Group 10
Morphological Drivers of Cell Motility

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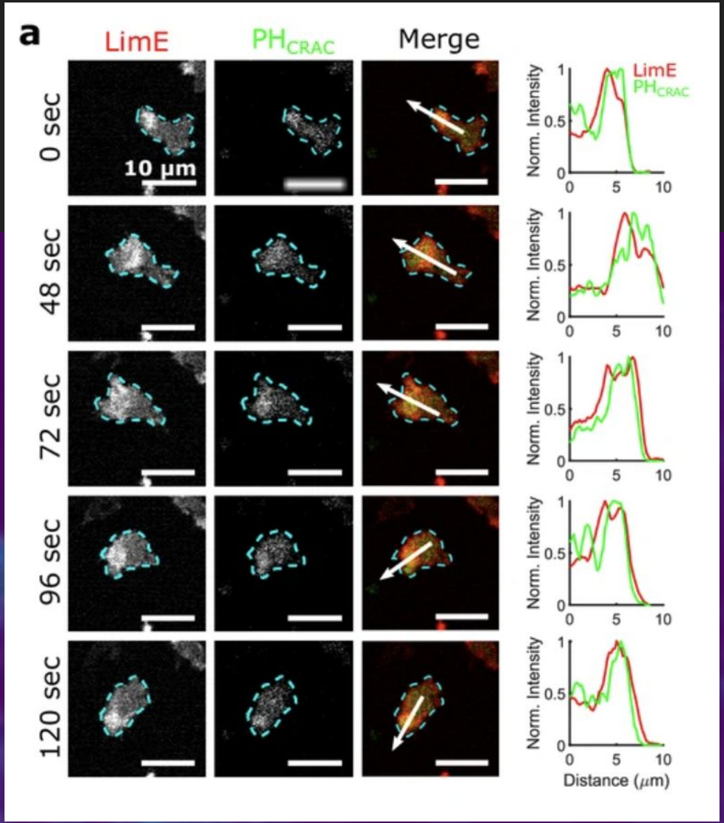
Problem Formulation and Motivation

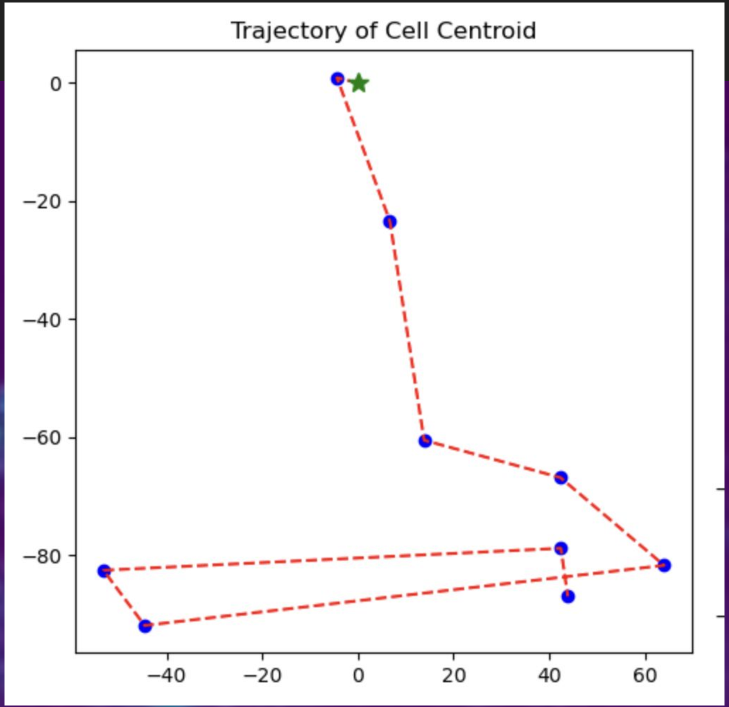
- Goal: Assess how fluorescent signals along Cytoskeletal Excitable Network (CEN) drive cell morphology and motion
- 3D Fluorescent Videos captured via imaging of F-Actin in *Dictyostelium discoideum*
- Supervised Motion Prediction + Unsupervised Cell Characterization

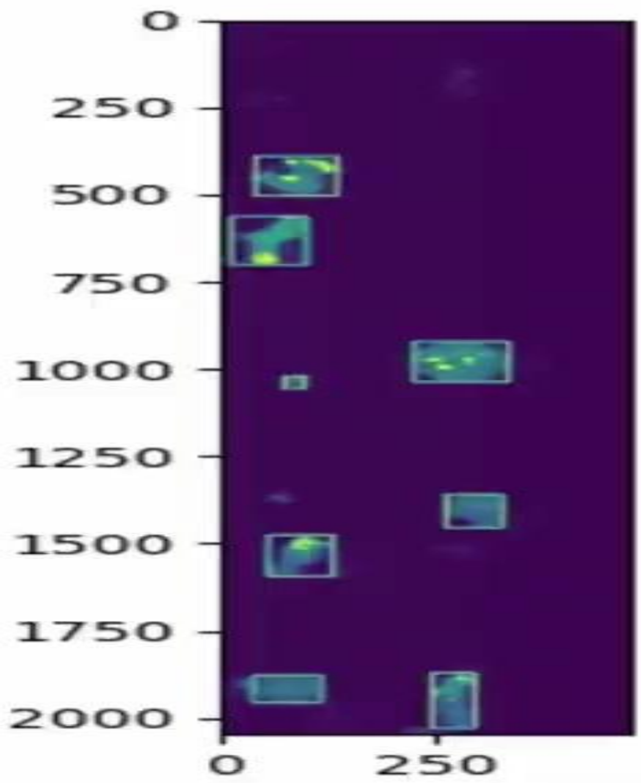


Data Pipeline - Object Detection and Cell Segmentation

1. Videos are up to 100 GB- speed was critical methodological factor
2. Apply background-foreground otsu thresholding to focus on Regions of Interest
3. Find contours and label connected components using regionprops filtering
    a. Filter by Cell Area for robustness
4. Track bounding boxes by ensuring cell areas and positions stay within localized radius of previous frame
5. Track Trajectories of Cell Centroids weighted by cell shape

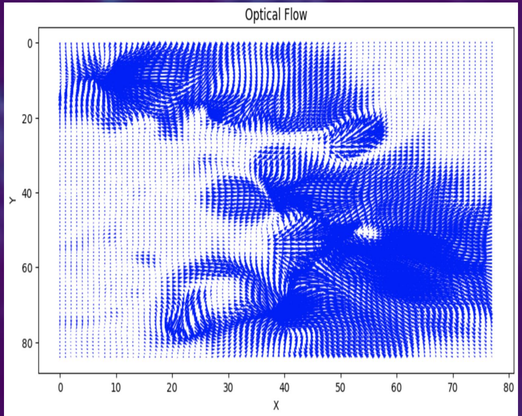
Cell Trajectory in 2D Plane

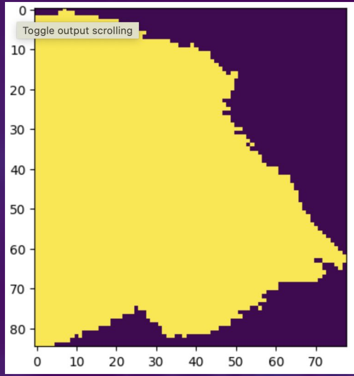


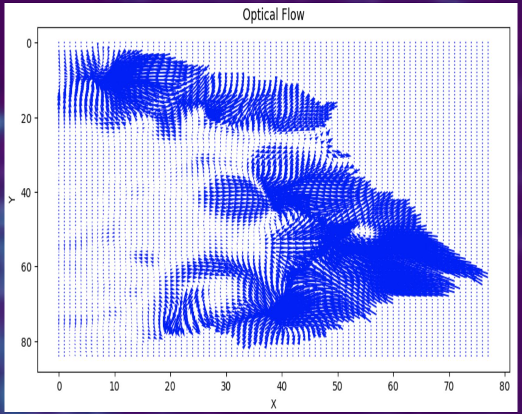

0
250
500
750
1000
1250
1500
1750
2000
0
250

Optical Flow

- Smoothing over n-2 to n+1 frames
- Use Lucas-Kanade method to compute optical flow using smoothed frames n and n+1
- Use binary mask to isolate OF vectors of cell
- Take an average of isolated vectors and add to centroid to find next centroid (frame n+2)

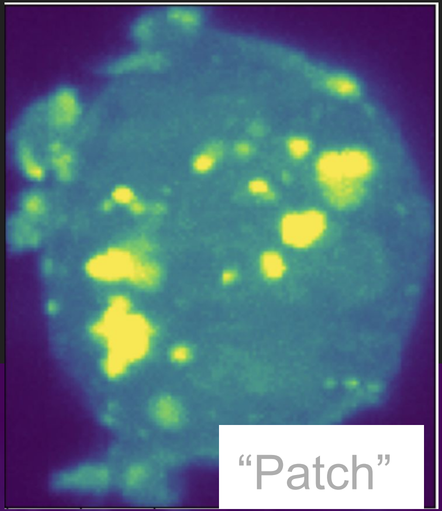




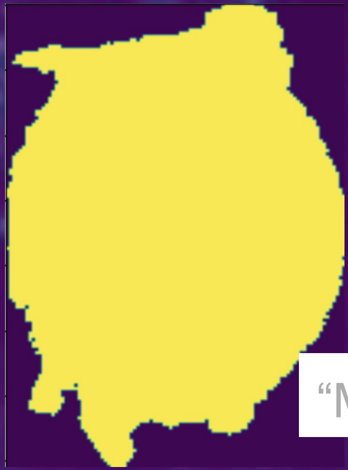


Learning Representation - LSTM Model

- Goal: Identify relevant information for Cell Movement.
- If CEN waves dictate cell movement, the images with the fluorescence (patches) will do better than the images with no Actin data (the masks)
- Training LSTM RNN on sequence prediction task using 3 different data types (“boxes”, “ masks”and “patches”
- Takes X-1 cells and predicts Xth cell
- Loss: Mean Squared Error between the Centroids

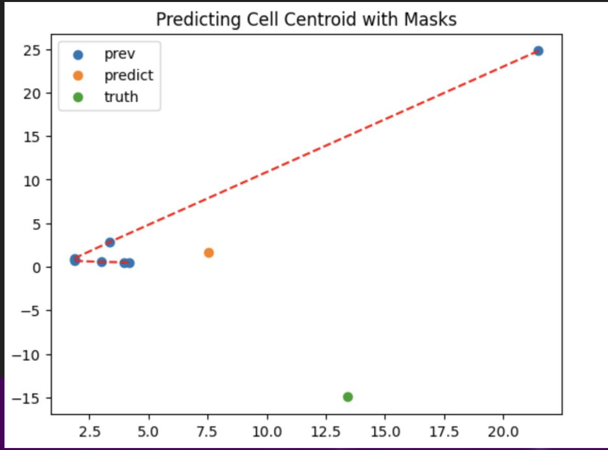

“Patch”

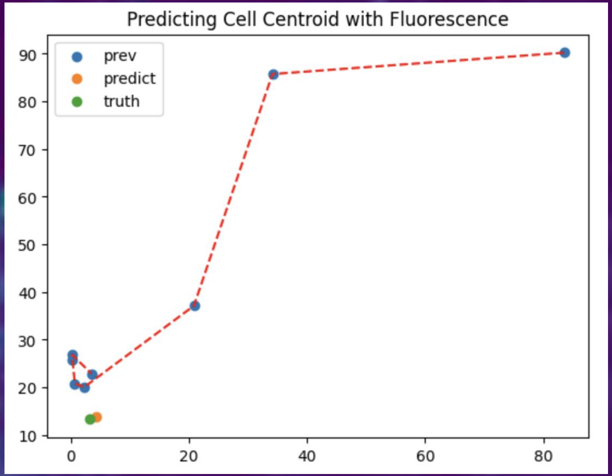

“Box”


“Mask”

LSTM Model Results

- The graph generated from input of boxes and masks leads to a highly inaccurate prediction vs the actual location of the Xth cell.
- The graph on the bottom is uses an input of boxes and fluorescence labels





Modeling Wave Dynamics

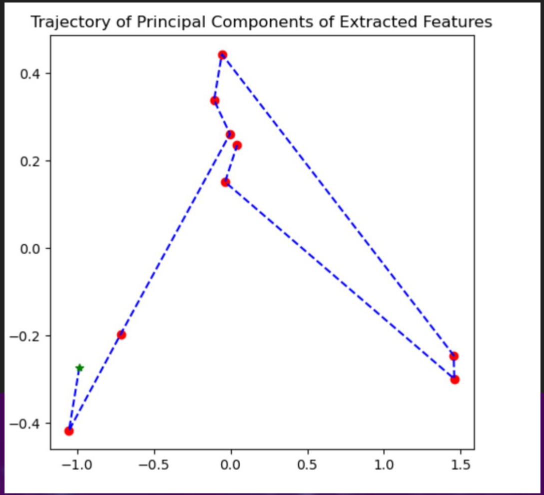
- Goal: learn unsupervised representation of cell morphologies

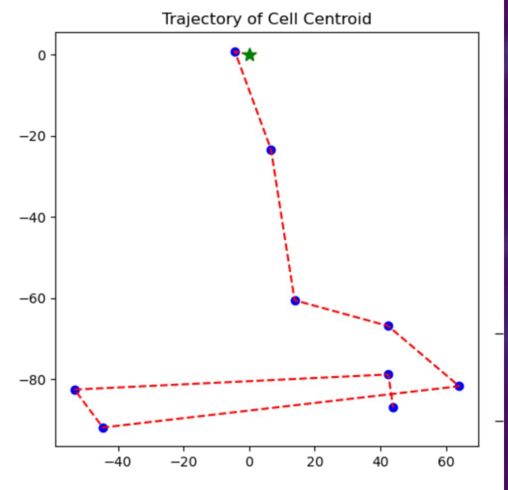
1. Zernike Moments to describe boundaries
2. Fourier Coefficients of Angular Distance to categorize radial stretching
3. Haralick Texture Features

→ Concatenated into 57 dimensional feature vector

Principal Components Provide Snapshot representation of a given cell at a given time

- Variation in PCA embeddings seems to mirror centroid trajectories, even though they are computed from completely non-overlapping data sources!
- Large jumps in position accompanied by large jumps in PCA space

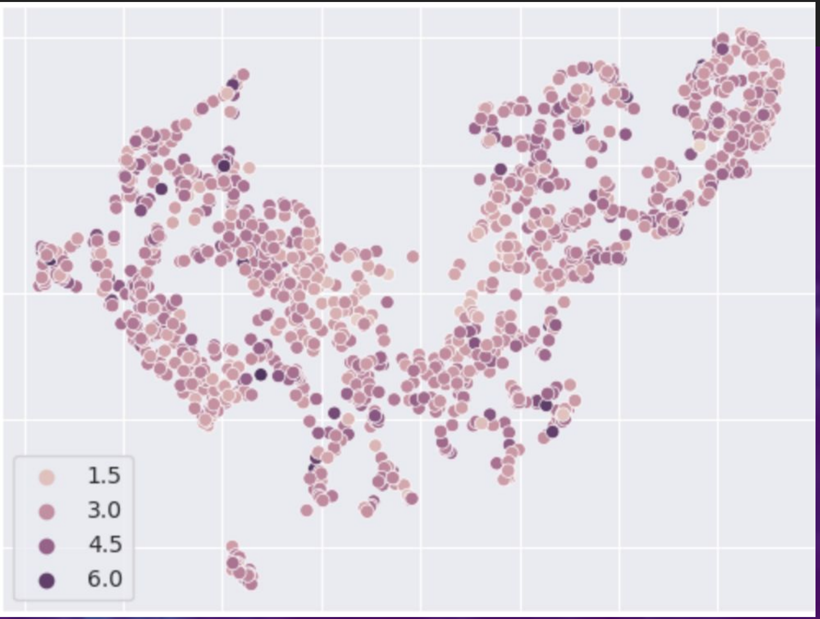




Embedding Trajectory Representations

- We can go beyond individual cell snapshots and try to obtain representations of trajectories themselves.
- Num_PCA_features x Num Timesteps → dat
  aggregated across entire cell history
- Embedded 1500 cells across videos using Uniform Manifold Approximation and Projection (UMAP)
- Next Steps: Further refine and explore semantic structure encoded by UMAP representations
- Try seeing if geometric features assist motion prediction

UMAP Embeddings



References

Unsupervised Representation Learning

1. Copperman, Jeremy, et al. "Morphodynamical cell state description via live-cell imaging trajectory embedding." *Communications Biology* 6.1 (2023): 484.
2. Alizadeh, Elaheh, et al. "TISMorph: A tool to quantify texture, irregularity and spreading of single cells." *PloS one* 14.6 (2019): e0217346.
3. McInnes, Leland, John Healy, and James Melville. "Umap: Uniform manifold approximation and projection for dimension reduction. arXiv 2018." arXiv preprint arXiv:1802.03426 10 (1802).
4. Yang, Qixin, et al. "Cortical waves mediate the cellular response to electric fields." *Elife* 11 (2022): e73198.
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