Research, Innovation and Dissemination Center for Neuromathematics

Report of Activities – 4th year

Period covered by this report: August 2015 – July 2017

1 RIDC 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

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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. 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.

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 and "Third Report of Activities 2015-2016." 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 report "Complementary Form 2013-2015", the NeuroMat research team has:

- published 83 papers;
- submitted or uploaded to arXiv 19 papers;

- 8 PhD dissertations concluded.

The full list of publications as well as rates of citations since NeuroMat's inception are provided in the appropriate section in this report.

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.

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 imple-

mentation. 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. A list of some of these

conferences and meetings in the period being assessed in this report is provided below. Presentations, programs and lists of participants are available on each meeting website.

2.4.1 Second NeuroMat Workshop: New Frontiers in NeuroMathematics (November 2016)

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.

2.4.2 High-Performance Computing, Stochastic Modeling and Databases in Neuroscience (April 2016)

To fully explore the scientific and experimental potential of the NeuroMat High-Performance Computational Center, NeuroMat organized the Workshop "High-Performance Computing, Stochastic Modeling and Databases in Neuroscience" from April 25-29, 2016. The workshop had the participation of representatives of the main world brain initiatives - the BRAIN Initiative and the Allen Institute (USA), the Human Brain Project and the Virtual Brain (Europe), the Brain/MINDS (Japan) and the International Neuroinformatics Coordinating Facility. Link for the event is neuromat.numec.prp.usp.br/hpcneuro.

2.4.3 VI Edition of the Latin American School on Computational Neuroscience (January 2016)

In January 2016, NeuroMat organized the VI Edition of the Latin American School on Computational Neuroscience (LASCON). LASCON is the first and foremost school of computational neuroscience in Latin America. It is a biennial school aimed at introducing advanced undergraduate, graduate students and young researchers to the use of mathematical and computational methods for modeling neurons and neural networks of the brain. It is an intensive four-week school with morning, afternoon and evening activities. The faculty is composed of researchers with large experience in computational neuroscience and the use of these programs. The VIII Edition of the Latin American School on Computational Neuroscience (LASCON) is currently being organized by NeuroMat and will be held in January, 2018. Link for the event is sisne.org/previous-editions/lascon-vi/?lang=en.

2.4.4 Random Graphs in the Brain (November 2015)

The model introduced in Galves and Löcherbach (2013) has as one of its components a graph of interactions between regions in the brain in several scales. The features characterizing the graph of interactions at different scales are one of the most important open questions in science. To address this question, NeuroMat organized the workshop "Random Graphs in the Brain," which took place from November 23-27, 2016. The workshop was coordinated by NeuroMat members C. Pouzat, A. Galves and C. Vargas, along with R. van der Hofstad. Link for the event is neuromat.numec.prp.usp.br/rgbrain.

2.4.5 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 Innovation and knowledge 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; this research was described on the section on Research Highlights, section 2.3. 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 Sections 2.3 and 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 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. 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 and AMPARO initiatives. NES is integrated to the Goalkeeper Game and to the NeuroMat Open Database. 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).

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 an 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. 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 scientific dissemination activities for 2015-2017 have followed directions established for 2013-2015 in its three main areas: education, communication and exhibition. This short report emphasizes achievements associated to NeuroMat's Wikipedia Initiative, a flagship of the RIDC's scientific-dissemination activities, which has reached over 14 million internet users globally.

4.1 Communication activities

Activity	**Description**	**Production**	**Impact**
NeuroMat website	Dissemination of results of each of the three RIDC areas	4,121 content pages, mostly in English	17,500 different users. 113,429 page views (since 2013)
Facebook page	Short posts on day-to-day activities at RIDC	on average, one post per day	914 community members
Newsletter	Monthly long report and short updates on NeuroMat breakthroughs	65 long reports in 40 issues	672 subscribers
Public relations	Systematic media outreach	21 releases; 7 visits by journalists since 2016	27 media pieces since January 2016
Video making	Movie production and streaming	7 releases, 8 under-production, since 2016	4,500 total views since January 2016
Blog Traço de Ciência	Reflections on scientific dissemination from the RIDC perspective	Biweekly posts	3,200 views in 2017
AMPARO website	Web production; news feeding	See section on Innovation and Knowledge Transfer	See section on Innovation and Knowledge Transfer
ABRAÇO website	Web production; news feeding	See section on Innovation and Knowledge Transfer	See section on Innovation and Knowledge Transfer

These activities are related to the general understanding that NeuroMat is a web media hub, to which interested audiences converge for high-quality information and resources. Newest communication activities in comparison to 2013-2015 are the Blog "Traço de Ciência" and the NeuroMat-led projects AMPARO and ABRAÇO. The blog has been a reference point to share learning and practice of the work

of the NeuroMat scientific dissemination team, thus being directed specifically to science communicators and educators. AMPARO and ABRAÇO are further presented in the section on Innovation and Knowledge Transfer in this report.

4.2 Education activities

4.2.1 Neuromat Wikipedia Initiative

The NeuroMat Wikipedia Initiative was launched in 2014 and has become a major element of the RIDC work in education. The focus has been the systematic improvement of content pertaining to Neuromathematics, such as topics in Probability, Statistics, Neurobiology and Stochastic Processes. As a go-to reference and the sixth most visited website in Brazil, Wikipedia attracts demographics the RIDC might have never been able to reach through other dissemination strategies; thus, improving the quality of science entries on this online encyclopedia may have an enduring impact on how top research results and processes are appropriated by general audiences. This impact has been broadened through systematic multimedia contributions to Wikipedia's media repository, the Wikimedia Commons. Per month files we have uploaded on this repository have reached over 8.5 million internet users globally. Recent highlights of the NeuroMat Wiki Initiative are: (a) 157 entries were created on Wikipedia in Portuguese by our team since August 2015; (b) 463 entries were substantially improved on Wikipedia in Portuguese by our team since August 2015; (c) 463,000 words were added to encyclopedia entries on Wikipedia in Portuguese by our team since August 2015; (d) 367,000 is the monthly average of views of articles our team has worked on Wikipedia in Portuguese since August 2015.

NeuroMat has become the largest institutional contributor to Wikipedia in Portuguese. Entries on basic mathematical terms we have worked on in Portuguese have been recognized as featured Wikipedia entries and were published on the first page of Wikipedia in Portuguese; because of our work, Wikipedia in Portuguese ranks first out of the 295 different versions of Wikipedias that exist in terms of best entries on Mathematics. Contributions to these entries are curated by NeuroMat's research team.

A relevant aspect of the work on Wikipedia is transmedia. We have produced a series of media files to illustrate Wikipedia entries, including pictures, short movies, GIFs and audio descriptions. Transmedia has been a strategy for increasing accessibility.

The NeuroMat scientific dissemination team has given 14 conferences and academic lectures on its ongoing Wikipedia initiative. Research activities associated to this initiative have led to three articles on academic journals —publications are listed on the general list of scientific production of the RIDC. Fourteen media pieces have been published on this initiative since January 2016. Four editing trainings —called "edit-a-thons"— have been promoted at the University of São Paulo since January 2016, in which dozens of new editors were recruited to improve scientific content on Wikimedia projects. A training on the use of Wikipedia in education was promoted in March, with the director of the North

American Wiki Education Foundation, LiAnna Davis.

In March 2017, the NeuroMat scientific dissemination team held a conference for RIDCs, in order to share knowledges and practices on how to use Wikimedia projects for scientific dissemination. As a first result of this conference, the NeuroMat team has provided training for the Center for the Study of Violence, which has launched its own Wikipedia initiative. Educational resources, such as introductory materials for editing science on Wikimedia projects, were produced by the NeuroMat dissemination team to foster new independent contributions.

The work of the NeuroMat scientific dissemination, especially the Wikipedia initiative, has resulted in external support, in parallel to six FAPESP-supported specific grants (Science & Media fellowships, listed below); external support is included in the specific section of additional funding sources.

4.2.2 Conferences and training

The NeuroMat scientific dissemination organized two conferences at the University of São Paulo in the period being assessed in this report: "Desafios da difusão científica," on June 9, 2016; "Cultura matemática no Brasil: diagnósticos e perspectivas," on May 16, 2017. The latter was part of the Brazil Biennial of Mathematics, to which NeuroMat is an official partner. NeuroMat-led conferences on scientific dissemination were a means of developing a general overview and grounded strategic planning for dissemination activities. The NeuroMat dissemination team took part in USP's 2015 Virada Científica and 2016 Semana de Ciência e Tecnologia, campus-wide events for disseminating science to broad audiences. Routine seminars have been organized, including a regular seminar for the team on Thursdays.

Pilots for the creation of training on topics pertaining to NeuroMat have been held with public-school teachers, in order to develop a full program and educational resources to be made available for teachers. This pilot has involved the student-led "Empresa Júnior de Informática, Matemática e Estatística," from USP.

4.3 Exhibition activities

In the context of the Wikipedia initiative, NeuroMat has established formal partnerships to promote the upload of collections of University of São Paulo museums onto the Wikimedia Commons. High-resolution images of collections of the Museum of Veterinary Anatomy and the Museum of Mathematics have been systematically released as open content. Three other museums of the University of São Paulo have worked with our team to upload their collections onto the Wikimedia Commons. As of June 2017, NeuroMat had uploaded 1,828 files, reaching typically 8 million views per month.The work with the Museum of Veterinary Anatomy has been associated to the exhibition "Inside the Brain," that was curated and developed by the NeuroMat team; this exhibition was launched in June 2017.

5 List of additional funding sources, except from FAPESP

Source of resources, except FAPESP (public or private, national or international funding agencies, universities, companies, etc)	**Equipament costs (verba de capital)**	**Other direct costs (verba de custeio)**	**Professor Salaries**	**Staff Salaries**	**Scholarships**
NUMEC – MacLinc – USP -2011-2018	R$1.488.925,25	R$503.096,75			R$18.633,84
FAPERJ-2017-2019 - E26/010.002474/ 2016 (sem previsão de depósito)	R$102.118,40	R$43.814,63			
FAPERJ-2015-2017 E26/010.002902/ 2014	R$33.130,00	R$89.000,00			
FAPERJ-2012-2015 E-26/110.526/2012	R$110.000,00	R$90.000,00			
FAPERJ PROINFRA 01.12.0308.00 (0366/11) – 2012-2015- LAboratorio de Neurociencias e Reabilitacao do INDC	R$330.000,00	R$409.000,00			
Edital Universal MCT/CNPq 14/2014-480108/2012-9	R$60.000,00	R$24.000,00			
IBRO (Inter .Brain Research Organization) – V LASCON 2014		R$53.726,40 (Euro 14.000,00 – bcb 18/08/2015)			
Edital Universal MCT/CNPq 14/2014 – 499335/2014-6	R$17.000,00	R$20.000,00			
PROBAL CAPES/DAAD – Proc. 430/15		R$33.748,00			
CAPES (PAEP 8621/2013-32) – V LASCON 2014		R$30.000,00			
Edital Universal MCT/CNPq 14/2012 478537/2012-3	R$9.000,00	R$12.000,00			R$12.960,00
Edital Universal MCT/CNPq Proc. 480053/2013-8	R$28.800,00	R$15.000,00			

CAPES/Brazilian Project Ciência Sem Fronteiras PVE 88881.068077/2014-01		R$115.695,00			
FADE/Boehringer-Ingelheim (Alemanha) – Contrato 270906	R$487.398,20 (134.000 Euros)				
Edital Universal MCT/CNPq Proc. 426579/2016-0	R$11.610,00	R$15.390,00			
CNPq (Eventos Nacionais 456821/2013-9 – V LASCON 2014		R$9.000,00			
Interdisciplinary Research Center					R$22.400,00 (US$7,000)
Wikimedia Foundation – Event Suport – Edit-a-thons on Neuroscience and Mathematics		R$5.760,00 (US$1,800)			
Wikimedia Foundation – Equipment – Museum collection upload	R$64.000,00 (US$20,000)				
Edital Universal CNPq – Proc. 426579/2016-0	R$11.610,00	R$15.390,00			
USP			R$6.190.979,13	R$1.003.132,92	R$17.600,00
UNICAMP			R$2.112.461,00		
UFRJ			R$431.400,00		
UFRN			R$203.834,10		
UFPE			R$411.137,80		
UFABC			R$48.529,16		
UFOP			R$234.443,30		
UFRGS			R$273.639,70		
UFMG			R$386.477,00		
UFSCar			R$281.031,40		
IMPA			R$360.000,00		
Bolsa de Produtividade em Pesquisa - CNPq					R$476.900,00 (RT-R$247.000,00)
Bolsas de Doutoramento - CAPES					R$330.000,00

Bolsas de Doutoramento – CNPq					R$105.600,00
Total	R$2.659.991,85	R$1.507.020,78	R$10.933.932,59	R$1.003.132,93	R$961.693,84

6 Evaluation of institutional support

The University of São Paulo has consistently supported NeuroMat efforts. Firstly, USP assigned an executive manager to NeuroMat, Magda Chang, in October 2015. Magda Chang has been on maternity leave from February to October, 2017.

Secondly, USP offered in 2016 an Assistant Professor position to each USP departments hosting an RIDC. In our case, this position was assigned to the Department of Statistics at IME-USP and for candidates working on stochastic modeling of neurobiological data. Four candidates have applied, including two NeuroMat postdoctoral researchers, and the selection procedure will be over by August, 2017.

Both the positions of the executive manager and the assistant professor are counterparts of USP to FAPESP's support to NeuroMat.

USP had previously assigned two other staff personnel to NAP NUMEC/MacLinC, coordinated by Antonio Galves, which was at the origin of the NeuroMat project. Carlos Eduardo Ribas is an IT analyst (IME/USP - Procontes); and Lourdes Netto (IME/USP) is an administrative assistant who was assigned to NAP NUMEC/MacLinC by the direction of IME-USP.

Several efforts have been made to have another staff member to work as a manager of the dissemination area. These efforts have not been successful yet.

7 Publications, citations URL and PhD dissertations

MyResearcherID: www.researcherid.com/rid/J-2428-2015

Google Scholar: scholar.google.com.br/citations?user=OaY57UIAAAAJ&hl=pt-BR

PhD dissertations: neuromat.numec.prp.usp.br/relatorio/2017/phd_dissertations.pdf

8 International advisory board reports

International advisory board reports are available at: files.numec.prp.usp.br/data/public/assessments. Password: neuromat2017

Full list:

- Annex_1_Leonardo_Cohen_February112014
- Annex_2_David_Brillinger_June_11_2015
- Annex_3_Charles NewmanAugust142015
- Annex_4_Wojciech_Szpankowski_November_2015_July_2017.pdf