UNITING BIOLOGY AND MATHS TO UNDERSTAND THE HUMAN BRAIN

Neurologist and computational neuroscientist Professor Bill Lytton and his colleagues at the Neurosimulation Laboratory of the State University of New York in Brooklyn are using computer simulation to investigate brain function and disease. Their research has far-reaching implications in addressing human illness.

Bringing Biology and Math Together

‘Everyone agrees that we need a paradigm shift – really several – before we can begin to understand the brain, and further understand the mind and brain in disease. For example, schizophrenia, stroke, epilepsy, Alzheimer’s and autism,’ Professor Lytton tells us. As with prior paradigm shifts, understanding comes from detailed observation using new technologies combined with changes in concepts from models. Think of how Galileo’s work with the telescope or Van Leeuwenhoek’s microscopy advanced the fields of observational astronomy and microbiology respectively. However, unlike prior shifts, nowadays new models will be based upon complex computer simulation rather than on closed form equations such as those used by Newton or Einstein.

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Simulation of a single cortical layer 5 neuron. The apical dendrite (top) extends upwards through many layers, gathering information from many sources to be conveyed to the soma near the bottom, at the centre of its web. Information then goes out through the axon at the bottom (purple line). The inset shows results of parameter exploration and indicates another difficulty of neural simulation: neurons are individuals that themselves learn specific attributes in concert with other neurons.

with experimentalists who measure wiring and activity in both normal and dysfunctional brain tissue. Looking from the bottom up, these simulations themselves become experimental objects. They are so complicated that one has to manipulate them experimentally to understand them. Through this interactive experimentation, the experimental objects (simulations) are repeatedly modified to provide clearer representations of the experimental models and to seek experimentally-verifiable predictions. Looking from the top down, one is then re-modelling the simulations themselves, using tools to understand how dynamics can be encapsulated and how activity can be understood in terms of information processing and of neural codes. Professor Lytton notes that it is great fun mentally to jump back and forth between the abstractions of math and the intricate details of biology.

Computer models are improved over time by additional mathematics, statistics, and computational techniques to incrementally fine-tune them to better fit the biological observations at multiple scales. The more the computer simulation allows scientists to find out about the brain, the more data from the brain they can feed into the simulation to make it more exact, and the more they learn about the brain. It’s almost as though Professor Lytton and his fellow researchers are themselves part of an algorithm that investigates the functioning of their own brains’ ability to function as an algorithm designed to learn about the brain. Circular investigations, perhaps like being part of the Matrix while trying to find out how the Matrix works. However, whether or not they are themselves part of the system they’re trying to study, they have made some real progress. The Simple is Really Quite Complex

The extraordinary success of artificial neural networks and computer learning in seemingly simulating the human mind – for example, computers playing chess and actually defeating human opponents – are not the things that are really difficult. They are also, of course, largely not the things that evolution has pressured human brains to be able to do. Instead, it’s the effortless things that we share with many other animals – acute visual and auditory perception under multiple conditions, control of locomotion across uneven terrain at different speeds – that really bring into play the complex processing for which brain coding is optimised. In fact, the inability to program these complex perceptual and motor skills have been a major impediment to the development of useful robots. News reports are quite glowing when someone exhibits a pondering metal being that can slowly negotiate complex terrain. It’s a difficult problem for robots and their programmers, even though human infants can usually walk over uneven ground with ease by the age of two, sometimes even earlier.

Look at the motor system generally. Beyond what other animals can do in terms of locomotion and other muscular activities, we humans have added fine motor control of hands and larynx to the basic mammalian substrate. With these two remarkable innovations in place, humans developed complex capabilities – namely language and tool-making – that made us human. This took place relatively recently and is quite important to our human existence as we know it. After all, without fine dexterity in our fingers and ability to conceptualise complex language, you wouldn’t be reading this article to begin with.

Professor Lytton’s interest in the brain’s motor cortex is precisely due to this being one of the areas – along with the cerebral cortex, thalamus, basal ganglia, red nucleus, anterior cord, etc. – that is responsible for the coordinated control of muscles to effect alterations in the environment. To attempt to understand how all of that works, what else would he do but build a cybernetic arm?

Driving an Arm with Multiscale Simulation! 

Professor Lytton and his team put together a biomimetic arm area, linked to a virtual arm, both running in computer simulation, finally all harnessed to an actual robotic arm with servos. The model, which can be seen at http://neurosimlab.org/BMIask, robot.mp4, is trained using a reinforcement learning algorithm.

The biomimetic model is programmed as a multiscale simulation. In this version of the model, there are three basic layers in the network that can be grossly mapped onto layers of cortex – a motor layer that outputs muscle excitations; a somatosensory layer that coordinates between the other two layers; and the proprioceptive layer that feeds back muscle lengths, i.e., the size of the virtual muscles as they contract and relax. These three layers are also divided into the various virtual muscles that control the extension and flexion of shoulder and elbow. Left to its own devices – that is, untrained – the virtual arm simply flails around without purpose, causing the same to happen with its robotic alter ego. With training, however, things are much different.

Programming the visual arm to pick up an object on a table is accomplished by reversing the arm for getting closer to the object or punishing it for getting further away. Of course, rewarding or punishing a computer program is obviously analogous to the human experience. In practice, what Professor Lytton’s team does is to potentiate or depress synapses based on spike timing depending on whether the arm wander closer or further from the target. This causes the virtual arm to ‘learn’ to get closer and closer to the object. When the hand is stabilised over the object, a grasping function, intrinsic to the robot arm, is
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What’s Next in This Research?

There is a great deal of technical work that Professor Lytton and his colleagues are doing to make massive multiscale simulations and their analysis possible on modern supercomputers. At the same time, they are working to incorporate new streams of data coming in from the US BRAIN project—Brain Research by Advancing Innovative Neurotechnologies—as well as the EU Human Brain Project, the Swiss Blue Brain Project and the Allen Institute brain projects. All of these are collaborative initiatives aimed at understanding brain function.

‘In applying our complex simulations to neurological and psychiatric disease, there is always a trade-off about what to include and what to omit in doing any model,’ Professor Lytton tells us. ‘Models for different purposes—e.g., conceptual versus clinical—need different details, different simulation experiments and different analyses. Schizophrenia is a disease of particular interest to us since it is a brain disease that presents as a disease of the mind. It may, therefore, offer insight into the classical duality of mind and brain.’ He and his team are examining the relationships among brain oscillations—popularly called brain waves—and information flow in the brain, their current, weak proxy for the information processing of mind. Just like the virtual computer arm modeling the function of the human arm, they hope to create more complex models for the more complex functions of the brain. In other words, they want to create functional cybernetic androids—brain region by brain region—so they can study biological human beings. Or is it the other way around?