A Rate Equation System Having a Mnemonic Function

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A chemical system having a mnemonic function is constructed and its behavior is analyzed. The system consists of a subsystem having seven steady states and, under suitable conditions, it stays in a stable steady state or in an oscillating state depending on the initial state. Moreover, the system can show an additional oscillating state around the oscillating state and transitions between two different oscillating states occur by a little change in a certain parameter value(input), which is the characteristic point in this system. Therefore, a response behavior of the system to an input differs drastically depending on the states, *i.e.*, oscillating or stationary. This property could be related to appearance of a mnemonic function. Moreover, it is demonstrated that the system could be linked with an excitable subsystem to show more clearly the mnemonic function proposed here.

It has been demonstrated that a chemical system far from an equilibrium state occasionally shows some peculiar behaviors like chemical oscillations,[1,2] periodic pattern formation,[3–5] excitation, [6–8] wave propagation,[9–11] etc. One of the most important points in this field is that these peculiar behaviors are very often observed in a living system,[2] and many articles discussed the behaviors with relation to the activities of the living system.[2,12,13] The chemical oscillation is also criticized in relation to the circadian rhythm,[14] beating of heart,[15] excitation of nerve membrane,[16] and the problem of pattern formation was first discussed in relation to morphogenesis in the living system by Turing.[17]

As one of the various activities of the living system, the functions of the living brain have been treated in various aspects. McCulloch and Pitts[18] analyzed the unidirectional travel of a signal from the output of a neuron to the input of the neurons connected to it. Caianiello developed their model and proposed a mnemonic equation in addition to the neuronic equation which includes absolutely and relatively refractory periods of each neuron.[19] He proposed an idea to treat mathematically the memory function of the brain; that is, the memory gained through experiences is stored in the coupling coefficients a_{ij} by the mechanism that the coupling coefficient a_{ij} increases as increasing number of pulses from neuron j to neuron i, and he led a mnemonic equation describing his idea. He developed his idea for thought-processes and thinking machines.

According to the Caianiello equation, the propagation of signal along the nerve of a living brain was studied by a computer simulation method, and the coexistence of a stably oscillating state and a stationary state was confirmed. Some investigators consider that the oscillating state is of the brain recalling a certain matter.[20] According to this explanation, any system that shows coexistence of a stably oscillating and a stationary states may be a candidate for the system having a mnemonic function. There are some model systems relating to this behavior.[21,22]

In this paper, we intend to analyze the mnemonic function in a chemical system with a different standpoint of views. We refer to the system with a mnemonic function as the system-M and consider that it should respond in quite different ways for an input dependently whether the system-M is storing a memory of not. We consider that there should be another external system-E, which utilize the memory stored in the system-M to attain its own specific purpose. The external system-E changes a given parameter value of the system-M to observe its response in order to draw an information from the system-M.

The essential point of the proposed equations is that there coexist one stable steady state and one stable oscillating state, around which another oscillating state appears by a little change in parameter values, and the system is stationary or oscillating dependently on its career it has experienced. Under this situation, we can say that the system remembers the past events. The phase diagram satisfying the steady state conditions is essential in this treatment and there is not a special meaning in the corresponding model reaction processes. Therefore, our main object in this article is not to construct a model system but to show a possibility of mnemonic function in a chemical reaction system.

In the following sections, the differential equations exhibiting a mnemonic function are proposed and the system behaviors are analyzed, and a little more functional system that an excitable system is linked with the original system is developed. In this system, the response caused by an input is more drastic and our idea about the mnemonic function is clearly shown.

Rate Equations Related to a Mnemonic Function

Let us consider the following rate equations without showing corresponding chemical reaction processes,

$$\frac{dE}{dt} = \alpha(b_1 - b_2EX - b_3X), \tag{1}$$

$$\frac{dX}{dt} = \beta(a_1X^9 - a_2X^8 + a_3X^7 - a_4X^6 - a_5X^5 + a_6X^4 - a_7X^3 + a_8X^2 - a_9X + a_{10} + E), \tag{2}$$

where E and X represent the concentrations of two intermediates E and X. The ninth order equation seems to be essential to display an expected mnemonic function, but it is not necessarily the simplest and the most realizable equation for the mnemonic function. It is considered that the system giving such rate equations is not difficult to be realized as being dis-

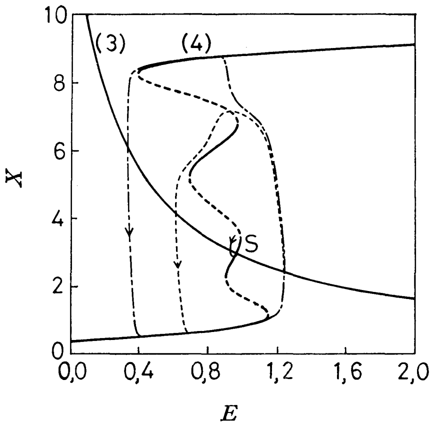

Fig. 1. Relationships between X and E determined by Eqs. 3 and 4.
The numbers in the figure correspond to the equation numbers. The crossing point S of the two curves (3) and (4) is a stable steady state. A thin solid line represents the route into the stable steady state, and a dotted line and a dot and rod line represent the routes of oscillating states of the system-M. Parameter values used for calculations are: $a_1=8.609\times10^{-6}$, $a_2=3.267\times10^{-4}$, $a_3=4.609\times10^{-3}$, $a_4=2.635\times10^{-2}$, $a_5=7.552\times10^{-3}$, $a_6=0.8573$, $a_7=4.3985$, $a_8=9.898$, $a_9=10.16$, $a_{10}=2.696$, $b_1=3.65$, $b_2=1.0$, $b_3=0.27$, $\alpha=0.25$, and $\beta=70.0$ for the dotted line and 75.0 for the dot and rod line.

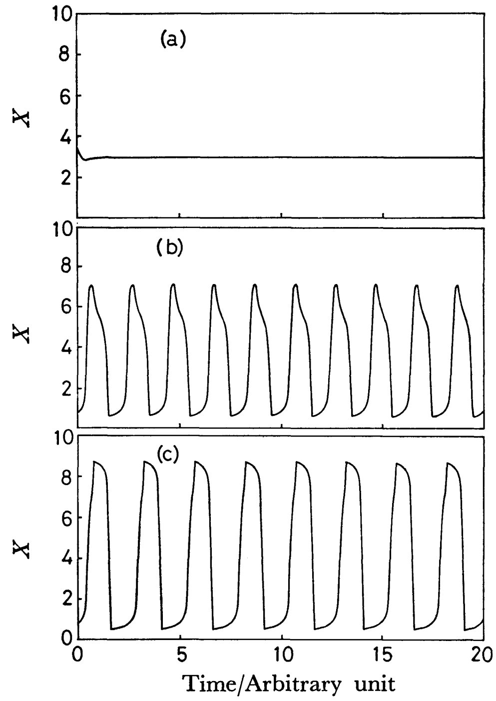

Fig. 2. System behaviors under various conditions.
(a), (b), and (c) show the responses corresponding to the behaviors as shown by solid, dotted, and dot and rod lines, respectively, in Fig. 1.

cussed later. Although the behaviors of the chemical system-M obeying Eqs. 1 and 2 can be determined by direct calculations of these equations with a digital computer, we first discuss the stability of the steady states in order to predict its behaviors. From the steady state conditions, $\mathrm{d}E/\mathrm{d}t=0$ and $\mathrm{d}X/\mathrm{d}t=0$, we have

$$b_1 - b_2EX - b_3X = 0, \tag{3}$$

$$a_1X^9 - a_2X^8 + a_3X^7 - a_4X^6 - a_5X^5 + a_6X^4 - a_7X^3 + a_8X^2 - a_9X + a_{10} + E = 0. \tag{4}$$

Equations 3 and 4 determine two relations between X and E at the steady state, which are displayed on the X-E phase plane in Fig. 1. The parameter values used for the calculations are as follows;

$a_1=8.609\times10^{-6}$, $a_2=3.267\times10^{-4}$, $a_3=4.609\times10^{-3}$,

$a_4=2.635\times10^{-2}$, $a_5=7.552\times10^{-3}$, $a_6=0.8573$,

$a_7=4.3985$, $a_8=9.898$, $a_9=10.16$, $a_{10}=2.696$,

$b_1=3.65$, $b_2=1.0$, and $b_3=0.27$.

These parameter values are arbitrarily chosen to produce an expected behavior. Of course, this selection is not unique for this purpose. The curve defined by Eq. 4 has six marginal points where $\mathrm{d}E/\mathrm{d}X$ is equal to zero. The states along the dotted lines are unstable; that is, when the rate equation 2 is solved for an initial state which is deviated a little from the dotted line at a fixed value of E, the value of X develops to another stable state apart from the dotted line.

The steady state is determined by the crossing point of the two curves defined by Eqs. 3 and 4. It is proved from the result by the standard stability analysis[1]) that the steady state is stable when the two curves intersect on the solid part of the line (4) in Fig. 1. The present system has a stable steady state S at $E=0.9561$ and $X=2.9770$. In this case, the system, which lies initially in the vicinity of the steady state, goes into and remains stable at this steady state. This behavior is shown with a thin solid line falling into the crossing point S from the initial state, $E=0.95$ and $X=3.5$, in Fig. 1. The values of $\alpha=0.25$ and $\beta=70.0$ are used for calculation. The arrow on the line represents the direction of the temporal change of the system. On the other hand, when the initial state of the system is far from the stable steady state S, say $E=1.0$ and $X=0.8$, the oscillating state shown by a closed cycle with a thin dotted line is realized as a final state for the parameter values, $\alpha=0.25$ and $\beta=70.0$. For the system having the parameter values, $\alpha=0.25$ and $\beta=75.0$, the oscillating state represented by a dot and rod line is realized as a final stable state.

These behaviors discussed above are shown as temporal changes of X in Fig. 2. (a) and (b) are of the steady state and the oscillating state, respectively, for $\alpha=0.25$ and $\beta=70.0$, and (c) is of the oscillating state solved for $\alpha=0.25$ and $\beta=75.0$.

Here, let us investigate how the system behaviors are affected by a change in β value. Initially the value of β is 70.0. Then, the system is stationary or oscillating. When the system lies in the oscillating state shown by a dotted line in Fig. 1, the oscillatory trajectory transfers to the cycle represented by a dot and rod line for an increasing value of β to 75.0. When β is brought back to the original value, the oscillating state regresses reversely to the original state of smaller amplitude. On the contrary, when the system is in

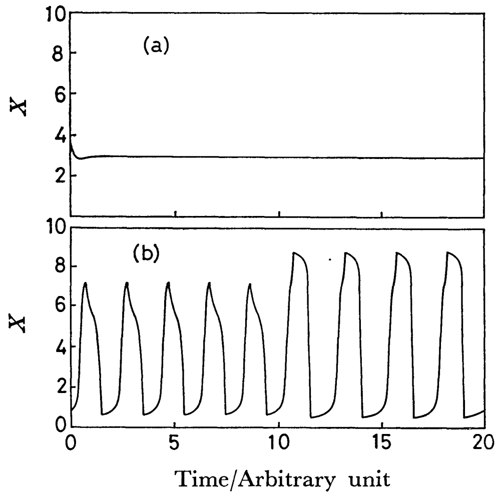

Fig. 3. Response behaviors of the system-M to change in β value.
In both (a) and (b), the value of β is changed from 70.0 to 75.0 at time 10. (a) shows a response of the system-M which is initially in the stable steady state and there is no detectable change. (b) is a response of the system which is initially in the stable oscillatory state and the behavior is suddenly changed in amplitude at time 10. All the parameter values are the same with those of Fig. 1.

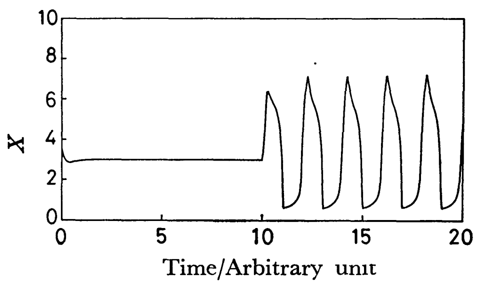

Fig. 4. Response of the system-M initially in the stable steady state to change in E value.
At time 10, the E value is changed into 1.1. The steady state is located at $X=2.9770$ and $E=0.9561$ and other parameter values are the same with those of Fig. 1.

the stable steady state, any changes can not be observed by this change in β value. These responses are demonstrated in Fig. 3. Initially, the system is in the steady state (case a) or in the oscillating state (case b). In both cases (a) and (b), the value of β is changed from 70.0 to 75.0 at time 10. Only the case (b) shows a noticeable response to the change in β value. This is the point on which we have an interest.

Now, let us examine the behavior of the system which is initially in the steady state, being subject to a certain deviation of E value as a result of external stimulus. As an example, when E increases beyond over a threshold value of 1.035, the system falls into the stably oscillating state as shown in Fig. 4. In this example, the E value is increased to 1.1 at time 10, and after that time, the system is in the oscillating state, storing with the memory of this stimulus.

Now, let us introduce another external system-E,

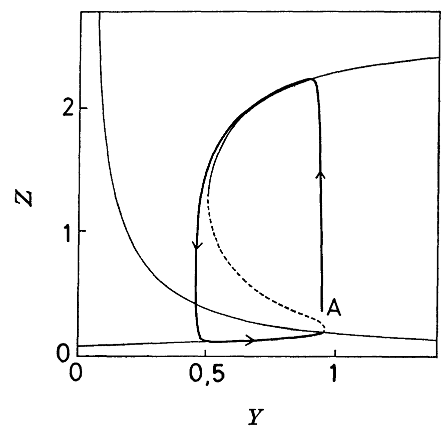

Fig. 5. System behaviors falling into the stable steady state from an initial state A.
Parameter values used for calculations are: $c_1=0.9$, $c_2=4.76$, $d_1=1.332\times10^3$, $d_2=4.864\times10^2$, $d_3=5.02\times10^2$, and $d_4=53.5$.

which may utilize the stored memory in the system-M in order to attain its own specific purpose. In order to draw the memory from the system-M, it should respond to a certain input depending on whether the system-M is storing with a memory or not, because the external system-E can not draw the memory without examining its response to an input. In this meaning, the system-M proposed here can be said that it has a mnemonic function as revealed by the system behaviors shown in Figs. 3 and 4.

System Linked with an Excitable System (System-M′)

In the preceding section, we have shown a series of differential equations related to the mnemonic function. Here, we develop a model by combining an excitable subsystem with the system-M in order to demonstrate more drastically the mnemonic function. The newly introduced system is referred hereafter as system-M′.

Let us introduce the following equations[7)]

$$\frac{dY}{dt} = c_1 - c_2YZ, \tag{5}$$

$$\frac{dZ}{dt} = d_1YZ^2 - d_2YZ^3 - d_3Z + d_4. \tag{6}$$

For the parameters we choose the following values;

$c_1=0.9$, $c_2=4.76$, $d_1=1.332\times10^3$, $d_2=4.864\times10^2$, $d_3=5.02\times10^2$, and $d_4=53.5$.

As is clear from Fig. 5, the system shows an excitation behavior when the Z value is increased beyond over the critical value on the dotted line.[7)] Now, let us construct a system which a large value of X causes an increase in Z. With this device, we could construct a mechanism which generates one pulse by each of the large amplitude oscillation (Fig. 2c) but no pulse by the small amplitude oscillation (Fig. 2b). To this end, Eq. 6 is modified as follows;

$$\frac{dZ}{dt} = d_1YZ^2 - d_2YZ^3 - d_3Z + d_4 + d_5X, \tag{7}$$

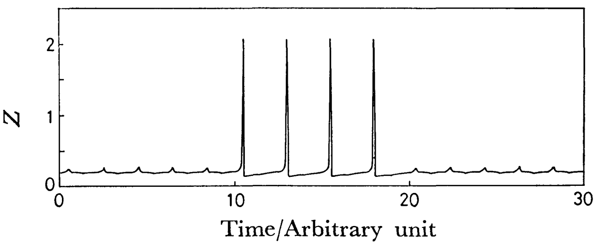

Fig. 6. Effect of change in β value on the behavior of the system-M′.
At time 10, the β value is changed from 70.0 to 75.0, and at time 20, the value is regressed to 70.0. The value of $d_5=0.39$ is used for calculations.

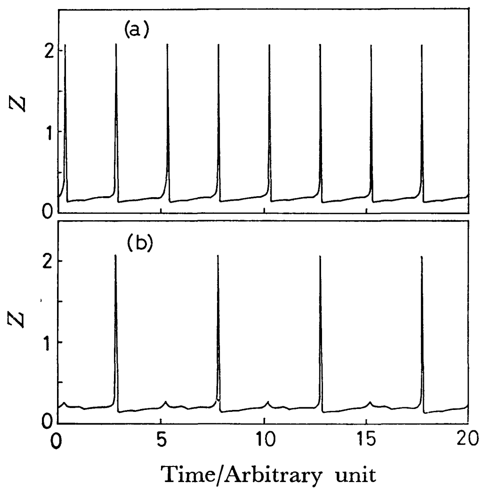

Fig. 7. Behaviors of the system-M′ for the two values of d_5.
(a) $d_5=0.39$ and (b) $d_5=0.38$.

where the last term represents a linkage between the two systems and insures an increase in the Z value owing to an increasing X value.

The behavior of the system-M′ thus constructed is determined by solving Eqs. 1, 2, 5, and 7 with a digital computer. Figure 6 is of an example of the calculated results and shows the response of the system-M′ due to an increase in the parameter β from 70.0 to 75.0 at time 10 and an decrease to its original value at time 20. The input given by the change in β gives large amplitude pulse-like oscillations when the system-M′ stores the memory of the past deviations. Reversely, when the system-M′ does not have any memories, it does not generate any pulses by an input. In this case, the coupling parameter d_5 is assumed to be 0.39

When the value of d_5 is shifted to 0.38, the system-M′ shows a peculiar behavior. Figure 7 shows the behaviors of the system having the d_5 values of 0.39(a) and 0.38(b). In the case of $d_5=0.39$, the excitable subsystem generates pulse-like oscillations as a response to every oscillation of the system-M. On the other hand, in the case of $d_5=0.38$, the excitable subsystem does not respond to every oscillation but responds to every second oscillation. This is because the excitable subsystem has a refractory period after an excitation. In such a situation, a skip of excitation occurs; when a succeeding oscillation of the system-M comes during the refractory period, the excitable subsystem can not respond to this stimulus.

Reaction Processes

In this article, we proposed an artificial rate equation system to show a mnemonic function in a chemical reaction system far from an equilibrium state. The rate equation (2) contains unnatural terms of higher orders than second order. In this section, we show a series of reaction processes to show appearance of a higher order polynomial by a proper selection of bimolecular reaction processes.

For example, let us presume the following consecutive reactions

$$X + X \rightleftharpoons X_2, \quad \text{(R1)}$$

$$X_2 + X \rightleftharpoons X_3, \quad \text{(R2)}$$

....

$$X_{i-1} + X \rightleftharpoons X_i, \quad \text{(R3)}$$

$$A + X_i \xrightarrow{k} P, \quad \text{(R4)}$$

where we presume that the rate constants of (R1)—(R3) are much larger than k of (R4) and the processes (R1)—(R3) attain nearly equilibria. Then, we get

$$X_i = K \cdot X^i, \quad (8)$$

where K is an overall equilibrium constant which is a product of equilibrium constants of the respective steps (R1)—(R3). Then, the decreasing rate of X in the reaction processes (R1)—(R4) is given by

$$\frac{dX}{dt} = -ikAX_i = -ikKAX^i, \quad (9)$$

this is the i-th order polynomial equation. With a similar procedure, we can deduce the rate equation (2) from a series of bimolecular elementary processes. But the scheme thus constructed is no more than one of the possible schemes and has no essential meaning in this work.

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