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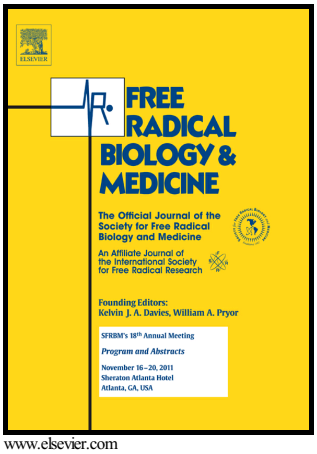

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Electrochemical Reverse Engineering: A Systems-Level Tool to Probe the Redox-Based Molecular Communication of Biology

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ABSTRACT

The intestine is the site of digestion and forms a critical interface between the host and the outside world. This interface is composed of host epithelium and a complex microbiota which is "connected" through an extensive web of chemical and biological interactions that determine the balance between health and disease for the host. This biology and the associated chemical dialogues occur within a context of a steep oxygen gradient that provides the driving force for a variety of reduction and oxidation (redox) reactions. While some redox couples (e.g., catecholics) can spontaneously exchange electrons, many others are kinetically "insulated" (e.g., biothiols) allowing the biology to set and control their redox states far from equilibrium. It is well known that within cells, such non-equilibrated redox couples are poised to transfer electrons to perform reactions essential to immune defense (e.g., transfer from NADH to O_2 for reactive oxygen species, ROS, generation) and protection from such oxidative stresses (e.g., glutathione-based reduction of ROS). More recently, it has been recognized that some of these redox-active species (e.g., H_2O_2) cross membranes and diffuse into the extracellular environment including lumen to transmit redox information that is received by atomically-specific receptors (e.g., cysteine-based sulfur switches) that regulate biological functions. Thus, redox has emerged as an important modality in the chemical signaling that occurs in the intestine and there have been emerging efforts to develop the experimental tools needed to probe this modality. We suggest that electrochemistry provides a unique tool to experimentally probe redox interactions at a systems level. Importantly, electrochemistry offers the potential to enlist the extensive theories established in signal processing in an effort to "reverse engineer" the molecular communication occurring in this complex biological system. Here, we review our efforts to develop this electrochemical tool for *in vitro* redox-probing.

I. Redox Biology of Intestine

1. Intestinal Anatomy and Physiology