Cell Segmentation, Tracking, and Mitosis Detection Using Temporal Context

Presentation by Warren Cheung for CMPT880

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Overview

What Does This Paper Address

- segmentation of cells
- 2D + time
- Identify cell clusters and cell division (mitosis)

Reasons

- automated system
- *LSDCAS*: Large-Scale Digital Cell Analysis System
- want to apply to cancerous cells — abnormal cells
  - variable cell shape
  - lots of cell contact
  - weak cell boundaries

Past Methods — Simple Image Segmentations

- using only image information
- techniques: thresholding, watershed
- give poor approximations of cell shape
- often need post-processing
- often do not produce closed shapes

Past Methods — Model-based

- exploit knowledge of cell shape
- techniques: active contours, *level sets*
- give closed boundaries
- interactive initialisation
- can allow tracking of cells through time (use prior time step to initialise next time step)

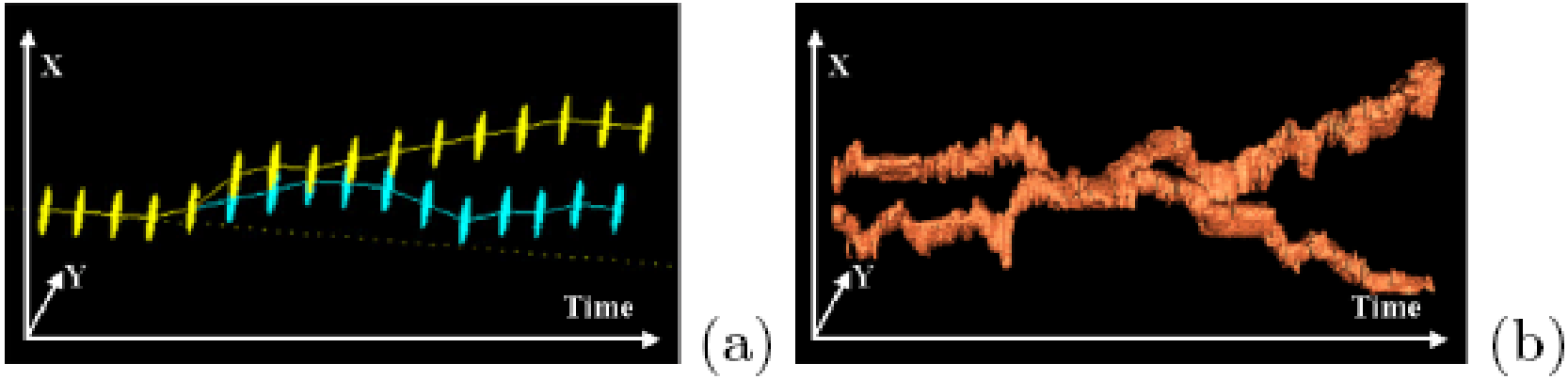
Past Methods — Pattern Recognition

- use machine learning (e.g. neural networks, genetic algorithms)
- distinguish cell from background — classification
- need to define rules and/or perform training

Claim to Fame

- high cell density — lots of contacts
- utilise temporal context
- can pick out abnormal cells

Cell Trajectories



- find space-time where cells are present
- Initialise using Image Boundaries
- Improve using Fast Marching method (front only moves in one direction) to get close to cell boundary
- Use Narrow Band Level Set on 2D+time image to refine image based on intensity + local variance

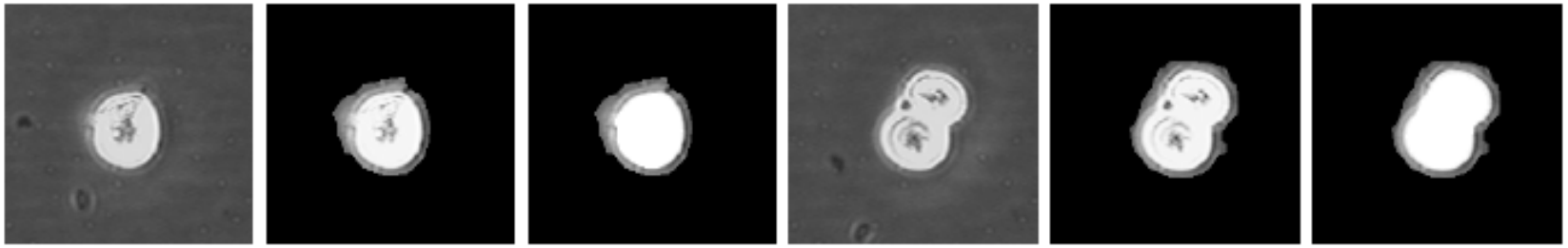
Cell Trajectories II

- Have a edge enhancement step (prevent bleeding across weak boundaries)
- get eigenvalues $\lambda_{\pm}$ (maximal and minimal change in the image) in Riemannian geometry

$$\lambda_{\pm} = \frac{s_{xx} + s_{yy} \pm \sqrt{(s_{xx} - s_{yy})^2 + 4s_{xy}}}{2}$$

- Force on the moving front is $F = e^{\rho*(\lambda_+ - \lambda_-)}$

Cell Mitosis

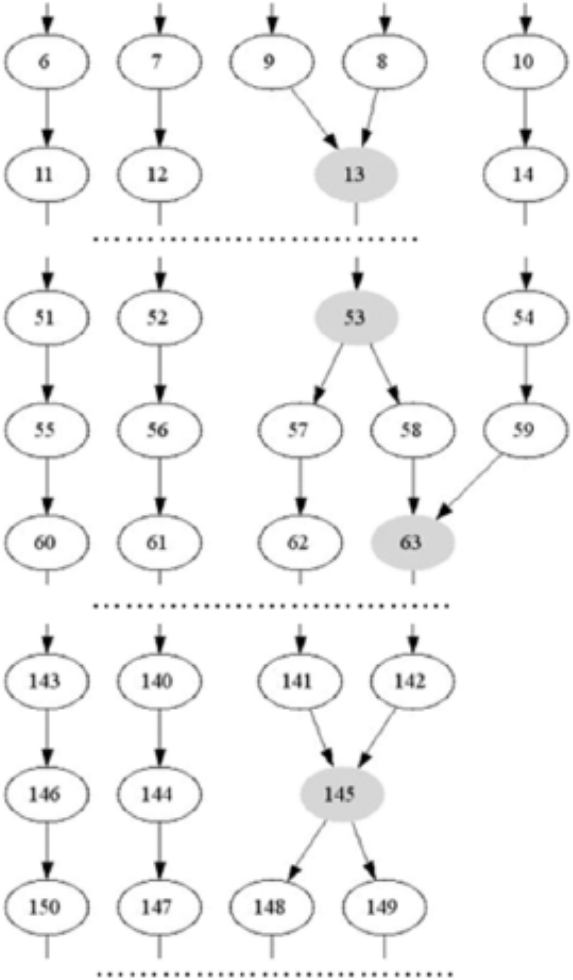


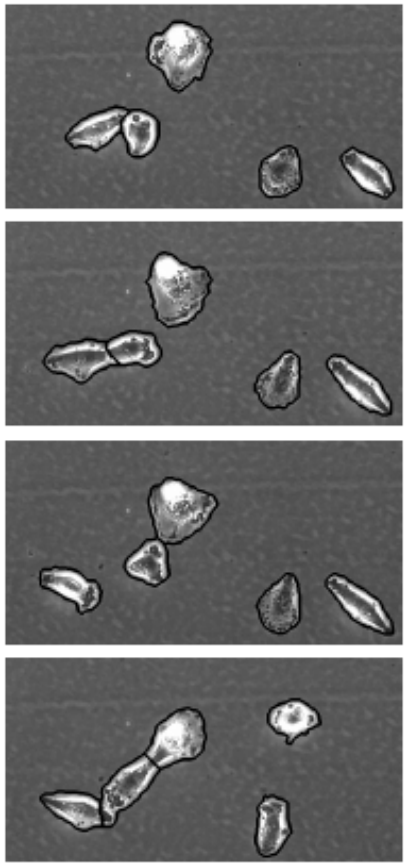
- detect cell division (change in number of cells)
- use thresholding to find possible regions where mitosis occurs
  - mitotic cells tend to be brighter than normal cells
- use Level Set method to get a smooth boundary
- identify mitosis
  - area and perimeter increases (increase in size)
  - circularity decreases (deformation)
  - average intensity remains the same (not caused by cell motion)
- use a trained classifier

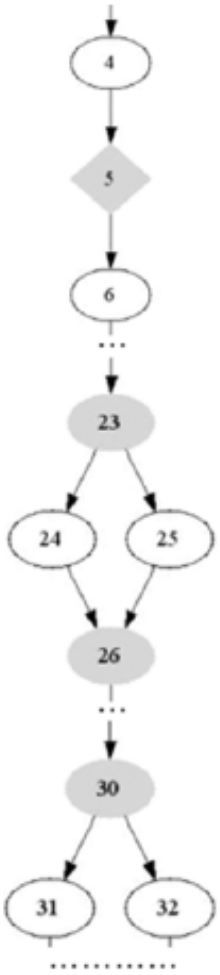
Cell Segmentation

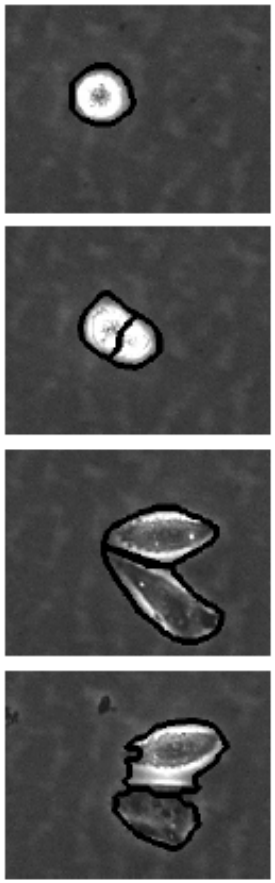
- trajectories described by *connection graph*
- use identified mitosis events
- track the evolution of changes in contact between cells/cell clusters
- process from known to unknown — use previously processed, neighbouring nodes to help segment current node
- use watershed segmentation (implemented via falling rain)
- mitosis simply divides the trajectory — cell count is constant before and after mitosis

Example of Segmentation

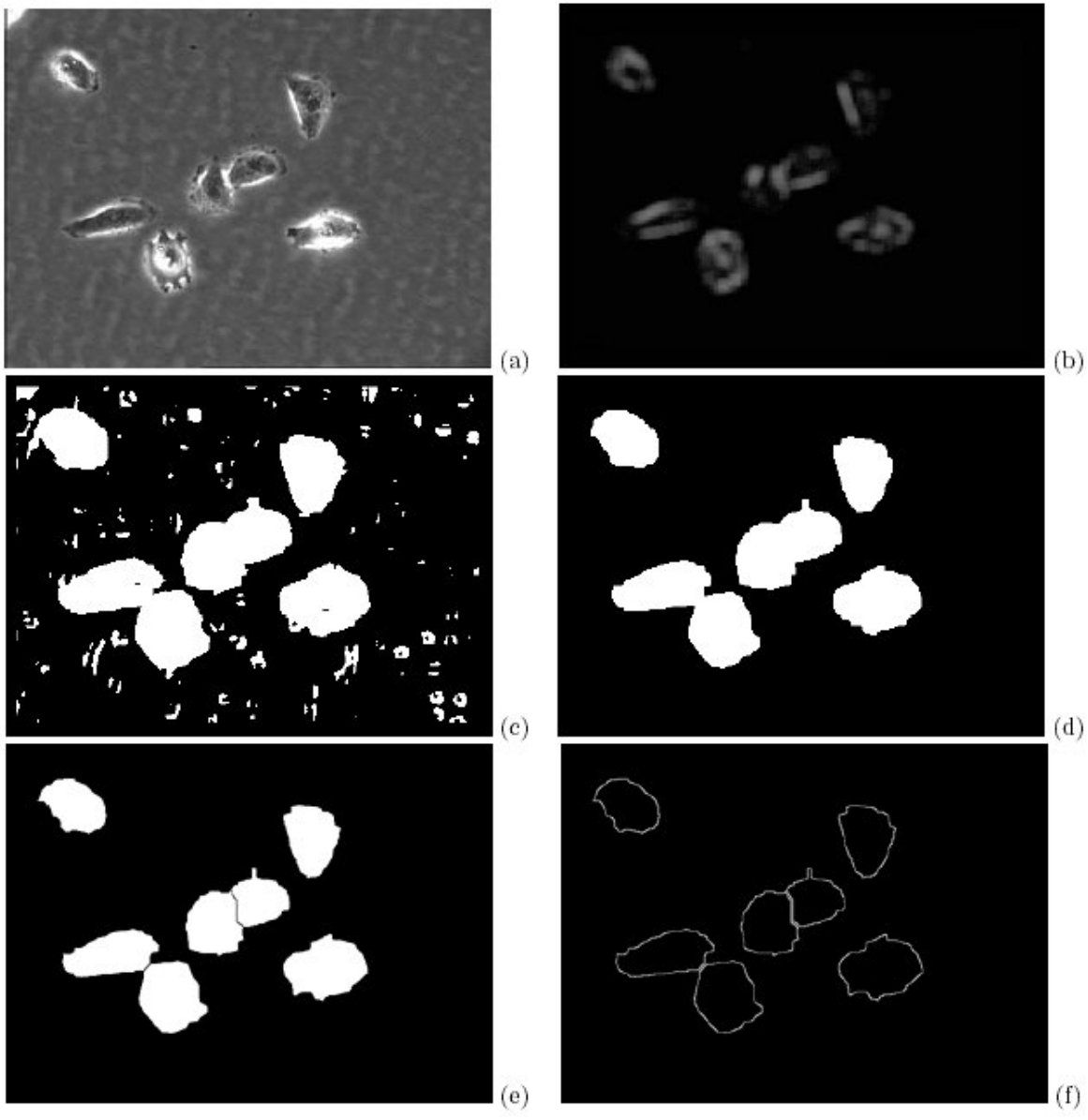








Summary of Segmentation Steps



Validation

- tested on evolution of U87-MG
- "gold standard" validation — manually segmented cells
- positioning — distance to closest "true" boundary
  - signed: inside vs. outside true contour
- Area of segmented cells
  - Kappa Index: $KI = 2 \times \frac{A \cap M}{A + M}$
  - overlap: $overlap = \frac{A \cap M}{A \cup M}$

Results

- 3368 2D+time frames
- 6654 cells
- All 26 mitosis events correctly identified
Mean positioning error	pixels	μm
absolute	4.2 ± 2.8	2.6 ± 1.7
signed	2.6 ± 3.4	1.6 ± 2.1
- Area error: $KI = 0.84 \pm 0.09$, $overlap = 0.74 \pm 0.12$

Conclusions

- extract both cells and "pedigree"
- exploit temporal information
- plan to incorporate more advanced (HMM-based) mitosis detection
  - abnormal cell divisions
  - interrupted cell division
  - cell death
- Almost available at `http://lsdcas.engineering.uiowa.edu/` under GPL