Introduction: It is not possible to emphasize enough the relevance of electrospray ionization (ESI) to the advancement of science. The shared award of the 2002 Nobel Prize in Chemistry to John Fenn clearly reinforces the significance of the discovery of ESI. Electrospray ionization plays a central role in converting solutes into gas phase ions, allowing the hyphenation of liquid phase separations to MS detectors used in proteomics and metabonomic studies, the investigation of charge-state dependent gas-phase ion reactions and fragmentation and the development of high-throughput drug discovery and ADME studies.

Methods: The micromachined ultrasonic electrospray device presented here consists of three main components: 1) A piezoelectric transducer operating in the ~1-5 MHz range to generate resonant ultrasonic waves within a reservoir filled with the analyte sample, 2) A micromachined silicon wafer which contains pyramidally shaped cavities (255 per chip) that focus the ultrasonic waves thus amplifying the pressure around the 3-10µm diameter nozzle at the apex of the pyramid and 3) A spacer layer to prevent solid-to-solid contact between the silicon wafer and the piezoelectric transducer so that the ultrasonic energy is primarily and efficiently transferred to the sample solution. During operation, the high pressure gradient close to the nozzle produces ejection of a droplet stream.

Preliminary Results: Conventional electrospray ionization relies on the formation of a Taylor cone to produce a charged spray. Due to the decoupling of the droplet formation and droplet charging processes, the piezo-assisted micromachined electrospray source presented here should require lower DC potentials to produce a charged spray. We have first performed a critical proof-of-concept experiment to explore the feasibility of generating charged droplets with a DC electrospray voltage as low as a few tens of Volts. By placing a metallized droplet collector in front of the micromachined ejector array we have measured the current produced upon impingement of the charged droplets as a function of the applied DC spray voltage. We have observed that, with voltages as low as 80-100 V DC, there is significant electrical charging of the droplets, resulting in an increase in the collected current. However, charged droplet production does not demonstrate per se the ability to form charged ions in the gas-phase. We have then interfaced the ultrasonic ESI microarray with the inlet port of an orthogonal time-of-flight mass spectrometer (AccuTOF MS, JEOL Inc.). The instrumental setup is identical to the one used for charged droplet detection, with the exception that the charged droplet stream was directed towards the MS. A sample containing the standard calibration compound reserpine (molecular weight 609.2 Da, 10µM) in MeOH:H2O:Acetic Acid (50:49.9:0.1) solvent was ejected using an applied DC spray voltage of 250V. The mass spectrum obtained after acoustic ejection of the charged solution showed a strong and clear peak at 609.2 Da with 197-to-1 signal-to-noise ratio.