RIDC NeuroMat

Fourth Report of Activities

Jun 30, 2016 - Jun 30, 2017

Contents

1 RIDC NeuroMat Identification

RIDC: Research, Innovation and Dissemination Center for Neuromathematics (NeuroMat)

Grant number: 2013/07699-0

Host institution: Instituto de Matemática e Estatística da Universidade de São Paulo

Associated institutions: CNRS; Gran Sasso Science Institute (GSSI); IBM Thomas J. Watson Research Center; Instituto de Matemática Pura e Aplicada (IMPA); Universidad de Buenos Aires, Argentina; Universidad de la Republica, Uruguay; Universidad de San Andrés, Argentina; Universidade Estadual de Campinas (UNICAMP); Universidade Federal de Minas Gerais (UFMG); Universidade Federal de Ouro Preto (UFOP); Universidade Federal de Pernambuco (UFPE); Universidade Federal do Rio de Janeiro (UFRJ); Universidade Federal do Rio Grande do Norte (UFRN); Universidade Federal do Rio Grande do Sul (UFRGS); Universidade Federal de São Carlos (UFSCar); Université de Cergy-Pontoise; Université Paris Descartes; University of Memphis; Princeton University; Universiteit Utrecht.

Webpage: http://neuromat.numec.prp.usp.br

Principal Investigator/Center Director: Jefferson Antonio Galves

Vice Director: Pablo Augusto Ferrari

Co-Principal Investigators: Antonio Carlos Roque da Silva Filho; Claudia D. Vargas; Ernst Hamburger; Fernando da Paixão; Jorge Stolfi; Pablo Augusto Ferrari; Yoshiharu Kohayakawa

Education and Knowledge Dissemination Coordinator: Fernando Jorge da Paixão Filho

Technology Transfer Coordinator: Antonio Carlos Roque da Silva Filho

RIDC Executive Manager: Magda Holan Yu Chang

System analyst: Carlos Eduardo Ribas - IME/USP (Procontes)

Administrative assistant: Lourdes Vaz da Silva Netto - IME/USP

Manager of Education and Dissemination of Knowledge:

Manager of Technology Transfer:

The Research, Innovation and Dissemination Center for Neuromathematics (RIDC NeuroMat) is a center of mathematics whose mission is to develop the new mathematics needed to construct a Theory of the Brain accounting for the experimental data gathered by neuroscience research. Mathematician Antonio Galves coordinates this center. Hosted by the University of São Paulo, the RIDC NeuroMat was established in 2013, with support from the São Paulo Research Foundation (FAPESP), grant 2013/07699-0.

The RIDC NeuroMat has an interdisciplinary team, bringing together researchers in mathematics, computer science, statistics, neuroscience, biology, physiotherapy, medicine, physics and communication, among other disciplines. RIDC NeuroMat leads a worldwide university network, with ramifications that sprawl to several high-level research institutions in Brazil, Latin America, the United States and Europe (Annex 1). Most research output has had co-authors from more than one country, thus contributing to put NeuroMat at the center of a blossoming international scientific cooperation around Neuromathematics (Annex 2).

Alongside a research team that focuses on the scientific challenges pertaining to Neuromathematics, NeuroMat has active technology-transfer and dissemination teams. The technology-transfer effort is concentrated on devising renewed tools for diagnosing and clinical guidelines for neurological conditions, and on developing free, open-source computational tools to manage and compile experimental and clinical data. This development team is part of a joint effort to create an international open database for neuroscientific data. The dissemination-team effort includes a nonstatic web portal (Creative Commons license), open multimedia productions and training projects with public-school teachers. A distinctive feature of this effort is that it relies on web-2.0 media tools as a means of communicating on-the-go scientific endeavors as well as involving a scientific and broad community around bridging the high-level science that this RIDC develops and general audiences.

Pablo Augusto Ferrari (UBA and USP), Antonio Carlos Roque da Silva Filho (USP), Fernando Jorge da Paixão Filho (UNICAMP), Ernst Wolfgang Hamburger (USP), Jorge Stolfi (UNICAMP), Claudia Domingues Vargas (UFRJ), and Yoshiharu Kohayakawa (USP) remain co-principal investigators, along with PI Antonio Galves (USP). Bella Bollobás (Cambridge/Memphis), Charles Newman (NYU), David Brillinger (UCBerkeley), Leonard Cohen (National Institute of Neurological Disorders and Stroke),and Wojciech Szpankowski (Purdue and NSF Center for Science of Information) take part in NeuroMat's International Advisory Board. NeuroMat's main laboratory and offices are located on a three-story building, with approximately 1,000 square meters, at 1171 Prof. Luciano Gualberto Avenue, at USP's central campus, in São Paulo. NeuroMat's main building has recently gone through an extension (+175 square meters) and renovation to support new laboratory facilities; the construction cost was BRL R$ 1,603,339 and was fully covered by USP, MaCLinC grant (recipient: Antonio Galves). NeuroMat has set up a High Performance Computational Center at the USP's Ribeirão Preto campus. NeuroMat's administrative staff team is composed of two administrative assistants, an IT professional, and an executive manager. These positions are supported by USP.

2 Scientific report

2.1 Mission

The mission of NeuroMat is to develop the new mathematics which is deemed necessary to account for 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 neuroscientific phenomena, with focus on plasticity mechanisms underlying learning and memory neurorehabilitation and rewiring. This Neuromathematics is envisioned, at this time, as conjoining probability theory, combinatorics, statistics, and neuroscience. This requires the definition of a full new class of mathematical models to describe and explain in a parsimonious way the different scales of neural activity and the relationship between them. The construction of these models should occur together with the development of suitable statistical and computational methods, including model selection principles and results.

2.2 Executive summary

The main goal of NeuroMat is to build the new mathematical, statistical and computational framework which is necessary to address the challenges of neurobiology. Activities presented in this report strictly relate to the goals announced in the document submitted to FAPESP in November 2012, in the third and final step of the selection process. The general goals of this research project are the following:

- Development of new classes of stochastic processes which are necessary to model brain functioning;
- Development of the statistical tools required by this new class of stochastic processes.

Detailed progresses on these two goals were reported in the documents "First Report of Activities 2013-2014", "Second Report of Activities 2014-2015", "Complementary Form 2013-2015", the Evaluation by FAPESP International Committee in November 2015, "Third Report of Activities 2015-2016," and the "Complementary Form 2015-2017." The progresses achieved in the first two years opened up the path for a new stage of development. In its third year, NeuroMat started the construction of innovative applications of the new stochastic models and statistical tools developed in the previous years, aiming at concrete questions of Neuromathematics and computational modeling in neurobiology, electroencephalographic recordings analysis, and neurorehabilitative therapy. Research highlights and corresponding published works are listed below, in the appropriate section. Since the "Third Report of Activities 2015-2016", the NeuroMat research team has:

- published 32 papers;
- submitted or uploaded to arXiv 43 papers;

- 6 communications in meetings with referee

NeuroMat scientific publications in the period being assessed in this report are listed on Annex 3a, 3b and 3c. A full list of publications since the inception of NeuroMat is presented on Annex 3d and 3e. Citations to these publications across the years are available on Annex 4.

In parallel to the mathematical and theoretical bioligical developments which are necessary to foster the scientific project of NeuroMat, the RIDC has also created two new laboratories. In April 2016, NeuroMat launched a new research facility: the NeuroMat High-Performance Computational Center. The simulation of large-scale network models remains a key activity to test analytical results, and the NeuroMat HPC will be a laboratory allowing for such tests, providing the NeuroMat team with a new experimental tool to test and construct large-scale computational implementations of NeuroMat newly developed models (over 100,000 neurons). The NeuroMat HPC is installed at the Laboratory of Neural Systems (SisNe) of the Department of Physics of USP Ribeirão Preto, under the direction of NeuroMat PI and Technology transfer coordinator A.C. R. da Silva Filho (USP-Ribeirão Preto). In July 2017, NeuroMat launched an Electroencephalography Laboratory, with an EEG DC actiCHamp 128CH System. The creation of NeuroMat's EEG lab was made possible by the expansion of the building, through a grant from the University of São Paulo (value of support: BRL R$ 1,603,339).

2.3 Research results highlights

The most general challenge the NeuroMat team faces is the development of new classes of probabilistic models to study different aspects of brain functioning. Aspects of this challenge are at least threefold.

Firstly, it has been necessary to develop a new class of stochastic processes describing nets of spiking neurons. The article Galves and Loecherbach (2013) has been the initial achievement in this direction.

Secondly, we are making steps towards a mathematical and statistical framework to formulate the phenomenon of brain plasticity.

Last but not least, we have made efforts to develop stochastic models, statistical procedures and neurobiological experimental protocols to address the classical conjecture of the Statistician Brain. The article Duarte et al. (2016) is a first important step in this direction.

Subsequent sections provide detailed accounts of NeuroMat's research main accomplishments, following these lines. These sections rest upon and strictly recompile achievements presented in the "Complementary Form 2015-2017," submitted a month ago.

2.3.1 RIDC main accomplishments

2.3.1.1 A new class of models describing systems of spiking neurons

The article Galves and Loecherbach (2013) introduced a new class of stochastic processes aimed to a realistic description of nets of spiking neurons. These processes are systems with a large number of interacting chains with memory of variable length. The original paper established conditions for the mathematical existence of the process and also a perfect simulation algorithm for its numerical implementation. The model was subsequently studied in a series of articles by different authors, not all members of the NeuroMat team. Duarte and Ost (2016) proves that a finite system in the absence of external stimuli stops spiking almost surely in a finite time. De Masi et al. (2015) and Duarte et al. (2015) study the hydrodynamical limit of processes in this class. This is an important step to relate different scales of description of the system: from the microscopic level modelling multi-unitary register to the mesoscopic and macroscopic levels describing EEG and fMRI data. Obviously it is still too early to be sure of that, but the increasing number of articles and PhD dissertations dedicated to the class of stochastic processes introduced in Galves and Loecherbach (2013) suggests that this article was the starting point of a new direction of research in Probability Theory.

2.3.1.2 Inferring neural interactions

The question of how to infer neural interactions from the activity of an ensemble of neurons is one of the most important contemporary issues in Neurobiology. In Duarte et al. (2016) we propose a novel estimator of the interaction graph based on a sample of spike activity of a finite set of neurons. We also prove the strong consistency of the estimator. The results do not require stationarity nor uniqueness of the invariant measure of the process, posing a great advantage in comparison with commonly used methods of functional connectivity inference.

In Brochini et al. (2017) we apply this statistical selection procedure to real electrophysiological data. We propose improvements to the original procedure in order to deal with small sample sizes. We show that the estimator can be used to real data by inferring the interaction graph from multi-unit recordings of neural activity of the first olfactory relay of the locust Schistocerca americana. All codes were made available online in order to encourage the usage of the proposed estimator. Recent accomplishments include results on non-parametric estimation of the spiking rate function and results on the optimal speed of convergence in L2 of the error for a given Hölder class of functions (Hodara et al. 2016).

2.3.1.3 Computer simulation of large-scale neural networks

We implemented a stochastic model of a cortical column (Cordeiro et al., 2016) based on the connectivity map compiled by Potjans and Diesmann (2014) from anatomical and physiological data. The model size (about 80,000 neurons and 0.3 billion synapses) and connectivity correspond to the cortical microcircuit under a surface of $1mm^2$. The stochastic neurons of the model are described by the Brochini et al. (2016) version of the Galves and Löcherbach (2013) model. The model was later refined by using empirically determined parameters to mimic the firing behavior of regular and fast spiking neurons, which are respectively the most common types of cortical excitatory and inhibitory cells. Simulations of the model for different parameter values show that it can display collective oscillatory activity over a broad range of frequencies similar to the ones observed experimentally. This is the first time that the aforementioned stochastic neuron model is compared with a widely used deterministic model for cortical activity in numerical experimentation, showing that the stochastic model is able to produce qualitatively similar results with much lower computational cost.

2.3.1.4 Phase transitions, criticality and oscillations in stochastic neuronal networks

We performed numerical experiments for large all-to-all networks and analytical mean field calculations for the stochastic spiking neuron model (Galves and Locherbach, 2013). We found that the model undergoes first and second order phase transitions, studied in Brochini et al. (2016) for the case where the model is a Markov chain and in Brochini et al. (2017) for the case of stochastic chain with memory of variable length.

In Brochini et al. (2016) we introduced a new model for neuronal avalanches where the critical region is achieved by a homeostatic mechanism of the neuronal gain leading the system to tune towards a slightly supercritical state instead of a purely critical one. We observed outlier avalanches, related in the literature to epilepsy and hyper excitability and we called this new dynamical state self-organized super criticality. This work is in consonance with recent rigorous mathematical findings that information propagation should be maximal in a supercritical state for a simpler stochastic model (Cassandro, Galves & Locherbach, 2017)

In Brochini et al. (2017) we propose a simplified version of the homeostatic neuronal gain. We observe that the mean-field fixed point for the gain turns out unstable, leading to collective oscillations of the neurons activity. Hence, we get both neuronal avalanches and oscillations coexisting in the same model for the same parameters. This result is surprising and new, and promises to unify two different approaches to the study of brain dynamics: critical (or supercritical) states and collective oscillations.

2.3.1.5 The statistician brain conjecture

It has been repeatedly conjectured that the brain retrieves statistical regularities from stimuli, so that their structural features are separated from noise. The article Duarte et al. 2016 presents a new statistical approach allowing to address this conjecture. This approach is based on a new class of stochastic processes driven by chains with memory of variable length. It leads to a new experimental protocol in which structured auditory sequences are presented to volunteers while electroencephalographic signals are recorded from their scalp. This article introduces a new statistical model selection procedure to analyze electroencephalographic signals (EEG). This procedure is proved to be consistent. Applied to samples of EEG data collected during structured auditory stimuli presentation, it produces results supporting the conjecture that the brain effectively identifies the context tree characterizing the source.

2.3.1.6 Brain plasticity

Recent accomplishments include detecting changes induced by brachial plexus injury (BPI) in upright stance (Souza et al., 2016). Furthermore, the analysis of empirical functional correlations between neighbouring voxels in the primary motor cortex in BPI patients reveal faster correlation decay as a function of distance bilaterally in the region corresponding to the upper trunk and arm as compared to an age-paired control group, suggesting that the lack of motor synergies induced by the total limb disconnection strongly disorganises the corresponding motor maps in the motor cortex (Fraiman et al., 2016). Tools to explore the cerebral dynamics associated to postural instability (Martins et al., 2017) and hand kinematics (Esteves et al., 2016) have been recently developed. We have also investigated in a small cohort of patients if somatosensory electrical stimulation can relieve spasticity in post-stroke patients (Garcia et al., 2016, Peres et al., 2017). We are now investing in new protocols to access plastic changes in the healthy brain as well as those induced by central and peripheral lesions employing context tree models. This initiative is intrinsically associated to the development of the experimental protocol presented in the article by Duarte et al., (2016).

2.3.1.7 Random graphs and computational psychiatry

Our group has pioneered the used of word graph analysis for computational phenotyping in psychiatry, neurology and education (Mota et al., 2016a). Word graphs provide a fast and low-cost tool to quantify psychopathological symptoms previously accessible only through the qualitative examination of specialists. In the past few years, we have successfully applied graph analysis to 1) differentially diagnose psychosis between schizophrenia and bipolar disorder (Mota et al., 2014), 2) sort Alzheimer's disease from mild cognitive impairment (Bertola et al., 2014), 3) track the cognitive gains of healthy children undergoing literacy acquisition, and 4) compare the structural development of speech and literature (Mota et al., 2016b). The most recent advance shows that the degree of speech disorganization measured during the first psychiatric interview of a psychotic teenager can predict the schizophrenia diagnosis 6 months later (Mota et al., 2017). We have also been interested in the use of semantic tools for similar purposes (Bedi et al., 2015). Altogether, these methods show wide applicability far beyond psychology, reaching the various mental realms induced by sleep and dream states, mood and attention variations, medication, drug use, nutrition, and the onset of psychiatric and neurological diseases. The methods also have potential to reveal new perspectives on the mental correlates of talking, reading, writing and, most importantly, learning.

2.3.2 Corresponding published works

2.3.2.1 A new class of models describing systems of spiking neurons

- Galves, A; Löcherbach, E. "Infinite systems of interacting chains with memory of variable length—a stochastic model for biological neural nets." Journal of Statistical Physics 151.5 (2013): 896-921.
- De Masi, A; Galves, A; Löcherbach, E; Presutti, E. (2015). Hydrodynamic limit for interacting neurons. Journal of Statistical Physics, 158(4), 866-902.
- Duarte, A; Ost, G. A model for neural activity in the absence of external stimuli. Markov Processes and Related Fields 22, 37–52 (2016)
- Duarte, A; Ost, G; Rodríguez, AA. (2015). Hydrodynamic Limit for Spatially Structured Interacting Neurons. Journal of Statistical Physics. 161(5), 1163–1202.

2.3.2.2 Inferring neural interactions

- Duarte, A; Galves, A; Löcherbach, E; Ost, G. Estimating the interaction graph of stochastic neural dynamics. arXiv:1604.00419
- Brochini, L; Hodara, P; Pouzat, C; Galves, A. Interaction graph estimation for the first olfactory relay of an insect. arXiv:1612.05226
- Hodara, P; Krell, N; Löcherbach, E. Non-parametric estimation of the spiking rate in systems of interacting neurons. arXiv:1604.07300

2.3.2.3 Computer simulation of large-scale neural networks

- Cordeiro VL; Shimoura RO; Kamiji NL; Kinouchi O; Roque AC (2016). A stochastic version of the Potjans-Diesmann cortical column model. Front. Neuroinform. Conference Abstract: Neuroinformatics 2016. doi: 10.3389/conf.fninf.2016.20.00060
- Potjans, TC; Diesmann, M. (2014), The cell-type specific cortical microcircuit: relating structure and activity in a full-scale spiking network model. Cereb. Cortex 24, 785-806. (Non NeuroMat referenced paper.)
- Brochini L; Costa AA; Abadi M; Roque AC; Stolfi J; Kinouchi O. Phase transitions and self-organized criticality in networks of stochastic spiking neurons. Sci Rep 2016, 6:35831.
- Galves A; Löcherbach E: Infinite systems of interacting chains with memory of variable length: a stochastic model for biological neural nets. J Stat Phys 2013, 151:896-921.

2.3.2.4 Phase transitions, criticality and oscillations in stochastic neuronal networks

- Galves, A; Löcherbach, E. "Infinite systems of interacting chains with memory of variable length—a stochastic model for biological neural nets." Journal of Statistical Physics 151.5 (2013): 896-921.
- Brochini, L; Costa, AA; Abadi, M; Roque, AC; Stolfi, J; Kinouchi, O. (2016) Phase transitions and self-organized criticality in networks of stochastic spiking neurons. Scientific Reports 6. doi:10.1038/srep35831
- Costa, AA; Brochini, L; Kinouchi, O. (2017) Self-Organised Supercriticality and Oscillations in Networks of Stochastic Spiking Neurons. arXiv:1705.08549
- Cassandro, M; Galves, A; Löcherbach, E. (2017) Information transmission and criticality in the contact process. arXiv:1705.11150

2.3.2.5 The statistician brain conjecture

- Duarte, A; Fraiman, R; Galves, A; Ost, G; Vargas, CD. Retrieving a context tree from EEG data. arXiv:1602.00579

2.3.2.6 Brain plasticity

- Souza, L; Lemos, T; Silva, DC; et al. (2016). Balance Impairments after Brachial Plexus Injury as Assessed through Clinical and Posturographic Evaluation. Frontiers in Human Neuroscience, 9, 715.
- Fraiman, D; Miranda, MF; Erthal, F; et al. (2016). Reduced functional connectivity within the primary motor cortex of patients with brachial plexus injury. NeuroImage: Clinical, 12, 277–284. http://doi.org/10.1016/j.nicl.2016.07.008
- Martins, EF; Lemos, T; Saunier, G; et al. (2017). Cerebral Dynamics during the Observation of Point-Light Displays Depicting Postural Adjustments. Frontiers in Human Neuroscience, 11, 217. http://doi.org/10.3389/fnhum.2017.00217
- Esteves, PO. et al. Motor planning of goal-directed action is tuned by the emotional valence of the stimulus: a kinematic study. Sci. Rep. 6, 28780; doi: 10.1038/srep28780 (2016).
- Garcia, MAC; Catunda, JMY; Souza, MN; et al. “Is the Frequency in Somatosensory Electrical Stimulation the Key Parameter in Modulating the Corticospinal Excitability of Healthy Volunteers and Stroke Patients with Spasticity?,” Neural Plasticity, vol. 2016, Article ID 3034963, 11 pages, 2016. doi:10.1155/2016/3034963

- Peres, A; Souza, V; Catunda, J. et al. (2017). Can somatosensory electrical stimulation relieve spasticity in post-stroke patients? A TMS pilot study. Biomedical Engineering / Biomedizinische Technik, 0(0), pp. -. Retrieved 17 Jul. 2017, from doi:10.1515/bmt-2016-0162.
- Duarte, A; Fraiman, R; Galves, A; Ost, G; Vargas, CD. Retrieving a context tree from EEG data. arXiv:1602.00579

2.3.2.7 Random graphs and computational psychiatry

- Bedi G; Carrillo F; Cecchi GA; Slezak DF; Sigman M; Mota NB; Ribeiro S; Javitt DC; Copelli M. Corcoran CM (2015). Automated analysis of free speech predicts psychosis onset in high-risk youths. npj Schizophrenia 1:15030.
- Bertola L. Mota NB; Copelli M; Rivero T; Diniz BS; Romano-Silva MA; Ribeiro S; Malloy-Diniz LF (2014). Graph analysis of verbal fluency test discriminate between patients with Alzheimer's disease, mild cognitive impairment and normal elderly controls. Front Aging Neurosci 6:185.
- Mota NB; Copelli M; Ribeiro S (2016a). Computational Tracking of Mental Health in Youth: Latin American Contributions to a Low-Cost and Effective Solution for Early Psychiatric Diagnosis. New Dir Child Adolesc Dev 152:59-69.
- Mota NB; Copelli M; Ribeiro S (2017). Thought disorder measured as random speech structure classifies negative symptoms and Schizophrenia diagnosis 6 months in advance. npj Schizophrenia 3:1.
- Mota NB; Furtado R; Maia PP; Copelli M; Ribeiro S (2014). Graph analysis of dream reports is especially informative about psychosis. Sci Rep 4:3691.
- Mota NB; Pinheiro S; Sigman M; Fernandez-Slezak D; Cecchi GA; Copelli M; Ribeiro S (2016b). The ontogeny of discourse structure mimics the development of literature. arXiv:1612.09268v1.

2.4 Scientific meetings organized by NeuroMat in the period

An important aspect of the work NeuroMat produces depends on fostering a tight relationship among members of the NeuroMat worldwide. As emphasized in our interaction with FAPESP International Committee, we are especially aware of this challenge, and we have sustained partnerships among scientists from different parts of the world —of which the high rate of papers with co-authors from different countries is an evidence. The fostering of a tight community around Neuromathematics strongly meets the expectations of FAPESP's Committee.

A key part of the community-building entrepreneurship NeuroMat has sustained relates to organizing frequent conferences and meetings on topics pertaining to Neuromathematics. In November 2016, NeuroMat held the Second NeuroMat Workshop: New Frontiers in NeuroMathematics. The goal of this event was to provide an overview of research trends and processes within the RIDC in accordance with the most important aim of the project, to propose new models for systems of interacting neurons and to develop new statistical tools to analyze neural datasets. Link for this event is neuromat.numec.prp.usp.br/nm2w.

2.4.1 Research events & seminars

During the period of activities being reported in this document, the NeuroMat team has also taken part in smaller-scale research events and seminars. An illustration is the NeuroMat-sponsored Statistic, probabilistic and computational methods in neurobiology, held in June, 2016; BIN@SP 2016 (November 2016); and INFIERI 2016 (January 2017). NeuroMat has also organized two courses at its High-Performance Computing Center in Ribeirão Preto: the I NeuroMat Course on Parallel and GPU Programming for Neuroscience and Mini-Workshop on Computational Neuroscience (PPNeuro) in December 2016 and the Practical Course of Computational Modeling in Neuroscience (PractiCoNeuro), in July 2017.

3 Technology transfer report

NeuroMat's Innovation and Technology Transfer has changed focus areas of activity since August 2015, in accordance to recommendations from the International Committee of Evaluation. In this context, A. C. Roque da Silva Filho (FFCLRP/USP) has been appointed the new director of Innovation and Technology Transfer. The creation and development of two new neuro-rehabilitation and diagnosis initiatives, directed to Parkinson's Disease (AMPARO) and Brachial Plexus Injuries (ABRAÇO), has been a main focus area of activity. Both initiatives took advantage of a computational tool NeuroMat had previously developed, namely the Neuroscience Experiments System (NES). Recent developments of NES and the ongoing work for the creation of the NeuroMat Open Database have been oriented towards the needs of AMPARO and ABRAÇO.

During this period, NeuroMat has also developed a new tool for neuro-rehabilitation and diagnosis, the Goalkeeper Game. This tool is a direct result of the theoretical and experimental research developed by NeuroMat around brain functioning. By doing this NeuroMat reaches one of its main goals, which is to produce new technology based on new scientific results.

3.1 Neuro-rehabilitation and diagnosis

3.1.1 AMPARO Initiative

The NeuroMat focus area towards Parkinson's Disease is called AMPARO Initiative, or Rede de Apoio NeuroMat a Amigos e Pessoas com Doença de Parkinson. Link for the website is amparo.numec.prp.usp.br.

3.1.1.1 A tool for early Parkinson's Disease diagnosis The team led by NeuroMat researcher Maria Elisa Pimentel Piemonte (FM-USP) is using the Goalkeeper Game (see Section 3.2.1) to study putative novel relationships between the main cardinal Parkinson's Disease symptom, bradykinesia, and implicit probabilistic learning and lack of ability in automatic motor control. The study aims at developing a new measure and typology to establish the limits between normal decline associated to aging process and abnormal alterations associated the onset of the pathological process of Parkinson's Disease. The clinical implication of this work is to offer a free and friendly test to early diagnosis of Parkinson's Disease by e.g. cell phones using the Goalkeeper Game. A pilot with 48 patients was conducted in 2016-2017. This work is currently going through a validation process. Data of these patients have fed NeuroMat's database.

The new approach developed by NeuroMat using the Goalkeeper Game together with the preliminary analysis of the data was presented at the 21st International Congress of Parkinson's Disease and Movement Disorders. In this meeting NeuroMat researcher and leader of the AMPARO Initiative, Maria Elisa Pimentel Piemonte, was elected the chair of Allied Health Professionals and of the pan-american chapter of the Movement Disorder Society.

3.1.1.2 Collaborative network for Parkinson's Disease clinical guideline

AMPARO Initiative organizes monthly meetings with NeuroMat members, professionals, patients and caregivers. The goal is to share knowledge towards the collaborative building of guidelines for Parkinson's Disease in Brazil, especially for the public health system. Comments are also gathered through online interactions and web surveys, as meetings are video streamed. Relevant early findings suggest the need to build instructions for clinical professionals, such as easing diagnosis and collaborating with an interprofessional team, and caregivers, especially around motricity, sleep and emotional support. Summaries of meetings are being produced as educational resources.

3.1.2 ABRAÇO Initiative

NeuroMat's Brachial Plexus Injuries focus area is called ABRAÇO Initiative, or Ação NeuroMat para a Lesão do Plexo Braquial. A reference website may be found at: abraco.numec.prp.usp.br. This website is the first worldwide platform devoted to this health condition and is aimed at being both a source of help and support for patients, caregivers, students and professionals, and a powerful scientific knowledge sharing platform.

3.1.2.1 Assessing plasticity associated to Brachial Plexus Injuries

The team led by NeuroMat CO-PI Claudia Domingues Vargas (INDC/UFRJ) is using the Goalkeeper Game (Section 3.2.1) to study mechanisms of plasticity in the brain after a brachial plexus injury aiming at developing new tools to assess plastic changes in the brain induced by this traumatic injury. In the motor context, prediction can be seen as an automatic process of choosing and implementing a next step in a sequence of events. Tests are being conducted with human subjects playing the Goalkeeper Game to determine which parameters of the context tree generating stochastic sequences of events in the Goalkeeper Game are best associated with the optimal processing of sequences of motor events. The objective is to check the possibility of using the Goalkeeper Game as a tool for rehabilitation of brachial plexus injury patients. This work is currently going through a validation process. Data of these patients have fed NeuroMat's database.

3.2 Computational tools

3.2.1 Goalkeeper Game

NeuroMat researchers devised experimental protocols to test the performance of human subjects in identifying sequences of stimuli represented by context trees. An innovation spin-off from NeuroMat's research project is the "Goalkeeper Game". It is an online game with desktop and mobile device versions (the latter under development) in which the player, taking the role of a goalkeeper in a penalty shootout, guesses the position in the goal where the ball will hit (left side, right side or center) after being kicked by the opponent. The game consists in a sequence of penalty kicks in which the ball positions are generated by a context tree model. As the player (the goalkeeper) succeeds in guessing the right sequence, the complexity of context tree model increases and the game becomes more difficult. The goalkeeper game has potential to be used as diagnosis and rehabilitation tool in neurology, and the NeuroMat technology transfer team is currently testing its applicability in its two main clinical development fronts: Parkinson's Disease and Brachial Plexus Injuries (see Sections 3.1.1.1 and 3.1.2.1). The game is openly, freely available at: game.numec.prp.usp.br. The development team of the Goalkeeper Game is led by Marcos Dimas Gubitoso (IME/USP).

3.2.2 Neuroscience Experiments System

The Neuroscience Experiments System (NES) is a free software to manage data and metadata from neuroscience experiments. It integrates data records from different types such as clinical, electrophysiological, and behavioral. NES is currently being used by the teams involved in both ABRAÇO (Section 3.1.2) and AMPARO (Section 3.1.1) initiatives. NES is integrated to the Goalkeeper Game (Section 3.2.1) and to the NeuroMat Open Database (Section 3.2.3). The main functionalities which were developed since August, 2015, include: an Electrophysiology module, for registering data and metadata from EEG, EMG and TMS experiments; and an Export module, for exporting all data stored from an experiment, including experimental subjects' data, e.g., questionnaire responses, clinical diagnoses, electrophysiological raw data, and experimental protocol metadata. NeuroMat's technology transfer team has formalized a collaboration with the International Neuroinformatics Coordinating Facility (INCF). Currently, there is a link to NES source-code repository at the INCF page on GitHub (github.com/INCF/nes). The development team of the Neuroscience Experiments System is led by Kelly Rosa Braghetto (IME/USP). Progress on the development of new functionalities is provided in Annex 11.

NES has been presented in a demonstration session at INCF's annual congress in 2016 and in a poster session at the 46th annual meeting of the Society for Neuroscience (Annex 12). In these events, the newest features of NES were presented to the international neuroscience community.

3.2.3 NeuroMat open database

The NeuroMat open database provides an open-access platform for sharing and searching data and metadata from neuroscience experiments. The platform is constituted by a web portal and a REST (Representational State Transfer) API (Application Programming Interface). The web portal is being designed to have a user-friendly interface. The REST API is used to feed the open database with experimental data generated by NeuroMat's researchers. Currently, the API intermediates the receiving and retrieving of data from research laboratories which use NES (Section 3.2.2). It can be can easily adapted to receive (or transfer) data from (for) other client systems. The development team of the NeuroMat open database is led by Kelly Rosa Braghetto (IME/USP).

Link to the RIDC Intellectual Property webpage: neuromat.numec.prp.usp.br/open-science.

4 Dissemination report

NeuroMat's dissemination activities have as guideline to work as a collaborative web-2.0 hub, developing web-2.0 media tools as a means of communicating on-the-go scientific endeavors as well as involving a scientific and broad community around the high-level science that this RIDC develops.

The dissemination team is committed on the development of a new language for NeuroMat's communication and education efforts, so as to bring the scientific frontier to general audiences. As part of this effort, the dissemination team creates its own media, like the Web Portal and the newsletter, promotes educational activities in schools and invests in the use of collaborative electronic platforms, like Wikipedia, to improve science contents available to the public. NeuroMat's dissemination activities are:

- the Wikipedia Initiative
- the Wikimedia Commons Initiative
- Training course for teachers
- Media Exposure and Newsletter
- Web resources: portal, Facebook page, dissemination blog
- NeuroCineMat
- Research on Communication Science
- Dissemination events
- Exhibitions

4.1 Wikipedia Initiative

NeuroMat's Wikipedia Initiative has become a strategic activity at the interface of communication and education. It has been recognized in Brazilian and foreign outlets as "success case" of the use of Wikipedia and other collaborative projects as a means of scientific dissemination. The project has been supported by seven scholarships and has been able to secure two small external grants, as described in Annex 13.

Achievements of this initiative from its inception from January 2016 to September 2017 are presented on Annex 14. Main achievements are:

- 5,010,076 content viewers in Portuguese Wikipedia;
- 672,000 words added to Portuguese Wikipedia;
- 227 entries created on Portuguese Wikipedias; and

- 854 entries improved on Portuguese Wikipedias.

The control panel of the NeuroMat Wikipedia Initiative is available at: goo.gl/v4Q1LD.

4.2 Wikimedia Commons Initiative

NeuroMat has been engaged in uploading media files to the open repository Wikimedia Commons. As of September 2017, 976 files had been uploaded by the NeuroMat team in this repository.

Files NeuroMat added to Wikimedia Commons were viewed 7,687,538 times in August. In July and June, views were respectively 8,288,448 and 9,425,437. These figures are obtained from the web visualization control tool GLAMorgan (https://goo.gl/U6V7e4).

4.3 Training course for teachers

Since July 2015, the NeuroMat educational effort has been directed towards the development of new educational strategies to broaden its outreach and impact on the public education system. As an outcome, NeuroMat has established as the strategic guideline of its educational activities the development of free and widely available online materials and lectures to empower the public school teachers to understand the state of art in the scientific interface between neurobiology and mathematics, and to develop science related activities with students in their classrooms.

The development of these materials encompasses educational texts and videos, as well as lessons plans and classroom activities. This effort is being collectively thought and designed by the NeuroMat educational team with public school teachers from Escola de Aplicação of School of Education of the University of São Paulo and undergraduate students from the Institute of Mathematics and Statistics from University of São Paulo.

4.4 Media Exposure and Newsletter

Activities from FAPESP'S RIDC NeuroMat were featured in fifty three external media outlets since its inception, in 2013. Since July 2016, there have been twenty three media publications. Coverage from FAPESP and USP media outlets have been continuous.

NeuroMat's media clipping for this year is attached to this report as Annex 15. NeuroMat's newsletter has had 43 issues since it was first released in February 2014. It runs monthly, generally being sent to subscribers at the end of each month. It is distributed to around 675 people, always in English. NeuroMat's newsletter compilation is attached to this report as Annex 16.

4.5 Web resources: portal, Facebook page, dissemination blog

NeuroMat's web portal was launched in early February 2014, and is thought of as the main official reference of the RIDC. It provides robust updates on research, technology transfer and dissemination activities. Publications are in English and Portuguese. 20,279 different users —53,32% of whom were identified as non-Brazilian users– have visited NeuroMat's webpage since its inception, with 106,921 page views, as of September, 2017. Average session duration was approximately 3 minutes and a half, with a bounce rate of 56,71%. A website analytics report is attached as Annex 17.

NeuroMat's Facebook page was launched in September 2014 to serve as a reference space for the diverse community that is involved with and interested in Neuromathematics. Since its creation (9/20/2014), the page has reached 934 followers, as of September 20, 2017, with steady progress. The community growth has been organic.

Since April 2016, the NeuroMat dissemination team has sustained a blog on scientific challenges and activities pertaining to science communication, especially relying on web-2.0 platforms. The blog is called "Traço de Ciência." The blog has been viewed 6,982, since its inception as of September, 2016. 213 posts were published on this platform in the period of activities that is reported in this document; this figure is illustrated on Annex 18.

References are:

- web portal: neuromat.numec.prp.usp.br
- Facebook page: www.facebook.com/neuromathematics
- blog: difusaoneuromat.wordpress.com

4.6 NeuroCineMat

The NeuroMat dissemination team has fully produced four movies—on the mathematical theory of the brain, on brain functioning, on NeuroMat's Network on Parkinson's Disease and on NeuroMat's Network on Brachial Plexus Injuries. Three other movies are under production: on open science, on an experiment on brain functioning and rhythms, and on the trajectory of Ernesto Hamburger. A full list is available on: neuromat.numec.prp.usp.br/streaming

4.7 Research on Communication Science

The NeuroMat dissemination team has presented six conference papers, included in the annals of the Congresso Brasileiro de Ciências da Comunicação, COMPÓS and ABCiber. Details of the research activity of the NeuroMat dissemination team are described on Annex 19.

4.8 Dissemination events

The NeuroMat scientific dissemination team has organized the following events:

- "Cultura Matemática no Brasil: diagnósticos e perspectivas", May 16, 2017. This event provided an opportunity for discussions and proposals to improve numeracy in Brazil. Data from the 2015 Programme for International Student Assessment (PISA), a triennial assessment of the educational system in dozens of countries in the world, have appeared to corroborate a general understanding that the level of mathematical literacy in Brazil was worrying. Mathematical literacy, as assessed by PISA, included understanding the role of Mathematics in making sense of the world and engaging with Mathematics in a way that corresponds to basic skills of establishing connections, reasoning, problem solving and representation. As a keynote speaker, PISA specialist Esther Carvalhaes was responsible for providing an understanding of the 2015 report of mathematical literacy. Official website: neuromat.numec.prp.usp.br/cmb.

- Edit-a-thons Neuroscience and Mathematics (editions II, III, IV). Enabling participants to contribute to topics pertaining to the RIDC NeuroMat on the Portuguese Wikipedia, in September 2016 and in March and June 2017.

- "O uso da Wikipédia na educação", training seminar with the director of the Wiki Education Foundation LiAnna Davis, in March 2017. Video available here: https://goo.gl/i8SXux.

- "Treinamento em difusão científica web 2.0", training seminar on the use of collaborative technologies in scientific dissemination, in December 2016. Official website: https://goo.gl/tZGMit

4.9 Exhibitions

The exhibition "Inside the Brain," at the Museum of Veterinary Anatomy, was inaugurated in 2017. This exhibition was the basis for an extended partnership between NeuroMat and the Museum of Veterinary Anatomy, that resulted in what is called a GLAM project, the publication on Wikimedia Commons of the museum image repository, photographed by a University of São Paulo journalism professor.

In tune with the initiative with the Museum of Veterinary Anatomy, the RIDC NeuroMat scientific dissemination team has also established partnerships with Matemateca IME-USP and Museu Paulista, from the University of São Paulo, to release images of their collection onto open repositories.

5 Annexes

Annex 1 - NeuroMat global network of scientific, institutional affiliations

Annex 2 - Graph of Interactions of the NeuroMat Research Team

Annex 3 - NeuroMat Scientific Publications

Annex 3a - Articles published or accepted for publication

Annex 3b - Articles submitted or uploaded to arXiv

Annex 3c - Communications in meetings with referee

Annex 3d - Articles published or accepted since NeuroMat's inception until July 2016

Annex 3e - Communications in meetings with referee since NeuroMat's inception until July 2016

Annex 4 - NeuroMat Scientic Publications: Citations

Annex 5 - Scientific missions

Annex 6 - Scientific meetings and Schools

Annex 7 - Seminars

Annex 8 - Post-doctoral fellows

Annex 9 - PhD dissertations

Annex 10 - MSc dissertations

Annex 11 - NES development report

Annex 12 - Communications in meetings with referee from the NES development team

Annex 13 - NeuroMat's Wikipedia Initiative scholarships and external grants

Annex 14 - NeuroMat's Wikipedia Initiative achievements

Annex 15 - NeuroMat's media clipping

Annex 16 - NeuroMat's newsletter

Annex 17 - NeuroMat's web portal

Annex 18 - NeuroMat dissemination blog "Traço de Ciência"

Annex 19 - NeuroMat Research on Communication Science

Annex 20 - Reports from FAPESP scholarships

- Annex 20a – Michelle Ferreira Miranda – II
- Annex 20b – Michelle Ferreira Miranda – III
- Annex 20c – Guillem Via Rodriguez
  - Annex 20c_1_Guillem
  - Annex 20c_2_Guillem
- Annex 20d – Achillefs Tzioufas
- Annex 20e - Antonio Ferrão Neto
- Annex 20f – Roberto Freitas Parente
- Annex 20g_1 – Margarita Ramos Ruiz Olazar I
- Annex 20g_2 – Margarita Ramos Ruiz Olazar II
- Annex 20h – Sidnéia Sousa França
- Annex 20i – Morgan Florian Thibault André
- Annex 20j_1 – David Fernando Levon Alves I
  - Annex 20j_1-1_Anexo_I_-_Tabela de Verbetes Editados
  - Annex 20j_1-2_Anexo_II_-_Tabela do Blog de Difusao Cientifica do Neuro
  - Annex 20j_1-3_Anexo_III_-_Certificado - Apresentacao de artigo academi

- Annex 20j_1-4_Anexo_IV_-_Certificado - Curso de Jornalismo Cientifico
  - Annex 20j_1-5_Anexo_V_-_Cartilha - Usando a Wikipedia na difusao cient
- Annex 20j_2 – David Fernando Levon Alves II
- Annex 20k – Marília Reinato Carrera
  - Annex 20k_1-I Tabela de verbetes lidos na Wikipedia carregados no Wikimedia Commons
  - Annex 20k_2-II Tabela de verbetes lidos na Wikipedia carregados no Pydio
  - Annex 20k_3-III Tabela de verbetes revisados na Wikipedia
  - Annex 20k_4-IV Pagina do Projeto Wikipedia Falada
  - Annex 20k_5-V Tabela de publicacoes de artigos sobre a atuacao do CEPID
  - NeuroMat em difusao
  - Annex 20k 6-VI Tabela de postagens no blog Traco de Ciencia
  - Annex 20k_7-VII Troca de email para o agendamento da visita
  - Annex 20k_8-VIII Confirmacao de submissao do artigo academico
  - Annex20k_9-IX Certificado do Online Course in Science Journalism
  - Annex20k_10-X Certificado do Treinamento em Difusao Cientifica
  - Annex20k_11-XI Confirmacao de inscricao no IV Forum de Discus
  - Annex20k_12-XII Lista de aprovados no processo seletivo para aluno
- Annex 20l – Giulia Modupe Ebohon
  - Annex_20l_1-Anexo I - video no wikimedia commons
  - Annex_20l_2-Anexo II - video no wikimedia common
  - Annex_20l_3-Anexo III - lista de postagens no blog
  - Annex_20l_4-Anexo IV - confirmacao da submissao do artigo
  - Annex_20l_5-Anexo V - certificado curso de jornalismo cientifico
  - Annex_20l-6-Anexo VI - certificado treinamento de difusao
- Annex 20m – Karolina de Souza Bergamo Almeida
- Annex 20n – Wilson Krugner Vicentim
  - Annex_20n_1-Anexo I-Lista de artigos criados e melhorados
  - Annex_20n_2-Anexo II-Número de visualizações de artigos criados e me

- Annex_20n_3-Anexo III-Lista de arquivos carregados no Wikimedia Comm
- Annex_20n_4-Anexo IV-Lista de publicações feitas no blog Traço de Ci
- Annex_20n_5-Anexo V-Resultados da análise quantitativa do artigo aca
- Annex_20n_6-Anexo VI-Certificado de conclusão de Curso de Introdução

- Annex 20o – Daniel Almeida Abrahão Dieb
  - Annex_20o_1-Anexo I - Modos de Organização e Financiamento dos Siste
  - Annex_20o_2-Anexo II - História da Ciência e da Tecnologia
  - Annex_20o_3-Anexo III -Gráfico - Mundo
  - Annex_20o_4-Anexo IV - Gráfico - Am. Latina e Caribe
  - Annex_20o_5-Anexo V - Gráfico - Invest em pesquisa e desenvolvimento
  - Annex_20o_6-Anexo VI - Gastos em CTI
  - Annex_20o_7-Anexo VII - Tabela do blog
  - Annex_20o_8-Anexo VIII - Atividades de difusão
  - Annex_20o_9-Anexo IX - Artigo acadêmico
  - Annex_20o_10-Anexo X - Aceite Intercom
  - Annex_20o_11-Anexo XI - Perfil no Centro Knight
  - Annex_20o_12-Anexo XII - Mensagens no fórum
  - Annex_20o_13-Anexo XIII - Certificate WFSJ
- Annex_21 - Technical Training.pdf
- Annex_22 - Scientific journalism.pdf