Modelling GCaMP responses: From spikes to fluorescence

The use of fluorescent calcium indicators, such as GCaMP6 to monitor neuronal activity is widespread. But relationship between GCaMP6 fluorescence and action potential firing is poorly understood. Furthermore, the effects of the indicator characteristics on this fluorescence signal are unknown. For example, it is known that the GCaMP indicator accumulates within neurons over weeks and months, which creates difficulties in comparing activity statistics across timepoints. As a result, whether or not spike train inference is always possible using GCaMP6 fluorescence remains unknown.

The aim of this project was to simulate the fluorescence traces produced by a fluorescent calcium indicator in a neuron soma, given parameters such as binding rate, dissociation rate, and molecular concentration from a specified spike train. The ultimate goal of the simulations were to allow benchmarking of the various spike inference algorithms that thave been developed (Theis et al, 2016), and to understand how indicator characteristics affect the quality of spike train inference.

The modelled cell contents consisted of free calcium, fluorescent indicator molecules, and mobile and immobile endogenous calcium buffers. The indicator molecules which were bound to a calcium molecule could be either excited, i.e. able to release a photon, or relaxed. In order to reproduce the noise in the system dynamics and the photon capturing process, the system was modelled as a piecewise-deterministic Markov process.

The fluorescence traces produced by the simulation were calibrated to reproduce the signal-to-noise ratio of observed in GCaMP6 data (Chen et al, 2013). The noise level was then varied to examine how this affect spike train inference. Then, the parameters of the model, i.e. GCaMP concentration, binding and dissociation rates, and endogenous buffer properties were varied, again to examine the effects on spike inference.