Modelling GcaMP responses: From spikes to fluorescence

The use of fluorescent calcium indicators, such as GCaMP6 to monitor neuronal activity is widespread. But methods for converting a single trial fluorescence trace into a single trial spike train are still under development.

The forward mapping between spikes and GCaMP fluorescence is poorly understood. Furthermore, how this mapping is affected by characteristics of the indicator is also unknown. For example, it is known that GCaMP expression accumulates over weeks and months, which introduces a significant confound in any longitudinal studies. Because of this, the upper limit on spike train inference from GCaMP6 is currently unknown.

The aim of this project was to simulate the fluorescence traces produced by a fluorescent calcium indicator in a neuron soma with user defined parameters (binding rate, dissociation rate, and molar concentration) for a given spike train (spike times decided by the user), to benchmark various spike inference algorithms [REFS], and to understand how the quality of the inference depends on GCaMP parameters.

The modelled cell contents consisted of free calcium, fluorescent indicator molecules, endogenous mobile and immobile calcium buffers, and their reactions (including the photo emission process). In order to reproduce the noise in both the system dynamics and experimental photon capturing processes, we simulated the model as a piecewise-deterministic Markov process (PDMP). The probability of a BCa molecule becoming excited and relaxing was determined by the Markov process and it was assumed that the fluoresence was proportional to the number of BCa\* molecules in each time step.

First, we calibrated the model’s fluouresecence traces to reproduce the signal-to-noise ratio of published GCaMP6 data (REF), and asked how varying the noise level affects spike inference. Second, we varied the key model parameters such as GCaMP concentration, forward and backward kinetics, cell size, endongeneous buffer properties, to ask how they affect spike inference.