Supporting Text

Mathematical Model

In what follows, we use the notation X cell to refer to any of the O, I, E or D cells, respectively. When necessary, V_X^k refers to the membrane potential of the k^{th} X cell, $I_{syn,X}^k$ refers to the synaptic input to the k^{th} X cell. The current-balance equations (CBE) for the O, I, E and D cells are as follows:

$$C_O\, dV_O/dt = I_{app,O} - I_{Na,O} - I_{K,O} - I_{L,O} - I_{h,O} - I_{A,O} - I_{syn,O},$$
$$C_I\, dV_I/dt = I_{app,I} - I_{Na,I} - I_{K,I} - I_{L,I} - I_{syn,I},$$
$$C_E\, dV_E/dt = I_{app,E} - I_{Na,E} - I_{K,E} - I_{L,E} - I_{syn,E} + I_{conn,E},$$
$$C_D\, dV_D/dt = I_{app,D} - I_{Na,D} - I_{K,D} - I_{L,D} - I_{syn,D} + I_{conn,D},$$

where V_X are the membrane potentials (mV), C_X are the membrane capacitances ($\mu F/cm^2$), $I_{syn,X}$ are the synaptic currents, and $I_{app,X}$ are the applied bias (DC) currents (or tonic drives). In the CBE, I_{Na}, I_K, I_L, I_h, and I_A are the transient sodium, delayed rectifier potassium, leak, hyperpolarization-activated (or h) mixed-cation and A currents, respectively. All the currents have units of $\mu A/cm^2$. The ionic currents are given by

$$I_{Na} = G_{Na}\, m^3\, h\, (V - E_{Na}),$$

$$I_K = G_K\, n^4\, (V - E_K),$$

$$I_L = G_L\, (V - E_L),$$

$$I_h = G_h\, r\, (V - E_h),$$

and

$$I_A = G_A\, a\, b\, (V - E_A),$$

where $m, h, n, r, a,$ and b are the gating variables, and G_Z and E_Z ($Z = Na, K, L, h,$ and A) are the maximal conductances ($\mu S/cm^2$) and reversal potentials (mV), respectively. Note that the subscripts referring to the type of cells ($X = O, I, E,$ and D) have been omitted for simplicity. For the O cells we used the following parameters: $G_{Na} = 107$, $G_K = 319$, $G_L = 0.5$, $G_A = 2$, $G_h = 20$, $E_{Na} = 90$, $E_K = -100$, $E_L = -70$, $E_A = -90$, $E_h = -32.9$, $C_O = 1.3$, and $I_{app,O} = 0.8$. For the I, E and D cells, we used the following parameters: $G_{Na} = 100$, $G_K = 80$, $G_L = -0.1$, $E_{Na} = 50$, $E_K = -100$, $E_L = -67$, $C_I = C_E = C_D = 1.0$, $I_{app,I} = 0.6$, $I_{app,E} = 1.4$, $I_{app,D} = 0.12$, $G_{ED} = 0.3$, and $G_{DE} = 0.05$.

For $k = 1, 2$, the synaptic currents are given by

$$\begin{aligned}
I^k_{syn,O} &= G^{1,k}_{IO} S_{IO,1}(V^k_O - E_{in}) + G^{2,k}_{IO} S_{IO,2}(V^k_O - E_{in}) + G^k_{EO} S_{EO}(V^k_O - E_{ex}),\\
I^k_{syn,I} &= G^{1,k}_{II} S_{II,1}(V^k_I - E_{in}) + G^{2,k}_{II} S_{II,2}(V^k_I - E_{in}) + G^{1,k}_{OI} S_{OI,1}(V^k_I - E_{in}) +\\
&\quad G^{2,k}_{OI} S_{OI,2}(V^k_I - E_{in}) + G^k_{EI} S_{EI}(V^k_I - E_{ex}),\\
I_{syn,E} &= G^1_{IE} S_{IE,1}(V_E - E_{in}) + G^2_{IE} S_{IE,2}(V_E - E_{in}),
\end{aligned}$$

and

$$I_{syn,D} = G^1_{OD} s_{OD,1}(V_D - E_{in}) + G^2_{OD} s_{OD,2}(V_D - E_{in}),$$

where $E_{in} = -80$ and $E_{ex} = 0$ are the inhibitory and excitatory reversal potentials (mV), respectively. The electrical coupling between the E and D compartments are given by

$$I_{conn,E} = G_{ED}(V_D - V_E) \qquad \text{and} \qquad I_{conn,D} = G_{DE}(V_E - V_D).$$

The gating variables obey kinetic equations of the form ($x = m, n, h, r, a,$ and b)

$$\frac{dx}{dt} = \frac{x_\infty(V) - x}{\tau_x(V)},$$

where

$$x_\infty(V) = \frac{\alpha_x(V)}{\alpha_x(V)+\beta_x(V)} \qquad \text{and} \qquad \tau_x(V) = \frac{1}{\alpha_x(V)+\beta_x(V)}.$$

For the O cells,

$\alpha_m(V) = -0.1\,(V+38)/(exp(-(V+38)/10)-1)$,

$\beta_m(V) = 4\,exp(-(V+65)/18)$,

$\alpha_h(V) = 0.07\,exp(-(V+63)/20)$,

$\beta_h(V) = 1/(1+exp(-(V+33)/10))$,

$\alpha_n(V) = 0.018\,(V-25)/(1-exp(-(V-25)/25))$,

$\beta_n(V) = 0.0036\,(V-35)/(exp((V-35)/12)-1)$,

$\alpha_b(V) = 0.000009/exp((V-26)/18.5)$,

$\beta_b(V) = 0.014/(0.2+exp(-(V+70)/11))$,

$a_\infty(V) = 1/(1+exp(-(V+14)/16.6))$,

$b_\infty(V) = 1/(1+exp((V+71)/7.3))$,

$r_\infty(V) = 1/(1+exp((V+84)/10.2))$,

$\tau_r(V) = 1/(exp(-17.9-0.116\,V)+exp(-1.84+0.09\,V))+0.1$,

and

$\tau_a(V) = 5$.

For the I, E and D cells,

$\alpha_m(V) = 0.32\,(54+V)/(1-exp(-(V+54)/4))$,

$\beta_m(V) = 0.28\,(V+27)/(exp((V+27)/5)-1)$,

$\alpha_h(V) = 0.128\,exp(-(50+V)/18)$,

$\beta_h(V) = 4/(1+exp(-(V+27)/5))$,

$\alpha_n(V) = 0.032\,(V+52)/(1-exp(-(V+52)/5))$,

and

$\beta_n(V) = 0.5\,exp(-(57+V)/40)$.

The synaptic variables obey a kinetic equation of the form

$$\frac{dS}{dt} = N(V)\,(1-S) - \bar{\beta}\,S$$

where

$$N(V) = \bar{\alpha}\,(1 + tanh(V/0.1))/2.$$

For S_{OI} and S_{OD}, we use $\bar{\alpha} = 5$ and $\bar{\beta} = 0.05$. For S_{IO}, S_{II}, and S_{IE}, we use $\bar{\alpha} = 15$ and $\bar{\beta} = 0.011$. For S_{EI} and S_{EO} we use $\bar{\alpha} = 20$ and $\bar{\beta} = 0.19$. The values of the maximal synaptic conductivities are divided into two groups. The first group contains a set of parameters that are common to all cases (theta, gamma, and theta/gamma). These are $G_{IO}^{1,1} = G_{IO}^{2,2} = 0.05$, $G_{IO}^{1,2} = G_{IO}^{2,1} = 0.04$, $G_{II}^{1,1} = G_{II}^{2,2} = 0.02$, $G_{II}^{1,2} = G_{II}^{2,1} = 0.015$, and $G_{IE}^{1} = G_{IE}^{2} = 0.01$. The second group contains three sets of parameters, one for each case (theta, gamma and theta/gamma). They are as follows:

I (gamma): $G_{OI}^{1,1} = G_{OI}^{2,2} = 0.015$, $G_{OI}^{1,2} = G_{OI}^{2,1} = 0.008$, $G_{EO}^{1} = G_{EO}^{2} = 0.03$, $G_{EI}^{1} = G_{EI}^{2} = 0.1$, and $G_{OE}^{1} = G_{OE}^{2} = 0.02$.

II (theta): $G_{OI}^{1,1} = G_{OI}^{2,2} = 0.04$, $G_{OI}^{1,2} = G_{OI}^{2,1} = 0.03$, $G_{EO}^{1} = G_{EO}^{2} = 0.005$, $G_{EI}^{1} = G_{EI}^{2} = 0.01$, and $G_{OE}^{1} = G_{OE}^{2} = 0.5$.

III (theta/gamma): $G_{OI}^{1,1} = G_{OI}^{2,2} = 0.02$, $G_{OI}^{1,2} = G_{OI}^{2,1} = 0.01$, $G_{EO}^{1} = G_{EO}^{2} = 0.013$, $G_{EI}^{1} = G_{EI}^{2} = 0.1$, and $G_{OE}^{1} = G_{OE}^{2} = 0.042$.

Data Analysis

The power spectra P_{xx} and P_{yy} of two signals is calculated by using the Fourier transform and presented as power spectral density. The coherence K_{xy} for two signals x and y is equal to the average cross power spectrum P_{xy} normalized by the averaged power spectra of the signals:

$$K_{xy} = \frac{|P_{xy}|^2}{P_{xx}P_{yy}}.$$

The coherence measures the strength of the linear relationship between two signals at every frequency f. Its values are between 0 and 1. $K_{xy} = 0$ means phases are evenly dispersed among all epochs. $K_{xy} = 1$ means phases of two signals are identical in all epochs; i.e., the two signals are totally phase-locked at this frequency.

Bispectral analysis gives information about two component oscillations within a signal (defined by their respective frequencies f_1 and f_2) and a harmonic component (defined by the sum of the frequencies, $f_1 + f_2$). The bispectrum, B, is calculated by computing the triple product $X_j(f_1)X_j(f_2)X_j^*(f_1 + f_2)$ for each window, j, of data time, then summing up over all windows and finally taking the sum's magnitude:

$$B(f_1, f_2) = \left| \sum_j X_j(f_1)X_j(f_2)X_j^*(f_1 + f_2) \right|,$$

where $X_j(f_1)$, $X_j(f_2)$ and $X_j^*(f_1 + f_2)$ are the Fourier transform components of the signal (calculated by using Fast-Fourier Transformation). X^* is the complex conjugate of X. Although the bispectrum may increase with phase coupling, it may also increase due to signal strength and other circumstances. By normalizing the bispectrum, the degree of phase coupling can be estimated by using a quantity known as bicoherence, BIC:

$$BIC(f_1, f_2) = \frac{B(f_1, f_2)}{\sum_j \sqrt{RTP_j(f_1, f_2)}},$$

where

$$RTP_j(f_1, f_2) = P_j(f_1)P_j(f_2)P_j(f_1 + f_2)$$

is the triple product of the power spectrums, P_j.

The bicoherence gives values between 0 and 1, and, specifically, it can quantify the degree of phase coupling between the component oscillations and the harmonic due to their sum. For more detailed information about bispectral analysis, see (1).

References

1. Hagihira, S., Takashina, M., Mori, T., Mashimo, T. & Yoshiya, I. (2001) *Anesth. Analg.*, **93**, 966–970.