MACACC – Modeling the Activity in the Cortex and Analysing the Cortical neural Code.

ALCHEMY (INRIA); CORTEX (INRIA); INCM (CNRS); LJAD (U Nice-CNRS); ODYSSEE (INRIA).

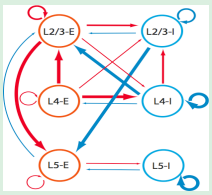
Neuronal information processing is related to the **brain bio-electrical activity**. Current **neuro imaging techniques** allow the measurement of this bio-electrical activity at different **scales of time and space**, from neurons to the brain as a whole (e.g. LFP, ECoG, EEG, MEG). But the analysis of data coming from these measurements requires the parallel development of **suitable models**. Namely, these models have to be, on one hand, **close enough to phenomenology**, taking into account the various types of bio-electrical activity and their scales relations, in order to propose a **coherent representation** of **information processing in the brain** (from neurons to neuronal populations, cortical columns, brain area, etc). On the other hand, these models must be **well posed** and **analytically tractable**. This requires a **constant interaction** between **neurobiology, modeling** and **mathematics**. In this spirit, this project aims to tackle the following questions.

Mesoscopic modeling of cortical columns, bifurcations, and imaging.

CORTEX – INCM – LJAD - ODYSSEE.

Goals. **Brain imaging techniques**, like **optical imaging** or **MEG-EEG**, require a **modeling** of **cortical brain activity** at a spatial scale of order 0.1-1 mm2. The goal of this project is to propose a **mesoscopic model** of the **measured biological signa**l, at the space scale of a **cortical column**, and to analyse this model **dynamics**, using analytical methods and numerical simulations. These theoretical predictions will be then compared to the cortical activity of the visual system (area V1-V2), measured by **optical imaging** and **MEG-EEG,** in order to better understand the link between **what is measured** and the **underlying cortical activity** .

Methods. We want to characterize the **activity** of P **neuronal populations** in a **cortical column**, including non **stationary dynamics** and **local field potential fluctuations**. This is achieved by using **dynamic mean-field** methods and **bifurcations analysis**. This is a first step towards a **mathematical** and **numerical** characterization of **local field potentials**, exhibited by a **realistic model** of a cortical column with a connectivity scheme based on **anatomic data**, at a scale corresponding precisely to the **resolution** of **optical imaging** or **MEG-EEG**.



Then, we will compare the **dynamical behaviour** predicted by our analysis to **real experimental data** of the cortical activity of the visual system (V1/V2). This will help us to constrain the **model parameters** and structure in order to fit the **real data**,.

Microscopic equations

$$d\widetilde{V}^{(N)}(t) = \left(\mathrm{L}^{(N)}(t)\widetilde{V}^{(N)}(t) + \widetilde{U}_t^{(N)} + \widetilde{I}_t^{(N)}\right)dt + \Lambda^{(N)}(t)\cdot d\mathbf{W}_t^{(N)},$$

$$\widetilde{U}_t^{(N)} = \begin{bmatrix} 0 \\ \vdots \\ 0 \\ \jmath(N)\cdot \tilde{s}^{(N)}(\widetilde{V}_G(t)) \end{bmatrix} \text{ and } \widetilde{I}_t^{(N)} = \begin{bmatrix} 0 \\ \vdots \\ 0 \\ \mathrm{I}^{(N)}(t) \end{bmatrix}.$$

Mesoscopic equations

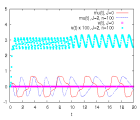
Effective interaction process

$$\begin{cases} \mathbb{E}\left[U^X_{\alpha\beta}(t)\right] = \bar{J}_{\alpha\beta} m^X_{\alpha\beta}(t) \text{ where } m^X_{\alpha\beta}(t) \overset{\text{def}}{=} \mathbb{E}[S_{\alpha\beta}(X_\beta(t))]; \\ \mathrm{Cov}(U^X_{\alpha\beta}(t), U^X_{\alpha\beta}(s)) = \sigma^2_{\alpha\beta}\Delta^X_{\alpha\beta}(t,s) \text{ where} \\ \qquad \Delta^X_{\alpha\beta}(t,s) \overset{\text{def}}{=} \mathbb{E}\left[S_{\alpha\beta}(X_\beta(t))S_{\alpha\beta}(X_\beta(s))\right]; \\ \mathrm{Cov}(U^X_{\alpha\beta}(t), U^X_{\gamma\delta}(s)) = 0 \text{ if } \alpha \neq \gamma \text{ or } \beta \neq \delta. \end{cases}$$

Dynamic mean-field equations.

$$d\widetilde{V}(t) = \left(\mathrm{L}(t)\widetilde{V}(t) + \widetilde{U}_t^{\mathrm{V}} + \widetilde{\mathrm{I}}(t)\right)dt + \Lambda(t)\cdot d\mathbf{W}_t,$$

Example: two populations model.



Evolution of the mean $\mu_1(t)$ and variance $v_1(t)$ for the mean field of population 1, over a time window [0,20]. Though Gaussian fluctuations are small, they have a strong influence on $\mu_1(t)$.

Results.

1) Mean-field equations. Considering the evolution of an assembly of N **neurons** belonging to **P populations** where neurons are described by **stochastic differential equations** and are coupled by **random synaptic connections,** we have shown that the **average activity** of a population is described, when N is large, by **explicit and well posed functional equations** Moreover, we provide a **constructive** and **numerically tractable** method for effectively computing their unique solution. These results shed new light on such neural mass models as the one of **Jansen and Rit:** their dynamics only **approximate** the **much richer dynamics** that emerge from our analysis because their approach **neglects the random fluctuations around the mean values and their correlations** [1].

2) Bifurcation analysis. Assuming that **orientation columns** in the visual cortex are coupled with **symmetries** allows an analysis of **bifurcations** via the study of **spontaneous symmetries breaking**. As a preliminary (master) work we have reconsidered the seminal work of Bressloff et al [2] about **visual hallucinations** using more recent techniques in **bifurcation analysis of systems with symmetries** [3].

Next steps. On the basis of these theoretical results we intend to analyse what are the **biological parameters** compatible with **experimental measurements** in **optical imaging** and **MEG-EEG**. This will allow to determine **precise constraints** that must be introduced in **neural masses models**, for example the **functional distinction between excitatory and inhibitory neurons**, the **dendritic** and **axonal activity**, and the **cortex laminar structure**. As an important application, in the continuity of **F. Grimbert's thesis** [4], such models of cortical activity are prototypes for biological sources of **voltage sensitive dye** (VSD) imaging, at a mesoscopic scale corresponding to **one pixel of optical imaging** (~ 50µm). In a recent paper S. Chemla et al [5] have shown, using numerical simulations on an accurate model of cortical column, that the contribution of **inhibitory cells**, **spiking activity** and **deep layers** to the VSD signal is stronger than initially thought. It would be interesting to compare these results to a **bifurcation analysis** of a **mesoscopic mean-field model**.

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Statistical analysis of spike trains

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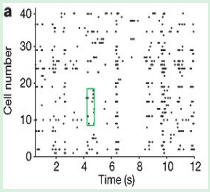
Goals. **Information transport** by neurons is mediated by **spikes trains**. How information is **encoded** remains however an open issue. Thus, the **analysis of spike trains** obtained from **in vivo** or **in vitro experimental data**, requires suitable **statistical models**. Our goal is to propose a **generic method** to construct **optimized statistical models** from **empirical data**, using an approach combining mathematical modelling and analysis from **in vivo experiments**, together with **numerical treatments**. Beyond theoretical aspects, this approach is intended to provide **new algorithms** to improve **spike trains analysis**.



Methods. We want to characterize the **spike dynamics** of **neural models**, close enough to **real neurons** so that this analysis provides relevant issues in **theoretical and experimental neuroscience**. Using methods from **ergodic theory** and **statistical physics** we propose to approximate the **empirical measure** generated by a spike train by a **Gibbs distribution**, whose form is imposed by a **variational principle**. A special emphasis is put on the effects of **synaptic plasticity,** which leads to specific forms of spike probability distributions.

These theoretical foundations provide **new algorithms** for the analysis of real data provided by our **biologist** and **neurophysiologist** partners, taking a step further in the **characterization** of spike trains obtained from **in vivo** and **in vitro** data with the scope of providing a **software** allowing an **automatic treatment** of **experimental data**.

Results.

1) Neuron dynamics. We have made the first **complete characterization** of **conductance based Integrate and Fire models** dynamics with discrete time [1,2].

2) Gibbs measures. In these models, we have shown that the spikes train statistics, given the **average value** C_α of some **specified** observables ϕ_α, can be **best approximated** by a **Gibbs measure** with a **specific potential** [2], [3].

3) Synaptic plasticity. In this context, a general class of **synaptic plasticity** rules can be formulated as a variational principle. The **spikes trains produced after adaptation** are described by a **Gibbs distribution** that we have **explicitly written down** [3,4].

For the analysis of spike trains coming from **numerical models** or **real data,** we have developed **numerical codes** available at http://enas.gforge.inria.fr.

Next steps. Three complementary directions are investigated.

Microscopic equations

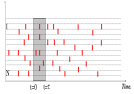
$$C\frac{dV_k}{dt} + g_k V_k = i_k \qquad g_k(t,\vec{\omega}) = g_L + \sum_{j=1}^{N} G_{kj} \sum_{n=1}^{M_j(L\Delta)} \alpha(t - t_j^n)$$

There is a ***weak form of initial condition sensitivity.***

Attractors are generically ***stable period orbits.***

The number of stable periodic orbit ***diverges exponentially*** with the number of neurons.

Depending on parameters (synaptic weights, input current), periods ***can be*** beyond ***any accessible computational time.***



$$R = [\omega(1)\ldots\omega(\tau)]\ \omega(t) = [\omega_i(t)]_{i=1}^{N}$$

$$P[R|S] \Longrightarrow P[S|R]$$

$$\pi_{\vec{\omega}}^{(\gamma)}(\phi) = \frac{1}{T}\sum_{t=1}^{T}\phi(\sigma^t\vec{\omega})$$

Large deviations

$$\nu\left\{\vec{\omega} \;\middle|\; \left|\pi_{\vec{\omega}}^{(T)}(\phi_\alpha) - C_\alpha\right| \geq \epsilon\right\} \sim e^{-TI(\alpha,\epsilon)}$$

$$I(\alpha,\gamma) = \sup_{\gamma}\{\gamma\cdot\alpha - F(\alpha,\gamma)\}$$

$$F(\alpha,u) = \lim_{T\to\infty}\frac{1}{T}\log\nu\left[e^{u\pi_{\vec{\omega}}^{(T)}(\phi_\alpha)}\right]$$

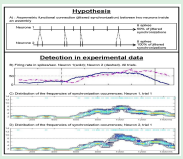
Entropy maximisation

$$P[\vec{\lambda}] = \sup_{\mu\in\mathcal{M}_{\mathrm{inv}}}\left\{h(\mu) + \sum_{\alpha=1}^{K}\lambda_\alpha\mu(\phi_\alpha)\right\}$$

$$P[\vec{\lambda}] = h(\nu) + \sum_{\alpha=1}^{K}\lambda_\alpha\nu(\phi_\alpha)$$

$$\frac{\partial P}{\partial\lambda_\alpha} = \nu(\phi_\alpha) = C_\alpha$$

$$\nu[R] \sim \frac{1}{Z_n(\vec{\lambda})}\sum_{\vec{\omega}\subset[R]}\exp\left[\sum_{\alpha=1}^{K}\lambda_\alpha\sum_{t=1}^{n}\phi_\alpha(\sigma^t\vec{\omega})\right]$$



1) Analysis of experimental data. We are currently working on data obtained by **INCM** in experiments with **monkeys**. Recent investigations [5] suggest that two **synchronized neurons** may be **asymmetrically connected** to each other in functional terms, even with **a similar firing rate** and a **common synchronized state** (A&B). This implies that each neuron is able to **join a synchronized assembly** with its **own dynamic**s, that fluctuates from trial to trial (C&D). We analyse this issue with our statistical tools [6].

2) Plasticity. Our results on synaptic plasticity open up the possibility of solving **variational problems** using **spiking neural networks** after a **suitable training**. Also, the role of **specific neural architectures** constrained by **plasticity mechanisms** will be investigated, in the continuity of [7] with possible extensions to **intrinsic plasticity** [8].

3) Application to vision tasks. Spikes appearing in **vision processing** can be precisely reproduced thanks to **simulators** [9]. Modeling further the vision system in a spiking architecture can also be considered for **higher level tasks**. For example, we showed in [10] that **action recognition** could be performed thanks to a **spiking model of cortical layers V1-MT**. Future work will focus on proposing plausible spiking models of **vision-related cortical layers** and see how the induced spiking activity can be analyzed for a **vision task**.

References.
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Conclusions. The present work relies on an approach combining **theoretical methods** from physics and mathematics, **numerical treatments**, and **biological modeling / experimentation.** At the present stage the two directions developed concerns **different scales** in the brain, but this separation is only apparent. As possible extensions we plan to study **mean field methods for spiking neuron models** and apply **Gibbs statistical methods for the analysis of data at the scale of cortical columns**.