

Neural Networks, The Brain And The Connectome

Cell robustness and complexity have been recognized as unique features of biological systems. In studying metabolic-reaction systems we have discovered multiple flux distributions and redundant pathways that lead to a given external state. Can a computational method identify such states? A way to do this has been found to do this. It identifies metabolic flux analysis (MFD) and multiple metabolic pathways analysis (MMP). MFD uses linear programming and MMP uses graph-theoretic methods

The BRAIN initiative expenditures for 2014 used \$110 million from DARPA, NIH and NSF. The program was to map the dynamics of neuron activity in the caenorhabditis elegans, drosophila, zebrafish and the Etruscan shrew and ultimately primates and humans. The functional connectome was to be achieved. This is a goal that will be very hard to achieve. This paper suggests methods to help. One can use structures and functions to enumerate neural networks which we can attempt. Nanoparticles were to be used as voltage sensors to detect action potentials and nanopores that could serve as electrophysiological multielectrode arrays. Neuronal activity detection can use microelectronic integration (based on synthetic biology). High throughput DNA sequencing for rapidly mapping neural conductivity was performed.

The human brain contains around 100,000,000,000 neurons (primary signaling cells), and maybe 10 to 50 times as many glial cells (supportive of neurons). We may consider neurons as variations on a common structural theme. Different types of neurons include Purkinje, Granule, motor, tripolar, pyramidal, chandelier spindle and stellate cells. Neurons can be classified into four groups differing in shape that include unipolar, bipolar, pseudo-unipolar and tripolar cells. They can also be categorized by function such as sensory, motor, and interneurons. So neurons differ structurally, functionally and genetically in how they form connections with other cells. Therefore neuron taxonomy has at least hundreds of types and subtypes. NeuroMpho.org is a database of digitally reconstructed neurons by species, brain region and cell type. fMRI of single cells could ensure activity levels of brain regions. Nanotechnology could help make brain activity maps. The program of Fan and Friedler can be adapted to accomplish such a goal.

In representing a neural network of the brain we need to have both a symbolic and a cognitive part that are combined. It must show the connections and the cognitive outline in the diagram. This neuromorphic diagram can be shown as a point, neglecting the shape of the neuron, at first, but depicting the connections symbolically. These connections leading to the connectome can appear later. However, the cognitive map will be composed of associative indexing and organization of indicative memories and path-finding spaces. There also should be a unique and central notion of the "self" in the map. This theoretical framework of the network will then integrate both the cognitive and pathway seeking scheme of the neural network.

Nexus

Synchronized firing of millions of neurons in the brain appears to be essential to some of the most basic functions of perception. Unraveling the tangle of several billion neurons in the human nervous system is still beyond scientific capabilities. Brenner tried to understand complex biological networks.

Scientists tried to map out the network of connections among the nematode worm *Caenorhabditis elegans* because it has only 979 cells and only 282 neurons. Most of the neuron's axons in the hippocampus or **Broca regions** link up with neurons in the neighboring brain regions

In the brain there are a few local connections and a few long range connections that begins to feel like a small-world pattern. The neural networks are highly clustered. The mammalian brain generates efficient reflex responses which hang together under adversity. The extreme flexibility is complex with great adaptability. Neurons store information not only at the group level with synchrony but also at the individual level. There is quick response and compact storing of information. This plays a role in how the organized activity that under lies consciousness.

Several years ago I attended a symposium paper presentation by Dr. F. Friedler and Dr. L. T. Fan that impressed me greatly. They were using their program for process pathway analysis and to design optimum plants to produce chemicals and refine oil. The program had been used to primarily reduce pollution from commercial plants, determine best pathways to produce essential products, etc. Molecular Engineering of materials and devices can extend the capabilities of technology many times in many areas. I suggested to a class of Ph. D. candidates of Dr. Friedler of Veszprem University in Hungary that they extend its use in the "new" field of molecular biology and that they use a variation of the program to design optimum structures for molecules with desired properties. Also, I suggested that they design a program simulating biochemical cycles. In 2005 D.Y. Lee, L. T. Fan, S. Park, S. Lee, S. Shafie, B. Bartok and F. Friedler published a paper entitled "Complementary Identification of Multiple Distributions and Metabolic Pathways." This paper was published in English and Chinese journals. It identified and varied the known and other metabolic cycles of great interest to medical people and is destined to be a grand step forward in drug discovery, synthetic biology, etc. It may be possible that the paper just cited can be of interest to those now concerned with the Brain initiative and the functional connectome of humans.

A program was used at DuPont during 1958-1964 for generating high energy rocket propellants by generating molecular structures capable of delivering high specific impulse and other properties. An additional program would have proposed pathways to synthesize such molecules. Other programs such as CHEMKIN were used in conjunction with these programs.

Science Pathways Discovery

Cajal advanced the principal of connection specificity and dynamic polarization. Later resting potential and of the action potential was explained in terms of the movement of specific ions of potassium and sodium through pores (ion channels) in the axonal membrane. Excitatory synaptic ion channels are gated chemically by ligands such as the transmitter acetylcholine. Other receptors were discovered later.

Parkinson's disease, Huntington's disease and Alzheimer's disease involved in clinical medicine have benefited from molecular neuroscience. The number of neurons and the details of their connectivity distinguishes one species from another. The brain's computational power comes from interactions among billions of nerve cells assembled into circuits that carry out specific operations in support of behavior and cognition. Functional neuroimaging by PET (positron resonance tomography) and fMRI magnetic resonance imaging have helped in these cases. Memory studies on humans and parallel studies on nonhuman primates have also helped.

Neuroscience concerned with both biology and psychology have emerged and is helping to bring about productive results. Mental processes (perception, memory and cognition) are emerging from the study of neurons, circuits, and brain systems and computational studies are providing models that guide experimental work.

This work concentrates on the human brain which weighs only three pounds. The behavior, thoughts and experience is attached to a wet chemical and electrical network called the CNS (central nervous system). This control center has many feedback loops. We underestimate its complexity. The circuits are complex but we take them for granted. Also there are many neural transmitters that affect cognition and emotion.

The firing of neurons occur in various patterns; controlled by physics and not under our will. It bears some resemblance to ants making a trail that emerges from chaos. The voltage impulses are provoked by interneurons and the total extract is from pulses of neuro transmitters and other factors coming in from other neurons. The brain is composed of two hemispheres with changing synaptic structures that in some cases lead to learning or memories that originated in our ancestors. There are billions of global qualities coded into the neurons. There are threshold currents for firing, tempered by the resistances of the axons. The reverberations of the neurons occur from forcing feelings of emotions that produce showers of electrochemical activity that lead to various neural pathways inside your brain.

In reference 8, chapter 10 on Networks and Flow there is a program that can be found at <http://www.netlib.org/toms/608>. This leads to a paper, Implementing Dense Linear Algebra Algorithms Using Multitasking on the Cray X-MP-4. It is possible to use a Quasi-Chemical description on the shape and functions of the neurons. The connectome is a very dense space of neurons connected in a combinatorial fashion described by equations that describe a multitude of connections that create potentials from their firing across the synapses, the sodium and potassium ion potential changes, the axon resistances, etc. These can be all additive and furthermore the connections can be very loopy. These can be described by a linear preponderance of algebraic equations that can be solved by a super computer such as the Cray X-P-4. This will be the next phase of the work on the connectome together with the laboratory work that will be necessary.

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