



Bioinformatics on the Brink

Companies struggle to diversify after disappointing software sales sink the sector | By Kate Fodor

When a working map of the human genome was announced in June 2000, it was immediately clear that it would open new avenues of study and transform the life sciences, both in academia and in industry. One of the many new opportunities was in bioinformatics: the use of computers to rapidly scan databases, analyze sequence data, and help predict protein structure based on DNA sequence. Companies and universities would be eager to purchase bioinformatics tools to help them manage the massive amounts of genomics and proteomics data they would be generating.

That has, indeed, turned out to be true. But for a number of reasons, the market opportunity for bioinformatics tools hasn't been as expansive as was thought, and many companies have suffered as a result. Now companies are trying to diversify their product lines or adopt more successful business models. Some are merging to attract clients needing more complete solutions rather than individual tools, while others are expanding into drug discovery.

"The bioinformatics industry kind of exploded onto the life science scene when the human genome was sequenced," says Zachary Zimmerman, a senior research analyst with Framingham, Mass.-based Life Science Insights. "The companies said that everybody needed to have bioinformatics tools and to buy all these software applications, and they told the investment community that bioinformatics would be a billion-dollar industry, maybe even a multibillion dollar industry. But the truth of the matter is that it's nowhere near that size."

Earlier this year, San Mateo, Calif.-based Navigant Consulting released a report on the bioinformatics analytical software market forecasting a compound annual growth rate of 9.3% over the next five years. Even that relatively optimistic report, however, pegged the worldwide market at only \$245 million for 2004, with growth to \$375 million by 2009—

figures that don't come close to the industry's heady early predictions.

"The early companies were exaggerating the size of the market," says Zimmerman. "Maybe they believed it, but they were wrong." He thinks part of the reason that the market is smaller than originally expected is that potential customers have chosen to keep a large amount of the work in-house. "They'd rather develop stuff in-house, because it's cheap and it's proprietary and it's customized. As a scientist, you think that you know everything, so can a product out of a box possibly do what you want it to do?"

Zimmerman adds that, although bioinformatics tools are becoming both cheaper and more reliable, some potential buyers were turned off by the inaccuracies and expense of the early products. "The earlier products were extremely expensive and didn't do what customers were told they would do, so of course that's bad business, and that's why a lot of the early bioinformatics companies went under," says Zimmerman. "Today there are companies, like Gene Logic and Accelrys and Spotfire, that sell products and do pretty well in the bioinformatics space," but even those companies are facing challenges, he says.

Andrew Kim, a senior consultant for Navigant Consulting who was one of the authors of the firm's recent report, adds that bioinformatics companies have had difficulty proving the worth of their products to the biotech, pharma, and drug-discovery companies that are their potential clients. "The key factor is return-on-investment," he says. "The [client] companies can't really quantify how much gain they ultimately get from using the bioinformatics systems."

SURVIVING BUT STRUGGLING Third-quarter 2004 sales were disappointing across the board in the bioinformatics sector. Gaithersburg, Md.-based Gene Logic, which Zimmerman and others have pegged as one of the success stories in the industry, saw revenues drop to \$17 million from \$17.7 million in the same period last

year. The company is undergoing management changes aimed at improving its sales.

Accelrys, another favorite of analysts, saw a drop in revenues from \$17.7 million to \$14.3 million. The San Diego-based firm recently reported that its chief financial officer would resign.

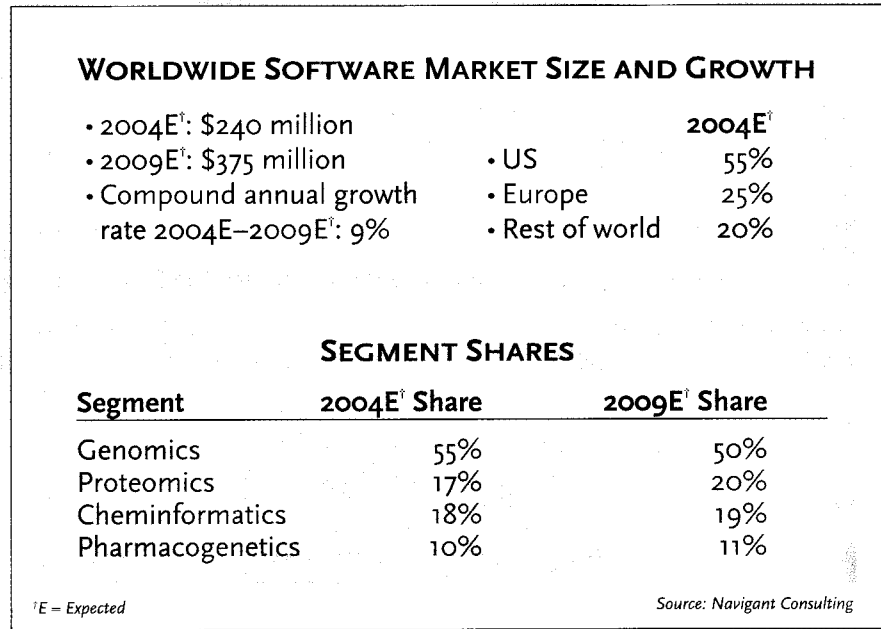
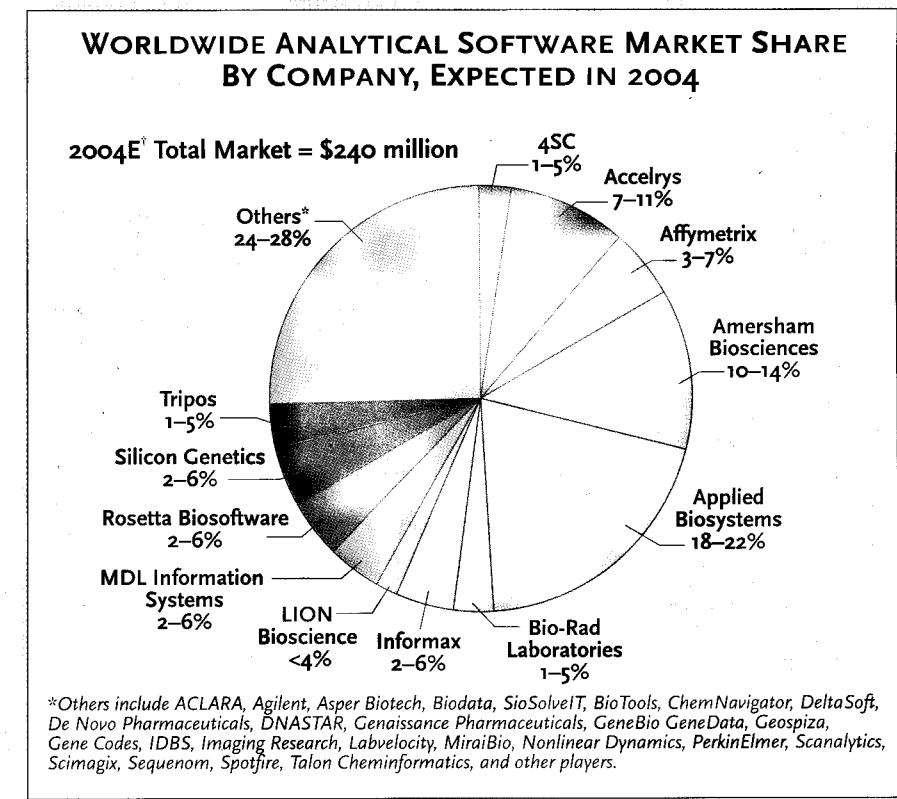
Germany's Lion Bioscience, which has undertaken a major realignment and sizable lay-offs, reported that its quarterly revenues had fallen from 5 million Euro to 2.6 million Euro. Shortly afterward, the company announced that it was de-listing from the NASDAQ stock market, apparently due in large part to the prohibitive expense of listing both in the United States and other countries.

The list of struggling companies goes on, with no clear end in sight to the sector's troubles. "I think it's going to stay tough for at least the next five years or so," Kim says.

BRANCHING OUT Arthur Pappas, managing general partner of life-science investment firm A.M. Pappas & Associates, Research Triangle Park, NC, agrees that the climate is difficult. However, he does see some hope for companies that are willing to adapt to the new environment and change the way they do business.

"What is developing quite nicely—although we still don't know how the business value of it is going to develop—is a model where bioinformatics companies have expanded their platforms so that they become more end-to-end biology solutions platforms," says Pappas. The approach does away with "the silos of data in bioinformatics" in favor of offering a more complete solution, he says. For example, while in the past a bioinformatics tool might have had only a single application, many newer systems can handle various types of research and so can be used through a project's entire duration. This strategy cuts down on the hassle and expense of manually moving data from one bioinformatics system to another, and it could also open up new uses for the technology. "We're all looking at it to see how it might apply to more predictive types of medicine and even streamlining of clinical trials," Pappas says.

Pappas cited one of his firm's portfolio companies, Cambridge, Mass.-based Genstruct, as an example of a business that is taking this new tack. In 2003, Genstruct, which focuses on using high-throughput biology to identify and validate disease mechanisms and compound mechanisms of action, acquired another of Pappas' portfolio companies, Incellico, a basic bioinformatics company.



"We moved Incellico into Genstruct in order to create this kind of end-to-end biology solution," Pappas says.

The merged company offers its partners resources in systems biology, expression analysis, disease biology, knowledge modeling, and experimental design and implementation. In November it announced an expansion of its existing

relationship with pharma giant Pfizer. Working with several of Pfizer's research units, it will use its high-throughput Molecular Epistemics Platform to help reveal the mechanisms of action and toxicity of new drugs for complex diseases.

DO-IT-YOURSELF Some bioinformatics companies may eventually improve their prospects by giving up on trying to sell

their research tools to pharma companies and focusing instead on using those tools to make their own discoveries, says Kim. "Some companies will actually try to come up with their own products and their own drug-discovery systems," he predicts. "They may try to merge with other companies that have the potential to develop their own molecules, and they'll try to apply the tools they have to optimize that process ... In a way, it's a logical evolutionary step, going somewhere where there's more ROI [return-on-investment] potential."

Kim points to Wilmington, Del.-based Incyte as an example of a company that has managed to make the shift from bioinformatics firm to drug-discovery company. "They wanted to focus more on the drug-discovery side, because they felt that there was a limit to how much they could sell the systems and platforms they had," he says. "They wanted to move into the next generation." Incyte now has an HIV drug candidate, Reverset, in Phase II clinical trials, as well as other drugs in earlier-stage trials.

The evolution from selling technology to clients to using that technology for in-house discoveries has precedence in other corners of biotech, according to Kim. "It's the way biotech works in general," he says. One example is Protein Design Labs, a Fremont, Calif.-based company focused on humanized monoclonal antibody technologies. The company was founded to out-license its technology to drug-discovery firms, but it has recently decided to focus instead on using its tools to discover its own drugs. The firm says it hopes to have its first proprietary medicine on the North American market within about three years.

"By selling their technologies, they had a short-term capital gain," Kim says. "Using that short-term capital gain, they could invest in something that would give them a long-term gain."

THE HEAVYWEIGHTS Despite the struggles that bioinformatics companies are experiencing, heavyweight, diversified IT companies such as IBM and Sun Microsystems show no signs of shying away from partnerships with the smaller companies or giving up on the bioinformatics market. "All the large IT vendors are getting very involved in life science," Zimmerman says. The big companies don't actually develop bioinformatics software, but they see opportunity in partnering with the software developers by providing hardware, service, and support for bioinformatics tools, and selling the complete package to firms involved in drug discovery.

"We're very involved in bioinformatics," says Loralyn Mears, Sun's life science market segment manager. "Ten years ago, we were dabbling in it. We had informal efforts. Five years ago, we formalized it, and it continues to grow. We continue to add headcount and to invest time and money in marketing campaigns around it, as well as to add new partners."

For firms like Sun, involvement in bioinformatics probably makes sense, because making relatively small changes to existing technologies can create saleable products, says Kim. "These companies already have experience with [creating similar support systems for] retail business—how to manage data, how to manage consumers, how to optimize communications," he says. "So all they have to do is come up with a different platform on the surface that will meet the needs of the biotech and pharma industries. It's pretty easy for them."

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Mears agrees that the fit is an easy one for Sun. "Computational biology has become extremely complicated," she says. "This is perfect for us, because since Sun's inception, we've been designing systems—not pieces, not a box, but whole systems." Because of Sun's experience and its many bioinformatics partnerships (about 400), the company is able to provide bioinformatics platforms that are more appealing to customers than they have been in the past, she says.

"Sun's been on a real kick for the past couple of years of attacking cost and complexity," says Mears. "We're making life easier for customers by providing integrated, pretested solutions that are actually much cheaper than custom-building a solution in-house."

For example, in November, Sun launched a DNA sequencing solution with Seattle-based bioinformatics partner Geospiza that it claims costs clients about one-tenth of a custom-built solution. The technology bundle provides Geospiza's software for DNA sequencing data collec-

tion, management, and analysis together with Sun's Sun Fire servers running Solaris or Linux operating systems. The system is targeted to cost-conscious biotech companies and academic labs, the company says.

The cost of the bundle is \$13,995, according to Mears. "In Geospiza's studies, they found that companies or organizations were typically spending at least \$100,000 in order to do a home-grown system, and that's just the cost of the development," she says. "It doesn't even get into the cost of the long-term maintenance." As a result of Sun's new focus on meeting customers' needs for cheap and simple solutions, the company's bioinformatics business is healthy, Mears says. "There were some dark days there, but overall, in 2004 we've had tremendous uptick."

Still, Pappas is skeptical that the bioinformatics market will turn out to be much friendlier to large IT companies than it has been to smaller software companies. "The big pharma companies and the biotech companies have in fact all built their own informatics platforms," he says. "At the end of the day, if a bioinformatics [software] company has not been able to sell its program to someone who wants to pay money for it, then it doesn't matter what kind of hardware these bigger companies are providing."

Kim points out that even if partnerships between software companies and IT giants can offer bioinformatics bundles that are relatively inexpensive and easy to use, some clients may avoid them simply because they are freely available to other pharmaceutical companies and aren't proprietary. "Often, they don't want to share the technologies," he says.

That issue could ultimately lead to small bioinformatics firms tying the knot with another kind of heavyweight—Big Pharma. Kim predicts that more and more bioinformatics vendors may be acquired by pharma companies that want the option of keeping at least some of the technology all to themselves. When Merck wanted access to the drug-discovery technology of the bioinformatics firm Rosetta Inpharmatics, Kim notes, it found a way to keep control by buying the company rather than just a license.

As a wholly owned subsidiary of Merck, Rosetta now enjoys a level of safety and shelter that independent bioinformatics companies don't begin to approach. For companies going it alone, the only certainty seems to be that those that can't find new ways of adapting will not survive. ☉

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