Real-time Biophotonic Oxygen Monitoring with Fluorescent Nanosensors and Hydrogel Fiber Optics

Elijah C. Feret, Department of Nanoscale Science and Engineering, University at Albany – SUNY, Albany, NY, USA
Nathaniel Cady, Department of Nanoscale Science and Engineering, University at Albany – SUNY, RNA Institute, Albany, NY, USA
Yubing Xie, Department of Nanoscale Science and Engineering, University at Albany – SUNY, Albany, NY, USA
Susan T. Sharfstein, Department of Nanoscale Science and Engineering, University at Albany – SUNY, RNA Institute, Albany, NY, USA

Abstract

A major constraint in the development and application of engineered tissue constructs is the inability to monitor the internal physical and chemical states. These states, including internal strain and oxygenation, are key parameters governing cell proliferation, differentiation, and survival, as well as the simulated tissue's functional mimicry of native constructs. Methods for real-time monitoring require the development of sensors that can be incorporated into tissue constructs.

Oxygen is a critical metabolite for cellular proliferation but is subject to mass transfer limitations due to high demand and low solubility. Here, we demonstrate the use of oxygen-sensitive fluorescent polymeric nanoparticles to spatially resolve dissolved oxygen concentrations in cell-laden hydrogel constructs. The nanoparticles were created by encapsulating Pt(II) meso-Tetra(pentafluorophenyl)porphine (PtTFPP), an oxygen-quenched fluorophore, and a reference dye in poly(styrene-maleic anhydride).

Following confirmation of nanoparticle biocompatibility, nanosensors were incorporated into cell-laden alginate hydrogels to model oxygen limitations in tissue constructs. Confocal microscopy was used to visualize oxygen concentration gradients. Future work will use the particles to evaluate oxygen transfer limitations in tissue constructs providing guidance for disease modeling and next-generation 3D tissue cultures.

In parallel, nanosensors will be incorporated into step-index hydrogel optical fibers to create a dissolved oxygen sensor to be incorporated into complex 3D tissue cultures, such as organoids. Step-index hydrogel fibers are fabricated

using a novel, extrusion-based method of creating alginate-PEGDA hybrid fibers. Total internal reflection optimized fibers will be tested for their ability to transmit light.

Optical fiber sensors will incorporate the previously developed oxygen nanosensors into the core. The nanoparticles will be excited in the fibers using a single wavelength. The output signal from the fiber will be measured spectrally, quantifying the intensity at the excitation and emission wavelengths. The excitation wavelength will be attenuated depending on the strain on the sensing fiber, whereas the sensor emission from PtTFPP will be inversely proportional to the dissolved oxygen concentration and the reference dye will remain as a reference to normalize interstrand variability.

Together, these complementary sensing strategies address distinct measurement needs in 3D tissue culture systems, enabling both spatially resolved imaging and fiber-integrated sensing within engineered tissue constructs.