Transmission Mode Desorption Electrospray Ionization (TM-DESI)

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Introduction
A new DESI sample preparation method is presented in which the electrospray is not deflected off of a sampling surface but instead transmitted through a sampling mesh at an angle of zero degrees between the electrospray tip, sample mesh and capillary inlet of a mass spectrometer. In this configuration both solid resins and liquids can be analyzed rapidly without rigorous optimization of spray distances or angles and without the preparation time associated with solvent evaporation. The transmission mode is not applicable to analysis of compounds in bulk form, but rather to any DESI analysis involving sample deposition. Results are presented to highlight both the similarities to traditional DESI analysis and the nuances associated with the transmission mode.

Methods
All experiments were performed on a Thermo Fisher Scientific LTQ XL
A modified Omni Spray™ from ProSci Inc. was used as the electrospray source
Nicotine and cotinine were purchased from Sigma-Aldrich
Peptides were purchased from Bachem
Mesh materials purchased from Small Parts Inc. and InterMet

Mesh Dependent TM-DESI Signal

Figure 4: TM-DESI signal of 10 pg of Rhodamine 6G from five different mesh materials with similar transmission characteristics (i.e., strand thickness of ~200-250 µm and five space of ~300-350 µm). Samples were spotted using 1 µL of methanol and allowed to dry prior to analysis.

Optimization
- Blue Sharpe® marker containing Blue 7 was used to spot a nylon mesh
- Electrospray solvent flow rate tested between 1 and 10 µL/min
- Optimization flow rate found to be between 5 and 10 µL/min
- Electrospray nebulizing gas (N₂) pressure tested between 40 and 140 psi
- Optimum pressure found to be 100-120 psi
- Electrospray voltage tested between 0.0 and 5.5 kV
- Minimum voltage found to be between 3.0 and 5.5 kV
- All results correlate well with what has been reported for traditional DESI

Transmission Mode Geometry

Figure 1: Transmission mode desorption electrospray involves depositing a sample from solution onto a transmissive mesh and passing an electrospray through it. Key advantages of TM-DESI lie in its simplified geometry and ability to rapidly analyze solutions that are suspended between the strands of the mesh.

Figure 2: TM-DESI mesh configurations A, B, C: a close-up of two 5 mesh samples with large pore and mesh size differences. B: 14 mesh samples with large pore and mesh size differences. C: 34 mesh samples with large pore and mesh size differences.

- 65 different mesh screens currently being investigated
- Mesh composed of Nylon, Polyester, Polypropylene, PEEK, Fluorotex, Stainless Steel, Brass and Nickel
- Various strand sizes and open spaces create specific transmittance for each mesh
- Open spaces range from 64 to 800 micron
- Rigid meshes utilize design A, while thinner, film-like meshes utilize design B
- Multi-layer TM-DESI (results not shown) can be accomplished using design C

Figure 3: Contour plot summarizing the optimization of the geometric variables DTC and DTC₂. Although the maximum response was recorded when DTC₂ = 10 mm and DTC = 12 mm, a range of values (depicted in red) produced similar results as long as the difference DTC₁ ≅ DTC₂ was approximately 2 mm.

Figure 5: Relative percent response of nicotine and bradykinin allowed to dry on a Nylon sampling mesh before analysis via TM-DESI. The impact of varying the electrospray solvent observed in traditional DESI is also observed here. In this case, methanol is shown to be the best electrospray solvent for nicotine, while water or a mixture of water and methanol (50:50 by volume) is best for bradykinin.

Applications

Peptides: 1 µM in Methanol (Substance P [M+2H]⁺

Figure 7: TM-DESI spectrum of a mixture of peptides at a concentration of 1 µM in Methanol. The spectrum was collected using a Link & spray methodology where a Nylon sample mesh was simply immersed in the solution and then analyzed without any additional sample preparation or drying.

Cotinine: 100 pg/µL in Diluted Urine

Figure 8: TM-DESI spectrum of urine containing cotinine, the primary urinary metabolite of nicotine. Urine samples were spiked with cotinine to give a concentration of 100 pg/µL in urine. Samples were then diluted 1:100 with methanol to reduce ion suppression from the urine matrix and analytes immediately following spotting of 1 µL of sample to a 300 micron PEEK mesh. The MS/MS spectrum of the ion at m/z 177 shown in the inset was used to confirm the presence of the protonated cotinine species.

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