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EDITORIAL

From McCulloch–Pitts Neurons Toward Biology

Peter beim Graben · James Wright

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Traditionally, the *Bulletin of Mathematical Biology* has not published Special Issues focused on a particular scientific problem on a regular basis. A recent change in policy, coinciding with the increase in journal issues published per year, alters this tradition and this is the first such issue. The paper "A logical calculus of the ideas immanent in nervous activity" by Pitts and McCulloch (1943) is one of the most important published in this journal, and in this first Special Issue we consider some approaches to the biological implications of the great work, continuing to move toward McCulloch's own goal—an "*experimental epistemology*—to understand the mind in terms of the brain" (Arbib 1987).

McCulloch, the physician/psychiatrist and Pitts, the logician, achieved conjunction of biology and mathematics about a central issue. While the resulting lines of development have proved fruitful, the subsequent scientific history has again reflected a schism between mathematical applications and their biological aspects. Arbib (2000) identifies two main lines of intellectual descent from the 1943 paper. One line—logical operations by gated neuron-like elements—was utilized early, and to enormous effect, by von Neumann (1945), leading to the digital computer and the modern age. The other line, arising via the work of Lettvin and Maturana with Pitts and McCulloch (1959) on the frog's retina, is closely engaged with the classical methods of

P. beim Graben (✉)
Department of German Language and Linguistics, Humboldt-Universität zu Berlin, Unter den Linden 6, 10099 Berlin, Germany
e-mail: peter.beim.graben@hu-berlin.de

J. Wright
Liggins Institute and Department of Psychological Medicine, University of Auckland, Auckland, New Zealand
e-mail: jj.w@xtra.co.nz

single-cell neurophysiology, with the feed-forward neural network models of Rosenblatt (1958) and related work. This approach emphasizes piece-meal, layer-by-layer, analysis of the function of the brain in terms of local interactions among neurons. Eventually, this approach has led to local neural field theories established by Griffith (1963, 1965), Amari (1977) and others. Earlier still, a linkage with psychological theory was opened when Hebb (1949) formulated his famous hypothesis for synaptic consolidation. In that era there appeared hope that correlation networks would be developed progressively, until the brain's function was understood. This has not been achieved, opinions differ as to why this is the case, and McCulloch's goal remains elusive. An "experimental epistemology" remains both theoretically and experimentally problematic, despite the enormous progress created by advances in cell biology, in single-cell physiology, and by techniques for scanning function of the living brain.

One major reason for the difficulty is philosophical, and can be illustrated by an example from Pitts and McCulloch (1943). Developing their neuron model as a binary threshold device, McCulloch and Pitts abstracted biological properties in a particular way. They were acutely aware that this abstraction was not the only possible one (Arbib 1987). In this sense, the McCulloch-Pitts model is contextual, where one particular context, distinguishing the relevant from the irrelevant features, has been deliberately chosen by the researchers. The role of contextual information in scientific methodology has recently been investigated in the framework of *contextual emergence* (e.g. Atmanspacher 2009), and was applied implicitly in the neurosciences by Amari (1974). A recent explicit account was given by beim Graben et al. (2009). A context—e.g., an experimental situation—sets bounds in both the neural, and the phenomenal, state spaces under consideration; but in setting these bounds, contexts partition these spaces in arbitrary ways. Not every deliberately chosen context leads to descriptions in phenomenal and neural phase spaces which are "stable" in the sense that one space can be mapped to the other. A contextual description is (maximally) stable if the resulting coarse-grained dynamics is ergodic and irreducible. Therefore, the two stable descriptions are topologically equivalent and hence compatible with each other. A priori determination of contexts which permit stable identifications is not generally practicable.

Added to this contextual limitation to development of theory, are both the problem of defining mental phenomena in objective terms, and the enormous wealth of neurobiological detail. There are thus many different contexts and criteria to be considered. Advances in understanding of the individual neuron made in cell and molecular biology have opened a wide and ever-expanding, landscape, it seems. But this has not yet added obviously to our understanding of the collective operation of large neural networks. Single-cell physiology has been rigorously applied in all locales of the brain, with *in vivo* observations in almost every conceivable behavioral paradigm, yet the insight gained in this way has largely supplemented conclusions drawn by earlier generations of neurophysiologists using lesion techniques to deduce brain function from induced behavioral deficit—a procedure originating with Galen; and contextual again: one tries to understand a functioning system by means of its malfunctions. There have been exceptions to this continuity with earlier tradition. One such was the discovery of synchronous oscillation among cortical neurons engaged in cognitive and perceptual processing (Eckhorn et al. 1988; Gray and Singer 1989). These findings, as much as any others, have changed the emphasis of physiological analysis toward co-operative properties of neurons, rather than the identification of correlations of single cells with behavioral specifics.

Escape from the restrictions of study of only one or a few neurons, to deal instead with the mind-brain mapping problem at a larger scale, has been partially achieved using advanced developments of the electroencephalogram (EEG), the magnetoencephalogram (MEG), and the scanning techniques of functional magnetic resonance imaging (fMRI), and positron emission tomography (PET). A limiting factor with these methods has been the difficulty of obtaining sufficient concurrent resolution of events in space, and in time, within the brain. EEG and MEG resolve rapidly in time, but poorly in space, and fMRI and PET are limited in the reverse way (Nunez 1995). Consequently, while these techniques have offered us beautiful and more detailed images of the brain's function, interpretations of findings generally remain bound in the same terms as do single-cell and lesion-based analyses. Since a purely empirical approach will not serve, there remains a largely unfulfilled need for theoretical models to provide a scaffold for observations made by all the means mentioned above, and more. A general theory would assist us in linking together observation models, each derived for some limited context.

Ideally, such observation models need to be simple enough to be tractable analytically and/or numerically, yet complicated enough to retain physiological realism (Freeman 1975). Sadly, we do not know which physiological properties are truly the essential, nor even whether such a distinction can be made. Therefore, scientists have to make the choice: what is essential with respect to their scientific goals, their modeling aims and also to the general zeitgeist? They are embedded into one or the other epistemic context. In the case of macroscopic observation models, contextual aspects lead to different coarse-grainings of the microscopic neurodynamics that are not necessarily compatible to each other (beim Graben et al. 2009).

Obviously, then, provision of an adequate theory is a tall order to fill, and this Special Issue will not do so. Yet the following papers, we believe, tend in useful and not widely known directions toward McCulloch's goal. Interestingly, contextuality itself appears as a leitmotif through the different contributions, and overlaps between the contexts of relevance to the different papers are frequent—suggesting that a synthesis may be possible.

In alphabetical order of authors:

Afraimovich et al. use competitive mode dynamics of two coupled systems: one describing cognitive computations by stable heteroclinic sequences, the other one describing emotional context dynamics. At an abstract and general level, this offers rules for dynamics in a neural state space, sufficient to capture complex neural systems such as those envisaged by Jirsa and Stefanescu.

Galka et al. compare different algorithms for source separation of macroscopically observable neurophysiological signals such as EEG or MEG. State space modeling is compared with independent component analysis, requiring the estimation of parameters for both the hidden dynamics and for a contextual observation model, by maximizing appropriate objective functions.

Jirsa and Stefanescu derive a coarse-grained neural mass model from a large-scale neural network and prove that its dynamical characteristics are comparable to that of the large-scale network. They describe the construction of modules, each a continuum approximation of a substantial cortical neural network, and show the computational advantages of this treatment over more conventional neural networks. Their goal is the assembly of modules to approximate the brain's many specialized and interactive subsystems.

Kay and Phillips show how physiologically realistic learning rules, akin to those described by Tsukada and Fukushima, can operate within a neural field. Crucially, their account also depends upon the physiological property of synchronous oscillation as a mediator of contextual information. Distinguishing between receptive fields and contextual fields of neurons in a neural network, the authors suggest a learning scheme for synaptic weights by maximizing coherent infomax as an objective function.

Mizraji and Lin discuss different ways to deal with contextual information in neural networks. Contexts are represented by tensor product states for generalized Hebbian learning of associative memories. Incidentally, they offer the important, and re-assuring, finding that dynamic neural systems organized as associative networks have the power to execute all logical operations, as is the case for McCulloch-Pitts neurons. Thus, the move to a biologically more plausible formulation has not come at the price of loss of generality.

Tsukada and Fukushima prove the coexistence of Hebbian learning and the spatiotemporal learning rule in real neural networks. While Hebbian learning is suitable for pattern completion and generalization, the STLR exhibits some context-dependency by the ability of pattern separation.

Steyn-Ross et al. offer a way in which the fast time events observed by the EEG, and in studies of synchronous oscillation, may be linked to slower brain events observed by functional MRI. Their paper applies electrical synapses (gap junctions) as well as chemical synapses in a continuum model.

In the final paper, Wright continues discussion of continuum models of the cortex in a manner close in spirit to that of Jirsa and Stefanescu, along lines pioneered by the findings of Freeman and colleagues. The paper addresses the long-standing puzzle of the relationship of single-cell action potentials to gross EEG. In the context of directed attention, and the attaining of a stationary state in cortical activity, emergent properties analogous to those seen in equilibrium thermodynamics offer an explanation of cortical attractor dynamics and synchronous oscillation.

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