Networks of computers analyze how networks of nerves in your brain talk to each other

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Computational scientist Mark Hereld explains how he uses large systems of interconnected computers, called supercomputers, to analyze the electrical signals that nerve cells in your brain use to talk to one another. Behind him -- diagrams of the variables he adjusts and sample electroencephalography tests, which measure impulses between nerve cells in the brain.



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A diagnostic tool sits in a room, lights blinking. If it had a brain, it would be contemplating the immense puzzle of just how your brain works.

But it's not capable of human thought – it's just a machine.

And no, it's not an MRI machine, and it's not in a hospital. It probably wouldn't even fit in most operating rooms.

The place: Argonne National Laboratory. The instrument: Jazz. But it plays no music other than a gentle humming, just loud enough that those around it must raise their voices.

This is no musical instrument – it's a supercomputer.

The machine, installed in November 2002, was the first teraflop computer at Argonne's National Computer Leadership

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Facility on the lab site, about 25 miles southwest of Chicago. Teraflop is a measurement of the computer's speed – meaning it can perform a trillion multiplication problems in a second. Imagine how much easier that might have made high school calculus.

The machine functions on the precept of parallel computing – the idea that many small machines working together are vastly more efficient than either one small machine or one large machine. Jazz is comprised of 350 smaller computers, or nodes. Each node, if left running continuously for a year, could perform the calculations it would take a human 20 years to hammer out.

Computational scientist Mark Hereld and his colleagues create thousands of different simulations that enable them to look at thousands of nerve cells, or neurons. They have presented their work at many conferences, and most recently published two papers in the April 2007 Journal of Clinical Neurophysiology. But because of the many levels of nuance to the brain, the research continues, with no signs of letting up anytime soon.

This research looks at how impulses travel between nerve cells in the brain, which allows messages to be sent to muscles throughout the body. Understanding how this communication works could help doctors figure out how to prevent seizures in patients with epilepsy. This knowledge would also help doctors and pharmacists adjust medications and surgeries so they are more effective for patients. The implications would extend to better comprehension of a variety of neurological conditions, including Parkinson's and Alzheimer's diseases. HereId says he is fascinated by the mathematical puzzle that is the human brain.

"Healthy brains are quite mysterious. It's very interesting because some aspects of it are genetically engineered into place, common to everybody. At some level, there are places where wiring does not depend on 5 billion years of specific evolution, but is learned through a lifetime of the owner of the brain. The dividing line between those effects is interesting," says Hereld.

Because these changes are so complex, there is a vast amount of information that can't be seen with something as general as electroencephalography, otherwise known as an EEG, which measures electrical activity in the brain, Hereld says.

EEGs print out a map of the electrical activity in the brain, resulting in a set of wavy lines that look to the untrained eye like a child's drawing of waves on the beach.

An EEG measures impulses in the brain, but takes the measurement from the outside. For the test, minute electrical contacts are placed on a patient's head and electrical signals are measured at those particular places. Each sensor is measuring electrical potential transmitted from the surface of the brain.

But, Hereld says, this test is merely an average of the signals passing through millions and millions of cells in the brain. To reach electrical contacts, this average of signals must pass through bone and skin, extremely thick and dense materials, which can obscure the readings. When EEGs are used to look at the brain, Hereld and his team simply can't get the amount of detail they need, which is why creating neural models using a very powerful computer is necessary.

"It allows us to think about the problem in principle from the bottom all the way up to the top, to develop models that look at the genetic relationship of proteins, all the way up to computations that analyze an aggregation of signals, which can then be compared to an EEG," says Hereld.

Another reason neural modeling is essential is mathematicians' human brains simply don't have the capability to do the sheer number of calculations required to examine different scenarios, or to analyze the millions of cells in the brain. Simulations enable the computer to look at the intricate systems in the organ, and calculate what would happen if impulses started at different places in the neural system. This is important because, Hereld says, "[epilepsy] is a complicated disease, and it has ramifications at the molecular level. These molecules intercede and mediate electrical communication in the synapses," small gaps between brain cells.

While other researchers around the nation are modeling the brain, Hereld says his simulation has a greater level of detail. "Some simulations look at a simple model of the neuron, and see whether it fires a signal or it doesn't. We are able to look at where that signal goes, how it gets there, and what part of the neuron is affected."

But in the five years the simulation has been running, Hereld says his team has barely begun to make discoveries.

The simulation is designed to examine how neurons are connected. Distinct types of synapses attach cells to one another. But more than 30 types of cells exist in the neocortex, the part of the brain Hereld's team is currently examining. Every time one type of neural cell connects to another type, it requires a different type of connection. And new cell types are still being discovered. One thing the scientists do know: There are 100 billion cells in the brain. And that's a lot of calculations.

To get a deeper understanding of the brain's anatomy and function and to analyze more cell types at once, Hereld uses the parallel computing technology at Argonne. That means the simulation has to be divided into smaller sections, compartmentalized pieces of computer code used to divide up very large programs so they can be run on many smaller computers in parallel. The size of these pieces varies depending on the supercomputer's power. A piece of code can include anywhere from 20 to 70,000 cells.

Right now, the simulations are small enough to run on one computer within the larger supercomputer, but they are being run with hundreds of adjustments to multiple variables. For example, the team can look at how changing the strength of the wire-like connection between cells affects the accuracy of a neural signal reaching where it needs to go.

The result of the simulations so far? The scientists adjusted the signals either to excite or to inhibit brain activity. "You might expect that excitation would cause more seizures, but what we found is quite the opposite, it's the inhibitory," says Hereld. "It took hundreds of simulations to look at every possible option in the spectrum, and each of these simulations looked at between a few thousand and ten thousand cells."

But using so many computers at once is not without its problems. Even as each computer calculates the necessary information for a certain group of cells, getting computers to communicate quickly with one another can be difficult, according to Paul Messina, director of science at Argonne's Leadership Computing Facility.

"If you only have a few highways and lots of cars trying to get onto them, you get congestion. For the same reason, lots of wires are needed to connect the computers to each other, but that makes it more expensive to build," he says.

Wim van Drongelen heads a team at the University of Chicago Hospitals that works with Hereld. Van Drongelen and an interdisciplinary group of doctors and researchers are following young epilepsy patients, treating them with drugs and surgery. They work with the Argonne team to try to reproduce the behavior of actual tissue in the simulation. Van Drongelen says a virtual model of the brain is key to providing the detail necessary to understanding how nerve cells go awry during a seizure.

"If you understand the mechanism, maybe you can fix it, or do something to help patients avoid seizures," says van Drongelen, who heads the research at the Pediatric Epilepsy Center at the University of Chicago Hospitals.

Hereld agrees: "We can perform experiments more simply in the simulation. Because everything is virtual and we can touch whatever we want, we can grab any knob, do what we want to a cell or signal, and ask how that affects overall behavior. That's considerably different than experimenting with people or even cell tissue; you can't adjust just one variable, such as the strength of a signal going from one place to another."

Dr. John Ruge thinks a better understanding of how neurons work is extremely important for the field of neurology. The chief of pediatric neurosurgery at Advocate Lutheran General Hospital in northwest suburban Park Ridge says the brain still holds puzzles for many doctors and scientists. "I've been studying the brain for 30 years. It's the size of a shoebox, and I feel we haven't even scratched the surface of understanding it."

"What's relevant is understanding neural pathways and how we can work with them, when using minimally invasive techniques," he says. "We are always looking for greater precision, and as surgeons we want to know, 'How do we get in and get out?' We want to make it so the fact that we're passing through is less obvious to the patient."

To work on finding the answer, Hereld says the research requires a large supercomputer "because there is so much to be modeled in order to provide sufficient detail. It's just not doable with a normal personal computer."

Argonne's Lab Director Eric Isaacs agrees.

"Computers are just another experimental channel to test theories, it allows you to test ideas," he says emphatically. "Normally you do it in a beaker, but this is just another way to test, and at least narrow the outcome of the experiment and do something about it. It helps us make decisions much more intelligently, and look at questions you just can't answer any other way."

Hereld's research is an example of a problem that needs a computer to analyze biology at a very high level of detail.

"It's hard to explain why certain epilepsy drugs help or hurt a patient; for each one, the mechanism is different, and until you understand, it's a little like fishing in the dark," says Hereld.

In addition to Argonne, other supercomputing sites make possible a wide range of biological and physical research. Physicist Klaus Schulten studies the function of cells in the human body at the National Center for Supercomputing Applications at the University of Illinois, where he is a member of the faculty. Schulten heads the Theoretical and Computational Biophysics Group there.

He says 10 to 15 years ago, he worked on computers that had the power and speed only to stretch out small proteins and to show how they worked, but today he can analyze structures that are much more medically relevant.

Schulten says biological computing is particularly essential. "Mathematical theory just doesn't work as well in biology as in physics and chemistry, because biological materials are so very complex."

For Schulten, it's fundamentally important to understand biological functions across the body. "Science is all about discovery, and what we are doing is using the computer like a microscope, so we can see things that we never could have seen before," he says.