Mathematical Neuroscience

What is mathematical neuroscience? Is it simply an interdisciplinary field that aims at modelling neural processes using mathematics? Most likely this is a perfectly respectable working definition, though probably worth qualifying with the statement that it has both practical and theoretical applications in neurobiology. However, when one digs a bit deeper into the historical use of mathematics in neuroscience it may be more useful to distinguish between *computational*, *theoretical*, and *mathematical* neuroscience proper. Computational neuroscience aims to be quantitative and often involves building detailed biophysical models of neurons and networks to study specific neuronal phenomena (such as network oscillations, learning, and memory). In this field mathematics is most often used hand-in-hand with computational tools to numerically explore model behaviour. The theoretical neuroscientist is more concerned with building testable, possibly metaphorical, theories for understanding the operation of neurobiological circuits. As such theoretical neuroscience also makes use of quantitative tools, which often, though not necessarily, include mathematics and computation. So that brings us back again to the question of what is mathematical neuroscience?

Mathematical neuroscience is certainly not just the reserve of the formally trained mathematician. Rather it is an area of neuroscience where the use of mathematics is key in elucidating the fundamental mechanism responsible for experimentally observed behaviour. In illustration of this point it is worth mentioning some success stories, perhaps foremost being the work of Alan Hodgkin and Andrew Huxley on a mathematical model of the action potential (reviewed in [1]). The conceptual idea behind their work is that cell membranes behave like electrical circuits, and that the flow of ionic current in their circuit model is gated by state-dependent conductances. The great insight of Hodgkin and Huxley was to express (and subsequently fit) the dynamics of these gating variables (representing membrane channels) using the mathematical language of nonlinear ODEs. Together with Sir John Eccles, the pair received the Nobel Prize in Physiology or Medicine in 1963 "for their discoveries concerning the ionic mechanisms involved in excitation and inhibition in the peripheral and central portions of the nerve cell membrane". In essence their mathematical work describes a model of excitable tissue that remains the basis of pretty much all conductance based neural models to date.

Another notable success in mathematical neuroscience can be attributed to Wilfrid Rall, who in the 1960's developed the cable model of the dendritic tree (see [2] for a survey of his work). Dendrites are strikingly exquisite and unique structures. They are the largest component in both surface area and volume of the brain and their specific morphology is used to classify neurons into classes: pyramidal, Purkinje, amacrine, stellate, etc. Cable theory uses coupled PDEs to describes how membrane potential spreads along the dendritic branches in response to a local conductance change (synaptic input). Using his mathematical formalism, Rall showed that there is a subclass of trees that are electrically equivalent to a single cylinder whose diameter is that of the stem (near the soma) dendrite. To a first approximation, many neurons (e.g. α-motoneuron), belong to this subclass, though cortical and hippocampal pyramidal cells do not. Importantly Rall's "equivalent cylinder" model for dendritic trees allows for a simple analytical solution and this has provided the main insights regarding the spread of electrical signals in passive dendritic trees.

As a final example we turn to work on neural field equations in the 1970's, by people such as Hugh Wilson, Jack Cowan, Shun-ichi Amari, Paul Nunez and Hermann Haken (for a recent overview see [3]). These are tissue level models that describe the spatio-temporal evolution of coarse-grained variables such as synaptic or firing rate activity in populations of neurons, and often take the form of integro-differential equations. The sorts of dynamic behaviour that are typically observed in neural field models include spatially and temporally periodic patterns (beyond a Turing instability), localised regions of activity and travelling waves. The mathematical study of such equations and their solutions has proven relevant to understanding EEG rhythms, mechanisms for short term memory, motion perception and drug-induced visual hallucinations. In this latter context the use of symmetric bifurcation theory has shown that neural activity patterns underlying common visual hallucinations can be accounted for in terms of certain symmetry properties of the anisotropic synaptic connections in visual cortex (requiring the use of a novel representation of the planar Euclidean group) [4].

As well as the above exemplars of the practice of mathematical neuroscience, it is appropriate to mention some of the tools in the arsenal of the mathematical neuroscientist. It is clear that techniques from nonlinear dynamical systems theory and mathematical physics have proven useful to date. Indeed, seeded by successes in understanding nerve action potentials, dendritic processing, and the neural basis of EEG, mathematical neuroscience has moved on to encompass increasingly sophisticated tools of modern applied mathematics. Included among these are Evans function techniques for studying wave stability and bifurcation in tissue level models of synaptic and EEG activity, heteroclinic cycling in theories of olfactory coding, the use of geometric singular perturbation theory in understanding rhythmogenesis, using stochastic differential equations to treat inherent neuronal noise, spike-density approaches for modelling network evolution, the weakly nonlinear analysis of pattern formation, the role of canards in organising neural dynamics, and the use of information geometry in developing novel brain-style computations. The field is now in the healthy state where not only is mathematics having an impact on neuroscience, it is simultaneously motivating important research in mathematics. In recent years a number of high profile mathematical institutes, including the Mathematical Sciences Research Institute (Berkeley; 2004), the International Centre for Mathematical Sciences (Edinburgh; 2005), and the Centre de Recerca Matemàtica (Andorra; 2006), have all held workshops with the title "Mathematical Neuroscience". As a further indication of the vitality of the field it is noteworthy that the recently formed Mathematical Biosciences Institute (Ohio) devoted its first year focus (2002–2003) to mathematical neuroscience.

New directions of research that will have most impact on neuroscience are likely to include advances in the analysis of systems with asymmetry and inhomogeneity, and in the understanding of the role that noise, delays, feedback and plasticity play in shaping the dynamic states of biological neural networks. Precisely these topics will be treated at the upcoming "Mathematical Neuroscience" workshop to be held at the Centre de Recherches Mathématiques, Université de Montréal in September 2007. It would appear that the field of mathematical neuroscience is rife with good problems and wide open for fun to be had with mathematics, by both mathematicians and neurobiologists alike.

References

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