Electronic Supplementary Information

A compartmentalized microfluidic chip with crisscross microgrooves and electrophysiological electrodes for modeling the blood-retinal barrier

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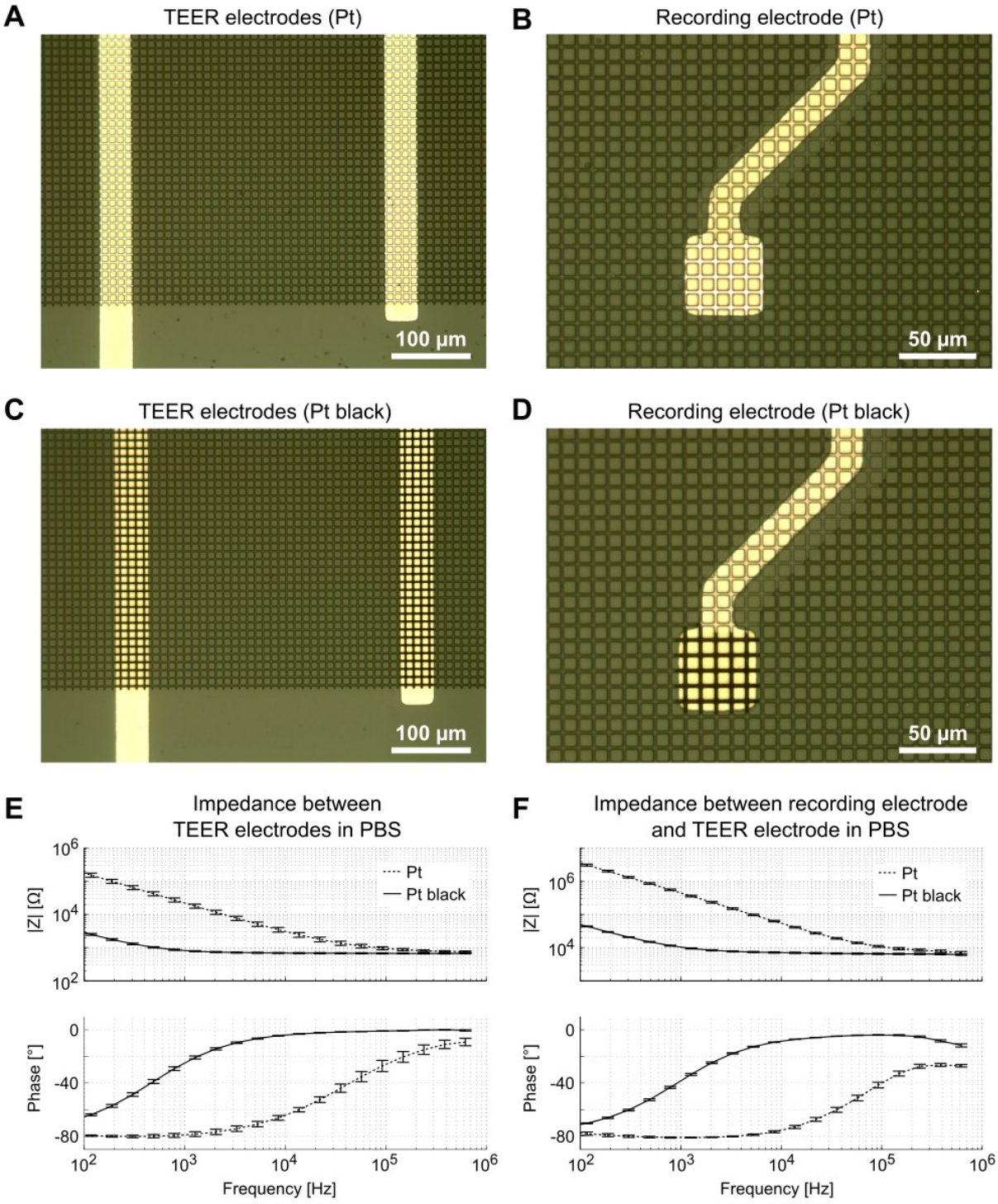

Fig. S1 Electrochemical coating of platinum (Pt) black. (A-B) Microscope images of TEER and recording electrodes before platinization. (C-D) TEER and recording electrodes after being electrochemically coated with a layer of Pt black. Pt black was deposited by constant potential amperometry applying -0.2 V for 12.5 s on the electrodes against an Ag/AgCl reference electrode. (E-F) Impedance spectra measured between (E) TEER electrodes and between (F) a recording electrode and a TEER electrode in phosphate-buffered saline (PBS) (0.9 % NaCl, w/v) (n = 8).

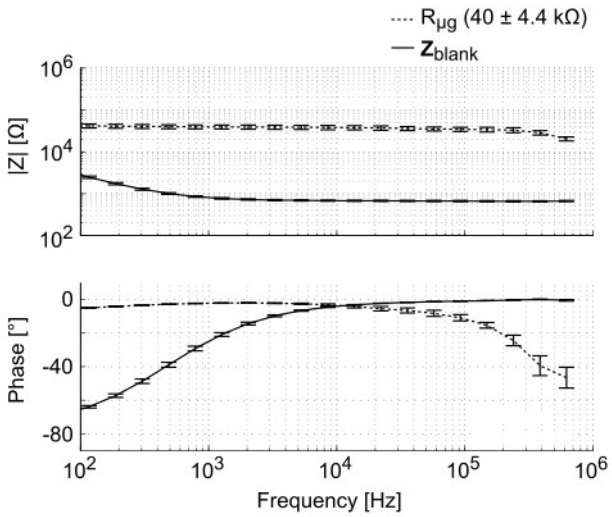

Fig. S2 Bode representation of the Impedance of the solution contained in the microgrooves ($R_{\mu g}$). This measurement was performed pouring a drop of PBS over the chip and pressing the drop with a piece of flat PDMS. $R_{\mu g}$ was 40 ± 4.4 kΩ (n = 8). There is also included in the figure the impedance spectra measured without the PDMS.

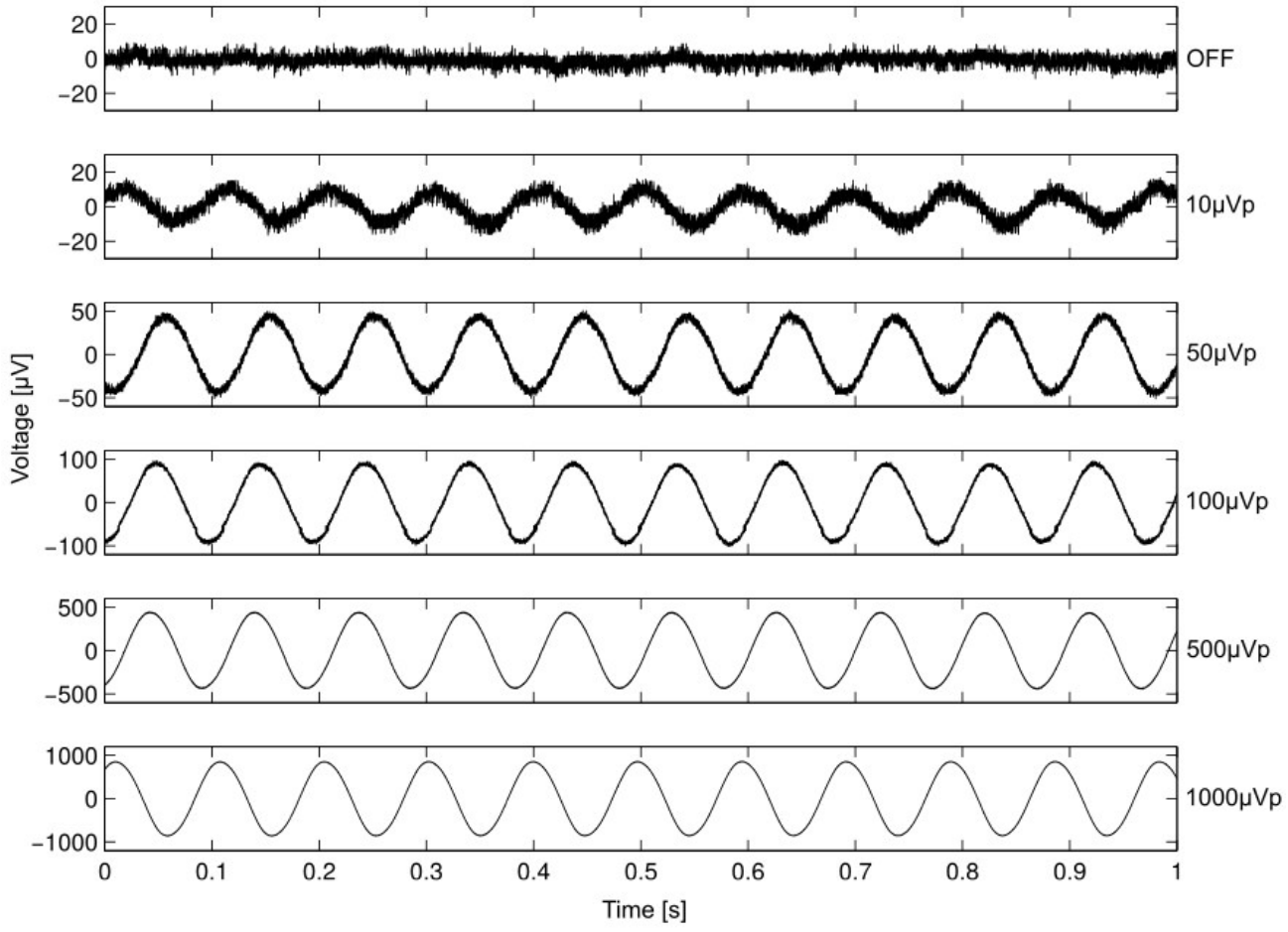

Fig. S3 Validation of the electrodes for recording of extracellular field potential. Recording electrodes were validated by measuring a simulated signal of 10 Hz and 0, 10, 50, 100, 500, and 1000 µVp. This signal was generated with a sine wave generator (g.SIGgen, Guger Technologies OG, AT) and applied to the PBS solution through an external Pt wire electrode. Recording was made using an open-sourced tool for electrophysiology (Open Ephys, www.open-ephys.org). The average noise value for 24 electrodes of a device was lower than 5 μV_{rms}.

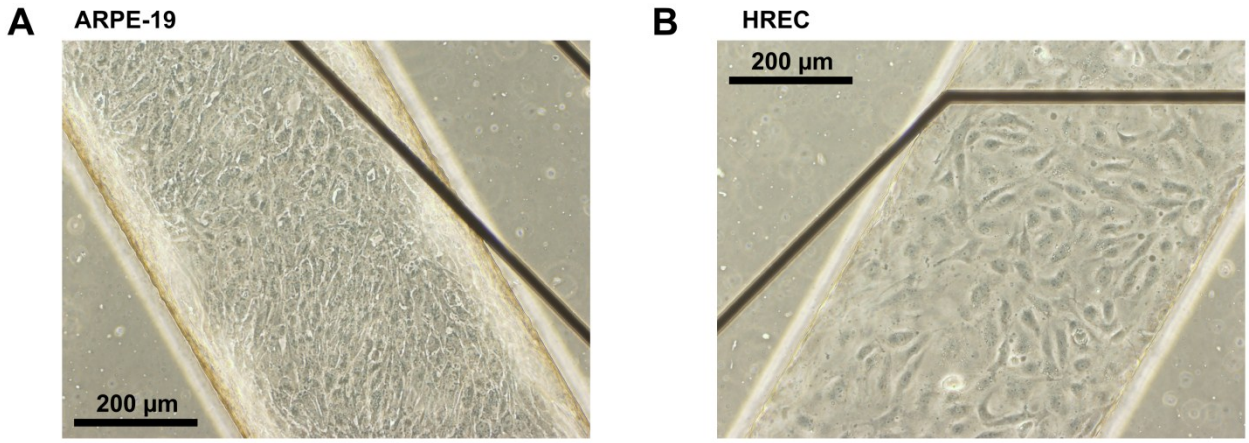

Fig. S4 Light microscopy of ARPE-19 (A) cells and HREC (B) after 3 days in the µBRB. Images were taken in the microfluidic inlets outside the grid of microgrooves. Note that black lines are the electrical tracks that connect the electrodes with the pads.

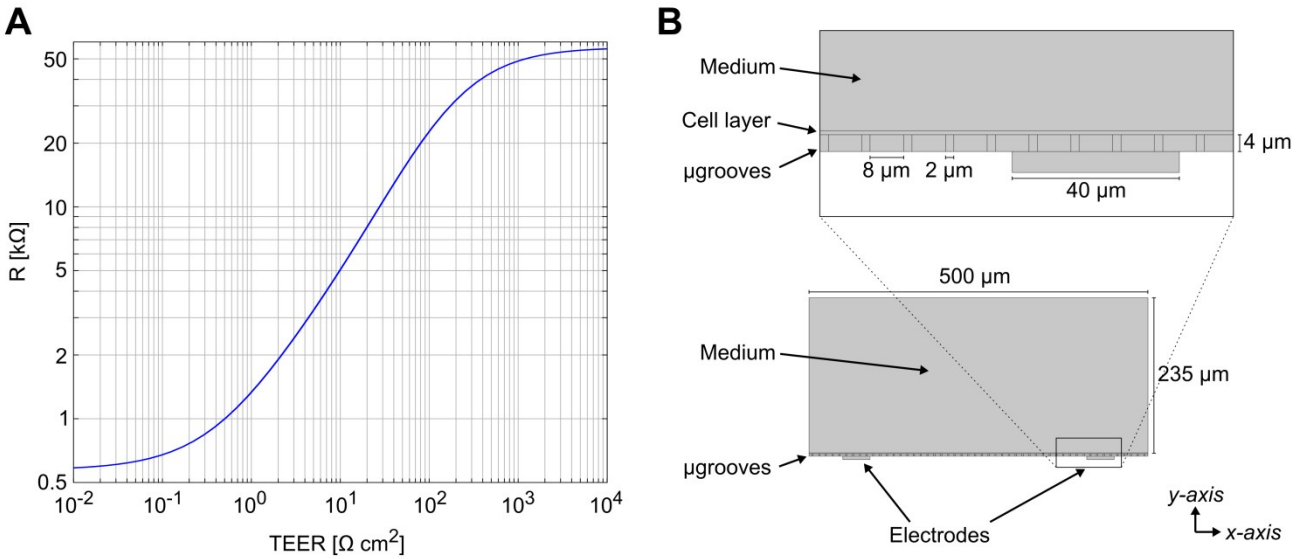

Fig. S5 TEER normalization to area obtained by numerical study. (A) Resistance measured (R) with the system as a function of the TEER in units of $\Omega\,cm^2$. The numerical study was performed according to our previous study[1] using a commercial software package for finite element method analysis (COMSOL Multiphysics version 5.1 and its AC/DC module). (B) Schematic representation of the simulated model with dimensions. The model is a 2D vertical cross-section of the microfluidic system including a cell layer, a medium compartment, microgrooves and electrodes. Cell barriers with different TEER values were simulated by changing the conductivity of the area of the cell layer. Electrical conductivity of the medium and the microgrooves was 1.5 $S\,m^{-1}$. The conductivity in the space of 8 µm between microgrooves was 0.3 $S\,m^{-1}$ (microgroove separation was divided by the width of microgrooves (10 µm / 2 µm)) to account for the microgrooves in the *x-axis* direction.

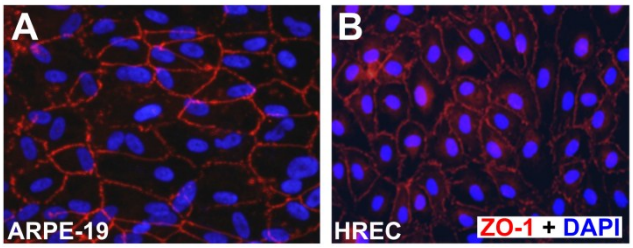

Fig. S6 Merge of ZO-1 (red) and DAPI (blue) immunofluorescence in (A) ARPE-19 cells and (B) HREC in cell monolayers (X20) at the 3rd day of culture.

References

1 J. Yeste, X. Illa, C. Gutiérrez, M. Solé, A. Guimerà and R. Villa, *J. Phys. Appl. Phys.*, 2016, **49**, 375401.