Updates from the OpenWorm project: incorporating NeuroPAL data and ASH neuron electrophysiological recordings

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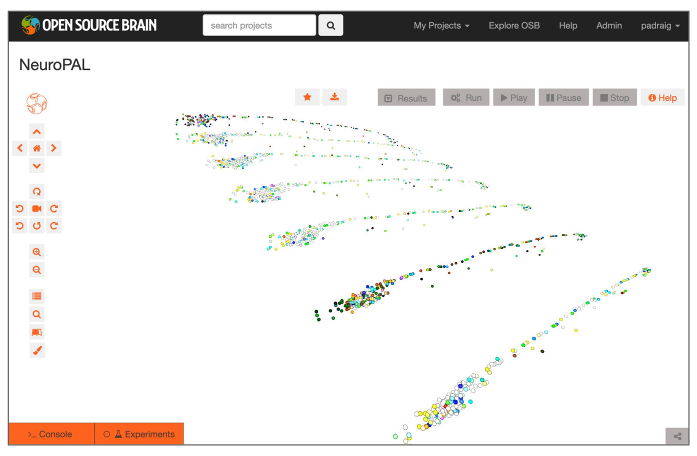
Introduction

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 approach provides community resources which consolidate our anatomical and physiological knowledge of the worm, and allows 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.

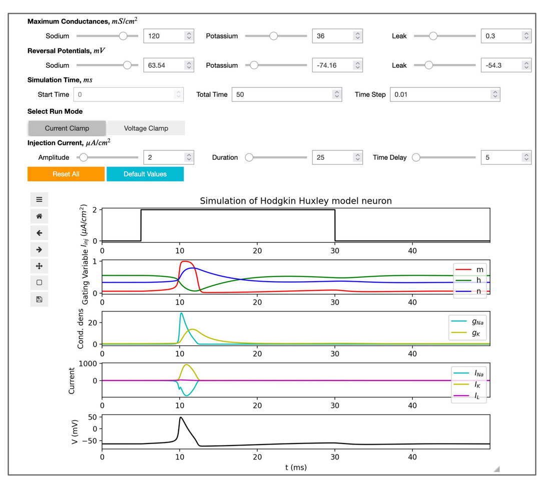
A number of activities are happening in parallel, focused on different areas and the resources developed have been brought together into a single simulation stack based on **Docker**. We highlight here some of the recent work in the project.

NeuroPAL



The recently developed NeuroPAL [4] is a groundbreaking new technique to create a genetic strain of the worm where each neuron is labelled with a fluorescent marker of a specific color, allowing easy identification of neurons across experiments and animals. We have converted datasets containing positions of cell bodies and the expressed NeuroPAL colors to **NeuroML** [5], to allow them to be used in OpenWorm models and associated applications.

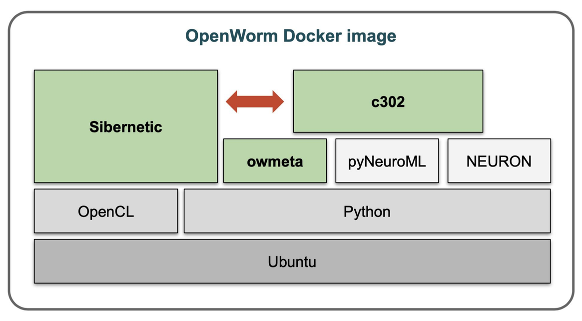
Hodgkin Huxley interactive tutorial

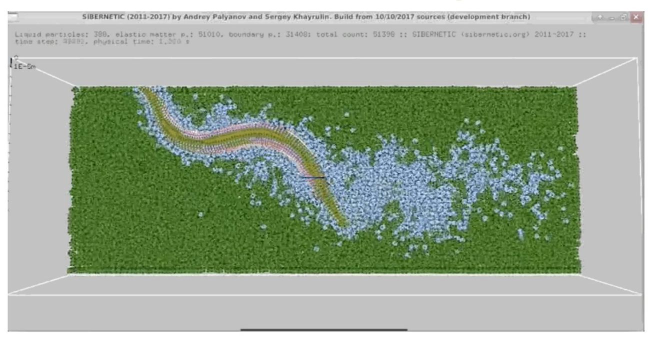


OpenWorm is keen to develop and promote educational material related to our modelling goals. As part of a recent Google Summer of Code project by Rahul Sonkar, an interactive tutorial for the Hodgkin Huxley model of neuronal activity was developed.

This Jupyter notebook based tutorial [6] can be used to investigate how ion channel dynamical properties underlie the generation of the action potential in neurons.

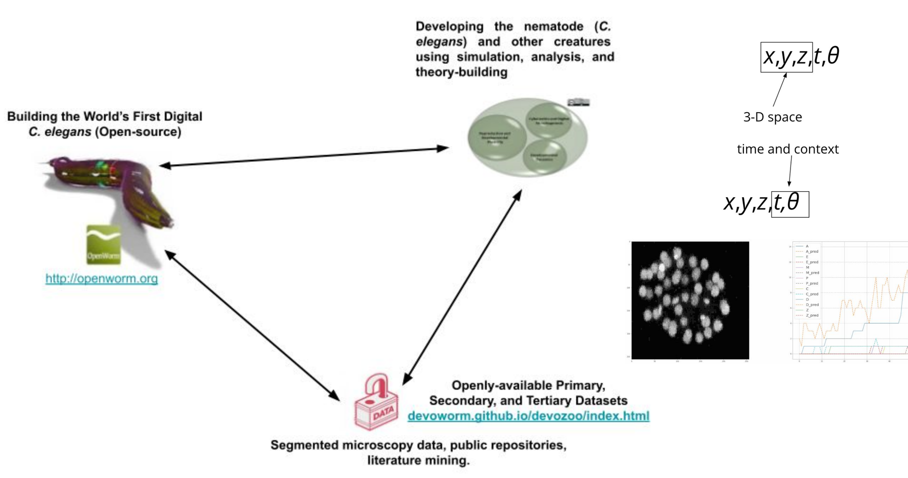
Simulation stack in Docker image





The software packages produced by the project (including Sibernetic [7] and the c302 nervous system model [8]) have been gathered in a single installable image based on **Docker**, and is available online at http://github.com/openworm/OpenWorm. This image can be run on Mac, Linux or Windows and provides a starting point for understanding the various subprojects of OpenWorm and how they come together.

DevoWorm and DevoLearn



The DevoWorm group [9] utilizes computational and theoretical models to investigate development of the worm and other organisms. Recent work has focused on four approaches: Machine Learning/Deep Learning, Complex Networks, Evo-Devo, and Theory-building/Simulation.

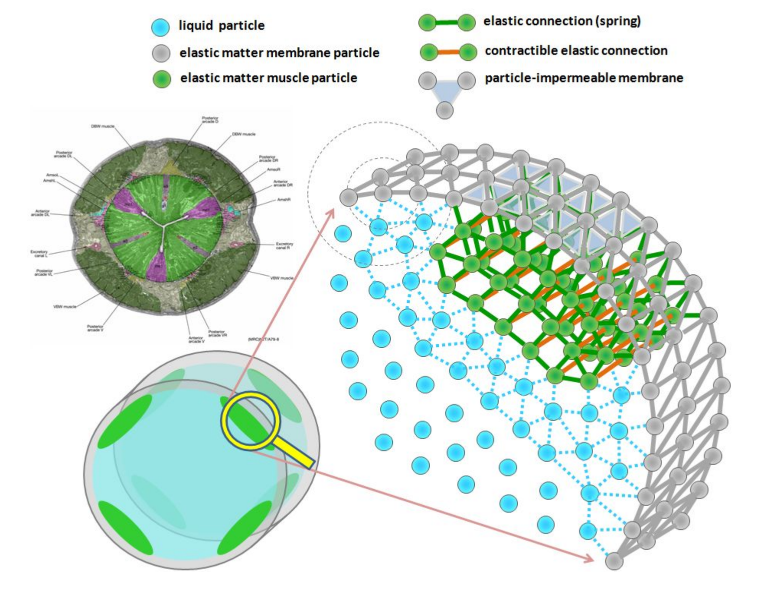
OpenWorm Studentships

OpenWorm Studentships are a new way to incentivize contribution to the project, offering small stipends and recognition to junior researchers who want to spend time bringing their research into the OpenWorm project and making it more accessible for the wider community. These are open to anyone involved in *C. elegans* research who has (or whose lab has) produced data, models or software, which has been publicly released and which would be useful for the OpenWorm project.

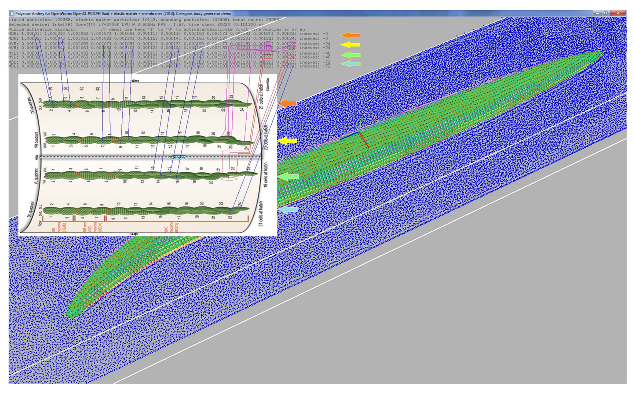
See https://openworm.org/studentships for more details.

3D worm body & environment - Sibernetic

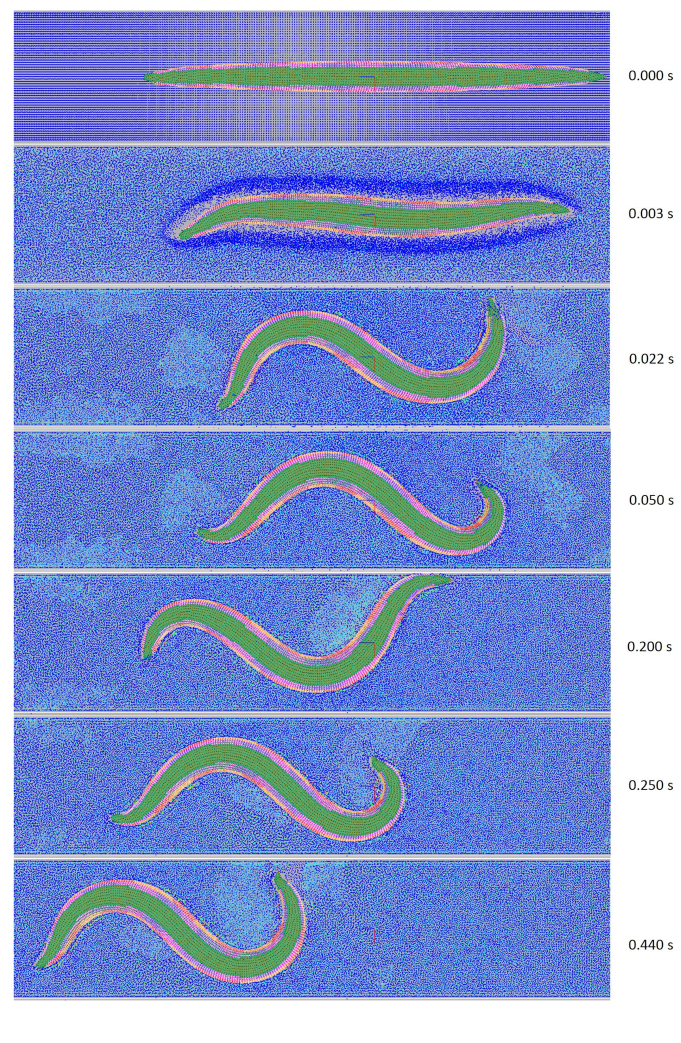
The **Sibernetic** physics engine [7,10] was developed to simulate the biomechanics of soft tissue and the environment of the worm. It can handle the simulation of liquids, elastic matter and solids with various physical properties. Sibernetic is based on the predictive-corrective incompressible smoothed particle hydrodynamics (PCISPH) algorithm [11] 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. Sibernetic has also been linked to the simulated neural network of **c302**, allowing the worm to be driven by generated neuronal activity.



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

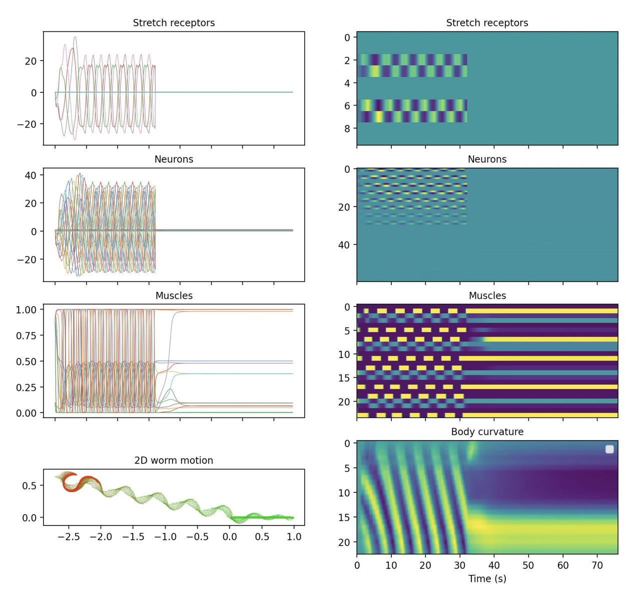


Main graphical interface of Sibernetic showing worm body (green) and simulated fluid (blue). Inset shows anatomical layout of 95 muscle cells, arranged in 4 quadrants.



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.

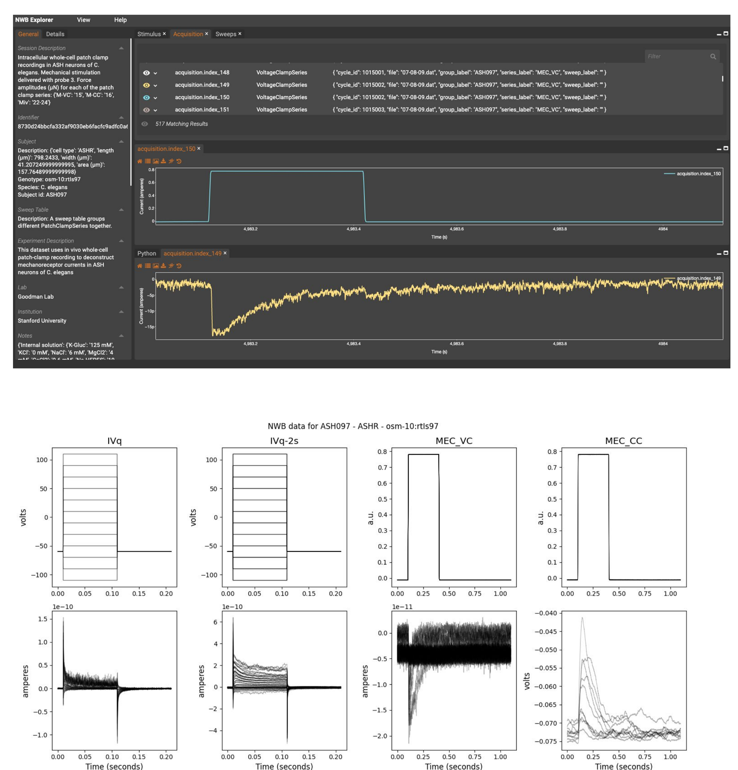
2D worm body models



While a full 3D model of the worm interacting with its environment, with closed loop feedback between the nervous system and body is a long term goal, much of the work of constraining the parameters of the model can be achieved with more computationally efficient 2D worm body models.

We aim to build on previous work to build and optimise such 2D models [12,13] and link these to the same biophysically detailed neuronal network models as our full 3D model.

ASH neuron electrophysiological recordings



Electrical recordings from individual neurons of *C. elegans* are crucial experimental data required for creating biologically realistic computational models of the worm.

Electrophysiological recordings of the activity of the ASH neuron made by the **Wormsense Lab of Miriam Goodman** were converted to the open, standardized format **Neurodata Without Borders (NWB)** as part of a Google Summer of Code project by Steph Prince [14].

Once standardised, these can be automatically visualised and analysed on our **Open Source Brain** platform [15].

Ongoing and future work

- Link 2D worm body models to neuronal networks expressed in NeuroML
- 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
- Constraining network model against whole animal *in-vivo* calcium imaging data
- Conversion of more open experimental data resources for use by the community

References

1. OpenWorm website: http://www.openworm.org; Documentation: http://docs.openworm.org
2. Szigeti B, Gleeson P, Vella M, Khayrulin S, Palyanov A, Hokanson J, Currie M, Cantarelli M, Idili G, Larson SD (2014). OpenWorm: an open-science approach to modelling Caenorhabditis elegans. Frontiers in Computational Neuroscience, 8, 137. doi:10.3389/fncom.2014.00137
3. Sarma GP, Lee CW, Portegys T, Ghayoomie V, Jacobs T, Alicea B, Cantarelli M, Currie M, Gerkin RC, Gingell S, Gleeson P, Gordon R, Hasani RM, Idili G, Khayrulin S, Lung D, Palyanov A, Watts M and Larson SD, OpenWorm: overview and recent advances in integrative biological simulation of *Caenorhabditis elegans*, Philosophical Transactions of the Royal Society B, 373, 20170382. doi: 10.1098/rstb.2017.0382
4. Yemini, E et al. , NeuroPAL: A Multicolor Atlas for Whole-Brain Neuronal Identification in C. elegans, Cell, Volume 184, Issue 1,2021
5. Cannon RC, Gleeson P, Crook S, Ganapathy G., Marin B, Piasini E, Silver RA. LEMS: a language for expressing complex biological models in concise and hierarchical form and its use in underpinning NeuroML2. Frontiers in Neuroinformatics 2014, 8: 79.
6. Hodgkin Huxley tutorial: https://github.com/openworm/hodgkin_huxley_tutorial
7. Sibernetic website: http://sibernetic.org
8. Gleeson P, Lung D, Grosu R, Hasani R, Larson SD, (2018) c302: a multiscale framework for modelling the nervous system of *Caenorhabditis elegans*. Philosophical Transactions of the Royal Society B, 373, 20170379. doi: 10.1098/rstb.2017.0379
9. DevoWorm: https://devoworm.weebly.com, DevoLearn: https://github.com/devolearn
10. Palyanov A, Khayrulin S, and Larson SD (2018) Three-dimensional simulation of the *Caenorhabditis elegans* body and muscle cells in liquid and gel environments for behavioural analysis. Philosophical Transactions of the Royal Society B, 373, 20170376. doi: 10.1098/rstb.2017.0376
11. Solenthaler B, and Pajarola R (2009). Predictive-corrective incompressible SPH, in ACM Transactions on Graphics (TOG), Vol. 28 (Geneva), 40.
12. Boyle J, Berri S and Cohen N, (2012). Gait Modulation in C. elegans: An Integrated Neuromechanical Model, Front. Comput. Neurosci. 6:10. doi: 10.3389/fncom.2012.00010
13. Olivares E, Izquierdo EJ and Beer RD (2021) A Neuromechanical Model of Multiple Network Rhythmic Pattern Generators for Forward Locomotion in C. elegans. Front. Comput. Neurosci. 15:572339. doi: 10.3389/fncom.2021.572339
14. ASH neuron electrophysiological recordings: https://github.com/openworm/WormsenseLab_ASH
15. Open Source Brain website: https://www.v2.opensourcebrain.org

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http://openworm.org

http://github.com/openworm

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