Mathematical Neuroscience Network

Scientific basis

"Mathematical neuroscience" here means an area of neuroscience where mathematics is the primary tool for elucidating the fundamental mechanisms responsible for experimentally observed behaviour. Drawing together the field provides the possibility of a critical discussion of the relevant experimental facts and of various mathematical methods and techniques that have been successfully applied to date. More importantly, it can draw attention to, and develop, those pieces of mathematical theory which are likely to be relevant to future studies of the brain [1]. In illustration of this point it is worth telling the story of Wilfrid Rall, who in the 1960s developed the cable model of the dendritic tree (see [2] for a survey of his work). Cable theory uses coupled PDEs to describe 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 is electrically equivalent to a single cylinder whose diameter is that of the stem 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 allows for a simple analytical solution and this has provided the main insights regarding the spread of electrical signals in passive dendritic trees. Indeed Rall's work seeded a whole new field of computational neuroscience, especially that concerned with the compartmental modelling of single neurons. As another example we turn to work on neural field equations in the 1970s, by people such as Hugh Wilson, Jack Cowan, Bard Ermentrout, 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 as well 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 [5], heteroclinic cycling in theories of olfactory coding [6], the use of geometric singular perturbation theory in understanding rhythmogenesis [7], using stochastic differential equations to treat inherent neuronal noise [8], spike-density approaches for modelling network evolution [9], the weakly nonlinear analysis of pattern formation [10], the role of canards in organising neural dynamics [11], and the use of information geometry in developing novel brain-style computations [12].

The field is now in the healthy state where not only is mathematics having an impact on neuroscience, the latter 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 held workshops with the title "Mathematical Neuroscience" (of at least three days duration). 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.

One area in which neuroscience has already prompted the development of novel mathematics is that of neurological disease associated with abnormalities in neural network synchrony. In particular, there is now a concerted attempt by the mathematical neuroscience community to uncover just how deep-brain-stimulation (a surgical treatment involving the implantation of a device which sends electrical impulses to specific parts of the brain) affects neuronal dynamics in a curative manner for Parkinson's disease [13]. This will form a sub-topic at the upcoming "Mathematical Neuroscience" workshop to be held at the Centre de Recherches Mathématiques, Université de Montréal in September 2007 (co-organised by S Coombes, with A Longtin and J Rubin). The issue of "synchrony" is a good example of the relevance of mathematics in neuroscience, where it is perhaps more well known for its discussion in relation to the binding problem [14] and brain rhythms in general [15]. Indeed, there are many current advances in neuroscience that have identified further need for mathematicians involvement. For example, one area that a Mathematical Neuroscience Network can make a significant contribution to is the recent discovery that cannabinoids can desynchronise neuronal assemblies (without affecting average firing rates), and that this effect correlates with memory deficits in individuals [16]. Another is the discovery of *grid cells*, which fire strongly when an animal is in locations that tessellate the environment in a hexagonal pattern [17]. The effect is believed to be crucially involved in self-motion based map generation of the spatial environment and the challenge remains as to how information about location, direction, and distance is integrated in the grid-cell network. As a final example we mention event-related desynchronisation/synchronisation (ERD/ERS), associated with a decrease/increase of the amplitude of the EEG α rhythm, and in particular how performing certain motor tasks can lead to patterns of "focal ERD/surround ERS" [18]. Here it remains an open question as to how such patterns of spatio-temporal activity are generated and whether they are critical for brain computation or are merely epiphenomena. The tools of modern applied mathematics are ideally suited for such challenges, and indeed are currently being used to great effect by physical and life scientists broadly interested in the development of a framework to underpin the understanding of complex systems in general.

The Network

Despite growing UK activity in both computational and theoretical neuroscience as evidenced by the Leverhulme Trust theoretical neuroscience network (LTTNN)[1], and the newly established UK Neuroinformatics Network[2] (UKNN), there is a lack of UK activity in promoting the direct use of mathematics in neuroscience. Moreover, both the LTTNN and UKNN Networks have already identified the necessity for far greater input from mathematicians in tackling problems arising in current neuroscience research. Now is an ideal time to create a mathematical forum to support such needs. Importantly a UK Mathematical Neuroscience Network would be able to address fundamental neuroscience problems, such as the ones described in the paragraph above, by developing the analysis of systems with asymmetry and inhomogeneity, understanding the role that noise, delays, feedback and plasticity play in shaping the dynamic states of biological neural networks, developing techniques from statistics and information theory for the analysis of neural coding, and contributing further to mathematical models of neuronal development. By working with the LTTNN and UKNN we will also have a direct conduit to the wider community. In particular, the LTNN already has a strong biological and clinical component and solid links with groups involved in the brain recording technologies of EEG, MEG, and fMRI. Importantly, the UKNN is well placed to identify the hot problems where mathematical neuroscientsists can have the most impact.

[1] http://theoreticalneuroscience.org.uk/
[2] http://www.neuroinformatics.org.uk/

Initial membership

To tackle the important future directions for neuroscience research described above necessarily requires the correct mix of skills. A substantial body of UK researchers have already given their enthusiastic support for the establishment of a Mathematical Neuroscience Network and have agreed to be core members. We list them here.

- **Cardiff University**: Prof. Vincenzo Crunelli & Dr Stuart Hughes (School of Biosciences) – electrical activity in the thalamocortical system underlying consciousness, sleep and absence seizures.
- **Heriot-Watt University**: Dr Gabriel Lord – Modelling in neuroscience, applied computational mathematics, stochastic differential equations.
- **Imperial College London**: Dr Simon Schultz and Dr Mauricio Barahona (Neural Computation Research Laboratory) – Computational neuroscience, information theory, neural coding and nonlinear dynamical systems.
- **University of Bristol**: Dr John Terry (Engineering Maths) – Dynamical systems, time-series analysis, delay equations, mathematical models of EEG. Dr Rafal Bogacz (Computer Science) – Computational neuroscience, neural bases of decision making and recognition memory.
- **University of Cambridge**: Dr Hugh Robinson (Development and Neuroscience) – Synaptic mechanisms, spike generation in cortical neurons, dynamical types of cortical neuron, development of conductance injection. Dr Stephen J Eglen & Dr Jonathan Dawes (Department of Applied Mathematics and Theoretical Physics) – Development of the nervous system, and bifurcation theory for systems with symmetry, pattern formation.
- **University College London**: Prof. Peter Dayan (Gatsby Computational Neuroscience Unit) – Mathematical and computational models of neural processing, representation and learning. Dr Zhaoping Li (Psychology) – Computation in biological systems, visual attention, sensory coding, nonlinear neural dynamics.
- **University of Edinburgh**: Prof. David Willshaw – Modelling of the development and functioning of specific neural systems. Dr Mark van Rossum – Mathematical and computational neuroscience, synaptic plasticity, noise in neural systems, modelling of the retina and sensory systems.
- **University of Exeter**: Prof. Peter Ashwin (Computer Science and Mathematics) – Bifurcation theory and dynamical systems, coupled oscillator dynamics and its applications to neural computing.
- **University of Leeds**: Dr Alastair Rucklidge (Applied Mathematics) – Pattern formation, bifurcation theory for systems with symmetry, dynamics of networks of coupled cells.
- **University of Manchester**: Prof. David Broomhead (School of Mathematics) – Dynamical systems and mathematical biology. Dr Stefano Panzeri & Dr Rasmus Petersen (Computational Neuroscience) – representation and transmission of sensory information using information theory and computational models.
- **University of Newcastle**: Dr Marcus Kaiser (Computing Science) – complex networks, error-tolerance, structure, and function of biological networks. Dr Stuart Baker (Institute of Neuroscience) – neural control of movement, oscillations and the role of synchronous neural activity in information processing, spike train analysis.
- **University of Nottingham**: Prof. Stephen Coombes, Dr Markus Owen & Dr Paul Mathews (School of Mathematical Sciences) – Mathematical neuroscience, nonlinear dynamical systems, pattern formation, bifurcation theory for systems with symmetry. Prof. Charles Marsden (School of Biomedical Sciences) – Neuroimaging, Molecular Neuroscience & Neuropharmacology.

- **University of Oxford**: Dr Wyeth Bair (Physiology) – computational modelling and electrophysiology to study neural coding and cortical circuitry in the visual system.
- **University of Plymouth**: Prof. Roman Borisyuk & Dr Thomas Wennekers (Centre for Theoretical and Computational Neuroscience) – Synchronisation-based neural network models of cognitive functions, dynamics of spatio-temporal receptive fields, synfire chains, Hebbian cell assemblies.
- **University of Sheffield**: Dr Kevin Gurney & Dr Mark Humphries (Adaptive Behaviour Research Group) – Computational models of action selection, information theoretic models of neurons, spike train analysis techniques, neural substrate of decision making, neural inspired robotics.
- **University of Surrey**: Prof. Björn Sandstede (Mathematics and Statistics) – dynamical systems, ordinary and partial differential equations, dynamics of patterns, nonlinear waves, symmetry in dynamical systems.
- **University of Warwick**: Prof. Jianfeng Feng & Dr Yulia Timofeeva (Computer Science) – Computational neuroscience, stochastic and deterministic dynamical systems, biological and optimal control of Parkinson disease, dendritic modelling. Dr Magnus Richardson (Systems Biology) – Synaptic plasticity, network dynamics, subthreshold resonance. Prof. Robert MacKay & Dr Markus Kirkilionis (Mathematics) – Dynamical systems, complexity science, and mathematical and computational biology.

The Network will be flexible, allowing new members to join as its profile is raised.

Objectives

The Network will provide a focus for the use of mathematical approaches to problems in the applied Neurosciences. Importantly the Network will allow and encourage more UK mathematicians to engage in fundamental neuroscience and at the same time tackle substantial mathematical challenges that will be of broader scientific interest to the nonlinear and complex systems community. By maintaining close links with the UK Neuroinformatics and Theoretical Neuroscience communities the Network will be ideally positioned to contribute to areas including neural engineering, neuro databases, applications to clinical data, imaging technologies, and other areas where the need to make a bridge from the maths community to the neuroscience community can be identified.

Activities & Organisation

The Network will comprise the core members listed above with a steering committee consisting of Prof. Coombes (chair), Dr Timofeeva, Prof. Willshaw, Dr Terry, and Prof. Marsden. As well as his research strengths in the mathematics of developmental neurobiology Prof. Willshaw is well known in his role as coordinator of the UKNN, thus providing us with a bridge to the wider neuroinformatics community. Likewise Dr Terry is not only known for his work on neural field models he is coordinator of the LTTNN, and will act as a liaison to the biological and clinical neuroscience communities. As director of the Nottingham Institute of Neuroscience[3] Prof. Marsden is ideally suited to ensuring that the Network focusses on areas of research that will have the greatest impact in other areas of neuroscience.

The Network will have an annual meeting of three days consisting of core members, registered participants and invited speakers, together with a one-day training workshop just beforehand. Reduced fees will be offered to PhD students and post-docs. Throughout the year we envisage running one-day hot-topic workshops hosted by core members. The remainder of the Network activity will be based around short collaborative visits. Working on a 3-month review cycle, funds will be allocated (by the steering committee) with priority to those without other financial resources to pursue a novel pairing of skills.

[3]http://www.nottingham.ac.uk/neuroscience/

Before the first annual meeting we will run a two-day meeting at Warwick (in Dec 2007) comprising core members and representatives from the Neuroinformatics and Neuroscience communities. As well as presentations to seed further research collaboration ideas there will be panel led discussions on topics including i) identification of remaining areas where math–neuroscience bridges need to be built, ii) the staging of hot-topic and training workshops, and iii) the evolution of the network.

The structure of the first annual meeting has already been planned and will follow quite closely that of the three-day Mathematical Neuroscience meeting (comprising seventy participants) organised by Prof. Coombes and Dr Lord in Edinburgh 2005[4]. Again this will be in Edinburgh (Mar 2008) and will make use of the excellent services offered by the International Centre for Mathematical Sciences. Our current list of provisionally accepted international speakers is: P Bressloff (Utah, USA), A Longtin (Ottawa, Canada), D Terman (Ohio, USA), D Liley (Melbourne, Australia), D Pinto (Rochester, USA), B Doiron (Pittsburgh, USA), R Curtu (Brasov, Romania). Remaining speakers will be drawn from the UK maths and neuroscience community after discussion at the first Network meeting. In order to minimise administrative overheads we envisage running the proposed training workshops in conjunction with the annual meetings. The first of these will be: "An introduction to Mathematical Neuroscience" (with lectures by Prof. Coombes, Dr Timofeeva and some of the invited speakers from the main meeting).

By having available a ring-fenced amount for hot-topic workshops the Network will be able to react quickly to the need to discuss important emerging areas of mathematical neuroscience. One initial topic requested by the Edinburgh group for discussion is on scale-free dynamics (mirroring a recent event at the Computational Neurobiology Laboratory at the Salk Institute). We will view support from 50% of the core membership as sufficient to trigger the running of a workshop within any one year and do not expect to run more than three a year.

The PI and co-I will take overall responsibility for administering the funds of the Network, running the first meeting at Warwick and the first Annual meeting in Edinburgh. They will also ensure that information about Network activities is regularly circulated so that the group as a whole can monitor Network evolution and ensure that cliques do not emerge. The running of other annual events, hot-topic workshops and training workshops will be organised in conjunction with members of the core.

Plans for dissemination

Beyond dissemination by annual meetings, hot-topic and training workshops, and collaborative visits we will manage a Network web-site and a mailing list. This will be used to advertise and promote activities of the network, make available collaborative work (in the form of both code and publications), and material associated with training workshops. Some of the core members already have experience running summer schools and training workshops. For example, Edinburgh (with its Doctoral Training Centre in Neuroinformatics) has run very successful summer schools[5] teaching a mix of modellers and experimentalists. In particular such workshops would allow for dissemination of results on new topics, directions, and techniques that are not covered by textbooks along lines of the events being run by the Surrey group[6]. We will work with Biomed Central (the open access publisher) to establish a Journal of Mathematical Neuroscience. This will provide a natural forum for publishing scholarly research on the types of problems that will be considered by Network members and furnish a lasting contribution to the field well beyond the lifespan of the Network. Any mathematical tools that are developed specifically for the analysis and modelling of neuroscience data will be made widely available via the CARMEN

[4]http://icms.org.uk/archive/meetings/2005/neuro2/index.html
[5]see http://anc.ed.ac.uk/school/
[6]see http://www.maths.surrey.ac.uk/personal/st/B.Sandstede/

GRID infrastructure. CARMEN[7] is an EPSRC e-Science pilot project that will officially launch in April 2007.

Potential for collaboration

As can be seen from the quality of people already signed up to our provisional members list, the potential for collaboration between scientists with varied research skills on areas of common interest in mathematical neuroscience is very strong. By offering mathematical support to the UK neuroinformatics and theoretical neuroscience communities we will be able to develop large collaborations that would ultimately allow those more distant from mathematics, and in particular neurologists, to benefit from more focused UK research in mathematical neuroscience.

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