High Throughput Genotyping and Mutation Detection by Rotating Field Mass Spectrometry (RFMS)

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NASA and the NCI require instrumentation useful in the early detection and treatment of cancer. The recent JPL development of the Miniature Rotating Field Mass Spectrometer (RFMS) will enable new biomedical and space in situe field measurements to be made. The RMS is very small (20 x 2 x 2 mm), and has mass resolution exceeding one part in 500, as well as a proven upper mass limit of 14,500 Dalton. No high-precision parts are needed. Operating RF frequencies are at the Megahertz level or lower. No magnetic fields are required. A direct liquid to vacuum nanospray ion source is used, with very low vacuum pumping loads. Ion beam production is good even in fairly poor (milli-Torr vacuum) settings.

The work is divided into three sections.
1. Steven J Smith: Refinement of Current RFMS design for DNA genotyping.
2. Ted Krontiris: Mismatch scanning strategy for sample multiplexing.
3. Terry Lee: Adaptation of the RFMS to analysis of biomacro-molecules.

The samples to be analyzed would contain a mixture of 4-50 polynucleotides closely grouped in sizes from 20-100 nucleotides (6600-33000 Dalton) and would require 1 nucleotide resolution. Presently such analyses can be done on state of the art MALDI-TOF instruments costing $200,000-$3000,000. The Rotating Field mass Spec would be ideal in this application since the number of components in the mixture can be predefined, the mass values for the components of interest are known, and there is no requirement for MS /MS analyses. The potential exists to develop a low cost system suitable for clinical or research applications.

The presentation will outline the work needed to:
1. Optimize the RFMS performance including ion detection for high mass ions.
2. Develop an electrospray source capable of ionizing large DNA fragments.
3. Develop efficient sample preparation methods, as well as develop data analysis software.

In the JPL-City of Hope collaboration we have:

1. JPL expertise in ion optics, RF technology, ion detection and mechanical engineering. Well established miniature flight hardware heritage.

2. City of Hope expertise in biological applications, biological mass spectrometry, sample preparation, and data analysis. The cancer genetics study provides an immediate and important application of technology emerging from collaboration.