The Mesoscopic Brain

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Synchronization

Both fMRI and MEG are based on synchronization phenomena (Strogatz, 2003).

We would'nt have anything to measure unless neurons were also able to synchronize (their post-synaptic or membrane potentials).

Neurons are most sensitive to incoming signals if the incoming spikes are synchronised (Wang, 2010).

Hence spike-to-spike synchrony and field synchrony are important.

Synchronization

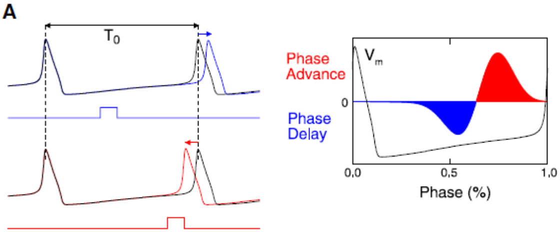
Whether two or more neurons will synchronize depends on at least two characteristics

- Membrane Dynamics. How sensitive spiking is to perturbations in the membrane potential. This is described by the Phase Response Curve (PRC).
- Synaptic Dynamics. What perturbation is delivered to the membrane potential by an incoming spike. This is quantified by the perturbation function.

Both of these criteria are taken into account by the theory of Weakly Coupled Oscillators (WCOs).

Neuronal Phase Response Curves

Stimulus at time t, or equivalently phase ϕ, induces an earlier or later spike.



V_m is the membrane potential. The change in phase is

$$z = \frac{t_0 - t_1}{t_0}$$

As a function of stimulus phase we have $z(\phi)$ the Phase Response Curve (PRC).

Can be found experimentally using a perturbation method, from models using analytical or numerical method, or analytically for oscillations arising from certain classes of dynamical bifurcations.

Hodgkin Huxley PRC

If an HH cell receives a spike just after firing, this will delay the emission of the next spike. This is because recovery processes are delayed (negative lobe).

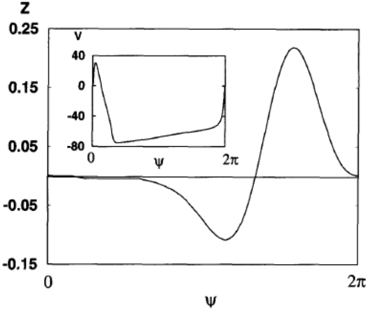


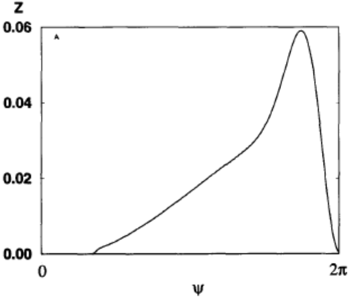
Figure 2: The response function Z along one cycle of the HH model. The frequency of the neuron is approximately 68 Hz. The inset shows the evolution of the membrane potential during the oscillation.

If it receives a spike later on, this will advance the firing of the next spike (positive lobe). Plot from Hansel et al (1995).

Connor-Stevens PRC

Conner and Stevens have added a slow K current, the so-called A-current, to the Hodgkin Huxley model so that it better reproduces the range of firing rates of human cortical neurons.

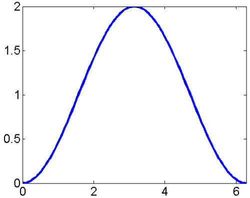
A reduced version of this model, the Hindmarsh-Rose model, was presented in the last lecture.



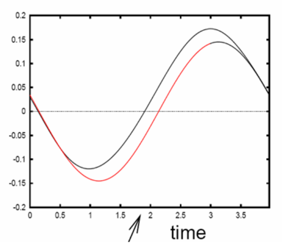
The Connor-Stevens PRC (Hansel et al 1995)

Type 1 and 2 PRCs

Type 1 PRCs are strictly positive.

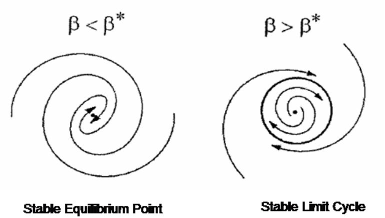


Type 2 PRCs are positive and negative.

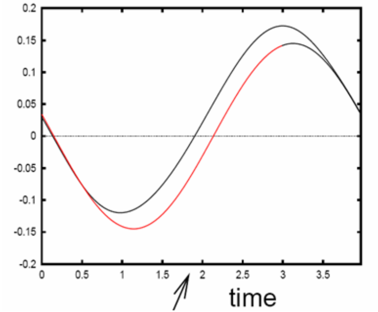


Hopf PRC

Oscillations produced by Hopf bifurcations

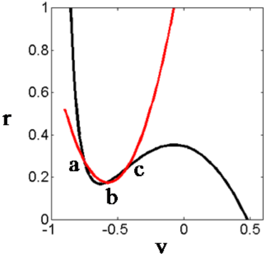


have $z(\phi) = a\cos\phi + b\sin\phi$ (Ermentrout and Terman, 2010)

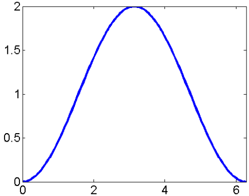


Saddle Node PRC

Oscillations produced by Saddle Node bifurcations



have $z(\phi) = 1 - \cos\phi$ (Ermentrout and Terman, 2010)



Integrate and Fire

The Integrate and Fire (IF) model neuron avoids a biophysical description of action potential generation. It models only subthreshold membrane dynamics. In its simplest form we have

$$C_m \dot{v} = -g_L(v - E_L) + I_e$$

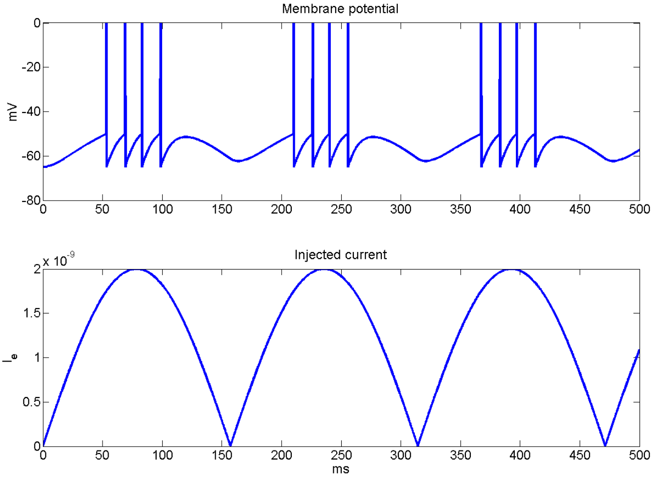
where g_L is a leak conductance and E_L is the leak equilibrium potential. I_e is applied current.

When the potential, v reaches a threshold, v_T, a supplementary rule resets it to resting potential, v_r, and a spike (delta function) is emitted at that time point.

Later on, we will add synapses

$$C_m \dot{v} = -g_L(v - E_L) - g_s(v - E_s) + I_e$$

Integrate and Fire



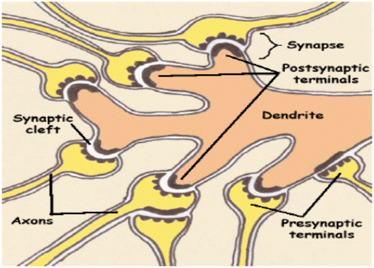
Synapses

Synapses can be incorporated into conductance based models with additional terms

$$C_m \dot{v} = -g_L(v - E_L) - g_s(v - E_s)$$

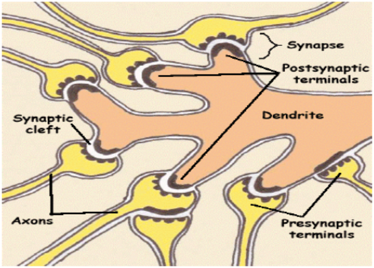
where g_s is the conductivity of a particular synaptic type and E_s is the equilibrium potential. If E_s is above spiking threshold the synapse is excitatory.

Differential equations for g_s can describe the presynaptic release of neurotransmitter, and opening of postsynaptic channels, up to various levels of detail.



Synapses

Glutamate and GABA are the major excitatory and inhibitory neurotransmitters.



The principal receptors for glutamate are AMPA and NMDA.

The principal receptors for GABA are GABA-A and GABA-B.

See eg. Dayan and Abbott (2001) for more.

Integrate and Fire Synapses

In the Integrate and Fire framework one can add conductance-based synapses as previously

$$C_m \dot{v} = -g_L(v - E_L) - g_s(v - E_s)$$

and add differential equations for g_s.

Or one can work with synaptic kernels

$$C_m \dot{v} = -g_L(v - E_L) - a_{max} \sum_i s(t - t_i)$$

where a_{max} is the maximum response, t_i indexes the time of the ith received spike, and $s(t)$ describes the synaptic kernel that produces the postsynaptic response. These are excitatory/inhibitory for positive/negative a_{max}.

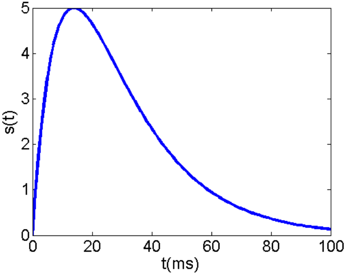
Difference of Exponentials Kernel

A common choice for the synaptic kernel, $s(t)$, is the difference of exponentials function

$$s(t) = a\left(\exp(-t/\tau_1) - \exp(-t/\tau_2)\right)$$

with rise and fall times

$$\begin{aligned} \tau_{rise} &= \frac{\tau_1 \tau_2}{\tau_1 - \tau_2} \\ \tau_{fall} &= \tau_1 \end{aligned}$$



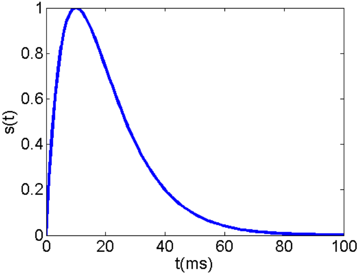
The parameter $a = 1/5$ here will ensure a normalised response.

Alpha Function Kernel

An alpha function synapse

$$s(t) = \frac{t}{\tau_s} \exp[1 - (t/\tau_s)]$$

reaches its peak at τ_s and decays with time constant τ_s.



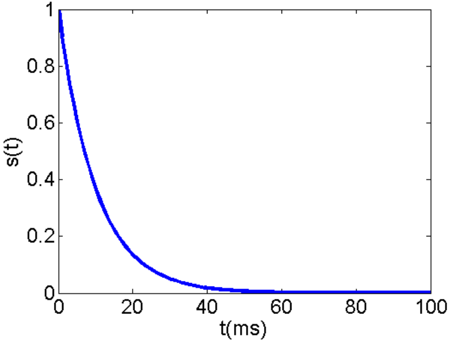
Alpha functions correspond to synaptic dynamics described by second order differential equations. See eg Grimbert and Faugeras (2006) in the context of Neural Mass Models.

Exponential Kernel

An exponential synapse

$$s(t) = \exp(-t/\tau_s)$$

has time constant τ_s.



Typical decay times are $2-3$ms for AMPA, about 100ms for NMDA, $5-10$ms for GABA-A and about 100ms for GABA-B.

Weakly Coupled Oscillators

The theory of Weakly Coupled Oscillators applies to dynamics close to limit cycles.

By assuming weak coupling leads to only small perturbations away from these cycles, one can reduce a high dimensional system of differential equations to one based solely on the phases of the oscillators and pairwise interactions between them.

Dynamics on the limit cycle are given by

$$\begin{aligned} \dot{x}_0 &= F(x_0) \\ x_0(t+T) &= x_0(t) \\ \dot{\phi}(x_0) &= f \end{aligned}$$

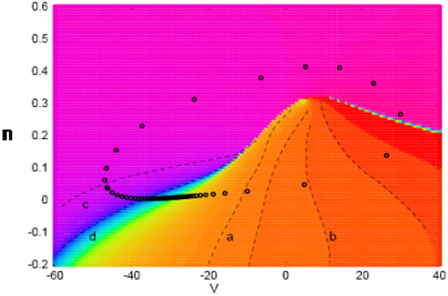
where $f = 1/T$ is the oscillator frequency.

Asymptotic Phase

Morris-Lecar model of a spiking neuron

$$\begin{aligned} C_m\dot{v} &= I_{app} - g_L(v-E_L) - g_K n(v-E_K) - g_{Ca} m(v)(v-E_{ca}) \\ \tau_n(v)\dot{n} &= \phi(n(v)-n) \end{aligned}$$

showing membrane voltage, v, and K activation level.



Isochrons (dashed line) have the same asymptotic phase. From Ermentrout and Terman (2010).

Phase Reduction

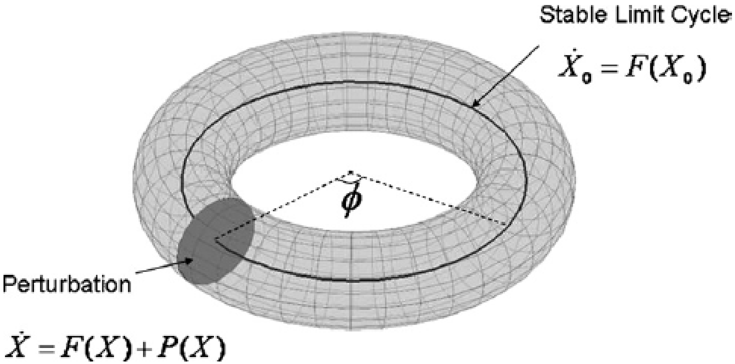


Fig. 1. Phase reduction. The solid circular line shows the state space X_0 of a system on a limit cycle. The limit cycle is assumed stable so that after a small perturbation, the system returns to X_0. Although X_0 may be high-dimensional the state will be uniquely determined by its position around the orbit, or the 'phase', $\phi(X_0)$. The dynamics of perturbed solutions are constrained to the space X shown by the torus. The solid disc corresponds to an 'isochron', meaning that all points on this disc have the same asymptotic phase. Using this notion, as we show in the main text, the high-dimensional state equation can be reduced to the one-dimensional system $\dot{\phi} = f + z(\phi)p(\phi)$. This is known as a *phase reduction*.

Weak Coupling

Dynamics close to the limit cycle are described by

$$\dot{x} = F(x) + P(x)$$

where $P(x)$ is a perturbation. If phase is defined asymptotically then the chain rule gives

$$\begin{aligned} \frac{d\phi(x)}{dt} &= \frac{d\phi(x)}{dx}\frac{dx}{dt} \\ &= \frac{d\phi(x)}{dx}F(x) + \frac{d\phi(x)}{dx}P(x) \end{aligned}$$

We now make use of a *weak coupling* assumption which is that the perturbations are sufficiently small that all terms can be equivalently evaluated at x_0 instead of x. This gives

$$\frac{d\phi(x)}{dt} = \frac{d\phi(x_0)}{dx_0}F(x_0) + \frac{d\phi(x_0)}{dx_0}P(x_0)$$

Perturbation function

Because x_0 maps on to phase via the function $\phi(x_0)$ we can rewrite $P(x_0)$ as $p(\phi)$, known as a perturbation function.

Second, the first term can be written simply as

$$\begin{aligned} \frac{d\phi(x_0)}{dx_0} F(x_0) &= \frac{d\phi(x_0)}{dx_0} \frac{dx_0}{dt} \\ &= \frac{d\phi(x_0)}{dt} \\ &= f \end{aligned}$$

Third, we recognize the PRC as

$$z(\phi) = \frac{d\phi(x_0)}{dx_0}$$

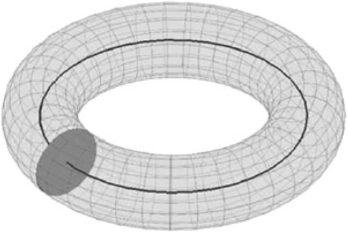
Overall, we can now write

$$\dot{\phi} = f + z(\phi)p(\phi)$$

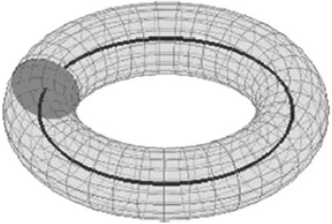
Pair of Oscillators

The same analysis can be applied to a pair of oscillators where the perturbation now depends on both phases

$$\dot{\phi}_1 = f + z(\phi_1) p(\phi_1, \phi_2)$$



$$\dot{\phi}_2 = f + z(\phi_2) p(\phi_2, \phi_1)$$



Phase Interaction Function

We now make a second assumption. This is that the interaction terms are much smaller than the oscillation frequency.

$$z(\phi)p(\phi_1,\phi_2) << f$$

This implies that the phase changes due to interactions are much slower than the speed of the oscillation itself. This allows us to replace the interaction term with its average over a cycle

$$\Gamma_{ij} = \frac{1}{2\pi}\int_0^{2\pi} z_i(\psi)p_{ij}(\psi,\psi+\phi)d\psi$$

which is known as the Phase Interaction Function (PIF). Hence

$$\begin{aligned}\dot{\phi}_1 &= f + \Gamma_{12}(\phi_1 - \phi_2)\\ \dot{\phi}_2 &= f + \Gamma_{21}(\phi_2 - \phi_1)\end{aligned}$$

Multiple Oscillators

The theory applies readily to multiple oscillators

$$\dot{\phi}_i = f_i + \Gamma_{ij}(\phi_i - \phi_j)$$

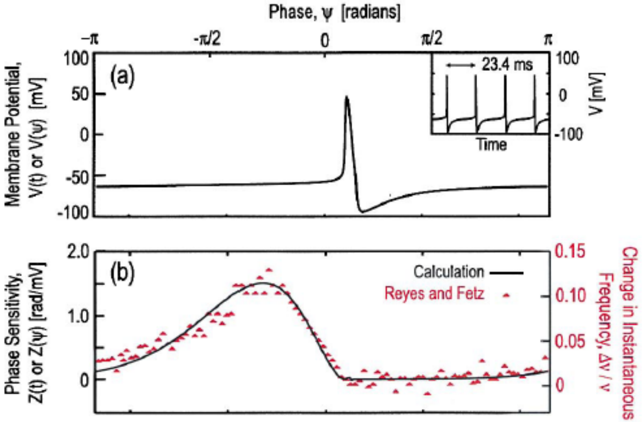
These models can be fitted to phase time series data using an arbitrary order Fourier series representation of the PIFs (Penny et al. 2009).

Bayesian model comparison can be used to select the appropriate Fourier order and to find out which oscillators are enslaved or are mutually entrained (more next lecture).

Oscillators can only be synchronized if the frequencies are sufficiently similar. See Kuramoto (1984) for quantitative results in the context of stochastic WCOs. This has been viewed as a shortcoming (Bartos, 2007) but this selectivity may in fact be an advantage (Hopfield and Brody, 2001).

Motor Neuron

Ermentrout and Kleinfeld (2001) modelled a motor neuron using a HH-type formalism. They computed the PRC. Red dotted lines show PRC measured experimentally.

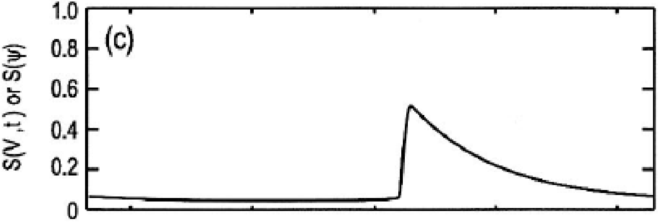


Synaptic Perturbation

The perturbation term for a synapse is

$$p(\phi_i, \phi_j) = -\frac{g_{max}}{C_m} S(\phi_j)[v(\phi_i) - E_{syn}]$$

where g_{max} is the maximum conductance, C_m is the membrane conductance, E_{syn} is the equilibrium potential. Synapses in this model had finite rise and fall times.

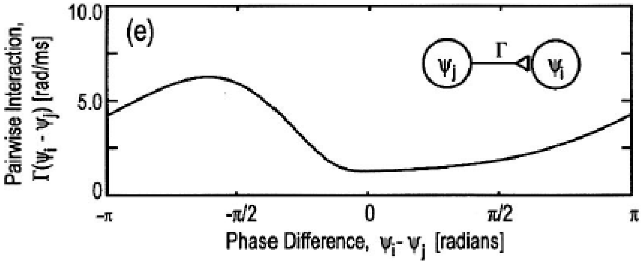


We consider excitatory synapses.

Phase Interaction Function

The Phase Interaction Function (PIF) is then

$$\Gamma_{ij} = \frac{1}{2\pi} \int_0^{2\pi} z_i(\psi) p_{ij}(\psi, \psi + \phi) d\psi$$



Synchronization Dynamics

If we have two oscillators

$$\begin{aligned}\dot{\phi}_1 &= f + \Gamma_{12}(\phi_1 - \phi_2)\\ \dot{\phi}_2 &= f + \Gamma_{21}(\phi_2 - \phi_1)\end{aligned}$$

then the relative phase is given by

$$\phi = \phi_1 - \phi_2$$

The stable fixed points of this one-dimensional system then indicate at what phase synchronization is achieved (if at all). We have

$$\begin{aligned}\dot{\phi} &= \dot{\phi}_1 - \dot{\phi}_2\\ &= \Gamma_{12}(\phi) - \Gamma_{21}(-\phi)\end{aligned}$$

If the PIFs are the same for each neuron we have

$$\dot{\phi} = \Gamma_{odd}(\phi)$$

where

$$\Gamma_{odd}(\phi) = \Gamma(\phi) - \Gamma(-\phi)$$

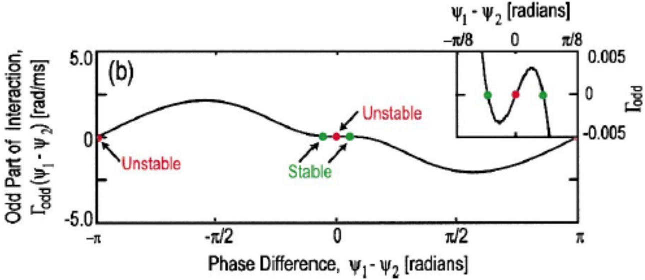
which is the odd part of the PIF.

Synchronization Dynamics

The fixed points ϕ_{FP} are the values of ϕ for which $\Gamma_{odd}(\phi) = 0$. A local first order Taylor expansion

$$\Gamma_{odd}(\phi) = \Gamma_{odd}(\phi_{FP}) + \frac{d\Gamma_{odd}}{d\phi}(\phi - \phi_{FP}) + \ldots$$

then shows that fixed points for which the derivative is negative, will be stable.

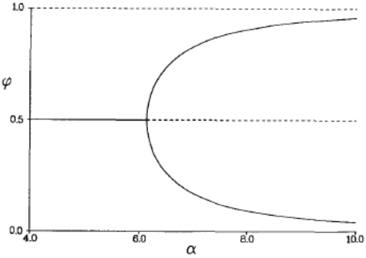


For the motor neuron, the two points each side of $\phi = 0$ are stable.

Mutual Excitation

Van Vreeswijk et al. (1994) have shown using WCO theory that cells having synapses with fast rise times (relative to the oscillation frequency) can be synchronized in-phase by mutual excitation.

For slower synapses, mutual excitation leads to out-of-phase sync. So unless oscillation is slow mutual excitation will not produce in-phase sync. Mutual excitation can produce in-phase sync at theta, alpha frequencies (Wang, 2010).

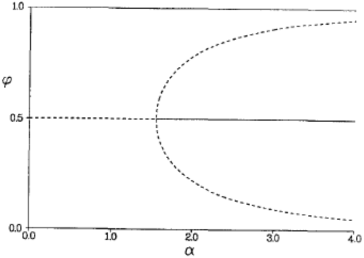


IF cells with alpha function synapses, where α is speed of synapse relative to oscillation frequency. Solid line for stable, dotted for unstable.

Mutual Inhibition

For fast rise times (relative to the oscillation frequency) mutual inhibition produces in-phase or out-of-phase sync. For slower rise times (or higher frequencies) mutual inhibition produces in-sync phase.

In practice, mutual inhibition produces in-phase sync at gamma frequencies (Wang, 2010).



IF cells with alpha function synapses, where α is speed of synapse relative to oscillation frequency. Solid line for stable, dotted for unstable.

Spike Frequency Adaptation

For constant current inputs the spike rates of neuronal cells are known to reduce over time. This is known as Spike Rate or Spike Frequency Adaptation (SFA).

A calcium activated potassium current, I_{KCa}, is thought to underlie this phenomenon. And to a lesser degree the I_M potassium current (Wang, 2010). These currents can be modelled in detail.

Changing the I_M current can change the PRC of a cell from type 1 to type 2.

Spike Frequency Adaptation

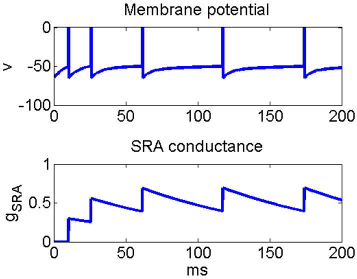
They can also be modelled using IF cells by including an additional current (Ch5, Dayan and Abbott, 2001)

$$\tau \dot{v} = E_L - v - r_m g_{sra}(v - E_k) + r_m I_e$$

which when activated will hyperpolarize the neuron. This current evolves according to

$$\tau_{sra} \dot{g}_{sra} = -g_{sra}$$

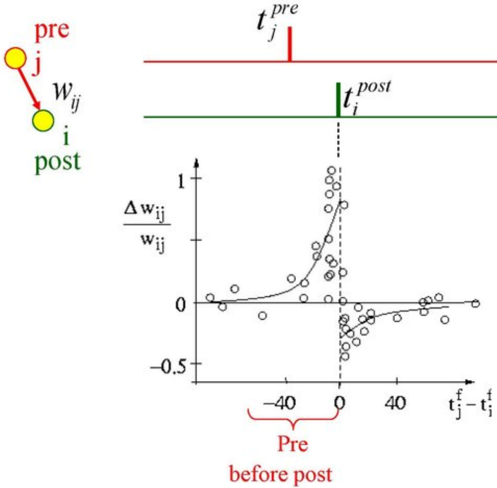
and whenever the cell fires a spike g_{sra} is incremented by Δg.



This current will build up after repeated firing and so cause firing rate adaptation ($\tau_{sra} = 100$ms).

Spike Timing Dependent Plasticity

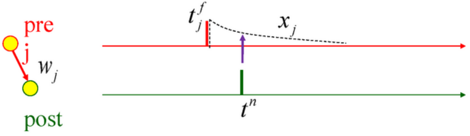
This is a timing-based form of Hebbian learning that allows for increases and decreases in synaptic strength.

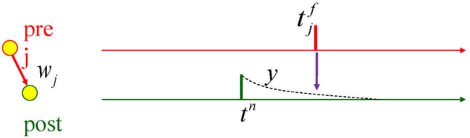


From Sjostrom and Gerstner (2010), Scholarpedia, 5(2):1362.

Spike Timing Dependent Plasticity

STDP can be implemented by local variables. The top trace shows a presynaptic spike t_j^f exciting activity of a variable x_j which then decays. This might be the proportion of open NMDA channels. Synapses are increased by the value of x_j at the time of the postsynaptic spike t^n.





The bottom trace shows a postsynaptic spike t_n exciting activity of a variable y which then decays. This might be the proportion of calcium that has entered the cell. Synapses are decreased by the value of y at the time of the presynaptic spike.

Transient Synchronization

Hopfield and Brody (2001) proposed a model, based on a transient synchronization mechanism, for recognising temporal patterns such as speech.

Each input feature (see later) is coded by a set of neurons having a range of SFA rates.

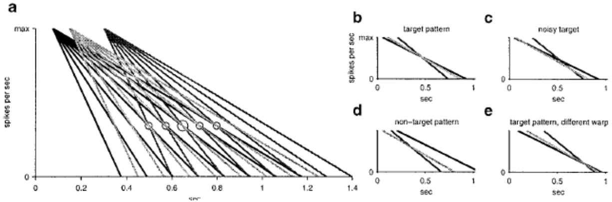
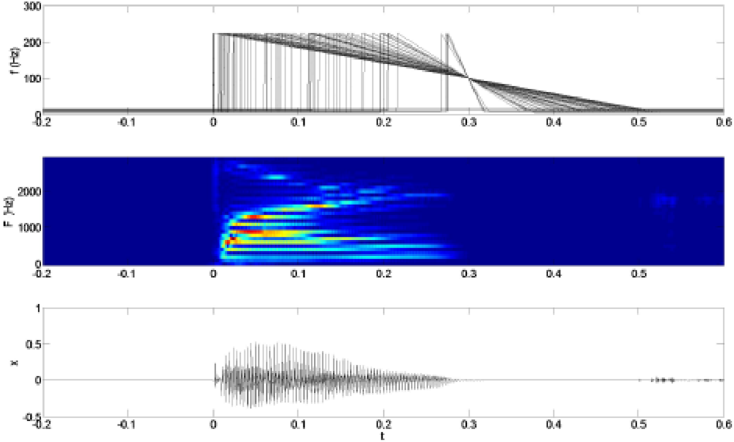


Fig. 1. Time-warp invariant convergence of decaying currents. (*a*) Decaying currents triggered by events in three different channels: one current at 0.075 sec, one at 0.15 sec, and one at 0.3 sec. Responses for different channels are shown in different shades of gray. The rings identify points at which three currents, one for each channel, converge. (*b*) The converging currents for the three currents selected by the larger ring in *a*. (c) An input pattern that is a noisy version of the target pattern. (*d*) A temporal pattern very different from the target pattern. (*e*) A time-warped version of the original pattern.

A subset of these cells will be oscillating at a similar frequency. This means, for a limited period of time, they can potentially synchronize. This representation is time-warp invariant.

Transient Synchronization

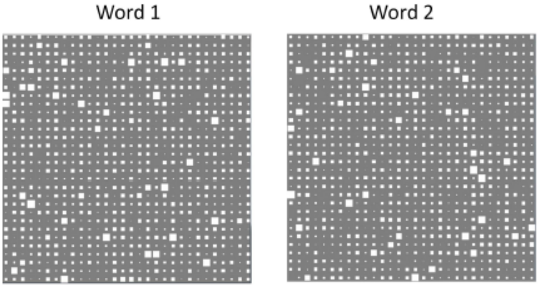


Transient Synchronization

The cells are in a recurrent network.

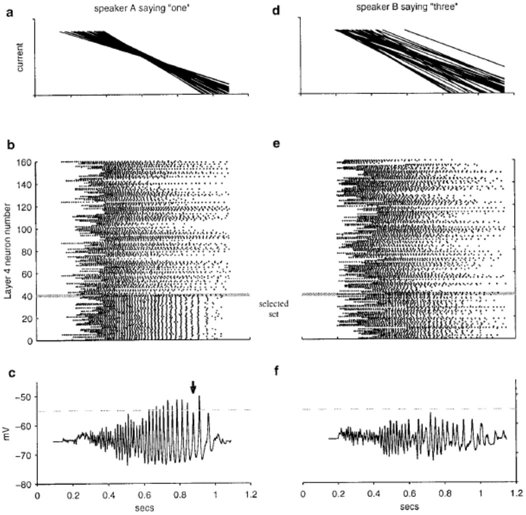
Given sufficient presentations of the temporal patterns, STDP should strengthen synapses between those cells that are firing at similar frequencies.

Hopfield and Brody hand-crafted these connections (using a balance of fast excitation and slow inhibition to the relevant ensembles).



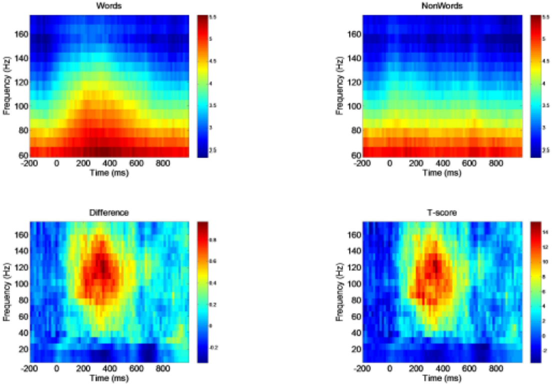
Transient Synchronization

A trained network then encourages synchronization of cells that are firing at similar rates.



Transient Synchronization

This produces transient spike-to-spike synchrony which can be read off by downstream neurons. It will also produce a transient gamma burst in the local field. This is what is observed empirically in ECOG data (Canolty et al. 2007).



But this may be due to sparse syncronization where field activity is synchronized but individual cells fire only rarely ie no spike field coherence (Brunel and Hakim, 2008).

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