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Abstract: The present paper seeks to explore factors related to the types, influences, reasons for influences, and how entrepreneurship ecosystems developed in the biopharmaceutical sector in select regions of Central Europe. It is motivated by specific gaps in the literature related to entrepreneurial ecosystems. Findings from a survey of multiple actors' perceptions in these areas are presented. Findings show that most ecosystems reside in areas with multiple innovative industries, that this has a slight positive influence on the development of this sector, and that over time these entrepreneurial ecosystems are becoming more directed as opposed to growing spontaneously.

Keywords: entrepreneurship ecosystems; development; Central Europe.

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Biographical notes: David R. Williams is a former senior healthcare executive and began his career in academia in 2003. His research interests lie in strategic management and entrepreneurship in healthcare organisations with a special interest in biopharmaceutical IPOs and regions. He is a Fellow in the American College of Health Care Executives and a Fulbright Scholar alumnus.

1 Introduction

It has been noted that the performance of firms and industries is related to space and place (Maskell and Malmberg, 1999). This is particularly true for those associated with innovation (Landabaso, 1997; Howells, 2005). In more recent years, the innovation literature has widened its scope from addressing areas that examine a firm's competitiveness to becoming the centre piece of a socio-economic development model for cities and regions (Rabelo and Bemus, 2015). An emerging literature that describes this phenomenon is the ecosystem literature. The ecosystem construct is a way of viewing various actor interdependencies and has gained prominence among both scholars and practitioners (Adner and Kapoor, 2010). The ecosystem literature includes the business ecosystem, knowledge ecosystem, innovation ecosystem, and entrepreneurial ecosystem

(EE) literatures. It has been noted that at times researchers and practitioners alike intermingle the concepts in an indistinguishable manner given their relatedness (Oh et al., 2016; Thomas and Autio, 2019). The present study borrows from these streams to examine various actors' perspectives on the development of the biopharmaceutical sector in select Central European EEs. Specifically, the study is interested in the perceived type and diversity of innovation that exists in each environment and how these environments developed over time.

The biopharmaceutical sector is an appropriate setting to study innovation and entrepreneurship, as it is a sector dominated by small growth-oriented firms, with extant research suggesting that these firms' external relationships play a central role in sector development (Xia and Roper, 2016). The European Union (EU) has included the biopharmaceutical sector as one of the sectors worthy of smart specialised development and support due to its perceived growth potential and high average annual wage (Vezzani et al., 2017). In addition to established firms, it is a sector that is energised by innovators in academia, incubators, and virtual companies (Robinson, 2020), as such it has important implications for theory and practice (Lim et al., 2006).

The present paper examines the biopharmaceutical sector in multiple EEs in Austria, Germany, Italy, and Switzerland. These areas are chosen as they are in proximity to one another with each having experience with this sector to varying degrees. Additionally, three of the four countries are members of the EU with its above-mentioned stated goals, with Switzerland and these EU economies overall also being in stages that are innovation-driven (Liñán and Fernandez-Serrano, 2014). Furthermore, the study addresses questions surrounding sectors and EEs related to industry types, influences, and development over time which are under-represented in the literature (Malecki, 2018; Cavallo et al., 2019).

2 Literature review

Moore (1993) was among the first to bring an ecological view via ecosystems to the business sector. He saw firms co-evolving in a coopetition manner around new innovations. He called the environment around these relationships a business ecosystem. Clarysse et al. (2014) observe that it is the competition between ecosystems, not individual firms, that brings about the subsequent rounds of innovation in an ecosystem. They (Clarysse et al., 2014) examine knowledge ecosystems – ecosystems built around academia. Clarysse et al. (2014) observe that business ecosystems bring the customer or demand side to the equation, whereas knowledge ecosystems do not. They note two other differences when comparing a business ecosystem to a knowledge ecosystem:

1 the connectivity of the players is a value network that may be globally dispersed compared with geographically clustered

2 the key player is a large corporation compared with a university or research organisation (Clarysse et al., 2014).

Another ecosystem stream, the innovation ecosystem literature, seeks to combine the commercial side of this literature (e.g., business ecosystems) with the knowledge generating side (e.g., knowledge ecosystem) (Oh et al., 2016; Xu et al., 2018). Knowledge-based technological innovations (such as biopharmaceutical products) come

from dynamic ecosystems that include not only firms, universities, and research organisations, but also government agencies and other actors described by those studying innovation systems (Frenkel and Maital, 2014). Smorodinskaya et al. (2017, p.5251) observe "the term 'innovation ecosystem' symbolizes the newly emerging, network mode of arranging business activity and economic governance, which enables companies and territories to master innovation-led growth and benefit from rapid technological changes."

An important aspect of an innovation ecosystem is that the knowledge ecosystem in part is funded (via taxes, grants, and other means) by the business ecosystem. In this regard, an innovation ecosystem is deemed to be healthy (and sustainable) when the resources invested in the knowledge ecosystem is replenished by the innovation profit accrued in the business ecosystem (Jackson, 2011).

A premise of the innovation ecosystem literature is that new knowledge creation and innovations do not occur in isolation. However, this literature stream remains lacking in theoretical development, and has often been used as a useful metaphor in a 'fuzzy-logic' manner (Oh et al., 2016). In practice, the term innovation ecosystem can refer to local hubs or regional clusters, networks, or technology platforms (Oksanen and Hautamäki, 2015). In this respect, an innovation ecosystem as applied in the literature is a hybrid of varying networks or systems (Durst and Poutanen, 2013).

For some time, innovation also has been linked with the concept of entrepreneurship (e.g., Schumpeter, 1934; Drucker, 1985). Given this, it is not unexpected that within the ecosystem literature, a more recent stream would emerge – that of the entrepreneurship ecosystem. From a scholarly perspective, entrepreneurship can be defined as the "examination of how, by whom, and with what effects opportunities to create future goods and services are discovered, evaluated, and exploited" [Shane and Venkataraman, (2000), p.18]. The EE literature has followed a path in scholarly work similar to the early entrepreneurship literature in that it has mainly focused on individuals (Stam, 2015) and new venture or firm creation. For example, Feld (2012) examined start-up communities in Boulder Colorado. Mack and Mayer (2016, p.2131) performed a case study on the 'lower-tier' EE of Phoenix Arizona. Breznitz and Zhang (2019) studied start-ups founded by student entrepreneurs associated with university accelerators.

Isenberg (2014) notes, however, that there is no one specific actor, not even the entrepreneur, that 'drives' the entrepreneurship ecosystem – it is entrepreneurship that 'drives' it. Therefore, an EE can be defined as a "set of interdependent actors and factors coordinated in such a way that they enable productive entrepreneurship within a particular territory" (Stam and Spigel, 2017). This differs from most of the focus of innovation ecosystems and business ecosystems which usually centre on a lead firm or technology platform. Similarly, it also differs from an innovation ecosystem in that in an EE there is no ecosystem value offering targeted at a specified audience (Thomas and Autio, 2019). In this regard, its focus is on value creation in the aggregate (Acs et al., 2017). However, it also differs from other literature streams, such as the systems of innovation literature (e.g., Cooke, 2008), where active policy making is a direct intention of many scholars and actors. Indeed, in an entrepreneurship ecosystem value for the actors and the system as a whole is most added when the system is mainly independent of central control; the system is as Isenberg (2016, p.565) notes relatively 'self-organising and self-sustaining'

The EE literature is relatively new (Alvedalen and Boschma, 2017; Stam and van de Ven, 2019). Like the business and innovation ecosystem literatures its bounds and theoretical underpinnings remain yet unknown (Stam, 2015; Acs et al., 2017). The extant literature, however, suggests the heterogeneous nature of EE, with different ecosystems being influenced by different actors. Yet, we know little about the differences of these actors' roles and influence. Given this, Acs et al. (2017) asks the question of whether these actors and institutions are all equally important or are some more important than others. Similarly, in a review paper Cavallo et al. (2019, p.1312) states "[s]cholars should advance the current understanding of how to create an EE, what makes it grow and, ultimately, what leads to a sustainable EE." Malecki (2018) observes that we do not know about the industrial type, scope or focus of EEs. Alvedalen and Boschma (2017) note that we know little about how an EE changes or evolves over time.

Considering the above outstanding questions, the present paper seeks to advance our knowledge on EEs. Stam and van de Ven (2019) note that the appropriate level of analysis could be a city, region, nation, technology, or sector, with Thomas and Autio (2019, p.21) noting that EEs are 'predominantly a regional phenomenon'. The present study takes an ambidextrous manner of analysis by utilising perceptions of multiple types of actors in a given sector – the biopharmaceutical sector—in select EEs in Central Europe. The study chose regions in Central Europe that have themselves chosen to pursue entrepreneurial growth in this sector as noted by their organised sectoral and regional trade associations. The study seeks to describe via survey responses many of the above noted questions.

3 Methods

After a review of both the academic literature and trade press, and communications with select actors in this sector, an electronic survey was sent to 601 actors involved with the biopharmaceutical sector in the Central European regions surrounding the cities of Basel, Graz, Innsbruck, Lausanne, Milan, Munich, Rome, Salzburg, Vienna, and Zurich. These actors included those who worked in academia, biopharmaceutical firms, biotechnology firms, consulting firms, contract manufacturing organisations, contract research organisations, financial organisations (venture capital and non-venture capital organisations), government agencies, hospitals, incubators and accelerators, industry trade associations, pharmaceutical firms, regional and national development agencies, and suppliers. The survey was given (with follow-up requests) between the dates of 15 April and 30 September 2020. It should be noted that this was during the COVID-19 pandemic, a particularly industrious time for these actors. One hundred two individuals started the survey with respondents at times skipping questions. The names and e-mail addresses of the actors were obtained via an Internet search, relying heavily upon contact lists provided within regional and national industry trade associations' websites. Multiple industry trade associations and other individuals posted information about the survey and/or otherwise forwarded the survey to various actors of the above-mentioned institutions and groups. Additionally, actors in ecosystems not solicited provided responses, and these responses are included herein. For comparative purposes, results are shown in the aggregate, and then broken down by region, country, and respondents' employer type. With respect to country, the survey means aggregated results for the regions surveyed within a particular country and not that these results reflect the country

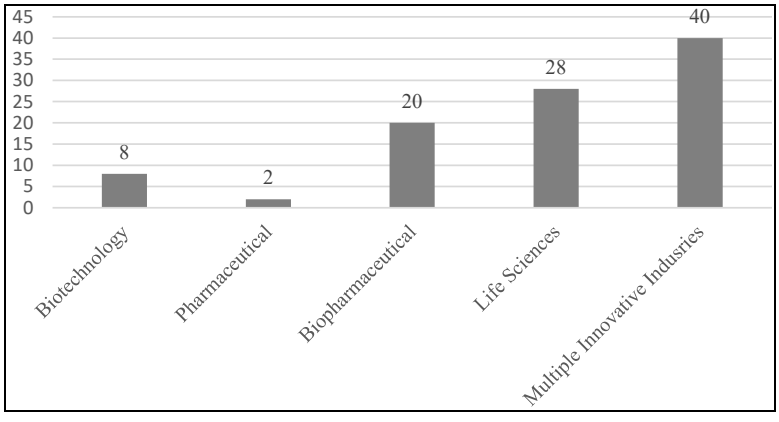
in its entirety. The e-mail recipients were given the option of taking the survey in either the English, German or Italian language, with several of the follow-up e-mails themselves sent in the actors' native languages. Participants received anonymous summary results at the survey's completion. The author communicated with several actors before, during, and after the survey to discuss the survey's purpose, questions, and results.

4 Results

4.1 Type of EE

Actors were asked to classify their ecosystem as being primarily either a biotechnology, pharmaceutical, biopharmaceutical (i.e., both biotechnology and pharmaceutical), life sciences (i.e., a mix of biopharmaceutical, medical devices, eHealth, etc.) or multiple innovation industry ecosystem (i.e., life sciences, information technologies, nanotechnology, etc.). Figure 1 shows their responses. Ninety-eight individuals responded, with nearly 41% responding that their EE was a multiple innovation industry EE.

Figure 1 Type of EE



Note: N = 98.

Table 1 shows the percentage of respondents by type of ecosystem by region and country. By country, it is not meant to represent the country as a whole, but rather, the aggregated EEs that are under study within those countries based on the actors' perceptions. The previous statement related to country is true for all tables going forward. The first interesting item to note is that to some degree there is variation with respect to perspectives of type of ecosystem. Here, it may be best to describe the ecosystem based on the mode of responses for those areas where there are multiple responses (and ignoring those with a single response). Given this, one can see that for EEs with multiple respondents, with the exception of Munich, all EEs are classified as either life sciences or multiple innovation industry ecosystems. If one were to extrapolate from the ecosystem literature, one could say that there are nested ecosystems within the EEs. This is to say that in a particular EE, say Zurich, there may be a small start-up firm with a handful of

network relations (i.e., an innovation ecosystem) with one of those relations being a larger established firm with a different (larger) set of network relations (i.e., its own innovation ecosystem of which the small firm is a part). These two innovation ecosystems may reside and tangentially engage other actors in a region with multiple innovative industries and ecosystems, with networks extending, perhaps, to a global reach. In this regard, a multi-innovative industry EE may portray a type of multi-modal meta-system.

Secondly, one can see that from the perspectives of the respondents that the EEs under study in Austria, Germany, and Italy are collectively viewed as being more of a multiple innovative industry EEs whereas, Switzerland is viewed as more of a life science EE based on the respondents in Basel and Lausanne.

Table 1 Type of EE by region and country

	Biotechnology	*Pharmaceutical*	*Biopharmaceutical*	*Life sciences*	*Multiple innovative industries*
Basel (13)	7.7	0	38.5	46.2	7.7
Dortmund (1)	0	0	0	0	100
Graz (8)	0	0	0	62.5	37.5
Habach (1)	0	0	0	100	0
Innsbruck (7)	0	14.3	28.6	28.6	28.6
Lausanne (8)	0	0	0	62.5	37.5
Milan (7)	14.3	0	14.3	0	71.4
Munich (10)	50	0	10	0	40
Regensburg (1)	0	0	0	0	100
Rhein-Neckar (1)	0	100	0	0	100
Rome (1)	0	0	100	0	0
Salzburg (2)	0	0	0	50	50
Solothurn (1)	0	0	0	100	0
Valais (1)	0	0	0	100	0
Vienna (22)	0	0	40.9	9.1	50
Wurzburg (1)	0	0	0	100	0
Zurich (13)	7.7	0	7.7	23.1	61.5
Austria (39)	0	2.6	28.2	25.6	43.6
Germany (15)	33.3	6.7	6.7	13.3	40
Italy (8)	12.5	0	25	0	62.5
Switzerland (36)	5.6	0	16.7	44.4	33.3

Notes: N = 98; numbers in parentheses represent number of respondents.

4.2 Diversity of innovative industries

Figure 2 shows the collective diversity of innovative industries for all EEs. Fifty-four (or 56%) perceived their EE to be somewhat diversified (i.e., from slightly diversified to broadly diversified) with respect to innovation activity compared to other EEs' diversity

of innovative industries of which the actors were familiar. This is congruent with the findings from Figure 1.

Table 2 Diversity of innovative industries by region, country, and employer type

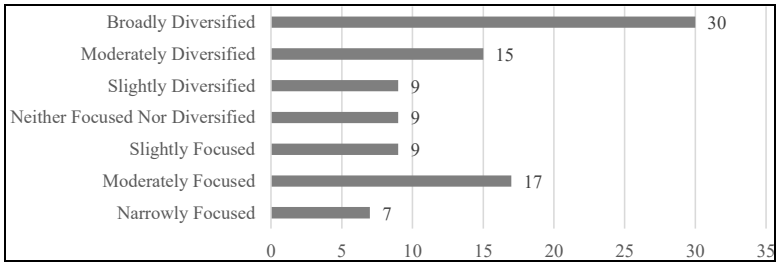
	Mean
Basel (13)	3.5
Dortmund (1)	6.0
Graz (8)	4.1
Habach (1)	7.0
Innsbruck (7)	5.0
Lausanne (8)	6.1
Milan (6)	2.7
Munich (10)	5.0
Regensburg (1)	4.0
Rhein-Neckar (1)	2.0
Rome (1)	1.0
Salzburg (2)	4.5
Solothurn (1)	2.0
Valais (1)	7.0
Vienna (22)	5.2
Wurzburg (1)	7.0
Zurich (12)	5.1
Austria (39)	4.9
Germany (15)	5.4
Italy (7)	2.4
Switzerland (35)	4.7
Academia (16)	5.1
Biotech firms (21)	5.2
Biopharma firms (8)	4.6
Pharma firms (2)	1.5
CRO (8)	4.2
CMO (3)	6.7
Suppliers (2)	2.0
Consulting (6)	3.8
Industry trade assoc. (4)	4.3
Government assoc. or agency (6)	6.2
Other (20)	4.0

Notes: N = 96; numbers in parentheses represent number of respondents.

Table 2 shows the mean perceptions of diversity of innovative industries by region, country, and employer type (1 = totally focused; 4 = neither focused nor diversified; 7 = totally diversified). Here, one can see that for EEs with multiple responses that respondents from Basel and Milan perceive these EEs to be more focused than diversified

compared with the other EEs. Within Switzerland, Basel and Lausanne both consider themselves to be life science EEs, with Lausanne respondents viewing this EE (within the life sciences) as being much more diverse than Basel. This is to say that even within a sector (e.g., life sciences) and proximate EEs, there is some heterogeneity with respect to diversity of industries.

Figure 2 Diversity of innovative industries

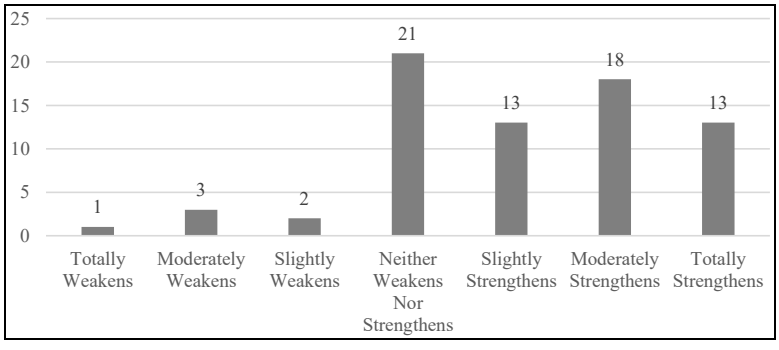


Note: N = 96.

4.3 Effect of other innovative industries on sector

Next, it might be helpful to know the effect of having other innovative industries within one's EE would have on the biopharmaceutical sector. Figure 3 illustrates the respondents' perceptions. Seventy-one individuals responded with nearly 62% perceiving a positive effect to some degree on the biopharmaceutical sector in the EE. Only about 8.5% of the respondents perceived a negative effect, with almost 30% perceiving neither a positive nor negative effect.

Figure 3 Effect of other innovative industries



Note: N = 71.

Table 3 shows the percentages and mean perceived effect of other non-biopharmaceutical innovative industries within the EE on the biopharmaceutical sector. Interestingly, on average, the CMOs and CROs perceived that having other innovative industries within the EE weakened this sector, with industry trade and government associations perceiving that other innovative industries strengthened this sector. Of note, the aggregated EEs in Switzerland (which considers itself more of a life science EE, per Table 1) views other innovative industries as strengthening the sector the most on average. Lausanne, which

according to Table 2 perceives itself as more diverse than Basel also views other innovative industries in a more favourable light.

Table 3 Effect of other innovative industries by region, country, and employer type

	Totally weakens	*Moderately weakens*	*Slightly weakens*	*Neither weakens nor strengthens*	*Slightly strengthens*	*Moderately strengthens*	*Totally strengthens*	*Mean*
Basel (11)	9.1	9.1	0.0	9.1	18.2	36.4	18.2	5.0
Dortmund (1)	0.0	0.0	0.0	0.0	100.0	0.0	0.0	5.0
Graz (5)	0.0	40.0	0.0	20.0	0.0	0.0	40.0	4.4
Habach (1)	0.0	0.0	0.0	100.0	0.0	0.0	0.0	4.0
Innsbruck (5)	0.0	0.0	0.0	40.0	20.0	20.0	20.0	5.2
Lausanne (7)	0.0	0.0	0.0	14.3	14.3	0.0	71.4	6.3
Milan (4)	0.0	0.0	0.0	0.0	75.0	25.0	0.0	5.3
Munich (7)	0.0	0.0	14.3	57.1	0.0	28.6	0.0	4.4
Rome (1)	0.0	0.0	0.0	0.0	0.0	100.0	0.0	6.0
Salzburg (1)	0.0	0.0	0.0	0.0	0.0	100.0	0.0	6.0
Solothurn (1)	0.0	0.0	0.0	0.0	0.0	100.0	0.0	6.0
Valais (1)	0.0	0.0	0.0	100.0	0.0	0.0	0.0	4.0
Vienna (17)	0.0	0.0	5.9	47.1	17.6	17.6	11.8	4.8
Wurzburg (1)	0.0	0.0	0.0	100.0	0.0	0.0	0.0	4.0
Zurich (8)	0.0	0.0	0.0	12.5	25.0	50.0	12.5	5.3
Austria (28)	0.0	7.1	3.6	39.3	14.3	17.9	17.9	4.9
Germany (10)	0.0	0.0	10.0	60.0	10.0	20.0	0.0	4.4
Italy (5)	0.0	0.0	0.0	0.0	60.0	40.0	0.0	5.4
Switzerland (28)	3.6	3.5	0.0	14.3	17.9	32.1	28.6	5.5
Academia (12)	0.0	0.0	0.0	25.0	25.0	16.7	33.3	5.6
Biotech (17)	0.0	0.0	5.9	29.4	23.5	29.4	11.8	5.1
Biopharma (5)	0.0	0.0	0.0	16.7	50.0	0.0	33.3	4.8
Pharma firms (2)	0.0	0.0	0.0	0.0	0.0	100.0	0.0	6.0
CRO (7)	0.0	28.6	0.0	57.1	28.6	0.0	0.0	3.6
CMO (2)	0.0	50.0	0.0	50.0	0.0	0.0	0.0	3.0
Suppliers (2)	0.0	0.0	0.0	50.0	0.0	50.0	0.0	5.0
Consulting (3)	0.0	0.0	33.3	33.3	0.0	33.3	0.0	4.3
Ind. trade ass. (3)	0.0	0.0	0.0	0.0	33.3	0.0	66.8	6.3
Government assoc. (4)	0.0	0.0	0.0	0.0	0.0	25.0	75.0	6.8
Other (14)	7.1	14.3	0.0	21.4	21.4	0.0	35.7	5.1

Note: N = 71; numbers in parentheses represent number of respondents.

Table 4 Reasons for others' effect on the sector by region, country and employer type

	Access to capital	*Access to facilities and/or land*	*Access to qualified personnel*	*Buyers and suppliers*	*Regional infrastructure*	*Taxes and/or government regulations*
Basel (10)	4.5	3.6	4.5	4.4	5.1	5
Dortmund (1)	3	5	5	3	4	3
Graz (5)	5	5	5.8	4	5.2	4.6
Habach (1)	4	4	4	4	4	4
Innsbruck (5)	3.6	3.8	3.8	4.4	4.6	4.2
Lausanne (7)	5.1	4.9	5.7	5	6.1	4.9
Milan (4)	3.5	4	4.3	4.8	4.3	3.5
Munich (7)	4.1	3.3	3.6	3.7	4.3	3.4
Rome (1)	4	4	6	6	1	1
Salzburg (1)	4	4	4	4	4	4
Solothurn (1)	6	5	4	5	6	4
Valais (1)	4	4	4	4	4	4
Vienna (16)	3.9	4.2	4.9	4.1	4.3	3.8
Wurzburg (1)	4	4	4	4	4	4
Zurich (8)	4.9	5	4.6	4.6	5.3	5
Austria (27)	4.1	4.3	4.9	4.1	4.5	4
Germany (10)	3.6	3.9	3.5	4.3	4	3.5
Italy (5)	3.6	4	4.6	5	4.3	3.5
Switzerland (27)	4.7	4.4	4.9	4.6	5.4	5
Academia (11)	4	4.5	5.2	4.5	4.9	4.5
Biotech firms (16)	4.4	4	4.4	4.5	4.8	4.3
Biopharma firms (6)	4.5	4.3	4	4.3	5	4.5
Pharma firms (1)	4	4	5	4	5	4
CRO (7)	4.7	4.3	4.3	4	4.6	4.1
CMO (2)	3.5	2.5	5	5.5	5	5
Suppliers (2)	4.5	3.5	3.5	4.5	4.5	4.5
Consulting (4)	2.8	3.5	4	3.5	3.8	3.3
Ind. trade assoc. (3)	3.7	3.3	4	3.7	4.7	4.3
Government agency (3)	4.7	4.3	6	4.7	5.3	3.7
Other (14)	4.7	4.9	5.1	4.4	5.1	4.5

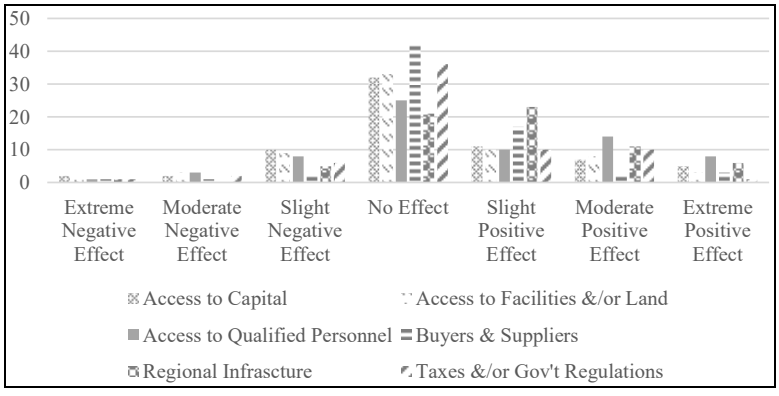
Note: N = 69; numbers in parentheses represent number of respondents.

4.4 Reasons for others' effect on sector

Related to the effect of other non-biopharmaceutical innovative industries on the sector, individuals were asked why this was so. Figure 4 illustrates this with 1 referring to an extreme negative effect and 7 referring to an extreme positive effect, with 4 having

neither a negative nor positive effect. The overall means are as follows: access to capital 4.3; access to facilities and/or land 4.2; access to qualified personnel 4.7; access to buyers and suppliers 4.3; regional infrastructure 4.8; and taxes and/or government regulations 4.3. Thus, having other innovative industries is perceived to affect most positively the regional infrastructure and access to qualified personnel. Yet, even so, these findings show that the 'no effect' answer had the single most responses for all categories except for regional infrastructure.

Figure 4 Reasons for others' effect on sector



Note: N = 69.

Table 4 shows these reasons for other innovative industries effect by region, country, and employer type. Of note, the aggregated EEs in Germany perceive other innovative industries to have a slight negative effect in 4 of the 6 areas (i.e., access to capital, facilities, qualified personnel, and taxes/government regulations). This despite Table 3 results for the aggregated German EEs seeing other innovative industries overall in a positive manner. In Italy, Milan perceived other innovative industries as having a slightly negative effect on access to capital and taxes and government regulations.

4.5 Development over time

Within the literature there is discussion as to the nature of how change occurs within an ecosystem – whether this change is evolutionary or by design. As noted previously, much of innovation ecosystems (e.g., Ritala and Almpanopoulou, 2017; Granstrand and Holgersson, 2020) literature notes the evolutionary nature of these relationships. However, writing broadly about ecosystems from a strategic management perspective, Jacobides et al. (2018, p.2263) observe: "[e]cosystems, of course, do not just 'emerge' spontaneously. They are at least, in part, the result of deliberate experimentation and engineering from different parties." Isenberg (2010) suggest that EEs should grow organically. Yet, we know little as to how EEs have developed over time (Alvedalen and Boschma, 2017). To address this issue, respondents were asked whether the region developed spontaneously/organically by firms focusing on their own efforts compared with the region being developed via directed/concerted efforts of multiple actors (i.e., firms, government agencies, industry trade associations, etc.) seeking to promote the development of the sector in the region.

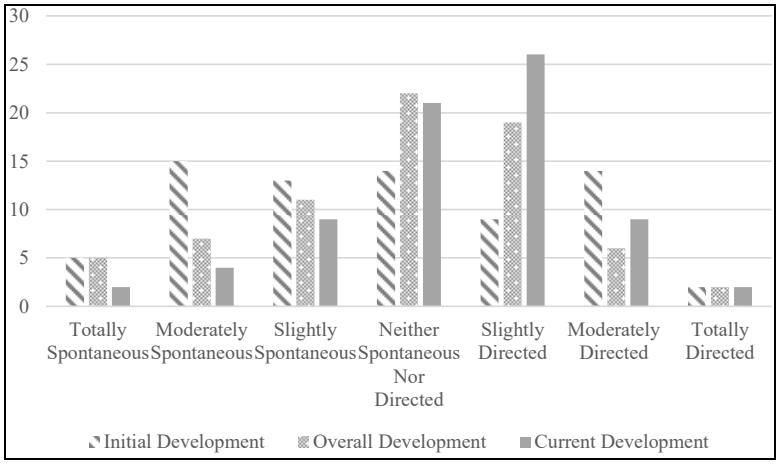
Table 5 Development over time by region, country and employer type

	Initial development	*Current development*	*Overall, historical development*
Basel (11)	3.1	4.2	3.7
Dortmund (1)	5.0	5.0	4.0
Graz (5)	3.0	4.0	3.4
Habach (1)	6.0	5.0	6.0
Innsbruck (5)	3.2	3.6	3.2
Lausanne (7)	4.0	4.9	4.6
Milan (4)	3.5	4.0	4.0
Munich (8)	5.5	4.3	4.9
Rome (1)	6.0	1.0	3.0
Salzburg (1)	7.0	6.0	6.0
Solothurn (1)	3.0	4.0	3.0
Valais (1)	1.0	2.0	2.0
Vienna (18)	3.9	4.8	4.2
Wurzburg (1)	4.0	4.0	5.0
Zurich (8)	2.4	4.3	2.6
Austria (29)	3.7	4.5	3.9
Germany (11)	5.4	4.4	4.9
Italy (5)	4.0	4.0	3.8
Switzerland (28)	3.2	4.3	3.5
Academia (12)	3.6	4.6	3.6
Biotech firms (17)	3.2	4.4	4.1
Biopharma firms (6)	4.2	4.5	3.5
Pharma firms (2)	5.5	4.0	4.5
CRO (8)	4.0	4.5	4.5
CMO (2)	6.0	4.5	4.0
Suppliers (2)	3.5	5.0	4.0
Consulting (4)	3.3	3.8	3.3
Industry trade assoc. (3)	3.0	3.0	3.0
Government assoc. (4)	4.0	3.8	4.3
Other (13)	4.3	4.6	4.2

Note: N = 73.

Figure 5 illustrates the respondents' overall perceptions. The question used a continuous scale with 1 equalling totally spontaneous/organic; 4 equalling neither spontaneous nor directed; and 7 equalling totally directed. The overall mean for all regions related to the initial development of all EEs is 3.8. The overall mean for the overall, historical development of all EEs is 4.0; whereas the overall mean for the current development of all EEs is 4.4. This may suggest that overall, the EEs' development is becoming more directed by the multiple actors over time.

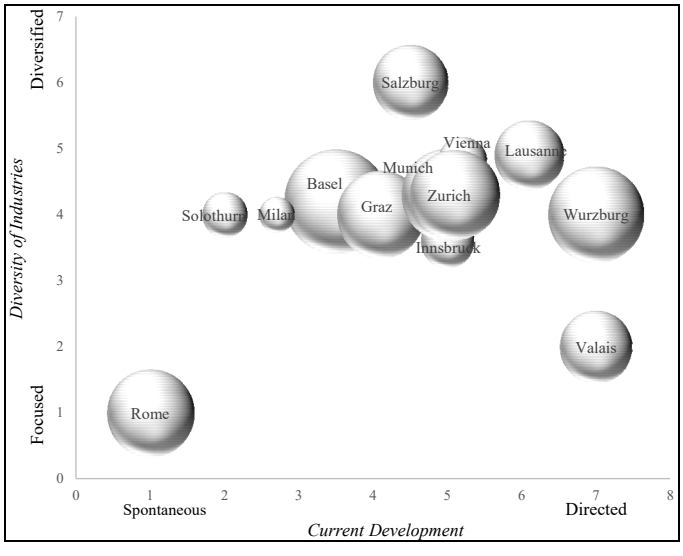
Figure 5 Development over time



Note: N = 73.

Malerba (2002) observes that for evolutionary theorists, the environment and conditions may vary drastically. Table 5 shows the mean responses for the development over time by region, country, and employer type. Similar to Figure 5, with the exception of Munich, the EEs with multiple responses all show a movement toward a more directed approach. Both Austria and Switzerland are perceived as becoming more directed over time. However, German EEs collectively which were viewed as initially the most directed are currently seen as becoming less directed. It is interesting that academia and the firms currently see the EEs as being more directed; yet the trade associations and government agencies or associations see the EEs' development as more spontaneous relatively speaking.

Figure 6 Diversity of industries and current development



Next, it may be useful to simultaneously examine the diversity of industries within the EE with the current development of the sector (i.e., combining Tables 2 and 5 data). Figure 6 illustrates this. The size of the bubbles represents a three-year (2016–2018) mean of the regions' per capita gross domestic product (GDP) growth rate. This is a very loose proxy for Isenberg's (2014, 2016) view that entrepreneurial growth should be the focus of an EE. All GDP data are the latest data available from the Organisation for Economic Co-operation and Development (OECD), except that the 2018 data for Swiss regions were not available and therefore the study used data provided by the Swiss Federal Statistical Office for 2018 related to the Swiss regions. Focusing only on areas with multiple responses, one can see that Milan and Basel are the only two areas whose current development are of a more spontaneous nature (with different results related to per capita GDP growth). Interestingly, of those areas with multiple responses, Lausanne is the most diverse and directed, yet its three-year GDP per capita growth rate is less than its Swiss counterparts.

5 Discussion

The present paper begins to address gaps related to the EE's types, influences, and development over time which are lacking in the literature (Alvedalen and Boschma, 2017; Malecki, 2018; Cavallo et al., 2019). Results from a comparative study of actors' perceptions show that there is heterogeneity among the EEs in this sector. Many of the EE actors perceived themselves to reside in EEs that had multiple innovative industries, with a slight majority of actors perceiving their EE's innovative activity to be diverse compared with other EEs in which they were familiar. The overwhelming majority of actors viewed this to be a positive outcome, with this most positively affecting the region's infrastructure and access to quality personnel. Actors also perceived their sector's development as changing over time – from initially developing somewhat organically to developing in a slightly more directed manner.

With respect to type of industry (and looking at the mode of those with multiple responses), only one EE (e.g., Munich) viewed itself as primarily a single (biotechnology) industry EE (with some respondents from Munich offering a different view). Basel, Lausanne, and Graz respondents primarily considered their EEs as life science EEs. Milan, Vienna, and Zurich respondents primarily viewed their EEs as multiple innovative industries EEs. This heterogeneity suggests a need to examine each EE separately with respect to policy implications (Isenberg, 2016; Horváth and Rabetino, 2019), as each EE and type of EE may have different resources, capabilities, and knowledge bases (Carlsson et al., 2002) and respond differently based upon their history, cognition, culture, and other factors (Nelson, 1993; Malerba, 2004; Thomas and Autio, 2019).

The study's results with respect to diversity of innovative industries and their effect on the EE is noteworthy. Within the different types (e.g., life sciences, multi-innovative industries), the study finds differences of perspective with regard to both the diversity of industries and its effects. For example, respondents view Basel, Graz, and Lausanne as life sciences EEs, with Basel (3.5) respondents perceiving it as being more focused, Graz (4.1) barely diverse, and Lausanne (6.1) much more diverse. All three see diversity of industries as strengthening the EE, but at different levels (with Lausanne the most) and for different reasons (i.e., the two Swiss EEs see the effect on infrastructure as the top

reason, whereas Graz sees access to qualified personnel). Similar results are found when one examines the muti-innovative industry EEs of Milan, Vienna, and Zurich – a diversity of views on the focused/diversity continuum with diversity of industries viewed as positively affecting the EEs by all three but with a difference in the ranking of reasons. Perhaps most interestingly, government agencies/associations were the top employer type in its perception that other innovative industries strengthen the EE; yet it also was among the top employer type for the negative effects of taxes and/or government regulations. Given the above, entrepreneurs, employers, and policymakers may wish to think carefully about aligning their locations and/or policies with the changing nature of these EEs. As Isenberg (2010) warns, EEs may wish to be sector neutral. It would be useful to know how specific other innovative industries (e.g., electronics, telecommunications) affected the EEs.

Given the sample, it may be argued that with respect to the findings related to the development over time that it depends upon one's perspective as to whether this is a positive or negative phenomenon. For example, from a systems of innovation perspective (which tends to have a more active policy orientation), it could be argued that these areas that are moving more toward being directed is a positive outcome – that policymakers are focusing on areas as they present themselves. If one were to pursue Isenberg's (2011, p.4) EE reasoning, however, then moving away from an organic development could be seen as negatively affecting the long-term development of the EE, as it 'dulls the entrepreneurial spirit'. A third explanation may be that some EEs and sectors may require regional support while others do not (Horváth and Rabetino, 2019). Milan and Basel are the two areas with multiple responses that are somewhat seen as developing spontaneously compared with the other areas. Yet, in terms of the limited proxy used for entrepreneurial productivity (per capita GDP growth rates) they have opposite results compared with each other. More research is needed in this area to determine the effect of type of development on entrepreneurial productivity, especially over time.

The study is not without limitations. First, it relied upon perceptions of the actors and not objective empirical evidence, such as examining the number and type of different innovative firms and industries within the EEs. Second, the study is limited by the number of respondents, with some of the (unsolicited) EEs only having one response, and thus it uses descriptive statistics of the perceptions which limits the ability to test hypotheses. Third, it used per capita GDP growth rate as a proxy for entrepreneurial productivity without taking into consideration the effects of other industries on this growth. Fourth, it relied upon perceptions from only one sector (e.g., biopharmaceutical), with it being acknowledged that actors from other sectors or industries might, perhaps, have different perspectives.

The study's reliance on perceptions of multiple actors is also a strength. Most studies examining actual EEs rely on case studies (e.g., Feld, 2012; Mack and Mayer, 2016) or secondary data (e.g., Stam, 2018). The present study presents results from a survey of multiple types of actors actively engaged in multiple EEs in the biopharmaceutical sector. It finds that most ecosystems reside in areas with multiple innovative industries, that this has a slight positive influence on the development of this sector (especially related to infrastructure and qualified personnel), and that over time these EEs are becoming more directed. The results should be of interest to scholars, policymakers, entrepreneurs, and others engaged in EE and biopharmaceutical development.

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