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## Inclusion of noise in iterated firing time maps based on the PRC Fred H Sieling\*1, Carmen C Canavier<sup>2</sup> and Astrid A Prinz<sup>1,3</sup>

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Methods using the phase response curves (PRCs) of component neurons to predict network activity suffer from biological variability intrinsic to the studied neural oscillators, often described as noise. To make analytical predictions, researchers minimize this noise either by averaging the measured PRC or by controlling the period of oscillation. Here, we present an alternate method that incorporates measured noise into PRCs. In a hybrid network of two bursting neural oscillators coupled via synaptic excitation ( $t_{\rm syn} \approx 10$  ms), we found that this method could accurately predict phase locking in the presence of variability in the intrinsic period of 10%.

We modeled our hybrid networks using the experimentally obtained PRCs of component neurons as well as their noise envelopes. We represented the first and second order PRCs (F1 and F2)

$$F1 = PRC^{fit}(\psi) + X \cdot \sigma(\psi), \quad F2 = PRC^{fit}(\psi - 1) + X \cdot \sigma(\psi - 1)$$

where  $\sigma$  was the standard deviation of the experimental PRC as a function of stimulus phase  $\psi$  on the interval (0,1), X was a normally distributed random variable with mean 0 and standard deviation 1, and PRCfit indicates a polynomial fit of the experimental PRC. PRCs are defined as in [1]. For each component neuron j, interburst intervals (IBI) were calculated iteratively according to a modified Winfree model [2]

$$IBI[n]_{j} = P_{0,j} \cdot \left[ 1 + \sum_{k=1}^{k} F1_{j}(\phi_{j,k}[n]) + \sum_{k=1}^{l} F2_{j}(\phi_{j,l}[n-1]) \right]$$

where  $P_0$  is the intrinsic period,  $f_{j,\ k}$  [n] is the phase at which neuron j receives the  $k^{th}$  input in the current cycle, and  $f_{j,\ l}$  [n-1] is the phase at which the  $l^{th}$  input was received by neuron j in the previous cycle. We defined time of input as the start of a burst in the presynaptic neuron. To simulate a reduction in the overall amount of noise in the system, we scaled the noise envelope by a factor less than 1. The inclusion of noise in the PRC-based iterative map is similar to those of [3]; the major difference is the use of F2 in addition to F1 in our method.

We compared experimental observations to predictions made using a noiseless model of pulsatile coupling [4] and to the predictions of our iterated map. Out of 86 networks tested [5], the noiseless model was incorrect 16 times and the iterative map was able to make the correct prediction for 12 of those networks. Further, the success of the iterative map method was predictable by inspection of the PRCs and noise envelopes.

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