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Title:

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

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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.

Keywords:

medical devices; social network analysis; bibliometrics; technological innovation systems

MSC Classification:

05C – Graph Theory

JEL Classification:

D85 **-** Network Formation and Analysis: Theory

O32 **-** Management of Technological Innovation and R&D

O33 **-** Technological Change: Choices and Consequences • Diffusion Processes

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Text:

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[1] and other supporting sectors, including government and non-government organisations (Chimhundu, et al., 2015) (de Jager, et al., 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.

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.

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, et al., 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, et al., 2007). Hekkert et al. (2007) and Bergek et al. (2008) 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. (2008) 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, et al., 2008). '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, et al., 2015)

Several authors have recently stressed the importance of considering context in TIS analysis. While the TIS framework may be universally applicable (Bergek, et al., 2008) (Hekkert, et al., 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, 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

[1] The term "science council" is widely used in South Africa. Scholes et al. (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).

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, 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, et al., 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, et al., 2014) (Wieczorek, et al., 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, et al., 2015) (Tigabu, et al., 2015). 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, et al., 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.

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, et al., 2008).

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.

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.

Collaboration networks

The collaboration networks were generated using UCINET 6 (V 6.573) (Borgatti, et al., 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 1, is the node's degree, $u(y)$, divided by the maximum possible degree in the network, u_{max}.

$$|D(y)| = \frac{u(y)}{u_{max}} \quad (1)$$

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:

$$B(y) = \sum_{x \neq y \neq z} \frac{\delta_{xz}(y)}{\delta_{xz}} \quad (2)$$

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 3:

$$|B(y)| = \frac{B(y)}{B_{max}} \quad (3)$$

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 4.

$$N = \frac{\sum L_i - \sum L_e}{\sum L_i + \sum L_e} \quad (4)$$

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 5, 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.

$$S = \frac{\sum s_i - \sum s_{e,}}{\sum s_i + \sum s_e} \quad (5)$$

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.

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 1 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 1: 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 (1st timeframe) and ending at 2011-2015 (12th 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 1). 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 2. Each actor is represented by a node in the network. Full names of the actors along with their abbreviations are presented in Appendix B.

Fig. 1 Number of publications and number of national and international actors in each of the timeframe networks of the orthopaedic device development network

Fig. 2 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 3. 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).

Fig. 3 Highest-ranked actors by degree centrality. A list of actor abbreviations and their full names can be found in Appendix B

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 4. This metric is presented similarly to degree centrality in Figure 3, 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 4.

Fig. 4 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 B

The actors having high degree centrality also have high betweenness centrality, i.e. all the actors that appear in Figure 3 also appear in Figure 4. There are two more actors in Figure 4 than Figure 3 – 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 2) 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 5. 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.

Fig. 5 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 6, where the overlap of subgroups is indicated by actors belonging to more than one subgroup. Considering Figures 5 and 6 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.

Fig. 6 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 B. 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 7. 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 Figures 2 and 6) 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.

Fig.7 Sectorisation index of the orthopaedic device development networks over the 12 timeframes

Discussion

We have shown that the rate of scientific publication output in orthopaedic device development in South Africa increases over the 12 timeframes. Makhoba and 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 affiliatec 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., 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 (2013) 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 devices 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, n.d.). 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, n.d.). 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.

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 et al., 2008). 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.

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.

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Appendix A

Scopus search term:

(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

Thomson Reuters WoK search term:

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

Table 2: Full name of institutions comprising the orthopaedic device development networks.

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

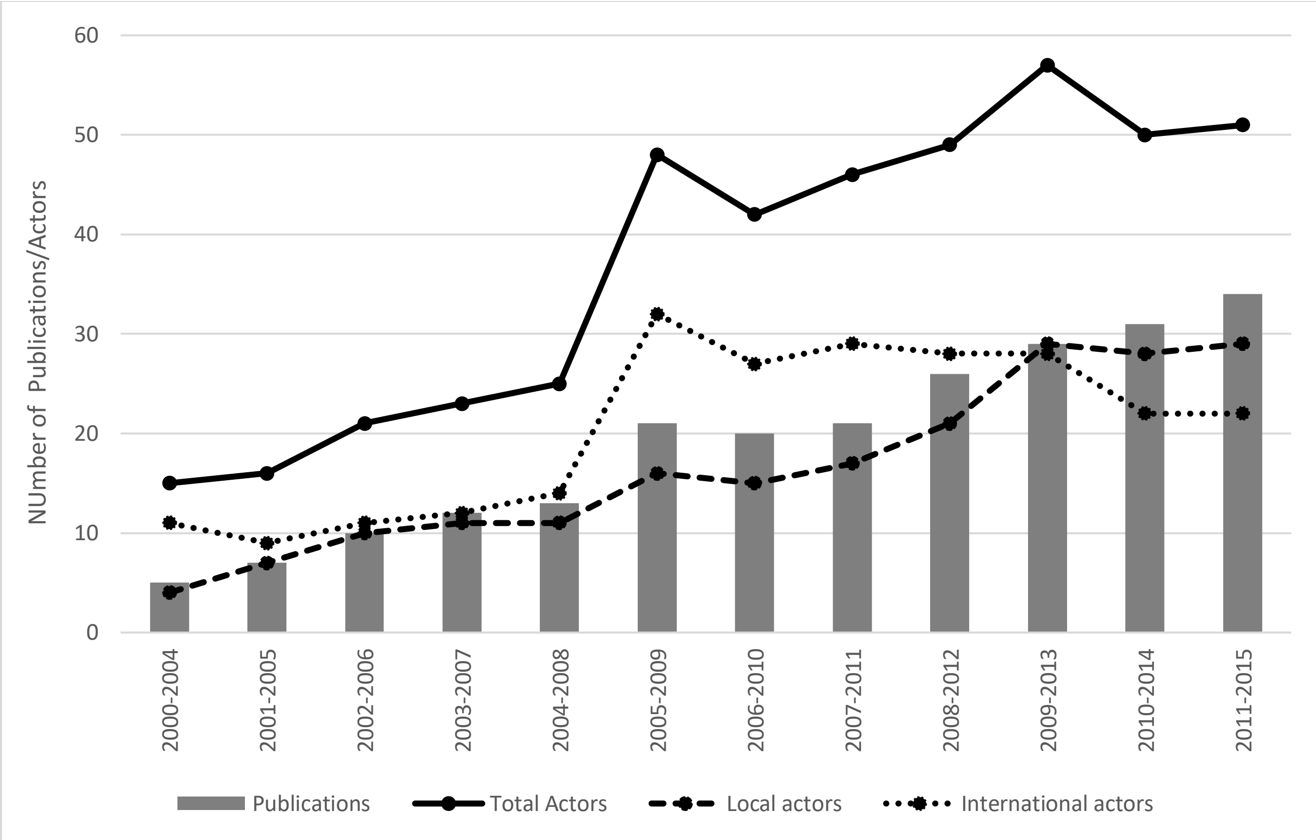
SSSA	Scualo Superiore Sant’Anna	International
TB	Telecom Bretagne	International
TUHH	Hamburg University of Technology	International
TUT	Tshwane University of Technology	National
UBRI	University of Bristol	International
UCAL	University of California	International
UCD	University College Dublin	International
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
EMG	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
IMATRI	Imatri Medical	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

Figures:

Fig. 1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International actors

Fig. 2a

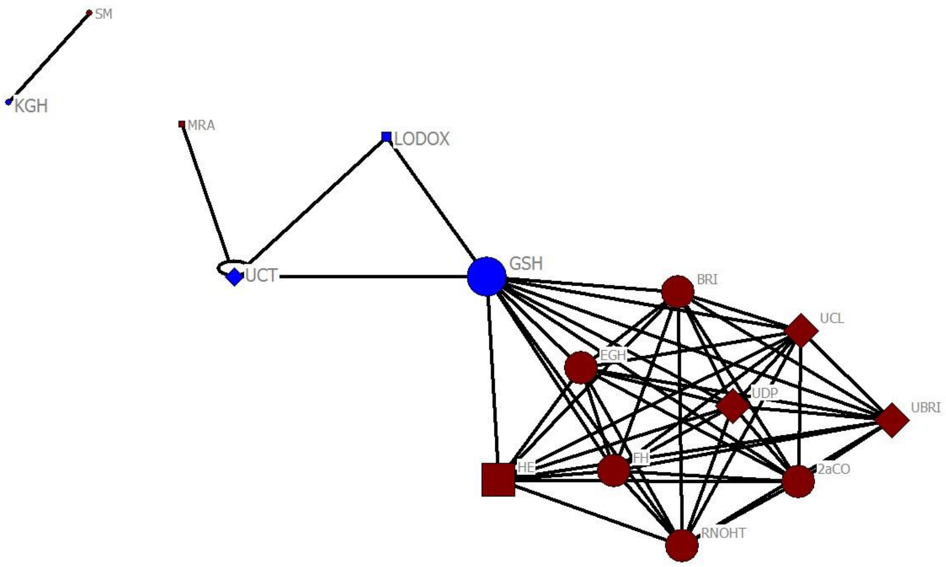
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Fig. 2b

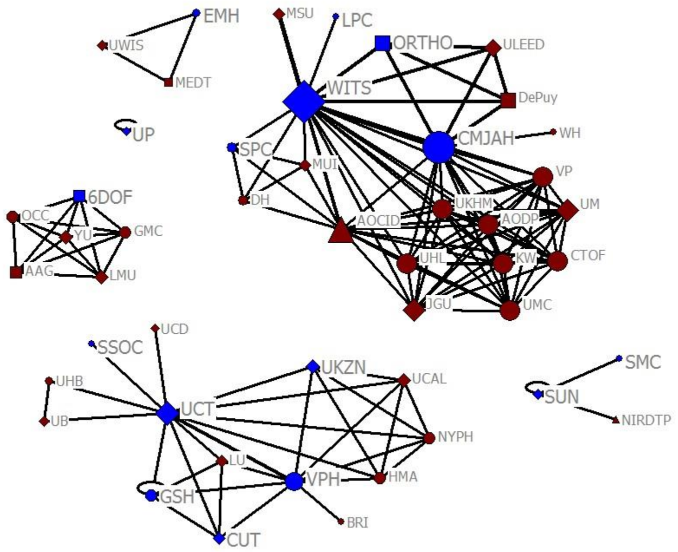
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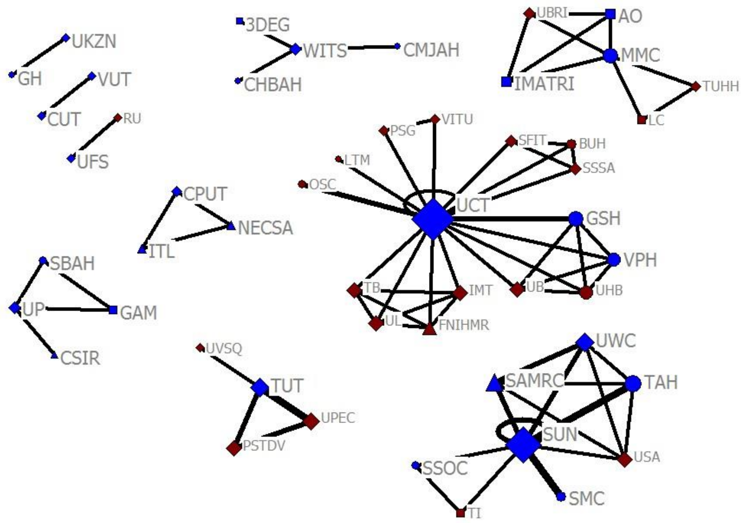
Fig. 2c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CMJAH
CHBAH
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AO
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IMATRI
TUHH
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CSIR
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PSTDV
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SSOC
SMC
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Fig. 3

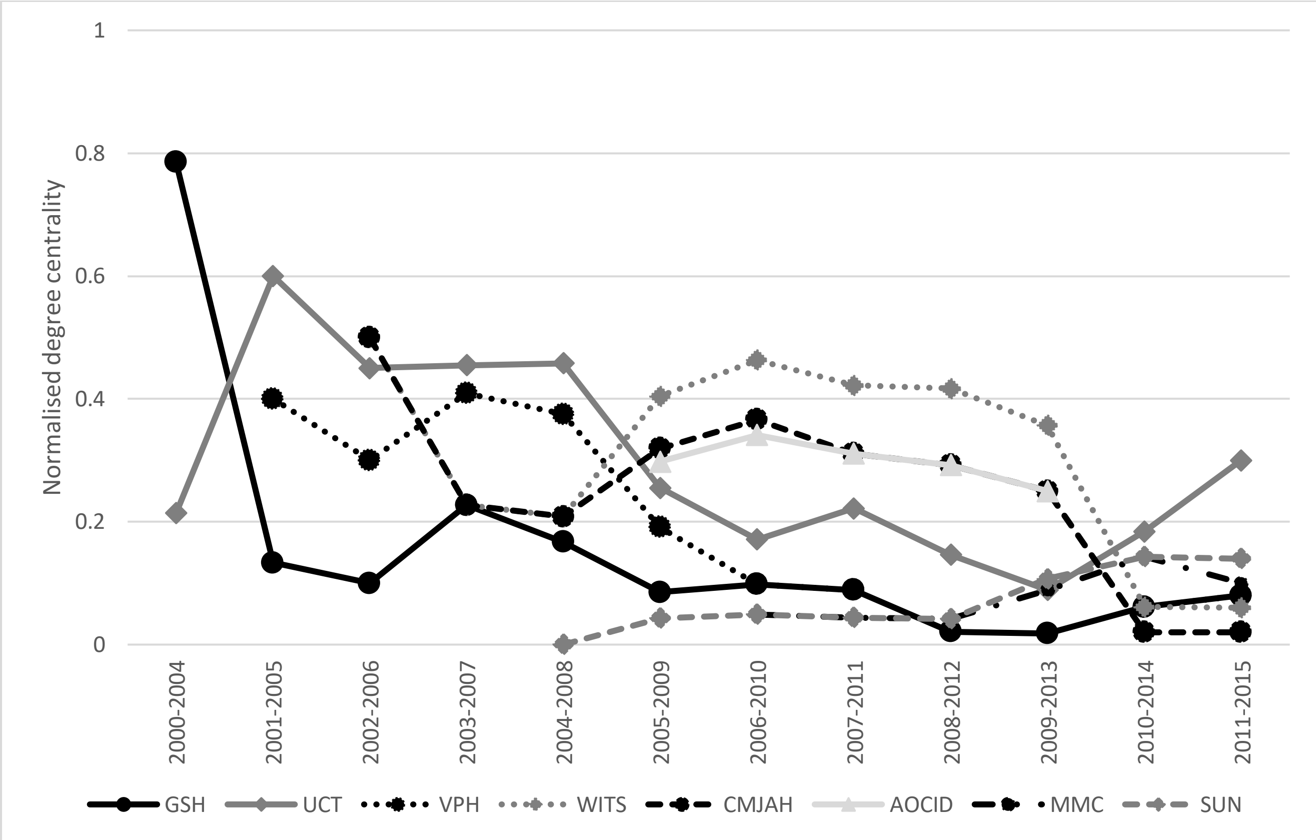


Fig. 4

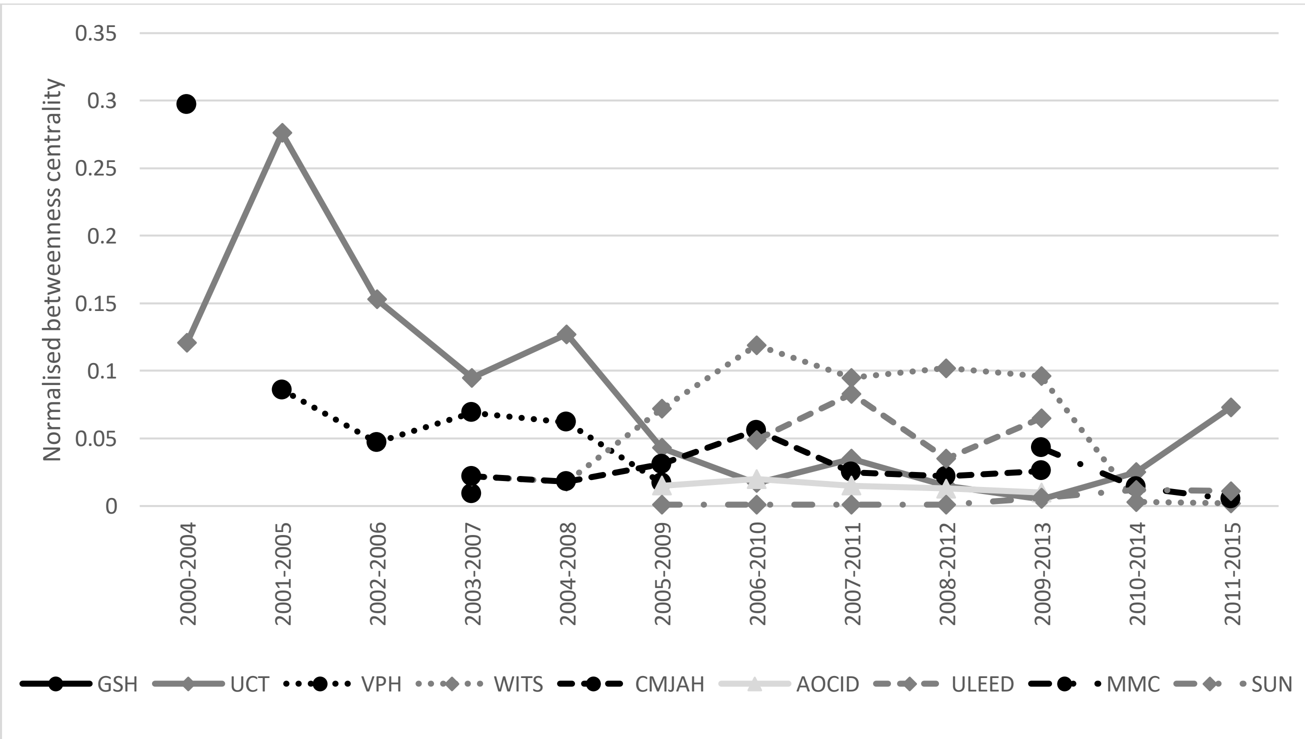
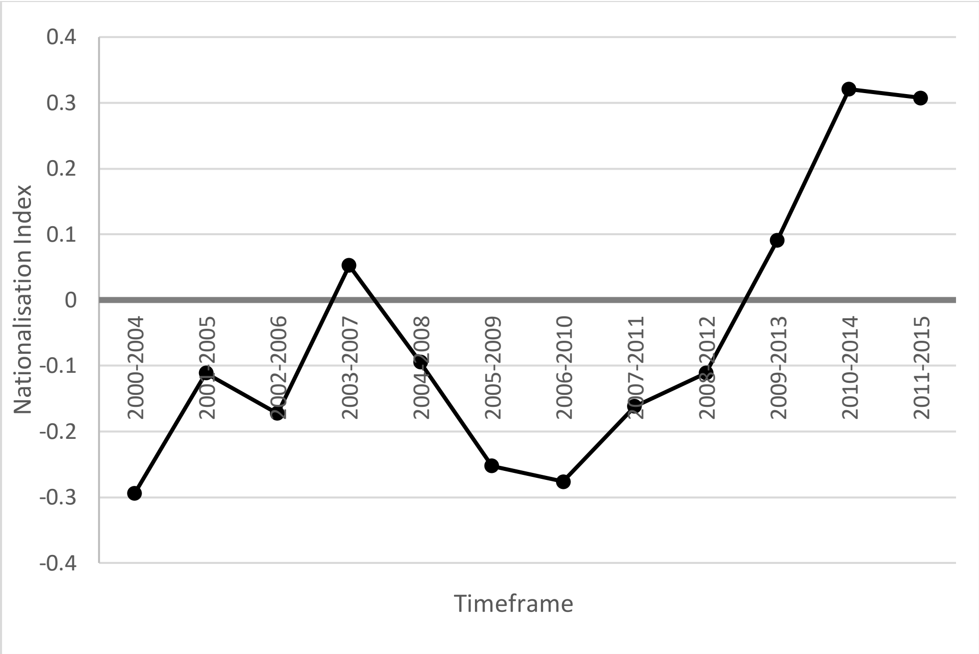


Fig. 5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Nationalisation Index
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2001-2005
2002-2006
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2004-2008
2005-2009
2006-2010
2007-2011
2008-2012
2009-2013
2010-2014
2011-2015
Timeframe

Fig. 6a

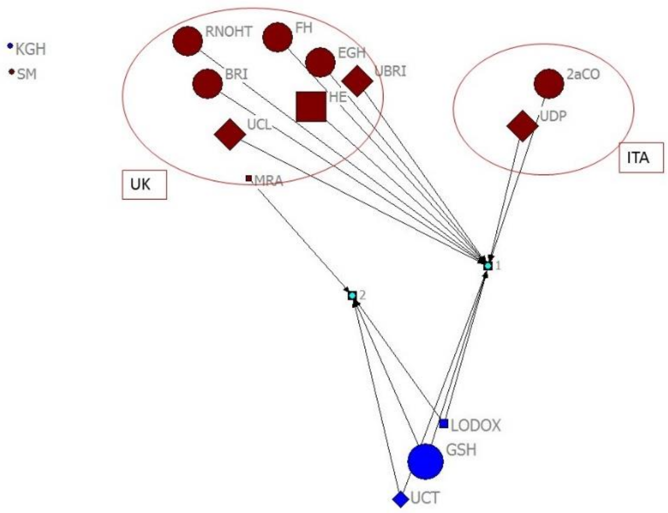
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Fig. 6b

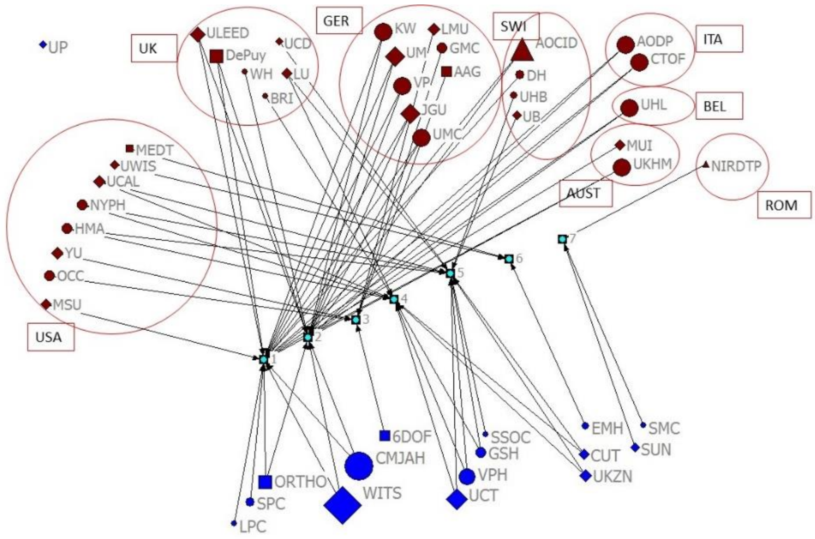
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Fig. 6c

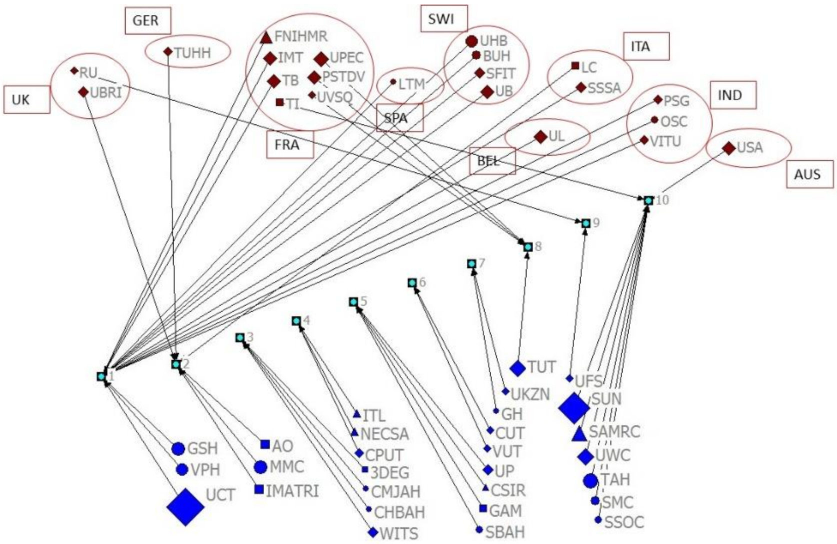
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Fig.7