TOPOLOGICAL DATA ANALYSIS FOR BIOLOGICAL RING CHANNELS

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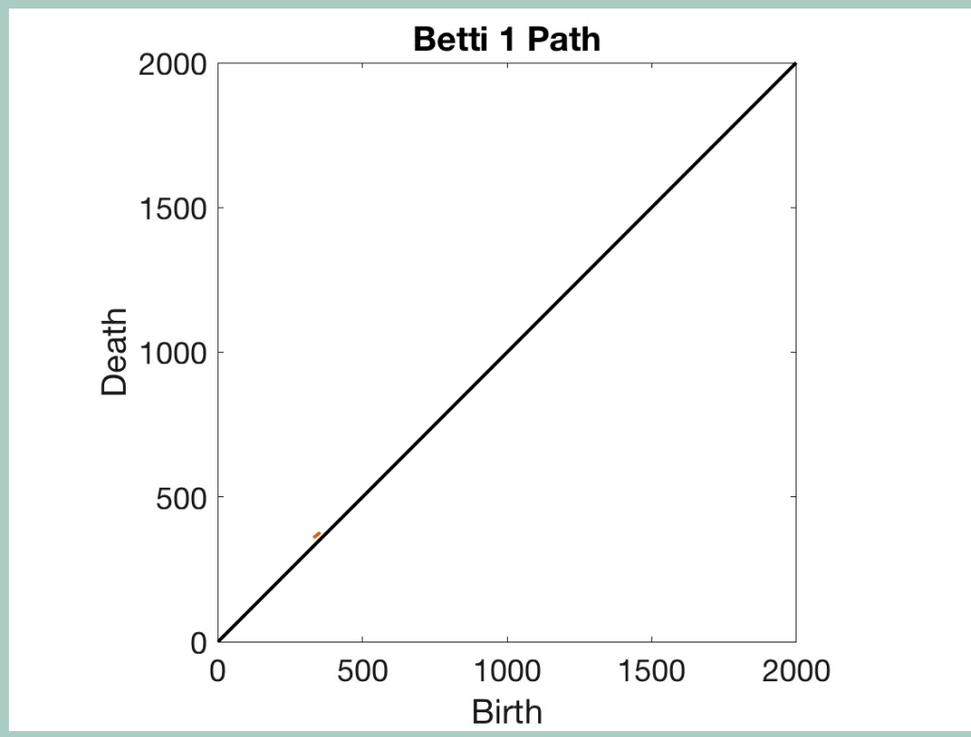
The Ohio State University

Tutorial Workshop on Parameter Estimation for Biological Models

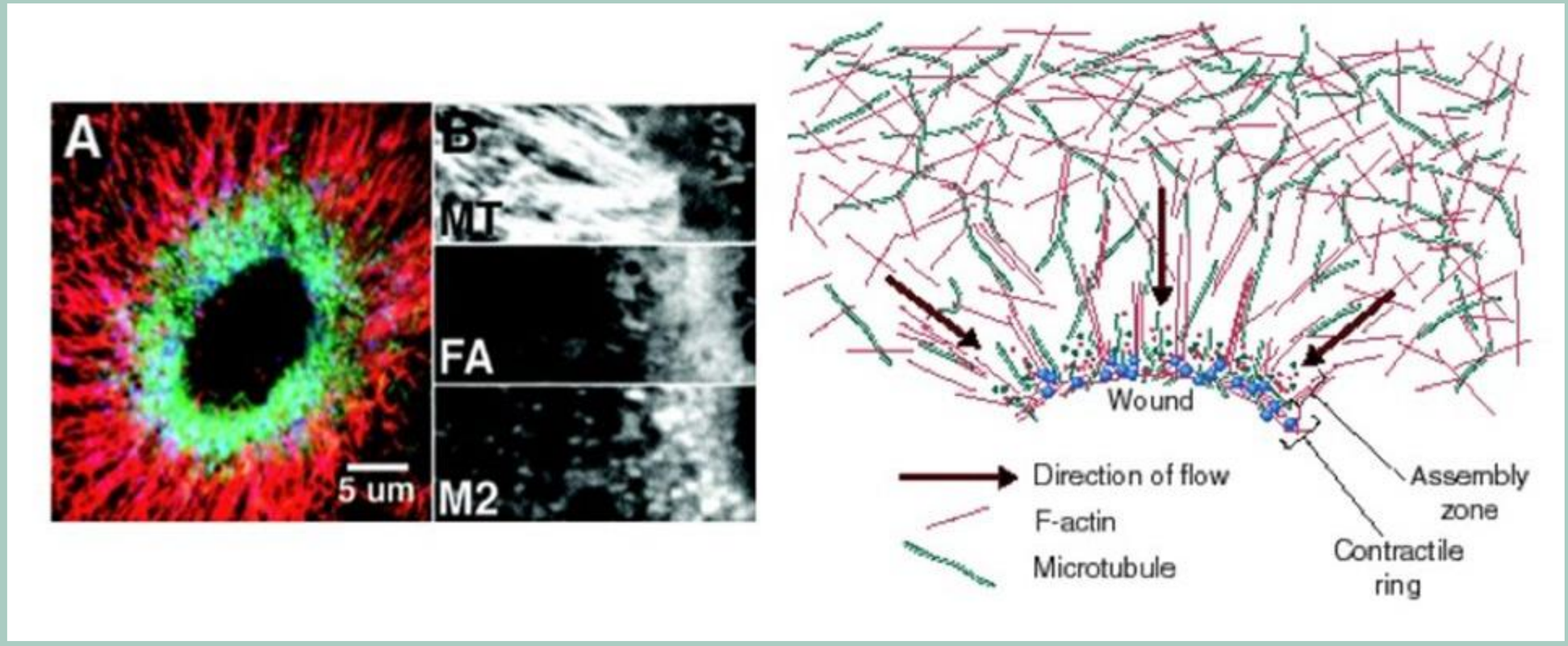
NCSU, Raleigh, NC

July 29th 2019



MOTIVATION

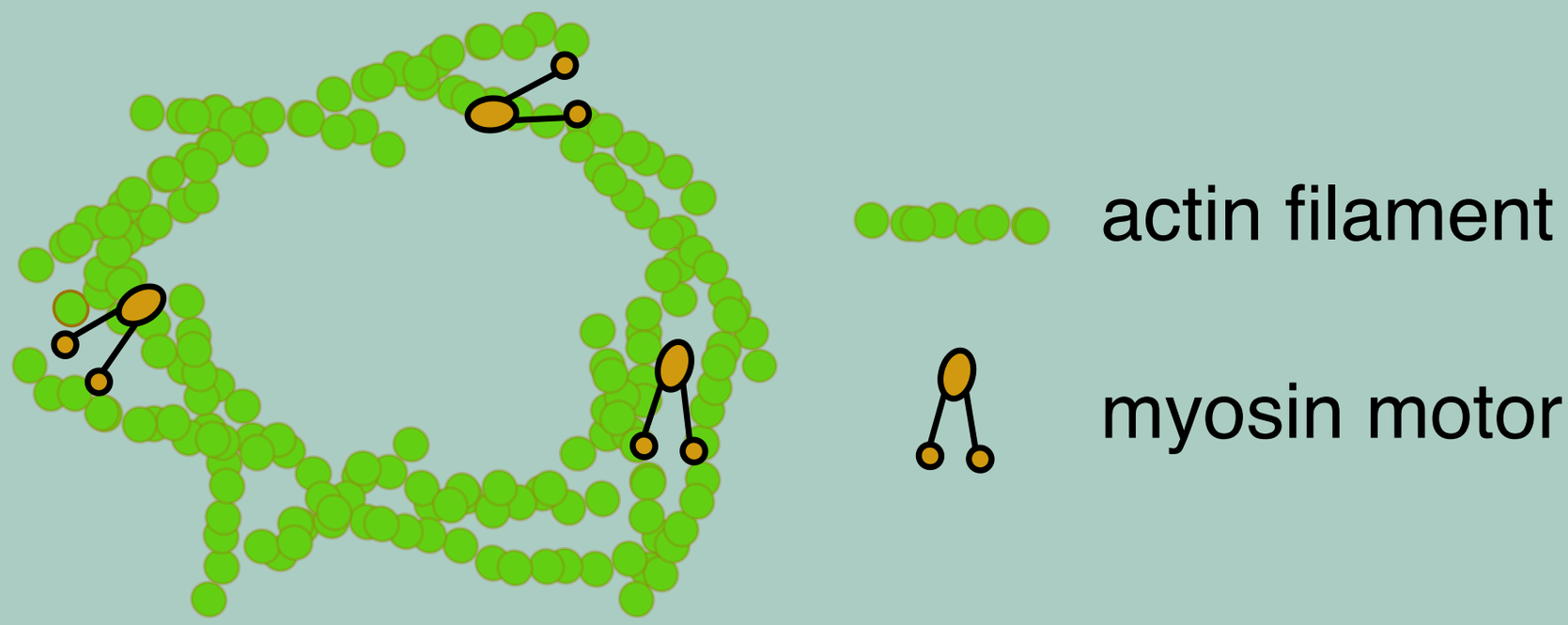
- Cells use many channels to communicate, each with different functions.
- **Ring channels** play critical roles in oogenesis, wound healing, and cell division.



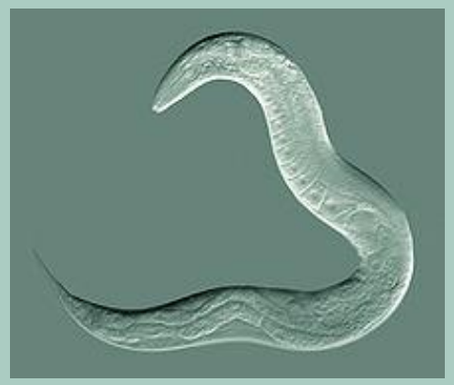
http://rusty.fhl.washington.edu/celldynamics/events/workshops/archive/2003/cytomod_abstracts/BBement/index.html

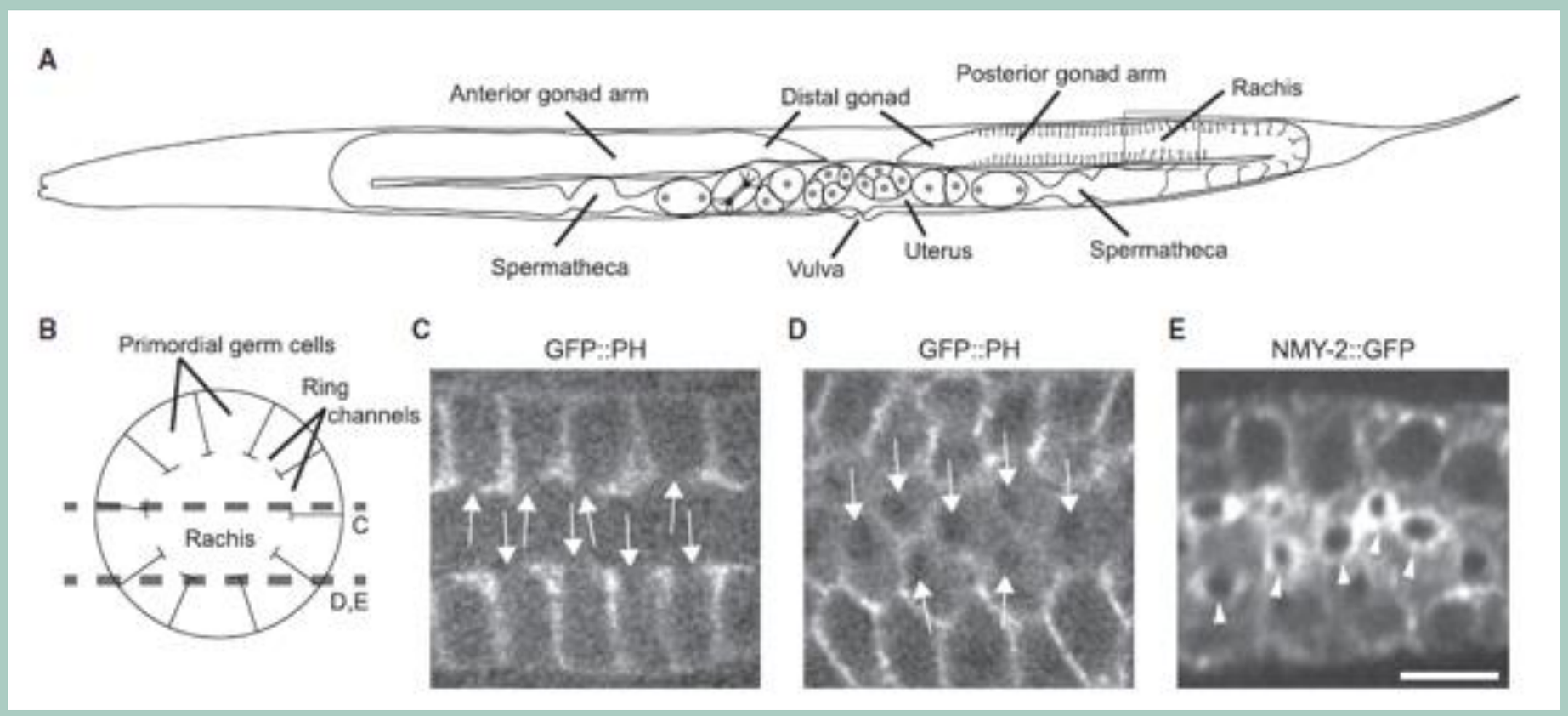
MOTIVATION

- Often, ring channels maintain precise diameters over a large time scale.
- Non-muscle myosin motor proteins are often “in charge” of creating appropriate constriction of the ring.



SPECIFIC MOTIVATION





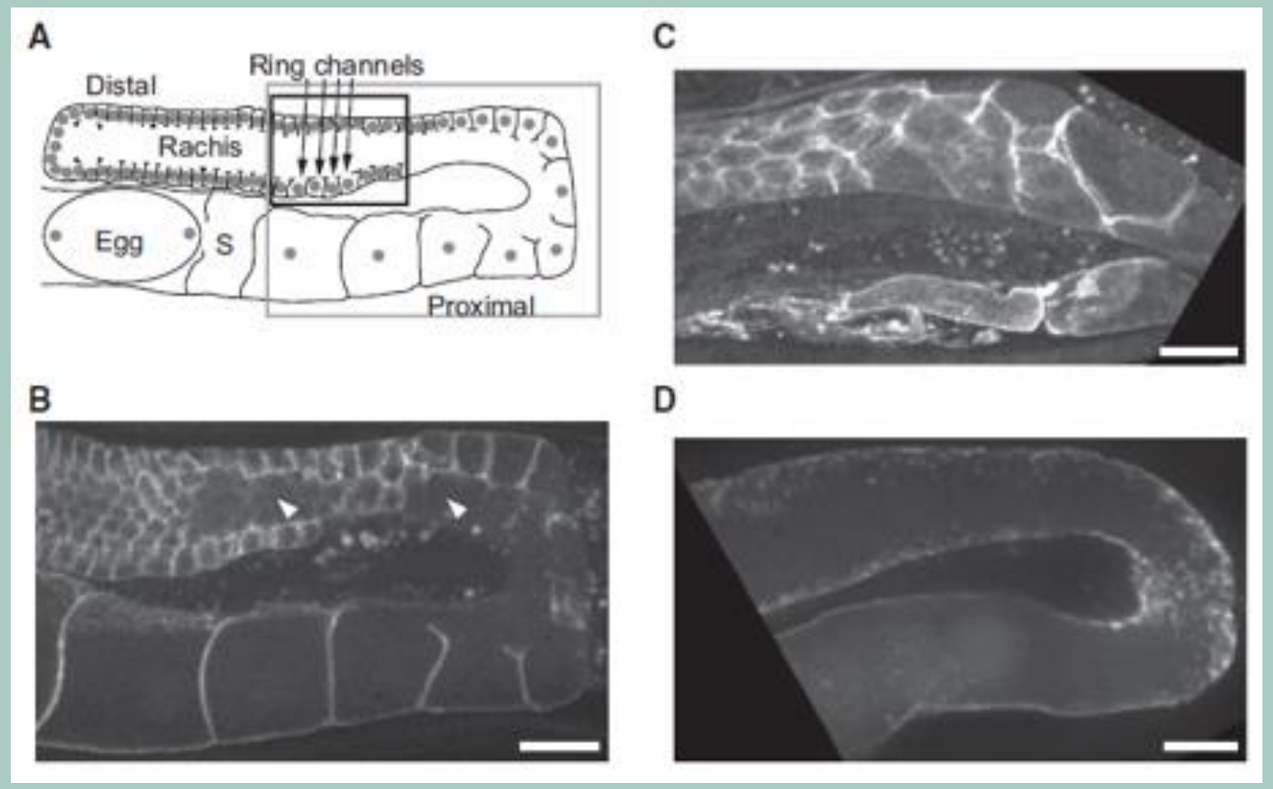
Adriana Dawes

OSU

- In the worm *C. elegans*: ring channels (made by actin) allow for nutrient exchange in development.

Coffman et al, 2016

THE QUESTION



Knockdown motor 1

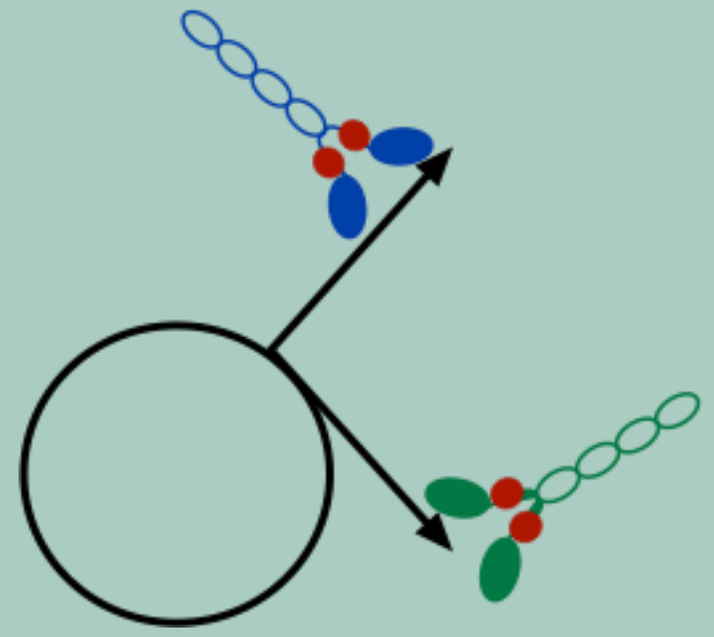
Knockdown motor 2

- Two types of motors, believed to function similarly, are involved in ring channel dynamics.
- Experiments show that they antagonize each other with respect to cellularization.

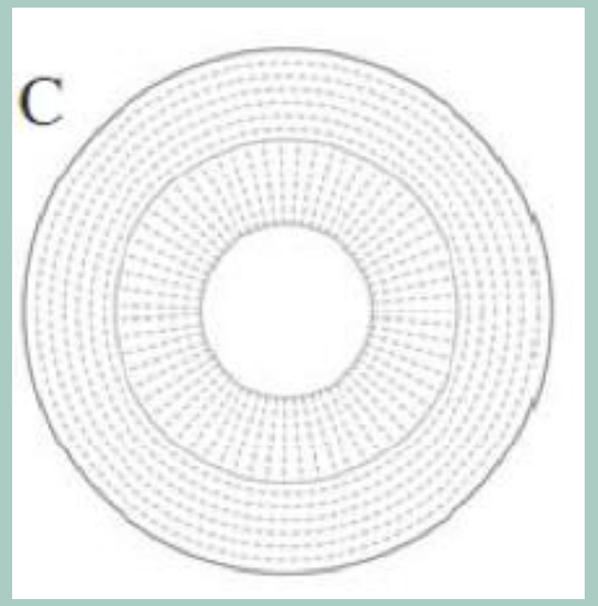
Coffman et al, 2016

GOALS

- Investigate ring formation using agent-based models for actin filaments and motors.

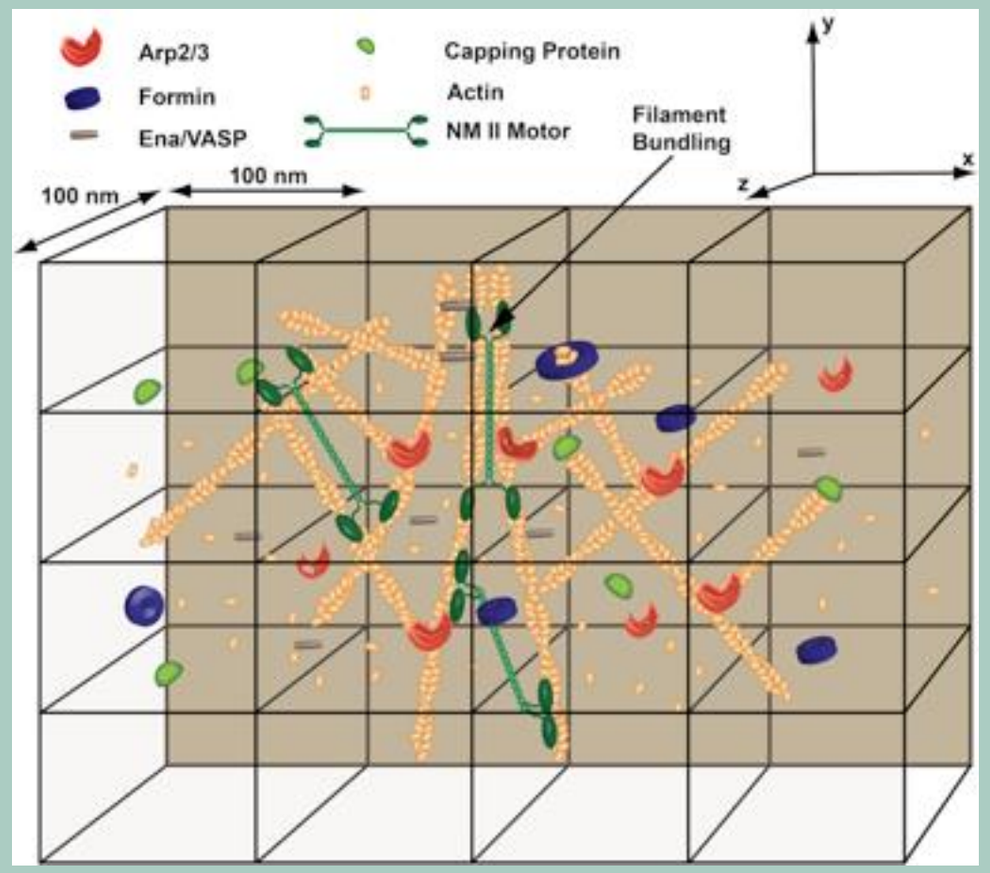


- Identify potential mechanistic differences between motors.



1. AGENT-BASED MODELING AND SIMULATION

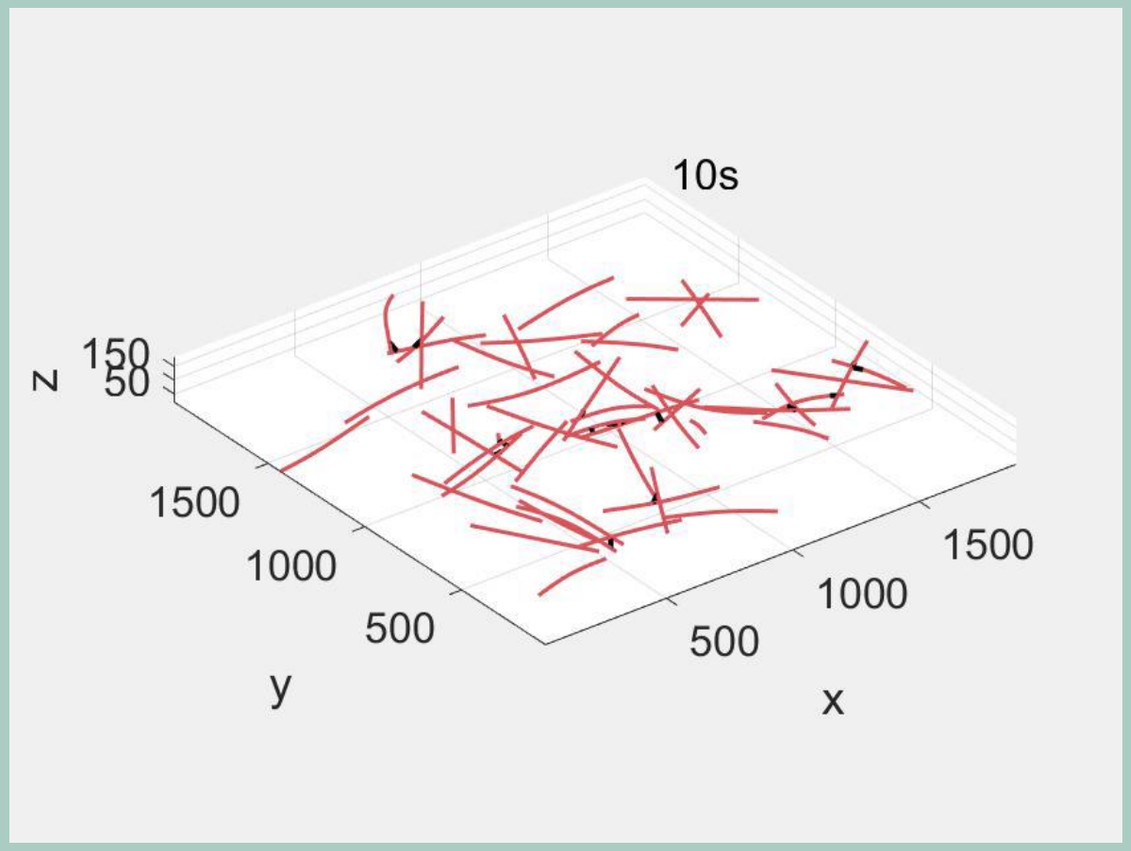
- Accounts for dynamics and molecular transport of chemical species.
- Diffusion and active transport are modeled as stochastic jumps between compartments.
- Is based on energy minimization.



Medyan (Papoian Lab)

Papoian Lab, University of Maryland; Popov, Komianos, and Papoian, 2016

DATA ANALYSIS MEASURES



Riley Juenemann, Tulane University

Scott McKinley, Tulane University

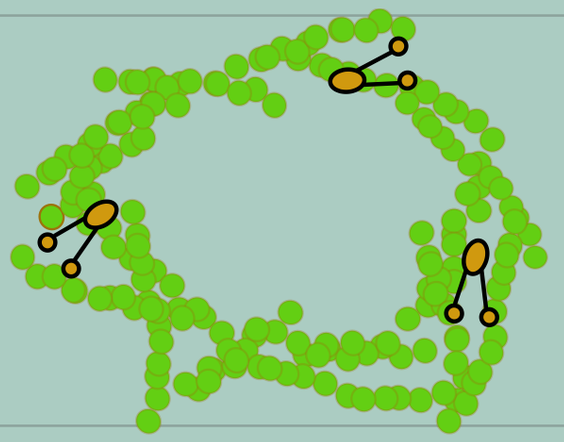
actin filament

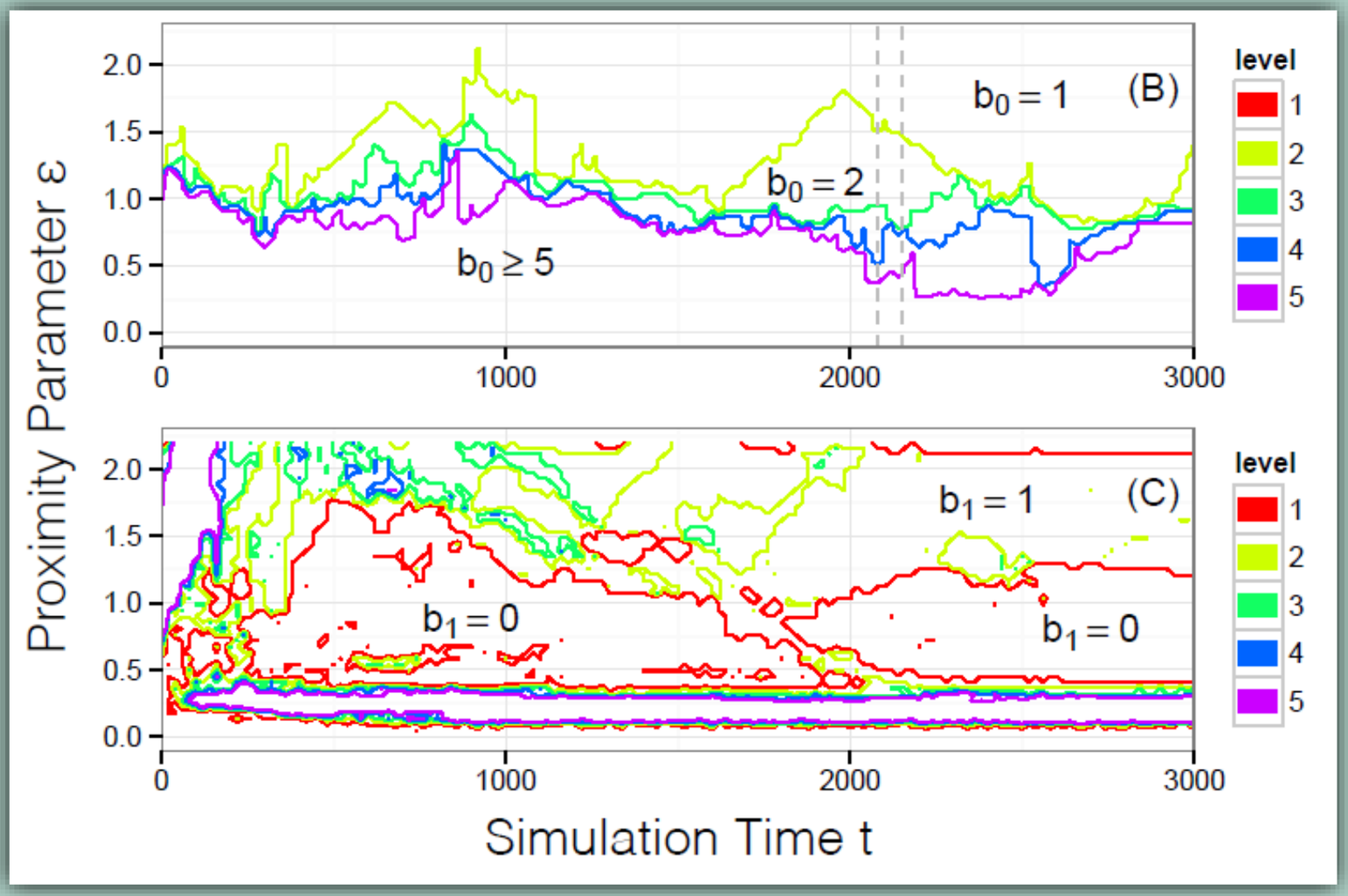
myosin motor

cross-linker

- Contractility, alignment, filament length distributions

2. DETECTING RING STRUCTURE



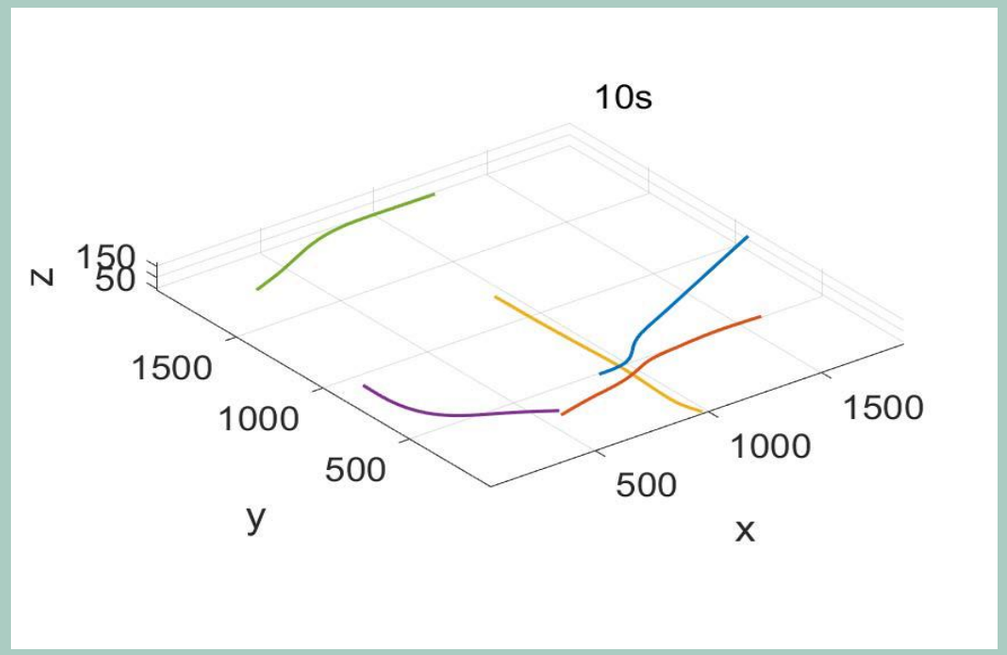


Chad Topaz, Williams College

- Inspiration: Crocker plots (Topaz, Zieglemeier, Halverson)

Topaz, Zieglemeier, Halverson, 2015

FRAMEWORK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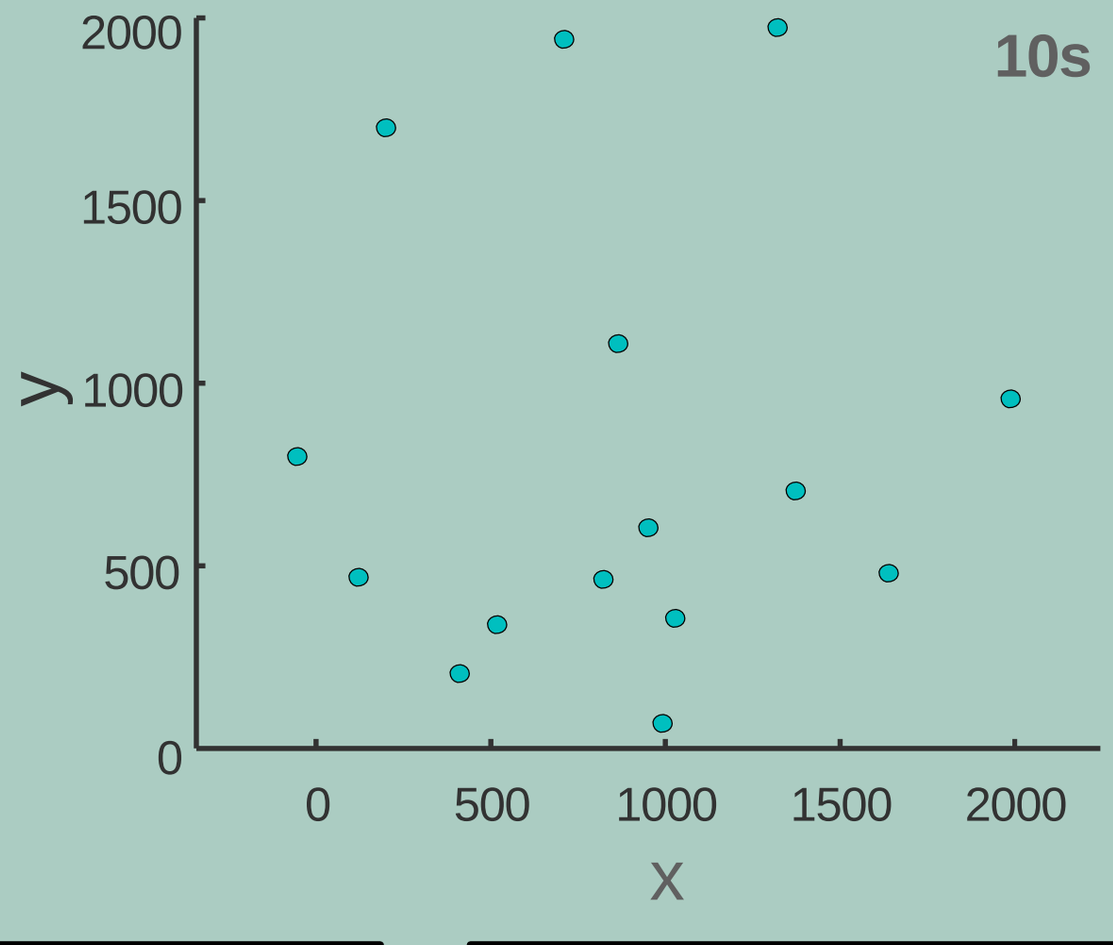
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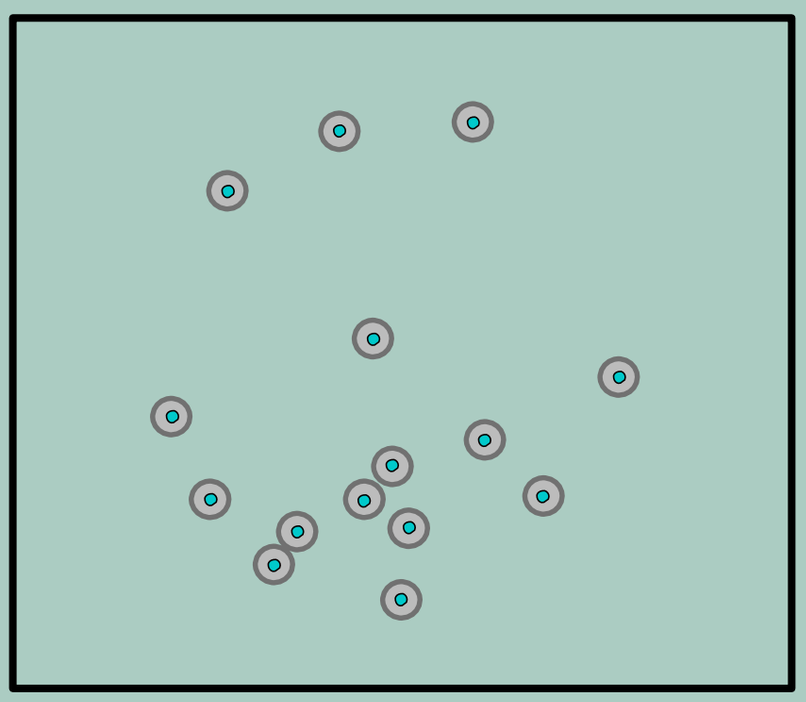

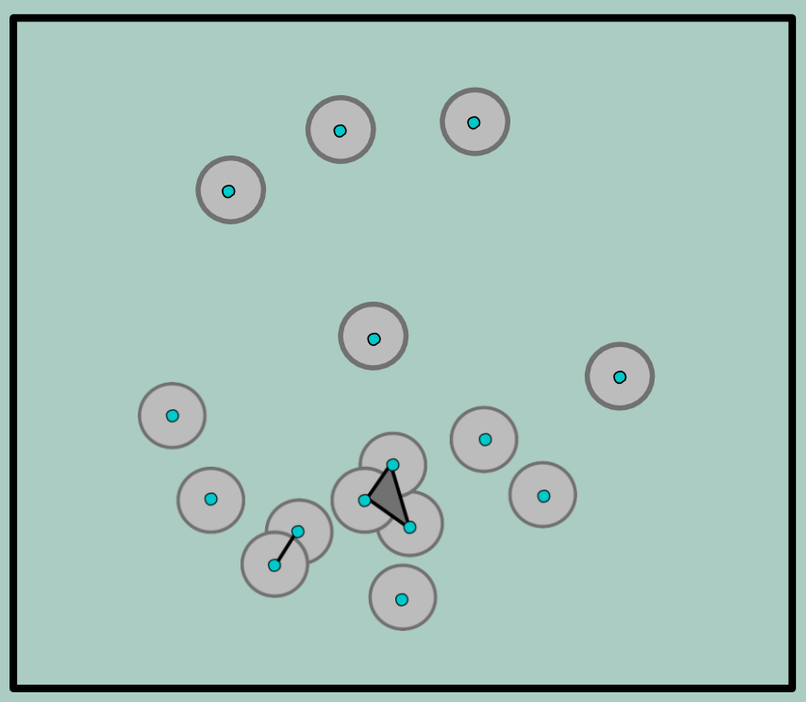

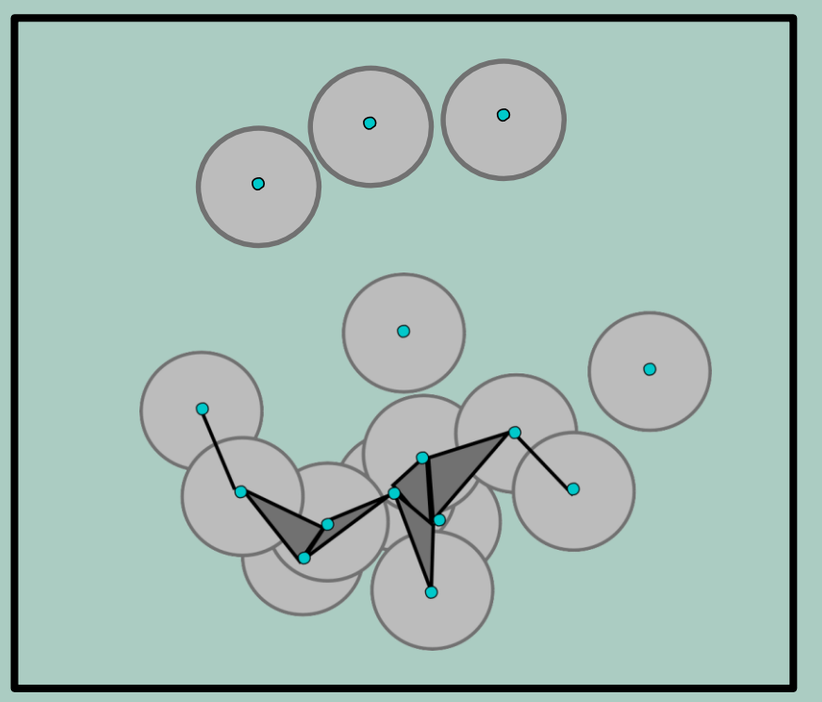

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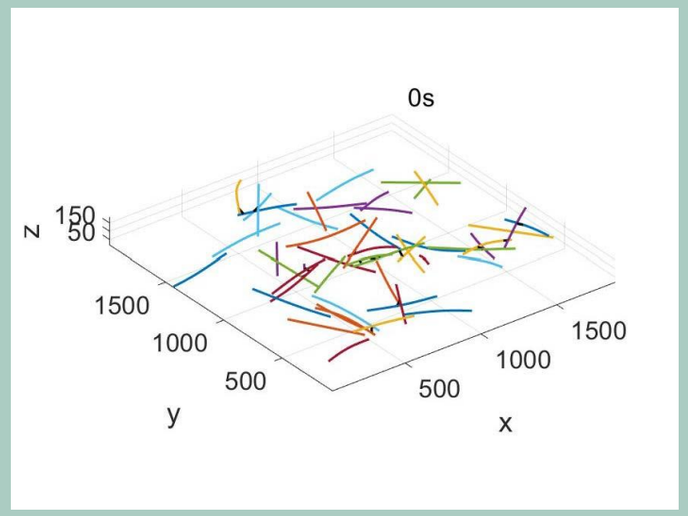
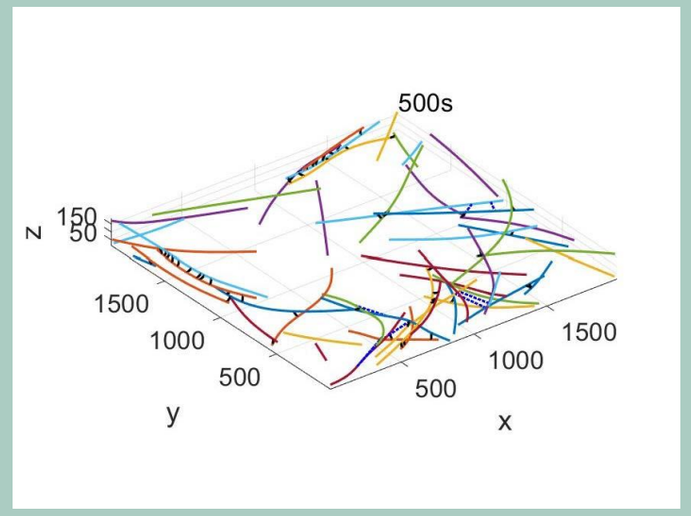
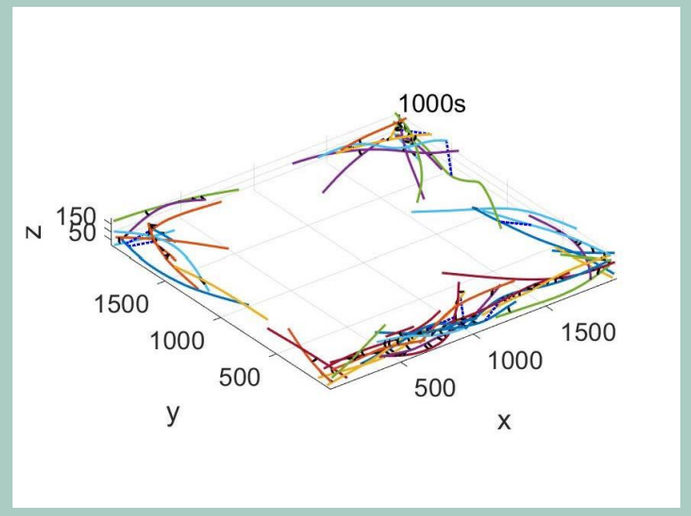
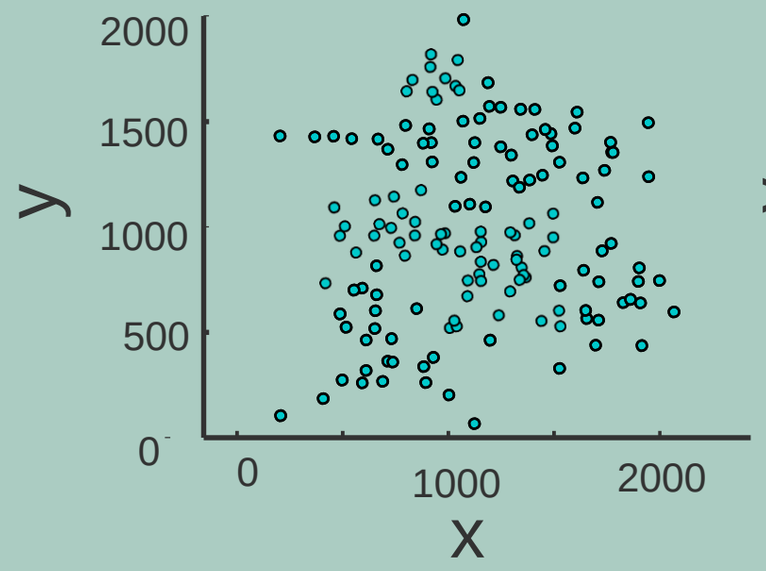


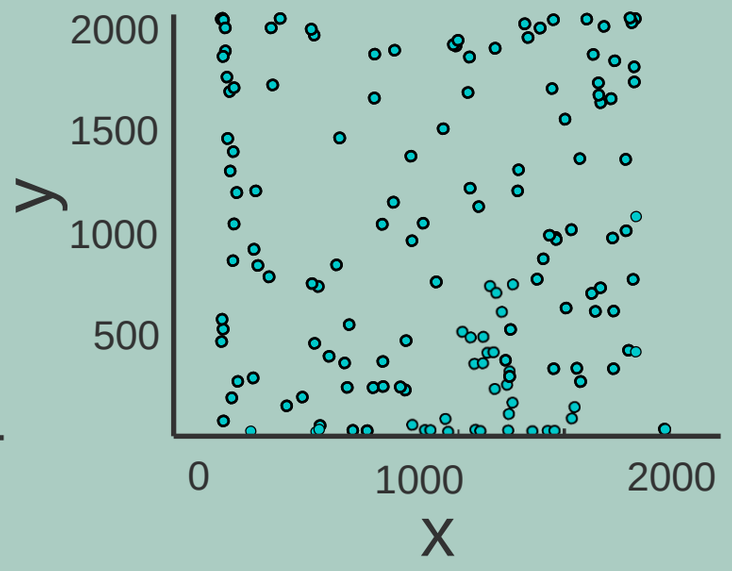
500s

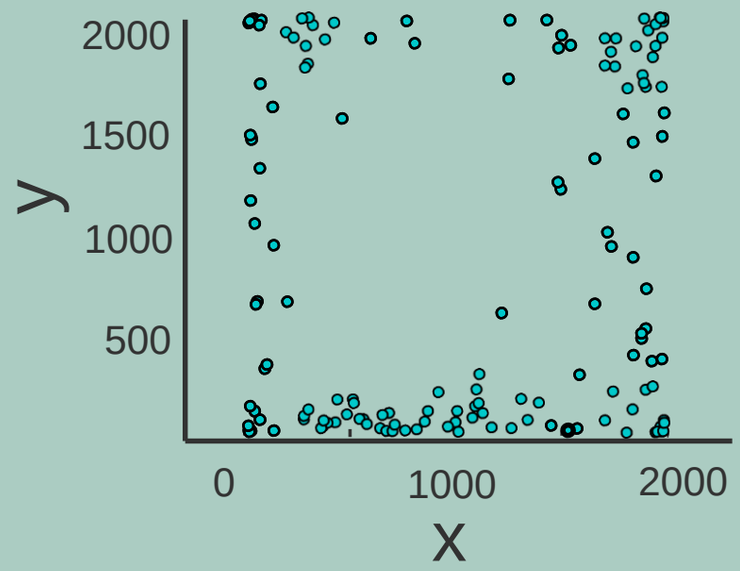


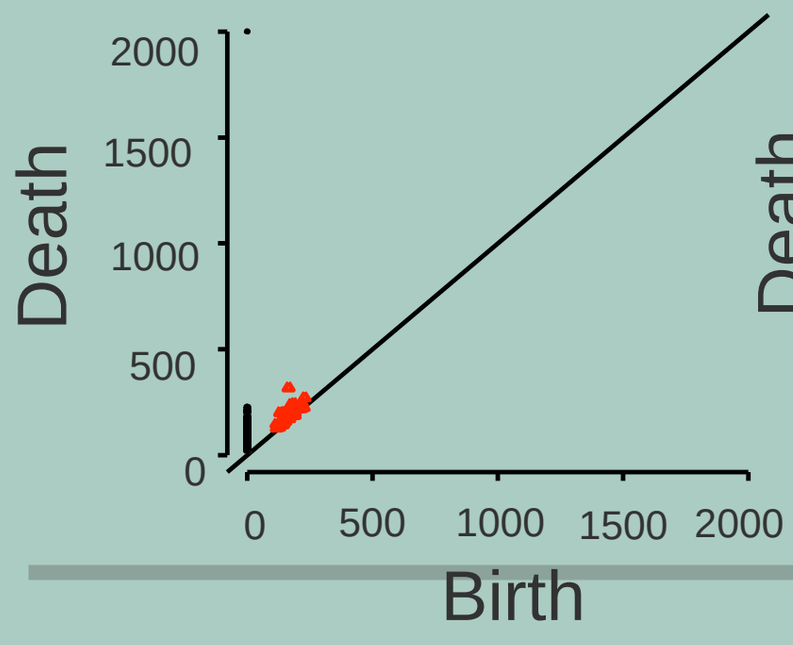
1000s

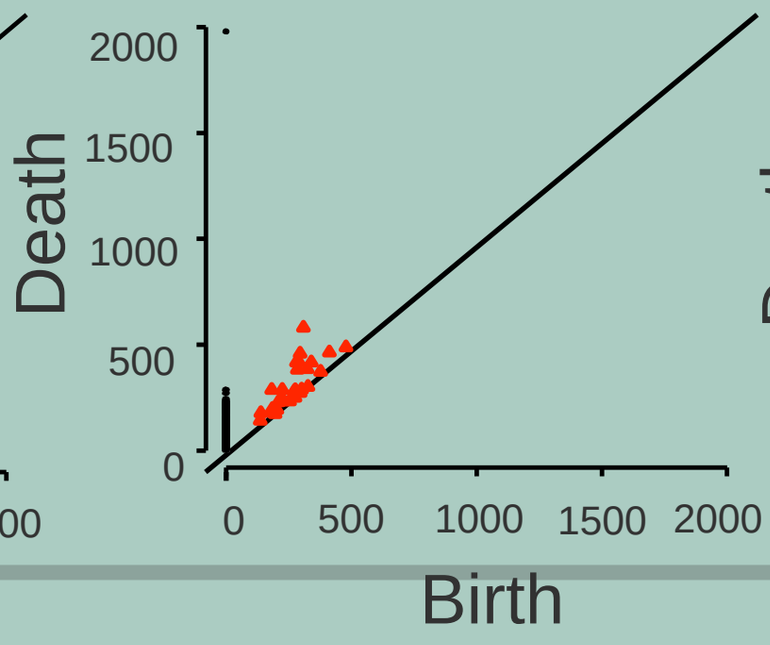


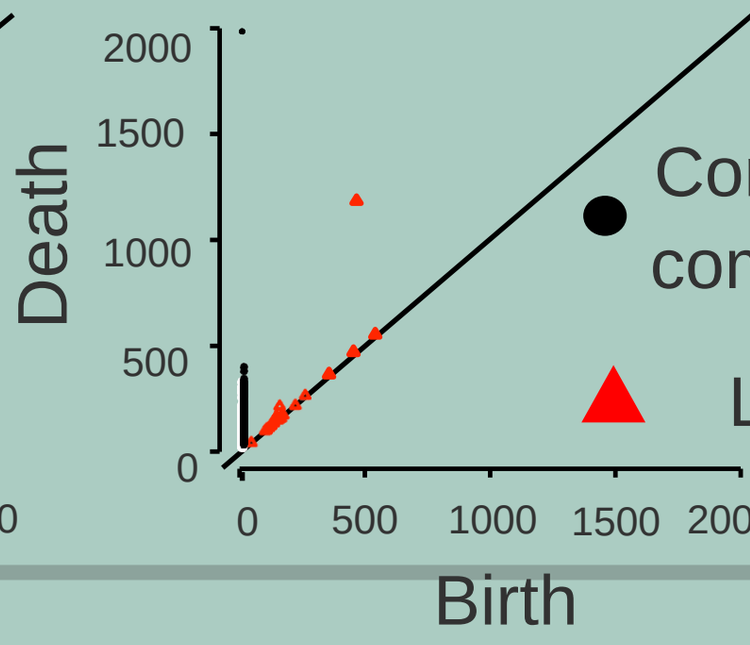






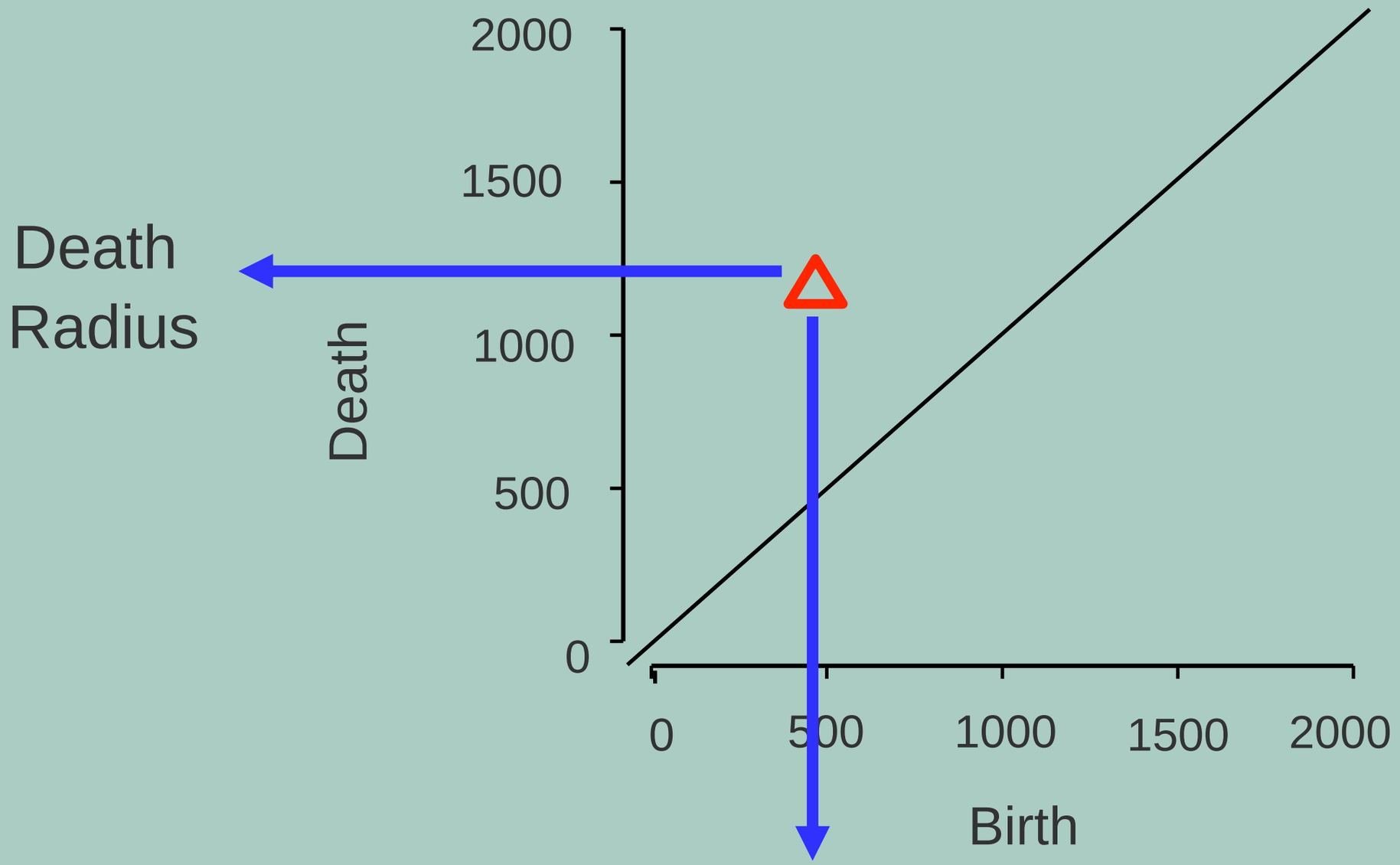






Connected component

Loop


2000
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1000
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0
Death
Death
Radius
0
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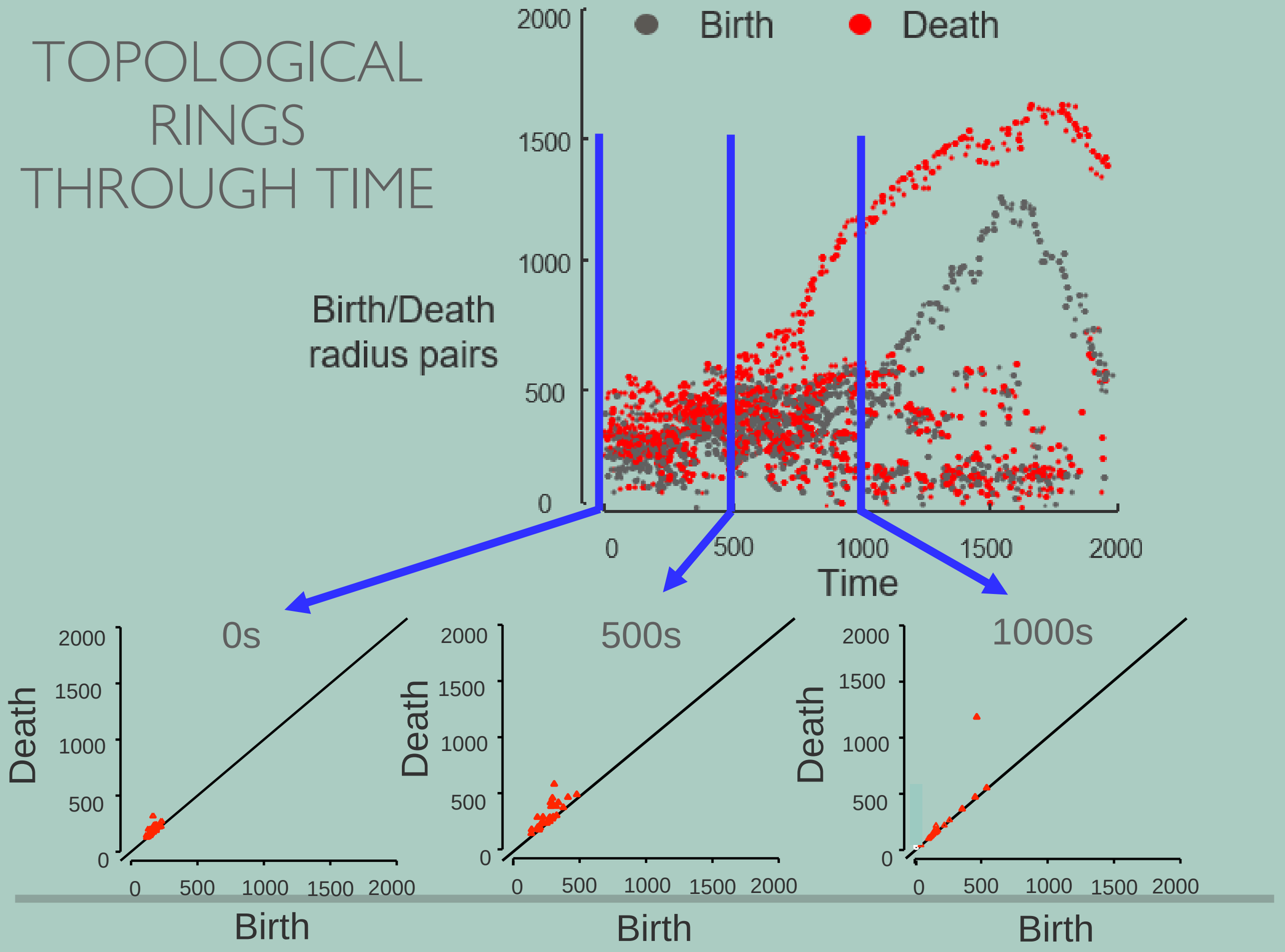
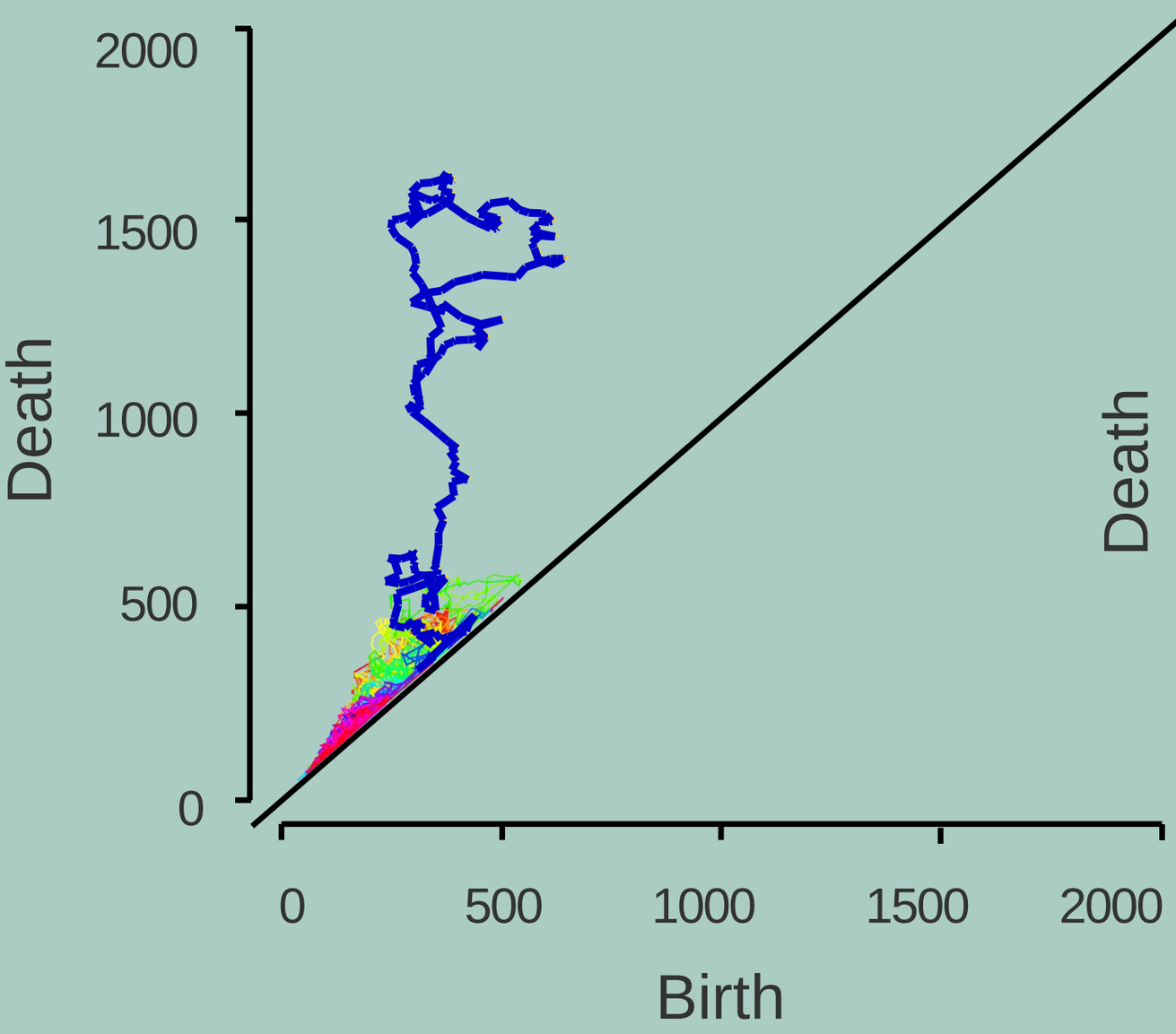
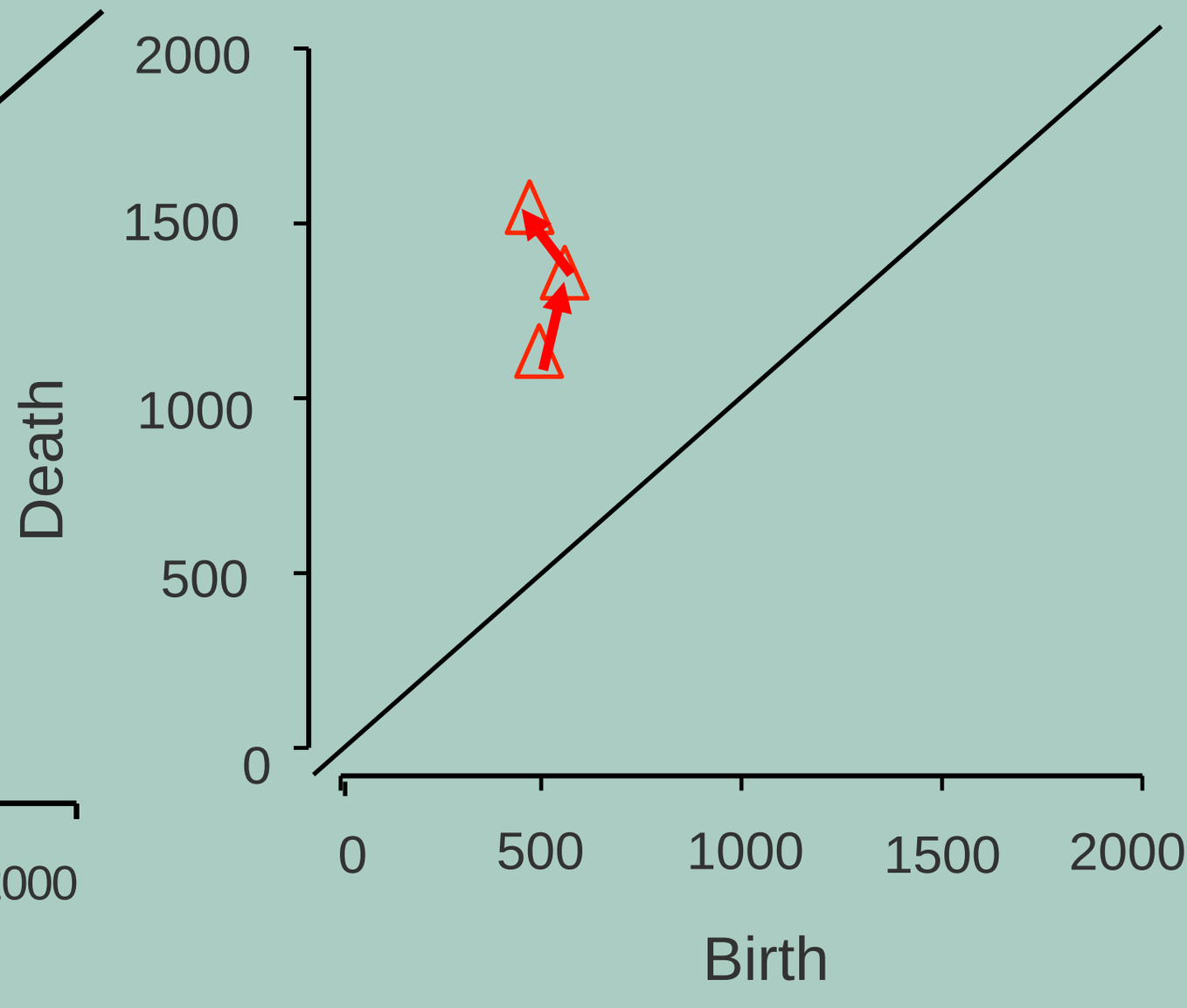
2000
Birth
Birth
Radius

TOPOLOGICAL RINGS THROUGH TIME



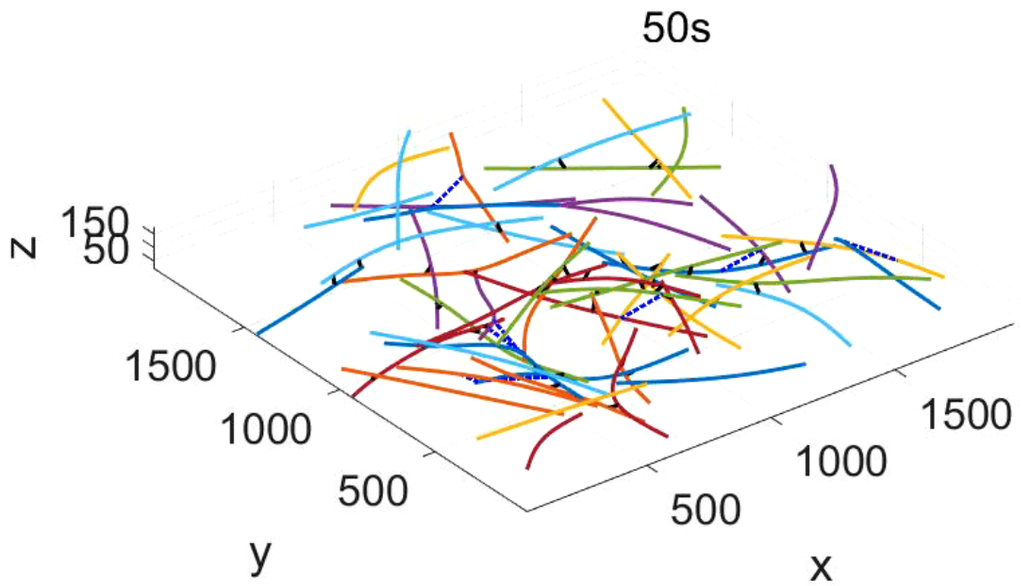
- ❑ Propose a method for connecting pairs through time.
- ❑ Extract the most significant Betti 1 path.

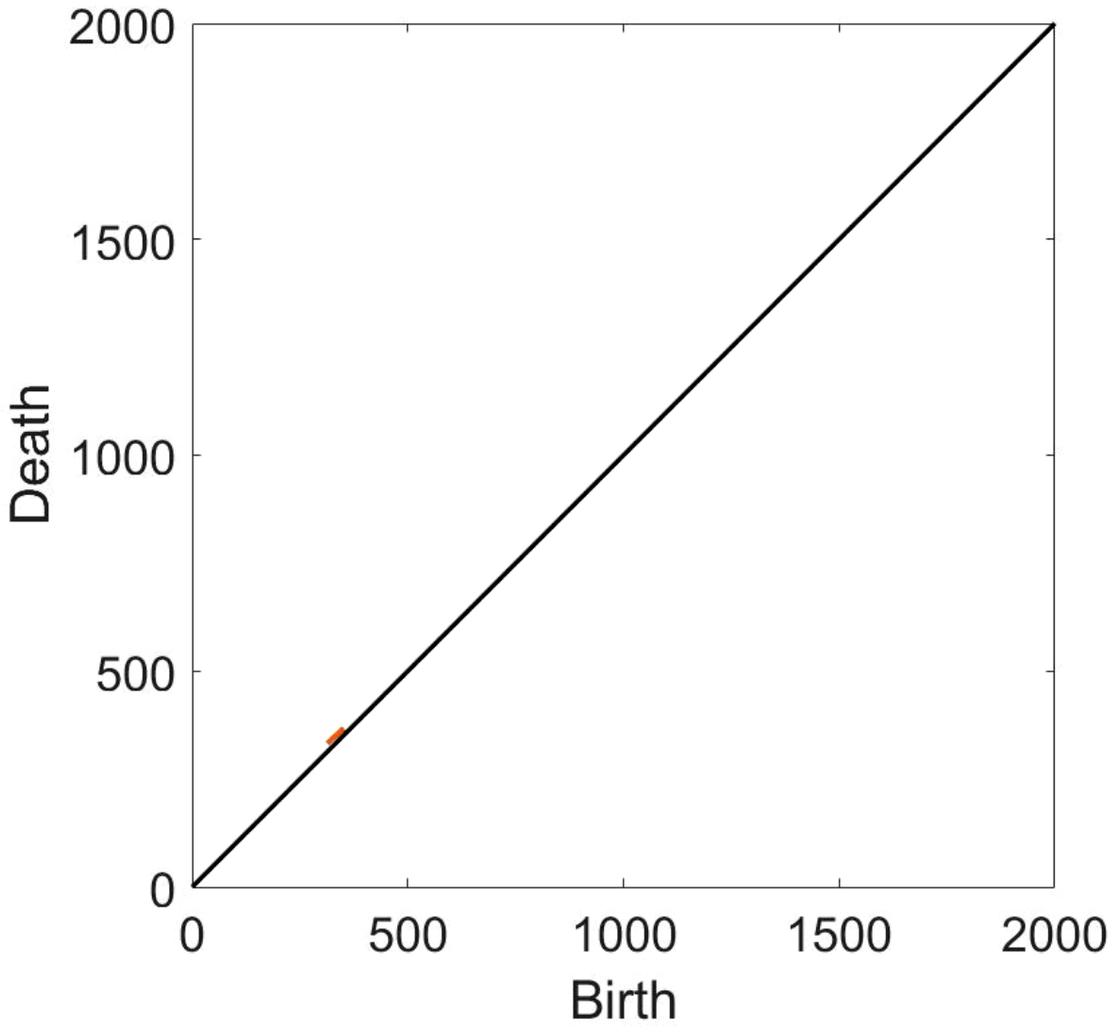




With Riley Juenemann, Adriana Dawes, and Scott McKinley (in preparation)

VISUALIZATION OF SIGNIFICANT PATH (RING STRUCTURE) EMERGENCE





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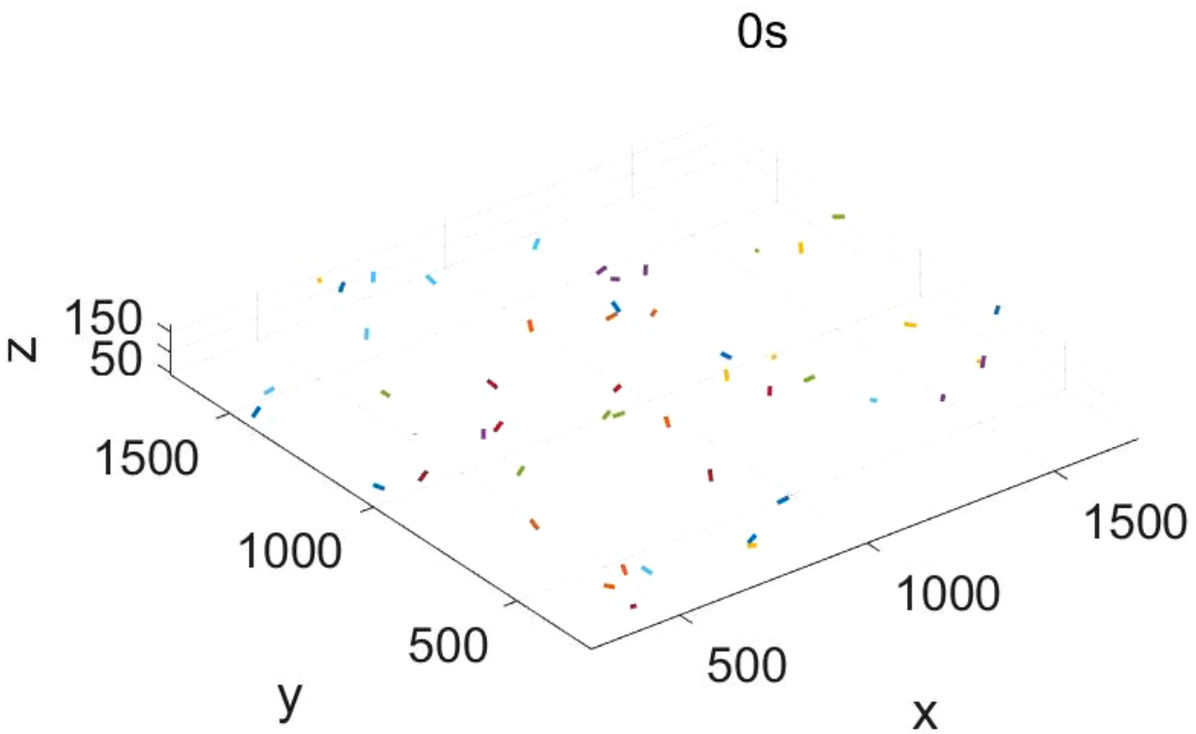
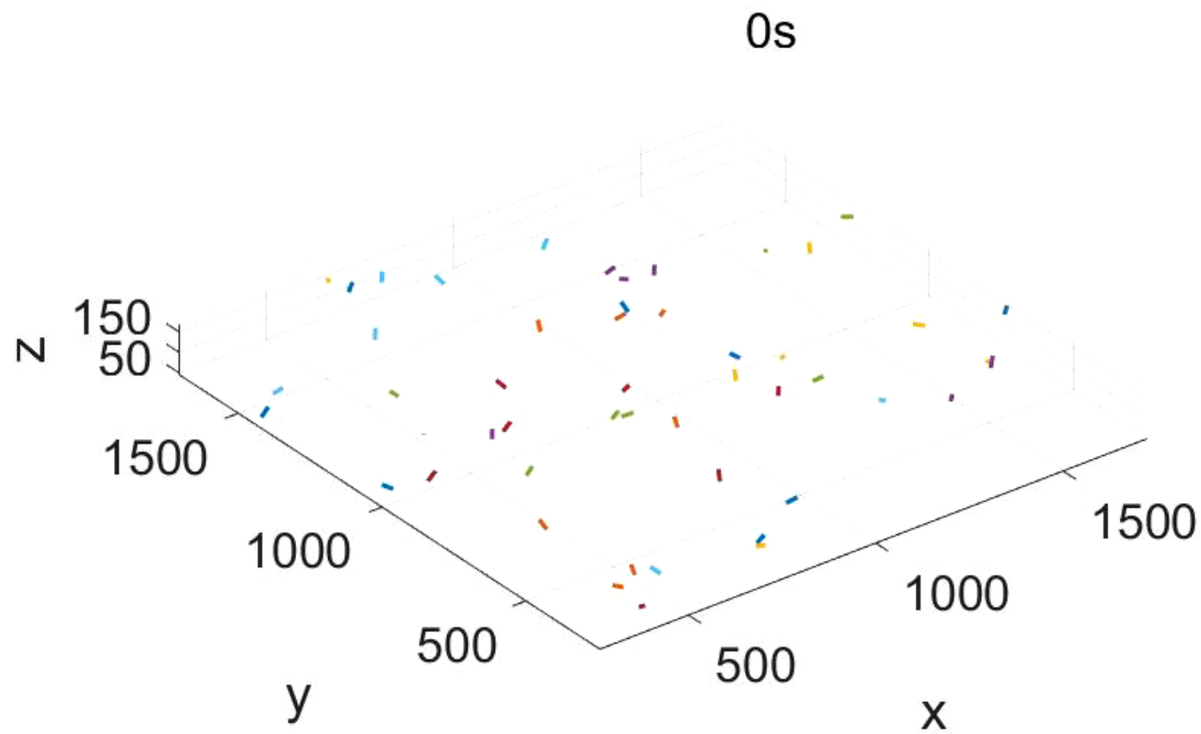
EXPLORE PARAMETER DIFFERENCES: ON-RATE



Small on-rate



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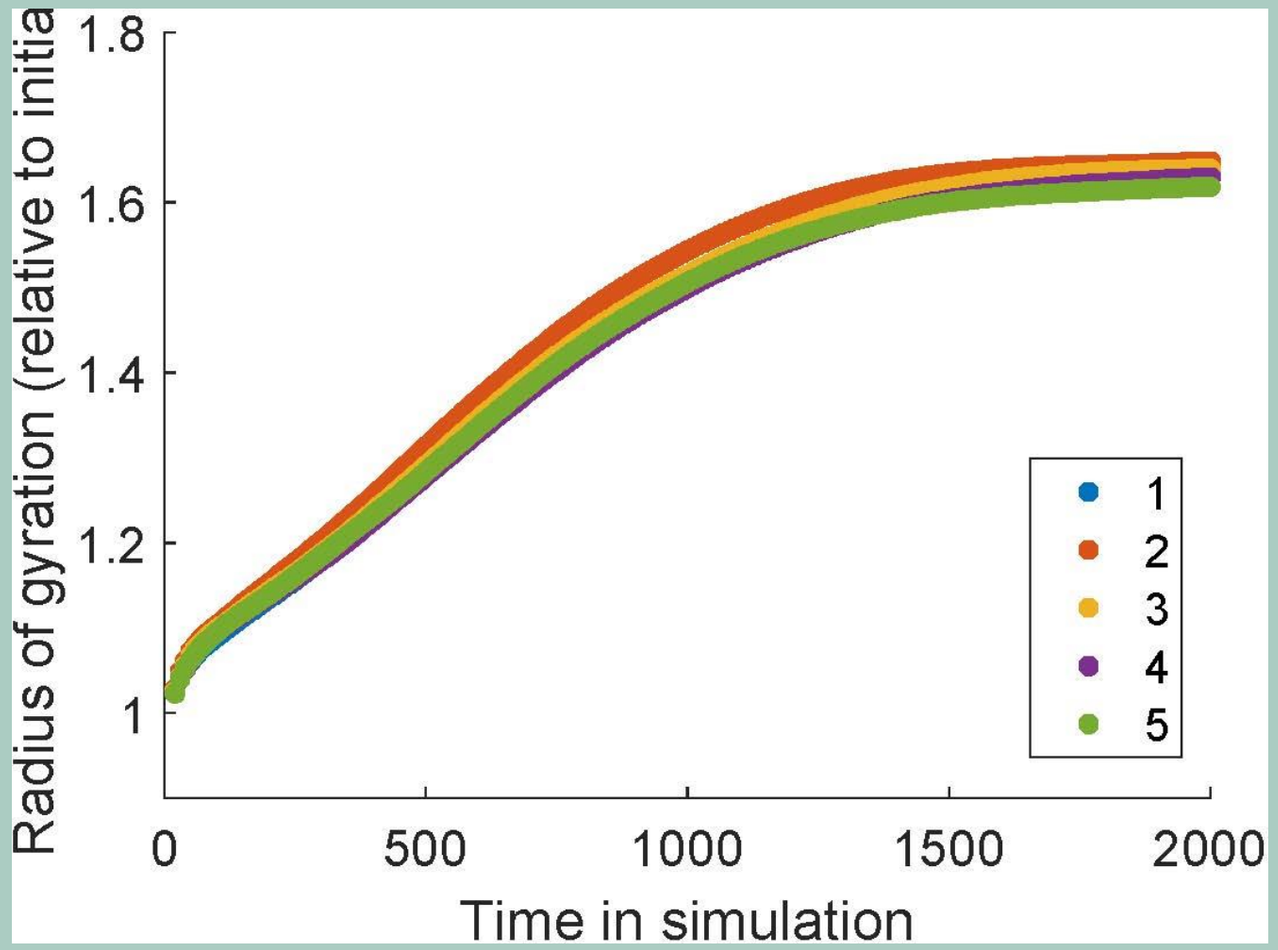
EXPLORE PARAMETER DIFFERENCES: ON-RATE

Contractility



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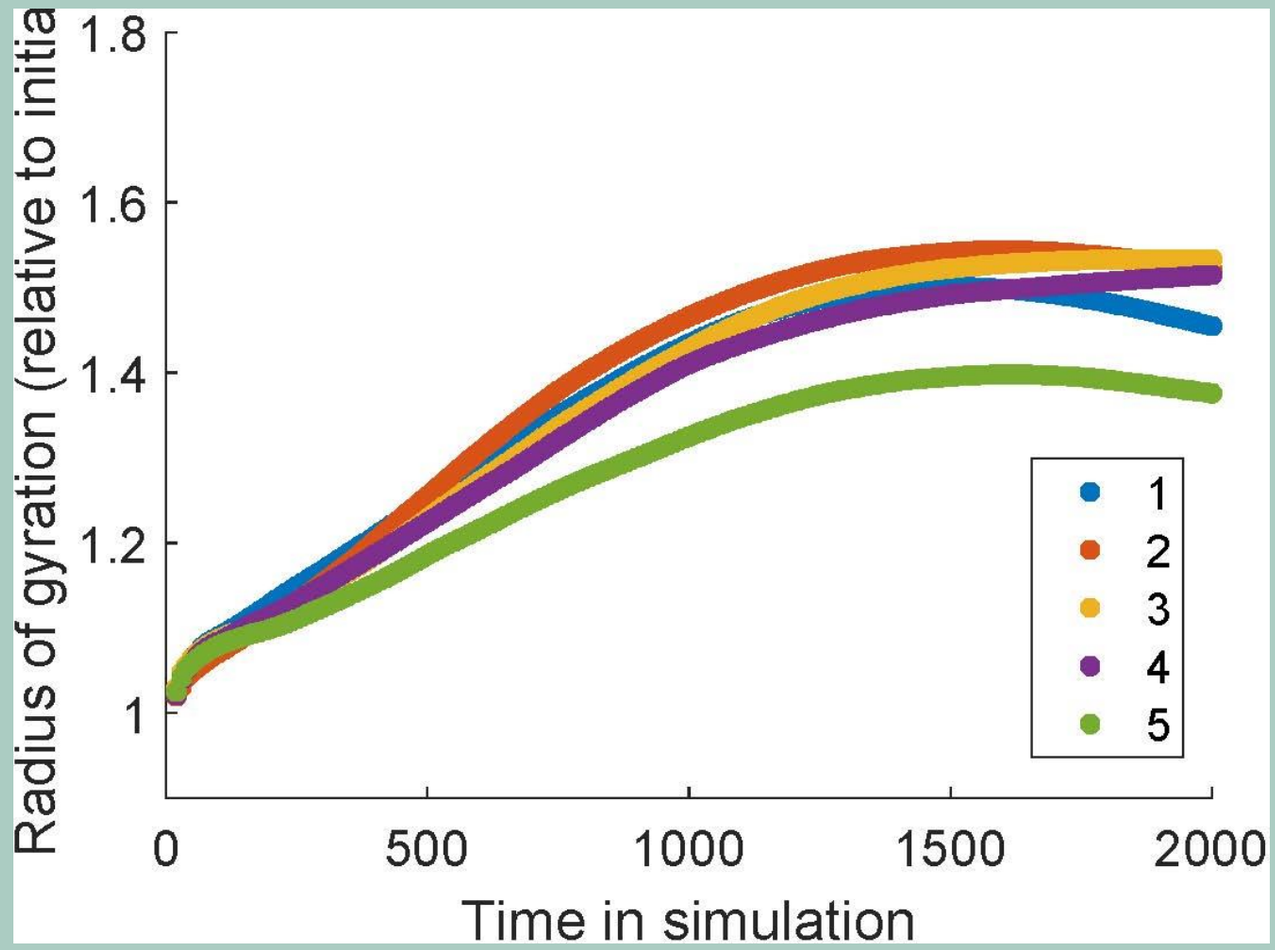

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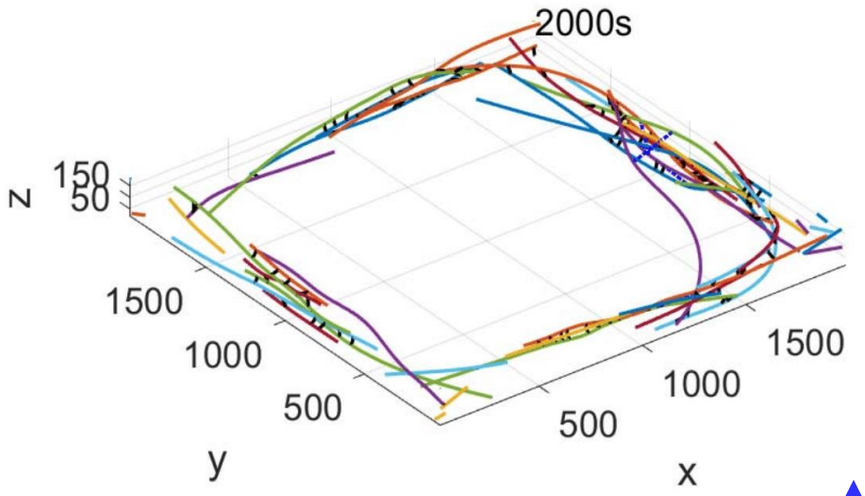

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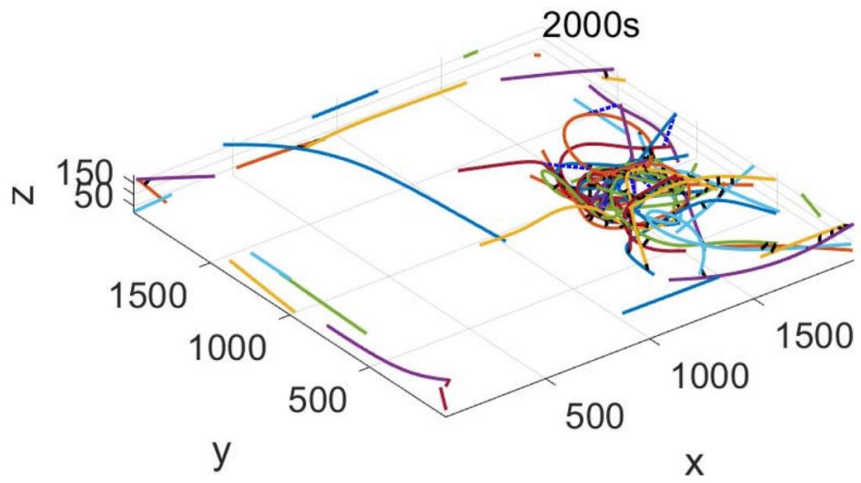
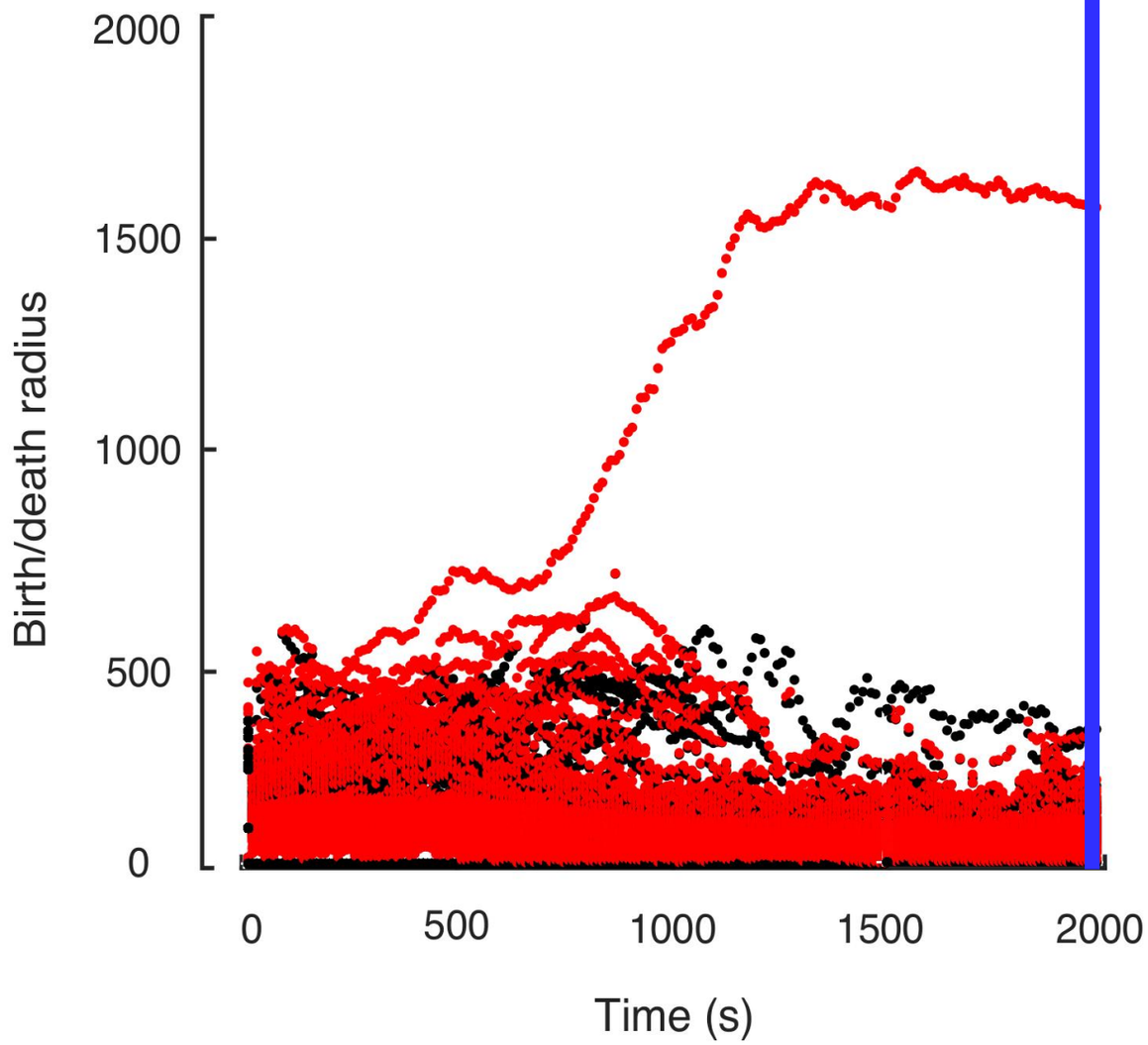
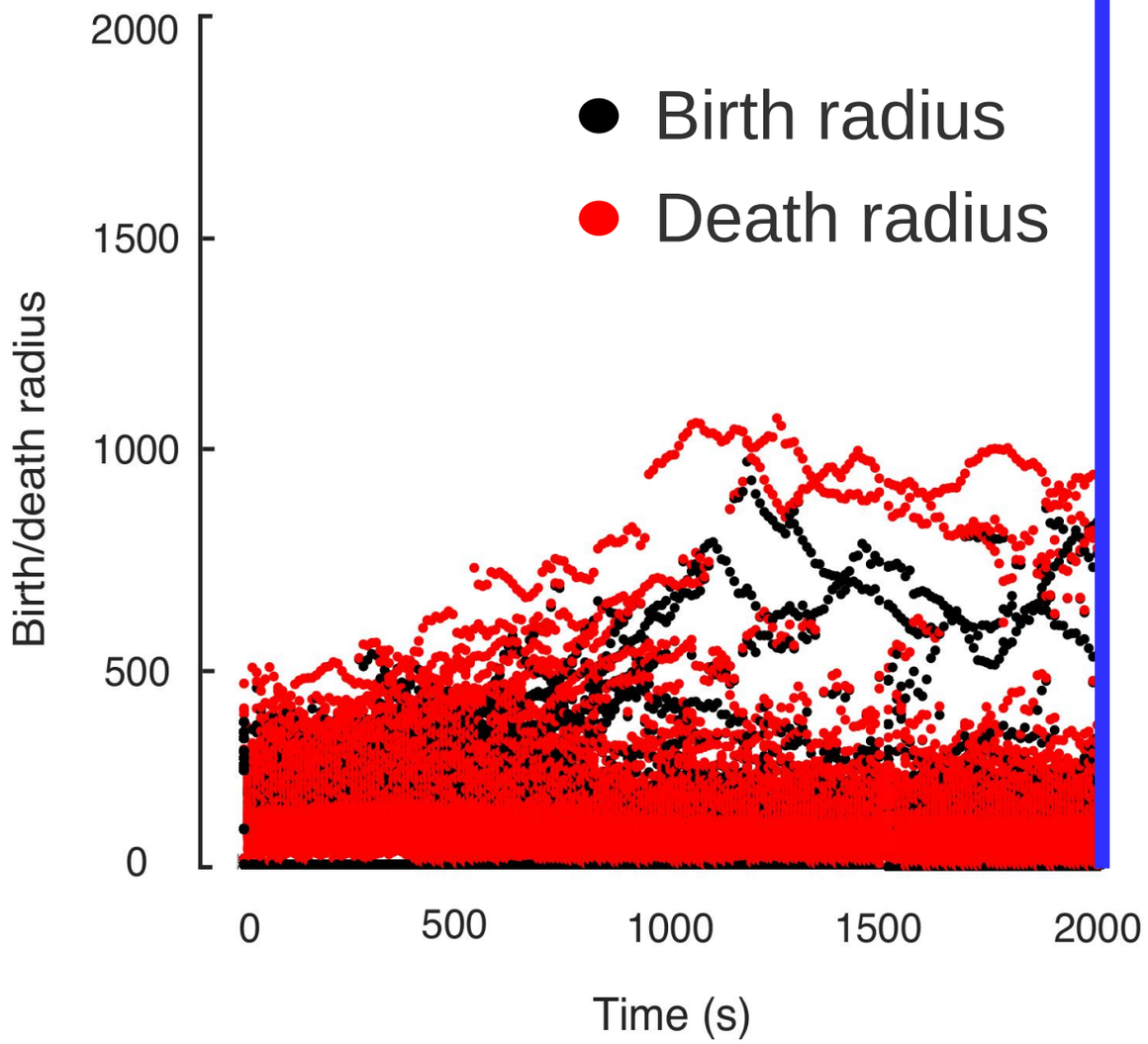
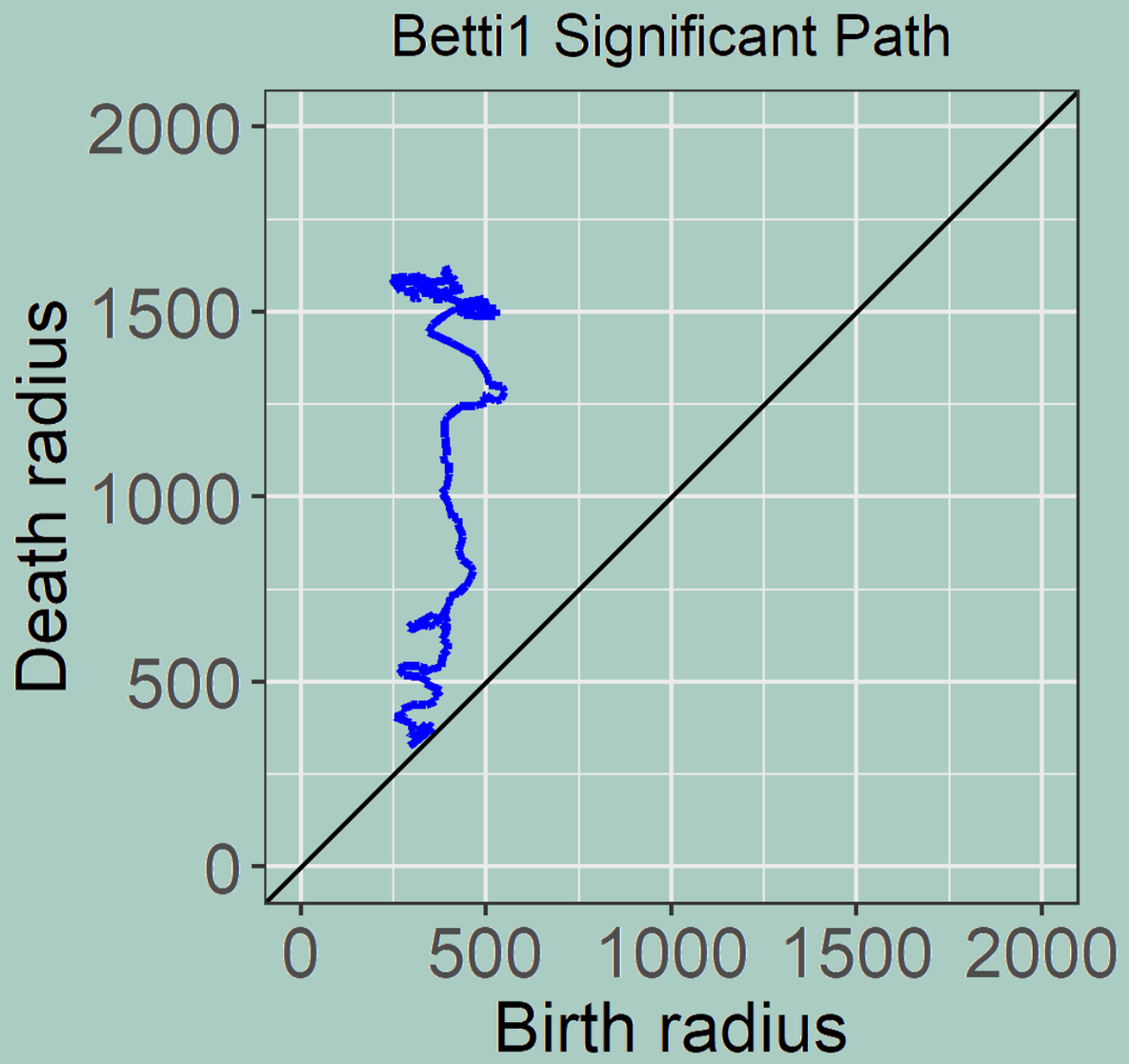






With Riley Juenemann, Adriana Dawes, and Scott McKinley (in preparation)

DETECTING RING STRUCTURE



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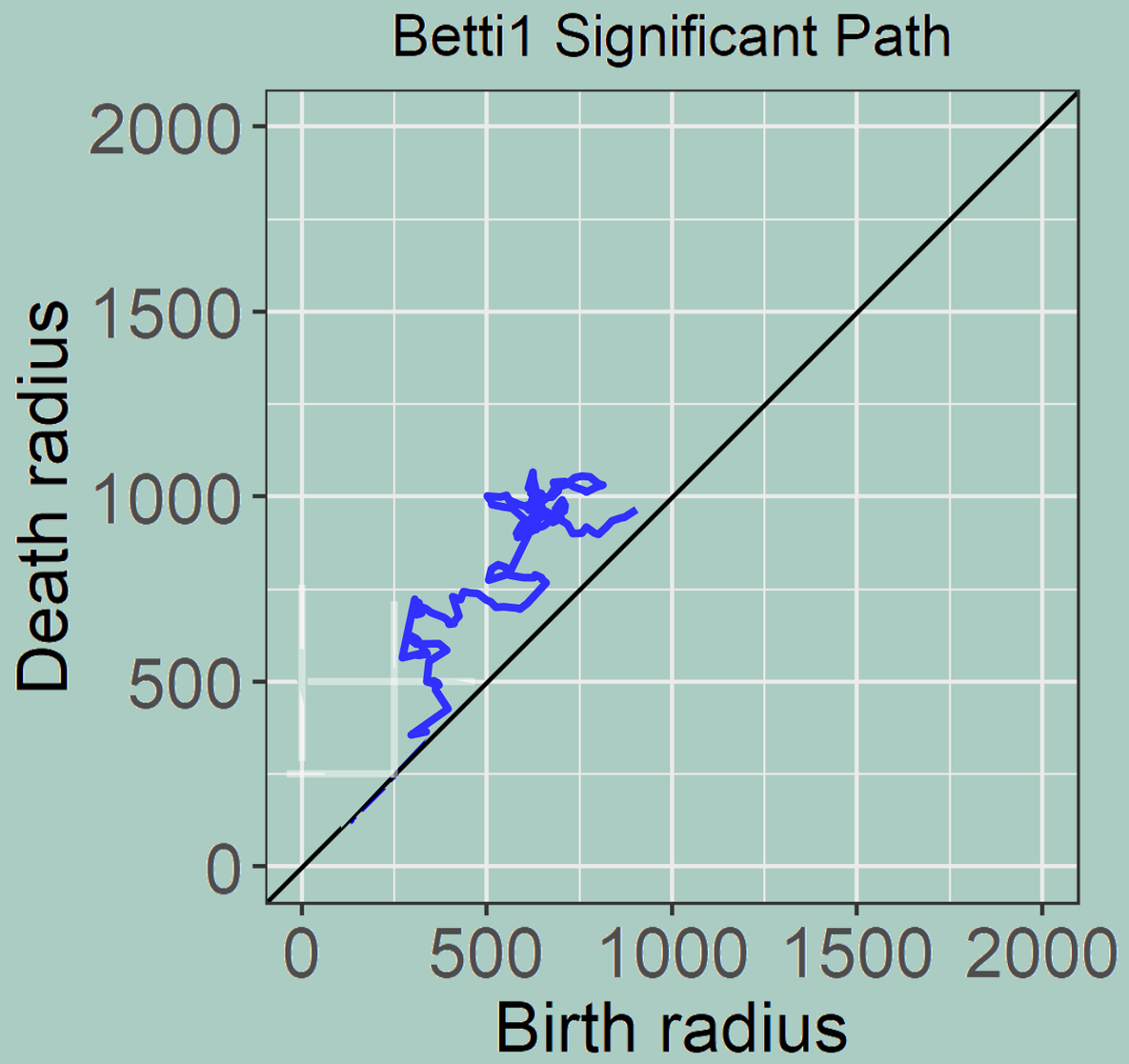

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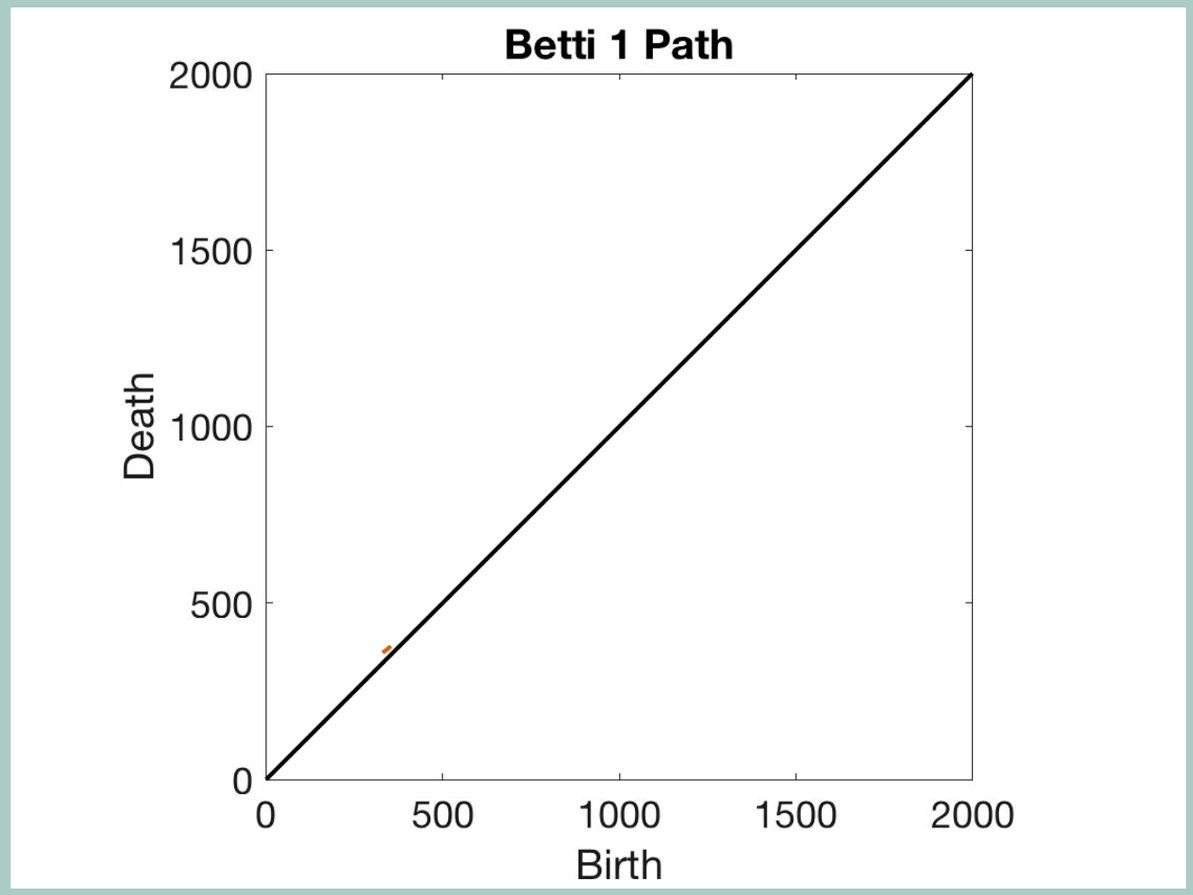
With Riley Juenemann, Adriana Dawes, and Scott McKinley (in preparation)

FUTURE WORK

- Modeling and simulation of ring formation and maintenance with realistic biological mechanisms.
- Exploration of parameters that may distinguish between motors.
- Stability? Rigorous measure of significant paths?



ACKNOWLEDGMENTS

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Thank you for your attention!

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