Supplementary Information

"On-chip lysis of mammalian cells through a handheld corona device"
Manuscript ID LC-TIN-09-2014-001042

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S1. Control experiment - Electrical lysis

As a control experiment cells were electroporated in a previously reported microsystem [1]. The methods are summarized as follows: Cells were harvested from culture flasks by trypsinization and re-suspended in isotonic sucrose buffer (adjusted to pH 7.4). For discrimination of live and dead cells the isotonic sucrose buffer was supplemented with the fluorescent live stain calcein AM and the dead stain propidium iodide. The cell suspension was loaded into a 100 uL glass syringe (ILS, Germany). Flow was provided by a syringe pump (nemesys, Cetoni GmbH, Germany) and the cells were injected into a microfluidic chip via a glass capillary (see supplementary Fig. 1). The chip was fabricated as a glass - SU-8 - glass sandwich device with facing platinum electrodes. These 18 um wide electrodes at the top and bottom of a channel (40 µm x 40 µm cross section) provided an electrical interface to the cells flowing through the channel. An AC voltage of 8 V amplitude and a frequency of 10 kHz was applied between the electrodes. This electric field was switched on for one single passage of a cell between the electrodes. The chip was placed on top of an inverted fluorescence microscope (DMI 6000, Leica Microsystems, Switzerland), and imaging was performed using a DFC340 camera (Leica Microsystems, Switzerland). For observation of the cells, the flow was inverted and the cell was shuttled back-and-forth for several minutes to allow for assessing the electroporation effects.

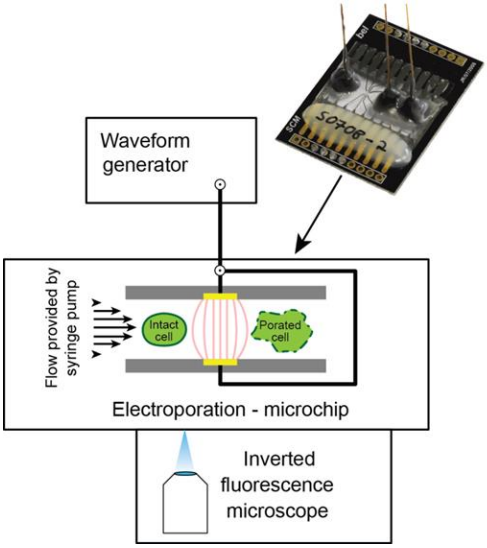

Fig. S1 Schematic representation of the control experiment for conventional electrical lysis in an integrated microfluidic platform.

S2. Dielectrophoretic forces

The DEP forces exerted on a particle with spheroid-like morphology in a fluid is:

$$F_{DEP} = 2\pi R^3 \varepsilon_m Re(f_{CM}) \nabla {E_{RMS}}^2 \quad \text{(S2.1)}$$

where R is the radius of the particle, ε_m is the permittivity of the medium, E_{RMS} is the root-mean-square of the alternating-current external electric field and $Re(f_{CM})$ is the real part of the Clausius-Mossotti (CM) factor depending on the complex permittivity of the particle and the medium, ε_p^* and ε_m^*, as follows:

$$f_{CM} = \left[\frac{\varepsilon_p^* - \varepsilon_m^*}{\varepsilon_p^* + 2\varepsilon_m^*}\right] \quad \text{(S2.2)}$$

As indicated by the literature, the dielectrophoretic properties of mammalian cells generally correspond to one of three different frequency groups. The dominant factor at frequencies under the 10^2 Hz mark is the surface charge of the cell, whereas the dielectric permittivity of the cell rules at frequencies above ~10^3 Hz.[1] Determination of the dielectric properties of mammalian cells can be approached by using a proposed protoplast model by neglecting the conductance of the cell membrane,[2] which leads to a CM factor defined by the following expression for viable cells:[1, 2]

$$f_{CM}(\omega) = -\frac{\omega^2(\tau_m\tau_c^* - \tau_c\tau_m^*) + j\omega(\tau_m^* - \tau_m - \tau_c^*) - 1}{\omega^2(2\tau_m\tau_c^* + \tau_c\tau_m^*) - j\omega(\tau_m^* + 2\tau_m + \tau_c^*) - 2} \quad \text{(S2.3)}$$

where $\tau_c^* = c_m R/\sigma_c$ and $\tau_c = \varepsilon_c/\sigma_c$ are time constants, c_m is the cell membrane capacitance, and σ_c and ε_c are the cytoplasm electrical conductivity and permittivity. In previous studies, mammalian cells have shown strong nDEP at low frequencies and strong pDEP at high frequencies. This characteristic difference have enabled sorting of viable and non-viable cells due to their inherent dielectric characteristics.[3] Specifically, for frequencies higher than 10 kHz and less than MHz, experimental studies demonstrate that cells experience strong pDEP within the high electric field region that decays exponentially with distance due to the force dependence on the field gradient.[1, 4, 5] A schematic representation of the particle (i.e. the cell) under the influence of a DEP force is shown in Fig. S2.

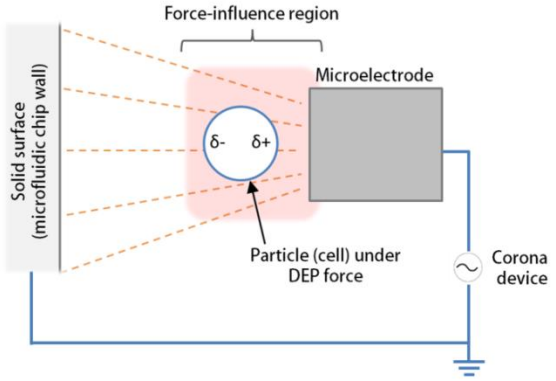

Fig. S2 Schematic representation of a pDEP force acting on a particle, due to an electric discharge from a handheld corona device.

Under the influence of DEP forces, particles, such as cells, may follow different traveling behaviors when they are close to microelectrodes.[6] This traveling behavior depends on the CM factor and travelling motion forces due to induced electrokinetics. Particles may experience both pDEP and motion forces, and the ratio of these defines the regions in which the particle is attracted or repelled. If the real component of the CM factor is dominant, the particle will be attracted to the electrode, but if the real part is small and the imaginary part is dominant, for instance, the particle may exhibit an apparent erratic motion along the edges of the electrode. This means, as explained by Hughes,[6] that the attracting forces and the motion forces are of similar magnitude (i.e. $|Im[f_{CM}(\omega)]| > 4Re[f_{CM}(\omega)]\ and\ Re[f_{CM}(\omega)] > 0$) then the net force depends on whichever force prevails due to, for instance, local electric field gradients. The effect of the force is spatially variable and, at shorter distances, pDEP may dominate. The particle, or cell, may also experience some motion even within a region close to the microelectrode. The strength of the force, however, decays with distance and cells at a certain distance from the electrode may actually be pushed away due to other forces (e.g. electro-hydrodynamic), also observed in the experiments in this study. The direction of the resulting force vector in DEP is characterized by a cross-over frequency. Experimental studies have demonstrated that viable cells may experience a transition from nDEP to pDEP, and *vice versa*, depending on the combination of the real and the imaginary components of the CM factor.[7] It is important to note that the complete picture involves a more complex electro-hydrodynamic scenario with additional hydrodynamic and electrothermal-induced forces occurring in the bulk liquid. Our experimental observations, however, agree well with the study reported by Menachery et al. and confirm that cells experience a pDEP force past the crossover frequency. Figure S3 shows that this field region lies within ~10 microns from the microelectrode, which is a length scale comparable to the size of one cell. For this reason, the cells within this region are strongly influenced by the DEP force, while the cells in the more distant regions experience a combination of forces including, for instance, hydrodynamic effects.[8, 9] Only the cells in the vicinity of the electrode get strongly attracted, experience the high electric field and get lysed: the force decays by about 3 orders of magnitude within a distance of ~30 microns.

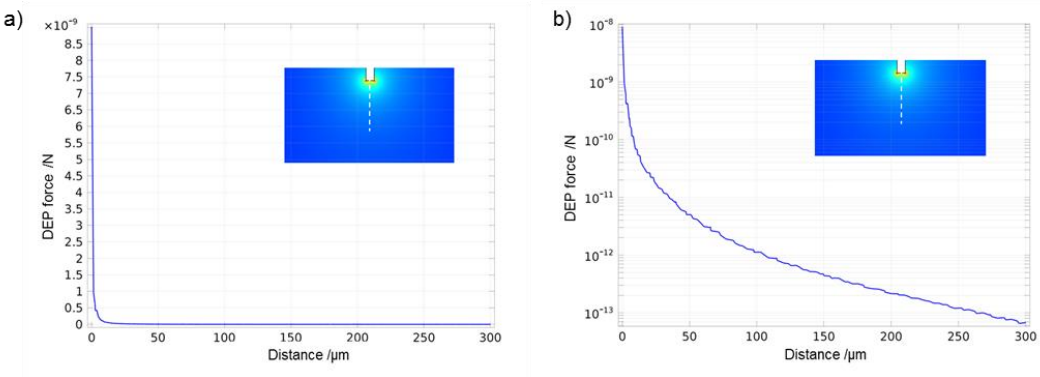

Fig. S3 Dielectrophoretic (DEP) force results from FEA simulations in a) normal and b) semi-logarithmic scale. The forces are plotted along the dashed line shown in the figure inset as a function of distance from the electrode. The inset shows the electric field results of the same simulation in color code.

S3. Finite Element Model Simulation

The simulations were performed using the Microfluidics, Particle Tracing and Electric Currents modules in COMSOL Multiphysics 5.0 software. The simulations rely on a 2D model of the 20-micron-width microelectrode integrated into the microfluidic chamber. The mesh of the geometry was formed by free-triangular elements with extra-fine refinement at the interface between the electrode and the medium (i.e., the dielectric). The minimum element quality of the mesh was 0.8 as observed in Figure S4. If not otherwise stated, water standard values were used for the density and dynamic viscosity of the medium, while the conductivity was set to 87 mS/cm. The electric current component of the model included the simulation of a 4.5 MHz AC electric field using the frequency domain feature in the electric current module. Creeping flow was used for the microfluidic component of the simulation, setting no-slip conditions at all boundaries. The dielectrophoretic (DEP) force was simulated using the Shell feature of the Particle Tracing module, assuming a thin-shell cell model. The parameters used for the shell model are: cell density 1050 kg/m^3, cell diameter 10 µm, cell conductivity 0.25 S/m, shell electrical conductivity 10^{-6} S/m, shell relative permittivity 20, shell thickness 8 nm, particle density 1050 kg/m^3, medium viscosity 10^{-3} Pa*s and medium density 10^3 kg/m^3.

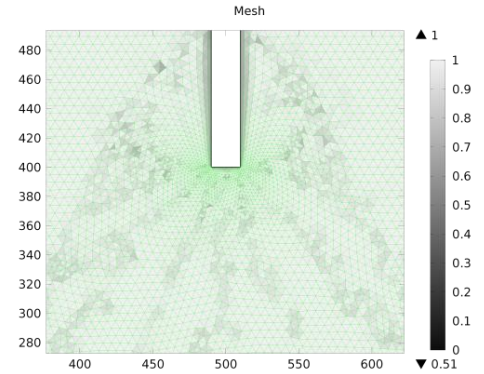

Fig. S4 Mesh quality image of the FEA simulation model in COMSOL.

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