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.

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

"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."

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

CREDITS (TOP TO BOTTOM): DAVID PINCUS; K. GUENTHER the Institute for Systems Biology in Seattle, Washington (see p. 1305). Aebersold returned to Europe at the end of 2004 and got involved with SystemsX, a collaboration between the universities of Basel and Zurich and ETH Zurich. Systems biology is a priority area in the European Commission's 7th Framework Programme, and the E.U. has just funded a €9 million pan-European systems biology project called Experimental Network for Functional Integration (ENFIN), among other projects. Most of Europe's national governments are making sizable bets—millions of euros—on systems biology projects. Large-scale collaborations are up and running, and more—such as SystemsX and ENFIN—are starting up. "In the way that molecular biology dominated the last half-century, systems biology will dominate the next half-century," predicts French systems biologist Nicolas Le Novère, a group leader at the European Bioinformatics Institute (EBI) in Hinxton, U.K. "Systems biology is here to stay."

De Silva. Moonlights as a biology student.

Building human networks

The systems biology workforce comprises classical experimental biologists, clinical scientists, mathematicians, computer scientists, physicists, engineers, and other specialists. Most research groups collaborate with researchers outside their specialties and often outside their own institutes. Edda Klipp heads the kinetic-modeling group at the Max Planck Institute for Molecular Genetics in Berlin; she is also an ENFIN partner. She says her group is "interested in trying to represent [biological] networks in mathematical terms" and in figuring out why certain features of a system evolve the way they do. Klipp's group is entirely theoretical, but she believes that "if you want to be close to nature, you need to have real data," so her group collaborates with several experimental groups. Some of her students have spent weeks or months in wet labs, learning new skills and cementing relationships.

Learning to collaborate—to get along with other scientists in a productive way—takes time, says Ewan Birney, a bioinformaticist at EBI and the coordinator of ENFIN. A big part of his role at ENFIN, he says, is "managing expectations: Experimentalists and theorists have different perspectives." It can be a difficult challenge, but it's essential. "Experimentalists have certain views," notes Klipp. "Models need different parameters; sometimes we"—theorists and modelers—"are aware of aspects they haven't discovered." Reality checks are also common the other way around. "We run our ideas by biologists," says de Silva, "and sometimes they rightly say, 'That is nonsense.' "

Sometimes the boundaries of communication are pushed. "Communication has always been one of the problems" of systems biology, says Le Novère. "It's not a dialogue between two disciplines; it's more like three or four." The key, say experienced systems biologists, is to be patient and give professional networks time. "At the start, you are kind of learning a language," says Klipp. Jörg Stelling, a systems biology group leader and assistant professor of bioinformatics at ETH Zurich, calls it "an investment." In his experience, learning to communicate adequately with collaborators "can take one to one-and-a-half years. But it's worth the effort," he adds.

Training as a systems biologist

Like de Silva, most of today's systems biologists come from traditional backgrounds and had to learn the systems biology ropes ad hoc. Le Novère trained in molecular and cellular pharmacology and taught himself computer programming and bioinformatics. His training, he says, "was not adequate." De Silva, who made the switch from astrophysics to biology, first got exposure to biology on the statistics end of a genetic-population project, which prompted him to read those biology books by moonlight.

Le Novère. Sees career potential for postdocs in systems biology.

So what kind of training, whether systematic or ad hoc, should aspiring systems biologists pursue? Stelling recommends "learning the basics in certain areas: stats, calculus, and linear algebra." Biologists "need to know how models can be set up." De Silva adds: "Be able to program." With these combined skills, he feels that researchers will be able "to analyze data sets themselves, quickly and easily." At the same time, "mathematicians and computer scientists need to acquire a biological way of thinking," says Stelling. "You need to learn the fundamentals in cell biology, molecular biology, and biochemistry."

Michael Stump, a group leader at Imperial College London and part of Imperial's new Centre for Integrative Systems Biology, advises students to "do what undergraduate degree you are most interested in, and do a master's course afterward." A number of master's-level courses that build bridges between disciplines have come on stream in recent years.

Gianni Cesareni—who has a hybrid computational and experimental lab at the University of Rome Tor Vergata and is part of the ENFIN initiative—believes that balance is key: "At the level of Ph.D., you need some specialist expertise, but you also need some interdisciplinary exposure." He recommends that researchers at the postgraduate level talk to students with different backgrounds. "Students need to go to common meetings," he says.

Job-market growth

Such training investments are likely to pay off for researchers with a talent for biological systems, because job opportunities are increasing rapidly. "At the moment, the mood is very good; there are a lot of things to do," says Klipp. And with funding levels high, the trend is likely to continue, say researchers in the field. Le Novère says that "the most striking effect is the number of new group-leader positions. It's one of the areas as a postdoc that you have a chance to become a group leader early."

But biologists who avoid mathematics should also avoid systems biology. "You need to have some maths mentality, and there are some students who deliberately pick biology because they want to avoid maths," says Cesareni. "It's not for everyone," says Stump—but he also predicts an era in biological research when "it will be hard to get a job if you are innumerate."

For Stump and ENFIN's Birney, these challenges are offset by substantial rewards. "It's a learning process, but great fun and adventure," says Stump. Birney adds, "It's a pleasure to coordinate; people want to collaborate."

As for de Silva, his appetite for biology is not yet quenched. "I feel I would be missing out a lot if I hadn't entered the world of biology. I thought there couldn't be anything as complicated as the universe until I started reading about the cell."

–ANNE FORDE

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