Analysis of orthopaedic device development in South Africa: Mapping the landscape and understanding the drivers of knowledge development and knowledge diffusion through networks

By Faatiema Salie

Thesis presented in fulfilment of the requirements for the degree of

Doctor of Philosophy (Health Innovation)

at the University of Cape Town

January 2021

Plagiarism declaration

I, *Faatiema Salie*, hereby declare that the work on which this thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature: Signed by candidate

……………………………

Date: 25 March 2021 ……………………………………….

Declaration: Inclusion of publications

I confirm that I have been granted permission by the University of Cape Town's Doctoral Degrees Board to include the following publication in my PhD thesis, and where co-authorships are involved, my co-authors have agreed that I may include the publication:

Salie, F; de Jager, K; Dreher, C and Douglas TS. 2019. The scientific base for orthoapedic device development in South Africa: spatial and sectoral evolution of knowledge development. Scientometrics, 119(1), 31-54, https://doi.org/10.1007/s11192-019-03041-y.

Signature: Signed by candidate ……………………………

Date: 25 March 2021 ……………………………………….

Abstract

An orthopaedic medical device refers to a part, implant, prosthetic or orthotic which is used to address damage to the body's musculoskeletal system, primarily by providing stability and mobility. Orthopaedic medical devices play a role in injury-related disorders, which have been highlighted as a key element of the quadruple burden of disease in South Africa.

In this thesis, orthopaedic devices are conceptualised as a technological field and a technological innovation system (TIS) framework is applied to understand orthopaedic device development in South Africa. Knowledge development and knowledge diffusion are fundamental components of any innovation system. The thesis hypothesises that the functions "knowledge development" and "knowledge diffusion through networks" of the orthopaedic devices TIS are influenced by contextual factors. The objectives of the study are: to identify the actors who generate knowledge for orthopaedic device development and to characterise the relationships between them; to identify focus areas of orthopaedic device development; to provide insight into the drivers and barriers to knowledge development and diffusion in the TIS; and to identify the contextual factors that influence knowledge dynamics in the TIS. These objectives are investigated using social network analysis based on bibliometric data (scientific publications and patents), keyword networks, a review of institutions, and a set of case studies where the primary data source are interviews with actors.

Actors producing knowledge were from the university, healthcare, industry and science council sectors, although science councils played a small role. International actors were shown to bring new ideas into the TIS. The networks were fragmented, illustrating that knowledge diffusion through the networks was limited. This was especially the case in the patent networks as many actors patent in isolation. The keyword networks highlighted unrealised collaboration potential between actors based on their common research interests. The case studies revealed features of cross-sector interaction for orthopaedic device development not evident from network analysis based on bibliometric data.

Drivers of knowledge development and knowledge diffusion were: inter-sectoral collaboration; the availability of resources; the affordability of available devices; and the positive externalities of allied TISs. The main barrier to knowledge development and diffusion was in the form of barriers to inter-sectoral collaboration. These include unmatched expectations from partners in collaboration, different views on intellectual property ownership, and burdensome university administrative processes. The orthopaedic devices TIS was structurally coupled to the embedded TIS and sectoral contexts, and externally linked and structurally coupled to its political context. Knowledge development and diffusion was found to be positively enhanced by innovation in the additive manufacturing TIS, with shared structural elements and resources. Knowledge development and diffusion was influenced by sectoral dynamics of the university, healthcare and industry sectors.

This thesis makes the following contributions. First, it applies the TIS framework to a new focus area, namely medical device development, in a developing country context. Second, it makes two unique methodological contributions: it presents an index to capture the extent of sectoral collaboration in a network; and it develops a method for determining the collaboration potential of actors in a network based on cognitive distance.

Acknowledgements

There are many people who have taken this journey with me, whom I would like to acknowledge.

I would like to thank my supervisor, Professor Tania Douglas, for presenting this opportunity to me. There have been great achievements and also really challenging times these past few years, and throughout, you have been a constant source of encouragement and inspiration. I am blessed to have taken this journey under your leadership.

To my co-supervisor, Dr Kylie de Jager, who showed me what it is to be a node in the network. There are some theories to challenge about the distance between nodes and strength of ties!

Thank you to Professor Carsten Dreher and Ms Jessica Lawniczak of the Freie Universitat of Berlin who taught me how to put the theoretical framework into context.

Thank you to Dr Trust Saidi for mentoring me through the development of the theoretical framework and interviews of the case studies and for his assistance in the keyword networks.

Thank you to Dr Nailah Conrad and the dynamic Health Innovation Research Group at the University of Cape Town for the support over the past few years. I am also very grateful to colleagues at the University of Cape Town's Research Contracts and Innovation Department – Mr Philip Hoekstra, Mr Francois Oosthuizen and Mr Saberi Marais, for being available to all the queries on technology transfer and case study design.

Above all else, I am thankful to the Almighty for blessing me with my love and support network: my mother, Fadealah, and father, Fuad; my husband, Tauhir; my children, Israail, Hannah and Shafi'I; my sisters, Zainab, Gameema, Gouwa and Shakira; my mother-in-law, Ahdela; and my very best friend Gadija. Thank *you*.

Table of Contents

List of Figures

List of Tables

List of Abbreviations

AM	Additive Manufacturing
AU	African Union
CAT	Computer Aided Tomography
CE	Conformité Européenne
CMD	Cardiovascular Medical Device
CRPM	Centre for Rapid Prototyping and Manufacturing
DHET	Department of Higher Education and Training
DST	Department of Science and Technology
DTI or dti	Department of Trade and Industry
FDA	Food and Drug Administration
GHIA	Global Health Innovation Accelerator
HIV	Human Immune Virus
ICASA	Independent Communications Authority of South Africa
IDC	Industrial Development Corporation
IP	Intellectual Property
IPAP	Industrial Policy Action Plan
MCC	Medicines Control Council
MD2M	Medical Devices to Market
MDMSA	Medical Device Manufacturers South Africa
MRC	See SAMRC
NAPPI	National Pharmaceutical Product Index
NEPAD	New Partnership for African Development
NDoH	National Department of Health
NGO	Non-Governmental Organisation
NHLS	National Health Laboratory Service
NIPMO	National Intellectual Property Management Office
NPO	Non-Profit Organisation
NRCS	National Regulator for Compulsory Specifications
NRF	National Research Foundation
PCT	Patent Co-operation Treaty
PDoH	Provincial Departments of Health
R&D	Research and Development
SADC	Southern African Development Community
SAHPRA	South African Health Products Regulatory Authority
SAMED	South African Medical Device Industry Association
SAMRC	South African Medical Research Council
SME	Small and Medium Sized Enterprises
SMME	Small Medium Micro Enterprises
SNA	Social Network Analysis

SSM	Statistical Shape Modelling
TB	Tuberculosis
TIA	Technology Innovation Agency
TIS	Technological Innovation System
TRL	Technology Readiness Level
TTO	Technology Transfer Office
UN	United Nations
USA	United States of America
VC	Venture Capitalists
WIPO	World Intellectual Property Office
YLD	Years Lived with Disability
ZAR	South African Rands

Definitions

Actor	A person or organisation that participates in a situation or process (Macmillan Dictionary, 2020).
Arthroplasty	A surgical procedure to restore the function of a joint (Johns Hopkins Medicine, 2020).
Assignee	The assignee of a patent is the individual or entity who holds the patent rights.
Author-inventor	An individual identified in the network analysis of this thesis as having contributed to authoring a scientific publication and inventing a patent.
Clinical trial	"A systematic study involving humans that aims to answer specific questions about the safety or efficacy of a medicine or method of treatment" (National Health Act, Act 61 of 2003).
Cognitive distance	A measure of the similarity of the knowledge base of researchers (Yan & Ding, 2012).
Institutions	Institutions are constraints and norms, devised by humans, that shape human interaction (Hekkert, Negro, Heimriks, & Harmsen, 2011).
Intellectual Property	Creative outputs "that can be protected either statutorily or not, within any jurisdiction, including but not limited to all forms of copyright, design right, whether registered or unregistered, patent, patentable material, trademarks, know-how, trade secrets, rights in databases, information, data, discoveries, mathematical formulae, specifications, diagrams, expertise, techniques, research results, inventions, computer software and programs, algorithms, laboratory notebooks, business and research methods, actual and potential teaching and distance learning material" and trademarks (University of Cape Town, 2011).
Inter-sectoral collaboration	A collaborative relationship between actors of (at least two) different sectors.
Intra-sectoral collaboration	A collaborative relationship between actors of the same sector.
Inventor	The inventor on a patent is the creator of the invention; the inventor must have made "a certain level of contribution to the development of the creative elements of an invention" (European IP Helpdesk, 2020).
Manufacturer	"Any natural or legal person with responsibility for design and/or manufacture of a medical device with the intention of making the medical device available for use, under their name; whether or not such a medical device is designed and/or manufactured by that person themselves or on their behalf by another person(s)" (International Medical Device Regulators Forum, 2018).
Networks	A group of interdependent entities (often actors) and the relationships between them (Brittanica, 2017).
Organisation	"A group of people who work together in an organised way for a shared purpose" (Cambridge, 2020).
Orthopaedics	A branch of medicine concerned with the musculoskeletal system and the correction of deformities or disorders thereof.

Orthopaedic device	A medical device for the treatment or correction of deformities of the musculoskeletal system.
Orthotic	"A support, brace, or splint used to support, align, prevent, or correct the function of movable parts of the body" (MedicineNet, 2018).
Patent Co-Operation Treaty	The Patent Co-Operation Treaty (PCT), administered by the WIPO, allows for the simultaneous filing for patent protection in several countries by filing a single "international" patent application in one language (World Intellectual Property Organization, 2007).
Prosthetic	An artificial body part.
Self-reflecting tie	An "edge" in a network diagram which links the node (usually an actor) to itself. In a collaboration network, it indicates the event occurred due to the contribution of that node only.
Spin-off	In particular, university spin-offs. A company formed to commercialise university intellectual property.
Start-up	A start-up company has different, often philosophical, definitions. In this project it refers to companies which have been initiated by an entrepreneur to develop a product or service to be scalable and grow.
Technology Transfer	The sharing of knowledge, skills, technologies, methods and infrastructure in order to make scientific and technological developments accessible to a wide range of stakeholders and users, and for the benefit of society (Cape Peninsula University of Technology, 2010).
Technology Transfer Office	The office at public universities and research councils responsible for technology transfer processes.
Translational collaboration	Collaboration involving all three of the university, healthcare and industry sectors (de Jager, Chimhundu, Saidi, & Douglas, 2017).

1. Introduction

The term “orthopaedics” refers to a branch of medicine concerned with the correction of deformities of the musculoskeletal system (The American Heritage Science Dictionary, 2011). While orthopaedics may be easy to define, the orthopaedic burden of disease could be classified under different causes. The “Revised Burden of Disease Estimates for the Comparative Risk Factor Assessment, South Africa 2000” (Bradshaw, Schneider, & Groenewald, 2006) includes an estimate for morbidity and non-fatal injuries due to a disease, i.e. years lived with disability (YLD). Of the top 20 leading causes of YLD, four categories are addressed by the orthopaedics speciality: interpersonal injuries (ranked 3rd), falls (ranked 8th), osteoarthritis (ranked 12th) and road traffic accidents (ranked 16th). Injury-related disorders have been highlighted as one of the four elements of the quadruple burden of disease in South Africa (Mayosi, et al., 2009). An orthopaedic medical device is a part, implant, prosthetic or orthotic that is used to address injuries or diseases of the musculoskeletal system. The primary purpose is to provide stability and mobility.

South Africa’s medical device industry is made up of many small players (600 to 700 companies) and a handful of large multinational corporations (MNCs), with very little known about the value of local manufacturing and about who is producing what (Trade & Industrial Policy Strategies, 2018). The market however is dominated by large MNCs, with approximately 90% of all products being imported (Deloitte, 2014). Sixty-eight percent of local medical devices companies are solely distributing imported devices, and 26% of local medical devices companies manufacture devices locally (Trade & Industrial Policy Strategies, 2018). Approximately 90% of the local manufacturers also act as distributors of imported devices, suggesting that it may be difficult to act as a local manufacturer (only) in the current South African market (Trade & Industrial Policy Strategies, 2018). Total imports for the medical device industry was valued at ZAR11.07 billion, and total exports at ZAR1.08 billion, in 2013 (Deloitte, 2014). The latter figure shows some local activity and opportunity in the South African medical device market. It is however not clear what percentage of the export figure represents products manufactured locally in South Africa, as it could also include re-export value, where suppliers use South Africa as an export gateway. Most exports are to other African countries (KPMG, 2014). Of the ZAR13.05 billion of products imported in the period 2004-2013 in the category “Surgical Appliances and Surgical Supplies”, 65% (ZAR8.5 billion) comprised products listed as “orthopaedic appliances” (Deloitte, 2014). These “orthopaedic appliances” were grouped as “artificial joints”, “other artificial parts of the body, not elsewhere specified” and “other appliances which are worn or carried or implanted in the body, not elsewhere specified.” In 2016, “orthopaedics and prosthetics” medical devices accounted for 11% of the medical device market in South Africa (Department of Trade and Industry, 2018a). Of the top ten groups of medical devices most imported into South Africa in 2013, four were classified as orthopaedic devices, with a combined value of ZAR1.8 billion. Of the top ten groups of most exported medical devices, only one was classified as orthopaedic devices, with a value of ZAR50 million. These figures indicate the substantial value of imported orthopaedic devices. They also suggest that the supply of such devices by the domestic medical device market in South Africa may be limited. This study investigates the orthopaedic devices innovation system in South Africa and how such an innovation system may address the South African orthopaedic burden of disease. In this study, the orthopaedic devices innovation system is analysed using a technological innovation system (TIS) framework (described below). The starting point of the TIS is the technology, in this case orthopaedic devices, and the emphasis is on interacting agents. The orthopaedic devices TIS co-exists with the National System of Innovation (NSI). An NSI is described by Metcalfe (1995) as "the set of distinct institutions which jointly and individually contribute to the development and diffusion of new technologies and which provides the framework within which governments form and implement policies to influence innovation processes". The starting point of the NSI is usually a geographic area (Hekkert, Suurs, Negro, Kuhlmann, & Smits, 2007), a country.

Thus, the TIS and the NIS offer different perspectives on, and consider different aspects of, innovation. The use of the TIS as a framework in this study enables a focus on orthopaedic devices, with the aim of identifying factors that may support orthopaedic device innovation in South Africa.

1.1 Technological innovation systems as a framework for the study

A technological innovation system (TIS) has been defined as a "network of agents interacting in a specific economic/industrial area under a particular institutional infrastructure or set of infrastructures" which "is involved in the generation, diffusion, and utilisation of technology" (Carlsson & Stankiewicz, 1991). The TIS comprises structure and functions. The structure comprises actors, networks and institutions of the TIS. Functions refer to core processes of the innovation system to move the technology forward. Hekkert et al. (2007) refer to seven functions of the TIS, including "entrepreneurial experimentation and production", "knowledge development", "knowledge diffusion through networks", "guidance of the search", "market formation", "resource mobilisation" and "counteract resistance to change/legitimacy creation".

As this study is concerned with the *development* of orthopaedic devices, the functions "knowledge development" and "knowledge diffusion through networks" are explored. A study of these functions would reveal the existing capabilities within the TIS. Knowledge development is described by Bergek et al. (2008a) as learning and involving activities in which learning takes place. Indicators of knowledge development include the number of scientific publications and patents produced by actors of the TIS

(Hekkert, Negro, Heimriks, & Harmsen, 2011). Knowledge diffusion through networks relates to the exchange of information within and between actors in the networks. Indicators of knowledge exchange include the types of knowledge exchange occurring in the network as well as the number of networks (Hekkert, Negro, Heimriks, & Harmsen, 2011).

Several authors have emphasised the importance of examining context in TIS analysis. Technology evolves differently in different contexts, resulting in TIS outcomes that are context-specific. Bergek et al. (2015) posited that TIS-contextual factors could present in several forms, including: the effect of different TISs in which the focal TIS is embedded; the sectors of which the TIS forms a part; geographical factors; and political factors. In this thesis, the author argues that "knowledge development" and "knowledge diffusion through networks" of the orthopaedic devices TIS in South Africa are influenced by TIS-contextual factors. This is achieved by regarding orthopaedic device development in South Africa as a technological innovation system and applying the TIS framework to guide the study. The orthopaedic devices TIS in this project, is therefore defined as the networks of actors who interact under a set of institutional infrastructures and are involved in the generation, diffusion and use of orthopaedic devices in South Africa. By identifying TIS-contextual factors, this study highlights drivers and obstacles for the orthopaedic devices TIS in South Africa.

1.2 Aims and objectives

The aim of the study is to investigate knowledge dynamics in the orthopaedics devices TIS and the effect of the South African context on knowledge development and exchange in the TIS. The specific objectives of this thesis are:

1. To identify the actors who develop knowledge in the orthopaedic devices TIS in South Africa and to characterise the relationships between them.
2. To identify the focus areas of orthopaedic device development in South Africa.
3. To provide insight into what drives and hinders "knowledge development" and "knowledge diffusion through networks" in the orthopaedic devices TIS in South Africa.
4. To identify the TIS-contextual factors that influence "knowledge development" and "knowledge diffusion through networks" in the orthopaedic devices TIS.

This study has a quantitative and a qualitative component. The actors who develop knowledge in the orthopaedic devices TIS are identified using bibliometric data of scientific publications and patents and are related using co-authorship and co-inventorship as a proxy for collaboration. Using social network analysis (SNA) techniques, relationships between actors are quantified and knowledge diffusion in the networks is characterised. The research focus areas are identified through keyword networks; further relationships between actors are established through the consideration of their cognitive distance. The analysis of actor-collaboration and keyword networks comprises the quantitative component of the study. The institutions that impact orthopaedic device innovation in South Africa are reviewed, providing evidence for the political context in which the orthopaedic devices TIS is embedded. Case studies exploring knowledge development and diffusion dynamics present actor experiences of their participation in the orthopaedic devices TIS. The case studies reveal how actors are structurally coupled to the embedded TIS and the sectors to which they belong. The institutional review and the case studies comprise the qualitative component of the study.

This research contributes towards the knowledge base on TIS by identifying contextual factors that affect the TIS for orthopaedic medical devices in South Africa. In doing so, it responds to the lack of literature on application of the TIS framework in developing countries, and it expands the set of technological fields to which the TIS framework has been applied.

1.3 Thesis structure

A literature overview is presented in Chapter 2 and the conceptual framework for the project is presented in Chapter 3. Chapter 4 presents the social network analysis methodology to be employed in Chapters 5, 6 and 7. The scientific base for orthopaedic device development in South Africa, which has been published in Scientometrics (Salie, de Jager, Dreher, & Douglas, 2019) is presented in Chapter 5. The technological base of orthopaedic device development in South Africa is presented in Chapter 6, through the analysis of actor-collaboration networks from patent bibliographic data. In Chapter 7, the research areas, and actors' interests within the scientific base, of the orthopaedic devices TIS are explored through keyword networks. Chapter 8 reviews the institutions that impact the orthopaedic devices TIS in South Africa. Chapter 9 presents case studies of the orthopaedic devices TIS. The research is concluded in Chapter 10.

2. Literature overview

In this thesis, it is hypothesised that "knowledge development" and "knowledge diffusion through networks" of the orthopaedic devices technological innovation system (TIS) in South Africa is influenced by TIS-contextual factors. In this chapter, the pertinent literature is reviewed. The chapter starts by introducing the biomedical innovation system and its relation to the medical devices and healthcare ecosystems in South Africa. The concepts of knowledge and learning are introduced and the TIS framework and its knowledge functions are reviewed. The chapter ends with a critical review of the literature and highlights the gap that this study aims to address.

2.1 The biomedical innovation system

Medical device development involves different sectors, each of which plays a different role in innovation. The healthcare sector identifies patient needs, has access to patients and their data and ensures that suitable technology reaches the patient; universities and science councils are platforms for research and development, and have advanced or specialised resources, instrumentation and expertise; and industry focuses on the development, production and commercialisation of technologies (Lander, 2014; Chimhundu, de Jager, & Douglas, 2015; de Jager, Chimhundu, Saidi, & Douglas, 2017). Collaboration between these sectors enables knowledge transfer and the sharing of capital across sectors, while ensuring that technologies match patient needs and ultimately reach the market. Through collaboration, organisations can create social networks, gain complementary expertise and share resources, which often results in the integration of knowledge, efforts and capabilities, and enhances productivity (Powell, Koput, & Smith-Doer, 1996).

In a study of the British research system, Hicks & Katz (1996) identified two clusters of organisations – one cluster linked to industry, and the other cluster linked to healthcare facilities – which could serve as a source of technical opportunity and sites of application. In the healthcare facilities cluster, the site of application was hospitals, which were connected to sources of biomedical technical opportunity, i.e. non-profit organisations, special health authorities, and through them, research councils and universities. Hospitals were the site at which much of biomedical research activity in the UK research system was ultimately applied. The analysis suggests the co-existence of a biomedical innovation system with the more commonly acknowledged industry-oriented system. The biomedical system, however, is quite different: hospitals contribute more substantially to the science base than does industry, and access to patients is needed for biomedical research. Hicks & Katz conclude that better knowledge of the biomedical system would support insights into its innovation activities and its contributions to the UK science base.

Lander & Atkinson-Grosjean (2011) and Lander (2013) deem the biomedical innovation system to be the clinical pathway of innovation. The biomedical innovation system relies on public sector institutions, including universities and hospitals, as well as private sector industry actors (Lander & Atkinson-Grosjean, 2011). Lander (2013) showed that the infection and immunity network in Vancouver, Canada, is dominated by interactions between two non-commercial sectors, i.e. universities and hospitals. They highlighted the roles of different sectors in research and development, and showed that alternate innovation pathways, dominated by the public rather than the private sector, exist and are successful. Lander & Atkinson-Grosjean (2011) showed that translational science occurs between the university and academic hospitals in biomedical innovations; this translation is often not recognised because the university and the academic hospital are considered to be a single entity.

The South African Medical Research Council (SAMRC) and PATH[1] (South African Medical Research Council and PATH, 2014) investigated the development of an ecosystem to support a medical devices and diagnostics industry for South Africa. They interviewed different stakeholders – government, healthcare, industry, research organisations (including science councils) and private investment organisations, and made recommendations aimed at building the local medical devices and diagnostic industry, reducing the country's trade deficit, improving access to healthcare, and reducing unemployment by developing local business opportunities through innovation. Many of the recommendations required government engagement and initiatives that government would need to pursue to create a favourable ecosystem for the local medical devices and diagnostics industry to flourish. The success of the medical device and diagnostics industry was said to lie within different stakeholders having a unified vision and collaboration among the different stakeholders towards that vision. Lack of alignment within the current ecosystem was identified as a barrier to existing innovation processes, where innovations arising from universities were not being translated to commercial products. Contributing factors reported were the many research focus areas within the university healthcare space and the lack of commitment to South Africa's healthcare and health technology requirements. Current innovation incentives were also reported to be misaligned and therefore unable to maximise the market impact of research and development through to commercialisation. In universities and science councils, research was publication driven, rather than focused on product development. The lack of incentives to procure locally manufactured devices, and the inability of government sponsorship for device development to translate into preferential treatment in the public healthcare space, were also cited.

[1] PATH is a global team of innovators working towards health equity; services include advising and working with different stakeholders to solve health issues (PATH, 2020).

The South African medical device innovation ecosystem, adapted from Bunn (2018), is presented in Figure 1.

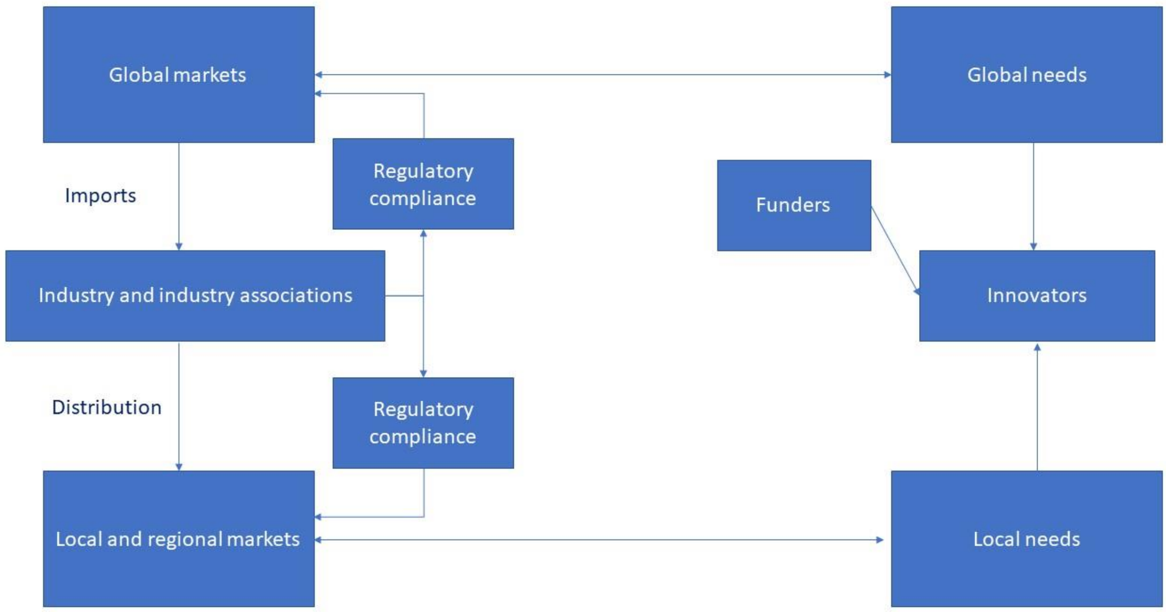


Figure 1: The South African medical device innovation ecosystem, adapted from Bunn (2018)

The South African medical device innovation ecosystem comprises stakeholders from different sectors. Industry associations, the South African Medical Device Industry Association (SAMED) and the Medical Device Manufacturers South Africa (MDMSA), are addressing import substitution of medical devices into South Africa. SAMED is an industry association, comprising members from local companies and multinational corporations (MNCs), which oversees medical device policies, innovation, and ethical principles and practices among its members within South Africa (South African Medical Technology Industry Association, 2018). The MDMSA is an industry association of companies that manufacture medical devices in South Africa (Medical Device Manufacturers Association of South Africa, 2015). These industry associations engage with government departments, such as the Department of Trade and Industry (dti) to support the domestic medical device industry. There are bi-directional flows between (local and global) needs and (local and global) markets. Public and private healthcare, health professionals, and national and provincial departments of health are responsible for identifying the local needs. The local needs also inform the devices to be developed for local/regional markets. Local and global needs are fed to the innovators – science councils, universities, not-for-profit organisations, local manufacturers and start-ups – which are self-funded or funded through various mechanisms of the Department of Science and Technology (DST), SAMRC, the Technology Innovation Agency (TIA), the Industrial Development Corporation (IDC), venture capitalists and international donors. The end-users in global markets identify global needs; the global needs inform the devices to be developed for global markets. Developments addressing local and global needs feed to the MDMSA, and after several regulatory processes, feed into the local and international markets.

Trade & Industrial Policy Strategies (2018) investigated the Johannesburg health cluster, providing a motivation to develop a medical devices cluster for the City of Johannesburg. In the report, medical device manufacturers and suppliers were positioned as healthcare service providers to the South African health cluster as described in Figure 2.

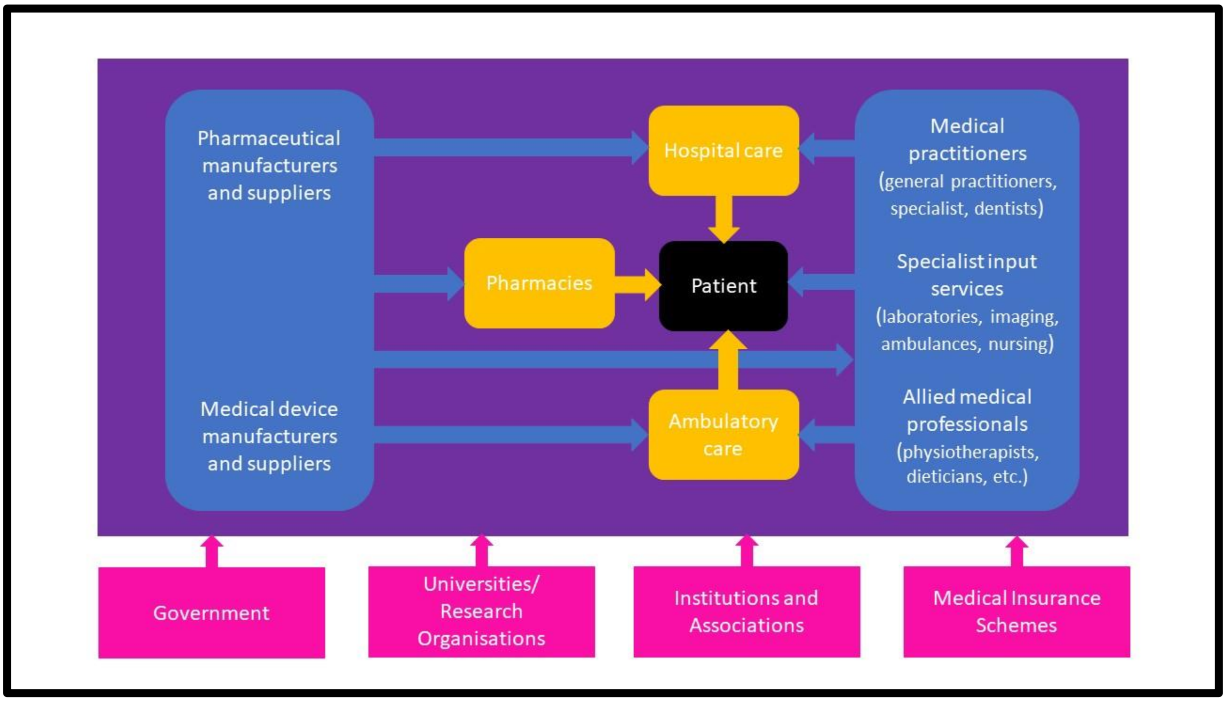


Figure 2: The health cluster, as described in Trade & Industrial Policy Strategies (2018). Activities in the purple space are core cluster activities aimed at providing healthcare to patients. Pink boxes, below the purple box, are facilitators to the healthcare cluster. Yellow boxes lying within the purple space are providers of healthcare. Blue boxes are the providers of healthcare services.

Core cluster activities provide healthcare to patients. The providers (medical practitioners, specialist input services and allied medical practitioners) of the core cluster services interface with the patient either through hospital or ambulatory care. Government, universities/research organisations, institutions and associations, and medical insurance schemes do not form part of the core activities; however, they are facilitators that enable and direct healthcare to patients within the health cluster. The report also focussed on problems faced within the existing medical device industry and on what would enable its growth. Two key emergent growth opportunities were uncovered: mass production at the lower-end medical consumables market (import substitution) and high-end, high-value new product development (for local and export markets). The report found that many of the constraints within the medical device industry could only be alleviated with government interventions.

The main difference between the biomedical innovation system described by Hicks & Katz (1996), Lander & Atkinson-Grosjean (2011) and Lander (2013), and the South African medical devices innovation ecosystem (Bunn, 2018), is that in the latter, members of the healthcare sector are not regarded as innovators; their role appears to be limited to identifying local needs in medical device innovation and being the users of such devices. This is despite the scientific evidence provided by Hicks & Katz (1996), Lander & Atkinson-Grosjean (2011) and Lander (2013), which identifies the healthcare actor as critical in the biomedical innovation system. Hicks& Katz (1996) showed that hospitals were the site of application, and that hospitals contributed towards the scientific base for biomedical innovation and are an even bigger contributor to the science base than industry. The health cluster put forth by Trade & Industry Policy Strategies (2018) identifies the critical role of other actors, like medical insurance companies, which facilitate or hinder the implementation of developed devices in the local market. According to the General Household Survey of 2014 (Statistics South Africa, 2015), medical insurance coverage in South Africa was at 18.1% in 2014. This puts medical insurance companies in a gate-keeping position where they can accept or refuse costs delegated to them. Thus, the available South African frameworks that capture or allude to the medical devices innovation system (Figures 1 and 2) do not capture the roles of all the actors in the innovation system, nor do they illustrate a co-ordinated innovation system.

To investigate the performance of an innovation system, several frameworks exist. These include the National System of Innovation (Lundvall, 2016), the Sectoral System of Innovation and Production (Malerba, 2002), Technological Innovation Systems (Hekkert, Suurs, Negro, Kuhlmann, & Smits, 2007; Bergek, Jacobsson, Carlsson, Lindmark, & Rickne, 2008a), the Triple Helix Model of Innovation (Leydesdorff & Erkowitz, 1998) and the Quadruple Helix Model of Innovation (Carayannis & Campbell, 2009), among others. The technological innovation system (TIS) framework is used in this research project as it places the development of technology in a central position, and it explores how the actors, networks and institutions perform functions necessary for the technology to develop. Central to this framework is knowledge development and exchange. While the TIS conceptual framework use in this project is presented in Chapter 3, literature on knowledge development and exchange is reviewed in the next section.

2.2 Knowledge development and exchange

2.2.1 Knowledge development

Van Raan (2004) distinguishes two different types of knowledge: basic, which relates to understanding, or applied, which relates to use. This knowledge could be codified – sometimes referred to as explicit knowledge – or tacit. Tacit knowledge has a technical and cognitive component;

the technical component refers to “know how” while the cognitive component is implicit, formed by mental models and beliefs that shape the way the individual perceives the world (Nonaka & Takeuchi, 1995). Examples of codified knowledge include patents and publications. Tacit knowledge is more personal and may be hard to communicate or share with others (Nonaka & Takeuchi, 1995); examples include formal and informal contacts and networks, shared technical facilities, human resources and mobility, and spin-off or start-up companies (Tijssen, 2004). Nonaka & Takeuchi (1995) developed a theoretical framework of organisational knowledge creation based on knowledge conversion between tacit and codified knowledge. Four modes of knowledge conversion were described, including socialisation (tacit to tacit), externalisation (tacit to codified), combination (codified to codified) and internalisation (codified to tacit). Tijssen describes a sequence of five stages in knowledge creation and utilisation: creation, dissemination, acquisition, storage and absorption of knowledge. While the results of these stages may be codified, the entire process results mainly from human actions and interaction generating tacit knowledge. Knowledge development builds on what has already been learned or is already known. As Powell et al. (1996) put it: “Knowledge facilitates the use of other knowledge. What can be learned is crucially affected by what is already known”.

Forms of basic and applied knowledge are scientific and technological knowledge, respectively. With scientific knowledge, communication of the research results is part of the scientific endeavour. This usually takes the form of scientific publications, like journal articles. However, it is not the only communication channel. Acceptance of a paper for publication in a well-known refereed journal is an indication that it reports meaningful research (Braun, 2004). The citation of a publication is an acknowledgement of research, usually by other scientists, and citation has been used as an indicator to illustrate how new research builds from older publications. Journal articles are not the main vehicle for scientific knowledge in all research fields (van Raan, 2004). Patents provide details on the technological characterisation of a patented invention (Gittelman, 2008) and have been used as output-based indicators of technological knowledge (Park & Park, 2006). The number of patents, or patent count, has been adopted as a measure of the amount of technological knowledge produced by an organisation or country (OECD, 2001; Lach, 1995). Similar to the citation of journal articles, patent citation shows how new technologies are related to previously patented technologies.

Knowledge is coupled to learning. Typically, two modes of learning are distinguished: the science, technology and innovation (STI) mode and the doing, using and interacting (DUI) mode. The STI mode relies on formal processes of research and development that explicitly produce codified knowledge, while the DUI mode focuses on learning via informal interaction within and between organisations where the end result is building competencies, usually associated with tacit elements (Jensen, Johnson, Lorenz, & Lundvall, 2016). The STI mode is usually applied in research fields associated with analytical processes that identify natural principles such as, for example, chemical, pharmaceutical, biotechnology and nanomaterials; it requires investment into research and development activity to generate knowledge, and is therefore associated with new and high technology industries (Gonzalez-Pernia, Parrilli, & Pena, 2012). Knowledge is acquired through the DUI mode by finding solutions to problems that arise and is tacit and often highly localised (Jensen, Johnson, Lorenz, & Lundvall, 2016). The DUI mode is an experience-based learning mode and promotes the translation of scientific knowledge inputs into knowledge that drives outputs associated with engineering-based and manufacturing industries (Asheim & Coenen, 2005). The two modes of learning are not mutually exclusive; elements of both are present in almost all innovation activity, and strategies that promote innovation need to consider both (Jensen, Johnson, Lorenz, & Lundvall, 2016).

Associated with the STI and DUI modes of learning, is the distinction of product innovation and process innovation. Product innovation refers to goods or services that are new or significantly improved regarding their characteristics or use (Parrilli & Heras, 2016). Process innovation refers to the implementation of a new or significantly improved technique, equipment, production or delivery method, and/or software (Parrilli & Heras, 2016) and is expected to yield efficiency and product gains through the introduction of better performing production processes (Gonzalez-Pernia, Parrilli, & Pena, 2012). Process innovation may be further delineated according to technological or non-technological innovation, where technological innovation refers to the definition above, and non-technological innovation refers to commercialisation and organizational innovations.

2.2.2 Knowledge exchange

Organisational learning is a function of both access to knowledge and the ability to use and build on such knowledge (Powell, Koput, & Smith-Doer, 1996). To stay current in an evolving research field where know-how is critical, requires that organisations be involved in the research process and be experts in both in-house research and in collaborative research with partners from various sectors (Powell, Koput, & Smith-Doer, 1996). In the innovation systems literature, “knowledge exchange” has become almost synonymous with “collaboration” or “partnership”. However, collaboration or partnership is one mechanism of knowledge exchange, and other forms of knowledge exchange do exist. The technological innovation systems function “knowledge diffusion through networks” of Hekkert et al. (2007) extends to learning by DUI.

Powell et al. (1996) refer to two types of learning associated with collaboration. The first type is strategic and based on risk vs return; the decision to collaborate is dependent on factors such as the size of the organisation and its position in industry, technological sophistication, resource constraints and previous collaborations. It also appears to depend on the specific types of skills or resources exchanged (Hennart, 1988; Pisano, 1989; Parkhe, 1993). The second type is a process of social construction (Brown & Duguid, 1991), where the learning is associated with the conditions under which it is learned. The sources of innovation are not limited to one organisation, instead, innovation occurs where firms, universities, research laboratories, and other actors in the innovation chain, meet. Social networks matter because face-to-face contacts between knowledge developers are necessary to transfer knowledge which escapes codification. This knowledge includes skills, which may be facilitated though practical demonstration, and scientific and technical jargon necessary for engagement (Breschi & Lissoni, 2004). While the DUI mode may be inherent in organisational operations, Jensen et al. (2016) point out that the DUI mode can also be intentionally adopted through building structures and relationships that enhance and utilise doing, using and interacting, such as, for example, project teams, problem-solving groups, and personnel rotation that promotes knowledge exchange. A mechanism to emphasise this localised knowledge, and diffuse it more broadly, is through interaction with external actors. Organisational knowledge creation in Japanese companies, described by Nonaka & Takeuchi (1995), refers to their capacity to create new knowledge, disseminate it through the company, and embody this knowledge in its products, services and systems. Here, knowledge is sought outside the organisation from suppliers, customers, distributors, government and competitors and this knowledge becomes part of the organisation's knowledge base, feeding into the development of new products and technologies. The knowledge is then transferred outside the organisation in the form of the product or technology. This internal-external cycle encourages continuous innovation in Japanese organisations.

The STI mode supports interactions with new knowledge producers, like universities and public research organisations, which generate codified knowledge that can be exploited by industry to produce innovations (Fitjar & Rodriguez-Pose, 2013). In fact, university-industry collaboration is an important manifestation of the STI mode of learning (Gonzalez-Pernia, Parrilli, & Pena-Legazkue, 2015). Gonzalez-Pernia et al. investigated the separate and combined effects of STI and DUI modes of learning on companies collaborating with universities, other scientific knowledge producers (technology centres, research laboratories, and consulting services) and DUI partners such as customers, suppliers and competitors. They found that company partnerships with universities, without engaging other STI and DUI partners, were weak for product innovation, while simultaneous STI and DUI partnerships, were found to be linked to a higher probability of product innovation. Process innovation was found to be more likely with the simultaneous engagement of other STI partners (not universities) and DUI partners. Their findings highlight the importance of combining strengths and complementarities of different partners through the innovation chain.

2.2.3 Knowledge development and exchange in biomedical innovation systems

The idea of innovation being a linear process of ideas born in universities, developed into new products by industry and then used by clinicians in healthcare facilities, is an oversimplification of the iterative process of discovery and development in medical research (Academy of Medical Sciences, 2010). Moon (2004) showed that the great mechanical innovations in history were as a result of both technological evolution and complex social networks, and that new technological products were usually preceded by other emergent technologies. In medical device development, actors from different sectors collaborate, and each actor plays a different role in the collaboration. This networking is necessary because it results in knowledge transfer and sharing of capital across sectors, while ensuring that developed technologies meet patient needs and reach the market. This interaction could also be measured, within limits, using codified indicators of knowledge development, i.e. scientific publications and patents (Hekkert, Negro, Heimriks, & Harmsen, 2011). Co-authorship of scientific publications and co-inventorship of patents, which serve as proxies for collaboration, have been used in social network analysis (SNA) studies to quantify knowledge exchange between actors. Newman (2001) used co-authorship of scientific publications to illustrate scientific collaboration networks. Fleming & Marx (2006) illustrated that collaborations recorded in patent data captured personal and professional ties between inventors.

The SNA literature using scientific publications, patents, or a combination of both, is abundant. In the latter the focus is often on university-industry interaction and the translation of basic science to commercialising technologies. Within this body of literature, work on medical device development is limited and therefore literature on medical and biomedical applications more broadly, is reviewed here. These include biotechnology (Powell, Koput, & Smith-Doer, 1996), tissue engineering (Murray, 2002), cancer research centres (Long, Cunningham, & BraithWaite, 2012; Long, Cunningham, Wiley, Carswell, & Braithwaite, 2013), medical research (Chinchilla-Rodriguez, Benavent-Perez, De Moya-Anegon, & Miguel, 2012), infection and immunity (Lander & Atkinson-Grosjean, 2011; Lander, 2013; Lander, 2014) and medical devices (Chimhundu, de Jager, & Douglas, 2015; de Jager, Chimhundu, Saidi, & Douglas, 2017).

Powell et al. (1996) mapped the emerging biotechnology industry to explain the extensive inter-organisational collaboration in that field. They put forward that, “when the knowledge base of an industry is both complex and expanding, and the sources of expertise are widely dispersed, the locus of innovation will be found in networks of learning, rather than individual firms.” They found that the age of a company was not a predictor for network behaviour. Growth was a process that required time; organisational growth stemmed from the initiation of collaborations and was stimulated by centrality. Centrality was produced by research and development ties, experience and diversity. This central connectedness cycled back to intensify a company's commitment to exploration through its network.

Murray (2002) investigated the communication between science and technology networks in cartilage tissue engineering. Using interviews, patents, scientific publications, and archival analysis, Murray showed distinct scientific and technological networks, with bidirectional communication between the two networks. Bibliometric indicators showed that a few key scientists published in both domains, while industry actors did not really participate in scientific publications. The interviews, however, highlighted considerable overlap between the two networks, not captured in bibliometric data. Reasons for this overlap included the involvement of key scientists in patenting and technology development, forming start-up companies, consulting, mentoring and informal advice. In particular, Murray found that academic scientists actively shape the co-evolution of patent and publication networks.

Long et al. (2012) and Long et al. (2013) investigated the importance of actors' position and strategic activities in a translational cancer research network. Translational research centres were a strategy developed to overcome gaps between clinicians and biomedical researchers. Gaps included administrative structures for shared resources, social structures in hospitals and universities which facilitate collaboration, and mechanisms for information and knowledge transfer between biomedical and clinical disciplines. Using online surveys and semi-structured interviews, their network analysis revealed that key network actors were a well-connected group with positions in the network that denoted high centrality and brokerage potential.

Chinchilla-Rodriguez et al. (2012) investigated international collaboration in medical research in Latin America and the Caribbean. Their study aimed to determine the countries' capacity to engage in scientific collaboration both intra- and extra-regionally, as a means of identifying the countries that hold central and strategic positions in collaboration networks, and determining the countries benefitting most from the relationship dynamic in terms of productivity. They found that all countries in the region tended towards internationalisation. The network was found to be occupied by three dominant trios of countries, which were the region's largest publication producers, with low collaboration rates. Thus, countries with the largest outputs had low international collaboration rates, and collaboration would not seem to affect publication production in such countries. In contrast, smaller countries had relatively high collaboration rates, and satellite countries had small output with high collaboration rates. International collaboration enhanced visibility, however, not all countries were equally effective in this way, and not all countries benefitted from collaboration to the same degree. Using citation analysis, the authors showed that the most productive countries used knowledge generated domestically or by their neighbours.

More recently, collaboration for medical device development has been investigated in South Africa. Chimhundu et al. (2015) investigated the types of collaboration within and between sectors in cardiovascular medical device (CMD) development in South Africa and the extent of collaboration within and between sectors, and analysed collaboration trends for the period 2000 to 2014. A network analysis was performed, with co-authorship data obtained from scientific publications to indicate collaboration across four sectors, i.e. industry, universities, healthcare services, and science councils and facilities. Two networks were defined, namely local (South African organisations only) and global (South African and foreign organisations). Results showed that the university and healthcare sectors were the most active in CMD development in the global network. The most prevalent type of inter-sectoral collaboration was between the university and healthcare sectors. The CMD development network was found to be improved by the presence of foreign organisations, as the global network absorbed some of the local actors that were isolated in the local network; foreign actors thus provided alternative pathways for knowledge exchange. Results further showed considerable unrealised collaboration potential in both networks and that university actors played a considerable role in determining the behaviour of the network.

De Jager et al. (2017) investigated the medical device development landscape in South Africa. SNA using co-authorship of scientific publications was used to identify organisations and sectors active in medical device development in South Africa, quantify the extent of intra- and inter-sectoral collaboration, and investigate the influence of international actors. The central actors were seven South African organisations. Four were from the university sector, two were from the healthcare sector (both academic hospitals) and one was from the science and support sector. Universities collaborated extensively both intra- and inter-sectorally. Universities formed hubs in the network that could facilitate knowledge exchange and potentially help to establish new collaborations. The healthcare sector actors also collaborated extensively with each other. This practice may be attributed to many healthcare actors present in the network being academic hospitals which may have mimicked university behaviour. Small sectors, like the science and support sectors, were involved extensively in inter-sectoral collaboration, while larger sectors did not necessarily engage as extensively in inter-sectoral collaboration. Even though international actors were found to have a presence, local actors collaborated more extensively with each other than with international actors. De Jager et al. further investigated the presence of "translational collaboration", defined as collaboration across three sectors – university, healthcare and industry – which are considered to be essential if biomedical discoveries are to be translated into clinical practice (Academy of Medical Sciences, 2010). Only 7 % of the publications of the dataset were due to translational collaboration. The authors suggested that this might be an indication that the biomedical innovation system in South Africa was not fully utilising innovation pathways described in Lander & Atkinson-Grosjean (2011).

Sooryamoorthy (2010) also identified government as a contributing sector in medical research in South Africa. The trends seen in Chimhundu et al. (2015) and de Jager et al. (2017) reflect the contributions by different sectors to scientific output in South Arica more generally. In 2013, 90% of South Africa's research output had at least one author from the university sector, while only 10% of research output was from the science council sector and 0.9% from the business sector (National Advisory Council on Innovation, 2014). The National Advisory Council on Innovation report showed that industry and science councils collaborated mainly with universities; however, there was a low level of research collaboration between industry and science councils, and businesses undertook limited research. Universities appeared to be the driving force in intersectoral collaboration producing more co-authored articles with other universities, science councils and industry, compared to the number of co-authored publications among the other sectors combined. Additionally, most international collaborations involving South African researchers were with developed countries.

2.3 Summary

In this literature review, the concepts of codified and tacit knowledge were introduced, the STI and DUI modes of learning were described, as were organisational knowledge and learning. The South African medical device innovation system was considered in the context of the literature on biomedical innovation systems. There is some discrepancy between the biomedical innovation system described in the literature (by Hicks & Katz (1996) and Lander (2013)) and that presented in recent reports from South African organisations. Frameworks describing the South African medical device innovation system were found lacking in terms of recognising healthcare actors as knowledge creators and in not recognising all actors who facilitate knowledge development processes.

Quantitative studies on medical device innovation systems are available, while qualitative enquiry to investigate innovation system dynamics, such as the learning processes that occur for knowledge development and exchange and the interactions between actors that enable such learning, are lacking.

Central to innovation system frameworks are knowledge development and exchange. A fundamental point made by Powell et al. (1996) is that expertise is widely dispersed and the locus of innovation is found in networks of learning and not in individual organisations. Thus, the technological innovation systems framework, given its emphasis on networks, may present a route to examining how knowledge is developed and exchanged among actors in medical device innovation systems. The literature review has also highlighted the potential of social network analysis in identifying knowledge creators and establishing knowledge flows in networks of actors.

3. Overall conceptual framework

This chapter presents the overall conceptual framework applied in the study. Certain elements of this conceptual framework are presented in Section 5.3, as Chapter 5 contains a verbatim account of a publication (Salie, de Jager, Dreher, & Douglas, 2019). There are therefore areas of overlap between this chapter and Section 5.3, which are included here in order to present a complete conceptual framework.

A technological innovation system (TIS) is a "network of agents interacting in a specific economic/industrial area under a particular institutional infrastructure or set of infrastructures" which "is involved in the generation, diffusion, and utilisation of technology" (Carlsson & Stankiewicz, 1991). TIS structures include actors, institutions and networks which contribute to the generation, diffusion and utilisation of a new technology.

A structural analysis can answer the following questions: "Which parties develop knowledge?", "Where are the knowledge producers located?", "How much knowledge is being developed?" and "What types of organisations are involved in knowledge production?" (Hekkert, Negro, Heimriks, & Harmsen, 2011). Structural analysis is useful because it enables the identification of actors and networks in the TIS, the sectors and countries to which they belong and their relationships. Hekkert et al. (2011) concisely described the elements of the structure of the TIS, namely actors, networks, institutions and technology. The actors are individuals or organisations contributing to the TIS through the generation, utilisation and diffusion of the technology. The network is the interaction between the actors of the TIS. Institutions are the human-derived constraints, such as policies, laws and rules, that shape the interactions of the TIS and influence the behaviour of the actors (organisations) (Hekkert, Negro, Heimriks, & Harmsen, 2011). The technology enables and constrains the activities of innovation system actors and therefore forms part of the innovation system. Functions are core processes in a TIS that are complementary to the structure (Hekkert, Suurs, Negro, Kuhlmann, & Smits, 2007). Hekkert et al. (Functions of innovation systems: A new approach for analysing technological change, 2007) and Bergek et al. (2008a) each describe seven functions of a TIS, with slightly different formulations. The functions described by Hekkert et al. (2007), are used in this research project, and are presented in Table 1. The functions of interest are "knowledge development" and "knowledge diffusion through networks".

Table 1:The functions of the TIS as described in Hekkert et al. (2007)

Function	**Description**
F1: Entrepreneurial experimentation and production	Activities relating to the commercialisation of a technology.
F2: Knowledge development	Activities in which learning takes place.
F3: Knowledge diffusion through networks	Learning through the exchange of information within and between networks.
F4: Guidance of the search	Activities that positively affect the visibility and clarity of specific desires among technology users.
F5: Market formation	Activities for the creation of markets where new technologies may grow.
F6: Resource mobilisation	The mobilisation of resources for the development of the innovation system.
F7: Legitimacy creation OR Counteract resistance to change	Activities related to advocacy for enhancing stakeholder support for the new technology.

Bergek et al. (2008a) compress the knowledge functions into “knowledge development and diffusion”. They introduce the function “development of positive externalities”, which reflects the development or strengthening of one function in the TIS in stimulating or positively influencing the development of other structural components or functions in the TIS. Both Hekkert et al. (2007) and Bergek et al. (2008a) present comprehensive frameworks to analyse TISs.

Knowledge development and diffusion are said to be “at the heart of the TIS” (Bergek, Jacobsson, Carlsson, Lindmark, & Rickne, 2008a). Bergek et al. describe knowledge development involving activities in which learning takes place. “Knowledge diffusion” describes the exchange of information within and between networks; it extends to activities of learning involving use and interaction (Blum, Bening, & Schmidt, 2015).

Several authors have emphasised the role of context in TIS analyses. Although the TIS framework is universally applicable (Bergek, Jacobsson, Carlsson, Lindmark, & Rickne, 2008a; Hekkert, Suurs, Negro, Kuhlmann, & Smits, 2007), technology development proceeds differently in different contexts, producing context-specific TIS outcomes. In addition, context is not static, but changes over time. Delineating favourable contexts enables the identification of opportunities that favour the development of new technologies (Bergek A. , et al., 2015). The way in which the TIS is linked to its context is illustrated in Figure 3.

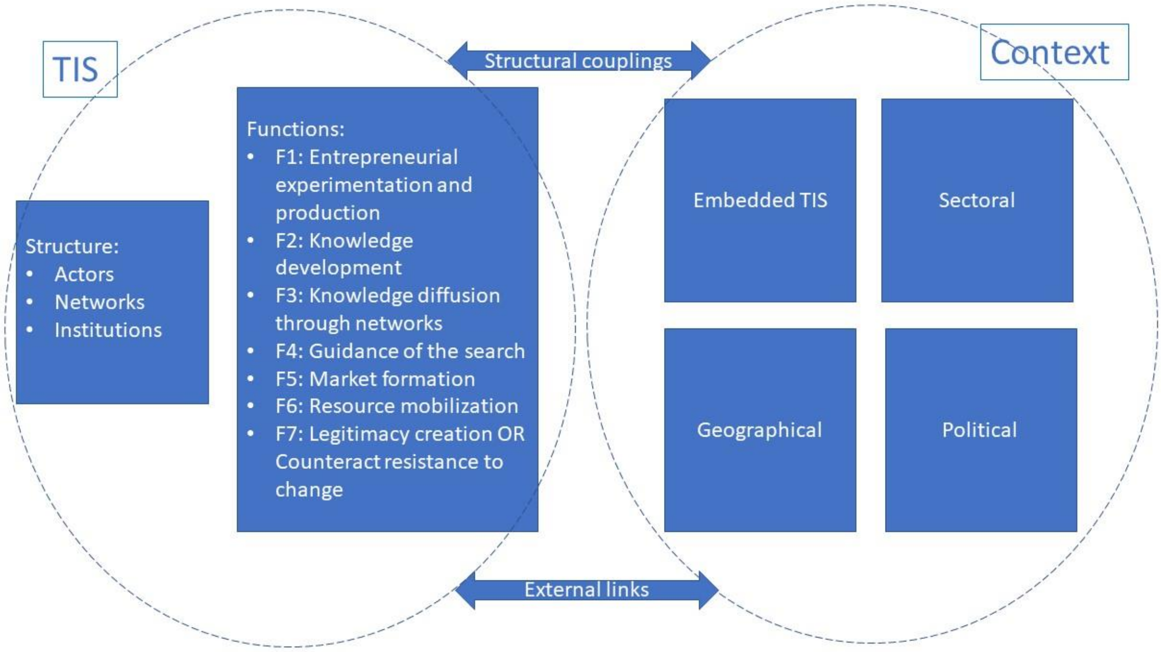


Figure 3: Relationship of the TIS to its context.

On the right-hand side of Figure 3 is the context of the TIS. Bergek et al. (2015) describe three types of contexts. The first type is the surrounding and related TIS where the context may be the result of how geographical or technological boundaries between the focal TIS and others are drawn (the embedded TIS). This means that other TISs that are dependent on the focal TIS, or other TISs on which the focal TIS is dependent, may influence its development. The focal TIS may therefore be embedded in the development of other TISs, or vice versa. The second type is related to pre-existing infrastructure and institutions (sectoral and geographical). Sectors and countries may already have established infrastructure and institutions which influence the TIS. When a new TIS develops, actors may come from already established sectors or countries, which may have habits and formal institutions which the new TIS may adopt, or adapt to its context, or challenge and change. The TIS is therefore influenced by the sectoral and geographical context, and it may influence the sectoral and geographical contexts. The third context type is political and related to the provision of system-level assets. This may present in the form of political support for technology-specific policies. On the left-hand side of Figure 3 is the TIS, which comprises the structure (actors, networks and institutions) and functions (F1 to F7). The TIS interacts with the context in one of two ways: “structural couplings” or “external links”. Structural couplings are shared elements (actors, networks, institutions, technology) between a TIS and a specific context structure. External links are influences or resources or assets that are shared between a TIS and a specific context that may impact the development of the TIS; these external links are not affected by TIS-internal processes. External links may be distant forces affecting macro-level developments; external links may also be close to the TIS, such as national innovation policy, market conditions, etc. The distinction between external links and structural couplings can be determined by the ability of the actors to influence the underlying contextual elements. If the actors can't influence the underlying contextual elements, then the interaction is externally linked; if the actors can, then it is structurally coupled.

When the TIS is contextually linked to an embedded TIS, there is an interdependence in the interaction of the two technologies (or technological fields). Different technologies may compete and complement each other in different ways and the coevolution of these inter-related TISs will influence the dynamics in each of them, as follows (Bergek A. , et al., 2015). Each TIS may form an important context for other TISs. The TIS-TIS interactions may be vertically- or horizontally-related. The focal TIS may require resources provided by other TISs. The development of up-stream TISs may influence the focal TIS positively or negatively. Up- or down-stream TISs (vertical relationships) may become bottlenecks for "knowledge development" in the focal TIS if complementary technologies are not developing at the same pace as the focal TIS. The focal TIS may also produce products required by downstream TISs. The development of the focal TIS then influences downstream TISs, and may affect certain functions, like "guidance of the search". TISs may be horizontally related if they share the same inputs and have complementary assets, or they have similar outputs as that of the focal TIS. Resultant interactions could be in the form of competition for resources, or structural couplings of actors and institutions.

The dynamics of a given TIS are intertwined with the structure and dynamics of the sector(s) of which it is part. Sectors are composed of the same type of structural elements as TISs, but they rely on a larger set of technologies in different stages of maturity and on several different TISs, to provide their overall function (Bergek A. , et al., 2015). In sectoral systems of innovation and production, institutions shape the interaction between actors in terms of processes of communication, exchange, co-operation, competition and command (Malerba, 2002). Sectors provide a stable context; individual TISs either have to adapt to this context, or they have to try to change it to their own benefit (Bergek A. , et al., 2015). Many TISs are part of several sectors. Interactions do not only occur in the sector in which the focal TIS is mainly embedded, but also with other sectors to which it is related. In particular, actors that enter an emerging TIS often come from other sectors. Because of such structural couplings, sectoral dynamics in adjoining sectors can influence the functional dynamics of the focal TIS.

Coenen et al. (2012) emphasise the geographical context of TISs. They explain that space affects relationships, i.e. the distance between actors affects how they interact – regular interactions between actors result in more solid connections, institutions and networks. Their geographical analysis allows for the understanding of a phenomenon with space-specific impacts. The absence of a conceptualisation of space results in an underestimation of the coupling structures between the TIS and the sectoral and contextual systems (Rochracher, Truffer, & Markard, 2010). It also results in an under-conceptualisation of relationships between different sub-system structures. By understanding how the TIS is coupled to its spatial context, case-specific findings in the literature could be made more general and comparable. The geographical context of TISs has been highlighted by several studies in recent years (Binz, Truffer, & Coenen, 2014; Wieczorek, Hekkert, Coenen, & Harmsen, 2015; Murphy, 2015). Binz et al. (2014) developed an analytical framework, incorporating indices and spatial classifications, to evaluate the geographical or spatial dimension of the TIS and map the dynamics of the knowledge functions in membrane bioreactor (MBR) technology. They performed a network analysis of the actors over time to identify relevant actor locations and spatial levels of the TIS. Spatial levels may refer to local, sub-national, national, regional or international delineations. The authors explain that the spatial set-up of the TIS is specific to the technology in focus, and to the resources and relationships between actors involved in driving that technology.

The political context in which the TIS is embedded is important to its development as it may impact the manner in which institutions are aligned. Government strategy and policy could result in actors in the TIS aligning their institutions to synchronise with those of government, and enable the provision of specific resources that are necessary for further maturation of the TIS (Bergek A. , et al., 2015). Bergek et al. highlight the importance of the political context, and the analysis of the political context, of the TIS for its development. Political support may present in the form of financial resources for research and development, formation of markets, legitimacy creation for the technology which may positively impact on the entry of new actors to the TIS, which may bring resources to the TIS. The analysis of the political context of the TIS should characterise the political system, including the way in which it may constrain or enable further development of the TIS.

It has been pointed out that the TIS approach has enjoyed limited application in developing world contexts and that examination of emerging TISs in developing countries would contribute to conceptual development of the TIS framework (Blum, Bening, & Schmidt, 2015; Tigabu, Berkhout, & van Beukering, 2015a). Coenen et al. (2012) suggest that actors may have substantially different access to resources at different geographical levels, contrary to the assumptions of a “global opportunity set” (Carlsson, Jacobsson, Holmen, & Rickne, 2002) in which all actors are assumed to have equal access to external resources. This is evident in studies applying the TIS framework in developing and least developed country settings. Schmidt & Dabur (2014) delineated a “national TIS” and “international TIS” in their framework for the diffusion of biomethanation in India. They found that the role of the international TIS only contributed to a few functions, but these functions were the most developed in the TIS and relevant in the removal of barriers that were less rooted in national institutions. Blum et al. (2015) used the TIS approach to derive policy recommendations to increase the diffusion rate of remote electric mini-grids in Laos. In delimiting their spatial contexts, they drew three geographical levels - local, national and international. They found that the low diffusion rates were due to institutional mismatches within and across geographical levels as well as hampered flows of resources across the geographical levels. Their geographical classification allowed for the identification of bottlenecks at geographical interfaces, which was important in understanding the functions in the Laotian context. Tigabu et al. (2015a) investigated the development of a bio-digestion TIS in Rwanda and mapped the dynamics of the bio-digestion TIS to understand how its functions influence the diffusion of the technology and to understand the determinants of the functioning of the TIS, so that ultimately, insight into policy measures could be generated. A process analysis was performed, where activities and processes related key actors, and their collaborations and institutions were analysed from a historical perspective. Tigabu et al. (2015b) performed a comparative analysis of the diffusion of biogas between Kenya and Rwanda. They showed that the pattern of accumulation of TIS functions may determine the rate of diffusion of the technology, and argued that it shapes technology diffusion in least-developed countries. Kebede & Mitsufuji (2017) used the TIS framework to discuss the diffusion of solar photo voltaic (PV) systems and the build-up of associated PV TIS in Ethiopia. They delineated a TIS into a research & development (R&D)-based TIS and a diffusion-based TIS. A diffusion-based TIS was defined as actors, networks and institutions "that interact and contribute to the diffusion of an existing technology along with building absorptive and innovative capacity for further improvement and diffusion of the technology". In a diffusion-based TIS, the emphasis of context involves relying on the introduction of technology from industrialised countries, where the aim may be to adapt and use the technology, and for the generation of further innovations over time. Kebede & Mitsufuji adapted function indicators to be more suitable to the developing country. As an example, in the knowledge development function, the usual indicator is the number of scientific publications and patents related to the technology. These indicators are more suited to the R&D-based TIS than to the diffusion-based TIS. Indicators for knowledge development used in the diffusion-based TIS context, where learning by doing, using and interacting was more prevalent, included feasibility studies, market assessment, testing new business models, and the adoption of technology from developed countries.

3.1 Application of the conceptual framework in this research project

The orthopaedic devices TIS in South Africa is investigated in this project, with orthopaedic devices considered the technological field. In particular, this project investigates the functions "knowledge development" and "knowledge diffusion through networks" of the orthopaedic devices TIS. Actors who contribute towards scientific knowledge production in the TIS are identified through scientific publications and actors who contribute towards technological knowledge production are identified through patents. Actor-collaboration networks are drawn based on bibliometric data on co-authorship and co-inventorship. These publications serve as indicators of "knowledge development" while the actor-collaboration networks represent "knowledge diffusion through networks". By only considering the contribution of South African knowledge creators, a geographical boundary is drawn which sets the limits to the analysis of the TIS, although international actors that collaborate with national actors are considered. As medical device development involves inter-sectoral collaboration, the way in which the TIS is linked to its sectoral context is also considered. A spatial and sectoral analysis of knowledge development and exchange in the TIS is performed using the framework presented in Binz et al. (2014). The analysis as it pertains to scientific knowledge production is presented in Chapter 5, and the analysis as it pertains to technological knowledge production is presented in Chapter 6.

To identify the focus areas of orthopaedic device development in South Africa, a keyword network analysis is performed. This keyword network analysis stems from a different conceptual framework which relates actors based on their cognitive distance. The framework, presented in Chapter 7, presents a methodology that may capture knowledge diffusion dynamics in actor-collaboration networks.

A review of the institutions to which the actors of the TIS subscribe to may reveal norms, standards, laws and regulations of the TIS. It may also reveal institutional alignment of the TIS to its political context. An institutional review, presented in Chapter 8, along with the actor-collaboration networks in Chapters 5 and 6, identify the structure of the orthopaedic devices TIS. Case studies, using interviews as the primary data source, present actor experiences of knowledge development and exchange in the TIS, and present the way in which knowledge is developed and exchanged for orthopaedic device development in the South African context.

4. Social network analysis

Social network analysis (SNA) is employed to address objective 1 of the thesis: “to identify the actors in the orthopaedic devices technological innovation system (TIS) in South Africa and to characterise the relationship between them”. The SNA in this thesis is performed using bibliometric data of scientific publications and patents. Scientific publications and patents are considered formal (i.e. codified) indicators of knowledge development in an innovation system (Hekkert, Negro, Heimriks, & Harmsen, 2011).

In this chapter, an overview of the methodology employed in the subsequent SNA-related chapters (Chapters 5, 6 and 7) is presented. This chapter is a step-by-step account of the methodology to identify actors of the TIS, and to characterise relationships between them. As scientific publications and patents are different knowledge indicators, the actor-collaboration networks are defined and constructed separately, and are presented in Chapters 5 and 6, respectively. SNA has its roots in graph theory. While the keyword networks of Chapter 7 also lie in this domain, the nature of the networks differs from those in Chapters 5 and 6, and distinctions are presented in Chapter 7.

4.1 Sourcing bibliometric data

Search terms were used in Scopus and Thomson Reuters Web of Knowledge (WoK) to find journal articles and conference proceedings (jointly “scientific publications”), and in TotalPatent from LexisNexis to find patents that demonstrate orthopaedic device development. Conference proceedings may not be subject to the same level of peer review as journal articles (Franco, Malhotra, & Simonovits, 2014); however, only conference proceedings that have been captured by Scopus and WoK have been included in this study. Only full-text conference papers are captured by Scopus; conference papers in the Scopus database are selected on relevance and quality of the conference relative to the subject field (Elsevier, n.d.). Clarivate has specific criteria upon which conference proceedings are considered for the WoK database and its Conference Proceedings Citation Index; it includes considerations regarding basic publishing standards, content, copyright and conference date (Clarivate, 2019).

The search phrases for the Scopus and Thomson Reuters WoK are provided in Appendix A, and the search phrase for TotalPatent is provided in Appendix B. The searches were performed for the period 2000 to 2015. The year 2000 was chosen as a start date because from the year 2000 there is a steady increase in scientific activity captured in the Scopus and Thomson Reuters WoK relating to orthopaedic device development in South Africa.

Search results were manually assessed to determine if the scientific publications and patents contributed to orthopaedic device development in South Africa. The retrieval of bibliometric data from scientific publications and patents differed. Each process is described below including the way author or inventor affiliation was established.

4.1.1 Scientific publications

Scientific publications retrieved using the search phrases were screened against the following criteria to be retained in the dataset:

1. Publications had to show evidence of development of an orthopaedic device, based on the definition of an orthopaedic device.
2. The publication had to have at least one author affiliated with a South African organisation.
3. Retrospective clinical studies which showed the performance of orthopaedic devices were included, as clinical performance of the orthopaedic device could lead to ancillary studies for further device modification and development.
4. Morphometric studies that were explicitly performed to bridge the gap between structural anatomy and device development, were included, as these studies directly contribute to the development of the device.
5. New applications of an existing device were included, as a new application was considered to contribute to the device development through broadening the scope of application of the device. This did not extend to new surgical techniques developed for existing devices.
6. Publications related to dental, orthodontic or maxillo-facial research were excluded. However, where publications showed extension to orthopaedic applications, they were retained.
7. Publications relating to tissue engineering were largely excluded, except where they explicitly showed an extension to orthopaedic device development.
8. Publications related to sports science were included only if they contributed to the development of an orthopaedic device but were excluded if the developed device was solely for improved sports performance.

Once the full list of publications was finalised, author-affiliation data were extracted from publications and used to draw actor-collaboration networks. The relationships that may arise in the actor-collaboration network are best illustrated through an example. Figure 4 shows an excerpt of the author affiliation details from Truscott et al. (2007), one of the publications included in the scientific publication dataset. This publication has seven authors affiliated with five organisations. Organisations are of interest in the actor-collaboration networks. Each organisation appearing in the dataset was given an abbreviation. In this example, the organisations were Central University of Technology (CUT), University of Cape Town (UCT), Groote Schuur Hospital (GSH), Vincent Palotti Hospital (VPH) and Loughborough University (LU).

Using RP to promote collaborative design of customised medical implants

Michèle Truscott and Deon de Beer
Central University of Technology, Bloemfontein, Free State, South Africa

George Vicatos
University of Cape Town, Cape Town, South Africa

Keith Hosking
Grootte Schuur and Vincent Palotti Hospitals, Cape Town, South Africa

Ludrick Barnard and Gerrie Booysen
Central University of Technology, Bloemfontein, Free State, South Africa, and

R. Ian Campbell
Central University of Technology, Bloemfontein, Free State, South Africa and
Department of Design and Technology, Loughborough University, Loughborough, UK

Figure 4: Author affiliations for the publication by Truscott et al. (2007).

Authors and affiliations appeared in different forms in the dataset. The following list explains how consistency was achieved across the dataset for incorporation into the actor-collaboration networks:

1. Departmental affiliations were not considered; only parent organisations were retained. An exception was the case of academic hospitals. Also, private hospitals belonging to a hospital group (e.g. Life Healthcare, Netcare, MediClinic) were considered as individual hospitals. This was thought to better reflect inter-organisational collaboration.
2. In the case of a publication from a single author having a single affiliation OR multiple authors having a single affiliation, the publication results from knowledge created within a single organisation.
3. In the case of a single author having multiple affiliations, each organisational affiliation was retained, co-authorship between those organisations was considered to have taken place. Using the example above of Figure 4, Keith Hosking works at both GSH and VPH, and the knowledge he created and possessed, was exchanged between these organisations.
4. Where university-affiliated authors had listed their clinical department (i.e. authors who were clinical academic staff), the associated academic hospital was also assigned a node. Figure 5 is an excerpt of the author-affiliated data from Janson & Rossouw (2013). The authors are from the Department of Surgery at the University of Stellenbosch (SUN), which is located at Tygerberg Academic Hospital (TAH). The resulting actor-collaboration network would show a collaboration between SUN and TAH. As in 3, above, knowledge was assumed to have been exchanged between the two organisations.


A New Technique for Repair of a Dislocated Sternoclavicular Joint Using a Sternal Tension Cable System

Jacques T. Janson, FCS(SA), and Gawie J. Rossouw, FCS(SA)

Department of Surgery, Division of Cardiothoracic Surgery, Faculty of Medicine and Health Sciences, University of Stellenbosch, Tygerberg, South Africa

Figure 5: Author affiliations for the publication by Janson & Rossouw (2013).

4.1.2 Patents

Each patent retained in the data set had to show evidence of orthopaedic device development, with the primary inclusion criterion of at least one inventor listing a South African address. On patents, inventors are only required to provide a full name and an address. Organisational affiliations of inventors could not simply be extrapolated from organisational affiliations as could be done with scientific publications, as patent data do not link the inventors to their affiliations.

To overcome some of the biographical shortcomings of patents, a series of steps was followed to determine the affiliation of the inventor at the time of first application, i.e. at the priority date. Figure 6 is an excerpt of the first page of a patent by Plugmacher et al. (2011) in the study dataset and is used to illustrate the extrapolation from inventor to organisational affiliation.

EP2526882A1 2012-11-28 **Surgical instrument for spreading bone** (en)

English Abstract:

Surgical **instrument** (1) having a proximal portion and a distal portion, the distal portion arranged for separating tissue. The **instrument** comprises a substantially rigid first elongated member (3) and a second elongated member (5). The first and second members extend adjacent each other, and are longitudinally translatable along each other. In the distal portion, the first and second members are connected with a first lever (7), which is rotatable with respect to the first and second members about a first hinge (13) and a second hinge (15), respectively, such that by a longitudinal translation of the first and second members the lever rotates for spreading tissue and the angle (α) enclosed between the first member and an imaginary line crossing the first and second hinges increases.

Standardized Assignees: VA VIJF MANAGEMENT

Original Assignees: VA-Vijf management BV, Prof Eijkmanstraat 18, 8415 EK Deventer, Kingdom of the Netherlands

Current Assignees: VA-Vijf management BV, Prof Eijkmanstraat 18, 8415 EK Deventer, NL

Inventors: Plugmacher, Robert, Gardeschutzenweg 96, 12203, Berlin, Federal Republic of Germany;
Becker, Gert, 1378b Beyers ave, Waverley Pretoria, Republic of **South Africa**;
Van Asselt, Peter Gerrit Hendrikus, Prof Eijkmanstraat 18, 7415 EK, Deventer, Kingdom of the Netherlands

Attorneys: De Vries & Metman, Overschiestraat 180, 1062 XK Amsterdam, Kingdom of the Netherlands

Application Number: EP11167493

Application/Filing Date: 2011-05-25
European Patent Office Register Plus

Priority Number and Date: EP11167493 2011-05-25

Designated Contracting States: AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR

Designated Extended States: BA, ME

Figure 6: An excerpt from a patent by Plugmacher et al. (2011).

The following steps were taken in extrapolating inventor data to organisational data:

1. The inventor name was cross-checked against names of authors in the scientific publication dataset. If the inventor was also an author of a scientific publication published at the time of patenting, then the affiliation listed on the scientific publication was used. This approach is similar to that of Tijssen (2004) who matched inventor names to authors of scientific publications in the Science Citation Index (SCI) database and had success in finding affiliations for inventors who were active in science-based technical areas. The "same time" refers to a one-year window with the priority date of the patent application at its centre.

2. A Google Scholar search of the inventor was performed. If the inventor had a Google Scholar profile listing their publications, then the publications were screened to retrieve all affiliations within one year of the priority date of the patent.

3. A LinkedIn search of the inventor was performed. If the inventor had a LinkedIn profile, the "Experience" section of the inventor's profile was viewed to establish their affiliation at the priority date of the patent.
4. A Google search of the inventor was performed. Google searches often resulted in links to social and academic networking platforms, including Facebook and ResearchGate. In the case of clinicians, often the clinician's practice would be found. In these instances, inventors were contacted (via email, social and academic networking messaging platforms, or phone calls) to confirm their affiliations at the priority date of the patent.
5. Where multiple affiliations were retrieved per inventor in the above steps, all affiliations for that inventor were captured.

Several factors must be considered when dealing with patent data. A patent is applied for, and granted, at different times. This time lag underscores the importance of choosing the appropriate date in a patent analysis (Hinze & Schmoch, 2004). Hinze & Schmoch suggest that the patent's priority date is most closely related to the time of invention and recommend this date to be used in patent analyses to reflect the applied research and development activities of companies and research organisations. For this reason, the priority date of the patent was used in this research.

Another factor considered in patent analysis is the assignment of countries of origin. Hinze & Schmoch (2004) described three options. First, the country can be assigned as that of the office to which the priority application was submitted; all patent databases record the priority country. Second, the inventor country information could be used for country assignment. It is assumed that the location of the research and development organisation generally coincides with the inventor's country of residence. The third option is the applicant country. This last option is less clearly defined. Some international groups have the parent company apply for all patents, and in other instances, the affiliated organisations appear as applicants. In this research, the inventor country information was used.

The patent family must also be considered in patent analysis. A patent family contains a set of patent documents which refer to the same technical topic (Michel & Bettels, 2001). An applicant usually makes a first filing at a patent office of their choice. The first filing is linked to the priority date. The applicant may file extensions of the same technical topic in other countries within one year of the priority date. In this research, patent families were considered as a unit. Inventor data at the priority date were recorded.

4.2 Drawing actor-collaboration networks

Actor-collaboration networks were generated using UCINet 6 (Version 6.573) (Borgatti, Everett, & Freeman, 2002) and NetDraw (Version 2.152) (Borgatti, 2002). UCINet is a software package used for SNA, and NetDraw, which is embedded within UCINet, is a software package to draw social network diagrams (Analytic Technologies, 2010). NetDraw's spring embedded algorithm was used to draw the network and nodes were manually manipulated to best illustrate network dynamics and relationships. A spring-embedded algorithm is used to sort randomly placed nodes into a desirable and legible layout for better visual representations (InfoVis Cyberinfrastructure, 2004). In the actor-collaboration network, the organisations to which the authors and inventors were affiliated are the nodes (actors). Each instance of co-authorship or co-inventorship is an edge between nodes. The thickness of the edge is weighted according to the number of co-authored publications or co-invented patents produced by the two nodes that it connects. Edges are undirected as co-authorship and co-inventorship are reciprocal relationships. The nodes and edges combine to form components. Two nodes are part of the same component if there is a path connecting them. Where the publication was co-authored or the patent was co-invented by individuals of the same organisation, the "collaboration" is represented by a self-reflecting tie.

Once the full list of publications was finalised, author- and inventor-affiliation data were extracted from scientific publications and patents and used to draw actor-collaboration networks using UCINet and NetDraw. The input file for UCINet was a node matrix which related nodes in the network. Following from the example of Plugmacher et al. (2011) (Figure 6), the following inventor-affiliations were established: Robert Plugmacher was found to be affiliated with Klinik und Poliklinik fur Orthopadie und Unfallchirurgie (KPOU), Gert Becker was found to be affiliated with Saspine, a South African medical device manufacturer, and Peter Van Asselt was found to be affiliated with Design 4 Spine (D4SBV) at the time of patenting. The resulting matrix required for UciNet is shown in Table 2.

Table 2: Node matrix illustrating collaboration in Plugmacher et al. (2011)

	D4SBV	Saspine	KPOU
D4SBV	0	1	1
Saspine	1	0	1
KOPU	1	1	0

NetDraw requires an attribute file, which assigns attributes to nodes. Each node was assigned attributes based on the sector to which it belonged and on its geographical location. All South African organisations were attributed "national" and all organisations who were not located in South Africa were attributed "international". Each node was assigned to one of the following four sectors:

1. Healthcare, which includes all hospital types, including academic hospitals, clinics and specialised healthcare facilities.
2. University, which includes all forms of higher education organisations, such as universities, universities of technology, colleges, etc.
3. Science council, which includes research organisations other than universities.
4. Industry, which includes individuals and organisations whose aim is to take products to market, usually to make a profit.

The attribute file for the Plugmacher et al. (2011) example would resemble Table 3 below, and the actor-collaboration network diagram could be drawn as in Figure 7. The assignation of attributes to respective nodes is represented in the shapes and colours in the actor-collaboration network. The attributes also allow for further analysis based on location and sector.

Table 3: Attribute file illustrating attributes ascribed to nodes of Table 2

*node data		
ID	**Location**	**Sector**
D4SBV	International	Industry
Saspine	National	Industry
KPOU	International	Healthcare

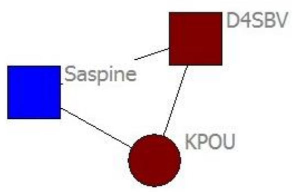


Figure 7: Simple actor-collaboration network diagram illustrating co-inventorship for Plugmacher et al. (2011).

Each organisation appearing on a scientific publication or patent has been counted only once, regardless of the number of authors or inventors affiliated with that organisation. Furthermore, where one author or inventor was affiliated with several organisations, a link was created between those organisations.

In order to build the actor-collaboration network, all the publications which formed part of the network dataset were needed: the affiliation data had to be built into a matrix; the attribute data of the nodes in the network had to be built into a file. The actor-collaboration networks were analysed in UCINet and network metrics were calculated to analyse the networks quantitatively. The following three chapters (Chapters 5, 6 and 7) use the methodology that has been described in this chapter and may have elements that differ according to their distinct analyses.

5. The scientific base for orthopaedic device development in South Africa: spatial and sectoral evolution of knowledge development

This chapter presents verbatim a journal article (Salie, de Jager, Dreher, & Douglas, 2019) which has been approved by the Doctoral Degrees Board to be included in this thesis. The article has been formatted to match the rest of the thesis.

The chapter investigates the scientific base for orthopaedic device development in South Africa. It partially addresses objective 1 of the study “to identify the actors in the orthopaedic devices TIS in South Africa and to characterise the relationship between them” by identifying the actors that contribute towards the scientific base, and using social network analysis, relating the actors to each other based on co-authorship of scientific publications. Methods employed in this chapter allow for examination of the spatial and sectoral evolution of knowledge development in the TIS. Through understanding the development of knowledge in orthopaedic device innovation and an assessment of how well the functions of the TIS are performing, the capacity of the innovation system is revealed. By highlighting trends in the TIS on the spatial and sectoral levels, the chapter partially addresses objective 3 of the study “to provide insight into what drives or hinders knowledge development and knowledge diffusion through networks of the orthopaedic devices TIS” and objective 4 “to identify the TIS-contextual factors that influence knowledge development and knowledge diffusion through networks in the orthopaedic devices TIS”.

As this chapter provides concise explanations of the methodology employed in the study, a more detailed explanation has been presented in Chapter 4. The conceptual framework as it applies to the entire project has been presented in Chapter 3, but elements are presented in Section 5.3. This chapter only presents selected timeframes of the evolution of the TIS over time. All twelve timeframes of the evolution network are presented in Appendices D and E. The scientific publications on which the networks are based, are presented in Appendix F. A postface discussion is presented in Section 5.8.

5.1 Abstract

We assess knowledge development and knowledge diffusion for orthopaedic device innovation in South Africa over the period 2000-2015. A structural network analysis is performed on bibliometric data using co-authorship on scientific publications as an indicator of collaboration between different organisations. We apply a Technological Innovation System (TIS) framework, quantitatively assessing the TIS functions “knowledge creation” and “knowledge diffusion” in their spatial and sectoral contexts. Network metrics (degree and betweenness centralities), and empirical TIS analyses are used

to describe the knowledge functions of the TIS. Our results show that scientific knowledge development has increased as time has progressed, and that university and healthcare sectors have largely been responsible. Results further indicate that, for the national healthcare and national industry sector actors, ties to university and science council actors support scientific knowledge creation. The collaboration networks were found to be sparse, and disjointed, with many actors largely unreachable, indicating barriers to knowledge exchange between actors. Initially the network displayed spatial elements of an internationalised TIS, but over time, the spatial typology changed to that of a nationalised TIS. This shift may be a positive one, as South African research and development activity shifts towards being driven by local actors and towards medical devices which address the South African burden of disease.

5.2 Introduction

Orthopaedic devices comprise a substantial component of medical device imports to South Africa, with up to 65% of all surgical appliances imported between 2004 and 2013 comprising products categorised as "orthopaedic appliances" (Deloitte, 2014). The export value of orthopaedic devices from South Africa is low in comparison. This suggests that the domestic orthopaedic market is not able to supply devices as needed and may present opportunities for local manufacture of orthopaedic devices, to replace imports. A characterisation of the nature and extent of innovation activity for orthopaedic devices in South Africa would form a basis from which to develop this area of activity.

Medical device development involves different sectors – university, healthcare, industry (Lander & Atkinson-Grosjean, 2011; Lander, 2013) and science councils[2] and other supporting sectors, including government and non-government organisations (Chimhundu, de Jager, & Douglas, 2015; de Jager, Chimhundu, Saidi, & Douglas, 2017) – each of which plays a different role in the innovation network. Collaboration between these sectors results in knowledge transfer and access to different forms of capital across sectors, while ensuring that developed technologies address patient needs and reach the market (Lander, 2014). An understanding of collaboration in orthopaedic device development networks could inform strategies to promote knowledge exchange between actors, to enhance research, development and commercialisation.

[2] The term "science council" is widely used in South Africa. Scholes et al. (Science councils in South Africa, 2008) described the term as being shorthand for a variety of public sector, not-for-profit research and development organisations, which have been established by statutes, and are dependent on public funding. Organisations in the science council sector typically conduct fundamental and applied industrial research, are involved in the experimental development of innovative technologies, and provide training, consulting and other services (National Treasury, 2014).

We investigate the scientific base for orthopaedic device development, focussing on collaboration for the creation and exchange of scientific knowledge. Our approach lies in conceptualising orthopaedic devices as a technological field, and applying a technological innovation system (TIS) framework to assess the development of aspects of the orthopaedic device TIS over time. We employ social network analysis as an analytical framework to analyse knowledge creation and knowledge diffusion among actors in the network, focusing on the spatial and sectoral context. An understanding of the development of knowledge in orthopaedic device innovation, and an assessment of how well the functions of the TIS are performing, reveal the capacity of the TIS. An analysis of the spatial and sectoral context of knowledge creation of the TIS may be used to inform policy to encourage development of orthopaedic devices which addresses local needs.

5.3 Conceptual framework

A TIS has been defined as a "network of agents interacting in a specific economic/industrial area under a particular institutional infrastructure or set of infrastructures" which "is involved in the generation, diffusion, and utilisation of technology" (Carlsson & Stankiewicz, 1991). TIS structures include actors, institutions and networks which contribute to the generation, diffusion and utilisation of a new technology. A structural analysis can answer the following questions: "Which parties develop knowledge?", "Where are the knowledge producers located?", "How much knowledge is being developed?" and "What types of organisations are involved in knowledge production?" (Hekkert, Negro, Heimriks, & Harmsen, 2011). Structural analysis is useful because it allows for the identification of actors and networks in the TIS, the countries and sectors to which they belong and their relation (if any) to each other. "Functions" refer to core processes in a TIS, complementary to the structure (Hekkert, Suurs, Negro, Kuhlmann, & Smits, 2007). Hekkert et al. (2007) and Bergek et al. (2008a) both describe seven functions of a TIS, but their formulations differ slightly. The functions described by Hekkert et al. (2007) include entrepreneurial activities; knowledge development; knowledge diffusion through networks; guidance of the search; market formation; resource mobilisation; and creation of legitimacy. Bergek et al. (2008a) compress the knowledge functions into "knowledge development and diffusion", and introduces the function "development of positive externalities" which is dependent on the other six functions. Both publications present comprehensive frameworks to analyse TISs. Knowledge development and diffusion are said to be "at the heart of the TIS" (Bergek, Jacobsson, Carlsson, Lindmark, & Rickne, 2008a). "Knowledge development" is described by Bergek et al. as learning, and involves activities in which learning takes place. "Knowledge diffusion" relates to the exchange of information within and between networks and extends to activities of learning involving interaction and use (Blum, Bening, & Schmidt, 2015).

Several authors have recently stressed the importance of considering context in TIS analysis. While the TIS framework may be universally applicable (Bergek, Jacobsson, Carlsson, Lindmark, & Rickne, 2008a; Hekkert, Suurs, Negro, Kuhlmann, & Smits, 2007), technology develops differently in different contexts, resulting in the context-specific TIS outcomes. Context is also not static, and changes over time. Identifying favourable contexts allows for the identification of favourable opportunities for the development of new technologies (Bergek A. , et al., 2015). The dynamics of a given TIS are intertwined with the structure and dynamics of the sector(s) of which it is part. Sectors are composed of the same type of structural elements as TISs, but they rely on a larger set of technologies in different stages of maturity and on several different TISs, to provide their overall function (Bergek A. , et al., 2015). They may exhibit high degrees of institutionalisation in terms of well-defined division of labour and stable network relationships and technological infrastructures (Malerba, 2002; Smith & Raven, 2012). A sector therefore provides quite a stable context, to which individual TISs either have to adapt or which they have to try to change to their own benefit. Many TISs are part of several sectors. Interactions do not only occur in the sector in which the focal TIS is mainly embedded, but also with other sectors to which it is related. In particular, actors that enter an emerging TIS often come from other sectors. Because of such structural couplings, sectoral dynamics in adjoining sectors can influence the functional dynamics of the focal TIS.

Coenen et al. (2012) emphasise the geographical context of TISs. They explain that space affects relationships, i.e. the distance between actors affects how they interact – regular interactions between actors result in more solid connections, institutions and networks. Their geographical analysis allows for the understanding of a phenomenon with space-specific impacts. The absence of a conceptualisation of space results in an underestimation of the coupling structures between the TIS and the sectoral and contextual systems (Rochracher, Truffer, & Markard, 2010). It also results in an under-conceptualisation of relationships between different sub-system structures. By understanding how the TIS is coupled to its spatial context, case-specific findings currently found in the literature could be made more general and comparable. The geographical context of TISs has been highlighted by several studies in recent years (Binz, Truffer, & Coenen, 2014; Wieczorek, Hekkert, Coenen, & Harmsen, 2015; Murphy, 2015).

It has been pointed out that the TIS approach has enjoyed limited application in developing world contexts and that examination of emerging TISs in developing countries would contribute to conceptual development of the TIS framework (Blum, Bening, & Schmidt, 2015; Tigabu, Berkhout, & van Beukering, 2015a). Coenen et al. (2012) suggest that actors may have substantially different access to resources at different geographical levels , contrary to the assumptions of a “global opportunity set” (Carlsson, Jacobsson, Holmen, & Rickne, 2002) in which all actors are assumed to have equal access to external resources. This is evident in studies applying the TIS framework in developing and least developed country settings. Schmidt & Dabur (2014) delineated a “national TIS” and “international TIS” in their framework for the diffusion of biomethanation in India. They found that the role of the international TIS only contributed to a few functions, but these functions were the most developed in the TIS and relevant in the removal of barriers which were less rooted in national institutions. Blum et al. (2015) used the TIS approach to derive policy recommendations to increase the diffusion rate of remote electric mini-grids in Laos. In delimiting their spatial contexts, they drew three geographical levels - local, national and international. They found that the low diffusion rates were due to institutional mismatches within and across geographical levels as well as hampered flows of resources across the geographical levels. Their geographical classification allowed for the identification of bottlenecks at geographical interfaces, which was important in understanding the functions in the Laotian context.

Binz et al. (2014) developed an analytical framework, incorporating indices and spatial classifications, to evaluate the geographical or spatial dimension of the TIS and map the dynamics of the knowledge functions in membrane bioreactor (MBR) technology. They performed a network analysis of the actors over time to identify relevant actor locations and spatial levels of the TIS. Spatial levels may refer to local, sub-national, national, regional or international delineations. The authors explain that, while technology and technological fields may span across countries, the spatial set-up of the TIS is specific to the technology in focus, and to the resources and relationships between actors involved in driving that technology.

Newman (2001) shows how the network structure of scientific communities has implications for the diffusion of information. He found “small-world” properties – high clustering, and low average path length – to be a crucial feature of a functional scientific community. A high clustering coefficient means that actors are highly connected, while a short average path length means that the distance between actors is small, usually only a few actors. Binz et al. (2014) assert that small-world networks increase TIS creative output as they combine local and trustful collaborative innovative processes with ties to more distant, complementary ideas.

5.3.1 Focus of the study

We examine the TIS for orthopaedic device development in South Africa. We identify the structure of the TIS by drawing collaboration networks based on bibliometric data, particularly co-authorship of scientific publications.

These publications serve as indicators of “knowledge development” while the collaboration networks represent “knowledge diffusion”. By only considering South Africa, a geographical boundary is drawn which sets the limits to the analysis of the TIS, although international actors that play a role in the national TIS are considered. The technological field is orthopaedic devices. We are concerned with the development of new devices, or the extension of functionality of existing devices. The spatial context arises from the collaboration of South African organisational actors with each other and with international actors. We are concerned with the functions "knowledge development" and "knowledge diffusion through networks" described by Hekkert et al. (2007).

As medical device development involves inter-sectoral collaboration, we draw from the ideas of TIS-sectoral interaction from Bergek et al. (2015). We perform an empirical analysis of the focal TIS using the framework presented by Binz et al. (2014), which relies on social network analysis. While geographic delimitation is of interest in our orthopaedic device development network, drawing boundaries between sectors is also of interest in understanding the behaviour of actors from different sectors. We have created distinct national and international boundaries, as in Schmidt & Dabur (2014). Here, we assess knowledge development and diffusion in the orthopaedic device development network in South Africa, in terms of its relative "goodness" as a desirable network (Bergek, Jacobsson, Carlsson, Lindmark, & Rickne, 2008a).

5.4 Methodology

A bibliometric study was used to investigate the network of actors involved in orthopaedic device development in South Africa. Using author affiliation listed on scientific publications, we were able to identify the organisations that contribute to orthopaedic device development in South Africa. Co-authorship on scientific publications served as an indicator of collaboration between authors from different organisations. The primary inclusion criterion for a scientific publication was affiliation of at least one author to a South African organisation. Once the organisations were identified, we could determine their location and sector, which were used for further analysis, described below.

5.4.1 Definition of an orthopaedic device

We developed a definition for an orthopaedic medical device using a similar approach to that of Chimhundu et al. (2015) for cardiovascular medical devices. We started with the medical device definition of the Global Harmonisation Task Force (Global Harmonisation Task Force, 2012) which is endorsed by the WHO, and modified it for orthopaedic devices (modifications are shown in bold):

*An **[orthopaedic]** medical device means any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent or calibrator, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings for one or more specific purposes of diagnosis, prevention monitoring, treatment or alleviation of disease**[s associated with the musculoskeletal system]**; the compensation for an injury; the investigation, replacement,* *modification or support of **[the musculoskeletal system]**; or for providing information for diagnostic purposes by means of in vitro examination of specimens **[of the musculoskeletal system]**; and does not achieve its primary intended action in or on the body**['s musculoskeletal system]** solely by pharmacological, immunological or metabolic means.*

The definition informed the search terms used in Scopus and Thomson Reuters Web of Knowledge (WoK) to find journal articles and conference proceedings for the period 2000-2015. These search terms are presented in Appendix A. Search results were manually assessed to determine if the articles contributed to orthopaedic device development.

5.4.2 Collaboration networks

The collaboration networks were generated using UCINET 6 (V 6.573) (Borgatti, Everett, & Freeman, 2002) and NetDraw (V 2.152) (Borgatti, 2002). In the network, the actors are the organisations to which the co-authors are affiliated; each actor is represented as a node. The actors were classified into four sectors – universities, healthcare, industry and science councils. While it is easy to classify national actors as belonging to the science council sector, international actors were classified with caution. Actors that have been designated as international science councils, are those that conduct research, but are not of the university sector, and not explicitly a healthcare organisation. Examples include the French National Institute for Health and Medical Research (FNIHMR) - a publicly funded research institute in France, and the National Institute of Research and Development for Theoretical Physics (NIRDTP) – a publicly funded Romanian organisation involved in basic and applied research.

In the collaboration networks, each publication is represented as an edge between collaborating nodes. The size of the node is scaled to the degree (discussed later) of the node. The thickness of the edge is weighted according to the number of co-authored publications produced by the two nodes that it connects. The nodes and edges combine to form components. Two nodes are part of the same component if there is a path connecting them. The network as a whole may consist of several components. Co-authorship of a publication by individuals of the same organisation is represented with a self-reflecting tie. While these publications do not display collaboration, they do indicate activity towards orthopaedic device development, and have thus been included in the analysis. We used a five-year moving window to assess our publication dataset. Eslami et al. (2013) assumed the life-span of network links based on co-authorship to be five-years, based on previous studies and on the argument that information exchange takes place between co-authors for some time during a collaboration.

The following metrics (Hanneman & Riddle, 2005) were used to analyse the network.

Degree centrality

The degree centrality is a measure of the number of collaborations in which the node is involved, thereby serving as an indicator of how active the node is. It is calculated as the number of ties between a given node and other nodes in the network, including any self-reflecting ties the node may have. As we are comparing networks, we report normalised degree centrality. The normalised degree centrality, as reported in Equation 6, is the node's degree, $u(y)$, divided by the maximum possible degree in the network, u_{max}.

$$|D(y)| = \frac{u(y)}{u_{max}} \text{ … Equation 6}$$

Betweenness centrality

Betweenness centrality is a measure of how often a node lies on the shortest path between two other nodes. From Batool & Niazi (2014), it is calculated by Equation 7:

$$B(y) = \sum_{x \neq y \neq z} \frac{\delta_{xz}(y)}{\delta_{xz}} \text{ … Equation 7}$$

Nodes with high betweenness centrality are considered to influence the flow of information across the network. As we are comparing networks, we report normalised betweenness centrality. The normalised betweenness centrality is the node's betweenness centrality divided by the maximum possible betweenness of the network, and is reported as a percentage, as in Equation 8:

$$|B(y)| = \frac{B(y)}{B_{max}} \text{ … Equation 8}$$

5.4.3 TIS analytical framework

Binz et al. (2014) present metrics and typologies to analyse networks spatially. This section draws strongly from their analytical framework, and allows us to characterise the innovation network in terms of a spatial topology. Three broad network patterns are described by Binz et al.:

1. Localised – where innovation is based on processes emerging in largely unrelated subsystems in the network, and the network may be localised regionally or nationally. We have localised at the national level.
2. Globalised – where innovation spans actors from different countries.
3. Multi-scalar – where the actor network incorporates both national and international ties. This set-up essentially represents a small-world network, efficiently connecting tight clusters of national interaction, with occasional distant links to other clusters.

Nationalisation index

Binz et al. (2014) developed a nationalisation index, to measure the level of cooperation within vs outside national borders. It is based on the external-internal (E-I) index by Krackhardt & Stern (1988), and is defined as the ratio of links among actors inside one country to links with actors outside that country. We have applied the nationalisation index of Binz et al. to compare the number of ties among South African actors, L_i, to the number of ties South African actors have with actors in other countries, L_e. This nationalisation index, N, is given by Equation 9.

$$N = \frac{\sum L_i - \sum L_e}{\sum L_i + \sum L_e} \text{ … Equation 9}$$

This index measures the dominance of national over international ties. If most actors are cooperating in a national context, the index would be positive and tend towards one. If national and international cooperation are equally present, the index would be close to zero. If international cooperation is dominant, the index would be negative, and tend towards -1.

Sectorisation index

Adapted from Binz et al.'s nationalisation index, we present the sectorisation index, S, as shown in Equation 10, which compares the number of collaborations between South African actors within the same sector (i.e. universities, healthcare, industry or science councils), s_i, to that with South African actors outside the sector, s_e. This metric is calculated separately for each sector.

$$S = \frac{\sum s_i - \sum s_{e,}}{\sum s_i + \sum s_e} \text{ … Equation 10}$$

n-clan analysis

Binz et al. (2014) use n-clan analysis to identify subgroups within components of the network. N-clans are defined as subgraphs in which the largest (geodesic) distance between any two nodes is not greater than "n". Based on this description, two nodes may form part of the same subgroup, even if they have not collaborated. By using n-clan analysis to identify subgroups in the orthopaedic device collaboration network, we can assess the network spatially to determine whether the network has national, global or multi-scalar dimensionality.

As in Binz et al. (2014), "n" is equal to 2, implying that all nodes are separated by no more than one other node in the subgroup. The n-clan function in UCINET requires that a minimum number of actors in a subgroup be set. We have set this to be the diameter of the network, which is the maximum geodesic distance in the network (within a component) (Hanneman & Riddle, 2005). Thus all nodes that meet the definition of the n-clan subgroup will be included.

Binz et al. (2014) present a typology of spatial TIS set-ups, based on the nationalisation index as well as the extent of cohesiveness of the network's subgroups. The cohesiveness of subgroups refers to the formation and interrelation of subgroups. The cohesiveness of the network is assessed by visualising the overlap of n-clan subgroups. The typologies may be:

1. Nationalised innovation networks – no cohesive subgroups and nationalisation index $N > 0$
2. International innovation networks – no cohesive subgroups and $N < 0$
3. Nationalised TIS – internal cohesive subgroups, weak overlap of subgroups and $N > 0$
4. Internationalised TIS – external cohesive subgroups, weak overlap of subgroups and $N < 0$
5. Multi-scalar TIS – internal and external cohesive subgroups, weak overlap of subgroups and $N \approx 0$
6. Global TIS – internal and external cohesive subgroups, strong overlap of subgroups and $N \approx 0$

Our network structures were analysed spatially using these typologies.

5.5 Results

In our manual assessment of the search results, publications were eliminated if their title and abstract did not show evidence of the development of an orthopaedic device. Where it was unclear from these sources whether the publication did indeed show evidence of orthopaedics device development, the first author read the publication to determine if the publication fell in the scope of orthopaedic device development. The publication had to clearly illustrate what "device" was being developed and it had to illustrate "development".

The Scopus search yielded 59 publications which met the inclusion criteria. The Thomson Reuters WoK search yielded 20 publications, of which four were not included in the Scopus results. Consequently, a total of 63 publications were retained for use in the bibliometric study. Ninety-nine actors were identified from the publications. Table 4 presents a spatial and sectoral breakdown of the actors. One hundred and ninety-eight unique authors were identified in the 63 publications. Of these authors, 99 had South African affiliations, 88 had international affiliations, seven had listed both South African and international affiliations, two had not listed their affiliations, and one publication did not distinguish affiliations when listing authors. The network is dominated by actors from the university and healthcare sectors, jointly accounting for almost 80% of the actors. There is a large international presence in the network, with more than 60% of all actors representing international organisations. Within the university and healthcare sectors, the majority of the actors were international.

Table 4: Sectoral breakdown of actors in the orthopaedic device development network.

Sector	National	International	Total
Universities	11	29	40
Healthcare	14	24	38
Industry	7	7	14
Science Councils	4	3	7
	36	**63**	**99**

Seven of the 63 publications arose from internal collaboration within the same organisation. Six of these were from the university sector, and one from the healthcare sector. All the actors who had publications resulting from internal collaboration, were high degree actors (discussed later).

For the period 2000-2015, 12 overlapping timeframes were distinguished, starting from 2000-2004 (1^{st} timeframe) and ending at 2011-2015 (12^{th} timeframe), and assessed. For each timeframe, the number of national and international actors, and the number of scientific publications for that period were counted (see Figure 8). There is a gradual increase in the number of publications produced by actors as time progresses. The total number of actors increases over time. The number of national and international actors are similar in the early timeframes. There is a sudden increase in international actors in the sixth timeframe (2005-2009), resulting in an increase of the total number of actors. Beyond the sixth timeframe, the number of international actors is slowly decreasing, and the number of national actors steadily increasing. The number of national actors exceeds the number of international actors in the latter years. Selected timeframes of the orthopaedic device development network are presented in Figure 9. Each actor is represented by a node in the network. Full names of the actors along with their abbreviations are presented in Appendix C.

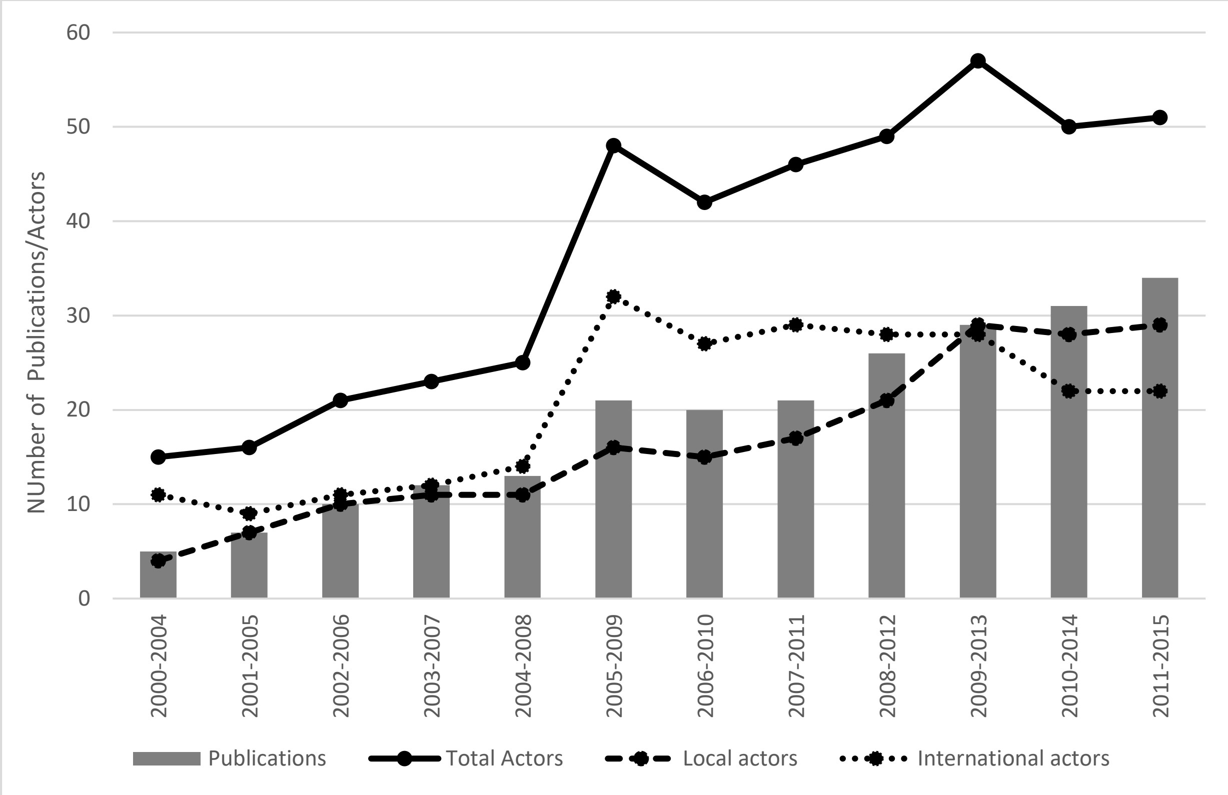


Figure 8: Number of publications and number of national and international actors in each of the timeframe networks of the orthopaedic device development network

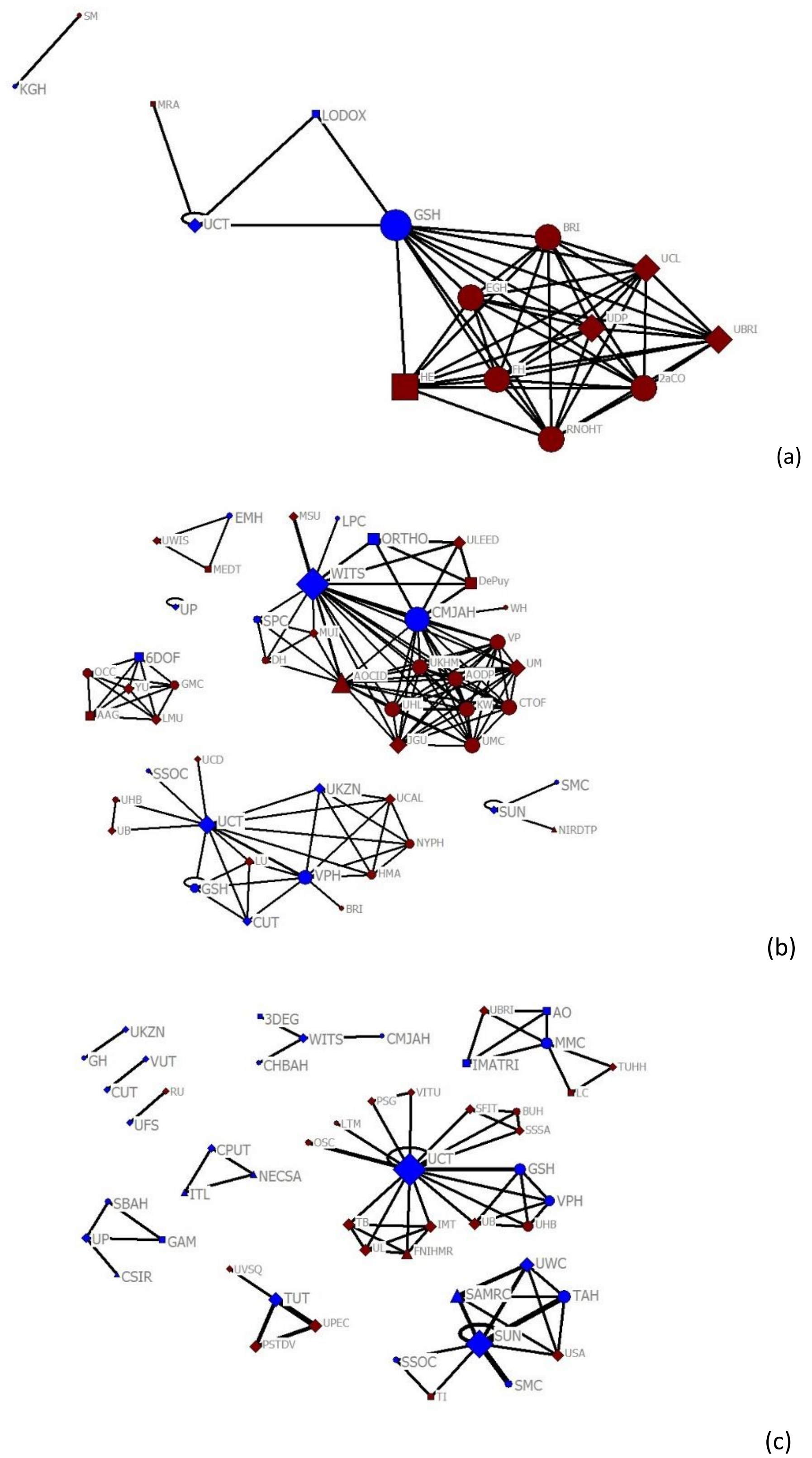


Figure 9: Orthopaedic device development network of South Africa for selected timeframes (a) 2000-2004 (b) 2005-2009 and (c) 2011-2015. All national nodes are blue, and all international nodes are maroon. Nodes are shaped according to sector [circle=healthcare, diamond=universities, square=industry and triangle=science councils]

The publication dataset of the bibliometric study showed low initial levels of publication in the early years, with no publications in 2001 and 2004. This may be the result of the fledgling orthopaedic device development network at that time, with very few actors – 15 in the first timeframe – able to make contributions to the network. As time progresses, there is an increase in the rate of knowledge production, determined by the increasing rate of publications.

For each of the 12 timeframe networks, the top three actors with the highest degree centrality values are reported. Where fewer than three actors are reported, several actors in the network would have been tied for the third position. Once the top actors were identified, the degree centrality for all time periods were extracted to assess actor evolution over the 12 timeframes. These results are presented in Figure 10. They are reported in this way for two reasons. The first is to show who the high-degree actors are for a specific timeframe (vertical axis). The second is to show the evolution of these high-degree actors over time (horizontal axis).

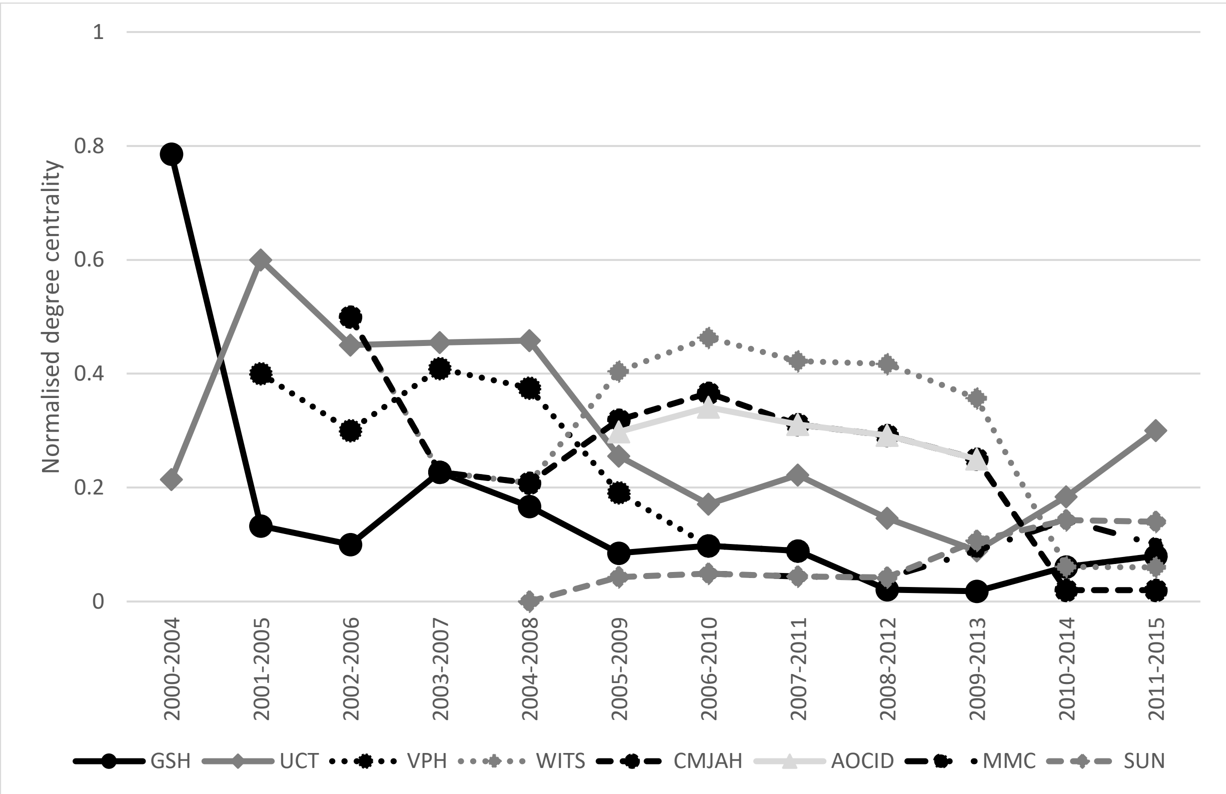


Figure 10: Highest-ranked actors by degree centrality. A list of actor abbreviations and their full names can be found in Appendix C

In the first timeframe, Groote Schuur Hospital (GSH) is the highest degree actor. In the next four timeframes, the highest degree actors are the University of Cape Town (UCT) and Vincent Palotti Hospital (VPH). In the sixth (2005-2009) and seventh (2006-2010) timeframes, the highest degree actors are University of Witwatersrand (WITS), Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), and AO Clinical Investigation and Documentation (AOCID). WITS and AOCID continue to be high degree actors up to the tenth timeframe (2009-2013). In the last two timeframes, UCT, the University of Stellenbosch (SUN) and Morningside MediClinic (MMC) are the highest degree actors. Most of these high-degree actors are from the national university and national healthcare sectors. The only exception is the AOCID, which is classified as an international science council.

The actors having highest betweenness centrality over the 12 timeframes are presented in Figure 11. This metric is presented similarly to degree centrality in Figure 10, where the highest ranked actors by degree centrality are presented along the vertical axis, and the evolution of these actors over time can be seen across the horizontal axis. While all actors present in a network has degree centrality, not all actors lie between other actors, and hence, not all have betweenness centrality. We report as many as five top betweenness centrality actors per timeframe in Figure 11.

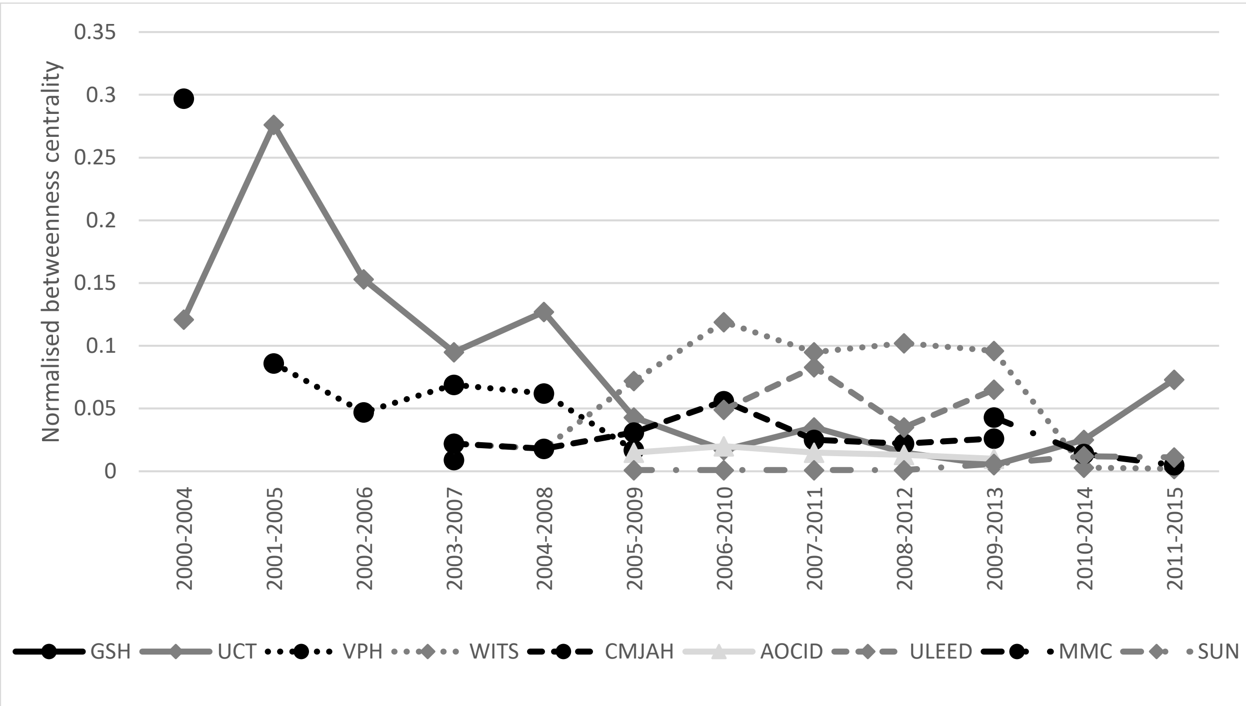


Figure 11: Highest-ranked actors according to betweenness centrality over the 12 timeframes. A list of actor abbreviations and their full names can be found in Appendix C.

The actors having high degree centrality also have high betweenness centrality, i.e. all the actors that appear in Figure 10 also appear in Figure 11. There are two more actors in Figure 11 than Figure 10 – the University of Leeds (ULEED) and the University of Pretoria (UP). In the first timeframe (2000-2004), GSH and UCT are the actors with highest betweenness centrality. In the second (2001-2005) and third (2002-2006) timeframes, UCT and VPH have betweenness centrality, and here, the value captures their role in the main component of the network. The addition of WITS and CMJAH to the network in the fourth timeframe (2003-2007) results in two distinct network components (see Figure 9) forming the UCT/VPH component and the WITS/CMJAH component. Over time the WITS/CMJAH component grows (timeframe 4 (2003-2007) to 7 (2006-2010)), stabilises (timeframe 8 (2007-2011) to 10 (2009-

2013)) and shrinks (timeframe 11 (2010-2014) and 12 (2011-2015)). The UCT/VPH component shrinks over time, with a slight increase in the last timeframe. The AOCID and the University of Leeds (ULEED) also have betweenness centrality in the WITS/CMJAH component. MMC enters the network in the seventh timeframe (2006-2010), but only gains betweenness centrality in the tenth timeframe (2009-2013). As the SUN component grows in the later years, so too does the betweenness centrality of SUN.

The network is dynamic and the actors change over time, particularly the international actors, many of whom only appear on one publication. The national actors appear to evolve – their collaboration choices and role within the evolutionary networks change. As an example, UCT shows growth in terms of increasing its degree centrality in the first five timeframes, followed by a period of decreasing degree centrality over the next five timeframes, and then increasing degree centrality in the last two timeframes. The actor SUN demonstrates more consistent growth. SUN first presents in the fifth timeframe (2004-2008) as a self-reflecting tie, illustrating internal collaboration. As time goes by it increases its degree centrality and betweenness centrality, by collaborating with other actors and across other sectors. By the eleventh timeframe (2010-2014), SUN has the second highest degree and betweenness centralities, creating a knowledge hub within the network. The evolution of most of the national actors (WITS, CMJAH, UP, GSH, VPH) across the timeframes is similar. These evolving actors are from the university and healthcare sectors and display co-dependence on the actors to which they have strong ties, as an example, the evolution of GSH with UCT.

Science councils are slowly introduced into the network, first presenting in the sixth timeframe (2005-2009), with international actors only. National science councils only present in the ninth timeframe (2008-2012). Across all timeframes, there is no instance of collaboration between the science council and industry sectors.

The Nationalisation Index is presented in Figure 12. Across all timeframes there is neither a strong tendency towards internationalisation (-1) nor towards nationalisation (+1). Till the ninth (2008-2012) timeframe, there is a preference for international collaboration, with a mostly negative index. There is preference for national collaboration from the tenth (2009-2013) to the twelfth (2011-2015) timeframe.

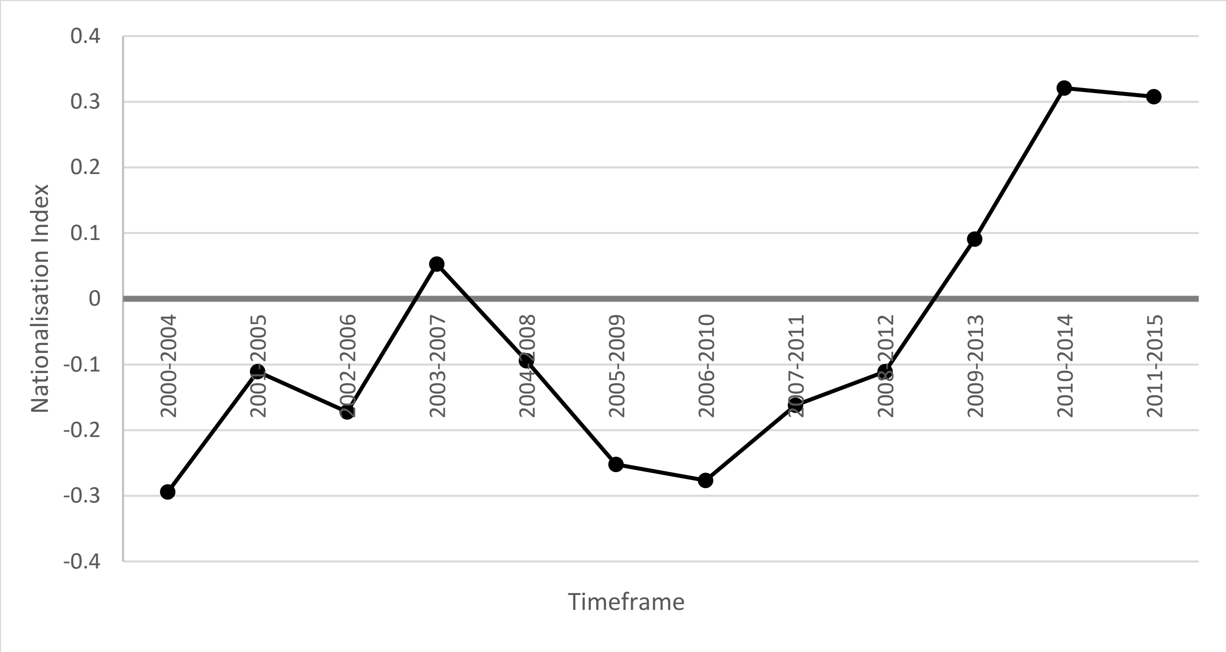
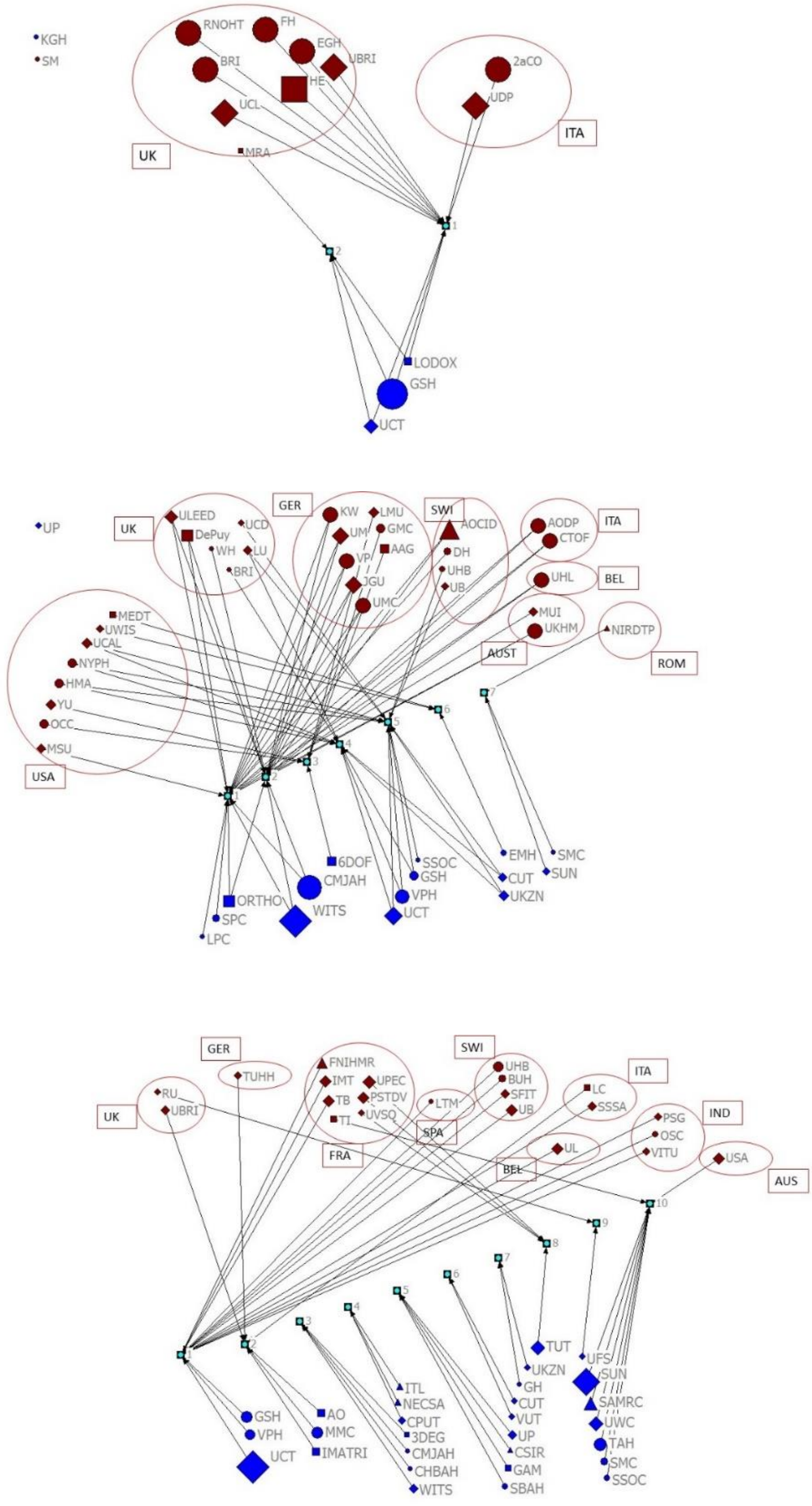


Figure 12: Nationalisation index of the orthopaedic device development networks over the 12 timeframes

We used 2-clan analysis to identify cohesive subgroups in the networks, and how these subgroups overlap. Subgroup overlap presents greater opportunity for knowledge diffusion across the network. Over the 12 timeframes, the number of 2-clans is ever increasing, with two 2-clans in the first timeframe, and ten in the last timeframe. The 2-clan subgroups of the selected timeframes are presented in Figure 13, where the overlap of subgroups is indicated by actors belonging to more than one subgroup. Considering Figure 12 and Figure 13 together, the spatial typology of each network was assessed. According to the classifications presented in Binz et al. (2014), the first three timeframes can be classified as being an internationalised TIS based on their negative nationalisation index and weak overlap of subgroups. The nationalisation index of the fourth timeframe (2003-2007) is positive, but very close to zero (N=0.05), and this network is classified as being a multiscalar TIS. From the fifth (2004-2008) to the tenth (2009-2013) timeframe, the networks are classified as internationalised TIS. In the last two timeframes, the networks have nationalised TIS typology due to their positive nationalisation index and no overlap in subgroups. It is worth pointing out that in all timeframes, a TIS, rather than an innovation network, is present, as there are always cohesive subgroups in each timeframe network.

The international actors of the orthopaedic device development network come from 14 different countries. These include the United Kingdom (UK), Italy (ITA), the United States of America (USA), Switzerland (SWI), Germany (GER), Austria (AUST), Belgium (BEL), Romania (ROM), Netherlands (NED), China (CHI), Australia (AUS), France (FRA), India (IND) and Spain (SPA). The UK appears in all 12 timeframes. In the first timeframe (2000-2004), international actors are from Italy and the UK. In the next three timeframes, international actors are from the USA and the UK. Switzerland is introduced in the fifth timeframe (2004-2008), joining the USA and the UK. There is an influx of European actors into the network from the sixth timeframe (2005-2009), originating from Germany, Switzerland, Austria, Italy, Belgium and Romania. China enters in the seventh timeframe (2006-2010) and Australia in the tenth timeframe (2009-2013). As the number of European actors grows over time, the number of American actors decreases; the USA is absent in the last two timeframes. India and France join the network in the eleventh timeframe (2010-2014), and Spain in the last timeframe (2011-2015). By the eleventh timeframe, the number of European countries present is higher, but the number of actors is lower. There are no collaborations with actors from other African countries. There are also no collaborations with actors from South American countries. On the national front, most of the national actors in the first six timeframes belong to overlapping 2-clan subgroups. From the eighth timeframe (2007-2011), national 2-clan subgroups, i.e. comprising only South African actors, start forming. There is one national 2-clan subgroup in timeframes eight, nine and ten; three national 2-clan subgroups in the eleventh timeframe; and five national 2-clan subgroups in the last timeframe. These national 2-clan subgroups never overlap.



(a)

(b)

(c)

Figure 13: 2-clan subgroups for selected timeframes (a) 2000-2004 (b) 2005-2009 and (c) 2011-2015. 2-clan subgroups are drawn across the diagonal, national actors are drawn below the diagonal and international actors above the diagonal. International actors are grouped according to the countries in which they are located. Overlap of subgroups can be seen where nodes belong to more than one 2-clan group. A list of actor abbreviations and their full names can be found in Appendix C. Isolated actors shown in the top left-hand corner form part of the timeframe network, but do not belong to any 2-clans.

The sectorisation indices are presented in Figure 14. A positive index indicates a sector's preference to participate in intra-sector collaborations, while a negative index indicates a tendency for involvement in inter-sector collaboration. An index of zero implies equal preference for intra-and inter-sectoral ties. All national sectors prefer inter-sectoral collaboration, however the degree of inter-sectoral collaboration differs greatly. The national healthcare sector shows strong preference for national inter-sectoral collaboration throughout all timeframes. This is different from the behaviour of the university sector, which shows preference for intra-sectoral collaboration from the second (2001-2005) to fifth (2004-2008) timeframes, and then again in the latter years. This is emphasised by the disjoint components (See Figure 9 and Figure 13) in later timeframes, driven by national universities. The industry sector is always involved in inter-sectoral collaboration. The national industry actors, however, are only involved in inter-sectoral collaboration till the ninth (2008-2012) timeframe when they start interacting with other national industry actors. National science councils were seen to enter the network in the ninth (2008-2012) timeframe and show evidence of collaborating with other national science councils as well as inter-sectorally. These trends suggest that for national healthcare and national industry sector actors, ties to university and science council actors promote scientific knowledge creation.

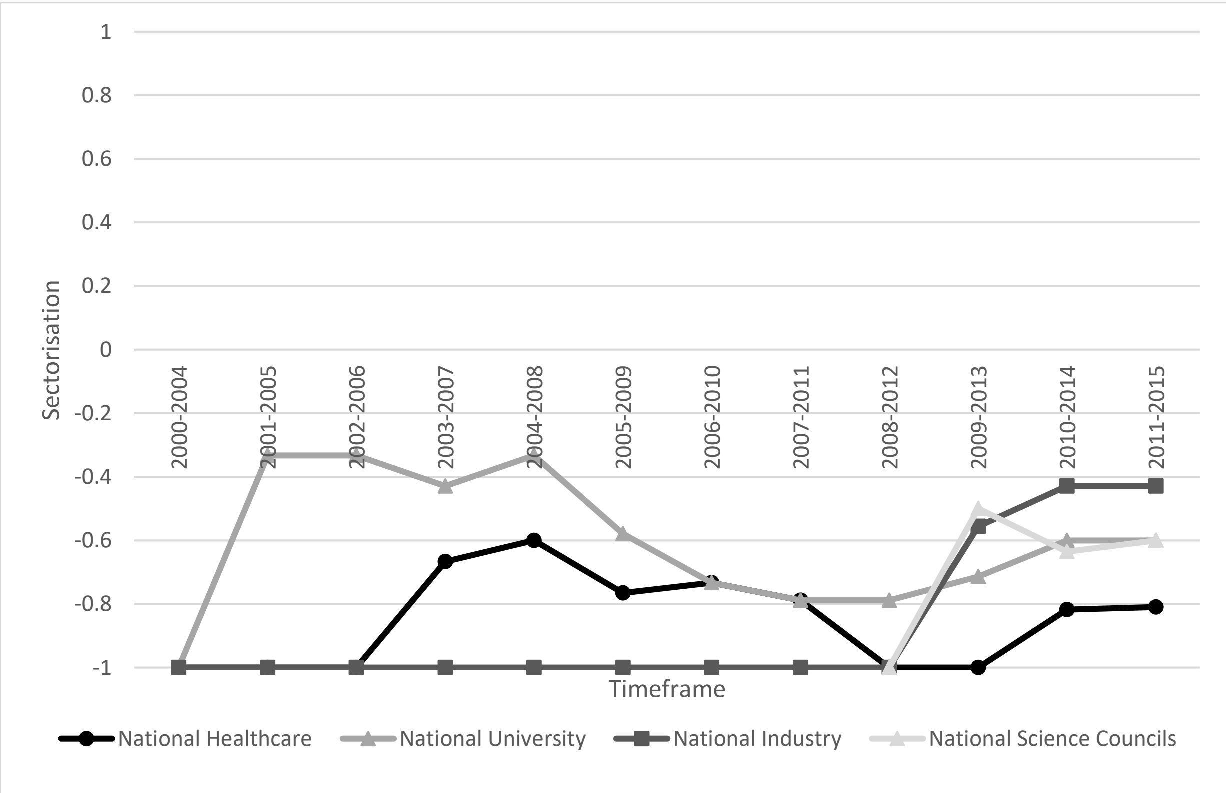


Figure 14: Sectorisation index of the orthopaedic device development networks over the 12 timeframes.

5.6 Discussion

We have shown that the rate of scientific publication output in orthopaedic device development in South Africa increases over the 12 timeframes. Makhoba & Pouris (2016) have argued that increased scientific output in South Africa in recent years could be due to concerted efforts made by the government to promote scientific publication. One such effort is the New Funding Framework which provides cash incentives to higher education organisations for each publication produced.

In our network, most of the actors, and therefore the knowledge creators, belonged to the university and healthcare sectors. Our results confirm the suggestion by Lander (2013) that the "biomedical innovation system", the clinical pathway of innovation, is dominated by interactions between two non-commercial sectors i.e. universities and hospitals. Shown using normalised degree centrality as an indicator for knowledge development – actors who publish more are likely to have more connections in the network – the key actors contributing to knowledge development are national research-intensive universities (UCT, WITS and SUN) and national healthcare facilities (VPH and CMJAH), which show strong ties (by repeat collaborations) to the national universities. The strong ties may be the result of single authors listing multiple affiliations, for instance when an author is affiliated with both the university and an associated academic hospital.

Some of our findings are consistent with those of Chimhundu et al. (2015) for cardiovascular medical devices (CMD). They defined two types of networks, i.e. local (South African organisations only) and global (South African and foreign entities). Universities and healthcare services were found to be the most active sectors in CMD development between 2000 and 2014 in the global network. The CMD development network was found to be improved by the presence of foreign entities, as some of the entities isolated in the local network, were absorbed into the global network by their presence; thus, foreign institutions created alternative pathways for knowledge transfer. Their results further showed there was substantial unrealised collaboration potential in both networks and that the universities played a substantial role in dictating the behaviour of the network. Our results differ from those of Chimhundu et al. (2015) who found that inter-sectoral collaboration increased over time. While our study shows a general preference among all sectors for inter-sectoral collaboration, the national science councils and universities tend toward intra-sectoral collaboration with other national actors in the latter timeframes. This suggests knowledge development rather than diffusion activity. Our findings also differ from those of Chimhundu et al. in terms of the role of international nodes. The isolated components in our network are consistent over all periods – international nodes did not link previously disconnected national actors, and the absence of international nodes did not hinder knowledge development. This confirms the assertion of Binz et al. (2014) that the spatial set-up of the

TIS is specific to the technology in focus (orthopaedic devices vs CMD), and to the resources and relationships between actors involved in driving that technology.

We showed that over all the timeframes, the interaction of actors resulted in a TIS typology, rather than an "innovation network" typology. This means that the actors are not creating knowledge in isolation. Those actors who have published by internal collaboration were found to be key actors, having high degree and betweenness centrality. The network evolves from having an internationalised TIS typology in the first three timeframes, multi-scalar TIS typology in the fourth timeframe (2003-2007), internationalised TIS typology from the fifth to the ninth timeframes, and then having nationalised TIS typology in the last three timeframes. Binz et al. (2014) suggest that the internationalised TIS typology could be a result of the TIS being driven by different international networks, e.g. multinational companies. This is certainly plausible in the network presented here with the presence of large industry sector actors Medtronic (MEDT), DePuy, Howmedica Europe (HE) (which had been a part of Pfizer), and Aesculap AG (AAG). Coenen et al. (2012) suggests that globally active actors depend on places to which they are structurally coupled to advance their own agendas. In the last timeframe, the national universities were the knowledge developers, creating small components of activity in the network. There are 11 national universities in the last timeframe network, belonging to nine of the ten components. The components however are disjoint, and diffusion is impaired. Further study is needed to determine the motivation for the more recent preferential collaboration among national actors, after initial international collaboration, and the role of international actors in driving collaboration.

While we have used the tools provided by Binz et al. (2014), our area of interest and spatial scales differ. Using co-authorship on scientific publications of MBR technology as an indicator of collaboration, Binz et al. were able to describe different phases of the MBR TIS, on a global scale, for the period 1990 to 2009. We have found the Binz et al. methodology to be valuable in understanding knowledge creation dynamics at a national and sectoral level.

The limitation of describing a network as having small world properties, is that a network can only truly be considered small world if all the actors are connected, i.e. all actors lie in the same component. Several authors, including Eslami et al. (2013) and Fleming et al. (Small worlds and regional innovation, 2007), have worked around this limitation, by considering only the largest component in the network in their analysis. We have not performed our analysis in this way, because for many of our timeframes, the number of actors in the largest component is only a fraction of the actors in the network. As an example, only 16 of the 51 actors (31%) present in the last timeframe belong to the largest component. Our network briefly displays multi-scalarity in the fourth (2003-2007) timeframe, but for the most part has internationalised TIS typology, with nationalised TIS typology in more recent times. In the fourth timeframe, 12 of the 23 actors (52%) form part of the largest component. Therefore, even at the point where the network displays multi-scalar traits, a small world analysis on the largest component would miss the influence of half the actors in the network. We have found the framework of Binz et al. especially useful in analysing our network, as it presents a methodology for analysing knowledge development and diffusion in networks that lack small-world properties.

Throughout the period of our study, many actors are unreachable from each other in the network due to disconnected components. While knowledge is certainly being developed, and being developed at an increasing rate, knowledge is not being diffused with increasing efficiency. Thus, learning is taking place in the absence of interaction and use. While there are tight clusters of activity driven by national university and healthcare actors, the key university actors – UCT, WITS, SUN – never collaborate with each other. While further analysis is required to ascertain reasons for this, Pouris & Ho (2014) have posed that the government subsidy system aimed at incentivising publication at South African universities, penalises co-authorship with other institutions and in fact disincentivises collaboration. If the reason for collaboration is to access capital, and that capital shapes the interactions within scientific fields (Lander, 2014), it appears that national universities have become more established, have better access to resources, and have become attractive collaborators, in later years. While universities and science councils both serve as research platforms in the network, there is an obvious preference for the healthcare sector to collaborate with the university sector. National science council actors only enter the network very late, and may not be experienced in orthopaedic device development, and may therefore not be an attractive collaboration choice in this TIS. Furthermore, the mandates of science councils may not necessarily be aligned to medical (or orthopaedic) device development, and their contribution to the network may be a reflection of their primary research focus. Bergek et al. (2015) explained that the dynamics of the TIS are related to the structure and dynamics of the sectors of which it is part, which may open or close markets for the new technologies. Our TIS could be displaying the consequences of existing sectoral dynamics.

The broader context of the orthopaedic devices TIS includes efforts towards the promotion of medical device development in South Africa. The South African Department of Trade and Industry (dti) commissioned an investigation of medical device industry in South Africa (Deloitte, 2014), with the aim of gaining insights for strategy and policy interventions to support long term growth of this industry. Stakeholder collaboration and the introduction and enforcement of effective regulatory policy were elements identified as necessary for growth of the medical device industry. Medical device regulations have since been introduced, effective since December 2016 (Department of Health, 2016). Codes of practice encouraging ethical principles among medical device manufacturers have been in practice since 2012 (SAMED). There are government incentives for investment into medical device development in South Africa, including support for: business development in both the healthcare and education sectors; manufacturing of medical devices; seed funding and patenting; foreign investment through a foreign investment grant; and developing innovative and competitive products or processes (SAMED). The TIS functions affected by these incentives should be examined. Another area for further exploration, is the impact of the promotional interventions on the knowledge functions of the orthopaedic device development TIS; the work presented in this paper would form the foundation for such a study.

5.6.1 Limitations of the study

As the network was investigated using a bibliometric study, institutions and sectors that publish scientific output are favoured, i.e. universities and academic healthcare facilities. This may explain why these institutions are more prominent in the network. Alternative outputs which also show collaboration for orthopaedic device development, such as patents, have not been captured and presented here, but may be more representative of collaboration trends in the industry sector, and will be analysed in a future study.

An analysis of a TIS should include examination of international influence because a spatially limited part of a global TIS cannot be understood or assessed without an understanding of the global context (Bergek, Jacobsson, Carlsson, Lindmark, & Rickne, 2008a). We present the role of international actors in the South African network but do not assess the global orthopaedic device innovation TIS, of which the South African TIS forms part.

5.7 Conclusions

We have identified the organisations contribute to the scientific base of orthopaedic device development in South Africa, the sectors to which they belong, and characterised the interaction between national and international actors by performing a spatial and sectoral analysis. We have shown that knowledge has been created at an increasing rate over time. We have further shown that the diffusion of knowledge is inefficient. We could present this in two (positive) ways. The first is that the TIS has the capacity to produce knowledge. Secondly, the sparsity of the network is an opportunity for collaboration, as the actors creating knowledge have been identified, and have, through this study, been made visible. The shift towards a nationalised TIS may be important in the developing country context, if the aim is to build national knowledge-generation capacity and address diseases and conditions that are nationally relevant. We have further shown that, at a national level, there is a great difference in preference for inter-sectoral collaboration among actors from different sectors, and that, for national healthcare and national industry sector actors, ties to university and science council actors support scientific knowledge creation. Further study is needed to explore any causal links between these network features and the context of South Africa as a developing country.

We have expanded the application of social network analysis to TIS, which was demonstrated by Binz et al. (2014), to a different knowledge field and to the early stages of a TIS in a developing country setting. We have adapted the tools proposed by Binz et al. to consider the technology in focus in a national context, and included a sectorisation index. Thus, we have extended the tools presented by Binz et al. into a methodology for assessment of the knowledge functions of an emerging TIS.

This study will in future be complemented by an analysis of the patenting activities of the actors. An understanding of knowledge development and diffusion through social network analysis of publications and patents will form the basis for case studies for further examination of knowledge dynamics for orthopaedic device innovation in South Africa.

5.8 Post-face discussion

This section discusses additional considerations that have arisen related to the actor-collaboration networks based on scientific publications, since publication of Salie et al. (2019).

The discussion (Section 5.6) and conclusions (Section 5.7) are based on a relatively small dataset, comprising 63 publications, presenting actor collaboration networks with only 99 organisational actors. These networks, though small, are similar in size to the national actor-collaboration networks that have been examined for cardiovascular medical devices (Chimhundu, de Jager, & Douglas, 2015) and medical devices (de Jager, Chimhundu, Saidi, & Douglas, 2017) in South Africa. Chimhundu et al. performed an analysis on 123 journal articles, resulting in networks comprising 155 organisational actors; de Jager et al. performed an analysis on 171 scientific publications, resulting in networks comprising 116 organisations. The conclusions drawn of networks being sparse and actors being unreachable in the scientific publications network, illustrating barriers to knowledge exchange displayed in these networks, is based on the scientific publication dataset only. Further work in later chapters on the patent actor-collaboration networks and case studies provides a more holistic picture of knowledge development and exchange of actors in the TIS. Additionally, the effect of sectoral dynamics on knowledge development and exchange is further explored in the case studies. The findings and conclusions of this Chapter are considered in Chapter 10 within the broader context of the analyses present in the chapters that follow.

The actor-collaboration networks based on scientific publications were shown to have a large international presence. Participation of national actors in large international projects may potentially crowd them into large networks with increased visibility. Kahn (2018) has described the impact on measuring collaboration of participation in mega science projects in BRICS countries, and the increased visibility of these publications due to their high citation rates; such crowding in may result in publications with hundreds of contributing authors, many of whom will never meet each other. In the scientific publication networks, the greatest number of organisations linked by one publication is 12. The networks are therefore unlikely to be influenced by the crowding-in resulting from mega science projects.

The multiple affiliations due to the joint assignation of clinical academics to a university and an academic hospital, contributed to the strong ties between the university and healthcare sectors in the scientific publication networks. Lander & Atkinson-Grosjean (2011) highlighted that these connections are often overlooked in biomedical innovation studies, where the two organisations are considered a single entity, with the result that the relational flow between the organisations that is important for translational sciences, is not recognised.

Clinicians are the de facto "users" of orthopaedic devices and the healthcare actors provide a demand-side input into the innovation system. The demand side of the innovation system would consider users of the devices and their experiences and preferences related to a device, and whether it meets the (clinical) need; this would feed back into the innovation process. In the actor-collaboration networks, the strong presence of the healthcare sector actors suggests that the (potential) users are active participants in the innovation system. Their role within the innovation system is further described in the case studies of Chapter 9.

6. The technological base for orthopaedic device development in South Africa: spatial and sectoral evolution of knowledge development

In this chapter, the technological base for orthopaedic device development in South Africa is explored through patent bibliometrics. The chapter begins by describing how patents are used as an indicator for collaboration in technological innovation, and then presents the results of the social network analysis using patent data of orthopaedic inventions stemming from South Africa. The discussion later in the chapter relates the patent and scientific publication actor-collaboration networks (the latter having been presented in Chapter 5), which together contribute to the structure of the orthopaedic devices technological innovation systems (TIS) in South Africa.

6.1 Patents as indicators of collaboration for technological innovation

A patent is a legal document claiming intellectual property (IP) protection, which gives the patent owner certain rights in exchange for public disclosure of the invention. In order for a patent application to be granted it has to meet all three of the following criteria: (1) novelty, (2) inventive activity, and (3) industrial applicability (Michel & Bettels, 2001). Because a patent must show novelty, it has been used as an economic indicator of the rate and direction of technological progress and innovation (Andersen, 2004). Patents, however, do not capture innovation in the economic sense, where a new or improved product or service has been commercialised into a market. The fact that an invention has been patented, does not mean that it will have commercial success. Patenting is used in this project to illustrate a form of knowledge development and exchange in the innovation chain. Patents and scientific publications represent different dimensions of innovation, and combined analysis may assist in the evaluation of knowledge transfer between scientific discovery and technological outcome.

Fleming & Marx (2006) illustrated that collaborations recorded in patent data captured personal and professional ties between inventors. Co-inventors may have collaborated intensively over extended periods of time towards novel inventions (Singh, 2005). Patents, therefore, serve as tools indicative of a collaborative event (Balconi, Breschi, & Lissoni, 2004) and could be exploited to map social ties among inventors (Breschi & Lissoni, 2004). Several authors have used co-inventorship of patents as a proxy for collaboration in network analysis studies. To the author's knowledge, the first true attempt was presented by Balconi et al. (2004). Balconi et al. mimicked the approach used by Newman (2001), which examined social networks arising from co-authorship in scientific publications, by linking co-inventors of patents in a network. Newman derived implications for knowledge exchange in the network from the structure of the network. Functional scientific networks were found to have "small world” characteristics, i.e. high clustering and low average path length. High clustering implied that actors were highly connected, and short average path length meant that the distance between actors was small. Small world networks increased creative output as they linked local collaborative innovation to more distant, complementary ideas (Binz, Truffer, & Coenen, 2014). Balconi et al. (2004) found that, except for a few technological fields, networks of inventors were more fragmented than networks of scientists. In the cases where network fragmentation was less pronounced between scientists and inventors, this was possibly related to technologies where scientific input was important for the commercialisation of those technologies. An objection raised against co-inventorship to illustrate knowledge exchange among inventors is that inventorship only reflects a small subset of the knowledge exchange that takes place for technological development; examples of other types of knowledge exchange are personal contacts with non-inventors, which may include academic researchers and technologists (Breschi & Lissoni, 2004).

Social network analysis (SNA) literature using scientific publications, patents, or a combination of both, is abundant. In the latter the focus is often on university-industry interaction and the translation of basic science to commercialising technologies. Within this body of literature, work on medical device development is limited. To the authors knowledge, the only such study was performed by Murray (2002), who investigated the communication between science and technology networks in cartilage tissue engineering. Murray discovered that one of the motivations for tissue engineering applications was grounded in the need to find real solutions to an existing medical problem i.e. real solutions for organ failure. Bibliometric indicators showed that a few key scientists published in both domains; also, industry actors did not really participate in scientific publications. Interviews conducted for Murray’s study, however, highlighted overlap between the two networks, not captured in bibliometric data. Reasons for this overlap included the involvement of key scientists in technology development and patenting, forming start-up companies, consulting, mentoring and informal advice. Through these activities, scientists become active participants in both the scientific and the technical community.

The conceptual framework employed in this chapter has been presented in Chapter 3, and the methodology implemented in this chapter has been presented in Chapters 4 and 5.

6.2 Results

The search phrase used to extract patents showing evidence of orthopaedic device development by South African inventors (individuals or organisations), is shown in Appendix B. The definition of an orthopaedic medical device (see Section 5.4.1) was used to develop the search phrase. A TotalPatent search was performed on 12 June 2018 and yielded 1,926 results. Patents were manually examined to extract those related to orthopaedic devices, which had priority dates between 1 January 2000 and 31 December 2015. Seventy-three patents having unique names and showing evidence of orthopaedic device development by inventors having a South African address, were retained.

Inventor affiliation data for 11 of the 73 patents could not be established. Some inventors had no internet presence at all. For some patents, affiliation data for some of the inventors, but not all, were obtained. These patents were excluded from the dataset. The results reported here are from 62 patents filed between 2000 and 2015. Fifty-seven organisational actors were identified; Table 5 presents a spatial and sectoral breakdown of the actors. Thirty-five (61%) of the actors are South African. The organisations are represented in fairly equal numbers from the university, healthcare and industry sectors. National and international university actors are represented in similar numbers. The number of national healthcare and industry actors present is twice that of their international counterparts.

Table 5: Spatial and sectoral breakdown of inventors who patent in orthopaedic device development in South Africa

Sector	**National**	**International**	**Total**
Universities	7	9	16
Healthcare	14	7	21
Industry	14	5	19
Science Councils	1	0	1
Total	**35**	**22**	**57**

For the period 2000-2015, 12 overlapping timeframes were assessed, starting from 2000-2004 (1st timeframe) and ending at 2011-2015 (12th timeframe). For each timeframe, the number of national and international actors and the patents for that period were counted (see Figure 15). There is a gradual increase in the number of patents produced by actors as time progresses, peaking in the 9th (2008-2012) timeframe. The total number of actors increases over time; the number of national actors is always greater than the number of international actors. There is a sudden increase in the number of international actors in the ninth timeframe (2008-2012). Selected timeframes of the orthopaedic device development network are presented in Figure 16. Each actor is represented by a node in the network. Full names of the actors along with their abbreviations are presented in Appendix F. The actor-collaboration networks for all 12 timeframes are presented in Appendix G.

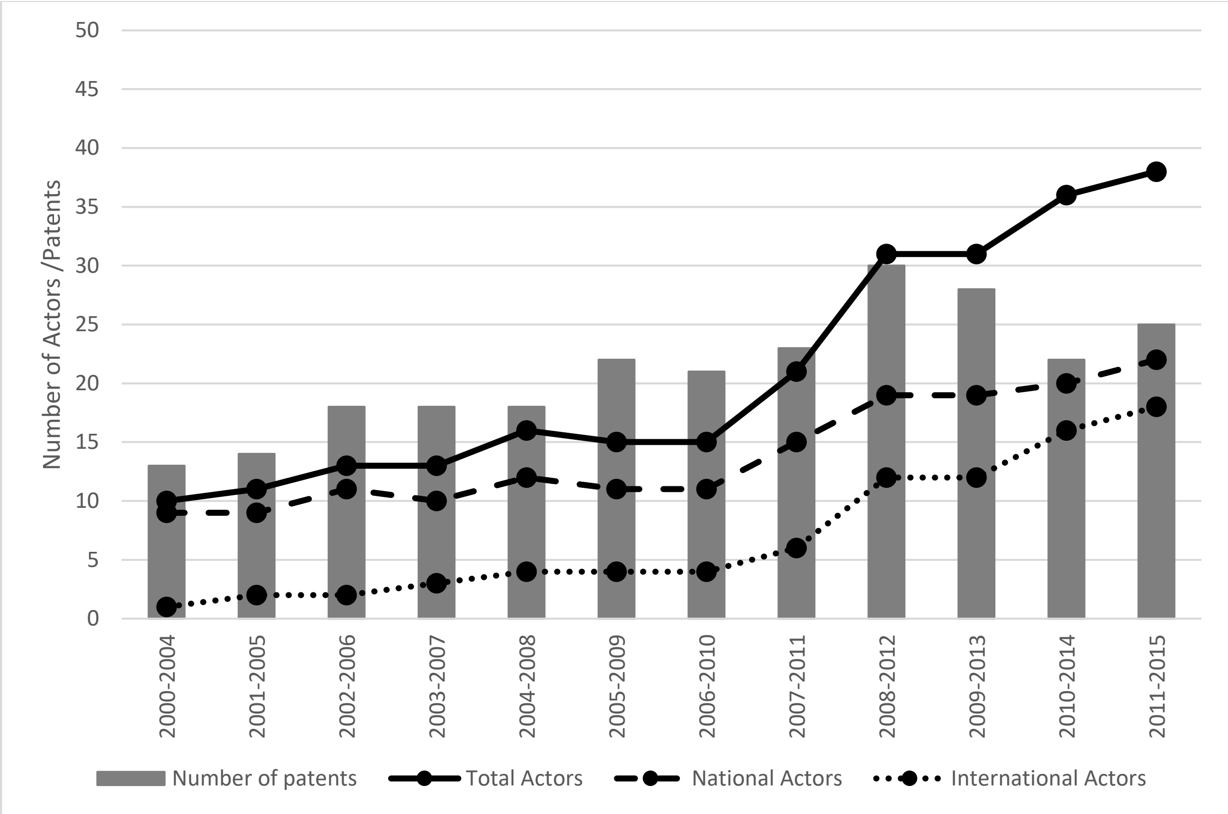


Figure 15: Number of patents and number of national and international actors affiliated with patent inventors

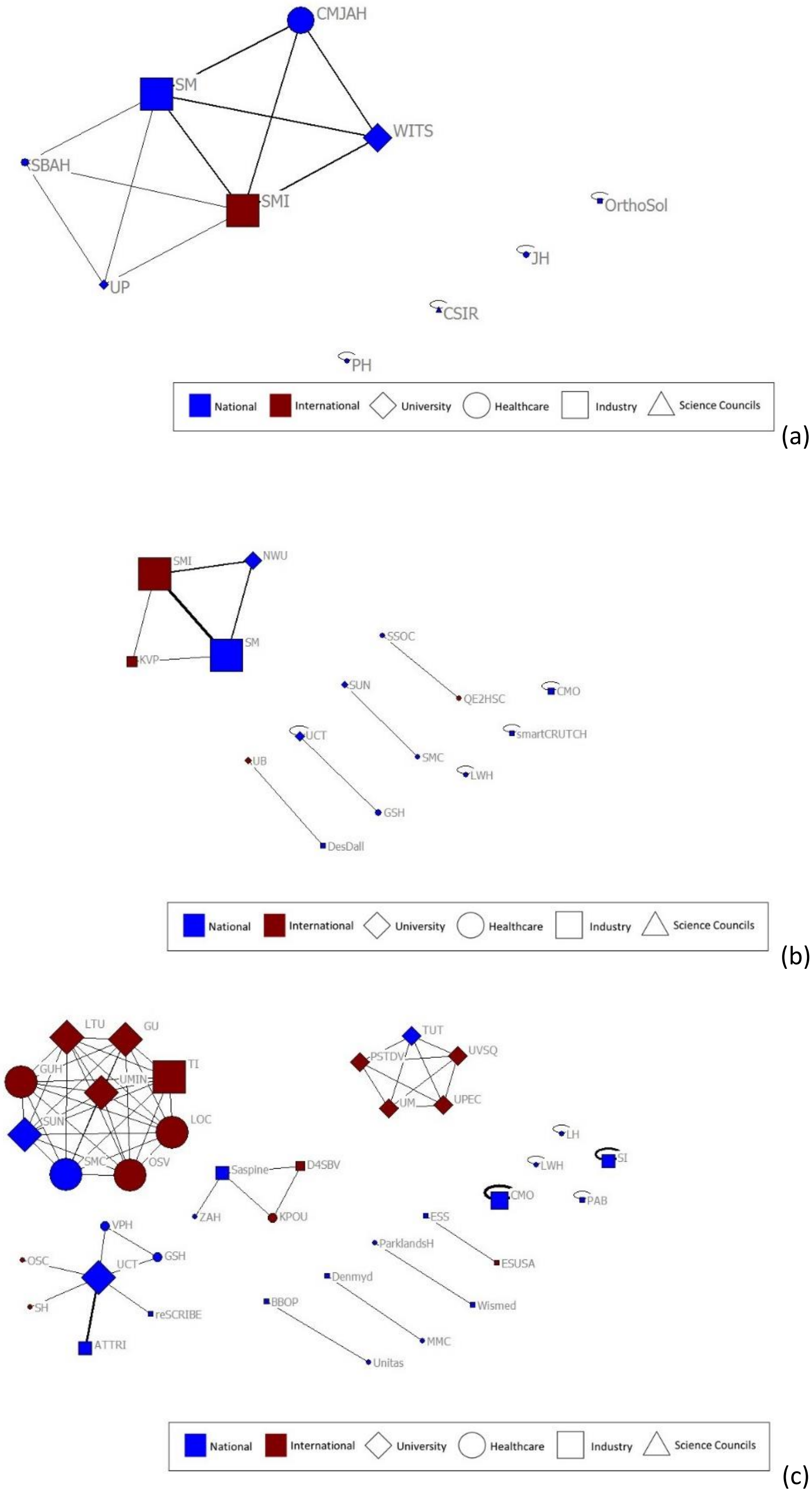


Figure 16: Orthopaedic device development actor-collaboration *network of South Africa based on patents for (a) 2000-2004, (b) 2005-2009 and (c) 2011-2015. Nodes are sized according to weighted degree centrality. Thickness of edges have been weighted to tie strength.*

In the 2000-2004 timeframe (Figure 16a), 13 patents were produced by inventors affiliated to ten organisations. In this timeframe, only one international organisation is present – Spinal Motion Inc. (SMI). SMI was, at the time of patent priority date, an American partner to domestic company Southern Medical (SM). The network component to which SMI and SM belong (i.e. the group of nodes of which SM and SMI and connected by edges), is largely involved in the development of spinal disc arthroplasty[3]. The other components in the first timeframe are all from patents arising from within the same organisation. In the 2005-2009 timeframe (Figure 16b), 22 patents were produced by inventors affiliated with 15 organisations. The SM/SMI component evolves – some previous actors have disappeared, and new actors appear. The patents of this component comprise inventions in spinal fusion devices and disc and lower-arm arthroplasty. The rest of the actor-collaboration network comprises either single-node or two-node groups, where the inventors were either from a single organisation, the inventors were from two different organisations, or the single inventor was affiliated with two organisations. An example is the UCT/GSH component, where the (single) inventor is affiliated to both the University of Cape Town (UCT) and one of its academic hospitals, Groote Schuur Hospital (GSH). The 2011-2015 timeframe (Figure 16c) comprises 25 patents from inventors affiliated with 38 organisations. The single-node CMO (Custom Med Orthopaedics) has repeat patents for orthopaedic instrumentation involving inventors only affiliated with its own organisation. Three components in this network have greater international presence – inventor(s) from Saspine are collaborating with inventors affiliated with international healthcare and international industry organisations; inventor(s) from Tshwane University of Technology (TUT) are collaborating with inventors affiliated with international universities; and inventors from Stellenbosch University (SUN) and Stellenbosch MediClinic (SMC) are collaborating with inventors affiliated with international university, healthcare and industry organisations. While UCT appears to have a central role in this network, it is largely in that position because of the multiple affiliations of its inventors.

Across all timeframes, there are inventors who chose to patent in isolation. Apart from the Council for Scientific and Industrial Research (CSIR), these inventors are largely from the national healthcare and national industry sectors. These isolated inventors from the national healthcare sector are almost exclusively affiliated with private healthcare facilities, including Netcare Jakaranda Hospital (JH), Life Wilgeleugen Hospital (LWH), Netcare Pinehaven Hospital (PH), Netcare Parklands Hospital (ParklandsH), Netcare Unitas Hospital (Unitas) and Zuid-Afrikaans Hospital (ZAH). The actor-collaboration network contains many actors who have patented only once. On the other end of the spectrum, there are a few actors who patented many inventions. SM/SMI contribute to 21(34%) of

[3]SM is a South African company and has SMI is its American partner. The SM/SMI partnership is occasionally due to one individual having both affiliations, but mostly, there are inventors from both companies.

the 62 patents; their parent company, Southern Implants (SI), contributes to a further three patents. CMO contributes to six patents. This is consistent with Balconi et al. (2004), who found that very few inventors produce a high number of patents, while most inventors produce just one.

Figure 17 presents the evolution of high degree centrality actors of the patent actor-collaboration network over the 12 timeframes. If an actor had the highest degree in any timeframe, its degree centrality over all 12 timeframes is reported. In some cases, pairs/groups of actors are presented because they are so closely related. This deviates from their presentation in the scientific publication actor-collaboration networks of Chapter 5. It is presented in this way because in some instances the nodes are solely due to the dual-affiliations of the inventors, as in the case of WITS/CMJAH and UP/SBAH, or in other cases, inventors have worked together on multiple patents and some have dual affiliations. This is the case for SM/SMI. SM/SMI are high degree actors for the first eight timeframes, with their degree centrality decreasing as time progresses. WITS/CMJAH and UP/SBAH are high degree actors in the first five timeframes. Their degree centrality values are identical and decreasing. These pairs are only present in the first five timeframes and result from university-affiliated clinicians who co-invent patents with the SM/SMI pair. Nine actors, UMIN, TI, SUN, SMC, OSV, LTU, LOC, GU and GUH, are high degree actors in the last four timeframes. They collaborate on a 2013 patent for a set of femoral implants for knee prosthesis. Their presence is due to the number of inventors listed on the patent, the biggest in the dataset.

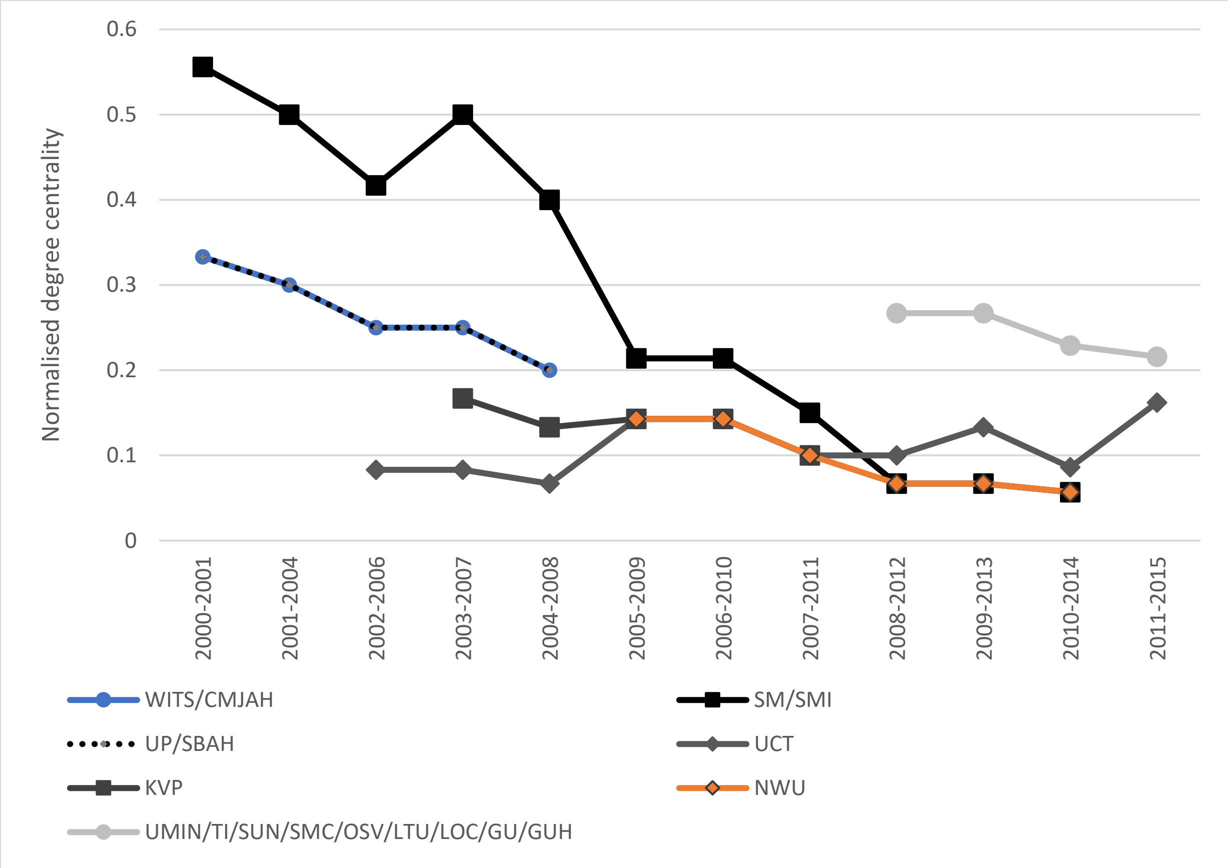


Figure 17: Actors having high degree centrality in the patent actor-collaboration networks

Figure 18 presents the evolution of actors having high betweenness centrality. In the entire period, only four actors have betweenness centrality. This includes the SM/SMI pair, UCT and Saspine. These actors have very limited potential to influence the flow of knowledge in the network; this influence is limited to the component in which they operate, as the networks remain fragmented across all timeframes.

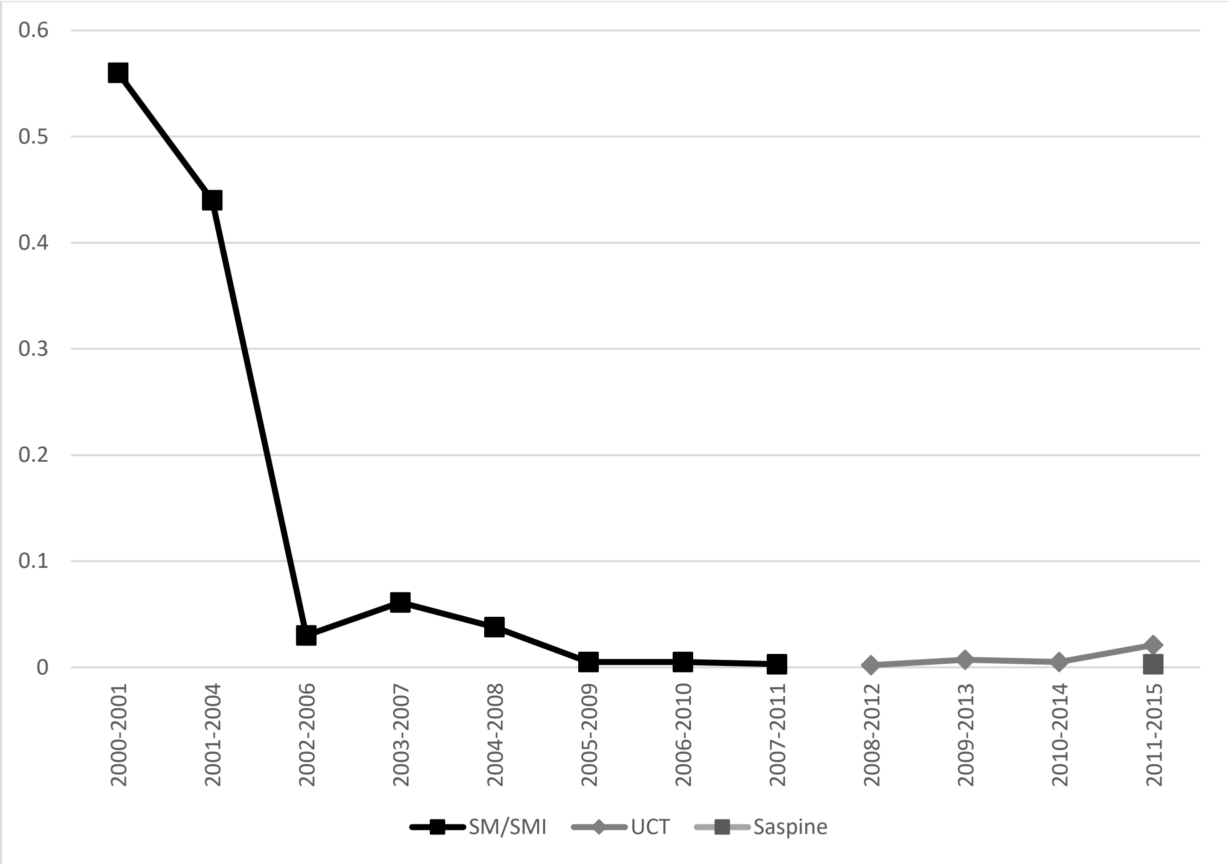


Figure 18: Normalised betweenness centrality for patent actor-collaboration networks

The nationalisation index of the patent actor-collaboration networks is presented in Figure 19. The nationalisation index is positive for the first five timeframes, but it is ever decreasing. As the network grows, the collaborations become more internationalised, with a negative index between the sixth (2005-2009) and the 11th (2010-2014) timeframes. Beyond the fifth timeframe, the index increases to zero, and then edges positively, suggesting that collaborations become nationalised again. However, the index is very close to zero beyond the seventh timeframe, suggesting that the collaborating actors do not show any preference between national and international collaborations.

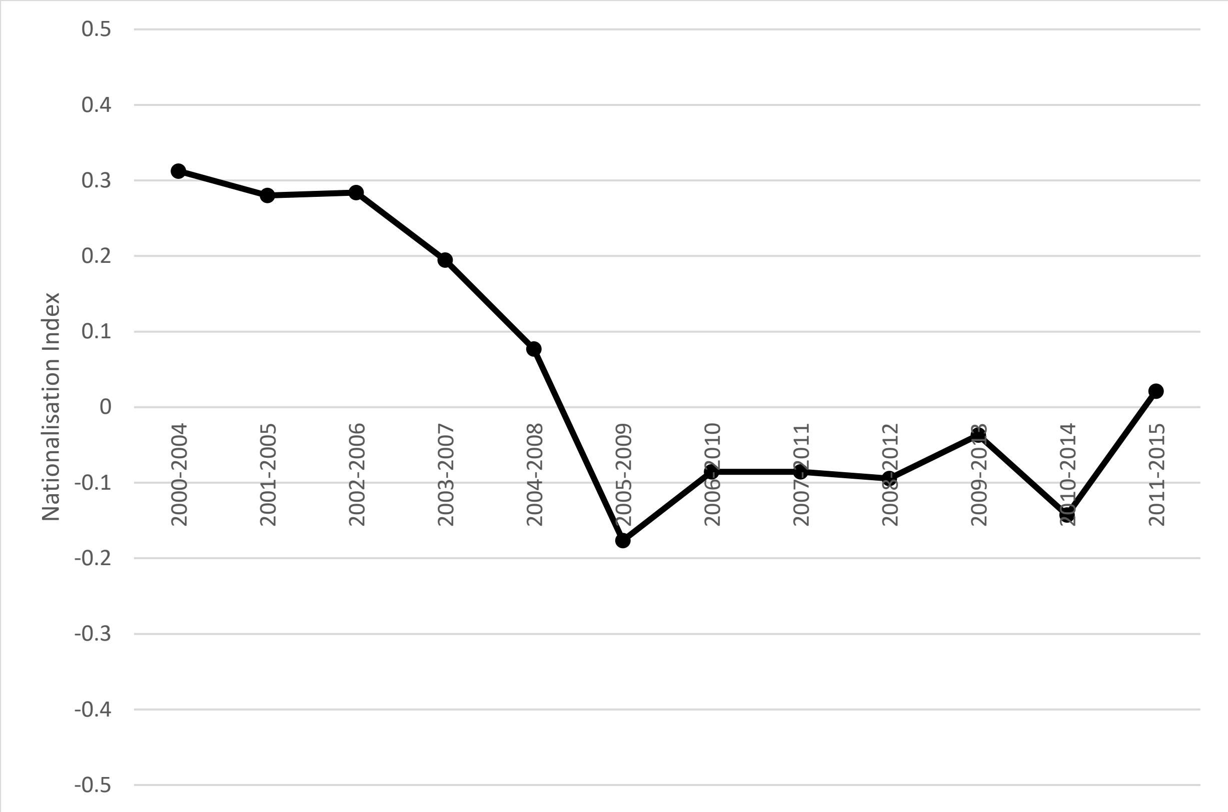


Figure 19: Nationalisation index of the patent actor-collaboration *networks across all 12 timeframes*

No 2-clan networks were drawn for the patent actor-collaboration networks as it was apparent from the actor-collaboration networks in Figure 16 that very few timeframes, or rather components within timeframes, would meet the requirements to be part of the 2-clan analysis.

The international actors of the patent actor-collaboration network are from nine different countries, including France (5 actors), the United States of America (4 actors), the United Kingdom (3 actors), Belgium (2 actors), Australia (2 actors), Canada (1 actor), Germany (1 actor), the Netherlands (1 actor), and India (1 actor). Canada is the only country appearing in the patent actor-collaboration network that did not appear in the scientific publication actor-collaboration network.

The sectorisation indices of the local healthcare, university and industry sectors, for the patent actor-collaboration networks across the 12 timeframes, are presented in Figure 20. A positive index indicates a sector's preference to participate in intra-sectoral collaborations, while a negative index indicates a tendency for involvement in inter-sectoral collaboration. In Figure 20, the sectorisation index is -1 across all timeframes expect for the last one.

Overall, collaborating actors from the national university and industry sectors are largely involved in inter-sectoral collaboration with other national organisations. Across all timeframes, the national university and industry actors do not participate in intra-sectoral collaboration with other national actors. This is also the case for the national healthcare sector, except in the very last timeframe, where there is a link between two national healthcare actors, GSH and VPH.

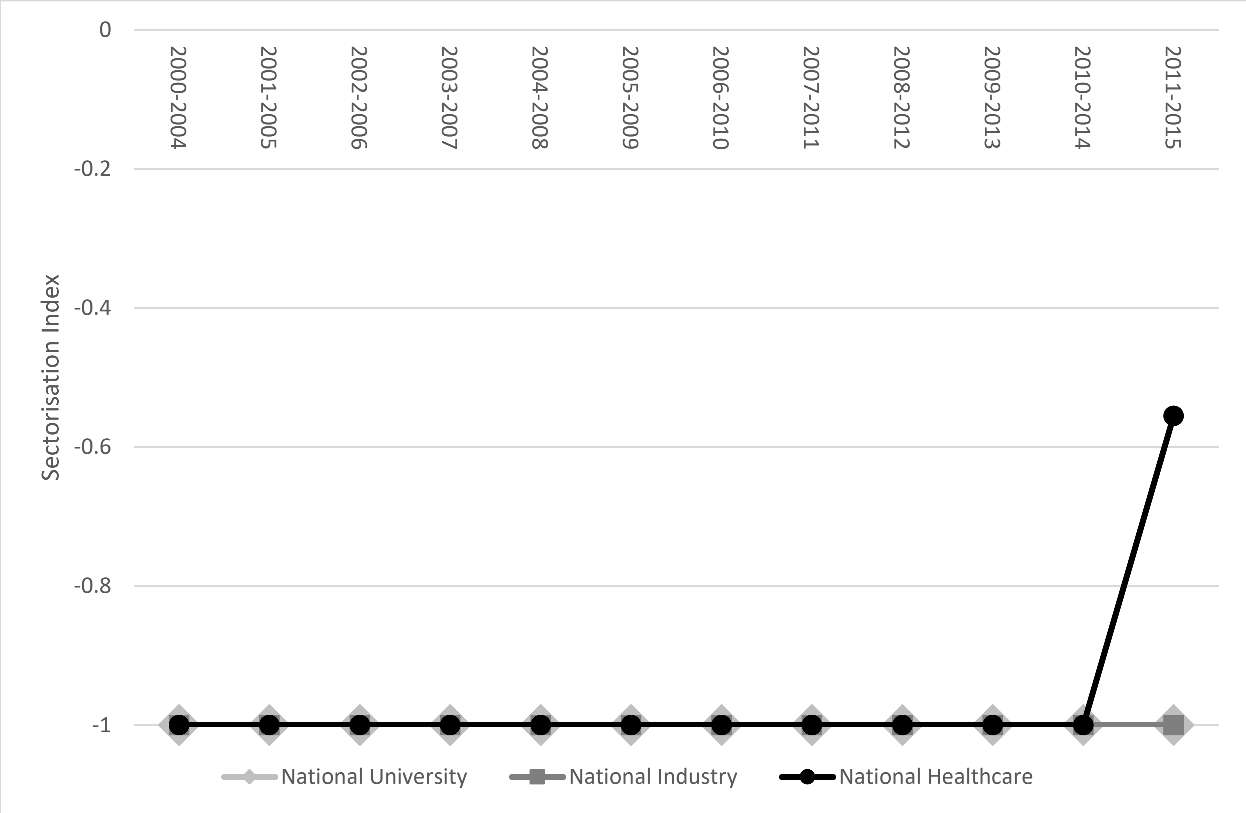


Figure 20: Sectorisation indices of the patent actor-collaboration *network across the 12 timeframes*

6.3 Discussion

The Intellectual Property Rights from Publicly Financed Research and Development Act, Act 51 of 2008, led to the establishment of the National Intellectual Property Management Office (NIPMO) and the Intellectual Property Fund in South Africa. The Act provides for more efficient utilisation of intellectual property resulting from publicly financed research and development, and for the establishment of technology transfer offices (TTOs) at publicly financed research organisations (e.g. universities and science councils). Public organisations like universities, academic hospitals and science councils are bound by the Act, while the Act does not apply to private sector actors from the healthcare and industry sectors.

Patenting activity from South African universities prior to the Act was low, with a total of only 24 patents emanating from South African universities in 2008 (Alessandrini, Klose, & Pepper, 2013); by 2015 South African universities accounted for 14% of the South African portfolio of patents (Patra &

Muchi, 2018). The effects of the Act appear to not (yet) have increased patenting in the orthopedic devices TIS. Seven national university actors appear in the patent actor-collaboration networks. However, the number of inventors affiliated with national universities in any given timeframe is very low, the highest number being four.

The Act may however have changed certain behaviours of actors in the TIS. The university-affiliated clinicians (from UP/SBAH and WITS/CMJAH) who collaborate in the SM/SMI components have their patents assigned to the SM/SMI conglomerate. In this way, university-affiliated clinicians may serve as consultants to industry and transfer their IP rights to the industry actor, on agreed-upon terms. These are earlier patents (between 2000 and 2008) and patenting activity may not yet have been affected by initiatives undertaken by universities to promote patenting. The inventors who have gone through national university channels to patent, i.e. where the university was the assignee on the patent, include inventors from SUN, VUT, TUT and UCT. All these patents have been filed since 2008.

Each of the national university actors has formalised structures for the protection of IP emanating from university research. In the UCT component, the UCT/GSH link is due to university-affiliated clinicians who have patented inventions in their own capacity[4], even though the clinician had been affiliated with both organisations. This appears to be a practice by clinicians, especially orthopaedic surgeons, who can be remunerated for consultation services and earn royalties on inventions (South African Orthopaedic Association, 2019). There does however exist opportunity for university TTOs to identify inventions by university employees, create an entrepreneurial culture among university-affiliated clinicians (and the university at large), and encourage employees to disclose inventions to the university and pursue university IP processes. Owen-Smith & Powell (2001) found that a crucial first step in the university environment is to convince academics to disclose their potentially valuable innovations to the TTOs. The perception of local patenting processes among academics and the meanings that academics attach to their IP colour their decisions to disclose these innovations (*ibid*). Owen-Smith & Powell suggest that creating an entrepreneurial culture among academics is a key step in successful technology transfer. In South African universities, successful technology transfer efforts lie in proactive engagement by the TTOs with inventors (Alessandrini, Klose, & Pepper, 2013) and effective and trustworthy relationships between TTO staff and inventors (Sibanda, 2009).

While national university actors produced many scientific publications related to orthoapedic device development, national university actors have been involved in relatively few patents. It could be that university faculty are not incentivized in the same way to patent as they are to produce scientific publications. Academics who patent are listed as inventors on university patents and can earn

[4] These clinicians were both the inventors and assignees listed on the patent.

royalties therefrom. Incentives available to produce scientific publications may bring more immediate gain, in the form of promotion and the subsidy from the Department of Education and Training's Research Outputs Policy. The Department of Higher Education and Training has changed the incentive structure, effective in the 2021-22 financial year, to give equal weighting to innovations such as patents and scientific publications under the recognised research outputs for which universities may earn subsidies (Department of Higher Education and Training, 2018).

The Act and its Regulations have been criticised for their approach to IP protection, which may present obstacles to scholarly publishing (Gray, 2009). Rapid publication of new research relating to potentially patentable inventions may be delayed to prevent compromising the novelty requirement for patentability; routine delays may affect scientific publication rates, making South African academics less competitive in open knowledge exchange (Ncube, Abrahams, & Akinsanmi, 2013).

The number of clinicians from the private healthcare sector in the orthopaedic devices TIS who patent in their own capacity is noteworthy. Of the 14 national healthcare actors present in the patent actor-collaboration network, ten are from the private healthcare sector. The actors from the private healthcare sector mainly operate on their own or with one other actor, contributing to the large number of separate components in the network (SMC is the exception). These private healthcare actors are largely from the three big private healthcare providers in South Africa, i.e. Netcare Group, Life Healthcare and Mediclinic. Medical practitioners, such as doctors and specialists, are not employed by the private healthcare groups in South Africa (Health Professions Council of South Africa, 2016b). A common business model employed in private hospitals has the medical practitioner working from, but not employed by, the hospitals; these hospital-based practitioners either deal only with inpatients admitted to the hospital, or have a dual business model where they treat private, ambulatory, in-care and hospital patients (Trade & Industrial Policy Strategies, 2018). Even though these doctors are not employed by the large private healthcare provider groups, there exists opportunity for private healthcare groups to facilitate and exploit innovations arising from clinicians affiliated with the private healthcare group.

There are a few ways in which the scientific publication actor-collaboration network (Chapter 5) and the patent actor-collaboration networks presented here differ. First, the scientific publication actor-collaboration network comprises actors largely from the university and healthcare sectors, with very few industry and science council sector actors present. In the patent actor-collaboration network, the inventors are affiliated with organisations from the university, healthcare and industry sectors in almost equal proportion, and the science council sector is mainly absent. Only one science council actor, the CSIR, appears early in the network, contributing to a single patent.

Second, the scientific publication actor-collaboration network had a large international presence, whereas the patent actor-collaboration network is made up mainly by inventors affiliated to South African organisations. Third, the key actors identified in the scientific publication actor-collaboration network were found to be national research-intensive universities and their associated academic hospitals. The key actors identified in the patent actor-collaboration network are a pair of industry actors who patent many innovations, and an inventor affiliated to a private healthcare facility, who has ties to university, healthcare and industry sector actors. In the scientific publication actor-collaboration network, only seven national industry actors and seven international industry actors were identified. In the patent actor-collaboration networks, 14 national industry actors (11 not previously identified in the scientific publication actor-collaboration network) and five international industry actors (four not previously identified in the scientific publication actor-collaboration network) were identified. These national industry actors are largely small, medium and micro enterprises; two of these are university spin-outs, both from UCT. Of the international industry actors, Tornier Inc. (TI), now merged with Wright Medical Group to form Wright Medical Group N.V. (Healio, 2014), is the only large corporation.

It is recognized that South African business makes a very small contribution to scientific knowledge output in South Africa (National Advisory Council on Innovation, 2014; National Advisory Council on Innovation, 2016). Industry actors who do patent may well be doing research that they prefer not to publish. As Breschi & Lissoni (2004) highlighted, patent inventorship only reveals a tiny subset of the activity towards development. Nonetheless, the patent actor-collaboration network analysis has identified actors, especially those in the industry sector, who were not identified in the scientific publication actor-collaboration network, including key contributors to the technological knowledge base, the SM/SMI pair.

The patent actor-collaboration networks are sparse, with many single-actor and double-actor components. In the case of single actor components, the benefits of inter-sectoral collaboration are absent in the development of devices. In the case of double-actor components, translational collaborations do not occur. The SM/SMI component is the main component participating in translational collaborations; however, its key role in the patent actor-collaboration network may be attributable to factors beyond its participation in such collaborations, which cannot be assessed through network analysis.

As seen in the sectorisation index, national intra-sectoral collaboration is absent. Intra-sectoral collaboration takes place between national and international actors in the patent actor-collaboration network; but within South Africa, South African universities are not patenting jointly, healthcare actors are not patenting jointly, and industry actors are not patenting jointly. The presence of intra-sectoral collaboration at an international scale, and not a national scale, suggests some benefit of international ties within the same sector offer over local ties. These could include access to foreign markets, access to different patient demographics, access to specialized infrastructure and resources, and access to patenting expertise.

Patra & Muchie (2018) found that approximately 20% of South African university patents were collaborative. Approximately 40% of these collaborative patents were with national science council actors, and approximately 17% were with international multinational companies. Joint patents with national industry actors were very low. Patenting between national universities and national industry actors is low in the orthopaedic devices TIS as well as more broadly in South Africa. In a study by Ncube (2013), one university warned that provisions in the Act would result in a loss of industry-contracted research due to requirements for permissions from NIPMO and the uncompetitive nature of the full-cost model, while another university considered the full-cost model a necessary approach to university-industry collaboration. According to the full-cost model, if a private entity or organisation covers the full cost (both direct and indirect) of research and development in collaboration with a public research organisation, the project is not considered to be publicly financed, and the provisions of the Act no longer apply (NIPMO, 2019). Knowledge is a localised phenomenon and knowledge exchange among the same set of co-located actors lose value over time; as the value of knowledge and the recombination thereof fades (Boschman & Frenken, 2010), collaboration with outside partners becomes important to prevent over-embeddedness (Breschi & Lenzi, 2015). Patenting only captures a small proportion of links relevant to knowledge exchange, although the network of collaborators is the most immediate and influential environment from which inventors draw ideas and information (Breschi & Lenzi, 2015).

Twenty-three organisations appear in both the scientific publication and the patent actor-collaboration networks – 11 from the university sector, eight from the healthcare sector, three from the industry sector and one from the science council sector. Many, but not all, organisations that appear in both networks, have the author and inventor as the same person. This suggests that there is some translation of scientific knowledge to commercial applications. Some patent-paper pairs are present in the actor-collaboration networks, i.e. the same idea described in different ways, resulting in a patent and journal paper (Murray, 2002). The paper would usually describe experimental results, whereas the patent would define utility and claims of inventiveness. Examples of such pairs from the university sector include paper and patent of the TUT-component on a mechatronic system for assisting an individual attaining a standing position. In the scientific publication actor-collaboration network, some of these TUT component inventors co-author a series of papers on the biomechanics of knee and ankle trajectories. The inventors of a patent by the SUN/SMC pair on the method for designing a knee prosthesis in the patent actor-collaboration network, are co-authors of several papers on the development and testing of patient-specific knee implants. There are several such examples, and it is evident that the orthopaedic device development network arises from the interaction between science and technology spheres.

6.3.1 Limitations of the study

Eleven of the 73 patents had incomplete inventor affiliation data and were subsequently omitted from further analysis in this research project. This means that many organisational actors may not have been identified. The second limitation is that the organisational affiliations associated with each inventor relied on the methodology described in Chapter 4. The inventors themselves did not provide their affiliations, and some affiliations may have errors. The multiple affiliations of the inventor captured at the priority date may not have been associated with work carried out at all of those organisations; this may result in the network presenting collaborative ties where there were none, or not formally. Multiple affiliations due to the joint assignation of university and hospital by clinical academic contributed toward the strong ties between the university and healthcare sectors in the scientific publication actor-collaboration networks.

Both the scientific publication and patent actor-collaboration networks were small, developed from 63 and 62 publications respectively, presenting networks of 99 and 57 organisations respectively. These networks, though small, are similar in size to those presented by Chimhundu et al. (2015) and de Jager et al. (2017).

6.4 Conclusion

The goal of any innovation system is to develop, apply and diffuse new technological knowledge (Hekkert, Suurs, Negro, Kuhlmann, & Smits, 2007). The organisations contributing to the technological knowledge base for orthopaedic device development in South Africa and the sectors to which they belong have been identified and the nature of the relations among them have been characterised. While technological knowledge is being created at an increasing rate over time, knowledge diffusion among actors is in the network is limited.

The patent network complements the scientific publication network presented in Chapter 5. The combined analysis presents an overview of knowledge generating capabilities and activities of the actors contributing to the orthopaedic devices TIS. Overlap between the two domains has been highlighted. Notable differences between the two networks is the small patenting contribution of national university actors, who were the main contributors of scientific knowledge production, as well as the significant contribution made by private healthcare actors patenting in isolation. The results of the chapter would be enhanced by further exploration of translation between science and technology in the orthopaedics devices TIS.

7. Keyword networks

In this chapter, keyword networks are used to identify the orthopaedic devices being developed, the areas of innovation, and the underlying cause, disease or anatomy addressed by the devices. The objectives of the chapter are to:

1. Identify the areas of interest in orthopaedic device development in South Africa and the links between these areas of interest.
2. Highlight the collaboration potential that exists for actors of the orthopaedic devices TIS based on common areas of interest.

The chapter begins with a literature overview of keyword networks and their applications, which extends to capturing the relationships between social and cognitive interaction in different types of scholarly networks. The conceptual framework and methodology as it has been developed for this chapter is then presented. This chapter makes unique methodological contributions in the development of tools to relate actors in a network based on their intellectual similarity in a particular context.

7.1 Background literature

Keyword networks (also referred to as co-word networks[5]) are approaches to reveal inter-related areas of knowledge. Keywords listed on scientific publications have been used as a data source in network analysis; by applying traditional network metric analysis, such studies have achieved several different aims. Choi et al. (2011) investigated the organisation and evolution of knowledge and research themes in five major journals. Important keywords were identified by their frequency of appearance on publications and their centrality in the network. They found that, in their context, the more popular a keyword became, the more frequently it was used by researchers in future publications, and the more often it was associated with other keywords. They inferred that keywords having a central position in the network usually become connected to many neighbouring keywords based on a process of preferential attachment. The latter occurs when new nodes attach preferentially to existing nodes in the network that are already well-connected (Barabasi & Albert, 1999). In the Choi et al. study, central keywords played a role in integrating distinct clusters of highly connected keywords into a unified network. Yi & Choi (2012) investigated the organisation and evolution of scientific knowledge by exploring the mechanisms underlying observed patterns of keyword networks. The study compared keyword networks to citation networks and showed that keyword network

[5] Co-word networks may have their data from several sources, including keywords, journal titles and journal abstracts.

analysis could be used as an alternative to citation network analysis. Citation networks were typically small-world networks (i.e. they had high clustering coefficients with short path lengths), had power-law degree distribution, and had hierarchical structure. The structure of keyword networks differed from that of citation networks as keyword networks were not small-world networks (i.e. they had high clustering coefficients without short path lengths), they were scale-free (power-law degree distribution with a scaling factor between 2 and 3) and had a hierarchical structure (due to scale-free topology and high clustering co-efficient).

By investigating the number of connections of keywords to others, Yi & Choi established a power-law between the nodal degree and its cumulative distribution. This power-law distribution takes the form of $x^{-\gamma}$; the probability of a keyword having x connections is proportional to $x^{-\gamma}$, where γ is a scaling factor. Most keywords would have a small number of connections, and certain keywords would have many connections. Yi & Choi showed that γ had a value between 2 and 3 in all their application areas. The implication of this range is that the keyword network optimises the association of keywords at low cost in terms of the number of links due to the role of hub keywords (Sole, Corominas-Murtra, Valverde, & Steels, 2010). The definition of a scale-free network is that γ has a value between 2 and 3. Outside of this range, the network may become too disconnected ($\gamma > 3$) or too dense ($\gamma < 2$).

Using keywords listed on conference proceedings, Santonen & Conn (2016) used keyword networks to investigate how different keywords were interlinked with each other to illustrate the interrelationship between research fields. Khan & Wood (2015) used keyword networks to uncover emerging themes in the information technology management domain.

Keyword networks potentially lie in the same domain as co-citation networks. Co-citation is considered to be a proxy for intellectual similarity (Small, 1973). Co-citation networks are based on the number of times two publications are cited together in other publications; co-citation networks indicate clusters of related scientific work (van Raan, 2004). They differ from keyword networks in that they may relay cognitive and social network relations, whereas keyword network analysis may only reveal the cognitive relations.

Yan & Ding (2012) explored the similarity between six different types of scholar networks and investigated the use of hybrid network approaches to identify research areas. The six networks included: bibliographic coupling, citation, co-citation, topical, co-authorship and co-word. Co-citation, bibliographic coupling and co-word networks were referred to as similarity-based networks and focussed on identifying research topics. Factors that contributed to the similarities among networks included edge types (real vs. artificial) and network types (social networks vs. information networks). Co-authorship networks were found to have the lowest density and number of links among all the networks, which suggested that real social connections were harder to establish than similarity approximations. Co-word networks were found to be most similar to bibliographic coupling networks. Yan & Ding also identified two types of similarity dimensions among the six networks: “citation-based vs. non-citation based” and “social vs. cognitive”. One of the recommendations of their study was to use hybrid networks to comprehensively capture complex research communication and interaction. A proposed hybrid model, which explored the second similarity dimension “social vs. cognitive”, combined co-authorship and co-word networks.

Khan & Wood (2016) explored the use of social network analysis in the information technology domain at the individual, organisational, country, source (i.e. journal) and keyword level in an attempt to answer the question “What is the network structure of information technology management knowledge infrastructure?” For the period 1995-2014, they found this domain to be highly fragmented, with new nodes (individuals and organisations) entering the network preferentially attaching themselves to established nodes in the network. They were able to establish unique characteristics of the information technology management community, showing that the community comprised several distinct schools of thought in which different hypotheses were pursued by individuals in the same organisation, who did not collaborate.

Vida (2018) investigated the effect of distance on co-authorship of scientific publications and its impact on the formation and intensity of relationships. Three different types of distances influencing the formation of scientific collaborations were identified: geographic, social and cognitive. Vida measured geographic distance by the physical distance between co-authors, social distance through co-authorship, and cognitive distance through author bibliographic coupling based on common references (co-citation) between pairs of scientific publications. Vida used the common journal article to inform the co-citation network. Khan & Wood (2016) used source co-citation, where the source was the journal in which the article was published, and constructed a source bibliographic coupling network. Vida (2018) proposed a way to measure pure cognitive distance (illustrated in Equation 11) of an author. The cognitive distance is a measure of the similarity of the knowledge base of researchers (Yan & Ding, 2012), as assessed by relations such as co-citation, bibliographic coupling, co-word occurrences and common topics (Vida, 2018).

$$Pure\ cognitive\ distance = Full\ cognitive\ distance - Social\ distance \ldots \text{ Equation 11}$$

In Equation 11, the full cognitive distance is established from a similarity matrix derived from the number of shared references between author pairs[6]. The social distance is established from a similarity matrix containing the number of co-authored publications for each pair of authors. Pure cognitive distance identifies potential future collaborations, since those authors who are close to each other in the cognitive dimension, work in the same research domain but are not (yet) connected by co-authorship (Vida, 2018).

The establishment of pure cognitive distance in Vida's approach is comprehensive, yet cumbersome; all author pairs for the given dataset would need to be established based on common citations, as well as co-authorship relations of authors. It is proposed here that the keywords listed on scientific publications be used as an indicator of cognitive distance and that keyword networks could similarly be used to highlight collaboration potential within co-authorship networks.

7.2 Conceptual framework

This conceptual framework is based on the literature described above. The keywork network is used to relate keywords listed on scientific publications using network theory. Network theory is rooted in graph theory and involves the mapping and visualizing of different relationships (e.g. co-authorship or co-words) among "nodes" of the graph (Wasserman & Faust, 1994). While network theory has been used extensively to characterise relationships among actors in a network, this study uses network theory to uncover relationships between keywords (or areas of innovation), similarly to the approaches presented in Choi et al. (2011) and Santonen & Conn (2016). The keyword network is used to establish key research areas in the publication set, links between different keywords, and relationships described in previous literature, such as preferential attachment and the formation of research domain hubs.

Based on the approach of Vida (2018), the cognitive distance between authors of scientific publications is established. In the approach presented in this thesis, the keyword an author lists on a scientific publication is an indicator of their research focus area. By relating keywords that appear on a scientific publication, a network of research focus areas can be formed. By linking authors to keywords listed on the same scientific publication within a network, an analogue to Vida's full cognitive distance is established. The difference here is that keywords, rather than co-citation, are used as the relationship linking authors. Collaboration potential in the network can then be calculated by subtracting the social component, which has already been established in the co-authorship

[6] The author pairs were derived from a set of scientific publications which meet the inclusion criteria; the set of scientific publications was in Economics and Physical Geography with at least one author affiliated to a Hungarian organisation (Vida, 2018).

networks, from the full cognitive component, namely the author-keyword network. To the author's knowledge, no previous keyword network study has attempted to connect author affiliations to the keywords listed on the same publication for this purpose. This thesis therefore adds a new approach to the set of tools available for analysing relationships in keyword network analysis.

7.3 Methodology

Using the dataset of scientific publications used to inform the scientific publication networks of Chapter 5, keyword networks were generated from keywords listed on the publications. Three types of keyword networks, namely a keyword-only network, a two-mode keyword-actor network, and a collaboration-potential network, were drawn and analysed; these are described below. These networks depict cognitive links between actors and are useful in illustrating the collaboration-potential which exists for actors in the scientific publication actor-collaboration network, based on common research interests.

7.3.1 Keyword-only network

Each keyword is represented as a node in the network, and an edge between two nodes indicates that those nodes appear on the same scientific publication. Metrics of interest were degree centrality and betweenness centrality, which have been described in Chapter 4. The popularity of a keyword, as described in Choi et al (2011), was investigated. Popularity is based on frequency of use of keywords, i.e. how often they appear in publications.

To determine if the keyword-only network displayed small world properties, the clustering co-efficient and the average path length were calculated, and a hierarchical dendrogram drawn. In a small world network, the clustering co-efficient is high and the average path length is low. The clustering co-efficient[7] is a measure of the degree to which nodes in the network cluster together and is calculated by Equation 12 (Wasserman & Faust, 1994). The clustering co-efficient is calculated by the number of closed triplets in a network divided by all the triplets (which may be open or closed) in the network. The term "triplet" here refers to three nodes in the network that are connected by either two edges (open) or three edges (closed).

$$C = \frac{number\ of\ closed\ triplets}{number\ of\ all\ triplets} \ldots \text{ Equation 12}$$

[7] In this project the clustering co-efficient refers to the global clustering co-efficient of the network. This is not to be confused with local clustering co-efficient of the node, which is not used.

The average path length[8] is calculated using Equation 13 (Nykamp, n.d.) and measures the average number of edges on the shortest path between pairs of nodes in the network.

$$l_N = \frac{1}{n.(n-1)} \sum_{i \neq j} d(v_i, v_j) \text{ … Equation 13}$$

In Equation 13, l_N is the average path length in the network, N, which is of size n, and d is the shortest path between the nodes (or vertices), v.

A measure to determine whether or not the network is indeed small-world is to validate the average path length against the criteria of Equation 14 (Yi & Choi, 2012):

$$l_n < 1 + log_{100}n \text{ … Equation 14}$$

7.3.2 Two-mode keyword-actor networks

The keyword-actor networks were drawn using a two-mode network. Two-mode networks are also referred to as affiliation or bipartite networks (Borgatti & Everett, 1997) and involve two sets of nodes, with the ties between the nodes belonging to different sets. A common distinction made between the two sets of nodes is that one set of nodes is more responsible for creating the tie (primary nodes) than the other (secondary nodes) (Opsahl, 2013). In the keyword networks of this thesis, the primary nodes are the actors, and the secondary nodes are the keywords. Using a two-mode network in UCINet, actors were related to keywords if the actors and keywords appeared on the same publication. The resulting node matrix relating actors and keywords is not symmetric; both the actor-collaboration network of Chapter 5 and the keyword-only network (above) are built with a symmetric node matrix. In the keyword-actor network, the node matrix is of size $n \times m$, where n is the number of actors and m is the number of keywords. In the actor-collaboration networks of Chapter 5 and the keyword networks described above, the node matrix of size $m \times m$, where m was the actors and the keywords, respectively. The keyword-actor network illustrates the areas of orthopaedic device innovation in which actors are working, based on their publications.

Popular keywords were used to draw two-mode actor networks, linking the actor to the area of interest. Popular keywords were those appearing with highest frequency in the data set. The two-mode keyword-actor network is useful in determining the capacity of actors to contribute to the innovation domains of, and their relation to popular areas of interest in, the orthopaedic devices TIS.

7.3.3 Collaboration-potential network

The actor-collaboration networks (based on co-authorship as shown in Chapter 5) were redrawn to show edges between nodes as keywords, to illustrate the relationship between actors based on

[8] The average path length is also called the geodesic distance. The geodesic distance calculator in UCINet was used to calculate average path length.

common research areas. To draw the network, UCINet requires an input relationship matrix. The two-mode keyword-actor matrix was converted to a one-mode matrix – $[N]_{keywords}$ – in which actors were related by keywords. This is different from the conventional actor-collaboration network node matrix – $[N]_{co-authorship}$ – in which actors were related by co-authorship. The collaboration-potential matrix was calculated by Equation 15:

$$[N]_{Collaboration-potential} = [N]_{keywords} - [N]_{co-authorship} \text{ … Equation 15}$$

The collaboration-potential network highlights presently unutilised opportunities for collaboration in orthopaedic device development in South Africa, based on common areas of interest.

7.4 Results

Fourty of the 63 scientific publications, which had formed part of the scientific publication dataset of Chapter 5, had author-assigned keywords. Twenty-two of the publications did not have author-assigned keywords, and keywords were assigned independently by the author and another researcher who had read the title and abstract of the publications. These assigned keywords were compared and reconciled by the author to determine a set of keywords for this set of publications. One publication did not have an abstract. The author read this publication and assigned keywords to it. As authors of the scientific publications would define a similar concept differently, keywords were standardised. For example, the term “prostheses and implants” encompass keywords described by authors as “biomechanical implants”, “cervical implant”, “implants”, “prostheses and implants” and “prosthesis”. A full list of the standardised keywords can be found in Appendix J.

In total, 271 unique keywords were identified. After standardising, 205 keywords were retained for further analysis. From the standardised list, the popularity of a given keyword was determined based on its frequency of appearance on publications. Most keywords only appeared on one publication; of the 205 keywords, 42 appeared on two or more publications, and 18 appeared on three or more publications. These 18 keywords are referred to here as popular keywords.

7.4.1 Keyword-only network

The keyword-only network is presented in Figure 21. The network comprises 8 components; 167 keywords, including all 18 popular keywords, appear in the main component. The clustering co-efficient of the keyword network is 1.004, and the average path length (among reachable pairs) is 3.804. The keyword network is of size 205 nodes, and the average path length is considered long in this network. To meet small-world length criteria, the average path length should have been smaller than 2.156 steps. The keywork network is therefore not a small-world network. It also has hierarchic structure, and its dendrogram is presented in Appendix K. The keyword network therefore has the structural elements as described in Yan & Ding (2012).

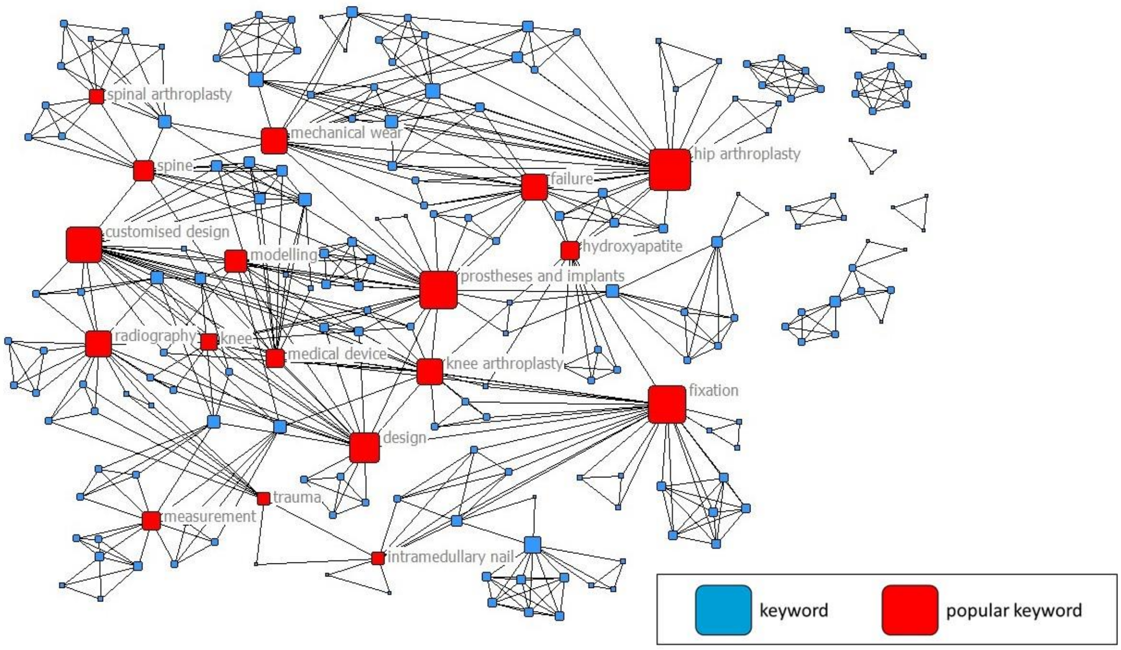


Figure 21:Keyword network drawn from keywords appearing in scientific publications on orthopaedic device development in South Africa. The nodes have been scaled to the degree centrality metric; edge thickness is unweighted. Only the labels of popular keywords have been included for legibility.

The top five keywords by popularity, degree centrality and betweenness centrality are presented in Table 6. The high-ranking keywords are research areas typically associated with orthopaedic devices, including the arthroplasty of major joints (hips and knees), and “fixation” which has the highest betweenness centrality and is a cross-cutting research focus in orthopaedics. More recently, developments by some South African actors have been focussed on “customised design” of devices. In Table 6, “hydroxyapatite” had the third highest betweenness centrality but does not appear as a high-ranking popular keyword or high-ranking degree centrality keyword. Hydroxyapatite is used as a coating on hip and knee implants, as well as in bone grafting, as it encourages bone growth after surgery. Like “fixation”, it cuts across different orthopaedic applications.

The agreement between degree and betweenness centrality is consistent with Choi et al. (Analysis of keyword networks in MIS research and implications for predicting knowledge evolution, 2011) who showed a strong correlation between these two metrics, but noted that the correlation is not typical of natural and artificial networks. In addition to highlighting the popular areas of interest of orthopaedic device development in South Africa, the connections between keywords can also be highlighted. In the keyword network, the strongest ties were between “knee arthroplasty” and “customised design”, the result of co-occurrence on four publications.

Table 6: Highest-ranked keywords by popularity, degree centrality and betweenness centrality

Popularity		***Degree Centrality***		***Betweenness Centrality***	
Keyword	**Value**	**Keyword**	**Value**	**Keyword**	**Value**
hip arthroplasty	8	hip arthroplasty	28	fixation	9180
prostheses and implants	8	prostheses and implants	26	prostheses and implants	8868
fixation	7	fixation	26	hydroxyapatite	5045
customised design	7	customised design	26	hip arthroplasty	4492
knee arthroplasty	7	design	20	mechanical wear	4480

7.4.2 Two-mode keyword-actor network

A two-mode keyword-actor network based on the 18 popular keywords was drawn and is presented in Figure 22. The network is a single component network comprising 77 of the 99 actors. Stellenbosch University (SUN) and Stellenbosch MediClinic (SMC) have strong ties to "knee arthroplasty" and "customised design". The University of Cape Town (UCT) has strong ties to "radiography" and "design"'. Even though "hip arthroplasty" and "prostheses and implants" are the most popular keywords, the biggest nodes in this network are "fixation" and "intramedullary nail", indicating that more actors are involved in these areas. The two-mode keyword-actor network is useful in highlighting the areas of orthopaedic device development in which actors are publishing. Figure 22 is limited to actors involved in research areas described by popular keywords, for legibility of the network.

Of the 22 actors absent from this network (shown on the left-hand side of Figure 22), only two are national actors. The other 20 are international actors, 12 of which are international universities. There was a total of 63 international actors in the scientific publication actor-collaboration network. This finding suggests that international actors bring new areas of interest into the orthopaedic device innovation network as well as contributing to the established research areas.

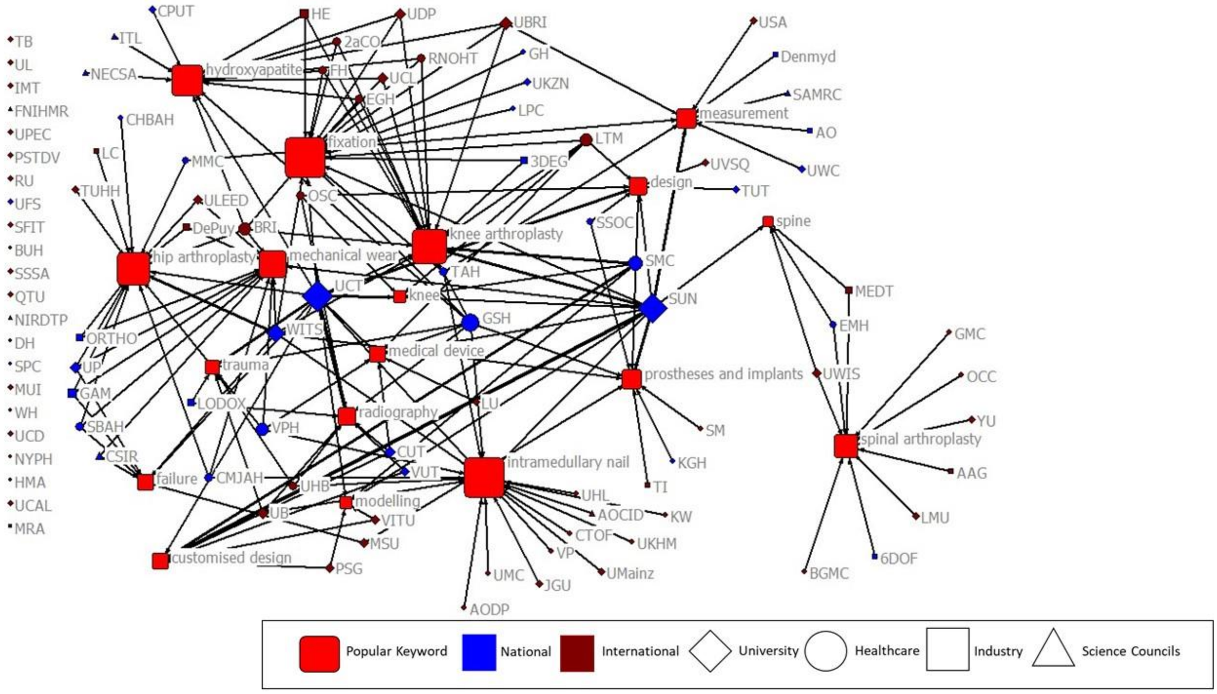


Figure 22: Two-mode actor-keyword network based on popular keywords of scientific publications of orthopaedic device development in South Africa. The actors appearing on the left-hand side do not work in the areas described by the popular keywords. The nodes have been scaled to the degree centrality metric, and edge thickness has been scaled to tie strength.

National actors appear to be involved in specific niche areas of orthopaedic device development and the fragmentation displayed in the actor-collaboration networks of Chapter 5 could be a result of these niche areas. This can be illustrated by considering the example of national university actors. SUN, for example, had focussed on the customised design of implants for knee and spine applications and a posture analysis tool. Tshwane University of Technology (TUT) had focussed on rehabilitative orthoses. The University of the Witwatersrand (WITS) and UCT were involved in many different developments, each collaborating with several actors in the network. WITS had focussed on hip implants, materials for hip implants and instrumentation for fatigue monitoring of biomechanical implants. UCT had focussed on surgical instrumentation, radiography for orthopaedic applications and software development with orthopaedic applications.

7.4.3 Collaboration-potential network

In Chapter 5, the actor-collaboration networks (Figure 9) had been presented in five-year moving-window timeframes. In Figure 23, the actor network is drawn for the period 2000 to 2015. Network metrics of degree centrality are reported in Section 5.4.

The scientific publication actor-collaboration network is sparse, with a density of 0.064, indicating that only 6.4% of all possible connections in the network have been made. The actor-collaboration network comprises nine components, with 74 actors present in the largest component. The most prominent nodes (by degree centrality) are national research-intensive universities – UCT, WITS and SUN – and national healthcare actors – Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), Groote Schuur Hospital (GSH) and Vincent Palotti Hospital (VPH). The strongest ties, i.e. the thickest edges in the network due to repeat collaborations between actors, was between the national universities and national healthcare facilities; examples include UCT and GSH (5 instances), UCT and VPH (3 instances), and WITS and CMJAH (3 instances). The other eight components in the network form isolated pockets of activity – five of these components have a national university actor present. Even within these isolated components, repeat collaborations occurred. The Six Degrees of Freedom (6DOF) component is due to two publications, largely from the same group of authors and the TUT component is due to three publications, with common authors across the three publications.

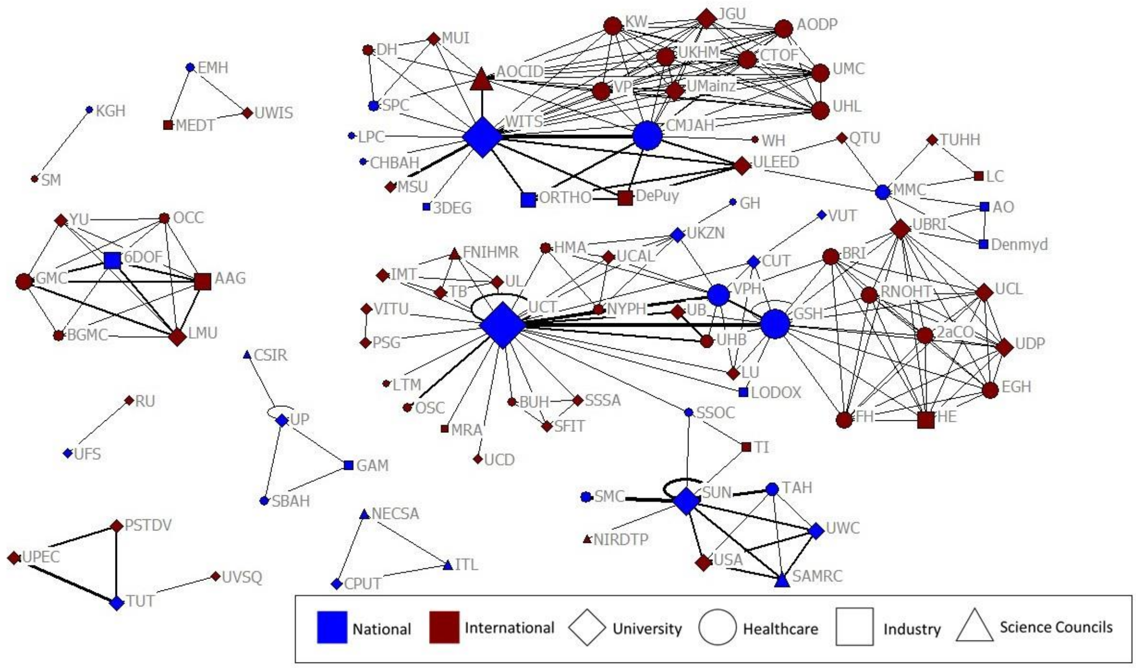


Figure 23: Scientific publication actor-collaboration *network for the period 2000 to 2015, where the links between nodes are indicative of a co-authorship event. Nodes are sized according to degree centrality. Thickness of edges have been weighted to tie strength.*

The nodes having the highest degree centrality are presented in Table 7. The three highest ranked nodes are national universities UCT, WITS and SUN, each of which are located at the centre of hubs within the main component. Each of these universities co-author publications with several other organisations in the actor-collaboration network, but not with each other. UCT, WITS and SUN are linked to each other through the activity of their collaborators.

Table 7: Actors having high degree centrality in the scientific publication actor-collaboration *network for the period 2000 to 2015*

Degree Centrality					
Rank	**Node**	**Actor**	**Sector**	**Location**	**Value***
1.	UCT	University of Cape Town	University	Local	33
2.	WITS	University of Witwatersrand	University	Local	30
3.	CMJAH	Charlotte Maxeke Johannesburg Academic Hospital	Healthcare	Local	21
4.	GSH	Groote Schuur Hospital	Healthcare	Local	20
5.	SUN	University of Stellenbosch	University	Local	16

*The degree centrality value is the weighted degree centrality, excluding self-reflecting ties.

In Figure 24, the actor network for the period 2000 – 2015 is redrawn with the edges between nodes as keywords. The result is a highly connected network, with 97 of the 99 actors connected in the main component. The actors University of the Free State (UFS) and Roehampton University (RU) appear in the scientific publication actor-collaboration network for the development of materials for use in orthotics.; no other actors in the scientific publication actor-collaboration network had published in this research area. This network illustrates common areas of interest among actors, and shows that actors may in fact be more closely related to each other in terms of research interest than suggested in the actor-collaboration network based on co-authorship in Figure 23.

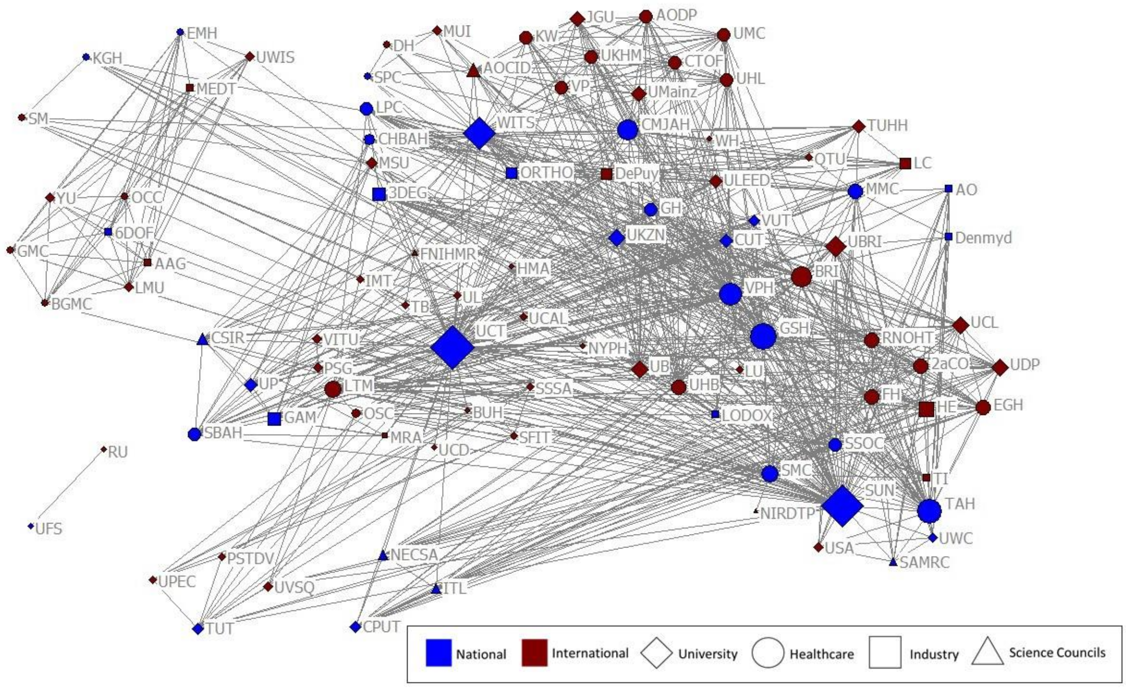


Figure 24: Redrawn actor network for the period 2000-2015 where the edges between actors are keyword links. The nodes have been scaled to the degree centrality metric, and the edges are unweighted.

The collaboration-potential network, presented in Figure 25, has been derived by subtracting the scientific publication actor-collaboration network from the keyword actor network. The nodes have been scaled to the degree centrality metric. This network illustrates the potential that exists for collaboration based on common areas of interest. Figure 24 illustrates how closely actors are related in the cognitive dimension; Figure 25 highlights the connections that could be made should actors exploit their relationships in the cognitive dimension to establish relationships in the social dimension through collaboration.

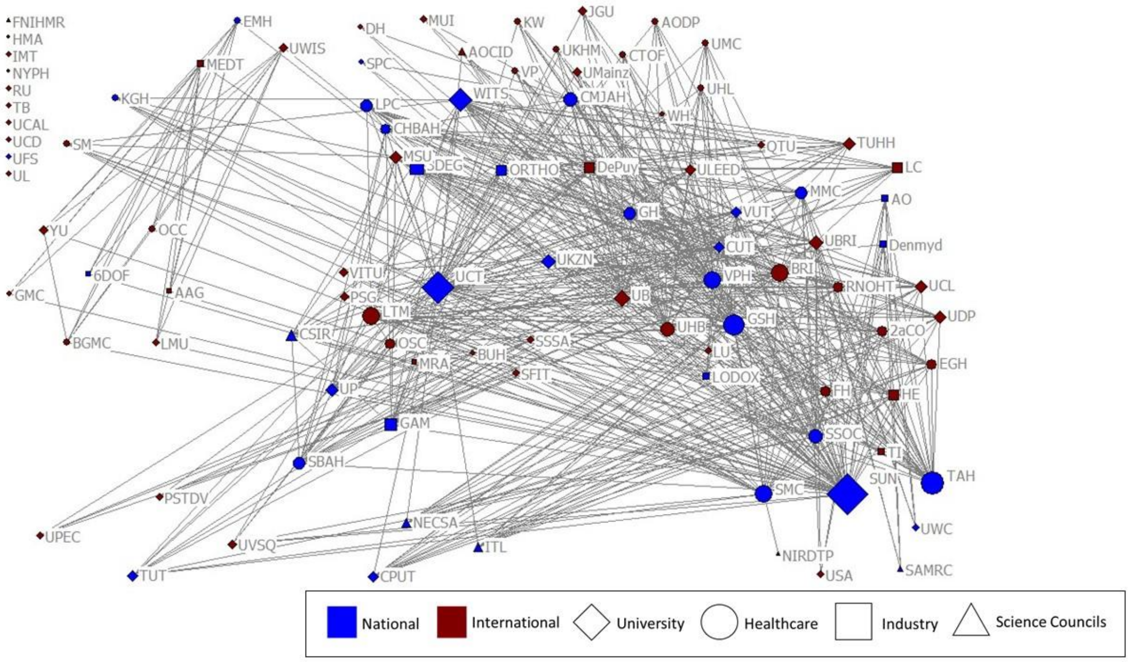


Figure 25:Collaboration potential of actors in the scientific publication network. Thickness of edges are unweighted.

The ten actors shown on the left-hand side of Figure 25 are isolated in this network because they are either already connected to the actors via the actor-collaboration network (Figure 23), or they work in more specialised areas which sets them apart from the interests of the other actors. As an example, in the actor-collaboration network of Figure 23, Telecom Bretagne (TB), Institut Mines-Telecom (IMT) and University of Liege (UL) co-author a publication with UCT on an automated statistical shape model of the human scapula and humerus. The choice of keywords by the authors were “statistical shape model”, “scapula” and “humerus”. These keywords do not overlap with any other actors’ areas of interest. Of these ten actors, nine are international actors, further supporting the suggestion that international actors bring new ideas into the network.

The highest-ranked actors in the collaboration potential network are presented in Table 8. The actors having the greatest collaboration opportunities are again national research-intensive universities (SUN, UCT and WITS) and national healthcare actors (TAH and VPH) that collaborate with them. These research-intensive universities have worked in many areas of innovation in orthopaedic device development and can therefore connect with other smaller degree actors who are more closely related in the cognitive dimension. In Figure 23, national university actors UCT, WITS and SUN showed no social ties in the orthopaedic devices TIS, as these universities never co-authored any of the scientific publications in the dataset. Some opinions about this absence of social ties have been offered in the discussion of Chapter 5. Figure 25 shows direct links between these universities based on their cognitive distance, and supports the assertions made by Yan & Ding (2012) that real social connections are harder to establish than similarity approximations.

Table 8:High-degree actors of the collaboration potential network

Degree Centrality					
Rank	**Node**	**Actor**	**Sector**	**Location**	**Value**
1.	SUN	Stellenbosch University	University	Local	65
2.	UCT	University of Cape Town	University	Local	50
3.	TAH	Tygerberg Academic Hospital	Healthcare	Local	37
4.	WITS	University of the Witwatersrand	University	Local	32
5.	VPH	Vincent Palotti Hospital	Healthcare	Local	27

7.5 Discussion

The keyword network is useful in several ways. At the superficial level it shows the research areas in which South African organisations are pursuing scientific knowledge in orthopaedic device development. The keyword network highlights which areas are of greatest focus and how these research areas are connected. Most keywords only appear on one publication, indicating a vast array of areas of innovation in which actors are independently conducting research. At the other end of the scale, popular keywords are connected to many of these hapax keywords. This can be seen in the keyword network (Figure 21) where the 18 popular keywords are connected to 149 other keywords in the main component of the network. These popular keywords are typically associated with traditional research areas for orthopaedic devices (e.g. prostheses and implants, fixation, hip arthroplasty, etc.). On the one hand it appears that innovation continues and expands in these traditional research areas, while on the other hand, these traditional areas are being combined with new areas as shown by the lower-frequency keywords to which the popular keywords are connected.

The two-mode keyword-actor network illustrated how key actors in the network are related to popular keywords. It is clear from Figure 22 that high-ranking actors are working in research areas described by popular keywords. However, it may also be true that the high-ranking actors are driving the focus of the research making these research areas appear popular, at least in terms of the number of publications produced. UCT, WITS and SUN are linked to several popular keywords.

In their study of the evolution of knowledge and research themes in five major journals, Choi et al. (2011) found a strong correlation between degree centrality and betweenness centrality in their keyword networks, which is uncharacteristic of most natural or artificial networks. In this study, keywords having high betweenness centrality also had high degree centrality. This suggests that the research areas connecting the network are also the research areas in which most knowledge is being produced.

The collaboration potential network highlights links that could be made between actors based on their cognitive distance. This network presents an opportunity for actors who have weak social ties in the network, in that it reveals potential collaborators who are similar in the cognitive dimension.

The approach presented responds to the recommendation by Yan & Ding (2012) to investigate hybrid network approaches when studying social and cognitive relations among actors in scientific knowledge production. The collaboration-potential network yields the same outcome as that of Vida (2018), i.e. determining the cognitive distance between actors, but with a simpler methodology. Author-assigned keywords on scientific publications can be retrieved with ease from scientific publication databases and combined with the two-mode network to link actors to keywords. In contrast, author bibliographic coupling through co-citation, suggested by Vida for the determination of cognitive distance, is time consuming and cumbersome with currently available bibliometric tools.

7.5.1 Limitations of the study

The keyword networks are based on author-assigned keywords and the keywords assigned by researchers in the present study to publications not having author-assigned keywords. The results are therefore somewhat subjective, i.e. the collaboration potential is only as good as the choice of keywords. The visibility of a publication is related to the choice of keywords. While keywords reflect the content of the publication, the choice by the author of a specific keyword could affect reach in the reader audience and encourage preferential attachment. Choosing keywords that are already prominent in orthopaedic device development, could connect a publication to an array of keywords already connected to that choice of keyword. In this way, authors may become more strongly associated with a research area. The keywords selected by authors in this set of scientific publications were highly specialised. None of the scientific publications have a keyword “orthopaedic device” or similar, and only three of the scientific publications had “medical device” as an assigned keyword. The keyword network is also sensitive to the generalised choice of keywords in the standardisation process, which, moving from 271 keywords to 205 keywords, aimed not to miss new research areas or oversimplify existing ones.

The approach to establish collaboration potential among actors in a network has been presented as an alternative to Vida's (Distance on scientific collaboration networks, 2018) use of author bibliographic coupling to determine cognitive distance. Direct comparison in future studies of the Vida approach and the new approach presented here, would reveal the extent to which they yield similar results.

7.6 Conclusion

This study has identified the scientific research areas of interest in the orthopaedic devices TIS and illustrated the linkages between these research areas. It has shown that actors of the orthopaedic devices TIS may be closer in their cognitive distance than suggested by the actor-collaboration networks of Chapter 5. The study has proposed a new approach for determining the cognitive distance among actors in a social network. The new methodology has been applied to show the collaboration potential that exists between actors of the orthopaedics devices TIS, which could be exploited for the creation of ties to facilitate knowledge diffusion through the scientific network.

8. Institutions that impact orthopaedic device development in South Africa

Institutions are considered to be the "rules of the game" in society; they are humanly devised constraints that shape human interaction (Hekkert, Negro, Heimriks, & Harmsen, 2011). Institutions may be formal or informal. Formal institutions are those rules that are codified and may be enforced by an authority, for example supportive legislation and technology standards, whereas informal institutions are shaped by the collective interaction of actors *(ibid)*. The creation of a favourable ecosystem for the local medical device and diagnostics industries to flourish, requires government engagement and intervention (South African Medical Research Council and PATH, 2014; Trade & Industrial Policy Strategies, 2018). It is therefore fitting to consider the institutions of government and how they impact on orthopaedic device innovation in South Africa.

This chapter identifies institutions that impact orthopaedic device development in South Africa. It presents government institutions that support innovation as well as institutions that support the realisation of a medical device industry in South Africa. The chapter also presents institutions that shape actors' roles in the innovation system. The performance of institutions is not assessed. The discussion at the end of the chapter relates the institutions to the orthopaedic devices technological innovations system (TIS) in South Africa and highlights the role of the political context in the TIS.

8.1 Methodology

Formal (codified) institutions likely to affect the development of orthopaedic devices and therefore the orthopaedic devices TIS, were investigated. While informal institutions may have a strong influence on innovation dynamics, it is impossible to map them systematically (Hekkert, Negro, Heimriks, & Harmsen, 2011).In the scientific publication and patent actor-collaboration networks, a list of actors involved in orthopaedic device knowledge development within South Africa, was generated. This actor list is distinguished by location (national and international) and sector (university, healthcare, industry and science councils). For each of the four sectors, institutional documents relevant to those sectors and actors belonging to those sectors, were identified as described below. Furthermore, knowledge creation for orthopaedic device development may be influenced by other national and international governance structures. The following sections describe the approaches taken to identify relevant institutional documents.

8.1.1 Government departments

In the scientific publication and patent actor-collaboration networks, no South African government departments were identified as knowledge creators in the orthopaedic devices TIS. However, government has the important role in enabling and facilitating the growth of the medical device industry in South Africa. Four government departments were identified either to be involved in medical device development or to contribute more broadly towards knowledge development and exchange. These are:

1. Department of Science and Technology[9]
2. Department of Health
3. Department of Higher Education and Training
4. Department of Trade and Industry

The websites of these departments were searched for institutional documents (acts, bills, other legislation, annual reports and strategy documents) which may speak to knowledge development and exchange for (orthopaedic) medical device development in South Africa.

8.1.2 Universities

Different university institutions may support the creation, exchange and dissemination of knowledge to deliver and improve healthcare in South Africa. For each identified university actor in the scientific publication and patent actor-collaboration networks, a search of its website was performed to capture:

1. The vision and mission statements of the university.
2. Policy and strategy documents that provide information on knowledge development and knowledge exchange in the scientific and technological domains, in general.
3. Policy and strategy documents that provide information on knowledge development and knowledge exchange in the scientific and technological domains of medical device development.

8.1.3 Healthcare

Many of the authors and inventors affiliated with the healthcare sector were clinicians, including, among others, medical officers, orthopaedic surgeons and neurosurgeons. Clinicians subscribe to certain ethical institutions and practices, which were searched for on the websites of the Health Professions Council of South Africa (HPCSA) and the South African Orthopaedic Association (SAOA).

In South Africa, the healthcare delivery system is divided into the public and private sectors. There are three large private hospital groups in South Africa, namely Netcare, Life Healthcare and Mediclinic.

[9] At the time of performing this institutional review, this was the name of the department. It has since changed to the Department of Science and Innovation.

The websites of public and private healthcare services providers were explored for relevant institutions.

While actors identified in the actor-collaboration networks were knowledge creators for orthopaedic device development, the healthcare sector actors, at large, would be users of orthoapedic devices. The institutions searched for included those addressing both knowledge development and exchange and the procurement and use of devices.

8.1.4 Industry

Several of the identified industry actors were members of either, or both, the South African Medical Technology Industry Association (SAMED) and the Medical Device Manufacturers Association of South Africa (MDMSA)[10]. The websites of these organisations were searched for relevant documents.

All actors who manufacture medical devices must have certain regulatory pathways in place, e.g. ISO, CE or FDA approval. In South Africa, medical device regulations were passed in December 2016, and are overseen by the South African Health Products Regulatory Authority (SAHPRA). ISO, CE, FDA and SAHPRA regulatory pathways were investigated.

8.1.5 Science councils

The websites of all the science council actors identified in the actor-collaboration networks were searched to identify relevant institutional documents.

8.2 Results

Most of the identified actors of the actor-collaboration networks do not exist for the sole purpose of developing and/or commercialising orthopaedic devices. Except for a few industry sectors actors who may be orthopaedics or medical device companies and specialist orthopaedic hospitals, the other actors offer a diverse spectrum of services.

8.2.1 Government institutions

An overview of the government institutions identified and presented here is shown in chronological order in Figure 26. During the review of the government institutions, it became apparent that the institutions of government departments were aligned to the National Development Plan Vision 2030 (National Planning Commission, 2012), which are South Africa’s long-term socio-economic development goals - hereafter referred to as NDP2030. The NDP2030 was only published in 2012, and the more recent institutions refer to its goals. The NDP2030 identifies 11 focus areas, one of which is

[10] Industry actors who are members of either SAMED or the MDMSA appear on the member lists on their websites.

"Improving Health". Government's strategic plans are further communicated through the Medium Strategic Framework (MTSF); the MTSF provides a five-year framework for the alignment of other government plans at national, provincial and local level, and is intended to bring coherence and continuity to the country's long-term plan. Institutions like the 1974 Health Professions Act, the 1988 Scientific Research Act, and the 1991 South African Medical Research Act, established the Health Professionals Council, the Council for Scientific and Industrial Research and the South African Medical Research Council. They are described in their respective sector sections below. The rest of this section describes the government institutions chronologically.

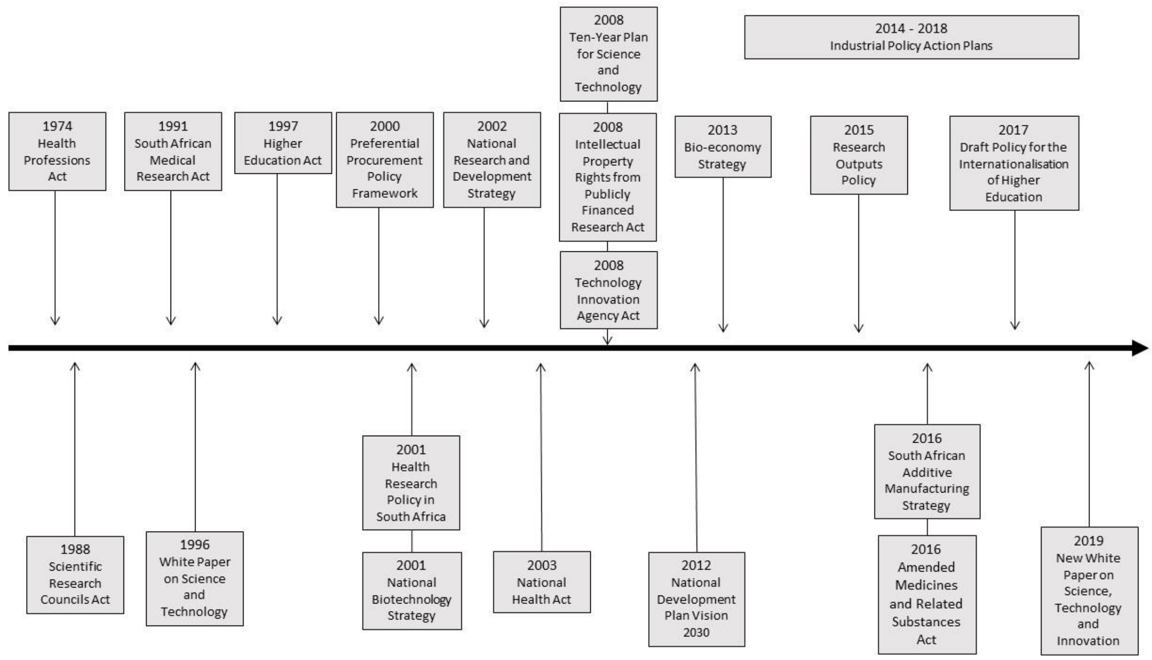


Figure 26: Government institutions that may impact the orthopaedic devices TIS in South Africa

The White Paper on Science and Technology (Department of Arts, Culture, Science and Technology, 1996), introduced the concept of a National System of Innovation (NSI). The NSI is the set of organisations and networks working towards the development and diffusion of new technologies that are economically useful. Within the NSI are certain public organisations, which are categorised into the funding bodies, science councils, universities, government departments, state-owned enterprises and regulators (Department of Science and Technology, 2017). Funding bodies include organisations that fund research and development activities, e.g. the SAMRC, the National Research Foundation (NRF) and the Technology Innovation Agency (TIA). Science councils perform basic and applied research and development across the entire innovation chain and include organisations such as the

CSIR and (again) the SAMRC. Science councils may also perform research with the private sector or through contractual research and formal research training, however, the research activity of science councils is in line with their respective government department's functions, i.e. research performed by the SAMRC would be in line with that of the NDoH. Universities operate in the same research space as science councils, however, universities have the responsibility of formal research training. Universities and science councils were established through individual legislation (Acts). Government departments, state-owned enterprises and regulators may also perform research in line with their mandates. The DST is the custodial co-ordinator for the development of the NSI and influences the NSI through strategies (Department of Science and Technology, n.d.(c)). The 1996 White Paper presented a broad vision to maintain South Africa's (then) areas of global competitiveness and address the needs of South Africans. It set forth the establishment of several organisations or bodies, including the National Advisory Council on Innovation (NACI), the NRF, the Innovation Fund and the National Facilities for Research. Among the objectives of the Innovation Fund, was the promotion of increased networking and cross-sectoral collaboration within the South African NSI.

The National Biotechnology Strategy (Department of Science and Technology, 2001) and the Health Research Policy of South Africa (Department of Health, 2001) were both published in 2001. The aim of the National Biotechnology Strategy was the development of services and technologies to support science-based innovation in the health, industrial and agricultural sectors of South Africa. The purpose of the Health Research Policy in South Africa (Department of Health, 2001) was to provide an enabling framework to conduct research that improves health and wellbeing in South Africa. Among its objectives were: to develop a communication strategy that establishes mechanisms for the dissemination of research and to ensure that the benefits of research are systematically and effectively translated into practice; and to establish links, locally and internationally, between partners involved in health, health research, funders of research, research organisations and users of research in public and private sectors.

South Africa's National Research and Development Strategy (Department of Science and Technology, 2002) was introduced in 2002 as an implement for publicly financed science and technology to create an enabling environment for the NSI. It was based on three pillars: (1) innovation; (2) science, engineering and technology (SET) human resources and transformation; and (3) creating an effective government science and technology system. The innovation pillar includes the establishment and funding of technology missions necessary for the promotion of economic and social development. These include technology platforms for biotechnology and information technology, and technology for manufacturing, indigenous resources, and poverty reduction. The NRF was identified as the key organisation for promoting this strategy as it links to the university sector.

The National Health Act, Act 61 of 2003, provides a framework for a structured uniform health system in South Africa. At national level, the Act gives the National Health Council (NHC) the role of advising the Minister of Health on the health technology development, procurement and use. It also gives the NHC the role of advising the Minister on the development of an integrated strategy for health research. The National Health Research Committee (NHRC) identifies, and advises the Minister on, health research priorities, considering the burden of disease and the cost-effectiveness of solutions aimed at reducing the burden of disease. At the provincial level, the general functions of the provincial health departments include conducting or facilitating research in health and health services. The Minister may also make any regulations concerning, and including, the development of an essential drug list and a medical and other assistive devices list, health technology, and health research.

In 2008, three pieces of related legislature were introduced: The Ten-Year Plan for Science and Technology (Department of Science and Technology, 2008), the Intellectual Property Rights from Publicly Financed Research and Development Act[11], Act 51 of 2008, and the Technology Innovation Act, Act 26 of 2008. The Ten-Year Plan for Science and Technology (Department of Science and Technology, 2008) was developed to transform South Africa from a resource-based economy towards a knowledge-based economy, where the production and dissemination of knowledge would lead to economic benefits in South Africa. The knowledge-based economy is underpinned by four interconnected and interdependent pillars, including innovation; economic and institutional infrastructure; information infrastructure; and education. Progress towards a knowledge-based economy would be driven by investment into four elements, including human capital development; knowledge generation and exploitation; knowledge infrastructure; and enablers to address the "innovation chasm" between research results and socio-economic outcomes. Attempts to address the "innovation chasm" have focused on connecting the knowledge generators (universities) more closely to the market (Department of Science and Technology, 2002). The Ten-Year Plan for Science and Technology introduced the establishment of TIA to address fragmentation of (the then) existing funding instruments and stressed the need to establish an Intellectual Property Management Office for the enhancement of intellectual property (IP) protection, and to develop capacity to manage technology licenses and commercialisation. The Intellectual Property Rights from Publicly Financed Research and Development Act provides for effective utilisation of IP arising from publicly financed research and development, to establish the National Intellectual Property Management Office (NIPMO), and to provide for the establishment of technology transfer offices (TTOs) at publicly

[11] "Publicly financed" or publicly funded means research and development performed using funds made available by the South African government, or an agency of the South African government as defined in the Act; this excludes bursaries and scholarship.

financed research organisations. The objective of the Act is to make provision for IP stemming from publicly financed research and development to be identified, protected, utilised and commercialised for the benefit of South Africans. Twelve months after the Act came into effect, publicly financed research organisations were to establish and maintain a TTO. TIA was established through the Technology Innovation Act, Act 26 of 2008, with the intention to promote the development and exploitation of discoveries, inventions, innovations and improvement, which are of the public's interest. TIA complements the National Intellectual Property Management Office (NIPMO) by actively promoting technology transfer and commercialisation by South African research organisations (Department of Science and Technology). TIA has health as a focus area. Its objectives in health include (Technology Innovation Agency, 2018): investing in the development of affordable and adaptable novel health technologies aimed at addressing the Southern African burden of disease; and strengthening the current portfolio of health technologies, developing point-of-care diagnostics for tuberculosis, and exploiting expertise in cardiac and orthopaedic devices in South Africa.

The Bio-economy[12] Strategy (Department of Science and Technology, 2013), introduced in 2013, aimed to coordinate innovation among different actors, to promote opportunities, resources and outcomes in agriculture, health, industry and the environment, and to guide research and investment in biosciences. South Africa's Bio-economy Strategy builds on the foundation set by The National Biotechnology Strategy (Department of Science and Technology, 2001) and the Ten-year Plan for Science and Technology (Department of Science and Technology, 2008). Within its health scope, the Bio-economy strategy identifies medical device development as a key intervention to address the South African burden of disease. It mentions government's approach in using the "quadruple helix" model to integrate actors from government, industry, universities and civil society into a coordinated system. In the quadruple helix model, government provides the framework to co-ordinate relationships; industry has a key role in production; universities generate new knowledge, innovation and technology; and civil society is consulted as co-innovators, end-users and holders of traditional knowledge. The NDoH sets the health research and innovation priorities for the Bio-economy Strategy.

The Research Outputs Policy (Department of Higher Education and Training, 2015), revised in 2015, is aimed at sustaining current research strengths and promoting the kinds of research and knowledge outputs which would be required to meet the South African national development needs. The policy encourages research productivity and rewards research output from universities, through the

[12] "The term "Bio-economy" encompasses biotechnological activities and processes that translate into economic outputs, particularly those with industrial application"; it may include the "technological and non-technological exploitation of natural resources, such as animals, plant biodiversity, micro-organisms and minerals to improve human health, address food security and subsequently contribute to economic growth and improved quality of life" (Department of Science and Technology, 2013).

distribution of a research subsidy to universities based on their research outputs (journal and conference papers, and master's and doctoral degrees). The research outputs subsidy has historically not recognised creative outputs, artefacts and patents. Innovations, such as patents, will be evaluated for the first time in 2020 and will receive equal weighting to journal articles and conference proceedings (Department of Higher Education and Training, 2018).

In 2016, A South African Additive Manufacturing Strategy (Department of Science and Technology, 2016) was introduced, and the 1965 Medicines and Related Substance Act, was amended. A South African Additive Manufacturing Strategy speaks explicitly to medical implants and the promotion of knowledge development and exchange among different stakeholders for the use of additive manufacturing (AM) platforms for medical implants. The AM strategy identifies products and future market opportunities where AM technology development might place South Africa in a competitive position in the global market. The AM Strategy recognises AM as having the potential to impact product manufacturing, especially in areas with mass customisation or relatively low volume production and to improve the competitiveness of the South African manufacturing sector. South Africa already has AM centres including the Vaal University of Technology South Gauteng Science and Technology Park and the Centre for Rapid Prototyping and Manufacturing at the Central University of Technology. The amended Medicines and Related Substances Act incorporates regulations relating to medical devices and invitro diagnostic medical devices. The South African Health Product Regulatory Authority (SAHPRA) was established in February 2018, with the responsibility of the regulation of medicines for human and animals, complementary medicines, medical devices, radiation emitting devices and radioactive nucleotides (South African Health Products Regulatory Authority, 2019). SAHPRA operates independently of the NDoH. Prior to the Amendment of the Act, there was no medical devices regulator in South Africa. However, there was a Medicines Control Council (MCC) which served as the national medicines regulatory authority with the aim of ensuring that medicines available in South Africa met quality, efficacy and safety standards (Medicines Control Council, 2012). The MCC transitioned to becoming SAHPRA, with additional role of regulatory oversight of medical devices and complementary medicines in South Africa. Prior to the establishment of SAHPRA, the sale and use of medical devices in South Africa were largely unregulated (Saidi, 2016), with only electromagnetic medical devices or radiation-emitting devices being subject to certain regulatory criteria under the Hazardous Substance Act, Act 15 of 1973.

In 2017, the DHET released the "Draft Policy Framework for the Internationalisation of Higher Education in South Africa" [13] (Department of Higher Education and Training, 2017), which provides a

[13] In this DHET report, internationalisation refers to "cross-border movement of students and staff; international research collaboration; offering joint degrees by universities in different countries; establishment of campuses

national framework for internationalisation for higher education organisations, which comprises high-level principles and guidelines, to which individual organisations may align their policies and strategies. The policy framework describes South Africa as being a "knowledge hub on the African continent", where South Africa offers attractive research opportunities to international researchers and is a gateway to Africa (and the Global South) for researchers from other countries (Department of Higher Education and Training, 2017).

A strategic objective of the Department of Trade and Industry (dti) is to grow manufacturing in South Africa towards industrial development, job creation, investment and exports. Current strategies for medical device development in South Africa by the dti are addressed in a series of annual documents, the Industrial Policy Action Plan (IPAP). In the Industrial Policy Action Plan 2014/15 – 2016/17 (IPAP2014) (Department of Trade and Industry, 2014), the key opportunities and constraints of a potential medical devices sector was to be identified through a study of the medical devices sector, later published as (Deloitte, 2014). Key action programmes in the IPAP2014 was the development of a strategy for the medical device sector. The strategy would be developed with stakeholders in the South African medical device sector, the NDoH and the SAMRC. The absence of an internationally recognised South African Medical Devices Certification Authority was also highlighted as an impedance on South African exports. The Deloitte (2014) report found that the medical device sector will only develop if university, industry and government initiatives are aligned and these sectors co-ordinate their growth plans and activities. The report further suggests that such collaboration will need to take place within a formalised structure. Another recommendation made in this report is for government to consider and analyse the potential effects of product designation[14]. This avenue could create demand in the domestic medical device market for locally produced medical devices. It is suggested that product designation via the Preferential Procurement Policy Framework Act, Act 5 of 2000, may be an instrument to ensure demand for locally manufactured medical devices.

Key opportunities identified in IPAP2015 (Department of Trade and Industry, 2015) for the medical device sector was expanding co-operation and exports of medical products to the Southern African Development Community (SADC) and other African markets. Two key action programmes were developed in IPAP2015: the development of an industrial strategy for the medical device sector; and optimising procurement of medical consumables in the public sector. An industrial strategy for the

by universities outside of their home country; the growth of satellite learning and online distance education, including online educational institutions; arrangements between countries for the mutual recognition of qualifications; regional harmonization of qualification systems; and the increasing inclusion of international, intercultural and global dimensions in university curricula."

[14] Product designation refers to the setting of specific requirements, such as designating a portion of government funds to be spent on locally manufactured products, which would encourage innovation by local manufacturers, and result in the demand for the procurement of local products.

medical device sector would be jointly developed by government, industry, labour, universities and NGOs. The strategy was expected to optimise manufacturing and trade in the medical devices sector, meet government's health needs, as well as gradually decrease the sector's trade deficit. The strategy would support the design of regulatory and economic measures to exploit the potential of the medical device and pharmaceutical industries in South Africa.

The key action programmes in IPAP2016 (Department of Trade and Industry, 2016) for the medical devices sector include: the facilitation of the development of regulatory standards and certification in South Africa; and the facilitation of the development of support mechanisms to subsidise compliance to ISO13485. These interventions would address challenges and opportunities in the sector, including quality assurance, and public and private procurement, which would promote exports and where possible, enable import substitution, which may result in increased capacity to access new and existing markets, and promote further investment in manufacturing in South Africa. In facilitating the development of support mechanisms to subsidise compliance to regulatory requirement of ISO13485, interventions would seek to address the challenges in adherence to this internationally recognised standard.

IPAP2017 comprises two parts. Some of the key opportunities for the medical device sector identified in IPAP2017 (Department of Trade and Industry, 2017b) include developing improved health technology innovation capabilities, and leveraging South Africa's geographic location in relation to the rest of Africa, and its BRICS status. The key action programme is the Medical Devices Supplier Development programme. This intervention calls for the investigation into local supplier development programmes, in collaboration with the private sector, to capture an increasing share of the private market, provided the correct mechanisms are put in place to meet the necessary requirements for supply into this sector of the economy. The intervention aims to facilitate increased local production of medical devices for the domestic as well as regional and international markets. Within IPAP2017 (Department of Trade and Industry, 2017a) is the proclamation of six cluster development programmes, one of which is for the medical device sector.

The key action plan for the medical device sector in IPAP2018 (Department of Trade and Industry, 2018b) was the establishment of a Technology Innovation Cluster Programme (TICP) to promote collaborative initiatives between university, industry and government, to enable high-impact industrialisation in the medical device sector. The TICP brings together the TIA, CSIR, IDC, DST, dti and the MDMSA for this intervention to strengthen ecosystems using a cluster-based approach. The TIA-TICP intends to establish a national initiative, the Medical Device and Diagnostic Technology Innovation Cluster (MDDTIC), to stimulate technology innovation and competitiveness in the medical device sector.

A new White Paper on Science, Technology and Innovation was put forth to develop new policy approaches to respond to an ever-changing innovation environment, as well as address some challenges which constrain the NSI in attaining the NDP2030 objectives. The new White Paper on Science, Technology and Innovation (Department of Science and Technology, 2019) sets the medium- to long-term policy direction of government for science, technology and innovation policy; it will be implemented through a series of decadal plans to be developed with actors from government, universities, industry, and civil society. In selecting and supporting research focus areas, the new White Paper proposes that, among other factors, science, technology and innovation priorities should be based on the sustainable development goals (SDGs) and the objectives of the NDP2030. The new White Paper calls for sector and thematic co-ordination, where integrated science, technology and innovation planning for priority sectors will be adopted, resulting in sector science, technology and innovation plans. These plans will be used to co-ordinate research efforts across the university, science council and industry sectors, and to concentrate funding on priority initiatives. Universities are proposed to continue playing a central role; science councils, NGOs and state-owned enterprises may also have a role. Regarding medical device development, the new White Paper aims to provide a supportive legislative environment for new industries, for example, government procurement.

8.2.2 Institutions of university actors

This section is divided into three sub-sections: Innovation policy of university actors; Traditional universities; and Universities of technology. In the scientific publication and patent actor-collaboration networks presented in Chapters 5 and 6, respectively, 12 South African universities were identified as actors of the orthopaedic devices TIS. There are many commonalities among the institutional documents of university actors, and rather than presenting them individually, they are presented as a whole, with outliers mentioned or discussed where relevant, or specific universities discussed for illustrative purposes.

Innovation policy of university actors

All 12 South Africa universities identified in the scientific publication and patents actor-collaboration networks had an established TTO and an innovation or IP policy. IP policy covers the establishment of the TTO, IP advisory committees and their roles, IP as it relates to university employees, students and visitors, and technology development and commercialisation strategies. It also provides for the recognition of, and the provision of incentives for, contributions made by researchers, and supports more effective utilisation of IP. The university allocates an annual budget to its TTO; NIPMO also supports the TTO by providing rebates of fees associated with protecting university IP. TTOs may also offer seed and innovation funding, or rely on support from other agencies, such as TIA or the SAMRC, which have dedicated funding for technology transfer and commercialisation of technology out of the university. The TTO serves as a liaison between the university and industry regarding IP protection and technology development, commercialisation and business development.

The Department of Research Contracts & Innovation at the University of Cape Town (UCT) – the TTO of UCT - through NIPMO funding, is developing a series of booklets called Route to Market (R2M) which focusses on specific sectors or products and highlights key steps and consideration for bringing such a product to market in the South African context. The booklets are released under a Creative Commons license which will enable other organisations to customise the booklet for their own use. "Medical Devices: An Innovation Guide from Lab to Commercialisation" (University of Cape Town, 2018) is one such booklet released in the series. In this guide, the innovation pipeline of publicly financed developments and can be illustrated, as in Table 15 in Appendix L, according to different technology readiness levels (TRL). TRLs are used to classify technology maturity as technology develops from TRL 1 – research initiation – towards TRL 9 – where the technology has been commercialised and has a market presence.

Typically, the university is the default owner of the IP generated from research activity. This translates to the university being the "applicant" or "assignee" on a patent application; inventors – which may be university employees, students or visitors – are also formally associated with the patent. There are conditions where IP may be assigned to the funder. This usually results from a "full cost model", where the funder pays for direct, indirect and, in some instances, a margin of the, project costs, which is declared and approved by NIPMO. There may also be instances of co-ownership of IP, resulting from collaborative research. The share of the IP is often determined and agreed upon through the terms set in the collaborative agreement, and/or may be based on the financial and intellectual contributions made by parties involved.

Commercialisation of university IP is usually done on a case-by-case basis. University-owned IP can usually be accessed in one of three ways: exclusive license; non-exclusive license and assignment. Other arrangements include the formation of start-up and spin-out companies, occasionally with the inventors of the IP themselves. The university may also seek industry assistance and partnerships to access funding to support innovation through technology development, scale-up, piloting and marketing trials. The nature and conditions of license agreements are usually determined by the university, however, certain NIPMO preferences need to be considered. Exclusive licenses are not preferred and are only granted where the IP is commercialised in a manner that benefits South Africa; the State retains "walk-in rights" for IP related to health, security and emergency needs of South Africa (Research Contract and Innovation, 2014). All off-shore IP transactions must be approved by NIPMO.

A favourable scenario for product development is for the university to partner with an industry partner that already has the appropriate regulatory infrastructure, which is willing and able to develop the device, secure regulatory approval, and manufacture the device for the market (University of Cape Town, 2018). Due to the limited size of South African medical device industry, very few opportunities exist to map new products to companies with existing infrastructure (*ibid*). The creation of a company may be undertaken to take the device to market. However, this is usually done at a late stage in the innovation pipeline, once all risks have been identified and minimised. The cost associated with establishing a company for a device, and its potential in the market, must be weighed (*ibid*).

Traditional universities

Traditional universities offer formal and professional academic programmes in undergraduate and postgraduate degrees (Department of Higher Education and Training, 2019). Nine traditional universities were identified in the scientific publication and patent actor-collaboration networks. In their vision statements, six of the universities identified themselves as being an African university. Common threads running through these vision statements were to be an internationally recognised university, favouring engaged scholarship and social responsiveness, contributing to the development of social justice, creating knowledge and advancing knowledge in the service of society.

The common threads in the mission statements of universities were excelling in innovative learning, teaching, scholarship and cutting-edge research which benefits society and the environment through knowledge and adding to the local, regional and global knowledge base; improved student success and well-being, and the opportunity for lifelong learning; advancing African scholarship through strategic partnerships on the continent, with the Global South and with the rest of the world; producing graduates and future leaders who were influential locally and globally; producing qualifications that are locally applicable and internationally acclaimed; producing qualifications underpinned by values of engaged citizenship, engaged scholarship and social justice; advancing the transformation within the university, its curriculum, and beyond; and nurturing an inclusive institutional culture that embraces diversity and redresses the disadvantages and inequality of the past.

Universities of technology

Universities of technology offer programmes (mainly undergraduate) that are career-focused (Department of Higher Education and Training, 2019) and usually have a work-integrated component. Universities of technology are distinguished by their focus on technology innovation and technology transfer (Bridge, 2020). Four universities of technology identified in the scientific publication and patent actor-collaboration networks. Three of the four vision statements of the universities of technology spoke of "innovation" to different ends. These included being "at the heart of technology education and innovation in Africa"; being "an engaged university that focused on producing quality social and technological innovations for socio-economic development…"; and being "a university that leads in innovative knowledge and quality technology education." The mission statements presented the aims in which the universities of technology would pursue their vision. The common threads running through the mission statements were to build universities of technology that were sustainable and environmentally conscious; known for providing a high quality of education and fostering a scholarship of teaching and learning; known for having a relevant and competitive curriculum; creating a well-resourced living and learning environment for its students; enhancing and developing the quality and effectiveness of (relevant) research and knowledge production and promoting innovation, engagement and social enterprise for the African continent, and beyond; and investing in state-of-the-art technology and teaching methods. Each of these universities of technology had a health sciences faculty.

In health technology innovation and medical device development, universities of technology are providing innovation and manufacturing platforms, and are involved in community based and SMME projects, often projects that focus on commercialisation of technology and provide platforms for technology transfer and spin-off technology companies. A special mention here is the CRPM which was established 1997 as "a centre for commercial work as well as research using rapid prototyping, rapid manufacturing, rapid tooling and medical product development technologies" (Central University of Technology, 2010). It was realised that infrastructure at CRPM could benefit industry through offering rapid prototyping services, and in fulfilling one of CUT's missions, the CRPM was able to introduce new technology to the South African manufacturing industry (Centre for Rapid Prototyping and Manufacturing, n.d.). The CRPM received ISO 13485 certification for 3D printing of medical devices making it the first accredited centre of its kind in Africa (*ibid*).

8.2.3 Institutions of healthcare actors

The Health Professions Act, Act 56 of 1974, established the Health Professions Council of South (HPCSA) and professional boards who provide control over the education, training, registration and practice of health professions. The mission of the HPCSA is to enhance the quality of healthcare for all South Africans by developing policy frameworks for effective and efficient co-ordination and guidance of the health professions (Health Professions Council of South Africa, 2018). The HPCSA guides the behaviour of healthcare professionals who may be involved in the research, development and commercialisation of medicines and medical devices, as well as their relationship with industry. A health professional may not be involved in any commercial activity (manufacture, promotion, sale, etc.) related to medicines or medical devices (Health Professions Council of South Africa, 2016a). Furthermore, the health professional may not engage in or advocate for the preferential use of a medicine or medical device, except where, through valuable consideration by the health professional, the patient is provided with the clinically most appropriate or the most cost-effective option (*ibid*).

The HPCSA has explicit guidelines for the involvement of health professionals in certain health technologies, including biotechnology (Health Professions Council of South Africa, 2008) and telemedicine (Health Professions Council of South Africa, 2014). The HPCSA also has a policy document to regulate business practices of healthcare professionals (Health Professions Council of South Africa, 2016b). There are limitations in which private hospitals may not employ HPCSA healthcare professionals, because of the profit-driven motive of such organisations.

Related to the institutions set by the HPCSA, are the institutions of the South African Orthopaedics Association (SAOA). The SAOA has "Principles of Medical Ethics" (South African Orthopaedic Association, 2019), which are not laws, but are standards of conduct for the behaviour of the orthopaedic surgeon, and are aligned with those guidelines of the HPCSA. The SAOA "Principles of Medical Ethics" details the orthopaedic surgeon's involvement with industry, including any consulting services offered by the surgeon to industry. Surgeons acting as consultants to industry providing a genuine service can receive reasonable compensation for their services. Industry-sponsored health research was previously seen as inappropriate because of the bias it may have introduced. The SAOA "Principle of Medical Ethics" outlines sponsorship and remuneration details for health research involving researchers, research organisations and funding corporations.

Twenty-one South African healthcare sector actors (all hospitals) were identified in the orthopaedic devices TIS in South Africa. Eight of these actors were from the public sector, all academic or tertiary hospitals. In the actor-collaboration networks, each of these eight hospitals were linked to university actors, the exception being Livingstone Hospital (LH) which appears in isolation in the patent actor-collaboration network. The other 13 identified hospitals were from the private sector, largely from the Netcare, Life Healthcare and MediClinic groups, the exceptions being the Sports Science Orthopaedic Clinic (SSOC), and the Zuid-Afrikaans Hospital (ZAH).

The webpages of all the public healthcare facilities were linked to their respective provincial Department of Health. Only Groote Schuur Hospital (GSH) and Steve Biko Academic Hospital (SBAH) also had their own websites. The websites of Netcare, Life Healthcare and MediClinic were patient-centric and focussed on the services available to patients and related procedures, both clinical and administrative. The policies available on the websites of Netcare, Life Healthcare and MediClinic were largely related to quality assurance, procurement, transformation and employment equality, and the environment. Each of these private healthcare service providers also had their own learning academies offering accredited training in nursing and healthcare sciences (examples include pharmacy and emergency medical response).

8.2.4 Institutions of industry actors

Twenty South African industry actors were identified in the scientific publication and patent actor-collaboration networks. Denmyd Medical Equipment (Denmyd) is the only industry actor appearing in both networks. Several of the South African industry actors belong to one or both local medical industry associations SAMED or the MDMSA. SAMED members comprise local and multinational industry actors that are involved in the manufacture, import, selling, marketing and distribution of medical technologies in South Africa (South African Medical Technology Industry Association, 2018). The objectives of SAMED are to (South African Medical Technology Industry Association):

1. Promote a balanced and harmonised policy environment – this is pursued by engaging with policymakers, regulators, politicians, health professional societies, funders and international organisations to develop and propose patient-centred policies and provide solutions that increase productivity and efficiency of healthcare systems.
2. Provide membership services - SAMED comprises various committees dealing with issues such as regulations, government procurement processes, reimbursement, transformation, ethics, congresses and health policy.
3. Promote ethical principles and practices.

One of the SAMED committees, is the Orthopaedic Suppliers Committee, which is involved in elective orthopaedics, trauma and spinal applications. This committee works closely with SAOA, and engages with SAOA on congresses, venues, fair market value and fellowships (South African Medical Technology Industry Association).

The MDMSA is an association of companies in South Africa that manufacture medical devices; it serves as a platform for manufacturers and others involved in the South African medical device sector to discuss matters that are important to industry, in support of the latter’s growth and sustainability (Medical Device Manufacturers Association of South Africa, 2015). The MDMSA has been instrumental in creating a strong partnership with the dti, towards continuous engagement on how to expand and grow the local medical technology manufacturing industry (South African Medical Technology Industry Association).

Medical device regulations for industry actors

The SAHPRA medical device regulations are to comply with the Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices (International Medical Device Regulators

Forum, 2018). The purpose of these guidelines is to provide harmonised essential principles for the design and manufacture of medical devices to ensure that devices are safe and perform as designed. The guidelines were written with reference to several available standards in medical device development, including ISO 13485 Medical Devices.

The market in which the medical device is sold will have certain regulatory requirements and sets the regulatory compliance needed for the device to enter that market. There are many markets which accept the CE marking, or where work done for CE marking compliance is directly or partially applicable. Under European law, the CE regulations for medical device are Medical Device Directive - 93/42/EEC – MDD.

In terms of the new South African medical device regulations, all companies that handle medical devices must be licensed. The license requires that devices handled by the company be listed, that an authorised representative be appointed, and that a quality management system be in place at the company. A company whose name appears on the medical device (the legal manufacturer) is required to hold the regulatory approvals (University of Cape Town, 2018).

SAHPRA is establishing capacity to approve devices under their regulations. This may take several years. In the interim, recognised regulatory approval such as CE markings and FDA approvals may be the quickest route to bring a product to the South African market (University of Cape Town, 2018).

8.2.5 Institutions of science council actors

The CSIR was formed under the Scientific Research Council Act, Act 46 of 1988. The work of the CSIR aims to support industrial development and to enhance government capabilities in the areas of service delivery, policy development and information management (Council for Scientific and Industrial Research, 2015). Their focus area of Health Technology has objectives of addressing the South African burden of disease through developing cost-effective bio-therapeutic technologies and health infrastructure as well as medical devices, sensors and information systems. The CSIR has begun to investigate the establishment of an incubator for medical devices and diagnostics, to assist local medical device manufacturers (Council for Scientific and Industrial Research, 2018).

The SAMRC is a public entity reporting to the NDoH and was established in terms of the South African Medical Research Council Act, Act 58 of 1991. The Intellectual Property Rights from Publicly Financed Research and Development Act, Act 51 of 2008, also informs the mandate of the SAMRC. The SAMRC has a mandate to improve health and quality of life through research, development and technology transfer. The SAMRC has four strategic goals which are aligned with the SDGs and the NDP2030 and contribute to the strategic objectives of the NDoH (South African Medical Research Council, 2018):

1. Efficiently and effectively administer health research in South Africa.

2. Lead knowledge generation and facilitate knowledge translation into policy and practice for improved health.
3. Support innovation to improve health.
4. Build capacity for long-term sustainability of health research.

Performance indicators of Goal 2 include the number of scientific publications published by the SAMRC's divisions and bibliometrics associated with it (e.g. authorship, citation, etc.). A performance indicator of Goal 3 is the number of innovation and technology projects which are funded by the SAMRC to develop new health technologies. In its quest to achieve these strategic goals, the SAMRC is an actor whose objective it is to develop and translate (new) knowledge for health technology in South Africa.

The SAMRC is the largest local funder of health research in South Africa. It also funds programmes focused on health innovation through strategic partnerships. Funding is directed at major health concerns that affect South Africa and the rest of the world.

The SAMRC Strategic Health Innovation Partnership (SHIP), a partnership between the SAMRC and the DST, is a programme for health technology product innovation. SHIP funds and manages projects that focus on the development of new pharmaceuticals, treatments, vaccines, medical devices and prevention strategies. Through partnerships with local universities, science councils and industry, SHIP aims to facilitate the translation of research results into improved health outcomes and social benefit. The focus areas of research and development are those which are relevant to South Africa's burden of disease, i.e. HIV/AIDS, TB, malaria, non-communicable diseases and maternal and child health (South African Medical Research Council and PATH, 2014). SHIP, together with the SAMRC's TTO, aims to enable technology transfer for the movement of new products to market.

8.3 Discussion

In this section, the main findings of the institutional review are discussed with reference to the scientific publication and patent actor-collaboration networks, to provide a comprehensive picture of the structure of the orthopaedics devices TIS. The discussion considers the TIS-contextual factors described by Bergek et al. (2015).

The orthopaedic devices TIS is externally linked to the broader innovation system in South Africa, i.e. the National System of Innovation (NSI). The actors who work in the orthopaedics devices TIS, especially the public sector actors (science councils, universities and public healthcare actors), may be influenced by broader innovation policy, such as the Ten-Year Plan for Science and Technology and the White Paper on Science, Technology and Innovation. The NSI assigns roles to different classes of actors. Among the group of actors not previously identified in the scientific publications and patent actor-collaboration networks are funding bodies, government departments, state-owned enterprises and regulators. While these actors do not explicitly develop knowledge in the TIS, they play a role in the facilitation of knowledge development and exchange among actors who do create knowledge in the TIS. Key among these are the regulators, such as NIPMO and SAHPRA, who have the authority to establish pathways for technology development (i.e. NIPMO) and regulate markets (i.e. SAHPRA). While regulators appear to have their roles in the later stages of the innovation pipeline, being cognisant of their regulations is important in the earlier phases of the innovation pipeline, as their regulations may determine market entry of developed devices, which directly relates to the success of the device. TIA plays a fundamental role in bridging the gap between knowledge created at universities and science councils from publicly funded research and its commercialisation, by funding technology development activity. TIA makes explicit contributions towards technology transfer for medical and orthopaedic devices, towards addressing the South African burden of disease and exploiting South Africa's local expertise.

Across government policy are examples of initiatives and strategies where the NSI learns, adapts and changes. Examples include the move towards a knowledge-based economy, the establishment of agencies to address the "innovation chasm" and playing to South African strengths by investing into focus areas where South Africa has competitive or comparative advantage. The move from the National Biotechnology Strategy to the Bio-economy Strategy has reflected an emphasis on the medical device sector in the latter. A co-ordination strategy proposed for medical device innovation in the Bio-economy Strategy is the use of the quadruple helix model and assigning roles to actors - industry, government (including science councils), university and civil society. The Bio-economy Strategy does not explicitly mention who "civil society" is, but according to the model, civil society provides inputs as users of the innovations, holds traditional knowledge and are co-innovators through consultation. These are all characteristics of clinicians, healthcare professionals and others belonging to the healthcare sector. It may also be the characteristics of NGOs and NPOs. Leaving the definition of "civil society" broad has two consequences. The first is that it excludes the healthcare sector from being a recognised helix in the proposed innovation model, despite its crucial role in medical device innovation. The second is that the institutions of healthcare actors may not expand and adapt towards innovation policy or encourage innovation within the healthcare sector, causing a potential gap in the outcomes of the Bio-economy Strategy.

The institutional review has highlighted certain sector-specific opportunities and challenges for the orthopaedics devices TIS, illustrating the way in which the TIS is structurally coupled to its context at both the sectoral and geographic levels. Universities are encouraged to be differentiated so that they make unique contributions towards knowledge production and national development by responding to the needs of their immediate environment, the African region and are globally competitive. Traditional universities largely identified themselves as being African universities, and their vision statements spoke of being internationally recognised, having engaged scholarship and developing or advancing knowledge for the service of society. Research-intensive universities are important in developing countries to address issues of relevance in the developing world (Department of Higher Education and Training, 2013). South Africa is considered a gateway to the African continent. In the new White Paper on Science, Technology and Innovation, the importance of international engagement for the evolution of the NSI is emphasised. The new White Paper's focus is on building African science, technology and innovation capacity, and acknowledges that the South African NSI will flourish as part of the innovation systems of the SADC and Africa as a whole. Africa is the biggest destination for medical device exports out of South Africa. Of the estimated domestic production of medical devices of around ZAR2.6 billion in 2014, more than ZAR1.5 billion was to African markets (Department of Trade and Industry, 2016). The African agenda, including its burden of disease, is therefore critical in developing the medical device market in South Africa. However, there is no evidence of collaboration with other African organisations in the scientific publication and patent actor-collaboration networks.

Innovation is central to the mission of universities of technology. Universities of technology were found to be active in creating innovation and manufacturing platforms for technology development; these areas overlap with science council mandates. While the Higher Education Act encourages collaboration of universities, primarily for sharing resources, the effects of the current university funding framework, including the Research Output Policy – a major driver of knowledge production from the university sector - does not *encourage* collaboration. Collaborating South African universities must share Research Output Policy incentives, essentially diluting would-be-funding into the university. Scientific knowledge production in universities has been favoured over technological knowledge production, as previously, only scientific research outputs were incentivised in the policy. This may be a reason why such few South African universities have contributed towards the patent actor-collaboration network.

The HPCSA guidelines steer the behaviour of healthcare professionals involved in research, development and commercialisation of medical devices, and influence their relationships with industry. The SAOA further builds on these guidelines as they would be appropriate to orthopaedic surgeons. These guidelines have resulted in healthcare professionals serving as consultants to industry. This is especially evident in the patent actor-collaboration network where surgeons co-invent devices with industry actors, suggesting that consulting to industry is a favourable pathway for getting innovations to market. The HPCSA also regulates business practices for healthcare professionals. One such measure is that private hospital groups may not employ HPCSA healthcare professionals, because of the profit-driven nature of such organisations. In the patent actor-collaboration network it had been highlighted that inventors affiliated with private healthcare providers make a large contribution towards technological knowledge production in the TIS. There is an opportunity for private healthcare groups to facilitate or support knowledge development for individuals already active in the orthopaedics devices TIS who are resident in their facilities.

The institutional review highlighted roles in medical device development of science councils (CSIR and SAMRC) which had not been considered in this research project before. Science councils are major funders of research and development activity, and fund knowledge exchange endeavours, such as local and international conferences. Science councils have also created innovation pathways for technology transfer from publicly financed research and development.

Since 2014, the Industrial Policy Action Plans (IPAPs) of the Department of Trade and Industry (dti) have addressed the building of a medical devices sector in South Africa in their key action plans. These key action plans always involve partnerships with, or the inclusion of, actors from different sectors, including government, universities, science councils, NGOs, labour and industry. The IPAPs also address issues that directly impact the industry actors of the medical device sector. As an example, the key action plans of IPAP2016 were to facilitate the development of regulatory standards and to support certification in South Africa, and to facilitate the development of support mechanisms for compliance to the regulatory requirements of ISO 13485. These key action plans directly address challenges of industry where local manufacturers are not able to trade in certain areas in the South African market or they aren't able to expand export markets, because they do not meet regulatory requirements. ISO 13485 is an expensive process and is beyond the reach of many local manufacturers. The dti response was therefore to investigate processes that would help support local manufacturers to comply with this well-established regulation.

The institutional review has highlighted the desire of the South African government to create an environment for medical device development to prosper in South Africa. Such a conducive environment would result in institutions that structurally couple the TIS to its political context. The first steps came as recognition of the potential shown by existing actors in the field. Government strategies like the Bio-economy Strategy and the South African Additive Manufacturing Strategy put forward mechanisms for different stakeholders to participate in the innovation chain in a formal, co-ordinated way. The Strategies also draw strongly on skills, capabilities and competitive/comparative advantages of actors who participate in the innovation chain. Several other government initiatives targeting medical devices have emerged to support the medical device sector over the past few years, including medical device regulations and the establishment of SAHPRA as a body to regulate medical devices. Other larger strategies have medical devices as streams and aim to accelerate the sector. These include medical device platforms in TIA, key action plans from the dti, a medical device cluster programme, and initiatives and platforms created by both the SAMRC and the CSIR. These initiatives and interventions are still in early stages of implementation and are facing challenges, one of which is not having the (human resource) capacity to fulfil the ambitious tasks that lie ahead.

8.3.1 Limitations of the study

A limitation of this study is that only formal codified institutions were reported on. Informal institutions, due to the impracticality of mapping such institutions, have not been considered at all. Additionally, it proved impractical to assess all formal institutions from all organisations who contribute towards the knowledge base of the TIS. Institutional documents such as annual reports and audits, for instance, were largely omitted from this exercise. This institutional review extended to South African organisations involved in knowledge development and exchange for orthopaedic device development in South Africa. Limiting the review to South African organisations may have led to the omission of drivers for international organisations to be involved in orthoapedic device development in South Africa.

8.4 Conclusion

This institutional review has identified actors that facilitate knowledge development and exchange within the orthopaedic devices TIS in South Africa, which had not been identified in the scientific publication and patent actor-collaboration networks. Further roles of those actors that had previously been identified in the orthopaedic devices TIS have been highlighted. The institutional review also highlighted how the orthopaedic devices TIS is related to its context, both externally linked and structurally coupled to the political contexts, and structurally coupled to the sectoral and geographical contexts. Strategies relating to medical device development address the burden of disease and focus on the capabilities of actors and the competitive/comparative advantage of actors in the NSI. Finally, the institutional review has shown inter-relationships between, and co-existence of, three well accepted and documented innovation frameworks, i.e. the NSI, the TIS and the quadruple helix model, in South Africa.

9. Case studies: Knowledge development and knowledge diffusion through networks in the orthopaedic devices TIS

This chapter presents case studies designed to investigate how knowledge is developed and exchanged among actors of the orthopaedic devices TIS, and through actor experiences, how the knowledge functions are influenced by TIS-contextual factors.

Yin (2003) defined a case study as an "empirical enquiry that investigates a contemporary phenomenon within its real-life context, where the boundaries between the phenomenon and context are clearly not evident, and in which multiple sources of evidence are used." Eisenhardt (1989) defined a case study as "a research strategy which focussed on understanding the dynamics present within single settings".

9.1 Methodology

The case study design for this study has been influenced by the case study design theory presented in Eisenhardt (1989), Yin (2011) and Gibbert (2015), and the case study design of Lander (2014). The case study design is broken down below.

9.1.1 Case selection

The case selection was based on descriptors for the functions "knowledge development" and "knowledge diffusion through networks" of the orthopaedic devices TIS in South Africa. The findings of the scientific publication and patent actor-collaboration networks presented in Chapters 5 and 6 inform the case selection, as do theories of knowledge development and exchange presented in the literature. Two cases – translational collaboration and author-inventors – were examined.

9.1.1.1 Translational collaboration

Translational collaboration occurs when the orthopaedic device developed resulted from the collaboration between actors from the university, healthcare and industry sectors. This type of collaboration has been presented by the Academy of Medical Sciences (2010), and investigated by de Jager et al. (2017). These sectors serve the public in different ways, and organisations in these sectors have different mandates; their motives for participating in the orthopaedic devices TIS may be different. Each of these sectors also brings capital to the collaboration, which may benefit other sectors depending on the needs of the latter. The translational collaboration case is explored because it involves different actors that are assumed to provide complementary skills and resources. In the scientific publication and patent actor-collaboration networks, if the scientific publication or patent resulted from the co-authorship or co-inventorship of actors from these three sectors, that collaboration was considered to form part of the population for this case. The co-authors and co-inventors who appear in these publications were invited to participate in the study.

The unit of analysis in this case is the interviewed individual (co-author or co-inventor). By inviting individuals of different sectors to participate in the study, the sample of participants would cover experiences from individuals from all three sectors. Actors from different sectors may offer contrary evidence or views.

9.1.1.2 Author-Inventors

Author-inventors are individuals who had contributed to both the scientific publications and patents in the datasets of the networks. The author-inventor case explores cases where the same actors produce different types of knowledge, working in scientific discovery as well as technological application. The unit of analysis is the individual. Investigating author-inventors was expected to reveal development dynamics in both the scientific and technological dimensions, as well as knowledge translation dynamics between the scientific and technological domains.

9.1.2 Data sources

The primary data source for the case studies were semi-structured interviews with individuals who met case criteria. Approval for the case studies was obtained from the Human Research Ethics Committee of the Faculty of Health Sciences at the University of Cape Town (HREC 860/2015).

Secondary data gathering techniques included a review of the institutional documents of actors creating knowledge in the orthopaedic devices TIS (see Chapter 8), published literature, and the analysis of other documents from the respondent's organisational websites. The findings of the scientific publication, patent and keyword networks were used as additional data sources.

9.1.3 Field data collection

For each respondent, a resource pack was created. Each pack included:

1. An informed consent form.
2. The scientific publication(s) and/or patent(s) to which the individual had contributed, and which had formed part of the scientific publication or patent actor-collaboration network.
3. Collected data about the respondent's career path and publications.
4. The scientific publication and patent actor-collaboration networks for the period 2000-2015.
5. The interview protocol.

The questions used in the semi-structured interviews were derived from the diagnostic questions for analysing the "knowledge development" and "knowledge exchange" functions of the TIS, presented in Hekkert et al. (2011, p. 10). To test the appropriateness of the questions and to expose the author to interviewing practice, a set of preliminary interviews was conducted.

9.1.3.1 Preliminary interviews

Invitations were sent to 10 individuals from the University of Cape Town known to be working in either orthopaedic device development or innovation management, and who did not meet the criteria for the case selection described above. Four individuals agreed to be interviewed, and a researcher who had experience in case study research agreed to a meeting discussing the proposed interview protocol.

The preliminary interviews were conducted in the same way the case interviews were planned to take place. In three of the interviews, a researcher with interviewing experience was present. The author asked the questions, and after all questions had been asked, the second researcher raised additional questions that he thought were relevant. Once the interview was over and the interviewee had left, the author and the researcher discussed the interview, the topics discussed, the respondent's interpretation of the questions, the achievements and gaps of the interview, and strategies for improving future interviews.

9.1.3.2 Interviews

Each respondent was asked to sign an informed consent form and permission was sought to record the interview. The interview was divided into three parts. The first part aimed to collect demographic data of the interviewee including educational background and career path choices of the respondent. It included questions like "Can you tell me about your tertiary education?" and "What is your current role(s) at your organisation(s)?". The questions were broad and open-ended to allow for the interviewee to provide an account of their career in orthopaedic device development, and how they came to their current role in their current organisation. The second part of the interview was a discussion on the scientific publication and patent actor-collaboration networks, and how the interviewee formed part of the network. The questions in this part of the interview reflected how well knowledge development and diffusion activity had been captured in the scientific publication and patent actor-collaboration networks. The third part of the interview addressed the respondent's perceptions about "knowledge development" and "knowledge diffusion through networks" within the orthopaedic device development TIS in South Africa. An interview protocol, presented in Appendix M, was developed, and contains the list of questions developed for the interview. The protocol served as a guide on topics to be covered, rather than rigid questions to be posed.

9.1.4 Data analysis

The data analysis followed a similar path to that presented in Yin (2011), and comprised the following five phases:

1. Assembly – the compilation and assembly of data into a database.
2. Disassembly – iterations of coding to disassemble the data.
3. Reassembly – identification of emerging patterns from disassembled data.
4. Interpretation – interpretation of the reassembled data, which forms the key analytic portion of the study.
5. Concluding – drawing conclusions from the study.

Validity of the data analysis has also been considered, as discussed later.

9.1.4.1 Assembling, disassembling and reassembling data

NVivo software (QSR International Pty Ltd, 2015) was used in the assembly, disassembly and reassembly of data. Codes were developed to capture the functions of the TIS framework, with a special focus on the "knowledge development" and "knowledge diffusion through networks" functions, and their relation to specific contextual conditions. As coding progressed, concepts not captured by the TIS functions gave rise to additional codes. The codes were reassembled and formed the basis for the theory developed in the study. Theory refers to an account of how a phenomenon operates and why it operates in the way that it does (Johnson, 1997); it is based on a collection of concepts which may be assembled in some logical order about the events that have been studied (Yin, 2011). The study's findings should demonstrate whether and how the results support or challenge the theory (Yin, 2011).

In developing theory, within-case data analysis, cross-case patterns and the development of hypotheses, described by Eisenhardt (1989), were considered. Within-case data analysis allowed the author to become familiar with each case. It allowed for unique patterns to emerge from each case before the author moved to generalisation across cases. Cross-case patterns were explored by examining the data in divergent ways. Three methods are discussed by Eisenhardt. The first is category or dimension selection, where within-group similarities and inter-group differences are determined on a set of categories or dimensions. The second method involves comparing a pair of selected cases and examining the subtle similarities and differences between them. The third method involves dividing cases according to the data source. In this chapter, only within-group similarities and inter-group differences are compared across cases. The cases are not designed to illustrate differences which may exist between them; both cases explore the development of knowledge for orthopaedic device development in the TIS. The translational collaboration case explores knowledge development for orthopaedic device development under pre-defined conditions. Theory may be generated when within-case analysis, cross-case analysis and overall impressions reveal emergent themes and concepts.

9.1.4.2 Interpreting and concluding

The interpretation phase connects the ideas of interest, which may be supported by literature, to the reassembled data (Yin, 2011). In this study, the interpretation phase links the reassembled data to the broader TIS framework, and explicitly addresses the TIS-contextual factors. Interpretation takes the form of developing theory, where context-specific findings may be linked to the objectives of the thesis. Interpretation is supported by the available literature; in the absence of available literature, it adds to the body of TIS literature for medical device development in/and developing country contexts. In interpreting findings, there is a possibility that others might interpret the findings differently, thus alternatives to the findings and their explanations, which may be less compelling, are also considered (Yin, 2011).

9.1.4.3 Validity

A valid study is one that has properly collected data and has interpreted the data in a way that the conclusions accurately reflect and represent the studied setting (Yin, 2011). Research validity is a criterion that denotes qualitative research that is credible, plausible, trustworthy and defensible (Johnson, 1997).

There are different strategies to promote validity in qualitative research, as described by Johnson (1997) and discussed below. Among them is triangulation, which is the cross-checking of information and conclusions using multiple methods or sources; "corroboration" occurs when the different methods or sources agree. When using methods triangulation, more than one research method is used in a single study. In this definition, the term method is used broadly to describe different methods of research as well as different procedures of collecting data. The purpose of triangulation is to combine different methodologies that have strengths and weaknesses that do not overlap, so that in their combination, "the whole is better than its parts". Data triangulation refers to using multiple data sources in a single method. As an example, if an interview method is used, multiple interviews would be the multiple sources of data. In this research project, triangulation is performed at both levels. For methods triangulation, the scientific publication, patent and keyword networks, as well as the institutional review, are sources employed to triangulate the developed theory. For data triangulation, each interview serves as a standalone source of data, so that several interviews could triangulate emerging theory.

9.2 Results

In the translational collaboration case, 21 e-mail invitations were sent to individuals from South African organisations who met the inclusion criteria. In the author-inventor case, 11 e-mail invitations were sent to individuals from South African organisations meeting the inclusion criteria. Nine positive responses were received for 32 invitations, translating to a 28% response rate. The interviews for the translational collaboration case were conducted before those for the author-inventor case.

9.2.1 Interview transcription and coding of transcripts

Interviews were recorded and uploaded to a secure drive. All interviews were professionally transcribed by a third party. All interview transcripts were confirmed against the audio by the author. Interview transcripts were coded using NVivo software; a database was created for each case. Prior to coding the first transcript, the author identified codes based on the TIS framework. Initially, there were seven codes corresponding to the seven functions of the TIS framework. As coding progressed, concepts not captured by the seven functions gave rise to additional codes. Coding was performed according to an iterative cycle, presented in Appendix N, which produced a total of 14 codes based on themes derived from interview responses. A brief explanation of each of these codes is presented in Table 9; these codes were used in both cases. As this study is concerned with the functions "knowledge development" and "knowledge diffusion through networks", the areas of interest in the interviews were those coded by either "knowledge development" or "knowledge diffusion through networks", those coded simultaneously by "knowledge development" and "knowledge diffusion through networks", or where any of the other codes are coded simultaneously with either "knowledge development" or "knowledge diffusion through networks" or both. While the primary focus of the study was the knowledge functions, relationships between the knowledge functions and the other five functions were anticipated, hence all the functions were coded for.

Table 9:Descriptions of codes used in interview transcripts for the translational collaboration and author-inventor cases

Code	Description
*F1: Entrepreneurial experimentation and production	All events or activities described by interviewees dealing with the commercialising of the technology.
F2: Knowledge development	All events or activities described by interviewees where learning took place, i.e. where knowledge was acquired. Learning may occur in several forms, including the STI and DUI modes.
F3: Knowledge diffusion through networks	All events or activities described by interviewees where learning occurred through the exchange of information, or interactions between individuals or with the technology.
F4: Guidance of the search	All events or activities described by interviewees that affect the visibility of specific objectives or goals of the users of the technology.
F5: Market formation	All events or activities described by interviewees that were pursued to form a market for the technology.
F6: Resource mobilisation	All events or activities described by interviewees that were undertaken to access and secure resources, including human, financial and infrastructural resources.
F7: Counteract resistance to change OR Legitimacy creation	All events or activities described by interviewees that were undertaken to promote acceptance of a technology.
Extension of knowledge or technology	All events or activities described by the interviewee that moved the technology beyond its intended use. This includes events or activities that showed the diffusion of the technology outside the networks displayed in this project.
Innovation in allied fields	All events or activities described by interviewees involving innovation or technology development in fields associated with orthopaedic device development. This code has similarities to the function "development of positive externalities" described by Bergek et al. (2008b). This function emphasises the "collective dimension" of innovation and illustrates how externalities amplify the other functions.
Innovation in other fields	All events or activities described by interviewees involving innovation or technology development not associated with orthopaedic device development.
Network familiarity	Interviewees' familiarity with other actors in the actor-collaboration network. This extends only to the scientific publication and patent actor-collaboration networks which were presented to interviewees in the interview.
Network limitations	Occasions highlighted by the interviewee where the scientific publications and patent actor-collaboration networks presented to the interviewee failed to capture relationships among actors.
South African context	Factors described by interviewees that were specific to South Africa.
Success factors	This code resulted from the question "If you were part of a successful collaborative project, how would you go about replicating those factors that made that project successful?". It codes factors described by interviewees that were necessary in collaborative projects for the technology to be successful.

*In the table, F refers to function, and "F1" refers to function 1 of the functional approach to the TIS framework as described by Hekkert et al. (2007).

9.2.2 The translational collaborations case

Five interviews were conducted in person in December 2017 and January 2018: three at the interviewee's office or board room at their place of work; one at a coffee shop in a business park where the interviewee's office was located; and one at the home of the interviewee. Basic demographic data of the interviewees are presented in Table 10. The interviewee responses will henceforth be referred to using their allocated pseudonym, P1, P2, P3, P4 and P5, where P1 was the first individual interviewed, P2 the second individual interviewed, and so forth. There are also some relations between the interviewees. P1 and P5 are co-inventors of a patent in the patent actor-collaboration network, and P2 and P3 are co-authors of a scientific publication in the scientific publication actor-collaboration network.

Table 10: Basic demographic data of interviewees of translational collaboration case at the time of the interview

Interviewee	Highest academic qualification	Primary professional designation	Current role in current setting	Sector represented in network	Experience
P1	PhD	Engineer	Managing Director	Industry	31 years in medical device industry
P2	MSc	Engineer	Chief Executive Officer	Industry	23 years in medical device industry
P3	MSc, MBA	Engineer	Founder/ Director	Industry	7 years in medical device industry
P4	DSc	Scientist	Retired	Industry	Over 40 years in medical device industry
P5	DSc	Surgeon	Surgeon in Private Practice	University and Healthcare	Over 50 years in medicine and 40 years in medical device development

All interviewees held post-graduate qualifications. Three of the interviewees were engineers, one was a scientist, and one was an orthopaedic surgeon. Four of the five interviewees were from the industry sector, however, the fifth served also served as a consultant to industry. Before joining the medical device industry, P2 had been employed as a university lecturer. P4 also lectured at a university and P5 had been a university-affiliated clinician. The interviewees had worked in medical device development for periods ranging from 7 years to over 40 years.

As the interviewees were identified using scientific publications and patents, discussions initially focussed on experiences in the development phase of orthopaedic devices, and how knowledge is created and exchanged among actors. However, in these experiences, many lessons were revealed by the interviewees about the manufacture and commercialisation of devices.

9.2.2.1 Knowledge development

Interviewees were involved in the development of an array of orthopaedic devices, including orthopaedic software, instrumentation, biomaterials, plates, and prostheses of major and minor joints. P4 and P5 were the only interviewees who spoke of research in basic sciences. Industry actors rarely co-authored scientific publications, and patents only reflect a portion of their device development activity. Patenting is an expensive exercise and was only pursued where developments showed promise and needed early-stage protection in sought-after economies. Provisional patent applications were also exploited to capitalise on development time; provisional patents establish the priority date and expire after twelve months, as per the Paris Convention (Southern African Research and Innovation Management Association, 2018), and result in a “patent pending” designation.

Patenting did not always have a favourable outcome. P3 said that the company “didn’t win” anything out of the patent; patenting was done because it was encouraged by peers as the device showed clinical promise. P4 highlighted that margins on medical devices were low, and the return on investment took many years from the time of the initial patent application. Patenting in South African universities is also a relatively new concept. P4 shared experiences of faculty peers at the university who were intent on publishing research (in journal articles and presenting at conferences), in which opportunities to potentially protect IP were missed; faculty had to be educated on the value of IP and were encouraged to give the university the opportunity to explore IP protection.

The interviewer enquired about scientific publication decisions that were made. P1 pointed out that much of medical device development work of his company was presented at conferences and congresses, which would not be reflected in the scientific publication actor-collaboration networks[15]. P3 indicated that he was not really interested in authorship other than promoting the product.

After clinical introduction of the device, research continued into the clinical performance of devices, i.e. time saved in surgery, reduction of hospital stays, blood loss, etc. While one interviewee (P3) indicated that none of this clinical data had been published, he did mention that clinical data were initially used to motivate the use of the device by surgeons to medical insurance companies. Some devices developed were used for purposes other than those initially intended. For example, a plate developed by P5 saw dental, maxillo-facial and veterinary applications by other clinicians and researchers.

[15] While conference proceedings have been captured in the scientific publication actor-collaboration network, the coverage by Scopus and Web of Knowledge (WoK) may not be comprehensive. Conferences, especially those at the national level, of the medical and orthopaedic associations may not be reflected in the Scopus and WoK databases.

Knowledge development occurred alongside innovations in allied fields. These included process innovations which fed back to product innovation. Examples include innovations in 3D printing and additive manufacturing. Another example is the development of materials, especially polymers, which directly impacted the development of prostheses for arthroplasty. Knowledge development was also hampered because of limitations in allied fields. P5 had worked in orthopaedic device development since the late 1970s, and at that time standards for using biomaterials were not available; material selection was a learning process, by trial and error. P2 spoke of a novel hip implant that had been patented, and for which funds had been raised for research and development, yet the device never reached the market because, at that stage, the biomaterials available were not suitable for the device.

9.2.2.2 Knowledge diffusion through networks

Interviewees shared many stories of orthopaedic devices being developed from collaboration between engineers/technicians and clinicians (e.g. orthopaedic- and neurosurgeons); however, the knowledge exchange described differed among the interviewees. P1 spoke of taking researched ideas from engineers to surgeons to provide insight about the practical implementations of the engineer's ideas. P3 spoke of the surgeon identifying a gap and developing the specifications for the device, and then passing those ideas to the engineers for calculations and conceptual designs. P5 identified the clinical need, developed a simple prototype of a device in his home garage and requested a biomechanical engineer to build prototypes for cadaver and animal studies. In these cases, the developments arose from the interaction between the engineer and the surgeon. Arenas for (tacit) knowledge exchange were mechanical workshops and operating theatres. P1 also mentioned that biomedical engineers must be in the operating theatre to explain the use of the device and experience its challenges first-hand. Three of the interviewees highlighted the significance of the biomedical/biomechanical engineer in orthopaedic device development. P2 considered the biomedical engineer to be the interface between a traditional engineer (mechanical, electrical, material, metallurgical, etc.) and the surgeon.

When presenting the networks to the interviewees, two interviewees indicated that the networks did not truly reflect their contributions to orthopaedic device development in South Africa. These interviewees were familiar with the other actors in the network, and highlighted links between themselves and other actors which were not reflected in the networks. Among the ways in which the industry actors shared knowledge with the orthopaedic community, was attending and speaking at conferences/congresses, and inviting surgeons to their facilities.

The interviewer enquired about the way in which the collaborations, reflected in the scientific publication and patent networks, had come about. P1 and P5 were co-inventors of a patent, and P5 was a consultant to P1's company, working on many other developments. P2 and P3 were co-authors on the same scientific publication and had worked with each other intermittently for almost ten years. They had been introduced through a surgeon, who was also a co-author on the scientific publication. P4 indicated that a university-affiliated surgeon had visited him at his (then) place of work, and presented the problem to him, which resulted in their joint work on the project. The two had never interacted before, and the surgeon only knew of him because he (P4) was a specialist in his research field.

Four of the interviewees indicated development of orthopaedic devices in the absence of university actors. The reasons given for the absence of university partners was that universities have a long turn-around time in development, and that universities were unable to attach reasonable fees to the services provided. Other issues highlighted were burdensome university administrative processes and IP ownership barriers. When asked whether university actors were necessary in the orthopaedic device innovation chain, P1 acknowledged that universities had expertise or specialised equipment that was otherwise out of reach of their companies. P2 indicated that certain (false) boundaries exist between industry and universities, and that as an industry actor he was aware of the specialised facilities of the university but felt that he could not access them. Interviewees also accessed expertise at universities outside South Africa. P1 mentioned that collaborations with universities were in fact collaborations with clinicians associated with universities who had approached the industry actor and needed assistance in practical implementation of their ideas. In the patent network, P5 is a university-affiliated clinician. In his earlier developments (from the late 1970s), he used university research facilities (workshops, cadavers from anatomy department and animal research centre). Publications generated from the research were published with the university affiliation. P5 and the university received royalties from the patented device. Lack of resources at the university drove P5 away from doing research at the university.

Even though some developments occurred in the absence of university actors in the translational collaboration case, P2 mentioned that all the actors (referring to the network diagram) had some academic background and some sort of link to the university. Two of the interviewees mentioned that they served as external examiners of theses, and two interviewees were guest lecturers at universities. P2 gave the example of a university actor who is consulting him concerning mechanical testing of prostheses.

P3 explained his design philosophy for the orthopaedic software that he had a part in developing. The software was designed to measure certain parameters of implants once implanted. This resulted in a baseline establishment of the parameters, and the parameters could be measured over time in follow-up visits. By establishing these parameters, interventions could be pursued earlier, possibly in the planning phase of an arthroplasty. P3 posed that the idea of the establishment of a baseline, and knowing where errors were made, was not well received by surgeons to whom the software had been promoted. P3 attributes this to the difference in operating modalities between engineers and surgeons.

Knowledge exchange also occurred across geographic boundaries. Four of the interviewees presented work at international conferences/congresses. Research and development of a device would occur in South Africa with the intent of taking the product to international markets or selling the IP to big international corporations. Knowledge exchange between South African and international industry actors sometimes occurred to enable clinical trials of devices in that country, and commercialisation in those markets. International surgeons also visit local industry actors to do surgeries and experience the local devices.

In addition to knowledge exchange described above, one interviewee was also instrumental in starting an international electronic magazine for his speciality, the aim of which was to develop a communication channel between members of an international organisation who hold a conference once every three years. This electronic magazine, published quarterly, would ensure communication on a more regular basis. Two of the interviewees were reviewers for scientific journals and two of the interviewees served in administrative roles in either the Medical Device Manufacturers of South Africa (MDMSA) or the South African Medical Technology Industry Association (SAMED).

9.2.2.3 Links between knowledge functions and other TIS functions

In the translational collaboration case, the "knowledge development" and "knowledge diffusion through networks" functions were coupled to three of the other five TIS functions – F5: Market formation, F6: Resource mobilisation and F7: Legitimacy creation. These links are illustrated in Figure 27. While links between the other five functions were discovered in the case studies, they have not been presented here, because these links would be incomplete as the interview questions were not designed to address them all. Only the links between the knowledge functions and the other functions are described here.

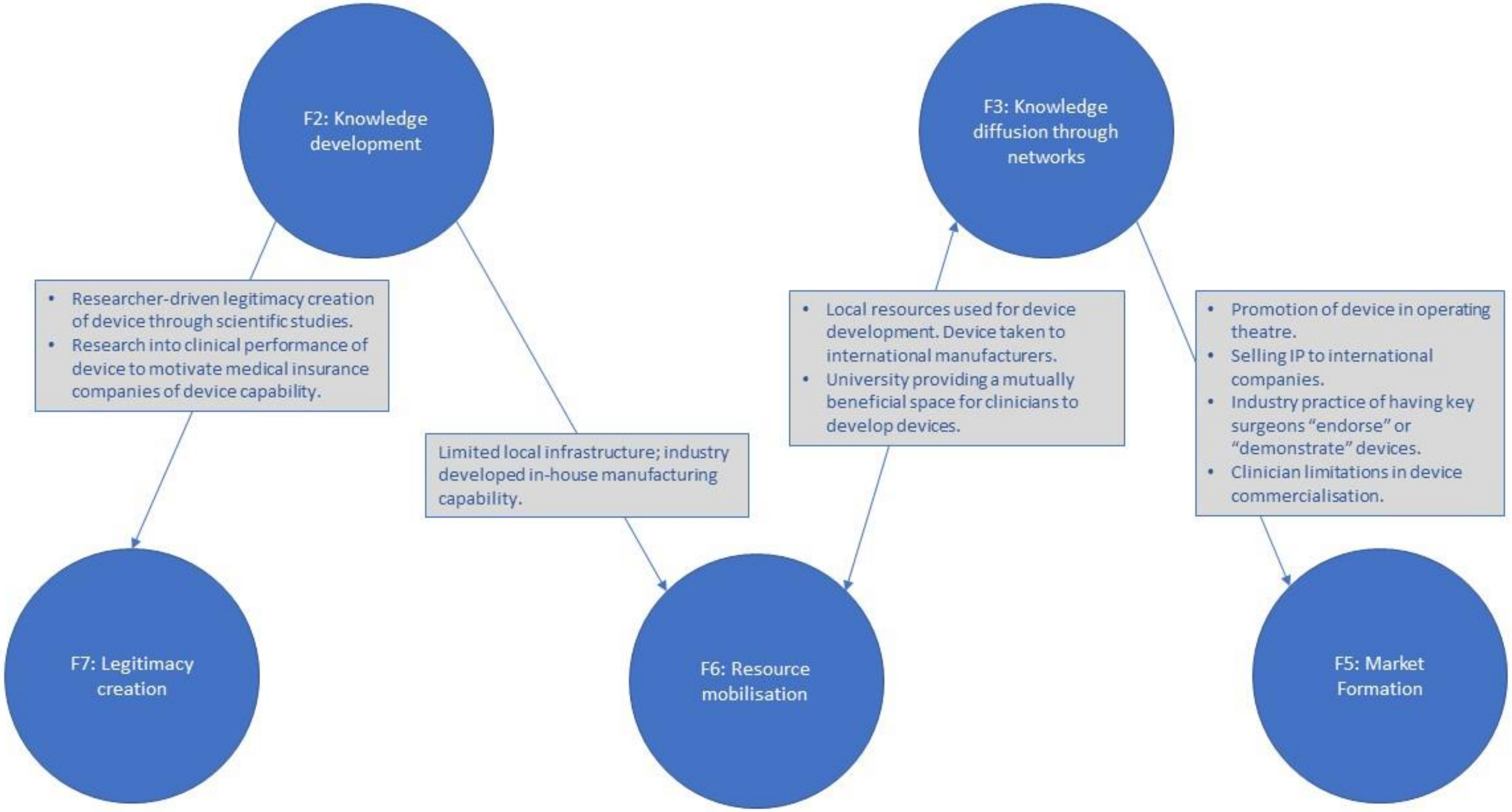


Figure 27: Connections between the knowledge functions and other TIS functions in the translational collaboration case; arrows indicate direction of relationship.

F2: Knowledge development ➔ F7: Legitimacy creation

Knowledge development was driven by the desire to create legitimacy for devices. P1 had been part of the development of a novel implant, at a time where there was still controversy around this class of implant. The knowledge created by P1 and his peers over the years created legitimacy (or acceptance) of the implant by demonstrating its abilities. This ultimately translated to codified sources of knowledge, including patents and scientific publications, driven by the clinician on the team, who addressed challenges associated with the implant, including basic kinematics, medium and long-term outcomes, etc. Knowledge development also occurred with the aim of producing good science, i.e. statistically meaningful results.

In the past, a surgeon could write a motivational letter to a medical insurance company motivating the use of a specific device, and this motivational letter would be sufficient for the medical insurance company to settle payment. In the present environment, a motivation is assessed by the medical insurance company, which determines if the device is relevant. A formal process for receiving a National Pharmaceutical Product Index (NAPPI[16]) code for a device ensues, requiring proof of regulatory approval (ISO, CE or FDA) and clinical evidence of performance. Clinical evidence would be collected on the device's performance mainly to demonstrate to a medical insurance company the device's capability; if the device does not have regulatory approval, then medical insurance companies will not finance its use.

F2: Knowledge development ➔ F6: Resource mobilisation

The resource mobilisation function describes activities to access or secure resources, including human, financial and infrastructural resources. Lack of resources negatively affected knowledge development in orthopaedic device development – clinical performance of devices remained unpublished and aesthetics of the product were compromised. Lack of resources at the university also drove researchers away from the university. While many products of the industry actors were privately funded by the company, where the device showed promise, funding was sought through venture capitalists and a local funding agency, the Industrial Development Corporation. P5 described difficulties associated with applying for external funding, including burdensome administration, pre-trial proofs, and late financing of projects. While P1's company had a wide portfolio of orthopaedic devices, he mentioned that they could do much more had they the money and resources to do so.

[16] A NAPPI code is a unique identifier that enables electronic transfer of information related to a product through the healthcare delivery system (MediKredit, 2009).

F3: Knowledge diffusion through networks ➔ F6: Resource mobilisation

Interviews illustrated access to resources as a barrier to knowledge diffusion through networks. In university-industry interaction, universities expect funding for the research that students would perform. This is not attractive to industry as they could perform research and development inhouse at university rates, with a shorter turn-around time. P2 shared that inventors were utilising resources at local universities and local industry, with the aim of taking the developments to international companies; the intention of these inventors was not to develop devices to be manufactured locally, even though local resources were used in their development.

F3: Knowledge diffusion through networks ➔ F5: Market formation

The market formation function describes initiatives undertaken by interviewees to create a market presence for the device. Market formation strategies discussed included after-sales services, tapping into the network of private hospital groups, committing instrumentation sets to hospitals, and developing and sharing (including selling) IP with international collaborators to extend the market to other countries. In building a market presence for a medical device, many medical device companies have sales representatives or sales engineers who go out to clinicians to promote and sell the device. Engineers also visit operating theatres to explain instrumentation sets and envisaged clinical procedures of the implant. P2 had mentioned that his company did not have the resources to pursue this line of marketing.

P3 mentioned that having a well-known surgeon's name associated with a device, gives the device traction in establishing a market. It was also the practice of big international companies to have key surgeons endorse or demonstrate a product to build a market for a device. Endorsements/demonstrations were often presented at congresses and conferences, which were an arena to promote technologies.

P2 also highlighted some limitations of clinicians in the commercialisation of devices. In the past, clinicians could be involved in the running of medical devices companies and other commercial ventures. This has changed, and in the current environment, clinicians can only consult to medical devices company and earn royalties on IP.

9.2.2.4 Relating knowledge functions to TIS-contextual factors

The findings presented above are grouped according to the TIS-contextual factor categories of Bergek et al. (2015) in Table 11. "Knowledge development" and "knowledge diffusion through networks" were most strongly influenced by the sectoral context (activities taking place in other sectors) driven by developments between the engineer and surgeon, and the various arenas for knowledge exchange.

Knowledge functions were also linked to the embedded TIS (activities taking place in related TISs) and geographical contexts (activities taking place internationally). No political contextual factors were raised by the interviewees concerning in the interviews the knowledge functions.

Table 11: Knowledge development and knowledge diffusion through networks grouped according to the TIS-contextual factors of Bergek et al. (2015) in the translational collaboration case

	Embedded TIS	**Sectoral context**	**Geographical context**
Knowledge development	Knowledge development occurs alongside innovation in allied fields, e.g. biomaterials and additive manufacturing, which are embedded TISs that influence the development of orthopaedic devices.	Industry actors seldom participate in scientific publications.	Clinical trials for FDA approval of a device were performed in the USA.
Knowledge diffusion through networks		Industry actors present their developments at conferences and congresses, which are academic venues.	Developments presented at international conferences.
		Orthopaedic devices are developed by collaborating surgeons and engineers.	Locally developed devices are taken to international markets, or IP is sold to international manufacturers.
		Arenas for tacit knowledge exchange include mechanical workshops, operating theatres, conferences and congresses, industry facility visits, and lecturing.	
		Arenas for codified knowledge exchange include thesis examination and journal review.	

9.2.3 The author-inventor case

Four interviews were conducted in person in March 2018. All four interviews were conducted in the interviewee's office at their place of work. Basic demographic data of the interviewees are presented in Table 12. These interviewees are not related to each other in the networks as was the case with interviewees in the translational collaboration case. The interviewee responses will henceforth be referred to using their allocated pseudonyms, P6, P7, P8 and P9.

Table 12: Basic demographic data of interviewees of the author-inventor case at the time of the interview

Interviewee	Highest academic qualification	Primary qualification	Current role in current setting	Sector represented in network	Experience
P6	PhD	Engineer	University Professor	University and Industry	26 years in biomedical research; 15 years in medical device industry
P7	PhD	Engineer	University Lecturer	University	10 years in biomedical research
P8	DSc	Engineer	Chief Executive Officer*	University	32 years in biomedical research; 20 years in medical device industry
P9	PhD	Engineer	University Associate Professor	University	12 years in biomedical research

*In the scientific publication and patent actor-collaboration networks, P8 had been a university professor and affiliated with the university sector. He has since moved to industry where he is a CEO of medical devices company.

All the interviewees in the author-inventor case held doctoral qualifications. All the interviewees had in the actor-collaboration networks been affiliated with the university sector, and P6 had additionally been affiliated with the industry sector. Interviewees worked in application areas including in medical imaging, neurology, cancer, leprosy, and sports and exercise technology. This included knowledge development in both basic and applied science. They were involved in the development of an array of orthopaedic devices, including diagnostic equipment, braces, cages, customised implants, software, instrumentation and prostheses of various joints.

9.2.3.1 Knowledge development

Two modes of knowledge development were described in the author-inventor case. The first was of developments arising out of post-graduate student projects. The second was the establishment of specialised laboratories or facilities at the university or associated facilities.

Patenting and publishing

In the author-inventor case, the interviewer enquired when interviewees chose to publish and when they chose to patent: "Patent first, publish after, that's the rule here" – P7. This sentiment was expressed by all the interviewees. The project through which P7 was identified in the actor-collaboration network had a conference proceeding and a journal article stemming from a patent. Patenting was done when a quick commercialisation of the device could be seen, and the patent offered design protection before the product went to the market, as going to the market could be a slow process. P8 mentioned that both publishing and patenting were important. P9 explored a more commercial route to research rather than a scientific one; much of the work done in his laboratory remains unpublished.

Creating specialised laboratories and facilities

All four interviewees described involvement in the creation of specialised laboratories or facilities in the university sector, not necessarily at their home university. P6 had been part of the establishment of a new manufacturing facility for medical implants. P8 contributed to setting up a research laboratory, and later started a research unit that had ties to the research laboratory, but whose research focus was different to that of the research laboratory.

P9, in conjunction with a clinician at his university's academic hospital, started a laboratory focussing on prostheses development. Rather than focusing on designing a new prosthesis, the laboratory initially focussed on basic science around design, including understanding design parameters.

9.2.3.2 Knowledge diffusion through networks

The interviewer enquired about how the actors involved in the patent or scientific publication had come together. Regarding the scientific publication P6 had been part of, the co-authors had different interests or roles in the project. The instigator of the project was a university professor who wanted to start a centre of excellence. P6 had an orthopaedic implant company, was keen on using a facility of that kind, and his company contributed financially to its establishment. A third co-author was an international university professor who was a specialist in the technology. Together they developed an implant that was the first of its kind in South Africa.

P7's patents and scientific publications stem from his PhD research. The project came about because his co-supervisor, a clinician, was having to fit standardised implants into patients, which was not ideal, while the clinician wanted to be involved in the development of custom implants. P7's PhD research led to research questions for another PhD project, the focus of which was to develop a pipeline for commercialisation of the technology.

The first scientific publication to which P8 contributed, was co-authored with a post-graduate student and a clinician. The clinician had previously been a student of P8's and approached P8 to work on a device. The research focus areas of the student, P8 and the clinician all aligned towards development of the device.

All four interviewees spoke positively about the role of the university in orthopaedic device development in South Africa. While perceived challenges raised by interaction with other sectors were acknowledged, intra- and inter-sectoral collaboration was a regular occurrence, and in many instances, delivered positive outcomes. P9 mentioned that inter-sectoral collaboration was almost non-existent when he had arrived at his current university in 2011. P8 felt that inter-sectoral collaboration was improving and that there is a recognition among actors that inter-sectoral collaboration is necessary in orthopaedic device development. He referred to meetings held by healthcare and university actors to facilitate discussion among all sectors involved in research, development and commercialisation.

University-university interaction

Interviewees indicated that the disconnect between universities highlighted in the actor-collaboration networks, specifically within the scientific publication actor-collaboration network, were not a fair reflection of collaboration activity between those organisations. All four interviewees highlighted past and on-going collaborations between the universities, including joint supervision of post-graduate students, curriculum advice, examination of theses, joint workshops and training, joint conferences, and mutual access to laboratory facilities. These types of collaborative activities are localised and mostly tacit in nature, and rarely result in codified knowledge. Furthermore, P7 highlighted that the scientific publication actor-collaboration network depended on the affiliations the authors had listed. One of the co-authors on P7's publications always listed himself as being affiliated with a private healthcare actor, omitting his appointment as an honorary professor at the same university as P7.

P7 had mentioned visiting a national university with the aim of connecting to, and collaborating with, its biomedical engineering group; it has since resulted in external examinations of post-graduate students with no real research collaboration between the two groups. P9 mentioned that while it is easy for research units within a university to collaborate, barriers still exist to collaboration with other universities, in the form of researchers being unwilling to collaborate and the cultural differences that exist between universities.

University-healthcare interaction

Interactions between universities and their associated academic hospitals included accessing facilities, mechanical workshops[17] and motion laboratories. Interviewees, who were all engineers, reported accounts of collaboration with both public and private healthcare sector actors. However, many of the interactions are with university-affiliated clinicians. Some university-affiliated clinicians also have a private medical practice, and research and efforts from clinicians often include activity in their private capacity as well as activity from the university side. One interviewee served in both a biomedical engineer role at the academic hospital and was appointed as a lecturer at the university. This shows that engineers may also be affiliated concurrently with the university and healthcare sectors.

P6 shared that, in the operating theatre, he learns the surgical technique, and how he can update designs based on a generic surgical technique. He shares this knowledge with his students and mentees.

Some of the challenges arising out of co-invention between different parties is IP ownership. P9 pointed out that it could be unclear who owns a solution when a surgeon brings an idea or problem and an engineer develops the idea or solves the problem. In the university patenting process, the fact that the university "owns" the patent, discourages some clinicians from participating in collaborative research. P9 suggested a perception among clinicians that the university will profit from the patent, to the clinician's detriment. P9 emphasised that clinicians need to be educated on the role of the university in the patenting process; beyond the cost of the patent, which is borne by the university, much time is invested by technology transfer office staff in the patenting process. In the patent actor-collaboration network, two patents in the dataset belonged to clinicians who patented in their own capacity, despite being affiliated concurrently with a university and a healthcare facility.

P9 expanded his research collaborations by tapping into the clinician network of his clinical collaborator. This fostered new collaboration, in that the network of clinicians started collaborating with colleagues of P9, who were also involved in other (engineering-based) research areas. Interacting with more clinicians resulted in more research directions; however, a commonality was the aim of improving surgical experiences.

The interviewer asked P9 how one could measure what is learnt between the engineer and the surgeon. He replied, "by the amount of time we spend together." This time is a reflection of the

[17] Both universities and academic hospitals had mechanical workshops, which were accessed in collaborative research.

collaboration. Beyond patenting and publishing, day-to-day needs are met, including 3D printing and visualisation and advisory meetings, which are not documented.

The absence of a clinical collaborator could be a barrier to device development. P9 mentioned that his first venture in orthopaedic commercialisation had failed because there was no clinician to champion the device. In P6's first exposure in orthopaedic device development in the late 1990s, P6 developed a tool for a clinician, who then left South Africa while the tool was still in the development phase, with the result that development stopped.

P9 speaks of the "operating barrier" which exists between the researcher and the surgeon. The surgeon is almost instantaneous in providing a solution "…they open up a body, they fix the body, close the body, they go in, they finish it, they come out…" The researcher works on a substantially longer timescale. Thus, the clinician must be educated on how engineering design is done, and the biomedical engineer has to learn how to communicate with the clinician.

University-Industry interaction

University and industry interacted in various ways, including industry accessing university resources and university actors supporting the national medical device industry. P8 did the latter through helping to start-up companies in the medical device industry. P6's company was approached by a different university from his home university, to assist in financing a specialised facility at that university. Because P6's company was keen to use such a facility, they contributed towards machinery costs. Research between P6 and the other university continued, resulting in mutual access to facilities, including facilities of P6's home university.

As a university actor, P7 would like to work with industry in developing student projects which industry may not have time to work on. In turn, industry could fund those student projects. P7 had mentioned that such discussions do happen at networking events but are rarely realised. The interviewer shared with P7 responses from industry sector actors, including, universities have a long turnaround time as they are tied to an academic cycle, and that universities do not know what to charge for services offered. P7 was not aware of this barrier perceived by industry but acknowledged that that was a fair comment.

One interviewee mentioned that the industry actor is not necessary for the development of a device; one can protect the idea and licence it to a manufacturer.

Technology transfer offices and spin-off companies

Three of the four interviewees spoke about their interactions with their respective universities' TTOs. P6 had eight patents, all owned by the university and commercialised through his spin-off company.

The relationship between P6 and the university is mutually beneficial. P6 saw spin-off companies as an expansion of the university's boundaries and a solution to commercialising university IP. The TTO at P7's university examines project proposals that faculty believe may have commercial promise. The TTO offered to do prior art searches, identify gaps and give advice in steering the project towards outputs that might be suitable for commercialisation.

Other modes of knowledge exchange

Inter-organisational knowledge exchange occurred in student exchange programmes, visiting professorships, and sabbaticals spent at other universities. This results in collaborative research and joint publications. Intra-organisation knowledge exchange occurred at strategy meetings of collaborating departments, and in mechanical workshops between engineers and technicians. Teaching responsibility at the university also enabled knowledge development and exchange. P8 introduced a new course at an international university at which he was lecturing, which introduced students to principles of IP. Part of the course involved spending an afternoon with patent lawyers to learn and share experiences. P9 has lectured (by invitation) biomechanics to orthopaedics registrars.

Location

The location of specialised facilities and departments of the university further enabled certain channels for knowledge exchange. An example given, was university departments having a research base in sports performance centres. As other individuals and centres also reside at the sports performance centre, including specialist orthopaedic centres, further collaboration between these centres and universities could arise.

9.2.3.3 Links between knowledge functions to other TIS functions

The knowledge functions were linked to three of the five other TIS functions – F1: Entrepreneurial experimentation and production, F4: Guidance of the search and F6: Resource mobilisation. The relationships are illustrated in Figure 28, which is a summary of the discussion presented in the rest of the section.

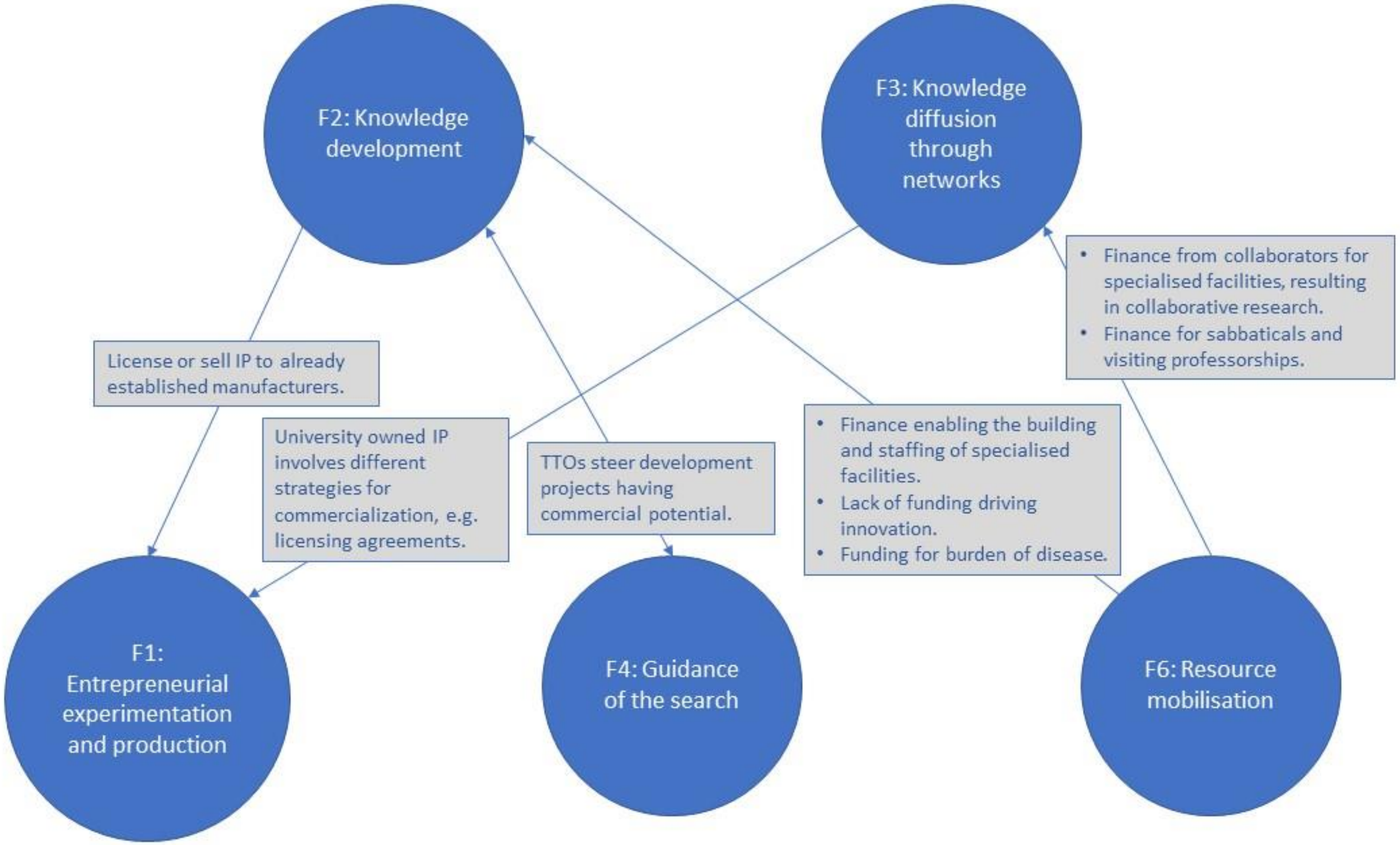


Figure 28: Connections between the knowledge functions and the other TIS functions in the author-inventor case, arrows indicate the interrelation between functions.

F2: Knowledge development → F1: Entrepreneurial experimentation and production

Knowledge is developed through entrepreneurial experiences when establishing companies and commercialising the product. Through experiential learning, actors have moved from customised to modular implants.

F3: Knowledge diffusion though networks → F1: Entrepreneurial experimentation and production

Knowledge is diffused through the network from the university where developments are commercialised. Innovation in academia is limited to the ideation and proof of concept phases. After those phases, companies and entities must be started which would have to do the technology development and commercialisation of university IP. This includes selling and licensing IP. University actors have sought DUI (doing, using and interacting) partnerships with established manufacturers who have necessary infrastructure to build devices and served as consultants to established manufacturers, creating links between STI and DUI learning modalities.

F6: Resource mobilisation → F2: Knowledge development

In the author-inventor case, financial resources were the enabler to build infrastructure which was not available, and ensure a stream of human resources to perform research and development activities. All interviewees shared experiences of raising funds, domestically and internationally, for building research and manufacturing spaces. The availability of funding enabled the recruitment of researchers and post-graduate students to work on projects. South African organisations funding research and development discussed in these endeavours were the National Research Foundation, South African Medical Research Council, and the Industrial Development Corporation. International funding organisations included the National Institute of Health and the Wellcome Trust. Funding was also sought from collaborators, and through writing joint funding applications with collaborators.

Lack of funding also drove innovation and knowledge development. P6 and P9 shared experiences on the need to develop devices because the options available were so expensive it had motivated them to develop alternatives. P9 further mentioned that limited funding resulted in more responsible choices of research projects to pursue, focusing on projects which would result in greater per capita returns, rather than "blue-sky" projects.

F6: Resource mobilisation → F3: Knowledge diffusion through networks

Funding enabled visiting professorships and sabbaticals, which were means of knowledge diffusion.

9.2.3.4 Relating the knowledge functions to TIS-contextual factors

The findings presented in this section were grouped according to the TIS-contextual factor categories of Bergek et al. (2015) as presented in Table 13. "Knowledge development" and "knowledge diffusion through networks" was most strongly influenced by the sectoral and geographical contexts. As in the translational collaboration case, no findings were categorised as political factors.

Table 13: Knowledge development and knowledge diffusion through networks functions grouped according to the TIS-contextual factors of Bergek et al. (2015) in the author-inventor case

	Sectoral context	**Geographical context**
Knowledge development	University actors have a limited role in the orthoapedic devices TIS.	National and international funding agencies support the establishment of facilities, device development, and knowledge exchange activities.
Knowledge diffusion through networks	University actors create partnerships with manufacturers to commercialise devices. In this way they create STI-DUI partnerships.	Collaboration with international universities enables access to specialists to establish local facilities.
	University and industry actors collaborate to establish specialised facilities.	Collaboration with international universities is based on common research areas.
	University and healthcare actors collaborate in post-graduate student projects. Healthcare actors are usually co-supervisors and provide access to resources.	
	Universities usually own IP in collaborative projects; this discourages collaboration with other sectors.	
	There are operating barriers between engineers and surgeons in collaboration. Education on how actors from other sectors operate is needed in collaboration.	

9.2.4 Analysis of the South African context

In this section, findings that were coded as “South African context” are reported as themes related to factors that influence the TIS which may be specific to South Africa. The responses were largely drawn from four questions posed to interviewees in part three of the interview about their perceptions of knowledge development and exchange in the orthopaedic devices TIS in South Africa. The questions were:

1. Are the types of devices South African organisations focussing on addressing the needs of the country?
2. Is there enough inter-sectoral collaboration in orthopaedic device development in South Africa?
3. Is there adequate knowledge exchange across geographical borders? Whom are we learning from? Whom are we influencing?
4. What is your opinion about the quality of work produced by South African actors in orthopaedic device development with whom you have worked? Are there South African actors with whom you wish to work? Are there international actors with whom you wish to work?

9.2.4.1 Addressing the South African burden of disease

There were varying responses from interviewees about their perception of South African organisations addressing the orthopaedic burden of disease in South Africa. Those interviewees who were of the opinion that South African organisations are addressing the South African burden of disease, indicated that locally developed and manufactured devices were of good quality and were sold at a fraction of the cost of imported devices. One interviewee from the university sector pointed out that, while the need may be addressed, the solution is rarely implemented: “…there’s always a need and we identify and we really try to find a solution for the need. The issue is, it never gets to the people, it’s always in the academic exercise - the person finishes his masters and that’s where it stops … we rarely build on projects … We never actually take whatever they found, whether bad or good and do another run of iterations and refine and get a product out … it never gets to that point where we actually implement what we are doing.”

Those interviewees who agreed that South African organisations were not addressing the orthopaedic burden of disease offered some insights. These include that developments from industry actors were focussed on earning and export potential, and that locally developed devices had limited acceptance in the domestic market.

9.2.4.2 Inter-sectoral collaboration for orthopaedic device development in South Africa

The following emerged from the interviewees' responses on inter-sectoral collaboration.

1. Actors recognise that inter-sectoral collaboration is necessary for orthoapedic device development in South Africa.
2. While inter-sectoral collaboration has not always been present in orthopaedic device development in South Africa, it is improving.

Actors from different sectors may have different expectations which limit or discourage collaboration for orthoapedic device development. One way to overcome these is through education and setting realistic expectations in collaborative research.

9.2.4.3 International collaboration for orthopaedic device development in South Africa

P1, P7 and P8 indicated that there was enough international collaboration. P1 indicated that South African professionals in other countries were a valuable resource and an opportunity to develop devices and introduce products into those markets. The interviewee responses suggest that collaboration with international partners is taking place, at a sufficient scale.

9.2.4.4 Quality and stigma of South African developments

While the quality of South African developments was reported to vary, the introduction of medical device regulations is expected to regulate and standardise the industry. Several interviewees were proud of the good quality work done by their organisations as well as fellow South African organisations; there was however some concern over quality control and stigma attached to South African developments – of products not being well researched and being produced in facilities of big international organisations.

Beyond these four questions, there were other instances that were coded as "South African context". Only South African contextual factors related to "knowledge development" and "knowledge diffusion through networks" have been discussed here. Interviewees mentioned the weak South African currency (the Rand) and its attraction for local device development and import substitution, as well as South Africa as an attractive destination for development, due to lower costs than in other parts of the world.

9.3 Development of theory

Some of the findings from the interviews suggests that multiple perspectives exist. In other instances, the results of the interviews converge towards a single perspective. The development of theory from the cases presented and strengthened by triangulation with the findings presented in the earlier chapters. The propositions of the theory, along with supporting evidence, are summarised in Table 14, and discussed later in this section.

Table 14:Propositions and evidence showing that "knowledge development" and "knowledge diffusion through networks" of the orthopaedics devices TIS are influenced by TIS-contextual factors

Proposition	**Source of Findings**	**Findings**
1. Inter-sectoral collaboration supports orthopaedic device development.	Interviews	• Interviewees acknowledged that inter-sectoral collaboration is necessary for orthoapedic device development in both cases.
	Networks	• In the scientific publication actor-collaboration network, the sectorisation index shows a preference of national actors to participate in inter-sectoral collaboration with other national actors. • In the patent actor-collaboration networks, the sectorisation index shows a preference of national actors to participate (almost exclusively) in inter-sectoral collaboration with other national actors.
	Literature	• Lander & Atkinson Grosjean (2011) and Lander (2013) illustrated the importance of inter-sectoral collaboration in the biomedical innovation chain. • Chimhundu et al. (2015) and de Jager et al. (2017) illustrated inter-sectoral collaboration in cardiovascular medical devices and medical device development in South Africa, respectively.
2. The university actor has an important, but limited role, in the orthopaedic devices TIS.	Interviews	• Results from translational collaboration case interviews illustrate absence of university actors in device development. • In the author-inventor case, interviewees described the limited role of the university actor in orthopaedic device development: scientific discovery, initial research and prototyping, and the protection of IP. Partnerships with DUI partners are created for technology development and commercialisation of devices.
	Institutional review	• The TTO and TTO institutions may limit university involvement beyond the research and development phase.
	Networks	• National research-intensive universities had key positions (high degree and betweenness centrality) in the scientific publication actor-collaboration network.
	Literature	• Lander (2013), Chimhundu et al. (2015) and de Jager et al. (2017) showed that university actors were key actors, having high degree and betweenness centrality, in their respective biomedical innovation networks.
3. The healthcare sector has an important role in knowledge development.	Interviews	• Interview results confirm that development occurs in collaboration with healthcare actors.
	Networks	• Healthcare actors are present in the scientific publication and patent actor-collaboration networks.
	Literature	• Healthcare sector actors are present in development networks for cardiovascular devices (Chimhundu et al. (2015) and medical devices more broadly (de Jager, Chimhundu, Saidi, & Douglas, 2017) in South Africa. • Hicks & Katz (1996) identified hospitals as an application site where biomedical research activity takes place.

	Institutional review (negative evidence)	• The Bio-economy Strategy does not explicitly include the healthcare actor in the quadruple helix model. • Other healthcare related institutions may promote or hinder healthcare actor participation in biomedical innovation. As an example, HPCSA regulations limit the role of the healthcare professional in commercialisation of medical devices.
4. Knowledge development and exchange create legitimacy to support the acceptance of developed devices.	Interviews	• Knowledge is developed on clinical performance of novel implants on for devices to be accredited by medical insurance companies. • Clinical trials are conducted for regulatory approval of medical devices.
	Institutional review	• Knowledge development is necessary for devices to comply to medical device regulations, national and international, including FDA, CE and SAHPRA. • Medical insurance companies require evidence for approval of devices and reimbursement for their use.
	Literature or other documentation	• Research evidence is included in information relating to what knowledge is required for regulatory approval (FDA, CE) from respective websites. • NAPPI registration requires regulatory approval and clinical evidence of performance (www.medikredit.co.za).
5. Affordability of available devices is a driver of knowledge development.	Interviews	• Innovations are sometimes a response to options available on the market being too expensive.
	Institutional review	• National Health Act promotes cost-effective solutions to deliver healthcare. • Initiatives of SAMRC/PATH and TIA to support the development of cost-effective medical device solutions.
6. Knowledge development is enhanced by innovation in allied fields.	Interviews	• Advances in process innovations (3D printing and additive manufacturing) have given rise to advances in orthoapedic device development. • Advances in biomaterials have made certain implants more realisable.
	Institutional review	• The South African Additive Manufacturing Strategy supports orthoapedic device development.
	Literature	• Bergek et al’s (2008b) discussion on “development of positive externalities” presents a TIS function that captures the dynamics between innovation in related research fields.

Proposition 1: Inter-sectoral collaboration supports orthopaedic device development

While there are differences in the types of inter-sectoral collaboration described by interviewees, there is acknowledgement that successful innovation in orthopaedic device development arises from collaboration across sectors, particularly between engineers/technicians and surgeons. The arenas where inter-sectoral knowledge exchange takes place were at conferences and congresses, operating theatres and mechanical workshops. Other knowledge exchange modalities include thesis examination and lecturing. These knowledge exchange modalities are largely tacit in nature.

In the scientific publication and patent actor-collaboration networks presented in earlier chapters, the sectorisation index reveals the preference of national actors to participate in inter- or intra-sectoral collaboration with other national actors. In the scientific publication actor-collaboration network, all national sectors prefer inter-sectoral collaboration, to varying degrees. The healthcare and industry actors showed preference for inter-sectoral collaboration across all timeframes. The university sector largely showed preference for inter-sectoral collaboration but did show preference for intra-sectoral collaboration in some of the timeframes. In the patent actor-collaboration networks, of the national actors who do participate in collaboration, actors from the university, healthcare and industry sectors prefer inter-sectoral collaboration.

Lander & Atkinson-Grosjean (2011) and Lander (2013) put forward that the "biomedical innovation system" relies on public sector institutions, including universities and hospitals, as well as the private sector industry. Lander (2013) showed that in the infection and immunity network in Vancouver, Canada, innovation is dominated by interactions between universities and hospitals, both non-commercial sectors. Chimhundu et al. (2015) found inter-sectoral collaboration between the university and healthcare sector to be the most prominent type of collaboration in scientific knowledge production for cardiovascular medical device development in South Africa. de Jager et al. (2017) identified organisations and sectors active in medical device development in South Africa and quantified the extent of intra- and inter-sectoral collaboration. They found the university and healthcare sectors collaborated extensively both intra- and inter-sectorally.

Both cases reported orthopaedic device development in the absence of a specific sector. In the translational collaboration case, developments occurred in the absence of university actors; in the author-inventor case, developments occurred in the absence of industry actors. In both cases however, the healthcare actor was highlighted as being a significant actor in the development of orthopaedic devices. Approximately 15% of the publications in the publication and patent actor-collaboration networks emanated from translational collaboration, which suggest orthopaedic device development can take place in the absence of translational collaboration across three sectors.

There is however evidence in the actor-collaboration networks of knowledge being developed by one actor (self-reflecting ties), and therefore one sector, in a small number of cases. There are also instances where scientific publications and patents arose from intra-sectoral collaboration only. There are also barriers to inter-sectoral collaboration, which include unmatched expectations from partners in collaboration, different perspectives on IP ownership, and burdensome university administrative processes. Education on the roles and limitations of each sector in the collaborative partnership is necessary to address these barriers.

Proposition 2: The university sector has an important, but limited, role in the orthopaedic devices TIS

In the translational collaboration case, interviewees described device development in the absence of university actors. Universities do have their place in orthopaedic device development, in providing access to infrastructure that industry could not afford to build. Interviewees in the author-inventor case pointed out the limited role that universities play in orthoapedic device development. Much university-based work towards orthopaedic device development never reaches implementation.

The institutional review presented the typical innovation pipeline for medical device development emanating from universities (Appendix L), which often ends at research or early-stage development, with TTOs playing a role in liaising with industry to further develop and commercialise the technology.

Universities were found to be key actors in the scientific publication actor-collaboration networks and were instrumental in developing knowledge and diffusing it through the network. The industry actors who collaborate with university actors towards scientific knowledge production are largely multinational corporations, and South African entities running local operations of the multinational corporations. This suggests that national university actors are attractive collaborators for multinational corporations for scientific knowledge production. As these multinational corporations do not appear in the patent actor-collaboration network, it suggests that national university actors are sought for their early phase research and development discoveries, i.e. national universities are STI partners. In the patent actor-collaboration network, only seven national universities are represented, and the creation of spin-off companies to develop and commercialise technology is evident. This evidence from the scientific publication and patent actor-collaboration networks illustrates that the university has an important role in the knowledge development and exchange in the orthopaedic devices TIS, while the interviews have shown this role to be limited.

Proposition 3: The healthcare sector has an important role in knowledge development

In addition to identifying clinical needs, healthcare actors conceive design ideas, and offer ideas on the practical implementation of device design and surgical techniques. Healthcare actors also have specialised resources and infrastructure, including operating theatres and access to patients.

In the scientific publication and patent actor-collaboration networks, healthcare actors account for approximately 40% of the actors. In the scientific publication actor-collaboration network, healthcare actors having high degree centrality were academic hospitals with close ties to research intensive universities. In the patent actor-collaboration network, many healthcare actors were private sector clinicians who patent in isolation. Chimhundu et al. (2015) and de Jager et al. (2017) found the healthcare sector to be significant contributor to cardiovascular medical device development and medical device development, respectively, in South Africa. Hicks & Katz (1996) found hospitals to be a site of application for biomedical research in the UK research system; hospitals made a more substantial contribution than industry to the science base in the biomedical innovation system.

While the important contribution the healthcare sector makes towards knowledge development in health technology has been shown, in the South African medical devices ecosystem presented in Bunn (2018), the healthcare sector was not regarded as an innovator in the innovation ecosystem. The role of healthcare actor in the South African medical device ecosystem appears to be limited to identifying the local needs in medical device innovation and being the users of medical devices. As presented in the institutional review, the Bio-economy Strategy recommends a “quadruple helix” model of innovation in medical device development to address the South African burden of disease, which does not explicitly include healthcare as one of the helices in the innovation model. The patent actor-collaboration networks and the institutional review have highlighted underutilisation of innovation potential in the healthcare sector, showing that opportunities exist for private healthcare groups to exploit and promote the knowledge already being created by individuals within their healthcare facilities.

The actor-collaboration network analyses have shown that orthopaedic device development also takes place in the absence of healthcare actors.

Proposition 4: Knowledge development and exchange create legitimacy to support the acceptance of developed devices

Legitimation is the socio-political process of creating legitimacy for a technology through the actions of actors; it includes formation of the actors’ expectations and visions and extends to compliance with relevant institutions and social acceptance (Bergek, Jacobsson, & Sanden, 2008b). Legitimacy is necessary for resource mobilisation, demand creation, and attainment of political strength by actors in the TIS (Aldrich & Fiol, 1994). Legitimacy is required for the formation of new industries and new TISs, and for having new technologies accepted as alternatives to existing ones (Bergek, Jacobsson, & Sanden, 2008b).

In the interviews, four scenarios were reported which illustrated that knowledge was developed and/or exchanged to create legitimacy for orthopaedic devices. These are:

1. Knowledge was created on the clinical performance of the device for reimbursement by medical insurance companies.
2. Knowledge was created to show acceptable clinical performance of novel implants.
3. Knowledge was created through clinical trials for Food and Drug Administration regulatory approval, so that the device could be sold in the American (and other international) markets.
4. Knowledge was developed and exchanged by key orthopaedic surgeons to endorse or demonstrate a device; this was often shared at conferences/congresses which were an arena to promote the technology, an example of expert legitimation as described by Bergek et al. (2008b).

The market in which the medical device is sold has certain regulatory requirements for the device to enter the market. South African medical device regulations were passed in December 2016; and the South African Health Product Regulatory Authority (SAHPRA) is still establishing capacity to review and approve medical devices. This may take several years. In the interim, recognised regulatory approval such as CE markings and FDA approvals may be the quickest route to bring a product to the South African market (University of Cape Town, 2018). Both the CE and FDA systems clearly require knowledge development on the device for it to receive its regulatory approval, a key form of legitimacy.

Proposition 5: Affordability of available devices a driver of knowledge development

In the interviews, there were two instances – both in the author-inventor case – which illustrated that knowledge development and exchange occurred due to the options available on the market not being affordable and alternatives being developed that were cost effective.

The institutional review showed that innovation in medical device development, and health research in general, directed at cost-effective solutions, is encouraged or incentivised. This is evident in the National Health Act, Act 61 of 2003, which mandates that the cost-effectiveness be considered of interventions aimed at reducing the burden of disease. The SAMRC has an agreement with PATH which involves activities for the promotion of *access to affordable and appropriate medical device*s, diagnostics and vaccines in South Africa through research and development, technology transfer, and local manufacture (South African Medical Research Council and PATH, 2014). Under the health focus of TIA, the objectives include investing in projects that focus on the development of affordable health products that address the South African burden of disease. This evidence from the institutional review illustrates how government and its agencies are promoting cost-effective solutions in health technology research. Espoused support for medical device innovation by government institutions can't be assumed to be causative factors for the findings of the case studies; the presence of supportive institutions has however been noted.

The finding of affordability of available devices as a driver of knowledge development exists alongside available resources as an enabler of knowledge development, which is an accepted feature of TISs and for which evidence was shown in the interviews.

Proposition 6: Knowledge development is enhanced by innovation in allied fields

The code "Innovation in allied fields" has similar elements to that described by the function "development of positive externalities" of Bergek et al. (2008b). In their framework, two or more emerging TISs are related if they share structural elements (actors, networks, technology or institutions). Bergek et al. explain that the related TISs may mutually benefit from functions moulding these elements. This means that the strengthening of one TIS function may result in positive externalities that promote the development of the structural elements of another (related) TIS.

In the interviews two points were raised which highlighted that knowledge created in the orthopaedic devices TIS was enhanced by innovations in allied fields:

1. Advances in 3D printing and additive manufacturing resulted in advances in orthopaedic device development.
2. Advances in biomaterials made certain implants more realisable.

Additive manufacturing is a process innovation, the implementation of which is expected to yield product gains through better performing production processes. Additive manufacturing has made patient-specific orthopaedic implants realisable.

The orthopaedic devices TIS and the additive manufacturing TIS share two structural elements: actors and institutions. As an institution, A South African Additive Manufacturing Strategy (Department of Science and Technology, 2016) speaks explicitly to medical implants, including orthopaedic applications, and to the promotion of knowledge development and exchange among different stakeholders for the use of additive manufacturing platforms for medical implants. South Africa already has an additive manufacturing centre which has ISO 13485 quality assurance to manufacture medical implants at the Centre for Rapid Prototyping and Manufacturing (CRPM) at the Central University of Technology.

One of the authors of A South African Additive Manufacturing Strategy, Professor Deon de Beer, is also a co-author on two articles in the scientific publication actor-collaboration network. Professor de Beer has been a knowledge creator in rapid prototyping/3D printing/additive manufacturing with focusses on final parts manufacturing, new material development, impact and economic aspects, as well as foundry, casting and medical industry focusses (Oxford, 2015). He, an actor, is therefore evidence of a shared structural element between the two TISs. The point made here is that, while Professor de Beer is an actor in orthopaedic devices, his academic profile lies more broadly in additive manufacturing theory and applications, and this academic profile may have enhanced his contribution to orthopaedic device innovation.

9.4 Limitations of the study

Each of the interviewees brought their career experience to the interviews. Their unique experiences and contributions towards knowledge development and exchange in the orthopaedic devices TIS adds to the findings, interpretations and conclusions drawn in this study. The response rate to the call for participation into the case studies was low. More interviewee experiences would certainly have added richness to the findings presented here. Additionally, only one interviewee was from the healthcare sector.

The interviewees highlighted how the actor-collaboration networks did not truly capture knowledge development and exchange activity of the orthopaedic devices TIS. Since interviewees were drawn from the pool of individuals identified through the scientific publications and patents which inform the actor-collaboration networks, those actors who do participate in creating knowledge in the TIS outside of what is captured by these two codified indicators, may have been missed.

9.5 Conclusion

This chapter has presented two case studies exploring aspects of knowledge development and diffusion in the orthopaedic devices TIS and have proposed theory that captures the findings from the case studies and from earlier chapters. The chapter has shown that inter-sectoral collaboration supports knowledge development in the TIS and highlighted the roles of actors from different sectors, particularly those of university and healthcare actors. Knowledge development was highlighted as being an important process, particularly in creating legitimacy for the device. Within the South African context, innovation in the orthoapedic devices TIS was found to have been driven by the affordability of available devices, and positively influenced by innovation in the additive manufacturing TIS.

These findings have provided an understanding of the way in which knowledge is developed and diffused through networks and of the processes and contexts that affect knowledge development and diffusion through networks in the TIS.

10. Conclusion

This thesis hypothesised that “knowledge development” and “knowledge diffusion through networks” of the orthopaedic devices technological innovation system (TIS) are influenced by TIS-contextual factors. While the hypothesis is broad, the objectives provide a narrower focus. In addressing the objectives of the study, evidence has been found to support the hypothesis. The project identified knowledge creators using codified knowledge indicators and related them in a social network analysis through co-authorship and co-inventorship to examine knowledge diffusion through networks in the orthopaedics devices TIS. A keyword network analysis was performed, which identified research focus areas in the TIS and related the actors based on their cognitive distance, highlighting collaboration potential in the actor-collaboration network. The institutions that impact the TIS were reviewed, completing the structural analysis of the TIS. A set of case studies, in which actors of the TIS were interviewed, investigated knowledge development and diffusion to determine contextual factors that may influence TIS development. This chapter concludes the thesis by illustrating how the objectives of the research have been achieved and linking the objectives to propositions developed in the case studies.

10.1 Objective 1: Nature of relationships among actors

The first objective of this thesis was to identify the actors that develop knowledge in the orthopaedic devices TIS and to characterise the relationships between them. The actors were identified, and the relationships between them were determined using analysis of scientific publication and patent actor-collaboration networks.

Creators of scientific knowledge, as determined by analysis of scientific publications, were found to be largely from the university and healthcare sectors; industry and science council actors played a lesser role. Key actors in the actor-collaboration network were largely research-intensive national universities and their associated academic hospitals. Scientific knowledge production was shown to be collaborative; knowledge diffusion through the network, however, was shown to be limited and localised to components of the network dominated by national universities. The TIS was largely internationalised, becoming more nationalised over time. The shift towards a nationalised TIS was attributed to national actors becoming more established and being able to create knowledge among themselves. This positive shift could facilitate development focussed on national interests.

Technological knowledge, as determined by analysis of patenting activity, was found to be produced largely by South African actors, in almost equal shares by university, healthcare and industry actors. A few actors patented many inventions, while many inventors only filed one patent. The patent actor-collaboration network showed that actors, particularly private healthcare actors, patent in isolation resulting in highly fragmented networks, with many inventors patenting in their personal capacity. There was evidence that knowledge translation occurs between the scientific and technological domains in the TIS, with the presence of patent-paper and author-inventor pairs.

In the case studies (Chapter 9), several interviewees indicated that the scientific publication and patent actor-collaboration networks did not truly capture knowledge development and exchange activity in the orthopaedic devices TIS, based on absent links between themselves and other actors. Other knowledge development and exchange activities include: the supervision of post-graduate students; curriculum advice, lecturing and teaching responsibilities; student exchange programmes; visiting professorships and sabbaticals; examination of theses; workshops and training; hosting, attending and presenting at conferences; accessing laboratories of other universities; consulting; creating media; inviting surgeons to industry facilities; the interaction of surgeons and engineers/technicians in mechanical workshops and operating theatres; participation in industry associations; and day-to-day interactions.

The institutional review of Chapter 8 identified actors that facilitate knowledge development and exchange in the TIS and highlighted further roles of actors already identified in the orthopaedic devices TIS through patent and publication actor-collaboration networks. The institutional review has presented a set of institutions intended to support medical device innovation in South Africa, which may influence the behaviour of actors of the TIS. The case studies have enriched the network analysis presented in the earlier chapters, by providing a more holistic picture of knowledge development and exchange in the TIS. The case studies also showed that beyond research and development activity, knowledge development and exchange create legitimacy to support acceptance of developed devices (Proposition 4).

10.2 Objective 2: Research focus areas

The second objective of the project was to establish the focus areas of orthopaedic device development in South Africa. The research areas of scientific knowledge development were identified in the keywork networks presented in Chapter 7. The actors create knowledge in a wide range of orthopaedic applications, in both traditional and new orthopaedic research areas, including orthopaedic software, instrumentation, diagnostic equipment, biomaterials, braces, cages, plates, prostheses for major and minor joints, and customised implants.

10.3 Objective 3: Drivers and barriers

The third objective of the project was to provide insight into what drives and hinders “knowledge development” and “knowledge diffusion through networks” in the orthopaedic devices TIS in South Africa.

The drivers of knowledge development and exchange were found to be: inter-sectoral collaboration (Proposition 1); the availability of resources; affordability of available devices (Proposition 5); and the positive externalities of allied TISs (Proposition 6).

Actors from different sectors have different and defined roles in inter-sectoral collaboration (Propositions 2 and 3), and successful developments arise where partners are aware of each other’s mode of operation and have reasonable expectations from the collaboration. Funding enables knowledge development and exchange; it can translate into resources of other kinds, including human resources and infrastructure, which further advance knowledge development and exchange. The affordability of available devices stimulates innovation in a different way, resulting in more responsible use of resources with cost-effective solutions (Proposition 5).

Progress in the additive manufacturing TIS positively influenced knowledge development and exchange in the orthopaedic devices TIS. Even though the TISs may exist and mature separately from each other, they have become mutually enabling, with shared structural elements. Thus, knowledge development is enhanced by innovation in allied fields (Proposition 6).

The main barrier to knowledge development and knowledge diffusion through networks of the orthopaedic devices TIS were barriers to inter-sectoral collaboration. These include unmatched expectations from partners in collaboration, different perspectives on IP ownership, and burdensome university administrative processes.

10.4 Objective 4: Contextual factors

Bergek et al. (Technological innovation systems in contexts: Conceptualizing contextual structures and interaction dynamics , 2015) explained that technologies develop differently in different contexts. Through the explicit consideration of context, an increased understanding of the peculiarities of individual TISs is achieved and provides a basis for a classification, generalisation and transfer of findings, which is important for TIS-based policy making. The aim here was not to generalise findings but to highlight the way in which knowledge development and exchange in the orthopaedic devices TIS is influenced by its contextual factors.

The findings of the case studies revealed that the TIS is influenced by the embedded TIS and sectoral contextual factors. Evidence has been found to support the hypothesis of this thesis, that “knowledge development” and “knowledge diffusion through networks” of the orthopaedic devices TIS are influenced by TIS-contextual factors. The knowledge functions were shown to be structurally coupled to the embedded and sectoral contexts, and externally linked and structurally coupled to the political context.

The orthoapedic devices TIS in South Africa was shown to be structurally coupled to the additive manufacturing TIS in South Africa. The horizontal linking between these TISs has shown that the maturation of each of these TISs positively enhances that of the other.

Sectoral dynamics are certainly at play in the TIS. In both forms of knowledge production, science council actors were found to play a lesser role in creating knowledge, but were however shown to be funders of medical device development and knowledge exchange initiatives, as well as creators of innovation pathways to facilitate technology transfer from publicly financed research. The bureaucratic nature of universities, accompanied by burdensome administration, dependence on an academic cycle, and unrealistic costs of research, discourage inter-sectoral collaboration. While healthcare actors are central to orthopaedic device development, they lack supportive institutions. This may be a deterrent to innovation by clinicians; however, a favourable pathway for healthcare actors to get their product to market – by serving as consultants to industry – was identified.

The orthopaedic devices TIS is part of the broader national system of innovation (NSI) in South Africa and is affected by innovation policy from various government departments. On the political front, government policy and initiatives in innovation, and specifically in medical device innovation, have been introduced with the intention of promoting knowledge development and exchange. However, clear causal pathways from these policies and initiatives, to the development of the orthopaedic devices TIS, cannot be concluded, as an analysis of policy implementation was beyond the scope of the study. Nonetheless, an effect of the Intellectual Property Rights by Publicly Financed Research Act, Act 51 of 2008, on behaviour change by university actors, was suggested in the patent actor-collaboration networks of Chapter 6. Patenting by universities is further expected to increase with the Department of Higher Education and Training rewarding patents with equal weighting to journal articles in its revised Research Output Policy.

South Africa’s NSI comprises a wide variety of institutions and organisations playing complementary roles in scientific and technological knowledge production in the country (Manzini, 2012). Success of the TIS lies in having institutional alignment between those policies that steer actor behaviour in the NSI, and specific policies geared towards the TIS. While government strategies are attempting to co-ordinate engagement among actors from different sectors, healthcare actors must be recognised as knowledge creators in the innovation chain, and attempts should be made to allow for institutional alignment of the healthcare sector to those of the government strategy (the Bio-economy Strategy as an example). Geographical factors played a lesser role. While international actors have a strong presence in terms of the number of actors contributing towards the actor-collaboration networks, many only appear on one publication. Their presence, however, is noted with the contribution of bringing new ideas into the network. Of concern is that, in both publication and patent actor-collaboration networks, there is no evidence of co-authorship and co-inventorship with actors from other African countries, despite government policies having been written with the African and SADC agenda in mind and national universities identifying themselves as being African universities.

10.5 Limitations and recommendations

Co-authorship as a proxy for collaboration has been used extensively in SNA studies. In this study, co-authorship was used to characterise the relationships among actors who produce scientific publications for orthopaedic devices in and with South African organisations. Co-authorship of publications captured activity from a very specific tier of knowledge generation. Within this tier, funding detail was not captured, and citation analysis was not performed to explore broader knowledge diffusion than that captured within the network. Co-inventorship as a proxy for collaboration has been used less extensively in SNA studies. The lack of bibliographic detail available in patent data, limits the use of patents. An objection raised against co-inventorship to illustrate knowledge exchange among inventors, is that inventorship only reflects a small subset of the knowledge exchange that takes place for technological development. The case studies revealed that the scientific publication and patent networks did not truly capture knowledge development and exchange activity in the orthopaedic devices TIS. Furthermore, the institutional review identified actors who are able to facilitate knowledge development and exchange in the TIS. It is important to acknowledge here that the scientific and patent networks, based on co-authorship and co-inventorship, are not sufficient on their own to capture knowledge development and diffusion through networks.

Knowledge networks that aim to capture innovation in developing countries should be based on appropriate indicators. Kebede & Mitsufuji (2017) proposed an approach to distinguish between research and development-based TISs and diffusion-based TISs, using knowledge indicators that would be suited to developing countries. These knowledge indicators inlude feasablity studies, market assessments, and technology adapted from developed economies. This research has revealed some sources of such indicators for the orthopaedic devices TIS in South Africa; these include national conferences of importance to the orthopaedic community, joint meetings involving different stakeholders, and activity in mechanical workshops and operating theatres. Future studies on TIS knowledge development and exchange for orthopaedic device development in South Africa, would benefit from an exploration of knowledge indicators derived from these sources, and from the development of approaches for their analysis.

In the patent actor-collaboration network, more than 10% of the retained patents had incomplete affiliation data and were omitted from further analysis. Strategies to link inventors to their organisational affiliations in a formal and robust manner would aid more comprehensive analyses. In the absence of a more robust system of establishing affiliations from patent bibliographic data, the methodology presented in Chapter 4 is a start to understanding these collaborative activities at an organisational level. Further work in this area is recommended.

Chapter 7 has presented a methodology for the analysis of keyword networks to highlight collaboration potential among actors in a network based on their cognitive distance, as an alternative to the co-citation analysis presented by Vida (2018). Comparative studies would reveal the relative strengths and weaknesses of the two approaches.

The institutional review of Chapter 8 presented formal (codified) institutions that impact the orthopaedic devices TIS. An analysis of how these institutions have been put into practice and their performance was beyond the scope of the project; such analysis in future work would provide understanding of how the espoused government support for medical device innovation translates into, or hinders, innovation.

The response rate for the case studies was poor and resulted in nine interviews. Only one of these interviews was with an actor from the healthcare sector. Given that the research has highlighted the important role of the healthcare sector in the orthopaedic devices TIS, greater representation from the healthcare sector would have enhanced the case studies.

10.6 Original contribution and implications

This thesis makes two methodological contributions. First, it extends the spatial indices presented by Binz et al. (2014) to sectoral indices to capture preferences among actors who participate in intra- and inter-sectoral collaboration. Second, it builds on keyword network methodologies to add a new approach for analysing social relationships among actors through cognitive distance.

This thesis adds to the body of knowledge on the application of the TIS framework in the developing country context, by examining a new setting and a new technological field. Previous studies using the functional approach of the TIS framework in a developing country setting have applied the framework to renewable energy applications.

The findings of the research suggest that certain contextual factors play a role in the orthopaedic devices TIS, as captured in the propositions derived in Chapter 9. Thus, evidence has been found to support the hypothesis that “knowledge development” and “knowledge diffusion through networks” of the orthopaedic devices TIS are influenced by TIS-contextual factors. In addition, the neglect of the role of healthcare actors as innovators has been highlighted.

The findings presented in this thesis may inform strategies towards the promotion of knowledge development and exchange for orthopaedic device innovation that are relevant to the South African context. Specifically, this thesis has highlighted the roles of the university and healthcare actors in creating knowledge in the orthopaedic devices TIS. It has also highlighted barriers to inter-sectoral collaboration, especially those stemming from universities. In a co-ordinated National System of Innovation, actors have defined roles and established pathways for collaboration. By highlighting the roles that different actors play and the barriers they experience in collaboration, the findings of this study address limitations in the current conceptualisation of medical device innovation in South Africa and may inform national strategies such as the Bio-economy Strategy, as well as university strategies for collaboration.

References

Academy of Medical Sciences. (2010). *Academia, industry and the NHS: Collaboration and innovation. Meeting report.* The Academy of Medical Sciences FORUM.

Aldrich, H., & Fiol, M. (1994). Fools rush in? The institutional context of industry creation . *Academy of Management Review, 19*(4), 645-670.

Alessandrini, M., Klose, K., & Pepper, M. (2013). University entrepreneurship in South Africa: Developments in technology transfer practices. *Innovation, 15*(2), 205-214. doi:10.5172/impp.2013.15.2.205

Analytic Technologies. (2010). *Description*. Retrieved April 12, 2019, from http://www.analytictech.com/ucinet/description.htm

Andersen, B. (2004). Paradigms and trajectories of technological opportunities 1890-1990. In H. Moed, W. Glanzel, & U. Schmoch (Eds.), *Handbook of quantitative science and techology research - The use of publication and patents statistics in studies of S&T systems* (pp. 133-162). Kluwer Academic Publishers.

Asheim, B., & Coenen, L. (2005). Knowledge bases and regional innovation systems: Comparing Nordic clusters. *Research Policy, 34*, 1173-1190.

Balconi, M., Breschi, S., & Lissoni, F. (2004). Networks of inventors and the role of academia: an exploration of Italian patent data. *Research Policy, 33*, 127-145.

Barabasi, A., & Albert, R. (1999). Emergence of scaling in random networks. *Science, 286*(5439), 509-512.

Batool, K., & Niazi, M. (2014). Towards a methodology for validation of centrality measures in complex networks. *PlosONE, 9*(4), 1-14. Retrieved from https://doi.org/10.1371/journal.pone.0090283

Bergek, A., Hekkert, M., Jacobsson, S., Markard, J., Sanden, B., & Truffer, B. (2015). Technological innovation systems in contexts: Conceptualizing contextual structures and interaction dynamics . *Environmental Innovation and Societal Transitions , 16*, 51–64 .

Bergek, A., Jacobsson, S., Carlsson, B., Lindmark, S., & Rickne, A. (2008a). Analysing the functional dynamics of technological innovation systems: A scheme analysis. *Research Policy*, 37, 407-429.

Bergek, A., Jacobsson, S., & Sanden, B. (2008b). 'Legitimation' and 'development of positive externalaties': Two key processes in the formation phase of technological innovation systems. *Technology Analysis & Strategic Management, 20*(5), 575-592.

Binz, C., Truffer, B., & Coenen, L. (2014). Why space matters in technological innovation systems—Mapping global knowledge dynamics of membrane bioreactor technology . *Research Policy, 43*, 138–155 .

Blum, N., Bening, C., & Schmidt, T. (2015). An analysis of remote electric mini-grids in Laos using the Technological Innovation Systems approach. *Technological Forecasting & Social Change, 95*, 218-233.

Borgatti, S. (2002). Netdraw software for network visualisation. Lexington, KY: Analytic Technologies.

Borgatti, S., & Everett, M. (1997). Network analysis of 2-mode data. *Social Networks, 19*(3), 243-269.

Borgatti, S., Everett, M., & Freeman, L. (2002). Ucinet for Windows: Software for social network analysis. Harvard, MA: Analytic Technologies.

Boschman, R., & Frenken, K. (2010). The spatial evolution of innovation networks. A proximity perspective. In R. Boschma, & R. Martin (Eds.), *Handbook of Evolutionary Geography* (pp. 120-135).

Bradshaw, N., Schneider, P. D., & Groenewald, P. (2006). *Revised burden of disease estimates for the comparitive risk factor assessment, South Africa 2000. Methodological Note.* Cape Town: South African Medical Research Council.

Braun, T. (2004). Keeping the gates of science journals - Gatekeeping indicators of national performace in the sciences. In H. Moed, W. Glanzel, & U. Schmoch (Eds.), *Handbook of quantitative science and technology research: The use of publication and patent statistics in studies of S&T systems* (pp. 95-114). Kluwer Academic Publishers.

Breschi, S., & Lenzi, C. (2015). The role of external linkages and gatekeepers for the renewal and expansion of US cities' knowledge base, 1990-2004. *Regional Studies, 49*(5), 782-797. doi:10.1080/00343404.2014.95434

Breschi, S., & Lissoni, F. (2004). Knowledge networks from patent data: Methodological issues and research targets. In H. Moed, W. Glanzel, & U. Schmoch (Eds.), *Handbook of quantitative science and technology research - The use of publication and patent statistics in studies of S&T systems* (pp. 613-643). Kluwer Academic Publishers.

Bridge. (2020). *Universities of technology*. Retrieved December 15, 2020, from https://www.bridge.org.za/knowledge-hub/psam/he/universities-of-technology/

Brittanica. (2017). *Network Sociology*. Retrieved February 2, 2020, from https://www.britannica.com/topic/idea

Brown, J., & Duguid, P. (1991). Organisational learning and communities-of-practice: Toward a unified view of working, learning and innovation. *Organisational Science, 2*, 40-57.

Bunn, T. (2018). Initiatives to strengthen academia-industry linkages and grow the local manufacturing sector through medical device innovation and commercialisation. Stellenbosch: South African Biomedical Engineering Conference.

Cambridge. (2020). *Organization*. Retrieved February 2, 2020, from https://dictionary.cambridge.org/dictionary/english/organization

Cape Peninsula University of Technology. (2010). *Technology transfer and industrial linkages*. Retrieved July 12, 2019, from https://www.cput.ac.za/research-technology-and-innovation/tto

Carayannis, E., & Campbell, D. (2009). 'Mode 3' and 'Quadruple Helix': toward a 21st century fractal innovation ecosystem. *International Journal of Technology Management, 46*(3/4), 201-234.

Carlsson, B., & Stankiewicz, R. (1991). On the nature, function, and composition of technological systems. *Journal of Evolutionary Economics*, *1,* 93-118.

Carlsson, B., Jacobsson, S., Holmen, M., & Rickne, A. (2002). Innovation systems: analytical and methodological issues. *Research Policy*, 233-245.

Central University of Technology. (2010). *Technology & Innovation*. Retrieved July 22, 2019, from https://www.cut.ac.za/technology-innovation

Centre for Rapid Prototyping and Manufacturing. (n.d.). *About Us*. Retrieved July 24, 2019, from https://www.crpm.co.za/

Chimhundu, C., de Jager, K., & Douglas, T. (2015). Sectoral collaboration networks for cardiovascular medical device development in South Africa. *Scientometrics, 105*, 1721-1741.

Chinchilla-Rodriguez, Z., Benavent-Perez, M., De Moya-Anegon, F., & Miguel, S. (2012). International collaboration in medical research in Latin America and the Caribbean (2003-2007). *Journal of the American Society of Information Science and Technology, 63*(11), 2223-2238.

Choi, J., Yi, S., & Lee, K. (2011). Analysis of keyword networks in MIS research and implications for predicting knowledge evolution. *Information & Management, 48*(8), 371-381.

Clarivate. (2019). *Web of Science conference proceedings selection process*. Retrieved December 15, 2020, from https://clarivate.com/webofsciencegroup/essays/web-science-conference-proceedings-selection-process/

Coenen, L., Benneworth, P., & Truffer, B. (2012). Toward a spatial perspective on sustainability transitions. *Research Policy, 41*(6), 968-979.

Council for Scientific and Industrial Research. (2015). *CSIR Shareholder's Compact - Cycle commencing 1 April 2015.* Retrieved January 22, 2019, from https://www.csir.co.za/csir-shareholders-compat-2015

Council for Scientific and Industrial Research. (2018). *CSIR Shareholder's Compact - Cycle commencing 1 April 2018.* Retrieved January 22, 2019, from https://www.csir.co.za/csir-shareholders-compact-201819

de Jager, K., Chimhundu, C., Saidi, T., & Douglas, T. (2017). The medical device landscape in South Africa: Institutions,sectors and collaboration. *South African Journal of Science, 113*(5/6), 1-8.

Deloitte. (2014). *Research to guide the development of strategy for the Medical Devices Sector of South Africa - prepared in partnership with the dti.* Retrieved February 9, 2020, from http://www.samed.org.za/DynamicData/LibraryDownloads/60.pdf

Department of Arts, Culture, Science and Technology. (1996). *White paper on science & technology.* Retrieved February 12, 2020, from https://www.gov.za/sites/default/files/gcis_document/201409/sciencetechnologywhitepaper.pdf

Department of Health. (2001). *Health research policy in South Africa.* Retrieved February 12, 2020, from https://www.gov.za/sites/default/files/gcis_document/201409/healthresearch0.pdf

Department of Health. (2016). Medicines and related substances Act, 1965 (Act No.101 of 1965) Regulations relating to medical devices and in vitro diagnostic medical devices (IVDs). Retrieved May 30, 2017, from https://www.emergogroup.com/sites/default/files/south-africa-regulations-medical-devices-ivds.pdf

Department of Higher Education and Training. (2013). *Report of the Ministerial Committee for the Review of the Funding of Universities.* Retrieved February 12, 2020, from http://www.dhet.gov.za/Financial%20and%20Physical%20Planning/Report%20of%20the%2

0Ministerial%20Committee%20for%20the%20Review%20of%20the%20Funding%20of%20Universities.pdf

Department of Higher Education and Training. (2015). *Research outputs policy.* Retrieved February 12, 2020, from https://libguides.wits.ac.za/ld.php?content_id=21220905

Department of Higher Education and Training. (2017). *Draft policy framework for the internationalisation of higher education in South Africa.* Retrieved February 12, 2020, from http://www.dhet.gov.za/Policy%20and%20Development%20Support/Draft%20Policy%20framework%20for%20the%20internalisation%20of%20Higher%20Education%20in%20Suth%20Africa.pdf

Department of Higher Education and Training. (2018). *Ministerial statement on university funding: 2019/20 - 2020/2021.* Retrieved June 14, 2019, from http://www.dhet.gov.za/SiteAssets/18%2012%2007%20Ministerial%20Statement.pdf

Department of Higher Education and Training. (2019). *Post-school education and training monitor - Macro-indicator trends.* Retrieved February 12, 2020, from http://www.dhet.gov.za/SiteAssets/Post-School%20Education%20and%20Training%20Monitor%20Report_March%202019.pdf

Department of Science and Technology. (2001). *A national biotechnology strategy for South Africa.* Retrieved February 12, 2020, from https://www.gov.za/sites/default/files/gcis_document/201409/biotechstrat0.pdf

Department of Science and Technology. (2002). *South Africa's national research and development strategy.* Retrieved February 12, 2020, from https://www.gov.za/sites/default/files/gcis_document/201409/rdstrat0.pdf

Department of Science and Technology. (2008). *The ten year plan for science and technology.* Retrieved February 12, 2020, from https://www.dst.gov.za/images/pdfs/The%20Ten-Year%20Plan%20for%20Science%20and%20Technology.pdf

Department of Science and Technology. (2013). *The bio-economy strategy.* Retrieved February 12, 2020, from https://www.gov.za/sites/default/files/gcis_document/201409/bioeconomy-strategya.pdf

Department of Science and Technology. (2016). *A South African additive manufacturing strategy.* Retrieved February 12, 2020, from https://www.dst.gov.za/images/2018/Additive%20Manufacturing%20Strategy.pdf

Department of Science and Technology. (2017). *Ke nako research and innovation for socio-economic impact now! A review of South African science, technology and innovation institutional landscape.* Retrieved February 12, 2020, from https://www.dst.gov.za/images/DST-institutional-review_Single-Page.pdf

Department of Science and Technology. (2019). *White paper of science, technology and innovation.* Retrieved February 12, 2020, from https://www.dst.gov.za/images/2019/WHITE_PAPER_ON_SCIENCE_AND_TECHNOLOGY_web.pdf

Department of Science and Technology. (n.d.). *Department of Science and Technology strategic plan for the fiscal years 2011-2016.* Retrieved February 12, 2020, from https://www.dst.gov.za/images/pdfs/DST_STRAT_PLAN_2011.pdf

Department of Science and Technology. (n.d.(c)). *Vote no. 30 - annual report 2017/2018.* Retrieved February 12, 2020, from https://www.dst.gov.za/images/2018/DST-AR-2017-18.pdf

Department of Trade and Industry. (2014). *Industrial Policy Action Plan: Economics sectors and employment cluster 2014/15 - 2016/17.* Retrieved February 18, 2020, from https://www.idc.co.za/wp-content/uploads/2019/02/IPAP2014.pdf

Department of Trade and Industry. (2015). *Industrial Action Policy Plan 2015: Economic sectors, employment and infrastructure development cluster IPAP 2015/16 - 2017/18.* Retrieved February 18, 2020, from http://pmg-assets.s3-website-eu-west-1.amazonaws.com/150804IPAP2015.pdf

Department of Trade and Industry. (2016). *Industrial Policy Action Plan IPAP 2016/17 - 2018/19 Economic sectors, employment and infrastructure development cluster.* Retrieved February 18, 2020, from https://www.gov.za/sites/default/files/gcis_document/201607/ipap-2016.pdf

Department of Trade and Industry. (2017a). *Industrial Policy Action Plan 2017/18 - 2019/20 Economic sectors, employment and infrastructure development cluster Part 1: A Brief Overview.* Retrieved February 18, 2020, from https://www.gov.za/sites/default/files/gcis_document/201705/ipap17181920.pdf

Department of Trade and Industry. (2017b). *Industrial Policy Action Plan 2017/18 - 2019/20 Economic sectors, employment and infrastructure development cluster Part 2: The Engine Room of Change.* Retrieved February 18, 2020, from http://www.itac.org.za/upload/Industrial%20Policy%20Action%20Plan%20Part%202%2017-18%20-%2019-20.pdf

Department of Trade and Industry. (2018a). *A guide to the dti incentive schemes 2018/19.* Retrieved February 12, 2020, from http://letamik.co.za/images/H_Factor/DTI_Incentive-Schemes_by_Donald_Mabusela.pdf

Department of Trade and Industry. (2018b). *Industrial policy action plan: Economic sectors, employment and infrastructure development cluster 2018/19 - 2020/2021.* Retrieved February 18, 2020, from https://www.gov.za/sites/default/files/gcis_document/201805/industrial-policy-action-plan.pdf

Eisenhardt, K. (1989). Building theories from case study research. *The Academy of Management Review, 14*(4), 532-550.

Elsevier. (n.d.). *Content policy and selection*. Retrieved December 15, 2020, from https://www.elsevier.com/solutions/scopus/how-scopus-works/content/content-policy-and-selection

Eslami, H., Ebadi, A., & Schiffauerova, A. (2013). Effect of collaboration network structure on knowledge creation and technoogical performance: The case of biotechnology in Canada. *Scientometrics, 97*(1), 99-119.

European IP Helpdesk. (2020). *What's the difference between the inventor, the applicant and the owner in a patent?* Retrieved January 14, 2020, from http://www.iprhelpdesk.eu/node/2593

Fitjar, R., & Rodriguez-Pose, A. (2013). Firm collaboration and modes of innovation in Norway. *Research Policy, 42*, 128-138.

Fleming, L., & Marx, M. (2006). Managing creativity in small worlds. *California Management Review, 48*(4), 6-27.

Fleming, L., King, C., & Juda, A. (2007). Small worlds and regional innovation. *Organization Science*, 938-954.

Franco, A., Malhotra, N., & Simonovits, G. (2014). Publication bias in the social sciences: Unlocking the file drawer. *Science, 345*(6203), 1502-1505. doi:10.1126/science.1255484

Gibbert, M. (2015, June). Case Studies: A Research Strategy. *Lecture Notes: Designing, doing and publishing case studies*. Stellenbosch.

Gittelman, M. (2008). A note on the value of patents as indicators of innovation: Implications for management research . *Academy of Management Perspectives, 22*(3), 21-27.

Global Harmonisation Task Force. (2012). *Definition of the terms 'medical device' and 'in vitro diagnostic (IVD) medical device'.* Retrieved February 18, 2020, from http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n071-2012-definition-of-terms-120516.pdf

Gonzalez-Pernia, J., Parrilli, M., & Pena, I. (2012). Learning modes, types of innovation and economic performance. *Orkestra Working Paper Series in Territorial Competitiveness*.

Gonzalez-Pernia, J., Parrilli, M., & Pena-Legazkue, I. (2015). STI-DUI learning modes, firm-university collaboration and innovation. *Journal of Technology Transfer, 40*, 475-492.

Gray, E. (2009). *National environmental scan of South African scholarly publishing.* Retrieved October 4, 2020, from https://open.uct.ac.za/bitstream/handle/11427/29095/Position_Paper_2_National_environmental_scan_of_So.pdf?sequence=1&isAllowed=y

Hanneman, R., & Riddle, M. (2005). Introduction to social network methods. Riverside, CA, California: University of California.

Healio. (2014). *Wright Medical and Tornier announce merger*. Retrieved October 4, 2020, from https://www.healio.com/news/orthopedics/20141028/wright-medical-and-tornier-announce-merger

Health Professions Council of South Africa. (2008). *Guidelines for good practice in the healthcare professions: General ethical guidelines for biotechnology research in South Africa Booklet 14.* Retrieved February 18, 2020, from https://www.hpcsa.co.za/Uploads/Professional_Practice/Conduct%20%26%20Ethics/Booklet%2014%20Gen%20Ethical%20Guidelines%20for%20%20health%20researchers.pdf

Health Professions Council of South Africa. (2014). *Guidelines for the good practice in the healthcare professions: General ethical guidelines for good ractice in telemedicine.* Retrieved February 18, 2020, from https://www.hpcsa.co.za/Uploads/Professional_Practice/Conduct%20%26%20Ethics/Booklet%2010%20Telemedicine%20September%20%202016.pdf

Health Professions Council of South Africa. (2016a). *Guidelines for good practice in the healthcare professions: Ethical and professional rules of the Health Professions Council of South Africa.* Retrieved February 18, 2020, from https://www.hpcsa.co.za/Uploads/Professional_Practice/Conduct%20%26%20Ethics/Booklet%202%20Generic%20Ethical%20Rules%20with%20anexures%20September%202016.pdf

Health Professions Council of South Africa. (2016b). *Policy document on business practices.* Retrieved February 18, 2020, from https://www.hpcsa.co.za/Uploads/PSB_2019/Policy_on_Business_Practices_final%20-%202016.pdf

Hekkert, M., Negro, S., Heimriks, G., & Harmsen, G. (2011). *Technological innovation system analysis - A manual for analysts.* Universiteit Utrecht, Faculty of Geosciences. Utrecht: Universiteit Utrecht.

Hekkert, M., Suurs, R., Negro, S., Kuhlmann, S., & Smits, R. (2007). Functions of innovation systems: A new approach for analysing technological change. *Technological Forecasting and Social Change, 74*, 413-432.

Hennart, J. (1988). A transaction cost theory of equity joint ventures. *Strategic Management Journal, 9*, 361-374.

Hicks, D., & Katz, J. (1996). Hospitals: The hidden research system. *Science and Public Policy, 23*(5), 297-304.

Hinze, S., & Schmoch, U. (2004). Opening the black box: Analytical approaches and their impact on the outcome of statistical patent analyses. In H. Moed, W. Glanzel, & U. Schmoch (Eds.), *Handbook of quantitative science and technology - The use of publication and patent statistics in studies of S&T systems* (pp. 215-235). Kluwer Academic Publishers.

InfoVis Cyberinfrastructure. (2004). *Software>Forced Directed Placement Algorithm*. Retrieved June 9, 2019, from http://iv.slis.indiana.edu/sw/spring.html#Eades

International Medical Device Regulators Forum. (2018). *Essential principles of safety and performance of medical devices and IVD medical devices.* Retrieved February 19, 2020, from http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-181031-grrp-essential-principles-n47.pdf

Janson, J., & Rossouw, G. (2013). A new technique for repair of a dislocated sternoclavicular joint using a sternal tension cable system. *The Annals of Thoracic Surgery, 95*(2), 53-55.

Jensen, M., Johnson, B., Lorenz, E., & Lundvall, B.-A. (2016). Forms of knowledge and modes of innovation. In B.-A. Lundvall (Ed.), *The Learning Economy and the Economics of Hope* (pp. 155-182). Anthem Press.

Johns Hopkins Medicine. (2020). *Arthroplasty*. Retrieved January 13, 2020, from https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/arthroplasty

Johnson, R. (1997). Examining the validity structure of qualitative research. *Education, 118*(2), 282-292.

Kebede, K., & Mitsufuji, T. (2017). Technological innovation system building for diffusion of renewable energy technology: A case of solar PV systems in Ethiopia. *Technological Forecasting & Social Change, 114*, 242-253.

Khan, G., & Wood, J. (2015). Information technology management domain: emerging themes and keyword analysis. *Scientometrics, 105*, 959-972.

Khan, G., & Wood, J. (2016). Knowledge networks of the information technology management domain: A social network analysis approach. *Communications of the Association for Information Systems, 39*(18), 367-397.

KPMG. (2014). *South African medical technology industry - Industry overview and economic impact assessment.* Retrieved February 19, 2020, from https://pdf4pro.com/cdn/prepared-for-the-south-african-medical-device-efb1a.pdf

Krackhardt, D., & Stern, R. (1988). Informal networks and organizational crises: An experimental simulation. *Social Psychology Quarterly, 51*(2), 123-140.

Lach, S. (1995). Patents and productivity growth at the industry level: a first look. *Economics Letters, 49*, 101-108.

Lander, B. (2013). Sectoral collaboration in biomedical research and development. *Scientometrics, 94*, 343-357.

Lander, B. (2014). The role of institutions and capital in intersectoral collaboration: Infection and immunity research and development collaboration in Vancouver. *Review of Policy Research, 31*(5), 390-406.

Lander, B., & Atkinson-Grosjean, J. (2011). Translational science and the hidden research system in universities and academic hospitals: A case study. *Social Science & Medicine, 72*(4), 537-544.

Leydesdorff, L., & Erkowitz, H. (1998). The Triple Helix as a model for innovation studies. *Science and Public Policy, 22*(3), 195-203.

Long, J., Cunningham, F., & BraithWaite, J. (2012). Network structure and the role of key players in a translational cancer research network: a study protocol. *BMJ Open*. doi:10.1136/bmjopen-2012-001434

Long, J., Cunningham, F., Wiley, J., Carswell, P., & Braithwaite, J. (2013). Leadership in complex networks: the importance of network position and strategic action in a translational cancer research network. *Implementation Science, 8*(122).

Lundvall, B.-A. (2016). National systems of innovation: Towards a theory of innovation and interactive learning. In B.-A. Lundvall (Ed.), *The Learning Economy and the Economics of Hope* (pp. 85-106). Anthem Press.

Macmillan Dictionary. (2020). *Actor*. Retrieved January 13, 2020, from https://www.macmillandictionary.com/dictionary/british/actor

Makhoba, X., & Pouris, A. (2016). Scientometric assessment of selected R&D priority areas in South Africa: A comparison with other BRICS countries. *African Journal of Science, Technology, Innovation and Development, 8*(2), 187-196.

Malerba, F. (2002). Sectoral systems of innovation and production. *Research Policy, 31*(2), 247-264.

Manzini, S. (2012). The national system of innovation concept: An ontological review and critique. *South African Journal of Science, 108*(9/10).

Mayosi, B., Fisher, A., Lalloo, U., Sitas, F., Tollman, S., & Bradshaw, D. (2009). The burden on non-communicable diseases in South Africa. *The Lancet, 374*(9693), 934-947.

Medical Device Manufacturers Association of South Africa. (2015). *About*. Retrieved September 18, 2019, from http://www.mdmsa.co.za/?page_id=2111

MedicineNet. (2018). *Medical definition of orthotic*. Retrieved February 2, 2020, from https://www.medicinenet.com/script/main/art.asp?articlekey=40206

Medicines Control Council. (2012). *Registration of Medicines - General Information.* Retrieved December 13, 2020, from http://www.rrfa.co.za/wp-content/uploads/2012/11/General-information-Jul12-v8-showing-changes.pdf

MediKredit. (2009). *National Pharmaceutical Product Index (NAPPI) Product Suite*. Retrieved February 18, 2020, from https://www.medikredit.co.za/index.php?option=com_content&view=article&id=21&Itemid=179

Metcalfe, J. (1995). The economic foundations of technology policy: Equilibrium and evolutionary perspectives. In P. Stoneman (Ed.), *Handbook of economics of innovation and technological change* (pp. 409-512). Oxford: Blackwell.

Michel, J., & Bettels, B. (2001). Patent citation analysis: A closer look at the basic input data from patent search reports. *Scientometrics, 51*(1), 185-201.

Moon, F. (2004). Social networks in the history of innovation and invention. In M. Ceccarelli (Ed.), *History of mechanism and machine science* (Vol. 22). Cassino, Italy: Springer.

Murphy, J. (2015). Human geography and socio-technical transition studies: Promising intersections . *Environmental Innovation and Societal Transitions , 17*, 73–91.

Murray, F. (2002). Innovation as co-evolution of scientific and technological networks: Exploring tissue engineering. *Research Policy, 31*, 1389-1403.

National Advisory Council on Innovation. (2014). *South African Science, Technology and Innovation Indicators.* Retrieved February 19, 2020, from http://www.naci.org.za/wp-content/uploads/South-African-STI-Indicators-2014.pdf

National Advisory Council on Innovation. (2016). *South African Science, Technology and Innovation Indicators.* Retrieved February 19, 2020, from http://www.naci.org.za/wp-content/uploads/2017/09/South-African-Science-Technology-and-Innovation-Indicators-2016-web.pdf

National Planning Commission. (2012). *National development plan vision 2030. Our future - make it work.* Retrieved March 27, 2019, from https://www.poa.gov.za/news/Documents/NPC%20National%20Development%20Plan%20Vision%202030%20-lo-res.pdf

National Treasury. (2014). *Expenditure and performance review #56206 assessment of the effective partnering of science councils with the private sector.* Retrieved March 23, 2018, from https://www.gtac.gov.za/perdetail/16.2%20Technical%20report.pdf

Ncube, C., Abrahams, L., & Akinsanmi, T. (2013). Effects of the South African IP regime on generating value from publicly funded research: An exploratory study of two universities. In J. de Beer, C. Armstrong, C. Oguamanam, & T. Schonwetter (Eds.), *Innovation and Intellectual Property: Collaborative Dynamics in Africa* (pp. 282-315).

Newman, M. (2001). The structure of scientific collaboration networks. *PNAS, 98*(2), 404-409.

NIPMO. (2019). *NIPMO interpretation note 13: Everything you need to know about full cost.* Retrieved October 4, 2020, from https://nipmo.dst.gov.za/uploads/files/NIN13_Fullcost_6-Aug-19.pdf

Nonaka, I., & Takeuchi, H. (1995). *The knowledge creating company - How Japanese companies create the dynamics of innovation.* New York: Oxford University Press.

Nykamp, D. (n.d.). *Mean path length definition*. Retrieved March 29, 2020, from http://mathinsight.org/definition/network_mean_path_length

OECD. (2001). *Special Issue on New Science and Technology Indicators.* Paris: OECD.

Opsahl, T. (2013). Triadic closure in two-mode networks: Redefining the global and local clustering coefficients. *Social Networks, 35*(2), 159-167.

Owen-Smith, J., & Powell, W. (2001). To patent or not: Faculty decisions and institutional success at technology transfer. *Journal of Technology Transfer, 26*, 99-114.

Oxford, T. (2015). *Accessible additive manufacturing.* Retrieved December 20, 2019, from https://mg.co.za/article/2015-07-10-00-accessible-additive-manufacturing

Park, G., & Park, Y. (2006). On the measurement of patent stock as knowledge indicators. *Technological Forecasting & Social Change, 73*, 793-812.

Parkhe, A. (1993). Strategic alliances structuring: A game theoretic and transaction cost examination of interfirm cooperation. *Academy of Management Journal, 36*, 794-829.

Parrilli, M., & Heras, H. (2016). STI and DUI innovation modes: Scientific-technological and context-specific nuances. *Research Policy, 45*, 747-756.

PATH. (2020). *About*. Retrieved February 8, 2020, from https://www.path.org/about/

Patra, S., & Muchi, M. (2018). Research and innovation in South African universities: from the triple helix's perspective. *Scientometrics, 116*, 51-76.

Pisano, G. (1989). Using equity participation of support exchange: Evidence from the biotechnology industry. *Journal of Law, Economics and Organisation, 5*, 109-126.

Plugmacher, R., Becker, G. & Van Asselt, P. (2011). Surgical instrument for spreading bone. European Patent Office, Patent No. EP11167493.

Pouris, A., & Ho, Y.-S. (2014). Research emphasis and collaboration in Africa. *Scientometrics, 98*, 2169-2184.

Powell, W., Koput, K., & Smith-Doer, L. (1996). Interorganisational collaboration and the locus of innovation: Networks of learning in Biotechnology. *Administrative Science Quarterly, 41*(1), 116-145.

QSR International Pty Ltd. (2015). NVivo qualitative data analysis software. *Version 11*. QSR International Pty Ltd.

Research Contract and Innovation. (2014). *Publicly-funded Research Act*. Retrieved August 27, 2019, from http://www.rci.uct.ac.za/rcips/ip/pfbill

Rochracher, H., Truffer, B., & Markard, J. (2010). Doing institutional analysis of innovations systems: A conceptual framework. Copenhagen: DRUID Summer Conference.

Saidi, T. (2016). Towards a medical device regulation in South Africa: An assessment of the medicines and related substances amendment act of 2015. *Health Technology, 6*, 83-88.

Salie, F., de Jager, K., Dreher, C., & Douglas, T. (2019). The scientific base for orthopaedic device development in South Africa: spatial and sectoral evolution of knowledge development. *Scientometrics, 119*(1), 31-54.

SAMED. (n.d.). *The South African medical device industry - facts.* Retrieved May 30, 2017, from http://www.samed.org.za/DynamicData/LibraryDownloads/224.pdf

Santonen, T., & Conn, S. (2016). Social network analysis based keyword analysis of ISPIM research topics. *Social network analysis based keyword analysis of ISPIM research topics.* Porto: The XXVII ISPIM Innovation Conference.

Schmidt, T., & Dabur, S. (2014). Explaining the diffusion of biogas in India: a new functional approach considering national borders and technology transfer. *Environmental Economics and Policy Studies*, *16,* 171-199.

Scholes, R., Anderson, F., Kenyon, C., Napier, J., Ngoepe, P., van Wilgen, B., & Weaver, A. (2008). Science councils in South Africa. *South African Journal of Science, 104*, 435-438.

Sibanda, M. (2009). Intellectual property, commercialisation and institutional arrangements at South African public research institutions. In *The Economics of Intellectual Property in South Africa* (pp. 113-145). WIPO.

Singh, J. (2005). Collaborative networks as determinants of knowledge diffusion patterns. *Management Science, 51*(5), 756-770.

Small, H. (1973). Co-citation in the scientific literature: A new measure of the relationship between two documents. *Journal of the American Society for Information Science, 24*, 265-269.

Smith, A., & Raven, R. (2012). What is protective space?Reconsidering niches in transitions to sustainability. *Research Policy, 41*(6), 1025-1036.

Sole, R., Corominas-Murtra, B., Valverde, S., & Steels, L. (2010). Language networks: their structure, function, and evolution. *Complexity, 15*(6), 20-26.

Sooryamoorthy, R. (2010). Medical research in South Africa: a scientometric analysis of trends, patterns, productivity and partnership. *Scientometrics, 84*, 863-885.

South African Health Products Regulatory Authority. (2019). *Annual performance Plan for the fiscal year 2019/2020.* Retrieved February 20, 2020, from http://pmg-assets.s3-website-eu-west-1.amazonaws.com/SAHPRA_APP_2019_2020.pdf

South African Medical Research Council. (2018). *SAMRC annual performance plan for 2018/2019.* Retrieved January 23, 2019, from http://www.samrc.ac.za/sites/default/files/attachments/2018-12-10/SAMRCAnnualPerfomancePlan.pdf

South African Medical Research Council and PATH. (2014). *Developing an ecosystem to support the local medical device & diagnostics industry in South Africa - Recommendations from an international perspective.* Retrieved February 20, 2020, from http://www.samed.org.za/Filemanager/userfiles/MRC-PATH-%20Medtronic%20Report%202014.pdf

South African Medical Technology Industry Association. (2018). *About SAMED*. Retrieved February 2, 2019, from http://www.samed.org.za/About.aspx

South African Medical Technology Industry Association. (n.d.). *Who we are and what we do.* Retrieved February 20, 2020, from http://www.samed.org.za/Filemanager/userfiles/Who%20we%20are%20and%20what%20we%20do.pdf

South African Orthopaedic Association. (2019). *Principles of medical ethics*. Retrieved June 13, 2019, from https://saoa.org.za/about/medicalethics/

Southern African Research and Innovation Management Association. (2018). *Technology transfer and innovation management: A handbook for Southern African Technology Transfer Offices.* Retrieved January 15, 2020, from https://www.sarima.co.za/wp-content/uploads/2019/04/TTIM-Handbook-v3-jc.pdf

Statistics South Africa. (2015). *General Household Survey 2014.* Retrieved February 21, 2020, from http://www.statssa.gov.za/publications/P0318/P03182014.pdf

Technology Innovation Agency. (2018). *Health*. Retrieved August 20, 2019, from https://www.tia.org.za/health/

The American Heritage Science Dictionary. (2011). *Dictionary.com*. Retrieved 12 20, 2018, from https://www.dictionary.com/browse/orthopaedics

Tigabu, A., Berkhout, F., & van Beukering, P. (2015a). Technology innovation systems and technology diffusion: Adoption of bio-digestion in an emerging innovation system in Rwanda. *Technological Forecasting & Social Change, 90*, 318-330.

Tigabu, A., Berhout, F., & van Beukering, P. (2015b). The diffusion of a renewable energy technology and innovation system functioning: Comparing bio-digestion in Kenya and Rwanda. *Technological Forecasting & Social Change, 90*, 331-345.

Tijssen, R. (2004). Measuring and evaluating science-technology connections and interactions. In H. Moed, W. Glanzel, & U. Schmoch (Eds.), *Handbook of quantitative sceince and technology research - The use of publication and patent statistics in studies of S&T systems* (pp. 694-715). Kluwer Academic Publishers.

Trade & Industrial Policy Strategies. (2018). *The Johannesburg Health Cluster.* Retrieved May 30, 2019, from http://www.tips.org.za/research-archive/trade-and-industry/item/3530-the-johannesburg-health-cluster

Truscott, M., de Beer, D., Vicatos, G., Hosking, K., Barnard, L., Booysen, G., & Campbell, R. (2007). Using RP to promote collaborative design of customised medical implants. *Rapid Prototyping Journal, 13*(2), 107-114.

University of Cape Town. (2011). *Intellectual Property Policy.* Retrieved February 21, 2020, from https://www.uct.ac.za/sites/default/files/image_tool/images/328/about/policies/Policy_Intellectual_Property_2011.pdf

University of Cape Town. (2018). *Medical devices: An innovation guide from lab to commercialisation.* Retrieved February 21, 2020, from https://www.sarima.co.za/wp-content/uploads/2019/01/r2m_guide_01.pdf

van Raan, A. (2004). Measuring Science - Capita selecta of current main issues. In H. Moed, W. Glanzel, & U. Schmoch (Eds.), *Handbook of quantitative science and technology research - The use of publication and patent statistics in studies of S&T systems* (pp. 19-50). Kluwer Academic Publishers.

Vida, Z. (2018). Distance on scientific collaboration networks. Budapest, Hungary: Eötvös Loránd University.

Wasserman, S., & Faust, K. (1994). *Social network analysis: Methods and applications.* University of Cambridge.

Wieczorek, A., Hekkert, M., Coenen, L., & Harmsen, R. (2015). Broadening the national focus in technological innovation system analysis: The case of offshore wind. *Environmental Innovation and Societal Transitions , 14*, 128–148 .

World Intellectual Property Organization. (2007). *Patents*. Retrieved February 2, 2020, from https://www.wipo.int/patents/en/

Yan, E., & Ding, Y. (2012). Scholarly network similarities: How bibliographic coupling networks, citation networks, cocitation networks, topical networks, coauthorship networks, and coword networks relate to each other. *Journal of the American Society for Information Science and Technology, 63*(7), 1313-1326.

Yi, S., & Choi, J. (2012). The organisation of scientific knowledge: the structural characteristics of keyword networks. *Scientometrics, 90*, 1015-1026.

Yin, R. (2003). *Case Study Research: Design and Methods.* SAGE Publications.

Yin, R. (2011). *Qualitative research from start to finish.* New York: The Guilford Press.

APPENDIX A – Search phrases for the scientific publication actor-collaboration network

The following search phrase was used to extract scientific publications from Scopus.

(AFFILCOUNTRY (south africa) AND TITLE-ABS-KEY (biomechanical OR bone OR joint OR muscle OR tendon OR ligament OR muscul* OR skelet*) AND TITLE-ABS-KEY (replacement OR arthroplasty* OR device OR tool OR instrument OR apparatus OR implement OR implant OR prosthe* OR orthotic OR orthoses OR machine OR appliance OR software OR material OR design* OR develop* OR concept*) AND NOT TITLE-ABS-KEY (dental OR orthodont* OR archaeolog* OR immunolog* OR pharmacolog* OR metaboli* OR evolution*)) AND PUBYEAR > 1999

The following search phrase was used to extract scientific publications from Thomson Reuters Web of Knowledge:

CU=(South Africa) AND PY=(2000-2015) AND SU=(Orthopedics OR Surgery OR Sports Sciences OR Engineering,Biomedical) AND TS=((joint OR bone OR tendon OR muscle OR ligament OR muscul* OR skeleton OR skeletal OR biomechanical) AND (arthroplast* OR medical device OR device OR tool OR instrument OR apparatus OR implement OR implant OR machine OR appliance OR prostheses OR prosthetic OR orthotic OR orthoses OR software OR material OR design OR concept* OR develop* OR replacement) NOT (pharmacolog* OR immunolog* OR metaboli* OR dental OR orthodont* OR archaeolog* OR evolution))

APPENDIX B – Search phrase used for the patent actor-collaboration network

The following search terms were used to extract patent data from LexisNexis TotalPatent.

((biomechanical OR bone OR joint OR muscle OR tendon OR ligament OR muscul* OR skelet*) AND (replacement OR arthroplast* OR device OR tool OR instrument OR apparatus OR implement OR implant OR prosthe* OR orthotic OR orthoses OR machine OR appliance OR software OR material OR design* OR develop* OR concept*) AND (Inventor-Res(South Africa) OR Inventor-Nat(South Africa) OR Assignee(South Africa) OR APC(South Africa) OR Applicant-Nat(South Africa) OR Applicant-Res(South Africa))) and DATE(>2000-01-01)

APPENDIX C – Actors of the scientific publication network

Abbreviation	Organisation	Location
	University sector	
CPUT	Cape Peninsula University of Technology	National
CUT	Central University of Technology	National
IMT	Institut Mines Telecom	International
JGU	Johannes Gutenburg University	International
LMU	Ludwig Maximillian University	International
LU	Loughborough University	International
MSU	Michigan State University	International
MU	Massey University	International
MUI	Medical University of Innsbruck	International
NWU	North Western University	National
PSG	PSG Tech	International
PSTDV	Pole Scientifique Et Technologique de Vlizy	International
QTU	Qinglao Technological University	International
RU	Roehampton University	International
SFIT	Swiss Federal Institute of Technology	International
SSSA	Scualo Superiore Sant'Anna	International
TB	Telecom Bretagne	International
TUHH	Hamburg University of Technology	International
TUT	Tshwane University of Technology	National
UBRI	University of Bristol	International
UCAL	University of California	International
UCD	University College Dublin	International
UCL	University College London	International
UCT	University of Cape Town	National
UDP	University de Pisa	International
UFS	University of the Free State	National
UKZN	University of KwaZulu Natal	National
UL	University of Liege	International
ULEED	University of Leeds	International
UM	University Mainz	International
UP	University of Pretoria	National
UPEC	University of Paris East Central	International
USA	University of South Australia	International
SUN	University of Stellenbosch	National
UVSQ	University de Versailles Saint-Quentin-en-Evelines	International
UWC	University of the Western Cape	National
UWIS	University of Wisconsin	International

VITU	VIT University	International
VU	Vrije University	International
VUT	Vaal University of Technology	National
WITS	University of the Witwatersrand	National
YU	Yale University	International
	Healthcare sector	
2aCO	2a Clinical Ortopedica	International
AODP	Azianda Ospedaliera di Padova	International
BUH	Balgrist University Hospital	International
BGMC	BG Medical Centre	International
BRI	Bristol Royal Infirmary	International
CMJAH	Charlotte Maxeke Johannesburg Academic Hospital	National
CTOF	Centro Traumalogico Ortopedico Firenze	International
CHBAH	Chris Hani Baragwanath Academic Hospital	National
DH	Davis Hospital	International
EGH	Epsom General Hospital	International
EMH	Eugene Marais Hospital	National
FH	Freeman Hospital	International
GH	Greys Hospital	National
GSH	Groote Schuur Hospital	National
GMC	Grosshadern Medical Centre	International
HMA	Hand and Microsurgery Associates	International
KGH	King George Hospital	National
KW	Klinikum Worms	International
LTM	Learning Trauma Med	International
LPC	Linksfield Park Clinic	National
MMC	Morningside MediClinic	National
NYPH	New York Presbyterian Hospital	International
OSC	Orthoone Speciality Clinic	International
OCC	Orthopaedic Care Centre	International
RNOHT	Royal National Orthopaedic Hospital Trust	International
SM	Sint Maartenskliniek	International
SSOC	Sports Science Orthopaedic Clinic	National
SPC	Springs Parkland Clinic	National
SMC	Stellenbosch MediClinic	National
SBAH	Steve Biko Academic Hospital	National
TAH	Tygerberg Academic Hospital	National
UKHM	Unfalkrakenhaus Meidling	International
UHB	University Hospital Berlin	International
UHL	University Hospital Leuven	International
UMC	University Medical Centre	International

VPH	Vincent Palotti Hospital	National
VP	VogtlanklinikumPlauen	International
WH	Wrightington Hospital	International
	Science Councils sector	
AOCID	AO Clinical Investigation and Documentation	International
CSIR	Council for Scientific and Industrial Research	National
FNIHMR	French National Institute for Health and Medical Research	International
ITL	Ithemba Labs	National
NIRDTP	National Institute of Research and Development for Theoretical Physics	International
NECSA	Nuclear Engineering Council of South Africa	National
SAMRC	South Africa Medical Research Council	National
	Industry sector	
3DEG	3 Degree Research and Consulting (Pty) Ltd	National
6DOF	6 Degrees of Freedom	National
AO	Advanced Orthopaedics	National
AAG	Aesculap AG	International
DePuy	DePuy International Ltd	International
HE	Howmedica Europe	International
Denmyd	Denmyd Medical Pty (Ltd)	National
LC	Lima Corporate	International
LODOX	Lodox	National
MRA	Marcus Riley Associates Ltd	International
MEDT	Medtronic	International
ORTHO	Orthomedics Pty Ltd	National
TI	Tornier Inc	International

APPENDIX D – Evolution of scientific publication actor-collaboration networks over all 12 timeframes

Each image presented in this appendix is an actor-collaboration network of the actors involved in the scientific publication network, in a five-year window over the period 2000-2015.

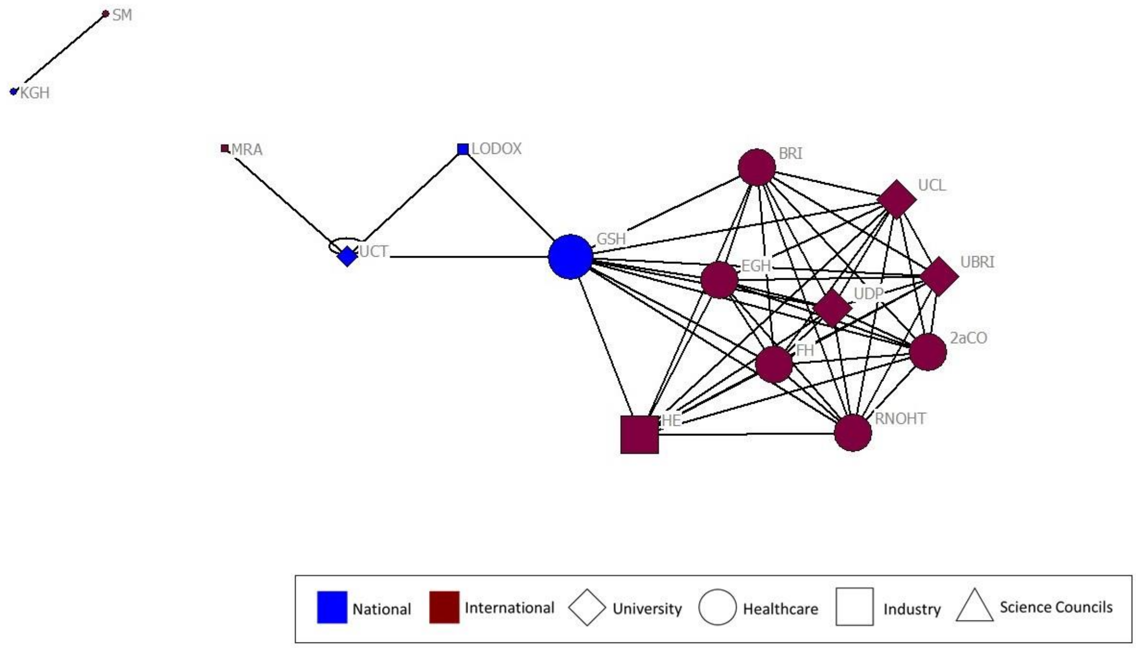


Figure 29: Actor-collaboration network based on scientific publication data for the period 2000 – 2004

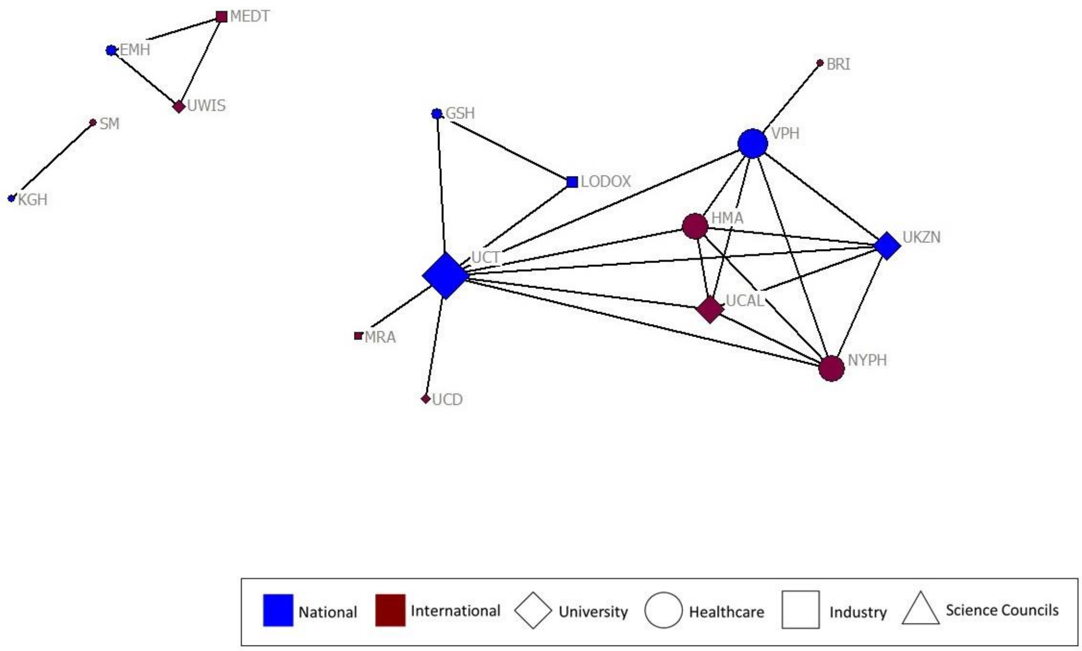


Figure 30: Actor-collaboration network based on scientific publication data for the period 2001 - 2005

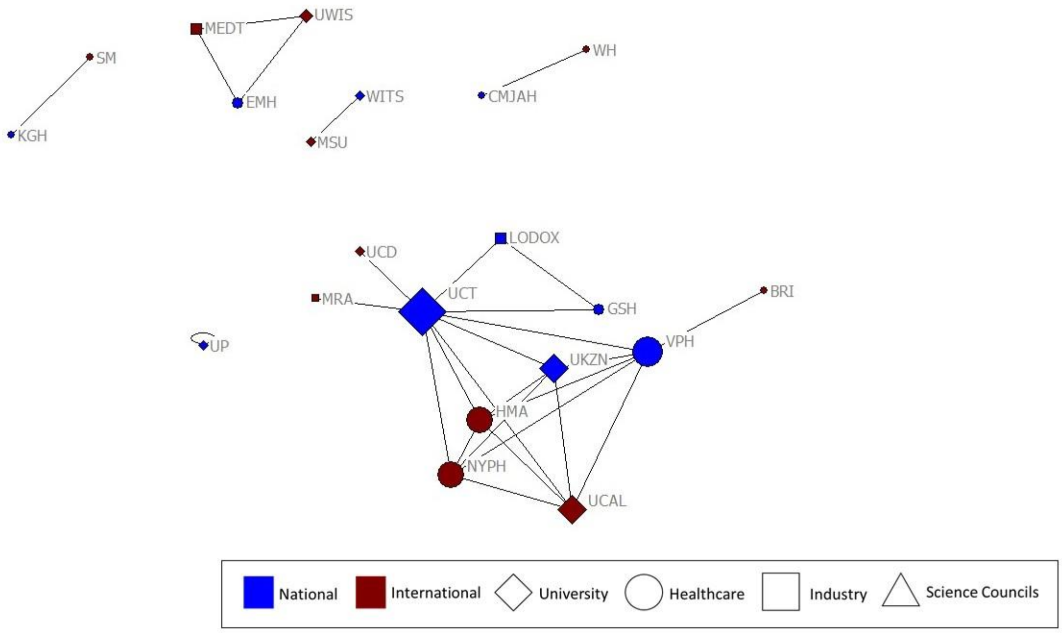


Figure 31: Actor collaboration network based on scientific publication data for the period 2002 – 2006

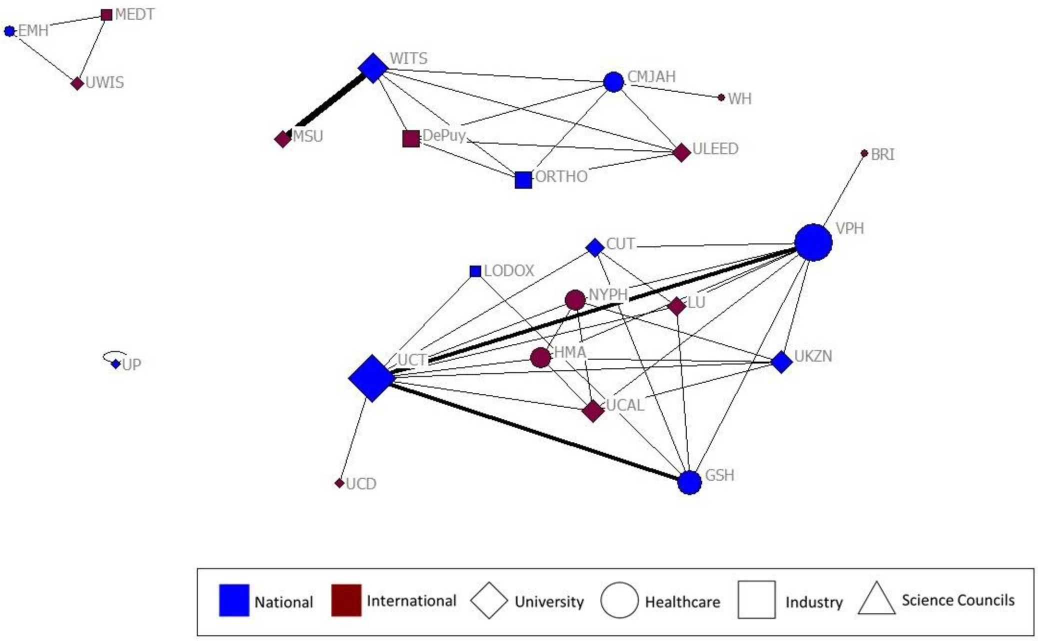


Figure 32: Actor collaboration network based on scientific publication data for the period 2003 - 2007

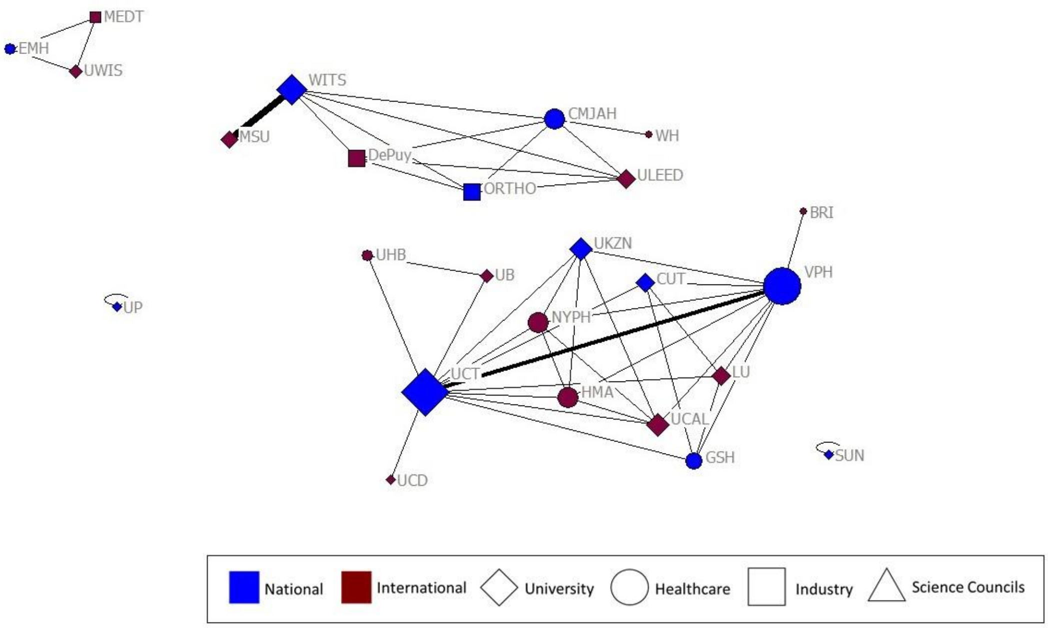


Figure 33: Actor-collaboration network based on scientific publication data for the period 2004 - 2008

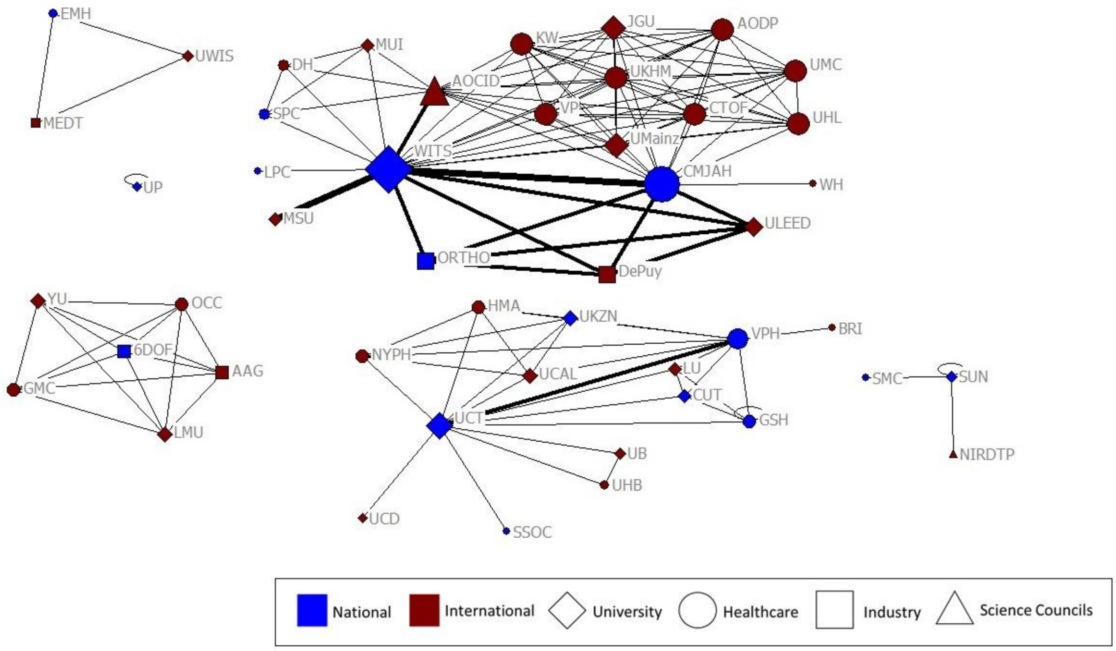


Figure 34: Actor-collaboration network based on scientific publication data for the period 2005 - 2009

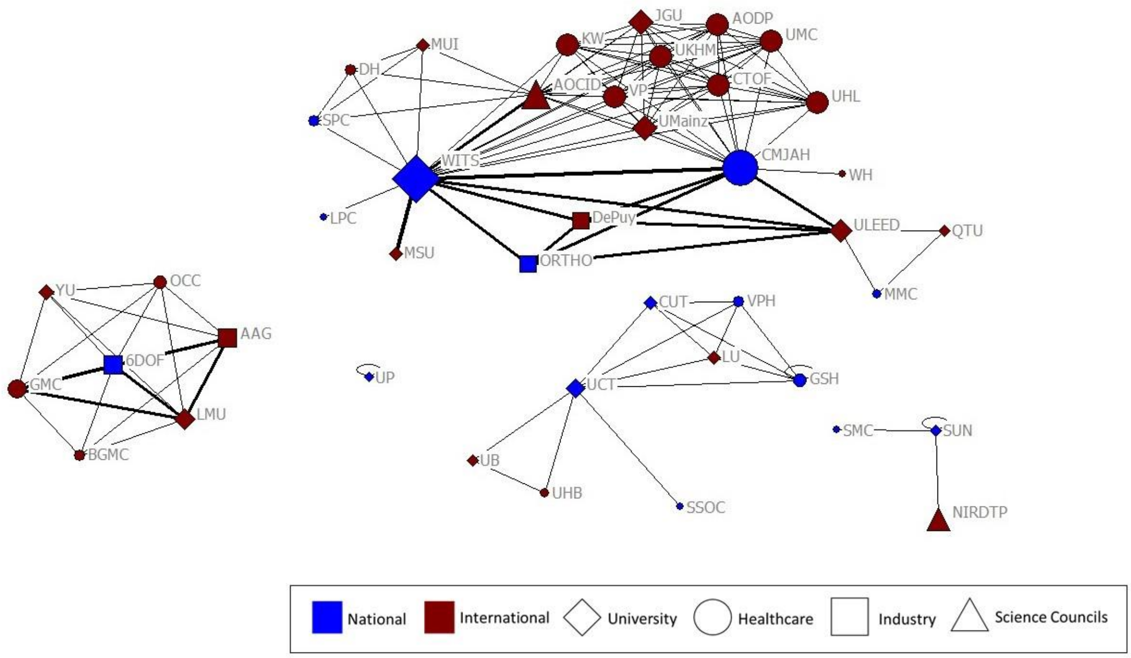


Figure 35: Actor-collaboration network based on scientific publication data for the period 2006 - 2010

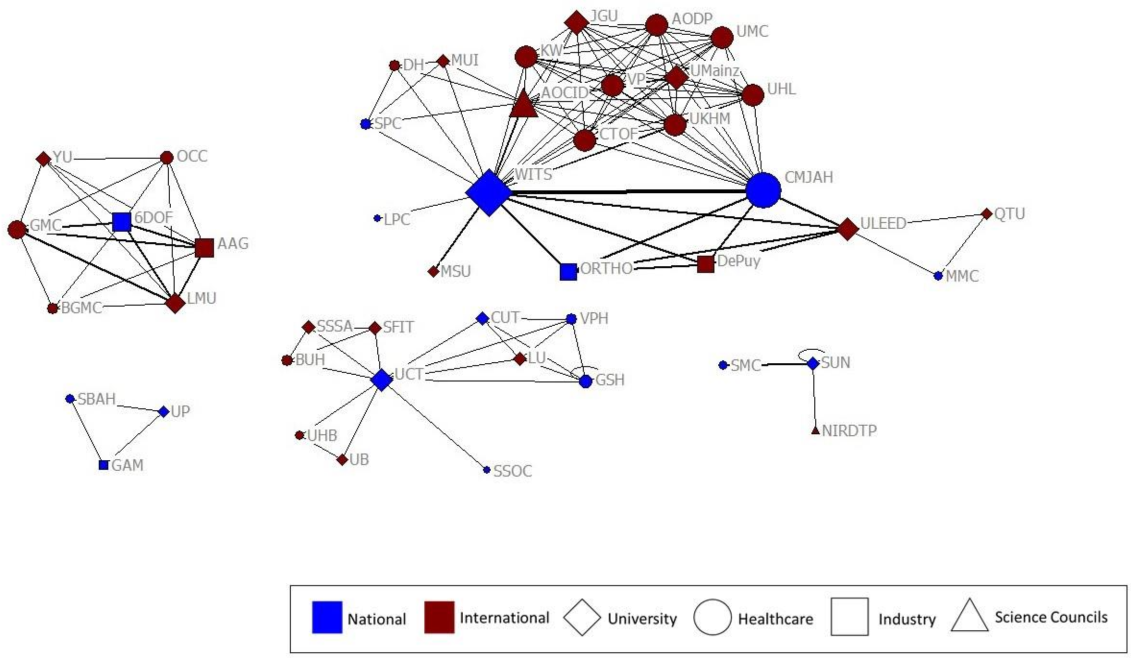


Figure 36: Actor-collaboration network based on scientific publication data for the period 2007 - 2011

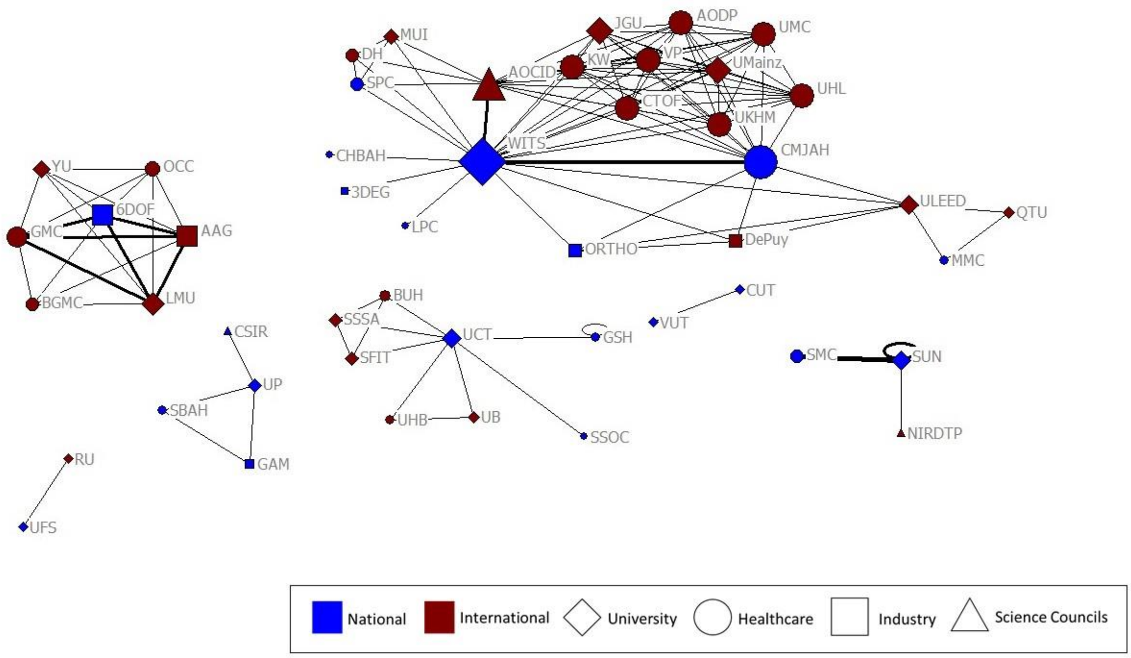


Figure 37: Actor-collaboration network based on scientific publication data for the period 2008 - 2012

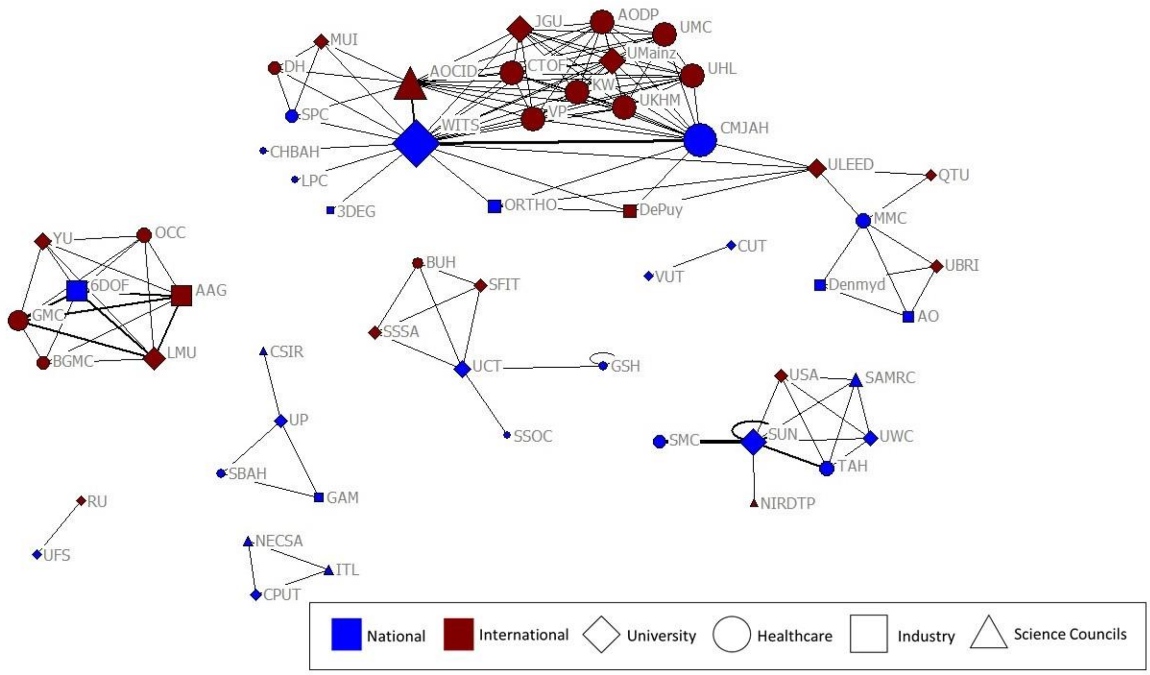


Figure 38: Actor-collaboration network based on scientific publication data for the period 2009 - 2013

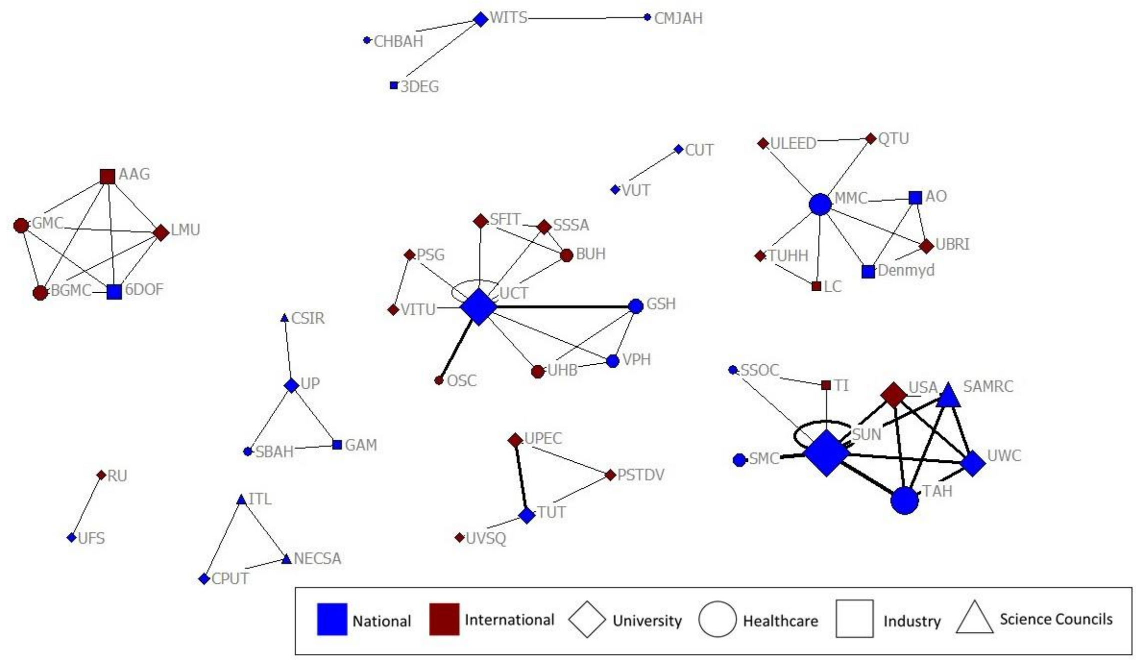


Figure 39: Actor-collaboration network based on scientific publication data for the period 2010 - 2014

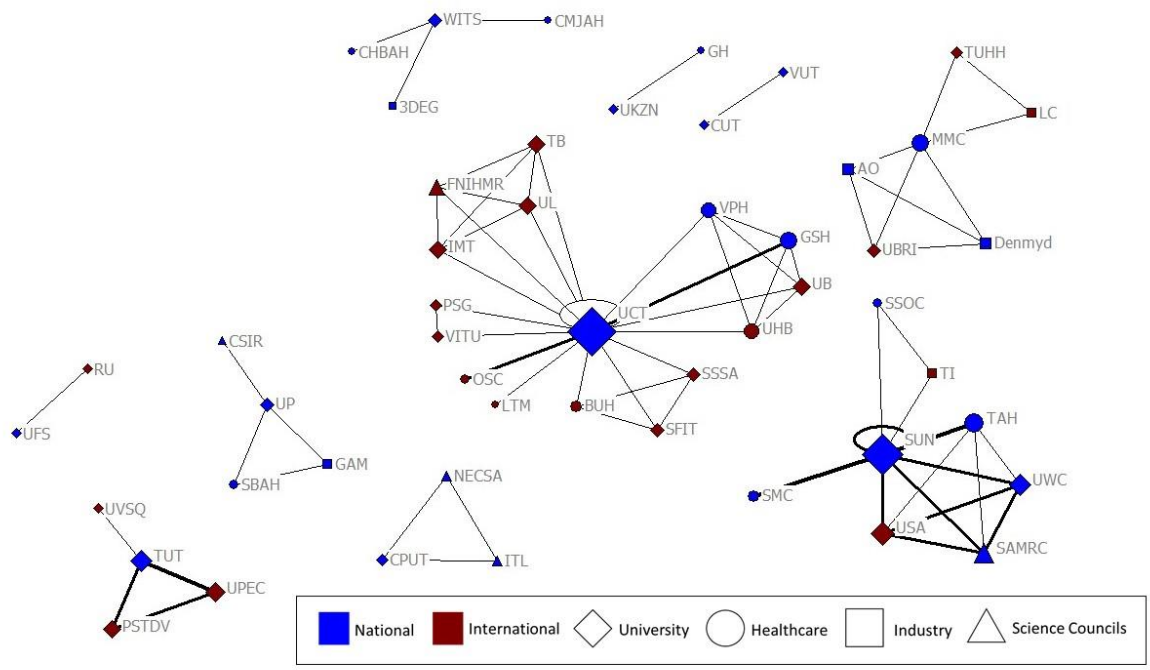


Figure 40: Actor-collaboration network based on scientific publication data for the period 2011 - 2015

APPENDIX E – Evolution of the 2-clan networks over all 12 timeframes

Each figure in this appendix is a 2-clan drawing of actors collaborating in the scientific publication network, in a five-year window over the period 2000-2015. In each diagram, national actors are drawn below the diagonal and international actors are drawn above the diagonal. International actors are grouped according to their country of origin. Overlap of subgroups can be seen where nodes belong to more than one 2-clan group. Isolated actors shown in the top left-hand corner form part of the timeframe network, but do not belong to any 2-clans.

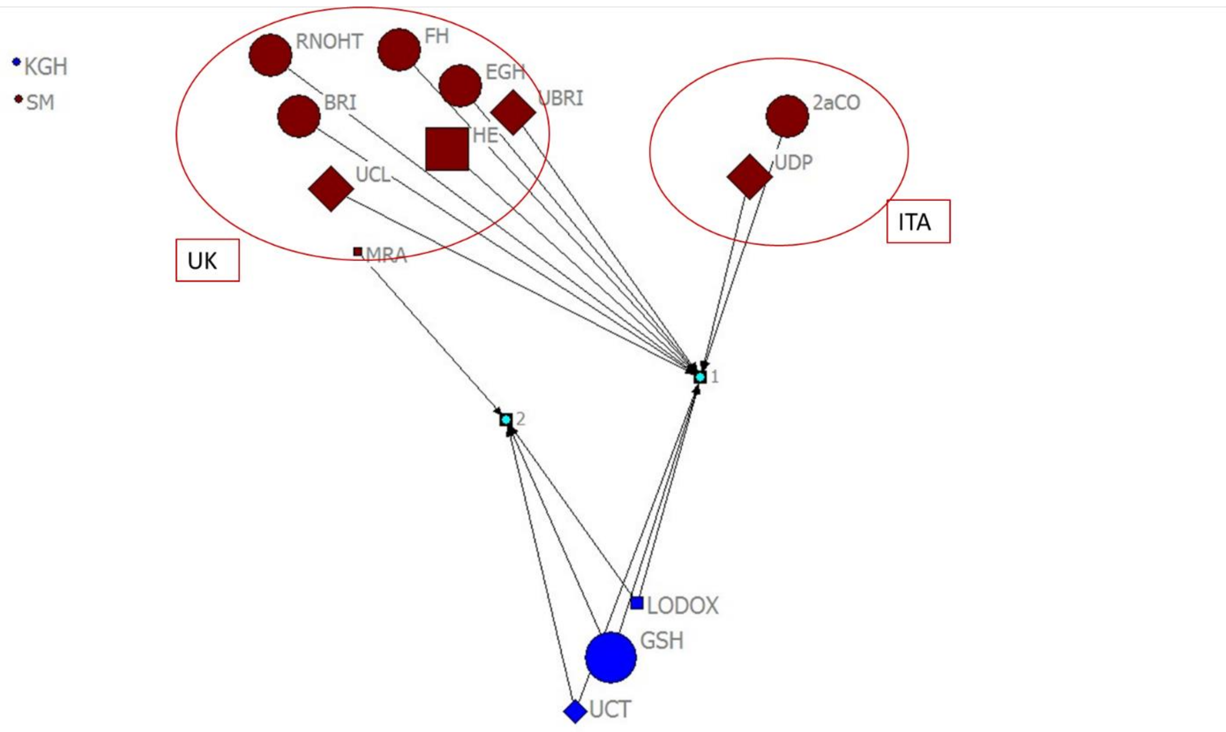


Figure 41: 2-clan subgroups for the period 2000-2004

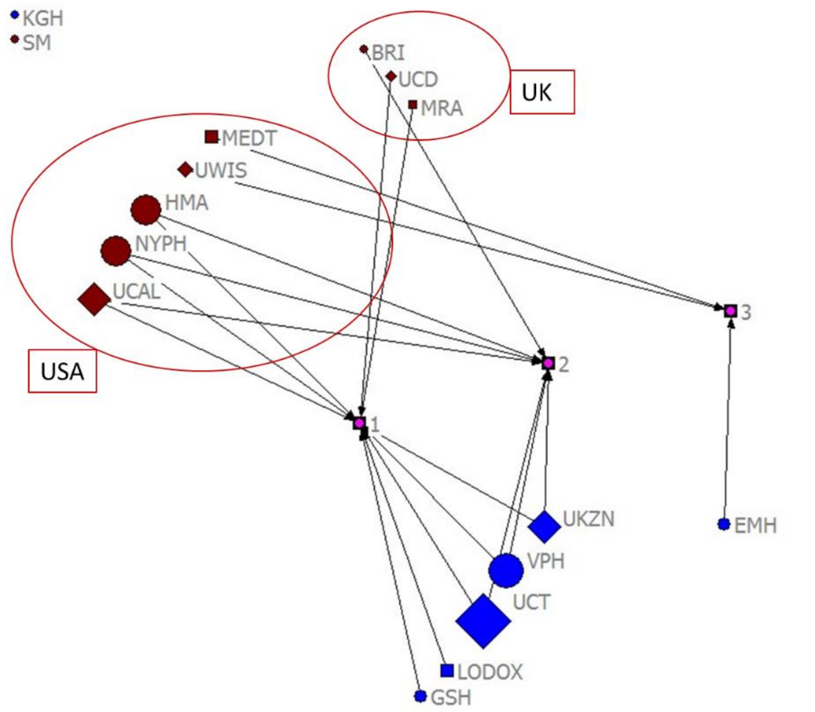


Figure 42: 2-clan subgroups for the period 2001-2005

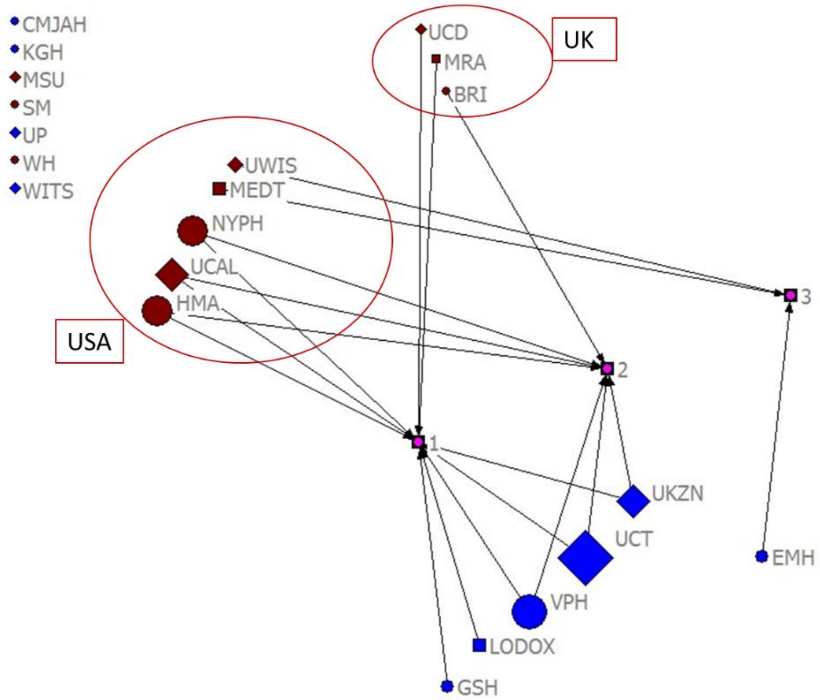


Figure 43: 2-clan subgroups for the period 2002-2006

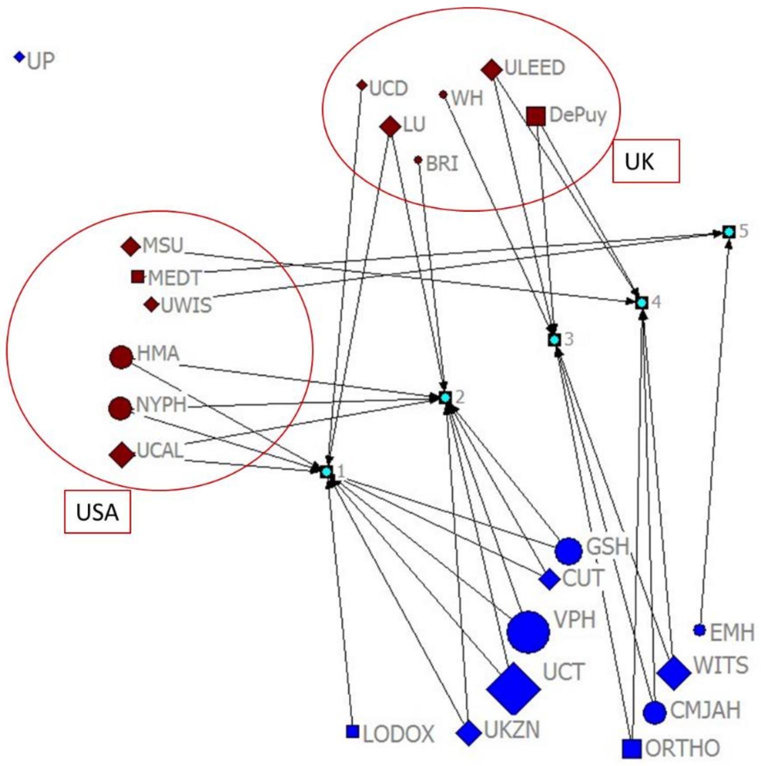


Figure 44: 2-clan subgroups for the period 2003-2007

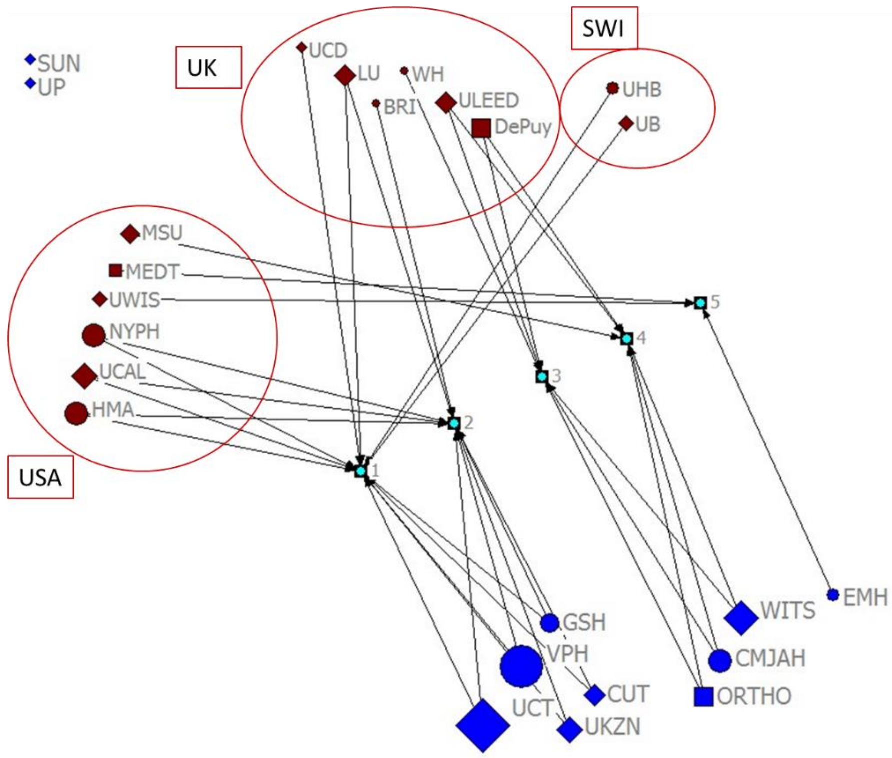


Figure 45: 2-clan subgroups for the period 2004-2008

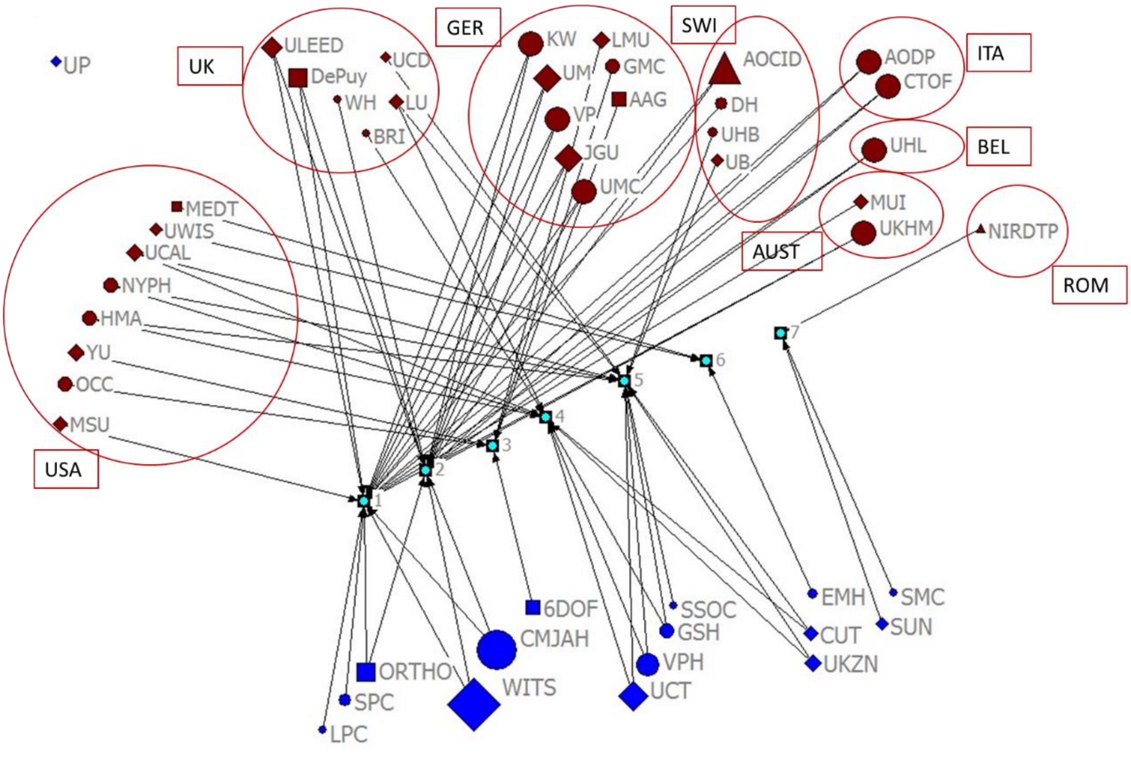


Figure 46: 2-clan subgroups for the period 2005-2009

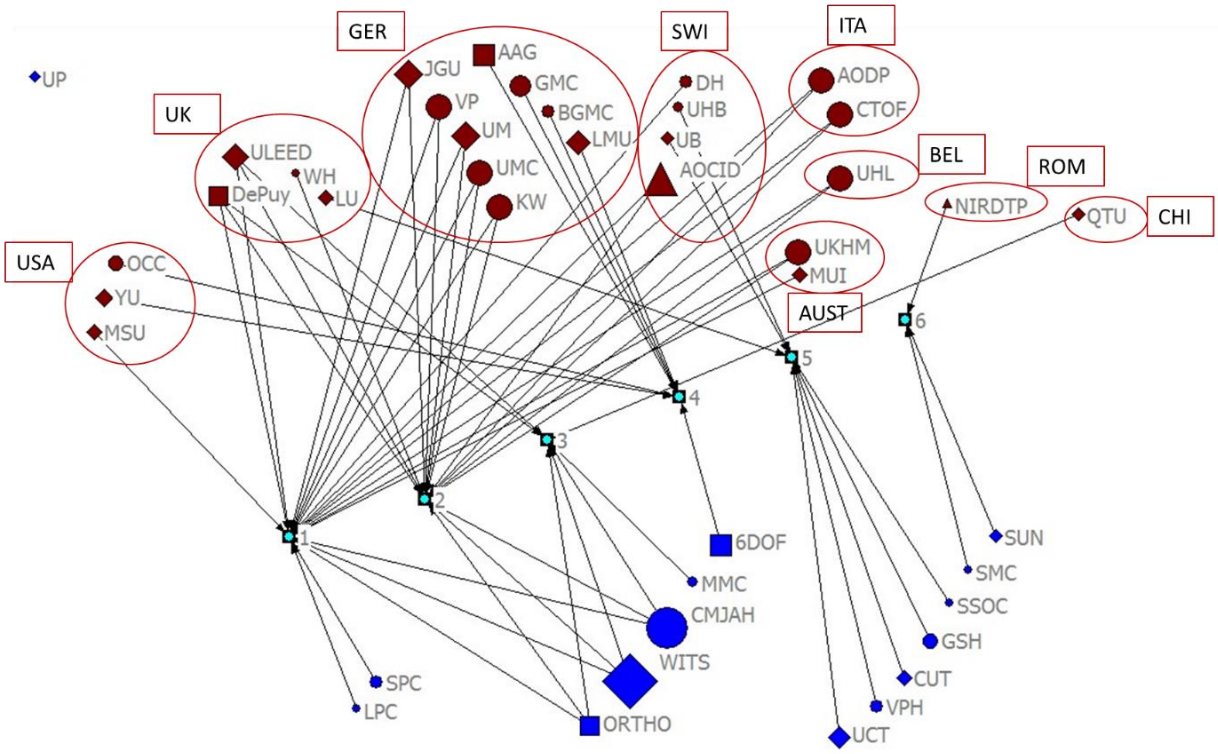


Figure 47: 2-clan subgroups for the period 2006-2010

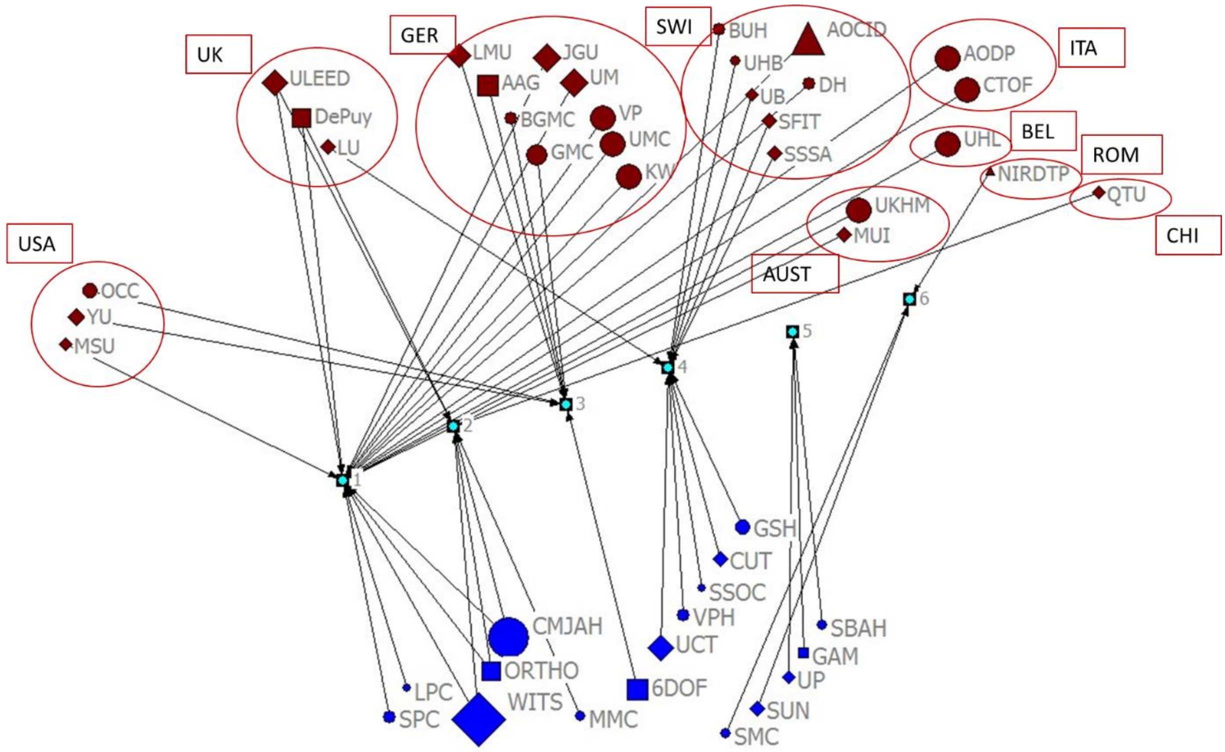


Figure 48: 2-clan subgroups for the period 2007-2011

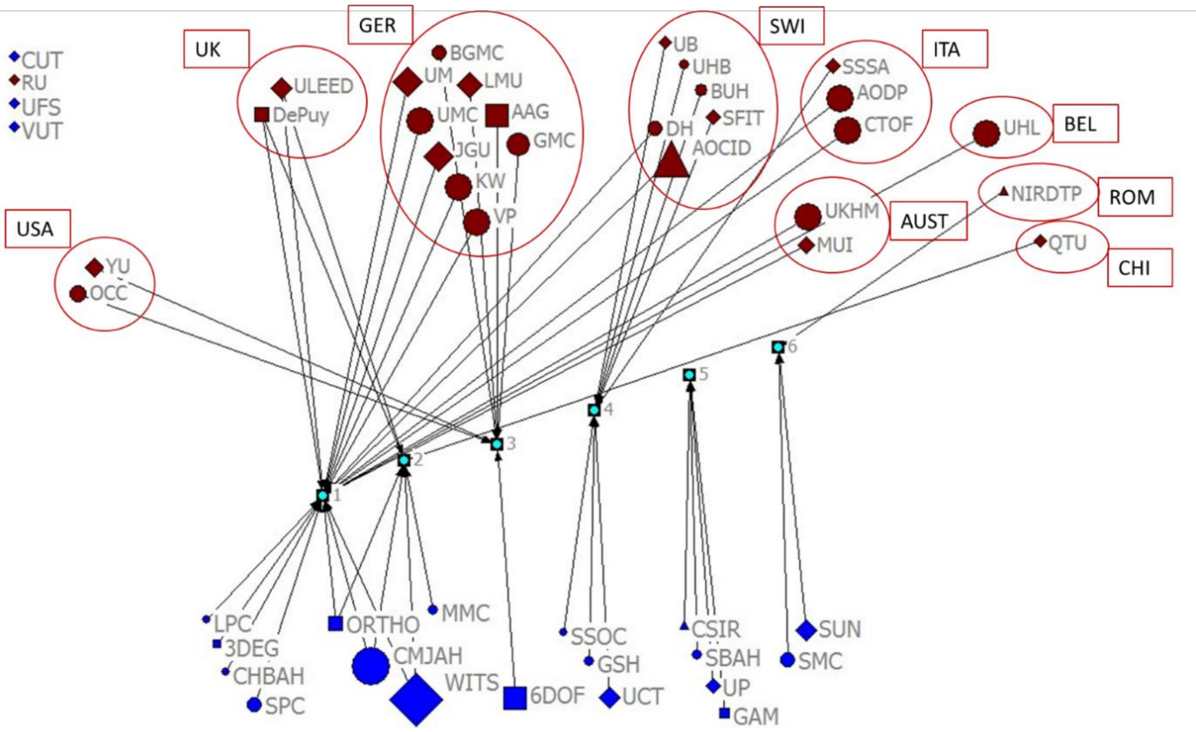


Figure 49: 2-clan subgroups for the period 2008-2012

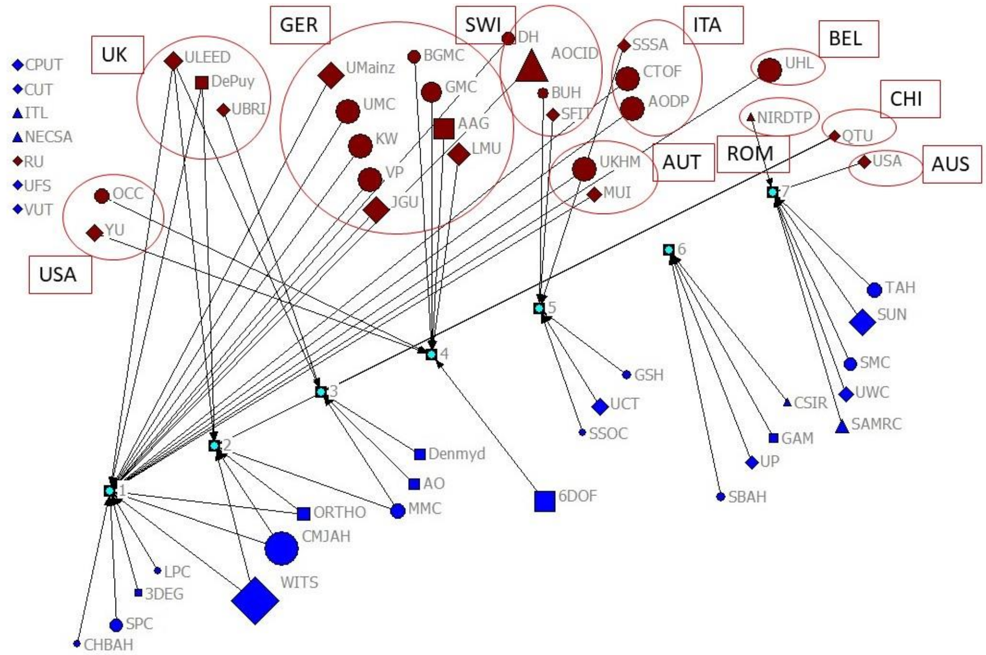


Figure 50: 2-clan subgroups for the period 2009-2013

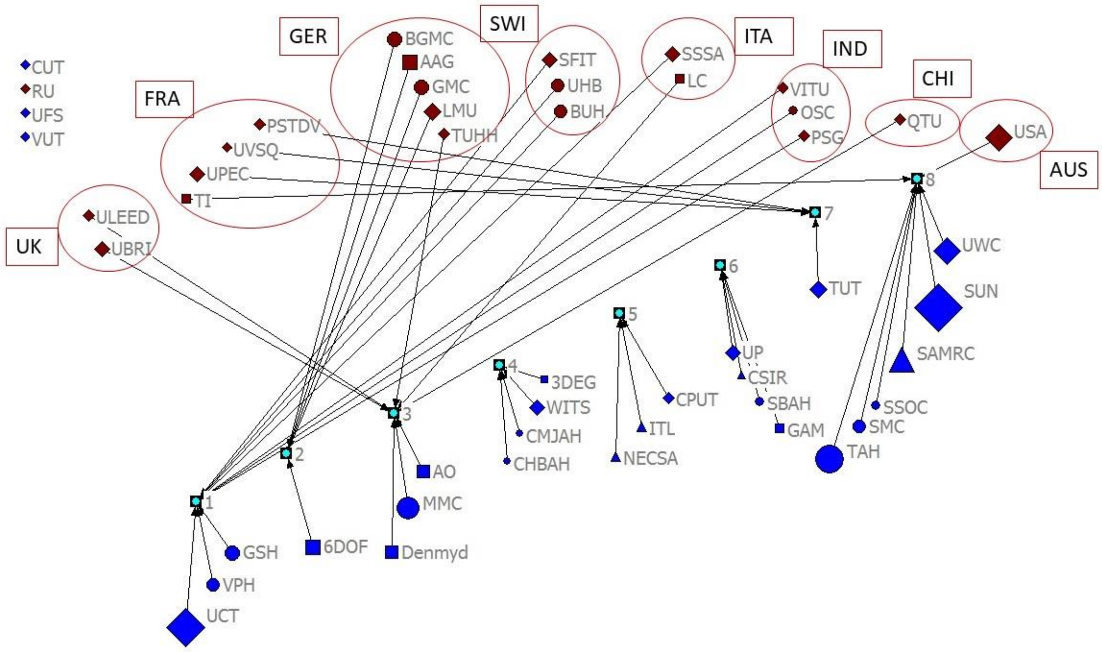


Figure 51: 2-clan subgroups for the period 2010-2014

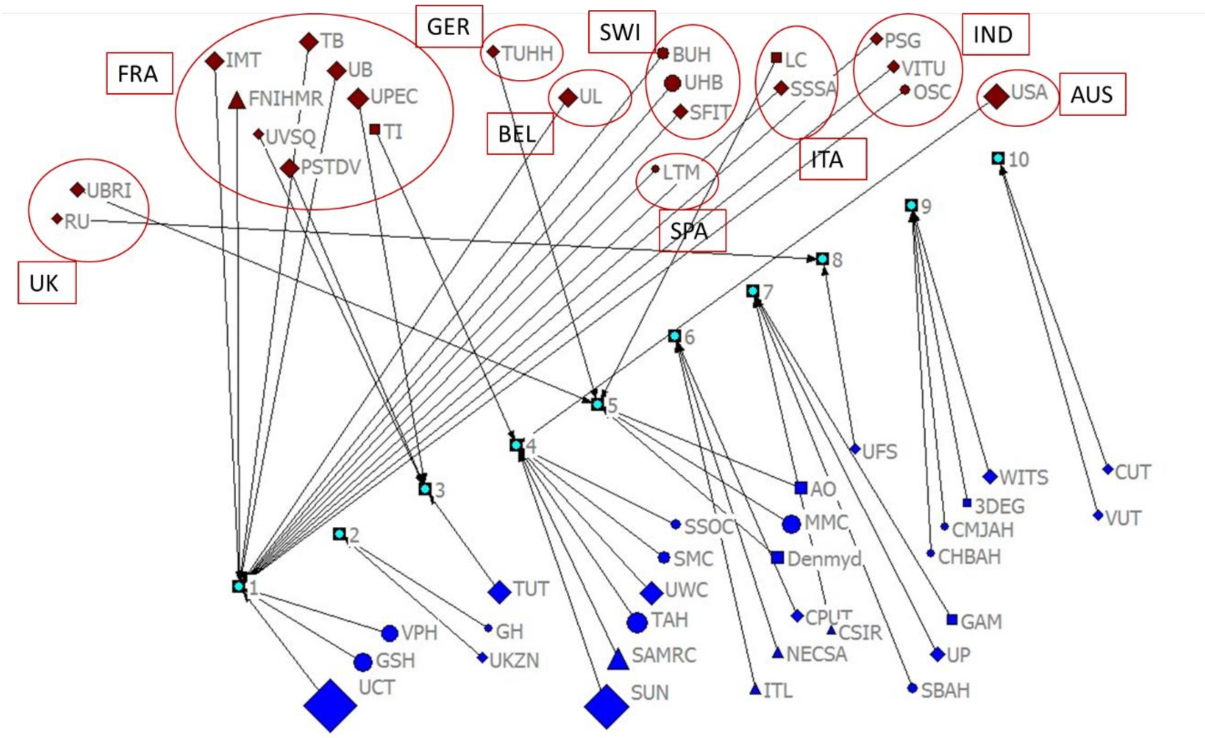


Figure 52: 2-clan subgroups for the period 2011 - 2015

APPENDIX F – List of scientific publications

Harting, M. & Hempel, M. 2000. Characterisation of residual stress and microstructure in bioactive coatings for titanium alloy hip implants. *Material Science Forum*. Volumes 347-349, pp. 580-585.

Walker, P.S.; Sathasivam, S; Cobb, A; Learmonth, I.D.; Grobler, G.P.; Pinder, I.M.; Marchetti, N. Spinelli, M.D. and Welsby, A. 2000. A comparison between cemented, press-fit, and HA-coated interfaces in Kinemax total knee replacement. *Knee*. Volume 7 (2), pp. 71-78.

Lambert, M.I.; Marcus, P.; Burgess, T. and Noakes, T.D. 2002. Electro-membrane microcurrent therapy reduces signs and symptoms of muscle damage. Medicine & Science in Sports & Exercise. Volume 34(4). pp. 602-607.

Spruit, M.; Pavlov, P.W.; Leitao, J.; de Kleuver, M.; Anderson, P.G. and den Boer, F. 2002. Posterior reduction and anterior lumbar interbody fusion in symptomatic low-grade adult isthmic spondylolisthesis: short-term radiological and functional outcome. *European Spine Journal*. Volume 11, pp. 428-433.

Beningfield, S.; Potgieter, H.; Nicol, A.; van As, S.; Bowie, G.; Hering, E. and Latti, E. 2003. Report on a new type of trauma full-body digital X-ray machine. *Emergency Radiology*. Volume 10, pp. 23-29.

Su, B.; Solomon, M.D.; Barrow, A.; Senogo, M.E.; Gilberti, M.; Lubbers, L.; Diao, E.; Quitkin, H.M. and Rosenwasser, M.P. 2005. Device for zone-II flexor tendon repair: A multicenter, randomized, blinded, clinical trial. *The Journal of Bone & Joint Surgery*. Volume 87(5), pp. 923-935.

Grobler, G.P.; Learmonth, I.D.; Bernstein, B.P. and Dower, B.J. 2005. Ten-year results of a press-fit, porous-coated acetabular component. *The Journal of Bone & Joint Surgery*. Volume 87-B(6), pp. 786-789.

Vaughan, C.L. and O'Malley, M.J. 2005. A gait nomogram used with fuzzy clustering to monitor functional status of children and young adults with cerebral palsy. *Developmental Medicine & Child Neurology*. Volume 47, pp. 377-383.

Jensen, W.K.; Anderson, P.A.; Nel, L. and Rouleau, J.P. 2005. Bone ingrowth in retrieved Bryan cervical disc prostheses: (Presented at the 2004 CSRS Meeting). *Spine*. Volume 30(22), pp. 2497-2502.

Burger, N.D.L.; de Vaal, P.L. and Meyer, J.P. 2006. Failure criteria for polyethylene acetabular cups. *South African Journal of Science*. Volume 102, pp. 572-574.

Haines, J.F.; Trail, I.A.; Nuttall, D.; Birch, A. and Barrow, A. 2006. The results of arthroplasty in osteoarthritis of the shoulder. *The Journal of Bone & Joint Surgery*. Volume 88-B, pp. 496-501.

Lajnef, N.; Chakrabartty, S.; Elvin, N. and Elvin, A. 2006. A sub-microwatt piezo-floating-gate sensor for long-term fatigue monitoring in biomechanical implants. Proceedings of the 28th IEEE EMBS Annual International Conference, New York City, USA.

Truscott, M.; de Beer, D.; Vicatos, G.; Hosking, K.; Barnard, L.; Booysen, G. and Campbell, R.I. 2007. Using RP to promote collaborative design of customised medical implants. *Rapid Prototyping Journal*. Volume 13(2), pp. 107-114.

Elvin, N.G.; Elvin, A. A. and Arnoczky, S.P. 2007. Correlation between ground reaction force and tibial acceleration in vertical jumping. *Journal of Applied Biomechanics*. Volume 23, pp. 180-189.

Lajnef, N.; Chakrabartty, S.; Elvin, N. and Elvin, A. 2007. Piezo-powered floating gate injector for self-powered fatigue monitoring in biomechanical implants. Proceedings of the IEEE International Symposium on Circuits and Systems, Los Alamito, USA.

Williams, S.; Schepers, A.; Isaac, G.; Hardaker, C.; Ingham, E.; van der Jagt, D.; Breckon, A. and Fisher, J. 2007. Ceramic-on-metal hip arthroplasties: A comparative in vitro and in vivo study. *Clinical Orthopaedics and Related Research*. Volume 465, pp. 23-32.

Exadaktylos, A.K.; Benneker, L.M.; Jeger, V.; Martinolli, L.; Bonel, H.M.; Eggli, S.; Potgieter, H. and Zimmermann, H. 2008. Total-body digital X-ray in trauma: An experience report on the first operational full body scanner in Europe and its possible role in ATLS. *Injury*. Volume 39(5), pp. 525-529.

de Jongh, C.U.; Basson, A.H. and Scheffer, C. Predictive modelling of cervical disc implant wear. *Journal of Biomechanics*. Volume 41(15), pp. 3177-3183.

Grupp, T.M.; Yue, J.J.; Garcia, R.; Basson, J.; Schwiesau, J.; Fritz, B. and Blomer, W. 2009. Biotribiological evaluation of artificial disc arthroplasty devices: influence of loading and kinematic patterns during in vitro wear simulation. *European Spine Journal*. Volume 18(1), pp. 98-108.

Hemmerich, A.; van der Merwe, W. and Vaughan, C.L. 2009. Measuring three-dimensional knee kinematics under torsional loading. *Journal of Biomechanics*. Volume 42(2), pp. 183-186.

Doppen, P.; Solomons, M. and Kritzinger, S. 2009. Osseointegrated finger prostheses. *The Journal of Hand Surgery*. European Volume 2008, pp. 1-6.

Ryf, C.; Goldhahn, S.; Radziejowski, M.; Blauth, M. and Hanson, B. 2009. A new injectable brushite cement: First results in distal radius and proximal tibia fractures. *European Journal of Trauma and Emergency Surgery,* Volume 35, pp. 89-96.

Isaac, G.H.; Brockett, C.; Breckon, A.; van der Jagt, D.; Williams, S.; Hardaker, C.; Fisher, J. and Schepers, A. 2009. Ceramic-on-metal bearings in total hip replacement: Whole blood metal ion levels and analysis of retrieved components. *The Journal of Bone & Joint Surgery*. Volume 91-B, pp. 1134-1141.

Saragas, N.P. 2009. Proximal opening-wedge osteotomy of the first metatarsal for hallux valgus using a low profile plate. *Foot & Ankle International*. Volume 30(10), pp. 976-980.

Blum, J.; Hansen, M.; Muller, M.; Rommens, P.M.; Matuschka, H.; Olmeda, A.; Radziesjowski, M.J.; Merbold, W.; Nijs, S. and Angeloni, R. 2009. Proximal humeral fractures and intramedullary nailing: Experience with a new nail system. *European Journal of Trauma and Emergency Surgery*. Volume 35(5), pp. 489-498.

Giouroudi, I.; Kosel, J.; Chiriac, H. and Scheffer, C. 2009. Evaluation of CoFeSiB microwires for biomechanical stress studies. *Sensor Letters*. Volume 7(3), pp. 378-382.

van den Heever, D.J.; Scheffer, C.; Erasmus, P.J. and Dillon, E.M. 2009. Development of a patient-specific femoral component for unicompartmental knee replacement. Proceedings of 31st Annual International Conference of the IEEE EMBS, Minnesota, USA.

Grupp, T.M.; Meisel, H-J.; Cotton, J.A.; Schwiesau, J.; Fritz, B.; Blomer, W. and Jansson, V. 2010. Alternative bearing materials for intervertebral disc arthroplasty. *Biomaterials*. Volume 31(3), pp. 523-531.

Gao, L.; Yang, P.; Dymond, I.; Fisher, J. and Jin, Z. 2010. Effect of surface texturing on the elastohydrodynamic lubrication analysis of metal-on-metal hip implants. *Tribology International*. Volume 43(10), pp. 1851-1860.

Grobbelaar, C.J.; du Plessis, T.A.; Steffens, F.E. and van der Linde, M.J. 2011. Longterm evaluation of polyethylene wear in total hip replacement - a statistical analysis of the association between the degree of wear versus pain, interface change, osteolysis and implant failure. *South African Orthopaedic Journal*. Volume 10(1), pp. 49-56.

Pikor, T.D. and Kyte, R.D. 2011. Evaluation of peri-articular aggressive benign bone tumours treated with cementation and a locked plate. *South African Orthopaedic Journal*. Volume 10(2), pp. 48-55.

van den Heever, D.J.; Scheffer, C.; Erasmus, P. and Dillon, E. 2011. Contact stresses in a patient-specific unicompartmental knee replacement. *Clinical Biomechanics*. Volume (26(2), pp. 159-166.

Crema, A.; McNaught, A.; Albissr, U.; Bolliger, M.; Micera, S.; Curt, A. and Morari, M. 2011. A hybrid tool for reaching and grasping rehabilitation: The ArmeoFES. Proceedings of the 33rd Annual International Conference of the IEEE EMBS, Boston, Massachusetts, USA.

van Staden, A.D. and Dicks, M.T. 2012. Calcium orthophosphate-based bone cements (CPCs): Applications, antibiotic release and alternatives to antibiotics. Journal of Applied Biomaterials and Functional Materials. Volume 10(1), pp. 2-11.

Truscott, M.; Booysen, G.J. and de Beer, D.J. Additive manufacturing for soft tissue geometries for reconstruction purposes. Innovative Developments in Virtual and Physical Prototyping - Proceedings of the 5th International Conference on Research and Rapid Prototyping.

Schepers, A.; Cullingworth, L. and van der Jagt, D.R. 2012. A prospective randomized clinical trial comparing tibial baseplate fixation with or without screws in total knee arthroplasty: A radiographic evaluation. *The Journal of Arthroplasty*. Volume 27(3), pp. 454-460.

McGuire, D.T.; White, C.D.; Carter, S.L. and Solomons, M.W. 2012. Pyrocarbon proximal interphalangeal joint arthroplasty: Outcomes of a cohort study. *Journal of Hand Surgery: European Volume*. Volume 37(6), pp. 490-496.

Peters, F.M.; Greeff, R.; Goldstein, N. and Frey, C.T. 2012. Improving acetabular cup orientation in total hip arthroplasty by using smartphone technology. *The Journal of Arthroplasty*. Volume 27(7), pp. 1324-1330.

Strike, S.C.; Wickett, O.; Schoeman, M. and Diss, C.E. 2012. Mechanisms to absorb load in amputee running. *Prosthetics and Orthotics International*. Volume 36(3), pp. 318-323.

Wepener, I.; Richter, W.; van Papendorp, D. and Joubert, A.M. 2012. In vitro osteoclasts-like and osteoblast cell's response to electrospun calcium phosphate biphasic candidate scaffolds for bone tissue engineering. *Journal of Materials Science*. Volume 23(12), pp. 3029-3040.

Mueller, J.H.; Erasmus, P.J. and Scheffer, C. 2012. Comparison of commercial patellofemoral arthroplasty systems on the basis of patella kinematics, peri-patellar soft tissue tension and prosthesis design. Journal of Mechanics in Medicine and Biology. Volume 12(5)

van den Heever, D.; Scheffer, C.; Erasmus, P. and Dillon, E. 2012. Development and testing of patient-specific knee replacements. Proceedings of the 34th Annual International Conference of the IEEE EMBS, California, USA.

Janson, J.T. and Rossouw, G.J. 2013. A new technique for repair of a dislocated sternoclavicular joint using a sternal tension cable system. *The Annals of Thoracic Surgery*. Volume 95(2), pp. 53-55.

de Beer, N. and van der Merwe, A. 2013. Patient-specific intervertebral disc implants using rapid manufacturing technology. *Rapid Prototyping Journal*. Volume 19(2), pp. 126-139.

Pineda-Vargas, C.A.; Topic, M. and Ntsoane, T. 2013. Micro-PIXE analysis of bioconductive hydroxyapatite coatings on titanium alloy. *Journal of Radioanalytical and Nuclear Chemistry*. Volume 297(3), pp. 457-461.

Dymond, I.W.; Ashforth, J.A.; Dymond, G.F.; Spirakis, T. and Learmonth, I.D. The usage of image trigonometry in bone measurements. *HIP International*. Volume 23(6), pp. 590-595.

Brink, Y.; Louw, Q.; Grimmer, K.; Schreve, K.; van der Westhuizen, G. and Jordaan, E. 2013. Development of a cost-effective three-dimensional posture analysis tool: validity and reliability. *BMC Musculoskeletal Disorders.* Volume 14(1), https://doi.org/10.1186/1471-2474-14-335.

Morlock, M.M.; Witt, F.; Bishop, N.; Behn, R.; Pria, P.D.; Barrow, R. and Dymond, I. 2014. Wear of a composite ceramic head caused by a liner fracture. *Orthopedics*. Volume 37(7), pp. 653-656.

Sivarasu, S. and Patnaik, S. 2014. Novel device for measuring knee laxity at various flexion angles – Laxmeter. *Journal of Medical Devices*. Volume 8(2), https://doi.org/10.1115/1.4026995.

Trenoras, L.; Gregory, U.; Monacelli, E. and Hugel, V. 2014. Mechatronic design of the Gyrolift verticalization wheelchair. Proceedings of the 2014 IEEE/ASME International Conference on Advanced Intelligent Mechatronics, Besancon, France.

Madani, T.; Daachi, B. and Djouani, K. 2014. Finite-time control of an actuated orthosis using fast terminal sliding mode. *IFAC Proceedings Volumes*. Volume 47(3), pp. 4607-4612.

Maqungo, S.; Horn, A.; Bernstein, B.; Keel, M. and Roche, S. 2014. Distal interlocking screw placement in the femur: Free-hand versus electromagnetic assisted techniques (Sureshot). *Journal of Orthopaedic Trauma*. Volume 28(12), pp. 281-283.

Sivarasu, S. and Patnaik, S. Design and prototype development of a novel low cost stress radiographic device – laxmeter (an Indo-Africa invention). Proceedings of Appropriate Healthcare Technologies for Low Resource Settings (AHT 2014), London, UK.

Dendere, R.; Whiley, S.P. and Douglas, T.S. 2014. Computed digital absorptiometry for measurement of phalangeal bone mineral mass on a slot-scanning digital radiography system. *Osteoporosis International*. Volume 25(11), pp. 2625-2630.

Muller, J.H.; Zakaria, T.; Renault, E. and van der Merwe, W. 2014. Application of an in-vivo validated lower body musculoskeletal model as a test platform for different total knee prostheses. Proceedings of the 9th South African Conference on Computational and Applied Mechanics, Somerset West, South Africa.

Ajayi, M.O.; Djouani, K. and Hamam, Y. 2014. Analysis of knee-ankle orthosis modelling: An inverse dynamics approach using adaptive coupled oscillator. *Lecture Notes in Computer Science*. Volume 8810, https://doi.org/10.1007/978-3-319-11900-7_11.

Sivarsu, S.; James, S.P. and Mather, L. 2014. 3D reconstruction of knee joint from CT images and customized meniscus development. *Biomed Tech*. Volume 59(s1).

Brink, Y.; Louw, Q.; Grimmer, K. and Jordaan, E. 2014. The spinal posture of computing adolescents in a real-life setting. *BMC Musculoskeletal Disorders*. Volume 15(1), https://doi.org/10.1186/1471-2474-15-212.

King, P.R.; Ikram, A. and Lamberts, R.P. 2015. The treatment of clavicular shaft fractures with an innovative locked intramedullary device. *Journal of Shoulder and Elbow Surgery*. Volume 24(1), pp. 1-6.

Ajayi, M.O.; Djouani, K. and Hamam, Y. 2015. Shank-foot trajectory control: A forward dynamics approach using computed-torque control. Proceedings of the 2014 IEEE-RAS International Conference on Humanoid Robots, Madrid, Spain.

Patnaik, S. and Sivarasu, S. 2015. Patellofixator rig – Design specifications of a device assisting medical patello femoral ligament (MPFL) reconstruction. Proceedings of the 7th WACBE Congress on Bioengineering, Singapore.

Ferreira, N. and Marais, L.C. 2015. Bone transport through an induced membrane in the management of tibial bone defects resulting from chronic osteomyelitis. *Strategies in Trauma and Limb Reconstruction.* Volume 10(1), pp. 27-33.

Mutsvangwa, T.; Burdin, V.; Schwartz, C. and Roux, C. 2015. An automated statistical shape model development pipeline: Application to the human scapula and humerus. *IEEE Transactions on Biomedical Engineering*. Volume 62(4), pp. 1098-1107.

APPENDIX G – Actors of the patent actor-collaboration network

Abbreviation	Full name	Location
	Healthcare sector	
CMJAH	Charlotte Maxeke Johannesburg Academic Hospital	National
GUH	Ghent University Hospital	International
GSH	Groote Schuur Hospital	National
JH	Jakaranda Hospital	National
KPOU	Klinik und Poliklinik fur Orthopadie und Unfallchirurgie	International
LH	Livingstone Hospital	National
LWH	Life Wilgeleugen Hospital	National
LOC	Lyon Ortho Clinic	International
MMC	Morningside MediClinic	National
OSC	Ortho One Sports Clinic	International
OSV	OrthoSport Victoria	International
ParklandsH	Parklands Hospital	National
PH	Pinehaven Hospital	National
QE2HSC	Queen Elizabeth 2nd Health Sciences Centre	International
SBAH	Steve Biko Academic Hospital	National
SH	Sunshine Hospital	International
SSOC	Sports Science Orthopaedic Clinic	National
SMC	Stellenbosch MediClinic	National
Unitas	Unitas Hospital	National
VPH	Vincent Palotti Hospital	National
ZAH	Zuid Afrikaans Hospital	National
	Industry sector	
ATTRI	ATTRI	National
BBOP	Bradley Beckerleg Orthotic & Prosthetics	National
CMO	Custom Med Orthopaedics (Pty) Ltd	National
DenMyd	Denmyd Medical Equipment	National
DesDall	Desmond Dall	National
D4SBV	Design4Spine BV	International
ESS	Elite Surgical Supplies	National
ESUSA	Elite Surgical USA	International
KVP	Kearny Venture Partners	International

OrthoSol	Ortho-Sol Pty Ltd	National
PAB	Pressure Air Biofeedback CC	National
reSCRIBE	reSCRIBE	National
Saspine	Saspine	National
SmartCrutch	smartCRUTCH	National
SI	Southern Implants (Pty) Ltd	National
SM	Southern Medical (Pty) Ltd	National
SMI	Spinal Motion Inc	International
TI	Tornier Inc	International
Wismed	Wismed	National
	Science Council sector	
CSIR	Council for Scientific and Industrial Research	National
	University sector	
GU	Ghent University	International
LTU	La Trobe University	International
LU	Loughborough University	International
NWU	North-West University	National
PSTDV	Pole Scientifique Et Technologique de Volzy	International
SUN	Stellenbosch University	National
TUT	Tshwane University of Technology	National
UVSQ	Universite de Versailles Saint-Quentin-en-Evelines	International
UB	University of Bath	International
UCT	University of Cape Town	National
UM	University of Manchester	International
UMIN	University of Minnesota	International
UP	University of Pretoria	National
UPEC	Universite Paris East Central	International
WITS	University of Witwatersrand	National
VUT	Vaal University of Technology	National

APPENDIX H - Patent actor-collaboration networks

Each image presented in this appendix is an actor-collaboration network of in a five-year window over the period 2000-2015.

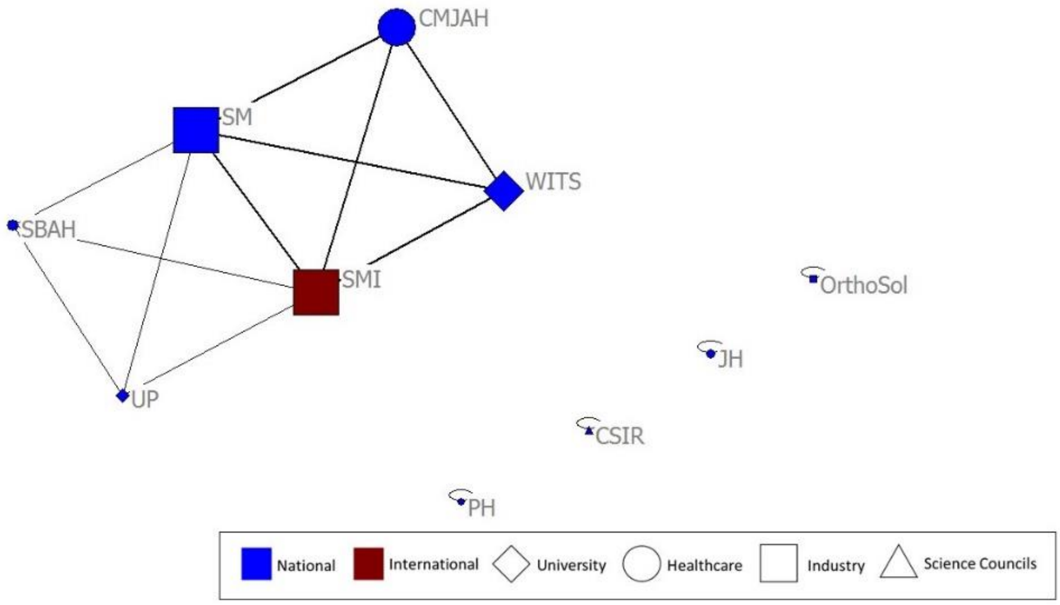


Figure 53: Actor-collaboration network based on patent data for the period 2000-2004

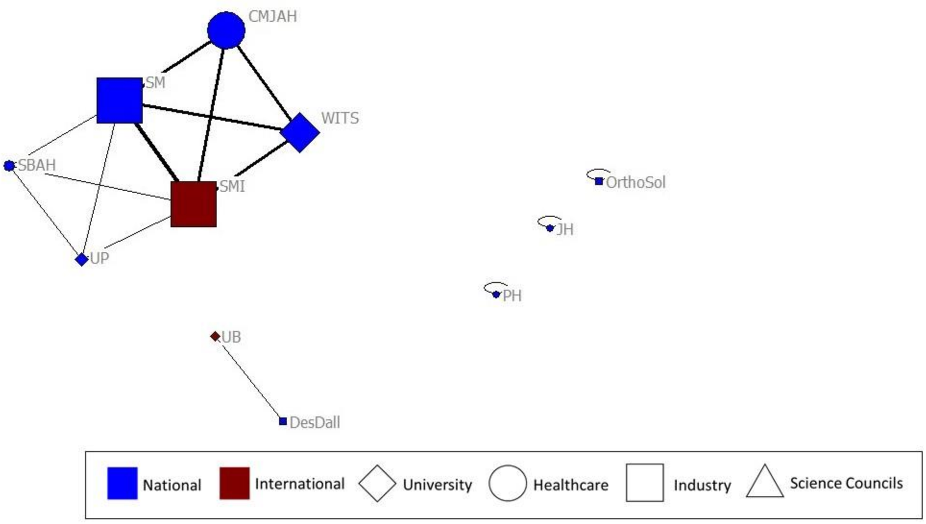


Figure 54: Actor-collaboration network based on patent data for the period 2001-2005

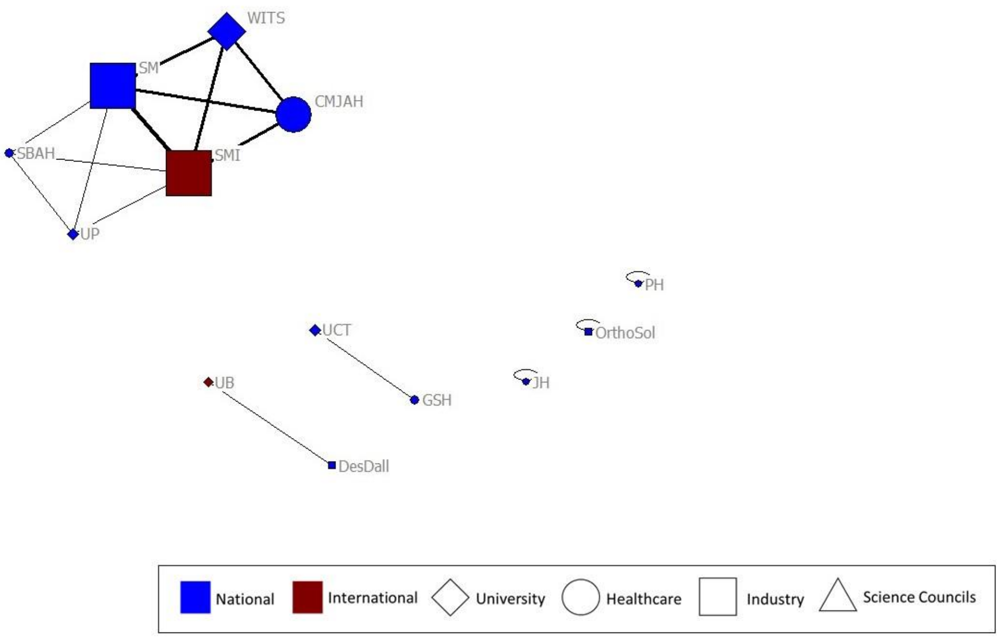


Figure 55: Actor-collaboration network based on patent data for the period 2002-2006

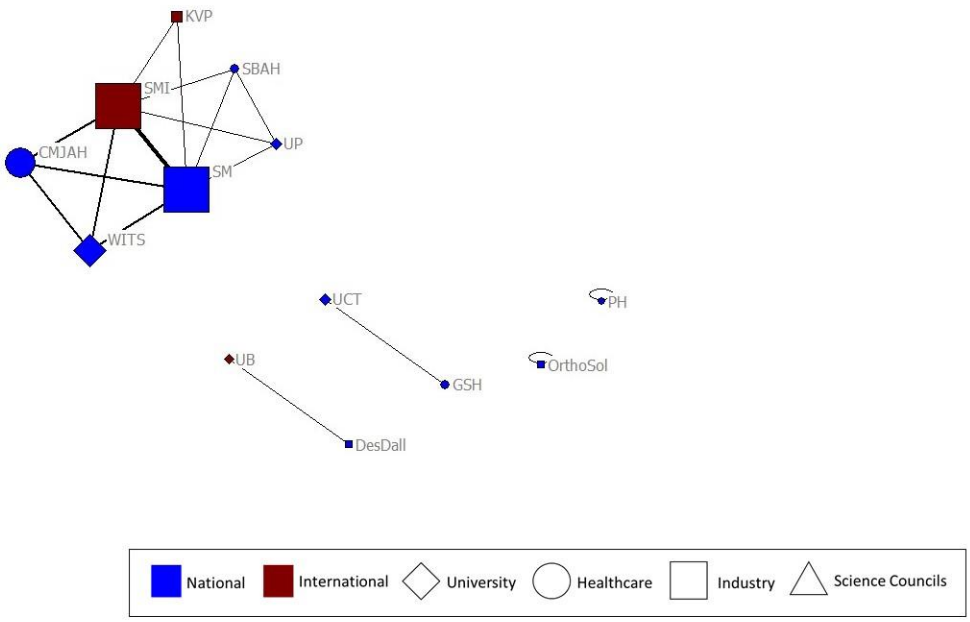


Figure 56: Actor-collaboration network based on patent data for the period 2003-2007

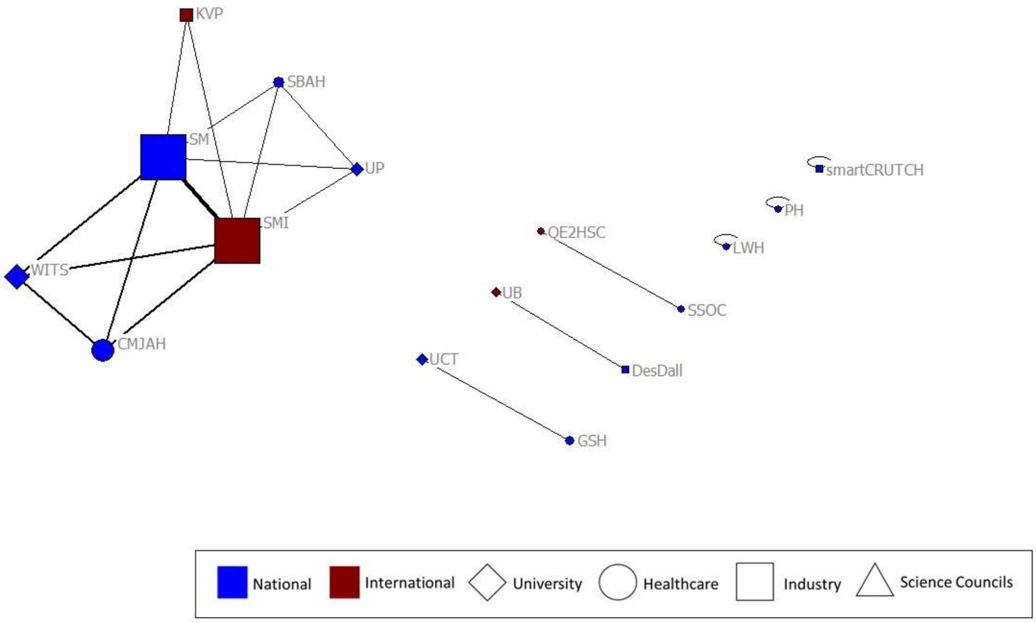


Figure 57: Actor-collaboration network based on patent data for the period 2004-2008

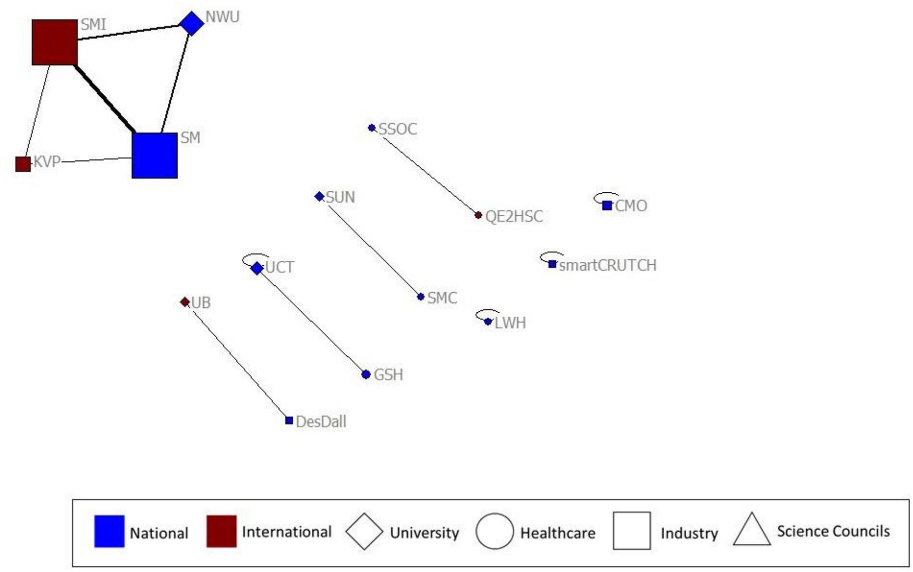


Figure 58: Actor-collaboration network based on patent data for the period 2005-2009

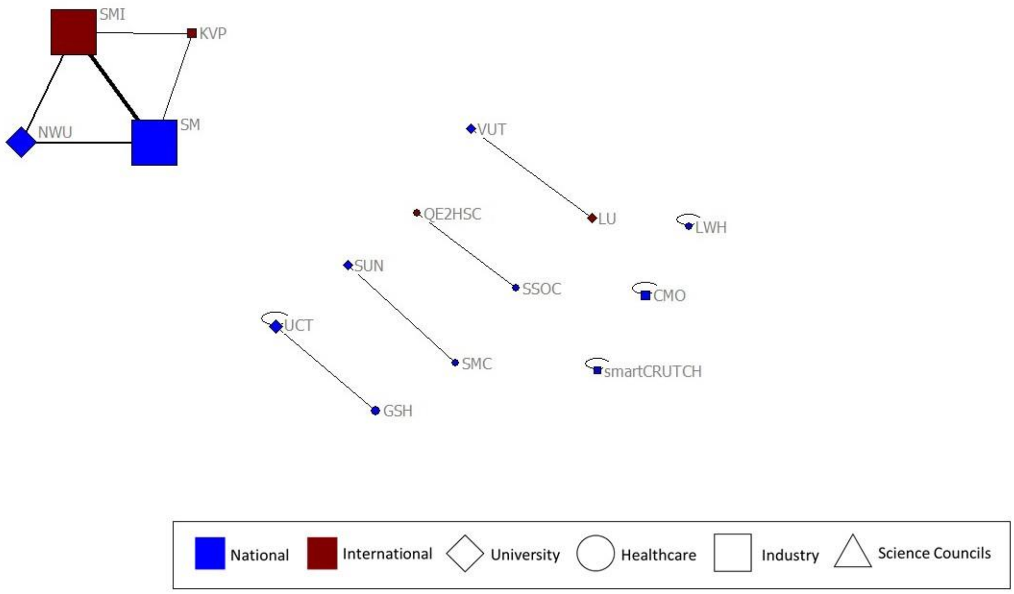


Figure 59: Actor-collaboration network based on patent data for the period 2006-2010

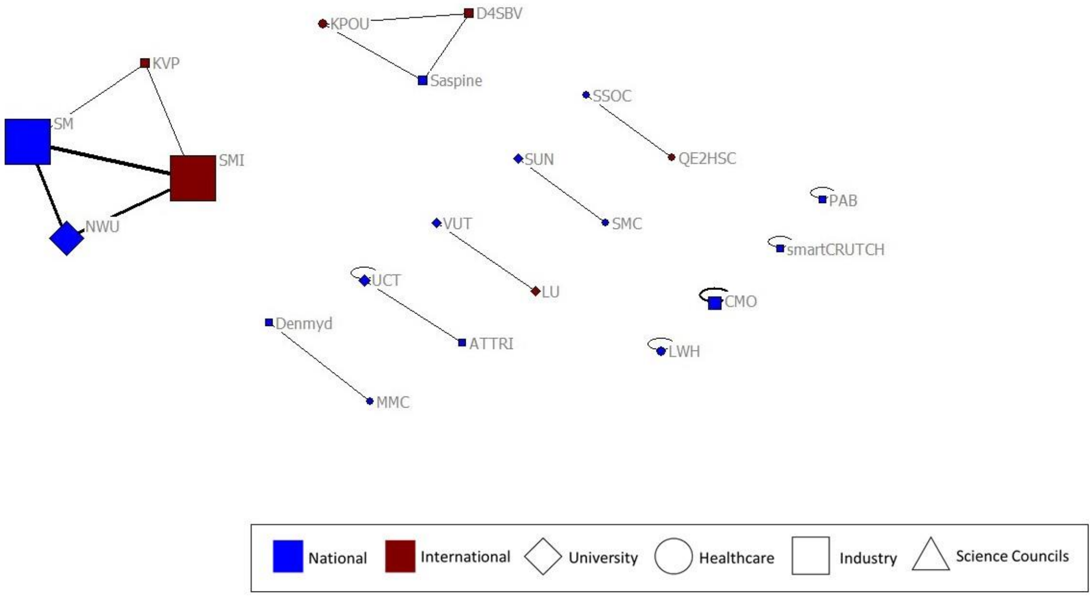


Figure 60: Actor-collaboration network based on patent data for the period 2007-2011

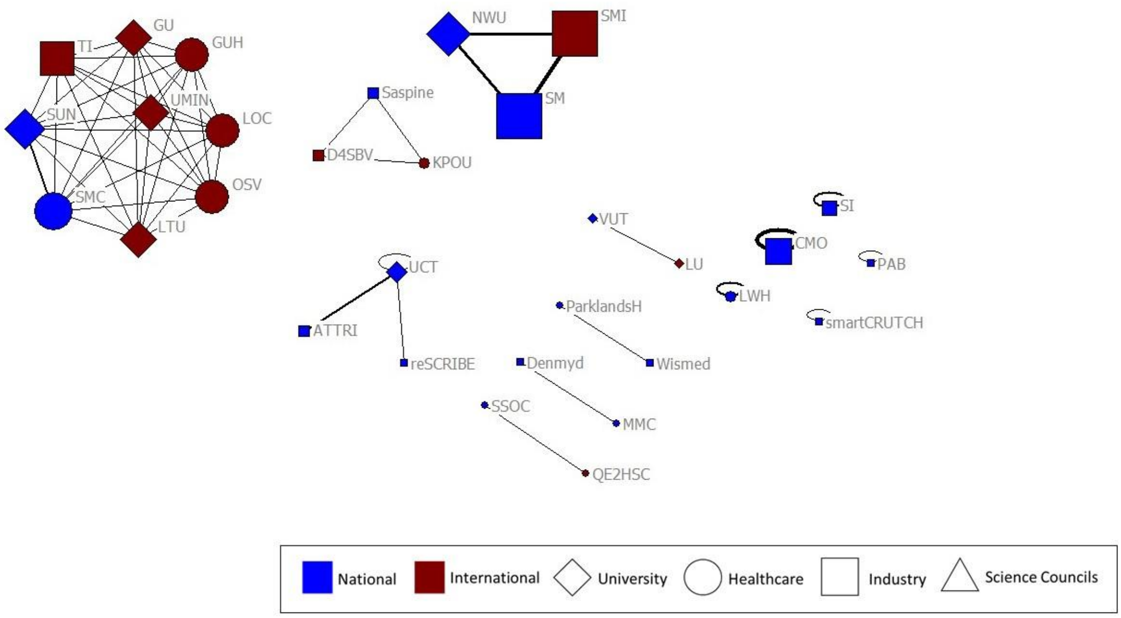


Figure 61: Actor-collaboration network based on patent data for the period 2008-2012

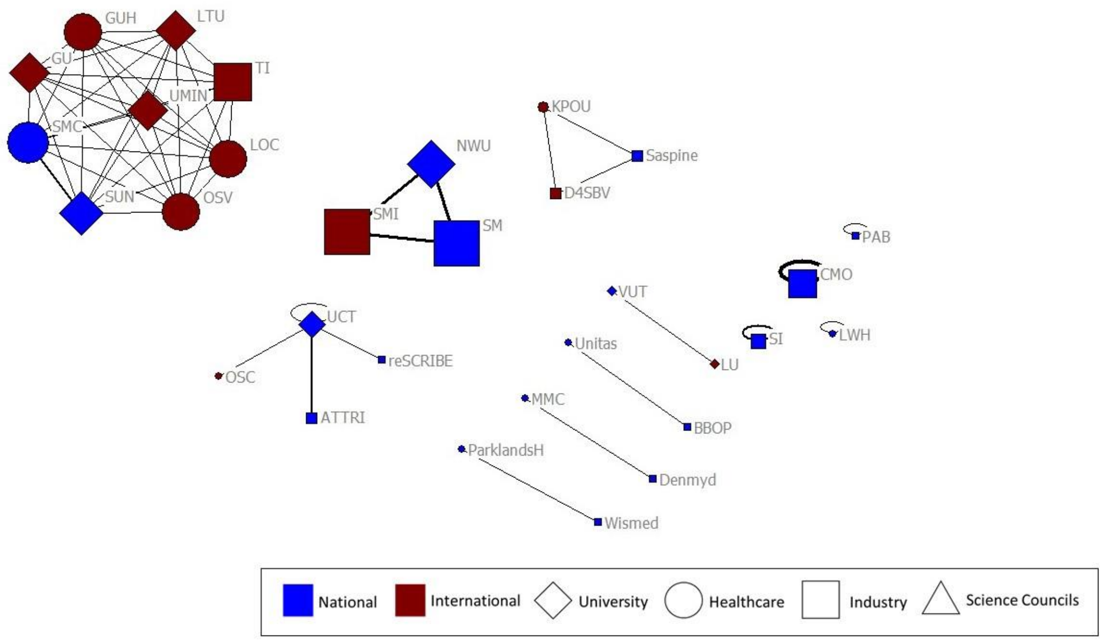


Figure 62: Actor-collaboration network based on patent data for the period 2009-2013

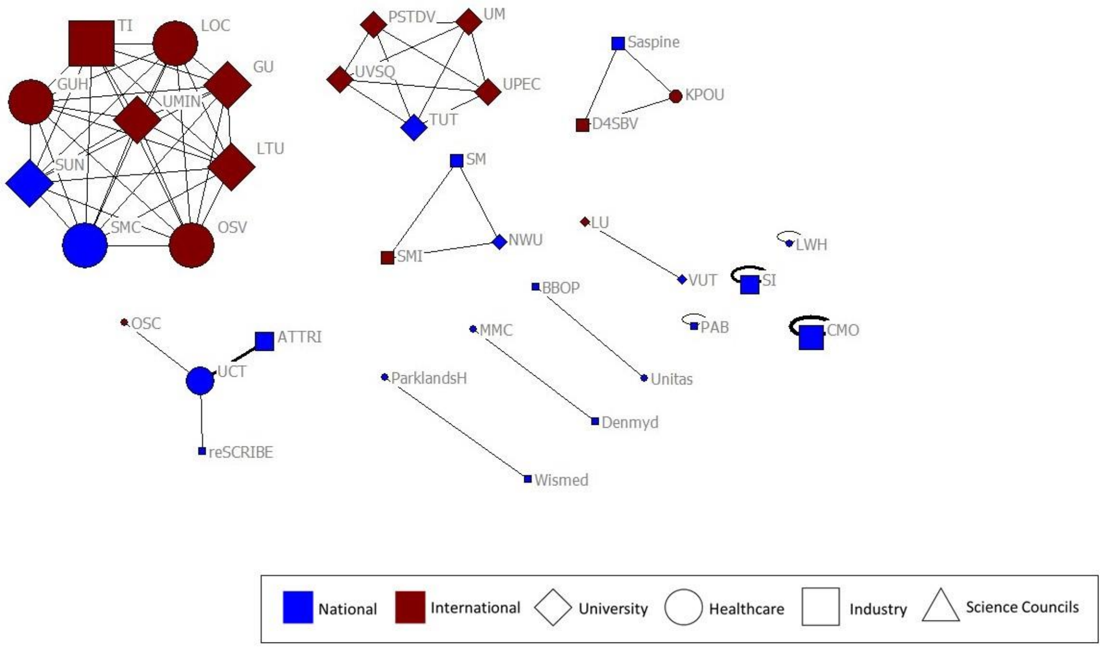


Figure 63: Actor-collaboration network based on patent data for the period 2010-2014

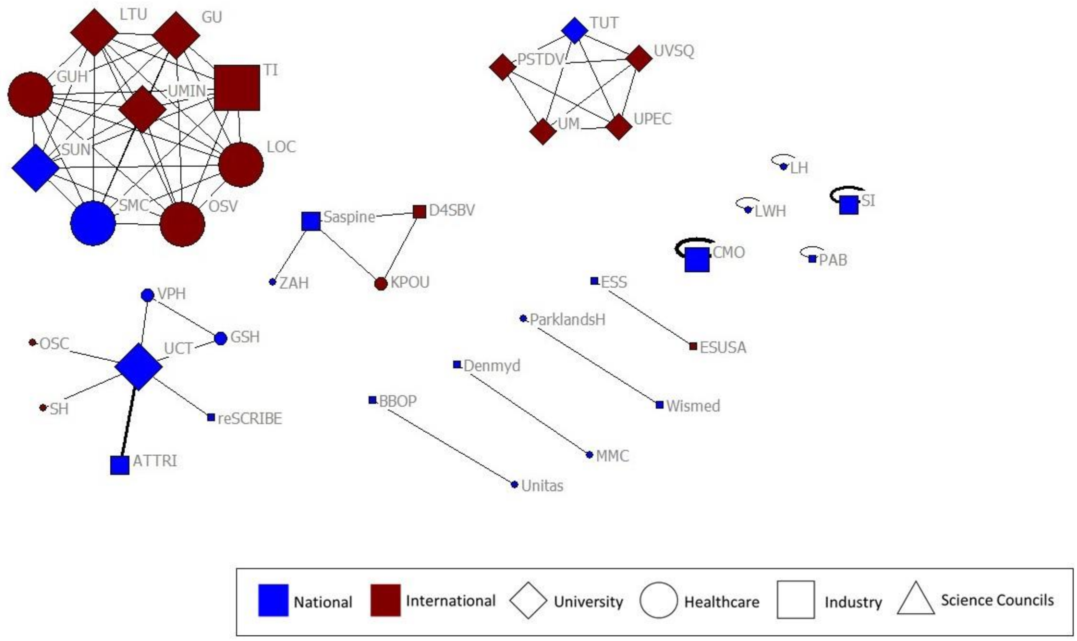


Figure 64: Actor-collaboration network based on patent data for the period 2011-2015

APPENDIX I – Patents

Richter, P.W. and Thomas, M.E. 2000. Implant including a body of non-resorbable bioactive material. ZA200001247A.

Roesch, T.G. 2000. Suture anchor. ZA2000/1282.

Roesch, T.G. 2002. A method of feeding a suture element. ZA200208423A.

de Villers, M. 2002. Arthroplasty implant. ZA200207516.

de Villiers, M. and Hahnle, U.R. 2002. Intervertebral prosthesis. ZA200207517.

Walker, R.M. 2003. An intervertebral prosthesis. ZA200309312A.

de Villiers, M. and Hahnle, U. 2003. A method for assembling a prosthetic disc for intervertebral insertion. US60473802.

de Villiers, M. and Hahnle, U. 2003. Intervertebral prosthetic disc. US60473803.

de Villiers, M. and Hahnle, U. 2004. Prosthetic disc for intervertebral insertion. WOUS04016789.

de Villiers, M. and Mennen, U. 2004. Digital joint arthroplasty. ZA2004/4961.

de Villiers, M.; Hahnle, U. and Hovda, D. 2004. Intervertebral prosthetic disc with metallic core. US903913.

Botha, P. J. 2004. Joint prosthesis component. US60610563P.

de Villiers, M.; Hovda, D. and Shapiro, J. 2005. Intervertebral prosthetic disc with shock absorption. US11051513.

Dall, D.M. and Miles, A.W. 2005. Configurable bone fixation system. GB0505505.

de Villiers, M. 2005. Spinal fusion device. ZA2005/02948.

de Villiers, M. 2006. Lower arm arthroplasty. ZA200607160A.

Kairinos, N. 2006. Orthopaedic pin isolator. ZA2006/04593.

de Villiers, M. and Hovda, M. 2006. Posterior spinal device and method. US60744710.

de Villiers, M. and Hovda, D. 2006. Spinal prosthesis with offset anchors. US60820769.

Solomons, M.W. 2006. Trapezium prosthesis. ZA2006/05686.

de Villiers, M.; Hovda, D. and Shapiro, J. 2007. Customised intervertebral prosthetic disc with shock absorption. US11836684.

de Villiers, M. and Hovda, D. 2007. Spinal prosthesis with multiple anchors. US11829056A.

Hovda, D.; Arramon, Y.; Jansen, N. and de Villiers, M. 2008. Dynamic spacer device and method for spanning a space formed upon removal of an intervertebral disc. WOUS08080804.

van der Merwe, W.M. and Wilson, D.A.J. 2008. Surgical drill aimer. ZA2008/07781.

Albertyn, C.P. 2008. Crutch. ZA2008/6795.

Oorthuizen, C.R. 2008. Orthopaedic prosthesis. ZA200805596.

Arramon, Y.; Jansen, N. and de Villiers, M. 2008. Polyaryletherketone artificial intervertebral disc. US61050455.

Jansen, N. and de Villiers, M. 2009. Artificial intervertebral disc placement system. US12504033.

de Villiers, M.; Jansen, N. and Arramon, Y. 2009. Artificial intervertebral disc with lower height. US12400221.

Arramon, Y.; de Villiers, M. and Jansen, N. 2009. Intervertebral prosthetic disc with shock absorbing core formed with disc springs. US12358716.

de Villiers, M. and Jansen, N. 2009. Posterior prosthetic intervertebral disc. US12504042.

Scheffer, C.; van den Heever, D.J.; Erasmus, P.J. and Dillon, E.M. 2009. A method of designing a knee prosthesis. ZA200903924A.

Honiball, J.R. 2009. A positioning guide and a femur bone cutting guide system. ZA200904421.

Honiball, J.R. 2009. A positioning guide and a bone cutting guide system. ZA200904421.

John, L. R. 2009. Non-invasive deep muscle electromyography. ZA200905309.

Campbell, R.I. and de Beer, D.J. 2010. Articulating prosthesis. ZA201005077A.

de Villiers, M. and Jansen, N. 2011. Prosthetic intervertebral disc with moveable core. US13094131.

Plugmacher, R.; Becker, G, and van Asselt, P.G.H. 2011. Surgical instrument for spreading bone. EP11167493.

Dymond, I.W.D. and Dymond, G.F.D. 2011. A retractor for use in surgery. ZA201100153.

Oosthuizen, C.R. 2011. A tibial component. ZA201107123.

Vicatos, G.; Ginsberg, S.I. and Parsons, A.T. 2011. An endoprosthesis. ZA201104740.

Honiball, J.R. 2011. An orthopaedic apparatus. ZA201107190.

Pienaar, A.W. 2011. Device of medical readjustment. DE202011 107911.

Gerhardt, T. 2012. Bone distractor. ZAF2012/00870.

Gerhardt, T. and Pieterse, R.K. 2012. Flexible drive assembly and bone distraction apparatus in which the drive assemble is used. ZA201204176.

Honiball, J.R. 2012. A positioning guide for positioning a bone cutting guide assembly and a bone cutting guide system. ZA20121993.

Honiball, J.R. 2012. A surgical tool guide. ZA201205808.

Brijlal, Y.; John, L.R. and Sivarasu, S. 2012. Hand exoskeleton. ZA201208238.

Wisniewski, P. 2012. Precision use enabling forceps. US61796731.

Vicatos, G. 2012. Rotating hinge knee prosthesis. ZA2012/01641.

Faure, E.; Goubet, N.; Dejour, D.; Erasmus, S.; Arendt, E.; Feller, J. and Almqvist, F. 2012. Set of femoral implants for a knee prosthesis. FR12055798.

Honiball, J.R. 2012. A bone cutting guide and a bone cutting guide system. ZA20121998.

Patnaik, S. and Sivarasu, S. 2013. Anatomical support facilitating medical imaging of the hip, leg and knee. GB1319689.

Birkholtz, F.F. and Beckerleg, B.J. 2013. Foot supporting device. ZA201306674A.

Monacelli, E.; Djouni, K.D.A; Gregory, U.N. and Hamam, Y. 2014. Mechatronic system for assisting an individual in obtaining a standing position. ZA201402346.

Tenim, S. and Vicatos, G. 2014. Underactuated prosthetic hand. GB1412034.

Nel, L.J. and Becker, G.S. 2015. Pedicle mountable retractor system. ZA2015/04028.

Verbeek, R. and O'Toole, B. 2015. Inter-body spacer. US62114742.

Patnaik, S. and Sivarasu, S. 2015. Accessory for conducting patella surgery. GB1511597.

Theunissen, H.B. 2015. A fastening device. ZA201506500.

Badenhorst, D.L.R.H.S.; and Davis, J.H. 2015. Cervical spine traction apparatus. ZA201508967.

Grobler, G.P. and Dower, B.J. 2015. Femoral head measurement device. ZA201502483.

APPENDIX J – Standardised keywords of the keyword networks

The following steps were taken to standardise keywords:

1. If any of the arthroplasty terms appeared alongside the term “surgery”, the term “surgery” was removed, as arthroplasty is the surgical replacement of the respective joint. Therefore, the term “surgery” does not appear in the list of keywords. The respective arthroplasty term was thought to better represent the research area of interest of the author than a generic “surgery” term.
2. Where keyword lists had both “medical” and “devices” listed, these terms were replaced by a single term “medical device”.
3. The keyword term “new products” was removed as it was redundant.
4. The term “custom implant” was replaced by both “customised design” and “prostheses and implants”.
5. The terms “customised soft tissue modelling” and “subject-specific musculoskeletal model” were each replaced by both “customized design” and “modelling”.
6. The term “implant wear” was replaced by both “prostheses and implants” and “mechanical wear”.

Standalone keywords	**Consolidated keywords**
3D reconstruction	arthritis includes arthritis and osteoarthritis
abnormalities	bone cement includes bone cement; calcium phosphate bone cement and cementation
absorptiometry	customised deign includes customised design; custom implant; customised soft tissue modelling; patient-specific and subject-specific musculoskeletal model
accelerometer	design includes design; design innovation; design methodology; equipment design and mechatronic design
accuracy	device migration includes device migration and migration
acetabular cup orientation	digital arthroplasty includes finger reconstruction and proximal interphalangeal joint replacement
adaptive coupled oscillators	exoskeleton includes exoskeleton and robotic exoskeleton
additive manufacturing	failure includes failure criteria; failure prediction and material failure
adolescent	fixation includes circular external fixation; fixation; joint fixation and tibial fixation
adult spondylolisthesis	fracture includes fracture and radius fracture
aluminium step wedge	hip arthroplasty includes hip arthroplasty and total hip arthroplasty
amorphous glass-covered microwires	hydroxyapatite includes hydroxyapatite and plasma sprayed HA coatings
ArmeoSpring	intramedullary nailing includes intramedullary nail and intramedullary nailing of long bones

arthroscopy	kinematics includes kinematics and 3D kinematics
bacteriocins	knee includes knee; knee geometries; knee joint and patella
battery-less monitoring	knee arthroplasty includes knee arthroplasty; patellofemoral arthroplasty; total knee prosthesis; total knee replacement and unicompartmental knee replacement
benign bone lesions	measurement includes 3D measurement; measurement and stress measurements
bilateral imaging	mechanical wear includes adhesion wear; cup wear; implant wear; plastic flow and wear
biocompatible scaffolds	medical device includes device; medical devices; medical equipment and medical scanners
bioconductive coating	metal-on-metal bearings includes metal-on-metal bearings and metal-on-metal hip joint
biological tissues	modelling includes modelling; musculoskeletal computational model; subject-specific musculoskeletal model and customised soft tissue modelling
biomechanics	osteolysis includes osteolysis; acetabular osteolysis and pelvic osteolysis
body weight	prostheses and implants include biomechanical implants; cervical implants; implants; prostheses and implants and prosthesis
bone	radiography includes CT; digital radiography; radiographic devices; radiography; x-ray and x-ray computed tomography scanners
bone ingrowth	repeatability of results includes repeatability and repeatability of results
bone mineral mass	shoulder arthroplasty includes hemiarthroplasty and shoulder arthroplasty
bone replacement	spinal arthroplasty includes cervical total disc arthroplasty; lumbar total disc arthroplasty and spinal arthroplasty
bone substitutes	spine includes cervical spine; intervertebral disc; spinal cord and spine
bone transport	trauma includes multiple injuries; multiple trauma and trauma
cementless	wear simulation includes wear simulation and simulation
ceramic liner	
ceramic-on-ceramic bearings	
ceramic-on-metal bearings	
ceramics	
cerebral palsy	
chronic osteomyelitis	
clavicle	
clinical utility	
collarbone	
collateral ligament tension	
computed torque	
computers	
contact stress	

creatine kinase activity	
CRx	
deep squat	
degenerative disc disease	
digital amputation	
dimpled surface texturing	
disabled	
distal locking	
distraction	
Duraloc 300 cup	
early mobilisation	
economic alternative	
electrospinning technique	
extracellular matrix	
fast terminal sliding mode control	
fatigue monitoring sensor	
femoral transverse movement	
finite element analysis	
finite-time convergence	
fuzzy clustering	
gait nomogram	
gamma crosslinked cup	
glenoid erosion	
Gyrolift	
hallux valgus	
hand grasp	
head-shaft angle	
hip	
hip joint simulator	
humerus	
induced membrane	
interface effects	
in-vivo calibration	
iPhone	
joint-preserving method	
jump height	
Kleinert rehabilitation technique	
knee-ankle orthosis	
landing impact	
ligament laxity	
limb disorders	

loading phase	
locked plate	
lucent lines	
magnetic sensor	
man-in-the-loop control approach	
manufacture	
masquelet technique	
maximum voluntary contraction	
mechanical damage	
mediolateral patellofemoral ligament	
metal debris	
metal ion levels	
microcurrent therapy	
microstructural characterisation	
mixed lubrication	
modified ATLS () algorithm	
MRI	
musculoskeletal system	
nano/microparticles	
nanotechnology	
neuromuscular function	
non-compliant patients	
opening wedge osteotomy	
osseointegration	
osteoblasts	
osteogenesis	
osteoporosis	
pain	
particle analysis	
particle release	
pattern of movement	
piezoelectric transducer	
PIXE	
polyaryletherketones	
polyethylene acetabular cup	
polymer-on-polymer articulation	
porous coating	
posture	
press-fit	
product development	
prosthetic joint infection	

proton microprobe	
proximal first metatarsal	
pyrocarbon	
radiographic image enhancement	
range of motion	
rapid availability	
rapid manufacturing	
rapid prototypes	
rehabilitation robotics	
rehabilitation	
reliability	
repair	
residual stress	
robot-assisted platform	
rotational knee laxity	
running	
rupture rates	
scapula	
screw	
screwless	
shank-foot	
shock absorbing pylon	
shoulder and hand	
silicone	
skeletal muscle	
smartphone technology	
South Africa	
spastic displegia	
specialised imaging software	
spinal fusion	
SSM	
stability	
Statscan	
sternal cable system	
sternoclavicular joint dislocation	
stress	
subsidence	
suture repair	
Teno Fix tendon-repair device	
Ti-alloy	
tibiofemoral reaction forces	

tilted liner	
trajectory	
transtibial amputee	
trauma centres	
Validity	
verticalization	
wear rates	
wheelchair	
x-ray diffraction	

APPENDIX K - Keyword network dendrogram

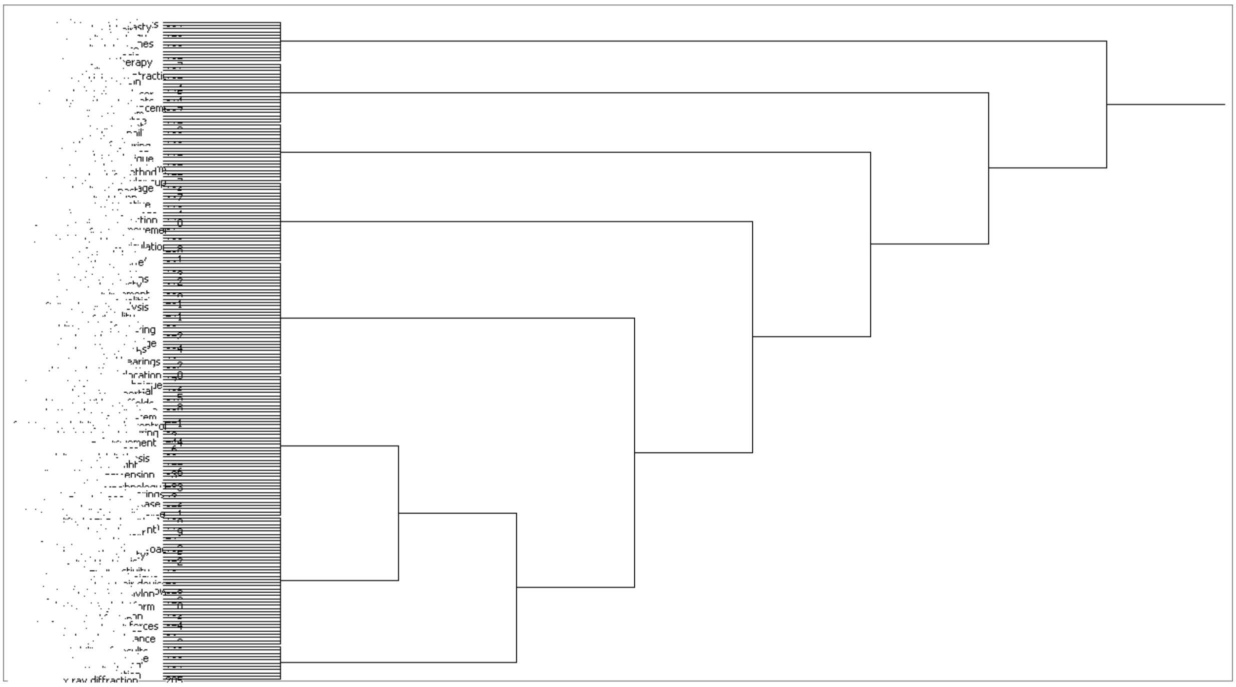


Figure 65: Keyword network hierarchical dendrogram. The dendrogram does not produce legible information in terms of the keywords that make up this network at this scale. It is presented here to show the hierarchical structure of the network.

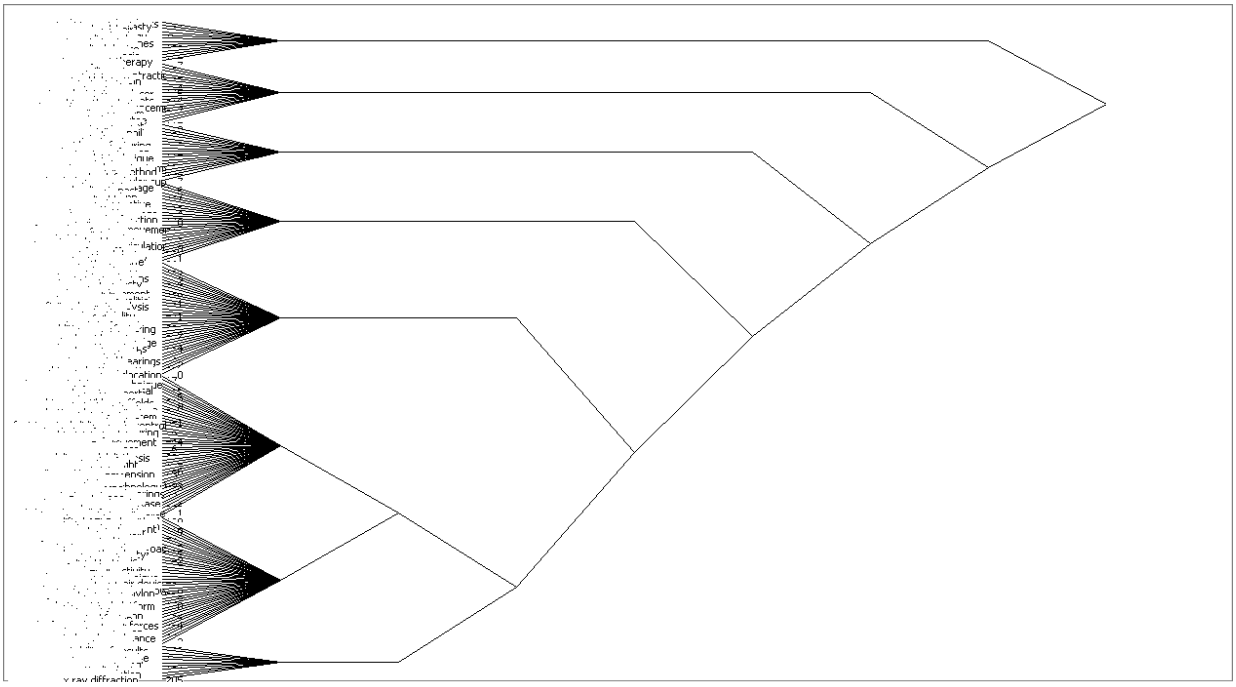


Figure 66: Keyword network hierarchical cluster diagram. The cluster diagram does not produce legible information in terms of the keywords that make up this network at this scale. It is presented here to show the hierarchical structure and node clustering of the network.

APPENDIX L – Medical device innovation pipeline for publicly financed developments

Table 15: TRL medical device innovation pipeline, adapted from (University of Cape Town, 2018)

Level	TRL 1	TRL 2	TRL 3	TRL 4	TRL 5	TRL 6	TRL 7	TRL 8	TRL 9
	Basic research		Pre-clinical research		Late pre-clinical research	Possible clinical trials and clinical investigations (Medical device dependent)			
	Basic idea	Concept developed	Experimental proof of concept	Laboratory demonstration: component/system validation in a laboratory environment	Laboratory scale validation: similar system performs in relevant environment	Prototype demonstration: engineering or pilot scale validation in relevant environment	Full scale /similar pilot system demonstrated in relevant environment. Capability validated on an economic scale.	Capability validated over a range of systems. Actual system completed, qualified through test and demonstration. Incorporated into commercial design.	Capability validated on full range of parts over long periods. Proven system ready for full deployment. Actual system operated over the full range of mission conditions.
Phase	Research		Translation/Development				Commercialisation		

Table 15 is an adaptation of the process developed by UCT's Department of Research Contract & Innovation, and how it may apply to the medical device innovation pipeline.

APPENDIX M - Interview questions

1. Basic Demographic questions:
    a. Can you tell us about your tertiary education?
        - Need to establish highest qualification
    b. What is your current role(s) at your current institution(s)?
        - This should tell us to what extent the author/inventor is (still) involved in orthopaedic device development.
2. The networks. The network to which the author/inventor would be part of is printed and the "case" which we are exploring is shown to the author/inventor. The network diagram is fully explained to the author, i.e. how it is drawn, betweenness and degree centrality, etc. The contribution of the author/inventor is then pointed out and discussed:
    a. Do you feel that this representation reflects your contribution to the orthopaedic device development network in South Africa? If yes, how? If no, then why not? Are there contributions which we may have missed?
    b. We have assigned you as belonging to the (insert sectoral and geographic classification here). Would you say that this is a fair assignation?
    c. In the project leading to this paper/patent, what was your role?
    d. How do you fit among the other authors/inventors on this publication/patent? DO you know their educational background? qualifications? capacity?
    e. Who funded this project/patent? What resources were provided by your organisation?
    f. Did this device reach the market? What is its market presence?
3. Section three deals with knowledge creation and knowledge diffusion
    a. Are the types of devices South African organisations focussing on addressing the needs of the country?
    b. Is there enough cross-sectoral collaboration in orthopaedic device development in South Africa?
    c. Is there sufficient knowledge exchange across geographical borders? Who are we 'learning' from? Or who are we influencing?

d. What is your opinion about the quality of work produced by South African actors in orthopaedic device development that you have worked with? Are there South African actors who you wish to work with? Are there international actors who you wish to work with?

e. If you were part of a successful collaborative project, how would you go about replicating those factors that made that project successful?

f. What is your vision for the future?

APPENDIX N – Iterative coding cycle of interview transcripts

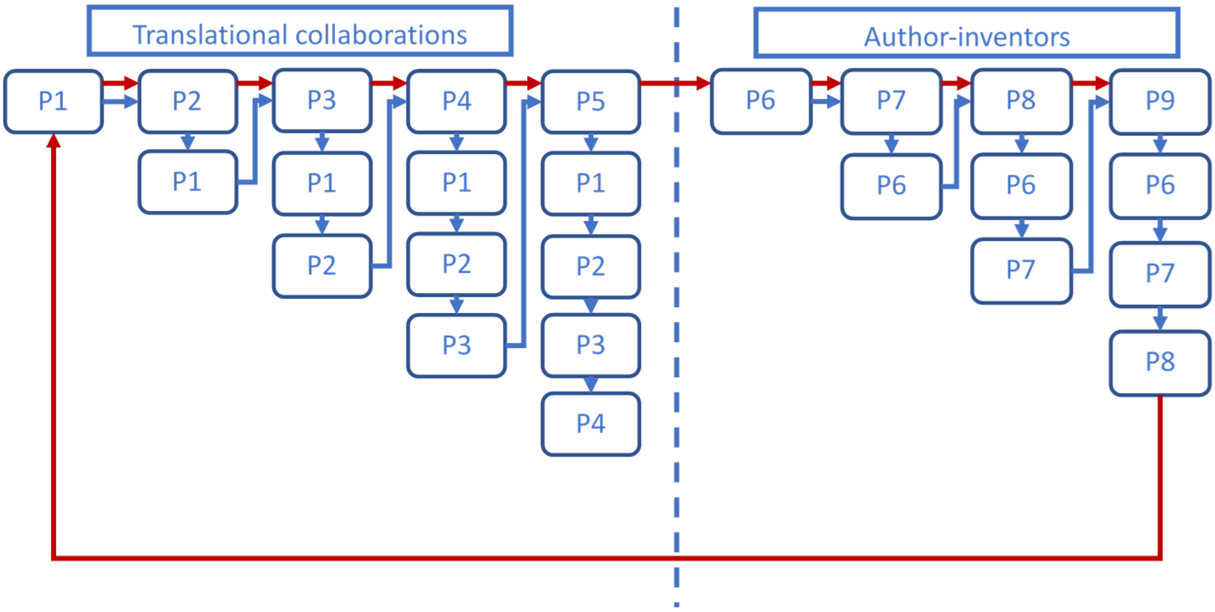


Figure 67: Iterative coding cycle of the interview transcript