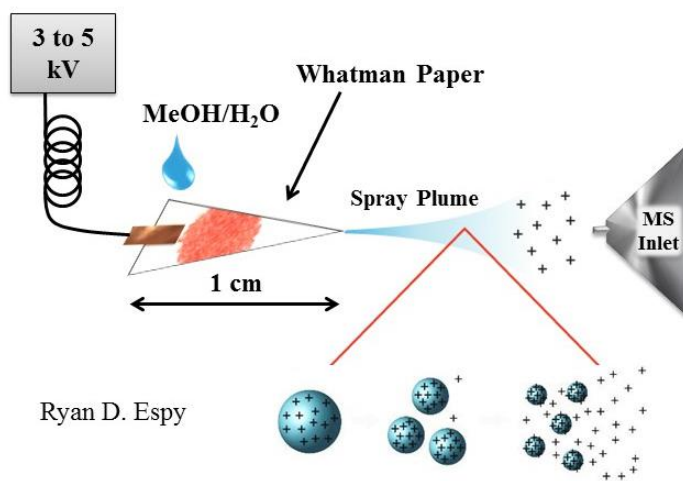


## Biofluid Analysis by Paper Spray Mass Spectrometry

### Introduction

Paper spray (PS) is an emerging ionization technique that combines sample collection, preparation and ionization for rapid direct analysis by mass spectrometry (MS) [1]. PS is currently one of the most developed ambient MS techniques for rapid and quantitative analyses for clinical and toxicological applications.

Conventionally, PS uses a small amount of sample (2-20  $\mu\text{L}$ ), e.g. biofluids, spotted onto a triangular piece of paper, such as cellulose filter paper. After the sample is dried, a spray solution and high voltage (3.5 kV) are applied to the paper to create ions off the paper's tip via ionization mechanisms similar to electrospray [2]. The biological matrix interacts with and is partially retained on the cellulose-based paper while the analyte is released and is ionized. The partitioning of analyte and matrix minimizes the need for multistep sample pretreatment.



**Figure 1.** Schematics of paper spray analysis. Samples can be preloaded onto the paper, added with the wetting solution or transferred from surfaces using the paper as a wipe. After the application of a high voltage to a paper triangle wetted with a small volume (< 10  $\mu\text{L}$ ) of solution, a spray plume of charged droplets via a Taylor cone is formed, producing ions. The charged droplets appear to be formed by breakup of larger droplets.

PS has been used for direct analysis of various biological matrices, including blood, oral fluid, urine and cerebral spinal fluid, to analyze both exogenous and endogenous analytes. Such methodology has proved amenable for point-of-care testing and therapeutic drug monitoring [3,4].

When developing a PS method, the paper substrate, spray solvent, volume spotted and volume sprayed all must be optimized. Paper spray analysis can be performed manually by cutting paper into a triangle using scissors and applying solvent with a pipette. However, an automated ionization source has been commercialized which uses single-use cartridges containing precut paper (Prosolia Inc., Indianapolis, IN).

### **Aims**

- Perform a PS-MS/MS experiment for the detection of drugs in various biological matrices.
- Build a calibration curve for quantitative analysis by PS-MS/MS.
- Understand quantitative performance of PS, e.g. measurement accuracy and reproducibility.

### **Experimental procedure**

1. Introduction to tandem MS. Basics of a triple quadrupole mass spectrometer and MS/MS methodology.
2. Basics of paper spray ionization. Visualization of the paper spray experiment set-up (cutting paper, sample spotting, solvent addition and troubleshooting).
3. Observe data acquisition by PS-MS/MS experiments.
4. Analyze drugs in various biological matrices. Build a calibration curve based on premade standards in biological fluids.
5. Discuss matrix ion suppression and the use of calibrators for quantitative analysis.

### **References**

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