

Innovation and corporate growth in the evolution of the drug industry

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Abstract

This work studies the processes of growth of the worlds top 150 pharmaceutical firms, on the grounds of an original database which also allows disaggregate analysis at the level of single therapeutical classes and chemical entities. Our findings show that the industry — whose long-term evolution is driven by innovation, imitation and permanent creation of new markets — displays (i) “fat tails” in the distribution of growth shocks, present at all levels of aggregation, with (relatively rare) big “spurs of growth”, (ii) a significant autocorrelation of growth rates, (iii) a fall of variance of growth rates with size entirely dependent on corporate diversification patterns, in turn plausibly shaped by the “competence scope” of each firm, and (iv) different “lifecycles” of diverse types of products, and persistent forms of heterogeneity across firms in terms of innovative output, which, however, do not seem to affect comparative growth performances. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

This work investigates the patterns of change in the international pharmaceutical industry, in particular with respect to the industry structure and the growth

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processes of a large sample of incumbents, against the background of the observed patterns of innovation.

Pharmaceuticals are indeed an archetypical example of a “science-based” industry, wherein innovation — in the form of new therapeutical entities, and imitation/improvements of existing ones — is the fundamental source of competitiveness within the industry, largely shaping the dynamics of growth and decline of different firms.

As such, the industry also represents a rich domain for the analysis of the properties of microeconomic processes of growth — touching upon the dynamics of innovation arrival and imitation, the processes of inter-product and inter-firm competition, corporate diversification across markets, and the ensuing characteristics of industrial structures. These are indeed the main topics addressed in this work. In particular, we shall primarily address three (inter-related) questions, namely, first, the relationship between firm size and growth, second, and more generally, the statistical properties, both at aggregate and disaggregate (market-specific) levels, of corporate growth and, third, the relations between the latter and the process of technological innovation, imitation and market competition.

Our analysis, based on longitudinal data, disaggregated down to single product markets, allows one to characterize, at least qualitatively, the systematic forces driving the evolution of the industry, the sources of heterogeneity across firms and the nature of “technological shocks” and of competition processes. Putting it another way, one is able to investigate the statistical properties which are “emergent” from specific evolutionary dynamics of heterogenous learning and market selection.

In Section 2 we shall briefly recall some major features of the secular evolution of the drug industry. This also sets the background of the subsequent analysis, developed in Section 3, addressing (i) the size distribution of the 150 top firms operating in the seven major Western countries, (ii) the properties of “growth shocks” at both levels of firms as a whole and of disaggregated markets, and (iii) the relationship between corporate size, diversification patterns and variances in growth rates. Finally, Section 3.5 explores the process of the arrival of innovations and their impact upon corporate growth and market dynamics. Finer statistical details along a similar interpretative thread may be found in Bottazzi et al. (2000).

2. The evolution of the industry: an overview

The history of the international pharmaceutical industry, dating back to its origin in the 19th century, has already been extensively analyzed by several scholars.¹ Here, let us just mention a few major characteristics of the processes of technological learning and market competition.

¹See, among others, Aftalion (1959), Arora and Gambardella (1998), Chandler (1990), Freeman (1982), Gambardella (1995), and Henderson et al. (1999).

Let us begin with the latter. Competition has always centered around the discovery and introduction to the market of new products, often subject to rather quick incremental improvements, as well as to imitation and generic products competition.

Notwithstanding the historically high R&D intensity of the industry, the successful introduction of major innovations, in the form of new molecules (New Chemical Entities, NCEs) with novel therapeutical properties, has always been a rather rare event. For example, Barral (1996) estimates the total number of NCEs introduced throughout the world over the period 1975–1994 to be 154. While major innovative breakthroughs arrive quite rarely, after arrival they experience extremely high rates of market growth (more on this point in Grabowski and Vernon, 1992).

NCEs, however, only capture a part of the innovative activities within the industry. In fact, pharmaceutical innovations, broadly defined, include “inventing-around” existing molecules, new combinations among them, new ways of delivery, etc.

Remarkably, the degree to which early innovators have enjoyed an advantage in later introducing major drugs within the same family has traditionally been fairly limited (see Sutton, 1998). That, together with the coexistence of several compounds or variations thereupon targeted to the same pathology, generally hinders the persistence of dominant positions in a single market (cf. also Temin, 1980). In fact, in most single markets and in the industry as a whole, one observes the (*persistent*) coexistence of two basic types of firms, mapping into distinct technological ensembles of competencies and competitive strategies. Briefly, the first group, closely corresponding to some “oligopolistic core” of the industry, undertakes what is sometimes called “pioneering R&D” (Grabowski and Vernon, 1987), generates the overwhelming majority of NCEs and, when successful, enjoys large, albeit not very long-lasting, first-mover advantages, and charges premium prices. The second group undertakes primarily “imitative R&D”, generates incremental innovations and more competitively priced “me-too” drugs, and takes up licenses from the core and is present to different degrees in the “generic” markets, after patent expirations.²

The qualitative historical evidence hints, in fact, at a long-term “ecology” of the industry relying on the competition, but also the complementarity, between two organizational populations, whose relative sizes is shaped by diverse competencies in accessing innovative opportunities (and, to some extent, also by Intellectual Property Right regimes, influencing the span and length of legal protection for temporary monopolies on innovation). Some of the statistical properties of such an ecology will indeed be explored below.

In a nutshell, the archetypical evolutionary story concerning each “disaggre-

²The two basic types are not evenly distributed across countries. Firms belonging to the former come almost exclusively from the USA, Germany, the UK and Switzerland, while France, Italy and Japan (not included in our sample) show up primarily in the second group.

gate” market (i.e. a market aimed at one particular pathology) runs more or less as follows.

A few firms — generally from the “core” — search for NCEs with the desired properties. Some of them (a small minority) achieve the stage of clinical trials. Even among these, only very few immediately fulfill therapeutic efficacy and required safety standards. Many NCE prototypes, on the contrary, show various clinical shortcomings, which might sometimes be overcome by alterations to the original chemical structures, the introduction of compound combinations, or different ways of administering them. In some cases these changes are undertaken by the original discoverer of the compound itself, while frequently the project based on that particular NCE is abandoned — leaving potential room for the development of modified analogues by other firms. Moreover, even when the original innovator carries the project through to a marketable product, molecular modifications of prototypes often enable followers within any chemical/therapeutic trajectory to introduce drugs with equivalent (or even superior) pharmaceutical activities, side-effect profiles, patient tolerability, etc.³

Come as it may, when the first NCE successfully reaches the market, it generally undergoes a very rapid market diffusion (cf. the examples in Figs. 1–3 below), partly through the competitive displacement of “older” drugs — whenever they exist for that particular therapeutic application — and, even more importantly, through the creation of its own fast-growing market niche. Quite soon, however, the niche, i.e. the product market, is invaded by competing NCEs and/or “creative analogues” which curb the growth of the early monopolist. All this might happen well before the expiration of the original patent — even if the latter event generally marks another “market shock”, with generic drugs and firms expanding in the market.

Note that, in the evolutionary story we have just sketched, there are two basic dynamic processes at work. The first concerns the multiplication of markets through the introduction of new families of products roughly aimed at the same therapeutic targets (either “old” targets with new methods or “new” pathologies, yet unchallenged). The second process regards competition *stricto sensu* amongst firms within each “micro” market. Clearly, the growth of firm size depends on both, with the timing of entry into each “micro market” being an important factor in the combination of the two effects.

Figs. 1–3 illustrate the market dynamics associated with the evolutionary patterns sketched above. Fig. 1 shows the profile of an entirely novel market, angiotensin-II antagonists, in the cardiovascular area. The new niche expands very fast allowing for the steady growth of both the first-comer and other early innovators. Here, in a sense, a fast expanding market provides “room for

³ Sneider (1996) presents a detailed analysis of 244 currently employed drug prototypes, showing that, out of these, more than 1200 medical compounds have been derived.

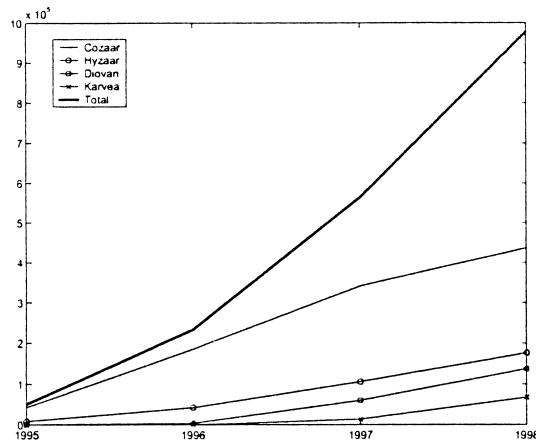


Fig. 1. Angiotensin-II antagonists: size of the market and firms/products sales, 1987–1998 (US\$ millions).

everyone” — and with that, also expanding sizes (in that market) for all early incumbents. Fig. 2 illustrates the case of antiulcerants, with two families of products, namely H2 antagonists, the older product, and acid pump inhibitors, the new product, which over time crowds out the former. All this goes together with the fate of the two leading NCEs/products (Zantac and Losec, respectively), while new “innovative invaders” begin to enter the younger niche only in the late 1990s. Finally, Fig. 3 depicts a relatively “old” market, antivirals, where the first innovative mover (Zovirax), despite a steady erosion of its market share by

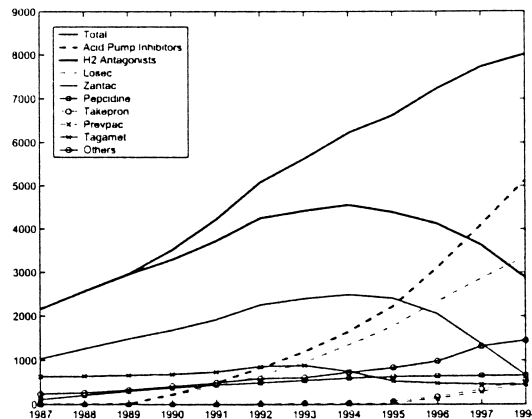


Fig. 2. Antiulcerants: acid pump inhibitors and H2 antagonists: size of the market and firms/products sales, 1987–1998 (US\$ millions).

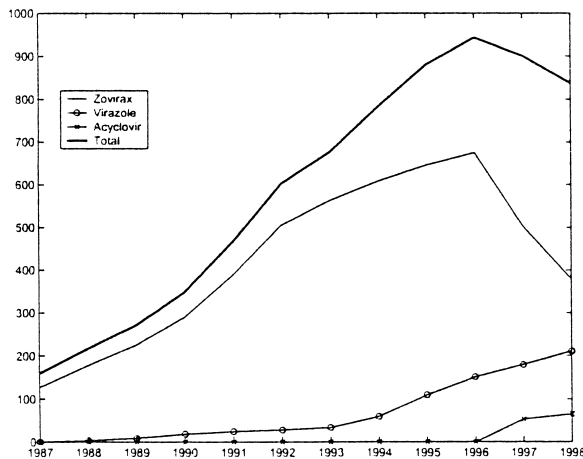


Fig. 3. Antivirals, excl. vaccines: size of the market and firms/products sales, 1987–1998 (US\$ millions).

late-coming innovators and analogues, maintained its dominance until patent expiration, in 1997, by which date a swarm of generic competitors entered the market.⁴

A final set of characteristics of the evolutionary dynamics of the industry that we want to recall concerns the nature of product markets themselves. Indeed, one observes a highly skewed distribution both of product market sizes and of intra-firm distribution of sales across products. So “a few *blockbusters* dominate the product range of all major firms” (Matraves, 1999; cf. also Sutton, 1998; Bottazzi et al., 2000).⁵

In an extreme synthesis, the evolutionary patterns of the industry display:

- rare arrivals of major innovations (new chemical entities with novel therapeutical targets or pharmacological mechanisms) often associated with the emergence of new markets;
- a more steady activity of incremental innovation, development of therapeutic analogues, imitation, licensing;
- systematic forms of heterogeneity, even amongst incumbents, distinguishing a few rather persistent innovators from the rest of the organizational population;
- “hierarchically nested” competitive mechanisms⁶ involving, at one level,

⁴Note that the decrease in the total “size” of the market after 1996 is entirely due to price reductions, with quantities still rising.

⁵In our database the three most important products of the top five firms account for more than 50% of the total sales. Matraves (1999) also suggests that only the top 30 drugs worldwide cover average R&D costs.

⁶We borrow the expression from Warglien (1995).

innovation/imitation and market share dynamics within single product groups, and, on a longer time scale, the generation of new markets and the diversification processes across them.

Given all this, what are the resulting statistical properties of the evolution of the industry, in terms of relative sizes, rates of growth, etc.? This is what we shall explore in the following.

3. Patterns of corporate growth

Let us begin by noting that the foregoing pieces of qualitative evidence suggest that the process of corporate growth is likely to display more structure than what would be predicted on the grounds of uncorrelated idiosyncratic shocks, i.e. a so-called Gibrat-type process.

In the following, in order to disentangle the actual growth patterns, after a summary description of our database (Section 3.1), we shall analyze the main properties of size distributions (Section 3.2) and growth processes (Section 3.3). Possible departures from the Gibrat hypothesis are studied by means of basic non-parametric methods. In particular, we shall study: (a) the shape of the tails in the observed growth distribution; (b) the time autocorrelation in growth profiles; and (c) the relationship between size and growth. Systematic departures from the “null” (Gibrat) hypothesis are indeed identified in all three domains of analysis.

Next, we present an interpretative framework able to account for the observed properties of growth processes, concerning in particular: (i) the relationship between size, diversification across different markets and growth variance (Section 3.4), and (ii) the effects of product innovation, entry and imitation upon the growth of markets and of the firms within them (Section 3.5).

3.1. *The data set*

Our statistical analysis in the following is based on the dataset PHID (Pharmaceutical Industry Database) developed at the University of Siena. It covers the top 100 companies in the seven major Western markets (USA, United Kingdom, France, Germany, Spain, Italy, Canada) with 10 to 20 years of observations (depending on the variables). In this paper we aggregate the respective figures in the different national markets and consider the resulting top 150 firms.⁷ Both sales figures and market shares are available for each firm from 1987 to 1997, disaggregated up to the four-digit level of the Anatomical Therapeutic Classification scheme (ATC) in 517 microclasses.

⁷In consequence, firms which are “big” in one single national market but smaller at the aggregate level are neglected.

The database also contains detailed information on the sales of 7654 drugs commercialized in the US by 57 major pharmaceutical companies. The launch date is reported for 4921 of them (64.29%). Launches are evenly distributed over the last 20 years, so we are able to track the lifecycle of 1600 products over 10 years after their launch. Products are distinguished according to whether they are a New Chemical Entity (NCE), a patented innovation that is not an NCE, or an unpatented product (including both products whose patents expired before the years under observation and products licensed from other firms).

As already mentioned, this work is focused on the processes of *internal* growth. Hence, to take into account mergers and acquisitions during the period of observation, we have constructed “super firms” which correspond to the end-of-period actual entity (so, for example, if any two firms merged during the observed history, we consider them merged from the start). This procedure might bias intertemporal comparisons on actual size distributions, but it helps to highlight those changes in the distributions themselves which are due to processes of intra-market competition and inter-market diversification.⁸

Finally, when studying the relationship between innovation and growth (Section 3.5) we shall confine the analysis to the US market wherein the overwhelming majority of innovative products were first introduced.⁹

3.2. Size distributions

Let us begin with a descriptive analysis of size distributions. Let $S_i(t)$ be the sales of firm i ($i \in [1, \dots, 150]$) at time t ($t \in [0, \dots, 10]$). The evidence (see Bottazzi et al., 2000, for more details) shows that the ratio of the standard deviation to the mean as well as the skewness and the kurtosis are nearly constant over time. These properties imply that the “normalized size” $G_i(t) = S_i(t) / \langle S_i(t) \rangle$ (the brackets $\langle \dots \rangle$ denote the average over all firm sizes in a given year) is stationary over time.¹⁰ This quantity is proportional to the market share when the number of firms is constant, but provides two advantages: first, it can also be used to characterize distributions whenever the number of firms changes over time (while the shares distribution would yield a spurious shift of their means) and, second, it provides an easy way of comparing distributions with different numbers of observations.¹¹ In Fig. 4 we plot the distribution function for $g_i(t) = \log(G_i(t))$. The normal fit (dotted line in Fig. 4) clearly shows that the distribution possesses a fatter upper tail than a Gaussian. Think of a growth process as

⁸In particular, our analysis is intended, purposely, to entirely wash away the effects upon industrial concentration of acquisition processes.

⁹We choose to do this in order to avoid problems of international comparisons between different institutional and regulatory systems.

¹⁰For a discussion of the accuracy of this procedure, see Bottazzi et al. (2000).

¹¹The analysis of G is fully equivalent to the analysis of S apart from a scale factor. A similar approach is adopted in Kalecki (1945) and Hart and Prais (1956).

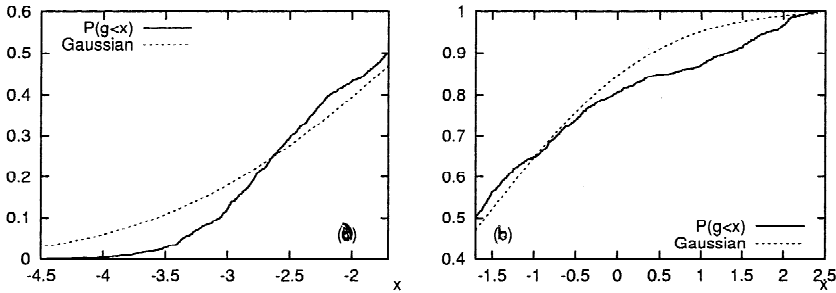


Fig. 4. Distribution function of firm sizes (lower half (a), upper half (b)). A fit with the normal distribution is also shown (· · ·).

$$g_i(t+1) = g_i(t) + h_i(t), \quad (1)$$

with $h_i(t)$ independent random variables. Under mild assumptions on the distribution of h , the size distribution should asymptotically tend to a Gaussian distribution.¹² We checked, however, that this trend is absent from the data (see Bottazzi et al., 2000). As such, this property may already be considered as a piece of circumstantial evidence against a simple Gibrat model. However, let us explicitly examine the properties of the growth process both at aggregate and disaggregate levels.

3.3. Corporate growth dynamics

As already mentioned, a classic benchmark in the analysis of growth processes addresses the relationship between size and growth and, in particular, possible departure from the so-called “Law of Proportionate Effect”.¹³ A first step is to check for possible “reversion to the mean” in our data. In order to do that we estimated the model $g_i(t+1) = \beta g_i(t) + \varepsilon_i(t)$ cross-sectionally for all the years, finding values for β statistically equal to one, thus rejecting the “reversion” hypothesis (see Appendix A for more details). Consequently, one is entitled to refer to (1) and confine the analysis to the properties of h . Fig. 5 reports the distribution for h averaged over time together with the distribution for some time

¹²For the Central Limit Theorem the n th normalized cumulant $\lambda_n = c_n/\sigma^n$ of the size distribution $\Sigma_{t=0}^T h_i(t)$ would behave as $\lambda_n \sim T^{1-n/2}$ where T are the total time steps. In particular, the third and fourth normalized cumulants, the skewness and the kurtosis, would decrease respectively as $T^{-0.5}$ and T^{-1} .

¹³The literature on the subject is vast and cannot be surveyed here: cf. Ijiri and Simon (1977) and for recent critical discussions of both the evidence and the related theoretical implications, Boeri (1989), Brock and Evans (1986), Sutton (1997) and Geroski (2000).

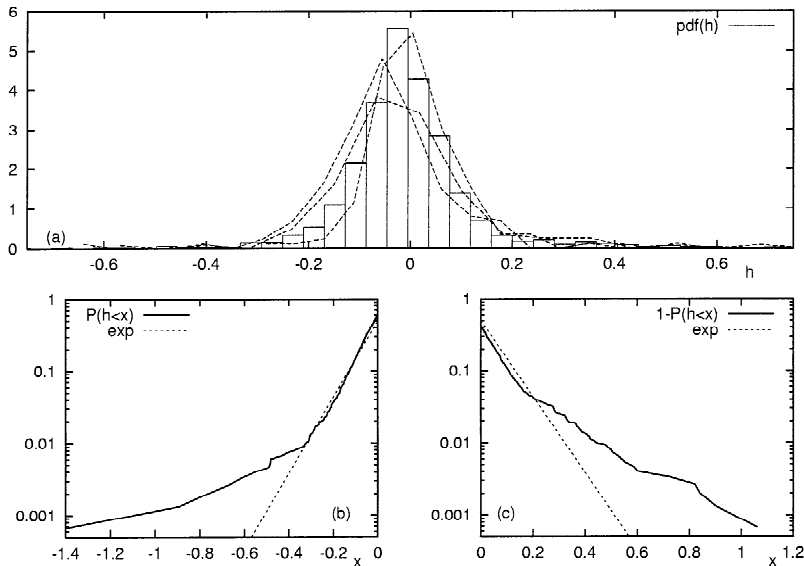


Fig. 5. (a) Probability density for growth obtained with bins (quantiles) of 100 values. The bars show the “average” distribution and the dotted lines the distributions at different time steps. (b) Distribution function for h (lower half). (c) Distribution function for h (upper half). The fit is performed with the exponential distribution.

steps ($t = 0, 5, 10$). As can be seen, differences are small, supporting the assumption, from now onward, that the distribution of h is stationary over time. However, such a distribution is highly non-Gaussian (see Fig. 5) and a fit with a symmetric exponential

$$p(h = x) = \frac{\alpha}{2} e^{-\alpha|x-m|} \quad (2)$$

provides a good description of its central part. Moreover, the distribution is asymmetric with fat tails corresponding to spurs of growth that are more frequent than those predictable on the grounds of a Gaussian noise process (see Fig. 5).

We have previously argued that the stability and the shape of the size distribution can hardly be explained using the simplest Gibrat-type model in (1) with independent increments. An interesting problem indeed concerns the identification of possible sources of “dependence” in the growth process governing this industry. The first effect to analyze is the possible autocorrelation in time of firm growth. In Fig. 6 we plot the autocorrelation coefficient of the logarithmic growth $c(t, \tau)$. The plotted line is the average $\bar{c}(\tau) = \sum_t^T c(t, \tau) / T$, where T is the number of

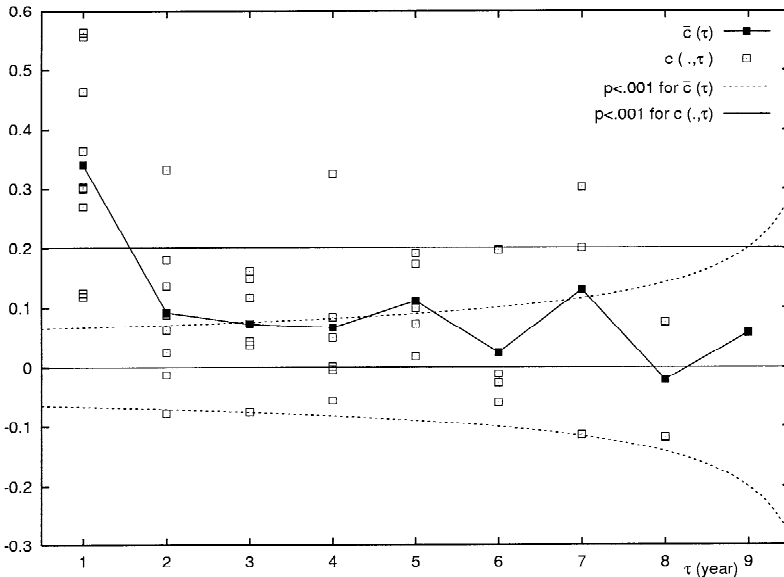


Fig. 6. Time autocorrelation of firm growth. The points are the values $c(t, \tau)$ for different times t plotted against τ . The line is the mean value $\bar{C}(\tau)$. The significance line for $P = 0.001$ (about 2.46 standard deviations) is plotted for both the single points and the average.

years covered in our database and τ is the time lag.¹⁴ If one considers the average correlation $\bar{c}(\tau)$, contrary to the prevailing results in the literature (for a critical discussion, cf. Geroski, 2000) our data do highlight, on average, a significant ($P < 0.001$) positive autocorrelation until the second lag $\tau = 1, 2$ (while we do not dare to make any claim on longer time lags).¹⁵

Fig. 6 refers to the growth of firms as a whole. However, in order to fully understand corporate growth, it is necessary to investigate the persistency profiles by firms within single therapeutic categories (“sub-markets”). Indeed, this is a level of observation nearer to the actual competition process, where innovative shocks are likely to exert their effect. Let us look at the distribution function of the autocorrelation $\bar{c}_j(\tau)$ over the set of all sub-markets and plot it for different τ lags.

¹⁴The data points relative to the same lag τ but different initial time t are dispersed, partly due to the relatively small number of observations and partly for a seemingly “true” difference in the growth from time to time (indeed, there are points separated by more than three standard deviations). In any case, the hypothesis $c(t, 1) = 0$ is rejected with a significance greater than 0.001 in seven over nine time steps t .

¹⁵Notice, however, that one should be cautious about the procedure of taking the average correlation as an estimate of a “true” (stationary) correlation, due to the high dispersion of $c(t, \tau)$ for different initial times t .

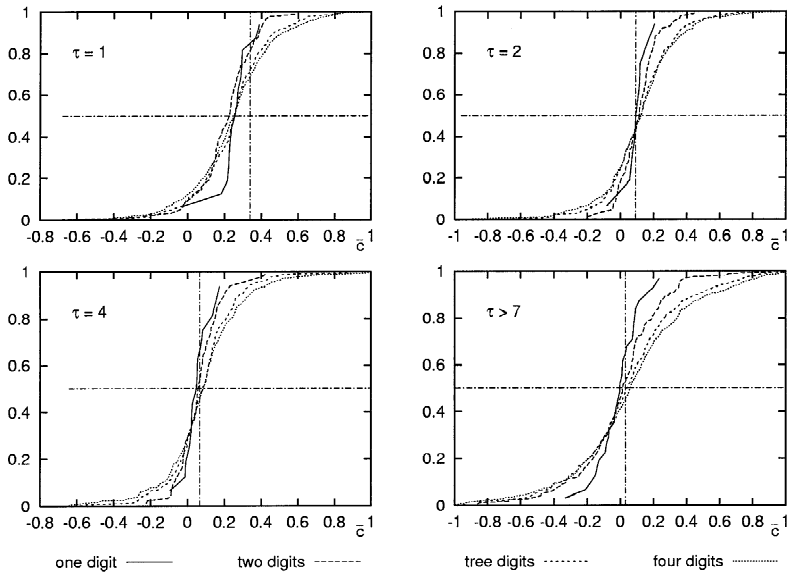


Fig. 7. Distribution function of the autocorrelation coefficients $\bar{c}_j(\tau)$. Different aggregation levels and time lags τ are plotted. The vertical lines correspond to “aggregate” values at the firm level. The horizontal line is centered at 0.5.

Fig. 7 presents the results for different levels of disaggregation (one, two and three digits, according to the therapeutical classification; see above). As can be seen the distributions are similar for different disaggregation levels and, remarkably, sales aggregation at the firm level does *not* wash away autocorrelation in growth; on the contrary, for $\tau = 1$, *firm-level autocorrelations* are significantly *higher* than the average *autocorrelation* calculated at any disaggregation level (this property disappears for $\tau > 1$). Moreover, a positive average autocorrelation seems to survive for a long time even if of negligible magnitude.¹⁶

Interestingly, one is also able to observe important market-specific characteristics in the competitive dynamics. In fact, as shown in Bottazzi et al. (2000), the distribution of the growth correlation of the two leading firms for each sub-market is U-shaped, suggesting that different market-specific growth processes coexist within the industry, including both highly correlated and anti-correlated patterns. The inter-market heterogeneity might indeed be the effect of considering statistics over different “windows of observation” of a “technology cycle” shaping the

¹⁶We also searched for a possible dependence of the autocorrelation $\bar{c}_j(\tau)$ on the size M_j of the sub-markets themselves, but no evidence of any such dependence was found.

growth process in each sub-market.¹⁷ So, for example, one might expect a positive correlation in the stages of penetration of new products and an anti-correlation associated with imitative entry and patent expirations (for an illustrative example, see Section 2).

To further investigate the growth structure we computed the 1-year transition matrices of the stochastic variable h both at the aggregate and at the three-digit sub-market levels. Having controlled the robustness of our results for different numbers of bins¹⁸ (ranging from 20 to more than 200) without revealing remarkable variations, let us present the analysis at the highest level of resolution supported by the data. More precisely, the actual rate of variation over time of the aggregate standardized growth (h_i) and disaggregate one (h_{ij}) were uniformly divided into 50 quantiles and every firm was assigned to them in each year. Since the transition matrices of h do not change substantially over time (as well as the distribution of h itself, see Fig. 5), we analyzed jointly the 1-year transition probability matrices. Two transition matrices were computed, at the aggregate (Π_a) and at the sub-market level (Π_d):

$$[h_i(t)] = \Pi_a[h_i(t-1)], \quad (3)$$

$$[h_{ij}(t)] = \Pi_d[h_{ij}(t-1)], \quad (4)$$

where $[h_{i(j)}(t)]$ are column vectors of binned growth at time t and each row of Π_a and Π_d represents the conditional probability vector of moving through the grid. Figs. 8 and 9 show the three-dimensional plot of transition matrices Π_a and Π_d . To interpret the graphs, take any point on the $[h_{i(j)}(t-1)]$ axis and look in the direction parallel to the other axis in order to trace out the probability density describing the transition to different parts of the growth distributions (more details on discrete stochastic kernel analysis can be found in Quah, 1996). If the graphs pile up on the positive sloped diagonal this may be interpreted as evidence of high persistence and “inertia”. Actually, Fig. 8, in line with our previous findings, shows a significant autocorrelation in growth rates at the aggregate firm level: more specifically, an oblique shape clearly emerges which may be fitted by a line with slope 0.38 passing through the mean values of $h_i(t)$ and $h_{ij}(t-1)$. Over time, the growth distribution converges towards its mean value where most of the observations are concentrated. However, note that the autocorrelation appears to be highly dependent on relatively rare events of sustained growth represented by the spikes in the top right quadrant of the transition matrix. Remarkably, qualitative inspection shows that the majority of these growth events corresponds to large innovation breakthroughs.

¹⁷Our statistics cannot discriminate between purely random micro-processes and more systematic competition processes observed at random times.

¹⁸The “bins” are the different intervals of values (quantiles) by which the data are partitioned.

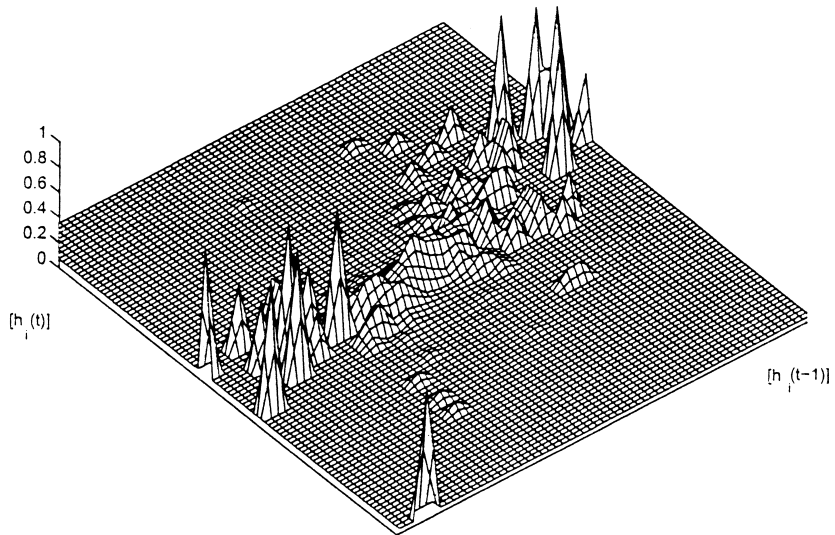


Fig. 8. Growth transition matrix at the aggregate level.

The companion Fig. 9, computed at the sub-market level, enables us to disentangle growth autocorrelation in terms of single market dynamics. Two different regimes are clearly distinguishable. The products that at time $t - 1$ experienced growth above the average are sharply divided into two groups: some

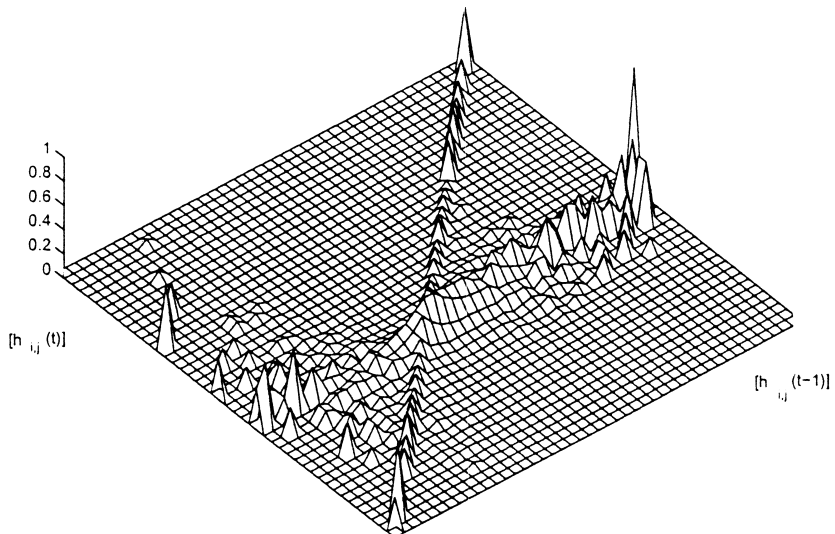


Fig. 9. Growth transition matrix at the sub-market level.

of them maintain their growth pace unchanged, while most of them subsequently drop on the mean. Conversely, the mean growth level also represents an absorptive state for slow (below the mean) growing products, but the phase transition is considerably smoother. New products burst onto the market and grow swiftly for a short period of time, then a cluster of analogue drugs enter (and possibly licensing begins also). As a result, innovative drug growth slows down. After a while, all incumbents tend to grow approximately at the same rate, even if with highly asymmetric shares in favor of the early movers.

Given the foregoing features of growth processes, at both corporate and disaggregate market levels, let us suggest some elements of an interpretation drawing upon possible forms of heterogeneity across firms, in particular with reference to diversification profiles and innovative patterns.

3.4. *Size, diversification across sub-markets and Gibrat violations*

The tangled and “classic” question concerning the possible dependence of the distributions of the growth rates on the initial firm size is, of course, not exhausted by the forgoing (negative) findings on correlation measures between growth and size. While the existence of correlation in a Gibrat-type test between growth and size would be sufficient to reveal dependence, the converse does not hold: dependence might just show up at higher moments of the conditional distributions. In Fig. 10 we plot the moments of the growth distribution for different size classes built considering, at each time step, all the firms with a size in a given range.

In line with a few contributions in the literature,¹⁹ as Fig. 10 shows, no dependence of mean growth appears, and neither does dependence in auto-correlation. However, a clear pattern emerges concerning the variance of growth rates, decreasing with increasing size. Fitting the relation between growth variance and size with an exponential law:

$$\sigma(h) \sim e^{\beta g}, \quad (5)$$

we obtain a value $\beta \sim 0.2 \pm 0.02$, which is strikingly similar to the value found in other analyses of different data sets (cf. Stanley et al., 1996; Lee et al., 1998).

The rather unique possibility offered by the PHID database is to break down sales until the fourth digit of the ATC code, allowing, as mentioned, the identification of sub-markets that are “specific” enough to be considered the loci of competition among firms, and also a more accurate evaluation of the relationship between diversification, and variance of growth and size.

Were one to assume that firms are collections of independent elementary lines of business, roughly of the same size, whose number is proportional to the overall size of the firm, then the Law of Large Numbers would predict a relation between variance of aggregate growth and firm size of the form $\text{var}(h) \sim g^{0.5}$. However,

¹⁹cf. Boeri (1989), Evans (1987), Geroski (2000), Geroski et al. (1998), Hall (1987), Hymer and Pashigian (1962), Mansfield (1962) and Sutton (1997) among others.

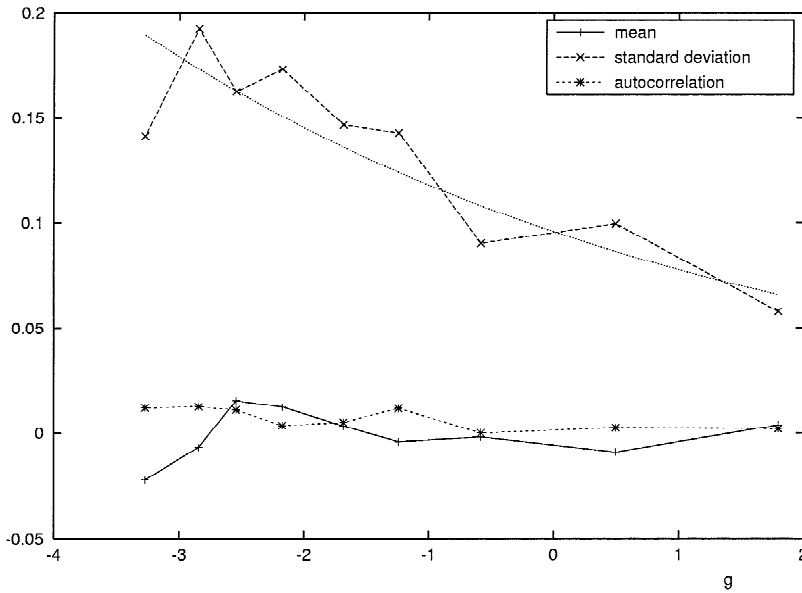


Fig. 10. Mean, standard deviation and autocorrelation of growth h computed for different size bins plotted against the average size in the bin. The exponential fit to the standard deviation (see (5)) gives a value $\beta = -0.20 \pm 0.03$.

both the existing literature and our data (see Fig. 10) show a *smaller* exponent.

In the literature, this departure from the predictions of the Law of Large Numbers is typically imputed to some interrelation between the “components” that make up each firm²⁰ (cf. Boeri, 1989; Stanley et al., 1996).

Conversely, as we shall do, one could relax the assumption of (unobserved) elementary components and measure the actual relationship between aggregate firm size and the number and size of its lines of business. In fact, our analysis shows that the Law of Large Numbers does explain the observed relationship between size and variance of growth if one considers as elementary lines of business the different sub-markets in which each firm operates. This result comes from two observations: first, that the correlation across sub-markets is negligible and, second, that the number of active sub-markets of a given firm increases, on average, with its size following a non-linear scaling law.

More formally, let $S_{i,j}(t)$ be the size of firm i in sub-market j at time t , and $S_i(t) = \sum_j S_{i,j}(t)$ its total size. The aggregate growth of each firm can be written as

$$\frac{S_i(t+1)}{S_i(t)} = \sum_j \frac{S_{i,j}(t+1)}{S_i(t)} \tag{6}$$

²⁰Note that imposing a simple correlation in components growth is not enough to explain the small value of γ .

We computed the correlation of $S_{i,j}(t+1)/S_{i,j}(t)$ for all firms in all sub-markets, obtaining a distribution sharply centered around zero.²¹ For any practical purpose, the growth in different sub-markets can then be considered uncorrelated and, therefore, the variance of the aggregate growth is the sum of the variances of growth in each sub-market.

Defining $R_{i,j}(t) = S_{i,j}(t+1)/S_{i,j}(t)$ and $\Delta_{i,j}(t) = N_i(t)S_{i,j}(t)/S_i(t)$, where $N_i(t)$ is the number of sub-markets in which firm i operates at time t (active sub-markets), the variance of the growth of the “normalized” size G becomes

$$\text{var}_{i,t}[H_i(t)] = \text{var}_{i,t} \left[\frac{G_i(t+1)}{G_i(t)} \right] = \sum_j \text{var}_{i,t} \left[\frac{M(t)}{M(t+1)} R_{i,j}(t) \frac{\Delta_{i,j}(t)}{N_i(t)} \right], \quad (7)$$

where $M(t)$ is the average (aggregate) size of the firm at time t and the ratio $M(t)/M(t+1)$ is a normalization factor (proportional to the rate of growth of the total industry). Here, $\text{var}_{i,t}$ denotes the variance of the distribution obtained using the complete panel (all firms at all time steps).

In (7) the contribution of each sub-market factorizes in three terms, namely, first, $R_{i,j}(t)$, the actual growth of firm i in sub-market j ; second, the inverse number of active markets, $1/N_i(t)$; and, third, $\Delta_{i,j}(t)/N_i(t)$, a weighting coefficient describing the “diversification asymmetry” of firm i .²² It happens that the mean and variance of the distribution of $R_{i,j}(t)$ and $\Delta_{i,j}(t)$ obtained using different size bins do not show any clear dependence on the average size of the firms in each bin (see Bottazzi et al., 2000). Therefore, the number of active sub-markets, $N_i(t)$, must be solely responsible for the observed dependence of the variance over the aggregate size. Fitting on a log–log scale the average number of active sub-markets for each bin against the average size of the bin, one obtains a slope $\alpha = 0.39 \pm 0.02$ and an intercept $q = 6 \pm 0.12$ (see Fig. 11). The Law of Large Numbers would predict a relation between the exponent in Fig. 5 and the slope in Fig. 11 of the form $\beta = -\alpha/2$ which is in perfect agreement with our evidence.²³

Summarizing, our evidence shows (i) that the number of sub-markets in which a firm operates increases non-linearly with firm size and (ii) that such a number fully accounts for the observed relationship between growth variance and size.

The relation provided by the Law of Large Numbers is valid as long as one considers the actual number of sub-markets a firm operates in. In order to demonstrate this statement, it was necessary to rule out two possible sources of functional dependence between aggregate growth variance and size, namely, first, the possibility that the mean and the variance of firm growth in individual

²¹ With a standard deviation of 0.388×10^{-4} and an average deviation of 0.24×10^{-5} .

²² This term captures the asymmetry in the contribution of each sub-market to the overall sales of the firm. If firm i at time t is symmetrically diversified over its active sub-markets, the distribution of $\Delta_{i,j}(t)$ in j is centered around 1, otherwise it is more broadly distributed.

²³ Notice that there is a weak relationship between the variance of $\Delta_{i,j}(t)$ and the aggregate size. A linear fit provides a slope of 0.09, which is, however, negligible compared to the effect of the number of active sub-markets.

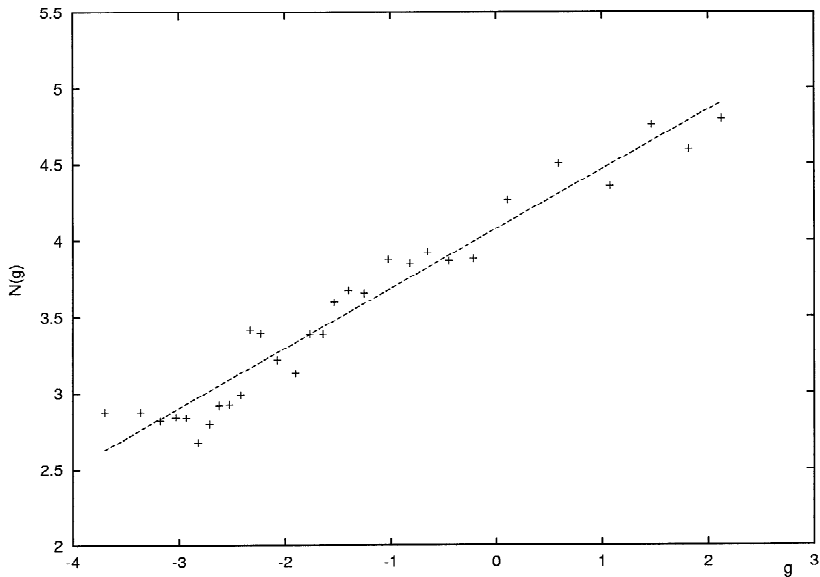


Fig. 11. Number of sub-markets a firm operates in vs. the firm's size (log–log scale).

sub-markets depend (on average) on its total size and, second, the possibility that the diversification pattern of a firm varies (on average) with its size.²⁴

In turn, however, a puzzling implication of these findings (as already pointed out by Boeri, 1989) is that a large firm is more “risky” than a collection of smaller firms: a notional investor would face a lower risk by diversifying their portfolio in N (independent) firms of size S rather than betting on one single firm of size NS .

From an interpretative perspective all this militates against the hypothesis that diversification is driven by risk-minimizing considerations. Rather, the evidence may be plausibly interpreted in terms of *competence-driven* diversification processes, in the presence of knowledge spillovers across products and lines of search. In fact, as formally discussed in Bottazzi (2000), the observed diversification patterns can essentially be described by a stochastic branching process: its economic interpretation may be plausibly grounded in the incremental development of knowledge bases, driving the exploration of an expanding range of products/markets.

3.5. Innovation and growth

A major tenet of evolutionary theories of industrial dynamics is indeed the general conjecture that the processes of technological innovation and imitation are

²⁴ Both these possibilities are actually discussed in the literature as possible sources of violation of Gibrat Law (see, for instance, Hart and Prais, 1956).

major drivers of industrial dynamics and also of the competitive fate of individual firms.²⁵ How does our evidence bear on this proposition?

Let us begin by considering the process of the introduction of innovative drugs, both New Chemical Entities and patented products,²⁶ into the US market. Consider first the distribution of NCE launches over the population of firms throughout the 11 years of observation (1987–97). In fact, the number of NCEs that a firm introduces over a given period may be understood as one proxy for its “degree of innovativeness”, and as such contributes to the possible revelation of underlying forms of heterogeneity across firms in their ability to innovate.

As a benchmark, let us model what would happen with technologically homogeneous firms. Under these circumstances, as a first approximation, one may consider the arrival of different NCEs as independent events. This means that, given a set of N NCEs introduced by a population of F firms, the probability of finding a firm which introduced exactly k NCEs is given by the binomial distribution

$$p_{M.B.}(k) = \binom{N}{k} \left(\frac{1}{F}\right)^k \left(1 - \frac{1}{F}\right)^{N-k} \quad (8)$$

As shown in Fig. 12, this model (known as Maxwell–Boltzmann statistics) provides a poor description of the observed frequencies.

Indeed, the assumption of random independent assignments is at odds with the qualitative evidence of whole families of research projects conducted by each firm over several years, often entailing knowledge spillovers across them. Hence, one may conjecture some correlation amongst NCE arrivals due to learning effects across individual research projects. In order to check this hypothesis empirically, one should check whether the random assignments of innovations to individual firms indeed concern “packets” of NCEs rather than single products. Under the assumption of equiprobability of the packet sizes, the appropriate statistics, known in physics as the Bose–Einstein statistics (Reichl, 1980), consider the probability of finding a firm who introduced exactly k NCEs:

$$p_{B.E.}(k) = \frac{\binom{F+N-k-2}{N-k}}{\binom{F+N-1}{N-1}} \quad (9)$$

As can be seen from Fig. 12, the latter distribution provides an excellent description for low to average NCE numbers and only fails for the very large assignments. It is also interesting to note that the propensity to introduce NCEs is not monotonic in the size of the innovative firms themselves (so that, for example, the upper tail in the distribution in Fig. 12 does not feature the largest firms in the

²⁵For theoretical arguments, cf., among others, Nelson and Winter (1982) and Dosi et al. (1995, 1997), and for qualitative historical discussions, Freeman (1982) and Pavitt (1999).

²⁶Note that the former are a small subset of the latter.

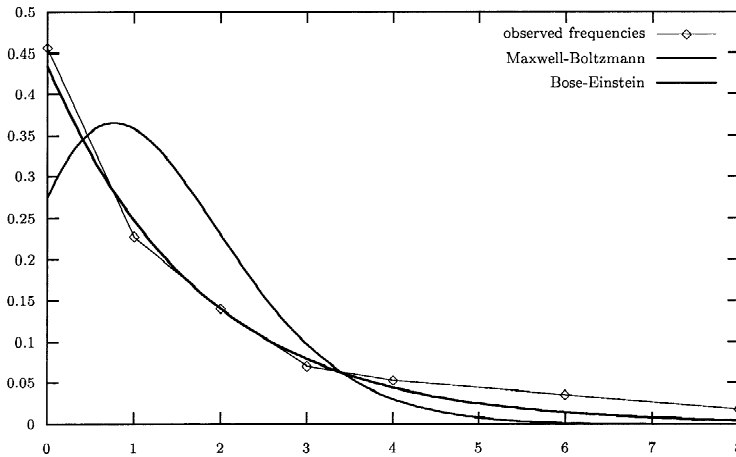


Fig. 12. Frequencies of total NCEs introduced over the firms population (x-axis, firms introducing 0,1,...,8 NCEs; y-axis, frequencies thereof).

industry). This evidence hints at some underlying forms of heterogeneity in search competences and/or search orientation (e.g., biased in favor or against the quest for relatively major innovations). Together, the widespread occurrence of “clustering” in the arrivals of NCEs does suggest the importance of firm-specific learning effects across different research projects.

Given the foregoing evidence, a crucial question concerns if (and how much) the introduction of a NCE during a firm’s history affects its growth performance. One can start by partitioning the set of firms depending on the number of NCEs they have introduced during the time window of observation. In Bottazzi et al. (2000) we show that no relationship appears between the number of NCEs and firm performance: indeed, “more innovative” firms do not seem to gain, on average, market shares with respect to “less innovative” firms.

As another, broader, proxy for the innovative capability, let us consider the *patent intensity* of each given firm, defined as the share of patented products present in its products portfolio.²⁷ Again, we observe that, first, the distribution of patent intensity on the population of firms is very heterogeneous; second, larger firms tend to show lower than average patent intensity in their product portfolios, while some of the smaller firms have a value near to unity; and, third, no systematic relationship appears between the structure of product portfolios and growth performance. Taken together, all the foregoing pieces of evidence suggest that firms embody rather idiosyncratic bundles of products, characterized by varying degrees of innovativeness, without, however, systematic effects of the “technological ID” of the firm itself upon its global growth performances (more on this in Bottazzi et al., 2000).

²⁷ Recall that patents, often based on “creative analogues”, new ways of combining existing NCEs, etc. are much more frequent than NCEs.

Note that all this does not imply homogeneous market dynamics of the three groups of products (NCEs, patented drugs and non-patented drugs) in the four-digit sub-markets in which they compete. Let us consider $S_{i,j,k}$, the sales of product k of firm i in sub-market j , and define the “normalized” sales with respect to all other products in the same four-digit sub-market as

$$G_{i,j,k} = \frac{S_{i,j,k}}{\langle S_{i,j,k} \rangle_{i,k}} \tag{10}$$

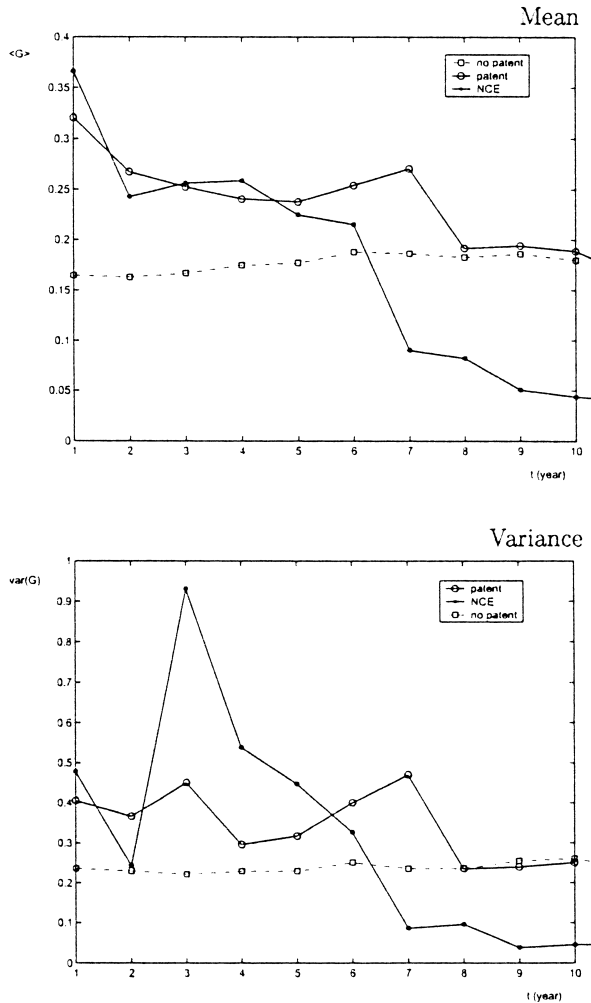


Fig. 13. Mean and variance of sales distribution for NCEs, and patented and non-patented products. At any given time we consider only sub-markets with at least 10 products. The product sales are rescaled by the average sales of the sub-market where the product is launched.

Fig. 13 reports the mean and variance of $G_{i,j,k}$ for three categories of products (i.e. NCEs, patented products and all others) as a function of the time elapsed since their introduction (so that on the x -axis one reads the “market age” of each product). Here, one observes a pronounced “market cycle” of NCEs which tends to “hit the market big” and decline relatively soon thereafter, with a burst in the variance (intuitively, a burst in competition with an ensuing high turbulence in market shares) early in their life cycle. The much more numerous family of patented drugs follows, on average, a “market cycle” loosely similar to NCEs, but with much less pronounced changes in both their means and variances. Finally, non-patented drugs appear to be highly stable and occupy from the start their long-term market position.

Therefore, innovation does indeed drive the evolution of each sub-market, but the competitive regime is not such as to guarantee a sustained competitive advantage and systematic above-average growth to the individual innovators either in the affected sub-markets or for the firms as a whole. Rather, one may think of some analogue to population-level mixed-strategy equilibria (here, populations of innovative vs. imitative and “old” products) which persistently coexists within sub-markets and also within single firms. Innovations continue to upset this population, but imitations, analogue developments, etc. are fast enough to curb any long-term advantage to specific products.

4. Conclusions and conjectural implications for the theory

In this work we have explored the statistical properties of the dynamics of an industry — pharmaceuticals — whose long-term evolution is fueled by innovation, imitation and the creation of new markets, trying to identify the possible links between the fundamental features of such evolutionary patterns and the quantitative evidence on corporate growth.

Here — as well as in several studies of this *genre* — a benchmark of departure was the so-called Gibrat Law. However, such a “law”, as Brock (1999) emphasizes, “is useful as a rough approximation to the unconditional distribution of rates of growth of firm sizes, which is especially pertinent to illustrating the degree of accuracy of the ‘Law of Proportionate Growth’; [however] it has poor power to discriminate across different plausible stochastic processes that might fit the stochastic dynamics of firm growth” (p. 432). Our data, breaking down firms’ dynamics over highly disaggregated product markets, as well as complementary pieces of evidence on innovation and competitive patterns, allows us to discriminate the finer structure of the growth processes and their links with size distributions, on one hand, and innovative activities, on the other.

The evidence shows: (a) fat tails in the distribution of growth shocks, present at all levels of aggregation, with (relatively rare) large “spurs of growth”; (b) a significant autocorrelation in growth rates, again at all aggregation levels; (c) a fall

of the variance of growth rate with size (in line with previous findings) which, at closer inspection, is entirely dependent on diversification patterns, in turn plausibly shaped by the “competence scope” of each firm; (d) different “lifecycles” of diverse types of products (defined in terms of their degrees of innovativeness) displaying equally diverse growth profiles; and (e) a persistent form of heterogeneity across firms in terms of innovative output, which, however, does not appear to affect their comparative growth performances.

Our results, on the negative side, allow us to rule out some interpretations of the growth processes as the sum of independent events. For example, the fat-tailed growth distribution and its departure from a Gaussian distribution, even in its central part, is at odds with a “pure Gibrat process”. In this respect, note that if Gibrat dynamics were a strict description of the process this should apply to all time scales (e.g., on monthly or weekly bases, etc.). But then, pushing the reasoning to the extreme, “years” should display a much more Gaussian profile — for the Central Limit Theorem — irrespective of the original distribution of events.

On the positive side, our evidence, first of all, is well in tune with the conjecture (Geroski, 2000) that the time scale of the arrival of “big” growth impulses associated with the arrival of major innovations — i.e. in the case of pharmaceuticals, New Chemical Entities — is different from the scale on which corporate growth is measured (i.e. accounting years). Such shocks are quite rare, are persistently generated by a relatively small number of innovators (indeed, a subset of the population of top incumbents considered in this work), but any one innovator is unlikely to hit the same market twice. Moreover, NCEs a few times *create new markets*.

Hence, the overall, industry-wide growth dynamics is likely to be the mixing of two different underlying evolutionary processes. The first, driven by major, rather rare, innovations, often entails the generation of new market niches (new therapeutic targets, etc.). The second (“faster”) process is associated with imitation, development of analogue drugs, incremental therapeutic improvements, etc., and drives the competition process within already existing markets.

Our analysis also reveals persistent forms of heterogeneity across firms. First, the autocorrelation in firm growth, increasing with the scale of observation, does indeed hint at some significant firm-specific structure in the growth process, possibly related, we conjecture, to firm-specific organizational competences in the search for and introduction of products in different markets. Second, firms systematically differ in their innovative propensity (either when measured in terms of NCEs or of patented products).

However, the diversity in the technological profile of each firm does not appear to influence long-term growth performance. Rather, our evidence appears to support some sort of “ecology” of heterogeneous firms (and of products at different stages of their lifecycle within single firms) holding some sort of long-term evolutionary complementarity.

Further corroborations of this interpretation will also involve conditioning the observed dynamics upon finer proxies for the technological characteristics of firms

and upon the “stages” of market development. We would like to consider this work as an initial exploration of links between some basic features of industrial evolution — so far analyzed empirically in a largely qualitative manner — on the one hand, and the “emergent” statistical properties of industrial structures and growth dynamics, on the other.

Acknowledgements

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Appendix A. A linear test of the Gibrat Law

A common procedure to analyze growth processes, to which we shall adhere, is to check for departures from the so-called Gibrat Law, that is for growth patterns deviating from the proportionality of mean growth to size. The “law” may be stated in different but statistically equivalent forms.²⁸

In the version proposed by Kalecki (1945) and adopted, among others, by Hart and Prais (1956) and Chesher (1979), the Gibrat linear test refers to the dynamics of the deviations of natural logarithms of firm sizes from their means ($g_{i(j)}(t) = s_{i(j)}(t) - \langle s_{i(j)}(t) \rangle$) and it is meant to provide an estimate of the divergence/convergence of the size distribution toward its mean. In that vein, one tests the model

$$g_i(t) = \beta g_i(t-1) + \varepsilon_i(t), \quad (\text{A.1})$$

and one typically concludes that the Gibrat Law is satisfied if the OLS estimator of $\beta(t)$ is close to unity.

We apply this analysis on our panel, testing the model cross-sectionally for each time step. Let $\beta(t)$ be the OLS estimation of the coefficient in (A.1) at time t :

$$\beta(t) = \frac{\sigma_g(t)}{\sigma_g(t-1)} \rho_g(t), \quad (\text{A.2})$$

where $\sigma_g^2(t) = \langle g_i(t)^2 \rangle$ is the variance of g at time t and $\rho_g(t) = \langle g_i(t)g_i(t-1) \rangle$ is the autocorrelation.

²⁸Cf., among others, Mansfield (1962), Ijiri and Simon (1977), Geroski (2000) and Sutton (1997).

Table 1
Gibrat test results — aggregate level, 1-year time lag. R^2 is always greater than 0.98

t	β	ξ
1988	0.982	0.998
1989	0.991	0.989
1990	1.006	1.006
1991	1.008	0.958
1992	1.017	1.004
1993	0.997	0.982
1994	1.004	0.938
1995	1.001	0.953
1996	1.000	0.959
1997	1.005	0.978

From (A.2) it immediately follows that the variance of the size distribution decreases at time t when $\beta(t) < \rho(t) \leq 1$. Table 1 reports the statistics resulting from the tests carried out over the period 1987–1997. As shown, $\beta(t)$ and $\xi(t) = \sigma_g^2(t)/\sigma_g^2(t-1)$ are always very close to unity, indicating that size does not exert a significant influence on expected growth, with the variance of the size distribution remaining constant over time. In fact, given these results, one is entitled, as we did, to refer constantly to (1) and analyze the distribution of h defined there (since this analysis is fully equivalent to the analysis of errors ε of (A.1)).

Let $h_{i,j}(t) = g_{i,j}(t) - g_{i,j}(t-1)$ be the (logarithmic) growth of firm i in sub-market j . Remember that g is defined as the logarithm of the “normalized” size G .

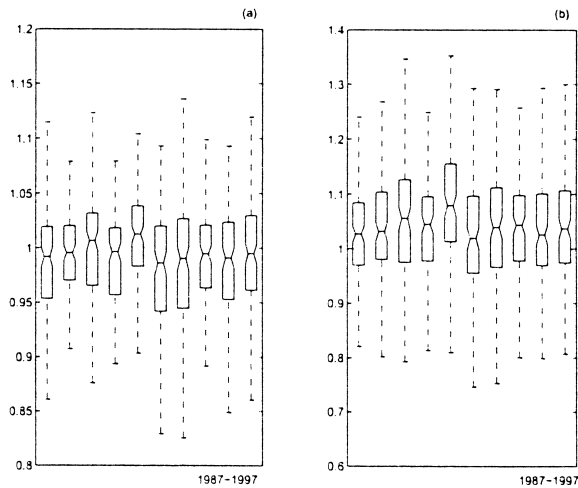


Fig. 14. Gibrat test at the three-digit sub-market level, 1 year time lag. Boxplot (a) reports the distributions of $\beta_j(t)$, while (b) depicts the distributions of $\xi_j(t)$ (cf. Eq. (A.1)).

Here, $G_{i,j}(t)$ is normalized using the size of the j th sub-market $M_j(t)$. We then test the analogue to (A.1) at the disaggregate level.²⁹ Fig. 14 reports the values of $\beta_j(t)$ and $\xi_j(t)$ for each sub-market j . In line with the aggregate results, the median of $\beta_j(t)$ stays quite close to unity over time, but the distribution of $\beta_j(t)$ display a remarkable degree of heterogeneity among sub-markets, ranging from 0.82 to 1.14. On the contrary, the median of the $\xi_j(t)$ distribution is constantly above unity, indicating that the variance of firm sizes in individual sub-markets increases (on average) over time.

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²⁹We considered the 180 sub-markets including at least 20 firms out of the 302 covered by PHID. They account for 85.6% of the pharmaceutical market. Furthermore, we checked the invariance of our results considering sub-markets with different numbers of competitors.

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