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Processes of corporate growth in the evolution of an innovation-driven industry. The case of pharmaceuticals.

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1 Introduction

This work — which is part of a larger on-going research on industrial dynamics — investigates the patterns of change in the international pharmaceutical industry, in particular with respect to the industry structure and the growth 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, whereby innovation is driven, to a large extent, by joint advances in pure and applied sciences, together with complementary progress in research technologies — undertaken both within public research institutions and business firms.

In turn, innovation itself, 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 represents also a rich domain for the analysis of the properties of microeconomic processes of growth, possibly with theoretical implications well beyond its sectoral boundaries — touching the characteristics (and time profiles) of industrial structures, the underlying dynamics of inter-product/inter-firm competition and of corporate diversification across markets.

Indeed, one of the questions that this work addresses concerns the statistical properties of firm growth — and the ensuing size distributions — over the "window of observation" of around a decade, taken within a longer process of industrial evolution which we shall qualitatively characterize in its basic features below.

In the pharmaceutical industry, since its origin, innovation — *in primis*, in the form of new therapeutical products — has been a fundamental determinant of the competitive strength, profitability and market shares of each firm. Circumstantial evidence suggests that "big innovations" — i.e. compounds which address previously uncured diseases or substitute existing treatments with different biochemical mechanisms and outcomes — come relatively rarely, often marking the competitive position of whole firms (think of aspirin with respect to Bayer or, more recently, the anti-ulcer Zantac in the case of Glaxo...). At the same time, an intense activity of improvements, "inventing around", and licensing, generally allows late comers to each therapeutical market to gain relevant shares, even well before patent expirations of the early "prototypical" innovation. These, intra-market dynamics, together with the processes of diversification across markets, determine the dynamics of internal growth of firms.

In Section 2, we shall reconstruct some characteristics of these basic evolutionary patterns. Given them, in Section 3 we shall study the resulting properties of corporate growth and international industrial structures, with respect to the top 150 incumbents operating on the 7 major western markets.

A classic benchmark in this type of analysis is a Gibrat-type question, addressing the relationship between size and growth over time and in particular possible departures from the so-called "Law of Proportionate Effect", entailing processes of stochastic growth uncorrelated with firm sizes.

The literature on the subject is vast and cannot be surveyed in any detail here (cf. Ijiri and Simon, 1977, and for recent critical discussions of both the evidence and the related theoretical implications, Boeri, 1989a; Brock, Evans, 1986; Sutton, 1997 and Geroski, 1999).

Telegraphically, the existing empirical evidence appears to suggest erratic growth rates (with low or inexistent autocorrelation over time) — often found to be uninfluenced by initial size in their means and (negatively) influenced in their variances — and rather high persistence of sizes themselves (thus conflicting with any notion of a transitory dynamics toward some "optimal" size)[1].

There are some important limitations to the quality of many data samples on which these conclusions are based. One of them, which we shall avoid in this work, is that many studies are undertaken using firms as sole unit of analysis even, when they embody a collection of different production activities and operate in different markets. In turn, this type of aggregation might wash away more systematic but technology-specific effects.

All this notwithstanding, it remains true that the foregoing evidence raises a few theoretically puzzling issues. For example, could it be taken to mean that constant return to scale are the norm throughout modern industry and that growth is basically driven by several small and idiosyncratic events (as Ijiri and Simon, 1977 suggest)? How does this statistical evidence stand vis-à-vis other more microeconomic-based evidence on systematic and long-standing differences in technological and organizational competencies across firms?[2]

An analysis based (as we do in the following) on longitudinal data in a well-defined industry — with also disaggregate observations down to individual product markets — allows to shed new light on these questions, in that one is able 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

[1] cf. among others Boeri, 1989a; and 1989b; Geroski, Urga, Walters, 1997; Geroski, 1999; Hall, 1987; Leonard, 1988; Sutton, 1997.

[2] The point is discussed from different angles in Dosi et al, 1995, 1997 and Geroski, 1999.

Company	Rank	M.Share	Company	Rank	M.Share	Date
Roche	6	3.73	Boehringer M.	67	0.24	5/97
Sandoz	11	2.63	Ciba-Geigy	13	2.56	3/96
Rhone-P. R.	16	2.14	Fisions	61	0.36	12/95
Pharmacia	29	1.27	Upjohn	20	1.60	11/95
Hoechst	4	3,20	Marion M. D.	23	1.50	7/95
Glaxo	2	4.52	B. Wellcome	19	1.63	3/95
Am. Home Pr.	11	2.54	Am. Cyanamid	21	1.52	12/94
Rhone-Poulenc	20	1.75	Rorer	36	0.92	7/90
Am. Home Pr.	7	2.59	Robins A. H.	62	0.39	12/89
Bristol-Myers	13	2.02	Squibb	18	1.78	10/89
SmithKline	23	1.60	Beecham	22	1.61	7/89

Table 1: M&A activity among the top100 firms, 1987 - 1997 (sources: Scrip League Tables)

processes. Putting it the other way round, one is able to investigate the statistical properties which are "emergent" from specific evolutionary dynamics of heterogenous learning and market selection.

Our results, while broadly in line with previous findings corroborating "weak" versions of the Gibrat Law (i.e. independence of growth rates from size) highlight also a much richer structure of the growth process than previously found, with significant autocorrelation appearing at all levels of aggregation, a fat tail of "big" growth events, plausibly associated with major innovations and with the emergence of new product markets, and the stability of an oligopolistic core of the industry which maintains itself via diversification across diverse therapeutic markets and "horizontal" innovative capabilities across them.

2 The evolution of the industry: an overview

The history of the international pharmaceutical industry has already been extensively analyzed by several scholars[3]. Here let us first mention a few major characteristics of innovation processes, competition and industrial structures.

The origin of the industry dates back to the late 19th century and is indeed one of the early examples of commercial exploitation in organized manners of scientific search and discoveries, beginning with the emergence of the synthetic dye production and the discovery of the therapeutic effects of dyestuff components and other organic chemicals.

Before the 1930s, pharmaceutical innovation was almost completely dependent upon few large, diversified, and vertically integrated German and Swiss firms, such as Hoechst, Bayer, Ciba, Sandoz. These firms entered the industry in the late nineteenth century and manufactured drugs based on synthetic dyes, being able to leverage their scientific and technical competencies in organic chemistry, chemical synthesis and medicinal chemistry.

On the contrary, until the 1920s, the US and UK pharmaceutical industries consisted largely of relatively small and focused firms (Glaxo, Wyeth, Pfizer, Eli Lilly, Warner-Lambert, Burroughs-Wellcome), and relied upon imported technology for a large part of pharmaceuticals, as well as for other important segments of the chemical industry (dyestuffs, fine chemicals), drawing upon subsidiaries and affiliates of foreign firms (Arora and Gambardella, 1998).

The early emergence of a restricted group of firms with large-scale in-house R&D capabilities was a consequence of the nature of pharmaceutical R&D in the chemical synthesis paradigm and, in particular, of the appearance of a dominant routinized regime of search — paraphrasing Nelson and Winter (1982) — based on extensive exploration of chemical compounds and on incremental structural modifications of *drug prototypes*, organized around highly structured processes for carrying out mass screening programs (cf. Schwartzman, 1976). Throughout the evolution of the industry "the organizational capabilities developed to manage the process of drug development and delivery — competencies in the management of large-scale clinical trials, the process of gaining regulatory approval, and marketing and distribution — also have acted as powerful barriers to entry into the industry" (Henderson, Orsenigo, Pisano, 1999).

[3]See Aftalion, 1959; Ackerknecht, 1973; Arora, Gambardella, 1998; Bovet, 1988; Chandler, 1990; Freeman, 1982; Gambardella, 1995; Henderson, Orsenigo, Pisano, 1999; Orsenigo, 1989; Pammolli, 1996.

NCE	Major Marketing Corp.	1992	1993	1994	1995	1996
Total Number		23	20	15	24	29
Risperidone	Johnson & Johnson	0	6	173	344	522
Finasterine	Merck & Co.	34	173	293	365	389
Paclitaxel	Bristol Myers Squibb	0	124	206	288	380
Fluvastatin	Novartis	0	0	38	156	291
Losartan	Merck & Co.	0	0	0	60	271
Cefprozil	Bristol Myers Squibb	78	138	176	209	242
Alendronic Acid	Merck & Co.	0	0	11	45	221
Venflaxine	American Home	0	0	62	122	206
Epinastine	Boeheringer Ing.	0	0	73	225	186
Lamivudine	Glaxo Wellcome	0	0	0	7	181
Loracarbef	Lilly	14	80	122	158	160
Gabapentin	Warner Lambert	0	1	28	76	158
Dorzolamide	Merck	0	0	0	32	126
Abciximab	Lilly	0	0	0	16	117
Aniracetam	Roche	0	17	52	95	115
Pantoprazole	Altana	0	0	8	50	114
Saquinavir	Roche	0	0	0	4	110
Ceftibuten	Sharing Plough	3	23	44	67	95
Tazobactam	America Home	0	4	41	68	91
Famciclovir	SmithKline Beecham	0	0	19	50	87
Nefazodone	Bristol Myers	0	0	1	44	86
Rocuronium B.	Akzo Nobel	0	0	17	53	81
Trandolapril	Hoechst	0	11	26	45	76
Cefpirome	Hoechst	0	19	82	106	75
Dornase Alfa	Roche	0	0	40	62	72
Aceclofenac	Bristol Myers	12	26	36	51	70
Bicalutamide	Zeneca	0	0	0	6	70
Stavudine	Bristol Myers	0	0	6	32	69
Desflurane	Pharmacia & Upjohn	0	13	45	59	65

Table 2: Sales of New Chemical Entities in USD millions, 1992-1996 (source: our elaborations on IMS International)

War World II induced a massive jump in research and production efforts, sponsored by the US government — especially in the field of antibiotics — which fostered accumulation of vast search capabilities in US firms and their entry into the international oligopolistic core.

Following World War II and the commercialization of penicillin, pharmaceutical companies embarked on a period of massive investment in R&D and built large-scale internal R&D capabilities (Henderson, Orsenigo, Pisano, 1999). Also benefiting from the dramatic increase of public support of biomedical research and health care expenditure in the post war period, the international pharmaceutical industry experienced a significant wave of discovery, with the introduction of several hundreds of new chemical entities in the 1950s and 1960s, from hydrocortisone and several other corticoids, to the thiazide diuretic drugs, to major and minor tranquilizers, to the initial birth control products (Grabowski and Vernon, 2000).

Throughout its evolution, the industry has been characterized by a significant heterogeneity in terms of firms strategic orientations and innovative capabilities. Competition has always centered around new product introductions, often undertaken by the oligopolistic core of the industry, subject to both incremental advances over time, as well as to imitation and generic competition after patent expiration (allowing a large "fringe" of firms to thrive). In a good approximation, the "oligopolistic core" of the industry has been composed by the early innovative entrants joined after World War II by few American and British firms. At the same time, until the mid-1970s a relatively small number of new firms entered the industry, and even less in its "core".

However, things began to change since, with a major transition in the "technological paradigm" underlying search activities, from one based on pragmatic knowledge and quasi-random screening to another one of "guided discovery" (or "discovery by design"). This is linked with major advances in biological sciences, including

Year	'87	'88	' 89	'90	'91	'92	'93	'94	'95	'96	'97
Total	919	994	1360	1287	1407	1345	1465	1214	1369	1687	2391
% top 25	85	84	85	83	83	81	78	78	79	76	77

Table 3: Patents granted to the top 100 firms, 1987-1997 (source: our elaborations on USPTO)

molecular and cell biology, biochemistry, protein and peptide chemistry and physiology[4]. The application of these new bodies of knowledge to the pharmaceutical industry has had a paramount impact on the nature of R&D activities and on the organizational capabilities required to introduce new drugs[5].

Together the "molecular biology" revolution has had (and is having) also major consequences on the patterns of "division of innovative labor" (Arora and Gambardella, 1994; Gambardella, 1995) fostering the emergence of specialized suppliers and pure *search firms*; moreover, the dramatic increase of plausible disease targets offered novel opportunities of entry for a few new small firms into new product markets.

However, this transformation in the knowledge bases of the industry does not appear to have eroded the advantages of incumbency (in particular, *core* incumbency) in the industry.

First, sunk costs required for discovery/development/testing have increased dramatically, due also to the introduction of more stringent efficacy and safety regulations. Nowadays, an R&D project for a new drug is likely to last 12-14 years, with a cost in the range of $ 350-600 millions. And to all that one ought to add the "sunkness" associated with marketing infrastructures (More on these aspects of the industry in Sutton, 1998).

Second, while the "molecular biology" paradigm has increased the importance of publicly generated (scientific) knowledge, it appears also to have increased firm-specific economies of scope related to serendipity in search competencies and knowledge spillover across projects (cf. Henderson and Cockburn, 1996; Henderson, Orsenigo and Pisano, 1999).

Third, the oligopolistic core of the industry has been playing a crucial integrative role across different bodies of knowledge, as well as providing critical complementary assets in clinical development, regulatory affairs and distribution channels.

Indeed, the last two decades have witnessed two major waves of Mergers and Acquisitions deeply affecting the levels of concentration of the industry. The first, at the end of the Eighties, involved top firms like Smithkline and Beecham, Bristol Myers and Squibb, Rhone Poulenc and Rorer. Even more so, the second wave started in the mid-90s, has involved well established members of the *core* like Hoechst and Marion Merrell Dow, Pharmacia and Upjohn, Glaxo and Wellcome, Ciba Geigy and Sandoz, Roche and Boehringer and more recently Glaxo Wellcome and SmithKline Beecham.

For a qualitative appreciation of the magnitude of the M&A process, Table 1 lists all the events concerning the top 100 firms over the period 1987-97. The oligopolistic core of the industry has continued to be up to present the overwhelming originator of "major" innovations — i.e. New Chemical Entities (NCEs) with novel pharmacological activities. So, for example, over period 1992-96 — on which we were able to elaborate the data — the top 25 firms were responsible for more than 90% of the NCEs launched on the major European and North American markets (see Table 2, reporting the list of the top-selling NCEs: all but one were marketed by the top 25 companies). A similar proportion emerges from the list — based on marginally less demanding criteria — complied by Barral (1996) on the period 75-94.

It is important to notice also that, notwithstanding the high R&D intensity of the industry, the successful introduction of NCEs has to be considered as a quite *rare event*. Indeed, estimates suggest that, out of all new compounds that are discovered only one over 5,000 reaches the market (Holliday, Walker and Lumley, 1992). So, as Table 2 shows, the rate of introduction has been of the order of a couple of dozens per year, and concentrated in some fast-growing areas such as central nervous system, cardiac therapy, anti-infectives and cytostatics. Similarly, Barral (1996) estimates the total number of NCEs introduced throughout the world over the period 75-94 to be 154. Innovative new drugs arrive quite rarely but after the arrival they experience extremely high rates of market growth: cf. Table 2 (more on this point in Gorecki, 1986; Grabowski and Vernon, 1992; Robinson, Kalyanaram, Urban, 1994; Dranove and Meltzer, 1994; Office of Technological Assessment, 1993).

New Chemical Entities, however, only capture a part of innovative activities, broadly defined — including

[4]During the Nineties, the new research paradigm has been associated also with new research technologies which achieve a higher breadth of applications in terms of both disease areas and biological targets - including Polymerase Chain Reaction; protein structure modeling; rapid computer based drug assay and testing; recombinant chemistry; chemical separation and purification techniques and combinatorial chemistry that allow to screen thousands of potentially promising compounds and to generate a large number of peptides and other organic molecules (Sneader, 1996; Orsenigo, Pammolli, Riccaboni, 2000).

[5]cf. Henderson and Cockburn, 1994, 1996; Galambos, Sturchio, 1996; Orsenigo, Pammolli, Riccaboni, 2000.

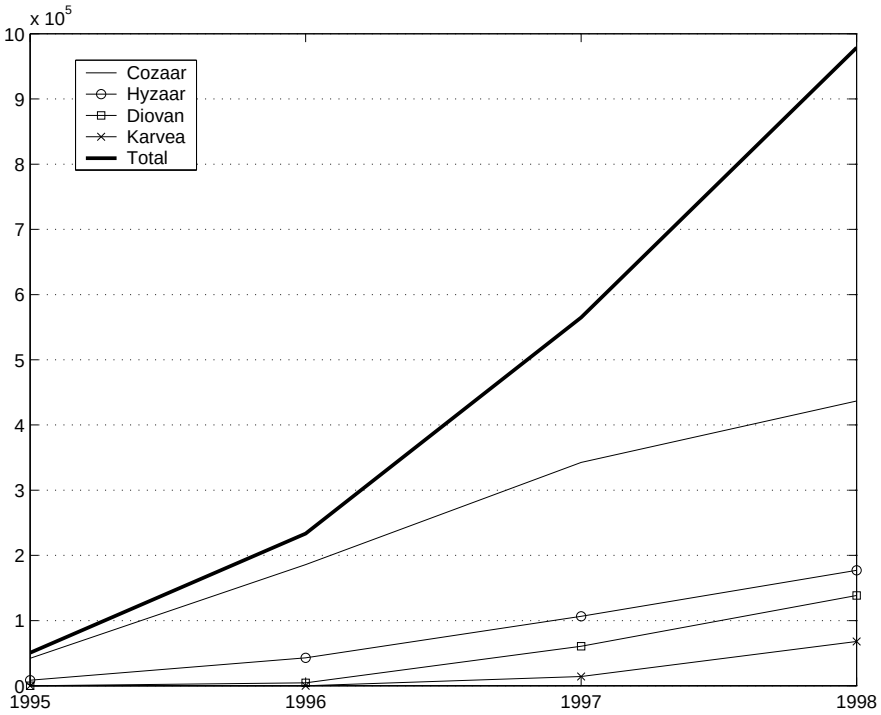

Figure 1: Angiotensin-II Antagonists: Size of the market and firms/products sales, 1987-1998 (US.$ millions)

"inventing-around" existing molecules, new combinations among them, new ways of delivering them, etc. In order to get a rough order of magnitude compare the foregoing data on NCEs with the number of patents granted in the US to the top 100 companies in the sample described in detail below (Table 3). The share of the "oligopolistic core" is also lower — around 80% of the total is accounted by the top 25 firms.

Another remarkable phenomenon is that persistency in the innovative record applies to the oligopolistic core *as a whole* and also to individual core firms when observed across the whole spectrum of therapeutic classes but does *not* apply within single classes. As Sutton (1998) points out the degree to which early innovators enjoy an advantage in introducing later major drugs within the same family has traditionally been fairy limited (p. 198). That, together with the coexistence-existence 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*) co-existence of two basic types of firms, mapping into distinct technological competencies and competitive strategies.

In a shorthand, the first group, closely corresponding to the *core,* undertakes what is sometimes called "pioneering R&D" (Grabowski and Vernon, 1987); generates the overwhelming majority of NCEs; when successful enjoys big, 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; takes up licenses from the core and is present to different degrees in the "generic" markets, after patent expirations[6].

One is tempted to depict 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).

In a nutshell, the archetypical evolutionary story concerning each "disaggregate" 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 them only very few happen to immediately

[6]The 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.

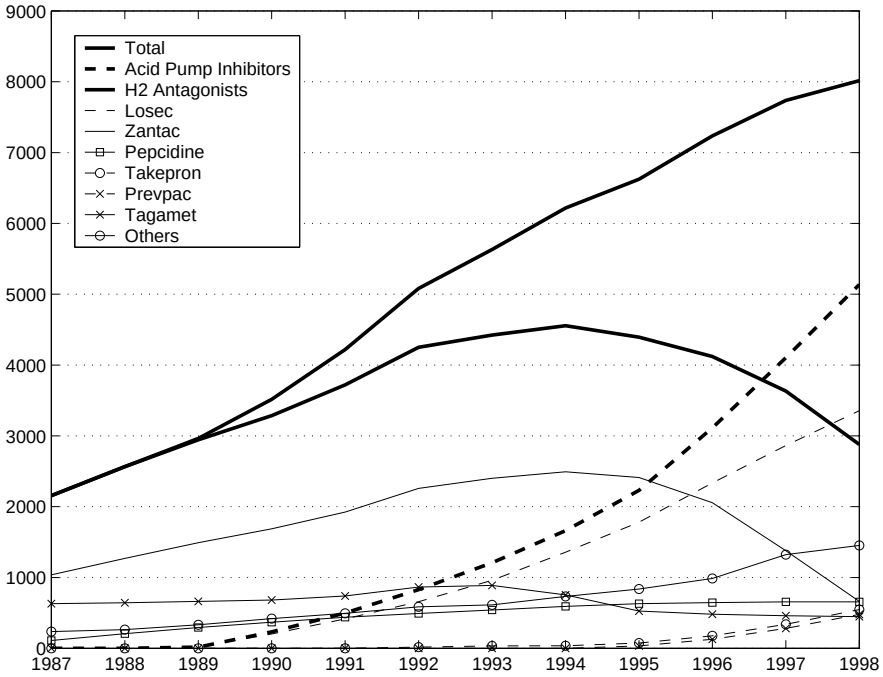

Figure 2: Antiulcerants: Acid pump inhibitors and H2 antagonists: Size of the markets and firms/products sales, 1987-1998 (US.$ millions)

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 unable followers within any chemical/therapeutic trajectory to introduce drugs with equivalent (or even superior) pharmaceutical activities, side-effect profiles, patient tolerability, etc[7].

Come as it may, when the first-coming NCE successfully reaches the market, it generally undergoes a very fast market diffusion (cf. the examples in Tables 2 and Figures 1,2,3 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, correspondingly the second type of firms, as discussed above) expanding on the market.

Note that in the evolutionary story we have just sketched there are two basic dynamic processes at work. A first one concerns the multiplication of markets (i.e. families of products based on similar chemical compounds and aimed at the same therapeutic targets) and, to varying degrees, the competition amongst them. The second process regards competition *stricto sensu* amongst firms within each market. Clearly the growth of firm size depend on both, with the timing of entry being an important factor in the combination of the two effects.

Figure 1 to 3 illustrate the market dynamics associated with evolutionary patterns sketched above. The first case show the profile of a 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 everyone" — and with that also expanding sizes (in that market) for all early incumbents.

[7]Sneader (1996) presents a detailed analysis of 244 currently employed drug prototypes, showing that out of them more than 1200 medical compounds have been derived.

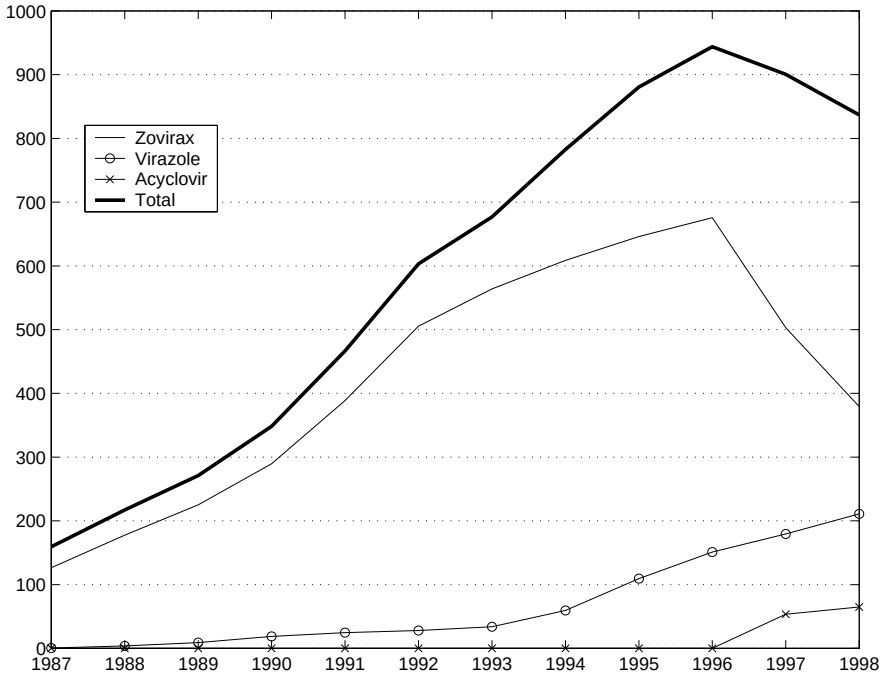

Figure 3: Antivirals, excl. vaccines: Size of the market and firms/products sales, 1987-1998 (US.$ millions)

Firm	% on total sales
Glaxo	75
Pfizer	60
Upjohn	58
Eli Lilly	56
SmithKline Beecham	53
Merck&Co.	52
Marion Merrell Dow	50
American Home Products	32
Johnson&Johnson	30
Bristol Myers Squibb	28

Table 4: % on total sales, three most important products, 1995 (source: Datamonitor)

Figure 2 illustrates the case of antiulcerants, with two families of products (i.e. two niches), namely H2 antagonists — the older one — and acid pump inhibitors — the new one, which over time crowds out the former. All that goes together with the fate of the two leading NCEs/products (Zantac and Losec, respectively), while new "innovative invaders" only in the late 90s begin to enter the younger niche.

Finally, Figure 3 depicts a market, antivirals, where the first innovative mover (Zovirax), despite a steady erosion of its market shares by late-coming innovators and analogues, maintained its dominance until patent expiration, in 1997, by which date a swarm of generic competitors entered the market[8].

A final set of characteristics of the evolutionary dynamics of the industry that we want to recall concern the nature of product market themselves. In line with other findings on e.g. the size distribution of returns on innovation (see among others, Scherer, Harhoff, Kukies, 2000, and more specifically on pharmaceuticals, Office of Technological Assessment, 1993) one observe a highly skewed distribution of product market sizes. Figure 4 presents the distribution of the top 1,000 products in 1997 [9]. A similar phenomenon appears when looking at the intra-firm distribution of sales across products. So "a few 'blockbusters' dominate the product

[8]Note that the decrease in the total "size" of the market after 1996 is entirely due to price restrictions, with quantities still rising

[9]Product sales are calculated calculated summing the 7 major western national markets (see below).

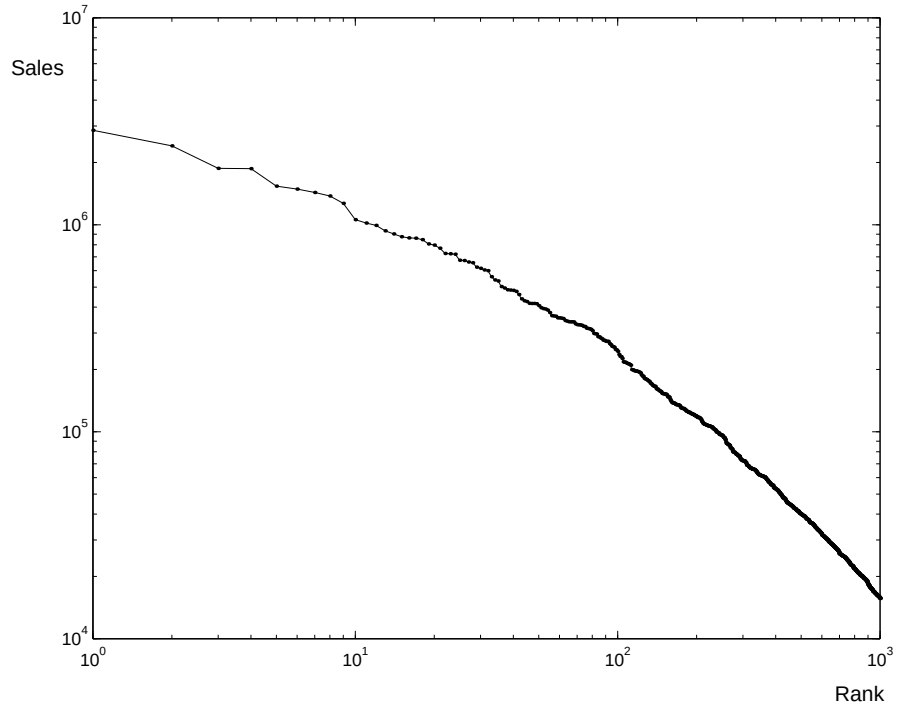

Figure 4: Rank and product sales (log scale), top 1000 products, 1997.

range of all major firms" (Matraves, 1999, p.180; Sutton, 1998)[10]: Table 4 illustrates the share of the first three most important products over the total sales of some major firms.

In an extreme synthesis, the evolutionary patterns of the industry display (see also Sec. 3.4):

- rare arrivals of major innovations (new chemical entities with novel therapeutical targets or pharmacological mechanisms) 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 mechanisms[11] involving, at one level, 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 that, what are the properties of statistical magnitudes summarizing the structure and collective evolution of the industry, in terms of relative sizes, rates of growth, etc.? This is what we shall analyze in the following.

3 Patterns of corporate growth: data and statistical evidence

Our statistical analysis in the following is based on the dataset PHID (Pharmaceutical Industry Database) developed at the University of Siena. It covers top incumbents 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). Sales by each firm stand for the sum of its sales in each of the national markets. The sample of the top 210 firms is obtained as the intersection of the top 100 (in terms of sales) in each national market, at the beginning of the period of observation. The choice of the time-zero ranking is obviously meant to avoid a

[10] Matraves, 1999 also suggests that only the top 30 drugs worldwide cover average R&D costs.

[11] We borrow the expression from Warglien, 1995.

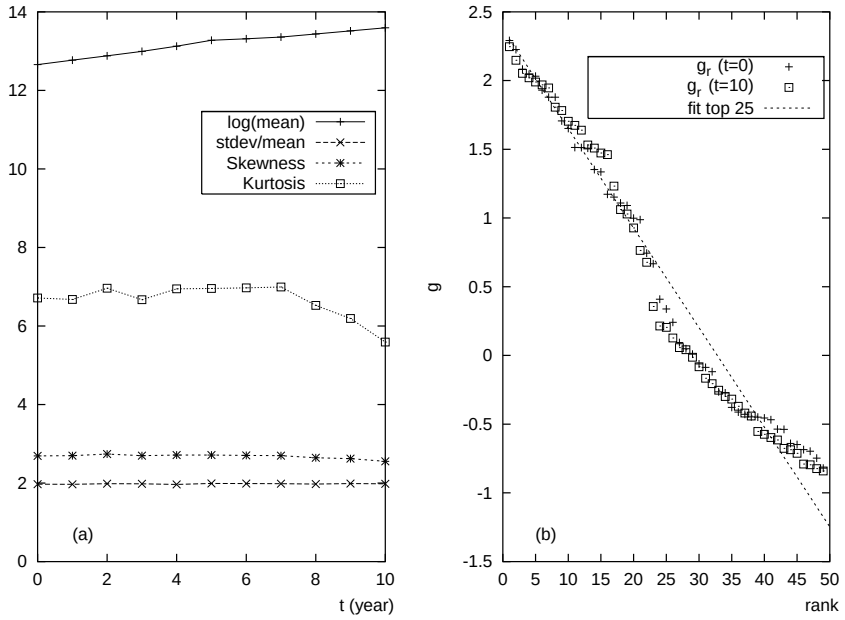

Figure 5: **(a)** The first moments of the size distribution S computed at different time **(b)** Pareto plot: log of size vs. rank. Both the initial $t = 0$ and final $t = 10$ distribution are shown. The linear fit is performed over the "average" distribution from rank 1 to 25.

sample selection bias in favor of the most successful ones, even if at the cost of censoring some (in actual fact very few) entrants among the top ranks [12]. Both sales figures and market shares are available for each firm from 1987 to 1997, disaggregated up to the 4-digit-level of the Anatomical Therapeutic Classification scheme (ATC) in 517 microclasses.

Our database contains information about sales of 7654 drugs commercialized in the US by 57 major pharmaceutical companies. The data of launch is reported for 4921 of them (64.29%). Launches are quite evenly distributed over the last 20 years, so one is able to track the life cycle for only 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, and unpatented product (including both products whose patents expired before the "windows of observation" spread 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 clearly biases 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.

Finally, note that when studying the relationship between innovation and growth (Sec. 3.4 below) we shall confine the analysis to new product launched on the US market and, symmetrically, to the dynamics of US sales. We choose to do that since institutional and regulatory differences are likely to introduce country-specific biases in the apparent "innovativeness" of any drug. In any case, the US represents by far the largest market, wherein the overwhelming majority of innovative products are introduced.

3.1 Size distributions

Let us begin with a descriptive analysis of size distributions (with the above caveats in mind). Let $S_i(t)$ be the sales of firm i ($i \in [1, \ldots, 150]$) at time t ($i \in [0, \ldots, 10]$). In Figure 5 we plot the first moments of the $S(t)$ distribution as a function of time: the ratio of the standard deviation to the mean is constant as well as skewness and kurtosis, suggesting the stationarity of the distribution. Given this, in the following we shall study the "normalized size" $G_i(t) = S_i(t) / < S_i(t) >$ (brackets $< \ldots >$ denote the average over all firms under

[12] In the following we consider only the top 150, for several reasons of statistical cleanliness, the most important being the possibility that the lower ranks include national firms which are "big" in one single market but smaller than other firms, left out of the sample, operating on other markets.

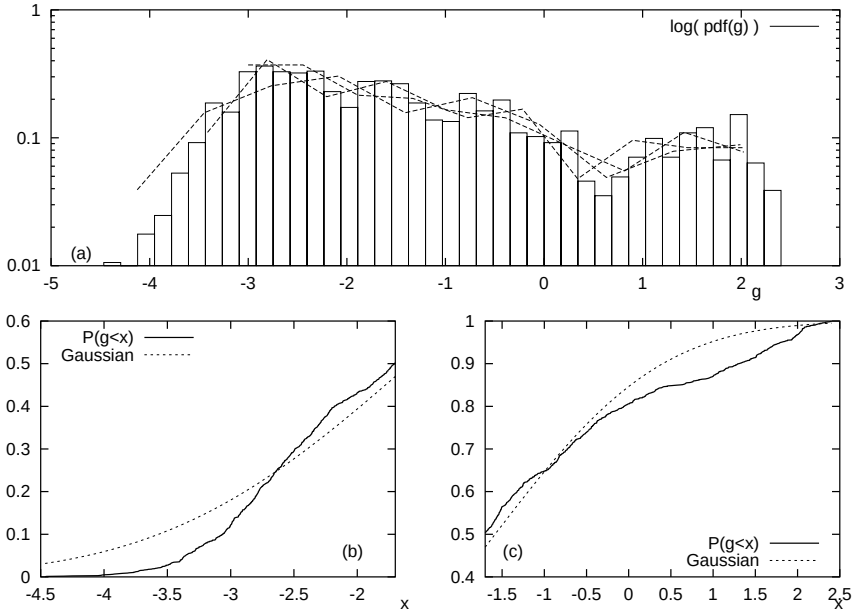

Figure 6: **(a)** Probability density for firm size. The "average" distribution obtained using values from all the time steps is plotted with bars. Lines show the distribution computed using values from one time step only. **(b)** Size distribution function (lower half) **(c)** Size distribution function (upper half). A fit with the normal distribution is also shown.

consideration). This quantity is proportional to the market share when the number of firms is constant but provides two advantages: first, it can be used also 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 number of observations.

The higher moments of G and S suggest a highly skewed and "fat tailed" distribution. We consider the logarithm of the normalized size $g_i(t) = \log(G_i(t))$. In Figure 6 we plot the probability density and the distribution function for g. On the assumption that the size distribution is stationary we estimate an "average" distribution using the complete time series for each firm[13] (For an illustration of the degrees of accuracy of such an approximation, we present in Figure 6a also the probability density for g at $t = 0$ and $t = 10$).

The size distribution shows a distinct shape over firms until the $20-25$ rank in term of size (see Figure 5b), which rather closely correspond to the boundaries of the *oligopolistic core* of the industry.

Since the higher moments of the g distribution are low (cf. Figure. 5a) one may perform a Gaussian fit. While we would not trust too much any analysis of the lower tail of the distribution due to possible sample selection biases for smaller firms, some interesting properties nonetheless emerge. The fit (Figure 6b and c) clearly shows that the distribution possess a fatter upper tail than the Gaussian approximation and can hardly be approximated by a lognormal. Moreover there is no evidence of any regression toward a Gaussian distribution as time goes on. Think of a growth process as:

$$g_i(t+1) = g_i(t) + h_i(t) \tag{1}$$

with $h_i(t)$ independent random variables. For the Central Limit Theorem the n-th normalized cumulant[14] $\lambda_n = c_n/\sigma^n$ of the size distribution $\sum_{t=0}^{T} h_i(t)$ 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}. This trend is absent from data (see Figure 5). Moreover the distribution of size shows clearly a bimodal nature which is stationary over time[15]. This bimodality would be erased by a process as the one described in (1). Conversely, its persistence can be seen as a signal of a non trivial growth structure and of possible violations of the so called "law of proportionate effect". This evidence demand a deeper analysis of the underlying growth processes, which will be performed next.

[13] The "binning" procedure involves averaging over a certain quantile of observations.

[14] c_n is the n-th cumulant, i.e. the n-th derivative of the logarithm of the characteristic function of the h distribution and σ is the standard deviation of the same distribution.

[15] We have checked that this bimodality is not produced by aggregating sales in different countries.

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

Table 5: Gibrat test results - aggregate level, one-year time lag. R^2 are always greater than 0.98.

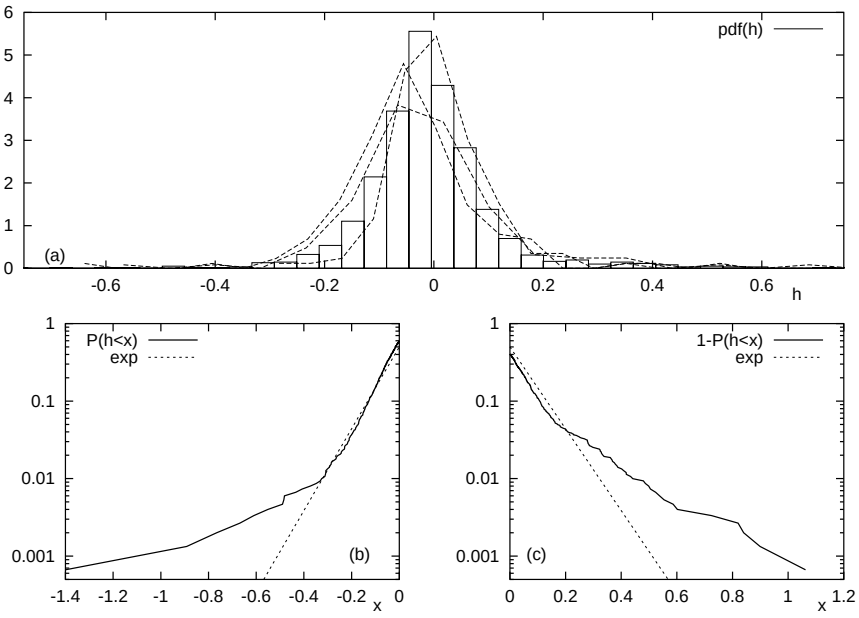

Figure 7: **(a)** Probability density for the growth obtained with bins of 100 values. The bars show the "average" distribution and the dotted lines the distributions at different time steps; **(b)** Distribution function for h (lower half). **(c)** Distribution function for h (upper half). The fit is performed with the exponential distribution

3.2 Patterns of corporate growth

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 proportionality of mean growth to size. The "law" may be stated in different but statistically equivalent forms[16].

In the version proposed by Kalecki (1945) and adopted, among others, by Hall 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 ($g_{i(j)}(t) = s_{i(j)}(t) - < s_{i(j)}(t) >$) and it is meant to provide an estimate of the divergence/convergence of the size distribution toward its mean. In that vein, we test the following model

$$g_i(t) = \beta g_i(t-\delta) + \varepsilon_i(t). \tag{2}$$

One typically concludes that the Gibrat Law is satisfied if the OLS estimator of β is close to unity.

After an OLS estimation of β, the quantities ε_i become uncorrelated to g and then the relationship between the variances in time is given by

$$\sigma^2(g_i(t)) = \beta^2\sigma^2(g_i(t-\delta)) + \sigma^2(\varepsilon_i(t)) \tag{3}$$

and the correlation coefficient ρ becomes

$$\rho^2 = 1 - \frac{\sigma^2(\varepsilon_i(t))}{\sigma^2(g_i(t))}\,. \tag{4}$$

Substituting (4) in (3), it immediately follows that

$$\xi(t) = \frac{\sigma^2(g_i(t))}{\sigma^2(g_i(t-\delta))} = \frac{\beta^2}{\rho^2}\,. \tag{5}$$

[16]cf. among others Mansfield; 1962; Ijiri and Simon, 1977; Geroski, 1999; Sutton, 1997.

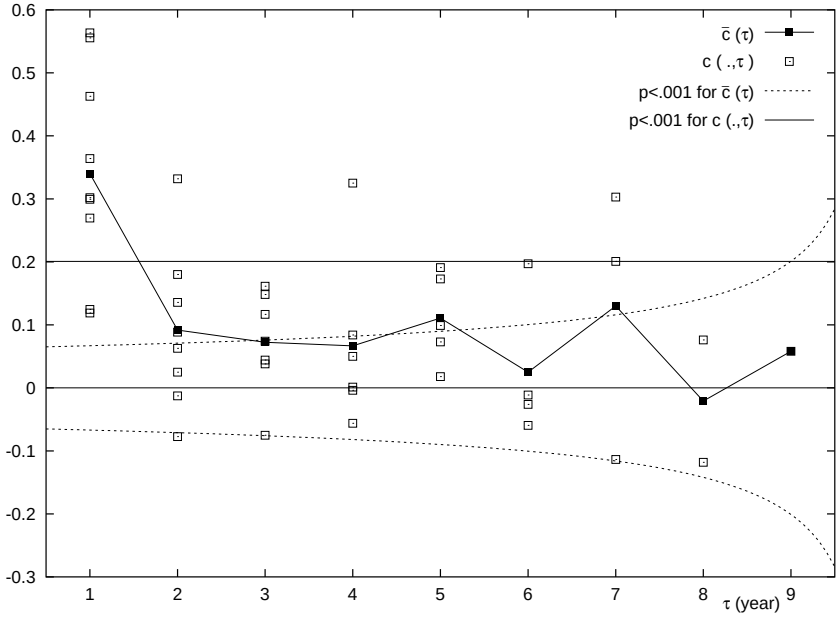

Figure 8: Time autocorrelation of the firm growth. The points are the values $c(t,\tau)$ for different time t plotted against τ. The line is the mean value $\bar{C}(\tau)$. The significance line for $p = .001$ (about 2.46 standard deviations) is plotted for both the single points and the average.

As a result, the variance of size distribution decreases in time iif $\beta < \rho \leq 1$. Table 5 reports the statistics resulting from the tests carried out over the period 1987-1997 with a one-year time lag ($\delta = 1$). As shown there, β, ρ, ξ are always very close to unity, meaning 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 shall do, to refer constantly to (1) and analyze the distribution of h — as defined there — since this analysis is fully equivalent to the analysis of errors (e) of (2).

In Figure 7 we plot the distribution for h averaged over all the time horizon of the sample together with the distribution for some time steps ($t = 0, 5, 10$). As can be seen differences are small, bearing the assumption, for now onward, that the distribution of h_i is stationary over time. Even if stationary, however, the distribution plotted in Figure 7 is highly non-Gaussian. A fit with a symmetric exponential

$$p(h = x) = \frac{\alpha}{2} e^{-\alpha |x - m|} \tag{6}$$

provides a good description of the central part even if the tails/ are fatter. Notice also that the distribution is asymmetric, as can be seen both from the binned density and from the distribution function in Figure 7, with a higher probability of relative large positive growth and few extremely large negative events, with the former effect being statistically more relevant. Another way of stating this evidence is that the dynamics display "spurs of growth" that are bigger and more frequent that those predictable on the ground of a noise-driven process.

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 concerns indeed the identification of possible sources of "dependence" in the growth process governing this industry.

The first effect to analysis is the possible autocorrelation in time of a firm's growth. In Figure 8 we plot the autocorrelation coefficient of the logarithmic growth $c(t,\tau)$. The plotted line is the average $\overline{c}(\tau) = \sum_t^T c(t,\tau)/T$, where T is the number of years covered in our database[17].

If one considers the average correlation $\bar{C}(\tau)$, contrary to the prevailing results in the literature (for a critical discussion cf. Geroski (1998) and (1999)) our data do highlight on average a significant ($p < .001$) positive autocorrelation until the second lag $\tau = 1, 2$ (while we do not dare making any claim on longer time

[17]The points relative to the same lag τ but different initial time t are dispersed, partly for 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 3 standard deviations). In any case, the hypothesis $c(t,1) = 0$ is rejected with a significance greater than .001 in 7 over 9 time steps t.

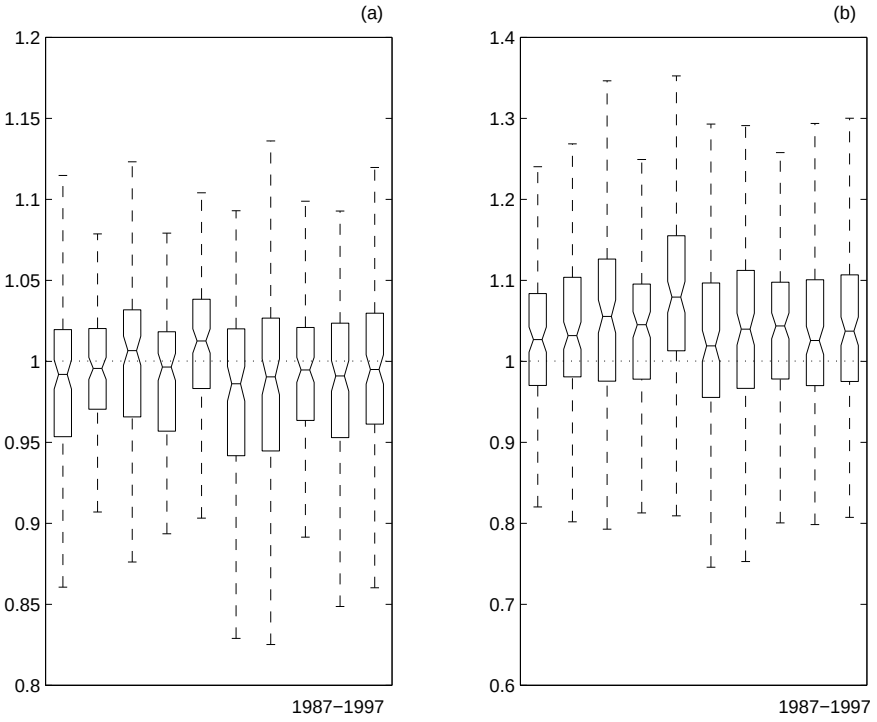

Figure 9: Gibrat test at the 3-digits submarket level, one year time lag. Boxplot **(a)** reports the distributions of $\beta_j(t)$ while **(b)** depicts the distributions of $\xi_j(t)$. (cf. (2) and (5))

lags)[18]. Figure 8 refers to the growth of firms as a whole. However, it is equally interesting 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 (after all, cardiovascular drugs do not compete with antibiotics etc.).

Let $h_{i,j}(t) = g_{i,j}(t) - g_{i,j}(t-1)$ be the (logarithmic) growth of the firm i in the sub-market j. Remember that g is defined as the logarithm of the "normalized" size G. Here the $G_{i,j}(t)$ is normalized using the size of the j-th sub-market $M_j(t)$. We then test the analogous to (2) and (5) at the disaggregate level[19]. Figure 9 reports the values of $\beta(t)$ and $\xi(t)$ for each sub-market j. Notably in line with the aggregate results, the median of $\beta_j(t)$ stays quite close to unity over time even if the distribution of $\beta_j(t)$ denotes a certain degree of heterogeneity among sub-markets ranging from 0.82 to 1.14. On the contrary, the median of $\xi_j(t)$ distribution is constantly above unity meaning that the variance of the firm size in sub-markets increases over time.

Next, let us look at the distribution function of the autocorrelation $\overline{c}_j(\tau)$ over the set of all the sub-markets and plot it for different τ lags. Figure 10 presents the results for different level of disaggregation (1–, 2– and 3– digits, according to the therapeutical classification; see above). As can be seen the distributions are similar for different disaggregations (with the *caveat* of different number of observations across markets for different disaggregation level). Moreover, even if the distributions in Figure 10 have wide support, they are strongly symmetric with small variance and Gaussian shaped.

Furthermore, Figure 11 reports the growth correlation of the two leading firms for each submarket $c_j^{1,2}(\tau)$. Remarkably, the distribution is U-shape peaked on the extreme values.

Taken together, Figure 10 and Figure 11 suggest 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 growth process in each sub-markets. Our statistics cannot discriminate between purely random micro processes and more systematic competition processes observed at random times, but the qualitative evidence discussed in Section 2 seems to support the latter hypothesis. So, for example, one

[18]Notice, however, that the procedure of taking the average correlation as an estimate of a "true" (stationary) correlation is not well grounded due to the high dispersion of $c(t,\tau)$ for different initial time t.

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

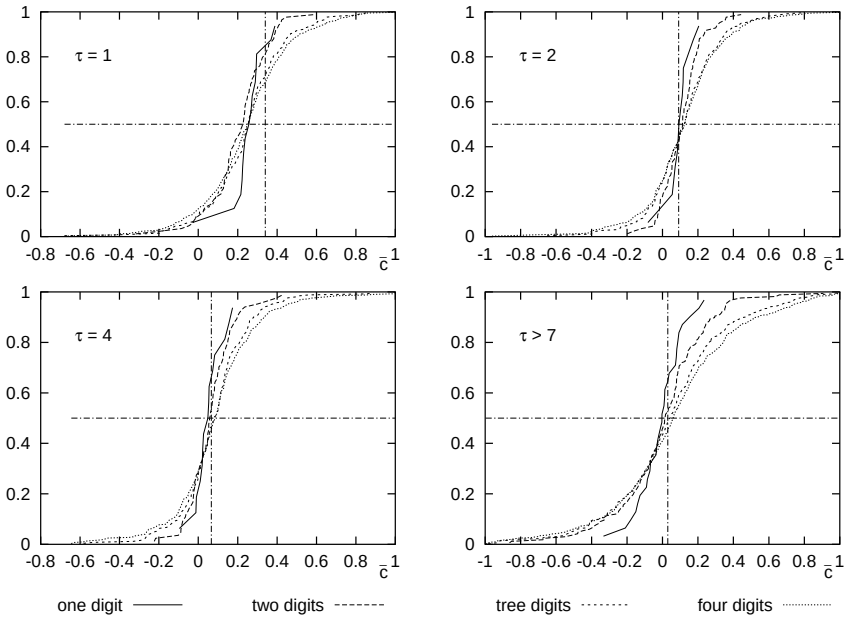

Figure 10: Distribution function of the autocorrelation coefficients $\overline{c}_j(\tau)$. Different aggregation levels and time lags τ are plotted. The vertical lines correspond to "aggregate" values at the firm-level. The horizontal line is centered at 0.5.

might expect positive correlation in $c_j^{1,2}(\tau)$ in the stages of penetration of new products and anti-correlation associated with imitative entry and patent expirations.

A further piece of information is obtained by comparing market-specific autocorrelations and firm-level ones. In this respect, recall that most of the firm in our sample are diversified across different markets. Moreover, for each diversified firm the weight of each market depends on both market size and the share of each firm in that market. Remarkably firm-specific aggregation does not wash away autocorrelation in growth: on the contrary, for $\tau = 1$, firm-level correlations are significantly higher than the average correlation calculated at any disaggregation levels. This property disappears for $\tau > 1$. A positive average correlation seems to survive for a long time even if of negligible magnitude[20]

To further investigate the growth structure we have computed the one-year transition matrices of the stochastic variable h both at the aggregate and at the 3-digit-submarket levels. Having controlled the robustness of our results for different numbers of bins (ranging from 20 to more than 200) without revealing remarkable variations, let us present the analysis at the highest level of resolution supported by data. More precisely, the actual rate of variation over time of the aggregate standardize growth (h_i) and disaggregate ones (h_{ij}) have been uniformly divided into 50 quantiles and every firm has been univocally 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 Figure 7), we analyze jointly the one-year transition probability matrices. Two transition matrices have been computed, at the aggregate (Π_a) and at the submarket level (Π_d)

$$[h_i(t)] = \Pi_a[h_i(t-1)] \quad (7)$$

$$[h_{ij}(t)] = \Pi_d[h_{ij}(t-1)] \quad (8)$$

where $[h_{i(j)}(t)]$ are column vectors of binned growth at time t and each row of Π_a and Π_d represent the conditional probability vector of moving through the grid[21]. Figure 12 and Figure 13 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 are in Quah, 1993). If the graphs pile up on the positive sloped diagonal this may be interpreted as evidence of high persistence and "inertia". Actually, Figure 12 shows that a significant auto-correlation in growth rates

[20] We searched also for a possible dependence of the autocorrelation $\overline{c}_j(\tau)$ on the size M_j of the sub-markets themselves, but no evidence of any such dependence has been found.

[21] The exercise is similar to that presented in Quah, 1993, 1996.

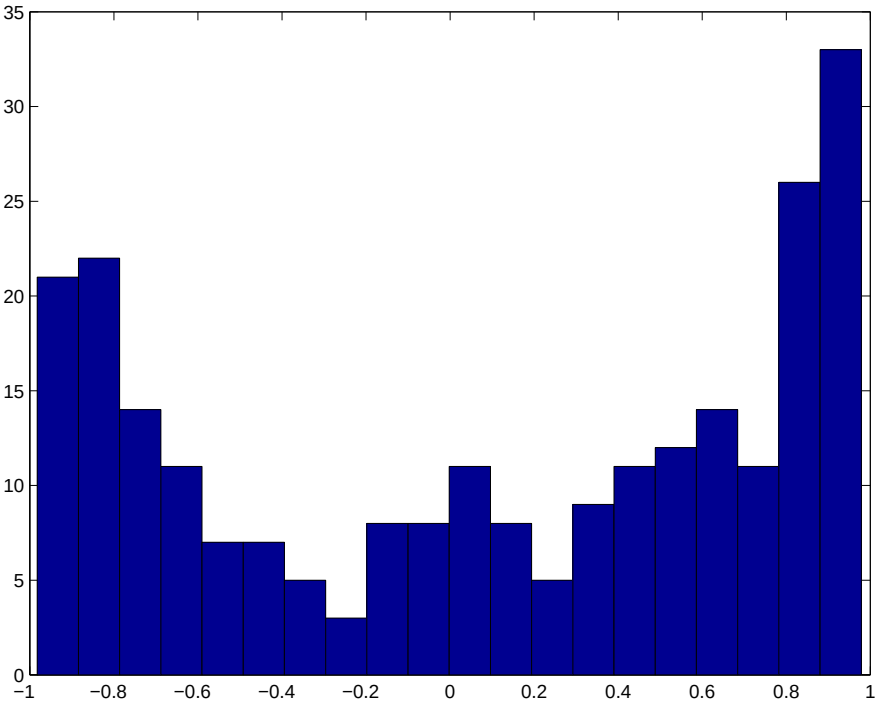

Figure 11: Correlations of the first and second firms growth in each submarket, $c_j^{1,2}(\tau)$.

is in place at the aggregate level. Specifically, a slantwise shape clearly emerges which may be fitted by a line with slope 0.38 passing through the mean values of $h_i(t)$ and $h_{ij}(t-1)$, in line with our previous finding. Over time, the growth distribution converge toward its mean value where most of the observations are concentrated. However note that auto-correlation appears to be highly dependent on relatively rare events of sustained growth represented by the spikes on the top right quadrant of the transition matrix. The companion Figure 13, computed at the submarket level enables us to disentangle growth autocorrelation in terms of single markets dynamics.

Two different regimes are clearly distinguishable. The products that at time $t-1$ experienced a growth above the average are sharply divided into two groups: some of them keep their growth pace unchanged, while most of them subsequently drop on the mean. Conversely, the mean growth level represents an absorptive state for slow (below the mean) growing products too, but the phase transition is considerably smoother.

New products bust into the market and growth swiftly for a short period of time, then a cluster of analogue drugs enter (and possibly licensing begins, too). As a result, innovative drugs growth slows down. After a while, all incumbents tend to growth approximately at the same rate, even if with highly asymmetric shares, in favor of the early movers.

A tangled and "classic" question concerns the possible dependence of the distributions the growth rates on the initial firm size. The answer, of course, is not exhausted by the above (negative) finding 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 Figure 14 we plot the moments of the growth distribution for different size classes built considering, at each time step, all the firms with size in a given range.

In line with a few contributions in the literature[22], as Figure 14 shows, no dependence of mean growth appears, and neither does dependence in autocorrelation. 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

$$\sigma(h) \sim e^{\beta g} \tag{9}$$

we obtain a value $\beta \sim .2 \pm 0.02$ which is striking similar to the one found in other analyses on different datasets (cf. Stanley et al., 1996, Lee et al., 1998).

[22] cf. Boeri, 1989a; Evans, 1987; Geroski, 1999; Hall, 1987; Hymer, Pashigian, 1962; Mansfield, 1962; Sutton, 1997 among others.

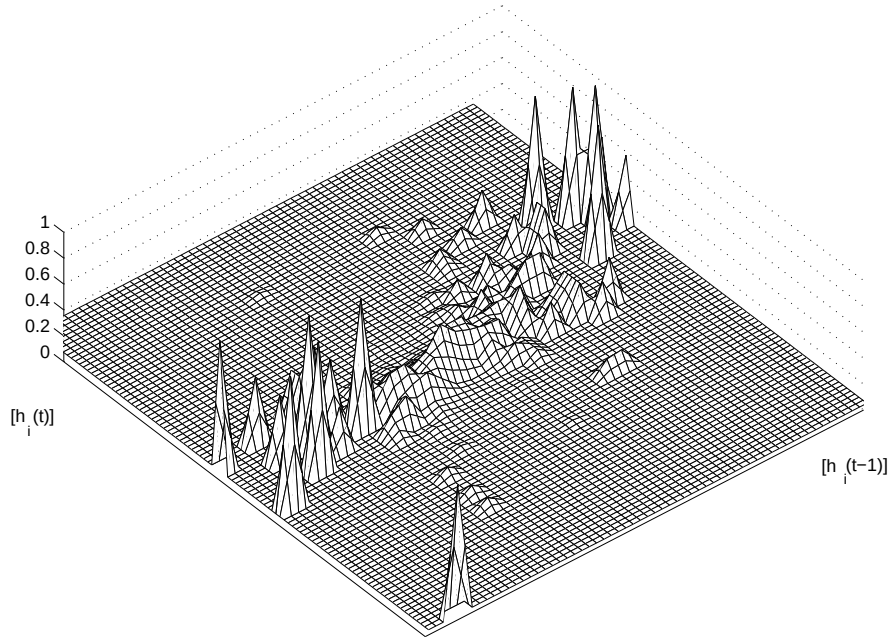

Figure 12: Growth transition matrix at the aggregate level

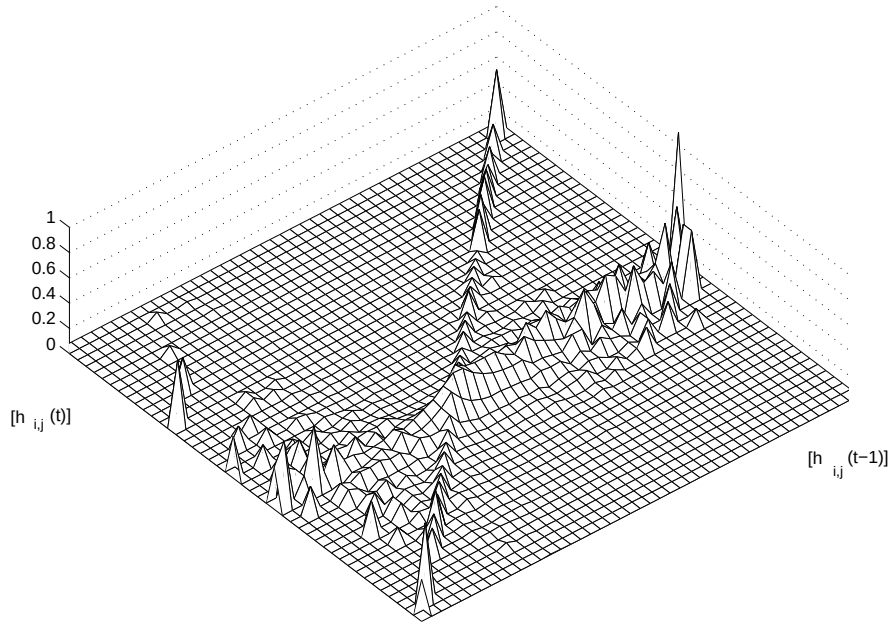

Figure 13: Growth transition matrix at the submarket level

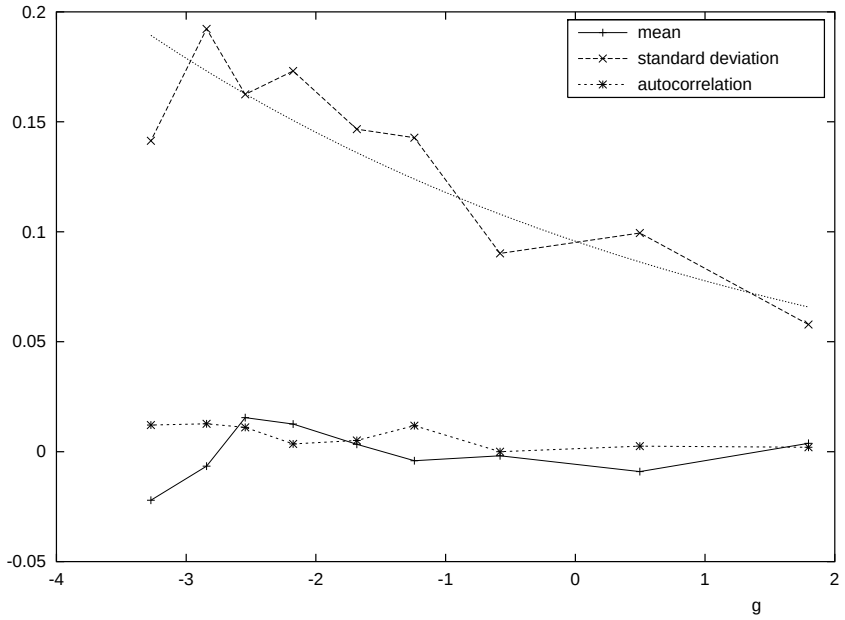

Figure 14: Mean, standard deviation and autocorrelation of growth h computed for different size bins plotted againts the average size in the bin. The exponential fit to the standard deviation (see (9)) gives a value $\beta = -0.20 + / - 0.03$

To further investigate the relation between size and growth we look at the dynamics of firms across ranks. One can then plot the frequency at which a given rank is crossed during the observed period. Take the two dimensional plane having time as x coordinate and log sizes as y coordinate. Think of the growth of a given firm as a continuous line in this plane with equation $y = g_i(t)$ (of course due to the data grid resolution, one can actually plot only a piecewise straight line). A given rank is then crossed when the lines pertaining to the firm associated to this rank meet another line. We record at each time step which ranks has been crossed, i.e. which rank was associated to firms that have met other firms since the last period, and then calculate the new ranking for all firms. In such a way is possible to obtain a statistic on how often a given rank is crossed during the growth process, i.e. the probability of crossing for this rank. Such probabilities are plotted in Figure 15 (they are grossly discretized because the time series used in the calculation contains only eleven time steps, so that only a rough analysis is possible). A first noticeable effect is that the "rank mobility" increase with rank until 50-60, then becomes stationary (this is approximately the minimum point between the two maxima in the size distribution, cf. Figure 6). Moreover, one observes the presence of a sort of "barrier" between the 20-25 positions which is seldom crossed. This is due to the presence in the size distribution of a large size gap (cf. Figure 5) and to the low variance of the growth rates for bigger firms. This "barrier", together with the change of "Pareto regime" discussed earlier, further reinforces the notion of a sort of separation between the "oligopolistic core" and the rest of the firms in the sample.

3.3 Diversification across sub-markets and Gibrat violations

One of the peculiar feature of the PHID database is the possibility of disaggregate sales until the 4-th digit of the ATC code. This level of disaggregation allows us to identify sub-markets that are "specific" enough to be considered the *loci* of competition among firms. In this section we focus on the relationship between the variance of growth and size.

If one assumes 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 predicts a relation between variance of aggregate growth and firm size of the form $var(h) \sim g^{0.5}$. However, both the existing literature and our data (see Figure 14), show a *lower* exponent.

In the literature, this departure from the predictions of the Law of Large Numbers is typically imputed to some interrelation between firm components[23] (cf. Boeri, 1989; Stanley et al., 1996).

[23]Note that imposing a simple correlation in components growth is not enough to explain the low value of γ.

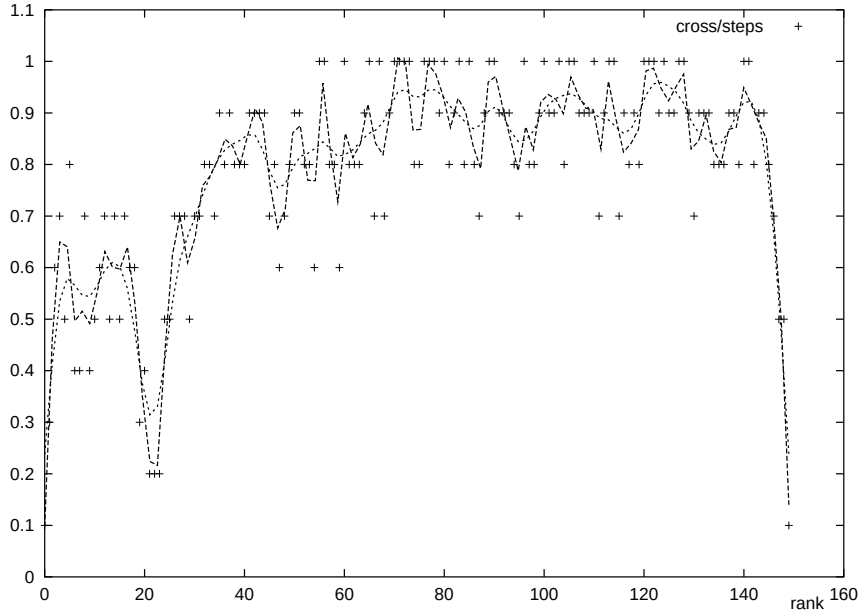

Figure 15: Probability of rank crossing. The smoothing approximations are performed using spline with different windows

In principle, one could relax the assumption of elementary components and measure the real 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 can explain the observed relationship between size and variance of growth if one consider as elementary lines of business the sales of firms in the different submarkets. This result comes from two observations: first, correlation across sub-market is negligible and second, the number of active sub-markets of a given firm is, on average, increasing with size.

To make the argument clear, let us introduce a bit of notation. $S_{i,j}(t)$ is 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

$$\frac{S_i(t+1)}{S_i(t)} = \sum_j \frac{S_{i,j}(t+1)}{S_i(t)} \,. \tag{10}$$

If one computes the correlation of $S_{i,j}(t+1)/S_i(t)$ for all firms in all submarkets, one obtains a distribution sharply centered around zero[24]. For any practical purpose, the growth on different sub-markets can be considered uncorrelated and 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

$$\mathrm{var}_{i,t}[H_i(t)] = \mathrm{var}_{i,t}\left[\frac{G_i(t+1)}{G_i(t)}\right] = \sum_j \mathrm{var}_{i,t}\left[\frac{M(t)}{M(t+1)} R_{i,j}(t) \frac{\Delta_{i,j}(t)}{N_i(t)}\right] \tag{11}$$

where $M(t)$ is the average (aggregate) size of 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 $\mathrm{var}_{i,t}$ denotes the variance of the distribution obtained using the complete panel (all firms at all time steps).

In Eq. (11) the contribution of each submarket factorizes in three terms: $R_{i,j}(t)$, that is the actual growth of the firm i in sub-market j; the inverse number of active markets $1/N_i(t)$ and $\Delta_{i,j}(t)/N_i(t)$, the weighting coefficient describing the "diversification asymmetry" of firm i[25] 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

[24] With a standard deviation of $.388\ 10^{-4}$ and an average deviation of $.24\ 10^{-5}$

[25] If the firm i at time t is symmetrically diversified over its active submarkets, the distribution of $\Delta_{i,j}(t)$ in j is centered around 1, otherwise it is broadly distributed.

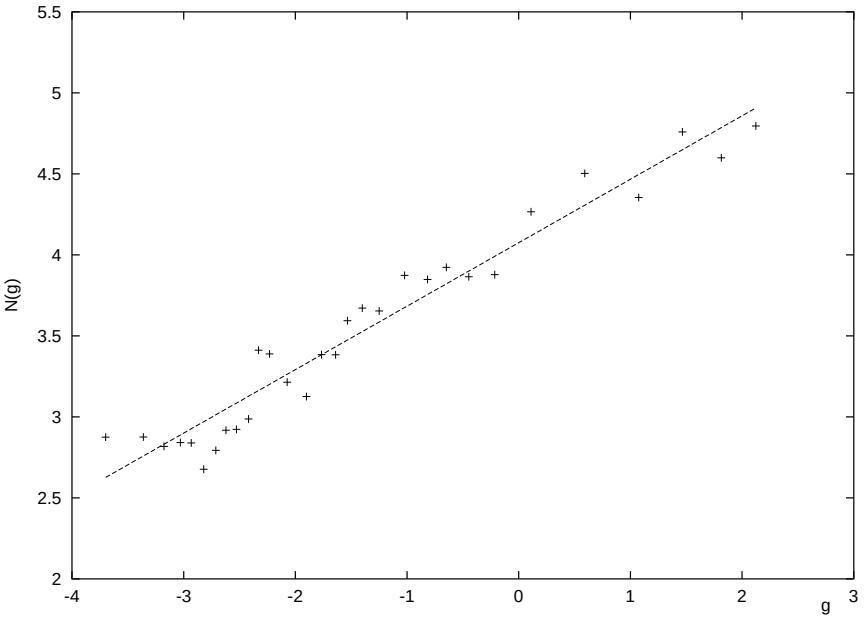

Figure 16: Number of submarkets a firm operates in vs. firm's size (log-log scale)

of the bins. Then the number of active submarkets $N_i(t)$ must be responsible for the observed dependence of variance over the aggregate size. Fitting on a log-log scale the average number of active submarkets for each bin against the average size of the bin one obtains a slope $\alpha = .39 + .02$ and an intercept $q = 6 + -.12$ (see Figure 16). The Law of Large Numbers would predict a relation between the exponent in 9 and the slope in Figure 16 of the form $\beta = -\alpha/2$ which is in perfect agreement[26].

In conclusion, 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 has been necessary to rule out two possible sources of functional dependence between aggregate growth variance and size: first, the possibility that the variance and mean of a firm growth in a sub-markets depends (on average) on its total size and, second, the possibility that the diversification pattern of a firm varies (on average) with its size. Both these possibilities are actually discussed in the literature as possible sources of violation to the Gibrat law (see for instance Hart, Prais, 1956).

3.4 Innovation and growth

A major tenet of evolutionary interpretation of industrial dynamics is indeed the general conjecture that the process of technological innovation and imitation are a major driver of industrial dynamics and also of the competitive fate of industrial firms. How does our evidence bear on this proposition? Let us beginning by considering the process of introduction of innovative drugs, both New Chemical Entities and patented products[27], in the US market. Consider first the distribution of NCE launches over the population of firms throughout the 11 years of observation (1987-97). Indeed, 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 contribute to detect possible underlying forms of heterogeneity across firms in their ability to innovate.

As a benchmark, let us model what would happen with "technologically homogeneous" firms. In 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 population of F firms, the probability to find a firm who introduced exactly k NCEs is given by the binomial distribution:

$$p_{\text{M.B.}}(k) = \binom{N}{k} \left(\frac{1}{F}\right)^k \left(1 - \frac{1}{F}\right)^{N-k} \quad . \tag{12}$$

[26]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 .09 that is negligible compared to the effect of the number of active submarkets.

[27]Note that the former are a small subset of the latter.

								Tot
NCE	0	1	2	3	4	6	8	73
firms	26	13	8	4	3	2	1	57

Table 6: Number of firms that introduce a given number of NCEs.

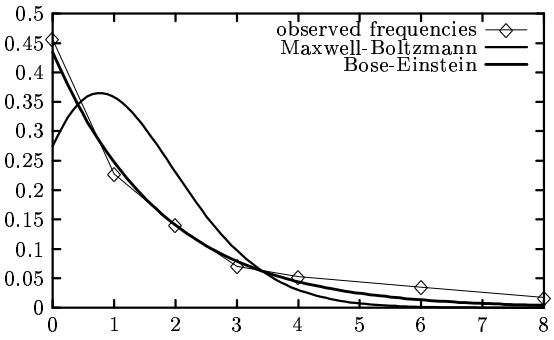

Figure 17: The frequencies of total NCE introduced over the firms population.

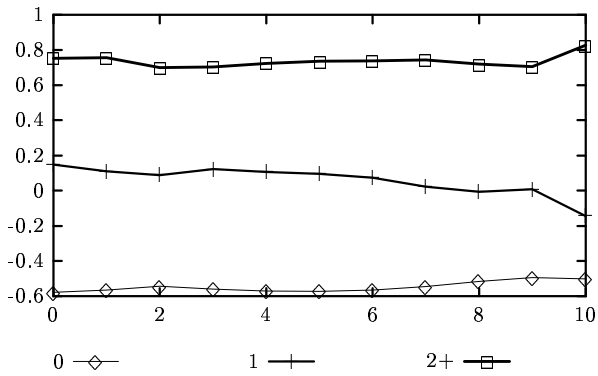

Figure 18: Average (rescaled) sales per firm for each "innovative propensity" group.

This model is known as Maxwell-Boltzmann statistics (Feller, 1968). However as shown in Fig.17 it is a poor description of the observed frequencies (cf. Tab.6).

Indeed the assumption of random independent assignment is at odds with the qualitative evidence on whole families of research projects conducted by each firm over several years, often entailing knowledge spill-overs across them. Hence, one may conjecture some correlation amongst arrivals of NCE due to learning effects across individual research projects. In order to empirically check this hypothesis one ought to check whether the random assignments of innovations to individual firms concern indeed "packets" of NCEs rather then 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 the probability to find a firm who introduced exactly k NCE:

$$p_{\text{B.E.}}(k) = \frac{\binom{F+N-k-2}{N-k}}{\binom{F+N-1}{N-1}} \cdot \tag{13}$$

As can be seen from Fig. 17 the previous distribution provides an excellent description for low to average NCE numbers and only fails for the very large assignments. It is also interesting to notice that the propensity to introduce NCE is not monotonic in the size of the innovative firms themselves (so that for example the upper tail in the distribution in Fig. 17 does not feature the biggest firms in the industry). This evidence, taken together with the observation that R&D expenditures do shows indeed a monotonically growing relation with size, hints of 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).

Conversely, when considering the distribution of NCEs across all firms in our sample independently from their size, as we do in Fig. 17, one does not need to invoke any further factor of heterogeneity in order to interpret the observed innovative patterns, except maybe for the few firms displaying the highest innovative intensity[28]. Together the widespread occurrence of "clustering" in the arrivals of NCEs suggest the importance of firm-specific learning effects across different research projects.

Given the foregoing evidence a crucial quantity concerns if (and how much) the introduction of NCE during a firm history does affect its growth performance. Firms sizes are computed as aggregate sales and growth performances are measured as variations in market shares. One can start by partitioning the set of firms based on the number of NCEs they have introduced during the time window of observation. Fig. 18 shows the average firm shares for three such subsets. Clearly appears a relation between the number of NCEs introduced and the size, with bigger firm introducing "on average" more NCEs, but no relation is apparent between the

[28]Note however that this statements concerns in any case the top tail of the distribution of firms in US market, in term of sales and generation of innovation. Deeper competence-related sources of heterogeneity might well apply when comparing our sample with the rest of the firms in the industry.

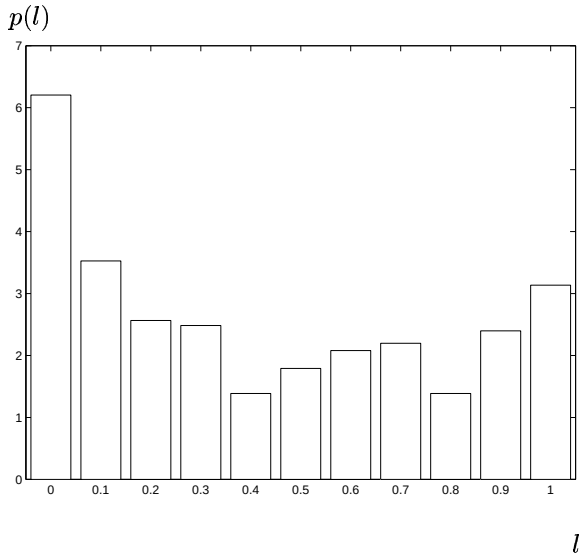

Figure 19: The frequency of different values of l on the firms population. A log scale has been introduced on the y-axis.

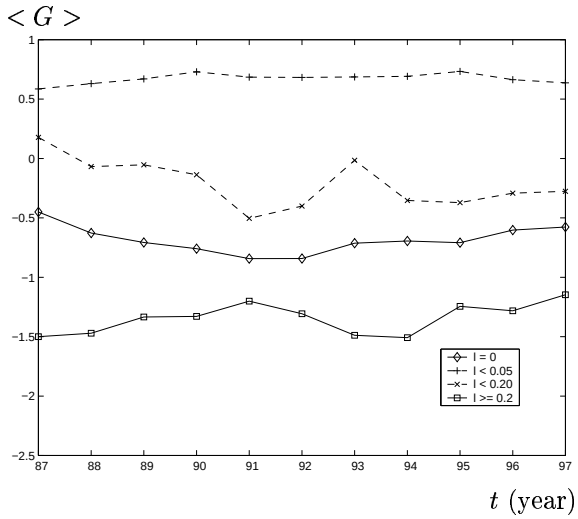

Figure 20: Average (rescaled) sales per firm relative to each l bin computed for the different years.

number of NCEs and firm performances: indeed more "innovative" firms do not seem to gain, on average, market share with respect to less "innovative" firms.

As already mentioned, the rates of arrival of NCEs are very low. Conversely, all firms introduce much more frequently patented innovations which more often do not involve NCE but e.g. "creative analogues", new ways of combining already existing NCEs, etc. Let us define $l_i(t)$ as the share of patented products present at time t in the total products portfolio of firm i. This can be taken as another broader proxy for the innovative capability of firm i. As shown in Fig. 19, note that the distribution of patent intensity on the population of firms is very heterogeneous, with the vast majority of firms possessing a very low l. Moreover, unlike the case of NCEs, a systematic relation appears between l and size with, interestingly, bigger firms displaying low to average values of l and many relatively small ones with values near unity. Finally, in terms of growth profile, again, no systematic relation appears between the structure of product portfolios and growth performance (cf. also Fig. 20). Rather, all the foregoing evidences 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. However, all this does not imply homogeneous market dynamics of the three groups of products (NCEs, patented drugs and no patented ones) in the 4-digit submarkets in which they compete.

Let us consider $S_{i,j,k}$, the sales of the product k of firm i in submarket j and define the "normalized" sales with respect to all other products in the same 4-digit submarket as

$$G_{i,j,k} = \frac{S_{i,j,k}}{< S_{i,j,k} >_{i,k}} \quad . \tag{14}$$

Fig. 21 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).

Note, first, the pronounced "market cycle" of NCEs which tend to "hit the market big" and decline relatively soon, thereafter with a burst in the variance (intuitively, a burst in the competition with the ensuing high turbulence in market shares) early in their life cycle. Interestingly, qualitative inspection of the big growth shocks described in section 3.2 reveals that they corresponds to a good extent to the introduction of NCEs. The much more numerous family of patented drugs follows, on average, a "market cycle" loosely similar to NCE but much less pronounced in both their changes in means and variances. Finally, non-patented drugs appears to occupy from the start their long term market position (plausibly at the expense of patented ones in general and NCE in particular).

In all that, innovation does indeed drive the evolution of each submarkets, but the competitive regime is not such as to guarantee a sustained competitive advantage to the individual innovators either in the affected submarkets or, even less so, for the firms as a whole. Rather, one may think to some analogue to

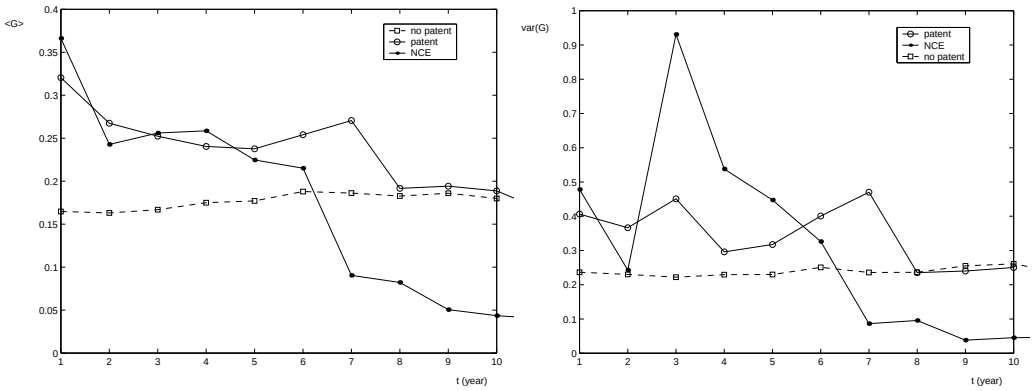

Figure 21: The mean (left) and variance (right) of the (rescaled) sales for the three groups of products computed for different "market ages". At any given time we take into consideration only submarkets with at least 10 products. The product sales are rescaled by the average sales of the submarket where the product is launched.

population-level mixed-strategy equilibria (here, populations of innovative vs. imitative and "old" products) which persistently coexists between submarkets and between firms.

4 Conclusions and conjectural implications for the theory

In this work we have tried to explore the statistical properties of growth dynamics in an industry — pharmaceuticals — whose long-term evolution is fueled by innovation, imitation and creation of new markets. The fundamental features of such evolutionary patterns, sketched out in the first part of this work, have proved to be also a fruitful heuristic guide in the interpretation of the statistical regularities identified in the second part of the analysis. There — as well as in several studies of this *genre* — the benchmark of departure has been 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 to discriminate the finer structure of the growth processes and their links with size distributions.

The evidence show, together, a) a "double-humped" size distribution, stable over the observation period, with its upper tail corresponding to a sort of *oligopolistic core* of the industry; b) fat tails in the distribution of growth shocks, present at all levels of aggregation, with (relatively rare) big "spurs of growth"; c) a significant autocorrelation in growth rates, again at all aggregation levels; d) 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.

Our results, on the negative side, allow us to rule out some interpretations of the growth processes as seemingly in conflict with the evidence. For example, the fat-tailed growth distribution and its departure from a Gaussian even in its central part is at odds with a "pure Gibrat process" purportedly driven by the sum of independent events. 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 — irrespectively of the original distribution of events.

On the positive side, our evidence, first, is well in tune with the conjecture (Geroski, 1999) that the time scale of 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). Indeed, such shocks are quite rare, are persistently generated by a relatively small club of innovators, but any one innovator is unlikely to hit the same market twice. Rather, NCEs often *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 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. The two processes, we suggest, approximately map also into a persistent heterogeneity — in terms of organizational competencies and competitive strategies — between, first, what we called the *oligopolistic core*, and, second the rest of incumbents.

Further corroborations of this interpretation will involve also conditioning the observed dynamics upon explicit proxies for the technological characteristics of firms and upon the "stages" of market development. We would like to consider this work just as an initial exploration of links between some basic features of industrial evolution — so far empirically analyzed in largely qualitative manners — on the one hand, and "emergent" statistical properties of industrial structures and growth dynamics, on the other.

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