Evidence for a nonlinear coupling between firing threshold and subthreshold membrane potential

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Abstract

In a rate-based framework, individual neurons are often characterized by f-I curves: functions that map constant inputs onto steady-state output rates. While the experimentally observed f-I curves of fast spiking interneurons are in good agreement with the ones predicted by generalized integrate-and-fire (GIF) models, the same is not true for excitatory pyramidal neurons.

To solve this issue, we propose a model in which a subthreshold adaptation mechanism complements spike-dependent adaptation. This mechanism implements a nonlinear coupling between the firing threshold and the membrane potential. Importantly, all the model parameters, including the timescale and the functional shape of the nonlinear coupling, are not assumed *a priori* but are extracted from *in vitro* recordings using a convex optimization procedure.

Our results demonstrate that the firing threshold and the subthreshold membrane potential are indeed nonlinearly coupled. This mechanism, consistent with subthreshold Na⁺-channel inactivation, operates on a relatively short timescale (5 ms) and makes the firing threshold dependent on the speed at which the threshold is approached.

The precise shape of the nonlinear coupling extracted from the experimental data accounts for both the saturation and the noise sensitivity that characterize f-I curves of pyramidal neurons. Moreover, the model predicts the occurrence of individual spikes with millisecond precision.

Why a nonlinear coupling between the membrane potential and the firing threshold?

(Platkiewicz and Brette, PLOS Comp. Biol. 2011)

Following the approximation used to reduce the HH model to the EIF model:

$$C\dot{V} = g_L k_a h \exp\left(\frac{V - V_T}{k_a}\right) + \ldots$$

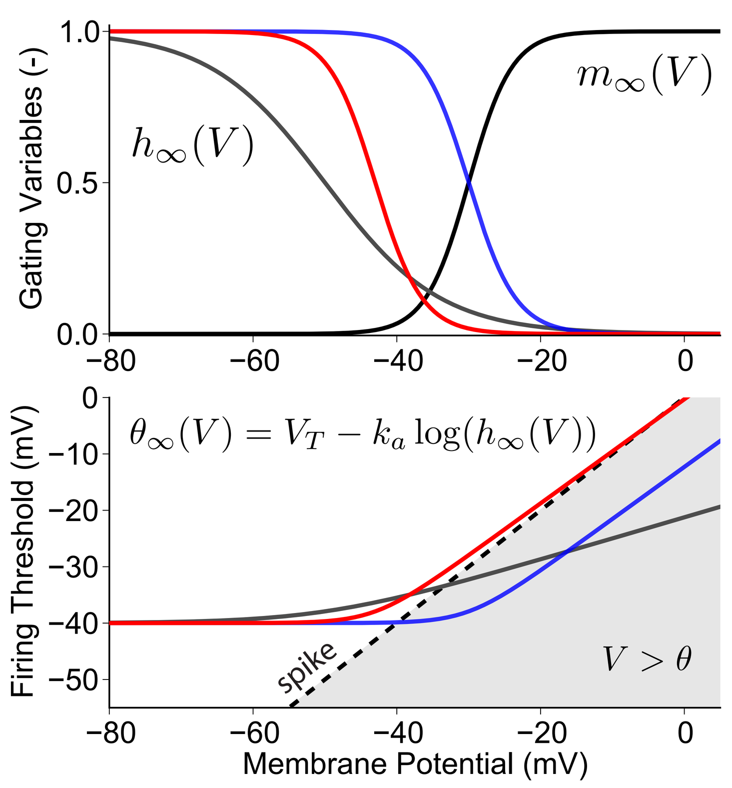
$$\tau_h \dot{h} = -h + h_\infty(V)$$

The effective threshold is therefore:

$$\theta = V_T - k_a \log(h)$$

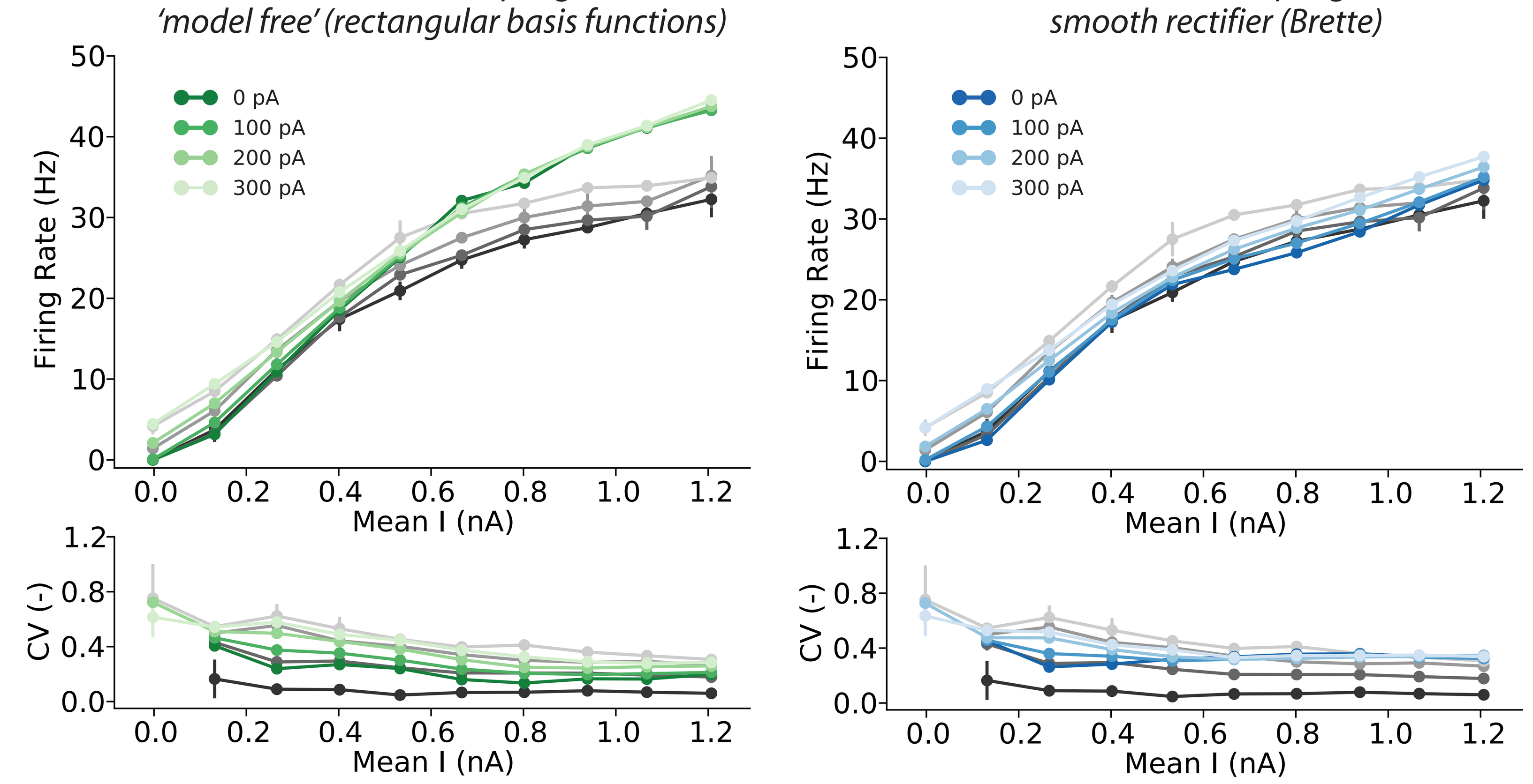
And its dynamics can be approximated by:

$$\tau_\theta \dot{\theta} = -\theta + \theta_\infty(V)$$

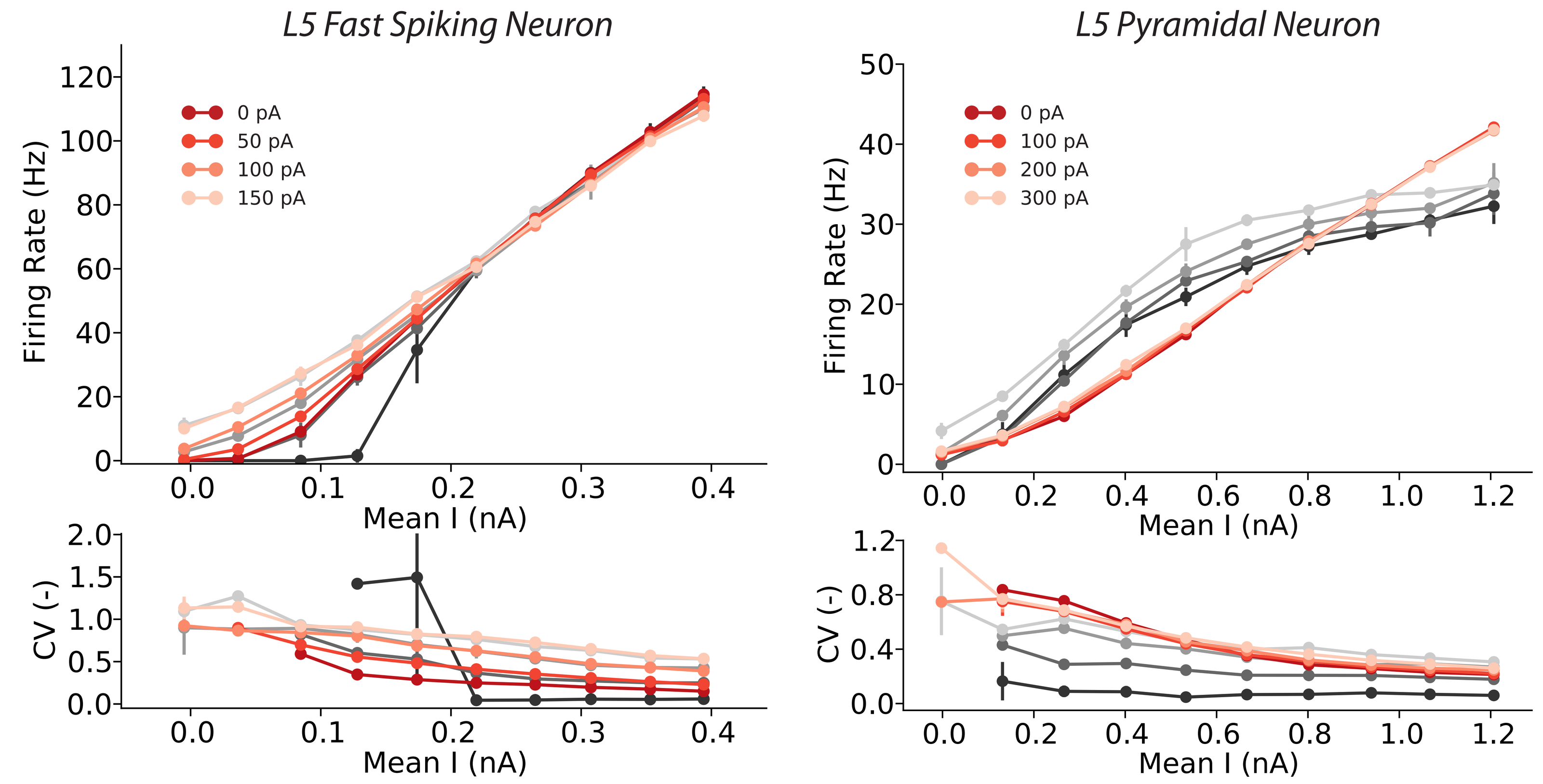


The nonlinear threshold explains the f-I curves

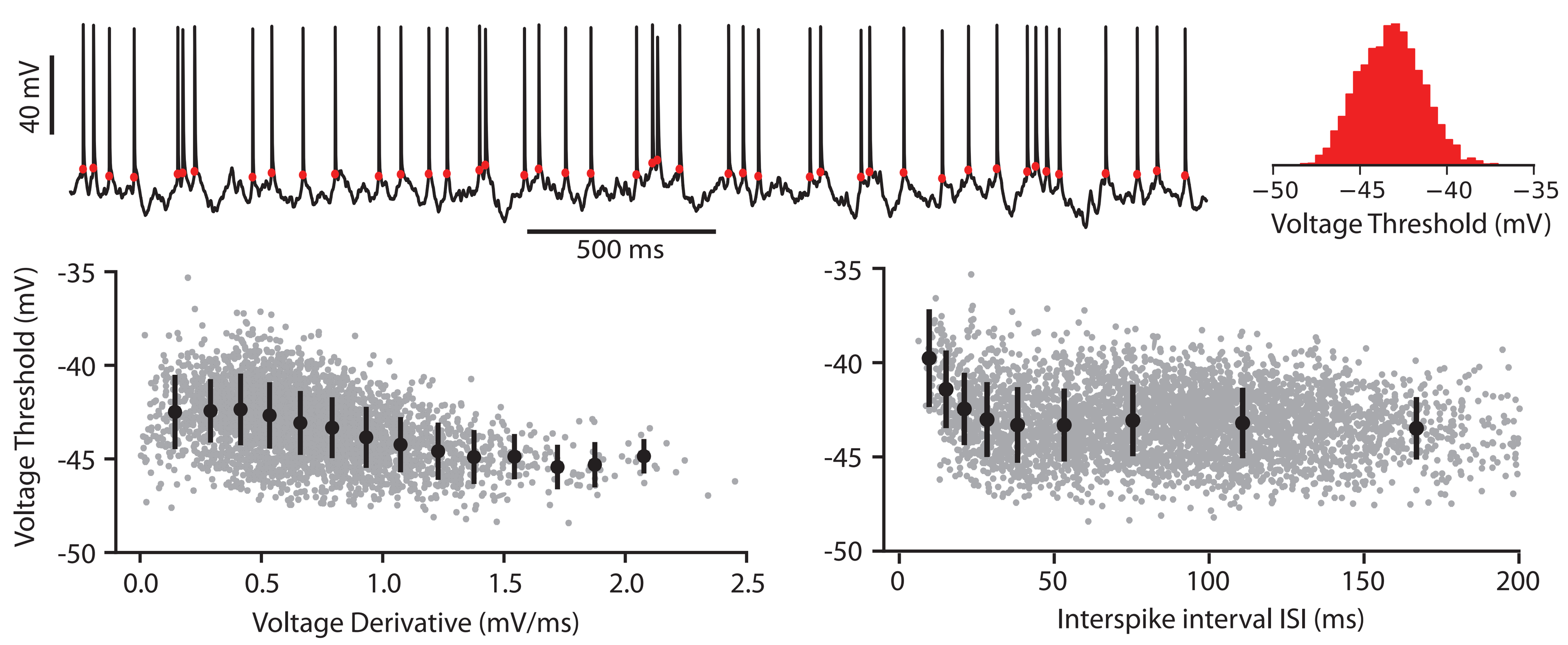
Nonlinear coupling: 'model free' (rectangular basis functions) — *Nonlinear coupling: smooth rectifier (Brette)*



Standard GIF models do not capture f-I curves of somatosensory L5 pyramidal neurons



The firing threshold depends on the membrane potential derivative



Spiking Neuron Model

Spikes are emitted stochastically according to the escape rate mechanism.

Each spike triggers both a movement of the firing threshold and an adaptation current.

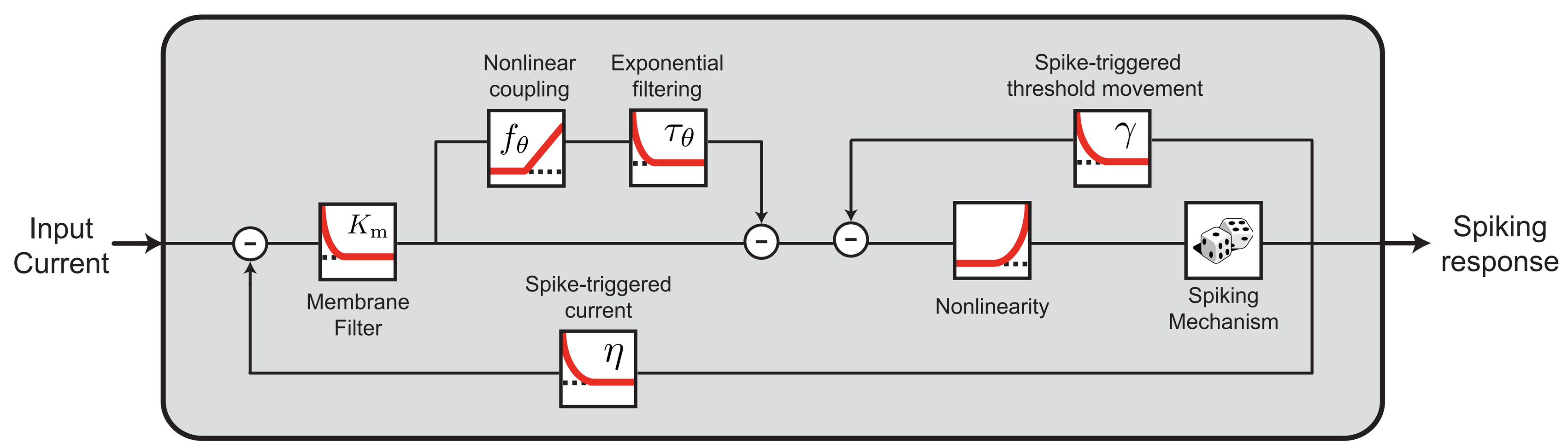
A nonlinear coupling between the membrane potential and the firing threshold constitutes a source of feed-foreward subthreshold adaptation.

$$\lambda(t) = \lambda_0 \exp\left(\frac{V(t) - V_T(t)}{\Delta V}\right)$$

$$C\dot{V} = -g_L(V - E_L) + I_{\text{ext}} - \sum_{\hat{t}_j < t} \eta(t - \hat{t}_j)$$

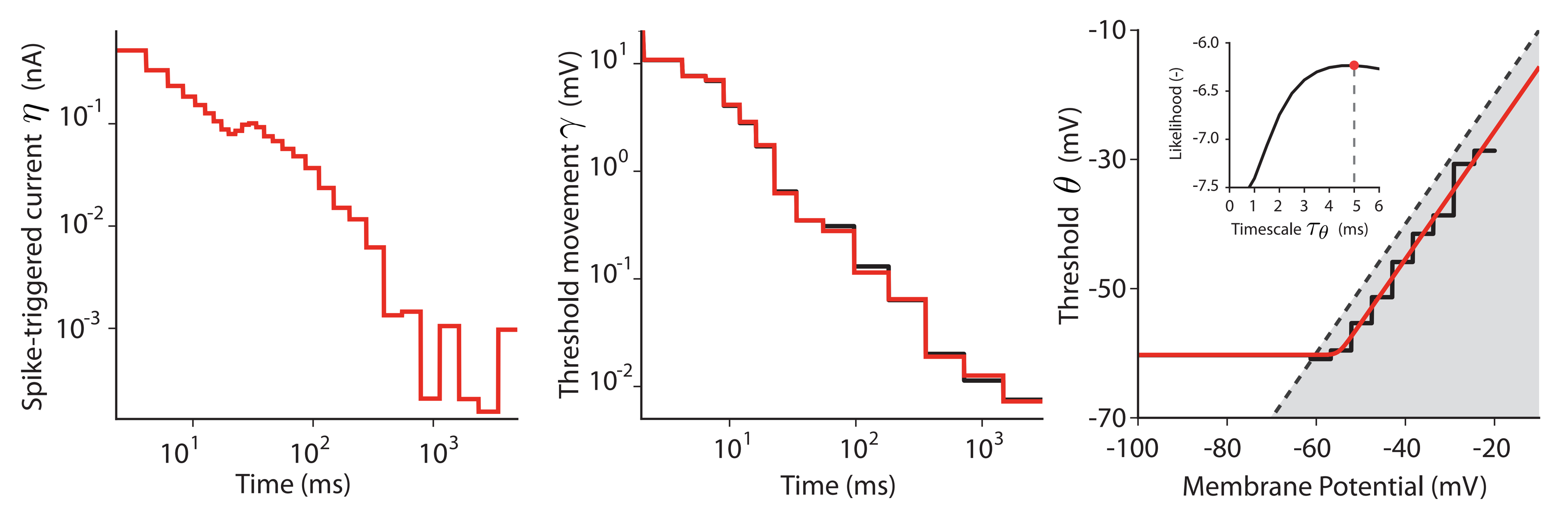
$$V_T(t) = V_T^* + \theta(t) + \sum_{\hat{t}_j} \gamma(t - \hat{t}_j)$$

$$\tau_\theta \dot{\theta} = -\theta + f_\theta(V)$$



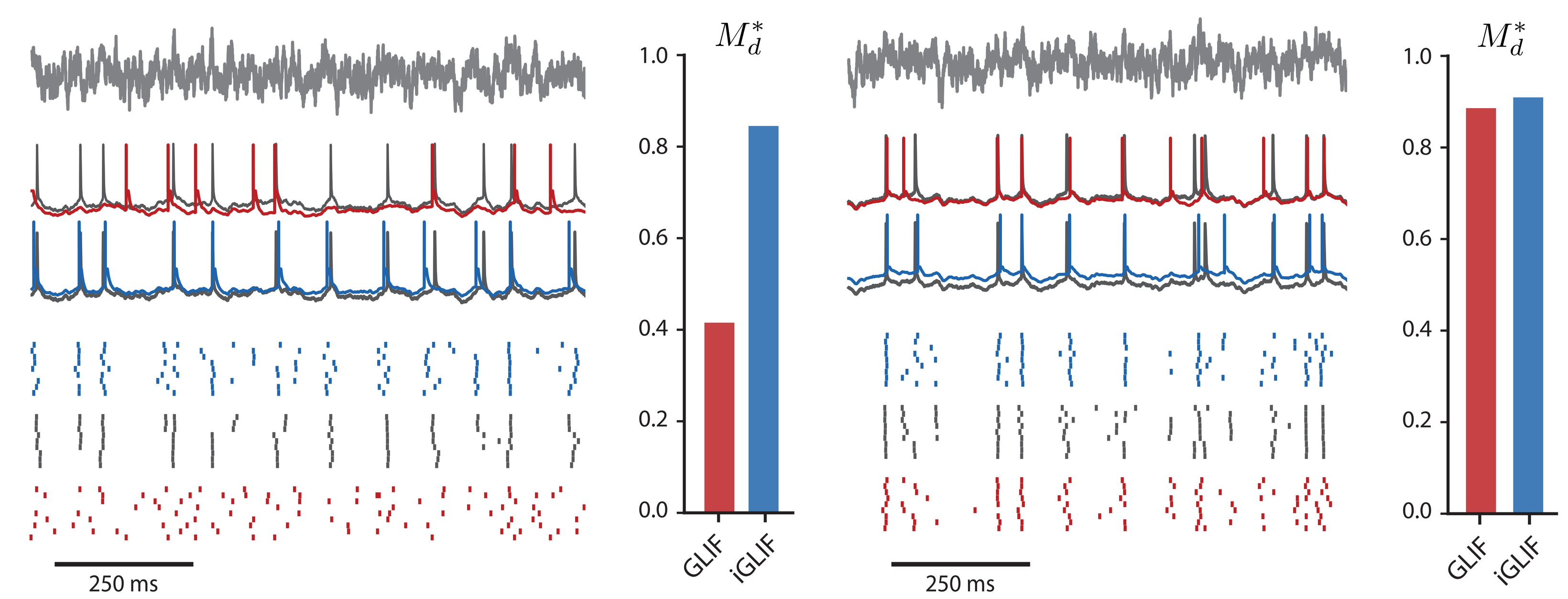
Parameters extracted from *in vitro* recordings

All model parameters are extracted from intracellular recordings using a new fitting procedure. Any *a priori* assumption is made on the functional shape of the different filters. The results reveal a strong coupling between the subthreshold membrane potential and the firing threshold.



Spike-timing prediction

The model not only predicts the mean firing rate observed in response to stationary inputs, but is also able to account for occurence of individual spikes with millisecond precision.

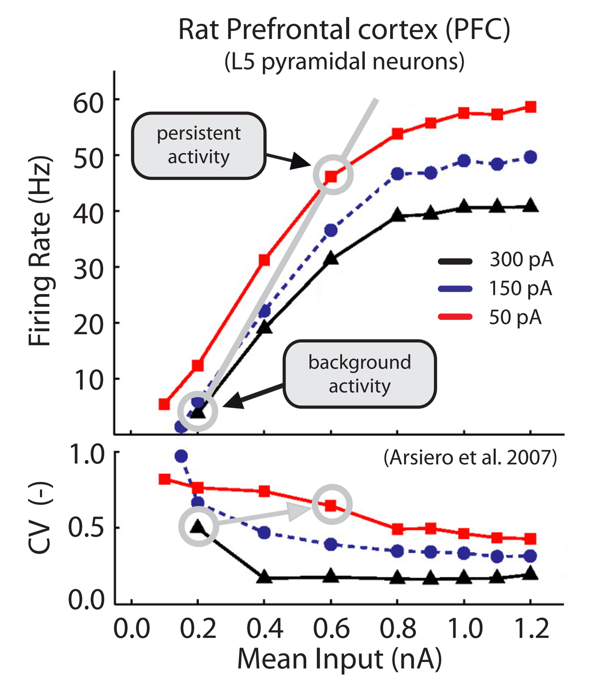


Functional implications

In rat prefrontal cortex (PFC), pyramidal neurons saturate at low rates and retain sensitivity to current fluctuations (Arsiero *et al.*, 2007).

In PFC, during working memory tasks, certain neurons show persistent activity. This phenomeon is usually interpreted as a bistability of the network. However, it is problematic to account for the high variability (high CV) observed during persistent activity.

Compared to standard LIF models, the nonlinear coupling between membrane potential and firing threshold might explain, at least partially, the high variability observed *in vivo*.



References

Platkiewicz and Brette, *"Impact of fast sodium channel inactivation on spike threshold dynamics and synaptic integration."* PLoS computational biology (2011)

Arsiero et al., *"The impact of input fluctuations on the frequency–current relationships of layer 5 pyramidal neurons in the rat medial prefrontal cortex."* The Journal of neuroscience (2007).