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

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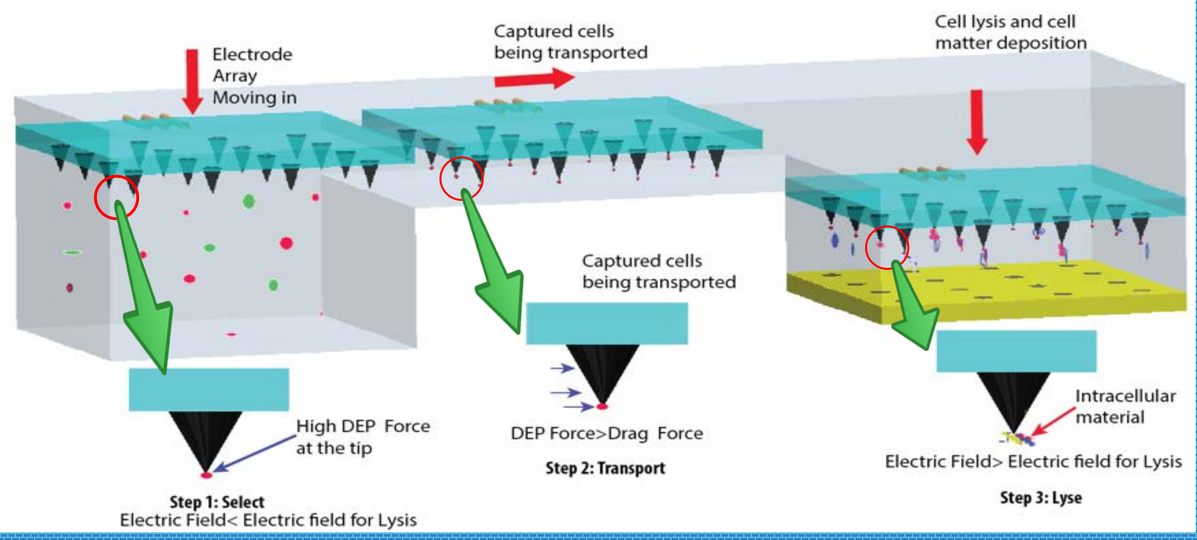
Introduction

- Here we present initial experiments towards an integrated platform for single cell selection, manipulation and lysis.
- An array of polarized conical carbon electrodes can 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.
- Our contribution in this work is the modeling of the electric field and its gradient around carbon cones, as well as initial cone fabrication results.

Why single cell Analysis?

In vitro Fertilization | Next Generation Sequencing | Analysis of Biomolecules | Diagnostics

Schematic of the proposed set up



Results

Geometric Optimization

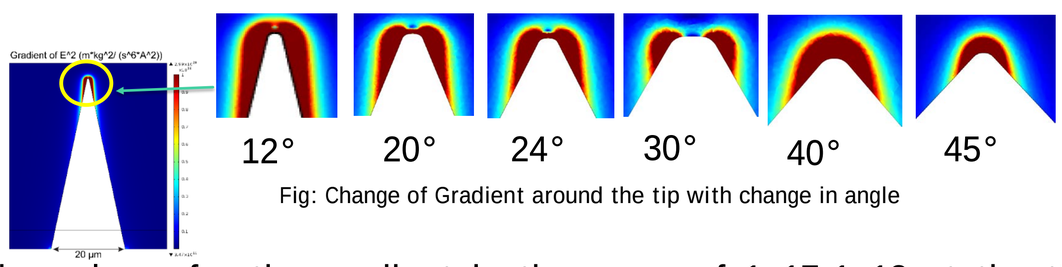


Fig: Change of Gradient around the tip with change in angle

The volume for the gradient in the range of 1e17-1e18 at the tip was obtained to be around 10 μm^3 which enables capture of single cell.

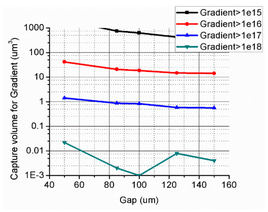


Fig: Volume captured for different gaps at tip

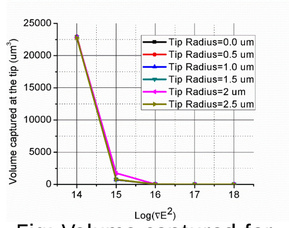


Fig: Volume captured for different tip radii

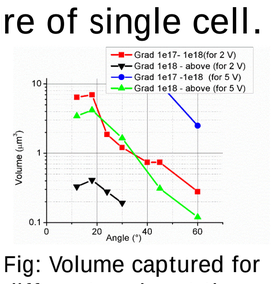


Fig: Volume captured for different angles at tip

Voltage Optimization

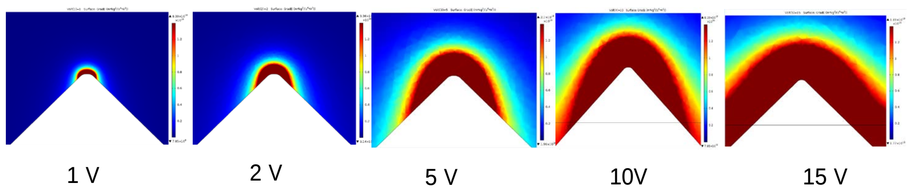


Fig: Change of Gradient around the tip with change in angle

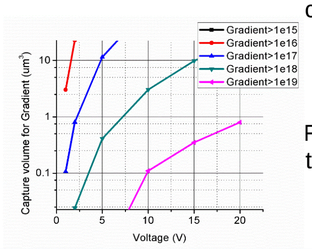


Fig: Volume captured for at tip for different voltages

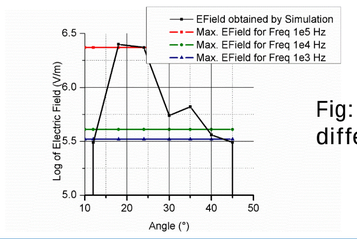


Fig: Max. Electric Field at different angles

Independent Parameters	Dependent Parameters
Geometry of Electrodes (angle α)	Drag Force : $6*\pi*r*\eta*v$
Polarizing Voltage(V) and Frequency(f) and Electric Field(E)	DEP Force: $2*\pi*r^3*Re(Fcm)*\nabla E^2$
Medium type (Conductivity(σm) and Viscosity(η))	Cell Membrane Potential: $\frac{1.5*E*r*cos\alpha}{\sqrt{1+(2*\pi*f*\tau)}}$
Velocity of transport(V)	Where τ = r*(Cmem)*$(\frac{1}{\sigma cyto}+\frac{1}{\sigma m})$
Particle Type (Radius , Capacitance of Membrane Cmem, Conductivity of cytoplasm σctyo)	Gradient for the Electric Field and volume for each gradient

Targets for the Process

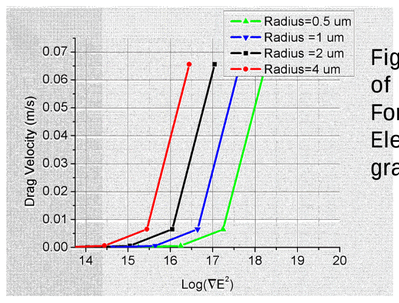


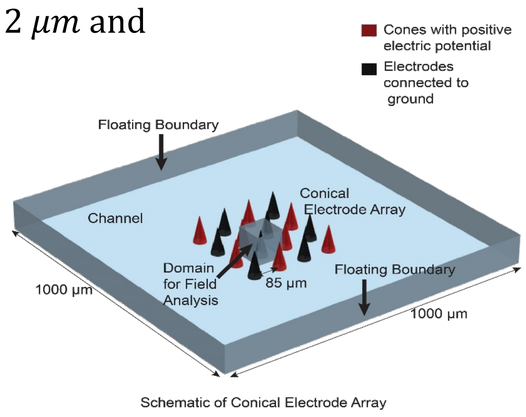
Fig: Graph of Drag Force and Electric gradient

Table: Signal Frequency and corresponding Field to capture live cells

Signal Frequency (Hz)	Max. Electric Field that can capture viable cells (V/m)
10^5	$2.34*10^6$
10^4	$4.0*10^5$
10^3	$3.31*10^5$

Methodology

- COMSOL Simulations for various electrode geometries was performed
- Cells assumed were yeast cells which are round with the radius of 2 μm and



Schematic of Conical Electrode Array

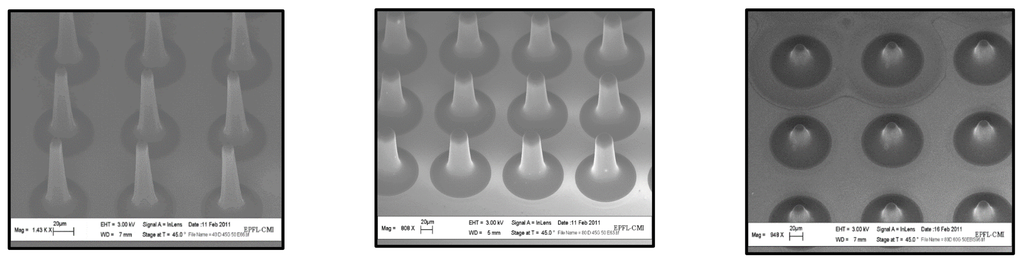
Table: simulation parameters

Parameter	Value
Voltage	1-20V
Radius	20 & 25 µm
Angle at tip	12˚-60˚
Radius at tip	0.5- 2 µm
Gap	50 -120 µm

Conclusion and ongoing work

- The volumes obtained at the tips of conical electrodes for considered gradient range justify that single yeast cell capture is possible in this region.
- Study for different media: Medium conductivity used for current models is 0.001 S/m, but other physiological media and cells will be targeted as well.

SEM image of conical carbon posts



- **Fabrication of cones:** Use of carbon electrodes has advantages over expensive metal electrodes and insulator based high voltage electrodes. Conical structures have been successfully fabricated in carbon. Further work in attending specific geometries is being done.

References:
- Rodrigo Martinez-Duarte, SU-8 Photolithography as a Toolbox for Carbon MEMS, Micromachines 2014, *5*(3),766-782;
- Aleksandra A.Kolodziejczyk, et al., The technology and biology of single cell RNA Sequencing, Molecular Cell, Volume 58, Issue 4, 2015, 610-620

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