

7 Networks of Phase Coupled Neuronal Oscillators

We consider small networks or simple networks in which cells are coupled only weakly, in the sense that they can affect each other's timing but do not necessarily turn each other on or off.

7.1 Basic formalism

Equation of motion for a general dynamical system

$$\frac{d\vec{X}}{dt} = F(\vec{X}; \mu) \quad (7.1)$$

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

$$\frac{d\vec{X}_0}{dt} = F(\vec{X}_0; \mu) \quad (7.2)$$

where a closed orbit satisfies

$$\vec{X}_0(t + T) = \vec{X}_0(t) \quad (7.3)$$

FIGURE - chapt-12-kuromoto-1-2-3.eps

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, C , to all points within a tube around C 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 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. The main idea is that the physical perturbation can be transformed into a phase shift along the original limit cycle, C , 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

$$\frac{d\psi(\vec{X})}{dt} = \omega \quad (7.4)$$

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

$$\begin{aligned} \frac{d\psi}{dt} &= \sum_i \frac{\partial\psi}{\partial X_i} \frac{\partial X_i}{\partial t} \\ &= \vec{\nabla}_{\vec{X}} \psi \cdot \frac{d\vec{X}}{dt} \\ &= \vec{\nabla}_{\vec{X}} \psi \cdot \vec{F}(\vec{X}) \end{aligned} \quad (7.5)$$

Let's perturb the motion by

$$\vec{F}(\vec{X}) \rightarrow \vec{F}(\vec{X}) + \epsilon \vec{P}(\vec{X}, \vec{X}') \quad (7.6)$$

where ϵ is small in the sense that the shape of the original trajectory is unchanged as $\epsilon \rightarrow 0$ 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

$$\begin{aligned} \frac{d\psi}{dt} &= \vec{\nabla}_{\vec{X}} \psi \cdot [F(\vec{X}) + \epsilon \vec{P}(\vec{X}, \vec{X}')] \\ &= \omega + \epsilon \vec{\nabla}_{\vec{X}} \psi \cdot \vec{P}(\vec{X}, \vec{X}') \end{aligned} \quad (7.7)$$

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 $|\vec{X}(t) - \vec{X}_0(t)| \rightarrow 0$ as $t \rightarrow \infty$, 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

$$\psi = 2\pi \frac{t}{T} \text{ modulo}(2\pi) \quad (7.8)$$

Using

$$\vec{X}(t) \rightarrow \vec{X}_0(\psi) \quad (7.9)$$

we have

$$\begin{aligned} \frac{d\psi}{dt} &= \omega + \epsilon \vec{\nabla}_{\vec{X}_0(\psi)} \psi \cdot \vec{P}[\vec{X}_0(\psi), \vec{X}'_0(\psi')] \\ &\equiv \omega + \epsilon \vec{Z}(\psi) \cdot \vec{P}(\psi, \psi') \end{aligned} \quad (7.10)$$

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 is 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

$$\psi = \delta\psi + \omega t \quad (7.11)$$

Then the relative motion is given by

$$\begin{aligned} \frac{d\delta\psi}{dt} &= \epsilon \vec{Z}(\psi) \cdot \vec{P}(\psi, \psi') \\ &= \epsilon \vec{Z}(\delta\psi + \omega t) \cdot \vec{P}(\delta\psi + \omega t, \delta\psi' + \omega t) \end{aligned} \quad (7.12)$$

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

$$\frac{d\delta\psi}{dt} = \Gamma(\delta\psi, \delta\psi') \quad (7.13)$$

where

$$\Gamma(\delta\psi, \delta\psi') = \frac{\epsilon}{2\pi} \int_{-\pi}^{\pi} d\theta \vec{Z}(\delta\psi + \theta) \cdot \vec{P}(\delta\psi + \theta, \delta\psi' + \theta) \quad (7.14)$$

FIGURE - panel from research talk

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

$$\frac{d\delta\psi}{dt} = \Gamma(\delta\psi, \delta\psi') + \delta\omega \quad (7.15)$$

7.2 Simplified interaction among 2 oscillators.

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

$$\Gamma(\delta\psi, \delta\psi') = \frac{\epsilon}{2\pi} \int_{-\pi}^{\pi} d\theta \vec{Z}(\delta\psi + \theta) \cdot \vec{P}(\delta\psi' + \theta) \quad (7.16)$$

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

$$\Gamma(\delta\psi' - \delta\psi) = \frac{\epsilon}{2\pi} \int_{-\pi}^{\pi} d\theta \vec{Z}(\theta - (\delta\psi' - \delta\psi)) \cdot \vec{P}(\theta) \quad (7.17)$$

So that a system of two oscillators obeys

$$\begin{aligned} \frac{d\delta\psi}{dt} &= \Gamma(\delta\psi' - \delta\psi) \\ \frac{d\psi'}{dt} &= \Gamma(\delta\psi - \delta\psi') \end{aligned} \quad (7.18)$$

We subtract the two equations of motion for the phase to get

$$\begin{aligned} \frac{d(\delta\psi - \delta\psi')}{dt} &= [\Gamma(\delta\psi' - \delta\psi) - \Gamma(\delta\psi - \delta\psi')] \\ &\equiv \tilde{\Gamma}(\delta\psi' - \delta\psi) \\ &\equiv -\tilde{\Gamma}(\delta\psi - \delta\psi') \end{aligned} \quad (7.19)$$

FIGURES - 5 panels from research talk

The term $\tilde{\Gamma}(\delta\psi - \delta\psi')$ is an odd function with period T , with zeros at

$$x_0 \equiv \delta\psi - \delta\psi' = n\frac{T}{2} \quad n = 1, 2, 3, \dots \quad (7.20)$$

and possibly other places. By way of analysis,

- The zeros correspond to phase locking.
- The stability depends on the sign of $\left. \frac{d\tilde{\Gamma}(x)}{dx} \right|_{x_0}$
- $\left. \frac{d\tilde{\Gamma}}{dx} \right|_{x_0} < 0$ implies stability with even n ; attractive - phases converge.
- $\left. \frac{d\tilde{\Gamma}}{dx} \right|_{x_0} > 0$ implies stability with odd n ; repulsive - phases diverge.

7.3 Examples

7.3.1 Two oscillators with delayed coupling.

An interesting example due to Ermentrout is to consider two oscillators that interact by a synapse with a noninstantaneous rise time. Before we choose a realistic cell model, let's try some analytical methods and choose a form of $\vec{Z}(\delta\psi)$ that has variable sensitivity along the limit cycle. The simplest choice is $Z(t) = \sin \omega t$, or

$$Z(\delta\psi) = \sin(\delta\psi) \quad (7.21)$$

The interaction is given by an "α" function, i.e., $P(t) = \frac{g}{\tau} e^{-t/\tau}$ with $\phi = \omega t \text{ modulo}(2\pi)$, i.e.,

$$P(\delta\psi') = \frac{g}{\tau} \frac{\delta\psi'}{\omega\tau} e^{-\delta\psi'/\omega\tau} \quad (7.22)$$

The convolutions for $\tilde{\Gamma}$ can be done explicitly to yield

$$(\tilde{\Gamma}(\delta\psi - \delta\psi')) = g(8\pi^2) \frac{(\omega\tau)^2 - 1}{[1 + (\omega\tau)^2]^2} \sin(\delta\psi - \delta\psi') \quad (7.23)$$

This says that, for excitatory connections ($g > 0$), 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. The opposite condition holds for inhibitory connections ($g < 0$).

FIGURE - 2 panels from research talk

Interestingly, synchronous, all inhibitory networks are observed experimentally!

7.3.2 Two identical Hodgkin Huxley oscillators.

How well does the above analysis hold with more realistic cells.

FIGURE - chapt-12-if-syn-phase-calc.eps

Recall the Hodgkin Huxley equations for a point neuron, where $\vec{X} = (V, h, m, n)^T$, i.e.,

$$\begin{aligned} \frac{\partial V(t)}{\partial t} &= \frac{-r_m}{2\pi a\tau} \left(\bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_K n^4 (V - V_K) + \bar{g}_{leak} (V - V_i) + I_{syn} \right) \\ \frac{dh(V, t)}{dt} &= \frac{h_\infty(V) - h(V, t)}{\tau_h(V)} \\ \frac{dm(V, t)}{dt} &= \frac{m_\infty(V) - m(V, t)}{\tau_m(V)} \\ \frac{dn(V, t)}{dt} &= \frac{n_\infty(V) - n(V, t)}{\tau_n(V)} \end{aligned} \quad (7.24)$$

Hansel and later van Vreeswijk considered two Hodgkin Huxley cells with a synaptic current given by

$$I_{syn} = -G_{syn} [V(t) - V_{syn}] \sum_i^{spikes} f(t - t_i) \quad (7.25)$$

where he used an "alpha" function for $f(t)$. The form of $\vec{Z}(\psi + t)$ is found from directly evaluating perturbations to the limit cycle, which is found from the Hodgkin-Huxley equations with $I_{syn} = 0$. The perturbation is given by

$$P(\psi + t, \psi' + t) = -G_{syn} [V(\psi + \omega t) - V_{syn}] \sum_i^{spikes} f(\psi' + \omega t - \omega t_i) \quad (7.26)$$

The systematics as a function of α for fixed ω were explored by van Vreeswijk

FIGURE - chapt-12-hh-phase-model.eps

The phase as a function of I_{ext} , really ω , for fixed α were explored by Hansel. He also examined where in the cycle the neuron is most sensitive to perturbations.

7.3.3 Two oscillators with different intrinsic frequency.

We take

$$\Gamma(\delta\psi - \delta\psi') \equiv -\Gamma_0 \sin(\delta\psi - \delta\psi') \quad (7.27)$$

Then

$$\begin{aligned} \frac{d\delta\psi}{dt} &= \Gamma_0 \sin(\delta\psi' - \delta\psi) + \delta\omega \\ \frac{d\delta\psi'}{dt} &= \Gamma_0 \sin(\delta\psi - \delta\psi') + \delta\omega' \end{aligned} \quad (7.28)$$

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

$$\tilde{\Gamma} = \Gamma_0 \sin(\delta\psi' - \delta\psi) - \Gamma_0 \sin(\delta\psi - \delta\psi') \quad (7.29)$$

$$= -2\Gamma_0 \sin(\delta\psi - \delta\psi') = \delta\omega - \delta\omega' \quad (7.30)$$

or

$$\frac{2\Gamma_0}{|\delta\omega' - \delta\omega|} > 1 \quad (7.31)$$

The phase shift is just

$$\delta\psi - \delta\psi' = \sin^{-1} \left(\frac{\delta\omega' - \delta\omega}{2\Gamma_0} \right) \quad (7.32)$$

and the frequency under phase lock is

$$\omega_{observed} = \omega + \frac{\delta\omega + \delta\omega'}{2} \quad (7.33)$$

The above are the two quantities are the ones measured in the lab!

FIGURE - panel from research talk

Outside of the phase locked region, the system undergoes quasiperiodic motion with a time varying phase shift given by

$$\delta\psi - \delta\psi' = 2 \tan^{-1} \left[\frac{\sqrt{(\delta\omega - \delta\omega')^2 - 4\Gamma_0^2} \tan\left(\frac{\sqrt{(\delta\omega - \delta\omega')^2 - 4\Gamma_0^2} t}{2}\right) + 2\Gamma_0}{\delta\omega - \delta\omega'} \right] \quad (7.34)$$

7.3.4 Chain of oscillators with $\delta\omega \propto \Delta x$: The example of Limax.

$$\frac{d\delta\psi_x}{dt} = \delta\omega_x + \sum_{x \neq x'} \Gamma(\delta\psi_x - \delta\psi_{x'}) \quad (7.35)$$

with

$$\delta\omega_x \propto x + \text{constant} \quad (7.36)$$

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 $\frac{\Delta\psi_x}{dx} \propto \text{constant}$, 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.

FIGURES - 4 panels from research talk

7.3.5 Two oscillators with propagation delays.

We again take

$$\Gamma(\delta\psi - \delta\psi') \equiv -\Gamma_0 \sin(\delta\psi - \delta\psi') \quad (7.37)$$

Then

$$\begin{aligned} \frac{d\delta\psi}{dt} &= \Gamma_0 \sin(\delta\psi'(t - \tau_D) - \delta\psi(t)) + \delta\omega_0 \\ \frac{d\delta\psi'}{dt} &= \Gamma_0 \sin(\delta\psi(t - \tau_D) - \delta\psi'(t)) + \delta\omega_0 \end{aligned} \quad (7.38)$$

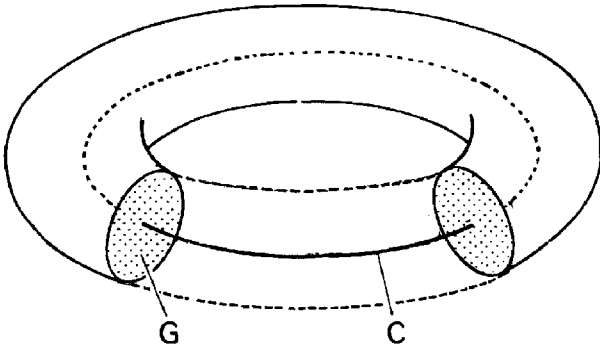
where the frequencies $\delta\omega_0$ are assumed to be equal. We assume a solution of the form

$$\delta\omega = \delta\omega_0 - \Gamma_0 \cos \alpha \sin \delta\omega \tau_D \quad (7.39)$$

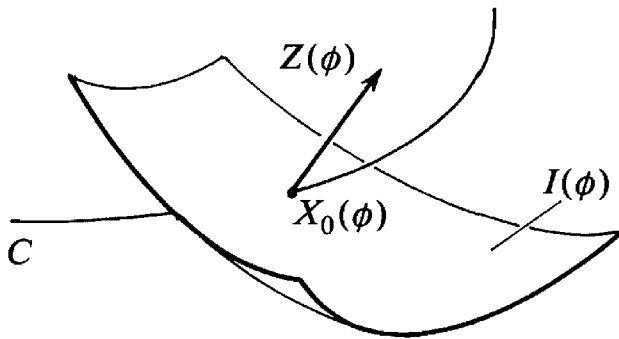
This is satisfied for

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

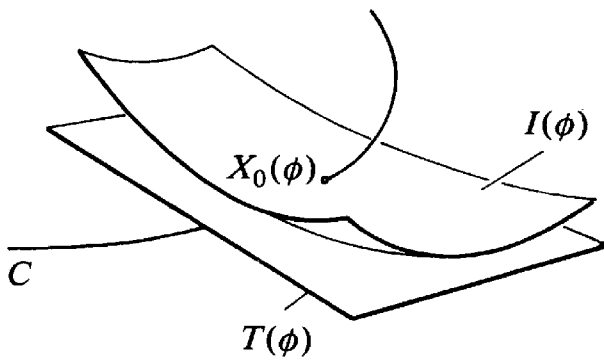
Thus we observe both frequency shifts and potential phase shifts. The synchronous state is stable only for $0 < \tau_D < \frac{\pi}{2\delta\omega}$. The details of this relation will change if the symmetry of the waveform changes, but the gist is correct.



Limit cycle orbit enclosed in a thin tube



Geometrical meaning of $Z(\phi)$



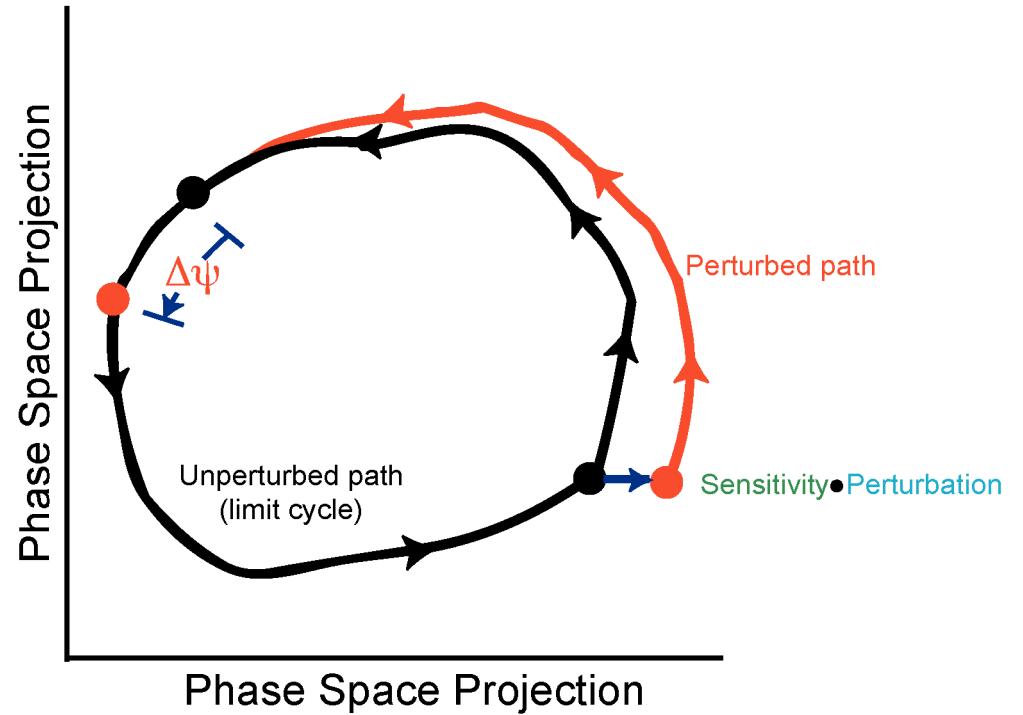
$(n - 1)$ -dimensional hyperplane $T(\phi)$ tangent to the isochron $I(\phi)$ at point $X_0(\phi)$ lying on the limit cycle orbit C

Transformation of a Dynamic System (N-dim) into a "Phase" System (1-dim)

Closed Orbits

Conditions (met only approximately in practice): **Weak Perturbations**
Infinite Relaxation Time

Perturbation → **Phase Shift ($\Delta\psi$)**



$$\frac{d\psi_i(t)}{dt} = \omega + \sum_{\text{neighbors, } j} \Gamma(\psi_i - \psi_j)$$

$$\Gamma(\psi_i - \psi_j) = \frac{\varepsilon}{2\pi} \int_{-\pi}^{\pi} d\theta \mathbf{Z}(\psi_i + \theta) \cdot \mathbf{P}(\psi_i + \theta, \psi_j + \theta)$$

Perturbation
Sensitivity $\propto \left(\frac{\partial \psi_i}{\partial V}, \dots \right)$

The Phase Sensitivity Function

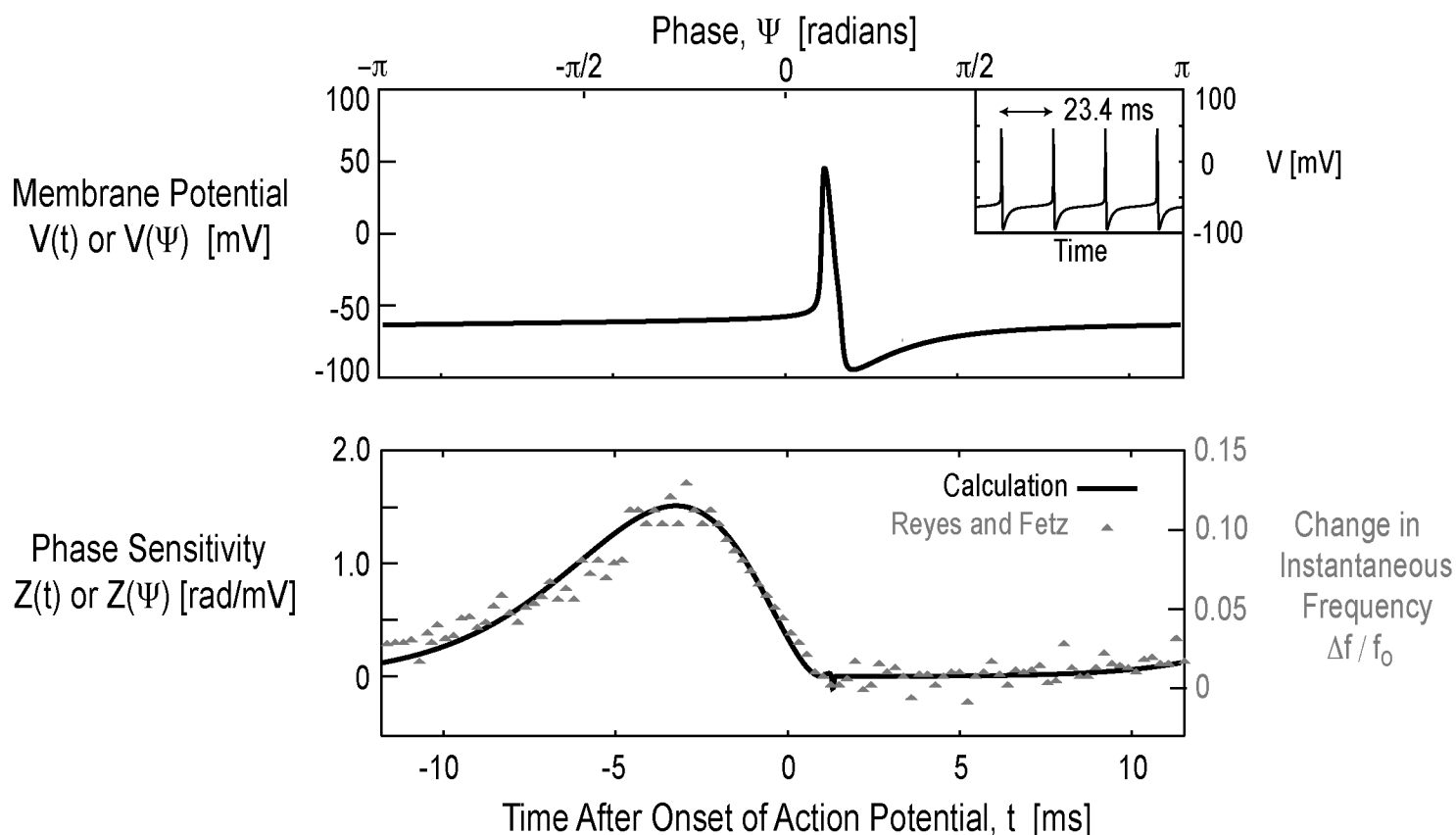
Calculation (Ermentrout & Kleinfeld 2000) vs. Experimental Data (Reyes & Fetz 1993)

Real system: $\frac{\partial V}{\partial t} = \dots$; $\frac{\partial n}{\partial t} = \dots$; etcetera

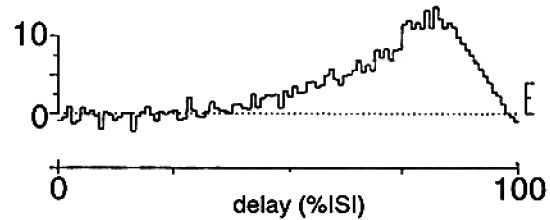
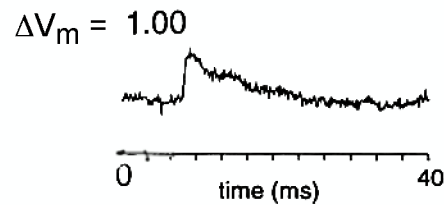
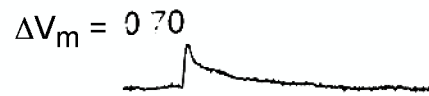
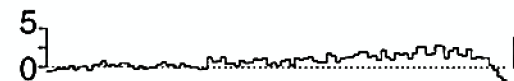
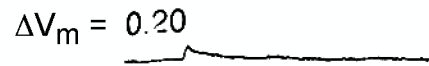
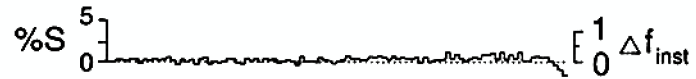
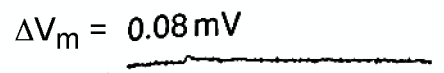
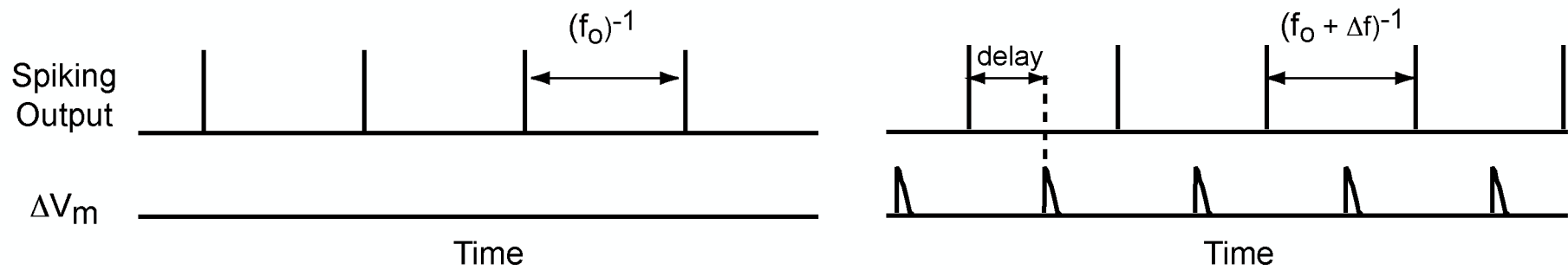
Phase reduction: $\frac{\partial \Psi_i}{\partial t} = \omega + \Gamma(\Psi_i - \Psi_j)$

$$\frac{\varepsilon}{2\pi} \int_{-\pi}^{\pi} d\theta \mathbf{Z}(\Psi_i - \theta) \cdot \mathbf{P}(\Psi_i - \theta; \Psi_j - \theta)$$

For perturbation solely in V: $\mathbf{Z}(\Psi) = \frac{\partial \Psi}{\partial V} \approx \frac{2\pi}{f_0} \frac{\Delta f}{\Delta V}$



Experiment of Reyes and Fetz (J. Neurophysiol. 1993)

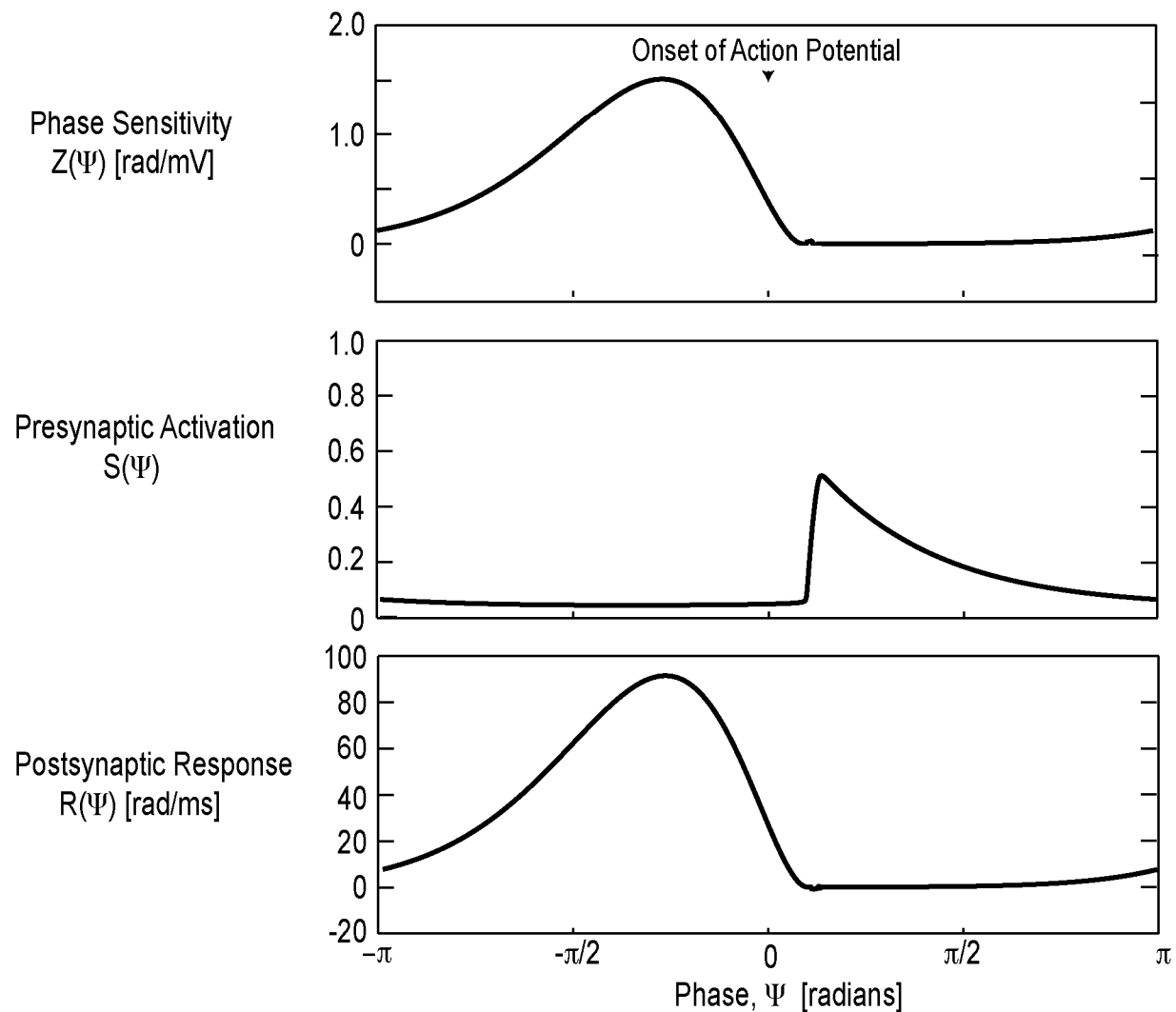


Pairwise Interaction between Neuronal Oscillators, $\Gamma(\psi_i - \psi_j)$
 is the Correlation of Presynaptic Activation with Postsynaptic Response

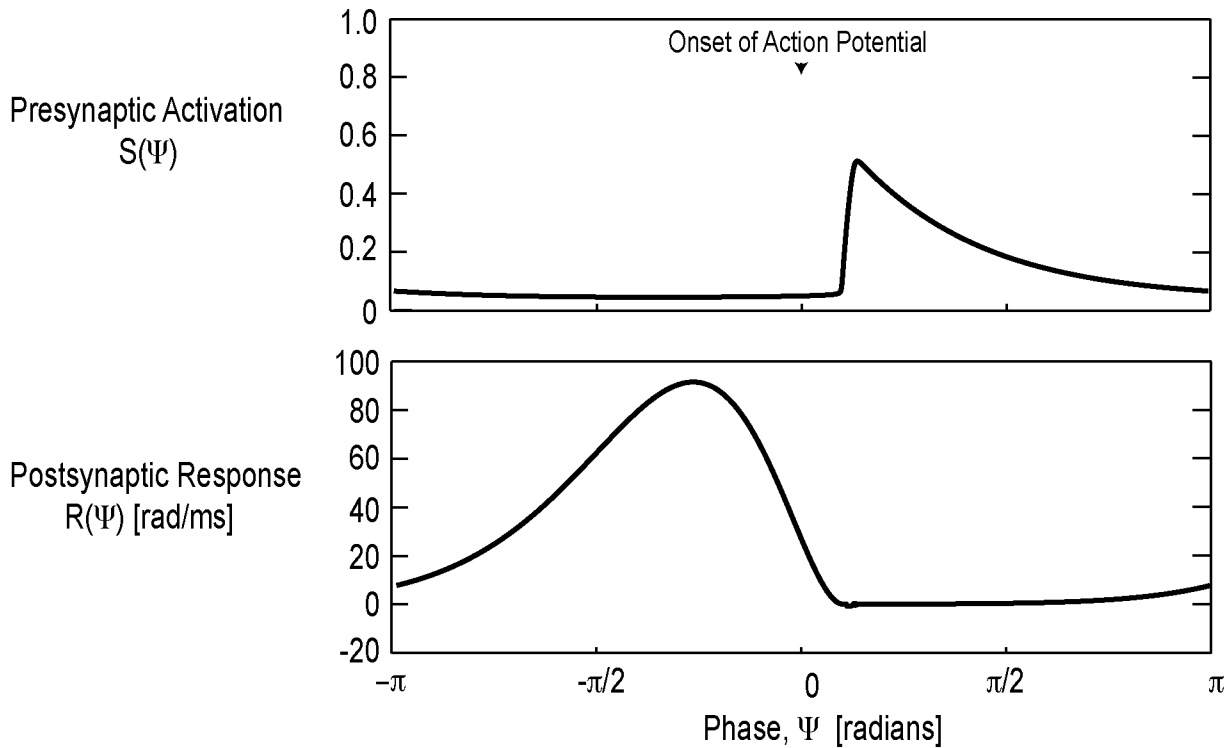
$$\Gamma(\Psi_i - \Psi_j) = \frac{\varepsilon}{2\pi} \int_{-\pi}^{\pi} d\theta \mathbf{Z}(\Psi_i + \theta) \mathbf{P}(\Psi_i + \theta; \Psi_j + \theta)$$

$$= \frac{\varepsilon}{2\pi} \int_{-\pi}^{\pi} d\theta \frac{g_{\text{synapse}}}{C_m} \mathbf{Z}(\Psi_i + \theta) [E_{\text{synapse}} - \mathbf{V}(\Psi_i + \theta)] \mathbf{S}(\Psi_j + \theta)$$

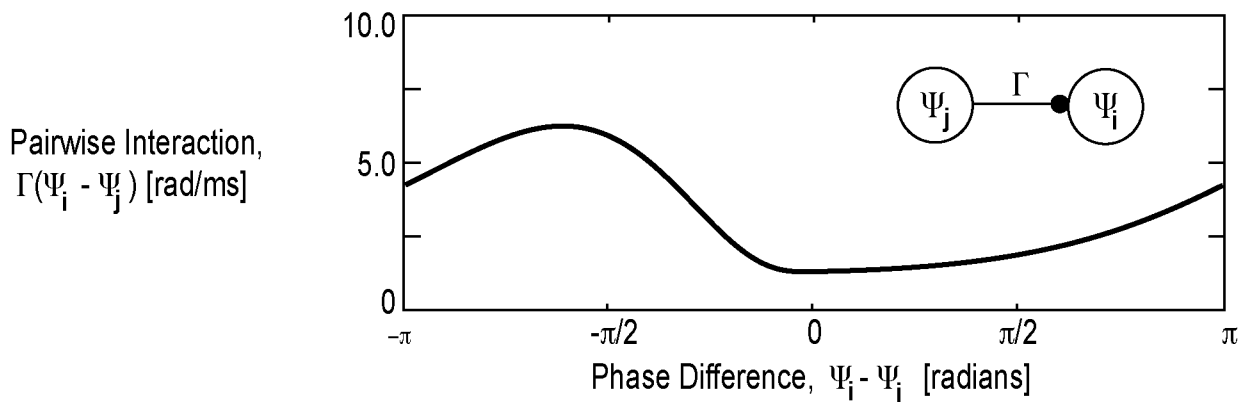
$$= \frac{\varepsilon}{2\pi} \int_{-\pi}^{\pi} d\theta \mathbf{R}(\Psi_i + \theta) \mathbf{S}(\Psi_j + \theta)$$



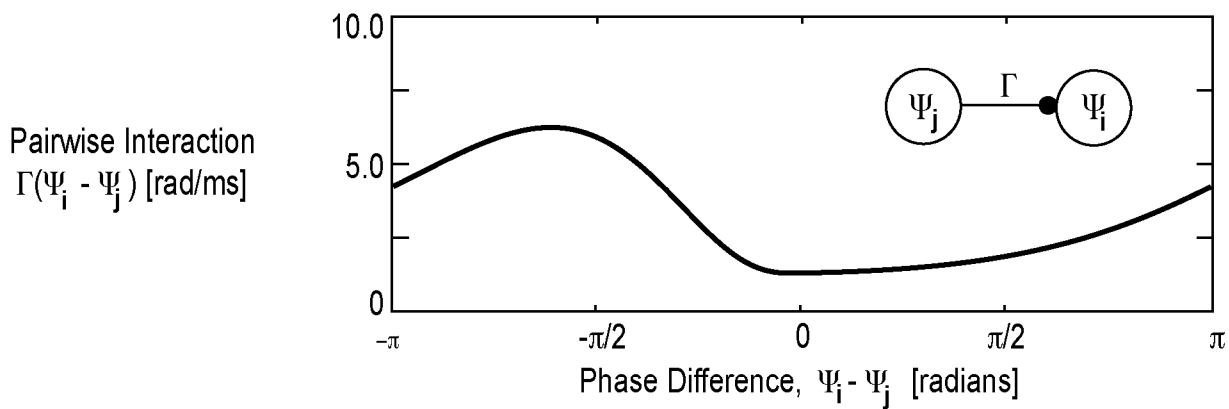
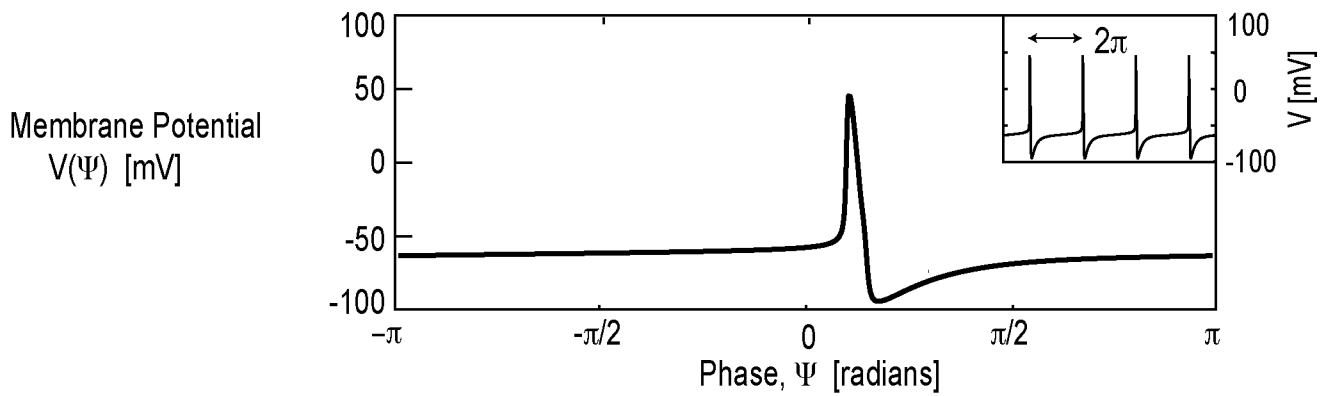
Pairwise Interaction between Neuronal Oscillators, $\Gamma(\psi_i - \psi_j)$ is the Correlation of Presynaptic Activation with Postsynaptic Response



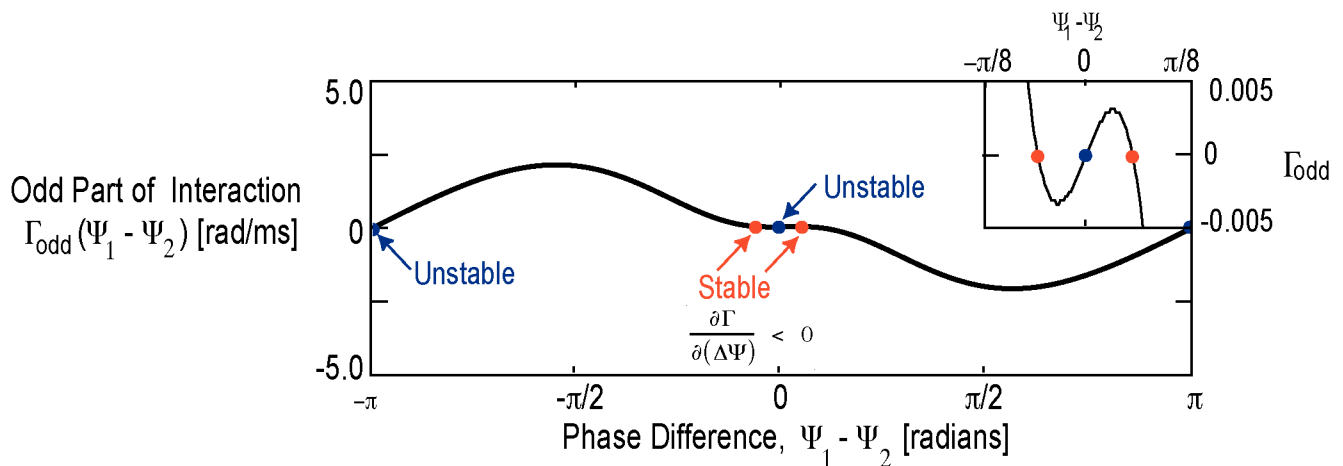
$$\begin{aligned} \Gamma(\Psi_i - \Psi_j) &= \frac{\varepsilon}{2\pi} \int_{-\pi}^{\pi} d\theta \mathbf{R}(\Psi_i + \theta) \mathbf{S}(\Psi_j + \theta) \\ &= \frac{\varepsilon}{2\pi} \int_{-\pi}^{\pi} d\theta \mathbf{R}(\theta) \mathbf{S}\left[\theta - \underbrace{(\Psi_i - \Psi_j)}_{\text{Phase difference}}\right] \end{aligned}$$



Nature of the Pairwise Interaction is Revealed by the Phase Shifts Between Two Reciprocally Connected Neuronal Oscillators



$$\begin{aligned} \frac{\partial \Psi_i}{\partial t} &= \omega + \Gamma(\Psi_i - \Psi_j) \\ \frac{\partial \Psi_j}{\partial t} &= \omega + \Gamma(\Psi_j - \Psi_i) \end{aligned} \quad \Rightarrow \quad \frac{\partial(\Psi_i - \Psi_j)}{\partial t} = \Gamma(\Psi_i - \Psi_j) - \Gamma(\Psi_j - \Psi_i)$$



Two Neuronal Oscillators with Synaptic Coupling

Minimal Model for Insight into Network Behavior

(Hansel, Mato & Meunier 1993, 1995; von der Vreeswijk, Abbott & Ermentrout 1994)

Simpliest phase sensitivity function: $Z(\psi) = \sin(\psi)$ with $\psi = \omega t \text{ modulo}(2\pi)$

Perturbation given by: $P(\psi) = \frac{g}{\tau} \frac{\psi}{\omega\tau} e^{-\psi/\omega\tau}$

Asymmetric part of the interaction controls $\Delta\psi \equiv \psi - \psi'$

$$\Gamma(\Delta\psi) - \Gamma(-\Delta\psi) = \frac{\epsilon}{2\pi} \int_{-\pi}^{\pi} d\theta \vec{Z}(\psi + \theta) \cdot \vec{P}(\psi' + \theta) \propto g \frac{(\omega\tau)^2 - 1}{[1 + (\omega\tau)^2]^2} \sin(\Delta\psi)$$

Stability (with our sign convention) requires $\frac{\partial [\Gamma(\Delta\psi) - \Gamma(-\Delta\psi)]}{\Delta\psi} < 0$

For inhibition ($g < 0$), synchrony ($\psi' = \psi$) is stable for $\tau > \frac{1}{\omega}$

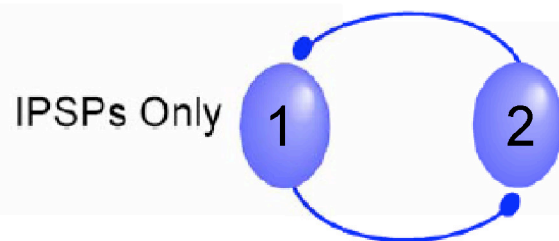
Synchronous, all inhibitory networks are observed!

Reciprocal, Kuromoto-like Inhibitory Coupling Among Pairs of Neurons

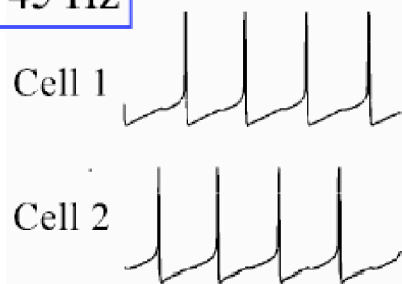
Firing Switches from Antisynchrony to Synchrony near 80 Hz

(data from Barry Connors Laboratory)

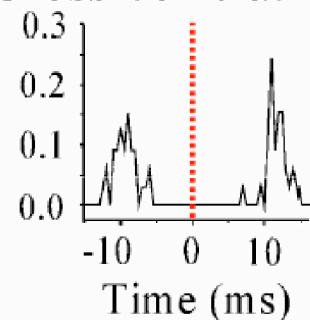
$$\Gamma(\Delta\psi) - \Gamma(-\Delta\psi) = g \frac{(\omega\tau)^2 - 1}{[1 + (\omega\tau)^2]^2} \sin(\Delta\psi) < 0 \text{ for } \omega > \tau^{-1}$$



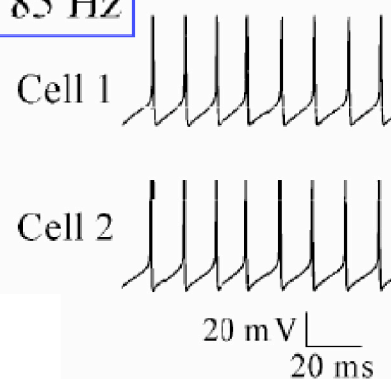
45 Hz



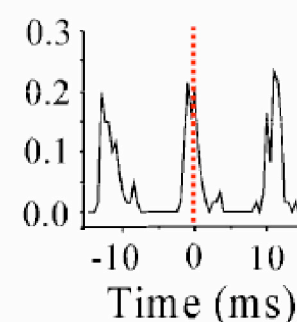
Cross-correlation



85 Hz

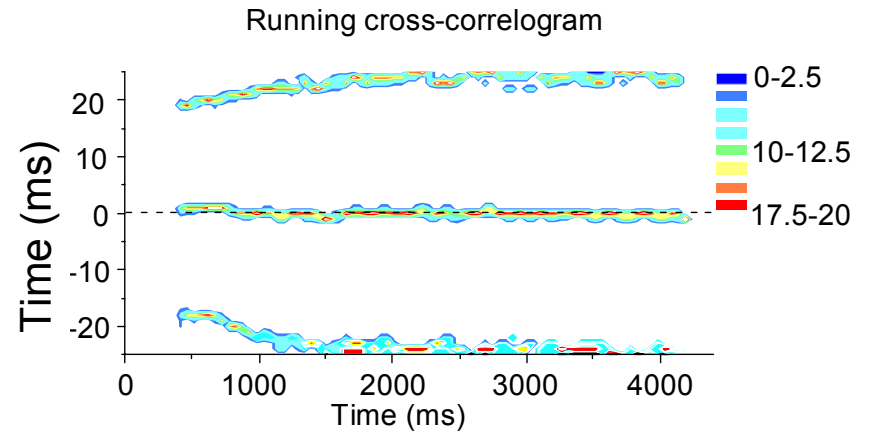
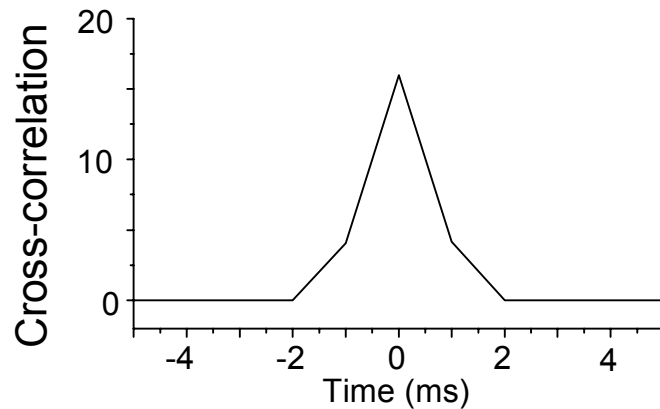
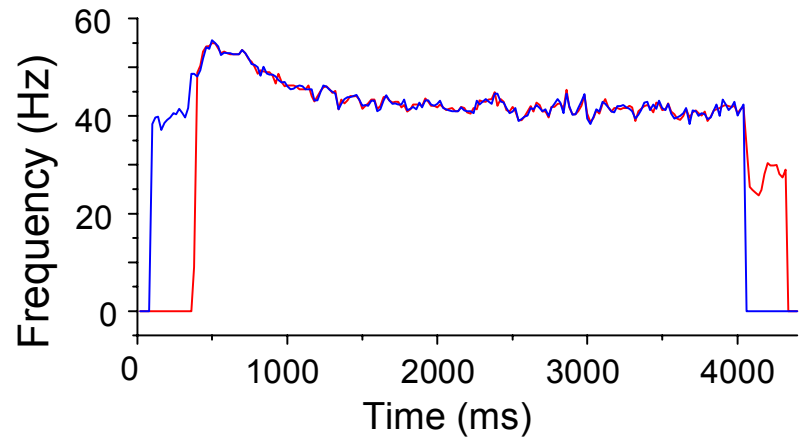
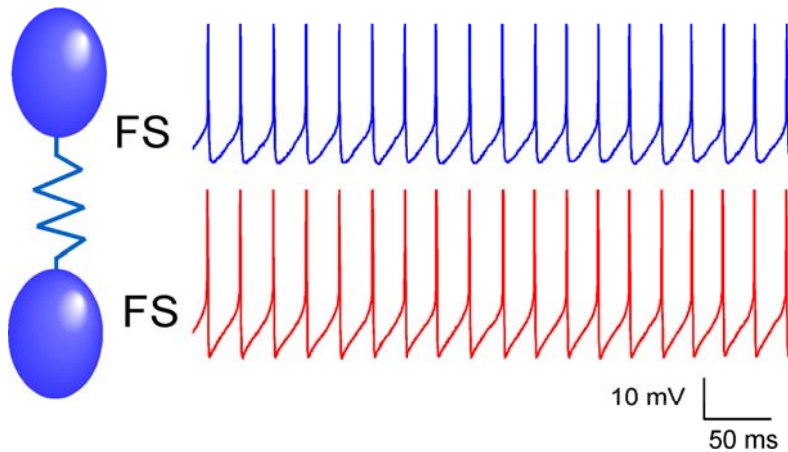


Cross-correlation

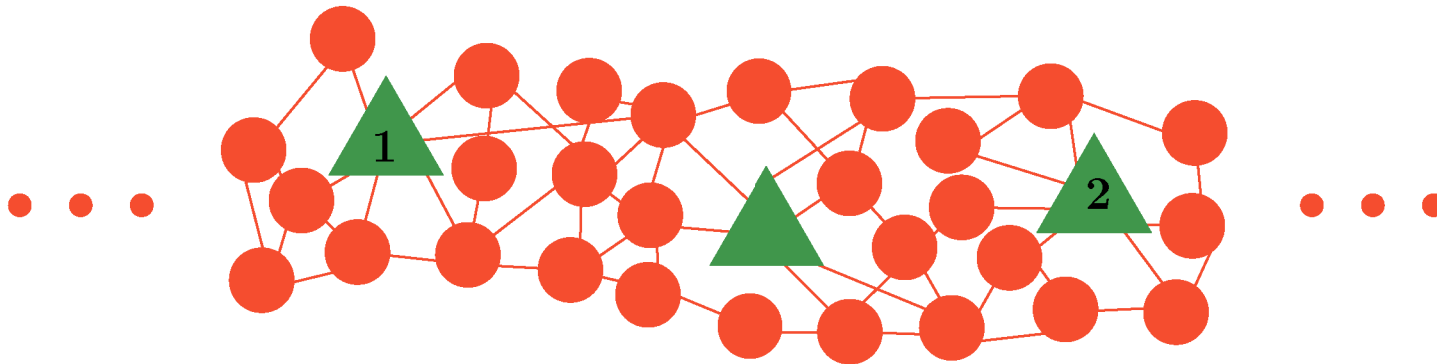


NEOCORTEX

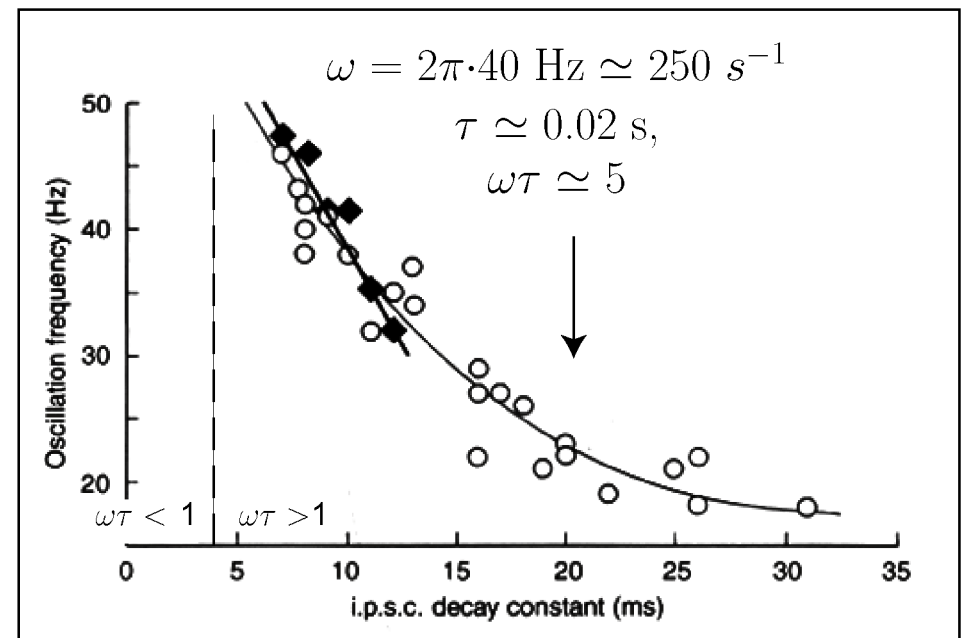
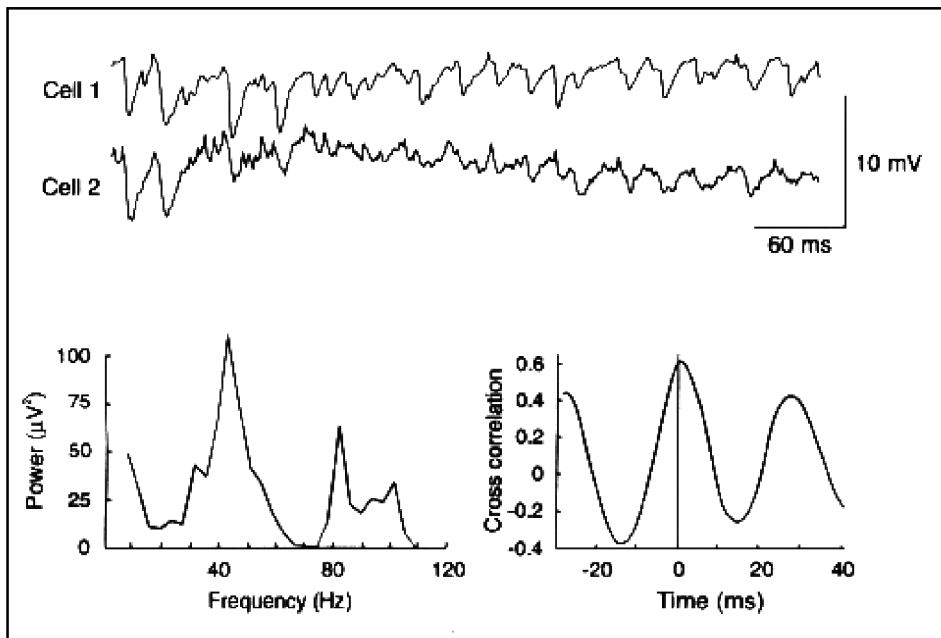
Electrical synapses can promote close spike synchrony



Synchronized Oscillations in Interneuron (all inhibitory) Networks (Whittington, Traub and Jeffreys 1995)



$$\Gamma(\Delta\psi) - \Gamma(-\Delta\psi) = g \frac{(\omega\tau)^2 - 1}{[1 + (\omega\tau)^2]^2} \sin(\Delta\psi)$$



$t e^{-\alpha t}$ Coupling between Hodgken-Huxley Neurons

