6   Circuits of Phase-Coupled Neuronal Oscillators: Basics

Rhythmic output is a hallmark of most motor output - almost by design when we think of locomotion and homeostatic functions like breathing and pumping blood. But neuronal systems also show rhythmic output - a state that on the surface appears very different than the random spiking we discussed for balanced networks - during different brain states. One example occurs during attention, when neurons in cortex have a field potential and modulated rate at the gamma (roughly 40 Hz) band (Figure 1). We will discuss how conductance-based neuronal dynamics can be reduced to all the way down to one dimension per neuron. Then each neuron is represented by a single variable, which will represent the phase in a limit cycles that can be coupled to all other neurons. This approach leads to insights, such as space-time waves as the origin of coordinated limb movement, for networks of neurons with largely rhythmic behavior. It also leads, as will discuss in the second lecture on this topic, to wave patterns in two and three dimensions (Figure 2).

Figure 1: Gamma oscillation. Example traces of the local field potential during spontaneous activity and visually driven activity in primary visual cortex of primate. The power spectra for the two conditions From Jia and Kohn, 2011
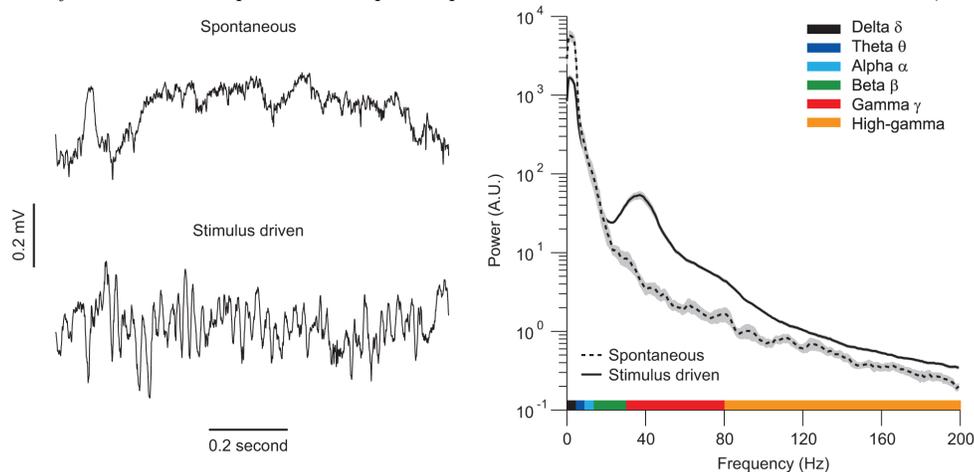
Our theoretical approach follows primarily from the work of the great Japanese physicist Yoshiki Kuramoto. We consider small networks in which identical or nearly identical neurons fire rhythmically and are coupled to each other only weakly. In this sense they effect each others timing but do not effect the shape of each others limit cycle. The interactions depend sinusoidally on the phase difference between each pair of neurons. Thus synapses are no longer excitatory or inhibitory. Rather, they are "synchronizing" versus "desynchronizing", depending on how they change the spike pattern between pair

Figure 2: Electrical rotating wave in tangental slice of layer 4 from mouse that has inhibited blocked with bicuculine. From Huang, Troy, Yang, Ma, Laing, Schiff and Wu, 2004

.
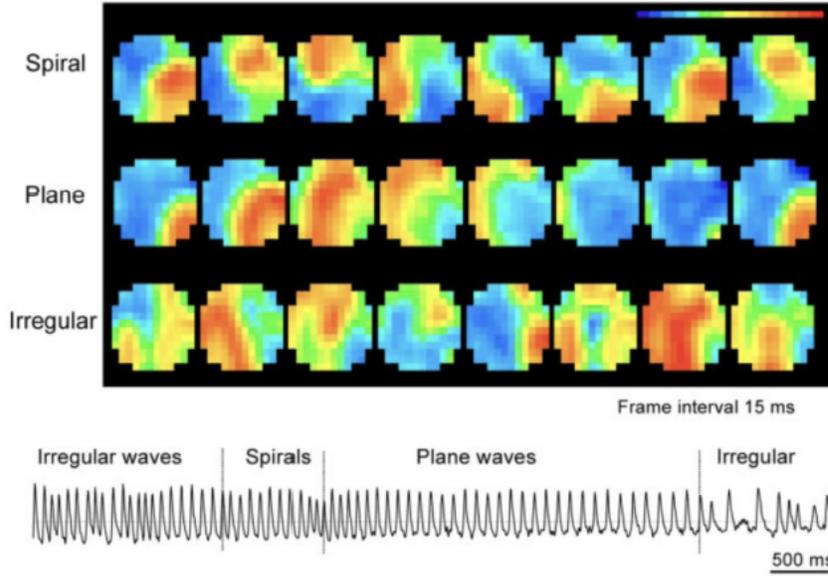
of neuronal oscillators. The effect on synchrony depends on the sign of the synapse, the time-delay of the synapse, and the frequency of the neuronal oscillations.

6.1 Basic formalism

The equation of motion for a general dynamical system

$$\frac{d\vec{X}}{dt} = F(\vec{X}; \mu) \tag{6.1}$$

where the $\vec{X}$ is a vector that contains all the dynamical variables and the μ are parameters. At steady state

$$\frac{d\vec{X}_{ss}}{dt} = F(\vec{X}_{ss}; \mu) \tag{6.2}$$

where a closed orbit satisfies

$$\vec{X}_{ss}(t + T) = \vec{X}_{ss}(t). \tag{6.3}$$

We associate a value of ψ with each point along $\vec{X}_{ss}(t)$. Thus the multidimensional trajectory is reduced to a single variable. It is useful to extend the definition of ψ off of the limit cycle, or contour, to all points within a tube around the limit cycle so that ψ is defined for all $\vec{X}_{ss}$ in the tube. This will allow us to study perturbations to the original limit cycle.

Look on a point just off the limit cycle This point will follow the nearly same trajectory as the closed orbit of the limit cycle and gradually converge back. There will be a phase difference between a point on the limit cycle and one just off the limit cycle (Figure 3). This is equivalent to an initial phase difference among the points. This is the main idea: a

2

physical perturbation can be transformed into a phase shift along the original limit cycle if the perturbed point collapses to or forever parallels the original limit cycle.

Figure 3: Weak interactions between two oscillators lead to a phase shift.

.
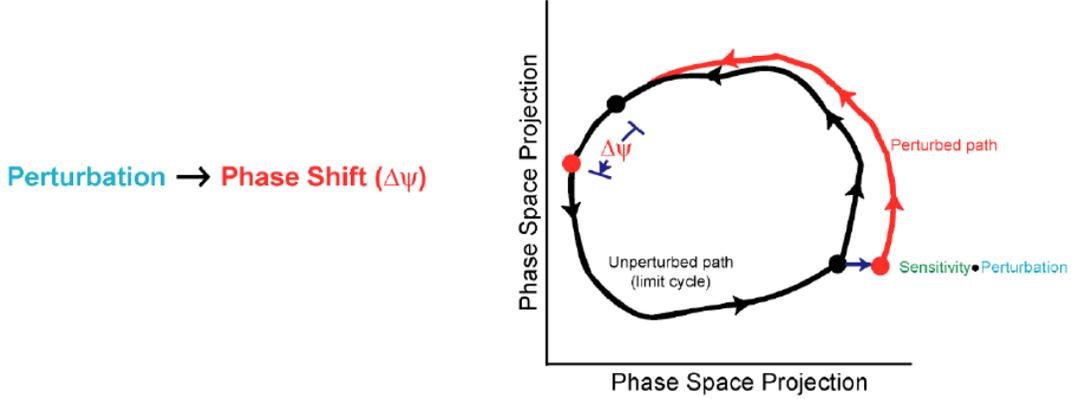
There are a set of points in the tube that will lead to the same phase shift (Figure 4). These define a surface of constant phase shifts, that is denoted $I(\psi)$. For all points $\vec{X}_{ss}$ on $I(\psi)$ we define the phase through

$$\frac{d\psi(\vec{X}_{ss})}{dt} = \omega \tag{6.4}$$

for the unperturbed system. Equal intervals in phase are proportional to equal intervals in time in the original system given the choice of a linear dependence between phase and time; other choices are possible.

So far everything is exact, that is, all calculations are done with respect to the perturbed orbit. The difficulty is that the orbits are not necessarily closed. But if we can make ϵ small enough so that $|\vec{X}(t) - \vec{X}_{ss}(t)| \to 0$ as $t \to \infty$, the perturbation will lead to a closed path. This results in periodic orbits, so that the independent variable can now be taken as the phase, $\psi = \omega t$, rather than time, t. Using the chain rule,

$$\begin{aligned} \frac{d\psi}{dt} &= \sum_i \frac{\partial \psi}{\partial X_{ss,i}} \frac{\partial X_{ss,i}}{\partial t} \\ &= \vec{\nabla}_{\vec{X}_{ss}} \psi \cdot \frac{d\vec{X}_{ss}}{dt} \\ &= \vec{\nabla}_{\vec{X}_{ss}} \psi \cdot \vec{F}(\vec{X}_{ss}). \end{aligned} \tag{6.5}$$

We add a perturbation to the motion by

$$\vec{F}(\vec{X}_{ss}) \to \vec{F}(\vec{X}_{ss}) + \epsilon \vec{P}(\vec{X}_{ss}, \vec{X'}_{ss}) \tag{6.6}$$

where ϵ is small in the sense that the shape of the original trajectory in unchanged as $\epsilon \to 0$ and $\vec{X'}_{ss}$ contains all the variables that define the perturbation, e.g, the trajectory

3

Figure 4: Details of perturbations as a phase shift. Consider a surface, denoted G, normal to and in the neighborhood of C. Let P be a point on G and Q be the point on C, the limit cycle, that passes through the same surface. We posit that as the trajectories evolve, the point P will approach the closed orbit defined by C. There will be a phase difference between P and Q. This is equivalent to an initial phase difference among the points. From Kuramoto 1984
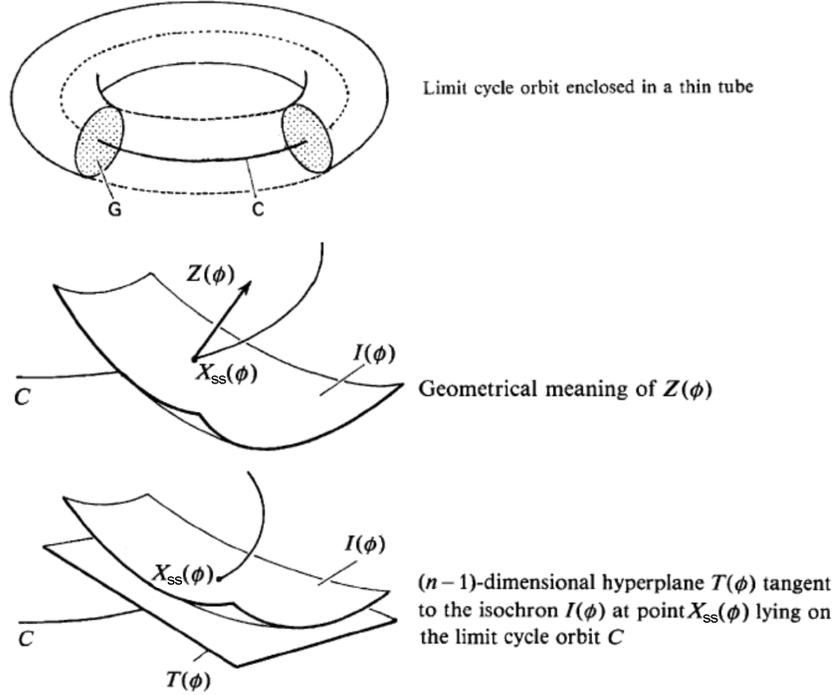
of a neighboring oscillator and the interaction between the two oscillating systems. Then

$$\frac{d\psi}{dt} = \omega + \epsilon \vec{\nabla}_{\vec{X}_{ss}(\psi)} \psi \cdot \vec{P}\left[\vec{X}_{ss}(\psi), \vec{X'}_{ss}(\psi')\right] \quad (6.7)$$

$$\equiv \omega + \epsilon \vec{Z}(\psi) \cdot \vec{P}(\psi, \psi').$$

The term $\vec{Z}(\psi)$ depends only on the limit cycle of the oscillator and defines the sensitivity of the phase to perturbation. It clearly varies along the limit cycle and is sometimes called a "phase-dependent sensitivity". It may be calculated directly by evaluating the trajectory of points inside a tube around the original limit cycle, or more expeditiously using a trick due to Bowtell, in which the perturbed system is rewritten in the form $\frac{d\vec{X}_{ss}}{dt} = \mathbf{A}(t)\vec{X}_{ss}$, with $\mathbf{A}(t) = \mathbf{A}(t+T)$, which can be shown to have only one periodic solution. A cute way to find the periodic solution is to solve the adjoint problem, $\frac{d\vec{Y}}{dt} = \mathbf{A}^T(t)\vec{Y}$, for which all of the solutions decay except for the periodic one. From this one backs out $\vec{Z}(\psi)$. The cool thing in that the oscillator is seen to rotate freely (ω term) with phase-shifts and frequency shifts that are determined solely by the perturbations. The term $\vec{P}(\psi, \psi')$, which can be calculated from the perturbation, allows these perturbations to be interactions with neighbors.

Let's look at the nature of the perturbation term. The idea is that this is small, so that the shift in frequency on one cycle is small. We consider

$$\psi = \delta\psi + \omega t. \quad (6.8)$$

4

Then the relative motion is given by

$$\begin{aligned}\frac{d\delta\psi}{dt} &= \epsilon\vec{Z}(\psi)\cdot\vec{P}(\psi,\psi')\\ &= \epsilon\vec{Z}(\delta\psi+\omega t)\cdot\vec{P}(\delta\psi+\omega t,\delta\psi'+\omega t).\end{aligned} \tag{6.9}$$

This expression may be further simplified. To the extent that the change in ψ is small over one cycle, i.e., $\frac{d\delta\psi}{dt} << \omega$, we can average the perturbation over a full cycle. We write

$$\frac{d\delta\psi}{dt} = \Gamma(\delta\psi,\delta\psi') \tag{6.10}$$

where

$$\Gamma(\delta\psi,\ \delta\psi') = \frac{\epsilon}{2\pi}\int_{-\pi}^{\pi} d\theta\ \vec{Z}(\delta\psi+\theta)\cdot\vec{P}(\delta\psi+\theta,\delta\psi'+\theta). \tag{6.11}$$

The above result can be generalized to the case where the internal parameters, i.e., the $\vec{X}_{ss}$'s are a bit different between oscillators, so that the underlying oscillations are slightly different frequency. We then have

$$\frac{d\delta\psi}{dt} = \Gamma(\delta\psi,\delta\psi') + \delta\omega. \tag{6.12}$$

6.1.1   Relation to measurements on neurons

We return to the general expression

$$\Gamma(\delta\psi,\ \delta\psi') = \frac{\epsilon}{2\pi}\int_{-\pi}^{\pi} d\theta\ \vec{Z}(\delta\psi+\theta)\cdot\vec{P}(\delta\psi+\theta,\delta\psi'+\theta) \tag{6.13}$$

where we identity $\delta\psi$ as the phase shift of the postsynaptic cell and $\delta\psi'$ as the phase shift of the presynaptic cell. The perturbation may be written (Figure 5)

$$\vec{P}(\delta\psi+\theta,\delta\psi'+\theta) = \frac{g_{syn}}{c_m}\vec{S}(\delta\psi'+\theta)\left(V_{syn}^{Nernst}-V(\delta\psi+\theta)\right) \tag{6.14}$$

where $\vec{S}(\delta\psi'+\theta)$ is the presynaptic activation, so

$$\Gamma(\delta\psi,\delta\psi') = \frac{\epsilon}{2\pi}\int_{-\pi}^{\pi} d\theta\ \vec{Z}(\delta\psi+\theta)\left(V_{syn}^{Nernst}-V(\delta\psi+\theta)\right)\cdot\frac{g_{syn}}{c_m}\vec{S}(\delta\psi'+\theta). \tag{6.15}$$

The interaction factors into post- and presynaptic terms, i.e.,

$$\Gamma(\delta\psi,\ \delta\psi') = \frac{\epsilon}{2\pi}\int_{-\pi}^{\pi} d\theta\ \vec{R}(\delta\psi+\theta)\cdot\vec{S}(\delta\psi'+\theta) \tag{6.16}$$

where we collected the postsynaptic response as

$$\vec{R}(\delta\psi+\theta) = \frac{g_{syn}}{c_m}\vec{Z}(\delta\psi+\theta)\left(V_{syn}^{Nernst}-V(\delta\psi+\theta)\right). \tag{6.17}$$

The interaction depends only on the phase difference, i.e.,

$$\begin{aligned}\Gamma(\delta\psi,\ \delta\psi') &= \frac{\epsilon}{2\pi}\int_{-\pi}^{\pi} d\theta\ \vec{R}\left(\theta-(\delta\psi'-\delta\psi)\right)\cdot\vec{S}(\theta)\\ &= \Gamma(\delta\psi'-\delta\psi)\end{aligned} \tag{6.18}$$

The contributions may be found from experiment since the interaction of neuronal oscillators is given by the correlation between the presynaptic spikes and the post-synaptic potentials (Figure 5).

Figure 5: The phase sensitivity function for perturbation in voltage. Data from Reyes and Fetz, 1993. Analysis from Ermentrout and Kleinfeld 2000
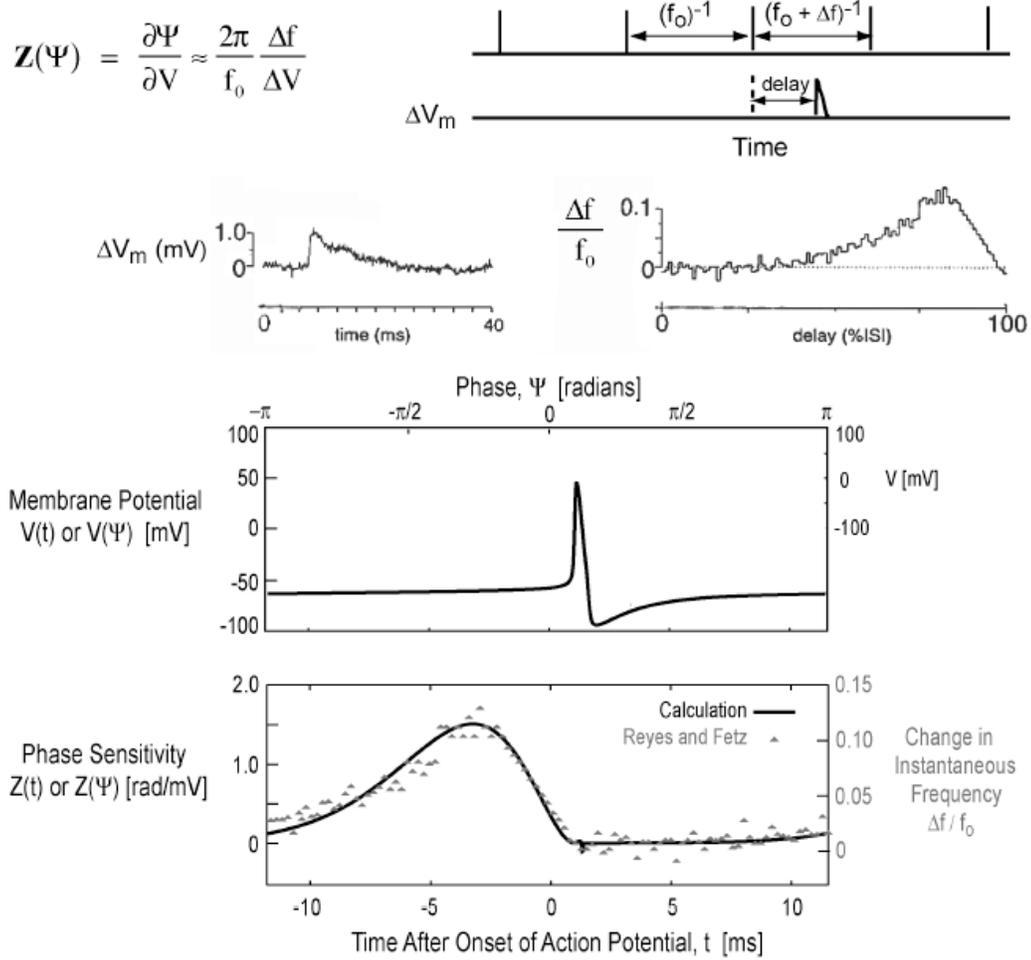
6.2 Stability of phase shifts among two oscillators.

Let's look at a pair of neurons when the interaction is a function of phase difference of the a pair of oscillators (Equation 6.18). The system of two oscillators obeys

$$\frac{d\delta\psi}{dt} = \Gamma(\delta\psi' - \delta\psi) \tag{6.19}$$

and

$$\frac{d\delta\psi'}{dt} = \Gamma(\delta\psi - \delta\psi'). \tag{6.20}$$

We subtract the two equations of motion for the phase to get the difference, i.e.,

$$\begin{aligned}
\frac{d(\delta\psi - \delta\psi')}{dt} &= [\Gamma(\delta\psi' - \delta\psi) - \Gamma(\delta\psi - \delta\psi')] \tag{6.21}\\
&\equiv \tilde{\Gamma}(\delta\psi' - \delta\psi)\\
&\equiv -\tilde{\Gamma}(\delta\psi - \delta\psi').
\end{aligned}$$

6

By way of analysis,

- The term $\tilde{\Gamma}(\delta\psi - \delta\psi')$ is an odd function with a period of 2π and with zeros at $\delta\psi - \delta\psi' = 0, \pm\pi$ and possibly other places.

- The zeros correspond to potential phase locking.

- We can determine the stability of each of these zeros by expanding $\tilde{\Gamma}(\delta\psi - \delta\psi')$ around each zero with a small perturbation to the phase, denoted Δ. That is

$$\frac{d(\delta\psi - \delta\psi')}{dt} = -\left.\frac{d\tilde{\Gamma}(\delta\psi - \delta\psi')}{d(\delta\psi - \delta\psi')}\right|_{\tilde{\Gamma}(\delta\psi - \delta\psi')=0} \Delta \tag{6.22}$$

- The stability depends on the sign of the slope of

$$\left.\frac{d\tilde{\Gamma}(\delta\psi - \delta\psi')}{d(\delta\psi - \delta\psi')}\right|_{\tilde{\Gamma}(\delta\psi - \delta\psi')=0}$$

which corresponds to a "restoring force". We want $\frac{d(\delta\psi - \delta\psi')}{dt}$ to be negative when Δ is positive, and vice versa.

- $\left.\frac{d\tilde{\Gamma}(\delta\psi - \delta\psi')}{d(\delta\psi - \delta\psi')}\right|_{(\delta\psi - \delta\psi')=0} > 0$ implies stability.

- $\left.\frac{d\tilde{\Gamma}(\delta\psi - \delta\psi')}{d(\delta\psi - \delta\psi')}\right|_{(\delta\psi - \delta\psi')=0} < 0$ implies instability.

This is illustrated for the case of $\tilde{\Gamma}(\mathbf{x}) = \sin\mathbf{x}$, for which $\frac{d\tilde{\Gamma}(\mathbf{x})}{d\mathbf{x}} = \cos\mathbf{x}$ is positive at $\mathbf{x}_0 = 0$ so the system is stable at this point (Figure 6).

.

Figure 6: Stability analysis
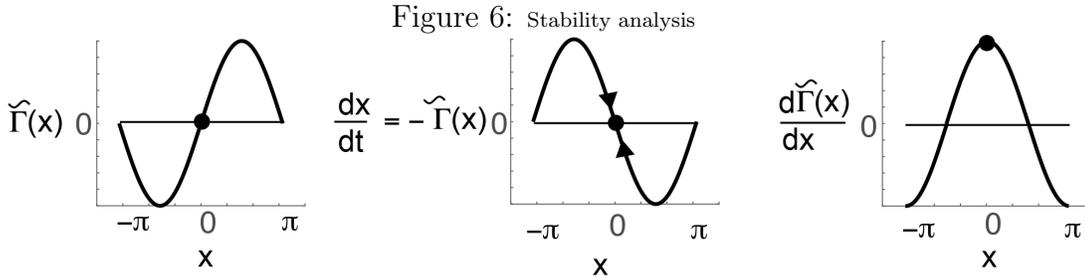
We return to the interaction between two neurons, with a model of a motor neuron used to calculate $\vec{Z}(\theta)$. Ee find that there are two points close to but not at the origin that are stable (Figure 7). The phase difference can, in the presence of variability, jump between these phase shifts.

Figure 7: Pairwise interaction is revealed by the phase shifts between two reciprocally connected neurons. Data from Reyes and Fetz, 1993. Analysis from Ermentrout and Kleinfeld, 2000