Robustness in Neurological Systems

13 - 15 November, 2015
Center for Philosophy of Science

ABSTRACTS

Alison Barth, Professor, Department of Biology, and Head, Barth Lab, Carnegie Mellon University

Functional Connectivity is Regulated by SOM Interneurons Spontaneous Activity

Understanding the dynamic range for synaptic transmission is a critical component of building a functional circuit diagram for the mammalian brain. We find that excitatory synaptic strength between neocortical neurons is markedly suppressed during network activity in mouse somatosensory cortex, with smaller EPSP amplitudes and high failure rates than previously reported. This phenomenon is regulated by tonic activation of presynaptic GABAb receptors via the activity of somatostatin-expressing interneurons. Optogenetic suppression of somatostatin neural firing was sufficient to enhance EPSP amplitude and reduce failure rates, effects that were fully reversible and also occluded by GABAb antagonists. These data indicate that somatostatin-expressing interneurons can rapidly and reversibly rewire neocortical networks through synaptic silencing, and suggest a critical role for these neurons in gating perception and plasticity.

Emilio Bizzi, Department of Brain and Cognitive Sciences and McGovern Institute for Brain Research, MIT

Muscle Synergies, Concept, Principles, and Potential use in Neurorehabilitation

When the central nervous system (CNS) generates voluntary movement, many muscles, each comprising thousands of motor units, are simultaneously activated and coordinated. Computationally, this is a daunting task, and investigators have strived to understand whether and how the CNS's burden is reduced to a much smaller set of variables. In the last few years, we and our collaborators have searched for physiological evidence of simplifying strategies by exploring whether the motor system makes use of motor modules, to construct a large set of movement.

The core argument for the neural origin of motor modules rests on studies of the spinal cord in several vertebral species, conducted using a variety of techniques. With these approaches, we and others were able to provide the experimental basis for a modular organization of the spinal cord circuitry in vertebrates. A spinal module is a functional unit of spinal interneurons that generates a specific motor output by imposing a specific pattern of muscle activated with a muscle synergy.

Muscle synergies are neural coordinative structures that function to alleviate the computational burden associated with the control of movement and posture. In my presentation, I will address two critical questions: 1) are muscle synergies explicitly encoded in the nervous system? And, 2) how do muscle synergies simplify movement production? I will argue that shared and task-specific muscle synergies are neurophysiological entities whose combination, orchestrated by the motor cortical areas and the afferent systems, facilitates motor control and motor learning.

Trey Boone, Department of History and Philosophy of Science, University of Pittsburgh

Temporal Organization and Robustness in Neural Systems

Neural circuits exhibit a delicate balance between sensitivity to and robustness over neuromodulatory inputs. Sensitivity to neuromodulatory inputs allows a single circuit to switch between a range of different functional states, while robustness enables a circuit to maintain stable performance of a particular function over variations in circuit parameters. Understanding the balance between sensitivity and robustness is fundamental to proper understanding neural circuit function. However, developing such understanding requires taking into account different sets of mechanisms that operate over a wide range of timescales. In particular, the biochemical mechanisms that modulate synaptic strength and intrinsic properties of cells often occur over much longer timescales than the relevant timecourse over which a circuit performs a particular function. As a result, proper understanding of both robustness and sensitivity of circuit function requires careful consideration of the temporal organization of those circuits and the processes that modulate them. The concept of temporal organization—i.e. which processes occur at what times and how processes occurring at different timescales interact—has received some attention in philosophy of neuroscience, but extant accounts—e.g. of ‘active’ or ‘dynamic’ organization in mechanistic explanation—do not seem up to the task when multiple timescales are involved. My talk will be largely exploratory. After discussing some of the basic issues of temporal organization implicated in the interplay between sensitivity and robustness, I will discuss some limitations of extant accounts of temporal organization in philosophy of neuroscience, and conclude by offering some of positive remarks about what sort of framework would be needed to address these issues.

Raffaella Campaner, Department of Philosophy, University of Bologna

Robustness Notions and Physiological Adaptability: Philosophical and Biomedical Reflections on the Neurological Basis of Disorders

Notions of robustness and invariance have recently been the objects of a pretty wide philosophical debate. In this joint paper we question whether and to which extent some philosophical reflections on the topic can profitably intertwine with reflections on the robustness of neuropsychiatric disorders as conceived of from within neurophysiology itself. As a matter of fact, the complex arrangement of causal factors bringing about, and reinforcing, neuropsychiatric disorders is in many cases still poorly understood. Such disorders lie at the crossroad of a number of disciplinary interests (e.g. physiology, psychology, neuroscience, psychiatry, genetics, epidemiology, pharmacology, etc.), which appeal to a variety of conceptual and methodological tools and whose models are supported by different kinds of evidence, which ought to be integrated, especially for explanatory purposes. With respect to this scenario, we will question whether the notion of robustness – and which notion of robustness – can be taken as a "picklock" to deal with the very idea of *disease*, its relations with the organism's overall behaviour and with its coping with changing conditions and environmental variations. Our reflections will be developed along two main lines:

- Does some notion of robustness help identifying a given neurobiological disorder over and above disciplinary-specific approaches, distinct models and ways to gather and integrate evidential data? How does the notion of "interactome" contribute to grasp the status of a disorder as a cluster of interplaying factors? Which idea of robustness does it assume and vehicle? To what extent can it – by showing overlappings and disease-disease relationships – help unravel invariant, "trans-diseases", relations?

- How does invariance relate to the intrinsically dynamic equilibrium (homeostasis) that characterizes every living systems? Which relations hold between stability of the organism and stability of the disorder, and between stability of the organism and arousal of the disorder? How does reversibility or irreversibility of a disorder impact on the robustness of a system and its capacity to adapt to changes and variations?

These issues will be tackled from both the vantage points of philosophy and physiology, looking for fruitful interactions between them and some joint rethinking of the very idea of neuropsychiatric disorder.

Mazviita Chirimuuta and Sandra Mitchell, Department of History and Philosophy of Science, University of Pittsburgh

Robustness in Contemporary Science and Philosophy

Robustness is a system-level property that allows the maintenance of function in response to external and internal perturbations. Kitano (2004) argues that, "Robustness is an inherent property of evolving, complex dynamic systems." What challenges do the study of robustness raise for our understanding of causal models, experimental protocols, and clinical practices? We will explore some of the ways robustness is characterized in biological systems generally and in neuroscience more specifically. We will present some examples to illustrate robust system behavior and the trade-offs between robustness and fragility. In particular, we will discuss the features of brain systems which make discussions of robustness particularly interesting in this area of biology. First, one of the most functionally significant features of the brain is its plasticity. The capacity of neural circuits and connections to reorganize themselves in response to new experience, and in the aftermath of damage to the brain, is what makes possible both lifelong learning and recovery from strokes and other brain injuries. Yet of course in many cases recovery is minimal or partial. A key question for advancing clinical neuroscience is to understand what the limits of the brain's robust mechanisms are, and how they can be altered through clinical manipulations. Second, theoretical neuroscientists following Barlow (1961) have often argued that evolution has worked to minimize the cost of biological information processing by reducing the number of redundant computations. This would, it seems, result in less robust systems. So an important question is how robustness in neural systems is achieved without sacrificing efficiency, and vice versa. Answering such questions would lead to insights into the general "design principles" (Sterling and Laughlin, 2015) of neural systems.

Flavio Keller M.D., Nicola Di Stefano Ph.D.
Laboratory of Developmental Neuroscience and *Istituto dell'Agire Scientifico e Tecnologico* , Università Campus Bio-Medico

Achieving Robustness in Perception Through Perception-Action Loops

To achieve perceptive stability and avoid perceptual ambiguities, perception must solve the problem of instability that arises both from changes in the external world, and from the intrinsic properties of the sensory organs. To bring just an example: if the eyes could assume different orientations for each gaze direction, it would be impossible to know whether a change in visual perception arises from a change in the world, or from a change in eye orientation. On the contrary, the eye takes always the same orientation for each gaze direction. This phenomenon, known as Donders' law, is but one of the many strategies by which sensorimotor systems solve the problem of perceptual ambiguities. In other situations, perceptive systems rely on perception-action loops to achieve stability.

One field that is very interesting in the context of robustness in perception is music: music is almost the quintessence of integration between perception and action. The human hear can tolerate small changes in the frequency of two simultaneous sounds without perceiving a change of harmony. Within a specific chord, one note is usually more critical than others for the character of the chord, and changing this note changes the harmonic character of the whole chord. In this paper we will present experimental data on the development of the discrimination between consonant and dissonant chords in children, exploiting the perception-action principle to establish when and how such capacity arises.

Arnon Levy, Department of Philosophy, Program in History and Philosophy of Science, The Hebrew University of Jerusalem

Causal Order and Types of Robustness

This talk is part of a project dealing with the notion of *causal order*. I use this term to signify two kinds of parts-whole dependence. Orderly systems have rich, decomposable, internal structure: specifically, parts play differential roles, and interactions are primarily local. Disorderly systems are aggregates of the activities of their parts, such that internal causal distinctions are of minor significance.
My focus here will be the connection between order and robustness, i.e. resilience in the face of internal or environmental perturbations. I distinguish three varieties of robustness. <u>Ordered robustness</u> is grounded on the system's specific organizational pattern, such as integral feedback or proofreading. In contrast, <u>Disorderly robustness</u> stems from the aggregate outcome of many similar parts, performing a form of trial and order on a massive scale. In between, we find <u>semi-ordered robustness</u>, wherein a messy ensemble of elements is subjected to a selection or stabilization mechanism. I'll discuss examples in each category and look at the prospects of this taxonomy to illuminate robustness across biological contexts and the relations between robustness and plasticity.

Timothy O'Leary, Marder Lab, Volen Center for Complex Systems, Brandeis University

Reconciling Variability with Robust Behavior at the Single-Neuron Level

Nervous system function depends on the electrical properties of neurons and these properties are largely determined by the types and distribution of signaling proteins, such as receptors and ion channels found in neuronal membranes and the connectivity between neurons. Perhaps surprisingly, the combination of important signaling components is found to be extremely variable even in neurons that have very stereotyped properties. How can this variability be reconciled with stable function? And what does variability tell us about the underlying regulation mechanisms in neurons? I will discuss recent theoretical work that offers simple conceptual answers to these questions and which implicates regulation, or 'homeostasis' in nervous system dysfunction as well as its robustness. Furthermore, I will argue that robust function is entirely compatible with significant variability in nervous system composition.

Acknowledgements
This work is supported by the Charles A King Trust and the NIH.