The OpenWorm Project: progress update, available resources and future plans

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Introduction

OpenWorm [1-3] is a global, online collaboration of computational and experimental neuroscientists, software developers and interested volunteers with an ambitious long-term goal: to create a cell-by-cell computer model of *C. elegans* which reproduces the behaviour of the real animal in as much biological detail as possible. The project takes a unique **Open Science** approach to development, making all code, data and documentation publicly available at the time of production. This will provide a community resource which consolidates our anatomical and physiological knowledge of the worm, and will allow investigators to examine the mechanistic underpinnings of how behaviour is generated by a complete nervous system.

The first concrete milestone for the project is an accurate simulation of **locomotion** including the motor system, with realistic electrophysiology of the muscle cells and connected neurons to reproduce the crawling gait. A prototype of this simulation has been released, and the model is being validated by comparison with crawling behaviour from experimental recordings.

A number of **subprojects** are focused on different areas and the resources developed have been brought together into a single simulation stack based on **Docker**.

Data management - owmeta and ChannelWorm

The fidelity of OpenWorm to its biological counterpart, *C. elegans*, depends on the realism of its constituent parts, such as computationally-modelled cells. To facilitate this we have developed a Python module **owmeta** [7] (previously PyOpenWorm), a framework for accessing and sharing anatomical and physiological data on *C. elegans*, facilitating their use in computational models.

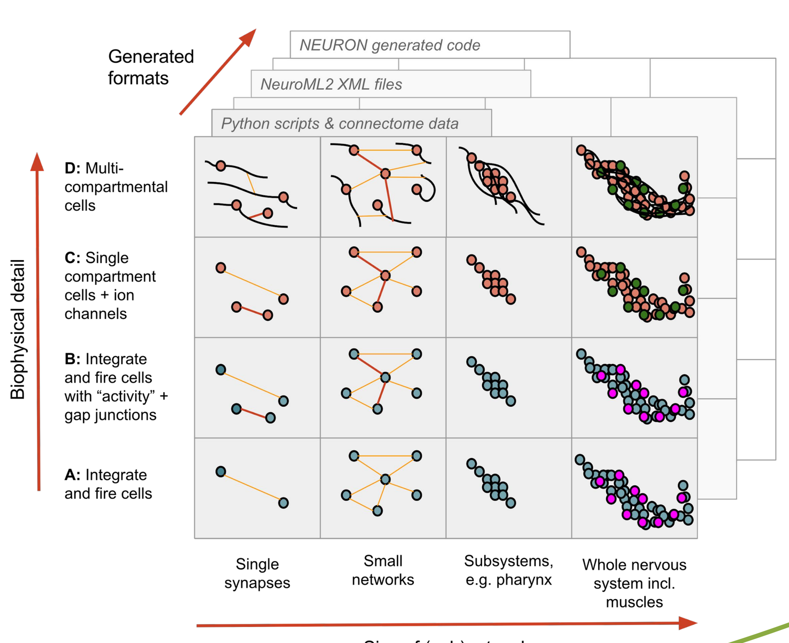
A related subproject, **ChannelWorm** [8], is being developed to support the production and provenance of detailed ion channel dynamic models as well as testing them rigorously against existing data, which supports detailed muscle and neuronal electrical models.

Neuronal simulations

c302 [9,10] is a framework for generating network models in NeuroML 2 [11] format based on the *C. elegans* connectome.

It uses information on the synaptic connectivity between the neurons to generate a network in valid NeuroML, which can be run in pyNeuroML or in the NEURON simulator.

Models can be generated at different levels of cellular complexity (from abstract point neurons to multicompartmental cells) and for the whole network or interesting subsets of cells. The output of c302 models can visualised on Geppetto/Open Source Brain, or can be used to drive whole body simulations in Sibernetic.

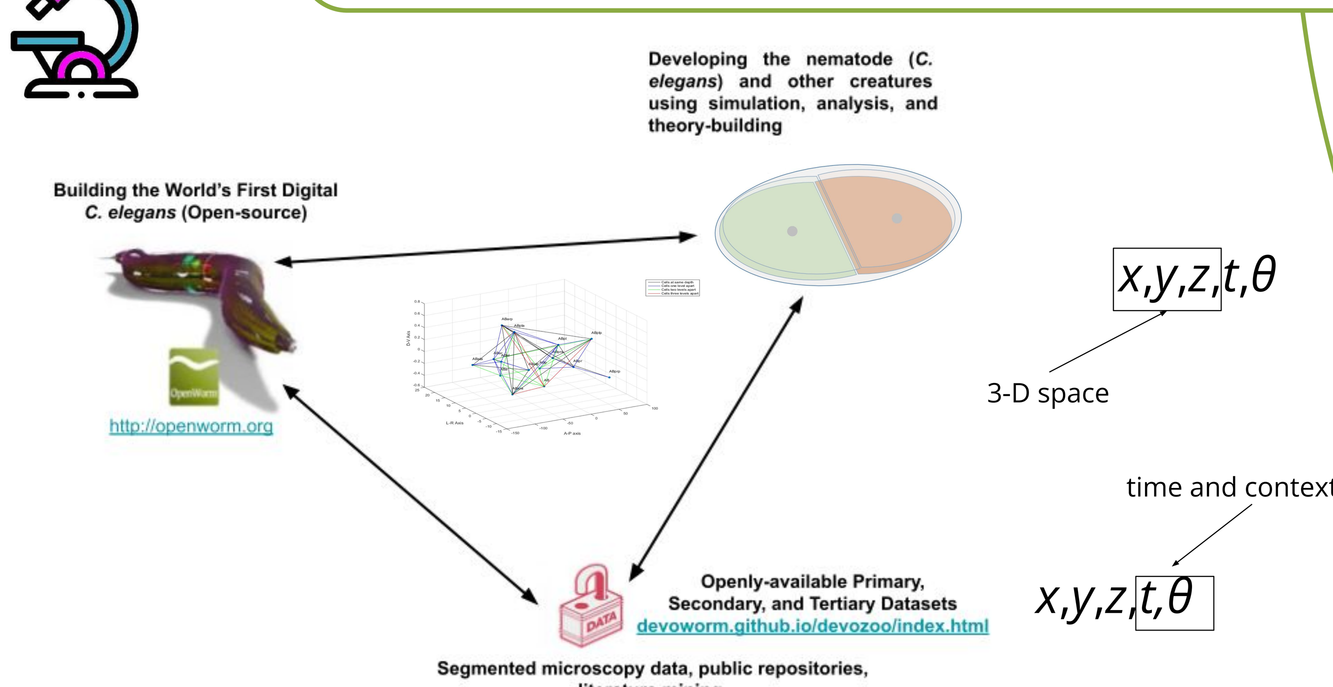


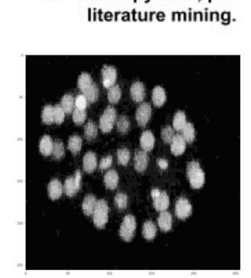
DevoWorm

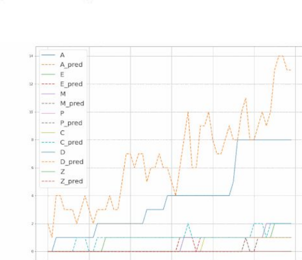
The **DevoWorm** group utilizes computational and theoretical models to investigate development of the worm. Recent work has focused on three approaches: Machine Learning [16], Complex Networks, and Comparative methods.

Machine and Deep Learning can be used to extract static and dynamic information from microscopy images. For the latter, our efforts have led to a pre-trained model and educational initiative called DevoLearn.

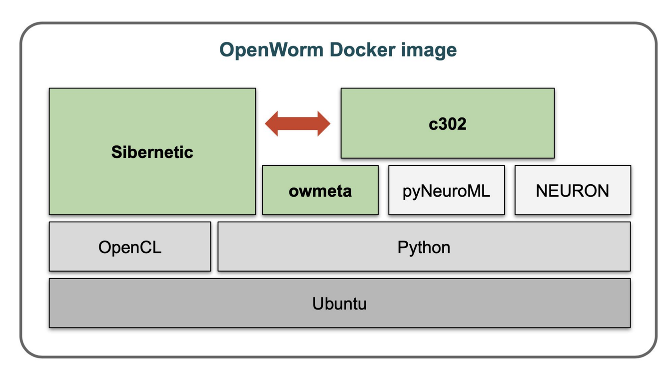
We also utilize complex network theory to investigate networks in the embryo and particularly the emerging connectome [17]. To place the development of *C. elegans* in a broader context, we utilize a comparative biology perspective to understand potential universal aspects of development.

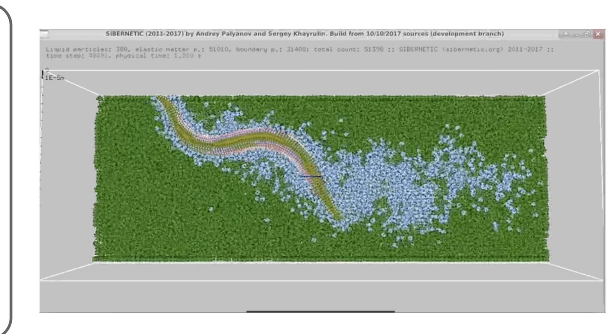






Current release of simulation stack in Docker image



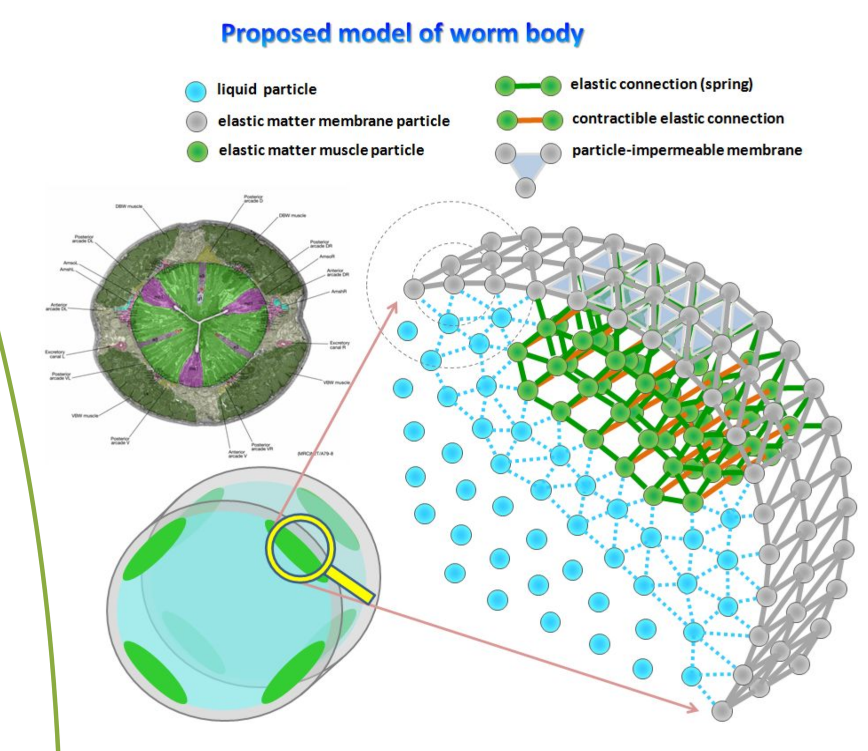


The software packages produced by the project are being gathered in a single installable image based on **Docker** online at http://github.com/openworm/OpenWorm. This image can be installed on Mac, Linux or Windows and provides a starting point for understanding the various subprojects of OpenWorm and how they come together.

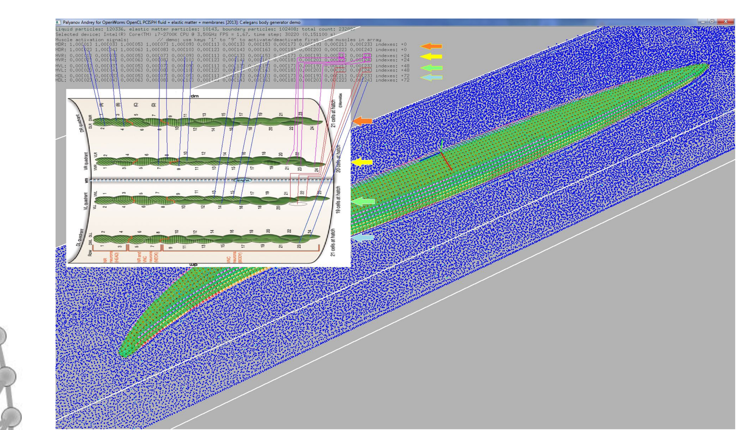
Worm body and environment - Sibernetic

The **Sibernetic** physics engine [4,5] was developed to simulate the biomechanics of soft tissues and the environment of the worm. It can handle the simulation of liquids, elastic matter and solids with various physical properties. Sibernetic is based on the predictive-corrective incompressible smoothed particle hydrodynamics (PCISPH) algorithm [6] with modifications to incorporate boundary-handling and a surface tension model.

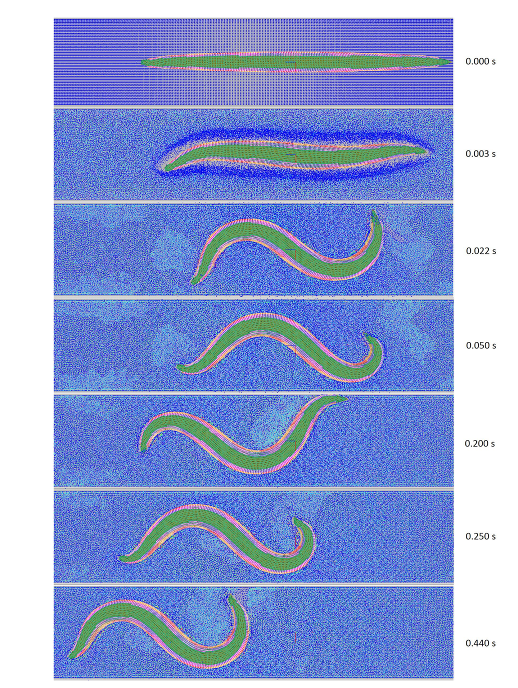
Sibernetic, to the best of our knowledge, is the first open source, parallel OpenCL/C++ PCISPH high-performance physics engine. A high-resolution 3D worm body provided with a full set of 95 body wall muscles was developed and its ability to simulate worm movement has been investigated.



Types of particles used in the Sibernetic simulation framework for creating a model of the worm body with cuticle, muscle quadrants and internal liquid.



Main GUI of Sibernetic showing worm body (green) and simulated fluid (blue). Inset shows anatomical layout of 95 muscle cells, arranged in 4 quadrants.

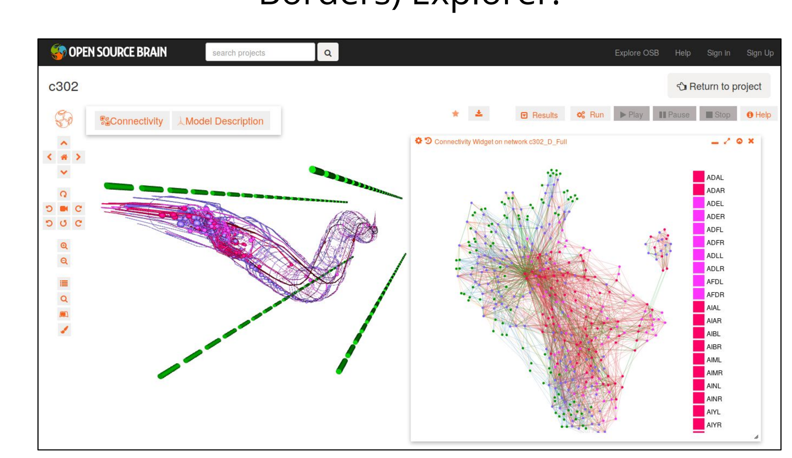


Simulation of *C. elegans* body crawling over a wet surface. Sequence of muscle contractions is artificially generated using travelling sine waves. Velocity is comparable to that of real worm - 0.1-0.3 mm/s.

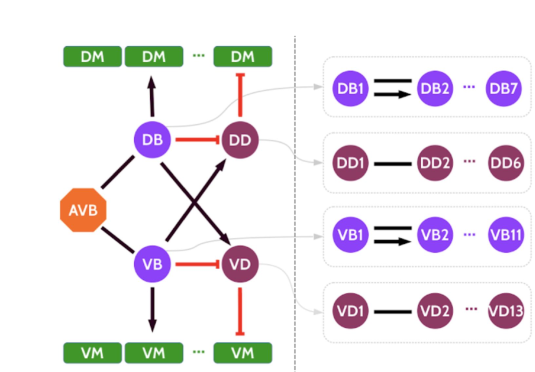
geppetto

A significant output of the OpenWorm project has been Geppetto [12,13], a web-based platform designed to enable the visualization, integration and simulation of neuroscience models and data. Geppetto is capable of visualizing and simulating networks of single and multi-compartment cells. Many of these features were developed following our Kickstarter campaign [14], which developed WormSim.

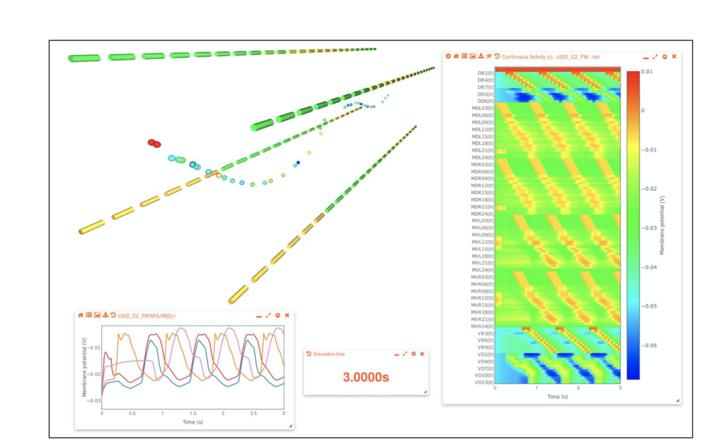
Geppetto is currently used in the Open Source Brain (OSB) platform [15] where the worm network models produced by c302 can be visualised and simulated. In addition to use in OpenWorm, Geppetto has been used as the basis for other neuroscience applications such as NetPyNE-UI, Virtual Fly Brain and NWB (Neurodata Without Borders) Explorer.



Geppetto based visualisation from OSB showing full multicompartmental neuronal network with 4 green rows of muscles generated by c302 (left) with graph of connections between cells (right)



Simplified neural circuit composed of AVB interneurons, B-type and D-type motor neurons and muscles for generation of the forward crawling activity.



Visualisation on OSB of muscles and subset of neurons used for forward locomotion activity generation. Membrane potentials shown in subplots, illustrating travelling waves.

Ongoing and future work

- Incorporation of sensory feedback between worm body/environment and neural network
- Investigating the influence of gap junctions between adjacent muscles on synchronization of their activity, and incorporation of proprioceptive feedback from stretch sensitive motoneurons
- ChannelWorm curating published data on ion channel properties in *C. elegans*
- Constraining network model against whole animal *in-vivo* calcium imaging data

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