Development of a micro-Differential Scanning Calorimetry thermal analysis device for clinical diagnostics

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Abstract

Our pioneering work, validated by other research groups in multiple disease settings, has shown that thermal analysis of blood plasma via Differential Scanning Calorimetry (DSC) can be used to differentiate clinical samples . DSC thermal profiles of plasma are sensitive to proteomic changes associated with disease due to detectable differences in the thermodynamic properties of human plasma proteins. However, despite 10 years of promising results, clinical development of DSC has been hampered by low experimental throughput and the requirement for expensive instrumentation and specialized expertise. We are currently working towards an inexpensive clinical device that can rapidly analyze a patient blood plasma sample using a microfabricated DSC sensor with a simple user interface. The sensors being evaluated consist of a thin-film polyimide membrane (~5μm) with 10μm wide gold electrical/heating traces (two designs, ~80Ω and ~200Ω) and an aluminum backside coating (~100Å) to distrubute heat across the membrane. Experiments are ongoing to electrically cycle the sensors (~ 1h 10V 1Hz sine wave) to remove residual stresses caused by thermal mismatch between layers. Post electrical cycling consists of a 20min controlled current ramp (~1mA/min) up to 20-40mA (depending on device resistance). This process yields sensors with linear applied power vs. resistance curves that will be used to identify matched sensor pairs (target variability <5%). Future work includes differential heating of sample vs. buffer using lysozyme as a DSC reference protein. This project fuses the Garbett and Roussel research groups with unique expertise in DSC and sensors/instrumentation.

Presenter biography

Nichola Garbett, Ph.D. is a co-inventor of the DSC blood plasma diagnostic assay. She is an Associate Professor in the Department of Medicine at the University of Louisville (UofL) with expertise in the biophysical analysis of biomolecules and biomarker interactions, focusing on technology development for medical diagnostics. As PI on multiple NIH, DoD and foundation grants spanning >15 diseases her research has shown that DSC is a sensitive reporter of proteomic changes associated with disease status.

Thomas Roussel, Ph.D., has 20+ years of experience in the research and development of multiple medical and industrial device prototypes that integrate custom and off-the-shelf sensor applications. Currently an Associate Professor in the Department of Bioengineering at UofL, he also serves as Director of the Bioinstrumentation and Controls R&D Laboratory and Associate Director of LARRI, the UofL Robotics Institute. His research has been supported by NASA, NSF, NIH, the Wallace H. Coulter Translational Partnership, and various UofL internal grant programs.