Background: The real-time monitoring of changes in intracellular metabolites will improve upon traditional assays for the analysis of patient health and the prediction of future cellular changes. Although metabolite abundance levels can be quantified by mass spectrometry (MS), large-scale real-time monitoring of metabolite flux and abundance has yet to be realized because of technological limitations for fast extraction of metabolites from cells and biological fluids.

Problem: In general, time-course metabolic experiments are several orders of magnitude slower than the capability of modern mass spectrometers to collect data. Bottlenecks slowing the process have been the amount of time it takes to extract metabolites as well as the computational interpretation of the data. Additionally, laborious, time-consuming sample preparation techniques involving multiple extractions from cell culture or biofluid, purification, sample concentration by repeated centrifugation, filtration, drying steps, and derivatization reactions frustrate fast extraction thus precluding real-time monitoring of metabolite abundance. In order for metabolomics to be a tool in patient care, these slow processes must be addressed.

Solution: Researchers at MSU have engineered a system for extracting small molecules from biologically relevant fluids using a microfluidic-based metabolite extraction chip (MEC), which is directly coupled to a mass spectrometer. This technology facilitates continuous automated biomolecule extraction, dramatically increasing the temporal resolution over standard metabolomics studies. The MEC will vastly increase the information recovery from metabolomics experiments through the detection of oscillating metabolic transient states. The overall setup is semi-supervised and can be controlled wirelessly providing a basis for cloud-based computational analysis and real-time predictive metabolomics.

Benefit of the MEC:
- Enables large-scale real-time monitoring of metabolite abundance
- Increases temporal resolution compared to standard metabolomics studies
- Proven in bacteria, blood and urine. Other biofluids have not yet been tested.
- Enables metabolite forecasting of disease progression
- Biomolecules obtained directly from living systems without sample preparation
- Time and cost savings in routine measurement of high throughput applications

Applications:
- Disease diagnosis
- Monitoring disease progression, timing treatment – patients in treatment
- Tracking physiology – military personnel, athletes, patients in recovery
- Process monitoring – food, beverage, pharmaceuticals
- Research – subject monitoring, experiment monitoring

Supporting Documents:
Patent Application Title: Automated, continuous microfluidic-based biomolecule extraction device for real-time biomolecule abundance digitization directly from living systems, comprising Bernoulli spiral microchannels, inlets and outlets for diffusion-directed extraction, and an integrated detector for detection and analysis. Available under CDA.

This discovery was made at Montana State University by Brian Bothner, Ph.D., and Joshua Heinemann, Department of Chemistry/Biochemistry

Contact: Gary Bloomer, Montana State University, 406-994-7483

Binary setup of integrated syringe pump, valve, solvents, MEC, and mass spectrometer, (a) valve is in position 1, syringe pump is set to draw from cells and solvents; (b) valve is in position 2, syringe pump is set to pump to MEC