Firing rate of neurons with dendrites, soma and axon in the fluctuation-driven, low-rate limit

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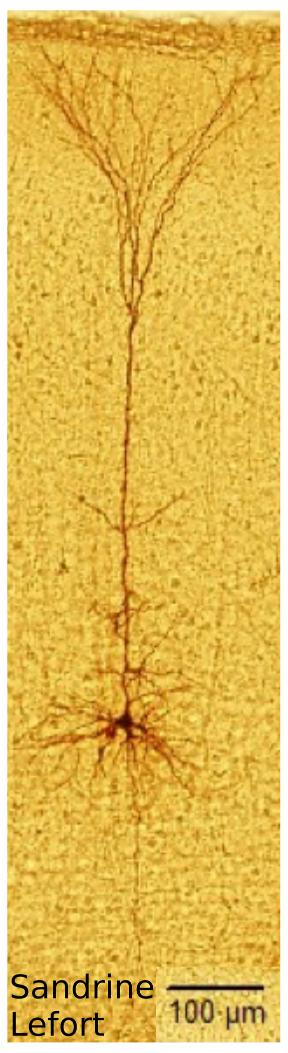
Abstract

- Framework developed for modelling neurons with dendrites receiving distributed stochastic drive [1].
- Firing rate independent of length constant for a neuron with identical semi-infinite dendrites but distinct from that of a point neuron.
- Addition of an axon significantly reduces the firing in spatial neuron models.
- Non-monotonic relationship found between the number of dendrites and the fluctuation-driven firing rate.

Background

- How neurons integrate stochastic synaptic inputs throughout their dendritic arbours is an active area of research.
- Neuronal firing properties are affected by spatial separation between the soma and the action potential (AP) initiation site in the axon initial segment (AIS), and the conductance load of the axon.
- These properties include: rapidity of spike onset, effective threshold at soma in comparison with AIS, and back-propagation of APs [2].
- This has led to the simulation of multi-compartmental models, with dendrites, soma and axon [3].
- Multi-compartmental models have provided useful insights and qualitatively different behaviour to point-neuron models.
- A theoretical framework for calculating the firing of neurons with spatially distributed synaptic input would provide a basis to assess the effect of electrotonic length.



Thick-tufted layer 5 pyramidal cell

Modelling Framework

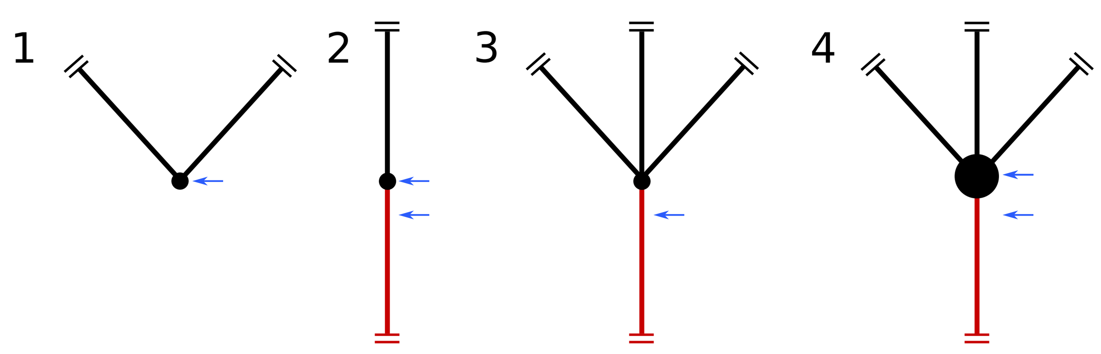
- Passive dendrites (but quasi-active I_h can easily be added), soma and axon have threshold voltage.
- Synaptic drive uniform across dendritic segments.
- Potential v measured from E_L evolves according to cable equation driven by spatially white but temporally filtered noise

$$\tau_v \frac{\partial v}{\partial t} = \mu - v + \lambda^2 \frac{\partial^2 v}{\partial x^2} + s,$$
$$\tau_s \frac{\partial s}{\partial t} = -s + 2\sigma_s \sqrt{\tau_s \lambda}\, \xi(x,t).$$

- Soma modelled as lumped conductance and capacitance. For n neurites radiating from soma

$$\tau_0 \frac{\mathrm{d}v_0}{\mathrm{d}t} = \mu_0 - v_0 + \sum_{k=1}^{n} \rho_k \lambda_k \left.\frac{\partial v_k}{\partial x_k}\right|_{x_k=0} + s_0.$$

- The dendritic dominance factor ρ is the conductance ratio between an electrotonic length constant λ of dendrite and the soma.
- When v at a trigger position $x_{\rm th}$ exceeds threshold $v_{\rm th}$, the potential across the structure is reset to $v_{\rm re}$.

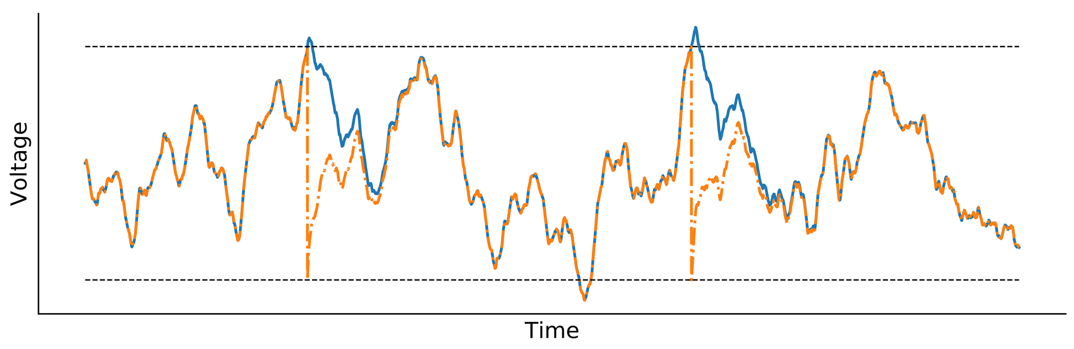


Morphologies: (1) Two dendrites, (2) Dendrite and axon (red), (3) Multiple dendrites and axon (4) Dendrites, large soma and axon. Blue arrows indicate possible locations for the trigger position $x_{\rm th}$.

Analysis

- The stochastic cable equation is a linear system so can be solved using Green's functions.
- In the fluctuation-driven regime, we can approximate the firing rate using the upcrossing method [4]

$$r = \frac{\sigma_{\dot v}}{2\pi\sigma_v} \exp\left[-\frac{(v_{\rm th} - \langle v\rangle)^2}{2\sigma_v^2}\right].$$

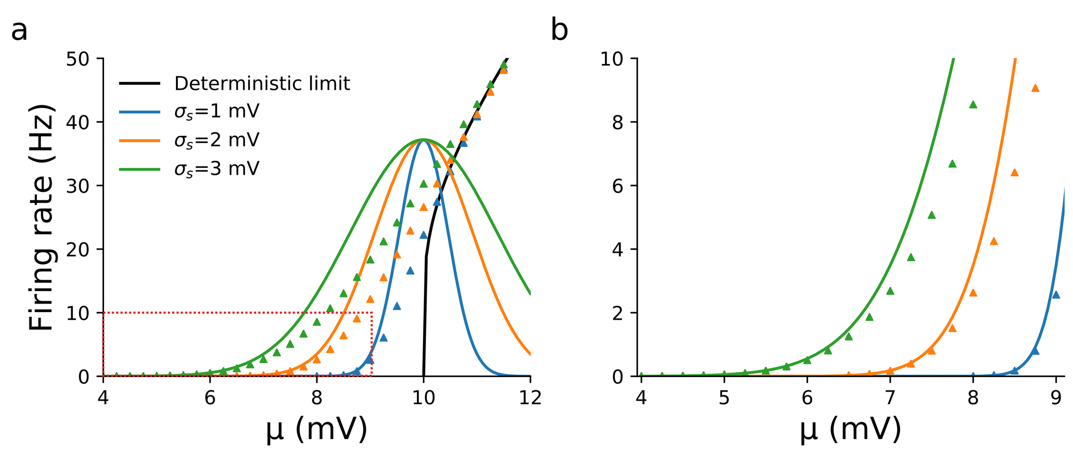


- Strategy to obtain the fluctuation-driven firing rate: calculate the mean $\langle v\rangle$, variance σ_v^2 and variance of the time-derivative $\sigma_{\dot v}^2$.
- Deterministic firing from input current injection calculable by considering zero-noise limit, setting $v(x_{\rm th}, t) = v_{\rm th}$ and solving for time.

Model 1: Two Radiating Dendrites

- Represents two dendrites radiating from a small (negligible conductance) soma.
- Dendrites with identical properties can be modelled as an infinite cable with the soma located at $x = 0$.
- Second moments do not depend on length constant λ but functionally different to point neuron

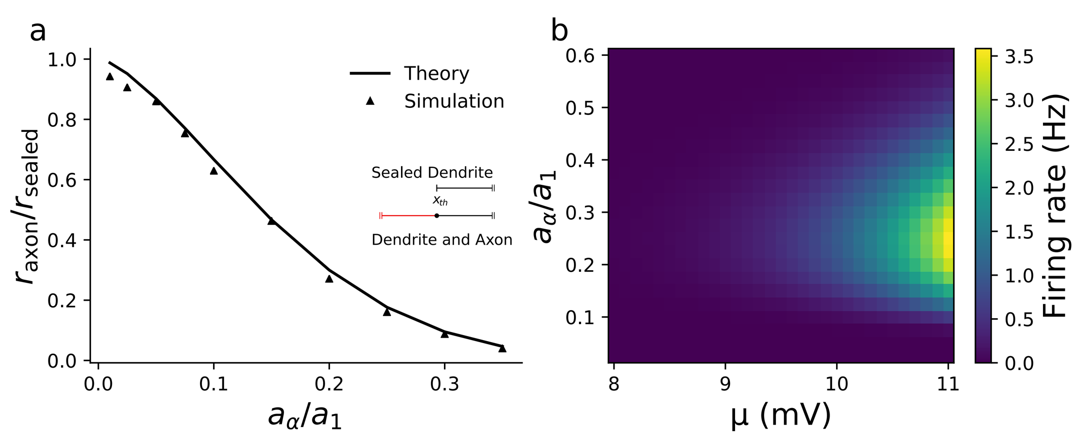
$$\sigma_v^2 = \sigma_s^2 \frac{\tau_s}{\tau_v}\left(1 - \sqrt{\frac{\tau_s}{\tau_s + \tau_v}}\right), \quad \sigma_{\dot v}^2 = \frac{\sigma_s^2}{\tau_s \tau_v}\sqrt{\frac{\tau_s}{\tau_s + \tau_v}}.$$



The upcrossing approximation works well for firing rates <5Hz. The region with the firing rate <10Hz in (a) has been expanded in (b). Here $\lambda_1 = 200\mu$m, $\tau_s/\tau_v = 0.5$, $\tau_v = 10$ ms, $v_{\rm th} = 10$ mV, $v_{\rm re} = 0$ mV. These values of τ_s, τ_v, $v_{\rm th}$, $v_{\rm re}$ are used for all future plots.

Model 2: Dendrite and Axon

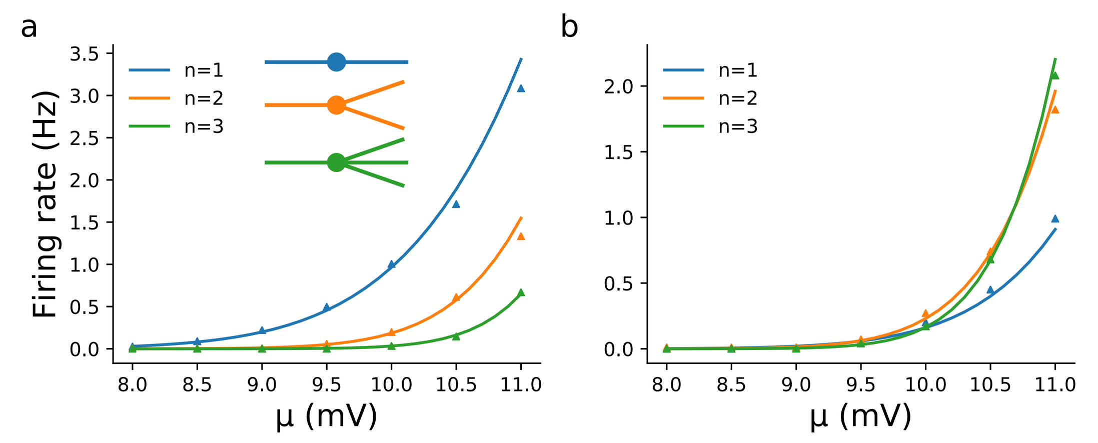
- Dendrite and axon (α) with different properties connected at $x = 0$ (nominal soma). Synaptic drive only placed in dendrite.
- Noise from the dendrite has additional spatial filtering in the axon.
- Axon reduces the input resistance at $x = 0$, significantly reducing the firing rate.
- Trigger position can be placed at any point along the axon. $x_{\rm th} = 0$ and $x_{\rm th} = 30\mu$m chosen here.
- For $x_{\rm th} = 30\mu$m, the ratio of axonal to dendritic radius a_α/a_1 that maximises firing is similar to physiologically found values in pyramidal cells.



(a) The lower the resistance of the axon (a_α/a_1 increasing), the lower the firing rate at $x_{\rm th} = 0$ relative to a sealed dendrite with the same input drive. (b) For $x_{\rm th} > 0$, the firing rate varies non-monotonically with the ratio a_α/a_1.

Model 3: Multiple Dendrites

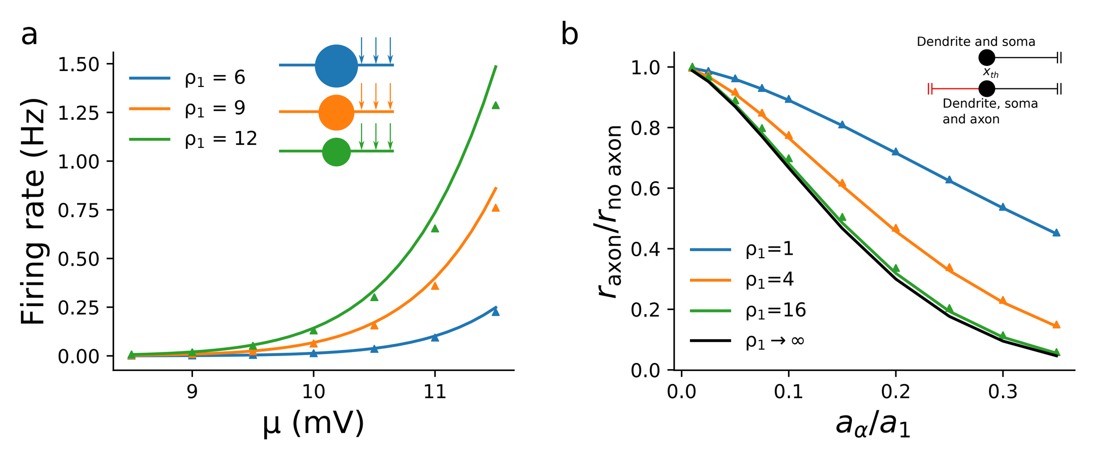
- Each dendrite in this model has the same properties but statistically independent input.
- More synaptic input sources, but a lower input resistance.
- Surprisingly, the variance falls as more dendrites are added, while the mean increases towards μ.
- For low mean synaptic drive μ and shorter axonal length constant λ_α, more dendrites results in a lower firing rate.
- For higher μ and λ_α, increasing the number of dendrites initially increases the firing rate.



(a) For $\lambda_\alpha = 100\mu$m increasing n decreases the firing rate. (b) With $\lambda_\alpha = 150\mu$m, increasing n for higher μ increases the firing rate. $x_{\rm th} = 30\mu$m.

Model 4: Effect of a Large Soma

- We tested the effect of a non-negligible soma on the firing rate with the dendrite and axon model.
- As dominance factor $\rho \to \infty$, the effect of a soma is negligible.
- For smaller ρ the firing rate in the axon decreases, since the somatic conductance is larger.
- In comparison to a model with a dendrite and soma only, the relative effect of the axonal load is smaller for lower ρ.



(a) The upcrossing approximation works well for various soma sizes. $x_{\rm th} = 30\mu$m, $\lambda_\alpha = 100\mu$m. (b) The axon reduces firing less significantly for smaller ρ for the same output firing rate. $x_{\rm th} = 0$.

Conclusions

- Fluctuation and mean-driven firing of neurons with spatially distributed input can be approximated.
- For simple models with identical dendrites, the firing rate is independent of the length constant.
- The axonal and somatic conductances have a significant effect on the firing rate.
- Adding more dendrites to the soma can decrease the fluctuation-driven firing rate, however in general it has a non-monotonic relationship.

References

[1] R. P. Gowers, Y. Timofeeva, and M. J. E. Richardson, "Low-rate firing limit for neurons with axon, soma and dendrites driven by spatially distributed stochastic synapses," *bioRxiv*, June 2019.

[2] M. H. P. Kole and G. J. Stuart, "Signal Processing in the Axon Initial Segment," *Neuron*, vol. 73, no. 2, pp. 235–247, 2012.

[3] G. Eyal, H. D. Mansvelder, C. P. J. de Kock, and I. Segev, "Dendrites impact the encoding capabilities of the axon," *Journal of Neuroscience*, vol. 34, no. 24, pp. 8063–8071, 2014.

[4] S. O. Rice, "Mathematical analysis of random noise Part III," *The Bell System Technical Journal*, vol. 24, no. 1, pp. 46–156, 1945.