Capacitance clamp

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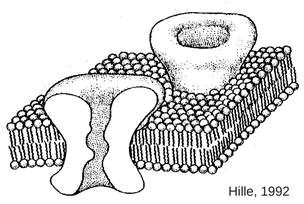
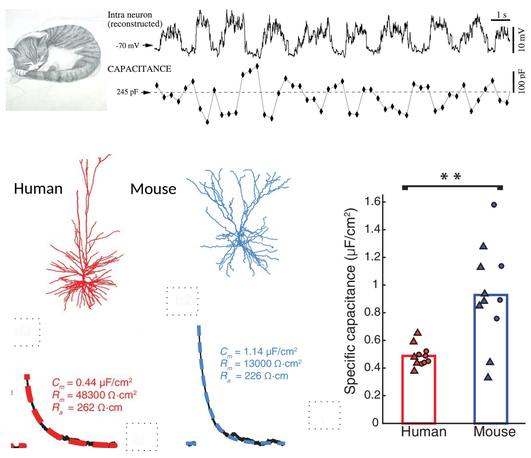
Motivation

Membrane capacitance translates ionic and synaptic membrane currents into voltage responses. Importantly, it sets the membrane time constant and hence fundamentally affects neural signal transmission and processing.


Hille, 1992



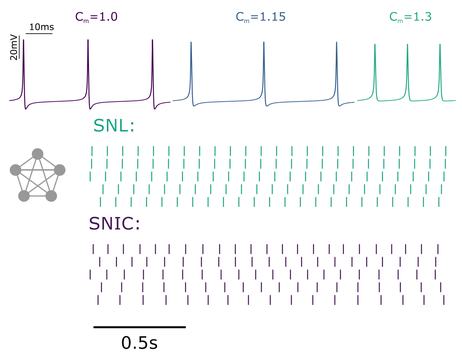
C_m is not a (boring) constant

The membrane capacitance of neurons and glia changes during physiological states like slow wave sleep probably by swelling[1]. An altered membrane capacitance is also observed in pathological conditions like Alzheimers[2].

The specific membrane capacitance is commonly assumed to be a universal constant of 1 µF/cm². However, it seems to vary across species and can change during development[3].

Capacitance as a critical switch

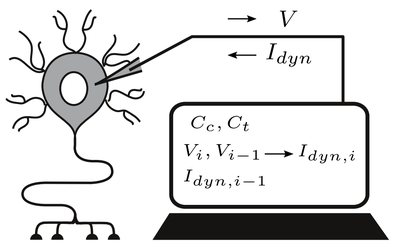
Changes in capacitance alter the relative speed of ionic currents and the membrane potential. Modelling predicts that capacitance changes, like temperature increase or exhaustion of ionic concentration gradients, can induce a switch in action potential generation, which affects the coding ability of single neurons, but also network phenomena like synchronization[4].



Control of capacitace in experiments

Manipulation of capacitance by pharmacological or genetical means is hard to control. Here, we propose the capacitance clamp, which uses the dynamic clamp to precisely and robustly control the capacitance of an excitable cell.

Clamp capacitance via dynamic clamp



Dynamic clamp

Fast feedback loop between recorded voltage and injected current to mimic changes in the electrical properties of a neuron[5].

$$C_m \frac{\mathrm{d}V}{\mathrm{d}t} = I(V) + I_{dyn}$$

Classical conductance clamp

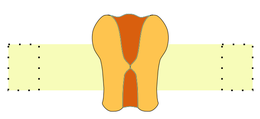
Aim: mimic additional ion channels

$$C_m \frac{\mathrm{d}V}{\mathrm{d}t} = I(V) + g(V - E)$$

$$\Rightarrow I_{dyn} = g(V - E)$$

$$\approx g(V_i - E)$$

Proposal capacitance clamp

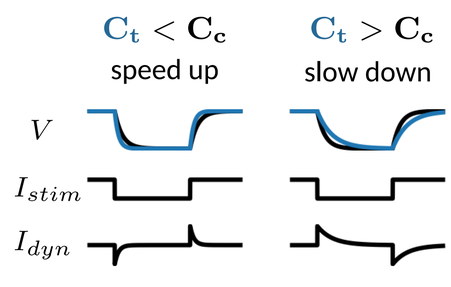


Aim: mimic a modified membrane

$$C_t \frac{\mathrm{d}V}{\mathrm{d}t} = I(V)$$

$$\Rightarrow I_{dyn} = \frac{C_c - C_t}{C_t} I(V)$$

$$\approx \frac{C_c - C_t}{C_t} \left(\frac{V_i - V_{i-1}}{C_c \Delta t} - I_{dyn,i-1} \right)$$



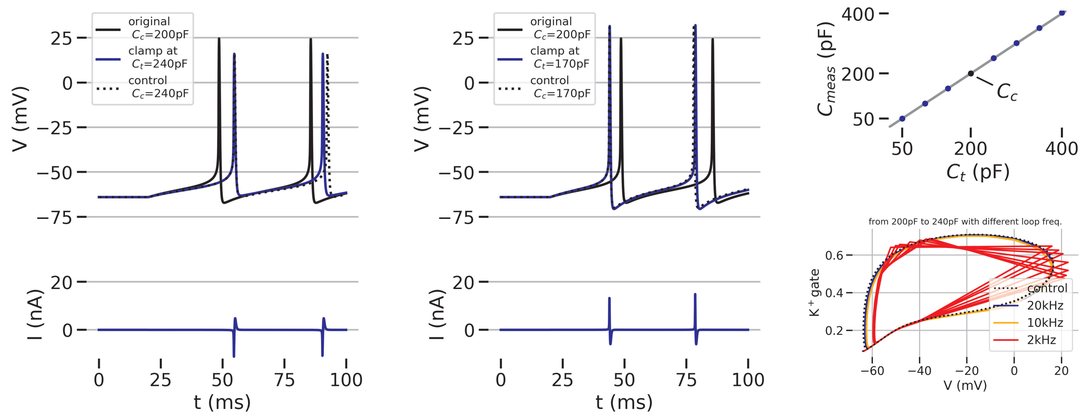
Capacitance clamp allows the experimenter to precisely control the capacitance of an excitable cell.

Only requires to measure the cell capacitance C_c; in particular no needs for a detailed model of the present ionic currents.

Results

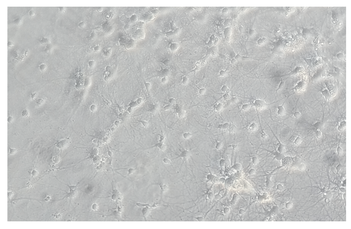
Capacitance clamp in silico

We simulated the capacitance clamp with conductance-based neuron models and compared the electrical activity of a neuron clamped at a target capacitance with a "control" neuron at this capacitance.

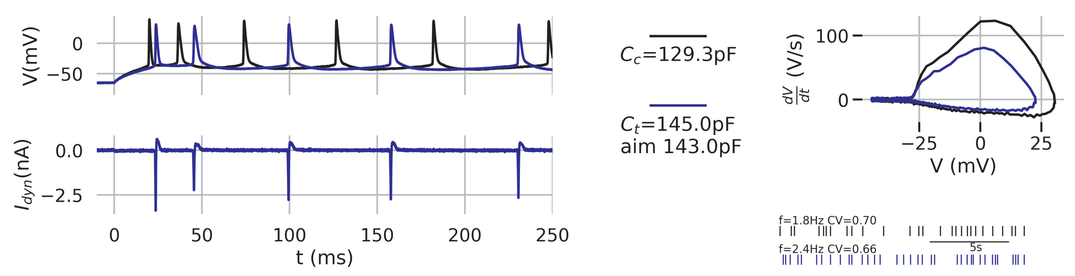


Capacitance clamp in vitro

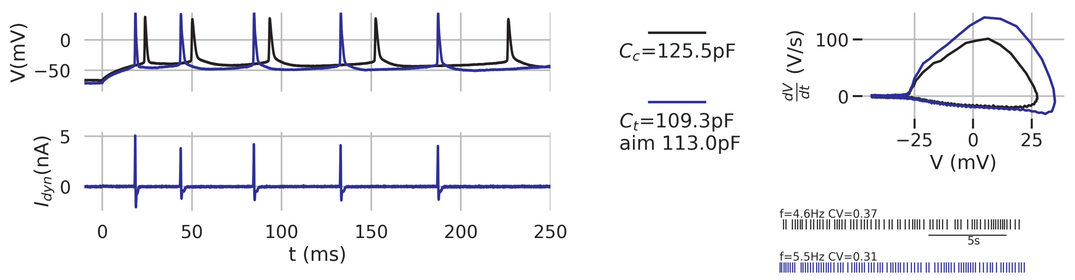
We tested the capacitance clamp in cultured hippocampal neurons. We used step pulses to measure the capacitance and then compared spiking close to the threshold at different capacitances. The software for dynamic clamp was RELACS[6].



Increasing capacitance $C_t > C_c$



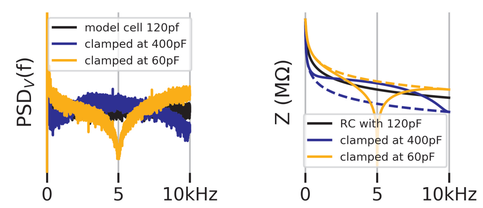
Decreasing capacitance $C_t < C_c$



Outlook

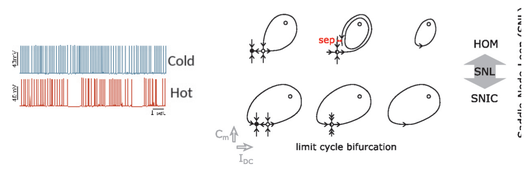
We present a novel tool for electrophysiology: the capacitance clamp provides reliable control over the capacitance of a neuron and thereby opens a new way to study the temporal dynamics of excitable cells.

Robustness



We work on an optimal filter design to make the capacitance clamp less noisy and more robust against imperfect electrode compensation.

Applications



We apply the capacitance clamp to study how close neurons are to a critcal switch in spike generation, the SNL bifurcation, which has widespread implications from coding to epilepsy.

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