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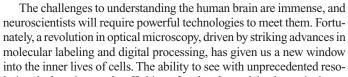
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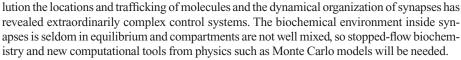
Understanding the Human Brain

LIKE MOST FIELDS IN BIOLOGY, NEUROSCIENCE IS SUCCUMBING TO AN "EPIDOMIC" OF DATA collecting. There are major projects under way to completely characterize the proteomic, metabolomic, genomic, and methylomic signatures for all of the different types of neurons and glial cells in the human brain. In addition, "connectomics" plans to provide the complete network structure of brains, and "synaptomics" aims to uncover all molecules and their interactions at synapses. This is a good time to pause and ask ourselves what we expect to find at the end of this immense omic brainbow.

Linnaeus's catalog of species and the classifications he imposed on them turned data into knowledge, but it did not lead to an understanding of why they were all there. That had to wait for Darwin's theory of evolution and the development of genetics. All the lists that we will accumulate about the brain, although necessary, will be far from sufficient for understanding. The human brain contains an estimated 86 billion neurons and an equal number of glial cells. The complete structure of the enormously simpler 302-neuron network of the nematode worm *Caenorhabditis elegans* was published in 1986. But without the activities of neurons and their synapses, it was far from a complete "wiring diagram." Today, with genetically encoded calcium sensors, with better knowledge of the molecules present at synapses, and by integrating the omic catalogs with developmental and dynamical data, we may finally be in sight of completing the worm wiring diagram, as required for a full understanding of this one relatively simple nervous system.

The challenges to understanding the human brain are immense, and neuroscientists will require powerful technologies to meet them. Fortunately, a revolution in optical microscopy, driven by striking advances in molecular labeling and digital processing, has given us a new window into the inner lives of cells. The ability to see with unprecedented resolution the locations and trafficking of molecules and the dynamical organization of synapses has revealed extraordinarily complex control systems. The biochemical environment inside synapses is seldom in equilibrium and compartments are not well mixed, so stopped-flow biochemistry and new computational tools from physics such as Monte Carlo models will be needed.

Electrical recordings from one neuron at a time deep in the brain can give us clues to what information has passed through a brain area. But neurons are not independent, interacting with each other and the world on a wide range of time scales. New techniques have been developed to simultaneously record from and manipulate many neurons in several brain areas that can give us a picture of how interacting neural populations give rise to behavior.

Since the 1980s, neuroscience has received visionary financial support from private foundations, jump-starting new fields including cognitive neuroscience and computational neuroscience based on new techniques for imaging and modeling the human brain. The global view of human brain activity thus far obtained from imaging experiments has changed the way we think about ourselves. *Homo neuroeconomicus* has replaced the rational-agent model of human behavior, neuroeducators want to make children better learners, and neuroethicists have been inspired by the discovery of biological links to aggression, trust, and affiliation. However, individual differences often dominate. Although expensive bets are being placed on explaining the diversity of human behavior and mental disorders with genetic polymorphisms, gene mutations, and chromosomal rearrangements, the results so far have been modest.

The Internet is making neuroscience more accessible to the public. The Society for Neuroscience, which convenes its annual meeting next week, will soon launch BrainFacts.org, a reliable source of information about the brain. In-depth interviews with neuroscientists can be found online at thesciencenetwork.org. And a Neuroeducation X Prize is being planned to encourage innovation in online computer games that enhance cognitive skills. Let us celebrate what our brains have discovered and what they can tell us about themselves.

– **Sydney Brenner and Terrence J. Sejnowski**