Market Structure in Biotechnology: Implications for Long-Run Comparative Advantage*

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Abstract:

A country specializing in a high technology industry may find that excess returns stemming from innovation are reallocated overseas as foreign-based multinationals access ongoing domestic R&D through alliances with or acquisition of established domestic start-ups. Computer simulation illustrates this process in the context of the current US specialization in biotechnology.

Keywords: Biotechnology, market structure, comparative advantage

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1. Introduction

In a recent paper, Lavoie and Sheldon (2000) advance the hypothesis that the empirically observed US comparative advantage in biotechnology can be explained by sources of heterogeneity within the biotechnology R&D investment process. Using a real options approach, they illustrate how international differences in the per-period rate of investment and the level of domestic regulatory uncertainty could be sufficient to explain the emergence of US biotechnology firms as the world leaders in the industry, as measured by industry aggregates.

Specialization in high technology carries the implication that domestic firms will enjoy *Schumpeterian* excess returns. However, the accumulation of rents stemming from innovative activity could be diminished by the growing presence of foreign-based multinationals in the domestic industry. In particular, foreign multinationals can enter into alliances with or even acquire established domestic start-ups, and in doing so, obtain access to proprietary knowledge stocks generated from ongoing domestic R&D. This in turn implies that the current and future rents embodied in these knowledge stocks will be partially or fully appropriated by overseas entities.

Recent dynamics in the biotechnology industry suggest that this process may be underway. Sharp (1996) observes that,

"… European multinationals are penetrating and exploiting American capabilities in biotechnology … The large European-based multinationals in chemicals and pharmaceuticals, in pursuit of the necessary knowledge and skills in biotechnology, have through arrangements of one sort or another widely penetrated the American knowledge base."

Recent examples of this process include a $45 million deal between German-based Hoechst Schering AgrEvo and US-based Gene Logic to discover genes useful for crop protection

and improvement products, an agreement between Hoffman-LaRoche and California-based Agouron to develop anti-cancer drugs, the establishment of a 5-year R&D collaboration between BASF AG and Massachusetts-based Mitotix, and even the $25 million research alliance between the plant biology department at the University of California at Berkeley and Swiss-based Novartis.

In this paper, the implications of foreign-based multinational activity for the current US comparative advantage in biotechnology are considered. In particular, a two-tiered industry structure for biotechnology is posited: start-ups, who pioneered the industry, and multinationals, who are relatively late entrants. Sources of heterogeneity within the biotechnology R&D process led to the emergence of US start-ups as the world leaders in biotechnology *vis-à-vis* their European rivals. Although many of these start-ups are yet to be profitable, they have accumulated valuable assets in the form of proprietary knowledge stocks originating from ongoing R&D projects. By either forming alliances with or even acquiring American start-ups, European multinationals gain access to the knowledge stocks arising from US R&D, and in doing so, establish a claim on the excess returns these stocks may produce in the future through successful commercialization.

In section 2, a characterization of industry dynamics in a biotechnology industry populated by start-ups and multinationals is developed. This allows an examination of how late entry by European multinationals could result in a re-allocation of ownership rights to the potential excess returns from innovation embodied in proprietary US knowledge stocks. In section 3, some of the implications of this characterization are illustrated using computer simulation, based on a refinement to Lavoie and Sheldon's (*op.cit.*) real options model of biotechnology R&D investment. Essentially, the model is extended to include the possibility

that multinational firms may acquire R&D undertaken by domestic start-ups. Finally in section 4, the policy and trade implications stemming from foreign European penetration of the US biotechnology industry are discussed.

2. A Characterization of Industry Dynamics in Biotechnology

The essential premise of Lavoie and Sheldon (*ibid*.) is that traditional explanations for the pattern of specialization in high technology industries are poor indicators *a priori* of the eventual emergence of US firms as world leaders in biotechnology *vis-à-vis* European firms. This point can be illustrated by considering the Grossman and Helpman (1991) endogenous innovation model of dynamic comparative advantage.

In this particular model, comparative advantage in high technology industries emanates from one of two sources: relative factor endowments or initial conditions in the form of inherited knowledge stocks. These elements impact the innovation process by creating asymmetries in the cost of R&D. If knowledge spillovers are international in scope, Grossman and Helpman predict that relative factor endowments will determine the pattern of specialization. Alternatively, if relative factor endowments are similar across countries, the pattern of trade can still be fixed if knowledge spillovers are restricted to be national in scope. In this interpretation, one country begins with favorable initial conditions in the form of relatively more "inherited blueprints" than its trading partner. This country will then enjoy a "head start" in innovation, and since knowledge spillovers are national in scope, it will perpetuate its lead through declining R&D costs.

Neither of these sources of heterogeneity, factor endowments or initial knowledge stocks, seem especially appealing as explanations for the US comparative advantage in biotechnology.

The convergence of the industrialized countries since 1945 in terms of traditional sources of comparative advantage such as factor endowments has been well documented. Furthermore, initial knowledge stocks likely took the form of basic scientific research preceding the commercialization of biotechnology, much of which occurred outside the US. While proprietary knowledge originating from the process of commercialization may be restricted on a national basis, basic scientific research, which likely constitutes initial knowledge stocks, was readily available internationally.

As an alternative approach, Lavoie and Sheldon developed a real options approach to explain the US comparative advantage in biotechnology. They formulate a firm's decision to invest in biotechnology R&D as analogous to holding a financial option - i.e., the right, but not the obligation, to invest in an R&D program. Comparative advantage then evolves into a question of option management: i.e., what incentives caused US biotechnology firms to exercise their options to invest earlier than their European rivals? Lavoie and Sheldon find that the presence of international differences in the form of a higher US per-period rate of investment and a less uncertain US regulatory environment yields the result that US biotechnology firms, on average, initiate more R&D projects, begin investment sooner, innovate more rapidly, persevere longer in the face of mounting R&D costs, and successfully complete more projects than their European rivals.

Typically, it is assumed that a country specializing in a high technology sector will enjoy the super-normal rents associated with innovation. Indeed, public policy has often stressed the need to promote high technology industries, as opposed to mature, "commodity" industries with little or no excess returns, for this very reason (Krugman, 1984). However, the recent history of the biotechnology industry suggests that this assumption may be too simplistic.

As noted earlier, the biotechnology industry is currently undergoing a period of consolidation, in which multinational corporations have acquired or formed alliances with many of the smaller start-up companies who pioneered the industry. It is significant to note that many of these alliances and acquisitions have been transatlantic in nature - in particular, European multinationals operating in the US biotechnology industry.

Given these conditions, it can be hypothesized that the penetration of the US biotechnology industry by foreign multinationals serves to dilute the concentration of current or future rents associated with biotechnological innovation in the United States. In other words, the *Schumpeterian* returns to innovation expected to accrue to domestic firms specializing in high technology industries like biotechnology may be dissipated by the increased presence of foreign-based multinationals in the domestic market. We elaborate on this theme with the following characterization of the dynamics of the biotechnology industry.

There are two distinct classes of firms present in the biotechnology industry: start-ups and multinationals. Start-ups are relatively small, un-diversified firms who were essentially built "from the ground up" for the sole purpose of exploiting opportunities in the commercialization of biotechnology. Typically, their capital is obtained from external sources. Start-ups are often the result of a union between bench scientists and venture capitalists; the latter provide the seed capital to form the company and begin operations. After a time, it is not uncommon for the start-up to be taken public through an initial public offering, which provides a further infusion of capital for the start-up's research efforts.

Multinationals, on the other hand, are relatively large, diversified firms with access to internally generated capital and operations in more than one country. In general, start-ups were the earliest entrants to the biotechnology industry, followed by entry of the multinationals, who

are currently initiating consolidation in the industry through the acquisition of and alliances with established start-ups and other multinationals.

The early entry of the start-ups into biotechnology may be explained as a result of competition for external capital combined with the start-ups' greater flexibility to undertake the R&D projects that pioneered the biotechnology industry. As Lavoie and Sheldon note, however, conditions in the US, greater access to capital and less regulatory uncertainty, fostered more rapid growth in start-ups there than in Europe. In other words, US biotechnology firms innovated more rapidly and on a larger scale than firms in other countries.

Multinationals, on the other hand, were, in general, late entrants to the biotechnology industry relative to start-ups. Sharp (*op.cit*.) notes that,

"[a] combination of uncertainty, skepticism, and inexperience led to what may be called a 'a minimalist strategy' on the part of most large firms. While avoiding large investments most of the companies built up teams of researchers large enough to keep abreast of the science and to monitor developments and competitors … One consequence of this strategy of 'watching and waiting' was that it conceded leadership in development of the new technology to the small companies which were so closely linked to the academic base".

It was noted earlier that in general, the start-ups that pioneered the biotechnology industry started with the same baseline "knowledge stock", scientific information published in the literature. However, as R&D programs commence, and the projects are gradually completed, research results and experiences accumulate. These results and experiences are closely guarded proprietary assets of the firms that produce them. Thus, the conduct of R&D is synonymous with the creation of the type of proprietary knowledge stocks to which Grossman and Helpman (*ibid*.) refer in their model of endogenous innovation. The value of a firm, especially in a relatively

young industry such as biotechnology, is often heavily based on the creation of these proprietary knowledge stocks, in that they serve as an indicator of the firm's future ability to successfully commercialize valuable biotechnology products.

Therefore, in the biotechnology industry's nascent stages, the industry is populated mainly by US-based start-ups, conducting ongoing R&D, and transforming the initial knowledge stocks, which were available equally to all firms regardless of national origin, into proprietary knowledge stocks representing closely guarded assets of the firm. Conditions in the biotechnology R&D process lead to a US comparative advantage in biotechnology, which is then reinforced and perpetuated by the development of proprietary knowledge stocks on the part of US start-ups, a result reminiscent of the Grossman and Helpman framework.

At this point, the following question must be posed: what precipitated the entry of multinationals into the biotechnology industry? Sharp notes that,

"by the mid-1980s, the period of watching and waiting was over. Most of these large companies recognized that, whatever their original reservations, biotechnology had established itself as an important enabling technology, i.e., a route to new product development, and would be essential for future product innovation."

An heuristic formulation of the multinationals' entry decision can be developed using a real options framework similar to that employed by Lavoie and Sheldon in detailing the start-ups' investment decision. In the early stages of the biotechnology industry, multinationals, in addition to the start-ups, acquire an option to invest in biotechnology R&D. However, the multinationals use different criteria to mange the option than the start-ups. In particular, it can be hypothesized that start-ups invest first relative to the multinationals, possibly as a result of competition for external investment capital. At this stage of industry development, comparative

advantage in biotechnology is determined by factors within the biotechnology R&D investment process. The sources of comparative advantage relevant at this formative stage of the biotechnology industry favor the US, resulting in an industry dominated by US start-ups.

Rather than exercising their options to invest immediately, the multinationals choose to wait and observe conditions in the investment environment. In particular, they monitor the performance of the start-ups. Most of the start-ups cannot be considered profitable, so it is unlikely that the multinationals use profitability as the performance metric, rather, they monitor developments in the start-ups' ongoing R&D - in other words, the accumulation of proprietary knowledge stocks. Once these stocks reach a critical level, the multinationals exercise their option to invest, possibly by direct in-house investment, but also through alliances with or acquisition of established start-ups.

Multinationals entering the industry must select the start-ups they choose to form alliances with or acquire. It seems likely that this selection will be based on the pattern of specialization established in the industry through the R&D activity of the start-ups. In particular, it is surmised that multinationals will be more likely to invest in start-ups located in the country holding the comparative advantage in biotechnology R&D and production, which as Lavoie and Sheldon observe, appears to be the United States. Two explanations can be used to justify this behavior. First, since the US has established a comparative advantage, investment conditions must be more favorable in that country than elsewhere. Second, the fact that US firms are the world leaders in the industry suggest that the knowledge stocks they have accumulated exceed, on average, those of their European counterparts. Therefore, it may be expected that multinational penetration of the American biotechnology industry will be greater than that observed in the European industry.

This in turn implies that European multinationals will have a greater propensity to acquire US start-ups than European ones, resulting in a cross-country pattern of ownership of the assets of the US start-ups in the form of European claims on the proprietary knowledge stocks of US-based start-ups. This has the ancillary effect of re-allocating the current and future rents embodied in these knowledge stocks from their originators - the US start-ups - to the European multinationals. Thus, an asymmetry emerges in the long-run structure of the industry, in that biotechnology R&D and production is concentrated in the United States, based on the comparative advantage established early in the time-line of the industry by the US start-ups, but the long-run allocation of the excess returns arising from this specialization is more evenly distributed across US and European enterprises.

3. Analysis

In this section, an illustration is offered of how the acquisition and alliance activity of foreign-based multinationals can reduce the concentration of excess returns accruing to start-up firms in the country specializing in biotechnology. The implications of the hypothesized industry dynamics discussed above are examined using a refinement of the simulation techniques employed in Lavoie and Sheldon.

Lavoie and Sheldon suggest that the issue of comparative advantage in biotechnology can be usefully examined in the context of a real options framework. Real options investment models rely on three characteristics of investment: irreversibility, ongoing uncertainty, and a firm's discretion to control the timing of its investment. Given these characteristics, the opportunity to invest is analogous to holding a financial option, with the exception that the option is "written" on a real asset, rather than a financial security. The option confers the right, but not the

obligation, to initiate investment. By investing, the firm irrevocably "kills" the option to delay; therefore, the value of this lost flexibility is part of the investment cost. Techniques for pricing financial options can be used to determine a firm's optimal investment strategy. The decision rules for managing the option are influenced by factors such as the necessity to invest incrementally, the presence of time to build, the degree and type of uncertainty, and the rate of productive investment. These factors coincide with a stylized view of the structure of R&D investment in the biotechnology industry.

In Lavoie and Sheldon's formulation, a biotechnology firm acquires an opportunity, or option, to invest in an R&D program. The firm can either invest immediately, if current conditions warrant, or hold the option while observing the evolution of investment conditions over time. The option can be exercised at a later date if conditions change such that investing becomes economically desirable. Once the firm exercises its option, it invests incrementally over multiple time periods. At the same time, the stochastic investment conditions continue to fluctuate, driven by two sources of uncertainty: 1) technical factors, corresponding to the physical difficulty of completing the investment, and 2) external factors, such as uncertainty over the domestic biotechnology regulatory regime, or the results of basic research conducted by the scientific community. These sources of uncertainty may combine to make the R&D proceed faster or slower than anticipated. If the R&D expenditures accumulate to the point that the investment no longer appears profitable, the firm can terminate the R&D midstream. Alternatively, the investment might terminate immediately, rather than through a gradual process, if for example scientific research indicates that the R&D is based on erroneous assumptions. This abrupt cessation of the R&D is called a termination event.

Given this scenario, the firm's investment strategy can be summarized by an indicator known as the expected cost to completion, *K*. At each stage of the investment, the firm completes part of the R&D, and also obtains new information associated with the uncertain elements of the investment environment. Based on these factors, the firm re-evaluates its expectation of how much it will cost to complete the project from that time forward. A critical level of cost to completion, *K**, exists, such that, if the expected cost to completion exceeds this level, it is not optimal for the firm to exercise its option to invest, or to continue the R&D if it has already been initiated. Conversely, if expected cost to completion is below the critical level, the firm should go ahead and initiate investment if it has not done so already, or carry on with the next stage of the investment.

To model these conditions, Lavoie and Sheldon extend Pindyck's (1993) real options model of uncertain investment cost. A biotechnology firm acquires an opportunity to invest in a new R&D project. When completed, the project yields a product or process innovation worth *V* with certainty. However, the cost to complete the project is uncertain. 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:

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

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*. Equation (1) represents the law of motion for expected cost to completion, driven by the investment activity of the firm (the first term), the evolution of technical uncertainty (the second term), and the evolution of regulatory uncertainty (the third term).

The value of the investment opportunity, $F(K,q)$, is impacted by the possibility of a random Poisson termination event, q, which takes the form:

$$\xi dq, \tag{2}$$

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. Recall that a termination event may be attributed to the results of basic research conducted in an external scientific community which reveals that the scientific principles upon which the research is based are in error. According to Equation (2), occurrence of the event implies that the value of the project instantaneously falls to zero, and the project is therefore immediately abandoned.

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

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

where time to build, T, is stochastic. Asset valuation in a risk-neutral economy is subject to the following relation:

$$rF = -I + E[dF/dt]. \tag{4}$$

Equation (4) states that the risk-free return from holding the asset must equal the expected net cash flow plus the expected capital gain. Applying Ito's Lemma yields:

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

Therefore:

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

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^*.

Equation (6) is then solved numerically for K^*, which is the critical cost to completion.

The mathematics presented above can be summarized as follows. In the extended Pindyck model, the biotechnology firm acquires an option to invest in an R&D project of certain value V. Investment is constrained to proceed at the maximum per-period rate I. Expected cost to completion K evolves stochastically according to the uncertainty in the investment environment. Technical uncertainty and regulatory uncertainty are represented respectively by the parameters β and γ, which are scalars for uncorrelated standard Weiner processes. Uncertainty in the scientific environment is represented by a Poisson process, the mean arrival rate being λ. The risk-free rate of interest is given by the parameter r. Given values for the parameters V, I, r, λ, β, γ, the model can be solved numerically for the firm's critical cost to completion K^*: the maximum level of cost to completion for which it is economically feasible to either initiate the investment or continue an ongoing R&D project. If the initial expected cost to completion K exceeds K^*, the firm will delay investment. If the investment has already been initiated when the evolution of K exceeds K^*, the firm abandons the project midstream.

Dynamic stochastic simulation is employed to consider the implications of the investment model discussed above. An iteration of the simulation begins with random draws to obtain an initial expected cost to completion K, and a waiting time for the first occurrence of a Poisson termination event. At time t = 0, the firm determines if the initial K exceeds K^*: if so, the firm delays investment to observe the stochastic evolution of K, driven by the random component

associated with regulatory uncertainty. If the current value of K eventually falls below K^*, the firm exercises its option to invest at that time. Otherwise, the firm observes K until the termination event occurs, rendering the investment option worthless.

If the option is exercised, investment proceeds as follows. For each time period, the expected cost to completion is incremented by subtracting the firm's current resource allocation to the investment, and adding on the (positive or negative) random components embodied in the technical and regulatory uncertainty. The firm compares the current K to K^*; if K exceeds K^*, the project is abandoned midstream; else, incremental investment continues until expected cost to completion equals zero, at which point the R&D project is considered successfully completed. If at any time the current period coincides with the random time corresponding to the occurrence of the termination event, the project is terminated immediately.

Heterogeneity is introduced into the simulation by designating different values for I and γ for representative US and European firms. Simulation results suggest that based on this heterogeneity, the representative US firm on average 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 than the representative European firm. This suggests that US biotechnology firms will eventually emerge as the world leaders in the industry, and by extension, acquire the assets and excess returns associated with innovation in high technology industries.

This simulation is used as the basis for the analysis in the present paper. First, an industry populated solely by American and European start-ups is considered. Estimates place the number of start-ups in the US in 1996 at 1,287, compared to 716 European firms: these estimates are utilized in the simulation. At time $t = 0$, each biotechnology firm acquires an option to invest in a

real asset, in other words, the right, but not the obligation, to initiate an irreversible investment in an uncertain R&D project. The model is parameterized using the combination of 1996 industry aggregates and *ad hoc* values employed by Lavoie and Sheldon. In particular, the value of R&D, the risk-free rate of interest, λ, and β are assumed to be the same for both types of firms, and are parameterized as \$262 million, 0.055, 0.067, and 0.5, respectively. Heterogeneity takes the form of the maximum per-period rate of investment, set to \$16 million per year for the US firm, and \$6 million per year for the European firm, and the level of regulatory uncertainty, γ, set to 0.1 for the US firm, and 0.2 for the European firm.

Using the parameterization detailed above, 1,287 iterations were run representing the number of US biotechnology start-ups in 1996; in addition, 716 iterations were conducted to represent the number of European start-ups that same year. Given these 2,003 total iterations, Table 1 below reports the share of successfully completed R&D projects owned by US and European start-ups.

Table 1: Share of Successfully Completed R&D Projects (% owned)

US Start-ups	91
European Start-ups	9

In an industry populated solely by start-ups, the sources of heterogeneity, embodied in the per-period rate of investment and the level of regulatory uncertainty, result in the majority of successful R&D projects belonging to US firms. This corroborates the previous results reported by Lavoie and Sheldon. By extension, and absent the presence of multinationals, it is also the case that the excess returns from innovation embodied in these projects are also concentrated in the United States.

Multinationals are introduced into the analysis in the form of a random process representing multinational penetration of the biotechnology industry. This process is intended to be suggestive of the option management problem underlying the multinationals' entry decision; however, at this stage the specifics of the problem are not modeled. Instead, a function f(*t*) is defined to be the probability at time *t* that a start-up's R&D will be acquired by a multinational, where $f(t) = 1/[(\gamma_F/\gamma_D)\rho t+1]$, defined on the interval (0,1]. In this equation, γ_F and γ_D are the levels of regulatory uncertainty in the foreign and domestic biotechnology industries, and ρ is a constant scalar set to 0.001. The function f(*t*) equals one at time $t = 0$, and converges to zero in the limit as *t* goes to infinity. This function is used to characterize the probability that a multinational acquires the R&D of a start-up. At the commencement of each iteration, a random draw *u* is made from the uniform distribution, on the range [0,1]. For each time period *t*, *u* is compared to the contemporaneous level of f(t). If $u > f(t)$, then the R&D is acquired by a multinational; else, the start-up continues to retain ownership. Note that the probability of a multinational acquiring the R&D increases with *t*, corresponding to the idea that the value of ongoing R&D increases over time, as proprietary knowledge stocks develop and mature.

The ratio (γ_F/γ_D) is positively correlated with f(t). In other words, an increase in the level of regulatory uncertainty in the foreign industry, or a decrease in the level of uncertainty in the domestic industry, increases the probability that a domestic start-up's R&D will be acquired by a multinational. This is because, *ceteris paribus*, a multinational would prefer to minimize the risk associated with its investment by operating in a relatively certain regulatory environment.

If the random process determines that a start-up's R&D is acquired by a multinational, a second random draw, *uu*, from the uniform distribution determines the geographical origins of the purchaser. For simplicity, it is assumed that US and European multinationals are equally

likely to purchase ongoing start-up R&D. Therefore, if *uu* > 0.5, the multinational is considered US-based; else, the multinational is considered European-based.

It is assumed that multinationals do not perform R&D internally, and that the potential for multinational acquisition does not enter the start-up investment decision process. Given this characterization of the activity of multinationals, the simulations for US and European biotechnology firms are re-run, with the added refinement of the possibility of multinational acquisition. The following results are obtained.

Table 2: Share of Successfully Completed R&D Projects (% owned)

	US	**European**
Start-ups	51	9
Multinationals	21	19

The introduction of multinationals into the industry has the effect of transferring control of a portion of the successful R&D projects to multinationals: approximately 60 percent of the projects are owned by the start-ups who originated them, while the remaining 40 percent have been acquired by multinationals. The penetration of multinationals into the market is not symmetric across countries, however. In Table 3, the level of multinational penetration in the US and European industries is reported.

Table 3: Level of Multinational Penetration (%)

US Industry:	42
European Industry:	26

Penetration of the US biotechnology industry by multinationals is greater than that of the European industry, brought about by the higher level of regulatory uncertainty associated with the latter; in other words, multinationals are more likely to acquire the R&D of US-based start-

ups than their European counterparts. This result can be sharpened by examining cross-country ownership of biotechnology assets, reported in Table 4 .

Table 4: Cross-Country Multinational Penetration (%)

R&D Originated by US Start-up, Owned by European Multinational:	19
R&D Originated by European Start-up, Owned by US Multinational:	10

These results suggest that the concentration in the United States of assets and returns generated from the successful R&D projects has been diluted compared to the case of a start-ups-only industry, as control of R&D shifts from US start-ups to European-based multinationals. Thus the result is obtained that, despite the US comparative advantage in biotechnology, embodied in international differences in the per-period rate of investment and the level of regulatory uncertainty, and exploited by the US start-ups to emerge as world leaders in the industry, European entities control a substantial portion of the market. Specifically, US firms, start-ups and multinationals, control 72 percent of the R&D, while European firms control the remaining 38 percent. This can be compared to the benchmark start-ups only case, where US firms controlled over 90 percent of the R&D. Ironically, this re-allocation of returns is the result of one of the very sources of heterogeneity which established the US comparative advantage in the first place, the lower level of regulatory uncertainty.

To sharpen understanding of the effect of regulatory uncertainty on multinationals' decisions to acquire ongoing start-up research, a comparative statics analysis is undertaken in the form of increasing the level of European regulatory uncertainty to 0.5. Re-running the simulations with this change in place yields the following results.

Table 5: Share of Successfully Completed R&D Projects (% owned)

	US	European
Start-ups	34	15
Multinationals	24	27

The increase in European regulatory uncertainty has the effect of reducing still further the share of the industry controlled by US start-ups (from 51 to 34 percent), and simultaneously increasing the share held by multinationals. Multinational penetration of the US and European industries is reported in Table 6.

Table 6: Level of Multinational Penetration (%)

US Industry:	60
European Industry:	7

The increase in the level of regulatory uncertainty in the European industry has the effect of increasing the presence of multinationals in the US market from 42 to 60 percent, while, at the same time, reducing penetration of the European market from 26 to 7 percent. This point is corroborated through an examination of the cross-country ownership of biotechnology R&D.

Table 7: Cross-Country Multinational Penetration (% owned)

R&D Originated by US Start-up, Owned by European Multinational:	32
R&D Originated by European Start-up, Owned by US Multinational:	5

The presence of European-based multinationals grows from 19 to 32 percent, indicating a significant transfer of assets and returns from US entities to European ones. Specifically, US firms now control only 58 percent of the global industry, while the European share has climbed to 42 percent. As regulatory uncertainty increases in Europe relative to the US, start-ups in the US become correspondingly more attractive relative to European start-ups as acquisition targets for multinationals. This result has important implications in the context of events currently

witnessed in the biotechnology industry. As the European Union continues to tighten its regulatory regime governing biotechnology, this translates into a higher value of γ for the European industry. As the results above suggest, a higher European γ has the dual effect of increasing both multinational penetration of the US industry, and also the number of alliances and acquisitions effected between European multinationals and US-based start-ups.

4. Implications for Trade Equilibrium and Policy

In this paper, the issue of multinationals and the international allocation of assets and rents arising from biotechnology R&D were considered. Using the real options model of biotechnology R&D developed by Lavoie and Sheldon, modified to include a simple process by which multinationals acquired ongoing R&D conducted by start-ups, computer simulation illustrates that the presence of international differences in the form of the level of regulatory uncertainty, while contributing toward the US comparative advantage in biotechnology established by US start-ups, also serves to increase the attractiveness of US R&D as targets for multinational acquisition. Thus, the assets and excess returns one would expect to accrue to US firms based on their comparative advantage are at least partially re-allocated overseas.

The presence of European multinationals in the US biotechnology industry raises an interesting policy issue for US trade authorities. The implication of the above analysis is that as the regulatory environment in the European Union toughens, the alliance and acquisition activity of European multinationals in the US biotechnology industry should increase. But this implies that even as the European Union restricts biotechnology activity within its own sphere of influence, by imposing such measures as the moratorium on further approvals of biotechnology products (Nelson, *et al*., 1999), they still enjoy the fruits of biotechnology in the form of

European multinationals' claims on the excess returns from innovation embodied in the proprietary knowledge stocks originating from American start-ups. This suggests the following question: should the US impose policies to protect ownership of its biotechnology assets in response to Europe's tightening of its regulatory restrictions, and if so, what form should these policies take?

Another issue is the long-term trade equilibrium that will emerge in biotechnology, given the industry's structure and dynamics. It might be expected that, given the favorable R&D investment conditions in the United States, which initially established comparative advantage, firms located in the United States will continue to specialize in biotechnology R&D and production. These firms will be either independent start-ups, start-ups in R&D alliances with multinationals, or start-ups that are wholly or partially-owned by multinationals. This pattern of specialization suggests that in the long run, the US will be a net exporter of biotechnology products. However, the rents commonly associated with high technology production will not be entirely captured by US enterprises: rather, a portion of these rents will be appropriated by foreign-based multinationals, in the form of intra-firm transfers from US subsidiaries or profits shared with US partners.

It is interesting to note that in the food and agricultural sector, two trading patterns could arise. In the first, the US exports "intermediate" biotechnology products in the form of genetically modified seeds, that embody the proprietary R&D, and subsequently imports the "finished" product in the form of processed food containing genetically modified ingredients derived from the seeds. In this case, the rents from innovation accruing to US entrepreneurs are dissipated on two levels: first, through the capture of rents brought about by the European multinationals' penetration of the US biotechnology industry, and secondly, through capture of

the rents generated in the final consumer market in the form of the premiums commanded by differentiated goods, specifically, genetically engineered "designer" foods.

In the second case, the US exports either agricultural commodities or/and finished food products that embody the proprietary R&D. In this case, the rents from innovation accruing to US entrepreneurs are also dissipated on two levels: first, through the capture of rents brought about by the European multinationals' penetration of the US biotechnology industry, and, second, through the extent to which European multinational firms have also acquired the ability to deliver biotechnology via either acquisition or alliance with US seed and food processing firms.

References

Ernst & Young. *Biotech 97: The Eleventh Industry Annual Report*. Ernst & Young LLP, 1997a.

Ernst & Young. *European Biotech 97: A New Economy: The Fourth Annual Ernst & Young Report on the European Biotechnology Industry*. Ernst & Young LLP, 1997b.

Grossman, G.M. and E. Helpman. *Innovation and Growth in the Global Economy*. Cambridge, MA: MIT Press, 1991.

Krugman, P.R. "Import Protection as Export Promotion: International Competition in Presence of Oligopoly and Economies of Scale." In H. Kierzkowski, *Monopolistic Competition and International Trade*. Oxford, UK: Oxford University Press, 1984.

Lavoie, B.F. and I.M. Sheldon. "The Source of Comparative Advantage in the Biotechnology Industry: A Real Options Approach." *Agribusiness – An International Journal*, 16 (2000): 56-67.

Nelson, G.C., Josling, T., Bullock, D., Unnevehr, L., Rosegrant, M. and Hill. L. "The Economics and Politics of Genetically Modified Organisms in Agriculture: Implications for WTO 2000." Bulletin, 809, Office of Research: University of Illinois at Urbana-Champaign, 1999.

Pindyck, R. "Investments of Uncertain Cost", *Journal of Financial Economics* 34 (1993): 53-76.

Sharp, M. "The Science of Nations: European Multinationals and American Biotechnology" STEEP Discussion Paper #28, Science Policy Research Unit, University of Sussex, 1996 (available at: http://www.sussex.ac.uk/spru/docs/steepdps/28/steep28.txt)