Electrochemistry of DNA Monolayers: from Biophysics to Biosensing

Current approaches towards drug dosing rely on venous draws measurements performed on test patients with long time intervals that are then laboratory-analyzed and returned the following days. This practice forces physicians to administer potentially toxic or ineffective concentrations of drugs to patients since dosages are determined based on weight and age of this test group even though pharmacokinetics may differ in each individuals. Having a technology that would in contrast allow, direct, continuous, real-time monitoring of drugs in the living body would revolutionize healthcare and allow personalized drug dosage and adjustment while enabling the development of artificial organs responsible of adjusting these levels.

Motivated by this goal, we and others have developed a class of electrochemical aptamer-based (E-AB) sensors[1], which has been used for the detection of a variety of targets including small molecules. These sensors are comprised of a redox-reporter-modified DNA "probe" that is attached by one terminus to a self-assembled monolayer deposited on an interrogating electrode. The binding of an analyte to this probe alters the kinetics with which electrons exchange to/from the redox reporter via binding-induced conformational changes producing an easily measured change in current when the sensor is interrogated using square-wave voltammetry (see Figure) [2]. Because E-AB sensors rely on a biology-inspired conformational change in which a biomolecule receptor transduce a molecular recognition event into a specific output, these sensors are capable of detecting with high specificity their molecular targets in flowing whole blood and in the living body. I will demonstrate the latest by deploying E-AB sensors in the living body of sedated rats to monitor the pharmacokinetics of tobramycin[3-4], an aminoglycoside antibiotic, and this with second resolution towards solving the paradigm of personalized medicine.

[1]: **Dauphin Ducharme, P.** and Plaxco, K. W. *Anal. Chem.* **2016** 88: 11654–11662.

[2]: Li, H., **Dauphin Ducharme, P.**, Ortega, G., Plaxco, K. W. *J Am. Chem. Soc.* **2017**, *139*, 11207-11213.

[3]: **Dauphin Ducharme, P.**, Arroyo-Currás, N., Pleonse, K. L., Kippin, T. E., Plaxco, K. W. **2018** In preparation.

[4]: Arroyo-Currás, N., **Dauphin Ducharme, P.**, Ortega, G., Pleonse, K. L., Kippin, T. E., Plaxco, K. W. *ACS Sensors* **2018**, *3*, 360-366.