**SPATIAL ORGANIZATION OF FIRMS:
INTERNAL AND EXTERNAL AGGLOMERATION ECONOMIES AND LOCATION
CHOICES THROUGH THE VALUE CHAIN**

by

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Abstract

We explore the impact of geographically bounded intra-firm spillovers (internal agglomeration economies) and geographically bounded inter-firm spillovers (external agglomeration economies) on firms' location strategies. Using data from the Census Bureau's Longitudinal Business Database and the U.S. Cluster Mapping Project, we analyze organic expansions of biopharmaceutical firms (by both new establishments and employment increase in existing establishments) in the U.S. in 1993–2005. We consider all activities in the value chain and allow location choices to vary by R&D, manufacturing, and sales. Our findings suggest that (1) internal and external agglomeration economies have separate, positive impacts on location, with relevant differences by activity; (2) internal economies of agglomeration arise within an activity (e.g., among plants) and across activities (e.g., between manufacturing and sales); (3) the effects of internal economies across and within activities vary by activity and type of organic expansion; and (4) across-activity internal economies are asymmetric.

Keywords: Location choices, agglomeration economies, value chain, organization theory.

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1. Introduction

The determinants of firms' location choices are the subject of a large body of research spanning multiple disciplinary fields. Most research in economics and management argues that elements of the external environment—most notably, location endowments and agglomeration economies—drive location choices. This focus overlooks the significant role of internal drivers such as geographically bounded intra-firm spillovers. The omission is particularly surprising in the strategy literature, which recognizes that links between activities across the value chain are important levers for developing competitive advantage (Porter 1996). The scarce research that does consider internal drivers focuses on links across pairs of activities, typically manufacturing and R&D. This approach obscures the effect of internal collocation forces acting *across* the value chain and *within* each value chain activity (e.g., multiple plants of the same firm).

Our objective is to identify the extent to which the locations of distinct activities in the value chain (manufacturing, R&D, or sales) are explained by the external environment and by internal drivers (i.e., the locations of a firm's pre-existing facilities). Due to the breadth and variation of prior empirical findings in this area, and to the dearth of relevant theoretical models, we do not approach our data with a set of testable hypotheses. Instead we present several streams of prior research that shape our expectations about the drivers of firm location and that guide our empirical analysis. Our conceptual section reviews and synthesizes previous research scattered across fields to provide a comprehensive view of the location decision, which we then translate to our data. This process allows us to identify limitations in the current studies and to propose a new, more comprehensive empirical framework that uses both external and internal location drivers to examine firms' location decisions across the value chain.

We conceptualize the location decision as a tradeoff between two sets of forces. The first set is external agglomeration economies, centrifugal forces that drive firms to disperse their activities geographically. The second set is internal agglomeration economies, centripetal forces that drive within-firm collocation, either across activities (e.g., manufacturing and R&D) or within activities (e.g., multiple R&D labs). Our theoretical review begins in Section 2.2 with the most prolific area of research, external drivers of location, covering both endowment-related drivers and agglomeration economies. Section 2.3 introduces the idea of internal agglomeration economies—productivity gains achieved when same-firm activities are collocated—as a conceptual tool encompassing a wide set of empirical findings in economics and management research. We argue that internal agglomeration economies (1) vary by focal activity (e.g., manufacturing has a different influence on sales location than on R&D location); (2) that they are asymmetric (e.g., the effect of manufacturing on the location of sales does not equal that of sales

on the location of manufacturing); and that they are (3) firm-specific (e.g., a firm may develop unique routines to facilitate the geographic separation of manufacturing from R&D).

Empirically, we contribute new empirical methods and findings that are important for analyzing firm location choices through the value chain. Using data from the Census Bureau's Longitudinal Business Database, we focus specifically on expansions (both through new openings and through employment increases at existing establishments) of biopharmaceutical firms between 1993 and 2005 and ask to what extent the location of a firm's new activities—a new site for manufacturing, R&D, or sales—can be explained by the location of a firm's pre-existing sites as compared to the external environment. To our knowledge, this is the first study to systematically explore collocation decisions for *all* firm activities rather than for subsets of activities. We introduce our data and explain our econometric approach in Section 3. We emphasize that our measure of internal economies is firm-specific, acknowledging that firms may develop specific capabilities that affect interdependency across activities. We present our results in Section 4 highlighting that (1) internal and external agglomeration economies have separate, positive impacts on location, with relevant differences by activity; (2) internal economies of agglomeration arise within an activity (e.g., among plants) and across activities (e.g., between manufacturing and sales); (3) the effects of internal economies across and within activities vary by activity and type of organic expansion; and (4) across-activity internal economies are asymmetric. We summarize and conclude in Section 5.

2. External and internal drivers for multiunit firms' locations

There has been a dearth of systematic theoretical and empirical research that bears directly on the extent to which the locations of various value chain activities can be explained by internal or external drivers. There are nonetheless several streams of prior research that influence our expectations about external drivers and, to lesser extent, internal drivers, and these guide our empirical analysis. We will first provide a concise summary of the literature on external drivers and then delve deeply into the important but less developed literature on internal drivers.

2.1. External drivers of location: driving firm activities apart?

Two set of external drivers have been commonly studied in the literature: unique location endowments and agglomeration economies. Ricardo (1817) was the first to posit that a stochastic distribution of natural resources across the geographic space drives economic exchanges, an idea that is at the core of economic geography and international economics today. Some studies have since expanded Ricardo's view of endowments to encompass a location's institutional features, such as IP regimes, labor regulation, and the unique technological knowledge present in universities. This literature primarily

predicts that firms will flock to locations where they can tap (1) abundant inputs at low costs (e.g., labor in China), (2) rare and unique resource (e.g., knowledge from universities), or (3) location-specific incentive programs (e.g., tax policies).

Marshall (1920) introduced a second and related external driver to explain location choices: agglomeration economies. He argued that collocated firms would enjoy higher productivity because geographic concentrations of firms would attract larger pools of specialized labor and suppliers, and would also facilitate the flow of knowledge from one firm to another. These agglomeration economies exert a multiplier effect on firm productivity by increasing the benefits that firms would otherwise receive only from a location's physical and institutional endowments, a concept that has been adopted and expanded by researchers in various fields, including Porter (1998) in strategy, Jacobs in urban economics (1984), and Krugman (1991) in international economics.

This rich tradition of research in agglomeration economies has been revitalized in related but diverse areas in recent years. Some studies have focused on developing new methods to isolate agglomerations—the geographic density of same-industry activity caused by broadly defined endowments—from agglomeration economies—positive spillovers from collocated firms (Ellison and Glaeser 1997; Glaeser and Kerr, 2009). Porter (2003) and Delgado et al. (2010a, 2010b) conceptualized agglomeration economies within regional clusters of related and complementary industries (in both manufacturing and services).¹

A second research stream has focused on how agglomeration economies vary by firm and by industry. In strategy, Shaver and Flyer (2001) and Alcacer and Chung (2006) identified conditions under which collocation may affect firms negatively. In economics, Henderson (2003) and Rosenthal and Strange (2009), among others, suggested that agglomeration benefits depend on firm size. In terms of industry determinants, Henderson et al. (1995) and Duranton and Puga (2001) found differences in agglomeration patterns between low- and high-tech industries and between new and mature industries.

While some of these recent papers have identified negative effects from external drivers—the incentives to *avoid* collocating—most empirical and theoretical models suggest the effect of agglomeration economies on location choices will be positive. And while the evidence overall is somewhat thin, previous research also suggests that the strength of external location drivers will vary by

¹ Regional clusters group industries related by various types of interdependencies (skills, demand, knowledge, supply, and others) rather than focusing on a particular type of externality. See Porter (2003) and Delgado, Porter and Stern (2012).

value chain activity. For example, Audrestch and Feldman (1996) found that innovation in the U.S. is more concentrated than manufacturing; and Alcacer (2006) found that competition and external agglomeration economies exert different effects on inter-firm collocation for R&D, manufacturing, and sales in the wireless handset industry. Thus, we argue that in the absence of countervailing forces, external drivers might be magnets for some activities but not for others, inducing firms to geographically disperse particular activities in the value chain. A biotechnology firm, for example, might locate its R&D labs near Cambridge because MIT is a unique source of knowledge, conduct its manufacturing in Puerto Rico because of low-cost labor and land, and site its headquarters in Washington, DC, to facilitate access to the NIH and FDA.

From this literature on the external drivers of location choices we can establish our first prior: that external agglomeration forces influence location choices, and that their effect will vary by activity (with some evidence that the effects are stronger for R&D, followed by manufacturing). Additionally, we can expect that, because activities may be attracted to different features in the external environment, firms will adopt a basic level of geographic dispersion for different value chain activities.

2.2. Internal drivers of location: bringing firm activities together?

The research on internal drivers of location choices has been more fragmented and lacks an organizing framework. Most papers have examined collocation across pairs of activities (e.g., manufacturing and R&D) and, to a lesser extent, within an activity (e.g., collocation of two plants manufacturing the same or different products) (Ketokivi 2006). Taken as a whole, this research suggests that interdependency between a firm's value chain activities (due to supply, demand, skills, knowledge, or other interdependencies) may induce a firm to collocate those activities. Interdependencies that are sufficiently strong might even swamp any dispersion effect promoted by external drivers.

2.2.1. Internal drivers across activities

Previous empirical research has focused on pairs of activities, normally manufacturing and R&D. These studies find high levels of collocation and positive, although asymmetric, performance effects on collocated activities.

In terms of location patterns across activities, these studies suggest that the extent of collocation between manufacturing and R&D depends on the type of R&D. Looking at Japanese investments in Europe, Mariani (2001) found that R&D sites were likely to be located close to manufacturing, but that this link was weaker in science-oriented industries. Using survey data for Japanese firms in biotech and electronics, Kenney and Florida (1994) found that interactions between R&D and manufacturing sites

were higher for applied R&D than for basic R&D, and therefore the location of basic R&D sites were less influenced by pre-existing manufacturing sites.

In terms of the effect of collocation for manufacturing and R&D, prior studies have examined the unidirectional effect of manufacturing on R&D performance (Tecu 2011) or the reverse effect of R&D on manufacturing (Jaffe 1996), but rarely have studies examined both effects simultaneously or explored their asymmetry. Tecu (2011) used patent data as an output measurement to find that R&D in pharmaceuticals was 2.5 times more productive in locations where manufacturing was also present (after controlling for external drivers of innovation such as proximity to universities and peer firms). Examining the reverse effect, in the case of R&D on manufacturing, Adams and Jaffee (1996) demonstrated that the positive effect of parent-firm R&D on plant productivity diminishes with geographic distance.

Studies that examine the collocation of other activities, such as sales or support, are scarce and offer inconclusive findings. Kleinbaum et al. (2008) used email frequency as a proxy for coordination needs in a large technology firm and found above average information exchanges between sales and R&D and between sales and supporting services. However, information exchanges between these activities may not require collocation. Van den Bulte and Moensert (1998) found no changes in information flows between R&D and sales even after dispersed R&D personnel were geographically concentrated.

For support activities, the role of firm headquarters has received special attention. Focusing on the dependency between HQ and manufacturing sites, Henderson and Ono (2008) found that, after controlling for external drivers, such as access to specific services in metropolitan areas, firms prefer to keep HQs close to their manufacturing bases.

Generating strong priors on collocation levels across value chain activities is problematic for different reasons. First, with the probable exception of collocation for manufacturing and R&D, we don't know of any studies that systematically examine collocation for *all* firm activities. Failing to consider all activities leads to an omitted variable problem, in which collocation levels between sales and manufacturing may be overestimated (or underestimated) by failing to control for the locations of another activity such as R&D. Second, although most studies suggest *potential* mechanisms for positive spillovers between establishments, they fall short of identifying those mechanisms empirically. As a consequence, it is difficult to build hypotheses based only on universal primitives—such as the nature of knowledge, the need for coordination, the complexity of interactions—that underlie a specific activity.² Third, findings that make productivity comparisons between collocated and non-collocated activities may not be adequate

² A notable exception is Ketokivi (2006), who suggested a fine-grained interdependency framework for manufacturing and R&D.

tests of causality because of endogeneity issues between location choice and performance (i.e., firms choose locations based on their expected subsequent performance).

For all these reasons, we believe that, given the state of the theoretical and empirical development in this area, the level of same-firm collocation for any pair of activities is an empirical question. As such, we approached our data without strong priors.

2.2.2. Internal drivers within activity

Among all the drivers of location, internal drivers within an activity (e.g., the collocation of same-firm, same-product plants) have received the least attention (Ketokivi 2006). In fact, the scant existing research focuses on explaining the dispersion, not the collocation, of same-activity, same-firm establishments. In most cases, external drivers (e.g., access to markets) overcome any implicit benefit from collocating the same activity of a firm.

The starting, implicit assumption is that activities of a particular type should be performed at a single location to achieve economies of scale (for single-product firms) or economies of scope (for multi-product firms). Dispersion would occur only when external drivers (e.g., access to markets) overcome any implicit benefit of same-activity collocation. Weber (1909) introduced the idea that transportation costs to final consumers might push firms to geographically disperse same-product plants. Krugman (1991) proposed that specialization of intermediate inputs produced in the lowest-cost production location is an important driver for trade. Thus, the manufacture of complex products will be divided into components and each component will be produced in the location with the lowest factor costs. The international business literature introduced market frictions that may trigger horizontal foreign direct investment. For example, the legal environment, regulation that favors local production, or intangibles that are not transferable through markets might all prompt firms to disperse the same activity across countries (Caves 1996).

Even when dispersion is desirable, firms must develop capabilities to make it feasible. Exploring when U.S. manufacturing firms fragment production across locations, Fort (2011) suggested that production fragmentation occurs with the use of communication technology—only then would firms find it profitable to geographically disperse production to tap lower costs or closer-to-demand locations. Also, highlighting the role of information as a driver of within-firm same-activity collocation, Kleinbaum et al. (2008) found that most information exchanges happened within activities, with the highest level of intra-unit emails found in R&D, followed by support activities. Given that R&D relies on the continuous exchange of tacit knowledge, it is not surprising to expect that R&D sites will be more likely to collocate. For example, Van Den Bulte and Moenaert (1998) found that information flows among R&D personnel

increased when dispersed teams were geographically concentrated, suggesting there are informational benefits from collocation.

The previous studies assumed single-product firms, but many geographically dispersed firms are also multi-product firms.³ Although some activities, such as support, are likely to spread across multiple products, others, such as manufacturing, sales, and even R&D, are likely to be product-specific. In such cases, will there be benefits from collocating R&D, manufacturing, or sales sites associated with different products? We argue that the answer is yes for two reasons. First, although geography is absent in the diversification literature, the idea of industry relatedness (Collis and Montgomery 1997) would suggest that same-activity sites of related products (e.g., manufacturing soap and oil) may benefit from collocation. Second, if a firm is active in two value chains and the product/service behind one of them is an input for the product/service of the other, one could expect benefits from collocation of all (or some) activities in the value chains. After all, the argument for positive externalities from proximate specialized suppliers (Marshall 1929) does not require those suppliers to be independent firms.

As in the case of internal agglomeration across activities, the lack of well-developed theories and the sparse set of empirical findings do not facilitate our building a strong hypothesis with which to approach the data. Abstracting from external forces, the received wisdom would suggest that single-product firms would favor collocation for establishments that perform the same activity. Where the activity belongs to a separate value chain—e.g., to a different product/service—we can expect firms to prefer collocation for products/services that are related.

Whether the locus of attention is across or within activities, the literature on the internal drivers of location provides three main insights. First, if meaningful linkages or interdependencies exist across or within activities, in the form of knowledge or information flows, intermediate inputs, or labor sharing, firms will be more likely to collocate those activities. These linkages, which we call internal agglomeration economies, will vary by activity and appear to be asymmetric.

Second, even if those links are desirable and exist, firms may have developed firm-specific capabilities—for example, through investment in IT or organizational practices—that render geographic collocation unnecessary. Thus, location patterns observed in the data will be the result of both underlying linkages across and within activities as well as of firm-specific decisions that make those linkages more or less geographically bounded.

³ After all, Chandler's explanation for the emergence of multiunit firms is more focused on horizontal or vertical diversification rather than on the geographic dispersion of establishments performing the same activity.

Third, there are tradeoffs between internal and external location drivers and, more importantly, those tradeoffs vary by activity; for instance, even if R&D would benefit from collocating with same-firm manufacturing, its final location may be determined by the overwhelming advantage of collocating with external knowledge sources such as a research university. These tradeoffs will also vary by firm because firms can take actions to neutralize the effect of distance. For example, a firm can collocate R&D and manufacturing activities and also tap a research university in another location by promoting internships and other collaborations between the university and firm personnel.

3. Empirical design

Our empirical design examines the location decisions of organic expansions of biopharmaceutical firms in 1993–2005. Organic expansions include opening new establishments (organic external expansion) and increasing employment above a threshold in existing establishments (organic internal expansion).⁴ There is strong evidence of internal agglomeration economies when firms grow within the same establishment. Thus, failing to account for organic internal expansions could underestimate the relevance of internal economies. Furthermore, if the locations where the firm is already present are rich with external agglomeration economies, abstracting from organic internal expansions may also underestimate the importance of external agglomeration economies.

The biopharmaceutical industry is an ideal setting for several reasons. First, previous research has shown that biopharmaceutical firms tend to cluster, suggesting the existence of agglomeration economies (see, e.g., Zucker et al. 1998, Feldman and Schreuder 1996, Feldman 2003). Second, Pisano (1997) found high levels of interdependencies among activities in the value chain, suggesting the presence of potential internal agglomeration economies.⁵ Third, the industry experienced an important period of growth during our sample period. Two critical parts of this transformation were the shift from drug development, normally triggered by basic research in universities, to more applied development and the scaling-up of manufacturing. A third critical factor was the development of new activities for commercialization and support, a development which allows us to capture geographic dispersion of multiple activities within the value chain.

⁴ We exclude acquired establishments and their expansions during 1993–2005.

⁵ The biopharmaceutical applied R&D and manufacturing functions of a firm may have meaningful interdependencies since they often share similar technologies, and many doses of a drug are produced during the R&D process. There are also basic R&D activities related to the creation of new molecules that may not be linked with the manufacturing process, but are instead linked to other R&D and support activities of the firm.

3.1. Sample

Our primary data source is the establishment-level Longitudinal Business Database (LBD) of the Census Bureau. The LBD provides annual observations of the universe of U.S. establishments with payroll in the years 1976–2005, including each establishment’s date of entry, physical location, industry code, and number of employees.

Our first challenge was to identify firms in biopharmaceuticals. The traditional approach has been to select firms in a particular set of SIC codes. For example, Toole (2003) and Cortright and Mayer (2002) defined biopharmaceuticals firms as those with establishments in SIC-283 – manufacturing of medicinal chemicals and botanical products (SIC-2833), pharmaceutical preparations (SIC-2834), diagnostic substances (SIC-2835), and biological products (SIC-2836) – and in SIC-8731 (commercial R&D in the physical, engineering and life sciences research). Another approach is to identify firms using firm directories (e.g., see Zucker et al. 1998). Both approaches have pros and cons. SIC-based sampling captures all firms, whether well-known or not, but it may include firms whose scope reaches beyond biopharmaceuticals.⁶ Directory-based sampling guarantees that firms are in biopharmaceuticals, but it does not cover all firms.

We followed a hybrid approach to define our sample. Specifically, we matched LBD data to BioScan (1992), a detailed (but not exhaustive) directory of worldwide biopharmaceutical firms also used by Zucker et al. (1998), to obtain frequencies of establishments’ SIC codes for the matched firms (see Table 1.a). Three features in Table 1.a deserve to be highlighted. First, approximately 75% of Bioscan-matched firms had at least one establishment in SIC-283 or SIC-8731, suggesting that membership in these SIC codes is an appropriate criteria to identify whether a firm in LBD is in biopharmaceuticals. Second, the frequency of SIC codes allowed us to identify activities in the biopharmaceutical value chain (referred to hereafter as the *Bio-VC*): R&D (associated with SIC-8731), manufacturing (associated with SIC-283), sales (associated with SIC-5120). Third, there were establishments with SIC codes outside Bio-VC. We aggregated these other firm activities into other value chains (referred to hereafter as *Other-VCs*) that include Other-R&D (SICs 8732 to 8734), Other-Manufacturing (SICs 20 to 39; except 2830) and Other-Sales activities (SICs 50 to 59; except 5120).⁷ The rest of firm activities were classified as support for any value chain, including Bio-VC. The main support activities included business services (including headquarters), medical labs, and financial, insurance, and real estate activities (e.g., holding companies).

⁶ This is particularly the case when firms are in SIC-8731, a very aggregated group that includes labs that may not be associated with biopharmaceuticals.

⁷ Many of our base biopharmaceutical firms had facilities in both Bio-VC and Other-VCs.

Thus, our final sample spanned around 600 multi-unit firms in the LBD database, with at least one establishment in either the 3-digit SIC 283 or in SIC 8731 as of 1992 (of these, 112 firms also appeared in BioScan).⁸ A total of 335 of these firms experienced expansion in an existing establishment in Bio-VC, and 157 of them opened a new biopharmaceutical establishment during 1993–2005. Our analysis focuses on the location choices for these biopharmaceutical expansions.

3.2. Econometric Specification

The empirical analysis examines the relationship between the location of organic expansion of biopharmaceutical firms and internal and external agglomeration economies. The baseline econometric specification is as follows:

$$Expansion_{fijrt} = \beta_1 Ln(X_{fijrt-1}^{internal}) + \beta_2 Ln(X_{fijrt-1}^{external}) + \beta_3 z_{firt-1} + \gamma_r + \varepsilon_{firt} \quad (1)$$

Where $Expansion_{fijrt}$ is equal to 1 if firm f chooses economic area (EA)⁹ r to expand in industry j that is part of focal bio activity i (R&D, manufacturing, or sales)¹⁰ at time t ; $X_{fijrt-1}^{internal}$ is a set of variables that capture firm f 's geographic footprint of activities (i.e., $\square$ activity i in Bio-VC or Other-VCs) in EA r at time $t-1$; $X_{fijrt-1}^{external}$ is a set of variables that capture potential external agglomeration economies for focal activity i , in EA r at time $t-1$; z_{firt-1} is a variable that indicates whether firm f had any employment in activity i in EA r at $t-1$, γ_r is a vector of EA fixed effects, and ε_{firt} is the error term.

Recall that we considered two types of organic expansion. *External Expansion* $_{fijrt}$ is equal to 1 if firm f choose EA r to open a new establishment in industry j that is part of bio activity i at time t . There were more than 1200 external-expansions in Bio-VC activities.¹¹ *Internal Expansion* $_{fijrt}$ is equal to 1 if firm f chooses EA r to increase employment in an existing establishment in industry j that is part of bio activity i at time t at a level that is larger than the median size of new establishments opened during 1993–

⁸ We focus on multi-unit firms because it is a more homogeneous group with a portfolio of locations (at least two establishments).

⁹ Economic areas (EAs) are defined by the Bureau of Economic Analysis (BEA). There are 179 EAs covering the entire United States. To minimize concerns about differences in transportation costs, we excluded EAs in Alaska and Hawaii. EA boundaries are drawn to reflect meaningful economic regions and to ensure comprehensive regional coverage, and they have been highly stable over time (Johnson and Kort 2004).

¹⁰ There is not always a 1-to-1 map between our concept of activities and our data. Because our dependent variable is based on the expansion at the 4-digit SIC, and our independent variables are built using 4-digit employment figures, we used subscript i for activities and j for the industry within an activity. In some cases, for example, Bio-R&D, the activity consists of a single 4-digit SIC industry. In the case of Bio-Manufacturing, the activity consists of multiple 4-digit SIC industries and we need to aggregate at the activity level. Note that this aggregation, if needed, applies only to our independent variables. Our dependent variable is always at the 4-digit SIC code.

¹¹ Over 700 entries in R&D, 92 in manufacturing and 408 in sales.

2005 for the same bio-activity.¹² In other words, we assume that an increase in employment above a certain threshold is equivalent to opening a new establishment in an existing location. There were 2337 internal expansions in Bio-VC in our sample (See Table 1b).¹³

We estimated equation (1) using conditional logit models of the location decision of organic expansions for each activity in the Bio-VC (i.e., manufacturing, SIC-283; R&D, SIC 8731; and sales, SIC 5120). Because the data may include multiple observations from the same firm (i.e., firms may open multiple bio establishments over time), and because a firm's subsequent location decisions are likely to be correlated, we clustered the standard errors by firm.¹⁴

3.2.1. *External economies of agglomeration*

We built on Porter (2003) and Delgado et al. (2010a) to compute our main variables of external economies of agglomeration. Specifically, we used two measures of external economies computed the year prior to the expansion of an establishment.¹⁵ First, external agglomeration benefits may arise from the specialization of a region in the focal activity of the establishment. To capture this, we defined the specialization of region r in the activity i (*Same Bio-activity Spec_{irt}*) as its location quotient, i.e., the share of regional employment in the region–activity as compared to the share of U.S. employment in the U.S.–activity. More formally:

$$\text{Same Bio} - \text{activity Spec}_{irt} = \frac{emp_{irt}}{emp_{rt}} * \left[\frac{emp_{iUS}}{emp_{US}} \right]^{-1} \quad (2a)$$

where emp_{irt} and emp_{iUS} are employment in activity i at time t for EA r and the U.S., respectively, and emp_{rt} and emp_{US} are total employment for r and for the U.S.

Because biopharmaceutical manufacturing encompasses multiple 4-digit SICs, we needed to aggregate employment data at the activity level. Recognizing that not all pairs of industries are equally related, we aggregated employment data using weights that capture pairwise industry relatedness. Specifically, we used locational correlation of employment between industries j and k (LC_{jk}) as the building block for our relatedness weights. Locational correlation captures any type of externalities across

¹² The pseudo median size of new establishments was computed using the range of percentiles 40 to 60 to avoid disclosure problems. The thresholds corresponded to values of 7, 45 and 21 employees for Bio-R&D, Bio-Mfg, and Bio-Sales, respectively. In the sensitivity analysis we considered alternative thresholds.

¹³ Of these, 1282 in R&D, 546 in manufacturing, and 509 in sales.

¹⁴ The choice set corresponds to the group of EAs selected for expansion in our sample in 1993–2005. The selected EAs vary by biopharmaceutical activity and type of organic expansion. When we consider all biopharmaceutical organic expansions all the EAs are chosen for expansion.

¹⁵ The extent of external benefits will depend on a firm's ability to interact with other firms in the region. In this paper, we abstract from the firm-level mechanisms that facilitate external benefits.

industries (e.g., technology, skills, supply, demand, or others).¹⁶ We then transformed LC_{jk} to w_{jk} by replacing negative correlation coefficients with 0 (thus $w_{jk} \in [0,1]$) and defined $w_{jj}=1$.¹⁷ The final definition becomes:

$$\text{Same Bio} - \text{activity Spec}_{ijrt} = \frac{\sum_k w_{jk} * emp_{krt}}{emp_{rt}} * \left[\frac{\sum_k w_{jk} * emp_{kUSt}}{emp_{USt}} \right]^{-1} \quad (2b)$$

where j is the 4-digit SIC of the establishment, k indices all 4-digit SICs that map to the focal activity i , emp_{krt} and emp_{kUSt} are employment in industry k at time t for EA r and the U.S., respectively, and emp_{rt} and emp_{USt} are total employment for r and for the U.S.

A value of *Same Bio-activity Spec* greater than 1 indicates that the activity was over-represented (in terms of employment) in the EA r . For example, among the top EAs in *Same Bio-activity Spec* for Bio-R&D in the base year (1992) were Idaho Falls-Blackfoot, ID, Washington-Baltimore-Northern Virginia, DC-MD-VA-WV, Colorado Springs, CO, Austin-Round Rock, TX (with values greater than 3). In our sample, this variable had a mean of 0.783 and a standard deviation of 2.061 (see Table 1.b).

Second, agglomeration benefits may also arise from a regional specialization in other activities related to activity i . Thus, we defined the specialization of a region r in activities related to focal bio-activity i at time t (*Related Activities Spec_{irt}*) as

$$\text{Related Activities Spec}_{ijrt} = \frac{\sum_{k \neq i} w_{jk} * emp_{krt}}{emp_{rt}} * \left[\frac{\sum_{k \neq i} w_{jk} * emp_{kUSt}}{emp_{USt}} \right]^{-1} \quad (3)$$

where w_{jk} is the pairwise industry relatedness ($w_{jk} \in [0,1]$), k indices any other 4-digit SIC *traded* industry¹⁸ excluding those used to compute the *Same Bio-activity Spec* ($-i$), and the employment variables are defined as above. An EA with a *Related Activities Spec* greater than 1 provided high external agglomeration potential (i.e., the presence of related activities was greater than expected given the size of the EA); values close to 0 are associated with EAs with low external agglomeration potential. For example, among the top EAs in *Related Activities Spec* for Bio-R&D in the base year were Syracuse-Auburn, NY, Burlington-South Burlington, VT, Boston-Worcester-Manchester, MA-NH, and

¹⁶ Specifically, LC_{jk} is the correlation coefficient between regional (EA) employment in industry j and regional employment in industry k ($\text{corr}(emp_{jr}, emp_{kr})$; see Porter (2003) for further detail). Delgado et al. (2012) demonstrated that LC_{jj} significantly correlates with other pairwise activity relatedness measures, including input-output links (Ellison et al. 2010) and the coagglomeration index used by Ellison and Glaeser (1997).

¹⁷ Note that Bio-R&D and Bio-Sales activities are mapped to unique 4-digit SIC codes. Thus, equation (2b) becomes

$$\text{Same Bio} - \text{activity Spec} = \frac{emp_{jrt}}{emp_{rt}} * \left[\frac{emp_{jUSt}}{emp_{USt}} \right]^{-1}.$$

¹⁸ In contrast to *local* industries (e.g., utilities) that serve primarily the local market, *traded* industries concentrate in particular regions and sell products or services across regions. Porter (2003) identified 589 traded 4-digit SIC industries.

Washington-Baltimore-Northern Virginia, DC-MD-VA-WV (with values greater than 1.3). This variable had a mean of 0.858 and a standard deviation of 0.193 in the main sample (see Table 1.b).¹⁹

3.2.2. *Internal Economies*

Internal economies are geographically bounded intra-firm spillovers. Note that to properly estimate their impact on firms' location strategies, we needed to account for firm-level heterogeneity in the extent of relatedness between activities of the value chain. For some firms two activities may have meaningful linkages (knowledge flows, input-output links, and/or shared labor) and could then benefit from collocation, while for other firms the same activities may be unrelated. There is also heterogeneity between firms' ability to coordinate across locations. Some firms may have developed management practices (e.g., communication technologies) that allow them to break down the value chain across locations (Fort 2011). In this case, even two activities with meaningful linkages might not be geographically bounded.²⁰

To capture internal economies while recognizing firm heterogeneity, we developed various firm–region–year variables that account for the spatial organization of a firm's activities and are consistent with our measures of external agglomeration economies in equations 2 and 3. However, departing from our measures of external economies, our measures for related activities were more granular. Specifically we grouped related activities by value chain (*Bio-VC* and *Other-VCs*) and by activity (R&D, manufacturing, sales, and support).

Our measure of firm-level regional specialization by bio activity captures whether the firm employment in an activity is over-represented in a particular location (given the size of the firm and its portfolio of activities and locations), and is defined as

$$Firm\ Bio - i\ Spec_{fijrt} = \frac{\sum_k w_{fjkt} * emp_{fkrt}}{emp_{frt}} * \left[\frac{\sum_k w_{fjkt} * emp_{fkt}}{emp_{ft}} \right]^{-1} \quad (4)$$

where k indexes all 4-digit SIC codes that map to activity i ; j is the 4-digit SIC of the establishment, w_{fjkt} the firm-specific relatedness between industries j and k ; and the employment variables are as follows: emp_{fkrt} and emp_{frt} are employment in firm-EA-industry-year and in firm-EA-year, emp_{fkt} aggregates

¹⁹ We also computed an alternative measure of *Related Activities Spec* based on Porter's (2003) biopharmaceutical cluster definition, which includes twenty six industries with high interdependencies. Our findings are robust to using this measure.

²⁰ Communication technologies may work better to coordinate certain activities (well defined input–output links) than others (tacit knowledge flows). In some cases, communication technologies could increase the collocation benefits by allowing a more efficient coordination of facilities within a given location.

employment by firm-industry-year, and emp_{ft} is firm-year employment.²¹ We calculated firm-level cross-industry relatedness (w_{fjkt}) as the employment locational correlation (LC_{fjkt}) of any pair of industries across EAs where the firm had any employment.²² The variable was then transformed to values between 0 and 1 by replacing negative correlation coefficients with 0.²³ If a pair of activities of the firm tended to collocate across locations in the past ($w_{fjk}>0$), we assumed that there were meaningful geographically bounded intra-firm linkages that offered potential collocation benefits.

Analogously, we calculated firm-level regional specialization by activity in Other-VCs with the equation:

$$Firm\ Other - i\ Spec_{fijrt} = \frac{\sum_k w_{fjkt} * emp_{fkrt}}{emp_{frt}} * \left[\frac{\sum_k w_{fjkt} * emp_{fkrt}}{emp_{ft}} \right]^{-1} \quad (5)$$

Recall from Section 3.1 that the range of SICs used for *Bio-VC* and *Other-VCs* were mutually exclusive. Finally, equation 6 introduces our last main independent variable, *Firm Support Spec_{fjrt}*:

$$Firm\ Support\ Spec_{fjrt} = \frac{\sum_k w_{fjkt} * emp_{fkrt}}{emp_{frt}} * \left[\frac{\sum_k w_{fjkt} * emp_{fkrt}}{emp_{ft}} \right]^{-1} \quad (6)$$

with k indexing through any 4-digit SIC industry that maps into the support activity (as defined in Section 3.1). This variable captures the presence of a firm's support activities in region r at time t .

Table 1.b shows the descriptive statistics for each of these internal-economies variables: *Firm Bio-R&D Spec*, *Firm Bio-Mfg Spec*, *Firm Bio-Sales Spec*, *Firm Other-R&D Spec*, *Firm Other-Mfg Spec*, *Firm Other-Sales Spec*, and *Firm Support Spec*. It is worth emphasizing three features of our internal economies. First, our variables *aggregated* the presence of firms' employment across all industries k related to focal activity i (R&D, manufacturing and sales) as defined in a particular value chain across regions and time, and an observation is defined at the establishment's industry level. In this way, we were able to exploit the maximum level of heterogeneity available in our data. Second, the aggregation into activity and value chain was based on weights that emerged from actual geographic collocation patterns.

²¹ For example, if a firm has 50% of its employment in Bio-R&D and locates 100% of this activity in a single location, then *Firm Bio-R&D Spec* will be 2 in that location (and zero in all other locations).

²² We allowed the relatedness between a pair of industries to change by year because a firm's portfolio of EAs and industries changes as the firm expands (through acquisitions and new establishments). Note that this variable does not assume that benefits from collocating activities are common across firms; on the contrary, it is firm-specific and time variant.

²³ In the sensitivity analysis we used alternative measures of firm collocation patterns, including a Jaccard index and a simple matching score. For all these measures, we assumed that if a firm had only one EA, the activities located in that EA were related ($w_{fij}=1$). We also assumed that the firm's new activities (i.e., the firm diversified into new SICs) were unrelated to its existing activities ($w_{fjk}=0$). We relaxed these assumptions in the sensitivity analysis by using unweighted internal economies variables (i.e., $w_{fjk}=1$).

Third, although these variables used the same related industries as the ones we used to calculate external economies, they differed in terms of weights (firm- vs. industry-based weights) and levels of aggregation (Bio-VC, Other-VCs, and Support vs. same- and related- activity).

3.2.3. Controls

There are some potential trade-offs between internal and external location drivers that may induce firms to locate a new establishment in a new EA (i.e., in an EA where the firm had no prior employment). A decision to deviate from prior geographical patterns suggests that external benefits may dominate internal benefits. Because location into a new region could be driven by unobserved firm attributes (e.g., decreasing internal economies in existing facilities of the firm, firms with small portfolios of locations, R&D-oriented firms, etc.) and/or by changes in the external environment (e.g., radical innovations in the new location), we controlled for this by including a dummy equal to 1 if the firm had no employment in a location at $t-1$ (*Firm New EA*). This control does not apply to the models of organic internal expansions since this expansion always occur in an existing location.

Finally, we controlled for unobserved factors in an EA that could influence the extent of external and internal agglomeration benefits (e.g., physical endowments, policies that favor manufacturing activities, wages, and labor composition) by including EA fixed effects.²⁴

While we accounted for the past location patterns of any pair of firm activities, it is possible that additional, unobserved firm heterogeneity influenced firms' subsequent expansions and location decisions in our sample period. We addressed this concern in the sensitivity analysis by considering the geographical and activity specialization of firms as well as their diversification into new bio activities, since location choices in these cases could be more idiosyncratic.

4. Results

Table 2a introduces the results of estimating equation 1 using conditional logit for *all* organic expansions. Coefficients are transformed into odd-ratios to facilitate comparisons. In models 1 and 2 we examine location choices for all bio activities and in models 3, 4, and 5 for sub-samples of specific bio activities (R&D, manufacturing, and sales respectively). All models include EA fixed effects. Model 1 introduces our measures of external economies. As expected, both *Same Bio Activity Spec* and *Related Activities Spec* are positive and significant, indicating that external economies positively influence the locations where firms expand. Note that the odd ratio for *Same Bio Activity Spec* is significantly smaller

²⁴ Fixed effects by EA may also capture relevant external agglomeration economies because the external variables only vary at the EA–year in some specifications.

than odd ratio for *Related Activities Spec*. This suggests that agglomeration economies arising from activities related to the focal activity are the main external driver of location.²⁵

Model 3 adds our measures of internal economies for firm Bio-VC, Other-VCs, support activities, and the expansion into a new location (*Firm New EA*). Including these variables improves the model fit substantially; the log likelihood goes up by 3948 (41%), a significant change at the 1% level, suggesting the importance of considering internal economies in location choices. Note also that the estimated coefficients for external economies become smaller in magnitude, suggesting that not controlling for internal economies may bias the estimates of external economies.²⁶

Negative and statistically significant coefficients for *Firm New EA* across specifications provide the first piece of evidence that internal agglomerations matter.²⁷ Firms are less likely to expand in an EA where no previous activity, of any type, is located. Moving to more granular measures of internal economies, the coefficients for internal economies are positive and significant. The magnitude is statistically larger for internal economies in Bio-VC than in Other-VCs and support. The same pattern is found when focusing on the location of specific bio activities (models 3 through 5). The importance of collocating with same-firm Bio-VC is especially larger for bio manufacturing expansions, followed by R&D and sales expansions (as suggested by the magnitude of the odd ratios).

The impact of external economies varies by activity type as well. Surprisingly, the most robust findings refer to the coefficients for *Same Bio Activity Spec* being negative and significant. Statistical issues may be behind this counterintuitive finding: For models estimated using subsamples by activity, our external economies variables vary mainly by EA, with little variation over time and little or no industry variation; as such, they are highly correlated with the EA fixed effects. As a result, coefficients for external economy variables are often insignificant or have an unexpected sign. Therefore, we re-estimated all models with (1) just external economy variables or (2) just EA fixed effects.²⁸ Under both approaches, no relevant changes were observed in the coefficients of the internal economies variables across all models. With the exclusion of the EA fixed effects, the specialization of the region in activities

²⁵ This is consistent with Delgado et al. (2010a), who found that economies of agglomeration take place within clusters of related industries. They showed that clusters of industries that are related to a focal region–industry contribute to the region–industry creation of new establishments.

²⁶ We may not be able to properly disentangle the effect of external economies from the internal economies for firms that are born in a strong biopharmaceutical cluster and concentrate their facilities in that single location. The correlation of the external economies variables with the internal economies variables is small (from .03 to .14), reducing this concern. Additionally, in the sensitivity analysis we dropped firms with a single EA during the whole period and the findings are robust.

²⁷ We do not provide the coefficient of this variable because we have not tested whether it passes the LBD disclosure test.

²⁸ Results available from the authors upon request.

related to the bio-activity of the establishment (*Related Activities Spec*) has a positive and significant effect. The effect of *Same Bio Activity Spec* also becomes positive and significant with the exclusion of EAs (for all but manufacturing expansions), but the magnitude of its effect continues to be smaller than for *Related Activities Spec*.²⁹

Table 2b introduces results by organic expansion type: columns 1a to 5a for organic internal expansion (employment increases in existing establishments) and columns 1b to 5b for organic external expansion (opening of new establishments). Note that the results for organic internal expansion are very similar to those obtained for all organic expansions. All types of internal economies continue to matter for location choices, and their estimated coefficients are larger, suggesting a stronger role of internal economies on internal expansions than on the location of new establishments. The effects of external agglomerations are similar to those reported for Table 2a with and without EA fixed effects.³⁰ Finally note that the models' explanatory power is larger.

Results change when only organic external expansions are considered. Recall that they are new establishment's openings and they represent a more pure and direct location choice. Surprisingly, results in column 2b suggest that only internal economies in Other-VCs and support, and not in Bio-VC, have a positive and significant effect on new bio establishment locations. These results may be explained, in part, by differences in type of activity. Internal economies from collocating with same-firm Bio-VC have a significant positive effect only for manufacturing entry, indicating complementarities across new and existing plants. In contrast, internal economies in Other-VCs seem to matter for Bio-R&D. Insignificant estimates for *Firm Bio-VC Spec* for R&D are consistent with the idea that firms locate apart to tap new knowledge sources (Chung and Alcacer 2002) that may reside in another VC (thus the positive estimate for *Firm Other-VC Spec*). In the case of sales, new establishments would locate apart from existing sites to maximize the geographic coverage of demand. The effects of external agglomerations on organic-external expansions are similar to those reported for all organic expansions in Table 2a with and without EA fixed effects.³¹

Taken together, the results in Tables 2a and 2b reveal clear location patterns for biopharmaceutical activity. First, for all expansion types, *both* internal and external agglomerations play an important role. Second, both internal economies (as expected) and external economies (less expected) are larger in

²⁹ For Bio-Manufacturing organic expansions, the coefficient of (log of) *Same Bio Activity Spec* remains negative and significant, suggesting diseconomies from collocating with other firms' Bio-Manufacturing facilities.

³⁰ Even after the exclusion of EA fixed effects, the effect of *Same Bio Activity Spec* is noisy across specifications.

³¹ The only difference is for new Bio-Manufacturing establishments, for which neither external economies in same bio activity nor in related activities seem to matter. Further analysis reveals that new Bio-Manufacturing seems to locate in regions with specialization in same SIC (vs. in the broader same Bio activity).

models that include internal organic expansions, suggesting that research on location decisions must also consider the default option of growing in existing facilities. Third, while all types of internal economies matter for internal organic expansions, the main positive effect is, by far, for *Firm Bio-VC Spec*. In contrast, the effect of *Firm Bio-VC Spec* for new establishment expansions, although still positive, is insignificant with relevant differences by activity, as discussed above.

Now we turn to explore the extent of within- and across-activity collocation for organic internal and external expansions (Tables 3a and 3b). To do so, we break down the variables *Firm Bio-VC Spec* and *Firm Other-VCs Spec* into their component activities (R&D, manufacturing, and sales; models 1-3 and 4-6, respectively).³²

Examining organic internal expansions reveals that the positive effect of *Firm Bio-VC Spec* found in Table 2b is mostly driven by within-activity economies: The largest odd ratio for R&D is *Firm Bio-R&D Spec*, for manufacturing it is *Firm Bio-Mfg Spec*, and for sales it is *Firm Bio-Sales Spec*. Internal economies also arise across activities, but to a lesser extent than within an activity. Both Bio-R&D and Bio-Sales internal expansions are positively influenced by the specialization of the firm in Bio-Manufacturing in the location (models 1 and 3). However, neither firm Bio-R&D specialization nor Bio-Sales specialization seems relevant for the expansion of Bio-Manufacturing. These results reveal important asymmetries in the types and intensity of internal economies across activities.

The findings regarding collocation across and within activities in the Bio-VC are robust when we break down *Firm Other-VCs Spec* by activity (columns 4, 5, and 6 in Table 3a). Interesting patterns of collocation across value chains emerge. Internal expansions in manufacturing (sales) are more likely to occur in locations with a strong presence of same-firm manufacturing (sales) *regardless* of the VC type. That is not the case of R&D, where only the presence of R&D in Bio-VC has a positive effect.

Now we turn to review the results for external expansion in Table 3b. We find relevant differences between internal and external expansions for the location of bio R&D, an activity where accessing knowledge in new locations may be especially relevant. The insignificant effect of *Firm Bio-VC Spec* for Bio-R&D activities in Table 2b extends to each activity (insignificant coefficients for *Firm Bio-R&D Spec*, *Firm Bio-Mfg Spec* and *Firm Bio-Sales Spec* in models 1 and 4 in Table 3b). The lack of significant links between the location of new Bio-R&D establishments and the presence of same-firm Bio-Manufacturing seems to contradict previous research (Tecu 2011), and may emerge for different reasons. Bio-R&D may not have relevant (geographically bounded) interdependencies with Bio-Manufacturing,

³² Note that the findings in Tables 3a and 3b are consistent with those in Table 2b (i.e., findings for Other-VC Spec and Firm Support Spec that were significant in Table 2b remain significant in Tables 3a and 3b).

especially in the case of science-oriented R&D. It may also reflect the tradeoffs between internal and external drivers. If locations that are more conducive to knowledge spillovers are not good for manufacturing, then a firm that wants to exploit external economies (e.g., collocation with other R&D firms and universities) will decide not to collocate its manufacturing and R&D functions. Finally, new (large) manufacturing establishments may have an R&D team inside the plant, and this could explain why they do not collocate with R&D establishments of the same firm.

In contrast, we find evidence of within-activity and across-activity collocation for other bio activities. Results suggest strong within-activity dependencies for new bio manufacturing establishments, consistent with organic-internal expansions. New manufacturing establishments are more likely to be located in EAs where there is a higher presence of same-firm manufacturing in biopharmaceuticals (positive and significant coefficient for *Spec in Bio-Mfg* in models 2 and 5). In contrast, for Bio-Sales establishments we find weak within-activity interdependencies and strong across-activity interdependencies with bio-manufacturing (models 3 and 6). Sales activities that aim to cover geographically dispersed customers may account for low within-activity collocation.

The findings regarding collocation across and within activities in the Bio-VC are robust when we break down *Firm Other-VCs Spec* by activity (columns 4, 5, and 6 in Table 3b). We find relevant within-activity and across-activity collocation with Other-VCs with differences by the focal bio activity of the new establishment, but we need to be cautious since these variables are sparse (especially for *Firm Other-R&D Spec* in models 5 and 6). For Bio-R&D, the positive and significant effect of *Firm in Other-VCs Spec* found in Table 2b is driven by R&D and sales and no manufacturing (positive and significant coefficients for *Firm in Other-R&D Spec* and *Firm in Other-Sales Spec* in model 4). Although positive spillovers across labs in different knowledge domains may account for the positive and significant coefficient for *Firm Spec in Other-R&D*, it is harder to find a plausible mechanism through which sales in Other-VCs may positively impact R&D location (while sales in Bio-VC do not have a significant effect). For Bio-Manufacturing we find evidence of collocation with same-firm Other-R&D (model 5). For Bio-Sales we do not find evidence of internal economies with any activity in Other-VCs (model 6).

Tables 3a and 3b point to different effects of within and across activity internal economies. Internal expansions of Bio-R&D show strong internal economies with same bio activity. In contrast, new Bio-R&D establishments show within-activity economies but only across value chains (collocating with other

R&D).³³ Both types of R&D expansions seem to benefit from across-activity economies with sales. Manufacturing shows within-activity economies for all types of organic expansions. Sales shows within-activity economies only for internal organic expansions, and strong across-activity economies with Bio-Manufacturing for all types of organic expansions.

In summary, our findings offer relevant insights. First, both internal and external economies play a role in the location of biopharmaceutical activity. Second, internal economies of agglomeration arise within and across activities. Third, the effects of across-activity and within-activity internal economies vary by activity and type of organic expansion. Finally, the internal economies that arise across activities are asymmetric.

4.1. Sensitivity tests: alternative samples and variable definitions

To address some econometric concerns, we conducted several alternate tests using different variable definitions (both for internal and external economies) and samples.

In terms of internal economies, our definition used weights based on locational correlations to measure firm-specific relatedness between activities. We relaxed the concept of relatedness between firm activities by assuming that all activities are equally related and geographically bounded (i.e., $w_{ijk} = 1$ for all pair of 4-digit SICs). Results using this alternative definition of relatedness are similar in statistical significance to those in Table 2 and Table 3, with slight changes in the magnitude of the effects. For the models that examine collocation within and outside Bio-VC, we find that unweighted internal economies result in greater coefficients for *Firm Bio-VC Spec* for most models.³⁴ This increase seems driven by an increase in the magnitude of within-activity economies (especially for organic-internal expansions; Table 3a). The difference between weighted and unweighted results suggests that accounting for firm-specific interdependencies offers a more accurate estimate of the role of internal economies.

Additionally, we tested whether our mapping of Bio-VC activities to SICs drives our findings. Specifically, for the samples of organic biopharmaceutical expansions, we considered a single value chain and examined collocation across broadly defined activities (i.e., without separating out Bio-VC and Other-VCs). This redefinition has the benefit of reducing sparsity for the explanatory variables as well as relaxing the definition of the core value chain of a biopharmaceutical firm. Findings with this new

³³ When we consider the sample of all organic expansions (not reported), for Bio-R&D expansions the bio-activity that matters is the firm specialization in same activity. Bio-R&D also benefits of collocation with each activity in Other-VCs, consistent with the exploratory nature of R&D in biopharmaceuticals.

³⁴ The exception is for the location of new Bio-Manufacturing establishments, with a relevant decline in magnitude of *Firm Bio-VC Spec* that becomes insignificant (model 4b in Table 2b), which is also associated with a relevant decline in magnitude (though not in statistical significance) of *Firm Bio-Mfg Spec* (models 2 and 5 in Table 3b).

definition confirm prior results in Tables 3a and 3b regarding within-activity and across-activity internal economies.

In terms of sampling, we applied specific criteria to identify biopharmaceutical firms from the LBD data. Because it may be possible that some of these firms are not actually in biopharma, we re-estimated our models using only firms that were in the BioScan directory. Results using this subsample of firms are very similar to those obtained from the extended sample across specifications.³⁵ To further control for unobserved attributes of firms that could drive location decisions, we dropped different subsamples of expansions. First, we dropped organic expansions if a firm has a single EA at $t-1$. Firms that have a single location during the whole period could be especially problematic since the initial external drivers that pulled them to their current location may not be disentangled from the internal forces that induce them to expand in the same location. Very few firms in our sample fall into this group and, not surprisingly, our findings are robust to their exclusion. Second, we dropped entries if a firm has only a single bio-activity at $t-1$ (e.g., firm only has employment in SIC-8731 or only in SIC-2830), for several reasons. First, these specialized firms will not be exposed to internal economies across activities. Second, firms that during the period had only employment in Bio-R&D may not be biopharmaceutical firms. Although there are a non-negligible number of firms in this group, results obtained by dropping them are similar in sign, magnitude, and significance across specifications. Third, we also dropped expansions into new bio-activities (e.g., manufacturing firm opens a lab) because there could be unobserved firm attributes that induce diversification into new activities (e.g., younger or smaller firms). Our findings remain robust with the exclusion of these observations. Finally, we considered two alternative samples for organic-internal expansions. First, we dropped internal expansions of establishments that were created after 1992 (25% of the expansions) because new establishments are expected to grow in a given location across time. The results are very similar after dropping these observations. Second, we considered alternative thresholds to define internal-organic expansions that take into account the size of the expanding firms.³⁶ The number of organic expansions only increases slightly with this new criterion and the same findings hold.

In terms of external economies, Glaeser and Kerr (2009) have suggested alternative measures for external agglomeration economies that are orthogonal to agglomeration levels. While their measures work better to capture external economies among manufacturing activities, we used a variation of these variables proposed by Alcacer and Chung (2012) as an additional test. We re-ran the specifications in

³⁵ The main difference observed using the BioScan sample was for internal expansions of Bio-R&D. In this case the largest odd ratio was not for *Firm Bio R&D Spec* (within-activity collocation) but rather for *Firm Bio-Mfg Spec*. Furthermore, *Firm Bio-Sale Spec* also mattered.

³⁶ The new thresholds are based on the median size of new biopharmaceutical establishments by both bio-activity and firm size (small vs. large). This criterion takes into account that larger firms tend to open larger establishments.

Table 2a using these measures and the estimated coefficients of the internal economies are robust. The effects of the external economies are also consistent with our main findings.³⁷

5. Conclusions

This paper examined the extent to which the geographical location of distinct activities in the value chain (manufacturing, R&D, or sales) is explained by external agglomeration economies (i.e., geographically bounded inter-firm spillovers) and by internal agglomeration economies (i.e., geographically bounded intra-firm spillovers). We argued that the geographical location decision is a tradeoff between external drivers pulling firms to geographically disperse activities and internal drivers pushing within-firm collocation, either across activities (e.g., manufacturing and R&D) or within activities (e.g., multiple R&D labs).

We tested our conceptual framework using data for organic expansions in the U.S. by firms in biopharmaceuticals in 1993–2005. We considered two types of organic expansions: internal (an increase in employment in existing establishments) and external (opening new establishments). Our findings offer relevant insights. First, *both internal and external economies play a role in the location of biopharmaceutical activity*. Overall, we find that internal and external economies exert a greater influence on internal expansions than on the location of new establishments. Second, *internal economies of agglomeration arise within and across activities*. Third, *the effects of across-activity and within-activity internal economies vary by activity and type of organic expansion*. Internal expansions of Bio-R&D show strong internal economies with same bio activity. In contrast, new Bio-R&D establishments collocate with other R&D. Both types of R&D expansions seem to benefit from across-activity economies with sales. Manufacturing shows within-activity economies for all types of organic expansions. Sales shows within-activity economies only for internal organic expansions, and strong across-activity economies with bio-manufacturing for all types of organic expansions. Finally, *across-activity internal economies are asymmetric*. For example, organic expansions of Bio-Sales activity seem to collocate with existing manufacturing establishments, but organic manufacturing expansions do not collocate with sales.

These insights offer important contributions to the literature. They suggest that focusing on just one side of agglomeration economies may produce biased estimates due to omitted variables, e.g., the effects of external agglomeration economies may be overestimated if internal agglomerations are not included. Similarly, failing to consider all activities in the value chain may lead to omitted relationships that can also bias results. For example, estimates of the link between manufacturing and R&D may be biased if

³⁷ The level of employment in the focal bio-activity in a location has a small effect on firm expansion; and external economies seem to arise mainly from (demand) linkages with related activities in the location.

sales, which affects manufacturing and R&D in different ways, is not simultaneously considered. Also, considering just one type of expansion may mask actual relationships in the data. For example, we show that the role of internal and, to a lesser extent, external economies vary depending on whether firms expand by increasing activity levels in existing establishments instead of opening new establishments. After all, the default alternative to a new location is to stay in an existing location—an issue that is absent in most of the location literature. These three issues—internal and external economies being relevant, all activities in the value chain being related distinctly, and effects that vary by expansion type—emphasize the need for a comprehensive framework, both at the theoretical level and at the empirical level, to understand the spatial organization of firms.

Several avenues for further research remain. First, the current empirical analysis focuses on expansions of biopharmaceutical firms. One could extend the analysis to other industries, such as semiconductors and aerospace, to determine how general our findings are. Cross-industry studies would also help by bringing more variation across time and EAs, a requisite for better capturing external agglomeration economies. Second, the effect of internal and external economies may vary across time and our results may reflect a specific stage of the life cycle of biopharmaceuticals. Future research that explores these dynamics would greatly enrich our understanding of the spatial organization of firms. Third, in this paper we assumed that firms' location decisions are driven by the goal of maximizing profitability and we abstract from the role of location choices on firm performance. In related work, we plan to examine the effects of internal and external economies on the subsequent performance of new facilities and of the firm as a whole. Fourth, we have taken into account the spatial organization of firms with a novel approach, but we did not examine the business practices that shape firms' spatial organization. The location choice and performance of firms may depend on firm management practices that increase the extent of intra-firm and inter-firm interactions (e.g., outsourcing practices, labor mobility practices, IT investments; see e.g., Fort 2011). Fifth, we focused on expansion, but the allocation of activities may imply also contraction of an activity due to internal and external diseconomies. Thus research that focuses on variation in employment levels (both positive and negative) as the dependent variable may refine our findings. Finally, we did not look at overseas expansions due to data limitations. This omission is less important in our empirical setting since most American biopharmaceutical firms did not globalize during the period study, and the U.S. provided better biopharmaceutical clusters. Nonetheless, future research should consider the tradeoffs between internal and external economies when firms expand globally (see, e.g., Beugelsdijk et al. 2010).

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Table 1.a: Top-10 Industry codes (SICs) of BioScan firms in 1992

Value Chain Activity	SIC Label	SIC code	No. firms	% of firms (out of 395)
Bio-R&D	Commercial physical & biological research	8731	168	43%
Bio-Mfg	Includes SICs 2833-to-2836	2830*	127	32%
Bio-Mfg	Diagnostic substances	2835	55	14%
Bio-Mfg	Pharmaceutical preparations	2834	51	13%
Bio-Mfg	Biological products	2836	47	12%
Bio-Sales	Drugs, proprietaries, & sundries-wholesale	5120	45	15%
Support	Holding companies	6719	42	11%
Other-Mfg	Industrial organic chemicals, n.e.c.	2869	40	10%
Other-Sales	Medical & hospital equipment-wholesale	5169	37	9%
Support	Medical laboratories	8071	30	8%
Other-Mfg	Surgical medical instruments	3841	29	8%

Note: 2830 (sum firms in 2833-to-2836).

Table 1.b: Variables and descriptive statistics

	Definition	Organic-All Obs.=226k	Organic-Internal Obs.=156k	Organic-External Obs.=51k
Expansions_t	Dummy 1 if EA selected for expansion in industry j through an existing establishment (organic-internal) or a new establishment (organic-external)	.015 (.121)	.015 (.121)	.024 (.153)
Internal Economies_{t-1}				
Firm Bio-VC Spec	Firm Bio-Value chain (SICs 8731, 2830, 5120) employment specialization in EA	0.146 (10.235)	0.170 (11.757)	0.218 (7.328)
Firm Bio-R&D Spec	Firm Bio-R&D (SIC 8731) employment specialization in EA	0.050 (3.436)	0.061 (3.966)	0.086 (4.271)
Firm Bio-Mfg Spec	Firm Bio-Mfg (SIC 283) employment specialization in EA	0.033 (0.689)	0.042 (0.777)	0.026 (0.520)
Firm Bio-Sales Spec	Firm Bio-Sales (SIC 5120) employment specialization in EA	0.140 (9.957)	0.160 (11.344)	0.174 (6.441)
Firm Other-VCs Spec	Firm Other-Value Chains employment specialization in EA	0.093 (2.545)	0.119 (3.023)	0.083 (1.265)
Firm Other-R&D Spec	Firm Other-R&D employment specialization in EA	0.029 (2.713)	0.030 (2.723)	0.024 (2.034)
Firm Other-Mfg Spec	Firm Other-Mfg employment specialization in EA	0.022 (0.650)	0.027 (0.723)	0.032 (0.804)
Firm Other-Sales Spec	Firm Other-Sales employment specialization in EA	0.172 (11.526)	0.215 (13.725)	0.142 (3.601)
Firm Support Spec	Firm support activity employment specialization in EA	0.096 (3.159)	0.126 (3.612)	0.061 (2.138)
External Economies_{t-1}:				
Same Bio-activity Spec	EA specialization in same bio activity than focal establishment	0.783 (2.061)	0.958 (2.327)	0.728 (1.775)
Related Activities Spec	EA specialization in other activities related to the focal industry of establishment	0.858 (0.193)	0.892 (0.189)	0.860 (0.195)

Note: Number of observations is rounded to facilitate disclosure.

Table 2a: Biopharmaceutical organic expansions: Collocation within and outside the Bio Value Chain (Conditional Logit model; Odd ratios)

	Bio-VC (1)	Bio-VC (2)	Bio-R&D (SIC 8731) (3)	Bio-Mfg (SICs 283X) (4)	Bio-Sale (SIC 5120) (5)
Internal Economies					
Ln Firm Bio-VC Spec		1.446** (0.030)	1.349** (0.036)	1.690** (0.050)	1.269** (0.045)
Ln Firm Other-VCs Spec		1.093** (0.018)	1.146** (0.024)	1.078** (0.031)	1.055 (0.030)
Ln Firm Support Spec		1.092** (0.012)	1.096** (0.014)	1.120** (0.043)	1.068** (0.021)
Firm New EA		Neg**	Neg**	Neg**	Neg**
External Economies					
Ln Same Bio Activity Spec	1.207** (0.065)	1.026 (0.036)	0.831 (0.026)	0.682** (0.038)	0.542** (0.085)
Ln Related Activities Spec	94.096** (65.843)	18.803** (13.003)	0.612 (0.368)	90.327** (145.181)	1.460 (1.595)
EA Fixed Effects	Yes	Yes	Yes	Yes	Yes
Pseudo R-sq	0.268	0.573	0.572	0.726	0.431
Log Likelihood	-9470	-5521	-2764	-718	-1517
Firms	335	335	237	120	83
Obs	226k	226k	100k	37k	22k

Notes: Standard errors are clustered by firm. ** Significant at 1%, * significant at 5% level.

Table 2b: Biopharmaceutical organic expansions (Organic-internal vs. Organic-external): Collocation within and outside the Bio Value Chain (Conditional Logit model; Odd ratios)

	Organic-Internal					Organic-External (new establishments)				
	Bio-VC		Bio-R&D	Bio-Mfg	Bio-Sales	Bio-VC		Bio-R&D	Bio-Mfg	Bio-Sales
	(1a)	(2a)	(3a)	(4a)	(5a)	(1b)	(2b)	(3b)	(4b)	(5b)
Ln Firm Bio-VC		2.402**	2.459**	2.373**	1.997**		1.045	1.001	1.276**	0.970
Spec		(0.070)	(0.103)	(0.115)	(0.133)		(0.035)	(0.060)	(0.087)	(0.052)
Ln Firm Other-VCs		1.138**	1.148**	1.099*	1.113**		1.053*	1.153**	1.002	1.011
Spec		(.024)	(0.028)	(0.047)	(0.035)		(0.024)	(.038)	(0.044)	(0.036)
Ln Firm Support		1.146**	1.126**	1.155**	1.159**		1.034*	1.031	0.996	1.015
Spec		(0.018)	(0.021)	(0.056)	(0.042)		(0.017)	(0.025)	(0.055)	(0.034)
Firm New EA							Neg**	Neg**	Neg**	Neg**
Ln Same Bio	1.168*	0.947	0.848**	0.549**	0.318**	1.274**	1.215**	0.929	0.764*	0.880
Activity Spec	(0.086)	(0.046)	(0.040)	(0.062)	(0.134)	(0.093)	(0.070)	(0.040)	(0.081)	(0.199)
Ln Related	257.8**	59.91**	1.166	331.2*	17.9	13.27**	6.510**	0.702	1.922	0.999
Activities Spec	(223.8)	(60.64)	(1.061)	(831.9)	(53.3)	(8.301)	(3.877)	(0.593)	(3.080)	(1.569)
EA Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pseudo R-sq	0.250	0.738	0.734	0.818	0.655	0.227	0.258	0.255	0.223	0.208
Log Likelihood	-7027	-2451	-1246	-395	-559	-3086	-2962	-1603	-257	-852
Firms	317	317	222	107	66	157	157	92	48	60
Obs.	156k	156k	67k	28k	13k	51k	51k	23k	3k	9k

Notes: Standard errors are clustered by firm. ** Significant at 1% level, * significant at 5% level.

Table 3a: Biopharmaceutical organic-internal expansions: Collocation within and across activities

	Bio-R&D (1)	Bio-Mfg (2)	Bio-Sales (3)	Bio-R&D (4)	Bio-Mfg (5)	Bio-Sales (6)
Ln Firm Bio-R&D Spec	3.606** (0.221)	1.108 (0.158)	1.063 (0.070)	3.605** (0.220)	1.111 (0.162)	1.104 (0.064)
Ln Firm Bio-Mfg Spec	2.080** (0.174)	2.149** (0.080)	1.311** (0.049)	1.974** (0.147)	2.149** (0.081)	1.319** (0.047)
Ln Firm Bio-Sales Spec	1.126 (0.217)	1.117 (0.065)	2.303** (0.169)	1.076 (0.155)	1.117 (0.066)	2.311** (0.172)
Ln Firm Other-VCs Spec	1.149** (0.029)	1.065 (0.045)	1.125** (0.040)			
Ln Firm Other-R&D Spec				1.042 (0.090)	2.507* (1.108)	2.197** (0.266)
Ln Firm Other-Mfg Spec				1.243** (0.055)	1.081* (0.034)	1.022 (0.058)
Ln Firm Other-Sales Spec				1.138** (0.056)	0.983 (0.043)	1.145** (0.032)
Ln Firm Support Spec	1.141** (0.021)	1.093 (0.052)	1.165** (0.040)	1.145** (0.020)	1.094 (0.054)	1.162** (0.038)
Ln Same Bio Activity Spec	0.840** (0.041)	0.619** (0.075)	0.347** (0.137)	0.843** (0.041)	0.624** (0.078)	0.344** (0.142)
Ln Related Activities Spec	1.131 (1.053)	45.761 (134.98)	17.390 (53.171)	1.107 (1.010)	47.001 (147.015)	16.223 (48.491)
EA Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
Log Likelihood	-1275	-336	-545	-1272	-333	-542

Notes: Table reports odd ratios. Standard errors are clustered by firm. ** Significant at 1% , * significant at 5% level.
Firm Other-R&D Spec has high sparsity in models 5-6 and so we are cautious about the estimated effect.

Table 3b: Biopharmaceutical organic-external expansions: Collocation within and across activities

	Bio-R&D (1)	Bio-Mfg (2)	Bio-Sales (3)	Bio-R&D (4)	Bio-Mfg (5)	Bio-Sales (6)
Ln Firm Bio-R&D Spec	1.001 (0.075)	1.208 (0.382)	1.209 (0.133)	1.002 (0.074)	1.172 (0.367)	1.197 (0.138)
Ln Firm Bio-Mfg Spec	1.051 (0.332)	1.524** (0.142)	1.241* (0.111)	1.057 (0.341)	1.501** (0.152)	1.230* (0.110)
Ln Firm Bio-Sales Spec	1.207 (0.160)	1.094 (0.094)	0.959 (0.058)	1.201 (0.161)	1.101 (0.093)	0.955 (0.060)
Ln Firm Other-VCs Spec	1.153** (0.038)	0.995 (0.046)	1.010 (0.036)			
Ln Firm Other-R&D Spec				1.263** (0.099)	16.272* (4.396)	Omitted
Ln Firm Other-Mfg Spec				1.065 (0.067)	0.999 (0.064)	1.044 (0.026)
Ln Firm Other-Sales Spec				1.241** (0.101)	0.883** (0.033)	1.018 (0.047)
Ln Firm Support Spec	1.031 (0.026)	0.978 (0.056)	0.999 (0.034)	0.989 (0.059)	0.978 (0.056)	0.994 (0.033)
Firm New EA	Neg**	Neg**	Neg**	Neg**	Neg**	Neg**
Ln Same Bio Activity Spec	0.929 (0.041)	0.784* (0.087)	0.906 (0.205)	0.783* (0.086)	0.784* (0.087)	0.906 (0.206)
Ln Related Activities Spec	0.716 (0.604)	1.457 (2.421)	0.966 (1.533)	1.629 (2.775)	1.457 (2.421)	0.851 (1.375)
EA Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
Log Likelihood	-1603	-256	-847	-1601	-252	-846

Notes: Table 3a notes apply.