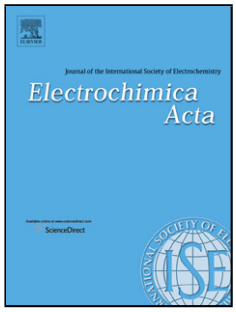

Title: pH fronts and tissue natural buffer interaction in gene electrotransfer protocols

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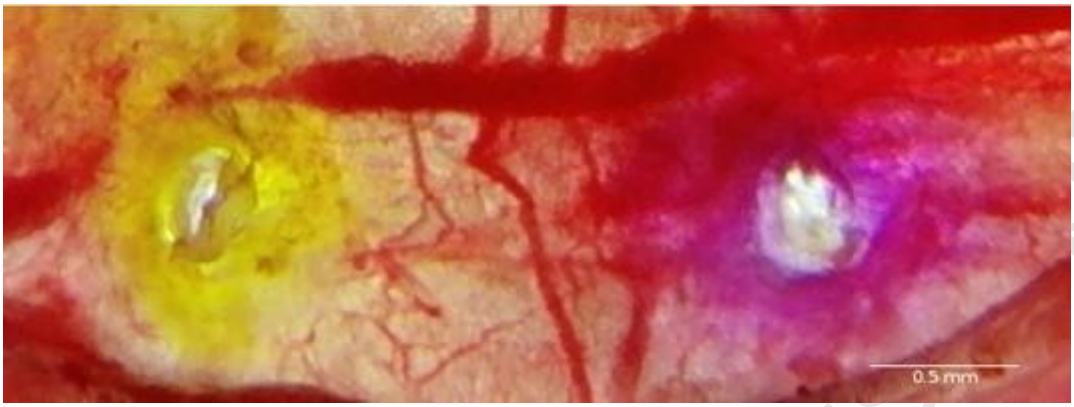
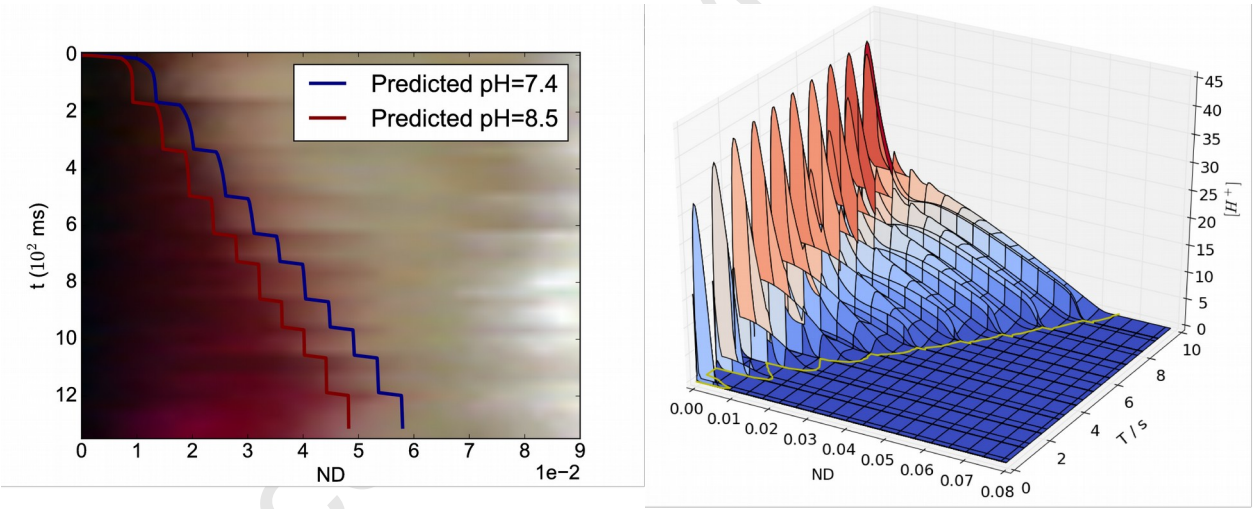


2D snapshot of pH fronts induced by GET (10 pulses of 40 V, 20 ms at 1Hz) in mice observed by intravital microscopy through a dorsal skinfold chamber. pH front visualization was done using phenol red as acid and basic indicator. Anodic acid front (left electrode) and cathodic basic front (right electrode) revealed as light yellow and pink-red areas, respectively. Thick and thin red stripes (hemoglobin) represent the capillary network. Image was taken 30 minutes after the end of the last pulse.



Left image: Experimental space-time (ms) diagram of the evolution of the pulse interaction with the pH front-buffer fluctuation in a zone close to the cathode induced by a GET protocol; red and blue lines are predicted pH=8.5 and 7.4 front trajectories. Right image: Simulated space-time evolution of the hydrogen ion concentration. The pH=5.5 yellow line separates non-physiological from physiological pH states. Images unveil a remarkable behavior tuned by pulse length and intensity: during the ON pulse pH fronts jump forward, during the OFF cycle, pH fronts recede due to tissue natural buffer neutralization.