

our productivity and growth," says Hartwig. Following a realization two years ago that it was no longer an innovative life science company and that a dramatic change was needed to haul it into the top 10, Bayer has been making a concerted effort to reinvent itself. "There is a narrow time window for investment in this gene rush," says Hartwig, referring to Bayer's lack of proprietary targets.

In order to surpass its competitors, Bayer calculates it must put two new chemical entities on the market every year. Given a 10% probability of success, this translates into 20 development candidates per year, a quadrupling of its output. High-throughput screening and combinatorial chemistry have been developed to a competitive level in-house, while genomics, bioinformatics, and functional genomics are covered in collaborations, the most notable of which is the

much-remarked upon deal with Millennium Pharmaceuticals (NBT, 16, 1005).

Having set up a competitive platform, "Bayer recognized that it faces a data handling problem that could prove fatal in a couple of years," says von Bohlen. "Information management is one of the biggest solutions for the future and Bayer wants to be the first to reserve a piece of that cake."

Bayer is proving to be one of the more aggressive companies in genomics, probably along with SmithKline Beecham, Roche, and Novartis in terms of external deals, says Hambrecht & Quist's Olan.

Lion's 50-strong fleet of bioinformatics specialists puts it in the same league as in-house development teams at such pharmas as SmithKline and GlaxoWellcome, claims von Bohlen. Although Olan says it's too

early to tell whether this will be enough to push Bayer into the top 10, "What is clear," he says, "is that bioinformaticists are expensive and are becoming more so, so if they can really deliver then again it will be cost effective [for Bayer]."

With Millennium, "Bayer bought the Ferrari, and Lion turbocharges it," says Michael King, biotechnology analyst at BancBoston Robertson Stephens (New York). However, "all this stuff is wonderful in theory," he cautions, "but the proof of the pudding's going to be when they finally get a product on the market or a target validated in X number of years—that's when people will really appreciate it."

Lion is expected to announce similar deals with other life science companies by the end of the year.

Emma Dorey

New institute to study systems biology

The creation of a new Institute for Quantitative Systems Biology was announced in spring by Leroy Hood, chair of the Department of Molecular Biotechnology at the University of Washington (Seattle, WA). Recognizing that neither academia nor industry is in a position to progress beyond the level of functional genomics, the institute aims to model complex biological systems, describe them quantitatively, and foster interdisciplinary interactions in the life sciences. Although many commend the project as a bridge between theoretical and applied biology, some question the use of computer models as a revolutionary tool for drug discovery.

Hood, whose work at the California Institute of Technology spawned Advanced Biosystems, Inc., a company that has given researchers DNA and protein sequencers as well as instruments to synthesize peptides and DNA fragments, has cofounded the institute with University of Washington professors Reudi Aebersold and Robert Franza. The institute will consist of a genome center, high-throughput analytical facilities, and cross-disciplinary faculty in biology, chemistry, physics, applied mathematics, engineering, and computer science. A major impetus behind starting the institute, says Hood, is the need to see biology transformed from the largely descriptive science it is now to a quantitative, predictive science.

The initial aim is to integrate data coming from all the various genomics technologies, such as DNA microarrays and proteomics,

and to generate information that describes biological systems (metabolic pathways, for example) quantitatively. The eventual goal is to be able to develop mathematical models that can accurately predict the behavior of complex systems containing, say, 50 proteins, as a way to test scientific hypotheses where it would be difficult to predict the outcome of changing any one parameter.

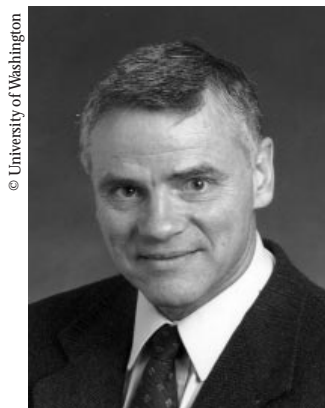
Amassing this quantitative information is key, says Hood, and the institute would be a place to develop the tools to do it. Although this overlaps with some of the university's

tative data is "the biggest challenge to biological modeling in general" at the moment, says Donna Rounds, vice president for external affairs at Physiome Sciences (Princeton, NJ), a 3-year-old company devoted to making computer models of biological systems. To get the sort of data it needs, Physiome scours the scientific literature and pays academic laboratories to provide it with kinetics data, for example, which often isn't available. "If Lee Hood is going after the right kind of data, that's great, we can all tap into that," she says.

However, some currently involved in one of the largest data-gathering exercises in biology—genomics—have reservations about the usefulness of models for drug discovery. Human Genome Sciences (Rockville, MD) president William Haseltine thinks that models will never be a primary discovery tool. "By the time you get the information you need to make those models reliable, you'll have the information you need to make a decision on whether to go forward with drugs or not."

Models would be of secondary importance in predicting the full range of responses, he adds. But Hood thinks this is "wisdom of someone of the past." In the future, he says, drug companies will need to understand informational pathways in a cell and how they can manipulate them. "They won't know what those [drug] targets are unless they understand the system," he says.

Thomas Caskey, senior vice president for research at Merck (Whitehouse Station, NJ), thinks that models could be a major time-saver. "I've looked for more and more computer power to reduce what we do at the bench, and [the use of models] would be one way of improving that," he says.



A major impetus behind starting the institute, says Leroy Hood (above), is the need to see biology transformed into a quantitative, predictive science.

work, he says the institute will be able to work on a much larger scale with less academic bureaucracy.

Companies already involved with complex modeling rarely generate the necessary experimental data themselves. Lack of quan-

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Nevertheless, it remains to be seen whether current genome centers will move from sequencing toward quantitative data and modeling. Francis Collins, director of the US National Human Genome Research Institute (NHGRI; Bethesda, MD), argues that the NHGRI will be a major player in this area in the future.

However, companies interested in modeling are skeptical that the large, publicly funded initiatives will be flexible enough to move into the area quickly. "It's like being the Titanic, it's hard to turn the ship," says Geoffrey Duyk, chief scientific officer of Exelixis Pharmaceuticals (South San Francisco, CA), a company that uses model organisms to define biochemical networks.

Hood describes his institute, which will be a nonprofit operating unit of the University of Washington, as halfway between academia and industry because it will have a less hierarchical infrastructure and more support than academia, but will be able to take a longer view than industry, which is driven by the need to add shareholder value on at least a quarterly basis. "I think Lee has the right vision here," says Caskey. "Within an institute the overall

dedication is to that end mission, and therefore people think and act cross-functionally."

Haseltine points out that making quantitative biochemical measurements is what many pharmaceutical companies do for a living. He admits, however, that an academic institute would have more freedom to study a broad range of questions that don't necessarily have direct medical relevance—something that companies can't justify.

The institute is applying for funding from many sources, including federal grants, private foundations, and large corporations for long-term support. Collaborations with biotechnology companies will allow the institute access to new technologies while giving small companies exposure to the institute's new intellectual property, methods, and technologies before they become commercially available. [A deal that is already in place with Orchid Biocomputer (Princeton, NJ), for example, allows the institute access to an automated genotyping system for single nucleotide polymorphisms.] Hood points out that because the institute is nonprofit, all the information generated will be publicly available, although publication could be delayed while companies obtain patents. The institute also

plans to offer academic laboratories access to technologies unavailable at most academic centers in exchange for access to good model systems.

In addition, an exchange program with the Keck Graduate Institute of Applied Life Sciences (Claremont, CA), announced in May will allow Hood to explore his ideas for teaching biology, while students and faculty from the Keck Institute can keep up to date on the latest technologies.

The need for more cross-disciplinary interactions has recently become a focus of both government and academic institutions. However, only the US National Institute of General Medical Sciences (NIGMS; Bethesda, MD) program has focused, not only on bringing together biologists and people from quantitative disciplines, but also on developing tools for making quantitative measurements. Since its creation in January 1998, though, relatively few applications have been received. NIGMS director Marvin Cassman attributes this to the lack of interaction between biologists and those in the quantitative sciences. An institute would help promote interactions just by having people next to each other and, he says, is a "terrific" idea.

Alka Agrawal

Japan starts its own SNP project

In another bullish attempt to kickstart its flailing genomics industry, the Japanese government on June 22 announced a "strategic plan" for a new national project to identify and map single nucleotide polymorphisms (SNPs) in the Japanese population. Although the government hopes the program will promote commercial growth in the sector, there is a distinct absence of corporate involvement. In addition, there is controversy—from both inside and outside the program—as to whether Japan has the right approach or the resources necessary for such an ambitious undertaking.

The project, which aims to map between 100,000 and 150,000 SNPs in two years, will be carried out jointly by science-related ministries, universities, and industry. "This is the first project to be carried out under a new scheme that encourages different government ministries to collaborate in genome research," says Yoshiyuki Sakaki, leader of the human genome group at the Genomic Sciences Centre (GSC; Saitama Prefecture) and professor at Tokyo University's Institute of Medical Sciences (IMS; Tokyo). "Which is why it is taking shape as a Japanese effort, and there is tremendous pressure for it to work."

The identification and mapping of SNPs will be performed by a central genome research center in order to ensure consistency of the

data. However, the effort will not take place at GSC, which is considered a flagship genome centre in Japan, but instead is likely to be carried out at the IMS.

Funding for the project will be provided entirely by the government which, in July, announced a five-year plan to increase biotechnology spending by ¥2 trillion (US\$16 billion). This would roughly double the amount of current funding for all biotechnology research, which received a total of ¥500 billion (US\$4 billion) in the 1999 fiscal year budget.

According to the government's ad hoc working group on SNP research, the new program aims to create, in parallel, a public database of SNP map data and a separate database of information based on disease correlation studies. The former will comprise SNPs within protein-coding sequences (cSNPs), identified by analyzing full-length human cDNA and expressed sequence tags obtained from at least 50 Japanese people.

Data from other populations may be added at a later stage by collaborating with research groups from other Asian nations, but the project will be a purely Japanese effort during its initial stages. According to the government, the project will go beyond those that have already started in Europe and the US because the Japanese population is more homogenous than Western populations, allowing disequilibria to be mapped in more weakly associated markers.

The second part of the SNP project will require an efficient mechanism for collecting vast amounts of DNA samples from diseased and healthy populations for association studies, and there are concerns that Japan lacks the ability to carry this out. "In a way, this is one of the most worrying aspects of the project, as we lack a strong infrastructure that would allow effective collaboration between clinicians and researchers from diverse areas of medicine," says Masaaki Terada, director of the National Cancer Centre (Tokyo). According to the SNP working group, workshops and meetings will be held in order to improve understanding of the project among clinicians and to discuss ethical issues surrounding the collection of such data.

Initially there was also controversy among members of the SNP working group concerning the cSNP approach, which differs from international efforts such as the SNP Consortium (Nat. Biotechnol. 17, 526, 1999), which focus on genomic SNPs (gSNPs). Because only 3–5% of the human DNA sequence encodes proteins, most SNPs are located outside the coding sequences. However, cSNPs are more likely than a random SNP to have functional significance, representing genotype–phenotype relationship in specific diseases. While many supported the cSNP approach in theory, some