How phase resetting curves influence excitation-inhibition-based synchronization

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The interplay between excitation (E) and inhibition (I) is a prominent mechanism of rhythmogenesis in neuronal networks [1]. Theoretical studies have shown that such E-I based rhythms —often referred to as Pyramidal-Interneuron Gamma (PING) oscillations— naturally emerge from reciprocal interactions between populations of excitatory and inhibitory neurons, when inhibition is delayed (or slower) relative to excitation [2]. In addition, recent theoretical results demonstrate that such PING rhythms can be thoroughly analyzed using a simple extension of the Kuramoto model of coupled oscillators [3].

Previous theoretical work has been made under the assumption that inhibitory cells have Type 1 *phase response curve* (PRC), that is, cells always advance their *phase* in response to excitatory pulses, see e.g. [1]. However, experimental studies show that inhibitory neurons often delay their phase in response to excitatory pulses as well, typically when the stimulus comes at the beginning of their cycle [4]. Given that PRC type critically influences synchronization, the features of PING oscillations may be altered in the presence of inhibitory neurons with PRC of Type 2.

Here we theoretically investigate the effects of the PRC-Type in the synchronization of an excitatory and an inhibitory neuron. Neurons are modeled using a variant of the Kuramoto model originally obtained in [5]. Though the Kuramoto model is ideally suited to theoretically investigate synchronization, thus far it has not been applied to investigate PING-mediated synchronization between oscillators with different PRC-Type. The Kuramoto model describing the evolution of the phases of a pair of coupled (synaptic strengths: $K_{E,I}$) excitatory and inhibitory neurons is

$$\begin{aligned}\dot{\theta}_E &= \omega_E - K_E \sin\beta_E - K_E \sin(\theta_I - \theta_E - \beta_E),\\ \dot{\theta}_I &= \omega_I + K_I \sin\beta_I + K_I \sin(\theta_E - \theta_I - \beta_I),\end{aligned}$$

where $\omega_{E,I}$ are the natural frequencies of the neurons, and parameters $\beta_{E,I}$ control the shape of the PRC of each neuron. Specifically, for $\beta_{E,I} = \pi/2$ the PRC is of Type 1, while $\beta_{E,I} \neq \pi/2$ corresponds to different types of Type 2 PRCs. The simplicity of the Kuramoto model allows one to write the two-dimensional dynamical equations as a single equation for the phase difference, $\phi = \theta_E - \theta_I$, as

$$\dot{\phi} = \Delta\omega + 2K \sin\bar{\beta}\Big[\cos(\phi + \frac{\Delta\beta}{2}) - \cos\frac{\Delta\beta}{2}\Big],$$

where we assumed symmetric coupling $K = K_E = K_I$, and defined the new parameters $\Delta\omega = \omega_E - \omega_I$, $\bar{\beta} = (\beta_E + \beta_I)/2$, and $\Delta\beta = \beta_E - \beta_I$. The stable fixed points of this equation are created in two Saddle-Node (SN) bifurcations, and they correspond to synchronous solutions. Consistent with biophysical data, we consider that the E neuron is Type 1, $\beta_E = \pi/2$, hereafter. In Fig. 1 we show the $(\Delta\omega, \beta_I)$ phase diagram, where the SN boundaries (thick blue lines) enclose the synchronization region (shaded). Remarkably, when the PRC of the I neuron deviates from $\pi/2$, the E-I network is able to synchronize even when the I neuron is faster than the E neuron —i.e. for $\Delta\omega < 0$. Moreover, if $\beta_I \in (-\pi/2, \pi/2)$, the I neuron can precede the E neuron ($\phi^* < 0$, see red shaded region in Fig. 1).

Our findings demonstrate that E-I based oscillations broadly considered in computational neurosciences can be investigated in the powerful theoretical framework of the Kuramoto model. This allows for a systematic exploration of the effects of biologically realistic Type-2 PRCs in neuronal synchronization. Our preliminary results already indicate that broadly accepted features of EI-based rhythms may be strongly altered if inhibitory neurons have Type-2 PRCs. For example, the oscillation cycle does not always begin with a boost of (fast) excitatory activity, followed by (slow/delayed) inhibition, but this can be reversed when inhibitory neurons have PRCs with $\beta_I \in (-\pi/2, \pi/2)$.

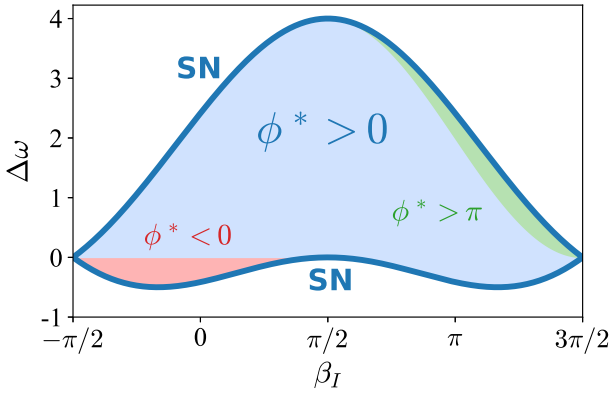

Fig. 1. Phase diagram of the Kuramoto model for a pair symmetrically coupled excitatory and inhibitory neurons. The shaded area corresponds to the synchronization region.

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