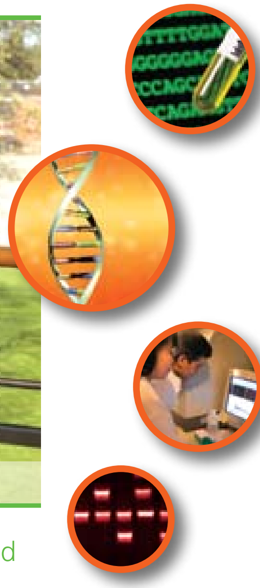
SYSTEMS BIOLOGY AND BIOINFORMATICS: SOMETHING FOR EVERYONE

Systems biology and bioinformatics want you. These highly collaborative fields are looking for biologists, engineers, chemists, mathematicians, and computer programmers. If you can work in a diverse team, says Bernhard Palsson of the University of California, San Diego, "It's an era of unprecedented opportunity." **By Chris Tachibana**

Janet Thornton



"Bioinformatics has evolved rapidly over the past 15 years and is now quite ubiquitous."

Lynn Hlatky, director of the center of cancer systems biology at St. Elizabeth's Medical Center, Tufts University, agrees, saying, "For people who are changing careers, and for new investigators, there is funding, and new systems biology centers are being established worldwide."

The job opportunities aren't necessarily tied to a specific geographic location, either. Collaborators can work remotely on a common project. Wet-lab data generated at one site might be analyzed by group members cyber-networking from a distance. "It's more about getting the right people together to address the problem, no matter where they are," says Hlatky. Systems biologists just need "the ability to see the big picture and to have an open mind. Anyone can get into this game."

Actually, all researchers need to get into the game, according to **Jens Nielsen,** professor of systems biology at Chalmers University of Technology, Göteborg, Sweden. "The tools, techniques, and approaches of systems biology are becoming standard in research and industry," he says. "To get a life science job in 10 or 20 years, you will simply be expected to have competency in these areas."

Combining High Tech with Old School

The list of specific areas within systems biology is almost comically long, and includes everything from cutting-edge computer science to traditional life sciences. Fortunately, in this field, collaboration is the name of the game. Galetti Professor of Bioengineering at the University of California, San Diego (UCSD) **Bernhard Palsson** says systems biology includes "an understanding of networks, biological systems and linear algebra, genomics and genetics, the biochemistry of gene products, and how everything fits into the three-dimensional architecture of the cell." Hlatky says that attacking the complex, nonlinear nature of biology requires "a team of individuals collectively versed in the traditional biological as well as the quantitative sciences, from cell and molecular biology to physics, chemistry, computer science, and mathematics."

Systems biology even needs expertise in fields that have fallen a bit out of fashion. Remember Linnaeus? "Taxonomy is a field of increasing importance, particularly combined with molecular techniques," says **Stephan Schuster** of the Center for Comparative Genomics and Bioinformatics at Penn State University and the Department of Biochemistry and Molecular Biology. Knowledge of physiology, "but now with quantitative and molecular tools," is valuable, says Hlatky. "We also need people who have training in population levels of thinking—developmental specialists, physicists, and ecologists."

The multidisciplinary systems biology group is like a multicellular organism, explains Hlatky, with robustness coming from specialization and a division of labor. This diversity allows the team to tackle dynamic problems with multiple variables. For example, she says, "In cancer biology, we used to think a number of oncogenes, tumor suppressors, and DNA repair genes drove the whole process, but now we are identifying thousands of genetic alterations in cancers. This means we're not going to figure it out by tracking a few or even dozens of genetic endpoints. We need computation and bioinformatics to address this part of the puzzle."

Like two organs in one body, systems analysis and bioinformatics are separate, but interdependent. "Bioinformatics extracts knowledge from the data that underlie systems biology, for creating hypotheses and models," says **Janet Thornton,** director of the European Molecular Biology Laboratory, European Bioinformatics Institute (EMBL-EBI). Bioinformatics is a growth area, says Thornton, because "almost every experiment now involves multiple sources of data, requiring the ability to handle those data and to draw out inferences and knowledge. Bioinformatics has evolved rapidly over the past 15 years and is now quite ubiquitous." continued »

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—Stephan Schuster

Bioinformatics Opportunities in Service and Discovery

Careers in bioinformatics can be in the applied or services field, or in basic research. These two areas are very different in philosophy and practice, offer diverse opportunities, and attract different personality types. Structured, long-term, large-scale thinkers excel in the services field. "These people deliver a professional service, so they have to have robust software, and a very clear development process," explains Thornton. "They serve a large community of users, so they can't just change things overnight. Changes are planned months in advance, and occur while running 24 hours a day, and accepting data from all over the world." This area especially needs developers and testers. "They say it takes one month to write a program, but 10 to make it robust," says Thornton. Bioinformatics service also involves curation, or annotation of genes, proteins, metabolites, and other elements. Here again, says Thornton, "the annotator has to follow clear processes, and do it the same way with every gene or protein. You can't suddenly decide to do it differently one day. The goals of service are reliability, robustness, utility, and ease of use."

Research opportunities in the bioinformatics service field usually focus on making databases faster and more efficient. But the bottom line for the service side is scheduling new releases and data exchanges, and sticking to clearly defined criteria, protocols, and deadlines. Also, Thornton acknowledges, "Service bioinformaticians must make absolutely sure that no data are lost, which is something research scientists have been known to do."

Bioinformatics discovery is "for blue sky researchers" who can think of new ways to apply bioinformatics techniques or new directions to take the field, says Thornton. "Bioinformatics researchers need curiosity to answer biological questions. They need to write good software, but it doesn't have to be perfect, and this is not usually the primary goal. It's more important for researchers to ask the right questions. In my opinion, most good bioinformatics research is rooted in answering a specific biological question, but these can be rather grand questions, such as, How does the expression of all genes change as an organism ages?" And bioinformatics researchers can go where their imagination and interests lead them. "They have the freedom to explore multiple organisms, which is usually not the situation for an experimental biologist," says Thornton. "To a computational biologist, it doesn't matter if the data are protein interactions or metabolism, the methods are the same. An attraction of this field is that you aren't spending your life looking at a single organism or protein, but can be flexible and take a broader view."

The future career possibilities are encouraging. Penn State's Schuster says that "together with genomics, the most important research will be in bioinformatics, where you can correlate temporal or genomic profiles with chemical, mass spectrometry, and genetic data. This really opens up opportunities for people who are coming from many different directions." But right now, Thornton says, "Bioinformatics needs people driven by biology questions who want to take computational routes to answering those questions."

Opportunities for Bioengineers, Entrepreneurs, and Academics

Systems biology needs all-around researchers, according to Nielsen of Chalmers. He advises his students and postdocs to get experience in as many areas as possible, "from engineering to statistical analysis to molecular verification," and to do this as part of their project. Palsson of UCSD agrees, saying, "The best training might be classwork in the quantitative methods, while at the same time doing hands-on research in the lab in an environment that provides an in-depth understanding of what biology is all about."

For scientists with a broad range of skills, Nielsen says, "job prospects in industry are fairly good right now, considering that it's a tough time everywhere." Many of his students train for careers in industry with applied projects, addressing issues like improving fungal strains for commodity chemical production. Nielsen says that drug development firms, pharmaceutical companies, and commodity producers have been "investing in systems biology technology, so now they need people who can use it." The demand is particularly great for "people who can analyze data, who approach biology in a quantitative fashion and can integrate information from different areas."

Palsson has been involved in several startup companies and holds 28 US patents. He says the current demand for systems entrepreneurs is in "bioprocessing and metabolic engineering to make commodity and fine chemicals, and biopolymers." Both Palsson and Schuster see renewable energy and biofuels as a potential growth area with many challenges to meet. "We already see money being earned in sustainable energy fields, and they need information from broad systems studies in environmental areas and biodiversity," says Schuster. EMBL-EBI's Thornton also sees business opportunities for bioinformaticians. "Large pharmaceutical companies are moving away from in-house bioinformatics resources," she explains. "There's too much data, and they can't handle the storage, and don't have the personnel to keep things running. There may be opportunities for small and medium enterprises to develop software solutions for companies to handle their data effectively."

Academics and educators are not left behind as the demand for systems analyzers and bioinformaticians grows. "In 10 or 20 years, systems biology will just be part of an integrated biology education, so the need for faculty in this area will increase dramatically in the future," says Nielsen. Universities also need bioinformaticians, says Thornton. "Every biology research department will need computational experts." continued »

FEATURED PARTICIPANTS

Chalmers University of Technology
www.chalmers.se/en

European Molecular Biology Laboratory, European Bioinformatics Institute
www.ebi.ac.uk

Institute for Systems Biology
www.systemsbiology.org

Penn State University
www.psu.edu

Tufts University
www.tufts.edu

University of California
www.universityofcalifornia.edu

Medicine in the Era of Systems Biology and Bioinformatics

Another booming area is systems medicine. Clinical applications are limited today, but leaders in the field believe that radical changes are coming to health care and medical research. Hlatky of Tufts predicts that progress in analyzing physiological networks, integrating data from multiple levels, and monitoring biological changes over time will have a major impact. Future physicians, take note. "We'll pay more attention to all the parts, and recognize connections between different medical disciplines, like cancer and cardiology," she says. "Medicine will become more of what it is supposed to be, an integrated treatment of the individual." Hlatky says that stem cell biology is another area where a systems approach has strong potential, because of the complexity of the cells, and their impact on everything from neurological diseases, to chronic conditions, to regenerative medicine.

Systems medicine will also create job opportunities in bioinformatics. Thornton says, "In the future, we'll need people at the interface of databases and clinical trials, people who can handle all that computational work. Those data will be used in many different ways, to identify and measure interactions, and to determine concentrations. We need to develop computational tools for handling those data, including the variants."

At a more personalized level, **Lee Hood,** founder of the Institute for Systems Biology in Seattle, put forward his vision of the future of diagnosis in a recent talk. He described "an annual wellness assessment by blood prick that will analyze 2,500 protein biomarkers, for an organ-by-organ report on an individual's health status." Accumulation of individual data points over time will make every person a little longitudinal study, and "every patient will be his or her own control." To make this happen, scientists need to advance nanotechnology and imaging technology, and to create new computational tools. For those interested in business-oriented careers, Hood predicts "an explosion in health care companies, as emphasis shifts from disease to wellness."

Penn State's Schuster has a different angle on how systems biology researchers and bioinformaticians will contribute to human health and welfare. "Changes to the environment will affect flora, fauna, microenvironments, and may have geologic aspects. This will shift patterns of pathogens, and changes in pathogens will impact human populations and food supplies. This will carry over to human health and the stability of societies." Awareness of how environmental changes affect health and society is growing, providing research opportunities for systems biologists. "I believe funding cycles for environmental projects are on the upswing," he says.

Seeing the Big Picture

To find other areas of expansion in systems biology and bioinformatics, you don't have to look very far. Analysis of the interactome, or how cell components interact with their neighbors, is "big in the field now" says Nielsen of Chalmers. "This will be especially challenging, because it is not a static thing. Protein A may act with Protein B, but that interaction depends on how we set up the experiments."

Tufts' Hlatky adds, "We need to take the multiscale, dynamic interactions among molecules, cells, and tissues and knit them together in a quantitative construct." Thornton of the EMBL-EBI also sees integrating different levels of information as the next step, particularly in processing, storing, and interpreting imaging data. "We're developing advanced imaging tools from the cellular, to the organ, and up to the whole organism level." These methods have to be automated, and the data they generate need to be processed, integrated, and analyzed. Thorton says, "The opportunities are clearly in understanding biology at all different scales, bridging information from molecules to cells to organs to the whole organism, and being able to bring all those aspects together, basically to interpret the entire genome at all levels."

The field needs researchers who are comfortable working with data from all these levels, and grand thinkers who can come up with unifying theories. Hlatky says the next goal is to find the overarching biological principles in systems data, the models that allow researchers to "explain and predict." In any case, there's no escaping the power of systems biology and bioinformatics. Echoing Nielsen's remark that systems methods and bioinformatics will become standard practice, Hlatky says, "It's how we do biology now."

Chris Tachibana is a science writer based in Seattle, USA, and Copenhagen, Denmark.

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