

MALDI and LDI-TOF Cryodetection Mass Spectrometry of Nanoparticles into the MegaDalton Mass Range



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NIST, Gaithersburg, MD 6-7 March, 2008

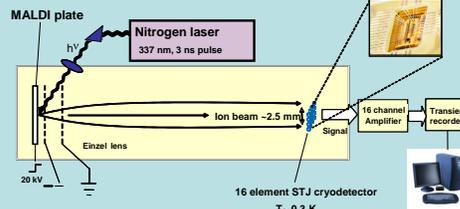
INTRODUCTION

The characterization of synthetic nanoparticles and very large macromolecules is difficult by conventional methods. In order to improve performance and decrease lot-to-lot variation in batches of large synthetic particles and macromolecules, it is desirable to develop new ultra-high mass spectrometry methods. Since these particles are large, it is necessary to develop MS instruments with good performance into a mass range extending into the megaDalton range. The current upper mass limit for MALDI TOF MS is believed to be due to the use of ionizing detectors and the MALDI technique which yields a declining signal as m/z increases. A novel superconducting tunnel junction (STJ) detector was introduced several years ago on a MALDI TOF MS (Macromizer, Comet AG) to overcome this detector limitation. Theoretically the STJ detector should exhibit mass independent 100% intrinsic detection. We have used this device to analyze several commercial preparations of nanoparticles.

EXPERIMENTAL

The mass spectrometer used for these studies was a Macromizer MALDI TOF system (Comet AG, Flammatt, Switzerland) equipped with sixteen STJ cryodetectors. A nitrogen pulsed laser operated at 337.1 nm was used for LDI or MALDI from a variety of matrix mixtures. This mass spectrometer is capable of energy analysis of the ions striking the detector to reveal the charge states making up a peak.

COMET Macromizer MALDI TOF MS with STJ Cryodetector



- TOF length (linear mode): ~1.5 m
- Resolution ~ 500
- Delayed extraction: 0.2-11.3 us
- Einzel lens ion beam focusing: beam diameter on detector ~2.5 mm
- 16 element STJ cryodetector, dimension 2.2 x 2.2 mm, active surface 0.64 mm²
- ~ 10% of the ion beam intercepted by the detector array

RESULTS

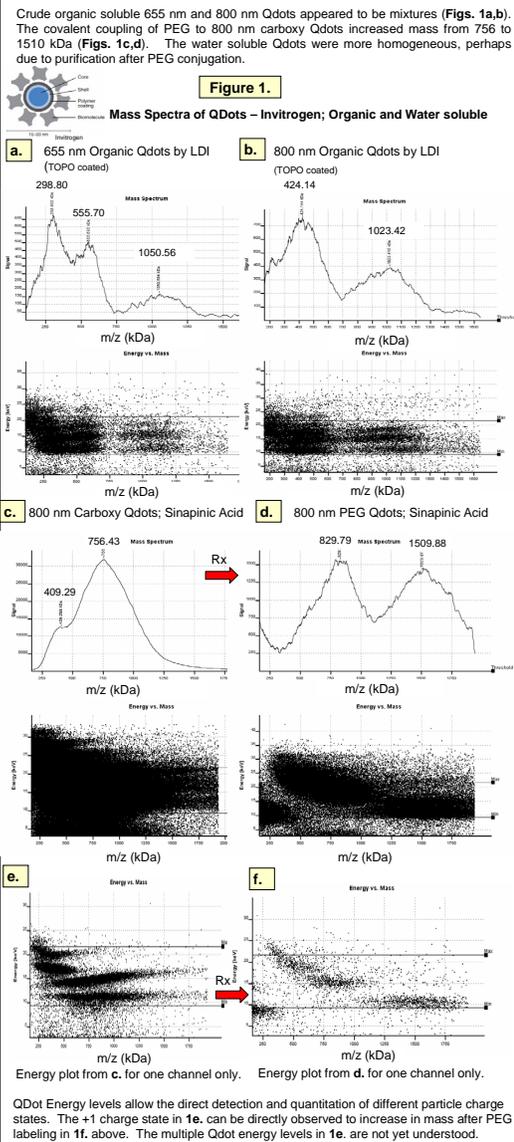
CdSe and CdTe Quantum Dots

Commercially available fluorescent QDotsTM (Invitrogen) are widely used in cell biology and biochemistry because of their intense fluorescence, which is very stable to photobleaching, and optimal absorbance (broad) and emission (very narrow) bands. The core is composed of nanocrystals of either CdSe, CdTe, or a combination. Fluorescence emission depends on both the composition and size of the nanocrystals. The 'cores' are then coated with a ZnS shell and a layer of organic R-groups, usually tri-n-octylphosphine oxide (TOPO) which may be subsequently coated with a layer of polymer (amphiphilic polyacrylic acid, AMP), then coupled with polyethylene glycol (PEG) - yielding water solubility. Qdots emitting at 655 nm and below are made of CdSe, those emitting above 705 nm are CdTe. Some sizes (nm, via TEM or gel filtration) of commercial Qdots are summarized in Table 1. Emission wavelengths are in color.

Table 1.

Emission Wavelengths (nm)	625	665	685	695nm	695nm	705nm	800nm
Materials							
Core-shells				8.2 x 4.4	6.0 x 12.5	5.8 x 10.1	
AMP	13.1	13.4	13.4	15.2	13.0	15.2	
AMP-PEG2K-30N (no barrier)	14.8	15.6	16.1	18.6	20.1	19.8	20.6
AMP-PEG2K-oMe (no barrier)		28.8			45.2		
Goat F(ab) ₂ (anti-His tag Core)							
Streptavidin Conjugate	16.1	17.1	20.1		22.9	21.8	
AMP-SAv (QTracker) TM							

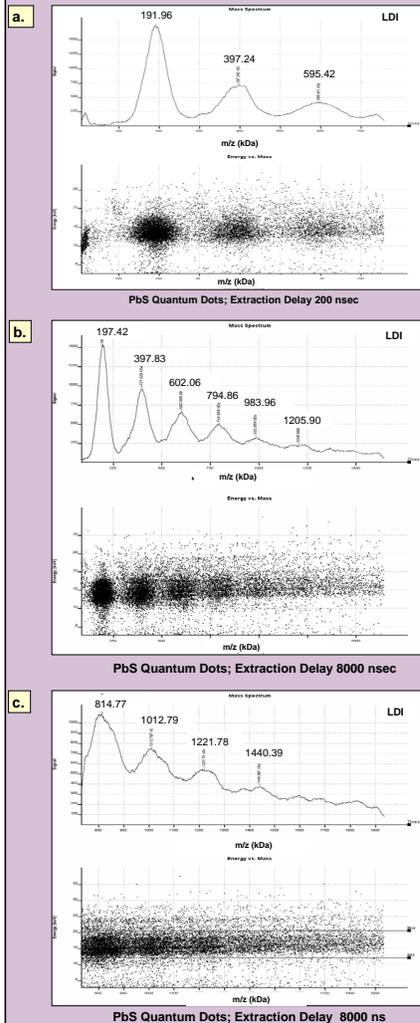
[#]Now at LGC, Inc., London, England



PbS Near-Infrared Quantum Dots

We also obtained mass spectra of PbS Qdots from Evident Technologies. Spectra are shown for 1311 nm emitting Qdots. Interestingly, these formed multimers of up to about six. The single Qdot mass was confirmed for an ~4.3 nm particle (191 kDa) and by results using a Voyager MALDI MS. Results are shown in Figures 2a-c.

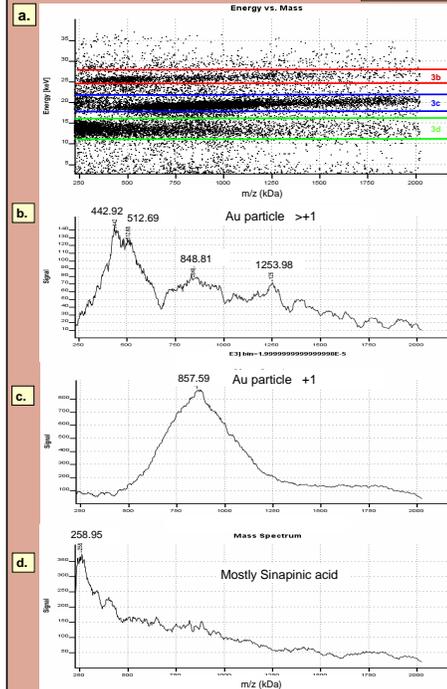
Figure 2.



5 nm Au Nanoparticles

Spectra were obtained for commercially available 5 nm Au nanoparticles (CV 15% by TEM) (citrate coated), using sinipinic acid. The energy plot is shown in 3a., followed by mass spectra obtained from three energy filters: high charge (3b.), Au particles (3c.), and matrix (3d.). As can be seen in 3c., the Au mass (858 kDa) is significantly higher than the calculated mass of 670 kDa, based on a 5 nm Au particle. Results demonstrate the great advantage of energy resolution in interpreting mass spectra. Gold energy bands are tighter than either of the quantum dots.

Figure 3.



CONCLUSIONS

The current STJ cryodetector allows the collection of mass spectra into the Mega Dalton mass range of CdSe, CdTe, PbS, and Au nanoparticles of commercial interest.

Organic soluble Qdots can be run via LDI. Water soluble Qdots require a matrix. Mass increased from 756 to 1509 kDa on coupling of PEG groups to Carboxy Qdots.

1311 nm-emitting PbS Qdots are observable with LDI, and readily form complexes of up to 6 Qdots.

Au nanoparticles have a broad mass distribution, but tight energy bands. The Energy vs. m/z plots allow the analysis of charge states directly, greatly aiding interpretation of MS data, and can help distinguish matrix from analyte ions.

This work was supported by NSF
Biological Infrastructure DBI 0454980