Approximate Bayesian Inference for a Mechanistic Model of Vesicle Release at a Ribbon Synapse

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Introduction

Photoreceptors and bipolar cells in the vertebrate retina are equipped with highly specialized ribbon synapses, able to simultaneously release multiple glutamatergic vesicles in a process known as multivesicular release, contributing to rapid and reliable information transmission.

We develop an approximate Bayesian inference scheme for a fully stochastic, biophysically inspired model of glutamate release at this specialised synapse. The model translates known structural features of the ribbon synapse into a set of stochastically coupled equations. We approximate the posterior distributions by updating a parametric prior distribution via Bayesian updating rules.

We show that model parameters can be efficiently estimated for synthetic and experimental data from in vivo two-photon experiments in bipolar cells of zebrafish. Also, we find that the model captures complex properties of the synaptic release such as the temporal precision.

Preprint availabel on bioRxiv:

Release Stage

The vesicle movement at the ribbon is modeled in a discrete way and the changing rates between the three vesicle pools are stochastic:

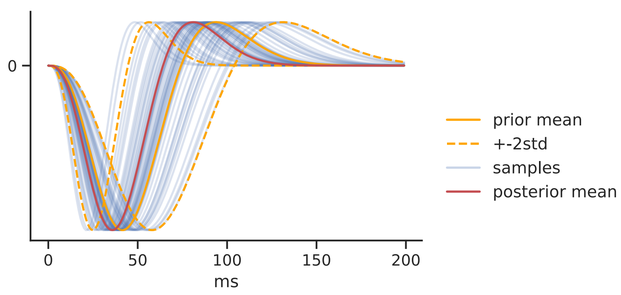
$$c(t) \sim Poisson(\lambda)$$
$$r(t) \sim Binomial(R_{t-1}, p_r)$$
$$d(t) \sim Beta\text{-}binomial(D_{t-1}, \alpha, \beta)$$
$$\text{with } \alpha = f\big(\rho, p_d(Ca)\big)$$
$$\text{and } \beta = g\big(\rho, p_d(Ca)\big)$$

Each rate depends on the current state of the model and is limited by the maximal pool size.

The parameters of r and c are constant over time whereas the distribution of the actual exocytosis d depends on the correlation ρ between vesicles, and in a non-linear way on the calcium concentration:

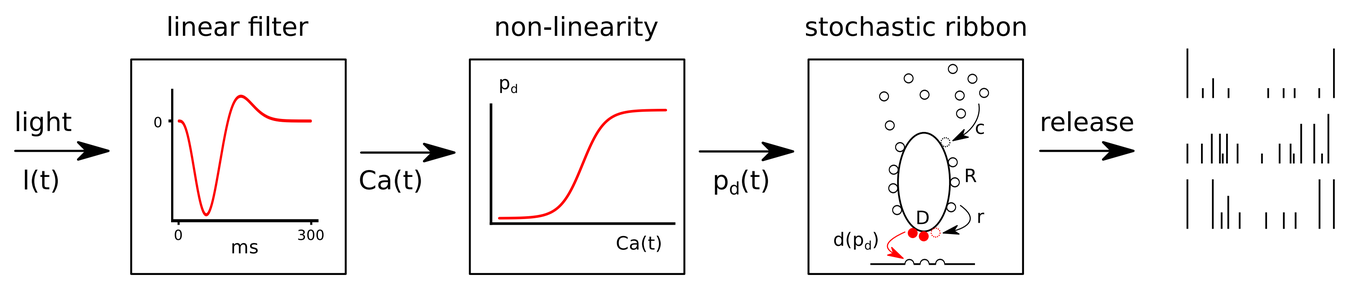
$$p_d = \frac{1}{(1 + \exp(-k(Ca - h))}$$

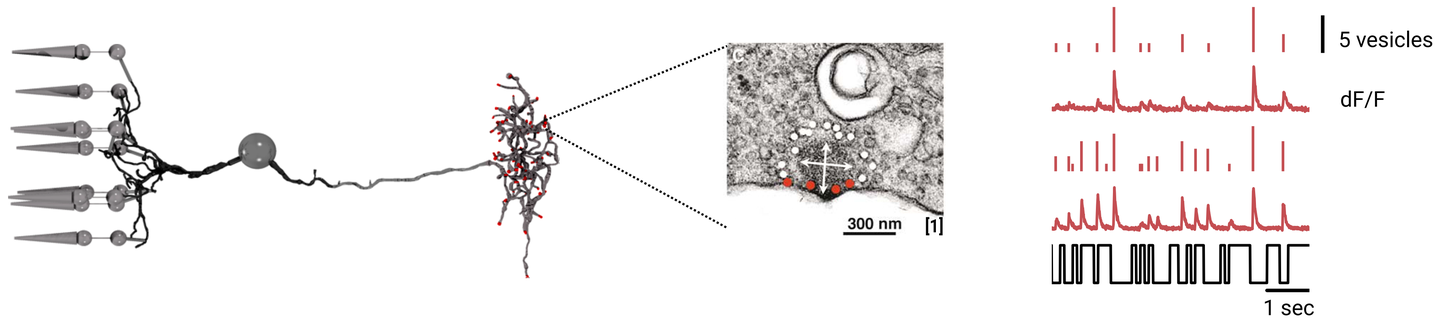
Linear kernel



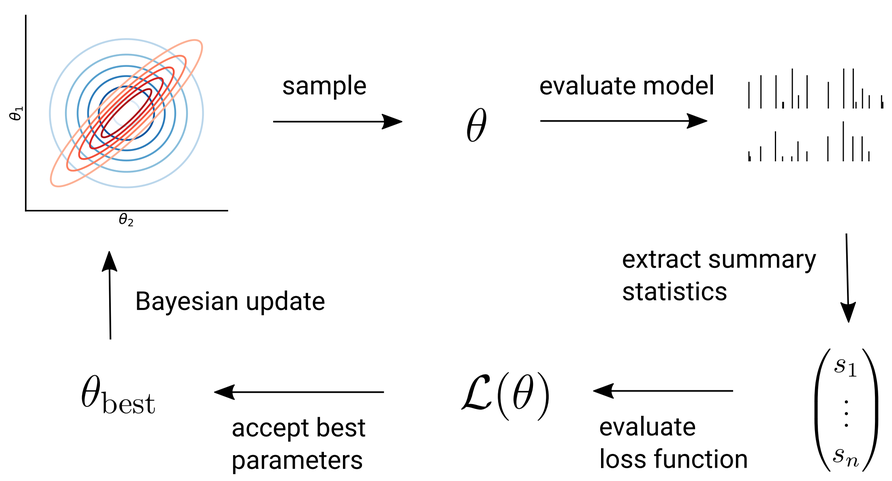
The biphasic kernel of the linear stage of the LNR model is parametrized by one single time stretching parameter γ.

Linear-Nonlinear-Release Model





Fitting procedure



Summary statistics:

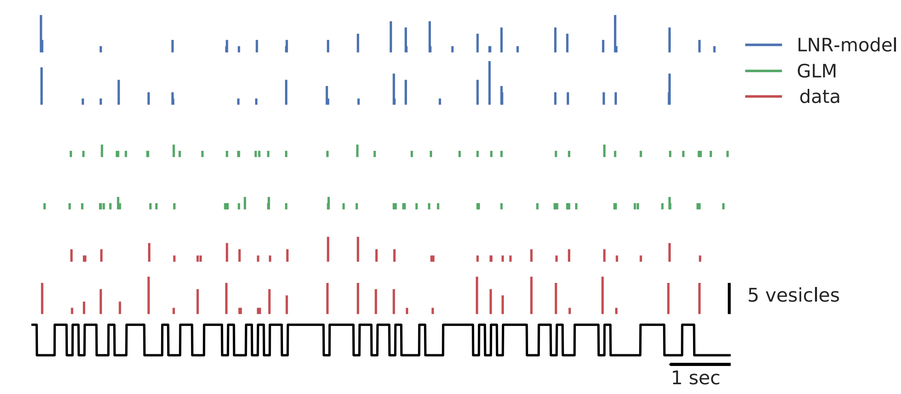
To compare the different discrete traces summary statistics s_1, ..., s_n are calculated and a weighted euclidean distance between these statistics gives the discrepancy for each parameter set.

Updating rules:

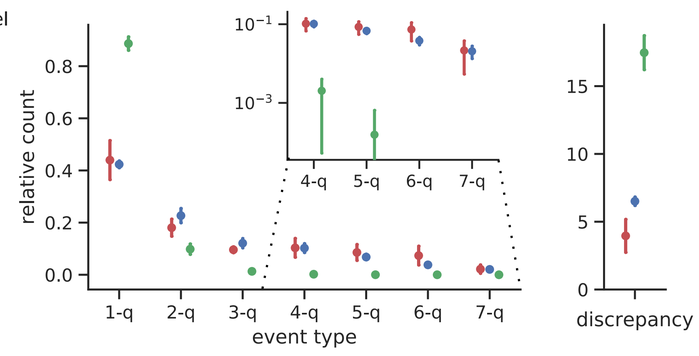
We assumed a Normal distribution as (proposal) prior which is updated by Bayesian updating rules with the best *n* parameters.

Results

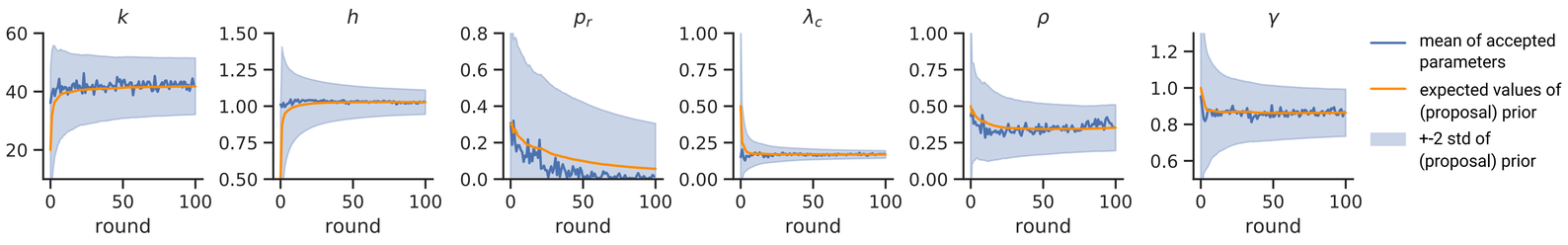
Data and simulations



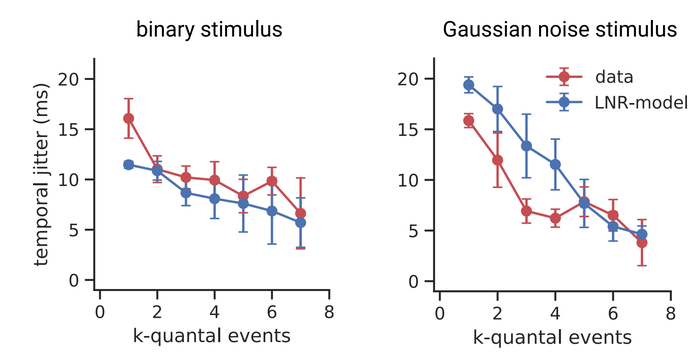
Summary statistics and discrepancy



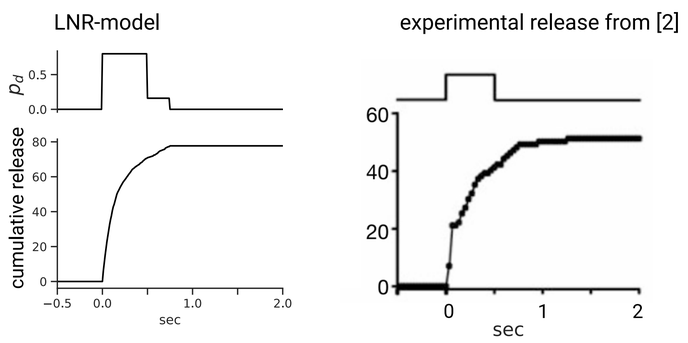
Posteriors



Temporal jitter



Cumulative release



Conclusions

- We developed a framework for linking mechanistic models of neural activity to measured data.
- Combining a system identification approach with a mechanistic, biophysically inspired component enables us to make biologically interpretable predictions.
- The presented linear-nonlinear-release model captures noise of glutamate release at a single synapse.
- Model parameters are infered via an Approximate Bayesian Inference Method.
- LNR model captures well complex features such as temporal precision.
- LNR model outperforms standard GLM.

References

[1] Holt, M. et al. (2004), Current Biology.
[2] Zenisek, D. et al. (2000), Nature.

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