

Performing Topological Data Analysis on T-Cell Dynamics

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Overview

- Background + Motivation
- Model, Data Generation, and Prior Results
- Description of Methods (TDA)
- Results
- Analysis
- Questions

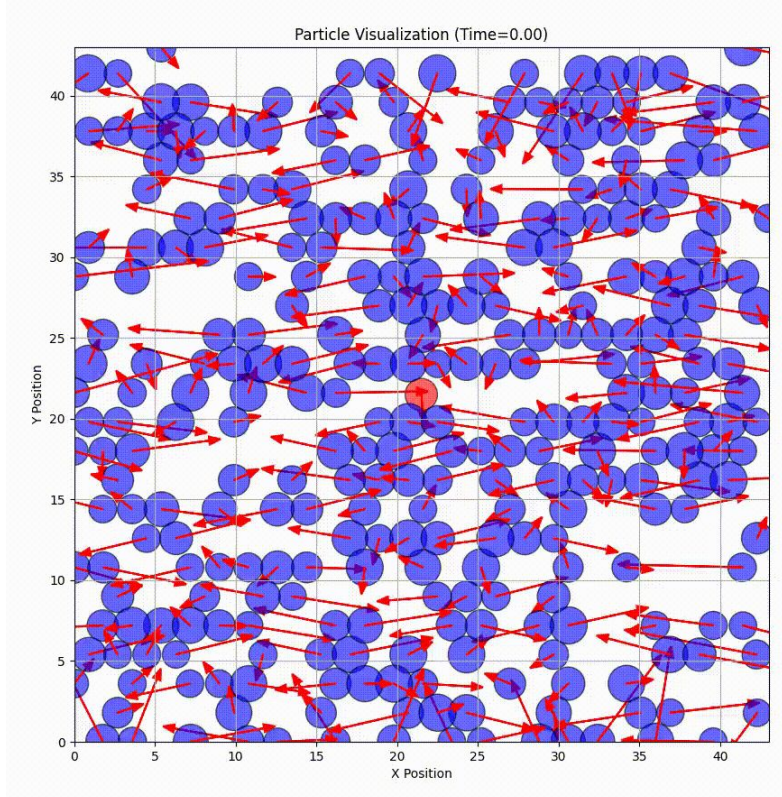
T-Cell Dynamics

- T-Cells are immune system response cells
- An APC cell first detects a foreign entity
- Multiple T-Cells must contact the APC cell to induce an immune response
 - Upon contacting the APC cell for the first time, the T-cell has a probability of spreading the information about the foreign entity
- Immune response time is minimized when T-Cells can efficiently respond to foreign entities/cells
 - Clusters and groups of T-Cells moving through body depend on cell deformation
 - If cells can efficiently deform, they can efficiently provide immune responses

Problem & Motivation

- Can we determine the quality of immune response from looking at how cells arrange themselves?
- How do T-Cells arrange themselves among foreign bodies?
- What topological behavior do T-Cells present? Can these topological behaviors provide insights into how cell arrangement works?
- Can we use topological behavior to quantitatively determine the quality of immune response?

Scanning Rate (Q)

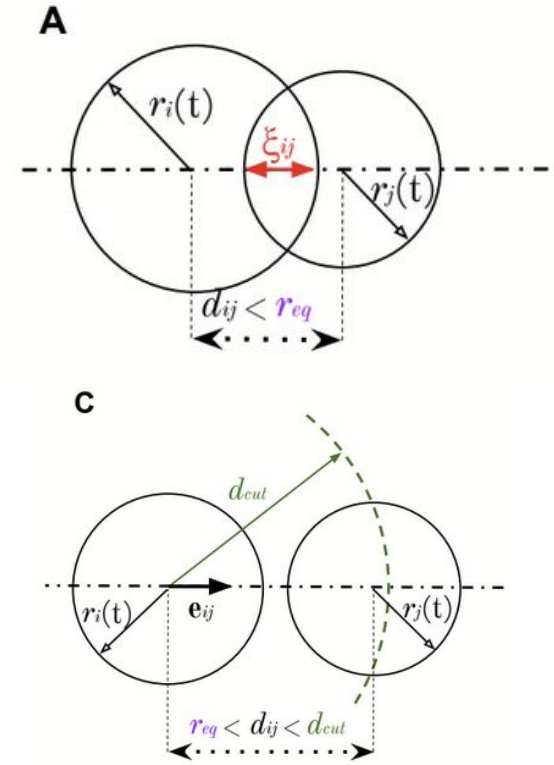


$$Q \equiv \frac{dN_{\text{contact}}}{dt},$$

Average growth rate of the number of contacts

The T-Cell Model

- Based on the study by L.E. Wiebke and D.R. Parisi
 - Wiebke, L. E., and D. R. Parisi. “Active Deformation Enhances Target Scanning in Crowded Two-Dimensional Self-Propelled Particle Simulations.” Oct. 2025
- Every cell is a circle of average radius 1
 - One APC cell in the center
 - T-cells deform by changing their radius at constant frequency
- Pseudo-periodic square boundaries
 - TDA used non-periodic boundaries
- Cell velocities are determined by intercellular forces
 - Adhesive force
 - Repulsive force
- Measure of performance: scanning rate



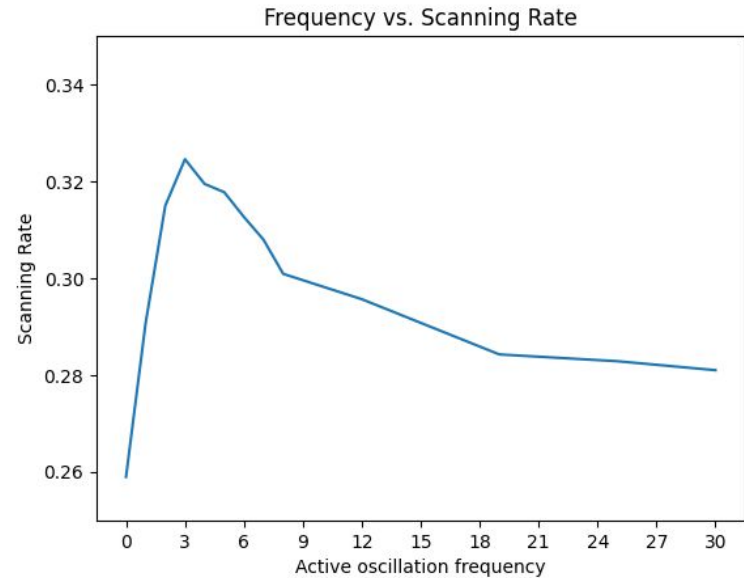
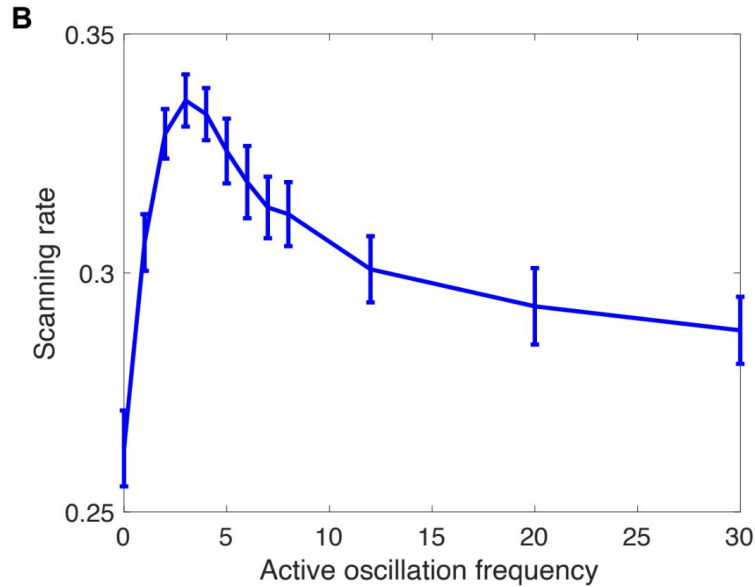
Wiebke et. al, “Optimum flow rate of actively deformable particles in the overdamped regime” (2024)

Data Generation

- As our base case, we simulate 300 particles in 43×43 grid with single APC cell in middle (same as in Wiebke and Parisi)
- Run for 1500 timesteps, with $dt = 0.005$, and frames recorded every 50 timesteps
- Cell radii are set to 1 and oscillate, with $\max F^{\text{rep}} = 20$ and $\max F^{\text{adh}} = 0.75$
- Simulations run for 30 realizations on each frequency from 0-30
- No randomly assigned particle velocities
- Lengths are scaled by $r_0 = 1$ and time is scaled by r_0 / v_0

Replicated Results

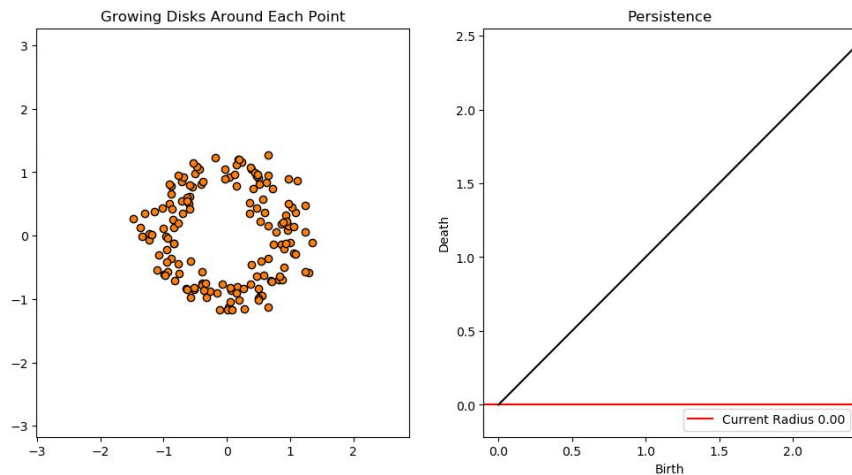
- Same base case parameters



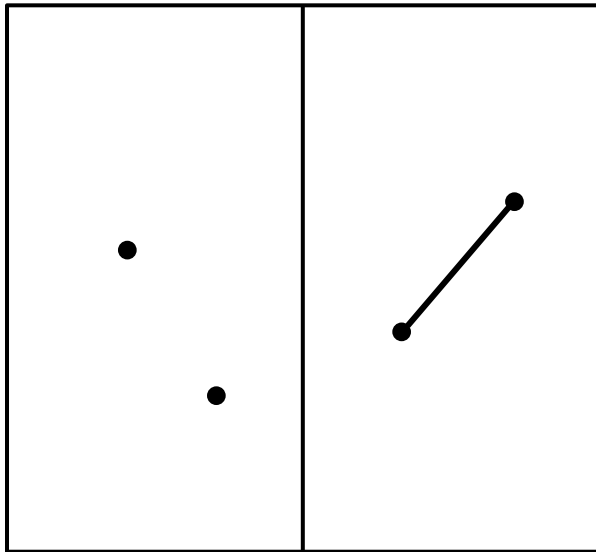
L. E. Wiebke and D. R. Parisi

Persistent Homology (PH)

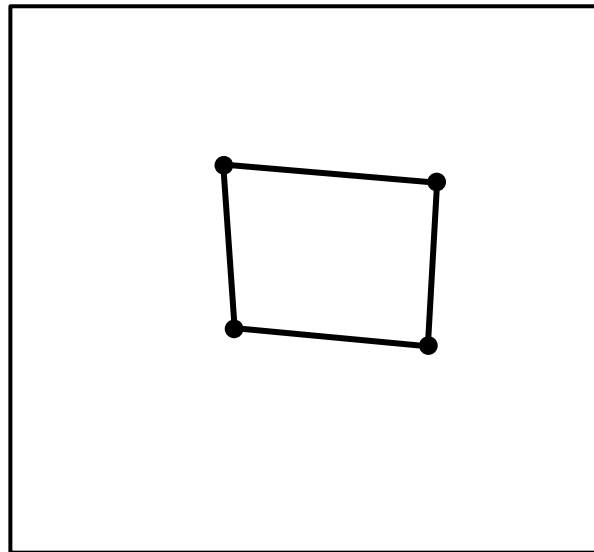
- Build shapes
- Use a **threshold**
- Track the threshold values that topological features **persist**



Homology?

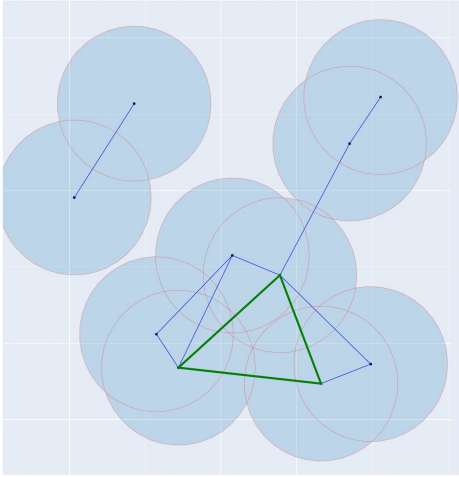


Dimension 0/Betti 0

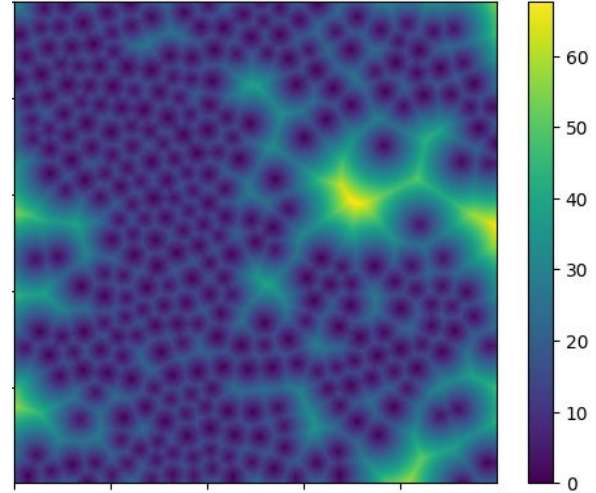


Dimension 1/Betti 1

Which PH Methods Do We Use?



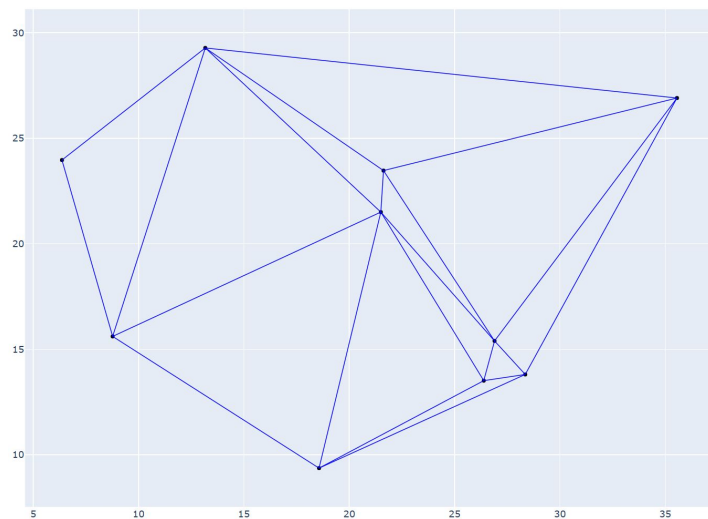
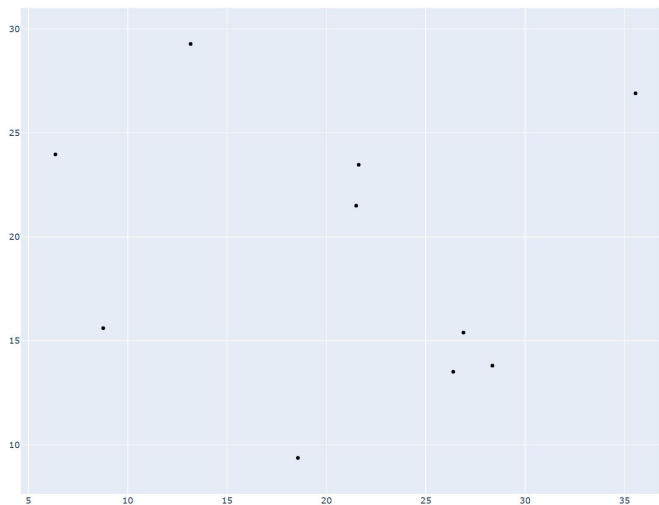
Alpha Complex



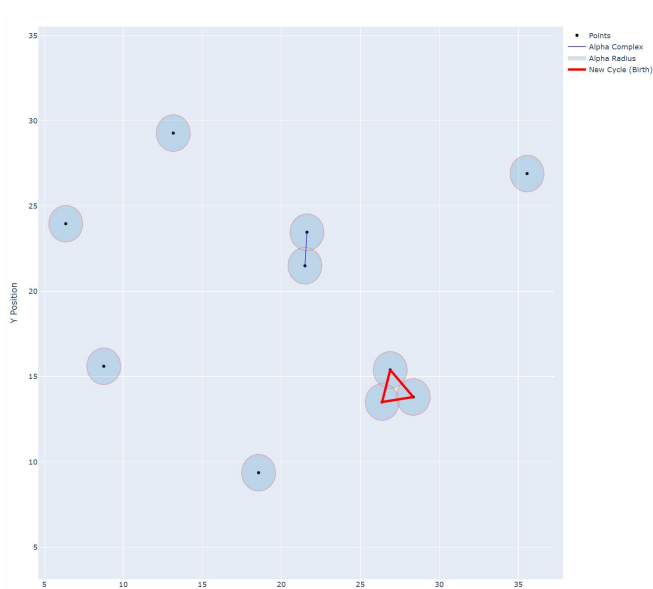
Euclidean Distance Transform

Alpha Complexes Background

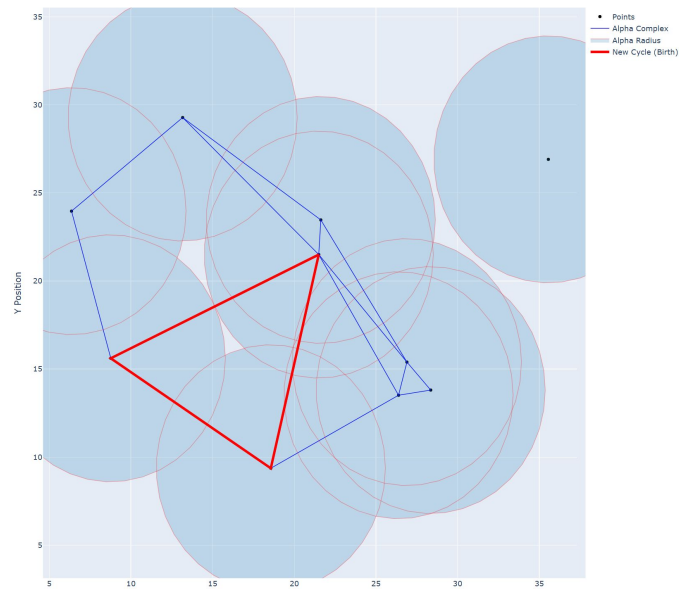
Goal: construct a simplicial complex from points to extract topological data



Constructing Simplicial Complex



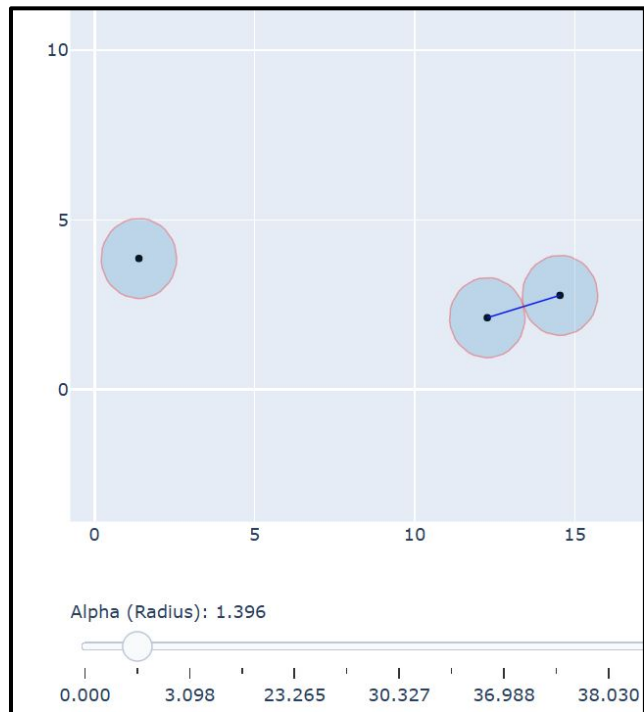
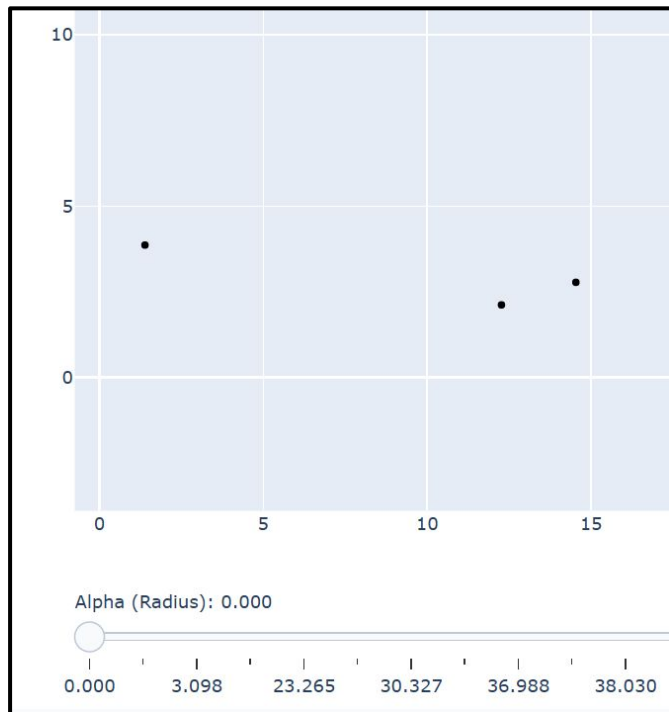
Radius: 1.2



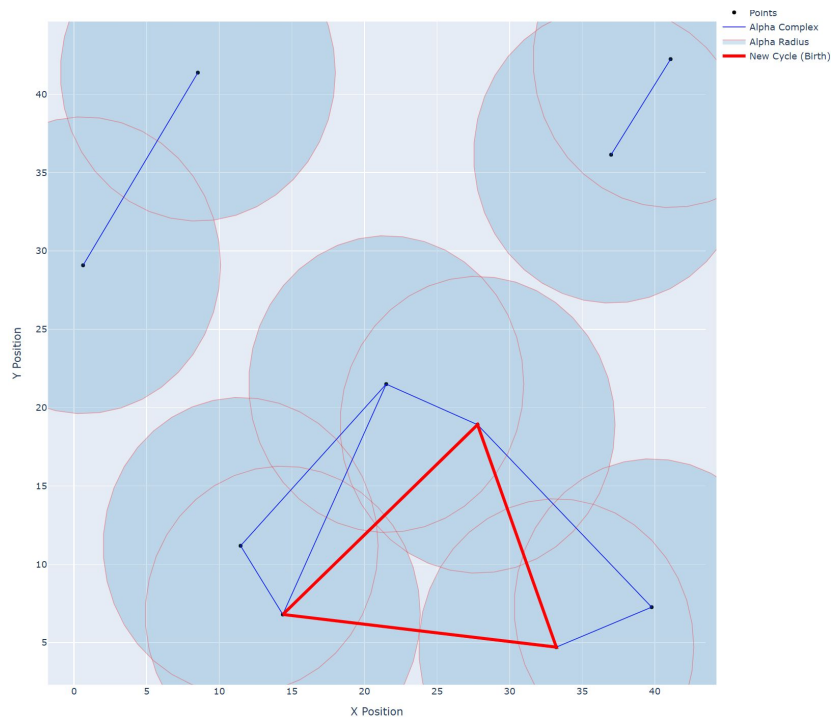
Radius: 49.2

Threshold: Radius of Circle

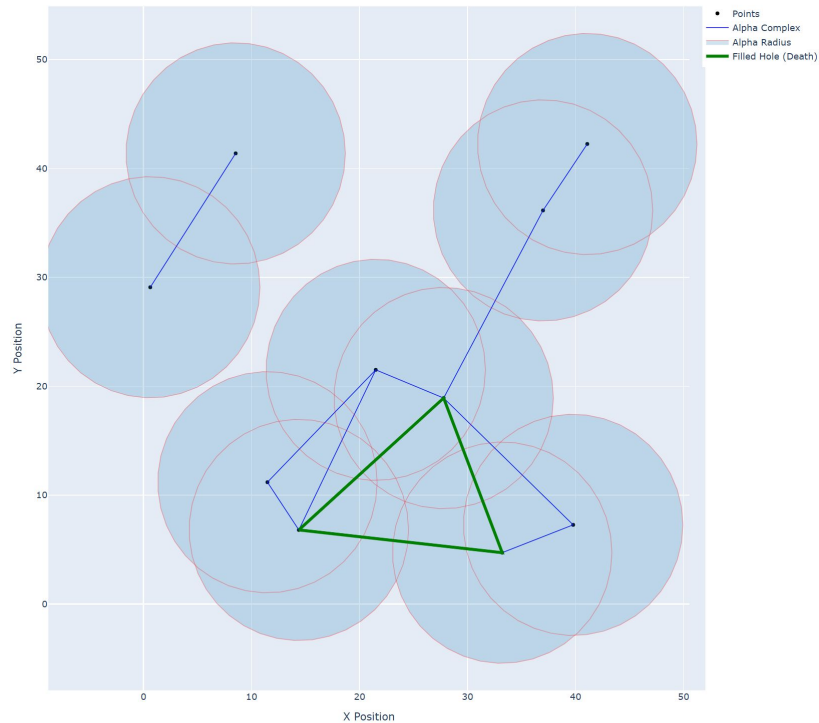
Dimension 0



Dimension 1

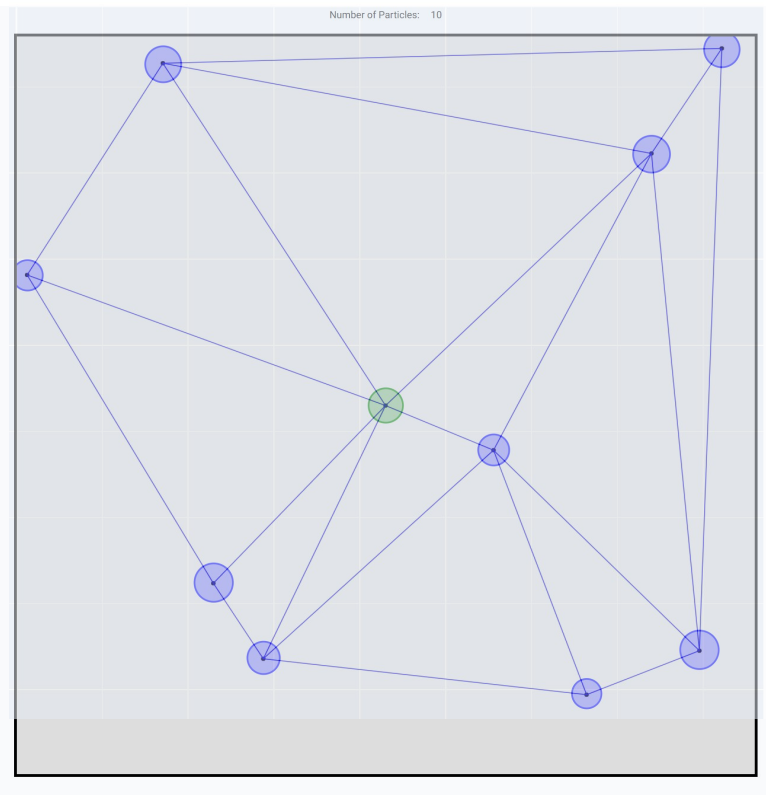
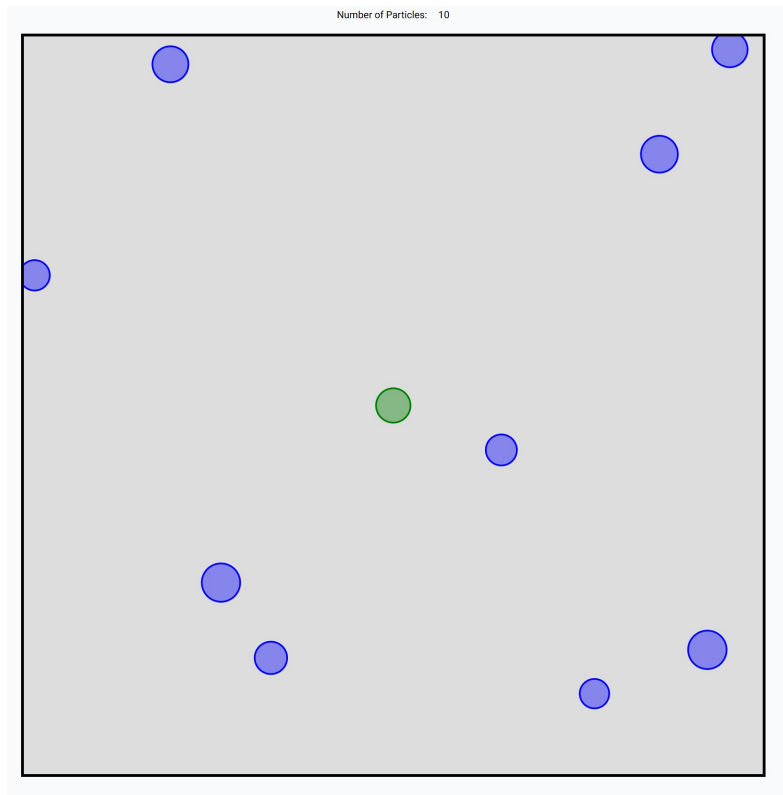


Radius: 89.7

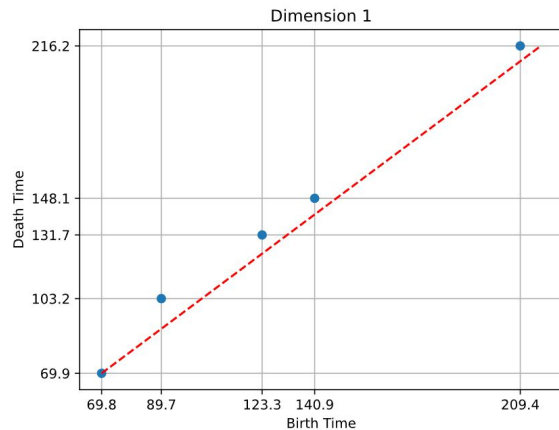
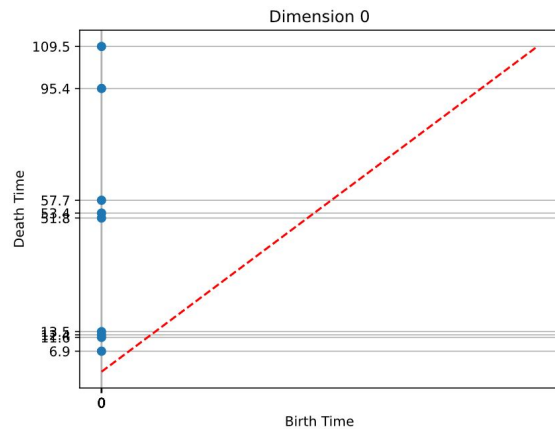
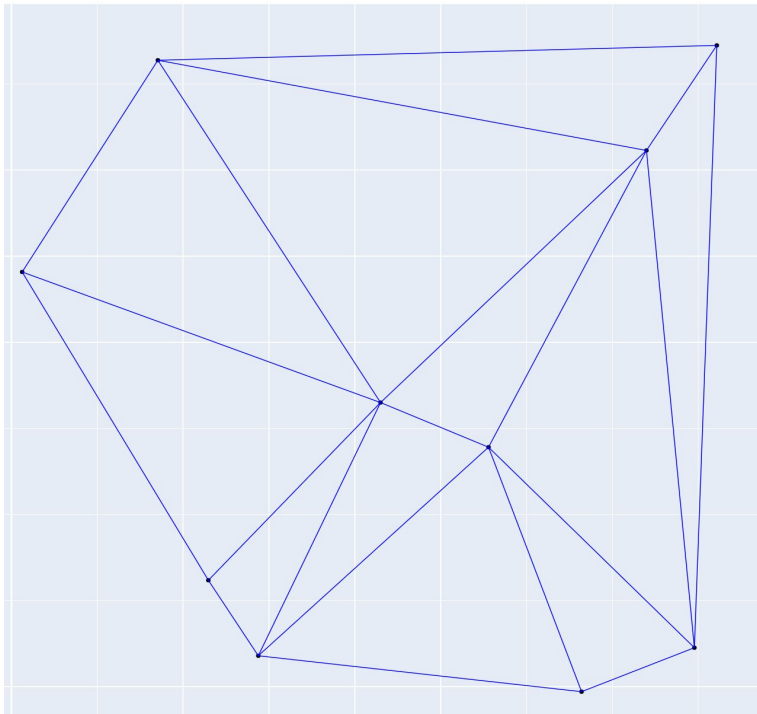


Radius: 103.2

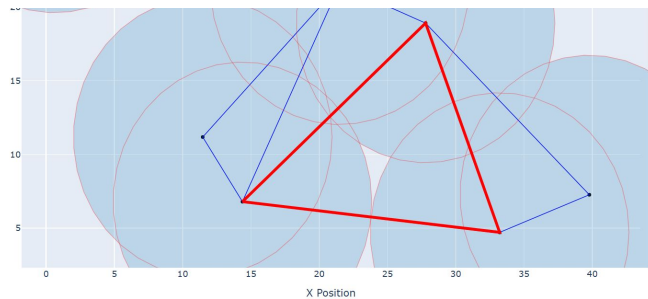
Applied to T-Cells



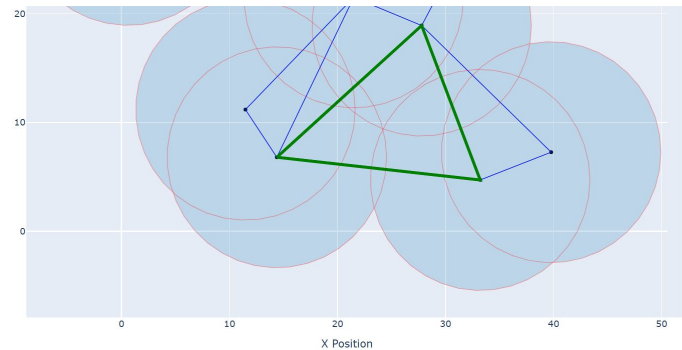
Applied to T-Cells (ctd.)



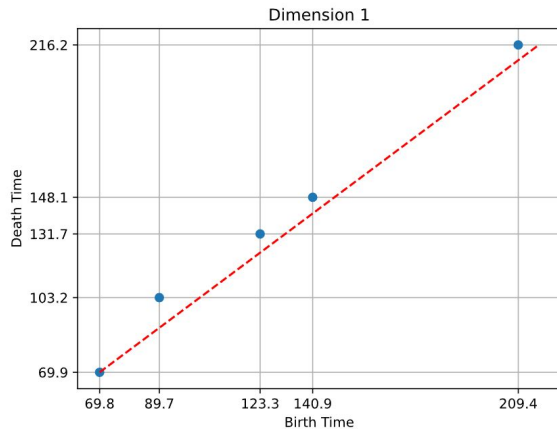
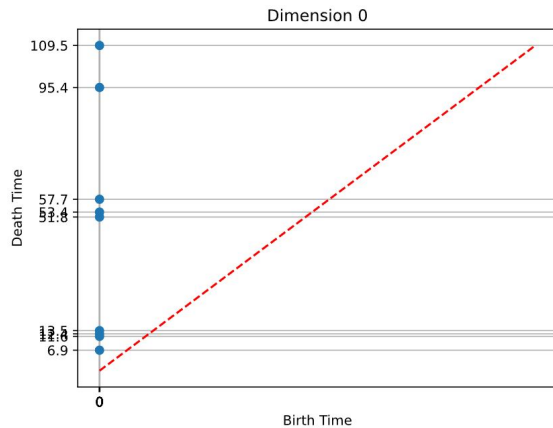
Applied to T-Cells (ctd.)



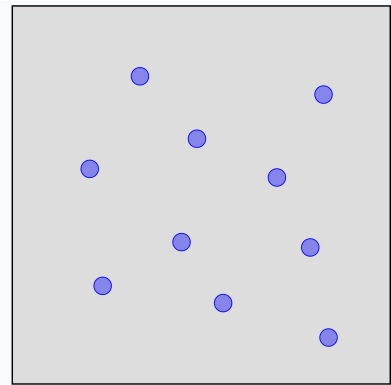
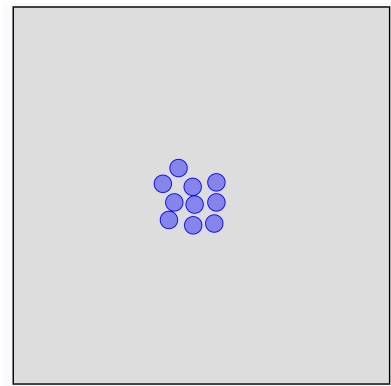
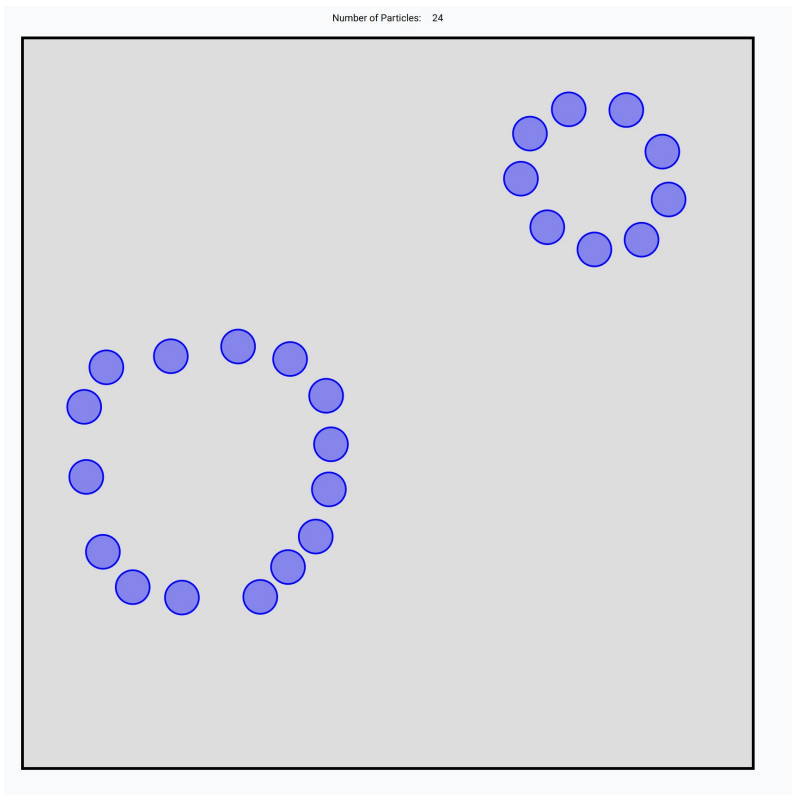
Radius: 89.7



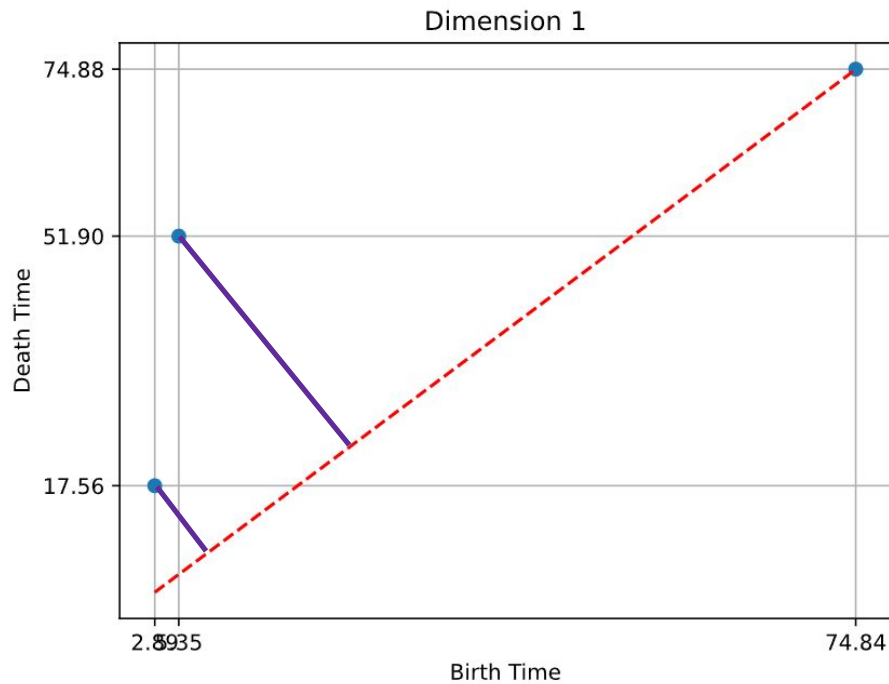
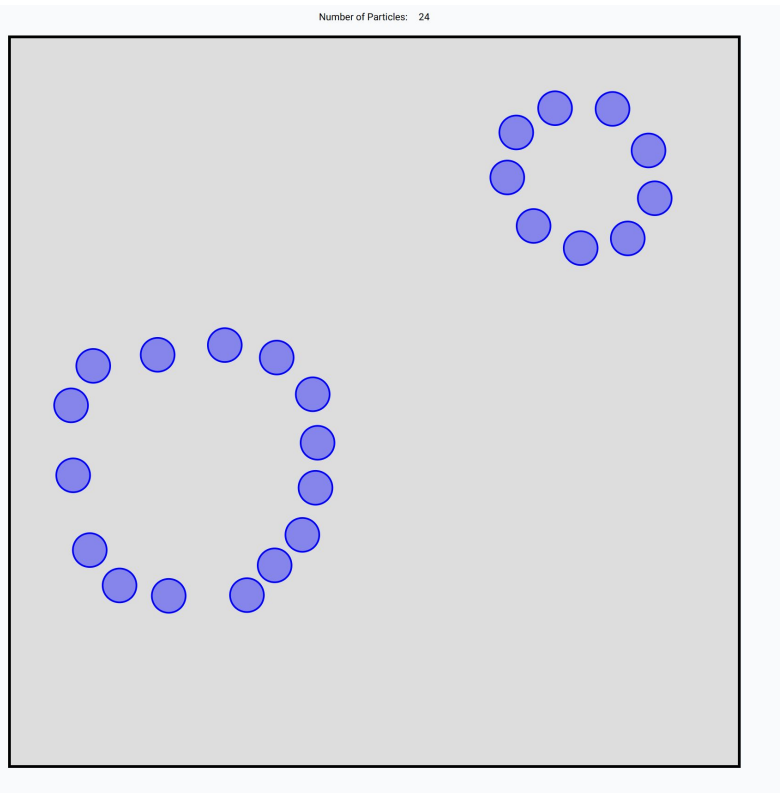
Radius: 103.2



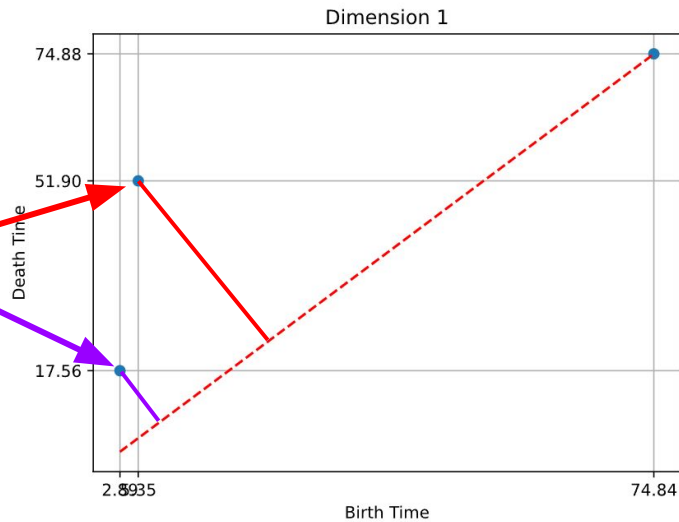
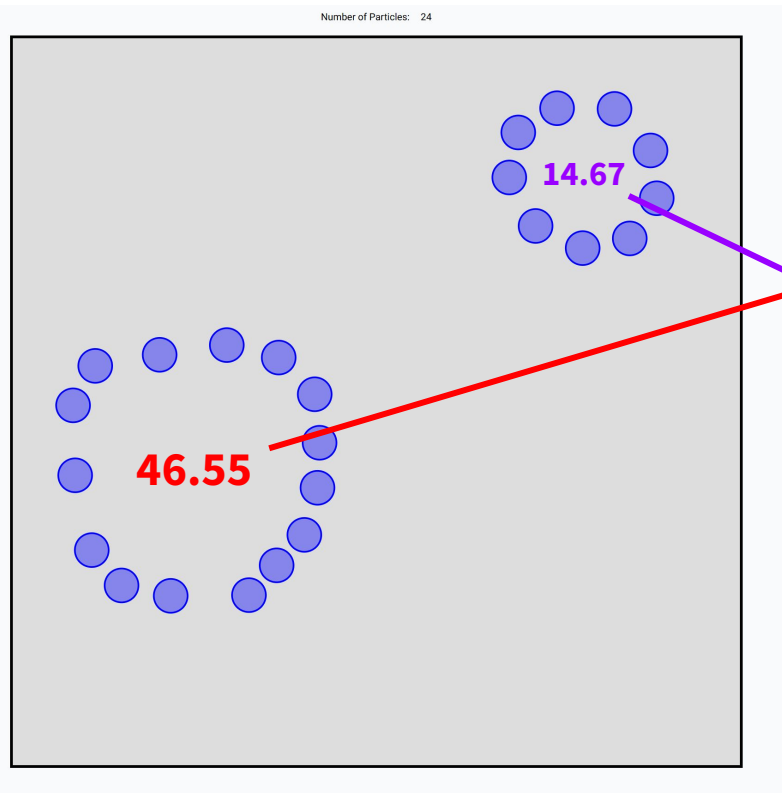
What Can This Tell Us About T-Cell Structure?



What Can Dimension 1 Tell Us?

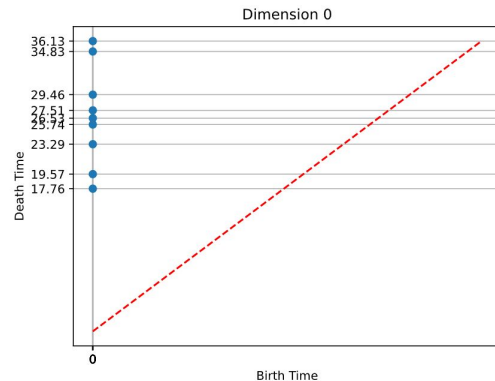
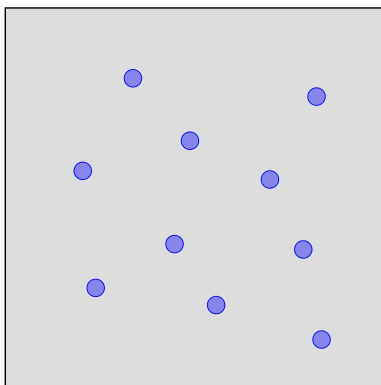
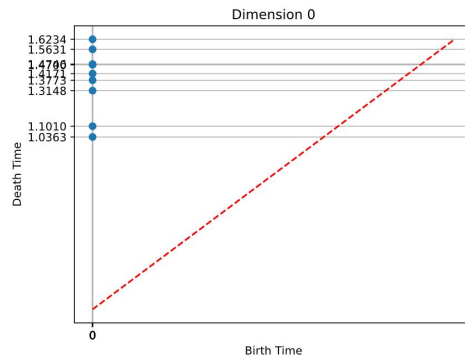
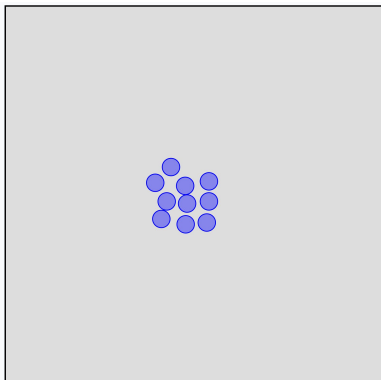


What Can Dimension 1 Tell Us? (ctd.)



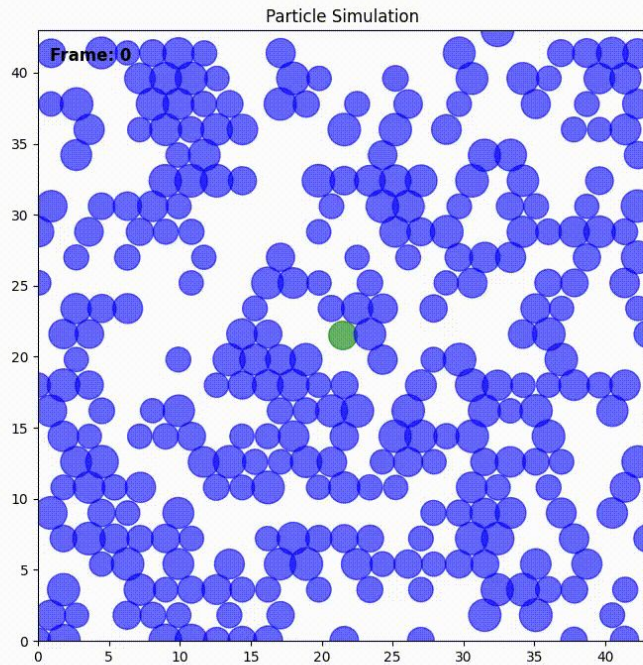
$$\text{Lifetime} = \text{Death} - \text{Birth}$$

What Can Dimension 0 Tell Us?

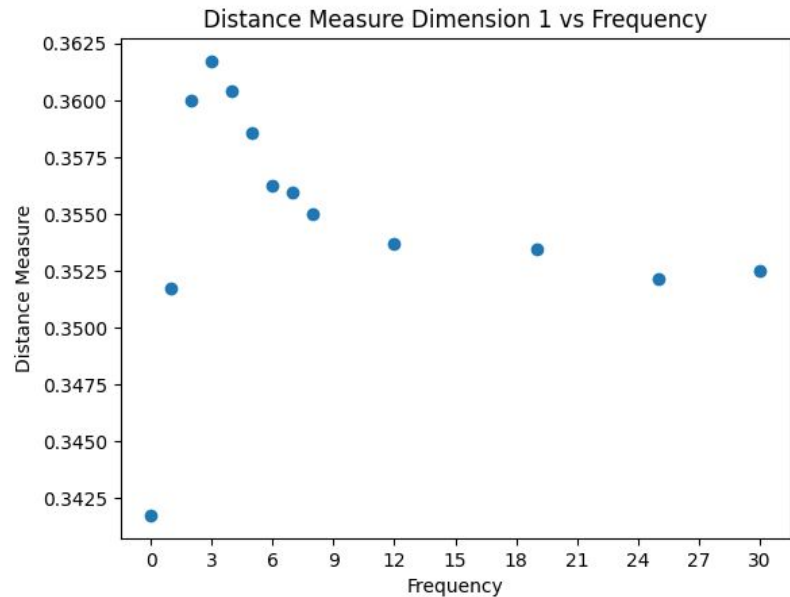
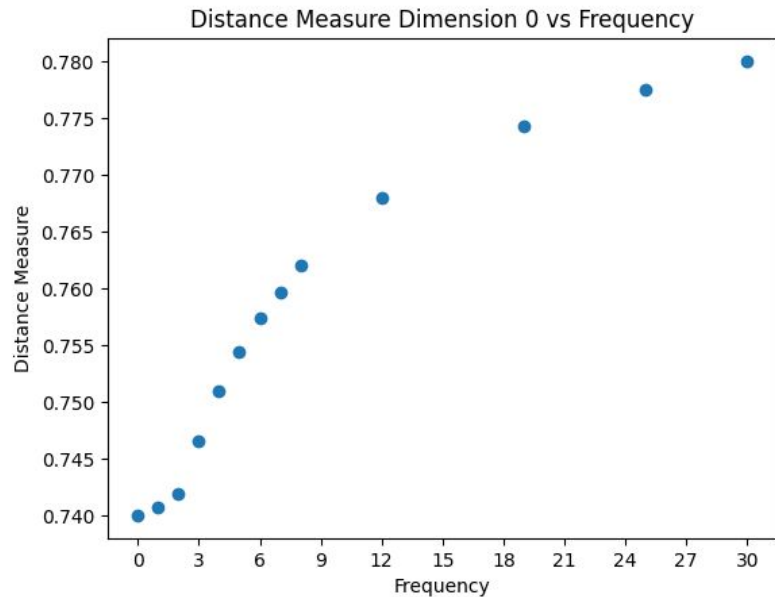


Lifetime = Death - Birth

Apply measure over all frames

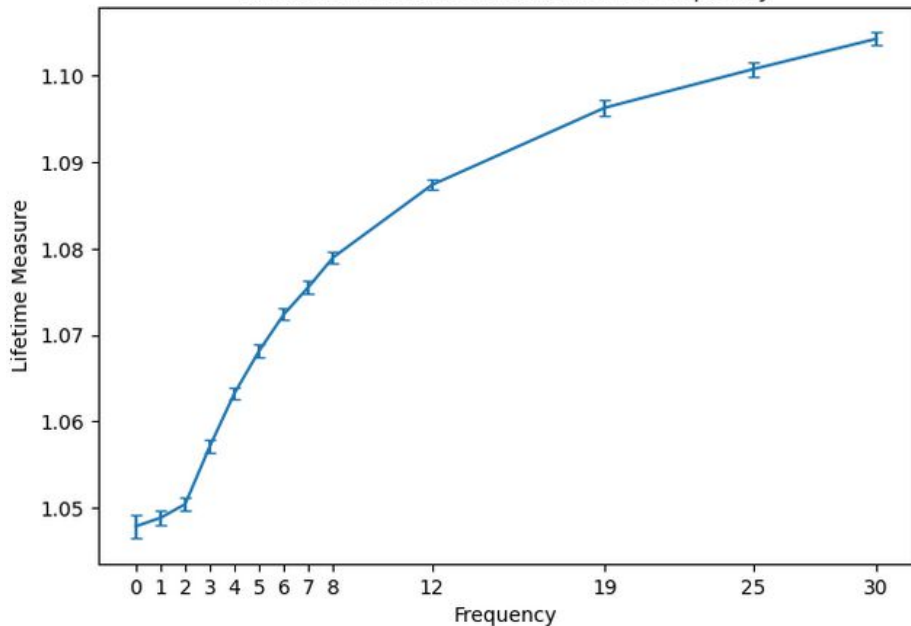


Lifetime measure depending on frequency

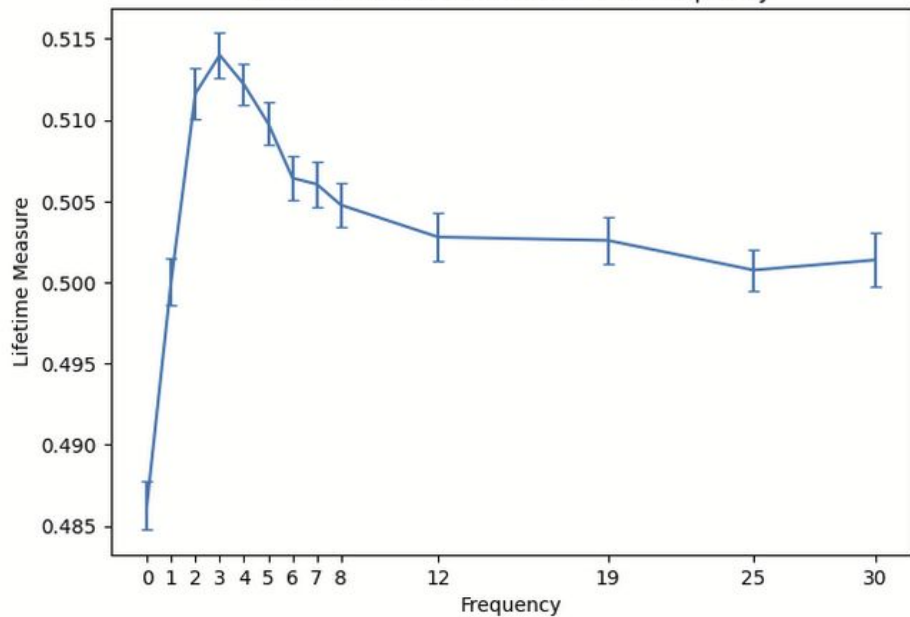


Lifetime measure depending on frequency

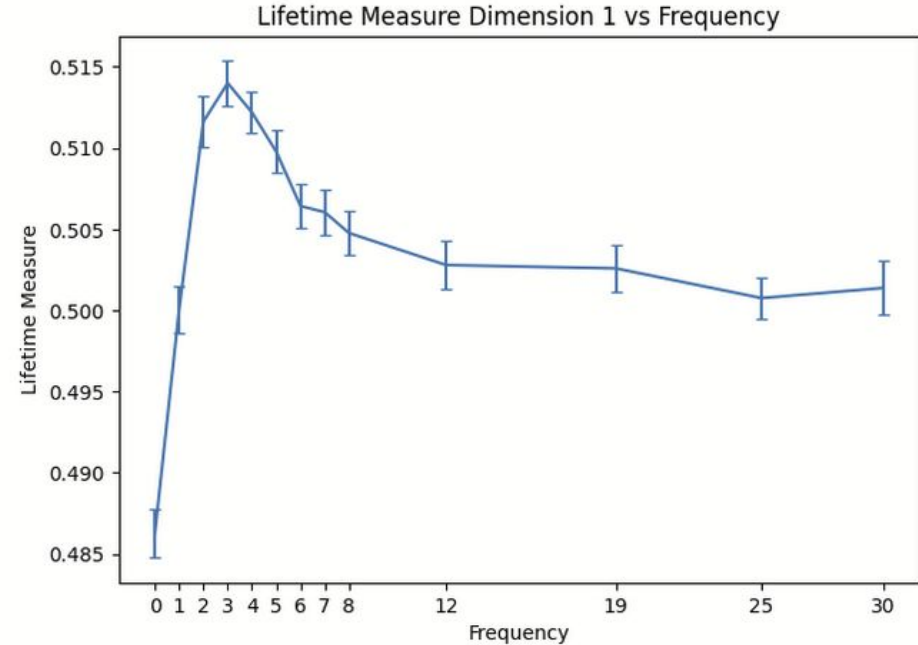
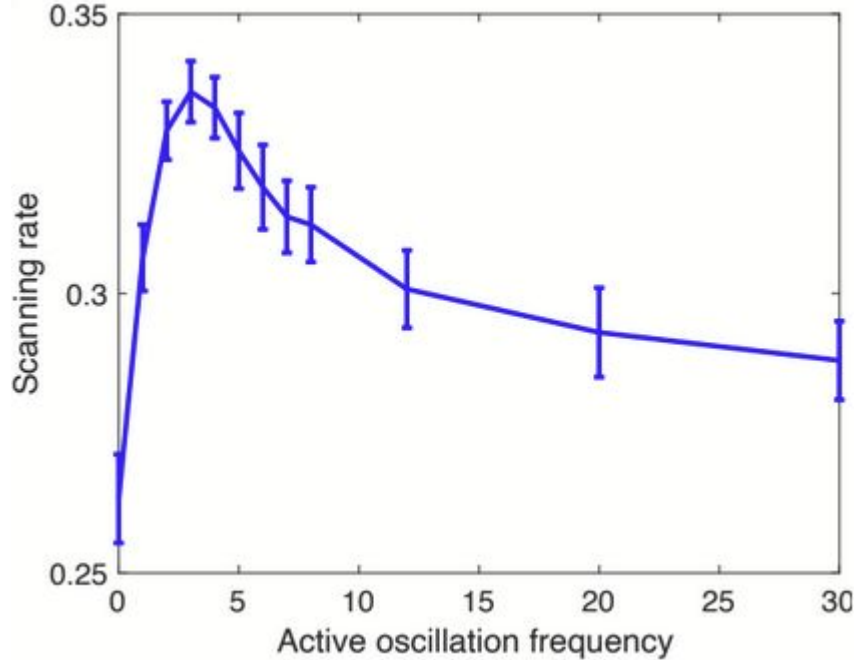
Lifetime Measure Dimension 0 vs Frequency



Lifetime Measure Dimension 1 vs Frequency



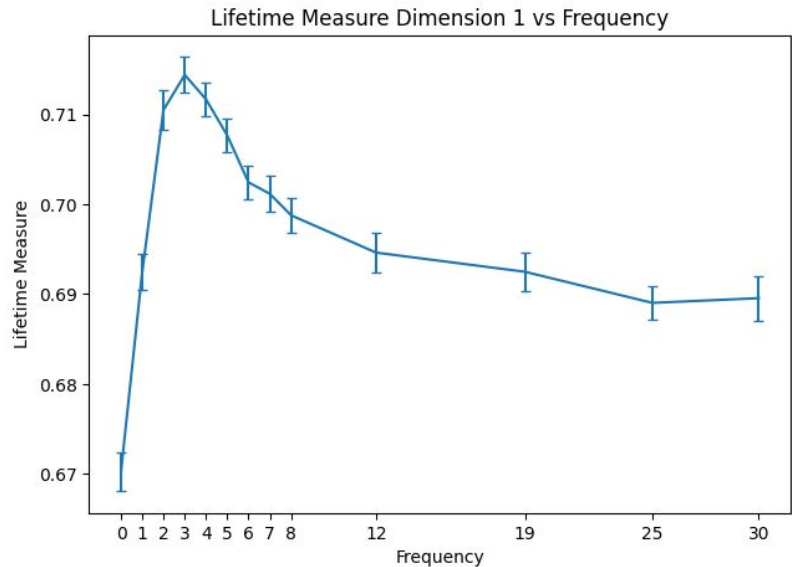
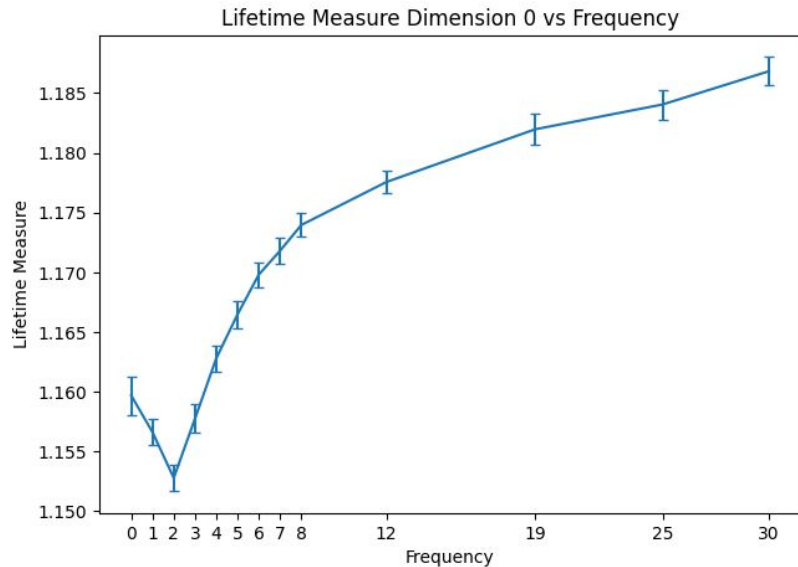
Lifetime measure depending on frequency (ctd.)



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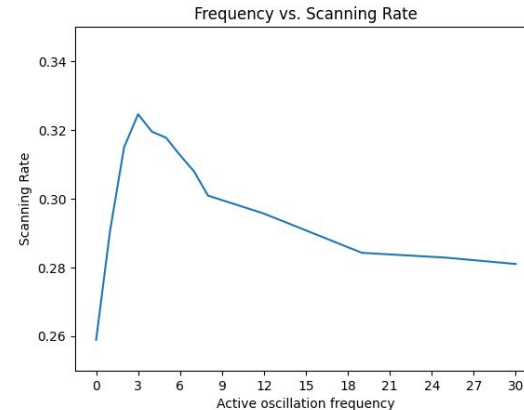
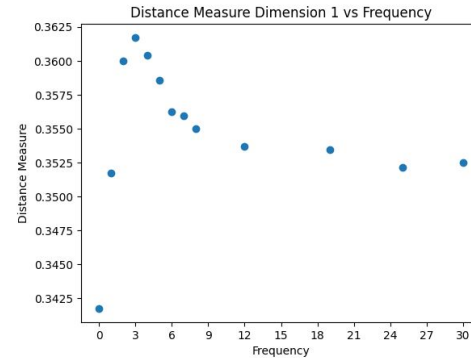
Culling Values

CULL: 30



Dimension 1 possible explanation

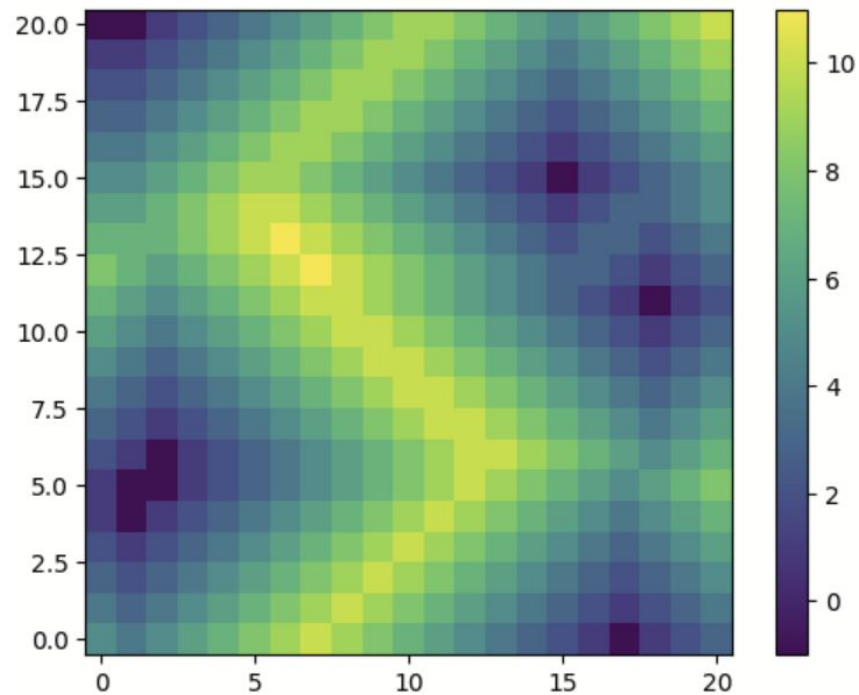
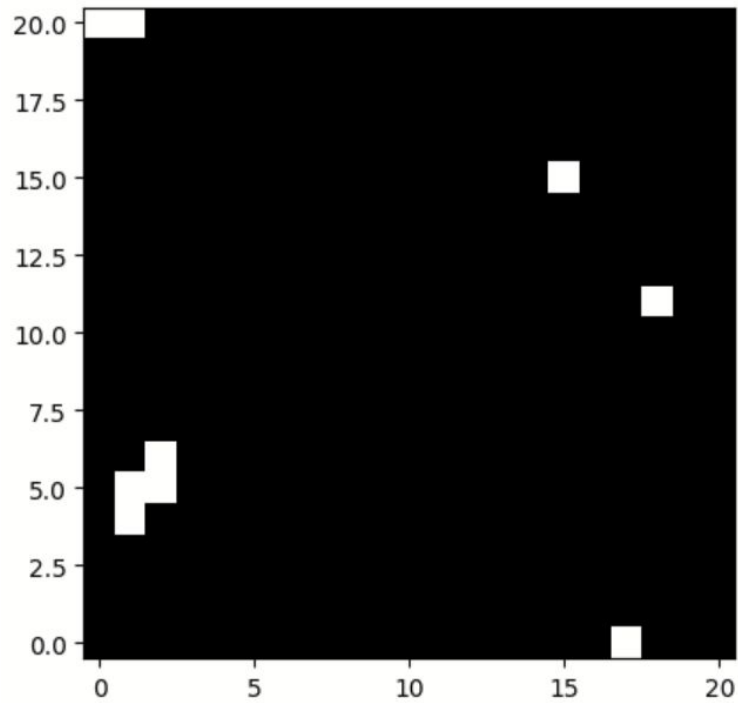
- Many holes formed at optimal frequency
- Correlation between cooperative motility and dimension 1 holes
- When cells move past each other easily instead of repelling or sticking, they form structures with holes



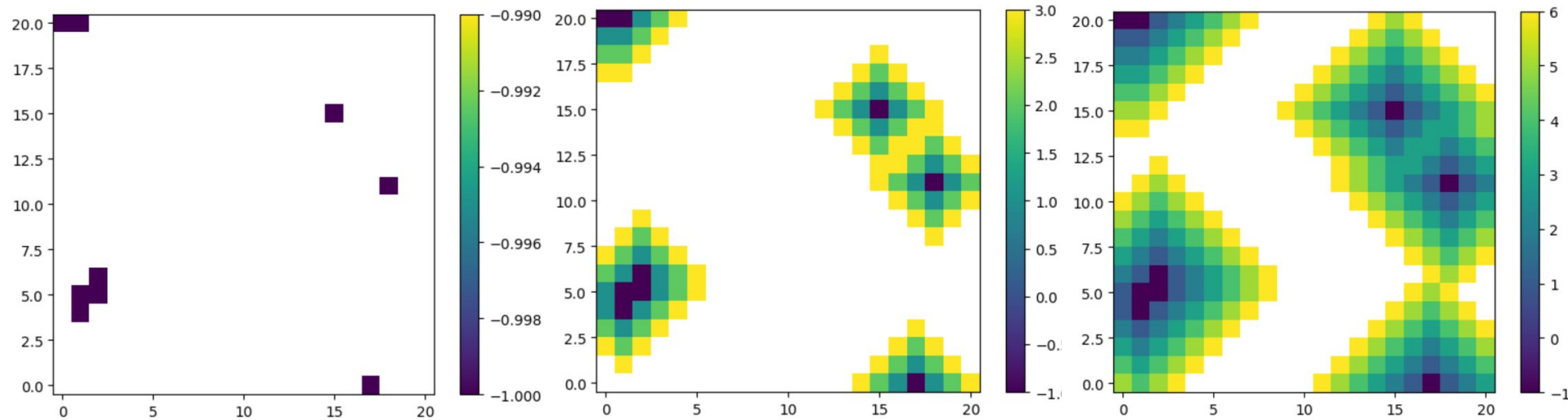
Distance Transform (DT)

- Convert the data (center + radius of cells) to binary image
- Perform signed distance transform
- Study uses Euclidean distance transform (EDT)
- Example uses L1/ taxicab norm for low-resolution visualization

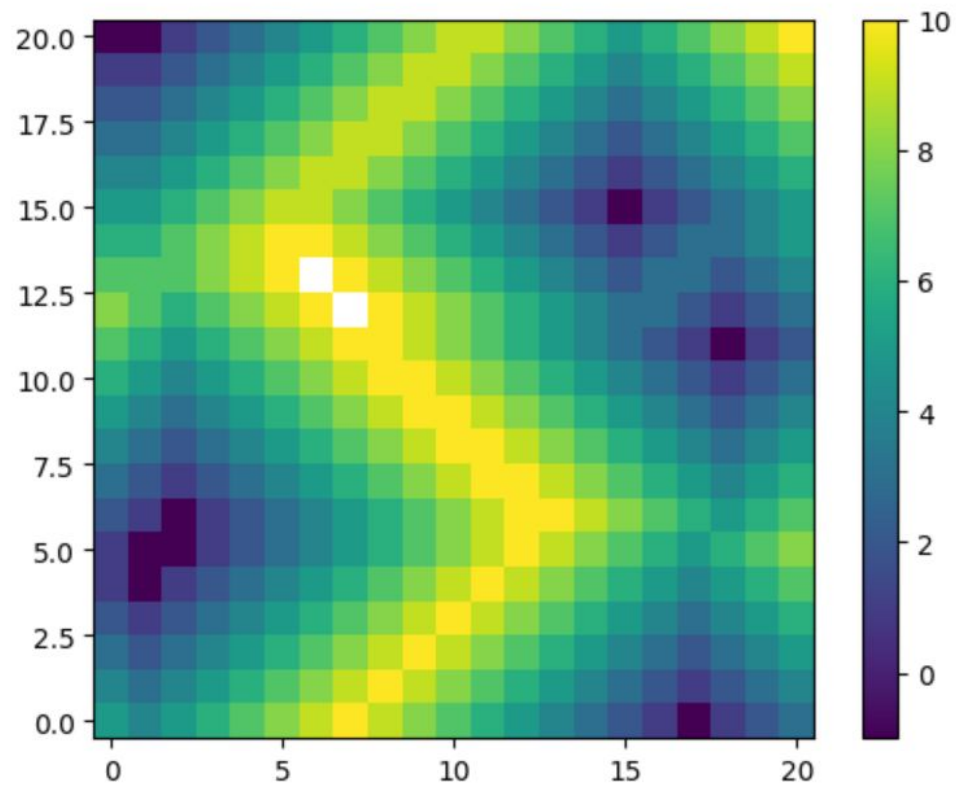
DT (ctd.)



DT (ctd.)

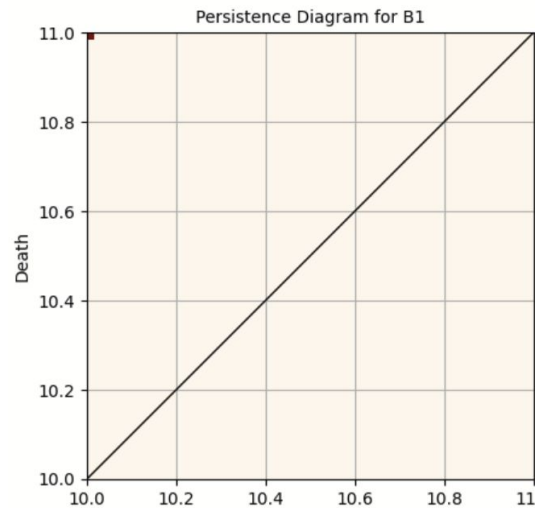
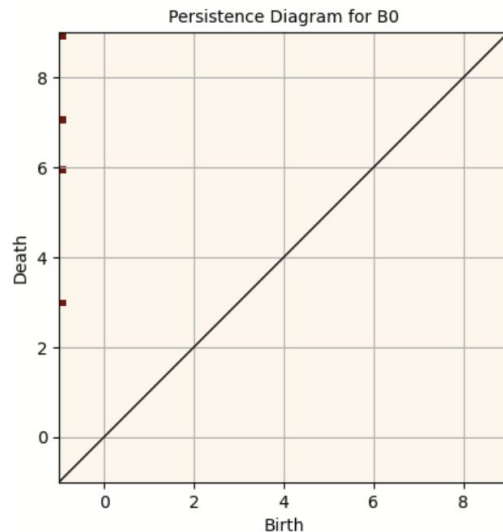
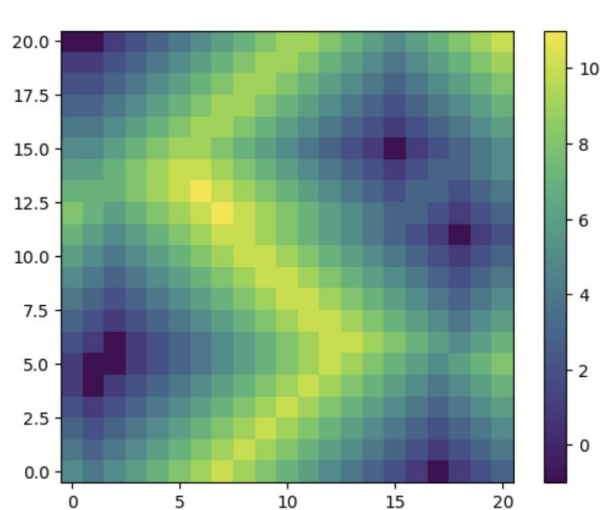


DT (ctd.)



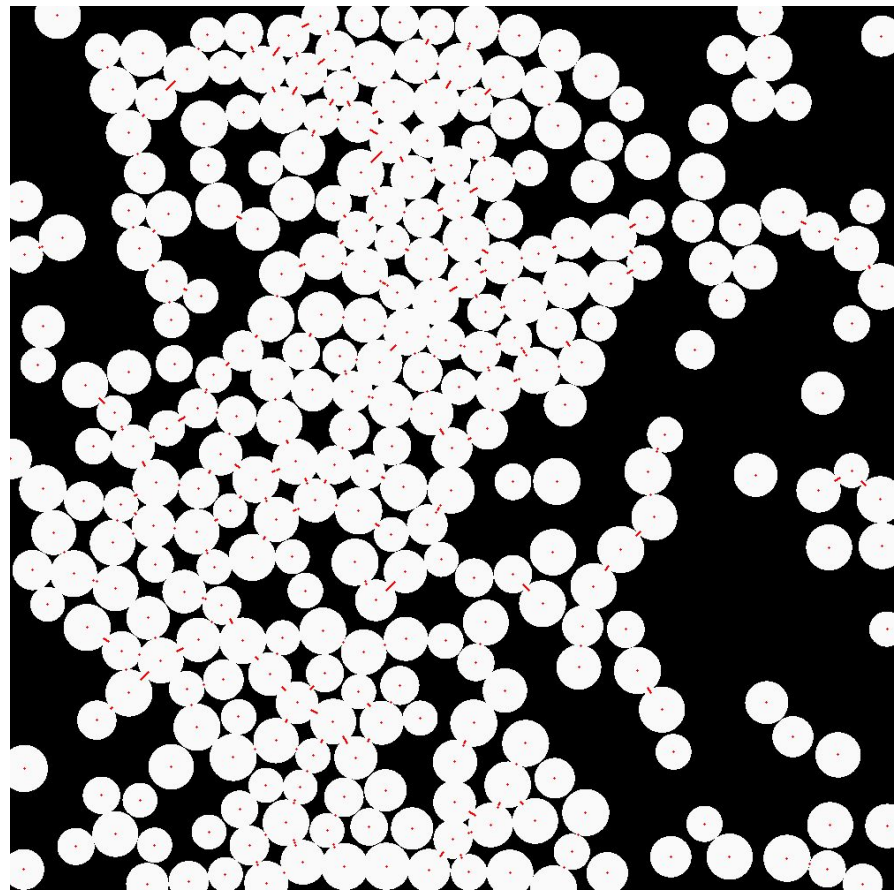
DT (ctd.)

- Generate a persistence diagram for each frame
 - Take the mean lifespan of all the points
 - Take the mean of all the frames and realizations for each frequency



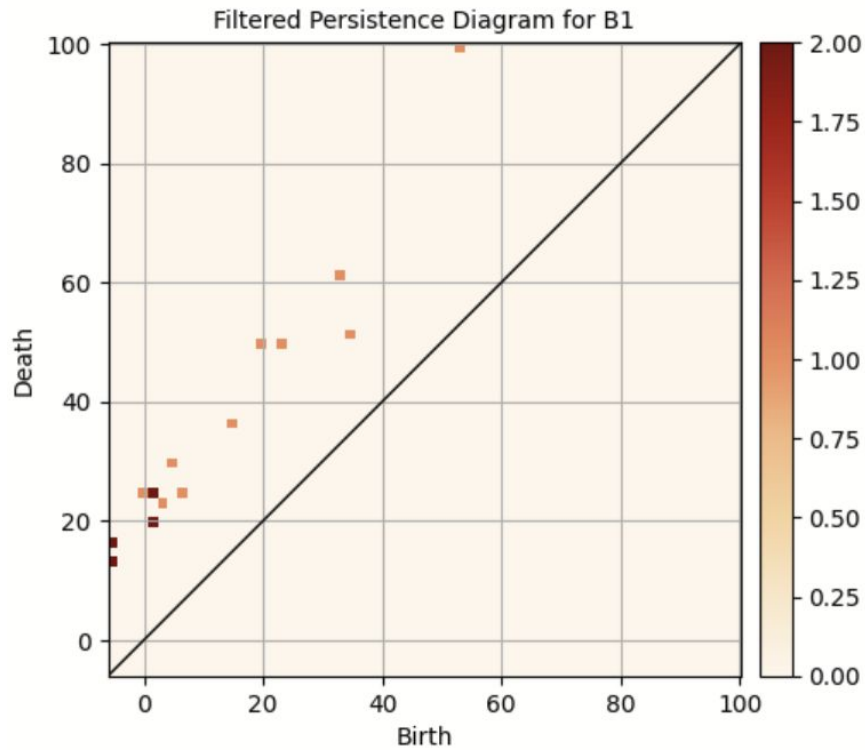
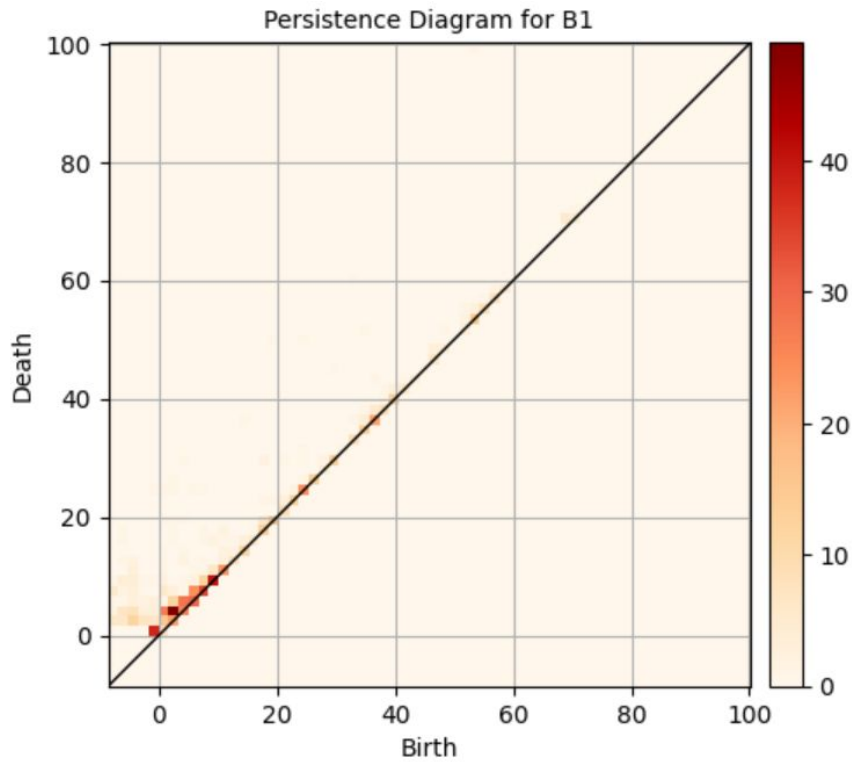
EDT (ctd.)

- Not every feature is taken into account
- Unnecessary generators $\Rightarrow$ noisy PD



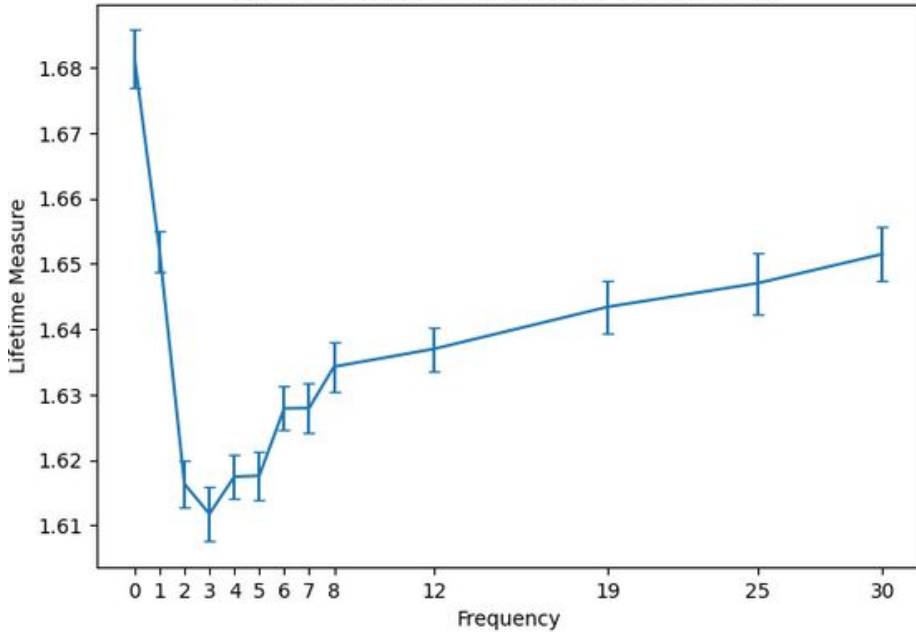
EDT (ctd.)

- Ex) Keeping only the 98th percentile of longest-lasting features

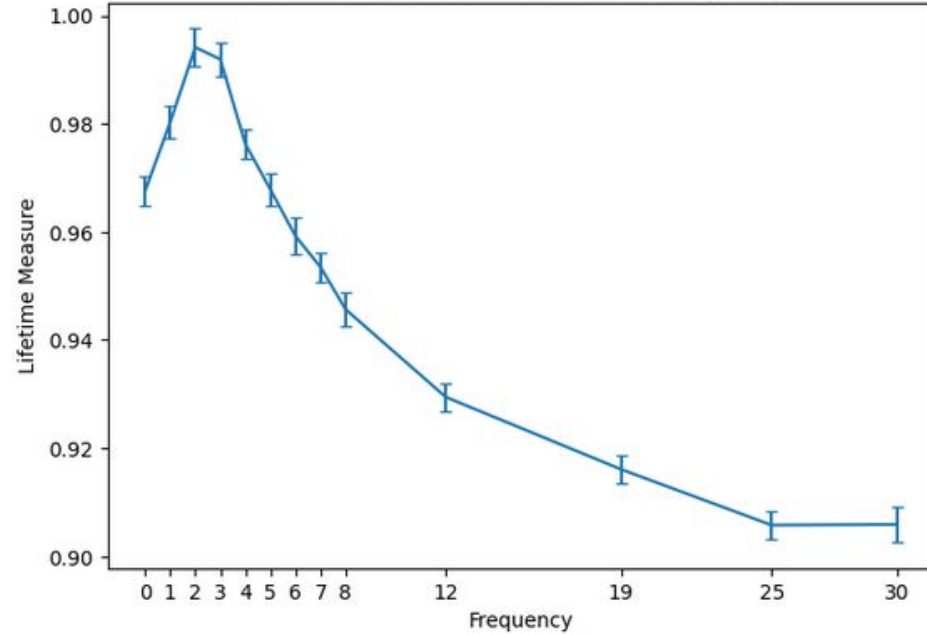


EDT (ctd.)

Lifetime Measure Dimension 0 vs Frequency

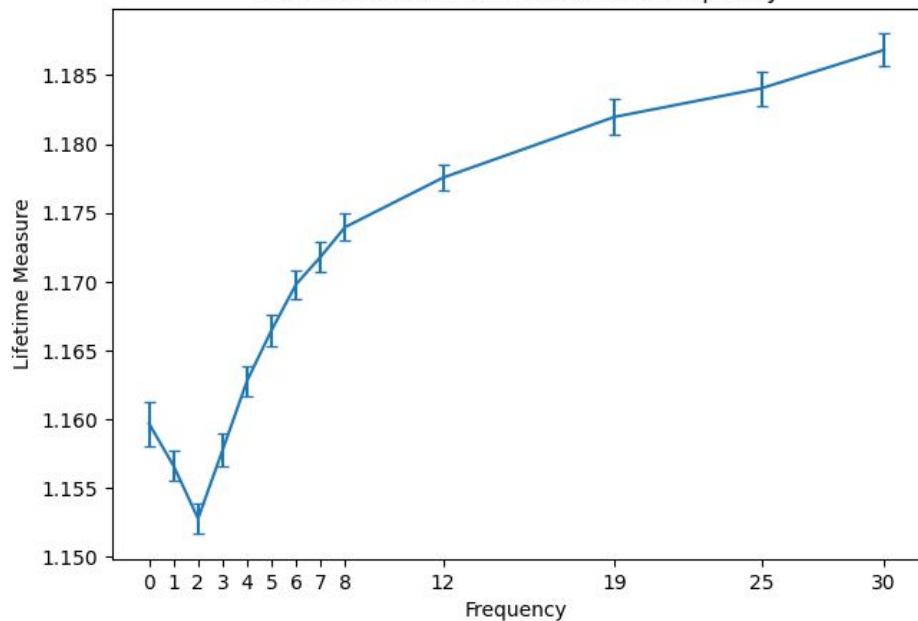


Lifetime Measure Dimension 1 vs Frequency

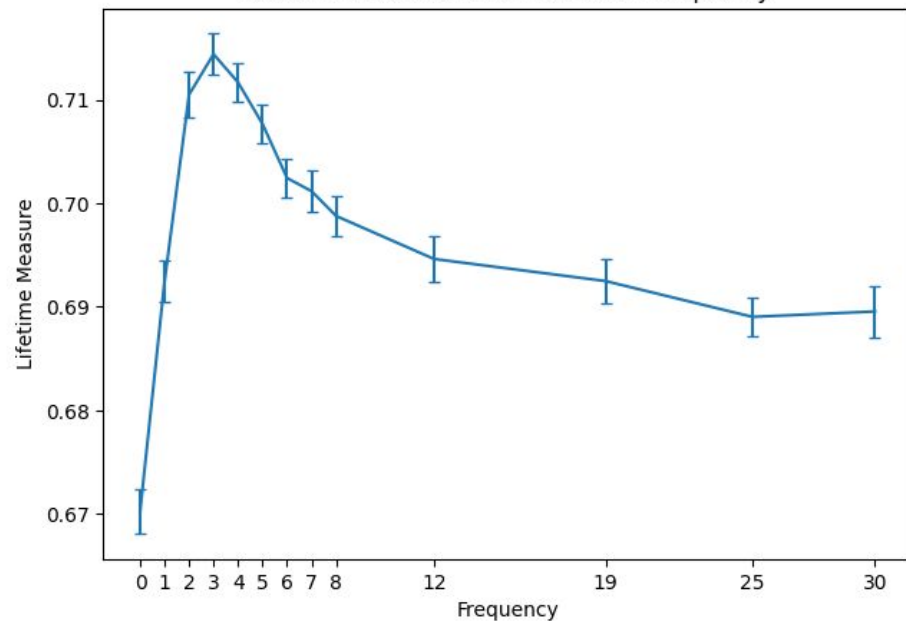


Alpha Complexes Filter 30%

Lifetime Measure Dimension 0 vs Frequency

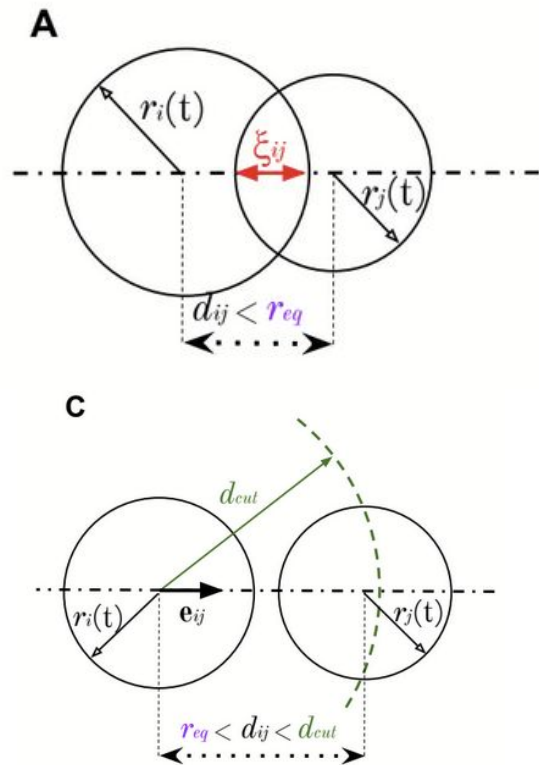


Lifetime Measure Dimension 1 vs Frequency



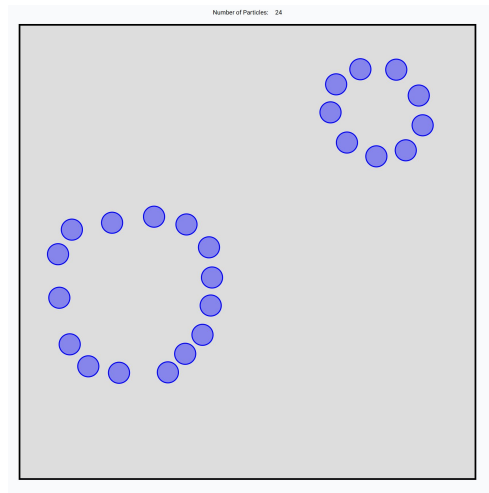
Connecting Scanning Rate & TDA

- Higher frequency => cells are more likely to break equilibrium
 - Cells in contact without overlapping => zero net force
 - Overlapped cells push each other away
 - Cells that are pushed away pull on each other until they overlap again => a cycle of push-and-pull => position locking
- Low frequencies
 - Cells experience little position locking
 - Cells slide past each other w/ little space between them
 - Low scanning rate
- High frequencies
 - Position locking becomes stronger (more prevalent & longer-lasting)
 - Cells become stuck in position
 - Low scanning rate

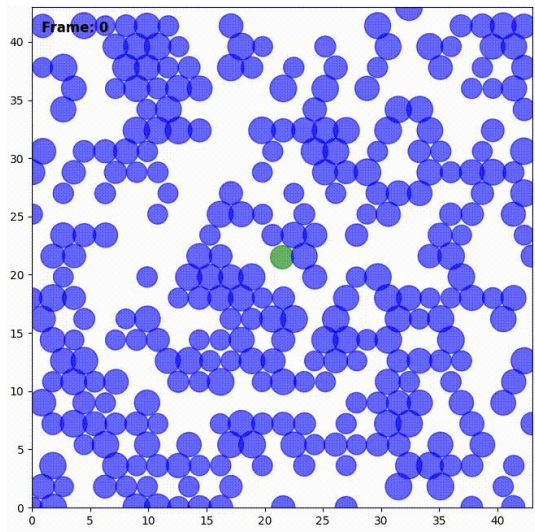


Connecting Scanning Rate & TDA (ctd.)

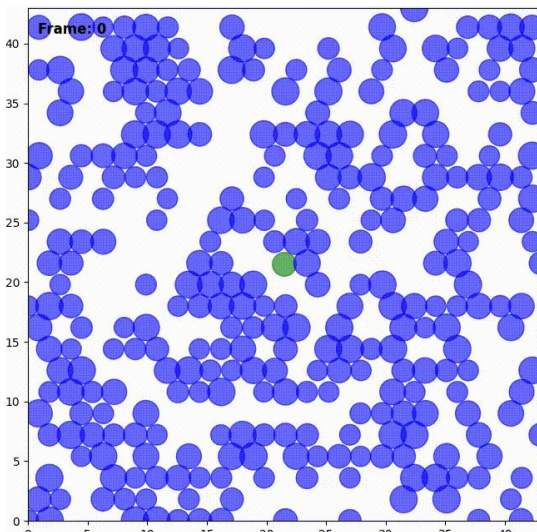
- At the optimal frequency ($w=3$)
 - Cells experience sufficient position locking
 - Strong enough to create some space between cells
 - Weak enough to not cause permanent position locking
 - Optimal motility & scanning rate
 - Sufficient space between cells => the cells enclose *apparent* dimension 1 holes
 - Large mean lifespan for both alpha complex and filtered EDT
 - Apparent dimension 1 holes => cells have less space to inhabit
 - Cells farthest from their neighbors have their space reduced the most
 - Minimized dim0 lifespan after filtration



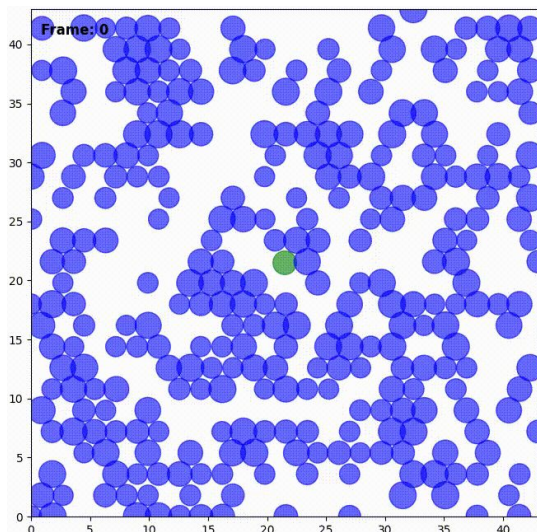
Animations at different frequencies



Frequency 0



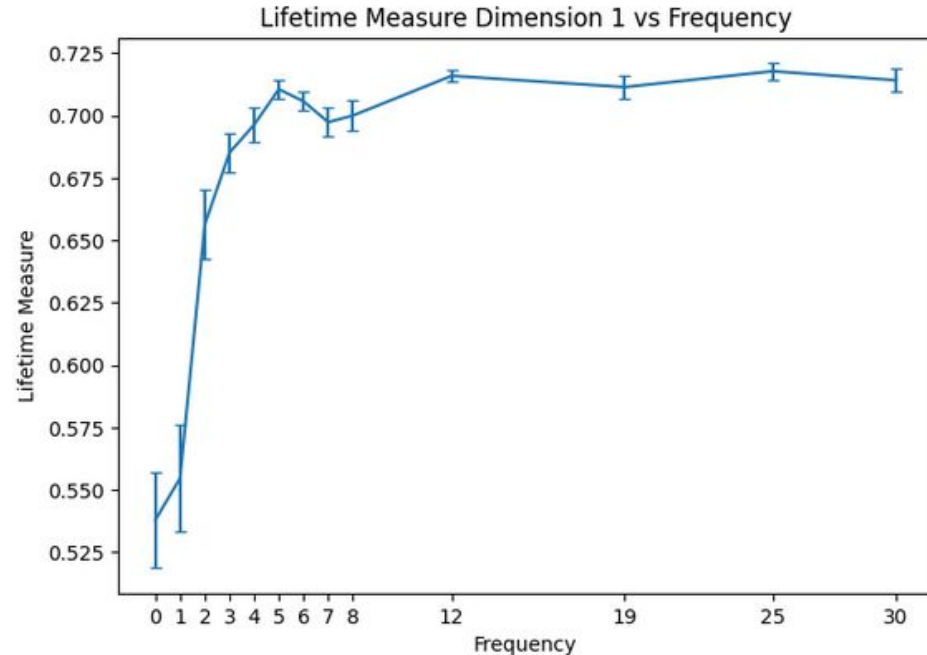
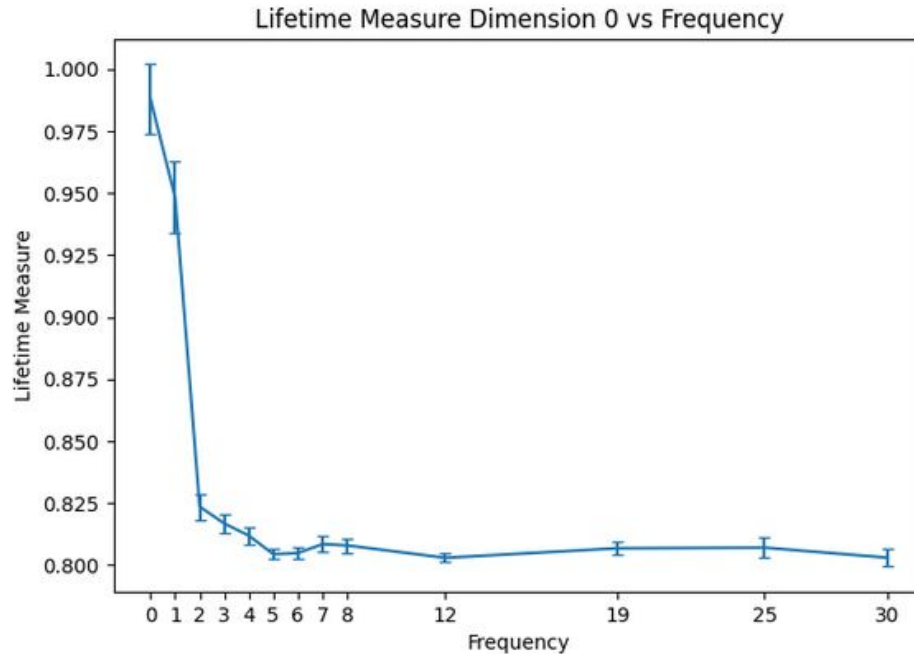
Frequency 3 (Optimal)



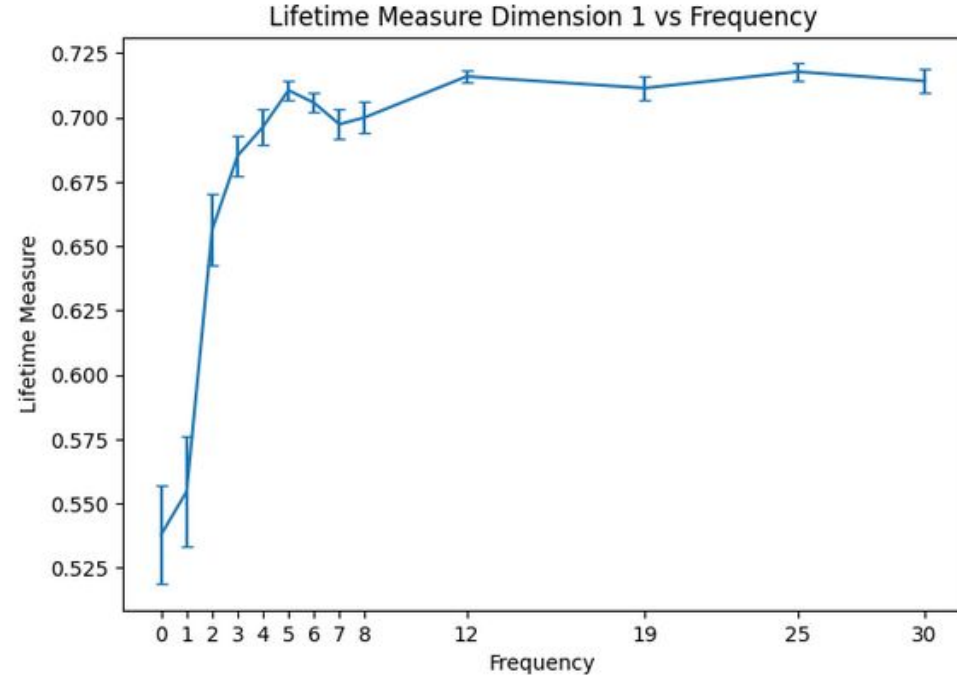
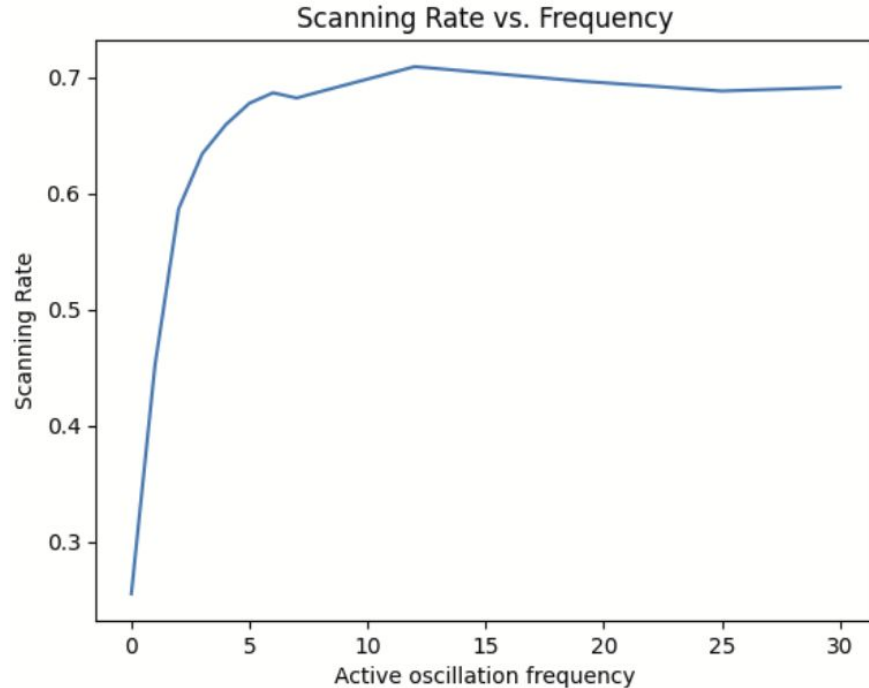
Frequency 20

Testing the Explanation (alpha complex)

- Set $F_{adh} = 0.75$ and $F_{rep} = 0 \Rightarrow$ no position locking

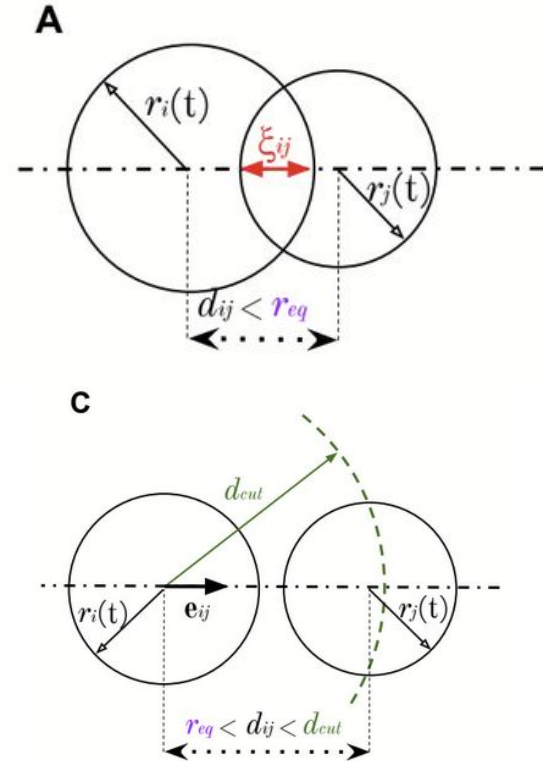


Testing the Explanation (ctd.)



Future Test Ideas

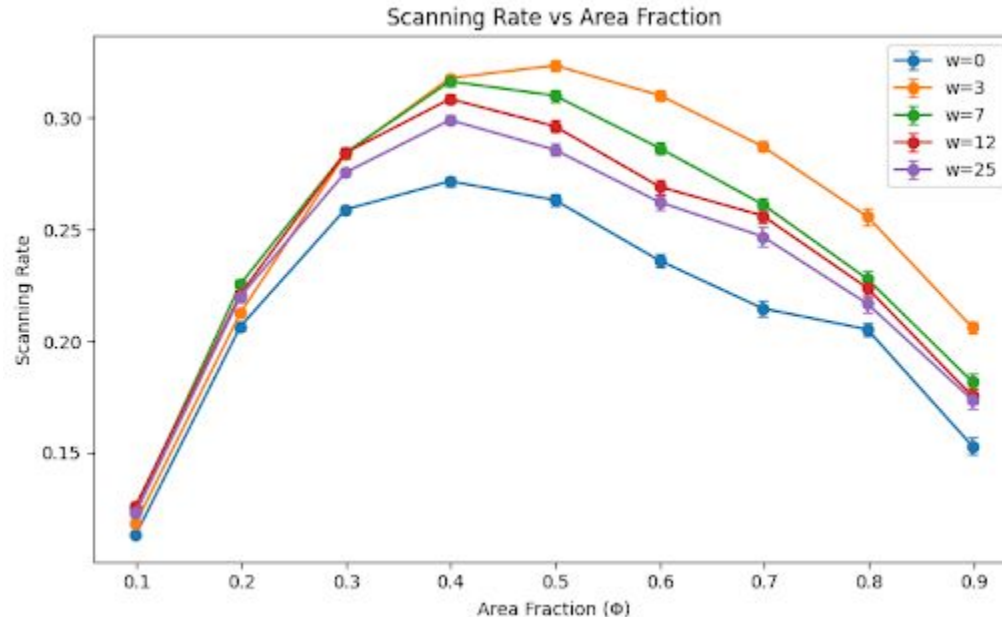
- Test different force values to verify the connection between scanning rate and dimension 1 mean lifespan
- Verify the position-locking explanation connecting scanning rate and TDA
- Track the direction of the velocity vectors of each cell
- If position locking is valid, at high frequencies, the velocities should be nearly parallel to the radial vector between nearest cells
 - Qualitatively assess animations
 - Measure the average angle (0 to 0.5π) between velocity and radial vector to the nearest cell
 - Measure the proportion of velocity vectors whose angles to the radial vector is below a certain threshold



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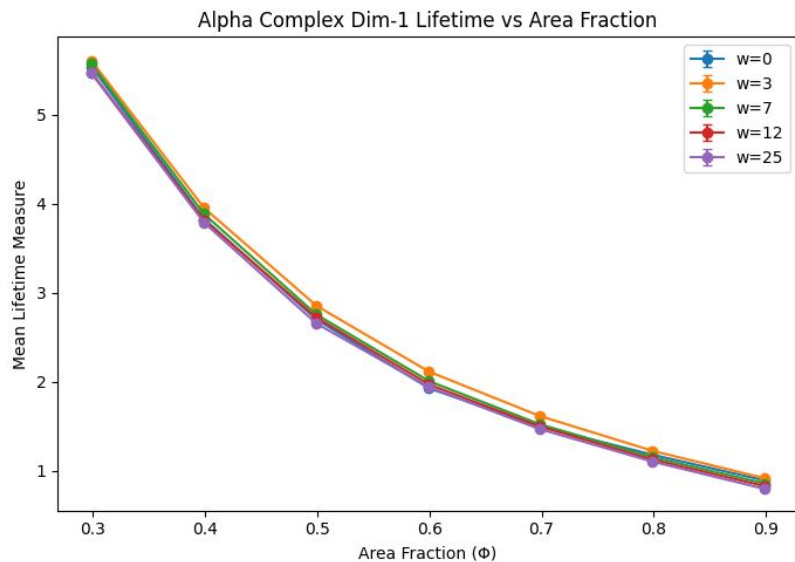
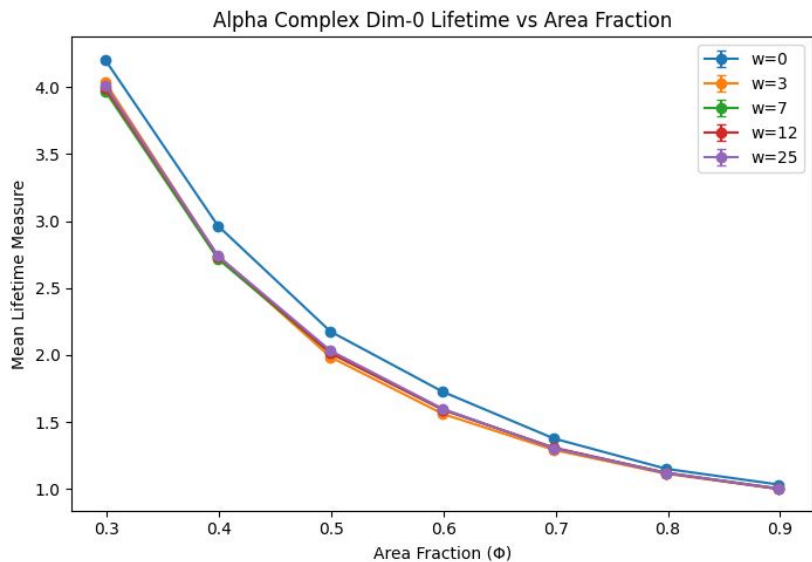
Scanning Rate Against Cell Density

- Previous work showed that scanning rate optimized at intermediate densities
- Similar to maximizing flow in pedestrian/vehicular traffic



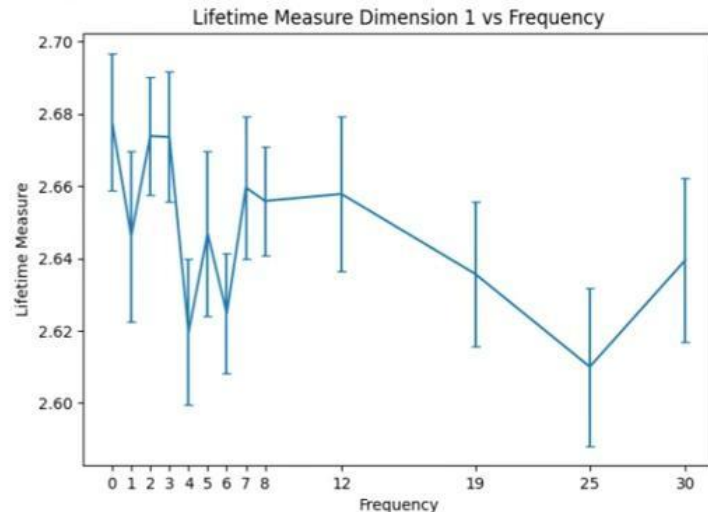
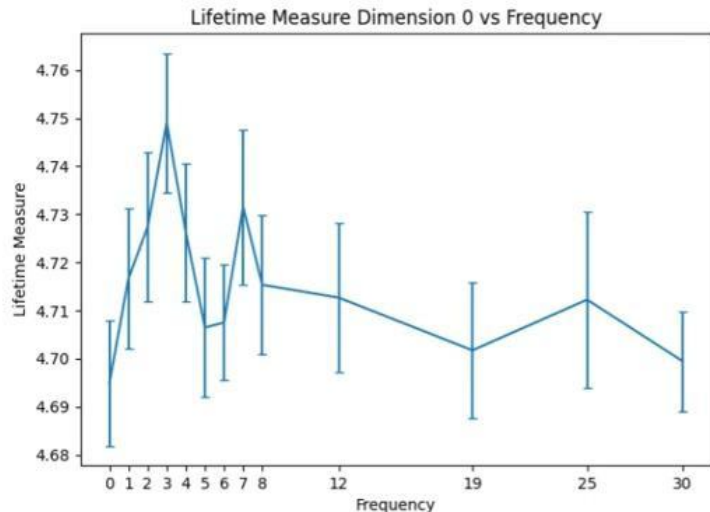
Topological Measures Against Cell Density

- Scale of features die off in general as cells get more packed



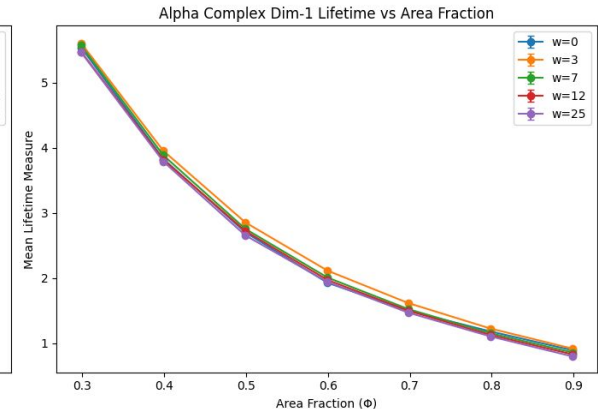
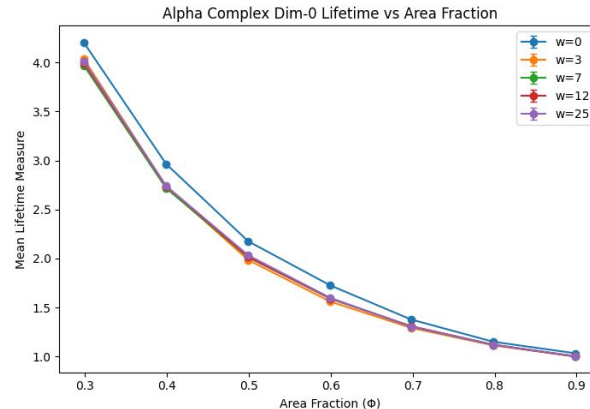
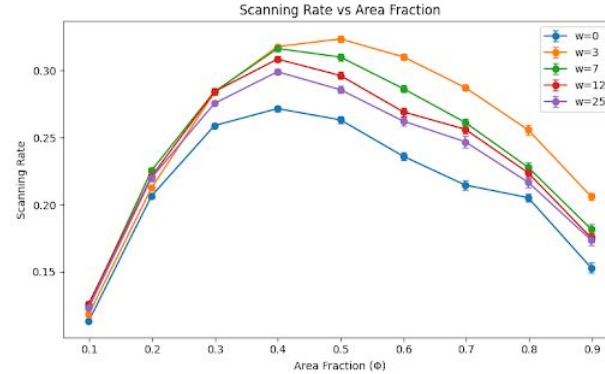
Topological Measures Across Area Fraction

Area Fraction: 0.1



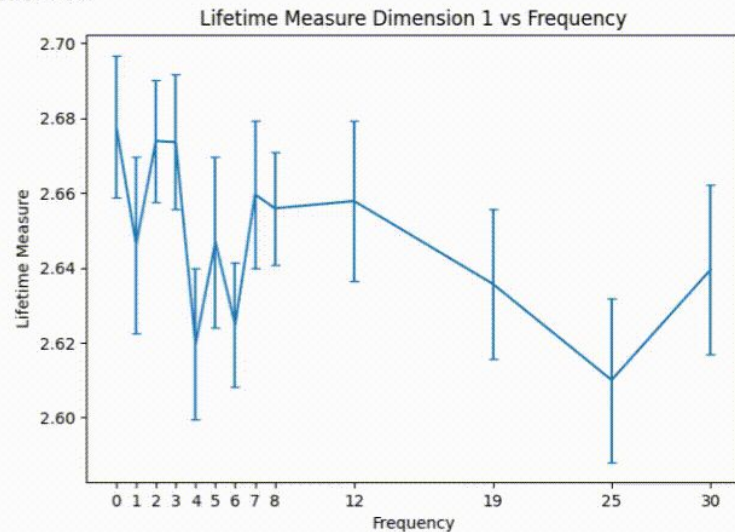
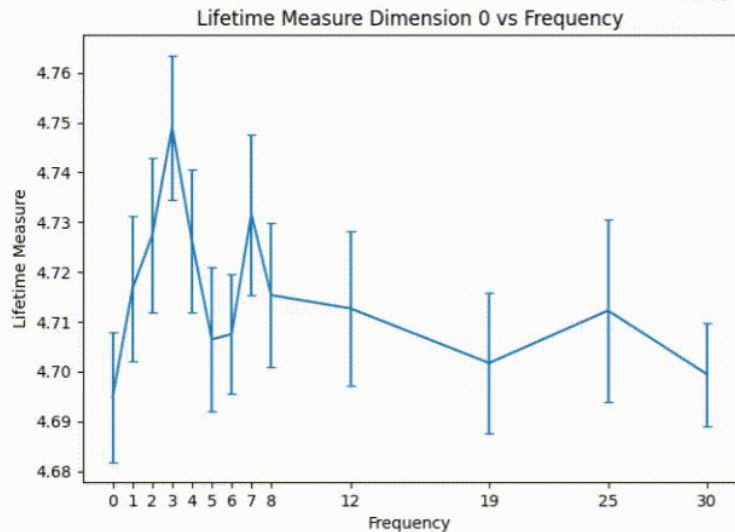
Topological Measures Across Area Fraction (ctd.)

- Cooperative Motility cares about crowded environments
 - Impediments are non-obstructing
 - Phenomena is best observed in extremely crowded environments



Topological Measures Across Area Fraction

Area Fraction: 0.1

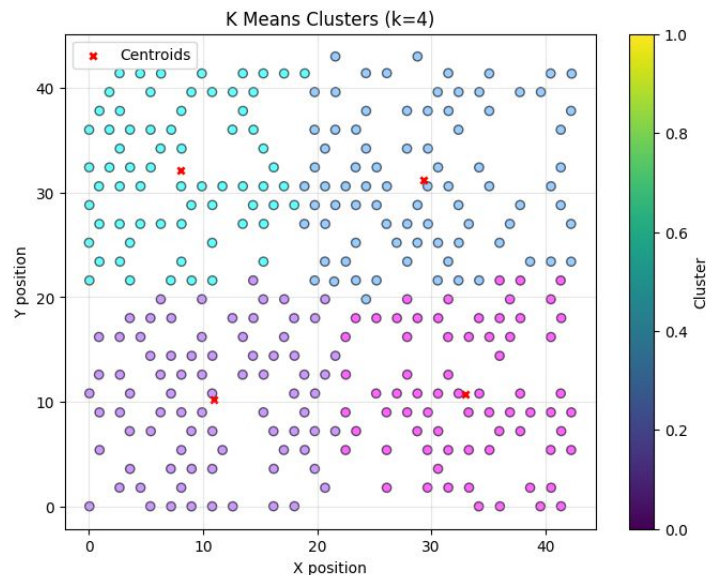


Clustering Analysis

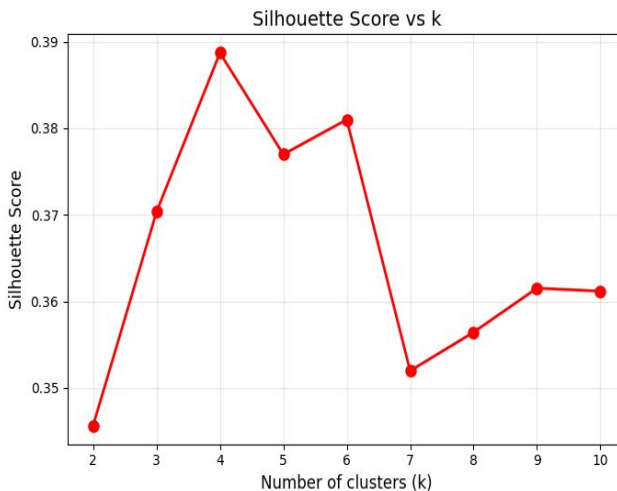
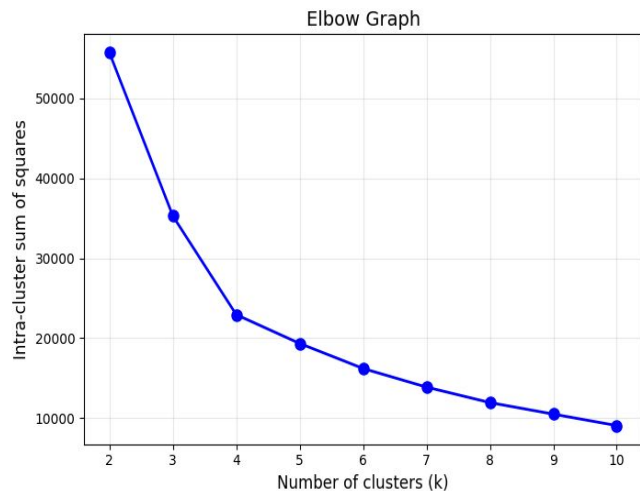
- We consider a basic approach to clustering
- Questions:
 - How and when do clusters of cells form?
 - Do frequency or scanning rate affect how clusters form?
 - Is the topological behavior of cells within respective clusters the same as compared to global behavior?

Cluster Formation

- Due to the geometry of the simulation grid and APC cell, cells form clusters within quadrants
 - APC cell inherently splits grid into 4 quadrants
- Centroids are positioned at center of each quadrant
- Provides insights into how cells will behave with multiple APC cells present



Cluster Formation



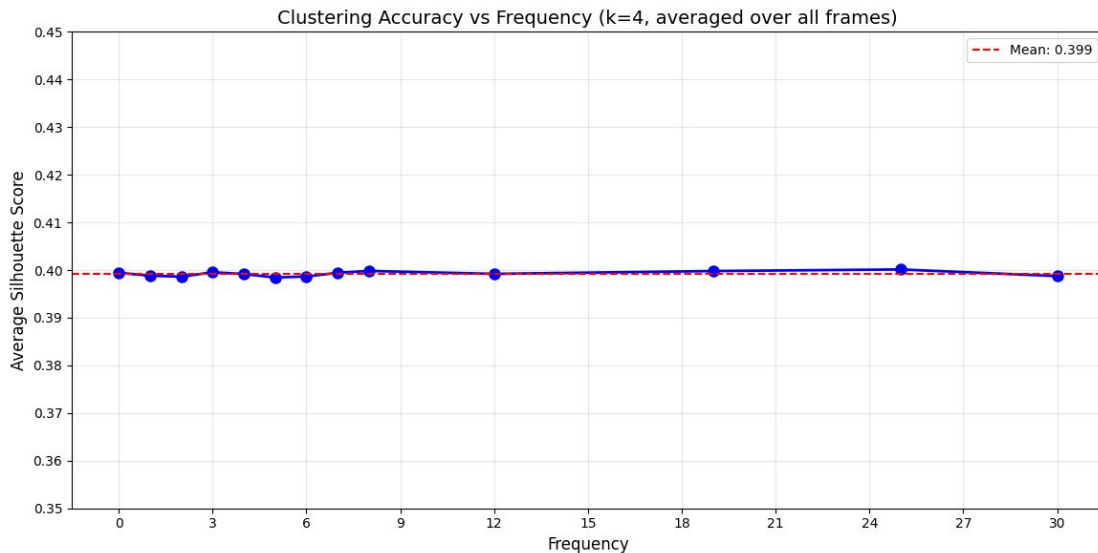
$$\sum_{C_k} \sum_{x_i \in C_k} (x_i - \mu_k)^2$$

$$s(i) = \frac{b(i) - a(i)}{\max\{a(i), b(i)\}}$$

The optimal number of clusters appears to be at $k = 4$, supporting the quadrant separation theory

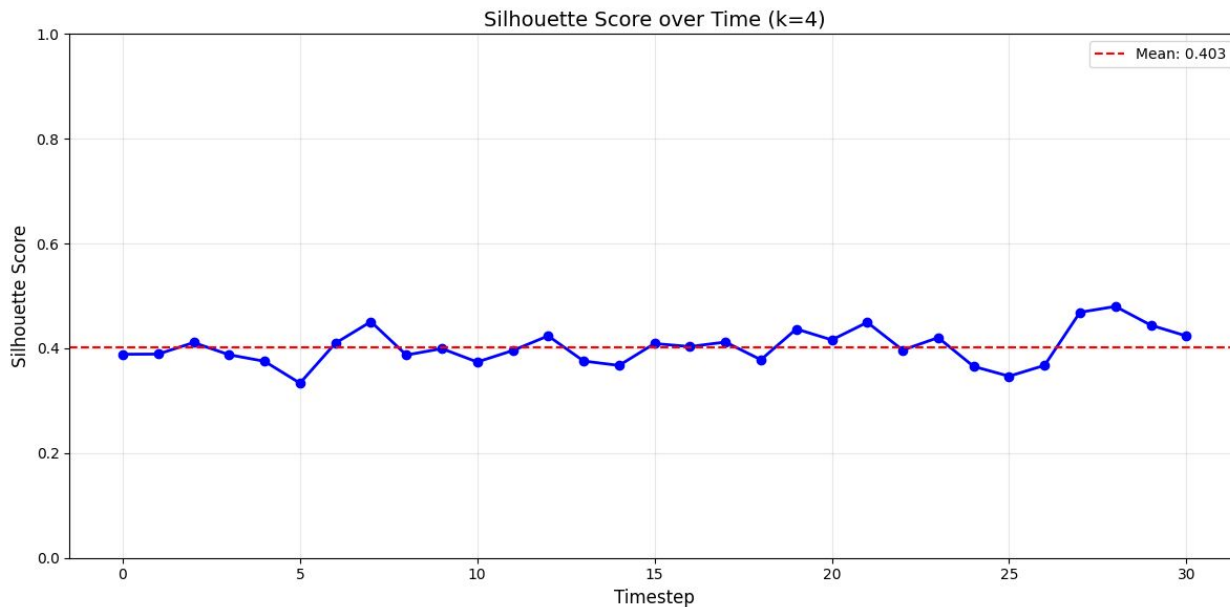
Clustering Across Frequency

- Accuracy does not change across each frequency, suggesting similar behaviors irrespective of frequency/scanning rate



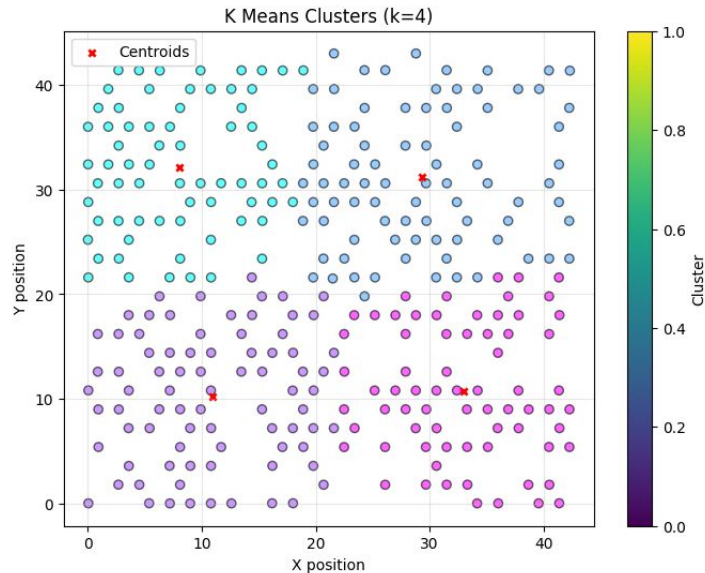
Clustering Across Time

- Relatively similar behavior across time as well
- Graph is for $w = 3$ (optimal scanning rate)

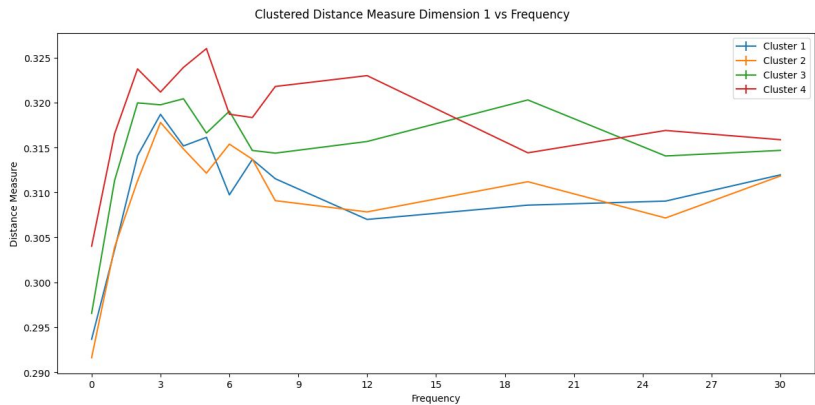
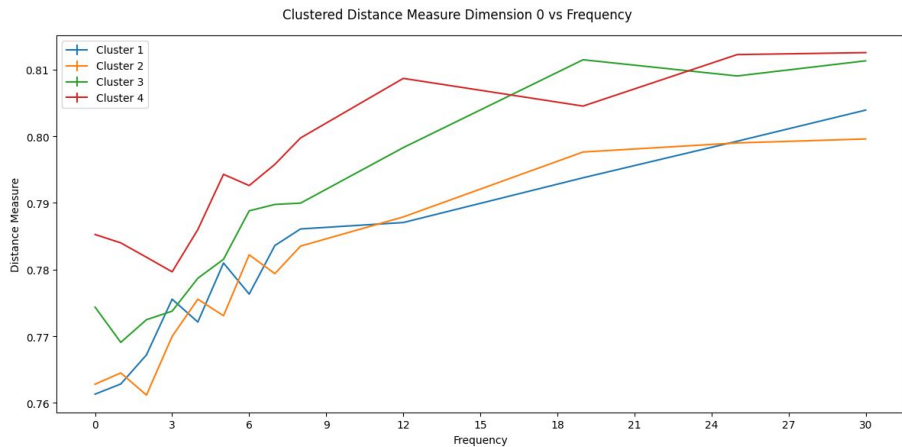
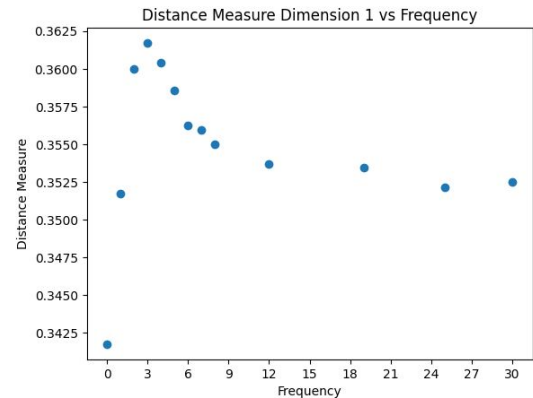
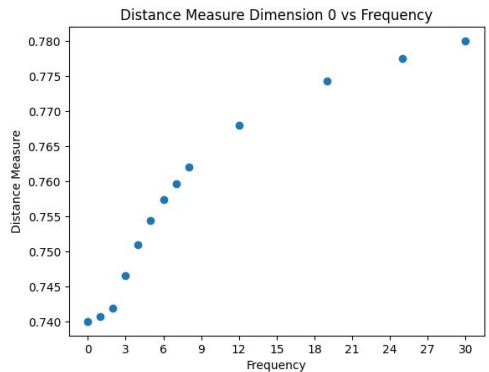


Topological Behavior of Clusters

- Within-quadrant behavior consistent with global behavior
- Not necessary to capture wide area of cells to compute topological measures



Topological Behavior of Clusters



Future Work

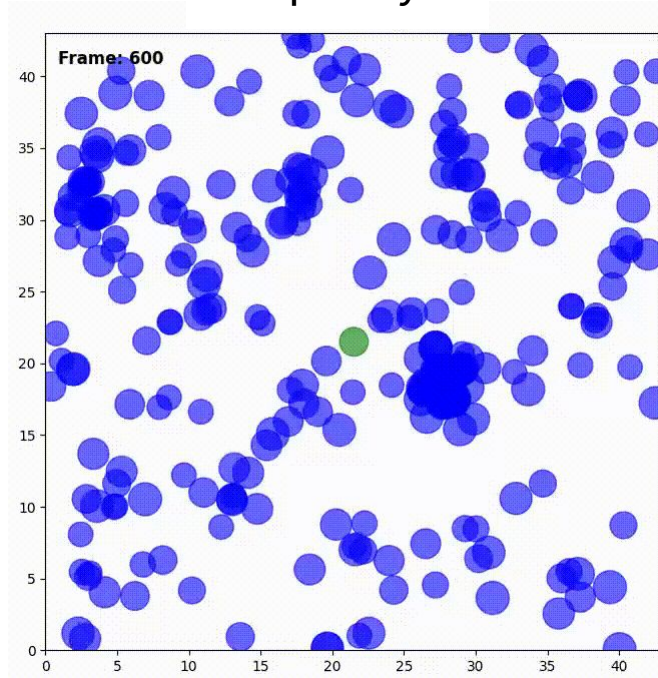
- Further exploration and verification of force dynamics of system
- More work into the effect of cell density (area fraction) on the system and stochasticity of cell orientations
- Topological Data Analysis on 3D simulation

Work Cited

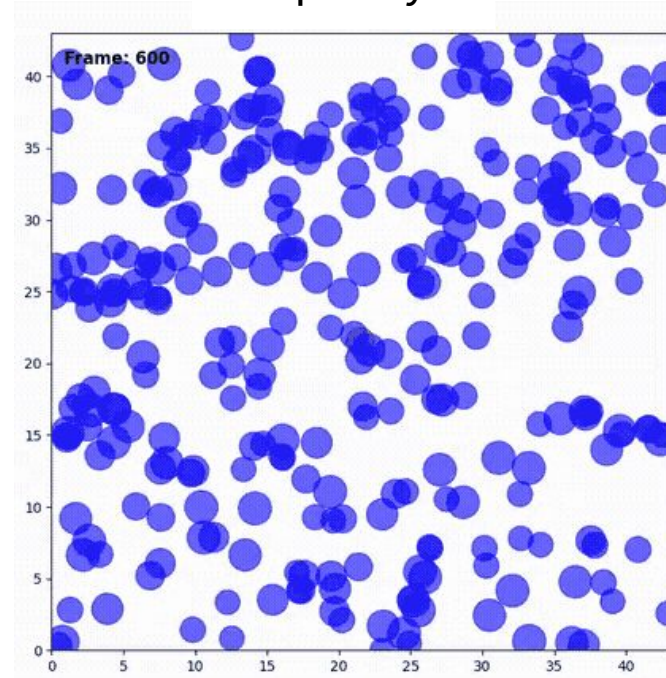
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Different Forces Animated

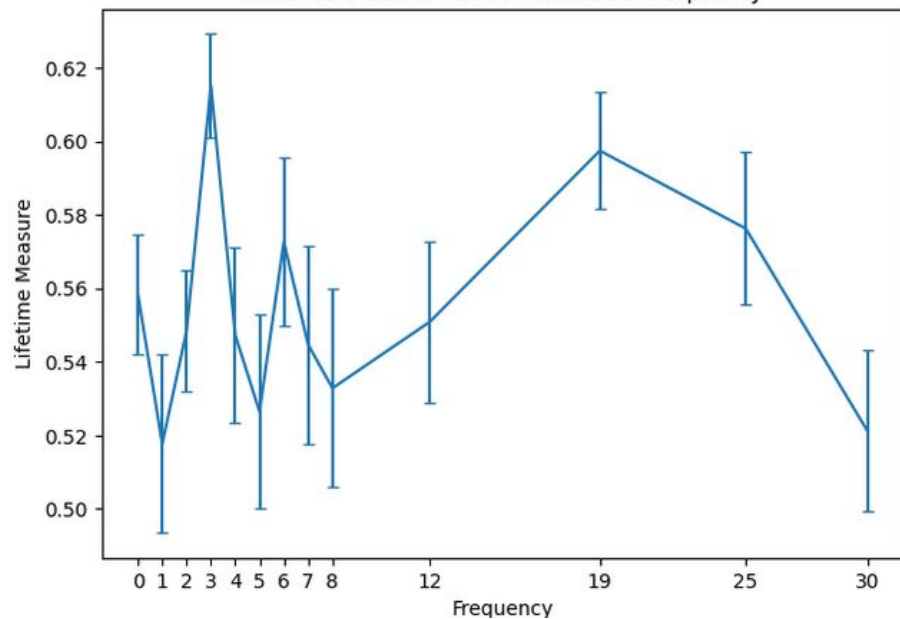
Frequency 0



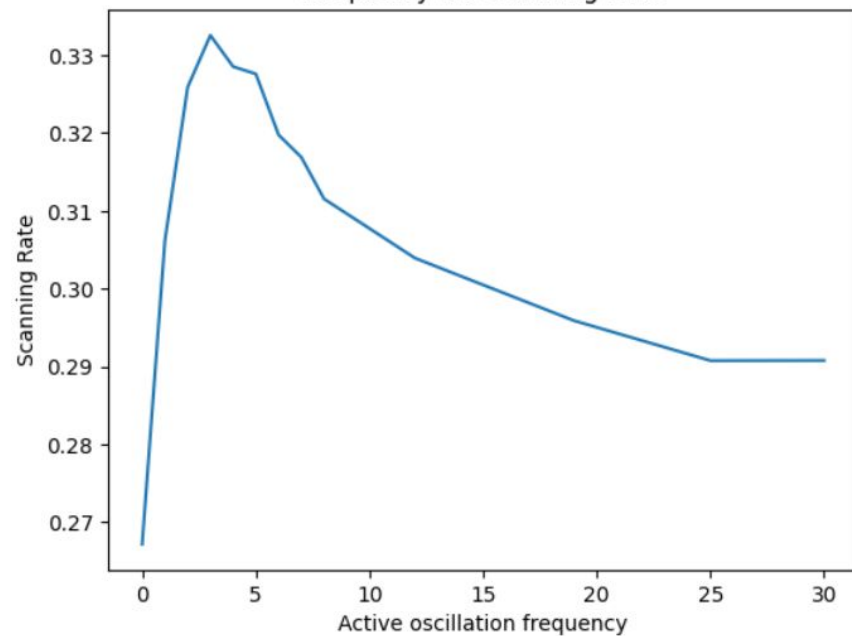
Frequency 3



Lifetime Measure Dimension 1 vs Frequency

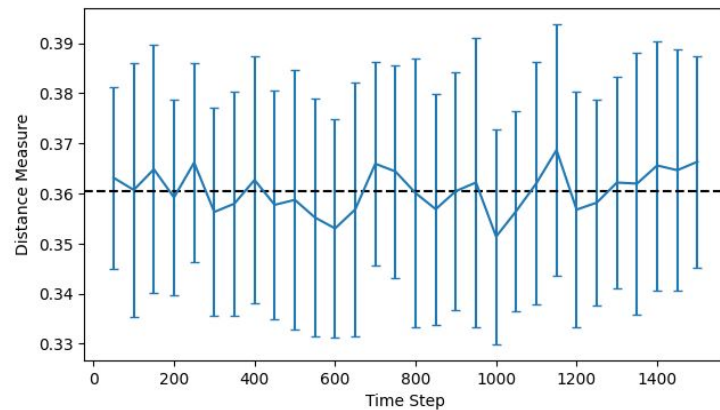
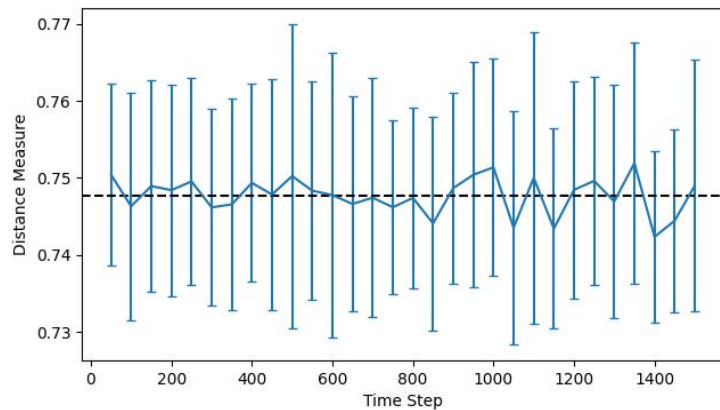


Frequency vs. Scanning Rate

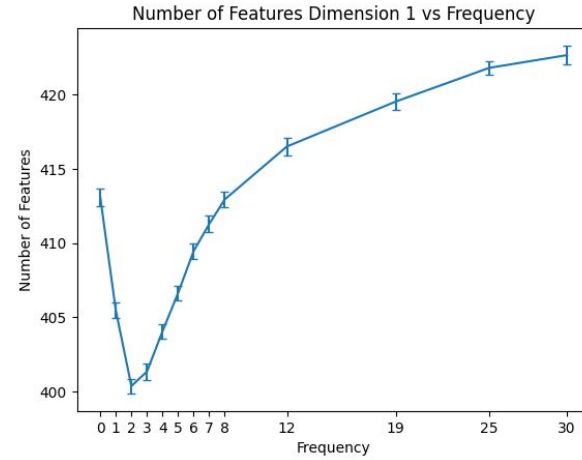
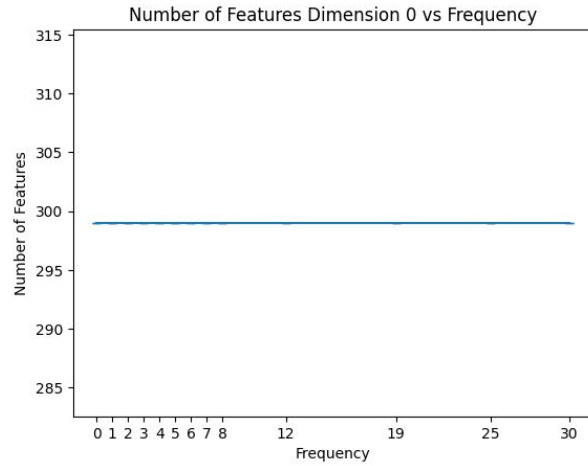


Consistency of Alpha Complex Distance Measure

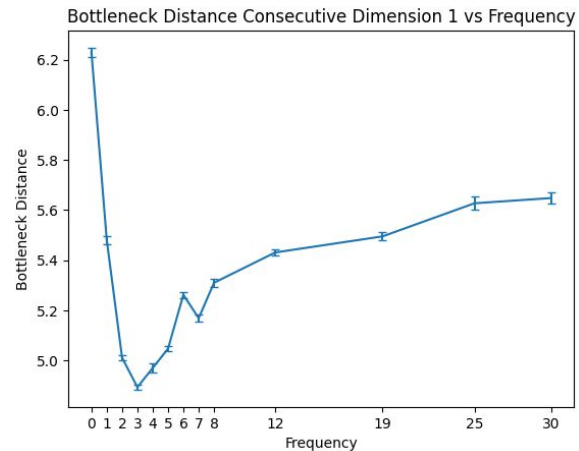
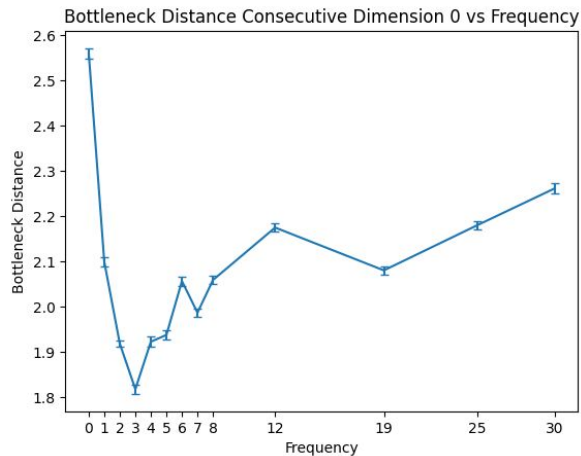
$w=3.0$



AC Number of features



AC Consecutive Bottleneck Distance



AC Contacted Cells

