Improved MALDI-TOF Performance with Practical Implementation of Very High Post-Acceleration

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Novel Aspect

The practical implementation of very high post-acceleration voltages can improve MALDI-TOF performance without adding substantial complexity to the system.

Introduction

The mass range of MALDI-TOF mass analyzers is unlimited, but applications to masses greater than ca. 100 kDa have been limited by the efficiency of electron multiplier detectors for ions of relatively low velocity. Sophisticated methods for improving the detection efficiency of very high mass ions have been developed, but these methods generally involve loss of resolving power and are often complex and expensive. A simple and practical method for improving the detection efficiency of high mass ions in MALDI-TOF has been developed and evaluated on a new high performance linear TOF instrument.

Methods

The new detector comprises a single microchannel plate, a high-speed scintillator, and a photomultiplier. Both the channel plate and the scintillator are independently mounted on insulators that allow them to be biased at up to 30 kV and light from the scintillator is focused to the cathode of the photomultiplier with the output anode at ground potential. For detection of positive ions a negative post-acceleration voltage is applied to the channel plate, and the scintillator is at ground. For negative ions the channel plate is biased up to +20 kV and the scintillator is an additional +10 kV relative to the channel plate. Experiments were performed using the linear TOF with variations in scintillator properties and optical coupling schemes.

Preliminary Data

A new linear MALDI-TOF analyzer was employed to evaluate the performance of the new detector. This analyzer provides simultaneous space and velocity focusing and a gridless ion optic system that efficiently transmits ions over a wide mass range. The ion source accelerates ions to initial energies up to 36 keV. With 30 kV post acceleration the maximum ion energy at the detector surface is 66 keV. The detection of an incoming high-mass ion by an electron multiplier is dependent on the incoming ion producing at least one secondary electron that reaches the multiplier input surface; thus detection efficiency for high mass ions is greatly enhanced by employing higher energy ions. The combination employed for most of the preliminary work provided very high gain giving single ion pulses limited only by saturation of the photomultiplier output at about 5 volts corresponding to a gain greater than 10^{10} with very low noise. Results from a detailed study of sensitivity as a function of ion mass and energy are presented with particular emphasis on applications to complex mixtures of proteins produced by tissue imaging and direct analysis of proteins separated on gels. Additional studies are planned to evaluate trade-offs between sensitivity and speed that can be achieved using a variety of scintillator materials and surface coatings.