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Automated Micro Robotic Manipulation using Optical Tweezers

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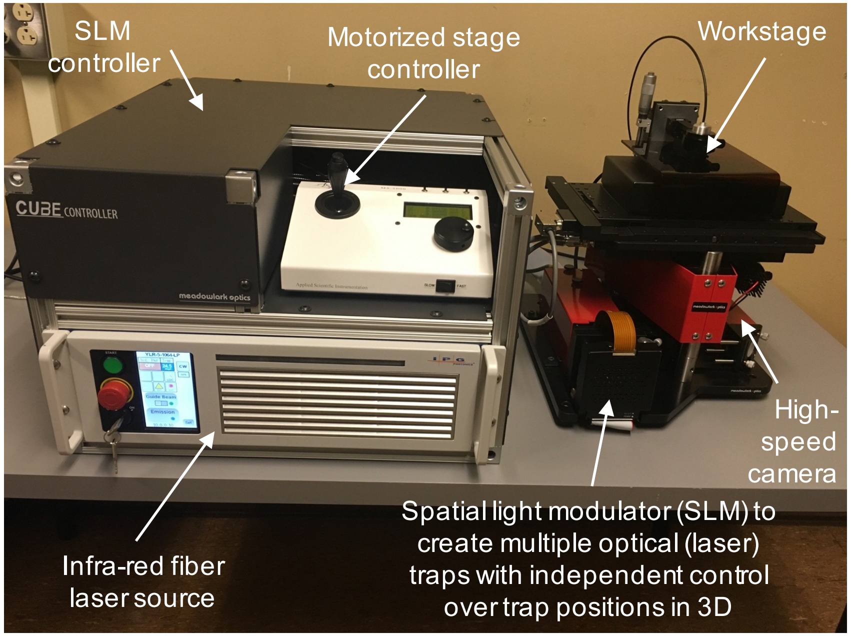
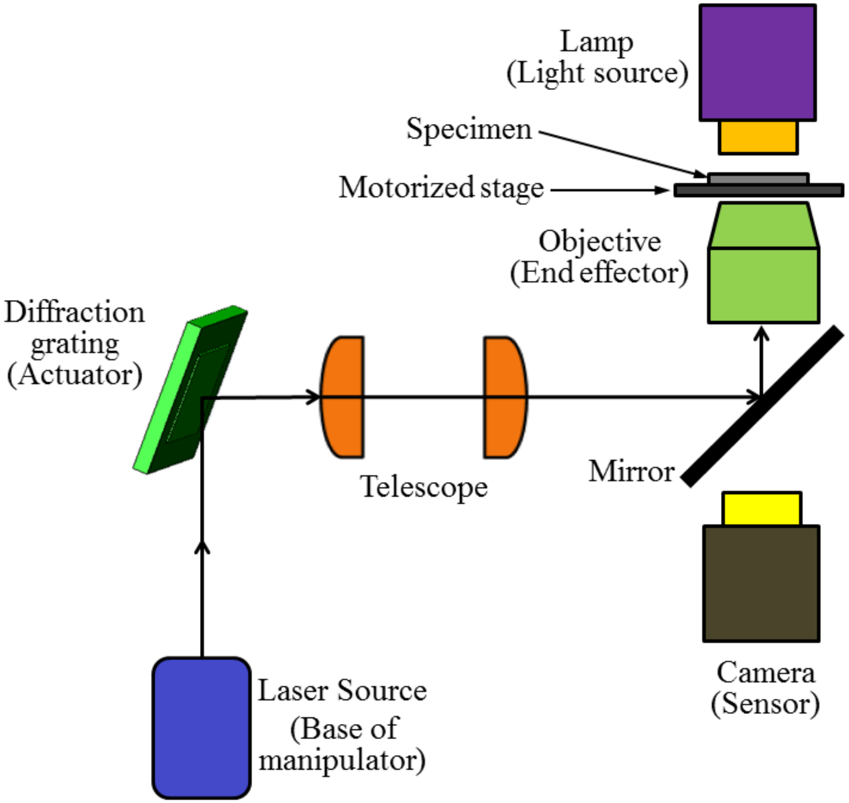
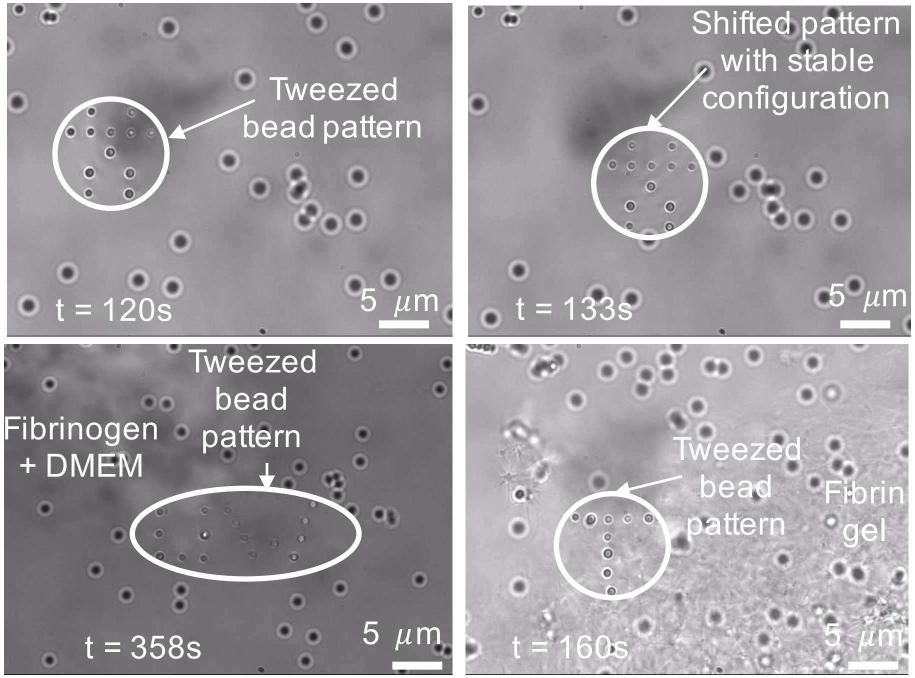
Optical Tweezers as Micro Robots





Why Optical Tweezers?

- Advantages
  - Multiplexing capability (up to 100 objects concurrently)
  - Precise and independent control over each object in 3D
  - Flexibility in choice of manipulated object (particles, cells, biomolecules, etc.) and medium
  - Easy to release trapped objects after manipulation
  - Minimal object damage during manipulation

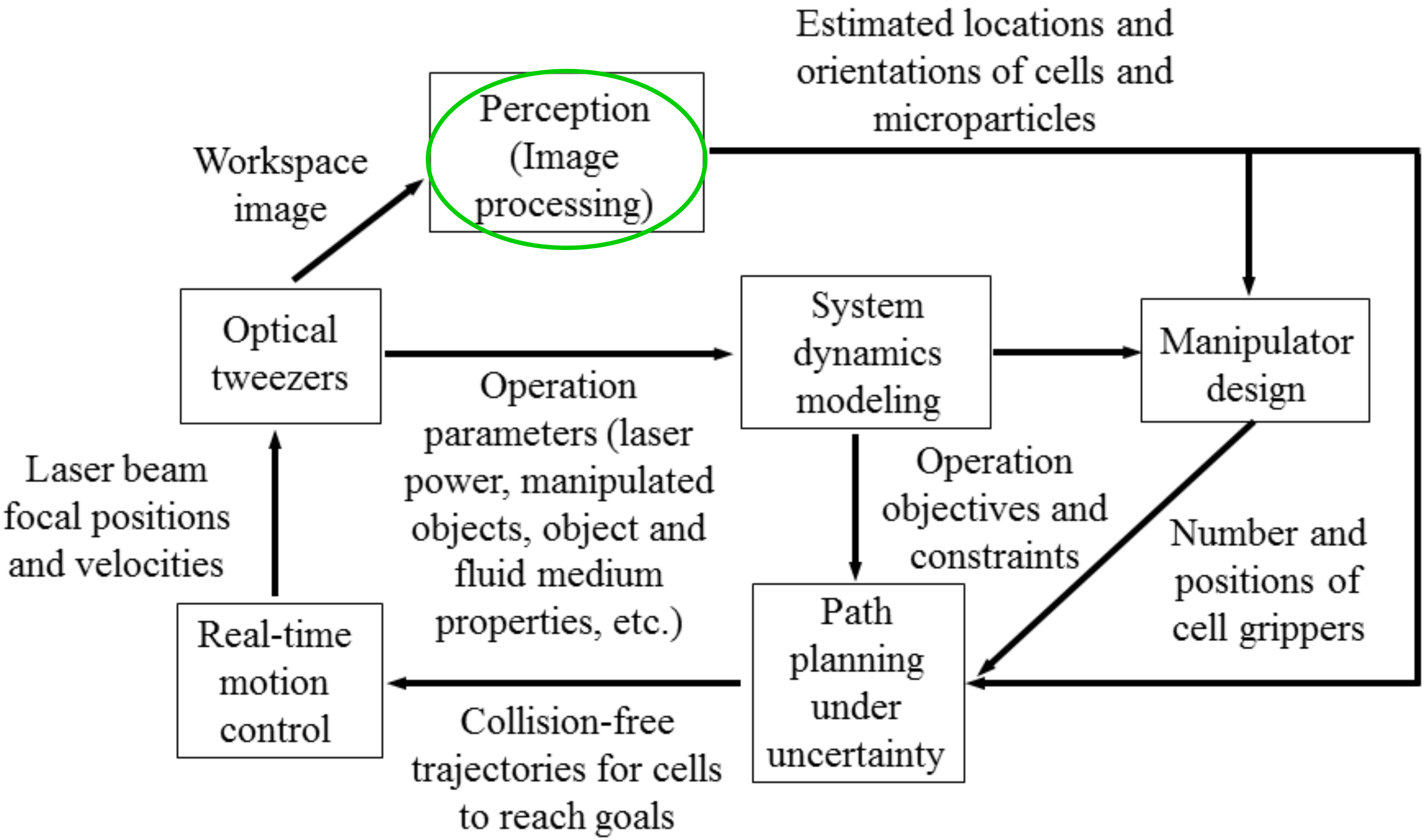


Automated Manipulation

- Motivation
  - Manipulate large number of objects in parallel
  - Reliable and efficient manipulation
- Challenges
  - Stochastic and non-linear system dynamics
  - Uncertainty in sensing (optical imaging) measurements
  - Fast motion control updates at rates of several Hz
  - Optimized manipulator design (number, positions, and intensities of traps for gripped object)
  - Real-time trajectory planning

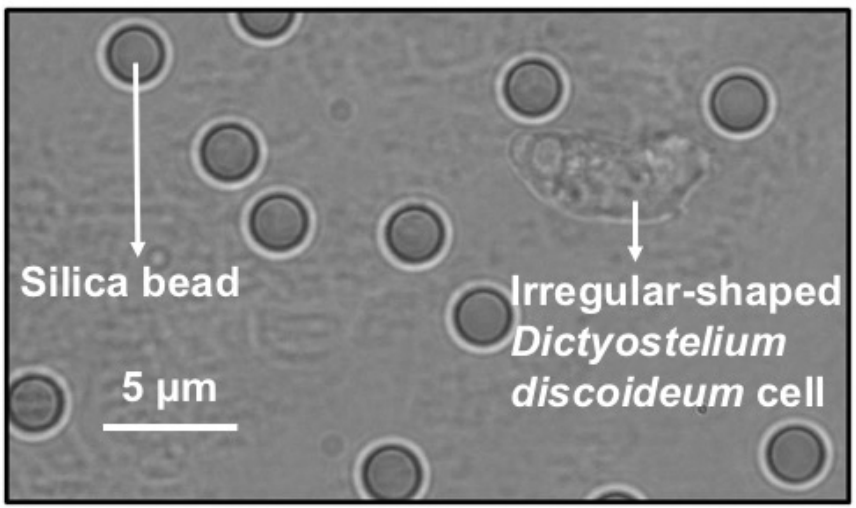
Focus on manipulation of cells using optically-trapped microspheres (beads) as grippers to minimize damage due to laser exposure

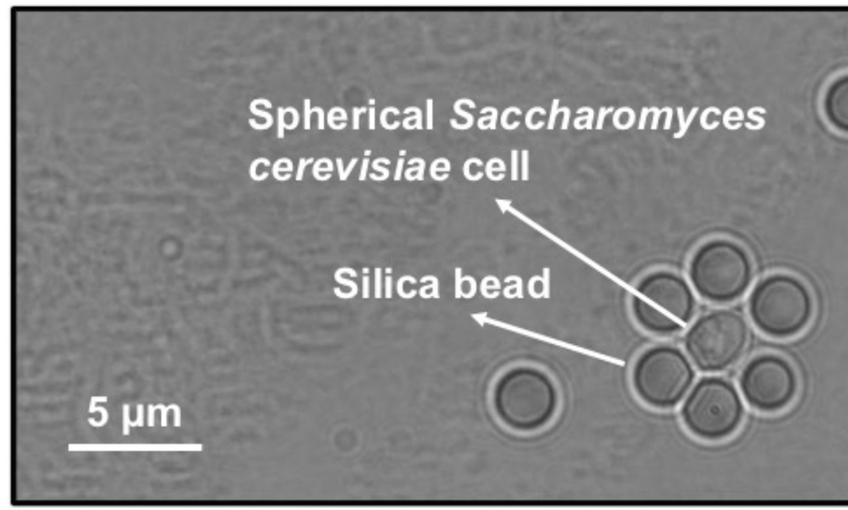
Automation: Need for Perception



Problem Formulation

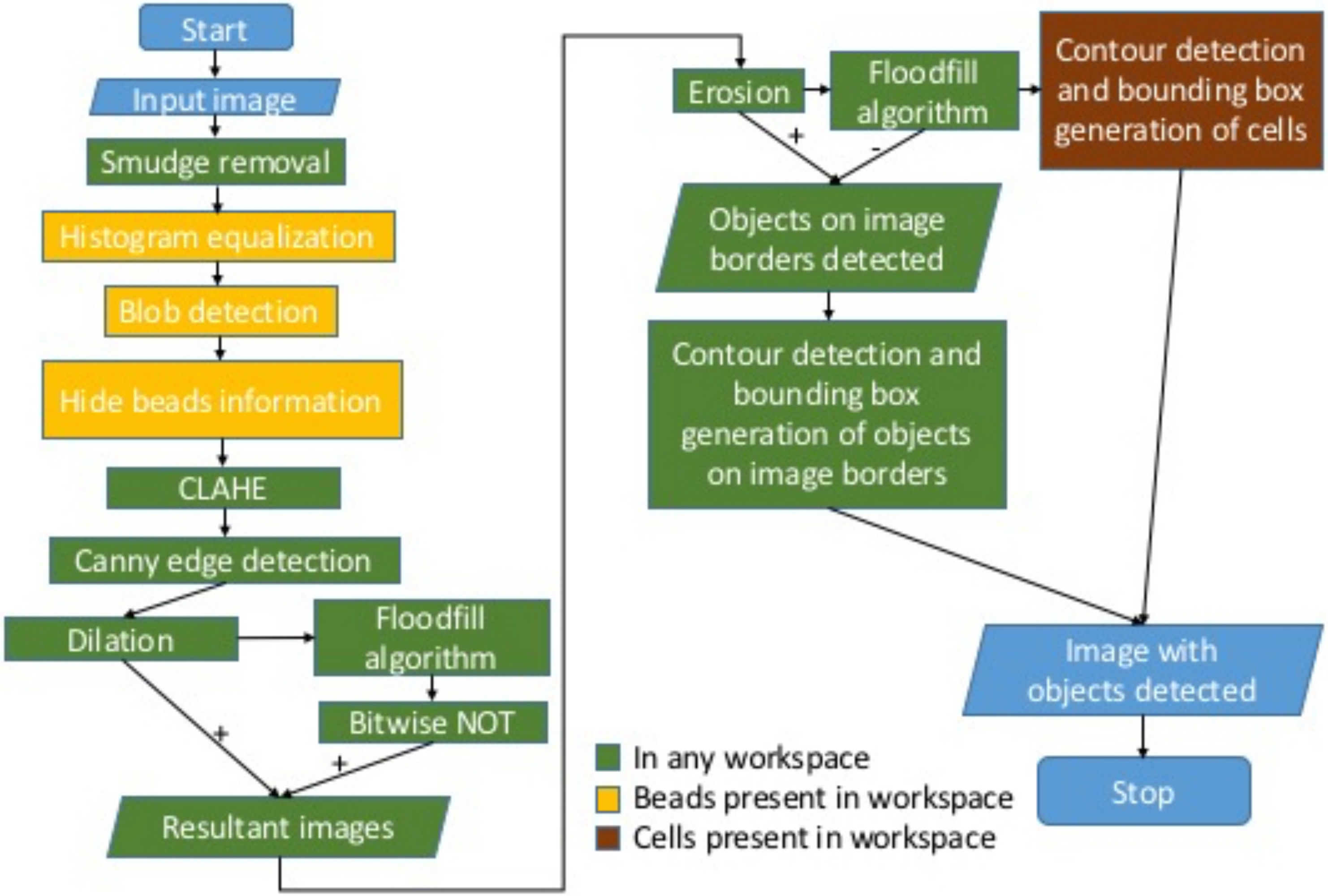
- Given input
  - Set of images from different time-lapse experiments
    - Beads and irregular-shaped cells
    - Beads and spherical cells





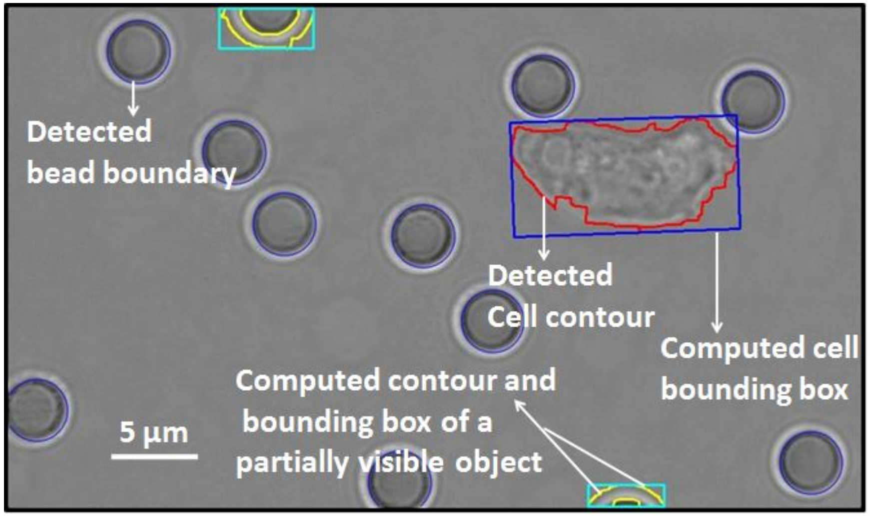
- Desired output
  - Centroids and diameters of beads; diameters and orientations of cell bounding boxes

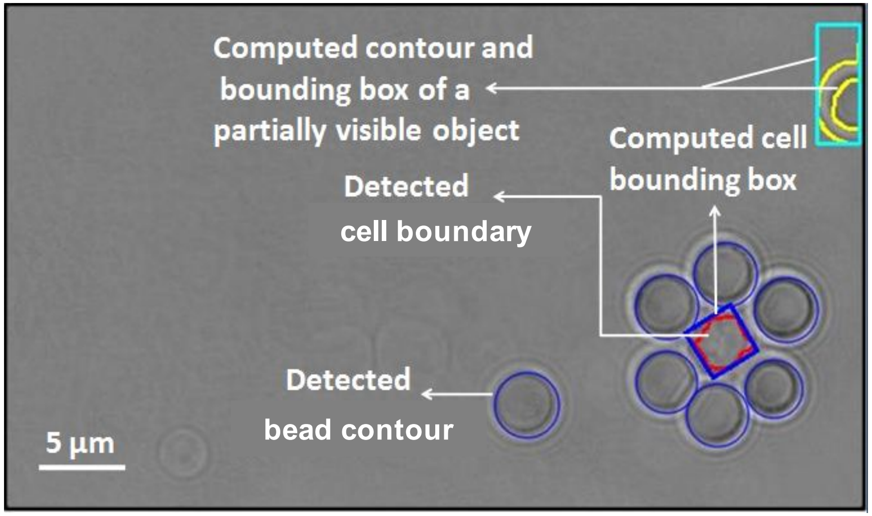
Robust Image Processing Method



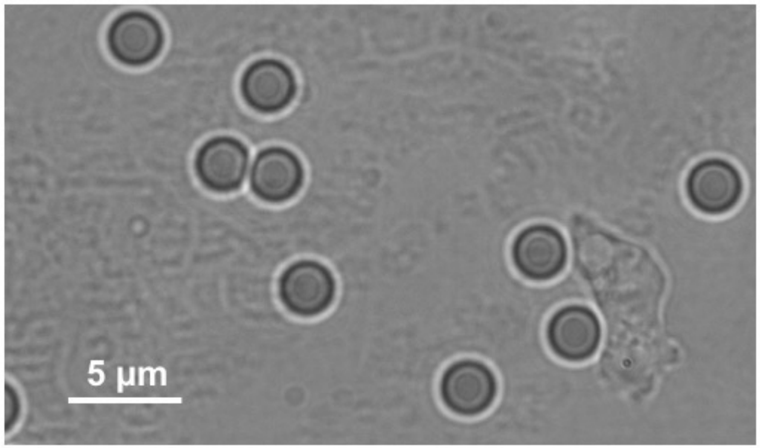
Examples of Processed Images

- Able to detect object positions and orientations even when they are of different types and located close to each other

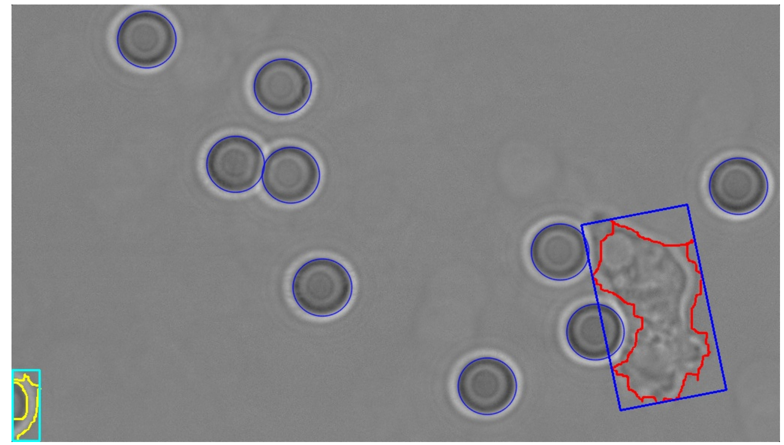




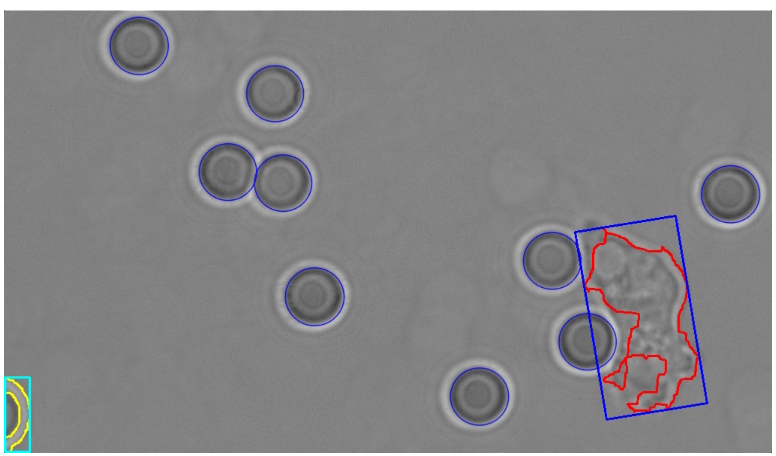
Detecting Irregular-Shaped Cells and Beads



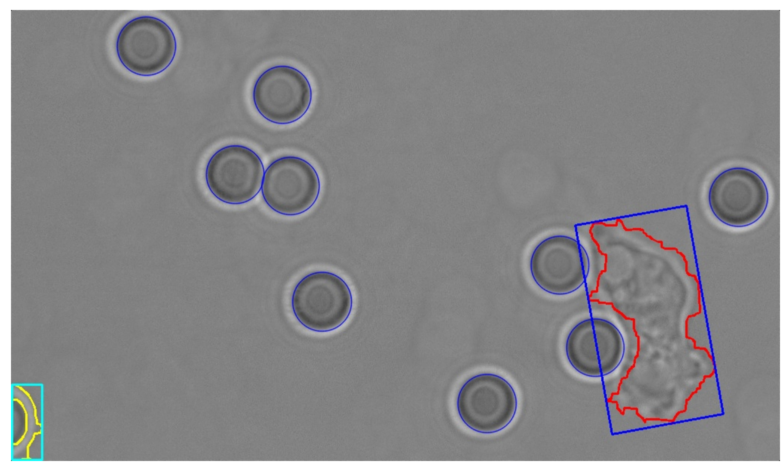
Test image



Our method

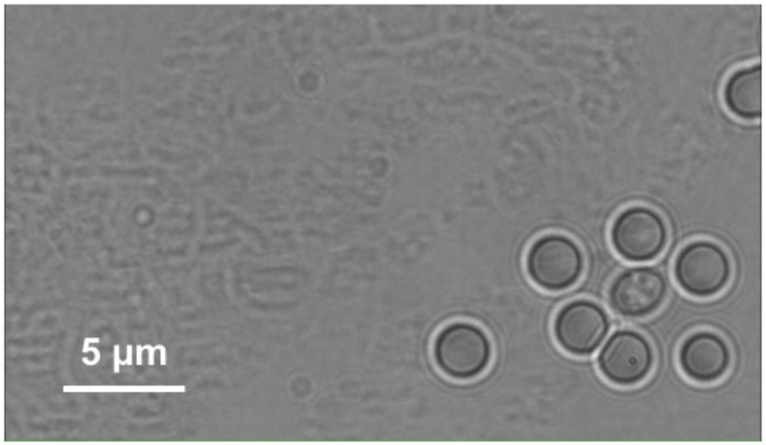


Otsu's thresholding

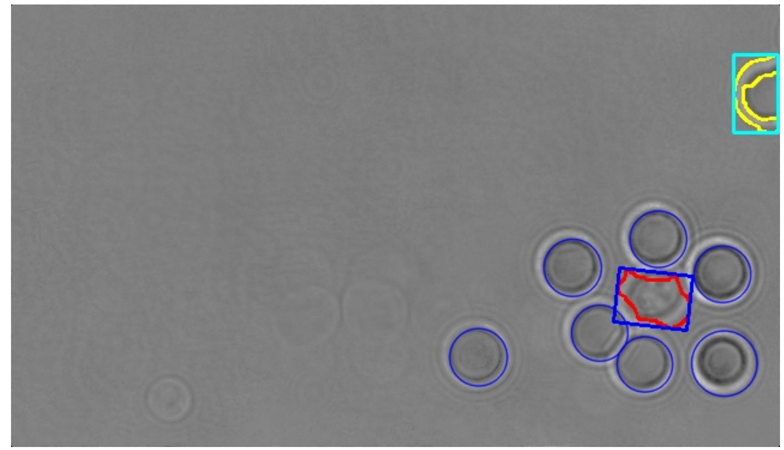


Histogram equalization & manual thresholding

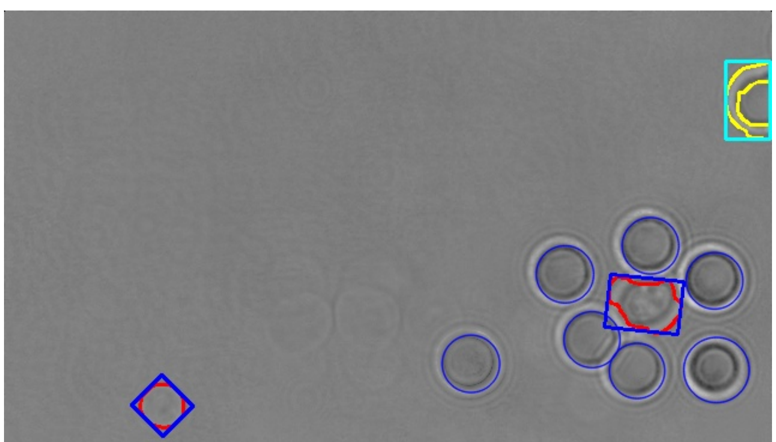
Detecting Spherical Cells and Beads



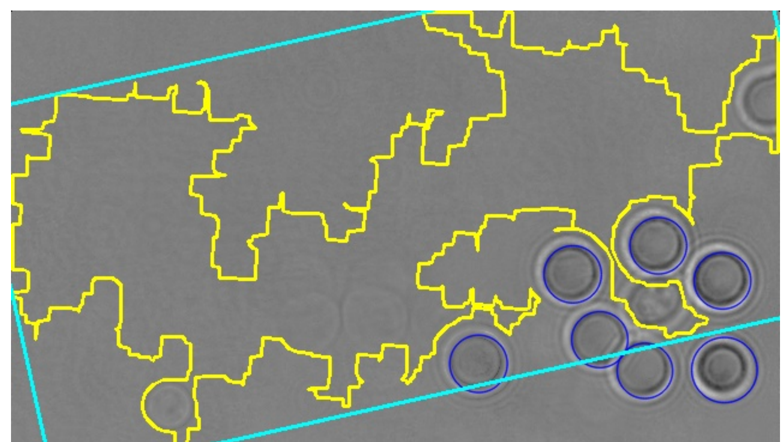
Test image



Our method

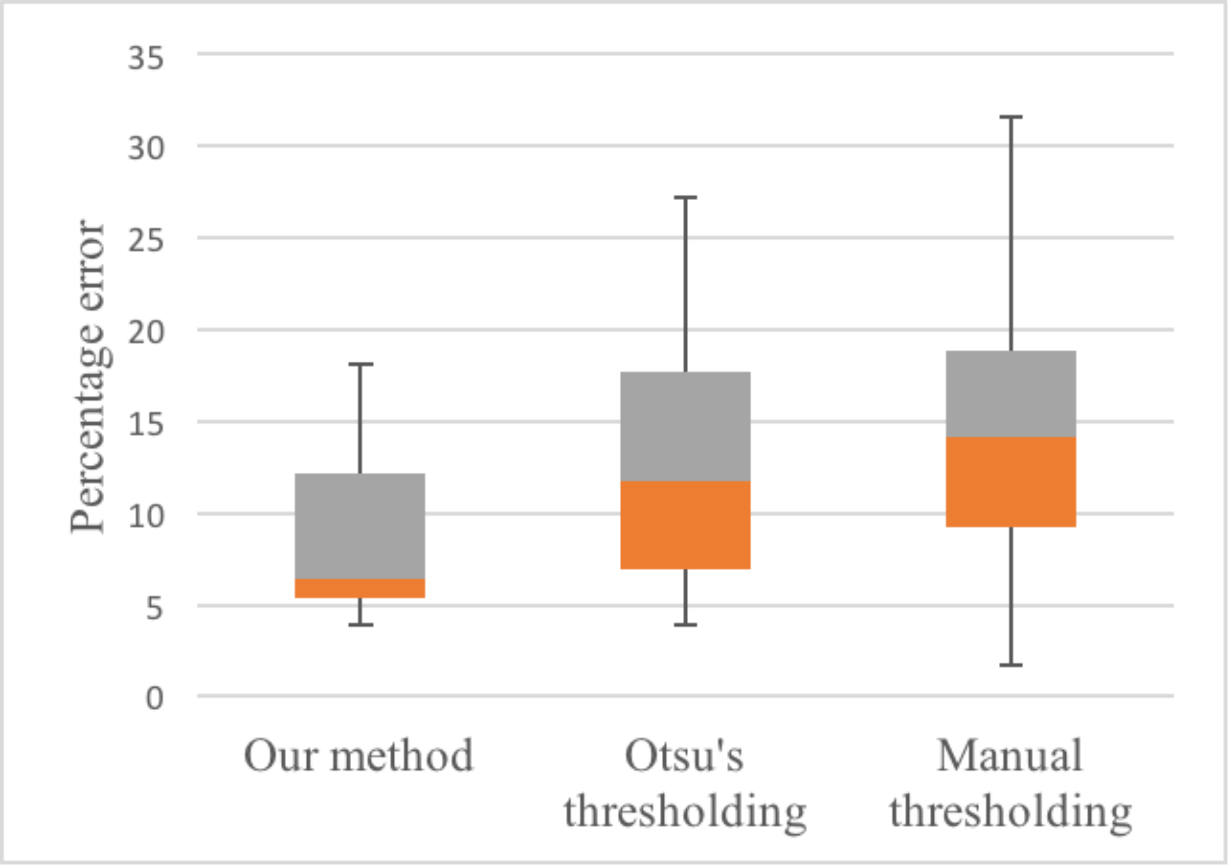


Otsu’s thresholding

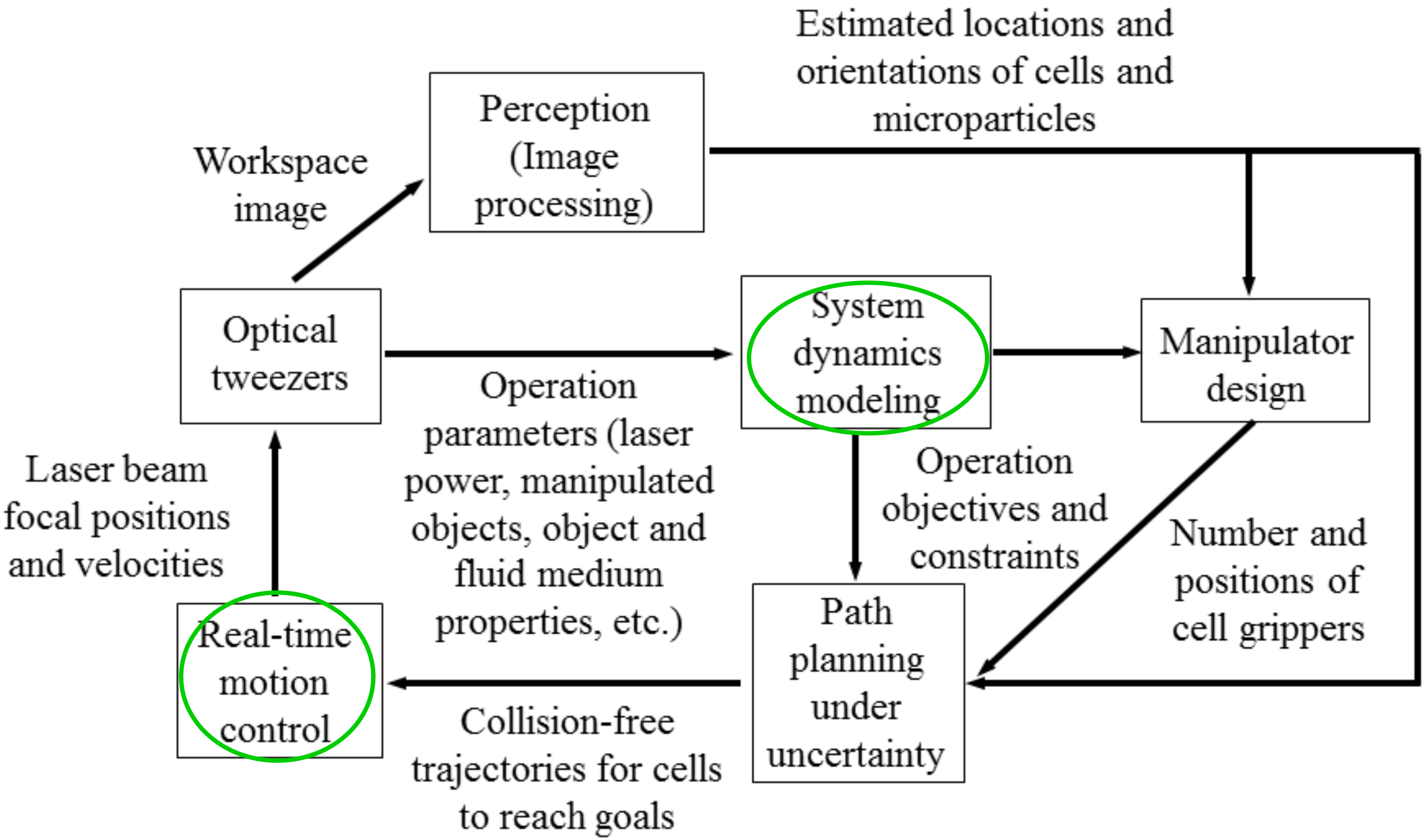


Manual thresholding

Performance Comparison



Automation: Need for Dynamics Modeling & Control



State-Space Representation

- States are bead positions; control inputs are optical trap (laser beam focus) positions
- Optical trapping forces on beads are modeled using combination of linear and non-linear spring stiffness with different axial and radial components
- Langevin (thermal) forces and observation disturbances are modeled using zero mean Gaussian distributions
- Viscous drag, buoyancy, and inertial forces are also considered

$$\boldsymbol{M}\ddot{\boldsymbol{x}} = \left(\boldsymbol{K}_{ln}(t) \circ (\boldsymbol{1} \otimes \boldsymbol{U}(t) - \boldsymbol{x} * \boldsymbol{1}^{T}) \circ e^{-\boldsymbol{K}_{en} \circ \left(\boldsymbol{1} \otimes \boldsymbol{U}(t) - \boldsymbol{x} * \boldsymbol{1}^{T}\right)^{.2}}\right)\boldsymbol{1} - \boldsymbol{B}_{\boldsymbol{drag}}\dot{\boldsymbol{x}}(t) - \boldsymbol{B}_{o} + \boldsymbol{F}\boldsymbol{\eta}$$

$$\boldsymbol{F} = \begin{bmatrix} \sqrt{2k_B T\gamma} & 0 & 0 \\ 0 & \sqrt{2k_B T\gamma} & 0 \\ 0 & 0 & \sqrt{2k_B T\gamma} \end{bmatrix} \qquad \gamma = 6\pi r\mu \qquad \eta_i \sim Normal\left(0, \sqrt{\delta t}\,\right)$$

$$\boldsymbol{y} = \boldsymbol{C}\boldsymbol{x} + \boldsymbol{\xi} \qquad \boldsymbol{\xi} \sim Normal(\boldsymbol{0}, \boldsymbol{\Sigma})$$

Model Predictive Controller (MPC)

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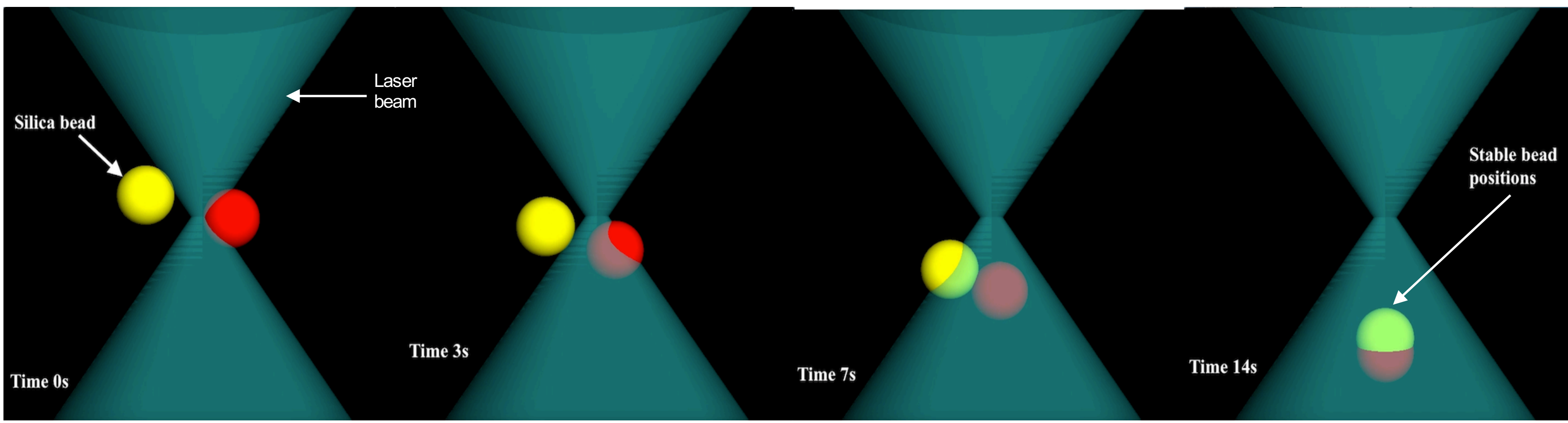
- MPC simulates system for certain time horizon to compute control trajectory, i.e., sequence of actions
  - Applies only first action
  - Receives feedback and simulates system once again for receding time horizon based on observed states

- Uses quadratic cost function to optimize each control input

$$J = \sum_{i}^{t} ((\boldsymbol{x}(i) - \boldsymbol{x}_d)^T (\boldsymbol{x}(\boldsymbol{i}) - \boldsymbol{x}_{\boldsymbol{d}}))$$

Dynamics Simulation

- Bead motions under influence of one or more optical traps correspond well to theoretical and experimental results
  - Optical trapping forces simulated using high-fidelity geometrical optics toolbox



Microsphere Arrangement Formation

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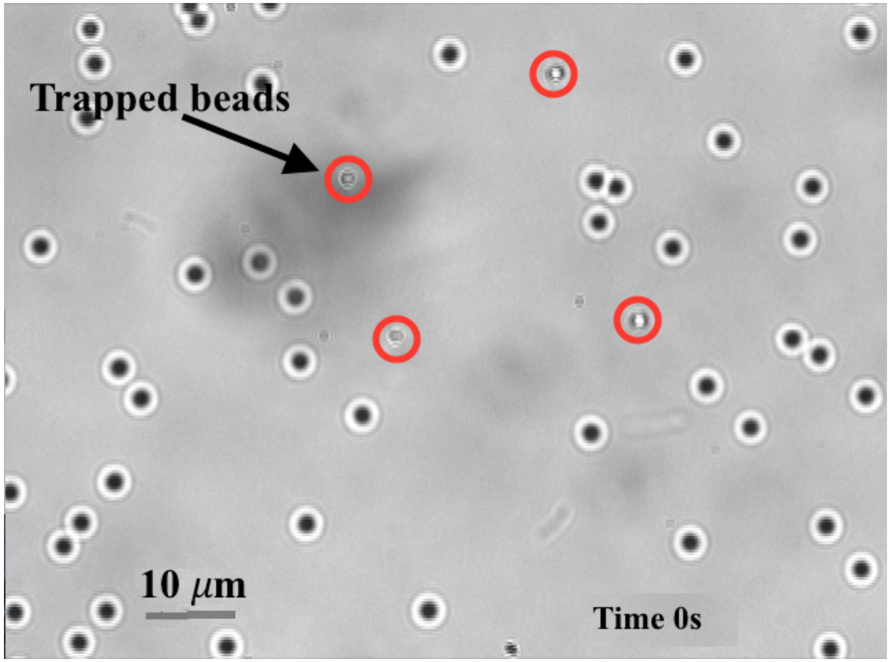
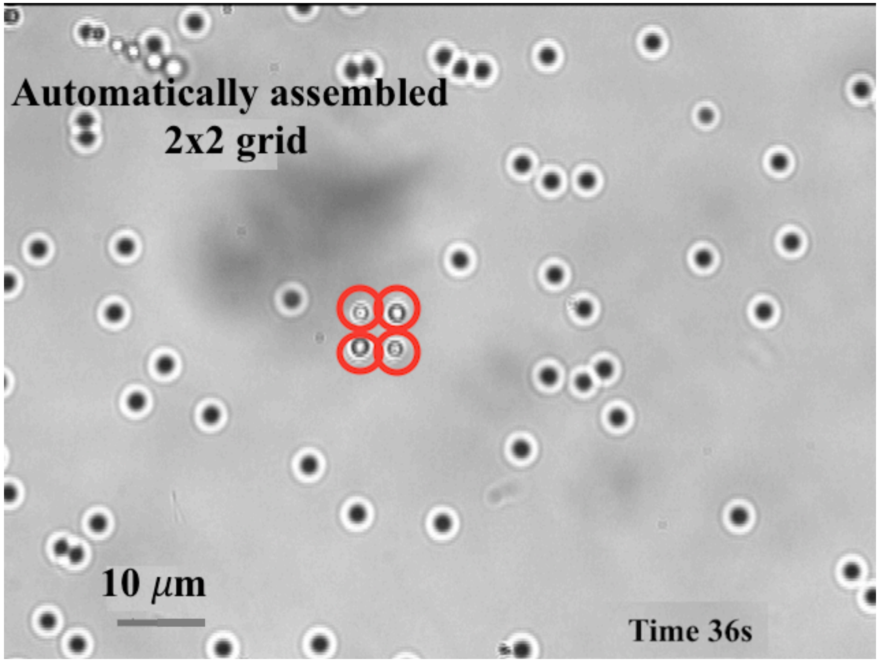
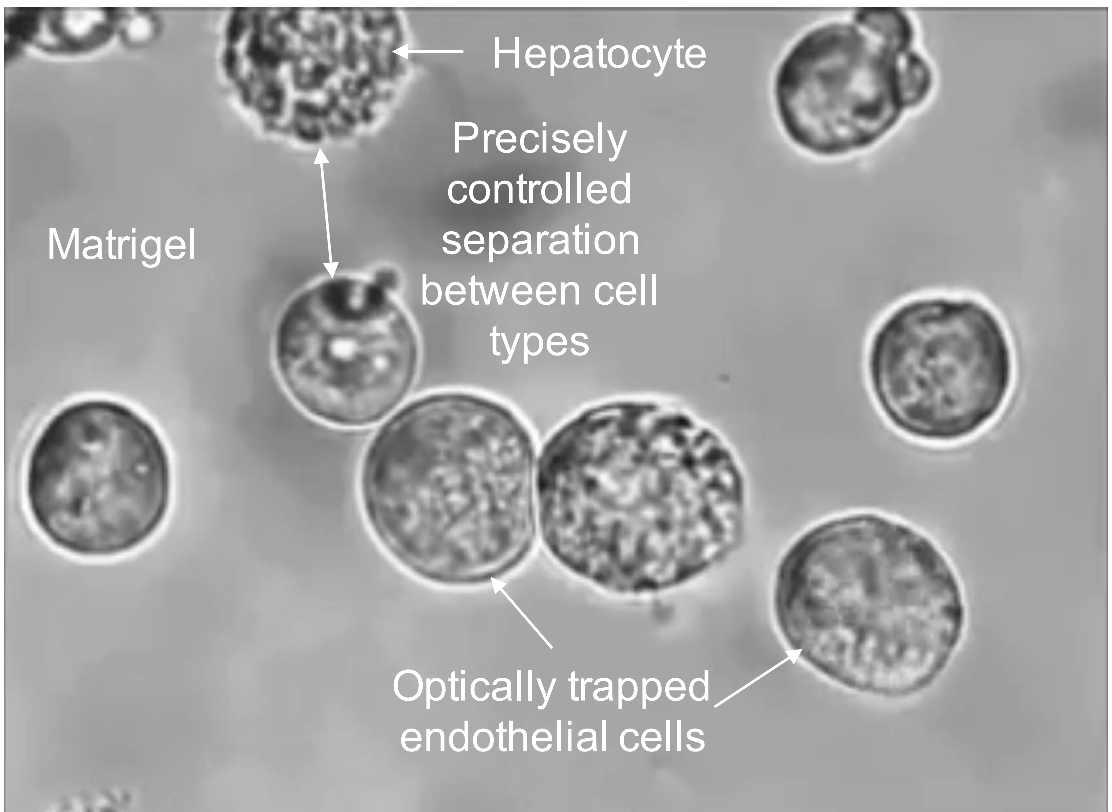
- Successful demonstration for simple arrangements in 2D
  - Further work needed for more complex-shaped arrangements involving larger number of objects in 3D





Ongoing Work: Multi-Cellular Arrangement Formation

- Investigate signaling between parenchymal and non-parenchymal cells as function of geometric shapes and distances



Participants

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  - Ph.D. student
    - Manasa Bollavaram
  - M.S. student
    - Keshav Rajasekaran
  - Undergraduate researchers
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    - John Stewart
- Collaborators
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    - Dr. Sagar Chowdhury
  - University of Southern California
    - Prof. Satyandra K. Gupta
  - University of Washington
    - Daniel Corbett (Bioengineering)
    - Chelsea Fortin (Bioengineering)
    - Dr. Andrea Leonard (Mechanical Engineering)
    - Prof. Nathan Sniadecki (Mechanical Engineering)
    - Prof. Kelly Stevens (Bioengineering and Pathology)