COMPUTATIONAL NEUROSCIENCE

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Contents

Summary

This chapter presents a broad perspective of the field of computational neuroscience focusing on general principles common to various computational models. Studies in computational neuroscience cover a wide range of topics from membrane currents and protein coupling at the level of the subcellular architecture to network properties of the nervous system, and then to the cognitive processes of learning, memory, attention, decision making and generating motor commands. General approaches towards an understanding of the functioning of such processes through modeling and simulation are outlined. The field of computational neuroscience is undergoing changes due to advances in neuroscience and computational science and through technological innovation.

1. What is Computational Neuroscience?

The ultimate goal of studies of computational neuroscience is to explain how the brain works through the modeling of information processing and motor control at various spatiotemporal scales, including the subcellular, neuronal, circuit, and system levels. Toward this end, experimental studies describe physiological phenomena to be explained, while studies in theoretical neuroscience provide mechanical or functional explanations for those observations, which become theories or hypotheses to be tested in subsequent experimental studies. To interconnect these studies, computational neuroscience intends to speculate on how the nervous system operates in three ways of mathematical models; computational theory guides research by giving functional explanations of entire system, models of hardware implementation gives details to simulation studies by giving mechanical explanations, and models of algorithms and representation are between them.

Simplified models are designed to capture the essential features of biological system, emphasizing the physiology and dynamics of functionally and biologically realistic system. Even perfect explanations are not sufficient to prove a theory. Therefore theories precisely formulated in computational neuroscience and expressed as computational models must be validated through computational simulation, analysis and experimentation. Numerical comparison of model predictions with experimental data enables one to validate the model. Without such validation, models cannot advance our understanding of the nervous system of natural life forms.

Computational neuroscience continues to change as a result of advances in neuroscience and computational science and through technological innovation. Studies in computational neuroscience cover a wide range of topics from membrane currents and protein coupling at the level of the subcellular architecture to network properties of the nervous system, and then to the cognitive processes of learning, memory, attention, decision making and generating motor commands. The studies have their counterparts in the diverse research fields of system neuroscience, biological neuroscience, cognitive neuroscience and psychophysics; in a variety of areas, including vision, sensory-motor integration, motor control, development and plasticity. This chapter will introduce the reader to some general concepts of the field. Readers desiring additional information on how to create and use computational models are referred to other textbooks focusing on models in each research field (for example, Sejnowski and Churchland (1992); Abbott and Dayan (2001); Koch (1999); Sterratt et al. (2011)).

2. Emergence of Computational Neuroscience

The term "computational neuroscience" was introduced by Eric Schwartz (1990). He organized a conference, held in 1985, to provide a summary of the status of a field, which at that time was referred to as neural modeling, brain theory or neural networks. The proceedings of that meeting were later published as a book, "*Computational Neuroscience*". However, the concept of computational neuroscience emerged much earlier among neuroscientists. Since the publication of "*Cybernetics*" by Norbert Wiener in 1948, there has been spectacular growth in the information available on the anatomy and physiology of the nervous system, as well as technological achievements such as the design of faster and more powerful computers. This has encouraged researchers to construct complex simulations of information processing and motor controls in the nervous system.

For more than a century mathematical models have been applied to explain various biological phenomena. In 1907, for example, Louis Lapicque introduced the integrate-and-fire model of the neuron to explain the generation of action potential on the basis of firing rates. This model continues to be used in computational neuroscience in both cellular studies and studies of neural networks. In addition, Warren McCulloch and Walter Pitts proposed a model of synaptic transmission with a binary threshold for generating action potential (McCulloch-Pitts model, 1943). In this model, each neuron was treated as a logical unit within a network. This type of rate-based model has been extensively applied to artificial neural networks. Beginning in the 1950's, experimental innovation enabled physiological studies to provide more specific data on some physiological phenomena.

After the invention of the voltage clamp technique, Alan Hodgkin and Andrew Huxley (1952) created the first biophysical model of the action potential. Subsequently, ion channels were discovered as the physical mediator of the membrane conductance described in their model. David Hubel and Torsten Wiesel (1959) discovered that neurons in the primary visual cortex are selective to orientation of contour lines. They showed that the orientation selectivity can be achieved through the hierarchical networks of neurons in the lateral geniculate nucleus and the primary visual cortex. Wilfrid Rall (1964) began biologically realistic anatomical modeling of neurons and dendrites, including the first multicompartment model using cable theory. Since experimental results were provided mainly for properties at the level of neurons at that point, these studies targeted the relationships between the input and output properties at the level of neurons. It is noteworthy that these pioneering works are not merely aged models; they are also the original models upon which many of the various computational models employed today are based.

In the 1970’s, computational theorists began to have the expectation that the study of information processing and motor control in the nervous system might lead to development of new kinds of computational machines and vice versa. Approach of David Marr (1969), which would take into account the quantitative network architecture of the brain system being modeled to produce a quantitative theory, has inspired physiologists to investigate how the cerebellar cortex might learn to associate motor commands with actions. Those investigators considered the cerebellar cortex as a kind of Perceptron (Marr, 1969, Arbus 1971), which was originally proposed as a learning system in a simple neural network (Rosenblatt 1958). However, it would be years before experimental studies were sufficiently advanced to provide enough data to develop biologically realistic models or to test his ideas experimentally. Marr himself tried to test his prediction that synapses between parallel fibers and Purkinje cells in the cerebellum would be modified through climbing fiber input to the Purkinje cells, but he did not succeed in confirming that prediction (Eccles *et al.*, 1967). Experimental proof of Marr’s fundamental idea of the mechanisms of learning in the brain would be obtained only later (Ito, 1984).

Since then, the tremendous growth of anatomical and physiological studies has provided the opportunity to generate empirically adequate computational theories at several levels, even at the level of higher cortical functions. However, more computational models were aimed at addressing specific questions and relied heavily on experimental data to constrain them, so that different models were constructed at different levels of detail. Moreover, the rapid and dramatic advances in the power of computers are making computational neuroscience comprehensive and essential for all neuroscientists.

3. What is the Role of Computational Neuroscience?

David Marr played a key role in the establishment and rapid growth of this area of computational neuroscience. In “Vision” (1982), he argued that an aim of neuroscience should be to reveal the underlying mechanisms at three levels of analysis.

1. *Computational Theory*. Studies at this level ask what problems does the processing solve, why does the system do what it does, what is the goal of the computation and

why is it appropriate, and what is the logic of the strategy by which it can be carried out? Here, models decompose the task into its main constituents to define the problem, set out how it can be solved, and predict new outcomes.

2. *Representations and Algorithms*. Studies at this level ask how a computational theory can be implemented. Clearly, the nervous system uses specific representations and algorithms to handle information, and it is the goal of computational neuroscience to help identify them.
3. *Hardware Implementation*. Studies at this level ask how the system physically realizes the algorithms and representations within the networks of the nervous system. Here the models are closely related to experimental data from anatomical, biological, physiological and psychological studies, and describe information processing and motor controls in a realistic manner.

This simple framework provides an important and influential starting point for thinking about conceptual levels in the context of computation by nervous structures.

Marr himself favored the idea that analyses at these three levels are weakly related, and inspiration and constraints from one level of analysis can guide research in another. Problems of computational theory can be studied without fully understanding the algorithm that executes the computation. Likewise, problems of algorithm can be solved without fully understanding their physical implementation in the nervous system. Thus, having a clear theory of what the brain is trying to accomplish can be a powerful research guide that can be further evaluated through research in computational neuroscience.

However, such a top-down strategy can be severely damaged by ill-posed questions, which make available several solutions for the same problem given by a computational theory. In such cases, models primarily driven by functional considerations can provide only general guidance about what might happen in the brain, which will make it difficult to achieve inspired consideration of hardware implementation. Furthermore, nervous systems are the products of evolution, so their solutions to problems may differ from those obtained through smart design. Thus, biological implementation of computational neuroscience plays an important role in analyzing the task, devising the algorithm, and providing computational insight to researchers as to an appropriate algorithm that will make a model biologically realistic. This means the aforementioned three levels of analysis are not independent, and there is much more coupling and interaction than was previously appreciated. Modern computational neuroscience expects that the appropriate algorithm will fill the gap between studies at the theoretical level and those at the hardware implementation level.

4. Property of Computational Modeling for Nervous Systems

Computational neuroscience can be viewed as a theoretical neuroscience specialized to employ mathematical models for simulating the physiological phenomena observed in experimental studies. To describe this, researchers borrow methods from a wide variety of disciplines, including mathematics, physics, computer science and statistics. However, computational neuroscience has its own specialization, which distinguishes its models from hypotheses or conventional self-standing theories, like theory of learning disciplines such as machine learning, artificial neural networks and computational learning theory.

To validate theoretical considerations, computational models need to be biologically plausible and to be testable by means of numerical simulations and further experimental studies.

4.1. Biological Constraints

As mentioned, experimental studies are vital for developing models and for setting the initial parameters into models. Although the field of computational science may be explored without the benefit of biological constraints, which may lead to technological innovations, only experimental measurements made within the nervous system can show what the system is actually doing in nature. Important experimental inputs to computational neuroscience come from anatomical studies of the morphology and functional connectivity of structures, from physiological studies of the behavior of neurons and networks within neuronal systems, and from psychological studies of the effects on animal behavior. With these data, biologically plausible speculations can be developed into testable hypotheses, realized in models, tested experimentally, and evaluated analytically. Thus, models in computational neuroscience do not escape biological constraints.

4.2. Simplifying Models

One modeling strategy is to produce a very large-scale simulation that incorporates as much cellular detail as is available. Such models are made increasingly realistic by adding more variables and more parameters. However, by keeping too many details that are not essential for the scientific argument, these models may miss some aspects of signals that are relevant and should be captured in the study. Managing realistic models requires a substantial experimental database and a great deal of computational power. Furthermore, we do not yet fully understand the cells themselves, so the results can be invalidated by the absence of important features. Finally, it is all too easy to make a complex model fit a limited set of data, resulting in a poor understanding of the nervous system. Hence, simplicity should be a major goal when designing a reference model that is appropriate for testing a particular aspect of a system or a hypothesis.

To better understand its behavior and underlying mechanisms, the nervous system is thought of as a kind of computational system. For this purpose, the functional elements involved in a specific functional task must be clarified within the system, so that the interaction among these elements can be investigated. Therefore, although models should be made as simple as possible, they must capture the main features of the data that should be captured. If this is achieved, modeling removes the ambiguity from theories and avoids the effects of unexpected aspects of data. On the other hand, a simplified model can become an end in itself and lose touch with nature. Some models have certainly been too abstract to justify the claims derived from them. Thus, models must be carefully constructed and reasonably simplified so that the results of careful scientific investigations lead to insight into natural processes. The aim of simplifying models in computational neuroscience is also to better comprehend the functionality of complex systems. It is not always possible to adequately justify all assumptions, but it is important to clarify which assumptions have been made and to debate them.

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Biographical Sketch

Minami Ito was born in 1959 in Canberra, Australia and returned to Japan at the age of three. He graduated from Osaka University in 1983 and obtained a Ph.D. (Engineering) (Osaka University) in 1994. He became a frontier researcher at the RIKEN Institute in 1989 and became a postdoctoral associate at The Rockefeller University in 1994. He was a C. H. Revson Fellow from 1994 to 1995. He returned to Japan and became an associate professor at the National Institute for Physiological Sciences in 1998 and then became an associate professor at The Graduate University for Advanced Sciences in 2004. Since April of 2012, he has been a professor at the Tokyo Medical and Dental University. His major is studies of neuronal mechanisms in the mammalian visual cortex using various methods of electrophysiology, psychophysics and computer simulations. He is a member of Japan Neuroscience Society, Society for Neuroscience and The Physiological Society of Japan.