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# Recent Biotechnology Development: challenges and opportunities to the consolidation of its knowledge "building blocks".

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## Abstract

One of the most interesting characteristics of the innovation process is that it can be regarded as a combination of different pieces of knowledge each acting as a "building block" The "building blocks" mechanism improves our capacity to break a complex scene down into parts using a wide variety of combinations which are neither arbitrary, nor deterministic, for they result from an objective process of search. It is a specific combination, among the great number of possibilities, that makes innovations available.Biotechnology has been defined as a robust block of knowledge which combines already existing research protocols with new scientific procedures derived from different disciplines such as biochemistry and molecular biology. This description of biotechnology holds a great potential for new combinations with other existing building blocks, such as the ones representing computer sciences. In fact, the information-based genetic approach becomes the *core* of a wide range of more complex scientific and technological blocks of knowledge

Up to this point, the main questions presented for the consolidation of the building blocks in biotechnological research and their institutional arrangements can be described as:

a) the new competitive profile which will emerge from the alliances between the large pharmaceutical companies, the specialized firms, the universities' research groups and governments;b) the continuation of the process of taking money for funding from financial markets, a very risky strategy adopted by most American specialized companies - particularly the new biotech companies - during the last fifteen years;c) the new intellectual property rights and other forms of protection that will emerge from the discussions about regulating trade in genetically modified organisms and from the debate concerning the monopoly of cloning techniques that are supposed to copy and to scale up the fundamental natural processes of life

To sum up, we present an analysis of recent biotechnology evolution and the main Brazilian features related to the developing of a the expertise in biotechnology fields, mostly in agriculture. After this we analyze the opportunities opened by the "Real plan", in terms of the new institutional environment to venture capital. We stress the nature of the recent biotechnology programs in Brazil, focused in long term results, as a main obstacle to develop new forms of finance biotechnology.

Key words: Biotechnology, Funding, Venture Capital, Knowledge Building Blocks, one, to, be, …

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## Elements for the current discussion on biotechnology

The emergence of biotechnology since the second half of the 1970's definitely cannot be treated in a conventional linear way, in which a scientific discovery is followed by developments that aim at commercial products. The continuous feed back between productive and scientific activities, and *vice-versa*, alert to the search of new forms of analysis of these activities currently identified as high technology sectors.

Some important studies, like those of Meyer and Nickerson (1998) and Pisano (1997), taking advantage of the existence of an emergent industry supported on recent results from biotechnology, discuss the emergence of transaction costs and governance problems typical of the industry, like monitoring problems between firms specialized in biotechnology and their suppliers and the presence of adverse selection on the relation between NEB´s (New Biotechnology Firms)and the incumbent firms. Audretsch & Stephan (1999), turn toward the relation between universities and biotechnology firms, tracing the profile of the professional from the university, responsible for the creation of a biotechnology firm. They show there is a positive correlation between academic performance (number of publications and citation index) and the trend of these professionals to create biotechnology firms, contrasting with the type represented by the successful Ph.D., that has greater propensity to follow a career in a big corporation. Hagedoorn (1992), in his turn, emphasized the role of pre-competitive alliances between corporations as one of the remarkable characteristic of the recent biotechnology development.

Even if these studies are of enormous interest to better characterize biotechnology as an economic activity, they strongly depend on the pre-supposed that biotechnology activities constitute an economic sector or a "auxiliary tool" of the technologies incorporated on productive routines and of corporate innovation of sectors that possess certain affinities with activities of biologic base.

The recent evolution of the industry attract attention to the fact that reductionist strategies in the use of recombinant DNA techniques aiming at new products or the revitalization of already consolidated markets, like herbicides, are very limited. The fact that projects like the Genome and the search of new strategies for the construction of new drugs (Nightingale, 1999) are gaining increasing room on biotechnology financing are indicators that little can be said on the future configuration of an "industry of biotechnology basis". The next item seeks to indicate some elements of an alternative analysis proposal that values some important characteristics of the activity that surrounds what we call biotechnological activities, utilizing the concept of "building blocks". However, before developing the basic elements related to the idea of "building blocks", it is interesting to present some view that, in our opinion, help us to introduce these new analytical tools applied to the peculiarities of biotechnology development.

Nightingale (1999) makes use of the concept of "technology tradition" to refer to a set of procedures, more or less standardized, used by technologists during determined period to solve problems known for their similar nature. With the passage of time, these "technological traditions" begin to be questioned for their own incapacity to solve certain problems. Besides, the advancement of scientific knowledge and instrumentation open new horizons for the resolution of these problems, changing even the perception of what are problems of similar nature. It is through this process that the technological communities begin to test and perfect new procedures and the "technological traditions" evolve, leading even to the redefinition of task division on R&D activities.

Olalde, Futino e Silveira (2000) point out that the concept of "technological tradition" resembles the notion of "routines" proposed by Nelson and Winter (1982), like a series of standardized processes that guide the practices of

"search" for innovation, whose goal is the creation and maintenance of competitive advantages on the entrepreneurial ambit. In the same sense, the concept of "technological paradigm" proposed Dosi (1982) could be cited, following the kuhnian tradition, like a heuristic that leads to the selection of certain problems and the proposal of a determined type of solution through certain period.

These approaches arise from the idea that technological knowledge goes beyond simple information processing, for this information needs to be interpreted by the agent, that, by using his capacity to associate ideas derived from experience (tacit knowledge), proposes solutions to determined problem situation. Then, changes in the innovation process can have its origin in the way information is processed, that is, on its "meaning" and not on its intrinsic characteristics. Thus, given that the recognition of similarity between two phenomena requires the participation of a cognitive agent, through his neurological process, the learning process cannot be seen in purely abstract terms. Nightingale (1999) criticizes the fact that firms are often treated as mere "information processors", when their main role is associated to the organizational knowledge accumulation. Because of that, the analysis of how certain technological community perceives problems and proposes solution may represent a significant advancement to open the "black box" of innovation.

On the other hand, the learning associated to innovative activities is not a purely individual phenomena, for the increasing complexity of innovation requires a collective and interactive process, including several individuals and corporations, even if recognizing that, as observed by Joly and Mangematin (1995), the greater part of the bibliography on the theme, the passage from Inter-personal to inter-entrepreneurial is an open question. On these approaches, there is also a differentiated interpretation of the role of science and academic institutions, questioning the linear model in which innovation derives mainly from the application of scientific discoveries.

On one hand, scientific knowledge cannot be directly applied to produce technological solutions. Besides, interactive models, as the one proposed by Kline and Rosenberg (1986), highlight the role of "feedback signals" between the different stages and agents that participate in the process. For these authors, the idea that innovation arises from science would be mistaken for the majority of cases. Many times, the technological communities guide themselves by "guided empiricism", resorting to science only when bottlenecks appear on the innovative process. The technologists would utilize, in first place, already available scientific knowledge and only when that was insufficient they would formulate research projects to be done in house or in co-operation with academic institutions.

Even if these approaches increasingly point out to the importance of constituting research networks (Bonacelli & Salles-filho, 1996), they lack an integrated proposal that account for the characteristics of recent biotechnology evolution. The case of the Gencell consortium (see Bonacell & Salles-Filho, 1998) and the example of Celera Genomics are very illustrative of the challenges imposed to the analysis of biotechnology. In the case of the American firm, the scientific activities, of research financing and the search for the best possible assignment of property rights on genetic sequences that do not even constitute an innovation, show that there is not anymore something like innovate first and then figure out ways to develop the product and guarantee property rights (by means of patents or other mechanisms), to organize the distribution network and then begin to commercialize products resulting from a biotechnological innovation.

When designing an investigation program in biotechnology, in the cases of greater impact, these questions are taken into account from the beginning, creating an anticipation power that, even if far from compatible with the idea of rational expectations, implies in choices, expenditure and investment decisions in the long run and on the formulation of intervention strategies for the creation of new institutional designs. However, when congregating distinct forms of knowl-

edge, agents of different nature, interests and expectational horizons, biotechnology demands a compatible approach, not only with the "architecture" complexity of its programs, but mainly with its fluid quality.

We believe that the idea of building blocks mechanisms helps to interpret these new forms of organizing the financing and conduction of the research, the production and constitution of property rights on current biotechnology.

## .Some new analytical tools to understand biotechnology complexity: The Building Blocks mechanism

The building blocks mechanism improves our capacity to break a complex scene down into parts using a wide variety of combinations that are neither arbitrary, nor deterministic, result from an objective process of search. It is a specific combination, among the great number of possibilities, that makes innovations available. The building blocks mechanism can be established as a unique of several possible combinations of structures in which the same blocks are systematically being arranged in a different order and position. The distinctive final combination is not known *ex-ante* and depends on the selection of vastly complex varieties of alternatives structures. The process of building the structures of innovations presents some basic properties and mechanisms that are presented in a way to emphasize the interrelationships and aggregation devices. The importance of this approach is that it helps us discover regularities and patterns in dynamic situations and evolving systems, for example, those related to biotechnology.

Building blocks mechanisms are based on three main "techniques": aggregation, networks and diversification.

Aggregation is a chief technique for constructing models in the course of which we are able to discern what is irrelevant and also decide which aspects of the problems can be ignored. In this process we decide which part of the details must be abandoned. The difference in the case of BB is that the categories we choose are reemployed and can be decomposed into familiar categories. Additionally we can create scenes never seen before by recombining the "blocks" beforehand (Holland,1994) Moreover we can see aggregation as the emergence of complex large scale behaviors from the aggregated interactions of less complicated structures or agents. Aggregating elements sometimes reveals the emergence of patterns of behavior that can not be observed in an individual and isolated agent. This is similar to the phenomena of coming out of meta-routines analyzed by Nelson and Winter (1982) with the difference that in this case we are looking to organizations, the meta -agents.

The idea of aggregation is related to other property, flows or network, which was inspired in economic theory (flow of goods, flow of capital etc). The same way economists have been using the analogy with natural selection, Holland (1995,1999)adopted it as a metaphor for modeling evolving systems[1]. One of attributes of flows is that they are comparable to the macroeconomic multiplier, e.g. We can think of a network as devices in which the nodes are processors and the connectors designates the possible interactions. Economic units of production may be the nodes and the motorways, the connectors for the flows of goods between factories. In a similar way computer stations, cables and information form the indisputable example for the flows property: the WEB. As time goes by, the network changes its form and the nodes and connections can emerge and withdraw, as agents adapt or fail to adapt (Holland 1995)

The multiplier effect is a major feature of networks and arises regardless of the nature of the resources (goods or bytes). It is relevant whenever innovations emerge and put at risk long-range predictions or when it is necessary to estimate the effect of some new resource in an evolutionary trajectory. The effect of cycles in the networks can , once more, be taken from the economy and Shows, e.g., how recycling the same raw material produces more resources at each node.

Diversity expresses the persistence of any individual agent, a firm or an organization, on the context or aggregation and networks. Diversity arises in two different ways (again, see Holland,1995):

a) when an agent is removed from its context, creating a gap in the structure that naturally respond with a stream of adaptation; the result might be the introduction of new elements filling the gap;

b) when the spread of an agent opens opportunities for new interactions that can be exploited by modifications of other agents.

Diversity is a dynamic pattern of evolving structures that Shows coherence and persistence. If there is a change in the way the components interact or if one of the elements disappears, the pattern re-establishes itself, but the result, the new pattern, may differ completely from the older. Diversity is an outcome of progressive adaptation of evolving structures (Holland,1995: 29). The decisive distinction related to dynamic interactions becomes visible as each new adaptation patterns evolves giving place to further interaction and to new niches for still newcomers. The agents that participate in *cyclic flows* cause the system to retain resources and this retention can be further exploited, opening new niches to be developed by new type of agents. The part of the structure that goes on with *recycling* will succeed. The part that fails, will lose its resources.

The evolutionary models studied by paleontologists illustrate a best comprehension of the appearance of new patterns of interaction. Curiously, it is a situation opposite to that of biotechnology, in the sense that is not an uncertain future, but a past without possible memory, from which one can use evidences to make the hypothesis more robust.. The emergence of a multifaceted hierarchical organization can be evidenced, initially, by a set of general pattern of behavior that satisfies numerous situations and presents some advantages[2]. In the paleontology method, the hypothetical rules are relatively easy to discover because they are simple and, therefore, can be investigated. Further, by repeated experimental tests, we can obtain a kind of "statistical" confirmation of the earlier conjectures. Once the generalists' patters of interactions are launched, they open possibilities for the discovery of other relations. As we can correct the initial mistakes, it is easier to obtain more sophisticated forms of organization (Holland, 1995).

A set of rules and procedures that enables agents to anticipate the consequences of actions is considered to be an" internal" model of knowledge to individuals and organizations[3]. From a simple form of life, like a bacterium, to great a sophisticated corporation, all agents improve mechanisms to deal with uncertainty and foresight. The patterns of reaction of the bacteria are pre-programmed by its genetic code, but human agents can develop more sophisticated models of knowledge and anticipation in spite of serious cognitive problems. (Simon, 1976)

So, what characterizes the internal models? The basic procedure to build a model can be resumed as a way of collecting features that we classify in the same category abandoning lots of details and idiosyncrasies. More formally, the objective of modeling can be described as a way of discovering regularities and selecting patterns in an evolving structure[4]. Initially the information collected from situations already experienced by agents can be thought as patterns of interaction.. Depending on that pattern of interaction, the regularities of certain kind of experience can be perceived even when there are random features among them. Afterwards, the perceived regularities are compressed in a *schema*. "The common features of all these processes is that in each one a complex adaptive system acquires information about the environment and its own interaction with that environment, identifying regularities in that information, condensing those regularities into a kind of "schema" or model, and acting in the real world on the basis of that schema." Holland (1999:17).

The internal models can be separated in two categories: tacit (or unconscious) and overt models. The former prescribes a current action under an implicit prescription of some desired future state. The latter is used when the agents are doing tentative explorations of alternatives lines of actions. Generally, natural environments adopt unconscious internal models while models used by economic agents are equally tacit and overt.

There is a pervasive mechanism that helps us in the identification of new patterns of aggregation and boundary formation. It is similar to using a flag to gather members of an army or people of similar politic affiliation. In the process of modeling the emergence of new patterns of interactions and creating building blocks, this feature improves our capacity to manipulate *symmetries*. They enable us to ignore certain details, focusing in others facilitating selective interactions and creating basis for specialization, and cooperation which , in turn, leads to the emergence of persistent hierarchical forms of organizations even when their internal parts are changing and evolving (Holland,1995)

One of the most operational examples of TAG is the *header* on a message of a bulletin. We can think of trademarks and logos as used by companies and firms to facilitate the identification of the product or service by the consumer. Classification of firms by classes of quality of methods and systems of production (ISO 9000/14000) and the creation of new categories of ecological and social labeling of commodities is a new forma of delimitating some limits of transactions in international trade.

[1] Actually, the idea of flows is derived from physical properties of the movements of fluids.

[2] Sometimes, they might be wrong but, on average, they shows that the associations are better than random

[3] Following the analysis proposed by Holland (1999) one can understand that the use of internal models, is an important *mechanism of anticipation*.

[4] Murray Gell-Mann, the Nobel winner, presents evolving complex systems as a pattern recognition device that seeks to obtain regularities in experience and compress them into a model or schema(1997:17).

## Recent Challenges to Biotech development

Biotechnology has been defined as a robust block of knowledge that combines already existing research protocols with new scientific procedures derived from different disciplines such as biochemistry and molecular biology. This description of biotechnology holds a great potential for new combinations with other existing paradigms, such as the ones representing computer sciences. In fact, the information-based genetic approach becomes the *core* of a wide range of more complex scientific and technological blocks of knowledge In both we can analyze the innovation process as a combination of different pieces of knowledge each acting as a "building block".

In the case of biotechnology, the particular combination of scientific protocols and technical devices corresponds to a kind of technological *guide-posts* for those companies and organizations which are engaged in R&D projects, but they also represent a benchmark for entrepreneurs who are engaged in the gene hunting race. However, this is a context in which nothing has been established already, neither the payoff nor the rules and norms. Basic research is still very expensive and the uncertainties associated with the development of new products currently are still too high. These uncertainties have been summed as the problems concerning the production of genetically modified food and the definitions of a new protocol to regulate basic research and trade.

Tabela 1 allows to see how R&D expenses are very important to US Biotech Firms and how high are the share of the losses in the total revenue of these enterprises in aggregate. Another interesting feature is that Public Companies are bigger in aggregate when compared whit "Other Companies", that reveals some barriers to achieve the equity market.

Tabela 1 Main US Biotech Figures (US$ billons)

| Variables | Public Companies | | Other Companies | |
|---|---|---|---|---|
| Year | 1999 | 1998 | 1999 | 1998 |
| Product Sales | 11 | 9.1 | 2.4 | 2.4 |
| Revenues | 15.2 | 12.6 | 3.4 | 3.5 |
| R&D Expenses (1) | 6.2 | 5.1 | 3.7 | 3.4 |
| Net Losses | 2.7 | 1.5 | 2.4 | 1.9 |
| Other Figures | | | | |
| Number of Biotech Firms | 327 | 317 | 956 | 957 |
| Number of employees | 106000 | 94000 | 47000 | 46000 |
| (1) Expenses to purchase technology not included | | | | |

Source: Ernest & Young (1999)

These characteristics of the "rising industry" – an idea that is completely maladjusted to the case of biotechnology – hampers, inclusively, the definition of what is the biotechnology industry and even more the definition of the typical biotechnology firm. Large corporations usually from the chemical/pharmaceutical sector have been preparing themselves through mergers, alliances and the creation of networks and consortia. As shown by Silveira (1993), not only the perception of risk, but also the need for monitoring of biotechnological progress motivates the creation of these hybrid forms of governance of high costs. Some of the new institutional arrangements established between business and science have been using risky forms of financing, such as Wall Street markets, burdening entrepreneurial expectations with more uncertainties and stress. Others, as the recent mergers in the pharmaceutical industry, are less uncertain.

Table 1 allows us to observe that for the three countries that invest the most in biotechnology in Europe there are

significant differences in the way of conducting the process by public agencies. Curiously, contrary to the intervention image, biotechnology in France is mainly financed by funds not directly aimed at this activity, contrasting with the greater allocation of funds by program in Germany (on more recent periods) and with the distribution of policy directed expenditure in the U.K. This variety Shows well that the patterns for financing arrangements and the combination of blocks that participate in biotechnology in innovation generators countries is still very fluid.

**Tabela 2 . Public Spending on Biotechnology Trhough Non-Policy-Directed Funding Mechanisms and Policy-directed Funding Mechanisms( 1994-1998)**

| Country | Non-policy directed | Policy-directed | |
|---|---|---|---|
| | Total public spending on biotech R&D (MECU) | Total public spending on biotech R&Dtrhorugh specific biotech programmes and other funding mechanism (MECU) | Total Public spedin on biotech R&D through genran funding mechanism (MECU) |
| Áustria | 50.87 | - | - |
| Belgium | 176 | 189 | 185.5 |
| Denmark | 39.8 | 42.4 | 54.87 |
| Finland | 210 | 72.5 | 3.9 |
| Frence | 1 539 | 114 | 44.4 |
| Germany | 1 616 | 1385 | 176 |
| Greece | n.a. | - | 19.7 |
| Iceland | 2.6 | - | - |
| Ireland | 12.2 | 14.5 | 18.75 |
| Italy | n. a. | 77.9 | 19.5 |
| Netherlands | 81.5 | 11 | 144 |
| Norway | 101.5 | 29.6 | 39.9 |
| Portugal | 23.3 | - | 34.8 |
| Spain | n.a. | 34 | 13 |
| Sueden | 125.5 | 50.6 | 22.6 |
| Switzerland | n.a. | 47.1 | 2.7 |
| U-K | 1 036 | 687.8 | 413.2 |
| Sub-total | 5 014.27 | 2 755.4 | 1 193.12 |
| Total | 8 962.79 | | |

Source: European Comission (1999)

Despite the query about genetically modified organisms, and the sharp fall of Monsanto's share price on Wall Street last year, the considerations about regulatory issues have not disrupted the new institutional solutions which have been giving support to the building of these blocks of knowledge in biotechnology. On the contrary, the role of basic research in biotechnology in the United States and Europe has been reinforced by centralized institutions which co-ordinate funding and regulatory recommendations, as well as planning programs for representing biotech companies in the government(McMeckin et Alii,2000). On these arrangements, there is room for the continuous emergence of small innovative firms in biotechnology and, almost as a consequence (without wanting to be deterministic) for co-operation deals that allow them to come closer to the market, financing the more expensive stages of the process, basically the stage of clynical experimentation.

An inventory of public programs in biotechnology done by the pelo Science Research Development, from the European Commission (1999) clearly shows that there are enourmous differences in the way biotechnology is financed and organized in the 18 countries under study, but those differences mainly refer to the degree of control that the financing agencies have on research activities, that is, on *ex-ante* evaluation activities than on the potential of the research (Assouline e Joly, 1999; Geopi, 2000).

Figure 1 shows that, on the different countries under study, despite the standard view of associating EU countries with a grater degree of intervention by the state, there are considerable differences, be it on the coordination between agencies that account for the development of biotechnology, be it on the way used by the public sector to finance them.

In sum, the organizational base of knowledge formation, based on "near-market" forms, reinforces the methodological importance of the Building block approach type, for it avoids previsions based on the market power of the leading firms interested in biotechnology (see Ronde, 1992, for a modeling based on this perspective.

Figure 1.Characteristics of Financing Systems and Biotechnology Research Control of European Countries
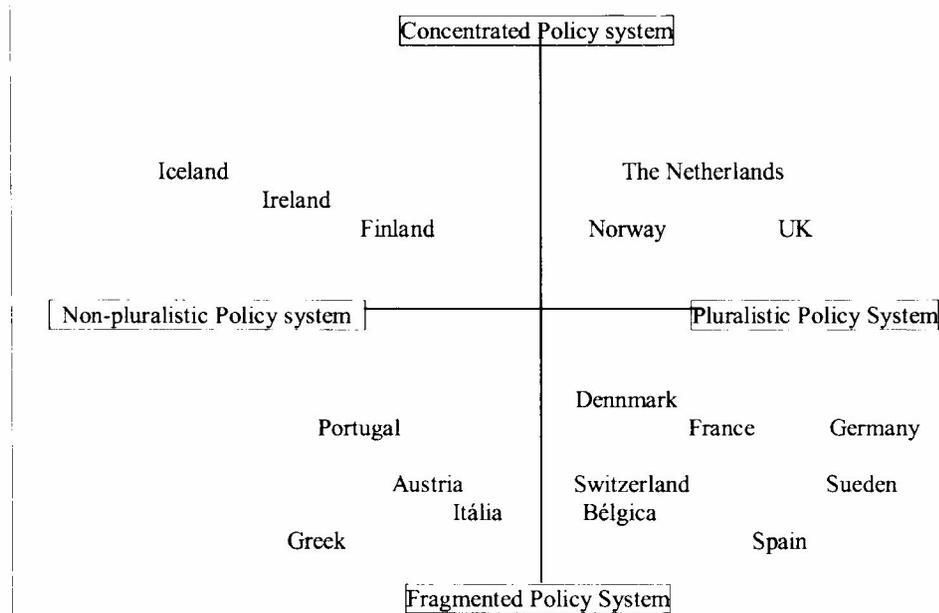


Up to this point, the main questions presented for the consolidation of the building blocks in biotechnological research and their institutional arrangements can be described as:

a) the new competitive profile which will emerge from the alliances between the large pharmaceutical companies, the specialized firms, the universities' research groups and governments;

b) the continuation of the process of taking money for funding from financial markets, a very risky strategy adopted by most American specialized companies - particularly the new biotech companies - during the last fifteen years. See Ostrovski(1998)[1].

c) the new intellectual property rights and other forms of protection that will emerge from the discussions about regulating trade in genetically modified organisms and from the debate concerning the monopoly of cloning techniques that are supposed to copy and to scale up the fundamental natural processes of life (see Fonseca et alii, 1999.).

Although the intellectual property protection laws, including patents, are seen as fundamental pre-requisites of co-operative research activities and funding, it is quite unlikely that regulating trade in GMOs, licensing cloning and creating protection to bio-diversity will be managed in the next few years. The discussion of these issues embodies a tremendous potential of conflict between different industry, companies, governmental and academic agencies, non-governmental organizations and, last but not least, countries. The consolidation of biotechnology blocks of knowledge

depends to a great extent on the acceptance of the same rules of the game by all of these agents.

## Some considerations on the development of biotechnology in Brazil

The development of new technologies in Brazil has suffered a great deal with the State crisis since 1980, with a greater negative impact on the incentive system for the stimulus of research activities by national firms, reaching areas like fine chemistry (Rebouças, 1997) and biotechnology (Bonacelli & Salles-Filho, 1996). Many attempts to create small biotechnology firms failed, mainly for being supported on traditional forms of financing. Some medium sized firms, especially those turned towards agriculture, like Agroceres, suffered a spin off of their biotechnological parts, acquired by Monsanto. The same thing happened to FT, a seed firm that became Monsoy, of the same corporation.

Brazilian biotechnology became basically restrict to the Empresa Brasileira de Pesquisa Agropecuária (Embrapa) and the Fundação Oswaldo Cruz (Fiocruz), institutions that act, respectively, on the agricultural area and human health, supported mainly by public financing, and recently developing near-market organizational forms of great importance and success.

From the theoretical perspective adopted here, it is curious how, with relatively small investment, some initiatives more complex than the simple creation of small NEB´s have been successful since the second half of the 1990´s. With financing from Fapesp (Fundação de Amparo à Pesquisa de São Paulo) of US$ 12 million, it was possible to sustain a research embryo in the line of GENOMA (Xyllela fastidiosa) which resulted in new processes (OREST, for example, to be patented) and unfolded itself in several other projects, like the Genoma-cancer and Genoma-sugarcane. Contrary to the organization visualized by the biotechnology programs from the 80´s, which had the creation of biotechnology firms as its objective, this program, involving 190 researchers and 32 research institutions, has basically turned towards the formation of the required BB for the development of biotechnology, with basis on pre-existing pure and applied research from the research institutes (Instituto Ludwig, Instituto Agronônomico de Campinas, among others) as well as from the three universities from São Paulo. At the same time, it was able to create the ONSA network, making fast use of the pre-existing competence, aggregating knowledge and specializing activities whose potential were not well defined *ex-ante*. This surprising combination of competencies originally different, like those required to the conception of a "cosmídeos" bank, its organization, the genetic sequencing, the information organization and depuration of chimeric forms allowed for a technological advancement recognized internationally which, inclusively shortens the search path of posterior use of this knowledge.

The result of this process is still incipient and uncertain, but clearly points at the overcoming of the linear path, in which the identification of productive potentialities is left to the will of isolated researchers and entrepreneurs. The extent of the research network for the creation of biotechnology firms is a challenge that recent experience has put upon biotechnology in Brazil and the world.

## References

Assouline, G & Joly, P.B. (1999) The Biotechnology Policy-Making and Research System in the Different Countries: convergences and specifics. in European Comission, SRD. vol.1.68p.

Audretsch, D. & Stephan, P (1999) Knowledge Spillovers in biotechnology: sources of incentives. Journal of Evolutionary Economics, vol 9(1:97-109).

Bonacelli, M.B. & Salles-Filho, S.L.M (1996) As especficidades do Processo de Mudança Tecnológica: uma análise aplicado ao caso da Biotecnologia. In Anais do XXIV Encontro da ANPEC, Águas de Lindóia.

Dosi G. (1982) "Technological paradigms and technological trajedtories" *Research Policy* 11, p. 147-162

Ernest & Young (1999) Biotech 99.An Industry Annual Report. Thought Leardship Series..

European Comission-SRD (1999) . Inventory of Public Biotechnolgy R&D Programmes in Europe. Vol 1. Analitycal Report. EU-Directorate-General Research. EUR-18886/1 en , 68pp.

Fonseca, M.G.*et alii* (1999) O Desenvolvimento da Biotecnologia no Brasil. Brasilia, DF. CNPQ-Produtividade em Pesquisa. mimeo, 315pp.

Gell-Mann, M. (1997) The Quark and the Jaguar. Adventures in the Simple and the Complex. Abacus. Little Brown and Co.

Hagedoorn, J (1992) Market Strcutural Hierarchies and Networks of Strategic Technology partnering. Linchburg, NE, MERIT, mimeo.

Holland, J (1995). The Hidden Order: How Adaptation Builds Complexity. Addison-Wesley.

Holland, J.(1999) Echoin Emergence:objectives, roghs definiitons and speculations from ECHO Class. in Cowan, G. Pines, D. and Meltzer, D. Metaphors, Models and Reality; Thee Adavanced, Book Program. Cambridge, MA. Perseus Books

Joly, P.B.& Mangematin, V. (1995) "Les acteurs sont-ils solubles dans le réseaux?", *Economies et Sociétes*, Série Dinamique technologique et organization, no 2, p. 17-50.

Kline,S. e Rosemberg, N. (1986) "overviw of innovation" In: LANDAU, R. e ROSENBERG, N (eds.) *The positive sum strategy*, Washington: National Academy Press, p. 275-305.

McMeekin, A.; Reed, A. & Tampubolon,G (2000). What Would Constitue Sucess for UK Biotechnolgy by 2005. ESCR/CRIC.

Meyer, K & Nikerson, J.(1998) Buyer-Supplier Contracting in Biotechnology. Berkeley, The Hass School of Business Working papers. mimeo, 40pp.

Nelson, R & Winter S. (1982) *Evolutionary theory of economic change*, Cambridge: Harvard University Press.

Nightingale, P (1999). Scientific Knowledge and the Dynamics of the Pharmaceutical Innovation Process, CoPS Working SPRU, University of Sussex, Brighton Paper,mimeo, 28pp.

Olalde, A.R., Futino, A.M. & Silveira, J.M.F.J. Os desafios impostos à microeconomia pelos setores de alta tecnologia: uma análise da biotecnologia. Paper apresentado no Encontro: "Situação Atual da Microeconomia em uma perspectiva metodológica". Doutorado em Economia da UFPR, Curitiba 16 e 17 de outubro de 2000.mimeo, 22pg.

Ostrovsky, C. (1998) The Feasibility Study For Research Venture Finance for Technology Firms inArgentina, Brazim, Chile and Uruguay. IDRC/CDRI:CIID-Montevideo, Ur. vencap.html.

Pisano, G (1997) R&D Perfomande, Collaborative Arrangementes and The Market-for-Know-How. Harvard, HBSchool Working paper. mimeo.36p.

Rebouças, M. (1997) A Indústria de Química Fina no Brasil. Tese de Doutoramento/IE-Unicamp.. mimeo, 254pp.

Silveira, J.M.F.J da (1993) ,."O Desenvolvimento da Biotecnologia e sua Repercussão nos Padrões de Concorrências Industriais. Porto Alegre, **Indicadores Econômicos**: Temas em Debate,p(130-143).

Simon, H (1979) From Substantive to Procedural rationality. in Latsis, SJ. (ed) Method and Apprasial in Economics. , pp 129-148. Cambridge, MA. Cambridge University Press.