

Propagation of rhythmic dorsoventral wave in a neuromechanical model of locomotion in *Caenorhabditis elegans*

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With 302 neurons and a fully reconstructed connectome, *Caenorhabditis elegans* is an ideal candidate organism to study how behavior is grounded in the interaction between an organism's brain, its body, and its environment. Since nearly its entire behavioral repertoire is expressed through movement, understanding the neuromechanical basis of locomotion is especially critical as a foundation upon which analyses of all other behaviors must build. In this extended abstract, we report on the evolution and analysis of an integrated neuromechanical model of forward locomotion.

C. elegans locomotes in an undulatory fashion, generating thrust by propagating dorso-ventral bends along its body. How the rhythmic patterns are generated and propagated is not yet understood. We focus here on the propagation of the dorsoventral body bend along the body.

To date there have been a handful of models of forward locomotion (see reviews by Gjorgjieva et al. (2014) and by Cohen and Sanders (2014)). However, recent experimental analysis of the structure of ventral cord circuitry (Haspel and O'Donovan, 2011) and the effect of local body curvature on nearby motor neurons (Wen et al., 2012) undermine some of the assumptions of these models. Furthermore, all current models have assumed specific answers to how the rhythmic movement is propagated, with little systematic exploration of the possibilities.

First, we reconstructed a biomechanical model of the worm's body and musculature from published descriptions (Boyle et al., 2012). The complete physical model consists of a set of 147 stiff, highly nonlinear differential-algebraic equations (Fig. 1A). Second, we developed a neural model of the ventral nerve cord subcircuit associated with forward locomotion, comprising four main classes of motor neurons: 12 neurons of class VB and VD, and 6 neurons of class DB and DD (Fig. 1B), separated into 6 repeating neural units derived from a statistical analysis of the connectome (Haspel and O'Donovan, 2011). Following previous work, neurons were modeled as passive, isopotential components, and the model includes chemical and electrical synapses (Izquierdo and Beer, 2013). Third, we incorporated stretch-receptors innervating B-motoneurons from

anterior body segments (Fig. 1B), based on recent findings (Wen et al., 2012). The generation of the rhythmic wave was modeled as originating in the head.

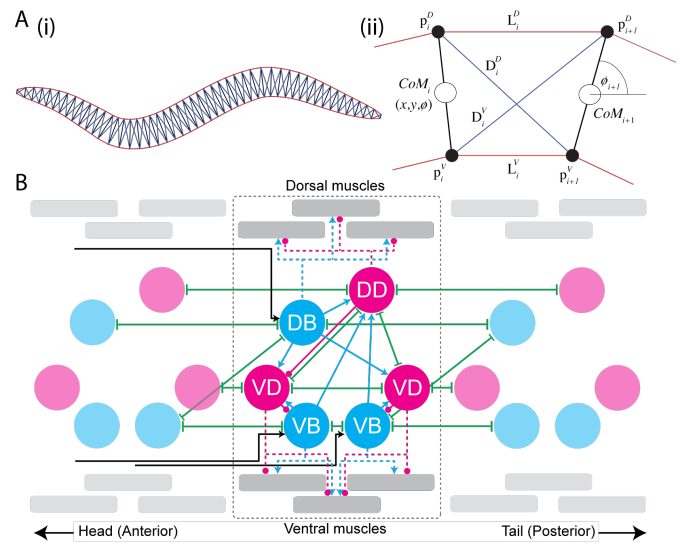


Figure 1: Neuromechanical model. (A) Complete physical model (i) and one of 49 individual segments (ii) adapted from (Boyle et al., 2012). (B) One of 6 repeating neuromuscular units, derived from a statistical analysis of the connectome (Haspel and O'Donovan, 2011). Each unit includes one dorsal and two ventral B- (cholinergic, blue) and D-class (GABAergic, magenta) motor neurons that connect to muscles (gray) on each side. The model includes all chemical synapses (blue excitatory and magenta inhibitory), gap junctions (green), and neuromuscular junctions (dashed). Additionally, B-class neurons receive stretch-receptor input from anterior muscles (black) (Wen et al., 2012).

Altogether, the model included 21 unknown electrophysiological parameters. An evolutionary algorithm was used to determine values of the unknown parameters that optimized behavioral performance. Solutions were evaluated on how closely they matched the speed of the worm on agar. We ran 100 evolutionary runs and consistently found elec-

trophysiological configurations that produced realistic control of movement when coupled to the biomechanical model of the body, and situated in a simulated agar environment.

Each successful search produced a distinct set of parameter values, leading to an ensemble of models that are consistent with the known biological constraints. The focus of our analysis was first to identify different possible classes of solutions through the exploration of electrophysiological configurations that produce realistic control of movement. The second part of the analysis was to understand the operation of the highest-performing exemplars of each class. We use this insight to propose experiments on the organism that test the hypotheses generated by the different classes.

In all evolved solutions, forward movement is produced with each body region alternating between positive and negative curvature, and bands of curvature propagating from head to tail as shown in a kymogram (Fig 2A). Emergent properties of the evolved networks reproduced key experimental observations that they were not designed to fit, including the curvature profile of the body's movement (i.e., curvatures near the head larger than curvatures near the tail) and the wavelength of the propagating wave. This suggests that the model may be operating according to principles similar to those of the biological network.

We analyzed the properties of the entire ensemble of solutions using a number of different techniques, including neuron recordings (Fig. 2B), neural and behavioral manipulations, and lesion studies. An examination of the ensemble revealed two broad classes of solutions: some where the D-class motoneuron did not play a role in forward locomotion and some where it did. All of the evolved solutions relied primarily on stretch-reception. Further analysis of the operation of these networks reveals the roles that the individual neural, synaptic and proprioceptive components of this system play in propagating and coordinating rhythmic undulatory waves from head to tail during locomotion.

C. elegans offers an unique opportunity to obtain a complete systems-level understanding of a locomotory circuit. As we better understand the operation of the ensemble of integrated neuromechanical model of locomotion, the insights will be used to propose novel experiments on the living organism that test the hypotheses generated by the different classes of solutions. The results of such neurobiological experiments can be used to constrain subsequent iterated optimizations, ultimately improving our understanding of the biological system, and more generally the generation of behavior in a coupled brain-body-environment system.

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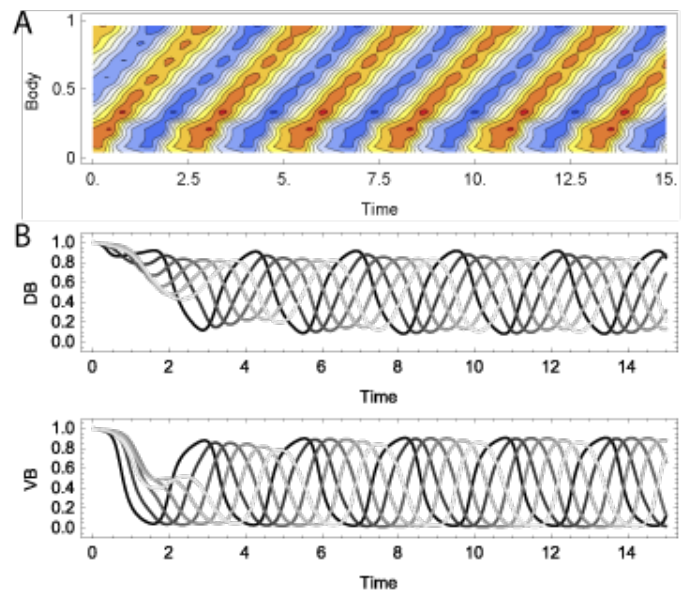


Figure 2: Characterizing evolved solutions. (A) Kymogram of time-varying curvature illustrating retrograde bending waves along the simulated worm (head = 0; tail = 1) responsible for forward movement. Wavelength and frequency in the model is similar to what has been observed in worm. (B) Neural activity in the Dorsal (top) and Ventral (bottom) B-class motoneuron for each of the six different neural units along the body (lighter shades of gray represent neurons in units closer to tail). Neural traces in the evolved circuits illustrate: (i) rhythmic patterns that are propagated anteriorly through the neural units with a phase lag, and (ii) anti-phase patterns of activity in dorsal and ventral units.

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