

Computational and Systems Biology Initiative

The MIT 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.

At its inception, the initiative was to develop and coordinate activities in the nascent computational and systems biology fields by building the CSBi Technology Platforms and programs in education and outreach. In the last year, CSBi has grown to over 90 faculty, and now includes three large research grants, two new PhD programs, and a successful outreach program. In a shift from its start-up phase, a new CSBi management structure has been installed to build on the existing resources. The new director, Professor Paul Matsudaira (Whitehead Institute, MIT Division of Biological Engineering [BE]), will chair the CSBi Research Committee that oversees CSBi research and technology. Professor Bruce Tidor (Department of Electrical Engineering and Computer Science [EECS] and BE), CSBi codirector, chairs the CSBi Education, Outreach and Community Committee. The Executive Committee consists of the heads of the departments of Biology, Electrical Engineering and Computer Science, and of the Biological Engineering Division; the deans of the schools of Science and Engineering; and the vice president for research and associate provost. This new management structure provides for a broader representation of the CSBi community through the two committees 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
- 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 include the following:

- Ensure 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 first-year students entering the program
- Launching a new CSBi research initiative, *Systems Biology of Stem Cells*, at the 4th Annual CSBi Symposium
- Encouraging economically disadvantaged, minority, and female students to consider careers at the biology-engineering interface.
- Strengthening ties with research entities at MIT and in the Boston area, including the Broad Institute, the Bauer Center for Genomics Research, and the Department of Systems Biology at Harvard Medical School

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. At the same time, CSBi recognizes the increasing dependence of biological research on multidisciplinary teams and sophisticated technologies.

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 second 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 first 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 study 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 will also emphasize 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 has employed seven research scientists in 2004–2005 to facilitate the development of technologies that are useful for the community and who are providing expertise to advance systems biology research. Successful high-end research platforms have been established, including microarray and bioinformatics (BioMicro), high-end computing and data storage (BioMicro and BioImaging), automated high-content imaging (BioImaging), advanced imaging (BioImaging), biophysics (Biophysics), and user groups have been established in high-performance computing and microarray analysis. CSBi held its first community-wide meetings to discuss the computing needs of its very large and diverse membership. These are first important steps in developing resources that are well maintained and sustainable in the long term. 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 that was jointly developed by the Department of Biology, the Department of Electrical Engineering and Computer Science, and the Biological Engineering Division. The program is a first of its kind in the U.S. and focuses on foundational material from computer science and engineering and its application to complex programs 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. In November 2004, 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 first class of students matriculates in Singapore in summer 2005 and will be in residence at MIT in spring 2006.

The Merck-CSBi fellowship program awarded four postdoctoral fellowships in 2004–2005, from four 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. Specific programs are being put in place 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 January 13–14, 2005. In addition, CSBi is organizing the 6th International Conference on Systems Biology, to be held in Boston October 19–22, 2005, in collaboration with the Broad Institute and Harvard's Bauer Center and Systems Biology Department.

CSBi received over 30 applications for the six student slots available in the 2004 summer internship research program. The 2004 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. Of the six students who participated in the 2004 program, four applied to MIT for graduate school; all four students were accepted and three chose to attend MIT beginning this fall.

In addition to undergraduate programs, CSBi has a six-month sabbatical for faculty at institutions serving significant numbers of economically disadvantaged and underrepresented minority students. In June 2005, Professor Carlos Ríos Velázquez from the University of Puerto Rico joined CSBi for the summer. At the high school level, CSBi sponsored the Women's Technology Program (WTP) in 2005. This four-week summer program in EECS introduces high school girls in their junior year to fundamental topics in electrical engineering and computer science through hands-on projects, guest speakers, and lab tours.

Community Building

In November 2004, the CSBi Graduate Education Committee launched the first in a series of presentations designed to highlight CSBi research activities for graduate students and postdocs throughout MIT. This event featured short oral and poster presentations by a broad range of engineering and science faculty, students, and postdocs. The goal of the event was to expose the new PhD students and researchers in the CSBi community to the breadth of systems biology research at MIT. Student-focused CSBi community events offer an excellent framework to catalyze collaborations among synergistic but heretofore disparate groups of investigators at MIT.

Finances and Funding

CSBi was successful in adding two new funding sources in 2004–2005, in addition to significant continuing support from a large federal grant awarded to the Cell Decision Processes (CDP) Center. With the addition of the CCR ICBP (\$14 million over a five-year period) NIH Roadmap Initiative grant to the current CDP center (\$16 million over a five-year period) grant, MIT becomes the only institution with multiple Roadmap grants. The CSB PhD program is also supported by an NIH Roadmap Initiative training grant. In addition, 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. The recently awarded SMA Computational and Systems Biology Program (\$10 million over an eight-year period) will provide support to the CSBi PhD program and research in tissue systems biology. EECS and CSBi were also honored to receive endowment support from an MIT alumnus for a new career development chair. 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. These research and instrumentation programs will collectively support a large proportion of the CSBi research, education, and outreach activities.

Future Directions

To build on CSBi's current success in the formation of new multi-investigator cross-disciplinary research programs, CSBi will launch the Systems Biology of Stem Cells initiative at the 2006 CSBi Symposium in January. By striving for the ambitious goal of understanding the embryonic stem cell, CSBi will join with other Boston institutions to expand the technologies and tools to understand complex biological systems and build predictive models that will have a biomedical impact. In addition, the CSBi is seeking to grow its research base with industry (Merck and Novartis) and universities (Imperial College, UK) through multi-investigator, peer-to-peer research collaborations.

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