# Zero-Current Chronopotentiometry with Wired Biosensors

Andrea Nonis, Polyxeni Damala, Eric Bakker

Department of Inorganic and Analytical Chemistry, (University of Geneva, Quai Ernest-Ansermet 30, 1211 Geneva, Switzerland)
Andrea.Nonis@unige.ch

Glucose biosensors are extremely important for point of care measurements and one of the major applications of electroanalytical chemistry. Theses sensors often use amperometric detection methods in which a redox mediator is used to shuttle electron between the electrode and the enzyme reaction site. Heller et al. developed the "wired" biosensor where the redox mediators are bound to the polymer containing the enzyme, thereby providing a connection to the electrode surface. [1] To achieve selectivity and avoid interference, a permselective layer is normally deposited which will also limit the diffusion of the analyte to the enzyme. The sensor is then no longer governed by the enzyme turnover rate but by the analyte diffusion, resulting in some protection from variations in enzyme kinetics and enzyme degradation. [2] Unfortunately, these sensors are subject to signal drift, which was attributed by Damala et al. to the charging of the redox polymer through the oxidation/reduction of redox center not connected to the enzyme. [3] Passive detection methods at open circuit may overcome some of these limitations. Nagy et al. introduced a chronopotentiometric method mased on the measurement of the open circuit potential (OCP) decay resulting from the reduction of an oxidized a redox mediator absorbed the electrode by NADH in solution. They correlated the initial slope of the potential decay to the NADH concentration. [4]

In this work we propose a new chronopotentiometric time dependent readout for a "wired" glucose biosensor based on glucose oxidase. A two-step process involving the oxidation of the redox polymer (ferrocene-modified branched poly(ethylenimine)) followed by the monitoring of the OCP over time allows one to measure a transition time characteristic to the glucose concentration in solution. The transition time ($t_r$) correspond to the potential jump due to the reduction of the previously oxidized ferrocene moieties by the electron generated by the enzyme converting glucose in gluconolactone. Thanks to an outer diffusion limiting membrane $t_r$ is related to the concentration of glucose Nafion and a blend of hydrophilic polyurethane and polyvinyl alcohol/vinyl butyral copolymer are used as outer permselective membrane to repel interference in phosphate buffered saline solution.

[1] A. Heller, Electrical wiring of redox enzymes, Acc. Chem. Res. **1990,** *23*, 5, 128-134.

[2] J. H. Han et al., Glucose biosensor with a hydrophilic polyurethane (HPU) blended with polyvinyl alcohol/vinyl butyral copolymer (PVAB) outer membrane, Sens. Actuators B Chem. **2007**, *123*, 384-390.

[3] P. Damala, N. Yu. Tiuftiakov, et E. Bakker, Avoiding Potential Pitfalls in Designing Wired Glucose Biosensors, ACS Sens., **2024**, *9*, 1, 2-8.

[4] A. Nagy, G. Nagy, et Z. Fehér, Investigation of a novel chronopotentiometric detection method using a redox mediator modified carbon electrode, Anal. Chim. Acta **1995**, *310*, 2, 241-249.