Innovation Networks in the Biotechnology-Based Sectors

by

Andreas Pyka♣ and Paolo Saviotti*
♣University of Augsburg, Economics Department, Universitätsstr. 16, D-86135 Augsburg
*INRA-SERD, Université Pieres Mendés France, BP47
F-38040 Grenoble, Cedéx 9, and CNRS-IDEFI, 250 rue A. Einstein, Sophia-Antipolis,
06560 Valbonne, France

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e-mail: andreas.pyka@wiso.uni-augsburg.de, saviotti@grenoble.inra.fr

Abstract

Technological progress in the biological sciences is now advancing across such a wide range and at such a pace, that, irrespective of size, no firm can hope to keep up in all the different areas. Participating in innovation networks, bundling of competencies and capabilities, therefore, offers an alternative to extremely expensive go-it-alone strategies, whether carried out by acquisition and mergers or by isolated R&D. This imbalance between the rate of growth of the biotechnology knowledge base and the capability of individual firms to access it can explain the persistence of cooperative R&D in the biotechnology-based sectors at the end of the 90s. Such imbalance is not due any more only to the lack of absorptive capacity of existing firms, because the large pharmaceutical firms have meanwhile developed considerable competencies in that field. This previous competence-gap was considered to be the reason for cooperative behaviour in the early phases of these industries in the end of the 70s and early 80s. To the extent that this was considered to be the only knowledge gap innovation networks were considered as a temporary phenomenon, which could not persist beyond the period required by large firms to catch up with the new technology. We are then proposing that a new role, that of explorers scanning parts of the knowledge space that LDFs (Large Diversified Firms) are capable of exploring but unwilling to commit themselves in an irreversible way, can be played by DBFs (Dedicated Biotechnology Firms) in innovation networks. Our simulation approach attempts to represent the emergence of these two roles as endogenous changes in the motivation for participating in innovation networks, allowing them to become an important and long-lasting organizational device for industrial R&D. Drawing on a history friendly modeling approach the decisive mechanisms responsible for the emergence of innovation networks in these industries are figured out and compared to real developments.

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1. Introduction

Innovation networks are a relatively new phenomenon which emerged in a significant way only since the beginning of the 1980s. Not only this new phenomenon was not predicted by economic theories, but its existence was considered to be an exception. The market and hierarchical organizations were considered to be the only stable and efficient forms of industrial organization. Networks were expected to have only a temporary existence or to survive in special niches. As it often happens, reality has taken science by surprise and the number of collaborative inter-institutional networks has steadily grown since the 1980s (EU Indicators Report, 1997). There is then a need to modify existing theories of industrial organization in order to explain the existence and the features of collaboration networks. The expression inter-institutional collaboration networks has been used before because the typical members of these networks are not only firms. Public research institutes or government departments participate quite often in these networks. Furthermore, in this paper we are only going to be concerned with innovation networks, that is with networks whose main objective is to create and adopt innovations. This is no the only type of network, but it is the dominant one.

In most of the research about networks the increased rate of creation of new knowledge and the shortening of the life cycles of products are two of the main factors associated with the existence of networks. Thus mechanisms of knowledge creation and utilization seem to be playing a very important role in the creation of networks. Networks can be considered a component of the emerging knowledge based society, in which knowledge is expected to

become the crucial factor leading to economic growth and to competitiveness. In a knowledge based society not only the quantity of knowledge used will be greater but its mechanisms of creation and utilization will change. According to Gibbons et al (1994) a new mode of knowledge generation and utilization, called Mode 2, is emerging in addition to the traditional one called Mode1. While in the latter the creation and utilization are clearly separated both chronologically and institutionally, in the former there is a continuous interaction between the two processes, which leads to the need for different institutional and organizational forms. Networks could then be a form of industrial organization appropriate to a knowledge based society.

Biotechnology is one of the fields that is at the forefront of the creation of a knowledge based society. This seems somewhat paradoxical, since it could be maintained that biotechnology is one of the oldest technologies used by mankind. Beer and yogurt making constitute two typical examples. However, modern biotechnology has been substantially changed by the advent of molecular biology, a new discipline which was founded in the 1930s based on the attempt to apply to biology the methods of physics. In the mid 1970s two discoveries, recombinant DNA and monoclonal antibodies, transformed a scientific discipline with a brilliant if distant future into a seedbed of industrial applications. Accordingly some authors now call this latest vintage of biotechnology third generation, to distinguish it from the completely empirical first generation and from the second generation, which began with the production of antibiotics. Second generation biotechnology used scientific methods but it did not have the knowledge required to change the genetic make-up of organisms. Such knowledge was only provided in a systematic way by molecular biology. In the mid 1970s very few research institutions did research in molecular biology and they were mostly in the USA. The industrial firms that in principle could have exploited molecular biology did not have a knowledge base or an absorptive capacity for it. Their competencies and knowledge bases were concentrated in more traditional disciplines such as organic chemistry or microbiology. In fact, this lack of knowledge hampered firms' recognition of the opportunities that could have been offered by molecular biology.

Biotechnology is not an industrial sector but a scientific field underlying a number of industrial sectors (pharmaceutical, agriculture, food, environment etc.), here called the biotechnology based sectors. Industrial applications of biotechnology are highly dependent on

new scientific developments, even on those that are the result of basic research. Although the lead times between the discovery of new knowledge and its final embodiment in new products may be very long, the time between the creation of new knowledge and the funding of industrial research aimed at its applications is in general very short. Basic research is not exclusively confined to public research institutions, but it is also carried out by firms. Thus, both for what concerns its intensity of knowledge utilization and for the mechanisms employed, biotechnology seems to be a very good example of industrial organization in a knowledge based society. Of course, the conclusions reached in this paper will depend on the specificity of biotechnology, but they will also have some general significance for the analysis of a knowledge based society.

The earliest analyses of networks of collaboration pointed to the possibility that they are only a temporary form of industrial organization. Such temporary character could be the result of discontinuities in knowledge generation, for example of the emergence of a new technological paradigm. It was argued that large diversified firms (LDFs) were committed to the old paradigm, in which all their competencies were concentrated, and that they could not easily internalise the new knowledge. Alternatively, LDFs did not have the absorptive capacity required to internalize the new paradigm and they were not capable of constructing it rapidly. A new type of industrial actor, small high technology firms, arose to bridge the institutional gap between public research institutions and LDFs. In the specific case of biotechnology such firms were called dedicated biotechnology firms (DBFs). DBFs were expected to act as intermediaries between LDFs and public research institutions. In the rest of the paper the DBFs performing this role will be called *translators*. In the course of time by collaborating with DBFs and with public research institutions, LDFs could construct a knowledge base and an absorptive capacity in biotechnology. Once this happened the role of DBFs would have become redundant and industrial organization would return to the traditional dichotomy between the market and hierarchical organizations.

As it was previously pointed out, the rate of creation of inter-institutional collaborative networks has been steadily increasing all throughout the 1980s and 1990s. Thus either LDFs have not internalized the new paradigm constituted by biotechnology or a new role for DBFs has emerged in innovation networks. The analysis of this problem constitutes one of the main objectives of the present paper. In the paper a second role for DBFs and thus for networks is

discussed. By the end of the 1980s LDFs in a number of industrial sectors had acquired a knowledge base in molecular biology (see for example Grabowski, Vernon, 1994) and yet they continued to enter into collaborative agreements with DBFs. In this paper we hypothesize a second role for DBFs, linked to the extremely rapid rate of creation of new knowledge. Even if LDFs have acquired an absorption capacity for it, the sheer rate of advance is such that no LDF could keep up with it all. LDFs might thus use agreements with DBFs within networks in order to keep abreast of new developments that could turn out to have important economic applications. The alternative course of action for an LDF would be to invest in research in the same fields of biotechnology. However, with a very high rate of growth of knowledge this strategy would involve a very heavy, irreversible and risky commitment. The collaboration with DBFs constitutes a more flexible and reversible strategy. It is to be observed that this role does not involve a qualitative difference in LDFs' ability to understand molecular biology, but only the attempt to reach a better trade-off between readiness to action if promising developments were to emerge in new subsets of the biotechnology knowledge space and the sunk costs that need to be faced in order to keep these windows open. Furthermore, it must be remembered hat the competitive advantage of LDFs is not constituted by their ability to understand new knowledge but by their capacity to combine the different competencies and complementary assets required to produce a final product. This second role that can be played by DBFs will be called of *explorers*.

In what follows we analyze biotechnology innovation networks with special emphasis on two types of actors, LDFs and DBFs. We compare the advantages and disadvantages for firms of going alone strategies and of networking strategies, taking into account the environmental factors influencing the formation of links between actors. Network formation will be shown to display a dynamics going beyond a first wave of networks and leading to a re-organization of the partnerships involved.

2. The Simulation Model

Before beginning to explain the basic structure of our model[1] some remarks with respect to the methodological framework we are adopting are order. In particular, we are going to use the methodology of the so-called *history friendly models*, recently introduced by Nelson,

Winter, Malerba and Orsenigo (1999). History friendly models are designed to capture, in a stylized form, the mechanisms and factors affecting industry evolution, technological advance and institutional change detected by empirical scholars of industrial economics, technological change, business organization and strategy, and other social scientists. Thus history friendly models can be considered the natural extension to modeling of qualitative and appreciative theories.

Obviously even in an evolutionary approach simulation models have to introduce a certain degree of abstraction and cannot reflect reality in all its complexity. The mechanisms built in the formal model have to be transparent enough, so that the analyst can figure out what are the causes of the observed effects. Therefore, in the first step of our modeling effort we have to carefully single out the relevant actors, bring together variables which are effective in the same direction and combine important developments and possibilities of action. Nevertheless, adopting the approach of evolutionary economics allows us to put emphasis on crucial features of innovation processes, such as non-linear dynamics, heterogeneity and true uncertainty, which are beyond the scope of traditional approaches.

In the following the basic building blocks of our modeling conception are introduced. In particular, we focus on the way we present the different agents in our model, the way we capture innovation processes, what we consider to be the prerequisites and consequences of networking as well as the representation of the economic realm in our simulation.

2.1 The Representation of Agents in the Model

Let us begin with the implementation of the agents. The agents we are explicitly considering in our model are Large Diversified Firms (LDFs) and Dedicated Biotechnology Firms (DBFs). They are described in terms of their competencies and capabilities. DBFs possess technological competencies while LDFs possess a mixture of economic and technological competencies.

[1] A comprehensive formal description of the simulation model can be found under http://www.uni-

- *Competencies*

Technological competencies are considered to be the components of the knowledge base required for building up production and innovation capabilities in a specific technology. In other words, before firms are able to develop new marketable outputs they have to develop the respective bio-technological competencies. Furthermore, technological competencies alone are not sufficient to achieve economic success with a new product. Economic competencies are necessary in order to successfully produce and market a new commodity. Examples of these economic competencies are experience in clinical trials, distribution channels and so on. Clearly this representation is somewhat simplified. The full range of competencies required by firms to conceive, develop, produce and market new products is very large and heterogeneous. However, given that most DBFs at the beginning of their life cycle do not possess any economic competencies and that LDFs in the 1970s were generally unable to acquire the knowledge required to use modern biotechnology, the representation in terms of technological and economic competencies adequately describes the difference between our two main agents. Moreover, we could consider technological competencies as the core competencies (Prahalad, Hamel, 1990) of firms and economic competencies as a large part of the complementary assets (Teece, 1986) required to produce and market a product.

The building up of technological B_i^t and economic competencies EC_i^t is described in equations (1) and (2) respectively:

(1) $$B_i^t = \frac{1}{1+\exp(const - NCOP_i^t \cdot t^{BIO})},$$

(2) $$EC_i^t = \frac{1}{1+\exp(const - NCOP_i^t \cdot t^{ECO})}.$$

B_i^t := technological competencies of firm *i* at time *t*
EC_i^t := economic competencies of firm *i* at time *t*
$NCOP_i^t$:= number of cooperations of firm *i* at time *t*
$t^{BIO/ECO}$:= time spent in particular activity

Figure 1 shows this function graphically for the case of technological competencies. In the early phases the building up of the knowledge base is a difficult process and progress is hard to achieve. However, after having developed a certain knowledge base it becomes easier to learn even more (*threshold effect*). Finally, marginal progress becomes progressively more

difficult as the knowledge frontier existing at a given time is approached. A function of this type implies variable returns to investment in the creation of new knowledge within a given field: very low at the beginning, positive and growing in the intermediate phase before diminishing returns set in as the potential of the new field has been exploited. The process of building up a knowledge base in biotechnology is supported by cooperative arrangements with firms who are already active in this field - an important part of the respective knowledge base is transferred by networking.

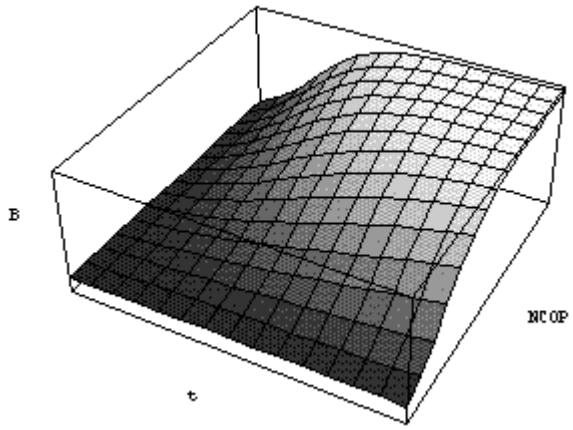

Fig. 1 Building up of a knowledge base in biotechnology

- *Discrimination between LDFs and DBFs*[2]

The two populations of firms which can be observed in the biotechnology-based industries can be distinguished on the basis of their relative technological and economic competencies. The first population of firms is that of LDFs, for example the large established pharmaceutical firms. Until the end of the 70s their research and development was mainly embedded in the paradigm of traditional organic chemistry. The coming up of the new bio-technological paradigm meant a *competence-destroying technological progress*[3] for them, as most of their competencies were threatened by the new ones. In our simulation this group of firms is represented in the starting distribution with well developed economic competencies but with almost no technological competencies in biotechnology.

[2] See e.g. Acharya, R. (1999), pp. 15 ff.
[3] Tushman, M. L., Anderson, P. (1986).

In the second population we find small start-up companies, often university spin-offs specialized in the biotechnology field. This group of firms, the so-called dedicated-biotechnology-firms or DBFs, by their very nature have highly developed technological competencies, but almost no economic competencies. When they start their existence DBFs depend on external funds for research and development. Accordingly, in our starting distribution they are represented just as having no economic competencies but highly developed technological competencies.

- *Venture Capital Firms and Universities*

In addition to these firms that we are explicitly taking into account, we also consider two further important groups of actors in our model: public research institutes or university labs and venture capital firms. In order to keep our model simple their behavior is not explicitly analyzed, but they are considered as an important component of the external environment of biotechnology firms. For example, in order to acquire the funds necessary to undertake R&D a DBF can cooperate either with a LDF or with a venture capital firm; similarly, the cooperation of a LDF with a DBF or with a public research institute leads almost to the same consequences for the LDF etc.

- *Capabilities*

Drawing on their competencies firms can accumulate technological capabilities in specific fields which allow them to explore the technological opportunity space. The firms in our model act in an environment which continuously force them to be engaged in such R&D processes. Not to innovate means to fall behind in the competitive environment of biotechnology. In order to increase the probability of an innovation firms accumulate technological capabilities in the course of time according to equation (3):

(3) $$C_i^t = \sum_t r_i^t \ .$$

C_i^t := capabilities of firm i at time t
R_i^t := R&D investment of firm i at time t

Together with the technological competencies B_i^t the technological capabilities determine the probability of an innovation Pr_i^t which is described in equation (4):

(4) $$\Pr_i^t = 1 - \exp(-B_i^t \cdot C_i^t) .$$

Pr_i^t := innovation probability of firm *i* at time *t*

To consider the intrinsic uncertainty of innovation processes the innovation probability of a firm is matched every period with a *Poisson-distributed random number* whose mean value is asymptotically reached by Pr^t_i. A firm is successful in its innovative efforts only if the innovation probability Pr^t_i is above the random number. [4]

However, technological capabilities are not sufficient for the successful introduction of a new product. To do this a firm also needs to acquire economic capabilities E^t_i as well as the economic competencies EC_i^t, e.g. in production, legal approval, marketing, distribution etc. The economic capabilities are accumulated in the same way as the technological capabilities and are responsible for incremental innovations on new technological trajectories opened up by a product innovation.

- *R&D decision rules*

The investment in R&D is no longer guided by an optimization calculus, but by a routinized behavior, as innovation goes hand in hand with true uncertainty.[5] Firms adopt certain rules, for example, *invest x% of your turnover in R&D, retain x% of your financial support in order to build up an own capital stock* etc. In the same way the distribution amongst different activities (e.g. between investing in the building up of technological or economic capabilities) is captured by referring to routines.

2.2 Networking

In order to carry out their innovation processes firms can choose different strategies. They can either decide to *go-it-alone*, which means not to draw on external knowledge sources and not to share their own new know-how with potential competitors, or they can decide to cooperate with other actors and build up collectively the new capabilities necessary for the introduction of a new commodity. Innovation networks emerge by this mutual cooperation, which gives

[4] In this respect, a major methodological advantage of simulation studies shows up in the construction of the innovation processes. Whereas in traditional optimization models there is no difference between the modeler and the modeled agents, simulation analysis allows programming random numbers their statistical distribution is unknown to the agents in the model (see Pyka, A. (1999, pp. 189 ff.)).

[5] E.g. Nelson, R. R., Winter, S. G. (1982), p. 132.

rise to channels for knowledge flows between the firms participating in the network. In particular, we are considering the evolution of innovation networks at three levels within the model: the environmental conditions favoring or inhibiting the growth of networks, the individual decisions of firms to cooperate or not, and a matching process bringing together firms willing to cooperate. This process creates a population of networks with its own dynamics. The formation of any network constitutes an act of birth or entry into the population. Conversely, the disappearance of a network constitutes an act of death or exit. The dynamics of birth and death of networks will be determined by the specific features of each network and by some features of the external environment. Accordingly we can calculate the probabilities of birth (P^t_B) and of death (P^t_D) that will contribute to the net probability of network creation (P^t_N).

- *Probability of Birth*

A number of environmental factors increase the probability of birth innovation networks. The growing complexity of innovation processes as well as a high degree of technological uncertainty play the most important role. Every time a firm is successfully introducing an innovation the number of knowledge fields *#KB* is assumed to grow. Given the *complementary and combinatorial nature*[6] of biotechnology, the technological space Ω, defined as the number of possible combinations of knowledge fields, increases in a nonlinear way (equation (5) and Fig. 2).

$$\Omega = \frac{\#KB!}{2!\#(KB-2)!} \tag{5}$$

Ω := technological space
#KB := number of different knowledge fields

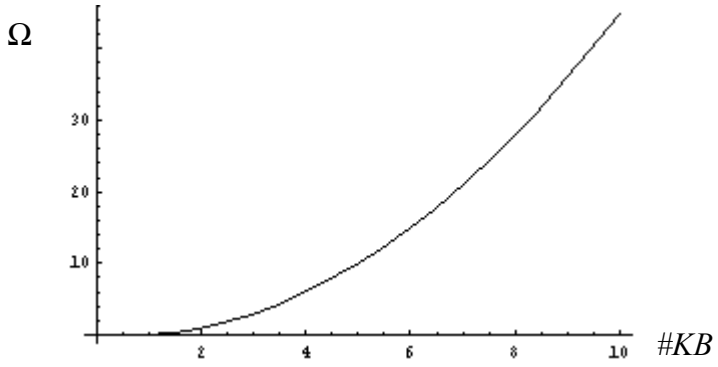

Fig.2: Increasing technological Space

Especially in the early phases of a technological life cycle (*TLC*) this increasing complexity is combined with a high technological uncertainty because specific research techniques or heuristics – e.g. how to handle this complexity - are not yet developed. In the model the phase of a technological life cycle is approximated very roughly by the average age of the different commodities on the product markets.

Additionally, R&D networks are dependent on a number of core technologies or core/central actors (M_N), who play a crucial role for the establishment of the networks.[7] In our model the population of LDFs is supposed to play this role. These factors influence the probability of birth of innovation networks P^t_B and are summarized in equation (6). The functional form of Eq 6 implies a sigmoid relationship, shown in fig. 3.

(6) $$P_t^B = \frac{1}{1+\exp(const - \frac{1}{TL}\cdot\frac{M_N^t}{N_N^t}\cdot\Omega)},$$

P_t^B := probability of birth of innovation networks
TL := age of technology life cycle
M^t_N := number of core actors
N^t_N := number of networking firms.

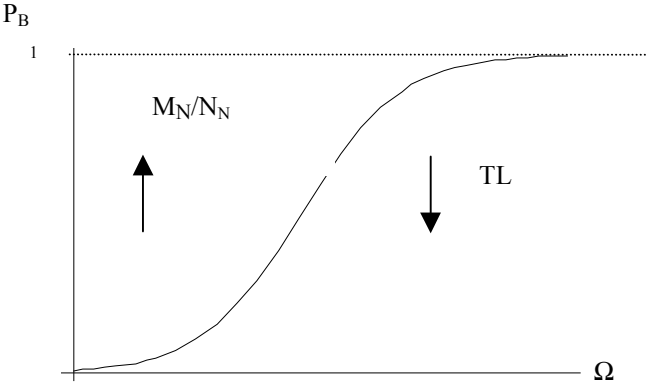

Fig.3: Probability of birth of innovation networks

In other words, the probability of birth of innovation networks increases with the complexity of the technological space and with the number of core actors, and it decreases with the age of the technological life cycle.

[6] Staropoli, C. (1998), p. 15.
[7] See e.g. Saviotti (1996), pp. 36-37.

- *Probability of death of innovation networks*

In addition to the previous network supporting effects, other influences decrease the probability of network formation, thus leading to network death. First, the degree of competition is crucial in this respect. In our model we use as an economic framework a heterogeneous oligopoly. We consider the degree of substitutability of the final products as a measure for the intensity of competition. We use the variance σ_a^t of the variables describing a firm's relative product quality a_{ij}^t as a measure of the product heterogeneity: the higher this variance, the lower is the competitive threat between the firms. Furthermore, we can expect demand saturation to decrease the rate of growth of the respective markets and thus the scope of cooperative R&D. In this phase of the industry life cycle minor improvements of the technology could lead to considerable advantages for a single firm. To capture this influence, we draw again on the life cycle *TLC* and assume that on later stages of this life cycle the rate of growth of demand is likely to decrease. Finally, the techno-economic performance of the k network members, again approximated by the relative quality $\underset{k}{a_k^t}$ compared to the average performance of all firms $\bar{a}^t$, is itself an indicator for the attractiveness of joining a network. In cases where the performance of network members is below average performance of the whole firm population, the networking strategy significantly loses attractiveness. These factors are summarized in equation (7) in the probability of network death P^t_D:

$$(7) \qquad P_D^t = \alpha \cdot \left| \bar{a}^t - \underset{k}{a_k^t} \right| \cdot \frac{1}{\sigma_a^t} \cdot TL \,,$$

P^t_D := probability of network death.

$\bar{a}^t$:= average quality at time t

$\underset{k}{a_k^t}$:= average quality of cooperating firms

σ_a^t := heterogeneity on product markets.

The net probability P^t_N of network creation at any given time is determined by the balance of births and deaths. The value of P^t_N in our firm population determines the decision of firms to engage or not to engage in cooperation:

$$(8) \qquad P_N^t = \frac{1 + P_B^t - P_D^t}{2};$$

P^t_N := net probability of innovation networks.

In cases where P^t_N is below 0.5, $2\cdot(0.5- P^t_N)\cdot 100\%$ of firms previously engaged in cooperation turn away from cooperation, if P^t_N is above 0.5, $2\cdot(P^t_N-0.5)\cdot 100\%$ of firms engage in further networking. Accordingly, the probability P^t_N determines the number of firms who decide to cooperate or not in every period t.

- *Networking Decisions*

Next, the firms have to decide whether they want to cooperate or not. Generally two forms of cooperation are possible:

i) *cooperation focussing on complementary assets*, i.e. firms are induced to cooperate to acquire technological or economic competencies that they do not posses but that they judge crucial for their economic success.

ii) *cooperation focussing on general complementarities* (i.e. the bundling of R&D efforts in a specific direction) *and synergies* (i.e. detecting potentials for cross-fertilization by the combination of different technological capabilities). It is to be noted that in this case cooperating firms can have competencies with a degree of overlap than in case i). For example, it is possible to conceive a division of labour in which firms pursue similar objectives using similar competencies, but they collaborate in order to speed up the innovation process and to spread the relative uncertainty over the network.

In the form of cooperation i) DBFs play the role of *translators*, while in form ii) they play the role of *explorers*. Consequently, the networking decision depends on the respective competencies and capabilities that firms have accumulated. For example, a small start-up DBF in its early phases is not able alone to raise funds for R&D and necessarily has to look for a partner in order to obtain funding. In the same way established LDFs which want to become active in the promising fields of biotechnology but have no internal technological competencies need collaboration partners experienced in these fields. On the other hand, firms with highly developed capabilities would not run the risk and share their knowledge with potential competitors in the stages immediately preceding the introduction of an innovation. The networking decisions are summarized in figure 4.

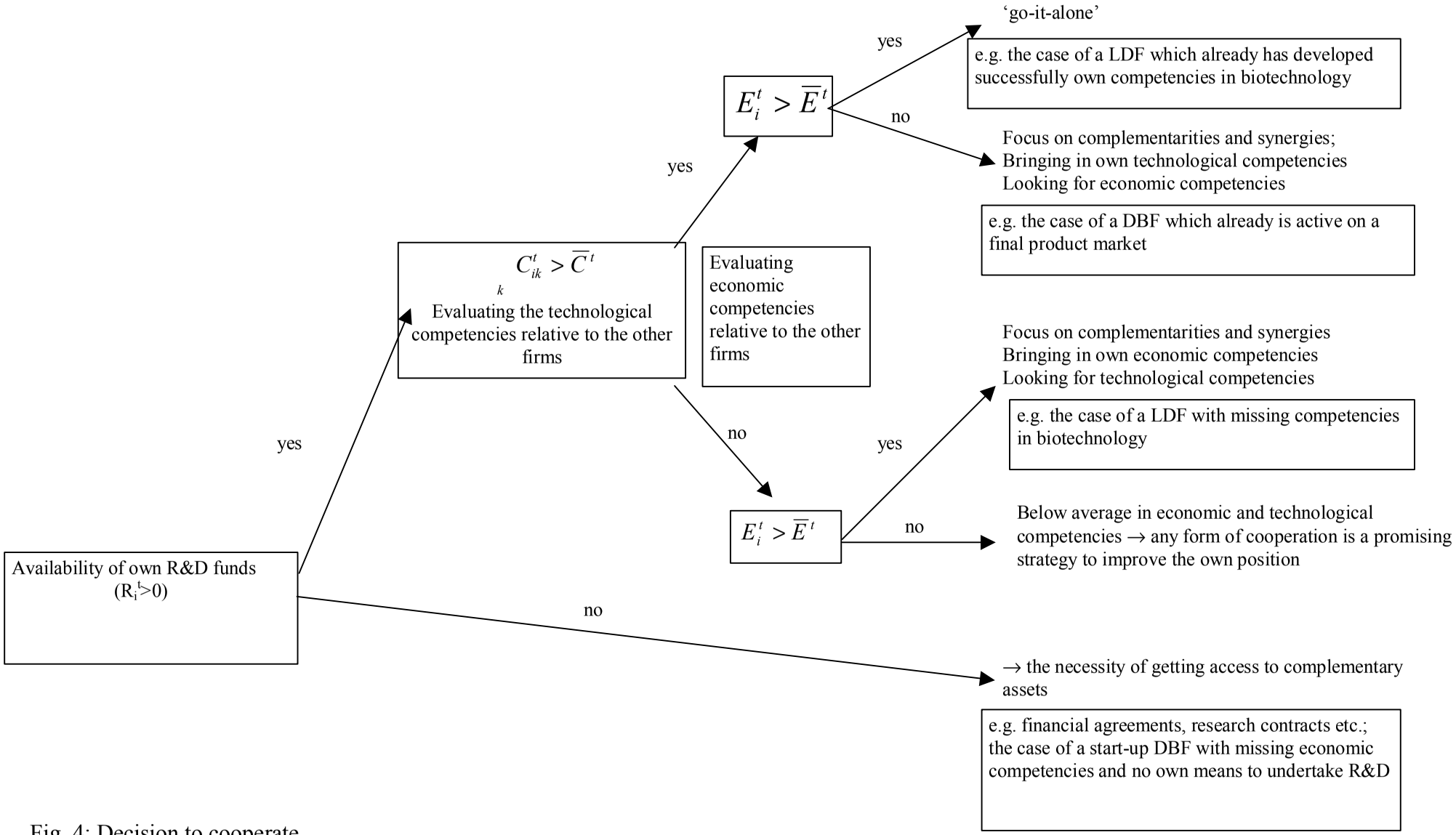

Fig. 4: Decision to cooperate

- *Matching Process*

Finally, we have to decide on the mechanism which brings together different firms willing to cooperate. Although different mechanisms are conceivably we think that a mechanism which could be labeled *success-breeds-success*[8] is best suitable for our purposes. Success-breeds-success means that firms would tend to pick collaborators with the highest technological and/or economic capabilities. We are here assuming that firms are in able to advertise their own capabilities and to value those of potential cooperating partners. This seems to be a realistic assumption, especially in the biotech industry, where firms are ranked on the basis of their technological performance, which is advertised by press announcements, publications, patents and even by the professional standing of the scientists hired by firms, including the Nobel prize winners present in their scientific committee.

2.3 Networking Consequences

After having introduced the way firms get together in innovation networks we now have to focus on the consequences of networking. By entering into a collaboration firms are exchanging their know-how. This means that firms can benefit from the efforts of other firms in order to build up their own capabilities.

- *Absorptive Capacities*

The extent to which a firm can benefit from the knowledge flow available by cooperation depends on its *absorptive capacity*[9]. In turn, absorptive capacity is expected to increase with the firm's previous experience in cooperation. This is represented by the *experience term* δ_i^t, which describes the amount of external competencies a firm is able to integrate – a kind of *absorptive capacity in networking*. This means that external knowledge is not easily integrated within the own knowledge stock, but certain prerequisites have to be fulfilled and a minimum amount of experience is necessary. This also means that the amount of knowledge which flows within the network is severely limited. The building up of the absorptive capacity is given in equation (9) where we draw on a firm's experience in cooperation as an approximation:

[8] Phillips, A. (1971).
[9] See Cohen/Levinthal (1989) and Cantner/Pyka (1998).

(9) $$\delta_i^t = \alpha \cdot NCOP_i^t ,$$

δ_i^t := absorptive capacities of firm *i* at time *t*.

- *Coordination Costs*

Cooperation also involves costs, which reduce R&D investments. If it were not for these costs we would get the unrealistic situation where everybody cooperates with everybody else. These costs together with the prevailing environmental conditions determine the potential number of collaborations in the industry while the decision rule described above determine the form of cooperation chosen. However, as in reality not all firms are engaged in cooperative relationships with all other firms, there also have to be certain limits to a cooperative strategy. An important factor limiting the growth of networks are the coordination costs, cr^t_i , which immediately appear together with cooperative R&D. We assume these coordination costs to be constant and equal for every form of cooperation.[10] These costs of cooperating with other firms decrease the budget for direct research r^t_i, since there is a trade-off between engagement in acquiring internal and external knowledge. Equation (10) shows this constraint:

(10) $$R^t_i = r^t_i + NCOP_i^t \cdot cr^t_i;$$

R^t_i := gross R&D budget of firm *i* at time *t*
cr_i^t := coordination costs.

Therefore, in deciding whether to engage in cooperative R&D or not firms also consider these coordination costs cr^t_i. For a firm *i* engaged in several cooperative relationships, coordination costs amount to $NCOP_i^t \cdot cr^t_i$. They should not exceed a certain percentage η of the gross R&D-budget R_i^t . Accordingly, the following decision rule (11) has to be considered by a firm additionally to the decision which specific form of cooperation it prefers:

(11) $$\begin{array}{l} \textit{if } NCOP_i^t \cdot cr_i^t \geq \eta \cdot R_i^t \quad \textit{then no further cooperation is intended} \\ \textit{else } NCOP_i^t \cdot cr_i^t < \eta \cdot R_i^t \quad \textit{then new cooperations are possible} \end{array}$$

- *Financial Flows*

Start-up DBFs with missing economic competencies cannot finance their own R&D and are obliged to find a cooperation partner. In this case an LDF cooperating with a DBF is supposed

to provide the required research funding. For a DBF *i* cooperating with an LDF *j* this means that its gross R&D budget R_i^t is financed in a part by the other firm's R&D budget. Of course, the DBF *i* will also retain a certain percentage κ of the funds as profits ($(1-\kappa)R_i^t = r_j^t$) thereby acquiring means which in future allow it to undertake R&D more independently. In the case of a successful innovation, the intellectual property rights belong to the LDF *j* which can start with the production on the final good markets.

Another possibility for DBFs to acquire R&D funds is to apply for venture capital, for which we assume an exogenous supply $VC^t = VC_0 \cdot (1+\alpha)$ growing with the rate α. Accordingly the number of firms which can be financed by venture capital is $n_{VC}^t = \frac{VC^t}{\overline{R}}$ ($\overline{R}$:= constant periodically paid amount of money). Also, we assume a constant period t^{VC} , so that the overall credit for a firm is $t^{VC} \cdot \overline{R}$. Access to venture capital is competitive. Amongst the firms applying only those which show the best record in bio-technological capabilities C_i^t as well as in previous cooperations $NCOP_i^t$ are funded.

- *Knowledge Flows*

One of the most important advantages of participating in an innovation network is the access to channels of knowledge flow. External knowledge exerts an impact on the innovation probability function and depends on the amount of absorptive capacities, as well as on the technological capabilities of the cooperating firms. For a firm participating in an innovation network and collaborating with *k* other firms the innovation probability function gets modified:

$$\text{(12)} \qquad \Pr_i^t = 1 - \exp\Big| - B_i^t \cdot C_i^t + \delta_i^t \cdot \underset{k}{} C_k^t \Big|,$$

C_k^t := capabilities of k cooperation partners.
k

Thus, participating in an innovation network exerts a threefold influence: first, the research budget of a firm is reduced due to coordination costs and, in the case of a cooperation with a DBF, by the financial support of this firm. Second, absorptive capacities are positively influenced by entering into a new collaboration as the experience with integrating external

[10] One also can consider the coordination costs to depend on the number of cooperations i.e. first they are decreasing (economies of scale in cooperating) and then they are increasing again after having passed a certain threshold.

knowledge is increasing. Finally, external knowledge becomes available via knowledge flows between the collaborating firms.

2.4 Competition Processes

The innovative activities of firms are undertaken in an economic environment which is characterized by a certain degree of competition. On the one hand, the firms offering products on the final market compete with each other in attracting demand. Also, those firms whose aim is to offer new technological knowledge compete in a particular way with other firms in acquiring the respective funds. Finally, firms who want to buy the respective knowledge also compete for the cooperation with the most attractive research laboratories.
The two levels of competition take place in two different market: the market for final products and the market for knowledge. Of course, we know that markets for knowledge cannot exist due to their imperfections. However, the existence of DBFs, which very often though not always function as contract research organizations, implies that within particular circumstances such imperfections can be reduced to a level where a market for knowledge, although very imperfect, can exist. In fact, cooperation often exists between firms operating in different markets (e.g. for final goods and for knowledge) and thus being in a complementary relationship. Of course, this does not exclude that firms operating in the same market can cooperate.

On the final markets firms compete in terms of prices and quality which are, in a dynamic context, determined by their innovative success. Generally, one would expect that a successful innovator will be able to attract demand away from its competitors because consumers can choose between several goods. These substitution effects are due to price and quality changes which are the results of the following actions and reactions:

- Introducing a new product with improved quality characteristics creates additional demand allowing the innovator to charge higher prices.
- In the case of an introduction of a new product by two or more vertically integrated firms who cooperated in the R&D stages the increase in demand is divided between the involved firms.

- As a reaction to this quality-induced substitution effect, non-innovators in related markets lower their prices in order to keep the loss in demand as small as possible.
- Exploitation of technological opportunities of an already existing technology allows the respective innovator to reduce its price, thereby increasing the demand for his product;
- As a reaction, non-innovators could fight their loss in demand by also lowering their prices, thereby, however, reducing their profit margin.

Another form of competition takes place in finding the most attractive network partner which is described with the help of the notion *success-breeds-success* (see above). Firms engaged in the search for a cooperation partner will match with those which show either the most developed technological or the most developed economic competencies.

By choosing a heterogeneous multi-product oligopoly[11] we allow for the relationships described above. Firms are offering their goods on a heterogeneous product market. By an innovation and the introduction of a new commodity on these markets the relative market share of the already existing goods gets eroded. By this, we also generate the endogenous incentives of the firms to engage in innovation, as they cannot survive in the long run by relying on their original established positions which are continuously threatened by the innovative actions of their competitors.

2.5 The Basic Structure of the Model

The following flow chart summarizes the basic structure of our model.[12] Starting with firms and industry characteristics of the previous round firms have to decide whether to go-it-alone or to cooperate. They are influenced by environmental conditions either favoring or inhibiting the growth of networks. After having found a cooperation partner in the matching process the firms enter the innovation stages which on the one hand influence the industry and firm characteristics, and on the other hand the market outcomes of the next round.

[11] See Kuenne (1992) and for an application in a simulation model Cantner/Pyka (1998).
[12] In the appendix a comprehensive description of the simulation model following the different stages of the flow chart can be found.

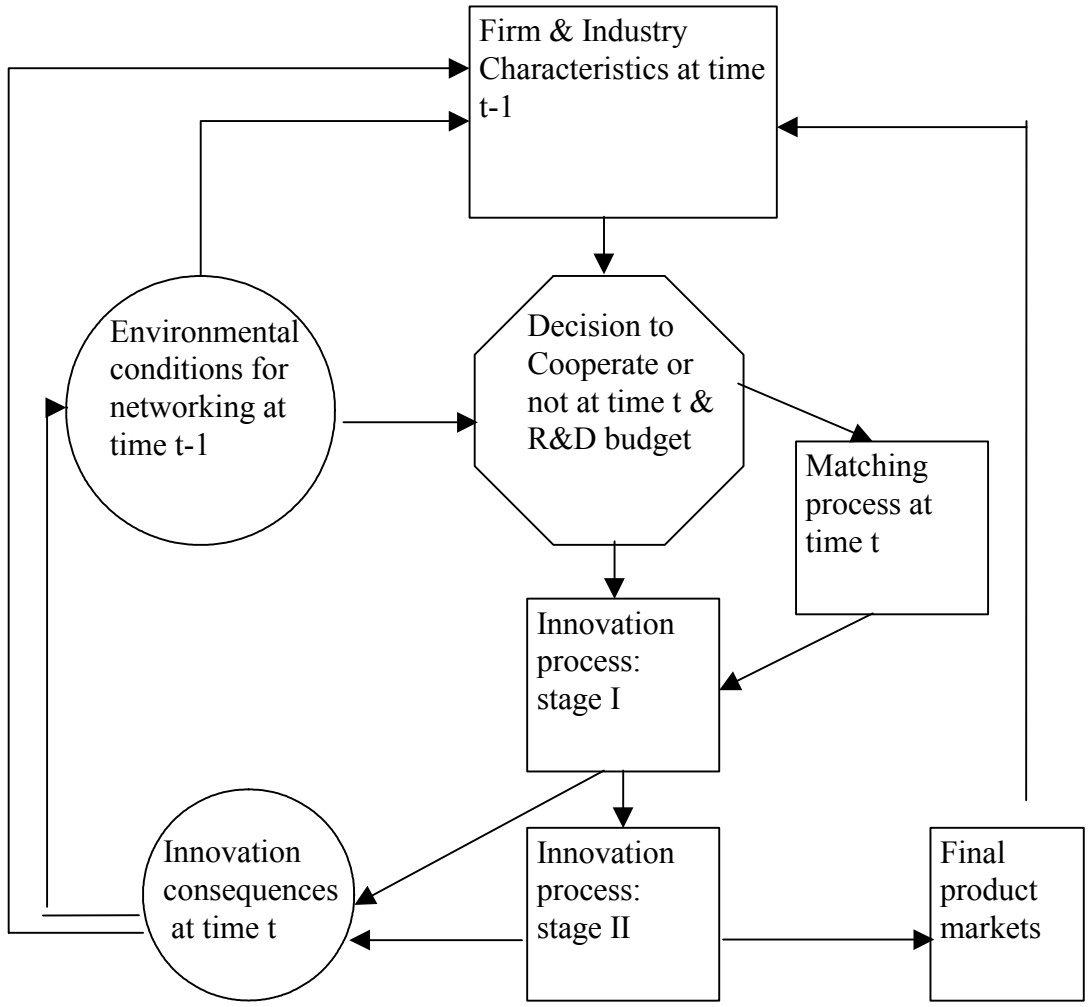

Fig. 5: Flow chart

3. The models results

The first simulation experiments are dealing with a purely theoretical case where we are considering a population of 12 firms, four of them being LDFs and eight DBFs. This step seems to be necessary to introduce to the model's results. Therefore, these first simulation results have to be seen as interim results demonstrating the basic functioning of our model as well as the plausibility of the implemented relationships and dynamics. In section 4 the network related results are then compared to real figures in a history friendly manner.

Before analyzing the development of the network structure we begin with the environmental conditions and some figures describing the typical course of single firms. In figure 6 we see how the number of successful innovations develop.

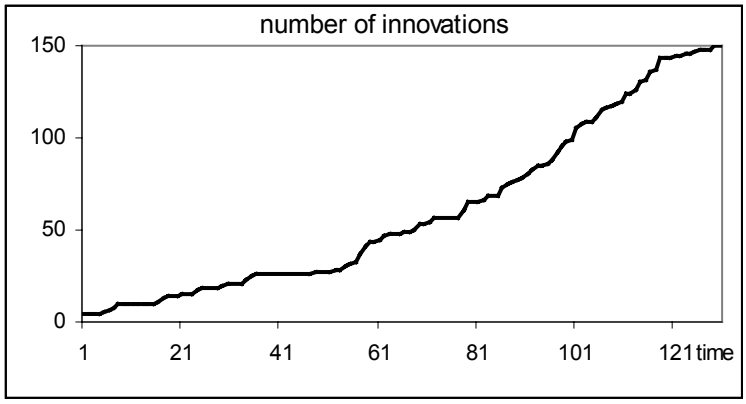

Fig. 6: Number of innovations

The first 50 periods are characterized by a slow introduction of innovations. During these periods firms are mainly occupied with building up the prerequisites to cope with the technological progress. The rate of creation of innovations starts accelerating only after period 45. During this period firms build up the required technological competencies and experience in networking (*absorptive capacities*). The introduction of innovations accelerates even further around period 55, where nearly after every second period a new commodity appears on the markets.

In figure 7 we find the development of the average age of the industry life cycle. The average age of the population of innovations introduced increases at a faster pace during the first 40 periods due to the slow rate of introduction of novelties. However, as innovative activity starts accelerating at the end of this period, the average age of innovations starts oscillating around a mean of 40. The aging process is thus reduced and with it the negative impacts on the incentives to collaborate. Later on, around period 165 the average age is increasing again which is caused by the co-existence of a larger variety of commodities introduced at different times. Here we find again the alternating sequence of low, growing and diminishing returns already found for the probability of network creation.

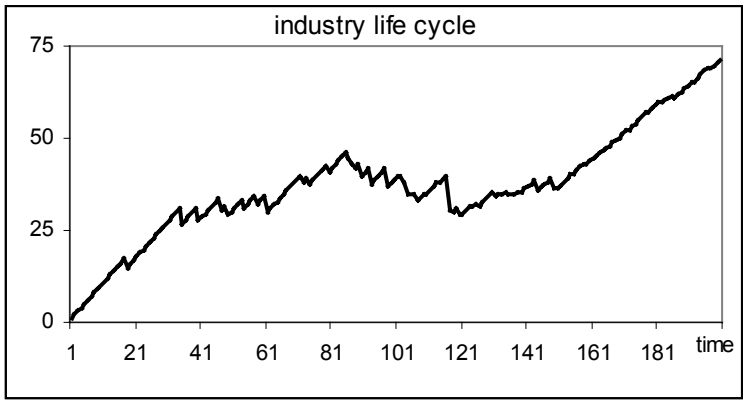

Fig. 7: Average age of the industry life cycle

Both effects determine the environmental conditions for networking. During the first 40 periods the combination of an increasing age of the industry life cycle and a relatively low rate of introduction of innovations worsens the environmental conditions for networking. After period 60 the increasing rate of creation of innovations favors the growth of networks, which can mainly be traced back to an increasing technological space. This effect even outweighs the further aging of the industry life cycle in later periods.

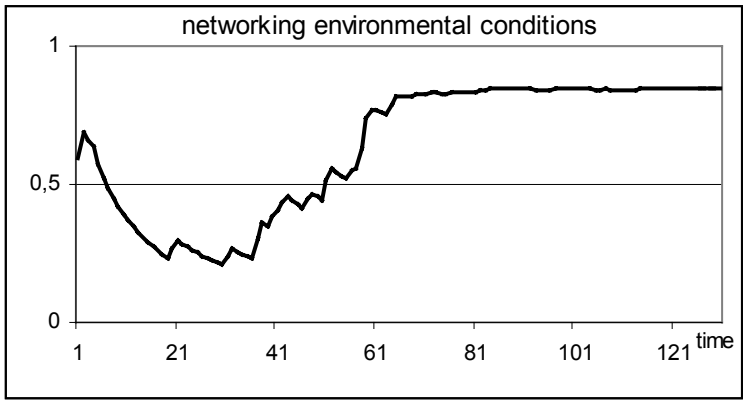

Fig. 8: Environmental conditions

Figure 9 shows the corresponding development of the network density. After a first increase in the density the dynamics of network growth come to a rest after around 10 periods, and even starts slightly decreasing until period 45. However, after that period network density starts increasing again, until it begins to oscillate around a value which is twice the average at the beginning. This can already be interpreted as evidence for the changed role of DBFs, which in the first periods find temporary collaboration partners in the population of LDFs. These collaborations are mainly oriented towards bridging the gap between the new bio-technologies

and the established industry. Later on, however, the DBFs are finally considered as an extension of internal R&D facilities, allowing LDFs to explore a wider opportunity space. Therefore, collaborations become more frequent and lasting in more advanced states of the industry evolution.

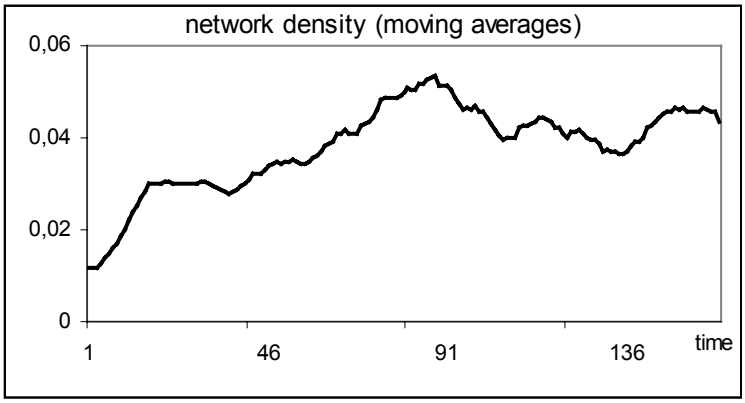

Fig. 9: Network density

This interpretation of the changed role of DBFs is supported when we analyze the developments at the firm level. Fig. 10 shows the process of building up of technological competencies by four LDFs. All of them begin with no technological competencies in biotechnology, but have to build them up by collaborating with firms specialized in these fields, namely DBFs. Two of the firms engage early in collaboration (thin curves) while the other two (bold curves) start only at a later stage. The two firms engaging early in collaboration improve more rapidly their competencies and accordingly reach sooner the second branch of the learning curve, with positive but decreasing rates. These firms develop considerable competencies in biotechnology more than 20 periods earlier than the two slow ones. We can observe that both for the fast and slow collaborating LDFs the shape of the learning curve is sigmoid and that the saturation level seems to be the same. From these results it seems that no penalty needs to be paid for late entry. While this result my depend on some features of our model that deserve further investigation, they are limited to learning and they do not take into account possible barriers of other types that might be created during the technological life cycle.

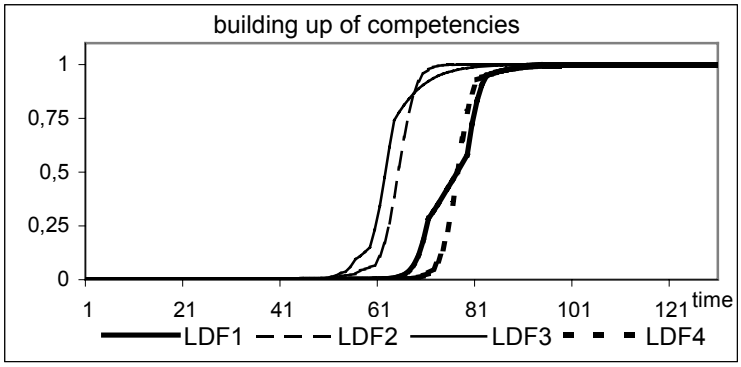

Fig. 10: The building up of technological competencies by LDFs

This building up of competencies has an immediate effect on the innovation probability, which is guided by the exponential relationship of equation (12) with positive but decreasing rates. Figure 11 shows the development of innovation probabilities of three DBFs (thin lines) and three LDFs (bold lines) in the starting periods.

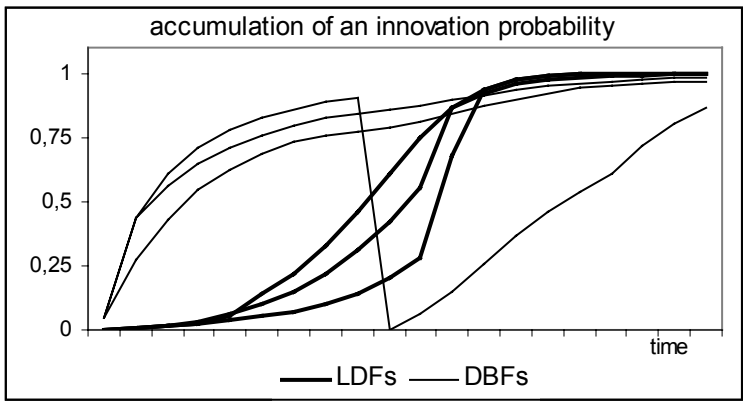

Fig. 11: Accumulation of innovation probabilities

The DBFs are able to accumulate quickly their innovation probabilities depending on their success in acquiring resources for R&D through. One of the three firms is even able to introduce a first innovation and to begin developing a second one go within the period shown in figure 11. Compared to DBFs, the population of LDFs is confronted with severe difficulties in exploiting their first trajectories. They need a considerably longer time to build up their technological competencies to the level required to innovate. Of course, this varies depending on the LDFs networking strategy. However, in general LDFs need more time to reach promising innovation capabilities. In the early period of biotechnology they depend on collaborations with firms from the population of DBFs in order to access the technological space offered by this new field.

In section 2 we argued that the persistence of innovation networks in the biotechnology-based industries could not be explained by means of only one role played by DBFs. Whereas in early stages the small technology-oriented firms play the role of *translators,* facilitating the absorption of the new technologies by LDFs, in later stages they become more emancipated as collaboration partners. This means that they do no longer serve solely as institutions transferring knowledge between academic and industrial research, but become explorers, allowing LDFs to investigate a broader technological portfolio in an increasing complex technological opportunity space. This changed role of the DBFs accordingly has to be observed also in the simulation as a development which endogenously takes place within our model's specification. In figure 12 we therefore plot the specific composition of collaborative agreements.

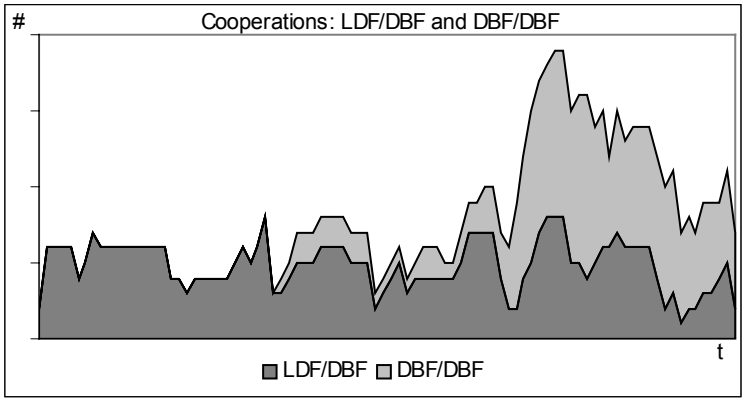

Fig. 12: Composition of collaborations

In the first part of the period investigated only cooperative arrangements between LDFs and DBFs are found: DBFs are supposed to support LDFs in building up their biotechnology competencies; and, as a compensation for their R&D efforts, they are funded by LDFs. As soon as some DBFs start to earn their own money they also initiate further collaborations in which they are no longer playing the role of translators but that of explorers. In the simulation we find that these collaborations between DBFs to become of increasing importance in later stages of the simulated time horizon. Now, the cooperative agreements aim at bundling know-how and joint exploration of the technological opportunities. At the end of the period studied the number of agreements between DBFs is becoming comparable to that of agreements between LDFs and DBFs.

This changed role played by DBFs is also mirrored in the decisions made by firms with respect to their collaboration policy. In the model we differ between three strategies: the go-it-alone strategy chosen by firms who are either at the technological frontier and don't want to share know-how with followers or by firms which already are engaged in several cooperations. The second strategy aims at attracting research funds; this strategy is adopted by the DBFs in their early phases, when they enter the scene with highly developed technological competencies but they have no economic competencies. Finally, the third strategy aims at the integration of external knowledge in order to build up jointly in a network the capabilities necessary for the introduction of an innovation.

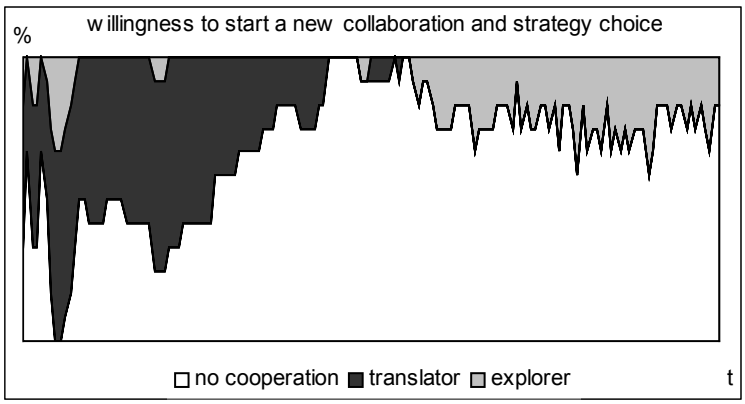

Fig. 13: Strategy choices

Fig. 13 shows the share of strategy choices the firms (LDFs and DBFs) make with respect to the specific form of cooperation they want to initiate. This decision, of course is always influenced by the position of the firm, in particular depending on whether the firm is already engaged in one or more cooperations. Therefore, the white area representing the proportion of firms who don't want to start a new cooperations has to grow with the number of already existing networks because of the increasing coordination costs. In the early stages almost all firms wish to start new cooperative relationships according to the translator's type (black shaded area). With the growing diffusion of technological competencies within the population of LDFs and as some successful DBFs become vertically integrated producers, this decision shifts nearly exclusively to collaborative relationships following the explorer's type (grey shaded area). This also means, that the new collaborative agreements to be started in later periods will almost only be of this latter type which is in line with the results shown in figure 12.

4. Comparing artifical and real networks

We can compare our artifical world with developments of the real world. In order to get a first idea of the respective artifical data, four selected periods are freeze framed in figure 14.

3	DBF_1	DBF_2	DBF_3	DBF_4	DBF_5	DBF_6	DBF_7	DBF_8
LDF_1	1	0	1	0	0	0	0	0
LDF_2	0	1	0	1	0	0	0	0
LDF_3	1	0	0	0	0	0	0	0
LDF_4	0	1	0	0	0	0	0	0
DBF_1	0	0	0	0	0	0	0	0
DBF_2	0	0	0	0	0	0	0	0
DBF_3	0	0	0	0	0	0	0	0
DBF_4	0	0	0	0	0	0	0	0
DBF_5	0	0	0	0	0	0	0	0
DBF_6	0	0	0	0	0	0	0	0
DBF_7	0	0	0	0	0	0	0	0
DBF_8	0	0	0	0	0	0	0	0

a)

48	DBF_1	DBF_2	DBF_3	DBF_4	DBF_5	DBF_6	DBF_7	DBF_8
LDF_1	0	0	0	1	0	0	0	0
LDF_2	0	0	1	1	0	0	0	0
LDF_3	0	1	1	0	0	0	0	0
LDF_4	0	0	0	0	0	0	0	0
DBF_1	0	1	1	1	0	0	0	0
DBF_2	1	0	0	0	0	0	0	0
DBF_3	1	0	0	0	0	0	0	0
DBF_4	1	0	0	0	0	0	0	0
DBF_5	0	0	0	0	0	0	0	0
DBF_6	0	0	0	0	0	0	0	0
DBF_7	0	0	0	0	0	0	0	0
DBF_8	0	0	0	0	0	0	0	0

b)

75	DBF_1	DBF_2	DBF_3	DBF_4	DBF_5	DBF_6	DBF_7	DBF_8
LDF_1	0	0	0	0	0	0	0	0
LDF_2	0	1	0	0	0	0	0	0
LDF_3	0	0	0	0	0	0	0	0
LDF_4	0	1	0	1	0	0	0	0
DBF_1	0	0	0	0	0	0	0	0
DBF_2	0	0	0	0	0	0	0	0
DBF_3	0	0	0	0	1	0	0	0
DBF_4	0	0	0	0	0	0	0	0
DBF_5	0	0	0	0	0	0	0	0
DBF_6	0	0	0	0	0	0	0	0
DBF_7	0	0	0	0	0	0	0	0
DBF_8	0	0	0	0	0	0	0	0

c)

95	DBF_1	DBF_2	DBF_3	DBF_4	DBF_5	DBF_6	DBF_7	DBF_8
LDF_1	0	0	0	0	0	1	0	0
LDF_2	0	0	0	0	1	0	1	0
LDF_3	0	0	0	0	1	1	1	0
LDF_4	0	1	0	1	0	0	1	0
DBF_1	0	1	0	0	0	0	0	0
DBF_2	1	0	1	0	0	0	0	0
DBF_3	0	1	0	0	1	0	1	1
DBF_4	0	0	0	0	0	0	0	0
DBF_5	0	0	1	0	0	0	0	0
DBF_6	0	0	0	0	0	0	0	0
DBF_7	1	0	1	0	0	0	0	0
DBF_8	0	0	1	0	0	0	0	0

d)

Fig. 14: Network structure for selected periods. Each gray box represents the collaboration of the firms corresponding to it on the horizontal and vertical axes.

Ad 14a) In the starting periods cooperations are focused on acquiring complementary assets, i.e. DBFs are looking for financial powerful partners whereas LDFs are looking for technologically interesting partners with core competencies in biotechnology. In this situation we end up with all firms in the population of DBFs collaborating with one or two partners out of the population of LDFs.

Ad 14b) In this period most of the early cooperations are terminated. This is caused mainly by two effects. On the one hand, a decreased network probability caused by an advanced age of the first technology life cycle leads to a canceling of less successful collaborations. On the other hand, some collaborations have led to an innovation and are terminated afterwards. As there are new collaborations, a re-orientation with

respect to the selection of partners has taken place. LDF_2 still participates a network with two DBFs and also LDF_3 has increased his cooperative engagement by now cooperating with two DBFs. The most significant change has taken place with respect to DBF_1 which obviously was successful in becoming a vertically integrated supplier. This firm no longer collaborates with any LDF but instead has built up a network with three other DBFs (DBF_2, DBF_3, DBF_4).

Ad 14c) When we look at the networking table of period 75 the situation has changed once more. Now we only find 4 collaborative agreements and none of the early cooperations is still in existence, however LDF_4 and DBF_2 are again collaborating in a network. This change is mainly caused by successful innovations as well as a still slow improvement of the environmental conditions for networking.

Ad 14d) In later stages (period 95) most of the indicators support the emergence of innovation networks and accordingly we find a dense network between LDFs and DBFs and between those DBFs who were successful in becoming vertically integrated producers (DBF_1, DBF_2, DBF_3). Also, all of our four LDFs are engaged again in eight different collaborations supporting our hypothesis that the role of DBFs is changing from translators to explorers in the course of time making innovation networks a persistent phenomenon.

The results on the network dynamics of our artifical biotechnology industries are at a first glance difficult to compare with data from the real world. In figure 15 we find for a single period (1998) a small selection of collaborations between LDFs and DBFs. However, graph theory[13] offers some measures to compare different networks from a structural perspective.[14] These measures describe, for example, the adjacency, the reachability and the connectivity of a network as well as the centrality of single actors.[15] By comparing these figures we will get some first insights whether we have caught the basic mechanisms of networking in our industries, or where we have to modify specific components of our model in order to improve our understanding.

[13] See e.g. Burt, R. S. (1980).
[14] An interesting application of graph theory on biotechnology innovation networks is in: Pammolli, F., Riccaboni, M. (1999).
[15] See e.g. Freeman, L. C. (1979).

LDF / DBF	AHP	Bayer	Boeh. Ingel.	Dupont Merck	Eli Lilly	Glaxo Wellc.	Hoechst	Ro-che	Merck &Co	Novar-tis	Pfi-zer	SKB	Warn. Lamb.	Ze-neca
Affymax	2					1	1		1	2				
Affymetrix	1							2			1			
ArQule	2							1						
Britisch Biotech.	1					2				1	1	2		
Celltech			1						2					2
Chiron							1	1		1			1	
CoCensys	1									1			1	
Human Genom Sci.								1				3		
Incyte Pharma.		1			1		1			1	1	1		1
Millenium Bio Therap.	1				2			1						
Neurogen	1										3			
Onyx		1			1								2	
Repligen					1	1			2	1	2			
Scios				1	1		1	1			1			
Sequana Therap.			1			1		1					1	
SIBIA					1	1				1				
Xenova													2	

Fig. 15: Collaborations in the biotechnology-based industries[16] (own datasources)

In the following we have applied three concepts, in particular the average distance, a network centralization index and the degree of centrality in order to compare time series of artifical networks with real networks. The computations are done with Ucinet[17], a software tool designed for network analysis.

Fig. 16 shows the development of the average distance, a measure for the average shortest path between two nodes for our artifical network as well as for our empirical database. This measure can be interpreted as an indicator for the diffusion of information in a network.

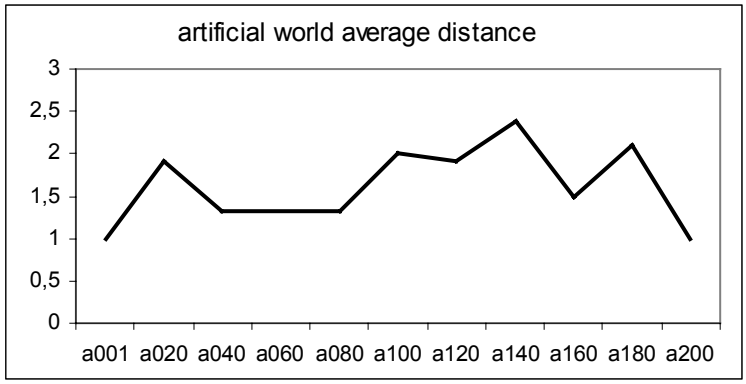

Fig. 16a: Average distance in the artifical world

[16] In total this is 113x704 matrix with around 1350 entries which exists for the years 1977 - 1999.
[17] Bogatti, S. P. et al. (1999).

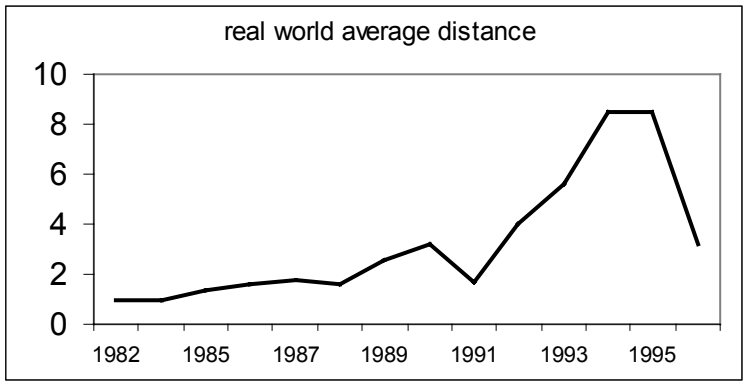

Fig. 16b: Average distance in the real world

First it is obvious that the scale of this measure is significantly larger for the real world compared to the simulated world. However, this measure is an absolute one and depends also on the size of a network. Therefore, the difference in scale can mainly be traced back to the difference in network sizes. Nevertheless, both figures show a structural similarity in a sequence of peaks which indicate a qualitative change in the network structure. Whereas these peaks grow in magnitude in the real world, their artifical counterpart stays almost on the same level and also the second peak is unimodal in the real world compared to the bimodal peak in the artifical world.

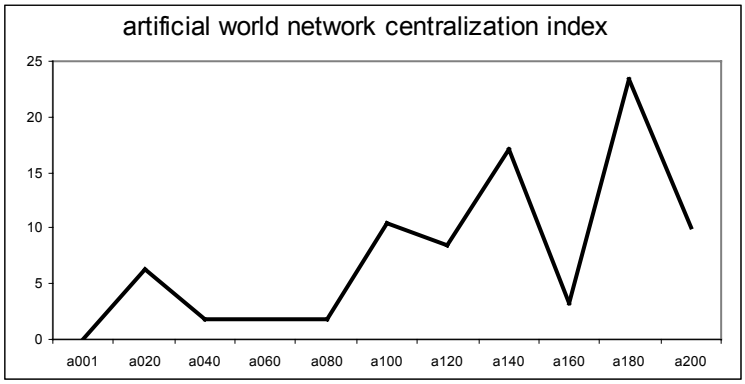

Fig. 16a: Network centralization index of the artifical world

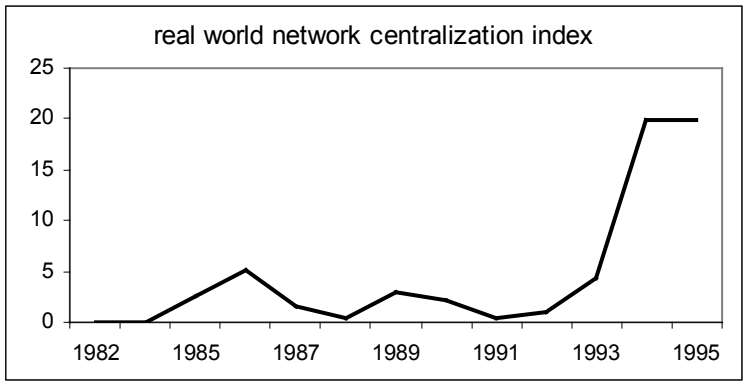

Fig. 16b: Network centralization index of the real world

To rule out the influence of network size, index oriented measures exist. In figure 17 we apply the so-called network centralization index which can be interpreted as a measure for the influence of core actors in a network. Again we find a sequence of peaks for both worlds which now are higher in magnitude in the artifical world. This difference in the impact can still be traced back to the different sample size: in the artifical world we consider for the moment only four LDFs which very likely play the role of core actors. Accordingly their relative impact in a population of 12 firms is likewise higher compared to a real world firm population of almost 1000 firms.

Finally we measured and calculated the degree centrality for both of our worlds. The degree centrality measures the asymmetry in the roles played by various actors in a network.

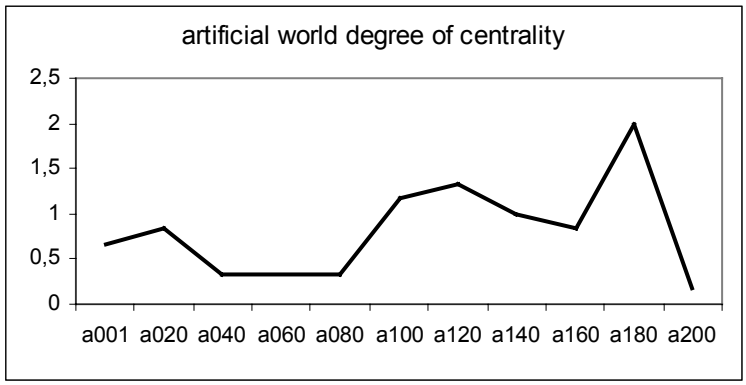

Fig. 18a: Degree of centrality in the artifical world

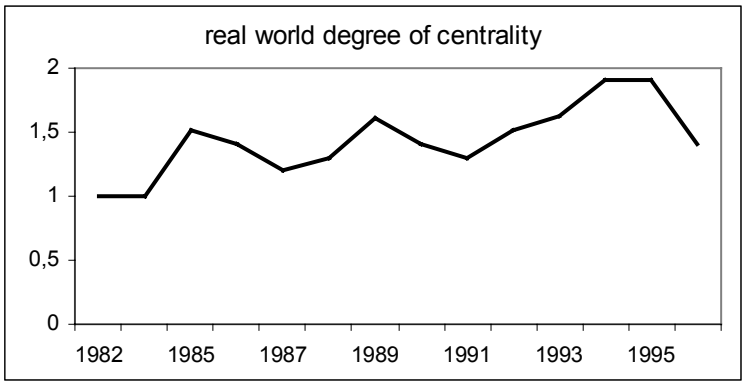

Fig. 18b: Degree of centrality in the real world

Also for this aspect of network activity we find a broad correspondence of our artifical and real worlds. The sequence of three peaks can be interpreted as a consequence of the changing role of DBFs in the networking processes. The first peak is caused by DBFs playing the role of translators supporting the LDFs in their efforts to overcome the gap between their dominant knowledge orientation and the upcoming new knowledge base in biotechnology. The second peak has to be characterized as an intermediate phase, with some DBFs who have already become vertically integrated producers and LDFs still mainly concerned with building up competencies in the new field. The third wave in networking then is caused by a tremendous growth in the technological opportunity space, where networking is considered to be a strategy to cope with the speed and complexity of technological development. In this phase DBFs play the role of explorers allowing the large and established firms to explore a wider range of technological approaches within biotechnology.

5. Conclusions

This paper provides a simulation analysis of the evolution of innovation networks in the biotechnology based industries. Since this is an applied simulation exercise, a great emphasis is placed on the characteristic features of this industry. Obviously the implementation of the model in the sense of a *history friendly model* is not an easy endeavor. The first step therefore was to analyze a prototypical case which allows to detect the interactions of the numerous mechanisms and interactions.

In a second step the results of the simulations are compared to developments of the real world by applying concepts of graph theory which provide us with some measurements of the overall network dynamics. Although there are still some significant differences between the

artifical evolution of network structures and the real world networks, the results look promising as they are able to reproduce at least qualitatively some developments which are observed in reality. The next steps have to be to balance the different mechanisms and to find relative weights in accordance to their specific impacts. Once such weights were attributed, different scenarios could be analyzed, showing the influence of different environments as well as of policy measures aiming at the establishment of these new biotechnology-based industries.

One final remark with respect to the stochastic influence of innovation processes on results seems to be necessary. By repeating the simulation experiment several times the Poisson-distributed random number, responsible for the innovation event leads to varying relationships between the firms in our sample. However, although collaboration partners change the overall network dynamics do not depend on stochastic influences, but remain rather stable over a large number of simulation experiments performed in a Monte-Carlo-method fashion..

To summarize, in our research we started from the empirical literature and from the existing case studies on the biotechnology-based sectors and developed a formal representation of innovation networks that, while abstract, matched a number of the observed features of innovation in these sectors. Going through this analytical exercise has significantly sharpened our theoretical understanding of the key factors behind the development of networking in the biotechnology-based sectors and contributed to a more general understanding of innovation networks in other sectors.

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