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State Space Analysis of the Crayfish Ganglionic Transmission Affected with Suppression of Inhibitory Synaptic Action

With 3 Text-figures

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ABSTRACT Transfer characteristics of the nerve signal through the cerebral and abdominal ganglia of the crayfish, *Procambarus clarkii*, were identified in the form of the linear state equation by use of Lee's sequential estimation method from data of the experiments in the normal van Harreveld's solution and in the test solution containing picrotoxin. The system order of the identified models were, respectively, the fifth for the cerebral ganglionic transmission in the normal solution, the fourth for the abdominal ganglionic transmission in the normal solution and the third for both kinds of ganglionic transmissions in the test solution. When the operator matrices obtained in the companion form were transformed into the Jordan canonical form in order to decompose them, one of the complex conjugate pairs in the diagonal elements of the canonical form operator under the normal condition disappeared under the test condition. Such change in the operator corresponded with the disappearance of the peak on the amplitude characteristics of the frequency response function derived from the same data. It is suggested that there exists an oscillatory neuronal system whose function is eliminated by suppression of the inhibitory synaptic action in the crayfish ganglion.

INTRODUCTION

The control theoretical study of the physiological systems has made startling progress recently. It is said that the control theory has made a change in and after 1969; worker's interest in this field has turned from the study in the frequency domain to the state variable method. The former is called the classical control theory and the latter, the modern control theory (Arimoto, 1976). When the problem is limited within the physiological study of the central nervous system on the basis of single neuron analysis, it is difficult to say that the classical theory has been applied with great success. This situation has been probably brought about from the reason that the structure of the central nervous system is too complicated to analyze within the classical theory. Although the modern theory has not been used so much in the experimental works of the central nervous system except the study of the excitable membrane, it is likely that the modern theory is more profitable for the processing of experimental data from the central nervous system than the classic one, because of the suitability in handling multi-variable systems. In the present study, derivation of the linear state model has been tried as the first step for application of the state space analysis through measurement of the nerve signal transmission in the crayfish ganglia. The effect of an inhibitory transmitter antagonist, picrotoxin, on the form of the state models of the ganglionic transmissions has also been studied.

Material and Methods

The data used in the present model derivation are the same as those used in the previous work on the crayfish ganglionic transmissions analyzed by Wiener's linear and nonlinear filter theories (Watanabe, 1979). They were gathered in the cerebral and abdominal ganglia of the crayfish, *Procambarus clarkii*, in the normal van Harreveld's solution (Van Harreveld, 1936) and in the test solution containing picrotoxin, 10^{-5} M. Each input-output pair consisted of the input signal which was a random electric pulse train for stimulation and the output signal which was the nerve impulse train transmitted through the ganglion by the stimulation. It has been seen in the previous analysis that these input-output pairs show nearly linear relation in the small signal range.

Theories. The signal intensity used in this study is the pulse number counted within each 10 msec; consequently, the input and output signals are the discrete time series. It is expedient at the first step that the ganglionic transmissions are approximated with the linear time invariant discrete state equations, since the present data are stationary and nearly linear. Then, they are represented by the following equations;

$$\begin{aligned} x(\mathrm{k}+1) &= \mathrm{A}x(\mathrm{k})+\mathrm{Bu}(\mathrm{k}) \\ \mathrm{y}(\mathrm{k}) &= \mathrm{C}x(\mathrm{k}) \\ \mathrm{k} &= 0, 1, 2, \ldots \end{aligned} \tag{1}$$

where k increases one by one every 10 msec, $x(\mathrm{k})$ is the state variable and the italics denote that it is vector (For details of the theories, see DeRusso, Roy and Close, 1965; Faurre and Depeyrot, 1977; Itô, 1973).

The present purpose is to find the system matrices A, B and C from the input signal u(k) and the output signal y(k). Since the data are the single input–single output observations, they have the corresponding z-transform transfer functions. Therefore, when the state models corresponding to them are looked for, it can be posturated that the present transmission systems are observable (and also controllable) and their A-matrices have the companion form. Then, A, B and C are given as follows;

$$A=\begin{bmatrix} 0 & 1 & 0\ldots 0 \\ 0 & 0 & 1\ldots 0 \\ \cdot & \cdot & \cdot \quad \cdot \\ \cdot & \cdot & \cdot \quad \cdot \\ 0 & 0 & 0\ldots 1 \\ a_1 & a_2 & a_3\ldots a_n \end{bmatrix} \tag{2}$$

$$B=[b_1 \ \ b_2 \ \ b_3\ldots b_n]'$$

$$C=[1 \ \ 0 \ \ 0\ldots 0].$$

Thus the problem is to find

$$\hat{a}=[a_1 \ \ a_2 \ldots . a_n] \tag{3}$$

$$\hat{b}=[b_1 \ \ b_2 \ldots b_n]',$$

instead of A, B and C. The prime denotes matrix transpose. The mini-computer used in this study had the user's area of about 1.2 K words (16-bit word) when the Fortran compiler was loaded, and all multiply/divide were performed by software. Because of these restrictions of memory amount and computation speed, the usual methods for linear system identification was avoided. When the memory and speed are not so small, the current methods are recommended (For example, see Akaike and Nakagawa, 1972).

Fundamental direction of the present parameter estimation is to obtain the solution of the discrete type Wiener-Khintchin equation

$$C_{uy}(k)=\sum_{i} h(i)C_{uu}(k-i) \tag{4}$$

by use of the autocorrelation function, C_{uu}, of the input and the crosscorrelation function, C_{uy}, between the input and the output, which have already been computed in the previous work (Watanabe, 1979); but direct derivation of the impulse response function, h(i), was not carried out for the reasons described above. Thus, $\hat{a}$ and $\hat{b}$ were estimated from C_{uu} and C_{uy}, which were regarded as the input and the output respectively, by means of Lee's sequential estimation method (Lee, 1964). Although it was known that this method yielded some estimation bias, it was emploied on account of very rapid convergence and small requirement of the memory. As the result, sometimes, appropriate adjustments were needed for the estimated parameters, but it was easy to see whole tendency of the model under our condition for computation.

The suffix "n" in the equations-(2) is the system order; it is unknown in principle in the central nervous system. This is different from some chemical reactions and electrical circuits which have theoretical bases for the choice of system order. Therefore, in the present study, it must be determined from the input-output data. Lee's and Woodside's methods for system order determination were tried but did not produce good results (Lee, 1964; Woodside, 1971). Details of system order determination in this study will be described in the results.

Results

Picrotoxin suppresses the inhibitory synaptic action in the crayfish abdominal ganglion. Then the shape of the post-synaptic potential varies strikingly and the postsynaptic spike train shows remarkably distinct temporal pattern from the transmission which is affected by the normal inhibitory synaptic action (Watanabe, 1979). One of the aims of the present study is to observe the influence of such change of the synaptic property upon the form of the state model of the ganglionic transmission. The typical process of system order determination can be seen in Fig. 1A for the model of the transmission through the cerebral ganglion in the normal solution. Firstly, the system parameters, $\hat{a}$ and $\hat{b}$, from the third order to the sixth order are calculated by use of the correlation functions through Lee's sequential estimation. Next, the frequency response functions (FRFs) are derived from the state equations

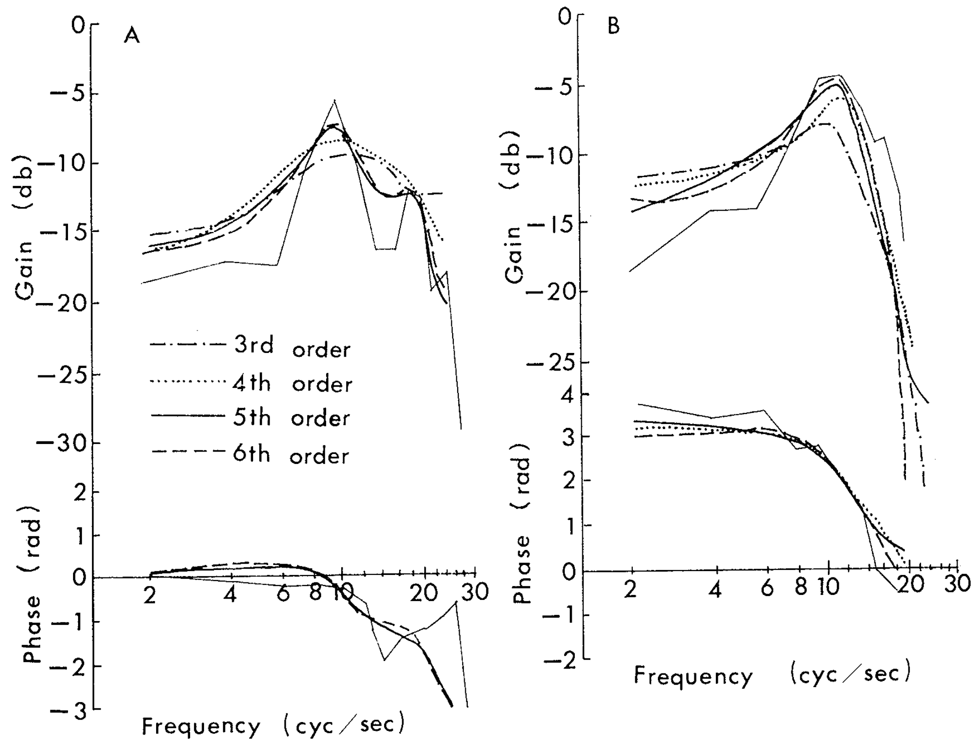

Fig. 1. Comparison between the FRF obtained through Fourier transform of the correlation functions (thin continuous curves) and the FRFs derived from the state models of various system orders (thick continuous and broken curves). A: FRFs of nerve signal transmission through the cerebral ganglion in the normal solution; corresponding operator is P_5 in Table 1. B: FRFs of nerve signal transmission through the abdominal ganglion; corresponding operator is P_6.

that the estimated parameters of the respective orders are substituted. Then, they are compared with the FRF obtained by the Fourier transform method (For Fourier transform method, see Watanabe, 1969). The details of the comparison are as follows; there are no large differences between the FRFs of the third order model and the fourth order one and between the FRFs of the fifth order model and the sixth order one, but the sudden and remarkable changes of the FRF-curves appear between the fourth order model and the fifth order one. By the similar comparison, the FRFs of the abdominal ganglionic transmission have the sudden change between the third order model and the fourth order one, although it is not so clear as the case of the cerebral ganglion. Thus the adopted system order are the fifth for the model of the transmission through the cerebral ganglion and the fourth for the transmission through the abdominal ganglion in the normal solution. When the estimated parameters are substituted in the equations-(1) which have the determined system order, the model of the cerebral ganglionic transmission shown in Fig. 1A is

$$x(\mathrm{k}+1)=\begin{bmatrix} 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \\ 0.176 & -0.066 & -0.065 & -0.094 & -0.200 \end{bmatrix} x(\mathrm{k})+\begin{bmatrix} 0.110 \\ 0.177 \\ -0.118 \\ -0.065 \\ 0.008 \end{bmatrix} \mathrm{u}(\mathrm{k}) \qquad (5)$$

$$\mathrm{y}(\mathrm{k})=[1 \quad 0 \quad 0 \quad 0 \quad 0]x(\mathrm{k}),$$

and the model of the abdominal ganglionic transmission shown in Fig. 1B is

$$x(\mathrm{k}+1)=\begin{bmatrix} 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0.066 & -0.138 & -0.200 & -0.090 \end{bmatrix} x(\mathrm{k})+\begin{bmatrix} -0.148 \\ -0.276 \\ -0.028 \\ 0.196 \end{bmatrix} \mathrm{u}(\mathrm{k}) \qquad (6)$$

$$\mathrm{y}(\mathrm{k})=[1 \quad 0 \quad 0 \quad 0]x(\mathrm{k}).$$

The FRFs of the transmission through the cerebral ganglion in the test solution containing picrotoxin and the FRFs of the transmission recovered partially in the surrounding solution that picrotoxin has been removed are shown in Figs. 2A and 2B. The curves of the former can be approximated with the third order model, while the fifth order model is required to get good approximation for the curves of the latter. Thus the system order of the cerebral transmission model in the picrotoxin solution, i. e. the model that the action of the GABA-synapse is suppressed with picrotoxin, is the third and the equations of the model are

$$x(\mathrm{k}+1)=\begin{bmatrix} 0 & 1 & 0 \\ 0 & 0 & 1 \\ 0.075 & 0.107 & 0.140 \end{bmatrix} x(\mathrm{k})+\begin{bmatrix} 0.131 \\ 0.420 \\ 0.278 \end{bmatrix} \mathrm{u}(\mathrm{k}) \qquad (7)$$

$$\mathrm{y}(\mathrm{k})=[1 \quad 0 \quad 0]x(\mathrm{k}).$$

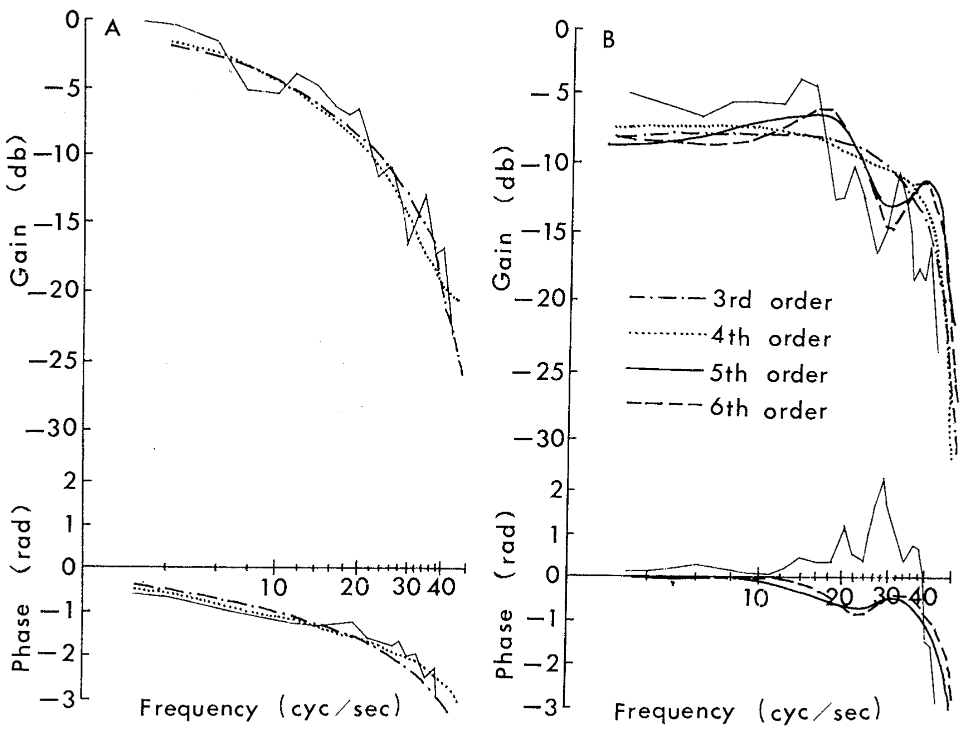

Fig. 2. Similar comparison between the FRFs of the cerebral ganglionic transmission to that shown in Fig. 1A. A: FRFs of nerve signal transmission in the test solution containing picrotoxin; corresponding operator is P_7 in Table 1. B: FRFs of nerve signal transmission whose property is recovering by removal of picrotoxin in the surrounding solution; corresponding operator is P_8.

And the system order of the model of the recovering cerebral transmission is the fifth, then the equation of the model are

$$x(k+1)=\begin{bmatrix} 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \\ 0.077 & -0.011 & -0.015 & 0.011 & 0.110 \end{bmatrix} x(k)+\begin{bmatrix} 0.372 \\ 0.295 \\ -0.031 \\ 0.011 \\ -0.132 \end{bmatrix} u(k) \quad (8)$$

$$y(k)=[1 \quad 0 \quad 0 \quad 0 \quad 0]x(k).$$

Figure 3A shows the FRFs of another abdominal ganglionic transmission than that shown in Fig. 1B in the normal solution, and the FRFs of the transmission through this ganglionic route in the picrotoxin solution are given in Fig. 3B. The former has the sudden change of the FRF curves between the fourth order model and the thrid order one, similarly to the case shown in Fig. 1B. Therefore, the fourth order was also adopted for the former model. For the latter case, the adopted system order was the third. After substitution of the estimated parameters, the state equations of the abdominal ganglionic transmissions in the normal solution and in the

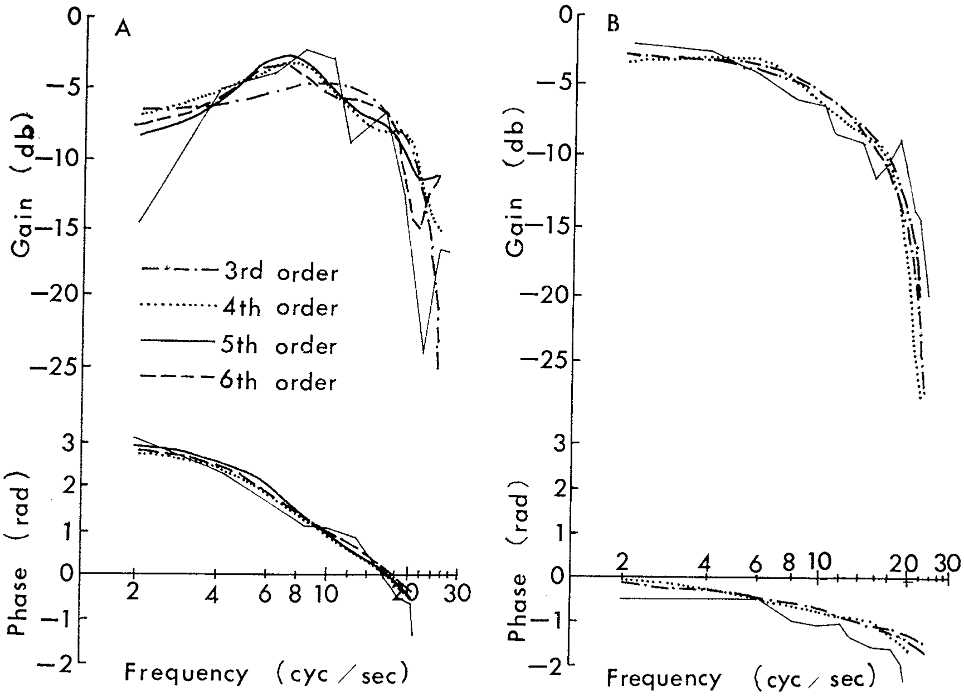

Fig. 3. Similar comparison between the FRFs of another abdominal ganglionic transmission than that shown in Fig. 1B. A: FRFs of nerve signal transmission in the normal solution; corresponding operator is P_9 in Table 1. B: FRFs of nerve signal transmission in the test solution; corresponding operator is P_{10}.

test one are respectively

$$x(k+1)=\begin{bmatrix} 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ -0.153 & -0.053 & -0.087 & -0.201 \end{bmatrix} x(k)+\begin{bmatrix} 0.177 \\ -0.395 \\ -0.405 \\ -0.039 \end{bmatrix} u(k) \tag{9}$$

$$y(k)=[1 \quad 0 \quad 0 \quad 0]x(k)$$

and

$$x(k+1)=\begin{bmatrix} 0 & 1 & 0 \\ 0 & 0 & 1 \\ -0.020 & 0.054 & -0.172 \end{bmatrix} x(k)+\begin{bmatrix} 0.326 \\ 0.346 \\ 0.037 \end{bmatrix} u(k) \tag{10}$$

$$y(k)=[1 \quad 0 \quad 0]x(k)\,.$$

DISCUSSION

The nerve signal transmissions through the crayfish ganglia have been approximated by linear state models with A-matrices in companion form. It is impossible to expect that the linear model obtained in this study can represent completely the quantitative property of the transmission characteristics, since the ganglionic transmission is merely approximately linear. However, it is sure that some qualitative property of the nonlinear model response remains in the linear model response, as revealed in the previous nonlinear analysis (Watanabe, 1979). Therefore, only the qualitative property which is inferred with the present linear model is considered. For this purpose, it is convenient to transform the companion form A-matrix into the representation in the modal domain, i. e. the Jordan canonical form (Kalman, 1968). This transformation can be carried out through the following procedure

$$P = M^{-1} A M , \tag{11}$$

where M is the modal matrix and M^{-1} is its inverse, then the companion form A is transformed into the diagonal matrix P (For detail, see Appendix). At the same time, the input and output coefficient matrices are transformed as $Q = M^{-1} B$, and $R = CM$, thus the representation of the equations-(1) in the modal domain becomes

$$\begin{aligned} z(k+1) &= Pz(k) + Qu(k) \\ y(k) &= Rz(k), \\ & k = 0, 1, 2, \ldots, \\ & z(k)\text{: new state variable.} \end{aligned} \tag{12}$$

Since our interest is confined within the qualitative property of the ganglionic transmission, the present discussion is concerned only with the P-matrix, i.e. the canonical form operator.

Table 1 shows the canonical form operators derived from the equations-(5) to -(10). The complex conjugate of the diagonal elements of the canonical form operator, which is replaced here by the quasi-diagonal form without the imaginary parts, corresponds to an oscillatory system, i.e. a second order system which can not be decomposed any longer (Takahashi, 1968). Therefore, the transmission characteristic through the cerebral ganglion in the normal solution (P_5-matrix) is decomposed into three parallel-connected components; one first order system and two second order oscillatory systems. One of the second order systems disappears by addition of picrotoxin (P_7-matrix) and recovers again by removal of picrotoxin to and from the surrounding solution (P_8-matrix). The behavior of this unstable second order system obviously coinsides with fall and rise of the peak in the amplitude characteristics of the FRF by application and removal of picrotoxin, as shown in Figs. 1A, 2A and 2B (For property of second order system, see Rosen, 1970; Takahashi, 1968). It may be concluded that one of the second order systems in the present cerebral transmission is an oscillator which is functioning by contribution of the inhibitory synaptic action and that it disappears when the action of the GABA-synapse is suppressed by application of picrotoxin.

The experimental conditions of the abdominal ganglion were more complex and obscure than those of the cerebral ganglion, because the recording neurons could

Table 1
Quasi-diagonal form operators of the state models of nerve signal transmissions through the cerebral and abdominal ganglia in the normal solution and the test one. Suffix of each P corresponds with the number of the state equation given in the results. Enclosed parts with broken rectangles indicate the decomposed and parallel-connected components which have the first order or the second order. (See Appendix.)

	Cerebral Ganglion	Abdominal Ganglion
Normal Solution	$P_5=\begin{bmatrix} 0.5893 & 0 & 0 & 0 & 0 \\ 0 & -0.6125 & 0.4403 & 0 & 0 \\ 0 & -0.4403 & -0.6125 & 0 & 0 \\ 0 & 0 & 0 & 0.2182 & 0.6901 \\ 0 & 0 & 0 & -0.6901 & 0.2182 \end{bmatrix}$	$P_6=\begin{bmatrix} 0.2880 & 0 & 0 & 0 \\ 0 & -0.5569 & 0 & 0 \\ 0 & 0 & 0.0894 & 0.6326 \\ 0 & 0 & -0.6326 & 0.0894 \end{bmatrix}$
	$P_8=\begin{bmatrix} 0.6074 & 0 & 0 & 0 & 0 \\ 0 & -0.4723 & 0.3508 & 0 & 0 \\ 0 & -0.3508 & -0.4723 & 0 & 0 \\ 0 & 0 & 0 & 0.2236 & 0.5626 \\ 0 & 0 & 0 & -0.5626 & 0.2236 \end{bmatrix}$	$P_9=\begin{bmatrix} -0.4719 & 0.4312 & 0 & 0 \\ -0.4312 & -0.4719 & 0 & 0 \\ 0 & 0 & 0.3692 & 0.4890 \\ 0 & 0 & -0.4890 & 0.3692 \end{bmatrix}$
Test Solution	$P_7=\begin{bmatrix} -0.2121 & 0.2964 & 0 \\ -0.2964 & -0.2121 & 0 \\ 0 & 0 & 0.5644 \end{bmatrix}$	$P_{10}=\begin{bmatrix} 0.1222 & -0.1813 & 0 \\ 0.1812 & 0.1222 & 0 \\ 0 & 0 & -0.4162 \end{bmatrix}$

not be identified and there existed many kinds of axons in the interganglionic connective to which the stimuli were applied. In addition, picrotoxin had dual effects on most neurons in the abdominal ganglion; not only the suppression of inhibitory synaptic action but the potentiation of the electrogenic ion-pump in the post-synaptic membrane (Watanabe, 1979). Therefore, there are considerable difficulties to interpret the present results on the abdominal ganglionic data. As a result of the formal procedure used in this study, the abdominal ganglionic transmissions in the normal solution can be approximated with the fourth order model, and it can be seen through operator diagonalization that the P_6-operator contains one second order system and the P_9-operator consists of two second order system (Table 1). Although the P_9-operator changes into the P_{10}-operator by application of picrotoxin, the results of the decomposition cannot be explained so clearly as in the case of cerebral ganglion. However, it seems likely that the elimination of the peak in the amplitude characteristics of the FRF of the abdominal ganglionic transmission corresponds to the disappearance of a second order system in the diagonalized operator by application of picrotoxin, similarly to the cerebral ganglion case (Fig. 3B and Table 1).

APPENDIX

An example of the operator diagonalization is shown here for the equations-(10) which represent the transmission characteristics through the abdominal ganglion in the picrotoxin solution. The three eigenvalues of the A-matrix

$$\begin{bmatrix} 0 & 1 & 0 \\ 0 & 1 & 0 \\ -0.020 & 0.054 & -0.172 \end{bmatrix}$$

of the equations-(10) are

1) $0.1222+0.1811j$
2) $0.1222-0.1811j$
3) -0.4162

and the corresponding eigenvectors are

1) $1.0 \quad 0.1222+0.1813j \quad -0.0179+0.0433j$
2) $1.0 \quad 0.1222-0.1813j \quad -0.0179-0.0433j$
3) $1.0 \quad -0.4162 \quad 0.1732$

respectively (Wilkinson, 1965). Then, the modal matrix is

$$M=\begin{bmatrix} 1.0 & 1.0 & 1.0 \\ 0.1222+0.1813j & 0.1222-0.1813j & -0.4162 \\ -0.0179+0.0443j & -0.0179-0.0443j & 0.1732 \end{bmatrix}$$

and its inverse is

$$M^{-1}=\begin{bmatrix} 0.4259+0.1171j & 0.3786-1.6335j & -1.5492-4.6008j \\ 0.4259-0.1171j & 0.3786+1.6335j & -1.5492+4.6008j \\ 0.1481 & -0.7572 & 3.0984 \end{bmatrix}.$$

Through the equation-(11), the diagonalized operator is

$$P=\begin{bmatrix} 0.1222+0.1811j & 0 & 0 \\ 0 & 0.1222-0.1811j & 0 \\ 0 & 0 & -0.4162 \end{bmatrix}$$

and its diagonal elements have the same values as the eigenvalues of the original A-matrix. At present, this is one of the axioms of the matrix calculation theory, but the present computations are not always of little significance as a check account in the practical problem like this study. After the transformation to eliminate the imaginary parts, the operator in the modal domain becomes so called quasi-diagonal form (Takahashi, 1968).

$$P_{10}=\begin{bmatrix} 0.1222 & -0.1813 & 0 \\ 0.1812 & 0.1222 & 0 \\ 0 & 0 & -0.4162 \end{bmatrix}.$$

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REFERENCES

Akaike, H., and T. Nakagawa, 1972. Stochastic Analysis and Control of Dynamical System. Saiensu Pub. Co., Tokyo. (In Japanese.)

Arimoto, S., 1976. *Seitai no Kagaku*, **27**: 306. (In Japanese.)

DeRusso, P. M., R. J. Roy and C. M. Close, 1965. State Variables for Engineers. John Wiley & Sons, Inc., New York.

Faurre, P., and M. Depeyrot, 1977. Elements of System Theory. North-Holland Pub. Co., Amsterdam.

Itô, M., 1973. System Control Theory. Shôkôdô Pub. Co., Tokyo. (In Japanese.)

Kalman, R. E., 1968. *In* Mesarovic, M. D. (ed), System Theory and Biology, p. 222. Springer-Verlag, Berlin.

Lee, R. C. K., 1964. Optimal Estimation, Identification and control. The MIT Press, Cambridge, Massachusetts.

Rosen, R., 1970. Dynamical System Theory in Biology. Wiley-Interscience, New York.

Takahashi, Y., 1968. System and Control. Iwanami Shoten, Tokyo. (In Japanese.)

Van Harreveld, A., 1936. *Proc. Soc. exptl. Biol. N. Y.*, **34**: 428.

Watanabe, Y., 1969. *Kybernetik*, **6**: 124.

——— 1979. *Annot. zool. Japon.*, **51**: 95.

Wilkinson, J. H., 1965. The Algebraic Eigenvalue Problems. Clarendon Press, Oxford.

Woodside, C. M., 1971. *Automatica*, **7**: 727.