EDITORIAL FEATURE

Working the Systems

Systems biology seeks to connect the dots between molecular data. It's a hot career field, but success requires making connections between disciplines

SEATTLE, WASHINGTON—The Institute for Systems Biology (ISB) here occupies a new building with large, rectangular panels of glass offset by brick. From the outside, the building has a vaguely modular feel, intended, perhaps, to evoke a system of linked components. Glass dominates the façade, providing those inside panoramic views of Seattle's Lake Union and the northwest's turbulent weather. Within, pastel walls and numerous cubbyholes and conference rooms encourage easy communication, and the design itself reflects some social engineering: "To get to the centrifuge, you may have to walk past the computational people," says Alan Aderem, a co-founder of the institute and one of its current directors. When you walk past the computational people, Aderem hopes you'll stop to strike up a conversation.

Six years after the building's construction, ISB remains the ambitious experiment in interdisciplinary research that began when founder and president Leroy Hood concluded that he couldn't arrange a successful marriage between computing and biology in the academic environment of the University of Washington. Six years on, there is no clear definition of systems biology, although most would agree it has something to do with understanding dynamic, molecular-level relationships among biological molecules in living systems. Like the building in Seattle, the new field brings together physiologists, molecular biologists, biochemists, computer scientists, mathematicians, engineers, physicists, and a few other specialists and encourages them to work together to look beyond individual genes and proteins to a holistic view of whole systems—like the view that dominated biology before the advent of molecular biology. But systems biology adds insights and an arsenal of techniques developed over the past half-century. There is little doubt about the power and potential of the systems approach, but have ISB's attempts at architectural, social, and scientific-systems engineering produced a smoothly operating new scientific discipline?

Not yet. "I underestimated how resistant people are to leaving their comfort zones," says John Aitchison, who joined ISB in 2000 from the University of Alberta, Canada. And that, in a nutshell, may define the opportunities and challenges of systems biology, as a field of science and as a career.

Opportunities

No question, systems biology is in heavy demand. "Systems biology is very fashionable. Until it is fully established in all of the major universities, there will be a lot of hires, either new hires or professors that are reminting themselves," predicts David Galas, a researcher at ISB and vice president and chief scientific officer of the Battelle Memorial Institute in Columbus, Ohio. Roger Brent, president and research director of the independent Molecular Sciences Institute (MSI) in Berkeley, California, agrees. "I'd say that this is a time in which a talented young person who demonstrates an ability to make real contributions can pretty close to write their own ticket in terms of what they can do academically and intellectually," he says.

One reason the outlook is so rosy is that "there are really very few" people who have the combination of biological and computational skills to fill those types of positions, says John Barnett, director of the center for immunopathology and microbial pathogenesis at West Virginia University in Morgantown. According to Barnett, those who have joint training "have a really good job market."

Industry has been cautious in embracing the new field, "and rightly so," says Galas. "They want to see how long it will take to benefit them. It's happening, but at a slower rate." The number of industry jobs may increase when the biotech market changes. "At the moment, funding in biotechnology is skewed toward later stages of research, where potential products are in clinical trials. I think where you will see it first is the larger companies that are trying to make long-term plays."

ISB is not a likely long-term career destination, because the institute hires few senior scientists. But it is an excellent training ground, with 50 or so postdoc positions opening every year. And according to Hood, "most people who have come through here have had no problem getting jobs."

In the blood. At the Institute for Systems Biology (*top pictures*), former bioengineer Nathan Price (*above*) looks for early fingerprints of cancer in patterns of blood proteins.

Challenges

Despite its opportunities, systems biology can be a difficult field to work in. It relies on collaborations, and ISB and similar centers have struggled to build them. "The differences [between biologists and

CREDITS (TOP): TEAM PHOTOGENIC; (BOTTOM) ISB

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A work in progress. Roger Brent says universities are still struggling to embrace the interdisciplinary research that is a hallmark of systems biology.

computational scientists] are really remarkable. They speak and think differently," says Aitchison. "Biologists think of themselves as wise, sagely knowledge banks, and they see computer people as keyboard jockeys. The computer guys think of themselves as mathematics-driven scientists. They think of biologists as lab technicians. [The problem is] getting people to bring appreciation for each other's work to the table. There is the potential for resentment."

Some of the problems have been a surprise. Says ISB's Aderem: "I expected hard-core mathematicians and physicists to have a relatively easy job learning biology because we're all inherently interested in life; we all hunted for frogs in a pond as a kid. I thought biologists would have more trouble, but it was the other way around. Biologists have some quantitative training, and with some work, they can learn [the computational side]. The mathematicians and physicists don't like complexity. They like an algorithm."

Nathan Price is learning how to tread that path between disciplines. A 2005 graduate of the University of California, San Diego, bioengineering department, he accepted a faculty position at the University of Illinois but decided first to do a postdoc at ISB to gain a better understanding of systems biology. In graduate school, he primarily modeled metabolic systems; at ISB, he uses systems biology to analyze secreted bloodstream proteins that might act as early-stage fingerprints for cancer diagnosis. The work is computationally intensive, but his research drove him toward the bench. "You need to be able to go where the problem takes you," he says. You need to be able to do some basic experiments, he says, because it can be difficult to find people to do work that they might not find intellectually stimulating. Despite the premium on teamwork, "you handicap yourself if you always have to find a collaborator when you want to validate something."

Costs and benefits

No one doubts that the focus on working together is a good thing for biology, but is it good for a researcher's career? As the number of authors on a paper grows, it becomes more difficult for potential employers to distinguish an individual's role. "A paper with 30 authors can stand in the way of recruitment," says Brent.

Academic environments can be particularly hard on work that resulted from a team approach. Tenure committees, for example, tend to evaluate a faculty member on the ability to conduct solo research—the traditional mark of the competent scientist. "They have to bend a bit and make it possible for teams of young people to work together across departments and forge relationships—to be respected for that work even if they're members of a coalition. That's a work in progress. It's why MSI is not affiliated with a university," Brent says.

Getting the proper training is another challenge. Even 6 years after the founding of ISB, few academic departments specialize in systems biology. Training should start as an undergraduate, says Hood, who advises every biologist to get a second major in computer science or mathematics. Barnett urges graduate students to find an adviser who will let them expand beyond the tight focus of the typical Ph.D. project. "It takes a unique adviser to let them do that," he says.

It also takes a unique scientist. "It takes the right kind of people. Some people don't want to be this diverse," says Hood. Brent agrees that work in systems biology can be difficult, noting that potential hires at MSI are subjected to an intense process of evaluation: "A candidate has to be quite committed to put up with the stress of the coming years. We are not unpassionate about what we do."

–JIM KLING

Jim Kling writes for ScienceCareers.org from Bellingham, Washington.

EDITORIAL FEATURE

A Meeting of Minds, Expertise, And Imagination

European systems biology is pushing the boundaries between disciplines and cultures

CAMBRIDGE, U.K.—British systems biologist Eric de Silva—an astrophysicist by training—began his systems biology education "by sitting at home reading popular science books." Later, he says he "was brave enough to pick up [the textbook] *The Cell*," and his biology education began in earnest. De Silva now investigates protein interaction networks as a postdoc at Imperial College London.

De Silva's experience is typical. Few of today's systems biology postgrads, postdocs, and group leaders were trained as interdisciplinary scientists. Most acquired the skills they need to work and communicate with scientists from different disciplinary backgrounds on their own, informally. As they struggle to piece together pathways and networks and map out relationships among the components of biological systems, they must also piece together professional networks and discover new ways to work together. But for those who manage to bridge different fields, prospects are promising. "It's a growth area and a young field with not a lot of senior people," says Rüdi Aebersold, a professor of systems biology at the Swiss Federal Institute of Technology Zurich (ETH Zurich) and the University of Zurich. "There's a great opportunity for young people starting out."

A model group. Edda Klipp's lab of modelers in Berlin sticks closely to experimental data.

Although the United States is the pioneer and still the world leader in the emerging field, "systems biology in Europe is very dynamic," says Aebersold, one of the founding members of

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