The Blurring Boundaries of Research: Towards a Property Rights Explanation of Knowledge Transfer In Biotechnology

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Abstract

This paper investigates how the different mechanisms for knowledge transfer are linked to the underlying technological life cycle. Following the most recent developments in the organizational economics literature, we analyze knowledge transfer from an incentive point of view. We modified the basic version of the incomplete contracts model (or property rights model) to include knowledge as an asset. The empirical hypotheses which can be derived from this model are contrasted to other streams of thought such as organizational ecology. Using this comparison as a guideline, we undertake a first empirical test of this property rights model in two technological subfields of biotechnology: monoclonal antibodies and protein engineering. The results, though tentative, are challenging: the property rights model clearly adds to our insights in spin-offs as a mechanism for knowledge transfer and in the incentive factors that influence an organization's decision to enter a technological collaboration with a university or another biotech firm.
Introduction

Worldwide, governments are looking for ways to commercialize the fundamental knowledge available in their public research laboratories and universities (Roberts and Malone, 1996; Aldrich and Sasaki, 1995). Universities themselves try heavily to appropriate financial benefits from the creativity of their academic research centers. Also at the demand side, rapid technological change and the increased complexity of knowledge has enlarged the interest of existing firms to set up research collaborations with academia (Rogers and Gibson, 1994; Clarysse et al., 1996). Both the industrial world represented by the existing companies and the academic world in which governments and universities take a major role, have constructed a wide range of governance mechanisms to stimulate collaborative research activities. However, practice shows that none of these initiatives proved to be a straight success. Research consortiums such as MCC in micro-electronics or SEMATECH in semi-conductors were only successful in a limited number of research fields, not seldom those where the technology was most mature (Rogers and Gibson, 1994). The use of patent offices to set up license contracts seems to be equally ineffective in most scientific domains (Nelsen, 1991). Finally, also policies aimed to stimulate entrepreneurial behavior are not an unambiguous success (Roberts and Malone, 1996; Roberts, 1991). As a result, practice demands for a better theory of the factors that determine the boundaries of research between universities and industry.

Confronted with this growing number of initiatives to stretch the classic boundaries of research and their mixed success, an increasing number of economic scholars have directed their attention towards explaining the causes and consequences of research collaborations. A first stream of research builds on the neo-classic economic premises and treats the choice to collaborate as a function of the appropriability regime (Grossman and Shapiro, 1985; Ordover and Willig, 1985; Katz, 1986; Levin and Reiss, 1988; Sinha and Cusumano, 1991; Kesteloot and DeBondt, 1993). The majority of these studies adopts a static (game theoretic) approach and focuses on pre-competitive research collaboration among rivals that already compete in existing markets. The results of these studies tend to be very
sensitive to the restricting assumptions that underlie the model\textsuperscript{44}, which limits their practical relevance in studying optimal forms of knowledge transfer.

A second group of economic scholars draws upon the insights which transaction cost economics offer to understand the evolution towards new structures of research governance (Williamson, 1975; Ouchi and Bolton, 1988; Tapon, 1989). Unlike the neo-classic stream which focuses on firms as production functions and for which the existing market structure is a main determinant of knowhow transfer, transaction cost economists stress the importance of the costs of organizing and transacting knowledge exchanges as a determinant of the research boundaries between industry and universities (Besanko et al., 1995). Pisano (1990) was among the first to empirically address some of the insights offered by this stream of thought. He explores the research boundaries of large firms in the pharmaceutical industry. Among other results, he finds that the 'number of available' suppliers of biotech research (namely small biotech companies) within a certain application influences the make-or-buy decision within large pharmaceutical companies. Based on this observation, he concludes that small-numbers bargaining stemming from specialized R&D capabilities is one of the driving forces behind the decision to do in-house research. The transaction cost framework relies very much on market imperfections which make collaboration between self-interested parties almost impossible. Although this framework introduces a possibility to analyze collaborations between small and large firms, its validity for analyzing knowledge transactions in which one or both partners are public institutes, remains weak. Both the neo-classic framework and the transaction cost model in itself are too weak to explain the changing research boundaries of firms.

In the meanwhile the institutional economic debate on the theory of the firm has taken some new directions, drawing the attention away from Williamson's version of transaction cost economics towards more rigorous models that explain the boundaries of the firm in terms of the incentives resulting from asset ownership (Hart, 1989) and the complementarities between the latter with job design and incentive systems as intra-firm.

\textsuperscript{44} Most studies focus on the incentives to collaborate that \textit{rivals} have in a \textit{symmetric} industry. This means that the results are very difficult to extrapolate to university-industry collaborations or to collaborations between very small and large companies.
practices (Holmstrom and Milgrom, 1994). While addressing the incentives issue related to asset ownership, Grossman, Hart and Moore (1986, 1990) introduced the 'incomplete contracts model'. The model explains how the inability to write complete contracts determines the distribution of asset ownership among various agents and is further elaborated by Brynjolfsson (1994) to include information as an asset. In line with Brynjolfsson’s (1994) pioneering efforts, we model knowledge as a separate asset in this paper. The model opens new perspectives for analyzing the incentives to transfer know how and will be used throughout the paper as a starting point for analyzing the optimal mode of technology transfer.

In addition to modeling knowledge as a separate asset, we address a second shortcoming of the current literature in explaining research collaboration, namely the “static” nature of most models. As shown previously, technological progress is a dynamic process in which the nature of the technology or knowledge changes over time. Continuous changes are often related to progress along a technological trajectory defined by a technological paradigm while discontinuities are associated with the emergence of a new paradigm (Dosi, 1982). It is likely that the diffusion of knowledge and the optimal governance modes to stimulate this knowledge transfer will be different in the different stages of technological development. Therefore, we explicitly model the stage of technological development as an explanation for differences in knowledge transfer.

The paper begins with a short literature review and an elaboration of the incomplete contracts model to include knowledge as an asset. Subsequent sections discuss the hypotheses which can be derived from this basic model and describe the data on which the empirical test of the model is based. Finally, we analyze the results and draw conclusions for further research.

**Model specification**

In order to come to a more comprehensive theory of the boundaries of the firm, Hart elaborated together with Grossman (1986) and Moore (1990) the "property rights model". A key assumption of this model is that, unlike in agency theory where the principal aims to write an optimal incentive contract, in practice, most contracts written by organizations are incomplete. Because, the scope of the contract will generally be a negative function of the complexity of the subject and the probability of unexpected contingencies during the term of the contract (uncertainty). In other words,
certain rights will be specified in the contract, but there remain "residual rights" that are not contracted for. In general, when these residual rights relate to the use of an asset, the owner of that asset will retain control over them. For instance, if a research contract between a university lab and a biotech firm says nothing about 'updating' the medical equipment used, then it is the owner of that equipment who decides whether to update it or not.

The property rights model suggests that the party that holds the residual rights to some of the essential assets or, more specifically, that is the owner of these assets will increase its ex post bargaining position in the deal. In our example, the owner of the medical equipment will decide whether to update it or not. If, for instance, the owner is the university lab and if an update of its medical equipment significantly increases the value of the output for the other party, i.e. the biotech firm, then the ex post bargaining power of the university lab will be inefficiently large. Basically, the biotech firm will rely on the goodwill of the lab to update its equipment (under the assumption that no comprehensive contract can be written to deal with this problem). If, on the other hand, the owner of the equipment is the biotech firm and if the update of the equipment is most beneficial for this firm, then the university lab will bear the risk of going unpaid for the re-training of its researchers to work with this new equipment.

The initial GHM framework only includes the physical, nonhuman assets such as machines or equipment. Of course, in many high technology industries not only the physical assets may play an important role in producing value. Also 'knowledge assets' will be an important part of the value creating chain. In line with Brynjolfsson's (1994) pioneering work, we have extended this initial model to include these knowledge assets in the property rights framework. Including knowledge as a separate asset in the model however introduces the question of alienability. Physical assets are almost by definition alienable. In our society, one can (for private goods) always trade the rights of ownership to that asset. For knowledge assets, alienability is not so straightforward. One of the key questions that should be addressed is: when is knowledge alienable and what are the underlying social and technical changes that make it alienable?

45 Brynjolfsson extended the property rights model with information assets as a variable.
Only if knowledge is alienable, one can consider the full option of jointly owning the physical and knowledge assets. When there is a high degree of complementarity between both assets, this may be considered as the most efficient way of organizing. The relative price at which one asset then can be transferred towards the owner of the other asset, will determine whether it is more efficient to transfer the know how assets towards the owner of the physical assets or the other way around. However, if knowledge is not alienable, one can only pose the question whether the party that has the knowledge should own the physical assets as well or whether another party should have the ownership rights to them. Under conditions of high complementarity between the two assets, this single ownership option may be a second-best alternative to the joint ownership option. Brynjolfsson (1994, pp. 1652) calls the difference between the values created between the two alternatives "the value of alienability". Both the alienability of knowledge as an asset and the complementarity between the physical and knowledge assets will shape the organizational structures in biotech research.

**A Dynamic View on the Property Rights Model.** A second shortcoming of economic models in assessing research collaboration or the boundaries of R&D is the static nature of most models. Using data from a number of industries, Tushman and Anderson (1986 ; 1990) show that technology evolves through periods of incremental change punctuated by technological breakthroughs that for the existing firms are either competence enhancing or competence destroying. Periods of technological breakthrough are often associated with the emergence of a new technological paradigm, while incremental changes are related to progress along a technological trajectory defined by a technological paradigm (Dosi, 1982). The technology distinguishes itself from basic science in the pre-paradigmal phase in the sense that it includes the search for an optimal set of heuristics to develop a new commercializable product, whereas basic scientific work aims to solve problems of scientific relevance taking the commercial side into account. Characteristic for the pre-paradigmal phase is that knowledge is difficult to communicate. Different research groups ‘compete’ to find the right set of solutions to further develop the technology. Once this set of solutions is found, a technological paradigm emerges which can be both competence enhancing or competence destroying. Competence enhancing means that the new technology enforces the value of the complementary assets in hands of the existing firms, while competence destroying means that new complementary assets are needed to commercialize the technology.
Let us depart from the initial situation in which knowledge is not alienable and there exists an optimal degree of complementarity between the knowledge and physical assets. This means that both the physical assets and knowledge assets can not create any value when they are not used in combination with each other. One can think of such situations in the pre-paradigmatic phases of technological development (Dosi, 1982). The knowledge assets are strongly tied with the top scientists or engineers that perform the research. The complementary physical assets are embodied in the (in some cases highly specialized) equipment these people use. Without the equipment, the scientists or engineers can not make any progress. The equipment itself does not add any value in the process of technological development unless it is used by those who control the knowledge assets.

Consider now the case in which these both assets are controlled by different agents. In the pre-paradigmatic phase of technological development, it is very difficult to predict the "outcome" of one's research efforts. In terms of the property rights model, there are too many contingencies involved to write a comprehensive contract. In the absence of such a contract, the engineer or scientist who creates some potential value is subject to hold-up by the agent who controls the physical assets. For instance, the university or company in which the researcher is employed can threaten to withhold the necessary equipment and use it for other purposes. On the other hand, also the employer faces a hold-up problem because the engineer or scientist can leave the company or university which makes the equipment obsolete. Therefore, both parties will bargain for the division of the total marginal benefit created by their marginal efforts (Under Nash bargaining, each party gets 1/2 of the marginal value). In the equilibrium, each party will invest till the marginal cost of the investment equals the marginal benefits. The property rights model, which includes knowledge as an asset then generates the following first order conditions (the top scientists are indexed by 1 and the other party by 2):

\[
\frac{1}{2}v^1(A_P, A_K) + \frac{1}{2}v^1(A_K) = c^1(x_1) \quad (1a)
\]

\[
\frac{1}{2}v^2(A_P, A_K) + \frac{1}{2}v^2(A_P) = c^2(x_2) \quad (1b)
\]

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46 It should be noted that in the pre-paradigmatic phase the complementary assets do not include the distribution channels and other assets needed to 'commercialize' the technology, but the equipment used to develop this technology.
with \( A_P = \) physical assets and \( A_K = \) knowledge assets
\[ v_1 \text{ and } v_2 \text{ the marginal benefit for each of the parties} \]
and \( c'_1, c'_2 \) the marginal cost of investment each of the parties faces.

As the second term in equation (1a) and (1b) is zero (the physical and knowledge assets are obsolete when they are not used in combination with each other), each party faces the total marginal cost of investment but only captures half of the marginal benefits. Therefore both parties will under-invest and asset ownership should be given to one of them.

From an incentive point of view, ownership on both assets should be given to either one of the parties. Which one ultimately depends upon the relative value of the physical assets versus the value of the technology. In the pre-paradigmatic stage, where knowledge is highly inalienable, it is clear that the best option would be to give the residual ownership rights to that party which possesses the knowledge as well, i.e. the engineers or scientists. In other words, the analytic model developed in equations (1a) and (1b) indicates that in the pre-paradigmatic phase, engineers or scientists will have optimal incentives to develop a technology if they receive the residual ownership rights to the physical assets as well. A practical implication of this analysis is that technology transfer, in such a pre-paradigmatic stage, should be realized through stimulating spin-off companies, in which the key researchers own the physical assets (Von Glinow and Mohrman, 1991).

Once a technological paradigm has emerged and knowledge becomes alienable at a decreasing price, the picture changes. Then, the relevant question is not anymore who should jointly own the knowledge and the physical assets, but which part of the knowledge or physical assets can "in an optimal solution" be transferred to a second party. Let us take the example of a new technology based firm which wants to pursue three research projects. It has the choice between "outsourcing" one of the projects to an agent who has the most up to date knowledge to finish this project (e.g. a research lab at the university) or to perform them all in-house. When research lab 1 owns the 'research project' or knowledge asset \( A_K I \) then the first order conditions for this research lab are\(^{47}\):

\(^{47}\) The division of bargaining power is calculated by using the Shapley value (Shapley, 1953). The Shaply value in the three agent case can be derived as follows: Agent 1 can be in four coalitions:
\[ \frac{1}{3}v^1(a_i, A_k^1, A_p^2, A_p^3) + \frac{1}{6}v^1(a_i, A_p^1, A_p^2, A_p^3) + \frac{1}{3}v^1(a_i, A_k^1) = c'_1(x_1) \]  
(2a)

with \( A_k^1 \) = knowledge asset for research project 1
and \( a_i \) = private information
\( v^1 \) the marginal benefit for party 1
and \( c'_1 \) the marginal cost of investment party 1 faces.

Alternatively, if all the "knowledge" is owned by the biotech firm, then the first order condition for our research lab can be written as:

\[ \frac{1}{2}v^1(a_i, A_k^1, A_p^2, A_p^3) = c'_1(x_1) \]  
(2b)

Again, in those cases where the knowledge which can be obtained from the research project is only "weakly complementary" with the other knowledge assets (other research programs) of the technology based firm, then it is beneficial from an incentive point of view to outsource the project while the specialized research lab itself retains the property rights to the knowledge involved in the latter project. One can think of such a situation as a research collaboration between a university and a new technology based firm in which the technology based firm licenses or outsources a part of its research program to the university. From the point of view of the university, this means that technology transfer becomes possible through patent vehicles.

Figure 1 gives a schematic overview of the most important policy insights which can be derived from the property rights model. The two key dimensions which play in the model are: (a) the degree of complementarity between the physical and knowledge assets or among the knowledge assets themselves and (b) the alienability of knowledge. The reasoning is as follows: in the pre-paradigmatic stages of technology development, knowledge is not alienable. If, in these stages, the physical assets to generate or further develop the technology are of crucial importance, then these assets should be in hands of the scientists or engineers that embody the knowledge assets (equations 1A and 1B). If not, the residual rights are in hands of the organization which owns the physical assets, which in turn

\{1,2,3\}, \{1,2\}, \{1,3\} and \{1\}. The probability of being in each of those coalitions is \(1/3\), \(1/6\), \(1/6\) and \(1/3\), respectively.
creates disincentives for the researchers. Hence, in the early stages of technological development, stimulating spin-off companies might be the most appropriate choice of technology transfer\textsuperscript{48}.

Once the technology becomes more mature (e.g. once a technological paradigm is established), knowledge turns out to be alienable through the use of property rights\textsuperscript{49}. At this stage, equations 2A and 2B suggest that new technology based firms have an incentive to look for other partners to perform their basic research activities with as long as the knowledge involved in these new activities is only 'weakly' complementary to the existing physical assets and to the existing knowledge assets. One can think of new technology based companies which have developed or commercialized their core technologies and now look for universities or specialized firms to supply knowledge which is complementary to but not too much entangled with the core knowledge they have in-house and with the different physical assets which they have accumulated. In these technical subfields, universities can set up patenting offices to commercialize their technology. In other words, research labs that want to perform contract research for existing companies should take into account that, from an incentive point of view, these companies will be most willing to outsource projects which belong to the technological subfields outlined above.

The analytic model also suggests two corollaries. First, in a pre-paradigmatic stage of technology development, it is useless to stimulate research collaboration between university and industry. The reason is straightforward: every time a research lab or a university department has developed a sufficient critical mass, the researchers have an optimal incentive to spin off their own company. Attempts from the university to commercialize their knowledge in research collaborations of any kind

\textsuperscript{48} Note that this argument does not depend on whether industry or universities are the main institutional sources of this technology. Spin-off occur from both types of organizations. In practice, the semi-conductors industry is an example where spin-offs mainly resulted from existing electronics companies, whereas the biotech industry represents a context where spin-offs were mainly industry driven.

\textsuperscript{49} Patents are only one form of property rights which guarantee knowledge alienability. Other property rights which are determined by common law include property rights and to a lesser extend trade secrets (which are covered by the trade secret law). Still other property rights do not find their roots in common law though in a kind of respect by the industrial partners or consumers. Reputation and to a lesser extent trademarks are an example of these kinds of property rights. We refer to Besen and Raskind (1991) for an oversight of the intellectual property rights and their impact on economic activity.
simply creates ex ante disincentives to invest in the development of this knowledge. On the other side, collaboration efforts undertaken by the industrial partners do not succeed because the researchers lack the incentive to collaborate on a long term basis. Second, once knowledge becomes alienable, this does not mean that spin-off companies are not fruitful anymore. The model only suggests that there is an incentive to collaborate, maybe on specialized subdomains, either with other new technology based companies or with the universities themselves. One can think of universities which choose to bundle their knowledge resources and form a semi-independent company that acts as a catalyst between the ‘generalist’ companies that already existed and the university labs themselves.

Figure 1: Technology Transfer From A Property Rights Point of View

So far, we specified how the incomplete contracts model might contribute to our insight in the process of knowledge transfer, defined from an incentives perspective. The analytic model generates a set of empirically testable hypotheses, which will be further developed in the next session.

Hypothesis development

One of the first insights derived from the property rights model is the relationship between the stage of technology development and the number of
foundings in the industry. The underlying rationale is that in the pre-paradigmatic stages of technology development, the knowledge associated with this technology is inalienable. From an incentive point of view, the model shows that in this case the scientists or engineers that develop the knowledge should own the physical assets needed to develop it. In other words, they should be stimulated to found their own technology based company. Once that knowledge becomes more alienable, we would expect less foundings based on this technology. Hence, a negative relationship is supposed between the number of new technology based foundings in a technological community and the alienability of knowledge in that community.

In order to empirically test this relationship, we should control for other competing or complementary theories which have been developed in the literature as (community-level) explanations for organizational founding. The most extensive and most elaborated among them is ‘organizational ecology’. Organizational ecologists have incorporated the study of foundings as a focal topic in their research agenda (see table 1, for an overview). Their main argument is that population-level dynamics shape the patterns of founding. In the early eighties, Delacroix and Carroll (1983) empirically investigated this hypothesis in a population of Argentine New Papers. They found a curvilinear relationship between population density, measured as the number of organizations at any period in time, and the founding rates in the populations under study. The theoretical explanation is as follows: organizational density is determined by the prior failures and the prior foundings in a population. Both dimensions have this curvilinear relations with founding patterns. Prior failures at first hand, create free-floating resources which could be accessed by newly founded organizations. However, this positive influence has an upper limit beyond which an even larger number of failures would signal that the environment is hostile towards potential entrepreneurs. Similarly, foundings initially encourage potential entrepreneurs because in a similar population or niche because they signal that the environment is fertile. But as the number of foundings increases, an upper limit is reached beyond which competition for resources in this environment discourages further foundings.

This initial hypothesis has been further elaborated as the ‘density-dependence’ hypothesis. The density dependence hypothesis states, in general, that initially population density legitimates the organizational form of a new population and helps to increase the founding rate of this new population. However, as population density increases further, the legitimacy
process becomes dominated by the competition effect and founding rates start to decrease. As a result, one expects an inverted U-shaped relation between population density and founding rates. The hypothesis has been validated in a large number of different populations, ranging from the US Brewery Industry towards US Semiconductor companies and even the US biotech industry. As shown by table 1, in most of these different populations, the density-dependence hypothesis has received empirical support. Therefore, we conclude that the evidence in support of the non-monotonic pattern is very strong and should be controlled for in our study of the effect of knowledge alienability on organizational foundings.

Based on the discussion of the previous paragraphs, a first hypothesis derived from the model is as follows:

*Research proposition 1: after controlling for population density, the alienability of knowledge in a new technological domain, will have a negative effect on the number of foundings in that domain.*

As a corollary to this, the model also predicts that the number of research collaborations in a particular technological domain will be a negative function of these organizational foundings. Organizations which want to collaborate with research groups do not have the possibility to do so, because the existing groups do not have enough incentives. On the contrary, once a research group obtains a critical mass of knowledge, it has an optimal incentive to spin-off its own company. Concluding, we can formulate the following corollary:

*Corollary 1: there is a negative relationship between the number of foundings in a particular domain and the number of research collaborations in that domain.*

The property rights model does not only focus on foundings as a viable strategy of technology transfer. Equation 2A and 2B show that, once knowledge has become alienable, new technology based firms have an incentive to enter research collaborations with external partners in those technological sub-fields where the knowledge involved is only weakly complementary to their physical assets and the knowledge assets within the company. In line with the core competence literature, new technology based companies are assumed to enter a research collaboration in those
technological subfields in which they do not have their core knowledge or physical assets.

Based on this, we can argue that, before an organization is willing to enter a research collaboration, be it with a university or another biotech firm, then this organization should already have developed a more or less coherent set of ‘knowledge’ and a well-elaborated set of physical assets which form the ‘core competence’ of the company (Prahalad and Hamel, 1990). Consequently, we state that the decision to enter a research collaboration is a positive function of the resources which a particular company has accumulated, both in terms of knowledge and physical assets. Hypothesis 2, derived from the property rights model is formulated as follows:

Research proposition 2A: after controlling for the level of knowledge alienability, we expect that the decision of a new technology based firm to enter a research collaboration is a positive function of its accumulated stock of knowledge in the technology.

Research proposition 2B: after controlling for the level of knowledge alienability, we expect that the decision of a new technology based firm to enter a research collaboration is a positive function of its accumulated stock of physical assets.

Both hypotheses will be tested in a particular research site within the biotech community. The next session defines the selection and definition of this site.

Research site:

Genetic engineering and hybridoma technology in the biotech community

Biotechnology is a heterogeneous set of biological techniques, which are used for a variety of purposes. The property rights model is not an a priori ‘industrial’ model, but a technology related one. Hence, not the industry, but the ‘technological domain’ or, to say it in organizational ecology terms, the homogenous population of companies that are interested in the development or commercialization of the same technology form the appropriate unit of analysis (Gray, 1985). For the purposes of this paper, we need to divide biotechnology in a number of homogenous technological subfields.
To do so, we used two steps. First, we traced back all companies which were active in biotech research with therapeutic purposes. Within this biopharmaceutical population, a number of different technological subfields can be distinguished (OTA, 1991). Based on a careful analysis of the relevant scientific journals in the field and in line with industry reports such as OTA (1991) and Ernst & Young (1995-2000) we were able to distinguish between seven technological subfields: (a) monoclonal antibodies, using hybridoma technology, (b) protein engineering using rDNA systems, (c) drug delivery systems, (d) antisense technology, (e) gene therapy, (f) intracellular receptors and (g) rational drug design (using computerized methods).

Within those technological sub-fields, there are very different types of organizations involved. 65% of all research and development activities in genetic engineering (rDNA) are performed in universities. Government funded labs account for about 10%. New biotech firms perform another 10% and about 15% is done in large established chemical or seed companies. The division of "research labor" in the biopharmaceuticals is more difficult to assess because the "research boundaries" are less clear to define. We estimated in previous research that for a particular stream of research, namely Hepatitis C, 50% of the research was done in universities and university-related hospitals. Another 20% was performed in government-related laboratories. 25% resulted from the efforts of new biotech companies and only a mere 5% is performed by large companies. Since we are interested in the foundings of independent new firms, we will focus on new biotech companies. Figure 2 shows the relative importance of each technological sub-field (in 1994) for the new biotech start-ups.

As shown by figure 2, the technological subfield of monoclonal antibodies (mabs) and genetic engineering of proteins (rDNA) are by far the largest biotechnology. Together, they account for about 45% of the new technology based companies involved in biopharmaceutical development. Although rational drug design has become a very popular concept in drug development, relatively little biotech start-ups focus on this sub-field. Increasingly popular are the domains of antisense technology and gene therapy. Gene therapy exists in the development of ‘therapies’ in adjunct to the recombinant drugs which are helpful in treating chronic diseases such as Cystic Fibrosis. Antisense technology is the newest subfield and targets the RNA instead of DNA strings. By using this kind of technology, companies hope to be able to inhibit the replication of viruses. So far, only a couple of
leads derived from antisense technology have entered clinical trials. Drug delivery companies focus on the development of novel delivery systems for biologics and genes. Most of these companies either focus on the use of liposomes (especially the older companies among them) or the use of ligands. Finally, quite recently, a whole stream of biotech companies has started to specialize their activities in the recombinant development of receptors (intracellular receptors). These companies are not interested in the development of real ‘drug agents’, but in the targets which enable the pharmaceutical companies to develop drug agents.

Figure 2: New Biotech Companies in Each Technological Sub-Field as a Percentage of the Total Population in 1994 (168 companies)

Legend: When a Biotech Company was involved in more than one technological subfield, it was given credit for that one in which the majority of its research efforts were.

Because the sub-fields of Monoclonal Antibodies (Hybridoma technology) and Genetic Engineering (rDNA technology) both really were at the origin of biotechnology as an industry, they show a similar life cycle. Moreover, as shown by figure 2, together they include over 45% of the new technology based companies involved in biopharmaceutical research. Therefore, we decided to focus in this paper on these two technological subfields as a population of organizations. Figure 3 then shows the foundings and dissolutions in this population. It is clear that the “big wave” of start-ups in this population is in the early eighties. From the mid-eighties on, an increasing number of these first generation companies disappear from the population. Most of these ‘exits’ result from mergers and acquisitions.
Model specification

Hypothesis set 1 and hypothesis set 2 are situated at different levels of analysis and need a different approach. To investigate hypothesis, we follow the previous organizational ecology studies, which have mostly used a kind of Poisson model (see table 1, for an overview of the models which have most frequently been used in the organizational ecology studies of founding). Hereafter, we shortly motivate why a Poisson version is an appropriate way to model foundings in a population or technological community.

Model Specification for research proposition 1. When modeling the founding of organizations in a population, the level of analysis is the population (Hannan and Carroll, 1992:236). We have to do with repeated events (Allison, 1984:51) occurring to one unit of analysis: the population of interest; this kind of process is easily modeled as an arrival or a point process (Cox and Isham, 1980:2). The entry rate is then the dependent variable in the analyses. The baseline model for comparison is always the constant rate, time independent Poisson model, also called the exponential model (Allison, 1984:23), describing a series of events, distributed randomly across time.
As shown by Barnett and Amburgey (1990), a Poisson process then provides a natural baseline model for organizational founding. The basic Poisson model for event count data can be described as in equation 6:

$$
\Pr(Y_t = y_t) = e^{-\lambda(x_t)} \left[ \frac{\lambda(x_t)^y_t}{y_t!} \right]
$$

(3)

The Poisson model holds the strong assumption that both the variance and the mean \( \Pr(Y_t = y_t) \) of the number of events are equal. Unobserved heterogeneity in the model always leads to overdispersion. A first way to correct for this heterogeneity would be to adopt a ‘fixed effects approach’ by including dummy variables which are niche-specific (e.g. a dummy variable for each of the different geographic locations or market niches). Hausman, Hall and Griliches (1984) have proposed to overcome these problems by letting \( l \) vary randomly across individual units. A common way to do so is by including equation 4 in equation 3 (the Poisson model), or if overdispersion is a problem, by incorporating equation 4 in the negative binomial specification which can be derived from the baseline model (see Hausman, Hall and Griliches, 1984:921):

$$
\lambda_{it} = \exp(p \otimes x_{it}) \varepsilon_{it}
$$

(4)

where the error term \( \varepsilon_{it} \) is assumed to follow a gamma distribution, \( i \) can be the number of different niches or populations and \( t \) is the time variable. Of course, the value of this random effects largely depends on the assumption that the errors really follow a gamma-like distribution, or in other words, that the errors will be larger for larger values of \( \lambda_{it} \) (in this case the number of foundings/niche/period of time).

**Model Specification for Research proposition 2A and 2B.** In these hypotheses, we study a classic make or buy decision. To study these decisions, previous research has used a kind of Probit or Logit specification (Pisano, 1990). In line with this research, we choose to use a *probit normal probability* model. This kind of model belongs to the family of binary choice models. This model suggests the use of a cumulative probability function, which is normally distributed. This probability function can be written as equation (5):

$$
P_i = F(a + bX_i) = F(Z_i)
$$

(5)
where $Z_i$ is a non-observable variable. Translated in terms of our unobserved continuous variable $Z_i$, we assume that $Y$ takes the value of 1 if the value of $Z_i$ is larger than a certain "critical" cut-off point $Z_i^{*}$ and $Y$ takes the value of 0 if the value of $Z_i$ is smaller than or equal to a certain "critical" cut-off point $Z_i^{*}$. The probit model assumes that this cut-off point is a normally distributed variable so that the probability that our unobserved continuous variable is larger than $Z_i$, can be computed from the cumulative normal probability function, which can be written in a standardized form as equation (6):

$$P_i = F(Z_i) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{z_i} e^{-s^2/2} \, ds$$

(6)

where $s$ is a normally distributed random variable (mean=0 and variance=1). By definition, the variable $P_i$ lies in the (0,1) interval. The model can be interpreted as the probability that a certain organization enters research agreements, conditioned upon the value of the explanatory variables.

**Construct operationalization and empirical results**

**Research proposition 1 and Corollary 1.** The operationalization of the density variable is straightforward: the number of organizations in the population.

Knowledge alienability is a much more difficult construct to operationalize than organizational density. Arrow (1962) has defined three characteristics which are typical for resource allocation on knowledge markets: *indivisibility*, *uncertainty* and *appropriability*. Indivisibility means that sometimes parts of the knowledge cannot be separated from other parts or even from the owner of that knowledge (since it may be a commodity if it is owned by anyone). Uncertainty refers to the fact that investing in knowledge does not straightforward result in output. Hence, existing firms may under-invest in knowledge because of the risk associated with it. Finally, knowledge appropriability refers to the extent that the owner of the knowledge is able to extract economic value from it. All three characteristics are related to the intangible or tacit nature of this knowledge. The more knowledge loses its intangible or tacit character which means the more it becomes codified, the better it can be traded on the spot market (Von Hippel, 1994). Hence, the codification of knowledge may be a good proxy for its alienability at any point in time. In pharmaceuticals, patents
have since long been a legal mechanism which was very useful both for information protection and codification.

Table 2 shows the results of the models in both the technological community of 'protein engineering companies' and the one of 'monoclonal antibody based' companies. Model (1) and (4) test the density-dependence model in these communities. Consistent with the large stream of organizational ecology research, both equations support the inverted-U relationship between the number of organizations that already exist in this industry and the number of foundings. Adding our knowledge alienability variable50 (see models (2) and (5)) to the model considerably adds to the explanatory power. In the case of monoclonal antibodies, the likelihood ratio increases with about 44% (the accompanying R² changes from 0.08 to 0.47), while in the case of protein engineering, the likelihood changes with 13% (the accompanying R² changes from 0.28 to 0.37). Also the individual signs of the coefficients point into the expected direction and are significantly different from 0.

In an auxiliary model, we also included a time trend in model (2) and model (5). Even after controlling for this time trend (which was significant in both cases), the results did not change. The slope of the PATENTS variable in model (5) was slightly smaller (-0.008) but that did not change the impact of this variable. In order to test how much these results are sensitive to the econometric specification we used, we used a negative binomial specification to check the stability of the results. The coefficients in equations (3) and (6) remain largely the same with slightly inflated standard errors. In none of both models was the overdispersion parameter statistically significant. The implications of these results are twofold: first, they provide an empirical test of a slightly modified version of the property rights model. Second, even after controlling for the most widely tested hypothesis on organizational foundings, the density-dependence model, the knowledge alienability hypothesis adds to the explained variance of the model.

Qualitative research on the incentive systems used in those start-ups confirm the empirical conclusions drawn from our quantitative models in the sense that they propose equity ownership as an important incentive. Kenney (1986: p. 96) for instance argued that leading researchers or founding

50 Measured as the annual patent activity in each technological community.
professors were given up to 10% of the initial equity. In addition to this, the remaining researchers were given stock options as incentives. Data on the motivations of those professors to spin off a new company also reveal that the equity shares and, related to this, the huge amounts of money that could be earned in case of a success are ranked as the number one reason. Moreover, cases in which the ownership of physical and knowledge assets remained separated clearly show examples of under-investment on both sides. Based on the same data, he describes how research labs at universities complain that they have not the necessary equipment to keep ahead with the biotech start-ups, whereas most research labs in the pharmaceutical and chemical firms were very skeptical towards the new biotech challenge.

We also stated, as a corollary, that we expected a positive correlation between the intensity of patent activity and the number of research collaborations in the domain. Unfortunately we were not able to split this variable up between the monoclonal antibodies and protein engineering. As a first indication, we calculated the Pearson point correlation between the number of research collaborations (between biotech companies and universities/other biotech companies) in which they are involved over the period 1982-1994. This correlation coefficient is 0.74, which again is a first indicator of empirical support for this hypothesis.

**Research proposition 2A and research proposition 2B.** The dependent variable is the same for both hypotheses, namely a dummy variable which takes the value of 1 if the company has entered a research collaboration in that particular year or not (see table 1 for a description of this variable). Research proposition 2A states that the accumulated stock of knowledge influences the decision to enter a research collaboration in a positive way. We have a direct measure of this accumulated stock of knowledge through the cumulated number of patents indicator (CUMPAT). Previous research has used this measure as an indicator of the knowledge stock in the company (Henderson and Cockburn, 1994). However, no direct measure is available to capture the amount of physical assets a biotech company has invested in. Instead, we use the number of projects this company has in clinical trials (CLINICAL) as a proxy. Previous researchers on biotechnology have argued that having products in clinical trials make it necessary to invest heavily in the physical assets needed to carry the clinical trials. Before testing these hypotheses, we controlled for a number of competing explanations. First, we included the total level of knowledge alienability by measuring the patenting activity during anyone year. This
variable is highly correlated with the time trend variable so that we omitted the latter one from the final analyses to avoid multicollinearity problems. We also controlled for the size of the company by using the number of employees in each company as a proxy (SIZE) and for the age of the company, measured as the number of years elapsed since company founding (AGE). Models (7) and (9) give respectively a Probit and a Logit estimation of this baseline model. As expected, it is mainly the patents variable which explains the probability of entering a research collaboration. AGE has a slightly significant and positive sign, which indicates that it are especially the more mature organizations which tend to enter such collaborations.

After controlling for AGE, SIZE and PATENTS, we included the explanatory variables in the model. The knowledge assets which organizations have accumulated in the field have a significant positive effect on the probability that these organizations enter a research collaboration, which supports research proposition 2A. The effect of the number of projects each organization has in clinical trials (CLINICALS) is slightly less, but still significant in the expected way. Hence, also research proposition 2B receives support from the data. Of course, the variables which we use in the model are only proxies for the constructs elaborated in the property rights model. Moreover, we have no variable which captures the degree of interrelatedness between the different knowledge assets on the one hand or the knowledge and physical assets on the other hand. We also have no idea how homogenous the existing knowledge base is and, related, how much it reflects a core competence in a certain domain.

Qualitative analysis of the data sources however revealed that in many cases research collaborations are formed between more mature companies involved in protein engineering and monoclonal antibodies and the newer biotech companies or university labs that are involved in newer technologies such as gene therapy and antisense technology, which is in the direction of our hypothesis.

Conclusions and directions for future research

In this paper, we analyzed how recent developments in organizational economics can help us understand the complex process of technology transfer. Organizational economics looks at the boundaries of the firm from a totally different perspective than the neo-classic economists. However, even within organizational economics, neither the principal-agent
perspective nor the transaction cost model really go to the heart of the institutional question: why do firms exist. In a response to this, GHM (1986; 1990) have developed an incomplete contracts model in which the asset ownership question is the central topic of interest. This incomplete contracts or property rights model has been the basis for many recent developments in principal-agency theory towards a full theory of the firm (Holmstrom, 1994).

The GHM model focuses on the incentives that agents have to cooperate or not, given the status of ownership of the complementary assets. We analytically modeled "knowledge" as an asset. When knowledge is not alienable, the model shows that those who possess the knowledge have the best incentive to develop this knowledge further if they also have the rights to the physical assets needed to develop this knowledge. Linking this result to the theories of technological evolution, this means that before a technological paradigm is established or, put differently, in the beginning of the technological life cycle (Foster, 1986), technology transfer should be stimulated through the spin-off of new technology based companies in which the key researchers receive equity rights.

Once knowledge becomes alienable, the model gives an insight in what kind of knowledge will be outsourced by which companies. The data suggest that probably the more mature companies which have already developed a research portfolio have the highest incentive to outsource these knowledge assets that are only weakly interrelated with either their existing portfolio nor the physical assets they have invested in order to further develop this portfolio. There are two interesting conclusions which can be drawn from this insight. First, research labs that want to perform contract research with existing companies should invest in this kind of knowledge. Second, high tech companies that belong to a second wave of foundings have an incentive to specialize in these technological sub-fields and act as brokers between universities and the more mature biotech or pharmaceutical companies.

In addition to these analytic derivations, we also undertook a first attempt to analyze how reality matches the predictions of the property rights model. Therefore, we developed a hypothetical framework. To empirically analyze the first hypothesis, we contrasted the predictions of the property rights model with the competing explanations derived from organizational ecology. The empirical results, derived from two biotech subfields are challenging. The knowledge alienability variable explains up to 0.39% of
the yearly variation in the number of foundings, after controlling for the generally accepted density dependence model. Of course, we should take some caution in interpreting these results because of the limited degrees of freedom in each model\(^{51}\). Still, the results open some challenging directions for further research on the incentive systems used in these new technology based companies. In the empirical operationalization, we assume that the key researchers receive equity ownership in these new companies. How does this degree of equity ownership change over time? Does it discriminate between successful and less successful new technology based companies? Is it a substitute for property rights in the initial stages of technological development? The incomplete contracts model, and its elaborated version analyzed by Holmstrom (1994) offers some strong, testable hypotheses for these questions.

The second set of hypotheses were more difficult to analyze (2A and 2B), because we have no data on the degree of interrelatedness between the different knowledge and physical assets, nor of the homogeneity of the existing knowledge base. The results are therefore indications rather than empirical tests. These indicators confirm direction of our hypothesis: companies which have accumulated a larger knowledge base and hence have more core competence in a certain core technology are more likely to enter a research collaboration (in what we assume to be a weakly related new technology) than those that did not accumulate this knowledge base yet. These results invite further research. Collaboration and more specifically outsourcing in basic research might be desirable from an incentive point of view. Further studies should go inside the firm and collect data at the project level so that the degree of interrelatedness between the different kinds of assets can be taken into account.

\(^{51}\) We only cover the period 1971-1994, which leaves us with 24 observations of the dependent variable. Still, this is a much longer period than Shan, Singh and Amburgey (1991) used to analyze foundings in the biotech industry.
Bibliography


Table 1: Variable Names and Sources

<table>
<thead>
<tr>
<th>Variable Name</th>
<th>Data Construction and Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPATENTS</td>
<td>number of US patents filed during that year of observation. The Derwent patent data base is used as the ‘population’.</td>
</tr>
<tr>
<td>MPATENTS</td>
<td>number of US patents filed during that year of observation. The Derwent patent data base is used as the ‘population’.</td>
</tr>
<tr>
<td>FOUNDINGS</td>
<td>Foundings of New Biotech Based Companies which are involved in biopharmaceutical research using techniques of protein engineering or monoclonal antibodies (<em>in vitro</em> diagnostic assays excluded) <em>and not</em> fully owned (i.e. at least 75% equity position) by another company.</td>
</tr>
<tr>
<td>RESEARCH COLLABORATIONS</td>
<td>The research collaboration variable is a variable collected from information available in the full text version of the NDA-pipeline (accessible through Dialog).</td>
</tr>
<tr>
<td>RESCO</td>
<td>Dummy variable variant of the RESEARCH COLLABORATIONS variable described in the previous paragraph.</td>
</tr>
<tr>
<td>CLINICALS</td>
<td>The number of projects this particular company has in clinical trials during the period of observation. This variable is computed from the NDA-pipeline data.</td>
</tr>
<tr>
<td>CUMPAT</td>
<td>Cumulative number of patents for each of the companies in our sample. This variable is drawn from DERWENT’s database on biotech patents.</td>
</tr>
<tr>
<td>AGE</td>
<td>Number of Years that the company exists.</td>
</tr>
<tr>
<td>SIZE</td>
<td>average size of the company in number of employees at each year of observation.</td>
</tr>
</tbody>
</table>

Table 2:
Determinants of New Tech Foundings
Poisson Regression/Negative Binomial.
Dependent Variable= Number of NDA/PLAs.

<table>
<thead>
<tr>
<th></th>
<th>RDNA sample</th>
<th>Mabs sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(1)</td>
<td>(2)</td>
</tr>
<tr>
<td>NUMBER</td>
<td>0.27**</td>
<td>0.197**</td>
</tr>
<tr>
<td>[number of companies in the sample]</td>
<td>(0.052)</td>
<td>(0.056)</td>
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<tr>
<td>NUMBER2</td>
<td>-0.006**</td>
<td>-0.003*</td>
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<tr>
<td>[number of companies squared in the sample]</td>
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<td>(0.0015)</td>
</tr>
<tr>
<td>PATENTS</td>
<td>-0.002**</td>
<td>-0.002**</td>
</tr>
<tr>
<td>[number of patent filings]</td>
<td>(0.000)</td>
<td>(0.000)</td>
</tr>
<tr>
<td>CONSTANT</td>
<td>-0.929</td>
<td>-0.623</td>
</tr>
<tr>
<td>[number of patent filings]</td>
<td>(0.477)</td>
<td>(0.459)</td>
</tr>
<tr>
<td>Overdispersion</td>
<td>N/A</td>
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</tr>
<tr>
<td>parameter</td>
<td></td>
<td>(71.90)</td>
</tr>
<tr>
<td>Log-likelihood</td>
<td>-39</td>
<td>-33.9</td>
</tr>
<tr>
<td>R^2</td>
<td>0.28</td>
<td>0.37</td>
</tr>
</tbody>
</table>
Table 3:
Determinants of the Decision to Enter a Research Collaboration
Probit/Logit Model.
Dependent Variable = 1 if involved in a Research Collaboration. 557 obs.

<table>
<thead>
<tr>
<th></th>
<th>Probit Regression</th>
<th>Logit Regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(7)</td>
<td>(8)</td>
</tr>
<tr>
<td>PATENTS</td>
<td>0.001**</td>
<td>0.001**</td>
</tr>
<tr>
<td>[total number of biotech patents]</td>
<td>(0.000)</td>
<td>(0.000)</td>
</tr>
<tr>
<td>SIZE</td>
<td>0.006</td>
<td>-0.006</td>
</tr>
<tr>
<td>[number of employees]</td>
<td>(0.003)</td>
<td>(0.000)</td>
</tr>
<tr>
<td>AGE</td>
<td>0.072*</td>
<td>-0.035</td>
</tr>
<tr>
<td>[number of years elapsed since company founding]</td>
<td>(0.0287)</td>
<td>(0.0244)</td>
</tr>
<tr>
<td>CUMPAT</td>
<td></td>
<td>0.0095**</td>
</tr>
<tr>
<td>[cumulative number of patents filed]</td>
<td></td>
<td>(0.0025)</td>
</tr>
<tr>
<td>CLINICALS</td>
<td>0.052*</td>
<td>0.0894*</td>
</tr>
<tr>
<td>[number of projects the organization has in clinical trials]</td>
<td>(0.0225)</td>
<td>(0.0379)</td>
</tr>
<tr>
<td>CONSTANT</td>
<td>-2.482**</td>
<td>-2.304**</td>
</tr>
<tr>
<td></td>
<td>(0.389)</td>
<td>(0.407)</td>
</tr>
<tr>
<td>Log-likelihood</td>
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<td>-288</td>
</tr>
<tr>
<td>R^2</td>
<td>0.05</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Notes to table 2 and 3:
* means significant at the 0.05-level
** means significant at the 0.01-level
standard errors in parentheses