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Editorial: Computational Neuroscience and Modeling of Diseases: Do We Need New Paradigms?

Computational Neuroscience has come out of age. The field emerged in the 1940s and 1950s under different names, such as biological cybernetics, neural networks, or brain theory. In 1985, Eric Schwartz coined the term “Computational Neuroscience”, and with the development of faster computers the field began to strongly expand. Computational neuroscience developed into a key discipline within system neuroscience providing the theoretical and computational tools which are necessary for understanding the brain as a complex dynamical information processing system. But computational neuroscience has also developed into an enabling technology for translational research. It provides new concepts and paradigms for intelligent systems and man-machine interfaces, and it has the potential of making strong impact on clinical research for understanding brain diseases and for designing therapeutic interventions. Computational neuroscience will help us to apply the accumulating knowledge of how the brain functions to understanding its dysfunction in disease.

Dynamics vs. Function

Theoretical approaches towards understanding the link between structure, dynamics, and response properties of neural systems are the success stories of modern computational neuroscience. Biophysical modeling of neurons and circuits using conductance-based models has been developed into research tools widely used by theoreticians and experimentalists. Biologically relevant abstractions of neurons and circuits have been created, simulation platforms have been designed, standardization is under way and efforts are being made to make the new methods widely accessible. Models of response properties and receptive fields have become common tools for the description and the analysis of neuronal response properties even in predominantly experimental laboratories and models underlying self-organization are frequently being used for the model-based analyses of experimental data.

Theoretical approaches towards computation in neural systems, however, are still in a much less mature stage. Although it is widely accepted that neural information processing can be understood through theoretically well-founded principles which generalize across brain structures and species, extracting those principles has turned out to be a hard task. Experiment-dominated bottom-up (data → computational models → functional concepts) and theory-dominated top-down approaches (functional hypotheses → computational models → testable predictions) have to go hand in hand, but top-down approaches are much less coherent and have not yet been developed into commonly used theoretical and computational tools.

Computational Models of Disease

Clinical research in neurology and psychiatry is currently facing a transition away from purely “descriptive” towards more “mechanistic” approaches that acknowledge the importance of interactions. Recently the concept of Dynamic Diseases has been developed stressing the fact that the properties of the whole may depend in a non-trivial way on the properties of its parts. This concept has been successfully applied to neurological disorders which are characterized by pathological network activity states. Dynamic Diseases include epilepsy, where pathological synchronized activity emerges within a large area of the cortex, Parkinson´s disease, which is characterized by abnormal rhythms in the basal ganglia, migraine, which is often associated with spreading depression waves travelling across cortex, and (though not a “disease” in the strict sense) the processes in the subacute phase and during recovery after stroke. While the origins of Dynamic Diseases can certainly be traced back to genes, receptors and molecules, a full understanding of these diseases requires an understanding of the network dynamics. This can then lead to novel therapeutic interventions as has for example been demonstrated by the application of delayed feedback control to deep brain stimulation in Parkinson´s disease. The full potential of the theoretical and computational concepts developed in the Computational Neuroscience field, however, has yet to be exploited.

A second group of neurological disorders is characterized by impairments of cognitive function which often affect the mechanisms underlying reward-based learning, adaptive decision making, working memory or emotional processing. Socially highly relevant disorders fall into this group, among them Alzheimer´s disease, bipolar disorders, mood disorders, and – although not "disorders" in the strict sense – alcohol and drug abuse and changes of cognitive performance with age. Much progress has been made tracing back the origins of these disorders to molecules and receptors, to neuromodulatory systems and genetic dispositions, and key therapeutic interventions have been derived from these insights.

A full understanding of these diseases, however, can only be achieved if we also understand the complex neuronal interactions in relation to the cognitive functions and learning processes they implement.

This is where theoretical and computational methods are required and have to enter clinical research. The computational analyses of the network dynamics, the plasticity of the interconnections and the plastic changes of neuronal response properties, have to go hand in hand with models of cognitive function and learning. The constructed computational models – properly calibrated against behavioral, imaging and genetic data – could then be of great help for designing novel therapeutic interventions. Computational models would allow the prediction of effects of these interventions as well as their neurophysiological correlates and would form a highly valuable component in the validation process.

Challenges

The design of computational models of brain function, however, faces two major challenges. Firstly, promising candidate hypotheses about brain computation must be identified. Inspiration is often gained from machine learning and AI, where optimal solutions are sought for tasks biological systems typically face as well and which provide formal ways of reasoning about computation and inductive learning. Secondly, experimental validation is a difficult task, because hypotheses about brain function (1) are related to performance measures which are often assigned to the whole organism and only indirectly to the neural circuit under study and (2) are formulated in computational or algorithmic terms. Putting them to test may require several additional assumptions regarding their implementation.

Basic concepts from the machine learning field have entered neuroscience and have stimulated research in a very productive way. Popular methods and paradigms include information theory, reinforcement and reward-based learning, Bayesian inference, Belief networks or Hidden Markov Models. Particularly promising are recent developments in the reward-based learning and decision making fields. Reinforcement learning models for example are well suited to quantify human behavior in non-stationary probabilistic environments and to identify individual and group differences. These models can then be correlated with data from imaging and genetic studies providing quantitative links between computation and the underlying neuronal response patterns. In recent years functional models were matched to network models of executive function systems in the brain, which were then successfully applied to explain changes observed in neurological disorders. The exploitation of the computational models for improving therapies will be a logical next step.

However, even reinforcement learning models are not yet used to their full power and theoretical approaches to "computation" have not yet turned into common and easy-to-apply research tools. The major reason for this is the small number of scientists who have expertise in both engineering oriented machine learning and brain oriented computational neuroscience. Educating young researchers at the interface of both fields is one of the important measures which we have to implement in the future.

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