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Abstract

Recently the knowledge base (KB) concept has been extended with combinational knowledge bases (CKB) in order to overcome the dichotomy between analytical, synthetic and symbolic KB. So far, however, empirical studies on these CKB have insufficiently focused on multi-scalar mechanisms, which is a gap we would like to fill with the help of this paper. Therefore, it aims at analyzing CKB from a proximity, agency and multi-scalar perspective. Through interviews with high-end medical device companies from Shanghai, findings show that, first, in this local industry a combination of analytical and synthetic knowledge prevail. Secondly, knowledge interactions differ at different spatial scales, which is strongly related to the characteristics of the local KB and the position of local knowledge in the global industrial knowledge value chain. Thirdly, in this industry cognitive proximity is the key factor facilitating combinatorial knowledge interactions at all spatial scales. Institutional and geographical proximity are obviously more important at the local scale. Fourthly, concerning the effect of agencies on proximities, place leadership and institutional entrepreneurship work respectively at the local and national level, while the role of innovative entrepreneurship is observed at all levels.

Key words: Combinational knowledge bases; proximity; agency; multi-scalar perspective

This is a pre-print version of a paper that will be submitted for publication to a journal.

1. Introduction

Knowledge bases (KB) are considered as a key asset which have the potential to enhance the capacity of regional or industrial innovation (Asheim et al., 2011) and therefore received much and increasing attention in the economic geography literature (Shearmur et al., 2016). Although there are several distinctions around knowledge, the KB concept is stronger connected to the knowledge creation dynamics that underlie innovation processes than other distinctions, such as high tech versus low tech, and codified knowledge versus tacit knowledge (Boschma 2018; OECD, 1996; Gertler, 2003). However, recently the KB concept has been extended with combinational knowledge bases (CKB), as empirical research showed that the too rigid distinction between the three KB cannot be observed in the reality of most local and regional industries (Asheim et al., 2017). With the help of CKB the characteristics of innovation associated to existing KB (i.e., knowledge breadth) can be expressed well in any industry.

Although there has been a strong focus on the role of a CKB in explaining innovativeness in regional economies, external knowledge linkages are central to CKB, as well. Trippl et al. (2018), for example, indicated that the crucial knowledge in emerging industries may be accessed from external areas. Grillitsch and Nilsson (2015) pointed out global linkages may offer complementary sources to areas with poor knowledge (see also Wiig et al., 2020). Another strand of literature emphasizes the significance of different kinds of proximities, including cognitive, institutional, organizational, geographical, and social proximity for knowledge production, knowledge interaction and innovation (Boschma, 2005). Moreover, the relationship between different dimensions of proximity such as substitution and overlap (Hansen, 2015), innovation networks and a dynamic proximity (Lazzeretti and Capone, 2016; Balland et al., 2015) has received much and increasing attention.

Although existing literatures contribute to our understanding of knowledge interactions and the innovation process, three research gaps can be identified. First, scholars tend to pay relatively little attention to multi-scalar CKB. Existing studies are often based on a single scale, such as at the local or national scale, which make knowledge flows in space fragmented. Secondly, although the role of different kind of proximities are emphasized in the literature on innovation (Boschma, 2005), so far, there has been little focus on a comparison of proximity related to CKB at different spatial scales in the same industry, and the role of agency in knowledge interaction. Thirdly, so far the empirical literature on CKB mainly focuses on cases in Europe (Northern Europe and Central Europe) (Grillitsch et al., 2017; Bennat and Sternberg, 2020).

In order to fill these gaps, this paper aims at analyzing CKB from a proximity,agency and multi-scalar perspective in the high-end medical device industry in Shanghai, through interviews with local companies (for more details, see Section 4), contributing to the understanding of combinatorial knowledge interactions across space and the related driving mechanisms. Shanghai is one of the earliest and strongest locations of the medical device industry in China.

The medical device industry is a multi-disciplinary, knowledge-intensive and capital-intensive high-tech industry (Davey et al., 2011; Zhao et al., 2018). “New medical devices are frequently a result of cooperation between academia and commercial interests” (Bergsland et al., 2014, 207). The reason why we choose the medical device industry is that we can expect a combination of several knowledge bases, as well knowledge interaction across space in this industry. In order to analyze and understand the case, we construct a new framework in which multi-scalar CKB, as well as several proximities and agencies are taken into account. It will help us to analyze and understand three phenomena. First, the whole process of knowledge interactions in space, which contributes to the understanding of the geography of knowledge (Shearmur et al., 2016). Second, the comparison of different kinds of proximity at different spatial scales provides insights in CKB and knowledge networks across space. Third, agencies linked to knowledge interactions and different kinds of proximity, extending our understanding of potential changes of the role of proximity at different spatial scales (Balland et al., 2015).

This paper is structured as follows. In the next section, we elaborate on the literature about CKB, proximity and agency, and then the new analytical framework is put forward in Section 3. Section 4 presents the case study, which consists of the specific industrial and regional-industrial context, the methodological approaches, and the empirical analysis of the medical device industry in Shanghai. Concluding remarks are presented in Section 5.

2. CKB, proximity and agency: a literature review

In this section, we will review the literature about CKB and knowledge interaction across space in section 2.1, and proximity and agency in section 2.2.

2.1 CKB and knowledge interaction across space

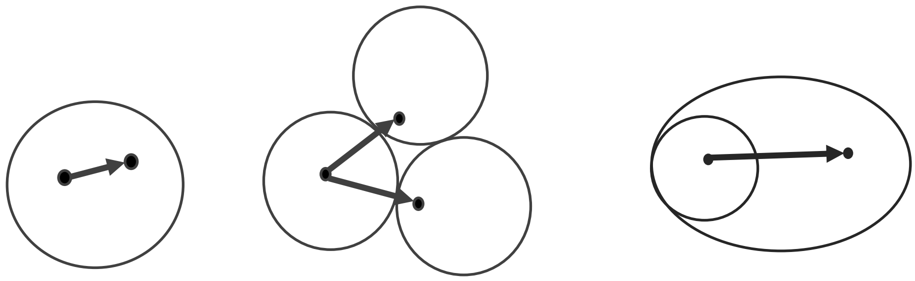
According to Boschma (2018, 24), "… the DKB literature shed light on the nature of knowledge sharing and its geographical extent which were claimed to vary between analytical, synthetic and symbolic knowledge bases (Manniche 2012; Martin 2012)", and is hence a good example of context-sensitive theorizing in economic geography (Gong and Hassink, 2020). The original theoretical literature states that analytical knowledge plays a vital role in the process of science-based industries, such as the pharmaceutical and biotechnology industries (Asheim and Gertler, 2005). In contrast, synthetic knowledge mainly refers to artefact engineering for electronics and construction industries (Asheim and Gertler, 2005). Symbolic knowledge is strongly related to cultural codes within the cultural and creative industries (Manniche and Larsen, 2013). If we compare the three different kinds of knowledge, analytical knowledge is easiest to absorb or transfer. In comparison to other distinctions and approaches such as high- vs. low-tech and codified vs. tacit knowledge, the KB approach is strongly connected to knowledge creation and innovation processes taking place within industries (Asheim and

Gertler, 2005).

Although one type of KB can represent the critical knowledge creation in the process of industrial development to some extent, empirical research has shown it is unrealistic to strictly separate KB from each other in one industry (Asheim et al., 2017; Manniche, 2012; Manniche et al., 2017). In many industries, such as the green building industry, knowledge and innovation have characteristics that cannot be covered by one KB only (Strambach, 2017). Moreover, when it comes to emerging and transforming industries, the nature of knowledge creation and industrial innovation may change through time and is difficult to be captured through ideal KB types. Based on these insights, the CKB approach has been suggested (Asheim et al., 2017; Manniche et al., 2017), which can be largely understood as the more advanced and complex alternative to DKB.

CKB is the combination of intra-KB or inter-KB leading to innovation (Asheim et al., 2017; Manniche, 2012; Manniche et al., 2017). Therefore, CKB offers a more nuanced insight into knowledge flows and innovation characteristics of regional industries. They can help to understand under which conditions combinations between intra-KB or inter-KB matter most for innovation in regional firms and industries.

Concerning scales, however, the KB literature has more to offer than the CKB literature. The KB literature emphasizes among others knowledge interaction (Boschma, 2018) how it relates to proximity and spatial scales, which has not been done to the same extent in the CKB literature. Moreover, we draw on the extensive body of literature about knowledge collaborations and innovations referring to proximity and spatial scales (Dierkes et al., 2003; Shearmur et al., 2016). In that literature, three types of spatial scales are identified, as is shown in Figure 1.



Intra-city cooperation Intra-nation Inter-city cooperation Local-global cooperation

Figure 1: Main spatial scales in existing studies

At present, most researches on CKB only refer to intra-nation inter-city knowledge learning (Grillitsch et al., 2017), whereas local-global interactions seem to be ignored. In addition, so far the empirical literature on CKB mainly focuses on cases in Europe (Northern Europe and Central Europe) (Grillitsch et al., 2017; Bennat and Sternberg, 2020).

2.2 Proximity and agency

In many cases, actors are the crucial research object in the field of knowledge creation and innovation. A group of relevant theories and concepts such as proximity and agency revolve around them.

In earlier times, economic geographers have highlighted the role of geographical proximity for knowledge interaction. With the cultural and institutional shift in economic geography, society and institutions have received increasing attention over the last few decades (Barnes and Christophers, 2018). Therefore, currently increasingly non-spatial factors are taken into account in the proximity framework. In this context, Boschma (2005) introduced, in addition to geographical proximity, four further dimensions of proximity, namely cognitive, institutional, organizational, and social. After the publication of Boschma's (2005) seminal paper, a number of studies examined the relationship between different kinds of proximity in the process of knowledge creation and innovation (Hansen, 2015; Leszczyńska and Khachlouf, 2018), as Figure 2 shows. Recently, scholars have been much concerned with a dynamic proximity framework and interpersonal relationships, such as personal proximity (Balland et al., 2015 and Sabbado et al., 2021). Although these studies contribute to knowledge, innovation and proximity, so far, a proximity comparison from a CKB perspective at different spatial scales has been hardly seen. More importantly, few papers analyze the dynamics of proximities from an agency perspective, that is, how agency has influenced proximities.

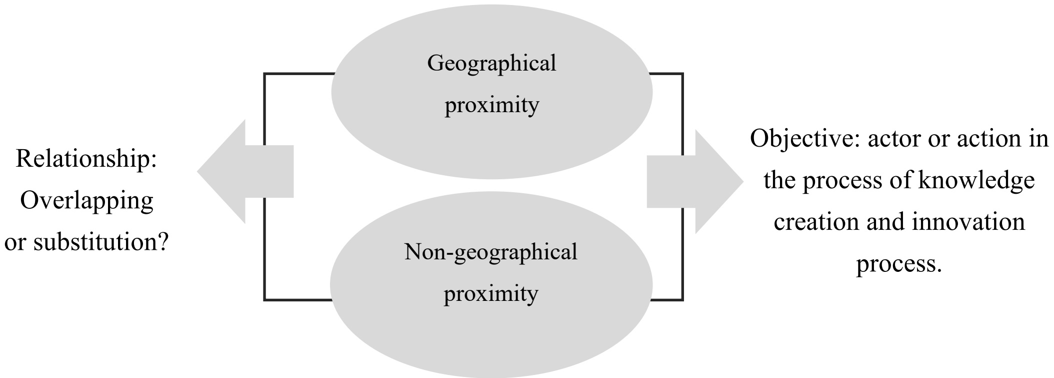


Figure 2: Main research directions in the framework of proximity

According to Giddens (1984, 14), agency is the ‘‘capability’’ to ‘‘make a difference’’, with agents viewed as ‘‘purposeful, knowledgeable and reflexive’’ (Sarason et al., 2006, 287; Giddens, 1984, 17). It has been constituted of resources and rules in the past, and is going to influence resources and rules in the future (Grillitsch and Sotarauta, 2018). On this basis, Grillitsch and Sotarauta (2020) identified three forms of agency, namely, Schumpeterian innovative entrepreneurship, institutional entrepreneurship and place leadership, potentially offering insights in the role of agency for knowledge creation and interaction in relation to different kinds of proximities. Innovative entrepreneurship concerns entrepreneurs ‘‘perceiving opportunities’’ within or outside the region, and ‘‘striving to realize these opportunities’’ such as niche market and new organization (Grillitsch and Sotarauta, 2020, 711). Institutional entrepreneurship refers to the ‘‘change processes contributing to the creation of new institutions and/or transformation of existing ones (Battilana et al., 2009)’’

(Grillitsch and Sotarauta 2020, 711). Place leadership is linked to the collaboration between local actors, ‘‘revealing the types of social processes involved in ‘making things happen’ and in ‘getting things done’ (or not getting things done)’’ (Sotarauta et al., 2017, 188).

3. Framework

3.1 CKB across space

Knowledge flows differ at different spatial scales. In order to gain insights into its characteristics at a deeper level, we are going to explore features of knowledge interactions at different spatial scales. In this framework, we categorize three levels, as Figure 3 shows, namely, intra-city collaborations (knowledge interactions within a city), intra-nation inter-city collaborations (knowledge interactions between the city and other cities located in that country) and local-global collaborations (knowledge interactions between the city and partners in foreign countries).

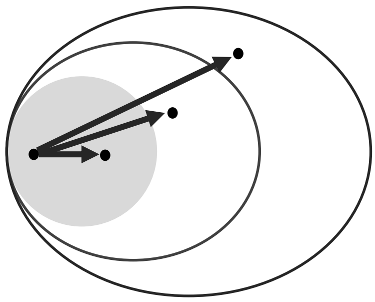


Figure 3: Multi-scalar collaboration

3.2 An analysis based on proximity and agency

After the identification of three spatial scales, the next step involves analyzing the mechanism behind knowledge interactions at local, national and international level. Concerning this point, a framework is put forward, in which proximity and agency are considered. As Figure 4 shows, we compare the effects of proximities on CKB at different spatial scales firstly.

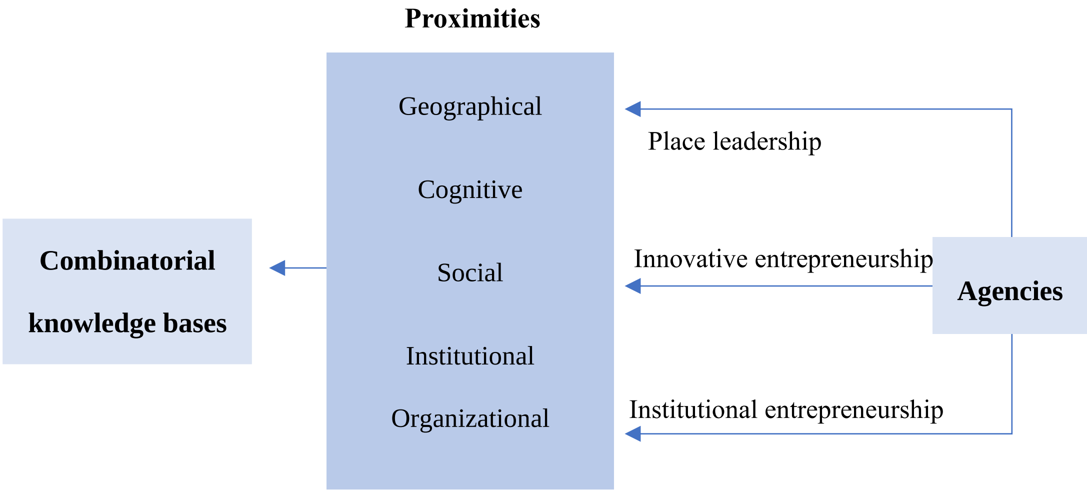


Figure 4: Key framework

Note that knowledge interactions are not stable, and the role of proximities may vary owing to agential forces. Agency is therefore linked to proximities to analyze how they influence knowledge interactions. Multiple possibilities are expected, instead of only one link between each agency and proximity. In order to better understand the possible linkages, we take some examples. First, Schumpeterian innovative entrepreneurship is connected to social proximity, which is necessary in order to perceive and create new demand for products and services and related new business opportunities. Secondly, institutional entrepreneurship may be linked to institutional and organizational proximity. In particular, the development of institutional reform or the issuing new industrial policies in certain regions may directly enhance institutional proximity, whereas the creation of new organizations or change of existing organizations, enhances organizational proximity. Thirdly, place leadership may be expected to be most strongly linked to geographical and social proximity, as it involves activating and enthusing local actors for a common vision or goal.

4. Case study

After describing the literature about CKB, proximity and agency, and presenting the new analytical framework, we will now apply this framework in our empirical analysis of the CKB from a proximity, agency and multi-scalar perspective in the high-end medical device industry in Shanghai. We will first introduce the industrial and regional-industrial context, then we will describe the methods, which will be followed by the empirical analysis.

4.1 Research context

The medical device industry is a multi-disciplinary, knowledge-intensive industry (Davey et al., 2011; Zhao et al., 2018), which refers to among others mathematics, physics, biology, engineering, and electronics. Therefore, in the process of R&D, cross-disciplinary collaborations are the main way of product innovation. Moreover, enterprises in this industry are mainly funded by themselves or venture investments.

Concerning the design of medical devices, given that they are directly related to the safety of people's lives, users' requirements (Privitera, et al., 2017), such as doctors' requirements, are necessary in medical device design and development. In addition, compared to public medical devices in hospitals, personal smart wearables are more concerned with aesthetic elements.

According to international regulations, medical devices can be divided into three categories (Kramer et al., 2012). Class I refers to medical devices that are safe and effective. Class II refers to medical devices for which safety and effectiveness can be controlled. Class III (the most stringent device management) includes those that are potentially dangerous to the human body, and the safety and effectiveness, therefore, must be strictly controlled (Kramer et al., 2012). In our paper, we are only concerned with high-end medical devices referring to Class II and Class III medical devices, for reasons, we will explain below.

Concerning the regional context, Shanghai, in addition to being the country's center for international economy, finance, trade and shipping (Shen and Li, 2014), is characterized by a high concentration of rich innovation sources, including organizations such as universities and public and private research institutes (Chen et al., 2017). In order to build Shanghai into a global technology innovation center (Du, 2018) (全球科技创新中心), the Shanghai government has developed policies to facilitate advanced knowledge creation and innovation, contributing to the development of local high-tech industries (Zeng et al., 2011; Cao et al., 2019). In 2019, the Shanghai Bureau of Statistics claimed that six key manufacturing industries contributed to 2327.915 billion yuan industrial output value, which accounts for more than 67.6% of the city's total. These six industries include electronic information, automobile, petrochemical and fine chemical manufacturing, fine steel, biopharmaceutical manufacturing (including medical device) and complete equipment/ complete set of equipment, such as industrial machinery.

Shanghai is one of the earliest cities in China developing medical device industries, having a strong historical endowment. After the establishment of new China in 1949, Shanghai Medical Instrument Factory and Shanghai Precision Instrument Factory jointly successfully developed the first 200 mA medical X-ray machine in China (中国第一台 200 毫安医用 X 光机) in 1952, which can be seen as a milestone in the history of medical devices in China (China Medical Device Industry Association 中国医疗器械行业协会 www.camdi.org /news/8416). After a long period of slow growth, more recently the Shanghai high-end medical device industry has developed into a strong agglomeration (See Table1).

Table1. The number of main agglomeration areas relevant to the Shanghai high-end medical device industry

Name	Criterion or evidence	The number in China	The number in Shanghai
Main agglomeration areas of the medical device industry	Criterion: the number of medical device manufacturing enterprises in the industrial park or in the industrial development area is more than 75.	50 areas (by the end of 2019)	7 areas (primarily referring to the high-end medical devices industry)
National innovative industrial clusters relevant to biological medicines and high-end medical devices	Evidence: it is published by the Ministry of Science and Technology of the People's Republic of China.	15 clusters (by the end of 2020)	1 cluster, namely the Zhangjiang biomedical medicine industrial cluster (including the high-end medical device industry)

Source: Zhongcheng medical device big data platform (众成医械大数据平台 https://www.joinchain.cn /home?timestamp=1619609904231), and the Ministry of Science and Technology of the People's Republic of China (中华人民共和国科技部)

Over time, the Shanghai medical device industry cluster has become a significant contributor to the innovativeness of the national medical device industry. First, the number of Shanghai's medical device company patents granted has exceeded 10,000 by the end of 2019, ranking second in the whole country, which accounted for about 6% of the nation's total (see Table 2). Secondly, the number of Shanghai's very innovative medical devices was 44 by the end of 2019, which accounted for about 20% of the nation's total (see Table 2). The latter has gone through a special review organized by the China Food and Drug Administration, which will be introduced in the last paragraph in Section 4.1.

As Figure 5 shows, seven areas are listed in the biomedical plan scheme in which five districts, including Pudong, Minhang, Fengxian, Songjiang and Xuhui districts, refer to high-end medical device industries. Our survey was conducted in these districts. According to the data from Zhongcheng medical device big data platform (众成医械大数据平台), by the end of 2019, 972 manufacturing medical device enterprises have been identified, of which 363 are regarded as innovative (see Table 2).

Figure 5: Shanghai industrial planning map for biological medicine

Table 2: Detailed information about medical device industry in the end of 2019

Name	Number
Shanghai's company patents granted	10413
China's company patents granted	173803
Shanghai's very innovative medical devices	44
China's very innovative medical devices	216
Shanghai's manufacturing enterprises	972
Shanghai's innovation enterprises	363

Source: Zhongcheng medical device big data platform (众成医械大数据平台) and China Food and Drug Administration (中国食品药品监督管理总局 https://www.cmde.org.cn/CL0004/index_12.html).

Recently, work on the Shanghai high-end medical device industry mainly focuses on two aspects. First, some work analyzes whether institutional entrepreneurship effectively promotes the development of the Shanghai high-end medical device industry. For example, Wang et al. (2021) evaluated the effects of a special review process. Such a review is compulsory for medical device companies in China before launching a new product on the market. Only companies with patents and advanced products can apply for this special review process, which speeds up the time to the market. Xu et al. (2019) analyzed the role of Marketing Authorization Holder (MAH), which is a national policy aiming at unbounding product registration and production license, which positively affected the high-end medical device industry in Shanghai. Secondly, some work focuses on the effects of ''…an industrial technological innovation alliance…'' on the Shanghai high-end medical device industry (Shi, 2016, 12, in Chinese, translation by the author). Shi (2016) showed that the establishment of this alliance supports enterprises to effectively obtain needed innovation resources, improving their innovation ability, which is beneficial to the technological innovativeness of the Shanghai high-end medical device industry.

4.2 Methods

In order to analyze the CKB, we decided to carry out a case study. Case studies are a preferred method to respond to 'how' and 'why' questions (Eisenhardt, 1989; Yin, 2003). Since we try to find answers to how and why questions concerning CKB at different spatial scales, we decided to use qualitative case study as our method. The fieldwork was conducted in Shanghai from August 2020 to November 2020. As Table 3 shows, in total 24 experts were interviewed in this period, consisting of seventeen experts in enterprises, including six CEOs and eleven R&D staff (indicated as CR), three scholars and experts from universities and public research institutes (SE), and four officials (OF). The interviews lasted on average forty-five minutes. The interview data were complemented with a large number of secondary data from various sources, including mainstream media reports, industrial reports and professional magazines.

Table 3: Detailed information around the survey of Shanghai high-end medical device industry

Interview groups	No. of interviews	Interview topics
CEOs and R&D staff (CR)	17	Classifications of technologies, detailed collaboration information, innovation entrepreneurship
Scholars and experts (SE)	3	Locally industrial endowment and absorb capacities
Official staffs (OF)	4	Institutions, especially institutional entrepreneurship and place leadership
Total	24	Proximity, agency and industrial embeddedness

Source: Our survey in Shanghai

After introducing the survey and the related secondary sources, we will elaborate on the definition of proximity dimensions in this paper. First, based on related studies by Boschma (2005) and Laursen et al. (2011), we argue that geographical proximity is high if firms are located close to collaborators in terms of geographical distance. Secondly, for what refers to the identification of cognitive, social, institutional and organizational proximity, we followed closely the definitions by Davids and Frenken (2018, 27) (see Table 4).

Table 4: The definition of five dimensions of proximity

Five proximity	High	Low
Geographical proximity	Close to collaborators in terms of geographical distance	Far away with collaborators in terms of geographical distance
Cognitive proximity	Similar knowledge	Different knowledge
Social proximity	Friendships, family ties and earlier collaboration	Absence of friendships, family ties and earlier collaboration
Institutional proximity	Co-location in same social subsystem (academia, industry, government) or same territory	Location in different social subsystems or territories
Organizational proximity	Intra-organizational	Inter-organizational

Source: Boschma (2005), Laursen et al. (2011) and Davids and Frenken (2018, 27).

4.3 Empirical analysis

In the following, we will present the results of our empirical analysis. The empirical analysis is divided into two periods, that is, the early development stage (1979-1999) and the main developmental stage (2000-). In the early development stage, knowledge interactions mainly took place within Shanghai. In the main development stage, we also look knowledge interactions at the national and international level.

4.3.1 Early development stage in the market-oriented economy (1979-1999)

As mentioned in Section 4.1, after the founding of the People's Republic of China in 1949, China's first 200 mA medical X-ray machine was developed in Shanghai (中国第一台 200 毫安医用 X 光机). After 1979, the Shanghai high-end medical device industry has started to rapidly develop. During that time, some research staff quit well known scientific institutes or state-owned medical device firms, and joined the world of start-ups (SE1 & OF2), which led subsequently to a strong growth of the number of small and medium-sized enterprises (SMEs). These start-ups and SMEs were mainly located in Puxi, central Shanghai (OF2). Most of these firms are located closely to their main collaborators, such as universities and research institutes, because local University-Industry collaborations are a significant way of product innovation in the process of R&D (geographical proximity) (CR2, 4, 8, 10, 15). This face-to-face communication has been facilitating interactive projects concerning software engineering (which is the combination of analytical knowledge and synthetic knowledge) and human factor engineering (which comes from the combination of three types of KB) (CR7, 8, 10, 15, 16; SE1).

In that era, old social connections (guanxi) such as old colleagues or old partners with similar KB were significant sources for CEOs for knowledge interactions, especially in analytical knowledge (CR1, 7, 9, 14, 16) (local cognitive proximity and social proximity). Moreover, due to low population mobility at that time, most entrepreneurs grew up and stayed in Shanghai. Their friends or relatives working in hospitals or engaging in high-end medical device industries provided some related knowledge resources in joint R&D and production (CR15) (local social proximity).

When old social linkages were not satisfactory anymore for knowledge interaction, new partners were recommended by acquaintances leading to a new combination within a KB. For example, in the 1980s, Liangju Chen, the leader of Yida Medical Equipment Co., Ltd, started his new project with the deformability tester of red blood cells with nuclear pore filtration membrane. According to foreign medical literature, the red blood cell population should pass through micro-pores, that is, each square centimeter has 400,000 micro-pores. His old partner, however, could not meet this new requirement. Therefore, he had to seek a new collaborator. One acquaintance, who worked at the Institute of Laser Technology of the Chinese Academy of Sciences, recommended him to go to a military institute in Jiading, Shanghai. Finally, he cooperated with that military institution to do that project, which won the third prize of Shanghai Municipal Science and Technology Progress (CR7). It shows that the lack of cognitive proximity at the beginning might be an advantage (no lock-in) and can be compensated for by other proximities, such as social proximity. In order to develop advanced products, this company choose a new partner, which shows that innovative entrepreneurship may change previous social networks.

4.3.2 Main developmental stage in the market-oriented economy (2000-)

After the 20^{th} Century, the Shanghai high-end medical device industry increasingly started to build knowledge networks related to different kinds of proximity beyond the local level. Therefore, we will analyze in this sub-section, three levels (local, national, international) separately.

Local level

After the 20th Century, the central government has paid more attention to the development of medical device and encouraged enterprise innovation through a related set of industrial policies. Partly because of this support, the number of medical device companies has been growing in Shanghai (SE2, OF1), locating in new districts, such as Pudong, Minhang, Fengxian, and Songjiang. Moreover, the number of public research institutes increased rapidly, significantly supporting industrial development. Within Shanghai there are by now about 50 universities, colleges and research institutes that refer to related disciplines or technologies, including biotechnology, medical science, artificial intelligence, mechanical engineering and electronics, primarily relevant to analytical and synthetic knowledge.

The concept of industrial parks and clusters (Brenner, 2004; Rodríguez-Pose and Hardy, 2014) has been widely applied in Shanghai urban planning and industrial development after 2000, also contributing to the local high-end medical device industrial development. For example, the Zhangjiang Modern Medical Device Park was founded in 2006 as one of the earliest specialized industrial parks in the medical device industry in China, and is meanwhile regarded as the core part of Pudong medical cluster. To further strengthen this cluster, the Pudong government encouraged related organizations that serve medical device firms to move into the Zhangjiang Modern Medical Device Park (OF3). In 2001, Fudan Fenglin Science Park was established, which is close to Fenglin Campus of Fudan University, where Fudan Medical School is located. It serves as an incubator of technological enterprises in Xuhui District, Shanghai. Overall, these cluster initiatives and parks provided a sound environment for medical device enterprises in industry-university-research-medicine cooperation and fostering product approval. So a lot of medical device enterprises and start-ups moved to these parks or became part of these clusters in order to get better interactions (CR1, 2, 5, 7, 8, 9) (geographical proximity was significant but in order to realize these parks and cluster initiatives place leadership was necessary). However, those interactions were primarily established through old connections (CR 1, 2, 5, 7, 8, 9) (local social proximity played a significant role in interactive learning).

Moreover, many preferential policies and relevant services given by cluster organizations or parks have become key advantages for SMEs, large firms and start-ups (local institutional proximity). For example, The China (Shanghai) Pilot Free Trade Zone (CSPFTZ)（中国（上海）自由贸易试验区), to which many enterprises would like to move, gives key advantages concerning a reduction of import fees, financial subsidies of enterprise income tax, and value-added tax and individual tax adjustment, to medical device companies (CR17). Fudan Fenglin Science Park is another park giving advantages to SMEs and start-ups. According to the CEO of a firm located in Fudan Fenglin Science Park, his company, which produces advanced combinatorial knowledge, received specialized financial subsidies, 300,000 yuan, from the Shanghai government and Fudan Fenglin Science Park in 2020, for being successfully listed as a Shanghai high-tech enterprise in 2020 (CR7). According to him, being based in Fudan Fenglin Science Park helped him to receive such a big financial subsidy.

National level

During the last ten years, Shanghai, Beijing, Tianjin, Zhejiang Province, Jiangsu Province and Guangdong Province, have developed into the main hotspots and clusters of the high-end medical device industry in China (SE1, 2, 3). Inter-city interactions at the national level, based on intra- or inter-KB, primarily take place between actors based in these cities and provinces, which are characterized by high cognitive proximity because of the same industrial and knowledge background (CR5, 6, 9, 11, 16). One researcher working for a high-end medical device company in Shanghai explained that due to interactive learning between actors in Shanghai and the other cities and provinces mentioned above, highly qualitative products with combinatorial knowledge are easier to create (CR8) (cognitive proximity).

In addition to cognitive proximity, the national level also plays a role concerning organizational proximity. Affiliates of Shanghai's large enterprises have been established in Shenzhen, Beijing and other cities in China, mainly through mergers and acquisitions (M&A), fostering organizational proximity at the national scale. For example, in 2012, Weichuang (微创), a medical device company located in Zhangjiang High-Tech Park, Pudong, Shanghai, specializing in orthopedic and implantable medical devices acquired D-Pulse Medical （Beijing） Co., Ltd.（龙脉医疗（北京）有限公司）with patents related to stent (CR16). In addition, jointly established institutes fostered cognitive proximity at the national level, such as the Shenzhen Lianying High-end Medical Equipment Innovation Institute (深圳联影高端医疗装备创新研究院), established in 2019, that is a private, non-profit organization jointly sponsored by Shanghai Lianying Medical Technology Co., Ltd.（上海联影医疗科技有限公司）and the Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences（中国科学院深圳先进技术研究院). It contributes to Shanghai Lianying's R&D on key technology and core components relevant to CKB (CR12). According to our survey, organizational proximity has a significant positive effect on product development of the large Shanghai-based high-end medical device companies (national organizational proximity).

Inter-city collaboration has also increased due to a change in policy regulation at the national level, namely the above-mentioned national regulation concerning unbounding product development and product license, MAH. The national state first published it and it was tried out in the Shanghai Free Trade Zone by the end of 2017 (OF4). In 2019, the trial of the MAH was extended to 21 provinces and cities, including, among others, Beijing, Shanghai, Shenzhen, Zhejiang Province, Guangdong Province and Jiangsu Province. Experts explained that, under this new condition, collaborations between firms and the CDMO (Contract Design & Manufacture Organization) platform at the national level increased (national institutional changes influence national institutional proximity) (SE1). For example, the CEO of Giant Yi Technology (Shanghai) Co., Ltd (one well-known CDMO platform) (巨翊科技（上海）有限公

司), explained that one client located in a province outside of Shanghai, specializing in R&D once operated a small plant, but the lack of experienced project managers led to some problems in the quality management system. After introducing the trial to the extended MAH, this client choose to collaborate with the Giant Yi CDMO platform in production. In addition to quality assurance of clients' products, the CEO said, Giant Yi offers services supporting R&D design or developing the next generation products for clients, which is the advantage of the CDMO platform, compared to other high-end medical device companies (Arterial Network - Future Medical Service Platform, https://vcbeat.top/ODBjZjExMzliMDQxNDNhODcyMzY1M2Rk ODdm ZDYxNTg=).

International level

Although the Shanghai high-end medical device industry has recently developed quickly, medical device products from America, Germany, Japan, Switzerland and the Netherlands have been imported to Shanghai and China for a long time. In specific fields, Shanghai industrial development have depended highly on international sources. Interviewees specializing in R&D acknowledged that Shanghai-international interactions primarily include optical engineering and electronic engineering (optical engineering knowledge consists of a combination of analytical and synthetic KB; electronic engineering is mainly based on intra-synthetic KB). Concerning optical engineering, collaborators mainly come from Germany, Japan and Switzerland, which have advanced optical engineering knowledge in this aspect (CR1, 5, 12, 13), while American collaborators are the biggest partners in R&D in electronic engineering, as they are renowned in this field (CR 9, 16) (international cognitive proximity).

In these international interactions, old social networks are the significant linkage between Shanghai and international sources. Several CEOs of large enterprises explained that these earlier collaborations or peer recommendations play an important role in facilitating current interactive learning (international social proximity). If the behavior of both partners is in line with their mutual expectations during earlier collaborations, they usually continue to work together in the future (international social and cognitive proximity). In addition to that, some entrepreneurs with overseas studying backgrounds use their foreign connections for help. Collaborating with alumni, laboratories and universities where they once studied is a common interactive mode (CR7, 13).

In addition to cognitive and social proximity, the international level also plays a role concerning organizational proximity. For large enterprises, many local-global interactions take place within the organization, which results from mergers and acquisitions (M&A) at the international level. The latter can often be recognized as a strategic global expansion in developing high-end medical devices. For example, in 2013, Weichuang (微创) acquired Wright's OrthoRecon business, which consists of hips and knee implant products, and set up Weichuang global orthopedics headquarters in Arlington, Tennessee, USA. Then it acquired the stent-related assets of Johnson & Johnson Cordis in 2014. Overall, in the process of organizational integration, in addition to the established effects of technological relatedness, the degree of organizational proximity has enhanced (SE3) (international organizational proximity). However, one CEO pointed out that M&As, particularly at the international level, are challenging, because entrepreneurs must deal well with organizational changes. Only innovative entrepreneurs with strong organizational skills are able to do reasonable M&As, propelling intra-organizational collaborations (innovative entrepreneurship may influence international organizational proximity).

4.3.3 A comparison of combinatorial knowledge interactions at different spatial scales

Our empirical case aims at analyzing CKB in terms of proximity and agency. By comparing combinatorial knowledge interaction at three spatial scales, we summarize the following interesting aspects. First, geographical, cognitive, social and institutional proximity are central for combinatorial knowledge interactions in the Shanghai high-end medical device industry at the local level. Although place leadership influenced local geographical proximity in the early 20th Century, it continued to play a significant role during later interactions. Moreover, innovative entrepreneurship may break old social connections. Secondly, cognitive and organizational proximity have an important effect on combinatorial knowledge interactions at the national level. Although, at this level, the role of institutions was weak for a long time, recently institutional entrepreneurship has the potential to enhance national institutional proximity. Thirdly, Shanghai-international collaboration is highly dependent on cognitive, social and organizational proximity. Innovative entrepreneurship with strong organizational skills is conducive to M&As, which is particularly evident at the international level.

5. Conclusions

Economic geographers have long shown an interest in knowledge flows at different spatial scales. So far, however, at least two weaknesses could be identified in the literature, namely, fragmented knowledge in space owing to single-scale researches, and a limited interpretation of driving mechanisms. By empirically investigating the Shanghai high-end medical device industry, we are able to fill these gaps and hence contribute to the understanding of combinatorial knowledge interactions across space and of driving mechanisms behind CKB.

Moreover, concerning the case study, we draw four conclusions. First of all, in the Shanghai high-end medical device industry, CKB, a combination of analytical and synthetic KB, prevails. Secondly, knowledge interactions differ at different spatial scales, which is strongly related to the specific characteristics of the local medical device industry, such as in the case of software engineering, and the position of local knowledge in the global industrial knowledge value chain, such as in the case of optical engineering. Thirdly, in the Shanghai high-end medical device industry cognitive proximity is the key factor facilitating combinatorial knowledge interactions at all spatial scales. Institutional and geographical proximity are obviously more important at the local scale. Fourthly, in this paper, proximity is firstly analyzed in terms of three kinds of agency. Among these, place leadership and institutional entrepreneurship work respectively at the local and national level, while the role of innovative entrepreneurship is observed at all levels.

Finally, three remaining interesting issues require future research. First, the analytical framework developed in this paper to analyze the Shanghai high-end medical device industry to study proximities and different kinds of agencies could be applied more widely in other empirical studies on CKB, regional innovation systems, industrial clusters, and global value chains. Secondly, within Shanghai more research could be done on other kinds of industries and the potential combinations of KB in order to compare features and characteristics of combinatorial knowledge flows. Thirdly, future research could be carried out on the medical device industry in other cities in China or abroad, in order to compare the results and to be able to generalize and have a deeper understanding of underlying mechanisms explaining combinatorial knowledge interaction across different geographical contexts.

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