

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.

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; by building the CSBi Technology Platform; and by launching programs in education and outreach. CSBi has grown to more than 90 faculty and now includes five large research projects, two PhD programs, and a successful outreach program.

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 micro-fabricated 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 2009 include the following:

- 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 approach 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 five large-scale research programs:

- The five-year Singapore-MIT Alliance for Research and Technology (SMART) program for infectious disease was funded in 2007. The program includes eight MIT faculty members and is led by Professor Jianzhu Chen. Research will take place in Singapore at the SMART Center as well as MIT, and it will foster collaborations between MIT faculty and Singapore faculty.
- The Center of Excellence program in cell decision processes (CDP), funded by the National Institutes of Health (NIH), is aimed at developing computational models of CDP in human cells.
- The NIH-funded MIT Integrative Cancer Biology Program (ICBP) completed its fourth year as a multi-investigator and cross-disciplinary research program focused on understanding cancer biology. ICBP is based in the Koch Institute for Integrative Cancer Research and links the Koch'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 create 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 (Koch 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

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 (EECS), and the Department of Biological Engineering (BE). The program is a first of its kind in the United States 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.

The successful Merck-CSBi fellowship program has been renewed for an additional four years through 2012. In the 2007–2008 year of the program, the two postdoctoral fellowships and two graduate fellowships from two academic units in the schools of Science and Engineering were awarded. 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.

Finances and Funding

In addition to driving the creation of the Cell Decision Processes Center in 2003 (\$16 million over a five-year period), and the Koch Institute's ICBP (\$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. In 2007, the Merck-CSBi fellowship program was renewed with a grant of \$1.5 million over three years.

The SMA Computational and Systems Biology Program, established in July 2005 (with an award of \$10 million over an eight-year period), provides support to the CSBi PhD program and research in tissue systems biology. The SMART-funded Infectious Disease Program (awarded in July 2007) will support research in infectious diseases. A National Cancer Institute collaborative agreement (awarded in January 2006) supports research projects for professors Steve Tannenbaum and Forest White. A collaboration initiated in 2006 among 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 instrumentation programs funded by NIH and the National Science Foundation (NSF). 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 CSBi's 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 its current success in the formation of new multi-investigator cross-disciplinary research programs, CSBi will continue to provide mechanisms of support for both the nonprofit and for-profit sectors. 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.

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