Computational model of the novel seizure pattern

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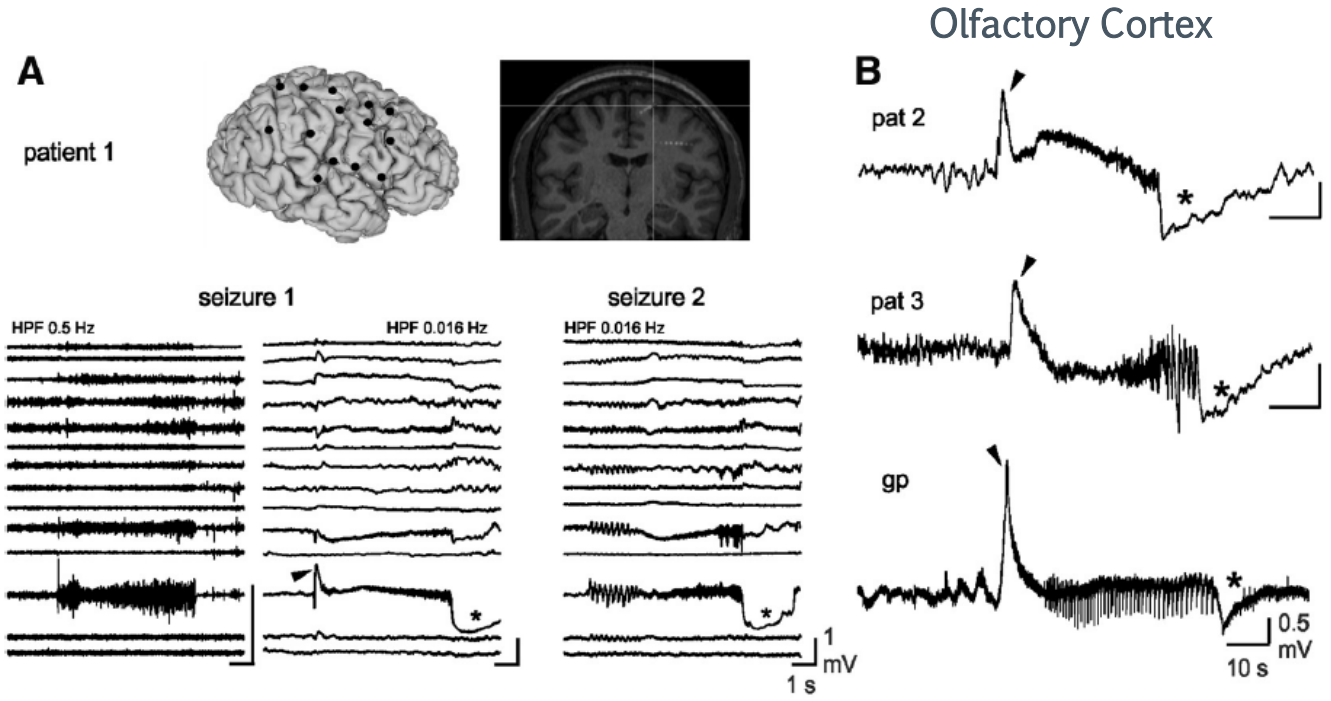
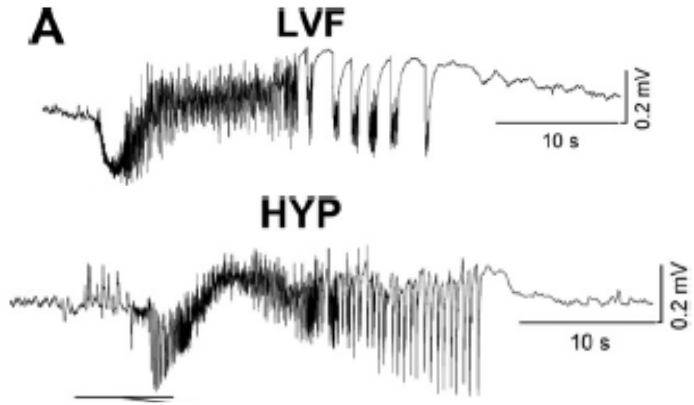
Novel seizure-like pattern

- Over a lifetime, **one in 26 people** will be diagnosed with epilepsy
- In many cases etiology remains unknown
- Standard filtering masks novel Seizure-like event (SLE)

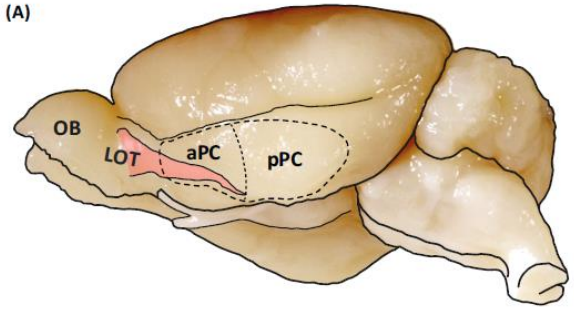


Source: Uva et. al. 2017 J. Neuroscience

„Normal" seizure
Temporal lobe



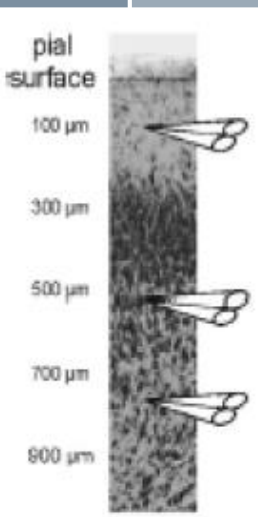
Source: Avoli et. al. 2016 J. Neurophysiol.

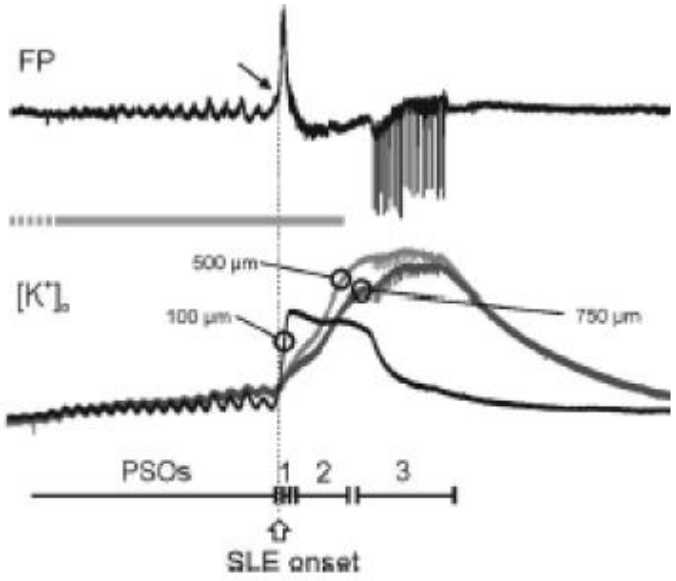


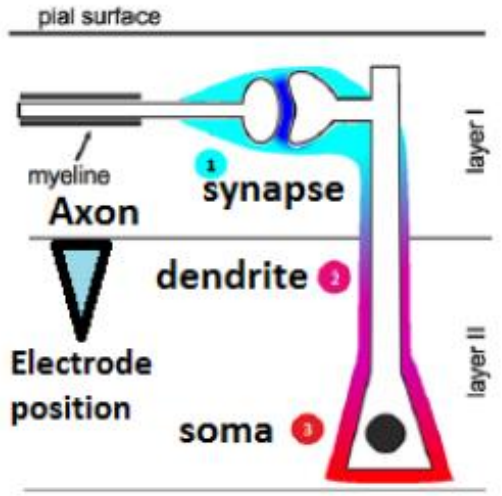
Source: Bekkers et. al. 2013 Trends in Neuroscience

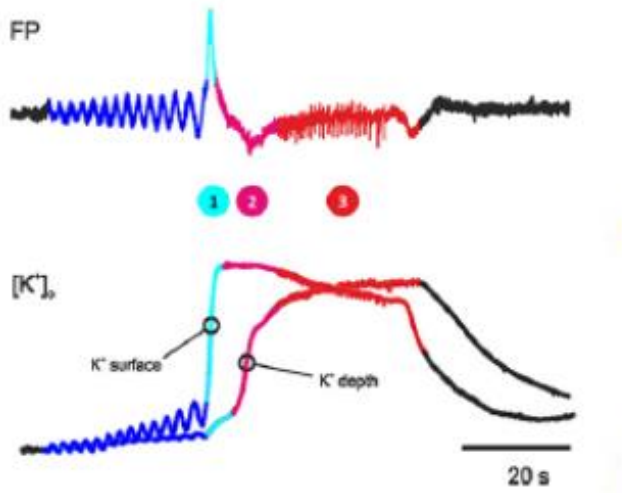
Experimental Data (*in vitro*) – Uva et. el. 2017

1. During Pre Seizure Oscillation (PSO) extracellular [K+] increases beyond the threshold of the buffering capability of astrocyte/glia (dark blue)
2. Potassium accumulates in layer 1 further depolarizing unmyelinated axon fibers and blocking synaptic transmission (light blue)
3. The accumulated potassium slowly diffuses to layer 2 and 3 (Pink)
4. Progressive recruitment of neuronal activity in layers 2 and 3 further increases [K+] in these layers (red)
5. Seizure-like event (SLE) terminates with return of [*K*+] to the level observed before SLE (black)



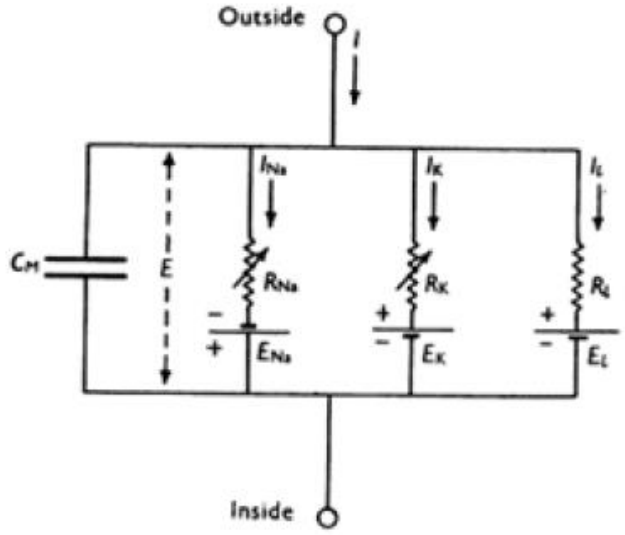






Methods – basic mechanisms

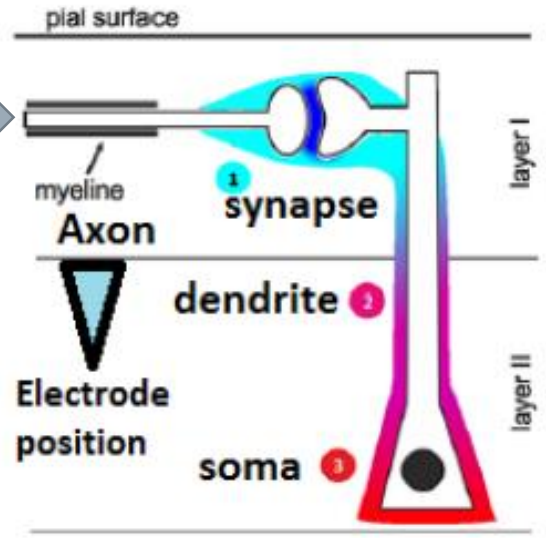
- NEURON v7.2 programming
- Hodgkin-Huxley set of membrane equations (axon, soma)
- Sodium/Potassium pump (axon, soma)
- Passive currents (dendrite)



Source: Hodgkin and Huxley 1952 J. Physiol.

Artificial spikes stimulation

Spikes freq: ~7 Hz



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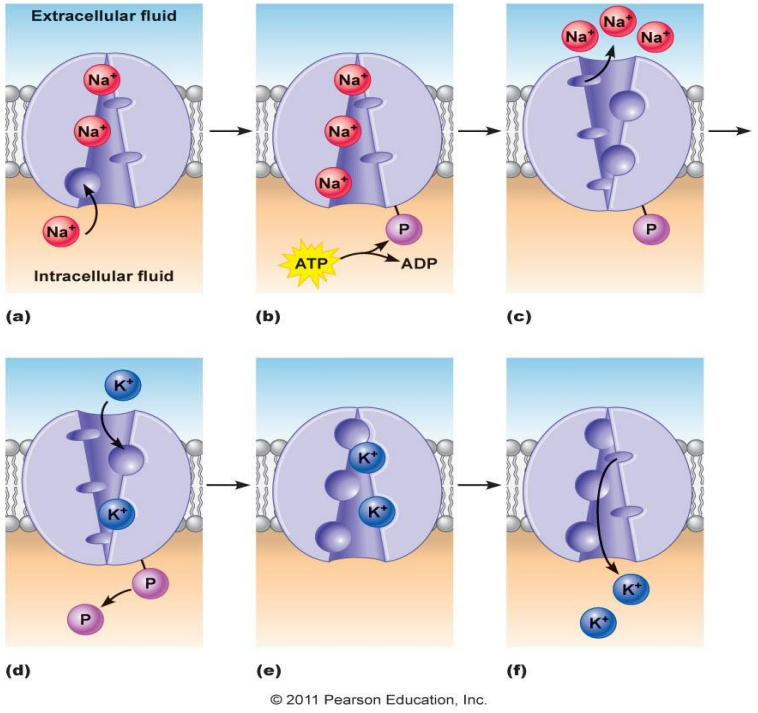
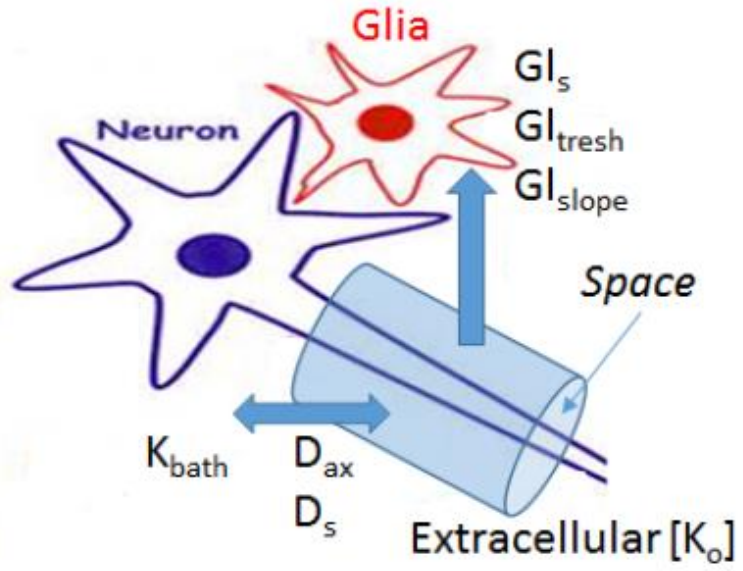


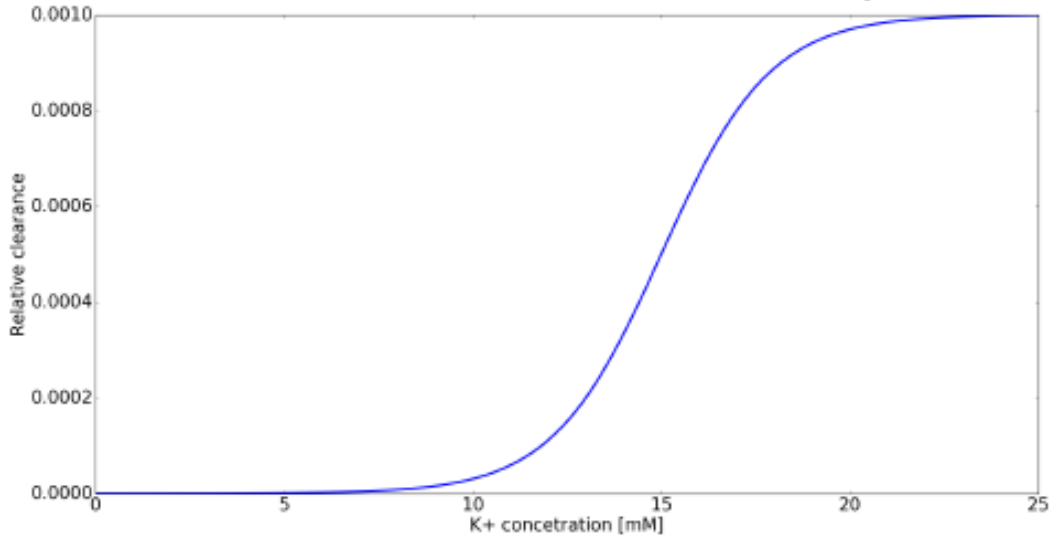
Methods – Extracellular potassium dynamics

- Diffusion
- Glial buffering

$$\frac{dK_o}{dt} = \text{Cell Spiking and Pump} - \text{Diffusion} - \text{Glia} - \text{Diffusion sup->deep}$$

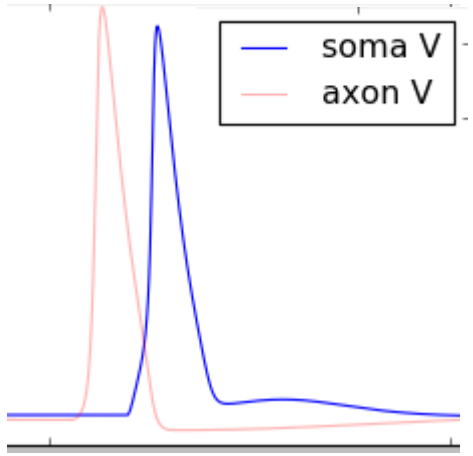


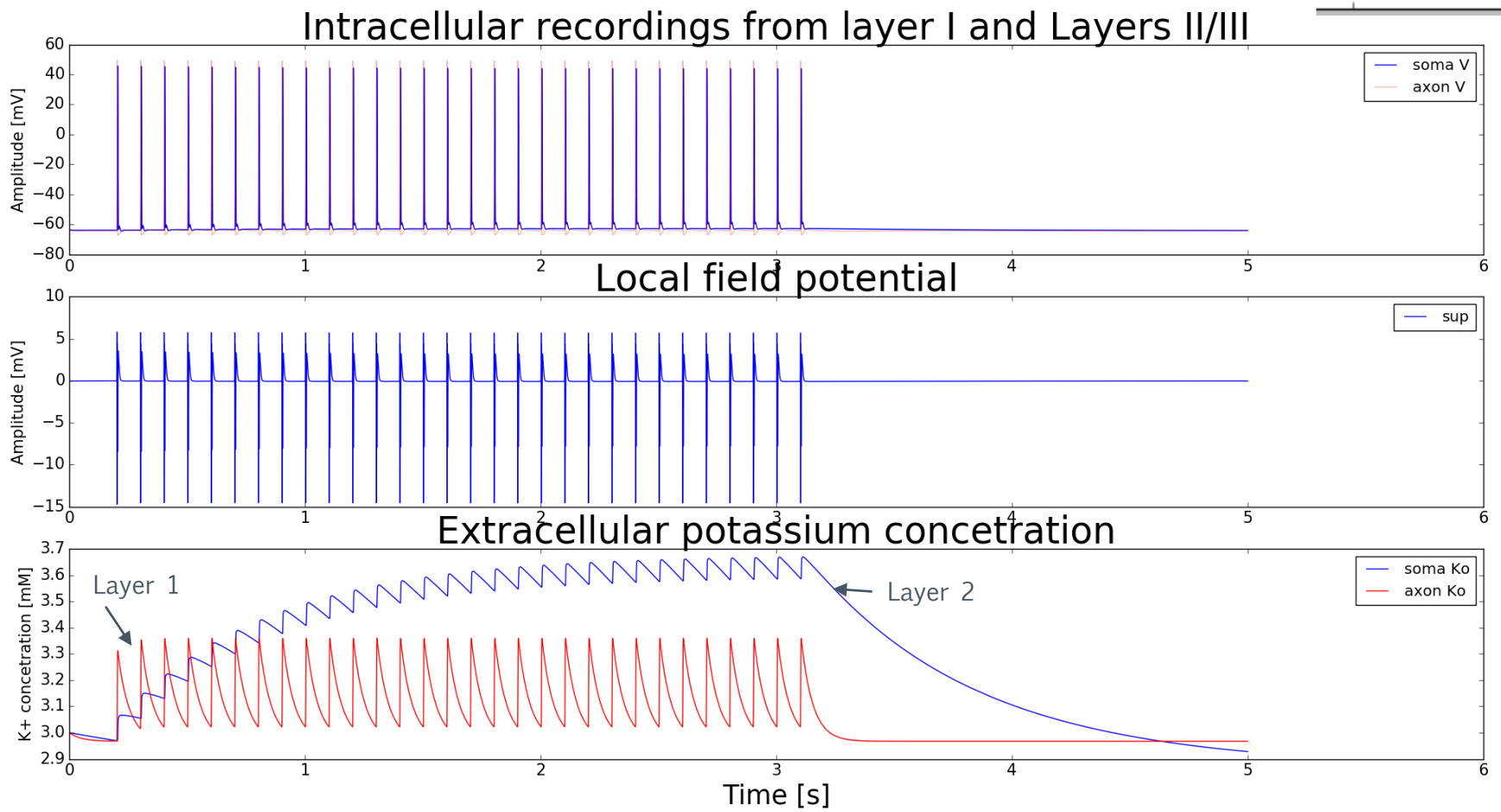
Glial [K+] clearance strength



Simulation results

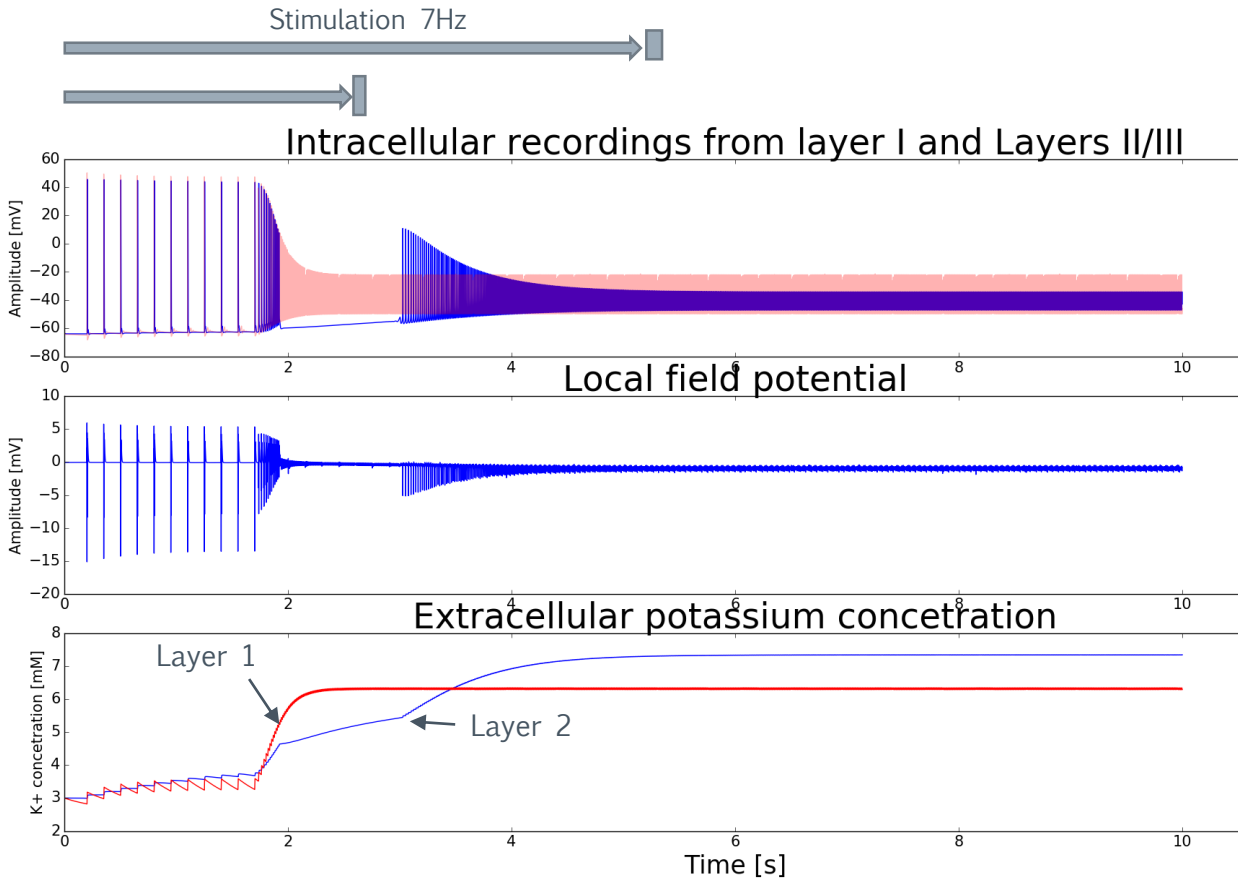
- Conditions: **strong** potassium clearance by glia

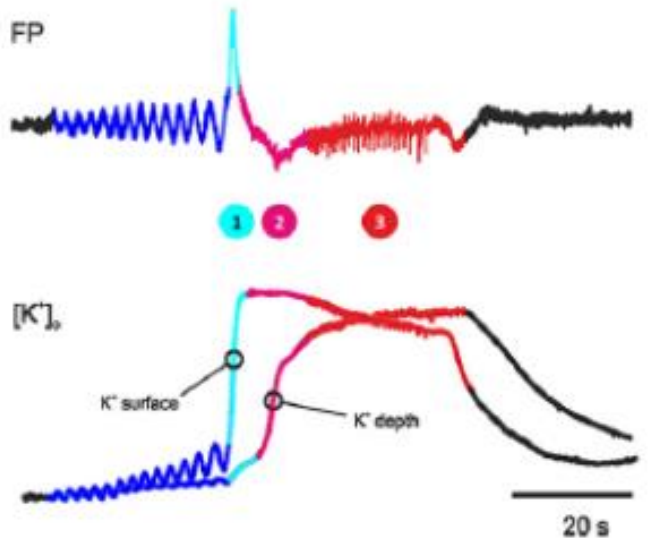




Results

- Conditions: **Low** potassium clearance by glia
- Model predicts silence period

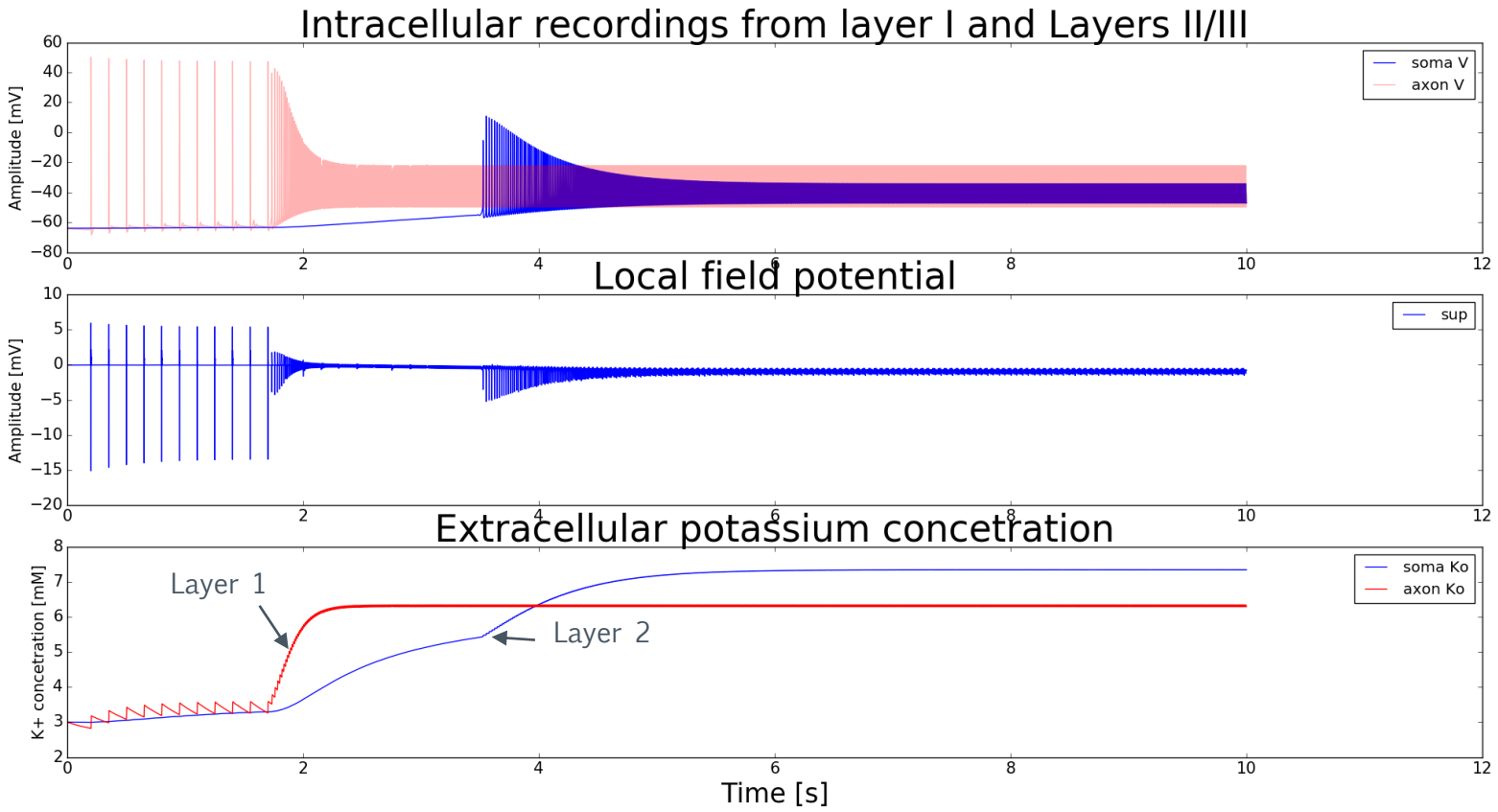




Results

Conditions:

- **Low** potassium clearance by glia
- **Blocked synaptic transmission**



Experimental data comparison

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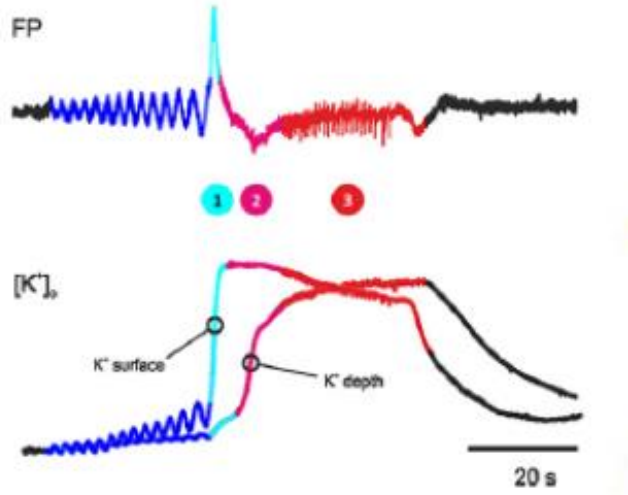
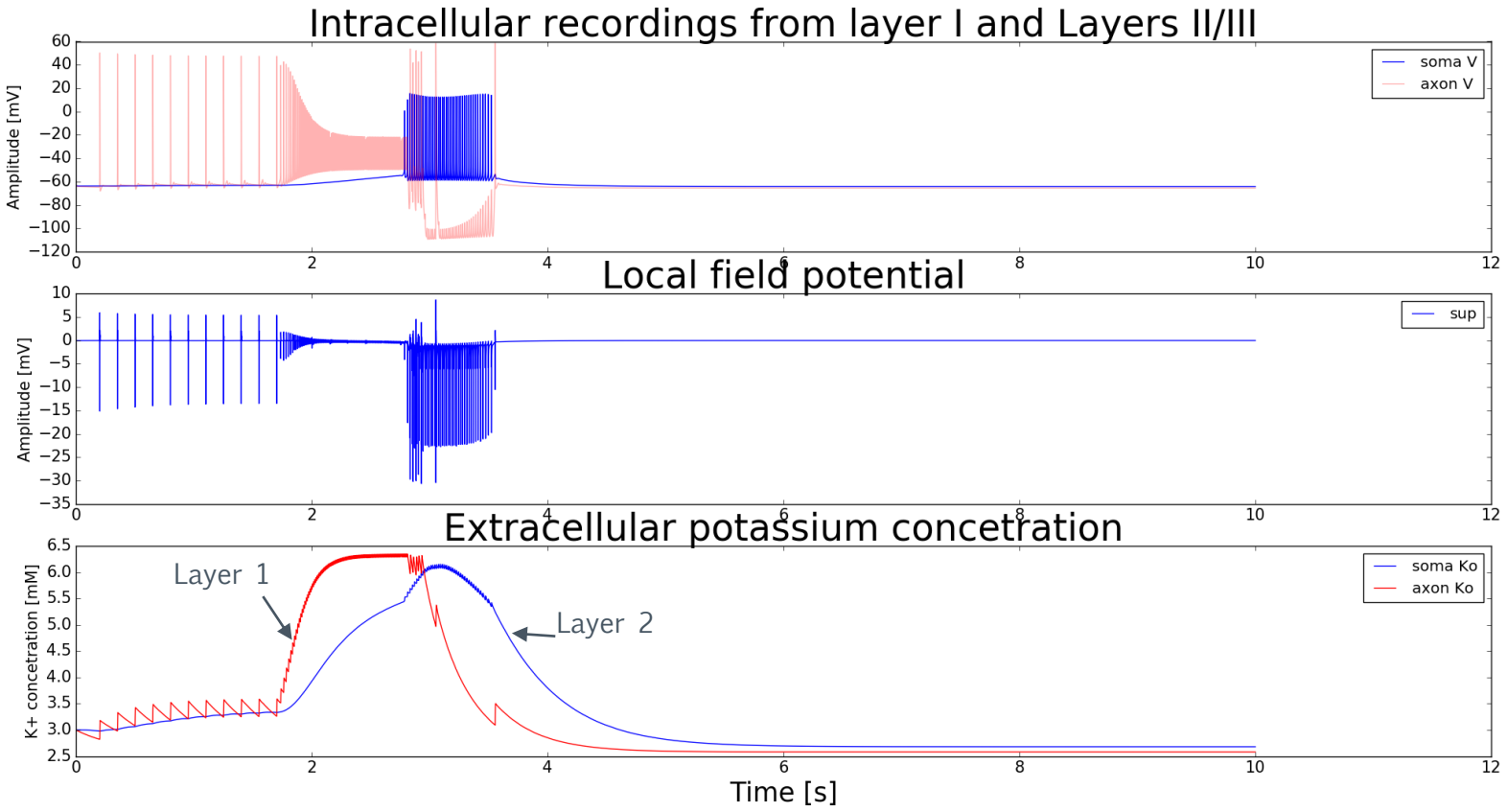


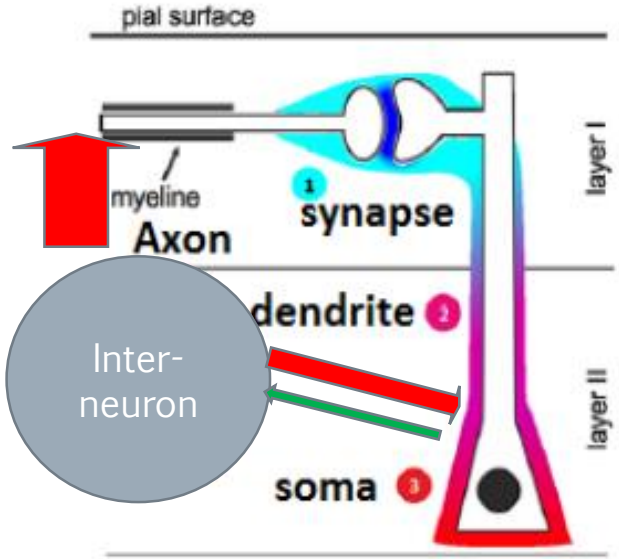
Seizure termination?

- Low potassium clearance by glia
- Blocked synaptic transmission
- Excitatory connection from soma to interneuron
- Strong inhibitory connection from interneuron to layer 1 and Layer 2/3

Inhibitiory connection

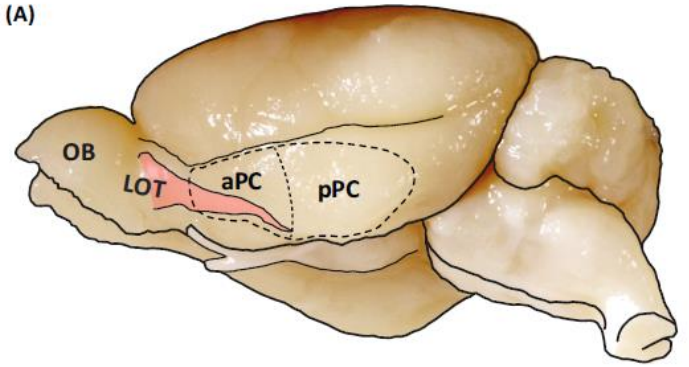
Excitatory connection





SUMMARY

- Very simple model that generated normal activity in high glia buffering conditions
- Model reproduced main stages of the of the novel seizure pattern observed in experimental studies
- Model exhibited stationary behavior in seizure-like state but still did not explain termination phase



ACKNOWLEDGEMENT AND BIBLIOGRAPHY

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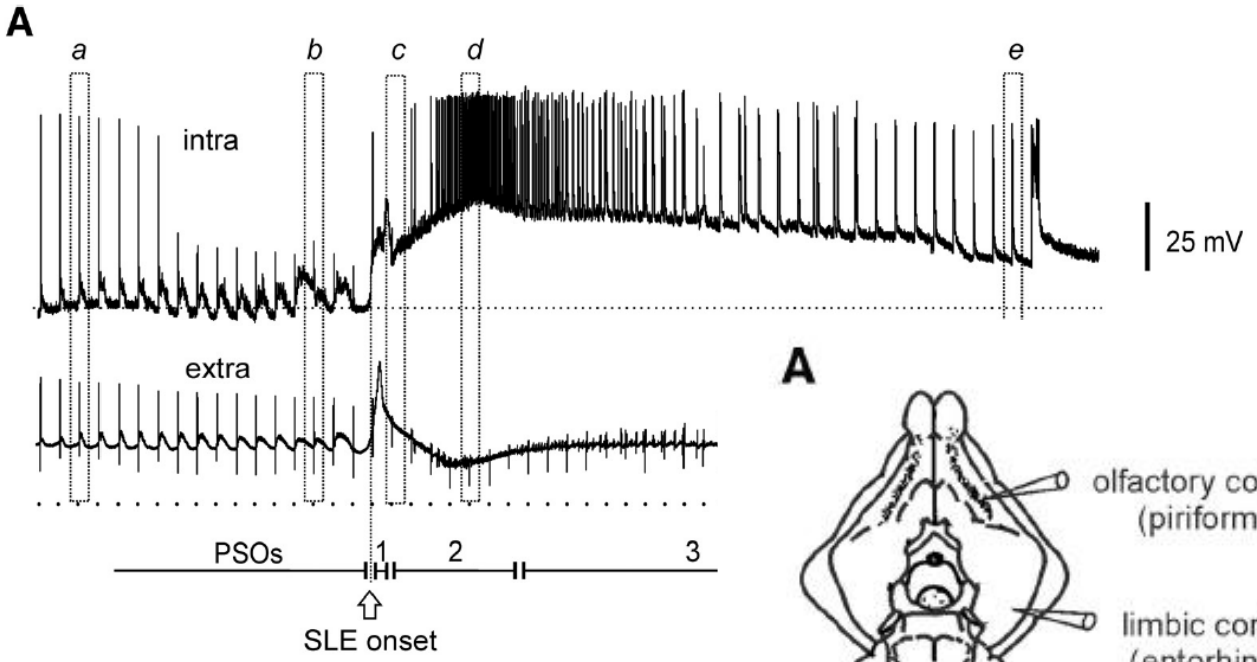

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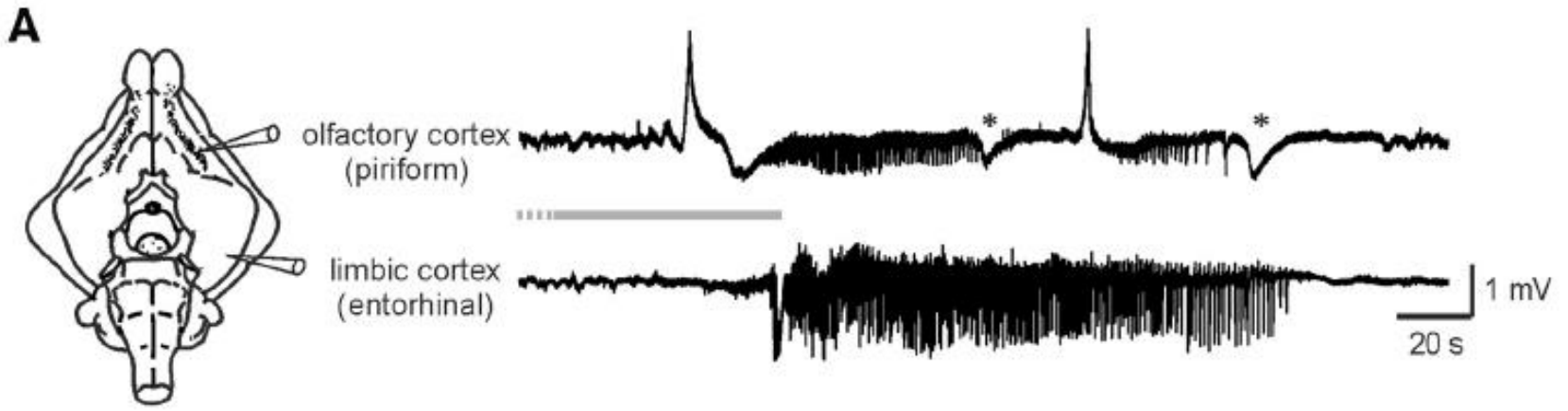

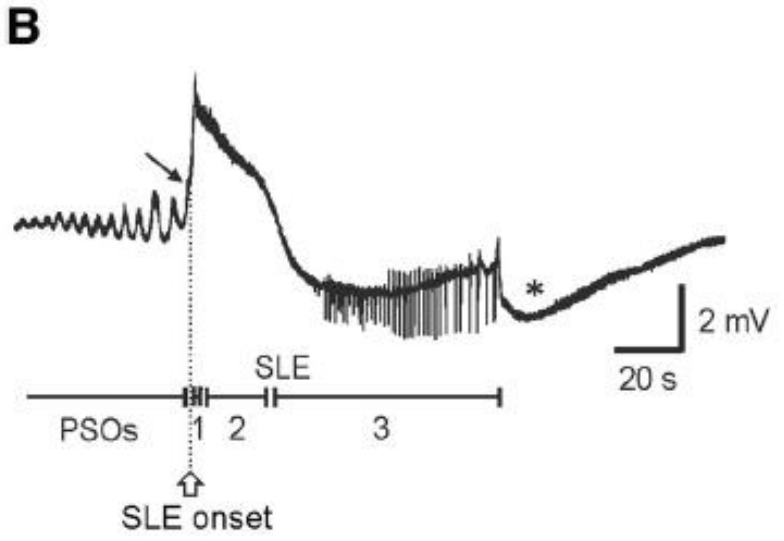

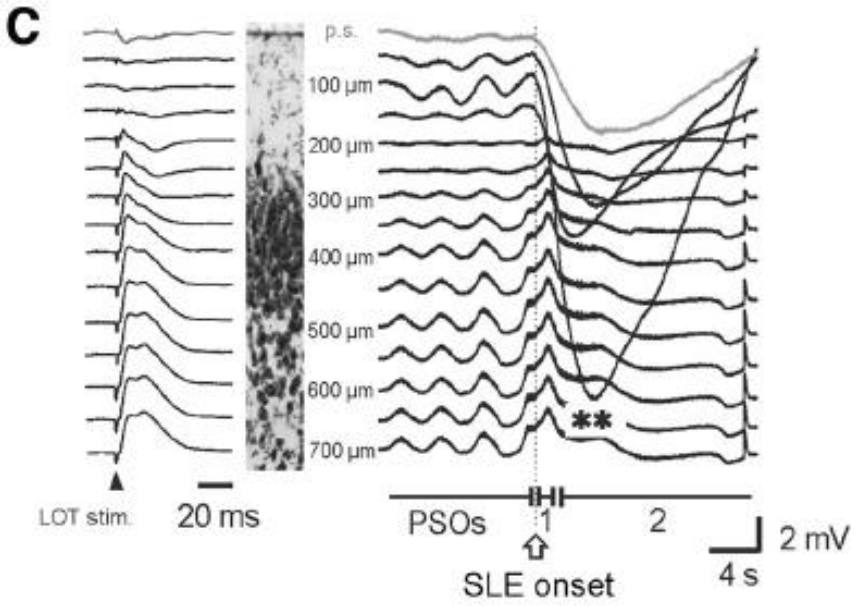

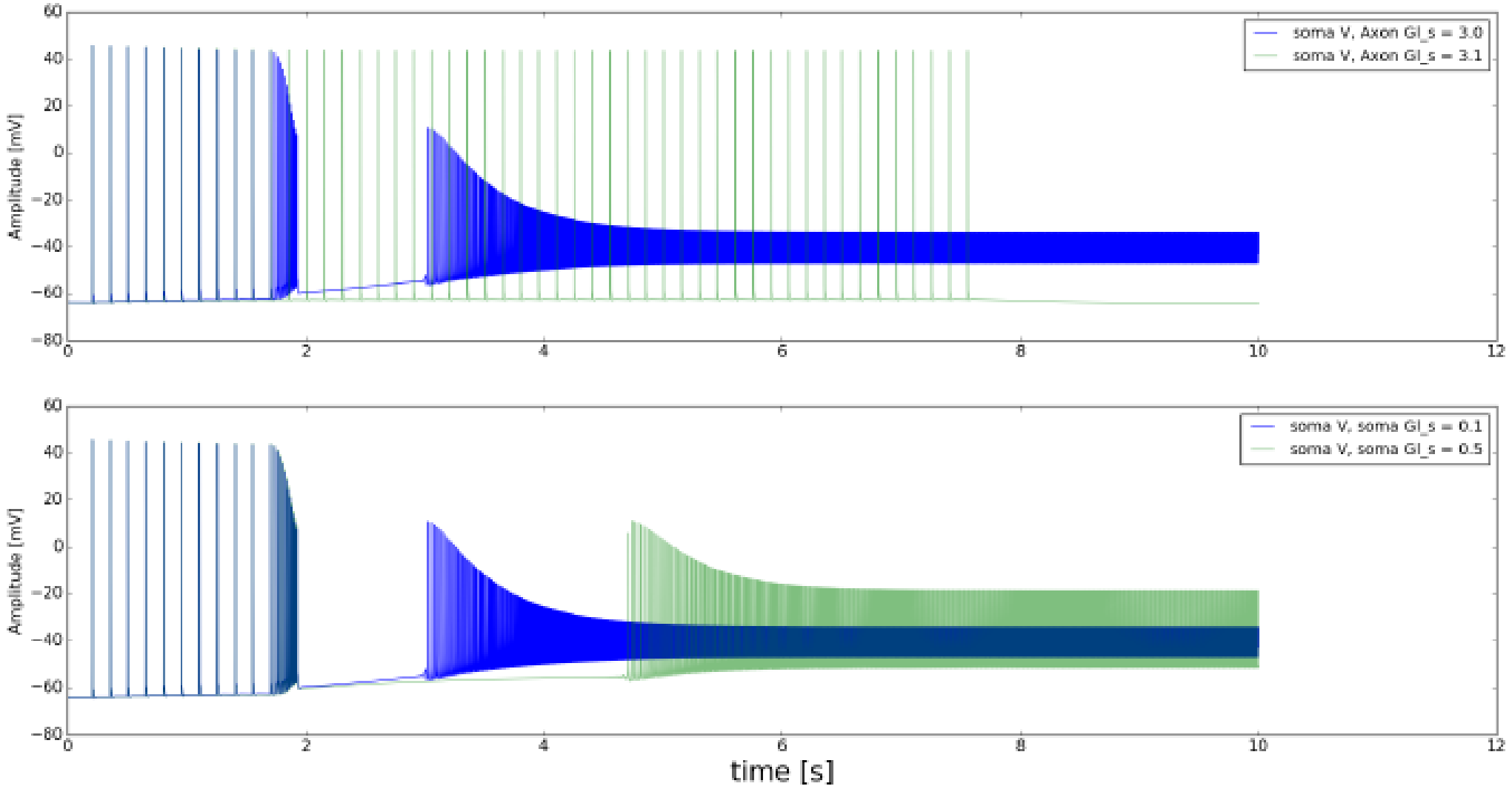
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soma V, Axon Gl_s = 3.1
soma V, soma Gl_s = 0.1
soma V, soma Gl_s = 0.5
Amplitude [mV]
time [s]