Droplet Injection Using Induction.

A 1000x Sample Input Rate Increase Compared To Sprays?

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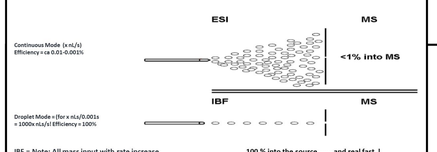
INTRODUCTION, Sprays vs. Droplets.

An inductive approach (IBF) has show the ability to dispense 100% of liquids in the nL/s range into ESI for infusion and UPLC MS.

Here we show "all in", fast (ms), droplet level control yields a sample rate input d(moles)/dt over sprays by up to ca. 1000x!

We discuss other droplet observations and issues.

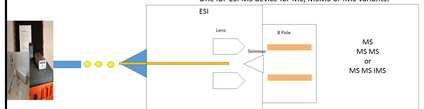


IBF = Note: All mass input with rate increase. 100 % into the source……. and real fast !

Droplets, "100% ALL IN" DROPLETS! THEN WHAT?

Here we report observations from ESI and MALDI experiments doing IBF.

One IBF ESI MS device for MS, MSMS or IMS variants.



We have employed IBF on many MS and MS/MS Systems, and noted that spectra observed were in agreement with what we'd expect from ESI mass spectra for metals, amines, Lanthanide chelates and other drugs/compounds. It's as if the ion inlet tube "standardizes" the ion product outlet. We're doing more work to investigate how one might improve this simple interface.

What is Induction Based Fluidics ?

Theory: One IBF device, a flowing or stop flow system. There are many IBF embodiments

The liquid volume passing through a tube is given to the Hagen Poiseuille equation. The volume of fluid (V) that flows down a small-diameter capillary tube per unit time (dV/dt) is proportional to the pressure (P) that reduce drifts in time (). The pressure pushing the fluid down the tube (P) is the fluidic ‘Ohm's Law'.

$$V = (\pi r^4 P)/8\eta l$$

Since electric fields can be rapidly toggled on and off, with great accuracy and precision, and since P= qE, the forces on liquid drops can be changed rapidly (because F is a vector, we can bend the drop as well.

$$F = qE$$

For a charged drop with initial volume, q0, with (ε a relaxation time, τ, where τ = (ε0ε / κ) where ε0 is the dielectric constant of free space, ε r is the relative permittivity and κ is the solution conductivity and t is time, we have q defined:

$$q = q_0 e^{(-t/\tau)}$$

Now, a charged liquid drop in an electric field, cannot only experience the qE force, but of course it experiences, differentforces as well in the atmosphere in, a and q space depending on the specific ofFire system. Using standard, well known physics, Newton's 2nd Law, we can equate the forces (electric, drag, buoyant, gravity and coulombic) acting on a drop to those acting in the direction x as:

$$F_x = m\,(a_x) = m\,(dv_x/dt) = F_{elec\,x} + F_{drag\,x} + F_{buoyant\,x} + F_{gravity\,x} + F_{coul\,x}$$

The same can be written for the y and z coordinates. Then with accurate model equations for Fy and Fz, we can actually calculate the trajectories of the drops (distances ofFlight) of the drops at any time t, knowing the initial position ofFire by: and final

$$V_x = dx/dt,\ V_y = dy/dt,\ V_z = dz/dt$$

$$V^2 = V_x^2 + V_y^2 + V_z^2.$$

EXPERIMENTAL

In all work reported either a digital Android or analogue energy source was employed to power inductors placed near Gaussian surfaces prior to commercially available ESI interfaces coupled to mass spectrometers of diverse types.

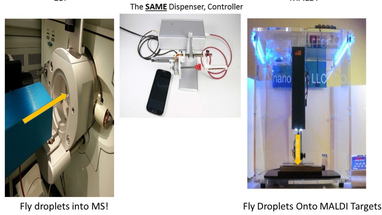
Droplets from Gaussian surfaces were inductively energized and shot into the ESI. In this mode, effectively all (100%) of nL sized samples are delivered into the ESI ion inlet tube and then to a mass spectrometer.

IBF systems were directly connected to ESI and ion traps, quadrupoles, Orbitraps, hybrid TOF mass spectrometers equipped with ion funnels and other ion optic devices.

Diverse liquids types were utilized, from aqueous salt solutions to aqueous mixtures of organic solvents, aliphatic alcohols, acetonitrile containing charged species, chelates or other compounds.

See the specific panels for exact references for any data set.

Here we seek **to begin to addresser** how qualitative and quantitative data varies for different chemical and analytical systems in the nL regime via IBF and to begin to see if there's a better arrangement for ion inlet tubes or other system components and variables.

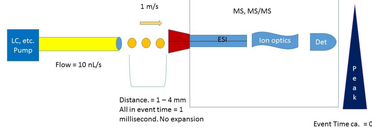


RESULTS AND DISCUSSION

Droplet typical launch configuration, d(moles)/dt > 1000x that of continuous sprays…..

While droplets can be shot over a m into an ESI, typically we employed in most early work ca, 1-4 mm distance of tip to ESI opening. Smith has indicted that at large distances, much of he sample is lost. Moving the device closer can cause poor desolvation.

Scheeline showed droplet velocity as 1 m/s for flight distances of a few mm. Sharp peaks result that are narrow given the supersonic heated gas velocity. Many examples are shown in this poster where the ESI appears to "standardize" droplet sample input across very different MS systems.



For a 1 mm distance shot at 1 m/s (See the Scheeline reference) d(moles)/ d(t) is ca. 1000x of a spray operating at some flow of x nLs/s.

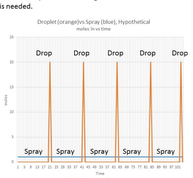
Droplets allow for major sample input rate increase of ca. 1000x compared to ESI?

While droplets can be shot over a m into an ESI, typically we employed in most early work ca, 2-4 mm distance of tip to ESI opening. Smith has indicted that at large distances, much of the sample is lost. Moving the device closer causes poor desolvation according to Smith, et al. A better solution is needed.

How does the IBF desolvation rate, discharging via the wall or other reactions, ion/liquid losses, compare to normal ESI ?

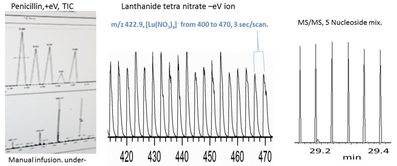
Many IBF mass spectra appear ESI like. What happens to observed ion current as a function of…..
- Droplet Input, d(moles)/dt.
- Droplet volume, penicillin 300 nLs, less i obsvd than 50 nLs!
- Droplet temperature, hotter better desolvation?
- Droplet path, physical distance, flight path, turbulence?
- Droplet physical form, pure droplet, mini spray, spray.
- Droplet composition, .
- Atmospheric variables, cover required.
- Data acquisition rate, ca. 2 Hz at least.
- m/z range, analyte dependent.
- System loses. (See Li+.). Need characterized.
- Mass Assignment.

Of course, then there's the consideration of different MS systems and sets of analytes … hard to establish

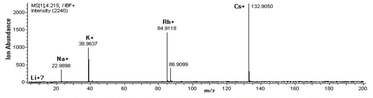


Droplet IBF peak shapes are reproducible & sharp. Probably best results are energy programmed, right two.

Best case precision can approach/exceed, ca. 5% RSD. Traditional ESI MS systems handle nL volumes quite easily.



Droplet: IBF MS of equimolar alkali metals. MS agrees w/ published ESI MS of van Dorsselaer.*



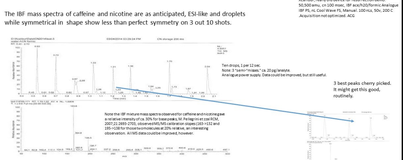
Enthalpy of hydration of alkali metal cations and relative ion abundances.). JEOL TOF at 10 Hz, pos. ion reflectron mode. Note alkali metals are near in m/z values, and have no other competing processes.

Cation	Enthalpy of Hydration (kJ/mole)	% Relative Ion Abundance ESI, H2O*	IBF, 50% MeOH/H2O
Cs+	260	100	100
Rb+	290	60	63
K+	335	20	44
Na+	405	7	16
Li+	535	2	0

* E. Leize, A. Jaffrezic, A. Van Dorsselaer, JMS, Vol., 31, 537-544,1996. G&D on the floor at Pittcon 2009.

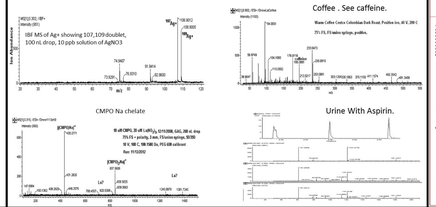
Droplets of Caffeine and Nicotine IBF MS for Merck At Caltech. Analogue IBF Dispenser.

Old Ion Trap Resurrection Demo Via IBF nL Cool Wave Dispensers
(Analogue nanoLiter Cool Wave Power Supply (Below) and Digital Energy Supply (next slide.).



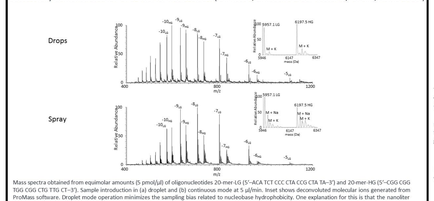
Droplet Qualitative: IBF MS are "ESI-like" for chemicals or mixtures. Observed elsewhere too.

Ag+, CMPO. Urine, coffee mixtures. + ion reflectron mode, ca. 10 Hz, 50-1500 amu.



Droplets vs Spray. IBF of oligonucleotides, are "similar", but note differences.

Successfully demonstrated IBF UPLC MS for nucleosides. (Dr. Ross's, Limbach's & our Poster w/ U. Cin., ASMS 2016.)

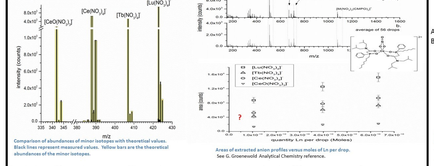


Mass spectra obtained from equimolar amounts (5 pmol/µl) of oligonucleotides 20-mer LG (5'-ACA TCT CCC CTA CCG CTA TA–3') and 20-mer HG (5'-CGG CGG TGG CGG CTG TTG CT–3'). Sample introduction in (a) droplet and (b) continuous mode at 5 µl/min. Inset shows deconvoluted molecular ions generated from ProMass software. Droplet mode operation minimizes the sampling bias related to nucleobase hydrophobicity. One explanation for this is that the nanoliter droplet produced by the IBF device desolvate better than sprays. Work is ongoing.

Droplet Quantitative Analysis,

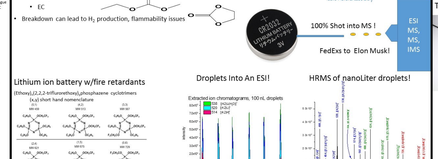
-eV, nitrato clusters + eV, Lanthanide CMPO chelates.

Excellent isotope ratios Of Lanthanides, (Actinides?) , Rapidly, > 1 Hz!



Comparison of abundances of minor isotopes with theoretical values. Black lines represent measured values. Yellow bars are the theoretical abundances of the minor isotopes.

Areas of extracted anion profiles versus molas of Ln per drop. See G. Groenewold Analytical Chemistry reference.

Substituting the IBF source for the standard ESI source did not appear to compromise the function of the MS mass spectrometer. The accurate m/z values for the nitrato clusters were within several ppm, and the relative abundances of the isotopic ions were very close to theoretical .

Droplet Qualitative: IBF MS of oligonucleotides, Lanthanide Chelates.