# Does Computational Neuroscience have a future in helping to understand how the brain works ?

Computational Neuroscience Coursework.
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October 22, 2002

An understanding the complex structures of the central nervous system requires the integration of many different scientific disciplines and descriptive levels. Computational Neuroscience (CN), as a specific computational modeling approach and as well as a general ethos is ideally suited to expediting integration this along both axes. A necessary prerequisite, however, is the development of a computational infrastructure to enable cross-fertilisation of data, as well as modeling and experimental methods.

## 1 Introduction

In the latter part of the last century, the field of Neuroscience has made unprecedented advances in our understanding of the brain. However, many unanswered questions remain, and in fact, knowing what questions to ask is a fundamental issue. Progress is advanced by continually defining new and difficult yet tractable problems. A list of important and difficult problems that have been currently earmarked for neuroscientists can be found at http://www.hirn.uni-dusseldorf.de/~rk/hilbert.htm. A unifying feature of these current problems is that they address fundamental structure-function relationships (ie relationships between morphological, physiological and behavioural aspects of information processing in nervous systems). For example, synaptic mechanisms of information storage. The nature of these problems requires integration both horizontally, across the various sub-disciplines of neuroscience, and vertically across different levels of description (molecular, cellular, network or organismic). It is argued that CN, both as a computational modeling approach and mental attitude, is key in the current climate, as it offers the potential for integration across both these dimensions.

## 2 CN as a computational modeling approach

For decades, CN has employed models across many levels of description: from the classic Hodgkin-Huxley equations, enabling membrane properties of the single neuron, to connectionist approaches that enable exploration of the dynamics of massively interconnected large-scale networks. Objections to these early models were aimed at their over-simplicity and neglect of physiology.

The latter objection can perhaps be most strongly made to connectionist models, where the single neuron is little more than a binary device. The swift rise and fall of connectionism is perhaps indicative of an overenthusiastic, under- uniformed trend. Although there has perhaps been a dip in both enthusiasm and funding since the 1980 'connectionist boom', this should not be seen to undermine the approach. An important contribution of neural network modeling was to negate the usefulness and arguably conceptual necessity of the software/hardware dualism in CN [4]. The passing of this 'modeling trend' is in some ways beneficial for the discipline, as the focus on 'computational' aspect of the approach is being balanced by a renewed interest in 'neuroscience'.

More fundamental criticisms note the incompatibility of the reverse engineering of CN with the fact that the brain exists as a product of evolution, not engineering. However, various areas of neural research are not amenable to solely experimental methods, and benefit greatly from this alternative approach. For example, computational modeling is essential in developing an understanding of the effect of subtle cellular changes on the macroscopic function of neural networks. Current work focuses on models of the activities and interactions of cells releasing the neuromodulators and their roles in behavioural and cognitive functions. (Neural Networks special issue 2002). Another crucial application is that of sub cellular models of information processing. Although, there is currently a deficit of models, the technical feasibility and scientific promise of such models have been demonstrated. [7]

In advancing understanding of structure-function relationships modeling is as essential as laboratory experimentation. Recent approaches such as De Schutter's [5] 'experiments in computo' are beginning to blur the boundaries between experimental and computational studies. He proposes a basic similarity between the two approaches, building realistic neuronal models for generating testable hypotheses with significant predictive power. Such advances in methodology together with the increasing complexity of computational methods promise imminent achievementf for computational neuroscientists in areas previously dominated by an experimental approach.

"The models are becoming complex enough to represent the electrical and chemical processes going on in brain tissue" Ellsiman, M. in [10]

This increase in complexity is accompanied by an increase in the dependency on experimental data. In the light of criticisms of biological neglect, this is a positive advancement. However, a frustration exists in that the necessary neurobiological data is not always readily available. A central problem is succinctly expressed [3] as 'the tyranny of the representative neuron': space restrictions in printed journals prevent publication of complete data sets, thus 'representative' neurons are described and erroneous or inexplicable results omitted. However, the selected neurons are arguably most representative of experimenter expectation and provide no information regarding the range or variance of responses. Full data and details of experimental procedures (such as recording place), are omitted, but it is precisely these details that are needed in the development of complexity computational models.

"It is useless to theorise about the brain without empirical data to shape one's modeling; however, empirical data can have little meaning without concepts and hypotheses to shape one's experiments". [1]pg 41.

If understanding of the brain is hindered by lack of empirical data to inform models, there is concomitant lack of theory to shape experimentation. Beside the practical limitations in financial and time costs of quantitative experiments, it has been suggested that systematic examination of cause and effect may have reached its potential in some areas. For example, the approach has been very successful in understanding the function (though not mechanisms) of V1 and MT, but have little notion of the other 36 visual areas. The parameter space is simply too large to be explored in this manner. The receptive fields of V1 can be described by relatively simple stimulus parameters, but even characterization of the complex fields in the inferotemporal cortex remains elusive under the traditional approach. Theory is essential for guiding experiments. Whilst neurobiologists are now accepting its' necessity the tradition of hostility toward theory means there is no established ground for theoretical development.

It seems palpable that the integration of experimental approaches and the theoretical models of CN may provide fertile ground for the growth of overarching theories. However, there is a bi- directional lack of communication between theoreticians and modelers. As mentioned above problems in experimental reporting techniques, hinder the development of neurobiologically accurate models, perpetuating experimentalist's skepticism of the approach. Similarly, lack of presentation standards in the modeling literature, as well as the fact that models with many key parameters are naturally prone to error, make it difficult to replicate experiments. This does nothing to encourage the already cynical experimenters to consider seriously any possible theoretical insights provided by the model. These pragmatic difficulties have been articulated repeatedly in the literature over the last decade [3][2], and efforts to remedy the situation, although slow are emerging. (see below)

## 3 CN as an Integrative Neuroscientific culture

The need to unite experimentalists and theoreticians epitomizes the need for a more general integration of the various sub-disciplines of neuroscience. This is perhaps more crucial than ever before as the investigation of currently earmarked structure-function relationships demand an interdisciplinary approach. The increasing number of collaboratorally authored articles in top neuroscientific journals, as well as the current increase in funding for co-operative projects [6], indicate a shift the appropriate direction. This has been realised in part, by the acceptance of broader spectrum of methods within the traditional disciplines. (e.g. anatomists applying molecular approaches, electro-physiologists embracing cell staining and network reconstruction and neuropsychologists using pharmacological manipulations in functional imaging). Whilst the merging of traditional approaches is encouraging, it bears problems in the early stages: communication is hampered by contrasting educational backgrounds, which may also bias opinions about what constitutes a key problem or its solution. In biological areas of science, where discovering the right questions is as challenging as finding the answers, this is a potentially significant predicament.

The solution lies in an integration at all levels - of ideas, education and administration - within a strong integrative neuroscientific culture. "Computational Neuroscience is representative of such an integrative culture as it is located at the crossroads of all neuroscientific disciplines across all levels of description combining empirical and theoretical approaches." [6]. As the contributing disciplines and subjects of study develop, CN constantly adapts, adjusting subjects, concepts and techniques. More than a computational discipline, CN can perhaps be conceived as a mental attitude.

Whilst CN may itself exists as an exemplary integrative approach, the collaboration necessary for the advancement of our understanding of the mind will be impeded until the practical communication problems are overcome. Efforts are being made toward this end in Europe in the form of Forums, workshops (http://itb.biologie.hu-berlin.de/neurinf98.html), creation of mailing lists (Comp-Neuro: cneuro@bbb.Caltech.edu), and comprehensive informative web sites (http://www.hirn.uni-duesseldorf.de˜ rk/cneuroeu.htm). However, Europe is arguably behind the U.S. where key projects are underway to develop a strong computational infrastructure including data dissemination and standardisation of modeling techniques.

## 4 Development of a computational infrastructure

The NCMIR has been collaborating with labs across the United States on various projects aimed to advance data collection, distribution and analysis and raise the sights of CN. Several leading neuroscience groups are working on a federating brain data project, aimed at developing a database focused on the structure and function of invertebrate nervous system. Other projects aim to facilitate the sharing and transmission of data e.g. the Neuroscience Data interchange System (Centre for Computational Biology, NCMIR, and labs at UCLA and Washington

University).

Another facet of the NCMIR thrust area is the Neuron Modeling Project. Tools such as GENESIS (GEneral NEural SImulation System) encourage confederation between labs and across disciplines. GENESIS is open-source theory-neutral software that models realistic systems at all levels: from subcellular biophysical mechanisms through single neurons and large-scale networks to entire neural systems. Models are based on details of relevant neuroanatomy, enabling the use of existing experimental data as constraints for model parameters. The popularity and extensive use means that this tool not only provides a flexible modeling platform, but also defines a community of investigators able to make their ideas about neural function intercomparable and quantifiable. Another component provides access to databases of existing neural models, fostering models sharing among neuroscientists, and enhancing accessibility of the accumulated knowledge. Such databases together with projects such as the federating brain data, suggest the possibility for global access to vast data caches. Such advancements are the necessary first step in the integration of the many sub-disciplines of neuroscience, a necessary precursor to development of neuroscientific theories and advancement of our understanding of the brain.

## 5 Conclusion

Increases in the complexity and physiological accuracy of the models of CN are producing promising insights into the structure and function of the central nervous system. However, the full potential of these models can only be achieved through the construction of an infrastructure that enables communication with the experimental approaches. CN is also well placed to contribute toward theoretical development. This also relies on an infrastructure and culture that fosters cross-fertilisation of ideas and data. Kotter [6] argues that the ethos of CN itself may help to instigate just such an integrative community, however in Europe in particular the practical problem of information sharing must be overcome. CN has a future in advancing our understanding of the brain by direct application of the increasingly detailed and physiologically relevant models: indirectly, as a flagship approach, it is currently of central importance in leading the crucial integration of the neuroscientific disciplines.

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