Bridging model and experiment in systems neuroscience with Cleo: the Closed-Loop, Electrophysiology, and Optophysiology simulation testbed

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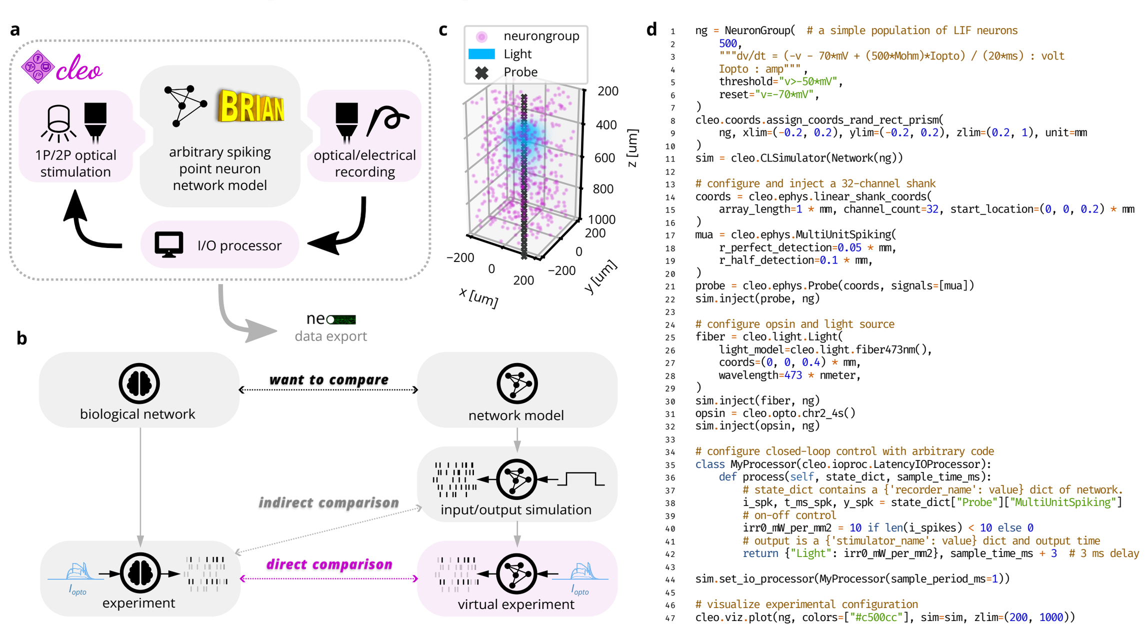
cleo

Simulate complex ephys, opto, and 2P imaging experiments with ease

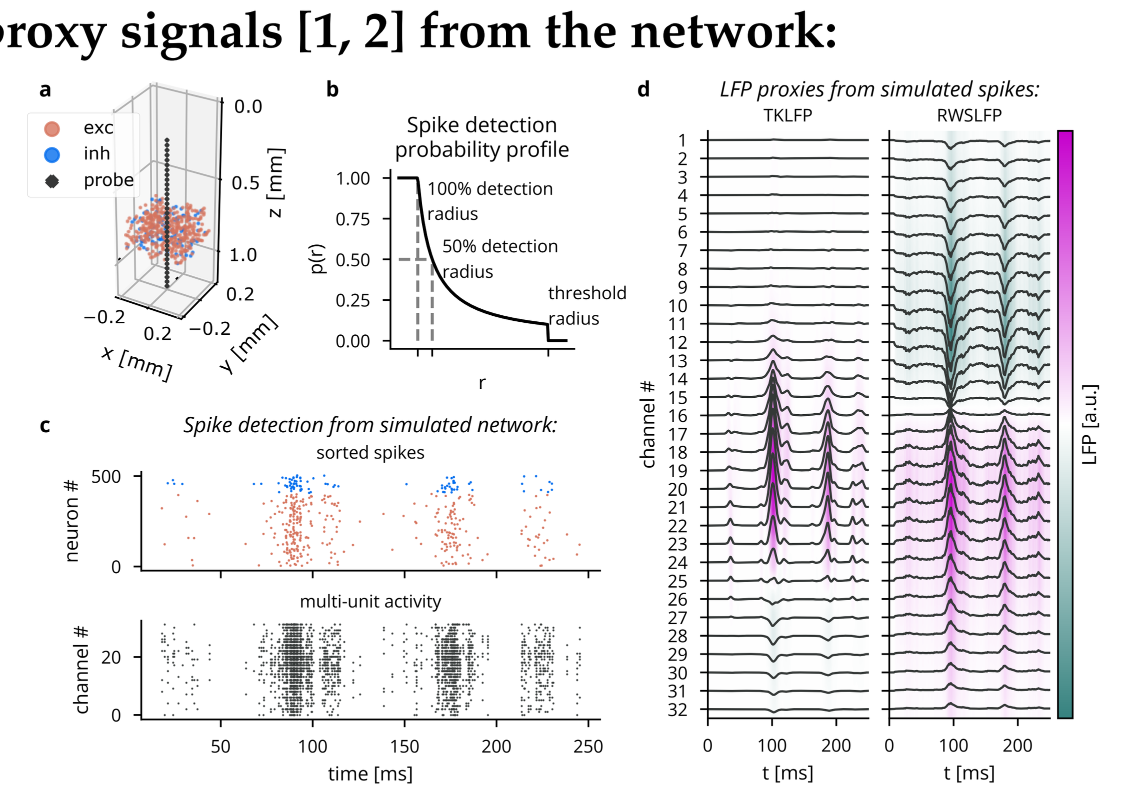
Introduction

Cleo turns a spiking neural network model into a virtual experiment—useful for experiment design, methods engineering, and model evaluation:



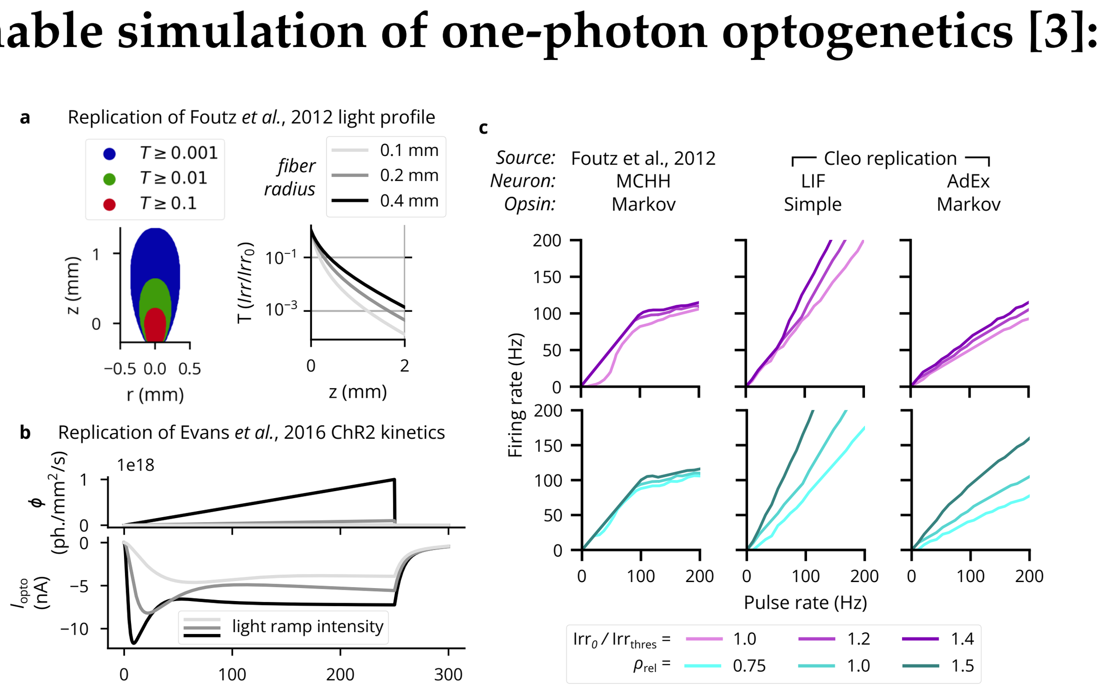
Electrophysiology

Virtual electrode contacts record spiking and LFP proxy signals [1, 2] from the network:

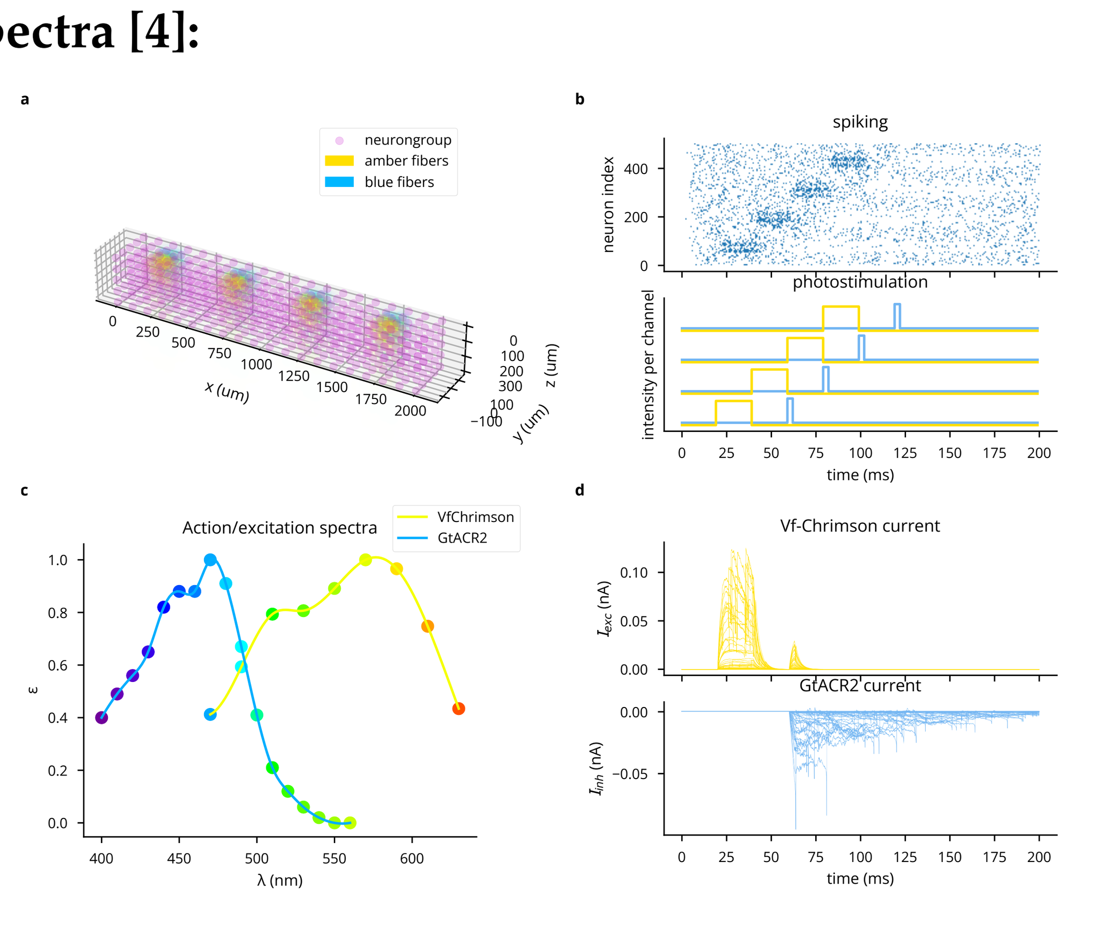


Optogenetics

Light propagation and opsin kinetics models enable simulation of one-photon optogenetics [3]:

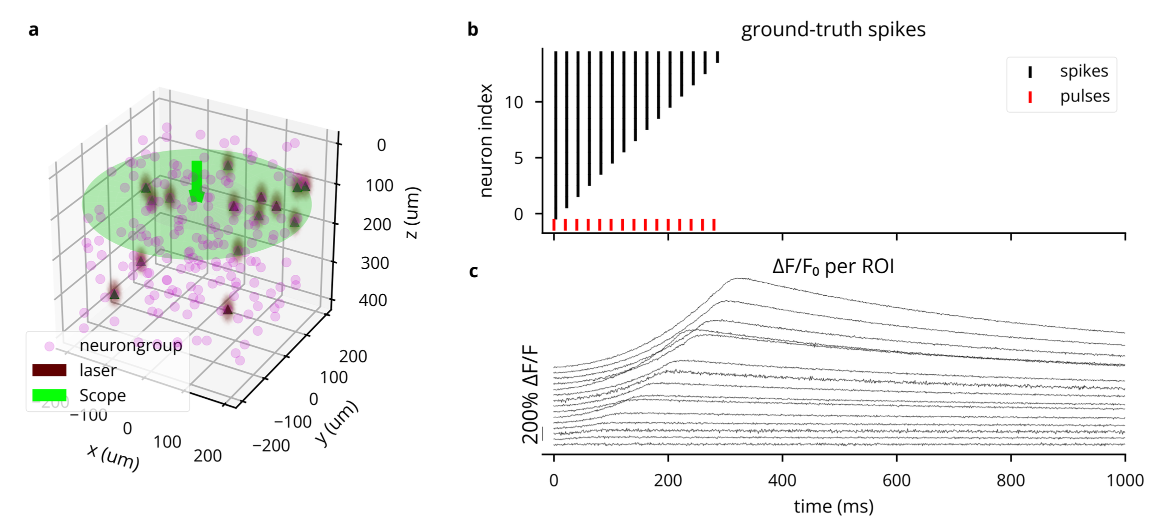


Cleo also simulates multi-site/opsin stimulation, including crosstalk from overlapping action spectra [4]:



Two-photon imaging and photostimulation

A microscope selects neurons in focus for imaging while a Gaussian ellipsoid models off-target 2P laser stimulation.



Signal and noise amplitude depend on the indicator, but are scaled by per-ROI expression level and pixels in focus:

$$\mathrm{SNR}_i = \frac{\Delta F/F_{01\mathrm{AP}}}{\sigma_{\mathrm{noise}}} \frac{\rho_{\mathrm{rel}\,i}}{1/\sqrt{N_i}}.$$

Detailed models of spike-driven calcium and GECI dynamics underlie fluorescence measurements [5]:

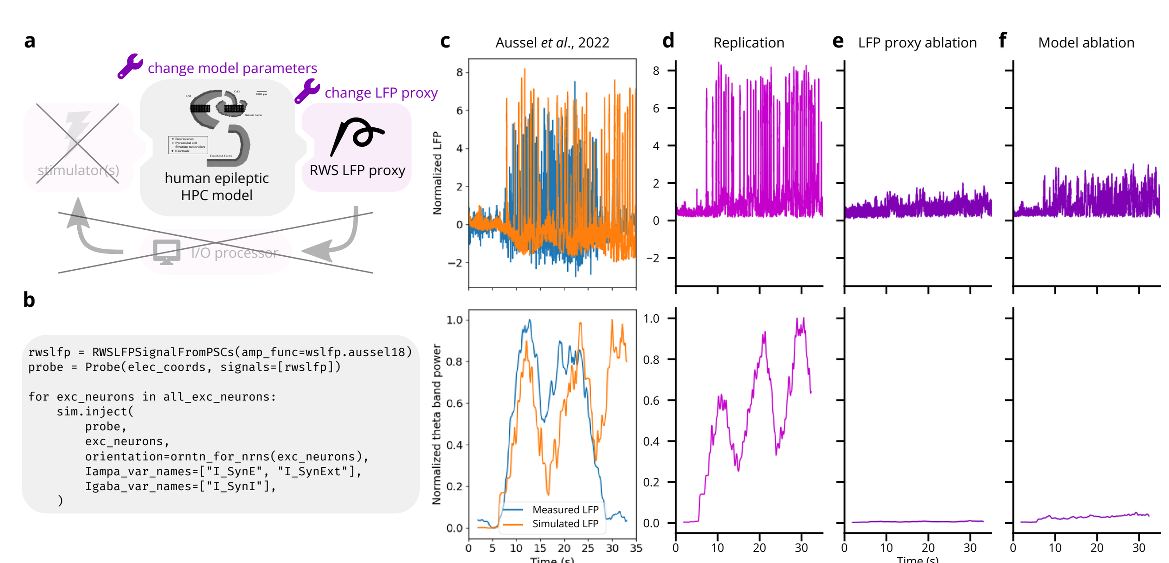
$$\Delta F/F_0 = \Delta F/F_{0\max}\left(\frac{1}{1+(K_d/[\mathrm{CaB}_{\mathrm{active}}])^{n_H}} - \frac{1}{1+\left(K_d/[\mathrm{Ca}^{2+}]_{\mathrm{rest}}\right)^{n_H}}\right)$$

$$\frac{\mathrm{d}\,[\mathrm{Ca}^{2+}]}{\mathrm{d}t} = -\gamma \frac{[\mathrm{Ca}^{2+}] - [\mathrm{Ca}^{2+}]_{\mathrm{rest}}}{1+\kappa_S+\kappa_B}$$

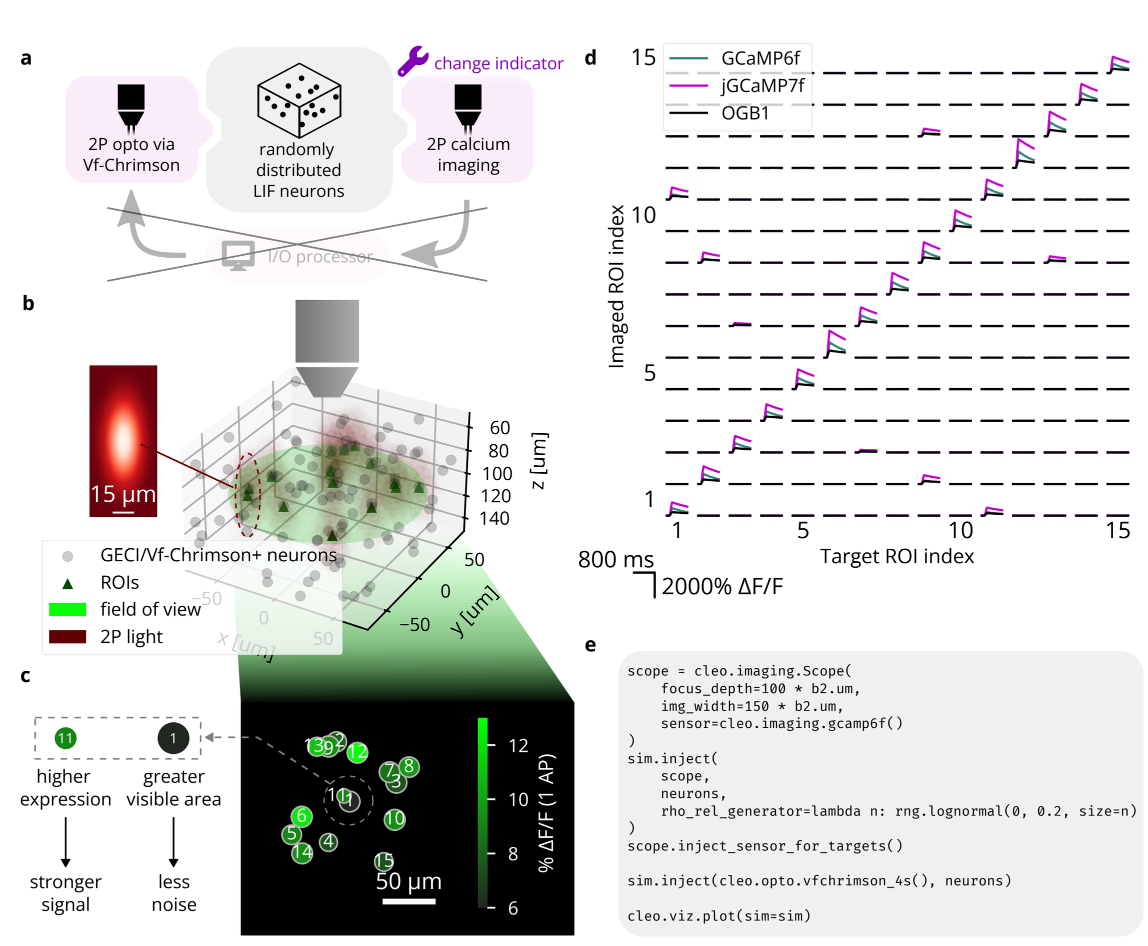
$$\Delta[\mathrm{Ca}^{2+}](t_{\mathrm{spike}}) = \frac{\Delta[\mathrm{Ca}^{2+}]_T}{1+\kappa_S+\kappa_B}.$$

End-to-end validation experiments

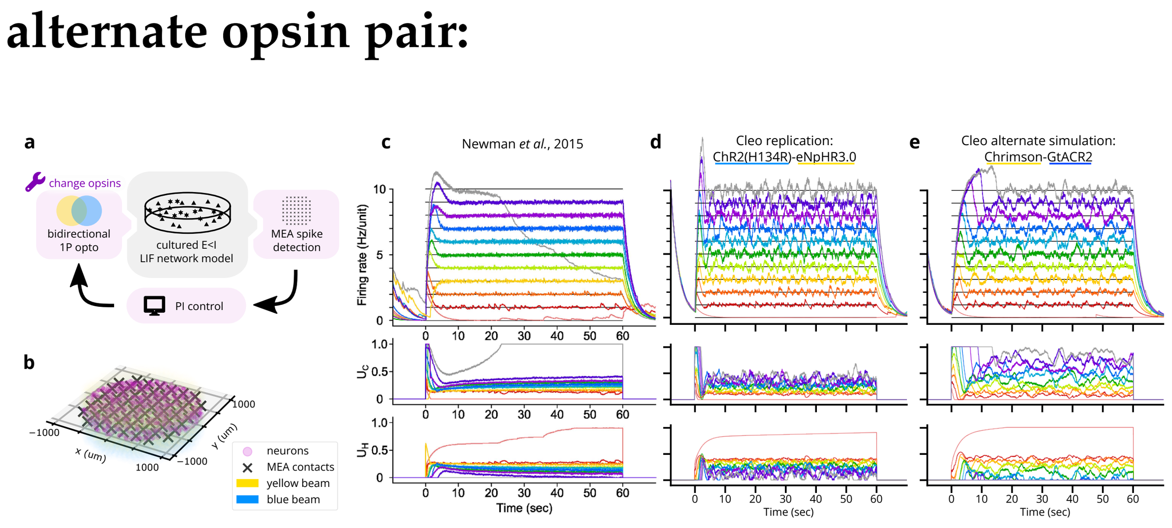
We reproduce LFP recordings of epileptiform activity from HPC model and data from Aussel et al. [6]. Ablations fail to do likewise:



Cleo is able to replicate the all-optical control experiment of Rickgauer et al. [7], using alternate opsin and calcium indicators:

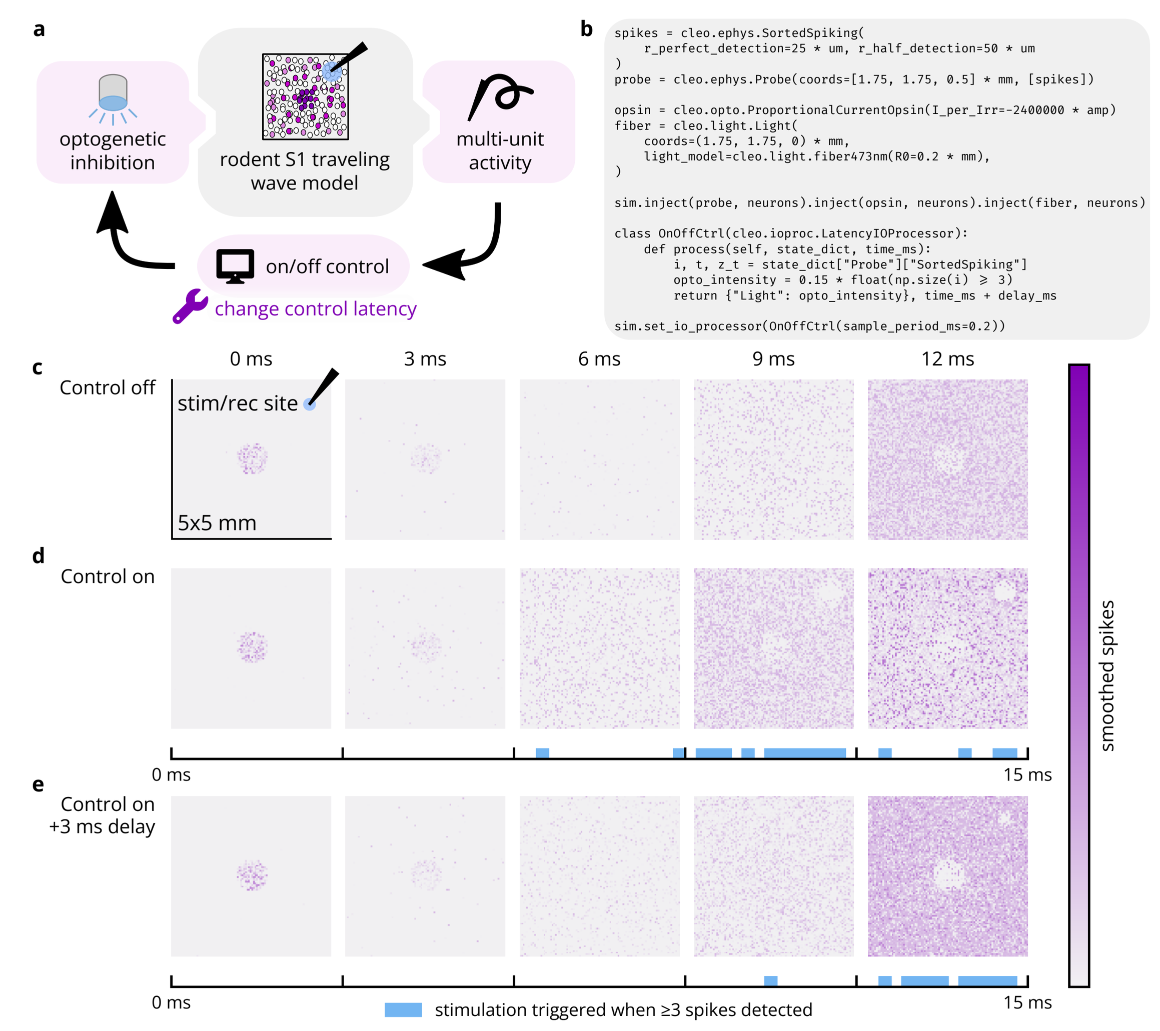


Using a simple E/I network model, we replicate Newman et al. [8]'s bidirectional "optoclamp" of *in vitro* firing rate. We use both the original and an alternate opsin pair:

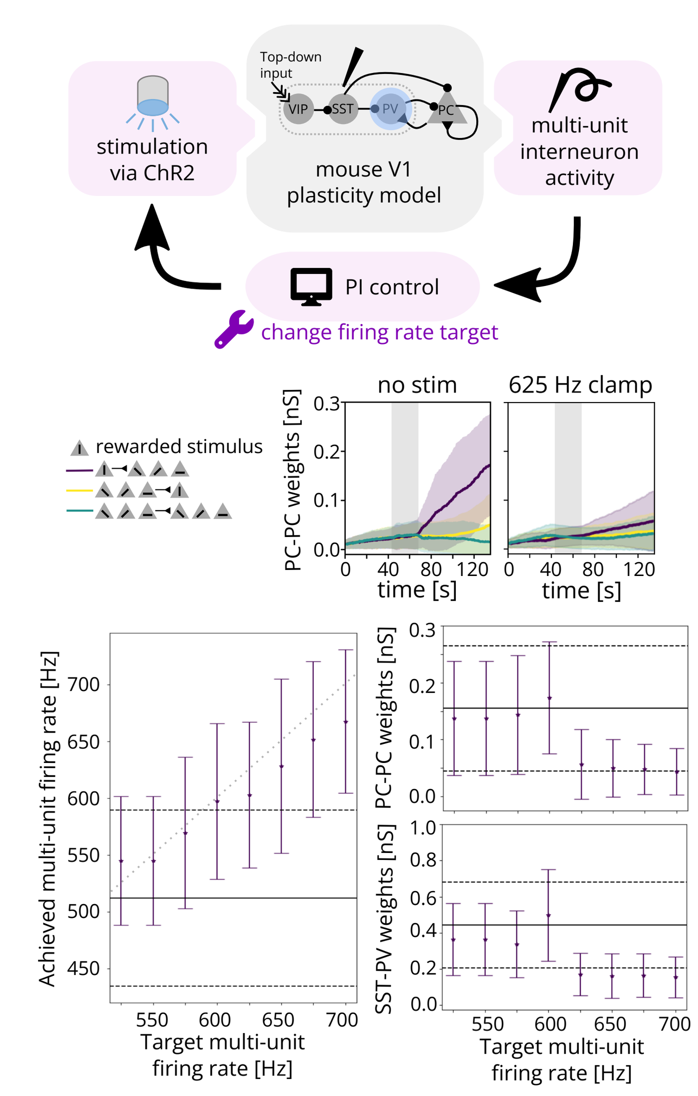


Prototyping novel experiments

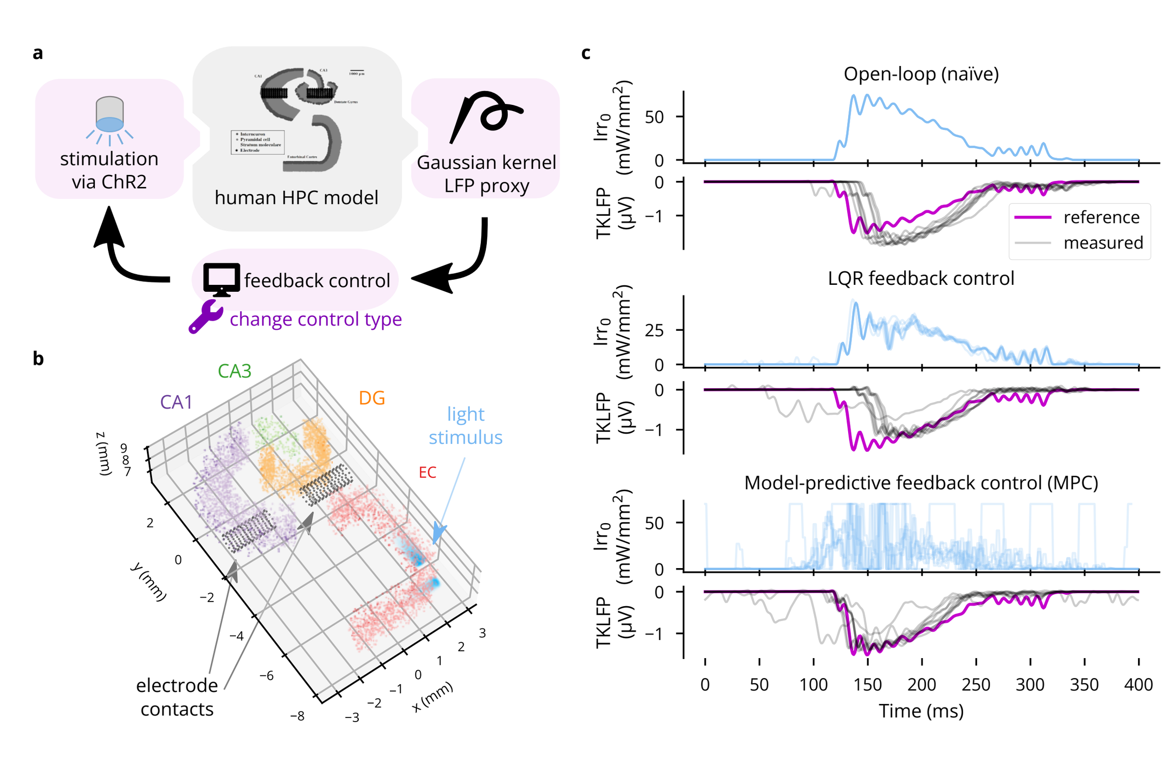
We reject a traveling wave via closed-loop inhibition in a rodent S1 model from Moldakarimov et al. [9] and simulate the effect of increased control latency:



By clamping PV firing rate to a range of targets, we find a threshold for disrupting plasticity in a V1 model by Wilmes and Clopath [10]:

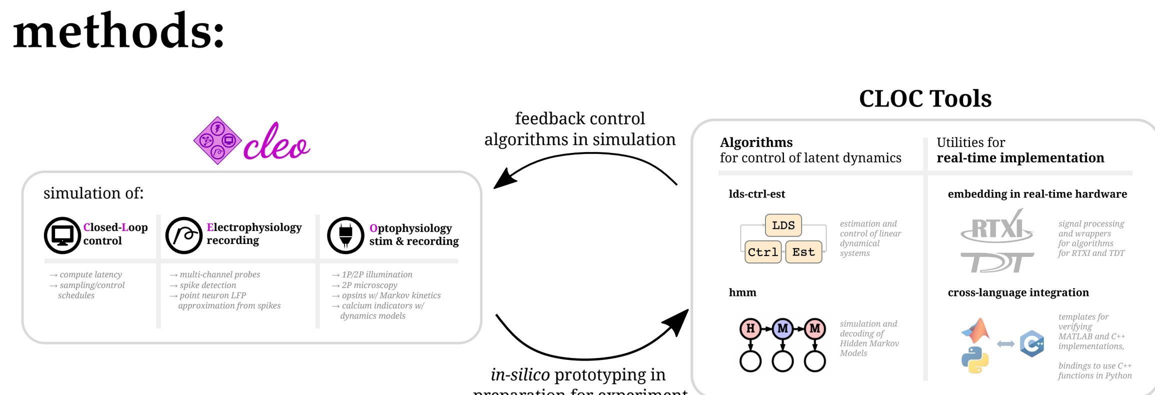


Feedback control can evoke a reference SWR-like oscillation in a HPC model [11] without manual stimulus design or calibration. Cleo makes it easy to try different control strategies:



Related work

Cleo is part of a larger effort developing and applying closed-loop optogenetic control (CLOC) methods:



See `https://cloctools.github.io` and Willats et al. [12, 13, 14], Bolus et al. [15, 16].

Acknowledgments

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