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The Evolution of Firm Growth Dynamics in the US Pharmaceutical Industry: Is 'Structure' in the Growth Process Related to Size and Location Dynamics?

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The Evolution of Firm Growth Dynamics in the US Pharmaceutical Industry: Is 'Structure' in the Growth Process Related to Size and Location Dynamics?

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Abstract:

The paper studies the dynamics of firm growth and the firm size distribution in the pharmaceutical industry from 1950 to 2003. Growth dynamics are studied in the context of how the size composition of firms changes, how innovation patterns (patents) change, and how location leads to growth differentials among US firms. It is found that the growth advantage of small pharmaceutical firms increases after the 1980s as small firms become more active in patenting and their patenting activities become more 'persistent'. Location is found to affect growth differences only for the most innovative firms (i.e. for non innovative firms, location does not matter). For this group of firms, California firms which are much smaller in size, yet more active and persistent in patenting are found to grow significantly faster than their counterparts in the New York-New Jersey-Connecticut Tri-State region. The bimodal shape of the firm size distribution is found to *emerge* towards the end of the 1970s precisely when a new division of labor between large and small firms sets in. Implications of location dynamics for firm growth and the non-gaussian behavior of the size distribution are highlighted.

Keywords: firm growth, innovation, industry dynamics, pharmaceutical industry.

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INTRODUCTION

The paper studies firm growth dynamics in the pharmaceutical industry between 1950 and 2003. The objective is to study the properties of firm growth in a particularly innovative sector which has undergone intense changes in its knowledge base over the last 50 years. We ask whether the (time series) patterns of firm growth, as well as the evolution of the firm size distribution, has changed alongside such transformations, and in particular, whether the degree to which firm growth can be described as "random"— as opposed to more "structured" (e.g., due to various types of increasing returns) — has changed over time. Central to this question is the different growth behaviour of (a) small and large firms and (b) firms located in different regions of the US. One of our key results, not found in the existing literature, concerns the facts that the presence of 'structure' is not a static characteristic of growth dynamics but *emerges* in a specific period of time (post-1980s), and that differs between geographic regions. Another key result is that regional differences only matter for the innovative firms.

(1) TRANSFORMATIONS IN THE PHARMACEUTICAL INDUSTRY

Innovation dynamics in the pharmaceutical industry went through significant changes in the 1970s and 1980s as the *guided search* techniques diffused among pharmaceutical firms, the biotechnology revolution initiated new avenues for drug discovery and innovations became less trial and error based and more incremental (GAMBARDELLA, 1995; HENDERSON et al.; 1999; NIGHTINGALE, 2000). The dominant search techniques in the pre-1980s have been described in the literature as **"random search"**, since a typical pharmaceutical research program would randomly screen through a massive number of molecules in search of a cure for a disease (GAMBARDELLA, 1995; NIGHTINGALE, 2000). With the radical developments in information technology, combinatorial chemistry, enzymology and bioinformatics (as well as increased public

expenditure in pharmaceutical research), the ability of scientists to understand the biological and chemical phenomena that underlie diseases was drastically improved. In the post-1980s, scientists were able to “design” an “ideal” molecule that would potentially cure a disease and hence this period is referred to as the **“guided search”** phase in the industry history (GALAMBOS and STURCHIO, 1998; GILSING and NOTEBOOM, 2006; LACETERA and ORSENIGO, 2001).

With the shift from random to guided search techniques, the industry witnessed the entry of many small pharmaceutical firms and these new firms started playing an increasingly important role in innovations of the post 1980 period. Emergence of the small pharmaceutical firms in the post 1980 period together with the biotechnology revolution led the way to the division of innovative labour between the small and large firms with small firms often playing an important role in the earlier stages of the drug discovery process while large firms took charge of drug development, clinical trials, the regulatory review process and marketing activities (GAMBARDELLA, 1995; PISANO, 1997; HOPKINS et al, 2007).

This paper addresses two specific aspects of firm growth behavior which have received relatively little attention in the literature: (a) the evolution of firm growth dynamics over the course of this industry’s evolution and (b) how geographical location affects the growth behavior of firms in an industry. We first briefly review in section 2 some of the literature that looks at firm growth behaviour, its evolution, and the relationship between firm growth and geographical location. Section 3 reviews the data and methodology. Section 4 discusses the results and the implications for our understanding of the presence of ‘structural’ factors behind firm growth. Section 5 concludes.

(2) FIRM GROWTH DYNAMICS

2.1. Evolution of Firm Growth

The few empirical studies which consider this issue suggest that firm growth dynamics indeed evolve over the course of industry evolution. For instance, CABRAL AND MATA (2003) observe that the firm size distribution is not log-normal throughout the history of an industry but starts off as an extremely right skewed distribution and then converges to log-normal distribution. They argue that this is related to the way that small and young firms gain more access to finance over time. LOTTI AND SANTARELLI (2004) highlight the inter-industry differences in terms of the pace and path of convergence to a log-normal distribution. They conclude that the convergence is much slower in mature and more traditional industries.

GEROSKI AND MAZZUCATO (2002) find the stochastic firm growth model in Gibrat's Law (GIBRAT, 1931) to accurately describe firm growth behavior only in early phases of the industry life cycle when innovation is more unsystematic and radical, and in which market shares are more unstable. LOTTI et al. (2007) note that firm growth process converges to a Gibrat-like behaviour through time as a result of market selection as well as the active and passive learning processes.

The paper adds to this literature by focusing on the way in which growth behavior evolves in an industry which has undergone major changes in the way that innovation is carried out, and in which the distribution of innovative firms has changed significantly both in terms of size and location. For instance, which phase(s) of the industry evolution- if any- can be characterized by random firm growth patterns? Does one find a stronger and more systematic (negative) relationship between firm size and firm growth

in periods when small firms innovate more actively? Do the answers to these questions depend on the location of firms?

2.2. Geographical Location as a Determinant of Firm Growth

The literature on firm growth spans a large spectrum from models where firm growth has no apparent underlying structure (quasi-random), to empirical studies that point to the presence of systematic economic factors at work in firm growth (See CAVES, 1998 and SUTTON, 1997 for a review). Empirical studies identify various forms of *structural dynamics* inherent to the growth process such as a negative relationship between firm size and growth rates (DUNNE AND HUGHES, 1994; EVANS, 1987; HART AND OULTON, 2001; PRAIS, 1976), a negative relationship between firm size and the variance of growth (DUNNE ET AL., 1989; HALL, 1987; HYMER AND PASHIGIAN, 1962), persistence in growth behavior (CHESHER, 1979; BOTAZZI ET AL., 2005; CONTINI AND REVELLI, 1989) as well as the presence of Non-gaussian properties in the (log) firm size distributions (i.e. multi-modality) and growth rate distributions (i.e. fat tails) (AXTELL, 2001; BOTTAZZI ET AL., 2003; REICHSTEIN AND JENSEN, 2005). Additionally, several systematic factors such as the innovative activities of firms (GEROSKI AND TOKER, 1996), ownership structure of the firm, links with external firms, founder specific characteristics and external factors related to the environment are found to determine the growth performance of firms (See ALMUS and NERLINGER, 1999 for a review).

Even though this body of literature offers a rigorous analysis of firm growth behaviour and its determinants, the implications of geographic location for firm growth have been mostly overlooked and location still remains a "*neglected determinant*" of firm growth in most of the firm growth literature (AUDRETSCH AND DOHSE, 2007).

The location of a firm is an important determinant of its growth performance due to factors like pooling of human capital, proximity to non-traded inputs and specialized goods as well as easy access to markets (AUDRETSCH and DOHSE, 2007).

More importantly, the cost of benefiting from knowledge spillovers is lowered by geographical proximity which becomes especially important for the assimilation of the tacit components of knowledge (AUDRETSCH and LEHMANN, 2005). Technological clusters drive dynamic increasing returns in innovation due to increased number of opportunities for socialization and knowledge sharing (in the form of formal and informal meetings) within a regional network of firms and other institutions such as universities and public research labs. Moreover, the concentration of other benefits such as the development of business networks (i.e. contacts and business relationships), venture capital availability, the size and growth of the market and quality of the local labour supply within a regional network contribute to the success of the firms in the region (BIRLEY and WESTHEAD, 1990; COOKE, 2002, 2005; FELDMAN AND MASSARD, 2002 among others).

Only recently a small number of empirical studies have investigated that locational divides are translated into growth differentials among firms. While these studies use different proxies for firm size and growth (e.g. employment, revenues or total assets), the general results confirm that location matters for the growth performance of firms. NORTH and SMALLBONE (1995) find that the employment growth of firms differs significantly in the three UK regions they consider: London, outer metropolitan areas of South East England and the remote areas of North England. They emphasize that firms in urban and rural areas follow different 'growth strategies'. In subsequent work, NORTH and SMALLBONE (2000) show that the 'hi-tech' firms located in *accessible* rural areas

of the UK grow faster than similar firms in *remote* rural areas, which have a lower concentration of hi-tech firms. ALMUS and NERLINGER (1999) find that location-specific factors such as population density and the wage rates of different counties determine the growth rates of the new technology based German firms.

Evidence also suggests that the impact of location on firm growth is stronger for manufacturing firms and in science based sectors. REICHSTEIN and DAHL's (2004) results based on 9000 Danish firms indicate that the increased clustering of an industry within a region affects the growth rates of firms in that industry positively. This applies mainly for science based industries. Similarly, AUDRETSCH and DOHSE (2007) show that the impact of location is most significant for small and young firms in the most knowledge intensive sectors: *"Regions abundant in knowledge resources appear to provide a particularly fertile soil for the growth of young, technology-oriented firms" (p.100).* HOOGSTRA and VAN DIJK (2004)'s results from the analysis of 35,000 Dutch firms between 1994 and 1999 indicate that the location-specific factors have an important role in determining the growth rates of firms especially in the manufacturing sector and not so much for the office related activities (e.g. business services).

This paper investigates regional differences in terms of the characteristics of pharmaceutical firms and their growth performance. As indicated in POWELL et al. (2002), the US life sciences industry is clustered in a relatively small number of geographical regions such as the NYC Tri-State region (including New Jersey and Connecticut) and the state of California where the San Francisco Bay Area (including Berkeley, Oakland and Silicon Valley) and San Diego are the two main clusters.

The Sorrento Valley biotechnology cluster is the main agglomeration in California around which the life sciences industry developed starting with the biotechnology revolution. Biotechnology opened up new research avenues for the pharmaceutical industry by making it easier to synthesize big and complex human proteins such as insulin by modifying the genetic material of living cells using recombinant techniques to produce the required proteins (DREWS, 2001; HENDERSON et al, 1999). As HOPKINS et al. (2007) show, the technology platform alliances between the pharmaceutical firms and biotechnology firms have exponentially increased over the years (see p.581). California presents a relatively young locational setting where pharmaceutical firms can be in close proximity to the leading biotechnology firms and hence, can tap into the most recent developments in the biotechnology field more easily.

The NYC Tri-State region, on the other hand, is an older cluster where more established pharmaceutical firms are located. These firms have stronger capabilities in chemistry based drug research techniques and stayed away from being involved in biotechnology research until the late 1990s (GALAMBOS and STURCHIO, 1998; MALERBA and ORSENIGO, 2002).

In what follows we question whether being located in one of these two regions is more advantageous for the growth performance of US pharmaceutical firms and if so, whether location affects the growth performance of all types of firms or only the “innovative” firms, as suggested in the literature. Hence, the paper fills an important gap in the literature by studying both the dynamic times series properties of growth rates, and the size distribution, while also emphasizing the role of location differences.

(3) DATA AND METHODOLOGY

An unbalanced panel of 256 pharmaceutical firms that were quoted on the US stock exchange between 1950 and 2003 constitutes the main dataset in this paper[1]. The data was purchased from the customized data department of Compustat and includes descriptive and geographic information on pharmaceutical firms from 16 different countries (82% of the firms have the USA as their country of domicile), along with industrial and financial data on these firms (all monthly data except for R&D, employment and net income which are only available on an annual basis)[2].

Firm size is measured in terms of (logarithm) revenues and the **firm growth rate** is the change in firm size from year t-1 to t. As an alternative measure of firm size, number of employees is also available in the dataset. However, because the reporting of firm employment is not as consistent as in the case of revenues, we prefer to use the revenues data as the proxy of firm size in the econometric regressions. Firm employment data, on the other hand is used to divide the firms into two categories: small firms and large firms[3]. Following ACS and AUDRETSCH (1988) and PAVITT et al. (1987), small firms are defined as those with fewer than 500 employees and large firms as those with a minimum of 500 employees.

[1] The original dataset which includes 323 pharmaceutical firms was cleaned to exclude the firms that report less than 7 years of consecutive data. This ensures that there is at least 5 years of data available in the equations where a 2 year lag of the firm size is used.

[2] Some firms have been subject to merger and acquisitions (M&A) during the period under observation. This creates a potential bias as it introduces an artificial "growth" for those firms that merged with, or acquired a small firm. It also overestimates the exit rates as the acquired and merged firms are counted as exits even though their economic activity has not completely ceased. Given this issue, there are two options for treating the data. The first is to simply leave the data in its raw form and ignore these events. In this case, the analysis is likely to suffer from the bias discussed above. The alternative method is Botazzi et al.'s (2001) methodology of forming "super-firms" by restructuring the dataset to adjust for M&A's that have taken place between firms while under observation. We have decided to utilize the first of these solutions and interpret our results with the limitations in mind. However, we have also formed an alternative dataset of super-firms so to check the robustness of our findings. The results proved robust irrespective of the dataset used.

[3] The number of employees is averaged throughout the life span of a firm to determine its classification as a small or large firm. This way, the problem of missing values in the employment data is tackled when firms are classified in one or the other size category.

In the following section, descriptive statistics are presented to highlight general trends related to the small and large firms as well as the firms in different regions of the US.

3.1. Descriptive Statistics

(a) Firm Size and Patenting Activities

The total number of pharmaceutical firms in the dataset are reported in Figure 1, including a breakdown of the firms by firm size. As can be clearly seen, the number of small pharmaceutical firms has increased in the post-1980 period which coincides with the guided search regime and the biotechnology revolution (GAMBARDELLA, 1995) while the number of large pharmaceutical firms stagnated.

Figure 1: Number of Pharmaceutical Firms

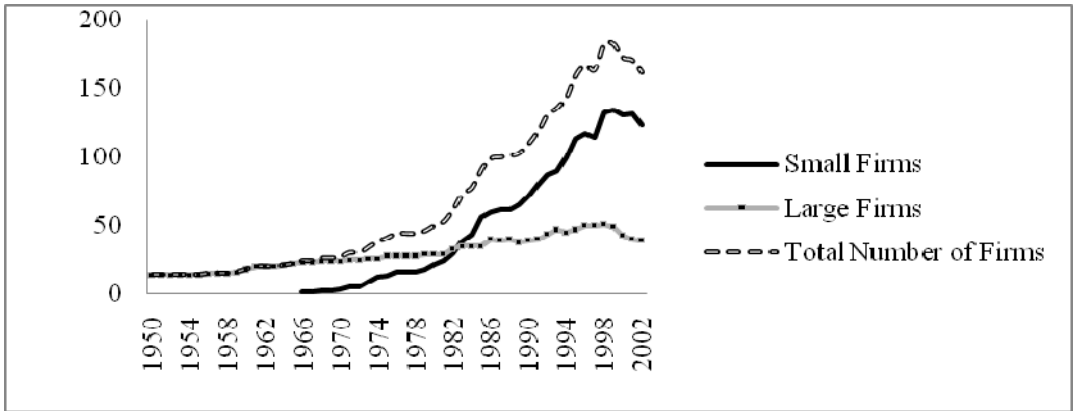
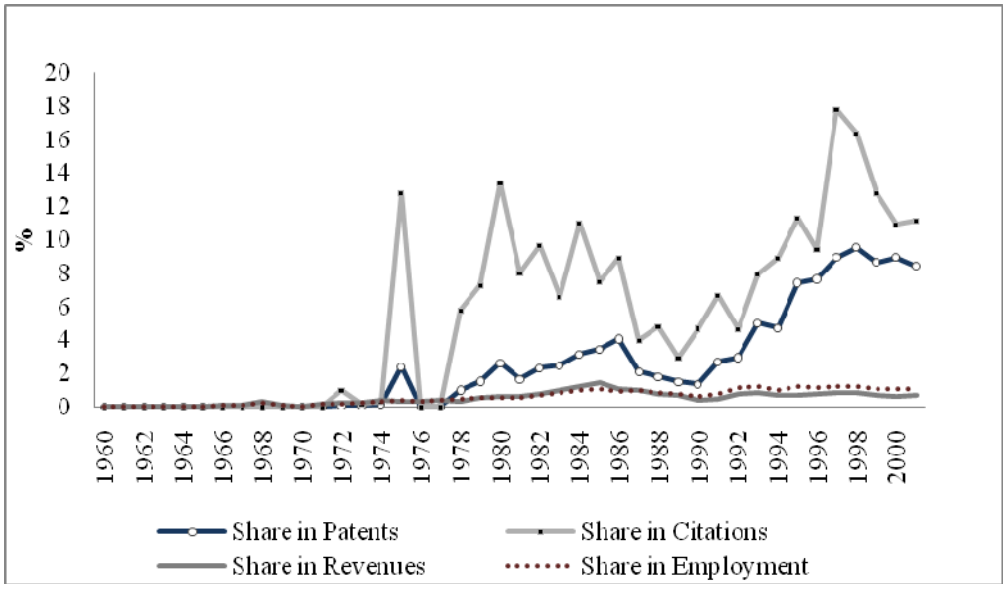


Figure 2 shows that despite the increasing number of small pharmaceutical firms, the share of small firms in total industry employment or revenues did not increase over the years. However, the share of small firm innovations measured by patents and citation

weighted patents increased significantly in the post-1980 period (Figure 2)[4]. Moreover, small firms not only increased their share in patenting but also became more "persistent" in their patenting activities (i.e. firms that patent for three consecutive years). Figure 3 which shows the size composition of firms that patent persistently reveals that the share of small firms among the persistent patentees increased dramatically in the post 1980 period[5]. Clearly, the post-1980 period is marked by an increase in the innovative activities of small firms in the pharmaceutical industry.

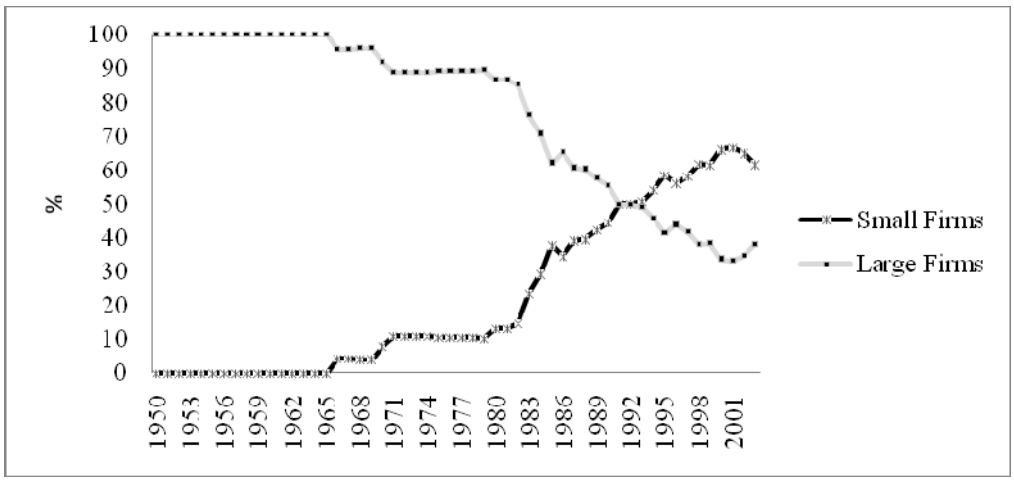
Figure 2: The Share of Small Firms in Industry Employment, Revenues and Innovations



[4] Patent data is taken from the NBER patent database (JAFFE and TRAJTENBERG, 2001). The use of patent data in the paper is limited and mainly aims to describe the innovative activities of firms in general way.

[5] Average length of the patent spells is 2.97 years.

Figure 3: Size Composition of Persistent Patentees



(b)Firm Location

Of the 256 pharmaceutical firms in the dataset, 210 are US firms while 46 are non-US firms[6]. Geographical distribution of the US firms is shown in Figure 4. California has the highest population of pharmaceutical firms followed by New Jersey and New York. Based on this information and POWELL et al.'s (2002) study of spatial clustering in the life sciences industry, we divide the firms into four categories according to their location:

(1) California

(2) NYC Tri-State region (New York, New Jersey and Connecticut)[7]

(3) Rest of the US

(4) Non-US

[6] Non-US category includes firms from Canada, UK, Germany, France, Ireland, Austria, Switzerland, Israel, Sweden, Bermuda, Chile, Denmark, India and Japan.

[7] Readers may find broader definitions of the NYC tri-state 'area' that replace Pennsylvania or Long Island with Connecticut. See footnote 8 below. (CNN)

Figure 4: Geographical Distribution of the US Firms in the Database

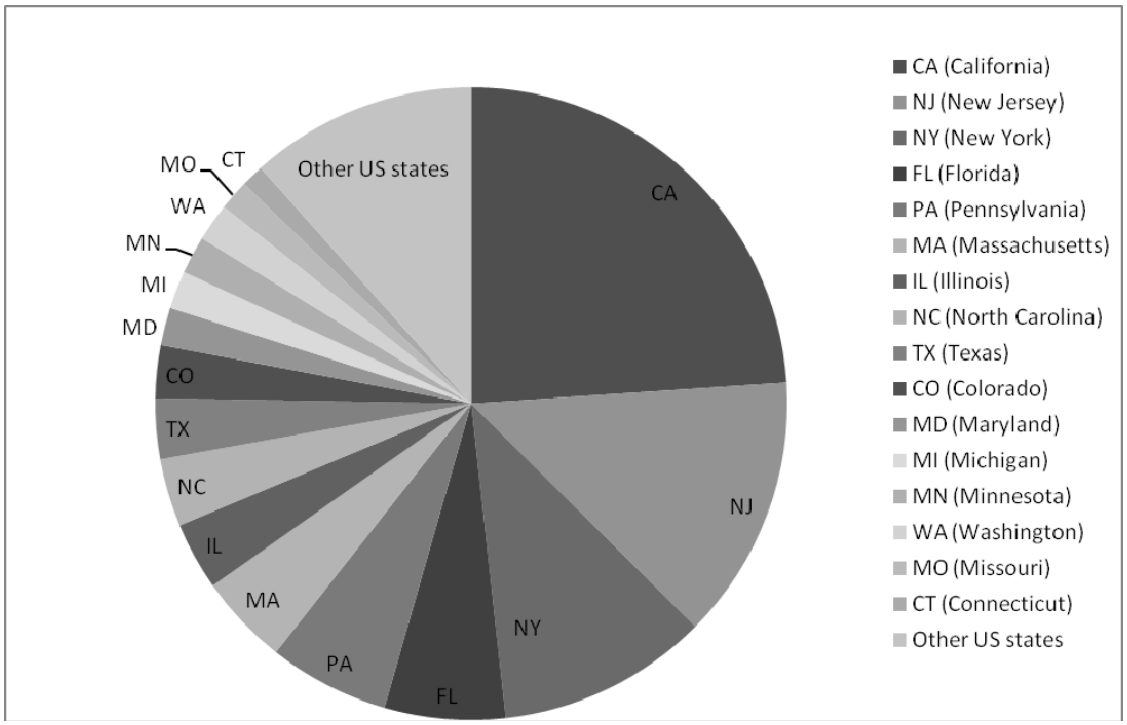


Table 1 reports the relevant descriptive statistics by firm location. The share of small firms is roughly the same for the California and the NYC Tri-State region while it is much higher for the rest of the US. The NYC Tri-State region lags behind other regions in terms of the innovativeness of the firms measured by the percentage of patentee firms and persistent patentees in the region.

Note that the California firms do not only score highest in terms of the percentage of patentee firms and persistent patentees, but also have the highest R&D intensity figures. The NYC Tri-State region, on the other hand, scores lowest on the R&D intensity figures and also has the lowest percentage of persistent patentees. The low innovativeness figures of the NYC Tri-State region are especially interesting because average firm size

measured by revenues is the highest in this region and large firms are known to patent more persistently compared to small firms (CEFIS, 2003). In contrast, the California region seems to show extraordinary innovative performance when one considers that the average firm size is the smallest in California, yet it has the highest shares of patentees and persistent patentees amongst all regions[8].

Table 1: Descriptive Statistics by Geographical Location

	Number of Firms	Number of Small Firms	Number of Patentees	Number of Persistent Patentees	Average Annual Revenues ($ mil.)	Average R&D intensity (R&D/Sales)
California	44	29 (66%)	34 (77%)	20 (45%)	98.8	12.7 (%)
NYC Tri-State	59	40 (68%)	39 (66%)	20 (34%)	1615.9	8.5 (%)
Rest of the US	107	88 (82%)	78 (73%)	46 (43%)	296.47	11 (%)
Non-US	46	25 (54%)	30 (65%)	19 (41%)	1331.3	12.2 (%)

Notes: Small firms have less than 500 employees. Patentee firms are firms that have been granted at least one patent between 1963 and 2002.

Persistent patentees are firms that have been granted at least one patent in each year for at least three consecutive years between 1963 and 2002. An alternative definition of persistent patentees, using at least five consecutive years of patenting, does not change the results.

3.2. Methodology

Having gained preliminary insights into the changing number of firms by size class, the changing role of small and large firms in patenting as well as how these vary across regions, we now look more carefully at the growth dynamics in the pharmaceutical industry to explore whether growth performance is affected by firm size and firm location. We follow the methodology used in firm growth studies in the industry dynamics tradition

[8] Excluding the Pennsylvania from the NYC Tri-State definition does not significantly alter the results. Alternative results for Tables 1, 3 and 4 that include the Pennsylvania firms in the NY Tri-State definition can be obtained from authors upon request.

(CABRAL and MATA, 2003; GEROSKI AND MAZZUCATO, 2002) which begin with the null hypothesis that the firm growth process is well approximated by a random walk: Gibrat's Law. The law, defined below, states that firms grow independently of their initial size and with small incremental stochastic shocks. Hence, the null hypothesis is that there is no 'structure' to growth. If instead there is structure, the question is whether this is related to firm characteristics, including location.

Conventionally, Gibrat's Law is formulated as:

$$y(i,t) = \alpha + \beta y(i,t-1) + \varepsilon(i,t) \quad (1)$$

where α is a constant term, $y(i,t)$ denotes the *natural logarithm* of firm size (i.e. revenues) for firm i at time t, and ε is an error term. If $\beta = 1$ (for every firm), growth follows a random walk. If $\beta > 1$, Gibrat's Law is violated because large firms grow faster than small firms (in the extreme case leading to monopoly), and if instead, $\beta < 1$, it is violated because small firms grow faster than large firms, i.e. "*reversion to mean*".

The paper utilises the panel estimation method used in GODDARD et al. (2002) to test for Gibrat's Law in the pre and post 1980 period for the pharmaceutical industry. Equation 2 is essentially the same as Equation 1, but is written in a specific form relevant for panel data estimations and also accounts for the possibility of persistence in growth rates $(y_{i,t-1} - y_{i,t-2})$.

$$y_{i,t} - y_{i,t-1} = (1-\rho)\alpha_i + (\delta_t - \rho\delta_{t-1}) + (\beta-1)y_{i,t-1} + \rho(y_{i,t-1} - y_{i,t-2}) + \vartheta_{i,t} \quad (2)$$

where $\vartheta_{i,t} = \varepsilon_{i,t} + \rho(1-\beta)y_{i,t-2}$ (note that $\vartheta_{i,t} = \varepsilon_{i,t}$ when Gibrat's law holds and β=1).

$y_{i,t}$ is the logarithm of firm revenues for firm i at time t. The $(y_{i,t} - y_{i,t-1})$ term on the left hand side is the firm growth variable (denoted $(gr_{i,t})$ from this point on). The right hand side variable $(y_{i,t-1} - y_{i,t-2})$ is the lagged growth variable ($gr_{i,t-1}$) and is included in the model to account for the possibility that firm growth may persist. In the case $\rho = 0$; the lagged growth variable becomes redundant, meaning that firm growth does not persist[9].

Following GODDARD et al.'s (2002) methodology, we estimate two different panel regression models using OLS. Model 1 includes only fixed time effects where the firm specific effects are pooled (i.e. $\alpha_i = \alpha$)[10]:

Model 1

$$y_{i,t} - y_{i,t-1} = (1-\rho)\alpha + (\delta_t - \rho\delta_{t-1}) + (\beta_1 - 1)y_{i,t-1} + \rho_1(y_{i,t-1} - y_{i,t-2}) + \vartheta_{i,t}$$

while Model 2 includes both fixed time and firm effects(i.e. $\alpha_i \neq \alpha$):

Model 2

$$y_{i,t} - y_{i,t-1} = (1-\rho)\alpha_i + (\delta_t - \rho\delta_{t-1}) + (\beta_2 - 1)y_{i,t-1} + \rho_2(y_{i,t-1} - y_{i,t-2}) + \vartheta_{i,t}$$

---

[9] (Note that the coefficient in front of $y_{i,t-1}$ is now formulated as $(\beta - 1)$ such that the left hand side variable is formulated as growth at time t.)

[10] The limitation of using Model 1 is that it does not allow for individual firm specific effects even though the ($\beta_1 - 1$) has a standard distribution and it is easy to test whether $\beta_1 = 1$. On the other hand, while Model 2 allows for the firm heterogeneity to be accounted with fixed firm effects, the β_2 coefficient has a downward bias in limited samples where T is small (GREENE, 2003). The data set used for the regressions has a 54 year span and the downward bias is especially significant when one looks at 10 year sub periods of the data. However as pointed out in GODDARD et al. (2002), this is a common issue for the panel data unit root tests (such as ADF) and does "*not present insurmountable obstacles*" to testing for Gibrat's Law.

In all the regressions, standard errors are heteroskedasticity robust White errors as the heteroskedasticity problem is commonly noted in similar studies (HYMER and PASHIGIAN, 1962).

In addition to testing whether Gibrat's law holds in *different periods of industry* evolution, we also use *kernel density estimation* techniques to explore the shape of the firm size distribution in the pharmaceutical industry and how this evolves over time[11]. This is important since those studies which have found that firm growth is not normally distributed (BOTTAZZI and SECCHI, 2005, LOTTI, 2004), have not actually shown how non-gaussian properties (fat tails, bi-modal) evolve over time as a response to changing innovation dynamics. Following the methodology of CABRAL and MATA (2003), we use a Normal Kernel function with an automatic Silverman bandwidth to estimate the firm size distribution. The results remain robust to the choice of the kernel function.

Finally, we compare the growth behaviour of firms in the California and NYC Tri-State region using ANOVA tests to see whether firm location creates growth differentials.

(4) RESULTS

4.1. Firm Growth

Table 2 reports the results of the regressions specified in Model 1 and Model 2 estimated using OLS. Results suggest that the β coefficient is significantly smaller than 1

[11] The Kernel density estimate of a series X at a point x is:

$$f(x) = \frac{1}{Nh}\sum_{i}^{N} K\left(\frac{x - X_i}{h}\right)$$

Here, K(.) is the Kernel density function and N is the number of data points in the empirical distribution. The Kernel density function K (.) determines shape of the bumps and can be chosen to be a function such as Epanechnikov, Gaussian (normal), and Uniform etc. "h" is called the "bandwidth" which is the smoothing parameter. A larger bandwidth leads to a smoother curve.

in the majority of the periods in both models. This implies that small firms grow faster than large firms: an indication that firm growth is not independent of initial firm size. Model 1 suggests that the earliest years of the industry history (1950-1960) is when β=1 and hence, the proportionate rate of growth is the same for all firms in the industry[12]. Since this period was one in which there was a prevalence of large firms in the pharmaceutical industry (Figure 3), these results support a set of earlier studies which confirm the validity of Gibrat's Law for the US economy only in the period around the 1950s and 60s when there was a prevalence of large firms in the economy (HART, 1962; PRAIS, 1974: SINGH AND WHITTINGTON, 1975).

The results from both models allow us to better understand Gibrat's Law in a dynamic context, i.e. how the β coefficient *evolves* over time*:* it declines over time suggesting an increased growth advantage for the small pharmaceutical firms over the course of industry evolution. Small firms grow especially faster in the post 1980 period which is when the number of small firms and their share in innovative activities increase.

The dynamics of *persistence* in growth also change in the post 1980 period. The ρ coefficient which measures the degree of persistence in firm growth (i.e. success breeds success) is significant in the pre-1980 period while it loses its significance in the post 1980 period. This can be related to the high levels of small firm activity in the post 1980 period as the growth performance of small firms tends to show lower degrees of persistence (CONTINI and REVELLI, 1989).

[12] Note that the β coefficient in Model 2 is also closer to 1 in the 1950-1960 period compared with other sub-periods.

Table 2: Estimation Results (Dependent Variable: Firm growth)

Time Period	MODEL 1 β_1	MODEL 2 β_2	MODEL 1 ρ_1	MODEL 2 ρ_2	Number of Cross Sections	Number of Observations	R^2 (Model1/Model2)
1950-1960	*0.976*	**0.78**	-0.023	-0.073	15	129	0.294/0.496
	(0.017)	*(0.010)*	*(0.076)*	*(0.08)*			
1961-1970	**0.967**	**0.59**	0.369[t]	0.065	26	211	0.327/0.645
	(0.015)	*(0.089)*	*(0.192)*	*(0.100)*			
1971-1980	0.996	**0.72**	0.360*	0.27*	44	355	0.224/0.4927
	(0.005)	*(0.067)*	*(0.09)*	*(0.083)*			
1981-1990	**0.962**	**0.52**	-0.039	0.056	110	650	0.056/0.423
	(0.011)	*(0.115)*	*(0.061)*	*(0.08)*			
1991-2000	**0.971**	**0.48**	-0.066	0.04	195	1109	0.027/0.397
	(0.009)	*(0.059)*	*(0.05)*	*(0.051)*			
1950-1980	**0.989**	**0.76**	0.362*	0.319*	44	695	0.273/0.459
	(0.005)	*(0.053)*	*(0.099)*	*(0.082)*			
1981-2003	***0.971***	**0.62**	-0.047	0.016	256	2081	0.027/0.329
	(0.006)	*(0.035)*	*(0.039)*	*(0.038)*			
1950-2003	**0.972**	**0.66**	-0.039	0.0117	256	2776	0.029/0.31
	(0.039)	*(0.031)*	(0.039)	*(0.036)*			

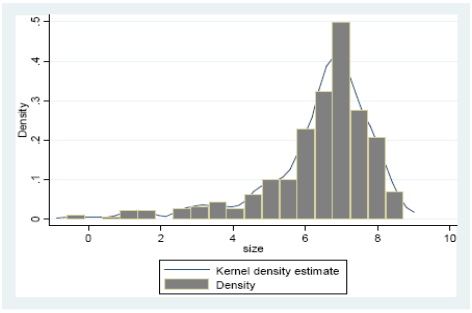
Source: Compustat Pharmaceutical Industry Database

Notes: Standard errors reported in paranthesis. The β_1 and β_2 coefficients in bold are significantly different from 1 at 5% significance level. * Significant at 5% level. [t] Significant at 10% level.

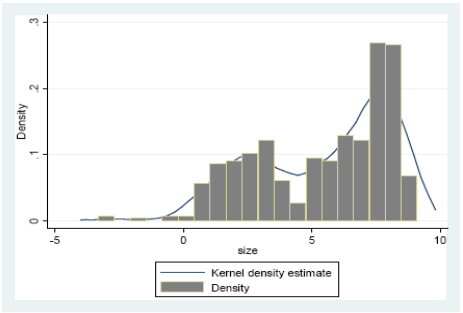
4.2 Firm Size Distribution

Having explored firm growth dynamics using an econometric methodology in Section 4.1, we now use non parametric techniques to explore the shape of the firm size distribution and its evolution over the years. Figure 5 shows the Kernel estimation of (log) firm size distributions for different periods of the industry history.

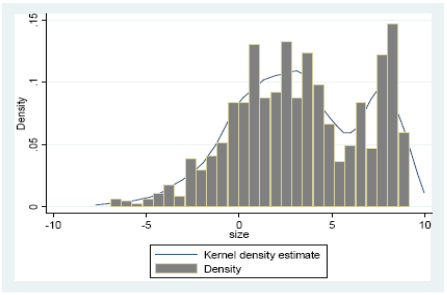
Figure 5: The Evolution of the FSD



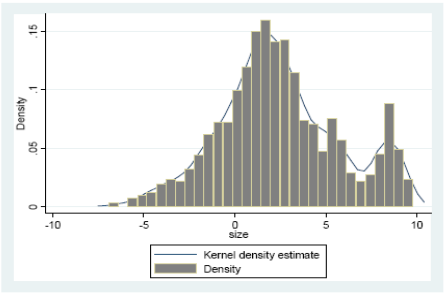
(a): *Pre-1970: 393 observations*



(b): *1970-1980: 425 observations*



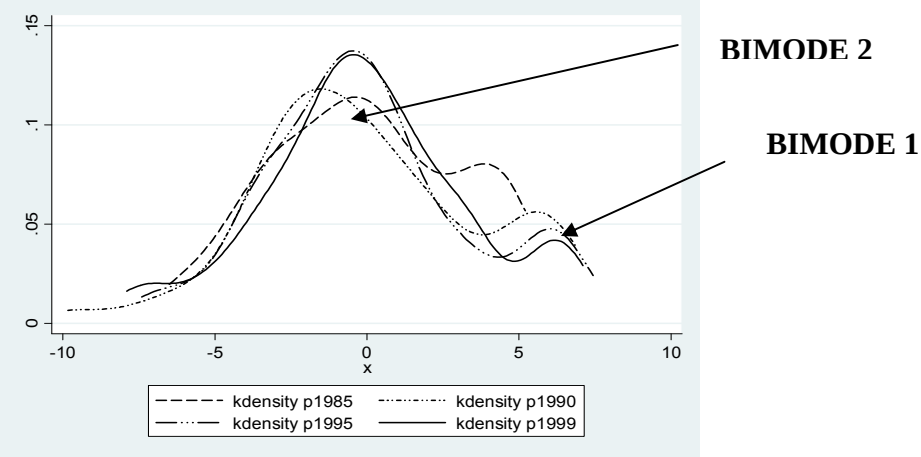
(c): *1981-1990:725observations*



(d): *1991-2003: 1597observations*

While BOTTAZZI and SECCHI (2005) have noted that the Firm Size Distribution (FSD) in the pharmaceutical industry has a bimodal character unlike the normal distribution, we show in Figure 5 that this complex feature of the FSD is not a static characteristic but *emerges* over time: in the post 1970 period. Prior to 1970 the FSD is uni-modal. Figure 6 shows that the bimodality feature becomes a stable and persistent characteristic of the FSD in the post 1980 period. The bimodality becomes established especially in the post 1980 period with the entry of small pharmaceutical firms. Hence, BIMODE 1 (on the right tail) can be interpreted as being due to a stable "core" of the industry that has persistently held a dominant position in the industry while BIMODE 2 is the "fringe" which is subject to more volatility (BOTTAZZI AND SECCHI, 2005).

Figure 6: Firm Size Distribution in 1985, 1990, 1995 and 1999



Further investigation of the firms in BIMODE 1 reveals more interesting facts. First of all, the identity of the firms in BIMODE 1 persists over time i.e. around 80% of the firms that are in BIMODE 1 in the mid 1970's are still in BIMODE 1 in the late 1990's[13].This is true even though certain periods (i.e. post 1980) are characterized by a shakeup of market shares among the top 10 pharmaceutical firms as shown in Figure 7[14].

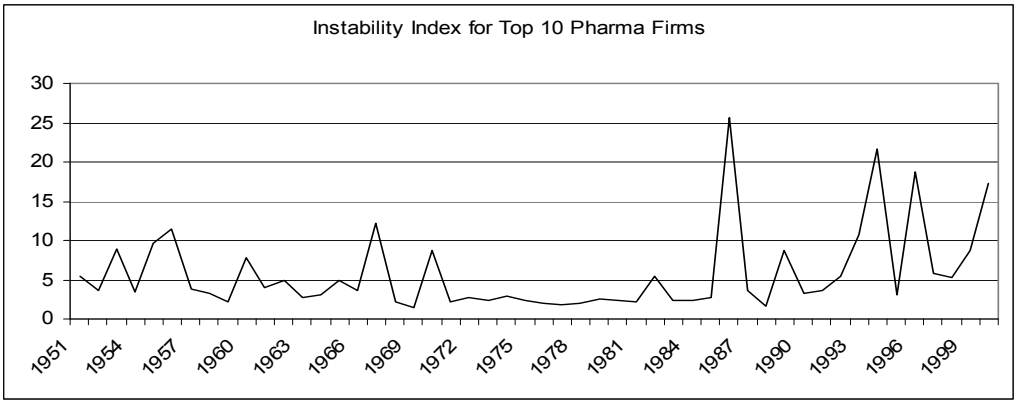
[13] The list of firms that have persisted in BIMODE 1: ABBOTT LABORATORIES, ASTRA ZENECA, AVENTIS SA -ADR, BRISTOL MYERS SQUIBB, GLAXOSMITHKLINE, JOHNSON & JOHNSON, LILLY (ELI) & CO, MERCK & CO, NOVARTIS, NOVO-NORDISK, PFIZER INC, PHARMACIA & UPJOHN INC, ROCHE, SMITHKLINE BEECHAM, WARNER-LAMBERT CO, WYETH.

[14] The market share instability index introduced in HYMER and PASHIGIAN (1962) is calculated as:

$$I = \sum_{i=1}^{n} [\,|\, s_{it} - s_{i,t-1} \,|\,]$$

where s_{it} = the market share of firm *i* at time *t*.

Figure 7: Instability index for Top 10 Pharmaceutical Firms



4.3 Firm Location and Firm Growth

Table 3 which reports results of the ANOVA tests that compare the average growth rates of the pharmaceutical firms in the two most populated regions of the US suggests that not only do the size properties and the patenting capabilities of the firms differ by location, but also there are significant growth differentials between firms located in California and the NYC Tri-State region of the US.

In general, California firms grow significantly faster than the NYC Tri-State firms. Yet, the regional growth differences are only significant for innovative (i.e. patentee) pharmaceutical firms. For non-patentee firms, we do not find that the growth performance differs by firm location.

This finding which suggests that location creates significant growth differentials among only the innovative firms adds to the existing literature that finds significant regional growth differentials mostly for the innovative industries (AUDRETSCH and DOHSE, 2007; REICHSTEIN and DAHL, 2004 and HOOGSTRA and VAN DIJK, 2004): Location seems to create growth differentials only for the innovative firms even within an

innovative industry, the pharmaceutical industry. In case of the pharmaceutical industry, being located in the dynamic California region and close to the biotechnology cluster seems to create growth advantages for only the patentee firms and not so for the non-patentees.

Table 3: Average Firm Growth Rates: California vs. NYC Tri-State

CALIFORNIA	Average Growth Rate (gr)	Number of Firms	NYC TRI-STATE	Average Growth Rate (gr)	Number of Firms	Difference Significant? ANOVA test results
Patentees	0.19	34	**Patentees**	0.053	39	F=0.03** Yes
Non-Patentees	0.08	10	**Non-Patentees**	0.14	20	F=0.88 No
Persistent Patentees	0.15	20	**Persistent Patentees**	0.04	20	F= 0.08* Yes
Non-Persistent Patentees	0.27	14	**Non-Persistent Patentees**	0.08	19	F=0.03** Yes
All California Firms	0.17	44	**All NYC Tri-State firms**	0.07	59	F=0.01** Yes

*Significant at 10%. **Significant at 5%.

The variance of firm growth also differs between California and the NYC Tri-State region as shown in Table 4. The growth of NYC Tri-State firms is much more stable compared to the growth of the California firms. Yet, the results again suggest that firm location only affects the growth performance of the patentee firms as the variance of firm growth is not significantly different between the non-patentee firms from these two locations.

Table 4: Variance of Firm Growth Rates: California vs. NYC Tri-State

CALIFORNIA	Variance of Firm Growth	Number of Firms	NYC TRI-STATE	Variance of Firm Growth	Number of Firms	Difference Significant? F test results
Patentees	0.82	34	**Patentees**	0.49	39	F=0.00** Yes
Non-Patentees	0.85	10	**Non-Patentees**	0.91	20	F=0.49 No
Persistent Patentees	0.63	20	**Persistent Patentees**	0.36	20	F=0.00** Yes
Non-Persistent Patentees	1.09	14	**Non-Persistent Patentees**	0.78	19	F=0.00** Yes
All California Firms	0.83	44	**All NYC Tri-State firms**	0.6	54	F=0.00** Yes

**Significant at 5%.

(5) DISCUSSION AND CONCLUSIONS

Analysis of firm growth dynamics in the US pharmaceutical industry reveals that the relationship between firm size and firm growth has *evolved* over time as the industry structure and the innovation dynamics changed. Firm growth behavior in this industry is structured, determined by various systematic factors, and evolves with time and industry evolution. Firm size and firm location are important factors.

Firstly, the results suggest that there is a negative size-growth relationship in the pharmaceutical industry. Smaller pharmaceutical firms grow faster than larger firms and this is more pronounced starting from 1970's. The specific characteristics of how innovation changed in the pharmaceutical industry from the 1970's onwards provide us with insights into this change.

Secondly, results suggest that the structure of firm growth in the pharmaceutical industry is partly rooted in regional growth differences. Pharmaceutical firms in the California and NYC Tri-State regions are very different in terms of firm size, R&D expenditures and patenting activities. These region-specific differences translate into growth differentials as the California firms which are more likely to patent, patent persistently and have higher R&D intensity figures, grow faster than the NYC Tri-State firms. However, these differences are only significant for the innovative firms (i.e. patentee firms) and do not apply to non-patentees which are less innovative.

This finding provides an important insight for our understanding of the role location plays in firm growth especially in innovative industries. As MAZZUCATO and DEMIREL (2008) find, different firm characteristics (firm size/patenting/persistence in

patenting/involvement in external research alliances) determine the growth performance of firms as well as the impact of innovation on firm growth. This paper similarly finds that different characteristics of firms (i.e. patenting ability) determines whether and how location affects firm growth.

Finally, we find that the (log) size distribution of firms in the pharmaceutical industry cannot be described by a normal distribution. It is a bimodal distribution, indicating the simultaneous existence of a core set of large firms and a fringe of small firms (BIMODE 1 and BIMODE 2 respectively). The bimodality feature of the firm size distribution, however, does not exist in the early years of the industry but emerges only in the late 1970s. This is a key result since most of the recent literature on non-gaussian properties of the firm size does not show the *evolution* of the firm size distribution nor its specific relationship to changing firm characteristics (BOTTAZZI and SECCHI; 2005; BOTTAZZI et al., 2003). The paper is an initial attempt to do both. And in fact, the results provide important supporting evidence to the claim that non-Gaussian features of the firm size distribution imply 'structure' (DOSI, 2005)[15]. Structure, as embodied in the bimodal firm size distribution, coincides with the emergence of small innovative pharmaceutical firms that play an ever growing role in the innovative division of labour in the life sciences industry.

The 'symbiotic relationship' between small (i.e. fringe) and large firms (i.e. core) is interestingly present even if we only include pharmaceutical firms, and not the biotechnology firms. Hence, the interpretation of the *division of innovative labour*

[15] DOSI (2005) notes that structure in firm growth is indeed good news for evolutionary economists because it provides evidence that the persistent heterogeneity of firm characteristics and the competitive market selection among them is translated differentials in the growth performance of firms. Yet it is difficult to speak about 'structure' without better understanding the underlying changes in production and technology and how these have impacted the dynamics between small and large firms.

between pharmaceutical and biotechnology firms needs to more carefully consider the role that small pharmaceutical firms play in this division. The results suggest the possibility that the literature has overlooked, or misunderstood, the important role that small pharmaceutical firms play in the innovative division of labour, possibly overemphasizing the role of large pharmaceutical firms and small biotechnology firms.

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