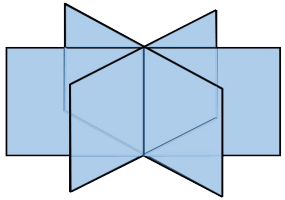
Process as Connectivity

towards biology-specific complex networks

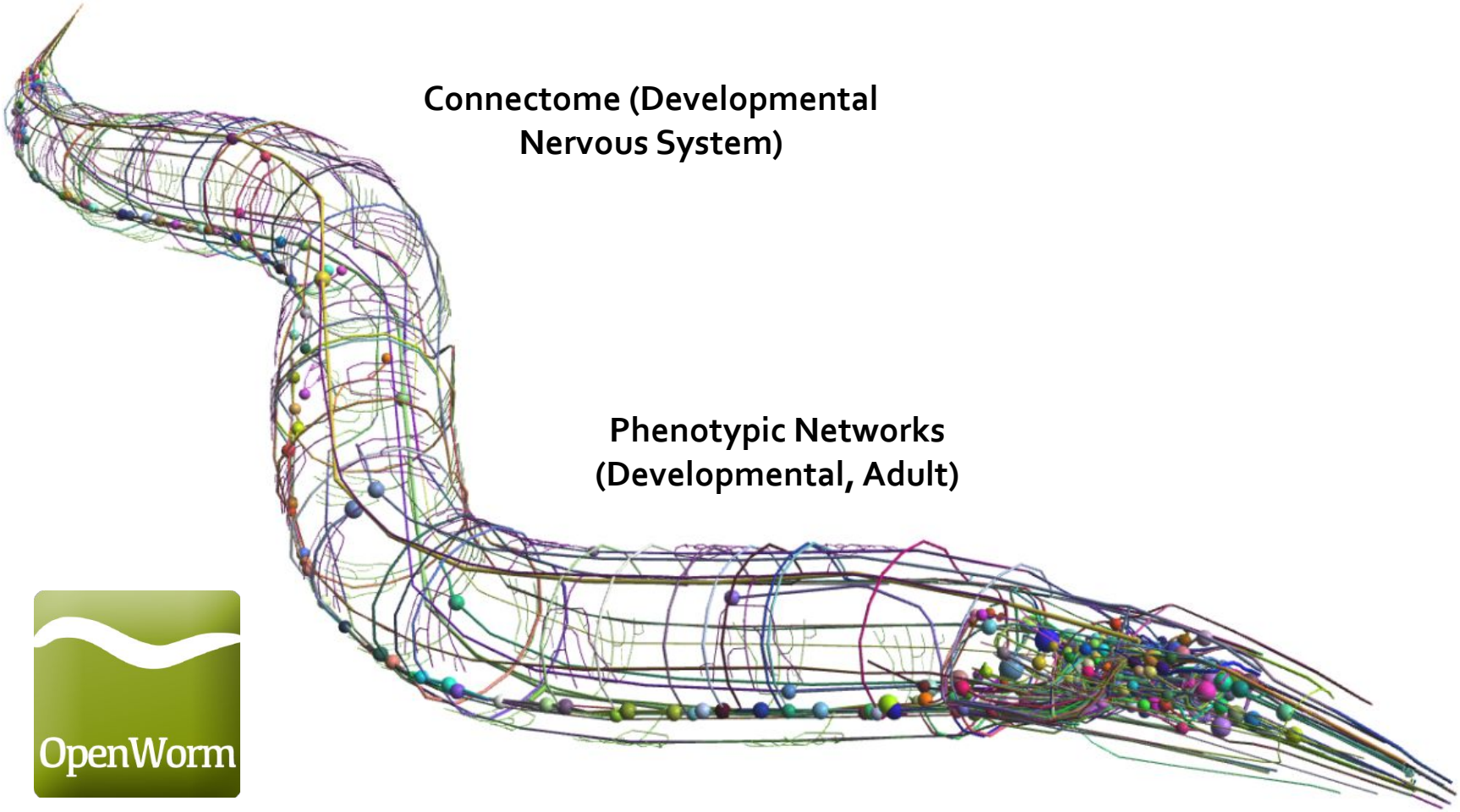


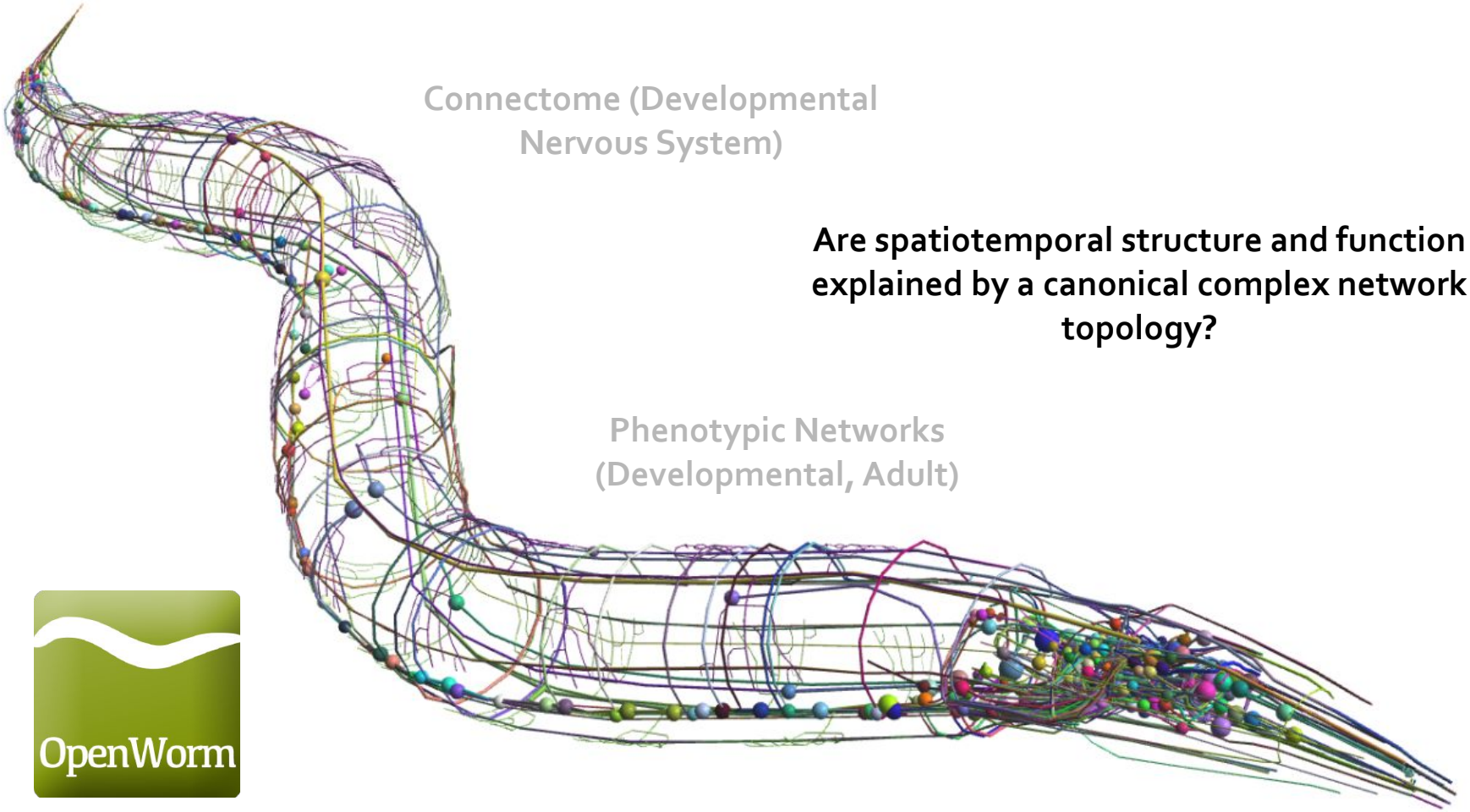
Orthogonal Research and Education Laboratory

Champaign-Urbana and Worldwide

Bradly Alicea

bradly-alicea.weebly.com


Connectome (Developmental Nervous System)
Phenotypic Networks (Developmental, Adult)
OpenWorm



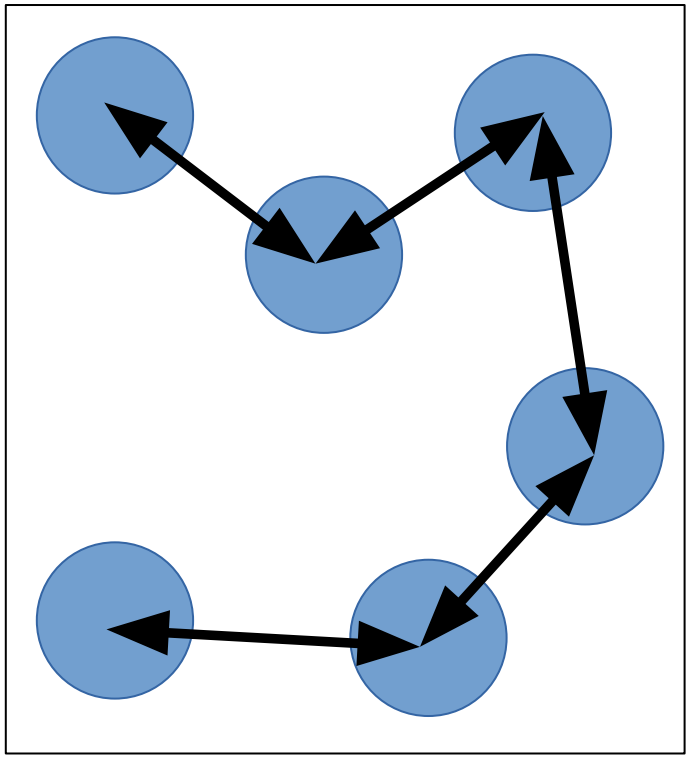
Connectome (Developmental Nervous System)

Phenotypic Networks (Developmental, Adult)

Are spatiotemporal structure and function explained by a canonical complex network topology?

OpenWorm

Embryo Networks



x,y,z,t,θ

3-D space

time and context

x,y,z,t,θ

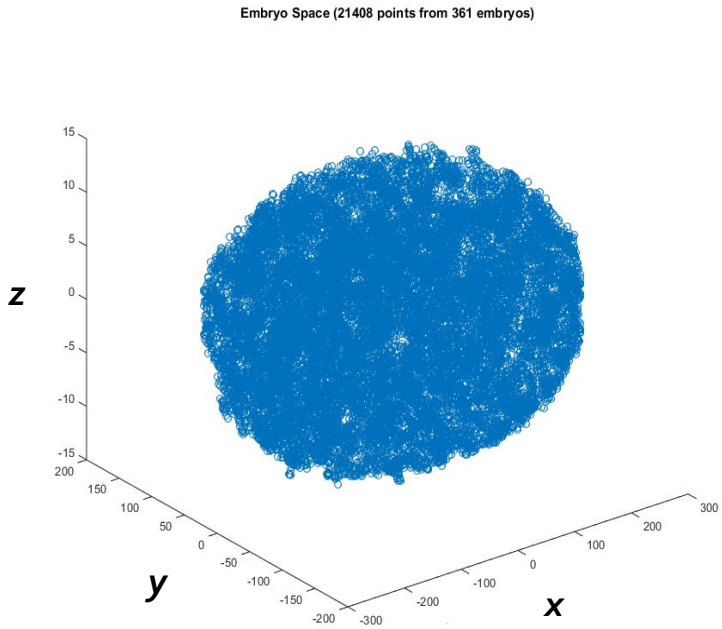
See our Jupyter Notebook for more information

GitHub

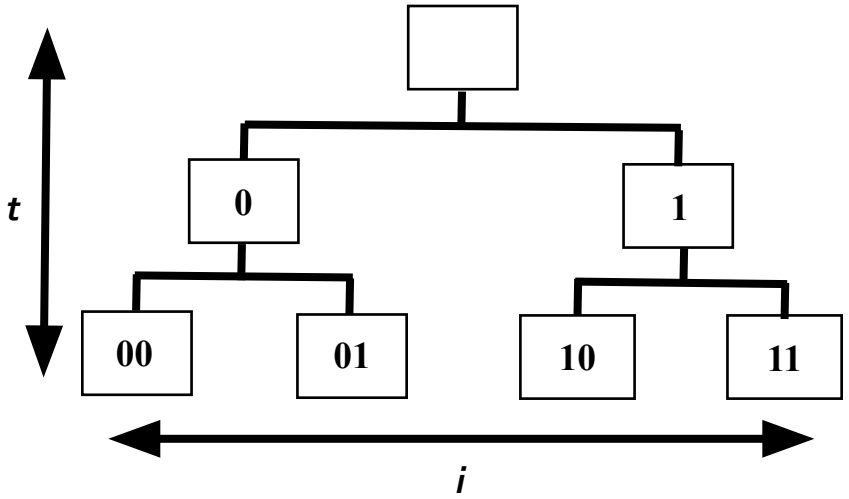
https://devoworm.github.io/

5-dimensional Data Structure

x, y, z, t, i

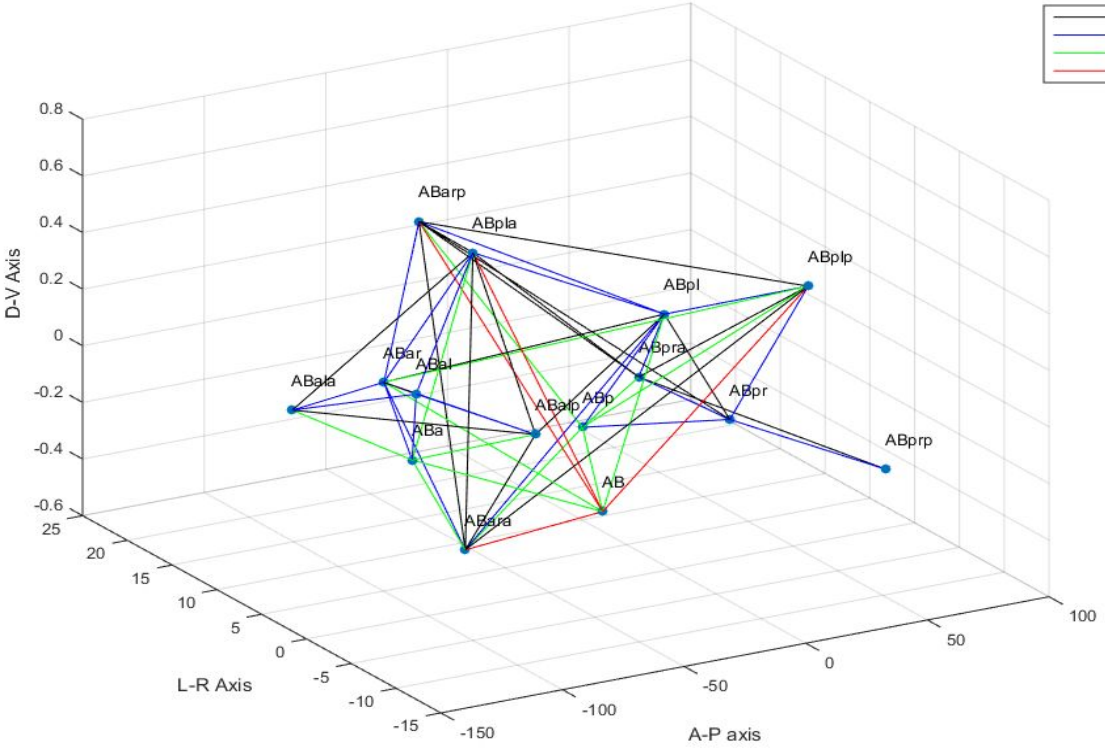


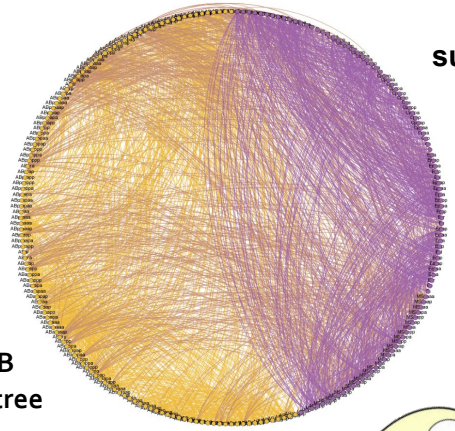
A generalized parameter space based on observations across *C. elegans* embryos (*x,y,z*)



A spatially-independent parameter space ordered by A-P axial order (*i*) and lineage time (*t,i*)

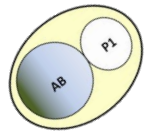
Spatial Connectivity (Interactome)

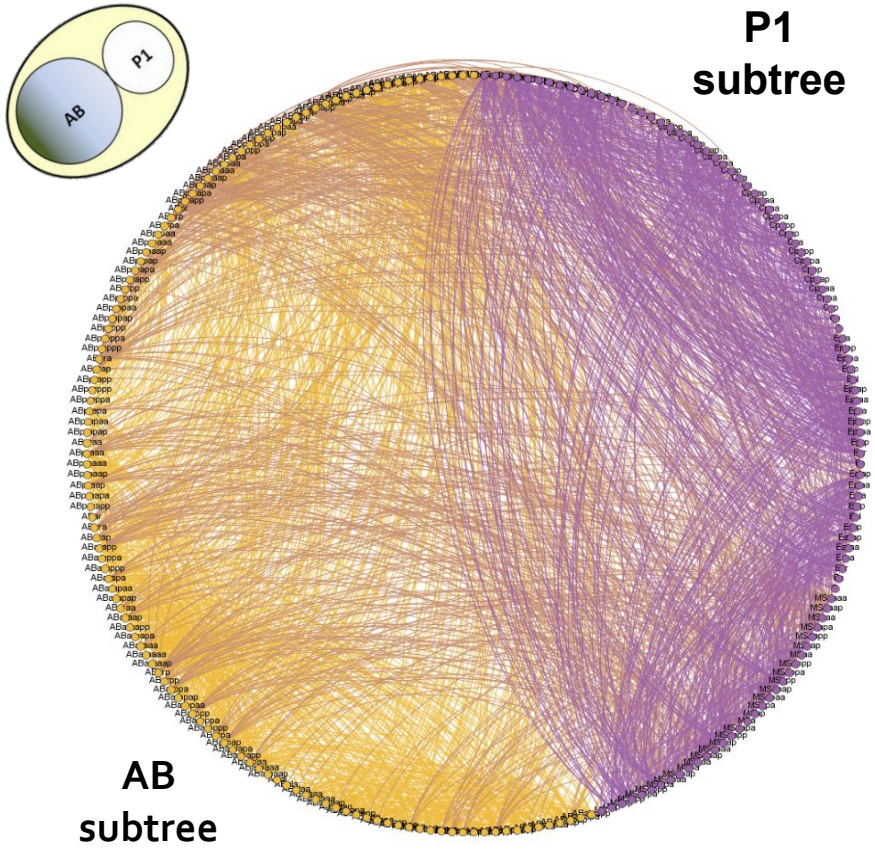




P1 subtree

AB subtree





Spatial Connectivity (Interactome)

Pairwise network that includes all cells from 3-layer tree to 8-layer tree (N = 224).

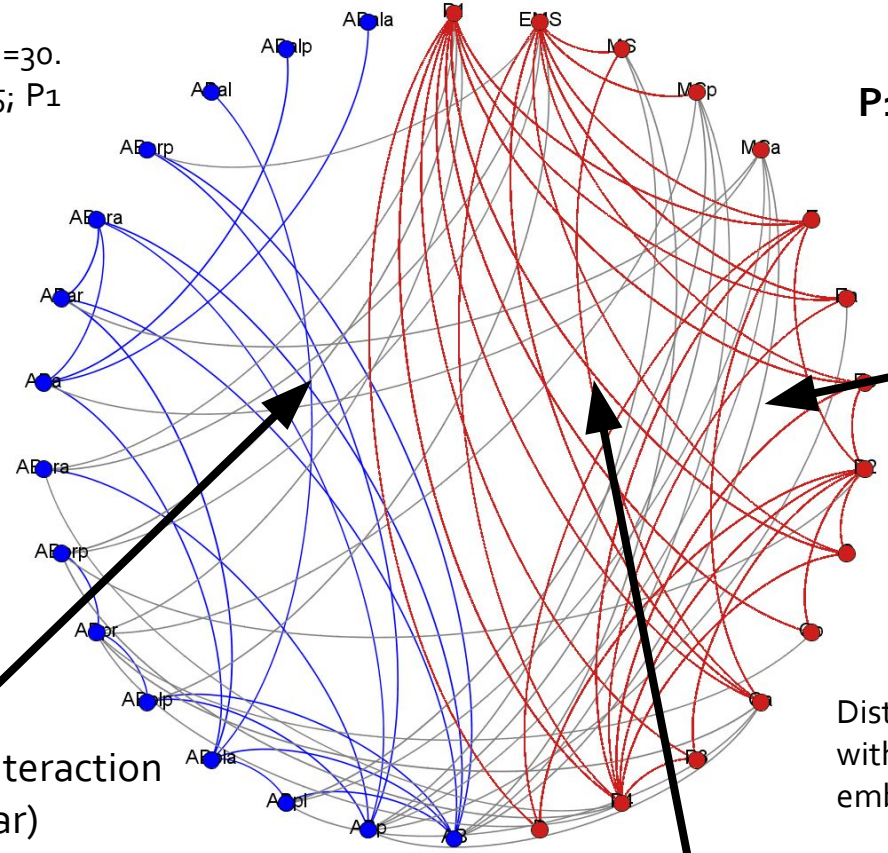
Distance threshold of 0.25 (all cells within 25% the maximum distance in embryo structure).

BioSystems, 173, 235-246 (2018).

Open Science Framework

"Embryo Networks" repository, https://osf.io/q9jvb/

4 level lineage tree: N=30. AB subtree (blue), *n*=15; P1 subtree (yellow), *n*=15.



P1 Subtree

Intra-subtree interaction
(P4, P2)

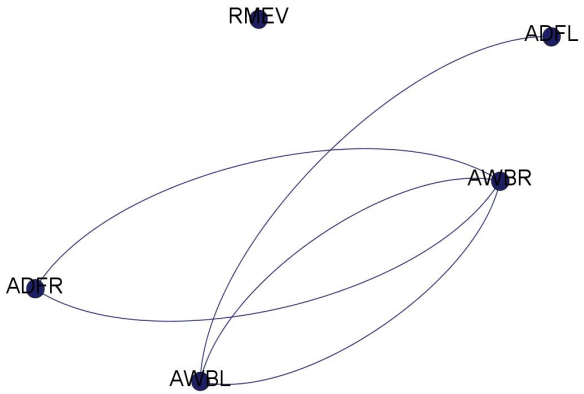
AB Subtree

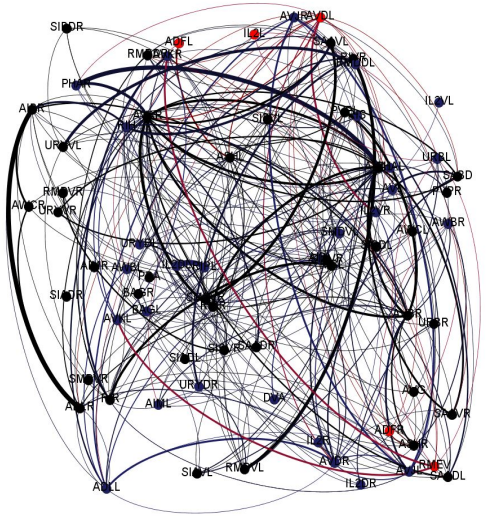
Intra-subtree interaction
(AB, ABar)

Distance threshold of 0.25 (all cells within 25% the maximum distance in embryo structure).

Inter-subtree interaction
(MSa, ABa)

Temporal Structure of Connectome Development

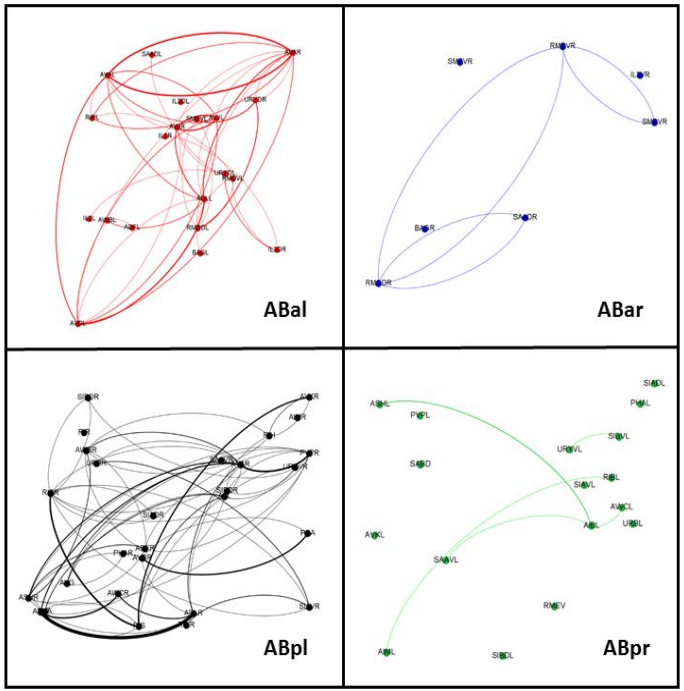


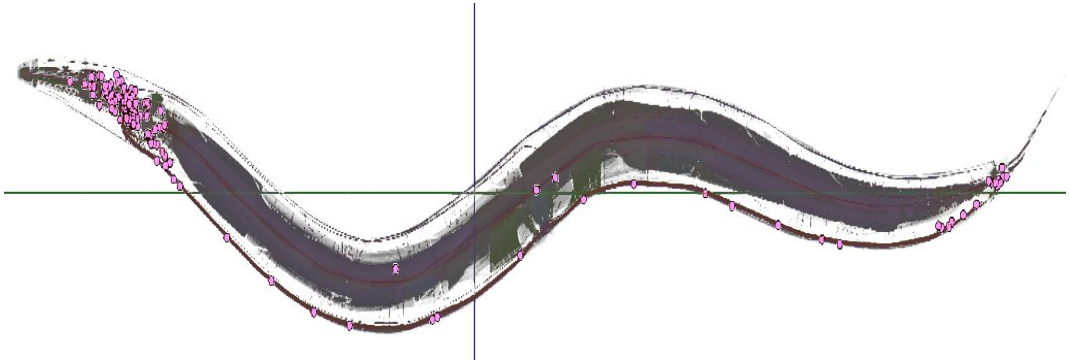


LEFT: adult connectome at 280 minutes post-fertilization. RIGHT: adult connectome at 300 minutes post-fertilization. Presence of terminally-differentiated cells pre- axonal outgrowth.

BioSystems, 173, 247-255 (2018).

Origin of Cells in Connectome Development

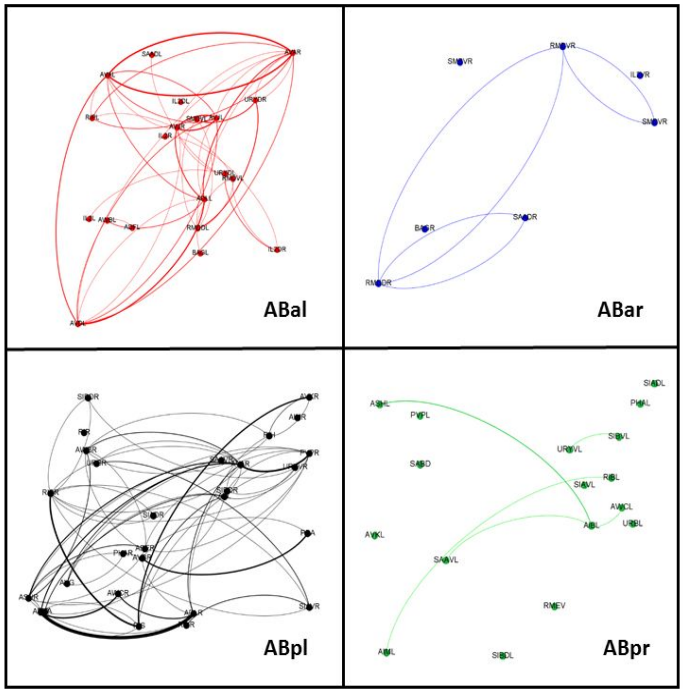


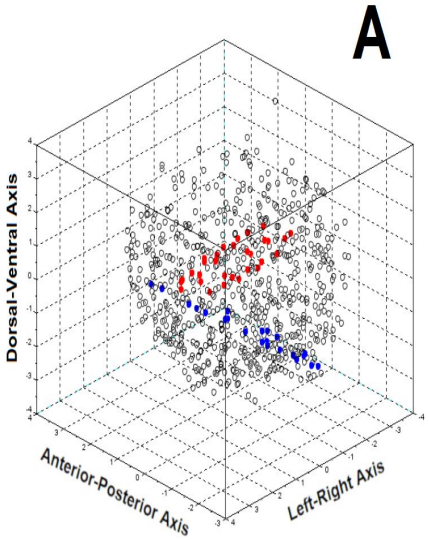


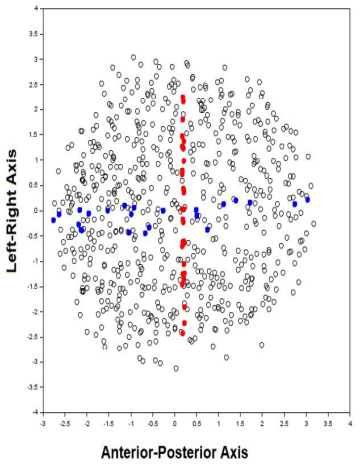
Negative color image of adult worm model generated in OpenWorm Browser:
http://browser.openworm.org/

BioSystems, 173, 247-255 (2018).

Origin of Cells in Connectome Development





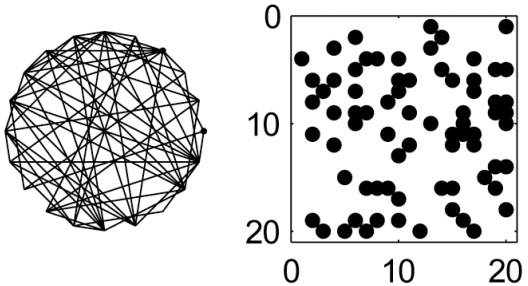


Location of embryonic neurons among cells in the embryo in 3-D (left) and 2-D space.

BioSystems, 173, 247-255 (2018).

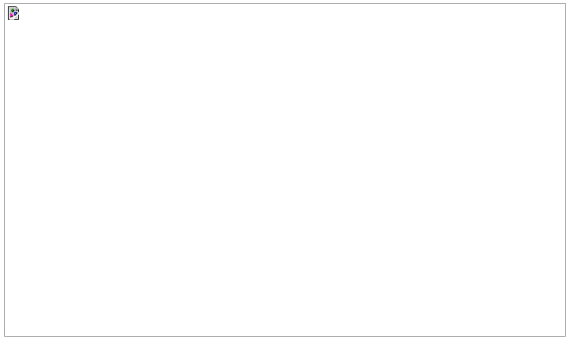
Developmental spatial connectivity and connectomes as complex networks?

Random

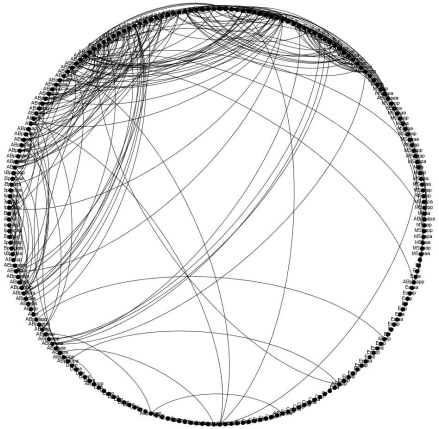


Scale-free

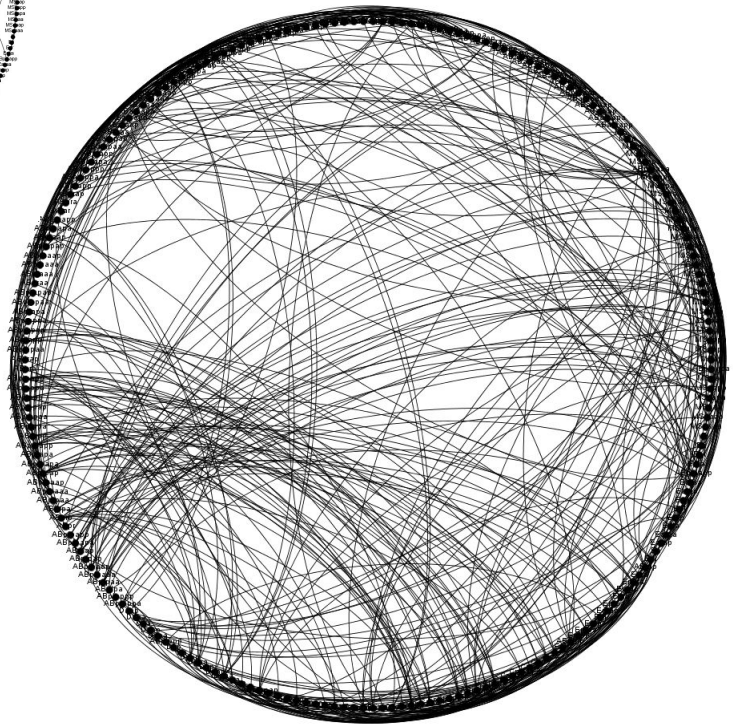
Small-world



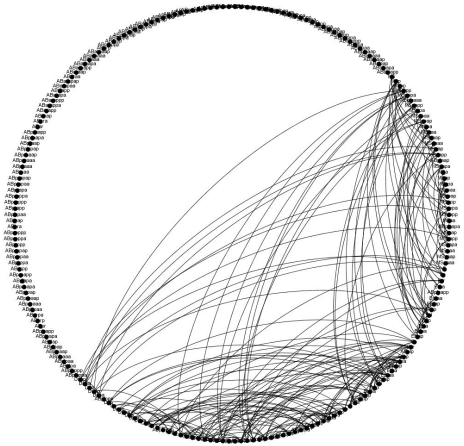
Stobb et.al, Graph Theoretical Model of a Sensorimotor Connectome in Zebrafish. PLoS One, 7(5), e37292.



Within AB sublineage



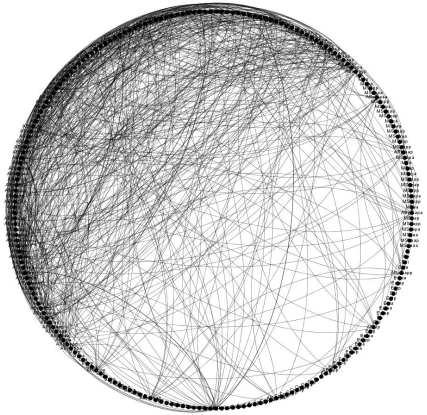
Within P1 sublineage



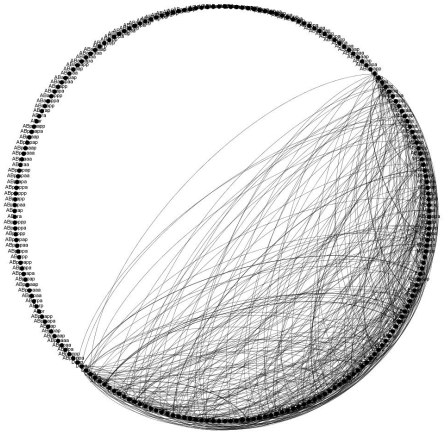
C. elegans

128-cell embryo,

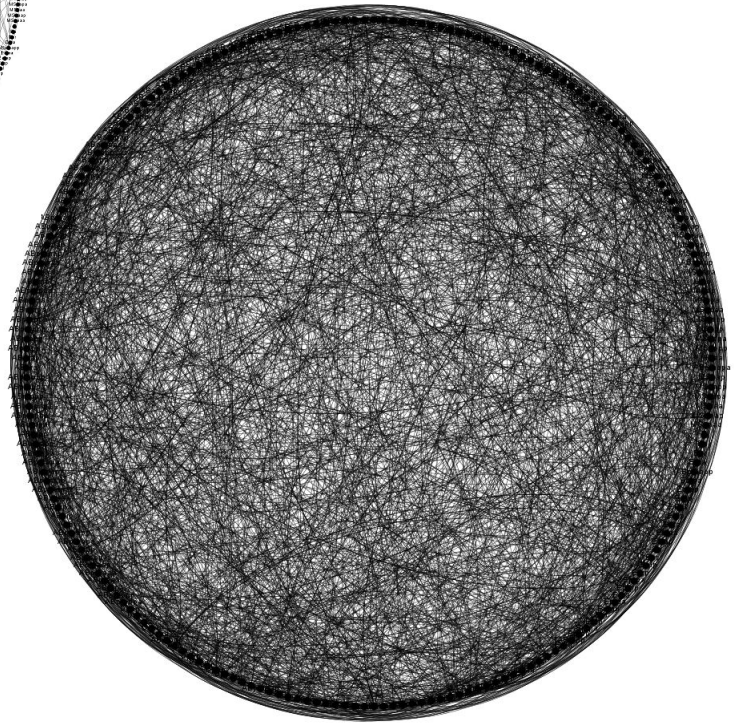
threshold = 0.05



Within AB sublineage



Within P1 sublineage



Random

based on *C. elegans* 128-cell embryo,

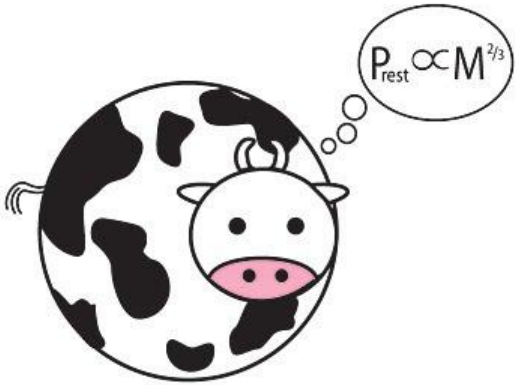
threshold = 0.05

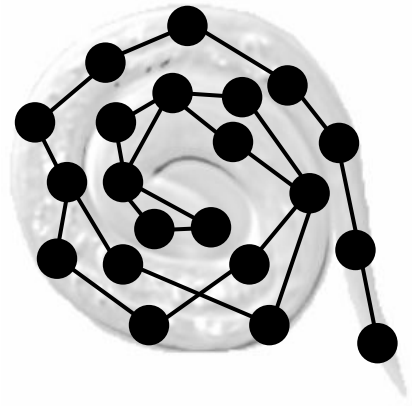
Biological Models: avoiding spherical cows

Spherical cow: oversimplifying a biological system.

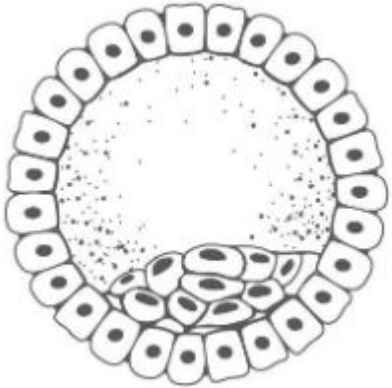
- "Beware of the Small-world Neuroscientist!" *Frontiers in Human Neuroscience*, doi:10.3389/fnhum.2016.00096 (2016).

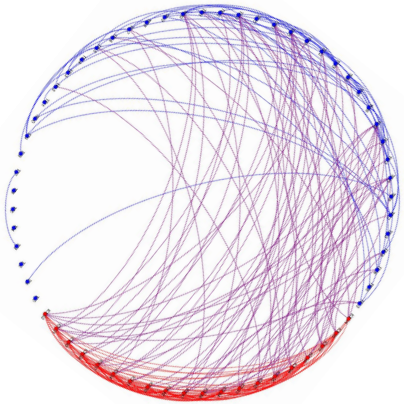
Development (and nervous systems) becomes less spherical over time.





Newly-hatched *C. elegans*





Mouse Blastocyst

Networks capture anatomical structures + functional relationships.

New World Networks (*Brain Structure and Function*, 221(4), 2361-2366 -- 2016):

- networks that expand (number of nodes) with time.

Connectivity reveals:

- anatomical and developmental lineage proximity.
- cells with a common function.
- symmetrical pairs.

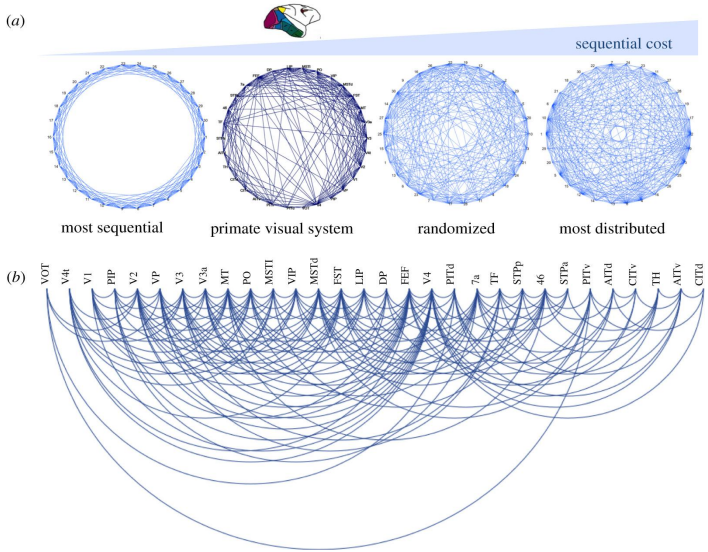
What if the correct model is not a complex (scale-free, small-world) network?

New World Network: small-world network with expansion
Brain Structure and Function, 221(4), 2361-2366 (2016).

Chimeric states: simultaneously coherent and incoherent.
Science Advances, eaah8535 (2019).

Network connectivity preferences influences later activity in ways that affect symmetry
PNAS, 116(41), 20360–20365.

Small-world constrained by spatiotemporal sampling
Chaos, 20, 013134 (2010).



Generalized Hierarchical Signatures
Phil. Trans. R. Soc. B, 375, 20190319 (2020).

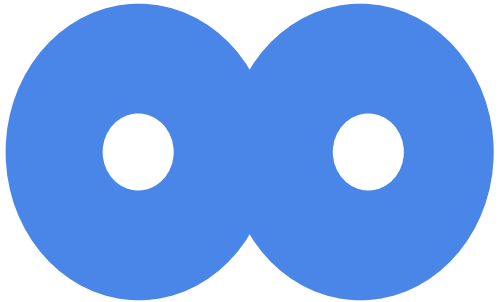
Cell Division

Graph diameter expands (growth in number of nodes)

Local connectivity increases (nodal density)

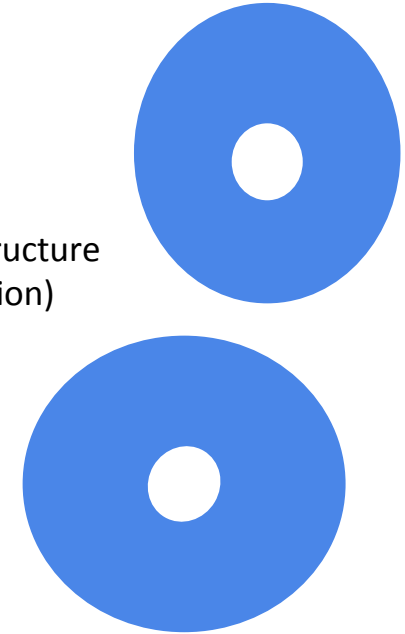
Global modularity increases (differentiation events, bifurcation)

Initial Condition



Expansion of Structure

Bipartite Structure (Bifurcation)

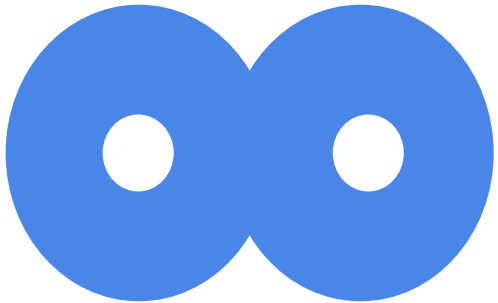


Cell Division

Measure added structure with convex hull analysis

- size and shape of internal features and how these are recapitulated across developmental sequence.

- expansion rate to differential path length ratio.

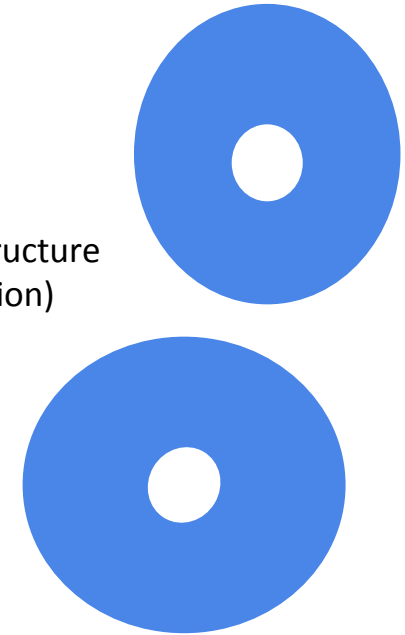


Expansion of Structure

Cell Division

Bifurcation: single network to bipartite.

- how many parts does the network fragment into over time?



Bipartite Structure
(Bifurcation)

New World Networks are Multilevel Networks

Proximity and Adjacency measurements:

- convex hull measurement over time (topological data analysis).
- differential network diameter (between time t_1 and t_n).

Expansion rate measurements:

- differential path length ratio (between time t_1 and t_n).
- differential clustering (between time t_1 and t_n).

New Types of Topologies

Feature-rich Networks:

- topological features capture fractals and fluid dynamics.

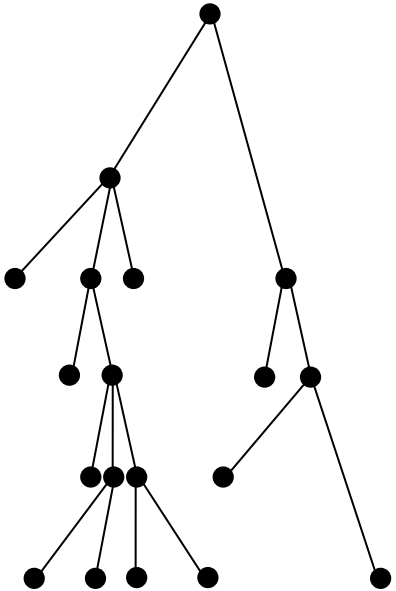
Multiple Worlds:

- different processes and structures captured in a *n*-partite network with weak connectors.

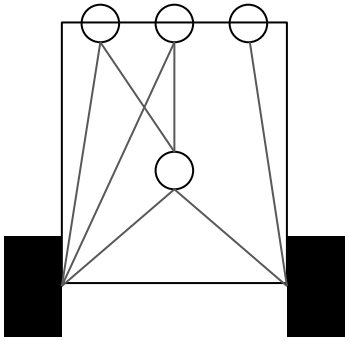
Semi-integrated Networks:

- interrelated phenotypic modules and functional systems (brain and body).

Generative Connectomes (with developmental Braitenberg Vehicles)



Generate a generic lineage tree (line of descent/timing)



Vehicle with connectome at time t_n (new world network with anatomical asymmetries).

	SL	SM	SR	IN	WL	WR
SL	0	0	0	1	1	0
SM	0	0	0	1	1	0
SR	0	0	0	0	0	1
IN	1	1	0	0	1	1
WL	1	1	0	1	0	0
WR	0	0	1	1	0	0

Connectivity matrix at time t_n

Check out our latest work!
arXiv:2003.07689

Thanks for Your Attention!

Acknowledgements

Google Summer of Code

OpenWorm

NetSci

Open Data Day

Finding Your Inner Modeler II
UNIVERSITY OF ILLINOIS AT CHICAGO
AUGUST 16-17, 2018