

COMSOL Multiphysics® as a Tool for Biomedical Engineering Students to Harness

Physical Processes

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INTRODUCTION: A curious approach for regenerative medical treatments utilizes electric fields to alter cell function and direct cell migration. In cartilage this is a critical approach as a common limiting factor in regeneration is the cells' ability to migrate to the site of the injury. We aim to gain a better understanding of the cells' local electrical field in both its native state and in an externally applied electric field. A device to apply electric fields to cells for experiments was also developed and modeled with COMSOL to study the electric field distribution and ion migration.

COMPUTATIONAL METHODS: The cellular electric field distribution is modeled using previously defined electrical properties for chondrocytes¹, the cells found in cartilage. Physiologically relevant electric fields of 10-1000 mV/mm in magnitude are applied across the cell to observe the extent at which a cell's membrane potential may warp the electrical field experienced by the cell. Multiple cells are distributed to observe how their own electrical fields interact with each other and how an externally applied field morphs through/around a region of cells.

A device was designed and 3D printed for applying electric fields of 100 mV/mm to cells within a 10x10x0.4 mm volume. To assess the uniformity of the electric field and electrophoretic ion mobilities, a COMSOL model was generated. The concentration of ion species common to cell culture media and their respective diffusivities were used in the 'Transport of Diluted Species' module coupled to the field value determined by the 'Electrical Currents' module. Flow rates of fresh media were studied to determine the minimum flow rate at which uniform ion distribution is maintained at intervals of 0.5, 4, 12 hours.

RESULTS: For a single cell applied EFs of at least 400 mV/mm localize the cell's EF almost entirely to one side; this EF magnitude has also been the limit at which directional migration began to diminish. The multi-cell models show the electrical shielding of cells within the region and concentration of the field on the outer cells. The device models demonstrate the extent at which ion gradients are developed over time and that a perpendicular media flow of 6 $\mu\text{L}/\text{min}$ is sufficient to maintain uniform ion distribution.

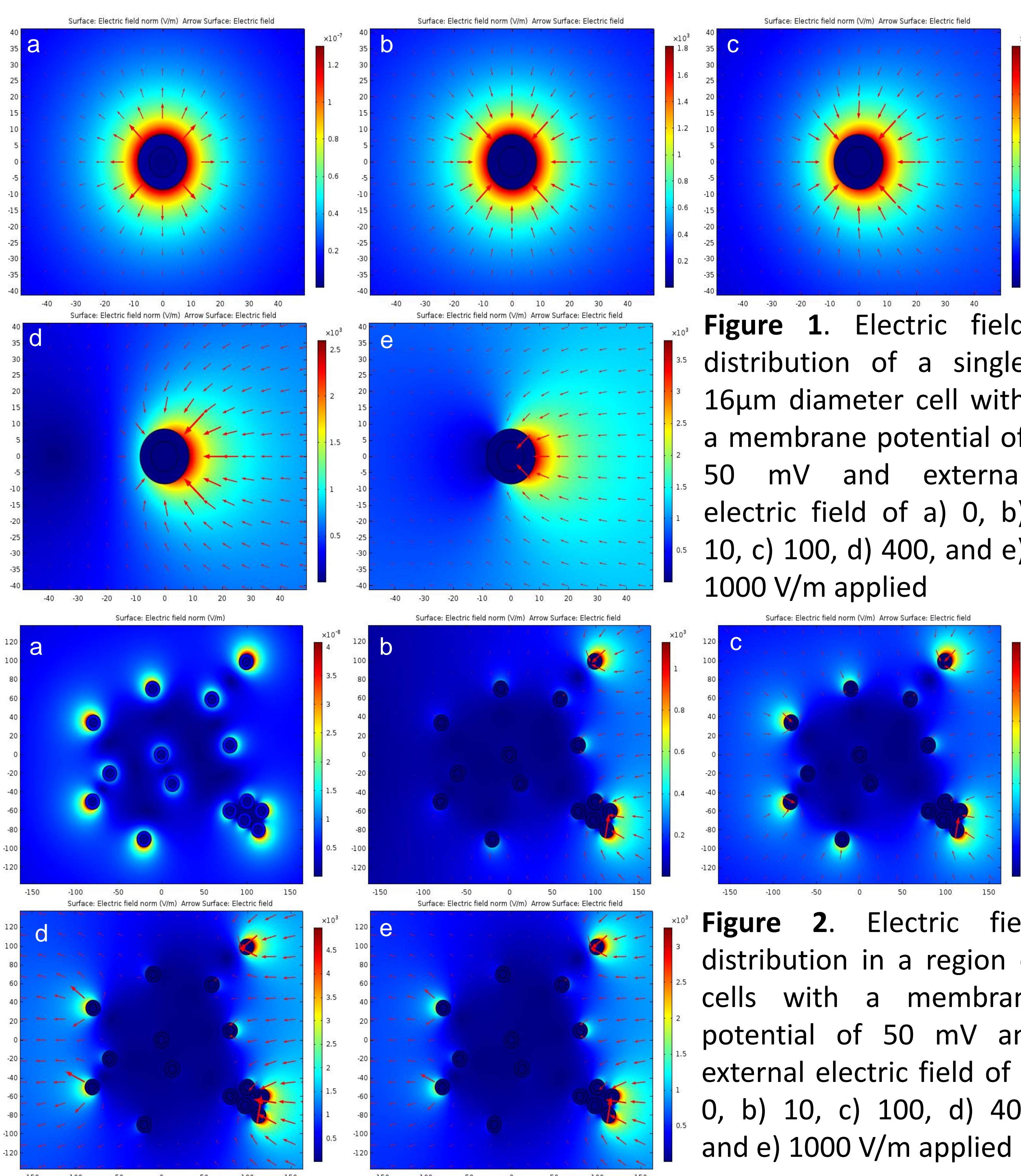


Figure 1. Electric field distribution of a single 16 μm diameter cell with a membrane potential of 50 mV and external electric field of a) 0, b) 10, c) 100, d) 400, and e) 1000 V/m applied

Figure 2. Electric field distribution in a region of cells with a membrane potential of 50 mV and external electric field of a) 0, b) 10, c) 100, d) 400, and e) 1000 V/m applied

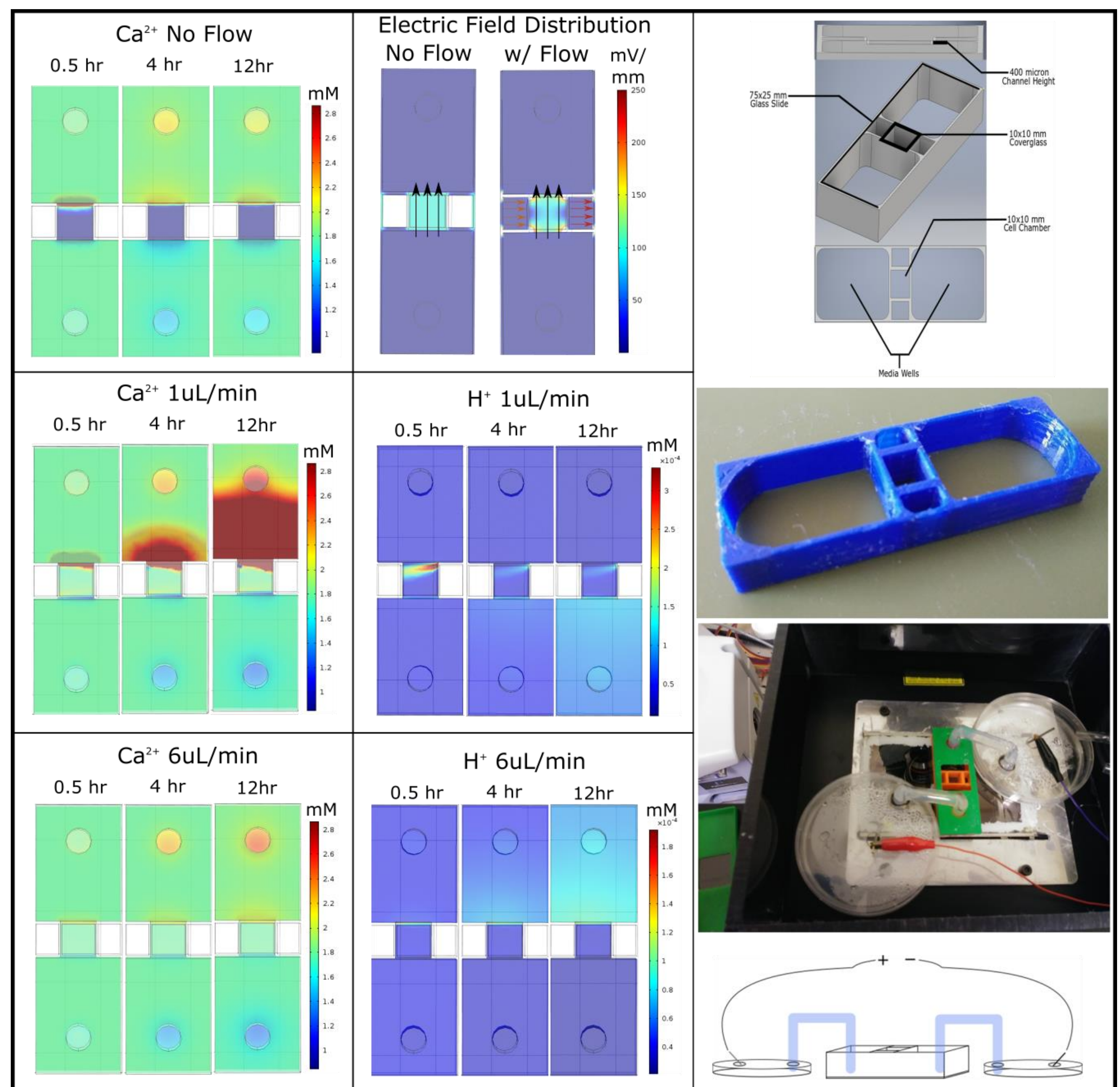


Figure 3. Electric field distribution; Calcium/Hydrogen concentration; 3D printed Device; Device Setup in use with an ITO Heater developed with COMSOL modeling; EF application schematic

Ion Species	Charge	Concentration (mM)	Diffusivity(m^2/s)* 10^{-9}
Ca	2	1.802	0.793
Cl	-1	118.4	2.03
Mg	2	0.8114	0.705
HSO_4	-1	0.8114	1.33
K	1	5.365	1.96
H_2PO_4	-1	0.9084	0.846
Na	1	154.4	1.33
H	1	0.00003981	9.31
OH	-1	0.0002511	5.27

Table 1. Modeled Ion concentrations of the inorganic salts present in DMEM cell culture media; Ion charge; and Ion diffusivity constants

CONCLUSIONS: COMSOL can be used to explore physical processes present in cells. This exploration can be beneficial for the teaching of physics concepts to curious biomedical engineering students. In conjunction with studying the physics of cells, COMSOL can be an invaluable tool in designing devices for accurate experiments.

REFERENCES:

1. M. W. Stacey, A. C. Sabuncu, A. Beskok; Dielectric Characterization of Costal Cartilage Chondrocytes, Biochim Biophys Acta (2014)