Miniaturized Mass Spectrometers

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Mobile Micro- and Nano-instruments

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Why Miniaturize?

- Mass spectrometers are bulky and expensive
- Scaling laws are drivers for miniaturization
  - Mean free path in gas with collision diameter d at temperature T, pressure P is $\lambda = kT/(2^{1/2}\pi d^2 P)$
  - Flight path L must be smaller than λ, so pressure must be $P < kT/(2^{1/2}\pi d^2 L)$.
  - If $d = 3.7 \times 10^{-10}$ m (N_2), $P = 6.8 \times 10^{-1}/L$ N/m^2 at 300 K (L in cm)
  - Miniaturization allows 1-2 orders of size reduction, so P can be higher. Pumps can be smaller, enabling portable and desktop systems.
- However, other scaling laws apply
  - Filter operation has scaling laws
  - Strong impact on sensitivity
  - Care also needed to avoid discharges

Frederick Aston
Cambridge ca 1920

Key Applications

- Portable systems for homeland security
  - Miniaturised vacuum components allow smaller pumps/batteries. Systems selling in quantity.
- Bench-top systems
  - Combination of separation and API allows improved LC-MS & CE-MS
- Many components being miniaturised
  - Ionisation by EI, plasma or ESI
  - Selection by magnetic sector, crossed field, travelling wave, time of flight, quadrupole, cylindrical ion trap, linear ion trap
  - Detection by Faraday cup arrays
- MEMS technologies increasingly employed
  - Activity since ca 1993 (Westinghouse)
  - Multiple efforts since 1995; portable MEMS 2005

Courtesy Naomi KisselJohns, Inficon

Microsaic Systems Chempack
Andrew Malcolm, Designer

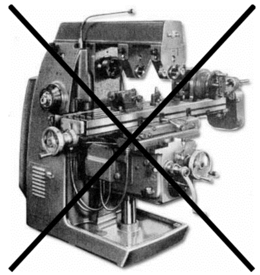
MEMS Technology (1)

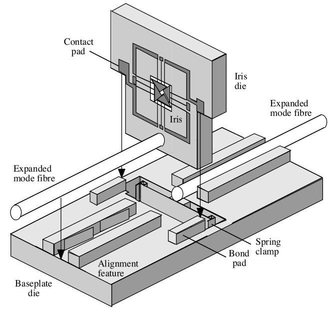
- Disadvantages
  - High infrastructure cost
  - High development cost; long development time
  - Hard to tackle 3D geometry of in-plane MS designs
  - Impact on mass resolution
  - Poor material quality (insulators, conductors, coatings)
  - Problems with RF - impact on mass range
  - Specialized packaging difficulties for vacuum systems
- Advantages
  - Ultimate miniaturization of in-chamber parts
  - Precise structuring and alignment
  - Allows mechanics, fluidics and ion optics on chip
  - Co-integration with electronics
  - Very low cost in volume

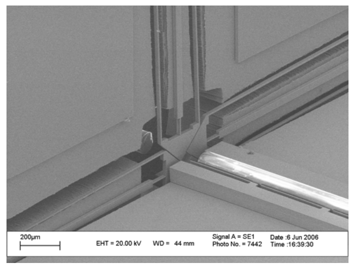
MEMS facilities,
Imperial College London

MEMS Technology (2)

- Different manufacturing approach
  - Limitations on achievable features
  - No possibility of rework
  - Batch development cycle
- Key enablers
  - Wafer bonding
  - Crystallographic etching of Si
  - Isotropic etching of nm-scale tips
  - Deep reactive ion etching for structuring Si
  - LIGA
  - Photopatterning of glass
  - Plastic substrate technologies
  - Wafer stacking and self-aligned micro-assembly
  - Packaging solutions from micro-optics



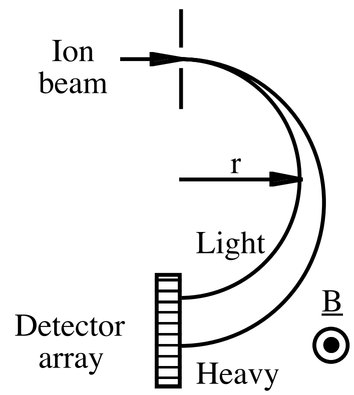


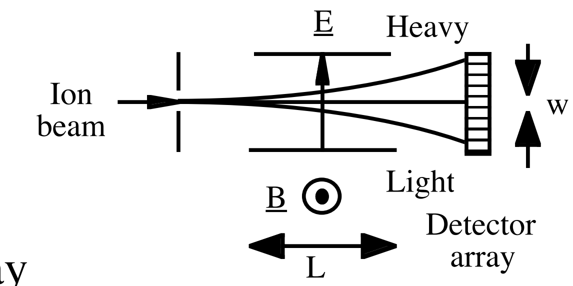


Veladi, Syms & Zou 2007

Magnetic Filters

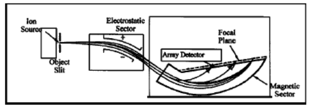
- Basic scaling laws:
  - Assume acceleration through potential V_a
  - Ion velocity is $v = (2qV_a/m)^{1/2}$
  - Trajectory radius is $r = (m/q)\ (v/B)$
  - Charge-to-mass ratio is $m/q = B^2r^2/2V_a$
- Radius is non-linear measure of m/q
  - Greater dispersion obtained by reducing ion energy V_a
  - However, V_a must be larger than thermal energy
- Small r only obtained with powerful magnet
  - Difficulties with saturation
  - Hard to scale into the MEMS size domain.
- High resolution requires high density detector array
  - Alternative is scanning in crossed field filter

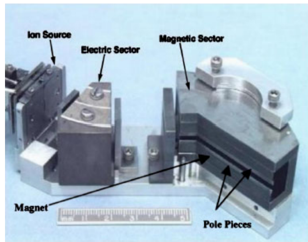


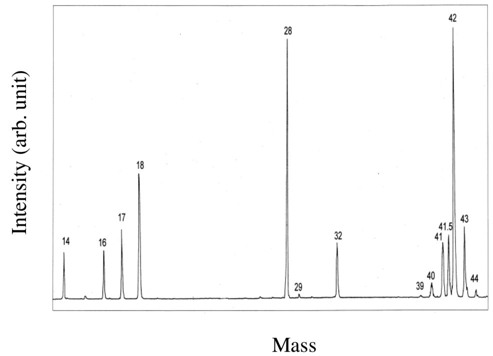


Miniature Magnetic Filters

- Magnetic separator
  - Sinha 2005
  - Mattauch-Herzog geometry
  - Nd-B-Fe magnet for reduced magnet mass
  - 1000 element CCD detector

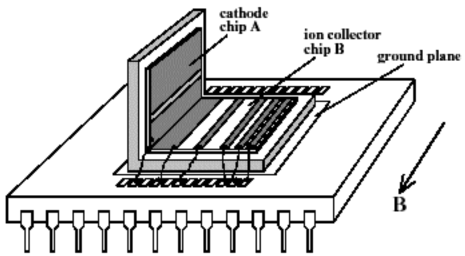


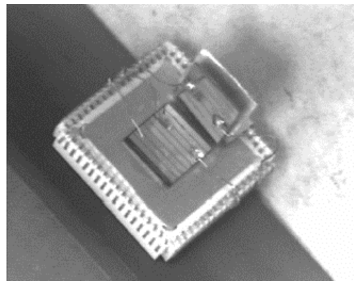




Courtesy Dr Mahadeva Sinha, JPL

- MEMS magnetic separator
  - Carr, Farmer & Sun 1998
  - Cold-cathode source
  - Strip array Faraday detector

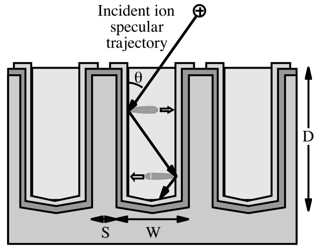


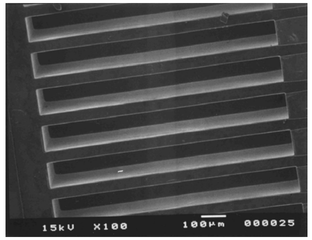


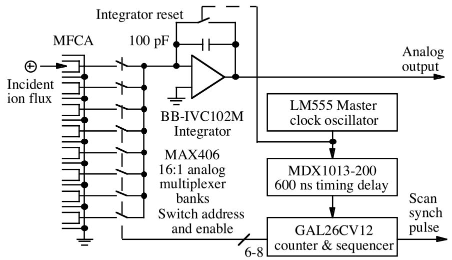
Courtesy Dr Beau Farmer, TSI

Detector Arrays

- Microfabricated Faraday cup arrays for linear dispersion magnetic mass spectrograph
  - Darling et al. 2002
  - DRIE used to form HAR trenches in Si, then oxidised and metallised to form array of independently addressable MOS capacitors
  - Arrays constructed with up to 256 elements and pitches down to 150 μm
  - Arrays combined with an electronic multiplexer to allow serial readout.



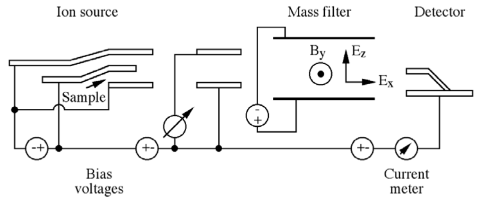




Courtesy Prof. Bruce Darling, Washington U.

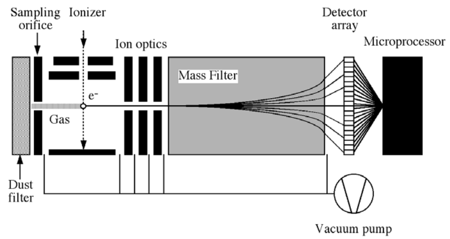
MEMS Wien Filters

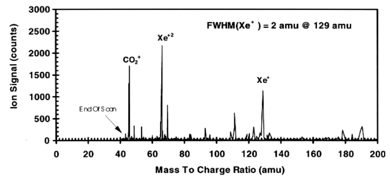
- Rosemount Analytical
  - Sittler 1995; Patent only



US 5,401,963

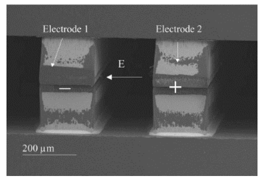
- Northrop Grumman
  - Freidhoff et al 1999
  - 1st working MEMS MS
  - Transverse electric field defined by 2D electrode array

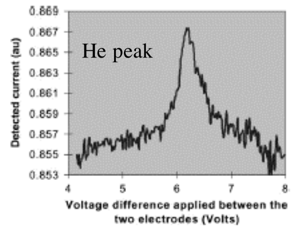




Courtesy Dr Carl Freidhoff, Northrop Grumman

- CEA/LETI
  - Sillon & Baptist 2002
  - Stacked wafer assembly
  - Transverse electric field defined by 3D electrodes

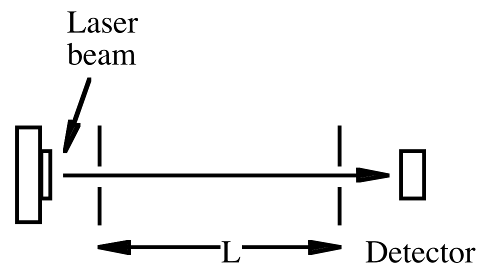




Courtesy Dr Nicolas Sillon, CEA LETI

Time-of-Flight Filters

- Basic scaling laws:
  - Assume acceleration through potential V_a
  - Ion velocity is $v = (2qV_a/m)^{1/2}$
  - Time of flight is $\tau = L/v$
  - Charge-to-mass ratio is $m/q = 2V_a\tau^2/L^2$

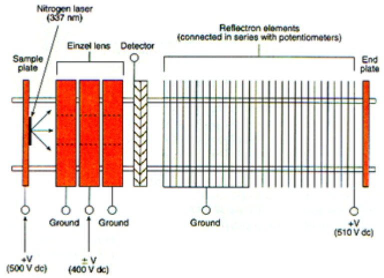


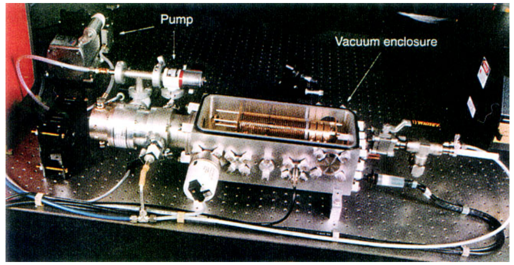
- Time-scale non-linear

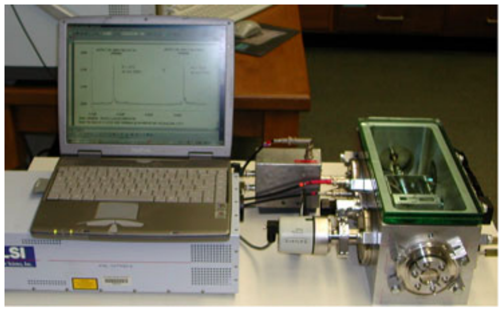
- Flight times reduce linearly with dimension L
  - Short pulses (MALDI), fast detectors needed
  - Standard correction methods (e.g. reflectron) also needed

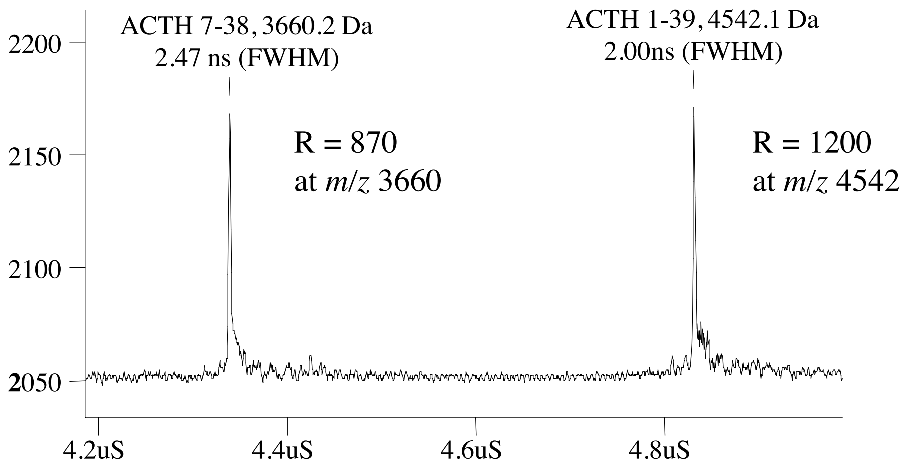
Miniature Time-of-Flight Filter

- Wiley-McLaren TOF with Mamyrin reflectron
  - Cotter et al 1992-
  - Tiny TOF; suitcase TOF
  - N_2 pulsed laser MALDI
  - Range 66 kDa; Resolution 1200
  - Bioagent detection





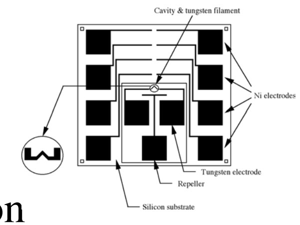


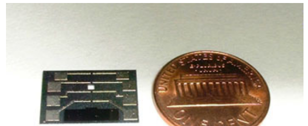


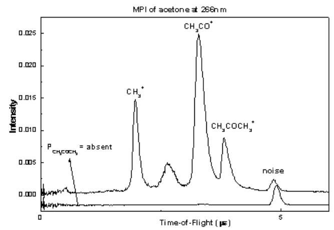
Courtesy Prof. Bob Cotter, Johns Hopkins U.

MEMS Time-of-Flight Filters

- MEMS TOF
  - Yoon et al 2002
  - Planar device with Wiley-McLaren geometry
  - Successful operation with pulsed Nd:YAG ionization

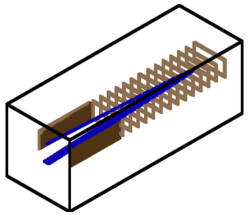


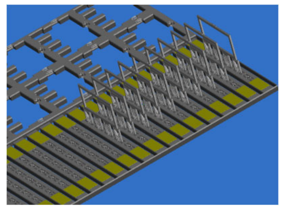


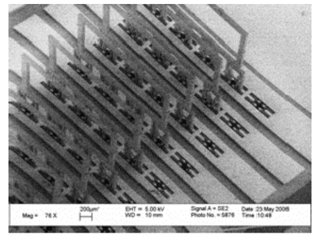


Courtesy Prof. Heung Joong Yoon, Ajou U. Korea

- MEMS reflectron
  - Verbeck 2007
  - Plug assembled electrode array



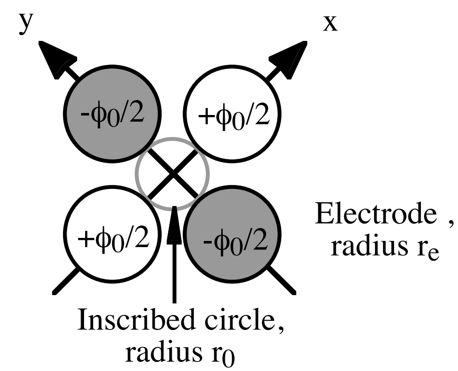


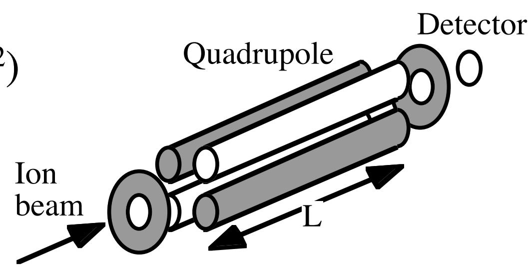


Courtesy Prof. Guido Verbeck, U. North Texas

Quadrupole Filters

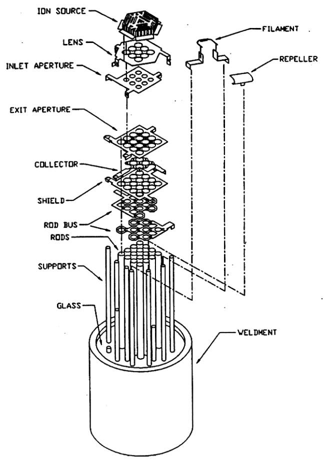
- Basic scaling laws
- Electrodes establish 2D potential $\phi = \phi_0(x^2 - y^2)/2r_0^2$.
  - Here r_0 is radius of inscribed circle, where $\phi = \pm \phi_0/2$.
  - Cylindrical electrode with optimised rod radius
- Forces on ion moving in z-direction:
  - $m\, d^2x/dt^2 = -e\phi_0 x/r_0^2 \quad md^2y/dt^2 = +e\phi_0 y/r_0^2$
- Potential is $\phi_0 = U - V\cos[\omega(t - t_0)]$
  - So $d^2u/d\zeta^2 + \{a_u - 2q_u \cos[2(\zeta - \zeta_0)]\}\, u = 0$
  - Here $\zeta = \omega t/2$, $a = 4eU/(m\omega^2 r_0^2)$ and $q = 2eV/(m\omega^2 r_0^2)$
  - u is x or y, and $a = a_x = -a_y$ and $q = q_x = -q_y$
  - U & V scale as $1/r_0^2$ - lower voltages
- Resolution is $m/\Delta m = n^2/20$, where n is no. of cycles
  - For axial energy V_a and length L, $\Delta m = 40eV_a/(f^2L^2)$
  - Frequency must increase with $1/L$

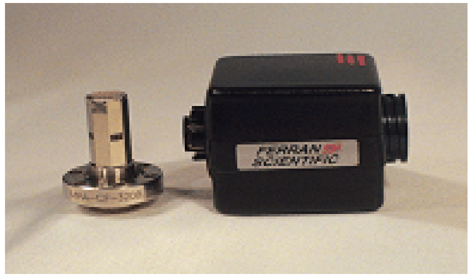




Miniature Quadrupole Arrays

- Rod-sharing arrays to recover sensitivity
- Ferran Micropole
  - Ferran et al. 1996
  - Precision glass assembly jig - limits to mechanical assembly?
- JPL Quadrupole array
  - Orient et al. 1997
  - Ceramic alignment jig
  - RGA for ammonia coolant detection
  - Self-contained unit for extra-vehicular activity





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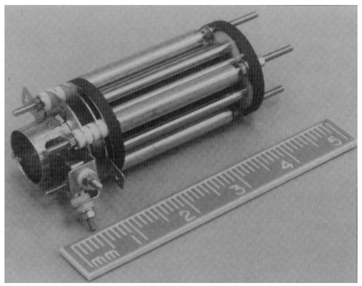
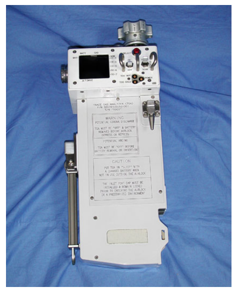
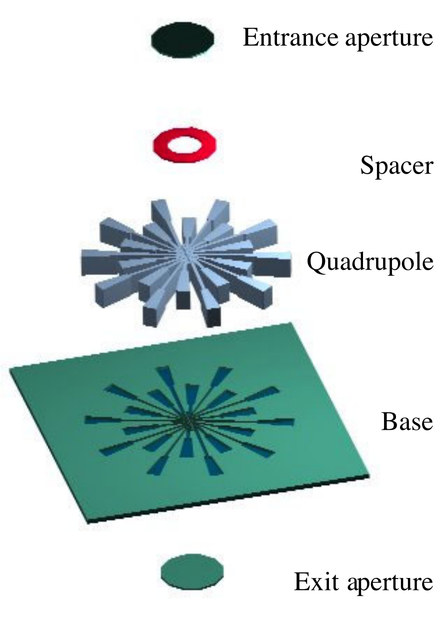


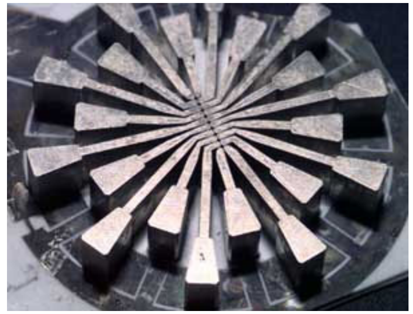


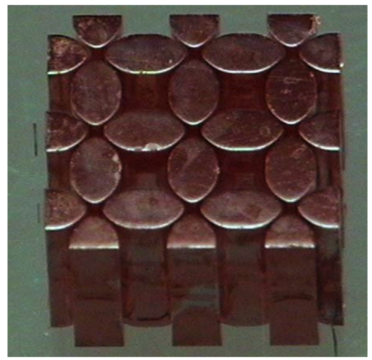
Courtesy Dr Ara Chutjian, JPL

LIGA Quadrupole Array

- JPL LIGA Quadrupole
  - Wiberg et al. 1997-
- Synchrotron exposure of thick resist.
  - Short wavelength and high energy ensures low diffraction, large exposure depth and vertical walls
- Hyperbolic electrode array
  - Electroplating to fill mould



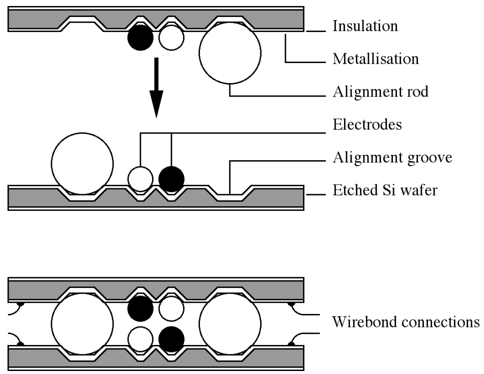


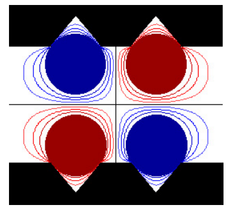


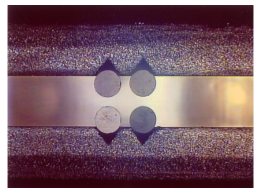
Courtesy Dr Dean Wiberg, JPL

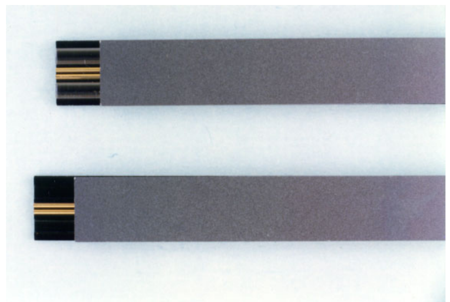
V-groove MEMS Quadrupole

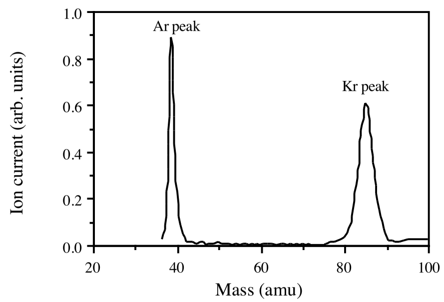
- 1st MEMS quadrupole
  - Syms, Taylor, Ahmad, Tindall 1995-1999
  - V-groove etched silicon; metallised glass electrodes; self-aligned spacer rods
  - Accurate alignment using crystal planes
- Limitations
  - Parasitic capacitance to substrate via oxide
  - Mass range & resolution limited by heating
  - Hard to add other features





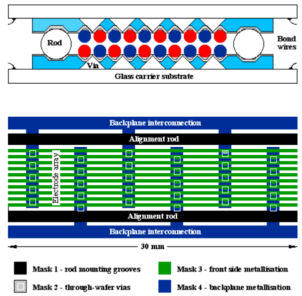


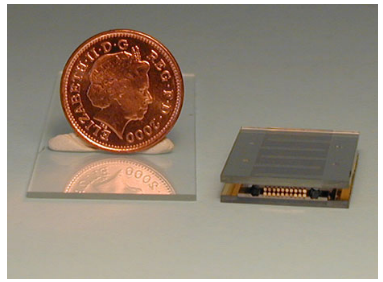




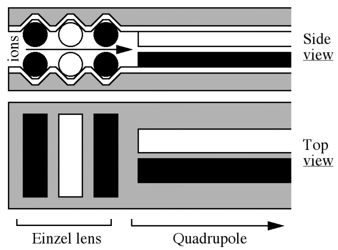
Advanced V-Groove Quadrupoles

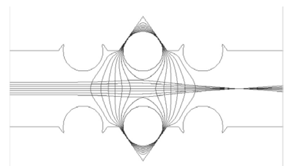
- Array-type quadrupole
  - Syms & Ahmad, 2001
  - Connection to rods via substrate
  - Parallel or independent operation

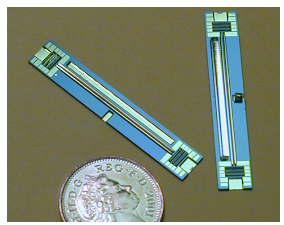


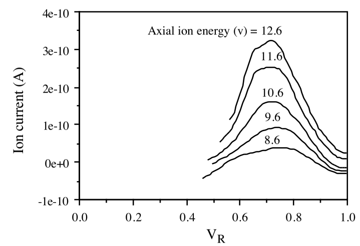


- Coupling optics
  - Syms, Michelutti & Ahmad 2003
  - Additional coupling optics
  - 1-D Einzel lens from cylindrical rods
  - Weak focusing into quad



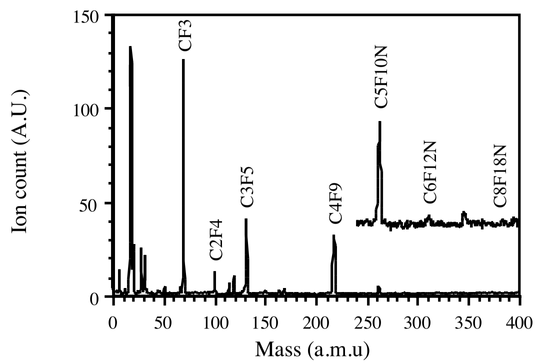


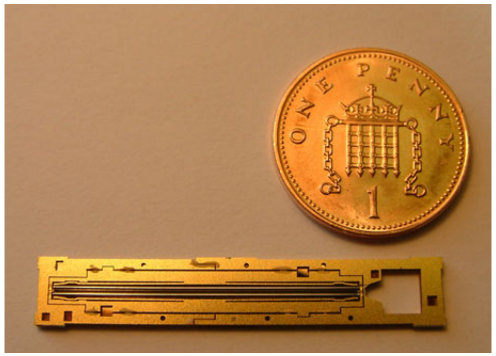




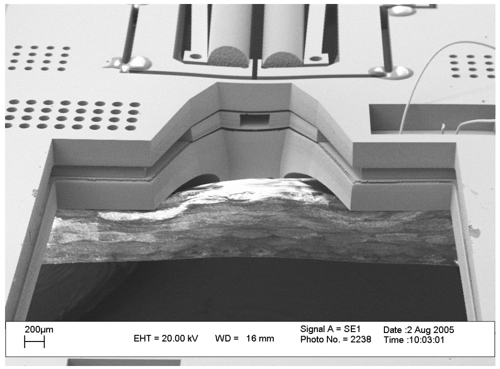
Microsaic Ionchip

- Monolithic construction
  - Geear, Syms, Wright & Holmes 2005
  - BSOI structured by DRIE
  - Stacked assembly with internal coupling optics and metal rods in spring retainers
  - 0.65 mm rods, 6 MHz operation
- Repeatable performance to 400 amu
  - Low RF heating



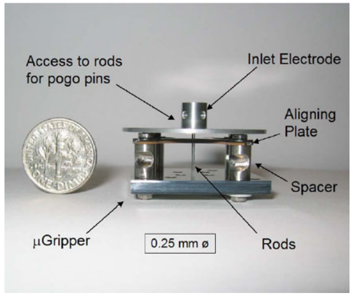


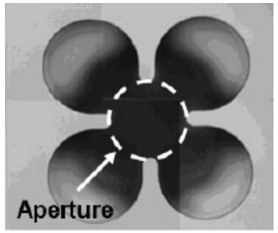
Microsaic Systems Ltd.

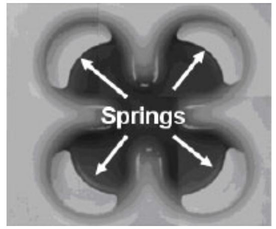


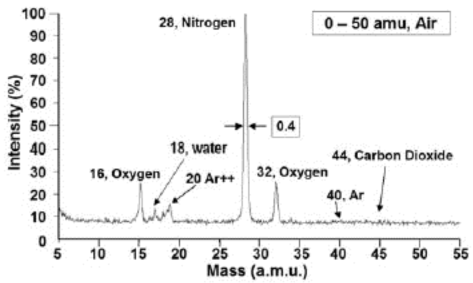
MIT Quadrupole

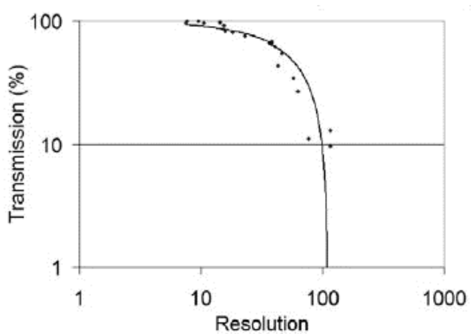
- Out-of-plane geometry
  - Velasquez-Garcia, Cheung, Akinwande 2007
- "μGripper" technology
  - BSOI alignment plates
  - 1.58 mm dia steel electrodes held in spring clips; 4 MHz operation
  - Carbon nanotube field emission ionizer being developed







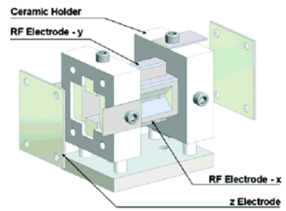


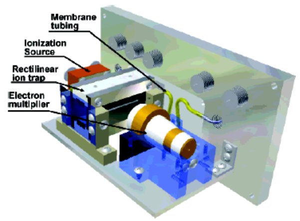


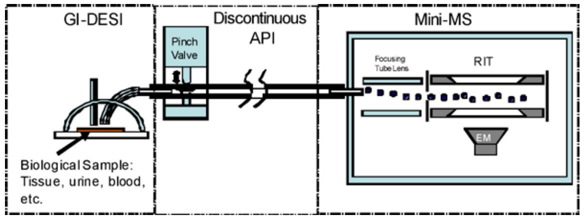
Courtesy Prof Luis Velasquez-Garcia,
Prof. Tayo Akinwande, MIT

Ion Traps

- Most popular form of miniature MS
- Hyperbolic traps by CNC machining
  - Kaiser & Cooks 1991
  - Difficult as size reduces
- Cylindrical electrode approximation
  - Simple to form by drilling, etching
- Rectilinear ion traps
  - Gao, Song, Patterson, Cooks & Ouyang 2006
  - Axially-ejecting Schwartz/Syka design
  - Greater ion storage capacity
  - Commercialised as Mini10
- Coupled with DESI by discontinuous API



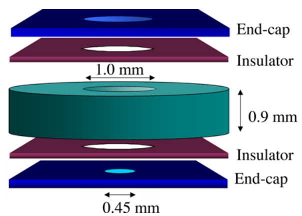




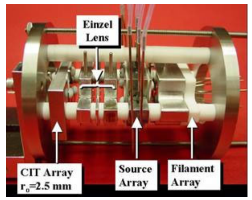
All courtesy Prof. Graham Cooks, Purdue U.

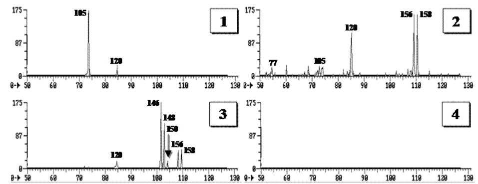
Cylindrical Ion Trap Arrays

- Cylindrical traps
  - Kornienko, Reilly, Whitten & Ramsey 1999
- Regular or chirped arrays
  - Badman & Cooks 2000
  - Mass selection by variation of trap dimension
- Microfabricated traps developed
  - Van Amerom et al 2006
  - DRIE & stacking of Si
- See also
  - Sandia trap array with air bridge interconnects (Blain et al 2004)

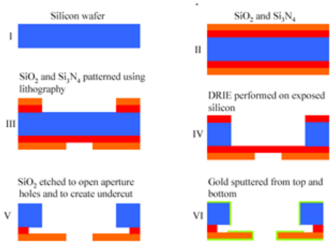


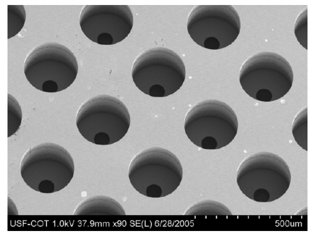
Courtesy Prof. Michael Ramsey, U. North Carolina





Courtesy Prof. Graham Cooks, Purdue U.

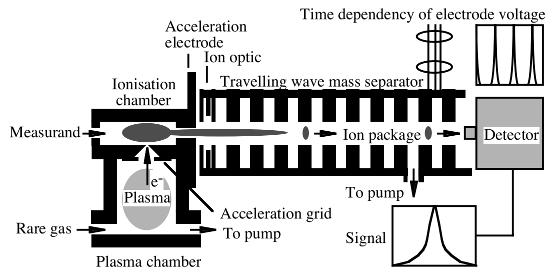




Courtesy Tim Short, Friso van Amerom & Ashish Chaudhary, SRI

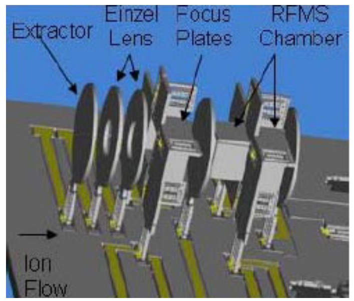
Novel MEMS Analyzers

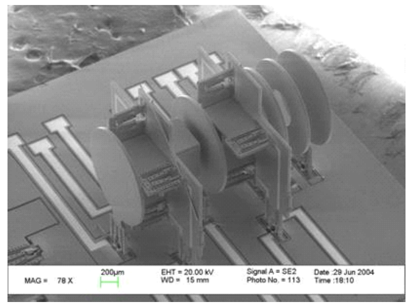
- Travelling wave mass spectrometer
  - Siebert et al. 1999
  - Stacked wafer assembly
  - Plasma ion source
  - Separation by travelling periodic electric field



Courtesy Prof. Jorg Muller, TU Hamburg-Harburg

- Rotating field mass spectrometer
  - Saini, Verbeck (Zyvex) & Smith (JPL) 2006
  - Separation by rotating electric field
  - Simple planar electrode structure
  - Plug assembled MEMS

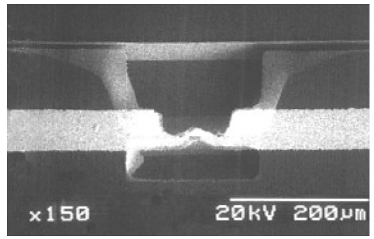


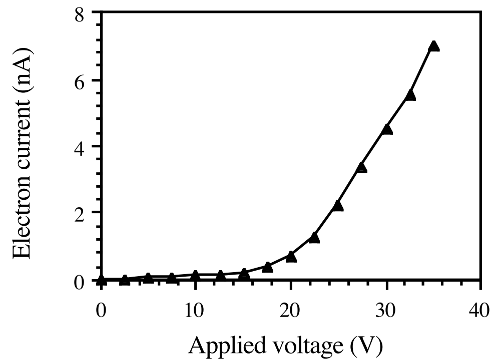


Courtesy Katherine Green, Zyvex Labs & Guido Verbeck, North Texas U.

MEMS Hot Cathode Ion Sources

- Current density J from electrically heated filament obeys the modified Richardson-Dushman equation $J = AT^2 \exp\{-(\phi - \Delta\phi)/kT\}$
  - Here E is field, ϕ is work function, $A = 4\pi m_\varepsilon k^2 \varepsilon / h^3$ is Richardson's constant, where m_e is electron mass and $h = 6.62 \times 10^{-34}$ J s.
  - Field-induced term is $\Delta\phi = (eE/4\pi\varepsilon_0)^{1/2}$, where $\varepsilon_0 = 8.85 \times 10^{-12}$ F/m
- Exponential variation requires low work function material (e.g. W) that can survive high temperature
  - Difficulties in fabrication and thermal management have hindered development of integrated sources
- Suspended filaments fabricated
  - Yoon et al. 2001

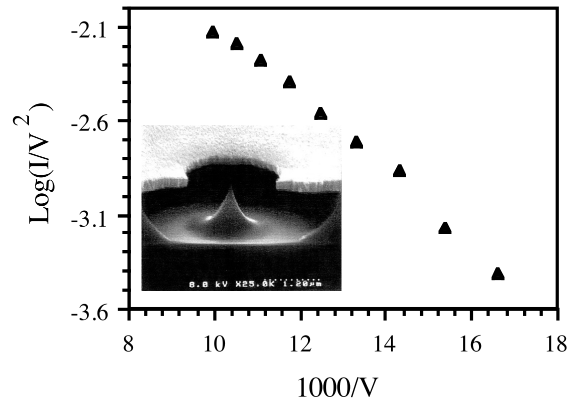




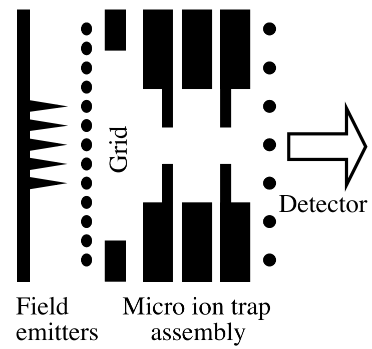
Courtesy Heung Joong Yoon, Ajou U. Korea

MEMS Cold Cathode Ion Sources

- Current density given by Fowler-Nordheim equation $J = AE^2 \exp(-B\phi^{3/2}/E)$.
  - Dominant factor is electric field. Suitable fields obtained at ≈ 100 V from tips with radii ≈ 1 nm, made by microfabrication.
  - Since $\log_e(J/AE^2\} = -B\phi^{3/2}/E$, plot of $\log_e(I/V^2)$ versus $1/V$ (where I is emission current and V is voltage) should be linear.
- Reduction in temperature and elimination of heater current important for portable systems.
- Sources fabricated and demonstrated with CITs
  - Main difficulty is limited lifetime, due to discharge and sputtering



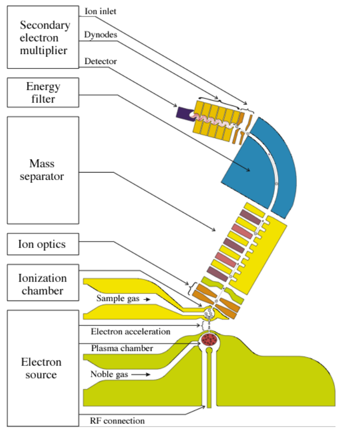
Courtesy Dr Ejaz Huq, RAL CMF

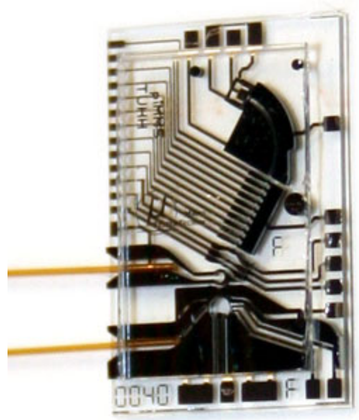


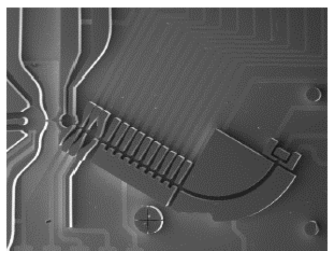
Courtesy Prof. Michael Ramsey, U. North Carolina

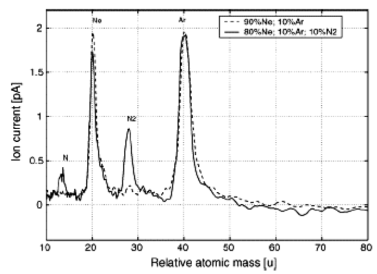
MEMS Plasma Ion Sources

- Planar integrated micro mass spectrometer (PIMMS)
  - Hauschild et al. 2007
  - Silicon-on-glass; features defined by 1 mask and deep silicon etch
- Plasma ion source
  - 50 Pa operation
- Synchronous ion shield (SIS) mass separator
  - 1 Pa operation
- 90^{o} sector energy filter
- Multiplying detector planned



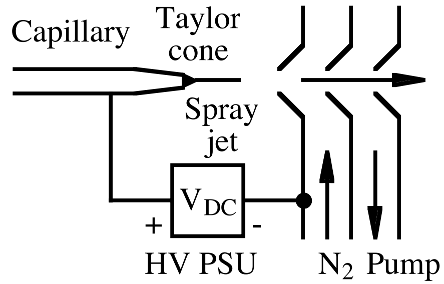




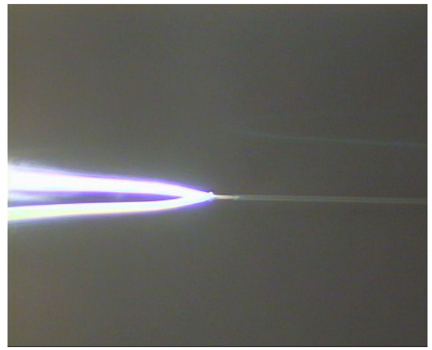


Courtesy Jörg Müller, Eric Wapelhurst & Jan-Peter Hauschild, TU Hamburg-Harburg

Nanoelectrospray

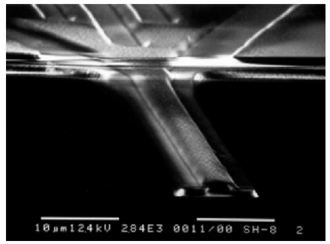


- Allows separation and analysis (LC-MS; CE-MS)
- Efficient formation of ions with high m/q. Depends on
  - Physical properties of analyte liquid (conductivity σ, dielectric constant ε, surface tension γ)
  - Geometric properties of set-up (capillary internal radius R and capillary-electrode separation D)
  - Operational parameters (applied voltage V, flow rate Q)
- Scaling laws
  - Droplet radius $r \sim (Q\varepsilon\varepsilon_0/\sigma)^{1/3}$
  - Ion current $I \sim (\gamma Q\sigma/\varepsilon)^{1/2}$
  - Threshold voltage $V_T \sim (\gamma D/\varepsilon_0)^{1/2}$
  - Decreasing D decreases V_T
  - Decreasing flow rate alters r and fission processes

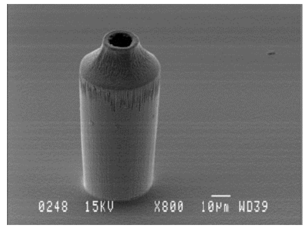


Chip-based Nanospray

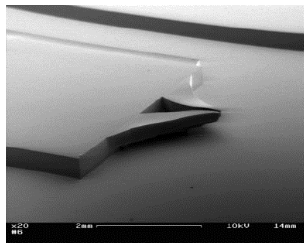
- Many variants demonstrated
  - Care needed to avoid Taylor cone spread in hydrophilic glass
  - Now formed in glass coated with e.g. parylene, plastic, Si and BSOI
- In-plane and through-wafer geometries
  - Linear and 2D arrays
  - Tip geometries now complex; include channels, open channels and nibs
  - Gaseous and ultrasonic nebulizers and signal enhancers being incorporated
- Generally omitting on-chip ion extraction
  - Signal stability variable

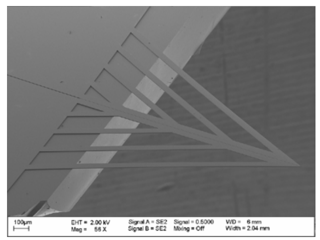


Courtesy
Prof. Yu-Chong Tai,
Caltech



Courtesy
Prof. Göran Stemme,
KTH Stockholm

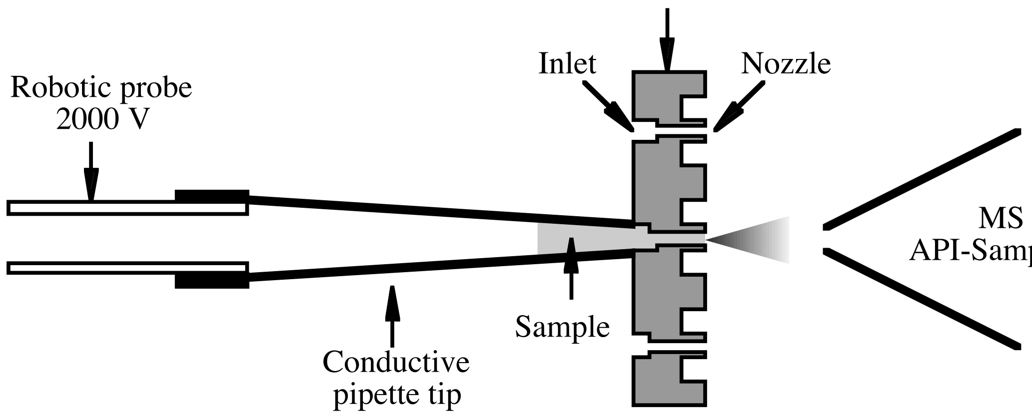


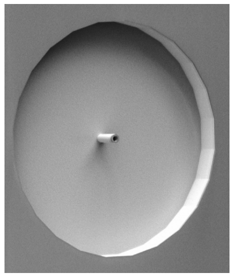


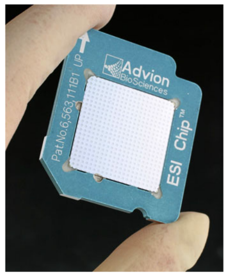
Courtesy Prof. Steve Arscott, Lille U.

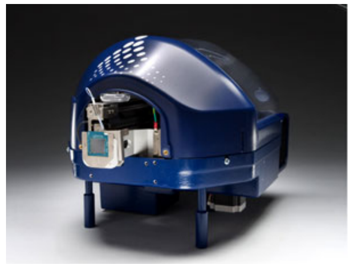
Advion TriVersa NanoMate

- Successful commercial system compatible with API-MS
  - Corso et al 2001
  - Chip-based infusion MS/MS
  - 400 nozzles in 2D array by DRIE of Si
  - Complete ion gun, insensitive to position wrt MS
  - Compatible with robotic handling





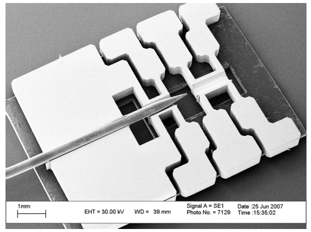


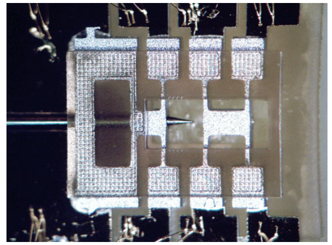


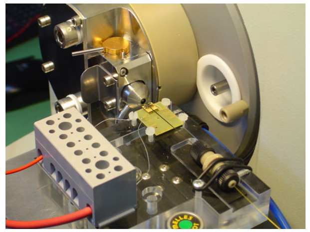
Courtesy Jack Henion, Advion Biosciences

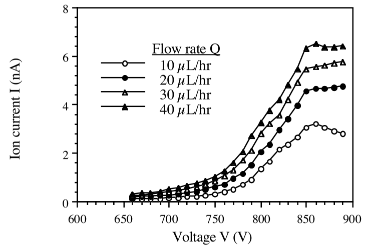
Microsaic Spraychip

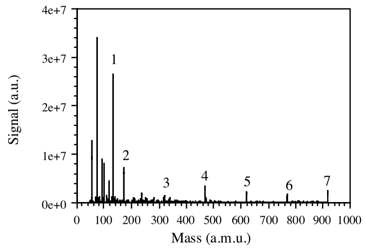
- Nanospray ion gun
  - Syms, Zou, Bardwell & Schwab 2007
- Batch produced MEMS device
  - Electrodes by DRIE of Si
  - Mount by V-groove etching of Si
  - Base in photopatterned epoxy resist
- Low voltage (800V) operation
  - Compatible with nanospray capillaries
  - On-chip spray detection
  - Stable spray; insensitive to position
- Good analytical performance
  - Low solvent contamination

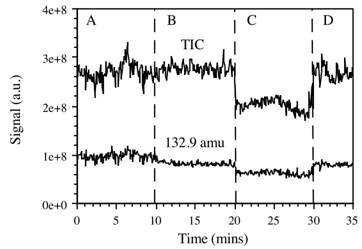










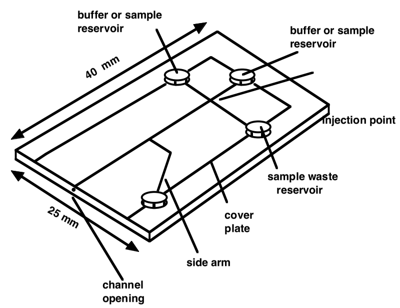


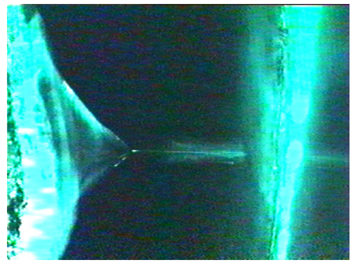
Microsaic Systems Ltd.

59th Ann. Pittsburgh Conf. on Analytical Chemistry and Applied Spectroscopy, New Orleans, March 2008
Mobile Micro- and Nano-instruments

Hyphenated Techniques

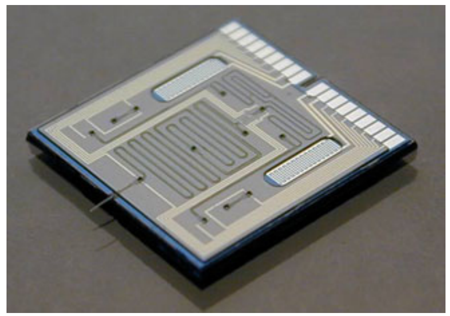
- CE-MS
  - Ramsey and Ramsey 1997
  - Electro-osmotic pumping & electrophoretic separation
  - Spray from CE separator chip with low peak broadening





Courtesy Prof. Michael Ramsey, U. North Carolina

- HPLC-MS
  - Tai et al 2007
  - Complete HPLC-ESI on chip
  - Pump, flow & gradient sensors, trap column, analytical column, electro-chemical sensors, filter and ESI nozzle

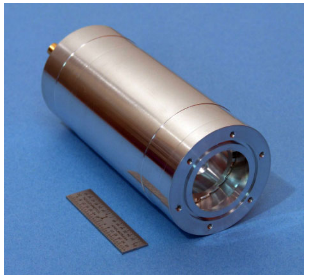


Courtesy Prof. Yu-Chong Tai, Caltech

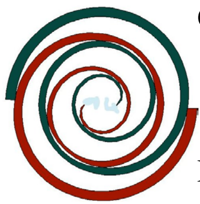
Vacuum Pumps

- Pfeiffer TPD 011 Turbo drag pump
  - 10 L/s pumping speed (N_2)
  - 860 g mass
- Creare Miniature TMP
  - 4 L/s pumping speed (air)
  - 550 g mass
  - 100,000 RPM rotor speed
- Creare Miniaturize Turbo-drag Pump
  - 130 g mass
  - 200,000 RPM rotor speed
- MEMS pumps
  - Scroll, getter and Knudsen types all investigated in recent years

Courtesy Peter Knight, Pfeiffer Vacuum UK



Courtesy Bob Kline-Schoder, Creare



Orbiting scroll

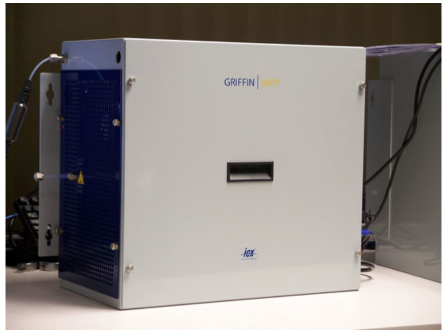
Fixed scroll

LIGA scroll

Courtesy Dr Dean Wiberg, JPL

Benchtop Systems

- Griffin Analytical 600P™
  - Cylindrical ion trap
  - 40-425 m/z
  - MS^n
  - 55 lbs



Courtesy Mitch Wells, Griffin Analytical
Adam Keil & Brent Rardin, designers

- Microsaic Systems Chemcube
  - Finlay, Syms, Wright, Malcolm 2006
  - MEMS quadrupole
  - 1-400 m/z
  - SPME interface
  - 35 lbs

Microsaic Systems Ltd.

Courtesy Microsaic Systems
Andrew Malcolm, designer

Conclusions

- Worldwide effort on miniaturizing mass spectrometers
  - Main drivers homeland security and pharma apps
- Miniaturized systems now extremely advanced
  - Complex systems developed
  - Traps, arrays, MS^n and API
- Portable and benchtop systems being developed
  - Pumps still difficult for portable systems
  - Personal mass spectrometer feasible
- Increasing use of MEMS technology
  - Especially fluidic separation/electrospray sources & mass filters
  - Considerable performance improvement
  - Confidence growing over outcome
  - Single-chip system developed