

SIMULATION AND ANALYSIS OF SEGMENTAL OSCILLATOR
MODELS FOR NEMATODE LOCOMOTION

by

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SUMMARY

We have applied a novel modeling and simulation methodology (Rockland, 1989; Rowley & Rockland, 1990) to analyze and test segmental oscillator models for nematode locomotion. Models of this type, based on anatomical and physiological studies of the motor nervous system of the nematode *Ascaris*, have been put forward (by Walrond & Stretton, 1985; Stretton *et al.* 1985) to account, as a first approximation, for propagation of the wave of muscle contraction-relaxation leading to locomotion. Our simulations, combined with mathematical analysis, yield a simple description of the possible model behaviors in terms of component oscillators with 1, 2 or 4 phases. Certain of these behaviors are suggestive of observed nematode behaviors, including "coiling" and "shrinking". An initial standing wave does not propagate; instead, it leads either to a coil or to a time-periodic (dorsal-ventral symmetric) pattern of muscle contraction-relaxation, depending on whether the synaptic connectivity of the model is based on physiological or anatomical data. Our results suggest that certain broad behavioral phenotypes do not depend on highly precise biological detail, but may instead be associated with "attractors" (e.g., fixed points, in the case of coiling) of simple dynamical models based on schematic biology. We conclude with a discussion of directions for further work on more elaborate models, suggested by our studies of such schematic models.

Page Heading: Simulation of segmental oscillators

Key Words: nematode, segmental oscillator, locomotion, simulation

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INTRODUCTION

The present study represents an initial step in a broader program of integrative modeling and analysis of the nervous systems of the nematodes *C. elegans* and *Ascaris* (Rockland, 1989). It is based on the application to the motor nervous system (more specifically to segmental oscillator models for the motor nervous system) of a novel modeling and simulation framework which we have begun to implement and develop (Rowley & Rockland, 1990). This framework is intended for the study of systems which exhibit the non-modularity (or multiple modularities) and heterogeneity characteristic of biological contexts.

The Motor Nervous System and Segmental Oscillator Models

Nematodes move by propagating a wave of muscle contraction-relaxation along the body. The pattern of innervation, with each motoneuron innervating either dorsal or ventral muscle, restricts the motion to the dorso-ventral plane. If the head and tail, with their associated neurons, are excised, thus removing peripheral neuronal input, the worm can still generate locomotory movements, although of a somewhat stereotyped form (Crofton, 1971). Thus, the remaining nervous system, approximately 90 motoneurons and interneurons out of a total 298 neurons, can control locomotion; this system (as reviewed in Stretton *et al.* 1985) is designated the motor nervous system.

The motoneurons in the motor nervous system consist of 7 classes, distinguished by their simple, characteristic morphologies. These are designated, primarily on the basis of physiological data, as DE1, DE2, DE3, the dorsal excitators; V-1, V-2, the ventral excitators; DI and VI, the dorsal and ventral inhibitors. The cell bodies all lie in the ventral nerve cord. The two ventral excitor classes have processes only in the ventral cord. The other classes have processes in both the ventral and dorsal nerve cords, linked by a lateral neuronal process, the commissure. The motoneurons are arranged anterior to posterior

along the body in periodic (though scaled) fashion as 5 "repeat units"; each consists of 11 neurons, namely 1 member from each of the DE2, DE3, and DI classes, and 2 members from each of the other classes. There is a characteristic pattern of synaptic connectivity, onto muscle and among pairs of motoneurons, both within and across the repeat units. In addition, five large interneurons and a somewhat larger number of small interneurons traverse all the repeat units, and synapse onto the dendrites of both the dorsal and ventral exciters, but not onto the inhibitors.

The segmental oscillator model (Fig. 1), both in its initial version put forward in (Walrond & Stretton, 1985), and in the subsequent version of (Stretton *et al.* 1985), is a provisional attempt to account for the mechanism of wave propagation. It is based on a schematic or summary of the anatomical and physiological data for *Ascaris*, representing the "lumped" synaptic connectivity of the motor nervous system. The schematic ignores neuronal geometry and details of connectivity, and lumps classes of neurons together; for example, all the interneurons are lumped into a single class IN, and all the dorsal excitor classes into a single class DE. The result is a linear chain of coupled units, each corresponding, more or less, to one of the anatomical repeat units, and each coupled to IN. In the tradition of central pattern generation schemata, both versions of the model propose that this chain functions as a chain of coupled oscillators driven by IN, thus providing the basic mechanism for wave propagation.

The two versions of the model in (Walrond & Stretton, 1985) and in (Stretton *et al.* 1985) differ in important respects. The former, or *anatomical version*, bases its connectivity on anatomical data, and thus incorporates excitatory synapses from DE to DI and from VE to VI. However, these synapses, while anatomically prominent, appear, based on physiological experiments, to be weak, and thus are not included in the alternative physiological version of the model. Instead, it was proposed in (Stretton *et al.* 1985) that a pattern-forming role is played by endogenous membrane-potential oscillations in DI and VI which are activated by depolarization.

Fig. 1
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In testing the behavior of a model it is necessary to know the underlying dynamics, i.e., the rules for time evolution of the model's state. However, in both versions of segmental oscillator model the dynamics, as opposed to structure, is not specified except schematically or implicitly. Thus, in our view, the segmental oscillator "model" is best regarded not as a model, but as a prototype for generating a succession of models; these models are to incorporate progressively more refined specifications of structure and dynamics, based on corresponding refinements in the underlying data.

Accordingly, we decided in our initial simulations to pair the anatomical and physiological structures with a simple choice of dynamics, to be subsequently refined. Our goals were to test whether wave propagation arises, and to determine the effects of anatomical vs. physiological connectivity. In view of the somewhat artificial dynamics, we were not surprised that waves do not propagate. On the contrary, we were surprised that the resulting model behaviors are sufficiently regular to admit of simple description and analysis, and that certain of these behaviors bear resemblance to actual nematode behaviors.

MATERIALS AND METHODS

For our studies of segmental oscillator models we applied a novel modeling and simulation framework, which we shall briefly describe here; more details may be found in (Rowley & Rockland, 1990). The framework is designed to deal with two characteristic features of biological systems: (1) Non-modularity or multiple modularities, i.e., the "overlap" of subsystems and components, resulting in an absence of clean system boundaries; (2) Heterogeneity, i.e., the fact that the appropriate mathematical format may vary from subsystem to subsystem, and indeed, that the same subsystem may require multiple formats, depending on context.

As in the case of the proposed segmental oscillator models, it is often necessary to test the behavior of the same structure under the action of multiple dynamics. To facilitate this process, our modeling framework maintains a separation of structure and dynamics,

via the introduction of two classes of modeling entity: *structures* and *models*. A *structure* consists of *parts* and *relations*, and may be recursive; i.e., parts may contain subparts. It may, but need not, correspond to an anatomical structure. A *model* associates state variables to the parts of the structure, and in addition imposes a set of mathematical relations among the state variables or their time histories. These relations in particular may assign dynamics, i.e., rules for the time-evolution of the state variables, to the structure; e.g., rules for interaction of the parts. The relations can take heterogeneous mathematical form. The same real "object" may be represented in multiple structures, each paired with multiple models. This allows examination of the same object from multiple aspects, as part of multiple functional subsystems, and at multiple levels of resolution or abstraction, as well as under the action of multiple hypothesized dynamics. It, in particular, permits the parallel examination of a specified motoneuron both as a branched neuronal structure with associated cable-theoretic dynamics, and as a lumped neuronal class within a segmental oscillator structure. The structures as well as the models may depend on parameters. This parametrization is intended to accommodate the variation inherent to biological systems, functional effects of structural perturbation, and time-varying structure, in particular structural modification induced by dynamics.

Our current computer implementation is written in Common Lisp (Steele, 1984) on Symbolics 3620 Lisp Machines (Symbolics, 1990) using CLOS (the Common Lisp Object System; Keene, 1989) for object-oriented programming. We make extensive use of the Symbolics Dynamic Windows system for graphical display of structures and their time evolution under model dynamics. The intuition into model behavior gained from these displays has been an invaluable foundation for our subsequent analysis.

We have studied three classes of structure: a basic structure, *segmental-oscillator* (Fig. 1), and two classes of compound structure, namely *segmental-linear-oscillator* (also shown in Fig. 1), formed by nearest-neighbor coupling of a sequence of segmental-oscillators, and *segmental-ring-oscillator* (Fig. 2), formed by coupling the two extreme

segments of a segmental-linear-oscillator. Both the basic structure and the associated compound structures exist in two variants, namely *anatomical*, resp. *physiological connectivity*; the coupling between nearest neighbors in the compound structures has been chosen of the same type (anatomical or physiological) as within the component segments. Although not necessarily indicated in our diagrams, IN makes synaptic contact with the DE and VE classes in each component segment. While the actual organism has 5 repeat units, we have considered compound oscillators of arbitrary length n , in order to test the resulting quantitative or qualitative effects. The purpose of the ring-oscillators is to test the effect of periodic boundary conditions, in particular to determine which behavior of linear-oscillators is due to edge effects, i.e., absence of anterior or posterior neighbors for the extreme segments.

Fig. 2
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Each class of structure, in both of its variants, was paired with three simple classes of model: *counting-model*, *probabilistic-counting-model*, and *probabilistic-interneuron-model*. As a basis for analysis of model behavior we simulated time evolution under the associated dynamics, starting from various initial states. We were primarily interested in a standing wave initial state, with adjacent segments alternating between dorsal or ventral muscle contraction (Fig. 1); our aim was to see whether such a wave would propagate along the structure, under the rules for time evolution specified by the given dynamics. We, in addition, considered more general initial states, both to determine the full range of model behavior, as well as to test the sensitivity of behavior to initial state.

The three classes of models considered are discrete: they assign discrete states to the structures, and their associated dynamics evolves in discrete time steps. More specifically, in these models each motoneuron class or muscle block has two possible states: 1 or 0 (on or off; resp., contracted or relaxed), and each synapse has "weight" 1 or -1 (excitatory or inhibitory). (Actually, our models allow the synaptic weights to be any real number. Positive weights are excitatory; negative weights are inhibitory; 0 weight

means that the synapse is inactive. We have not yet explored this additional degree of freedom in our models.)

Counting-model is deterministic. The next state of each element (neuron or muscle) is determined as follows from the current state of the oscillator structure: First, one computes the sum of the current states of all the neurons which synapse onto the element, weighted according to the signs (excitatory = 1, inhibitory = -1) of the corresponding synapses. The next state assigned to the element is 1 or 0, depending on whether or not this sum is ≥ 1 , a threshold value. (As with the synaptic weights, the threshold is actually a continuous parameter.) In this model, IN is taken to be always on (tonic interneuron excitation of DE and VE); if IN were turned off (equivalently, disconnected from the structure), the entire structure would turn off (and remain off), after 2 time steps.

The other two models modify *counting-model* dynamics by introducing stochastic elements; this is done in order to explore effects of perturbation and variation due, for example, to the more detailed biology not directly included in the segmental-oscillator "picture". *Probabilistic-interneuron-model* incorporates one continuous parameter, a probability that IN fails to excite DE or VE. *Probabilistic-counting-model* incorporates two parameters: a probability for below-threshold firing, and a probability for failure to fire when above threshold. Our detailed results thus far, to be described below, deal exclusively with *counting-model*. This is due to the fact that the behavior associated to this model is sufficiently regular so that direct visual inspection of simulation displays provides a sufficient basis for analysis. Analysis of the stochastic models will require a more elaborate facility for the computerized storage, analysis, and comparison of simulation runs, which we are in the process of constructing. Nevertheless, such visual inspection of simulation runs for the stochastic dynamics has been adequate to suggest to us directions for further research regarding the "quantitative" characterization of behaviors, to be discussed below. In addition, we have used the stochastic models to "randomize" the state of the segmental-oscillator structures. More precisely, starting from a particular initial

state, we have let the structure evolve for a number of time steps under the stochastic dynamics; the resulting state has then been taken as the initial state for evolution under *counting-model*.

The "true" dynamics for the segmental-oscillator structures should be, in some sense, the projection onto a simpler space of states of the dynamics associated with the underlying network of branched neurons in the motor nervous system. In view of the predominantly passive, graded character of neuronal interactions in the motor nervous system (Stretton *et al.* 1985), our decision to begin our study of segmental-oscillators with discrete models incorporating thresholds, as above, may thus appear puzzling. However, one of our aims has been to determine how refined a model must be, i.e., how much biological detail it must incorporate, in order to approximate to a given degree the actual behavior of the organism; we believe that this purpose is best served by a process of progressive model refinement. For example, we wished to see whether the physiological version of the segmental-oscillator structure would yield (as is, in fact, the case) some form of coupled oscillator mechanism under *counting-model* dynamics, despite the fact that this model does not incorporate the known membrane-potential oscillations in DI and VI. We should point out that, for the most part, the results that follow were first observed in "numerical experiments". The resulting intuition enabled us in certain cases to find an underlying mathematical explanation.

RESULTS

We shall begin by introducing some terminology, followed by a summary of the salient points regarding behavior of the segmental-oscillator structures under counting-model dynamics:

Terminology:

The *state* of a structure is specified by the states (on or off; contracted or relaxed) of the constituent neuron classes or muscle blocks. For example (ignoring muscle) segmental-oscillator (single segment) has $2^4=16$ possible states, corresponding to the possible on-off combinations of DE, VE, DI, and VI. By an *orbit* of the dynamics we refer to a temporal sequence of successive states. As we explain below, for the dynamics we are considering every state either lies on a periodic (i.e., temporally repeating) orbit, or eventually reaches a periodic orbit. For example, a 4-state periodic orbit consists of a cycle of 4 successive states s_1, s_2, s_3, s_4 which repeats *ad infinitum*, i.e., a 4-phase oscillator. A *fixed point*, i.e., a state which does not change under the time evolution, can be regarded as a 1-state (or period-1) orbit. The periodic orbits of the dynamics correspond to the stable behaviors of the model. An orbit is sometimes referred to as an *attractor*, to indicate that states not initially on the orbit may (after a finite number of time steps) reach, and thereafter stay on, the orbit; i.e., the orbit is stable with respect to small perturbations. The attractor is called *universal* if *every* state eventually reaches and stays on it.

Summary of results:

- (1) The standing wave of alternating dorsal-ventral muscle contraction fails to propagate. This holds for both the segmental-linear-oscillator and the segmental-ring-oscillator, in both the anatomical and physiological versions.
- (2) The segmental-oscillator (single segment) structure does, in fact, oscillate, but with fundamental differences in behavior between the anatomical and

physiological versions. In the anatomical case there is a universal 4-phase attractor which is reached from any initial state; in particular, information about initial state is lost. In the physiological case, on the contrary, every state is either a fixed point of the dynamics, or returns to itself after 2 or 4 time steps (i.e., constitutes one phase of a 1-, 2-, or 4-phase oscillator).

- (3) The behaviors of the segmental-linear-oscillator and segmental-ring-oscillator can be described in terms of coupling of the phases (and of the types) of oscillations associated with the component segmental-oscillator structures. Certain of these behaviors, such as "coiling" or "shrinking", are suggestive of observed nematode behaviors. Time period 4 plays a ubiquitous role in the resulting stable behavioral patterns and in their development.
- (4) For the segmental-linear-oscillator the length n has a quantitative but not qualitative effect on behavior. Edge effects, due to the special position of rostral and caudal segments, do arise.
- (5) The segmental-ring-oscillator introduces qualitatively novel behavior. In particular, in the physiological version inhomogeneities in initial state (introduced, for example, by choosing n odd) can lead to rotating patterns.

We pass next to the detailed results. We note that, under the dynamics considered, muscle state is a passive follower of motoneuron state and may, hence, be disregarded for purposes of analysis. Also, since the dynamics is first-order (i.e., next state depends on present state but not on past history), a return to an initial state after a finite number of time steps implies that the state lies on a periodic orbit. Even if a given initial state does not return to itself, some other state on its orbit must return to itself (since the total number of states is finite); thus, in any case, a periodic orbit is eventually reached. For the physiological versions of the oscillator structures a mathematical analysis is possible, due to a "hidden" linearity in the apparently nonlinear dynamics.

Segmental-oscillator

There are $2^4=16$ possible states, corresponding to the possible on-off combinations of DE, VE, DI, and VI. Thus each state may be represented by a 4-vector (DE, VE, DI, VI), where the symbols denote the binary values of the designated neuronal classes.

In the anatomical version, any initial state within 2 time steps reaches some state on the universal period-4 (4-phase) attractor (shown in Fig. 3A), and thereafter remains on this orbit; i.e., the subsequent time evolution involves only these 4 states.

In the physiological version, on the contrary, each state lies on a periodic orbit; i.e., the state space breaks up into a union of periodic orbits: 2 fixed points (orbits of period 1), 1 orbit of period 2, and 3 orbits of period 4 (thus accounting for all the states: $2 \times 1 + 1 \times 2 + 3 \times 4 = 16$), one of which is identical with the period-4 attractor of the anatomical version. (These orbits are shown in Fig. 3, together with the associated muscle innervation patterns.) There is a dorsal-ventral symmetry to the set of orbits: either an orbit is itself dorsal-ventral symmetric or its mirror image is also an orbit. This break-up of the state space into orbits stems from the following observations. For the physiological, but not the anatomical version, the state-transition operator T (which expresses how the next-state vector (DE', VE', DI', VI') is determined from the current-state vector (DE, VE, DI, VI)) is linear; more precisely, if the values 1, -1 rather than 1,0 are used to represent the binary states of individual neurons, then state-transition is computed via multiplication by

the 4x4 matrix

$$T = \begin{bmatrix} 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & -1 \\ 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 \end{bmatrix}$$

Consequently $T^4=I$, the 4x4 identity matrix; whence, for any state \vec{v} , $T^4 \vec{v} = \vec{v}$ (and, in some cases, one of the sharper statements $T^2 \vec{v} = \vec{v}$, or $T \vec{v} = \vec{v}$ holds). Thus, one returns to any initial state after 1, 2, or 4 time steps.

Fig. 3
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Segmental-linear-oscillator: anatomical version

A standing wave initial state, with successive segments alternating between dorsal and ventral muscle contraction evolves as follows (Fig. 4). Independent of the length of the segmental-linear-oscillator, after 2 time steps the state of each component segment lies on, and thenceforth (with the exception of the second segment) evolves according to the universal 4-phase attractor for a single segmental-oscillator. All the segments beyond the second are in phase, and lead by 1 the phase of the first (rostral) segment. Unless the linear-oscillator has exactly two segments, the second segment is "frustrated", in that it cannot be in phase both with its anterior and posterior neighbors; it adjusts by keeping in phase with the rostral segment for 1 time step, and with the caudal segments for 3 time steps. It does so by substituting for the second phase of the 4-phase attractor a second copy of the initial phase. Thus, starting from a standing wave, the resulting behavior of the segmental-linear-oscillator, after 2 time steps, is periodic of period 4, with dorsal-ventral muscle symmetry (i.e., simultaneous contraction or relaxation), with all the posterior segments (except the second) in phase, and leading the lead segment by 1 time step. The phase "frustration" at the second segment is reminiscent of the phenomenon of frequency "plateauing" of coupled oscillators (Winfree, 1980).

Fig. 4
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In the simulations we have run starting from other initial states, the system has evolved, after a small number of time steps, into periodic (period-4) behavior as above, but with all the segments in phase; i.e., the chain consists of multiple in phase copies of the universal period-4 attractor. The resulting muscle-excitation pattern is: all muscle (both dorsal and ventral) contracted for 1 time step and relaxed for 3 time steps, a kind of "shrinking" behavior. Based on these results, we anticipate that starting from arbitrary initial states the system will eventually settle into period-4 behavior as above, with regions of identical phase separated by individual "frustrated" segments; conceivably, there may be restrictions on the possible number and locations of the frustrated segments.

Segmental-linear-oscillator: physiological version

A standing wave initial state here gives rise to a different behavior pattern than it does for the anatomical version. The state of the initial, rostral, segment stays unchanged throughout the time evolution. After 2 time steps all the remaining segments are in an identical state, with all neurons (and muscle) off (resp., relaxed), i.e., the "first" phase of the universal (anatomical version) 4-phase attractor (Fig. 5). After 2 more time steps the second segment reaches, and thereafter remains in, the same state as the initial segment; during the interval from time 2 to time 6 the remaining $n-2$ posterior segments run, in phase, through the successive phases of the period-4 attractor, and thus have returned to the initial phase. This process continues, with an additional successive segment reaching the state of the leading segments after each 4 time steps. That is, a "kink" progresses from left to right until all the segments are in the same state as the initial segment. Thereafter, the resulting pattern (a "coil", with all the muscle contracted on one side and relaxed on the other) remains unchanged, a fixed point of the dynamics.

Fig. 5
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Arbitrary initial states give rise to analogous forms of behavior. This was suggested to us by observing simulations starting from selected initial states, and subsequently verified mathematically for the general case. As in the physiological version of the single segmental-oscillator, analysis of this behavior is facilitated by an underlying linearity. We begin with a description of the behavior, followed by the mathematical verification. Starting from an arbitrary initial state, the leading (rostral) segment evolves in time exactly as in the case of a single segmental-oscillator, and is totally independent of the remaining segments; that is, it evolves on one of the 1-, 2-, or 4-phase periodic orbits described above. After 4 more time steps the state of the second segment is exactly the same as that of the first; i.e., it is on the same periodic orbit as, and in phase with, the initial segment. After every 4 time steps the next remaining segment is on this orbit, and in phase with the initial segments. Eventually, all the segments are on the same orbit as, and in phase with, the lead segment. Thus, for the physiological version of the segmental-linear-oscillator, the

resulting stable behavior is that all oscillators are in the same orbit as the rostral one. That is, we can characterize the asymptotic behavior of the entire sequence of oscillators by the orbit of a single oscillator. Depending on the initial state of the rostral oscillator, there are 5 asymptotic behaviors:

- All oscillators go into a fixed point: a dorsal or ventral "coil", as in Figure 3B, top.
- All oscillators go into an orbit of period 2: all muscle relaxed throughout, as in Figure 3B, middle.
- All oscillators go into an orbit of period 4:
 - A periodic dorsal "coil," as in Figure 3B, bottom.
 - A periodic ventral "coil," as in the mirror image of Figure 3B, bottom.
 - A periodic "shrinker," as in Figure 3A. This is the same "shrinking" behavior as observed in the anatomical case.

The mathematical verification is as follows: First, there is no synaptic input from any segment to its anterior neighbor; hence, the initial segment (more generally, initial group of segments) behaves independently of posterior segments. Second (and this is the crux of the matter), for the segmental-linear-oscillator of length 2, starting from any initial state, the second segment, after at most 4 time steps, reaches and thereafter maintains the same state as the initial segment, i.e., the difference between the states vanishes. This leads us to suspect we should reformulate the problem in terms of *differences* of states of adjacent oscillators. When we do so, we discover two things:

- The time evolution of the difference of states depends only on the current value of that difference, and not the individual values.
- Moreover, the time evolution, while nonlinear, has its nonlinearity circumscribed within a linear framework. The existence of such a linear framework is reminiscent of the linearity of the state transition operator T for a single oscillator, discussed above.

The nonlinearity is described by a function Γ from the set of possible state differences, $\{-2, 0, 2\}$, to itself: $\Gamma(-2)=2$; $\Gamma(0)=0$; $\Gamma(2)=0$, i.e., the quadratic polynomial $\Gamma(x) = 1/4 x (x-2)$. Γ satisfies the identity $\Gamma \circ \Gamma = 0$, where \circ denotes function composition. Then the time evolution operator for differences, which we denote S , may be written in terms of Γ :

$$S = \begin{bmatrix} 0 & \Gamma & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & \Gamma \\ 1 & 0 & 0 & 0 \end{bmatrix}$$

It follows that

$$S^4 = \begin{bmatrix} \Gamma \circ \Gamma & 0 & 0 & 0 \\ 0 & \Gamma \circ \Gamma & 0 & 0 \\ 0 & 0 & \Gamma \circ \Gamma & 0 \\ 0 & 0 & 0 & \Gamma \circ \Gamma \end{bmatrix}$$

but this is the zero matrix, because $\Gamma \circ \Gamma = 0$. Thus $S^4 = 0$. That is, the difference between the states of adjacent oscillators must disappear within 4 time steps, just as T takes the state of a single oscillator back to itself in 4 time steps. The result for the linear-oscillator of length n then follows by iteration.

Segmental-ring-oscillator: anatomical version

The behavior here seems even more rigid than for the linear-oscillator. Independent of the initial states that we have tested, the system has evolved after a small number of time steps into period-4 behavior, with each segment evolving according to the universal period-4 attractor, and with all the segments in phase. In particular, unlike the linear-oscillator case, in phase behavior occurs even starting from the standing wave initial state of

alternating dorsal-ventral muscle contraction. We expect that such in phase behavior always results, regardless of initial state.

Segmental-ring-oscillator: physiological version

We begin with the case of an even number of segments n . If we take as initial state the standing wave of alternating dorsal-ventral muscle contraction (i.e., with successive individual segments alternating between the 2 fixed-point states), then after 2 time steps each segment reaches, and remains on, the universal period-4 attractor (of the anatomical segmental-oscillator), with all the segments in phase, i.e., the system evolves into the same period-4 behavior as the anatomical version. This behavior is quite different from that of the (physiological) linear-oscillator, discussed above, which is entrained to follow the behavior of the rostral segment. Instead, we have the following phenomenon: a ring of segments which individually, when uncoupled, are in equilibrium (i.e., at fixed-points), switches when the segments are coupled, to oscillatory behavior (of period 4). This is a particularly simple analogue of the corresponding phenomenon for reaction-diffusion systems (Turing, 1952).

We have found that starting from less homogeneous initial states, the system gives rise to counterclockwise (corresponding to anterior-to-posterior) rotation. More precisely, it reaches a sequence of 4 states each of which thereafter recurs periodically, but rotated 1 unit counterclockwise after every 4 time steps.

Such rotation arises also in the case of n odd (Fig. 2).. In fact, for odd n the standing wave initial state has an "inhomogeneity"; it is impossible for each pair of adjacent segments to be out of phase. Starting from this initial state, after 2 time steps the "rostral" segment (i.e., the unique segment in phase with its clockwise neighbor) is in its original configuration, and all the remaining segments are completely turned off. Thereafter, after every 4 time steps this configuration has rotated 1 unit counterclockwise. It is instructive to compare this behavior with that of the linear-oscillator (Fig. 5). We have not attempted to

carry out a mathematical analysis for the ring-oscillator akin to that for the (physiological) linear-oscillator, although we expect that this could be done.

DISCUSSION

In modeling neuronal control of behavior, a basic problem is to isolate the essential features of the underlying biology; i.e., how much detail must a model include in order to yield approximations (of a given degree) to particular behaviors of the organism? Segmental-oscillator models incorporate highly schematic representations of the anatomy and physiology of the *Ascaris* motor nervous system. In the studies described above, we sought to determine whether this class of models is adequate to provide a mechanism for propagation of the locomotory wave of muscle contraction-relaxation. Accordingly, we tested the behavior of two extreme variants of such models (the *anatomical*, resp. *physiological* versions) under a simple form of dynamics (*counting-model*). The physiological version yields a wider range of behaviors than the anatomical version, which is rather rigid; one of the behaviors ("shrinking"), though not its time-course of onset, is common to both versions. In neither case is an initial standing-wave pattern propagated along the body.

"Worm-like" behaviors

While these models do not yield wave-propagation, they do admit of an underlying coupled-oscillator description. Moreover they exhibit other behaviors reminiscent of normal nematode behavior. For example, "shrinking" is suggestive of the body shortening movements associated with feeding and defecation (Crofton, 1971). "Coiling" is reminiscent of the "omega-wave" described in (Croll, 1975) and, alternatively, of the "deep ventral bend that usually accompanies the transition from backward to forward motion" in *C. elegans* (White *et al.* 1976); Crofton (1971) refers to "long-maintained, more or less extensive, unilateral contractions in the ventral side" which may occur anywhere, but especially in the tail. Abnormal "coiling" and "shrinking" phenotypes are commonly observed in a wide variety of *unc* (uncoordinated locomotion) mutant strains (Wood, 1988, Appendix). We are not suggesting that our segmental-oscillator models can, in and of

themselves, "explain" either wild-type behavior or that of any particular mutant strain; in particular, these models are not sufficiently detailed to be linked to specific anatomical or physiological deficits. Rather, we are suggesting that certain broad behavioral phenotypes may not depend on highly precise biological detail; instead they may be associated with attractors (e.g., fixed points, in the case of "coiling") of simple dynamical models based on schematic biology.

The problem remains of how to account for wave propagation on the basis of motor nervous system biology. Three approaches suggest themselves: 1) Variants of segmental-oscillator models. 2) Models incorporating more refined biology. 3) Alternative schematic models.

Variants of segmental-oscillator models

Our negative results thus far on wave propagation have been derived for only two classes of segmental-oscillator structure (anatomical and physiological), paired with one class of model dynamics (counting-model). We intend to explore the behavior resulting from other choices of structures or models, still essentially of segmental-oscillator type (and level of resolution). We have in mind modifications which incorporate such additional features as: time delays (resulting from signal propagation or from synaptic mechanisms); membrane-potential oscillations in VI and DI motoneuron classes; different choices of synaptic weights (in particular, interpolation between the extreme anatomical and physiological weightings); modified connectivity patterns, including non-nearest neighbor coupling of individual segments; continuous vs. discrete dynamics; different patterns of "forcing" by IN; "electrotonic" coupling of muscle in adjacent segments.

More refined biological models

Here we refer to the introduction of structures and associated models which are based on progressively less schematic representations of biological information. For

example, the next "level" of structures to examine might be networks of individual neurons rather than lumped neuronal classes. The neurons would be represented with branched morphologies, and forming synapses, *en passant*, along their processes. The associated models would be based on cable-theoretic dynamics, together with more-or-less schematized representations of the membrane-potential oscillations in the VI and DI motoneurons. (Data to support such models are available; published data include Davis & Stretton, 1989a and 1989b, and Angstadt & Stretton, 1989.) It is possible that this, or some additional level of biological refinement may be necessary to account for wave propagation; i.e., while some form of segmental-oscillator model may be "consistent with" wave propagation, it may be too crude, in and of itself, to actually account for the propagation (let alone for such additional properties as bidirectionality or multiple speeds of propagation).

Alternative schematic models

Conceivably, the segmental-oscillator "picture" is fundamentally in error; even if not, some other form of schematic picture may be able to account for (or, at least, be consistent with) wave propagation. A natural source of alternative schematic models is the motor nervous system of *C. elegans*. Indeed, while the nervous systems of the two species are in many respects homologous, they exhibit ostensible differences in synaptic connectivity; for example, the DI → DE and VI → VE synapses, which appear in both the anatomical and the physiological versions of the segmental-oscillator model are not reported for *C. elegans* (White *et al.* 1986). A schematic for *C. elegans*, distinguishing motoneuron and interneuron classes believed to be associated with forward, resp. backward wave propagation, is presented in (Wood, 1988, Chapter 11).

"Quantitative" characterization and comparison of behaviors

As a basis for comparing models with each other and with experimentally observed behavior, it is desirable, where possible, to characterize "quantitatively" various facets of locomotory behavior. Such characterization is simplest in the case of "steady-state" behaviors (such as propagation of a traveling waveform). Indeed, the extreme difficulty in "quantitatively" characterizing the behavior of biological systems is due in no small measure to the inherent variability and nonstationarity of the associated dynamics; i.e., this dynamics is not primarily steady-state, but consists of patterns of transitions between several quasi-steady state "behaviors". Such nonstationarity comes clearly to the fore in our simulations of segmental-oscillator structures under our two classes of stochastic models. As noted above, these stochastic modifications (or perturbations) of the deterministic model were introduced to incorporate the effects of unmodeled dynamics (i.e., the effects of the "rest" of the organism) on the segmental-oscillator behavior. The resulting behavior patterns (when the continuous model parameters were chosen small, so as to remain close to the deterministic counting-model) were suggestive of a sequence of transitions among several behaviors, each of which was "close" to one of the steady-state behavior patterns of the deterministic model. This suggests one potentially instructive way to quantitatively describe (and compare) non-trivial classes of behaviors: namely, seek to represent the behavior as perturbations to an underlying (family of) deterministic model(s), and then describe the behavior in terms of the global (steady-state) attractors of the latter. The relevant quantitative measures include the amount of time the perturbed system spends near any attractor, the "allowed" sequences of transitions (or transition probabilities) between attractors, and the time between transitions. Two such behaviors would then be regarded as "equivalent" if their corresponding quantitative measures are (roughly) equal. One can then ask which choices of parameter values in the perturbed models lead to equivalent behaviors; conversely, parameter values leading to inequivalent behaviors may provide the organism with control mechanisms for switching between different behavior

patterns. Analogous considerations arise in the comparison and correlation of behaviors of more refined models (such as networks of branched neurons) with those of more schematic or abstract models (such as segmental-oscillator models). Related viewpoints are discussed in (Schöner & Kelso, 1988).

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REFERENCES

- Angstadt, J.D. & Stretton, A.O.W. (1989). Slow active potentials in ventral inhibitory motor neurons of the nematode *Ascaris*. *J. comp. Physiol. A* 166, 165-177.
- Crofton, H.D. (1971). Form, function, and behavior. In *Plant Parasitic Nematodes*, vol. III. (ed. B.M. Zuckerman, W.F. Mai & R.A. Rhode), pp. 83-113. New York: Academic Press.
- Croll, N.A. (1975). Components and patterns in the behavior of the nematode *Caenorhabditis elegans*. *J. Zool.* 176, 159-176.
- Davis, R.E. & Stretton, A.O.W. (1989a) Passive membrane properties of motoneurons and their role in long distance signaling in the nematode *Ascaris*. *J. Neurosci.* 9, 403-414.
- Davis, R.E. & Stretton, A.O.W. (1989b) Signaling properties of *Ascaris* motoneurons: Graded active responses, graded synaptic transmission, and tonic transmitter release. *J. Neurosci.* 9, 415-425.
- Keene, S.E. (1989). *Object -Oriented Programming in Common Lisp: A Programmer's Guide to CLOS*. Cambridge, MA: Symbolics Press.
- Rockland, C. (1989). *The Nematode as a Model Complex System: A Program of Research*. Laboratory for Information and Decision Systems, Working Paper WP-1865, Cambridge, MA

- Rowley, S. & Rockland, C. (1990). The design of simulation languages for systems with multiple modularities. (submitted to Simulation)
- Schöner, G. & Kelso, J.A.S. (1988). Dynamic pattern generation in behavioral and neural systems. *Science* 239, 1513-1520.
- Steele, G.L. (1984). *Common Lisp: The Language*. Digital Press.
- Stretton, A.O.W., Davis, R.E., Angstadt, J.D., Donmoyer, J.E. & Johnson, C.D. (1985). Neural control of behavior in *Ascaris*. *Trends Neurosci.* 8, 294-300.
- Symbolics (1990). *Genera 8.0 Reference Documentation*. Cambridge, MA: Symbolics Press.
- Turing, A.M. (1952). The chemical basis of morphogenesis. *Phil. Trans. R. Soc. Lond. B.* 237, 37-72.
- Walrond, J.P. & Stretton, A.O.W. (1985). Excitatory and inhibitory activity in the dorsal musculature of the nematode *Ascaris* evoked by single dorsal excitatory motoneurons. *J. Neurosci.* 5, 16-22.
- White, J.G., Southgate, E., Thomson, J.N. & Brenner, S. (1976). The structure of the ventral nerve cord of *Caenorhabditis elegans*. *Phil. Trans. R. Soc. Lond. B.* 275, 327-348.

White, J.G., Southgate, E., Thomson, J.N. & Brenner, S. (1986). The structure of the nervous system of *Caenorhabditis elegans*. Phil. Trans. R. Soc. Lond. B. 314, 1-340.

Winfree, A.T. (1980). The Geometry of Biological Time. New York: Springer-Verlag.

Wood, W.B. (1988). The Nematode *Caenorhabditis Elegans*. New York: Cold Spring Harbor Library.

FIGURE LEGENDS

Figure 1. (A) Anatomical version of segmental-oscillator (following Walrond & Stretton, 1985). Excitatory synapses are shown as open, and inhibitory synapses as filled.

(B) Physiological version of segmental-oscillator (following Stretton *et al.* 1985). This differs from the anatomical version by omitting the (excitatory) DE \rightarrow DI and VE \rightarrow VI synapses.

(C) Segmental-linear-oscillator, anatomical version, formed by connecting a chain of segmental-oscillators. The pattern of synapses is the same between adjacent segments as within an individual segment. Muscle blocks in adjacent segments are not coupled. (The physiological version, not shown, omits the DE \rightarrow DI and VE \rightarrow VI synapses.) The excitation pattern shown is a standing wave, with adjacent segments alternating between dorsal and ventral muscle contraction. Excited cells are shown as filled, i.e., have thickened outlines.

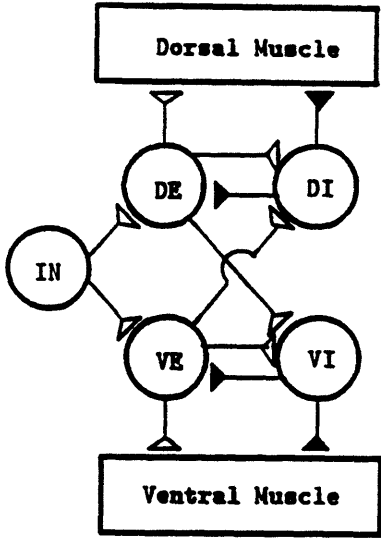
Figure 2. Segmental-ring-oscillator, physiological version, formed by connecting the rostral and caudal segments of a segmental-linear-oscillator, as if the rostral segment were the posterior neighbor of the caudal segment. The inside of the ring corresponds to the dorsal surface. As in Fig.1, and in all the subsequent figures, inhibitory synapses and excited cells are represented as filled. [Both (A) and (B) are copied from computer screen displays. The dotted lines indicate the absence of DE \rightarrow DI and VE \rightarrow VI synapses. The twigs adjacent to synapses onto muscle are purely artifacts of the display.] (A) Shows a standing wave excitation pattern. Since the number n of component segments in the figure is odd, one of the segments (in this case the bottom one) must be in phase with its clockwise neighbor (i.e., must have the same rather than opposite excitation state). (B) Shows the resulting excitation pattern after 2 time steps (under counting-model dynamics). After every additional 4 time steps the pattern has rotated 1 unit counterclockwise; more precisely, it is part of a temporal sequence of 4 excitation patterns which recurs periodically, but rotated 1 unit counterclockwise after every 4 time steps. This behavior should be compared with that of the corresponding segmental-linear-oscillator (Fig.5).

Figure 3. Periodic orbits for segmental-oscillator (single segment) under counting-model dynamics.

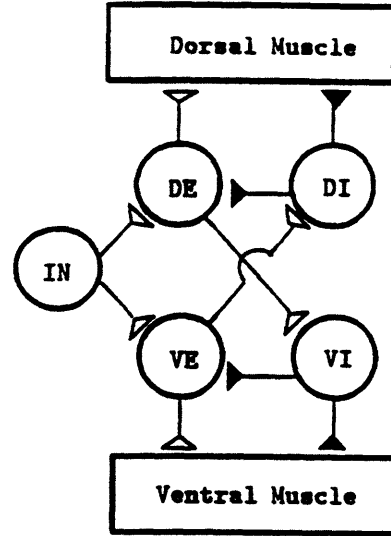
Each row represents a periodic orbit, i.e., periodically repeating successive excitation states of a single segment, and not the state of a segmental-linear-oscillator at a single time. The choice of initial state (i.e., where to put the time origin $t = 0$) is arbitrary. Synaptic contacts are omitted from the display for clarity. We note that the muscle excitation state at time t is induced by the neuronal excitation state at time $t - 1$. (A) The period-4 universal attractor for the anatomical version. This is also one of the 3 period-4 orbits for the physiological version. Note that it is dorsal-ventral symmetric. (B) Top: one of the 2 fixed points for the physiological version. The other fixed point is its dorsal-ventral mirror image. Middle: the period-2 orbit for the physiological version. It is dorsal-ventral symmetric. Bottom: one of the 2 remaining period-4 orbits for the physiological version. The other is its dorsal-ventral mirror image.

Figure 4. Segmental-linear-oscillator, anatomical version, shown at successive time steps. [The diagrams are copied from computer screen displays; the presence of 2 (vs. 1) synapses onto muscle by each neuron is an artifact of the displays.] The initial state (at $t = 0$) is a standing wave. In 2 time steps it reaches a periodic orbit, of period 4. That is, the state at $t = 6$ is identical to the state at $t = 2$, etc.

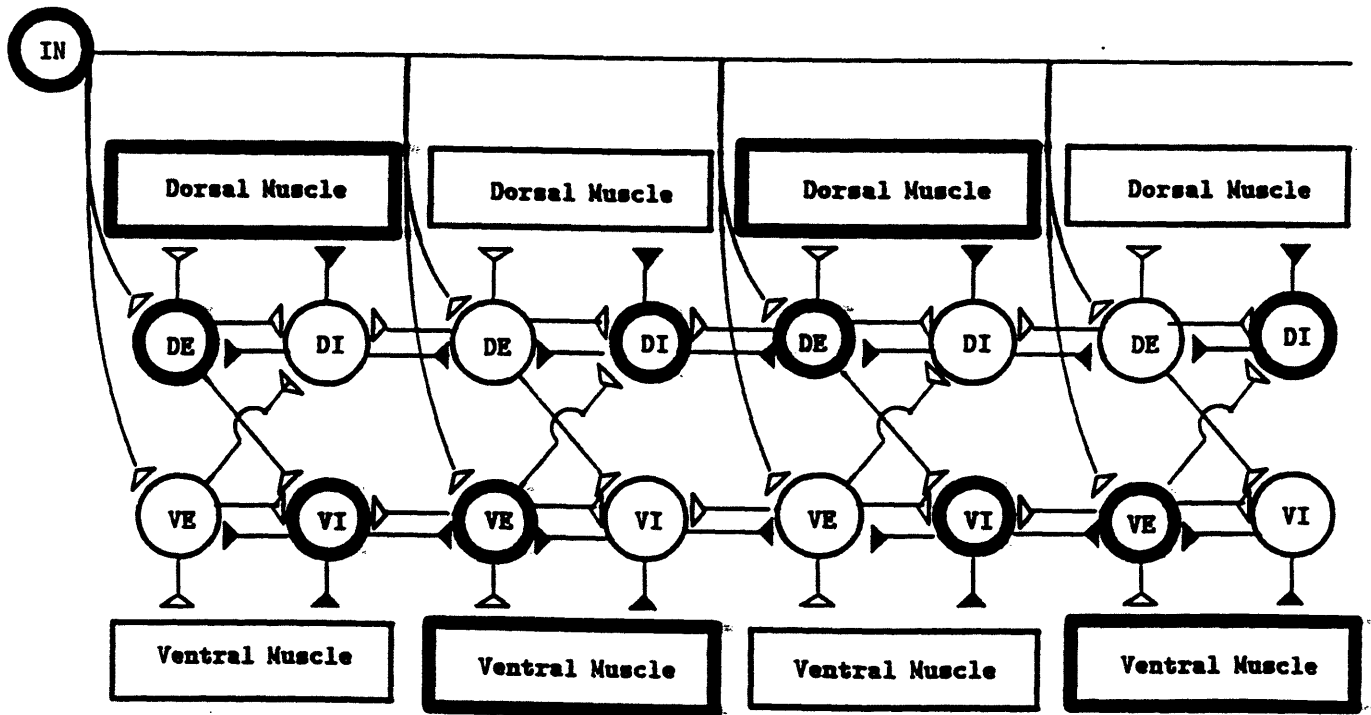
Figure 5. Segmental-linear-oscillator, physiological version, shown at successive time steps. As in Fig.4, the initial state (at $t = 0$) is a standing wave. The state of the anterior segment does not change over time. At $t = 2$ all the posterior $n - 1$ segments are in an identical state, the initial phase of the period-4 orbit in Fig. 3A. During the interval from $t = 2$ to $t = 6$, the posterior $n - 2$ segments run in phase through the successive states of this orbit, returning to the initial phase at $t = 6$. Meanwhile, at $t = 4$ the second segment has reached, and thereafter remains in, the same state as the anterior segment. Both processes repeat every 4 time steps, advancing one segment to the right at each repetition. Eventually, at $t = 4 (n - 1)$, a fixed point "coil" is reached.



(A)

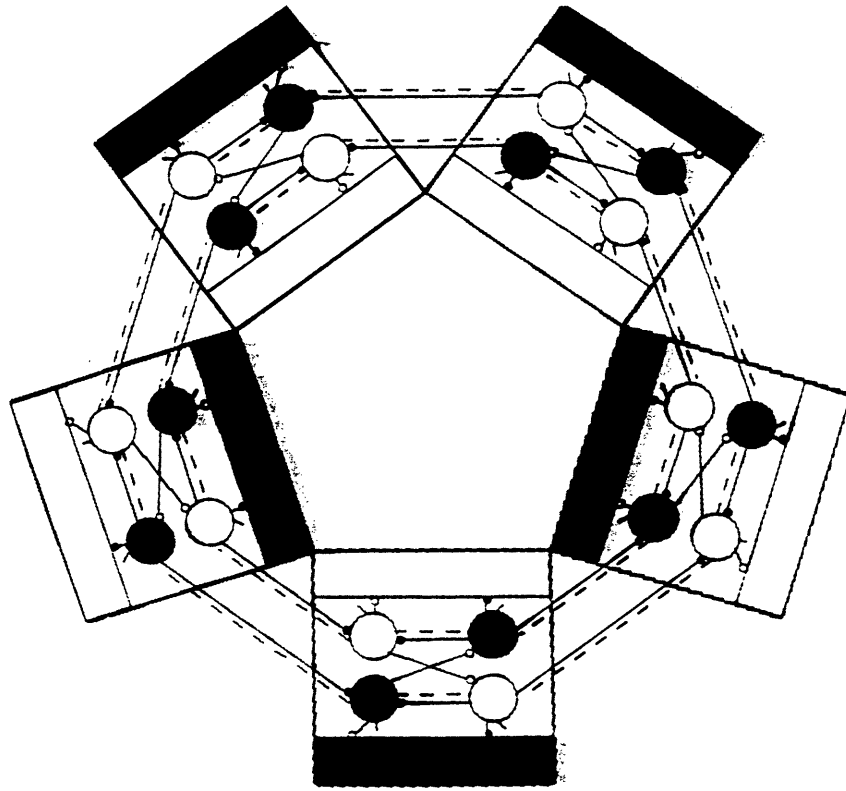


(B)

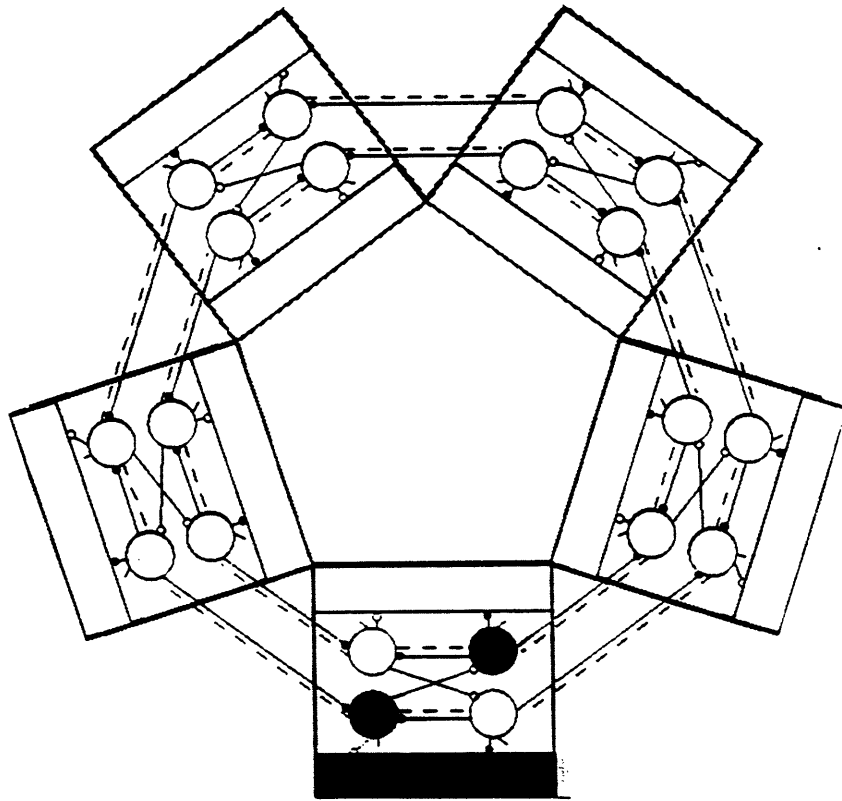


(C)

Figure 1

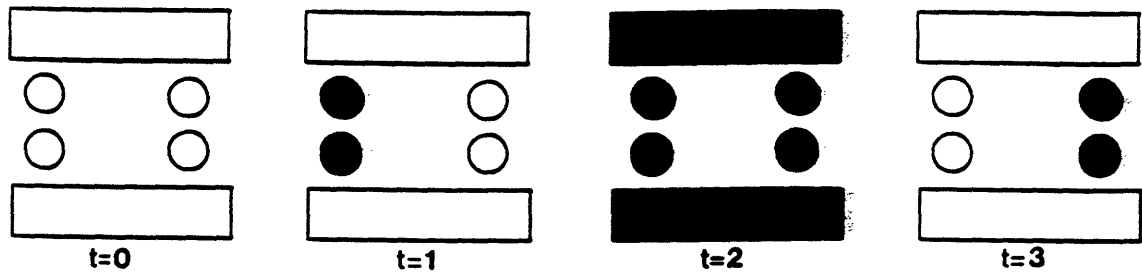


(A)

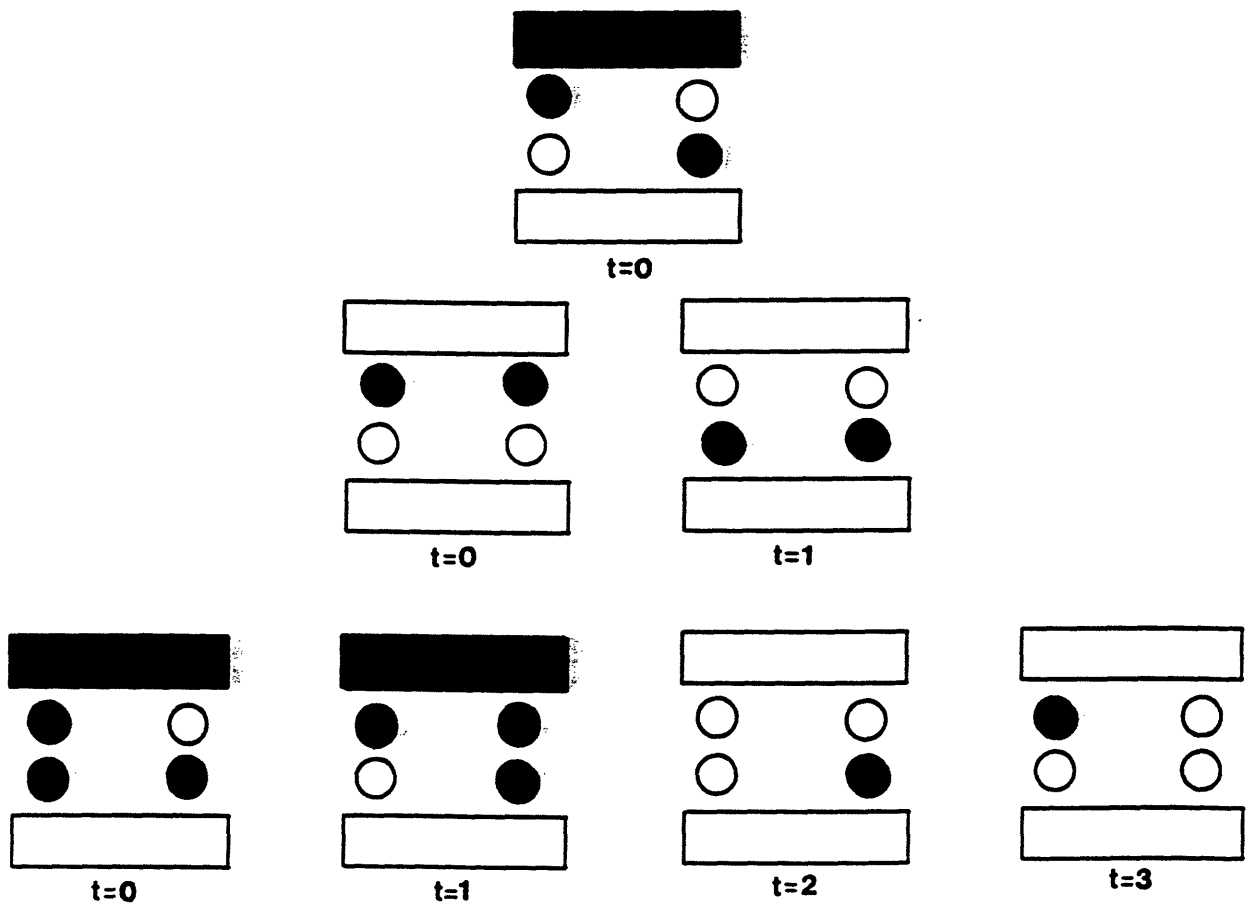


(B)

Figure 2



(A)



(B)

Figure 3

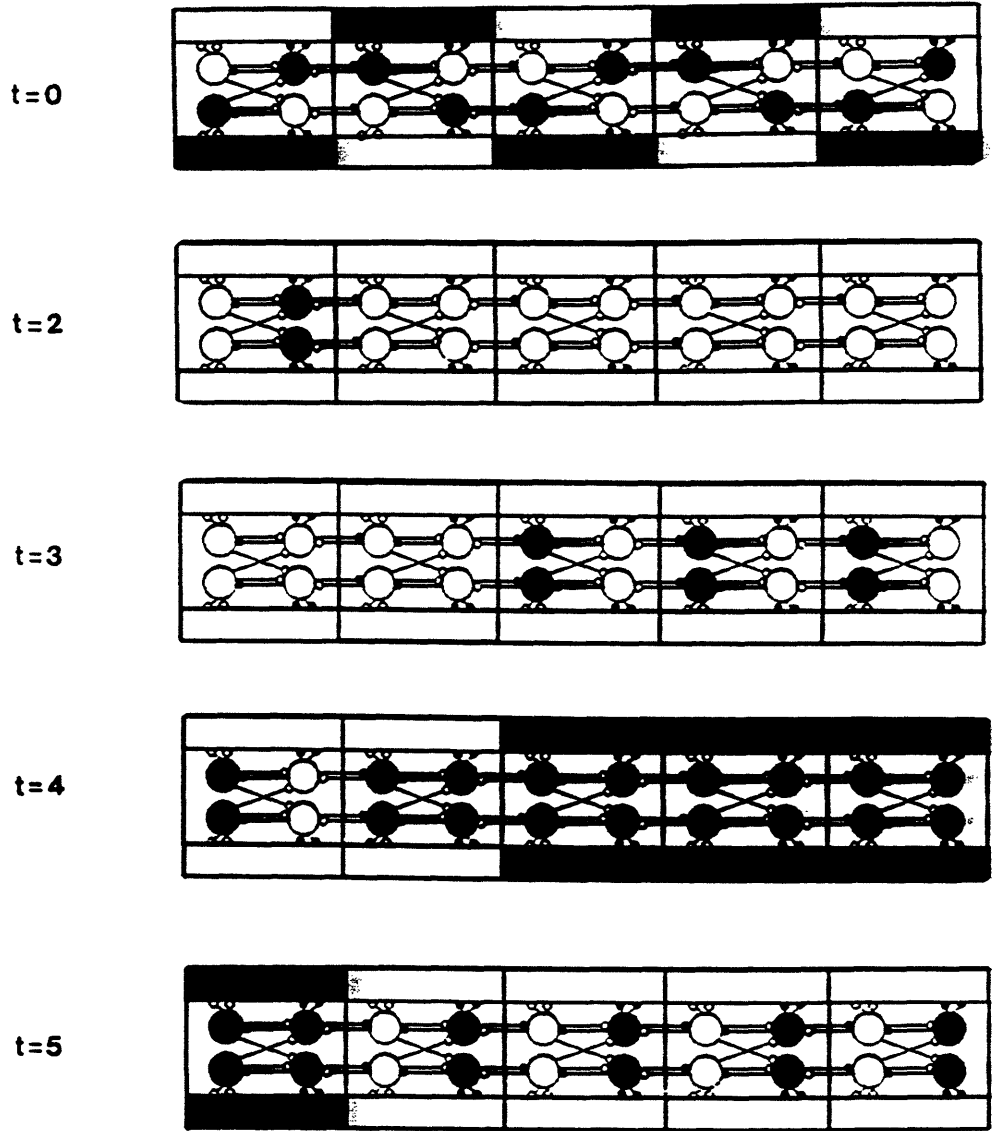


Figure 4

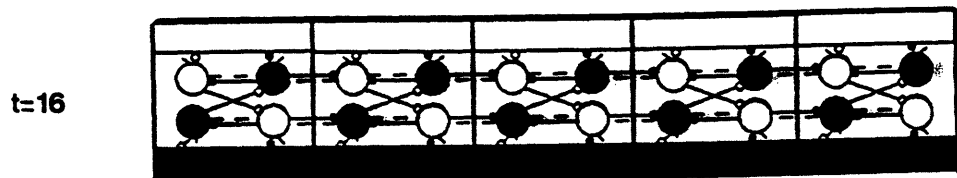
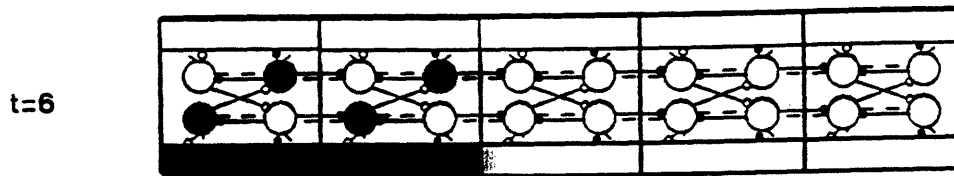
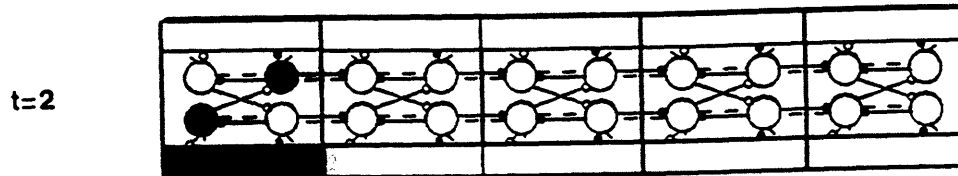
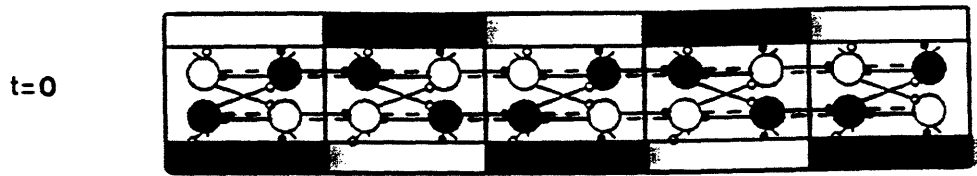


Figure 5