Invention of a New Class of Ultra-Fast, Ultra-Sensitive Mass Spectrometers for Kinetics, Reference Mass Spectrometry, and Homeland Defense Applications

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CSTL Program: *Measurement Science for Future Standards and Technology*

The project was designed to demonstrate the feasibility for improved mass spectrometers based on Hadamard-transform data acquisition. Hadamard mathematics describes the most accurate procedures for measuring properties of any ensemble. To the chemist, its most familiar form includes a digital representation of the fast-Fourier transform used in modern infrared spectrometers. A goal is to show that Hadamard MS/MS instruments are feasible and can rapidly resolve the chemical structures of components in a complex mixture. Hadamard mathematics suggest that such instruments can acquire comprehensive structure determination data of chemical unknowns as much as 3,000 to 600,000 times faster than current art.

CSTL researcher builds a prototype Hadamard time-of-flight mass spectrometer (HT-TOFMS), measures its performance, and uses test data to model a Hadamard-transform MS/MS instrument.

The first Hadamard time-of-flight (TOF) mass spectrometer incorporating an electron-impact ionizer has been invented, and constructed at NIST. The instrument appears similar to a commercial reflection TOF mass spectrometer; however, it contains a specialized electron gun, ion optics, and high-voltage electronics that are optimized for high-frequency modulation. Laboratory tests have demonstrated that this ionizer can switch ion streams on and off with a 5 ns rise-fall time when modulated at 13 MHz. These performance specifications will permit Hadamard operation. Integration of this hardware with the necessary software is in progress.

Preliminary numeric simulations have been conducted and suggest that useful Hadamard MS/MS instruments are possible. The incorporation of test results from the present HT-TOFMS will help us optimize trial instrument designs and data acquisition procedures.

Conventional TOFMS ion optics accelerate individual ion bunches down a flight tube to a detector. The detector signal is sent to a 1 GHz multi-channel scalar that counts the ions and measures their arrival times. The TOF spectrum is simply the graph of ion counts vs. time. Because a conventional TOFMS instrument flies each ion bunch individually, it has a duty cycle of only ≈ 2 %. When operating in Hadamard mode, the ionizer modulates the ion stream with a simplex code sequence that is derived from a Hadamard matrix. The simplex matrix is composed of rows of 1's and 0's that instruct the ionizer to switch the ion current on and off. With a Hadamard modulation frequency of 13 MHz, ≈ 500 distinct ion packets are simultaneously in flight. The signal from an HT-TOFMS initially looks like random noise. The mass spectrum is obtained by multiplying this "noise" by the inverse of the simplex matrix. The duty cycle of the HT-TOFMS is 50 %. Hence, the HT-TOFMS obtains a 25x to 50x sensitivity improvement from its higher duty-cycle. Other features of Hadamard mathematics further enhance sensitivity and reduce measurement uncertainties.

The demonstration that any conventional TOFMS can be converted into a more sensitive Hadamard instrument may accelerate adoption of this superior technology. Hadamard technology is expected to find application in fields of chemistry such as the study of the rates of chemical reaction or forensic analyses where high sensitivity, sample conservation, and high operational speed are essential. If Hadamard principles could be adapted to other variations of MS/MS, say those used in the drug discovery process, it would enable the acquisition of complete MS/MS data sets within the duration of a single high performance liquid chromatography (HPLC) peak. Currently, such data campaigns take days to execute and can require use of an expensive (≈$1M) ion cyclotron resonance MS in order to conserve sparse samples.

The present Hadamard mass spectrometer will be used to obtain feasibility data for an MS/MS instrument. The design target is an instrument that can measure the kinetics of complex hydrocarbon mixtures.

Plans include incorporating error correction algorithms into the NIST HT-TOFMS in order to generate benchmark reference data.

Algorithms that reduce the effects of mask errors (which in mass spectrometers arise from non-ideal ion current modulation) on the measurement quality are an active research area in mathematics. The community needs data from a well-characterized experiment to verify assumptions about the nature of Hadamard measurements. This data may facilitate improvements in other Hadamard application fields including microscopy, nuclear magnetic resonance (NMR), and medical magnetic resonance imaging (MRI).