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Bioinformatics Patents – Challenges and Opportunities

by James G. Gatto

By many measures, bioinformatics is one of the hottest technologies around. Industry researchers such as IDC estimate that this $2 billion market will expand to nearly $12 billion by 2004. IBM, whose Life Science group is its fastest growing group, pegs the market at closer to $43 billion over the next three years. IBM and Compaq have each ear-marked $100 million for investment in bioinformatics start-ups. IBM is spending another $100 million to develop "Blue Gene," which reportedly will be the world's fastest super computer, to tackle the computer intensive analysis needed to unravel proteomics. The October 2001 issue of *Red Herring* included a report on the few areas where first round venture funding is still occurring — bioinformatics was listed as one of the few "new and growing" areas.

In any technology industry, when investment dollars flow and market values grow, increased patent activities follow. Bioinformatics is no exception. As the bioinformatics industry continues to surge forward, two trends are emerging — the role and importance of bioinformatics patents continues to increase and the number of bioinformatics patents is rapidly growing. A few recent examples demonstrate some of the various ways in which bioinformatics patents have played a role.

In July 2001, Nanogen agreed to pay $5 million in cash and stock to Motorola, Genometrix and MIT to settle a bioinformatics patent infringement dispute. The allegedly infringing product was the NanoChip Molecular Biology Workstation, which is used in the clinical research market and is being developed for potential use in the clinical diagnostics market. The patent involved was U.S. Patent No. 5,653,939 *"Optical and Electrical Methods and Apparatus for Molecular Detection."* The settlement reportedly only gives Nanogen a license to certain claims of the patent and does not include any cross-licensing provisions to any of Nanogen's 26 issued U.S. patents.

Also in July 2001, Gene Logic announced that it completed the spinoff of its patented Flow-thru Chip™ technology into a new company, MetriGenix, Inc., and that MetriGenix secured $15 million in initial financing to further develop and commercialize the Flow-thru Chip™. Gene Logic's contribution to the new venture consisted mainly of relevant patents and other intellectual property associated with the Flow-thru Chip™ technology. Initial financing was provided by a group of investment partners consisting of Oxford Bioscience Partners, Burrill Biotechnology Capital Fund, L.P., Infineon Ventures GmbH and GE Equity. Gene Logic owns 54% of the new company. Gene Logic's results of operations have historically reflected expenses associated with its investment in the ongoing development of the Flow-thru Chip™ technology. As a result of the spinoff, Gene Logic expects that beginning with the fourth quarter of 2001, its results will cease to show any further expenses associated with MetriGenix.

In a press release dated August 16, 2001, LION Biosciences announced the filing of its *first* patent application on a lead compound series — only 16 months after starting drug discovery activities. According to the press release, the results confirm the acceleration that can be achieved by applying IT-solutions to drug discovery problems. LION stated that the tight integration of information driven biological research, assay development, computational chemistry and advanced combinatorial chemistry yielded a significant improvement from gene to lead, and that this project is just the first in a series of lead generation projects. Expect LION, and others, to file more patents for lead generation/drug discovery related inventions.

As further acknowledgement of the expected increase in the number of bioinformatics patent application filings, the United States Patent and Trademark Office (USPTO), has set up a special group ("Art Unit") to examine bioinformatics patent applications. This group, known as Art Unit 1631, has ten full time examiners with a broad range of technical expertise ranging from biology to physics to electrical engineering. These are just a few examples of the clear trends emerging regarding the increasing importance and number of bioinformatics patents.

More concrete evidence of the increasing number of bioinformatics patents can be found by analyzing the number of issued U.S. patents in bioinformatics-related categories. The USPTO classifies patents by a class/sub-class system. To convey some sense of the number of bioinformatics patents being issued, I have identified some of the patent classes and sub-classes relevant to bioinformatics and determined the number of patents within each class. Some of the classes/sub-classes include the following:

Selected US Patent Classes/Sub-classes Relevant to Bioinformatics

CLASS	Subclass	Name
707		DATA PROCESSING: DATABASE AND FILE MANAGEMENT, DATA STRUCTURES, OR DOCUMENT PROCESSING
	1	DATABASE OR FILE ACCESSING
	3	Query Processing (i.e., searching)
	6	Pattern matching access
	100	DATABASE SCHEMA OR DATA STRUCTURE
	104	Application of database or data structure (e.g., distributed, multimedia, image)
706		DATA PROCESSING: ARTIFICIAL INTELLIGENCE
		APPLICATION USING AI WITH DETAIL OF THE AI SYSTEM
	924	Medical
703		DATA PROCESSING: STRUCTURAL DESIGN, MODELING, SIMULATION, AND EMULATION
		SIMULATING NONELECTRICAL DEVICE OR SYSTEM
	11	Biological or biochemical
	12	Chemical
702		DATA PROCESSING: MEASURING, CALIBRATING, OR TESTING
		MEASUREMENT SYSTEM IN A SPECIFIC ENVIRONMENT
	19	Biological or biochemical
	20	Gene sequence determination
	21	Cell count or shape or size analysis (e.g., blood cell)
	22	Chemical analysis
	27	Molecular structure or composition determination
	31	Specific operation control system
	32	Specific signal data processing:
382		Image Analysis
		Applications
	128	Biomedical applications
	129	DNA or RNA pattern reading

It is interesting to analyze the number of patents issued in each of these sub-classes prior to 1996 and since then. Since 1996, the number of issued patents in these sub-classes has increased significantly. (Due to the USPTO practice of cross-referencing patents in multiple sub-classes, these numbers do not reflect the number of unique patents in these sub-classes.)

Number of Patents Issued in Selected Subclasses

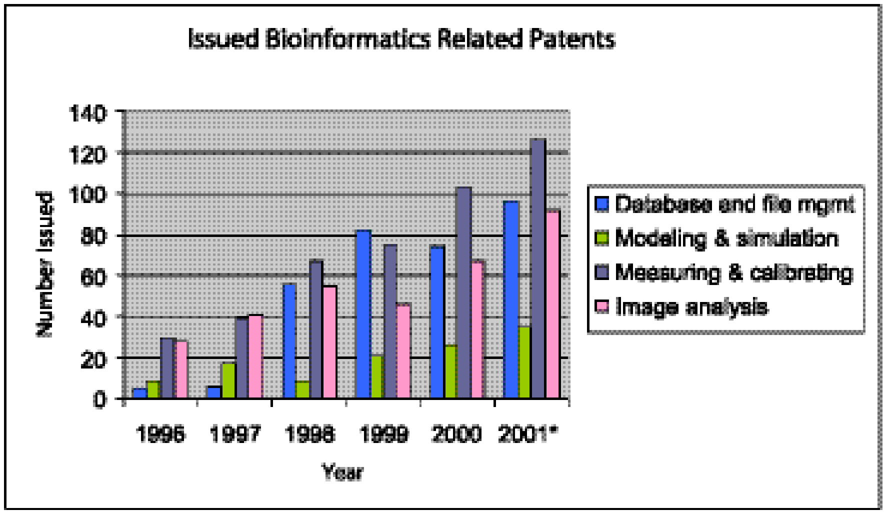
Description	class/sub	pre 1996	1996	1997	1998	1999	2000	2001	2001*	Total*	post 1996 % change
Data Processing: database and file management	707/1^	7	3	2	14	16	10	13	17	69	886
	707/3^	13	1	0	18	36	30	26	35	133	923
	707/6^	3	0	1	13	13	22	16	21	73	2333
	707/100^	2	1	3	11	17	12	8	11	57	2750
	707/104^	0	0	0	0	0	0	9	12	12	n/a
	Total 707	25	5	6	56	82	74	72	96	344	1278
Artificial Intelligence: medical	706/924	30	7	10	13	8	7	2	3	78	160
	Total 706	30	7	10	13	8	7	2	3	78	160
Data processing: modeling & simulation	703/11	22	4	10	7	12	12	14	19	86	291
	703/12	14	5	7	2	9	14	12	16	67	379
	Total 703	36	9	17	9	21	26	26	35	153	325
Data processing: measuring & calibrating	702/19	80	7	8	16	20	27	30	40	196	145
	702/20	10	3	2	5	9	15	12	16	60	500
	702/21	29	3	1	7	3	3	6	8	54	86
	702/22	45	8	10	19	18	19	14	19	138	207
	702/27	29	7	18	17	14	15	22	29	129	345
	702/31	31	1	0	0	6	9	2	3	50	61
	702/32	32	1	2	3	5	15	8	11	69	116
	Total 702	256	30	39	67	75	103	94	126	696	172
Image Analysis	382/128	150	22	35	50	39	59	62	83	438	192
	382/129	26	6	6	5	7	8	7	9	67	158
	Total 382	176	28	41	55	46	67	69	92	505	187

^ = Further limited by text search terms
* = Annualized

The trend is more clearly established when we aggregate the sub-classes by common class as depicted in the chart below.

Aggregate Number of Patents Issued in Selected Classes

Description	Class	1996	1997	1998	1999	2000	2001*	Total	Pre 1996 Total	% Change
Database & file mgmt	707	5	6	56	82	74	96	319	25	1176
Modeling & simulation	703	9	17	9	21	26	35	117	36	225
Measuring & calibrating	702	30	39	67	75	103	126	440	256	72
Image analysis	382	28	41	55		67	92	329	176	87



* = annualized

What aspects of Bioinformatics can be patented?

The bioinformatics industry provides the information technology tools that facilitate many aspects of biotechnology research and shave years off the drug discovery process. The explosion of new genomic and proteomic information has led to an increased demand for computational and statistical tools to analyze this information, and has accelerated the growth of the bioinformatics industry. Some examples include collecting, storing, analyzing and retrieving terabytes worth of genomic and proteomic data, data mining and data visualization tools, sequence alignment and pattern recognition tools, molecular modeling tools, and predictive tools. Many other types of bioinformatic tools exist and more will be developed. All of these tools are the types of things that can be patented. In the near future, bioinformatics tools will move out of the laboratory and be used in a commercial context. One of the most exciting commercial opportunities is in the field of personalized medicine. With "personalized medicine," doctors will soon be using individuals own genetic information to tailor treatment of disease, and more importantly, to proactively manage individual's health issues to prevent disease. Many business models relating to these and other uses of bioinformatics tools can also be patented.

Why should bioinformatics companies focus on patents?

The value of patents in general is at an all time high. As an example, Boston Scientific recently was awarded nearly $170 million in damages plus an injunction against Medtime on a stint patent. Hewlett Packard recently agreed to pay Pitney Bowes $400 million in an out of court settlement of a patent infringement case. Suing competitors for damages is a well-known use of patents. But it is not the only value of patents. Meaningful patents that protect the core features or functions of a company's technology or its basic business methods can create significant business leverage. Such patents provide offensive value, defensive value and other strategic benefits.

Offensive Uses

Examples of offensive uses of patents include the obvious — suing competitors for damages or licensing to generate royalties. Profits generated from licensing patents can be significant. For example, IBM reportedly generates over $1.7 billion annually from patent licensing.

The ability to sue a competitor to obtain an injunction can also be a significant offensive weapon. For example, during the peak of the holiday season, Amazon obtained an injunction against Barnes & Noble's use of a "one-click" feature on its online shopping site. In one of the most famous and devastating injunctions ever issued, Kodak was ordered to shut down its entire instant camera business because of infringement of Polaroid's patented technology.

Some less obvious offensive uses of patents include cross-licensing patents to obtain access to a competitor's patented technology, using patents to enhance bargaining positions in business deals (*e.g.,* joint ventures, divestitures, etc.) and using patents as a sales and marketing tool, especially when competing against competitors without patents.

Cross-licensing

An example of an offensive use of cross-licensing is to trade patents to obtain access to another company's technology. In many cases, competitors or even business partners have patented technology that the other wants to use. By cross-licensing, each party can obtain rights to technology to which it otherwise would not have rights, or for which it would have to pay potentially significant royalties to obtain.

Creating Leverage in Business Deals

When negotiating joint ventures, divestitures of business units and other transactions, patents can be leveraged as a valuable business asset. For example, suppose you have invented and patented valuable technology, but do not have or want to devote resources to the R&D and commercialization of the technology. You can leverage your patents by finding a joint venture partner that will commit the resources and you will contribute the patent(s). In this way, you can capitalize on an asset that otherwise may lay dormant, or avoid losses attributable to developing products. This is what Gene Logic did, as described above.

When selling a business unit or company, the valuation is often much greater if patents are part of the assets sold. It is increasingly common in the acquisition of small technology companies that the primary value of the company is its patents and other intellectual property. Without having obtained patents, such companies may not realize as much value in these transactions.

Sales and Marketing Tool

The exploitation of patents in connection with sales and marketing activities is another offensive use of patents. This advantage may be actual or apparent. For example, an actual marketing advantage can result from significant patents if you can accurately claim an exclusive right to the patented technology or feature. An apparent marketing advantage may result even if you do not have a dominant patent. More companies are advertising "patented technology" to create the perception that the product is unique or that the company is innovative. Many companies, like LION Biosciences, even advertise products that are "patent pending" to create the perception of uniqueness.

More frequently, companies that have patents are using this asset as a sales tool. Consider the situation where your company and a competitor sell a similar product. They have a patent and you do not. You run the risk that your competitor's salespeople will tell the prospective customer that it will be sued for patent infringement if it purchases your product instead of the competitor's patented product. In contrast, if you have the patented product and your competitor does not you may have the sales advantage.

Defensive Uses

Patents also may be used defensively. One defensive use of patents is the ability to protect your company's investment in R&D. Without patent protection, competitors are free to reverse engineer and copy the features and functions of your commercial products, subject to relatively minor exceptions. Additionally, if you do not timely file for a patent on a new invention in a timely manner, a competitor that independently develops a similar invention can obtain a patent and, in some cases, prevent you from using your invention even if you had the idea first.

Patents also have defensive value as a bargaining chip. For example, if you have patents, and a competitor asserts a patent infringement claim against you, you can consider cross-licensing to resolve the matter. If you do not have patents, your options are to pay significant legal fees to fight the allegations or pay royalties to your competitor. If you are sued for patent infringement, your patents may serve as the basis for a counterclaim. Having a counterclaim against your adversary will create significant leverage for you in connection with settlement negotiations. In many cases, this will facilitate a prompt settlement. If you do not have patents and are sued for patent infringement you often have little, if any, leverage. Typically, you are left with the undesirable choices of paying a significant amount of money to defend the lawsuit (usually with no potential upside) or pay to settle the case.

Another incredibly valuable defensive advantage of patents is one that you may never know you received. Before bringing a patent infringement lawsuit against you, most companies will often analyze your patents (if you have any) to determine whether you may raise any significant counterclaims. If you have potential counterclaims this may deter the competitor from suing you. This is obviously a significant benefit, but one you may never know you received. If you do not have patents, your competitor can sue you without fear of a patent infringement counterclaim.

Strategic Value

Patents also have other strategic value. One example of the strategic value of patents relates to finance activities. If you are a start-up or emerging growth company, having patents will not guarantee you get funded, but not having patents or a patent will hurt your chances of getting funded. Venture capitalists and other investors often want to know that your technology or business method is protected. For companies of all sizes, patents can facilitate the ability to obtain financing. Banks and other lenders are now more willing to use patents and other intellectual property as collateral to secure loans. Patents are now being pooled and "securitized" as an asset-backed security, similar to mortgages.

Bioinformatics Patent Challenges

Bioinformatics patents present some unique challenges — some obvious, some not so obvious. The obvious challenges relate to the multidisciplinary nature of the technology involved. The not so obvious challenges relate to the diversity in bioinformatics business models and the corresponding diversity of patent claim types that may be necessary to ensure maximum patent protection.

For many bioinformatics inventions, the obvious challenge is finding a patent attorney that understands both the IT and biotechnology aspects of the invention. Many have suggested using a pair of patent attorneys — an IT patent attorney and a biotech patent attorney to ensure that the technology aspects of a bioinformatics patent are covered. This "tag team" approach parallels how the USPTO examines bioinformatics patents. The tag team approach is a fall-back to the more desirable approach of finding an IT patent attorney who understands biotech. Moreover, while the tag team approach may help tackle the technical challenges, it alone is insufficient to realize maximum value from a bioinformatics patent portfolio. Another critical challenge is the need to understand the various business models relating to bioinformatics and the various types of patent claims potentially applicable to those models.

Some of the many bioinformatics business models include licensing data, licensing software, selling/licensing systems (hardware and software), selling components of a system, being an application service provider (ASP), selling test equipment, using test equipment to perform testing for others, among other things. For certain business models, reach-through provisions are used to capture a share of the revenue from products made using the invention.

This smorgasbord of business models impacts patents because the art of patent drafting involves more than just understanding the technology well enough to describe the invention. It further requires an understanding of the potential revenue sources for the invention and crafting the proper types of patent claims to cover those revenue models.

Patent claims are the numbered paragraphs at the end of a patent that define the legal scope of protection afforded by a patent. The significance of claim types is that they dictate what activities are covered by a patent and the potential royalty base for licensing. As an overly simplified example, if a claim covers a testing device incorporating a new gene chip, the claim would be infringed by someone who manufactured the device with the chip, but may not cover the manufacturer of the chip itself. If however, the patent includes claims to the chip itself and to a device with the chip, it may be infringed by both the chip manufacturer and the device manufacturer. As for the royalty base, assuming an arbitrary royalty rate of 10%, a 10% royalty on the cost of the device is likely to be much greater than 10% royalty on the cost of the chip. One might assume then that the device claims are always more desirable. This is not so. One reason is that the chips may be made in the U.S. and the devices made elsewhere. In this case, the device claims may not be infringed by the U.S. Patent. Additionally, the gene chip may be subsequently incorporated into another type of device different than the claimed device. For this reason, it is often desirable to include both device and component claims where applicable.

If the device is used as part of a system, it is often desirable to claim the system as well. The method of operating the device and system can be covered by method claims. One advantage to this approach is that if a competitor uses the device or system to perform services for others and charges a per-use fee, the royalty base may be much higher than the royalty base of the device or system itself. An analogous situation outside the bioinformatics arena is laser eye surgery. The patent license fees are based on cost per surgery, not just the cost of the system.

Beyond the basic system and method claims, lies an arsenal of other claim types relevant to bioinformatics. Understanding these options and when to use them can greatly enhance the potential value of a bioinformatics patent portfolio.

Business method claims can be used to cover unique aspects of a business model itself. For example, suppose a company creates a database of personal genetic information and other related information and offers unique services to individuals based on this information. The business method may be protected separate and apart from the technology used to implement the method.

Patent protection poses significant challenges for companies that sell data. Data itself is not patentable. Data structures are. An important aspect of bioinformatics is handling terabytes worth of data generated from genetic and proteomic research. Some of the inventions that relate to the technology for handling this data include unique ways of storing data. "Data structure" claims can be used to cover the way in which data is stored.

ASP models and other client/server inventions pose some unique international issues. If an ASP system claim includes interaction between a client terminal and a server, territoriality issues may be preclude a finding of infringement. For example, if a competitor operates the server outside the U.S. and it is accessed by a client terminal in the U.S. (or vice versa), a system claim may not cover this activity. The reason is that not all of the activity covered by the claim occurred in the U.S. A technique to overcome this is to draft separate "server-side" claims and separate "client-side" claims. This way, if either the client or the server is in the U.S., the patent may cover the activity.

A number of bioinformatics business models involve licensing data or tools used in research (research tools) and collecting, as part of the license fee, a royalty on any products developed as a result of use of the research tool. A product-by-process claim can be used to facilitate this type of patent license. A product-by-process claim covers a product made according to a particular process. If the patent adequately describes and claims how to make a product using the data or research tool, protection for this revenue source may be obtained.

The foregoing provides just some examples of claim types that can be used to enhance the value of bioinformatics patents. When to use each and what combinations to use requires an understanding of the various potential business models of the patent owner and its potential competitors or licensees.

Bioinformatic tools, as well as many of the business models relating to how these tools are used, can be patented and are being patented. Various indicators suggest that the number of bioinformatic patent filings will continue to increase. History has shown that as the number of patents filed in a particular industry increases, the ensuing years bring more patent licensing and litigation. Companies in the bioinformatics field need to understand this and take action now to maximize the value of their intellectual property and prepare for the bioinformatics patent race that is underway.

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