AI Magazine Volume 5 Number 4 (1984) (© AAAI)

Comparing Artificial Intelligence and Genetic Engineering:

Commercialization Lessons

Edward M. Dickson

Abstract

Artificial Intelligence is rapidly leaving its academic home and moving into the marketplace. There are few precedents for an arcane academic subject becoming commercialized so rapidly. But, genetic engineering, which recently burst forth from academia to become the foundation for the hot new biotechnology industry, provides useful insights into the rites of passage awaiting the commercialization of artificial intelligence. This article examines the structural similarities and dissimilarities in the two subjects and briefly summarizes the history of the commercialization of genetic engineering. It then proposes some lessons that would benefit the artificial intelligence industry

RARELY DOES A NEW INDUSTRY suddenly spring out of the most arcane corners of universities; we live in interesting times. Within a few short years AI and genetic engineering have burst their academic restraints and are on the way to being commercialized by industry throughout the developed world.

Genetic engineering, as a commercial endeavor, has about a five-year lead. AI is currently passing through rites of passage that resemble those already braved by the young genetic engineering industry. There are many striking similarities that suggest that examination of the commercialization of genetic engineering contains lessons valuable to the budding artificial intelligence industry.

Similarities.

- AI and genetic engineering both are esoteric subjects, previously considered at the purest end of the research spectrum of their disciplines Yet, both suddenly became viewed as practical, and, potentially, very valuable because they have such unbounded areas of application.
- Stanford and MIT are two of the three leading sources of inspiration and expertise in both subjects. Both are located in urban areas noted for their high technology and their entrepreneurial start-up companies which are often spin-offs of earlier start-ups In these areas, a spirit of risk-taking is in the air.
- The vicinities of Palo Alto and Cambridge abound with the venture capitalists needed to launch new, capital intensive high-tech companies Even banks in these areas look more favorably upon loaning to individuals with a bright new idea.
- Major pharmaceutical companies, in spite of their legions of microbiologists, neglected genetic engineering science much as the major computer companies treated AI with benign neglect—until brave entrepreneurs showed the way to commercialization
- Protection of intellectual property, through patents and copyrights, required the breaking of new legal ground, ground which remains uncomfortably shaky Moreover, even this protection may not be sufficient, because piracy of software or unique microbial strains is easier to accomplish than the protective laws are to enforce
- There is a sudden explosion of interest in corporate America as evidenced by the attendance at two symposia on the subjects sponsored by MIT's Industrial Liaison Program, with assistance from F Eberstadt and Company, a New York securities analysis firm. The March 1983 AI symposium attracted 764 registrants, making it the largest MIT has ever sponsored Until then, the record was held by the October 1980 Biotechnology symposium which attracted 536 registrants
- The United States has the technological lead in both subjects, but the Japanese government and industry have targeted both as growth industries for Japan. In both subjects, Japanese expertise is growing rapidly, and Japan is reckoned to pose the greatest long-term competition for the United States in the subjects.
- AI and genetic engineering are both names with which the general public cannot feel immediately comfortable. These futuristic names carry within them the hint of meddling in areas best left alone.

Differences. But the fields are not entirely similar, and some of the differences are big enough to ensure that commercialization lessons learned from genetic engineering may not always apply to artificial intelligence:

- AI research in universities was pursued by computer scientists who always had opportunities to consult with industry (even if it was in other aspects of computer science) Computer science graduates always could find well-paying employment By contrast, microbiologists were in over supply, pay was relatively low, and consulting opportunities were much scarcer.
- Computer software (except, indirectly, cryptography) is not a subject of governmental regulation and can be brought to market without having to prove that it is safe. Nearly every application of genetic engineering ventures into regulated arenas, usually those of the Food and Drug Administration

This article has benefited from conversations about AI with many people, but especially Prof Edward Fredkin of MIT and Mr J. Peter Bartl of MIT's Industrial Liaison Program.

FDA approval cycles are notoriously long, costly, and uncertain. A five to seven year approval cycle is normal.

- Genetic manipulation is well defined in that the genetic makeup of an organism is either altered or it is not.[1] AI, practically speaking, is that part of computer science that is always on the horizon, the most difficult to achieve at any given time. What seemed like artificial intelligence yesterday (for instance, voice recognition) may seem rather mundane today.
- Genetic engineering currently is of little value to the military because germ warfare is illegal by international agreement As a result, if any genetic engineering is being performed in the United States under Department of Defense funding, its very existence is very highly classified. By contrast, the use of AI techniques in warfare and intelligence interpretation is completely legitimate, and Department of Defense sponsorship of research and development is large and well known.

Intersections. Finally, there are a few places where the subjects of genetic engineering and AI actually intersect:

- The use of AI tools in the practice of genetic engineering. The start-up company, IntelliCorp, located in Menlo Park, provides such tools.
- The involvement of several venture capital companies in both subjects. Perhaps most notable is the role that Frederick Adler has played in both fields. (Adler was involved in the computer field long ago. His first venture investment was in Data General in 1968.)

Commercialization History of Genetic Engineering

The Dark Ages—1973 to 1982. Genetic engineering was proved feasible when Stanley Cohen and Herbert Boyer first transferred genetic material among microbes in 1973. In 1976, Boyer co-founded Genentech with Robert Swanson, a venture capitalist. Soon after, Biogen (1978) and Genex (1977) were formed. All three received substantial infusions of venture capital. Cetus, a Berkeley company, had been formed in 1971 to perform automated pharmaceutical-oriented screening of microbes. All four received substantial infusions of venture capital and early investments by chemical and oil companies. By 1980, these were the "big four" of the industry and remain in the top ranks today.

Quickly, university microbiologists caught the entrepreneurial fever, and in the quest for monetary rewards formerly unattainable in the subject, either formed small companies or joined with small new companies as consultants. The recruitment of the best and brightest minds moved rapidly, and many gave up their academic positions entirely. Established Fortune 500 pharmaceutical and chemical companies began to take the field seriously. Many established in-house genetic engineering teams and took equity positions in the start-up companies. The more risk-taking microbiologists tended to join the start-up companies and the more security-conscious ones stayed at or joined the Fortune 500 companies.

By 1982, over 160 companies were known to be doing genetic engineering using either recombinant DNA or hybridoma (monoclonal antibody) techniques. Most start-up companies targeted the pharmaceutical market, because it is conventional wisdom that profit margins are very high in pharmaceuticals. Moreover, the dominance of ex-academic professionals in the field ensured that there was a strong altruistic feeling that genetic engineering be first applied where it could most benefit mankind, which usually meant human health care products to microbiologists. A few companies targeted animal health care. However, few companies targeted agricultural markets because higher plants are vastly more complicated genetically than microbes, and no one yet knew how to manipulate specific genes.

To help keep bread on the table, most companies undertook contract research for large established companies, but few of the small companies had the foresight or the negotiating strength to retain important shares in the rights to the fruits of their research. The large companies who purchased the research were using the contracts as a "window" into the technology and as a means to evaluate companies in which they might invest.

"Going-Public" Fever and Other Changes. Genentech was among the first to go public and, in fact, the stock issue was sold while the 1980 MIT Biotechnology symposium was in progress. Genentech stock was sold at $35 per share, but in the first frenzied minutes, it shot up to $89 and took a long time to decline to reasonable levels justifiable by the company's performance and prospects. Nevertheless, this very well publicized episode greatly encouraged the formation of even more companies to pursue genetic engineering. The genetic engineering hype in the press gladdened the hearts of the company founders and early investors.

A profusion of "me-too" companies were founded, most pursuing similar goals. Dozens sought to develop microbes to produce commercial quantities of interferon, a very rare substance protein which many hoped would be a miracle cure for virtually everything from the common cold to cancer. For a while, the interferon fever gripped investors. Unless a company was working on interferon, it was very difficult or impossible to raise capital from "me-too" venture capitalists or from stock issues. For a long time, the largest source of income to biotechnology companies was interest earned on the money raised in public offerings For some of the start-up companies the only thing they ever sold was their stock.

Relatively few start-up companies brought in seasoned professional managers at the beginning. Inexperienced university professor-turned-entrepreneur company founders tended to launch research projects in their new companies on a broad front. Projects were almost always chosen without realistic prior market research to validate or refute the hunches of the company founders that the fruits of the research would have commercial potential. Some projects seem to have been chosen more on the basis of technical challenge than realistic market potential

Few paid attention to the smaller, less glamorous niche markets such as drugs for domesticated animal diseases, specialized reagents for performing genetic engineering itself, di-

[1] The definition of what constitutes AI changes with time

agnostic kits, or the automated "gene-machines" which could construct artificial segments of genes by carefully and sequentially adding the nucleotides of the genetic code in question. But, several companies did perfect gene machines. As a result, the practice of gene splicing became routine. Chemical tools and machines made it possible for technicians to do work that had required Ph.D scientists just two or three years earlier.

Company finances became strained by the pursuit of projects on too broad a front. New capital became more difficult to attract as investors began to realize that few could win in the interferon derby, that the efficacy of interferon was not even proved, and that marshalling new products through the regulatory maze would be arduous and extremely expensive. Start-ups depended increasingly on performing contract research for major corporations. This contract research increasingly was performed on terms less favorable to the small companies.

Current Situation. Now that the small genetic engineering companies have experienced a strong dose of commercial-world reality, research programs have narrowed and are more directed to products where there was less competition and faster regulatory approvals such as animal health products and diagnostic kits. The wiser companies which had recognized these advantages initially, now have significant competitive advantage over the converts. Companies, such as Enzo Biochem, that initially focused on providing the biochemical tools that the other companies needed did well. However, a few companies, such as Bethesda Research Laboratories, grew too ambitious, expanded quickly into the more glamorous areas, and finally got into financial trouble. Some companies that concentrated on diagnostic kits based on monoclonal antibodies have been shown to have had good foresight, because the regulatory maze facing commercialization of a product is less forbidding. Techniques for transferring genes among higher plants have been developed and some companies, such as Sungene, have specialized in a few key agricultural crops.

The original "big four" are still in the top rank, but they are no longer alone. Genentech which has raised financing of over $200 million, seems to have done everything best. It now employs about 550 people, a fifth of which have Ph.Ds. But, Genentech is fervently business-oriented and brought in professional management from the first. It has pursued narrowly defined, precisely targeted products. It has benefited from judicious alliances with investing companies and has several products on the market including human insulin, human growth hormone, and a kind of interferon. Its insulin is being brought to market by Eli Lilly, the company which dominates the U.S. insulin market.

Cetus, which has attracted over $270 million ($120 million of which was raised in its 1981 initial stock offering, setting a record), now employs about 500. At first, Cetus attempted to do everything, but since has greatly narrowed its scope, and changed its top management. Compared to the confident, deliberate advances of Genentech, Cetus still seems to be floundering, although it has commercialized several products including a vaccine against scours, a diarrhea that often kills newborn pigs. Its scours vaccine is being brought to market by Norden Laboratories, an animal health subsidiary of the pharmaceutical giant, Smith Kline Beckman.

Biogen, the only company in the world to have a Nobel Prizewinner as its Chairman of the Board, has raised $125 million but did not go public until 1983. Biogen now employs about 330 persons and is bringing an alpha interferon to market through Shering-Plough, a major player in pharmaceuticals and an owner of about 11% of Biogen.

Genex which first went public in 1982, has raised a total of $50 million and now employs about 230 persons. Genex is the least glamorous of the original big four because it has concentrated on using genetic engineering to produce valuable, biologically obtained specialty chemicals. Its big success is production of an amino acid used by G.D. Searle, to make aspartame, the new artificial sweetener that is gaining a large share of the soft drink sweetener market.

Several of the small companies are quite successful, including Genetic Systems which is marketing kits to diagnose venereal diseases; it has a marketing link with Syva, a Syntex subsidiary. Molecular genetics, which has raised over $50 million and first went public in 1982, employs about 110 persons. It is concentrating on animal health care products and has a vaccine against scours in calves. Enzo-Biochem, was the first biotechnology company to go public even though it was not well regarded within the industry. It has since confounded its skeptics and is now clearly profitable on operations.

By now, most companies now have brought in experienced management talent to guide them, often at the insistence of key investors. Some company founders stepped aside (sometimes reluctantly) in order to save the company.

Amazingly, only about five of the start-up companies have failed completely. However, large corporations which had been watching the field waiting for investment or acquisition opportunities have purchased some struggling companies and their research progress at bargain prices. Personnel have begun to move among the companies as the "golden handcuff" provisions of their profit sharing or stock options have expired or diminished in apparent value.

Thus, in summary, genetic engineering is beginning to deliver meaningful products to the market place, proving that it is a viable body of technology on which to base an industry. Its rites of passage serve to drive home the tired lessons that good technical ideas need to be complemented by good management, financial savvy, and an eye to the market to be successful. Scrutiny of the industry's rites of passage leads to a revision of the old aphorism: "Invent a better mousetrap and the world will beat a path to your door." In its place should be recited: "Invent a better mousetrap, and watch someone with better management and marketing skills emulate it and beat a path to the world's door."

Lessons for the Emerging AI Industry

The rapid passage of genetic engineering from being a basic research laboratory tool into a thriving young industry yields many worthwhile insights to the daring people seeking to commercialize AI. Among them are the following:

- Good ideas and technical expertise alone are insufficient to yield success in entrepreneurial endeavors. Companies, both large and small, must bring in experienced management that is able to strike a balance between expenditures on research, market assessment, and market development. Few academics possess these skills buttressed with sufficient knowledge in these areas to lead new companies for long after their formation Investors, especially venture capitalists, will want to see progress towards a commercial product and will not long tolerate a floundering company that makes scientific progress but scant commercial progress.

- Supplying tools of the trade to the innovators can be profitable—and often much earlier than selling the products of the technology itself. For AI, such tools include specialized computer hardware and software needed to streamline the development of AI products, such as the machines sold by Xerox, Symbolics, and Lisp Machines, Inc. AI software that will facilitate development of yet other AI products can be best sellers. For example, tool-bag expert systems made to aid in the design of other expert systems will be the analog of the gene machines that greatly facilitated gene splicing and allowed technicians to perform the jobs that had been performed by Ph D scientists Because such tools can relieve the impending AI talent bottleneck and can shorten and cheapen product development cycles, they can be seen as very valuable to the buyers and can command premium prices.

- Companies should pursue only a narrow range of alternative products to ensure that scarce financial backing is not squandered by being spread too thin. The markets for the potential products should be assessed early to be sure that buyers for the product really do exist and that the money spent developing the product is commensurate with the size of the market and the price buyers will be willing to pay. "Toy" expert systems are much more readily developed and more readily sold than larger, more comprehensive but much more costly systems. Genetically engineered drugs to prevent disease in piglets is less glamorous than developing interferon, but it was developed at a cost in keeping with the size of the market and, most importantly, it will be generating revenue before the more glamorous products

- Companies should target their markets and products with an eye to the number and strength of competitors. There was no need for scores of companies to be pursuing genetically engineered interferon, and the technically and financially weaker companies really did not have much chance of beating out their better financed rivals. Seeking out and serving buyers well in niche markets with little or no competition can be a viable survival strategy. Genetic engineering companies that targeted markets for specific animal diseases are generally bringing products to the market sooner than the companies that won the interferon derby. Me-too products in crowded markets seldom build successful companies

- The large companies with the deep pockets are jumping on the AI bandwagon market just as the pharmaceutical companies finally did with genetic engineering They have the financial staying power to sweat out the product development cycle. They also have experienced marketing teams that can decide on the proper means to market the product, either through their own existing channels or through alliances with other companies that have suitable marketing channels

- Judicious alliances between small and large companies can benefit both, much as Genentech formed an alliance with Eli Lilly to manufacture and market its human insulin, and Cetus has a relationship with Norden Laboratories to make and market its pig scours vaccine. Equity participation in the small company can often form the basis for such relationships The large company gets a window on the technology without having to build competing in-house capability that is constrained by the large-company culture and bureaucracy The small company gets a ready channel to the market, has made a powerful potential competitor into an ally from the start, and retains a substantial stake in the profits.

- Start-up genetic engineering companies that performed contract research for large companies as a means to generate early revenues frequently never broke out of the mold when the exigencies of the meeting diverted management attention from independent product development. Investors are less eager to invest in such companies because disputes over rights to product developments can result.

- Those purists who bemoan the commercialization of the technology before it is really ready will be ignored and the train will leave without them. They will lose control of the definition of what constitutes AI to the commercial sector which will shamelessly market products based upon well-known, decade-old technology Some products will even falsely purport to be forms of AI. Marketing people and journalists will then control the use of the name

- The door to the small, cozy, closed club will be wrenched open Ten years from now, those who fret about the loss of talent to the companies will have been found to have underestimated the resiliency and self-correcting nature of the American system of education and enterprise. New opportunities for recognition and advancement at universities (*e.g.*, large grants from industry to university programs) will arise that will continue to entice the most theoretically inclined. Meanwhile, the commercial outlet for AI expertise will draw in mature talent from other fields. These mature people will retrain themselves, largely on-the-job, and lessen the commercial appetite for people formally trained in AI.

The main lesson that members of the AI community can draw from the commercialization of genetic engineering is that the future will be good, but its evolution will be different than they imagine.