Pitt receives $2.5 million to simulate and analyze brain, immune system activity

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Models of how systems evolve and function under certain conditions could lead to better medical understanding of when and how to treat patients

In an effort to promote the application of mathematics to medical treatment, researchers in the University of Pittsburgh's Department of Mathematics will undertake a $2.5 million project to create models of how the brain and immune system function and change over time in response to certain illnesses, infections, and treatment. The models are intended to help doctors better understand and predict the possible short- and long-term responses of their patient's body to treatment.

The National Science Foundation awarded University professor G. Bard Ermentrout, assistant professor Beatrice Riviere, associate professor Jonathan Rubin, assistant professor David Swigon, and professor and interim chair Ivan Yotov a nearly $1.8 million Research Training Group (RTG) award. The RTG includes resources for creating training programs for mathematics students wherein they would work with physicians and biologists to help resolve complicated medical problems through mathematics. Pitt's School of Arts and Sciences—which houses the mathematics department—provided additional funds.

The team will create a variety of computer models based on differential equations—which predict how systems evolve over time—with the medical guidance of scientists and doctors in Pitt's Departments of Biological Sciences and Neuroscience, the Pitt School of Medicine, and UPMC, said Rubin, a coinvestigator on the project.

The immune system models will plot the various chemical and physical changes that occur as the body battles influenza, inflammation, sepsis and necrosis, and wounds. Ultimately, Rubin explained, the researchers want to pinpoint the origin of such conditions as multiple organ dysfunction syndrome (multiple organ failure), a potentially deadly, uncontrollable inflammation that usually strikes ailing patients with compromised immune systems.

"Infection and inflammation kill people in the intensive care unit," Rubin said. "We hope that by building this model and calculating how to control the system, we can help doctors design a clinical strategy for intervention based on a condition's progression."

The neurological models will outline the typical course of activity in various brain regions, communication among brain cells, and time-dependent changes in the synapses—the small gaps between cells through which they communicate. The team will look for how electrical signals and brain waves transmit between brain cells and, in turn, the manner in which those impulses alter the cells.

One clinical application, Rubin said, would be for improving therapies for neurological conditions, such as deep brain stimulation (DBS), which manipulates brain activity via a surgically implanted device that emits electric pulses. Despite DBS' effectiveness in treating such conditions as chronic pain and Parkinson's disease, how it works remains unknown, Rubin said. Once the pathways of brain activity are exposed, he continued, doctors could observe how DBS functions and better control the electrical currents to avoid the known psychological side effects.

The complicated models simulate the extensive, constant interaction of various cells and organs operating on multiple time scales, from the immeasurably swift to a full day. The complexity of these models will require the development of new simulation and mathematical techniques, but the work could apply to several other biological systems.

"We're exploring mathematical and computational territory that has not been understood yet," Rubin said. "For instance, the brain contains millions of neurons that in turn contain very small molecules [neurotransmitters]. This network functions on a time scale measured in submilliseconds, a scale so small that no one can really grasp how short it is. At the same time, the brain manages and abides by the circadian rhythm, the body's 24-hour cycle.

"If we make a breakthrough on how to map these time scales, it would apply to multiple systems," Rubin added.

Source: University of Pittsburgh