Proper Citation:
TURBO-CHARGING BIOINFORMATION FOR DRUG DISCOVERY

“Unlike material goods, information does not disappear by being consumed, and even more important, the value of information can be amplified indefinitely by constant additions of new information to the existing information. People will thus continue to utilize information which they and others have created, even after it has been used.”  
Yoneji Masuda.

1 From Gathering To Information Gathering

Since the dawn of modern civilization, we have witnessed at least three watershed revolutions. There are, in chronological order, Agrarian, Industrial and Information Revolutions. The first occurred when modern civilization transitioned from hunting and gathering into more a developed agricultural economy. Hunting and gathering lasted for hundreds of thousands of years. Since then, the duration of each successive economy has gotten shorter and shorter. Agricultural dominance persisted for less than ten thousand years. The industrial economy lasted for slightly less than two centuries (1760s to 1950s) globally, with something like ninety years (1860s to 1950s) in the United States. We are probably seeing the current information economy halfway through its seven- or eight- decade life span.¹

The industrial economy produces and emits waste by-products. We call them pollutants or consider them useless, but some of these by-products can be, and have been, put to better use. Natural gas is a classic example. Originally burned off at the wellhead as useless, it became a major industry when infrastructures and markets were developed. Turbo-chargers, another example, recycle engine exhaust fumes to greatly enhance performance and increase power.

2 Information Economy

The information economy also produces information exhaust, and it too can be turbo-charged. Information exhaust can be captured, processed, and recycled to improve business performance. Opportunities exist to provide turbo-charged information services in all businesses and industries. In fact, a new generation of enterprises built around information emitted from older business is already taking shape. The irony is that turbo-charged information service businesses often become worth more than the businesses from which the information is generated in the first place. And examples abound.

For example, Quotron provides information about security prices to brokerage companies. In 1986, Citicorp purchased it for US$628 million. Quotron did not possess proprietary access to securities information. It simply filled a need that brokers had not been attended to by simply capturing securities transaction information and recycling it back to the brokerage industry that generated the information in the first place. In doing so, it created a business with market value greater than the market values of the then leading brokerage firms such as Paine Webber and Smith Barney.

Similarly, Rupert Murdoch acquired TV Guide in 1987 for more than US$2 billion. This publication is essentially a well-packaged listing of TV broadcast schedules, information that is available to anyone from a number of sources. Despite this, the purchase price for TV Guide had a market valuation higher than any one of the major broadcast networks, ABC, CBS, or NBC at that time.

And, Official Airlines Guide (OAG), a listing of monthly flight schedules, sold in 1988 for US$750 million. OAG simply consolidates flight information, yet the basic concept created a business with a greater market value than most airlines, and only slightly less than the market valuation of US Air. More recent examples are Yellow Pages compiled by telecommunications companies, which scoop in more revenue than selling standard telephone services, Hotmail acquired by Microsoft, Infoseek bought out by Go Network (now defunct), and not to mention Yahoo!, eBay, Amazon.com, WebMD and many others.

These examples suffice to show that the proper order of things seems to be standing on its head. Someone, it would seem, has to perform brokerage services so that profits can be made selling financial information services. TV programs are produced and broadcast to create a need for TV Guide. During the downturns of the airline industry, it would seem as if someone has to fly airplanes so that money can be made selling flight information and reservation services. Telephone services are provided to stay in touch so that there is a need for Yellow Pages. Last but not least, the Internet was introduced to transcend socio- and geo-political barriers. Yet in each instance, the turbo-charged information is worth more than the primary business from which the information is derived!

We thus see that information offshoots represent a tremendous business opportunity, and if we take the cue from T.S. Eliot “The historical sense involves the perception not only of the pastness, but of its presence”, it would seem every business contains one or more latent info-businesses. And drug discovery is no exception.
3 Drug Discovery

The chronology in drug discovery in the past century is summarized in Figure 1.\(^2\)

Drug discovery has come a long way in the past century. In early days, drugs were discovered serendipitously. As the science advanced, more systematic and scientific means were used to develop new drugs. Classical drug discovery has been a process of trial and error involving use of natural products and synthetic compounds for the purpose of identifying new chemical entities, many of which fail and a few may reach the marketplace as pharmaceuticals. However, as easier to develop drugs have been “cherry-picked”, more and more involved techniques have to be developed to compensate for the complexity.

Currently, we are at the threshold of this classical way of developing new drugs. The cost of drug discovery and development has spiraled in recent decades because the process has become both very expensive and time-consuming. The cost for developing a new drug is about $400 million and it takes about 12 to 15 years. Figure 2 shows the cost increase in the past quarter of a century.

\(^2\) http://www.phrma.org.
Figure 2. The cost of developing new drugs has been spiraling in the past two and a half decades from $54 million in 1976 to about $400 million in 1990 and to about $700 million in 2001.

Other indicators abound. Table 1 presents the annual prevalence and the cost of the top eight uncured diseases in the U.S. in 1995-1996, while Table 2 lists the pharmaceutical and healthcare expenditures in the world’s ten most developed countries in 1994. These indicators suffice to show that if left unchecked, it is conceivable that pharmaceutical and healthcare expenditures will spiral out of reach of the most needy in the very foreseeable future. Thus there is a dire need for a revolution or paradigm shift in the drug discovery and development process.

Table 1. Despite all the news coverage of new discoveries and doctors’ claim that they can “cure” diseases, to date, there are only a dozen of curable diseases. The annual prevalence and cost of uncured diseases in the U.S. are rampant (data of 1994/5).

<table>
<thead>
<tr>
<th>Uncured Diseases</th>
<th>Approx. Annual Prevalence</th>
<th>Approx. Cost ($Billion)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>56,000,000</td>
<td>$128</td>
<td>Am. Heart Assoc.</td>
</tr>
<tr>
<td>Cancer</td>
<td>10,000,000</td>
<td>$104</td>
<td>Am. Cancer. Assoc.</td>
</tr>
<tr>
<td>Alzheimer's</td>
<td>4,000,000</td>
<td>$100</td>
<td>Alzheimer's Assoc.</td>
</tr>
<tr>
<td>Diabetes</td>
<td>16,000,000</td>
<td>$92</td>
<td>Am. Diabetes Assoc.</td>
</tr>
<tr>
<td>Arthritis</td>
<td>40,000,000</td>
<td>$65</td>
<td>Arthritis Assoc.</td>
</tr>
<tr>
<td>Depression</td>
<td>17,400,000</td>
<td>$44</td>
<td>Nat. Depression Assoc.</td>
</tr>
<tr>
<td>Stroke</td>
<td>3,000,000</td>
<td>$30</td>
<td>Nat. Stroke Assoc.</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>28,000,000</td>
<td>$10</td>
<td>Alliance of Aging Res.</td>
</tr>
</tbody>
</table>

Table 2. Pharmaceutical and healthcare expenditures are not only rampant in the U.S., they are also significant in other ten most developed nations in the world. Note that the expenditure on healthcare is about 5-10 times higher than the corresponding pharmaceutical expenditure. Note also that the expenditure on healthcare in the U.S. has exceeded $1 trillion.

<table>
<thead>
<tr>
<th>Countries</th>
<th>Pharma Expense $Million</th>
<th>Health Expense $Million</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>N/A</td>
<td>28,657</td>
</tr>
<tr>
<td>Canada</td>
<td>7,402</td>
<td>58,438</td>
</tr>
<tr>
<td>France</td>
<td>17,922</td>
<td>108,314</td>
</tr>
</tbody>
</table>
4 The Human Genome Project

The paradigm shift has been taking place. The archetypal and exemplar of this revolution is the Human Genome Project (HGP).\(^3\) HGP is often paralleled with the moon-shot program. While this metaphor may be useful in political and funding arenas, it does not convey the true significance of HGP. Moon race affected a negligible number of people substantially and had only negligible effect on a substantial number of people. The impact of HGP will be substantial and it will affect a substantial number of people. The primary purpose of HGP is to understand the molecular basis of human diseases. It will transform the lives of many people through the impact it will have on the pharmaceutical industry.

To the end of understanding human diseases on the molecular basis, HGP has already completed sequencing the first draft of the human genetic materials - the DNA sequences. A detailed sequence is expected in 2003. The human genome contains approximately 30,000-40,000 genes, out of which, by a conservative estimate, 5,000 genes may be associated with diseases.\(^4,5,6\)

5 Enabling Bioinformatics - The Enabler

“Necessity is the mother of invention”, and bioinformatics was born out of the need to manage genetic data. Bioinformatics is the study of information content and information flow in biological and biology-related systems. In its most restricted sense, it involves genetic, chemical, and healthcare data collection, management, analysis and dissemination.\(^7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23\) As such, it plays the

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\(^6\) Bioinformatics: A Strategic Business Analysis, (FrontLine Strategic Management Consulting Inc., Foster City, CA, USA, 1998).

offshoot role in genetic sequencing, biotechnology and pharmaceutical industries as a turbo-charger of genetic, chemical and healthcare information.

The marketplace for bioinformatics has been created by the emergence of new discovery paradigms in large-scale sequencing projects of HGP, which generate an astronomical amount of genetic data. Most of the data are irrelevant (“genetic waste” or “genetic exhaust”). Bioinformatics collects, manages, analyzes, and disseminates, as shown in the figure. In analogy to previous discussion, bioinformatics is enabled by HGP because HGP creates a niche for bioinformatics. However, bioinformatics is also enabling HGP because it creates a paradigm shift from classical drug discovery to a gene-based and chemical-based discovery program, as shown.

19 Molecular Bioinformatics - Sequence Analysis and the Genome Project, R. Hofestätde and Hwa A. Lim (Hrgs.), (Shaker Verlag, Aachen, Germany, 1997), 60 pages.
Figure 3. Large-scale sequencing produces a huge amount of genetic data. A large portion of the data is "genetic exhaust". Bioinformatics is the turbo-charger that collects, analyzes and disseminates the data and exhaust as useful information and knowledge.

Figure 4. A restricted definition of bioinformatics as applied to the new paradigm of drug discovery. The supply side shows that it is a specialized form of information technology (IT). Gene-based informatics comprises of hardware, database, and software tool components, while cheminformatics encompasses managing and analyzing small-molecule structures. The combination of gene-based and cheminformatics will likely drive the development of molecular diagnostics and therapeutics.

6 Proliferation Of Bioinformatics

A search for the word "bioinformatics" on the Internet using AltaVista search engine, for example, produces in excess of a hundred thousand matches, and a search for bioinformatics books using amazon.com produces more two dozen books. These are cyberspace evidences of the popularity of this relatively new field, almost 15 years old since the coinage of the word. In the physical world, the number of biotechnology, pharmaceutical, and information-based companies forming internal bioinformatics divisions is increasing daily. Fledging and emerging bioinformatics
companies arrive on the scene daily. These companies produce a plethora of similar but differentiated products and services. They vie for the same pie in the limited marketplace.

7 Market Structures

We alluded to the fact that a market for bioinformatics has been created by HGP. To better understand the bioinformatics market, let us take a cursory look at market structures. In general, there are four types of market structures: perfect competition, monopoly, monopolistic competition, and oligopoly.

7.1 Perfect Competition

A perfectly competitive market is characterized by many buyers and sellers who exchange a standardized or homogenous product. Buyers and sellers are fully informed of the price and availability of all resources and products. Firms and resources are freely mobile, with no obstacles such as patents, licenses to prevent new firms from entering or existing firms from exiting the market. Two classic examples which come close to this type of market structure are the stock market and the world grain market. The currently very lucrative Internet businesses are probably best described by this market structure. A participant in this market is a price-taker for it has to take or accept the market price.

7.2 Monopoly

“Monopoly” is a Greek word meaning “one seller”, just as we understand the word. A feature of this market is the high barrier to entry. Barriers to entry can be any impediments that prevent new firms from competing on an equal basis with existing firms in an industry. Three examples of barriers to entry are legal restrictions (e.g., patents and licenses), economies of scale (e.g., in the cable TV industry where once the cost for laying cable has been sunk, the cost for hooking up additional household declines), and control of essential resources (e.g., the diamond industry).

It is thus clear that in perfect competition, many suppliers offer a homogenous commodity to a market where firms can enter or exit the industry with ease. In contrast, monopoly involves only one seller offering a product with no close

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* In the United States, the economic downturn since the beginning of 2001 has put a halt to new companies entering the scene. The same can be said of other parts of the world, when the rippling effect is felt. In October of 2001, more than half of small German companies went under.

substitutes. These polar market structures are logically appealing, but most firms operate in market structures between these two polar structures.

7.3 Monopolistic Competition

As the name implies, inherent in the monopolistic competition market are both elements of monopoly and competition. In this market, many producers offer products with no close substitutes, but the barriers to entry are relatively low so that there are enough sellers to compete. Because of the monopoly, players in this market are price-searchers. The monopoly comes from product differentiation, in sharp contrast to the homogenous products in perfect competition. Product differentiation can be physical appearances (e.g., Burger King’s grilled Whopper versus McDonald’s fried Big Mac), location (e.g., Seven Eleven convenient stores which are actually selling the convenience of proximity to consumers and opening late hours), services (e.g., Domino Pizza stores who deliver), and product image (this is the image the producer tries to foster in the consumers’ mind. For example, Nike shoes are linked with quality and the “Just Do It” is imprinted in consumers’ mind).

7.4 Oligopoly

Oligopoly is a market dominated by a few sellers because of the high cost to entry, economies of scale or legal restrictions. In this market, the products can be homogenous, such as in the steel and oil industries, or the products can be differentiated, such as in the automobiles and tobacco industries.

These four market structures are presented pictorially in the figure for easy comparison. Based on these criteria, we shall now argue which of these market structures sequencing, biotechnology, pharmaceutical and bioinformatics companies belong to.

Figure 5. Figures to contrast the number of players, barriers to entry, the “size” and product homogeneity of industries in the four market structures. Note that we say “size”, which refers to the relative sizes in that particular market structure, and not size in its absolute sense. Perfect competition is
characterized by low entry barrier and product homogeneity. In contrast, monopoly is characterized by high entry barrier and low product homogeneity. Between these polar market structures are oligopoly and monopolistic competition. Note that an oligopolistic company can have homogenous products (for example, steel producers) or differentiated products (for example, automobile manufacturers).

8 Market Structures Of Bioinformatics, Sequencing, Biotechnology And Pharmaceutical Companies

The barrier to entry for high throughput sequencing companies is relatively high because it is costly to set up an enterprise large enough to have a sustainable competitive advantage. Once the system is in place, automation and ultra-high throughput technology provide economies of scale. They each produce raw data (homogenous products). Thus these companies are in the oligopolistic market with homogenous products.

Biotechnology and pharmaceutical companies are in the differentiated product oligopolistic market. For example, GlaxoWellcome has Zantac and SmithKline has Tagamet. Tagamet and Zantac serve more or less the same purpose (ulcer), yet they are not the same. The barrier to entry is extremely high. For example, in addition to patents, it costs about US$500M to discover and develop a drug. These companies are also interdependent, i.e., each firm must consider the effect of its own policies on competitors’ behavior. Thus biotechnology and pharmaceutical companies are in the oligopolistic differentiated product market structure.

Bioinformatics companies try to differentiate their products. For instance, the products are

- Web-based, graphical user interfaced, enterprise solution, integrated solution, task-specific (“physical appearance”) or neural-net based, hidden Markov approach (“approach appearance”)
- Platform-independent, flexibility, international convention compliant open system (“convenience”)
- Guaranteed 24×7×365 reliability (“post service”)
- Use of well-known engines, for example, Oracle for databases, or claim of product use by huge pharmaceutical colossi in press releases or third party validation (“product image”).

Many of the products perform similar task. They each claim reliability, accuracy and speed. The barriers to entry are relatively low, as is evident from the number of bioinformatics companies entering the marketplace each day. We thus argue that bioinformatics companies are monopolistically competitors.

An analogy will make the distinction clearer. A monopolistically competitive bioinformatics company is like a professional golf player. The player is striving for a personal best to win the tournament. In contrast, an oligopolistic biotechnology or pharmaceutical company is like a professional tennis player whose action and reaction depend on where the opponent hits the ball to outplay the opponent.
8.1 Goals of Bioinformatics Companies to Monopolize

We shall now investigate the monopoly component of monopolistically competitive bioinformatics industry.

Like any firms in other business sectors, bioinformatics companies would like to maximize profit by capturing a huge share of the market. In an attempt to do so, these companies try to follow the footsteps of successful products and may parallel their products with general-purpose software such as MS Office and AutoCAD. For example, they may see that MS Office is not necessarily the best software, yet through good promotion and marketing, Microsoft captures a significant market share. So these bioinformatics companies allocate huge sums for promotion in trade shows and workshops. Huge promotion is not an uncommon feature in a monopolistically competitive market.

Though their products are sometimes greeted with éclat in bio-publications, the actual sales may not quite live up to expectations. There are two plausible reasons for this:

- Most bio-publications are paid media for promotion. They are not an independent third party for evaluating products.
- There are many more players in the bioinformatics market, each vying to put the hole-in-one.

In addition, there are a number of distinctions between bioinformatics products and general-purpose software such as MS Office:

- MS Office’s latent client base is PC users in the private, public, and home-based sectors. The latent client base of bioinformatics companies is primarily oligopolistic biotechnology and pharmaceutical companies. This client base is not only much more limited, but they are also potential competitors for they may also develop their own bioinformatics tools in-house.
- PC users are likely to look for an easy-to-use software (such as MS Office) to get their work done. Expert users of bioinformatics products look for functionalities. It is unlikely that they will accept a product with “force down their throat” features. They likely would want to integrate the bioinformatics products into their in-house enterprise system for proprietary R&D.
- As shown in the figure, MS Office is product-focused, i.e. it requires little customization and sells in large volume. Bioinformatics products, in contrast, are highly customized.\(^{25}\)

Thus, in the current prevailing market, a monopoly of market share is likely an unattainable goal for bioinformatics companies.

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Figure 6. Bioinformatics software and databases for pharmaceutical and biotechnology companies are in the process focus category, i.e., high customization and small latent client base. Healthcare software and databases are in the intermediate focus category. In contrast, commonly used software such as desktop publishing software, MS Office, AutoCAD, is in the product focus category, i.e., low customization and large latent client base.

8.2 Competition

We now turn to the competition component of the monopolistically competitive bioinformatics industry.

Because of the large number of companies and the keen competitions, each company has to move with celerity to get to the market, sometimes with not fully tested products. Besides competing with each other, bioinformatics companies also have to compete with publicly funded institutions. Because of funding arrangements, these institutions normally provide their R&D results as freeware.

Perhaps the strongest competitions come from oligopolistic biotechnology and pharmaceutical companies integrating backward to form their own bioinformatics divisions. Examples of these include SmithKline, GlaxoWellcome and Wyeth-Ayerst, each of which have a sizable bioinformatics division. Another competition comes from information-based companies concentrically diversifying their business into bioinformatics to tap into the short-run profitability. Examples of these include Compaq Computers and the 1997 Reed Elsevier Publishing acquisition of Molecular Design Ltd. (MDL) in San Leandro, California, USA.

With their huge financial resources and established channels of distribution, they can in principle penetrate the market easier than fledgling and emerging

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\[^{a}\] Diversification into new product line that has technological and/or marketing synergies with existing product lines, even though the product themselves may appeal to a different group of customers.

bioinformatics companies. But size is a double edge sword. A larger size often allows for larger, more specialized machines, hardware and greater specialization of labor. This creates economies of scale. On the other hand, in the thicket of bureaucracy of larger companies, diseconomies of scale may result.

Let us now look at another market, the labor market.

9 Bioinformatics Entrepreneurs And New Entrants

The ranks of entrepreneurs are in constant flux as some emerge from the labor market to form their own enterprises and others return to the labor market after selling successfully or failing miserably. Whatever the reason, the supply of entrepreneurial ability is influenced by a variety of external forces. These forces include the pace of technological changes such as ultra throughput sequencing and computer technologies, government regulations and policies such as Small Business Innovations Research (SBIR) grants, or federal agencies’ recommendation to set up federally funded centers and institutions.27

Many entrepreneurs prefer the individual freedom that comes from self-employment. Some derive satisfaction from creative processes. Some dream of founding a corporate empire, and still some may have difficulty finding employment. Essentially, there are three typical roles played by entrepreneurs. They are not mutually exclusive. Entrepreneurs are either:

- **Broker**: These are the so-called “buy low and sell high” entrepreneurs. They contract with resource suppliers and combine the resources to form goods and services. They direct resources to the highest valued use, thus promoting economic efficiency. In such scenario, they attract rivals in the long run, forcing profit down to just a normal level.

- **Innovator**: These are the ones who can make an existing product for less than competitors do, or who introduce successful new products. In this scenario, the possibility of economic profit is a strong incentive for innovations. Whether the profit continues in the long run depends on whether competitors can imitate the cost-saving activities or the new products. Barriers to entry will help economic profit to continue into the long run as well.

- **Risk bearer**: These are those who venture into a world of uncertainty and get paid for their willingness to bear the risk. Examples of this are investment companies and angels.

With the exception of angels and venture capital firms, almost all bioinformatics companies are in categories 1 or 2. In category 1, the bioinformatics company functions like a “hollow corporation” or “network company”. It spends

most of its time on the telephone or the computer to coordinate suppliers. Examples of this category include bioinformatics companies that license to sell effectively through their distribution channels such as SinoGene.

In category 2, the bioinformatics company normally produces a flagship product, often times by combining products from various producers through licensing. Examples of this category include Compugen, D’Trends, DoubleTwist, Gene Logic, Genomica, NetGenics, and many others. The company can also integrate backward by hiring or buying-out those producers whose products (authors of software tools or databases) are critical to the company’s mission. Examples of this include Incyte and those who spend time developing their technologies in incubators, and bioinformatics companies spinning off publicly funded research institutions such as Human Genome Science spinning off The Institute for Genome Research (Bethesda, USA), and eBioinformatics spinning off the Australian National Genome Information Services (University of Sydney, Australia). Yet another category is those companies that farm out their development offshore (such as Russia) to cut down on cost. Examples include GeneGo and InforMax.

9.1 Bioinformatics Labor Supply

Having looked at entrepreneurs, we now turn to the behind-the-scene driving force of bioinformatics companies.

Like any other resources that produce goods and services, the demand for bioinformatics labor resources is a derived demand in the sense that companies looking for bioinformaticists do not value the labor resource itself, but rather the bioinformaticists’ ability to produce profitable products.

As depicted in Figure 6, bioinformatics is in the process-focused positioning strategy. This type of positioning requires a flexible work force. Members of a flexible work force are capable of doing many tasks, either at their own workstation or as they move from one workstation to another. This flexibility comes at a cost because it requires greater skill and thus more training and education. Though the cost is high, but the benefits can be large. It is probably the best way to achieve reliable customer service and alleviate capacity bottleneck. It helps absorb the feast-or-famine workloads.

Partially because bioinformatics is a relatively new field, it is still not a regular part of most teaching institutions’ curriculum, though the situation is changing rapidly. This, coupled with the rapid growth of organizations doing bioinformatics, creates a dearth of qualified bioinformaticists.\textsuperscript{28,29} The shortage is not very elastic in the sense that a qualified bioinformaticist acquires his/her qualification through

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\textsuperscript{28} “University reforms would help Germany to combat its worrying shortage of bioinformaticists”, \textit{Nature} 400, (Macmillan Publishers Ltd., 1999), pp. 93.

proper training, which takes time. This short differential should be corrected over
time. For now, we must make do and seek more mobile substitutes from closely
related disciplines of computer science, mathematics and life sciences.

Bioinformaticians - those who know how to operate bioinformatics packages -
on the other hand, are easier to come by. These technicians attend workshops and
evening classes, learn to use tools of the trade and graduate with certificates or
diplomas in short periods.

It is sometimes said that the private sector “is eating its own seed for
bioinformatics” because the private sector is recruiting faculty from the academia to
provide a ready source of knowledge and hence spillovers from the academia to the
private sector. The practice, where replacement is difficult, impairs the academia’s
capacity to continue training initiative.30 There are four interrelated explanations for
what appears to be the academia’s sluggish response to the dearth of
bioinformaticists.

- Individual faculty has no incentive to establish bioinformatics programs
  because traditionally, funding monies are primarily for research and
  researchers’ salaries.
- The education system responds differently when the demand is driven by
  the private sector. Life sciences are arguably not as responsive to demands
  driven by the private sector as are computer science and engineering.
- The interdisciplinary nature of the field creates disincentives to establish the
  program. The problems of working across departmental lines are difficult
  because of bureaucracies and turf issues within university administration.
- The quick fix of converting life scientists into bioinformaticists is not very
easy, given the lack of skills and quantitative abilities of life scientists. And
  the quick fix of augmenting computer scientists with life science encounters
  keen competition from the strong job market for computer scientists and
  engineers in the private sector.

Pressure from the labor market has changed many a risk-aversion university.

It is a noteworthy point that bioinformaticists are professionals. They are
typically different from nonprofessionals. They have a strong and long-term
commitment to their field of expertise. Their loyalty is more often to their
profession than to their employer. To keep current in their field, they need to
regularly update their knowledge. This explains the flourishing business of
bioinformatics publications (BioInform, BioVenture, BioWorld, Elsevier Trends
Series, Genome Technology, etc), bioinformatics reports,31 conferences (Cambridge
Healthtech Institute, Frost & Sullivan, etc), workshops, meetings and online training.

30 P.E. Stephan and G. Black, “Bioinformatics: does the US system lead to missed opportunities in
emerging fields?”, Report at National Research Council’s Committee on Science, Engineering and

31 An excellent example is Malorye A. Branca, T.V. Venkatesh, and Nathan Goodman, Bioinformatics:
Getting Results in the High Throughput Genomics, (Cambridge Healthtech Institute Publication, 2001),
178 pages.
There are other reasons why bioinformatics conferences, workshops, meetings and training are so successful. Though bioinformaticists and bioinformaticians are *Homo economicus*, lifetime income maximization is not their main interest. In a downsizing environment, job security has come on to be more important than maximum wages.\(^{32}\)

Having described the market structure and the labor market of bioinformatics, let us see how they interact.

### 10 Technology-Push, Market-Pull Or Interactive Marketing Strategies

In the days of “it is not what you manufacture, rather it is what you know that matters”, the distribution channel and marketing strategies are also different.

In the past, product development in the technology industry was largely driven by engineers, who usually designed products based on their own interests and left the marketing department with the task of finding consumers to buy them. This is the so-called bottom-up or technology-push approach:

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\text{Basic research} \rightarrow \text{Applied research} \rightarrow \text{Product development} \rightarrow \text{Pilot product trial} \rightarrow \text{Manufacturing} \rightarrow \text{Market/sales/services}
\]

With the accelerating pace of technology innovation, product cycles are measured in weeks rather than years. Many companies are finding that it makes more better business sense to design product based on what customers want rather than what engineers think they want. Increasing globalization of markets also makes the bottom-up approach impractical. For example, a black cellular phone with myriad functions designed for the U.S. market may hold little attention in Latin America, where bright colors and simpler designs are preferred. Thus a top-down approach or market-pull approach is better suited for current technology market environment:

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\text{Basic research} \leftarrow \text{Applied research} \leftarrow \text{Product development} \\
\leftarrow \text{Pilot product trial} \leftarrow \text{Manufacturing} \leftarrow \text{Market}
\]

Ethnography is a branch of anthropology that studies human culture. Social scientists hired by technology companies with the belief that their observations and insights will lead to the development of new products and services. Their task is like a reconnaissance mission - to map out the landscape, constantly foraging for opportunities for new technology. We thus propose an interactive scheme should be considered. The latter is a market-pull scheme couched in advances in the computer and the Internet technology. In this interactive mode, the market is identified through market survey and analysis. Then during development, there is a constant interaction (feedback) between the development team, the market forces, and the technology sector. Companies such as Microsoft and Perkin Elmer also organize

workshops to train clients to operate their products. Such a scheme is key in this fast-paced market and rapid advances in technologies. Any entrenched Luddith of new technologies will be permanently left behind.

Figure 7. Comparisons of technology-push, market-pull and interactive-pull marketing strategies. In recent product development, the traditional technology-push strategy has been replaced by market-pull strategy whereby the market is first identified and then a product is manufactured to satisfy the need. However, because of concurrent advances of computer and Internet technologies, basic market-pull strategy is quite inadequate to cope with the fast-pace marketplace. To keep abreast with rapid market changes, a more interactive strategy that maintains a constant interaction (feedback) between the development team, the market forces, and the technology sector, has to be adopted.

11 New Paradigm Adoption

We mentioned earlier that we are at the juncture of a new paradigm shift in drug discovery and bioinformatics is the turbo-charger. We now turn our attention to the adoption of this new paradigm.

Virtually all contemporary thinking about high-tech marketing strategy has its roots in the technology adoption curve, a model grew out of social research begun in the late 1950s about how communities respond to discontinuous innovations. Along a risk-aversion axis, adopters of the new paradigm self-segregate themselves into roughly a Gaussian distribution, with innovators (2.5%), early adopters (13.5%), early majority (34%), late majority (34%), and laggards (16%). The paradigm shift will be adopted from left to right, with each constituency coming to the fore in sequence. In high tech industries, we can re-label each of the five constituencies as (see figure):

- Innovators - technology enthusiasts: These are people who are fundamentally committed to new technology on the ground that sooner or later, it is bound to improve our lives. They derive pleasure from mastering the intricacies, in fiddling with, and love to get their hands on the latest and greatest inventions. They are driven to be the first to explore.

Early adopters - visionaries: These are the true revolutionaries who want to use the discontinuity of any innovation to make a break with the past and start an entire new future. Their expectation is that by being the first to exploit the new capability they can achieve a dramatic and insurmountable competitive advantage over the older order. In contrast to enthusiasts, they are driven to be the first to exploit.

Early majority - pragmatists: These people do not love technology for their own sake. They are neutral about technology and look to adopt innovations only after proven track record. They believe in evolution rather than revolution in the sense that they accept the new technology as a natural extension of the older order (evolution) rather than a paradigm shift (revolution or discontinuity).

Late majority - conservatives: These are pessimists who doubt their ability to gain any value from technology investments and undertake them only under duress—typically the only alternative is to let the rest of the world pass them by.

Laggard - skeptics: These are the gadflies of high tech, the ones who delight in challenging the hype and puffery of high technology.

Thus, we coin the five “e’s” of new paradigm adoption: technology enthusiasts explore, visionaries exploit, pragmatists evolve, conservatives employ, and skeptics elude.

Figure 8. In the adoption of a new innovation or a paradigm shift, adopters self-aggregate themselves into five constituencies. The most risk-immune are the technology enthusiasts, followed by visionaries. Pragmatists are neutral while conservatives are most risk-averse.
12 Who Prevails

With so many external factors - technology, federal policies, competitions, labor resource supply, technology adoption - to worry about, which bioinformatics companies will prevail eventually? To shed light on this important issue, let us look at the microeconomics of supply and demand of bioinformatics products.

Because each monopolistically competitive bioinformatics company offers a product or a gamut of products that differ somewhat from other competitors’ products, each company has some control over the price. This means that the demand curve slopes downward, i.e., not completely elastic, as shown in the figure. This is a reasonable assumption since if the quantity produced is decreased, the unit selling price should go up as the firm is a price searcher.

However, monopolistic competitive bioinformatics companies have no guarantee of economic profit, as we shall show presently.

12.1 Short-run Profit/Loss Optimization

If in the short-run, a period too brief to allow a bioinformatics company to enter or leave the market, the company can cover its variable cost\(^\beta\), it will increase output (sales) as long as marginal revenue (MR)\(^\chi\) exceeds marginal cost (MC)\(^\delta\). The opposite case of MR<MC means the company is operating at a loss and thus there is no reason to expand production. The profit-maximizing level of output occurs where MC intersects MR, and the corresponding profit-maximizing price (p) is the one on the demand curve at that level of output (q), as shown in Figure 9. At an average total cost (ATC)\(^\varepsilon\) of ATC', where ATC' is partially below the demand curve D [otherwise (p-c') will never be positive], the company will maximize a short-run profit of q×(p-c'). This is a profit because (p-c') is positive, and it is an extremum as can be seen by varying q. For other q values, (p-c') is smaller.

While at an average total cost of ATC'', where ATC'' is completely above the demand curve D so that (p-c'') is always negative, the company will minimize a short-run loss of q×(c''-p). Again this is an extremum as can be seen by varying q. For other q values, |(p-c'')| is larger.

So depending on along which ATC the company is operating, it may be making a profit or incurring a loss. In the latter case, the company may want to shut down temporarily to reevaluate itself. If the loss is expected to persist, the company should consider leaving the industry for good.

\[^\beta\] Any production cost that increases as output increases.

\[^\chi\] The change in total revenue resulting from a one-unit change in sales. In our examples of perfect competition, marginal revenue equals to market price.

\[^\delta\] The change in total cost resulting from a one-unit change in output. Mathematically, this is ratio of change in total cost to change in output, \(\Delta C/\Delta P\).

\[^\varepsilon\] Total cost divided by output, or the sum of average fixed cost and average variable cost.
Figure 9. Production level, price, short-run and long-run profit/loss of a monopolistically competitive bioinformatics company. If ATC (average total cost) is partially below the demand curve D so that the difference of unit selling price and cost of production \( (p-c') > 0 \), the maximum short-run profit is \( q \times (p-c') \). On the other hand, if ATC is completely above D, \( (p-c`) \) is always negative, the minimum short-run loss is \( q \times (c`-p) \). In the latter case (loss), the company must decide whether to produce or to shut down temporarily. Shutting down temporarily is not the same as going out of business. It allows the company to reevaluate and realign itself. However, if the loss is expected to persist, the company should consider leaving the industry permanently. The monopolistic competitive long-run scenario is depicted by ATC osculating D, in which the company will earn no economic profit.

12.2 Long-run Economic Profits

Since the barriers to entry are very low, short-run economic profits\(^6\) of existing bioinformatics companies will attract new entrants in the long-run. Because new entrants offer a product that is quite similar but differentiated to those offered by existing firms, they draw customers from existing firms thereby reducing the demand of each company. Entry will continue in the long-run until economic profit disappears.

On the other hand, if existing bioinformatics companies incur short-run losses, some of them will leave the industry in the long-run, redirecting their resources to activities that are expected to earn at least a normal profit\(^7\). As companies leave the industry, their customers will switch to remaining companies, increasing the demand for each remaining company’s products. Companies will continue to leave the industry in the long-run until remaining companies have enough customers to earn a normal profit (opportunity cost\(^8\)), but not economic profit (total revenue minus explicit and implicit costs).

In the long-run, entry and exit will alter each company’s demand curve until economic profit disappears. This situation is attained when ATC is tangential to D.

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\(^6\) A firm’s total revenue minus its explicit and implicit costs.

\(^7\) The accounting profit required to induce a firm's owners to employ their resources in the firm. This is also the accounting profit earned when the firm earns their opportunity cost.

\(^8\) The value of the best alternative foregone when an item or activity is chosen.
At the point of osculation, average total cost (ATC) equals the price. At all other level of output, the company’s average total cost is above its demand curve, so that the company will lose money if the company reduces or expands its output.

Thus, in the long-run, monopolistically competitive bioinformatics companies will earn no economic profit. The above model assumes that monopolistically competitive bioinformatics companies do not regularly come up with new innovations or that they do not integrate backward, or merge with competitors.

13 Perfect Versus Monopolistic

So what can we infer from the supply-demand of bioinformatics products? Let us compare and contrast bioinformatics business with one of its close relatives, the Internet business, which is probably better described by perfect competition.

In perfect competition, Curve D in Figure 9 is a horizontal line and points a and b collapse to a single concurrent point of intersection of MC, ATC and D at the extremum of ATC resulting in a higher level of output than q shown in Figure 9. Thus perfect competitors in the long-run produce at full capacity at the lowest cost (ATC). Monopolistic competitors have excess capacity. Excess capacity means they can serve more customers to lower the average cost. If the marginal value of production exceeds the marginal costs of production, expanding output would increase marginal value more than marginal cost, thereby increasing economic welfare. The latter scenario probably describes publicly-funded bioinformatics R&D.

We also point out a key difference between perfect competitors and monopolistic competitors. Monopolistic competitors tend to spend more on advertising and promotion to differentiate their products. These expenses are not reflected in Figure 9. Accounting for these expenses will shift the average cost curve higher. Some people argue that the product differentiation among monopolistic competitors is artificial, while others argue that consumers are willing to pay a little more for a greater selection.

14 Bioinformatics Gorillas, Chimpanzees And Monkeys

A good friend who is also a well-respected authority in bioinformatics once jokingly remarked, “If you want to be rich from bioinformatics, be an attorney”. He has a point. Legal matters can be pernicious to any organization. The only winning parties are the attorneys. Let us also not forget in business, one never makes an enemy. A whilom enemy may be a future strategic partner. And strategic partnerships seem to be a way to stay ahead in the competitive bioinformatics market because partnerships help get to the end results or new innovations sooner and more cost-effectively. Else, the god old aphorism of “publish or perish” in the
academic sector can be translated into “innovate or perish” in the bioinformatics business. The sole survivors are those who can perform best the funambulism of innovation and marketing, those who know how to introduce the future into the present. And ultimately, only a few will survive as oligopolistic bioinformatics companies, be it through mergers or hostile takeovers.

As of now, diseconomies of scale of large biotechnology and pharmaceutical companies are working in the favor of small savvy bioinformatics companies. Because of bureaucracies, large companies have more inertia than smaller bioinformatics to realign to the rapidly changing technologies. Also working in favor of bioinformatics companies are federal agencies’ effort to ensure that genetic data do not lie only in the hands of the private sector. Federal agencies do so by investing huge sums into large sequencing projects, two examples of which are the Whitehead Institute of MIT and the Department of Energy Joint Genome Institute in Walnut Creek, California.

As the turbo-charger of biotechnology and pharmaceutical discoveries, bioinformatics will remain popular for the new millennium. However, two to three more years (from 2001) will demarcate an evolutionary epoch of “survival of the operationally fittest” of many small monopolistic bioinformatics competitors. To conclude, we borrow the gorilla-chimpanzee-monkey terminology from Jeff Tarter, a software industry analyst and the editor of SoftLetter. By that time, a couple of dominant competitors, the gorillas, will have emerged; a handful strong market contenders, the chimpanzees, will have remained; and a score of opportunists, the monkeys, will seek a small piece of the left-over bioinformatics pie.

Though we like to use September 11, 2001 incident of the World Trade Center Twin Tower as an excuse, the first two quarters of 2001 was a dismaying period of deteriorating economies in the U.S. Poor market performance has ushered in the demise of many of these companies. September 11 incident is only a catalyst, NOT the cause.

15 Early And Late Majority Asian Bioinformatics And Biotechnology Countries

15.1 Singapore – One of the Four Tigers

During November 18-20, 1992, HAL visited the National University of Singapore. After a lot of hard work, Dr. Tan Tin Wee managed to set up the Bioinformatics Centre (BIC). In 2001, the Singaporean government announced another big investment into biotechnology.
Singapore has been a regular on the international biomedical arena. Of note is the recent Fugu Genome Project. The Fugu Genome Project was initiated in 1989 by Sydney Brenner, Molecular Research Center (MRC, Cambridge, England), along with colleagues Greg Elgar, Samuel Aparicio, and Byrappa Venkatesh. The International Fugu Genome Consortium was formed in November 2000, comprising of U.S. DoE Joint Genome Institute (JGI, Walnut Creek, California, Director: Trevor Hawkins), Singapore Biomedical Research Council’s Institute for Molecular and Cell Biology (IMCB, Director: Chris Tan), U.K. Human Genome Mapping Resource Centre (MGMP-RC, Cambridge, U.K.), Cambridge University Department of Oncology, Institute for Systems Biology (Seattle, Washington), Celera Genomics (Rockville, Maryland) and Myriad Genetics, Inc. (Salt Lake City, Utah).

At a recent conference, the Consortium announced the completion of a draft sequence of the genome of the Japanese pufferfish Fugu rubripes.\(^{35}\) This Fugu draft sequence is the first public assembly of an animal genome by the whole genome shotgun sequencing method. For reassembly, a new computational algorithm, JAZZ, that was developed at JGI was used.

The Fugu genome (365×10^6 bases) is only an eighth the size of the human genome (3×10^9 bases), but it has a similar complement of genes. With far less junk DNA in the Fugu genome to sort through, finding genes and controlling sequences should be a much easier task than doing the same in the human genome.

\(^{35}\) The 13th International Genome Sequencing and Analysis Conference, San Diego, California, October 26, 2001
Sydney Brenner, now a distinguished professor at the Salk Institute for Biological Studies, San Diego, and Board Director of the Singapore Biomedical Research Council, commented, “This represents the culmination of more than a decade of work at Cambridge and Singapore. Without JGI’s initiative and Singapore’s strong support, the project would have languished. We already know it will illuminate the human genome sequence and help us understand it.”

Chris Tan, founding director of IMCB, said, “The draft of the Fugu genome will yield much more accurate estimates of the gene repertoire in humans. We will now be able to refine many of the features of the non-coding regions that may prove to have regulatory control over genes expressed in the human genome.” Singapore’s IMCB is already leveraging the genome sequence through the creation of a live Fugu genome bioinformatics analysis pipeline producing annotations and comparisons for the genome community.36

15.2 Korea – A Tiger

During October 5-23, 1993, HAL visited the Korean Institute of Science and Technology (KIST) to evaluate the cell culture projects and bioinformatics program, and to present a series of lectures on bioinformatics. KIST has now been renamed the Korean Research Institute for Biosciences and Biotechnology.

Photo 2. Left: HAL preparing lectures in his office at the Korean Institute of Science and Technology (KIST), Daejon, Korea. HAL was at KIST from October 5-15, 1993. Right: Dr. Pal Hajas, CPO, Food and Agricultural Organization (FAO) of United Nations (UN), and HAL. HAL visited the FAO office in Rome, Italy from October 24-27, 1993 to present findings and recommendations after a United Nations mission.

15.3 The Republic of China – A Tiger

The Republic of China (ROC) has enjoyed phenomenal successes in the computer business in the closing decades of the twentieth century. Former Finance Minister

36 www.eurekalert.org
Sun Yun-xiang is credited with the successes of the semiconductor industry. Two other principal factors have fueled the successes: one is technology transfer from the United States, mainly in the form of U.S.-trained engineers and computer scientists. The second is the pursuit of a strategy of efficient manufacturing of generic components and computers.

ROC is an island of calm. It weathered the recent Asian financial tempest with business flexibility, low debt, high foreign reserve (US$84 billion), the wits of small- and medium-size businesses, spending heavily on education, and moving rapidly up the value-added chain. ROC’s strength has been to focus on specific product categories, build expertise and dominate the world market. The integrated circuit industry was $3.95 billion in Y1996, $4.9 billion in Y1997, $7 billion in Y1998, and an impressive $9.8 billion in Y2000 from wafer and dynamic RAM (DRAM). At the Investment Forum of September 10, 1998, HAL proposed it was high time for ROC to diversify into other technologies, particularly biotechnology because the worry is its increasing reliance on a single sector – electronics - is holding the nation hostage with price cycles.

From November 12 through 19 2000, HAL, as leader of the Biotechnology and Pharmaceutical Delegate at a week-long meeting organized by the Chinese Institute of Engineers (President: Dr. Chintay Shi), visited Taipei and vicinities. Delegate members visited and discussed with members of local scientific institutions and business enterprises. Upon completion of the mission, the Delegate met with President Chen Shui-bian, made a report to Premier Chang Chun-xiong and Former Finance Minister Sun Yun-xiang. HAL concluded that the biotechnology in Taipei was a few years behind that of the U.S., and recommended the Taipei government investing a sum of $5 billion over a 5-year period. HAL also encouraged Taipei to work with the People’s Republic of China, knowing that Taipei had unsuccessfully bid for being a member of the International Human Genome Consortium, and that PRC had been investing a lot of money into biotechnology. In April 2001, the Taipei government announced plans to invest NT$150 billion (~$5.0 billion) into the biotechnology and pharmaceutical sectors.

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Photo 3. President Chen Shui-bian of Republic of China (fifth from left), HAL (third from left), the Biotech Delegate, and the Local Delegate at the Presidential Mansion, Taipei, November 16, 2000. HAL made a brief report to the President on the findings and recommendations of the Biotech Delegate.


15.4 Enter the Dagon – People’s Republic of China

As program director of Computational Biophysics and Molecular Biology at the Supercomputer Computations Research Institute, Florida State University, HAL was a delegate member of US-China Joint Conference on Computer and Education, November 9-15, 1992, with a highlight of presentations on November 10th at the Great Hall of the People, Beijing, China. The goal of the conference was to promote the use of computers in specific areas.

From February 12 through March 7, 1999, HAL was at Zhongshan University, Guangzhou, China to help establish the biotechnology and bioinformatics programs in the region. Besides lectures, there were meetings with city officials and trips to
Beijing to meet with central authorities to discuss projects and to raise funding. One of the outcomes is the BioIsland in Guangzhou.

Photo 5. Left: HAL explaining to reporters the importance of bioinformatics in drug discovery at a press conference held at the Biopharmaceutical Center, Zhongshan University, Guangzhou, China. HAL was at the Department of Life Sciences of Zhongshan University from February 25 through March 5, 1999. Right: HAL at the entrance to the headquarters of Haizhu Industrial Park. The BioIsland of Guangzhou was at its formative stages then.

On March 2, 2000, the North Bioinformatics Association Establishment Conference and Academic Report Meeting was held at the Science Auditorium, Tsinghua University, Beijing. Tsinghua University/Peking University duo is sometimes regarded as the MIT/Harvard duo of the U.S. HAL took part at the Conference as a foreign expert speaker. Also taking part, besides other participants, were some 62 members of the Chinese Academy of Sciences who were very keen to get the bioinformatics efforts in China stepped up, particularly after the Chinese Genome Program had accomplished its goal of sequencing 1% of the human genome as part of the International Human Genome Consortium.
Lest us forget, we must mention the great effort initiated by Dr. Jingchu Luo of Peking University. Luo has made Peking University one of the hubs of bioinformation in China. He is currently working with Beijing Genomics Institute (now renamed Genomics and Bioinformatics Institute, Chinese Academy of Sciences) and has plans to work with Zhongshan University in Guangzhou.

15.5 Rise with the Dragon

The general impression is that these bioinformatics and biotechnology efforts are slightly behind those of the United States and Europe. In some countries along the Pacific Rim, bioinformatics and biotechnology are burgeoning fields. Along the Adoption Curve discussed earlier, most of our Asian colleagues tend to be more pragmatic, and a few are even very conservative. China is leading the pack. Besides Japan, China is the only Pacific Rim country that is a member of the International Human Genome Consortium.

In Y2000 and Y2001, China also has entertained a lot of private funding sources even when fundings are ebbing in other parts of the world. However, the funding levels are uncreatively uniform, always the order of $2 million whatever the projects. These projects are usually projects of returning scholars. The efforts are rather diffused. We anticipate most of these me-to companies, with no proprietary technologies, will not survive beyond first-round financing, or will falter within a year or two of operations. There are yet another mode of business conduct. The government has an invisible hand in most businesses in this vast country. In an effort to encourage a more uniform spread of high-tech pockets throughout China, an unwritten regulation is that in cities where there have not been IPOs, IPOs will be approved more easily. Because of this, new companies – aimed for a quick IPOs - are being formed in remote areas where the infrastructure and distribution logistics are still wanting. Feasibility studies will reveal that most, if not all, of these operations are not viable.

There are commendable exceptions. An example is the Beijing Genomics Institute (BGI). In 2001, BGI changed its name to Genomics and Bioinformatics Institute (GBI), Chinese Academy of Sciences. GBI has numerous very impressive achievements since it started in 1998. It made its name sequencing a part of human chromosome 3 as one of the 16 members of the International Human Genome Consortium. In October 2000, BGI opened a branch in Hangzhou. The two locations, Beijing and Hangzhou, together are churning out 10 megabases or 50,000 reactions a day. Aside from finishing chromosome 3, GBI has embarked on three new projects: finding single nucleotide polymorphisms (SNPs) of the Chinese population, shotgun sequencing the pig with a Danish consortium, and sequencing the Indica strain of rice. GBI also has plans for high throughput proteomics project based on traditional Chinese medicinal herbs.

The spin-off from Tsinghua University –Capital Biochip Corporation - is a result from the effort of Zhu Rongji – Premier of China, and Cheng Jing, a returning scholar from University of Pennsylvania. The corporation, based in Beijing and headed by Cheng Jing, specializes in microfluidics chip (lab-on-a-chip). The chips will be mainly used for laboratory preparation, upstream of microarray hybridization. Capital Biochip Corporation has plans to launch several products in the upcoming year. The company has a window in San Diego. Aviva, formerly Artloon, is doing very well financially.

The only commercial biochip company that currently has products in China is BioWindow Gene Development, Inc. - a holding company of United Gene Holdings, Ltd. Founded in March 1998, they have engaged in large-scale cDNA cloning and sequencing, functional genomics, drug discovery and drug development. Their operation is a copy cat of Incyte Genomics’ business model. They entered cDNA microarray field in 1999. The microarray products and services they currently offer are,

- **BioDoor™** Gene Expression Microarrays
- **BioDoor™** Classified Gene Expression Microarrays
- **BioDoor™** Disease Management Microarrays
- **BioDoor™** Diagnostic Microarrays
- **BioDoor™** Mouse Expression Microarrays
- Custom Made Microarrays
- Microarray Related Services

When BioWIndow first launched their microarray products in mid 2000, the initial market response was very positive. Their sales of all microarray related products and services since introduction exceeded $1 million. Despite the initial successes, the company just experienced a big layoff.
In Y2000, Peking University and Hong Kong University formed a consortium with Shenzhen Central Hospital. Also, the Tsinghua University Group has established business operations in Shenzhen.

The Zhongguancun Haidan Science Park started as an experimental zone for promoting new technology. It capitalizes on its strategic location in the capital city, and is being fueled by talents from 56 colleges such as Tsinghua University and Peking University, and 138 research institutes such as the Chinese Academy of Sciences. Its One-Four-Eight Project - One new industry policy, four bases of focus areas, and eight aspects of good environment – is on target. Proud spin-offs include Legend and Founder.

The Pudong District of Shanghai is exemplary. For example, recently, Professor Chen Zhu, Director of the Chinese National Human Genome Center in Shanghai and Vice President, Chinese Academy of Sciences, reported a new finding of a collaboration between Sino-German Genome Center and Hoffman-La Roche Genetics. Working as part of the collaboration, Dr. Liu Lisheng of Beijing-based Fuwai Hospital, has identified three to four genetic markers on chromosome 2 that likely cause strokes – the number one killer in China – from 3,000 DNA samples of Chinese stroke patients.

These are commendable business models. But, currently, the Chinese pharmaceutical industry does not have the ability to discover and develop new drugs. For years, the Chinese pharmaceutical companies have been making generic drugs. As a result, the Chinese pharmaceutical companies have never been considered a serious player in an industry that generates multi-billion dollars every year. As the date that China joins WTO approaches, the Chinese pharmaceutical industry is going to face fierce competition and threat from international drug companies even in the domestic market. To survive, Chinese pharmaceutical industry needs help to discover and develop new and effective drugs to meet patients’ needs.

15.6 Asia and Pacific Rim Rising

Besides these centers along the Pacific Rim, there are also bioinformatics centers in Australia, Indonesia, Japan, Malaysia, Myanmar (formerly Burma), the Philippines, Thailand and Vietnam. The Philippines is part of the International Rice Research Institute.

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* One policy: promote development of Haidan Science Park. Four bases: software, biology and medicine, high technology, and innovation. Eight aspects of better environments for: innovative activities, open mindedness, legal system, finance resources, intellectual talents, continuing education, industry development, and government management and social services.

Currently, HAL is helping establish other bioinformatics and biotechnology programs in the United States, China and India.

A general good sign, nevertheless, is that these Pacific Rim countries are putting in huge efforts and are making great strides. For example, the People’s Republic of China, the Republic of China and Singapore have each committed a handsome sum of money into biotechnology. Employing a catch up mode of development by attracting returning U.S.-trained and Europe-trained scholars, these countries should be able to catch up sooner than most people would think.

While we do not encourage outright patent or intellectual property infringements, we opine copying to catch up is simply the fastest way to advance for these countries. Why duplicate efforts when advances can be made much sooner and cheaper by following trodden research paths? However, this is normally more easily said than done. Most societies resist copying. The copying process has to start by admitting that there is something to learn or that someone else does it better. Believing that if that something was not invented domestically, it cannot be worth copying is a universal human egostic failing. In the 1980s, American firms narrowed the manufacturing quality gap with the Japanese by shamelessly copying them. So why not these countries?

Increasingly, the acquisition of information and knowledge is central for both catch-up countries and stay-ahead countries. Smart developing countries understand the reality facing them. Operating as a monopolist – a monopoly buyer – these developing countries use their domestic markets as enticements and carrot sticks. For example, China has been saving 30% of its income and has accumulated $100 billion in international exchange reserve. It does not need foreign capital for development. But it can demand the sharing of technology from companies that sell in their market.41

Stay-ahead countries deplore the demands. But they should remember how they got to the present position in the first place. For example, U.S. remembers fondly the clever Yankee engineer with a photographic memory who visited British textile mills in the early 1800s and then reconstructed mills in New England.

16 Who Owns What?

Capitalism began in Great Britain when the enclosure movement converted communal agricultural lands of feudalism into privately owned land. To have an enforceable property right in capitalism, who owns what has to be clearly defined.42

The private ownership of productive assets and the ability to appropriate the output that flows from those assets lies at the core of capitalism. But not all

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countries are capitalist countries. Different cultures in different parts of the world view and interpret intellectual property rights differently. The idea that people should be paid to be creative is a point of view stemming from the Judeo-Christian-Muslim belief in a God that created humanity in his image.\textsuperscript{43} It has no analogue in Hindu, Buddhist or Confucian societies. Knowledge is seen as a free good.

On the other hand, what everyone owns, no one owns. Consider environmental pollution, everyone has an incentive to pollute, to use the free disposal system that is available and let someone else downstream or downwind bear the cost of cleaning up. However, on land that is privately owned, pollution market works. Private owners do not let their neighbors dump waste on their property. Someone seize the opportunity and gets into the business of opening up a dump site. The only problem with these private dump sites is that their owners in turn have an incentive to abuse the free pollution rights.

Capitalism cannot deal with pollution because it cannot establish the ownership rights to clean the environment. In certain sense, we were extremely blessed that during the U.S. longest period of prosperity of the Clinton administration, we had an environmental champion Vice President Al Gore.

16.1 Loopholes In Intellectual Property System

In this new economy, raw materials can be bought and moved to wherever they are needed. Financial capital is a commodity that can be borrowed, or financed by venture capital. The knowledge that used to be tertiary after raw materials and capital in determining economic success is now primary. The source of future success of a business is apt to be buried in the software and hardware of its electronic information and logistics systems rather than the advertising or the novelty of its products. Intellectual property rights now affect all businesses. It has moved from the periphery to the center of economic success. Themost successful companies have some lock on some form of knowledge. So, without a clear and enforceable system, knowledge-based capitalism is not going to work.

Intelectual property is also being used strategically. Patent suits are used to create uncertainties, time delays, and higher start-up costs for competitors. Whether used as an incentive for creativity or as a business strategy, historically, efforts to establish and enforce ownership rights to intellectual property have revolved around patents, copyrights, trademarks, and trade secrets. But new technologies are eroding the applicability of this old system, which was designed essentially for the technology of the nineteenth century. For example, this old system allows one to go to a library and browse a book such as this one without paying the publisher or author. But is downloading a book from the Internet equivalent to browsing? If so, how does one sell books when the books can be electronically scanned or downloaded onto a computer free of charge?

The important point is that the current legal system, designed more than a hundred years ago to meet the simpler needs of an economy based on natural resources and mechanical devices, is no longer adequate. The system of intellectual property rights, couched in the language of the current legal system, is an undifferentiated, one-size-fits-all system.

The prevailing wisdom of those earning a living in the current legal system is that some minor tweaking here and there will fix the problem. Opening up the system would be equivalent to opening up Pandora’s box. Unfortunately, the time has come for a complete overhaul of the system from ground up. This is unlikely going to happen if left to those making a living in the current system. They have too many vested interests in preserving the system.

Without a reasonable system of protection, companies will defend their economic positions by keeping their knowledge secret. Secrecy is an enemy of knowledge expansion, more so than a monopolistic system of protection of intellectual rights. An investigator who knows what is already known can proceed to the next step, instead of groping in an intellectual wilderness looking for trodden paths. Indeed, a recent research found that 73% of private patents were based on knowledge generated by public sources such as universities and nonprofit or government laboratories.44

When it comes to biotechnology, the patent issue can be even more troubling. For example, no society will let anyone have a monopoly on the cure for cancer, nor will biologists be allowed to freely clone or own human beings. This is why the publicly funded consortia such as the Genome Consortium, the Fugu Fish Consortium are commendable worthy efforts. But it is clear that private companies must be allowed to own part of the human beings. Otherwise, no company will invest the funds necessary to find cures. Thus we have Celera Genomics, Human Genome Science and the like.

Biotechnology is a dual-use technologies. The same techniques that can cure human ailments can also be used to enhance humans or make humans more efficient such as smaller but smarter. Thus patents on genetic cures is difficult to differentiate from patents on human enhancements. A possible solution is to draw a distinction between fundamental advances in knowledge and logical extensions of existing knowledge. Inventing a new piece of biology that alters the natural characteristics of plants, animals or humans is not the same as discovering how an existing piece of biology works. What a patent means in these instances has to be different.

16.2 Brain Drain Or Gain?

Technology has juxtaposed intellectual property ahead of raw materials and capital. Other factors are also contributing to the need for a better system. From the Second World War to recently, knowledge has flowed freely and cheaply around the world. The U.S. financed for most of the basic research while most other countries invested mainly in development. With the exception of classified technologies, worldwide dissemination was encouraged. During the Cold War, the economic success of other countries was seen as important to the strategic geopolitical position of the U.S. as to its internal economic success.

But the world is now very different. U.S. economic dominance is not as clear as it used to be. As a vivid sign to control the flow of information, members of the Congress call to keep foreign students out of U.S. universities or laboratories. However, we must not forget that most of these people that we get are the cream from these foreign countries. These countries have footed for the most expensive part of their early education. If we retain them after training them, these foreign countries are losing and we are gaining. In fact, this is how the U.S. have come to attain its technologically dominance. We should be thankful that, given the option, these people would prefer to stay and contribute to this nation and call it home.

In summary, what different countries want, need, and should have from an intellectual property system is a function of the level of economic development. The U.S., which plays the role of stay-ahead, would like to have the national system evolve into a de facto international system. But this will not happen for countries playing the role of catch-up have the right to a world system that lets them succeed.

On the issue of brain drain or brain gain, it is a matter of perspectives.