Supporting Information

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SI Text

We assumed that the redox mediator (ferrocyanide) present in the solution underwent a simple one electron transfer as shown below and the tip was held at diffusion controlled potential to avoid any kinetics complications.

$$R(\text{soln}) \rightarrow O(\text{soln}) + \text{ne}$$

where, R represents ferrocyanide species and O represents ferricyanide species.

Because the redox species O and R moved toward and away from the electrode surface only by concentration gradient Fick's second law of diffusion was used in the simulation. The concentration of species R is given as $c_R(r,z,t)$ and the diffusion equation in cylindrical coordinates is described as

$$\frac{\partial c_R}{\partial t} = D\left(\frac{\partial^2 c_R}{\partial r^2} + \frac{1}{r}\frac{\partial c_R}{\partial r} + \frac{\partial^2 c_R}{\partial z^2}\right)$$

where r and z are the coordinates as shown in Fig. S4; t represents time; c and D represent the concentration and diffusion coefficient of species R.

The boundary conditions at $t > 0$

At the tip: $0 < r < a$, $z = h1$

$$c_R(r,h1) = 0$$

$$c_O(r,h1) = 4$$

At the substrate: $0 < r < r_m$, $z = h2$

$$\frac{\partial c}{\partial z} = 0$$

At the cell membrane: arc1, $d < z < h2$

$$\text{Flux of } R \text{ across the acr1} = P^*(R\text{-}R1)$$

where, P (m/s) is the permeability of species R across membrane or acr1 in the simulation. R and $R1$ represent the species outside and inside the cell respectively. Also, the glass sheath surrounding the electrode was considered as an insulator.

Initially the concentration inside the cell was zero and the concentration in the bulk solution was 4 mM or 4 mol/m^3. The species R was consumed by the cell depending on the permeability value of the membrane as well as by the tip located at 16 μm away from the substrate. The current at the electrode was determined by

$$I_{\text{tip}} = \int_{r=0}^{r=a} 2\pi n F D_R r \frac{\partial c_R(r,h2)}{\partial z} \text{dr}$$

Where, $n = 1$; $F = 96485$ C/mol; and $D_R = 1 \times 10^{-9}$ m^2/s;

The simulation model described above was solved by finite element method where the mesh was increased in exponential grid fashion to generate two-dimensional grid at the regions where sharp change in the concentration gradients were noticed.

X-Scan Simulation. HeLa cell was assumed to be semielliptical shape with symmetry along z-axis as showed in Fig. S4. In this model, permeability was assumed to be zero along cell membrane or arc 1 since topography was the subject of interest here. The 10 μm tip with RG = 10 was also considered symmetrical along z-axis (Fig. S4). The tip was held at diffusion controlled potential at all times over the cell or arc 1 and the model was solved in steady state solver condition with the aid of Comsol Multiphysics software. The tip to dish distance was maintained at 16 μm at all times. Each red dot in Fig. 3*B* corresponds to simulated tip current calculated over a specified position on arc 1. For example, the lowest normalized peak current in Fig. 3*B* was calculated over the highest point of arc 1 as showed in Fig. S4. To measure the tip current at different position over the cell, the arc 1 was moved toward left by a distance of 1 μm out of the active simulation sub domain instead of tip moving over the arc 1. This imitates the same condition such as a tip was moving over a cell in x-direction. Due to symmetry of cell along z-axis, scanning along arc 1 was adequate to obtain the full simulated x-scan over the cell. Both height and radius of cell were considered as adjustable simulation parameters and were fitted with experimental data as showed in Fig. 3*B*.

Permeability Measurement. Simulations were done first with $P = 0$ at arc1 (i.e., without any added surfactant) to determine the current at the tip for the certain fixed height of the cell. Then after that different value of P in the range of zero to 8.7×10^{-6} m/s was used in the simulation to fit the experiment data. The tip current was always calculated with the tip located right above the highest point of the cell height. For example, when $P = 1.5 \times 10^{-6}$ m/s the concentration inside and outside the cell was calculated until $t = 1$ min and then the tip was brought close to the cell top i.e. 16 μm away from the dish and held there for 0.1 s (because the speed of tip x-scan was 1 μm/0.1 s) to record the current at $t = 1.1$ min. The tip was then withdrawn from the top of the cell and the concentration gradient across the cell was again calculated with new value of parameter of P. The steps were repeated until $t = 60$ min.

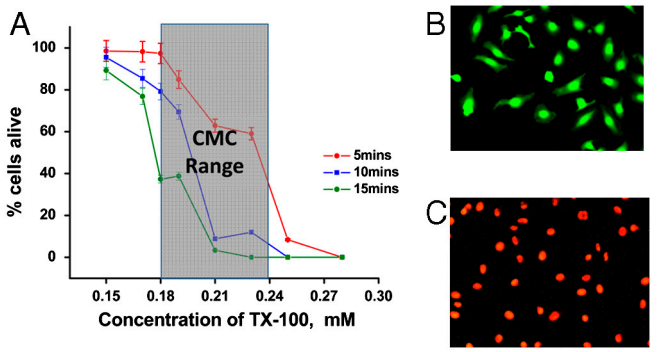

Fig. S1. (*A*) Fluorescence based viability assay to HeLa cells exposed to different concentrations of TX100 for 5, 10, and 15 min. (*B*) Optical microscope image of green dyed cells representing the intact membranes of living cells and (*C*) of red dyed cells representing the collapsed membrane of dead cells.

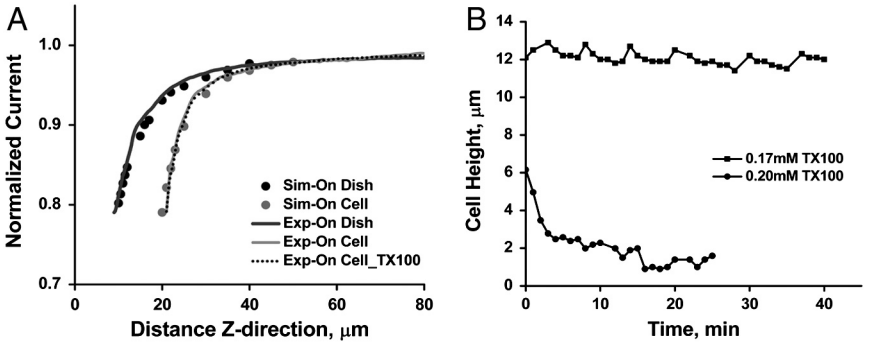

Fig. S2. (*A*) Approach curves over dish and on single cell in absence and presence of 0.17 mM of TX100 and 4 mM redox mediator in solution. The experimental approach curve fitted to theoretical negative feedback approach curve over dish and over cell to determine the pre-TX100 treated cell height. (*B*) The apparent cell height vs. time in presence of 0.17 mM and 0.20 mM of TX100 respectively.

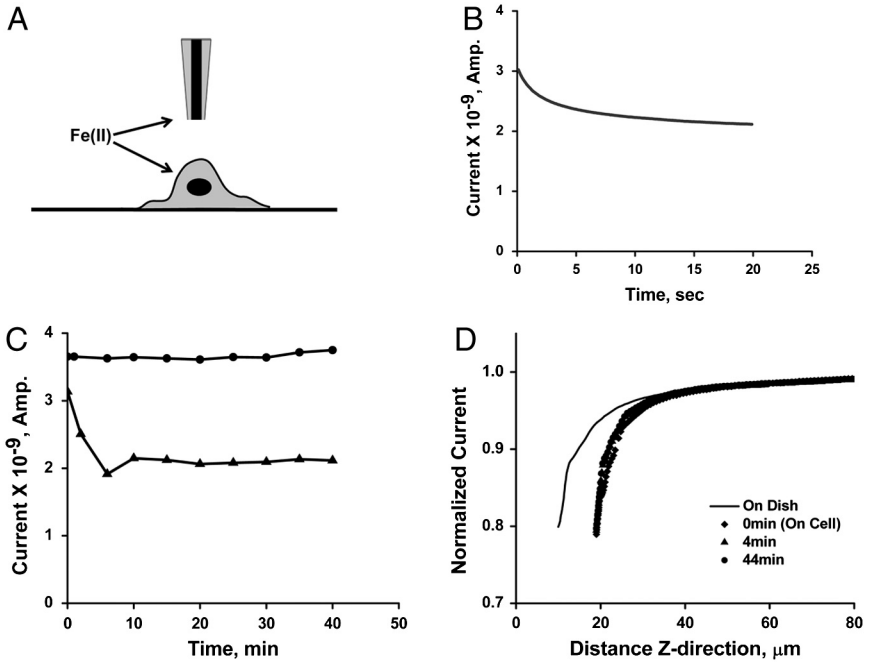

Fig. S3. Tip currents and approach curves after different exposure times. (*A*) Schematic representation of the 10 μm Pt tip held 5 μm above a single cell at a constant potential of 0.5 V in buffer containing 4 mM ferrocyanide and 0.17 mM of TX100. (*B*) Current-time response over the cell. (*C*) Sampled current at $t = 20$ s was plotted against time of exposure of cell to TX100. Red and blue lines represent the sampled current response in the bulk solution ($i_{T,\infty}$) and over the cell, respectively. (*D*) Approach curves over dish and over single cell in the absence and presence of 0.17 mM of TX100.

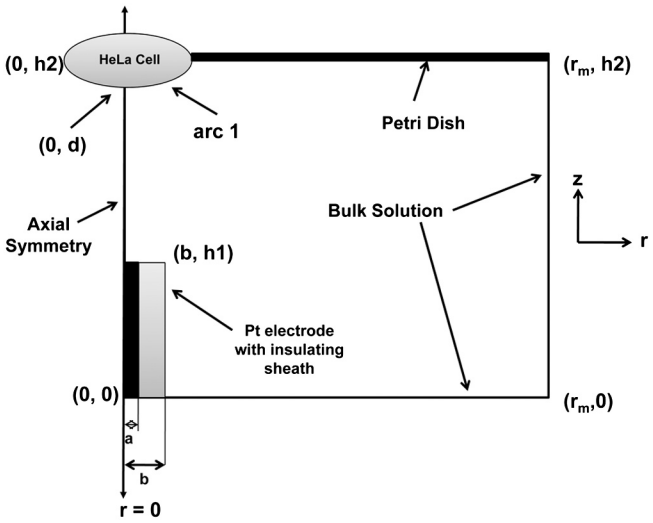

Fig. S4. The schematics of simulation model in 2D axial symmetry.