SPECIFICATION FOR A HIGH PERFORMANCE MASS SPECTROMETER AND DATA SYSTEM

A. Background

The Naval Research Laboratory (NRL) is engaged in research on protein expression. With the completion of an increasing number of genomic sequences, much attention is now focused on how the data contained in sequence databases can be interpreted in terms of the structure, function and control of biological systems. Global profiling of gene expression at the messenger ribonucleic acid (mRNA) level as a function of the cellular state is widely used to identify genes and clusters of genes for which expression is idiotypic for a specific state.

These methods, although sensitive, do not indicate exact changes in protein expression. Quantitative proteome analysis, the global analysis of protein expression, is a complementary method to study gene expression and perturbation-induced changes in cellular protein composition. In comparison to gene expression analysis at the mRNA level, proteome analysis provides more accurate information about biological systems and pathways because measurement directly focuses on the actual biological effector molecules (i.e., proteins).

The development of methods and instrumentation for automated high resolution electrospray mass spectrometry, in conjunction with microcapillary liquid chromatography – mass spectrometry (LC-MS) and advanced database searching, has been of critical importance in achieving increased speed and sensitivity for identification and quantitation of cellular protein components.

For NRL's intended applications, it has been determined that a hybrid quadrapole-time of flight (QTOF) mass spectrometer with MS-MS capability is required. Critical considerations include sample throughput, sensitivity, resolution, and accuracy. The mass spectrometer must meet or exceed the following minimum specifications:

B. Spectrometer Performance

1. The instrument must be capable of mass accuracy of 5 parts per million (ppm) or better.

2. The instrument must be capable of acquiring full scan mass spectra within the mass range from 5-12000 atomic mass units (amu) or higher.

3. The instrument must be capable of achieving mass resolution of 10,000 or higher in MS mode.

4. The instrument must be capable of performing tandem mass spectrometry (MS-MS) experiments on any selected ion using collisional activation with an inert target gas.

5. Parent ion selection of a minimum of 3000 amu must be possible with 1 amu resolution.

6. The instrument must be capable of fragmenting the selected ion with a collision energy that can be varied between 0 and 200 eV.

7. The mass resolution of fragment ions in the MS-MS mode must be no less than 7000.

8. The instrument must be capable of scanning in both product and precursor ion modes.

C. Liquid Chromatography (LC) System

A capillary LC system must be included with the mass spectrometer. The LC system must be capable of ternary gradient solvent delivery, automated sample management, and fully integrated MS interfacing capabilities. This system should include the following features, as a minimum:

1. An integrated autosampler must be provided with one or more of the following sample formats: a flexible format sample tray for a 48-position vial tray, a 96-well standard or deep well microtiter plate, or a 384-well microtiter plate.

2. Automated sample injection with programmable injection volumes for full loop, partial loop, and microliter pickup methods of injection.

D. Sample Introduction

A variety of sample introduction sources are required, with direct interface to analytical and microcapillary LC outputs. Direct infusion (flow injection analysis) via a syringe pump is also required. Sources must include:

1. A standard atmospheric pressure electrospray ionization (API) source allowing flow rates of 1-200 uL/min directly into the source.

2. An atmospheric pressure chemical ionization (APCI) source allowing flow rates up to 2 mL/min directly into the source.

3. A nanoflow electrospray source supporting continuous flow rates from 100-1000 nL/min, and which is designed for both flow injection analysis (FIA) and direct coupling to an on-line capillary LC column.

4. A nanovial (nanocapillary) electrospray source for single sample (approx. 1 microliter volume) analysis at a rate of < 30 nL/min.

5. All necessary viewing optics, lighting, and camera sources for nanospray interface.

E. Software

1. The instrument operating software must be a fully integrated suite which allows desktop control of all relevant instrument operating parameters. These parameters include the automated operation of any associated liquid chromatography systems and autosamplers.

2. The software must be compatible with commercially available personal computers or workstations running on a commercially available platform. The contractor shall provide a computer which will contain all necessary hardware and operating software required to operate all of the equipment specified herein. All hardware and software, including drivers, device interface cards, or controller cards must be pre-installed and pre-configured on the computer provided. The computer must have sufficient computational power and memory to use the features in the software. The computer must control the spectrometer and LC system in an integrated fashion, and provide useful data analysis and output. All necessary software licenses for the computer and software provided shall be included.

3. The software must include an integrated proteomics package which enables chemically meaningful knowledge to be extracted "in silico" from multi-dimensional datasets (e.g. m/z, intensity, retention time.) automatically. The ability to deconvolute complex biopolymer mass spectra containing molecular ions in multiple charge states is necessary to plot the spectra in homogeneous (virtual z = 0 or z = 1) charge state representations and to infer the molecular mass of large proteins.

4. Software for biopolymer sequencing must be included. This software must be capable of interactive de novo peptide sequencing for finding isotopic tags (ICAT experiments). This software must be capable of performing database searching for peptide mass fingerprints and/or peptide sequence tags.

5. A protein sequence editor, peptide targeting and matching capability, and a protein digestion simulator must be included.

6. A oligonucleotide sequencer for interpreting oligonucleotide sequences from MS-MS data must be included. A nucleic acid editor for editing sequences and calculating oligonucleotide composition from mass spectral data is also required.

7. The instrument must be capable of data dependent scanning. At minimum, the software must be capable of performing the following functions:1) obtaining a full scan spectrum, 2) determining charge states of ions in the spectrum 3) automatically selecting ions of specific charge states 4) determining whether ion abundances exceed preset thresholds, and 5) performing tandem mass spectrometry experiments on a specified number of ions that meet the aforementioned criteria. The data system should be capable of performing these experiments in sequence, repetitively, during the course of data acquisition runs.

F. Installation, Training and Documentation

1. The price of the system must include installation and pre-installation site inspections at NRL by the contractor.
2. Installation must be performed within 30 days of receipt of the equipment at NRL.
3. Installation of the mass spectrometer must include all software and hardware components necessary to operate the equipment.
4. Installation must include connection to all electrical, water and gas plumbing services.
5. The contractor shall demonstrate that the system is in compliance with any of the specifications contained herein, as deemed appropriate by the NRL representative.
6. At the completion of the installation and demonstration of the specifications, the contractor shall provide training for 2 people for a minimum of three days to familiarize the operators with proper operation and care of the instrument. This training may be conducted at either NRL or at the contractor's facility, but must be included in the price of the system.
7. A full set of all written documentation customarily provided to the public with a commercial item shall be provided. This shall include users manual(s) or equivalent as well as copies of any software, and any manuals for the software included with the system, if customarily provided. This documentation must be received at NRL with the system hardware, unless other arrangements are agreed to by the NRL representative.

G. Warranty

Warranty Conditions: The contractor shall offer the Government at least the same warranty terms, including offers of extended warranties, offered to the general public in customary commercial practice. These warranty terms must be included in the system price. The period of the warranty shall begin upon acceptance.

H. Used Equipment

Offers of used equipment which meet all other specifications herein will be considered acceptable, provided however, that such equipment is warranted by the contractor to have had no more than six months of prior use prior to installation and acceptance at NRL.