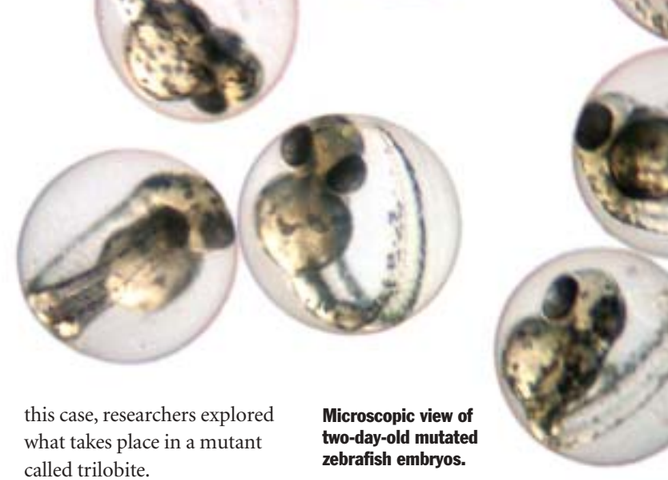
# Bright Ideas

**"It's something like a mob** *transforming into an army.*" —LILIANNA SOLNICA-KREZEL



Microscopic view of two-day-old mutated zebrafish embryos.

## Decentralization May Prove Key to Smart Structures

1. A NEW APPROACH may finally make "smart structures" practical.

The early promise of smart structures—equipping spacecraft, aircraft, automobiles and ships with networks of sensors and actuators that allow them to respond actively to changing environmental forces—was that they would revolutionize design, construction and performance. That promise never materialized. When such networks grew beyond a modest size of about 100 nodes, they became too complex for central computers to handle. In addition, the weight, power consumption and cost quickly became prohibitive. In other words, they could not be scaled up to large sizes.

Today, however, recent advances in MEMS (microelectromechanical systems) and distributed computing appear to be overcoming these limitations, reports Kenneth Frampton, assistant professor of mechanical engineering at Vanderbilt. Frampton, an expert in vibration and acoustics, and colleagues Akos Ledeczi, research assistant professor; Gabor Karsai, associate professor; and Gautam Biswas, associate professor—all from the Vanderbilt Department of Electrical Engineering and Computer Science—have designed embedded systems using a smart vibration-reduction system for a 15-foot-long rocket payload faring.

The high noise and vibration levels inside rockets when they are launched increases the cost of manufacturing satellites and other equipment boosted into space. So a system that reduces these levels by even a small amount would cut payload development costs substantially.

In the first phase of the project, Frampton's group prepared and ran a detailed computer simulation of the system that showed it should provide a degree of vibration reduction comparable to that of a centrally controlled smart system.

"The most important result of the simulation is that it shows that the embedded system is scalable," says Frampton. "That means we should be able to build it as big as we need to and it should continue to function."

In the older approach, all the sensors and actuators are connected to a central computer. It receives information from all the sensors, processes it, and then sends instructions to all the actuators on how they should respond. As the size of the structure and the number of sensors and actuators increase, the amount of wiring required increases. Difference in arrival times of information from the nearest and farthest sensors also increases, as does the time it takes the farthest sensors to receive their orders.

In an embedded system, on the other hand, each node contains a PC-strength microprocessor with a relatively simple program and modest amount of memory that allows it to directly control the sensors and actuators wired to its node. The microprocessor also communicates with its nearest neighbors so they can work together. Depending on how the system is set up, the processor also receives data from a certain number of its nearest neighbors so it can coordinate the actions of its actuators. Although each processor has less capability than that of a central computer, it has far less information to handle, and its workload does not increase as the system gets bigger.

"Embedded systems are also far more 'fault tolerant' than centrally controlled systems," Frampton points out. If the central processor breaks down, the entire system shuts down. But a decentralized system will continue to work even when several microprocessors fail, although probably with slightly diminished capability.

The second step in Frampton's project is to put a 100-node system into an actual rocket faring comparable to the simulated system. Then he will test how well it performs in the laboratory. This information will allow engineers to estimate the system's performance and its weight and cost.

Kenneth Frampton

NEIL BRAKE

## Discovery May Shed Light on Cell Movement During Development

2. BIOLOGISTS AT Vanderbilt and the University of Missouri have uncovered what could be a major clue into mysterious molecular processes that direct cells to the correct locations within a developing embryo. Understanding the molecular basis of these processes and how they can go wrong could lead to treatments for birth defects such as spina bifida.

In the August issue of the journal *Nature Cell Biology*, researchers report the discovery that a single protein facilitates movements of cells within the developing embryo of the zebrafish.

This protein plays an essential role in directing cell migration within the spherical egg to the head-tail axis where the body is beginning to take shape. Researchers found that disruption of the same protein inhibits normal migration of nerve cells within the developing zebrafish brain, a type of motion found in human brain development.

"Very little is known about how neurons move from one place to another," says Lilianna Solnica-Krezel, associate professor of biological sciences at Vanderbilt, who led the study with Anand Chandrasekhar, assistant professor of biological sciences at the University of Missouri, Columbia. Solnica-Krezel's research team included graduate student Florence Marlow, and research associates Jason R. Jessen, Jacek Topczewski and Diane S. Sepich.

Lilianna Solnica-Krezel

NEIL BRAKE

Zebrafish have become important in studying development of vertebrates. Their eggs are transparent and develop outside the body, making them particularly easy to study. The zebrafish genome is currently being sequenced, which allows researchers to employ the powerful tools of genomics to unravel complex molecular processes involved in the development process. One of these methods is to examine the impact of specific mutations. In this case, researchers explored what takes place in a mutant called trilobite.

During development, cells begin converging from all sides of the spherical egg to the embryonic axis where the body begins to form. What begins as a disordered, chaotic motion changes into an orderly movement. Cells change from a round to an elongated, spindle shape. "It's something like a mob transforming into an army," says Solnica-Krezel.

Her research group discovered that trilobite mutations prevent the army from forming. Cell motions continue to be disordered and do not develop the same sense of direction and purpose in the mutant as in normal embryos. As a result, trilobites' development is stunted. Scientists determined that the mutations disrupt activity of a specific membrane protein, called either Strabismus or Van Gogh.

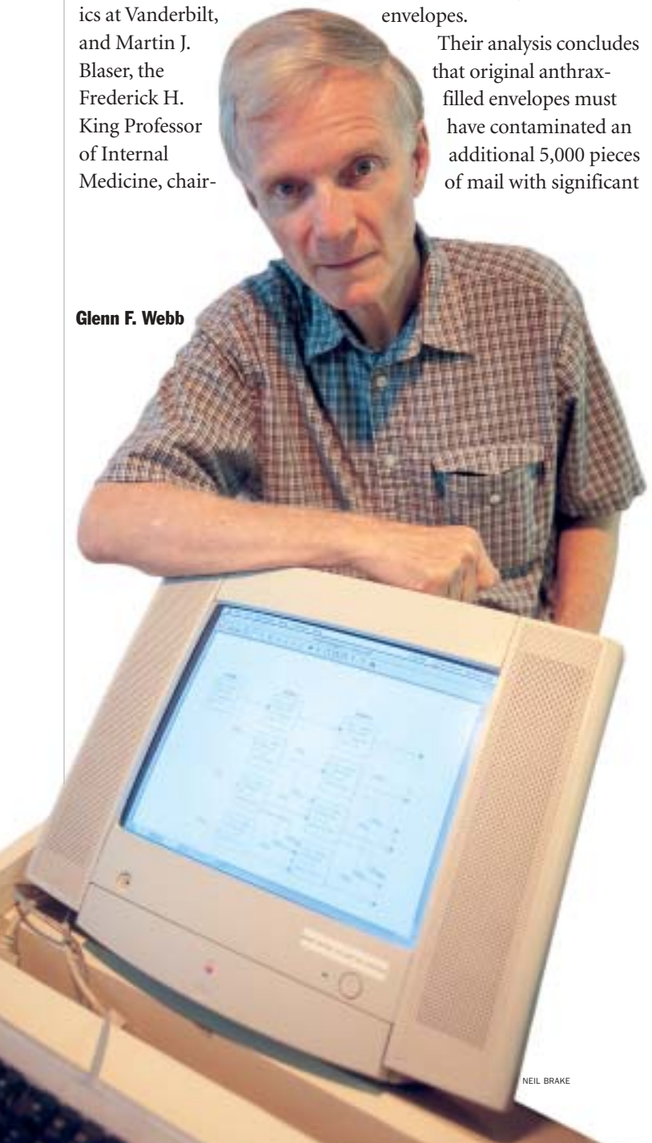
Somewhat later in zebrafish development, a number of motor neurons move from one part of the brain to another. "We don't understand why they move because they can form the connections they need from their original location," says Solnica-Krezel. But Chandrasekhar and his Missouri team discovered that this movement does not take place in trilobite embryos.

Researchers transplanted trilobite neurons into brains of normal embryos and normal neurons into trilobite brains. None of the normal motor neurons migrated when placed in a trilobite brain, whereas a third of the trilobite neurons migrated when placed in normal brains. Scientists concluded that the Strabismus/Van Gogh protein must have both cellular and extracellular effects.

The results of various tests suggest that the protein Strabismus/Van Gogh acts independently in mediating neuron movement. If this proves to be the case, then it provides an entry point to elucidate the molecular basis of this class of neuronal migration.

## Mathematician Tracks Anthrax Contamination

3. A MATHEMATICIAN at Vanderbilt and an expert in infectious diseases at the New York University School of Medicine have produced a mathematical model of how anthrax can be spread through the mail. The model was developed by Glenn F. Webb, professor of mathematics at Vanderbilt, and Martin J. Blaser, the Frederick H. King Professor of Internal Medicine, chairman of the department of medicine, and professor of microbiology at the NYU School of Medicine.



Glenn F. Webb

NEIL BRAKE

Their model, which appeared in the May 14 issue of *Proceedings of the National Academy of Sciences*, simulates the recent outbreak of mail-borne anthrax deaths in the United States and demonstrates that all known cases of infection can be explained by contamination spread through the mail from six original envelopes.

Their analysis concludes that original anthrax-filled envelopes must have contaminated an additional 5,000 pieces of mail with significant but much lower levels of anthrax spores in order to account for the two deaths that appear to have occurred from such cross-contamination. In the case of any future attacks of this type, the model provides a framework that can be used for the rapid identification and containment of any further outbreaks.

Blaser was tapped in the days following the Sept. 11 terrorist attacks to participate in a task force on bioterrorism. He began bouncing ideas off Webb, a longtime collaborator and friend. The two agreed to try to develop a mathematical model that adequately explains the basic facts of the fall outbreak based on cross-contamination. The model would not prove that contaminated letters caused all the cases, but it would demonstrate that the explanation is feasible, the scientists say. (The other hypothesis that has been proposed for the apparently unrelated deaths is that the victims were infected by anthrax spores carried downwind from contaminated postal facilities.)

Eighteen cases of anthrax infections have been reported since last October. Eleven were caused by inhalation of anthrax spores, and seven were caused by cutaneous (skin) contact. Five of the people who inhaled anthrax have died. The federal task force investigating the cases reports that four of the original letters have been recovered, and officials have stated that they believe at least two additional anthrax-laden letters passed through the postal system.

The mathematical model tracks contaminated letters through different "nodes" in the postal system. The first node is the point at which letters enter the system, either mailbox or post office. Then the letters move to local postal stations. From there they are transported to regional stations and back to local stations before delivery. Each node is assigned a different level of risk of spreading anthrax spores depending on how the letters are handled.

The scientists found that the model provides the best match for the fall outbreak when they assume that there were six original letters, each carrying trillions of anthrax spores. They calculate that these letters, although tightly sealed, contaminated about 5,000 other letters with much smaller numbers of spores, ranging from 10 to 10,000 apiece.

"Only one of the deaths was the recipient of an original letter," notes Webb. "The much greater danger is to postal workers and to the recipients of cross-contaminated letters. The threat is much greater than what people believed earlier."

If their model is correct, "the rapid and widespread usage of antibiotics among postal workers and persons in the immediate environment of the received original letters probably averted a substantial number of cases," Blaser and Webb write.

In the case of another mail-borne outbreak of anthrax, the model provides a framework that could help determine what is going on more rapidly than would otherwise be possible.

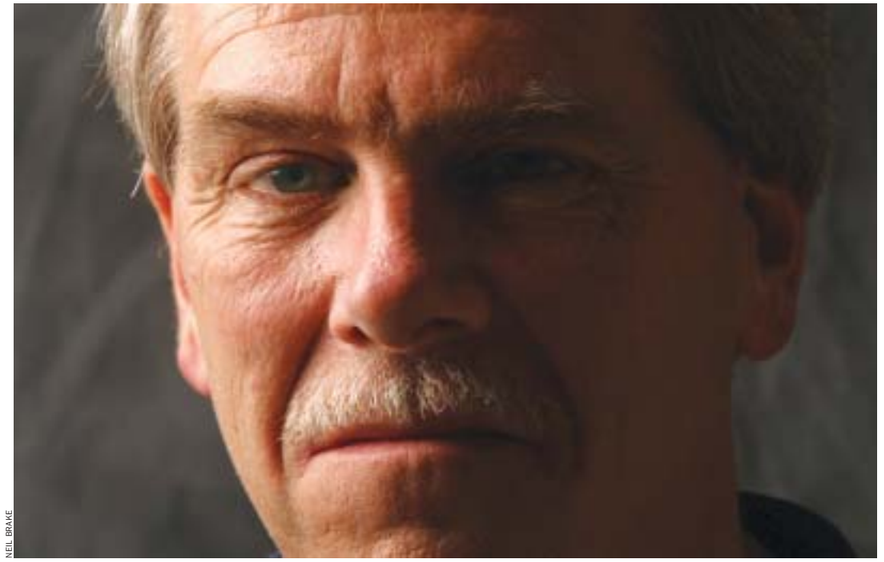
## Study Makes Case for Cognitive Therapy

4. A TYPE OF THERAPY that encourages severely depressed patients to challenge the judgments and misperceptions that underlie their condition can be as effective as medication over the long term.

That is the conclusion of a new study conducted by researchers at Vanderbilt University and the University of Pennsylvania comparing the relative effectiveness of cognitive therapy and medication for the long-term treatment of severe depression. The findings were discussed earlier this year at the annual conference of the American Psychiatric Association in Philadelphia.

Cognitive therapy was developed at Penn in the 1960s. Cognitive therapists lead patients to explore harmful ideas—such as "I'm a bad person and don't deserve to have any fun" or "I'll never get that job, so I won't even apply"—and encourage them to test the misperceptions that shape their negative feelings.

"In this study we looked at depression somewhat differently than prior studies," says Steven Hollon, professor of psychology at Vanderbilt, who co-directed the investigation with Robert DeRubeis, professor of psychology at Penn. "The question that has most often been asked in studies is, 'What gets people better faster?' We asked, 'What will keep depression away over the long term?'"



NEIL BRAKE

**Steven Hollon, professor of psychology at Vanderbilt, co-directed the investigation of cognitive therapy in severely depressed patients with Robert DeRubeis, professor of psychology at Penn.**

Compared to past research on more severely depressed patients—some depressed nearly enough to require hospitalization—Hollon and DeRubeis' study was unusually comprehensive in its size, 240 patients in Philadelphia and Nashville, and in its duration, 16 months. Other Vanderbilt researchers involved in the study include Richard Shelton, Ronald M. Solomon and Margaret L. Lovett of the Department of Psychiatry.

The study, funded by the National Institute of Mental Health and SmithKlineBeecham, involved a four-month period of acute treatment. Patients who responded to therapy then discontinued treatment, except for an occasional booster session. Those who responded to medications either continued to take meds or were withdrawn onto a placebo pill. The patients were then tracked for an additional year.

During the second phase of the study, 75 percent of patients who underwent cognitive therapy avoided a relapse, compared to 60 percent of patients who continued on medication and 19 percent of those withdrawn onto a placebo pill.

"Statistically, both cognitive therapy and medication were more effective than a placebo, and a brief course of cognitive therapy was better than a similarly brief course of medication in the yearlong continuation phase," DeRubeis says.

"These results suggest that even after termination, a brief course of cognitive therapy may offer enduring protection comparable to that provided by ongoing medication."

Hollon, DeRubeis and colleagues also found that cognitive therapy enjoys a long-term cost benefit compared to drugs. During the 16 months, treatment with medication cost an average of $2,590 compared with $2,250 for cognitive therapy. This gap grows with time, since antidepressants must be administered continually to be effective.

"Some proponents of medication for severely depressed patients have suggested that cognitive therapy is impractical on the basis of cost," DeRubeis says. "Our study indicates this isn't true, especially over the long term.

"This will be a surprising, controversial finding for many psychiatric professionals," he continues. "Most believe quite strongly in the efficacy of medication, and psychiatric treatment guidelines call unequivocally for medication in cases of severe depression."

*For more information on the stories in Bright Ideas, visit Vanderbilt's online research journal,* Exploration, *at http://exploration.vanderbilt.edu.*