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Neuronal synchronization through electrochemical ephaptic coupling

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Ephaptic coupling

Indirect neuronal communication through the extracellular space (ECS) is known as *ephaptic coupling*. Ephaptic coupling contributes to neuronal synchronization[1], an important property of healthy brain function[2]. In-silico studies on ephaptic coupling often focus on local field potentials, often assuming constant ion concentrations in the ECS. The chemical ephaptic effects remain largely unexplored. Here, we propose a minimal model for studying electrochemical ephaptic coupling.

An electrodiffusive model

We introduce an electrodiffusive Kirchhoff-Nernst-Planck[3] framework for modeling an arbitrary number of two-compartment neurons sharing a two-compartment extracellular space. The model describes the time evolution of the electrical potentials ϕ, and the ion concentrations of Na^+, K^+, Cl^- and Ca^{2+}. The ion concentrations and electric potentials are calculated in each compartment of both the ECS and the intracellular spaces (ICS).

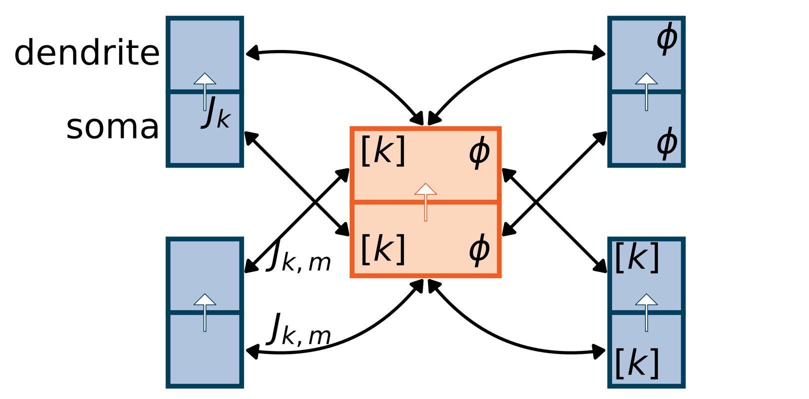

Figure 1: Network model schematic. Neurons are depicted in blue, while the ECS is orange.

Fluxes in the ECS and ICS are modelled with the Nernst-Planck equation for each ion species k

$$J_k = J_k^{\mathrm{diff}} + J_k^{\mathrm{drift}}. \quad (1)$$

Membrane fluxes $J_{k,m}$ due to ion channels and homeostatic mechanisms are modeled with a Hodgkin-Huxley type formalism.

Changes in ion concentrations affect the membrane fluxes through the dynamic reversal potentials:

$$E_k = \frac{RT}{F z_k} \ln \frac{[k]_{\mathrm{ECS}}}{[k]_{\mathrm{ICS}}}, \quad (2)$$

where $[k]$ denotes an ion concentration. Neuronal activity in a single neuron can impact the concentrations and electric field of the ECS, potentially influencing the behaviour of all neurons.

Each neuron is injected with a noisy stimulus current into the soma, where the start time of each neuron has an offset to avoid initial synchrony. Excitatory AMPA synapses will be added between neurons in future simulations.

Model limitations

The neuron morphology is simplified. Changes in the ECS are instantly homogenised, and distances between neurons are only implicitly accounted for by the ECS volume fraction.

Acknowledgements

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References

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2. Uhlhaas, P. *et al.* Neural synchrony in cortical networks: history, concept and current status. *Frontiers in Integrative Neuroscience* **3** (2009).
3. Sætra, M. J. *et al.* An electrodiffusive, ion conserving Pinsky-Rinzel model with homeostatic mechanisms. *PLOS Computational Biology* **16**, e1007661 (2020).

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In-silico electrochemical studies

Ephaptic coupling increases firing rates and synchrony

A study of an unconnected network, i.e. no synapses were added, was performed to isolate the overall impact of ephaptic coupling. Figure 2 shows the spike times of the neurons using a regular volume ratio between the ECS and the total ICS. By considerably increasing the ECS volume, we reran the study with reduced ephaptic effects (Figure 3).

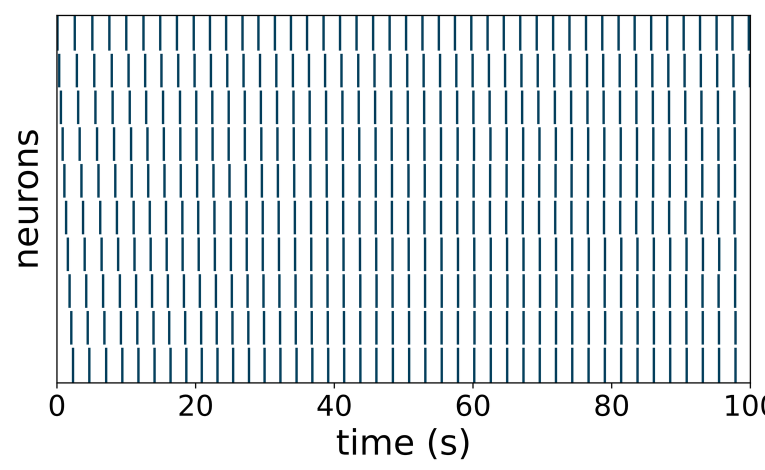

Figure 2: ECS/ICS volume ratio 1:2.

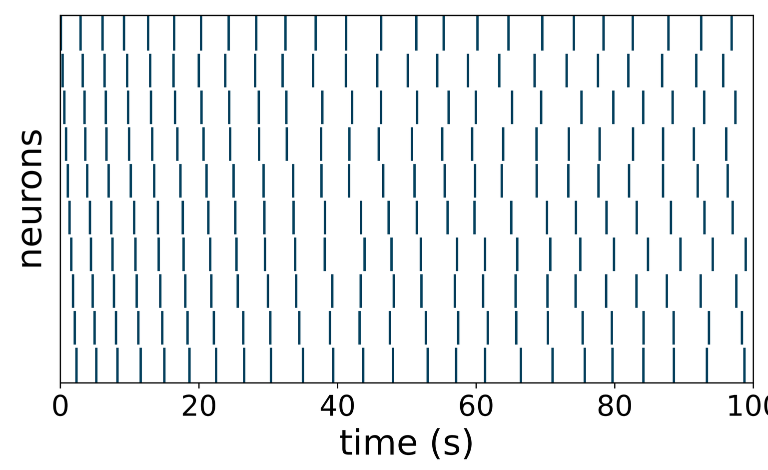

Figure 3: ECS/ICS volume ratio 10^4:2.

Chemical ephaptic effects dominate over the electric

Next, we study the importance of electrical versus chemical contributions to ephaptic coupling. The chemical effects were suppressed by fixing ion concentration parameters in the transmembrane fluxes to equilibrium values.

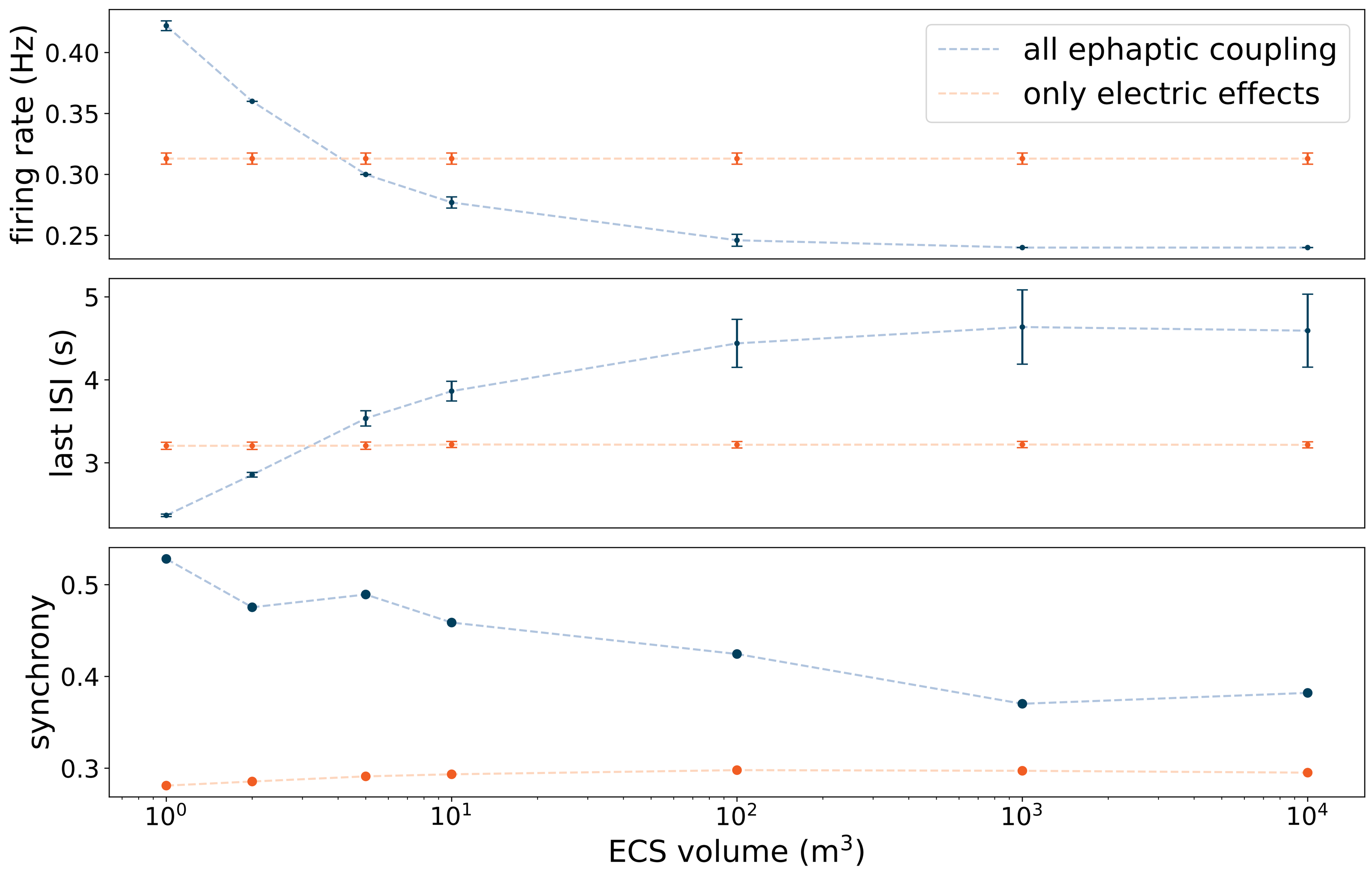

Figure 4: Network spiking properties of an unconnected 10-neuron network.

Network synchrony is based on membrane potentials, and lies between 0 (no synchrony) and 1 (complete synchrony). The last interspike interval (ISI) and the firing rates are provided as mean values with standard deviations.

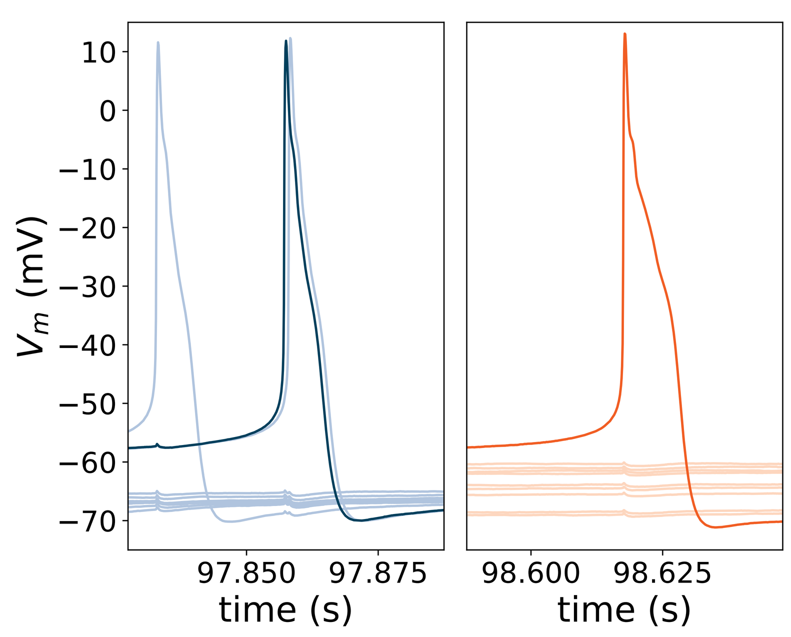

Figure 5: Last spike of neuron nr. 10.

While the effects of ephaptic coupling should decrease with increasing ECS volume, no such effect is visible without the chemical ephaptic coupling. The electrical effects were very small. Using the regular 1:2 volume ratio (Figure 5), one neuron firing causes a small fluctuation in the membrane potential of the other neurons, regardless of whether the chemical effects are suppressed or not.