Progress in the development of capillary Atmospheric Pressure Ionization Methods (cAPI)

Sonja Klee; Valerie Derpmann; Hendrik Kersten; Walter Wißdorf; David Müller; Yessica Brachthäuser; Sebastian Klopotowski; Klaus Brockmann; Thorsten Benter

Physical & Theoretical Chemistry
Wuppertal, Germany
Institute for Pure and Applied Mass Spectrometry

Introduction

Challenges

- Design AP ion sources which generate ion populations closely representing the neutral analyte composition *in the source*
  → Investigations of *ionization mechanisms*
- Design AP ion sources which operate kinetically controlled
  → Ionization within *reactive matrices* (e.g. effluent from smog chambers, ambient air)
- Design AP ion transfer stages which allow carefully controlled transport of ions from the source to the analyzer region
  → *Optimization* of ion transfer efficiency (instrument sensitivity)
  → *Controlled* ion activation (reagent ion reactivity)

State of Knowledge:

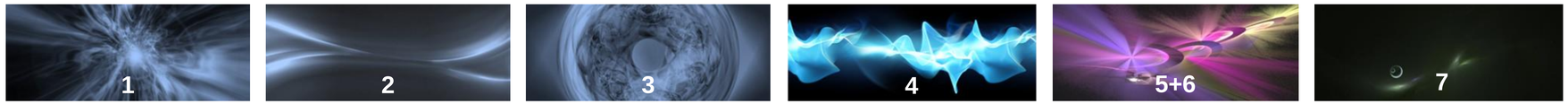
1. All *common* API sources are generating ion populations, which are thermodynamically controlled, *i.e.*, all ion concentrations present are *equilibrium* concentrations [1].
2. Thermodynamic control is governing the thermal ion source chemistry since the ion residence time in the source enclosure is generally ≥10 ms. Most bi- and termolecular ion molecule reaction rates are collision controlled leading to half lives of < 10^{-5} s (first order rates > 10^5 s^{-1}) when neutral reactants (*e.g.*, H_2O, dopants, solvents) are present at ppmV mixing ratios.
3. Thermal equilibrium ion concentrations do rarely reflect the true neutral analyte/matrix composition. For example most low mass ions are generally present in the source as charge bound clusters [2].
4. In the context of the present framework, "reactive" neutral matrices are depicted as containing ppmV (or above) mixing ratios of either *polar* compounds such as water or LC solvents (CH_3OH, CH_3CN) as well as molecular oxygen, due to its bi-radical character ($^3\Sigma$)

Methods

Experimental Setup

MS:	Bruker esquire6000 ion traps, Bruker micrOTOFs, TOFWerk HR-Tof with custom inlet and pumping stage, Thermo Exactive Orbitrap
Ion Sources:	Custom APPI, APCI, APECI, and APLI stages. Laminar flow ion source (LFIS). Bruker Apollo and MPIS [3] sources for comparison studies
Capillaries:	Borosilicate glass, stainless steel, aluminum
Gases:	Nitrogen (5.0), synth. air (5.0) < 1ppmV H_2O

General Considerations



1 ***Energy***, the hot zone of primary ion generation – essentially non-thermal chemistry

2 ***Relaxation***, the thermally equilibrated zone of the AP ion source enclosure – a reactive environment

3 ***Turbulence***, vigorous mixing of all compounds entering and flowing through the capillary duct

4 ***Compression/Expansion***, ion equilibria shift in response

5 ***Capture***, directing ions to the next stage, ion temperature rises (> 500 K)

6 ***Activation***, ion temperature may reach >> 1000K

7 ***Dispersion***, collision free analyzer region

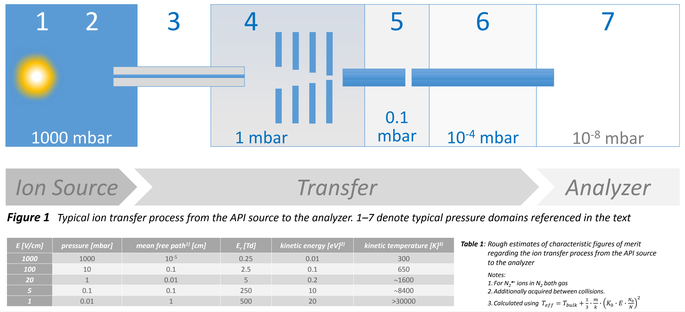


Figure 1 *Typical ion transfer process from the API source to the analyzer. 1–7 denote typical pressure domains referenced in the text*

E [V/cm]	pressure [mbar]	mean free path[1] [cm]	E/N [Td]	kinetic energy [eV][2]	kinetic temperature [K][2]
1000	1000	10^{-5}	0.25	0.01	300
100	10	0.1	2.5	0.1	650
20	1	0.01	5	0.2	~1600
5	0.1	0.1	250	10	~8400
1	0.01	1	500	20	>30000

Table 1: *Rough estimates of characteristic figures of merit regarding the ion transfer process from the API source to the analyzer*

Notes:
1. For $N_2^{+\bullet}$ ions in N_2 bath gas
2. Additionally acquired between collisions.
3. Calculated using $T_{eff} = T_{bulk} + \frac{1}{3}\frac{m}{k}\left(K_0 \cdot F \cdot \frac{N_0}{N}\right)^2$

1 Region of plasma chemistry (e.g., Corona discharge), VUV radiation, or laser radiation

2 Charge bound cluster formation, rapid thermal relaxation, leading to global ion concentration equilibrium

3 Equilibrated ion population is vigorously mixed. Depending on set-up, considerable chemical change occurs (curtain/dry gases, heat)

4 Repeating shock fronts generate regions of strongly changing conditions (pressure, temperature)

5 Electrical fields (DC and/or AC driven) "collect" and thus direct ions towards the next transfer stage.

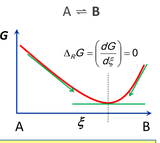
6 The lowered pressure leads to elevated reduced field strengths and thus *collision energies* – but also reduced *collision numbers*

7 No chemical change (other than unimolecular decay) possible

Thermodynamic vs. Kinetic Control

If the residence time of ions in domains 1-5 (cf. Figure 1) is significantly exceeding the half lives of one or several ion/molecule reactions, then $\Delta_R G$ governs the ion concentration distribution.

$$dG = \left(\frac{\partial G}{\partial p}\right)_{T,n} dp + \left(\frac{\partial G}{\partial T}\right)_{p,n} dT + \sum_i^n \left(\frac{\partial G}{\partial n_i}\right)_{T,p,n_j \neq n_i} dn_i$$



Kinetic control
The reaction system is *not* allowed to equilibrate before mass analysis.

The ion population resembles closely the neutral analyte composition in the matrix.

$\mathbf{A}_g^+ + \mathbf{B}_g \rightleftharpoons C_g^+ + D_g$

Typical Examples
- Radical cations $M^{+\bullet}$ are *not* oxidized in the presence of O_3 or OH to yield e.g. $[M+O_n]^{+\bullet}$
- Aromatic hydrocarbons, e.g., toluene, do *not* act as proton donors in complex matrices (and are thus *not* "suppressed")
- High IP analytes do *not* transfer charge

Thermodynamic control
The reaction system has time to equilibrate, driven by $\Delta_R G$. The ion population resembles the energetically lowest ion system. This *may* represent the neutral analyte composition, see insert in Fig. 2, but this is rarely the case.

$A_g^+ + B_g \rightleftharpoons \mathbf{C}_g^+ + \mathbf{D}_g$

Typical Examples
- H_2O^+ ions are rapidly converted to yield a thermally equilibrated distribution of $[H+(H_2O)_n]^+$ clusters
- Low mass analyte ions are generally clustering, mostly with background matrix water or polar LC solvents
- Ion "suppression" phenomena
- "Matrix effects"

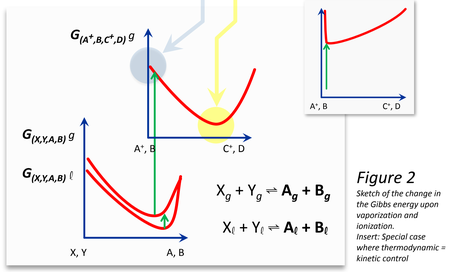


Figure 2
Sketch of the change in the Gibbs energy upon vaporization and ionization.
Insert: Special case where thermodynamic = kinetic control

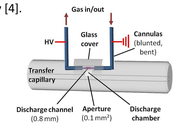
Capillary Ionization Methods

cAPPI *(see MOH PI 3:30 pm and MP15#276)*

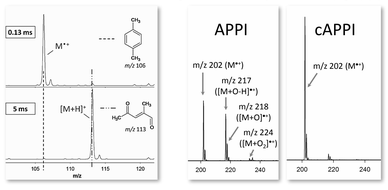
Purpose 1: Minimize the contact time between ions generated at high pressure and reactive neutrals such as radicals present in the gas matrix (t < 200 µs) thus pushing the chemical system towards kinetic control.

Approach: Miniature VUV lamp mounted windowless onto the inlet capillary [4].

Design:



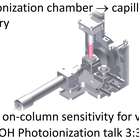
Results:
1. Mixture of p-xylene (D) and a 1,4-unsaturated dicarbonyl (A): Progress of the protonation reaction $D^{+\bullet} + A \rightarrow D\text{-}H + [A+H]^+$ for typical APPI dwell times (> 5ms; bottom left), in contrast to the kinetically controlled ion distribution obtained with cAPPI (< 0.13ms; top left) [4].
2. Pyrene radical cations (m/z 202) are oxidized in the presence of OH-radicals using APPI, but hardly with cAPPI (right) [5]



Purpose 2: Highly efficient direct (*no dopant*) VUV light driven generation of analyte radical cations in an ultra-clean environment. Application to GC-cAPPI-Orbitrap MS.

Approach: GC capillary effluent → transfer line → heated capillary ducts → APPI ionization chamber → capillary ducts → Orbitrap inlet capillary

Design:



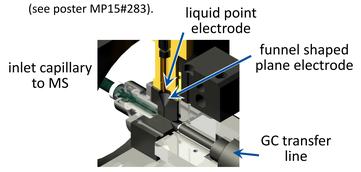
Results: Low fg on-column sensitivity for various analytes (as $M^{+\bullet}$)
See MOH Photoionization talk 3:30 pm / Room 103

cAPCI *(see MP15#274/5 and #283)*

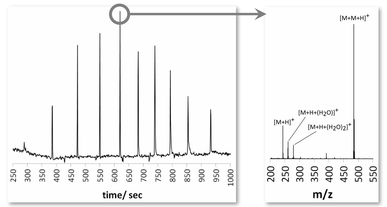
Purpose: Establish a selective *protonation* method for GC hyphenation without the adverse effects accompanied by the interaction of the hot Corona plasma zone with the analyte gas stream [2].

Approach: *Thermally equilibrated* proton bound clusters $[H+(H_2O)_n]^+$ are generated as reagent ions upstream of the capillary duct. The corona is operated with a liquid point electrode (highly purified, optionally acidified water pumped through a quartz capillary at nano-flow rates) and a funnel shaped plane counter electrode merging at the exit with the inlet capillary duct. Since the reagent ion clusters (n= 5 … 9) exhibit rather low proton acidities, an ion activation stage (domains 4-6) is required for high sensitivities towards less basic compounds (see poster MP15#283).

Design:



Results: cAPCI is a protonation-only API method. Charge transfer as well as oxidation reactions are generally not observed. The figure below shows the TIC for a GC-cAPCI-TOF MS analysis of a fatty acid ester mix (left panel). The corresponding mass spectra consist solely of a strongly concentration-dependent distribution of protonated molecule, proton bound analyte water clusters, and proton bound dimer ions, as expected (right panel). Carefully controlled ion activation in a dedicated rf funnel device (see poster M15#283) leads to exclusive $[M+H]^+$ formation.

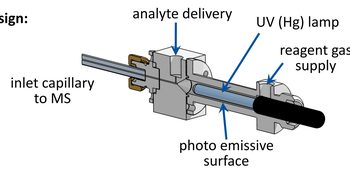


cAPECI *(see MP15#277/8)*

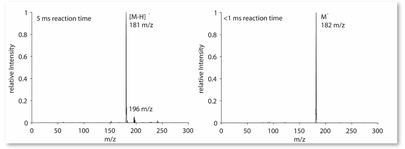
Purpose: Establish a selective kinetically controlled ionization method for analytes with elevated electron affinity or proton acidity [6]. Samples are either delivered from a GC with transferline stage or are directly sampled from ambient air. Future applications will include spatially resolved desorption stages coupled directly to the capillary duct (see below).

Approach: Selective generation of thermal electrons via the photo electric effect with long-term stability using anodize aluminum as photo emissive material. Quantitative capture of the photo electrons by oxygen to yield superoxide, $O_2^{-\bullet}$, as reagent ions.

Design:



Results: Typical minimum analyte/reagent reaction times in conventional APPI sources are > 10 ms. As shown below for 2,4 dinitro-toluene even a reaction time of 5 ms still leads to the formation of the thermodynamically preferred deprotonated and further oxidized molecule (left panel). With reaction times of < 1 ms, only the molecular radical anion is detected (right panel).



cAPECI was successfully coupled to GC (see MP15#277 for details). The method shows further exceptional performance for compounds sampled directly from ambient air.

Conclusions

- Capillary ionization methods are currently operated in the gas phase, i.e., require *vaporization* of the neutral analyte before ionization occurs
- For *direct cAPPI* (no dopants present) kinetic control is achieved. Thus complex mixtures with highly reactive neutrals present can be accurately analyzed. This is of particular interest to applications in atmospheric/environmental chemistry.
- The same arguments apply for cAPECI due to the high reactivity of superoxide
- cAPCI in positive mode using liquid point electrode configurations is fully compatible with cAPI – this method benefits strongly from a dedicated ion activation stage (within domains 4-6), since the reagent ions are fully thermally equilibrated $[H+(H_2O)_n]^+$ clusters.

References

[1] Dzidic, I.; Carroll, D.I.; Stillwell, R. N.; Horning, E.C. *"Comparison of Positive Ions Formed in Nickel-63 and Corona Discharge Ion Sources Using Nitrogen, Argon, Isobutane, Ammonia and Nitric Oxide as Reagents in Atmospheric Pressure Ionization Mass Spectrometry"* Anal. Chem. 1976, 48, 1763-1768.

[2] Klee, S.; Albrecht, S.; Derpmann, V.; Kersten, H.; Benter, Th. *„Generation of Ion Bound Solvent Clusters as Reactant Ions in Dopant Assisted APPI and APLI"* accepted for publication as "paper in forefront" in *Anal. Bioanal. Chem.* 2013.

[3] Schieweck, R.; Lorenz, M.; Giese, R.; Brockmann, K.J.; Benter, Th.; Gäb, S.; Schmitz, O.J. *"Development of a multi-purpose ionsource for LC-MS and GC-API MS" Anal. Bioanal. Chem.* 2008, 392, 87-96.

[4] Kersten, H. *"Development of an Atmospheric Pressure Ionization source for in situ monitoring of degradation products of atmospherically relevant volatile organic compounds"* Dissertation, Faculty of Mathematics and Natural Sciences, University of Wuppertal, Germany, 2011. *http://elpub.bib.uni-wuppertal.de/edocs/dokumente/fbc/chemie/diss2011/kersten*

[5] Kersten, H.; Funcke, V.; Lorenz, M.; Brockmann. K.J.; Benter, Th; O'Brien, R. *"Evidence of Neutral Radical Induced Analyte Ion Transformations in APPI and Near-VUV APLI" J. Am. Soc. Mass Spectrom.* 2009, 20, 1868-1880.

[6] Derpmann, V.; Albrecht, S.; Benter, Th. *"The role of ion-bound cluster formation in negative ion mass spectrometry" Rapid Commun. Mass Spectrom.* 2012, 26, 1923-1933.

Acknowledgement

Financial support is gratefully acknowledged

- Bruker Daltonics (Bremen, Germany)
- Thermo Fisher (Bremen, Germany)
- iGenTraX UG (Haan, Germany)
- DFG – German Research Foundation
- DAAD – German Academic Exchange Service
- BUW – University of Wuppertal, Germany
- iPAMS – Institute for Pure and Applied Mass Spectrometry, University of Wuppertal, Germany