FAPESP
SÃO PAULO RESEARCH FOUNDATION

The Scientific Project of NeuroMat High Performance Computing Center

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Ribeirão Preto, Brazil

Workshop on High-Performance Computing, Stochastic Modeling and Databases in Neuroscience
USP, São Paulo, Brazil
April 25, 2016

NeuroMat

Research, Dissemination and Innovation Center for NeuroMathematics

- FAPESP research center
- Established August 2013 at USP
- Mission: to integrate mathematical modeling and neuroscience

neuromat.numec.prp.usp.br
www.facebook.com/neuromathematics
https://github.com/neuromat

RIDC
Research, Innovation and Dissemination Centers

About the Program

RIDCs

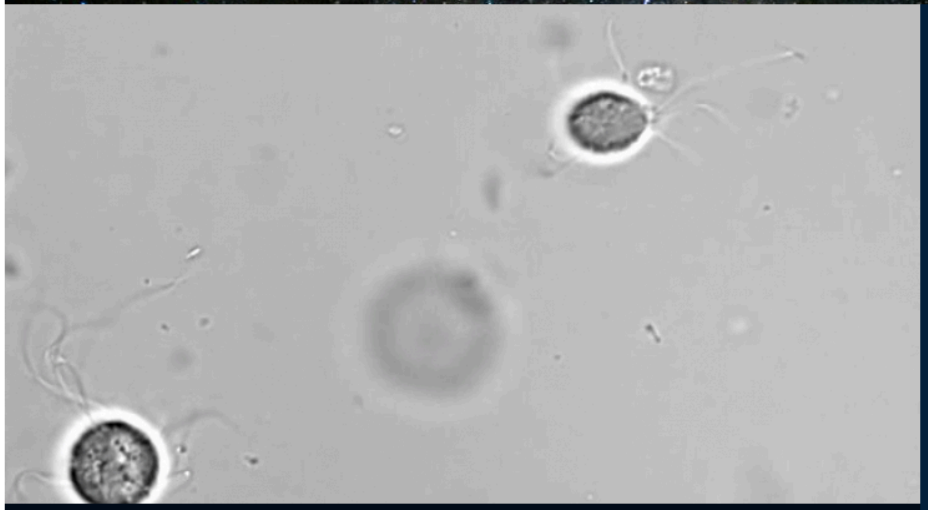
Center for Metropolitan Studies
Brazilian Research Institute for Neuroscience and Neurotechnology
Center for Cell-Based Therapy
Center for Computational Engineering and Sciences
Center for Research and Development of Functional Materials
Center for Research and Innovation in Biodiversity and Drug Discovery
Center for Research in Mathematical Sciences Applied to Industry
Center for Research on Inflammatory Diseases
Center for Research on Redox Processes in Biomedicine
Center for Research on Toxins, Immune-Response and Cell Signaling
Center for Research, Teaching, and Innovation in Glass
Center for the Study of Violence
Food Research Center
Human Genome and Stem-Cell Research Center
Obesity and Comorbidities Research Center
Optics and Photonics Research Center
Research, Innovation and Dissemination Center for Neuromathematics

2001-2013

Center Antonio Prudente for Research and Treatment of Cancer
Center for Research into Optics and Photonics - Campinas
Center for Sleep Studies

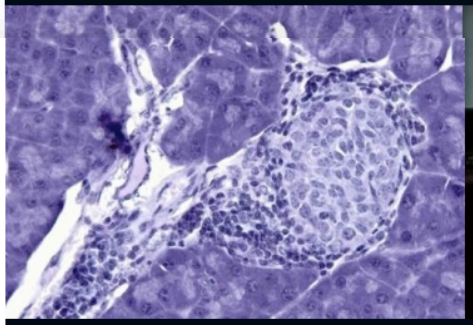
Research at the cutting edge of knowledge

The São Paulo Research Foundation (FAPESP) supports Research, Innovation and Dissemination Centers (RIDCs) selected for funding for a period of up to eleven years. Each RIDC is expected to establish hub of excellent research in focus area, and must actively seek out and develop opportunities to have its research results contribute to high-impact applications, as well as contributing to education and dissemination of knowledge.



Initial findings of BIPMed were presented during FAPESP Week

Data from a study involving carriers of dystonia presented in Michigan demonstrate the importance of gathering genetic data on reference populations in Brazil

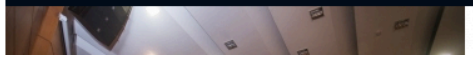


Study deepens understanding of molecular genetics in diabetes mellitus

Researchers find that microRNAs undermine the control of gene expression in T-lymphocytes, leading these defense cells to attack insulin-producing beta cells in the pancreas

Washington seminar scrutinizes reduction in Brazilian inequality

Researchers gathered to discuss how demographic and territorial disparities as well as inequality in gender, race, the labor market, access to education and political participation have changed in the last 50 years



RIDC in the news

Researchers share studies of glass and glass-ceramic materials
September 01, 2015
Glass On Web

Brazilian firm uses silver in plastic bottles to double shelf life of milk
August 05, 2015
Packaging News online

Nanoparticles in bottle plastic doubles shelf life of pasteurized fresh milk
August 04, 2015
Nanowerk

Brazilian company doubles shelf life of pasteurized fresh milk
August 04, 2015
Phys.Org

SPIE Spies Brazilian Photonics
March 10, 2014
Science for Brazil

New glass research center in Brazil - 2 unis, 16 profs, 11 years, $22 M - one big impact
July 8, 2013
The American Ceramic Society

Brazil puts $680m into innovation centres
June 4, 2013
Chemistry World - RSC

Brazil to Provide Funding to Research Centers under RIDC Program
May 30, 2013
The Optical Society

Brazil Announces Funding for a Second Round of Multidisciplinary Research Centers
May 24, 2013
Science online

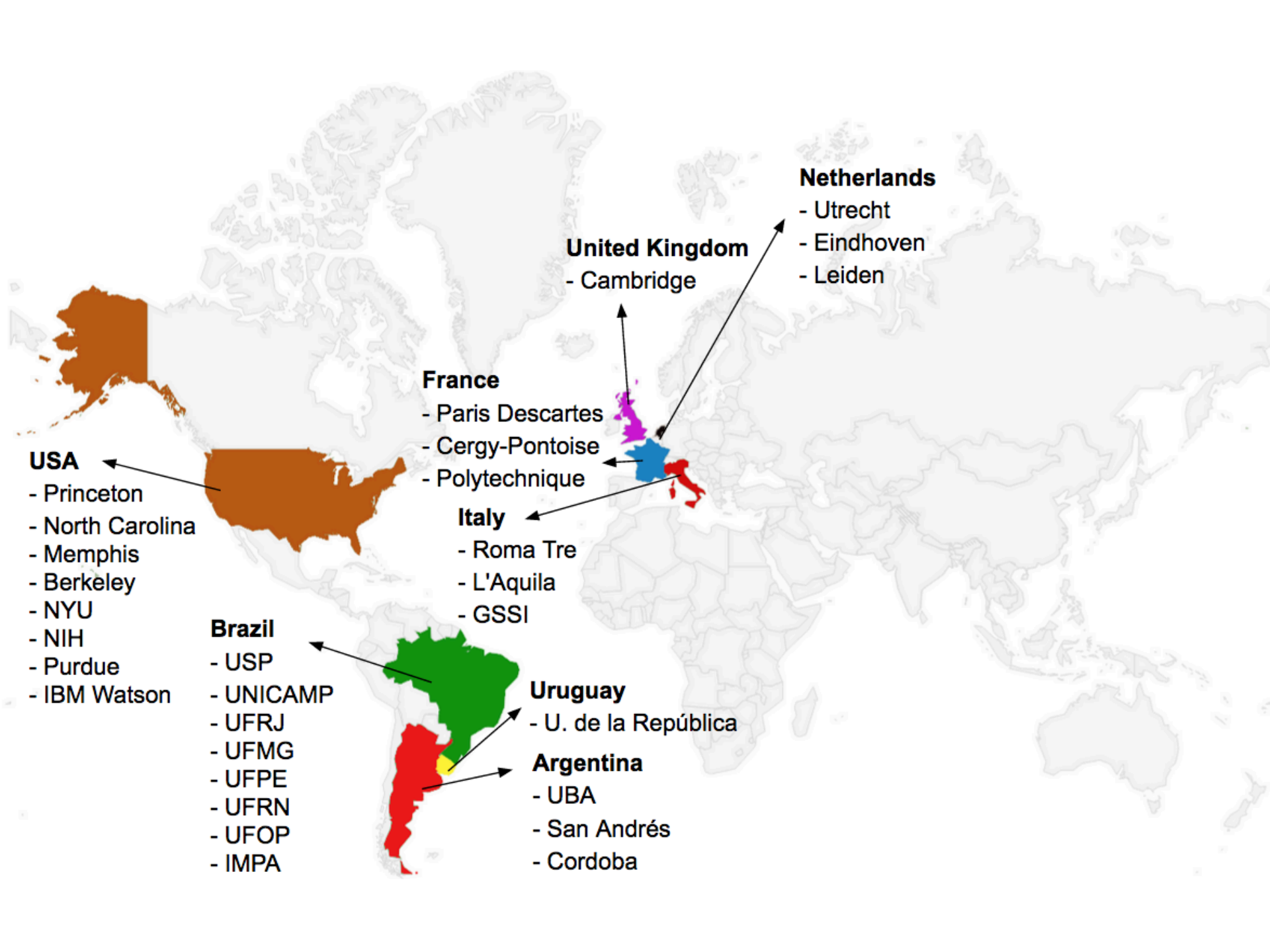
Brazil Plans $680M for Research Institutes; Includes Genomics Center
May 23, 2013
GenomeWeb

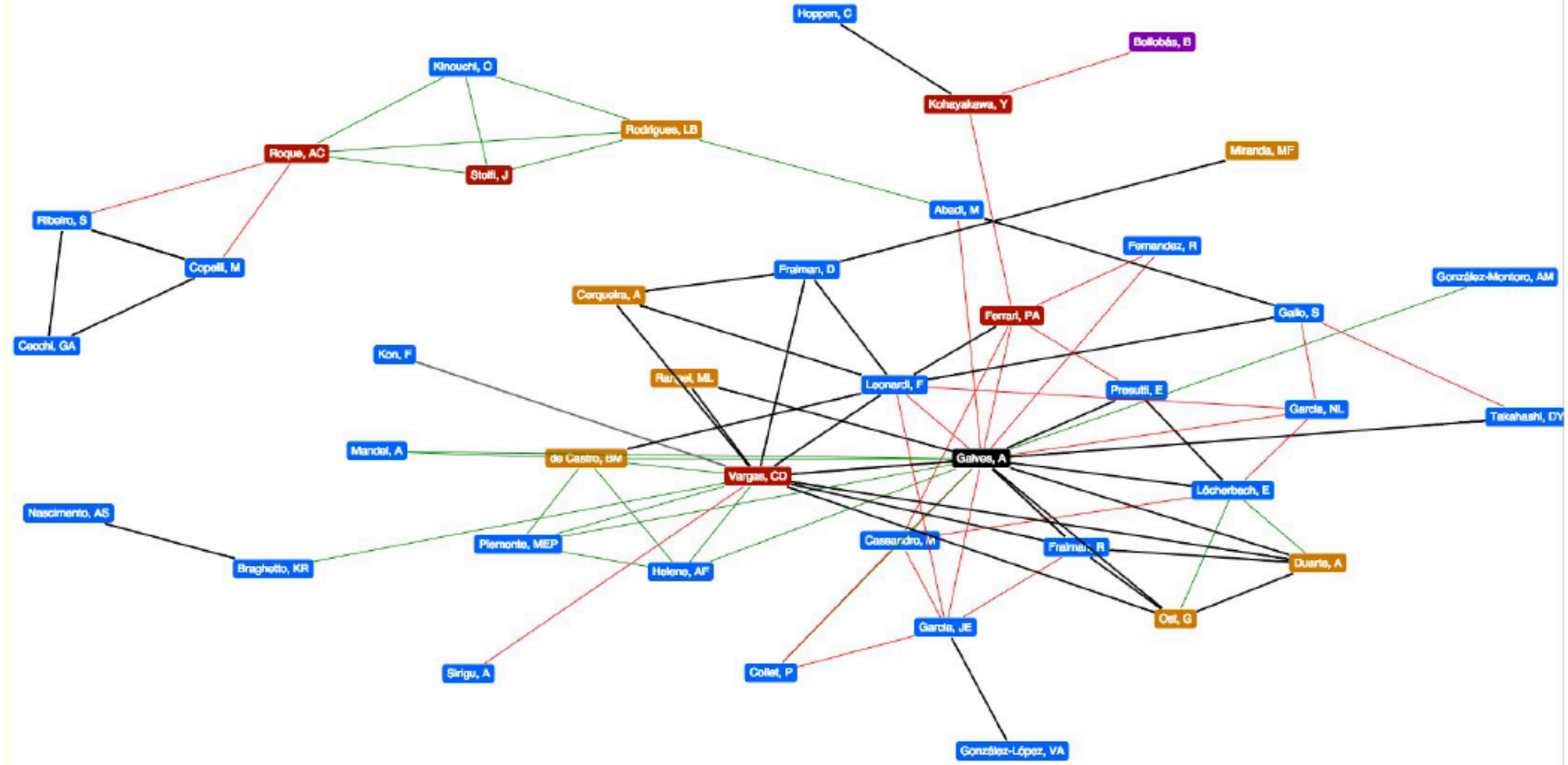
FAPESP funds $680 million to support 17 RIDCs
May 22, 2013
News Medical

All news

NeuroMat Structure

- Main node: USP (São Paulo)
- Vertices in departments of Mathematics, Statistics, Computer Science, Physics, Biology and Neuroscience
- Countries: Brazil (8), USA (8), Argentina (3), France (3), Italy (3), The Netherlands (3), UK (1), Uruguay (1)


Netherlands
- Utrecht
- Eindhoven
- Leiden
United Kingdom
- Cambridge
France
- Paris Descartes
- Cergy-Pontoise
- Polytechnique
Italy
- Roma Tre
- L'Aquila
- GSSI
USA
- Princeton
- North Carolina
- Memphis
- Berkeley
- NYU
- NIH
- Purdue
- IBM Watson
Brazil
- USP
- UNICAMP
- UFRJ
- UFMG
- UFPE
- UFRN
- UFOP
- IMPA
Uruguay
- U. de la República
Argentina
- UBA
- San Andrés
- Cordoba



Graph Lines Legend:
- Black: articles published during NeuroMat's project.
- Red: articles published before NeuroMat's project.
- Green: articles in progress.

Graph Authors Legend:
- Black: NeuroMat's Principal Investigator.
- Red: NeuroMat's Co-Principal Investigators.
- Blue: NeuroMat's Associate Investigators.
- Purple: Advisory Board Members.
- Orange: Post-doctoral fellows and Graduate Students.

NeuroMat: RID Center

- **Research**: Development of new mathematical tools to allow improved understanding of the brain
- **Innovation**: Development of free, open source computational tools to manage and compile experimental and clinical data
- **Dissemination**: Development of web portals, open multimedia productions and training projects for young researchers and teachers

NeuroMat Main Research Goal

To construct new mathematical models which could play in Neuroscience the same clarifying role that Gibbs models played in the Statistical Mechanics derivation of Thermodynamics

Neuromat Research Strategy

- To achieve the main research goal requires the initial development of two foundational aspects:
  - Development of a **new** class of stochastic processes
  - Development of the **statistical tools** required by this new class of stochastic processes

New class of stochastic processes

- We propose a new paradigm based on the idea that neuronal activity must be described as a **stochastic** system
  - With a **large** number of interacting components
  - Whose evolution depends on the **history** of the system

Basic features of these stochastic processes

- The activity of each component depends on the past history of its interacting neighborhood
- Both the size of the relevant past history and of the interaction neighborhood change as the process evolves

Double time evolution

- Therefore, there is a **double** time evolution
  - One describing the changes in neuronal activity
  - And another one describing changes in the graph of interactions among components

Statistical tools for this new class of stochastic processes

- Brain activity is underpinned by a double graph structure:
  - Physical graphs defined by connections between brain regions
  - Functional graphs relating regions recruited for each particular activity
- While the physical graphs can be directly observed, functional interactions can only be inferred from data

Inferring functional structures

- Traditionally done using **descriptive** statistical methods, which give little insight on the mechanism underlying the dynamics of neural activity
- An alternative to the descriptive statistical approach is to use **statistical model selection**
- Statistical model selection means: to assign models to samples following some optimality criterion

- Inference and model selection within this framework requires the development of **new** statistical methods

Developments (2013-2015)

- For an overview of what has been done so far see the 2nd report of activities:
  - neuromat.numec.prp.usp.br/relatorio/2015/relatorio.pdf

- And the two NeuroMat talks in this workshop (no spoilers here)

Stochastic model for systems of interacting neurons

J Stat Phys (2013) 151:896–921
DOI 10.1007/s10955-013-0733-9

Infinite Systems of Interacting Chains with Memory of Variable Length—A Stochastic Model for Biological Neural Nets

A. Galves · E. Löcherbach

Received: 21 December 2012 / Accepted: 8 March 2013 / Published online: 21 March 2013

Abstract We consider a new class of non Markovian processes with a countable number of interacting components. At each time unit, each component can take two values, indicating if it has a spike or not at this precise moment. The system evolves as follows. For each component, the probability of having a spike at the next time unit depends on the entire time evolution of the system after the last spike time of the component. This class of systems extends in a non trivial way both the interacting particle systems, which are Markovian (Spitzer in Adv. Math. 5:246–290, 1970) and the stochastic chains with memory of variable length which have finite state space (Rissanen in IEEE Trans. Inf. Theory 29(5):656–664, 1983). These features make it suitable to describe the time evolution of biological neural systems. We construct a stationary version of the process by using a probabilistic tool which is a Kalikow-type decomposition either in random environment or in space-time. This construction implies uniqueness of the stationary process. Finally we consider the case where the interactions between components are given by a critical directed Erdös-Rényi-type random graph with a large but finite number of components. In this framework we obtain an explicit upper-bound for the correlation between successive inter-spike intervals which is compatible with previous empirical findings.

Keywords Biological neural nets · Interacting particle systems · Chains of infinite memory · Chains of variable length memory · Hawkes process · Kalikow-decomposition

2 Systems of Interacting Chains with Memory of Variable Length: Existence, Uniqueness and Loss of Memory

We consider a stochastic chain $(X_t)_{t\in\mathbb{Z}}$ taking values in $\{0,1\}^I$ for some countable set of neurons I, defined on a suitable probability space $(\Omega, \mathcal{A}, P)$. For each neuron i at each time $t \in \mathbb{Z}$, $X_t(i) = 1$ if neuron i has a spike at that time t, and $X_t(i) = 0$ otherwise. The global configuration of neurons at time t is denoted $X_t = (X_t(i), i \in I)$. We define the filtration

$$\mathcal{F}_t = \sigma(X_s, s \in \mathbb{Z}, s \le t), \quad t \in \mathbb{Z}.$$

For each neuron $i \in I$ and each time $t \in \mathbb{Z}$ let

$$L_t^i = \sup\{s < t : X_s(i) = 1\} \tag{2.1}$$

be the last spike time of neuron i strictly before time t. We introduce a family of "synaptic" weights $W_{j\to i} \in \mathbb{R}$, for $j \neq i$, $W_{j\to j} = 0$ for all j. $W_{j\to i}$ is the "synaptic weight of neuron j on neuron i". We suppose that the synaptic weights have the following property of uniform summability

$$\sup_{i\in I} \sum_j |W_{j\to i}| < \infty. \tag{2.2}$$

Now we are ready to introduce the dynamics of our process. At each time t, conditionally on the whole past, sites update independently. This means that for any finite subset $J \subset I$, $a_i \in \{0,1\}, i \in J$, we have

$$P\big(X_t(i) = a_i, i \in J | \mathcal{F}_{t-1}\big) = \prod_{i\in J} P\big(X_t(i) = a_i | \mathcal{F}_{t-1}\big). \tag{2.3}$$

Moreover, the probability of having a spike in neuron i at time t is given by

$$P\big(X_t(i) = 1 | \mathcal{F}_{t-1}\big) = \phi_i\left(\sum_j W_{j\to i} \sum_{s=L_t^i}^{t-1} g_j(t-s) X_s(j), t - L_t^i\right), \tag{2.4}$$

The model for non-mathematicians

$$V_i(t+1) = \begin{cases} V_{\text{rest}} & \text{if} \quad X_i(t) = 1 \\ \mu V_i(t) + \sum_{j=1}^{N} w_{ij} X_j(t) & \text{if} \quad X_i(t) = 0 \end{cases}$$

- $V_i(t)$: time dependent membrane potential of neuron i at time t for $i = 1, \ldots, N$;
- t: discrete time given by integer multiples of constant step Δ small enough to exclude possibility of a neuron firing more than once during each step;
- $X_i(t)$: number of times neuron i fired between t and t+1, namely 0 or 1;
- If neuron fires between t and t+1, its potential drops to V_{rest} by time t+1;
- w_{ij}: weight of synapse from neuron j to neuron i;
- μ: decay factor (in the interval [0, 1]) due to leakage during time step Δ;
- $X_i(t) = 1$ with **probability** $\Phi(V_i(t))$;
- $\Phi(V)$ is assumed to be monotonically increasing;

Comments

- The model belongs to the class of models in the Galves-Löcherbach paper with:
  - $g_j(t-s) = \mu^{t-s-1}$
  - $\phi_i(V) = \Phi(V)$
  - $W_{j \to i} = w_{ij}$
- If $\Phi(V)$ is a Heaviside function with threshold V_{th}, i.e. $\Phi(V) = 0$ for $V < V_{\text{th}}$ and 1 for $V > V_{\text{th}}$, the model is basically a discrete-time version of the leaky integrate-and-fire model (LIF)
- Any other choice of $\Phi(V)$ gives a stochastic neuron

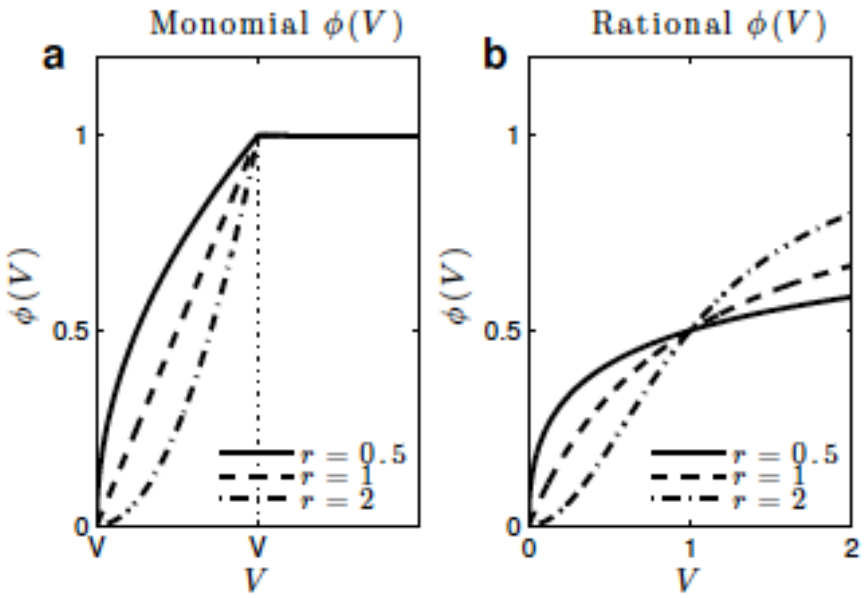
Examples of $\Phi(V)$

Piecewise monomial function of degree r

$$\Phi(V) = \begin{cases} \gamma(V - V_{\rm th})^r \Theta(V - V_{\rm th}) & \text{for } V < V_{\rm th} + 1/\gamma \\ 1 & \text{for } V > V_{\rm th} + 1/\gamma; \end{cases}$$

Rational function

$$\Phi(V) = \frac{[\gamma(V - V_{\rm th})]^r}{\left(1 + [\gamma(V - V_{\rm th})]^r\right)}$$



$\gamma = 1;\ V_{\rm th} = 0$

NB.: The deterministic LIF model corresponds to the monomial function with $\gamma \to \infty, r \to 0$

Brochini et al. (2016), in preparation

Questions

- A central question is to understand whether the initial history of the system affects its long term behavior. Is it possible to theoretically predict how the system will behave asymptotically in time?
- 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. What are the effects of the features that characterize this graph at different scales on the dynamics of the model?

More questions

- The behavior of the stochastic model depends on the parameters of the $\Phi(V)$ function and μ (leakage parameter). These parameters can be used to model different types of neurons. What are the effects of heterogeneous neuron populations on the activity patterns of the network?
- In the original Galves and Löcherbach paper the synaptic weights w_{ij} are fixed. What are the effects of introducing time-varying, i.e. plastic, synaptic weights on the network behavior?

NeuroMat and computer simulation

- NeuroMat's main focus is on rigorous analytical methods to model the brain
- An outcome of this has been the development of a stochastic model for systems of interacting neurons
- In parallel with formal analyses of this model, **large-scale computational implementations** are also needed to provide testing platforms for the models being developed

Large-scale models

- Anatomical estimates:
  - Probability of synaptic contact between two cortical neurons within 1 mm: $p \approx 0.1$
  - Mean number of synapses per cortical neuron: $\langle k \rangle \approx 10^4$
- Then, minimum number of neurons in a realistic network: $N \approx 10^5$
- This implies a total number of synapses of:

  $N_{syn} \approx 10^9$
- These figures determine the **minimum size** of a large-scale cortical model (local cortical network)

Multiscale Models

- A hierarchy of large-scale network models:
  - Local cortical network models;
  - Mesoscopic cortical network models (cortical areas);
  - Macroscopic cortical network model (brain size)
- Models will be built based on available connectivity data at micro-, meso- and macroscopic scales from various experimental techniques

NeuroMat HPC

- Dedicated supercomputer to simulation of stochastic networks of spiking neurons
- Location: Laboratory of Neural Systems (SisNe) USP @ Ribeirão Preto
- Current configuration:
  - 4 nodes with 8 Intel E5-2650 V3 processors with 10 cores each (128 GB RAM and 2TB HD per node)
  - 1 node with 2 Intel E5-2650 V3 processors (128 GB RAM and 6TB HD)
  - 1 NVDIA Tesla K40 GPU

NeuroMat HPC: a dedicated supercomputer for the Brazilian neuroscience community

- NeuroMat aims at turning its HPC center into an open research tool for the Brazilian neuroscience community
- Our goal:
  - User-friendly platforms for simulations and numerical studies;
  - Unified access via user accounts to registered members;
  - A national hub for collaborative research work;
  - Workshops, meetings and courses for students and researchers
  - Development of teaching material on computational neuroscience

NeuroMat and other brain projects

- With its emphasis on **mathematics**, NeuroMat presents a **complementary** view to other brain projects approaches
- The major goals of other brain projects have been:
  - Development and application of innovative **technologies**
  - Development of **database** platforms to bring together different types of **experimental data**
  - Development of large-scale **computer simulations** of biophysically detailed models of brain circuits