

## Computational and Systems Biology Initiative

MIT's Computational and Systems Biology Initiative (CSBi) is a campus-wide education and research program that links biologists, computer scientists, and engineers in a multidisciplinary approach to the systematic analysis of complex biological phenomena. CSBi places equal emphasis on computational and experimental methods and on molecular and systems views of biological function. Multi-investigator research in CSBi is supported through a sophisticated research infrastructure, the CSBi Technology Platform.

From its inception, CSBi has developed and coordinated activities in the nascent computational and systems biology (CSB) field by facilitating interaction at the interface of life science, engineering, and computation; building the CSBi Technology Platform; and launching programs in education and outreach. In the last year, CSBi has grown to over 90 faculty members, and now includes four large research projects, two new PhD programs, and a successful outreach program. In a shift from its startup phase, a new CSBi management structure has been installed to build on the existing resources. The director, Professor Paul Matsudaira (Whitehead Institute for Biomedical Research, Department of Biology, and Biological Engineering Division [BE]), chairs the CSBi Research Committee that oversees CSBi research and technology. The codirector, Professor Bruce Tidor (Department of Electrical Engineering and Computer Science [EECS] and BE) chairs the CSBi Education, Outreach, and Community Committee. The executive director, Dr. Lauren Linton, oversees administrative activities and fundraising. The Executive Committee consists of the heads of the Department of Biology, EECS, and BE; the deans of the Schools of Science and Engineering; and the vice president for research and associate provost. A group of stakeholders, including directors of linked centers and other leaders of other key activities, plays a strong advisory role. This structure provides for a broader representation of the CSBi community and will provide clear direction in this new phase of CSBi.

### Goals and Priorities

CSBi's mission is to advance research and education in the emerging field of systems biology and to pursue high-impact collaborations with companies engaged in biomedical and pharmaceutical research.

CSBi is currently active in five main areas:

- Multi-investigator research projects that integrate systematic experimentation and computational modeling
- Development of new technologies, particularly those involving microfabricated devices and sensors, for monitoring biological processes and manipulating biological systems
- Establishment of high-end instrumentation and computer facilities
- Creation of a new curriculum to educate the next generation of undergraduate and graduate students
- Outreach to a broad industrial and academic community interested in systems biology

The priorities for CSBi in 2006–2007 include:

- Developing new multi-investigator research initiatives in stem cell biology, infectious disease, and computational methods
- ensuring the continuing maintenance and support of current CSBi resources while continuing to meet the growing needs of the community
- Expanding and enhancing the CSB PhD program and securing a continuing source of funds for students entering the program
- Encouraging economically disadvantaged, minority, and female students to pursue careers at the biology-engineering interface
- Strengthening ties with research entities at MIT and in the Boston area

## Research

The overall goal of CSBi is to foster links among biology, engineering, and computer science, and to create interdisciplinary, multi-investigator teams to undertake the systematic analysis of complex biological phenomena. CSBi places equal emphasis on computational and experimental research and on molecular and systems-level views of biological function. CSBi retains a fundamental commitment to an academic tradition placing graduate students and postdoctoral fellows at the forefront of scientific inquiry. CSBi recognizes that significant research advances in this emerging cross-disciplinary field will come from integrating concepts, technologies, and tools from different disciplines. With this in mind, CSBi fosters the development and integration of multidisciplinary teams and sophisticated technologies to approaching problems at the frontiers of biomedical research. Cross-disciplinary research will also provide new concepts, technologies, and tools developed through studying biological systems that will have important applications in engineering and computer science.

CSBi currently has four large-scale research programs:

- The National Institutes of Health (NIH)-funded Center of Excellence program in Cell Decision Processes (CDP), under the direction of Professor Peter Sorger (Biology and BE), wrapped up its third year with a retreat of 80 researchers from 15 centers, labs, and groups across the Institute. The CDP project is aimed at developing computational models of cell decision processes in human cells.
- The NIH-funded MIT Integrative Cancer Biology Program (ICBP) completed its second year as a multi-investigator and cross-disciplinary research program focused on understanding cancer biology. The ICBP is based in the Center for Cancer Research (CCR) and links CCR's research on cancer biology with CSBi's emphasis on biological modeling and data systematics.
- The goal of the Tissue Systems Biology project of the Singapore-MIT Alliance (SMA) Computational and Systems Biology Program is to take a systematic and quantitative approach to studying problems in tissue biology, including stem cell differentiation, tissue morphogenesis and physiology, and tissue-based disease models. Funded by SMA, this multi-investigator and Pan-Pacific collaboration also emphasizes the development of advanced technologies to address complex problems in biology, including new imaging and image informatics technologies, biological/chemical probes, and computational tools.

- The Synthetic Biology research project is dedicated to developing the design and fabrication tools required to design and operate novel devices built from biological components (MIT's Registry of Standard Biological Parts). These devices will include intracellular sensors of cell physiology and biology-based logic circuits. The program also is taking a close look at the risks and benefits of this emerging technology through a study funded by the Alfred P. Sloan Foundation.

## Technology Development

The goal of the CSBi Technology Platform is to develop state-of-the-art technologies for systems biology research and to make them available to the research community at MIT. CSBi research scientists facilitate the development of technologies that are useful for the community and provide expertise to advance systems biology research. Successful high-end research platforms have been established, including microarray and bioinformatics (BioMicro Center), high-end computing and data storage (BioMicro and MIT-Whitehead BioImaging Center), automated high-content imaging (MIT-Whitehead BioImaging Center), advanced imaging (CCR and MIT-Whitehead BioImaging Center), and biophysics (Biophysics), and user groups have been established in high-performance computing and microarray analysis. CSBi is continuing to forge new corporate partnerships in technology development in an effort to continue to provide the latest technology to the MIT community.

## Education, Outreach, and Community Building

### Education

The CSB PhD program is an Institute-wide program jointly developed by the Department of Biology, EECS, and BE. The program is a first of its kind in the US and focuses on foundational material from computer science and engineering and its application to complex processes in biology. The program integrates biology, engineering, and computation to address complex problems in biological systems, and CSB PhD students have the opportunity to work with CSBi faculty from across the Institute. Additionally, in July 2005 CSBi was awarded a large research and education grant by SMA. The CSB/SMA PhD program is a specialized track of the CSB PhD program emphasizing tissue/stem cell biology using advanced imaging and computational technologies.

The Merck/CSBi fellowship program awarded two postdoctoral fellowships in 2006–2007 and two graduate fellowships from two academic units in the schools of Science and Engineering. In addition, CSBi supports the Intercollegiate Genetically Engineered Machine (iGEM) Competition sponsored by the MIT Synthetic Biology Working Group and Microsoft's iCampus program. The iGEM program provides a new opportunity to engage students from different backgrounds, such as engineering and physics, in thinking about biological systems. CSBi research scientists continue to coordinate and teach short courses and workshops for the CSBi community as well as hosting visiting students and faculty.

## Outreach

CSBi believes that open access to new ideas and data is essential to advancing research and training in systems biology. Programs are created to ensure the efficient dissemination of scientific tools, information, and educational material generated by CSBi activities. CSBi sponsored and hosted its Annual Symposium in Systems Biology at MIT on January 13, 2006. The CSBi symposium, “Systems Biology of the Stem Cell,” featured prominent speakers from MIT and other academic institutions in the US and abroad to address critical problems at the interface of stem cells and systems biology. It was attended by over 450 researchers from around the world.

CSBi received over 30 applications for the four slots available in the 2006 summer internship research program. The 2005 interns conducted supervised research in the labs of the CSBi Technology Platform in areas of imaging, proteomics, RNAi, technologies, and synthetic biology. The students also participated in the weekly lecture series given by MIT and CSBi faculty and the CSBi research scientists.

In addition to undergraduate programs, CSBi has a six-month sabbatical program for faculty at institutions serving significant numbers of economically disadvantaged and underrepresented minority students. In 2005–2006, Dr. Elba Serrano from New Mexico State University joined CSBi under the Visiting Faculty program.

At the high school level, CSBi was a coordinator and sponsor of the Women’s Technology Program (WTP) in 2006. This four-week summer program in EECS introduces high school girls in their junior year to fundamental topics in engineering through hands-on projects, guest speakers, and lab tours. The program included a unit on systems biology that included talks presented by CSBi faculty and tours of CSBi facilities. Program participants had an opportunity to see the wide range of activities open to graduates of programs focusing in engineering.

## Visiting Faculty

CSBi coordinated the visit of Dr. Elba Serrano in 2005–2006 through the CSBi/CDP Visiting Faculty program. Dr. Serrano was joined by several students and one postdoctoral fellow during the year and was able to start microarray and imaging projects to complement the studies that are continuing at her home institution of New Mexico State University. In addition, CSBi is in discussions with other minority faculty to develop future summer sabbatical visits.

## Community Building

As a followup activity to the visit of Carlos Rios Velazquez last summer, CSBi participated in a conference hosted by CoHemis, a hemispheric organization that promotes education, research and technology development. CSBi director Paul Matsudaira and codirector Bruce Tidor gave presentations on CSBi and MIT’s dedication to interdisciplinary research and education while research scientist James Evans presented his work in imaging technology development. In October 2006, CSBi will sponsor two sessions at the annual conference of the Society for Advancement of Chicanos and Native Americans in Science (SACNAS) in Tampa. Sabbatical visitor

Elba Serrano, together with MIT faculty, students, postdocs, and staff, will host a track entitled “Multidisciplinary Approaches to Biological and Computational Systems Research” and will lead a professional development workshop in bioinformatic tools for systems biology.

### **Finances and Funding**

In addition to continuing support from a large federal grant awarded to the Cell Decision Processes (CDP) Center in 2003 (\$16 million over a five-year period) and the CCR Integrative Cancer Biology Program NIH Roadmap Initiative Grant (\$14 million over a five-year period) in 2005, CSBi was awarded a \$4.25 million grant from an anonymous foundation for the CSBi Technology Platform and \$2 million for the Merck-CSBi fellowship program in systems biology in 2003. The SMA Computational and Systems Biology Program awarded in July 2005 (\$10 million over an eight-year period) will provide support to the CSBi PhD program and research in tissue systems biology. An NCI Collaborative agreement (awarded in January 2006) supports research projects for Professors Steve Tannenbaum and Forest White. Collaboration initiated in 2006 between Merck, the Whitehead Institute, and MIT supports research projects for Professors David Sabatini and Barbara Imperiali.

In addition, through CSBi support, the research platforms have been successful in building and growing their instrumentation through NIH- and National Science Foundation-funded instrumentation programs. In April 2006 CSBi received two shared instrumentation grants (\$400,000 from NIH and \$300,000 from NSF) to support the BioImaging Facility. These research and instrumentation programs will collectively support a large proportion of the CSBi research, education, and outreach activities. EECS and CSBi were also honored to receive endowment support from an MIT alumnus for a new career development chair.

### **Future Directions**

To build on CSBi’s current success in the formation of new multi-investigator cross-disciplinary research programs, CSBi will continue fundraising activities to provide sustainable mechanisms of nonprofit and for-profit sector support. CSBi will also seek to initiate research collaborations with new industry partners as well as expand successful ongoing industrial research collaborations (such as with Merck) to provide opportunities for crucial peer-to-peer collaboration with industry. Lastly, the value of CSBi outreach programs as well as graduate and postdoctoral fellowship programs is essential to the CSBi mission, and the further development of these programs will be explored.

**Paul Matsudaira, Director and Professor of Biology and Biological Engineering**

**Bruce Tidor, Codirector and Professor of Biological Engineering and Computer Science**

*More information about the Computational and Systems Biology Initiative can be found at <http://csbi.mit.edu/>.*