Research Development Fund: Fall 2021

Application title: High-Throughput Automated Desorption Electrospray Ionization Mass Spectrometry (DESI-MS) System for Reaction Screening, Bioassays and Small-Scale Synthesis

Lead contacts: R. Graham Cooks cooks@purdue.edu David Russell russell@chem.tamu.edu

Key Participating Unit: College of Science

Anticipated Request Amount ($): 1,326,000

Survey on Campus:

The current proposal has received extremely strong support from researchers in various areas at Texas A&M University including the departments of chemistry, chemical engineering, biomedical engineering, and veterinary integrative biosciences, and institute of biosciences and technology. There would be additional future users to the proposed facility because it fills gaps in capabilities inaccessible in the current mass spectrometric facilities on campus. The tremendous needs for facilities with innovative mass spectrometry-based technologies also include single-cell analysis, H/D exchange, and native mass spectrometry which could be future additions to the proposed facility.

A. EXECUTIVE SUMMARY

Construction of an automated high-throughput (HT) chemical analysis, enzyme assay and organic/catalyst synthesis facility is proposed. The system is based on mass spectrometry which is used here as both an analytical and a synthetic method. The facility will be valuable to scientists and engineers in the life and chemical sciences.

Personnel: Graham Cooks is a Hagler Fellow who plans to visit A&M repeatedly over the next three years. Prof. Cooks led the Purdue DARPA project which developed the first DESI-MS automated system and is well positioned to co-lead this proposed Texas A&M project. David Russell is well known on campus for his leadership in chemical instrumentation and mass spectrometry. Cooks will supply instrumentation designs and system control software and work with Russell, an instrumentation post-doctoral with expertise in instrumentation, and with Hagler graduate students Thomas Walker and Shuli Tang. TAMU faculty and staff members (Table 1) will comprise the Management Committee that oversees the construction, characterization and initial utilization phases and reports to TAMU administration. Each has research projects for which the facility will be invaluable.

System Capabilities: The system will be capable of analysis of 6,144 samples in an hour, with output processed as heat maps or in graphical form. Sample sizes are small (ca. 50 nL, 4 ng) and precision is high, typically RSD < 10%. The system uses ambient ionization ("analysis in the native environment with little or no sample preparation") with mass analysis to prioritize speed and simplicity of analysis while maintaining sensitivity and broad applicability. Samples are sprayed with solvent to generate ions by DESI. Small scale synthesis relies on the phenomenon of acceleration of chemical reactions in microdroplets.

Applications (selected): 1. Optimization of conditions for synthesis of drugs (as an example) by screening reaction mixtures for conditions and reagents at a rate of 6,144 reactions/hour. 2. Measurement of enzyme kinetics including Michaelis-Menten curves, maximum velocities and inhibition constants for hundreds of individual reactions, with data acquisition total times on the order of 15 min. 3. "Made-to-Measure" synthesis of target chemicals in nanogram amounts for bioassays made using the same instrumentation. 4. Molecular imaging, e.g. of tissues for endogenous lipids and metabolites, and xenobiotics.