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State-dependence of sensory-evoked responses in neocortex

Carina Curto*[1], Shuzo Sakata[1], Vladimir Itskov[2] and Kenneth D Harris[1]

Address: [1]CMBN, Rutgers University, Newark, NJ, USA and [2]CTN, Columbia University, New York, NY, USA

Email: Carina Curto* - ccurto@rutgers.edu

* Corresponding author

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The neocortex typically operates in one of two states. The activated (desynchronized) state, typical of alert wakefulness and REM sleep, is characterized by a high-frequency, low amplitude local field potential (LFP). The inactivated (synchronized) state exhibits high low-frequency power, and spontaneous transitions between UP states of widespread depolarization and spiking, and DOWN states of generalized silence.

Cortical responses to sensory stimuli exhibit enormous trial-to-trial variability, much of which is state-dependent. This presents a problem for averaging in order to find the "typical" response. One solution is to classify trials (repeated presentations of the same stimulus) into categories depending on the cortical state at the time of the stimulus (activated vs. inactivated, UP vs. DOWN, etc.). In this work, we are more interested in understanding how the intrinsic dynamics associated to different states controls population activity.

We investigated the state-dependence of sensory-evoked responses using a dynamical systems approach. Cortical LFPs and population spike trains were recorded from the auditory cortex of urethane-anesthetized rats using multisite silicon microelectrodes. 5 ms noise click stimuli were presented, and intervals of silence were used to investigate spontaneous activity. Activated states were induced by electrical stimulation of the pendunculo-pontine tegmental nucleus (PPT).

We quantified the strength of "initial" and "persistent" network responses using multiple unit activity (MUA). In the activated state, initial responses were more or less consistent, whereas persistent network activity merely reflected a return to baseline. In contrast, the inactivated state exhibited greater variability in initial responses, and persistent activity that often reflected transitions between UP and DOWN states. We found that a "past activity" variable, which summarizes recent network activity, is highly correlated to persistent network activity after a stimulus presentation. In the activated state, the correlation was strongly positive, whereas in the inactivated state, the correlation was strongly negative.

By viewing the MUA as the output of a dynamical system driven by external sensory stimuli, we constructed a simple nonlinear model that captures the essential dynamic differences between the activated and inactivated states, and explains much of the trial-to-trial variability of sensory-evoked responses. By fitting the model to data, we were able to determine the phase diagram associated to each kind of activity, and the bifurcation that transitions from activated to inactivated state. Furthermore, using the model we made predictions for initial and persistent responses that were better than those using past activity alone.

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