

Development of real-time control methodologies for tandem mass spectrometry

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One of the most important goals in the early detection of genomic-related disease, and the discovery of associated biomarkers, is to identify and characterize the proteins and protein complexes present in related cell lines. Tandem mass spectrometry (MS/MS) is a powerful tool for identifying and comparing the proteins expressed in complex biological systems. However, the performance of mass spectrometers remains limited in terms of the proportion of MS/MS data that can actually be interpreted. For example, up to 70% of the peptide MS/MS spectra generated by quadrupole-time of flight mass spectrometers, and up to 85% of those produced by ion trapping mass spectrometers cannot be interpreted using any available technique. Furthermore, a great deal of time is wasted in acquiring and attempting to interpret these poor-quality spectra. Based on our experience, literature review, and conversations with industry, it is apparent that the main obstacle to improving performance in protein mass spectrometry is the lack of fast, efficient algorithms capable of real-time detection and/or selection of target peptide ions for fragmentation and MS/MS analysis. The goal of the proposed research is to overcome this challenge, and hence, increase throughput and efficiency for protein mass spectrometry. This will be achieved by developing (a) an efficient algorithm for assessing the quality of peptide MS/MS spectra, and (b) a fast and accurate algorithm for on-line protein identification using verified peptide MS/MS spectra. The proposed research will significantly improve the performance of mass spectrometers by enabling the development of real-time control methodologies based upon the algorithms developed in this proposal.