NeuroMat RIDC Proposal – Goals for the first two years

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The mission of the Center is to develop the new mathematics needed to construct a Theory of the Brain accounting for the full experimental data gathered by neuroscience research. The long-term objective is to understand and explain complex neuronal phenomena, with focus on plasticity mechanisms underlying learning and memory, neurorecovery and adapted rewiring. This calls for the development of a new approach —*neuromathematics*— conjoining probability theory, combinatorics, statistics, computer science and neuroscience. In this approach, a new class of mathematical models must be introduced to describe and explain in a parsimonious way the different scales of neural activity and their relationship. The construction of these models, however, should marry the simultaneous development of suitable statistical and computational methods, including model selection principles and results.

The main strength of the Center relies on its innovative combination of scientific expertise. The prospect of very successful interactions among team members is guaranteed by the recognized scientific level of the participants. In particular the Center includes a team of first-level national and international neuroscientists, mathematicians, physicists, computer scientists, statisticians and clinicians. The Center is also connected to international institutions such as the NSF Science and Technology Center for the Science of Information and the Center of Cognitive Neurosciences of the CNRS, at Lyon. This team has been reinforced by a recently awarded Capes-Nuffic agreement with M. Malessy, Professor of Nerve Surgery at the Leiden University Medical Center in the Netherlands (LUMC). Collaborative interdisciplinary partnership in progress is described in Sections 2.7–2.8 (p. 10) of the Research Project of our proposal.

The following summarizes the activities planned for the first two years.

A new mathematical framework for neuroscience

In basic mathematical research it is unrealistic to establish concrete deadlines for particular results. Rather, research plans must refer to general objectives and directions of investigation. Success in this type of research comes from the careful combination of relevant research lines with qualified teams of mathematicians. The design of the Center is based on such a combination.

The development of the long-term goal of providing encompassing mathematical bases for neuroscience research requires the initial development of two foundational aspects, which will be addressed in the first two years:

Development of a new class of stochastic processes. We propose a new paradigm for Neuromathematics based on the idea that neuronal activity must be described as a stochastic process. This approach requires the development of a new class of process. Owing to the multiscale character of neural phenomena, these stochastic processes are systems with a large number of components, linked by interactions that evolve in time and depend on the history of the system. They are not Markovian in time, the activity of each component depending on the past history of its interaction neighborhood. Moreover, both the size of the relevant past history and of the interaction neighborhood change as the process evolves. Therefore there is a double time evolution: one describing the changes in neuronal activity, and another one describing changes in the graph of interactions among components.

The mathematical models of these evolving interaction graphs must access both "low dimensional" and "high-dimensional" aspects of neural systems, and lead to a revealing description of brain plasticity. In particular, models should provide appropriate degree distributions, clustering coefficients, average inter-vertex distance, as well as scale-free properties of the neural networks. Furthermore, evolutions should illustrate "repair mechanisms" of the brain, that is, change in graph properties due to localized destruction and the transitions leading to (partially) restored functionality.

The development of this new probabilistic theory is essential for a mathematical description of brain plasticity. A fundamental objective of the Center in the first two years is to lay down its foundations.

Development of the statistical tools required by this new class of stochastic processes. Brain activity is underpinned by a double graph structure: physical graphs defined by actual connections between neurons and brain regions, and functional graphs relating regions recruited for each particular activity. While the physical graphs can be directly observed, interactions between neural structures can only be inferred from data. Traditionally, this has been done using descriptive statistical methods which give little insight on the mechanism underlying the dynamics of the neural activity. The alternative to this naive descriptive statistical approach is to assign models to samples of neural data at different scales. Inference and model selection within this framework requires the development of new statistical results.

From a practical point of view, an inference problem can only be considered to be effectively solved if the resulting estimator is computationally efficient as well as theoretically sound. Progress in these directions will require cooperative work of computer scientists, mathematicians and statisticians. The NeuroMat team has the right blend of expertise needed to face this challenging issue. In the first two years, the Center aims to make noticeable progress in this direction.

A São Paulo School on Advanced Sciences on Neuromathematics. A proposal for a FAPESP advanced school will be submitted in the second year of the project. The research developed in the Center will require a new combination of skills, and the school will play an important role in attracting and giving the initial training to talented young researchers that will be able to join the team.

Technology transfer in years 1 and 2

The first activity of the Center in technology transfer will be the development of a collection of open source tools for basic neuroscience research, databases handling and clinical practice, in particular with respect to diagnostics and rehabilitation of stroke patients. These will evolve in tandem with the theory up to a point where sufficient utility can be amassed into an useable product.

The initial stage will be gathering typical data, in order to design, implement and test fundamental algorithms for data handling. These will be packaged into reusable containers, mostly libraries and possibly plug-ins for existing software products. The construction of test drivers will yield some experience on the useful characteristics of a productive user interface. The technology produced by the project will be released as free and open source software in all stages.

The initial two years will be highly experimental in the software front, and will comprise: (1) Data normalization within the project, with adoption of international open standards wherever applicable; (2) surveying existing products that may provide hooks and interfaces to the project yield; (3) implementing algorithms and incorporating the ensued software into the research cycle; (4) disseminating this production as free and open software, scientific and technical papers and workshops for medical and therapy personnel of Lucy Montoro and other rehabilitation centers, and to interested professionals.

Education and knowledge dissemination in years 1 and 2

The Center will produce instructional tools for general audiences, students at several levels and researchers in mathematics and neuroscience. These include: (1) Interactive contents for the web portal of the Center (already under construction), including texts, demonstrations, kits, exhibitions and videos; (2) communication channels with researchers, students, teachers and other interested parties; (3) videos on neuromathematical issues, made available on internet and exploiting the agreement with public TV channels of Fundação Padre Anchieta, TV Cultura and UNIVESP; (4) exhibitions and shows on Neurosciences at Science Centers and Museums of USP and UNICAMP, schools, Lucy Montoro Rehabilitation Network and other health centers and public places; (5) organisation of courses for teachers of mathematics and science to allow for future inclusion of neuromathematical topics in school curricula.