FINAL GRADE PROJECT

for obtaining the title in
Bachelor in Bioinformatics

Determination of a population rate model for slow oscillations using Bayesian inference

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***Abstract*— Signals and parameters that cause neural activity to occur can be inferred from several scales. In this project we focused in the network level, where our object of study, a population of neurons, is assumed to co-habit; two pools: excitatory and inhibitory, that are constantly shaping each others behaviour. The true signal of our model can only be measured indirectly through electrophysiological recordings, and with the presence of noise. Our aim is to determine a population rate model capable of replicating the dynamics of slow oscillations in the cerebral cortex, and applying to our simulated data a Bayesian inference technique, a Kalman filter, as a probabilistic interpretation of the problem to apply parameter estimation of our rate model.**

I. INTRODUCTION

Membrane potentials are the principal measurable signals in the brain, and hence, they constitute the main biophysical variables of neuron models. When we want to describe certain dynamics of the neuron, such as synaptic conductances, we derive our single neuron models from cable theory models, as we understand them as a biological circuit, with 'transistors' (ion channels) that can turn electrical signal on and off (Hodgkin and Huxley, [12]).

The sentence : "We can't explain how birds flight by modeling its feathers", in neuroscience would be translated into "in order to explain large-scale brain networks and eventually reconstructing complex brain systems, we need to integrate the micro and the macroscales, as there are millions of neurons linked up with one another constantly spiking, synchronizing or being inhibited".

That is why in our work we have used rate models instead of single channel ones. Those models assume an underlying dynamic of spatially localized populations that may contain both excitatory and inhibitory neural populations (Wilson and Cowan, [9]), ideal for studying relationships among interconnected brain areas and their relevance to several conditions (Basset et al, [11]). Our models are capable of replicating the dynamics of slow oscillations in the cerebral cortex, an activity pattern associated with cognitive processes such as memory consolidation, and that is altered in several pathologies (Capone et al, [3]). The general objective in long term of this project is to estimate all variables and parameters of our hidden system through the average activity of the network. One application of our long term objective is to adjust our model to experimental data, and implement it to a closed-loop system able to control the frequency of slow oscillations in real time, by injected current. (See for instance, D'Andola et al, [5])

In our rate model we got parameters and variables, and the unique observable variable is the rate r . We can use this average activity of the network to infer the other parameters and non-observable variables. All this process of parameter inference can entail uncertainty as multiple steps require rigorous methodology and noise can also be intrinsic of the neuron. That is why in this project we will use one of the most effective methods to approach this kind of estimations: bayesian inference, more specifically a Kalman filter.

Our main goal is to estimate the variables: the firing rate (r), spike-frequency adaptation (a) and synaptic depression (s) for the rate models (1), (3) and (4), through data given from simulations with process noise, using Bayesian inference, in concrete an Extended Kalman Filter. Those rate models have different levels of complexity, and we will add strong restrictions (fixing the values of the parameters) in order to simplify our problem and understand correctly our filtering technique.

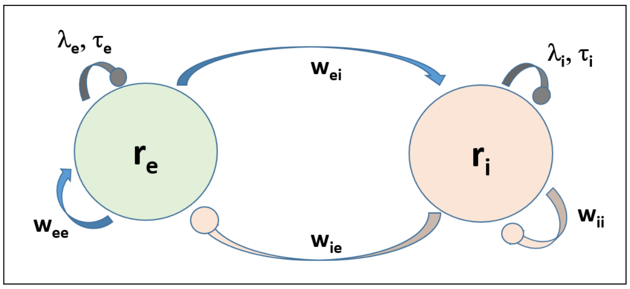

Fig. 1. Model 3 : Assumed hidden system

Figure 1 represents our assumed setup of the system, which is not measurable directly, composed of a hidden system, that contains an excitatory pool, our observed neuron, and an inhibitory pool. The main variables are the activity rates of each population $(r_e,\ r_i)$, and both adaptation $(\lambda_e,\ \lambda_i)$ and depression $(s_e,\ s_i)$ variables for each population, which are two different types of negative feedback (subtractive and divisive, respectively). Our model has different sets of parameters: connectivity strength among populations (ω_{ee}, ω_{ei}, ω_{ie}, ω_{ii}); adaptation (λ_e, λ_i), current input (I_e , I_i), time constants (τ_e, τ_i, τ_a, τ_s) and synaptic depression factor (δ_e, δ_i).

II. MATERIALS AND METHODS

In this section, we present the three different neural dynamical systems that we will use, the state-space formulation and the Extended Kalman Filter (EKF). This filtering method is proposed here, as the underlying dynamical models presented non-linearities, and the Kalman Filter algorithm is for liniar processes.

A. Neural dynamical models

We have chosen three different rate models with increasing order of complexity. The first one involves only one excitatory population of neurons endowed with some feedback adaptation mechanism. We can think that this is the minimal structure of a rate model, presenting two variables: the rate r of the population (representing the average firing of the neurons of the population) and the adaptation (or fatigue) term a. In the second model, we add a variable of synaptic depression and, finally, the third model involves two populations (excitatory and inhibitory) with adaptation and depression.

- The model with one excitatory population and adaptation is given by

$$\begin{cases} r' &= -r + \phi(\omega\, r - \lambda a + I), \\ \tau_a\, a' &= -a + r, \end{cases} \tag{1}$$

where $'$ denotes the derivative with respect to the time t; ϕ is known as the *activation function* and it is defined as:

$$\phi(x) = (1 + \exp(\frac{-(x-\theta)}{k})), \tag{2}$$

where θ and k are parameters that represent the threshold for activation and the slope of the activation function, respectively. Note that this implies a new set of parameters in the model apart from those mentioned in the Introduction.

- Adding the synaptic depression dynamics to (1), we get

$$\begin{cases} r' &= -r + \phi(\omega\, s\, r - \lambda a + I), \\ \tau_a\, a' &= -a + r, \\ \tau_s\, s' &= 1 - s - \delta\, s\, r, \end{cases} \tag{3}$$

- Finally, two populations of type (3), one excitatory and one inhibitory, can be coupled as

$$\begin{cases} \tau_e\, r_e' &= -r_e + \phi(\omega_{ee} s_e r_e - \omega_{ie} r_i s_i - \lambda_e a_e + I_e), \\ \tau_i\, r_i' &= -r_i + \phi(\omega_{ei} s_e r_e - \omega_{ii} r_i s_i - \lambda_i a_i + I_i), \\ \tau_a\, a_e' &= -a_e + r_e, \\ \tau_a\, a_i' &= -a_i + r_i, \\ \tau_s\, s_e' &= 1 - s_e + \delta_e\, s_e\, r_e, \\ \tau_s\, s_i' &= 1 - s_i + \delta_e\, s_i\, r_i. \end{cases} \tag{4}$$

We will apply the filtering methods to a discretized version of our systems. For this purpose, we use the Euler method. For instance, the discrete model corresponding to model (1) writes as

$$\begin{cases} r_{n+1} &= (1 - \Delta t)\, r_n + \Delta t\, \phi(\omega r_n - \lambda a_n + I), \\ a_{n+1} &= (1 - \frac{\Delta t}{\tau_a})\, a_n + \frac{\Delta t}{\tau_a} r_n, \end{cases} \tag{5}$$

where Δt is the step of the Euler method. Defining

$$x_k = \begin{pmatrix} r_k \\ a_k \end{pmatrix} \tag{6}$$

as our state-space variable, the solutions of (5) are then sequences $\{x_k\}_{k\geq 0}$.

B. State-space formulation

In order to apply the stochastic filtering tool, we assume that data are noisy by adding process noise to the state equation:

$$\begin{cases} x_k = x_{k-1} + \boldsymbol{Q}_{k-1}, \\ y_k = x_k + R, \end{cases} \tag{7}$$

where the noise terms $\boldsymbol{Q}$ and R, respectively for the model noise and the measurement noise, are a covariance matrix of the form, (keeping as example model (1))

$$\boldsymbol{Q} = \begin{pmatrix} \sigma_r^2 & 0 \\ 0 & \sigma_a^2 \end{pmatrix} \tag{8}$$

and peculiarly our structure is diagonal as we assume white processes, in the sense that no correlated noise appears in our model between the firing rate (r) and the spike-frequency adaptation (a).

C. Extended Kalman Filter

The Extended Kalman Filter (EKF) is an algorithm that uses series of measurements observed over time, containing statistical noise, and produce an estimate of the observed variable that tend to be more accurate than the measurements alone.

In order to implement the filtering method, we need the prediction equations, based on the theoretical model of the hidden system and the update equations, characteristic of each measurement in which the state and the error associated take role for the estimation. When applying the EKF, the discrete-time prediction equations used were

- Predicted state estimate

$$\hat{x}_{k|k-1} = f(\hat{x}_{k-1|k-1}, u_k). \tag{9}$$

  where f is the system of equations and $\hat{x}_{k-1|k-1}$ the a priori estimate.
- Predicted covariance estimate

$$P_{k|k-1} = F_k P_{k-1|k-1} F_k^T + Q_k, \tag{10}$$

  where both terms can be calculated directly from our discretized model and its Jacobian F_k, which is the state transition matrix defined as $F_k = \frac{\partial f}{\partial x}|_{\hat{x}_{k-1|k-1}}$.
  For the update equations, the following values were calculated
- Innovation or measurement residual:

$$\check{y}_k = z_k - h(\hat{x}_{k|k-1}), \tag{11}$$

- Innovation covariance:

$$S_k = H_k P_{k|k-1} H_k^T + R_k. \tag{12}$$

- Kalman gain:

$$K_k = P_{k|k-1} H_k^T S_k^{-1}, \tag{13}$$

- Updated state estimate:

$$\hat{x}_{k|k} = \hat{x}_{k|k-1} + K_k \check{y}_k, \tag{14}$$

- Updated covariance estimate:

$$P_{k|k} = (I - K_k H_k) P_{k|k-1}. \tag{15}$$

and when applying it $\check{y}_k$ was introduced as the input for each dt.

To understand over the mathematical layer what is the Extended Kalman Filter, we are going to describe it with plain language.

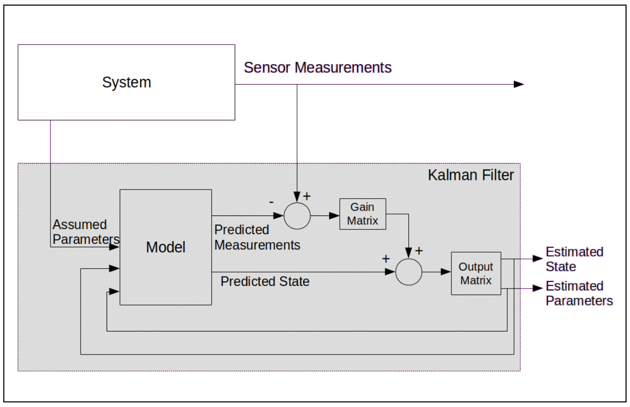

Fig. 2. Extended Kalman Filter Diagram

To calculate the updated state estimate, that is our final estimate, from the measurement (with error R) and our prediction (with error $\boldsymbol{Q}$), we first need the predicted covariance and the measurement covariance, to quantify both and obtain the Kalman gain, which will indicate which one of our two samples has less error related . The resulting estimate will be more accurate always than one of the previous samples.

III. RESULTS

We simulated the data of our populations using the rate models (1), (3) and (4). Our generated data sample had a sampling frequency of $f_s = 2kHz$. The model parameters were set constant, for connectivity: ω_{ee} and ω_{ii} = 0.2, ω_{ei} and ω_{ie} = 0.4; adaptation effect λ_e and λ_i = 0.9, current input I_e and I_i = 0, as we just want to add them for posterior tests (f.e. stochastic process Ornstein-Uhlenbeck); time constants τ_e = 3, τ_i = 5, τ_a = 400, τ_s = 100 and synaptic depression factor δ_e and δ_i = 0.3. For the activation function ϕ, the activation threshold was set to θ = 0.3 and the speed of change to k = 0.5. The values for the model were taken from paper [8], Table 1. For the model noise and the measurement noise, the values for σ_k, where $k = \{r, a, s\}$, were set to 0.003 each for the measurements and 0.0003 for the model.

Three sets of simulations are discussed, one for each model. Our main goal was to validate the filtering method. As mentioned in the Introduction, in our case the underlying model and our predicted model were identical, so in a sense, we have perfect knowledge of the model.

To evaluate the efficiency of the proposed filtering method, we computed the root mean square error (RMSE) for the measurements (raw RMSE) and for the filtering method (EKF RMSE), and compared them after averaging 1000 independent EKF trials for each model. For generic time series, the EKF RMSE is defined as

$$RMSE(\omega_k) = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(\omega_k - \hat{\omega}_k)^2},$$

where $\hat{\omega}_k$ is the estimate of ω_k, obtained from the EKF and M the number of iterations performed. The raw RMSE was calculated following the same equation but instead of using the estimate we used the measurement value, that is actually our noise associated σ_k.

Table I show the RMSE values for each variable of our presented models. All ekf RMSE have lower values than the raw measurements; for model (1), r has two orders of magnitude less of error while a has one. For model (3), r has two orders of magnitude less of error while a and s have one. For model (4), r_e has two orders of magnitude less of error while r_i, a_e, a_i, s_e, s_i

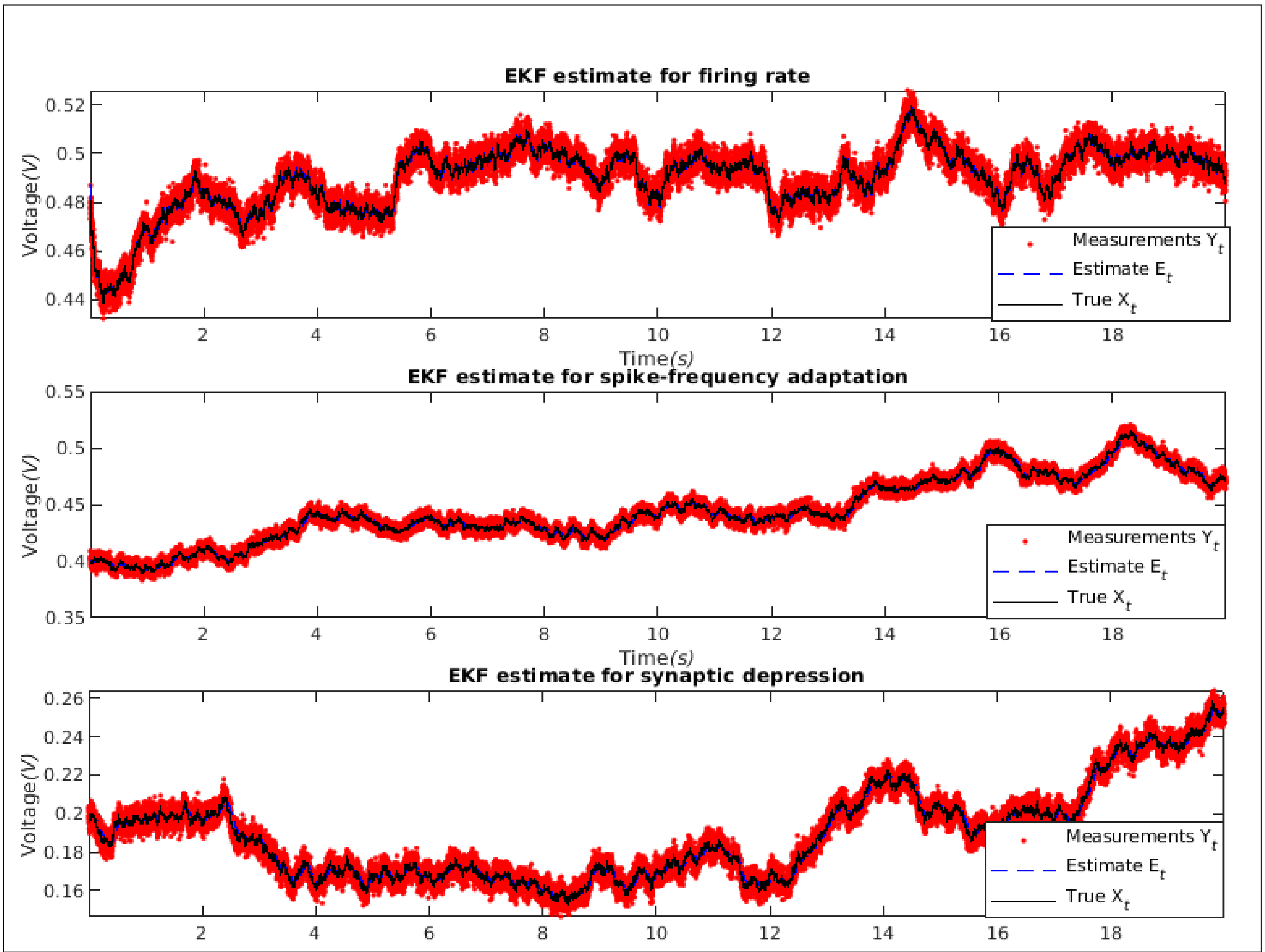

Fig. 3. A single realization of the EKF method for the model (3), for the variables firing rate (r), spike-frequency adaptation (a) and synaptic depression (s).

TABLE I
RMSE COMPARISON

		raw RMSE	ekf RMSE
Model 1	r	0.003	0.00092353
	a	0.003	0.0021
Model 2	r	0.003	0.00092326
	a	0.003	0.0021
	s	0.003	0.0021
Model 3	r_e	0.003	0.002
	r_i	0.003	0.00092542
	a_e	0.003	0.00092556
	a_i	0.003	0.00092504
	s_e	0.003	0.00092527
	s_i	0.003	0.00092493

have two orders of magnitude less of error. As we can observe, firing rate r is more accurately estimated for models (1) and (3), than for (4). That is explainable as the complexity of our last model has at least 3 degrees of freedom more than the previous ones.

As we can observe in Figure 3, our models can be estimated using the Extended Kalman Filter lowering the noise width in at least one order of magnitude. The covariance associated to the process noise has larger values than for the model noise, this allows the filter to reduce the RMSE of the estimation. The performance could be improved if the model inaccuracies are reduced, f.e. the parametrization of our models could have been more precise. We can observed in the table that the more complex our model is, the harder it is for the filter to reduce its noise, the subtractive feedback increases the complexity of the signal, and the addition of another population (inhibitory) makes it more inaccurate.

IV. CONCLUSIONS

For the parameters' estimation we have implemented a *alpha beta Kalman Filter* (GHKF), for one specific parameter (w) for the first model, but we have not been able to test it. We could have also tried other parameter estimators such as Metropolis Algorithm based on MonteCarlo Markov Chain (MCMC), but that work remains for posterior additions.

Another field that would had been interesting to prove is to estimate hidden variables (a,s) from experimental data, as we have 'assumed' our variables measurable, and even though it is feasible with more complex recording techniques, in reality we could had not been able to set the variables in a real experiment. In the near future, we plan to do these estimations with data from the Sánchez-Vives lab, eventually for other rate models that have not been treated here.

Finally, the EKF has been proven to work for different models, and hence, we can induce that has a high applicability for a different set of neuron models.

The MATLAB scripts of the project can be consulted at https://github.com/marcalbp98/TFG.

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