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PERIODIC AND NONPERIODIC RESPONSES OF MEMBRANE POTENTIALS IN SQUID GIANT AXONS DURING SINUSOIDAL CURRENT STIMULATION

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Abstract

Periodic and non-periodic responses of the membrane of squid giant axons to sinusoidal current stimulation were studied during spontaneous repetitive firing of action potentials. The periodic or non-periodic trains of action potentials were analyzed with stroboscopic plots, one-dimensional transfer functions and power spectrum analysis. These data processing techniques elucidated the dynamical structure of the axon during repetitive firing. It was reconfirmed that the state of spontaneous repetitive firing of action potentials corresponds to that of a dissipative structure with a stable limit-cycle. The oscillations exhibited by the axon during sinusoidal current stimulation were classified into four categories: (1) entrained oscillations, (2) 1/N entrained oscillations, where N stands for an integer equal to or larger than 2, (3) quasi-periodic oscillations and (4) chaotic oscillations.

1. Introduction

It has been demonstrated that dissipative structures are formed in nonlinear and nonequilibrium systems of fluid dynamics, chemical reactions and nerve excitation (Glansdorff and Prigogine, 1971; Nicolis and Prigogine, 1977; Haken, 1977; Matsumoto, 1981; Aihara and Matsumoto, 1982; Matsumoto and Shimizu, 1983). A dissipative structure shows remarkable temporal periodicity, or coherent time-order, so that it can be represented by a nonlinear oscillator with an orbitally stable limit-cycle. It is important to study the effect of periodic stimulation upon the nonlinear oscillator in order to clarify the characteristics of the dissipative structure. Application of the periodic stimulation to the oscillator brings about one more degree of freedom to the system, putting the system further from equilibrium (Nicolis and Prigogine, 1977). As a result, the periodic stimulation disturbs the periodic motion of the nonlinear oscillator. Whether or not it behaves periodically is determined by the frequency and the strength of the periodic stimulation and, at the same time, by the

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dynamic structure of the system. (Holden, 1976; Kai and Tomita, 1979; Matsumoto *et al.*, 1980; Guttman *et al.*, 1980; Ueda and Akamatsu, 1981; Nagashima 1982; Aihara *et al.*, 1982, 1983). Thus, we can get valuable information about the dynamic structure of the system by observing responses of the nonlinear oscillator to the periodic stimulation.

Here we report periodic, quasiperiodic and chaotic responses of squid giant axons to sinusoidal current stimulation during self-sustained oscillations of action potentials (Huxley, 1959; Guttman, 1969). The state of the self-sustained oscillation is in the spatio-temporally coherent order and can be understood as that of a typical dissipative structure with an orbitally stable limit-cycle (Matsumoto, 1978, 1981; Matsumoto and Shimizu, 1982; Matsumoto and Stühmer, 1978; Aihara and Matsumoto, 1982; Matsumoto, Aihara and Utsunomiya, 1982). Thus, we can regard the axon in the state of the self-sustained oscillation (the spontaneous repetitive firing) as a nonlinear neural oscillator. This study aims at elucidating the dynamical structure of the squid axon under repetitive firing by observing responses of membrane potentials to periodic current stimulation.

2. Materials and Methods

Materials

Giant axons of squid (*Doryteuthis bleekeri*) were used. The squid were collected in Sagami Bay, transported to the Electrotechnical Laboratory where the present experiments were performed, and maintained in a small, circular and closed-system aquarium tank (Matsumoto, 1976; Matsumoto and Shimada, 1980). It took 5 to 8 hours from the seashore to the Laboratory by truck. Although the aquarium system allowed the squid to survive in the tank for over 40–60 days they were usually used up within 2 weeks of delivery. Axon diameters were between 500 and 750 μm. The majority of the adherent tissues surrounding the axon was removed under a dissecting microscope. The axon was then transferred to a Lucite chamber filled with natural sea water (NSW; pH 8.2) for the physiological experiments described below.

Experimental methods

Intact axons were used. The external medium surrounding the axon was natural sea water (NSW) or a 1:9 mixture of NSW and 550 mM NaCl to induce the spontaneous repetitive firing of action potentials, the pH being adjusted to 8.2 with Tris.–HCl (Huxley, 1959; Guttman, 1969; Matsumoto, 1981; Aihara and Matsumoto, 1982). Membrane potentials were recorded through a pair of glass pipette Ag–AgCl electrodes filled with 550 mM KCl. The internal potential electrode with its tip of 80 μm in outer diameter was inserted inside and parallel to the axon. To reduce the electrode impedance, a platinum wire of 25 μm in diameter was inserted into the glass pipette up to the tip (Hodgkin and Katz, 1949). The external potential electrode was put in the external medium just outside the axon and faced the tip of the internal potential electrode across the membrane. Sinusoidal currents for stimulation were applied through an internal platinized platinum wire electrode (current electrode), 50 μm in diameter and exposed for 5 mm length. The current electrode was inserted into the axon with the internal potential electrode. The tip of the potential electrode was placed at the center of the conducting portion of the current electrode. The axon for the region where the conducting portion of the current electrode was located was spatially clamped, so that no spatial variation of membrane potentials could take place.

The sinusoidal current was superimposed on a d.c. bias current of 1.5 or 2.0 μA, which is just equal to the amplitude of the sinusoidal current. Responses of membrane potentials to the sinusoidal current stimulation were monitored on an oscilloscope (Yokogawa-Hewlett Packard 180C) and, at the same time, recorded on an FM tape recorder (Sony Magnescale Inc., type DFR-3415). The sinusoidal current used for the stimulation was also recorded on the recorder. All the experiments were carried out at room temperature (15–24°C).

Data Gathering and Processing

Analog data of the potential response and current stimulation, recorded at the same time as described above, were digitally processed with a microcomputer system (Sharp Inc., MZ 80B) after they were converted into digital data through a 12 bit A/D converter with 8 μsec in conversion time. Membrane potential record was sampled each 10 μsec and 3 subsequent data points were stored in the digital memory of the microcomputer system at each time-period T of current stimulation. The 3 digital data points were obtained so that the second point was sampled when the stimulating sinusoidal current is just crossing on the superimposed d.c. level in the direction from positive to negative values. From three subsequently-obtained values of membrane potentials $V_i(T)\ (i=1,2,3)$ for each period of time T, we got the average membrane potential V(T) at time T, defined by $V(T)=\frac{1}{4}(V_1(T)+2\ V_2(T)+V_3(T))$, and its time-differential $\frac{dV(T)}{dt}$, defined by $\frac{dV(T)}{dt}=\frac{V_3(T)-V_1(T)}{20\ \mu\text{sec}}$. The data thus obtained were displayed on an X–Y plotter (Watanaba Sokki Co. Ltd., WX4636R) in the following two ways; one was a set of $(V(T), V(2T)), (V(2T), V(3T)), \ldots\ldots, (V((N-1)T), V(NT))$, and the other was a set of $(V(T), \frac{dV(T)}{dt}), (V(2T), \frac{dV(2T)}{dt}), \ldots\ldots, (V(NT), \frac{dV(NT)}{dt})$, where N was an integer between 200 and 600. The former plot, $V(KT)\to V((K+1)T)$ where $K=1,\ldots\ldots,N-1$, is a one-dimensional transfer function or a kind of the Lorenz plot (Lorenz, 1963; Tomita and Kai, 1979). The latter one is related to a kind of Poincaré mapping and is called the stroboscopic plot (Minorsky, 1962; Kai and Tomita, 1979; Ueda and Akamatsu, 1981). It has been well known that both plots are useful to elucidate the dynamic structure of the nonlinear oscillator.

Fourier Analysis

Power spectral densities of the oscillating membrane potentials were calculated by a signal processor (Sanei Sokki, Co. Ltd., type 7T07A) and displayed on a CRT display. Analog data of membrane potentials recorded on the FM tape recorder were fed into the signal processor for the Fourier analysis after the data were filtered through a band-pass filter to avoid aliasing (Matsumoto and Shimizu, 1983).

3. Results

Periodic and non-periodic responses of membrane potentials to the sinusoidal current stimulation were observed in squid giant axons in the state of spontaneous repetitive firing of action potentials. The responses were found to be classified, judged from the stroboscopic and the Lorenz plots, into four classes; entrained, 1/N entrained, quasi-periodic and chaotic oscillations.

Entrained Oscillation

When the frequency f_s of the sinusoidal current stimulation is close to the natural frequency f_n of the spontaneous repetitive firing of action potentials, the firing frequency changes to keep in tune with the stimulation frequency f_s. It was reported (Matsumoto *et al.*, 1980) that the frequency range, where the firing frequency was in agreement with the stimulation frequency f_s, increased monotonically with the amplitude of sinusoidal current stimulation; the bigger the amplitude was, the wider the range became. This was reconfirmed in the present experiment. For example, Fig. 1(a) shows that the spontaneous repetitive firing of action potentials with a natural frequency of 228 Hz is entrained to repetitive firing with the frequency of 203 Hz when a sinusoidal current with a frequency of 203 Hz and a peak-to-peak amplitude of 4 µA is applied. The complete entrainment is more clearly seen in Fig. 1(b) (the stroboscopic plot), in Fig. 1(c) (the Lorenz plot) and in Fig. 1(d) (the power spectral density): Both stroboscopic and Lorenz plots are composed of a single point, which means that the forced firing frequency is completely entrained to the frequency of the sinusoidal current. The power spectral density consists of several discrete lines at the fundamental frequency (203 Hz) and its higher harmonics. A relatively large power spectral density at the higher harmonics is characteristic of a nonlinear oscillation.

In the case of detuning, that is, away from the ranges of the amplitude and the frequency of the sinusoidal current to which the repetitive firing frequency is entrained, the oscillations of action potentials become more complex, as described below.

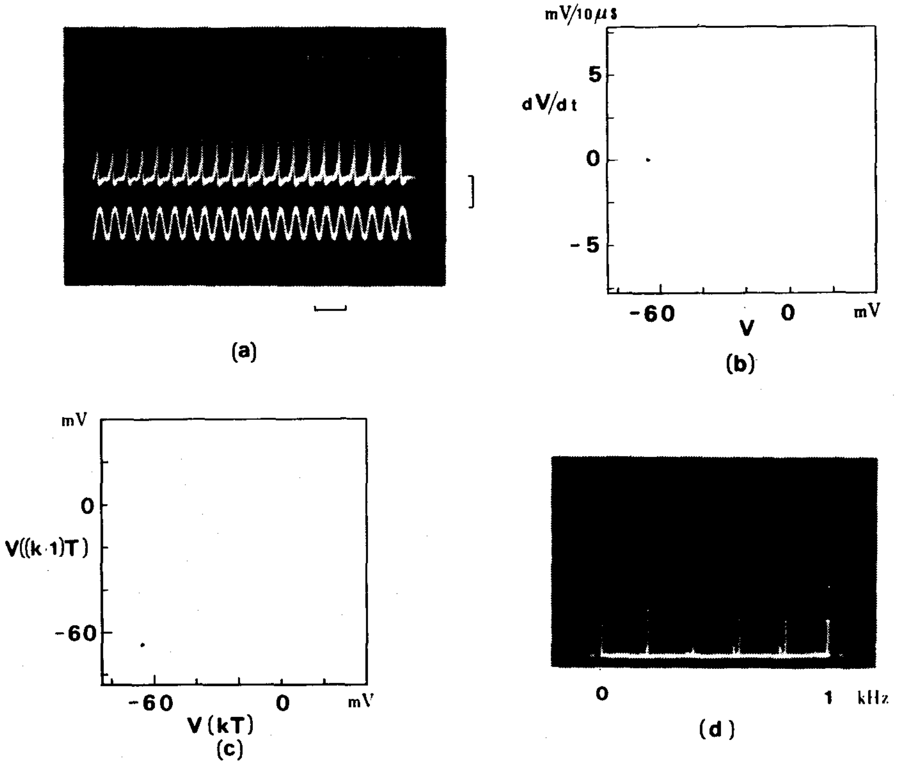

Fig. 1. Entrained Oscillation of the repetitive firing of action potentials when the sinusoidal current with the frequency of 203 Hz and the peak-to-peak amplitude 4µA was applied externally to the squid giant axon in the state of spontaneous repetitive firing with the natural repetitive frequency of 228 Hz. (a) The wave forms of the membrane potential (above) and the stimulating current (below). Vertical bar stands for 20mV and 4 µA. Horizontal bar denotes 10msec. (b) The stroboscopic plot on the membrane potential V and its time differential dV/dt. (c) The Lorenz plot on the membrane potential. (d) The power spectra of the oscillating membrane potential. Ordinate: Power spectrum density in an arbitrary scale. Abscissa: Frequency in linear scale. Full scale is 1 kHz.

1/N Entrained Oscillation

The next simplest oscillation of membrane potentials was found to be the 1/N entrained oscillation in which the period of the forced oscillation was N times the period of the sinusoidal current, where N stands for an integer equal to or larger than 2. In other words, the repetitive firing frequency synchronizes to the 1/N subharmonics of the stimulating frequency f_s. An example for $N = 2$ is shown in Fig. 2(a). The corresponding stroboscopic plot, Lorenz plot and power spectral densities are shown in Figs. 2(b)-(d). In this example, the natural frequency of spontaneous

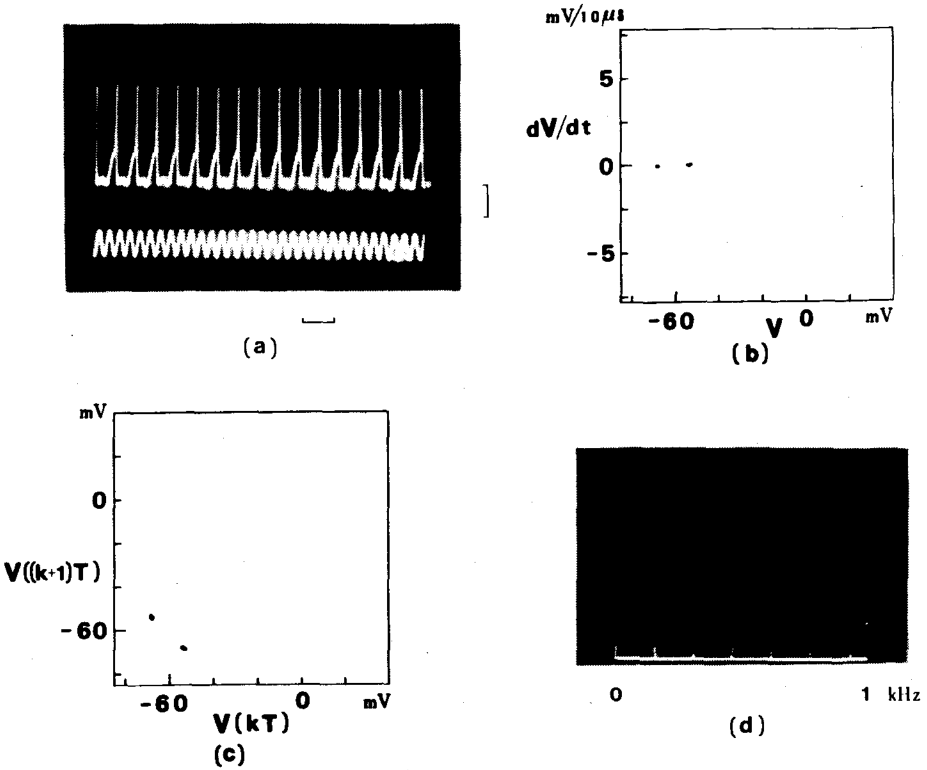

Fig. 2. The 1/2 entrained oscillation of the repetitive firing of action potentials (with the repetitive frequency of 156 Hz) when the sinusoidal current with the frequency of 311 Hz and the peak-to-peak amplitude of 3 μA was applied externally to the squid giant axon in the state of spontaneous repetitive firing with the natural firing frequency of 136 Hz. (a) The wave forms of the membrane potential (above) and the stimulating current (below). Vertical bar stands for 20mV and 4 μA. Horizontal bar denotes 10msec. (b) The stroboscopic plot on the membrane potential V and its time differential dV/dt. (c) The Lorenz plot on the membrane potential. (d) The power spectra of the oscillating membrane potential. Ordinate: Power spectrum density in an arbitrary scale. Abscissa: Frequency in linear scale. Full scale is 1 kHz.

repetitive firing was around 136 Hz. The repetitive firing frequency became 156 Hz (Fig. 2(d)) when a sinusoidal current with a frequency of 311 Hz and a peak-to-peak amplitude of 3 μA was applied. Occurrence of the 1/2 entrained oscillation was clearly seen in the stroboscopic and Lorenz plots (Figs. 2(b) and (c)). The power spectral densities consist of discrete lines at the fundamental frequency of 156 Hz and at its harmonics (Fig. 2(d)).

Quasi-Periodic Oscillation

The next simple oscillation of membrane potentials was found to be a quasi-periodic oscillation of action potentials that has two fundamental frequencies which are irrationally related (Moser, 1969; Sell, 1981; Ueda and Akamatsu, 1981; Zeeman, 1982). A typical example is shown in Fig. 3. As seen in Fig. 3(b), the stroboscopic plot asymptotically forms a closed curve. The closed curve given as a ω-limiting set in terms of the stroboscopic plot means that the forced neural oscillator has two fundamental frequencies which are irrationally related, as described above. This was confirmed by examining the power spectra of Fig. 3(d), which consist of two funda-

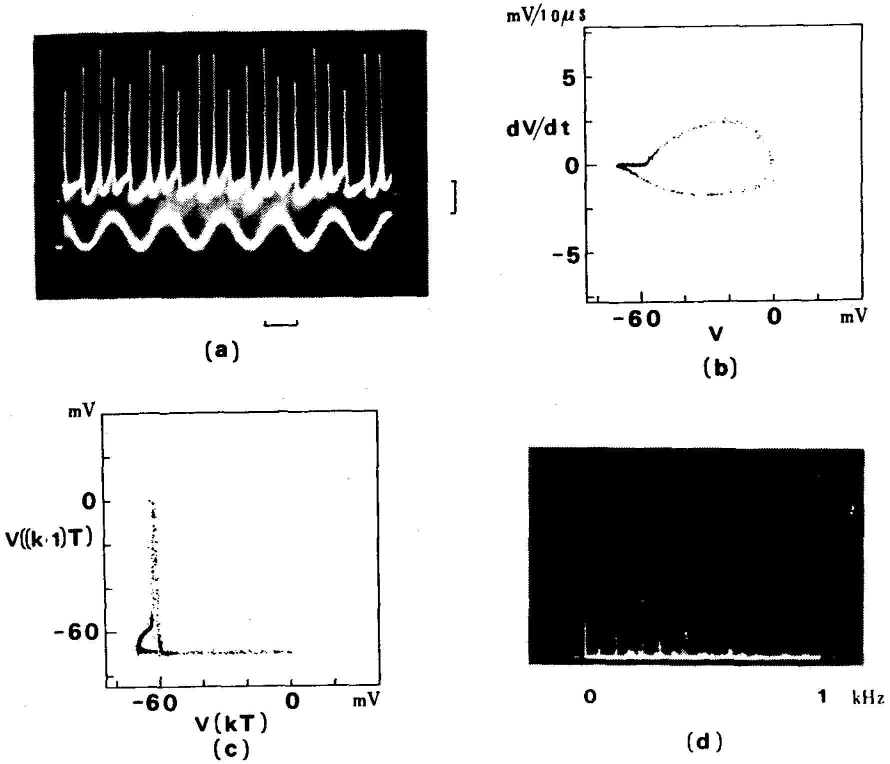

Fig. 3. Quasi-periodic oscillation of the repetitive firing of action potentials when the sinusoidal current with the frequency of 60 Hz and the peak-to-peak amplitude of 4 μA was applied externally to the squid giant axon in the state of spontaneous repetitive firing with the natural frequency of 187 Hz. (a) The wave forms of the membrane potential (above) and the stimulating current (below). Vertical bar stands for 20mV and 4 μA. Horizontal bar denotes 10msec. (b) The stroboscopic plot on the membrane potential V and its time differential dV/dt. (c) The Lorenz plot on the membrane potential. (d) The power spectra of the oscillating membrane potential. Ordinate: Power spectrum density in an arbitrary scale. Abscissa: Frequency in linear scale. Full scale is 1 kHz.

mental frequencies $f_1(=185$ Hz) and $f_2(=59$ Hz), and of their linear combinations nf_1+mf_2 (n,m: integers). In this example, the natural frequency f_n of spontaneous repetitive firing was 185 Hz, and the sinusoidal current with a frequency f_s of 60 Hz, and a peak-to-peak amplitude of 4 μA was applied externally. Note that $f_1=f_n$ and $f_2=f_s$.

Another example of the quasi-periodic oscillation is shown in the Fig. 4. In this example, the natural firing frequency f_n was 138 Hz, and the sinusoidal current with a frequency f_s of 450 Hz and a peak-to-peak amplitude of 3 μA was applied externally.

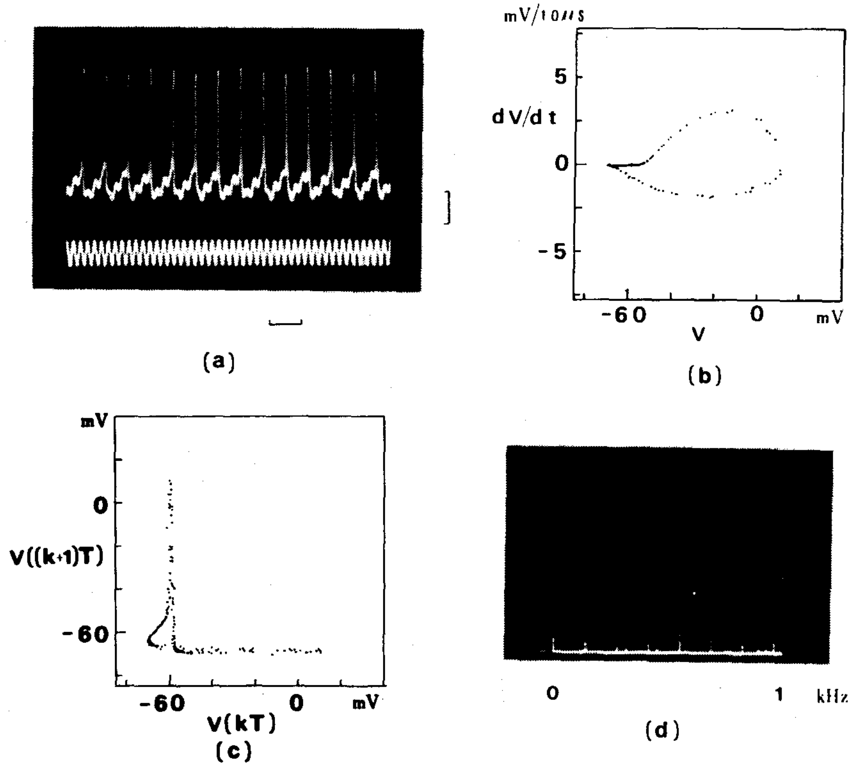

Fig. 4. Quasi-periodic oscillation of the repetitive firing of action potentials when the sinusoidal current with the frequency of 450 Hz and the peak-to-peak amplitude of 4 μA was applied externally to the squid giant axon in the state of spontaneous repetitive firing with the natural firing frequency of 138 Hz. (a) The wave forms of the membrane potential (above) and the stimulating current (below). Vertical bar stands for 20mV and 4 μA. Horizontal bar denotes 10msec. (b) The stroboscopic plot on the membrane potential V and its time differential dV/dt. (c) The Lorenz plot on the membrane potential. (d) The power spectra of the oscillating membrane potential. Ordinate: Power spectrum density in an arbitrary scale. Abscissa: Frequency in linear scale. Full scale is 1 kHz.

Since the frequency f_s of the sinusoidal current stimulation was considerably high as compared with the natural firing frequency f_n, there are small peaks in the membrane potential responding to peaks of the stimulating current between two adjacent action potentials (Fig. 4(a)). The stroboscopic plot also asymptotically forms a closed curve (Fig. 4(b)). The power spectrum analysis reveals that there are two fundamental frequencies of $f_1(=138$ Hz) and $f_2(=450$ Hz); in this case, it holds again that $f_1=f_n$ and $f_2=f_s$. However, action potentials with the frequency of f_1 are the major component (see Fig. 4(a) and (d)).

Chaotic Oscillation

Complex non-periodic oscillations of membrane potentials were found in squid giant axons under repetitive firing when the sinusoidal current with certain frequency and amplitude was externally applied (Fig. 5). It was suggested that these oscillations might be due to chaotic response of membrane potentials to the sinusoidal current stimulation (Matsumoto *et al.*, 1980). Exact nonlinear properties of these oscillations were studied by making the stroboscopic and Lorenz plots in the present experiments. A typical example is illustrated in Fig. 6. In this case, the sinusoidal current with a frequency of 332 Hz and a peak-to-peak amplitude of 4 μA was externally applied to the axon under repetitive firing with a natural frequency of about 228 Hz. The forced repetitive firing of action potentials on the CRT display is shown in Fig. 5 with the applied sinusoidal current. The stroboscopic plot of these complex oscillations shows that there is a complicated attractor, which is given as a ω-limiting set by the stroboscopic plot (Fig. 6(a)). This attractor evidently differs from other ordinary attractors consisting of a point, N points and a closed curve, and is named a strange attractor (Smale, 1967; Ruelle and Takens, 1971). In the Lorenz plot two curves with upward peaks are superposed and appear asymptotically (Fig. 6(b)). The power spectrum analysis reveals that there are two main components at frequencies of $f_1(=220$ Hz) and $f_2(=331$ Hz), and that each component does not consist of a simple line but of a band (Fig. 6(c)), which means that spectral broadening occurs (Fenstermacher *et al.*, 1979; Gollub and Benson, 1980; Vidal, 1981; Helleman, 1981; Ueda and Akamatsu, 1981; Zeeman, 1982). All these characteristics in the stroboscopic plot, the Lorenz plot and the power spectrum analysis show that the complex oscillations of membrane potentials as typically seen in Fig. 5 are chaotic.

4. Discussion

Various oscillatory behaviours of the membrane potentials in squid giant axons during repetitive firing when the sinusoidal current was externally applied were analysed in terms of the stroboscopic plot, the Lorenz plot and the power spectrum analysis of the oscillatory membrane potentials. The behaviours were qualitatively classified into the four classes according to the values of parameters (the frequency

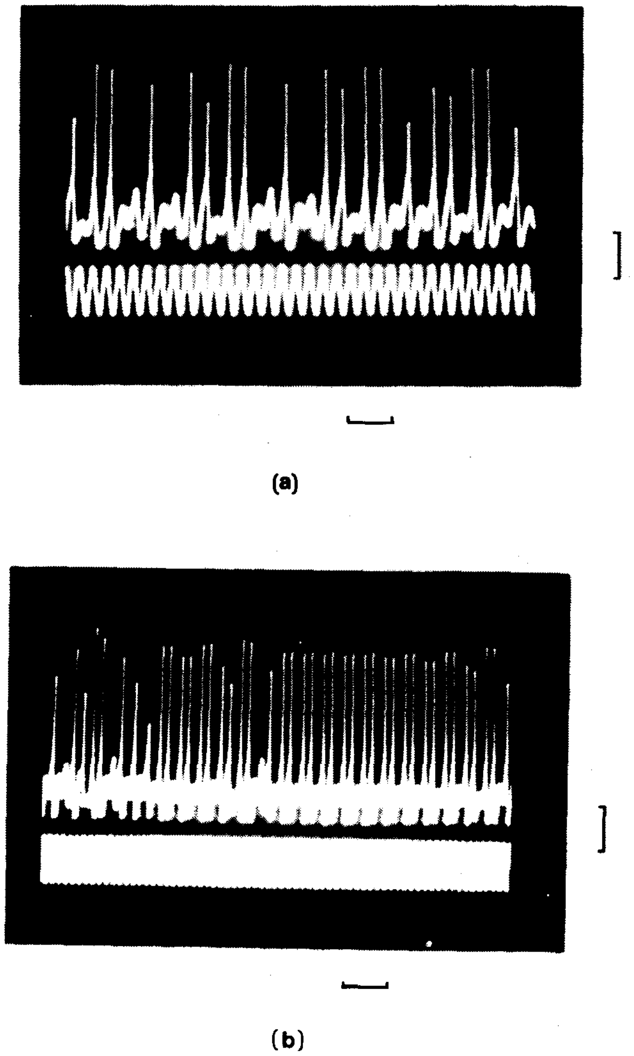

Fig. 5. The wave form of chaotic oscillation of the repetitive firing of action potentials when the sinusoidal current with the frequency of 332 Hz and the peak-to-peak amplitude of 4 μA was applied to the squid giant axon in the state of spontaneous repetitive firing with the natural frequency of 228 Hz. The upper and lower traces represent the membrane potential and the stimulating current, respectively. Vertical bar stands for 20mV and 4 μA. Horizontal bar denotes 10msec for (a) and 20msec for (b), respectively.

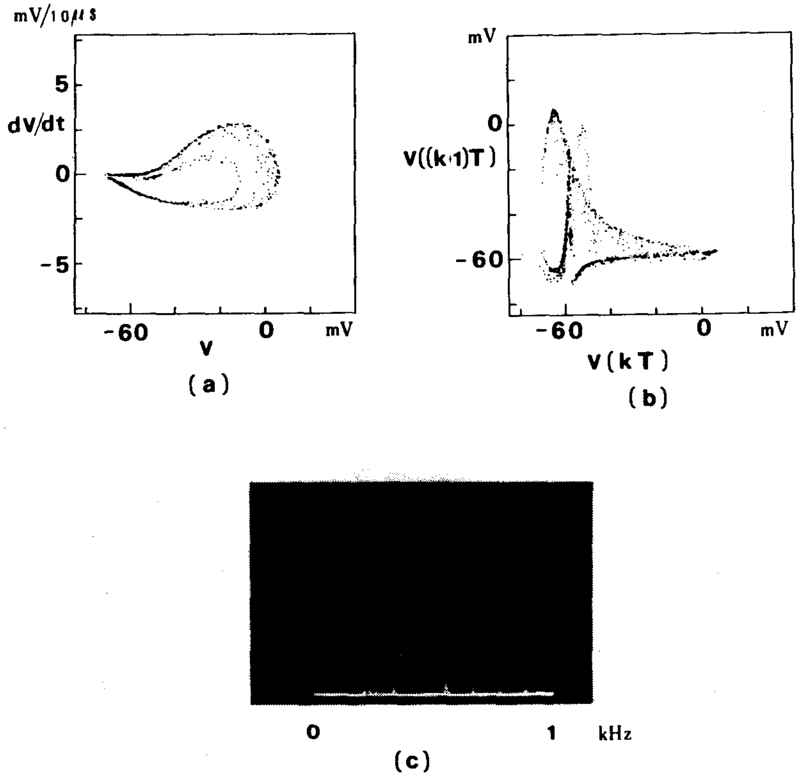

Fig. 6. Chaotic oscillation of the repetitive firing of action potentials in the squid giant axon under the same conditions as in Fig. 5. (a) The stroboscopic plot on the membrane potential V and its time differential dV/dt. (b) The Lorenz plot on the membrane potential. (c) The power spectra of the oscillating membrane potential. Ordinate: Power spectrum density in a relative measure. Abscissa: Frequency in linear scale. Full scale is 1 kHz.

and the amplitude) of the sinusoidal current: (1) entrained oscillations, (2) 1/N entrained oscillations, (3) quasi-periodic oscillations, and (4) chaotic oscillations. The entrained and 1/N entrained oscillations behave periodically, corresponding to harmonic and subharmonic synchronizations, respectively. The chaotic oscillation, obviously different from the quasi-periodic oscillation, was found to have the phenomenological characteristics, as follows: (1) appearance of the strange attractor in the stroboscopic plot, (2) existence of curved lines with upward peaks in the Lorenz plot, and (3) the spectral broadening observed in the power spectra. These properties have been commonly observed in chaotic phenomena in fluid dynamic, electrical circuits, chemical reactions and so on (eg, Lorenz, 1963; Fenstermacher *et al.*, 1979; Gollub and Benson, 1980; Ueda and Akamatsu, 1981; Vidal, 1982; Nagashima, 1982). The power spectral densities for the chaotic oscillations in Figs. 5 and 6 have two major bands with their respective peak frequencies $f_1(=220\,\mathrm{Hz})$ and $f_2(=331\,\mathrm{Hz})$. Note that the frequency ratio f_1/f_2 nearly equals 2/3. These characteristics that the rational value of the ratio f_1/f_2 and the frequency broadening in the power spectrum densities have been also observed in a turbulent flow preceded by quasi-periodicity and phase locking (Gollub and Benson, 1980; Zeeman, 1982).

The quasi-periodic and chaotic oscillations in Figs. 3–6 have remarkable aperiodicities and gradations in the action potentials. It was reported by Cole *et al.* (1970) that the response of squid giant axons to a stimulating current is a continuous graded function in a spatially-clamped condition. The fractional responses can easily be demonstrated in the quasi-periodic and chaotic oscillations. Such complex oscillations have been also found in many biological membranes such as quiescent membranes of squid giant axons stimulated by sinusoidal currents (Guttman *et al.*, 1980), cardiac cells (Guevara *et al.*, 1981), Molluscan neurons (Holden *et al.*, 1982) and Nitella internodal cells (Hayashi *et al.*, 1983). Guttman *et al.* (1980) also reported that the aperiodic oscillations in their modified Hodgkin-Huxley eqs. could be mostly ascribed to the imposed noise. On the other hand, it has been well known that the unmodified noise-free Hodgkin-Huxley eqs. (Hodgkin and Huxley, 1952) can describe not only various synchronized oscillations but also non-periodic oscillations (Nemoto *et al.*, 1975; Holden, 1976; Holden, 1980; Matsumoto *et al.*, 1980; Guttman *et al.*, 1980). Recently, the non-periodic oscillations in the Hodgkin-Huxley eqs. are analysed by the stroboscopic and Lorenz plots (Aihara *et al.*, 1982; Aihara *et al.*, 1983) and trajectories in in state spaces (Holden, a personal communication). It remains for a future problem to examine the relationship between the non-periodic oscillations experimentally observed under the existence of inevitable thermal noise and the deterministic and non-periodic oscillations in the Hodgkin-Huxley eqs., but the curves emerging asymptotically in the stroboscopic and Lorenz plots of Figs. 3, 4 and 6 seem to imply that the non-periodic oscillations obey macroscopic dynamics.

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References

Aihara, K. and Matsumoto, G. (1982). Temporarily coherent organization and instabilities in squid giant axons. *J. Theor. Biol.* **95**, 697–720.

Aihara, K., Matsumoto, G. and Ikegaya, Y. (1983). Periodic and nonperiodic responses of a periodically forced Hodgkin-Huxley oscillator. *J. Theor. Biol.* (in press).

Aihara, K., Utsunomiya, T., Matsumoto, G. and Hoshino, H. (1982). A chaotic behaviour of the membrane potential in squid giant axons. Proc. of the World Congress on Medical Physics and Biomedical Engineering **2**, 34.

Cole, K. S., Guttman, R. and Bezanilla, F. (1970). Nerve membrane excitation without threshold. *Proc. of Nat. Acad. Sci.* **65**, 4, 884–891.

Fenstermacher, P. R., Swinney, H. L. and Gollub, J. P. (1979). Dynamical instabilities and the transition to chaotic Taylor vortex flow. *J. Fluid. Mech.* **94**, 103–128.

Glansdorff, P. and Prigogine, I. (1971) *Thermodynamics theory of structure, stability and flucturation.* Wiley-Interscience, London.

Gollub, J. P. and Benson, S. V. (1980). Many routes to turbulent convection. *J. Fluid. Mech.* **100**, 3, 449–470.

Guevara, M. R., Glass, L. and Shrier, A. (1981). Phase locking, period-doubling bifurcations, and irregular dynamics in periodically stimulated cardiac cells. *Science* **218**, 1350–1353.

Guttman, R. (1969). Temperature dependence of oscillation in squid axons: comparison of experiments with computations. *Biophys. J.* **9**, 269–277.

Guttman, R., Feldman, L. and Jakobsson, E. (1980). Frequency entrainment of squid axon membrane. *J. Membrane Biol.* **56**, 9–18.

Haken, H. (1977). *Synergetics — an introduction. Nonequilibrium phase transitions and self-organization, in physics, chemistry and biology*, Springer-Verlag, Berlin, Heidelberg and New York.

Hayashi, H., Nakao, M. and Hirakawa, K. (1983). Entrained, harmonic, quasiperiodic and chaotic responses of the self-sustained oscillation of Nitella of sinusoidal stimulation. *J. Phys. Soc. Japan* **52**, 344–351.

Helleman, R. H. G. (1981). Feigenbaum sequences in conservative and dissipative systems. In: *Chaos and order in nature.* (Haken, H., Ed.) pp. 232–248. Springer-Verlag, Berlin, Heidelberg and New York.

Hodgkin, A. L. and Huxley, A. F. (1952). A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol.* (London) **117**, 500–544.

Hodgkin, A. L. and Katz, B. (1949). The effect of sodium ions on the electrical activity of the giant axons of the squid. *J. Physiol.* **108**, 37–77.

Holden, A. V. (1976). The response of excitable membrane models to a cyclic input. *Biol. Cybern.* **21**, 1–7.

Holden, A. V. (1980). Autorhythmicity and entrainment in excitable membrane. *Biol. Cybern.* **38**, 1–8.

Holden, A. V., Winlow, W. and Haydon, P. G. (1982). The induction of periodic and chaotic activity in a Molluscan Neurone. *Biol. Cybern.* **43**, 169–173.

Huxley, A. F. (1959). Ion movements during nerve activity. *Annals. N.Y. Acad. Science* **81**, 221–246.

Kai, T. and Tomita, K. (1979). Stroboscopic phase portrait of a forced nonlinear oscillator. *Prog. Theor. Phys.* **61**, 54–73.

Lorenz, E. N. (1963). Deterministic nonperiodic flow *J. Atoms. Sci.* **20**, 130–141.

Matsumoto, G. (1976). Transportation and maintenance of adult squid (*Doryteuthis bleekeri*) for physiological studies. *Biol. Bull* **150**, 279–285.

Matsumoto, G. (1978). Current fluctuation observed in squid giant axons. *J. Phys. Soc. Japan* **45**, 2047–2048.

Matsumoto, G. (1981). Long-range spatial interactions and a dissipative structure in squid giant axons and a proposed physical model of nerve excitation. In: *Nerve membrane — biochemistry and function of channel proteins.* (Matsumoto, G. and Kotani, H., Eds), pp. 203–220. University of Tokyo Press, and Tokyo.

Matsumoto, G., Aihara, K. and Utsunomiya, T. (1982). A spatially-ordered pacemaker observed in squid giant axons. *J. Phys. Soc. Japan* **51**, 942–950.

Matsumoto, G., Kim, K., Uehara, T. and Shimada, J. (1980). Electrical and computer simulations upon the nervous activities of squid giant axons at and around the state of spontaneous repetitive firing of action potentials. *J. Phys. Soc. Japan* **49**, 906–914.

Matsumoto, G. and Shimada, J. (1980). Further improvement upon maintenance of adult squid (*Doryteuthis bleekeri*) in a small circular and closed-system aquarium tank. *Biol. Bull.* **159**, 319–324.

Matsumoto, G. and Shimizu, H. (1978). A spatially organized structure observed in the time-ordered state of squid giant axons. *J. Phys. Soc. Japan* (*Letters*) **44**, 1399–1400.

Matsumoto, G. and Shimizu, H. (1983). Spatial coherence and formation of collectively-coupled local nonlinear oscillators in squid giant axons. *J. Theor. Neurobiol.* **2**, 29–46.

Matsumoto, G. and Stühmer, W. (1978). Cross-correlation of fluctuating membrane potentials in squid giant axons. *J. Phys. Soc. Japan* (*Letters*) **45**, 1069–1070.

Minorsky, N. (1962). *Nonlinear oscillations.* Van Nostrand, New York.

Moser, J. (1969). Perturbation theory of quasiperiotlic solutions of differential equations. In: *Bifurcation theory and nonlinear eigenvalue problems.* (Keller, J. B. and Antman, S., Eds), pp. 283–308, Benjamin, New York.

Nagashima, H. (1982). Experiment on chaotic responses of a forced Belousov-Zhabotinsky reaction. *J. Phys. Soc. Japan* **51**, 21–22.

Nemoto, I., Miyazaki, S., Saito, M. and Utsunomiya, T. (1975). Behaviour of solutions of the Hodgkin-Huxley equations and its relation to properties of mechanoreceptors. *Biophys. J.* **15**, 469–479.

Nicolis, G. and Prigogine, I. (1977). *Self-organization in nonequilibrium systems.* John Wiley & Sons, New York.

Ruelle, D. and Takens, F. (1971). On the nature of turbulence. *Comm. Math. Phys.* **20**, 167–192.

Sell, G. R. (1981). Hopf-Landau bifurcation near strange attractors. In: *Chaos and order in nature.* (Haken, H. Ed.), pp. 84–91. Springer-Verlag, Berlin, Heidelberg and New York.

Smale, S. (1967). Differential dynamical systems. *Bull. Amer. Math. Soc.* **73**, 747–817.

Tomita, K. and Kai, T. (1979). Chaotic response of a limit cycle. *J. Stat. Phys.* **21**, 65–86.

Ueda, Y. and Akamatsu, N. (1981). Chaotically transitional phenomena in the forced negative-resistance oscillator. *IEEE Trans. CAS.* **28**, 3, 217–224.

Vidal, C. (1981). Dynamic instabilities observed in the Belousov-Zhabotsinsky system. In: *Chaos and order in nature.* (Haken, H., Ed.), pp. 69–82. Springer-Verlag, Berlin, Heidelberg and New York.

Zeeman, E. C. (1982). Bifurcation, catastrophe and turbulence. In: *New Directions in applied mathematics.* (Hilton, P. J. and Young, G. S., Eds), pp. 109–154, Springer-Verlag, New York.