Postdoctoral Research Project (FMJH): Optimal Estimation of Synaptic Weights

Quentin Cormier

1 Scientific Context and Motivation

A fundamental challenge in neuroscience is the estimation of synaptic weights between neurons. This remains a largely open problem. A common experimental approach involves using multi-electrode arrays (MEAs) on cultured neurons. A typical setup consists of a few hundred neurons on an array with a few hundred electrodes. These extracellular electrodes do not directly measure the membrane potentials of individual neurons ; instead, they record the precise timings of their action potentials, or "spikes".

A key feature of these electrodes is that they are bidirectional: in addition to recording spike times, they can be used to externally stimulate a neuron, thereby increasing its probability of firing. To date, statistical methods developed to infer the network's interaction graph have generally not leveraged this bidirectional capability. The temporal resolution of the electrodes is excellent (on the order of a millisecond), and a typical experiment lasts about 15 minutes, with neurons firing at an average rate of 10 Hz.

2 Project Objective

The primary objective of this postdoctoral project is to address the following stochastic control problem:

How can we optimally stimulate the neurons via the electrodes to most effectively and accurately estimate their synaptic weights?

3 Mathematical framework

We propose the following mathematical model. We consider a network of N neurons, where the state of each neuron i is described by its membrane potential, V_t^i . The dynamics of each neuron are governed by the following stochastic differential equation:

$$\mathrm{d}V_t^i = \alpha_t^i \mathrm{d}t + \sum_{j=1}^{N} J_{j\to i} \mathrm{d}N_t^j - V_{t-}^i \mathrm{d}N_t^i.$$

The terms in this equation are defined as follows:

- $V_t^i \in \mathbb{R}$ is the membrane potential of neuron i.

- N_t^i is a Poisson point process with stochastic intensity $f(V_{t-}^i)$. This process represents the spike train of neuron i. The rate function $f(v)$ is assumed to be known and monotonically increasing, such that a higher membrane potential leads to a higher probability of firing an action potential.
- The term $-V_{t-}^i \mathrm{d}N_t^i$ models the reset mechanism: immediately following a spike, the neuron's membrane potential is reset to its resting value, which is set to zero in this model.
- When neuron j spikes, the membrane potential of a postsynaptic neuron i is instantaneously increased by the quantity $J_{j\to i}$. This is the **synaptic weight** we aim to estimate.
- Finally, (α_t^i) is the **stochastic control**, representing the current injected into neuron i through its corresponding electrode.

We assume that the observable data consists of the spike times of all N neurons, which corresponds to the filtration:

$$\mathcal{F}_t^N = \sigma(N_s^j, s \le t, j \in \{1, \dots, N\}).$$

Admissible controls are defined as predictable processes with respect to this filtration.

4 Bayesian Formulation and Optimization

We adopt a Bayesian perspective. We define a known prior distribution over the synaptic weights:

$$\mu_0 = \mathcal{L}((J_{j\to i}, i, j \in \{1, \dots, N\})).$$

The posterior distribution, μ_t, is then the law of the weights given the observed history of spikes:

$$\mu_t = \mathcal{L}((J_{j\to i}, i, j \in \{1, \dots, N\}) \mid \mathcal{F}_t^N).$$

The optimization problem is to determine the optimal control strategy: *How should we choose the controls (α_t^i) to minimize a variance-based criterion on the final posterior distribution μ_T?*

To tackle this problem, we will employ methodologies based on stochastic filtering for point processes, see [1].

5 Proposed Research Directions

This project open several research steps and directions:

1. **Theoretical Formulation:** Formalize the stochastic control problem using Girsanov's theorem to handle the change of measure induced by the control and the observations.
2. **Posterior Distribution Dynamics:** Derive the evolution of the posterior measure (μ_t) using a Zakai-type equation for point processes and study the structural properties of its solution.
3. **Algorithms to sample along the posterior distribution:** Develop and analyze algorithmic techniques, such as interacting particle systems (sequential Monte Carlo methods), to sample from the posterior distribution μ_t. A possible direction is to study the convergence properties of these algorithms.

4. **Measure-Valued Control Problem:** Conduct a theoretical analysis of the control problem by formulating and studying the corresponding Hamilton-Jacobi-Bellman (HJB) equation on the space of probability measures. The analysis will initially focus on simplified "toy model" (e.g., estimating a single synaptic weight).

5. **Numerical Solution:** Develop numerical methods to solve the control problem, particularly leveraging machine learning techniques suitable for high-dimensional stochastic control. This investigation will also begin with simpler toy problems before scaling to larger networks.

6. Candidate Profile

We are seeking a candidate with a strong background in either:

- Stochastic processes, with a focus on stochastic filtering or stochastic control or analysis of interacting particle system driven by jump processes.
- Scientific computing and machine learning, with an interest in solving high-dimensional stochastic control problems.

A candidate with expertise in both areas would be ideal.

7. Collaborations

The project will involve collaborations and discussions with experimental neuroscientists at the NeuroPSI institute (Paris-Saclay) and the NeuroMod institute (Nice) at various stages of the research.

References

[1] N. Baradel, Q. Cormier, *Optimal control under unknown intensity with Bayesian learning*, Preprint, 2025.