Complex systems science and brain dynamics

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Brain systems with their complex and temporally intricate dynamics have been difficult to unravel and comprehend. While great advances have been made in understanding genetics, neural behavior, gray versus white matter and synaptic plasticity, it remains a particular challenge to understand how human diseases and disorders develop from internal neural level irregularities, e.g., in channels, membranes and mutations before they lead to an observable disease. The field of system biology has advanced significantly, giving rise to high expectations of tying separate biological phenomena into more expansive rational systems. Denis Noble, a pioneer of systems biology, who developed the first viable mathematical model of the working heart in 1960, has been influential in calling the community to focus on creating computer and mathematical models of organic life to interpret functions from the molecular level to that of the whole organism (Noble, 2006). Our approach to modeling the brain and its intricate, interrelated network of systems is through the mathematical computational fields of complexity and dynamical systems.

Complexity explains the emergent behavior of interacting particles and is a theoretical approach inspired by physics, which has become a basis for computational simulations. *Dynamical systems* consist of equations governing the temporal evolution of values of interacting sets of variables and parameters (Alligood et al., 1997). This fundamental mathematical field is used to model complex phenomena like biological systems and diseases (Villanueva et al., 2008), behavioral aspects of societies and spread of viruses in epidemics (Rapatski et al., 2005), as well as to describe multi-agent computer networks (Olsen et al., 2008); and gives rise to subfields like chaos theory and complex systems theory. *Complex system science*, a combination of complexity and dynamical systems, is used to interpret, analyze and characterize systems behavior. This rapidly maturing science has the potential to close gaps in our knowledge and allow us to make connections between lower level brain functions and the higher level of human senses, behaviors and disorders.

In our own work, we have recently employed complex systems science to study the loss of synchronicity in the biological clock following travel (Leise and Siegelmann, 2006). In an effort to understand circadian inter-system synchronization, we built a multistage non-linear system level model of the biological clock governed by the suprachiasmatic nucleus (SCN) in the hypothalamus – known to regulate circadian rhythm. Prior to our work, organ de-synchronicity occurring after travel and in shift work was assumed to result in differing re-entrainment rates of system components following the phase update in the SCN. Employing our model and recent data about the relative dynamical properties of organs including their free dynamics and strength of connectivity, we were able to take a detailed look at the phenomenon of jet-lag and impediments to re-entrainment that lead to jet-lag. We found that the chief source of de-synchronicity occurs when some organs advance their clocks following the SCN update, a property termed "anti-dromic re-entrainment." Based on this model, we were able to suggest applications to avoid organs advancing their clocks in opposite directions, and thus avoid hard cases of jet-lag.

In another recent study, we used complex systems science to study the dynamics of re-consolidation in memory. Re-consolidation has been recognized as a storage process distinct from the one-time loading involved in consolidation. It serves to maintain, strengthen and modify existing memories shortly after their retrieval. Problems in re-consolidation have been implicated in diseases such as post-traumatic stress disorder (PTSD), obsessive compulsive disorder (OCD), and even addiction. Part of the growing interest in re-consolidation is the hope that controlling it may assist in psychiatric disorders, such as PTSD, or even in the permanent eradication of compulsive fears. Our initial efforts to understand the process focused on the dynamics occurring during and after the continuous update of memories (Siegelmann, 2008). Further work is needed to more fully comprehend the function and dynamics of re-consolidation, to map out its processes in greater detail, and identify potential remedies to systemic problems.

Dynamical diseases (Belair et al., 1995) methods have been used to qualify changes in the normal state or dynamics of physiological systems, like those occurring in heart arrhythmia (Glass and Mackey, 1988) and in schizophrenia (Loh et al., 2007). The value of analyzing disease through the mathematical view of dynamical systems is a greater, more detailed understanding of the system, and a more precise identification of the mechanisms of disease. Dynamical systems give us the ability to model the varying parameters of a disease, its host, and the conditions surrounding it – enabling us to identify mechanisms, predict outcomes, and suggest countermeasures. By taking advantage of advances in dynamical systems, the research community as a whole stands to gain a powerful new tool set to use in acquiring a more complete, more detailed understanding of brain processes and disorders.

This Special Topic in Frontiers in Computational Neuroscience contains diverse research articles describing successful uses of complex modeling to analyze various aspects of brain dynamics: Neural population-codes, which may underlie behavioral invariance as well as object recognition (Robbe L.T. Goris and Hans P. Op de Beeck). Modeling the mammalian neocortex with new self-organizing recurrent networks that incorporate various distinct forms of local plasticity to learn spatio-temporal patterns (Andreea Lazar, Gordon Pipa, and Jochen Triesch). An algorithm to analyze multichannel recordings (Barak Blumenfeld). Self-assembly processes such as the formation of DNA and protein oligomeric structures (Eugen Czeizler and Lila Kari). Determination of synaptic weight matrices

or kernels for neural networks and fields (Roland Potthast and Peter Beim Graben). Assessing and increasing quality in binary pairwise models for studying the statistics of spike trains of neuronal populations and inferring neuronal functional connectivities (Yasser Roudi, Erik Aurell, and John A. Hertz). And a hierarchical memory model based on the collaboration of slow bidirectional synaptic plasticity and homeostatic unit activity regulation and its application to face recognition (Jenia Jitsev and Christoph von der Malsburg).

Complex system science, both mathematically and computationally, gives us the tools to dissect, quantify and analyze organic life's most complex system set: the brain. In addition to aiding diverse fields of brain research by following brain system dynamics over time, we can detect systemic changes prior to them becoming problems or diseases. Additionally, medicine today tends to approach illness with a "fix-it-when-it's-broken" mentality; using dynamical systems to analyze and monitor brain systems results in a broader, more detailed view, and one that shows changes over time. These same attributes provide the means for early identification of disease, enable preventative measures, earlier fixes, and the identification of alternative methods and strategies for remedying problems. Ultimately, using these tools to follow the dynamics of individuals may provide the best approximation of their health, and the most exact picture of when their health is affected by different agents or ameliorated by specific treatments. It is possible then, that a dynamic understanding of the complex brain will yield early disease detection, novel treatments, and individual approaches in medical sciences.

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