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Inside the Biotech

A dialogue between Rosenberg, Babbage, Smith, and Schumpeter

Andrea Borsato[*1], Patrick Llerena[1]

Abstract

We provide a contribution to the understanding of the emergence of biotechnology as the result of a co-evolutionary process that required simultaneous innovations in four core domains: law, government policy, molecular biology, and finance. The result of these institutional changes had profound implications in terms of division of labour and division of knowledge that characterised the early biotech industry: the classical interpretation according to which the division of labour precedes and determines the division of knowledge *via* learning by doing might be challenged when the economic environment becomes uncertain. In this perspective, we posit that the division of knowledge may also precede the division of labour and that organisations make deliberate decisions regarding the allocation of resources to core and non-core competences. The different repartition of roles and institutions at work shaped the trajectories of early biotech start-up. These trajectories have epitomised in two theoretical variants in which the greater of lower emphasis on scientific research and commercialisation co-existed in differing degrees and determined long-term profitability and growth.

Keywords: Biotechnology, Dynamic complementarity, Division of labour, Division of knowledge, Entrepreneurial function.

JEL Classification: L2, L65, O3.

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1) Introduction

The emergence of biotechnology as a high-tech industry has caught economist's attention ever since early 1970s, when the Silicon Valley and other hotspots on both sides of the United States became the locus of major scientific discoveries. There has been a great deal of writing on this subject in the social sciences in general and in economics in particular: Orsenigo (1989), Arora and Gambardella (1990), and Padgett and Powell (2012), to name but a few, have offered important methodological contributions. They provided the interested reader with both the knowledge and the taste to form his or her own ideas about the emergence and development of biotechnology over time.

To place our contribution in this wide strand of literature, we start by recognizing the massive empirical evidence that, in every industry, there is a number of sources of knowledge that involves also non-firm actors and institutions that are able to significantly affect firm's innovative search. Moreover, industries differ to a good extent in terms of these dimensions, and it is not possible, nor very helpful, to come up with an ideal type of sectoral system (Malerba 2002). For instance, the pharmaceutical and biotech sector is composed of a variety of actors from large firms and small start-ups to universities, venture capital, and regulatory institutions, such that innovation results from the combination of advancement in science, networks, and division of labour (Malerba in Dosi 2023). These institutions complement one another, and the way in which they are combined differ from other industries, e.g., specialised machinery, software, and so on.

We offer three contributions to the literature. Firstly, using the lens of Rosenberg (1979, 1982), we explain the rise of biotechnology as the outcome of a co-evolutionary process in which several innovations in the fields of law, government policy and university-industry links, molecular biology, and finance, were introduced such that their integration formed an *architecture* that opened up the way for new technological opportunities, the most paramount of which was a new organisational model based on horizontal and information flows, porous boundaries that have strengthened the inter-institutional cooperation in R&D. Secondly, we analyse the implications of this architecture for the division of knowledge and the division of labour in the first generation of biotech start-ups. The classical Smithian interpretation argues that the progressive specialisation of work induces the creation of capabilities and a progressive increase in specialised knowledge *via* learning by doing. As Cohendet and Llerena (2010) challenged, things may not be that straightforward when the environment gets more uncertain. Therefore, firms need to create new knowledge from the inside out, and they cannot rely on a pre-existing division of labour, as claimed long ago by Babbage (1832). We show that the co-evolutionary process that characterises biotechnologies makes mechanisms *à la* Smith and *à la* Babbage more, or less, evident according to the specific link between institutions. In particular, the lack of vertical determinism from the *upstream* division of labour to the *downstream* division of knowledge typical of the Smithian argument, to the benefit of a horizontal configuration with several likely divisions of labour for any given division of knowledge, is visible in the two (theoretical) trajectories that an early biotech could choose to follow. These trajectories led to the emergence of two start-up *variants* (Padgett and Powell 2012, Powell and Sandholtz 2012). We discuss the reasons behind their scientific as well as financial success/failure with the emphasis Schumpeter (1934), Pavitt (1998), and Winter (2006), among the many others, have put on the entrepreneurial *vis à vis* administrative functions, and on the ability of each start-up to recruit managers with a long-term view that should characterise firms operating in high-tech sectors.

The paper is organised as follows: Section 2 discusses the broad institutional innovations that led to the emergence of the biotechnology's industry; Section 3 studies the co-evolutionary relationship between division of knowledge and division of labour; Section 4 focusses on the variants of biotech firms through the lens of their entrepreneurial behaviour; last Section concludes and offers some food for thought for future research.

2) Dynamic complementarities: institutional innovations behind the expansion of biotech

We describe the institutional environment that surrounded the early days of biotechnology by reconsidering the technological interdependencies of the American economy as described long ago by Rosenberg (1979, 1982). The basic idea behind was that "the social payoff of an innovation can rarely be identified in isolation" (Rosenberg 1982, p. 58). On the contrary, the growing productivity of modern industrial economies and the associated emergence of new sectors result from the complex diffusion of several innovations, often occurred in clusters and belonging to different fields. In other words, the emphasis on *complementarities*, on complementary innovations, is intended to argue that the alleged breakthrough technologies alone are not the only responsible for broad technological improvements. They are most often accompanied by other novelties in the larger economic and institutional system, whose arrival may also be "unnoticed".[1]

From this point of view, the emergence of biotechnology as a fast-growing and promising sector has benefitted from the occurrence of several innovations in four main domains: law, government policy and university-industry links, molecular biology, and finance. Innovations in each of these areas provided the institutional infrastructure that enabled early biotech start-ups to pave the way for the major change they brought to the research system: the replacement of the traditional divide between university science and pharmaceutical innovation by a system largely dependent on fluid boundaries that fostered joint R&D between university, government, and industrial scientists (Cockburn and Stern 2010, Padgett and Powell 2012). Figure 1 summarises what we consider to be the key institutional and technological innovations that lie behind the emergence of biotechnology as an industry.

Innovations in *law* and *regulatory aspects* concerned to taxes, university patents, and federal funding to research. The progressive increase in capital gains tax between late 1960 and early 1970s, and the "prudent man rule" that made fund managers personally liable for the economic performance of risky investments lifted disappointment among investors and venture capitalists.[2] The prospects of further increases in this tax during Carter's administration were strongly opposed, among the others, by the American Electronics Association (AEA) and by the National Venture Capital Association (NVCA). They allied and launched an important lobbying campaign for the introduction of tax cuts. In their argumentation, the disquieting trends of US productivity, the rising deficit in the balance of payments,

[1] "Complementarities exist when various activities reinforce each other in such a manner that performing multiple activities together lowers/(raises) cost, increase economies/(diseconomies) of scope, or otherwise improves/(depresses) payoff" (Teece 2010, p. 720). In other terms, complementarities make the combined value of two factors greater than the sum of the values of the same factors taken in isolation (Monteverde and Teece 1982, Teece 1980).

[2] The "prudent man rule" was a provision in the Employment Retirement Income Security Act (ERISA) that aimed at decreasing the abuse of pension funds: more on Berman (2012).

and the technological lag the US firms were starting accumulating with respect to international competitors could be stopped only through capital tax gain cuts. Indeed, they would have encouraged the availability of capital for the small enterprises in fast-growing sectors, e.g., microelectronics, that provided the thrust of new employment opportunities in the country (Berman 2012). The successful outcome of this lobbying activity was the Revenue Act of 1978 that reduced corporate tax rates from 48% to 46% and the rate of taxation on realised capital gains to 28%.

The second innovation was far less controversial and regarded the idea of allowing pensions funds to invest in venture capital, in a period in which high inflation rates were eroding incomes. The purpose came from the Department of Labor (DOL) that counteracted the prudent man rule and included the stocks of small companies of the emerging high-tech industries in the investment portfolio of pension funds. The wide consensus received helped this regulation go into effect in the first half of 1979.

The third key institutional change in law over the last quarter of the XX century was about the patentability of at least some of the results out of basic research. The Bayh-Dole Act of 1980 compelled universities to take out patents on the outcomes of their research for the alleged benefit to firms' innovative activity.[3] As also argued by Nelson (2004), it is worth emphasizing two consequences that have impacted on the concomitant emergence of biotechnologies. The first is the significant increase in firms involved in basic research activity with the aim of drawing income from the licensing of potential discoveries. Then, the Act changed the way in which universities gave access to their research results: "[a]s a result, important areas of science are now much more under the sway of market mechanisms than used to be the case" (Nelson 2004, p. 462).[4] This Act did not arrive alone. Soon after its introduction, the Bayh-Dole Act was accompanied by two other laws that have impacted most on the nascent biotech sector. In 1983, the Congress promulgated the Orphan Drug Act to encourage the research and development of drugs to fight diseases that hit a small number of patients, and for which there would not be "enough incentive" by firms to carry out expensive innovative search. This Act aimed at providing a quicker and less costly *iter* for FDA approval and an enhanced exclusivity period. Several nascent biotech firms - e.g., Genzyme - would have benefitted from the advantages of the Orphan Act in the following years, also because biotechnology seemed to suit the peculiarities of rare diseases. The year after, the Hatch-Waxman Act (1984) devised a regulatory framework in order to ensure a time lapse of exclusivity for the commercialisation of innovative drugs as well as a set of incentive mechanisms to spur the introduction of generics once the exclusivity period expired. These regulatory schemes have envisaged a *carrot-and-stick* "Market for Technology", in which the carrot of stronger intellectual property rights would be counterbalanced by the stick of innovation-led competition among both pharmaceutical and biotech firms (Cockburn and Stern 2010, Gans and Stern 2003).[5]

[3] The discussion of short-term and long-term pros and cons of this Act are beyond the scope of this paper. Nelson (2004), Mowery et al. (1999) and the references thereof are sufficiently *maieutic* to own ideas on the issue.

[4] Yet, we remind the differences in the way universities were (are?) organised on the East Coast and on the West Coast when the Act arrived. On the West Coast as in Stanford for instance, labour mobility and intense informal networks of collaboration between scientists and firms probably have made the application of the Bayh-Dole Act rather hard. Conversely, on the East Coast, the very structured and centralised organisation of universities, along with long-established legal departments, have made smoother its enforcement (Saxenian 1996).

[5] The interested reader may refer to Tab. 1 in Coriat and Orsi (2002) for further selected legislation enabling a competitiveness R&D policy.

These innovations in law occurred in a transition period of the university-industry link and government policy. WWII represented a first turning point in the organisation of the US research system, where the remarkable increases in federal funding transformed universities into centres of performance of scientific research (Mowery and Rosenberg 1993, Rosenberg and Nelson 1994). This rise in federal expenditure during the 1950s throughout the 1970s took three broad directions: all the programs with the aim of reducing the industrial R&D cost by means of grants, loans, and the like; *national priorities* in terms of security, defence, and health which ensured government payments to firms to carry out R&D activity through public procurement programs; and the establishment by US government of research infrastructure to fuel technology transfer within the industry (Dosi et al. 2006). An important, although sometimes rhetoric, change happened with the National Cancer Act (1971), which significantly increased funds allocated to the National Institute of Health (NIH) along with the foundation of several research centres. Even if *biased* in their purpose to focus on cancer, this Act has represented the base for a slow but steady growth in federal expenditure for life sciences with implications for molecular biology and genetics (Cockburn and Stern 2010).

This combination of supply-side and demand-side policies changed in early 1970s with the decline of US aggregate productivity growth and the catching-up of other Western economies. The superiority of the American economy was indeed challenged by the fast technological transfers of emerging sectors – e.g., semiconductors. To respond to these changes, public as well as private actors pursued several new organisational approaches to R&D that impacted upon the increasing global character of university-industry research linkages. As Mowery and Rosenberg (1993) argued, if the private sector accounted for a modest share of total US basic research in the years of the Golden Age (1950 – 1973), its share grew to one fifth of the total amount in mid-1980s. The connection between university research and industry became significant in biotechnology, in which genetic engineering techniques constituted a *ladder* technology (Blumenthal et al. 1986, Gomory 1988), in the sense that "the new idea is dominant and the product forms itself around the new idea or new technology" (Gomory 1988, p. 11), giving scientists the leading role in its introduction. Therefore, the life sciences industry was characterised by a commitment to a sustained step-by-step research process that has increasingly involved public-private partnerships (Cockburn and Stern 2010).

This line of reasoning introduces in broad terms what was the frame in which major innovations in scientific research have then paved the way to the rise of biotechnology. Though the origins should be dated back to 1953, when Watson and Crick discovered the double-helix structure of DNA, it is widely recognised that the crucial contributions to the birth of biotech domain should be dated in late 1960s and early 1970s. As Malerba and Orsenigo (2015) and Powell and Sandholtz (2012) argue, at the forefront of this breakthrough research were the University of California – San Francisco (UCSF), Harvard (MIT), Stanford, and the University of Cambridge (UK). Three contributions represented the core. Firstly, Peter Lobban and Dale Kaiser on the one hand, and Paul Berg independently on the other hand, developed the initial procedures for making recombinant DNA (Lobban 1969, Berg 1970, Lobban and Kaiser 1972).[6] Four key advances based recombinant techniques: the discovery of particular enzymes able to modify DNA molecules in order to combine them; the practical

[6] As often in science, the parenthood of recombinant DNA is a hot issue: working independently from the abovementioned, Herbert Boyer and Stanley Cohen published two seminal papers on the same topics (Cohen et al. 1974, Morrow et al. 1974).

demonstration that molecules could be cloned and expressed in bacteria; the development of chemical methods to sequence DNA and a DNA-amplifying change reaction *in vitro* (Berg and Mertz 2010). Although astonishing, such innovations largely emerged as extensions of existing knowledge: what was novel "was the numerous ways in which many investigators applied these technologies for analysing and modifying gene structure and the organisation of complex genomes" (Berg and Mertz 2010, p. 9).[7]

Indeed, the second major innovation was developed at UCSF, when William Rutter's lab was working on the isolation of the gene for insulin from rats and humans. In 1973, in collaboration with Boyer from UCSF and Cohen from Stanford, Rutter completed the structural and functional analysis of the human gene insulin by means of recombinant DNA techniques. Years afterward, these achievements represented the building block for the development of diagnostic tests, therapeutic drugs, and the devising of several vaccines.

The third key scientific discovery was developed on the East Coast by Walter Gilbert and by Frederick Sanger at the University of Cambridge (UK). What allowed them to share the Nobel Prize in Chemistry with Berg in 1980 concerned to discoveries about gene control and nucleoid acids that led to one of the first methods of DNA sequencing, an important *instrument* for biological research with potential applications in diagnostics, biotechnology, and virology. In other terms, their studies showed that an organism's genome could be mapped by ordering the nucleotides that compose a DNA molecule with radioactive substances (Maxam and Gilbert 1976, 1980).

What pools all the key innovations in molecular biology is their very theoretical aspect. Although they have triggered the emergence of biotech, they nonetheless could not be converted into market applications soon, even with consistent development expenditure. Moreover, the innovations in regulatory norms and law as the above represented a fuel for the fast-growing emergence of venture capitalism, which was still a cottage industry in the 1970s (Gompers 1994). As exemplified by the case of Genentech, "what was so different… was the astonishing amount of capital required" (Perkins 2002, p. 24). Without tangible and "ready" marketable products, traditional financial schemes were ill suited to the funding needs of biotech start-ups in both quantity and durability. What early venture capitalists in the Silicon Valley soon realised was that biotech would have continued to fail to attract investors without solving the problem of signalling the progress in their research. Since scientific output in terms of publications was the remarkable *good* produced by a biotech lab, venture capitalists understood that papers were the *calling cards* to demonstrate the worthiness of a small start-up (Powell and Sandholtz 2012): a worthiness to be sold to both Big Pharma companies for research partnerships and to wannabe investors operating in the broader world of financial markets.

[7] Therefore, these advances represented episodes of incremental technological progress along a given trajectory (Dosi 1982). What represented a paradigmatic change was the interaction of all the technological and institutional innovations that *jointly* paved the way for the emergence of the biotech sector: "[w]hile many discussions of potential technological solutions to pressing societal challenges often envision a single discrete "quantum leap" in technology, the history of life sciences innovation suggest that in many cases "breakthrough" technologies depend on a long-drawn out process of cumulative step-by-step innovation, which ultimately delivers significant results only after decades of sustained investment and development" (Cockburn and Stern 2010, p. 42). Seemingly, the evidence that biotechnology followed and follows a well-established incremental pattern of technical change goes against the existence of a biotech revolution (Hopkins et al. 2007, Nightingale and Martin 2004).

To this aim, novelties were introduced in finance: multiple layers in public offerings without preliminary commercial applications, tracking stocks, milestone agreements. Such innovations in finance have represented the seed-money that allowed early biotech start-ups to sustain their research and business until they could generate cash on their own, or until the next round of investments. But more importantly, these novelties were an example of *instrumentations à la* Rosenberg (1992): in that seminal article, Rosenberg suggested that a by-product of fundamental research is the devising and spreading of new research instrumentation, which is nothing else of a capital good in the scientific sector. The spread of such instruments – e.g., the microscope – has been a source for cross-realm, namely new collaborations between researchers working in different fields or the migration of researchers from one field to another – e.g., from physics gradually to chemistry. From this point of view, the arrival of a new technology in one scientific sector presents a form of *increasing returns* since the benefits are not circumscribed to those industries but diffuse across disciplines. We argue that the same has occurred with financial innovations. On the one hand, tracking stocks on multiple layers in public offerings were the means, or better, the instrumentations, that allowed venture capitalists and Big Pharma companies to get involved in the emerging biotech industry, a sector in which their competences and capabilities were yet to be developed enough, in earliest stage at least.[8] On the other hand, the same instrumentation was pivotal to the scientists that founded the first biotech start-ups to enter a world in which, as the founder of Genentech asserted, they found "returns, social benefits, the excitement, the technical prowess, and the fun" (Perkins 2002, p. 24). By the way, these were the means that also allowed early start-ups to fund the subsequent generations of biotech firms.

We claim that the emergence of biotechnology as one of the fast-growing sectors of the last quarter of the XX century was not (only) the result of major advances in molecular biology. As suggested by the enormous literature on the economics of innovation and technical change (see also Cowan et al. 2010, Pisano 1991, Saxenian 1996), improvements in one of the components of a system are of limited significance without simultaneous improvements in other parts. In this respect, technological innovations are the outcome of several interactions and cooperation between autonomous institutions that require complementary resources (Arora and Gambardella 1990). However, much of the analysis on the development of biotechnologies seemed to rely on some forms of *ex-ante* institutional complementarity that were "revealed" by some fortuitous events in the scientific realm, an event that subsequently unleashed the creation of early start-ups. We believe that no pending complementarity was in place. Or, rather, the rise of biotech was the outcome of a coevolutionary process in which several innovations were introduced in different domains such that their progressive integration formed a *platform* or an *architecture* that opened the way for new economic opportunities and became the backbone for the most remarkable innovation brought about by biotechnology: not (only) product innovations like therapeutic drugs, but the organisational model, that is the way in which early biotech carried out R&D activity.[9] The former hermetically sealed industrial R&D lab, as DuPont's in early

[8] "Minority participations in the capital stock of small biotech start-ups provide a means of monitoring the internal research of the NBFs [New Biotechnology Firms]. The objective of the large firm is to keep in touch and acquire some familiarity with the applied laboratory research skills […] and to establish a "preferential" link the biotech company" (Arora and Gambardella 1990, p. 364-365).

[9] In his review on biotech clustering, Orsenigo (2006, p. 27) seemed to recognise this aspect when he wrote: "[I]t has to be emphasised that these factors – industry-university relations, IPRs and venture capital – were not simply pre-existing at the onset of the biotechnology industry, but they co-evolved over time". Unfortunately, this assertion had no continuation in the subsequent analysis.

XX century, was indeed supplanted by fluid and porous organisational boundaries that fostered R&D as close interactions between university, government, and industrial scientists. Research was no longer a local enterprise but a collective and coordinated affair (Orsenigo 2006, Powell and Sandholtz 2007, Cockburn and Stern 2010).[10] But, once more, technological progress in one sector (biotech), regardless of its type, has become increasingly dependent upon technological change in other, perhaps unfamiliar at a first glance, industries or domains as law and finance (Rosenberg 1979, 1982).[11]

What are the implications for the division of knowledge and the division of labour in early biotech? The following pages offer a critical interpretation of the way such broad and multi-sectoral organisational changes have shaped the biotech industry.

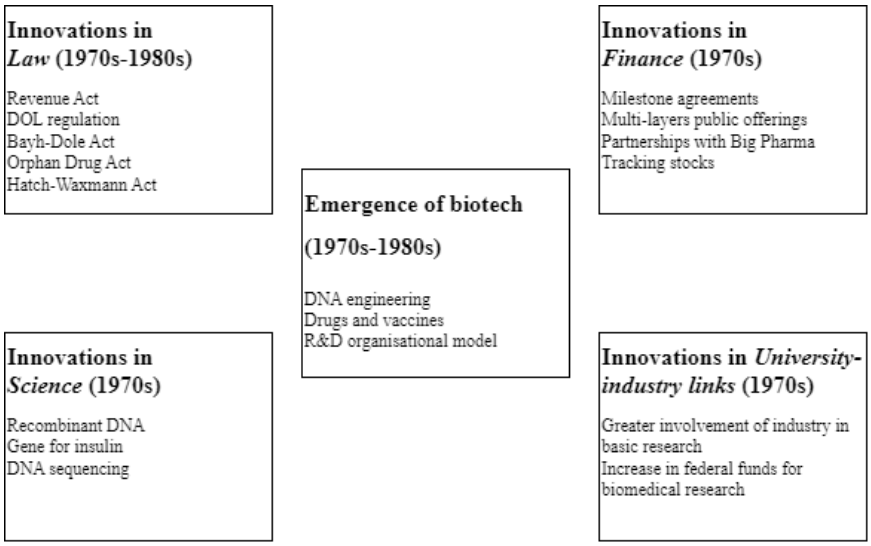

Figure 1. Institutional and scientific innovations linked to the emergence of the biotech industry

3) Division of knowledge and division of labour in biotechnology

The discussion above has offered a general overview of what was the institutional environment which has allowed the progressive emergence of biotechnology as a fast-growing and high-tech sector. The institutional framework and the several innovations that surrounded this development are pivotal to understanding how the *division of knowledge* – i.e., the distribution of interpretative capabilities between agents – and the *division of labour* – i.e., the distribution of tasks amongst agents, organised

[10] By the way, these organisational changes rather look like standard example of competence-destroying technologies *à la* Patel and Pavitt (1997).

[11] The notion of *technical imbalance à la* Rosenberg (1976) is not new in economics. Several examples can be drawn since the dawn of capitalism: spinning and weaving technologies (Landes 1969), numeric control technologies in the machine tool industry (Mazzoleni 1999) and the switch between hydromechanics to digital technologies in aircraft engine control systems (Brusoni et al. 2001). We are going to come back later to this issue, when a comparison between biotechnology and aircraft engine control system will be useful to grasp why firms know more than they make, and why the division of knowledge and the division of labour can be different.

in the (early) stages of the industry. To this aim, we believe with the help of Fig. 2 that it is useful to make a short comparison of the traditional technology-based firm *vis à vis* early biotech start-ups, as suggested by Malerba and Orsenigo (2015), Powell and Sandholtz (2012), and Rosenberg (2010, ch. 2).

3.1) The start-up as a multi-technology firm

The broad story that runs since the emergence and formation of the US national system of innovation is that an important part of scientific research has been motivated by some expectations towards private as well as social payoffs. Furthermore, during all the XIX century and the first decades of the XX century there were extensive changes in the nature of inputs and production technologies, and in the characteristics of industrial output that raised enormously the social payoff of the application of scientific knowledge to industry. These forces that step-by-step led to the establishment and the institutionalisation of the industrial research labs were not confined to sectors like chemistry and metallurgy, traditionally employing the highest number of scientists, but such processes were pervasive also in small sectors of the economy or in those industries that were traditionally considered as low-tech – e.g., food processing, packing, and canning.

Regardless of the idiosyncratic differences that permeate(d) the several sectors of the American economy, they nonetheless shared some key features about the increasing commitment to science. Firstly, there was a sustained growth in R&D expenditure by private industry, and within this community, the large bulk of the research activity was not conducted by sectoral associations of entrepreneurs but *within* firms.

Secondly, research activity at firm level was carried out by an expanding pool of engineers. However, and this represents a crucial difference with biotech, though engineers were (obviously) trained to the large body of scientific knowledge and methodology, they were not trained to work at the scientific frontier. Even much later, after the turn to the XX century, a major component of the job of scientists and engineers consisted of several tasks like quality control, grading and testing of materials, that "were elementary from *the point of view of the science content*" (Rosenberg 2010, Ch. 2, p. 26; italics in the original), even if absolutely vital to the development of the industry.

Thirdly, when engineers and scientists turned to be a source of ideas and "human capital" to be employed in the core of the innovation process (first decades of XX century), a good part of the firm core activity consisted of the conversion of knowledge into marketable products, hence not in basic research. And if this conversion led to a sufficiently *tangible* good, firms would try to codify the corresponding knowledge and apply for a patent. What indeed characterised the activity of internal laboratories in important firms such as DuPont, Kodak, or General Electric, was a sort of fear of losing the exclusivity of their core technologies and to be imitated by competitors.[12] In most of the examples, industrial R&D labs were hermetically sealed, and cooperations with university scientists were kept at minimum: universities were often regarded as source of talents that would populate the

[12] Cooperation among competitors involved most componentry, not core science. In the traditional pharmaceutical industry, practices of open science were believed as giving away the crown jewels (Saxenian 1996). As we will see later, this belief survived and sorted the behaviour of several early biotech firms.

firm as lifetime employees in firm's R&D laboratory. This situation persisted after WWII although for somehow different reasons: many high-tech firms were involved in national-security programs, and the most skilled scientists were engaged in military work. Therefore, their research was largely shrouded in secrecy (Powell and Sandholtz 2012).

Fourthly, traditional science-based firms attracted funds from investors through public equity markets and these investors used to take their decisions on company's sale records: in other words, there was not such a grand overlap between the knowledge of science and the flow of capital.

In this respect, biotech was "more the antithesis of the corporate labs than a lineage of them" (Powell and Sandholtz 2012, p. 400). Precisely, with the emergence of early biotech, the organisational model it has engendered differs from both the industrial science *à la* Big Pharma, as expected, and by the garage start-up model that characterised the nascent ICT (Padgett and Powell 2012). It is indeed different to imagine an industry that relies more on frontier knowledge than biotech for the life-sciences system of innovation is built on a stable foundation of high-levels of public support for basic research over the long term (Cockburn and Stern 2010, Orsenigo 2006).

All start-ups in life sciences combined resources, personnel, and practices from academy, venture capital, and (but not limited to) large pharmaceutical companies, even if different firms combined all these aspects in different degrees, as for instance, the establishment of research contracts with Big Pharma, oil companies, cosmetic markets that have often lent executives to start-ups. On the one hand, drug companies had huge difficulty in accessing and mastering frontier technical knowledge in molecular biology (Malerba and Orsenigo 2002, Orsenigo 1989). Moreover, their hermetically-organised laboratory was not very appealing to university researchers.[13] On the other hand, the founders of early start-ups realised that such contracts were a financial necessity for the conversion of knowledge into marketable products would take years: the *D* component of research and development indeed demands the greatest share of resources and often time too. Nevertheless, agreements with large enterprises and venture capitalists took several forms. For example, Cetus used partnerships with several corporations and then opened an important initial public offering (IPO) in 1981. Conversely, Genentech has preferred a form of financing through venture capital based on milestone payments – i.e., payments conditional to successful research. Still different was the case of Genzyme that financed the commercialisation of existing breakthrough by means of tracking stocks.

Additionally, before being entrepreneurs, investors or start-up founders, they were *scientists*. Boyer, Rutter, Gilbert, and most of the other first-rate researchers that founded the first generation of life-sciences firms, have never quitted academy. They retained their faculty positions and if they had to move to run a start-up as member of the board, it was just a temporary move out of the university. Padgett and Powell (2012) call them *amphibious* scientists that managed to combine scientific research and management, regardless of very different economic success. The trespassing of scientists

[13] This was already a problem in the early XX century. Hounshell et al. (1996, p. 27) reports an interview to James Conant, a former head of the Department of Chemistry at Harvard, in which he claimed to have hampered and stopped his best students (but not the less able) to go working to DuPont for he regarded DuPont chemists as "lacking in the fine critical judgement of the best teachers, and I wonder whether this is the cause or effect of their industrial relations". Many years later also William Rutter tried to start a collaboration with Eli Lilly, among the others, but he had to give up for contrasting viewpoints with the executives on the applicability of biotechnology to the pharmaceutical industry. This was one the reason that prompted him to found Chiron in 1981.

into the world of commerce and finance was pivotal to bring the college organisational model to industry: from a business model focussed on the traditional vertically-oriented corporate hierarchy to a cooperation model whereby information flows horizontally, in which organisational boundaries are rather porous, and collaboration in core science (not only componentry) occurs among start-ups, and with universities, government research centres, and industrial scientists.[14] Not only has trespassing occurred from college to industry and finance, but also the other way round, with the intermingling flows of ideas that have rebounded across the several domains. Universities became much more involved and interested in the commercial exploitation of basic research, and venture capitalists had to spend part of their time to devising novel practices on how to signal commercial progress without tangible achievements.

Therefore, we can portray the start-up in the life sciences industry as a *three-agent entity*, composed of a scientist, a venture capitalist, and a mid-career executive from an established large company, often from the pharmaceutical sector. This triple soul makes the start-up a *multi-technology firm* (Nelson 2000, Patel and Pavitt 1997, Pavitt 1998). According to this stream of literature, we should make a clear distinction between the artifacts of the innovative firm from the knowledge sources that underline the products. In particular, in every innovating firm two bodies of knowledge co-exist. The first is the *body of understanding* that reflects the qualifications of the technical trained personnel and the fields in which the firm applies for a patent or publishes: in our case, these realms concern to molecular biology, finance, and management. The second body of knowledge is the *body of practice* obtained through experimentation, experience, and information exchange with the different elements of the organisation. It consists to a large extent of the organisational knowledge that connects the body of understanding with the design, development, production and commercialisation of successful artifacts (Pavitt 1998). Each single and specific class of products – e.g., therapeutic drugs – cannot be associated only with a single peculiar body of technical knowledge, but it is the outcome of a broadened technological focus. In other terms, "firms are active in a range of technologies *broader* than the products that they make" (Pavitt 1998, p. 439; italics in the original). At firm level, such a broad technical diversity provides the source to make and further improve the products. In addition to this, at the level of the market or industry, the mix of technological knowhow is rather similar across firms, and the degree of technological diversity looks very low in those sectors that experience high rates of technological progress – e.g., pharmaceuticals and biotechnology. Conversely, the bodies of knowledge may widely vary across sectors, due also to the fact that such mixed bodies change slowly through time, again depending on sector-specific technological opportunities. The fact that firms know more than they make (Wang and von Tunzelmann 2000) impacts on their ability to further acquire new competencies and specialised knowledge, a process that happens incrementally and constrains innovative search. Accordingly, the knowledge boundaries of the firm stretch beyond its production boundaries, and knowledge and product domains move forward along different trajectories (Brusoni et al. 2001). In other words, the division of knowledge and the division of labour in biotechnology can be different.

[14] By the way, this is also one of the reasons why most first-generation biotech firms established in the university campus.

3.2) Implications in terms of division of knowledge and division of labour

To introduce this theme, we think that the development of biotechnology as a fast-growing industry, with firms that are characterised by a multi-technology organisational structure, could benefit from the parallelism with the aircraft engine control system. The analysis of engine control systems was extensive in Brusoni et al. (2001). We believe there are three key reasons to make such a comparative example. The first relates to the complex patterns of interdependencies that tie the production process. Both industries and their respective products rely on different technological fields characterized by uneven rates of development: in the case of aircraft control systems, scientific domains include, among the many others, aerodynamics, thermodynamics, and tribology; in the case of biotech, we have biology, finance, law, and management. The second reason is about the (radical) shift in the underlying technologies: as the engine control systems moved from hydromechanics to digital technologies, the biotechnology was triggered by increasing knowledge of DNA properties that allowed for its manipulation. Additionally, we consider these disruptive changes as instances of technological imbalances (Rosenberg 1976) for a novelty in one domain requires complementary improvements elsewhere – e.g., the elaboration of milestone agreements in finance was a necessity to establish a value upon an intangible product as basic scientific research performed at university. Both engine control systems and biotechnology products share a third and preliminary feature: once the transition to digital electronics was complete, the control system became a pivotal part of the engine system. The parallelism with biotechnologies is clear when we think that after the initial period of intensive and costly clinical trials and product development, both biotech start-ups and Big Pharma started reaping the fruits of their research collaboration, which consistently improved the corresponding bodies of knowledge. At the turn of the XXI century more than one-third of all pharmaceuticals found their origins in biotechnology, with significant payoff in human health and welfare benefits (Cockburn and Stern 2010, Orsenigo 2006).

In their analysis, Brusoni et al. (2001) showed that the three largest companies in engine control systems have often adopted very different organisational patterns, from a comprehensive vertical integration for a firm working with the military, to the opposite case in which a company had never designed or manufactured an engine control system because it was deemed as largely outside the range of core capabilities. Yet, in all cases, the firms "developed and maintained an understanding of the functioning and characteristics of the units in the engine control systems…[as] a necessary condition to integrate the different components together and within the engine system" (Brusoni et al. 2001, p. 606). This is important to understand why something similar occurred *within* the single biotech start-up and *between* this start-up and the large pharmaceutical company. On the one hand, within any start-up there was an *anchor tenant* (Powell et al. 2012) or a *system integrator* (Brusoni et al. 2001, Hopkins et al. 2007), namely a scaffolding firm, an agent, or an institution that led and coordinated from both a technological and organisational viewpoint the work of suppliers and customers involved in the network, or the work of the other agents in the firm whose competences lied partially outside firm's core activity.[15] Anchor tenants neither competed nor cannibalised the other members of the organisation but mobilised and coordinated resources to fostering collective

[15] While reconciling specific products and technologies, system integrators or anchor tenants govern their relationship with suppliers and customers with arm's-length contractual relationship, cost-sharing agreement, out-licensing of patents, as demonstrates the case of Alza, Cetus and Immunex, that used research partnerships with Big Pharma to generate funds.

growth. In the case of biotechnologies, this figure could be a venture capitalist as for most early biotech firms founded in San Francisco Bay Area – e.g., Bill Bowes for Amgen and Robert Swanson for Genentech. Conversely, since venture capital has not developed enough yet in the Boston cluster until the 1990s, this role of anchor tenant was taken on by somebody from academy or management, as in the case of Genzyme (Porter et al. 2005). On the other hand, the same applies between a biotech firm and pharmaceutical corporation. The small biotech most often could not meet the requirements for clinical trials, by far the largest expense in any drug development company. This expenditure was sustained by Big Pharma, as was the case of Chiron. In contrast, the difficulty of harnessing the technical knowledge of molecular biology on the part of Big Pharma was necessary for the growth of small biotech-s.

The essential point to understand was that the several agents involved needed not master all the technicalities of the value chain, from the procurement of initial resources to final product delivery, but the leading agent had to maintain a sufficient body of knowledge as to keep the whole system cohesive. This is far more paramount during the early stages of product developments, when interdependencies may be high as well as poorly understood (Williamson 1971). In this case, decisions to *outsource* parts of the production activities differ to a good extent from decisions to outsource technological knowledge. This is far truer for fast-changing technological fields – e.g., finance, biology, digital electronics – in which the leading firm in the production network must elaborate on some coordination mechanisms composed of the wider body of knowledge, as to bridle and govern the uneven development rates that impact on multi-technology products (Brusoni et al. 2001).[16] In accordance with the *dual theory* of the firm (Cohendet and Llerena 2005), key is here the figure of the manager, who is responsible for establishing an ex-ante vision of knowledge management within the firm. Managers are thus in charge of defining the frontier between the domains of competence and transaction. In this perspective the role of managers is to foster cognitive commonalities and socially shared interpretation patterns and frames. They also exert indirect influence over the routines at every level of the firm. Managers can orient the learning process and select the core competencies of the firm through acquisition and mergers, either by reinforcing existing core competencies or by allocating resources to accumulate new competitive knowledge in a specific and given core competence. In other words, managers must establish incentive mechanisms.[17]

The discussion has emphasised the building blocks of our analysis on the evolution of the division of labour and the division of knowledge in biotechnologies. Once ascertained that they might not be overlapped, some questions emerge: Who is determining whom? Who is the *first mover*? Are they co-evolutionary processes? To respond, let us remember what the benefits of the division of labour are as in Smith (1776). In the classical Smithian interpretation, the task or the set of activities assigned

[16] Some form of outsourcing is often necessary when the increasing specialisation in the body of knowledge becomes a hindrance for the effectiveness of vertical integration (Langlois 1992, Patel and Pavitt 1997). The existence of loose networks in drug development was further analysed by Orsenigo et al. (2001) and Orsenigo (2006).

[17] "Consequently, the benefits of new technologies do not come from only possessing firm specific assets or competencies, but instead require the dynamic capability to effectively transform them" (Hopkins et al. 2007, p. 568). This knowledge-based approach to the theory of the firm has been criticised for being too static and for neglecting the role of the entrepreneur: Cohendet et al. (2024) proposed an idea-driven perspective which "explicitly introduces goals and intentions that emphasize the firm's ability to generate, nurture, select, and implement ideas, thus better understanding the firm as a place of collective creation" (*ibid.*, p. 5).

to an employee determines the pattern of learning by carrying out that task. The progressive specialisation of work induces the creation of capabilities and a progressive increase of specialised knowledge, by mechanisms such as learning by doing (Becker et al. 2007, Cohendet and Llerena 2010). More precisely, two complementary types of specialisations have occurred in parallel (Pavitt 1998). On the one hand, the emergence of new disciplines becomes useful for an increasing spectrum of applications and surround the productions of several goods. This emergent process is what lies behind the multi-technology nature of products and firms and presents all the advantages of an extended division of labour, namely the subdivision of employment improves dexterity and saves time (Smith 1776).

On the other hand, and in addition to this *cognitive* dimension, the functional division of labour with the establishment of new business units or in-house R&D laboratories can speed up the rate of technological progress. As clearly asserted by Pavitt (1998), these corporate R&D labs, whose task consists of working full-time to innovative search, enable the firm to monitor and benefit systematically from scientific advances that are made outside – e.g., in academy. Moreover, the increasing specialisation, professionalisation, and new vintages of capital goods, together with a greater understanding of natural phenomena, have all become pivotal to enhancing the systematic experimentation of the wider ensemble of products and processes. From this accumulation, new gains in productivity can then be obtained in the society at large that lead to a virtuous extension of the markets, which in turn does trigger a new cycle of further division of labour (Cohendet and Llerena 2010).

The classical Smithian interpretation restricts the relationship between the division of labour, which distributes tasks amongst the agents, and the division of knowledge, which distributes interpretative capabilities between agents, to a mere causal relationship: the division of work *causes* the division of specialised knowledge. In other words, the division of labour defines the problem to be solved, the direction and the potential of learning. Then, the nature of competences and routines are *vertically* and *homothetically* determined accordingly.[18] However, entrepreneurial decisions include elements of uncertainty, opportunities, creation of knowledge, and the vision of the role of the division of labour as in Smith can be complemented by the point of view that Charles Babbage (1832) presented in his description of England's transition from an agricultural to an industrial economy. The notion of division of labour was applied to both physical and cognitive activities for while technical change had played a key role in the industrial take-off, manufacturing entrepreneurs had to spend a lot of effort in organisation and management issues. Even if it was not inconsistent with the classical interpretation of Smith, Babbage had emphasised the priority on skills in the sequence of steps that links division of labour to learning to further division of labour, based on the higher degrees of specialisation and knowledge. Furthermore, he put the emphasis on *skills* as the means to decide how to divide labour, thus presuming that the division of labour should itself be founded on differences in skills. Hence, the causality link is reversed: the division of labour *is caused* by the characteristics of the human resources, rather than the other way around (Cohendet and Llerena 2010), and there is not

[18] The reader may get confused by the distinction between competences and capabilities. Though usually used quite liberally and interchangeably, we confine *competences* to the ability to master specific body of knowledge, e.g., chemistry. Instead, *capabilities* ought to be confined to high-level tasks – e.g., making a chemical compound with desired properties. References are Dosi et al. (2000), Dosi et al. (2008), and Teece (2010).

a vertical deterministic process like in the Smithian argument. The lack of homotheticity implies a *horizontal* portfolio of different configurations of divisions of labour for any given division of knowledge.

What interpretation could we provide with reference to (early) biotechnology? We do know that the life-sciences system of innovation includes a number of institutions such as NIH, venture capital, public companies, start-ups, whereas the sources of knowledge are university research departments, academic medical centres, and private innovators. Instead, commercialisation occurs through to the supporting activities of large pharmaceutical corporations that provide with funds for clinical trials and offer legal services for FDA approval (Arora and Gambardella 1990, Orsenigo et al. 2001). We also know that since the 1980s, there has been an institutional change in the number and scope of graduate programs that has made the life sciences the leading field in hard sciences and engineering. Moreover, the NIH increased during the same period its funds for graduate as well as postdoc fellowships in order to exploit the high-technological opportunities of the field (Cockburn and Stern 2010), hence feeding the development of a skilled and specialised manpower.[19] The outcome of these policies was both the steady growth of the labour supply in the form of scientists, and the increased specialisation of individual researchers that were grouped to work on different projects (Wutchy et al. 2007). As argued by Jones (2008), the combination of specialisation and collaboration with the private sector has prompted individual scientists to master a larger ensemble of skills and knowledge, that could have led to find a job either as tenure track in academia or as an applied scientists in some biotech start-up in the nearby of the campus. Yet, this choice between the two jobs needed not be deemed as ultimate for the periods of employment in industry "need not come at the expense of returning to public sector scientific employment in the future" (Cockburn and Stern 2010, p. 30).

Rather than deciding what *came first* between division of labour and division of knowledge, we argue that they are intertwined in a co-evolutionary process in which one mechanism may prevail according to the institutional linkage. For what concerns the relationship between university, industry, and the market in early 1980s, there were several instances of mechanisms *à la* Smith.

First, as the economic environment has unleashed and revealed all the potential of biotechnologies, the growing demand for labour in the forms of scientists from start-ups encouraged the expansion of university programs grounded on the development of large workforce, which also increased the degree of specialisation of individuals. Postdoctoral students and early researchers were ready to populate the R&D laboratories of the early biotech industry not only with their strong background in the core competences of biology, but also with the expertise in nascent disciplines such as bioinformatics, genetics, and bioengineering. Broadly speaking, the life sciences system of innovation is indeed characterised by the fact the individual researchers can make very specific human capital investments at an early stage in their professional lives, reap the benefits of these investments through different types of employments, and work with researchers with complementary skills across organisational boundaries (Cockburn and Stern 2010). Among these specific investments, the career of young scholars often did and does present some entrepreneurial characteristics. Therefore, entrepreneurship could no longer be considered as a social attitude but a form of organisation of innovative search (Orsenigo 2006).

[19] A related outcome was the creation of new disciplines spanning bioinformatics over genetics.

Second, the demand for biopharmaceuticals had proved to be price inelastic contributing to a stable flux of demand for these products. Paraphrasing Smith (1776) from this point of view, the extent of the market limits and conditions the division of labour, and the other way around.

Third, the complex nature of the relevant knowledge makes innovations the results of the interactions between complementary resources and competencies. In this case, "it is the structure of the network and the position of the agents within it that fundamentally determine agents' access to relevant sources of scientific and technological knowledge and therefore innovative activities and performances" (Orsenigo 2006, p. 35).

Nevertheless, when observing the grounds behind early start-ups, we notice that the inherent uncertainty of the environment did, and does, constrain firms to create new knowledge *from the inside out* in order to cope with ever-changing environments. First, firms, summarised by a scientist, a venture capitalist, and an executive, cannot always rely on a pre-existing division of labour. And the figure of the *entrepreneur* is precisely the (collective) agent in charge of the creation of resources that ensure the connection between the internal and the external environments of the firm.

Second, the formation of successful clusters in the USA was due to the efficient division of (innovative) labour. Universities and small start-ups specialised in what they were (already) best at – i.e., research – whereas big established firms focussed on development. This attitude toward collaboration and division of labour, though varying in time and space, is a permanent feature of the industry, and engenders the emergence of networks whose ties "between these actors can provide the necessary coordination of the innovative process in a division of innovative labor" (Orsenigo 2006, pp. 34-35).[20] Put it differently, clusters were born and developed as the fruit of specific combinations of capabilities, incentives and opportunities. Capabilities were pivotal to the creation and definition of opportunities and on how to take advantage of them, triggering a feedback process of accumulation of new competencies. Yet, not all of them were pre-existing and the related process of construction emerged as itself a fundamental ingredient for an efficient division of labour.

In all these cases, the direction of causation is reversed, with cognitive processes *à la* Babbage come first and drive the division of labour. By the way, such mechanisms were evident in Chiron, a first-generation start-up with expertise in vaccines. As confirmed by William Greene in Padgett and Powell (2012, p. 418), its general counsel until 2004, Chiron's main advantage "was in having a very deep, early stage research competence […] Chiron didn't have the downstream skills to move that compound through development process or through pre-clinical or clinical testing […] so it depended upon its collaborators to execute the more traditional parts of pharmaceutical development processes". Likewise, the lack of pre-existing management capabilities to get oriented in the very uncertain environment was among the turmoil that characterised Cetus and Hybritech, despite some important research achievements. This inability of combining knowledge from different interfaces,

[20] Malerba and Orsenigo (2015) raised some concerns on the long-term viability of such division of labour, since biotech companies may be too small and too specialised to grab the fruits offered by scientific progress. The stronger integration of knowledge required by further division of labour may have led to some forms of diminishing returns in firms absorptive capabilities. The overall issue is for how long small and often transient organisations can be the vehicle for product innovations.

with their own routines and decision rules was often the cause of the high-failure rates of early biotech enterprises.

Therefore, we agree with Pisano (1991), Henderson and Stern (1994), and Cockburn and Stern (2010), that America's life-sciences innovation system emerged and evolved as the result of a co-evolutionary set of policy choices and a microeconomic environment where a series of nascent scientific discoveries were transformed into a platform for sustained innovation with major implications for human health and well-being. Fig. 2 summarises the main aspects. In this perspective, the outcomes of the co-evolutionary approach are rather visible in the examples of early start-ups that actually emerged. As we said, the key argument of Babbage was the absence of any vertical determinism that links the division of labour to the division of knowledge. Quite the opposite, the role of managers in the delimitation and selection of the core competences opens the way to a horizontal variety of configurations of divisions of labour for any *given* division of knowledge. The different repartition of roles and related institutions that were at work in the nascent industry contributed to determine the development trajectories of any biotech-s. These trajectories have epitomised in two *variants* (Powell and Sandholtz 2012), in which the greater of lower emphasis on scientific research and/or commercialisation co-existed in differing degrees. The next Section deals with this issue and discusses the implications for the evolution of the industry.

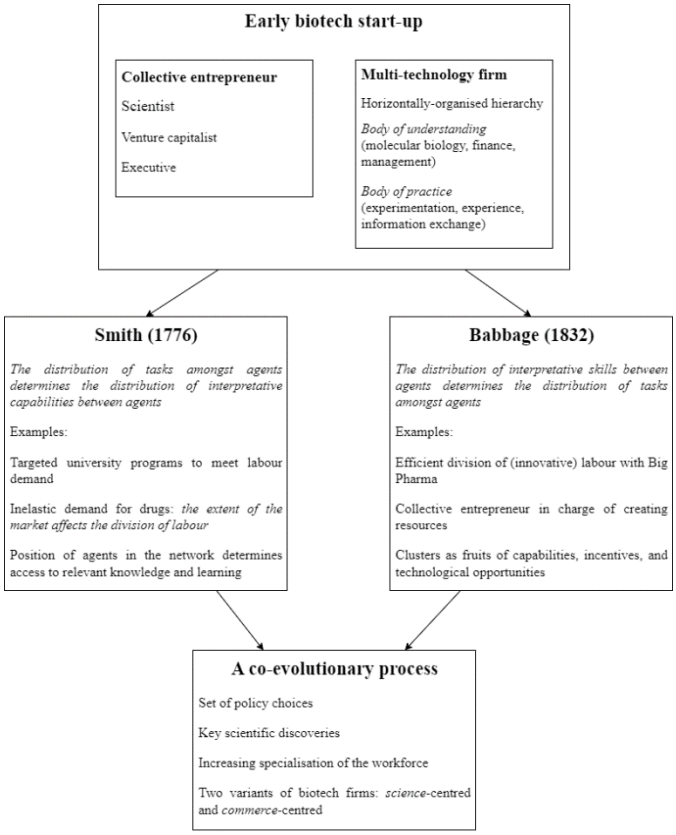

Figure 2. Characteristics of early start-ups in terms of division of labour and knowledge

4) Two variants of biotech start-ups: implications for the *entrepreneurial* and *administrative* functions

In very broad terms, the history of the pharmaceutical industry can be analysed as an evolutionary process of adaptation to major technological and institutional shocks. In the early decades after WWII the industry largely relied on random screening as a method to find new drugs. The advances in molecular biology, genetics, and enzymology have led to a transition toward the drug development *by design* (Malerba and Orsenigo 2002, 2015). This transition to biotechnologies can be considered as a change in the underlying technological paradigm (Dosi 1982; 2023, Ch. 2). The features that characterise each paradigm provide innovators with the boundaries to advance a technology along distinct technological trajectories, with improvements occurring along certain invariant directions in the characteristics of products, services, and methods of production. This holds for firm's configuration too. In the case of biotechnology, the foundation of several start-ups has envisaged the creation of an institution comprising three types of agents, horizontal flows of information, and a multi-technology structure. Proceeding along a trajectory, however, does not at all remove the persistent generation of *variety* (Dosi and Nelson 2010), as is clear from the emergence of two *variants* of biotech start-up, whose attributes appeared to concern the respective imprints of science and commerce (Powell and Sandholtz 2012). Fig. 3 summarises the main features of the two variants.

On the one side of the spectrum, we have what Padgett and Powell (2012) have labelled as *science-centred* variant, as were Cetus, Genentech, and Biogen. Three features marked this variant: scientists were encouraged to publish and to contribute to public science; founders retained their university position, and the biotech settled in the nearby of university campus. It is worth noting that such characteristics contrast with respect to the standard pharmaceutical company, in which appropriability concerns always took precedence over open science. Start-ups like Genentech and Biogen contributed to breaking the mold on publishing restriction and transposed the college model into the new companies. The interviews carried out by Padgett and Powell (2012) are quite revealing on this aspect. The Biogen's lab coordinated by Walter Gilbert was guided by intense curiosity and scepticism that drove all the research activity. Scientists wanted to publish on *Science* or *Nature* for they first aimed at being good researchers. Therefore, science and intellectual property were put to joint use (Powell and Sandholtz 2012).[21]

Furthermore, the science-centred variants tried to develop a hybrid organisational form in between academy and industry in which scientists were allowed to take equity and stocks to benefit from potential commercial success. Yet, this might have been among the reason on why these small companies started off with meagre capital, and firms like Biogen had to conduct research in the university laboratories of their founders. In other words, investors took an empirical approach (Powell and Sandholtz 2012): they financed the start-ups with "minimal" funds that could later be enhanced conditional to scientific results. For example, the founder of Genentech Robert Swanson ensured that firm's lawyers applied for patents as soon as the papers by Boyer's group were ready to submission to international peer-review journals. Regardless of their financial and commercial success, the

[21] Albeit scientists in Genentech, Biogen or Chiron would claim that working in those companies was more fun that the academy, the emphasis on publishing was also instrumental not to cut the threads with the university worlds, had not things worked out. A strong publishing record could be pivotal to go back to academia.

science-centred biotech-s gained a paramount scientific reputation that erased the stigma attached to research careers in an industrial environment (Levinson 20021, Kornberg 1995).

On the other side of the spectrum, Padgett and Powell (2012) position the *commerce-centred* variant, as were Amgen, Genex, or Genzyme. Most of these firms made the deliberate decision not to permit scientists to publish their (basic science) research and focussed more on applied and development activities. Since the absence of ready marketable products was binding, and publishing was deemed as the calling card to attract investors, the meagre emphasis in commerce-centred start-ups needed to be counterbalanced some way. The calling card was the establishment of all-star advisory boards that, albeit used as signal of credibility, such high-profile scientists had never engaged in shaping the direction and organisation of their firms. In fact, the lead was often taken by senior executives with experience in second-tier pharmaceutical companies like Abbott and Baxter that provided Amgen and Genzyme with managers. Venture capitalists and managers were tied to market opportunities, projected cash flow, and profitability that replaced the milestone payments conditional to scientific success, a method ruling in the science-centred variant. Moreover, commerce-centred firms were characterised by long-term relationships between managers and venture capitalists, as the case of Hybritech confirms. The scientists-founders left their university positions to become full-time entrepreneurs and contributed to found several start-ups across the years. This may have had an impact on the *nature* of such start-ups: leading scientists were neither involved nor interested in pursuing basic research projects and to transfer the college model to the industrial counterpart. Commerce-centred biotech-s were more involved in developing non-therapeutic applications and in the commercialisation of existing breakthroughs rather than focussing on new research -intensive drugs (Powell and Sandholtz 2012). [22]

Overall, this distinction and classification should not be thought of as absolute and sharp: the several elements of finance, science, and commerce often combined as to deliver composite organisational models. In addition to this, the entire field of life sciences collaborated with university and drew on basic science for continuing input thereof (Powell 1996).

We could move a criticism to what suggested by Padgett and Powell (2012), among the others. Their classification scheme seems the prelude to the idea that, in a hypothetical figurative battle between the two organisational models, the science-centred variant proved successful in the long run because of a higher commitment to publishing, despite the commerce-centred variant proved financially more successful in the short term. Beyond the issue of sharply grouping early start-ups in one category or in another, and beyond the empirical evidence that rather witnesses that only a small fraction of biotech-s have ever been profitable (Malerba and Orsenigo 2015) in the longer term – e.g., Genentech, Amgen, Genzyme – we suggest that absolute excellence in scientific research was a *necessary* but not *sufficient* condition for the successful development of biotechnology. The recruitment of managers needed to supervise and coordinate the functional activities and to allocate the several resources for future production and distribution was equally important. Indeed, what distinguishes an *innovator* from its competitor is the ability "to build an organisation appropriate to the new product or process and a capacity to build market share" (Teece 1993, p. 323).

[22] Genzyme benefitted from the Orphan Drug Act and became known as a success story of orphan drugs – e.g., the naturally derived enzyme at the base of the therapy against Gaucher's rare disease.

Biogen represents a first example. Founded in 1978 by Walter Gilbert – Nobelist in Chemistry in 1980 – this start-up was obviously a locus of scientific excellence and an instance of science-centred variant. Its business model could be summarized by the motto "a company run by its scientists" (Padgett and Powell 2012, p. 412), even though the scientific board was quite unfamiliar with managerial practices. Under Gilbert's leadership, Biogen did not achieve financial returns and nearly went bankrupt. Only the arrival of James Vincent, former manager from Abbott, brought an entrepreneurial attitude that turned Biogen to a profitable firm. Likewise, Genzyme is an example of long-run successful commerce-centred variant. This start-up became famous as a niche collector and a specialist in delivering orphan drugs – e.g., Ceredase to cure Gaucher's disease. Although publishing was never emphasised, managers stressed the importance to acquiring and maintaining manufacturing and scientific capabilities for drug production. The related purchase of a small British chemical company, combined with fiscal conservatism, allowed Genzyme to become a market leader in orphan drugs.

Therefore, we argue that it is not (only) scientific excellence *per se* from *within* which is the key to (long-term) profitability and growth, rather the ability to maintain a sufficient body of knowledge as to keep the whole system together, especially when the economic environment is characterised by uncertainty.[23] We have already emphasised this point. This represents an instance of what Schumpeter (1934), Winter (1967/2006) and Pavitt (1998), among the many others have denoted with *entrepreneurial function*. It sets out the strategies to maintain for the long-period formation of organisational skills, facilities, and capital, namely for the future health and growth of the enterprise. This soul is crucial for firms operating in environment with high technological opportunities and with significant costs for product and process development.[24]

By the way, successful start-ups developed along a trajectory which is quite different from the *abstract* picture science-centred v. commerce-centred variants. In fact, "they have transformed themselves into quasi-conventional pharmaceutical companies, vertically integrated into manufacturing and marketing" (Malerba and Orsenigo 2015, p. 679). To conclude, a last key ingredient to success was the relationship with big established firms that mastered complementary assets. Crucial for a start-up was the ability to sell itself as an *ideas factory* (Gans and Stern 2003), such that big firms could associate a start-up *modus operandi* not with creative destruction but with an opportunity to strengthen their incumbent market power.

[23] Sometimes scientific excellence is measured by the presence of star scientists in the scientific board. However, this indicator could be misleading for star scientists were often *used* as means to get funding rather than a way to signal commitment toward scientific excellence.

[24] The entrepreneurial, or value-creating, function is juxtaposed to the *administrative function*, who is rather a matter of loss prevention and it is important for firm's survival in late-stage industries, when the notional technological opportunities are low, or when the economic objective can be reached in a relatively short term. For a focus on large multidivisional structure of early 20th century firms, see Chandler (1990, 1991).

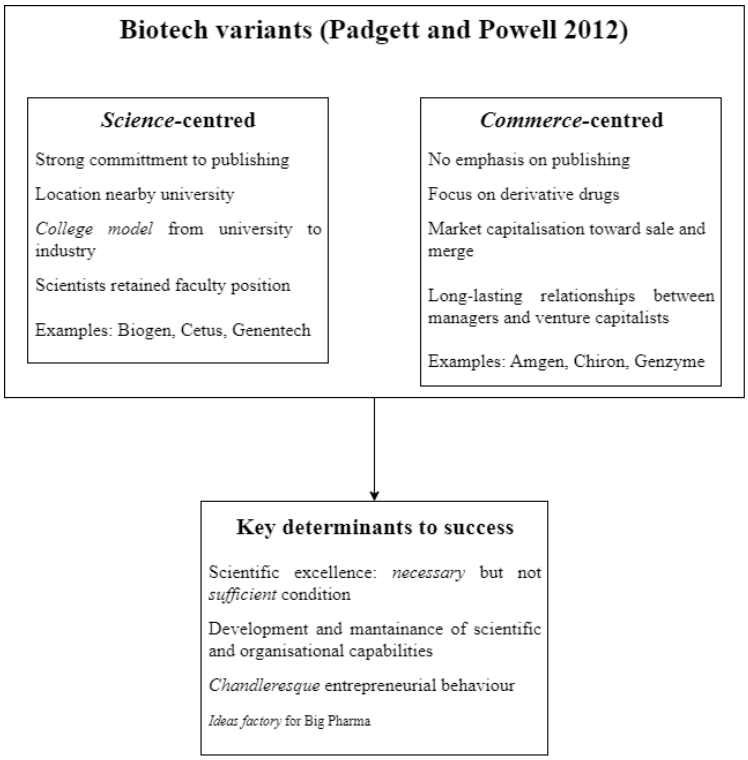

Figure 3. Main features of early biotech variants

5) Conclusions

In this article, the rise of life sciences as a fast-growing sector characterised by high technological opportunities was analysed as the result of a co-evolutionary process involving several innovations in law, government policy, science, and finance. All such novelties were pivotal to the most remarkable innovation brought about by biotechnologies – i.e., the substitution of fluid and porous organisational boundaries, that fostered inter-institutional cooperation in R&D, for the hermetically sealed industrial R&D lab typical of early XX century. Technological progress in one industry is indeed dependent on technological change in other domains (Rosenberg 1979).

Such a discussion on the surrounding architecture of biotechnology was preliminary to the issue of the relationship between division of knowledge and division of labour. As consequence of uncertain economic environment, the figure of the entrepreneur, be it a single or collective agent, is necessary to the process of creation of resources that ensure the proper linkage between the internal and external environments of the firm. In other terms, and with reference to the three-agent entity that composes a biotech start-up, the collective entrepreneur was the active element of the interaction between different realms, designing the internal organisation and being pro-active toward the external environment (Cohendet and Llerena 2005, 2010). But, had this been the case, such a reasoning challenges the Smithian interpretation according to which the task one is assigned to carry out – i.e., the division of labour – determines what one can learn by carrying out that task – i.e., the division of knowledge, and opens the possibility the skills and knowledge are the criteria that should decide how labour is divided (Babbage 1832, Becker et al. 2007).

However, rather than deciding who first determines whom, we have asserted that division of labour and division of knowledge are intermingled in the co-evolutionary process that shapes the relationship between biotechnology and broad institutions. For what concerns the relationship between university, industry, and the market, mechanisms *à la* Smith do appear. In general, the innovation system in life sciences allows individual researchers to make very specific investments in human capital early in their careers, to grab the benefits thereof through different types of jobs, and to collaborate across organisational boundaries with researchers with complementary skills (Henderson et al. 1999, Cockburn and Stern 2010). Nonetheless, observing the reasons behind early start-ups, we find that the inherent uncertainty of the environment – e.g., high drug development costs and hazards that fuelled agreements with Big Pharma - forced and forces firms to create new knowledge *from within*. Firms cannot always rely on a pre-existing division of labour between a scientist, a venture capitalist, and a manager. Entrepreneurs are responsible for creating resources which link a company's internal and external worlds. In that case, cognitive processes *à la* Babbage come first: they drive the division of labour.

Strictly connected was the role of managers in the delimitation and selection of the core competences that opened the way to a variety of configurations of division of labour for a given division of knowledge. This process was the mechanism behind the ongoing generation of variety along the trajectory of a given technological paradigm (Dosi and Nelson 2010). In the case of life sciences, this regarded two types of start-ups: the science-centred and the commerce-centred variants (Powell and Sandholtz 2012). The literature seems often to assume that excellence in scientific research was the key to long-run profitability and growth. Albeit we consider it as a necessary pre-requisite, we claim that it was not a sufficient condition. As case studies on the first generation of start-ups emphasise, the recruitment of managers to supervise and coordinate the different activities of production and distribution was equally important. The key to long-term profitability and growth was rather the ability to maintain a sufficient body of knowledge with respect to recent scientific advances, managerial practices and so on, in order to keep the whole system together in a situation of deep economic uncertainty. In other words, a collective entrepreneur exerting a strong entrepreneurial function (Schumpeter 1934) was pivotal.

Two remarks should conclude this article. Firstly, the kind of institutional network that established between university and industry in biotechnology is a very peculiar one and we shall not come to generalising the relationship between academy and industry. Lundvall (2007) and Cowan et al. (2010) suggest that these misunderstandings and crude interpretations have "inspired reforms that neglect that universities fulfil other and more important functions than being "immediate sources of innovation" such as educating critical and skilled knowledge workers" (Lundvall 2007, p. 97). The second remark concerns to the potential of our interpretation to shed light on emerging sectoral systems of innovation. For instance, the development of Artificial Intelligence (AI) as the next general-purpose technology (GPT) or as a large technical system (Vannuccini and Prytkova 2023) is the result of increasing cooperation between university and big tech-s like Google, Microsoft, and Amazon. Academy is the source of human capital, but it needs capital in the form of computers and data, which are in the hands of big tech-s. May our analysis on biotech-s contribute to explain how this innovation system is evolving? These and further research questions will guide our future research on the topic.

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References

Arora, A., & Gambardella, A. (1990). Complementarity and external linkages: The strategies of the large firms in biotechnology. *The journal of industrial economics*, 361–379. https://doi.org/10.2307/2098345

Babbage, C. (1832). *On the economy of machinery and manufactures*. *The London, Edinburgh, and Dublin Philosophical Magazine and Journal of Science*, *1*(3), 208–213. https://doi.org/10.1080/14786443208647876

Becker, M. C., Cohendet, P., & Llerena, P. (2007). Division of labor and division of knowledge: Why the nature of the causality matters for the evolutionary theory of the firm. In U. Cantner & F. Malerba (A c. Di), *Innovation, Industrial Dynamics and Structural Transformation* (pp. 49–63). Springer Berlin Heidelberg. https://doi.org/10.1007/978-3-540-49465-2_4

Berg, P. (1970). Viral oncogenesis and other problems of regulation. *American Cancer Society grant application, submitted November*.

Berg, P., & Mertz, J. E. (2010). Personal reflections on the origins and emergence of recombinant DNA technology. *Genetics*, *184*(1), 9–17. https://doi.org/10.1534/genetics.109.112144

Berman, E. P. (2012). Explaining the move toward the market in US academic science: How institutional logics can change without institutional entrepreneurs. *Theory and Society*, *41*(3), 261–299. https://doi.org/10.1007/s11186-012-9167-7

Blumenthal, D., Gluck, M., Louis, K. S., Stoto, M. A., & Wise, D. (1986). University-Industry Research Relationships in Biotechnology: Implications for the University. *Science*, *232*(4756), 1361–1366. https://doi.org/10.1126/science.3715452

Brusoni, S., Prencipe, A., & Pavitt, K. (2001). Knowledge Specialization, Organizational Coupling, and the Boundaries of the Firm: Why Do Firms Know More than They Make? *Administrative Science Quarterly*, *46*(4), 597–621. https://doi.org/10.2307/3094825

Chandler, A. D. (1991). The functions of the HQ unit in the multibusiness firm. *Strategic Management Journal*, *12*(S2), 31–50. https://doi.org/10.1002/smj.4250121004

Chandler, A. D. (2009). *Scale and scope: The dynamics of industrial capitalism*. Harvard University Press.

Cockburn, I. M., & Stern, S. (2010). Finding the Endless Frontier: Lessons from the Life Sciences Innovation System for Technology Policy. *Capitalism and Society*, *5*(1). https://doi.org/10.2202/1932-0213.1071

Cohen, S. N., Chang, A. C. Y., Boyer, H. W., & Helling, R. B. (1973). Construction of Biologically Functional Bacterial Plasmids *In Vitro*. *Proceedings of the National Academy of Sciences*, *70*(11), 3240–3244. https://doi.org/10.1073/pnas.70.11.3240

Cohendet, P., Dupouët, O., Llerena, P., Naggar, R., & Rampa, R. (2024). Knowledge-based approaches to the firm: an idea-driven perspective. *Industrial and Corporate Change*. https://doi.org/10.1093/icc/dtae032

Cohendet, P., & Llerena, P. (2005). A dual theory of the firm between transactions and competences: conceptual analysis and empirical considerations. *Revue d'économie industrielle*, *110*(1), 175-198.

Cohendet, P., & Llerena, P. (2010). The knowledge-based entrepreneur: The need for a relevant theory of the firm. In *Knowledge Intensive Entrepreneurship and Innovation Systems*, Malerba, F. (ed), 55–75. Routledge.

Coriat, B., & Orsi, F. (2002). Establishing a new intellectual property rights regime in the United States: Origins, content and problems. *Research Policy, 31(8-9)*, 1491-1507. https://doi.org/10.1016/S0048-7333(02)00078-1

Cowan, W. B., Cowan, R., & Llerena, P. (2010). 11. Running the marathon. *Learning to compete in European universities: From social institution to knowledge business*, McKelvey, M., & Holmén, M. (Eds.). Edward Elgar Publishing.

Dosi, G. (1982). Technological paradigms and technological trajectories: A suggested interpretation of the determinants and directions of technical change. *Research policy*, *11*(3), 147–162. https://doi.org/10.1016/0048-7333(82)90016-6

Dosi, G. (1988). Sources, procedures, and microeconomic effects of innovation. *Journal of economic literature*, 1120–1171. https://www.jstor.org/stable/2726526

Dosi, G. (2023). *The Foundations of Complex Evolving Economies: Part One: Innovation, Organization, and Industrial Dynamics*. Oxford University Press.

Dosi, G., Faillo, M., & Marengo, L. (2008). Organizational Capabilities, Patterns of Knowledge Accumulation and Governance Structures in Business Firms: An Introduction. *Organization Studies*, *29*(8–9), 1165–1185. https://doi.org/10.1177/0170840608094775

Dosi, G., Llerena, P., & Labini, M. S. (2006). The relationships between science, technologies and their industrial exploitation: An illustration through the myths and realities of the so-called 'European Paradox'. *Research policy*, *35*(10), 1450–1464. https://doi.org/10.1016/j.respol.2006.09.012

Dosi, G., & Nelson, R. R. (2010). Technical change and industrial dynamics as evolutionary processes. In *Handbook of the Economics of Innovation*, *1*, 51–127. https://doi.org/10.1016/S0169-7218(10)01003-8

Dosi, G., Nelson, R. R., & Winter, S. G. (2000). *The nature and dynamics of organizational capabilities*. Oxford University Press.

Gans, J. S., & Stern, S. (2003). The product market and the market for "ideas": commercialization strategies for technology entrepreneurs. *Research Policy, 32(2)*, 333-350. https://doi.org/10.1016/S0048-7333(02)00103-8

Gomory, R. E. (1988). Reduction to practice: The development and manufacturing cycle. *Proc. Symp. bid. R&D and US Technological Leadership*, 11–17.

Gompers, P. A. (1994). The rise and fall of venture capital. *Business and economic history*, 1–26. https://www.jstor.org/stable/23702914

Henderson, R., Orsenigo, L., & Pisano, G. P. (1999). The pharmaceutical industry and the revolution in molecular biology: Interactions among scientific, institutional, and organizational change. In *Sources of industrial leadership*, Mowery, D. C., & Nelson, R. R. (eds), 267–311. Cambridge University Press.

Hopkins, M. M., Martin, P. A., Nightingale, P., Kraft, A., & Mahdi, S. (2007). The myth of the biotech revolution: An assessment of technological, clinical and organisational change. *Research Policy*, *36*(4), 566-589. https://doi.org/10.1016/j.respol.2007.02.013

Hounshell, D. A., Rosenbloom, R. S., & Spencer, W. J. (1996). *The Evolution of Industrial Research in the United States.*

Kornberg, A. (2002). *The golden helix: Inside biotech ventures*. University Science Books.

Landes, D. S. (1969). *The unbound Prometheus: Technological change and development in Western Europe from 1750 to the present*. Cambridge University Press.

Langlois, R. N. (1992). Transaction-cost economics in real time. *Industrial and corporate change*, *1*(1), 99–127. https://doi.org/10.1093/icc/1.1.99

Levinson, A., D. (2001). Robert A. Swanson: Co–founder, CEO, and Chairman of Genentech, Inc., 1976–1996. Oral history conducted in 1996 and 1997 by Sally Smith Hughes, Regional Oral History Office, The Bancroft Library. *University of California–Berkeley*.

Lobban, P. E. (1969). The Generation of Transducing Phage in vitro. *Essay for third Ph. D. examination, Stanford University*, *6*.

Lobban, P. E., & Kaiser, A. D. (1973). Enzymatic end-to-end joining of DNA molecules. *Journal of molecular biology*, *78*(3), 453–471. https://doi.org/10.1016/0022-2836(73)90468-3

Lundvall, B. (2007). National Innovation Systems—Analytical Concept and Development Tool. *Industry & Innovation*, *14*(1), 95–119. https://doi.org/10.1080/13662710601130863

Malerba, F. (2002). Sectoral systems of innovation and production. *Research policy*, *31*(2), 247–264. https://doi.org/10.1016/S0048-7333(01)00139-1

Malerba, F., & Orsenigo, L. (2002). Innovation and market structure in the dynamics of the pharmaceutical industry and biotechnology: Towards a history-friendly model. *Industrial and corporate change*, *11*(4), 667–703. https://doi.org/10.1093/icc/11.4.667

Malerba, F., & Orsenigo, L. (2015). The evolution of the pharmaceutical industry. *Business History, 57(5)*, 664-687. https://doi.org/10.1080/00076791.2014.975119

Maxam, A. M., & Gilbert, W. (1977). A new method for sequencing DNA. *Proceedings of the National Academy of Sciences*, *74*(2), 560–564. https://doi.org/10.1073/pnas.74.2.560

Maxam, A. M., & Gilbert, W. (1980). [57] Sequencing end-labeled DNA with base-specific chemical cleavages. In *Methods in enzymology* (Vol. 65, pp. 499–560). Elsevier. https://www.sciencedirect.com/science/article/pii/S0076687980650599

Mazzoleni, R. (1999). Innovation in the machine tool industry: A historical perspective on the dynamics of comparative advantage. In *Sources of Industrial Leadership. Studies of Seven Industries*, Mowery, D. C., & Nelson, R. R. (eds), 169–216.

Monteverde, K., & Teece, D. J. (1982). Supplier switching costs and vertical integration in the automobile industry. *The Bell Journal of Economics*, 206–213. https://doi.org/10.2307/3003441

Morrow, J. F., Cohen, S. N., Chang, A. C. Y., Boyer, H. W., Goodman, H. M., & Helling, R. B. (1974). Replication and Transcription of Eukaryotic DNA in *Esherichia coli*. *Proceedings of the National Academy of Sciences*, *71*(5), 1743–1747. https://doi.org/10.1073/pnas.71.5.1743

Mowery, D. C., & Rosenberg, N. (1993). The US national innovation system. In *National innovation systems: A comparative analysis*, Nelson, R.R. (ed), 29–75.

Mowery, D., Nelson, R., Sampat, B., & Ziedonis, A. (1999). The effects of the Bayh-Dole Act on US university research and technology transfer. *Industrializing knowledge: University-industry linkages in Japan and the United States,* Branscomb, L. M., Kodama, F., Florida, R. (eds), 269-306.

Nightingale, P., & Martin, P. (2004). The myth of the biotech revolution. *TRENDS in Biotechnology*, *22*(11), 564-569. DOI: 10.1016/j.tibtech.2004.09.010

Nelson, R. R. (2000). *The sources of economic growth*. Harvard University Press.

Nelson, R. R. (2004). The market economy, and the scientific commons. *Research policy*, *33*(3), 455–471. https://doi.org/10.1016/j.respol.2003.09.008

Orsenigo, L. (1989). *The emergence of biotechnology: Institutions and markets in industrial innovation.* Pinter Publishers Ltd. https://www.cabdirect.org/cabdirect/abstract/19891607693

Orsenigo, L. (2006). Clusters and clustering in biotechnology: stylised facts, issues and theories.

Orsenigo, L., Pammolli, F., & Riccaboni, M. (2001). Technological change and network dynamics: Lessons from the pharmaceutical industry. *Research policy*, *30*(3), 485–508. https://doi.org/10.1016/S0048-7333(00)00094-9

Padgett, J. F., & Powell, W. W. (2012). *The emergence of organizations and markets*. Princeton University Press.

Patel, P., & Pavitt, K. (1997). The technological competencies of the world's largest firms: Complex and path-dependent, but not much variety. *Research policy*, *26*(2), 141–156. https://doi.org/10.1016/S0048-7333(97)00005-X

Pavitt, K. (1998). Technologies, products and organization in the innovating firm: What Adam Smith tells us and Joseph Schumpeter doesn't. *Industrial and Corporate change*, *7*(3), 433–452. https://doi.org/10.1093/icc/7.3.433

Perkins, T. J. (2001). Kleiner Perkins, venture capital, and the chairmanship of Genentech, 1976-1995. *An oral history conducted in*.

Pisano, G. P. (1991). The governance of innovation: Vertical integration and collaborative arrangements in the biotechnology industry. *Research Policy*, *20*(3), 237–249. https://doi.org/10.1016/0048-7333(91)90054-T

Porter, K., Whittington, K. B., & Powell, W. W. (2005). The institutional embeddedness of high-tech regions: Relational foundations of the Boston biotechnology community. In *Clusters, networks, and innovation*, Breschi, S., & Malerba, F. (eds), *261*, 296.

Powell, W. W. (1996). Inter-organizational collaboration in the biotechnology industry. *Journal of Institutional and Theoretical Economics (JITE)/Zeitschrift für die gesamte Staatswissenschaft*, 197–215. https://www.jstor.org/stable/40751919

Powell, W. W., & Brantley, P. (1996). Magic Bullets and Patent Wars: New Product Development. *Managing product development*, 233. https://doi.org/10.1093/oso/9780195074383.003.0010

Powell, W. W., Packalen, K., & Whittington, K. (2012). Organizational and institutional genesis and change: The emergence and transformation of the commercial life sciences. . In *The emergence of organizations and markets*, Padgett, J. F. & Powell, W.W. (eds), 379–433.

Powell, W. W., & Sandholtz, K. (2012). Chance, nécessité, et naïveté: Ingredients to create a new organizational form. In *The emergence of organizations and markets*, Padgett, J. F. & Powell, W.W. (eds), 379–433.

Rosenberg, N. (1976). Perspectives on technology. *Cambridge: Cambridge University Press*.

Rosenberg, N. (1979). Technological interdependence in the American economy. *Technology and Culture*, *20*(1), 25–50. https://muse.jhu.edu/article/890451.

Rosenberg, N. (1982). *Inside the black box: Technology and economics*. cambridge university press.

Rosenberg, N. (1992). Scientific instrumentation and university research. *Research Policy*, *21*(4), 381–390. https://doi.org/10.1016/0048-7333(92)90035-3

Rosenberg, N. (2010). *Studies on science and the innovation process: Selected works by Nathan Rosenberg*. World Scientific.

Rosenberg, N., & Nelson, R. R. (1994). American universities and technical advance in industry. *Research policy*, *23*(3), 323–348. https://doi.org/10.1016/0048-7333(94)90042-6

Saxenian, A. (1996). *Regional advantage: Culture and competition in silicon valley and route 128, with a new preface by the author*. Harvard University Press.

Schumpeter, J. (1934). *The theory of economic development*. Harvard Economic Studies.

Smith, A. (1776). *The Wealth of Nations: An inquiry into the nature and causes of the Wealth of Nations*. Harriman House Limited.

Teece, D. J. (1980). Economies of scope and the scope of the enterprise. *Journal of economic behavior & organization*, *1*(3), 223–247. https://doi.org/10.1016/0167-2681(80)90002-5

Teece, D. J. (1993). The dynamics of industrial capitalism: Perspectives on Alfred Chandler's scale and scope. *Journal of economic literature*, *31*(1), 199–225. https://www.jstor.org/stable/2728154

Teece, D. J. (2010). Technological innovation and the theory of the firm: The role of enterprise-level knowledge, complementarities, and (dynamic) capabilities. In *Handbook of the Economics of Innovation* (Vol. 1, pp. 679–730). Elsevier. https://doi.org/10.1016/S0169-7218(10)01016-6

Vannuccini, S., & Prytkova, E. (2023). Artificial Intelligence's new clothes? A system technology perspective. *Journal of Information Technology*, 02683962231197824. https://doi.org/10.1177/02683962231197824

Wang, Q., & von Tunzelmann, N. (2000). Complexity and the functions of the firm: Breadth and depth. *Research policy*, *29*(7–8), 805–818. https://doi.org/10.1016/S0048-7333(00)00106-2

Williamson, O. E. (1971). The vertical integration of production: Market failure considerations. *The American Economic Review*, *61*(2), 112–123. https://www.jstor.org/stable/1816983

Winter, S. G. (2006). Toward a neo-Schumpeterian theory of the firm. *Industrial and corporate change*, *15*(1), 125–141. https://doi.org/10.1093/icc/dtj006

Wuchty, S., Jones, B. F., & Uzzi, B. (2007). The Increasing Dominance of Teams in Production of Knowledge. *Science*, *316*(5827), 1036–1039. https://doi.org/10.1126/science.1136099