Supplemental Materials

**Phase transition model of neuronal network**

This theoretical model describes (1) the structure of network synchronous activity, (2) the internal state of single cells embedded in a network, and (3) the dynamics produced by them.

According to the Hopfield model, we first assume that the structure of network synchronous activity (Hopfield 1982, 1984), that is, the Hamiltonian of the network activity is described as:

$$H = -\frac{1}{2}\sum_{i,j} J_{ij} S_i S_j$$

at network temperature *T*.   $S_i$ is the firing state of neuron *i*, $S_i = 1$ shows "fire" and $S_i = -1$ shows "non-fire".   $J_{ij}$ represents the synaptic interaction from neuron *i* to neuron *j*.   Note that temperature *T* is not the real temperature, but rather it is used here as a parameter which represents a network activity statistic; that is, as *T* is higher, neurons become to act more randomly (Amit et al., 1985).
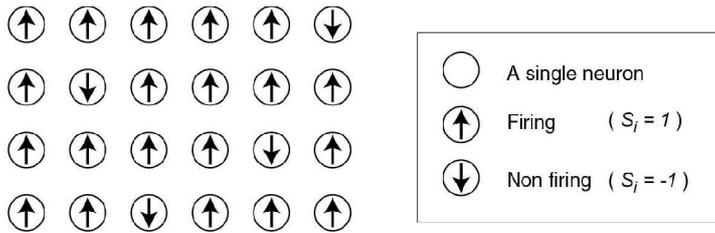


According to the model the mean field theory, the free-energy of the network synchronous state *F* is obtained as follows (Hertz et al., 1991; Nishimori 2001)

$$F = \mu(T - T_c)\varphi^2 + u\varphi^4$$

$\varphi$ represents the degree of synchronization of the states of neurons in this network; $\varphi = 0$ means that network firing activity is random, $\varphi > 0$ indicates that the "firing" states of individual neurons are more synchronized, and $\varphi < 0$ indicates that more neurons are synchronized at "non-firing" states.   $\mu$ and *u* are constants ($\mu = 1$; $u = 1$).

Network synchronous
state parameter

$\varphi$ ∝ Ratio of ↑ and ↓

| Random | Synchronous Firing | Synchronous non-firing |
|---|---|---|
| ↓ ↑ ↓ ↑ ↓ | ↑ ↑ ↑ ↑ ↑ | ↓ ↓ ↓ ↓ ↓ |
| ↓ ↑ ↓ ↓ ↑ | ↑ ↑ ↑ ↑ ↑ | ↓ ↓ ↓ ↓ ↑ |
| ↑ ↓ ↑ ↓ ↑ | ↑ ↑ ↑ ↑ ↓ | ↓ ↑ ↓ ↓ ↓ |
| ↓ ↑ ↓ ↓ ↑ | ↑ ↑ ↑ ↑ ↑ | ↓ ↓ ↓ ↓ ↓ |
| $\varphi = 0$ | $\varphi > 0$ | $\varphi < 0$ |
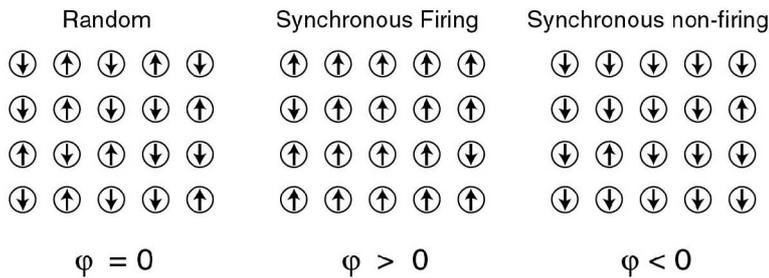
We next consider the critical temperature $T_c$. The shape of the free-energy function $F$ changes as a function of $T$, and $T_c$ is the temperature at which the number of the stable points (local minima) of the free energy function changes. When temperature is higher than the critical temperature ($T > T_c$), there is only one stable point at $\varphi = 0$, whereas there are two stable points when $T$ is less than $T_c$. This change in the number of the stable points represents a "phase transition" of the network synchrony state, i.e., a shift from random states to synchronous firing states (Amit et al., 1985). This is an analogy to structural analysis in solid-state physics in which temperature-dependent state changes is generally termed a phase transition (Landau 1980).

Free energy **F**

$T > T_c$

*Phase Transition*

$T < T_c$

-1  0  1
$\varphi$

-1  0  1
$\varphi$

| Random | Synchronous Firing / Synchronous non firing |
|---|---|
| ↓ ↑ ↓ ↑ ↓ | ↑ ↑ ↑ ↑ ↑ |
| ↓ ↑ ↓ ↓ ↑ | ↓ ↑ ↑ ↑ ↑ |
| ↑ ↓ ↑ ↓ ↑ | ↑ ↑ ↑ ↑ ↓ |
| ↓ ↑ ↓ ↓ ↑ | ↑ ↑ ↑ ↑ ↑ |
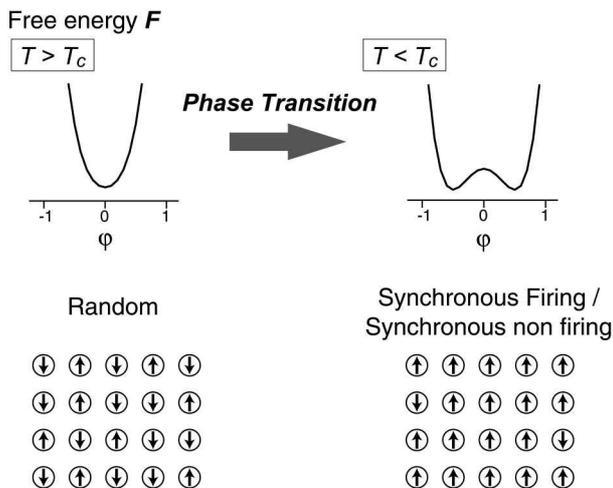
We hypothesize that a phase transition of network activity induces a change in the level of synchronous synaptic inputs from the network into individual neurons, resulting in a transition of the internal states (the pattern of membrane potential fluctuations) of these neurons. In other words, we think that the internal states of single cells reflect the phase of network activity states.

---------

Here we describe the dynamics of both network synchronization and membrane potential of a single cell. First, the dynamics of network synchronous state is given by

$$\tau_N \frac{d\varphi}{dt} = -\frac{\partial F}{\partial \varphi} + W + \xi_N$$

where $F$ is the free-energy of network synchronous state as defined above, and $\tau_N$ is the time constant of network dynamics (Langevin equation). $W$ represents the brain oscillations. We consider $W$ as slow-wave (<1 Hz) oscillations, i.e., $W(t) = A_w \times \sin(2\pi f t + \varepsilon)$, because this frequency range of oscillations is involved in generation of network synchronization such as UP/DOWN alternations *in vitro* (Sanchez-Vives and McCormick; 2000) and *in vivo* (Steriade et al., 1993). $\xi_N$ represents a stochastic component of synaptic inputs and denotes a zero-mean, Gaussian white noise with the autocorrelation function $\langle \xi_N(t)\xi_N(0) \rangle = 2D\delta(0)$, where $D$ is the intensity of noise, and $\delta(t)$ is the Dirac delta function. We used. $\tau_N = 1$ ms, $A_w = 0.1$, $f = 0.2$ Hz, and $D = 0.55$.

The dynamics of membrane potential is

$$C_m \frac{dV_m}{dt} = -g_L(V_m - E_L) - g_{balance}(V_m - E_{balance}) + \xi_m$$

where $C_m$ is cell capacitance, $\xi_m$ represents a stochastic component of synaptic inputs, $E_L$ represents the reversal potentials for leakage current components, and $g_L$ is leak conductance. $E_{balance}$ and $g_{balance}$ represents the reversal potential and conductance during UP depolarization, respectively. $E_{balance}$ is set to -30 mV, which was adopted from our experimental data (Fig. 8). This value is consistent with that reported by Shu et al. (2003a). In this equation, we do not take action potentials into consideration; instead we focus on the dynamics of subthreshold membrane potential. $C_m$ was set to 0.5 nF.

$g_{balence}$ ($\Delta$ conductance) is conductance due to balanced excitatory and inhibitory synaptic inputs, which are generated by synchronous synaptic inputs $s_\varphi$ as follows:

$$g_{balance}(t) = g_{unit} s_\varphi(t)$$

$g_{unit}$ is the unit conductance of a synchronous synaptic input. $g_{unit}$ is set to 10 pS because the conductance of a single AMPA channel is about 5 ~ 20 pS (Swanson et al., 1997; Rosenmund et al., 1998; Derkach et al., 1999), and that of a single GABA$_A$ channel is about 10 pS (Eghbali et al., 1997).

Synchronous synaptic inputs $s_\varphi$ is a function that depends on network synchronous state $\varphi$;

$$s_\varphi(t) = \begin{cases} a_\varphi \varphi & (\varphi > 0) \\ 0 & (\varphi \le 0) \end{cases}$$

where $a_\varphi$ is the coefficient of the number of synchronous synaptic inputs. The coefficient $a_\varphi$ is set to 2000 so that $\varphi = 1$ corresponds roughly to persistent UP depolarization; note that our experimental data showed that the $\Delta$ conductance is 10 ~ 20 nS during persistent UP periods (state V).

$\xi_m$ represents the stochastic component of synaptic inputs and denotes a zero-mean, Gaussian white noise with the autocorrelation function $\langle \xi_m(t)\xi_m(0) \rangle = 2d\delta(0)$, where $d$ is the intensity of noise, and $\delta(t)$ is the Dirac delta function. The intensity of stochastic input $d$ is also a function of the network synchronous state $\varphi$:

$$d = d_0 + d_\varphi \exp(-|\varphi|/\tau_d)$$

where $d_0$ is the baseline stochastic synaptic inputs, and $d_\varphi$ is the $\varphi$-dependent component. We used $d_0 =$

0.4 nA, $d_\varphi$= 0.4 nA, $\tau_d$= 1 ms.
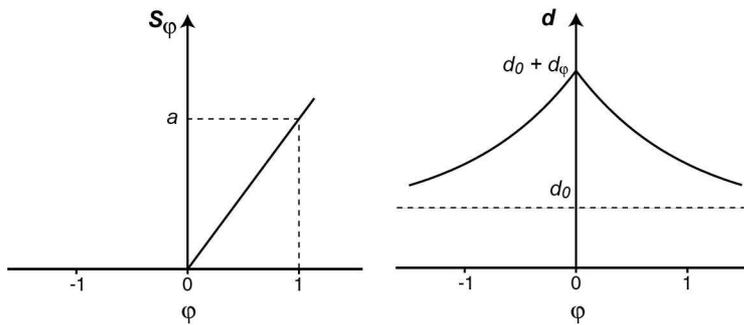


In summary, we assumed that membrane potential fluctuation depends on the Δ conductance generated by synchronous synaptic inputs, and the synchronous synaptic inputs depend on network synchronous states.

The figure below shows the dynamics of network synchrony, synchronous synaptic inputs (i.e., Δ conductance) and membrane potentials of single cells when $T$ is less than $T_c$. In this case, the free-energy of network synchronous states has two stable points, and the network synchrony levels transit periodically but stochastically between the double-well stable points. Such transitions induced by periodic and stochastic forces are known as stochastic resonance (Wiesenfeld and Moss 1995; Gammaitoni et al., 1998). This stochastic resonance of network synchronous levels contributes to UP/DOWN alterations in single neurons.
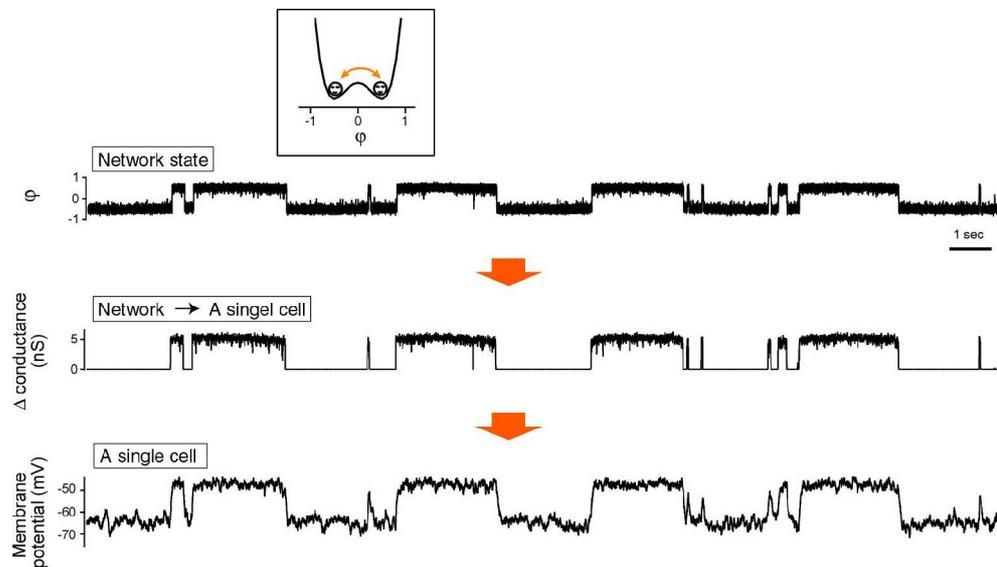


The results of computational simulation using this model are shown in the text (see Figure 9B).

REFERENCES

Amit DJ, Gutfreund H, Sompolinsky H (1985) Storing infinite numbers of patterns in a spin-glass model of neural networks. Phys Rev Lett 55: 1530-1533.

Derkach V, Barria A, Soderling TR (1999) Ca2+/calmodulin-kinase II enhances channel conductance of alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate type glutamate receptors. Proc Natl Acad Sci U S A 96: 3269-3274.

Eghbali M, Curmi JP, Birnir B, Gage PW (1997) Hippocampal GABA(A) channel conductance increased by diazepam. Nature 388: 71-75.

Gammaitoni L, Hanggi P, Jung P, Marchesoni F (1998) Stochastic resonance. Rev Mod Phys 70: 223-287.

Hertz J, Krogh A, Palmer RG (1991) Introduction to the theory of neural computation. New York: Westview Press.

Hopfield JJ (1982) Neural networks and physical systems with emergent collective computational abilities. Proc Natl Acad Sci U S A 79: 2554-2558.

Hopfield JJ (1984) Neurons with graded response have collective computational properties like those of two-state neurons. Proc Natl Acad Sci U S A 81: 3088-3092.

Landau LD, Lifshitz EM, Pitaevskii LP (1980) Statistical physics. New York: Pergamon.

Nishimori H (2001) Statistical Physics of Spin Glasses and Information Processing: An Introduction. New York: Oxford University Press.

Rosenmund C, Stern-Bach Y, Stevens CF (1998) The tetrameric structure of a glutamate receptor channel. Science 280: 1596-1599.

Sanchez-Vives MV, McCormick DA (2000) Cellular and network mechanisms of rhythmic recurrent activity in neocortex. Nat Neurosci 3: 1027-1034.

Shu YS, Hasenstaub A, McCormick DA (2003) Turning on and off recurrent balanced cortical activity. Nature 423: 288-293.

Steriade M, Nunez A, Amzica F (1993) A Novel Slow (Less-Than-1 Hz) Oscillation of Neocortical Neurons In-Vivo - Depolarizing and Hyperpolarizing Components. J Neurosci 13: 3252-3265.

Swanson GT, Kamboj SK, Cull-Candy SG (1997) Single-channel properties of recombinant AMPA receptors depend on RNA editing, splice variation, and subunit composition. J Neurosci 17: 58-69.

Wiesenfeld K, Moss F (1995) Stochastic resonance and the benefits of noise - from ice ages to crayfish and squids. Nature 373: 33-36.