Cell-material interface resolved with nanometer resolution *via* electron microscopy

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The interface between biological cells and non-biological materials has profound influences on cellular activities, chronic tissue responses, and ultimately the success of medical implants and bioelectronic devices. Materials in contact with cells can be metals, plastics, silicon, ceramics or other synthetic materials, and their surfaces vary widely in chemical compositions, stiffness and levels of roughness. For example, the success of bioelectronic devices for both *in vivo* and *in vitro* applications lies in the effective coupling of cells/tissues with the devices' surfaces. It is known how a large cleft between the cellular membrane and the electrode surface massively affects the quality of the recorded signals or ultimately the stimulation efficiency of a device. However, there remains a critical need to directly examine the aforementioned cleft at the relevant length scale of nanometers. Scanning electron microscopy (SEM) and focused ion beam (FIB) milling are powerful tools in analyzing interfaces for inorganic and organic materials. However, using FIB-SEM for interfaces involving biological specimens has been challenging due to the inherent low contrast of biological samples and the structural artifacts induced by sample drying. Here, we present a new FIB-SEM method that overcomes these limitations to resolve the cleft between cells and devices with 10 nm resolution. Furthermore, we present an overview of this methods application relevant to the material science field including the investigation of the interface between cells and 3D conductive and dielectric materials in a micro and nanostructured fashion such as nanopillars, PEDOT-based grooves and scaffolds.