RIDC NeuroMat

Eleventh Report of Activities

Aug 01, 2023 - Jul 30, 2024

Contents

1 Important Notice

Sadly, on September 5, 2023 professor Antonio Galves passed away unexpectedly. Professor Oswaldo Baffa was chosen by the RIDC PIs and approved by FAPESP to succeed professor Galves in the coordination of this project. The importance and achievements of professor Galves were recognized by the Instituto de Matemática e Estatistica (IME-USP) through the award of the Emeritus Professorship and nomination of the NeuroMat headquarter building as *Edifício Antonio Galves*. Other honors are being planned by other institutions.

2 Highlights of the period

- **Modeling networks of spiking neurons as systems of interacting point processes with memory of variable length.** The model introduced by Galves and Löcherbach (2013) is a microscopic model because it describes the neuronal dynamics with a single-cell resolution. Since then, population-based versions of the Galves-Löcherbach model have been put forth to model dynamic phenomena at mesoscopic and macroscopic levels, like EEG and fMRI. A major step in the population-based approach in the period was the publication of the article On a finite-size neuronal population equation, by V. Schmutz, the NeuroMat distinguished associate investigator outside São Paulo E. Löcherbach, and T. Schwalger, in *SIAM Journal of Applied Dynamical Systems* **vol. 22**, pp. 996-1029 (2023). The paper proves the well-posedness and stability of a finite size population model, which captures the effect of finite-size fluctuations of the average population activity on the system's dynamics.

- **Statistical model selection employing the Goalkeeper Game.** Two articles published by NeuroMat researchers, Response times are affected by mispredictions in a stochastic game, by P. R. Cabral-Passos, A. Galves, J. E. García and C, D. Vargas, in *Scientific Reports* **vol. 14**, 8446 (2024), and Probabilistic prediction and context tree identification in the Goalkeeper game, by N. Hernández, A. Galves, J. E. García, M. D. Gubitoso and C. D. Vargas, in *Scientific Reports* **vol. 14**, 15467 (2024), established the Goalkeeper Game as a new and promising protocol for studying sequence learning in humans. The article by Hernández et al (2024) identified which features of the context tree used to generate the sequence of events in the Goalkeeper Game make the sequence more difficult to learn. And the article by Cabral-Passos et al (2024) shows evidence that the response time during the game depends not only on the results of the choices made by the player but also on the predictability of the sequence of stimuli provided.

- **Construction of a robot arm to deliver transcranial magnetic stimulation (TMS) to specific cortical sites**. The major achievements in the period were the publications of the articles

Robotic–electronic platform for autonomous and accurate transcranial magnetic stimulation targeting, by R. H. Matsuda, V. H. Souza, T. C. Marchetti, A. M. Soto, O.-P. Kahilakoski, A. Zhdanov, V. H. E. Malheiro, M. Laine, M. Nyrhinen, H. Sinisalo, D. Kicic, P. Lioumis, R. J. Ilmoniemi and O. Baffa , in *Brain Stimulation* **vol. 17**, pp. 469-472 (2024), and MarLe: Markerless estimation of head pose for navigated transcranial magnetic stimulation, by R. H. Matsuda, V. H. Souza, P. N. Kirsten, R. J. Ilmoniemi and O. Baffa, in *Physical and Engineering Sciences in Medicine* **vol. 46**, pp. 887-896 (2023). The first paper discusses in detail the validation combination of the use of multi-locus TMS that enables the stimulation of nearby cortical regions electronically, without physically moving the coil set with a robotic system demonstrating that collaborative robots can improve the reproducibility and precision of TMS. The second paper introduces MarLe, a markerless head tracker neuronavigation software for TMS which uses computer-vision techniques combined with low-cost cameras to estimate the head pose for neuronavigation. MarLe makes navigated TMS easier and more precise with impact in the experiments being conducted by NeuroMat and other groups.

- **Innovation research related to the NeuroMat Parkinson Network (AMPARO)**. A new postural instability index (PII) was introduced in the article A non-expensive bidimensional kinematic balance assessment can detect early postural instability in people with Parkinson's disease, by G. V. Santos, M. S. d'Alencar, A. F. Helene, A. C. Roque, J. G. V. Miranda and M. E. P. Piemonte , in *Frontiers in Neurology* **vol. 14**, 1243445 (2023). The index is based on kinematic parameters generated by a two-dimensional movement analysis software and had a better performance in discriminating the decline in postural control across the first three stages of disease evolution than other clinical balance tests. The PII, together with the gait performance index (GPI) introduced earlier in the article A non-expensive bidimensional assessment can detect subtle alterations in gait performance in people in the early stages of Parkinson's disease, by M. S. d'Alencar, G. V. Santos, A. F. Helene, A. C. Roque, J. G. V. Miranda and M. E. P. Piemonte , in *Frontiers in Neurology* **vol. 14**, 1101650 (2023), are part of a suite of tests being developed by the NeuroMat AMPARO team to assess people in the early stages of Parkinson's disease.

- **Building on Models: Experiences from a Decade with the Microcircuit model** was a workshop held at the Käte Hamburger Kolleg, Aachen, Germany, 3-4 April, 2024. The purpose of the event was to celebrate the 10th anniversary of the publication of the Potjans-Diesmann cortical microcircuit model, which was the first full scale model of the neural circuitry under 1 mm^2 of sensory cortex surface. The NeuroMat SimLab, coordinated by A. C. R. da Silva Filho at USP in Ribeirão Preto, was the first to use the graph of neural connections of the Potjans-Diesmann model to implement a stochastic version of the cortical microcircuit using the Galves-Löcherbach neuron

model. Because of this, da Silva Filho was invited to participate in the event to give a talk about the SimLab's experience in simulating the Potjans-Diesmann model.

- **USP Thesis Award, 12th edition**. The former NeuroMat PhD student (now NeuroMat post-doctoral fellow) Renan H. Matsuda, co-advised by O. Baffa Filho and V. H. O. Souza, won the prize in the area of Technological Innovation with the thesis Robotized System for Navigated Transcranial Magnetic Stimulation. The thesis describes in detail the development and validation of the closed-loop control system for robotized TMS coil positioning, and the MarLe system for markerless navigated TMS head tracker.

- **Three PhD students and three MSc students under the supervision of NeuroMat PIs** obtained their respective degrees during the period assessed in this report. Details are provided in Annex 10.

- **The development of a comprehensive methodology and operational framework to preserve the center's decade-long legacy** in research, innovation, and dissemination was a central focus of NeuroMat's dissemination efforts during the reporting period. This initiative involved the systematic archiving of research outputs, software tools, and media content. Over 8,000 content files have been archived digitally. Preservation procedures adhered to an open-science commitment, utilizing free repositories and accessible formats. In addition to preservation, efforts included creating media content that offers time-based learning accounts of the work conducted at NeuroMat since 2013.

3 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: Aalto University; Centre National de la Recherche Scientifique - CNRS (Strasbourg); Faculdade Cásper Líbero; Forschungszentrum Jülich; Gran Sasso Science Institute (GSSI); IBM Thomas J. Watson Research Center; Instituto de Matemática Pura e Aplicada (IMPA); National Institute of Neurological Disorders and Stroke (NIH); New York University Shanghai; Universidad de Buenos Aires; Universidad de la Republica; Universidad de San Andrés; Universidade Estadual de Campinas (UNICAMP); Universidade Federal do ABC (UFABC); Universidade Federal do Pará (UFPA); 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); Universidade Federal de São Paulo (UNIFESP); Università

di Roma "La Sapienza"; Université Côte d'Azur; Université Paris 1 (Pantheon-Sorbonne); University of California, Berkeley.

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

Principal Investigator/Center Director: Oswaldo Baffa Filho; Jefferson Antonio Galves (*in memoriam*)

Vice Director: Pablo Augusto Ferrari

Co-Principal Investigators: Antônio Carlos Roque da Silva Filho; Claudia Domingues Vargas; Ernst Hamburger (*in memoriam*); Fernando Jorge da Paixão Filho; Florencia Graciela Leonardi; Jorge Stolfi; Osame Kinouchi Filho; Maria Elisa Pimentel Piemonte; Pablo Augusto Ferrari

Education and Knowledge Dissemination Coordinator: Fernando Jorge da Paixão Filho

Technology Transfer Coordinator: Antônio Carlos Roque da Silva Filho

RIDC Executive Manager:

System analyst:

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 which has as mission to develop the new mathematics needed to construct a Theory of the Brain accounting for the experimental data gathered by neuroscience research. Antonio Galves coordinated the center until his death on September 5, 2023, and Oswaldo Baffa has been coordinating it since October 4, 2023. 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, which will last until July 2025.

The RIDC NeuroMat has an interdisciplinary team, bringing together researchers in mathematics, statistics, physics, computer science, neuroscience, biology, physiotherapy, medicine 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, Europe and China (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.

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 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, *in memoriam*), Florencia Graciela Leonardi (USP), Jorge Stolfi (UNICAMP), Claudia Domingues Vargas (UFRJ), Maria Elisa Pimentel Piemonte (USP), and Osame Kinouchi Filho (USP) remain co-principal investigators, along with PI Oswaldo Baffa Filho (USP) and Jefferson Antonio Galves (USP, *in memoriam*). David Brillinger (UCBerkeley), Francesco Guerra (Universita di Roma "La Sapienza"), Leonard Cohen (National Institute of Neurological Disorders and Stroke), Markus Diesmann (Jülich Institute of Neuroscience and Medicine), 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 (now called Antonio Galves 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 three laboratory facilities: an EEG laboratory (EEG Lab) at its main building in São Paulo, and a Simulation Laboratory (SimLab) and a TMS experimental facility (TMS Lab) at the USP Ribeirão Preto campus. Multiuser experimental facilities in São Paulo and Ribeirão Preto are being planned. NeuroMat's administrative staff team is composed of one administrative assistant. This position is supported by USP.

4 Scientific report

4.1 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.

4.2 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 exhaustively 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," the "Complementary Form 2015-2017," "Fourth Report of Activities 2016-2017," the presentation "NeuroMat: first 5 next 6" to FAPESP's International Assessment Committee, the 2018 Statement of Impact (SoI), "Fifth Report of Activities 2017-2018," "Sixth Report of Activities January 2019-July 2019," "Seventh Report of Activities August 2019-October 2020," "Eighth Report of Activities November 2020-August 2021." "Ninth Report of Activities August 2021-July 2022.", "Complementary Form 2017-2022.", and "Tenth Report of Activities July 2022-August 2023." These documents were carefully reviewed by FAPESP. The SoI is a summary of main activities and highlights our main achievements. This statement is still up-to-date and informs substantially this report, along with relevant parts of the document for the renewal of the RIDC NeuroMat by FAPESP, the "Project for the period 2018-2024".

The research of the RIDC led to innovative applications of the new stochastic models and statistical tools to concrete questions of Neuromathematics and computational modeling in neurobiology, electroencephalographic recordings analysis, and neurorehabilitative therapy. Research highlights are given in Section 2 and corresponding published works are listed below, in the appropriate section. Since the "Tenth Report of Activities", the NeuroMat research team has:

- published 49 papers;
- submitted 13 online pre-prints;
- had 7 PhD theses concluded and 10 in progress;

- had 7 MSc dissertations concluded and 3 in progress.

NeuroMat scientific publications in the period being assessed in this report are listed on Annex 2. A full list of publications since the inception of NeuroMat can be viewed at NeuroMat's Google Scholar (https://goo.gl/LvZV4f). Citations to these publications across the years are available on Annex 3.

In parallel to the mathematical and theoretical biological developments which are necessary to foster the scientific project of NeuroMat, the RIDC has also sustained three laboratories. In April 2016, NeuroMat launched a new research facility: the NeuroMat Simulation Laboratory (SimLab). The simulation of large-scale network models remains a key activity to test analytical results, and the NeuroMat SimLab allows for such tests, providing the NeuroMat team with a new experimental tool to test and construct large-scale computational implementations of NeuroMat's newly developed models. The SimLab 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 (EEG Lab), with an EEG DC actiCHamp 128CH System. The creation of NeuroMat's EEG lab was made possible by the expansion of its main building, through a grant from the University of São Paulo (value of support: BRL R$ 1,603,339). A transcranial magnetic stimulation facility (TMS Lab) equipped with a robotic arm started operations in January 2020 at the Biomagnetism Laboratory (Biomag Lab) of the Department of Physics of USP Ribeirão Preto, under the direction of the NeuroMat Director O. Baffa Filho. Two multiuser experimental facilities equipped with high end equipment for data acquisition are being planned.

4.3 Research results highlights

There are two main axes in the NeuroMat research agenda, which follow:

- the development of a new class of stochastic processes aimed at a realistic description of nets of spiking neurons;

- the introduction of a new mathematical approach to address the classical conjecture that the brain retrieves statistical regularities from sequences of stimuli.

The first axis appears to be by now a well-established area of research in Probability Theory and Mathematical Neuroscience. For instance, according to Google Scholar, there have been around 150 papers with direct references to its foundational paper (Galves and Löcherbach (2013)). Since 2023, there have been 27 publications with direct references to this paper. A notable example is the 2023 paper On a finite-size neuronal population equation, highlighted in Section 2. While co-authored by Eva Löcherbach, a member of the NeuroMat team, the paper's primary author is Tilo Schwalger, who is not

affiliated with NeuroMat. This illustrates that the use of stochastic point processes with variable-length memory for modeling neuronal systems has now become a focus of research within the global scientific community.

Still related to the Galves-Löcherbach model, an important result during this period was the article Less is different: Why sparse networks with inhibition differ from complete graphs, by G. Menesse and O. Kinouchi, in *Physical Review E* **vol. 108**, 024315 (2023). In this article, co-authored by NeuroMat's co-PI Osame Kinouchi Filho (FFCLRP-USP), it is shown that for networks composed of excitatory and inhibitory Galves-Löcherbach neurons, the behavior of the network with sparse connectivity fundamentally differs from that of the network with a complete graph, unlike what occurs when only excitatory neurons are present, where the behavior is similar for both the complete graph and sparse connectivity.

The second research axis has evolved into a new research program in which statistical modeling of response times and choice rates in the Goalkeeper Game is used for parameterization of sequential learning in humans. Examples of recent works within this program are the articles by Hernández et al (2024) and Cabral-Passos et al (2024) mentioned in Section 2. Their results provide insights on how the brain deals with uncertain information by investigating simple aspects of behavior, such as response time.

A complete list of papers is available as Annex 2.

4.4 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 community 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 the period covered by this report, we continued with this endeavor and the meetings and training activities organized are listed below.

- XXVI Brazilian School of Probability (*XXVI Escola Brasileira de Probabilidade*, EBP), in honor of Antonio Galves, held at USP São Paulo from July 30 to August 5, 2023. The EBP is a traditional international event which has been running since 1997 by initiative of the Brazilian probability community. It represents a good opportunity for researchers and students from Brazil and abroad to interact, always at a very high scientific level with the participation of some of the best world

leaderships in the field. This time the EBP had a special emphasis on Neuromathematics, with courses by Eva Löcherbach and Patricia Reynaud-Bouret from the international NeuroMat team.

- RIDC NeuroMat Researchers Workshop 2023. The workshop was held October 25-26, 2023, at the main NeuroMat building. It was the first NeuroMat event after the death of Antonio Galves, and its objective was to give opportunity to NeuroMat's graduate students and postdocs to present their current work to all members of the RIDC.

- LASCON 2024 - IX Latin American School on Computational Neuroscience. This was the ninth edition of this traditional worldwide school on computational neuroscience, which since 2016 has been a NeuroMat activity. The school was held at the main NeuroMat building between January 8 and February 2, 2024. LASCON 2024 gathered 62 participants (lecturers plus students) from 16 different countries in the Americas, Europe and Asia.

- EEG Training ActiCHamp and ActiCHamp Plus. This was a training event with NeuroMat's EEG equipment, offered to interested students and researchers, which was held January 8-9, 2024, at NeuroMat's EEG Lab. The training provided complete introduction to EEG data acquisition using actiCHamp and actiCHamp Plus, with hands-on practices with 32 channels increasing up to 128 channels, plus auxiliary channels.

- *Da Teoria à Prática: Dominando Aplicações do fNIRS em Pesquisa Clínica*. The workshop was held on April 9, 2024, at the main NeuroMat building. It was organized by NeuroMat's AMPARO team to promote theoretical and practical training on functional near-infrared spectroscopy (fNIRS), which is a new technique to be used by NeuroMat members in their research.

- *Simpósio de pesquisadores do CEPID NeuroMat: rumo ao CEPIX NeuroMat*. The symposium was held June 26-27, 2024, at the main NeuroMat building. The symposium was planned to take place alongside the event *CEPIx USP: novas fronteiras de pesquisa*, promoted by USP with all the RIDCs linked to the university on the morning of June 27. On June 26, the symposium had talks by NeuroMat members presenting their latest research results. At the end of the day, there was a plaque unveiling ceremony in honor of Antonio Galves, which gave his name to the main NeuroMat building. On the afternoon of June 27, after the USP event, the symposium continued with presentations by invited researchers who are not part of NeuroMat, discussing potential research topics to integrate into the new CEPIx NeuroMat research project.

5 Technology transfer report

The main focuses of this area have been the development of supporting tools for the diagnosis and neuro-rehabilitation research being conducted by the AMPARO and ABRAÇO initiatives on Parkinson's Disease and Brachial Plexus Injury, respectively. These tools are the Goalkeeper Game, a robot arm for accurate real-time positioning of a transcranial magnetic stimulator on the head, and the Neuroscience Experiments System (NES). Details and links to the GitHub pages of the software developed by NeuroMat can be seen at NeuroMat's Intellectual Property webpage.

An important milestone was the introduction of the gait performance and postural instability indexes (GPI and PII) in the articles by d'Alencar et al. (2023) and Santos et al. highlighted in Section 2. Together, they are part of the Parkinson's Affordable Neuro-movement Detection and Analysis (PANDA) system being developed by the AMPARO team coordinated by Neuromat co-PI M. E. P. Piemonte (FM-USP). The PANDA system aims to offer a low-cost, fast, and user-friendly alternative for monitoring gait automaticity decline in people in the early stages of Parkinson's disease.

The highlight of the period was related to the robot arm development. The communication protocol between the robotic arms was improved by developing a hybrid system that integrates the Robot Operating System (ROS) with a socket-based communication framework. This system facilitates interaction between the robots, neuronavigation systems, electroencephalography (EEG), and electromyography (EMG), bringing more robustness and flexibility to the system. Additionally, an algorithm for synchronizing and executing experimental protocols was created. This code processes information from the neuronavigator and robotic positioning, controlling the brain stimulation device and the data acquisition equipment. It is designed to be flexible, allowing users to define and create new stimulation protocols, synchronized with the acquisition of physiological data. A new robotic arm (Dobot) with higher payload was acquired and fully integrated with the InVesalius Neuronavigator and a new infrared camera system (Polaris-Vega). The arm required the development of a stable stand made with aluminum structured profiles. New goggles with infrared markers were also tested and implemented. The system was entirely developed at the TMS Lab at USP Ribeirão Preto led by NeuroMat Director Oswaldo Baffa Filho, and is now ready to be used and tested in experimental neuroscience set ups. The first robotic arm (Han*s) is already in operation at the research group led by NeuroMat co-PI Claudia D. Vargas at the Federal University of Rio de Janeiro (UFRJ). Other research groups have been in contact with our group, as a multiuser experimental facility, to use the robotic arm in their experiments. The feedback of the performance of the two models of the robotic arm will be important to improve the whole system, making it more robust and resilient.

5.1 Neuro-rehabilitation and diagnosis

5.1.1 ABRAÇO Initiative

NeuroMat's Brachial Plexus Injuries focus area is called ABRAÇO Initiative, or Ação NeuroMat para a Lesão do Plexo Braquial. The ABRAÇO 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.

5.1.1.1 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 5.2.1) to study mechanisms of plasticity in the brain after a brachial plexus injury (TBPI) aiming at developing new tools to assess plastic changes in the brain induced by this traumatic injury. New evidence of these plastic changes were gathered recently by our team. The publication Plasticity of face–hand sensorimotor circuits after a traumatic brachial plexus injury, by F. F. Torres, B. L. Ramalho, M. R. Rodrigues, A. C. Schmaedeke, V. H. Moraes, K. T. Reilly, R. P. Carvalho, C. D. Vargas, in *Frontiers in Neuroscience* **17**:1221777 (2023), investigated bilateral changes in inhibitory circuits of the sensorimotor cortex after a traumatic brachial plexus injury. In the paper Upper limb joint coordination preserves hand kinematics after a traumatic brachial plexus injury, by L. Lustosa, A.E. Lemos Silva, R.P. Carvalho and C. D. Vargas, which appeared in *Frontiers in Human Neuroscience* **16**:944638 (2023), the authors suggest that upper limb coordination is reorganized after a traumatic brachial plexus injury so as to preserve hand kinematics. 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 healthy 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 first results have appeared in the article Probabilistic prediction and context tree identification in the Goalkeeper game, by N. Hernández, A. Galves, J. E. García, M. D. Gubitoso and C. D. Vargas, in *Scientific Reports* **vol. 14**, 15467 (2024). Furthermore, data collection from patients with brachial plexus injury has been made to investigate how this injury interferes in the ability of these individuals to predict events compared to healthy subjects. The first results and their analysis were reported in the article Response times are affected by mispredictions in a stochastic game, by P. R. Cabral-Passos, A. Galves, J. E. García and C, D. Vargas, in *Scientific Reports* **vol. 14**, 8446 (2024). This important step to better understanding the prediction process after a brachial plexus injury could help in the development of new treatments for this injury. More specifically, the objective is to check the possibility of using the Goalkeeper Game as a tool for rehabilitation of brachial plexus injury patients

5.1.1.2 New transcranial magnetic stimulation protocol

This endeavor involves a collaboration between NeuroMat Director Oswaldo Baffa Filho (FFCLRP/USP), NeuroMat CO-PI Claudia Domingues Vargas (INDC/UFRJ) and R. Ilnomiemi (Aalto) for the development of a closed-loop robotic system for the positioning of a transcranial magnetic stimulation (TMS) coil on a subject's scalp (see Section 5.3.1). Besides the technological aspects of this initiative, a team of researchers led by NeuroMat CO-PI Claudia Domingues Vargas is developing a new protocol to test whether the primary motor cortex (M1) holds the memory of a sequence of TMS pulses driven by a stochastic chain. If so, it should be possible to recover in the motor evoked response (MEP) a signature of a sequence of TMS pulses applied in M1. In other words, can a sequence of TMS pulses generated by a stochastic chain be recovered on the MEP response? Having this answer, then it would be interesting to test if this recovered signature is affected by a brachial plexus lesion.

5.1.2 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. The AMPARO website is a reference source on Parkinson's disease in Brazil, providing scientific and practical information, case histories and questions and answers for people with Parkinson's disease, their relatives and caregivers.

5.1.2.1 A tool for early Parkinson's Disease diagnosis

The team led by Neuromat CO-PI Maria Elisa Pimentel Piemonte (FM-USP) is using the Goalkeeper Game (see Section 5.2.1) 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 objective is to develop a new measure and typology to establish the limits between normal decline associated to aging process and abnormal alterations associated to 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. The main step towards this goal in the period has been the development, in collaboration with J. G. Vivas Miranda (UFBA), of two indexes based on a two-dimensional movement analysis that uses kinematic gait variables to detect subtle alterations in gait and postural control in early stages of Parkinson's disease. These indexes, named gait performance index (GPI) and postural instability index (PII), were introduced in the articles A non-expensive bidimensional assessment can detect subtle alterations in gait performance in people in the early stages of Parkinson's disease, by M. S. d'Alencar, G. V. Santos, A. F. Helene, A. C. Roque, J. G. V. Miranda and M. E. P. Piemonte , in *Frontiers in Neurology* **vol. 14**, 1101650 (2023), and A non-expensive bidimensional kinematic balance assessment can detect early postural instability in people with Parkinson's disease, by G. V. Santos, M. S. d'Alencar, A. F. Helene, A. C. Roque, J. G. V. Miranda and M. E. P. Piemonte , in *Frontiers in Neurology* **vol. 14**, 1243445 (2023). Currently, in

the clinical setting, these alterations can only be identified in moderate to advanced stages of the disease. The new indexes, which can be widely used in clinical practice, may open therapeutic windows for new interventions that can prevent falls and higher levels of disability in people with Parkinson's disease.

5.1.2.2 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. In particular, in collaboration with national and international institutions, including the Movement Disorder Society, which is a global reference in Parkinson's disease. An important contribution of the AMPARO network during this period was the publication of two articles: Comparison of disability level between Early and Late Onset Parkinson's Disease using WHODAS 2, by I. A. P. S. Nascimento, K. C. C. Nóbrega, B. R. A. Souza, I. C. Barone, G. Checchio, V. P. Ponciano, C. G. C. de Paula, A. N. Possani, N. C. Penha, A. F. Helene, A. C. Roque, R. Savica and M. E. P. Piemonte , in *Frontiers in Neurology* **vol. 14**, 1281537 (2023), and The impact of motor, non-motor, and social aspects on the sexual health of men living with Parkinson's disease, by B. R. A. Souza, K. C. C. Nóbrega, B. E. A. da Silva, R. A. Gonçalves, T. S. Martins, G. F. Santos, A. F. Helene, A. C. Roque, I. A. P. S. Nascimento and M. E. P. Piemonte , in *Journal of Parkinson's Disease* **vol. 14**, pp. 565–574 (2023). They report statistical studies with samples of Brazilians with Parkinson's disease, and their results are useful for helping to map the challenges faced by those living with Parkinson's in Brazil..

5.2 Computational tools

5.2.1 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 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 the 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: Brachial Plexus Injuries and Parkinson's Disease (see Sections 5.1.1.1 and 5.1.2.1). The game is openly, freely available at: game.numec.prp.usp.br and also at Apple Store and Google Play.

5.2.2 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 5.1.1) and AMPARO (Section 5.1.2) initiatives. NES is integrated to the Goalkeeper Game (Section 5.2.1) and to the NeuroMat Open Database (Section 5.2.3). The main functionalities, which include Electrophysiology and Export modules, were improved in the period, and modules that deal with data from machine learning tools are being developed. The development team of the Neuroscience Experiments System is led by the Associate Investigator Kelly R. Braghetto (IME/USP).

5.2.3 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 was 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 that use NES (Section 5.2.2). 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 the Associate Investigator Kelly R. Braghetto, and its source code is available at NeuroMat's GitHub portal.

5.3 Hardware tools

5.3.1 Closed-loop system of robotic stimulator positioning in the brain

The impact of transcranial magnetic stimulation (TMS) on the brain is remarkably precise; deviations of approximately 1 mm in positioning and a few degrees in coil angles can evoke significantly divergent responses. In addition, the patient or volunteer being awake throughout the procedure performs small involuntary movements, even with the head secured on a head strain. If the subject moves during stimulation, the stimulator must be repositioned. As a solution to this problem, robotic arms have been proposed to help position the TMS coil. Robotic positioning also enables the development of new methods for automated motor mapping. However, the combination of TMS and robotic arms is not yet commonly used by the clinical and scientific communities due to three main factors. The first is low portability, that is, the systems are fixed and cannot be transported between rooms and clinics. The second is the high cost of commercial equipment. And the third is that commercial navigation programs are closed systems, making it impossible for new tools to be developed to test different research protocols. A closed-loop system is a set of mechanical or electronic devices that automatically regulates a variable to the desired state, without human interaction. Closed-loop systems are designed to automatically achieve and

maintain the desired condition (exit condition), comparing it to its condition at the given moment (real condition). Since the last report, the team led by NeuroMat Director O. Baffa Filho and R. Ilmoniemi has completed the development of a novel methodology of an autonomous robotized multilocus TMS (mTMS) positioning system. The development of the mTMS stimulator continues at Aalto University and the postdoc Renan Matsuda spent one year in Helsinki working in this area also to ensure a smooth transfer of skills and technology from this group to Neuromat´s group. It is now possible to combine robotic positioning with mTMS electronic targeting, enabling the automation of TMS procedures, such as hotspot hunting and motor mapping. The robot control can accurately position the TMS coil on the target, and it can also follow the patient's head, performing an automated head move compensation. The robot control achieves superior accuracy than with manual positioning and comparable stability and accuracy to existing robotized TMS systems. The motor mapping experiment demonstrated the system's ability to perform high-density mappings in a fast and autonomous way. The new open-source platform for robotic control of mTMS transducer positioning represents an important step to increase the accuracy and reliability of TMS procedures. This platform facilitates the development of new tools and methods for brain investigation. The automation of mTMS procedures can bring more streamlined, safe, and reproducible applications in both clinical and research environments. For the next step, the real-time EMG and EEG analyses will be combined with the robot control, enabling coil positioning and targeting based on the physiological responses. This integration will, in turn, enable the development of new TMS protocols to test whether the primary motor cortex (M1) holds the memory of a sequence of TMS pulses driven by a stochastic chain.

The paper Robotic–electronic platform for autonomous and accurate transcranial magnetic stimulation targeting, by R. H. Matsuda, V. H. Souza, T. C. Marchetti, A. M. Soto, O.-P. Kahilakoski, A. Zhdanov, V. H. E. Malheiro, M. Laine, M. Nyrhinen, H. Sinisalo, D. Kicic, P. Lioumis, R. J. Ilmoniemi and O. Baffa , published in *Brain Stimulation* **vol. 17**, pp. 469-472 (2024), provides an in-depth analysis of the validation process for using mTMS. It also demonstrates how collaborative robots can enhance the reproducibility and precision of TMS. The paper MarLe: Markerless estimation of head pose for navigated transcranial magnetic stimulation, authored by R. H. Matsuda, V. H. Souza, P. N. Kirsten, R. J. Ilmoniemi and O. Baffa, published in *Physical and Engineering Sciences in Medicine* **46**, pp. 887–896 (2023), is an important step to improve the coil positioning by using face fiducial marks to guide the robotic arm. The Paper Real-time tractography-assisted neuronavigation for TMS, authored by D. B. Aydogan, V. H. Souza, R. H. Matsuda, P. Lioumis, R. J. Ilmoniemi, *bioRxiv* 2023.03.09.531565 (2023), demonstrates the incorporation of real-time tractography into the neuronavigation system, enabling the visualization of neural fiber networks at stimulation points. The combination of real-time tractography and TMS opens doors to the formulation of new protocols for defining the target brain areas for

stimulation. This combination allows for a deeper understanding of brain connectivity, facilitating the training of machine learning models for target stimulation identification through the analysis of cerebral nerve fibers. This study has the potential to automate the positioning of the stimulator at the hotspot and to identify stimulation targets in neurological diseases with greater accuracy. This approach is being developed by master's degree student Lucas dos Santos Betioli, under the supervision of NeuroMat's Director Oswaldo Baffa Filho and co-supervision of Renato Tinós (FFCLRP-USP), with collaboration from postdoctoral researcher Renan H. Matsuda.

6 Dissemination report

NeuroMat's dissemination activities have as a compass point working as a collaborative 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. Activities are envisioned to use innovative means to transform scientific culture, overcoming artificial field boundaries and contributing to foment an integrated and genuinely multidisciplinary approach to the study of the brain. These activities have seen a significant increase in production and viewers in the context of the pandemic.

NeuroMat's milestone dissemination activities include in the period of interest:

- the *A Matemática do Cérebro* podcast
- the Wikimedia Initiative
- Media Exposure
- Web resources: portal, Facebook page, dissemination blog
- NeuroCineMat
- the Introduction to Science Journalism course
- NeuroMat's science dashboard

6.1 The *A Matemática do Cérebro* podcast

The RIDC NeuroMat launched in August 2019 the podcast "A Matemática do Cérebro" – in Portuguese, Mathematics of the Brain. This resource is available on the most important podcast technologies and also hosted on its own website. The podcast was envisioned by former NeuroMat director Antonio Galves (in memoriam) and NeuroMat associate investigator Eduardo Vicente.

NeuroMat's podcast is aimed at covering three main topics: the model for systems of spiking neurons that the research team developed; the Statistician Brain conjecture; and pertaining institutional aspects of doing research in Brazil. The overall goal is to bring public awareness on work that is being done within the NeuroMat community.

NeuroMat podcasts have released 11 episodes, which have reached 1,459 plays on Spotify in the period of interest for this report. A new season is currently under production, supported by a science journalism fellowship.

6.2 The Wikimedia 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 a "success case" of the use of Wikipedia and other collaborative projects as a means of scientific dissemination.

Main achievements on Wikipedia have been:

- 322 million content viewers in Wikimedia; and
- 193 thousand words added to Portuguese Wikipedia and related projects.

Moreover, NeuroMat has been engaged in uploading media files to the open repository Wikimedia Commons. In the period assessed by this report, 4,442 files had been uploaded by the NeuroMat team in this repository. These files have reached 1,916,233 views per month, on average (from 2019 to 2023).

In the period covered by this report, an on-wiki portal for the Wikimedia Initiative has been launched at: https://pt.wikipedia.org/wiki/WikipÃ©dia:GLAM/CEPID_NeuroMat

The control panel of the NeuroMat Wikipedia Initiative is available at: https://outreachdashboard.wmflabs.org/campaigns/neuromat/programs.

The NeuroMat Wikipedia Initiative has been featured on a special paper at Pesquisa FAPESP, available at: https://revistapesquisa.fapesp.br/pesquisadores-e-estudantes-ajudam-a-melhorar-verbetes-da-wikipedia/.

6.3 Media Exposure

Activities from FAPESP'S RIDC NeuroMat were featured in around a hundred external media outlets since its inception in 2013. NeuroMat's media clipping for this year is attached to this report as Annex 4.

A highlight of the period were the interviews given by NeuroMat's Associate Investigator A. F. Helene (IB-USP) to the Hiperconectado program of the public network television *TV Cultura*. The interviews, available on the network's Youtube channel (Interview 1, Interview 2) took place at the Museum of Veterinary Anatomy of USP. They were centered around aspects of the nervous system's organization, using the backdrop of the exhibition set up under the scope of NeuroMat in 2018.

6.4 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. There have been 104,481 pageviews in the period of interest of this report.

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 4,661 followers, as of July, 2024, including complementary communities led by the ABRAÇO and AMPARO initiatives. Community growth has been organic.

Since April 2016, the NeuroMat dissemination team has maintained 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".

Posts on this resource have been published continuously; a detailed report is provided on Annex 6.

References are:

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

6.5 NeuroCineMat

The NeuroMat dissemination team has fully produced 385 movies. A full list is available on the NeuroMat Youtube channel. There has also been continuous streaming of activities on YouTube. A full list is available on:

https://www.youtube.com/user/neuromathematics

This material has been viewed on Youtube and Facebook 80,395 in the period of the interest of this report.

6.6 The Introduction to Science Journalism course

The NeuroMat dissemination team launched in 2021 an Introduction to Science Journalism course to contribute to capacity building of communications professionals who are interested in specializing in science coverage. The course strictly abides to curriculum expectations of the Mídia & Ciência call.

The course has been developed under the supervision of NeuroMat PI Fernando J. Paixão, supported by NeuroMat team members and FAPESP science-journalism fellows.

The course is available freely on Wikiversity:

https://pt.wikiversity.org/wiki/Introdução_ao_Jornalismo_Científico.

This course has become a major asset for FAPESP's journalism fellowships, for NeuroMat and for other scientific projects supported by FAPESP. Since 2017, 22 journalism fellows have been supervised by NeuroMat, most of them have gone through this course. At least seven people from other projects

have taken the course, including fellows from the University of São Paulo Physics Department and Engineering School. Noteworthily, fellows have later engaged professionally with science communication, mostly on digital outlets, or joined an academic path about journalism and science.

6.7 NeuroMat's science dashboard

A new institutional academic profile was developed at RIDC NeuroMat, based on Wikidata. Wikidata is a platform inspired by the vision of the Semantic Web, which was designed to allow computers and people to interact over a network. The Semantic Web presents knowledge in a form that is more easily machine-processable, enables data to be linked from a source to any other source, and to be understood by computers. This provides the opportunity to create inference rules and to manage automated reasoning both between people and between machines, so they could perform increasingly sophisticated tasks

The option for a new development was justified due to the disadvantages of the most common platforms, for example using closed code and having limited functionalities for data visualization and scientometric consultation. In contrast, Wikidata is a collaborative technology, under a free license, which allows queries and visualizations based on inferences made by the users themselves.

The dashboard is available freely on NeuroMat's website:
https://vitrine.numec.prp.usp.br/. Three papers on the dashboard methodology have been submitted.

7 Annexes

Annex 1 - NeuroMat global network of scientific, institutional affiliations

Annex 2 - NeuroMat scientific publications

Annex 3 - NeuroMat Scientific Publications: Citations

Annex 4 - NeuroMat's media clipping

Annex 5 - Website's analytics

- Annex 5a - NeuroMat's web portal
- Annex 5b - NeuroMat's podcast web portal
- Annex 5c - Abraço's web portal
- Annex 5d - Rede AMPARO's web portal

Annex 6 - NeuroMat dissemination blog "Traço de Ciência"

Annex 7 - Scientific Missions

Annex 8 - Seminars

Annex 9 - Post-doctoral fellows

Annex 10 - PhD dissertations

Annex 11 - MSc dissertations

Annex 12 - Scientific Initiation

Annex 13 - Scientific Journalism

Annex 14 - Technical Training

Annex 15 - AMPARO Technical Training

Annex 16 - Reports from FAPESP scholarships

- Annex 16a – Bia Ramalho dos Santos Lima
- Annex 16b – Carlo Rondinoni
- Annex 16c – Eduardo Janotti Cavalcante
- Annex 16d – Fernando Araujo Najman
- Annex 16e – Flávio Roberto Rusch
- Annex 16f – Isabela Tosta Ferreira
- Annex 16g – Kádmo de Souza Laxa
- Annex 16h – Luis Henrique dos Santos
- Annex 16i – Morgan Florian Thibault André
- Annex 16j – Paulo Roberto Cabral Passos
- Annex 16k – Renan Hitoshi Matsuda
- Annex 16l – Tahnee Valzachi Sugano