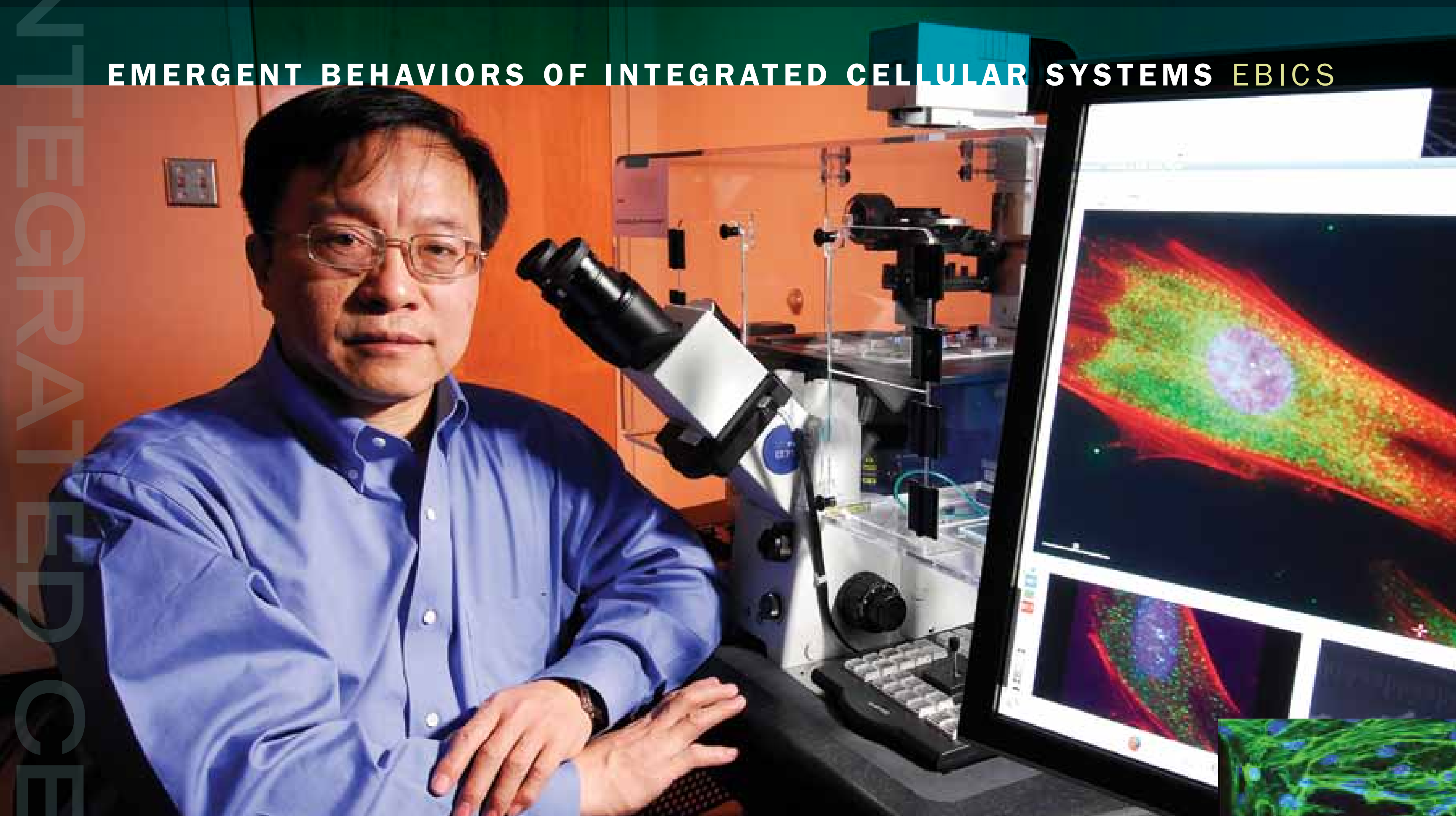
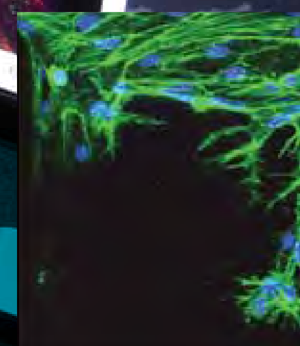




TOWARD BIOLOGICAL MACHINES

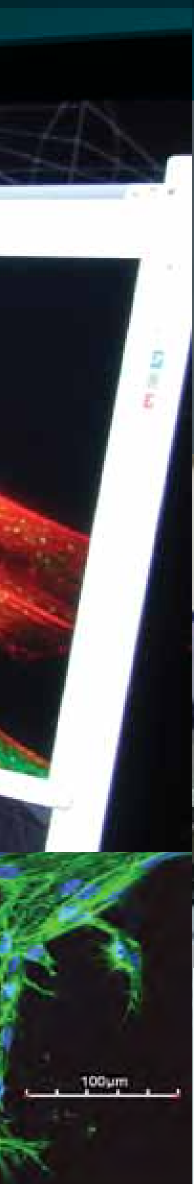
The mission of the center for Emergent Behaviors of Integrated Cellular Systems, or EBICS, is to create a new scientific discipline for building living, multicellular machines that can be applied to solving problems in health, security, and the environment.

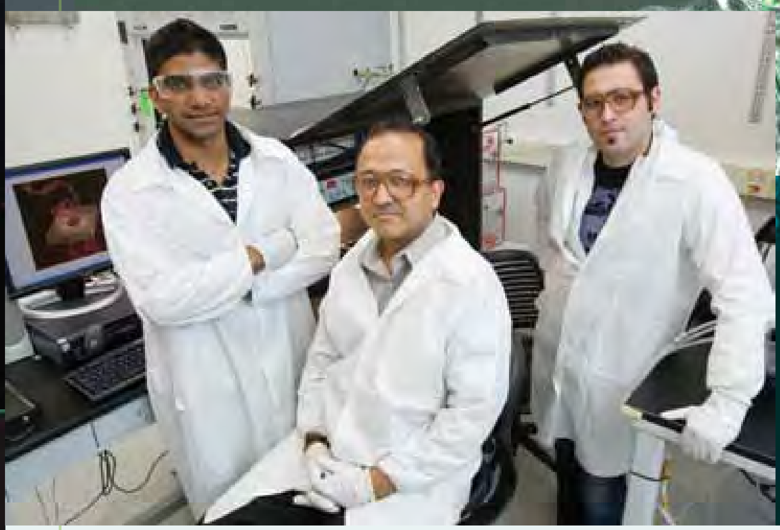
EBICS brings together scientists and engineers from the Massachusetts Institute of Technology, the Georgia Institute of Technology, the University of Illinois at Urbana-Champaign (UIUC), and seven other institutions to focus on developing biomachines that ultimately could, for example, clean up toxins in the environment or deliver life-saving therapies in the clinical setting. The center is led by professor Roger D. Kamm of MIT.

Center researchers are pursuing an array of programs to move this nascent field forward and provide educational opportunities to students."To effectively carry out EBICS-STC's mission, we need not only to produce innovative research results and develop new technologies, but also to train the next generation of research and education leaders," notes Kamm and members of the leadership team Robert M. Nerem, and K. Jimmy Hsia in the November 2010 issue of the journal *Mechanical Engineering.*

"The leaders of this new field should be knowledgeable in engineering and physical sciences, and in biology," note the authors. "They should be not only competent in these scientific disciplines, but also familiar with other big-picture issues such as public policies, intellectual property and patent law, entrepreneurship, and ethics. They should possess strong communication skills and leadership qualities. Furthermore, the new generation of research and education leaders should be a diverse group including women and underrepresented minorities."

Pictured above: Gang Bao, EBICS researcher at the Georgia Institute of Technology.
Photo: Gary Meek, Georgia Tech





Rashid Bashir (center) is a professor of electrical and computer engineering and of bioengineering at the University of Illinois at Urbana-Champaign. He is flanked by graduate students Murali Venkatesan (left), and Sukru Yemenicioglu (right). *Photo: L. Brian Stauffer, ScienceDaily.*

Ron Weiss of MIT

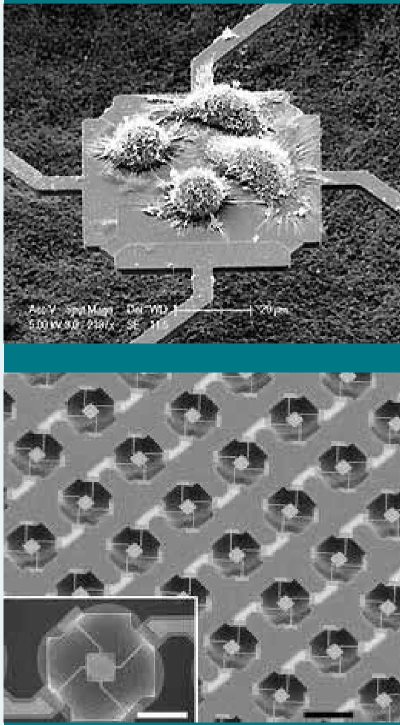
BIOBOTS ON THE MOVE

"I became fascinated about 15 years ago with the notion that we could program cells," says Ron Weiss, a biological engineering professor at MIT. "I started getting into synthetic biology. I'm a computer scientist by training, so I like to program stuff," he laughs. "I think biology is now the coolest thing that you can program, so that's my particular interest."

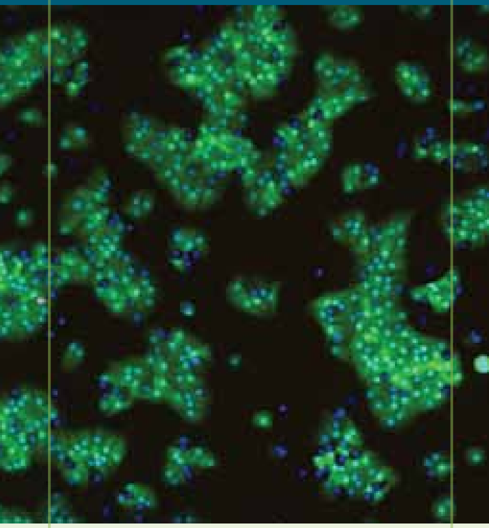
Weiss co-leads an EBICS research project with UIUC researcher Rashid Bashir working on so-called "biobots"–biological "robots" ultimately capable of moving, sensing, and carrying out actions of interest. These are assemblages made of groups of cells of different kinds, such as muscle cells to produce movement, cells to sense substances in the environment, and neurons to control the biobot's actions and motion. The long term goal is to develop biobots using muscle cells and neurons that can achieve net motion towards a chemical toxin and subsequently release chemicals to neutralize the toxins.

It's a field in its infancy: scientists currently are working on the most fundamental strategies for assembling the basic building blocks that would make up such biological machines. Weiss, Bashir and colleagues have outlined an ambitious 10-year plan to develop biobots of increasingly greater sophistication and capabilities.

They envision four basic levels. "The first would be what we're calling flapbot; it would just flap muscle cantilevers or muscle-actuated cantilevers. It would move around in one direction," Weiss explains. "Stopbot would move until its neuronal sensors detected a particular analyte–could be a toxin or other chemical in the environment--and then it would stop. Even if the analyte went away, it would still be stopped." In contrast, something at least for now he's calling "scaredy-bot" would move around randomly, and then when it sensed a toxin, it would move away forever in a particular direction. A "follow-bot" would move up a gradient toward increasing concentrations of a substance in the environment, such as a pheromone, a chemical substance produced by an animal, often as an attractant. □



Microsensors can measure cell mass like tiny scales.
Bottom: A scanning electron microscope image of a microsensor array. Inset: an individual sensor. Courtesy of Rashid Bashir. *Photos: www.pnas.org/cgi/doi/10.1073/pnas.1011365107*



Pancreatic beta cells.
Photo: Richard Lee

CELLULAR MACHINES FOR GLUCOSE BIOSENSING AND INSULIN RELEASE

EBICS researcher Richard Lee and colleagues are developing a cell-based system for monitoring glucose levels. The project targets "a big clinical problem that's been unsolved for a long time," says Lee, a Harvard professor of medicine in Cambridge, Mass.

"We have this problem in glucose monitoring," Lee explains. "A person with type I diabetes that's hard to control has very little insulin, and the reason that you can't give them enough insulin to keep their glucose in a normal range is because they'll have periods of hypoglycemia–low blood sugar. It's actually the high blood sugar levels that cause the organ damage, like to the eyes and kidneys–but it's the low blood levels that prevent you from giving enough insulin to prevent the high levels. So if we had ways of continuously monitoring glucose--particularly for the low blood sugar levels–we would be able to be more aggressive with insulin."

The strategy in this EBICS project is to take some of the patient's own cells, and make them able to sense and report out the glucose level. A small wearable device about the size of a large earring or a wristwatch would pick up that signal. In turn, the wristwatch would wirelessly transmit that information to an insulin pump, an existing technology in routine clinical use. Insulin pumps usually are worn on the belt, and a small needle near the belt administers the insulin.

"If one could actually monitor glucose incredibly accurately and in near-continuous fashion, one could get nearly perfect glucose levels in these patients," notes Lee. "That part has been proven. In effect, a big advance in Type I diabetes therapy is figuring out how to do the monitoring."

Researchers from a half dozen labs have participated in the work, both within and outside of the STC. "This has been an interesting experience because it's a real team effort," says Lee. "The funding from NSF is a small fraction of the project, but we were able to interest other labs because they were so excited about it. This is not just a 'cool' science project--this is a real life issue, and to remind myself of what patients are doing, I keep a glucose monitor on my desk and prick my finger to make a measurement a few times a week. For us, this is taking a bioengineering concept and putting it into an 'every minute counts' situation."

Pictured opposite right: Andres Garcia (right) and a student. *Photo: Georgia Tech*

Georgia Tech researcher Manu Platt. *Photo: Rob Felt, Georgia Tech*

> **"By emergent behavior we mean the characteristics and self assembly that occurs naturally for a population of cells due to their microenvironment and genetic programming–an order, structure, and complexity that arises due to the cues provided. Through the research of EBICS, our goal is to understand how this occurs and how we might control these processes so as to use this in the creation of biological machines."**
>
> — **ROBERT NEREM, EBICS Associate Director**
> **Parker H. Petit Distinguished Chair for Engineering in Medicine and Institute Professor Emeritus, Georgia Institute of Technology**

EDUCATIONAL PROGRAMS AT EBICS PREPARE STUDENTS FOR RESEARCH ON CELLULAR SYSTEMS

Graduate Teaching Consortium

In Fall 2011, EBICS launched its first full-scale Graduate Teaching Consortium (GTC) courses exploring the field of engineered biological systems. The classes are Internet-based and include asynchronous and synchronous lectures, live Q & A sessions, and discussion forums.

One of the offerings, entitled “Cell as a Machine,” was taught by professor Michael Sheetz of Columbia University and Hanry Yu of the National University of Singapore. The other, on “Principles of Synthetic Biology,” was taught by professors Ron Weiss of MIT and Adam Arkin of the University of California-Berkeley.

“The exciting thing about the Graduate Teaching Consortium is that it creates the opportunity for students at a fairly wide array of universities to have access to cutting-edge content taught by the leading researchers in the field around the new biology,” says Lizanne DeStefano, EBICS education co-director located at University of Illinois at Urbana - Champaign.

“Our students gain an advantage through the Graduate Teaching Consortium because they’re getting a course from the person in the field who’s doing the leading work in that area. And for our students at our minority serving institutions, we find that it really enhances the level of graduate coursework that they’re able to take, because they may not have people at their university who are doing work on that particular topic.”

In Their Own Words...

“As one can imagine, whenever the issue of creating living systems with new functionalities is raised, caution must be exercised. Indeed, a number of ethical issues will need to be addressed. Will these machines be endowed with the capability to self-repair, adapt, and self-replicate? If so, they become indistinguishable from natural organisms and need to be considered in a similar light. If stem cells are used, from what source may they be taken? What protections and regulations need to be in place? These and many other questions will be openly debated within EBICS and with the larger community in parallel with the development of advancing technologies.”

— **ROGER D. KAMM, ROBERT M. NEREM, AND K. JIMMY HSIA**
in “Cells into Systems,” *Mechanical Engineering,* November 2010
http://memagazine.asme.org/Articles/2010/November/Cells_Into_Systems.cfm

Roger Kamm

INTEGRATED CELLULAR SYSTEMS