Neural Oscillators: Weak Coupling

Part I:
Motivation, PTC, PRC, Isochron and Adjoint

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Single Neuron

[Diagram of a single neuron]

Networks of Neurons

[Diagram of a network of neurons]
An acrimonious battle!!!

Two main approaches:
- The details of the action potentials (spikes) matter a great deal,
- We are concerned only with the firing rates of populations.
Why oscillators?

If spikes matter, then it is important to understand how the spikes of one neuron affect the timing of the spikes of another neuron to which it is somehow (synaptically or ... ) connected.

A neuron with slowly varying input current can be regarded as an oscillator.
Why oscillators?

Oscillatory networks arise in many areas of neuroscience, like motor patterns for repetitive activity such as

- locomotion,
- feeding,
- breathing,
- and mating.

Why oscillators?

A binding problem: A major question in cognitive psychology concerns how different sensory modalities are brought together to produce a unified percept.

Neural oscillations could solve this problem. That is, different areas of the brain would synchronize when there was a common percept.[Von der Malsburg and Schneider]

Wolf Singers group found tantalizing evidence for this theory in electrical recordings of the cat visual cortex. So-called gamma oscillations (30-80 Hz) were found to have a high degree of synchrony under certain situations presumably related to perceptual grouping.
Neural Oscillators, Phase, and Isochrons

What is Isochron?

Consider the dynamical system derived by differential equation

\[
\frac{d}{dt} X = F(X),
\]

and let \( \Gamma \) be a \( T \)-periodic limit cycle. We can parameterize \( \Gamma \) by time and define a phase, \( \theta \in [0, T) \) along the limit cycle.
What is Isochron?

So I can define $\Theta : \Gamma \rightarrow [0, T)$. Let $\Gamma$ be a stable (attractive) limit cycle.

There exist a neighborhood of $\Gamma$, like $U_\Gamma$, such that for any $y \in U_\Gamma$, we have

$$d(\Gamma, X(y, t)) \rightarrow 0, \quad as \ t \rightarrow \infty.$$
What is Isochron?

So we can extend the function $\Theta$ over $U_\Gamma$, i.e. $\Theta : U_\Gamma \rightarrow [0, T)$, that is for any $y \in U_\Gamma$, we define $\Theta(y) = \Theta(x)$, where $x \in \Gamma$ such that

$$||X(x, t) - X(y, t)|| \rightarrow 0, \quad \text{as } t \rightarrow \infty.$$ 

We call the level sets of $\Theta$, set of points $y \in U_\Gamma$ with the same asymptotic phase, the **isochron of the limit cycle** $\Gamma$. 

![Diagram showing isochrons and limit cycle](image)
What is Isochron?

For any $x \in \Gamma$, We denote the isochron through a point $x$, as $N(x)$. Isochrons are local invariant sections; that is, for a point $y \in N(x)$, we have $X(T; y) \in N(x)$. The map $y \rightarrow X(T; y)$ is a Poincare map for the limit cycle which takes time exactly $T$ to return.

What is Isochron?

In practice, the isochrons can only be computed numerically, except for some simple models.

Morris-Lecar model:

\[
\begin{align*}
C \frac{dV}{dt} &= I - g_L(V - V_L) - g_{Ca} M_{ss}(V - V_{Ca}) - g_K N(V - V_K) \\
\frac{dN}{dt} &= \frac{N - N_{ss}}{\tau_N}
\end{align*}
\]

where

\[
\begin{align*}
M_{ss} &= \frac{1}{2} \cdot (1 + \tanh \left[ \frac{V - V_1}{V_2} \right]) \\
N_{ss} &= \frac{1}{2} \cdot (1 + \tanh \left[ \frac{V - V_3}{V_4} \right]) \\
\tau_N &= \frac{1}{\phi \cosh \left[ \frac{V - V_3}{2V_4} \right]}
\end{align*}
\]

and

\(V\): membrane potential,

\(N\): recovery variable: the probability that the \(K^+\) channel is conducting.
The function $\Theta(x)$ is not at all isotropic and shows very slow changes near the spike and very rapid changes near the ghost of the saddlenode bifurcation.
Phase resetting and transition curves

Rolling along the limit cycle, a brief stimulus is given, a perturbation to the vector field at phase $\phi$. This perturbation puts us on the isochron for $\phi'$ so that the phase of the oscillator is reset to a different value which depends on its initial phase.
Phase resetting and transition curves

For each phase $\phi$ at which the stimulus is applied, we get a new phase $\phi'$. The map from old phase $\phi$ to new phase $\phi'$ is called the phase transition curve (PTC), $\phi' = P(\phi)$. In fact, we have $P : [0, T) \rightarrow [0, T)$. 
Phase resetting and transition curves

Winfree and others have noted that the PTC has two different topological forms:

- **type 0 - strong resetting** - the map $P$ is **not** an invertible map of the interval $[0, T)$ to itself,
- **type 1 - weak resetting** - the map $P$ is an invertible map of the interval $[0, T)$ to itself.
Phase resetting and transition curves

Examples:

- If the stimulus is so strong that the phase is always reset to 0, that is, the neuron spikes immediately, then it is type 0 (strong).
- For the classic integrate-and-fire model, any finite increase of the voltage always results in type 0 resetting,
- For the quadratic integrate-and-fire model with infinite reset, all perturbations show type 1 resetting.
Experimentalists are often interested not in the PTC, but rather in the actual change in phase due to the perturbation.

**Phase Resetting Curve (PRC):** It is defined as the difference between the new phase and the old phase:

$$\Delta(\phi) := \phi' - \phi = P(\phi) - \phi$$
Phase resetting and transition curves

Some experimental results computed PRCs from cortical and related neurons, for excitatory (i) and inhibitory (ii) synaptic perturbations.
Phase resetting and transition curves

For any $x \in \Gamma$, we have that

$$\frac{d}{dt} \Theta = 1.$$ 

Suppose at time $\phi$ the stimulus is applied and this causes a shift to a new phase $\phi'$. The time until the next spike is just $\tau = T - \phi'$, so the time of the next spike is $T' = \phi + \tau = \phi + T - \phi' = T - \Delta(\phi)$. Thus, we have

$$\Delta(\phi) = T - T'.$$
Phase resetting and transition curves

Typically, if one is trying to measure a PRC either experimentally or from a numerical simulation, the time of the next event, e.g., is measured as a function of the time of the stimulus. This is just $T'$. If $T' < T$, then the stimulus advances the phase (speeds up the cycle) and vice versa.
Phase Resetting Curve and Phase function

Let \( x = X_0(\phi) \in \Gamma \) be the point on the limit cycle, \( X_0(t) \), with phase (time) \( \phi \in [0, T) \), i.e. \( \Theta(x) = \phi \). Consider an arbitrary perturbation, \( y \in \mathbb{R}^n \), of the vector field. The new phase is

\[
\phi' = \Theta(x + y) = \phi + \nabla_x \Theta(x) \cdot y + O(||y||^2).
\]

Thus, for small perturbations

\[
\Delta(\phi; y) = \phi' - \phi = \nabla_x \Theta(x) \cdot y + O(||y||^2) \approx \nabla_x \Theta(x) \cdot y.
\]

Define the vector function \( Z : [0, T) \to \mathbb{R}^n \) as

\[
Z(\phi) = \nabla_x \Theta(X_0(\phi))
\]
Phase Resetting Curve and Phase function

As we have

\[ \Delta(\phi; y) \approx \nabla_x \Theta(x) \cdot y = Z(\phi) \cdot y, \]

where \( \Theta(\phi) = x \), the function \( Z \) provides a complete description of how infinitesimal perturbations of the limit cycle change its phase.

Kuramoto introduced the function \( Z(\phi) \) and Winfree was a long-time proponent of the utility of the PRC. In the correct limit, we see that they are related. The PRC is exactly related to \( \Theta(X_0(\phi) + y) - \phi) \), but in practice the function \( \Theta(x) \), for arbitrary \( x \) is very difficult to calculate.

However, the gradient evaluated at the limit cycle, the function \( Z(\phi) \) is very simple to compute.
How to calculate $Z$?

The function $Z(\phi)$ could be computed by applying small stimuli to the limit cycle along each of the $n$ components of the limit cycle and then linearly interpolating the results to zero amplitude. Try it once!

However! However! However! However!

However, it turns out that the function $Z$ is the solution to a linear differential equation which is closely related to the linearization of

$$\frac{d}{dt}X = F(X),$$

about the limit cycle.
How to calculate $Z$?

Let $X_0(t)$ is a $T$-periodic limit cycle solution to

$$\frac{d}{dt} X = F(X)$$

and

$$A(t) := D_X F(X)|_{X_0(t)}$$

be the $n \times n$ matrix resulting from linearizing around the limit cycle. Then solutions to the linearized equation satisfy

$$(L y)(t) := \frac{d}{dt} y(t) - A(t)y(t) = 0.$$ 

For the adjoint of $L$, satisfies $< u, L v > = < L^* u, v >$ and therefore

$$(L^* y)(t) := -\frac{d}{dt} y(t) - A^H(t)y(t) = 0.$$
How to calculate $Z$?

Recall that the asymptotic phase to an infinitesimal perturbation $y(t)$ is given by $Z(t) \cdot y(t)$. By definition, this phase is independent of time. Note that since $y(t)$ is arbitrarily close to the limit cycle, its dynamics are linear, so $Ly = 0$. Thus,

$$
0 = \frac{d}{dt}Z(t) \cdot y(t) = \frac{dZ(t)}{dt} \cdot y(t) + Z(t) \cdot \frac{dy(t)}{dt} = \frac{dZ(t)}{dt} \cdot y(t) + Z(t) \cdot A(t)y(t) = \frac{dZ(t)}{dt} \cdot y(t) + A^H(t)Z(t) \cdot y(t) = \left[ \frac{dZ(t)}{dt} + A^H(t)Z(t) \right] \cdot y(t) = -L^*Z(t) \cdot y(t)
$$

Since $y(t)$ is arbitrary, we must have that

$$L^*Z(t) = 0$$
How to calculate $Z$?

If $X_0(t)$ is a stable limit cycle, then the operator $L$ has a nullspace spanned by scalar multiples of $\frac{dX_0(t)}{dt}$ which is a periodic function. The adjoint has a one-dimensional nullspace in the space of $T$-periodic functions in $\mathbb{R}^n$, so $Z(t)$ must be proportional to this eigenfunction.

$\Theta(X_0(\phi)) = \phi$. By Differentiating this with respect to $\phi$, we see that

$$Z(\phi) \cdot \frac{dX_0(\phi)}{d\phi} = 1.$$ 

This uniquely defines $Z(t)$. 
How to calculate $Z$?

Therefore $Z(t)$ is the (unique) solution of

$$\begin{cases}
    \mathbf{L}^*Z(t) = 0 \\
    Z(\phi) \cdot \frac{dX_0(\phi)}{d\phi} = 1
\end{cases}$$

Numerically solving $\ast y = 0$ is done by integrating the equation

$$\frac{dy}{dt} = -A^H(t)y(t)$$

backward in time. Since the limit cycle is asymptotically stable, backward integration damps out all components except the periodic one which is the solution of the adjoint equation. Suitable multiplication by a scalar provides the necessary normalization.
Ring Models

Consider the differential equation

\[ x' = f(x) \]

where \( f(x) > 0 \) and \( x \in S^1 \). Thus, \( f(x + 1) = f(x) \). This equation has a \( T \)-periodic solution \( x_0(t) \) with period

\[ T = \int_0^1 \frac{1}{f(x)} \, dx. \]

The adjoint is just

\[ z(t) = \frac{1}{f(x_0(t))}, \]

since

\[ z(t) \frac{dx_0}{dt} = 1. \]
Ring Models

Note that $z(t)$ is always positive and one can only phase-advance the oscillator when the stimulus is positive. On the other hand, plotting $-z(t)$ as would be the response to an inhibitory stimulus.

For example, consider the function $f(x) = 1 + a \cos(2\pi x)$, where $|a| < 1$. Then the period is

$$T = \frac{1}{\sqrt{1 - a^2}}$$

and a bit of algebra shows that the adjoint is just

$$z(t) = \frac{1 - a \cos(2\pi t/T)}{1 - a^2}$$
Kopell and Howard introduced a class of nonlinear oscillators described by

\[
\begin{align*}
    u' &= \lambda(\sqrt{u^2 + v^2})u - \omega(\sqrt{u^2 + v^2})v \\
    v' &= \lambda(\sqrt{u^2 + v^2})v + \omega(\sqrt{u^2 + v^2})u
\end{align*}
\]

Suppose \(\lambda(1) = 0, \omega(1) = 1\) and \(\lambda'(1) < 0\). Then there is a stable limit cycle solution

\[(u, v) = (\cos t, \sin t)\]

and the adjoint for this system is

\[(u^*, v^*) = (a \cos t - \sin t, a \sin t + \cos t)\]

where \(a = \omega'(1)/\lambda'(1)\).
Quadratic Integrate-and-Fire Model

The quadratic integrate-and-fire model with infinite reset,

\[ V' = V^2 + I, \]

is a singular example of a scalar ring model. The solution to this is

\[ V = -\sqrt{I} \cot(\sqrt{I} t). \]

So the adjoint is

\[ z(t) = \frac{1}{V'(t)} = \frac{\sin^2(\sqrt{I} t)}{I} = \frac{1 - \cos(2\sqrt{I} t)}{I}. \]