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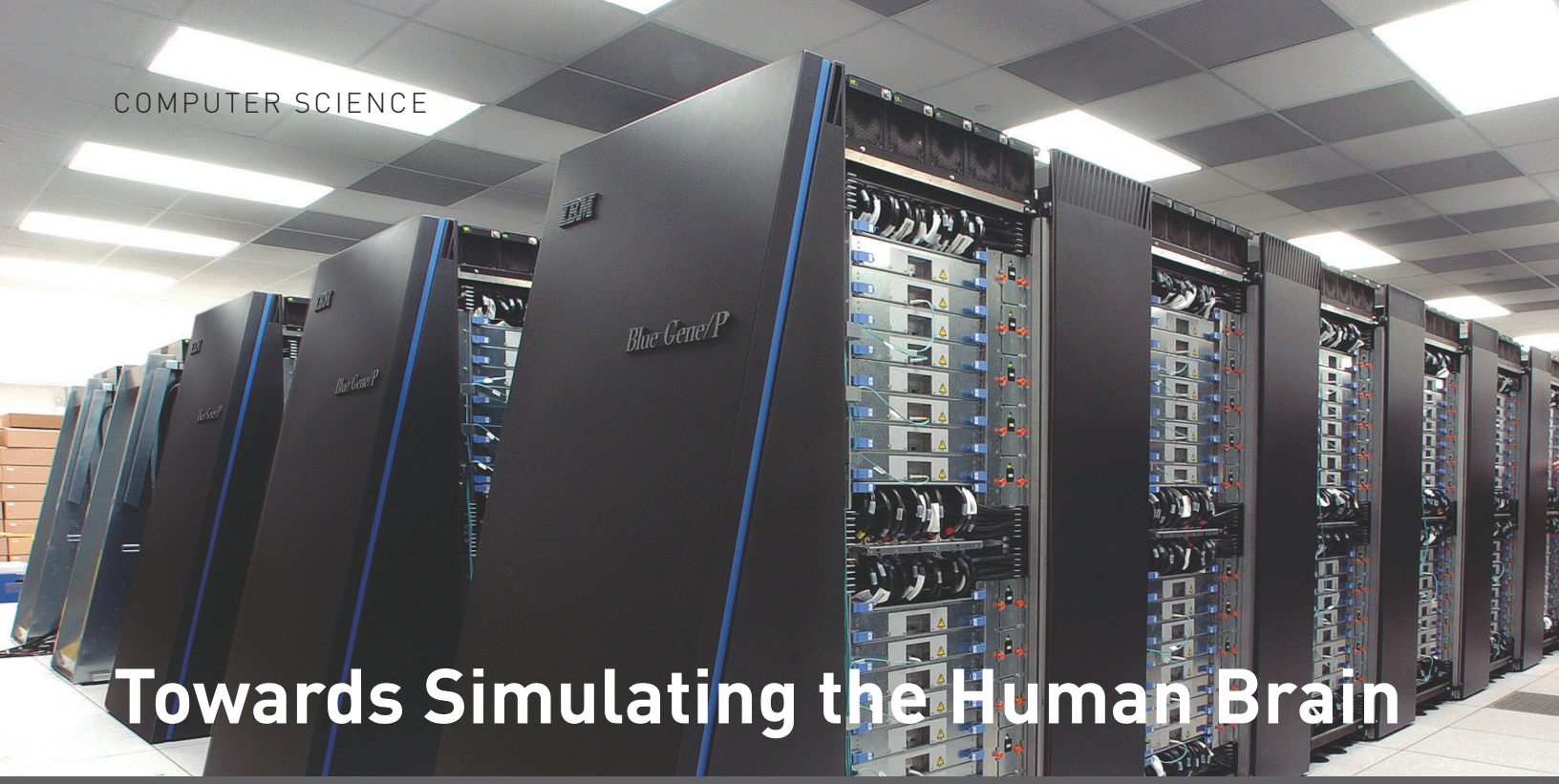

Towards Simulating the Human Brain

BY LOGAN COLLINS '19

The Potential of Brain Emulation

The human brain has been described as "the most complex object in the universe." Its meshwork of 86 billion neurons, 84 billion glial cells, and over 150 trillion synapses may seem intractable (Azevedo et al., 2009; Pakkenberg, 2003). Nonetheless, efforts to comprehensively map, understand, and even computationally reproduce this structure are underway. Large collectives of researchers have come together, working in concert towards these goals. The Human Brain Project (HBP) and its precursor, the Blue Brain Project, have spearheaded the brain simulation goal (Grillner et al., 2016). Some other notable organizations include the China Brain Project, the BRAIN Initiative. On a scale which parallels the space program and the Human Genome Project, neuroscience may be approaching a revolution.

Whole brain emulation (WBE), the computational simulation of the human brain with synaptic (or higher) resolution, would fundamentally change medicine, artificial intelligence, and neurotechnology. Modeling the brain with this level of detail could reveal new insights about the pathogenesis of mental illness (Markram et al., 2011). It would provide a virtual environment in which to conduct experiments, though researchers would need to develop guidelines regarding the ethics of these experiments, since such a construct may possess a form of consciousness. This virtual connectome could also vastly accelerate studies of human intelligence, leading to the possibility of implementing this new understanding of cognition in artificial intelligence and even developing intelligent machines. Brain-computer interfaces (BCIs) may also benefit from WBE since more precise neuronal codes for coding motor actions and sensory information could be uncovered. By studying WBEs, the "language" of the brain's operations could be revealed and may give rise to a rich array of new advances.

Foundations of Computational Neuroscience

Biologically accurate neuronal simulations usually employ conductance-based models. The canonical conductance-based model was developed by Alan Hodgkin and Andrew Huxley and published in 1952, later winning them the Nobel Prize in Physiology or Medicine (Hodgkin and Huxley, 1952). Current models still use the core principles from the Hodgkin-Huxley model.

This model is a differential equation which takes into account the conductances and equilibrium potentials of neuronal sodium channels, potassium channels, and channels that transport anions. The output of this equation is the total current across the membrane of the neuron, which can be converted to a voltage by multiplying by the total membrane resistance.

$$\frac{V_M}{R_M} = C\frac{dV}{dt} = I_{injected}(t) - [g_{Na}m^3h(V(t) - E_{Na}) + g_K n^4(V(t) - E_K) + g_L(V(-E_L t))]$$

Figure 1: This figure depicts a Blue Gene/P supercomputer.

Source: Wikimedia Commons (Credit: Argonne National Laboratory)

"Whole brain emulation (WBE), the computational simulation of the human brain with synaptic (or higher) resolution, would fundamentally change medicine, artificial intelligence, and neurotechnology."

"Multi-compartmental models use complicated partial differential equation extensions of the Hodgkin-Huxley equation. When solved, the resulting multivariable functions take both the location along the dendrite and the time as inputs."

The Hodgkin-Huxley equation (above) can generate biologically accurate predictions for the membrane voltage of a neuron at a given time. Using these membrane voltages and the firing threshold of the neuron in question, the timing of action potentials can be computationally predicted.

Another important concept in computational neuroscience is the multi-compartmental model. Consider an axon which synapses onto another neuron's dendrite. When the axon terminal releases neurotransmitters which depolarize the other neuron's dendritic membrane, the depolarization will need to travel down the dendrite, past the soma, and onto the axon of this post-synaptic neuron to contribute to the initiation of an action potential. Since the density of voltage-gated channels outside of the axon is relatively low, the depolarization decreases as it moves along this path. In order to accurately recreate a biological neuron in a computer, this process must also be modeled. To accomplish this, the model segments each portion of the neuronal membrane into multiple "compartments." In general, the higher the number of compartments, the more accurate the model, but also the more computational resources the model will require. Multi-compartmental models use complicated partial differential equation extensions of the Hodgkin-Huxley equation. When solved, the resulting multivariable functions take both the location along the dendrite and the time as inputs.

These methods form the fundamentals for constructing virtual neurons and assemblies of neurons. They have shown remarkable biological fidelity even in complex simulations. Multi-compartmental Hodgkin-Huxley models, given the proper parameters from experimental data, can make predictive approximations of biological activity.

The Blue Brain Project

The quest to simulate the human brain has largely emerged from The Blue Brain Project, a collaboration headed by Henry Markram (Figures 1 and 2). In 2007, Markram announced the completion of the Blue Brain Project's first phase, the detailed simulation of a rat neocortical column in IBM's Blue Gene supercomputer.

This achievement required a powerful engineering strategy that integrated the many components of the simulation (Markram, 2006). To start, gene expression data were used to determine the ion channel distributions in the membranes of various types of cortical neuron. Over twenty different types of ion channel were considered in this analysis. These ion channels were incorporated into extensions of the Hodgkin-Huxley model with additional terms for the many types of channel. Three-dimensional neuron morphologies were paired with appropriate ion channel distributions and a database of virtual neuron subtypes was assembled. Experimental data on axon and dendrite locations was collected to recreate the synaptic connections in the neocortical column. A collision detection algorithm was employed

Figure 2: Henry Markram explains neuronal function

Source: Wikimedia Commons (Credit: Steve Jurvetson)

Figure 3: Cajal Blue Brain research is ongoing in Spain

Source: Wikimedia Commons (Credit: Cesvima)

to adjust the three-dimensional arrangement of axons and dendrites by "jittering" them until they matched the experimental data. Physiological recordings provided membrane conductances, probabilities of synaptic release, and other biophysical parameters necessary to model each neuronal subtype. In addition, plasticity rules mirroring those found in biological neurons were applied to the virtual neurons to allow them to perform learning. Through a series of iterative tests and corrections, parameters were optimized.

By 2012, the project reached another milestone, the simulation of a cortical mesocircuit consisting of over 31,000 neurons in several hundred "minicolumns" (Markram et al., 2015). In this simulation, some of the details of synaptic connectivity were algorithmically predicted based on experimental data rather than strictly adhering to experimentally generated maps. Nevertheless, valuable insights were produced from the emulated mesocortical circuit. In vivo systems have shown puzzling bursts of uncorrelated activity. The simulation confirmed that this emergent property occurred as a consequence of excitatory and inhibitory signals canceling each other. The simulation also demonstrated that, during moments of imbalance between these signals, choreographed patterns of neuronal encoding can occur within the "overspill." Such observations in this virtual cortical circuit have increased understanding of the mechanisms of neural activity.

The Human Brain Project

As the Blue Brain Project developed, it was eventually rebranded as The Human Brain Project to reflect its overarching goal. In 2013, the HBP was selected as a European Union Flagship project and granted over 1 billion euros in funding (equivalent to slightly over 1 billion USD).

Criticisms inevitably arose. Some scientists feared that it would divert funding from other areas of research (Frégnac and Laurent, 2014). A major complaint was that the HBP was ignoring experimental neuroscience in favor of simulations. The simulation approach would need to be complemented by further data collection efforts since connectomic and functional mapping information is lacking. As a result, the HBP restructured to broaden its focus.

An array of neuroscience platforms with varying levels of experimental and computational focus were developed (Amunts et al., 2016). The Mouse Brain Organization and Human Brain Organization Platforms were initiated to further knowledge of brain structure and function through more experimentally centered approaches. The Systems and Cognitive Neuroscience Platform employ both computational and experimental approaches to study behavioral and cognitive phenomena such as context-dependent object recognition. The Theoretical Neuroscience Platform and Brain was created to build large computational models starting at the cellular level, closely mirroring the original Blue Brain Project.

In addition to these, several overlapping platforms were initiated (Amunts et al., 2016). The Neuroinformatics Platform seeks to organize databases containing comprehensive information on rodent and human brains as well as three-dimensional visualization tools. The High Performance Analytics and Computing Platform (HPAC) centers on managing and

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expanding the supercomputing resources involved in the HBP. In the longer term, HPAC may help the HBP obtain (projected) exascale computers, capable of running at least a quintillion floating point operations per second. Exascale computers would have the ability to simulate the entire human brain at the high level of detail found in the first simulated neocortical column from 2007 (Markram et al., 2011). The Medical Informatics platform focuses on collecting and analyzing medically relevant brain data, particularly for diagnostics (Amunts et al., 2016). The Brain Simulation Platform is related to the Theoretical Neuroscience Platform, but more broadly explores models at differing resolutions (i.e. molecular, subcellular, simplified cellular, and models which switch between resolutions during the simulation). The Neuromorphic Computing Platform tests models using computer hardware that more closely approximates the organization of nervous tissue than traditional computing systems. Finally, the Neurorobotics Platform develops simulated robots which use brain-inspired computational strategies to maneuver in their virtual environments.

Through the introduction of these platforms, the HBP collaborative may yield new insights in diverse areas of neuroscience and neurotechnology. The HBP's original mission of simulating the human brain will continue, but with along a more interdisciplinary path. The incorporation of experimental emphases may help build more complete maps of the brain at multiple scales, enabling superior simulated models as the project evolves.

"Insights into brain mechanisms may help to decipher the mystery of consciousness. Such understanding may open the door to constructing intelligent machines."

The Future

As a European Flagship, the HBP will receive funding over a ten year period that started in 2013 (Amunts et al., 2016). It may yield advances in numerous neuroscientific fields as well as in computer science and robotics. The HBP is also open to further collaboration with other neuroscience projects such as the American BRAIN Initiative. The Theoretical Neuroscience and Brain Simulation platforms may unify experimental knowledge and pave the way to emulating a brain in a supercomputer (Supercomputer shown in Figure 3). As exascale supercomputers emerge and the human connectome continues to be revealed, this challenging goal may be achievable. With the massive funding and resources available, the HBP may significantly advance understanding of the human brain and its operations.

The eventual completion of the HBP may have tremendous implications for the more distant future. Insights into brain mechanisms may help to decipher the mystery of consciousness. Such understanding may open the door to constructing intelligent machines (Markram et al., 2011). With the capacity to emulate consciousness in a computational substrate, prosthetic neurotechnologies may see remarkable advances (Deadwyler et al., 2016). We may uncover methods for gradually replacing portions of the brain with equivalent computational processing systems, enabling mind uploading. Although these possibilities currently seem fantastical, exponential trends in technological advancement suggest that they may transition into real possibilities within the next hundred years (Kurzweil, 2005). The HBP demonstrates that collaborative innovation is vital for building the future and continuing the human quest to invent, experience, and discover. D

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