Computational Neuroscience, from Multiple Levels to Multi-level

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Abstract

Despite the long and fruitful history of neuroscience, a global, multi-level description of cardinal brain functions is still far from reach. Using analytical or numerical approaches, *Computational Neuroscience* aims at the emergence of such common principles by using concepts from Dynamical Systems and Information Theory. The aim of this Special Issue of the Journal of Physiology (Paris) is to reflect the latest advances in this field which has been presented during the NeuroComp08 conference that took place in October 2008 in Marseille (France). By highlighting a selection of works presented at the conference, we wish to illustrate the intrinsic diversity of this field of research but also the need of an unification effort that is becoming more and more necessary to understand the brain in its full complexity, from multiple levels of description to a multi-level understanding.

1 Computational Neuroscience

As experimental tools are providing a better and more precise insight into the neural activity, the vision that we gain about brain functions is becoming more and more puzzling. In fact, we face the enormous diversity of neural cells, the intricacy of the connectivity patterns, the diversity of signaling mechanisms as well as both non-linearity and non-stationarity of individual responses. All this contrasts with the apparent noisiness of the neural activity and the intriguing self-organizing

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properties of the nervous system at its different levels of description. Thus, the brain appears as a complex ensemble for which general organizational and structural principles, linking the microscopic to the macroscopic scale, are still missing. Therefore, the Neuroscience community is constantly in needs of new insights to build a comprehensive and global view of brain functions.

To achieve such an unprecedented effort, the Neuroscience community is widely opening the door to scientists from the fields of physics or applied mathematics. By doing so, new standards and corpus of knowledge are keen to emerge before being popularised among biologists. Formal concepts are imported from various fields, namely artificial vision (mass action and reaction-diffusion equations), non-equilibrium physics (attractor, multi-stability and energy functions), artificial intelligence (probabilistic inference, artificial neural networks, theory of decision) or engineer sciences (backward and forward models, signal processing, robotics). *Computational Neuroscience* has emerged from these multi-disciplinary efforts.

The core approach of Computational Neuroscience is devoted to model brain functions in terms of *information processing* (Sejnowski et al., 1988). Despite a great diversity in neural structures, there is growing evidence that most of them share some common computational principles. In this respect, Computational Neuroscience differs from other functional approaches, such as Cognitive Neuroscience (which remains at the phenomenological level), functional brain imaging (giving functional schemes in terms of large scale dynamical interaction patterns), or biophysical models of the nervous system (looking at the scale of the single cell and/or small networks). The frontier is of course not strict between those different views. On one hand, notions which are rooted to the direct observation of biological activity have raised considerable interest in Computational Neuroscience because of their direct link with key concepts of information processing concepts. We can cite, among other, concepts such as “tuning curves” and “receptive fields” (Hubel and Wiesel, 1962), “phase precession” (O’Keefe and Recce, 1993), “rank-order coding” (Thorpe et al., 1996), “spike-timing dependent plasticity” (Bi and Poo, 1998), “high conductance states” (Destexhe A and Pare, 2003) or “feed-forward inhibition” (Wehr and Zador, 2003). On the other hand, there is a handful of new notions and tools which have been forged by Computational Neuroscientists and which are now popularized in neighboring neuroscience fields, such as, for instance, the notions of “itinerant dynamics” (Tsuda, 1992), “balanced networks” (van Vreeswijk and Sompolinsky, 1996), “sparse coding” and “over-complete representations" (Olshausen and Field, 1997) or "probabilistic population codes" (Pouget et al., 2003). This is one objective of this special issue to illustrate this fruitful handshaking between computational and "experimental" neurosciences which can arise at many different complexity levels of organization, from small networks to language processing.

2 The NeuroComp workgroup in France

Since 2005, the "NeuroComp" workgroup has done a significant effort to identify and structure a community from the different research teams having an activity in this field in France. It offers a centralized platform[1], with a list of active research teams, and gathers related information such as reference papers, softwares, databases, training, conferences or job opportunities. A scientific event is organized every year to foster the development of collaborations within the community, encouraging interdisciplinary exchanges between teams within Neuroscience, Information science, Physics, Statistics, Robotics. In particular, even if the focus is on activities in France, the NeuroComp conference is open to international submissions. A role of NeuroComp is also to promote computational neuroscience within the french education and research institutions. For instance, NeuroComp has contributed to the recent PIRSTEC initiative[2] supported by the *Agence Nationale de la Recherche*, the main funding agency for fundamental and applied research. This contribution highligh the links to be developed between Computational Neuroscience and Cognitive Sciences. Thus, the goal of the "NeuroComp" workgroup is not only to direct research initiative towards modeling higher cognitive functions but also to build new bridges between fundamental research in cognitive sciences and technological and industrial R&D.

The 2008 edition of the NeuroComp conference attracted about 180 participants from France and abroad, allowing wide and fruitful exchanges among the community. The peer-reviewed selection process, based on 6-pages abstracts, allowed to propose a scientific program made of 15 contributed talks and about 50 posters[3]. The key issues of the field were presented by four invited keynote speakers: Ad Aertsen (Freiburg, Germany), Gustavo Deco (Barcelona, Spain), Gregor Schöner (Bochum, Germany), Andrew B. Schwartz (Pittsburgh, USA). Two thematic workshops, one on brain-machine interfaces, the other on com-

[1] http://www.neurocomp.fr
[2] http://www.agence-nationale-recherche.fr/PIRSTEC
[3] These abstracts may be browsed on a dedicated preprint server http://hal.archives-ouvertes.fr/NEUROCOMP08.

putational vision concluded the edition.

To give a larger echo to the event, the NeuroComp committee, thanks to the editors of the Journal of Physiology (Paris), proposed to carry out a special issue for the most original contributions to the conference. Authors were asked to submit an extended version of their work. From the 13 full papers, 10 papers were selected out thanks to a 2-stage peer-reviewed process to build up the present issue. However, note that it is not a mere compilation of the best contributions to the conference. Compared to the respective abstracts, these are complete rewritings that contain new material and developments in order to scale them to full-size papers standards. Although a majority of the presented papers come from French teams, this issue is neither expected to give an overview of the all research tracks taking place in France. It rather aims at offering a selection of some significant advances recently carried out in the field.

3 A contextual presentation of the selected contributions

The contributions presented in this issue may appear diverse in both their topic and methodology and it is necessary to introduce them within a more general point of view, rooted in the historical context of the field. In fact, although recently identified as a distinct research track, the conceptual tools manipulated by Computational Neuroscience are the successors of many attempts implying the introduction of mathematical formalisms into the field of Neuroscience.

First to be mentioned is the description of the brain as a logic machine, similar to a logical circuit (McCulloch and Pitts, 1943) or a *digital computer* (von Neumann, 1958), though it has finally revealed to be ineffective. In fact, the physical substrate supporting cognition strongly differs from the computer both in its structure (i.e. its organization relies on decentralized and reconfigurable circuits), and in its function: a vast majority of the brain operations have little to do with the theory of logical reasoning. Even considered relevant to some point until the late nineties, the Turing computer metaphor is almost abandoned nowadays at the profit of concepts coming from theoretical physics, applied mathematics or statistics. The historically closer concept to have gained a large echoe in the field is *Shannon entropy* (Shannon, 1948) which was proposed in the forties as a measure of the total amount of information transiting through a physical channel. In Neuroscience, such typical channels are, for instance, a synapse, an axon, or whole populations of neurons. Derivative concepts such as Kullback-Leibler divergence or cross-entropy of a series of spikes is similarly offering quantitative bounds on the total amount of information a spike train can handle. The paper of Cessac et al presented in this issue offers a good overview of the main conclusions that can be drawn out of this family of concepts.

Many of the conceptual tools developed in the eighties and nineties in the *Neural Networks* community have proven to be relevant metaphor for brain processing, such as the stability/plasticity trade-off (Carpenter and Grossberg, 1987), the principles of parallel distributed processing (Rosenblatt, 1962) and distributed representation (Hopfield, 1982), the definition of main network architectures (such as feed-forward, lateral or recurrent) or the notion of self-organizing maps (Kohonen, 1982). All of those models have primarily been designed for other purpose than biological modeling. They have indeed no straightforward relationship with the nervous system, but can serve as a metaphor of the plasticity processes taking place in the brain. In particular, they should help in identifying the structural constraints that a physical substrate undergoes when the learning of a new item is imposed. Notions like the loading capacity, over-learning and forgetting are addressed by these sorts of models. The paper of Glotin et al presented in this issue illustrates this approach by comparing real learning curves with artificial ones obtained on simple ART neural network.

From the electrical engineer perspective, the brain is a complex device that is to be “back-engineered” in order to extract and identify the different functions at work. Under this approach, the specific nature of the components are not important, only the (input/output) relationship between the different components matters, in order to maintain the system between the bounds of some viability domain (Wiener, 1948). This approach has of course a long history in various fields. When used in brain modelling, the emphasis is put on the physical constraints (the so-called “embodiment”) and the fundamental and archaic orientation of nervous activity towards production of appropriate postural compensations, steering movements and locomotion. From this perspective, the paper of Portelli et al in the present volume gives the principles of an autonomous flying pilot whose control system is inspired from the brain of a fly.

Many advances in the field of nonlinear *dynamical systems* have proven to be effective at describing large populations of interacting neurons, the so-called “neural assemblies” (Hebb, 1949). The notion of attractor neural network has been popularized by Hopfield (Hopfield, 1982) which opened the way to many fruitful contributions of dynamical physicists to the domain. It is commonplace now to identify the field of Computational Neuroscience to a “dynamical system” oriented description of brain activity. The principles of dynamical systems are indeed relevant at different places, for giving a synthetic description of intricate EEG or fMRI signals in terms of chaotic attractors, long range synchronization, neural fields and other “mean field” descriptions. The paper by Chemla and Chavane gives examples of this approach by proposing different scales of analysis for identifying the sources of optical imaging signals. On the basis of computer simulations, the paper by Voges and Perrinet explores the parametric domain under which synchronous or asynchronous activities are made possible under various connectivity patterns between large populations of randomly coupled neurons.

The *signal processing* approach (including adaptive filtering, kernel-based decomposition and Bayesian inference) is another dominant field of Computational Neuroscience. Close from the machine learning and artificial vision framework, it addresses the question of how the brain may capture the principal features of its environment from a statistical point of view. Finding and describing such an extraction process and confront it to real brain activity may facilitate the understanding of the real underlying processes. Akin to this approach, the paper by Beck and Neumann explores how the form and motion pathways may interact in the first steps of high-level visual processing, while Raudies and Neumann address the question of transparent motion detection and processing.

The intrinsic characteristics of neuronal circuits also raise interesting computational issues. The microscopic organization of the neuronal substrate suggests various roles played by different classes of cells. *Computer simulation* of physiologically inspired neuronal models may allow to decipher the complex interaction of electrical and chemical signals and identify elementary mechanisms of feature extraction and decision making. In this perspective, the paper of Hugues and José addresses the question of the interaction between pyramidal cells and interneurons in V4 visual processing. Such numerical simulation are also important to study synaptic plasticity and its implication for neuronal coding, adaptation and memory. Since, intrinsic mechanism of synaptic plasticity are still not fully deciphered, computer simulations can give some cues about the putative large scale effects of the local plasticity mechanisms. Along the same lines, the contribution of Baroni and Varona analyses the role of intrinsic cell’s properties in shaping the receptive field of neurons with spike-timing dependent plasticity. In the field of electrophysiological studies, fast hardware simulations now allow to directly (and reciprocally) stimulate biological cells with realistic artificial signals. The paper of Boussa et al gives an insight in this type of work by studying the effect of artificial self-inhibition in cultured neurons.

4 Conclusion

Computational Neuroscience is intrinsically an integrative approach generating multiple interactions from biology to electronics, from *in vivo* to *in silico*. In the long-term scale, it is foreseen to propose major advances in three principal domains. First, even if a full suppletion of large neuronal populations seems out of reach at the present stage, a better understanding of brain processes will allow to build better interface devices to compensate for motor or sensory deficits (brain-computer interfaces, hybrid wet- and hard-ware devices). A second objective is to implement realistic simulations of the operations taking place in the brain. In this perspective, computer simulations of macroscopic brain activity could help in understanding the effect of focal lesions as well as allowing to explore the putative effects of of new drugs and treatments. Third, a better understanding of the key principles that make the brain learn and adapt itself over time could potentially pave the way to a new generation of artificial autonomous devices and robots but also to new ways of thinking about computational architectures for future computers.

As an emergent field, Computational Neuroscience has recently benefited from substantial institutional support and some international institutes have emerged to promote a coordinated development (INCF in Stockholm or Bernstein centers in Germany). This recent development is nonetheless rooted in the last 60 years history of information science and many of the research work enrolled under the “Computational Neuroscience” flag have a rather diverse conceptual background. Efforts to unify the theoretical basements are still to be tackled. The blooming of community based efforts in modeling (Davison et al., 2008) and the important flow of new students are encouraging signs that significant advances should take place in the future and that a common language may emerge from these scientific exchanges. This common language should finally allow to blend its original multi-disciplinary origin and to step over the different levels at which the brain is currently studied, from multiple levels to multi-level.

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