Orthogonal Control Systems for ESI-MS and Nanobore LC-MS

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Low flow rate ESI (i.e. nanospray and microspray) provides exceptional sensitivity, but subtle changes to electrospray plume morphology (size, shape, direction) can effect performance. It has been well established (1,2) that the liquid, and subsequent spray exiting the nozzle, may take on a wide variety of physical forms, or spray modes. The specific spray mode obtained depends strongly upon the geometry of the nozzle, the strength and shape of the electric field, and the mobile phase chemical composition. At low flow rates, the smaller, monodisperse droplets having a high charge-to-mass ratio, appear to offer analytical benefits including improved ionization efficiency (3,4) and a reduction in ion suppression (5). The most effective mode for producing such droplets is the cone-jet mode in which a stable, non-pulsating Taylor cone is observed (6). Tuning of the cone-jet mode is when using gradient chromatography since the mobile phase mobile phase surface tension, viscosity, and flow rate change dynamically during the run. This results in spray instabilities, shifts in charge state distribution, and decreased performance for a set of fixed tuning conditions. Current LC-MS sources provide no means to dynamically test or control cone/jet/plume geometry independently of spray or ion current.

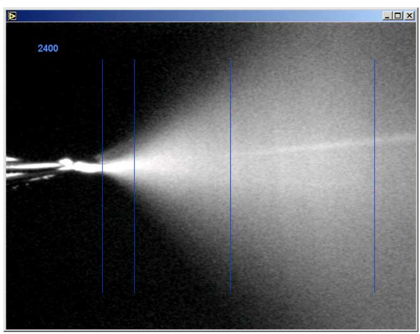
Rather than using an ion current based sensing scheme to detect and control the spray, we have investigated a number of opto-electronic schemes for the implementation of a self-tuning and self-adjusting ESI source. In these methods, optical channels of information are used to characterize and control the spray mode, in a manner that is completely independent of the spray or ion current. The advantage of this orthogonal approach is that the control system characteristics are independent of the chemical composition of the mobile phase. Thus such a system should be able to deal with the variable conditions of gradient chromatography. We present three general classes of feedback control system: static, dynamic, and hybrid. The static spray mode control system involves the use of a "machine vision" system in which an image acquisition and analysis computer determines the spray mode either through direct empirical measurements or through comparative analysis. This machine vision system forms the core of a feedback loop in which a control algorithm adjusts an experimental parameter so that a particular spray mode is obtained and maintained. The dynamic spray mode control system involves the use of an illuminator/ photo-detector pair to probe the temporal spray dynamics in the cone, jet, and/or plume regions. The photo-detector feeds signal to an acquisition computer containing an algorithm to characterize the spray mode either through direct empirical waveform measurements or through comparative waveform analysis. This system forms the core of a feedback loop in which a control algorithm adjusts an experimental parameter so that a particular spray mode is obtained and maintained. In the hybrid system elements of the static and dynamic systems are combined for increased "modal" reliability.

A static control system was developed on a bench-top spray apparatus was constructed on an optical breadboard. A fused-silica electrospray tip of 10, 15, or 30 µm ID (New Objective, Inc.) was mounted on an X,Y,Z positioning stage. A CCD camera based microscope of 200x total magnification (PicoView, New Objective, Inc.) was mounted with its optic axis perpendicular to the tip. The output of the CCD camera was connected to a PC with a frame grabber, running LabView 6.0 (National Instruments) for image acquisition. A 5 kV power supply (Stanford Research Systems Inc.) was controlled by the PC via GPIB interface bus. A fiber optic bundle provided (150 W) reflected-scattered light illumination. A program to analyze the content of the CCD images based on the scattered illumination scheme to automatically control the spray mode was written in LabView. Mobile phase was delivered from a split flow capillary HPLC (Agilent).

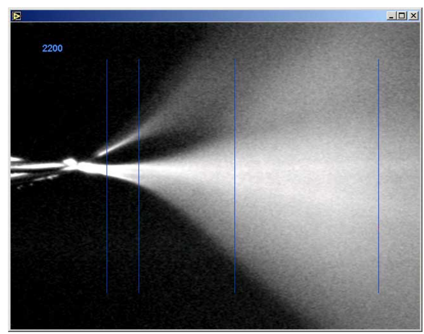
For static spray mode control using empirical measurement, the spray mode algorithm must be able to make quantitative measurements of the image to *a priori* determine the spray mode. In this example, the algorithm for mode determination is based upon analysis of image morphology. The algorithm works by dividing the image into regions of interest and determining the number of edges within each ROI. Based upon the number of edges found in each ROI, the voltage is increased, decreased, or left unchanged. In this example the control algorithm is designed to generate and maintain the cone-jet mode of operation. It could be modified so as to maintain other modes, such as controlling the number of jets in the multi-jet mode.

In the figures below, a 30 μm, coated, PicoTip™ was positioned 4mm in front of the counter-electrode. A 5% to 95% Acetonitrile gradient (0.1% formic acid) was delivered for a through-tip flow rate of 300 nL/min. Using a 4 zone system, the control system could establish and maintain a stable spray for both rapid (< 3 min) and slow (> 30 min) gradients. Unstable, multi-jet modes such as shown in the second photo, persisted only a second or two before the voltage was adjusted to re-establish a stable cone-jet spray. From 5% to 95% the applied voltage ranged from 2500 to 1500 V.

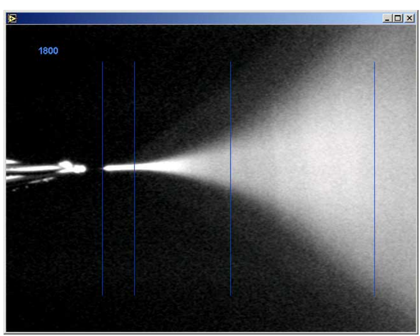
Many other implementations of spray mode control are possible. One limitation of the static system shown is poor discrimination between the pulsed cone-jet and pure cone-jet modes. The dynamic and hybrid systems should be able to precisely determine the spray mode, and establish and maintain truly optimal ESI conditions for gradient chromatography. These systems should dramatically improve the ease of use, reproducibility and productivity of low flow ESI. They will enable the automation of nanobore chromatography with “no compromise” electrospray.



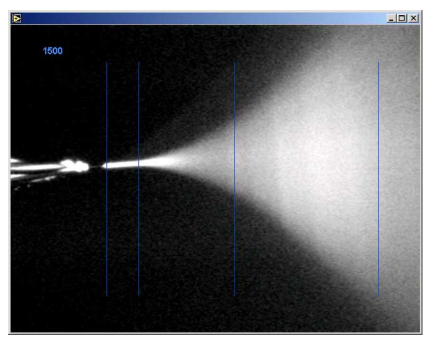
Start of Run, 5% ACN, 2400V



Brief Multi-Jet, Approx 20-30% ACN, 2200V



Stable cone-jet, Approx 50% ACN, 1800V



Stable cone-jet, 95% ACN, 1500V

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