



# OpenWorm

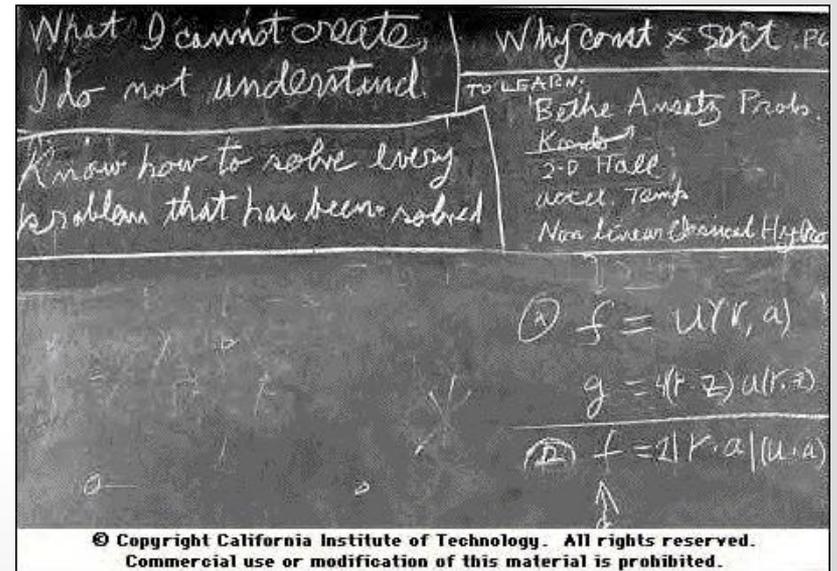
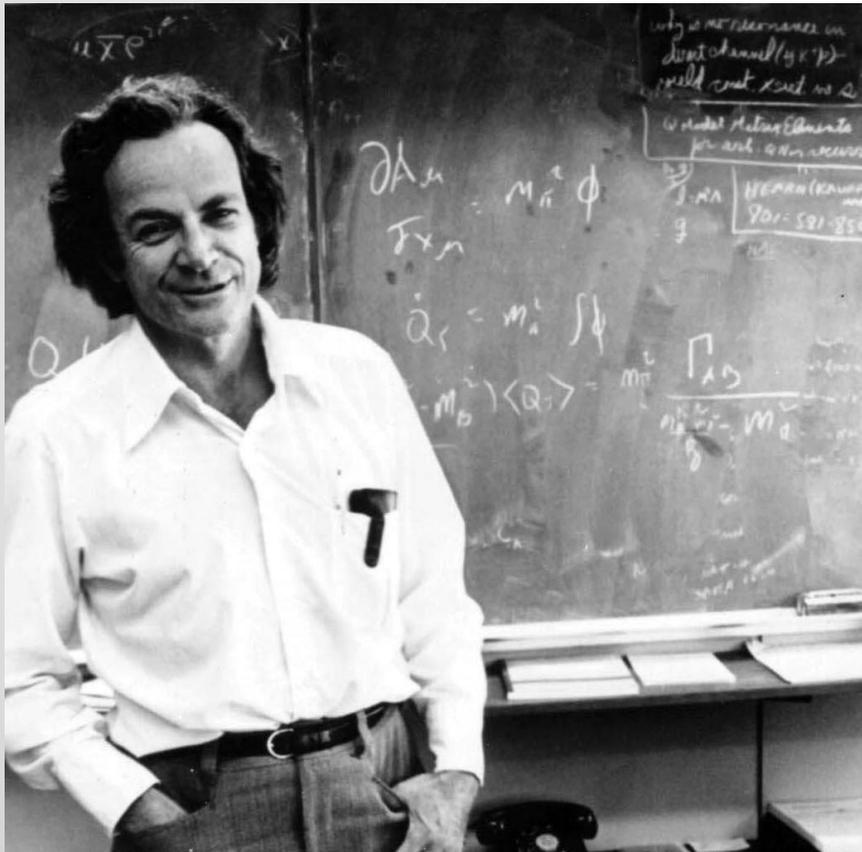
## Building an open digital organism

Matteo Cantarelli (@tarelli)  
fOSSA 2015

Co-founder, OpenWorm  
CTO, MetaCell

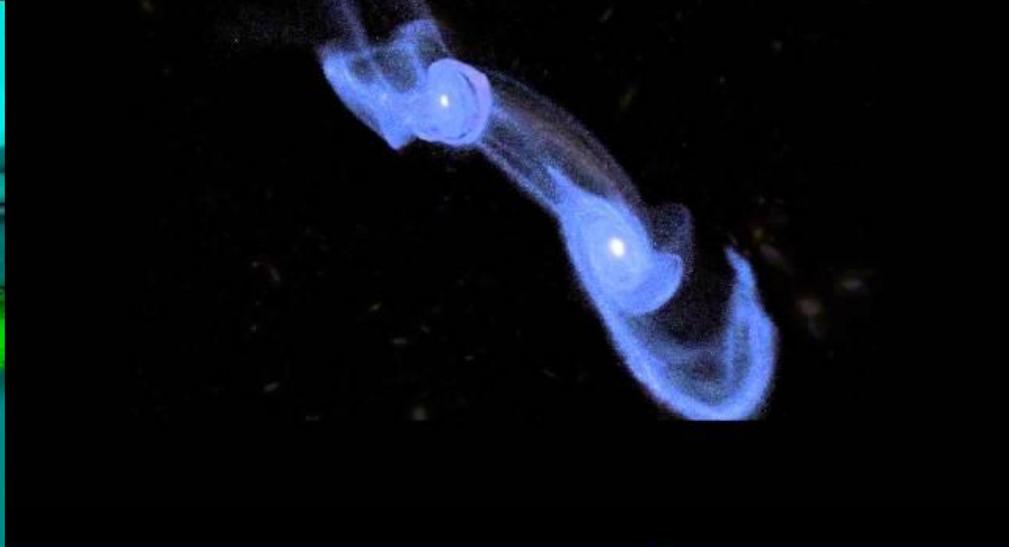
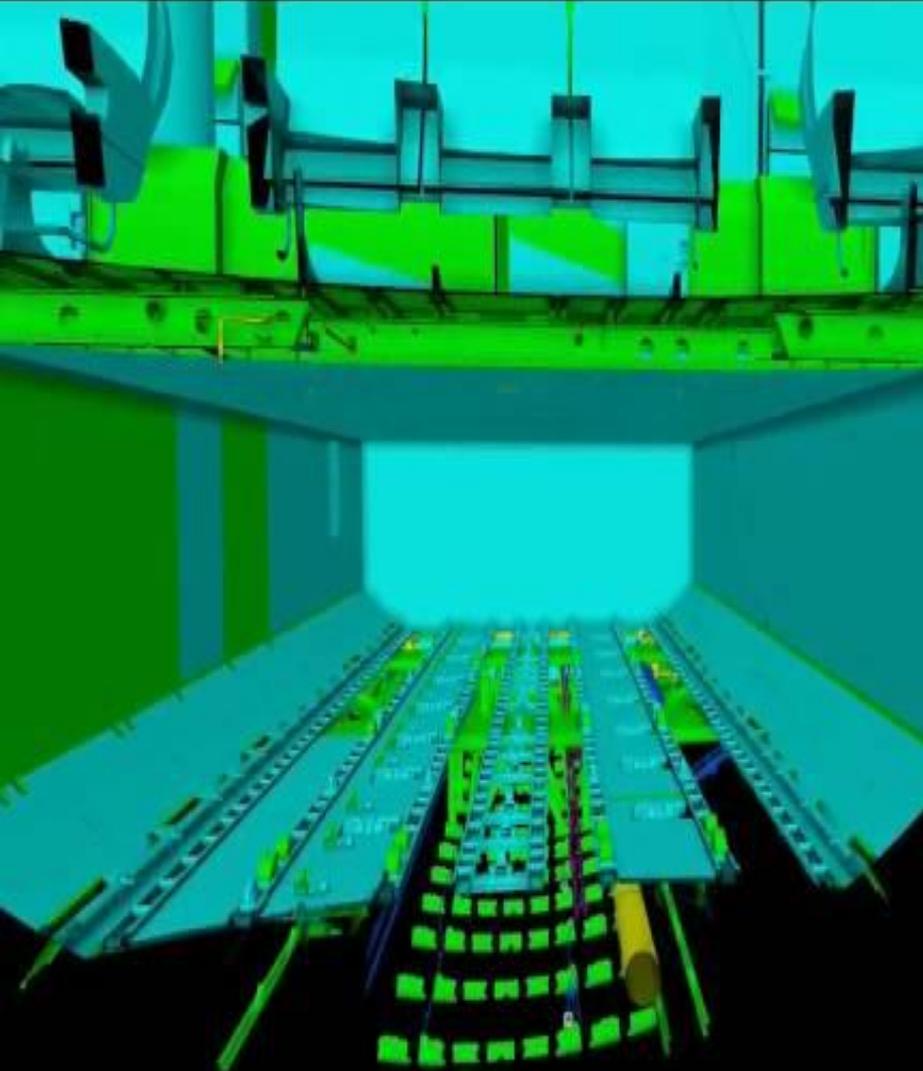
"What I cannot create, I do not understand"

- Richard P. Feynman



# Models help us understand

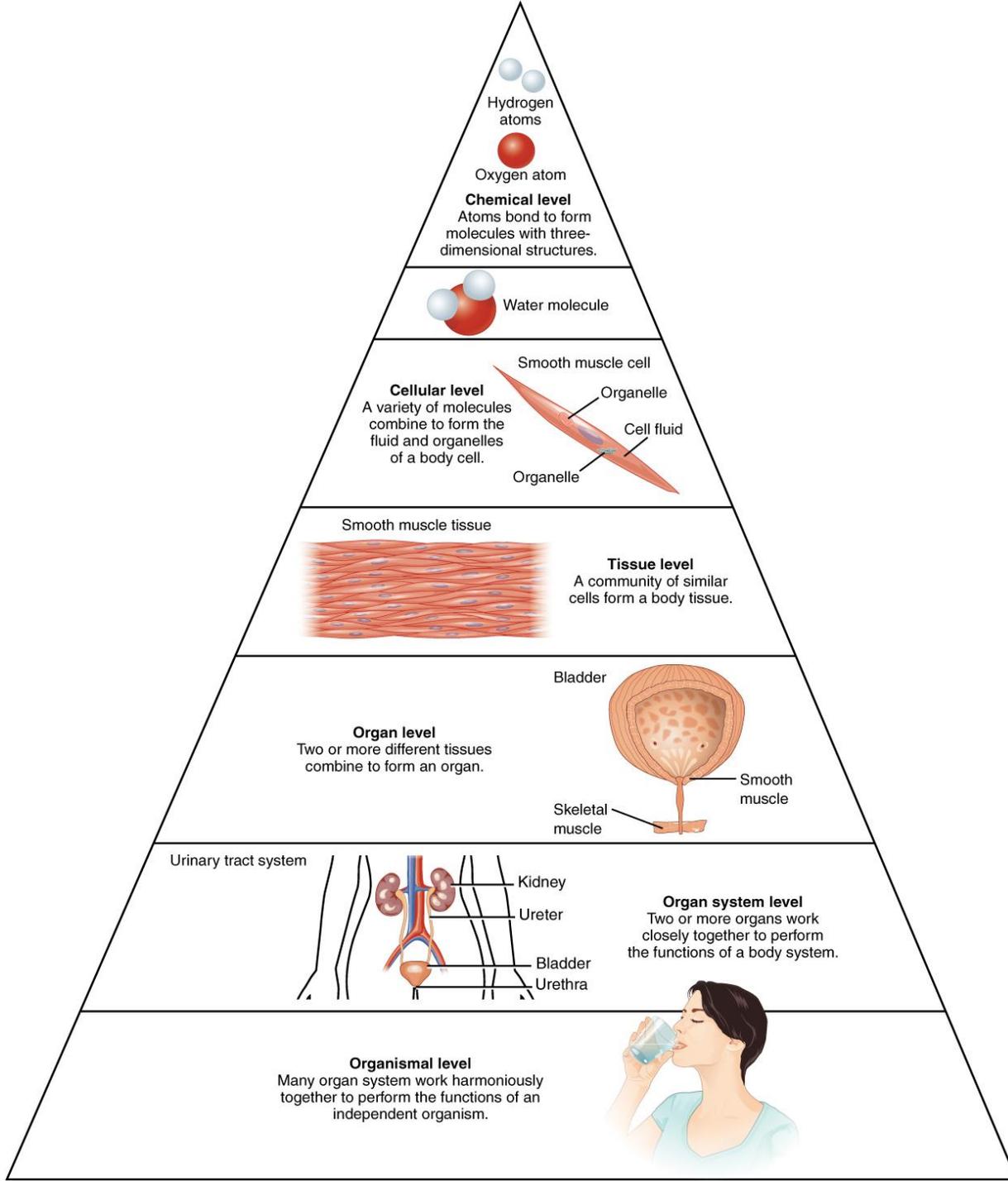
- Engineering disciplines are used with building models that describe the behaviour of complex systems and simulate them
- Boeing 777
  - “Boeing engineers designed and electronically pre-assembled the 777 using computers. New laboratory facilities enabled the various airplane systems to be tested together as a single integrated entity in simulated flight conditions, before the first jetliner took to the air.”
  - 3 million individual parts
  - 1.8 TB of data to make



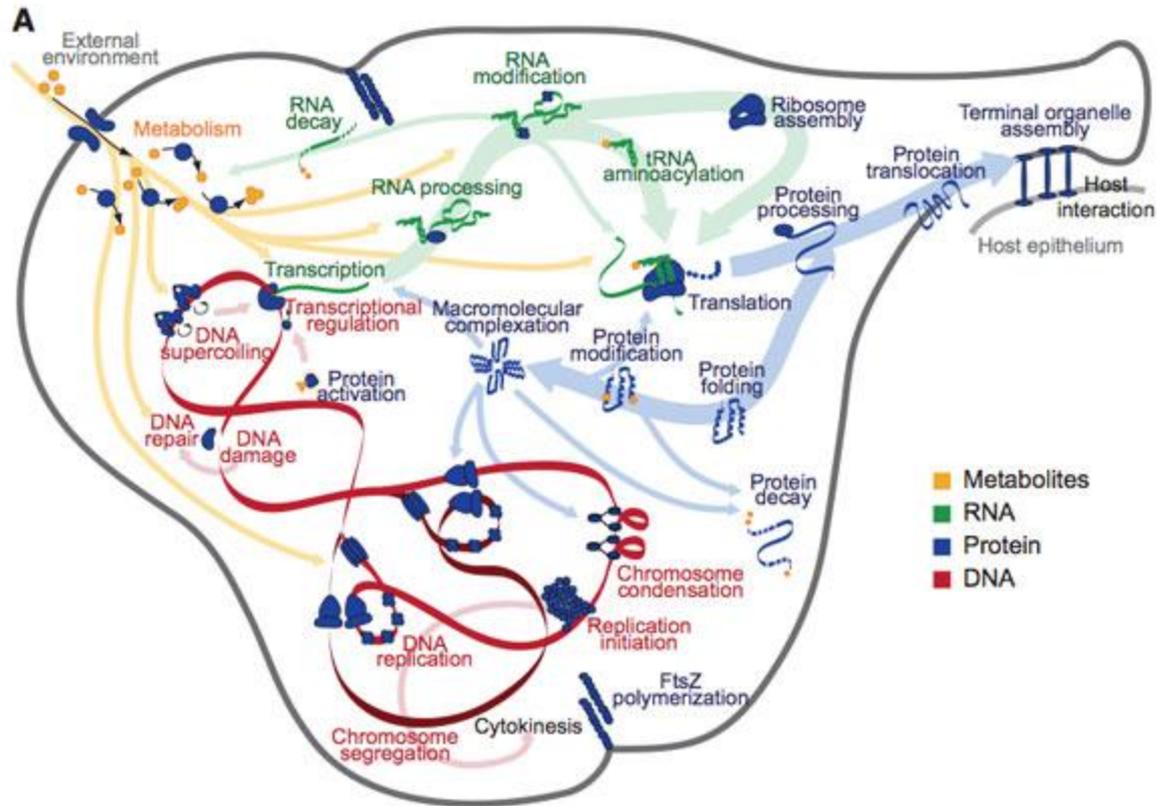
# How about biology?

- Can we understand and predict biology in the same way?
- Challenges
  - **Alien technology**
    - Gathering data is hard
    - Understanding data is even harder
  - **Multiscale problem**
    - Multiple algorithms involved
    - Different level of abstractions
    - Different skillsets needed

# Multiscale alien technology

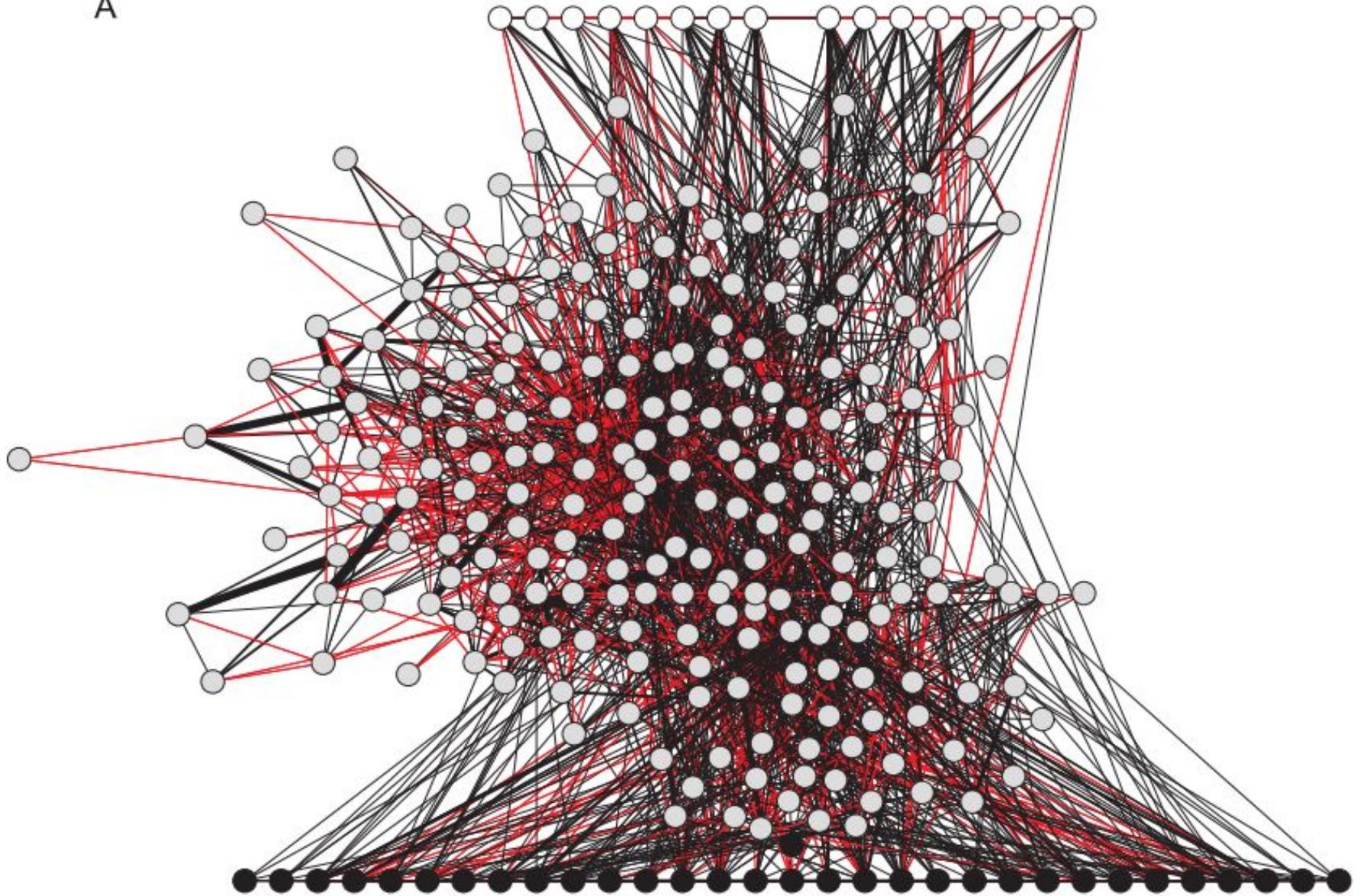


# Mycoplasma Genitalium



A Whole-Cell Computational Model Predicts Phenotype from Genotype (Karr et Al., Cell 2012)

A



C. elegans: White nodes are chemosensory neurons, Grey nodes are interneurons, Black nodes are neck motor neurons, red lines are gap junctions, black lines are chemical synapses

## The hard question

How much physics and biology do you have to include in your model before you can explain all the behaviours of the organism?

# Meet OpenWorm

Open science project aimed at creating a full scale model of the *C. elegans*, a tiny worm.



We are building the first digital life form.



# OpenWorm's Goal

Long term

Full scale **simulation** of **C. elegans**

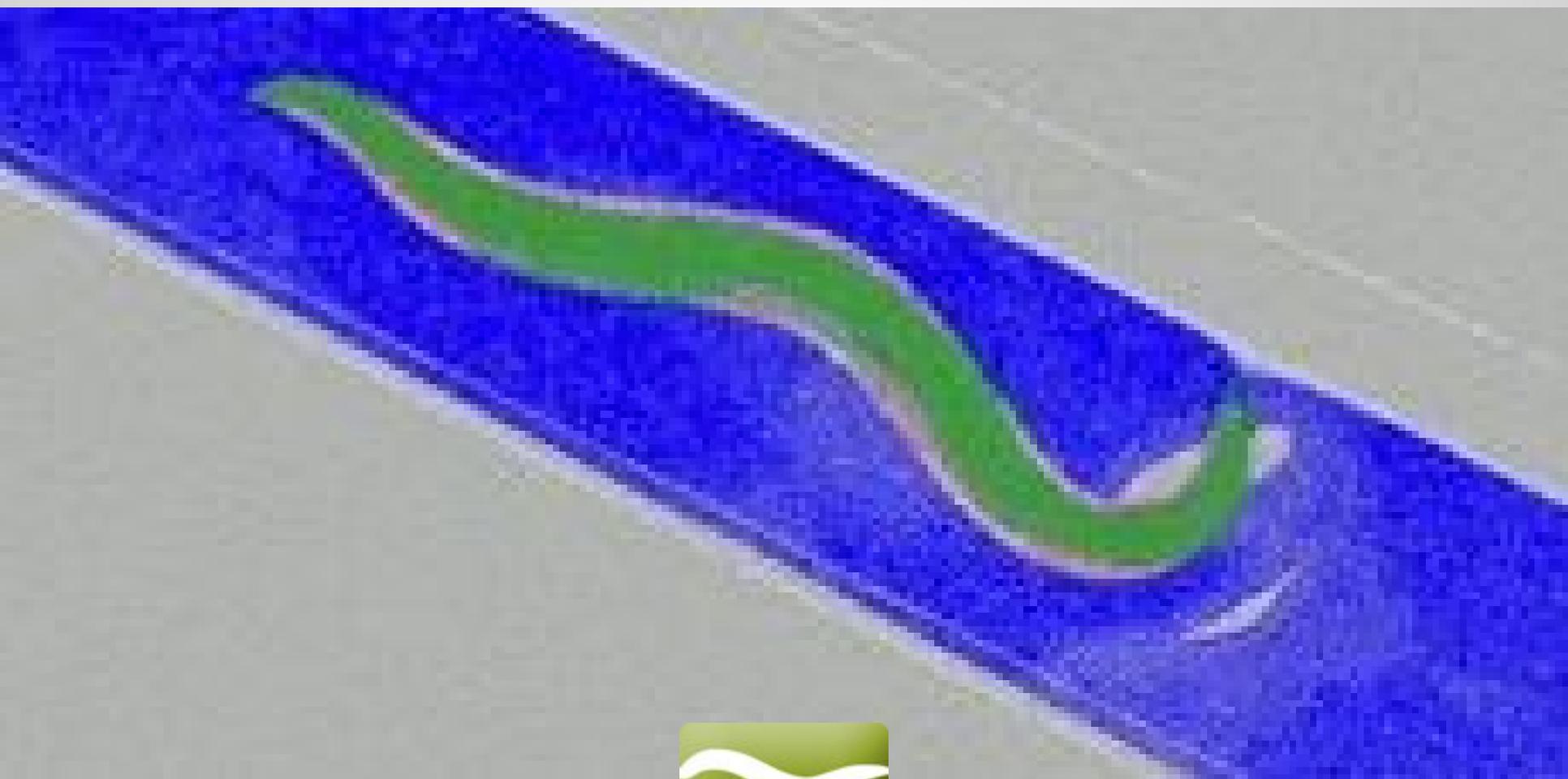
Medium term

Accurately predict **WormBehavior** database  
using data-driven, cell-by-cell **3D**  
**neuromechanical model**

*Szigeti et al, - Front. Comp. Neuro., 2014*

# Why the *C. elegans*?

- Wide range of behaviours
  - Locomotion, feeding, reproduction
  - Learning, mating, social behaviours
- How does it do it?
  - 1mm long
  - 302 neurons
  - 956 cells in total
- The first organism to have its genome **fully sequenced**
  - 100 million base pairs
    - 3 billion in mouse and humans

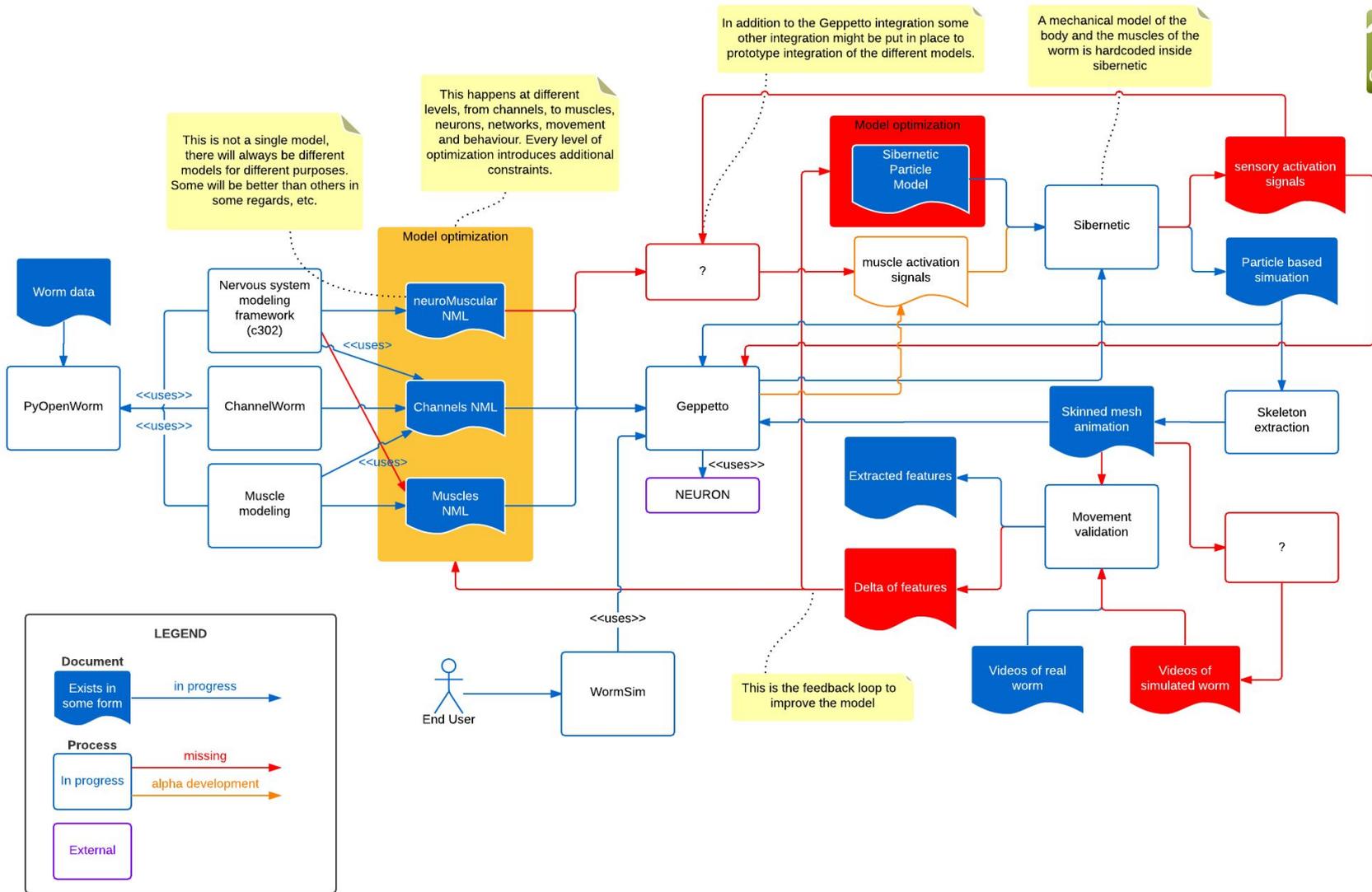


# Why?

- Increase our understanding of the biology of an organism as a whole
  - How does nature solve complex problems?
  - How do we program intelligence?
  - How can we build better drugs in a more efficient way?
  - How does life work?

# How do we do it?

- Open science model
  - Foster collaboration between different research groups and individuals
  - Reach out to different skillset
    - Scientists in academia
      - Biochemists, biologists, neuroscientists, computationalists
    - Engineers working in the industry
    - Curious citizen scientists



# OpenWorm open science community

- Independent international **open science** community
  - 9 **core** members
  - 20 **active members** & 40 **additional contributors** across 14 **countries**
- Networked science
  - >35 **Git repositories**
  - ~350 **mailing list** members
  - Streamed 40+ online meetings last year on YouTube
- Collaborative open source construction
  - Every line of code committed to GitHub
    - MIT Licensed

**How did we start?**



**Whole Brain Catalog**

@BrainCatalog

1 Jan 10

Do you have your new year's resolution figured out?



**Giovanni Idili**

@John\_Idol

 Follow

[@BrainCatalog](#) new year's resolution: simulate the whole C.Elegans brain (302 neurons)!

9:14 PM - 1 Jan 2010

   1



**Whole Brain Catalog**

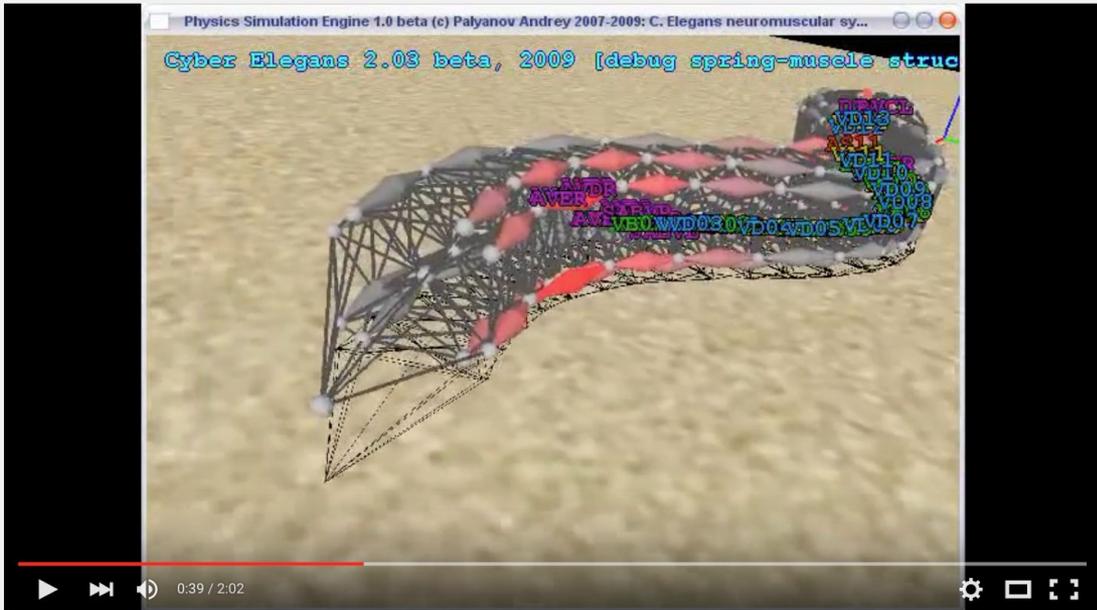
@BrainCatalog

 Follow

Nice! RT [@John\\_Idol](#): [@BrainCatalog](#) new year's resolution: simulate the whole C.Elegans brain (302 neurons)!

9:31 PM - 1 Jan 2010

   1



c\_elegans.avi



Andrey Palyanov

33

14,443

Up next

Autoplay

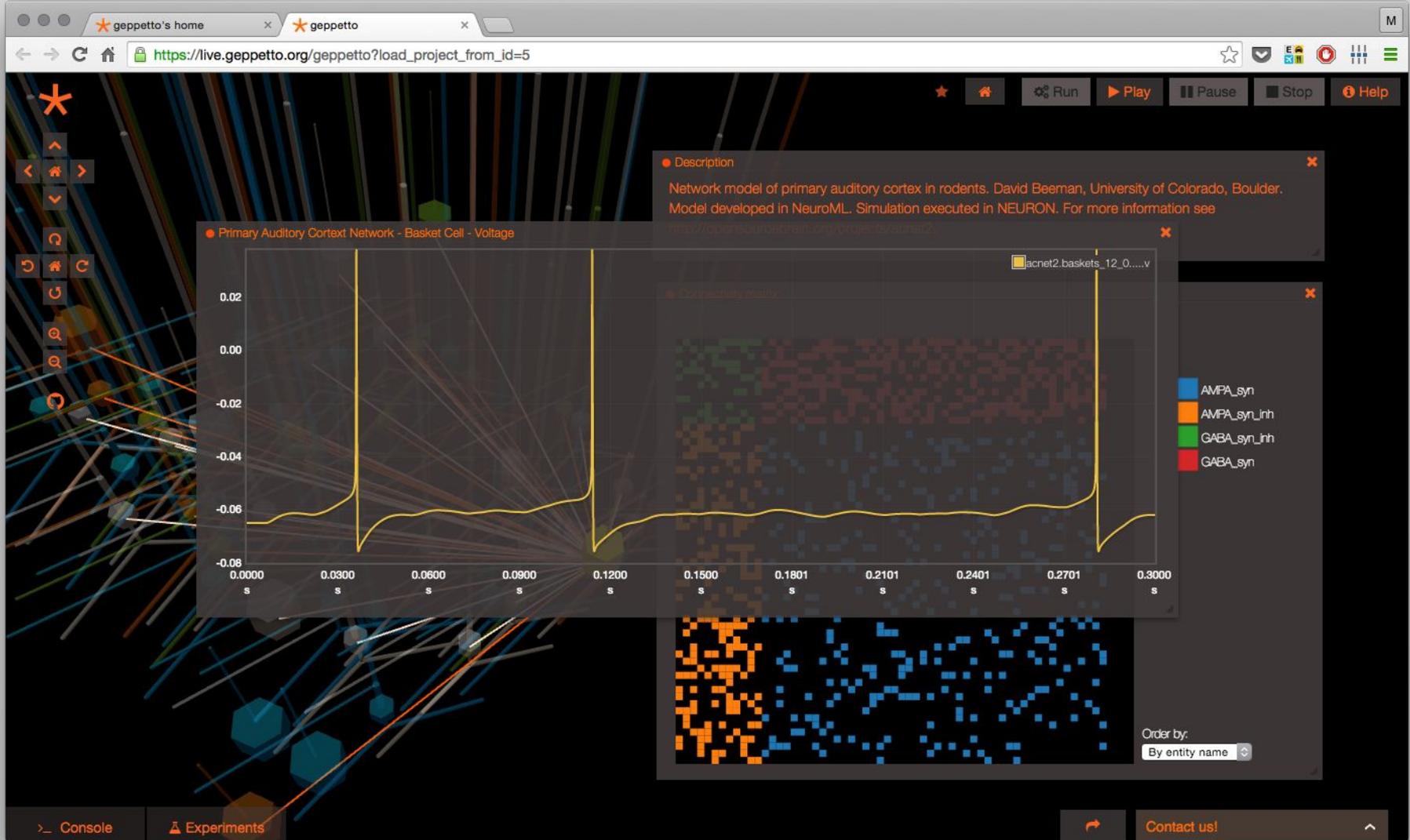
- Online Developmental Biology: Introduction to C. elegans**  
by Jason Pelletieri  
14,926 views
- Искусственная нервная система уже готова**  
by КристоРус - крионика в России  
13,629 views
- КиВиАИ - Дмитрий Дзюба - Нейронные сети**  
by grammariylabs  
6,859 views
- Ridley Scott's THE MARTIAN Viral Trailer (Science Fiction - 2015)**  
by Fresh Movie Trailers  
Recommended for you
- Нейронные сети - Временные ряды**  
by StatSoftRussia  
5,285 views
- Нейронные сети - Классификация**  
by StatSoftRussia  
3,089 views
- Embryonic development of C. elegans**  
by Hymanlab  
12,831 views

**How do we simulate a digital  
organism?**





- Web-based simulation **platform**
  - Support of multi-algorithm and multi-scale models
    - Neuroscience
    - Dynamical systems
    - Fluid dynamics
  - Allow for collaborative modeling
- Biggest scientific challenge is **lack of data and models**
  - Geppetto goal is to be completely **data driven**: new data and models can be fed to a simulation as they become available in a **standard** format



# What does Geppetto do?

- Provides a Web application to control the simulation through a web browser
- Provides a way to define what needs to be simulated in a data driven way
- Defines interfaces to allow third party simulators and model interpreters to extend the platform
- Provides a way to stream simulated data from the server to the client

# What does Geppetto do? (2/2)

- Provides a 3D engine to visualize in the browser what is being simulated
- Provides a way to define multiple computational experiments for a given model, allowing the user to change its parameters
- Provides an API to interact with the simulators in real time
- Provides an extensible widgets infrastructure to visualize and interact with the data

# How is it being developed?

Open Source, **MIT** License

Growing community

Bi-weekly Google Hangout open meetings

Open process

Regular Monthly Releases

(latest 0.2.5 alpha)

openworm/org.geppetto x MetaCell

GitHub, Inc. [US] <https://github.com/openworm/org.geppetto>

# Geppetto

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[Website](#) | [Documentation](#) | [Install Instructions](#) | [Releases](#)

[Contribution guidelines](#) | [Development progress](#)

Geppetto is a web-based multi-algorithm, multi-scale simulation platform engineered to support the simulation of complex biological systems and their surrounding environment.

Although Geppetto was designed with systems biology in mind, thanks to its generic architecture Geppetto can be used anywhere there is need to rely on a backend to perform any kind of simulation which then needs to be streamed to a web client, allowing the user to interact with the simulation remotely and through an API (accessible from an embedded Javascript console) and a set of customisable widget which allows visualising data in different ways.

Geppetto is a modular platform based on Java, OSGi and Spring and different modules (also named bundles) provide different functionalities.

This is the umbrella project that keeps together all the different modules currently available:

- Essential
  - [org.geppetto.core](#) build passing
  - [org.geppetto.simulation](#) build passing
  - [org.geppetto.frontend](#) build passing
- Domain Specific
  - Neuronal simulation
    - [org.geppetto.model.neuroml](#) build passing
    - [org.geppetto.simulator.jlems](#) build passing
  - Fluid mechanics simulation
    - [org.geppetto.model.sph](#) build passing
    - [org.geppetto.solver.sph](#) build passing
    - [org.geppetto.simulator.sph](#) build passing

Geppetto is an open-source project with a growing community, if you want to contribute (with either new simulators support, visualisation widgets or backend magic) please do get in touch at [info@geppetto.org](mailto:info@geppetto.org) or fork any of the bundles and do what you please.

[Website](#) | [Documentation](#) | [Install Instructions](#) | [Releases](#)

[Contribution guidelines](#) | [Development progress](#)

<https://github.com/openworm/org.geppetto>

openworm/org.geppetto x

MetaCell

https://waffle.io/openworm/org.geppetto

openworm/org.geppetto + Add Issue Filter Board

Ideas 39 58 Backlog 84 145 To do 16 57 In Progress 11 156 Needs review 15 58 Done 7 33

390 Main Eclipse plugin for installing and configuring geppetto

91 Skeleton extraction Making skeleton extraction very fast - maybe almost in real-time enhancement

366 Main Add attribute to Geppetto to optionally specify what to load

365 Main Add individual methods for known widgets enhancement

364 Main Add console option to change background colour from black in main 3D view enhancement

241 Frontend Drawing synaptic connections

309 Main Integrate NSDF format for neuroscience recordings

273 Frontend Tree visualizer right click menu for cell in network

65 Model-NeuroML Extra cell in ModelTree

42 WormSim The user must be logged in into wormsim to open wormsim custom geppetto instance bug wormsim

48 WormSim Review WormSim bug wormsim

378 Main Define API for time series/VariableNode design

259 Frontend VisualReferences in Connection Lines

263 Main Update how 3D objects are referenced enhancement

294 Main

391 Main Review Variable Watch changes Sprint 49

9 Main Compression of data transfer between server and client Sprint 49 enhancement

387 Main Release 0.2.3 Sprint 49

41 WormSim Implement logic from "submit" button on landing page Sprint 49 wormsim

46 WormSim Map model entity names to recording entity names wormsim

58 Core Update Javascript API to allow for calling conversion services

313 Main Design Export feature for a ModelInterpreter design

367 Main Centralize list of model formats in

388 Main Error in display of cell positions Sprint 49 bug

331 Main Add display of time global variable & scale bar on x axis of plots Sprint 48 bug

5 External simulator Finalise variable watch for external simulator Sprint 49

47 WormSim Style WormSim wormsim

379 Main Refactor simulation backend to add support for visual transformations in recordings Sprint 49 wormsim

376 Main Refactor run simulation workflows Sprint 48

248 Frontend Network activity widget design Sprint 49

380 Main Error Code: INITIALIZATION

66 Model-NeuroML Domain info

272 Frontend List watchable variables

68 Core List watchable variables

87 Simulation List watchable variables

67 Model-NeuroML List watchable variables

44 Simulator-jLEMS List watchable variables

36 Test backend List watchable variables

29 Samples List watchable variables

53 Solver-SPH

386 Main SetParameters frontend implementation Sprint 49

385 Main SetParameters backend implementation Sprint 49

1 Recording Add support for matrices

269 Frontend Extend widget API

389 Main Latest development version failing: org.geppetto.core.features.Feature not found Sprint 49 bug

382 Main Review Sprint 48 Sprint 48

384 Main Error in connectivity widget for ACNet Sprint 48 bug

<https://waffle.io/openworm/org.geppetto>

## How do I use it?

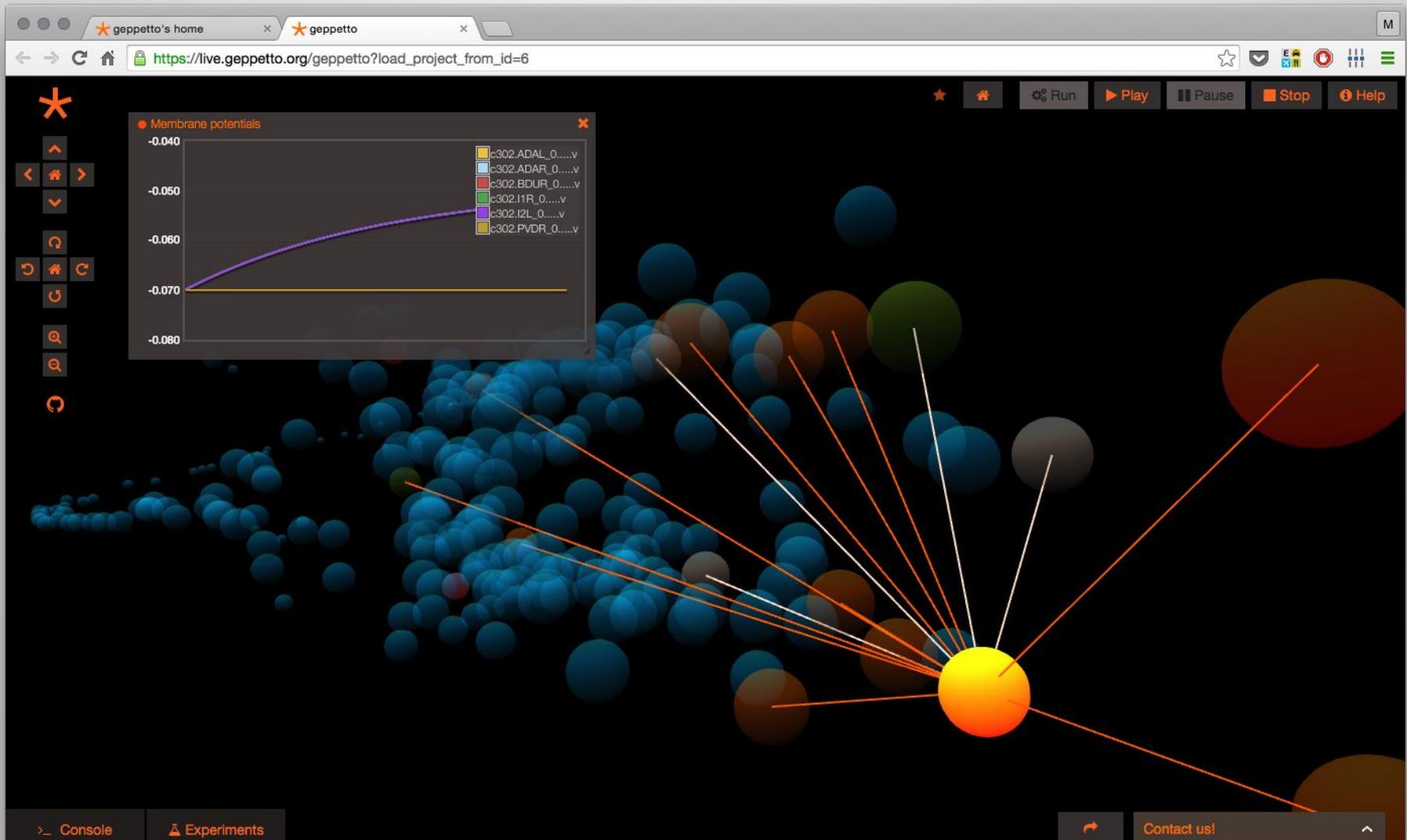
<https://live.geppetto.org>

<http://www.geppetto.org>

<http://docs.geppetto.org>

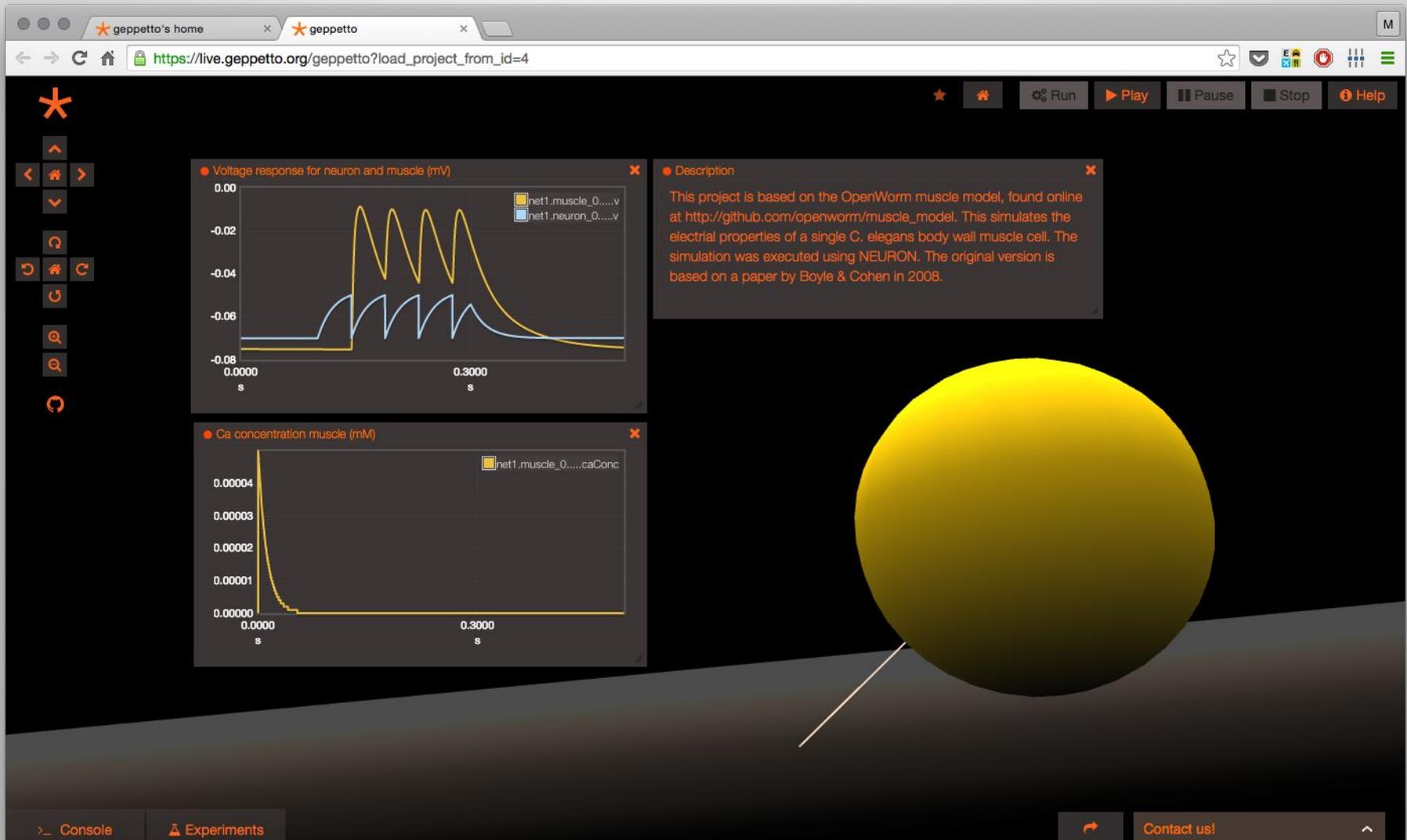
<https://github.com/openworm/org.geppetto>

# c302 generated network



<https://github.com/openworm/CElegansNeuroML/tree/master/CElegans/pythonScripts/c302>

# Model of a C. elegans muscle



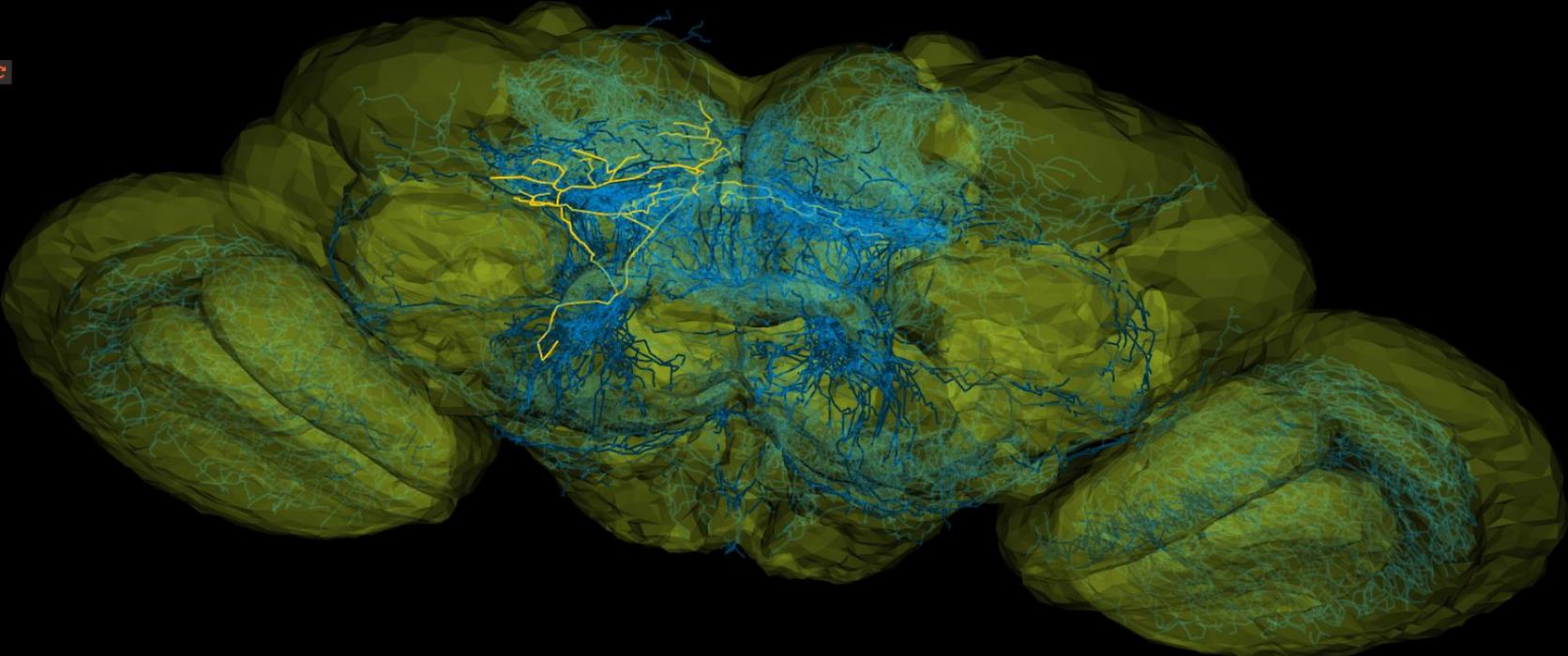
[http://github.com/openworm/muscle\\_model](http://github.com/openworm/muscle_model)

geppetto

127.0.0.1:8080/org.geppetto.frontend/geppetto?load\_project\_from\_url=SERVER\_ROOT/appdata/vfb/brain/brainTdc.json

Run Play Pause Stop Help

58 FPS (40-60)



> Console Experiments Contact us!

The image shows a 3D visualization of a brain model with a complex network of fibers overlaid. The brain is rendered in a greenish-yellow color, and the fibers are primarily blue and yellow. The visualization is displayed in a web browser window with a dark theme. The browser address bar shows the URL: 127.0.0.1:8080/org.geppetto.frontend/geppetto?load\_project\_from\_url=SERVER\_ROOT/appdata/vfb/brain/brainTdc.json. The interface includes a top navigation bar with a star icon, a 'Run' button, a 'Play' button, a 'Pause' button, a 'Stop' button, and a 'Help' button. A status bar in the top right corner displays '58 FPS (40-60)'. On the left side, there is a vertical toolbar with various navigation and interaction icons. At the bottom, there are buttons for 'Console', 'Experiments', and 'Contact us!'.

# WormSim

WormSim

org.geppetto.frontend/geppetto?load\_project\_from\_url=SERVER\_ROOT/appdata/wormsim/wormsim-project.json

Play Pause Stop

Muscle selection

DR4 DR16 VR12 VR20

Cuticle / Muscles toggle

~ Cuticle Muscles

Nonna / C. elegans mechanical simulation

The WormSim mechanical model is a model of the muscular system of the C. elegans worm. The simulation is based on a Smooth Particle Hydrodynamics (SPH) reconstruction of the body and muscles of the worm.

Guided tour

Hi Matteo Cantarelli! It's me, Nonna, crawling around! Welcome to WormSim! Hit 'next' below to start my guided tour!

<-- PREV NEXT -->

Console Experiments

<http://wormsim.org>



OpenWorm: A Digital Organism In Your Browser



OpenWorm is building the first complete simulation of an entire organism and bringing it to your web browser

[Add link](#)

Created by  
OpenWorm 

**799 backers** pledged \$121,076 to help bring this project to life.

WormSim x wormsim.org

Login



OpenWorm



# WormSim

[Tweet](#) [Share](#) [Share](#) [Share](#)

Request

Request an invitation. [Why?](#)

Explore a digital organism!

Play with OpenWorm in your browser!

Create & customize your own WormSim!

(c) 2011-2015 OpenWorm - All rights reserved. Code licensed under MIT, documentation under CC BY 3.0.



wellcome trust



Caltech



UC San Diego



### Core team



Our Superheroes.

- |                 |                  |                |              |                   |                |
|-----------------|------------------|----------------|--------------|-------------------|----------------|
| Andrey Palyanov | Balazs Szigeti   | Giovanni Idili | Jim Hokanson | Matteo Cantarelli | Michael Currie |
| Padraig Gleeson | Sergey Khayrulin | Stephen Larson |              |                   |                |

### Contributors



Helping us with amazing support. Thanks!

- |                   |                 |                   |                  |                   |                  |
|-------------------|-----------------|-------------------|------------------|-------------------|------------------|
| Abdullah Haroon   | Adrian Quintana | Alexander Dibert  | Alexander N      | Allie Love        | Andrew Leifer    |
| Andrew Papadopoli | Ari Richman     | Bóris Marin       | Bradley Alicia   | Charles Cooper    | Christian Grove  |
| Chris Jensen      | Christina Lee   | Christopher Perez | Credentiality    | Crystin Slade     | Dan Knudsen      |
| Dan Kruchinin     | David Dalrymple | Deanne Taylor     | Dmitriy Shabanov | Dmitar Shterionov | Dominic Denicola |
| Domenico Luciani  | Ellen McGowan   | Eviatar Yemini    | Gaston Gentile   | Gleb Kuznetsov    | Jay Coggan       |
| Jesus Martinez    | Joe Bowen       | Johannes Rieke    | John Hurliman    | John White        | Jordan Boyle     |
| Jinze Yu          | Marius Buibas   | Mariusz Sasinski  | Mark Watts       | Martin Madaras    | Matt Olson       |
| Mike Vella        | Mei Zhen        | Nathan Daly       | Netta Cohen      | Pedro Tabacof     | Peter McCluskey  |
| Petr Baudis       | Phil McElmurray | Rayner Lucas      | Richard Gordon   | Rich Stoner       | Rick Gerkin      |
| Steven Cook       | Steve McGrew    | Timothy Busbice   | Travis Jacobs    | Vanessa Adelman   | Vahid Ghayoomi   |

# Modelling the brain, together

**Open Source Brain** is a resource for sharing and collaboratively developing computational models of neural systems.

[Explore OSB](#)[Sign up](#)

Join us at the [Open Source Brain kickoff meeting](#) in Alghero, Sardinia in May 2013!

# Open Source Brain

- Open Source Brain is a resource for **sharing** and collaboratively **developing** computational models of neural systems.
  - Encourage the use of **open standards** such as NeuroML and PyNN, to ensure transparency, modularity, accessibility and portability
  - Provide advanced facilities to analyse, visualise and transform models
  - Helps **connecting** researchers interested in models of specific neurons, brain regions and disease states.



# The idea behind Open Source Brain

- Increasingly detailed single neuron and network models are becoming available
- Complex models take a **long time** to develop and are normally only available in one of many incompatible, **simulator specific** formats.
- Enabling these to be **analysed, reused** and critically **evaluated** by as many researchers as possible will increase the power and scientific rigour of neuronal models and make them more accessible to a wider range of neuroscientists.



# Goals

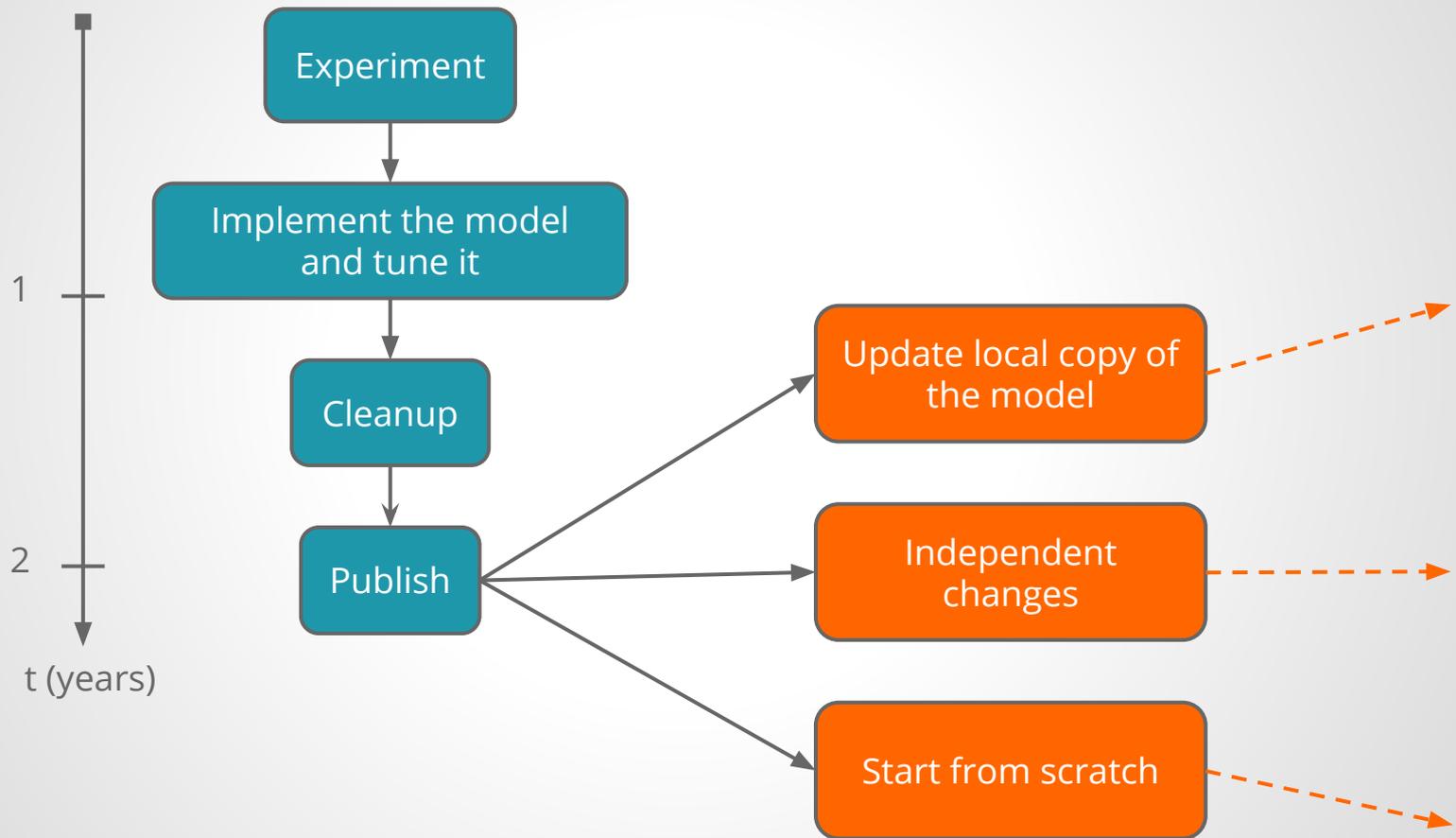


# Model development life-cycle

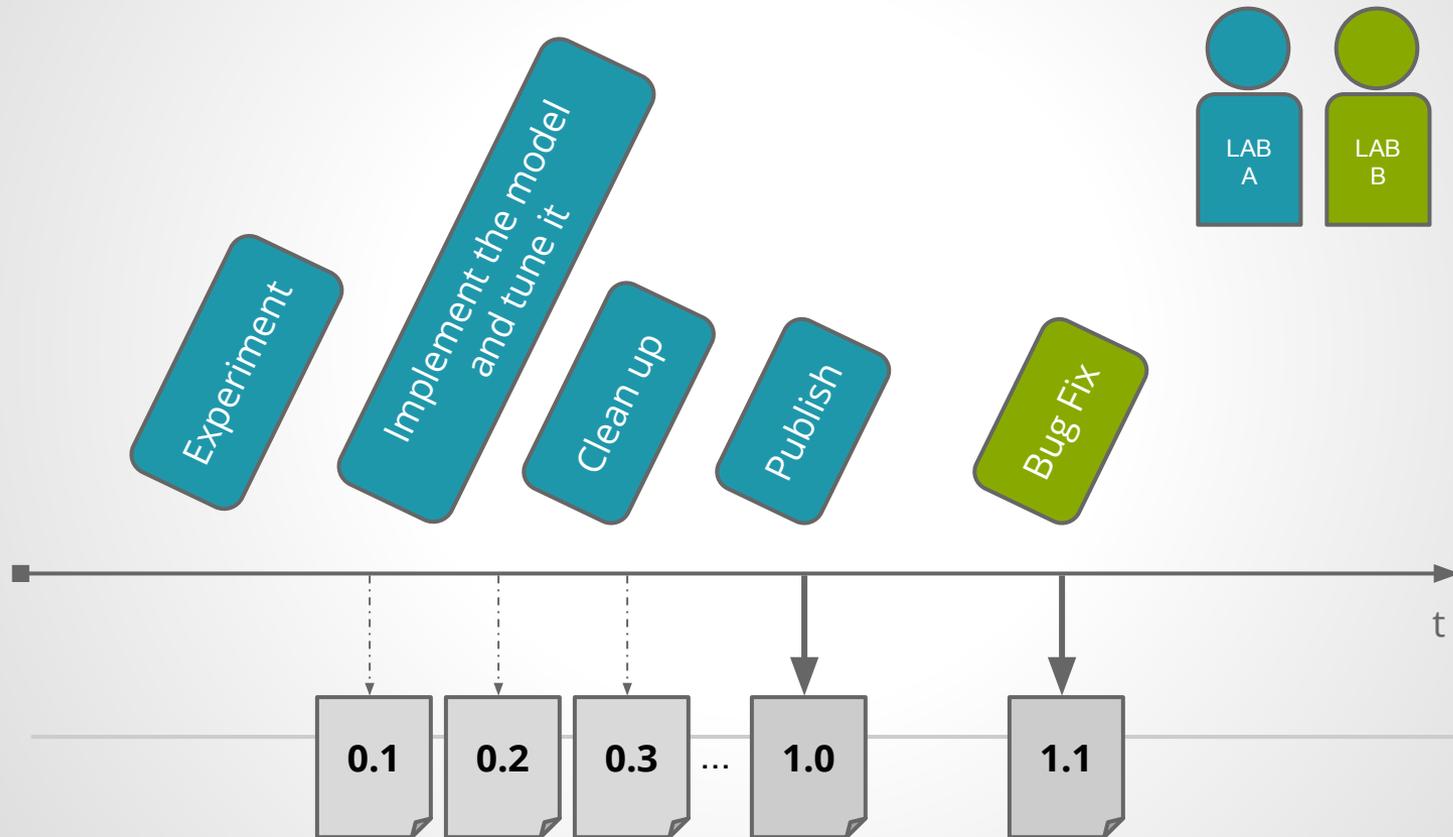
How are detailed neuronal models  
traditionally developed



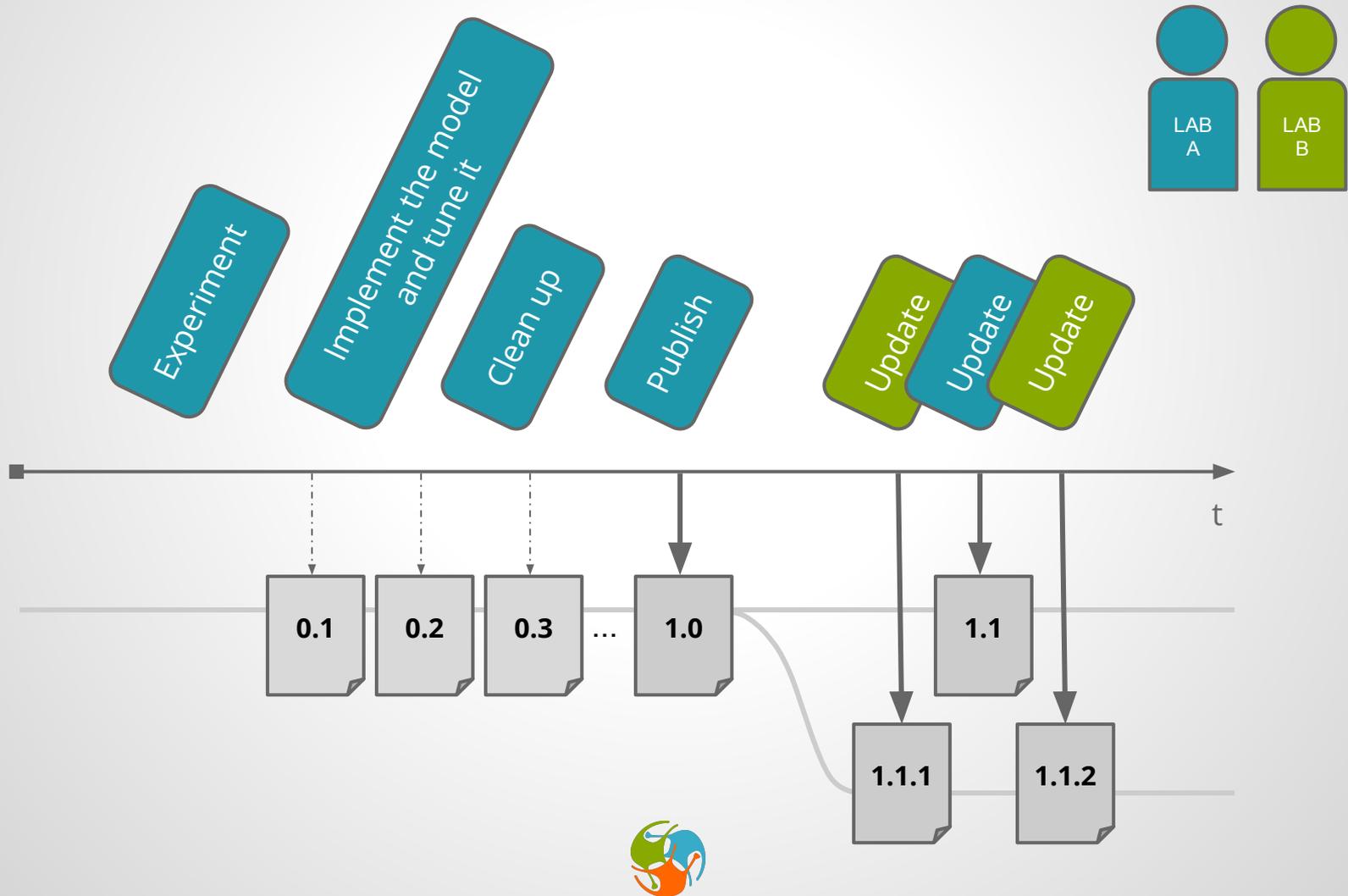
# Model development life-cycle



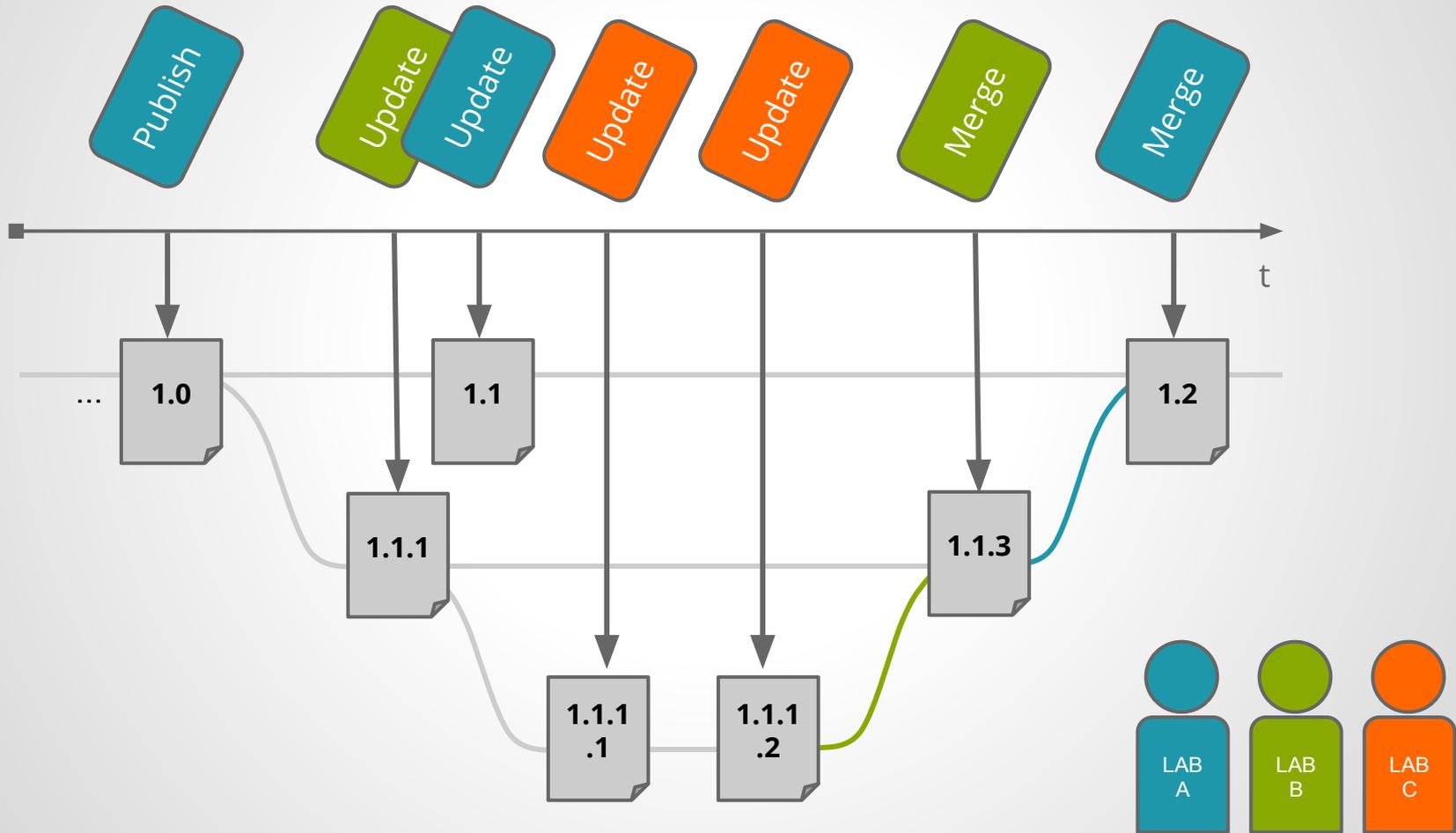
# Scenario 1: Bug fixing



# Scenario 2 - Parallel developments



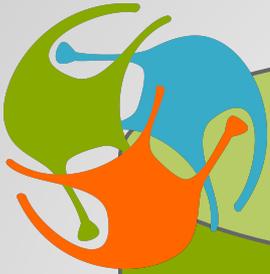
# Scenario 3 - Consolidation



# Model development life-cycle with OSB

- **Benefits**
  - Track all changes in the model since its creation
  - Allow anyone to comment on and **improve** the model
  - Convert to **simulator independent** formats
  - Facilitate and track **reuse** of model elements between models
- **Cons?**
  - Learn source-control
  - People are looking at my model!





## OSB Model Repository

Version 0.1

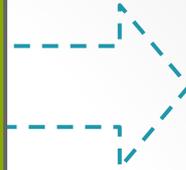
Version 0.n

Version x.x

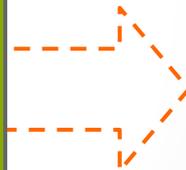
Updated model components



NeuroML model



**VISUALISE**



**SIMULATE**



**VALIDATE**

# Hello Matteo

[Explore OSB](#)

-  8 days ago  
**Matteo Cantarelli** edited **The Open Source Brain repository**  
 Wiki edit: [Meetings \(#34\)](#)

---

-  2 months ago  
**Matteo Cantarelli** edited **The Open Source Brain repository**  
 Wiki edit: [Meetings \(#20\)](#)

---

-  2 months ago  
**Matteo Cantarelli** edited **The Open Source Brain repository**  
 Wiki edit: [Meetings \(#19\)](#)

---

-  2 months ago  
**Matteo Cantarelli** edited **The Open Source Brain repository**  
 Wiki edit: [Meetings \(#18\)](#)

---

-  2 months ago  
**Matteo Cantarelli** edited **The Open Source Brain repository**  
 Wiki edit: [Meetings \(#17\)](#)

---

-  3 months ago  
**Matteo Cantarelli** edited **The Open Source Brain repository**  
 Feature #26 (Closed): [Breadcrumb trail on Project Overview page](#)  
Moved to GitHub

### Your projects

[+ New project](#)

-  [NeuroMorpho.org Showcase](#)
-  [OpenWorm C. elegans network model](#)
-  [Setting up a new project](#)
-  [TestProject](#)
-  [The Open Source Brain repository](#)
-  [VFB Showcase](#)

### Latest projects added on OSB

-  [SBMLShowcase](#)
-  [Multiscale Medium Spiny Neuron - Mattioni and Le Novere](#)
-  [Olfactory Bulb](#)



## Latest news

# Cerebellar Nucleus Neuron Steuber et al. 2011

OSB endorsed project 

Curation against published models: Low 

[Vertebrate](#) / [Mammalian](#) / [Rodent](#) / [Cerebellum](#) / [Cerebellar Nucleus Neuron](#) / Cerebellar Nucleus Neuron - Steuber et al. 2011

OSB Overview  OSB 3D Explorer  Activity Issues Wiki Forums Files Repository Model components

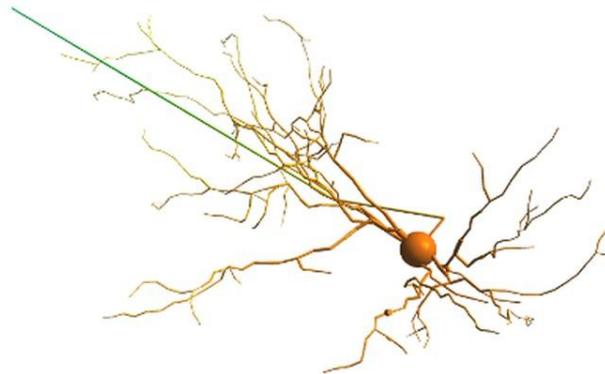
Description 

Status 

Members 

References 

## Description



[Deep cerebellar nucleus neuron](#) model from: Determinants of synaptic integration and heterogeneity in rebound firing explored with data-driven models of deep cerebellar nucleus cells. Steuber V, Schultheiss NW, Silver RA, De Schutter E, Jaeger D. J Comput Neurosci. 2011 Jun;30(3):633-58

[More...](#)

# 3D Olfactory Bulb Migliore et al. 2014

OSB endorsed project

Curation against published models: Low

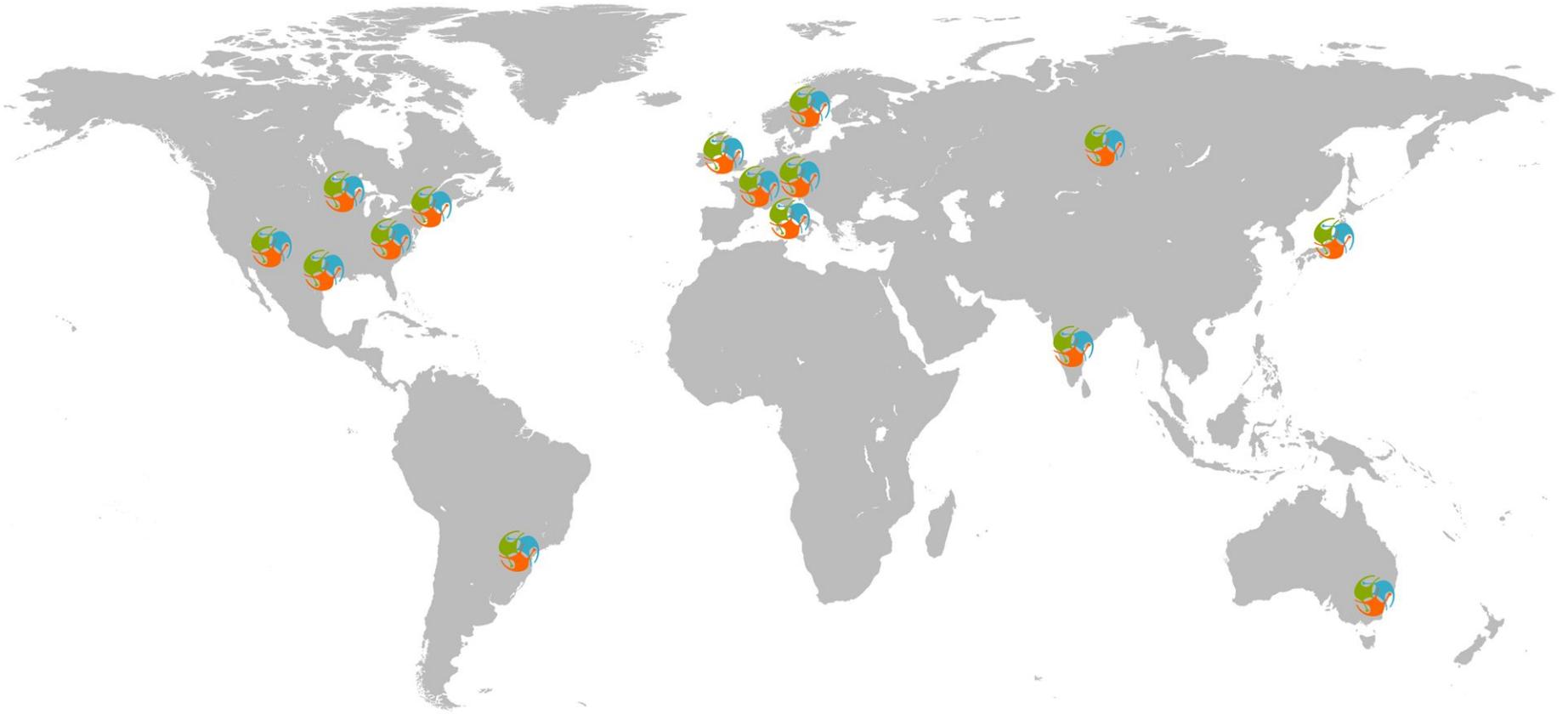
Vertebrate / Mammalian / Rodent / Olfactory bulb / Network model / 3D Olfactory Bulb - Migliore et al. 2014

Overview OSB 3D Explorer Wiki Other tools Settings

Full Screen

The image shows a 3D visualization of a neural network, likely representing the olfactory bulb. The network is composed of numerous blue lines representing axons and dendrites, forming a dense, interconnected structure. The visualization is displayed in a dark environment. Above the visualization, there is an "OSB Control Panel" with four tabs: "Connectivity", "Cell Info", "Channels", and "Cell Visual". To the right of the control panel, there is a toolbar with several icons: a star, a house, a gear labeled "Run", a play button labeled "Play", a pause button labeled "Pause", a stop button labeled "Stop", and a question mark labeled "Help". On the left side of the visualization, there is a vertical toolbar with various navigation and interaction icons, including arrows, a magnifying glass, and a refresh symbol.

**446** Members    **46** Research groups    **101** Projects



# Open Science Ecosystem



WormSim

\* geppetto

**Thanks for the attention!**

Matteo Cantarelli (@tarelli)  
fOSSA 2015