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Irregular firing, quasi-stationary state and spike-time dependent response

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Neurons *in vivo* emit action potentials in a highly irregular manner. One generic feature of the corresponding distribution of inter-spike intervals (ISIs) is the presence of long exponential tails, and neuronal firing is therefore often described as a Poisson process. Such a strong irregularity sharply contrasts with periodic firing elicited by a constant input current, so that the origin of the randomness in the firing has long been a matter of debate. It is nowadays considered that irregular neuronal firing is due to a highly fluctuating drive generated by a balance between excitatory and inhibitory synaptic inputs to the neuron. The statistical properties of the neuronal firing and the underlying membrane potential dynamics in response to such a noisy drive have remained difficult to fully characterize. In this study, we relate the Poisson-like firing to the existence of a quasi-stationary state of the underlying membrane potential dynamics, and explore the implications of the convergence to this state on the response properties of the neuron.

We study analytically the stochastic dynamics of the membrane potential distribution between two successive action potentials, for an integrate-and-fire neuron receiving noisy synaptic inputs. We find that for long enough periods since the firing of the previous action potential, the dynamics converge to a quasi-stationary state, in which the membrane potential distribution becomes independent of time except for a global exponential decay. Once this quasi-stationary distribution has been reached, the firing probability per unit time becomes constant, and the subsequent firing is a Poisson process with a rate that depends on the amplitude of background noise. For *in vivo*-like background noise amplitudes, the convergence time to the quasi-stationary state is significantly shorter than the mean ISI, so that the quasi-stationary state dominates the dynamics.

The fast convergence to the quasi-stationary state has important implications on the response properties of the neuron. We examine the spike-time dependent response (SDR), which we define as the modification in the timing of the next AP due to a given synaptic input, as function of the timing of this input. In absence of noise, the SDR is equivalent to the well studied Phase Response Curve and the response depends strongly on the timing of the input. In contrast, for *in vivo*-like background noise, the timing of the input quickly becomes irrelevant because of the fast convergence to the quasi-stationary state. These theoretical findings are corroborated by in vivo and in vitro experiments.

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