Explainable Prediction of Cell Events in Microscopic Videos

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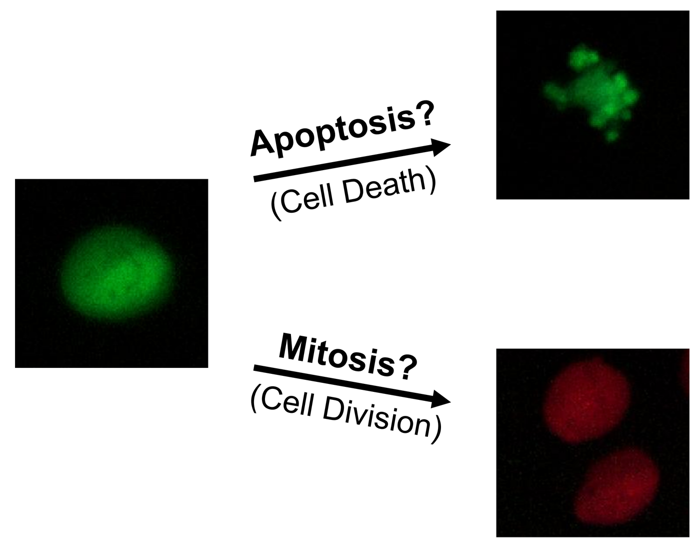
Introduction

- Time-lapse microscopy enables direct observation of dynamic cellular behaviors over time [1]
- Understanding how individual cells progress toward division or death is fundamental in biological systems
- Rules that determine individual cell fate are poorly understood [2]

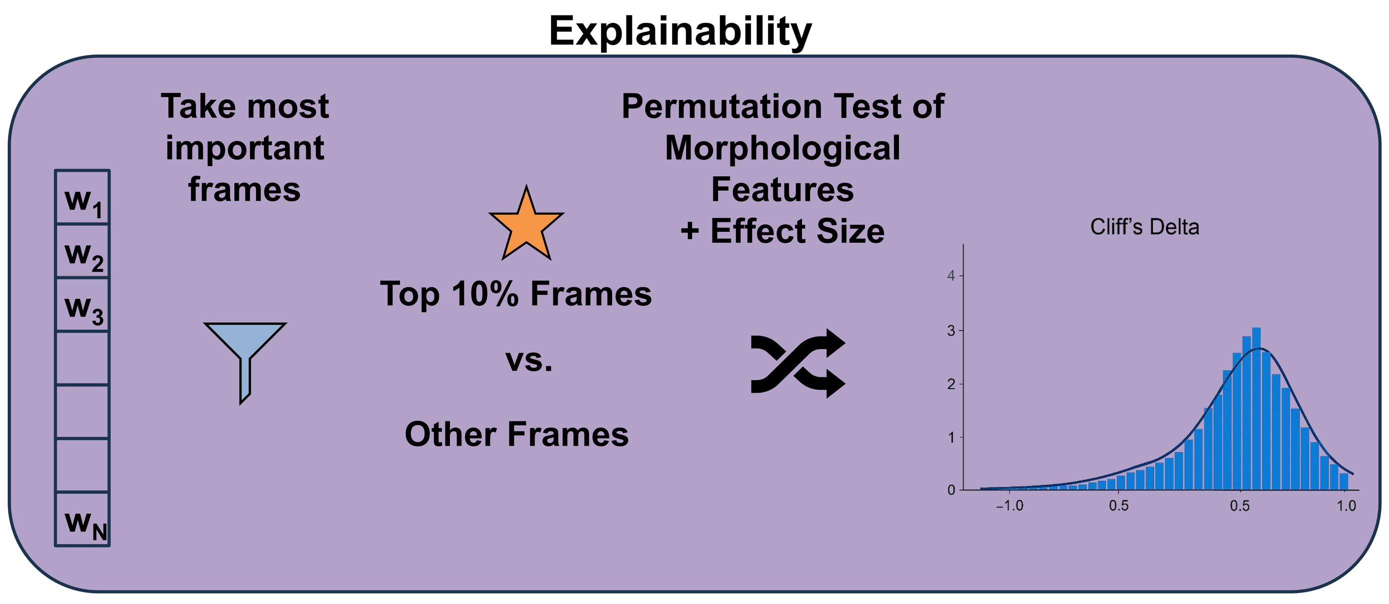
- Goal: Given a temporal sequence of a cell, can we predict whether the cell is about to divide or die?
  - If so, why?

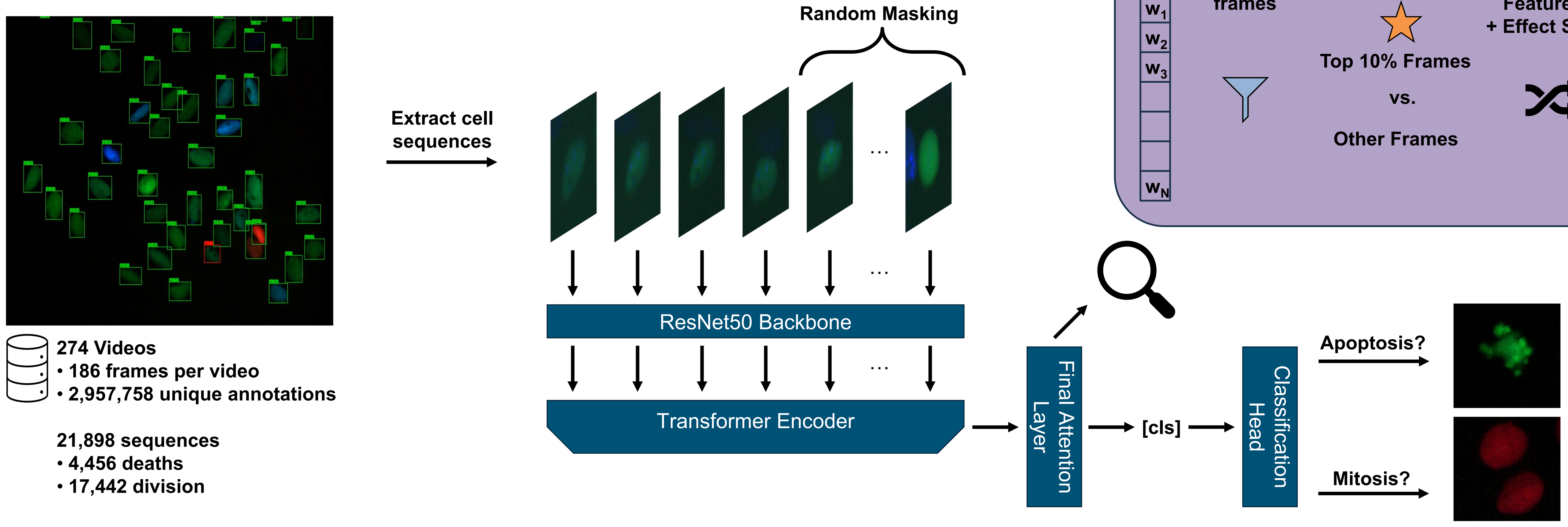
- Explainable models help identify key morphological cues driving cellular decision processes



Method

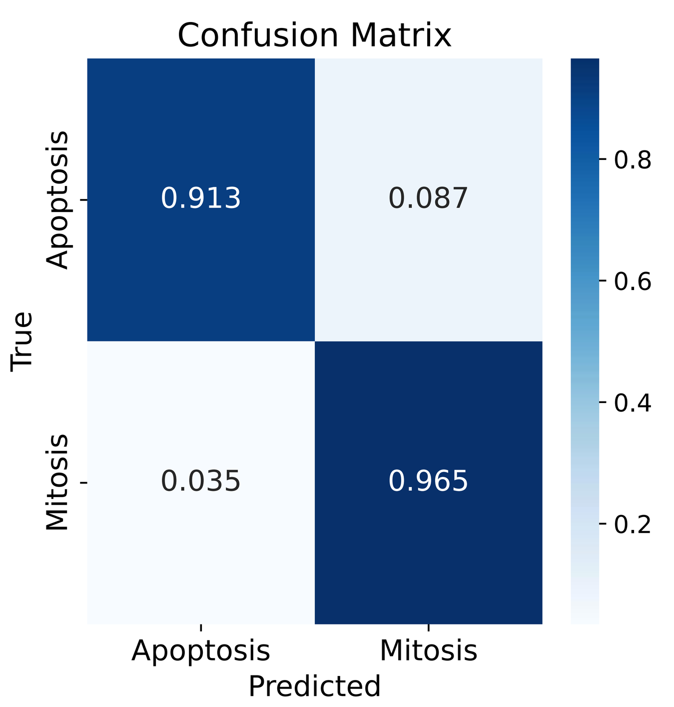
- Cell fate classification by Transformer Encoder architecture + Final Attention Layer + Classification Head
- Random masking of 10 - 50% of the sequence tail during training
- **Attention-based Explainability** framework:
  - Extract attention weights from the Final Attention Layer
  - Group frames into "Top 10%" (high attention) and "Others"
  - Perform permutation tests on morphological features to identify significant visual cues



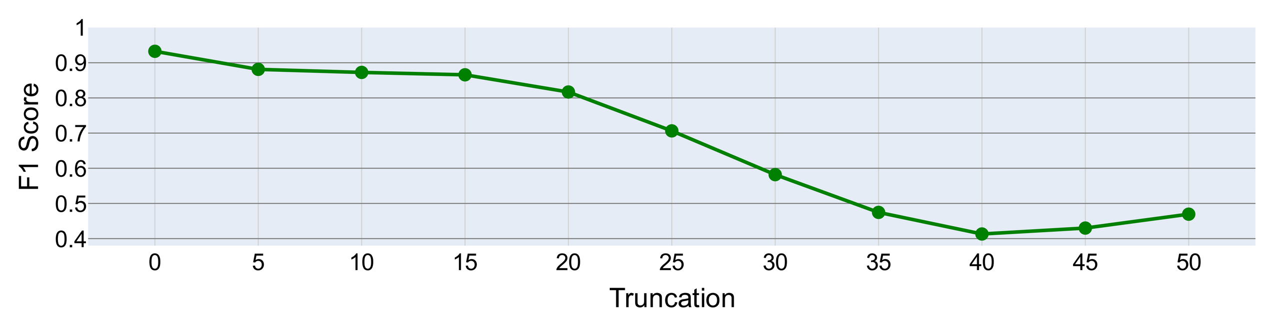


Results

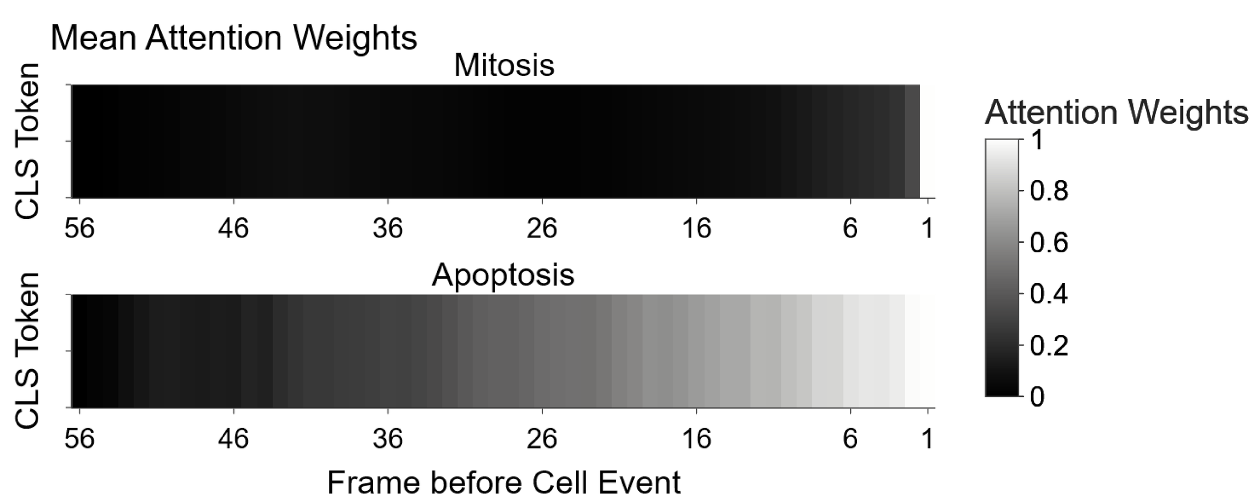
F1-Score: 0.93



How many frames can we truncate from the sequences?



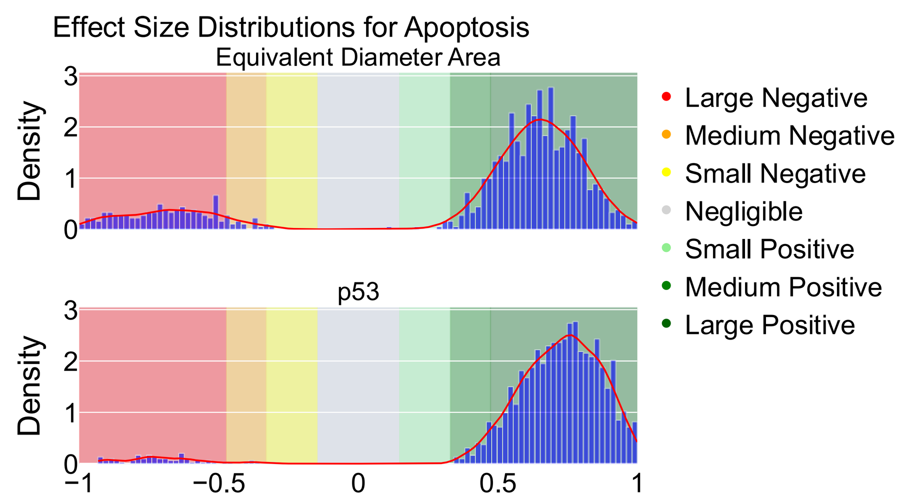
Which frames are important for classification?



Crucial Features

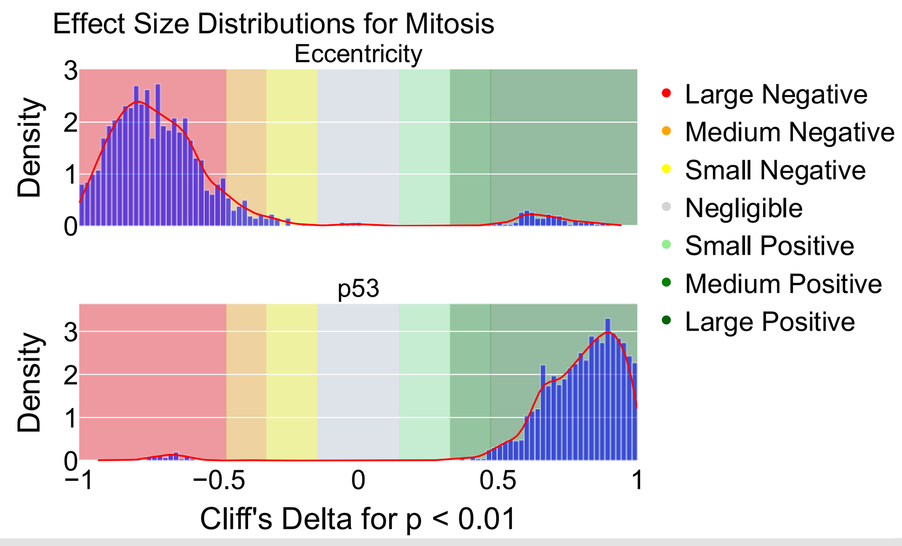
p-Value <	Ratio	Percentage
0.01	900 / 2987	30.13%
0.001	507 / 2987	16.97%
0.0001	225 / 2987	7.53%

p-Value <	Ratio	Percentage
0.01	1514 / 2984	50.74%
0.001	1102 / 2984	36.93%
0.0001	685 / 2984	22.96%



p-Value <	Ratio	Percentage
0.01	1332 / 5415	24.60%
0.001	665 / 5415	12.28%
0.0001	294 / 5415	5.43%

p-Value <	Ratio	Percentage
0.01	1514 / 2984	50.74%
0.001	1102 / 2984	36.93%
0.0001	685 / 2984	22.96%



Conclusion

- Reliable cell fate prediction, even when truncating up to 20 frames
- Apoptosis
  - Focus already on earlier frames
  - Features related to cell size are most crucial: Area, Equivalent Diameter Area
- Mitosis
  - Very last frames most important
  - Cell shape features are most crucial: Eccentricity, Circularity
- Beyond morphology, the cell fitness reporter p53 provides a distinctive marker of cell fate

References

[1] Granada, Adrián E., et al. "The effects of proliferation status and cell cycle phase on the responses of single cells to chemotherapy." Molecular Biology of the Cell (2020)
[2] Soelistyo, Christopher J., et al. "Learning biophysical determinants of cell fate with deep neural networks.", Nature machine intelligence (2022)