Nonlinear Prediction on Squid Axon Response

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ABSTRACT

Membrane response of squid giant axon stimulated by sinusoidal force is analyzed by deterministic nonlinear prediction in order to evaluate short-term predictability and long-term unpredictability, which are important properties peculiar to deterministic chaos. As a result, it is shown that correlation coefficients decrease with increase of prediction steps, which is due to sensitive dependence on initial conditions. In order to obtain more reliable results, the method of surrogate data is also applied to the time series data of squid axon response and statistical significances are calculated. The result shows a strong evidence that the squid giant axon response cannot be explained without nonlinear dynamics and implies that the approach with deterministic nonlinear prediction has potential ability for identification of deterministic chaos in a real world data, even though it is almost impossible to obtain information on deterministic models explicitly.

1. Introduction

A biological neuron, or the fundamental element of brains, is composed of nerve membranes. Nonlinear dynamics of nerve membranes produces various attractors and bifurcation structures according to nonequilibrium conditions such as ionic concentration and external force. Therefore, it is natural to expect existence of deterministic chaos, and actually, many interesting results of chaotic oscillations of nerve membranes have already been reported [1, 2, 3]. Among several kinds of attractors, deterministic chaos is most complicated but most interesting in nerve membranes especially from the viewpoint of dynamical systems theory.

It has been experimentally shown that when squid giant axons are forced by periodic pulses, timings of firing in the nerve membranes are irregular, or chaotic, under some conditions. We have already analyzed the real data on squid axon response to periodic pulses by deterministic nonlinear prediction and shown existence of chaotic dynamics behind a complex response of squid axon data quantitatively [4].

Membrane potential response of squid giant axons stimulated by sinusoidal currents has also been investigated [1, 2, 3], then existence of chaos is confirmed by examining bifurcations and structures of attractors both by experimentally with squid giant axons and numerically with the Hodgkin-Huxley equations.

In this paper, deterministic nonlinear prediction [5] is applied to real data on squid axon response that is stimulated by sinusoidal external force in order to show short-term predictability and long-term unpredictability, which are important properties peculiar to deterministic chaos. The method of surrogate data [11] is also applied to the real data of squid axon response to obtain more stronger evidence on existence of deterministic chaos. The differences between the original time series and surrogate data series are examined and statistical significances are also computed to reject the null hypotheses that complex behavior of squid giant axon data can be describe with linearity.

2. Application of deterministic nonlinear prediction to squid axon response

As for identification of deterministic chaos, deterministic nonlinear prediction is now becoming an important method [6]. The other methods of extracting dynamical invariants, for example, correlation dimensional analysis or Lyapunov spectral analysis, have several drawbacks on its application to real time series. Especially, if enough number of data points is not available, which is usual in analyzing real time series, deterministic nonlinear prediction is more reliable for identifying deterministic chaos [6]. It is almost impossible to record a number of data as large as enough for obtaining reliable estimates of fractal dimensions or Lyapunov exponents from squid giant axons because of unsteadiness. From this reason, we apply deterministic nonlinear prediction to real data of squid axon response in this paper.

Fig.1 is the time series of the membrane potential stroboscopically sampled. It is hard to find regularity or periodicity in Fig.1, from which we can confirm that the time series is not a periodic nor described as a superposition of periodicity.

Fig.2 is the corresponding power spectrum by calculating fast Fourier transform with the Hanning window.

In Fig.3, reconstructed attractors in two-dimensional state space are shown. These figures imply that the squid data have a kind of determinisity and steadiness.

For applying deterministic nonlinear prediction, we must reconstruct the orbit of the attractor from the single variable time series. Takens proved the method to embed the attractor by the delay time vectors [7, 8]. Let us denote the single variable time series by $y(t)$ and the number of data points by N. Assuming that the state space is a k-dimensional compact manifold and that the box-counting dimension of the attractor is D_0, it is proven that the transformation of Eq.(1) from the real time series to the m-dimensional vectors is an embedding if $m \geq 2k+1$ [7] and it is also embedding of smooth manifolds contained in the fractal attractor if $m > 2D_0$[8],

$$\boldsymbol{v}(t) = (y(t), y(t+1), \ldots, y(t+(m-1))). \quad (1)$$

These theorems [7, 8] show that through the transformation of Eq.(1) one-to-one property is at least preserved, then we can apply deterministic nonlinear prediction to the reconstructed attractors.

The prediction algorithm which we use in this paper is a kind of local linear approximation algorithm [5], which is quite simple but has high performance even if there are relatively high amount of observational noise. This algorithm first selects a set of near neighbors $\boldsymbol{v}_{k_i}$ of the predicted point $\boldsymbol{v}_T$, and its one-step-ahead point is predicted by the following equation:

$$\hat{\boldsymbol{v}}_{T+1} = \frac{\displaystyle\sum_{i=1}^{M} \frac{1}{|\boldsymbol{v}_{k_i} - \boldsymbol{v}_T|} \boldsymbol{v}_{k_i+1}}{\displaystyle\sum_{i=1}^{M} \frac{1}{|\boldsymbol{v}_{k_i} - \boldsymbol{v}_T|}}. \quad (2)$$

where M is the number of near neighbors. When we apply this algorithm to the real time series, singular cases with $\boldsymbol{v}_T = \boldsymbol{v}_{k_i}$ might happen, however, by introducing an exceptional rule that if $\boldsymbol{v}_T = \boldsymbol{v}_{k_1}$, then $\hat{\boldsymbol{v}}_{T+p} = \boldsymbol{v}_{k_1+p}$, we can avoid catastrophes due to such singularities [5].

We assume the existence of the deterministic model and make the data base for prediction with the first half ($t = 1, 2, \ldots, N/2$) of the real data. Next, the second half of the observed data, denoted by $y_T(T = N/2+1, \ldots, N)$, are also transformed by

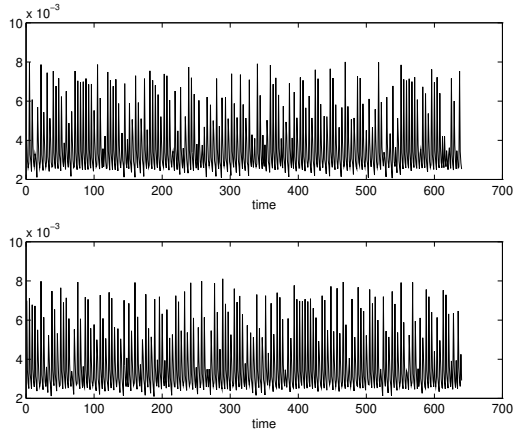

Fig. 1: The time series of the squid axon response. The top figure shows the first part and the bottom the second. Total number of data points is 1,280.

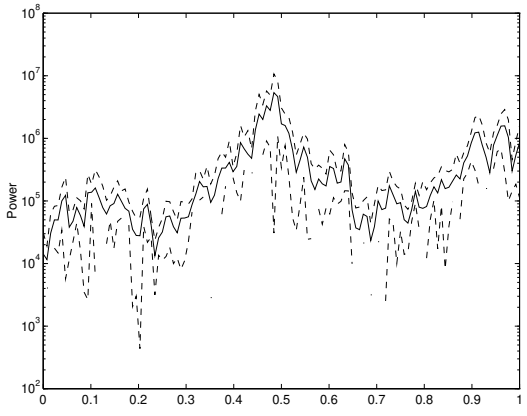

Fig. 2: Power spectrum of the squid data shown in Fig. 1. Computed with a Hanning window of the length 1,024. The dashed lines indicate 95% confidence intervals.

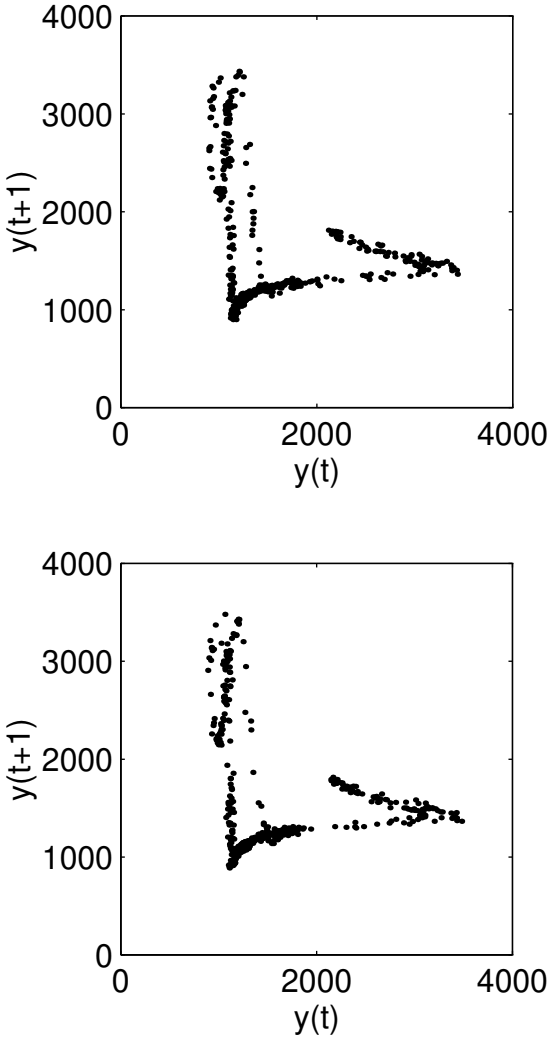

Fig. 3: Reconstruction of the squid data in two dimensional state space $(y(t), y(t+1))$ of the first half (the upper) and the second half (the lower) of 1,280 points.

Eq.(1) and deterministic nonlinear prediction is applied to these points. We reconstruct an attractor with the number of points $N = 1,024$ and the lag time $\tau = 1$. The predicted time series $\hat{z}(t)$ is constructed by the last component of each predicted vectors $\hat{\boldsymbol{v}}_{T+p}$ [5].

For evaluating prediction performances, we adopt the following two indexes between the real time series and the predicted time series. The first one is the real correlation coefficient r_1,

$$r_1 = \frac{\sum_{i=1}^{P}(z(t)-\bar{z})(\hat{z}(t)-\bar{\hat{z}})}{\sqrt{\sum_{i=1}^{P}(z(t)-\bar{z})^2}\sqrt{\sum_{i=1}^{P}(\hat{z}(t)-\bar{\hat{z}})^2}}, \qquad (3)$$

where $z(t)$ and $\hat{z}(t)$ are actual and predicted time series, $\bar{z}$ and $\bar{\hat{z}}$ are the averages, and P is the number of data points in the predicted time series. The second one is the delta correlation coefficient r_2 between the difference time series $\Delta z(t) = z(t+1) - z(t)$ and $\Delta\hat{z}(t) = \hat{z}(t+1) - z(t)$:

$$r_2 = \frac{\sum_{i=1}^{P'}(\Delta z(t)-\Delta\bar{z})(\Delta\hat{z}(t)-\Delta\bar{\hat{z}})}{\sqrt{\sum_{i=1}^{P'}(\Delta z(t)-\Delta\bar{z})^2}\sqrt{\sum_{i=1}^{P}(\Delta\hat{z}(t)-\Delta\bar{\hat{z}})^2}}, \qquad (4)$$

where P' is the number of data points of $\Delta z(t)$ and $\Delta\hat{z}(t)$. The delta correlation coefficient plays an important role for discrimination of deterministic chaos from colored noise with a power-law spectrum. If the observed time series is produced from deterministic dynamics, the real correlation coefficient decreases with prediction steps. On the other hand, even if the time series has a stochastic origin but the property that its power spectrum has the form of $1/f^{\alpha}$, the same tendency, or the decreasing property of prediction performance with prediction steps, is spuriously obtained [10]. However, if one calculates the delta correlation coefficients, it is likely to discriminate deterministic chaos from colored noise more easily [9] than the log-log and the semi-log plots approach [10]. Further studies on the discrimination performance on deterministic chaos and colored noise with the delta correlation coefficients will be discussed elsewhere [9].

In Figs.4(a) and 4(b) shown are the relation between the real correlation coefficients and the prediction steps and the relation between the delta correlation coefficients and the prediction steps, respectively.

From these figures, as the prediction steps increases, the correlation coefficients have a tendency to decrease; it comes from the existence of the positive Lyapunov exponent, which indicates one of the characteristic of deterministic chaos, sensitive dependence on initial conditions [6]. Moreover, in both Figs.4(a) and (b), the prediction performances, correlation coefficients in this case, are best in the case of the four dimensional reconstructed state space, which might be considered as a minimum embedding dimension.

3. The method of surrogate data

In the previous section, deterministic nonlinear prediction is applied to squid axon response directly and quantitative evidences of short-term predictability and long-term unpredictability are shown. In this section, we apply the method of surrogate data to real data of squid axon response in order to obtain more reliable results of nonlinear prediction.

The method of the surrogate data specifies a process against time series as a null hypothesis. Although several kinds of the null hypotheses against

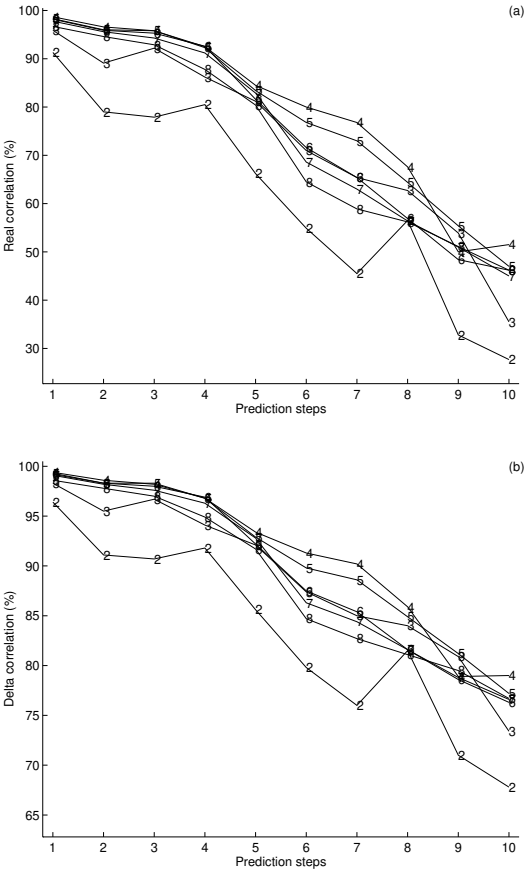

Fig. 4: (a) Real correlation coefficients and (b) delta correlation coefficients as a function of prediction steps for time series shown in Fig.1. For predicting more than one step, Eq.(2) is recursively applied to reconstructed data. The numbers on the lines show the reconstruction dimensions m.

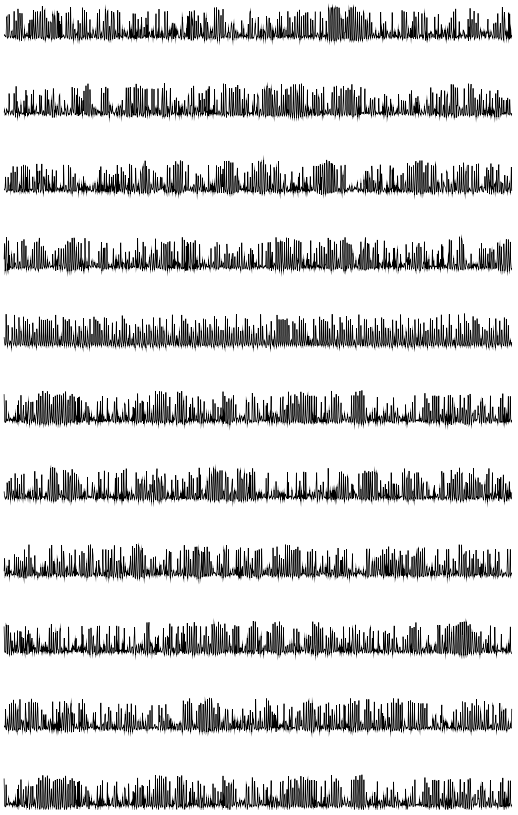

Fig. 5: Examples of surrogate data calculated for the squid data. In this figure, the third null hypothesis described in the text is used. Ten surrogates and the original time series are drawn. The original time series is drawn in the seventh row from the bottom.

nonlinear time series can be considered, the following three null hypotheses are introduced and often used [11]; namely, (i) the time series has no temporal correlation, (ii) the time series has a temporal correlation and can be characterized only by autocorrelation, and (iii) the time series is an output of an observation function, which is nonlinear *static* transformation, of linear stochastic time series [11]. For these null hypotheses, we made three kinds of surrogate data sets, called (i) random shuffle, (ii) Fourier transformed and (iii) amplitude adjusted Fourier transformed surrogates, respectively. The number of surrogate time series is 100 in each case.

In Fig.5 shown are examples of surrogate data of squid axon response by the original squid axon data. It is not easy to discriminate which is the original data only by observing the wave forms at a glance; the original time series is in the fifth row from the top. Fig.6 is the same plot as Fig.3 but for surrogate time series. Structures observed in Fig.3 are destroyed in Fig.6. Again we can obtain qualitative evidence that the squid data cannot be explained without nonlinearity.

Figs.7(a) and (b) are the results of applying deterministic nonlinear prediction to the surrogate data shown in the top of Fig.5. From the figures, we can see that there are different tendencies between Figs. 4 and 7. Although there are the same kind of decreasing property, even at one-step-ahead prediction, both correlation coefficients in Fig. 7 are very low, which are different from those obtained in Fig.4.

In order to obtain more quantitative discrimination and see whether the null hypotheses should be rejected or not, the statistical significances S are calculated:

$$S = \frac{|Q_o - \mu_S|}{\sigma_S} \tag{5}$$

where Q_o is a measure of an original time series, μ_S and σ_S are average and standard deviation calculated from the distribution of surrogate data set, respectively. In Fig.8, the ordinate shows statistical significances S and the abscissa the reconstruction dimensions.

The significances computed on all null hypothe-

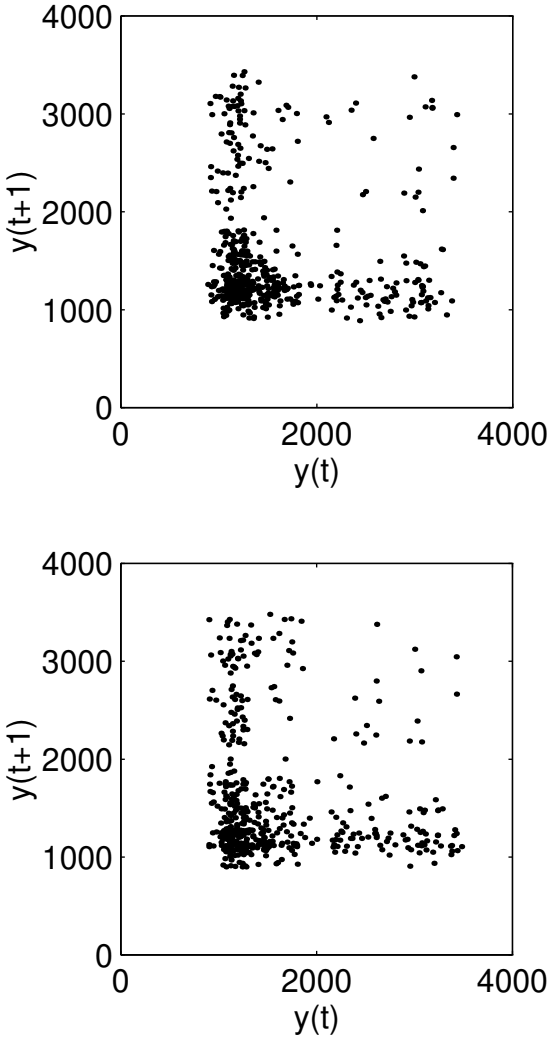

Fig. 6: Reconstruction of the surrogate data of the squid data in two dimensional state space $(y(t), y(t+1))$ of the first half (the upper) and the second half (the lower) of 1,024 points. The algorithm of amplitude adjusted Fourier transformed surrogate data is used.

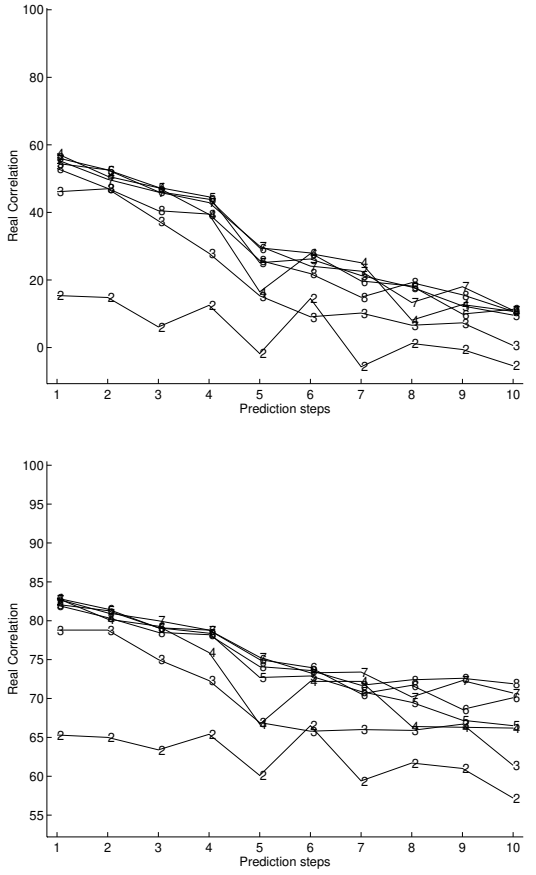

Fig. 7: The same figure as Fig.4 but for a surrogate data. In this figure, the third null hypothesis, or the algorithm of making amplitude adjusted Fourier transformed surrogates, is adopted.

ses are much larger than 2, at which the null hypothesis can be rejected with 95% confidence.

As a result, the results on analyzing squid axon response by deterministic nonlinear prediction indicate that complex response of squid axon data is possibly due to nonlinear determinisity.

4. Conclusions

We have applied deterministic nonlinear prediction to squid axon response in order to analyze short-term predictability and long-term unpredictability, which are one of the important properties peculiar to chaotic dynamics.

We have used a kind of local linear approximation algorithm of nonlinear prediction [5]. As a result, short-term predictability and long-term unpredictability have been confirmed by an application of deterministic nonlinear prediction. The results are also confirmed by the extra analysis with the method of surrogate data [11] by observing the reconstructed attractors qualitatively and calculating significant difference on predictability between the original time series and a set of surrogate data quantitatively.

Although existence of deterministic chaos of squid giant axon responses has already been demonstrated by other analyses [1, 2, 3], it is worth saying that deterministic nonlinear prediction is useful for detecting existence of deterministic chaos from real time series, such as squid giant axon response. Further studies with another dynamical measures should be discussed elsewhere [16].

In more complicated situations, for example, the case that interspike interval time series of successive outputs from neurons are only available, this kind of approach is also effective [12]. An application of the approach to interspike intervals driven by deterministic systems has already been discussed from theoretical point of view [13, 14], and its extensions are also considered from more realistic view points [15, 17]. It is an important future problem to clarify

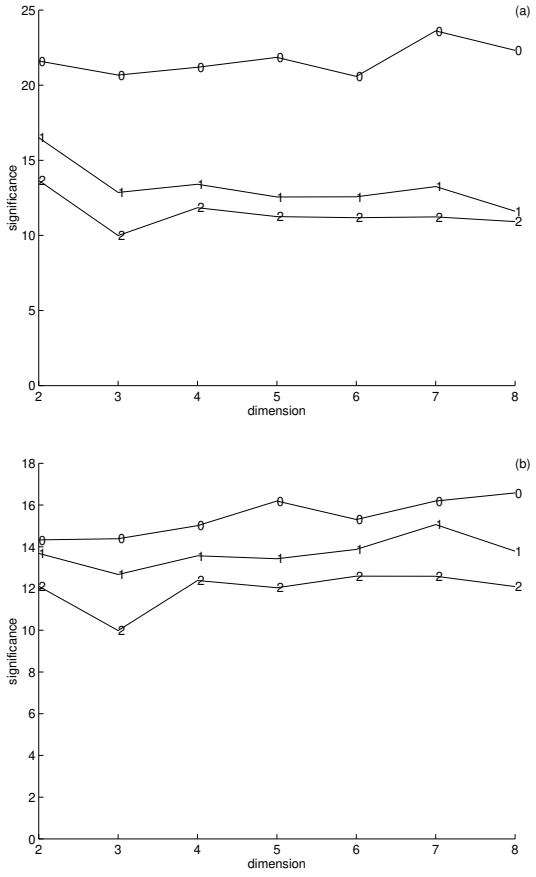

Fig. 8: Statistical significance between the original time series and the surrogate data sets. Discrimination measures are for (a) real correlation coefficients and (b) delta correlation coefficients of one-step-ahead prediction. The abscissa is the reconstructed dimensions and the ordinates are significances. The numbers in the figure describe which algorithm of making surrogate data sets is used: "0" is for random shuffle, "1" is for Fourier transformed and "2" is for amplitude adjusted, respectively.

how informations of driving sources are transformed by the neural dynamics in the case that driving time series are not only deterministic chaos but also the other kind of processes, such as colored noise and so on [17].

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References

[1] K. Aihara, G. Matsumoto and Y. Ikegaya : "Periodic and non-periodic responses of a periodically forced Hodgkin-Huxley oscillator," *Journal of Theoretical Biology*, Vol. 109, pp.249–267, 1982.

[2] K. Aihara and G. Matsumoto : "Chaotic Oscillations and bifurcations in squid giant axons," In A. V. Holden, editor, *Chaos*, pp.257–269, Manchester, Manchester University Press and, Princeton, Princeton University Press, 1986.

[3] K. Aihara and G. Matsumoto : "Forced oscillations and routes to chaos in the Hodgkin-Huxley axons and squid giant axons," In A. V. Holden H. Degn and L. F. Olsen, editors, *Chaos in Biological Systems*, pp.121–131, N.Y., Plenum Press, 1987.

[4] A. Mees, K. Aihara, M. Adachi, K. Judd, T. Ikeguchi, and G. Matsumoto : "Deterministic prediction and chaos in squid axon response," *Physics Letters*, Vol. 169, pp.41–45, 1992.

[5] T. Ikeguchi and K. Aihara : "Prediction of chaotic time series with noise," *Transactions of IEICE, Fundamentals*, Vol. E75, No. 10, 1995.

[6] G. Sugihara and R. M. May : "Nonlinear forecasting as a way of distinguishing chaos from measurement error in time series," *Nature*, Vol. 344, pp.734–741, April 1990.

[7] F. Takens : "Detecting strange attractors in turbulence," In D. A. Rand and B. S. Young, editors, *"Dynamical Systems of Turbulence,"* Vol. 898 of *Lecture Notes in Mathematics*, pp.366–381, Berlin, 1981. Springer-Verlag.

[8] T. Sauer, J. A. Yorke, and M. Casdagli : "Embedology," *Journal of Statistical Physics*, Vol. 65, No. 3/4, pp. 579–616, 1991.

[9] T. Ikeguchi and K. Aihara : "Delta correlation can distinguish deterministic chaos from colored noise," preprint, 1995.

[10] A. A. Tsonis and J. B. Elsner : "Nonlinear prediction as a way of distinguising chaos from random fractal sequences," *Nature*, Vol. 358, pp.217–220, July 1992.

[11] J. Theiler, S. Eubank, A. Longtin, B. Galdrikian, and J. D. Farmer : "Testing for nonlinearity in time series : the method of surrogate data," *Physica D*, Vol. 58, pp. 77–94, 1992.

[12] A. Longtin : "Nonlinear forcasting of spike trains from sensory neurons," *International Journal of Bifurcation and Chaos*, Vol. 3, No. 3, pp. 651–661, 1993.

[13] T. Sauer : "Reconstruction of dynamical systems from interspike intervals," *Physical Review Letters*, Vol. 72, No. 24, pp. 3811–3814, 1994.

[14] T. Sauer : "Interspike interval embedding of chaotic signals," *Chaos*, Vol. 5, No. 1, p. 127, 1995.

[15] D. Racicot and A. Longtin : "Reconstructing Dyanamics from Neural Spike Trains," to appear in *Proceedings of IEEE EMBS conference*, 1995.

[16] T. Ikeguchi and K. Aihara : in preparation.

[17] T. Ikeguchi and K. Aihara : "Nonliear prediction on interspike intervals produced from dynamical systems," to appear in *Proceedings of IEICE International symposium on Nonlinear Theory and Its Applications*, 1995.