

8 Circuits of Phase-Coupled Neuronal Oscillators: Time delays

We return to coupled oscillators and consider the effect of time delay, such as caused by propagation along long axons, among the communication between neurons.

8.1 Propagation delays

There are multiple biophysical mechanism that can delay the impact of one cell on another. The activation of a synapse is one, as are dendritic integration times. These are relatively fixed and typically of a few milliseconds. The longer delays are likely to result from the propagation along axons. If understand this, we return to our "brutalized" model of a neuron and estimate the propagation speed to together with related parameters.

8.1.1 Speed and width of the action potential

We are after the speed of the propagating front. We thus solve the cable equations with the fast onset current, the Na^+ current, which dominates the leading edge of the action potential. We ignore the slower potassium currents and sodium inactivation. In this limit the I-V relation for the Na^+ current can be assumed to follows a cubic dependence of $f(V)$, This yields an equation that is roughly valid on the time-scale of the leading edge of the spike - roughly the first 0.1 ms of the action potential, i.e.,

$$\begin{aligned} \tau \frac{\partial V(x, t)}{\partial t} - \lambda^2 \frac{\partial^2 V(x, t)}{\partial x^2} + \frac{r_m \bar{G}_{leak}}{2\pi a} (V - V_{leak}^{Nernst}) &= \text{Active Currents} \quad (8.1) \\ &= -\frac{r_m \bar{G}_{Na^+}}{2\pi a} f(V) \end{aligned}$$

where λ is the space constant and τ is the time constant of the cell. We recall that in the absence of active currents, the passive part is simply a cable equation. It supports the propagation of a pulse, with an exponentially decaying amplitude, whose front propagates with a speed, denoted μ , given by

$$u = \frac{\lambda}{2\tau}. \quad (8.2)$$

We next perform a self-consistent analysis to determine the speed of propagation and the width of the rising edge in the presence of active currents. We can estimate, from the form of Equation 8.2, that the space constant and the time constant are rescaled as

$$\Lambda \leftarrow \frac{\lambda}{\sqrt{r_m \bar{G}_{Na^+}}}. \quad (8.3)$$

with $r_m \bar{G}_{Na^+} \gg 1$ and

$$T \leftarrow \frac{\tau}{r_m \bar{G}_{Na^+}}, \quad (8.4)$$

respectively, so that that active speed is of order

$$U \sim \frac{u}{\sqrt{r_m \bar{G}_{Na^+}}}. \quad (8.5)$$

This is an increase by about an order of magnitude, and of course active pulses do not decay.

Box 1. A proper calculation of propagation speed

- We begin with the cable equation with the leakage rolled into the source term, i.e.,

$$\tau \frac{dV}{dt} = \lambda^2 \frac{d^2V}{dx^2} - r_m \bar{G}_{Na^+} \frac{(V - V_{rest})(V - V_{thresh})(V - V_{peak})}{v_o^2} \quad (8.6)$$

- Let $V(x, t) = V(x - Ut) \equiv V(z)$, so that

$$-\tau U \frac{dV}{dz} = \lambda^2 \frac{d^2V}{dz^2} - r_m \bar{G}_{Na^+} \frac{(V - V_{rest})(V - V_{thresh})(V - V_{peak})}{v_o^2} \quad (8.7)$$

- We define the width of the front as Λ , which has to be found self consistently. Assume that V propagates as a front when V is not near V_{rest} nor $V = V_{peak}$, where $\frac{dV}{dz} = 0$. We thus take

$$\begin{aligned} \frac{dV}{dz} &\equiv \dot{V} \\ &= \frac{1}{\Lambda} \frac{(V - V_{rest})(V - V_{peak})}{v_o} \end{aligned} \quad (8.8)$$

where the slope is negative as the propagating front moves from a region with $V \approx V_{peak}$ to a region with $V \approx V_{rest}$. Then by the chain rule

$$\begin{aligned} \frac{d^2V}{dz^2} &= \frac{d}{dz} \frac{dV}{dz} \\ &= \left(\frac{d}{dV} \frac{dV}{dz} \right) \frac{dV}{dz} \\ &= \frac{d\dot{V}}{dV} \dot{V} \end{aligned} \quad (8.9)$$

with

$$\begin{aligned} \frac{d\dot{V}}{dV} &= \frac{(V - V_{peak}) + (V - V_{rest})}{\Lambda v_o} \\ &= \frac{2V - (V_{peak} + V_{rest})}{\Lambda v_o}. \end{aligned} \quad (8.10)$$

- Take $V(z \rightarrow \pm\infty) = 0$

- Substitution gives

$$-\tau U \dot{V} = \lambda^2 \frac{d\dot{V}}{dV} \dot{V} - r_m \bar{G}_{Na^+} \Lambda \frac{(V - V_{thresh})}{v_o} \dot{V} \quad (8.11)$$

and we see that the \dot{V} terms cancel out. So

$$-\tau U = \lambda^2 \frac{2V - (V_{peak} + V_{rest})}{\Lambda v_o} - r_m \bar{G}_{Na^+} \Lambda \frac{(V - V_{thresh})}{v_o} \quad (8.12)$$

or

$$-U \frac{\tau}{\Lambda} + \frac{\lambda^2}{\Lambda^2} \frac{(V_{peak} + V_{rest})}{v_o} - r_m \bar{G}_{Na^+} \frac{V_{thresh}}{v_o} = \left(2 \frac{\lambda^2}{\Lambda^2} - r_m \bar{G}_{Na^+} \right) \frac{V}{v_o}. \quad (8.13)$$

Terms proportional to V and those independent of V must independently sum to zero. Thus

$$\Lambda = \lambda \sqrt{\frac{2}{r_m \bar{G}_{Na^+}}} \quad (8.14)$$

and we see that the space constant, or spatial width of the action potential, is shortened by a factor of $r_m \bar{G}_{Na^+}$ during an action potential, as expected. Further,

$$U = \frac{\lambda}{\tau} \sqrt{\frac{r_m \bar{G}_{Na^+}}{2}} \left[\frac{(V_{peak} - V_{thresh}) - (V_{thresh} - V_{rest})}{v_o} \right] \quad (8.15)$$

and we see that the speed is increased by a factor of $r_m \bar{G}_{Na^+}$ compared to λ/τ , as expected, as well as modulated by electrophysiological parameters, which could not be "guessed" at the onset of our calculation. Self consistency requires $V_{peak} > V_{thresh}$ and $V_{thresh} > V_{rest}$. Experimental reality enforces $(V_{peak} > V_{thresh}) > (V_{thresh} > V_{rest})$, with the expectation that $[\dots]$ is of $O(1)$.

When we put in numbers, we get speeds $U \approx 1$ mm/ms. The largest changes in a rhythm takes place over a quarter of a cycle. This for a 40 Hz gamma rhythm this corresponds to a time of 6 ms or a distance of about 6 mm. This is more than the width of one hemisphere for a mouse brain; not so much for a primate.

8.2 Two oscillators with propagation delays.

Let's see what time delays in signal propagation do to synchronization of neuronal signals. We again take

$$\Gamma(\delta\psi - \delta\psi') \equiv -\Gamma_0 \sin(\delta\psi - \delta\psi'). \quad (8.16)$$

Then

$$\begin{aligned} \frac{d\delta\psi(t)}{dt} &= \Gamma_0 \sin(\delta\psi'(t - \tau_D) - \delta\psi(t)) \\ \frac{d\delta\psi'(t)}{dt} &= \Gamma_0 \sin(\delta\psi(t - \tau_D) - \delta\psi'(t)). \end{aligned} \quad (8.17)$$

We assume a solution of the form

$$\begin{aligned}\delta\psi(t) &= \phi(t) + \alpha/2 \\ \delta\psi'(t) &= \phi(t) - \alpha/2\end{aligned}\tag{8.18}$$

where α is a phase shift. The equation for $\delta\psi(t)$ yields

$$\begin{aligned}\frac{d\delta\psi(t)}{dt} &= \Gamma_0 \sin [\phi(t - \tau_D) - \alpha/2 - \phi(t) - \alpha/2] \\ &= \Gamma_0 \sin [\phi(t - \tau_D) - \phi(t) - \alpha] \\ &= \Gamma_0 \sin [\phi(t - \tau_D) - \phi(t)] \cos \alpha - \Gamma_0 \cos [\phi(t - \tau_D) - \phi(t)] \sin \alpha\end{aligned}\tag{8.19}$$

while that for $\delta\psi'(t)$ yields

$$\begin{aligned}\frac{d\delta\psi'(t)}{dt} &= \Gamma_0 \sin [\phi(t - \tau_D) + \alpha/2 - \phi(t) + \alpha/2] \\ &= \Gamma_0 \sin [\phi(t - \tau_D) - \phi(t) + \alpha] \\ &= \Gamma_0 \sin [\phi(t - \tau_D) - \phi(t)] \cos \alpha + \Gamma_0 \cos [\phi(t) - \phi(t - \tau_D)] \sin \alpha\end{aligned}\tag{8.20}$$

The difference at equilibrium yields

$$\frac{d(\delta\psi(t) - \delta\psi'(t))}{dt} = -2\Gamma_0 \cos [\phi(t - \tau_D) - \phi(t)] \sin \alpha.\tag{8.21}$$

At phase locking this becomes

$$0 = \cos [\phi(t - \tau_D) - \phi(t)] \sin \alpha\tag{8.22}$$

Except for the case $\sin \alpha = 0$, we have phase locking for $\phi(t) - \phi(t - \tau_D) = \text{constant}$, so that

$$\phi(t) = \Omega t\tag{8.23}$$

satisfies

$$\frac{d\delta\psi(t)}{dt} = \frac{d\delta\psi'(t)}{dt} = \Omega\tag{8.24}$$

where Ω is the shift in frequency from intrinsic frequency ω , i.e.,

$$\frac{d\psi(t)}{dt} = \frac{d\psi'(t)}{dt} = \omega + \Omega\tag{8.25}$$

Then

$$0 = \cos [\Omega\tau_D] \sin \alpha,\tag{8.26}$$

which is consistent with a fixed shift in phase of $\alpha = 0, \pm\pi$. The sum at equilibrium yields

$$\begin{aligned}\frac{d(\delta\psi(t) + \delta\psi'(t))}{dt} &= 2\Gamma_0 \sin [\phi(t - \tau_D) - \phi(t)] \cos \alpha \\ &= 2\Gamma_0 \sin (\Omega\tau_D) \cos \alpha.\end{aligned}\tag{8.27}$$

When phase locking occurs this becomes

$$\Omega = \Gamma_0 \sin [\Omega \tau_D] \cos \alpha, \quad (8.28)$$

which must be satisfied for potential values of Ω and α .

We need one more relation to constrain Ω and α ; we achieve this by looking at the stability of $\delta\psi(t) - \delta\psi'(t)$. Expanding Equation 8.21 in a Taylor series with respect to α yields

$$\begin{aligned} \frac{d(\delta\psi(t) - \delta\psi'(t))}{dt} &= 0 - 2\Gamma_0 \cos [\phi(t - \tau_D) - \phi(t)] \Big|_{\phi=\Omega t} \frac{d \sin \alpha}{d\alpha} \Big|_{\alpha=0, \pm\pi} \Delta\alpha + \dots (8.29) \\ &= -2\Gamma_0 \cos [\tau_D \Omega] \cos \alpha \Big|_{\alpha=0, \pm\pi} \Delta\alpha \end{aligned}$$

and implies, to keep the sign of the RHS negative (see part 1 of oscillator series),

$$\alpha = \begin{cases} 0 & \text{if } \cos \Omega \tau_D \geq 0 \\ \pm\pi & \text{if } \cos \Omega \tau_D < 0 \end{cases} \quad (8.30)$$

or equivalently, with Equation 8.28, specifies that

$$\frac{\Omega \tau_D}{\Gamma_o \tau_D} = \begin{cases} +\sin(\Omega \tau_D) & \text{if } \cos \Omega \tau_D \geq 0 \\ -\sin(\Omega \tau_D) & \text{if } \cos \Omega \tau_D < 0 \end{cases} \quad (8.31)$$

and we immediately see that

$$\Omega = \begin{cases} 0 & \text{if } \Gamma_o \tau_D < 1 \\ \text{One or more values} & \text{if } \Gamma_o \tau_D > 1 \end{cases} \quad (8.32)$$

Thus small delays imply phase shifts of $\Omega = 0$. For $\Gamma_o \tau_D > 1$, these equations must be solved graphically (Figure 1) or numerically.

8.2.1 Case of $\alpha = 0$

Here $\Omega \tau_D$ must lie in the ranges $0 < \Omega \tau_D < \pi/2$, $3\pi/2 < \Omega \tau_D < 5\pi/2$, $7\pi/2 < \Omega \tau_D < 9\pi/2$, etc. The graphical solution, illustrated in Figure 1, is found for the interception of a line with positive slope of $1/\Gamma_o \tau_D$ with the positive part of a sine curve, or a line with negative slope of $-1/\Gamma_o \tau_D$ with the negative part of a sine curve.

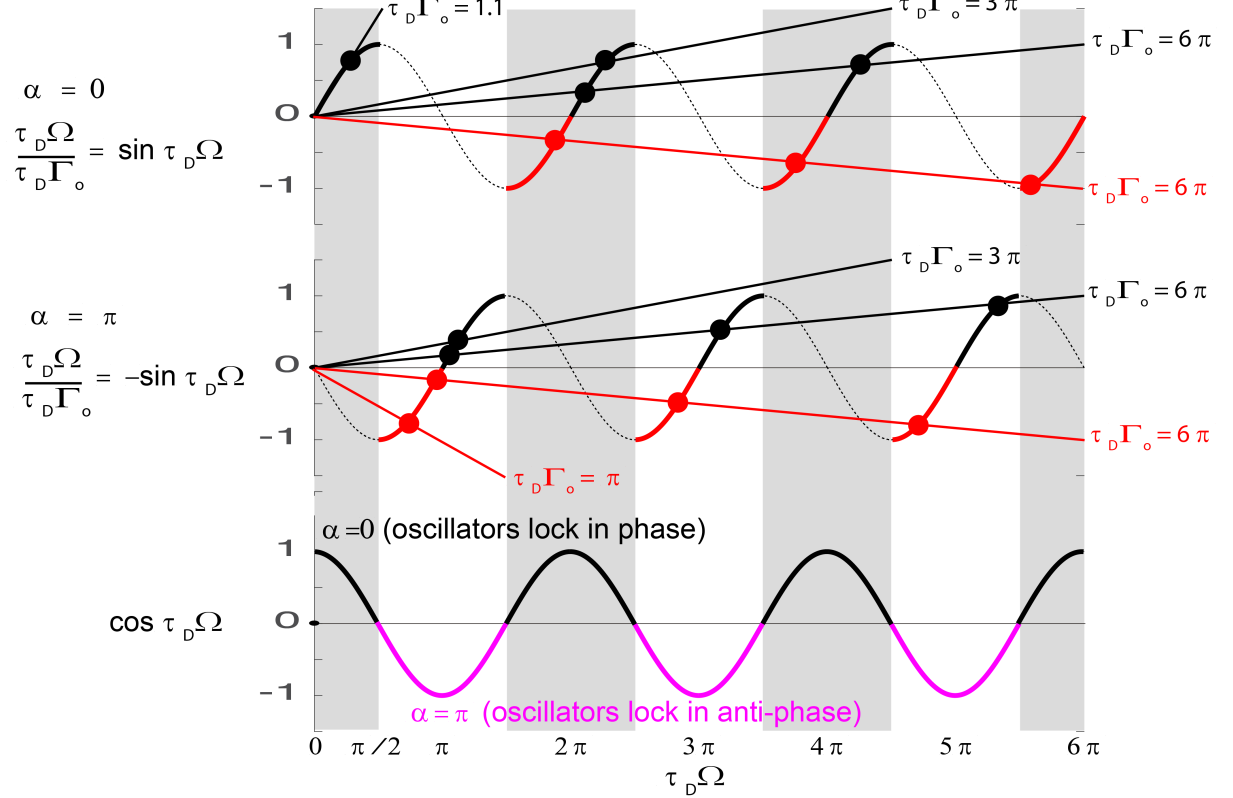
A little algebra shows that when $\Gamma_o \tau_D$ is barely larger than 1, the frequency shift Ω is arbitrarily small, i.e.,

$$\Omega \simeq \Gamma_o \sqrt{6(\Gamma_o \tau_D - 1)} \quad (8.33)$$

Increasing values of $\Gamma_o \tau_D$ lead to more solutions, i.e., multiple values of Ω for the same τ_D and Γ_o . A little more algebra shows that when $\Gamma_o \tau_D \rightarrow \infty$, the potential frequency shifts are

$$\Omega = \frac{2n}{\tau_D} \left(\frac{\pi}{\Gamma_o \tau_D} \right) \text{ for } n = 0, 1, 2, \dots \quad (8.34)$$

Figure 1: Graphical determination of the locking frequencies for two mutually coupled oscillators. Dots are stable equilibria. Black lines are for excitatory synapses ($\Gamma_o\tau_D > 0$ and red lines are for inhibitory synapses $\Gamma_o\tau_D < 0$).



8.2.2 Case of $\alpha = \pm\pi$

Here $\Omega\tau_D$ must lie in the ranges $\pi/2 < \Omega\tau_D < 3\pi/2$, $5\pi/2 < \Omega\tau_D < 7\pi/2$, etc. This case follows that for $\alpha = 0$, except as we are now looking for the interception of a line with a negated sine curve (Figure 1).

As above, a little algebra shows that when $\Gamma_o\tau_D \rightarrow \infty$, the potential frequency shifts are

$$\Omega = \frac{2n+1}{\tau_D} \left(\frac{\pi}{\Gamma_o\tau_D} \right) \text{ for } n = 0, 1, 2, \dots \quad (8.35)$$

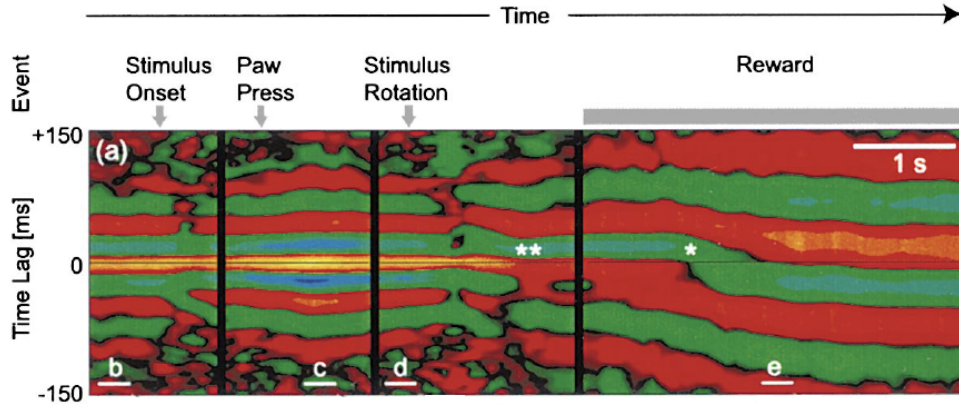
8.2.3 Summary on delays

- The frequency of oscillations are unshifted for small values of delay, i.e., $\Gamma_o\tau_D < 1$.
- The phase is similarly unshifted for small values of delay, i.e., $\Gamma_o\tau_D < 1$.
- There are frequency shifts for $\Gamma_o\tau_D > 1$.
- The synchronous state is stable only for $\tau_D < \pi/(2\Omega) \bmod 2\pi$. The first switch in phase first occurs for a delay of a quarter of a cycle.

- There are gaps in the spectrum for Ω .
- Large time delays can lead to multiple oscillation frequencies.

The evidence for the effect of delay of shifting frequencies and phase is fairly equivocal at present, but see Figure 2. Nonetheless, this is likely to become a major experimental issue as simultaneous recording across the brain becomes prevalent.

Figure 2: Correlated activity in across two regions in parietal association cortex in cat, i.e., areas 7 and 5, during a forced choice discrimination task in which the animal was trained to respond to a change in the orientation of a grating. (1) the onset of the grating stimulus, (2) pressing a level once the grating is perceived, (3) releasing the lever in response to a rotation of the grating, and (4) a period of food reward. Note the presence of a phase shift, **, that originates soon after the cat makes a behavioral choice, and a further flip of π radians (*) during the reward period. From Roelfsema, Engel, König and Singer, 1997.



8.3 Two oscillators with frequency differences and propagation delays.

Let's now see what combined frequency differences and time delays in signal propagation do to synchronization of neuronal signals. The procedure is similar to that above, with a bit more algebra. We take

$$\begin{aligned} \frac{d\delta\psi(t)}{dt} &= \delta\omega + \Gamma_0 \sin(\delta\psi'(t - \tau_D) - \delta\psi(t)) \\ \frac{d\delta\psi'(t)}{dt} &= \delta\omega' + \Gamma_0 \sin(\delta\psi(t - \tau_D) - \delta\psi'(t)) \end{aligned} \quad (8.36)$$

where the frequencies $\delta\omega$ and $\delta\omega'$ are in general different. We again assume a solution of the form

$$\begin{aligned} \delta\psi(t) &= \phi(t) + \alpha/2 \\ \delta\psi'(t) &= \phi(t) - \alpha/2 \end{aligned} \quad (8.37)$$

where α is a phase shift. The equation for $\delta\psi(t)$ yields

$$\begin{aligned} \frac{d\delta\psi(t)}{dt} &= \delta\omega + \Gamma_0 \sin[\phi(t) + \alpha/2 - \phi(t - \tau_D) + \alpha/2] \\ &= \delta\omega + \Gamma_0 \sin[\phi(t) - \phi(t - \tau_D)] \cos \alpha + \Gamma_0 \cos[\phi(t) - \phi(t - \tau_D)] \sin \alpha \end{aligned} \quad (8.38)$$

while that for $\delta\psi'(t)$ yields

$$\begin{aligned}\frac{d\delta\psi'(t)}{dt} &= \delta\omega' + \Gamma_0 \sin[\phi(t) - \alpha/2 - \phi(t - \tau_D) - \alpha/2] \\ &= \delta\omega' + \Gamma_0 \sin[\phi(t) - \phi(t - \tau_D)] \cos \alpha - \Gamma_0 \cos[\phi(t) - \phi(t - \tau_D)] \sin \alpha\end{aligned}\quad (8.39)$$

Thus the difference of the phase evolution yields

$$0 = \delta\omega - \delta\omega' + 2\Gamma_0 \cos[\phi(t) - \phi(t - \tau_D)] \sin \alpha \quad (8.40)$$

or

$$\cos[\phi(t) - \phi(t - \tau_D)] = \frac{\delta\omega - \delta\omega'}{2\Gamma_0 \sin \alpha}. \quad (8.41)$$

As in the case of solely delays, we have phase locking for $\phi(t) = \Omega t$, so that the difference yields

$$0 = \delta\omega - \delta\omega' - \Gamma_0 \cos \Omega\tau_D \sin \alpha. \quad (8.42)$$

Further, the sum yields

$$2\Omega = \delta\omega + \delta\omega' - 2\Gamma_0 \sin \Omega\tau_D \cos \alpha. \quad (8.43)$$

or

$$\Omega = \frac{\delta\omega + \delta\omega'}{2} - \Gamma_0 \sin \Omega\tau_D \cos \alpha. \quad (8.44)$$

We now have two equations and two unknowns. We rearrange these to solve for $\cos \alpha$, yielding

$$\cos \alpha = \frac{1}{\cos \Omega\tau_D} \sqrt{\cos^2 \Omega\tau_D - \left(\frac{\delta\omega + \delta\omega'}{2\Gamma_0}\right)^2}. \quad (8.45)$$

which has the correct limit of $\cos \alpha = 0$ for $\delta\omega = \delta\omega'$. We then form an expression solely in terms of the frequency shift Ω and known quantities. Valid values of Ω correspond to solutions of the transcendental equation

$$\frac{\delta\omega + \delta\omega'}{2\Gamma_0} = \tan \Omega\tau_D \sqrt{\cos^2 \Omega\tau_D - \left(\frac{\delta\omega + \delta\omega'}{2\Gamma_0}\right)^2}. \quad (8.46)$$

The numerical solution of this equation is shown for values of τ_D and Γ_0 (Figure 3). As in the above case of solely time delays, the number of solutions increases with τ_D and Γ_0 .

The stability of the solutions can be examined by expansion around the equilibrium, as shown by Schuster and Wagoner (Progress of Theoretical Physics, 1989). The stable solutions flip between shifts of 0 and π as the frequency increases (Figure 4).

8.4 Rotating waves in two dimensions

The extension of weakly coupled oscillators to lattices 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. Nonetheless, waves and especially rotating waves are observed in experiment (Figures 5, 6, 7, and 8) and apparently metastable patterns are observed in numerical examples.

Figure 3: Zeros of Equation 8.46 for the total frequency shift, found from the zeros of F in $F = \frac{\delta\omega + \delta\omega'}{2} - \Gamma_0 \tan \Omega \tau_D \sqrt{\cos^2 \Omega \tau_D - \left(\frac{\delta\omega + \delta\omega'}{2\Gamma_0}\right)^2}$. From Schuster and Wagoner, 1989

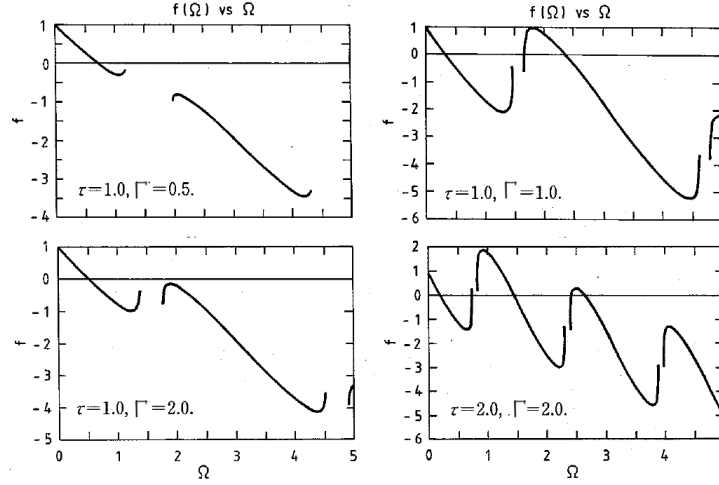


Figure 4: The synchronization frequency Ω and the phase shift α between the neuronal oscillators. From Schuster and Wagoner, 1989

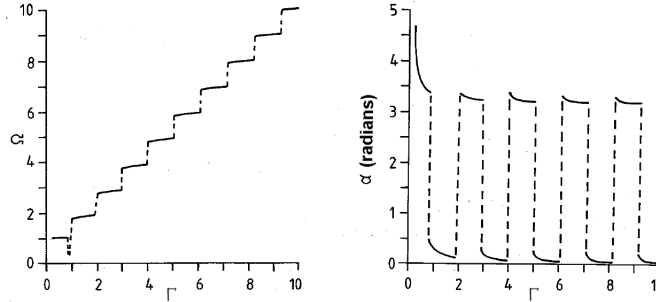


Figure 5: Measurement of oscillations across visual cortex in turtle in response to a looming stimulus. Note the peak response at 18 Hz. From Prechtl, Cohen, Pesaran, Mitra and Kleinfeld, 1997

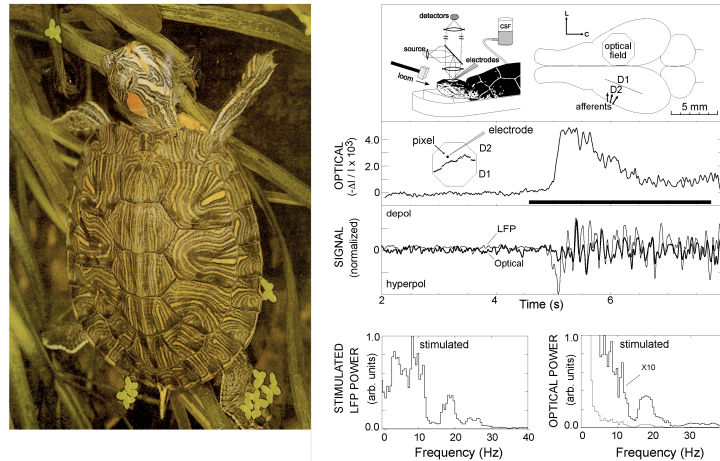


Figure 6: The spatiotemporal dynamics for the modulation of the 18 Hz rhythm in turtle visual cortex. Note the epoch of a rotating wave. From Prechtl, Cohen, Pesaran, Mitra and Kleinfeld, 1997

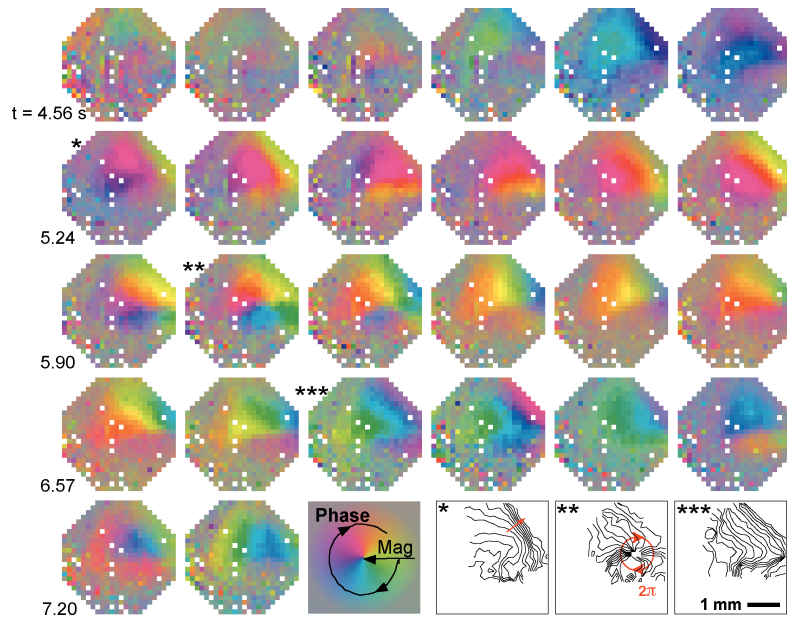


Figure 7: Images of two evoked waves and six spontaneous waves from the same field of view in the same animal. The evoked response showed a clear compression of activity at the V1/V2 border (*) in the middle of the imaging field. From Xu, Huang, Takagaki and Wu, 2007

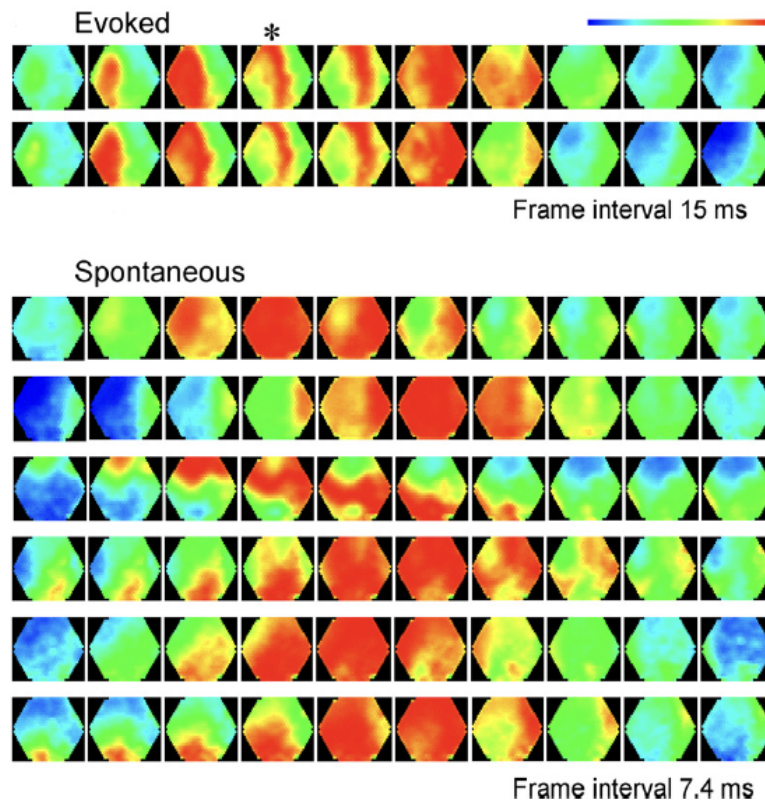


Figure 8: The present of traveling waves at the alpha rhythm frequency in human temporal cortex. From Muler, Piantoni, Koller, Cash, Halgren and Sejnowski, 1989

