1700 Biophysical Journal Volume 75 October 1998 1700–1711

Effect of Syncytium Structure of Receptor Systems on Stochastic Resonance Induced by Chaotic Potential Fluctuation

Yoshiki Kashimori, Hirofumi Funakubo, and Takeshi Kambara
Department of Applied Physics and Chemistry, The University of Electro-Communications, Chofu, Tokyo 182-8585, Japan

ABSTRACT To study a role of syncytium structure of sensory receptor systems in the detection of weak signals through stochastic resonance, we present a model of a receptor system with syncytium structure in which receptor cells are interconnected by gap junctions. The apical membrane of each cell includes two kinds of ion channels whose gating processes are described by the deterministic model. The membrane potential of each cell fluctuates chaotically or periodically, depending on the dynamical state of collective channel gating. The chaotic fluctuation of membrane potential acts as internal noise for the stochastic resonance. The detection ability of the system increases as the electric conductance between adjacent cells generated by the gap junction increases. This effect of gap junctions arises mainly from the fact that the synchronization of chaotic fluctuation of membrane potential between the receptor cells is strengthened as the density of gap junctions is increased.

INTRODUCTION

Some kinds of sensory receptor systems in visual, auditory, and gustatory systems have a syncytium structure in which receptor cells are interconnected through gap junctions (Attwell et al., 1984; Holland et al., 1989; Lamb and Simon, 1976; Schwartz, 1976; Ye et al., 1993). It is not clear yet what kind of role the syncytium structure plays in the function of receptor systems.

In the present paper, we study the role of the syncytium structure in the detection of weak signals, using a computer simulation of the dynamical response of syncytium to weak signals. It is one of the most important requirements of every sensory system that animals be able to sense weak external stimuli and distinguish weak signals embedded in a noisy environment (Tsong, 1994).

The presense of noise in a signal transduction system usually interferes with its ability to transfer information reliably. However, many nonlinear systems can use noise to enhance their ability. This phenomenon, called stochastic resonance, may underlie the remarkable ability of some biological systems to detect and amplify weak signals in a noisy environment (Moss and Wiesenfeld, 1995; Wiesenfeld and Moss, 1995). Stochastic resonance has been demonstrated to be functionally important in various biological systems. It is quite possible that stochastic resonance is a common phenomenon in sensory systems. We consider here the functional role of syncytium structure only in the weak signal detection made by sensory receptor systems through stochastic resonance, although the syncytium structure may play other functional roles in the sensory receptor systems.

We present a model of a typical sensory receptor system with syncytium structure, which consists of many receptor cells and a single afferent nerve innervating all of the cells. The apical membrane of each cell includes two kinds of voltage-dependent ion channels mimicking Na^+ and K^+ channels, whose gating processes are described by the deterministic model (Liebovitch and Toth, 1991). The adjacent cells are interconnected through gap junctions. We investigate the effect of the gap junctions on the ability of the afferent nerve to detect weak input signals applied to the receptor cells.

We found that there are two kinds of dynamical states of collective ion channel gating in the receptor cell syncytium, that is, periodic and chaotic states, depending on the value of parameter in the deterministic model. The membrane potential of each receptor cell fluctuates periodically or chaotically, depending on the collective gating state. Because the response of a receptor cell to an input signal is generated by a change in the membrane potential of the cell, which is induced by the signal, the chaotic fluctuation of the potential acts as internal noise in the response process.

It was found in the present work that the detection ability of the receptor system with syncytium structure depends on the dynamical state of the system, which is determined by the collective gating state of ion channels and the intercellular coupling due to gap junctions: 1) The receptor system in a chaotic state can detect a weak periodic signal without any assistance from external noise, whereas the system in a periodic state cannot detect the signal in the case of no assistance from external noise. 2) The detection ability of the system in a chaotic state increases as the electric conductance between adjacent receptor cells generated by the gap junctions increases. 3) Even if the weak periodic signal received by the receptor system is not completely coherent, that is, the signal received by each receptor cell is slightly different in its amplitude or its phase, the afferent nerve becomes able to detect the signal as the conductivity between the cells increases.

Received for publication 26 February 1998 and in final form 5 July 1998.

Address reprint requests to Dr. Y. Kashimori, Department of Applied Physics and Chemistry, The University of Electro-Communications, Chofu, Tokyo 182-8585, Japan. Tel: 81-424-43-5470, Fax: 81-424-89-9748; E-mail: kashi@nerve.pc.uec.ac.jp.

0006-3495/98/10/1700/12 $2.00

These effects of gap junctions arise mainly from the fact that the synchronization of chaotic fluctuation (internal noise) of membrane potential between the receptor cells is strengthened as the density of gap junction is increased.

To consider the meaning of the present work, we describe briefly the results obtained so far by experimental and theoretical studies of stochastic resonance in biological systems relevant to the sensory receptor systems. Stochastic resonance at the ion channel level has been demonstrated by Bezrukov and Vodyanoy (1995, 1997b), using voltage-dependent ion channels of alamethicin reconstituted in a lipid bilayer membrane. The addition of white noise at 10–20 mV to a small sine wave input signal increases the output signal by 20–40 dB, conserving the signal-to-noise ratio. Stochastic resonance at the cell level has also been demonstrated in several systems. Douglass et al. (1993) showed, by using external noise applied to crayfish mechanoreceptor cells, that individual receptor cells can provide a physiological substrate for stochastic resonance in sensory systems. Braun et al. (1994) showed, by recording from single electrosensory afferents of shark, that intrinsic oscillations in combination with noise can signal both environmental changes and modality-specific information. Wiesenfeld and Moss (1995) showed, based on the electrophysiological recordings from a single hair cell of mechanoreceptor of crayfish stimulated with a subthreshold signal, that noise serves well the detection of weak signals. Levin and Miller (1996) showed, by investigating the effect of ambient noise on signal encoding in the mechanosensory system of the cricket, that stochastic resonance can enhance the ability to detect broadband signals such as small-amplitude low-frequency air disturbances. Collins et al. (1996) showed, by observing the response of rat cutaneous mechanoreceptors to a perithreshold aperiodic stimulus plus noise, that noise can serve to enhance the response of a sensory neuron to a weak aperiodic signal.

The microscopic mechanism by which noise may enhance the ability of sensory systems to detect weak signals has been considered based mainly on the theoretical studies of stochastic resonance in relatively simple units such as a particle moving in a double-well potential with friction or some kinds of model neurons (Wiesenfeld and Moss, 1995). However, there are some problems in the straightforward application of the features of stochastic resonance in simple units to complex systems such as sensory systems:

1. It is required for stochastic resonance in a single-unit system such as an ion channel or a sensory neuron that the optimal intensity of the noise be adjusted, depending on the nature of the signals (Wiesenfeld et al., 1994). This has been thought to limit the application of stochastic resonance to biological systems. However, Pantazelou et al. (1993) have observed stochastic resonance in an array of uncoupled elements (Schmitt triggers) with summed outputs when each element was subject to an independent, incoherent noise. They have shown how the system can operate as an amplifier based on digital sampling of the input signal at random times governed by the noise. Furthermore, Collins et al. (1995) have shown that there is no optimal noise intensity for an array of model neurons, and the physiological mechanism for adjusting the internal noise intensity is not necessary for the application. They explained, by considering the response of the arrays, with each neuron subject to its own noise source, how these internal noise can average out across the array and enhance the coherent weak signal.

2. It has not yet been resolved whether the demonstrations of stochastic resonance at the ion channel and cellular levels can help to clarify the microscopic mechanism generating the remarkable sensitivity of animals to weak external stimuli. Astumian et al. (1997) showed, using the theory of Bezrukov and Vodyanoy (1997a), that with parameters appropriate for typical biological cells, adding noise does not make a far-from-detectable signal detectable. Moss (1997) suggested one possibility for a modulation of a few parts in a million to result in a detectable change in the spike rate of so noisy a detector as a single sensory neuron. That is, individual neurons and/or ion channels do not act alone, but collectively as a system with multiunits. The enhanced sensitivity may be a property of the systems.

3. The effect of interunit interaction on stochastic resonance in multiunit systems has been studied by using simple units. Jung et al. (1992) found an unusually large amplification of the periodic modulations for certain values of the noise strength due to collective dynamics of the coupled bistable units. Inchiosa and Bulsara (1995) showed, using a network of simple model neurons, that cooperative effects arising from the noise and the coupling lead to an enhancement of the response of the network over that of a single unit. However, it is not yet clear whether the coupling between complex systems such as sensory cells leads to a similar enhancement.

4. There are two kinds of noises, external and internal noises. In biological sensory systems, the contribution of internal noise to stochastic resonance seems essentially important, because each of the units that make up systems such as ion channels and receptor cells necessarily generate noises inherent in their functions. It has been shown in the observation of the response of crayfish mechanoreceptors to weak signals (Wiesenfeld and Moss, 1995) that the signal-to-noise ratio does not decrease rapidly for small external noise because of the residual internal noise of the receptor neuron. Pantazelou et al. (1995) have investigated the effect of the internal noise of the receptor cells on stochastic resonance by controlling the intensity of the noise with temperature. An optimal noise intensity was not observed in the dependence of the signal-to-noise ratio on the output noise, but an interesting general power law behavior of the signal-to-noise ratio on the noise intensity was observed. Collins et al. (1995) have explained how the internal noise inherent in each neuron works effectively for an array of the neurons to enhance the system's sensitivity to weak signals. Therefore, it is quite important for a clear understanding of stochastic resonance in biological systems to know how the internal noises are generated and how they serve a useful

function in the detection of weak signals in relatively complex systems such as ion channels and receptor cells. Petracchi et al. (1994) studied experimentally the role of internal noise in ion channels, but the results are inconclusive.

It would be quite useful to develop a further understanding of the microscopic mechanism of stochastic resonance in sensory systems. Hence the response properties of these systems to weak signals should be studied with more realistic models. Galvanovski and Sandblom (1997) have investigated theoretically the possibility of amplification of weak electromagnetic signals in cellular systems by considering the ion channel model whose gating properties are modulated by external noise fields. It was shown that a suitable choice of channel parameters can lead to a high degree of signal amplification.

In the present paper, using a relatively realistic model of a typical sensory system, we study the response property of an array of receptor cells under the application of weak input signals, the effect of gap junction on the response property, and the effect of collective gating dynamics of ion channels, in conjunction with the problems 1 and 2, problem 3, and problem 4, respectively.

MODEL

A model of a single ion channel

It has been considered in many models of ion channels that the gating of channels, that is, whether the gate of a channel is opened or closed, depends on a random process. However, recently it has been shown, based on an analysis of variation of transient charge distribution in single ion channels (Mika and Palti, 1994), that the transient variation associated with ion channel gating arises from the deterministic conformation change of the channels. Liebovitch and Toth (1991) analyzed the fluctuation of ionic current through ion channels, based on both a stochastic gating model and a deterministic one, and showed that it is highly possible for channel gating to be a deterministic process.

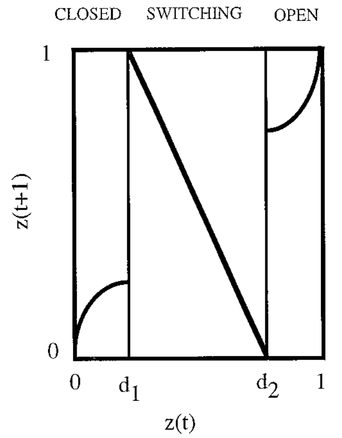


FIGURE 1 The mapping function describing the gating process of a single ion channel.

In the present model, we adopted the deterministic gating model presented by Liebovitch and Toth (1991). We used the mapping function, including two quadratic parts as shown in Fig. 1, because it generates periodic states as well as chaotic states. As shown in Fig. 1, the gating quantity $z(t)$ on the map is divided into three different regions: closed, switching, and open. In the closed region, the current through the channel is very low. In the open region, the current through the channel is very high. The switching region acts as a switch for the conversion between the open state and the closed one, when the gating quantity enters this region. The gating quantity $z(t + 1)$, representing a state of channel gating at the time $(t + 1)$, is given by $z(t)$ at the previous time t according to the mapping function

$$z(t+1) = \begin{cases} a_1(2d_1 - z(t))z(t); & 0 \le z(t) < d_1 \\ \dfrac{d_2 - z(t)}{d_2 - d_1}; & d_1 \le z(t) \le d_2 \\ a_2(z(t) - 1)(z(t) - 2d_2 + 1) + 1; & d_2 < z(t) \le 1, \end{cases} \tag{1}$$

where a_i and d_i $(i = 1, 2)$ are constant parameters. The gate is closed for $0 \le z(t) < d_1$ and opened for $d_2 < z(t) \le 1$. One time step in the function corresponds to t_m ms.

A model of a receptor cell syncytium system

To study the effect of intercellular coupling of ion channel gating through the gap junction on the response of the receptor system, we presented a model of the receptor cell syncytium system shown in Fig. 2. Each receptor cell includes p Na^+ channels and q K^+ channels in its apical membrane. N receptor cells are arrayed linearly, and the two adjacent cells are interconnected by gap junctions through which Na^+ and K^+ ions can pass smoothly.

We consider the temporal variation of the electric potential difference V_n across the apical membrane of nth cells $(n = 1 - N)$. The equations for $V_n(t)$ are derived from the conservation law of electric current in each cell,

$$C\frac{dV_n}{dt} + J_n(\text{Na}) + J_n(\text{K}) = I_{n-1} - I_n, \tag{2}$$

where $n = 1 - N$, $J_n(X)$ $(X = \text{Na, K})$ is the electric current through the X channels in the nth cell apical membrane, C is the membrane capacitance, and I_n is the electric current from the nth cell to the $(n + 1)$th cell through gap junctions as shown in Fig. 2. The channel currents are given by

$$J_n(\text{Na}) = g_{\text{Na}} \sum_{k=1}^{p} x_{n,k}(V_n - E_{\text{Na}}), \tag{3}$$

$$J_n(\text{K}) = g_{\text{K}} \sum_{k=1}^{q} y_{n,k}(V_n - E_{\text{K}}), \tag{4}$$

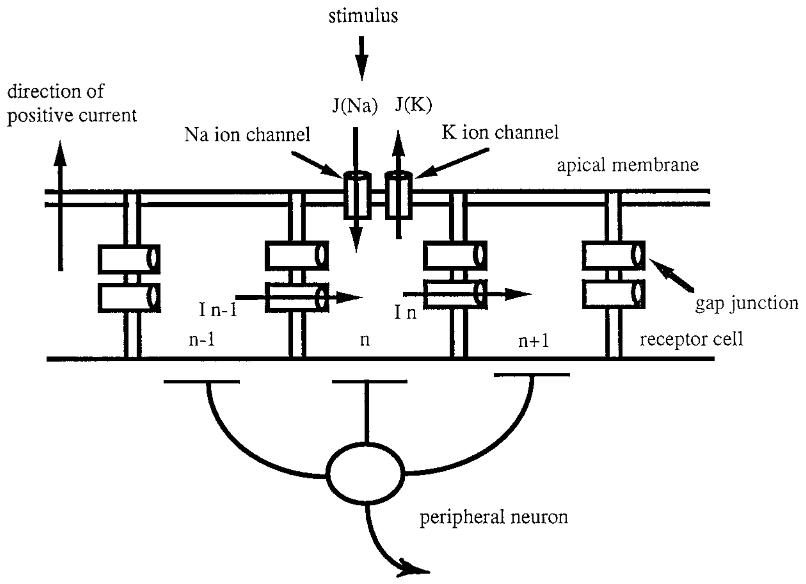


FIGURE 2 A model of receptor cell syncytium with a peripheral neuron. Each receptor cell includes p Na^+ and q K^+ channels in its apical membrane. The two adjacent cells are connected electrically through gap junctions in their basal membranes. The neuron innervates all of the cells equally.

where $x_{n,k}$ and $y_{n,k}$ are the gating quantities for the kth Na^+ channel and the kth K^+ channel in the nth cell, respectively; their temporal variation is given by Eq. 1. g_X is the electric conductance of an X channel, and E_X is the equilibrium potential for X ions. The electric current I_n is given by using the membrane potential V_n as

$$I_n = \frac{V_n - V_{n+1}}{r}, \tag{5}$$

where r is the electric resistivity of all of the gap junctions in the boundary between the two adjacent cells.

Equation 2 is reasonably approximated by using the Euler method as

$$\begin{aligned} V_n(t+\Delta t) = V_n(t) &- \sigma_{Na} \sum_{k=1}^{p} x_{n,k}(t)(V_n(t) - E_{Na}) \\ &- \sigma_K \sum_{k=1}^{q} y_{n,k}(t)(V_n(t) - E_K) \\ &+ \lambda\{V_{n+1}(t) + V_{n-1}(t) - 2V_n(t)\}, \end{aligned} \tag{6}$$

where $\sigma_{Na} = g_{Na}\Delta t/C$, $\sigma_K = g_K \Delta t/C$, $\lambda = \Delta t/(rC)$, and Δt is the unit of the time step.

Because we consider that the Na^+ and K^+ channels are voltage-dependent, we introduce the dependence of channel gating function on the membrane potential V_n, which is given through the voltage dependence of the branching parameter a_i ($i = 1, 2$) in Eq. 1, as

$$a_i(t+\Delta t) = a_{i0} \pm \epsilon \cdot \tanh\left[\frac{F(V_n(t) - E_n)}{2RT}\right], \quad i = 1, 2, \tag{7}$$

where + and − are used for $i = 1$ and 2, respectively, a_{i0} is the value for the resting state ($V_n = E_n$), E_n is the resting potential corresponding to the value of V_n in the steady state, where $I_n = I_{n-1}$, $J_n(Na) + J_n(K) = 0$, $dV_n/dt = 0$, and R, T, and F have their usual meanings. It is a result of this voltage dependence that as the membrane potential is depolarized, that is, as $V_n - E_n$ is increased, the probability that the channel is open increases.

A model of a peripheral neuron

To investigate the dependence of stochastic resonance on the dynamics of the receptor cell syncytium, we consider a peripheral neuron innervating each cell, as shown in Fig. 2. The outputs of receptor cells converge to the peripheral neuron. Then the membrane potential V_p of the neuron is determined by

$$\begin{aligned} C_p \frac{dV_p}{dt} = &-g_{Na}(V_p - V_{Na}) - g_K(V_p - V_K) \\ &-g_L(V_p - V_L) + w \sum_{n=1}^{N} \left[1 + \exp\left(-\frac{V_n - V_{th}}{B}\right)\right]^{-1}, \end{aligned} \tag{8}$$

where C_p is the capacitance of the membrane of the neuron; g_{Na} and g_K are the conductances of active Na^+ and K^+ channels, respectively; g_L is the conductance of a leak channel (Cl^- channel); and V_X is the equilibrium potential of ion X ($X = Na^+, K^+, L$). The last term of Eq. 8 means the postsynaptic current that is induced by the neural transmitter release from the presynaptic membrane of the receptor cells. In Eq. 8, w is the strength of synaptic connection, V_{th} is the threshold value, and B is the parameter determining the rising rate of the sigmoid curve. The temporal variations of conductances g_X (X = Na, K, L) are determined by using the Hodgkin-Huxley equations (Hodgkin and Huxley, 1952).

Preparation for numerical calculations

We adopted the values listed in Table 1 for the quantities used in the present model. We describe briefly the reasons why we adopted the values.

The values of quantities relevant to the mapping function for ion channel gating (d_i and a_{i0}) were chosen so that the mapping function (Eq. 1) becomes roughly equivalent to the piecewise linear function of Liebovitch and Toth (1991). The gating quantity $z(t)$ given by Eq. 1 changes periodically for $a_{i0} = 11.25$ and chaotically for $a_{i0} = 16.50$, in the case where $\epsilon = 0.1$ (see Eq. 7), but $z(t)$ changes chaotically for both of the values of a_{i0} in the case where $\epsilon = 0.0$. The values of t_m corresponding to the unit time step in Eq. 1 were chosen so that the temporal changes of $z(t)$ become quite similar to the observed changes in electric current through a single ion channel (Sakmann and Neher, 1983). The values of $z(t)$ for t between $(i - 1)t_m$ and it_m were determined by linear interpolation. The value of ϵ was chosen so that the voltage-dependent part of a_i becomes at most 1% of the independent part a_{i0}.

The numbers (p and q) of Na^+ and K^+ channels in a single cell and the number N of the cells were chosen tentatively, but the conclusions obtained based on the present calculation also hold in the case where much larger values are taken for p, q, and N.

We adjusted the values of effective conductances σ_{Na} and σ_K so that the amplitude of membrane potential fluctuation in a receptor cell becomes several millivolts. The values of effective conductance of gap junctions was obtained by using the values of $\Delta t = 0.1$ ms, $C = 1$ μF/cm^2, and $1/r =$ order of 1 mS/cm^2. In the case with no specification, we used 0.2 for λ.

The values of parameters w, V_{th}, and B, describing the synaptic connection between the receptor cells and the peripheral neuron, were adjusted so that the neuron can be activated occasionally by the sum of inputs from N receptor cells.

TABLE 1 The values of the quantities included in the model and the equations relevant to the definition of the quantities

Quantity	Definition (Eq.)	Value
d_i	1	$d_1 = 0.1$, $d_2 = 0.9$
t_m	1	2.5 ms
a_{i0}	7	$a_{10} = a_{20} = 11.25$, 16.50
ϵ	7	0.1
F/RT	7	38.755
N	2	10
p, q	6	$p = q = 5$
σ_{Na}, σ_K	6	$\sigma_{Na} = \sigma_K = 0.07$
λ	6	0–0.5, (0.2)
Δt	6	0.1 ms
E_{Na}, E_K	6	$E_{Na} = 60$ mV, $E_K = -90$ mV
w	8	3.15
V_{th}	8	13 mV
B	8	10 mV

RESULTS AND DISCUSSION

Dynamical properties of single ion channels

The gating dynamics of a single ion channel generated by the mapping function (Eq. 1) includes various kinds of periodic and chaotic oscillations. Fig. 3 shows the branching diagram of gating dynamics in the case where $a_1 = a_2$, and the value of a_1 is changed as the branching parameter.

There are many windows for periodic states in the chaotic region. As a_1 is increased, the period of oscillation decreases. In the region of relatively small values of a_1, the dynamics changes sensitively with the variation in a_1, but as a_1 increases, the dynamics becomes stable under a small change in a_1.

Dynamical properties of ion channel gating and membrane potential in the syncytium system

The syncytium model has two kinds of dynamical properties, depending on the value of parameter a_{i0}. The periodic state for collective ion channel gating is shown in Fig. 4 *a*, where $a_{i0} = 11.25$, and all of the ion channels show spatially synchronous and temporally periodic gating. As shown in Fig. 5 *a*, the membrane potential of every cell also oscillates periodically. Because the gating of an isolated single channel ($\epsilon = 0.0$) is chaotic for $a_{i0} = 11.25$, the synchronous collective gating is produced by the interchannel interaction through the membrane potential, which is represented by Eq. 7. The chaotic state for collective ion channel gating is shown in Fig. 4 *b*, where $a_{i0} = 16.50$ and the gating of every channel is chaotic. The membrane potential of every cell also fluctuates chaotically, as shown in Fig. 5 *b*.

Because the main purpose of the present paper is to investigate the effect of gap junctions on the response properties of the system under the application of a very weak signal, we calculated the dynamical properties of the syncytium system for the various values of conductivity λ of the gap junctions. The calculated patterns of the collec-

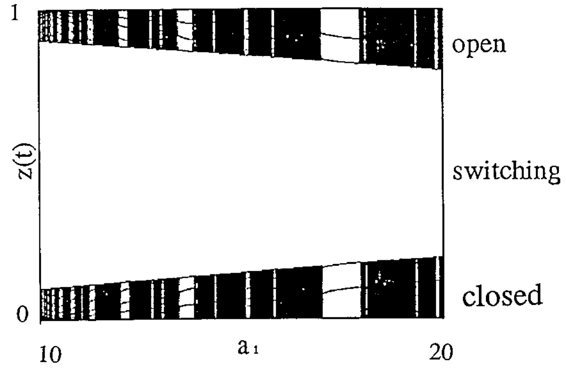
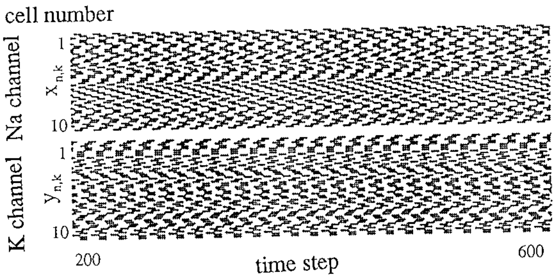


FIGURE 3 The branching diagram of gating dynamics of a single ion channel. The branching parameter is a_1 in Eq. 1. The parameter values used are $a_1 = a_2$, $d_1 = 0.1$, $d_2 = 0.9$, and $\epsilon = 0.0$. The black regions mean chaotic gating.

(a) Periodic state



(b) Chaotic state

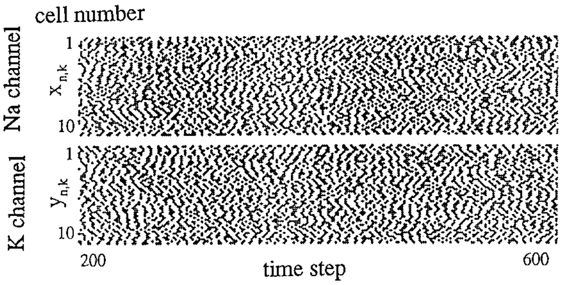


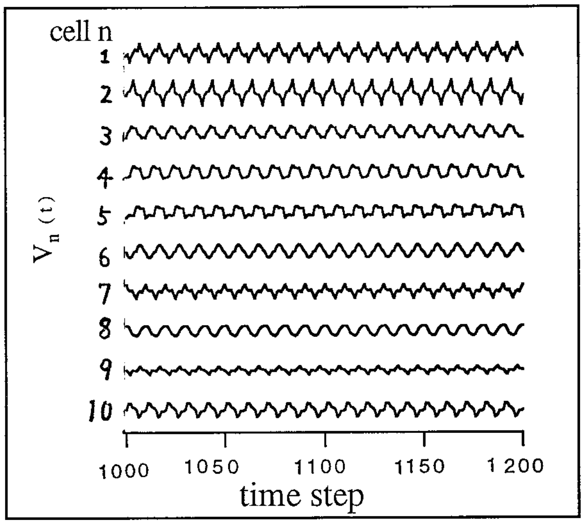
FIGURE 4 The two kinds of dynamical states for collective ion channel gating. (*a*) Periodic state ($a_{i0} = 11.25$). (*b*) Chaotic state ($a_{i0} = 16.5$). Each diagram shows the temporal variations of gating quantities (x_{nk},y_{nk}) for n = 1–10, k = 1–5, where the black and blank points mean open and close states, respectively. The parameter values used are given in Table 1.

tive channel gating for various values of λ are similar to the patterns shown in Fig. 4, and the calculated oscillation patterns of the membrane potentials are similar to the patterns shown in Fig. 5. However, we cannot clearly determine from these calculated patterns how the dynamical properties of the system depend on λ. Because the interaction between the receptor cells increases with λ, we calculated the correlation function between membrane potentials V_m and V_n of the two different cells m and n, respectively, which is defined by

$$C_V(m, n; \tau) = \lim_{T \to \infty} \frac{1}{T} \int_0^T V_m(t + \tau) V_n(t) \mathrm{d}t. \tag{9}$$

Fig. 6 shows the calculated correlation functions $C_V(m, n; \tau)$ in the chaotic state for the three values of λ as functions of τ, where m = 5 and n = 6, 7. The correlation of the membrane potential variation between the different cells increases with the gap junction conductivity, even when the system is in the chaotic state. This means that the synchronicity of the membrane potential fluctuation between the different cells increases as the cells are interconnected more strongly through the gap junctions.

(a) Periodic state



(b) Chaotic state

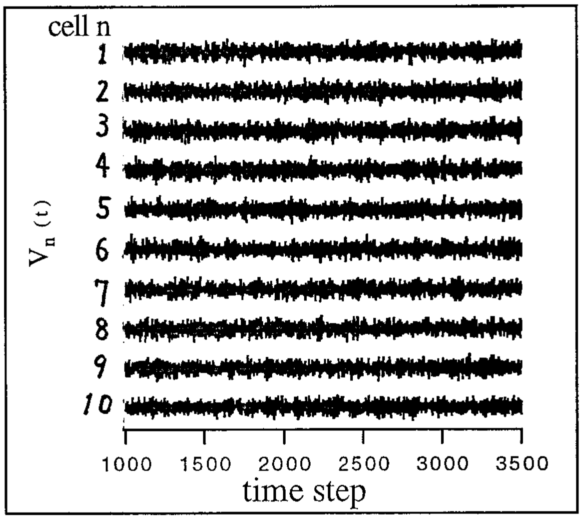


FIGURE 5 The two kinds of dynamical states for membrane potentials. (*a*) Periodic state (a_{i0} = 11.25). (*b*) Chaotic state (a_{i0} = 16.5). Each diagram shows the temporal variations of membrane potential of the *n*th cell, V_n (n = 1–10). The parameter values are the same as in Fig. 4.

Signal transduction across a single ion channel

To investigate the signal transduction properties of ion channels whose gating process is determined by Eq. 1, we calculated the electric current across the single channel under the application of a sinusoidal signal by using Eq. 3, where p = 1, ϵ = 0.0, $V_n = (V_h + V_s \sin 2\pi f_s t)$ mV, and f_s = 0.028 kHz. The spectral density of the current calculated for V_h = 30 mV and V_s = 0.5 mV is shown in Fig. 7. A sharp peak appeared at the frequency f_s of the signal. The calculated result is qualitatively quite similar to the observed spectral density for alamethicin ion channels (Bezrukov and Vodyanoy, 1997b).

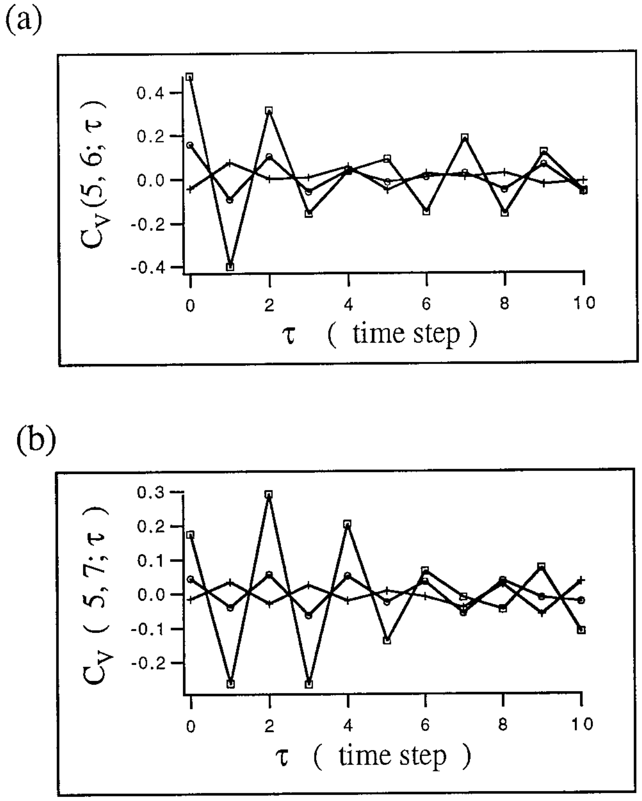


FIGURE 6 The correlation functions $C_V(m,n;\tau)$ between membrane potentials V_5 and V_n ($n = 6, 7$) in the chaotic state for the three cases ($\lambda = 0.0, 0.3$, and 0.5) of conductivity of gap junctions. +, ○, □: $\lambda = 0.0, 0.3$, and 0.5, respectively.

Effect of gap junctions on stochastic resonance with the assistance of chaotic potential fluctuation

The presence of noise is essential for the detection of weak signals by stochastic resonance. First, we investigated, using weak periodic signals without any external noise, whether the chaotic fluctuation of membrane potentials of the receptor system can act as internal noise for the stochastic resonance in the system. Fig. 8 shows the response of the system in the chaotic state and in the periodic state to a very weak sinusoidal current injected simultaneously into each receptor cell. The power spectra $P(\omega)$ of spike trains of the peripheral neuron clearly show that the peaks corresponding to the signal frequency ω_0 and its integral multiple frequencies appear in the chaotic state, as seen in Fig. 8 *a*. To clarify the role of the chaotic fluctuation of membrane potential in weak signal detection, we investigated the detection ability of the system in the state where the membrane potentials V_n fluctuate periodically, as shown in Fig. 8 *b*. There is no peak at ω_0 in the power spectra $P(\omega)$, as seen in Fig. 8 *b*. The peripheral neuron rarely fires in the periodic state, because the phase of periodic oscillation of the membrane potential in each cell differs constantly from the phase in the other cells, and as a result the sum of the instantaneous postsynaptic currents from all of the cells can hardly become so large that the peripheral neuron can fire. These results show clearly that the chaotic potential fluctuations work as an internal noise for the stochastic resonance in the system.

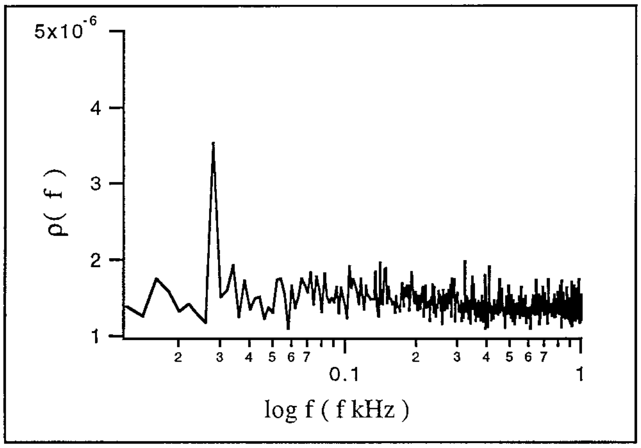


FIGURE 7 Spectral density of the electric current (Eq. 3) across the single ion channel under application of the voltage $V_n = V_h + V_s \sin(2\pi f_s t)$, where $a_{i0} = 16.5$, $\epsilon = 0.0$, $V_h = 30$ mV, $V_s = 0.5$ mV, and $f_s = 28$ Hz.

Second, to investigate the effect of syncytium structure on the capacity to detect weak signals, we calculated the dependence of the power spectra for the chaotic state on the strength of ionic conduction through gap junctions, which is proportional to λ in Eq. 6. Fig. 9 shows the values of peak height at the signal frequency ω_0 in the spectra as a function of λ. The capacity to detect weak signals has a tendency to increase with increasing λ. This tendency arises mainly from the property of the system that the synchronicity of potential fluctuation between the different cells increases with λ, as shown in Fig. 6, and as a result the sum of postsynaptic current from each cell increases with λ. This means that the gap junctions increase the detection capacity of the syncytium system by modifying the internal noise.

Response of the syncytium system to incoherent signals

The effect of multiunits on stochastic resonance has been considered in the case where the signal received by each unit is common, that is, coherent (Collins et al., 1995; Inchiosa and Bulsara, 1995; Moss, 1997). In the present paper, we investigated the effect of multiunits (syncytium structure) on the detection ability of weak signals in the case where the signal received by each receptor cell is slightly different from the input signals for the other cells. Fig. 10 shows the power spectra of response spike trains of the peripheral neuron as a function of λ for the two kinds of incoherent sinusoidal stimulations. The result for the stimulations, $I_0(0.95 + 0.1r_n) \sin \omega_0 t$ ($n = 1$–10), with a fluctuation in signal amplitude, is shown in Fig. 10 *a*, where r_n is a random number in the range of 0–1. The result for the stimulations, $I_0 \sin(\omega_0 t + r_n \pi/6)$ ($n = 1$–10), with a fluctuation of signal phase is shown in Fig. 10 *b*. A syncytium

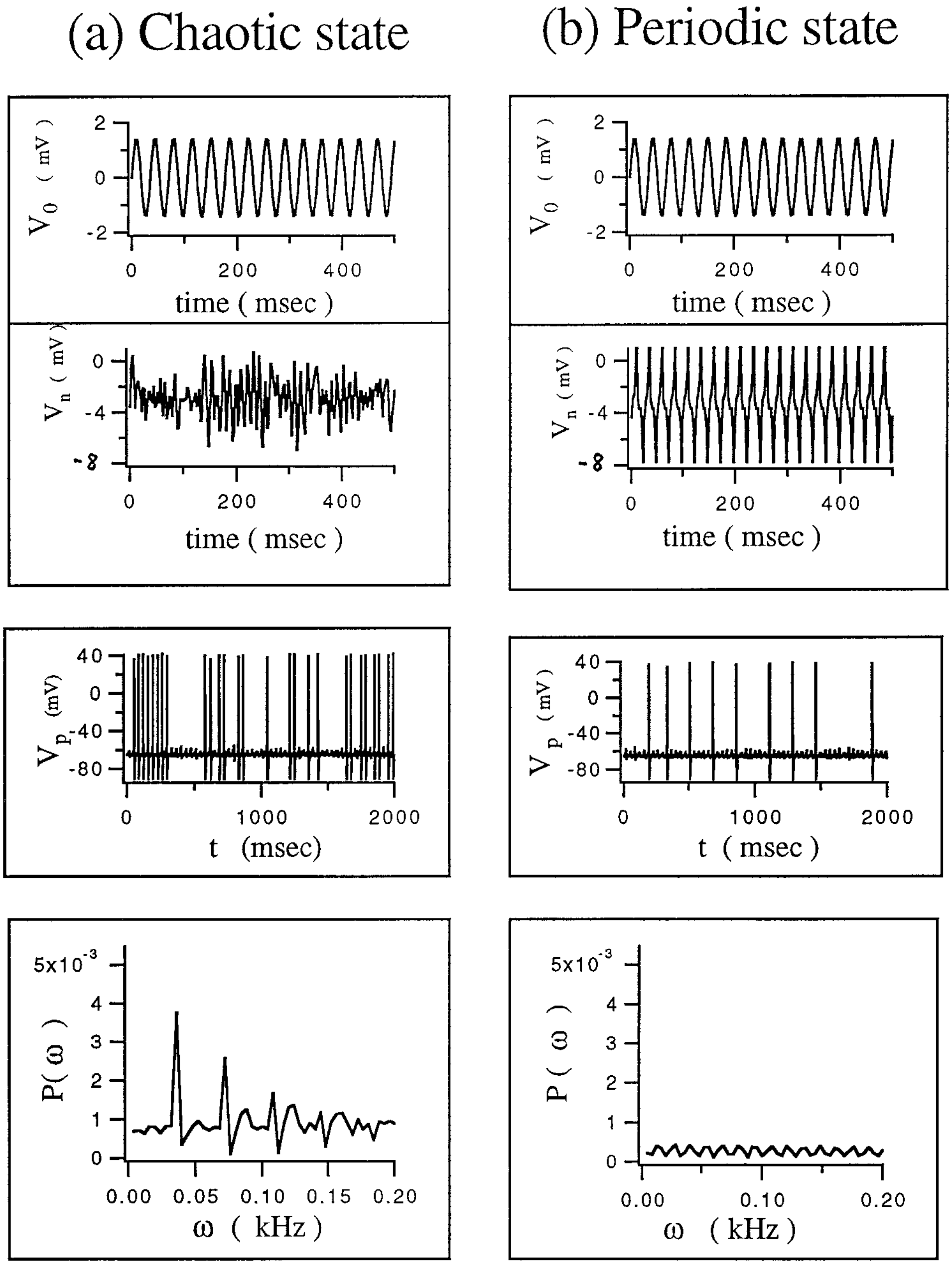


FIGURE 8 Responses of the syncytium system in the chaotic state (*a*) and in the periodic state (*b*) to a weak sinusoidal electric current $I_0 \sin \omega_0 t$ injected simultaneously into each receptor cell. V_n is the membrane potential of one receptor cell, where the input signal $V_0 \sin \omega_0 t$ ($V_0 = I_0 \Delta t / C$) is also shown in the top space, where $\omega_0 / 2\pi = 28$ Hz and $V_0 = 1.4$ mV. V_p is the response of the peripheral neuron. $P(\omega)$ is the power spectrum of the spike train V_p.

system constructed with enough gap junctions can clearly detect the weak signals, even if the signals include spatial fluctuation in their amplitude or their phase.

Stochastic resonance with the assistance of external noise

When the external noise is added to the weak periodic signal, the syncytium system becomes able to detect the signal, irrespective of the dynamical state of the system. The power spectra of response spike trains of the peripheral neuron are shown in Fig. 11 for the system in the chaotic state and in the periodic state. The system in the periodic state can detect the weak signal with assistance from external noise, as seen in Fig. 11 *b*, but the detection capacity is noticeably lower than the capacity in the chaotic state, where the system is assisted by both the internal and external noises.

It is required for the stochastic resonance generated by a single unit system that the optimal intensity of the external noise is adjusted as the nature of the signal is changed (Moss and Wiesenfeld, 1995). However, Collins et al. (1995) have shown that the ability of a summing network of excitable units to detect a range of weak aperiodic signals can be optimized by a fixed level of noise, irrespective of the nature of the input signal.

To investigate the dependence of detection capacity of the syncytium system on the intensity of external noise, we calculated the power spectra of the response spike trains of the peripheral neuron as a function of the intensity. Fig. 12

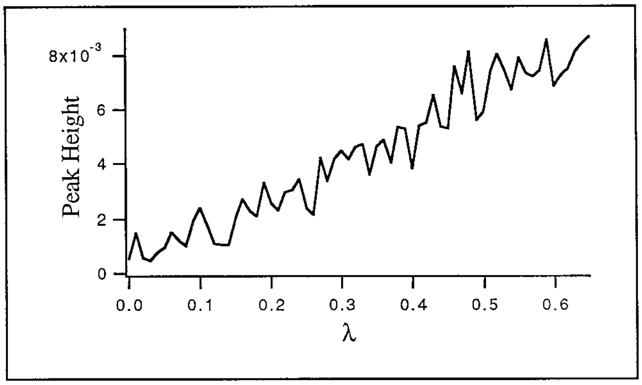


FIGURE 9 Dependence of peak height at ω_0 in the power spectra of response spike trains V_p on the conduction strength λ of gap junctions in the chaotic state. The parameter values used are the same as in Fig. 8.

shows the dependence of the effective signal-to-noise ratio (ESNR) on the external noise intensity for the three values of conduction strength λ of gap junctions, where ESNR means the ratio of the peak height at ω_0 of the power spectra to the level of the foot of the peak. There is no clear optimal intensity of the external noise, but the detection ability becomes optimal in a broad range of the intensity. The position and width of the optimal range change depending on λ.

The calculated dependence of ESNR on the intensity of external noise for $\lambda = 0.1$ is qualitatively similar to the dependence observed for crayfish mechanoreceptors (Wiesenfeld and Moss, 1995). It indicates the contribution of internal noise of the neuron to the stochastic resonance in the mechanoreceptors that the observed SNR data do not

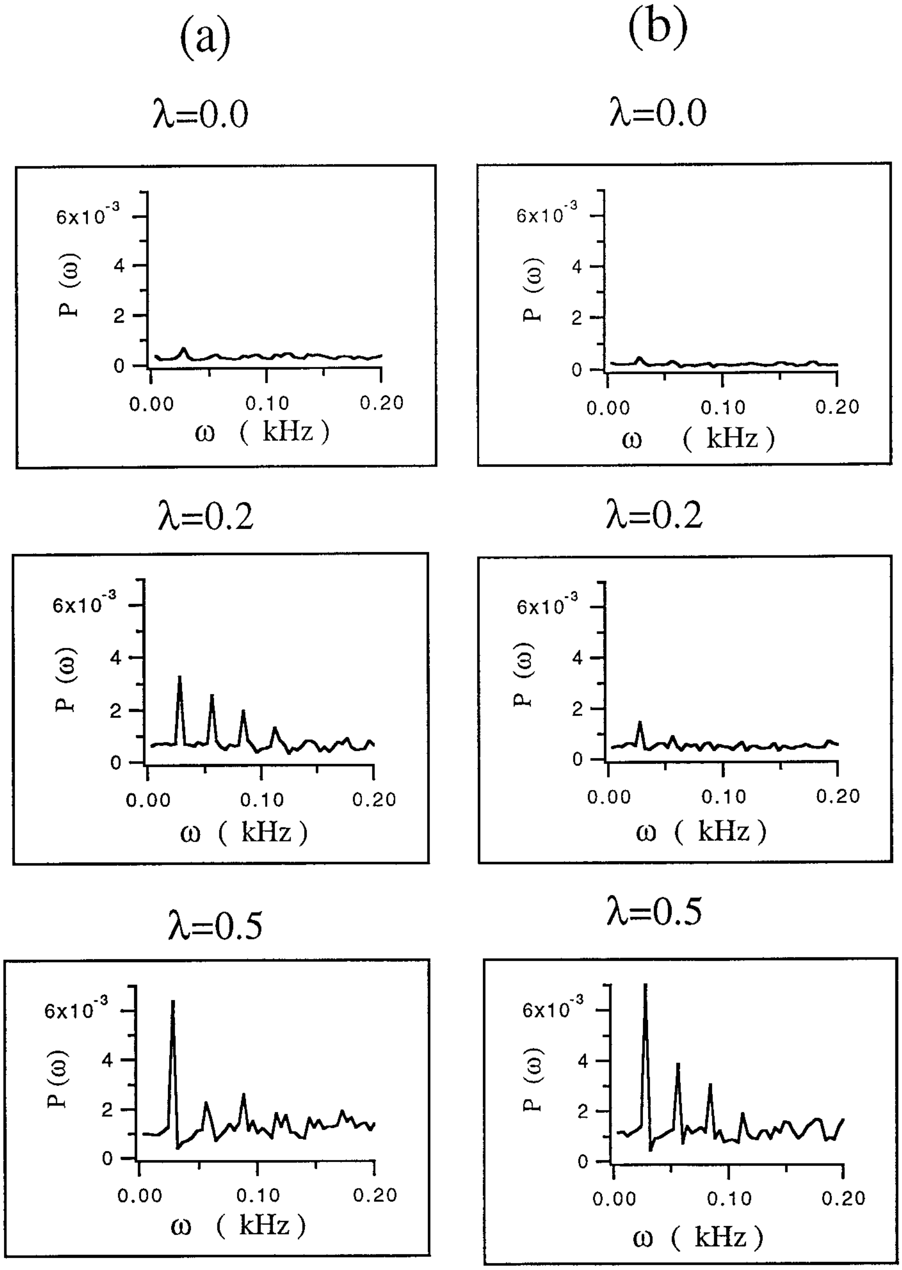


FIGURE 10 The power spectra of response spike trains of the peripheral neuron as a function of conductance λ of gap junctions in the case where the syncytium system is in the chaotic state ($a_{i0} = 16.5$). (*a*) Response to the sinusoidal currents with a spatial fluctuation of signal amplitude, where $I_n = I_0(0.95 + 0.1r_n) \sin \omega_0 t$ (n = 1–10) and r_n is a random number in the range of 0–1. (*b*) Response to the currents with a spatial fluctuation of signal phase, where $I_n = I_0 \sin(\omega t + r_n\pi/6)$ (n = 1–10). $I_0 = 1.4$ mV × $(C/\Delta t)$ and $\omega_0/2\pi = 28$ Hz.

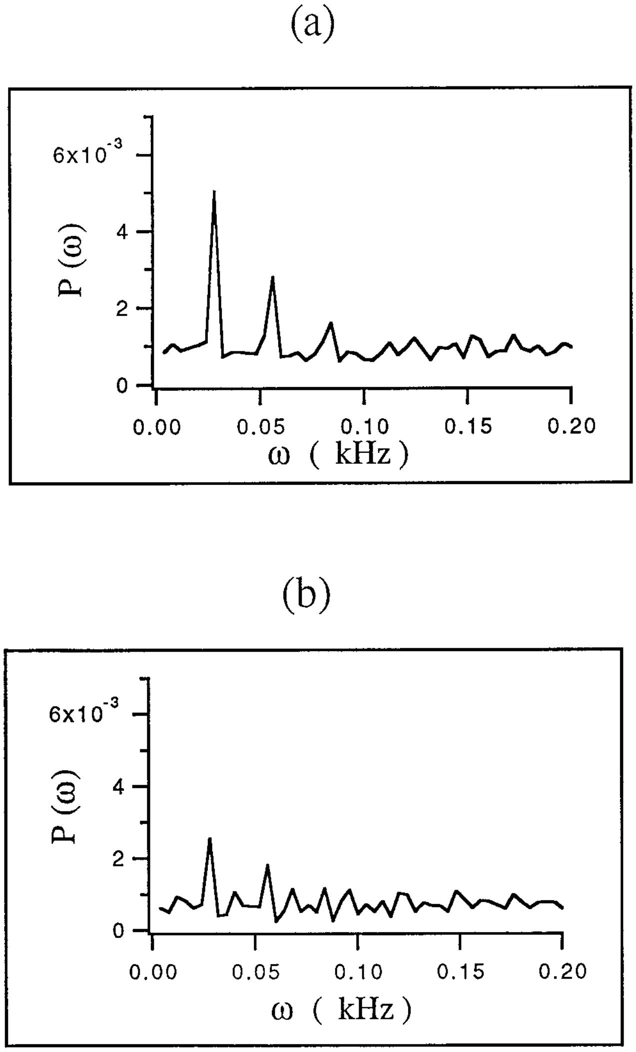


FIGURE 11 Power spectrum of response spike trains of the peripheral neuron induced by the weak current I_0 sin $\omega_0 t$ with the assistance of external noise, which is a white noise of intensity 2 mV ($C/\Delta t$). (*a*) In the chaotic state. (*b*) In the periodic state.

decrease rapidly for the small noise intensity. It has been suggested (Wiesenfeld and Moss, 1995) that the origin of internal noise is the spontaneous fluctuation of membrane potential of the receptor neuron.

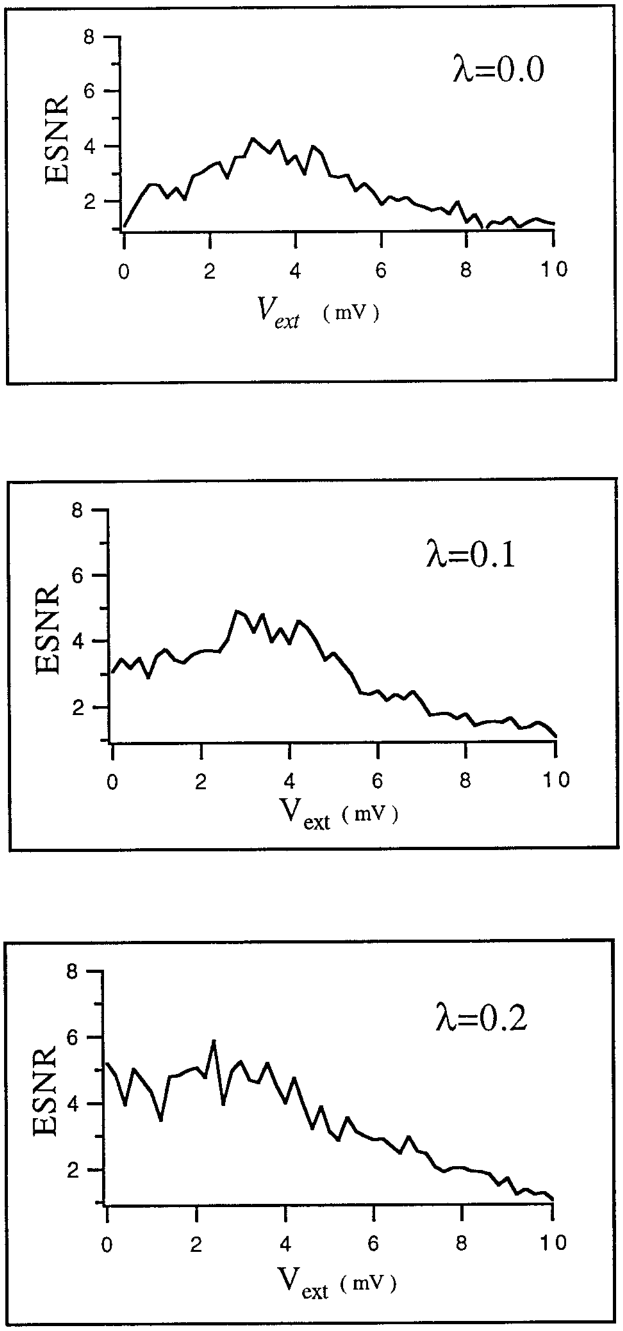


FIGURE 12 Dependence of the effective signal-to-noise peak ratio (ESNR) on the intensity V_{ext} of external noise for the three values of conductance strength λ of gap junctions in the chaotic state. ESNR means the ratio of the peak height at ω_0 in the power spectra to the level of foot of the peak. The parameter values used are the same as in Fig. 8. The noise is a white noise of intensity V_{ext}.

CONCLUDING REMARKS

Plausibility of the deterministic model of channel kinetics

Most models of ion channel kinetics have been based on stochastic processes such as the Markov process (Colquhorn and Hawkes, 1981; MacGee et al., 1988) and fractal processes (Liebovitch and Sullivan, 1987), in which switching between the open and closed states occurs randomly. These stochastic models have reasonably reproduced the channel kinetics observed in many ion channels. In the models, it was assumed that channel proteins are in local thermodynamic equilibrium with their environment, and as a result, switching between different conformations of the proteins is essentially a random process driven by the energy from thermal fluctuations. This assumption came mainly from the observed results that ionic currents through single ion channels change quite randomly.

However, nonlinear dynamics has shown us that not everything that looks random is stochastically random. The output from some nonlinear deterministic systems can be so complex that it (that is, chaos) mimics random behavior (Liebovitch, 1995). Mika and Palti (1994) have shown, based on analysis of variation of charge distribution in single ion channels, that the transient change associating with the ion channel gating arises from the deterministic conformation change of the channels.

Liebovitch and Toth (1991) proposed a deterministic model in which the switching of the channel gate is determined by an iterated map. They showed that the mapping function can reproduce several observed properties of single ion channels (Liebovitch and Toth, 1991). Lievobitch and Czegledy (1992) presented the ion channel kinetics based on deterministic motion in a potential with two local minima. The model has shown that the nonlinear interactions between the channel protein and the thermal fluctuations result in the protein spending long times in some locations in the energy landscape that are not at local energy minima. This means that long-lived states of the channel do not necessarily correspond to the stable conformations of the channel. This result is quite different from the usual assumption in the stochastic models that channel proteins are in local thermodynamic equilibrium with their environment. Thus the origin of the channel gating fluctuation in deterministic models is quite different from that in the stochastic model. It is chaos in the former models and thermal fluctuation in the latter ones.

We adopted the deterministic model in the present paper because the mapping function can simply represent the complex gating kinetics of some passive ion channels. We used the nonlinear mapping function given by Eq. 1, in which the linear functions on the piecewise linear map, studied in detail by Liebovitch and Toth (1991), were replaced with quadratic functions. The linear map generates only chaotic gating states, but the quadratic map generates periodic gating states in addition to chaotic ones by changing the value of a_1 and/or a_2, as seen in Fig. 3.

Chaotic oscillation of membrane potential

Chaotic oscillations of the membrane potential have been demonstrated experimentally and theoretically in various types of excitable membrane systems. The experimental study has been made for cardiac cells (Guevara et al., 1981), internodal cells of Nitella (Hayashi et al., 1982), giant axons of squids (Matsumoto et al., 1984), Purkinje fibers (Chialvo et al., 1990), and ventricular muscles (Chialvo et al., 1990). The chaotic oscillations in these systems are mainly driven by a periodic external current. There have been also theoretical identifications of autonomous (nondriven) chaos in various kinds of membrane models, such as bursting nerve cells (Chay, 1984), cardiac cells (Chay and Lee, 1984), and pancreatic β cells (Chay and Rinzel, 1985). The oscillation phenomena mentioned above arise from the electric excitation of membranes, which is driven by various types of voltage-gated (active) ion channels. In these models, it has been assumed that all of the same kind of active ion channels simultaneously change their gating state; that is, the channels behave cooperatively.

The chaotic potential oscillations in the lipid bilayer membranes including only passive ion channels or no ion channels have been studied theoretically (Yagisawa et al., 1993, 1994; Fuchikami et al., 1993). The chaotic oscillations in the membrane systems are generated by the repetitive, abrupt variation in the ion conductivity across the membrane, which is induced by cooperative interaction between ion channels or between lipid molecules. The nonlinear potential oscillations in lipid bilayer membranes have also been studied experimetally (Ishii et al., 1986; Toko et al., 1986).

The chaotic oscillations of membrane potentials in the present model arise from chaotic fluctuations in the ionic current through passive ion channels, the gating dynamics of which is chaotic. There is no direct interaction between the ion channels. That is, each channel opens its gate almost independently of the gate state of the other channels. Therefore, the observation of this type of potential oscillation may be difficult compared with the observation of oscillations induced by the cooperative channel gating. However, if there are ion channels whose gating dynamics is chaotic, it is quite possible that the potential of membranes including such ion channels oscillates choatically. Fatt and Katz (1950) showed by the reasonable consideration and observation of end-plate potential noise that the resting potential of nerve cell fluctuates because of thermal agitation of ions, and the fluctuation voltage becomes on the order of 1 mV. They suggested that the random potential fluctuation may produce important physiological effects.

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