

Spatiotemporal Cell Population Tracking & Lineage Construction

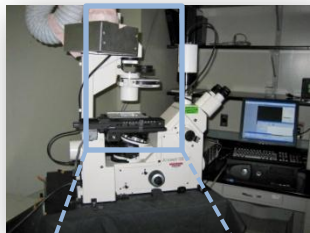
Kang Li, Takeo Kanade

Carnegie Mellon University

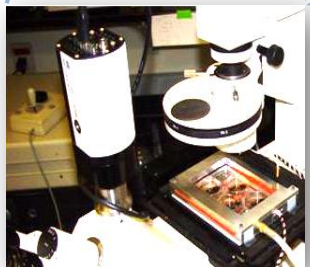
Mei Chen

Intel Research Pittsburgh

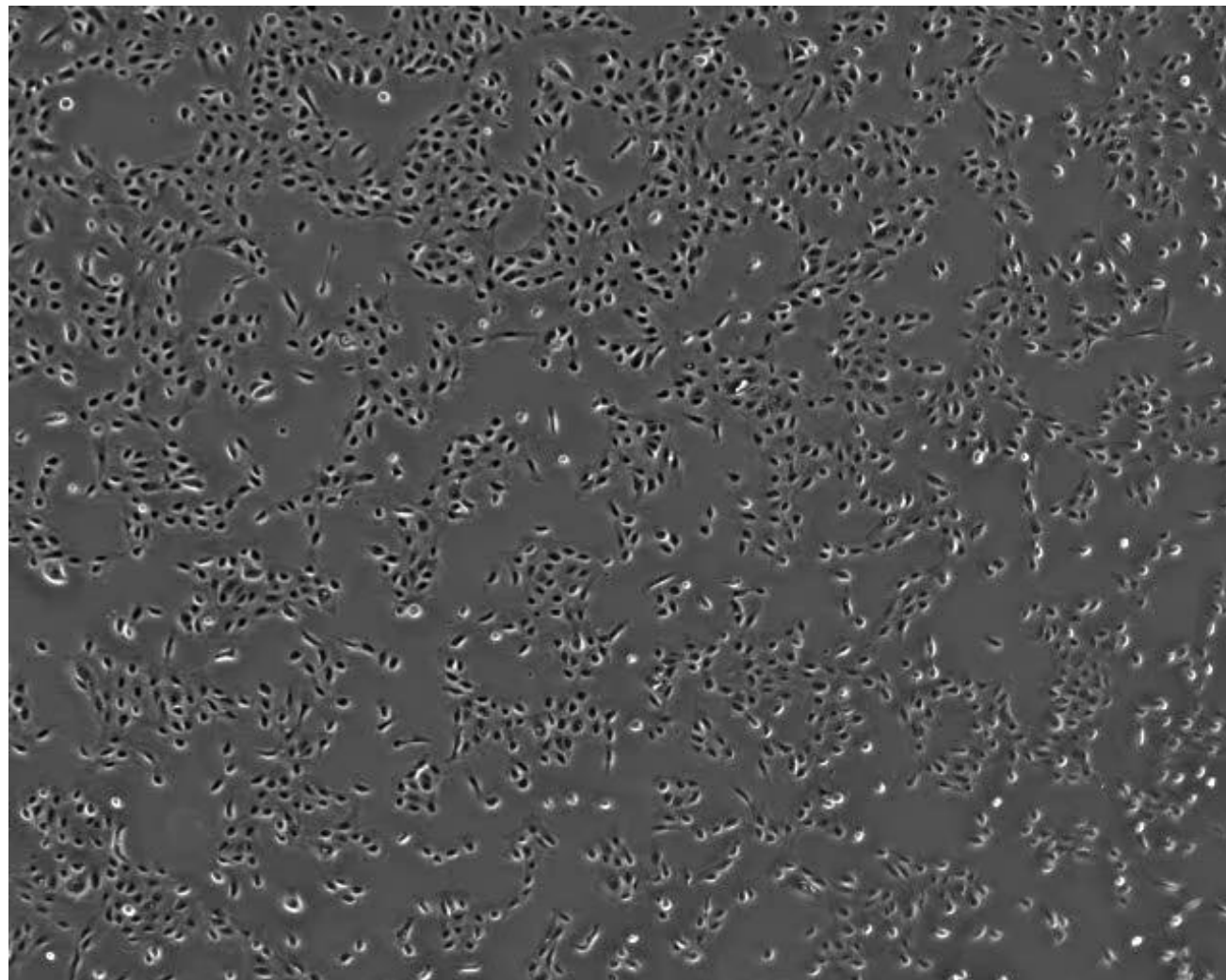
Cell Population Tracking



Phase-Contrast
Microscope

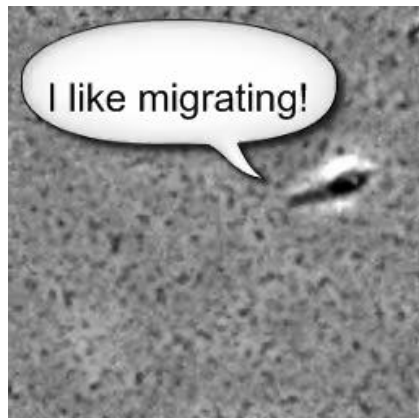


CCD Camera

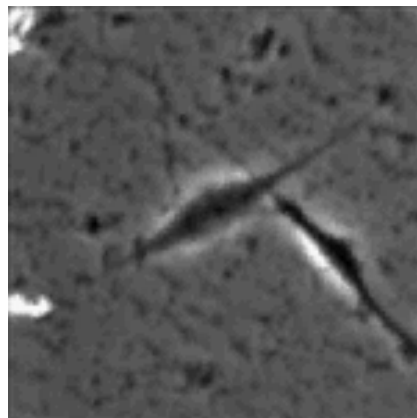


Human Amnion Epithelial (AE) Stem Cells in Growth Environment
1280×1024-Pixel Resolution, 10 Minutes/Frame, 42.5 hours

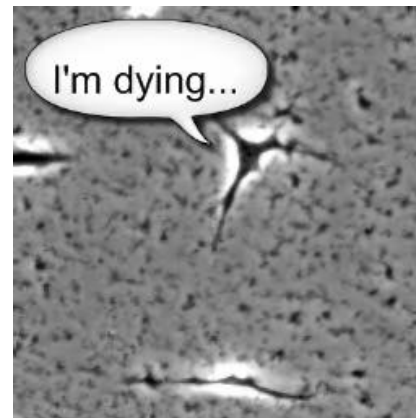
Migration, Mitosis, and Apoptosis



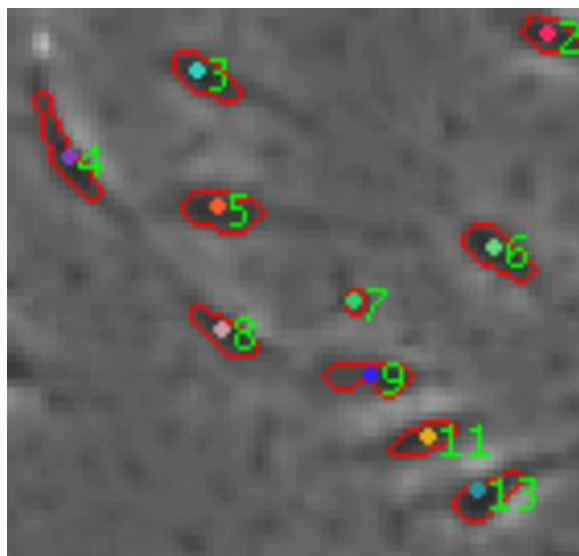
Migration



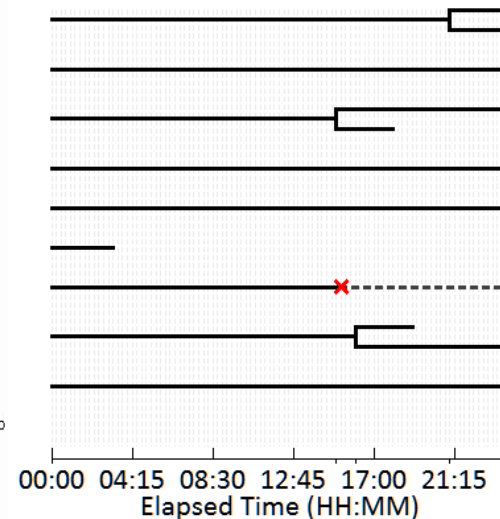
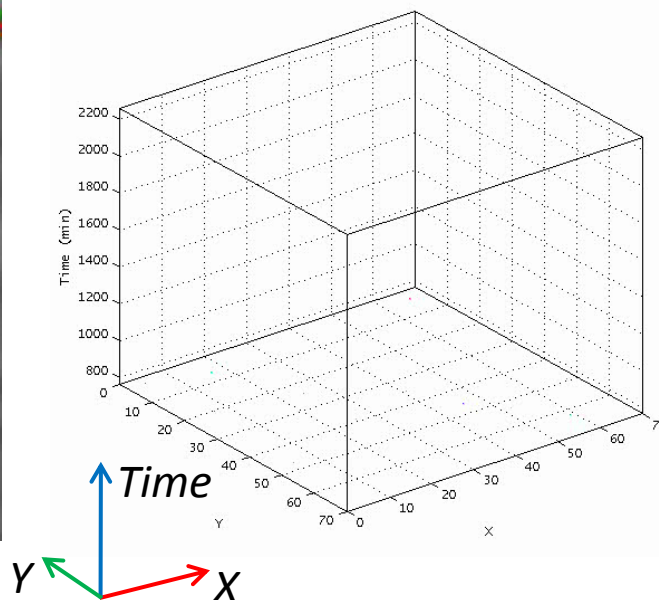
Mitosis



Apoptosis

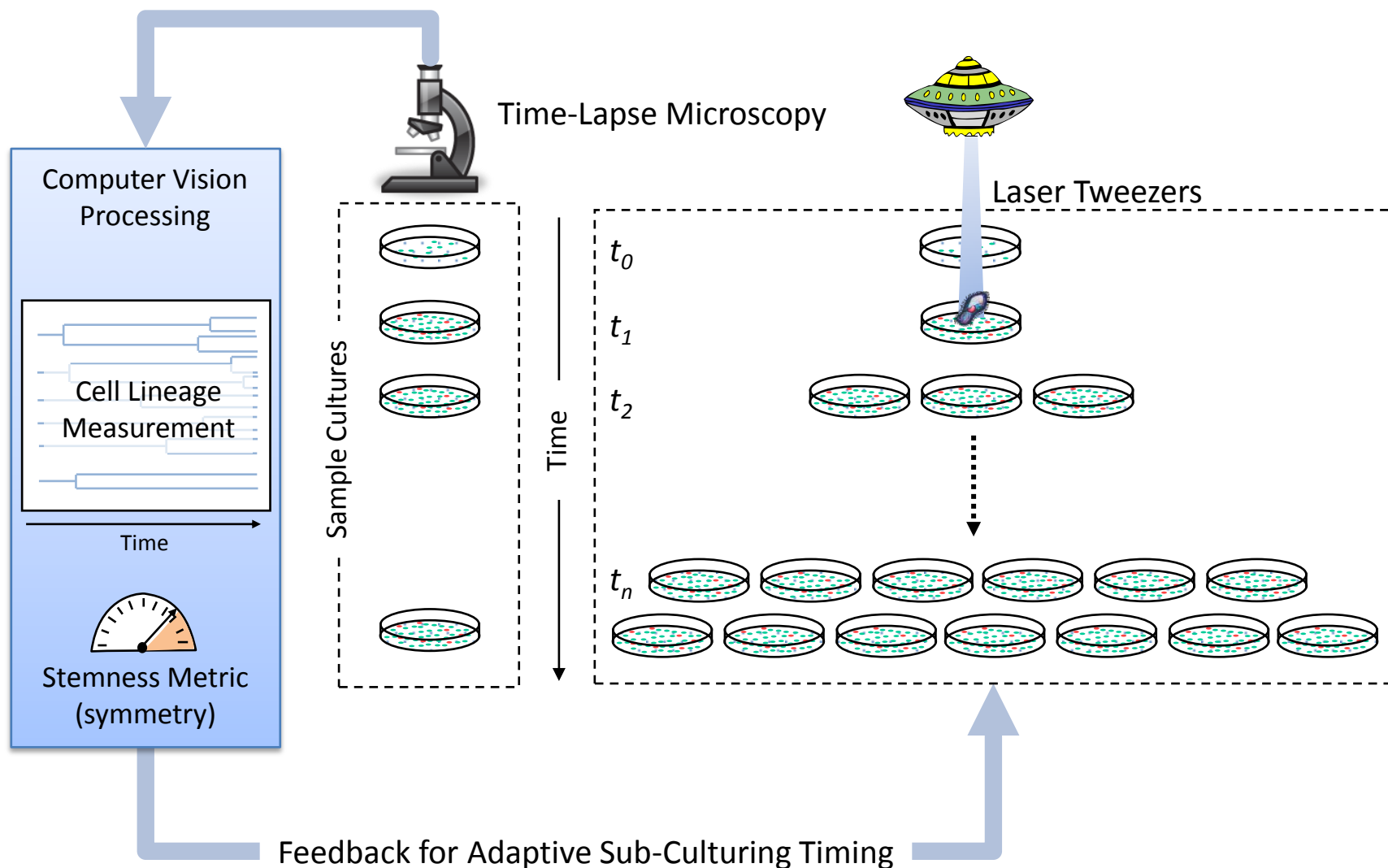


MG-63 Cells

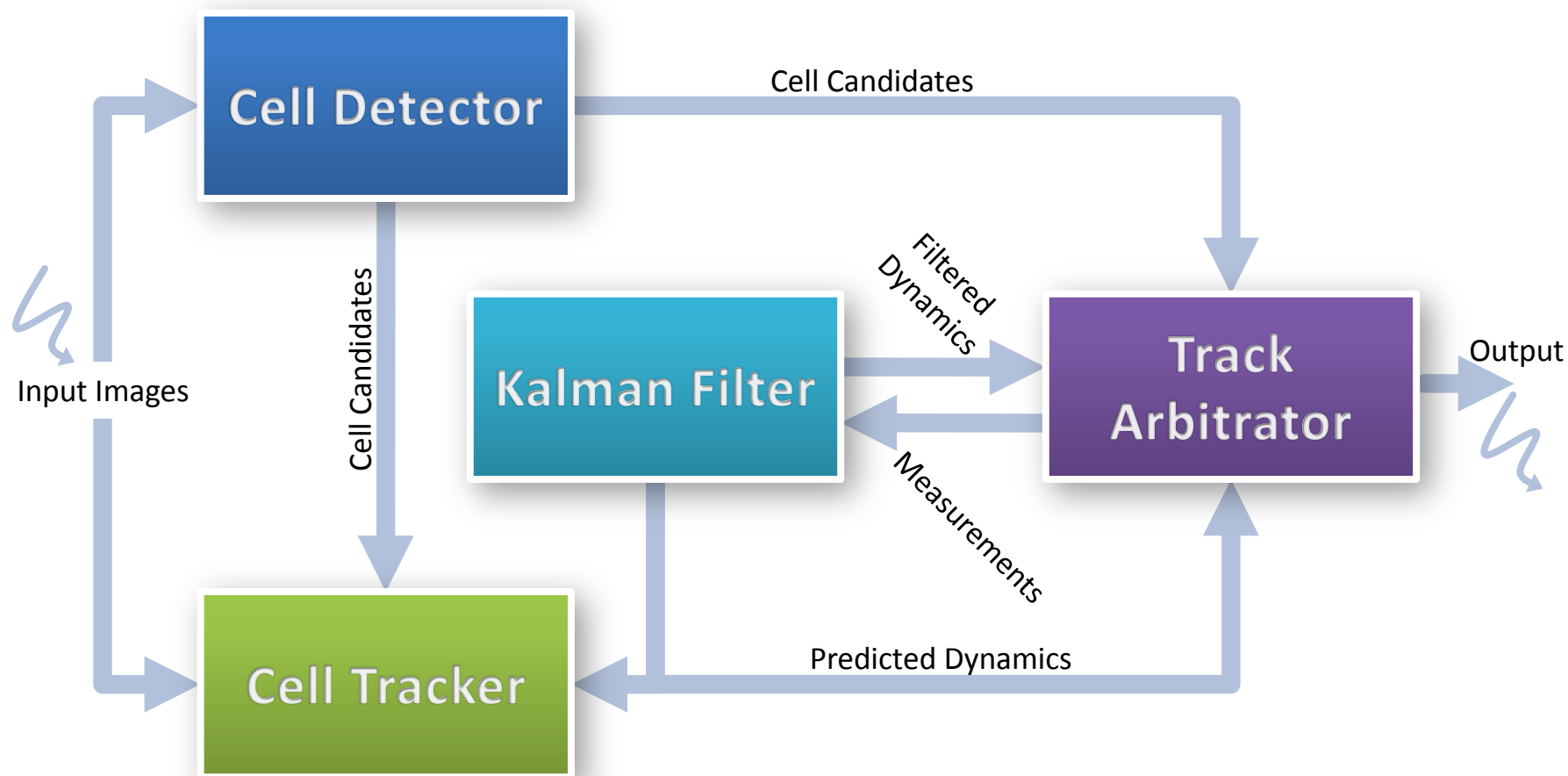


Lineage Trees

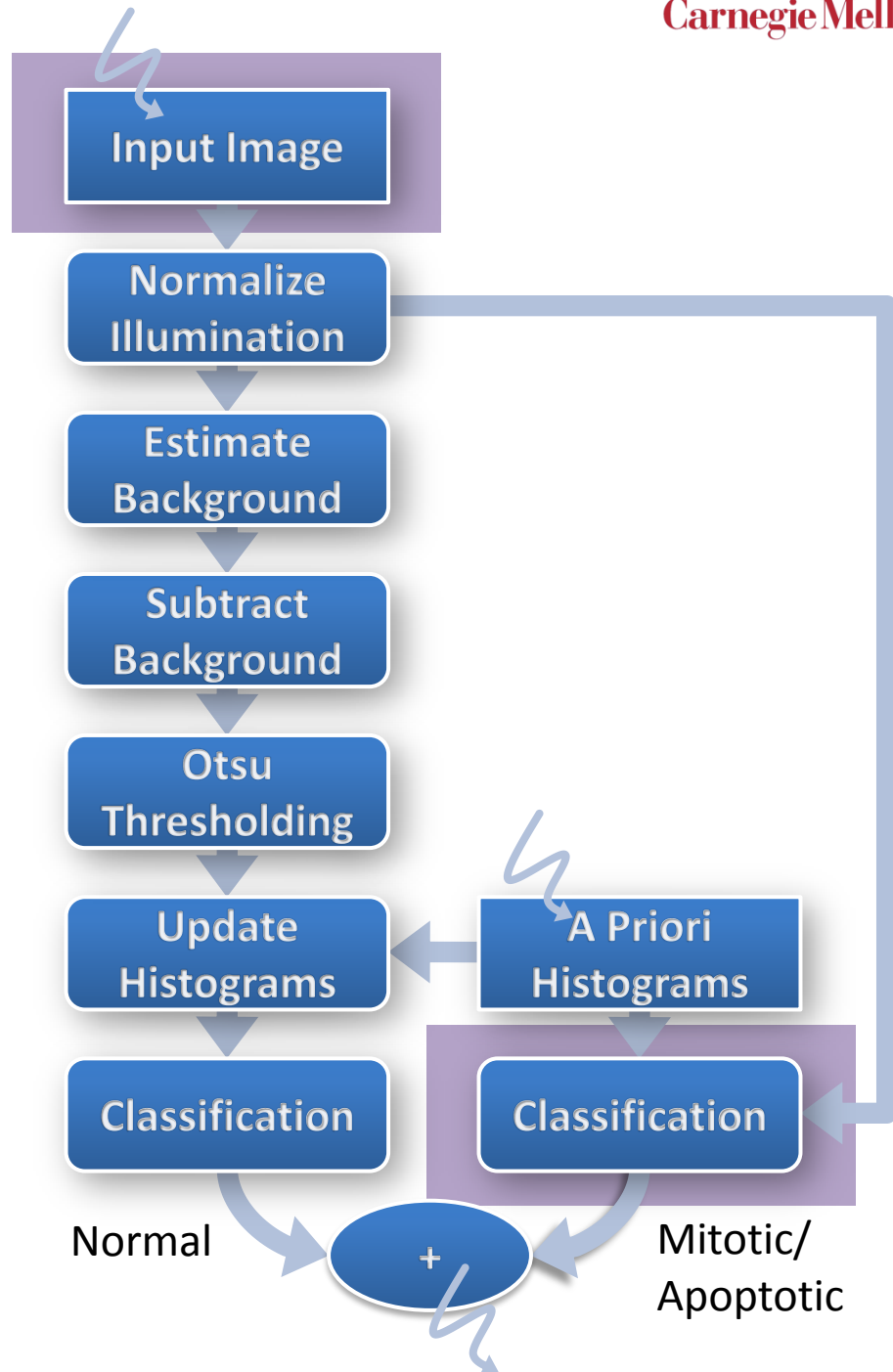
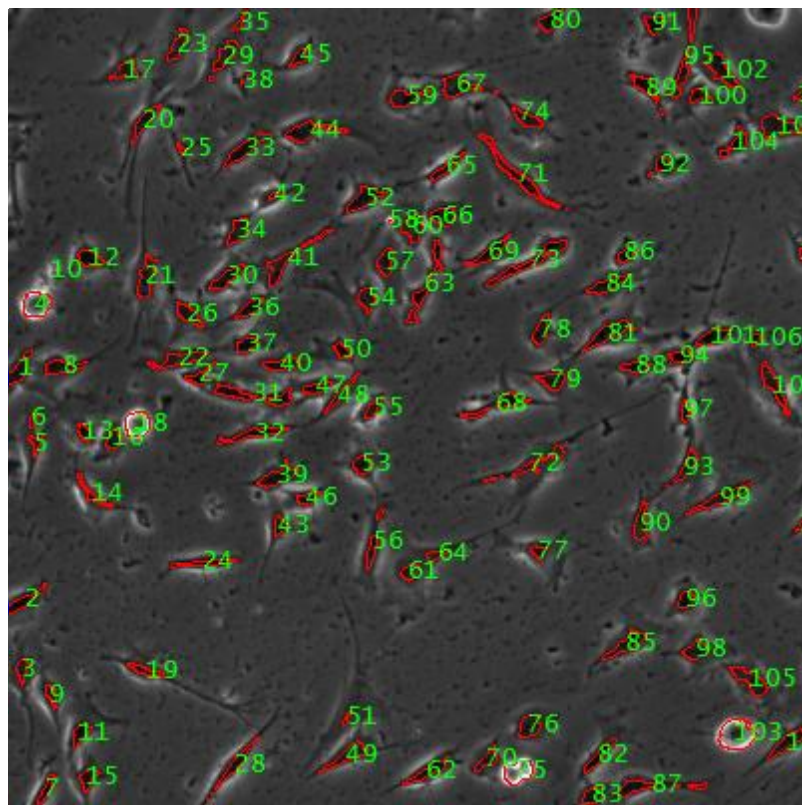
Stem Cell Culture Optimization



Tracking System Overview

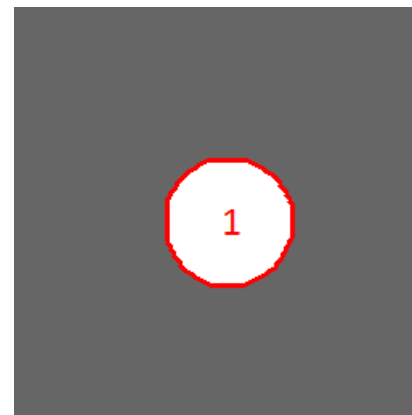
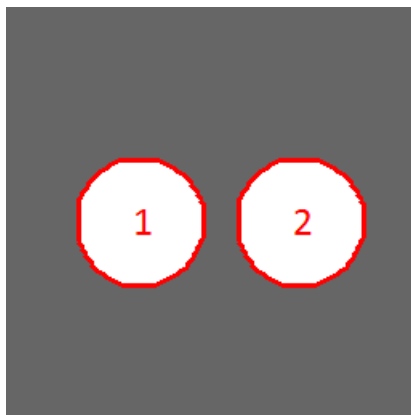


Cell Detector



Real-Time Level Set Cell Tracker

- Evolve level set to minimize three “energy” terms:
 - Region competition term
 - Geodesic active contour term
 - Cell dynamics prediction term (from Kalman filter)
- A region-labeling function identifies each unique cell region
- Cell regions with different IDs not allowed to “merge”

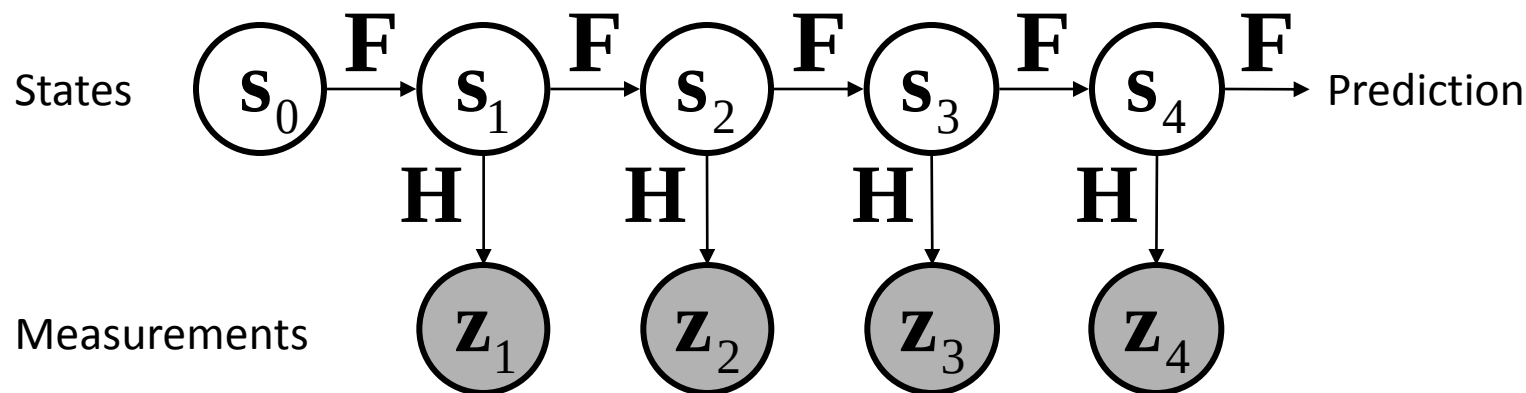


- Fast implementation [Y. Shi et al, 2005]

Kalman Filter

$$\mathbf{s}_k = \mathbf{F}\mathbf{s}_{k-1} + \mathbf{v}_{k-1}$$

$$\mathbf{z}_k = \mathbf{H}\mathbf{s}_{k-1} + \mathbf{w}_{k-1}$$



Track Arbitrator

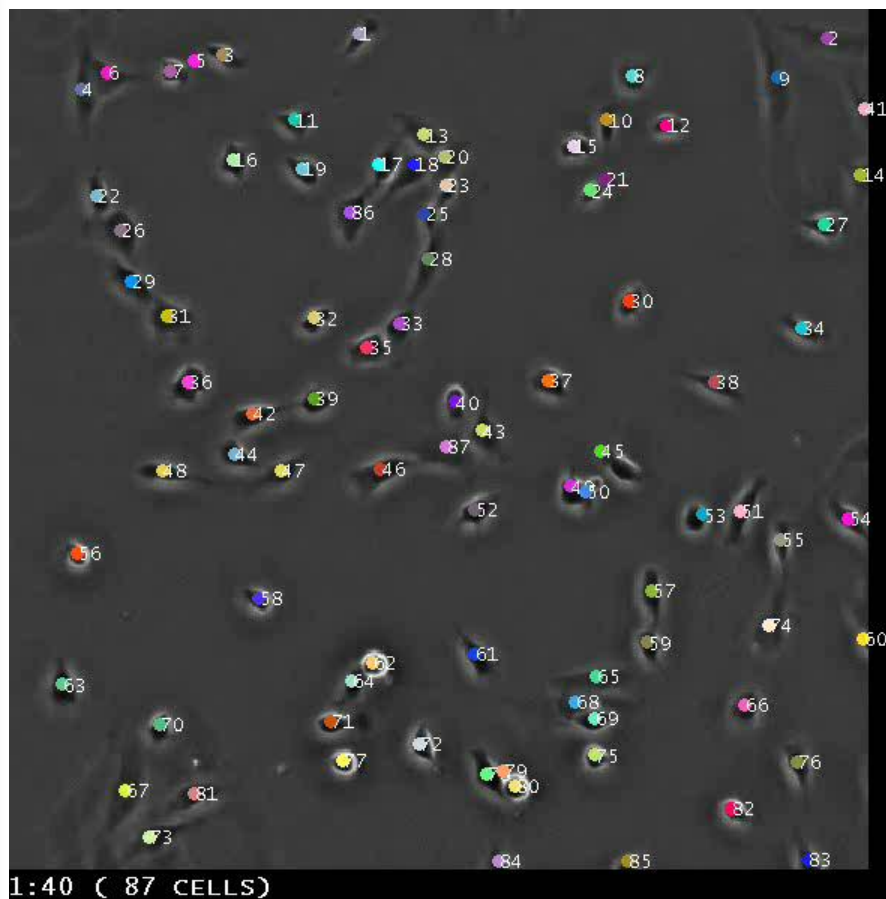
- Assign IDs to entered cells
- Establish parent-child lineages
- Terminate trajectories of departed cells
- Label mitotic, apoptotic & dead cells
- Recover trajectories of lost cells
 - Linear assignment algorithm
[S. Belongie et al, PAMI 2002]
[R. Jonker and A. Volgenant, 1987]
 - Frame-by-frame

Algorithm 1: TrackArbitration

```

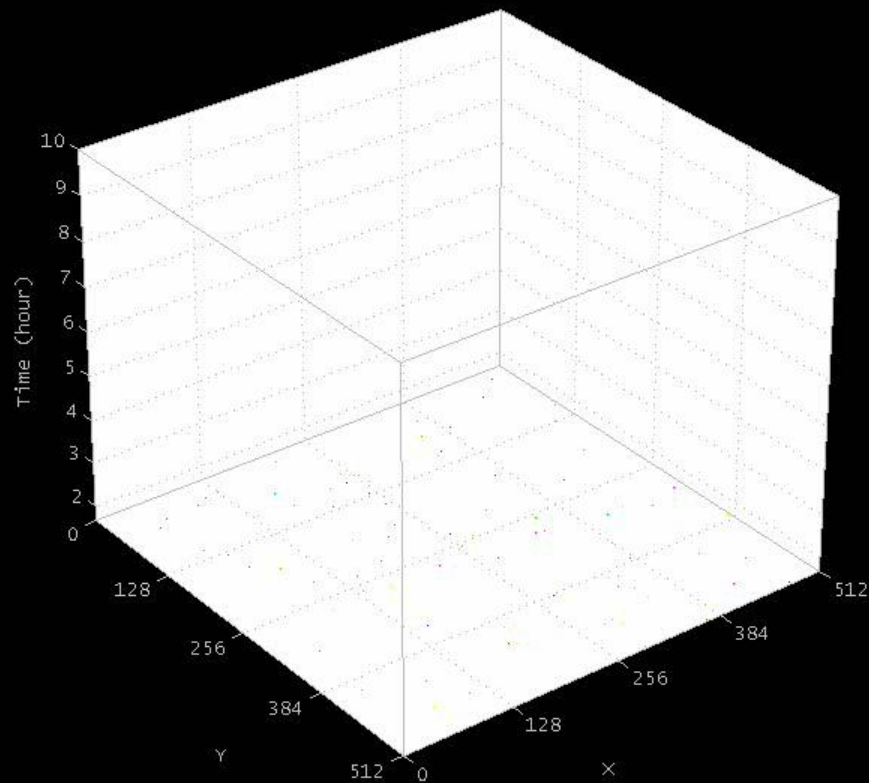
 $\mathbf{N}_{\text{lost}}, \Omega_{\text{no label}} \leftarrow \emptyset; \Omega_0 \leftarrow \{\mathbf{x} | \psi^k(\mathbf{x}) = 0\}$ 
1 foreach cell candidate  $\omega \in \zeta^k$  do
  | if  $\omega \in \Omega_0$  then Add  $\omega$  to  $\Omega_{\text{no label}}$ 
2 foreach  $n \in \mathbf{N}^{k-1}$  do
  |  $\Omega_n \leftarrow \{\mathbf{x} | \psi^k(\mathbf{x}) = n\}$ 
  | if  $\Omega_n = \emptyset$  then Add  $n$  to  $\mathbf{N}_{\text{lost}}$ 
3 else if  $\Omega_n$  is divided and detected mitotic then
  | Set status of cell  $n$  to mitotic
  | foreach connected subregion  $\omega \in \Omega_n$  do
  | | Assign a new unique label  $n_d$  to  $\omega$ 
  | | Set the parent of  $\omega$  to  $n$ 
  | | AddBranch( $n, n_d$ )
4 else if detected apoptotic then
  | Set status to dead and UpdateBranch( $n$ )
  | else UpdateBranch( $n$ )
5 Match cell candidates in  $\Omega_{\text{no label}}$  with labels in  $\mathbf{N}_{\text{lost}}$ 
6 foreach  $n \in \mathbf{N}_{\text{lost}}$  with no match in  $\Omega_{\text{no label}}$  do
  | if cell  $n$  is moving out of the border then
  | | Set status to departed and Terminate( $n$ )
  | else
  | | Set status of cell  $n$  to maybe-dead
  | | if the status continues for  $L$  frames then
  | | | Set status to dead and Terminate( $n$ )
7
8 foreach  $\omega \in \Omega_{\text{no label}}$  do
  | if  $\omega$  is labeled  $n$  then UpdateBranch( $n$ )
  | else if  $\omega$  is from the image border then
  | | Assign a new unique label  $n_n$  to  $\omega$ 
  | | AddTree( $n_d$ )
  | else Ignore
  
```

Tracking Example



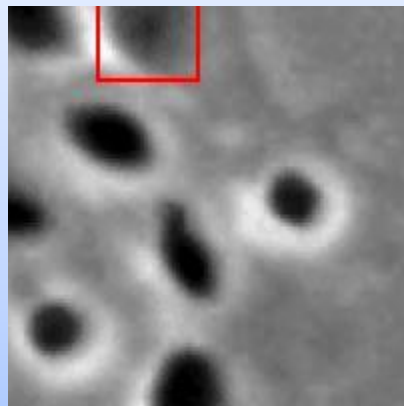
MG-63 Cells Imaged @ 4 Minutes/Frame

Tracking Accuracy: 88.4%

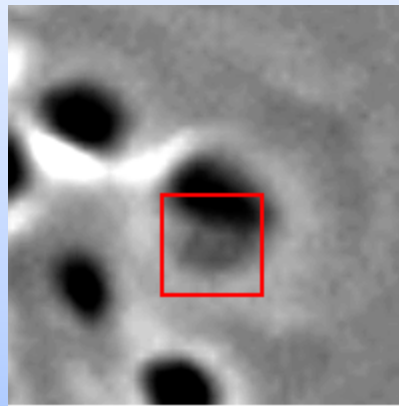


[K. Li et al, MMBIA 2006]

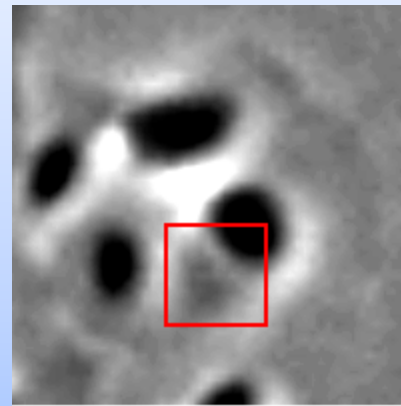
Example of Unsuccessful Tracking



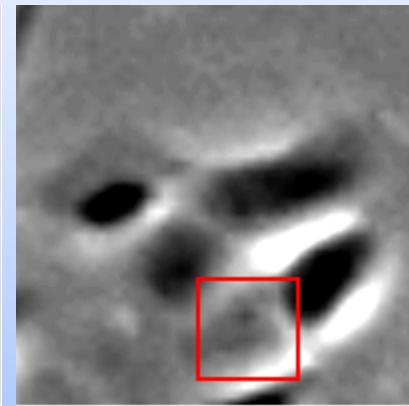
Original



Frame #33



Frame #36



Frame #46



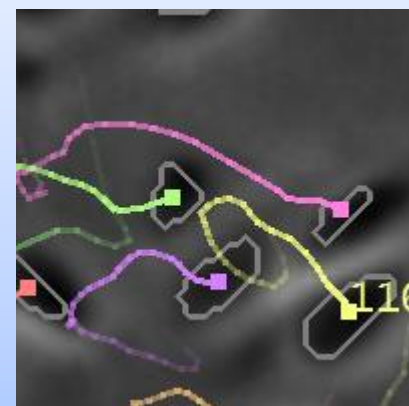
Result



Frame #33

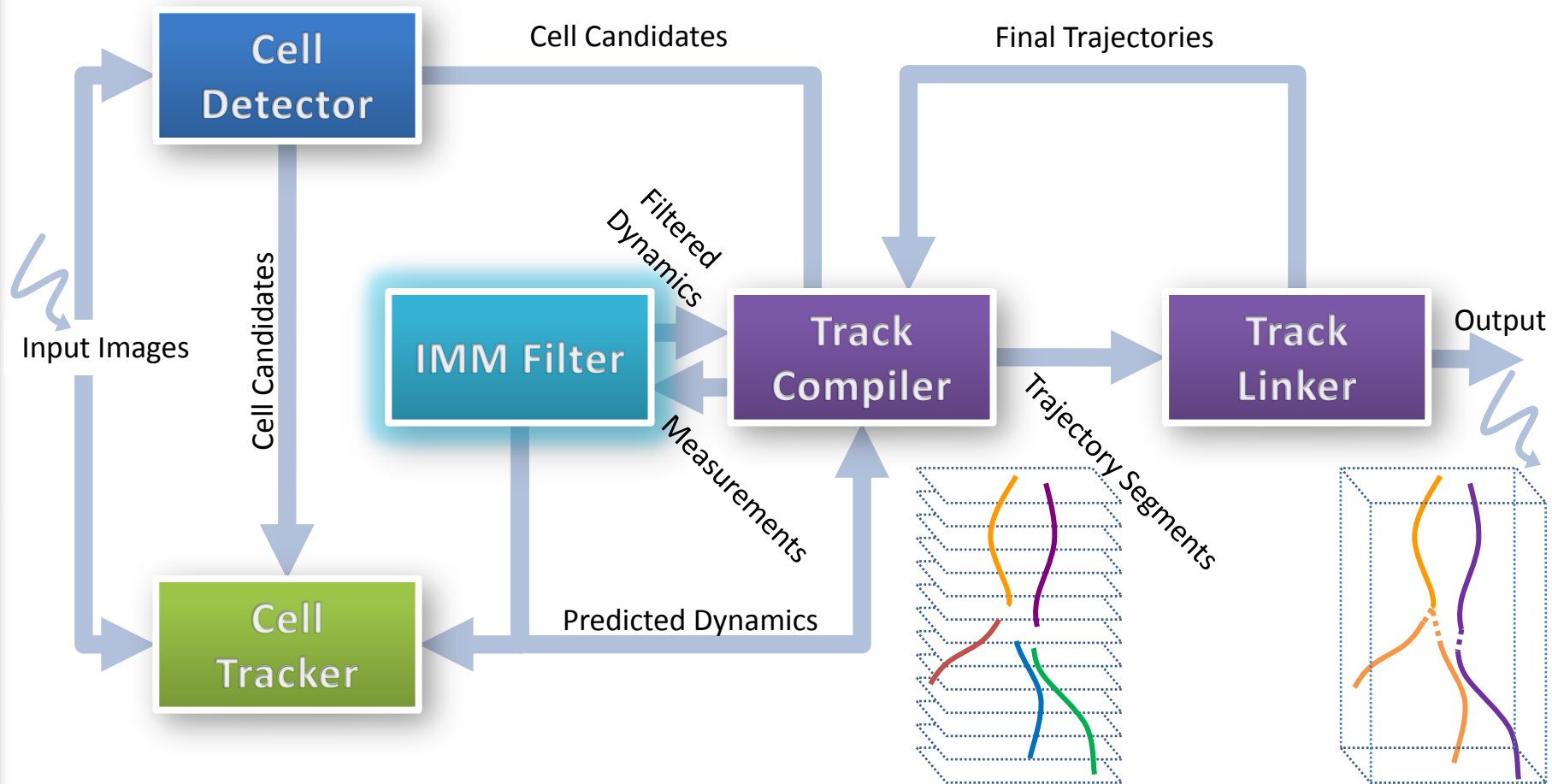


Frame #36



Frame #46

Tracking System 2.0



Multiple-Models Motion Filter

$$\mathbf{s}_k = \mathbf{F}^i \mathbf{s}_{k-1} + \mathbf{v}^i_{k-1}$$

$$\mathbf{z}_k = \mathbf{H} \mathbf{s}_{k-1} + \mathbf{w}_{k-1}$$

$$\mathbf{F}^1 = \begin{bmatrix} \mathbf{I} & 0 & 0 \\ \mathbf{I} & 0 & 0 \\ 0 & \mathbf{I} & 0 \end{bmatrix}$$

random walk

Interactive Multiple-Models (IMM) Filter

[Blom, 1984]

[Genovesio et al, 2006]

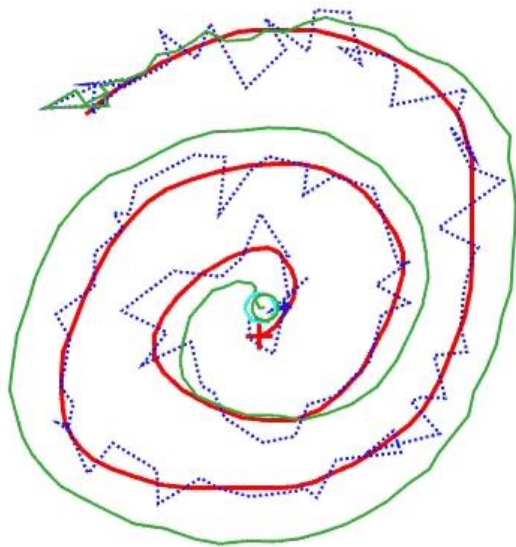
$$\mathbf{F}^2 = \begin{bmatrix} 2\mathbf{I} & -\mathbf{I} & 0 \\ \mathbf{I} & 0 & 0 \\ 0 & \mathbf{I} & 0 \end{bmatrix}$$

constant speed

$$\mathbf{F}^3 = \begin{bmatrix} 3\mathbf{I} & -3\mathbf{I} & \mathbf{I} \\ \mathbf{I} & 0 & 0 \\ 0 & \mathbf{I} & 0 \end{bmatrix}$$

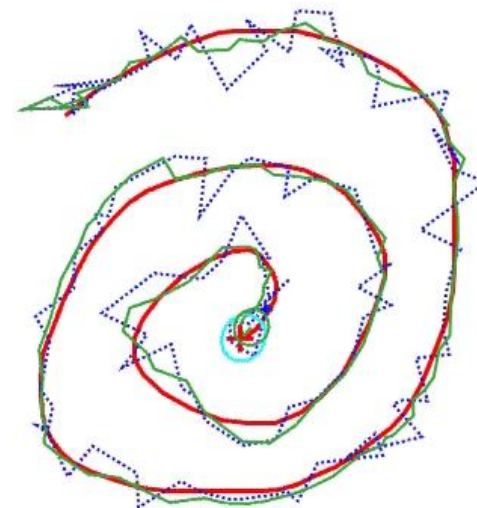
constant acceleration

Kalman Filter vs. IMM Filter



Kalman Filter

$$\mathbf{s}_k = \mathbf{s}_{k-1} + (\mathbf{s}_{k-1} - \mathbf{s}_{k-2}) + \mathbf{v}_{k-1}$$



IMM Filter

$$\mathbf{s}_k = \mathbf{s}_{k-1} + \mathbf{v}_{k-1}^1$$

$$\mathbf{s}_k = \mathbf{s}_{k-1} + (\mathbf{s}_{k-1} - \mathbf{s}_{k-2}) + \mathbf{v}_{k-1}^2$$

$$\mathbf{s}_k = \mathbf{s}_{k-1} + 2(\mathbf{s}_{k-1} - \mathbf{s}_{k-2}) - (\mathbf{s}_{k-2} - \mathbf{s}_{k-3}) + \mathbf{v}_{k-1}^3$$

Improved Results Using IMM Filter



Kalman



Frame #33



Frame #36



Frame #46



IMM



Frame #33

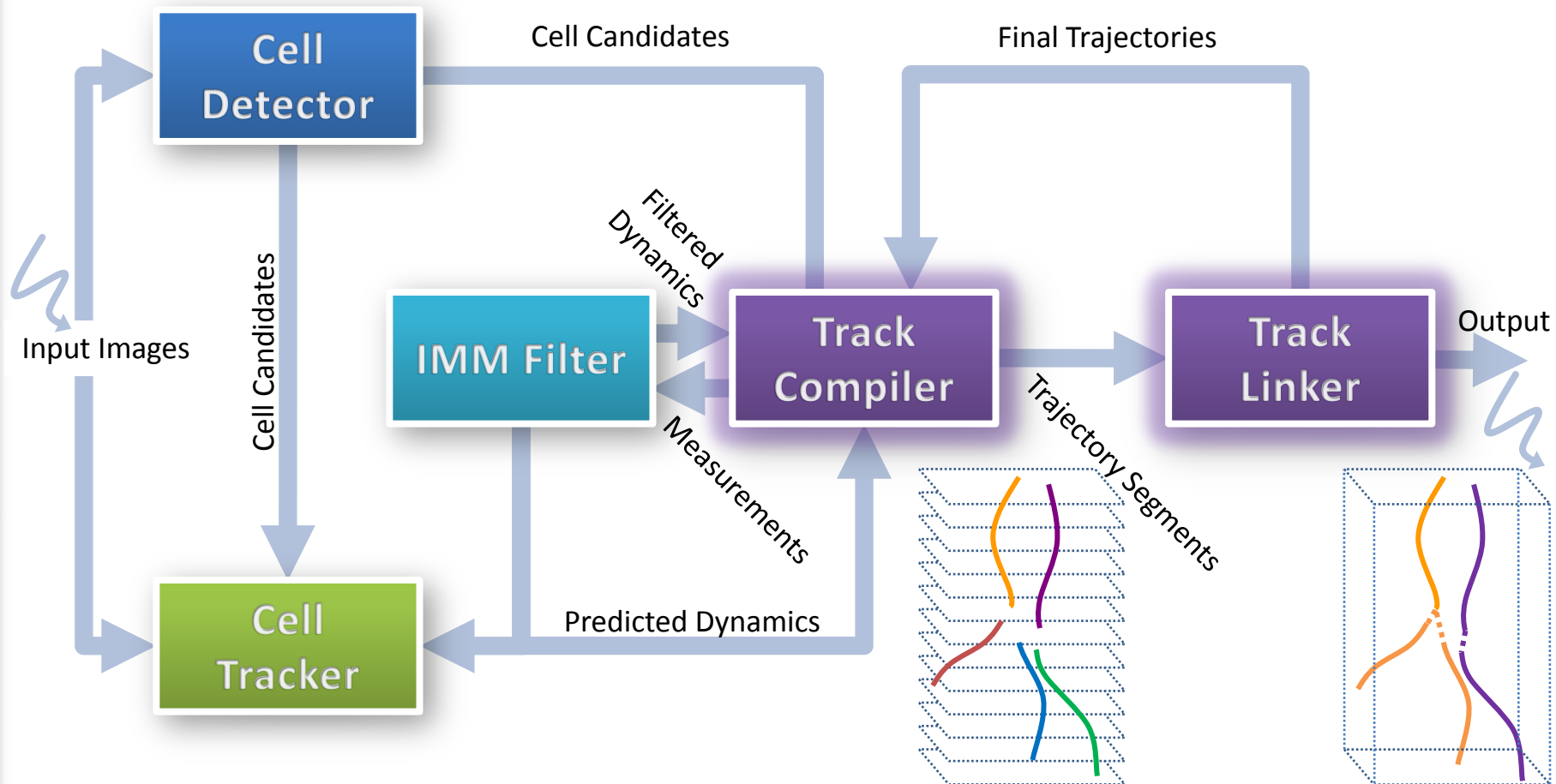


Frame #36

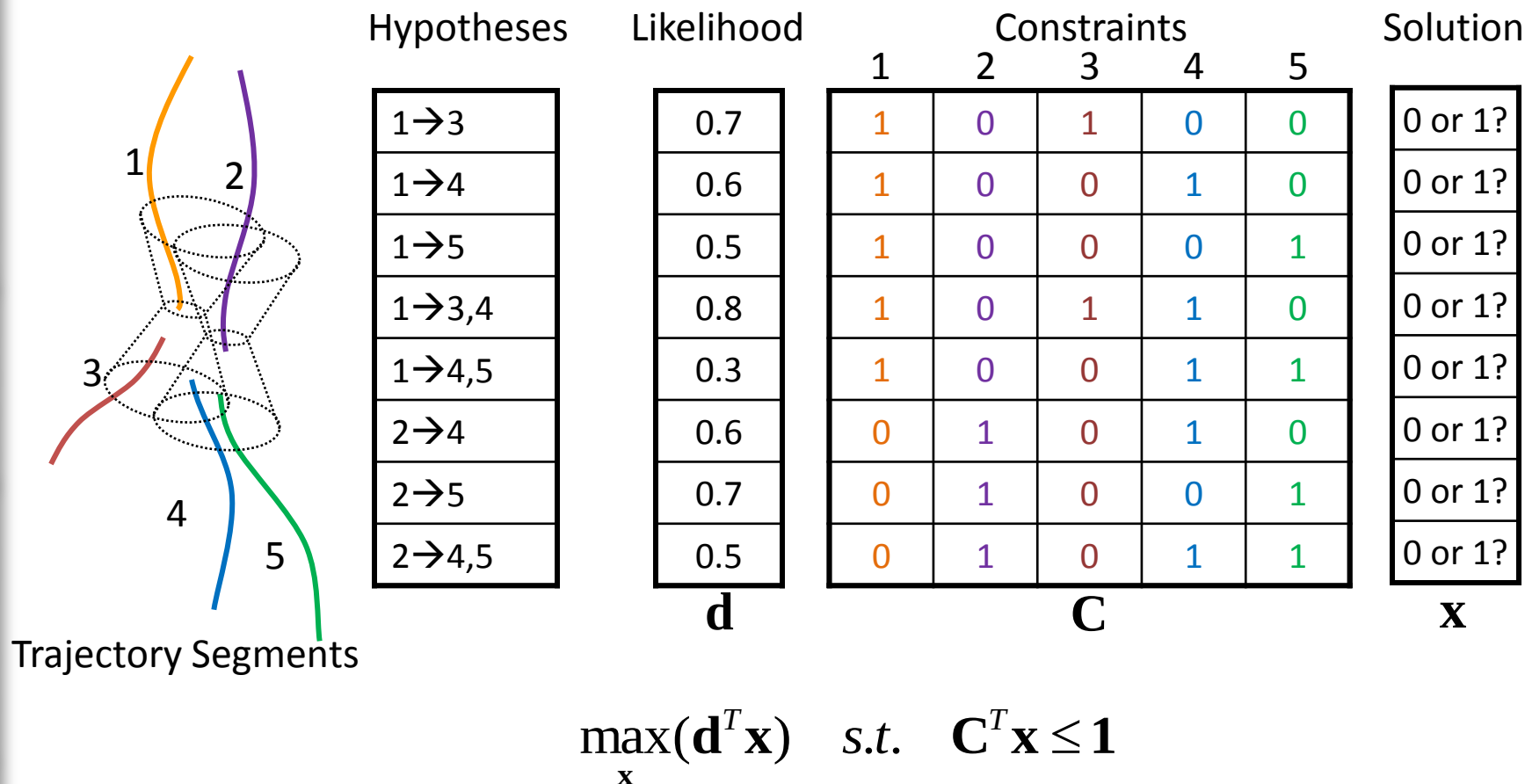


Frame #46

Tracking System 2.0

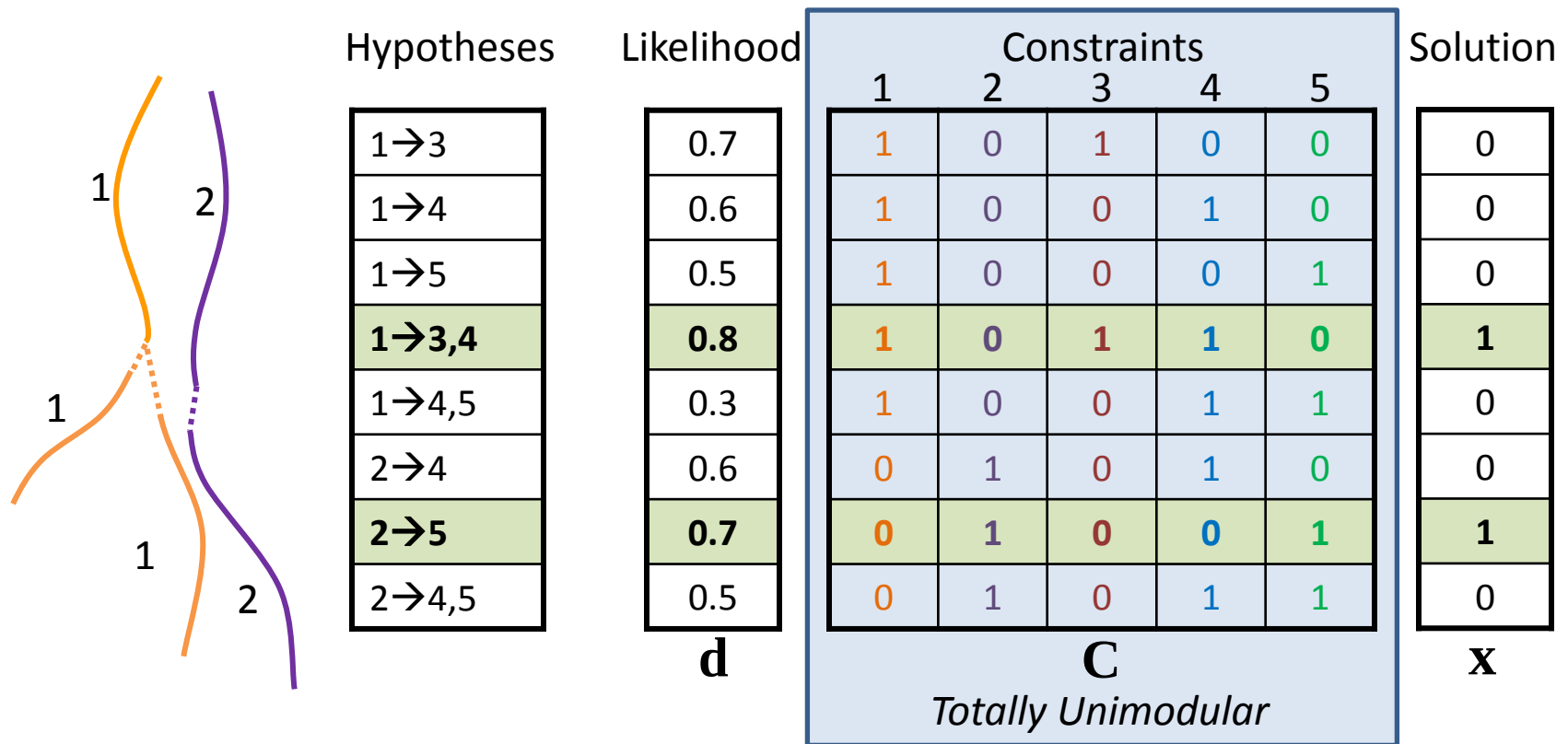


Track Compilation and Linking



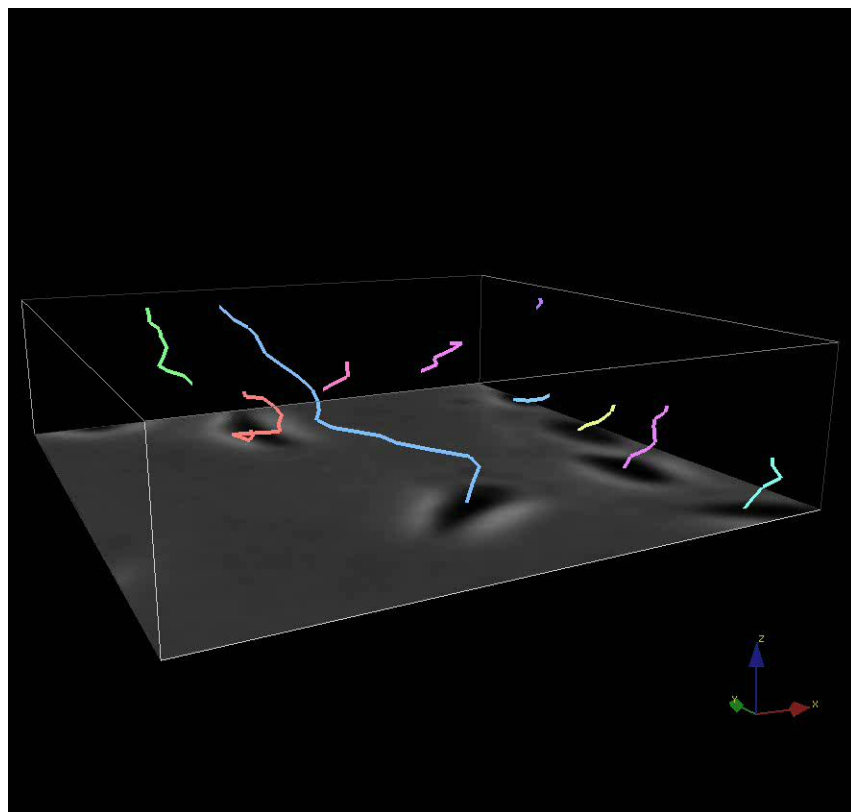
Track Compilation and Linking

- Integer programming problem: $\max_{\mathbf{x}}(\mathbf{d}^T \mathbf{x}) \quad s.t. \quad \mathbf{C}^T \mathbf{x} \leq \mathbf{1}$

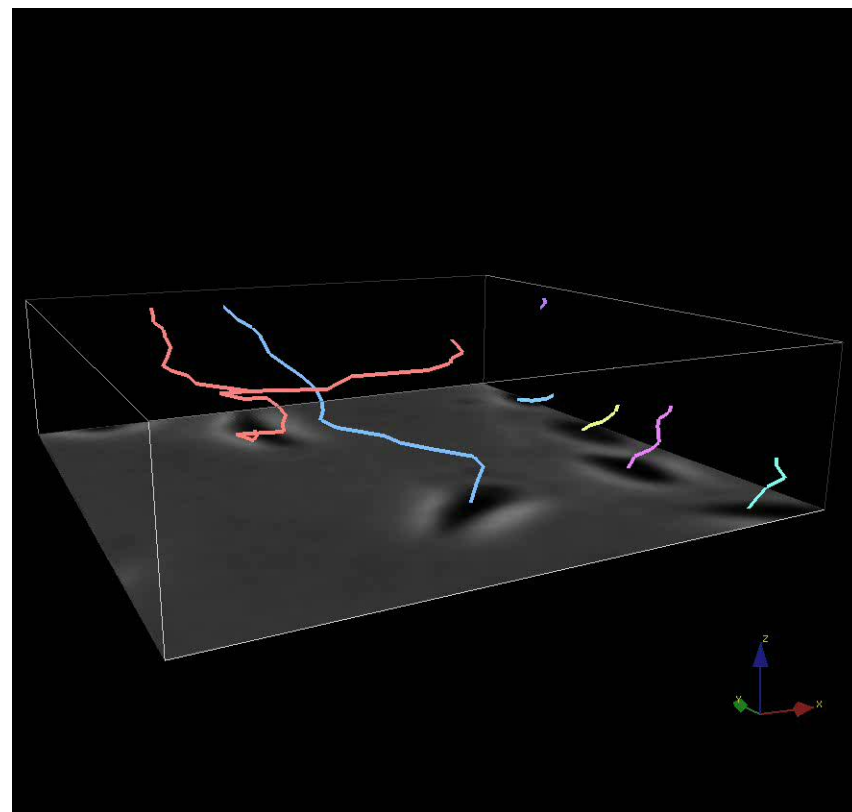


- Exactly solvable by **linear programming**

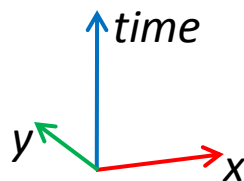
Spatiotemporal Track Linking



Before Linking



After Linking



Results after Spatiotemporal Linking



Frame-by-Frame



Frame #33



Frame #36



Frame #46



Spatiotemporal



Frame #33



Frame #36



Frame #46

Validation Using Real-World Data

Amnion Epithelial (AE) Stem Cells	MG-63 Human Osteosarcoma Cells
30 Sequences (2 Sub-Regions for Quantitative Validation)	2 Sequences
42.5 Hours/Sequence	10 Hours/Sequence
Polystyrene Dish	Polystyrene Dish
Zeiss Axiovert 135 TV Microscope (4.9× Magnification)	Zeiss Axiovert 135 TV Microscope (4.9× Magnification)
12-bit CCD Camera	12-bit CCD Camera
10 Minutes Frame Interval	4 minutes Frame Interval
1280×1024 Pixels/Frame	512×512 Pixels/Frame
1.9µm/Pixel	1.9µm/Pixel

Manual Validation

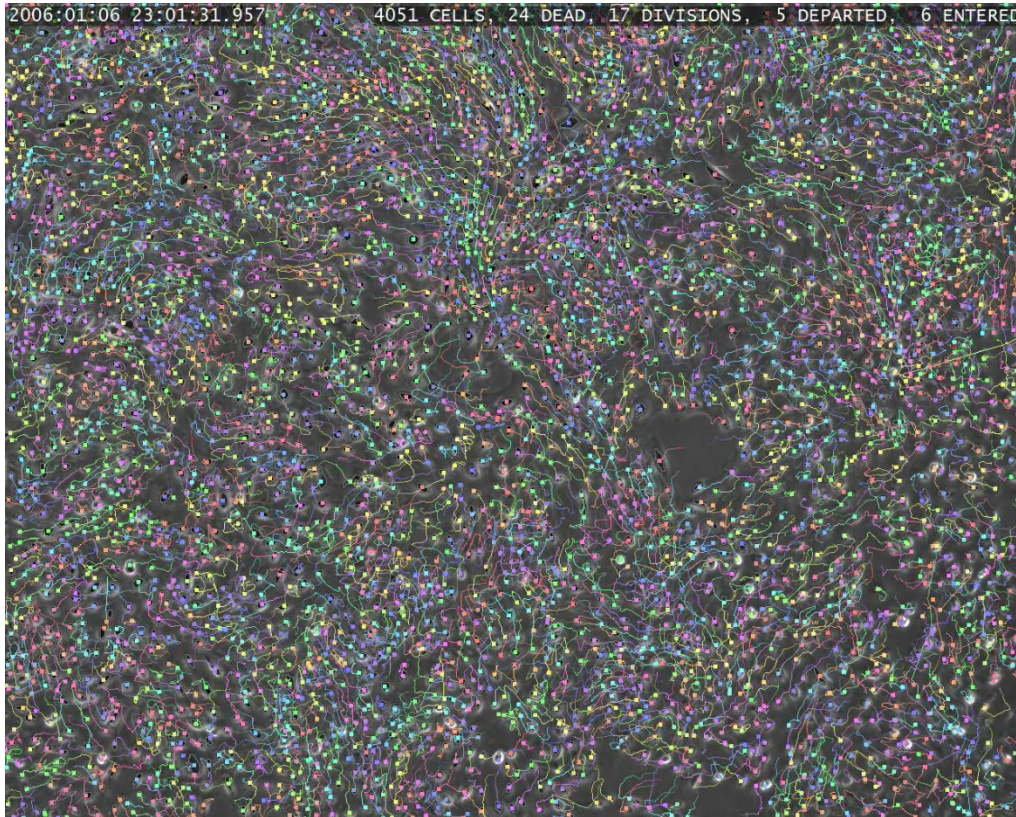
- Trajectory Validity

Sequence	Frame-by-Frame Only		Spatiotemporal	
AE (1)	70/92	76.1%	78/92	84.8%
AE (2)	90/117	76.9%	101/117	86.3%
MG-63 (1)	70/81	86.4%	74/81	91.4%
MG-63 (2)	82/93	88.2%	86/93	92.5%

- Division Tracking Validity

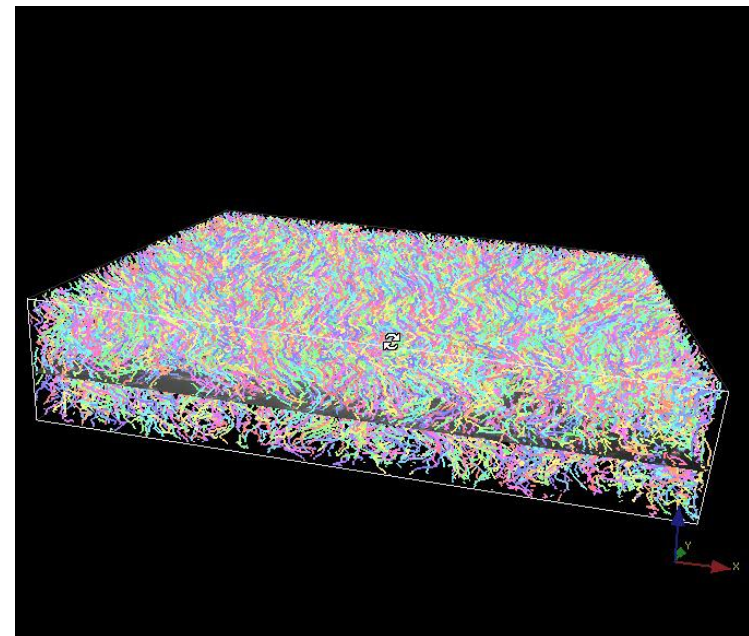
Sequence	Frame-by-Frame Only		Spatiotemporal	
AE (1)	43/55	78.2%	47/55	85.5%
AE (2)	41/52	78.8%	41/52	86.5%
MG-63 (1)	1/1	100%	1/1	100%
MG-63 (2)	0/0	N/A	0/0	N/A

Tracking Thousands of AE Stem Cells



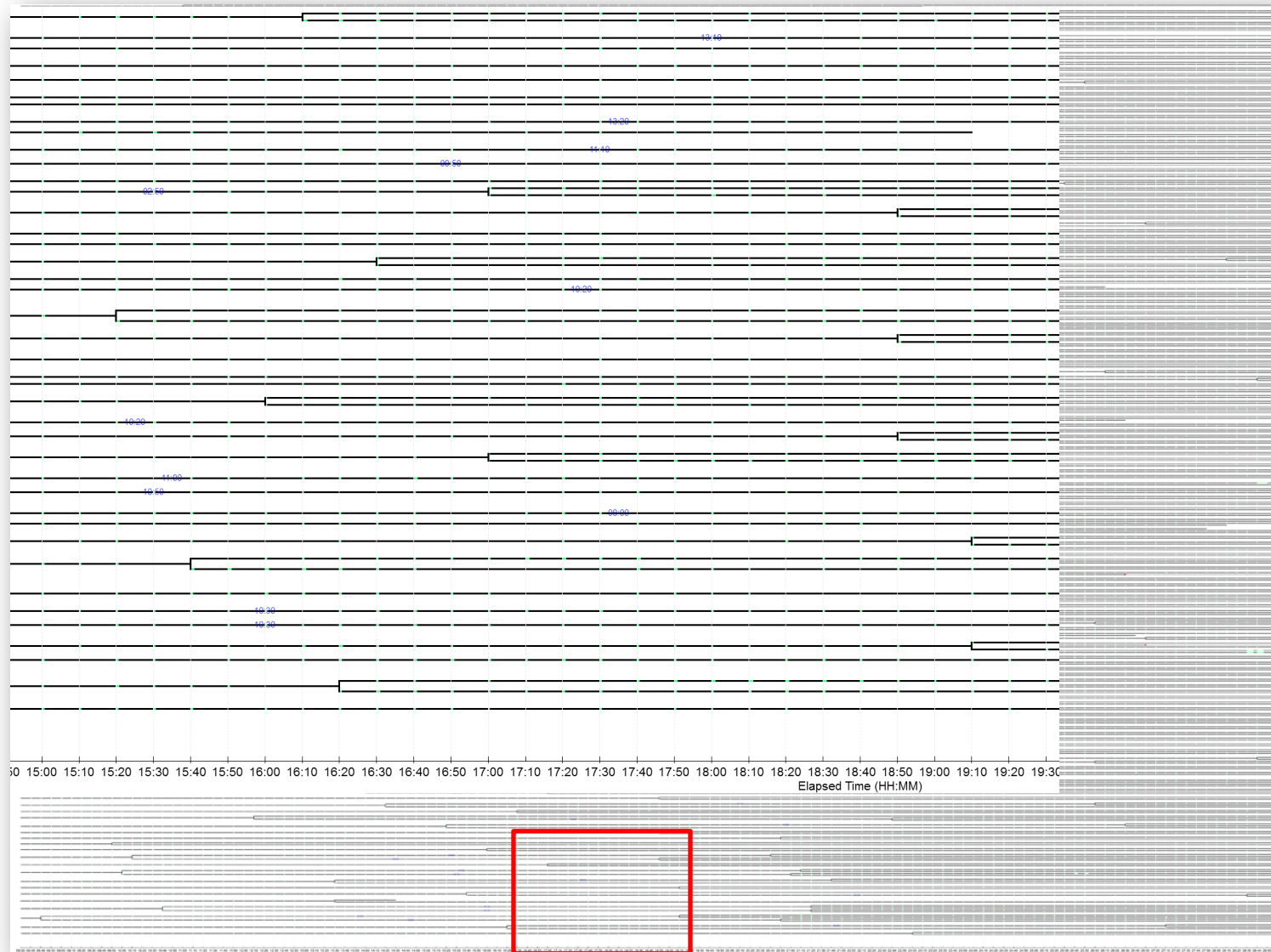
▲ Tracking Output

30 Seconds/Frame Tracking Time
Intel Xeon 2.66 GHz CPU
4Gb RAM



Spatiotemporal View of Cell Trajectories ►

Cell Population Lineage



Conclusions

- Automated system for tracking thousands of cells
 - **85.5—92.5%** accuracy
 - **30 seconds/frame** computation
- **9%** performance improvement achieved by
 - Multiple-models dynamics filter
 - Spatiotemporal trajectory optimization
- Applications: stem cell biology, cell culture optimization
- Future: more complex cell shapes/interactions

Acknowledgements

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- Intel Equipment Grant