

INSTITUTE
OF ECONOMICS



Scuola Superiore
Sant'Anna

LEM | Laboratory of Economics and Management

Institute of Economics
Scuola Superiore Sant'Anna

Piazza Martiri della Libertà, 33 - 56127 Pisa, Italy
ph. +39 050 88.33.43
institute.economics@sssup.it

LEM

WORKING PAPER SERIES

Big pharma and monopoly capitalism: A long-term view

Giovanni Dosi ^a
Luigi Marengo ^{b,a}
Jacopo Staccioli ^{c,a}
Maria Enrica Virgillito ^{a,c}

^a Institute of Economics and EMbeDS, Scuola Superiore Sant'Anna, Pisa, Italy.

^b Department of Business and Management, Luiss Guido Carli, Rome, Italy.

^c Department of Economic Policy, Università Cattolica del Sacro Cuore, Milan, Italy.

2021/26

August 2021

ISSN(ONLINE) 2284-0400

Big pharma and monopoly capitalism: A long-term view

GIOVANNI DOSI^{*1}, LUIGI MARENGO^{†2,1}, JACOPO STACCIOLI^{‡3,1}, AND MARIA
ENRICA VIRGILLITO^{§1,3}

¹*Scuola Superiore Sant'Anna*

²*Luiss Guido Carli*

³*Università Cattolica del Sacro Cuore*

Abstract

Are IPRs institutions meant to foster innovative activities or conversely to secure appropriation and profitability? Taking stock of a long-term empirical evidence on the pharmaceutical sector in the US, we can hardly support IPRs intended as an innovation rewarding institution. According to our analysis, pharma patents have constituted legal barriers to protect intellectual monopolies rather than an incentive and a reward to innovative efforts. Patenting strategies appear to be quite aggressive in extending knowledge borders and enlarging the space protected from the possibility of infringements. This is also witnessed by the fact that patent applications are very skewed in the covered trade names and patent thickness expands over time. Conversely, the number of patents protecting new drugs approved by the FDA which draw upon government-sponsored research – as such a mark for quality – falls. Firm-level analysis on profitability confirms strong correlation, restricted to listed pharmaceutical firms, between patent portfolio and profit margins.

JEL classification: L65, O31, O34.

Keywords: Intellectual property rights, patents, pharmaceutical industry.

^{*}Institute of Economics and EMbeDS, Scuola Superiore Sant'Anna, Piazza Martiri della Liberta' 33, 56127, Pisa, Italy. E-mail address: gdosì@santannapisa.it

[†]Corresponding author: Department of Business and Management, Luiss Guido Carli, Viale Romania 32, 00197, Rome, Italy. E-mail address: lmarengo@luiss.it

[‡]Department of Economic Policy, Università Cattolica del Sacro Cuore, Via Lodovico Necchi, 5, 20122, Milano, Italy. E-mail address: jaco. staccioli@unicatt.it

[§]Institute of Economics and EMbeDS, Scuola Superiore Sant'Anna, Piazza Martiri della Liberta' 33, 56127, Pisa, Italy. E-mail address: m.virgillito@santannapisa.it

1 Introduction

Two distinctive roles have been attributed to intellectual property rights (IPRs hereafter) by the economic literature, namely, IPRs as incentives to undertake innovative activities and IPRs as forms of appropriation (Dosi, Marengo, and Pasquali 2006). As well acknowledged for instance by Adam Smith, Karl Marx and Joseph Schumpeter, just to mention the classics, expensive search efforts by profit-motivated agents imply some departure from purely competitive conditions. However, the two crucial issues concern, first, the extent of such a departure, that is the actual or expected extra-profit necessary to trigger innovative search, and, second, the possible monotonicity in the relation between such a departure and the intensity of innovative effort. Such questions are particularly thorny with respect to the scope and breadth of patents. In one perspective, which we may call the *incentive view*, patents, by restricting the possibility of imitation, grant the innovator a monopoly rent which should motivate *ex-ante* and compensate *ex-post* the R&D investment. In the alternative perspective, which we may call the *opportunity view*, innovative activities are primarily driven by the richness of opportunities of technological advances, while patents represent intellectual barriers to innovation and obstacles to its diffusion. Whether being institutional forms embraced to secure rents or to ensure legitimate profits, both streams recognize patents as creators of intellectual monopolies, even if in the former case they are a necessary evil to drive the “unbound Prometheus” of innovation in capitalist societies, while in the latter case they are primarily a mechanism of generation of unproductive rents.

Among all sectors, the pharmaceutical one has been recognised to be one of the most dependent on patents in order to ensure its intellectual monopoly. The reliance of pharma on patents – it is commonly claimed – descends from the very nature of its production activity, based on very low reproduction costs, and facing instead almost exclusively entry costs in terms of knowledge generation. Given the potential easy replication of the knowledge embedded in a product (Dosi and Nelson 2010), patents ensure a temporary exclusive use of such knowledge which would instead be easily acquired by competitors. Additionally, the knowledge embedded into pharmaceutical patents is often discrete and might be well confined into claims, therefore quite apt to be patented (Orsenigo and Sterzi 2010).

Our evidence challenges the correspondence between patents and innovation and studies the behaviour of modern monopoly capitalism ensured by intellectual rents in the long run, adopting a historical perspective to detect the change in the IPRs system in the pharma industry (Khan and Sokoloff 2001) and the current evolution of capitalism direct toward an accelerated *commodification of knowledge* (Coriat and Weinstein 2012), or equivalently toward *rentification* (Dosi and Virgillito 2019). The historical analysis allows to frame the evolution of the patenting activities of the pharma indus-

tries also comparatively, to appreciate the *diversity of modern capitalism*, in the words of Amable (2003).

Let us start by noticing that historical records of drug search (see for instance the monumental history of drug discovery in Sneader (2005)) show that until very recently it has been mainly driven by search heuristics for discovery and experimentation very far from mere appropriation objectives, even when undertaken within corporate laboratories. More specifically, the modern pharmaceutical industry was born – mainly in Germany – under a regime of basically non-existent patent protection and then, after 1877, thrived under a regime of rather weak protection of processes rather than products. Still, the chemical/pharmaceutical oligopolies – later merged in 1925 into one monopolist firm, IG Farben¹ – were able to reap hefty profits stemming from the integration of “pure” scientific research in close collaboration with universities, applied product-oriented research, industrialization and scaling-up of production, market penetration, and product diversification. At the turn of the 20th century, the leading German dyestuff companies were paying annual dividends between 18 and 26% (Plumpe 1991).

The German chemical/pharmaceutical industry is the first one to enter the era of modern monopoly capitalism. We use this term as a shorthand to mean industrial regimes characterized by a) the *visible hand* (Chandler 1977) of either few oligopolistic firms, or indeed a monopoly like the one of IG Farben in 1920’s and 1930’s Germany, or of platform firms nowadays; and b) the ability of these oligopolists or monopolist to secure a sustained stream of differential profits/rents. Monopoly capitalism may be either due to complementary assets (Teece 1986) and distinct organizational capabilities (like those just mentioned with reference to the 19th century German chemical industry), or due to the consequences of the extreme increasing returns nature of information-intensive activities (such as those associated with the contemporary platform technologies), or due to the sheer outcome of monopolistic rights over crucial tangible or intangible assets such as patents.²

The very history of the pharmaceutical industry highlights that there is no necessary link between the profits/rents accruing to monopoly capitalists, as defined here, and rates of innovation, and even less so between the latter and the appropriation of knowledge via patents. The modern drug industry emerges basically out of the dyestuff one and the development of synthetic chemistry for new compounds (Beer 1959). In the early days, the “incorporation of science” and the “industrializa-

¹IG Farben, a short common name for Interessengemeinschaft Farbenindustrie AG, was formed in 1925 as the merger of the six main chemical/pharmaceutical German companies: BASF, Bayer, Hoechst, Agfa, Chemische Fabrik Griesheim-Elektron, and Weiler-Ter Meer. The company survived until 1951, when it was split in its originally constituent companies (Beer 1959).

²For an extensive discussion of the essence of competition in capitalism see the recent work by Ergen and Kohl (2020).

tion of invention” involve close connections between university and industry, between research and production, and the cooperation of chemists, engineers and technicians (Marsch 1994). In this, German-centred, institutional set-up, IPRs in the form of patents play no role at the start, and become important in the early 20th century only as a defensive weapon against foreign imitation. All this notwithstanding, or because of this, the rates of innovation have remained very high.

The US drug industry in the first 80 years or so plays a negligible role, also because, unlike Germany, it is largely separate from the chemical industry. Things change dramatically with World War II, and the mass production of penicillin is the archetype of such a change. Penicillin was discovered in the UK, but the industrialization and the scaling-up of production occurred in the US, under the guidance of the Federal Office of Scientific Research and Development, founded by the Federal Government, which retained all IPRs while freely sponsoring private production under non-exclusive conditions (Best and Bradley 2020, Gross and Sampat 2020). That was basically the template upon which the US drug industry surged to world leadership, with non-profit institutions (public laboratories and universities) undertaking a good deal of basic research and also product development. Under that institutional arrangement, private pharmaceutical companies were receiving publicly generated knowledge basically for free, but they were engaged into a good deal of basic research too, even if with the only purpose of efficiently absorbing, refining and industrializing it. Thus, when private appropriation was possible (it could not be done on the results of publicly financed research) it occurred quite “down the line” and still had very little to do with any incentive to search for innovative knowledge.

This picture started to change under the convergence of different factors. The Bayh-Dole Act of 1980 allowed patenting of the outcomes of publicly sponsored research. The jurisprudence increasingly enlarged the domain of patentability, while becoming much less demanding on the criterion of novelty. No refinement of comparability has even been put in place: that is patent applicants have to show that a certain drug somehow works, but not that it works better than the already existing ones.³ And, since the 90’s a good deal of the running costs of the US Food and Drug Administration, that is the regulator, have been put in charge of the drug companies, i.e. the regulated actors.

All in all, since the mid 70’s but more rapidly since the 80’s, patenting has exponentially increased, with no evidence, however, of any parallel increase in the rates of innovation. On the contrary, the pharmaceutical sector has been recently object of policy

³In fact, the regulatory framework has been even worse, neglecting basic safety requirements for a long time. Just as an example, in 1937 the company Massengill commercializing a poisonous antibiotic (Elixir Sulfanilamide) causing the death of more than 100 people could be prosecuted only for mislabelling. Even the Kefauver Harris amendment approved in 1962 after the thalidomide tragedy failed to provide general third-party checked requirements for safety (Temin 1985, Angell 2005, Avorn 2005).

and scientific concerns of an *innovation crisis*. Indeed, according to Light and Lexchin (2012) there is a myth of such a crisis in pharma but there is also a real innovation crisis of a different nature. The myth stands in the purported decline in the number of released New Molecular Entities, which however after the resolution of a backlog in applications, settled at an average between 15 and 25 drugs per year, with one NME per firm approved every six years, on average, with those most successful companies recording one NME per year, and with a constant production rate in the last fifty years (Munos 2009). The real innovation crisis comes from the lack of new therapeutical treatments in new drugs which since the eighties have been introduced at disappointingly low rates. Different studies agree that the innovativeness of therapeutic treatments has been quite low, with reference to new drugs approved in the EU (Motola, De Ponti, Poluzzi, Martini, Rossi, Silvani, Vaccheri, and Montanaro 2006, Van Luijn, Gribnau, and Leufkens 2010), Canada (Morgan, Bassett, Wright, Evans, Barer, Caetano, and Black 2005), and the US (Angell 2005).

The different phases of the patent regimes in the US described so far closely mimic the dating proposed in Coriat and Weinstein (2012) describing a *Pre-Fordist* phase, marked by the intention to reward the individual innovative activities and during which firms tend to acquire knowledge from outside, until the establishment of *Corporate Capitalism* in which innovation laboratories were created inside vertically integrated and hierarchical firms, mainly big ones, while structured relationship with universities and public laboratories arose. The third phase, initiated by the Bayh-Dole Act of 1980 (Coriat and Orsi 2002) defines instead an acceleration in the commodification of knowledge and paves the way for the rentification of innovative activities and the innovation crisis in pharma.

In the latest phase, most of new approvals appear to be defensive patenting around existing compounds and therapies, new applications of existing molecules, and “*me-too*” drugs. It is not easy to clearly identify “*me-too*” drugs, however Krieger, Li, and Papanikolaou (2018) provide compelling empirical evidence of their increase. They calculate an index of similarity between drugs by computing a Jaccard distance between chemical substructures. They then apply this measure to data in Thomson Reuters Cortellis’s Investigational Drugs database, which contains detailed development histories for over 64,067 drugs, and find that the number of drugs presenting a similarity score of 0.9 or above has more than doubled in the period 1999-2014.

Also the expenditure of large pharmaceutical companies in basic R&D has been dramatically low (Light and Lexchin 2005), in line with a general reduction of the involvement of private corporations in science (Arora, Belenzon, and Pataconi 2018). Public funding on the contrary has become more and more important for relevant discoveries. For instance, Cleary, Beierlein, Khanuja, McNamee, and Ledley (2018) report that the NIH funding contributed to published research associated with 210

NMEs approved in the period 2010-2016.

Coupling together the two latter trends, namely the innovation crisis and the decrease of breakthrough innovations produced by private companies, this paper provides a systematic analysis of the patenting activity in the pharmaceutical sector distinguishing between product and process innovations. By reconstructing the long-term evolution of all drugs approved in the Orange Book by the Food and Drug Administration, we disentangle the increasing role of public funding in process-based innovation (overall pharmaceutical patents) and the decreasing one in product-based innovations (Orange Book). After studying the evolution of standard quality indicators, we focus on a rarely used indicator of appropriability, namely extended patent families, and document the changing patterns over time of top collecting families and relative firm applicants.

Finally, leveraging on Compustat, we look at the dynamics of sales, profitability and R&D activities of top patenting listed firms. Our analysis reveals that inside a vast variety of firm level strategic behaviours in patenting activities, the stock of owned patents strongly correlates with profitability while it does less so with R&D expenses.

The rest of the paper is organized as follows. Section 2 presents the data and methods that have been used, section 3 provides evidence of the so called innovation crisis in the pharmaceutical sector, while section 4 explores the firm-level relationship between appropriability, profitability and R&D expenses. Finally, section 5 concludes.

2 Data and methods

We base our analysis on patents belonging to WIPO technical field 16 (which we shall call W16 patents), i.e. patents belonging to “Pharmaceuticals” within the 35-field WIPO classification. Then, we refer to the Orange Book (OB) in order to focus on patents that have yielded a new drug. The OB is a yearly publication of drug products, approved on the basis of safety and effectiveness by the Food and Drug Administration, containing related patent and exclusivity information. When not specified otherwise, the analysis in the remainder of the paper includes a concatenation of OB editions between 1985 and 2020. Figure 1 presents a concise description of how new drugs are classified in the OB. The most relevant information for us is:

- ◇ trade or generic name: it defines the commercial product name;
- ◇ therapeutical equivalent code (TE): it defines whether a product is a therapeutical equivalent. TEs are distinguished under label ‘A’ (“Drug products that FDA considers to be therapeutically equivalent to other pharmaceutically equivalent products”) and under label ‘B’ (“Drug products requiring further FDA investigation and review to determine therapeutic equivalence”);

- ◇ applicant to FDA: it represents the firm requiring approval which *does not* necessarily coincide with the original patent applicant.

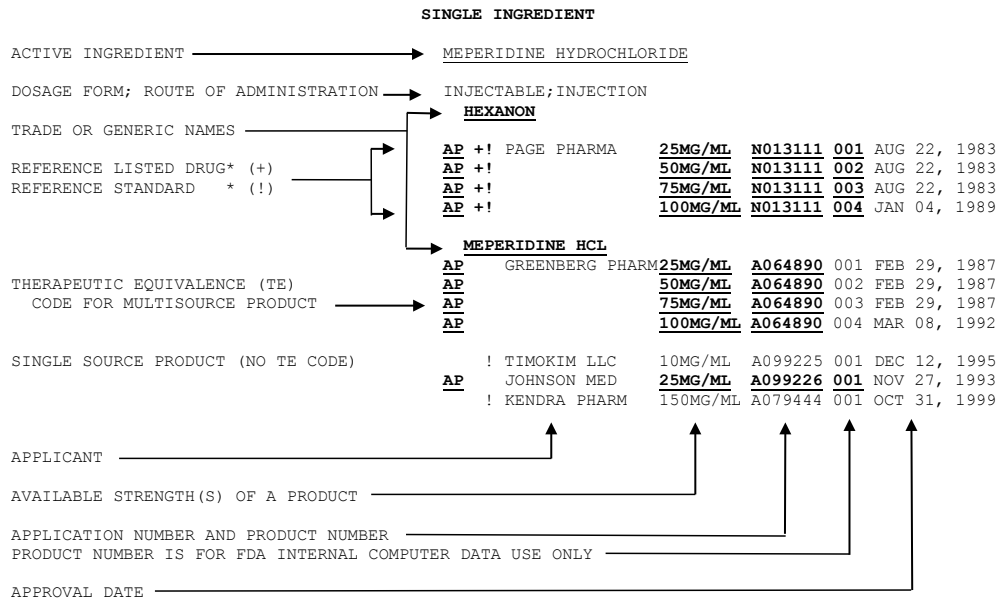


Figure 1: Drug product illustration. Source: Orange Book (2021).

Additionally, the section “Patent and exclusivity information addendum” allows to recover information on patent applications linked to drug applications submitted to the FDA. The Addendum contains patent and exclusivity information for the Prescription, OTC, Discontinued Drug Product Lists, and for the drug products with approval under Section 505 of the Federal Food, Drug, and Cosmetic Act administered by the Center for Biologics Evaluation and Research (CBER), i.e. the Center within FDA that regulates biological products for human use under applicable federal laws.

Public funding information are retrieved from PatentsView which provides information on government interest statements in USPTO patents. The dataset allows to break down the source of funding among the various US public institutes (e.g. National Institute of Health, Department of Health and Human Services, etc.). Additional general information on patents, patent citations and the like come from PATSTAT.

Firm-level information is retrieved from Orbis IP, which provides a 10-year rolling window for firm balance-sheet data, and Compustat, which provides long-term figures for listed companies.

Figure 2 presents a synthetic diagram of the analysis workflow, which also highlights relevant data sources and matching procedures.

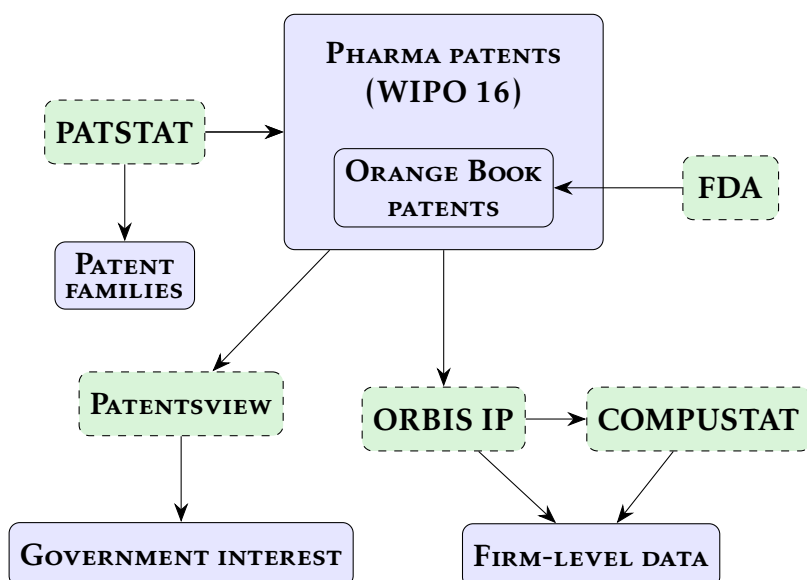


Figure 2: Flowchart of the empirical analysis.

3 Patent data analysis: in search of the innovation crisis

In this section we present our empirical evidence on the purported crisis of innovation in the pharmaceutical sector. We will start by analysing the underlying quality of patents in the industry by means of standard patent quality indicators in Section 3.1. We then analyse the role of governmental agencies in funding private patents in Section 3.2 and look at the patterns of appropriability conditions by the dynamics of extended patent families in Section 3.3.

3.1 Quality indicators of pharmaceutical patents

The PATSTAT database contains 177,040 W16 patents published since 1837, of which 171,743 ($\approx 97\%$) published since 1968. Figure 3(a) presents the long run trend since 1837 while Figure 3(b) shows the ratio of W16 patents over all published patents in each year. The ratio stays roughly constant for the first 25 years of the XX century, grows approximately linearly between 1925 and 1975, and after that shows a roughly quadratic increase. This acceleration is a sign of the institutional changes that we described in the introduction.

Of all pharmaceutical patents, 5,655 ($\approx 3.3\%$) are mentioned in the Orange Book (we shall call them OB patents). The time evolution of OB patents is presented in Figure 4(a) while the ratio is shown in Figure 4(b). Over time, the fraction of OB patents versus W16 patents does not present any remarkable steep trend. Figure 4(c) shows that OB patents are predominantly pharmaceutical, but also cover related fields such as organic chemistry, medical technology, biotech, and the like.

What are those patents about? Tables 1 and 2 present a breakdown of the relevant

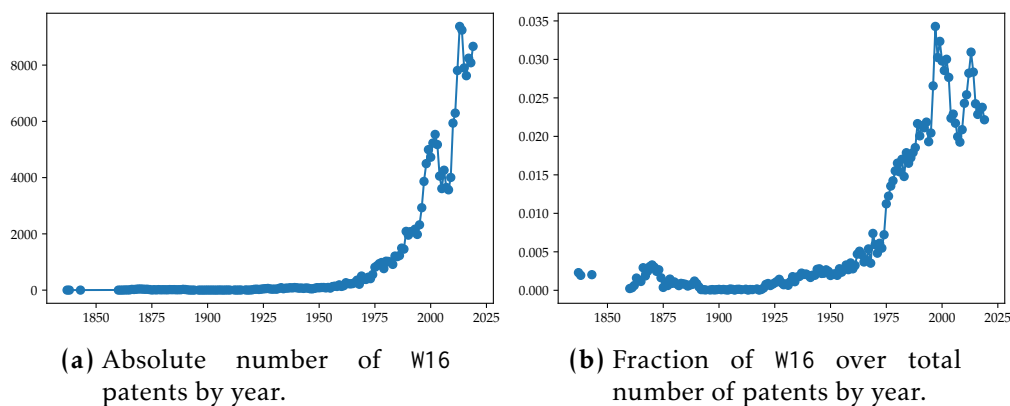


Figure 3: Long-run patenting activity in pharma (1837–2019).

CPC technological classification codes at the 4-digit level for the two sets of patents (W16 and 0B, respectively). In both cases, A61K (“Preparations for medical, dental, or toilet purposes”) is the dominant CPC code, a code typically assigned to pharmaceutical inventions. It is worth noting that the W16 set presents a strong presence of process innovations (e.g. methods and apparatus to sterilise materials), while 0B patents are essentially product innovations.

Unfortunately, we cannot distinguish between therapeutical equivalent products ‘A’ and ‘B’ for the whole set of 0B patents, but restricting the analysis to only the latest release of the Orange Book (2021), which covers 3,151 patents ($\approx 56\%$) of the overall 5,655 0B patents, we find that, among approved drugs, only 22 ($\approx 3\%$) over 764 therapeutical codes are listed under the B category. Figure 5 presents the cumulative distribution of trade names by patents. The top 20 trade names over a total of 988 distinct trade names (top 2%) are covered by approximately 10% of patents (388 of 3,714). This number shows that therapeutical equivalent treatments are quite concentrated in a relatively small group of commercial products. Table 3 presents a list of the top 20 products with the number of related patents.

We now ask the extent to which these patents present an innovative content by matching them with some patent quality indicators used in the literature (Squicciarini, Dernis, and Criscuolo 2013). We will make reference to five patent quality indicators, that we consider particularly relevant in our case:

Backward citations: patent applicants are asked to disclose the prior knowledge which they have relied upon and, in particular, cite existing patents and scientific publications which their purported innovation is somehow indebted to. These citations are used to assess patentability and evaluate the legitimacy of the claims. The number of citations can help estimate the degree of novelty of an invention (Criscuolo and Verspagen 2008). Backward citations either to patents or to

Code	Count	Definition
A61K	598,309	PREPARATIONS FOR MEDICAL, DENTAL, OR TOILET PU...
C07D	126,946	HETEROCYCLIC COMPOUNDS
C07K	80,802	PEPTIDES
C12N	55,074	MICROORGANISMS OR ENZYMES; COMPOSITIONS...
Y10S	38,854	TECHNICAL SUBJECTS COVERED BY FORMER USPC CROS...
C07C	23,419	ACYCLIC OR CARBOCYCLIC COMPOUNDS
G01N	18,659	INVESTIGATING OR ANALYSING MATERIALS BY DETERM...
A61L	17,036	METHODS OR APPARATUS FOR STERILISING MATERIALS...
Y02A	15,033	TECHNOLOGIES FOR ADAPTATION TO CLIMATE CHANGE
A23L	9,346	FOODS, FOODSTUFFS, OR NON-ALCOHOLIC BEVERAGES,...

Table 1: Top 10 CPC codes for W16 patents.

Code	Count	Definition
A61K	34,041	PREPARATIONS FOR MEDICAL, DENTAL, OR TOILET PU...
C07D	2,831	HETEROCYCLIC COMPOUNDS
Y10S	1,655	TECHNICAL SUBJECTS COVERED BY FORMER USPC CROS...
A61P	663	SPECIFIC THERAPEUTIC ACTIVITY OF CHEMICAL COMP..
C07C	591	ACYCLIC OR CARBOCYCLIC COMPOUNDS
A61M	509	DEVICES FOR INTRODUCING MEDIA INTO, OR ONTO, T...
C07K	408	PEPTIDES
G01N	398	INVESTIGATING OR ANALYSING MATERIALS BY DETERM...
Y02A	370	TECHNOLOGIES FOR ADAPTATION TO CLIMATE CHANGE
A61J	239	CONTAINERS SPECIALLY ADAPTED FOR MEDICAL OR PH...

Table 2: Top 10 CPC codes for 0B patents.

Trade name	# patents
VASCEPA	50
IMBRUVICA	31
HYSINGLA ER	24
ESBRIET	21
GATTEX KIT	20
XIFAXAN	19
VIEKIRA XR	18
SYMDEKO (COPACKAGED)	18
VYVANSE	18
ORKAMBI	16
OSMOLEX ER	16
TRIKAFTA (COPACKAGED)	16
ENVARUS XR	16
XTAMPZA ER	15
DSUVIA	15
BAFIERTAM	15
ZOHYDRO ER	15
BENDEKA	15
PENNSAID	15
OXYCONTIN	15

Table 3: Top 20 trade names by OB patents.

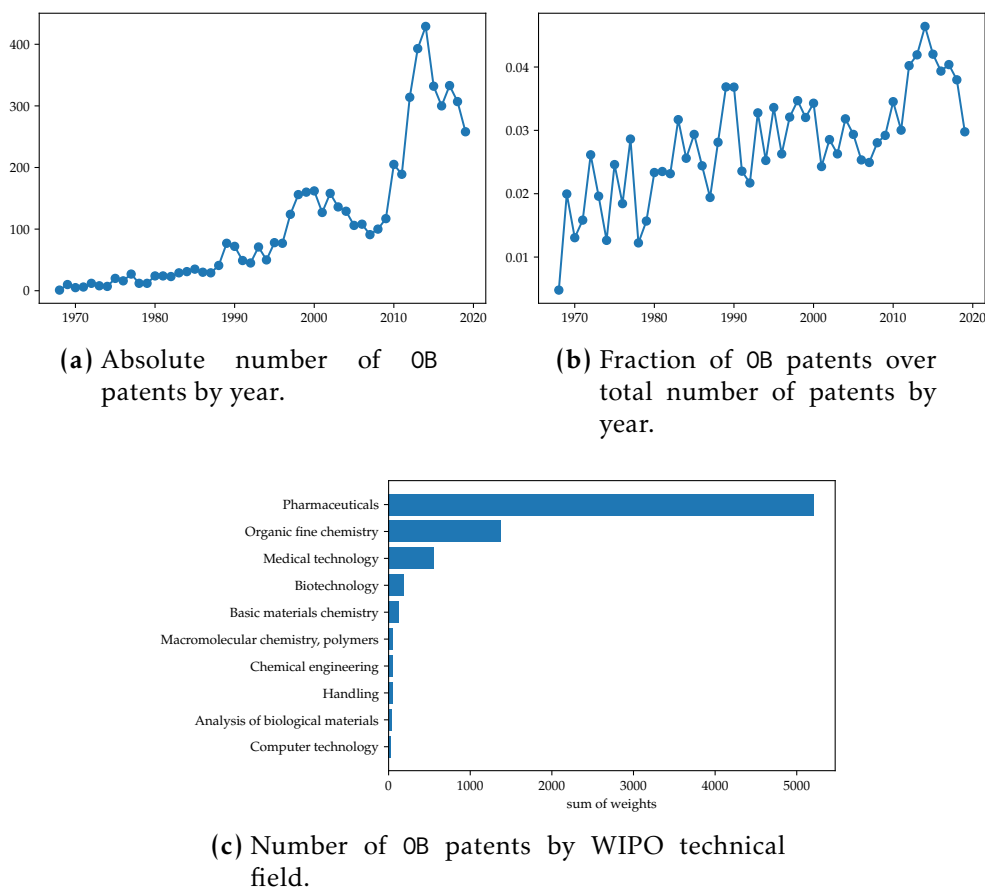


Figure 4: Patents treating diseases (1968–2019).

non-patent literature (NPL) is positively related to the value of a patent (Harhoff, Scherer, and Vopel 2003). However, many backward citations may signal a more *incremental* innovation (Lanjouw and Schankerman 2001). Our backward citations indicator excludes references to NPL, which is considered separately in our next indicator, and it does not particularly suffer from truncation error. Different technology fields share similar backward citation patterns, 5-10% of patents do not rely on prior art (i.e. they do not contain backward citations) and only a very small percentage of patent documents contain more than ten backward citations.

Citations to non-patent literature: backward citations to NPL can be considered as indicators of the contribution of public science to industrial technology (Narin, Hamilton, and Olivastro 1997). They reflect how close a patented invention is to scientific knowledge and help assess the proximity of technological and scientific development. Patents citing NPL tend to contain more complex and fundamental knowledge (Cassiman, Veugelers, and Zuniga 2008) and have significantly higher quality than patents that do not (Branstetter 2005). NPL citations represent a subset of the backward citations, as such, they do not suffer from truncation

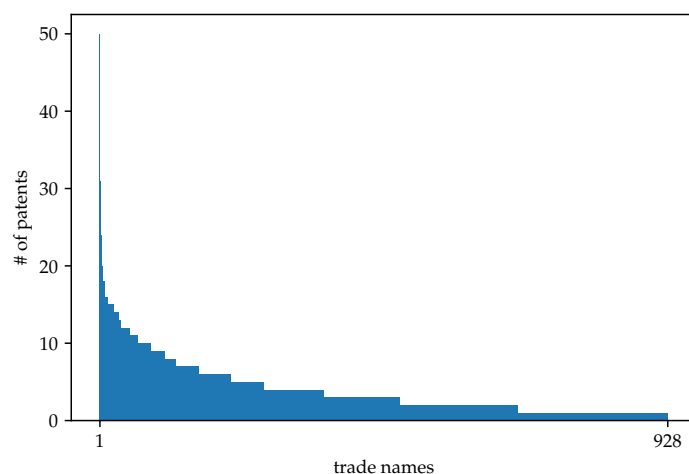


Figure 5: Distribution of 0B patents by trade name.

error. In the 1998-2009 period very few patents cite NPL. Sectors follow very similar pattern, with most patents in all sectors not citing any NPL.

Number of claims: claims determine the boundaries of patent protection. The number and content of claims determine the breadth of IPRs. Patent fees are also based on the number of claims. Hence, the number of claims not only reflects the technological breadth of a patent, but also its expected market value (Tong and Davidson Frame 1994, Lanjouw and Schankerman 2001, Lanjouw and Schankerman 2004). The indicator is defined as the number of claims per patent. Technology fields seem to vary in the average number of claims per patent. Caution should be used when making intertemporal comparisons because different averages might reflect different underlying distributions, for instance, biotech patents feature on average 22 claims per patent in 1999 and 13 in 2009, while the standard deviation above 16 in 1999 and 12 in 2009, micro and nano-tech patents contain on average 20 claims in 1999 and only 12 in 2009, while the standard deviation drops from 17 in 1999 to 8 in 2009.

Forward citations: the number of citations a given patent receives is an indicator of the technological importance of the patent for the development of subsequent technologies. To a certain extent, they also reflect the economic value of inventions (Trajtenberg 1990, Hall, Jaffe, and Trajtenberg 2005, Harhoff, Scherer, and Vopel 2003). Forward citations are counted over a period of five or seven years after publication and the count includes self-citations. The indicator is defined

as

$$\text{CIT}_{i,T} = \sum_{t=P_i}^{P_i+T} \sum_{j \in J(t)} C_{j,i} \quad T \leq 5$$

$\text{CIT}_{i,T}$: number of forward citations received by patent application i published in year P_i within T years from publication

$C_{j,i}$: dummy variable that gets value 1 if the patent j is citing patent i , and 0 otherwise

$J(t)$: set of all patents applications published in year t

The forward citation index has generally decreased over time and there is substantial heterogeneity across technology fields.

Breakthrough innovations: breakthrough innovations are high-impact innovations which serve as a basis for future technological developments, new products, or new services (Popp, Santen, Fisher-Vanden, and Webster 2013) and are defined as the 1% most cited patents. Also in this case truncation occurs.

Figure 6 presents the time evolution of the above mentioned quality indicators. Panels (a), (b), and (c) show the time evolution for W16, OB, and all patents in general, respectively. Each line shows a year-average taken across the population of interest (W16, OB, all patents). With respect to backward and NPL citations, the pharmaceutical sector, both overall and limited to OB patents only, presents a remarkable steep trend, by far more pronounced when compared to the set of all patents. Indeed, this evidence reflects the huge leverage the pharmaceutical sector does on both prior and scientific knowledge. Recall that while a high number of backward citations might signal quality because of the complex knowledge content embedded in patents, the latter can also be an indicator of more incremental innovation. The contribution of public science is instead a proxy of good quality but also signals that a large body of knowledge appropriated by pharmaceutical patents relies on public scientific knowledge.

With reference to patent breadth, reflected by the number of claims included in each patent document, we observe that W16 patents have a stable trend in the number of claims, ranging from 10 to 15 across our time frame. However, OB patents present a higher number of claims, ranging between 15 and 25, in the period under analysis. Therefore, recalling that the number of claims represents a direct expression of the extension of appropriability, patents linked to drugs approved by the FDA have a remarkable higher breadth. Higher breadth is also reflected into higher forward citations that OB patents on average receive, reaching approximately 30 citations in 2015 (the declining trend after 2015 is affected by truncation).

In order to better appreciate the difference among our patent samples, Figures 6(d), 6(e), and 6(f) plot, respectively, the ratios between OB and W16 patents, between W16 patents and patents in all technological fields, and between OB patents and patents in all technological fields. OB patents generally seem to display better quality compared to both W16 and all patents, especially in the two indicators of forward and NPL citations. The latter indicator is 5 to 8 times greater in pharmaceutical patents (with peaks in OB patents) than in the whole set of patents.

Figures 6(g), 6(h), and 6(i) plot the coefficients of variation of quality indicators for the three sets of patents: W16, OB and all. Tracking variability across patents is important in order to detect heterogeneity. Regarding W16 patents, indicators which present a decreasing variation over time are backward and NPL citations (except the spike after 2015). At the opposite, forward citations present a strong divergent trend over time, signalling how the between-patent variation is quite remarkable. OB patents show instead approximately mean-reverting trends. Forward citations show the highest variability across patents over time.

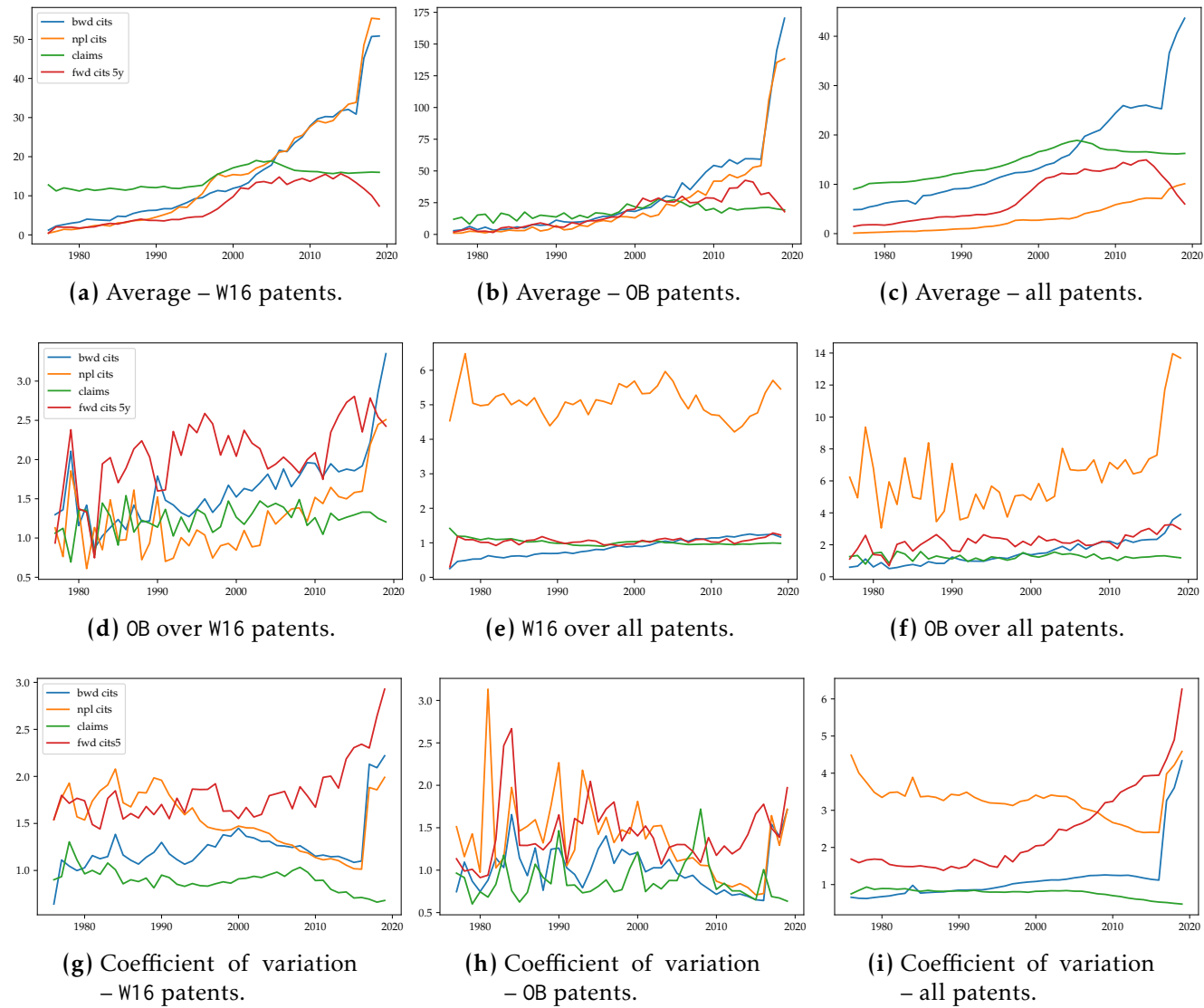


Figure 6: Time evolution of quality indicators – year average (first row), relative (second row), coefficient of variation (third row).

Finally, panels (a) and (b) of Figure 7 show the time evolution of the number of breakthrough patents, counting yearly the top 1% patents in terms of forward citations in the past five years, among all technological classes. In both sets, trends are increasing, however numbers are quite small, with peaks at 100 and 20 patents respectively. A more telling picture is presented in panels (c) and (d) of the same figure, where the ratio of breakthrough patents over total patents is dramatically low for W16, ranging from 0.2% to 1.75%, and notably with a declining trend since 2005. With respect to new drugs approved, the number of breakthrough patents, quite volatile because of small numbers, does not exceed 8%.

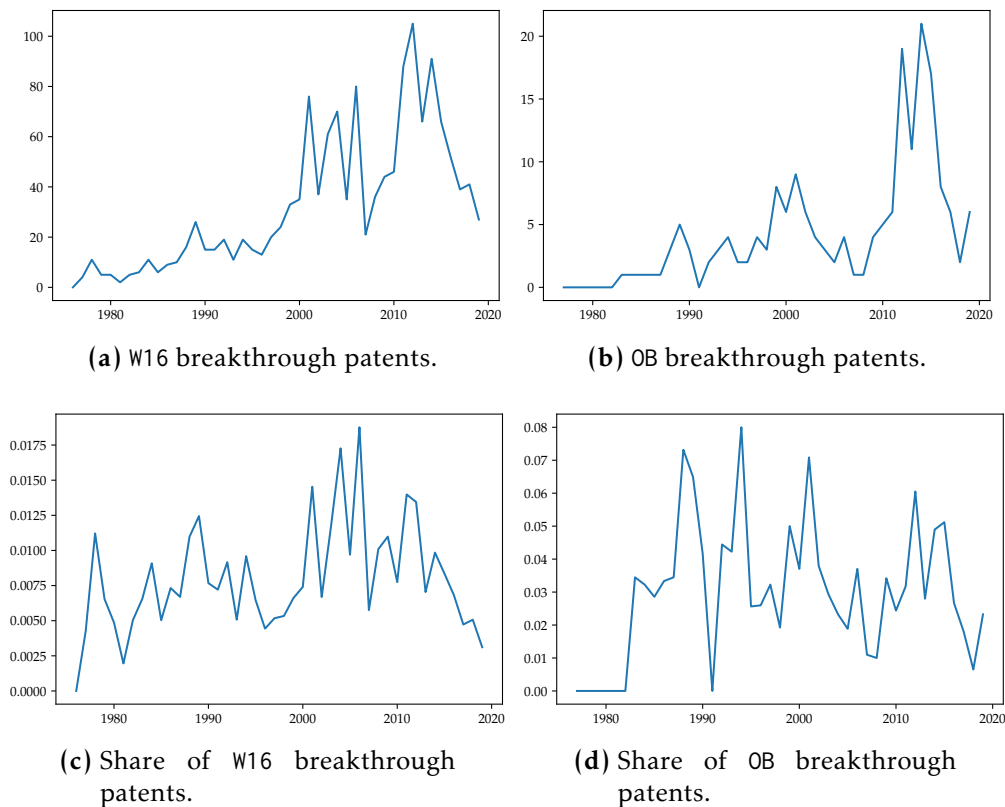


Figure 7: Breakthrough patents.

3.2 Public funding

We now turn to the role of public funds in the production of patented innovations. According to Light, Burke, and de Francisco (2005), big pharma has profoundly transformed its business model, devoting an ever declining fraction of expenditure to basic research. For example, with reference to so called *neglected diseases* (e.g. a vaccine for HIV/AIDS, more effective diagnostics for tuberculosis, and better treatments for leishmaniasis and sleeping sickness) Moran, Guzman, Ropars, McDonald, Jameson, Omune, Ryan, and Wu (2009) reports that public funding was responsible for 69%

	Agency	# patents
	Any agency	14,312
	National Institutes of Health	10,661
	National Cancer Institute	823
	United States Government	713
	Department of Health and Human Services	652
	National Science Foundation	537
	Department of Defense	380
	Army	369
	National Institute of Allergy and Infectious Diseases	335
	Public Health Service	308
	Department of Energy	276

Table 4: Public funding agencies of W16 patents.

of total R&D expenditure. Garattini and Chalmers (2009) reports that public funding is taking care of the most-risky drug developments while Stevens, Jensen, Wyller, Kilgore, Chatterjee, and Rohrbaugh (2011) finds that 153 new FDA-approved drugs, vaccines, or new uses of existing drugs were discovered through research carried out in public-sector research institutions. Beyond the pharmaceutical sector, an increasing role of public institutions in guiding the discovery and innovation process has been documented looking at prize winning innovations (Block and Keller 2009).

In order to detect forms of public funding in pharma patents we follow an alternative route: by means of the PatentsView dataset, we are able to identify the patents reporting some form of government interest. Tables 4 and 5 present a breakdown of W16 and OB patents reporting forms of public funding. Overall, we found 14,312 patents with public funding among all W16 patents, and 75 among OB patents. The National Institute of Health (NIH) provides by far the largest share of funding.

Figure 8 summarises the main results. Panels (a) and (b) present the time evolution in the number of patents receiving public funding from the NIH and their ratio over all W16 patents. A steep increasing trend is quite visible, with NIH funding being present in 12% of pharma patents in 2019. Panels (c) and (d) present the corresponding patterns for OB patents where, given the small numbers involved, we consider not only NIH but the top four funding agencies. Numbers are small and quite volatile, but the ratio shows a clearly declining trend. Table 6 presents the top assignees of patents receiving forms of government interest.

What can we infer from these two opposite trends? Considering the complementary evidence on the more prominent role played by the public funding in more risky and breakthrough research efforts (Moran, Guzman, Ropars, McDonald, Jameson, Omune, Ryan, and Wu 2009, Garattini and Chalmers 2009, Stevens, Jensen, Wyller, Kilgore,

Agency	# patents
Any agency	75
National Institutes of Health	47
Department of Health and Human Services	16
National Cancer Institute	10
United States Government	4
Public Health Service	4
Department of Veterans Affairs	3
Army	3
National Institute on Ageing	2
National Institute of Mental Health	2
National Institute of General Medical Sciences	2

Table 5: Public funding agencies of OB patents.

Chatterjee, and Rohrbaugh 2011), our evidence complements the declining innovative contents that OB patents deliver. Additionally, the government interest has shifted over time from funding product innovation to funding process innovation and this might indeed indicate that the true innovative contents embedded into OB patents went down over time.

3.3 Appropriability

The final piece of evidence we would like to add concerns the increasing similarity and decreasing innovative contents in newly released patents. Indeed, there are alternative ways to characterise similarity in patents, for example by looking at their technological classification. However, a quite straightforward but relatively unexploited piece of information comes from extended patent families.

According to the definition by the European Patent Office⁴ an extended patent family (also known as an INPADOC family) is “a collection of patent documents covering a technology. The technical content covered by the applications is similar, but not necessarily the same. Members of an extended patent family will have at least one priority in common with at least one other member – either directly or indirectly.” Extended families differ from “simple” families, which generally track applications of the very same innovation to different patent offices. Indeed, extended patent families are useful to understand the applicants’ strategy to gain patent protection on the basis of *cumulativeness of inventions and patent thickets*. Extended families are built by consolidating both direct and indirect priority links between patent applications within families. As a result, it is possible to find two patent documents with no priority in common, but which are

⁴<https://epo.org/searching-for-patents/helpful-resources/first-time-here/patent-families/inpadoc.html>

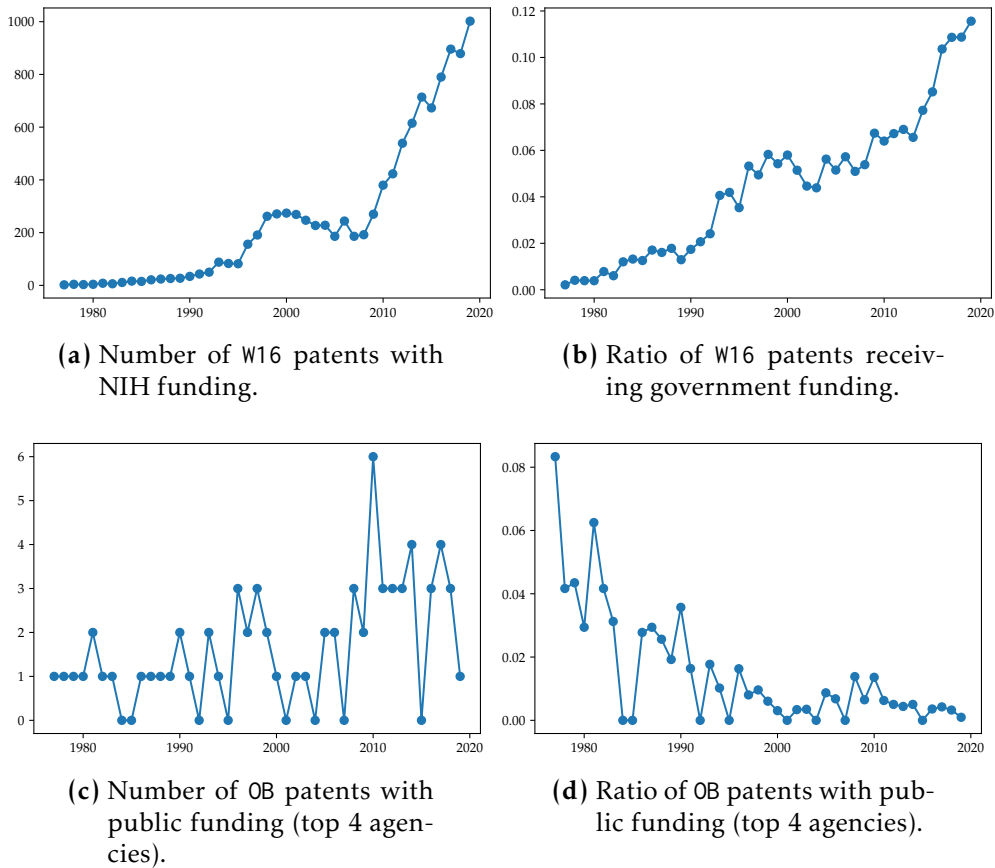


Figure 8: Public funding in W16 patents (NIH only) and OB patents (top 4 agencies).

indirectly related because they both share at least one priority with a third application (Martinez 2011).

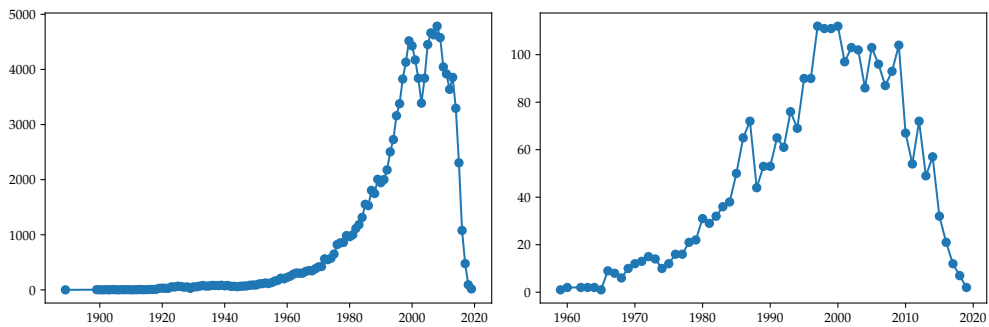
Although strong heterogeneity has been found in the dynamics of extended patent families, ranging from simpler (singleton) to complex structures, based on country of origin of the applicant and on technological fields, analysis of temporal evolution of extended patent families by industry is still missing. In Figures 9(a), 9(b), and 9(c) we present the long term evolution of newly entered families by year of observation, considering W16 and OB patents, and the ratio between new entries and the stock of existing families. The patterns show a long phase of technological diversification, during which new patents are assigned to new families, and a phase starting around 2000 in which technological diversification across patent classes seems to come to a halt. Indeed, the ratio between new entry and existing families shows two phases, one from 1940 up to mid 1990s with an increasing trend, and one from the 2000s onward with a declining trend.

More detailed information on the structure of patent families is provided in Tables 7 and 8 where we present for five decades (1970s, 1980s, 1990s, 2000s, and 2010s) the top ten families in terms of number of patents they collect, the top ten corresponding

Applicant	# patents
MERCK	7
KALA PHARMS INC	5
SIGA TECHNOLOGIES	4
JANSSEN BIOTECH	2
ASTELLAS	2
AVID RADIOPHARMS INC	2
CELGENE INTL	2
LAB HRA PHARMA	2
JANSSEN PHARMS	2
PALATIN TECHNOLOGIES	1
LIFE MOLECULAR	1
ACROTECH	1
ALEXZA PHARMS	1
GENZYME CORP	1
FOLDRX PHARMS	1
CARDINAL HEALTH 414	1
AZURITY	1
TITAN PHARMS	1

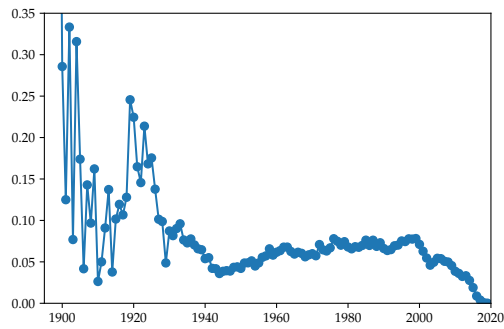
Table 6: Top 20 applicants (only listed companies) of OB patents receiving government interest.

applicants among listed firms (again in terms of number of patents), PATSTAT family identifiers and their year of birth. The evidence for both W16 and OB patents shows decreasing concentration of families in terms of number of firms and increasing size in terms of patents: while in the first two decades many families were single-firm, with the top patent assignee holding almost the entire family, since the nineties concentration has been declining. However, such higher diversification of families derives from a sizeable increase in the number of patents they collect. It is the case for example of family 5570 born in 1994, gathering 3,205 patents with Roche, the top applicant, holding only 26 of them. Bigger extended families, collecting more distinct firms, signal over time higher technological proximity of inventions and increasing similarity. OB patents present smaller and more stable values over time.



(a) Number of families by year with at least one W16 patent.

(b) Number of families by year with at least one OB patent.



(c) Ratio of new W16 families over existing W16 families.

Figure 9: Time trend evolution of extended patent families.

1970s																			
483109 (1973)	627642 (1972)		739332 (1975)		495087 (1976)		627715 (1972)		1888371 (1978)		573984 (1964)		4056068 (1976)		473664 (1969)		661755 (1972)		
Pfizer	20	Bayer	18	Roche	17	GlaxoSmithKline	16	Bayer	13	Pfizer	12	L'Oréal	12	Bristol-Myers Squibb	12	Merck	11	Procter & Gamble	11
TOTAL	21	TOTAL	18	TOTAL	25	TOTAL	16	TOTAL	16	TOTAL	14	TOTAL	24	TOTAL	12	TOTAL	19	TOTAL	12
1980s																			
508242 (1980)	514555 (1984)		514726 (1985)		320415 (1985)		1139385 (1983)		1114838 (1979)		519466 (1987)		2192055 (1985)		320133 (1984)		48772 (1981)		
Pfizer	16	Johnson & Johnson	13	Eli Lilly	13	GlaxoSmithKline	13	Pfizer	12	Merck	11	Regal Beloit	10	Pfizer	10	Bristol-Myers Squibb	9	Sanofi	9
TOTAL	18	TOTAL	13	TOTAL	16	TOTAL	13	TOTAL	12	TOTAL	12	TOTAL	29	TOTAL	12	TOTAL	19	TOTAL	9
1990s																			
67214 (1990)	1430 (1992)		515991 (1987)		5570 (1994)		159598 (1988)		1271007 (1992)		41529 (1988)		1230319 (1989)		206248 (1991)		160568 (1992)		
Ionis	156	Alnylam	58	Colgate-Palmolive	32	Roche	26	Stryker	24	Pfizer	25	Roche	22	AbbVie	21	Nektar	21	Discovery	19
Novartis	1	Novartis	1					Curis	2										
TOTAL	483	TOTAL	625	TOTAL	54	TOTAL	3,205	TOTAL	123	TOTAL	29	TOTAL	40	TOTAL	51	TOTAL	70	TOTAL	103
2000s																			
343028 (1991)	3196 (1996)		67214 (1990)		5570 (1994)		4990278 (2005)		987885 (1997)		47842 (2002)		41211 (1998)		80848 (2002)		1029037 (2000)		
Eli Lilly	57	Perrigo	32	Ionis	30	Roche	26	Medtronic	23	Roche	19	Xencor	18	Becton Dickinson	17	Vyne	15	AbbVie	15
TOTAL	312	TOTAL	122	TOTAL	483	TOTAL	3,205	TOTAL	63	TOTAL	42	TOTAL	218	TOTAL	136	TOTAL	115	TOTAL	18
2010s																			
37701 (1997)	337472490 (2010)		4848881 (2001)		405123419 (2011)		66176 (1997)		47842 (2002)		414841034 (2013)		459187117 (2015)		1862215 (2001)		406608378 (2011)		
Gilead	110	Johnson & Johnson	97	Neonode	43	Moderna	43	Conformis	35	Xencor	31	Sanofi	29	Axsome	26	Coherus	25	ThraapeuticsMD	22
																		Qualcomm	1
TOTAL	458	TOTAL	138	TOTAL	126	TOTAL	189	TOTAL	222	TOTAL	218	TOTAL	37	TOTAL	48	TOTAL	42	TOTAL	62

Table 7: Top 10 families per decade and underlying applicants (only listed companies) – W16 patents.

1970s																			
473664 (1969)	479595 (1972)		49269939 (1970)		485474 (1973)		476712 (1970)		498914 (1977)		752270 (1966)		500559 (1978)		486601 (1974)		473491 (1970)		
Merck	11	Johnson & Johnson	7	Johnson & Johnson	6	Eli Lilly	4	Bristol-Myes Squibb	4	Pfizer	4	GlaxoSmithKline	4	Eli Lilly	3	Eli Lilly	3	Pfizer	3
TOTAL	19	TOTAL	9	TOTAL	7	TOTAL	4	TOTAL	5	TOTAL	17	TOTAL	8	TOTAL	3	TOTAL	7	TOTAL	12
1980s																			
2192055 (1985)	48772 (1981)		498914 (1977)		509541 (1981)		186476 (1979)		511104 (1980)		983135 (1984)		554999 (1981)		468599 (1984)		1182369 (1986)		
Pfizer	10	Sanofi	9	Pfizer	7	Johnson & Johnson	6	Sanofi	6	Eli Lilly	4	Pfizer	4	Bayer	4	Dow Chemical	4	Merck	3
TOTAL	12	TOTAL	9	TOTAL	17	TOTAL	6	TOTAL	14	TOTAL	5	TOTAL	9	TOTAL	15	TOTAL	9	TOTAL	5
1990s																			
67214 (1990)	41529 (1988)		206248 (1991)		138292 (1991)		1233491 (1990)		1276895 (1992)		1290911 (1993)		1259335 (1991)		634113 (1988)		468971 (1992)		
Ionis	156	Roche	22	Nektar	21	GlaxoSmithKline	15	Teva	12	Alkermes	10	Bayer	10	Astra Zeneca	8	Novartis	8	Vertex	8
Novartis	1																		
TOTAL	483	TOTAL	40	TOTAL	70	TOTAL	40	TOTAL	19	TOTAL	24	TOTAL	10	TOTAL	14	TOTAL	14	TOTAL	15
2000s																			
67214 (1990)	80848 (2002)		1335994 (2996)		64475 (1995)		206248 (1991)		25322 (1996)		1006104 (1999)		1015414 (1998)		359007 (1999)		1276895 (1992)		
Ionis	30	Vyne	15	Actlax	10	Nurix	7	Nektar	6	Bristol-Myers Squibb	6	Alkermes	5	Abbott	5	Mannkind	4	Alkermes	4
TOTAL	483	TOTAL	115	TOTAL	14	TOTAL	18	TOTAL	70	TOTAL	21	TOTAL	13	TOTAL	12	TOTAL	15	TOTAL	24
2010s																			
406608378 (2011)	144435 (2002)		328538385 (2009)		413597801 (2012)		276781 (2002)		5160 (2004)		412034 (2006)		444207968 (2014)		80848 (2002)		329363474 (2009)		
TherapeuticsMD	22	Bristol-Myers Squibb	16	Amarin	16	Amarin	16	Mannkind	15	AbbVie	15	AbbVie	15	Thermo Fisher	15	Vyne	14	Vyne	14
Qualcomm	1																		
TOTAL	62	TOTAL	79	TOTAL	25	TOTAL	23	TOTAL	71	TOTAL	40	TOTAL	74	TOTAL	29	TOTAL	115	TOTAL	45

Table 8: Top 10 families per decade and underlying applicants (only listed companies) – OB patents.

W16 patents			OB patents		
Company	# patents	# patents/last sales (m\$)	Company	# patents	# patents/last sales (m\$)
Pfizer	4,228	0.1	Pfizer	206	0.0049
Sanofi	2,407	0.053	Ionis	205	0.2811
Merck	2,276	0.047	AbbVie	197	0.0043
GlaxoSmithKline	2,250	0.049	Johnson & Johnson	175	0.0021
Bristol-Myers Squibb	2,152	0.051	Merck	131	0.0027
Roche	2,116	0.032	GlaxoSmithKline	130	0.0028
Johnson & Johnson	1,858	0.022	Novartis	128	0.0026
Eli Lilly	1,832	0.075	Eli Lilly	122	0.0050
Bayer	1,699	0.034	Bristol-Myers Squibb	120	0.0028
AbbVie	1,411	0.031	AstraZeneca	119	0.0044

Table 9: Patents over sales of top ten patenting firms.

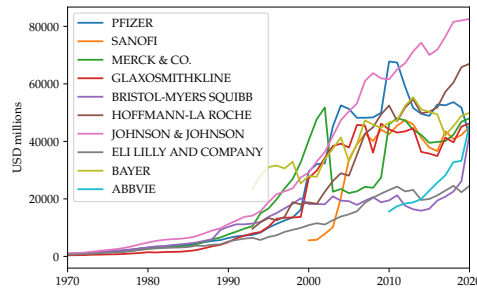
4 Firm-level analysis: appropriation, R&D expenses and profitability

In this section we present evidence on indicators of firm-level corporate performances, focusing on patterns of R&D expenses and profitability of top patenting firms. Applicants are retrieved from Orbis IP and matched with Compustat via thicker identifiers of their global ultimate owner. Our data base starts in 1950. The purpose of the analysis is to detect the extent to which (i) R&D expenses reflect into patenting activities, (ii) patenting and profitability have a positive association. Due to data limitation on corporate performances, in the following we limit the analysis to top ten patenting firms listed in Compustat.

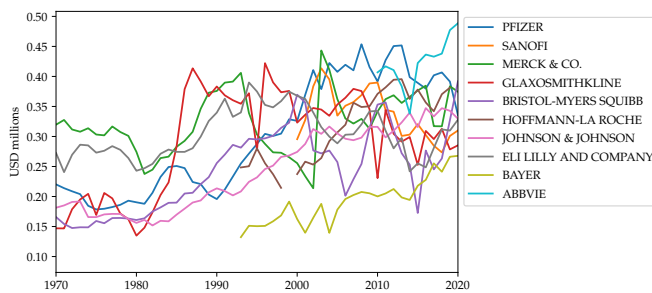
Table 9 presents descriptive statistics in terms of the top ten patenting firms, defined as the cumulative patent count, the number of patents and the ratio between patents over sales. Not surprisingly, such big pharma companies as Pfizer, Sanofi, Roche and GlaxoSmithKline appear among the top companies. Among top ten patenting firms two strong outliers emerge: the first is Pfizer which presents a W16 patents over sales ratio much higher than the other firms. However this anomaly of Pfizer tends to disappear when we consider the ratio between OB patents only and sales. The other outlier is represented by the company Ionis, which appears only among top 10 firms in OB patents. This firm presents a ratio close to 0.3, which indeed signals a completely different corporate strategy: Ionis is a biotech company specialised in drug discovery and potentially a patent-vendor to other firms.

Figure 10 shows the dynamics of corporate performances in terms of sales, EBITDA (Earnings Before Interest, Taxes, Depreciation, and Amortization) and R&D margins, calculated as ratios over total sales. It is interesting to observe the impressive increase of sales, and the two distinct dynamics characterizing profitability and patenting ratios. Albeit profitability stands between 15% and 45%, with an approximative average

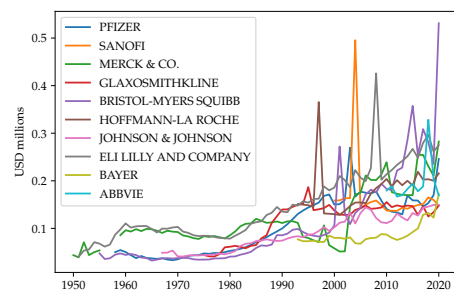
of 30% in the all period, the R&D ratio is quite smaller, ranging from 5% to 20%, with an approximate average value of 15%.



(a) Sales of top 10 patenting firms – W16 patents.



(b) EBITDA margins of top 10 patenting firms – W16 patents.

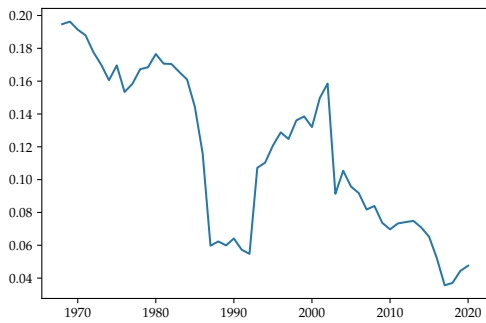


(c) R&D per sales of top 10 patenting firms – W16 patents.

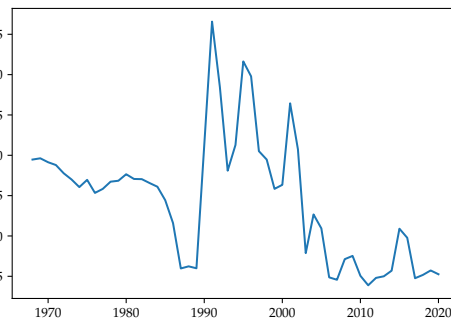
Figure 10: Corporate performances and R&D.

In order to understand the temporal variability of the between-firm heterogeneity we calculate the standard deviation among both EBITDA and R&D margins over time and plot results in Figure 11. EBITDA margins show a remarkable decreasing trend over time, hinting at a pattern of increasing similarity across firms in terms of profitability. R&D margins instead show an increasing trend in terms of between-firm differences. Overall, top ten patenting firms are more similar in their expenditure in R&D rather than in their profitability. The standard deviation of the OB set is highly influenced by the behaviour of Ionis.

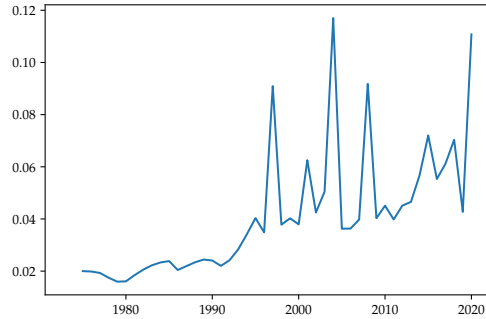
How do R&D expenses map into the number of patents? Figure 12 presents the correlation structure among the annual stock of patents, distinguishing between W16 and OB patents, and annual R&D expenses. Looking at the correlation structure among R&D levels and stock of patents (first row), in both sets we detect a quite remarkable correlation, but with considerable heterogeneity across firms. When looking at margins, a more telling figure, we confirm a positive correlation structure. However, we are not able to target the amount of R&D expenses devoted to each patent, but a simple stock-flow relation. In Figure 13 we perform the same exercise looking at EBITDA.



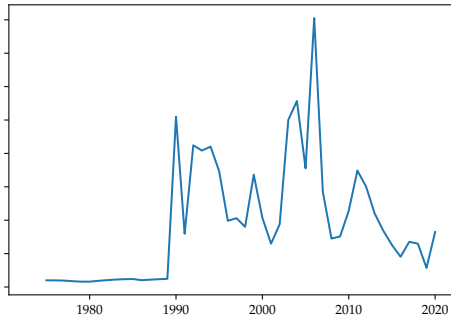
(a) Standard deviation in EBITDA margin – W16 patents.



(b) Standard deviation in EBITDA margin – OB patents.



(c) Standard deviation in R&D per sales – W16 patents.



(d) Standard deviation in R&D per sales – OB patents.

Figure 11: Between heterogeneity – top patenting firms.

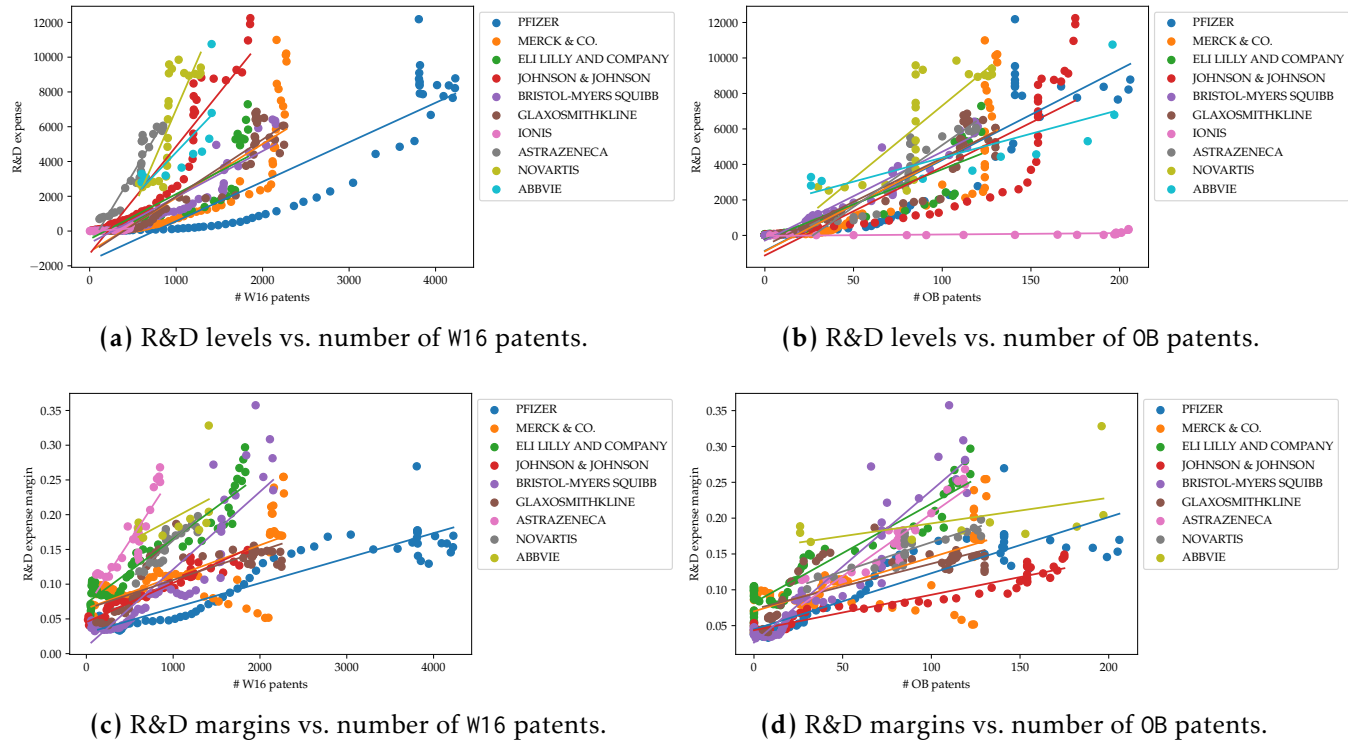
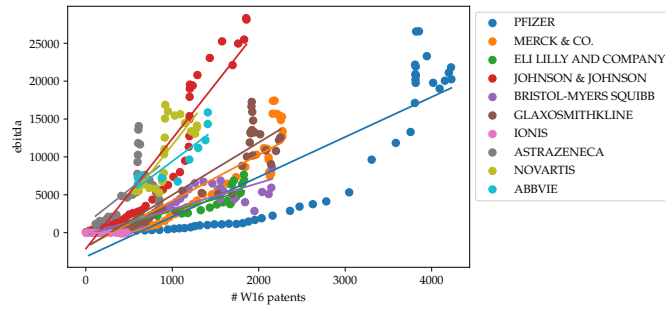
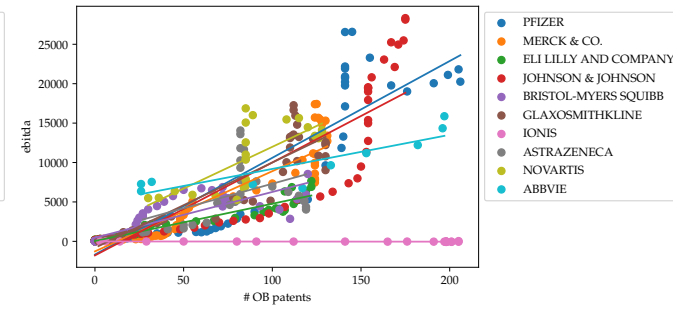


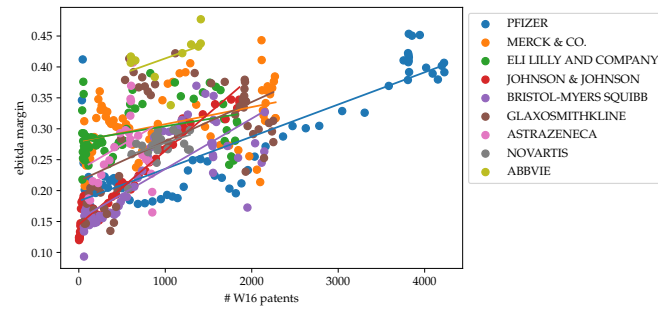
Figure 12: Bivariate correlations – R&D expenses and patenting activities.



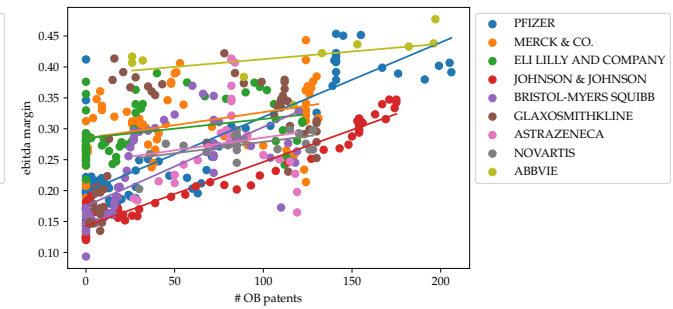
(a) EBITDA levels vs. number of W16 patents.



(b) EBITDA levels vs. number of OB patents.



(c) EBITDA margins vs. number of W16.



(d) EBITDA margins vs. number of OB.

Figure 13: Bivariate correlations – Profitability and patenting activities.

To what extent are patents the result of innovative activities or rather a strategy to secure profits? We conclude our empirical investigation by presenting the distribution of the correlation coefficients, now including all firms since the 1950 for which we find data. Given that, as shown above, top patenting firms all present a strong correlation in terms of both R&D and EBITDA margins, the question is now the extent to which the same pattern can be found in all firms in the dataset, and also whether correlations in R&D differ from correlations in profitability.

In Figure 14 we plot the histograms, restricting our analysis to those firms whose correlation coefficients are statistically significant (10% p-value). Correlation in patents vs. profitability is by far more prevalent across firms than correlation in patents vs. R&D. First, firms presenting a significant coefficient between R&D margins and stock of patents are fewer (37/38) than those ones having a significant correlation in profitability (55/56). Second, the distribution is more concentrated in positive values in EBITDA margins rather than in R&D margins.

The evidence presented so far shows that both R&D expenses and profit margins are positively associated with the stock of available patents. However, patenting activity seems to be a firm strategy to secure profits more than being the result of R&D efforts.

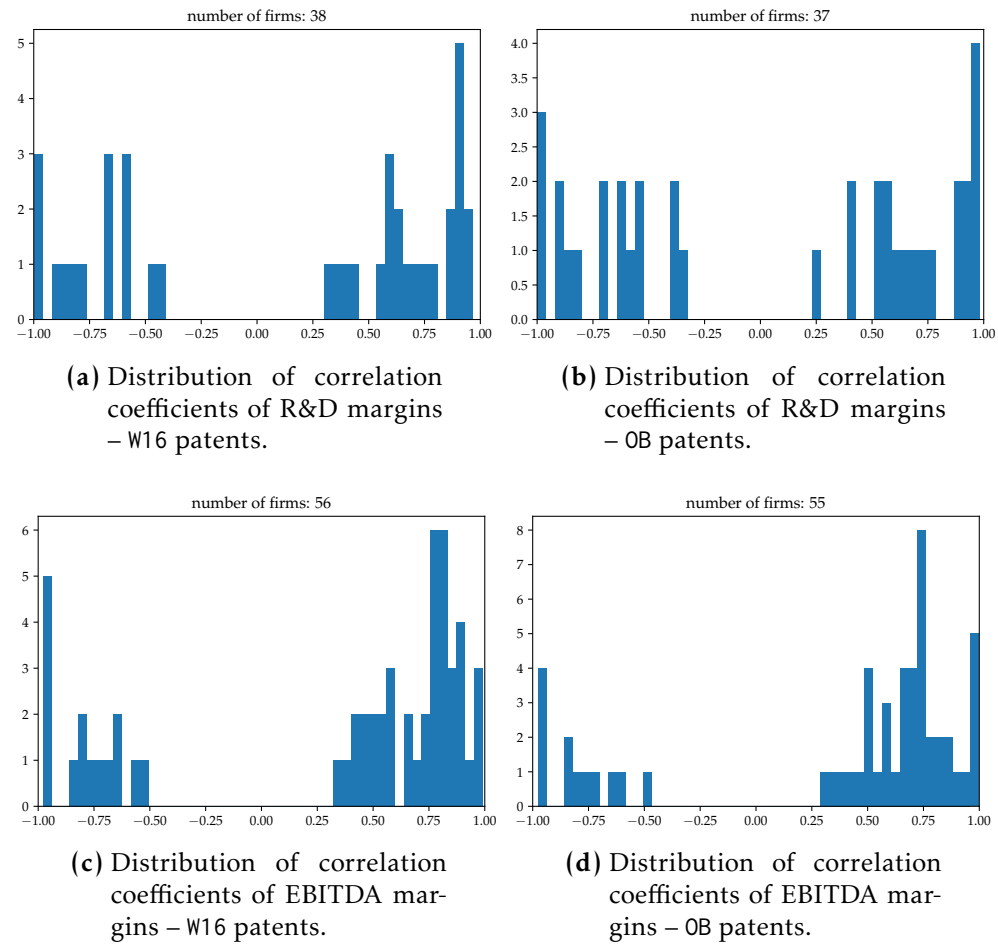


Figure 14: Correlation coefficient distributions – all available firms.

5 Conclusions

In this paper we have attempted a comprehensive empirical analysis by matching complementary data sources on patenting activities in pharma. Notably, our paper represents one of the few efforts linking new products included in the Orange Book and approved by the Food and Drug Administration with their patents.

We analyse pharmaceutical patents along three main lines. First, we look at their quality by employing standard indicators in terms of backward and forward citations, citations to non patent literature, number of claims, breakthrough innovations. While pharma patents strongly rely on prior and scientific knowledge, the amount of breakthrough innovations is remarkably low and decreases over time. Second, we identify and characterize those patents receiving forms of government interest – as such a mark for quality – and find that OB patents are relatively few, decrease over time and concentrate on a bunch of products. Third, we look at appropriability via extended patent families and we identify a declining pattern of new families vis-à-vis the stock of existing ones, coupling with an increasing family size, signalling therefore raising patent thickets and stronger barriers to imitations.

After documenting that the big explosion in patenting activities does not map into a corresponding explosion in innovative activities, we move to the firm-level analysis in order to understand the relationship between patenting activities, profitability and R&D expenses. We document that top patenting firms present converging profit margins over the period of interest while between-firm R&D margins look to be diverging over time. Additionally, we find that R&D and profitability margins are quite correlated with the stock of owned patents for the top patenting firms while, when considering all companies, correlation in R&D margins reveals to be lower than the correlation in profitability.

Taking stock of the empirical evidence collected in this paper and considering the starting empirical question, whether IPRs are an institution promoting innovative activities, with reference to the pharmaceutical sector we can hardly support a positive answer. According to our analysis, IPRs encoded in patents represent legal barriers to protect intellectual monopolies rather than an incentive and a reward to innovative efforts. Patenting strategies look to be quite aggressive in defining extensive knowledge borders and ample space of possibility of infringements.

ACKNOWLEDGEMENTS: The authors are in debt with Silvio Garattini. G.D. and M.E.V. acknowledge support from European Union's Horizon 2020 research and innovation programme under grant agreement No. 822781 *GROWINPRO – Growth Welfare Innovation Productivity*. J.S. acknowledges support by the Italian Ministero dell'Istruzione, dell'Università e della Ricerca, PRIN-2017 project 201799ZJSN: *Tech-*

nological change, industry evolution and employment dynamics.

References

- AMABLE, B. (2003): *The diversity of modern capitalism*. Oxford University Press on Demand.
- ANGELL, M. (2005): *The truth about the drug companies: How they deceive us and what to do about it*. Random House Incorporated.
- ARORA, A., S. BELENZON, AND A. PATACCONI (2018): “The decline of science in corporate R&D,” *Strategic Management Journal*, 39(1), 3–32.
- AVORN, J. (2005): *Powerful Medicines: The Benefits, Risks, and Costs of Prescription Drugs*. Vintage Books, New York.
- BEER, J. J. (1959): *The Emergence of the German Dye Industry*. University of Illinois Press, Urbana, IL.
- BEST, M., AND J. BRADLEY (2020): “World War II to Covid-19: Been Here Before and Done Better,” Discussion paper, Institute for New Economic Thinking.
- BLOCK, F., AND M. R. KELLER (2009): “Where do innovations come from? Transformations in the US economy, 1970–2006,” *Socio-Economic Review*, 7(3), 459–483.
- BRANSTETTER, L. (2005): “Exploring the Link Between Academic Science and Industrial Innovation,” *Annals of Economics and Statistics*, 79–80, 119–142.
- CASSIMAN, B., R. VEUGELERS, AND M. ZUNIGA (2008): “In search of performance effects of (in)direct industry science links,” *Industrial and Corporate Change*, 17, 611–646.
- CHANDLER, A. D. (1977): *The Visible Hand: The Managerial Revolution in American Business*. Belknap Press, Cambridge, MA.
- CLEARY, E. G., J. M. BEIERLEIN, N. S. KHANUJA, L. M. MCNAMEE, AND F. D. LEDLEY (2018): “Contribution of NIH funding to new drug approvals 2010–2016,” *Proceedings of the National Academy of Sciences*, 115(10), 2329–2334.
- CORIAT, B., AND F. ORSI (2002): “Establishing a new intellectual property rights regime in the United States: Origins, content and problems,” *Research policy*, 31(8-9), 1491–1507.

- CORIAT, B., AND O. WEINSTEIN (2012): "Patent regimes, firms and the commodification of knowledge," *Socio-Economic Review*, 10(2), 267–292.
- CRISCUOLO, P., AND B. VERSPAGEN (2008): "Does it matter where patent citations come from? Inventor vs. examiner citations in European patents," *Research Policy*, 37, 1892–1908.
- DOSI, G., L. MARENGO, AND C. PASQUALI (2006): "How much should society fuel the greed of innovators?: On the relations between appropriability, opportunities and rates of innovation," *Research Policy*, 35(8), 1110–1121.
- DOSI, G., AND R. R. NELSON (2010): "Technical change and industrial dynamics as evolutionary processes," *Handbook of the Economics of Innovation*, 1, 51–127.
- DOSI, G., AND M. E. VIRGILLITO (2019): "Whither the evolution of the contemporary social fabric? New technologies and old socio-economic trends," *International Labour Review*, 158(4), 593–625.
- ERGEN, T., AND S. KOHL (2020): "Rival views of economic competition," *Socio-Economic Review*, <https://doi.org/10.1093/ser/mwaa041>.
- GARATTINI, S., AND I. CHALMERS (2009): "Patients and the public deserve big changes in evaluation of drugs," *Bmj*, 338.
- GROSS, D. P., AND B. N. SAMPAT (2020): "Organizing Crisis Innovation: Lessons from World War II," Discussion paper, NBER Working Paper 27909.
- HALL, B., A. JAFFE, AND M. TRAJTENBERG (2005): "Market Value and Patent Citations," *RAND Journal of Economics*, 36, 16–38.
- HARHOFF, D., F. M. SCHERER, AND K. VOPEL (2003): "Citations, Family Size, Opposition and the Value of Patent Rights," *Research Policy*, 32(8), 1343–1363.
- KHAN, B. Z., AND K. L. SOKOLOFF (2001): "The early development of intellectual property institutions in the United States," *Journal of Economic Perspectives*, 15(3), 233–246.
- KRIEGER, J., D. LI, AND D. PAPANIKOLAOU (2018): "Developing novel drugs," Discussion paper, NBER Working Paper 24595.
- LANJOUW, J., AND M. SCHANKERMAN (2001): "Characteristics of Patent Litigation: A Window on Competition," *RAND Journal of Economics*, 32(1), 129–151.
- (2004): "Patent Quality and Research Productivity: Measuring Innovation with Multiple Indicators," *Economic Journal*, 114(495), 441–465.

- LIGHT, D., M. BURKE, AND A. DE FRANCISCO (2005): “Basic Research Funds to Discover Important New Drugs: Who Contributes how Much?,” *Global Forum for Health Research*.
- LIGHT, D. W., AND J. LEXCHIN (2005): “Foreign free riders and the high price of US medicines,” *Bmj*, 331(7522), 958–960.
- LIGHT, D. W., AND J. R. LEXCHIN (2012): “Pharmaceutical research and development: what do we get for all that money?,” *Bmj*, 345.
- MARSCH, U. (1994): “Strategies for success: research organization in German chemical companies and IG Farben until 1936,” *History and Technology*, 12, 23–77.
- MARTINEZ, C. (2011): “Patent families: When do different definitions really matter?,” *Scientometrics*, 86(1), 39–63.
- MORAN, M., J. GUZMAN, A.-L. ROPARS, A. McDONALD, N. JAMESON, B. OMUNE, S. RYAN, AND L. WU (2009): “Neglected disease research and development: how much are we really spending?,” *PLoS medicine*, 6(2), e1000030.
- MORGAN, S. G., K. L. BASSETT, J. M. WRIGHT, R. G. EVANS, M. L. BARER, P. A. CAETANO, AND C. D. BLACK (2005): ““Breakthrough” drugs and growth in expenditure on prescription drugs in Canada,” *Bmj*, 331(7520), 815–816.
- MOTOLA, D., F. DE PONTI, E. POLUZZI, N. MARTINI, P. ROSSI, M. C. SILVANI, A. VACCHERI, AND N. MONTANARO (2006): “An update on the first decade of the European centralized procedure: how many innovative drugs?,” *British journal of clinical pharmacology*, 62(5), 610–616.
- MUNOS, B. (2009): “Lessons from 60 years of pharmaceutical innovation,” *Nature reviews Drug discovery*, 8(12), 959–968.
- NARIN, F., K. HAMILTON, AND D. OLIVASTRO (1997): “The increasing linkage between U.S. technology and public science,” *Research Policy*, 26, 317–330.
- ORSENIGO, L., AND V. STERZI (2010): “Comparative study of the use of patents in different industries,” *Knowledge, Internationalization and Technology Studies (KITEs)*, 33.
- PLUMPE, G. (1991): “The Political Framework of Structural Modernisation : The I. G. Farbenindustrie Ag, 1904–1945,” in *German Industry and German Industrialisation: Essays in German Economic and Business History in the Nineteenth and Twentieth Centuries*, ed. by W. R. Lee, pp. 220–264. Routledge, London.

- POPP, D., N. SANTEN, K. FISHER-VANDEN, AND M. WEBSTER (2013): "Technology variation vs. R&D uncertainty: What matters most for energy patent success?," *Resource and Energy Economics*, 35(4), 505–533.
- SNEADER, W. (2005): *Drug Discovery: A History*. John Wiley & Sons, Chichester.
- SQUICCIARINI, M., H. DERNIS, AND C. CRISCUOLO (2013): "Measuring patent quality: Indicators of technological and economic value," Discussion paper, OECD Working Paper 2013/03.
- STEVENS, A. J., J. J. JENSEN, K. WYLLER, P. C. KILGORE, S. CHATTERJEE, AND M. L. ROHRBAUGH (2011): "The role of public-sector research in the discovery of drugs and vaccines," *New England Journal of Medicine*, 364(6), 535–541.
- TEECE, D. (1986): "Profiting from Technological Innovation: Implications for Integration, Collaboration, Licensing and Public Policy," *Research Policy*, 15, 285–305.
- TEMIN, P. (1985): "Government action in time of crisis: Lessons from the history of drug regulation," *Journal of Social History*, 18, 433–438.
- TONG, X., AND J. DAVIDSON FRAME (1994): "Measuring national technological performance with patent claims data," *Research Policy*, 23, 133–141.
- TRAJTENBERG, M. (1990): "A Penny for Your Quotes: Patent Citations and the Value of Innovations," *RAND Journal of Economics*, 21, 172–189.
- VAN LUIJN, J. C., F. W. GRIBNAU, AND H. G. LEUFKENS (2010): "Superior efficacy of new medicines?," *European journal of clinical pharmacology*, 66(5), 445–448.