Development of San Diego Life Sciences Ecosystem

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INTRODUCTION

Increasing competition in global markets requires many countries to seek new growth sectors. In addition, the nature of competition is changing. Competition takes place among business ecosystems that tie various actors together through knowledge flows and shared value creation processes (Moore, 1993; Iansiti and Levien, 2004). The business ecosystem concept is claimed to offer advantages over previous concepts, such as clusters (Porter, 2000) and value chains. These advantages include the capability to provide insights into change dynamics and related strategic consequences (Makinen and Dedehayir, 2012). Although cluster-thinking is widely used in innovation policy context, the cluster concept has also been criticized as being unable to explain the underlying factors contributing to the success of certain locations (Kim, 2013). This study aims to provide new insights into innovation policy in a spatial context by utilizing a business ecosystem perspective. While business ecosystems span over regional boundaries, many ecosystem actors have a local presence (Clarysse et al., 2014). Therefore, the business ecosystem view is relevant and can provide valuable insights in spatial contexts (Carayannis and Campbell, 2009).

Despite growing competition especially from Asian countries, the USA is still the undisputed global leader in life sciences. The leading life sciences areas in the USA include Greater Boston area, San Francisco Bay area, and San Diego (JLL, 2014). The first two have received most interest in literature, but interest in San Diego and its unique characteristics has grown recently. Previous studies and reports (e.g. Porter, 2001) provide information on many important factors that have contributed to the success of San Diego, including the roles of university, pioneer companies, and other institutions, and the importance of social networks, cultural aspects, and collaborative learning (Casper, 2007; Kim, 2013; Walshok and Shragge, 2014). This study was based on a single in-depth case of San Diego life sciences business ecosystem. Data were collected using (1) researcher observation and notes during a six-month field research, (2) analysis of previous studies of San Diego, and (3) interviews with key informants consisting of twenty individuals who possessed in-depth information on the ecosystem under study.

This study extends the current body of knowledge; a business ecosystem approach is adopted and the evolution of San Diego is studied as a spatial life sciences ecosystem. The paper analyzes and reports evolution of the ecosystem in each life-cycle phase: birth, expansion, leadership, and self-renewal. The aim is to identify issues that should be considered in design of innovation policies and regional industry development, i.e. how policy makers can effectively support the development of business ecosystems in a spatial context. In order to meet the aforementioned aim, the following research questions are addressed:

> *How has San Diego life sciences ecosystem evolved and what are the ecosystem's life-cycle phases?*

What are the key innovation policy measures utilized in each phase?
How does business ecosystem view affect innovation policy design?

This study focuses on one specific case: San Diego life sciences. However, the viewpoint adopted covers the entire evolution of the ecosystem and related innovation policy measures. The major contribution of this study is advancing innovation policy research in a spatial context by offering an analysis for the required measures to support ecosystem development in different evolution phases. In addition, this study provides a novel analysis on how San Diego life sciences ecosystem has evolved through its life-cycle phases.

SAN DIEGO LIFE SCIENCES ECOSYSTEM

Birth

The origins of San Diego life sciences ecosystem can be found already in the late 19th century. Due to the climate of the region, many people with health and respiratory issues moved to the area in search of health friendly environment. San Diego invested in sanitariums, hospitals, and health research clinics already in the 1880s (Walshok and Shragge, 2014). The Scripps Institution of Oceanography was founded in 1903 as a non-profit association and was funded by the Scripps family. It was acquired by University of California in 1912 (Walshok and West, 2014).

In the late 1950s and early 1960s, three major research institutions were founded in San Diego: The Scripps Research Institute, The Salk Institute, and University of California San Diego (Porter, 2001). Focus on clean industries was an obvious choice, since San Diego has limited natural resources and its remote location prevented establishing manufacturing and heavy industries. In the 1920s-1940s, the region benefitted from the rise of aviation industry (Walshok and Shragge, 2014). The Second World War led to the expansion of the military base and the aircraft industry in San Diego (Kim, 2013). However, a key event that enabled the birth of successful life sciences ecosystem was the establishment of University of California San Diego (UCSD). Prior to that, the city of San Diego had made land zoning decisions that enabled proximity of various ecosystem actors: UCSD, research institutes, and companies. In the late 1950s, the City of San Diego donated land for University of California and to Jonas Salk (polio vaccine discoverer) for his research institute (Anderson, 1993). In 1971, the city reinforced the plan for the Life Sciences-Research zone to create a campus-like environment that would attract talented people and enterprises (Kim, 2013).

A significant factor that drove the establishment of University of California campus in San Diego in 1960 was the research co-operation that had taken place between Scripps Institute of Oceanography and US Navy (Walshok and Shragge, 2014). In addition, the decision was heavily influenced by the trend in expanding basic science research and development in the 1950s and 1960s, especially science-driven engineering and technology development focusing on applications related to defense and aerospace. However, UCSD had a broader scope and its strategy was to build excellent science programs in biology, chemistry, mathematics, and physics. The strategy was aimed to be implemented by recruiting world-class scientists and researchers. (Walshok and West, 2014). The strategy proved successful: according to Casper (2014) “from the early 1970s onwards UCSD’s biomedical science departments had achieved an international reputation that was comparable to that of University of California San Francisco (UCSF).” Clinical and basic research integration in UCSD was performed in the similar way as in UCSF. UCSD

Medical School was started in 1968 and was integrated with the basic science departments. 1n 1972, 1000-bed veterans administration hospital was opened on the campus. (Casper, 2014).

Two important persons in the UCSD establishment and early years must be highlighted. First of all, the state governor Edmund Gerald "Pat" Brown got excited by the idea that any qualified individual could have an elite education through the University of California. The target was that UC San Diego would be another Berkeley; excellent but accessible unlike private universities. However, recruiting top scientists to San Diego was not that easy, since San Diego did not have a scientific reputation. The type of scientists that were recruited can be considered as risk takers; they were willing to leave traditional institutions to start something new without constraints of traditional institutions. Another key person was Richard C. Atkinson who was the chancellor of the UCSD from 1980–1995. Atkinson had a background in Stanford and National Science Foundation (NSF) and he was involved in many government activities, such as Small Business Innovation Research (SBIR), Small Business Technology Transfer Program (STTR), and the Bayh Dole act. The SBIR and STTR enabled the NSF and other agencies to fund university-industry research partnerships, whereas the Bayh Dole act has been pivotal in technology transfer in USA. Atkinson understood and encouraged the importance of collaboration between UCSD and industry.

Expansion

Starting from the 1970's, funding of life sciences increased. Federal government funding, especially National Institute of Health (NIH), and the partnership between UCSD, The Scripps Research Institute, and the Salk Institute increased San Diego's research capacity. In addition, the La Jolla Cancer Research Foundation (later known as Sanford-Burnham Medical Research Institute) was founded in 1976, and the La Jolla Institute for Allergy & Immunology was established in 1988. These five research institutions in San Diego acquired 707 million USD from the NIH in 2009 (Kim, 2013). By the mid-1980s, San Diego life sciences ecosystem had developed a critical mass of R&D capacity, which attracted international firms and venture investors. In addition, three pioneer startup companies, Linkabit (wireless), ISSCO (computer graphics), and Hybritech (biotechnology), played a key role (Jones, 2005; Kim, 2013; Walshok and Shragge, 2014).

Hybritech was founded in 1978. The scientist founder, Ivor Royston, was an assistant professor who focused on cancer research at UCSD. Royston conducted research on monoclonal antibodies and wanted to start a company to exploit the increasing demand for them (Jones, 2005). Co-founders Tim Wollaenger and Ted Green had both worked at Chicago's Baxter Travenol Pharmaceutical (Walcott, 2002). Hybritech hired people from research institutes and several managers with experience in R&D, marketing and plant management and several products were launched. A successful initial public offering took place in 1983 (Casper, 2014.) Hybritech was located close to the UCSD campus, which was very convenient for the former university employees. However, in contrast to another successful biotechnology company, Genentech, that had its background at UCSF, Hybritech did not pursue scientific achievements (i.e. publications) and had a more commercial orientation than Genentech. The success of Hybritech inspired professors at UCSD and The Scripps Research Institute to establish new companies. Yet, the growth of biotechnology in San Diego can be considered somewhat limited during the early 1980s. Eleven companies were established in 1975-1986 and few local venture capitalists existed. Venture capital money was coming from the San Francisco Bay area through syndication deals. Kleiner Perkins was the only active company supporting foundation of new companies. (Casper, 2014). The founders of the first biotech start-ups faced a recruiting challenge, since they had to lure management talent outside San Diego

region to an emerging high-risk industry. The recruited people were attracted by the opportunity to build something new in an environment that lacked traditional constraints. These people also leveraged their personal and professional relationships outside San Diego region and brought in additional resources related to business, science, capital, and business services. San Diego's remote location necessitated collaboration and partnering. Sharing resources and contacts became a key feature of San Diego's innovation ecosystem. (Global CONNECT, 2010).

In 1986, Eli Lilly acquired Hybritech for 413 million USD. The company became a subsidiary of its conservative parent company and many people left to start their own companies. According to Casper (2007), Hybritech managers established or assumed senior management position in at least twelve companies between 1986 and 1990. A study by Walcott (2002) reports over forty companies that were formed between 1983 and 1996 by former Hybritech employees. San Diego life sciences ecosystem benefitted from the experienced, wealthy, and high-status networks of managers and scientists linked to Hybritech. From the late 1980s through the 1990s, the ecosystem began to attract venture capitalists; Avalon Ventures was founded in 1983, Forward Ventures in 1993, and Kingsbury Capital Partners in 1994 (Casper, 2014).

In spite of Hybritech's initial success, gaps between science and business existed in San Diego. In addition, the region faced a lack of capital and intellectual property rights (IPR) competence. Due to reductions in military sector, the unemployment rate increased to 10 % in 1984. San Diego Economic Development Corporation contacted UCSD and initiated discussions on how to connect science and business. (Walshok and Shragge, 2014) The local leaders recognized the need to accelerate innovation, and a non-profit intermediary organization called CONNECT was established at the UCSD extension in 1985; the organization has been very successful in catalyzing local innovation. Prior to the CONNECT's establishment, San Diego had lost a bid to Austin, Texas for the Microelectronics and Computer Technology Corporation's (MCC) headquarters, which was a consortium of semiconductor and computer manufacturers. After the lost bid, a group of local business leaders worked with the UCSD Chancellor Richard Atkinson to develop an innovation and entrepreneurship acceleration program. The initiative was bottom-up and privately funded, and it was hosted by UCSD. CONNECT was selected to reside at the UCSD to ensure that it was perceived as a neutral actor in the ecosystem. (Global CONNECT, 2010).

The first CEO of CONNECT, Bill Otterson had a lot of connections, and he used them to create relationships between entrepreneurs, investors, and experts. Otterson was a former high-tech entrepreneur who sold his business, since he had had cancer. CONNECT as an organization does what Otterson started on a personal scale. The organization has developed the Springboard program which is now internationally recognized. CONNECT can be claimed to be a key reason behind San Diego's success in creating new innovations. Before CONNECT was founded, collaboration among companies in vertical industries was considered inappropriate as companies focused on their unique competitiveness. CONNECT's principles, which can be seen to be derived from the Otterson culture, included help each other – compete in the marketplace, the team above self, the region above company, political issues matter (e.g. Food and Drug Administration reform) and it is acceptable to fail as long as you try again. The implementation of CONNECT's strategies and business practices can been considered vital for building trust among actors in San Diego's life sciences ecosystem (Majava et al., 2016a).

In the early years of CONNECT, the members shared their contacts and networks to benefit others. Various networking events and lecture series including Meet the Researcher and Meet the Entrepreneur brought together different stakeholders of the ecosystem. CONNECT played a very valuable role in life

sciences, since in the mid-1980s a local industry association for life sciences did not exist. CONNECT's Biotechnology Corporate Partnership Forums attracted interest in San Diego's biotechnology industry from outside the region. The idea was to attract large pharmaceutical companies to visit San Diego and familiarize them with small biotechnology companies. The objective was to create new partnerships, supply agreements, or even acquisitions. After these activities, many large pharmaceutical companies established offices in San Diego for sales, R&D, and technology licensing purposes. CONNECT's activities can be considered essential in putting San Diego's biotechnology industry on the map. Later on, the Springboard Program offered a process of coaching and mentoring entrepreneurs. (Global CONNECT, 2010)

In addition to creating collaboration between research, start-ups, and investors, CONNECT has supported the creation of industry organizations, such as the Wireless-Life Science Alliance. The San Diego Biocommerce Association (BIOCOM) was founded in the early 1990s (Walcott, 2002). The foundation of BIOCOM was affected by severe draught some years earlier and the city of San Diego was planning to shut off the water. Since biotechnology companies are dependent on the water they saw the need to work together (BIOCOM, 2016). The leader of CONNECT, Bill Otterson, also understood that the unique requirements of life sciences industry and acknowledged that the life sciences companies needed their own voice.

Leadership

By the mid-1990s, the San Diego region had developed the third-largest bioscience industry in the world, after San Francisco and Boston. In addition to UCSD, the research institutes, such as the Scripps Research Institute and Salk institute played a major role. (Casper, 2014). Yet, apart from Hybritech and Idec, few large biotech firms were created in the region. In 1996, the number of life sciences firms in San Diego was approximately 430 (Walcott, 2002). In 2010, the ecosystem included approximately 500 life science firms, but only three of them - Illumina, Amylin Pharmaceuticals, and Life Technologies - had over 1000 employees (Global CONNECT, 2010). The number of employees in the life sciences industry in San Diego increased from 7548 in 1997 to 19 693 in 2002, and in 2007 the industry employed 22 719 people (Kim, 2013). With regards to federal R&D funding, in 2009 NIH awarded San Diego 919 million USD and the NSF 267 million USD (Global CONNECT, 2010).

Over the years, San Diego's life sciences ecosystem developed through a bottom-up nature to be very self-organized. The ecosystem's scientific base can be considered as diverse and dense. Cancer, neurosciences, and diagnostics research areas are strong, and the importance of genomics and the next generation sequencing is increasing. The ecosystem operates without a single leader although, for example, the leaders of CONNECT and Biocom play major roles. Thus, the life sciences ecosystem can be argued to differ considerably from the wireless technology ecosystem in San Diego that is led by Qualcomm. The life sciences lacks a big anchor company, although Hybritech had that role in the early 1980s and the genomics company Illumina's influence has increased in recent years. According to Majava et al. (2016b) various actors contribute to the San Diego ecosystem. The UCSD and research institutes provide a platform for new discoveries; these organizations acquire research funding, create new technologies and ideas to be commercialized, train new talent, and license technologies. Accelerators and incubators provide the start-ups with resources, space, mentoring, and coaching. They have important role in networking in the ecosystem and match companies with early stage funding opportunities. Angel investors, in turn, contribute to the ecosystem with seed investments and providing advice for start-ups. Venture capitalists invest to support innovation and company growth in the later

stage, whereas large pharmaceutical companies are potential partners and investors if the company becomes successful. Established life sciences companies offer a talent pool and contribute to the success of the ecosystem. Trade organizations offer advocacy and resources for member companies, and act local and global networking platforms. Health care providers are the target market, channel to end-customers, and important partner in clinical trials. Governmental actors in local state, and federal levels provide the ecosystem with the infrastructure, rules (including legislation, regulations, and taxes), policies, and research funding. The ecosystem also includes providers of business services, such as legal, financial, real estate, and human resources services. The business services providers offer contact networks that support the ecosystem.

Self-renewal

Currently, San Diego is especially strong in the sectors of wireless technology and life sciences and the region provides unique opportunities considering the convergence of wireless technology and healthcare (JLL, 2014; Walshok and West, 2014). The military sector continues to be important; it is responsible for approximately 328 000 (22 %), of the region's total jobs in 2015 if all the ripple effects of defense spending are taken into account (SDMAC, 2015). The main factor that drives the development of the ecosystem is constant innovation that typically originates from government funded basic research. Commercializing the invention is supported by accelerators, technology transfer organizations, incubators, angel investors, venture capitalists, local and external talent pools, and trade organizations. In case of success, an initial public offering (IPO), a merger, or acquisition by another company may occur. However, most life sciences inventions will not be seen in the market. In spite of failures, constant innovation in the ecosystem feeds the local resource pool. People also tend to reinvest in the local ecosystem either financially or by spending time in mentoring and coaching new entrepreneurs. (Majava et al., 2016b)

The life sciences ecosystem in San Diego has a lot of strengths in many areas. The ecosystem is growing and continuous learning takes place among actors. The convergence between life sciences and wireless, also known as connected health, contains many areas, such as digital health, mobile health, applications, use of sensors, big data, and personalized medicine. Examples of the convergence include the investments by Qualcomm to its Qualcomm Life activities and the collaboration between UCSD School of Medicine’s and the School of Engineering. The importance of genomics, sequencing, and stem cells are also increasing. A recent example is a company called Human Longevity that applies large-scale genomic and clinical data to improve medicine, which has raised over 220 million USD from investors that include Illumina, Celgene, GE Ventures, and individuals from the Americas, Europe, and Asia (Fikes, 2016).

The growth in initial public offerings (IPOs), which started in 2013, is likely to continue. This will bring more capital into the ecosystem. New forms of funding, including syndication and crowdfunding, are also developed. However, the level of federal research funding is a concern; this requires research institutes to change and focus more on commercialization and create public-private partnerships. Pharmaceutical companies are likely to become more interested in early stage opportunities. But the ecosystem also faces challenges. San Diego has a remote location and lacks capital and IT talent resources compared to the San Francisco Bay area. Global competition in life sciences is increasing. The high cost of doing business in California, water issues, and federal regulatory barriers are issues that may have significant effects on the ecosystem. The local government should be determined to develop San

Diego in order it to remain attractive base for the life sciences ecosystem in the future. (Majava et al., 2016b)

DISCUSSION: INNOVATION POLICY MEASURES

In recent years, many researchers have tried to explain the factors that have contributed to the success of life sciences industry in San Diego. In a study by Porter (2001) the following factors were emphasized: importance of educational and research institutions, the capability to attract federal and state research funding, the local talent pool, the role of local government in fostering a favorable business environment, formal and informal collaborations, and a location and climate that can attract external talent. Walcott (2002), in turn, claimed that the key success factors included a world-class research university, advocacy leadership, risk financing, an entrepreneurial culture, and appropriate real estate, combined with an intensive information exchange network. Jones (2005) and Casper (2007) focused in their analyses on the social networks and interactions as well as Hybritech and the startups that were established by former Hybritech employees. In a report by Global CONNECT (2010), San Diego was found to benefit from low barriers to entrepreneurs, experience in private-sector led initiatives, state infrastructure investments, self-organization capability (instead of relying on government-led programs), the ability to acquire federal research grants, highly interdisciplinary and entrepreneurial research institutions, strong personal networks and proactive engagement with resources and external decision makers, and pioneer companies such as Hybritech. Hwang and Horowitt (2012) argue that the growth of San Diego's ecosystem was catalyzed by enterprise-friendly policy changes, transparent laws (for real estate, intellectual property, agreements, and corporations), low enough taxes and cost of setting up a new corporation, a network of people with experience in technology, science, business and business-related services, and the capability to attract global talent. Kim (2013) emphasized in his findings the importance of learning and claimed that, "to a large extent, the emergence of the San Diego biotechnology community was a process of creating and circulating local knowledge and practices." Walshok and Shragge (2014) claimed that San Diego's civic culture is characterized by risk-orientation, entrepreneurial talent, integrative civic platforms, numerous gateways to develop ideas and opportunities, and a culture of reinvestment. They argued that San Diego's success was based on five critical factors: natural advantage of place, early settlers' values, organization of communities for economic promise, the resources and talents the community cultivated, and how citizens defined and promoted their place.

The San Diego biotechnology industry has also been argued to emerge from a different pattern of university-industry interaction compared to San Francisco (Casper, 2014). According to Powell et al. (2002), there is a strong pattern of spatial concentration in research organizations, biotechnology and venture capital. However, especially in the 1970s and 1980s San Diego lacked local venture capital. Casper (2014) claims that university-industry collaborations are much more common in the San Francisco biotechnology sector than in San Diego, and the San Francisco area's development resonates with broader research on Silicon Valley (e.g. Kenney, 2000; Saxenian, 1996). In San Diego, the key networks can be considered entrepreneurial and they surround a nucleus of commercially oriented managers and scientists with a background at Hybritech. The San Diego case suggests that access to strong entrepreneurial managers early in a firm's development can lead to a competitive success. Furthermore, Casper (2014) states that "this conclusion may be important for thinking about public policy toward cluster development. The inventor network theory of cluster success, which privileges scientific spillovers and thus investment primarily into creating world-class research, may not be the only way to

promote cluster formation." While a strong science base is vital, policies that focus on entrepreneurial network formation can also promote the development of regional network.

The literature and empirical data collected in this study indicate several elements of ecosystem-based policy that apply to San Diego in all development phases. These include for example feeding creativity by developing an attractive, close-proximity, environment for entrepreneurs and researchers, maintaining vivid testing and experimenting culture, building world-class research capacity, access to financial and social capital, cooperation networks, as well as promoting cooperation between universities and firms. Ecosystem policy is more orchestrating and facilitating instead of direct steering or too much interference in business. However, when examining the San Diego case more closely, some elements can be seen to be of special importance in particular phases of the ecosystem evolution.

The report by Global CONNECT (2010) articulates many interesting points regarding the role of government during the ecosystem's birth phase. The report points out that while a long history of defense spending has affected the US economy, one may argue whether the US has an industrial policy. The actions by federal, state, and local governments create an environment where institutions and companies compete for resources. The concrete actions, among others, include incentives, tax policy, regulatory policy, patent policy, bankruptcy laws, research and education funding. The report claims that San Diego benefitted from the interplay of federal, state, and local government actions which were often related, but initiated independently. The federal level activities have included private companies' mission-oriented contract work for the US military and other agencies, the funding for basic research at universities and research institutes, and regulatory processes (e.g. phased clinical trials required by the FDA). The activities by State of California, in turn, include funding for public universities and the facilities and infrastructure that support research. The most prominent example is naturally the decision to locate a UC campus in San Diego and provide funding for its facilities and laboratories. The local government's activities during the 1940s and 1950s included land use decisions in Torrey Pines Mesa that later became the heart of life sciences ecosystem.

For a spatial business ecosystem to be born common agenda and vision form an important strategy level base for other policy level decisions and actions that can affect the early phase development of a business ecosystem. Committing to common growth and development aims is a strategy-level decision effects of which become concrete and visual through for example regional and urban planning. San Diego case showed that at least in this case this has mattered, and creating favorable conditions for ecosystem development can start from decisions concerning land use, infrastructure and good living conditions. In life sciences ecosystem the seed of a new business lies often in a new idea that is a result of research work. This can be supported by developing research and development infrastructure and funding instruments that enable risk-taking and developing radical innovations. Universities and other research organizations can also be important platforms especially for cooperation between researchers and firms as well as platforms for spin offs that can become pioneer companies. In the early phase development public sector can also provide platforms for testing and piloting, in life sciences case for example in hospitals. Public procurements can also be another way foster demand for new innovations that could also foster new ecosystem development.

The expansion phase of San Diego's life sciences ecosystem that started in the early 1980s has been affected by the Bayh-Dole act in USA in 1980 and the establishment of Technology Transfer Offices (e.g. Grimaldi et al., 2011). In addition, the Small Business Innovation Research (SBIR) and Small Business Technology Transfer Program (STTR) can be considered important factors that have affected

the expansion. The most significant events in the expansion phase include the Eli Lilly's unsuccessful acquisition of Hybritech followed by a number of start-ups founded by its former employees and the establishment of CONNECT in 1985 (e.g. Jones, 2005; Casper, 2007; Majava et al., 2016a). In addition, during the late-1980s and early-1990s the City of San Diego considered water restrictions due to a long-lasting drought. Representatives of the local biotechnology industry demonstrated their self-organization capability and unitedly told the City Council how important water was for the industry. The restrictions were not implemented and the city started a new business impact assessment process for its decisions. (Global CONNECT, 2010).

From the business ecosystem policy perspective, the expansion phase calls for policy tools that support startup activity and the growth of small enterprises. Attracting and utilizing different funding sources helps new businesses to develop and grow. Availability of support systems and networks for startups, and business mentors and incubators is important in the expansion phase for new businesses to start and join the ecosystem. Platforms, such as CONNECT, can help bring different actors such as firms and investors together. The role of leading firms is important for the expansion, as the leading firms generate growth and attract skillful workforce. Removing unnecessary regulation and bureaucracy is of special importance from the policy point of view in the expansion phase. The strategy level common dedication to grow becomes concrete and visual in the expansion phase.

The ecosystem leadership phase can be considered to have started in the mid-1990s, when San Diego had developed the third-largest life sciences industry in the world, after San Francisco and Boston. In addition to continuous research funding by the federal government, the state government has also had a significant role in supporting the ecosystem. The state has had initiatives, such as California Institutes for Science and Innovation (Cal-ISI) in the early 2000s and the California Institute for Regenerative Medicine (CIRM) in 2005 related to a $3 billion bond that was distributed over 10 years. The bond was created to fund stem cell research in reaction to limitations placed on federal research grants. (Global CONNECT, 2010).

With regards to the ecosystem-oriented innovation policy, the role of successful enterprises is emphasized in the leadership phase. How to lead the ecosystem and ensure its continuous renewal? In this phase the ecosystem should work quite independently without any special policy support. However, in order to ensure the "vitality" and continuous renewal of the ecosystem, policies could continue to encourage open innovation, co-creation, and re-investment. The leadership phase and preparation for self-renewal can also be supported through long-term oriented research funding.

San Diego's life sciences ecosystem is entering self-renewal phase, which includes, for example, the convergence of life sciences and wireless. In self-renewal phase it is essential that policy supports specifically the renewal process instead of supporting old industries and structures that as such are no longer capable of showing future potential. Sotarauta (2005, see also Saarivirta, 2009; Ståhle, 1998) speaks of self-renewal capacity that consists of for example exploration, integration and leadership. The self-renewal capacity is of course built during the whole lifespan of the ecosystem, but its "strength" is tested especially when the ecosystem is about to or already has lost its leadership role in a particular field. In self-renewal phase the role of radical innovations and new unexpected combinations is again emphasized. Policies promoting interdisciplinary and diversity are needed as well as "looking for the unknown". San Diego has strengths in different fields and it has not been "locked" to its old development paths. The convergence between life sciences and wireless technology is a very potential and promising path for San Diego.

Finally, some unique characteristics of San Diego's life sciences ecosystem should be stressed. The proximity of actors, which can be affected by land use decisions, is one of the key differentiators of San Diego compared to San Francisco and Boston. In addition, the business and academic culture of San Diego is very entrepreneurial. The importance of university-industry collaboration was understood already when the UCSD was established, and the first scientists recruited were risk-takers who were willing to leave well-established universities to pursue their interests. The entrepreneurial culture grew stronger through the success of Hybritech and its heirs, and the local community and decision-makers saw that the science and business supplement each other. A large number of intermediary organizations that have been established since the 1980s also illustrate entrepreneurial orientation; when the actors see a gap in the ecosystem, they tend to fix it without top-down guidance. Furthermore, the relative smallness of San Diego has fostered collaborative culture.

CONCLUSIONS

This study documented the case of a successful spatial life sciences business ecosystem, its evolution, and analyzed related innovation policy measures. The results of the study support many of the policy remarks presented in previous studies, such as the importance of strong basic research and education, the need to support networking and knowledge exchange, and to build infrastructure. Our study contributes to business ecosystem research by offering an innovation policy perspective to business ecosystem evolution through its four different development phases recognized in previous literature. Contribution to policy practice is also related to examining the ecosystem development through four different phases; considering the evolution and development phase of an ecosystem when planning policy measures can help targeting policy support to where it is needed, and avoid creating unnecessary structures and incentives. Based on the results of the analysis we argue that the relevance of policy decisions and support is present throughout the ecosystem life cycle but the role of policy changes along with the different phases of the ecosystem's evolution.

In the birth phase the policy targets seem to be related to such things as common vision building and basic investments supporting the vision. This is often enabled by some strong personalities in the region. A successful process calls for a certain ability: regional visionary capability. The policy targets in the expansion phase are typically related to fostering brokerage functions and new startup generation in the region. The necessary capability for this is something we call general ability to build possible worlds. The leadership phase requires support for the key value networks and their keystone companies especially by research funding. Regional creative tension should be kept on, as well. A useful capability for these tasks is the regional leadership capability including needed creative social capital. The policy targets of the self-renewal phase are typically related to finding technology adjacencies and building related variety platforms in order utilize the opportunities emerging in the process. Regional self-renewal capacity has a decisive role in this phase.

In summary, the results of this study show that although some policy measures can have a positive effect on the ecosystem development throughout its evolution, the development phase of an ecosystem can also indicate what type of policy measures are needed and most effective. As presented in this study, San Diego life sciences ecosystem - as probably most spatial business ecosystems - has unique features related to ecosystem actors as well as to the features proceeding from local history and culture. From policy perspective, the right ecosystem policy mix needs to be created considering these features. As

successful spatial business ecosystems cannot be duplicated, neither can the mix of policy measures that have successfully supported the ecosystems throughout their evolution. Therefore, supporting policies require flexibility in taking into account the unique ecosystem characteristics and ability to respond to ecosystems' evolution. The challenge for policy planning and practice is how to support ecosystem birth, development and renewal without interfering too much with the ecosystems' self-organizing and self-renewal dynamics.

The findings presented in this study were based on a single case study, which limits generalizations. A single-case based research strategy was deemed appropriate by the researchers due to the opportunity to gain in-depth understanding of the phenomena under study. For the future studies, the authors propose analyzing other spatial contexts in order to generate broader understanding of life sciences ecosystems, as well as to compare and to validate the findings. In addition, future research can develop understanding of spatial ecosystems in other industry sectors, such as information and communication technology.

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