

A Neuromuscular Model of *C. elegans* with Directional Control

Michiyo Suzuki¹, Toshio Tsuji¹, Hisao Ohtake²

¹ Department of Artificial Complex Systems Engineering, Hiroshima University, Higashi-Hiroshima, Japan

² Department of Biotechnology, Osaka University, Suita, Japan

Abstract - This paper focuses on the nematode *C. elegans*, which has a relatively simple structure, and is one of the most analyzed organisms among multicellular ones. We aim to develop a computer model of this organism to analyze control mechanisms with respect to its movements. First, a neuronal circuit model for directional control and a kinematic model of the muscle body are proposed. Then, by integrating the two models, we construct the whole body model of *C. elegans*. The effectiveness of the proposed model is verified through a series of computer simulations.

Keywords - *C. elegans*; directional control; steering circuit model; kinematic model; computer simulation

I. INTRODUCTION

Multicellular organisms have special and complex mechanisms to adapt to various conditions of their external environment. However, despite of recent progress of the experimental techniques in biology, even the simple nematode has never been fully clarified. In recent years, a new approach for analyzing functional mechanisms of living organisms, a computer simulation of a mathematical model, has been developed [1]. Using a computer model instead of the actual corresponding 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 the computer model, these model could be some help for the biological experiments. Also, using the model may make it possible to clarify some characteristics that cannot be measured in actual experiments.

Caenorhabditis elegans (a non-parasitic soil nematode) has a simple cylindrical body approximately 1.2 mm long that includes such fundamental organs as a nervous system, muscles, a pharynx, a hypodermis, an alimentary canal and genitals. The neuronal circuit of *C. elegans* processes various stimulations from the environment and controls forward and backward movements, rest, and search movements [2]-[5].

Because all the neuronal cells (neurons) of *C. elegans* have been identified and the connections have been approximately clarified [3], several computer models of the neuronal circuit of *C. elegans* have been proposed in recent years [6]-[8]. Much interest is centered on how *C. elegans* uses its muscles to perform and control various motions, and some body models of motor control have been proposed [9],[10]. The authors have also focused on the sinusoidal movement that is peculiar to *C. elegans*, and developed both kinematic and dynamic models of the muscle body [11],[12]. These models can express some patterns of two-dimensional movement. In addition, we modeled a neuronal

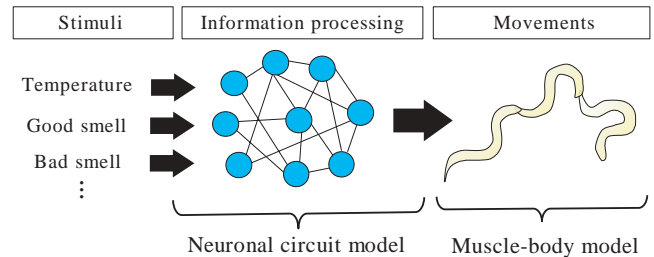


Fig. 1. Schematic diagram of the proposed model.

circuit for touch response and integrated it to the kinematic model of the muscle body. The model was able to simulate the motor control of responses to perceived touch stimulation [12].

In this paper, we propose a neuronal circuit model for directional control that realized movements such as turning in response to environment stimuli. Also, a three-dimensional kinematic model of the muscle body was constructed to realize the more complicated movements. As shown in Fig. 1, the proposed model consists of a neuronal circuit model, which processes stimuli and controls the muscles, and a muscle-body model, which executes movement. This paper is organized as follows: In Section II, the overview of *C. elegans* is explained. In Sections III and IV, a neuronal circuit model for direction control and a muscle-body model for movement are described in detail, respectively. In Section V, the behavior to environmental stimulation of the proposed model of *C. elegans* is verified through a series of computer simulations.

II. STRUCTURE AND MOVEMENT OF *C. ELEGANS*

The body is composed of 959 cells including the 302 neurons [2]-[5]. The body-wall consists of four quadrants of striated muscles enclosed by the hypodermis that execute forward, backward and turning movements. Each quadrant consists of two closely apposed rows of muscles, as shown in Fig. 2. The pharyngeal muscles are located in the anterior part of the body and assume a leading role in searching the environment, turning the body and opening and closing the mouth. The neurons are classified into three main groups by function: sensory neurons, interneurons and motoneurons [2]-[5]. The sensory neurons detect external stimuli, and then the interneurons process information from the stimuli. Finally, the motoneurons control the muscles on the basis of signals from the interneurons.

C. elegans exhibits various movements, such as going forward and backward, and stopping and turn, that are controlled by the neuronal circuits [2],[8]. For example, motoneurons DB(1-7) and VB(1-11) control contraction and relaxation of the body-wall muscles, and overall control

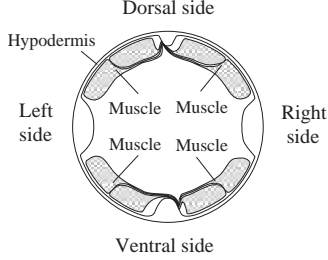


Fig. 2. Cross-section of the muscles.

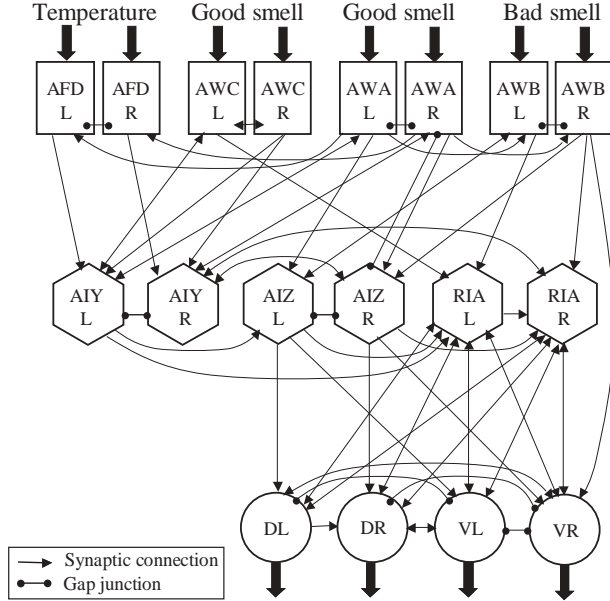


Fig. 3. A steering circuit model.

is performed by interneurons, AVB(L/R), in forward movement. DA(1-9), VA(1-12) and AVA(L/R) control backward movement [2]. Although the details of the neuronal circuit for directional control have not been clarified, Kawamura et al. identified the neurons that are likely concerned with directional control, and named the circuit that consists of these neurons “the steering circuit” [8].

C. elegans can respond to various kinds of environment stimuli. For example, *C. elegans* moves forward when it perceives a comfortable temperature or good smell, and turns when it perceives a bad smell. Although *C. elegans* also moves forward when it receives no stimulation, sometimes it stops or turns spontaneously.

In this paper, we focus especially on the steering circuit, and propose a model that controls the movement at the time a stimulus is received.

III. MODELING OF STEERING CIRCUIT

A. Steering circuit model

Only the neurons that are supposed according to the literature [8] to participate in the directional control were extracted from the neuronal circuit map of *C. elegans* published by J.G. White et al. in 1986 [3]. Although *C. elegans* has many sensory neurons, the neurons included in the

steering circuit are particularly those that sense temperature or smell.

This model aims to realize control of movements, such as forward movement and turning, stimulated by temperature and smell. The proposed steering circuit model of *C. elegans* for directional control is shown in Fig. 3. In the figure, eight sensory neurons are shown as rectangles, six interneurons as hexagons and four motoneurons as circles. AFD(L/R), which manage the sense of temperature, perceive comfortable temperatures. AWC(L/R) and AWA(L/R) perceive volatile attractants (good smells), although they perceive different kinds of chemical materials. The stimuli perceived by the six sensory neurons cause a positive response. To the contrary, AWB(L/R) perceives volatile repellents (bad smells), and these stimuli cause a negative response. The eight sensory neurons compose the amphid, which is the sense organ on the head tip, and play the main role in the perception of environment stimuli [4].

The 14 motoneurons of the pharynx, SMB(DL/DR/VL/VR), RMD(L/R), RMD(DL/DR/VL/VR) and SMD(DL/DR/VL/VR), are divided into four positional groups, DL, DR, VL and VR, for simplicity to confirm that the neuronal circuit model realizes directional control according to stimuli in this paper. On this occasion, multiple connections between two neurons are simply modeled as a single connection. These four motoneurons control the corresponding muscles that exist in the four directions, respectively.

B. Characteristics of neurons

The model supposes that the outputs of sensory neurons are not linear reactions to the strength of the stimulus, according to the general characteristics of neurons [15],[16], and they are expressed by the following nonlinear equation based on a neuron model [16].

$$O_n = \frac{c_n}{1 + \exp(-a_n(I_n - b_n))} \quad (1)$$

where a_n is an inclination with output function of sensory neuron n ($n \in \{AFD(L/R), AWC(L/R), AWA(L/R), AWB(L/R)\}$), b_n is the value of the stimulatory input at which the output of the neuron takes a central value, and c_n ($0 \leq c_n \leq 1$) is the output gain and is equivalent to the stimulation reception sensitivity. Therefore, O_n outputs the continuation value of $[0, 1]$, which is normalized by the maximum output from the actual neuron. The stimulation input I_n to a sensory neuron, n ($n \in \{AFD(L/R), AWC(L/R), AWA(L/R), AWB(L/R)\}$), is a stepless input of the range of $[0, 1]$, which quantifies the strength of the stimulation.

The characteristics of interneurons and motoneurons are also expressed by (1). The input I_n to the neuron, n ($n \in \{AIY(L/R), AIZ(L/R), RIA(L/R), DL, DR, VL, VR\}$), is the result of the multiplication of the connection weight by the output of the connected neuron i or m , and is calculated by the following equation.

$$I_n = \sum_i w_{i,n} O_i + \sum_m g_{m,n} O_m, \quad (2)$$

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 $g_{m,n} = g_{n,m}$).

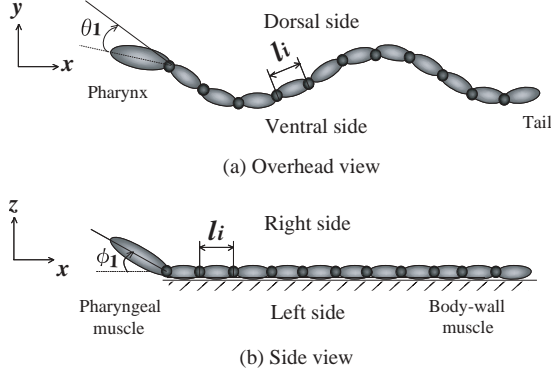


Fig. 4. The 12-link body model of *C. elegans*.

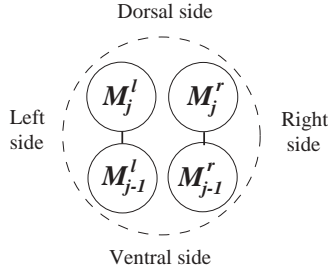


Fig. 5. Cross-section of the muscle model.

The muscle-body model of *C. elegans*, discussed in the next section, receives the outputs of motoneurons O_{DR} , O_{DL} , O_{VR} , and O_{VL} .

IV. MODELING OF MUSCLE BODY FOR MOVEMENT

A. Muscle-body model for movement

In this paper, the complete body of *C. elegans* is represented by a rigid 12-link model, which consists of 11 segments of body-wall muscles and one segment of pharyngeal muscle (Fig. 4). The relative angles, θ_i and ϕ_i , to the $(i+1)$ -th link of the i -th link ($i = 1, 2, \dots, 11$) are angles of the dorso-ventral and left-right directions of each joint, respectively ($-\pi \leq \theta_i, \phi_i \leq \pi$ [rad/sec]).

Four muscles shown in Fig. 2 are modeled at each joint as shown in Fig. 5. The internal states of the muscles on the dorsal and ventral sides on the left are denoted as M_j^l and M_{j-1}^l , and the internal states of the muscles on the right are M_j^r and M_{j-1}^r . Then, the i -th dorso-ventral joint angle, θ_i , is expressed by using the internal states of the muscles as follows:

$$\frac{d\theta_i}{dt} = \alpha_i \{ (M_j^l + M_j^r) - (M_{j-1}^l + M_{j-1}^r) \}, \quad (3)$$

where α_i is a positive constant ($-\pi \leq \alpha_i \leq \pi$ [rad/sec]), which is equivalent to the velocity gain for the i -th joint. The subscript, j and $j-1$, show the number of each muscle, the i -th muscle on the dorsal side is denoted by $j = 2i$ ($i = 1, 2, \dots, 11$), and the one on the ventral side by $j-1$. θ_i is decided by the difference between the sum of the dorsal internal states and one of the ventral. In the same

way, the i -th left-right joint angle, ϕ_i , is

$$\frac{d\phi_i}{dt} = \beta_i \{ (M_j^r + M_{j-1}^r) - (M_j^l + M_{j-1}^l) \}, \quad (4)$$

where β_i is a positive constant ($-\pi \leq \beta_i \leq \pi$ [rad/sec]) that is equivalent to the velocity gain. ϕ_i is decided by the difference between the sum of the right internal states and one of the left.

Because the internal state, M ($M \in \{M_j^l, M_j^r, M_{j-1}^l, M_{j-1}^r\}$), of the muscle is equivalent to the membrane potential, it is possible to express it as the sum of the direct current voltage ${}^D M$ corresponding to the bias component and the oscillating voltage ${}^A M$ corresponding to the frequency component. For example, the internal state of the j -th muscle on the right of the dorsal side, M_j^r , can be expressed as follows.

$$M_j^r = {}^D M_j^r + {}^A M_j^r \quad (5)$$

In this paper, the following assumptions are introduced.

A.1 Two pairs of components, ${}^A M_j^l$ and ${}^A M_{j-1}^l$, and ${}^A M_j^r$ and ${}^A M_{j-1}^r$, produce the oscillations with the same phase. In this paper, two pairs of components on the left and right sides oscillate identically at each joint.

$$\left. \begin{aligned} {}^A M_j^l &= {}^A M_j^r \\ {}^A M_{j-1}^l &= {}^A M_{j-1}^r \end{aligned} \right\} \quad (6)$$

A.2 The oscillation produced by each pair of components, ${}^A M$, is expressed by using Matsuoka's neuronal oscillator model [13]. For example, the frequency component, ${}^A M_j^r$, of the j -th muscle on the right of the dorsal side can be expressed as follows.

$$\frac{T_r}{\gamma} \frac{d {}^A M_j^r}{dt} + {}^A M_j^r = \sum_{n \neq j} v_{j,n}^r V_n^r - b_j^r f_j^r + \gamma s_j^r, \quad (7)$$

$$\frac{T_a}{\gamma} \frac{df_j^r}{dt} + f_j^r = V_j^r, \quad (8)$$

$$V_j^r = \begin{cases} {}^A M_j^r & ({}^A M_j^r \geq 0) \\ 0 & ({}^A M_j^r < 0), \end{cases} \quad (9)$$

where T_r and T_a are time constants; $v_{j,n}^r$ is the connection weight from the j -th oscillator to the n -th oscillator; b_j^r denotes a fatigue coefficient; f_j^r is the state of the oscillator; s_j^r is a tonic input from oscillators connecting with the j -th oscillator; and V_n^r is the output of the n -th oscillator. γ is a gain with respect to the time constants [12], and $\gamma = 1$ in Matsuoka's original model.

Under the above assumptions, (3) and (4) are respectively reduced to

$$\frac{d\theta_i}{dt} = \alpha_i \{ 4 {}^A M_j^l + ({}^D M_j^l + {}^D M_j^r) - ({}^D M_{j-1}^l + {}^D M_{j-1}^r) \}, \quad (10)$$

$$\frac{d\phi_i}{dt} = \beta_i \{ ({}^D M_j^r + {}^D M_{j-1}^r) - ({}^D M_j^l + {}^D M_{j-1}^l) \}, \quad (11)$$

where ${}^A M_j^l = -{}^A M_{j-1}^l$.

For example, if the following equality is true in (10), movement to the dorso-ventral direction is determined only

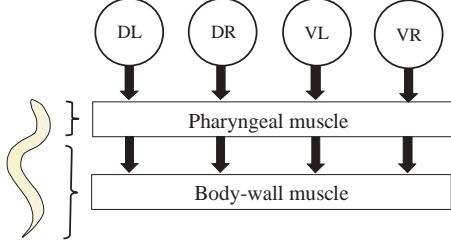


Fig. 6. Motor control by a steering circuit model.

by the frequency components, $^A M$, of the internal state of the muscle.

$${}^D M_j^l + {}^D M_j^r = {}^D M_{j-1}^l + {}^D M_{j-1}^r \quad (12)$$

Furthermore, from (11), the left-right joint angle, ϕ_1 , with respect to the pharyngeal movement is derived only by the bias components, ${}^D M$, of the internal states of muscles. If the right-hand side of (11) is positive, the pharynx lifts to the left. In this case, the dorso-ventral contraction and relaxation of the muscles are realized only by $^A M$ based on the neuronal oscillator model, and left-right contraction and relaxation only by ${}^D M$.

B. Integration of neuronal circuit model and muscle-body model

The steering circuit model described in Section III is connected to the muscle-body model in Section IV.

In this study, directional control of the muscle-body model in forward movement is realized by giving outputs of the steering circuit model to the muscle-body model as the bias components, ${}^D M_1^d$ and ${}^D M_2^d$ ($d \in \{l, r\}$). The relationship between outputs of motoneurons of the steering circuit model and the bias components of the muscle-body model is as follows:

$$\left. \begin{aligned} {}^D M_1^l &= O_{VL} \\ {}^D M_1^r &= O_{VR} \\ {}^D M_2^l &= O_{DL} \\ {}^D M_2^r &= O_{DR} \end{aligned} \right\} \quad (13)$$

The motoneurons of the pharynx and body-wall muscles are partially connected in the actual organism. As shown in Fig. 6, outputs of motoneurons of the pharynx are transmitted through the pharynx to body-wall muscles. Therefore, outputs of steering circuit model are given to the corresponding muscles as the bias component, ${}^D M_j^d$ and ${}^D M_{j-1}^d$ ($d \in \{l, r\}$; $j = 2i = 4, \dots, 22$), as well as those in the first joint. As mentioned in Section III, a sinusoidal wave of forward movement is realized in this model by adjusting the frequency component, $^A M$, based on Matsuoka's neuronal oscillator model [13].

Using the above system, directional control of the muscle-body model based on the outputs of the steering circuit model can be realized. In the next section, a computer simulation, which represents a series of stimulation responses by the integration model of *C. elegans*, is carried out.

TABLE I
DESIRED OUTPUTS OF MOTONEURONS FOR STIMULATION INPUTS TO SENSORY NEURONS.

	$u = 1$	$u = 2$	$u = 3$	$u = 4$	$u = 5$
$I_{AFD(L/R)}(u)$	1	0	0	0	0
$I_{AWC(L/R)}(u)$	0	1	0	0	0
$I_{AWA(L/R)}(u)$	0	0	1	0	0
$I_{AWB(L/R)}(u)$	0	0	0	1	0
$O_{DL}^*(u)$	0.1	0.1	0.1	0	0
$O_{DR}^*(u)$	0.1	0.1	0.1	0	0
$O_{VL}^*(u)$	0.1	0.1	0.1	0.1	0
$O_{VR}^*(u)$	0.1	0.1	0.1	0.1	0
movement	FD	FD	FD	TR	FD

V. COMPUTER SIMULATION

A. Simulation Settings

In this simulation, the coefficients for sensory neurons included in (1) are set as $a_n = 15$, $b_n = 0.6$ and $c_n = 1$, based on references giving data on the neuronal characteristics of higher organisms [14],[15]. Also, those for the interneurons and motoneurons are set as the same values except for $c_n = 0.1$ in motoneurons.

In the muscle-body model, the link lengths, l_i , are set to $l_1 = 0.2$, $l_2 = l_3 = \dots = l_{12} = 0.1$ [mm] to approximate the actual body length, which is about 1.2 [mm]. In the neuronal oscillators, the initial values of ${}^A M_k^d$ are all set to 1, $b_k^d = 18$, $f_k^d = 1$ and $s_k^d = 5$ ($d \in \{l, r\}$; $k = 1, 2, \dots, 22$), and the time constants are set to $T_r = 0.12$ [sec] and $T_a = 0.24$ [sec] by trial and error based on the literature such as [18]. Under the above setting, the differential equations included in (6), (7) and (8) are calculated every 1.0×10^{-3} [sec] by using the fourth-order Runge-Kutta method.

This simulation considers only whether each sensory neuron receives stimulation or not for simplicity, although the sensory neurons in this model can sense differences in stimulus strength. $I_n = 1$ when stimulation is given, and 0 when no stimulation is given. Also, since neurons AFDL and AFDR, AWCL and AWCR, AWAL and AWAR, and AWBL and AWBR are in the same class, they sense the same stimulation input at same time, respectively. In addition, some kinds of stimulation are not given at same time. Therefore, responses to five patterns of stimulation, i.e., four kinds of stimuli and non-stimulation are dealt with in this simulation. The desired outputs of four motoneurons, $O_n^*(u)$ ($n \in \{O_{DL}, O_{DR}, O_{VL}, O_{VR}\}$), for five patterns of stimulation inputs to eight sensory neurons, $I_n(u)$ ($n \in \{AFD(L/R), AWC(L/R), AWA(L/R), AWB(L/R)\}$; $u = 1, \dots, 5$), are shown in Table I. In the table, FD means forward movement, and TR turning.

As shown in the table, it is assumed that the body moves forward even when no stimulation is given ($u = 5$). Also, the body moves forward in response to stimulation when a suitable temperature or good smell is sensed ($u = 1, 2, 3$), and it turns when a bad smell is sensed ($u = 4$).

Although turns to the ventral and dorsal sides are possible, for simplicity it is assumed that a turn occurs always to the ventral side in this simulation. At each joint, the set value of bias components of the muscles for a turn is underspecified. It is assumed that motoneurons, DL and

