The Source of Comparative Advantage in the Biotechnology Industry:

A Real Options Approach*

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Abstract:

Sources of heterogeneity within the process of R&D investment, such as international differences in the maximum per-period rate of investment and level of regulatory uncertainty, offer a plausible explanation for US comparative advantage in biotechnology. Using dynamic stochastic simulation, the results presented in this paper suggest US biotechnology firms may initiate more R&D projects, innovate earlier and more rapidly, persevere longer in the face of mounting R&D costs, and successfully complete more R&D projects than European firms.

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Introduction

Commercial biotechnology has been and continues to be the nearly exclusive province of US enterprise. From the late 1970s to the present, biotechnology research and production has concentrated in the US, rather than in other industrialized regions such as Western Europe. Casual inspection of industry data confirms that early US dominance in biotechnology has been perpetuated over time. In 1996, US biotechnology firms numbered 1,287 and employed 118,000 workers, compared to 716 firms and 27,500 workers in all of Europe. US firms earned $14.6 billion in revenues, dwarfing the European total of $1.4 billion. Significantly, US biotechnology firms spent $7.9 billion on research and development (R&D); European firms spent only $1.2 billion (Ernst & Young, 1997a; 1997b). This evidence suggests that the US holds a comparative advantage in the biotechnology industry, *vis-à-vis* other Northern countries.

In this paper it is hypothesized that sources of heterogeneity within the structure of the R&D investment process offer a plausible explanation for US comparative advantage in biotechnology. This contrasts with existing models that ascribe heterogeneity to international differences in resource endowments such as productive factors and knowledge stocks (Grossman and Helpman, 1992). In section 1, a set of stylized facts is listed that characterize biotechnology R&D investment, and two candidate sources of heterogeneity that impact R&D investment are identified: the per-period rate of investment and the level of uncertainty pertaining to the domestic regulatory regime. In section 2, a model of biotechnology R&D investment is developed, based on an extension of Pindyck's (1993) real options model of irreversible investment with uncertain cost. The implications of this model for the issue of comparative advantage in the biotechnology industry are examined in sections 3 and 4. The paper is summarized in section 5.

1. Stylized Facts of Biotechnology R&D

To understand how one country can ultimately dominate an industry such as biotechnology, a promising avenue of inquiry is the actual process of R&D investment. An examination of this process in the biotechnology industry yields the following six stylized facts: (i) biotechnology R&D programs are lengthy; (ii) R&D costs are irreversible; (iii) R&D investment is made up-front; (iv) the total number of time periods required to complete an R&D program is unknown *a priori*; (v) the cost to complete an R&D program is subject to ongoing technical and regulatory uncertainty; and (vi) an R&D program is subject to discrete uncertainty in the form of the possibility that the value of an investment opportunity might instantaneously fall to zero midstream – known as a *termination event*.

The concepts of technical and regulatory uncertainty are borrowed from Pindyck. Technical uncertainty arises from the physical difficulty of completing an R&D project. At the time an R&D program is undertaken, limited information is available regarding the effort, resources and time required to successfully realize the future payoff. Initiating the project and completing successive stages will incrementally reveal information related to these issues. As the investment proceeds, the barriers to completion may become higher or lower, but the true cost of the investment is only known with certainty when the project is completed. Thus, the "information revealing" nature of technical uncertainty enhances the incentives to commence investment.

Regulatory uncertainty arises from unpredictable aspects of the regulatory regime governing the completion of R&D programs, which may take the form of unpredictable compliance costs incurred over the course of the R&D process. The level of these costs may be higher or lower depending on how regulators respond to factors such as public opinion or safety

concerns. In contrast to technical uncertainty, information about the regulatory regime proceeds regardless of whether or not the firm is investing. This tends to have a dampening effect on investment incentives, since the firm may benefit from delaying investment in order to observe the regulatory regime and thus obtain more information about its future trajectory.

A country's comparative advantage in commercializing new technologies can be thought of as the ability to innovate more rapidly than rival countries. The stylized facts listed above suggest at least two candidate sources of heterogeneity pertinent to this issue. First, since biotechnology R&D is lengthy, the rate at which a firm can invest will have important implications for average time to build, or equivalently, the rate of innovation. Secondly, the presence of regulatory uncertainty and its implications for investment incentives suggests that a reduction in the level of uncertainty surrounding the regulatory regime will reduce the incentive for firms to delay investment in order to obtain more information about the future path of the regulatory environment.

Evidence supports the contention that these sources of heterogeneity in fact exist in the biotechnology industry. "In America," *The Economist* (1996a, p.21) observes, "companies such as Netscape and Genentech have sprung up to lead the Internet or biotechnology even before such things can really be classified as industries." This disparity between the US and Europe may be in part attributable to the fact that European firms face more difficulties in obtaining investment capital. "... [Europe] seemingly has no shortage of venture capital," *The Economist* (1996b, p.89) notes. "But most of it has been going into relatively unadventurous investments … only a fraction has been invested in start-ups." In contrast, the US has a well-tested mechanism for channeling funds to risky high technology enterprises, notably the NASDAQ equity market.

Heterogeneity between the US and Europe also exists in the guise of domestic regulatory regimes, especially in terms of the relative ease with which biotechnology products can gain approval for release by national regulatory agencies. In Europe, product approval is a much more costly and uncertain prospect than in the US. For example, in 1992, the US Food and Drug Administration determined that genetically engineered foods would only have to satisfy the same health and safety standards imposed on naturally occurring foods. In contrast, European biotechnology firms face a protracted approval process, fraught with uncertainty.

It is reasonable to hypothesize, therefore, that the US biotechnology industry possesses certain advantages that have allowed it to move ahead of its rivals through more rapid innovation, independent of any international differences in inherited resource endowments

2. A Real Options Model of Biotechnology R&D Investment

Real options investment models are based on three observed characteristics of investment: it is at least partially irreversible; it is subject to ongoing uncertainty; and the timing of the investment is at the discretion of the firm. Taking these characteristics into account, the opportunity to invest is likened to holding a financial option, except that the option is "written" on a real asset, rather than a financial instrument. The firm holds the right, but not the obligation, to initiate investment. When a firm invests, it irrevocably "kills" the option to delay, and therefore the value of this lost flexibility must be included in the cost of investment. As a result, the return necessary to persuade a firm to invest will tend to exceed the direct cost of capital.

The model presented here is Pindyck's model of investment with uncertain cost, extended to include the possibility of a termination event. Consider a biotechnology firm faced with the opportunity to invest in a new R&D project. When completed, the project will yield an asset, i.e., a product or process innovation, worth V with certainty. The firm holds an option to invest in this

project which it has the right, but not the obligation, to exercise. The expected cost to completion, K, evolves according to:

$$dK = -Idt + \beta(IK)^{1/2}dW + \gamma KdZ. \quad (1)$$

I is the per-period rate of investment, β and γ are scalars representing the level of technical uncertainty and regulatory uncertainty, respectively, and dW and dZ are increments of standard Wiener processes, with mean zero and variance dt.

The value of the investment opportunity, $F(K,q)$, is subject to the possibility of a random Poisson termination event, q:

$$\xi dq, \quad (2)$$

where, $\xi = -F$, and $dq = 1$ with probability λdt, and 0 with probability $(1 - \lambda dt)$. λ is the constant mean arrival rate of a termination event. Occurrence of the event implies that the value of the project immediately falls to zero, and the project is abandoned.

In order to determine its optimal investment strategy, the firm solves the following infinite horizon optimal stopping problem using dynamic programming:

$$F(K,q) = \max E_0[Ve^{-\mu T} - \int_0^T I(t)e^{-\mu t}dt]. \quad (3)$$

Asset valuation in a risk-neutral economy is subject to the following relation:

$$rF = -I + E[dF/dt]. \quad (4)$$

Applying Ito's Lemma yields:

$$E[dF/dt] = -IF_K + 1/2\beta^2 IKF_{KK} + 1/2\gamma^2 K^2 F_{KK} - \lambda F. \quad (5)$$

Therefore:

$$(r+\lambda)F = -I - IF_K + 1/2\gamma^2 K^2 F_{KK} + 1/2\beta^2 IKF_{KK}, \quad (6)$$

which is subject to the boundary conditions:

$$F(0) = V$$
$$\lim_{K\to\infty} F(K) = 0$$
$$1/2\beta^2 K^* F_{KK}(K^*) - F_K(K^*) - 1 = 0$$
Value matching condition: $F(K)$ continuous at K^*.

(6) is solved numerically for K^*, which is the critical cost to completion. K^* represents the maximum level of cost to completion for which investment is economically feasible. If the initial expected cost to completion exceeds K^*, the firm will not undertake the investment. If the investment is already underway when the evolution of K crosses the K^* threshold, the firm will abandon the project midstream. The level that K^* takes will depend on the exogenous parameters in the model: V, I, r, λ, β, and γ. I and γ represent the sources of heterogeneity in the biotechnology industry.

3. Comparative Statics

To illustrate the comparative statics of the investment model described above, a benchmark vector of exogenous parameters, $[V, I, r, \lambda, \beta, \gamma]$, is constructed from 1996 US biotechnology industry data. In 1996, the total market capitalization of 294 publicly traded US biotechnology companies was $77 billion. This yields an average market capitalization of approximately $262 million per firm, which is used as a proxy for the capitalized value of a biotechnology firm's R&D. For simplicity, this value is assumed to be certain and time-invariant. In 1996, the 294 biotechnology firms collectively spent $4.7 billion on R&D, or about $16 million per firm. Therefore, the maximum per-period rate of investment, I, is set to $16 million per year. This figure can be interpreted as a supply constraint on the availability of investment capital, dictated by the willingness of the capital market to fund biotechnology R&D. Again, it is assumed that this figure is time-invariant. A value for λ is also needed: it is assumed that the mean arrival rate of an R&D termination event is 0.2 on a yearly basis. To complete the

calibration, the risk-free rate of interest r is set equal to the 1996 yearly average for the one-year Treasury index, or 5.5%.

Solving (6) numerically (see Fackler, 1996) over a range of values for β and γ yields a matrix of values for K^* illustrating the relative effects of technical and regulatory uncertainty on the critical value of cost to completion:

	$\gamma = 0.0$	$\gamma = 0.1$	$\gamma = 0.2$	$\gamma = 0.3$	$\gamma = 0.4$	$\gamma = 0.5$
$\beta = 0.0$	102.2	92.2	85.5	80.3	75.6	71.1
$\beta = 0.1$	103.5	93.0	86.2	80.9	76.2	71.6
$\beta = 0.2$	106.7	95.4	88.2	82.7	77.7	73.0
$\beta = 0.3$	111.4	99.3	91.6	85.6	80.3	75.3
$\beta = 0.4$	117.6	104.7	96.2	89.7	83.9	78.5
$\beta = 0.5$	125.3	111.4	102.0	94.8	88.5	82.7

The results confirm the point made earlier that increases in technical uncertainty tend to increase the critical cost to completion, i.e., enhance the incentive to invest, while increases in regulatory uncertainty have the opposite effect. In terms of the regulatory effect, differences in the level of γ, holding β and all other exogenous parameters constant, yields substantial differences in the critical level of cost to completion. For example, if $\beta = 0.5$, an increase in the level of regulatory uncertainty from 0.1 to 0.2 leads to a corresponding decrease in K^* of almost ten percent – from $111.4 million to $102.0 million.

In terms of cross-country differences in the maximum per-period rate of investment I, if $\beta = 0.5$ and $\gamma = 0.1$, the effects on K^* are as follows:

I	**1.0**	**8.0**	**16.0**	**24.0**	**32.0**
K*	21.1	78.6	111.4	132.6	148.0

As the maximum rate of investment increases, the critical value K^*, below which a firm will initiate investment or maintain an existing project, also increases. This suggests, *ceteris paribus*, that a firm exhibiting a higher value of I will invest under conditions that a firm with a lower I would find economically infeasible. Similarly, the firm with a higher I will maintain an R&D program under conditions that would cause a firm with a lower I to choose termination.

Cross-country differences in the maximum rate of investment or level of domestic regulatory uncertainty result in asymmetric decision rules governing investment. For example, a country whose capital markets are either "tight", or whose investors are averse to high-risk investments such as biotechnology, will tend to allocate capital less generously on a per-period basis to its domestic biotechnology firms. On the other hand, firms with access to more capital will tend to innovate faster, earlier, and exhibit more perseverance in the face of mounting R&D costs than firms less well supplied with capital. Therefore, if US biotechnology firms invest at a greater per-period rate, they will find a source of comparative advantage in this feature of the structure of biotechnology R&D.

4. Dynamic Stochastic Simulation

Dynamic stochastic simulation can be employed to assess the implications of the investment model discussed above. Specifically, the stochastic investment environment in which biotechnology firms operate is simulated, and the investment strategy summarized by the critical cost to completion K^* is applied within this environment, in order to generate simulated investment behavior.

The simulation can be summarized as follows. For each iteration, a random draw is made from a specified interval of an initial expected cost to completion. In addition, another random draw is made from an exponential distribution to obtain the waiting time for the first occurrence

of a Poisson termination event. With these values in hand, the investment begins. During the initial period of the investment, the firm checks to see if the initial K exceeds K^*: if so, the firm delays investment and observes the evolution of K, which is then driven entirely by the random component stemming from regulatory uncertainty. Should the current value of K fall below K^* at some future date, the firm initiates the R&D project at that time. Otherwise, the firm continues to observe K until the occurrence of the Poisson termination event, at which point the investment opportunity becomes worthless.

Once the R&D project is initiated, the investment proceeds as follows. For each time period, the expected cost to completion is incremented according to (1), which includes reducing K by the firm's maximum per-period R&D investment, and adding on the random components brought about by technical and regulatory uncertainty, which can be positive or negative. For each time period, the firm compares the current value of K to its critical value K^*; if K exceeds K^*, the project is abandoned midstream. Also, if the current time period coincides with the time period associated with the occurrence of the Poisson termination event, the project is terminated immediately. Otherwise, investment continues until expected cost to completion equals zero, at which point the R&D project has been successfully completed.

The simulation was carried out for representative US and European firms. Algorithms for generating the random sequences driving the stochastic processes in the model are from Press *et al*. (1992). The value of R&D, the risk-free rate of interest, λ, and β were assumed to be the same for both firms, and were parameterized as \$262 million, 0.055, 0.067, and 0.5, respectively. Heterogeneity was introduced by setting the maximum per-period rate of investment, I, to \$16 million per year for the US firm, and \$6 million per year for the European firm. These figures are based on the average R&D expenditure in 1996 for publicly-traded biotechnology firms in the

US and Europe. Finally, the level of regulatory uncertainty, γ, was set to 0.1 for the US firm, and 0.2 for the European firm, reflecting the observation that European firms are subject to a higher level of uncertainty pertaining to the regulatory regime than their US rivals. These exogenous parameters are sufficient to derive the critical cost to completion for both firms, which was $143 million for the US firm, and $87 million for the European firm.

Finally, the range of values, from which the initial expected cost to completion is drawn, was specified. This was chosen to be an interval with a lower endpoint equal to the value ten percent lower than the K^* for the European firm ($78 million), and with an upper endpoint equal to the value ten percent higher than the K^* for the US firm ($157 million). The simulation was iterated one million times each for the US firm and the European firm. The simulation results are summarized below:

	US Firm	**European Firm**
Mean Time to Build (successful only)	86 months	162 months
Projects Not Started in Initial Period	187,169	887,505
Projects Started After Delay	149,149	541,282
Projects Terminated due to Poisson Event	357,325	459,429
Projects Abandoned Midstream	126,053	442,142
Projects Successfully Completed	516,622	98,429

These results offer a striking illustration of how heterogeneity in the R&D investment process can result in one country rapidly dominating the industry in question. Note that the US firm exhibits, on average, a time to build of 86 months for successfully completed projects, almost half of the European result of 162 months. Clearly, the US firm innovates more rapidly on average than its European counterpart.

Other simulation results offers more insight into the relative performance of the US and European firms. A reason for the US firm's faster rate of innovation is the fact that, in almost 90 percent of the iterations, the European firm does not initiate investment right away, but, instead, delays investment until the current value of K drops below the critical value of cost to completion. In contrast, the US firm is forced to delay investment in only 20 percent of the iterations. The necessity of delaying investment has profound implications for time to build, as evidenced by the disparity between the US and European firms.

Another important factor contributing to the faster US innovation rate is that nearly half of the European iterations end in the project being abandoned midstream, as a result of cost to completion accumulating to the point that it exceeds the critical level. Clearly, this is a result of the much lower critical cost to completion employed by the European firm as its decision criterion for abandoning or continuing investment. This disparity has significant implications for the total number of R&D projects successfully completed by each type of firm: the US firm completes the project successfully in over half of the iterations, compared to less than ten percent of the iterations for the European firm.

In sum, as a result of the heterogeneity present in the R&D process, the simulation results indicate that, in contrast to its European rival, a representative US firm initiates more R&D projects, commences investment sooner, innovates more rapidly, perseveres longer in the face of mounting R&D costs, and ultimately, successfully completes more projects. Clearly, extension of these results to an industry-level setting suggests that US firms would rapidly dominate the industry, as in fact empirical evidence suggests has been the case in biotechnology. This in turn implies that the sources of heterogeneity present in the R&D process may offer a plausible

explanation for the US comparative advantage in biotechnology vis-à-vis other Northern countries.

5. Summary

In this paper it has been shown that a real options approach to investment provides a plausible explanation for the fact that the pattern of specialization has located the bulk of biotechnology R&D and production in the US, relative to other, relatively similar Northern countries. Contrary to other research on trade in high technology sectors, it was assumed in this paper that country's resource endowments are identical, and, that the source of comparative advantage lies within the R&D investment process. In a simulation analysis, it was shown that international differences in the maximum per-period rate of investment and the level of regulatory uncertainty are sufficient to generate asymmetric investment behavior, and therefore identify the world leader in biotechnology.

Given this, it is logical to ask if policy prescriptions, such as R&D subsidies, can "create" comparative advantage in science-based, high technology industries such as biotechnology. The answer is a qualified "yes": while government authorities can affect the rate of innovation, policy intervention cannot alter the probability distribution of success or failure; rather, it can only move firms more rapidly toward the realization of the outcome of their R&D initiatives.

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