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Abstract

This paper develops a framework to understand new industrial path development in peripheral regions based on notions of 'bricolage' and 'institutional relatedness'. While the first stresses the agency of (heterogeneous) actors' resourcefulness and strategic improvisation co-shaping new industrial paths, the latter highlights the transposition of related institutional settings within regions to amplify (or to limit) the search space for new industries. These arguments are used in conjunction to explain the development of an unlikely biotechnology path in the Portuguese Centro region, analysed since its emergence and over a period of more than ten years.

Keywords

Path creation, Bricolage, Institutional Relatedness, Biotechnology, Emergence, Peripheral regions

JEL

R11, O3, O43, D02

1. Introduction

Over the last decades, several studies have shown the difficulties to steer new, knowledge-intensive industrial change in peripheral regions (e.g. Tödtling and Trippl, 2005, Pike *et al.*, 2010, Vale, 2011, Dawley *et al.*, 2015). Notably, evolutionary economic geography (EEG) approaches stressed that new economic activity in such regions have limited chances beyond 'path extension' and can easily face 'path exhaustion' (Isaksen and Trippl, 2014). As they are often institutionally thin and lack technology-related industries that can branch out to one another (Boschma, 2009), pursuing 'high-road', knowledge-intensive strategies has many caveats and has led to countless cases of policy failure (e.g. Rodriguez-Pose, 2013).

The emergence of new, unrelated industrial paths and economic specializations has been shown to be an exception, notably in peripheral regions (Xiao et al., 2018). Yet, despite this general picture, evidence also shows that every now and then new industrial paths do emerge and endure in such places, contributing to economic diversification and talent retention (e.g. Nuur and Laestadius 2010, Rodríguez-Pose and Fitjar 2013, Dawley, 2014). Hence, economic geography and regional studies brought forward complementary frameworks to understand new path creation and 'unrelated diversification' (Boschma, 2017), notably in peripheral regions. This research stream highlights, among others, the generative role of external knowledge sources (e.g. Isaksen and Trippl, 2016; Vale and Carvalho, 2013); the role of state policy interventions and activism (MacKinnon *et al.*, 2009; Dawley *et al.*, 2015); endogenous knowledge accumulation in universities (Vallance, 2016); and the 'bricolage' of institutional entrepreneurs to align multiple resources and co-develop favourable institutional conditions (Boschma *et al.*, 2017; Sotarauta, 2016; Simmie, 2012).

This paper integrates and builds on insights from these literatures to explain processes of new path development in peripheral regions. We make two concrete contributions. First, we explore further the 'bricolage' hypothesis, which highlights actors' resourcefulness and strategic improvisation co-shaping emerging technological paths and new institutional

settings over time (Miner *et al.*, 2001; Garud and Karnøe, 2003). Bricolage and agency-driven explanations have been recently used in studies at the interface of economic geography and transition studies to explain the emergence of new industries beyond technology branching processes, but have essentially focused on 'green' and sustainability-related industrial niches (Binz *et al.* 2016) – here we intend to test the generalizability of this framework to other types of knowledge-intensive industries, namely in peripheral, institutionally-thin regions. Second, and in line with the call to expand the notion of relatedness beyond knowledge and skills (Content and Frenken, 2017), we build on a concept of 'institutional relatedness' to argue that, despite the lack of related technologies and skills, new industries can more easily emerge and develop in regions if they benefit from portfolios of related institutional settings associated with other (skill-unrelated) industries – such as knowledge transfer routines between university and companies, informal arrangements and relational ecologies –, thus bringing regional 'selection' environments more amenable for new industries. We thus suggest that one of the key roles of regional diversification agents and 'bricoleurs' is to transpose organizational forms and institutional practices not only across regions (Saxenian and Sabel, 2008) but also across industries within regions.

To explore these issues, the paper analyses the evolution of the biotechnology industry in the Portuguese Centro Region since its inception (early-2000s) and over a period of more than ten years. Biotechnology epitomizes the 'breakthrough', science-driven type of industry which several regions tried to emulate unsuccessfully, prospering in a selective group of places with robust endowments – e.g. strong research universities, established pharmaceutical firms (Cooke, 2001) – *and* favourable social and institutional environments – e.g. well-developed venture capital and knowledge transfer contexts (Casper, 2009). Because of this socio-institutional dimension, many studies have shown that regions with strong endowments failed to develop relevant biotechnology clusters over time (e.g. Powell *et al.*, 2012), but are relatively silent on why regions with modest endowments – i.e. limited technological capabilities, weak knowledge organizations and few interaction routines among actors – succeed. In this study, by building on the aforementioned frameworks, we provide an explanation for why a peripheral region, with modest endowments, succeeded in creating and maintaining a stream of new biotech ventures overtime, outperforming other

more likely candidates in the country, such as Lisbon or Porto. By doing so, it follows up on previous studies on Portuguese biotechnology, which focused essentially on emergence stages (Fontes, 2005; Vale and Carvalho, 2013) to understand regional variation as the industry unfolded in the country.

The paper is organised as follows. Section 2 reviews and elaborates on the notion of bricolage applied to industrial path creation in peripheral regions, and builds on a concept of institutional relatedness. Section 3 details the research setting, as well as the methods used, while Section 4 presents the empirics that illustrate the agents, resources and processes that enabled the development of an unlikely biotechnology path in Centro Region. Section 5 concludes and elaborates on how the elements of such a framework can add to more comprehensive explanations of new path creation and industrial diversification in peripheral regions.

2. Conceptual background

2.1 A renewed interest in path creation in the periphery

The policy and scholarly interest in industrial development in peripheral regions is hardly new. In fact, it dates from the 1950s – e.g. with the support to exogenously-driven 'growth poles' and branch plant relocations –, and went on through the last decades with different generations of firm subsidies, cluster policies, science park development, etc. (Pike *et al.* 2016). In most cases, the outcomes of these policies felt short of expectations. Newly supported industries rarely endured, often relocating or simply disappearing, leaving low socio-economic returns in regions (Massey *et al.*, 1992; Rodríguez-Pose and Fratesi, 2004).

Over the last decade, EEG proposed a Darwinism-inspired perspective to understand that phenomena. Based on notions of variety, selection, inheritance, retention and adaptation, it has been shown that firms and industries typically branch out to other activities to which they are technologically-related and share competences with (Neffke *et al.*, 2011; Boschma and Frenken, 2011). Therefore, regions tend to develop durable 'selection environments', such as pools of skills and industry-specific institutional settings that are appropriate to nurture some activities but hostile to others (Boschma, 2004). This makes it difficult for new skill-unrelated firms and industries to enter and stay in regions over time (Neffke *et*

al., 2014), especially in peripheral regions with thin institutional settings, fragile economic structures and limited industrial search spaces (Boschma, 2009).

In these regions, related diversification is the norm, with new growth paths emerging from the re-combination of previous (scarce) industrial competences (Xiao et al., 2018). Moreover, beyond skills and technological competences, peripheral regions are often associated with having adverse types of institutional settings – notably inward-looking and rent-seeking interactions among local actors in a few industries, favouring the formation of bounding social capital and overall closed groups that hamper the emergence of novelty in regions (e.g. Cortinovis et al., 2017). The textbook example of the previous is Southern Italy (Putnam, 1993), in which rent-seeking groups, the absence of social interactions among different types of knowledge communities and the dominance of homogeneous groups in industrial and policy spheres hampered knowledge circulation and the emergence of the proper institutional settings for new industry formation (Crescenzi et al., 2013).

Yet, in parallel to this constraining view on new path creation, and drawing on Martin (2010) and Martin and Sunley (2006), a stream of research has sought to understand the sources and mechanisms enabling industrial evolution and new path creation episodes that occasionally occur in peripheral regions, namely by moving beyond skills and firm-centric approaches towards more pluralistic explanations embracing policy activism, the access to exogenous resources and institutional change (e.g. MacKinnon *et al.*, 2009). For example, accessing and anchoring external knowledge – e.g. through scientists, branch companies, transnational entrepreneurs, etc. – has been highlighted as a fundamental source of new path development (e.g. Trippl *et al.*, 2017; Isaksen, 2014; Vale and Carvalho, 2013); beyond 'carrying' technical and market knowledge, these actors frequently bring in new organizational routines and institutional practices, which ultimately may contribute to regional institutional change (Saxenian and Sabel, 2008). Over time, ripple effects and heightened relations between new and old industries in the region and beyond contribute to change the regional 'selection' environment and anchor new industries (Isaksen and Trippl, 2016). In this context, state policy interventions and activism at various scales are also deemed pivotal, namely for attracting new actors, resources, implanting regulatory

frameworks and actively shaping the institutional environment for new industries (Dawley, 2014; Dawley *et al.*, 2015).

Also advancing previous EEG approaches, Vallance (2016) stresses that, in many occasions, universities were *per se* a central endogenous source of novelty and industrial change, even in the absence of technology-related industrial systems in place. Based on a complex adaptive systems framework, Vallance argues that the growth and accumulation of knowledge is in itself an important driver of regional (self-) transformation, which can ultimately spread out and lead to spin-offs, research collaborations and labour mobility into firms, in a co-evolutionary fashion. To be sure, these processes are not straightforward in peripheral regions – indigenous research may not be novel enough to support new paths, or there may be connectivity problems between universities and (nascent) industries, hampering co-evolution and new path development (Vallance, 2016; see also Feldman and Kogler, 2010). Hence a key challenge remains to unpack how connectivity and alignments between university's accumulated knowledge and nascent industries are achieved in regions with thin industrial-institutional contexts (Tödtling and Trippl, 2005).

2.2. Bricolage and the strategic alignments of multiple resources

An approach that helps integrating the previous insights – and shed light on the issue of connectivity and alignments – suggests that new regional path creation in resource-scarce regions may primarily rely on 'bricolage'-like innovation processes. The notion of bricolage – borrowed from innovation and organisation studies (Garud and Karnoe, 2003; Miner *et al.*, 2001) – was recently introduced in economic geography to better understand processes of unrelated diversification (Boschma *et al.*, 2017). In contrast to explanations based on regional knowledge endowments and firm´s capabilities, a notion of bricolage highlights the role of multiple, heterogeneous types of actors and their improvisations to align multiple resources and co-shape new relational and institutional environments (Binz *et al.*, 2016).

One of the most well-known illustrations on how bricolage has underpinned the emergence and consolidation of a new industry – described in Boschma *et al.* (2017) – has been provided by Garud and Karnoe (2003) comparing the development of the wind turbine

industry in the US and Denmark during the 1970s (see also Simmie. 2012), in which the latter ultimately outperformed the first. While the US wind turbine industry initially followed a breakthrough-type development process (drawing on the industrial absorption of high-tech endowments from leading scientific institutions), the central Jutland region in Denmark developed the industry based on bricolage: a step-wise process of trial-and-error and strategic collaboration among multiple actors (local producers, R&D institutes, owners-users, associations, policy-makers, etc.), aligning and connecting different types of (local and non-local) resources, which ultimately co-evolved and led to the emergence of a supportive institutional environment for the industry.

The concept of bricolage highlights that knowledge-technological capabilities are only one among other resources to be accessed and mobilized for new path development. Based on technological innovation system´s research, Binz *et al.* (2016) framed the development of a new water recycling industry in Beijing as a bricolage process requiring external *knowledge*, but also the active construction of *markets*, access to *finance* and *legitimacy*, involving several loosely coordinated actors such as endogenous and transnational firms, associations, users, R&D institutes, policy-makers, etc. Markets for new industries – at least national/regional markets – are often poorly developed, do not recognise or value new products, and niche segments have thus to be actively (co-) created by industry proponents and supported through subsidies, new regulatory frames, etc. Finance and specialized investors also absent, requiring the mobilization and networking among new industry proponents, funding agencies, ventures capitalists, policy-makers, among others. Finally, as there is often a mismatch between new industries and existing normative and cognitive frameworks, overall scepticism and incongruity between existing practices and new industry´s demands and expectations have to be overcome to enhance its legitimacy. Hence, new regional path creation through bricolage requires experimentation and active 'institutional work' (Boschma *et al.*, 2017, pp. 36).

Besides firm entrepreneurs, new (unrelated) regional path creation also involves institutional entrepreneurs, i.e. resourceful individuals or organizations with an interest in a new industry, which initiate and actively participate in building up new (deviant) institutional contexts, often taking up leadership roles in the process (e.g. Garud *et al.*,

2007; Battilana *et al.*, 2009; Sotarauta, 2016). Due to the paradoxical 'embedded agency' nature of institutional entrepreneurship (Garud *et al.*, 2007), research has also focused on the enabling conditions that drive actors to actually pursue such institutional work, namely filed-level conditions (e.g. economic crises, regulatory changes, technological discontinuities and opportunities) and actor´s interfacing positions within organizations and social networks. Building on this last point, Grillitsch (2017) argues that the transformative and resource-mobilization capacity of these actors rely on i) holding multiple positions, i.e. belonging to different social fields or organisational structures at a point in time (e.g. a university professor who is involved in a firm), ii) having positional mobility, i.e. moving across social fields and structures (e.g. a researcher who leaves the university to be involved in a firm) and/or iii) having social networks across different social structures (e.g. connections through personal ties). These contexts, alone or in combination, allow institutional entrepreneurs to connect and align resources across different social fields to co-shape new favourable institutional contexts for the industries they envision developing.

2.3. Institutional relatedness

The notion of bricolage highlights the relevance of multiple actors that strategically mobilize and iteratively co-align resources, ultimately leading to the formation of new regional institutional environments for nascent industries. Yet, there is a risk that by focusing too much on agency and actor´s mobilisation of (often external) resources, the role of previous regional institutional features is overlooked. This is problematic because although generally 'thin' (Tödtling and Trippl, 2005; Trippl *et al.*, 2017), peripheral regions are not institutionally empty. As stressed by Martin (2010), beyond just random accidents, previous economic, relational and institutional legacies of regions do play a role in explaining where new industrial paths emerge and how they get established over time (Storper and Walker, 1989; Storper *et al.*, 2015).

In order to better specify the role of institutions in new path development, Boschma and Capone (2015) show that unrelated diversification is more likely to occur in economies in which resources (e.g. labour, capital) can more easily switch across industries, and legal barriers to firm acquisition and new product development are lower (Boschma and Capone, 2015). Likewise, Menzel and Kammer (2017) suggest that when institutional constrains

associated with old industries are lower, resources are more easily transferred to new industries and firm entry patterns are higher. Although these studies focus at the country-level and measure largely static, higher-order institutions – thus overlooking informal, hard-to-measure regional and industry specific contexts – they hint that the transposition of resources across industries (including institutional practices, conventions and organizational arrangements) can underpin new path development processes, even if industries are skill- and technologically-unrelated.

In line with Frenken and Content (2017), an argument could thus be made to broaden the notion of relatedness beyond technology and skills (see also Tanner, 2014) and consider the role of 'institutional relatedness' as source of diversification and regional path development. As suggested by Frenken and Content (2017), regions are more likely to move into industries to which they are institutionally related, namely as actors can make use of previous arrangements and practices, and simultaneously face little resistance from incumbent industry´s actors and policies. This perspective resembles the notion of institutional relatedness as defined in management studies (Peng *et al.*, 2005), i.e. the 'degree of informal embeddedness with the dominant institutions in the environment that confer resources and legitimacy [to organisations]' (pp. 623). It posits that firms may conglomerate and move into product-unrelated industries if they can make use of non industry-specific competences, such as on how to acquire licences, how to source and finance technology, how to access and leverage relationships with policy organizations, etc. Peng *et al.* (2005) are primarily concerned with firms and their (national institutional) environment, but the argument can be extended to industries in their regional institutional environment as well.

The idea that existing relational and institutional settings are, in their own right, relevant resources that can be actively mobilized to support new (technology-unrelated) industries resembles the notion of 'shielding', developed in the field of sustainability transition studies (Smith and Raven, 2012). New industry proponents may protect or shield new activities from hostile selection environments by mobilising previously existing institutional settings – e.g. existing policies and funding sources, values, social networks, established knowledge transfer procedures – providing them with conditions to attract and

develop new knowledge, foster new social networks and enhance legitimacy (Verhees *et al.*, 2013). As many of these processes are socially dense and require multiple forms of physical and relational proximity, regions are often the locus in which these latent institutional settings are mobilized and reconfigured to support industry emergence (e.g. Coenen *et al.*, 2010; Carvalho *et al.*, 2012).

Specifying institutional relatedness requires an understanding of the ways through which previous institutional settings 'branch out' to provide the organizational and institutional backbone to nascent industries. For Padgett and Powell (2012), one key mechanism is transposition and refunctionality, i.e. 'the movement of a relational practice from one domain to another and its reuse for a different function or purpose' (pp. 12). Institutional and relational practices developed within a certain social field (e.g. an industry or activity) are purposefully borrowed and inserted in another social field (e.g. a nascent industry) and develop there further, eventually changing both fields in the process. This hints to the pivotal role of institutional entrepreneurs in the processes, namely when they are positioned at the interface of different social structures, thus with access to – and understanding of – different types of institutional and relational practices.

Drawing on the same argument, Storper *et al.* (2015) shows that the economic divergence between San Francisco and Los Angeles over the last decades is closely linked to the ways through which both regions managed to transpose and adapt institutional settings across activities and 'milieus', and much less to initial firm-level or regional knowledge endowments. For example, Storper *et al.* (2015) show that the interest on new technologies in Silicon Valley has not emerged from engineering communities alone, but from crosspollinations between engineering, hippie and localized alternative technology movements, resulting in new organizational practices and routines associated with openness and experimentation (see also Saxenian, 1994). Likewise, although Los Angeles was a first mover in biotechnology, with strong research institutes and the biggest firm in California (Amgen), it never created a strong industrial path in biotechnology. While Amgen inherited the 'scale-dominated managerial models that prevailed in Los Angeles (…) and became a commerce-dominated company' (Storper *et al.*, 2005, pp.199), new biotech companies in San Francisco borrowed and transposed the organizational practices and institutions of

leading research labs (e.g. open science models) and local entrepreneurial ecosystems, bridged by the venture capital industry, allowing then to grow in a distributed fashion, spin-off new companies and create a distinctive institutional environment that supported the industry further.

These examples suggest that, together with the agency of institutional entrepreneurs mobilizing and anchoring (diverse types of) resources – as in bricolage-related explanations (e.g. Binz *et al.*, 2016) – the emergence of new industrial paths may also be closely linked to the ways through which institutional and organizational settings in regions are borrowed and transposed, expanding (or, contrarily, constraining) the regional 'selection environment' for new industries. As transpositions have to be forged, this implies that one important role of institutional entrepreneurs and 'bricoleurs', namely in peripheral regions, is not only to build or transpose institutional forms and practices across regions (Saxenian and Sabel, 2008), but also across (institutionally-) related industries within regions.

3. Research setting

3.1 Regional development patterns in Portuguese biotechnology

This study explored the aforementioned propositions for the development of the biotechnology industry in Portugal, and in Centro Region in particular – the archetypal European peripheral region with modest knowledge endowments, characterized by incremental innovation processes and thin industrial-institutional structures (Cooke et al., 2000) – which nevertheless managed to develop a consistent and rising number of biotechnology activities over time.

The first Portuguese dedicated biotechnology firms (DBFs[1]), mostly start-ups and university spin-offs, date from the early 2000s. Fontes (2005) links their emergence to the accumulation of knowledge through public-funded doctoral education and university-based R&D in Portugal since the late 1980s (Fontes, 2005). As predicted by the literature, most DBFs emerged near large universities, namely in Lisbon, Porto (Norte region) and Coimbra

[1] A DBF is defined as a dedicated biotechnology active firm whose predominant activity involves the application of biotechnology techniques to produce goods or services and/or the performance of biotechnology R&D (OECD, 2005).

(Centro region), with whom their founders were affiliated to or had close relations with, notwithstanding the relevance of external knowledge sources since the early beginning (Vale and Carvalho, 2013).

Considering the metropolitan scale, presence of large pharmaceutical companies, and the strengths of biotechnology-related research institutions in Lisbon and Porto, those regions would be major candidates for DBF development in the country. However, the pattern proved more nuanced (Figure 1). Namely the continuous growth of DBFs in Centro over the last decade suggests the emergence of an unexpected industrial path in a largely rural-industrial region. As there is no evidence of specific regional markets for biotechnology in Portugal, two types of arguments are usually put forward to explain why Centro became so relatively preeminent in biotechnology vis-à-vis other regions, namely: i) the presence of a good hospital and an university with research in the field (University of Coimbra) and ii) the advantages that accrue form being a Convergence Region[2], thus eligible for heightened European Union´s (EU) Cohesion Policy funds in relation to Lisbon since 2007 (e.g. for R&D and innovation projects), which would act as a pull factor luring DBFs to settle operations in the region independently of its industrial structure and institutional settings.

[Insert Figure 1 about here]

However, a closer look at the evidence does not fully support either of the claims. First, the presence of good research universities does not explain the nuanced regional growth dynamics. Despite the sizable number of DBFs in Centro and its growth over time (Figure 1), the volume of high-quality scientific output is modest in relation to Lisbon and to Norte in particular (Figure 2). Second, the 'EU-funding' argument does not explain the growth of biotechnology in Centro before 2007-8, nor the difference vis-à-vis Norte – also a Convergence Region and thus eligible for the very same policy supports. In reality, the total amount of EU funds allocated to the biotechnology industry in Lisbon and Centro was relatively similar, though Centro´s DBFs managed to attract the highest number of biotechnology innovation projects in the county (Figure 3). The differences between Centro and Norte are again significant and cannot be explained by EU-funding frameworks alone.

[2] In the setting of European Union´s Cohesion Policy, Convergence Regions are the ones (NUTSII) with GDP/capita of less than 75% of the average of the average GDP/capita of EU-25.

[Insert Figure 2 and Figure 3 about here]

3.2 Research design and methods

In order to disentangle the processes behind the creation and consolidation of a biotechnology path in Centro – namely the role of bricolage and institutional transpositions from institutionally-related industries – we make use of qualitative evidence collected over about ten years (2007-2017)[3]. This longitudinal approach and follow-up of a contemporary case allowed iterating between theory and empirics to strengthen the underlying explanations for the phenomena (e.g. George and Bennett, 2005). Moreover, it also provided a reasonable time frame to assess whether the emerging industrial path endured after the early enthusiasm, or, in opposition, exhausted and declined (Isaksen and Trippl, 2014).

Besides several secondary sources (e.g. industry and company reports, statistics, press-releases) analysed over the years, the study relies on 76 in-depth interviews with a variety of actors – DBFs and other bio-related companies, research institutes, science parks and intermediaries, venture capital firms and policymakers – involved with the development of biotechnology in three regions (Centro, Lisbon and Norte) and beyond, e.g. venture capitalists and policymakers working at the national level (Table 1). Most interviews were carried out in tandem by the authors and transcribed afterwards. Variety within and across expert groups and regions allowed triangulating and increasing reliability and validity of the results, which together with secondary data allowed minimizing recall biases. Detailed investigation focused on Centro region as 'black swan' (Flyvbjerg, 2006) for new path development, with Norte and Lisbon being analysed mostly as contrasting cases (see also Binz *et al.*, 2016), allowing for punctual comparisons that highlight the reasons behind different regional industry patterns.

[Insert Table 1 about here]

Fieldwork took place during two main time periods (Table 1). During 2007-09, interviews focused on reconstructing the emergence and early development of the first DFB

[3] The fieldwork was conducted with the support of under course of 'Regional Trajectories to the Knowledge Economy (EURODITE), a FP6 project. In the course multiple follow-ups, the authors collected additional information.

companies in Portugal, with an emphasis on the role of local-global knowledge sources and institutional supports – e.g. broker´s intermediation, finance and policy (see also Vale and Carvalho, 2013). Subsequently, during 2010-2015, the case was followed-up through informal talks with key actors, analyses of press releases, sectoral trends and participation in biotechnology-related events. During 2016-17, a new round of systematic interviews was initiated to revisit the case, now with a focus on assessing path development in Centro vis-à-vis other Portuguese regions. Some firms and individuals where interviewed more than once during the course of this research, allowing to observe change in individual positions and strategies over time, while tracing and explaining path consolidation trajectories. Data codes evolved during the research process but were ultimately aligned and crystalized along the core constructs of the paper´s conceptual framework. In line with Binz *et al.* (2016), insight and evidence from interviews are cited according with the abbreviations in Table 1, being that e.g. a dedicated biotech firm (DBF) from Centro Region (C) is mentioned as DBFC, with the adjacent number (e.g. DBFC17) corresponding to the sequential order of the interview within the whole set.

4. Empirical analyses

4.1. Biotech by bricolage

Emergence (2000-2009)

The roots of the biotechnology industry in Centro date from the early 2000s, and can be traced to a technology-transfer project on recombinant protein applications (X-PROT), involving the Centre of Neuroscience and Cell Biology at the University of Coimbra (CNC), a medical research and technology association (AIBILI) and Bluepharma – a bio-pharma company founded in Coimbra (2001) by an university professor and a drugstore manager [e.g. R&DC4, GOVC25, SPC27]. During this project, some CNC´s researchers experienced the cultural and bureaucratic hurdles of working with the industry under the university umbrella and started looking for a new – physical and organisational – setting to promote market-oriented technology transfer [e.g. GOVC25, SPC27]. Simultaneously, the Mayor of Cantanhede (a small provincial town in the region) was looking for a scientific partner to develop a generalist business-science park in the municipality. Upon multiple

discussions, CNC´s representatives and the Mayor aligned their resources to develop a fully dedicated biotechnology park (named Biocant), with the ambition to commercialize university knowledge and support startups and university spinoffs [e.g. GOVC5, SPC16, 28, VCC24]. Despite the overall scepticism from the University´s deans [e.g. R&DC3, DBFC10, SPC27], Biocant was ultimately built and funded by the regional government in 2005; yet, it resembled a voluntaristic approach to develop a new industry based on accumulated academic knowledge, namely in the absence of industry-specific competences or policy incentives.

In order to create a favourable institutional context for the industry and enhance its *legitimacy*, an important step was the appointment of CNC´s vice-president as Biocant´s director and the investment in dedicated laboratorial facilities from the early beginning (Biocant Labs) [SPC28; SPN70, VCO72]. This was a deviant practice vis-à-vis other business-science parks in the country, primarily focused on undifferentiated office space and managed by the municipality [VCC24, GOVC25], but also compared with university research labs, in which academic research and startups compete with one another for space [VCO72]. Under the supervision of the park´s director, Biocant Labs provided fully dedicated state-of-the-art equipment and technology-transfer platforms for firms in a few selected areas (e.g. DNA-sequencing, microbiology, cell biology, bio-informatics), supervised by experienced scientists from the university and run by full-time technicians, tasked with conducting applied research and interacting with firms in a professional way [SPC16, 27, R&DC68].

Beyond providing infrastructure and services to a still incipient industry, the development of Biocant went hand-in-hand with strategic efforts to attract promising startups in the region, as well as returnee scientist-entrepreneurs in the director´s social network, notably former graduate students [e.g. SPC27]. Those included young researchers then in leading institutes – e.g. in Boston (Harvard, MIT), Houston (Baylor College) and Stockholm (Karolinska Institute) – inviting them to start a company and build research units in the park. As stressed, ‘the idea was not to offer space, but a life-changing project in the region’ [SPC53]. Beyond technical *knowledge* (e.g. publications and patents) and access to promising research and applications in many fields, these returnees brought new

organizational competences as well, including experience working with serial bio-entrepreneurs and bridging between business and academia worlds [DBFC9, 12, 13, 15]. While some ventures never took off [DBFC 17, 23], others grew fast and acquired sound national and international investments [DBF 9, 12, 14, 15, 67]; they soon became role models and their experience diffused in the park and in the region. A few early entrepreneurs created new spin-offs and founded their own research labs at Biocant and CNC (e.g. on tissue bio-engineering – DBFC9) while keeping their international affiliations, enhancing the legitimacy and building the reputation of the park nationally.

Biocant Labs and newly formed DBFs had also to create early biotechnology *markets* in the country from the early beginning. For example, a pioneer DBF that introduced a stem cell cryopreservation service built his own market together with pregnant women and young parents [DBFC16], as such a service was relatively new to the world and inexistent in the country, also requiring active institutional work with the Ministry of Health to adapt regulatory frameworks [DBFC64]. Simultaneously, Biocant Labs entailed with 'multiple dating' [R&DC68] and several talks with companies and associations in established industries beyond health segments to raise awareness about promising biotech applications – which were new to many companies – resulting in some early contracts for DNA-sequencing (e.g. cork oak) and other bio-applications and laboratorial services for wine and food industries [e.g. SPC27, R&DN48].

Related with the previous, as markets were underdeveloped and there was no investment experience in biotechnology in the country, finance was a major issue. To tackle this, Biocant developed his own early-stage venture capital (VC) fund – Biocant Ventures – with the support of generalist public-owned VC fund and other private investors (e.g. Bluepharma) [VCC24, 27]. Over time, Biocant's director and regional DBF´s founders became invited to the external advisory boards of national VCs, sometimes providing 'strong suggestions' [SPN70] towards company´s location in the region, while working together to bring international investors to meet promising startups in the region [DBFC66]. Moreover, in order to support new startups acquiring national and European innovation funding, Biocant teamed up the University´s incubation services (Institute Pedro Nunes – IPN), with longstanding experience supporting university spinoffs [SPC16]. Yet, as no

specific innovation funds existed for biotechnology, pioneer DBFs and Biocant lobbied nationally with the newly founded Health Cluster Portugal (in Porto), as well as with regional policy makers [DBFO42; SPN52]. Altogether, this made it possible to have a combined stream of VC funds, R&D projects and market-based contracts to support the early development of the industry in the region.

Early growth and development (2009-2016)

At the brink of the 2008-9 financial crisis, there were 20 DBFs in the region (Figure 1) and still some uncertainty about biotechnology´s prospects, as many DBFs were in early development stages, capital was scarce and institutional supports fragile. Yet, during 2009-2016, biotechnology industry gradually consolidated and developed in the region, supported by an increasingly dynamic regional ecosystem and fit institutional conditions. In 2009, a large US private equity firm bought and invested in one of the largest DBF in the region [SPC53]; during 2011, Biocant Labs reported a 30 percent increase in the volume of contract research (Biocant, 2012). The connection between university research centres, Biocant Labs and DBFs became increasingly fluid, with actors changing across and holding multiple positions [e.g. SPC53, DBFC62, R&DC69]; new university spin-offs and serial bio-entrepreneurs emerged, with CEOs and key individuals moving across management and technical positions [SPC54, DBFC55, 62]; new DBFs were founded while others closed down, and staff started moving across firms and labs in the region [DBFC64, R&DC68, 69]. Biocant kept attracting new international scientists, becoming an active member of multiple research and entrepreneurship networks (e.g. with the MIT) [SPO57, SPC60]. The park expanded, and the University of Coimbra re-organized and re-located their bio-related research centres from the city to Biocant, into a new building called UC-Biotech [SPC54].

Knowledge anchoring and *finance* attraction became increasingly intertwined. First-generation DBF founders and park managers became role models and active mentors of second-generation DBF, both through informal relations and through participation in company boards [e.g. DBFL29; SPC53, DBFC55]. Moreover, as influential researchers themselves, the connectivity between research labs, research projects and new company formation became gradually porous – e.g. with university researchers-entrepreneurs

actively scanning and supporting commercially-promising research projects [e.g. DBFC64, 67; R&DC69]. Spin offing and mobility between academia and biotechnology businesses became increasingly legitimated within the university, with the biggest companies (e.g. Bluepharma) launching their own investment funds to mentor and promote university spinoffs within the company [DBFC64; 67]. At the same time, UC-Biotech and Biocant Labs kept attracting international researchers – e.g. from the US, Germany and Italy –, who brought their own international funding (e.g. European Research Council grants) to launch new research labs [R&DC68], leading to further attraction of national innovation and R&D funds into the region [SPC54], at the same time as older DBFs got new rounds of VC investments [VCO72].

Biocant, Bluepharma, university research labs and a network of consolidating DBFs gave rise to the emergence of a supportive knowledge ecosystem, not only combining state-of-the-art scientific knowledge and experienced technicians, but also other tacit components on e.g. how to start a biotech company, how to acquire VC, regulatory issues associated with clinical trials, how to solve day-to-day issues in labs, roads to follow and to avoid, the right equipment and technological platforms, etc. [e.g. SPC53, R&DN75]. This actively constructed ecosystem contributed to reduce uncertainty among VC investors when investing in biotechnology in the region, and contributed to attract startups from other regions. During this period, while some DBFs moved form Lisbon primarily lured by EU funds for innovation projects (e.g. to develop new pilot testing facilities – see Section 3) [e.g. DBFL29, DBFC59], others relocated from their home university labs (both in Porto and Lisbon) because of the superior laboratorial conditions, market support, and because of the recommendation of their own VC investors [e.g. DBFC55, 56]. Yet, in both cases, DBFs from outside the region gradually established new connections with regional startups and Biocant Labs, becoming part of and contributing to the region´s knowledge and supportive ecosystem.

Over time, these developments added to the *legitimation* of the industry in the region, consolidating a hybrid model of scientific research and DBF formation increasingly recognised by the university and by regional policymakers themselves. Examples are the development of a new dedicated university building at Biocant (UC-Biotech) and the

launching of regional health-cluster networks and policy incentives to promote and fund the system further [SPC54, GOVC61]. Moreover, besides establishing new commercial and research partnerships with hospitals and medical service organizations in the country and beyond [e.g. SPC60, DBFC64], ripple effects are observable as regionally based DBFs and research labs progressively expanded the scope of their activities to work with large agro-food and other industrial companies nationwide and internationally, e.g. for the development of new fungicides, nano-particles applied in the construction industry, IT-services, among many others [e.g. DBFC62].

Summing up, and over about 15 years, a few committed institutional entrepreneurs (university professors, park director, mayor, DBF founders), positioned at and bridging across different social fields and locations, strategically influenced the formation of a biotechnology ecosystem and co-created a favourable institutional environment for it – despite the absence of any previously targeted policy support or closely related industry skills. This was achieved through an iterative *bricolage* process, involving the mobilisation, alignigment and anchoring of multiple scattered resources that contributed to knowledge, market, finance and legitimacy formation processes over time.

4.2. Institutional Relatedness

Active bricolage and the formation of a supportive biotechnology ecosystem occurred in Centro but not in Lisbon or Norte, despite the presence of stronger endowments (e.g. research institutions, established pharma companies) but also of pioneer and internationally connected DBFs and influential individuals at the firm-university interface, namely in Lisbon [e.g. DBFL30, 31, 35]. An explanation for this rests in the presence of nuanced regional institutional settings, which influenced the scope for bricolage and the way biotechnology selection environments unfolded in different regions. While institutional entrepreneurs in Centro could make use of – and transposed – related institutional and organizational settings to pave a new biotechnology path, institutions in Norte and Lisbon, on the contrary, constrained the selection environment and the scope of action for new industry formation.

The development of Biocant Labs and hybrid models of technology transfer between university and DBFs – which were the cornerstone of new path development in Centro – could actually emerge and consolidate relatively swiftly as they inherited related institutional norms and legitimized practices for the commercialization of academic research in the region, previously developed within the IT and engineering fields. During the 80s, the University of Coimbra was early in the country establishing a technology transfer model through a dedicated and independent arm´s length interface institute – Institute Pedro Nunes (IPN). One of the specificities of this model consisted in pursuing a '3-pillar' integration between technology-transfer, incubation and market support under the same organizational umbrella (SPC16); another feature was the establishment of independent technology transfer labs (e.g. informatics, automation) with a dual management, i.e. a 'daily' plus a 'scientific' director with well-defined reward systems – e.g. the second being typically a tenured professor whose additional remuneration was dependent on the lab´s profits (e.g. SPC53, 63). These institutional and organizational practices were strategically transposed from IT to biotechnology through Biocant and IPN´s directors – the latter also an early collaborator of one of the first DBFs in the park, who was initially incubated at IPN before moving to Biocant [DBFC14, 15]. As explained:

> The 'IPN model' closely inspired the model for Biocant (…). Just as we [IPN] did 30 years ago for engineering and mechanics, they [Biocant Labs] created distinct business units in the life sciences. You can see a lot of similarities because we also transferred all the pricing standards and contractual models there. We have been working closely together ever since [e.g. jointly incubating DBFs] although we never really signed any formal document about it. [SPC63].

These 'business units' or technology transfer labs facilitated the hybridization of research-business contexts in biotechnology, namely as

> (…) There is a sense of independence from hierarchical [university] structures. [University bio-research labs] have great equipment but often allocated to students or researchers doing one-time experiments, and when they leave all the knowledge is lost. Here we designed a structure with permanent staff that uses the equipment over time. [Moreover], there is not that kind of strong judgement and peer-pressure that

> you find in an academic lab. You see the same in IPN [engineering labs] – people come with the idea but they are heavily supported during the stage in which you need to change the mindset from research to business (SPC54).

Similar business-academia interfacing organizations also existed in Porto and Lisbon in the fields of engineering (e.g. van Winden and Carvalho, 2008), but their practices were never transposed to 'shield' biotechnology development. On the contrary, biotechnology and DBF development in these regions evolved around closed and fragmented ecosystems centred in a few individuals within leading academic research labs, with limited interactions among each other (e.g. SPL71; VCO72). These developments mirrored the fragmentation of Lisbon and Porto´s incubation spaces developed over the last decades, as well as of both region´s dispersed medical research institutes and in-fighting within universities (e.g. R&DC69). In Porto, a merger between three large bio-medical research institutes took place in 2015 only, with an eye to gain synergies and commercially exploit scientific knowledge; yet, despite a large investment in a new building and research infrastructure, no specific laboratorial facilities for companies were developed there or in the University´s incubator (SPN70, 76).

In both regions, research institutes' competition for resources – namely for scientific research funding and laboratorial space – hampered the development of integrated support ecosystems for biotechnology businesses (e.g. DBFC56). Although leading star scientists could be found in Porto or Lisbon, few if any of them became bio-entrepreneurs – 'there are well-established 'schools' focusing on high-quality and fundamental research' (SPC54), and this poses several problems for emerging DBFs. For example, some leading scientific institutes in Lisbon have strict 'no incubation' policies to avoid conflicts among researchers and businesses concerning information flows (VCO72); in Porto, tensions emerged between university spinoffs and scientific research labs. As explained by a national VC investor and former bio-entrepreneur,

> 'One of our companies lost already time and money with these [lab competition] issues [in Porto]. In a scientific research lab companies never have priority, and I know this from experience incubating my own [DBF] company [in Lisbon]. Biocant is well set in that respect as companies have more control on their own facilities.

> What they do is separating incubation from academic research, and by separating it [in space] a researcher can more easily move across the two [social] places. (VCO72)

An additional (constraining) institutional issue in Lisbon and Norte (namely in Porto) relates with rigid practices of academic technology transfer offices, in their relation between research, startups and venture capital firms. A number of offices developed and grew over the last two decades, frequently pursuing a 'gatekeeper', one-size-fits-all approach. Yet, from the perspective of VC investors in biotechnology,

> 'Their perception of reality is very different than ours, and this doesn't mean that they are right or wrong but they make it very hard for us. […] Instead of facilitating access to promising companies, they act as gatekeepers, which is not interesting, just boring. For example, even for starting PhD projects, in which there is nothing there yet, the rules and sharing barriers are already daunting.' (VCO72)

The University of Coimbra (Centro) has not been immune to these pressures and institutional rigidities, but their experience with IPN carved out the emergence of new mindsets and hybrid firm-university relations, which were appropriated by new DBFs and their founders [e.g. DBFC9, 62, 64, 67]. The case of a leading bio-pharma in Coimbra founded by a professor is illustrative, as expressed by a representative of the University:

> 'They [bio-pharma company] move around in the University as inside their own labs. All their recent spinoffs are, in reality, spinoffs of the University. Some people say they are parasitizing the University (…) but we do not buy those wars anymore. If we consider that parasitizing means being around, having an award for the best theses, knowing what is going on and pulling our students to do projects with them, then yes, they do that…' (R&DC69).

Finally, the mobilisation of resources for biotechnology in Centro – namely committed regional advocacy and public funding – also benefited from the relative absence of competing vested interest from other industries, as occurred in Norte. The creation of the 'Health Cluster Portugal (HCP)' in Norte is illustrative. It emerged roughly at the same time as Biocant, but while Biocant originated bottom-up from researchers with positional mobility, HCP was initially championed by a group of industrialists, involved with medical

devices, equipment and and engineering products, closely linked to regional industrial competences – 'the group of plastics and rust' (SPO52). The cluster initiative grew to involve the largest national pharma company (in Porto), as well as other sizable pharma and medical research organizations in the country. Although Biocant and other related DBFs joined latter on, HCP was based in Norte and primarily led by their group of founders to, among others, lobby and gain policy attention for their activities and attract public funding SPC60).

Large pharma companies in Porto and Lisbon have their own in-house research and long-term product development pipelines, and absorb substantial amounts of public funding (e.g. R&DN73). Yet, they are considered as conservative and closed, making it hard to develop partnerships with other parties or supporting new startups and spinoffs (DBFC66, R&DN74). As explained by a former collaborator, 'if somebody arrives there with an idea, or they like it and buy it on their own terms, or send the person away' (DBFC10). Likewise, as explained by an HCP board member involved in biotechnology, 'I have been trying to convince him [pharma company CEO] to spin off a lot of molecules that are just stuck there with no use, but I never really got a good answer from their side (…) these could be better used and improved by a [DBFs] ecosystem' (SPC54).

All in all, the way related institutional settings 'branched out' and were strategically transposed to biotechnology in Centro do contribute to complement bricolage-driven explanations behind new path development in the region. These related institutional settings provided the nascent industry and their proponents with fit organisational and institutional resources and legitimacy, shielding it from potentially hostile selection pressures – notwithstanding the absence of related industrial skills in the region. On the contrary, the presence of potentially related skills (e.g. in pharma industries) and strong university knowledge endowments were insufficient to support the emergence of biotechnology in other regions, namely as previous institutional settings and vested interest largely constrained the potential for resource mobilisation, bricolage and new firm development.

5. Conclusions

EEG approaches have been sustaining that regions diversify into new industrial paths by recombining inherited portfolios of knowledge and skills (Boschma and Frenken, 2011), thus limiting the ability of peripheral regions to move towards more knowledge-intensive types of activities. While this seems to be the norm (Xiao et al., 2018), every now and then dissonant activities do emerge and endure in those places, calling for a more multi-dimensional perspective to understand the causes and mechanisms behind industrial change (MacKinnon *et al.*, 2009). By combining and building on a number of extensions involving the role of external knowledge networks, policy activism, endogenous emergence and the agency of institutional entrepreneurs, this paper provided an explanation for new path development in the periphery based on the use, in conjunction, of two concepts: 'bricolage' and 'institutional relatedness'.

Starting from the work of Binz *et al.* (2016) and Boschma *et al.* (2017), our analysis shows that also the (unlikely) development and consolidation of biotechnology in Centro neatly resembles a bricolage process, in which heterogeneous types of actors iteratively mobilise and anchor distributed resources – knowledge, but also finance, markets and legitimation –, doing active institutional work with the purpose of creating a new path (university professors, mayors, new DBFs, science park managers, etc.). In this case, biotechnology did not develop because of knowledge endowments or targeted state policy intervention, but by forging new connections among distributed resources and by iteratively creating a new favourable institutional environment. The involvement of actors with positional mobility and with access to multiple social networks (e.g. university researchers), locally and globally, was fundamental to the process.

Yet, this study also highlights that these institutional environments were not created from scratch. They derived from related institutional norms and practices associated with the commercialization of academic research from engineering communities in the region (e.g. technology-transfer models, incubation, dual management of research labs). In this case, actors involved with bricolage and new path creation purposefully borrowed, transposed and provided refunctionality to portfolios of related institutions, expanding the regional space of search and making it more amenable to the biotechnology industry. This was contrary to what happened in other Portuguese regions, in which the influence of previous

institutional settings hampered new path creation in subtle yet influential ways – with the growth of biotech ventures in Lisbon essentially linked to a scale effect and the presence of many yet fragmented R&D institutions. Hence, this study suggests that institutional borrowing and transpositioning are not automatic processes but have to be forged. For example, beyond transposing institutional settings from the same industry in other regions (e.g. by attracting returnee scientists with bio-related commercialization knowledge from Boston), institutional entrepreneurs may also need to transpose practices across (institutionally-) related industries within regions.

The notion of institutional relatedness – or the degree to which institutions associated with certain industries or activities can be transposed to provide resources and legitimacy to new industries – may provide new avenues to understand path creation beyond technology branching (Content and Frenken, 2016), notably in peripheral regions (see also Peng *et al.*, 2005). Yet, further studies would still need to explore this notion in other industrial and regional contexts, in order to gain more insight on the mechanisms through which institutions may become transposed or not (Padgett and Powell, 2012), and where does it matter the most. For example, it could be hypothesised that institutional relatedness and institutional transpositions are more relevant for peripheral regions, as it would prevent the need to (struggle to) develop very different institutional practices anew to legitimize technologically deviant paths. Moreover, such a construct would certainly need more elaboration to become better operationalized and measured, namely for more quantitative analyses that may try to compare and distinguish the impact of institutional relatedness and technological relatedness across a number of regional development and new path creation variables.

Finally, this study shows that although related diversification and institutional adverse contexts are the norm in the periphery, not all peripheral regions are the same, and should be treated as such in policy terms. Therefore, in line with recent studies, a latent policy implication running through the paper is that a single focus on regional knowledge endowments and incumbent firm skills may overlook relevant actors and sources for new path development in peripheral regions. At the same time, strong policy interventions and funding may be insufficient when related institutional settings in regions are adverse to new

types of industries (as shown with the cases of Porto and Lisbon). Beyond assessing (existing and sought) skills and knowledge resources for new path development, policymakers in peripheral regions should also strive to identify which institutional configurations exist that may be mobilised to support new industries, and where the institutional gaps/contradictions are. These may be fundamental to anchor externally accessed resources in regions over time.

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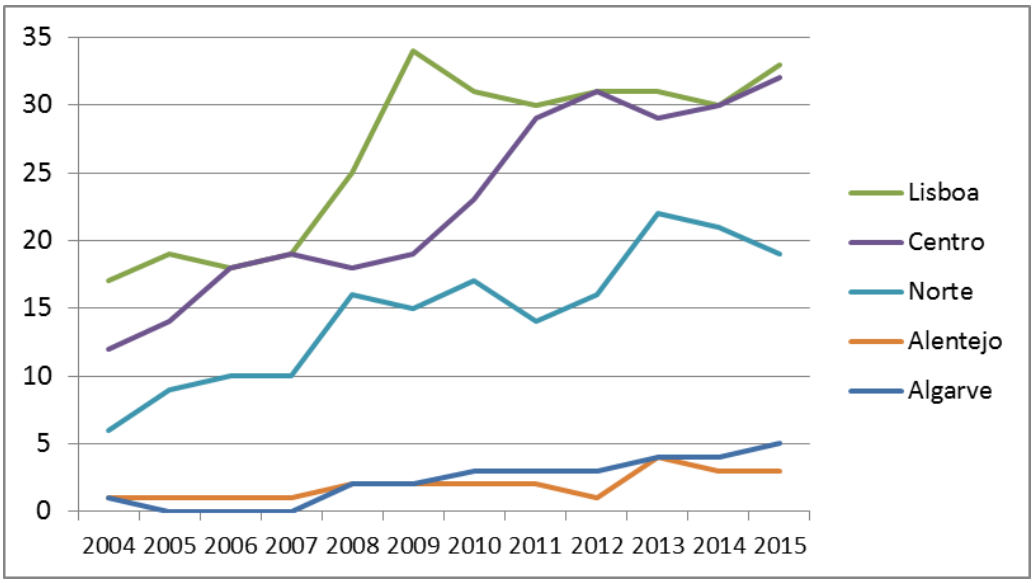

Figure 1. Registered Portuguese biotechnology companies (NACE 72110) by NUTS II regions, 2004-2015.
Source: INE – National Statistics Office (2017).

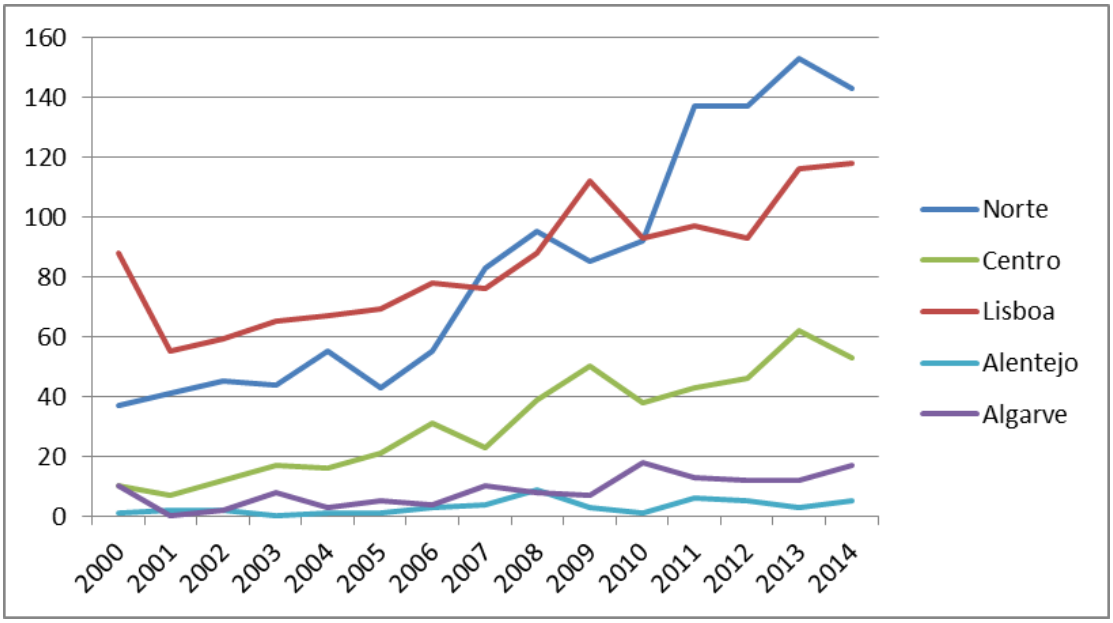

Figure 2. Scientific articles in the field of 'Biotechnology and Applied Microbiology' from Portuguese universities and research institutes, ISI web of knowledge, 2000-2014, NUTSII.

Note: 'Norte' incudes the University of Porto (U. Porto), Porto Technical School, U. Minho and U. Trás-os-Montes e Alto Douro; 'Centro' includes. U. Coimbra, Biocant and U. Beira Interior; 'Lisboa' includes U. Lisbon, Lisbon´s Technical School and Nova U. of Lisbon; 'Alentejo' includes U. Évora and Algarve includes. U. Algarve.

Source: Own calculations, based on ISI Web of Knowledge (as of 31 May 2016).

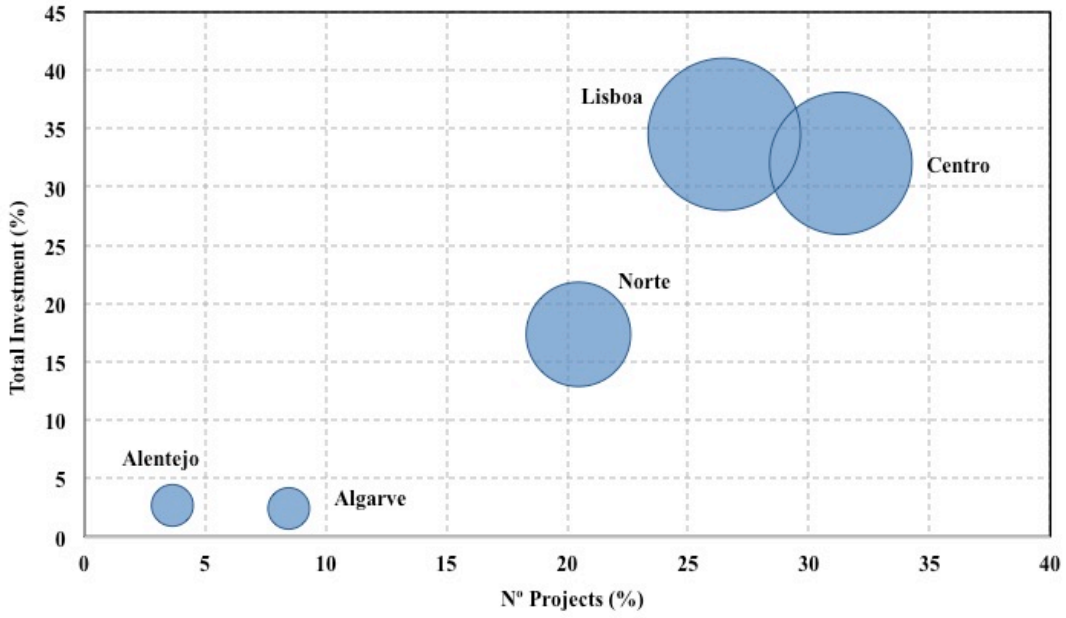

Figure 3. EU-funded R&D and innovation projects in Portuguese biotechnology companies (NACE 72110), NUTS III, 2007-2014, European Regional Development Fund (ERDF).
Note: Circle´s size is proportional to the amount of ERDF funding in the total investment.
Source: Own calculations, based on data from the Portuguese Operational Programme COMPETE 2007-2013.

Table 1. Interviews

Interview group	Norte (N)		Centro (C)		Lisbon (L)		Others (O)		Sum
	2008-9	2016-17	2008-9	2016-17	2008-9	2016-17	2008-9	2016-17	
Dedicated Biotech Firms (DBF)	6	-	14	8	13	-	-	-	41
Academia & R&D Centres (R&D)	1	4	7	1	1	-	-	-	14
Intermediaries (Science Parks, Associations, Incubators) (SP)	0	2	3	3	-	2	3	1	14
Venture Capitalists (VC)	0	-	1	-	-	-	-	2	3
Government/policy authorities (GOV)	0	-	2	1	-	-	1	-	4
Sum	7	6	27	13	14	2	4	3	76

Table 1. Interviews
Source: own elaboration, based on fieldwork