

### **531c Modeling of Oxygenation within a Hepatic Hollow Fiber Bioreactor with Modified Oxygen Carriers Supplemented to the Circulating Media**

*Jesse Sullivan and Andre Palmer*

Hollow fiber bioreactors mimic the 3D vessel arrangement within the liver sinusoid, allowing for cell attachment and cell-cell interactions, making them an ideal candidate for a bioartificial liver assist device. However, the low solubility of oxygen in aqueous solutions, the long diffusion distances within the hollow fiber membranes, and the high metabolic oxygen consumption of hepatocytes hinder the progress of this type of device. Additionally, hepatocytes in vivo experience a range of oxygen tensions (25-70 mmHg) that is important to the cultures differentiated function (zonation). We have previously proposed the use of whole, intact bovine red blood cells (bRBCs) as a supplemented oxygen carrier within the circulating media. These studies indicate, with both experimental data and computer modeling, that the addition of an oxygen carrier increases both the amount of oxygen delivered to the hepatocytes and the oxygen spectrum within the ECS of the device. However, the additional resistance to diffusional transport due to the membranes of the hollow fiber bioreactor causes native bRBCs to be suboptimal oxygen carriers. From the oxygen transport model developed, we observe that the maximum oxygen offloading within the device is located near the P50 of the bRBCs. We propose that by altering the bRBC oxygen-hemoglobin binding properties, and consequently the P50, of the bRBC the range of oxygen delivery could be targeted to ideal oxygenation conditions. Our simulations indicate that low oxygen affinity oxygen carriers (high P50) deliver the most oxygen to the hepatocytes cultures within the hollow fiber bioreactor studied. In addition to oxygen carrier characteristics, other parameters were varied to find the optimal bioreactor operating conditions (inlet pO<sub>2</sub>, flow rate, and oxygen carrier concentration). From these promising results, we conclude that an optimal oxygen carrier can be predicted by modeling the oxygen transport within this and other hollow fiber bioreactors.