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Functional localization of ion channel densities from calcium fluorescence

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Single cells learn by tuning their synaptic conductances and redistributing their excitable machinery. To reveal its learning rules, one must therefore know how the cell remaps its ion channels in response to physiological stimuli. We exploit the recent ability to dynamically monitor cytosolic dye-buffered calcium, throughout rat hippocampal pyramidal cells in slice, with sub-millisecond temporal resolution and sub-micron spatial resolution [1] in the construction of a functional map of calcium and potassium channel densities.

In the process we pose and solve [2] a number of inverse problems associated with converting dye recordings to current and voltage information through a series of experimental procedures:

(1) Focal uncaging of cytosolic calcium in the presence of dye to determine dye kinetics and intracellular calcium extrusion rates,
(2) Suprathreshold current injection at the soma to infer calcium current from calcium fluorescence using (1),
(3) Recovery of the calcium channel density and voltage information from the calcium current in (2),
(4) Recovery of various potassium channel densities through voltage information in (3) and the selective use of potassium channel blockers.

We demonstrate the validity of this algorithm on synthetic data generated from channel densities and morphologies consistent with previous experimental results [3]. Finally, we explore the robustness of this algorithm to experimental error and noise.

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