Hidden Markov models for the stimulus-response relationships of multi-state neurons

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Recent experimental results suggest that neural networks are associated with multiple firing regimes, or states, such as tonic and burst modes in thalamus (for review, see Sherman, Trends in Neuroscience, 2001) and UP and DOWN states in cortex (e.g. Anderson et al., Nature Neuroscience, 2000). It is reasonable to speculate that neurons in multi-state networks that are involved in sensory processing might display differential firing behaviors in response to the same stimulus in each of the states of the system, and, indeed, Bezdudnaya et al. (Neuron, 2006) showed that temporal receptive field properties change between tonic and burst states for relay cells in rabbit thalamus. Motivated by these results, we previously presented a general framework for estimating state-dependent neural response properties from paired spike-train and stimulus data assuming that neuronal assemblies transition between several discrete hidden states (Escola and Paninski, Cosyne, 2007). We modified the traditional hidden Markov model (HMM) framework to permit point-process observables such as spike-trains, and, for maximal flexibility in our model, we allowed an external, time-varying stimulus, if present, and the neurons' own spike histories to drive both the spiking behavior in each state and the transitioning behavior between states. We showed that an appropriately modified expectation-maximization algorithm could be constructed to learn the model parameters and gave preliminary results with simulated data. Although HMMs have been used previously to analyze neuronal data (e.g. Abeles et al., Proceedings of the National Academy of Sciences, 1995; Chen et al., Neural Computation, 2009), our model is an extension to the stimulus and history-dependent regime.

In this poster, we review this previous work and then apply our model to a recently published data set of known multi-state neuronal ensembles (Jones et al., Proceedings of the National Academy of Sciences, 2007). We show that inclusion of spike-history information significantly improves the fit of the model compared to the analysis given in Jones et al.. We then show that a simple reformulation of the state-space of the HMM's underlying Markov chain allows us to implement a hybrid half–multi-state/half-histogram model which captures more of the neuronal variability than either a simple HMM or a simple peri-stimulus time histogram (PSTH) model alone. This hybrid model learns firing-rate histograms that are triggered by the state-transition times rather than the trial start-times (i.e. these are state-dependent peri-transition time histograms or PTTHs as opposed to traditional PSTHs), and uncovers interesting and unexpected transition-locked dynamics in the data such as oscillations that are phase-locked to the transition times. We believe that techniques such as these may allow for the identification of data as multi-state that could not have been so identified by earlier methods, particularly data derived from neural systems where it is the network dynamics that are state-dependent rather than simple features such as firing rate, inter-spike interval distribution, or resting membrane potential.