TOPOLOGICAL DATA ANALYSIS FOR BIOLOGICAL RING CHANNELS

Veronica Ciocanel

OSU President's Postdoctoral Scholar

Mathematical Biosciences Institute

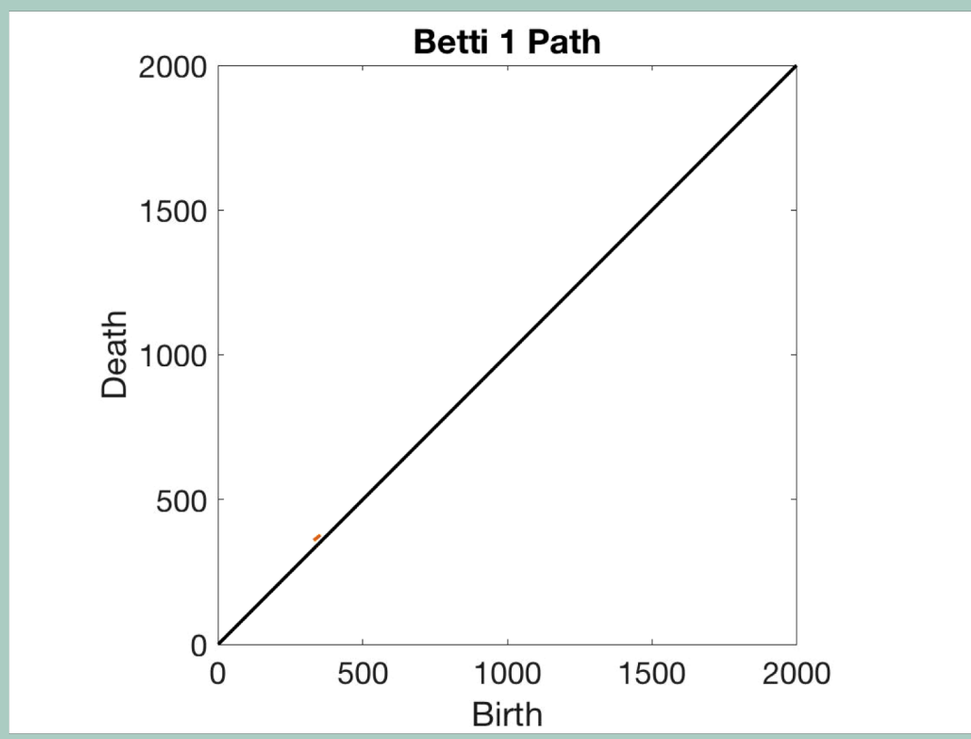
The Ohio State University

SIAM

Dynamical Systems

Snowbird, UT

May 21st 2019



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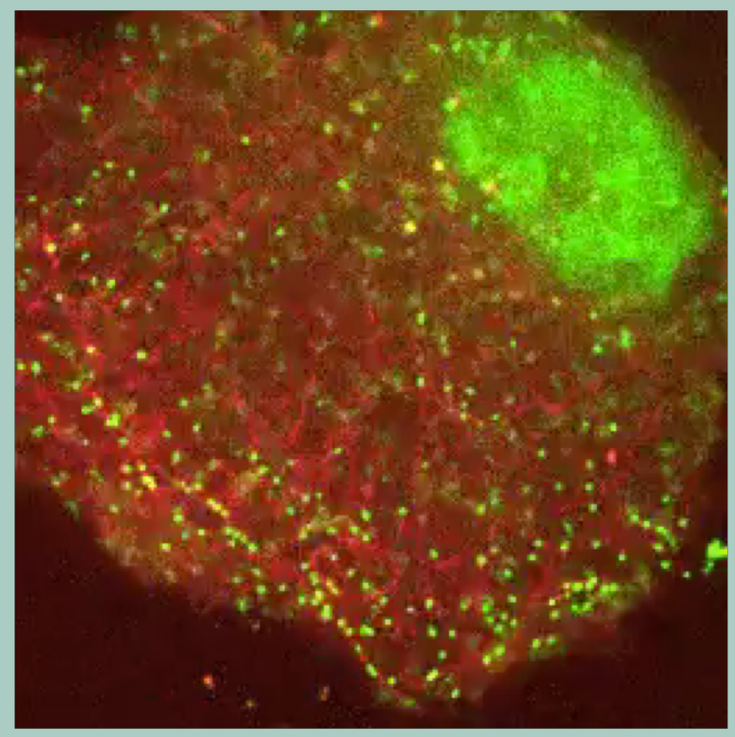
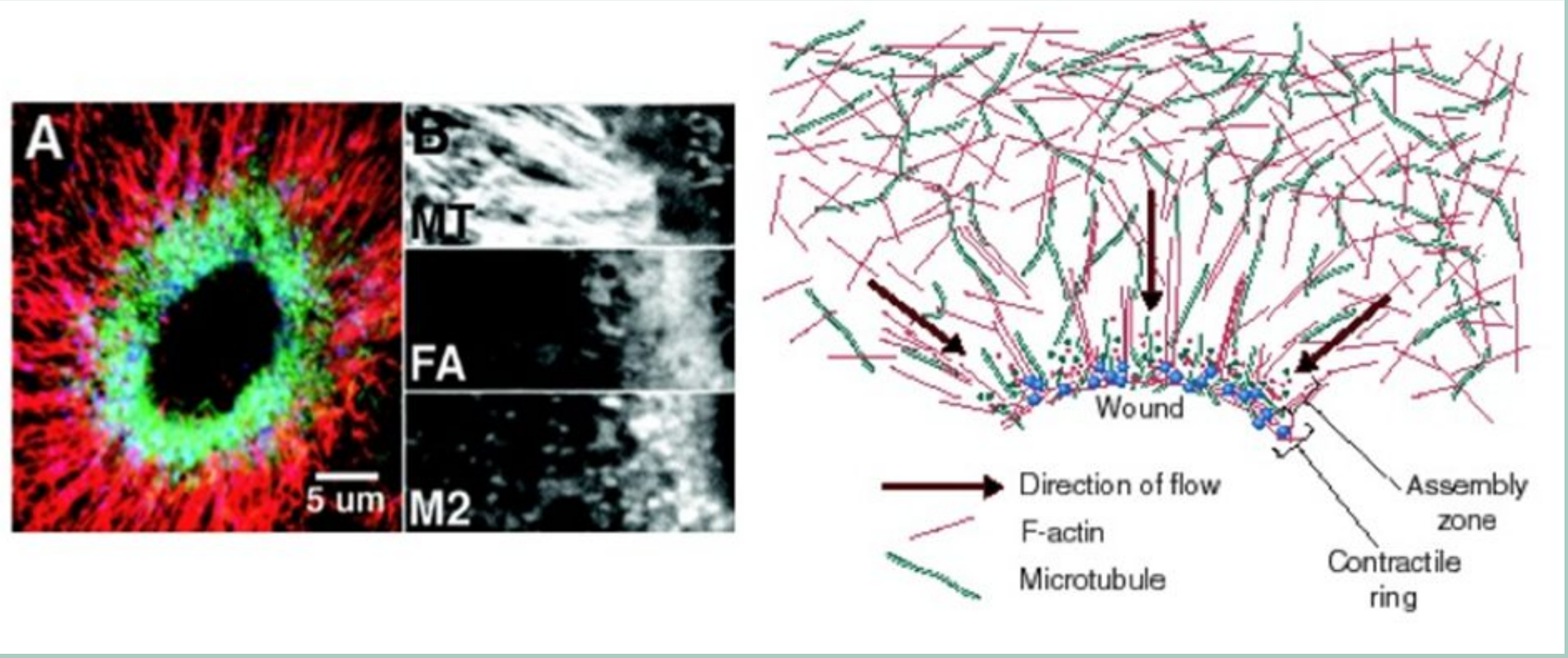


MOTIVATION

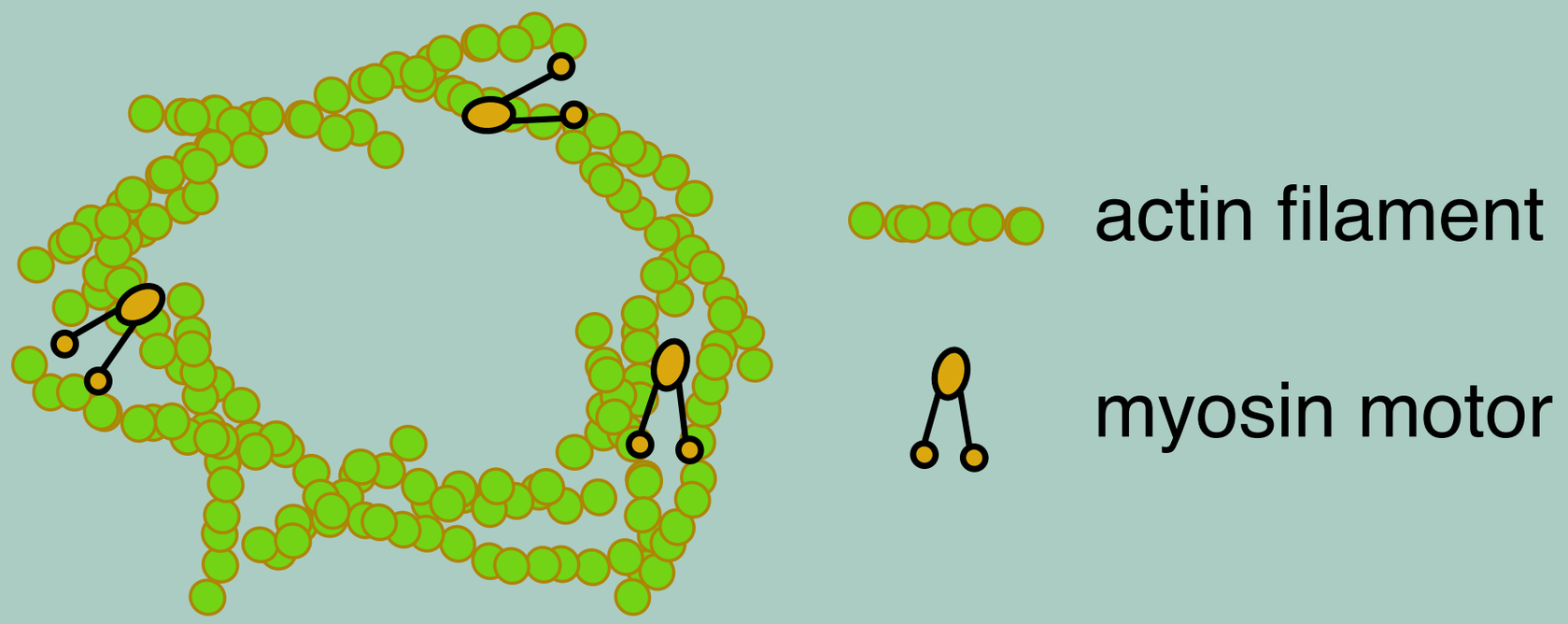
- Cells use many channels to communicate, each with different functions.
- **Ring channels** play critical roles in oogenesis, wound healing, and cell division.



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

Biophysical *Journal*
Article

Biophysical Society

Antagonistic Behaviors of NMY-1 and NMY-2 Maintain Ring Channels in the *C. elegans* Gonad

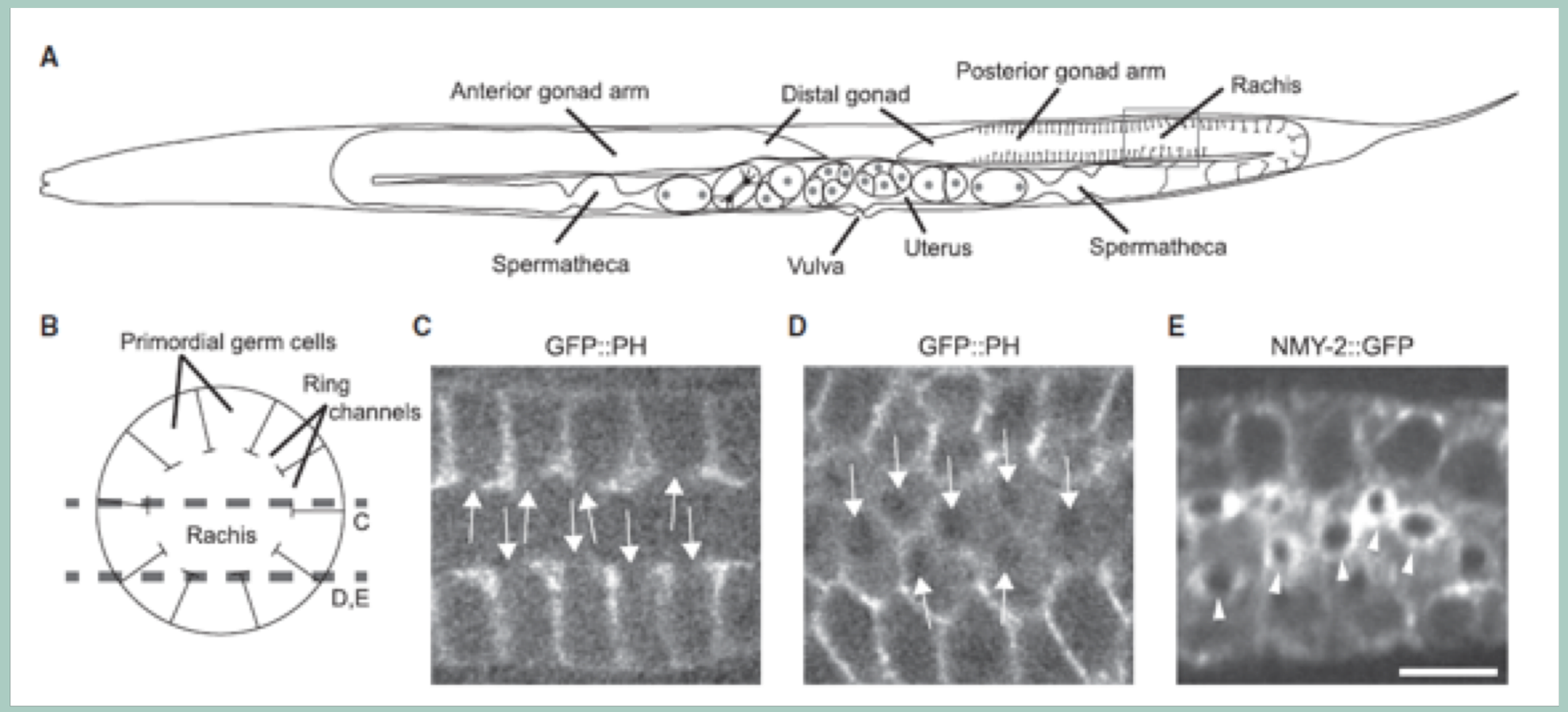
Valerie C. Coffman,[1] Torah M. Kachur,[2] David B. Pilgrim,[2] and Adriana T. Dawes[1,3,*]
[1]Department of Molecular Genetics, The Ohio State University, Columbus, Ohio; [2]Department of Biological Sciences, University of Alberta, Edmonton, Alberta Canada; and [3]Department of Mathematics, The Ohio State University, Columbus, Ohio

ABSTRACT Contractile rings play critical roles in a number of biological processes, including oogenesis, wound healing, and cytokinesis. In many cases, the activity of motor proteins such as nonmuscle myosins is required for appropriate constriction of these contractile rings. In the gonad of the nematode worm *Caenorhabditis elegans*, ring channels are a specialized form of contractile ring that are maintained at a constant diameter before oogenesis. We propose a model of ring channel maintenance that explicitly incorporates force generation by motor proteins that can act normally or tangentially to the ring channel opening. We find that both modes of force generation are needed to maintain the ring channels. We demonstrate experimentally that the type II myosins NMY-1 and NMY-2 antagonize each other in the ring channels by producing force in perpendicular directions: the experimental depletion of NMY-1/theoretical decrease in orthogonal force allows premature ring constriction and cellularization, whereas the experimental depletion of NMY-2/theoretical decrease in tangential force opens the ring channels and prevents cellularization. Together, our experimental and theoretical results show that both forces, mediated by NMY-1 and NMY-2, are crucial for maintaining the appropriate ring channel diameter and dynamics throughout the gonad.

Adriana Dawes, OSU

- In the worm *C. elegans*: ring channels allow for nutrient exchange in development.

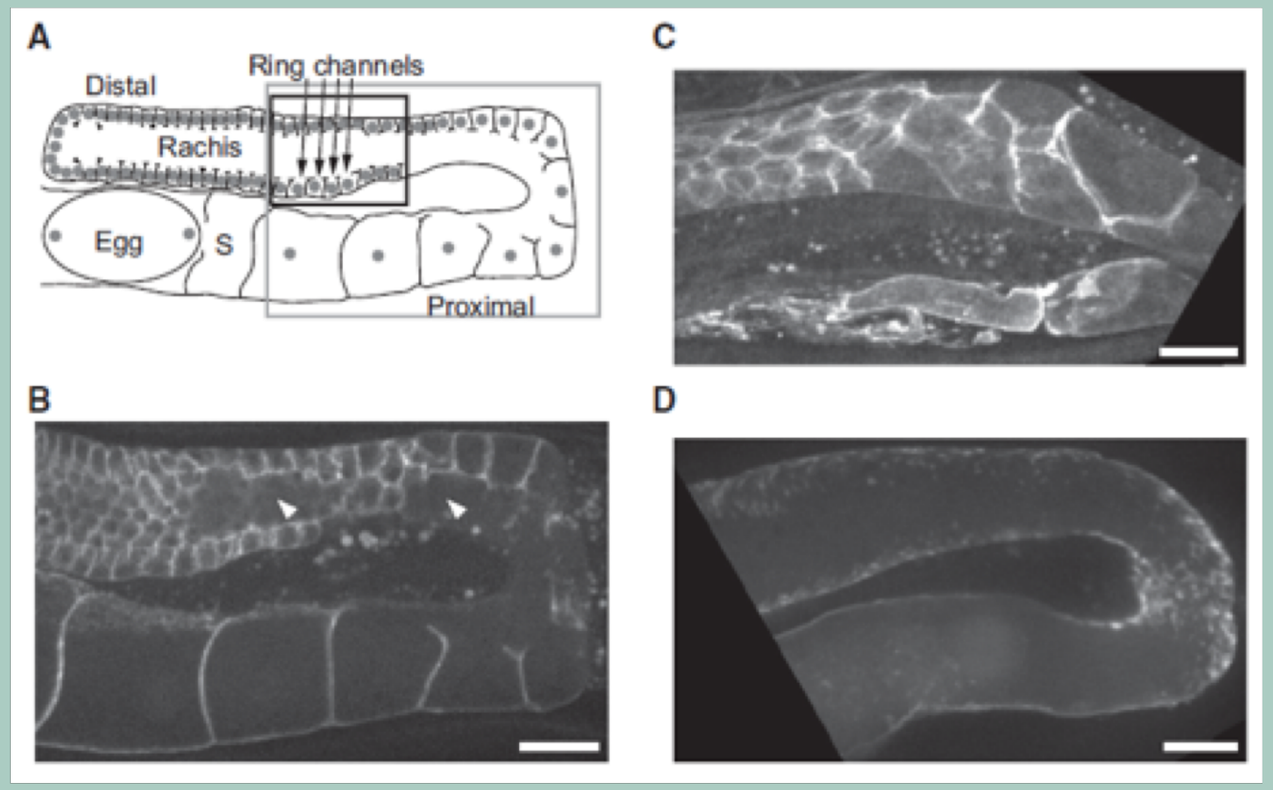
SPECIFIC MOTIVATION



- Ring channels (formed of actin polymers) in the worm.

Coffman et al, 2016

THE QUESTION



Knockdown motor 1

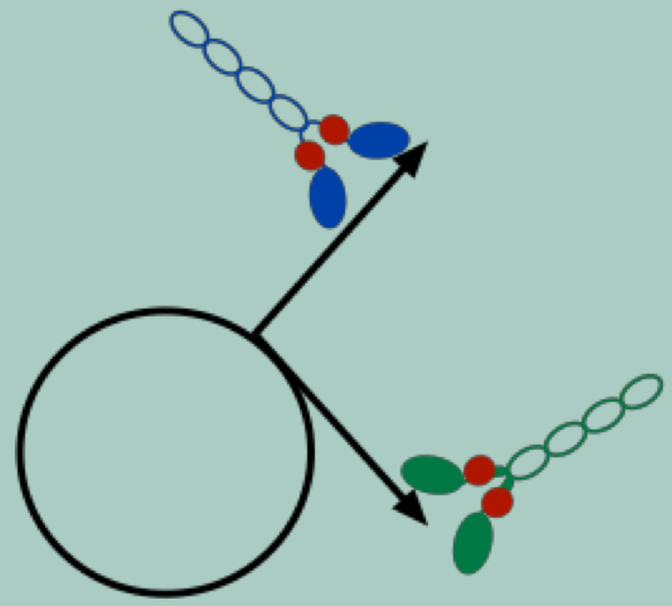
Knockdown motor 2

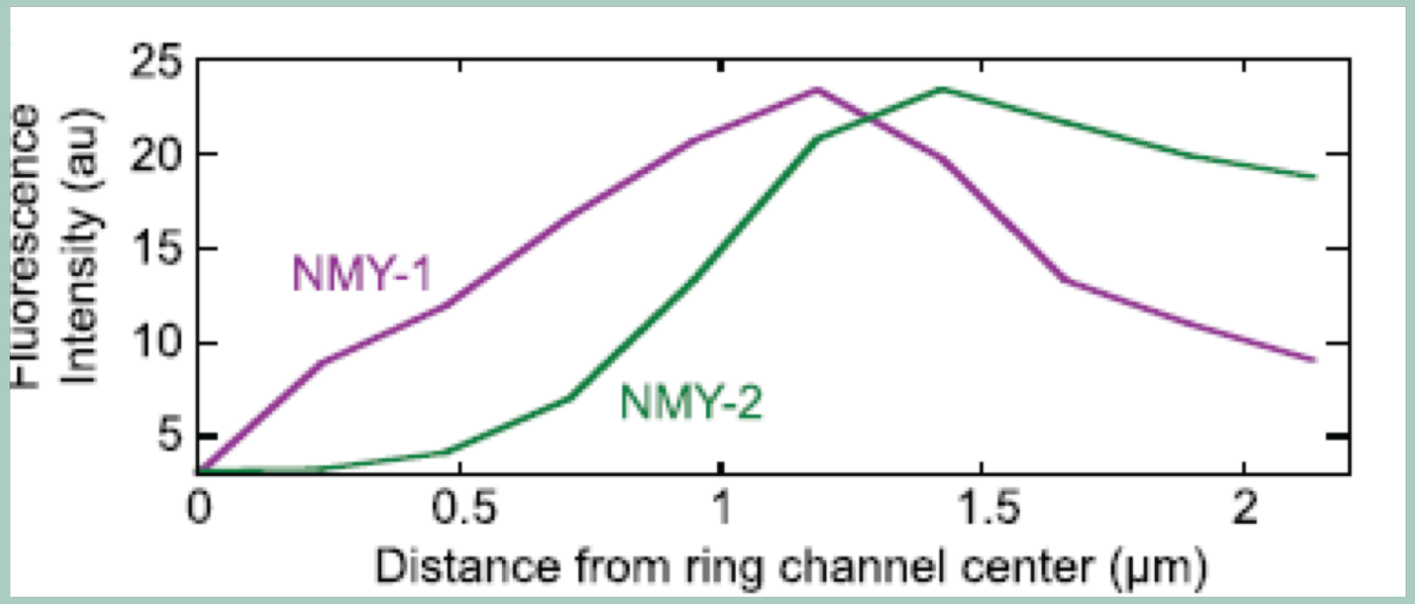
- Two types of myosin motors, believed to function similarly, are involved in ring channel dynamics.
- Experiments show that they antagonize each other with respect to cellularization.

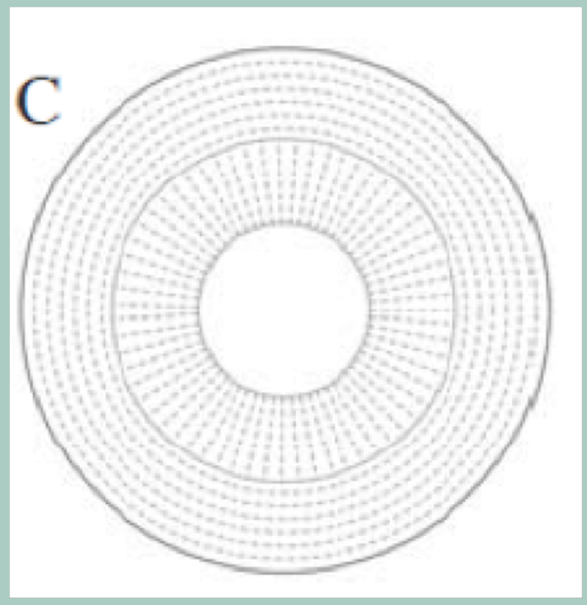
Coffman et al, 2016

GOALS

- Investigate ring formation using agent-based models for actin filaments and motors.
- Identify potential mechanistic differences between motors.







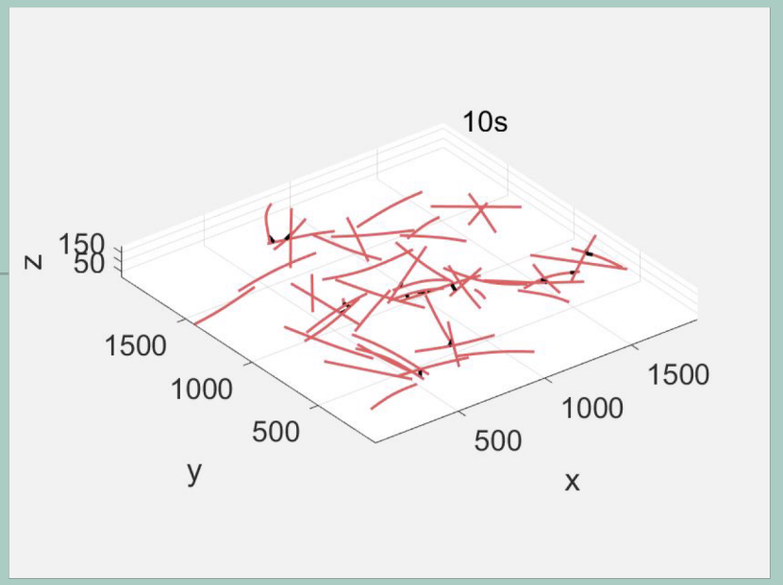
Coffman et al, 2016

OUTLINE

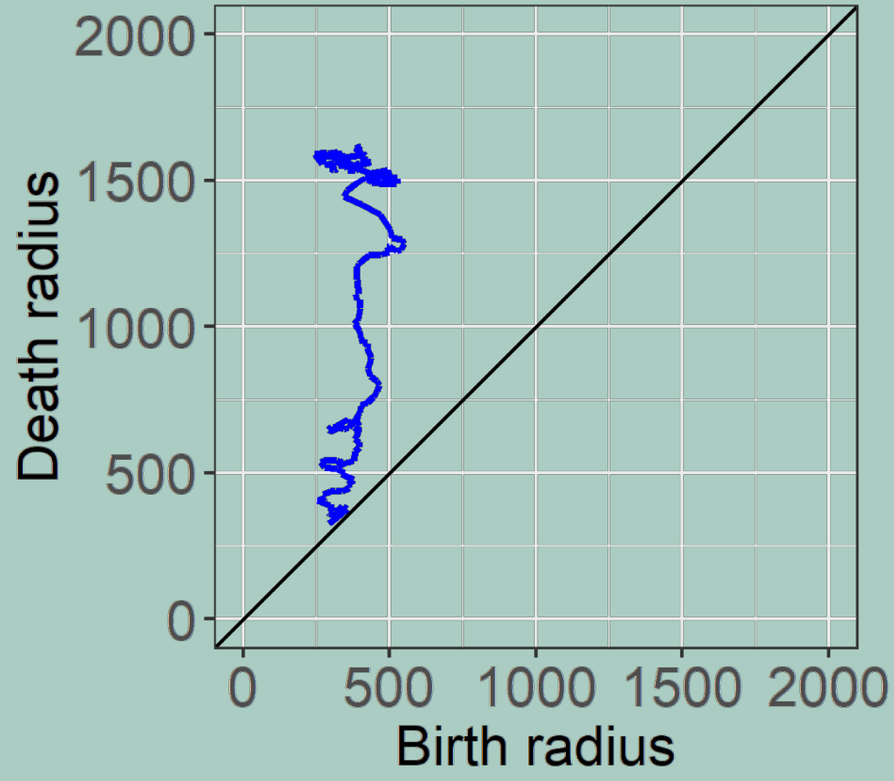
1. Agent-based model simulations of actin-myosin interactions and data analysis measures

2. Detecting ring structure in time-series simulation data

3. Connection with in vitro experimental data

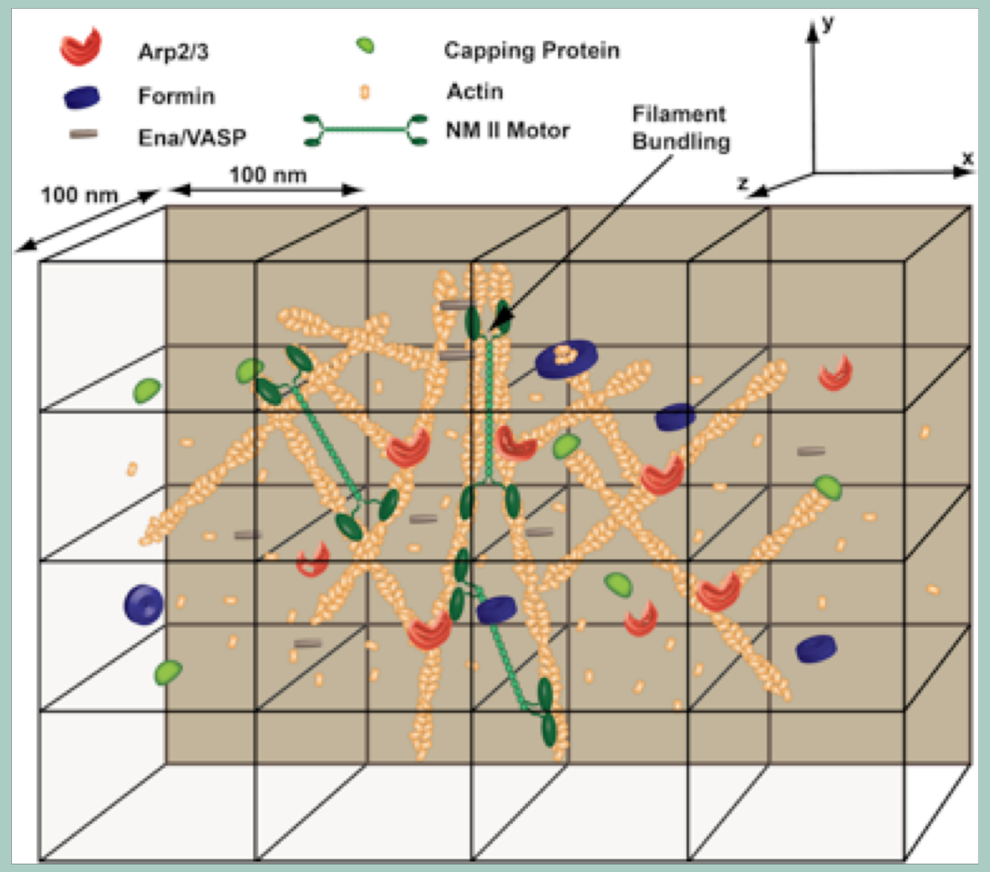


Betti1 Significant Path



1. AGENT-BASED MODELING AND SIMULATION

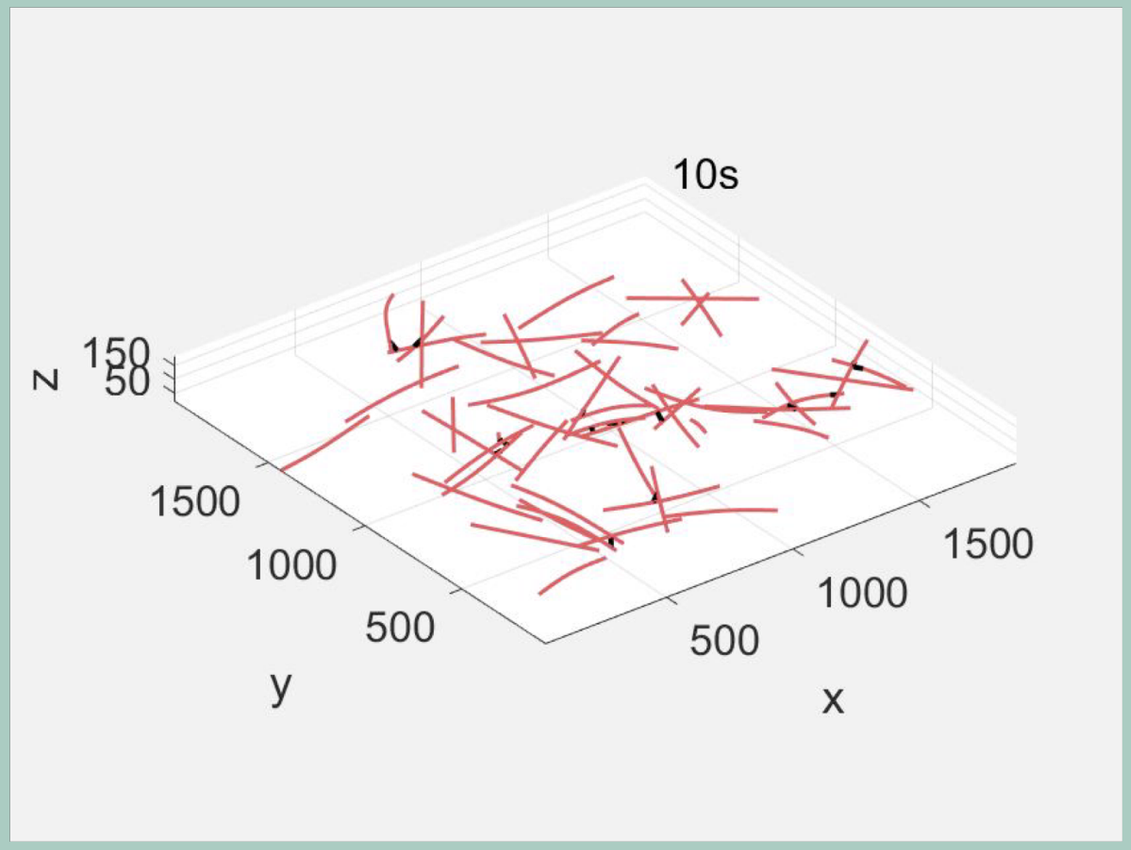
- Accounts for dynamics and molecular transport of chemical species.
- Diffusion and active transport are modeled as stochastic jumps between compartments.
- Is based on energy minimization.



Medyan (Papoian Lab)

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

DATA ANALYSIS MEASURES



Riley Juenemann, Tulane University

Scott McKinley, Tulane University

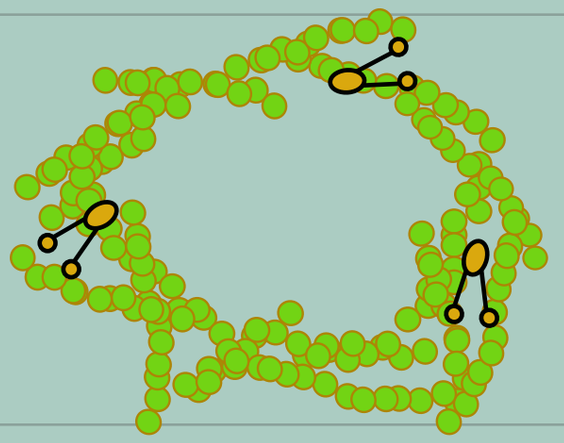
actin filament

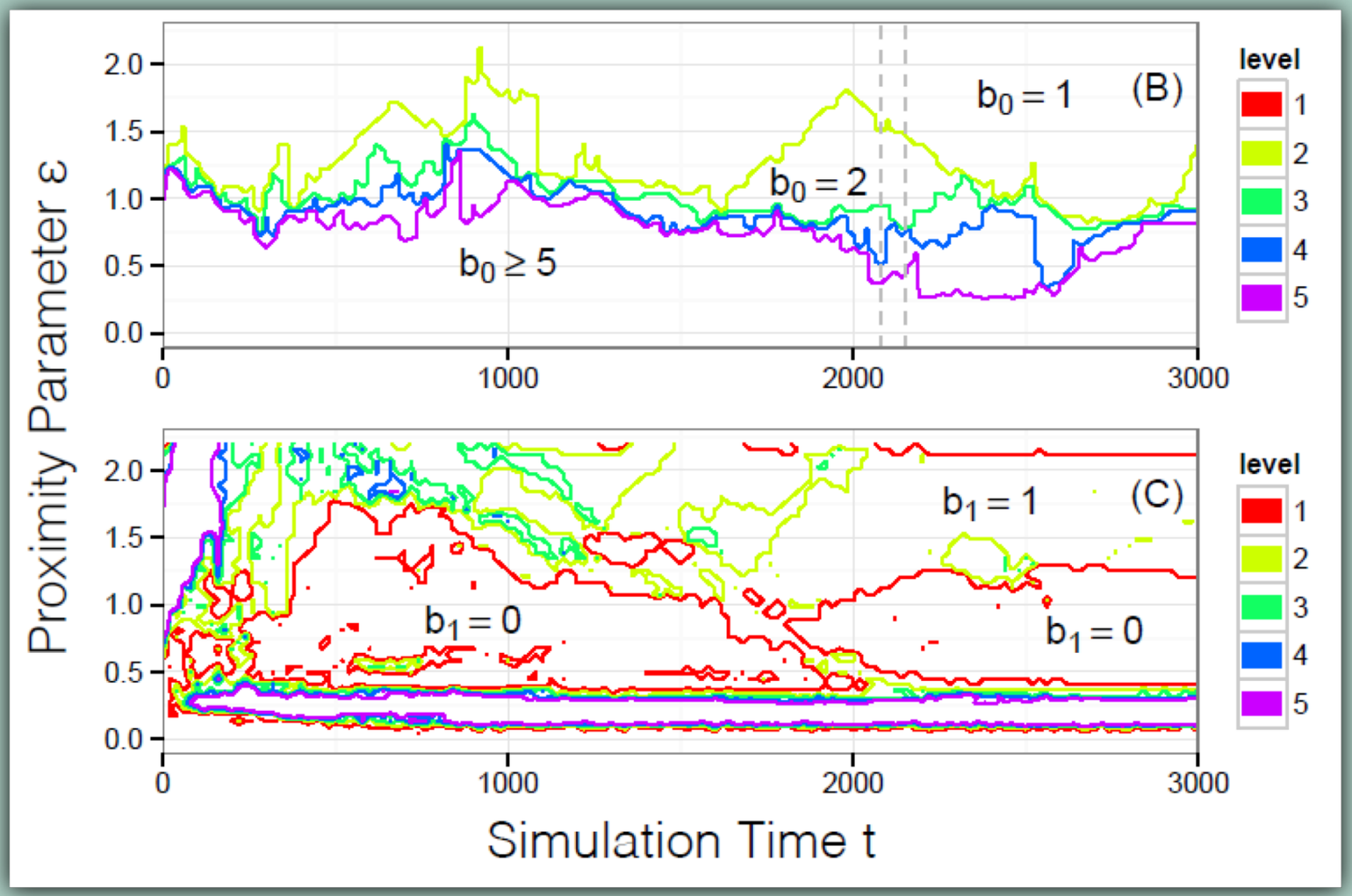
myosin motor

cross-linker

- Contractility, alignment, filament length distributions

2. DETECTING RING STRUCTURE



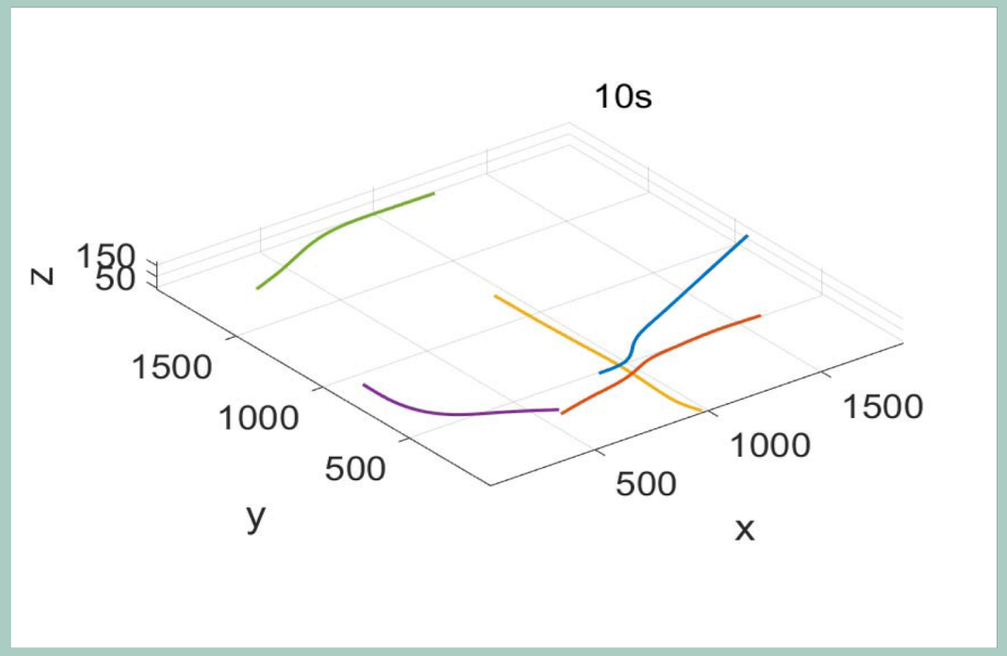


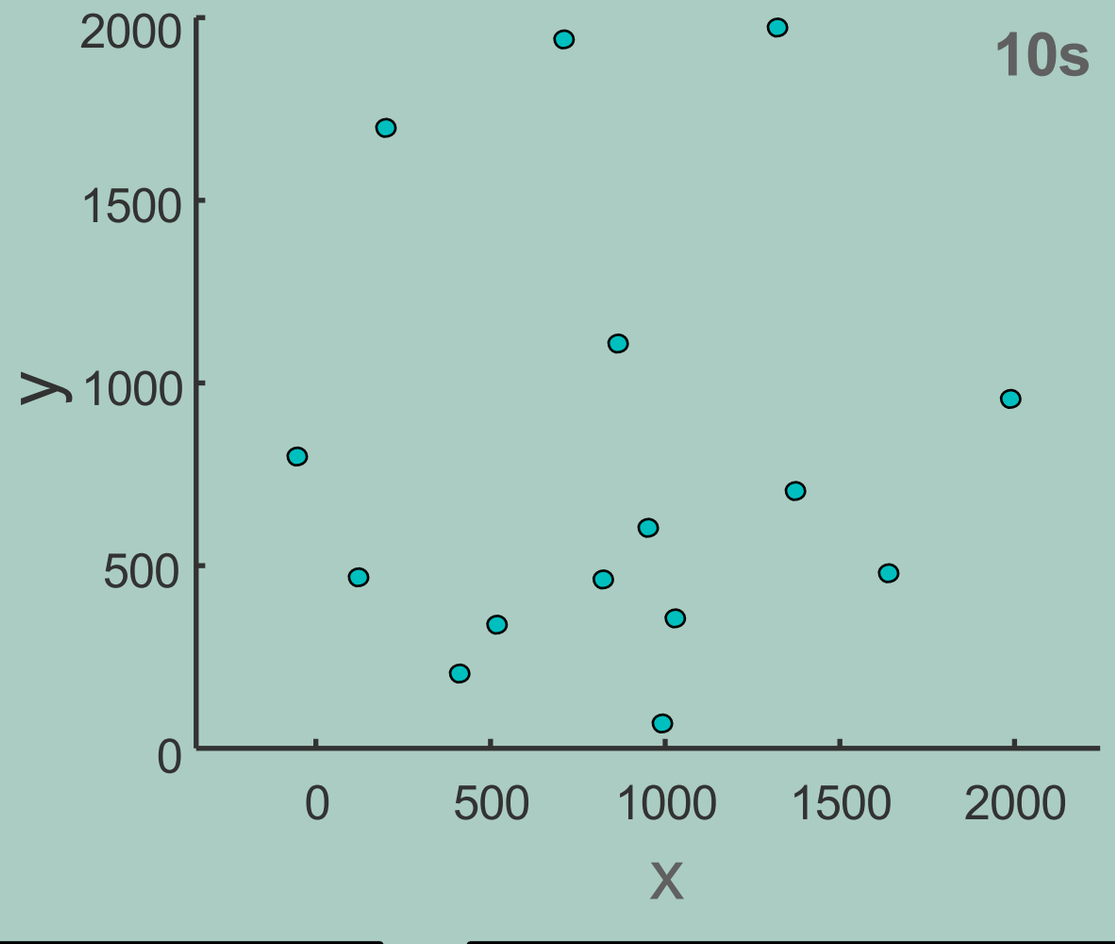
Chad Topaz, Williams College

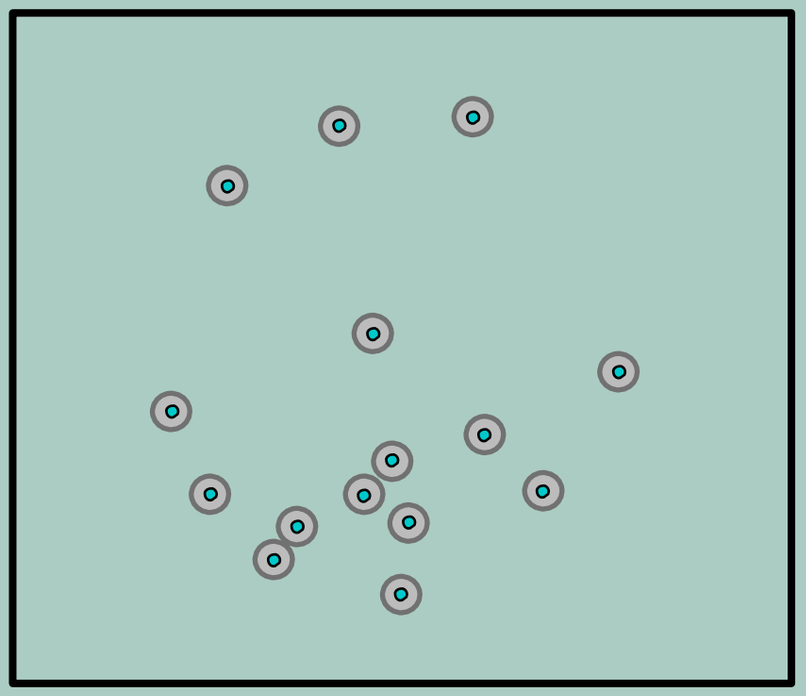
- Inspiration: Crocker plots (Topaz, Zieglemeier, Halverson)

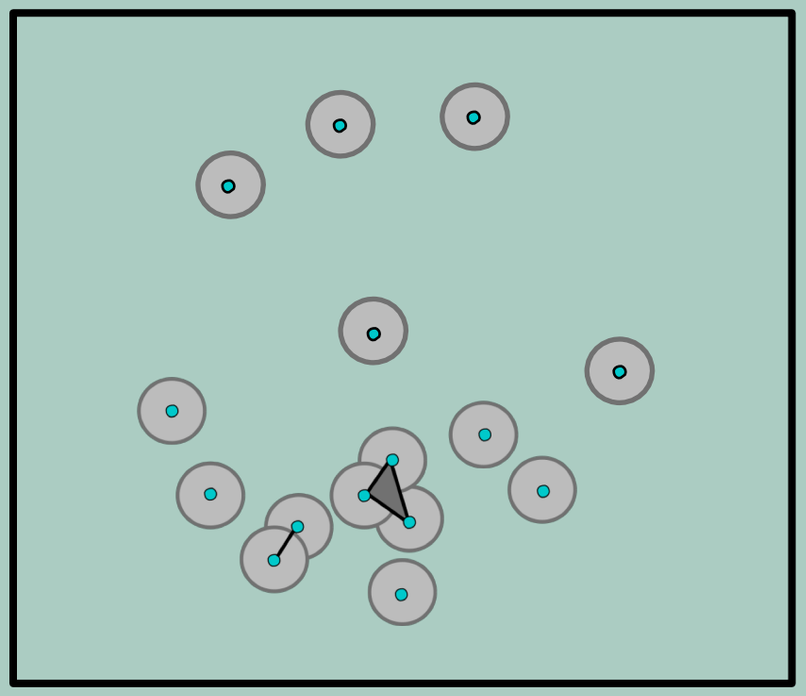
Topaz, Zieglemeier, Halverson, 2015

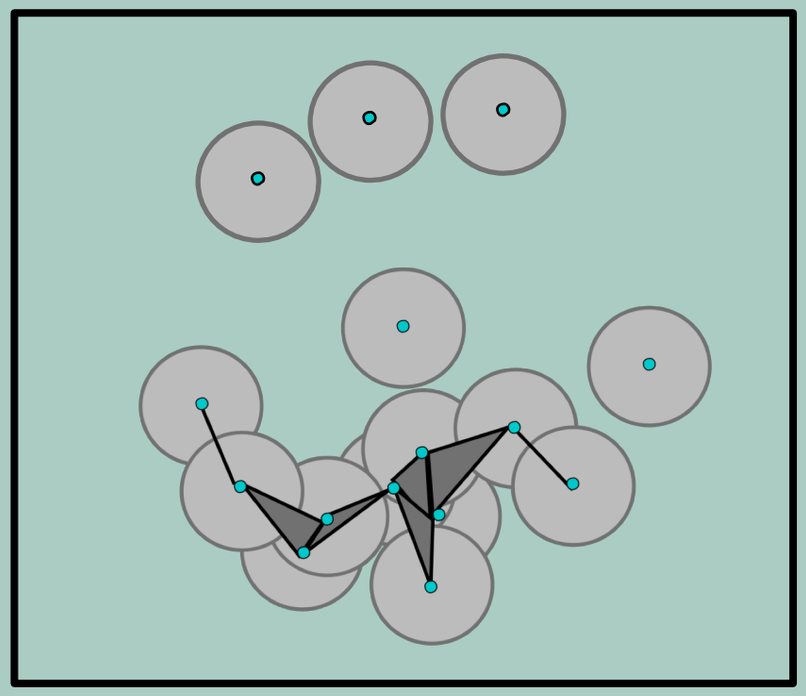
FRAMEWORK


10s
z
150
50
1500
1000
500
y
500
1000
1500
x

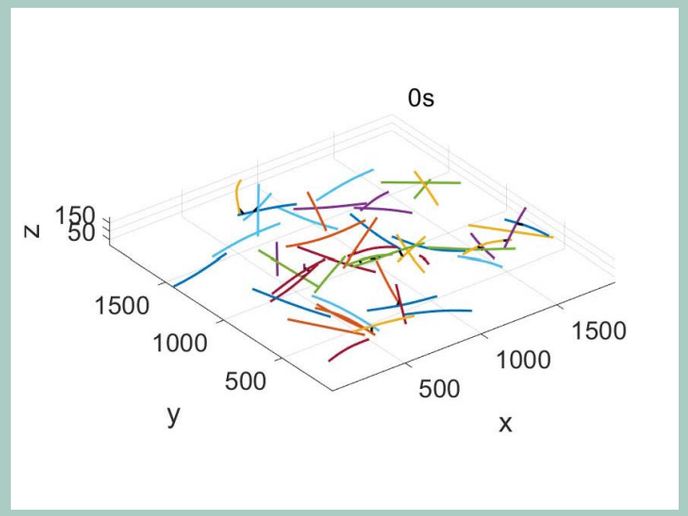

10s
2000
1500
1000
500
0
y
0
500
1000
1500
2000
x



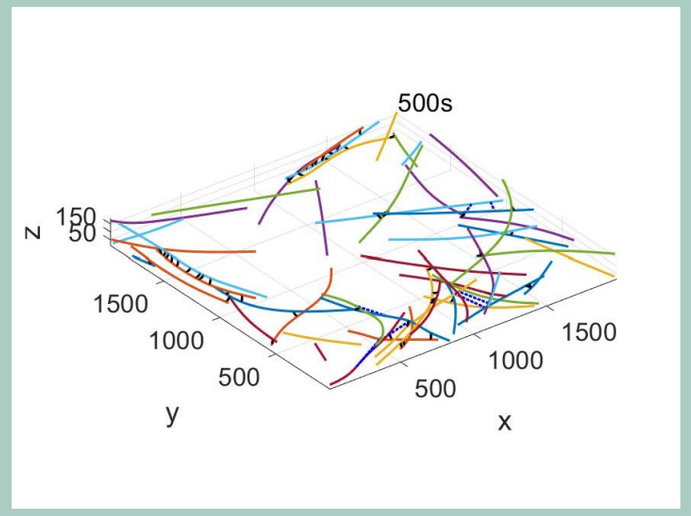




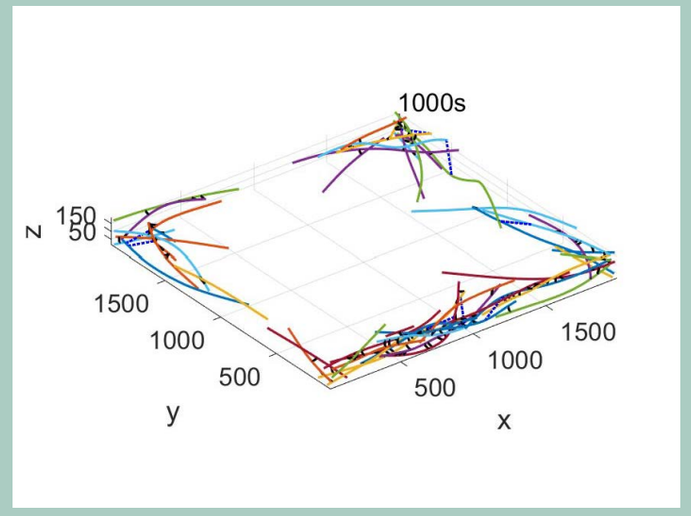
0s

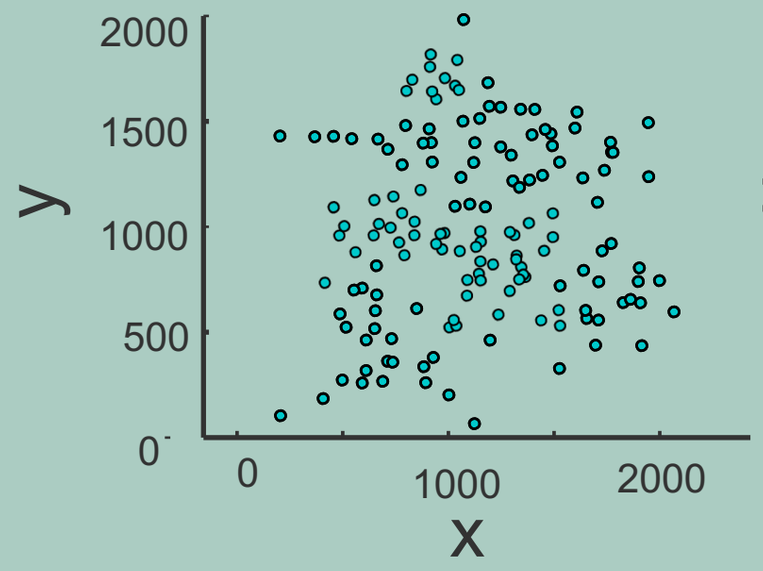


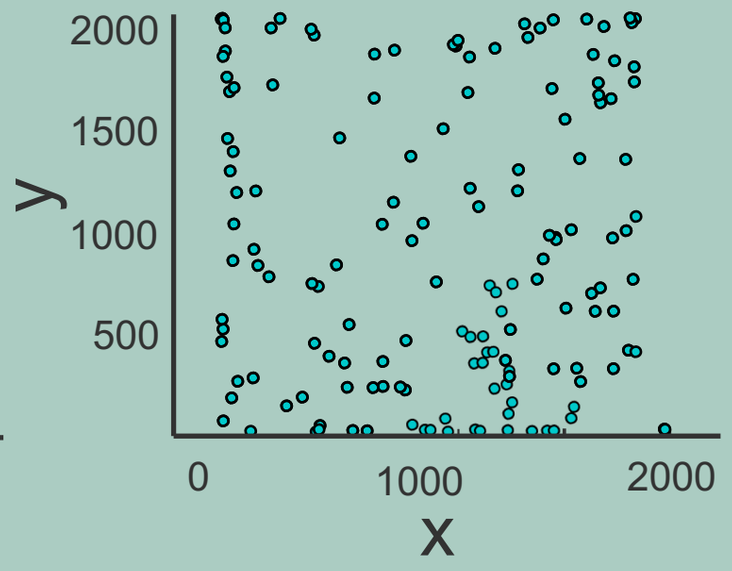
500s

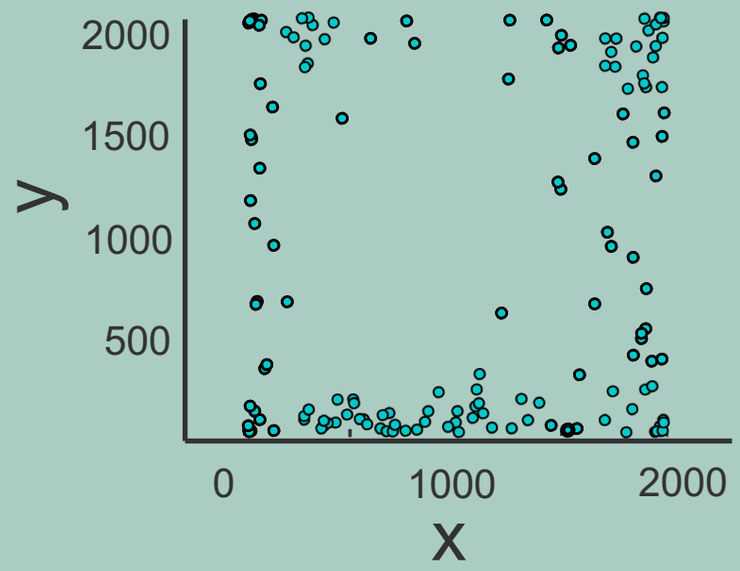


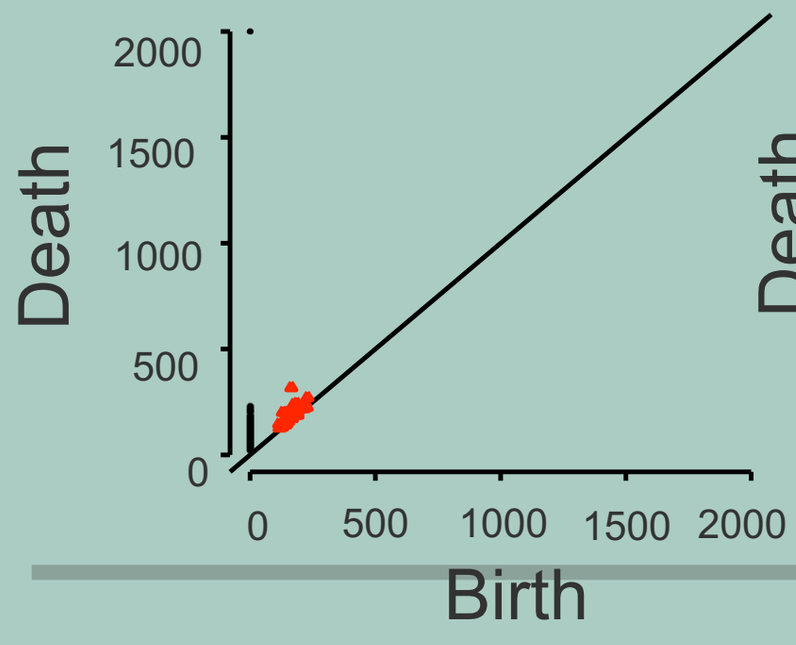
1000s

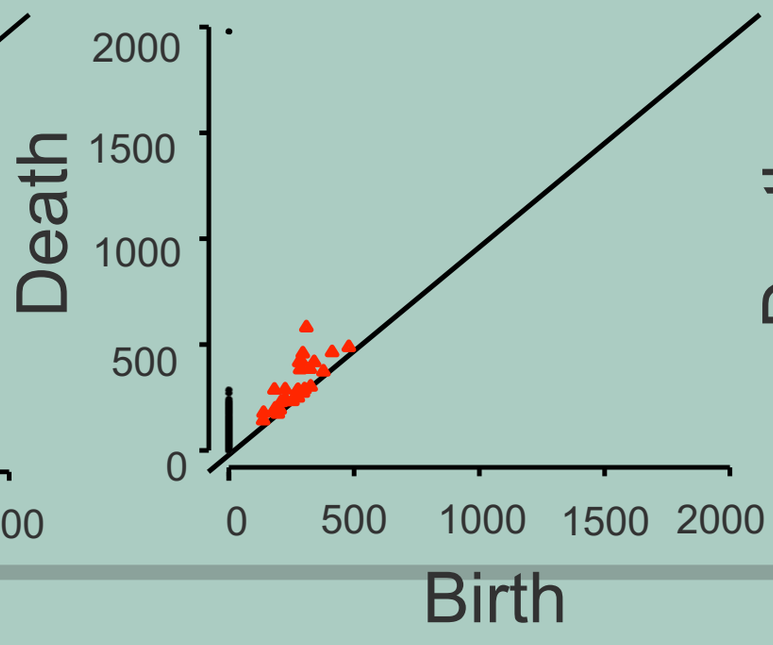


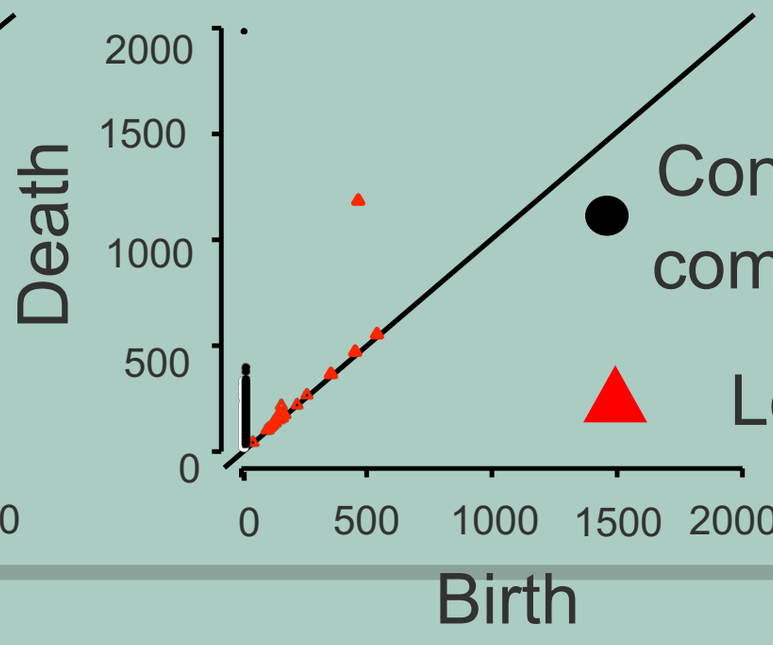






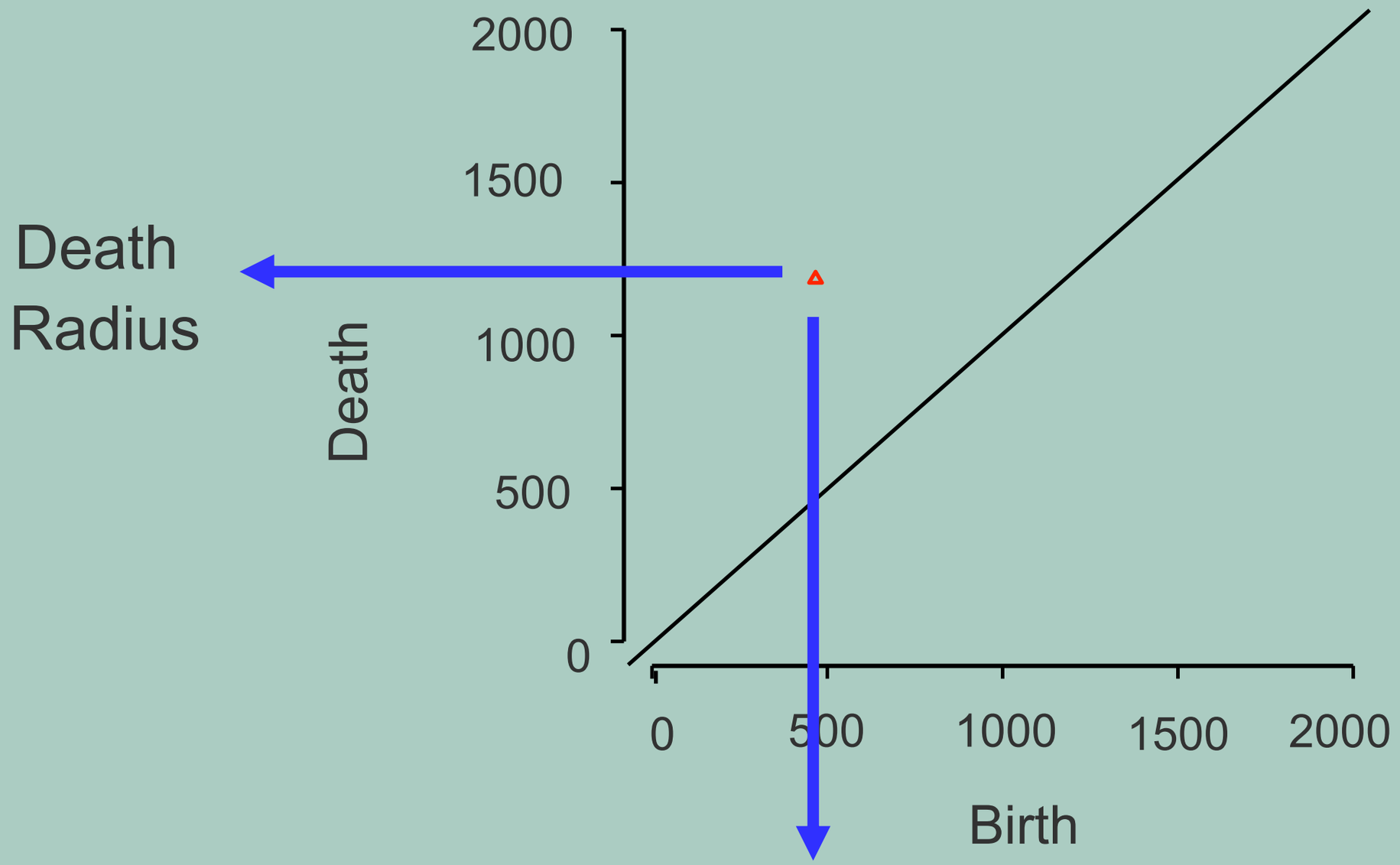




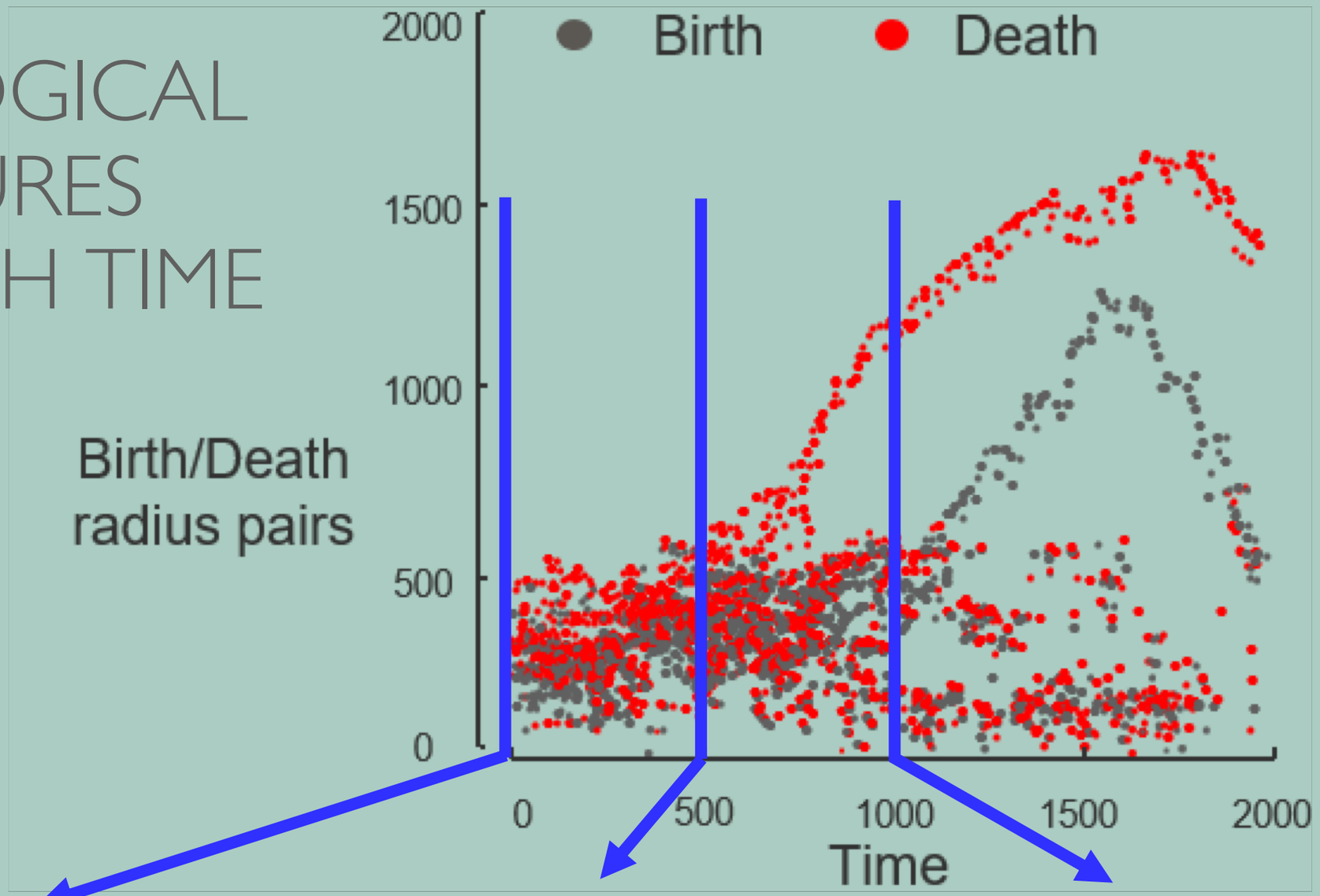


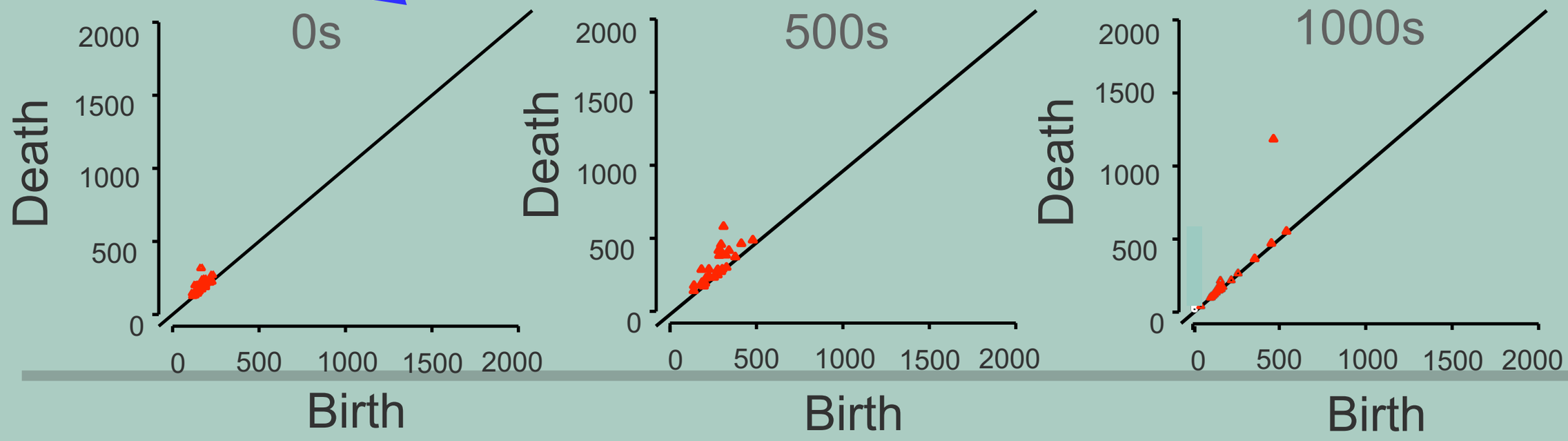
Connected component

Loop

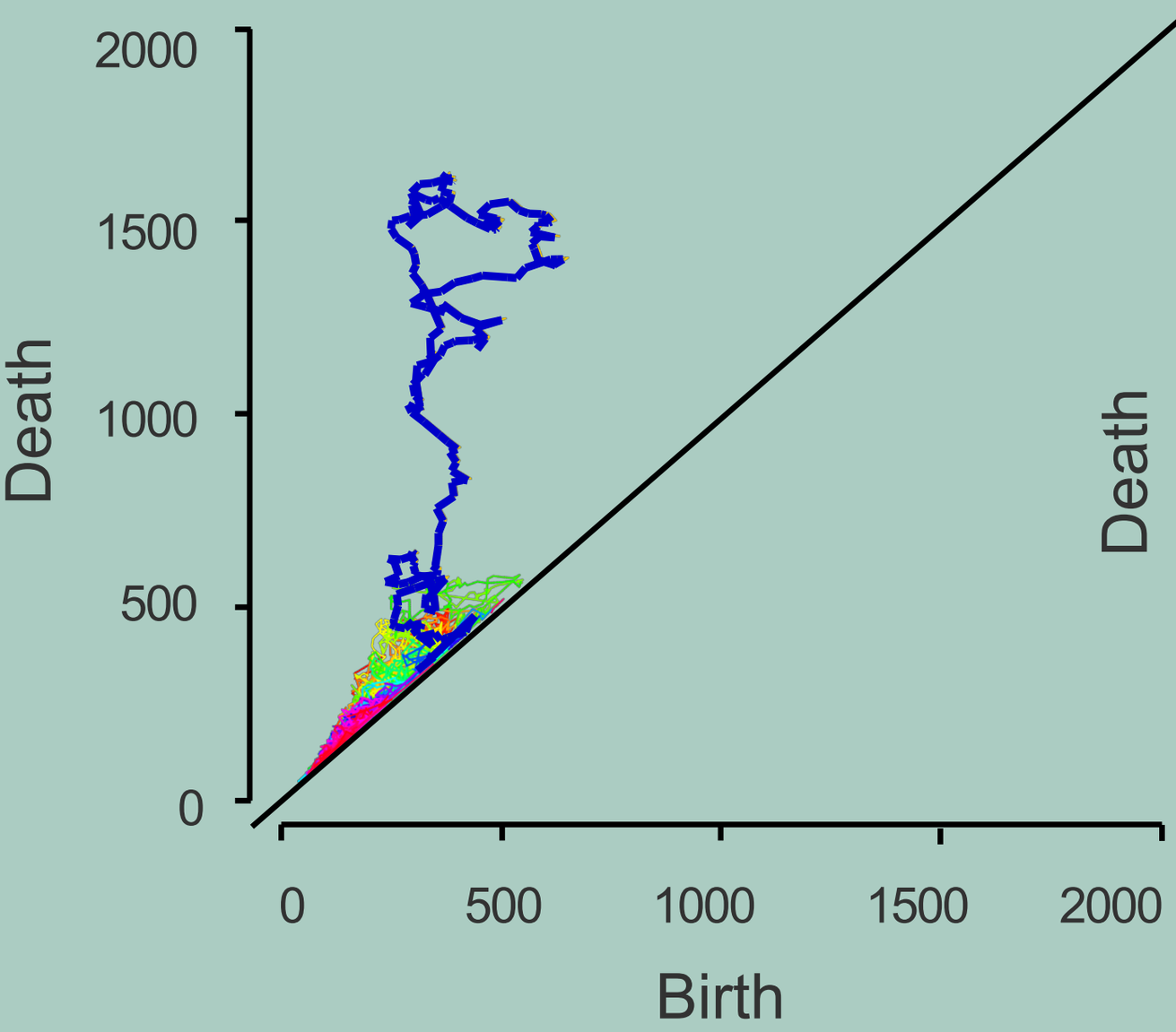

Death
Radius
2000
1500
1000
500
0
Death
0
500
1000
1500
2000
Birth
Birth
Radius

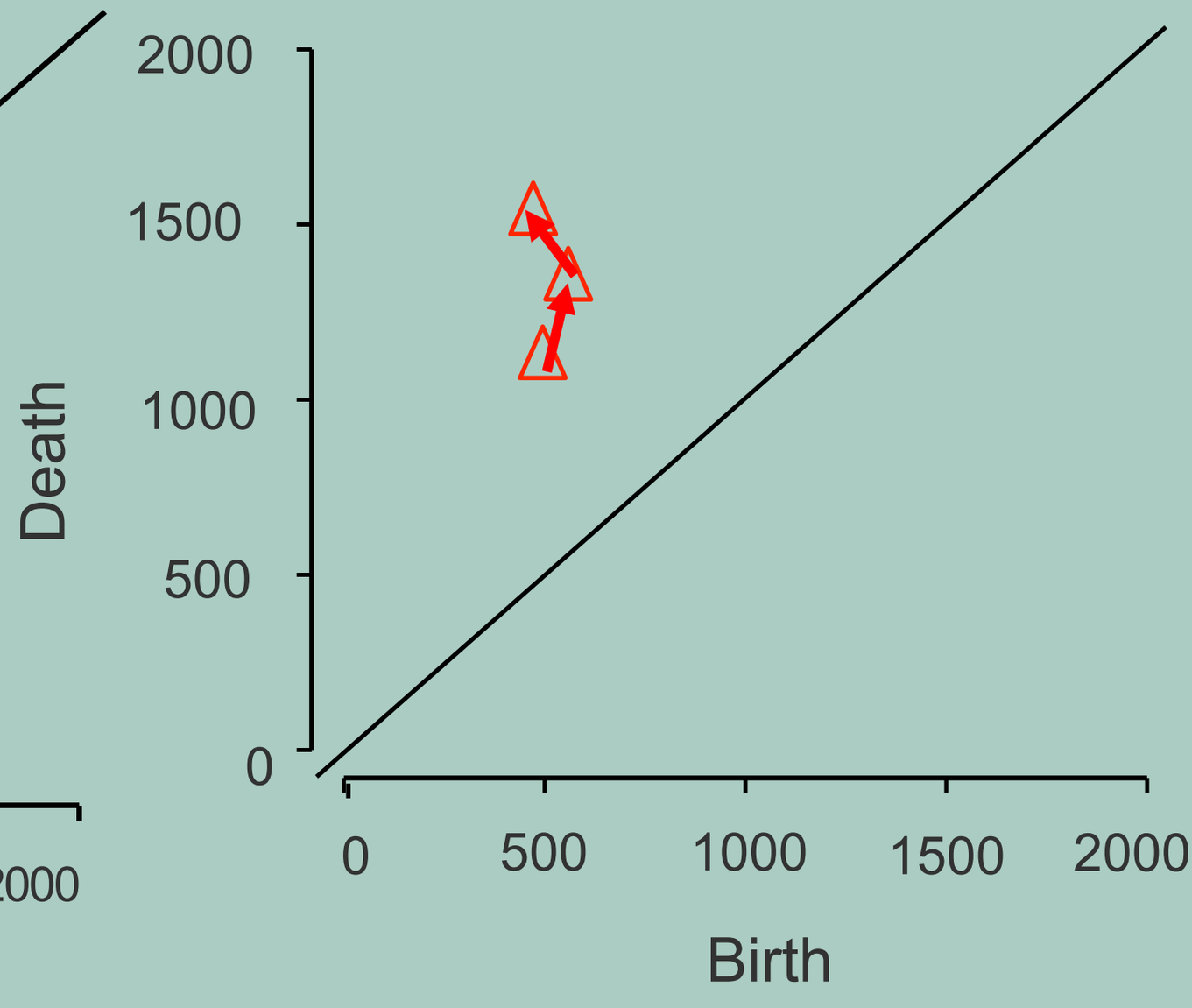
TOPOLOGICAL FEATURES THROUGH TIME





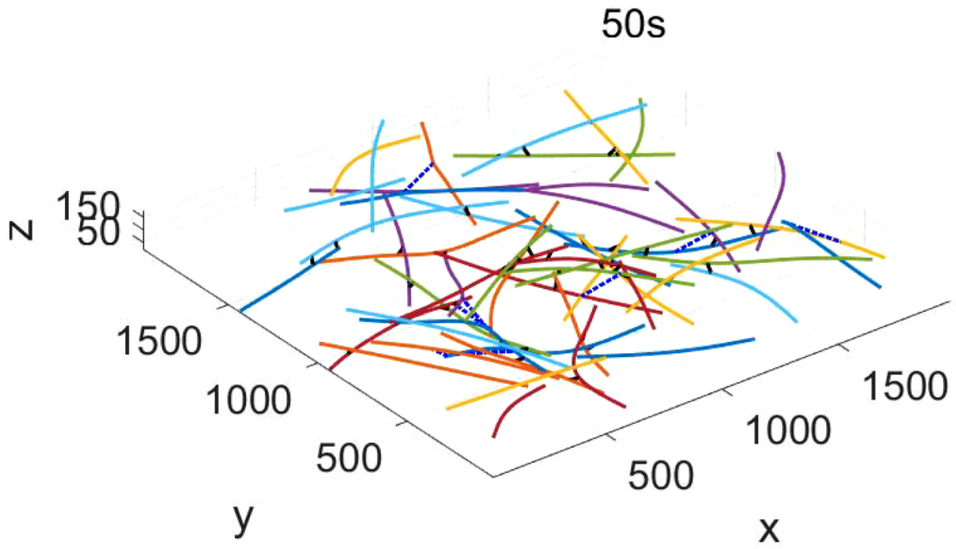
- Propose a method for connecting pairs through time.
- Extract the most significant Betti 1 path.

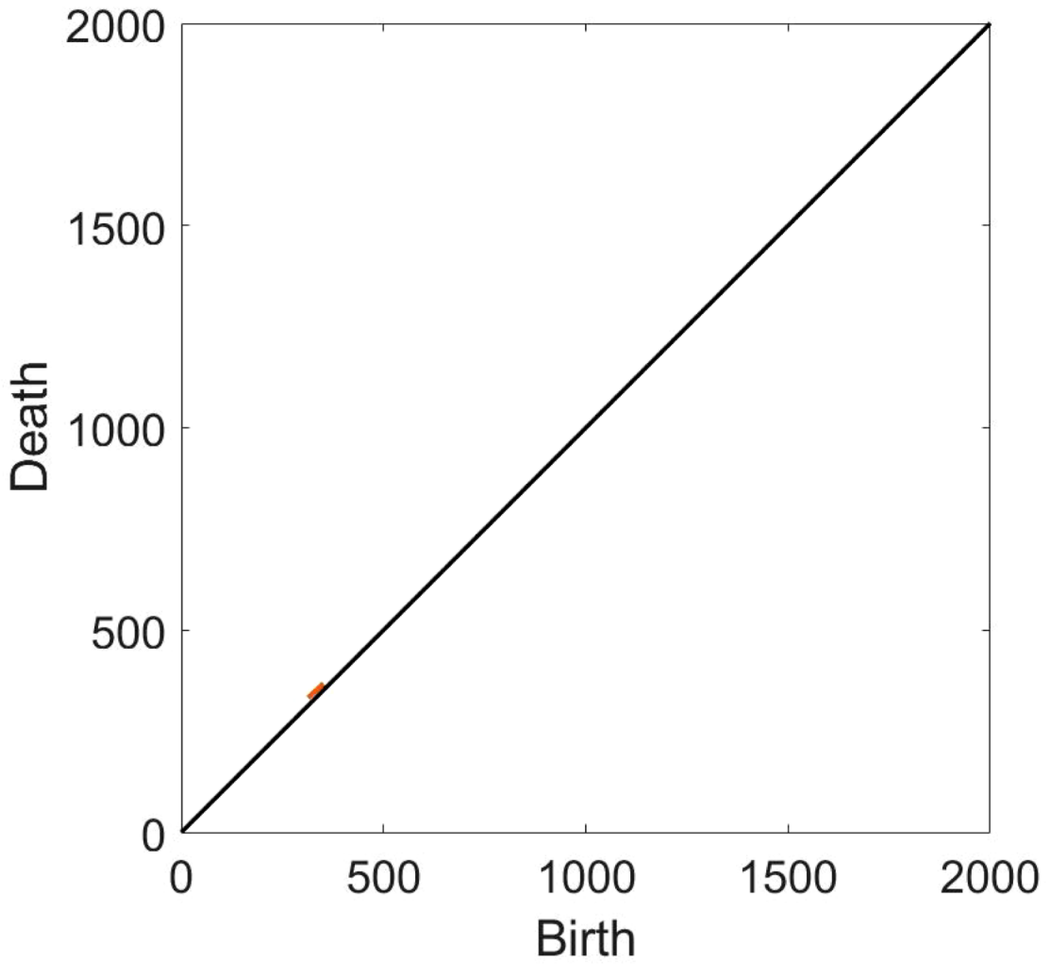




With Riley Juenemann and Scott McKinley (in preparation)

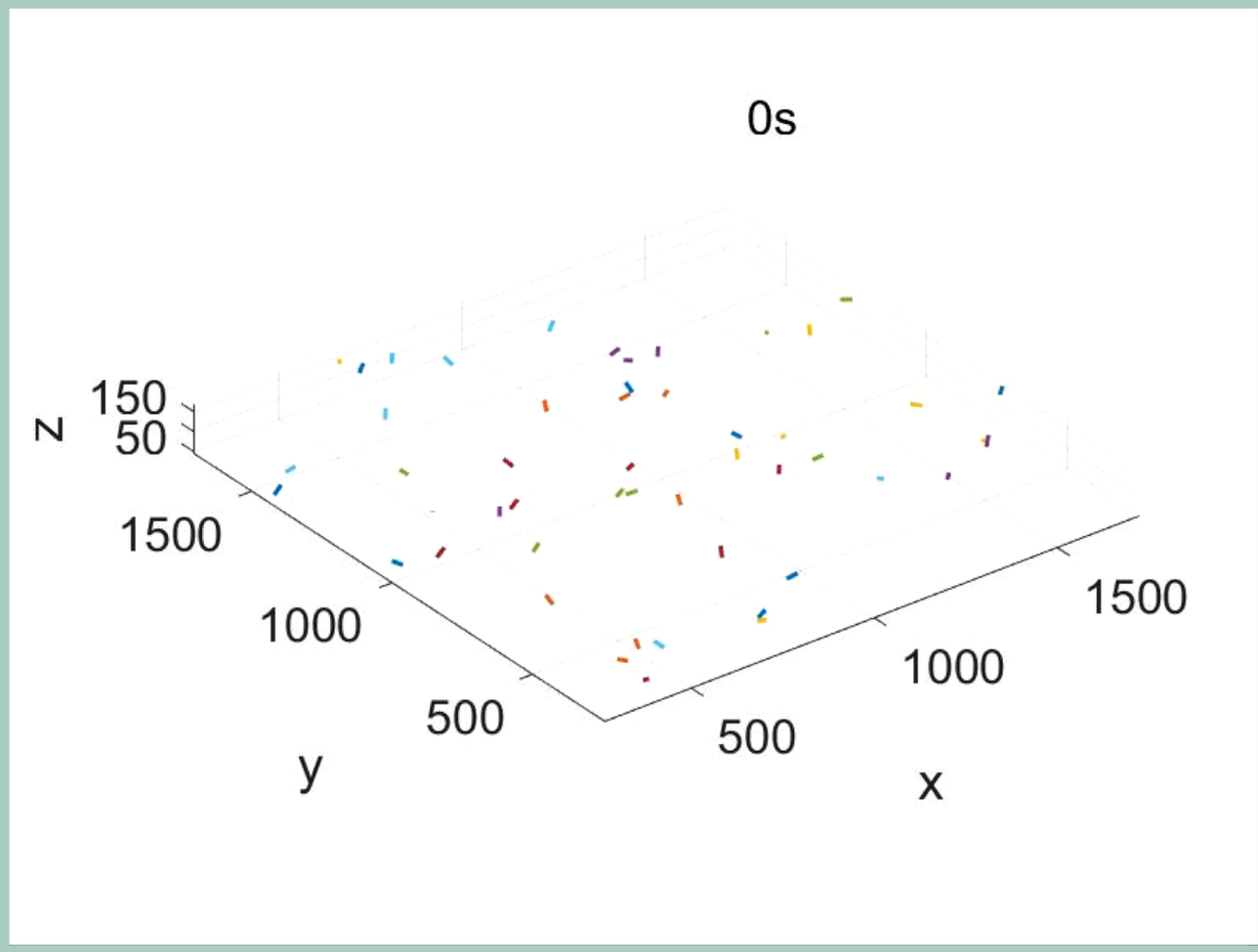
VISUALIZATION OF SIGNIFICANT PATH (RING STRUCTURE) EMERGENCE



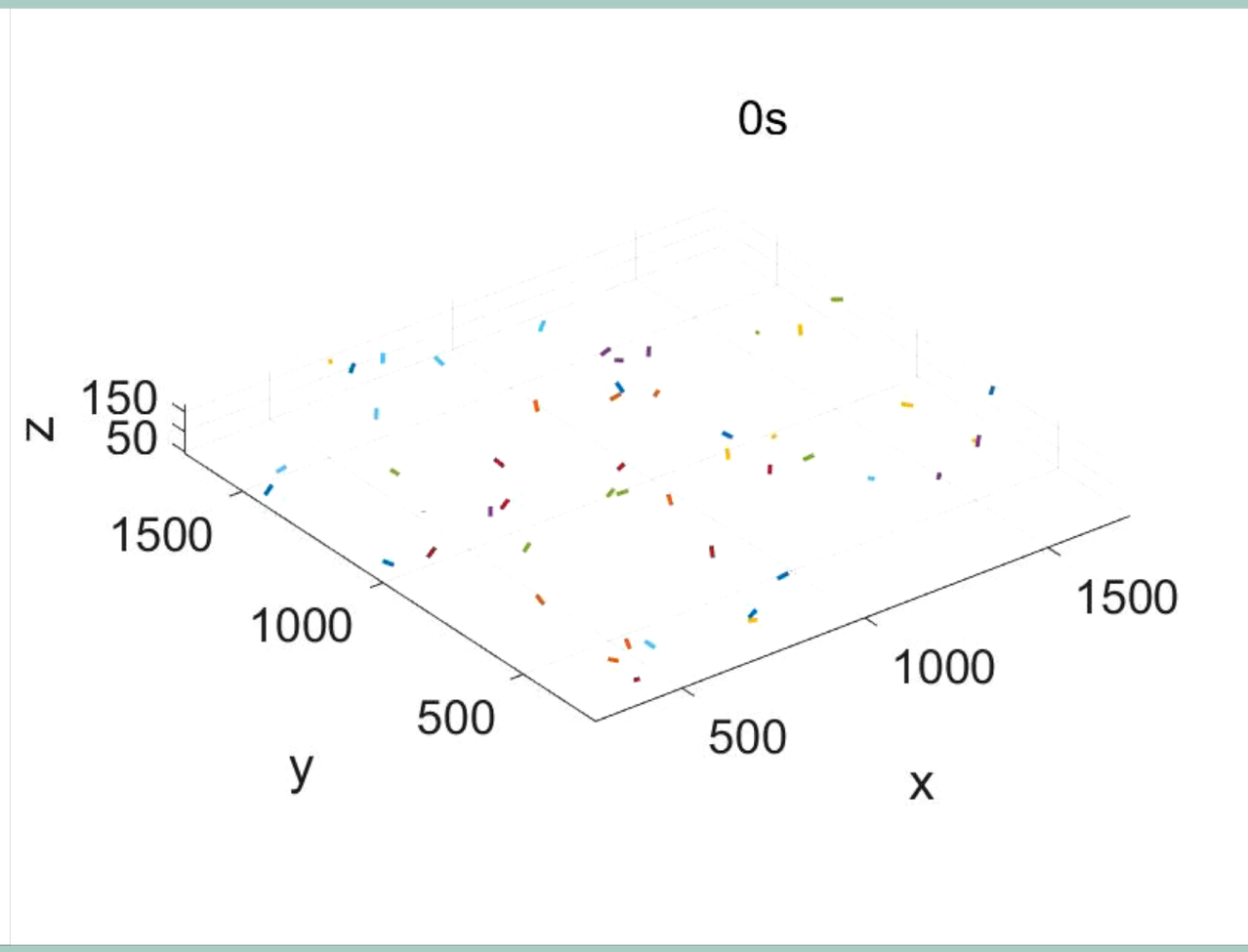


With Riley Juenemann and Scott McKinley (in preparation)

EXPLORE PARAMETER DIFFERENCES: ON-RATE

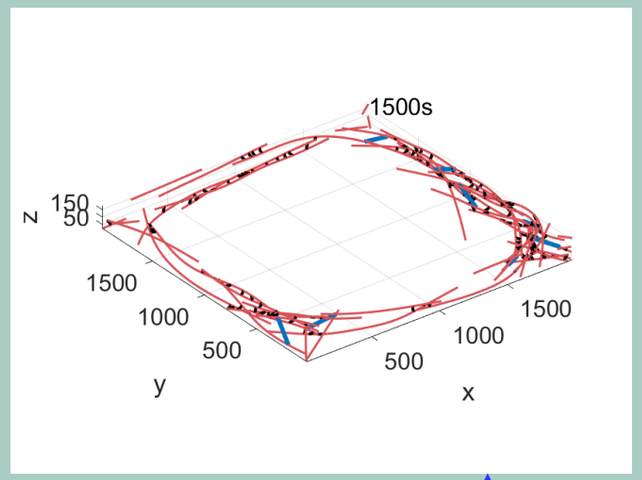


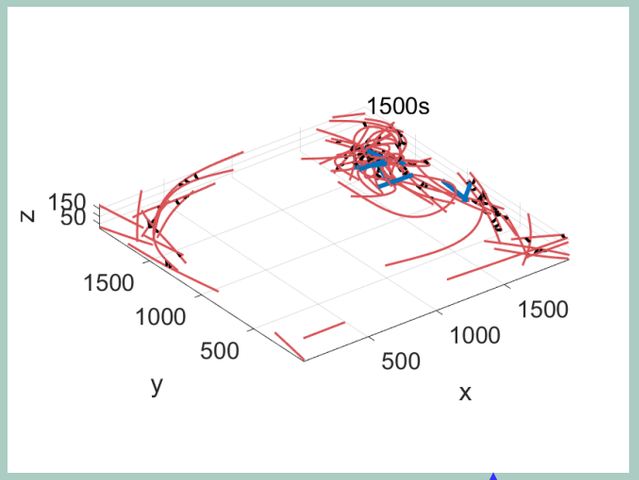
Small on-rate

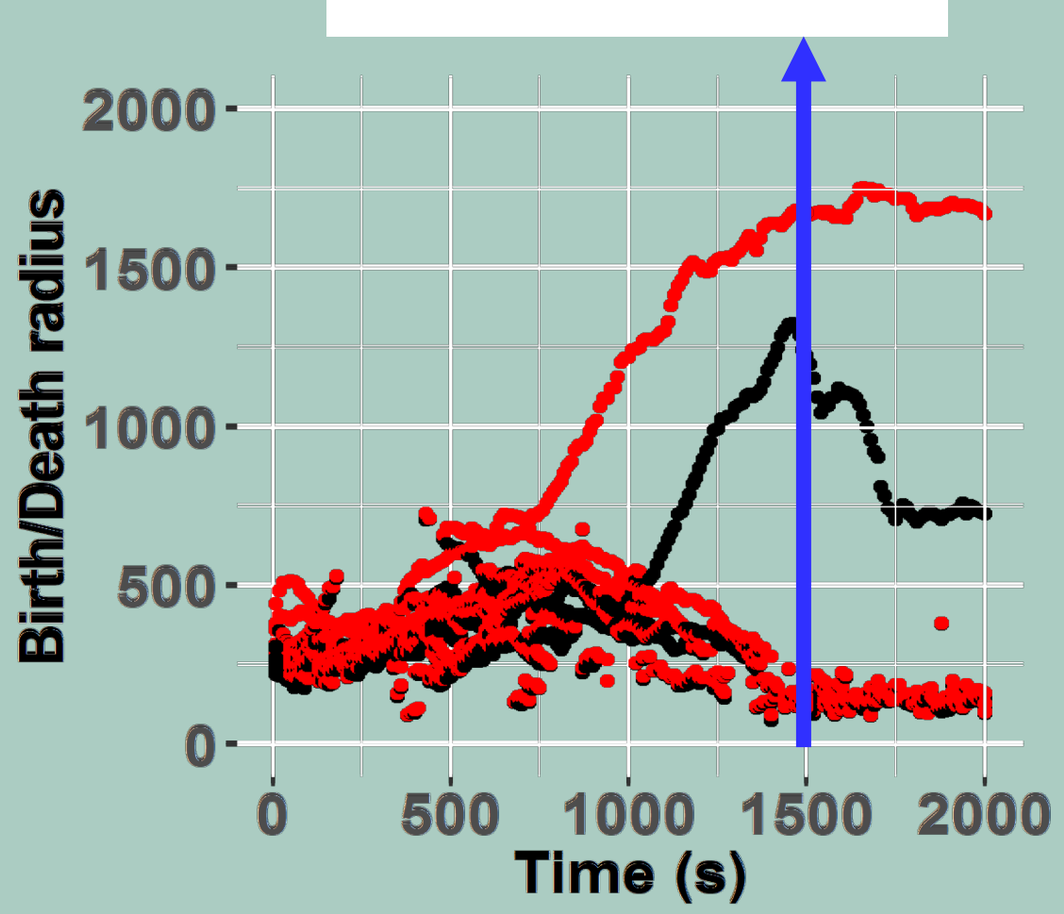


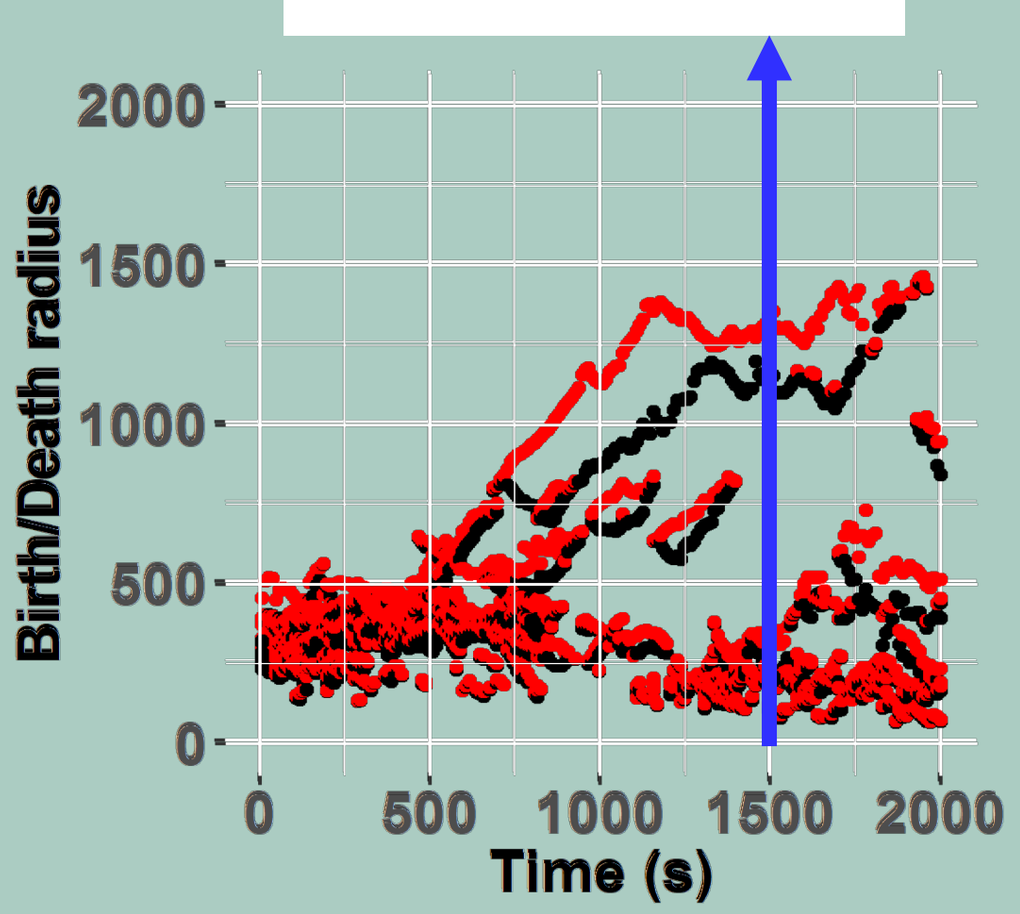
Large on-rate

TOPOLOGICAL FEATURES THROUGH TIME



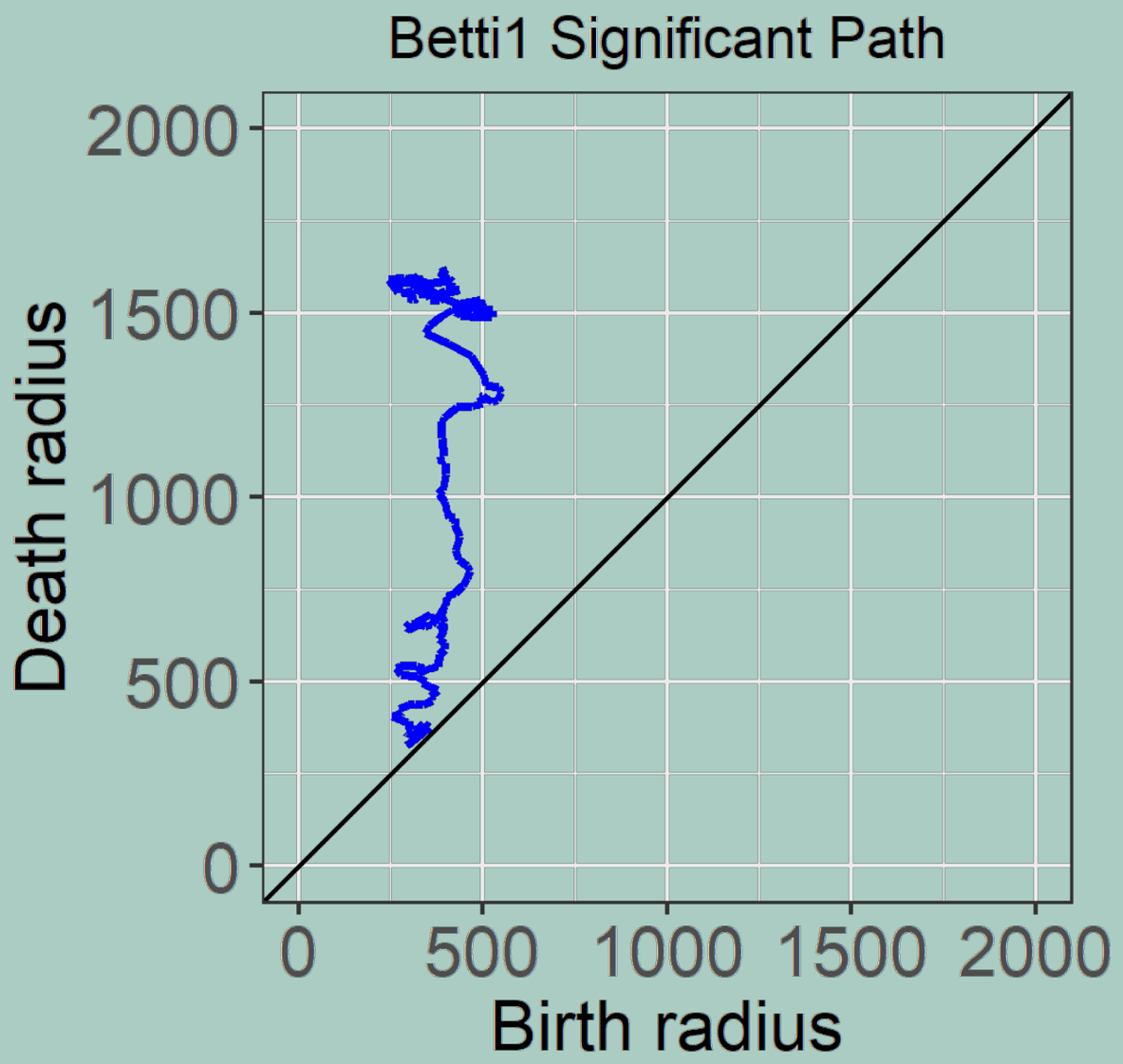






With Riley Juenemann and Scott McKinley (in preparation)

DETECTING RING STRUCTURE



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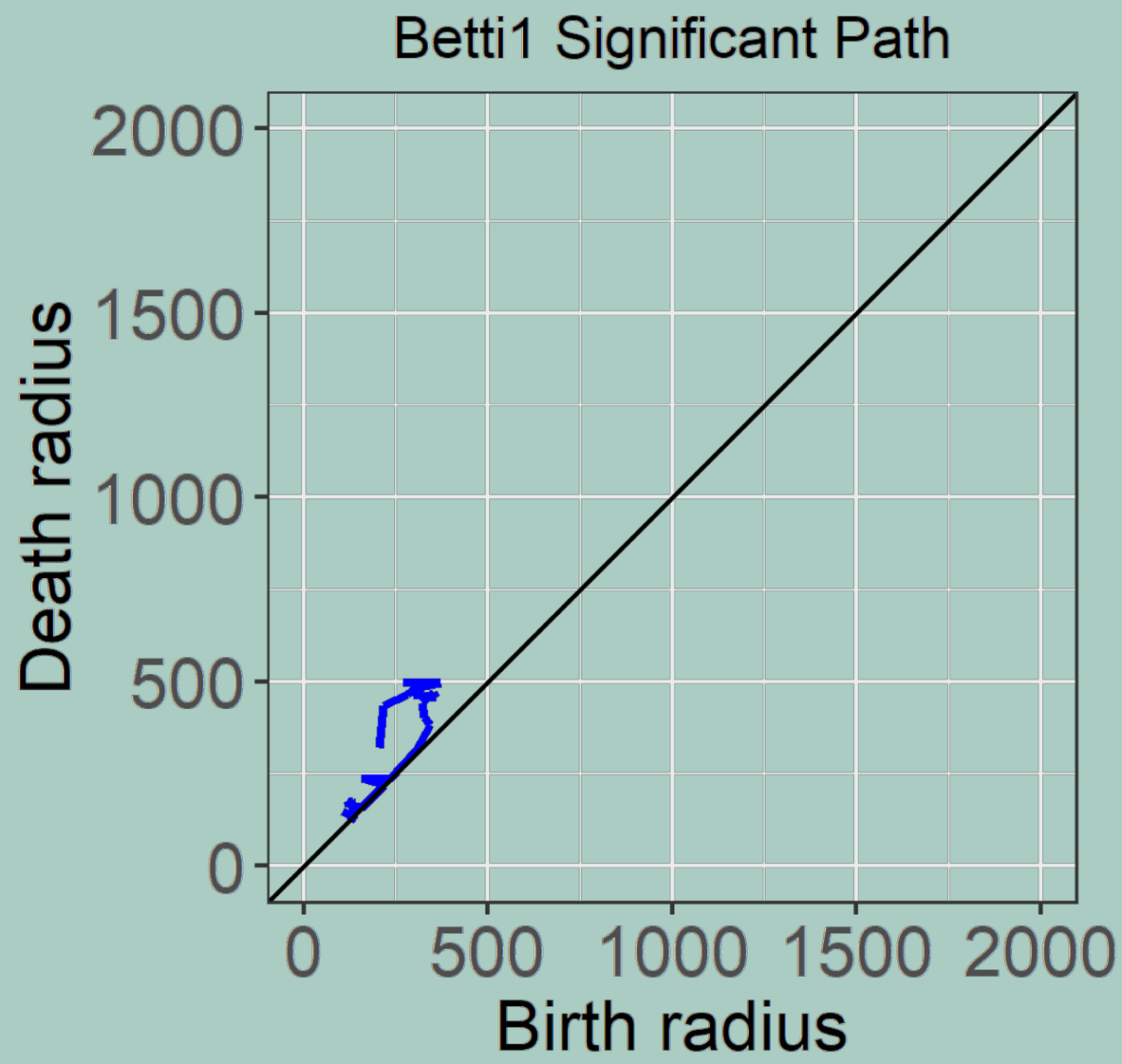
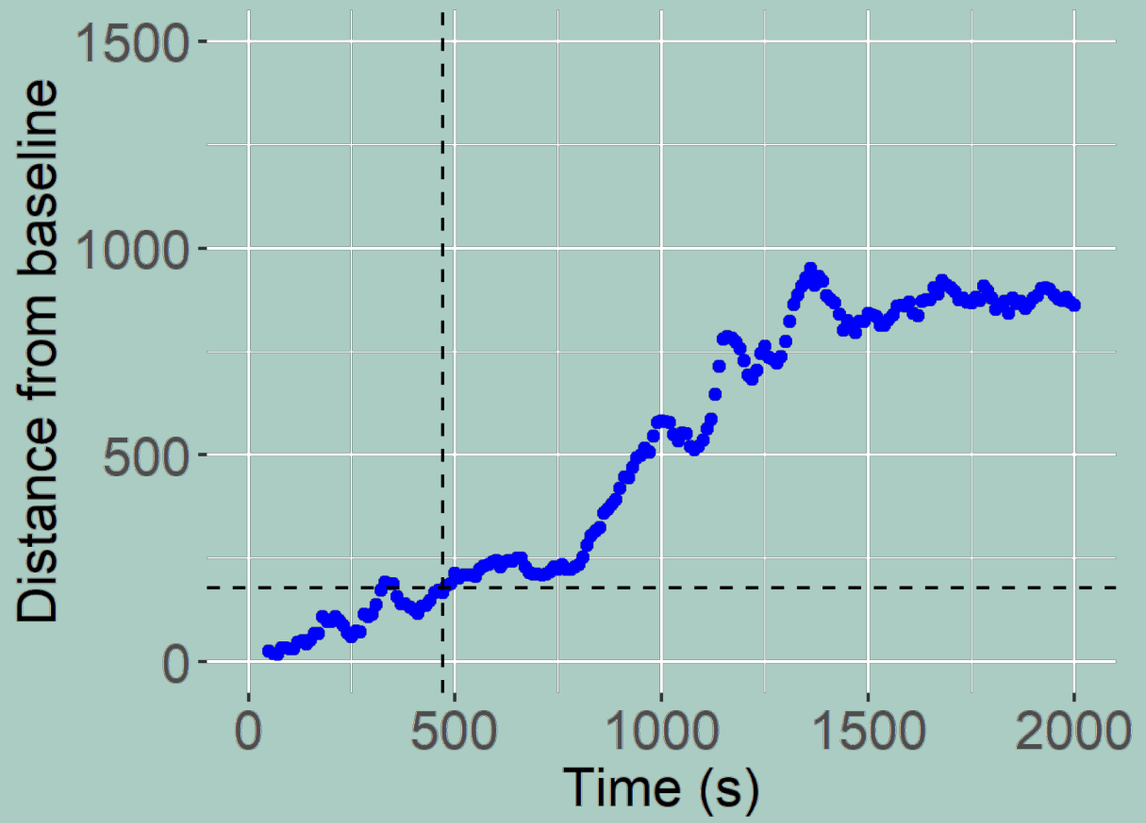


Large on-rate

With Riley Juenemann and Scott McKinley (in preparation)

DETECTING RING STRUCTURE



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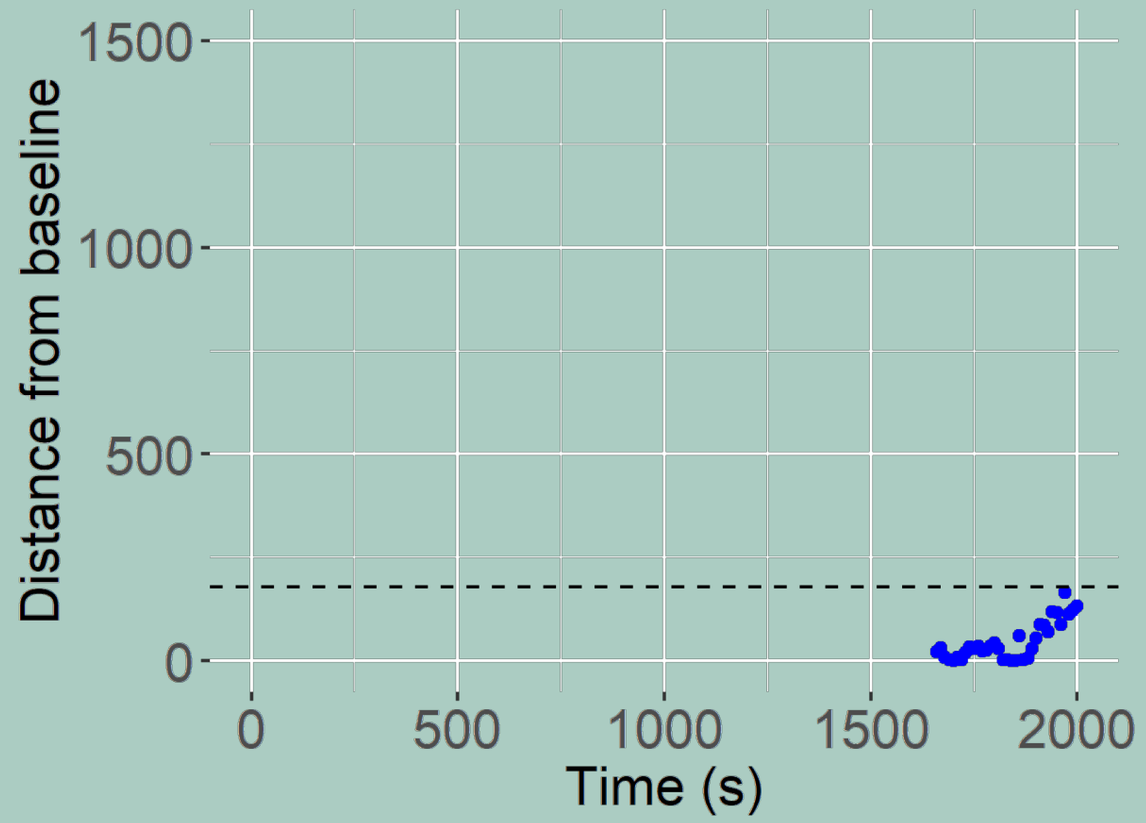
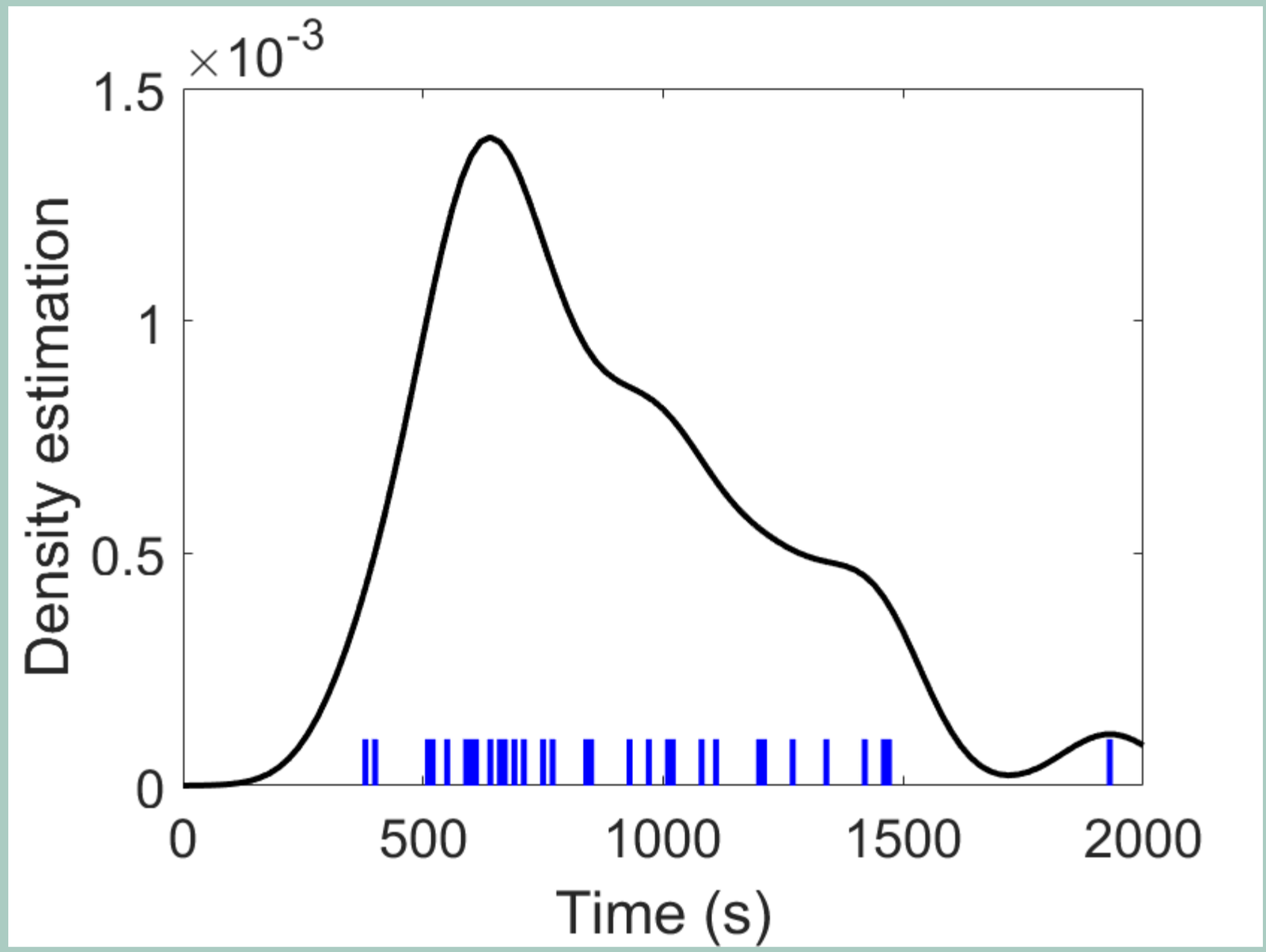


Large on-rate

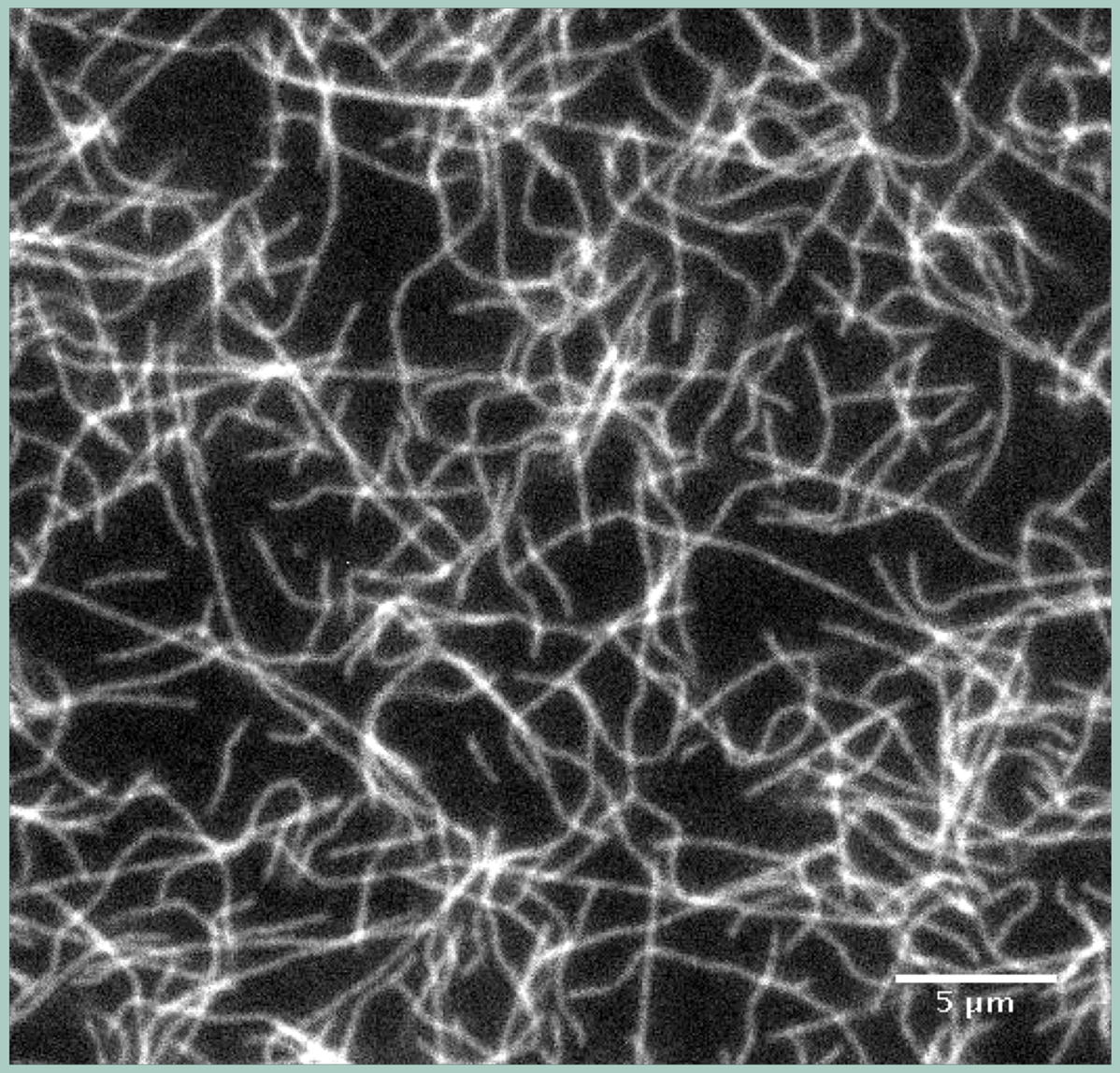
With Riley Juenemann and Scott McKinley (in preparation)

TIME OF RING FORMATION



With Riley Juenemann and Scott McKinley (in preparation)

3. CONNECTION TO IN-VITRO EXPERIMENTAL DATA



Myosin VI – actin interactions

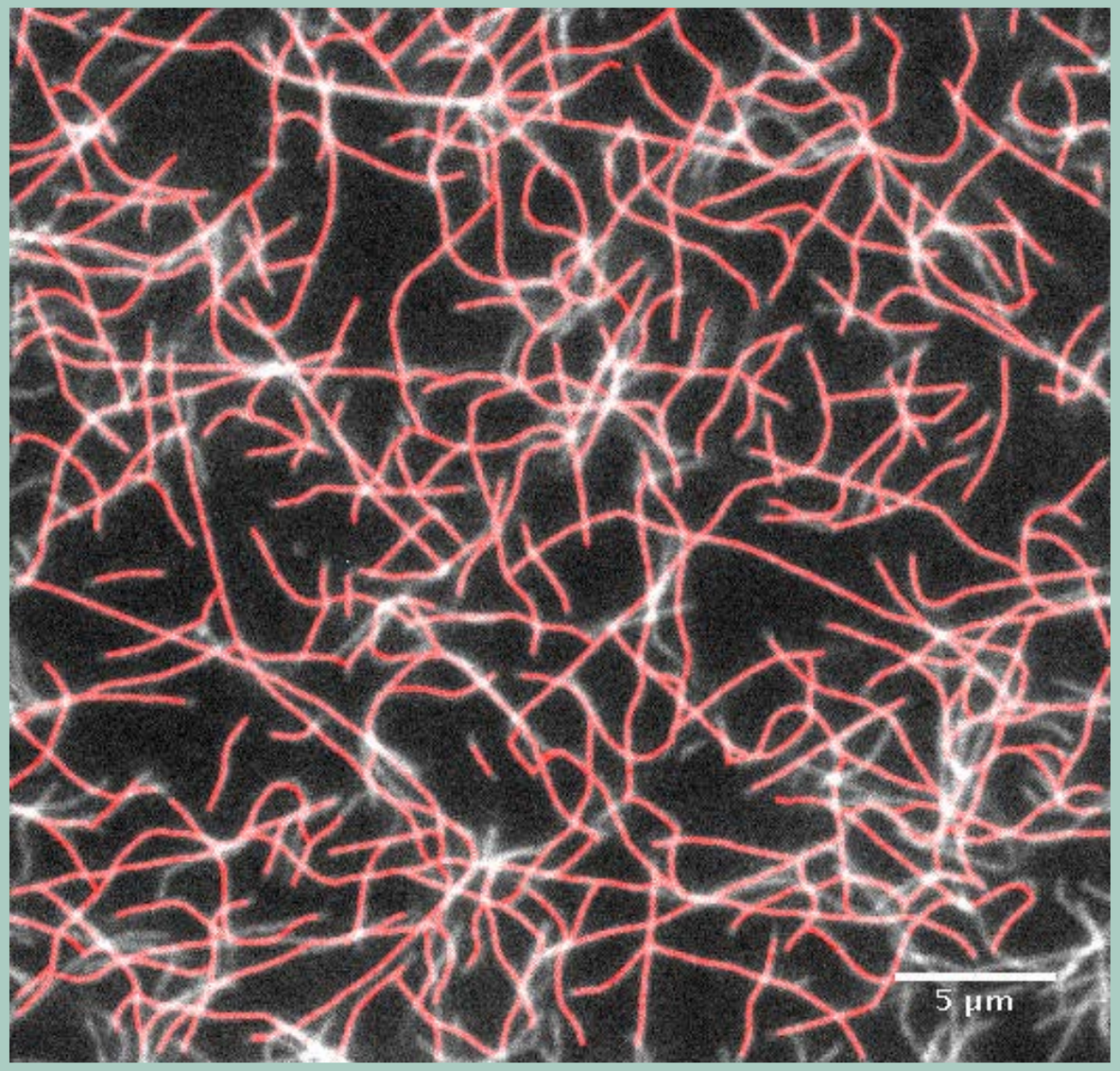
Tim Atherton

Tufts University

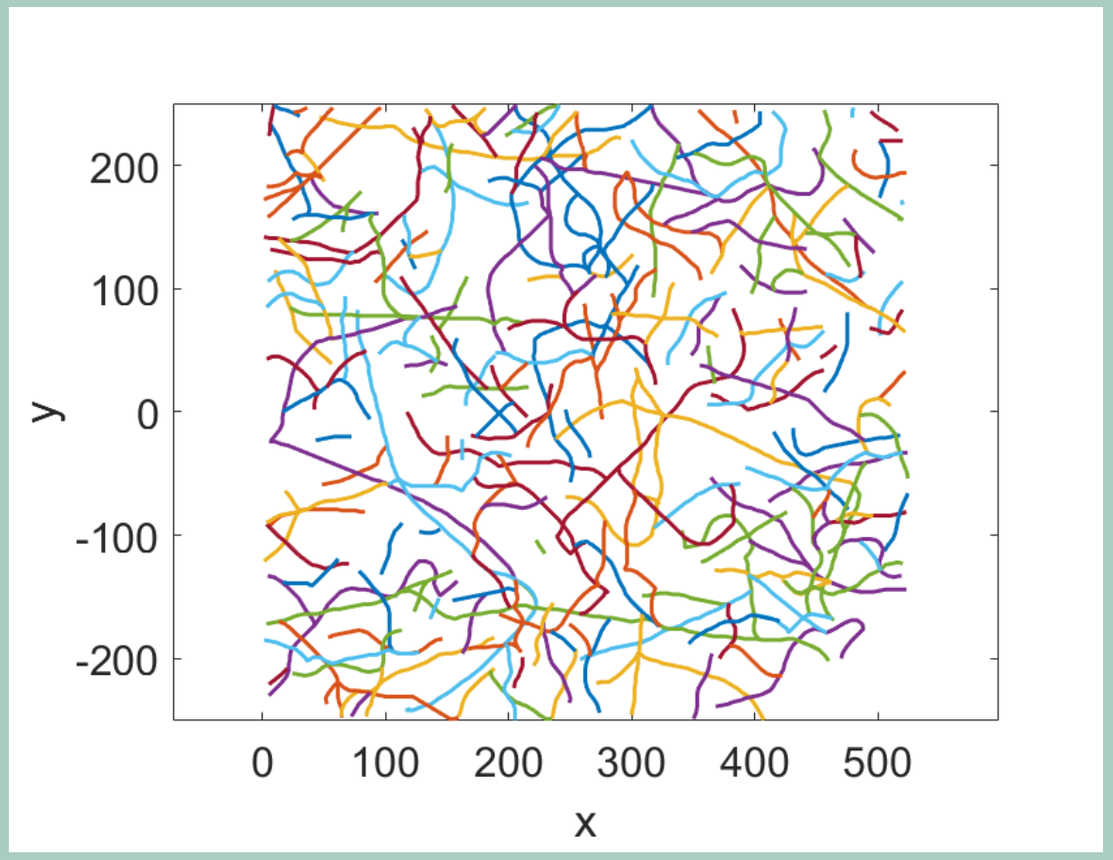
David Altman

Willamette University

CONNECTION TO IN-VITRO EXPERIMENTAL DATA

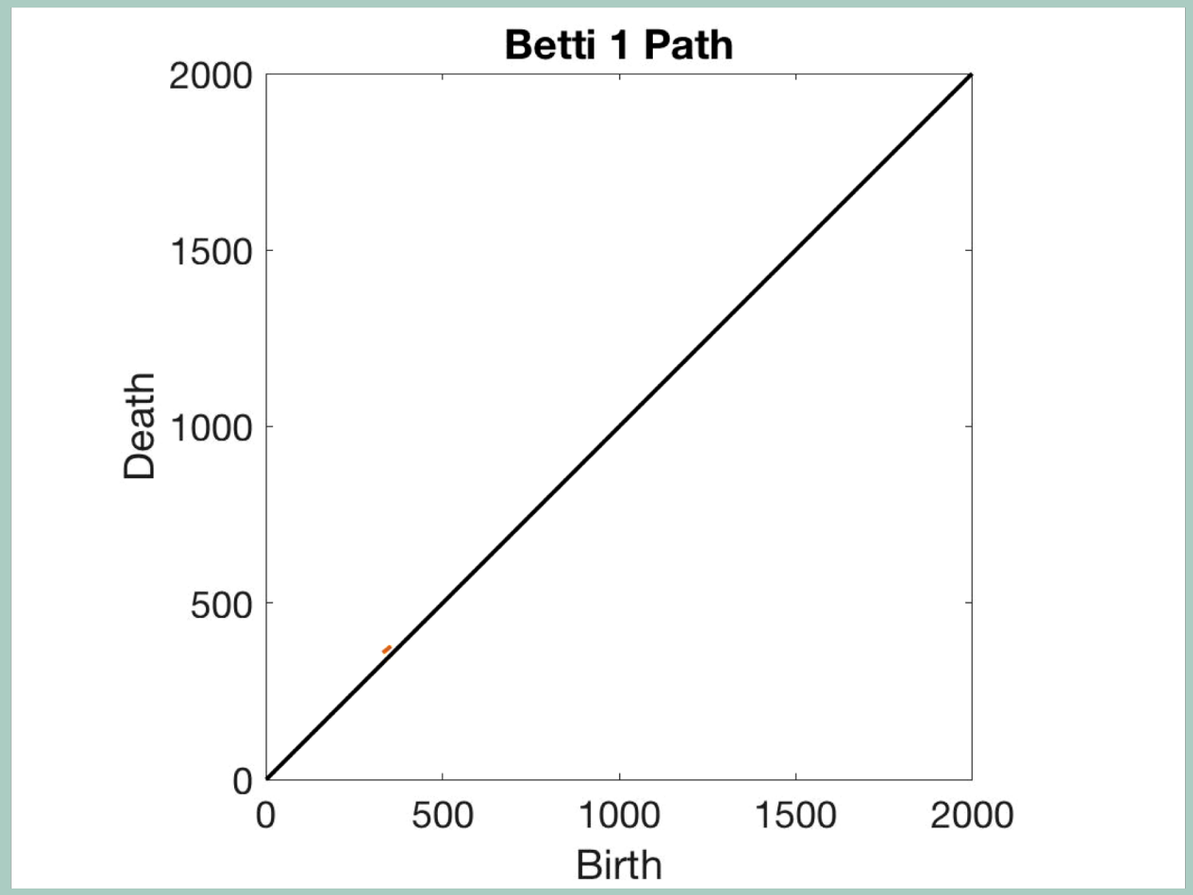


- Trace the actin filaments
- Apply data analysis measures and connect to simulations



FUTURE WORK

- Modeling and simulation of ring formation and maintenance with realistic biological mechanisms
- Stability? Rigorous measure of significant paths?
- Comparison/incorporation into vines and vineyards[1] framework.



[1] *Cohen-Steiner, Edelsbrunner, Morozov (2006)*

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Thank you for your attention!

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