

Supplementary Information

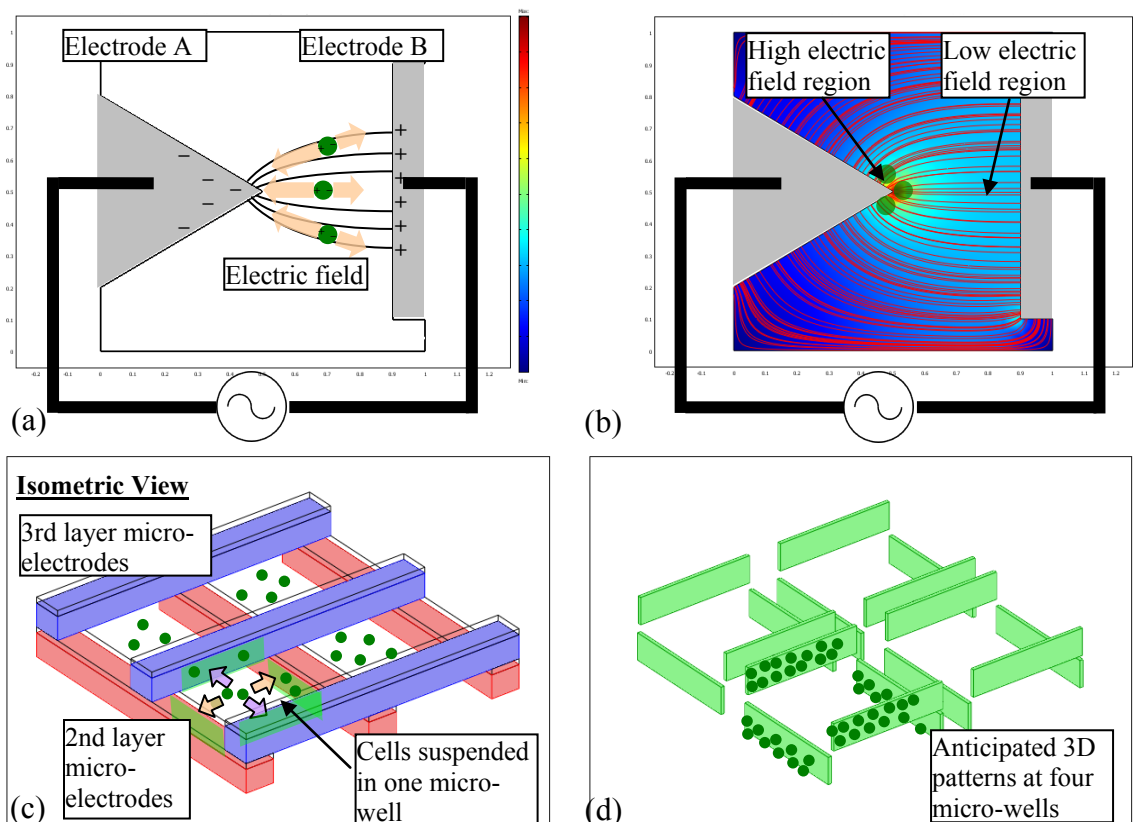
Title: Three-dimensional Cell Manipulation and Patterning using Dielectrophoresis via a Multi-layer Scaffold Structure

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Dielectrophoresis cell manipulation via the multi-layer scaffold

The multi-layer scaffold employed dielectrophoresis (DEP) to manipulate cells that were pipetted into the micro-wells of the scaffold, forming 3D cellular patterns for subsequent culture. In general, the mechanism of dielectrophoresis involves establishing a non-uniform electric field through electrode pairs as shown in Fig. S1(a). When the suspending cells are more polarizable than the surrounding medium, the induced DEP forces will manipulate the cells along the electric field gradient towards the high field regions as indicated in Fig. S1(b). In order to apply the DEP mechanism for 3D cell manipulation, the proposed scaffold utilized its multi-layer body as the electrodes to generate required non-uniform electric fields in the 3D domain. Based on the simulated result in Fig. 2(d) and (f), the suspending cells at different elevations were polarised by the field and manipulated towards the nearby micro-electrodes of the scaffold layers. Fig. S1(c) and (d) show the formation of the 3D cellular patterns from the stacked multi-layer scaffold structure. The cellular patterns that can be observed through the inverted microscope are shown in Fig. S1(e) and (f).

As discussed, the 3D cellular patterns are formed at the regions with high electric field and these regions are mainly dependent on the geometry of the integrated micro-electrodes in each scaffold layer. The proposed scaffold adopted a design that is similar to typical scaffold structures for cell and tissue cultures. With a supply voltage, high electric field regions were generated along the micro-electrodes facilitating cell manipulation via dielectrophoresis and the spatial resolution is correlated to the electric fields generated from the micro-electrodes. Through experiments, it is confirmed that a higher voltage input can generate higher electric field gradient at the micro-electrodes, inducing stronger DEP force on the suspending cells to construct denser 3D cellular patterns. Different types of biological cells were also examined. The cellular pattern from the HFF cells stained with LysoTracker Green is shown in Fig. S1(g) and (h), while the cellular pattern from another scaffold with 3T3 cells is shown in Fig. 5(b) and (c). Results showed that a wide range of cells can be seeded into the scaffold with this technique to culture cells and tissues for various applications.



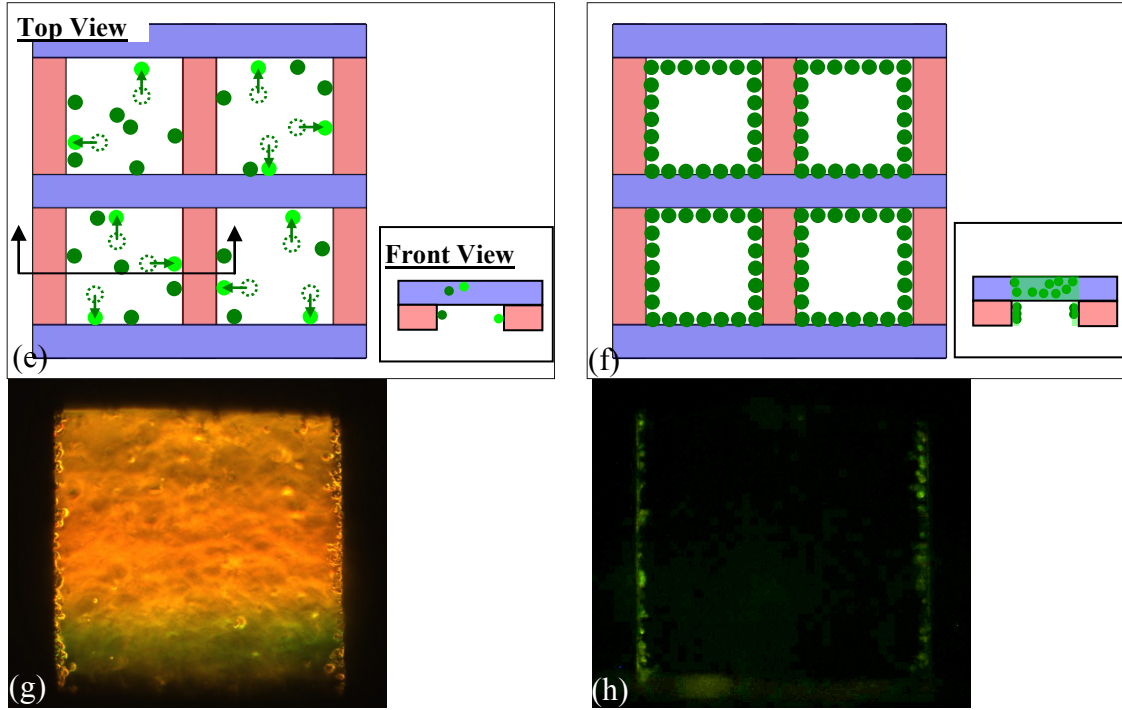


Fig. S1. (a) Cell manipulation via dielectrophoresis under a non-uniform electric field; (b) Cells manipulated towards the high electric field regions; (c) Cells suspended in different micro-wells of the scaffold; (d) Anticipated 3D cell pattern from the multi-layer scaffold; Cell pattern observed through the microscope: (e) at start; (f) at the end; 3D pattern from HFF cells: (g) brightfield image; (h) fluorescent image