News from Medicine

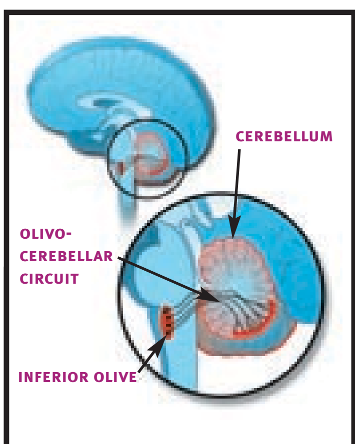
Robots on the Brain

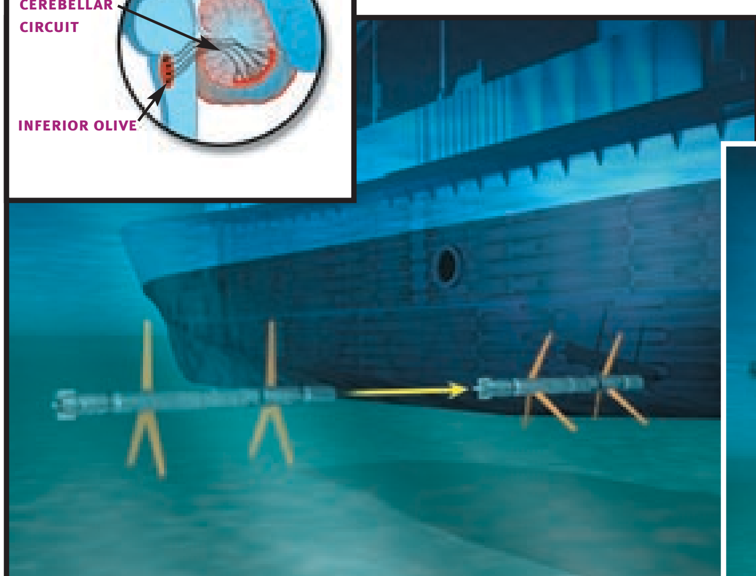
Computers are great for crunching large amounts of data, but when it comes to controlling robotic vehicles, they're surprisingly inept. Even the most advanced mobile robots are slow, clumsy, and unreliable. But this may soon change, thanks to a new type of control system inspired by a little-known component of the human brain called the olivo-cerebellar circuit. Rodolfo R. Llinás, M.D., Ph.D., the Thomas and Suzanne Murphy Professor of Neuroscience and Chairman of the Department of Physiology and Neuroscience, is working with scientists in Russia and the U.S. Navy to build electronic control systems for smart underwater robots—ones that can perform surveillance, rescue, and other high-risk maneuvers with agility and precision.

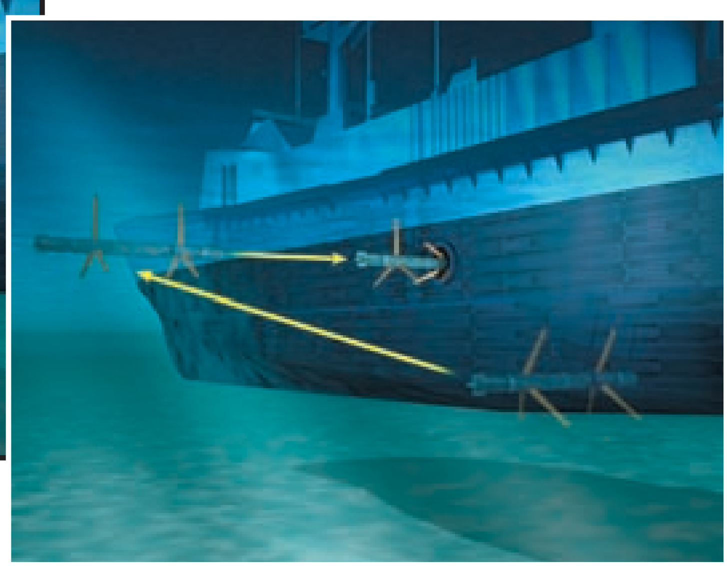
An expert on the cerebellum (the brain structure that helps to control movement and coordination), Dr. Llinás patterned this robot control system on the olivo-cerebellar circuit. That circuit—part of the inferior olive, a mass of neurons located near the cerebellum—directs the body's balance and limb movement. It performs so well, notes Dr. Llinás, that unlike many components of the brain, it has barely been tinkered with by nature for 400 million years of evolution. "All vertebrates have this circuit," he explains. "It embodies a very intelligent solution to motor coordination."

Dr. Llinás has been delving into this area of the brain for more than two decades. The cells of the inferior olive, he's learned, naturally generate oscillations, electrical waves with regular peaks and valleys. When signals for initiating movement reach the olive, clusters of nerve cells within it work in unison, producing large, coordinated electrical spikes instead of a jumble of separate electrical signals. The spikes are transmitted to the cerebellum and, ultimately, to the muscles. In turn, sensory input from the muscles is transmitted back to the cerebellum and then to the olive, allowing for the fine-tuning of movement. "It turns out that each cluster governs a set of muscles, and the clusters that are firing change as the muscles required for movement change," explains Dr. Llinás.

How Dr. Llinás' research led him to robotics is quite serendipitous: "My NYU colleagues Drs. Vladimir Makarenko and Mutsuyuki Sugimori and I felt that the only way to test the electrophysiological findings of the last 20 years about the olivo-cerebellar circuit







A new robotic control system developed with NYU researchers is based on the olivo-cerebellar circuit in the brain (left). This system gives an underwater robotic vehicle agility during such maneuvers as docking. When the robot first approaches the ship (bottom left), it is misaligned. The system enables the robot to automatically readjust position farther to the left, so it can dock with the ship (bottom right).

ILLUSTRATION © MATT ZANG

was to make a hardware model." The trio teamed up with Drs. Vladimir Nekorkin and Viktor Kazantsev at the Institute of Applied Physics of the Russian Academy of Sciences in Nizhni Novgorod, Russia, and the group commenced to build an artificial version of the biological circuit.

The project eventually caught the attention of the U.S. Office of Naval Research, which is seeking to build robots that can move with the dexterity and agility of animals and humans—a giant step beyond current robots, which slavishly follow instructions embedded in lines of computer code.

Dr. Llinás and his colleagues are now readying their artificial circuit for field tests at the Naval Undersea Warfare Center in Newport, R.I. Like the brain's olivo-cerebellar circuit, their control system is analog, which means it processes information as continuously varying signals, much like the electrical waves that carry information in the brain. Computers, by contrast, are digital; they store information discontinuously, in a series of switches that are either on or off—one or zero.

Analog controllers, Dr. Llinás notes, are simpler, more responsive, and more robust than digital ones. "In a computer, if even a single digit is dropped, the whole system may go down. With our analog controller, a good chunk of the system may be off and the robot will still work."

Dr. Llinás expects that analog controllers will have uses well beyond military applications. Smart robots could one day help disabled or paralyzed people with everyday tasks, such as dressing or eating. Says Dr. Llinás: "We are just beginning to scratch the surface of this technology." ■

— *By Gary Goldenberg*

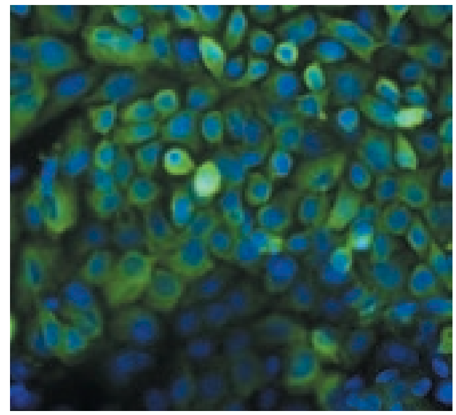
Proteins Move to Center Stage in Cancer Research

In the drama that is cancer, genes have long been thought to play a starring role and proteins only a bit part. But researchers at NYU are now bolstering the notion that in the development of cancer, proteins and genes share center stage.

Paul D. Walden, Ph.D., Associate Professor of Urology and Biochemistry, is among the scientists worldwide who are examining protein imbalances as potential culprits in the development of cancer. Genes provide the instructions for the creation of proteins, and it is these proteins that actually do most of the work inside cells. Dr. Walden's research suggests that some cancers might arise from an insufficient quantity of one or more particular proteins, rather than mutations in the genes that created these proteins.

Dr. Walden and his colleagues are focusing on a protein produced by a gene called BTG2, which is known to be involved in cell reproduction and DNA repair. As they reported in the October 2004 issue of the journal *Oncogene,* while there are no mutations in the BTG2 gene itself, they have found that the levels of its protein dropped dramatically in the early stages of breast cancer among women with no obvious predisposing factors.

Proteins are designed to exist for a finite period of time; once a protein has completed its job, it is dissolved by the cell's trash removal system. But the research team has found evidence that as a cell starts to become cancerous, it degrades BTG2 protein twice as fast as healthy cells do. With this protein gone, the cell begins to reproduce out of control. Previously, using a model of human prostate cancer in mice, the researchers reduced the growth and spread of prostate cancer cells by increasing the levels of BTG2 protein. Dr. Walden and his colleagues are now developing a mouse model in which the BTG2 gene has been removed, or knocked out, to better sort out how the protein functions in cells.



Healthy human prostate cells have high levels of the protein BTG2 (in blue).

PHOTOGRAPHY COURTESY OF PAUL D. WALDEN, PH.D.

Such changes in this and other proteins may soon be implicated in other cancers, says Dr. Walden, and could be a novel way of approaching cancer research, albeit not necessarily a simpler one. It's easier to find a mutation than to figure out how a cell suddenly starts to destroy selected proteins. The payoffs, however, could be great. Drugs that increase levels of BTG2 protein might even be used for tumor treatments. Additionally, the untimely exit of BTG2 and other proteins could someday provide an early warning sign of cancer. ■

— *By Fenella Saunders*