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Electrically shielded dielectric elastomer actuators for the study of the mechanical perturbation of cardiomyocytes

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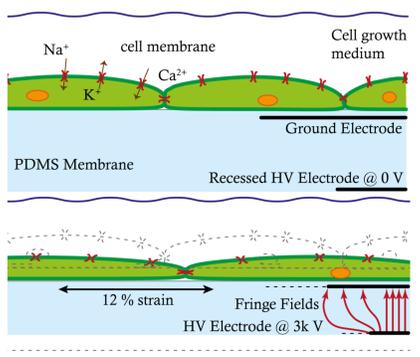
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Abstract

We present the development of a mechanically active bioreactor. Using dielectric elastomer actuators (DEA), we are able to mechanically perturb cell cultures in a controlled environment. With tailored pre-strain and compliant electrodes, it is possible to digitally control the strain state of the cell culture substrate and generate tensile strain exceeding 20%. This bioreactor enables new types of studies of cytomechanics. Specifically, we will use the bioreactor to study cellular mechanisms of cardiac arrhythmias that are related to mechano-electrical feedback. DEAs require high electric fields to generate physiologically relevant strain levels of 10%. Typically, potentials up to 5 kV are applied to electrodes that are located a few tens of microns from the cells. Resulting electrical fields may adversely affect cell physiology and mask the mechanosensitive response under study. To circumvent this problem, we present a stacked DEA design where the HV-electrode is embedded between grounded electrodes. This design practically eliminates the cells' exposure to fringe fields. Compared to a two-electrode configuration, it is shown that stray fields can be suppressed by six orders of magnitude. Tests on cardiomyocytes indicate that this layout is sufficient to prevent unwanted electrical triggering of the action potential. The device presented demonstrates the ability to combine electrically sensitive cells with mechanically active DEA bioreactors.

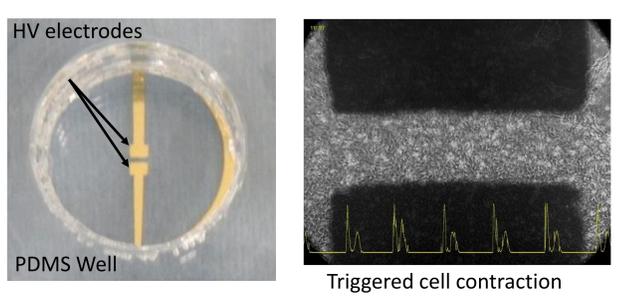
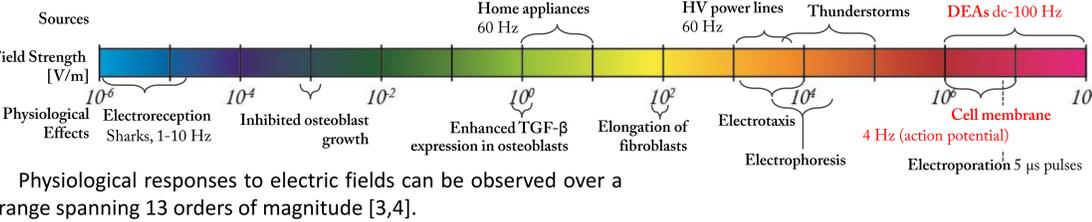
Introduction

We present the development of a mechanically active device suitable for new types of *in-vitro* cell physiology experiments. Using Dielectric Elastomer Actuators (DEA), a soft, stretchable, and compliant membrane replaces the static petri dish. Cells can be grown on such 'artificial muscles' and exposed to well defined strain, thereby approximating their native, dynamic environment. DEAs can add control over the mechanical degree of freedom for *in-vitro* studies, and thereby address the mechano-sensitive response of living cells. The strain is generated by applying a potential between conductive electrodes stamped on a prestretched PDMS membrane. To generate a linear strain of up to 20%, the applied electric field will reach an order of 10^8 V/m [1,2]. Naturally one must consider how such fields may influence the physiology of cells.



We determined the critical field experimentally by observing the response of cardiomyocytes to DEA activation in a static culture well. We then used finite element simulations to determine geometries that efficiently shield the cells. Finally, the fabrication steps to build a functioning device were established.

E-Fields in Biology and DEAs

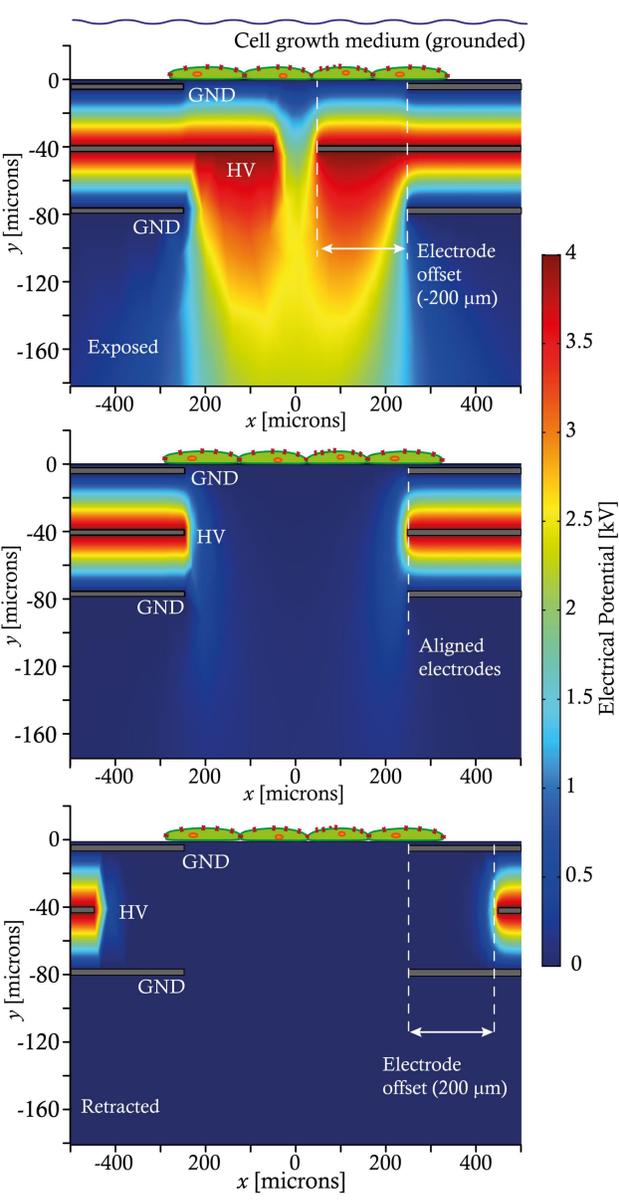
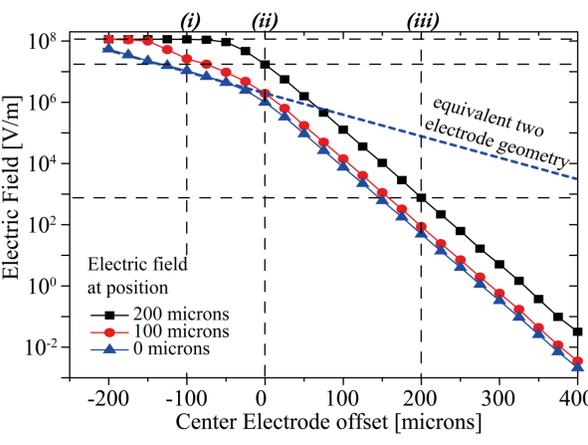


- #### Capacitive Coupling to Cardiomyocytes
- A 2 Hz 10^7 V/m square wave can trigger the action potentials in a cell culture
 - 6 hour exposure to electric fields of 4×10^7 V/m magnitude does not affect cell viability

To avoid unwanted electrical stimulation, cell cultures must be shielded from the electric fields generated in a DEA.

Finite Element Simulation of Shielded DEA

A finite element simulation can be used to determine the cells' exposure to an electric field generated by a DEA.

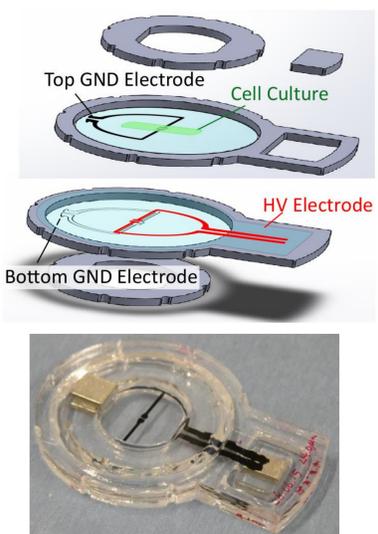


- Embedding the HV electrodes between ground planes suppresses the fringe field
- By retracting the HV electrodes by just 100 microns, the fringe field is suppressed by three orders of magnitude, in respect to the maximum electric field
- With maximum fields required for actuation in the order of 10^8 V/m, the resulting simulated fringe fields drop to 10^5 V/m, well below the critical fields observed to cause electrical activation of cardiomyocytes.

DEA with embedded HV-electrodes

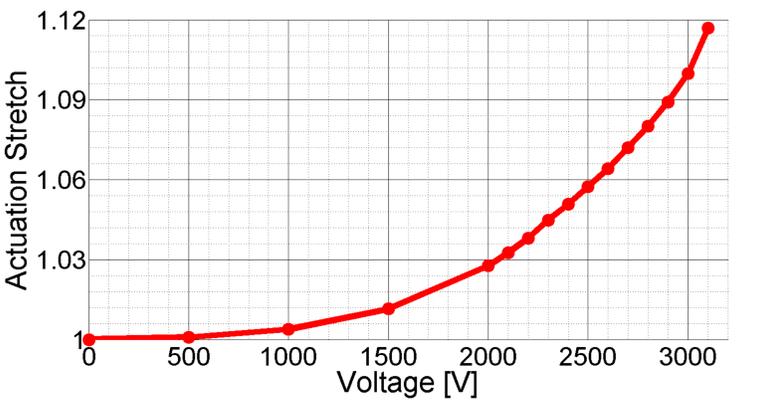
Fabrication steps (based on [5]):

- 1) Bi-axial pre-stretch of two PDMS membranes
- 2) Pad print the HV electrodes to one of the membranes
- 3) Combine the two membranes with oxygen plasma
- 4) Pad print GND electrodes on both outer surfaces of the stacked membranes



Electromechanical Response:

A uniaxial stretch reaching 12% is generated by a potential of 3.1 kV. Dielectric break-down occurs at 3.2 kV.



Conclusions

Cardiomyocytes can be capacitively triggered by electric fields exceeding 10^7 V/m. Finite element simulations illustrate how retracting an embedded HV electrode between two ground planes can strongly suppress the exposure of the cells to the electric fringe field. DEAs with embedded HV electrodes can be manufactured by bonding activated PDMS membranes with previously stamped electrodes. Given fabrication tolerances, it is shown that electric fields can be suppressed by three orders of magnitude while still exceeding 12% stretch.

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