

Computers + biology = bioinformatics

Here, we will explore one of the most intriguing areas within medicinal biotech: the nascent field of bioinformatics. The term "bioinformatics" was coined in 1987 in a journal article by Hwa Lim, the current president of the biotech consulting firm, D'Trends. Since then, the term has taken on a life of its own. Though notoriously hard to pin down, bioinformatics may be defined as the use of computer technology to organize and analyze genomic, biological, and chemical data in order to support the drug discovery process.

A brief history lesson might help to highlight the extraordinary value of bioinformatics. For decades, companies have taken the old-fashioned approach to drug discovery: the drug in question is put through a battery of preclinical safety tests, followed by a lengthy—and very expensive—set of clinical trials on animals and humans. At the end of this nearly decade-long process, drug developers cross their fingers in hopes that their drug will be approved by the Federal Drug Administration (FDA).

But usually, drug companies are not so lucky. According to the Boston Consulting Group, nearly 75 percent of the 5,000 drug candidates now in the trial stage will never make it to market. With such a high rate of failure and such extraordinarily high costs, researchers are eager to find ways to streamline and accelerate the drug discovery process.

Drug discovery in hyperspeed

This is where bioinformatics steps in. With bioinformatics technologies, drug companies can cut the cost of drug development in half and shave years off the development process. No wonder high-profile pharmaceutical companies

have been scrambling to jump on the bioinformatics bandwagon.

Pfizer, the world's largest pharmaceuticals company, currently partners with about fifteen major bioinformatics companies. And pharmaceuticals giant, Merck & Co., hoping to speed up its drug discovery process, forked out \$620 million to acquire the genomics data analysis company, Rosetta Inpharmatics, in May 2001. And that's just the beginning. According to a Frontline study, the worldwide bioinformatics market was estimated at roughly \$697 million in 2001 and is projected to grow to \$1.7 billion by 2006.

At the moment, bioinformatics companies work with drug companies primarily in the pre-clinical trial phase of the drug development process. Palo Altobased Incyte Genomics, for example, has developed powerful databases which provide researchers with a stable set of genes in order to facilitate drug discovery. Gene Logic provides drug companies with data mining and visualization tools to streamline the process of sifting through data.

From *in vitro* to *in silico*

However, some bioinformatics companies are moving higher up the drug discovery value chain by collaborating with companies at the clinical trial stage of the drug development process. In fact, *in silico* discovery—drug discovery on computersimulated models—has become the latest buzzword in the bioinformatics industry. Silicon Valley-based Entelos, for instance, has developed PhysioLab technology, enabling scientists to simulate experiments on a computer

instead of conducting costly clinical trials, which often take a number of years. Entelos' technology offers researchers a virtual research environment in which they can define virtual patients, virtual drugs, and experiment protocols to run rapid simulations that predict human clinical efficacy. *(Turn to "The Informer" on p.20 for a bioinformatics company that straddles both ends of the drug discovery chain.)*

This kind of technology holds extraordinary promise. A recent Price Waterhouse Coopers study estimates that in silico technologies can save a drug company about \$200 million and two to three years per drug.

Trying to stay afloat

For all its promise, bioinformatics has, strangely, left investors cold. Venture capitalists don't question the value of the technology but seem skeptical as to whether bioinformatics companies can come up with a viable business model. The key question seems to be: how will the market be able to sustain companies built around one or two high-cost software programs targeted to a relatively small user-group?

The unexpected demise of the bioinformatics firm, DoubleTwist, in March certainly hasn't helped to boost investor confidence. Founded in 1993, the Oakland-based gene database licensor managed to burn through \$37 million, before ending up in bankruptcy.

Meanwhile, the bioinformatics giant, LION Bioscience—as well as a number of smaller firms such as AxCell Biosciences and BioDiscovery—have adopted a hybrid business model, deriving significant revenues from collaborations with drug discovery

companies as well as from product licensing. The Burlington, MA-based bioinformatics company, AnVil, has abandoned the product-licensing model altogether—it derives all of its revenues from corporate partnerships.

Some investors remain uncertain about the potential for bioinformatics to penetrate the biotech market. Dr. Dinesh Patel, Managing Director at vSpring Capital, shares this uncertainty. "A lot of people are saying that it will be very simple for bioinformatics companies to achieve market penetration. I would say that it is not going to happen easily since most pharma or biotech companies already have huge bioinformatics groups inhouse within their own company. They are not going to outsource something that is so critical," insists Patel.

Cautious optimism?

However, others are more optimistic. "Outsourcing is certainly happening. There is a lot of outsourcing of medicinal chemistry today, for instance, which would have never happened ten years ago. That used to be the crown jewel that you would never outsource," says a biotech consultant.

Indeed, the trend among drug companies seems to confirm such optimism. Despite the fact that the major pharmaceuticals company, Bristol-Myers Squibb, built an in-house bioinformatics division in 1998, it still chooses to outsource most of its bioinformatics responsibilities. And the London-based pharma company, AstraZeneca, has embarked on a number of academic and corporate partnerships to complement its inhouse bioinformatics efforts.

It remains to be seen whether the

optimists or skeptics will rule the day. But it can safely be said that the future of bioinformatics lies in how effectively bioinformatics companies are able to shed the stigma of being "mere database-providers" and prove to be an integral part of the drug discovery process itself.

In fact, some bioinformatics firms—not satisfied with being on the platform side of things—are moving into the drug discovery arena themselves. High-profile bioinformatics company, Celera Genomics (partly responsible for the initial sequencing of the human genome in 2000), has recently begun to focus on developing therapeutic antibodies and cancer vaccines. LION Bioscience, meanwhile, has lately embarked on drug discovery for neuroreceptors. Only time will tell whether bioinformatics companies are successful in their quest for the perfect business model.

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