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# A model of motor control of the nematode *C. elegans* with neuronal circuits

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**Summary**

*Objective:* Living organisms have mechanisms to adapt to various conditions of external environments. If we can realize these mechanisms on the computer, it may be possible to apply methods of biological and biomimetic adaptation to the engineering of artificial machines. This paper focuses on the nematode *Caenorhabditis elegans* (*C. elegans*), which has a relatively simple structure and is one of the most studied multicellular organisms. We aim to develop its computer model, artificial *C. elegans*, to analyze control mechanisms with respect to motion. Although *C. elegans* processes many kinds of external stimuli, we focused on gentle touch stimulation.
*Methods:* The proposed model consists of a neuronal circuit model for motor control that responds to gentle touch stimuli and a kinematic model of the body for movement. All parameters included in the neuronal circuit model are adjusted by using the real-coded genetic algorithm. Also, the neuronal oscillator model is employed in the body model to generate the sinusoidal movement. The motion velocity of the body model is controlled by the neuronal circuit model so as to correspond to the touch stimuli that are received in sensory neurons.
*Conclusion:* The computer simulations confirmed that the proposed model is capable of realizing motor control similar to that of the actual organism qualitatively. By using the artificial organism it may be possible to clarify or predict some characteristics that cannot be measured in actual experiments. With the recent development of computer technology, such a computational analysis becomes a real possibility. The artificial *C. elegans* will contribute for studies in experimental biology in future, although it is still developing at present.


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## 1. Introduction

Living organisms such as human beings have mechanisms to adapt to various conditions of external environments. In the field of molecular biology, one research strategy uses comparatively simple organisms to analyze complicated organisms in detail. A gene that has an important function in the nervous system, for example, was identified in human beings after being discovered in nematodes, and the effectiveness of the analysis of simple organisms is widely recognized. However, despite the experimental techniques of biology, even the simple nematode has never been fully clarified. In recent years, a new approach for analyzing functional mechanisms of living organisms has been proposed, in which a computer simulation of a mathematical model is fully utilized [1]. Using an artificial organism instead of the corresponding actual organism makes it possible to change environmental conditions easily and to analyze behavior repeatedly under the same conditions. If the experimental results of an actual organism can be approximated with high precision by an artificial organism, experiments with the insistent necessity can be selectively done. Also, by using the artificial organism it may be possible to clarify some characteristics that cannot be measured in actual experiments.

Our group has developed computer models of two kinds of unicellular organisms, colibacillus and paramecium, based on knowledge of both biology and engineering [2,3]. By using these models, we were able to simulate the adaptive behavior of unicellular organisms. In addition, we confirmed that mobile robots can be controlled by these model based on the mechanisms of unicellular organisms [4—6]. Therefore, computer models of organisms are not only useful in biology, but can also be applied in engineering. If models of higher organisms can be constructed, the capability and usefulness of computer modeling will increase dramatically.

This study deals with multicellular organisms as the next step in the above-mentioned approach. Among multicellular organisms, we focused on *Caenorhabditis elegans* to model a series of mechanisms from the processing of stimulation information to representation of the behavior. By using such a model, the behavior of an actual organism is reproduced on the computer. The multicellular organism differs mainly from the unicellular organism in that it processes information by using neuronal circuits, in addition to a difference in the number of cells. All neuronal cells (neurons) of *C. elegans* have been identified and the connections have been approximately clarified [7].

These data have been gathered by Dr. Kawamura's group as a database [8] in a form that is easy for engineers to understand and is widely available to the public [9]. Therefore, several computer models of the neuronal circuit of *C. elegans* based on such biological data have been proposed in recent years [8,10—14]. On the other hand, much interest is centered on the control of movement by *C. elegans*, which uses only four muscles (Fig. 1 (b)) to realize various movements, as shown in Fig. 2, and several body models for motion control have been proposed [15,16].

The computer models of *C. elegans* can be classified into three main groups: (i) one that aimed only at understanding the processing of stimulation information in the neuronal circuit and tried to determine the flow of information processing in detail [8,10,11,13,14], (ii) one that examined only the movement of muscles and tried to express the muscles for motion generation in detail [15,16] and (iii) one that tried to integrate the flow series from reception of the stimulation to motion generation in a very simplified form [12]. However, a model that aims only at limited functions like (i) or (ii) cannot express a series of mechanisms from the reception of stimuli to the generation of motion specifically,

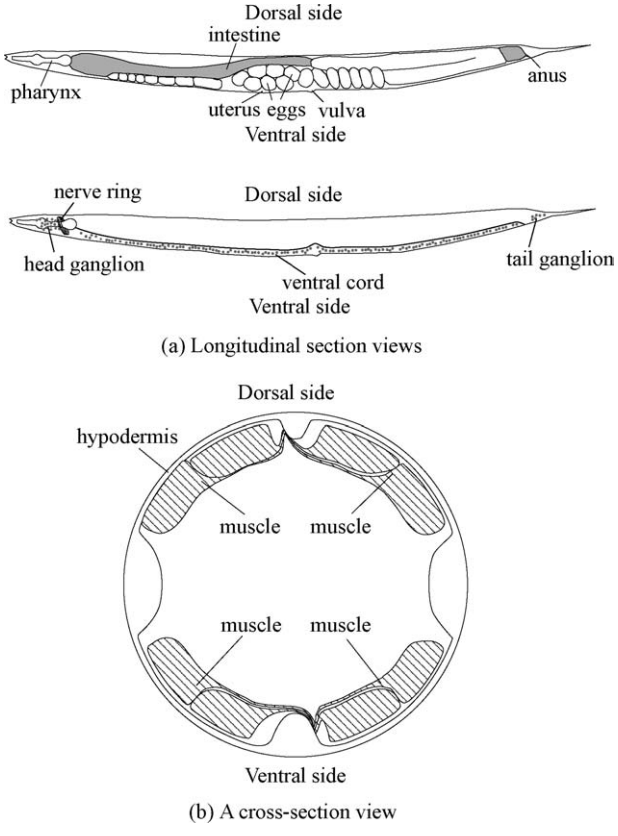


**Figure 1** The structure of *C. elegans* (revised from the figure in [7]).

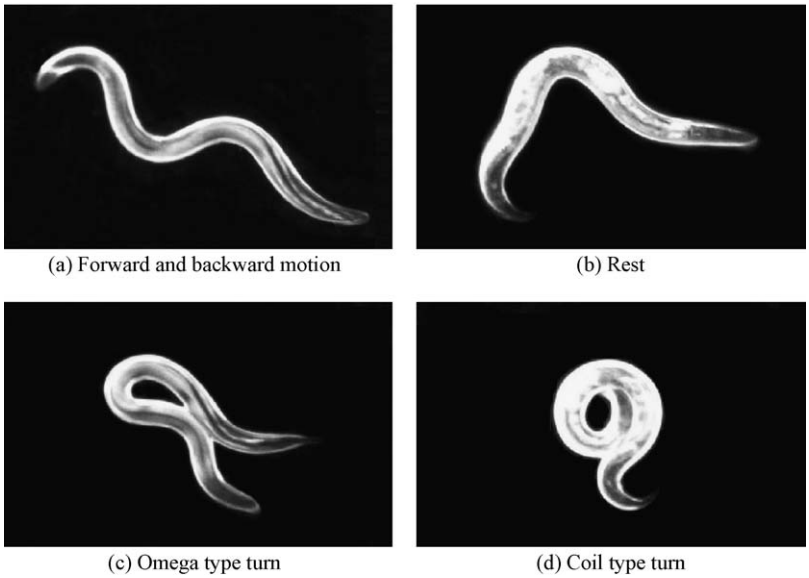


**Figure 2** Motion patterns of *C. elegans*.

and it is impossible to connect the models of (i) and (ii) to construct a whole body integration model because each model was produced separately. In addition, a very simplified model like (iii) imitates only an apparent aspect in the phenomenon of an organism. It is insufficient to explain a phenomenon that actually occurs inside an organism. Therefore, the representation of the actual response that controls a motion according to the stimuli based on the outputs of the neuronal circuit has not been accomplished by the models that were proposed so far.

In this study, we developed both a neuronal circuit model for touch stimulation and a kinematic model of the body, and constructed a whole body model of *C. elegans* by integrating the two models, which are capable of reproducing a flow series from the reception of stimulation to the generation of motion. Although *C. elegans* processes many kinds of external stimuli, we focused on gentle touch stimulation, and the effectiveness of our model is discussed through the simulation results.

## 2. Nervous system and motion of *C. elegans*

*C. elegans* (a non-parasitic soil nematode) has a simple cylindrical body whose length is about 1.2 mm. In the laboratory, they are fed *E. coli* on agar and generally breed at 20 °C. The body is composed of 959 cells and has fundamental organs such as a hypodermis, muscles, alimentary canal and nervous system (Fig. 1) [17]. The body musculature consists of four quadrants of striated muscles. Each quadrant co-nsists of two closely apposed rows of muscle cells [7].

In 1986 White et al. published a neuronal circuit map that includes 302 neurons, about 5000 chemical synaptic connections, about 600 gap junctions and about 2000 connections between neurons and muscles [7]. The neuronal circuit processes information from various kinds of stimuli inside and outside the body, and produces motion appropriate to each stimulus, for example, avoiding obstacles or repellent chemicals. These neurons are classified into three main groups by function: sensory neurons, interneurons and motoneurons. The sensory neurons detect external stimuli first, and then the interneurons process information from the stimuli. Finally, the motoneurons control the muscles on the basis of signals from the interneurons. These neuronal circuits play an important role in sensing, information processing and motor control. In addition to transient responses, *C. elegans* has the capability to learn some environmental information [18].

*C. elegans* moves sideways and sinuously like a snake. As shown in Fig. 2, there are five patterns of motion: forward and backward motion, rest, the omega type turn and the coil type turn. *C. elegans* chooses a suitable motion from these patterns in its search for food. Fig. 2(a) shows the posture of forward or backward motion. From the figure, it can be seen that the motion is achieved by wriggling the body in sinusoidal waves. The rest posture shown in Fig. 2(b) is led by a kink in the tail. The omega type turn is the distinguishing feature in the movements of *C. elegans*. As shown in Fig. 2(c), the body usually executes an " Ω" shape on agar. The coil

type turn, in which the body forms a flat spiral, shown in Fig. 2(d), occurs typically in water. *C. elegans* always moves forward, and the pattern of motion is changed spontaneously or by external stimuli. These movements are controlled by the motoneurons in the head ganglion and the ventral cord. In addition, it has been reported that the motoneurons in the ventral cord play an important role in motion.

## 3. Neuronal circuit model

The connection and feature of each neuron of *C. elegans* are shown in literature by White et al. in 1986 [7]. Also, information about the neurons concerned with response of touch stimulation is conversantly explained in Refs. [17,19]. We extracted the neurons and the connections concerned with touch stimulation based on the references. Therefore the circuit dealt in this paper is sufficient for response of touch stimulation, although there is the possibility that it contains the connections which do not concern with touch stimulation. In the neuronal circuit model, we aimed to represent the response of *C. elegans* to touch stimuli and realize its motor control by using outputs from the model on a computer.

### 3.1. Neuronal circuit model for gentle touch stimulation

When *C. elegans* receives gentle touch stimulation on the anterior part of the body, it moves backward, and it also moves forward when stimulated on the posterior part of the body. Gentle touch stimulation on the anterior part of the body is received by three sensory neurons: ALML, ALMR and AVM. Similarly, gentle touch stimulation on the posterior part of the body is received by PLML, PLMR and PVM. The positions of these sensory neurons are shown in Fig. 3 [7,17—20].

Although *C. elegans* also moves backward when it receives touch stimulation on the top of the head, the response is not dealt in this paper because we focus on only gentle touch stimulation. The sensory neuron which receives the touch stimulation on top of the head is ASH, and this neuron also receives chemical stimulation [17,18]. In modeling ASH, both the chemical and touch stimuli must be considered. However, it is not easy to determine the characteristics of ASH because the details of the mechanism which recieves two kinds of stimulation has not been identified so far. Future research will be directed at dealing with chemical stimulation as well as touch stimulation.

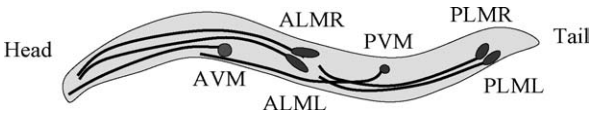


**Figure 3** Sensory neurons for touch stimuli.

The proposed neuronal circuit model of *C. elegans* for gentle touch stimuli is shown in Fig. 4. In the figure, six sensory neurons are shown as rectangles, 10 interneurons as hexagons and two motoneurons as circles. Each neuron is treated as the $n$th neuron $H_n(n = 1, 2, \ldots, 18)$ in this paper. Furthermore, since some parts of the connections with respect to PLM(L/R) and PVM have never been clarified, the connections are determined according to those of ALM(L/R) and AVM.

The movement of *C. elegans* is controlled by 50 motoneurons that can be classfied into five groups : DB$(1, 2, \ldots, 7)$ which controls the muscles on the dorsal side of the body in forward motion, VB$(1, 2, \ldots, 11)$ which controls the muscles on the ventral side of the body in forward motion, DA$(1, 2, \ldots, 9)$ which controls the muscles on the dorsal side of the body in backward motion, and VA$(1, 2, \ldots, 12)$ and AS$(1, 2, \ldots, 11)$ which control the muscles on the ventral side of the body in backward motion [17,18,20]. The neurons for forward motion are represented simply as a neuron, motoP ($H_{17}$), and the ones for backward motion as motoA ($H_{18}$), in order to confirm that the neuronal circuit model realizes control of forward and backward motion according to the position of touch stimuli in this study.

The details of the neuron model is described in the next subsection.

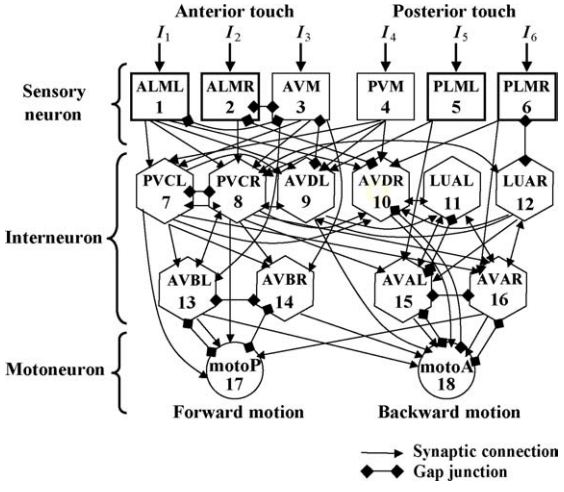


**Figure 4** Neuronal circuit model for touch stimuli.

### 3.2. Description of the characteristics of neurons

The sensory neurons ALML and ALMR receive gentle touch stimuli on the anterior part of the body. In particular, ALML receives stimuli on the left side and ALMR on the right side. Similarly, PLML and PLMR receive gentle touch stimuli on the posterior part of the body. Furthermore, AVM and PVM receive gentle touch stimuli on anterior and posterior parts of the body, respectively. These neurons are considered to have some or no involvement with reception of gentle touch stimuli. The six sensory neurons (Fig. 3) are different from each other in position and sensitivity to stimulation reception. These differences must be considered in the modeling of each neuron. The model supposes that the outputs of ALM(L/R) and PLM(L/R), $O_n(n = 1, 2, 5, 6)$, do not react linearly to the strength of the stimulation, according to the general characteristics of neurons [21,22], and they are expressed by the following equation based on a neuron model [23]:

$$O_n = \frac{c_n}{1 + e(-a_n(I_n - b_n))}, \tag{1}$$

where $a_n$ is an inclination with output function, $b_n$, the value of the stimulation input at which the output of the neuron takes a central value, and $c_n$ is a gain ($0 \leq c_n \leq 1$) to the output and is equivalent to the stimulation reception sensitivity. Touch stimulation inputs $I_n$ to ALM(L/R) and PLM(L/R) are the stepless inputs of the range of (0, 1) which quantifies the strength of the stimulation. Therefore, $O_n$ outputs the continuation value of (0, 1) which is normalized by the maximum output from the actual neuron. Since cases in which gentle touch stimuli are given to both anterior and posterior parts of the body at the same time are uncommon, such a case is not considered in this paper. It is assumed that ALM(L/R) and PLM(L/R) have the same characteristic, and the parameters included in Eq. (1) are set as $a_n = 15$, $b_n = 0.6$ and $c_n = 1$ ($n = 1, 2, 5, 6$) based on the references giving data on the neuronal characteristics of higher organisms [21,22]. Furthermore, the model considers the characteristics of the actual *C. elegans*, and it enters stimulation inputs to AVM and PVM as averages of ALML and ALMR and averages of PLML and PLMR, respectively, and it makes reception sensitivity 1/2 of ALM(L/R) and PLM(L/R).

The output characteristics of six sensory neurons are shown in Fig. 5. The output characteristics of interneurons are also represented by Eq. (1). The input $I_n(n = 7, 8, \ldots, 16)$ to the interneuron $H_n$ is the sum of a value that multiplies the connection weight

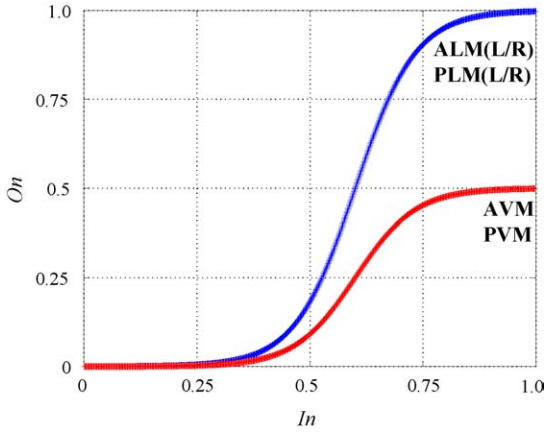


**Figure 5** Characteristics of sensory neurons.

by the output of the connected neuron $H_i$, for example, $I_7$ is calculated by the following equation:

$$I_7 = w_{1,7}O_1 + w_{3,7}O_3 + w_{4,7}O_4 + w_{8,7}O_8 + g_{8,7}O_8, \tag{2}$$

where $w_{i,n}$ and $g_{m,n}$ are the connection weights of synaptic connections (one-way) and gap junctions (interactive), respectively ($w_{i,n} \neq w_{n,i}$, and $g_{m,n} = g_{n,m}$).

The motoneurons, motoA and motoP, are neurons that fire when gentle touch stimuli are given to anterior and posterior parts of the body, respectively. These output characteristics, $O_{18}$ and $O_{17}$, are set as to have the same characteristics of ALM(L/R) and PLM(L/R), and fire corresponding to the strength of the touch stimulation.

In this section, the proposed neuronal circuit model for gentle touch stimulation was explained.

## 4. Body model

To reproduce forward and backward motion in response to gentle touch stimulation by the output signals from the neuronal circuit model described in Section 3, a body model of *C. elegans* was developed. The body musculature consists of four quadrants of striated muscles, and the body-wall muscles are inside the body (Fig. 1(b)). Each quadrant consists of two closely apposed rows of muscle cells [7,17], and sinusoidal motion is achieved by rhythmical dorso-ventral flexures of these muscles [7]. Neuronal control of the body-wall muscles for such sinusoidal motion is divided into 12 parts. Therefore, in this paper, the body-wall muscles of *C. elegans* are expressed by a multi-joint rigid link model with 12 joints in two-dimensional space, as shown in Fig. 6. Since the 50 motoneurons involved

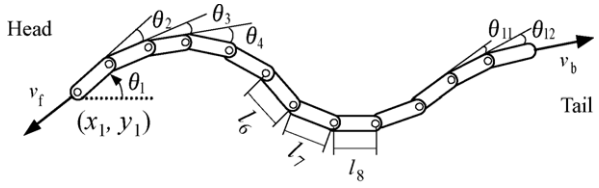


**Figure 6** The rigid-link body model of *C. elegans*.

with motion are simplified to two motoneurons in Section 2, only the direction of the motion (forward or backward) and the velocity are controlled by using the outputs of motoneurons included in the neuronal circuit model.

The head position in forward motion and the tail position in backward motion are calculated by using the velocities, $v_f$ and $v_b$, respectively. The head position in forward motion can be given by:

$$\frac{dx_1}{dt} = v_f \cos\theta_1, \qquad \frac{dy_1}{dt} = v_f \sin\theta_1, \tag{3}$$

where $\theta_1$ corresponds to the current direction of the head. In this paper, it is assumed that the velocities of forward and backward motion, $v_f$ and $v_b$, are controlled by the strength of stimulatory inputs. Thus, the velocities, $v_f$ and $v_b$, are given by the following equations using the outputs of motoneurons, $O_{17}$ and $O_{18}$:

$$v_f = O_{17}(v_f^{max} - v_f^{st}) + v_f^{st}, \qquad v_b = O_{18} v_b^{max} \tag{4}$$

where $v_f^{max}$ and $v_b^{max}$ are the maximum velocities of forward and backward motion, respectively. Furthermore, since *C. elegans* ordinarily moves forward, $v_f$ includes this velocity as $v_f^{st}$. Then, the positions $(x_i, y_i)$ of the $i$th joint $(i = 2, 3, \ldots, 12)$ are calculated by:

$$x_i = x_{i-1} - l_i \cos\theta_{i-1}, \qquad y_i = y_{i-1} - l_i \sin\theta_{i-1}, \tag{5}$$

where $l_i$ denotes the link length, as shown in Fig. 6. $\theta_i (i = 2, 3, \ldots, 12)$is the joint angle to the $(i-1)$th link ($-\pi \le \theta_i \le \pi$ (rad)).

Let us consider with controlling each joint angle respectively here by using one pair of neuronal oscillators. In this model, one pair of neuronal oscillators are set on the dorsal and ventral sides of each joint, and muscles are controlled by the output states of the neuronal oscillators, $M_j$ and $M_{j-1}$. The $i$th joint angle $\theta_i$ $(i = 1, 2, \ldots, 12)$ is expressed by using $M_j$ and $M_{j-1}$ as follows:

$$\frac{d\theta_i}{dt} = \alpha_i (M_j - M_{j-1}) \quad (i = 1, 2, \ldots, 12;\ j = 2i), \tag{6}$$

where $\alpha_i$ is the positive constant ($-\pi \le \alpha_i \le \pi$ (rad/s)) which is equivalent to the angular velocity gain. The subscripts, $j$ and $j-1$, show the number of the neuronal oscillator, where the neuronal oscillators on the ventral side are denoted by $j = 2i$, and the ones on the dorsal side $j-1$.

To realize the sinusoidal movement that is particular to *C. elegans*, it is important to generate the values of $M_j$ and $M_{j-1}$ in Eq. (6) to contract and relax the muscles on the dorsal and ventral sides of the body alternately. To generate this alternating oscillation, Matsuoka's neuronal oscillator model [24], which is a mathmatical model for mutual inhabitation networks that can generate oscillatory output [25], is employed in this paper. The output state $M_k (k = 1, 2, \ldots, 24)$ of the $k$th oscillator is expressed by the following equations [24]:

$$\frac{T_r}{\beta}\frac{dM_k}{dt} + M_k = -\sum_{l=0, l\neq k} a_{k,l} V_l + \beta s_k - b_k f_k, \tag{7}$$

$$\frac{T_a}{\beta}\frac{df_k}{dt} + f_k = V_k, \tag{8}$$

$$V_k = \begin{cases} M_k & (M_k \ge 0) \\ 0 & (M_k < 0), \end{cases} \tag{9}$$

where $M_k$ is the output of the $k$th oscillator; $a_{k,l} (l = 1, 2, \ldots, 24)$ is the connection weight from the $k$th oscillator to the $l$th oscillator; $T_r$ and $T_a$, the time constants; $b_k$ denotes a fatigue coefficient; $s_k$, the tonic input from neurons connecting with the $k$th oscillator; $f_k$, the internal state of the $k$th oscillator; and $V_l$ is the output state of the $l$th oscillator. Furthermore, the following trajectory modification gain $\beta$ is utilized as to maintain a constant trajectory regardless of the velocity:

$$\beta = \begin{cases} \dfrac{v_f^{max}}{v_f} & (\text{forward motion}) \\ \dfrac{v_b^{max}}{v_b} & (\text{backward motion}) \end{cases} \tag{10}$$

In this way, it becames possible to generate the sinusoidal motion of *C. elegans* by using the proposed rigid link model of a body with 12 joints that incorporates the neuronal oscillators. In the next section, we tried to represent the movement of *C. elegans* with the proposed model.

## 5. Simulation of motor control

### 5.1. Optimization of the neuronal circuit model by a real-coded GA

The connection weights of the chemical synaptic connection and the gap junction must be appropriately set to realize the desired output according to the stimulation of the neuronal circuit model described in Section 3. However, it is impossible to measure these values by biological experiments

with actual organisms. Therefore, in this paper, a real-coded genetic algorithm (GA) [26] was employed in which the mechanism of heredity or the evolution of organisms is simulated in order to adjust these connection weights, 56 chemical synaptic connections and 14 gap junctions. Since details of the characteristics of 10 interneurons are unknown, the coefficients $a_n$, $b_n$ and $c_n$ included in Eq. (1) cannot be set on the basis of the actual characteristic. Therefore, these values, which decide the properties of interneurons, are also adjusted by the same GA. Because the interneurons PVCL and PVCR are neurons in the same class, these coefficients are given by identical values, i.e. $a_7 = a_8$, $b_7 = b_8$ and $c_7 = c_8$, respectively. In the same way, because the neurons AVDL and AVDR, LUAL and LUAR, AVBL and AVBR, and AVAL and AVAR are in the same classes, each coefficient takes an identical value. In this paper, stimulation inputs with $v$ patterns of strength to sensory neurons ALML, ALMR, PLML and PLMR are considered, respectively. All connection weights and coefficients are adjusted to obtain the appropriate output to the $2v^2 = U$ patterns of gentle touch stimulation.

In this simulation, the stimulation inputs to the sensory neurons are set as six patterns ($v = 6$) of 0, 0.2, 0.4, 0.6, 0.8 and 1.0. First, all the parameters that are required to be well adjusted are included as the $r$th $(r = 1, 2, \ldots, 85)$ components in a GA string $q_p$ as shown in Fig. 7, where $p$is the serial number $(p = 1, 2, \ldots, P)$ of the individual. After making the above preparations, a method of real-coded GA [26] is employed, and the procedure used in this paper is described below;

Step 0: Initialization

The maximum generation number $G$ is set, and the initial individuals are produced with random real-codes within the initial domain which is set in advance. Also, the fitness function $F(p)$, which is the evaluation standard of the solutions, is given by Eq. (11) in order to reduce the difference between the desired output signal of the motoneurons, $D_n(u)$, and the actual output signal, ${}^pOn(u)$, where $n = 17, 18$. The neuronal circuit model is optimized to minimize the value of $F(p)$:

$$F(p) := \frac{1}{U}\sum_{u=1}^{U}(\{D_{17}(u) - {}^p O_{17}(u)\}^2 + \{D_{18}(u) - {}^pO_{18}(u)\}^2) \quad (p = 1, 2, \ldots, P) \tag{11}$$

The following three steps of (i) selection, (ii) crossover and (iii) mutation are carried out in each generation.

Step 1: Selection

Each individual $q_p$ is arranged in order based on $F(p)$. Then, $\gamma_E$ individuals with superior fitness values are selected and saved in the next generation.

Step 2: Crossover

The $\gamma_C$ individuals are generated by the crossover, where $\gamma_C = P - \gamma_E$. Two individuals $q_a$ and $q_b$ are chosen from among the superior $\gamma_E$ individuals, and new individuals $q_{c1}$ and $q_{c2}$ are generated by applying the following procedure to each $q_a(r)$ and $q_b(r)$ $(r = 1, 2, \ldots, 85)$:

$$q_c(r) = q_{sup}(r) \mp |q_a(r) - q_b(r)|/4, \tag{12}$$

where $q_{sup}$ in Eq. (12) refers to the individual with the superior fitness value, i.e., $q_a$ or $q_b$. If $q_{sup} = q_b$, Eq. (12) means that $\overrightarrow{q_a q_b} : \overrightarrow{q_b q_c} = 4 : \mp 1$.

Step 3: Mutation

Choose $\gamma_M$ individuals from among ones given by the crossover at random, and replace them with randomly determined values within the initial domain.

Step 4: Update

The procedure from steps 1–3 is repeated for G.

The motoneurons, motoA and motoP, are the neurons that fire according whether the anterior or posterior part of the body, respectively, is stimulated. Therefore, it is assumed that the characteristics of motoA and motoP are the same as that of sensory neurons ALM(L/R) and PLM(L/R), and the

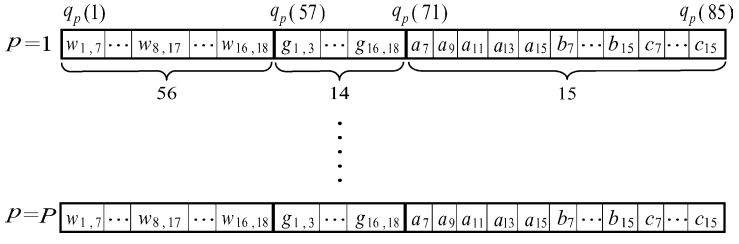


**Figure 7** Phenotype of a GA for connection-weight training.

desired output signals $D_{18}(u)$ and $D_{17}(u)$ of the two motoneurons are respectively given by the following equations:

$$D_{18}(u) = \frac{c_1}{1 + e(-a_1(I_3(u) - b_1))}, \quad (13)$$

$$D_{17}(u) = \frac{c_5}{1 + e(-a_5(I_4(u) - b_5))} \quad (14)$$

The fitness value of each individual is evaluated after the outputs of the neuronal circuit model reach the steady states, because the neuronal circuit of *C. elegans* is a recurrent type. In each generation, the elite individuals are chosen after the elapse of five sampling intervals which has been confirmed in preliminary simulations as enough time to reach the steady states.

## 5.2. Output results of the neuronal circuit model

The neuronal circuit model was optimized by stimulation inputs of $U = 72$ patterns with $P = 50$ individuals and $G = 500$ generations. Also, $\gamma_E$ and $\gamma_M$ were set to 20 and 10, respectively. The initial values of the connection weights, $w_{i,n}$ and $g_{m,n}$, were randomly determined by the normal distribution with $N(0, 0.01)$ and the uniform distribution $U_n(0, 0.001)$, and the parameters $a_n$, $b_n$ and $c_n (n = 7, 9, 11, 13, 15)$ by uniform distributions with $U_n(0, 10)$ for $a_n$, $U_n(0, 1)$ for $b_n$ and $U_n(0, 1)$ for $c_n$.

The evolution of the elite fitness, $F_{\text{sup}}$, is shown in Fig. 8. The figure confirms that the optimal set of 85 parameters was obtained at the 200th generation. Also, the output results of the neuronal circuit model by using the optimal set of 85 parameters at the 500th generation of a GA are shown in Fig. 9. The dotted line in the figure is the value of the desired output signal $D_n(u)$ of the motoneuron. The desired output is produced when the difference between the actual output $O_n(u)$ of the motoneurons of this model and $D_n(u)$ is small. Thus, it is possible to state that the connection weights and the coefficients included in the neuronal circuit model are appropriately adjusted by the GA, and the neuronal circuit model can generate the desired outputs to the various stimulation inputs.

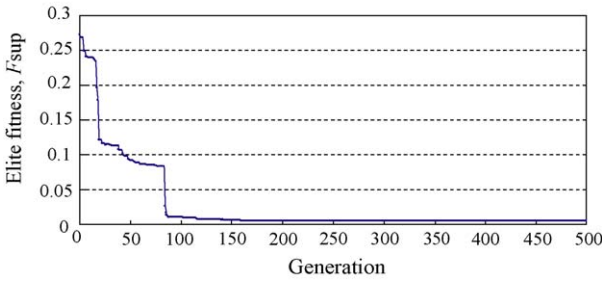


**Figure 8** Evolution of the elite fitness value.

## 5.3. Behaviors of the body model

Before integrating the neuronal circuit model described in Section 3, the behavior of the body model in Section 4 was confirmed. Considering the body length which is about 1.2 mm, the parameters were set as $v_{\text{f}}^{\max} = 1.2$ (mm/s), $v_{\text{b}}^{\max} = -0.8$ (mm/s), $v_{\text{f}}^{\text{st}} = 0.4$ (mm/s) and $l_1 = l_2 = \cdots = l_{12} = 0.1$ (mm). The initial value of $\theta_1$ was set to $\pi/4$ (rad), where $\theta_1$ specifies the direction of movement. Also the initial value of the joint angles $\theta_i$ $(i = 2, 3, \cdots, 12)$ were set to $\pi/4$ (rad). In the neuronal oscillators, the initial value of $M_k$ $(k = 1, 2, \ldots, 24)$ were all set to 1, $b_k = 18$, $f_k = 1$, $s_k = 5$, and the time constants were set to $T_r = 0.12$ (s) and $T_a = 2T_r = 0.24$ (s) by trial and error based on literature such as [25].

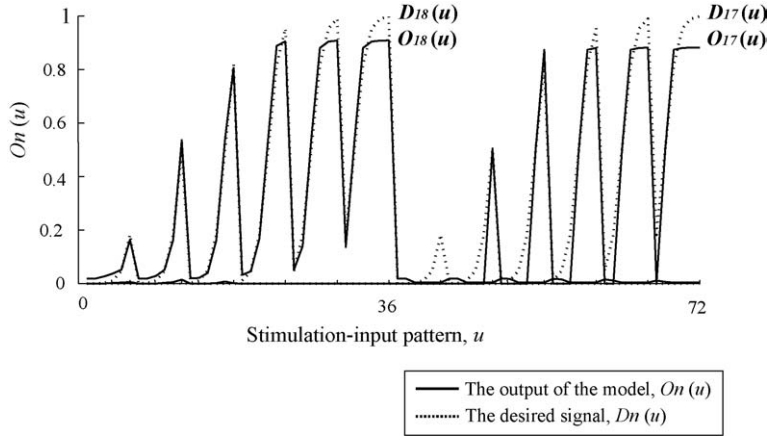


**Figure 9** Outputs of motoneurons in proposed neuronal circuit model.

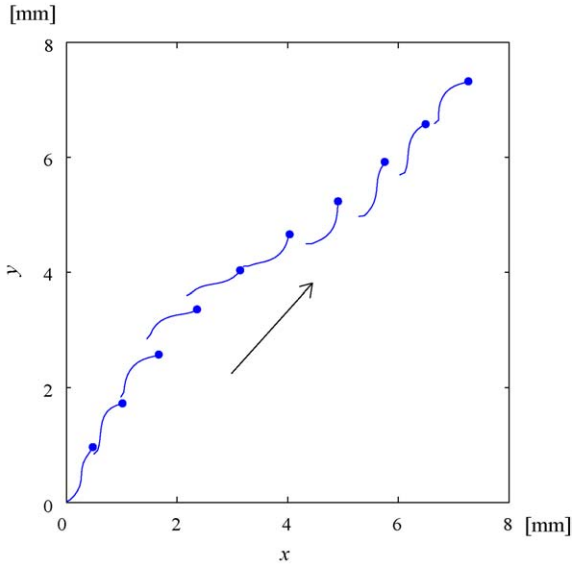


**Figure 10** Forward motion of the body model.

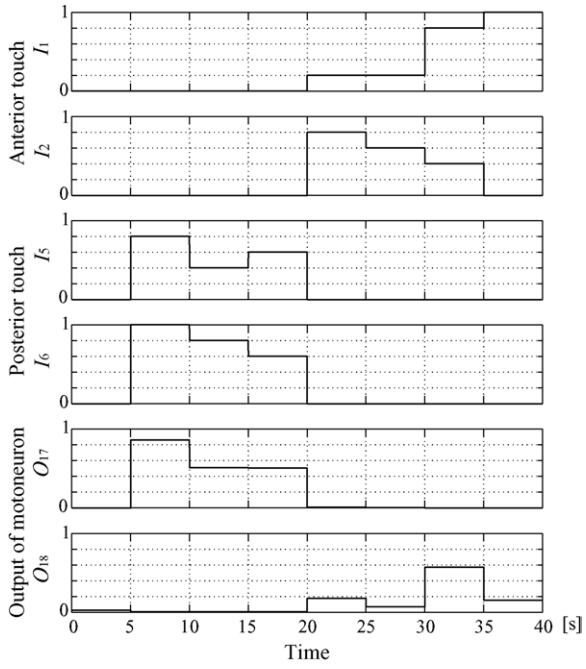


**Figure 11** Exsample of input—output responses of the proposed neuronal circuit model.

Under the above setting, the differential equations included in Eqs. (6)—(8) are calculated every $1.0 \times 10^{-3}$ (s) by using the fourth-order Runge-Kutta method. The result in forward motion with the velocity $v_f = v_f^{max} = 1.2$ (mm/s) is plotted every 1 (s) in Fig. 10. In the figure, '●' is the head of *C. elegans*. The figure shows that the sinusoidal movement can be expressed by the proposed model.

## 5.4. Integration of the neuronal circuit model and the body model

The neuronal circuit model described in Section 3 was connected to the motor control model of the body in Section 4. A computer simulation, which represents the series of stimuli processed with the total model of *C. elegans*, was carried out. In this model, the velocity and direction of the motion correspond to the stimuli that are received in sensory neurons. The various strengths of touch stimulation inputs $I_n (n = 1, 2, 5, 6)$ are given every 5 (s) for 40 (s) on the anterior and posterior parts of the body. The outputs of the motoneurons included in the neuronal circuit model is shown in Fig. 11. The figure demonstrates that touch stimulation of the body is processed adequately by the neuronal circuit model. By using the outputs of the motoneurons, the motion velocity of the body model is determined based on Eq. (4).

The head position for 20 (s) of the first half (forward motion) plotted every 0.1 (s) in Fig. 12. In the figure, a—d are the head positions at 5, 10, 15 and 20 (s), respectively. It is observed that the constant trajectory of the sinusoidal movement can be maintained regardless of the change of the motion velocity by introducing the trajectory modification gain $\beta$ into Eqs. (7) and (8). Motor control can be well realized by gentle touch stimuli to the anterior part of the body.

## 5.5. Reproduction of five motion patterns

As shown in Fig. 2, *C. elegans* has five patterns of motion. The tonic input to the neuronal oscillator $s_k = 5 (k = 1, 2, \ldots, 24)$ in forward or backward

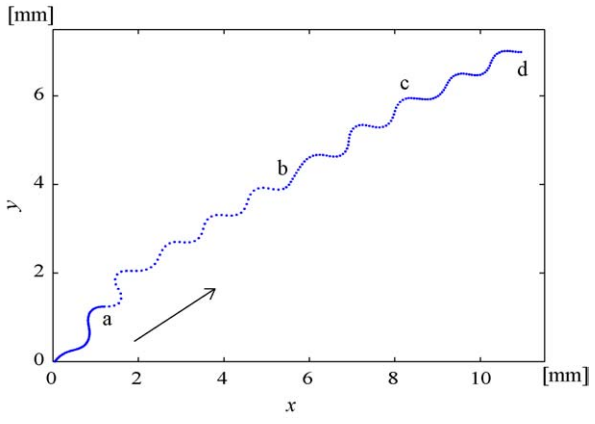


**Figure 12** Motion trajectory of the body model controlled by the neuronal circuit model.

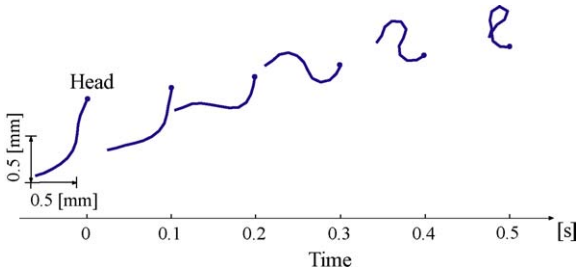


**Figure 13** Reproduction of the Ω type turn.

motion makes it possible to express some patterns of motion by changing the input to the specific neuronal oscillator and by tuning the balance of the motion.

The result in which the form changes to the Ω type turn from the forward motion is plotted every 0.1 (s) for 0.5 (s) in Fig. 13. At time 0 (s), the tonic inputs were strengthened for the center from the end of the body as follows:

$$s_1 = s_2 = s_{23} = s_{24} = 5, \qquad s_3 = s_4 = s_{21} = s_{22} = 6,$$

$$s_5 = s_6 = s_{19} = s_{20} = 7, \qquad s_7 = s_8 = s_{17} = s_{18} = 8,$$

$$s_9 = s_{10} = s_{15} = s_{16} = 9,$$

$$s_{11} = s_{12} = s_{13} = s_{14} = 10.$$

From the figure, the change to the Ω form from the sinusoidal form in forward motion can be confirmed.

The results that reproduced all of the motion patterns of Fig. 2 in the same manner, in addition to the Ω type turn, are shown in Fig. 14. In the figure, (a) is the form of forward and backward motion ($s_1 = s_2 = \cdots = s_{24} = 5$), and (b) is the form at rest, where only inputs $s_8$ and $s_{17}$ to the oscillators on the ventral side of the fourth joint and on the dorsal side of the ninth joint were rather strengthened, $s_8 = s_{17} = 10$. Fig. 14(c) is the form of the Ω type turn mentioned above, and (d) is the form of the coil type turn. In Fig. 14(d) only inputs to the oscillators on the ventral side were strengthened for the head from the center of the body as follows: $s_{14} = 6$, $s_{12} = 7$, $s_{10} = 8$, $s_8 = 9$, $s_6 = 10$, $s_4 = 11$and $s_2 = 12$. These results confirmed that the motor control model of the body in Section 4 can represent various patterns of motion by tuning the tonic input signal to each neuronal oscillator based on the desired body form. Actually, *C. elegans* has a steering circuit to control the motion direction. Although the escape reactions, such as forward and backward motion, are controlled by the neuronal circuit for touch stimulation that was extracted in this study, the turns are controlled by the steering circuit. However, it is unclear what control enters which part of the body-wall muscles. The ability of this simulation to freely change input to a specific part of the body-wall muscles is expected to provide an effective approach to finding new information about motion control.

The proposed model in this paper reproduced the actual behavior qualitatively. How to evaluate the behavior of the model is a particularly important and also difficult problem. The stricter evaluation such as the quantitative comparison with the actual one using the electrophysiologic states in neurons and muscular forces could be required, although the measurement of the biological data on *C. elegans* is

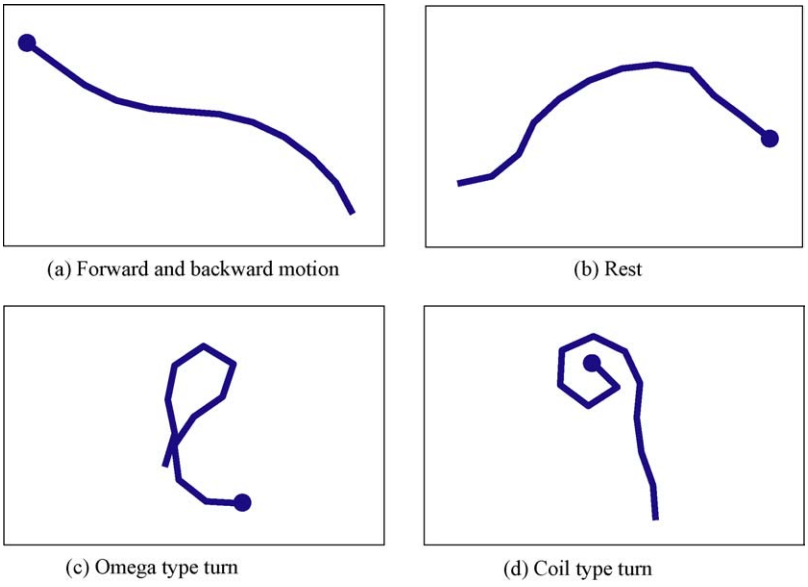


**Figure 14** Reproduction of motion patterns in Fig. 2.

difficult. Future research will be required to solve such a problem.

## 6. Conclusion

Toward the generalization of the computer analysis, this study focused on *C. elegans* and proposed its motor control model, *artificial C. elegans*, as one of examples of the *artificial* organism. This model consisted of a neuronal circuit model for motor control that responds to touch stimuli and a kinematic model of the body for movement. The computer simulations confirmed that the proposed model is capable of realizing motor control similar to that of the actual organism qualitatively.

Further research will be required to adapt the model to the actual characteristics based on experimental biological data such as that in Ref. [27]. Also, if a neuronal circuit can be constructed to model not only the touch-response circuit but also various functional circuits such as those concerned with chemotaxis or direction control, it will be possible to realize a more realistic model that represents complex mechanisms of behavior in the environment in response to various stimuli.

Sor far, we have been aimed at the development of computer models of organisms, *artificial* organisms, which could be used instead of the corresponding actual organisms in some biological experiments. The *artificial* organism enables us to change environmental conditions easily and to analyze behavior repeatedly under the same conditions. If the experimental results of an actual organism can be approximated with high precision by an *artificial* organism, experiments with the insistent necessity can be selectively done, and thus the computational analysis by using such an *artificial* organism could contribute for the reduction of the period for some kinds of biological experiments dramatically. Also, by using the *artificial* organism it may be possible to clarify or predict some characteristics that cannot be measured in actual experiments. With the recent development of computer technology, such a computational analysis becomes a real possibility. The *artificial C. elegans* will contribute for studies in experimental biology in future, although it is still developing at present.

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## References

[1] Ohtake H, Software of living organisms, Comput Today 104 (Saiensu, Tokyo) 2001;16—21 (in Japanese).
[2] Tsuji T, Hashigami K, Kaneko M, Ohtake H. Emerging chemotaxis of virtual bacteria using genetic algorithm. Trans IEE Jpn 2002;122—C(2):201—7 (in Japanese, with English abstract).
[3] Hirano A, Tsuji T, Tanaka Y, Ohtake H, Takiguchi N. Simulation of chemotactic response of paramecium. Softw Biol 2004;3:84—90 (in Japanese).
[4] Ohtake H, Yako T, Tsuji T, Kato J, Kuroda A, Kaneko M. An approach to molecular artificial life: bacterial intelligent behavior and its computer model. In: Langton CG, Shimohara K, editors. Artificial life V. Cambridge: The MIT Press; 1997. p. 395—401.
[5] Tsuji T, Sakane A, Fukuda O, Kaneko M, Ohtake H. Biomimetic control of mobile robots based on a model of bacterial chemotaxis. Trans Jpn Soc Mech Eng C 2002;68(673):171—8 (in Japanese, with English abstract).
[6] Hirano A, Suzuki M, Tsuji T, Takiguchi N, Ohtake H. Mobile robot control based on chemotaxis of paramecia. In: Proceedings of the 2004 JSME Conference on Robotics and Mechatronics, 1A1-L1-23. 2004. p. 1—2 (in Japanese).
[7] White JG, Southgate E, Thomson JN, Brenner S. The structure of the nervous system of the nematode *Caenorhabditis elegans*. Phil Trans R Soc Lond B 1986;314(1165):1—340.
[8] CCEP (Cybernetic Caenorhabditis Elegans Program), editor. Study on the nervous system of *C. elegans* as a biological information system, Annual Report of CCEP. Keio Future, Keio University, Yokohama, 2001 (in Japanese).
[9] Oshio K, Iwasaki Y, Morita S, Osana Y, Gomi G, Akiyama E, et al. Database of synaptic connectivity of *C. elegans* for computation, Technical Report of CCeP. Keio Future 3, Keio University, Yokohama, 2003.
[10] Wicks SR, Roehrig CJ, Rankin CH. A Dynamic network simulation of the nematode tap withdrawal circuit: predictions concerning synaptic function using behavioral criteria. J Neurosci 1996;16:4017—31.
[11] Cangelosi A, Parisi D. A neural network model of *Caenorhabditis elegans*: the circuit of touch sensitivity. In: Neural processing letters, vol. 6. Netherlands: Kluwer Academic Publishers; 1997. p. 91—8.
[12] Ferrée TC, Lockery SR. Computational rules for chemotaxis in the nematode *C. elegans*. J Comput Neurosci 1999;6:263—77.
[13] Morita S, Oshio K, Osana Y, Funabashi Y, Oka K, Kawamura K. Geometrocal structure of the neuronal network of *Caenorhabditis elegans*. Physica A 2001;298:553—61.
[14] Funabashi Y, Kawamura K, Oshio K, Morita S, Osana Y, Akiyama E, et al. Native response of *C. elegans* encoded in its neuron network. J Phys Soc Jpn 2001;70(4): 1154—61.

[15] Niebur E, Erdos P. Modeling locomotion and its neural control in nematodes. Comment Theor Biol 1993;3(2):109—39.
[16] Bryden Jhon. Cohen Netta. A simulation model of the locomotion controllers for the nematode *C. elegans*, From animals to animals 8. In: Schaal S, Ijspeert A, Billard A, Vijayakumar S, Hallam J, Jean-Arcady Meyer, editors. Proceedings of the Eighth International Conference on the Simulation of Adaptive Behavior. 2004. p. 183—92.
[17] Kohara Y, editor. Senchu, Kyoritsu Syuppan, Tokyo, 1997 (in Japanese).
[18] Riddle DL, Blumenthal T, Meyer BJ, Priess JR, editors. *C. elegans* II. New York: Cold Spring Harbor Laboratory Press, 1998.
[19] Chalfie M, Sulston JE, White JG, Southgate E, Thomson JN, Brenner S. The neural circuit for touch sensitivity in *C. elegans*. J Neurosci 1985;5:956—64.
[20] Hope IA, editor. *C. elegans* —A practical approach. New York: Oxford University Press, 1999.
[21] Delcomyn F. Foundations of neurobiology. New York: W.H. Freeman and Company, 1998.
[22] Fain GL. Molecular and cellular physiology of neurons. Cambridge: Harvard University Press, 1999.
[23] Rumellhart DE, McClelland JL. PDP Research Group. Parallel distributed processing volume 1: foundations. Cambridge: The MIT Press, 1986.
[24] Matsuoka K. Mechanisms of frequency and pattern control in the neural rhythm generators. Biol Cybern 1987;56:345—53.
[25] Kotosaka S, Schaal S. Synchronized robot drumming by neural oscillator. J Robot Soc of Jpn 2001;19(1):116—23 (in Japanese, with English abstract).
[26] For example;
Suzuki M, Yamamoto T, Tsuji T. A design of neural-net based PID controllers with evolutionary computation. IEICE Trans Fund 2004;E87-A(10):2761—8
[27] For example;
Suzuki H, Rexr Ker, Laura Bianchi, Christian Frøkjær-Jensen, Dan Slone, Jian Xue, et al. In vivo imaging of *C. elegans* mechanosensory neurons demonstrates a specific role for the MEC-4 channel in the process of gentle touch sensation. Neuron 2003;39:1005—17