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Carbon cone electrodes for Selection, Manipulation and Lysis of Single cells

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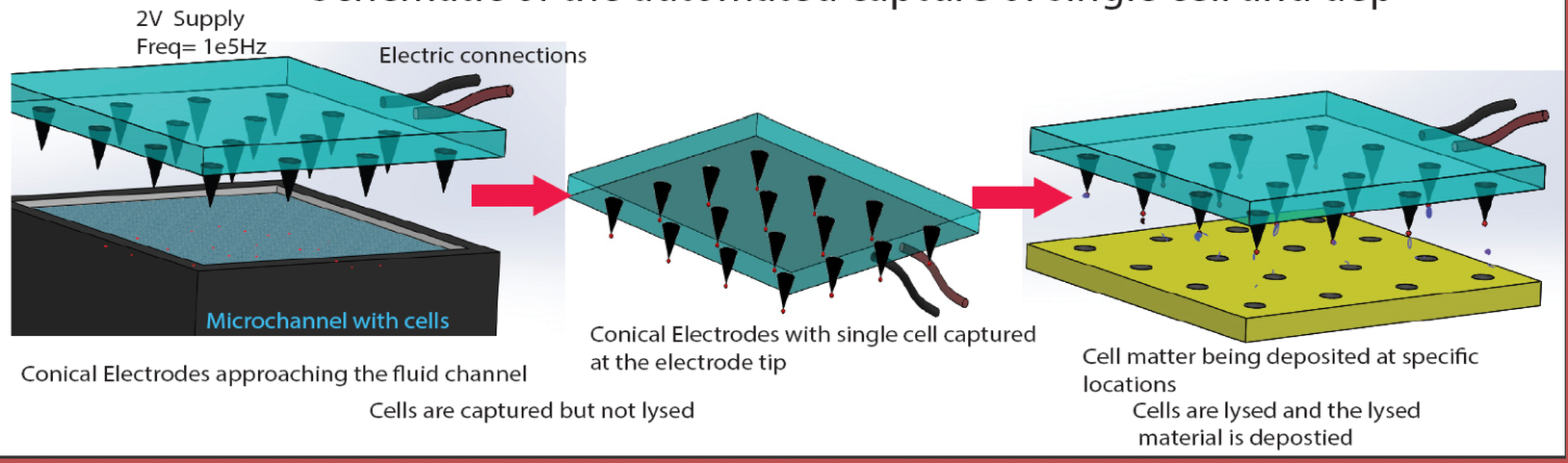
Introduction

Here we present initial experiments towards an integrated platform for single cell selection, manipulation and lysis. An array of polarized conical carbon electrodes can be dipped in a cell culture, trap cells of interest using dielectrophoresis and transport them to specific locations where they can be lyzed electrically to extract intracellular components from targeted particles over specific locations. What we contribute in this work is modeling of the electric field and its gradient around carbon cones, as well as initial cone fabrication results. Ongoing work is on demonstrating cell trapping and lysis using these conical electrodes by only varying the magnitude and frequency of their polarizing AC signal.

Here we use conical carbon electrode to trap volumes to keep a single particle in place and yields strong enough electric fields for lysing once the cell is on top of a specific location.

Schematic of the automated capture of single cell and dep-



Target parameters :

1. Extremely high electric gradient is needed to be localized at the tips of the cones

High Gradient at tips → **High DEP force** → **Localized Cell Capture**

2.Velocity required to transport the captured cells to the location for deposition

DEP Force on captured cells = **Drag force on the cells** → **Velocity of transport**

3. Cell lysis is desired only when the cells are positioned above the deposition sites

Electric Field at the tips during capture < **Cell Membrane potential**

Electric Field at the tips the deposition sites > **Cell Membrane potential**

Methodology:

- ❖ The process starts with moving the electrode plate in the vicinity of the cell culture
- ❖ The conical electrode array is supplied with 2V of potential difference at a specific frequency(currently used freq.=1e5Hz) and alternate electrodes are grounded.
- ❖ When the electrodes approach the cells, a single cell gets trapped at the tip because of the small volume of high gradient region
- ❖ At specific velocity(determined based on the gradient), the system of electrodes with captured cells is transported to the cell material deposition sites
- ❖ When the system is located above the deposition sites, by changing the frequency (1e6 Hz) cells are lysed and the cell material is deposited at individual sites
- ❖ Process is automated
- ❖ The cell matter of each cell can be obtained at separate locations for analysis

Graphical Representation of parameters

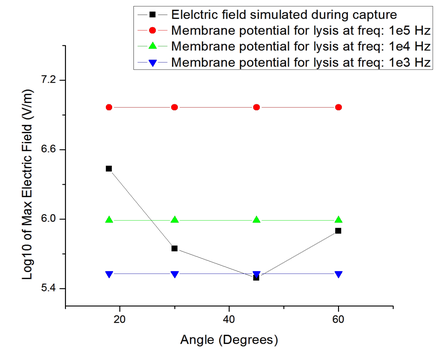


Fig: Electric field obtained at various angle by simulation and corresponding membrane potential for lysis of yeast cells

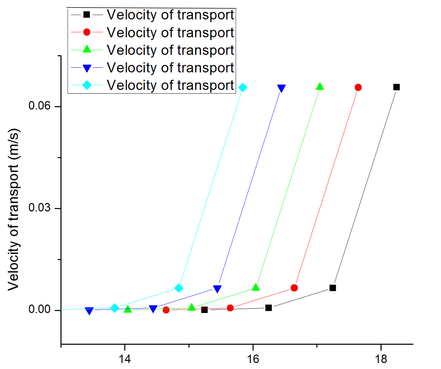
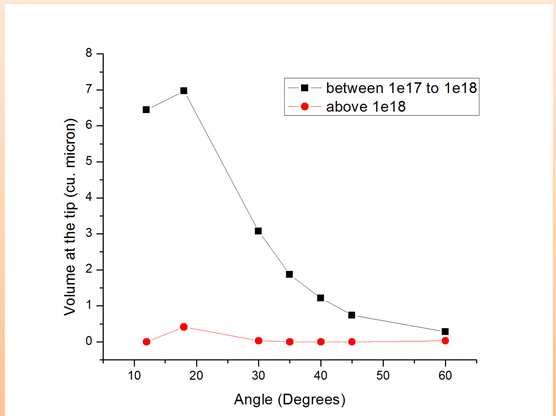


Fig: Maximum velocity that can be used for transport of the system against DEP force for various cell radii

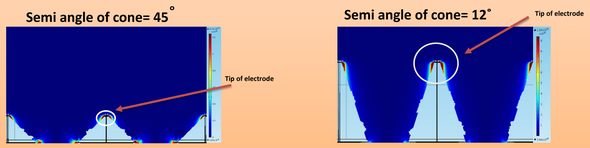
Volume captured at the tips of cones



Simulation Results for minimum and maximum angles

Simulation conditions in 500*500*100 cu. micron domain:

- Comsol based Electric Current model
- Media conductivity = 1e-3 S/m
- Relative permittivity of Media =80.3
- Cone dimensions: Base Radius=20.00 microns & Tip Radius=0.50 microns
- Range of semi angles studied: 12 degrees to 60 degrees



Carbon Electrode Fabrication:

- ❖ Carbon has large electrochemical stability window
- ❖ Obtained by photolithography process on negative photoresist SU8
- ❖ Back exposure is used to obtain the desired geometry
- ❖ The obtained posts are heat treated at temperatures upto 900˚C to obtain carbon structures
- ❖ Specific conical structures are obtained by optimizing the back exposure dose, post exposure bake temperature and time of the photolithography process

Conclusion:

The volumes obtained at the tips of conical electrodes for desired gradient range justify that single yeast cell capture is possible in this region. With higher voltages at the same conductivity, high gradient and membrane potential is obtained. Thus a study for different conductivities is desired. Fabrication of simulated geometries and further experimentation is needed.

Current Work:

- Study for various conductivities of media
- Fabrication of cones
- Assembly and automation of the system
- Experimentation for yeast cells
- Extending the concept to other cells