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Nanopiezoelectric biointerfaces

Michael McAlpine

Piezoelectric nanoribbons permit the electrical recording of cell's mechanical responses to electrical stimulation.

The ability to directly interface energy conversion materials with the body and with tissue could open new avenues for powering portable, wearable, and even implantable biomedical devices.[1,2] A promising approach is to harness mechanical interactions that are fundamental to cellular biology and physiology at the cellular level. For example, mechanical processes such as neurite elongation are vital to structural remodeling of neurons and synapse formation.[3] Simultaneous measurement of a cell's mechanical and electrical responses offers the best route to understanding its behavior.

Mechanical tension in the cell membrane plays a key role in axonal development, and mechanical stimulation can profoundly impact nerve regeneration. Notably, numerous studies have shown that there is a measurable volume change that accompanies membrane depolarization or action potentials.[4–6] In particular, nanometer-scale swelling has been measured in cells, including neurons, via atomic force microscopy (AFM). This voltage-induced membrane deformation is a universal property resulting from changes in membrane tension that can be explained by thermodynamics and basic mechanics.[7,8] The magnitude of this effect depends on cellular mechanical properties such as rigidity and elasticity.[7,9]

To date, a number of techniques have been developed to interrogate cellular mechanical interactions and rigidity, such as optical tweezers,[10,11] magnetic twisting cytometry,[12] and elastomeric posts.[13] Yet, for small, irregularly shaped cells with fragile membranes such as neurons, smaller tools are required.[14]

Electrical recording from cells, including neurons, can be successfully performed using nanoelectronic materials such as silicon nanowires and graphene.[15] These nanomaterials have a small active area, offering minimally-invasive electrical measurements of exceptional sensitivity and resolution. However, these nanosensors have not been used to probe mechanical deformations from cells, although some intriguing studies hint at this direction.[16,17] Atomic force microscopy is still the most commonly utilized tool for quantification of the cellular deformation, despite its complexity and invasiveness.

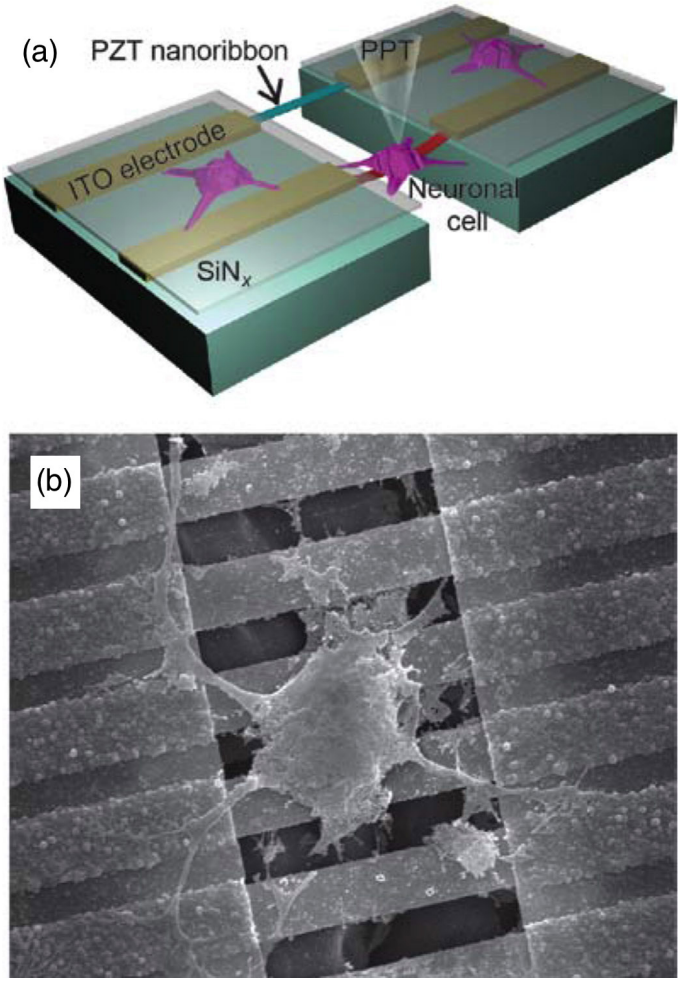

Figure 1. *(a) Schematic of cells interfaced on a piezoelectric nanoribbon device. (b) Image of a single neuronal cell interfaced with suspended lead zirconate titanate (PZT) nanoribbons. PPT: Pipette. ITO: Indium tin oxide. SiN_x: Silicon nitride.*

We have used high-performance piezoelectric nanomaterials such as lead zirconate titanate (PZT), which has charge constants up to 140pm/V,[1,18,19] in novel electromechanical biointerfaces for simultaneous imaging and electrical recording of small voltage-induced cellular deflections.[20]

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First, we used standard microfabrication techniques to make PZT nanoribbons, which we characterized using AFM to measure the voltage obtained from a known applied force.[1] We then designed and fabricated the nanoribbons to maximize the electromechanical response to small cellular deflections, and to allow for simultaneous imaging and electrical recording. A schematic of the experimental design is outlined in Figure 1, which shows several key features. First, PZT nanoribbons were suspended like plank bridges over a gap between two magnesium oxide substrate blocks: this enabled us to measure the deflection (stretching) of the nanoribbons, which would not have been possible if they had been fully supported along their length. Second, the underlying substrate of transparent magnesium oxide[18] and transparent indium tin oxide electrodes facilitated backside chip visualization during electrophysiology measurements. These electrodes were electrically isolated by coating them with silicon nitride to eliminate any cross-signal response when the chip was placed into solution.

We next cultured 'neuron-like' cells, known as PC12 cells, which acquire many of the characteristics of sympathetic neurons when treated with nerve growth factor.[21] We cultured these cells on the PZT chip, and used a standard glass electrode for membrane voltage stimulation of those cells located on the nanobeam arrays. Figure 1 shows a cultured PC12 cell that developed morphologically normal neurites directly on the PZT array. We showed that PZT nanoribbons can measure mechanical deformations of neuronal cells in response to electrical excitations. Cells deflect by 1nm when 120mV is applied to the cell membrane.[1]

Finally, we also transferred arrays of PZT nanoribbons onto a silicone elastomer and measured mechanical deformations on a cow lung that mimics respiration. We transferred the PZT nanoribbons onto the elastomer polydimethylsiloxane and interwove gold contacts. This device was then transferred onto the cow lung, which we alternately inflated and deflated with a bicycle pump to simulate breathing. In this way, we obtained voltages around 1V, showing the potential to harvest body energy for portable electronics.

In summary, we have shown that PZT nanoribbons can measure neuronal cells' mechanical responses to an applied voltage across the cell membrane. The nanoribbons offer a minimally-invasive and scalable platform for electromechanical biosensing. We are now scaling these devices to larger areas for more significant amounts of harvested power. This could ultimately enable advances in on-body energy scavenging for powering portable electronics.

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