CHEMOTAXIS CONTROL BY LINEAR RECURRENT NETWORKS

Computational Neuroscience: Trends in Research: 373-377. Plenum Press (1998).

Thomas C. Ferrée and Shawn R. Lockery

Institute of Neuroscience
University of Oregon
Eugene, OR 97403

INTRODUCTION

The nematode *Caenorhabditis elegans* provides an excellent opportunity to study biological computation. This is mainly because it has a very simple neuromuscular system, consisting of only 302 neurons and 95 muscle cells. Anatomical studies have revealed the morphology of every neuron and the location of nearly every electrical and chemical synapse[1], and it has recently become possible to make electrophysiological recordings from identified neurons in *C. elegans*[2].

Among its behaviors is chemotaxis[3], the ability to orient up gradients of chemical attractants (Fig. 1a). Laser ablation experiments have identified which neurons are important for chemotaxis in *C. elegans*[4]. The chemotaxis control circuit appears to involve a small number of chemosensory neurons, interneurons and motor neurons, with feedforward and feedback connections among them. In this paper, we seek to understand how small networks of this type might control chemotaxis in a nematode-like body.

LINEAR MODEL OF THE NEMATODE *C. ELEGANS*

In a recent paper[5], we derived a simple model of the nematode body and chemotaxis control circuit. The body model was based on the observation that, during much of their movement on a flat surface, nematodes move forward at constant speed[6].

Thus

$$\frac{dx}{dt} = v \ \cos\theta \tag{1}$$

$$\frac{dy}{dt} = v \ \sin\theta \tag{2}$$

where v is the speed, and θ is the direction of movement. The rate of turning of the model nematode was determined by the degree of bend in the neck, which in turn was determined by the relative voltage of dorsal (D) and ventral (V) motor neurons. Thus

$$\frac{d\theta}{dt} = \gamma \ \left(V_{\mathrm{D}} - V_{\mathrm{V}}\right) \tag{3}$$

where γ is a constant parameter. In the present model, however, lateral movement of the head during ordinary, sinusoidal locomotion was ignored. This model focuses, therefore, on chemotaxis control strategies which can be characterized by movement of the body center-of-mass alone.

The model network included a single chemosensory neuron (V_1), three interneurons (V_2–V_4) and two motor neurons (V_{D} and V_{V}). Each neuron was connected to each other neuron. Electrophysiological experiments suggest that many *C. elegans* neurons are effectively isopotential, and do not fire classical, all-or-none action potentials[2]. Simultaneous recordings from pairs of neurons in *Ascaris suum*, a related species of nematode, suggest that nematode chemical synapses release neurotransmitter tonically, and that postsynaptic voltage is a sigmoidal function of presynaptic voltage at steady state[7]. We therefore modeled the voltage of each neuron as

$$\tau_i \frac{dV_i}{dt} = -V_i + \tanh\left(\sum_{j=1}^{N} w_{ij} \ (V_j - \overline{V}_j)\right) + \delta_{i1} C(t) \tag{4}$$

where w_{ij} represents the strength of the synaptic connection from cell j to cell i, and $\overline{V}_j$ represents the presynaptic voltage at which no transmitter is released. Since *C. elegans* is believed to sense the chemical concentration at only a single point in space[3], we took $C(t) \equiv C(x(t), y(t))$, the instantaneous chemical concentration at the tip of the nose. We then used simulated annealing to find sets of network parameters: τ_i, w_{ij} and $\overline{V}_j$, which produced chemotaxis in the model. Many such sets were found. Because the network model was nonlinear, however, the neural computations underlying chemotaxis control in the model remained elusive.

While the chemotaxis network in *C. elegans* is likely to be nonlinear, chemotaxis control by this network may be effectively linear. To demonstrate that small linear networks of graded-potential neurons are capable of controlling nematode-like chemotaxis, here we linearized the voltage dependence of (4). Because recordings from *Ascaris suum* suggest that nematode neurons tend to rest near the middle of their voltage-sensitive range for neurotransmitter release, this linearization was carried out about the voltage $\overline{V}_j$ for each neuron. The resulting linear network can be written in the form

$$\frac{dV_i}{dt} = \sum_{j=1}^{N} A_{ij} \ V_j + b_i + c_i(t) \tag{5}$$

where the matrix $A_{ij} = (-\delta_{ij} + w_{ij})/\tau_i$, the vector $b_i = -\sum_{j=1}^{N} w_{ij}\overline{V}_j/\tau_i$, and the time-dependent input vector $c_i(t) = \delta_{i1}C(t)/\tau_1$. We again used simulated annealing to find parameter sets which produced chemotaxis. Figure 1b shows the result of one such optimization, for one initial condition. Like the real nematode in Fig. 1a, the model nematode oriented almost directly up the gradient and dwelled at the peak. Similar chemotaxis behavior was observed for a variety of other initial conditions. Similar behavior was also observed for other linear networks obtained by this optimization procedure.

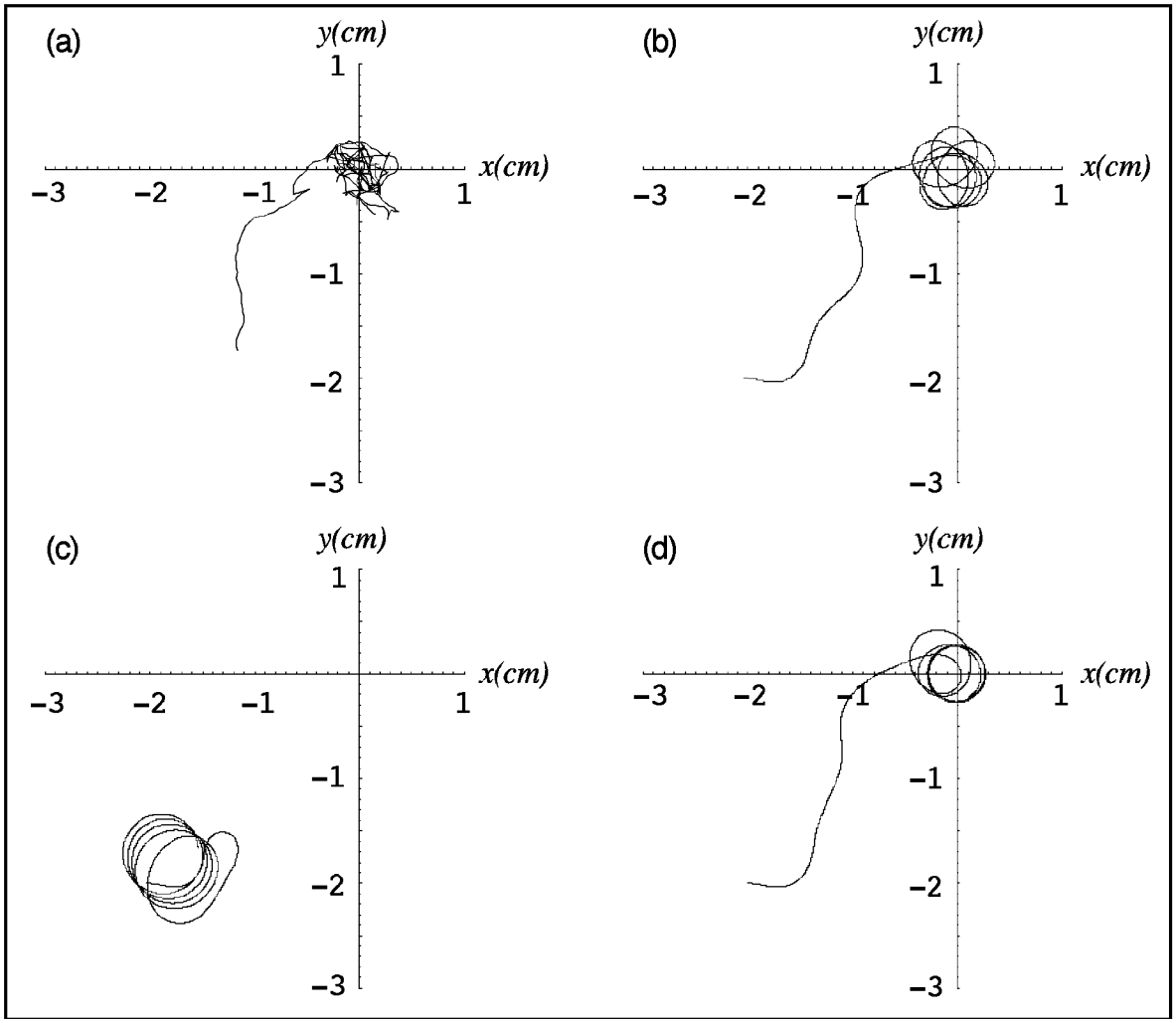

Figure 1: Nematodes chemotaxing in a Gaussian chemical gradient. (a) A real nematode[6]. (b) The model nematode controlled by the linear neural network (5). (c) The model nematode controlled by the computational rule (9), keeping terms only through $C(t)$. (d) Same as (c), but keeping terms through dC/dt.

COMPUTATIONAL RULES FOR CHEMOTAXIS

Because equations (5) are linear in voltage, they can be solved analytically. With

a convenient choice of initial conditions $V_i(t_0)$, the solution can be written in matrix form

$$\mathbf{V}(t) = -\mathbf{A}^{-1}\ \mathbf{b} + \int_{t_0}^{t} \mathbf{K}(t-t')\ \mathbf{c}(t')\ dt' \tag{6}$$

where the kernel $\mathbf{K}(t-t')$ is an $N \times N$ matrix involving the eigenvalues λ_i and eigenvectors of the matrix $\mathbf{A}$. Inserting (6) into (3) and using the fact that our model has only a single chemosensory neuron leads to

$$\frac{d\theta}{dt} = \Omega_{\text{bias}} + \int_{t_0}^{t} k(t-t')\ C(t')\ dt' \tag{7}$$

where Ω_{bias} is a constant turning bias, and the scalar kernel $k(t-t')$ is the impulse response of the turning rate to chemosensory input at the nose.

The second term in (7) indicates that, formally, the rate of turning at time t depends on the entire history of the stimulus $C(t')$. Previous studies of chemotaxis, however, have shown that many animals use time-derivatives of the stimulus to direct oriented movement[8]. We therefore sought an expansion of (7) in terms of the instantaneous stimulus $C(t)$ and its time-derivatives. Mathematically, this expansion can be justified as follows: The kernel $k(t-t')$ is a sum of exponentials of the form $\exp(\lambda_i(t-t'))$. For the system to be stable, i.e., for the voltages to remain finite at all times t, each eigenvalue λ_i must have negative real part. This condition is indeed satisfied by the network which produced Fig. 1b, and must be satisfied by any network optimized to control chemotaxis. Consequently, in practice the second term in (7) accumulates contributions from the stimulus $C(t')$ for times t' only in the *recent* past. We therefore expanded $C(t')$ in a Taylor series about the time t:

$$C(t') = C(t) + \frac{dC}{dt}(t'-t) + \ldots \tag{8}$$

Substituting (8) into (7) and regrouping terms gives

$$\frac{d\theta}{dt} = \Omega_{\text{bias}} + Z_0(t-t_0)C(t) + Z_1(t-t_0)\frac{dC}{dt} + \ldots \tag{9}$$

where the expansion coefficients are defined

$$Z_n(t-t_0) = \int_{t_0}^{t} k(t-t')\ (t'-t)^n\ dt' \tag{10}$$

Note that the functions $Z_n(t-t_0)$ do not depend on the stimulus, but are intrinsic to the network. Equation (9) constitutes a simple computational rule, which can be used in place of the network (5) to control chemotaxis in the model nematode.

To demonstrate that (9) controls chemotaxis effectively, we computed the expansion coefficients $Z_n(t-t_0)$ from the network parameters which generated Fig. 1b. Figure 1c shows the result of keeping only terms through $C(t)$. The initial transient behavior results from the explicit time dependence in $Z_0(t-t_0)$. This rule failed to produce chemotaxis, but instead led to circular movement whose center traveled along a line of equal concentration. Figure 1d shows the result of keeping all terms through dC/dt.

This rule led to oriented movement up the gradient and dwelling at the peak, much like the network behavior shown in Fig. 1b. Similar results were obtained for other initial positions and angles. This suggests that in order to control chemotaxis, the linear network computes the first time-derivative of the chemical stimulus.

DISCUSSION

We have shown that small networks of graded-potential neurons with linear voltage dependence are capable of controlling nematode-like chemotaxis. An expansion of the analytic solution in time derivatives of the stimulus led to simple, intuitive rules, which elucidate computations being performed implicitly by the network. The first time-derivative of the stimulus was shown to be necessary to control chemotaxis. These results have three interesting consequences. First, since the model network was linear, these results suggest that much of chemotaxis control in real nematodes may arise from linear computations only. Second, for a fully-connected recurrent network, each eigenvalue and eigenvector depends on *all* of the time constants τ_i and synaptic weights w_{ij}, and each voltage V_i depends on *all* of the eigenvalues and eigenvectors. Information processing in such a system is, in general, highly distributed. Third, since the analytic methods employed here made no assumption about the pattern of synaptic connectivity in the network, these results suggest that linear network models based more closely on the anatomical data are likely to evolve similar computational strategies for chemotaxis.

ACKNOWLEDGEMENTS

The authors thank C. I. Bargmann for providing unpublished data, and J. T. Pierce and T. M. Morse for helpful discussions. This work was supported by NIMH MH11373, NIMH MH51383, NSF IBN 9458102, ONR N00014-94-1-0642, the Sloan Foundation, and the Searle Scholars Program.

References

[1] White, J. G., E. Southgate, J. N. Thompson and S. Brenner (1986). The structure of the nervous system of *C. elegans*, *Phil. Trans. R. Soc. London* **314**:1-340.

[2] Goodman, M. B., D. H. Hall, L. Avery and S. R. Lockery (1998). Active currents regulate sensitivity and dynamic range in *C. elegans* neurons. Submitted to *Neuron.*

[3] Ward, S. (1973). Chemotaxis by the nematode *Caenorhabditis elegans*: Identification of attractants and analysis of the response by use of mutants. *Proc. Nat. Acad. Sci. USA* 70: 817-821.

[4] Bargmann, C. I., unpublished.

[5] Ferrée, T. C., B. A. Marcotte and S. R. Lockery (1997). Neural network models of chemotaxis in the nematode *Caenorhabditis elegans*. In: Mozer, M. C., M. I. Jordan and T. Petsche (Eds.) Advances in Neural Information Processing Systems 9. MIT Press. pp. 55-61.

[6] Pierce, J. T., and S. R. Lockery, unpublished.

[7] Davis, R. E., and A. O. W. Stretton (1989). Signaling properties of *Ascaris* motor neurons: Graded active responses, graded synaptic transmission, and tonic transmitter release, *J. Neurosci.* **9**:415-425.

[8] Dunn, G. A. (1990). Conceptual problems with kinesis and taxis. In: Armitage, J. P. and J. M. Lackie (Eds.) *Biology of the chemotactic response*. Cambridge University Press. pp. 1-13.