Physics 178/278 - David Kleinfeld - Winter 2021 - Lecture 13

Revised 23 Jan 2020 20:36 -s

13 Pairs and networks of Phase-coupled Neuronal Oscillators

Our 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 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.

13.1 Basic formalism

The equation of motion for a general dynamical system

$$\frac{d\vec{X}}{dt} = F(\vec{X};\mu) \tag{13.13}$$

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

$$\frac{d\vec{X}_0}{dt} = F(\vec{X}_0;\mu) \tag{13.14}$$

where a closed orbit satisfies

$$\vec{X}_0(t+T) = \vec{X}_0(t). \tag{13.15}$$

We associate a value of ψ with each point along $\vec{X}(t)$. 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, o all points within a tube around the limit cycle so that ψ is defined for all $\vec{X}$ 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. This is equivalent to an initial phase difference among the points. This is the main idea: a 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.

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

$$\frac{d\psi(\vec{X})}{dt} = \omega \tag{13.16}$$

for the unperturbed system. But, by the chain rule,

$$\begin{aligned} \frac{d\psi}{dt} &= \sum_i \frac{\partial \psi}{\partial X_i}\frac{\partial X_i}{\partial t} \\ &= \vec{\nabla}_{\vec{X}}\, \psi \cdot \frac{d\vec{X}}{dt} \\ &= \vec{\nabla}_{\vec{X}}\, \psi \cdot \vec{F}(\vec{X}). \end{aligned} \tag{13.17}$$

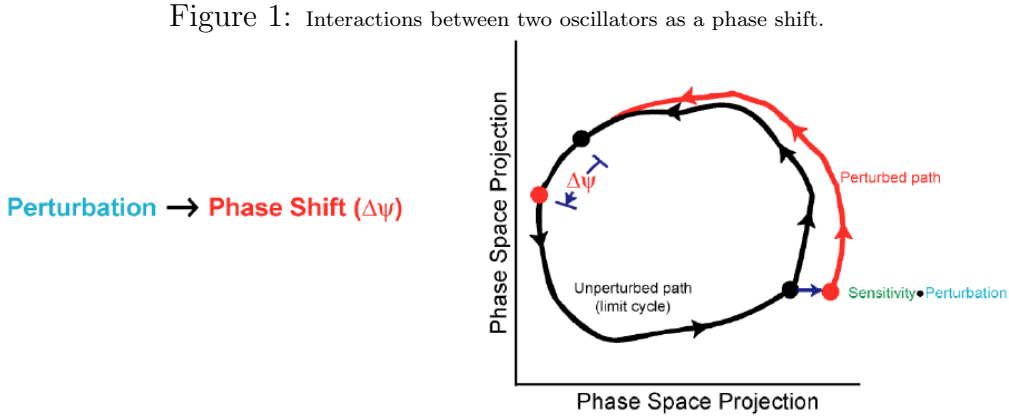
Let's perturb the motion by

$$\vec{F}(\vec{X}) \to \vec{F}(\vec{X}) + \epsilon \vec{P}(\vec{X}, \vec{X}') \tag{13.18}$$

where ϵ is small in the sense that the shape of the original trajectory in unchanged as $\epsilon \to 0$ and $\vec{X}'$ contains all the variables that define the perturbation, e.g, the trajectory of a neighboring oscillator and the interaction between the two oscillating systems. Then

$$\begin{aligned} \frac{d\psi}{dt} &= \vec{\nabla}_{\vec{X}}\, \psi \cdot \left[F(\vec{X}) + \epsilon \vec{P}(\vec{X}, \vec{X}')\right] \\ &= \vec{\nabla}_{\vec{X}}\, \psi \cdot F(\vec{X}) + \epsilon \vec{\nabla}_{\vec{X}}\, \psi \cdot \vec{P}(\vec{X}, \vec{X}') \\ &= \omega + \epsilon \vec{\nabla}_{\vec{X}}\, \psi \cdot \vec{P}(\vec{X}, \vec{X}'). \end{aligned} \tag{13.19}$$

Figure 1: Interactions between two oscillators as a phase shift.



.

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 $|\vec{X}(t) - \vec{X}_0(t)| \to 0$ 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, ψ, rather than time, t, where the two are related by

$$\psi = 2\pi \frac{t}{T} - \pi \;\; modulo(2\pi) \tag{13.20}$$

so that ψ ranges between $-\pi$ and π. Using

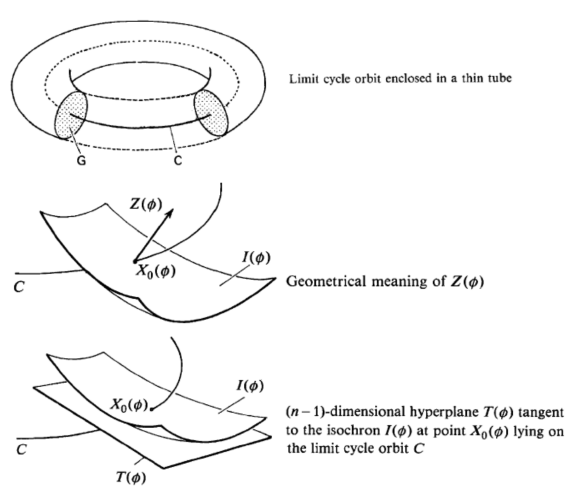
$$\vec{X}(t) \rightarrow \vec{X}_0(\psi) \tag{13.21}$$

we have

$$\begin{aligned} \frac{d\psi}{dt} &= \omega + \epsilon \vec{\nabla}_{\vec{X}_0(\psi)} \, \psi \cdot \vec{P}\left[\vec{X}_0(\psi), \vec{X'}_0(\psi')\right] \\ &\equiv \omega + \epsilon \vec{Z}(\psi) \cdot \vec{P}(\psi, \psi'). \end{aligned} \tag{13.22}$$

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 $\frac{d\vec{X}}{dt} = \mathbf{A}(t)\vec{X}$, 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.

Figure 2: Details of perturbations as a phase shift. tLook on 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 Kuramotor 1984



.

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

$$\psi = \delta\psi + \omega t. \tag{13.23}$$

Then the relative motion is given by

$$\begin{aligned} \frac{d\delta\psi}{dt} &= \epsilon \vec{Z}(\psi) \cdot \vec{P}(\psi, \psi') \\ &= \epsilon \vec{Z}(\delta\psi + \omega t) \cdot \vec{P}(\delta\psi + \omega t, \delta\psi' + \omega t). \end{aligned} \tag{13.24}$$

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

$$\frac{d\delta\psi}{dt} = \Gamma(\delta\psi, \delta\psi') \tag{13.25}$$

where

$$\Gamma(\delta\psi,\ \delta\psi') = \frac{\epsilon}{2\pi} \int_{-\pi}^{\pi} d\theta\ \vec{Z}(\delta\psi + \theta) \cdot \vec{P}(\delta\psi + \theta, \delta\psi' + \theta). \tag{13.26}$$

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

$$\frac{d\delta\psi}{dt} = \Gamma(\delta\psi, \delta\psi') + \delta\omega. \tag{13.27}$$

13.2 Simplified interaction among two oscillators.

We take the perturbation to be solely a function of the phase of the other oscillator. Thus

$$\Gamma(\delta\psi, \delta\psi') = \frac{\epsilon}{2\pi} \int_{-\pi}^{\pi} d\theta\ \vec{Z}(\delta\psi + \theta) \cdot \vec{P}(\delta\psi' + \theta). \tag{13.28}$$

But this is just a correlation integral that is proportion to the differences in phase, i.e.,

$$\Gamma(\delta\psi' - \delta\psi) = \frac{\epsilon}{2\pi} \int_{-\pi}^{\pi} d\theta\ \vec{Z}\left(\theta - (\delta\psi' - \delta\psi)\right) \cdot \vec{P}(\theta). \tag{13.29}$$

Thus a system of two oscillators obeys

$$\frac{d\delta\psi}{dt} = \Gamma(\delta\psi' - \delta\psi) \tag{13.30}$$

and

$$\frac{d\delta\psi'}{dt} = \Gamma(\delta\psi - \delta\psi'). \tag{13.31}$$

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

$$\begin{aligned}\frac{d(\delta\psi - \delta\psi')}{dt} &= [\Gamma(\delta\psi' - \delta\psi) - \Gamma(\delta\psi - \delta\psi')] \\ &\equiv \tilde{\Gamma}(\delta\psi' - \delta\psi) \\ &\equiv -\tilde{\Gamma}(\delta\psi - \delta\psi').\end{aligned} \tag{13.32}$$

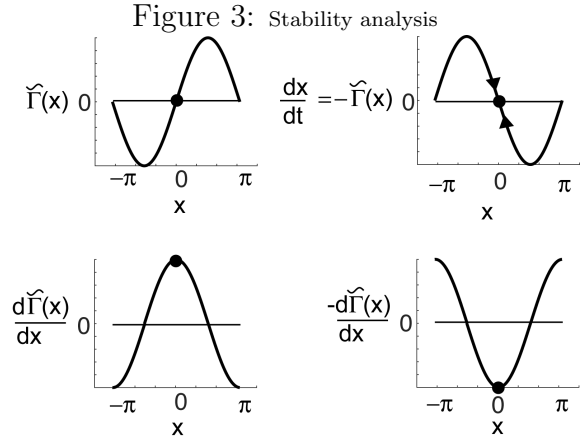
The term $\tilde{\Gamma}(\delta\psi - \delta\psi')$ is an odd function with a period of 2π and with zeros at $\delta\psi - \delta\psi = 0$, $\pm\pi$ and possibly other places.

By way of analysis,

- The zeros correspond to potential phase locking.
- The stability depends on the sign of the slope $-\frac{d\tilde{\Gamma}(x)}{dx}\Big|_{x_0}$, which corresponds to a "restoring force".
- $-\frac{d\tilde{\Gamma}}{dx}\Big|_{x_0} < 0$ at $x_0 = 0$ implies stability.
- $-\frac{d\tilde{\Gamma}}{dx}\Big|_{x_0} > 0$ at $x_0 = 0$ implies instability.
- The opposite conditions hold at $x_0 = \pm\pi$.

This is illustrated for the case of $\tilde{\Gamma}(x) = \sin x$, for which $-\frac{d\tilde{\Gamma}(x)}{dx} = -\cos x$ is negative at $x_0 = 0$ so the system is stable at this point.

Figure 3: Stability analysis



.

13.2.1 Relation to measurements on neurons

We return to the general expression

$$\Gamma(\delta\psi,\ \delta\psi') = \frac{\epsilon}{2\pi}\int_{-\pi}^{\pi} d\theta\ \vec{Z}(\delta\psi + \theta)\cdot\vec{P}(\delta\psi + \theta, \delta\psi' + \theta). \tag{13.33}$$

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

$$\vec{P}(\delta\psi+\theta,\delta\psi'+\theta)=\frac{g_{synapse}}{c_m}\vec{S}(\delta\psi'+\theta)\left(V_{synapse}-V(\delta\psi+\theta)\right) \tag{13.34}$$

so

$$\Gamma(\delta\psi,\ \delta\psi')=\frac{\epsilon}{2\pi}\int_{-\pi}^{\pi}d\theta\ \vec{Z}(\delta\psi+\theta)\left(V_{synapse}-V(\delta\psi+\theta)\right)\cdot\frac{g_{synapse}}{c_m}\vec{S}(\delta\psi'+\theta). \tag{13.35}$$

where $\vec{R}(\delta\psi'+\theta)$ is the presynaptic activation. This is of the form

$$\Gamma(\delta\psi,\ \delta\psi')=\frac{\epsilon}{2\pi}\int_{-\pi}^{\pi}d\theta\ \vec{R}(\delta\psi+\theta)\cdot\vec{S}(\delta\psi'+\theta) \tag{13.36}$$

where we collect the postsynaptic response as

$$\vec{R}(\delta\psi+\theta)=\frac{g_{synapse}}{c_m}\vec{Z}(\delta\psi+\theta)\left(V_{synapse}-V(\delta\psi+\theta)\right). \tag{13.37}$$

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

$$\begin{aligned}\Gamma(\delta\psi,\ \delta\psi') &= \Gamma(\delta\psi'-\delta\psi) \\ &= \frac{\epsilon}{2\pi}\int_{-\pi}^{\pi}d\theta\ \vec{R}\left(\theta-(\delta\psi'-\delta\psi)\right)\cdot\vec{S}(\theta).\end{aligned} \tag{13.38}$$

Thus the interaction of neuronal oscillators is given by the correlation between the presynaptic spikes and the post-synaptic response.

13.3 Examples

13.3.1 Two oscillators with "low-pass" coupling.

An interesting example due to Ermentrout and to Hansel is to consider two oscillators that interact by a synapse with a non-instantaneous rise time. Before we choose a realistic cell model, let's try some analytical methods and choose a form of $\vec{R}(\delta\psi)$ that has variable sensitivity along the limit cycle. The simplest choice is

$$R(t)=\sin\omega t \tag{13.39}$$

so

$$R(\theta)=\sin\theta. \tag{13.40}$$

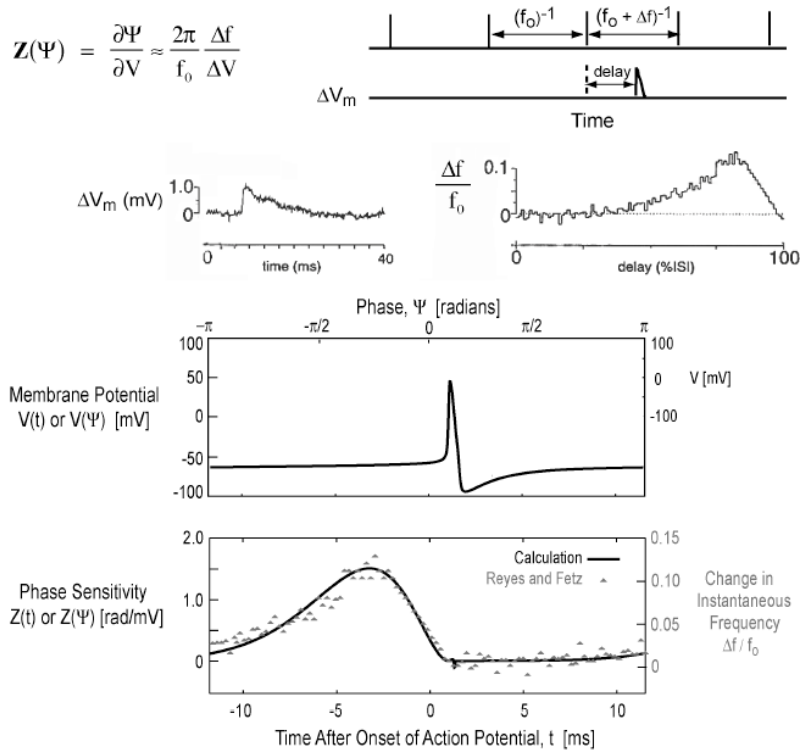
The interaction is given by an "α" function, i.e.,

$$S(t\geq 0)=\frac{g_{synapse}}{c_m}\frac{t}{\tau}e^{-t/\tau} \tag{13.41}$$

so

$$\begin{aligned}S(\theta) &= 0 && \theta<0 \\ &= \frac{g_{synapse}}{c_m}\frac{\theta}{\omega\tau}e^{-\theta/\omega\tau} && \theta\geq 0.\end{aligned} \tag{13.42}$$

Figure 4: The phase sensitivity function for perturbation in voltage. Data from Reyes and Fetz, 1993. Analysis from Ermentrout and Kleinfeld 2000



.

The convolution for $\tilde{\Gamma}(\delta\psi' - \delta\psi)$ can be done by extending the range of integration over all time, so that

$$
\begin{aligned}
\Gamma(\delta\psi' - \delta\psi) &= \frac{\epsilon}{2\pi}\int_0^\infty d\theta\ \vec{R}\left(\theta - (\delta\psi' - \delta\psi)\right)\cdot\vec{S}(\theta) \qquad (13.43)\\
&= \frac{g_{synapse}}{c_m}\ \frac{\epsilon}{2\pi}\ \omega\tau\int_0^\infty d\left(\frac{\theta}{\omega\tau}\right)\ \sin\left[\theta - (\delta\psi' - \delta\psi)\right]\left(\frac{\theta}{\omega\tau}\right)e^{-\theta/\omega\tau}\\
&= \frac{g_{synapse}}{c_m}\frac{\epsilon}{2\pi}\ \omega\tau\ \frac{1}{2i}\left(e^{-i(\delta\psi'-\delta\psi)}\int_0^\infty x\ dx\ e^{i\omega\tau x}\ e^{-x}\ -\ e^{i(\delta\psi'-\delta\psi)}\int_0^\infty x\ dx\ e^{-i\omega\tau x}\ e^{-x}\right)\\
&= \frac{g_{synapse}}{c_m}\frac{\epsilon}{2\pi}\ \omega\tau\ \frac{1}{2i}\left(\frac{e^{-i(\delta\psi'-\delta\psi)}}{(1-i\omega\tau)^2}\ -\ \frac{e^{i(\delta\psi'-\delta\psi)}}{(1+i\omega\tau)^2}\right)\int_0^\infty x\ dx\ e^{-x}\\
&= \frac{g_{synapse}}{c_m}\frac{\epsilon}{2\pi}\frac{\omega\tau}{[1+(\omega\tau)^2]^2}\left(\left[(\omega\tau)^2 - 1\right]\sin(\delta\psi' - \delta\psi)\ +\ 2\omega\tau\cos(\delta\psi' - \delta\psi)\right)
\end{aligned}
$$

and thus

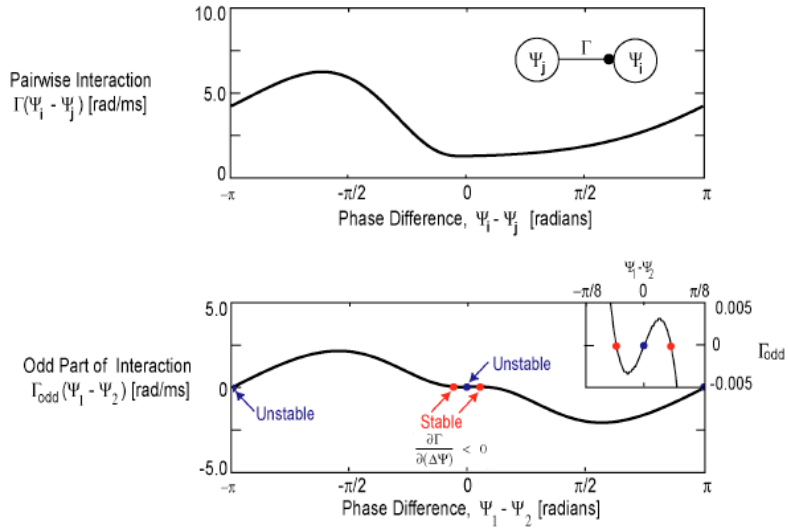
$$\tilde{\Gamma}(\delta\psi' - \delta\psi) = \frac{g_{synapse}}{c_m}\frac{\epsilon}{\pi}\frac{\omega\tau\left[(\omega\tau)^2 - 1\right]}{[1+(\omega\tau)^2]^2}\ \sin(\delta\psi' - \delta\psi) \qquad (13.44)$$

so that

$$\frac{d(\delta\psi - \delta\psi')}{dt} = \frac{g_{synapse}}{c_m}\frac{\epsilon}{\pi}\frac{\omega\tau\left[(\omega\tau)^2 - 1\right]}{[1+(\omega\tau)^2]^2}\ \sin(\delta\psi - \delta\psi') \qquad (13.45)$$

and the "restoring force" ensures stability.

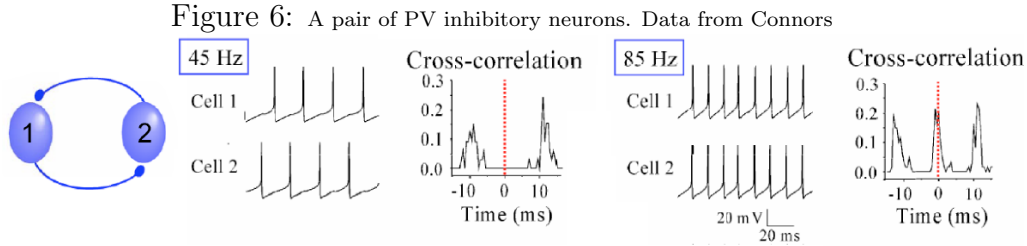
Figure 5: Pairwise nteraction is revealed by the phase shifts between two reciprocally connected neurons. Data from Reyes and Fetz, 1993. Analysis from Ermentrout and Kleinfeld, 2000



This result implies that, for excitatory connections ($g_{synapse} > 0$), the synchronized state, i.e., $\delta\psi' = \delta\psi$, is stable only for $\tau < \frac{1}{\omega}$. In contrast, for $\tau > \frac{1}{\omega}$ the antiphastic state with $\delta\psi' - \delta\psi = \pm\pi$ is stable.

This result further implies that, for inhibitory connections ($g_{synapse} < 0$), the synchronized state, i.e., $\delta\psi' = \delta\psi$, is stable only for $\tau > \frac{1}{\omega}$. In contrast, for $\tau < \frac{1}{\omega}$ the antiphastic state with $\delta\psi' - \delta\psi = \pm\pi$ is stable.

Figure 6: A pair of PV inhibitory neurons. Data from Connors



The appearance of synchrony with inhibitory connections was a prediction that has been born out by experiments on pairs of neurons bu Connors. Further, all inhibitory networks are observed experimentally, first by Jeffreys. The circular frequency at the peak amplitude is $f = \frac{1}{\tau}\frac{\sqrt{3+\sqrt{8}}}{2\pi} = \frac{0.384}{\tau}$, or about $f \approx 40Hz$ for a 10 ms time constant.

13.3.2 Two oscillators with different intrinsic frequencies.

We take

$$\Gamma(\theta) \equiv -\Gamma_0 \sin(\theta). \tag{13.46}$$

Then

$$\begin{aligned} \frac{d\delta\psi}{dt} &= \Gamma_0 \sin(\delta\psi' - \delta\psi) + \delta\omega \\ \frac{d\delta\psi'}{dt} &= \Gamma_0 \sin(\delta\psi - \delta\psi') + \delta\omega'. \end{aligned} \tag{13.47}$$

The system will phase lock, for which $\frac{d\delta\psi}{dt} = \frac{d\delta\psi'}{dt}$, so long as the interaction strength, i.e.,

$$\begin{aligned} \tilde{\Gamma} &= \Gamma_0 \sin(\delta\psi' - \delta\psi) - \Gamma_0 \sin(\delta\psi - \delta\psi') \\ &= 2\Gamma_0 \sin(\delta\psi' - \delta\psi) \end{aligned} \tag{13.48}$$

balances the difference in frequencies, i.e.,

$$2\Gamma_0 \sin(\delta\psi' - \delta\psi) = \delta\omega - \delta\omega'. \tag{13.49}$$

This requires

$$\frac{2\Gamma_0}{|\delta\omega' - \delta\omega|} > 1 \tag{13.50}$$

and the phase shift is just

$$\delta\psi - \delta\psi' = \sin^{-1}\left(\frac{\delta\omega - \delta\omega'}{2\Gamma_0}\right) \tag{13.51}$$

so that the oscillator with the higher uncoupled frequency leads. The frequency under phase lock, found by adding the equations, is

$$\omega_{observed} = \omega + \frac{\delta\omega + \delta\omega'}{2}. \tag{13.52}$$

The above are the two quantities that are measured in the laboratory.

Outside of the phase locked region, the system undergoes quasiperiodic motion and the time varying phase shift is found by integrating the equations of motion to yield

$$\delta\psi - \delta\psi' = 2\tan^{-1}\left[\frac{2\Gamma_0 + \sqrt{(\delta\omega - \delta\omega')^2 - 4\Gamma_0^2}\tan\left(\frac{\sqrt{(\delta\omega - \delta\omega')^2 - 4\Gamma_0^2}}{2}\, t\right)}{\delta\omega' - \delta\omega}\right] \tag{13.53}$$

13.3.3 Chain of oscillators with $\delta\omega \propto \Delta x$: Example of Limax maximus.

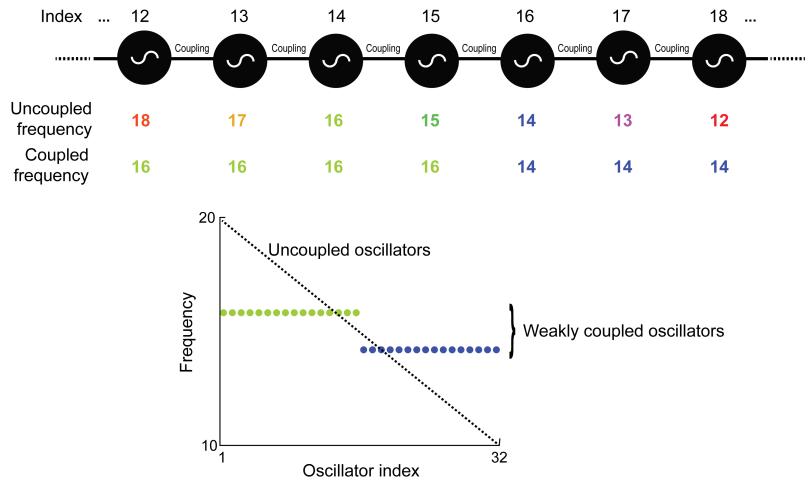
$$\frac{d\delta\psi_x}{dt} = \delta\omega_x + \sum_{x \neq x'} \Gamma(\delta\psi_x - \delta\psi_{x'}) \tag{13.54}$$

with

$$\delta\omega_x \propto x + constant. \tag{13.55}$$

When the system locks, there is a single frequency, but a gradient of phase shifts with $\frac{\Delta\psi_x}{dx}$ given by a monotonic function of x, like $\frac{\Delta\psi_x}{dx} \propto$ constant, i.e., the phase shift appears as a traveling wave. The data from Limax shows traveling waves and a gradient of intrinsic frequencies. The article by Ermentrout and Kleinfeld summarizes this and other data. The extension of weakly coupled oscillators to latices has proven to be largely analytically intractable. One interesting result is that the lattice will only synchronize for a coupling constant Γ_0 that scales as the size of the system, although (metastable?) patterns are observed in numerical examples.

Figure 7: Parcellation in one dimensionsl lattice of weakly coupled oscillators. From Ermentrout and Kopell, 1984



13.3.4 Two oscillators with propagation delays.

We again take

$$\Gamma(\delta\psi - \delta\psi') \equiv -\Gamma_0 \sin(\delta\psi - \delta\psi'). \tag{13.56}$$

Then

$$\begin{aligned} \frac{d\delta\psi}{dt} &= \Gamma_0 \sin(\delta\psi'(t-\tau_D) - \delta\psi(t)) + \delta\omega_0 \\ \frac{d\delta\psi'}{dt} &= \Gamma_0 \sin(\delta\psi(t-\tau_D) - \delta\psi'(t)) + \delta\omega_0 \end{aligned} \tag{13.57}$$

where the frequencies $\delta\omega_0$ are taken to be equal. We assume a solution of the form

$$\delta\omega = \delta\omega_0 - \Gamma_0 \cos\alpha \sin\delta\omega\tau_D. \tag{13.58}$$

This is satisfied for

$$\alpha = \begin{cases} 0 & \text{if } \cos\omega\tau_D \geq 0 \\ \pi & \text{if } \cos\omega\tau_D < 0 \end{cases}$$

Thus we observe both frequency shifts and potential phase shifts. The synchronous state is stable only for $0 < \tau_D < \frac{\pi}{2\delta\omega}$. The details of this relation will change if the 'symmetry of the waveform changes, but the gist is correct.