Michael Leopold, Ph.D.
University of Richmond

CHRB Grant Title: ***Amperometric Biosensors Incorporating Nanoparticle Networks: Monitoring Sepsis Using Lactate Measurement***

CHRB Project Summary:

Sepsis, a systemic inflammatory response triggered by infection, is the 10th leading cause of death in the U.S. with a 20% mortality rate. Identified through clinical presentation or from time-consuming laboratory blood tests, early diagnosis and monitoring of sepsis during antibiotic treatment is essential for improving patient survival from this condition. Recent clinical studies have identified lactate as a critical marker for sepsis and the ability to clear lactate from the blood as prognosticator of septic patient survival. Sensors that continuously monitor lactate in real time would represent a significant biotechnological advancement and a valuable clinical improvement for patients with sepsis. Amperometric biosensors, using enzymatic reactions to selectively detect physiological targets like lactate, can suffer from insufficient sensing performance of inadequate sensitivity. Incorporation of colloidal gold nanoparticle networks within biosensor schemes, the focus of this research proposal, may allow for improved sensing performance and miniaturization toward development of *in-vivo* devices.

CHRB Project Outcome:

Probably the most significant impact of our work is the successful adaptation of our materials and strategy to the creation of a uric acid sensor, technology that can be further developed into an actual sensor prototype that can potentially be commercialized for preemptive detection of pregnancy-induced hypertension (PIH) that can lead to a condition called preeclampsia. CHRB provided the "seed support" for the research to become more expansive and more influential years during and following the funding. Using CHRB support to generate preliminary results, we were able to procure a National Science Foundation (NSF) grant that will fund our work in this area through 2018, including exploration of signal enhancement strategies using nanomaterials and the successful adaptation of the technology to sensor designed for diagnosing galactosemia, prostate cancer, xanthinuria, as well as sepsis. The work will likely lead to significant future collaboration between the University of Richmond and neighboring Virginia schools and local biotechnology organizations.

CHRB funding has allowed for a significant number of undergraduate coauthors on publications and presentations at local and regional scientific conferences. The efforts of this research group have become nationally recognized program and the Principal Investigator was invited to give a presentation celebrating 30 years of electrochemistry at a symposium honoring all significant electrochemists in the southeastern United States. Additionally, the CHRB-funded research and the outcomes produced over the past year became part of the University of Richmond's successful bid to be awarded a Beckman Institutional Award for an unprecedented fourth straight cycle (2005-2018).

Comments regarding CHRB Grant Funding

The CHRB funding has facilitated our research by providing critical funding for preliminary findings, essentially "seeding" the foundation of a research program for meaningful progress and contribution to the field. The role of CHRB in the climate of the need for scientific research and the challenging current state of funding cannot be underestimated. CHRB represents the important first step towards humans solving the issues we all face.

Leveraged Funding as a result of CHRB Grant Award: $512,000

Awarded:

Project title: *Xerogel-Based Amperometric Biosensors Incorporating Nanoparticle Networks – Adaptable Templates for Clinically Relevant Measurements*
Principal Investigator: Michael Leopold, Ph.D.
Funding agency: National Science Foundation (NSF)
Awarded: September 2014 to September 2018
Amount awarded: $375,000 ($322,000 including institutional support of $52,000)

Project title: *Xerogel-Based Amperometric Biosensing for the Detection of a Diagnostic Marker*
Principal Investigator: William Case, Ph.D. and Co-Investigator, Michael Leopold, Ph.D.
Funding agency: National Institutes of Health (NIH)
Awarded: September 2015 to September 2017
Amount awarded: $100,000

Project title: *Sarcosine Biosensor for Early Detection of Prostate Cancer*
Principal Investigator: Michael Leopold, Ph.D.; (Michael Pannell, Undergraduate Researcher)
Funding agency: Arnold and Mabel Beckman Foundation
Awarded: Spring 2016 to Summer 2017
Amount awarded: $37,000 ($26,000 including institutional support of $11,000)

Publications *denotes undergraduate researchers

N. Poulos,* J. Hall,* and **M.C. Leopold**, "Functional Layer-By-Layer Design of Xerogel-Based 1st Generation Amperometric Glucose Biosensors," *Langmuir* **2015**, *31*(4), 1547-1555. (Featured: *Chemical & Engineering News*)

L. Finch,* M. Hillyer,* and **M.C. Leopold**, "Quantitative Analysis of Heavy Metals in Children's Toys and Jewelry: A Multi-Instrument, Multi-Technique Exercise in Analytical Chemistry and Public Health," *J. Chem. Edu.* **2015**, *92*(5), 849-854.

L. DiPasquale,* N. Poulos,* J. Hall,* A. Minocha,* T. Bui,* and **M.C. Leopold**, "Structure-Function Relationships Affecting the Sensing Mechanism of Monolayer-Protected Cluster Doped Xerogel Amperometric Glucose Biosensors," *J. Colloid and Interface Science* **2015**, *450*, 202-212.

M.C. Leopold, T.T. Doan,* M.J. Mullaney,* D.J. Tognarelli,* A.F. Loftus,* and C.M. Kidd,* "Electrochemical Characterization of Self-Assembled Monolayers on Gold Substrates Derived from Thermal Decomposition of Monolayer-Protected Cluster Films," in press, *J. Applied*

Electrochemistry **2015**, *45*(10), 1069-1084.

K. Chen,*[=] G.E. Conway,*[=] G.A. Hamilton,* M.L. Trawick, and **M.C. Leopold**, "Electropolymerized Layers As Selective Membranes in First Generation Uric Acid Biosensors," *J. Applied Electrochemistry* **2016**, *45*(5), 603-615.

G.E. Conway,*[=] R.H. Lambertson,*[=] M.A. Schwarzmann,* M.J. Pannell,* H.W. Kerins,* K.J. Rubenstein,* J.D. Dattelbaum, and **M.C. Leopold**, "Layer-by-Layer Design and Optimization of Xerogel-Based Amperometric First Generation Biosensors for Uric Acid," *J. Electroanalytical Chemistry* **2016**, *775*, 135-145. (Featured: *World Biomedical Frontiers*)

M.B. Wayu, M.J. Pannell, and **M.C. Leopold**, "Layered Xerogel Films Incorporating Monolayer Protected Cluster Networks on Platinum Black Modified Electrodes for Enhanced Sensitivity in 1st Generation Uric Acid Biosensing," *ChemElectroChem* **2016**, 3, 1245-1252.

K.W. Kittredge, J.T. Malinowski,* K.J. Dye,* R.W. Day,* and **M.C. Leopold**, "Assembled Nanoparticle Films with Crown Ether Derivatives as Sensors for Metal Ions," *Amer. J. Organic Chemistry* **2016**, *6*(3), 86-92.

M.B. Wayu, L. DiPasquale,* M. Schwarzmann,* S. Gillespie* and **M.C. Leopold**, "Electropolymerization of β-Cyclodextrin onto Multi-Walled Carbon Nanotube Composite Films for Enhanced Selective Detection of Uric Acid," *J. Electroanalytical Chemistry* **2016**, *783*, 192-200.

M.B. Wayu,[=] M.A. Schwarzmann,*[=] S.D. Gillespie,* and **M.C. Leopold**, "Enzyme–free Uric Acid Electrochemical Sensors Using β–cyclodextrin Modified Carboxylic Acid Functionalized Carbon Nanotubes," *J. Mater. Sci.* **2017**, *52*(10), 6050-6062.

M. Pannell,* E. Doll,* N. Labban,* M. Wayu, J. Pollock, and **M.C. Leopold**, "Versatile Sarcosine and Creatinine Biosensing Schemes Utilizing Layer-by-Layer Construction of Carbon Nanotube-Chitosan Composite Films," *J. Electroanalytical Chemistry* **2018**, 814, 20-30.

M. Wayu, M. Pannell,* W. Case, and **M.C. Leopold**, "Nanomaterial Adsorption Platforms for Electron Transfer Studies of Galactose Oxidase," submitted.

C. Steele,* N. Labban,* T. Munoz,* G. Horn,* A. Burton,* J. Pollock, **M.C. Leopold** and W. Case, "1st Generation Amperometric Biosensor to Detect Galactosemia," manuscript in preparation.