Applications in Mass Spectroscopy

Andrei Nomerotski,
Oxford University/CERN

DESY, 26 March 2012

Outline

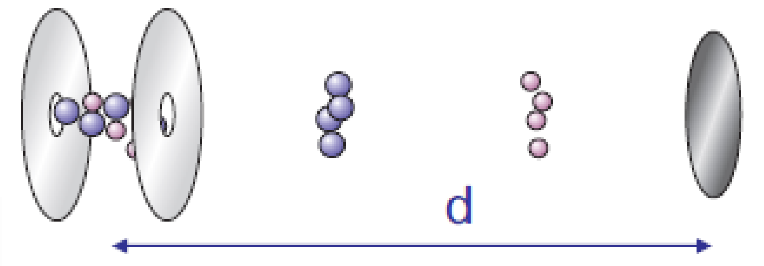
- Time-Of-Flight Mass Spectrometry
- Imaging Mass Spectrometry
  - Velocity Mapping
  - Surface Imaging
  - Timepix / PImMS sensors
- Direct detection of low energy ions

Mass Spectrometry

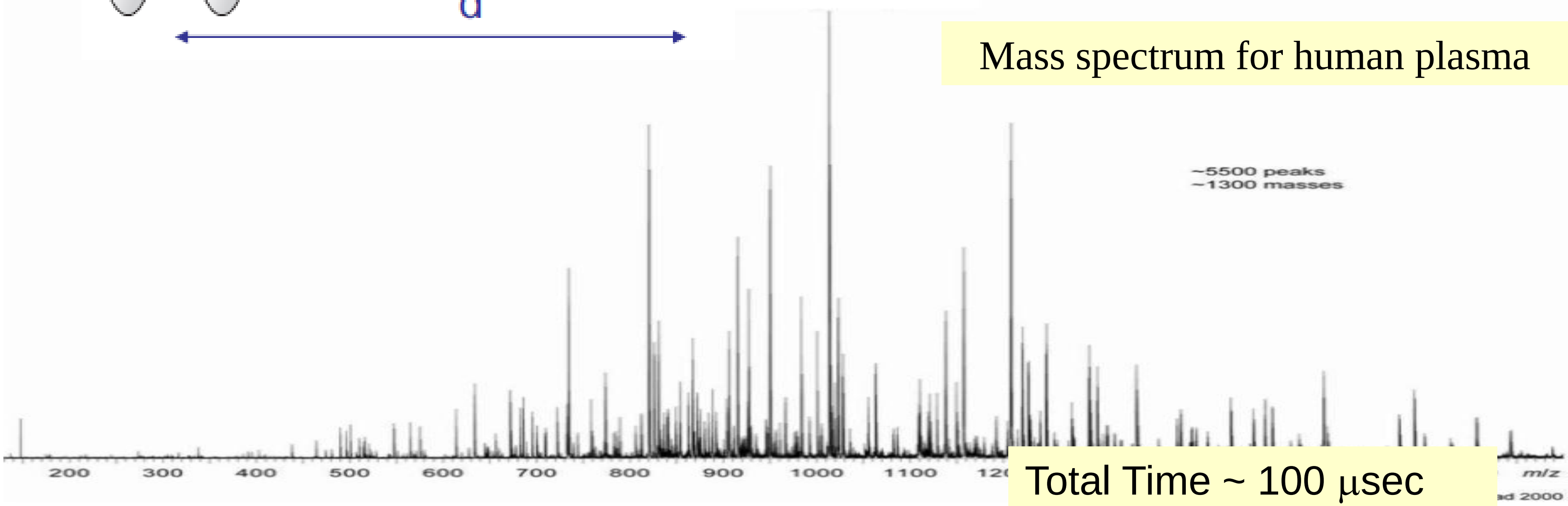
- Very popular tool in chemistry, biology, pharmaceutical industry etc.
- TOF MS: Heavier fragments fly slower

$$E = zV = \frac{1}{2}mv^2$$

$$t = d / v \propto (m/z)^{1/2}$$



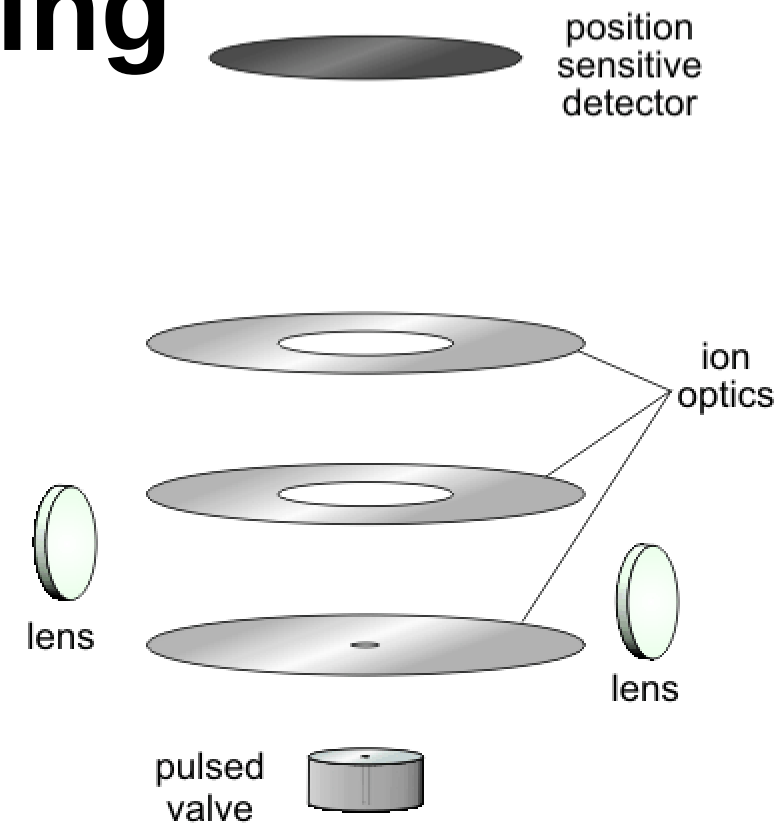
Mass spectrum for human plasma



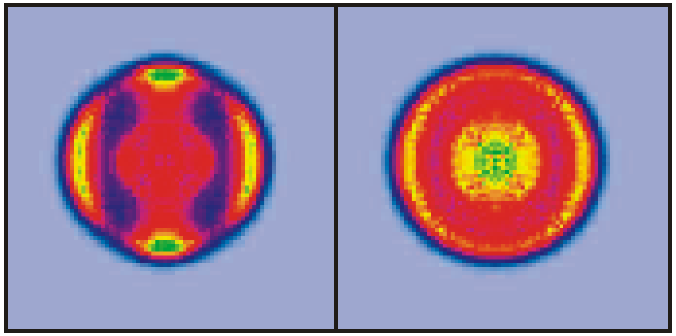
Total Time ~ 100 μsec

Measure detector current: limited to one dimension

Ion Imaging

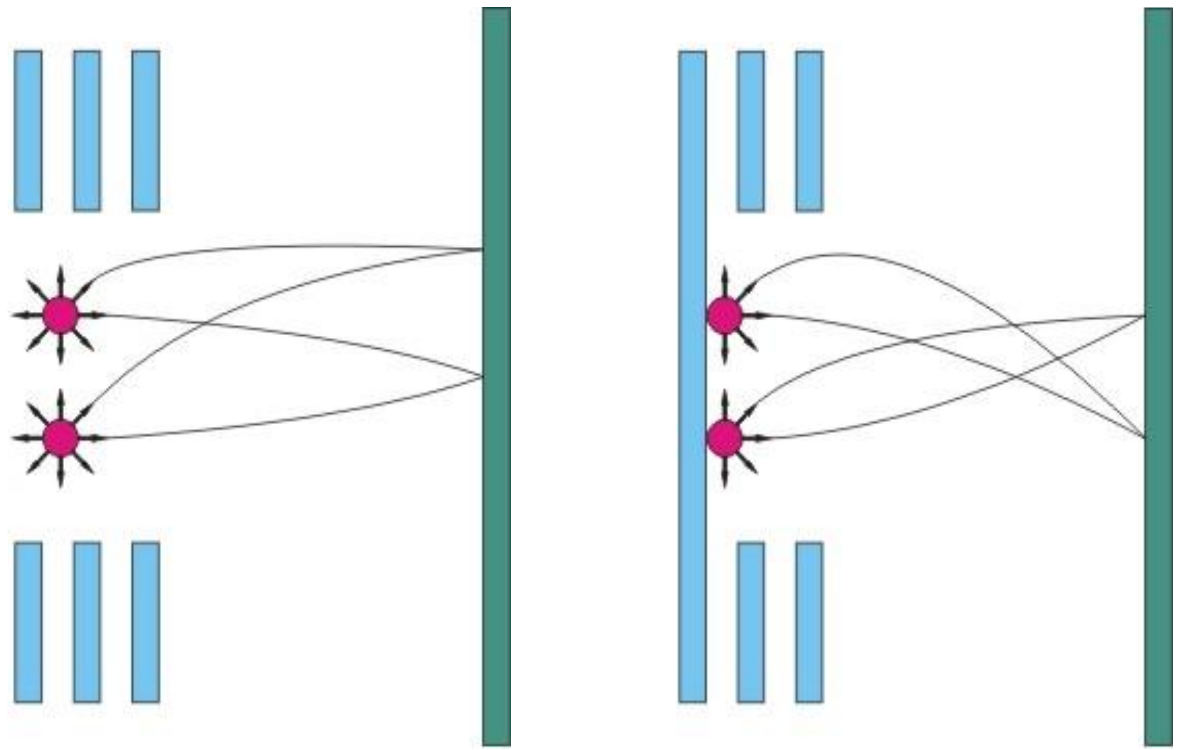


- Fix a mass peak by gating microchannel plate (MCP)
- Measure full scattering distribution of fragment ions
- Sensitive to fragmentation process



S atom ion images for OCS photodissociation at 248nm

Ion Imaging Modes

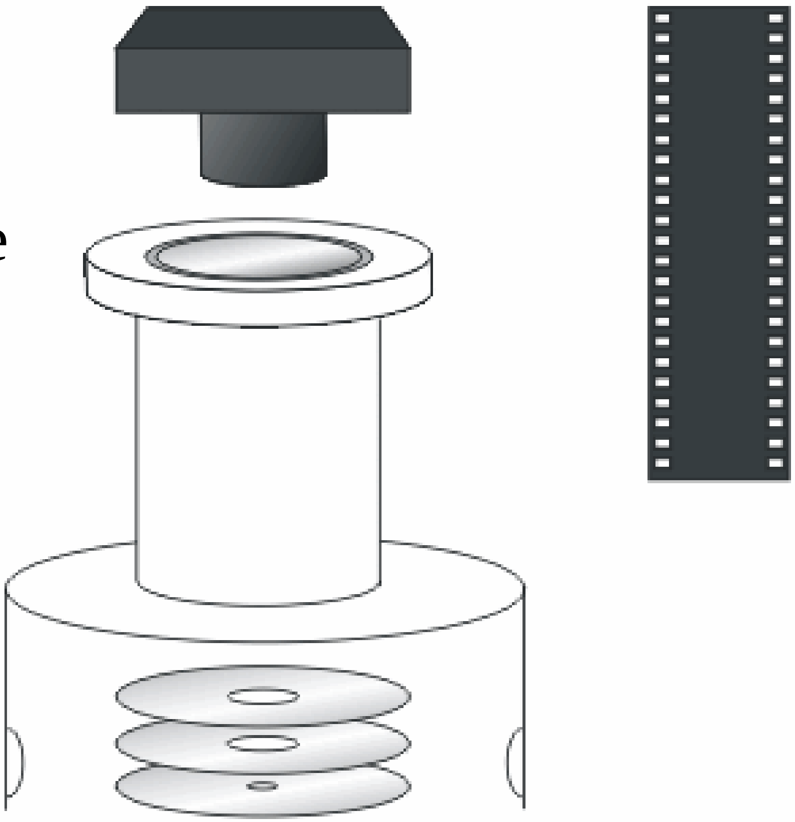


Velocity mapping Spatial mapping

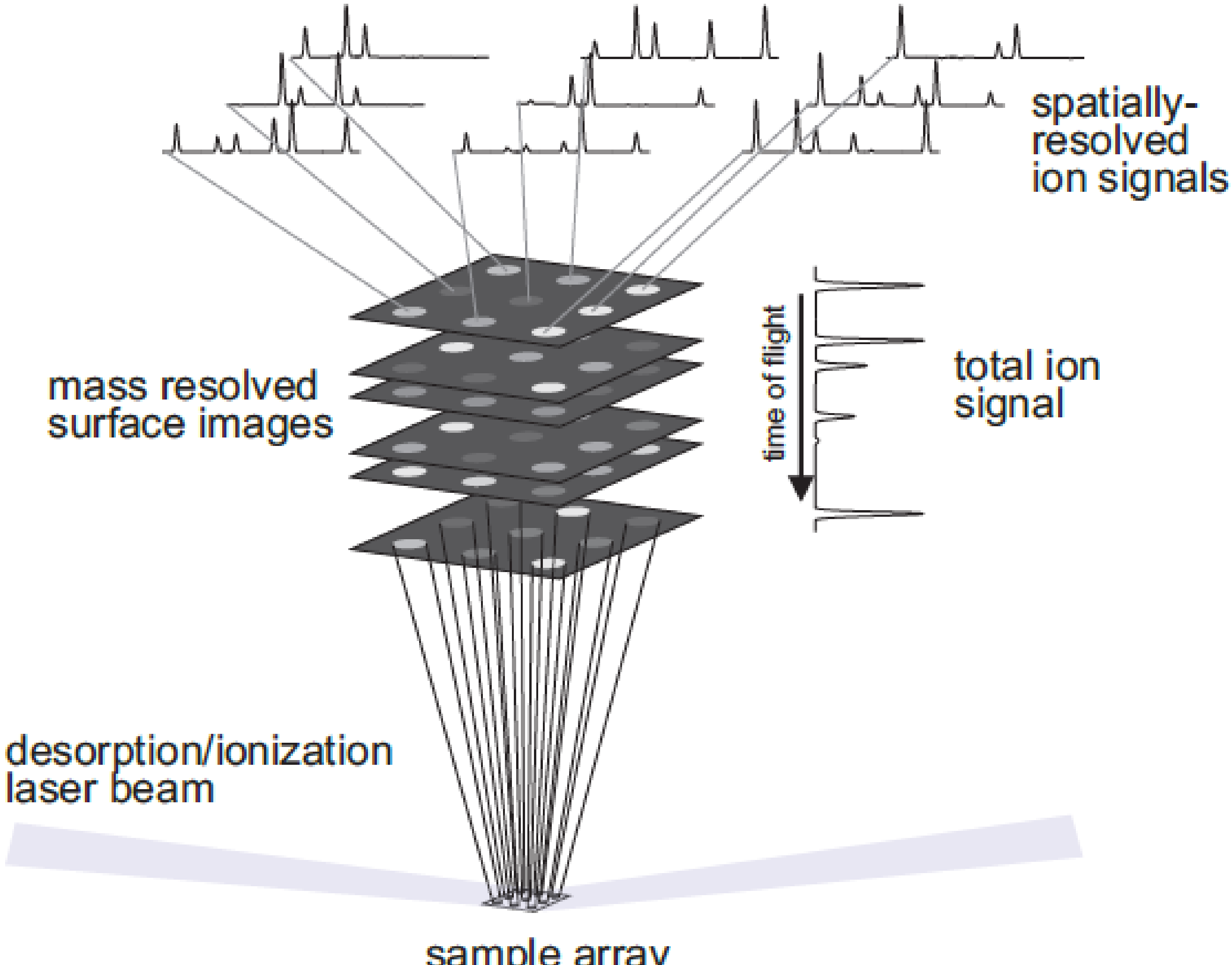
Imaging Mass Spectrometry with Fast Pixel Sensors

- Fast camera allows imaging of multiple masses in a single acquisition
- Mass resolution is determined by the camera speed

- Can measure full frames at high speed or directly measure time of arrival



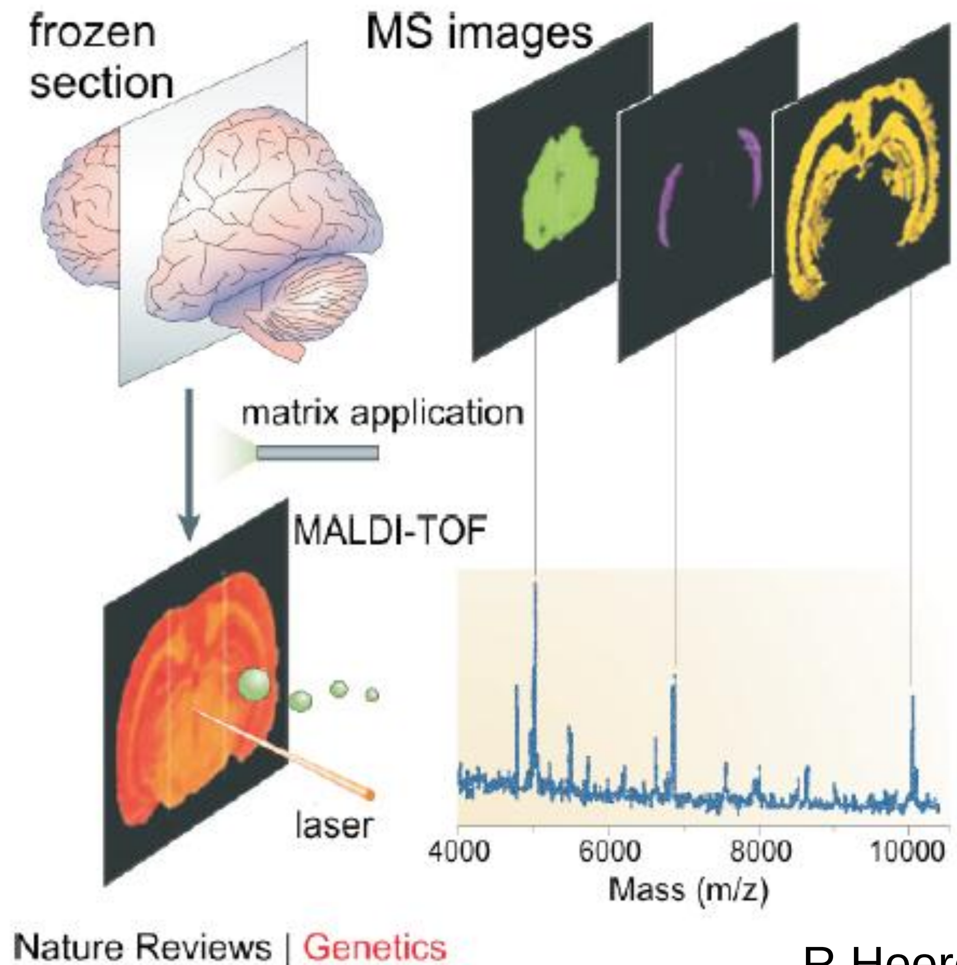
Possible applications (1)



- Parallel processing– high throughput sampling
- Example: analysis of biochips

Possible applications (2)

- Surface imaging for separate mass peaks
- Replace scanning with wide-field imaging
  - Faster by orders of magnitude

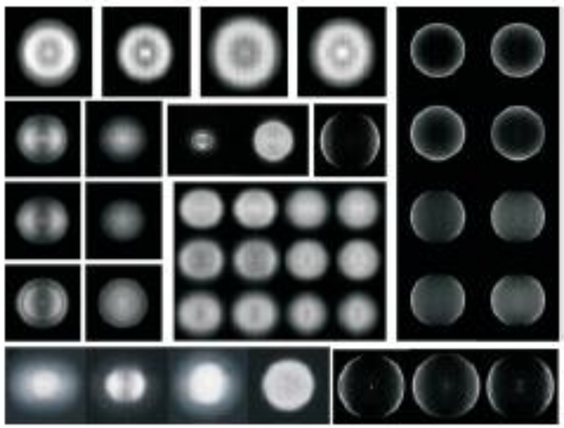


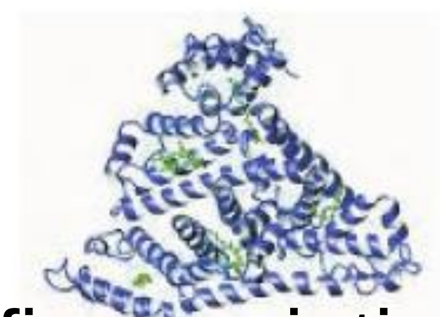
R.Heeren et al

MALDI imaging of tissue

Possible applications (3)

- Structural information: Fingerprinting of molecules



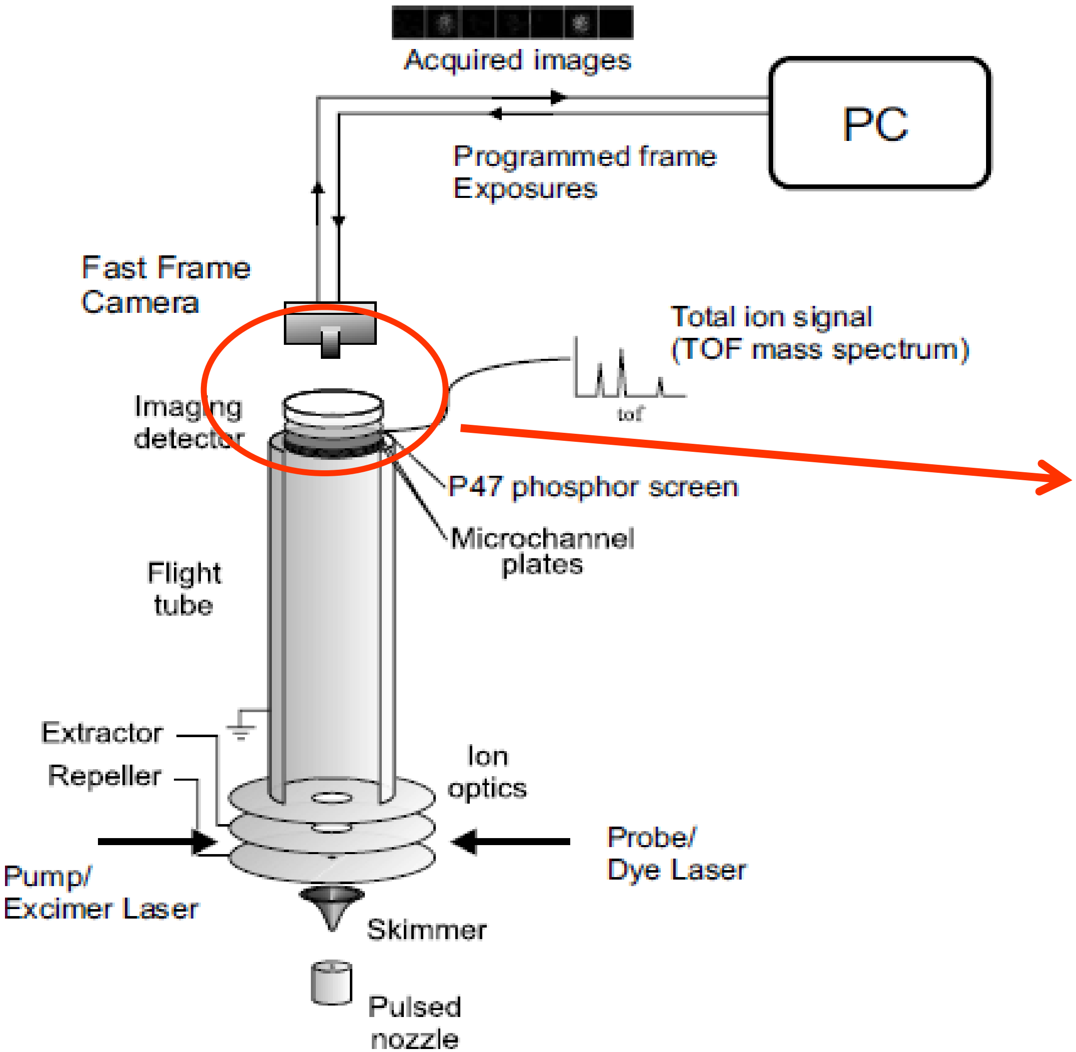


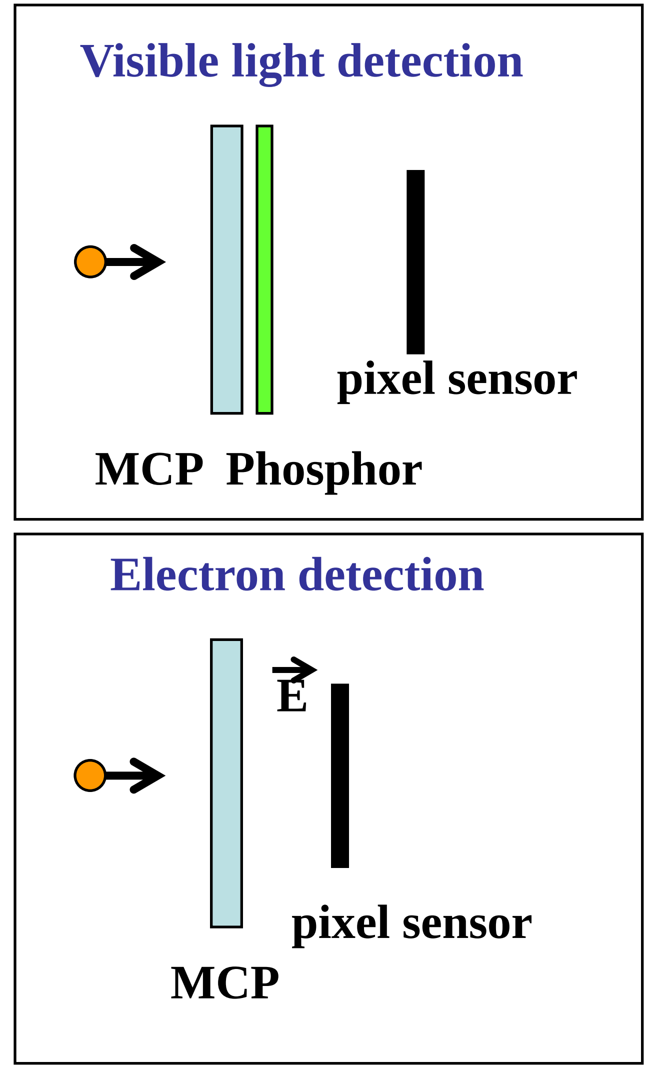
mass fingerprinting of human serum albumin

(from Wikipedia)

Visible Light vs Direct Detection

- Typically use visible light but direct detection of electrons after MCP is possible





Fast Framing

Velocity imaging experiments:

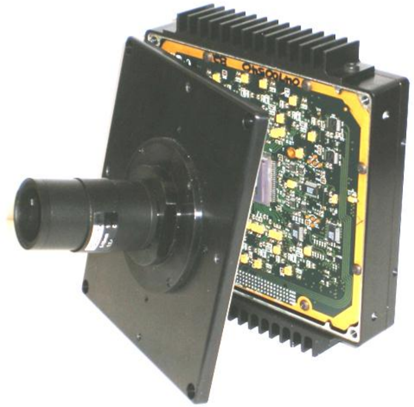
CCD camera by DALSA

16 sequential images at 64x64 resolution

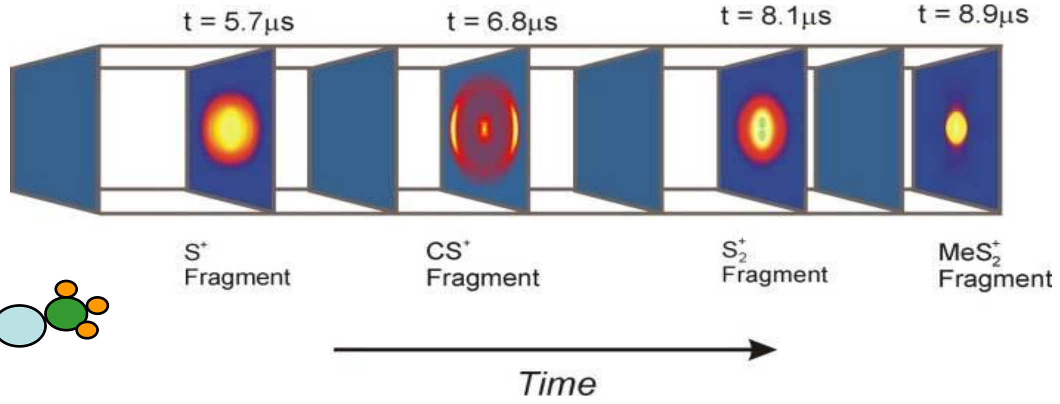
- Pixel : 100 x 100 sq.micron
- Frame rate 100 MHz → 10 ns resolution

Principle: local storage of charge in a CCD register at pixel level

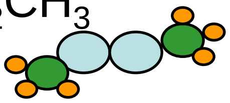
Limitation: number of frames

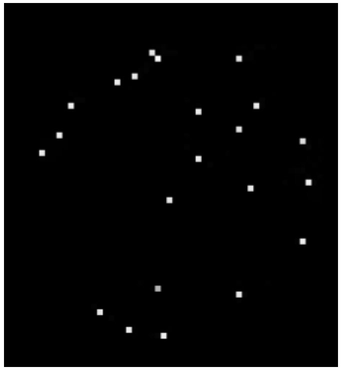


DALSA camera



$CH_3S_2CH_3$



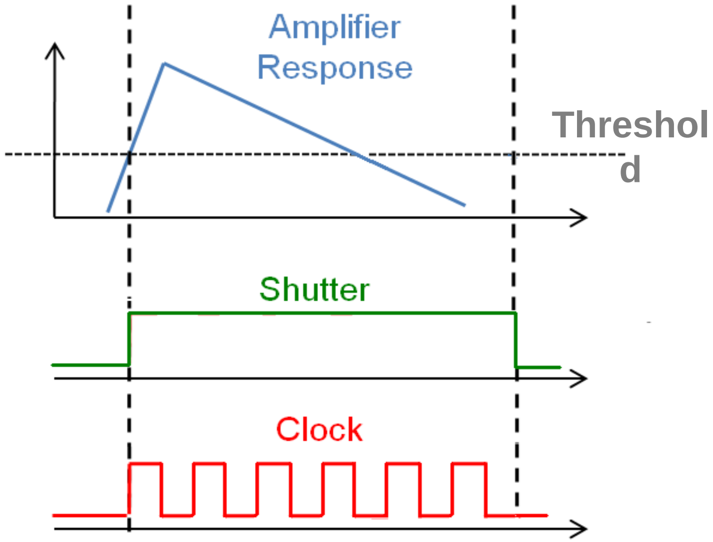


Single shot

3: M. Brouard, E.K. Campbell, A.J. Johnsen, C. Vallance, W.H. Yuen, and A. Nomerotski, *Rev. Sci. Instrum.* 79, 123115, (2008)

Time Stamping

- Time stamping is efficient way to have good time resolution generating much less data
- Need to do particle by particle → low intensity (one pixel hit only once or less)
- Measure Time of Arrival in each pixel

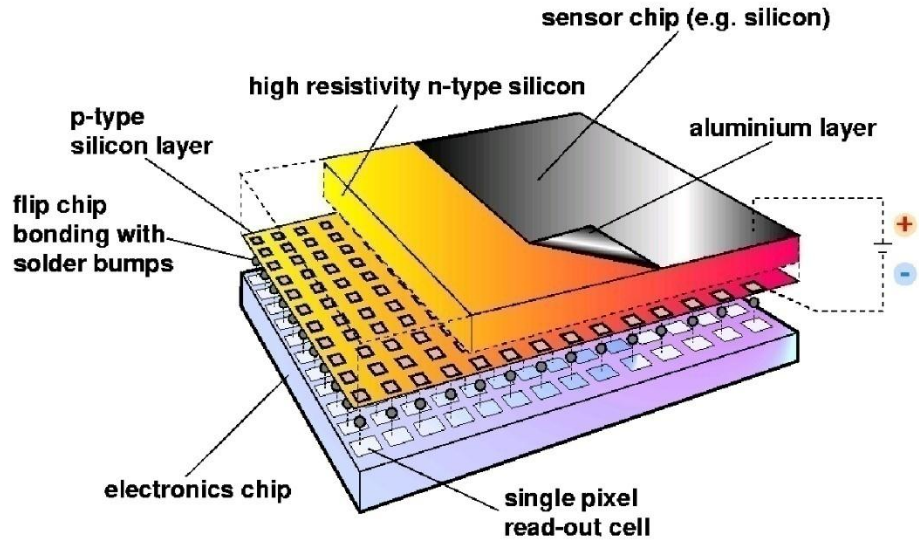


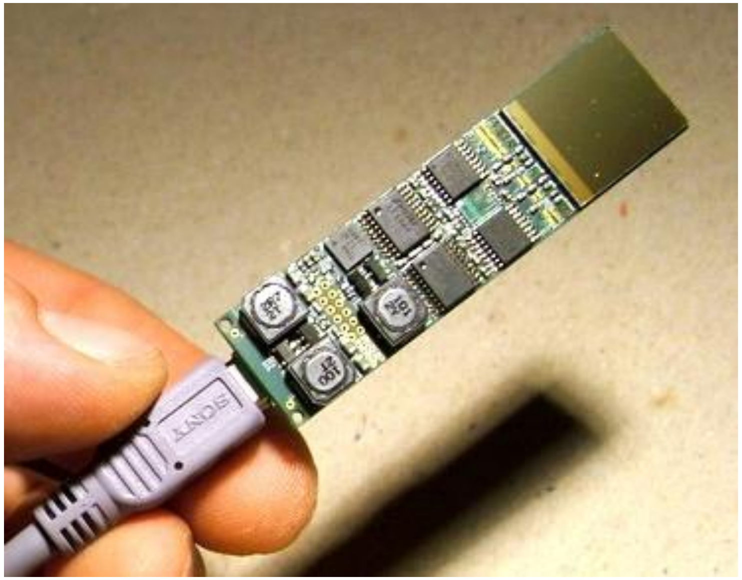
Can still do imaging!

Timepix

- 256 x 256 pixel array
- 55 um by 55 um pixel
  - 14 mm x 14 mm active area
- 10 ns timing resolution
- 14 bit time stamp

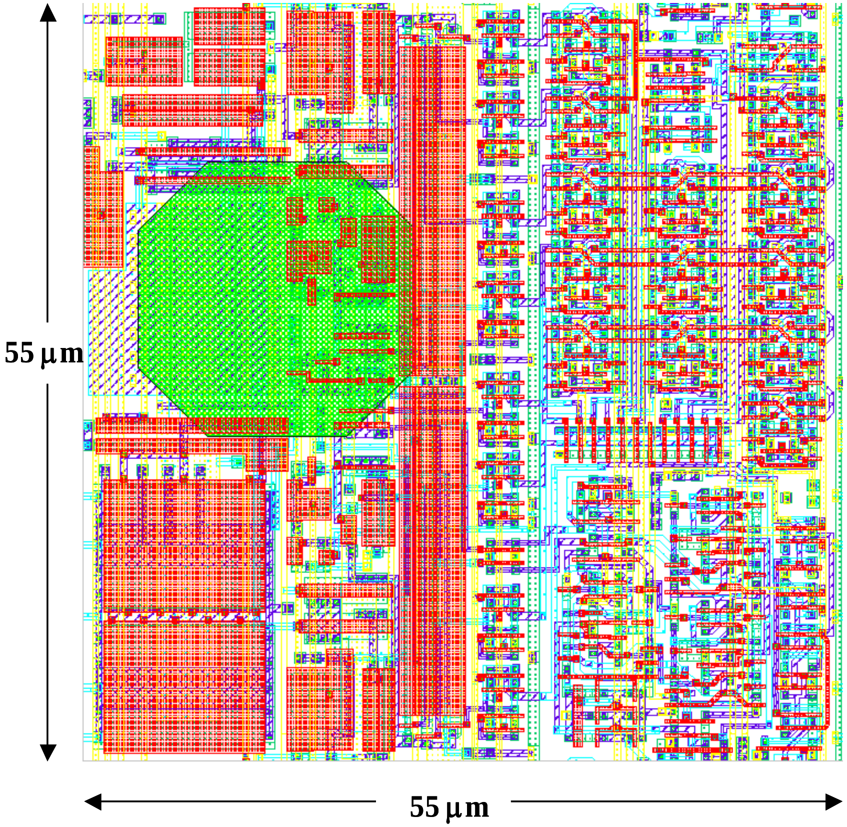
- First produced in 2006



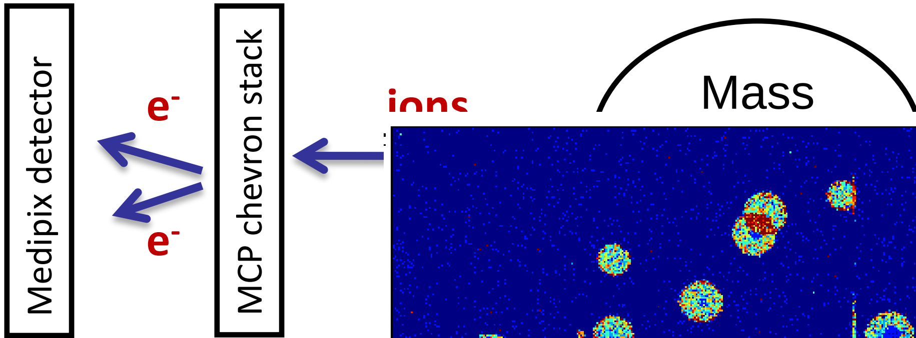


X. Llopart, R. Ballabriga, M. Campbell, L. Tlustos, and W. Wong, Nucl.Instrum.Methods Phys. Res. A **581**, 485 2007.

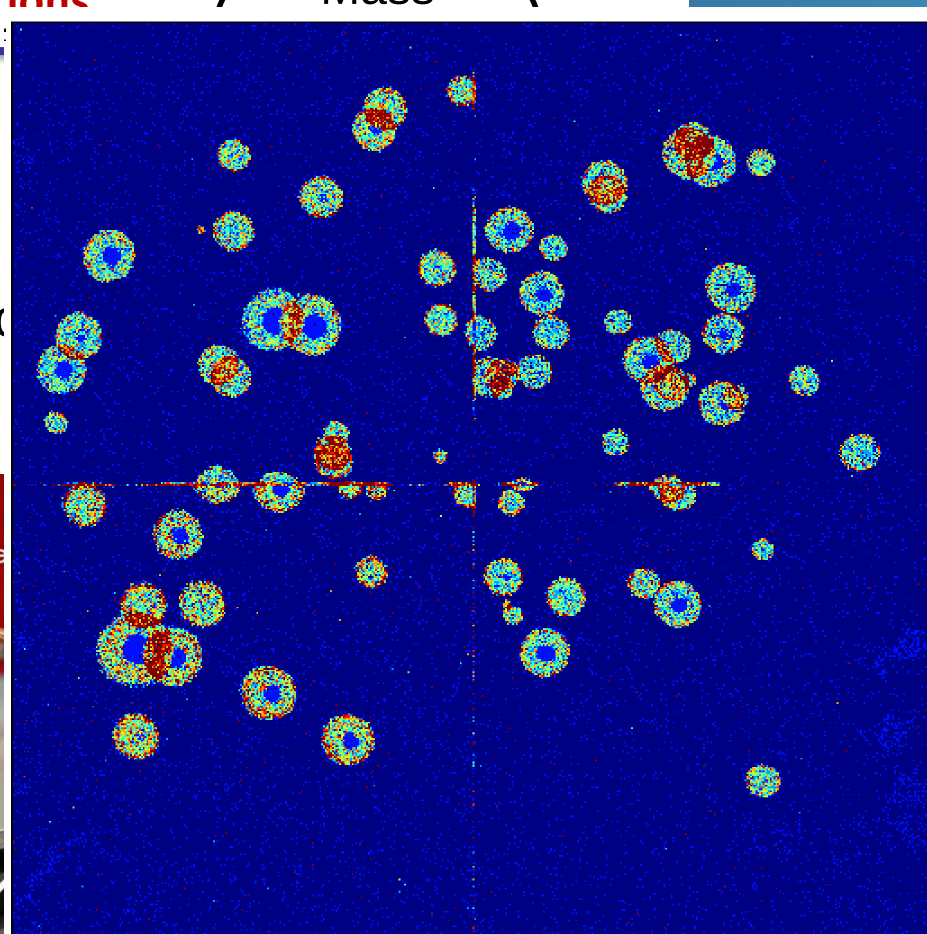
Timepix Pixel Layout

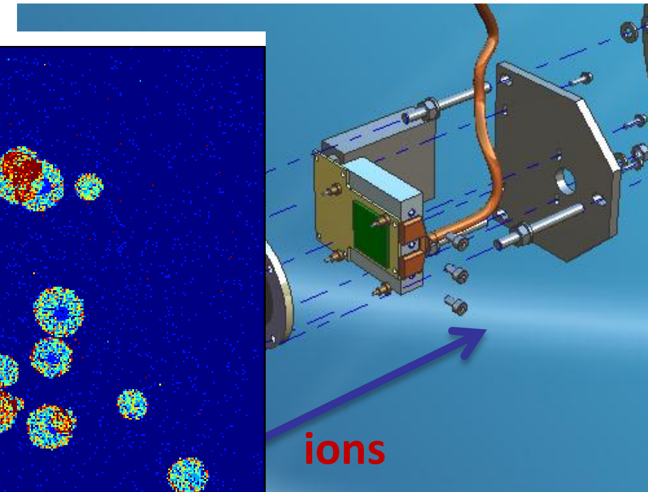


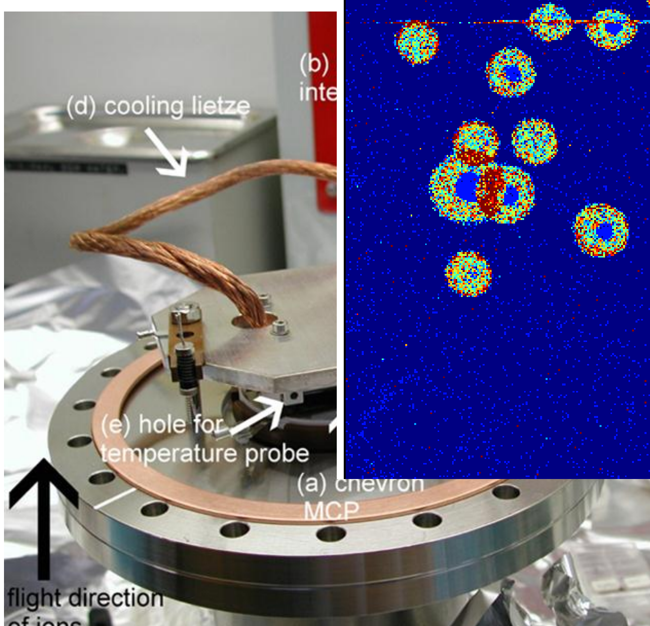
Direct Detection with Timepix

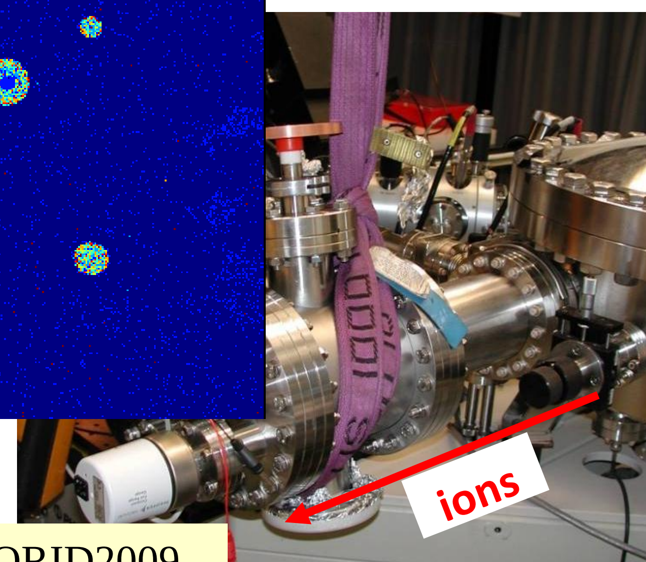


Non-trivial task to c



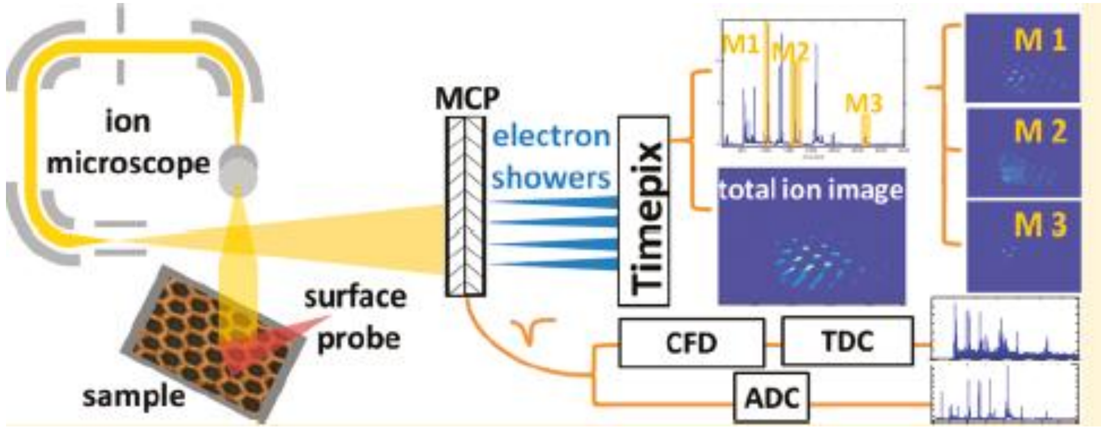




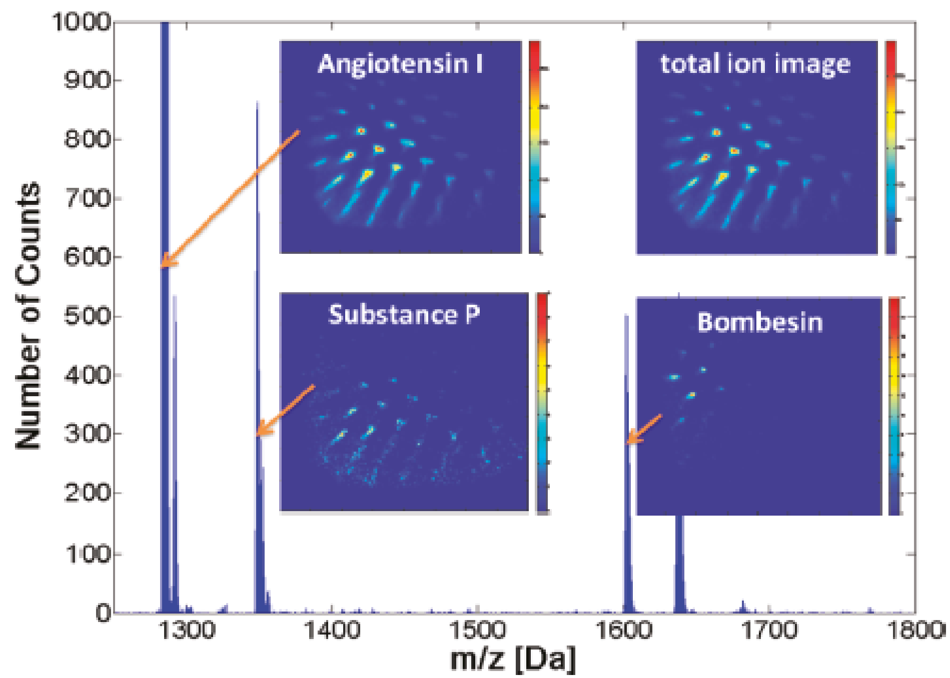


J.Jungmann, IWORID2009

Surface Imaging with Timepix (1)



- Surface imaging using matrix-assisted laser desorption ionization (MALDI) on a commercial ion microscope
- 512x512 pixel, bare 2x2 Timepix assembly combined with chevron MCP
- Oligomers of the protein ubiquitin were measured up to 78 kDa



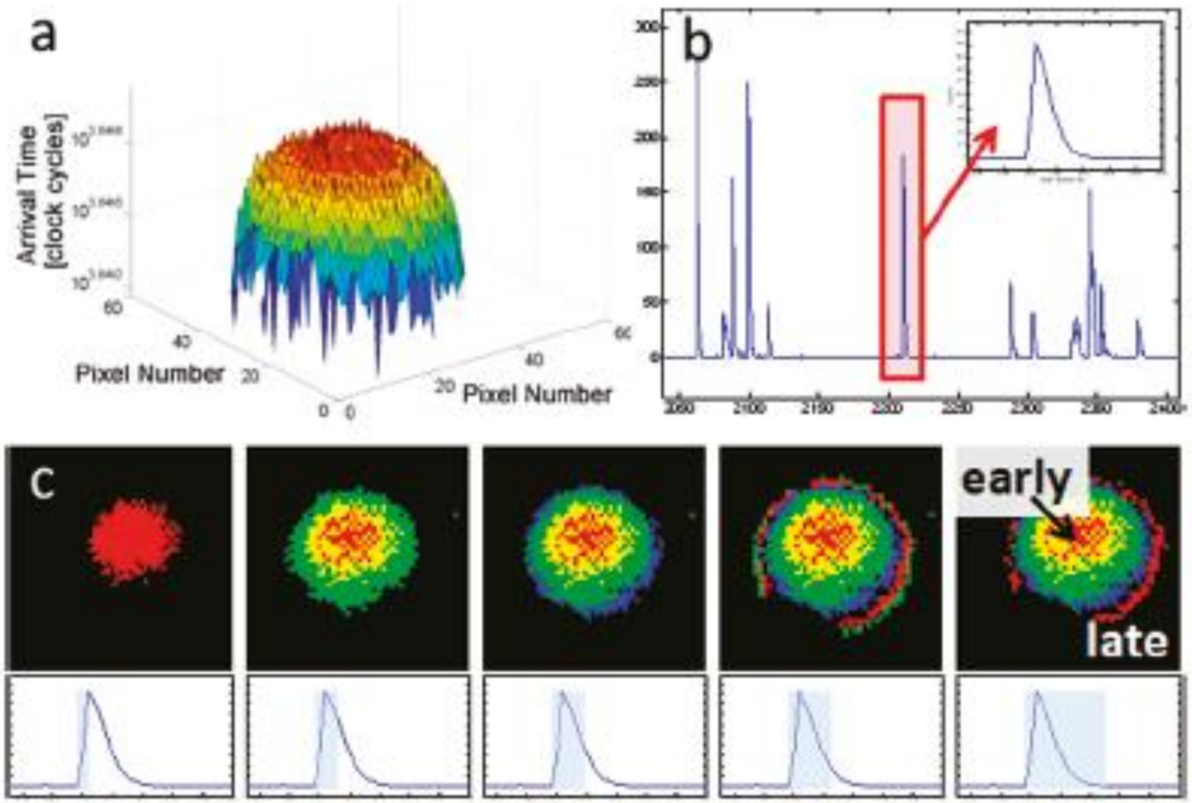
High Dynamic Range Bio-Molecular Ion Microscopy with the Timepix Detector

Julia H. Jungmann,[†] Luke MacAleese,[†,‖] Jan Visser,[‡] Marc J. J. Vrakking,[§,†] and Ron M. A. Heeren[*,†]

[†]FOM Institute for Atomic and Molecular Physics (AMOLF), Science Park 104, 1098 XG Amsterdam, The Netherlands
[‡]National Institute for Subatomic Physics (Nikhef), Science Park 105, 1098 XG Amsterdam, The Netherlands
[§]Max-Born-Institute, Max Born Straße 2A, D-12489, Berlin, Germany

Anal. Chem. 2011, 83, 7888–7894

Surface Imaging with Timepix (2)



- Cluster shape can be used to improve timing (hence mass) resolution
- Mass resolution: ~10 Da for 3000 Da
- Spatial resolution: ~ 3 micron

Anal. Chem. 2011, 83, 7888–7894

High Dynamic Range Bio-Molecular Ion Microscopy with the Timepix Detector

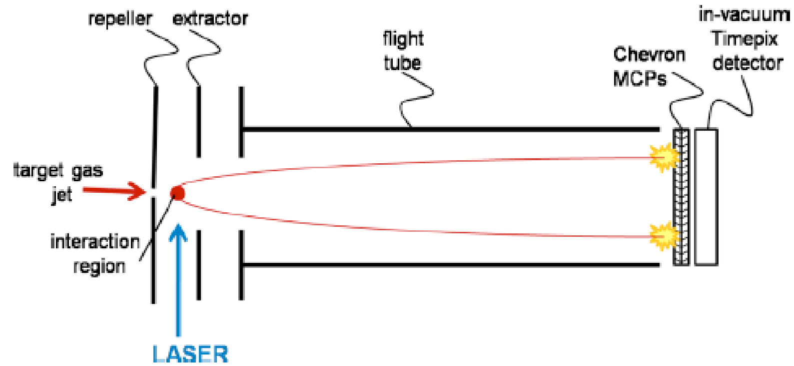
Julia H. Jungmann,[†] Luke MacAleese,[†,‡,∥] Jan Visser,[‡] Marc J. J. Vrakking,[§,†] and Ron M. A. Heeren[*,†]

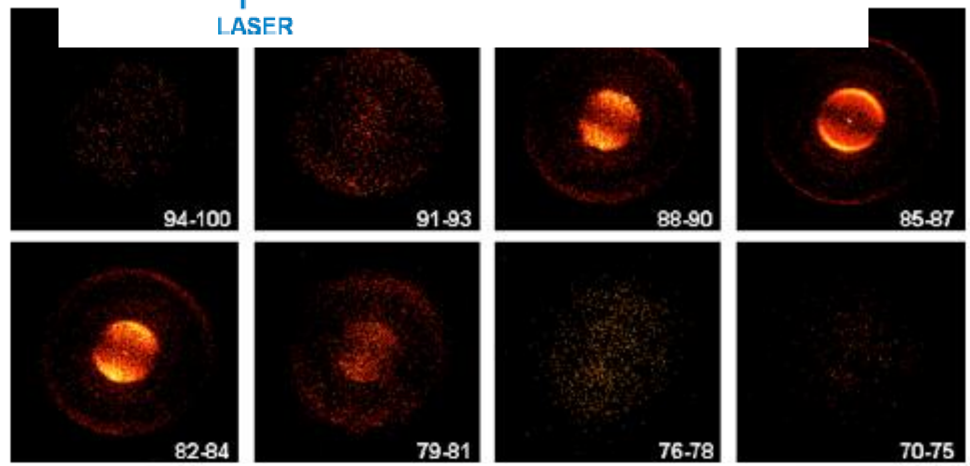
[†]FOM Institute for Atomic and Molecular Physics (AMOLF), Science Park 104, 1098 XG Amsterdam, The Netherlands
[‡]National Institute for Subatomic Physics (Nikhef), Science Park 105, 1098 XG Amsterdam, The Netherlands
[§]Max-Born-Institute, Max Born Straße 2A, D-12489, Berlin, Germany

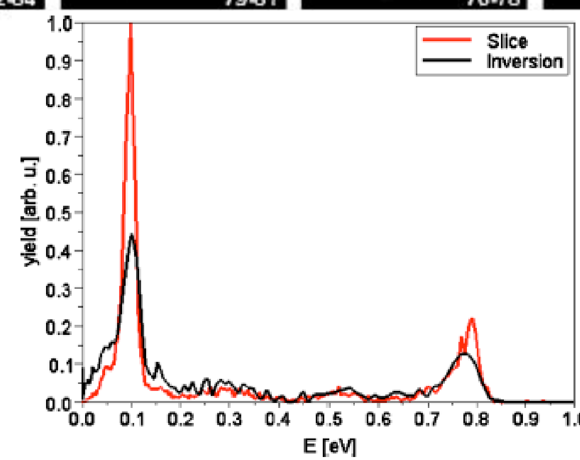
Velocity Mapping with Timepix

- Photodissociation of NO_2 at 452 nm
- Rings in scattering distribution can be interpreted as various transition paths in photodissociation

- Slicing technique improves the energy resolution
- The energy resolution observed in the experiment, dE/E=0.05, was limited by the experimental setup rather than by the detector







REVIEW OF SCIENTIFIC INSTRUMENTS **81**, 103112 (2010)

A new imaging method for understanding chemical dynamics: Efficient slice imaging using an in-vacuum pixel detector

J. H. Jungmann,[1] A. Gijsbertsen,[1] J. Visser,[2] J. Visschers,[2] R. M. A. Heeren,[1] and M. J. J. Vrakking[1,3]
[1]*FOM Institute for Atomic and Molecular Physics (AMOLF), Science Park 104, 1098 XG Amsterdam, The Netherlands*
[2]*National Institute for Subatomic Physics (Nikhef), Science Park 105, 1098 XG Amsterdam, The Netherlands*
[3]*Max-Born-Institut, Max Born Straße 2A, D-12489 Berlin, Germany*

Next Step: Timepix3

- wide range of non-HEP applications:
  - X-ray imaging
  - Dosimetry
  - Compton camera, gamma polarization camera, fast neutron camera, nuclear fission, astrophysics ...

- time-resolved imaging
- hit (photon) → ToA & ToT
- continuous & sparse readout
- minimum dead time

Christoph Brezina[3], Martin van Beuzekom[2], Michael Campbell [1], Klaus Desch[3], Vladimir Gromov[2], Xiaochao Fang[3], Ruud Kluit [2], Andre Kruth[3], Tuomas Poikela[1,4], Xavi Llopart [1], Francesco Zappon[2] ,Vladimir Zivkovic[2]

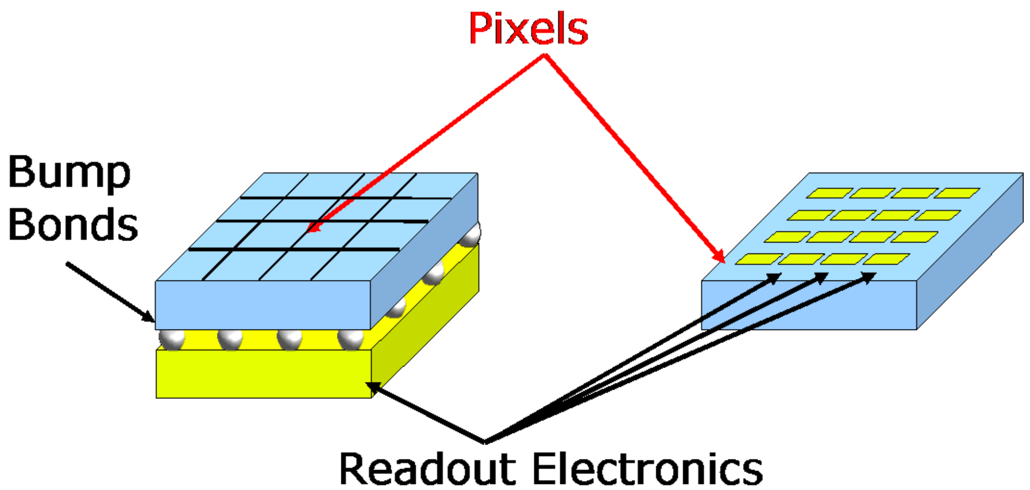
[1] CERN, Geneve, Switzerland,
[2] National Institute for Subatomic Physics (Nikhef), Amsterdam, the Netherlands
[3] Institute of Physics, Bonn University, Germany
[4] University of Turku, Finland

Vertex2011, Rust, Austria.
June 24, 2011

- suitable for HEP applications

- 256x256 55x55 sq.micron pixels – same as Timepix
- Time resolution : 1.6 ns
- Will allow for multi-hit operation for each pixel
- Ready in the end of 2012

Monolithic Pixel Sensors



- Monolithic Active Pixel Sensors (MAPS): Detector and electronics are integrated in same sensor
- Normally used as imager but can detect charged particles as well

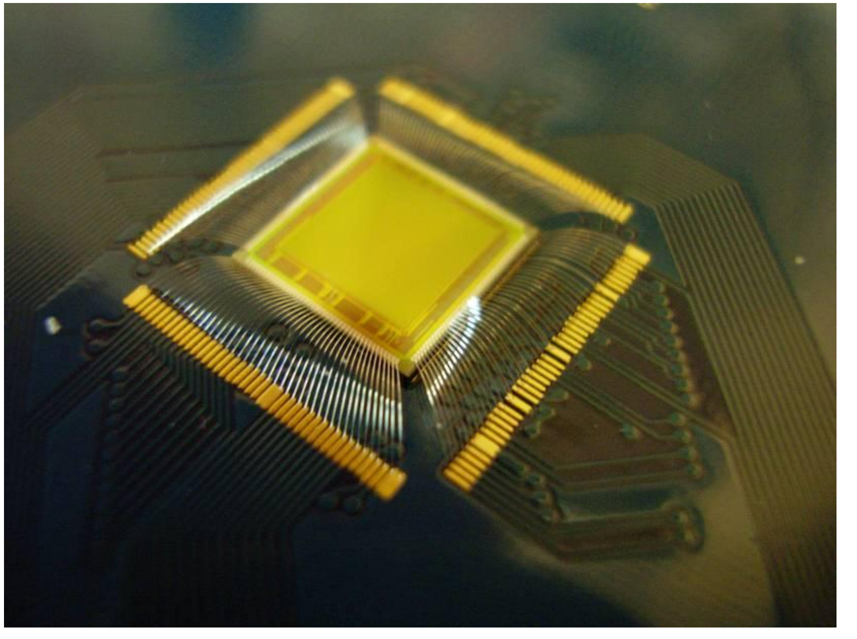
PImMS1 Sensor: CMOS Imager with Time Stamping

- PImMS: Pixel Imaging Mass Spectrometry
  - Collaboration of Oxford and RAL
    www.physics.ox.ac.uk/LCFI/PImMS.html

- 72 by 72 pixel array
- 70 um by 70 um pixel
  - 5 mm x 5 mm active area
- 25 ns timing resolution
- 12 bit time stamp storage
  - 4 memories per pixel
- 500 experiments/sec

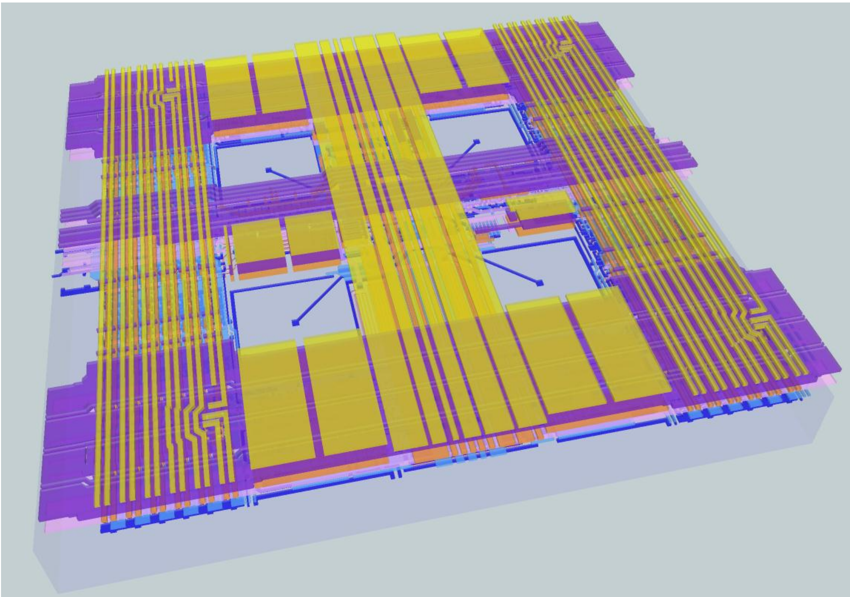
- Produced in Nov 2010

- **Pixel Imaging Mass Spectrometry with fast and intelligent pixel detectors** A Nomerotski *et al* 2010 *JINST* **5** C07007

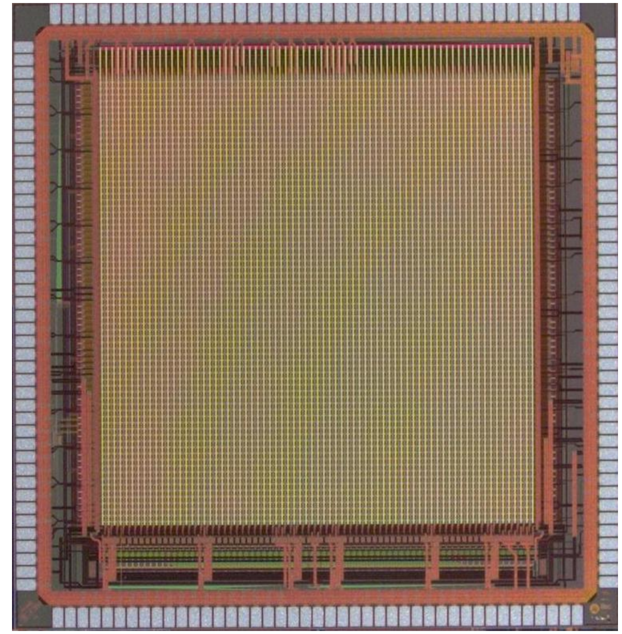


Design: A.Clark, J.Crooks, I.Sedgwick, R.Turchetta (RAL)
Testing: J.J.John, L.Hill (Oxford Physics)

PImMS Pixel, Sensor and Camera

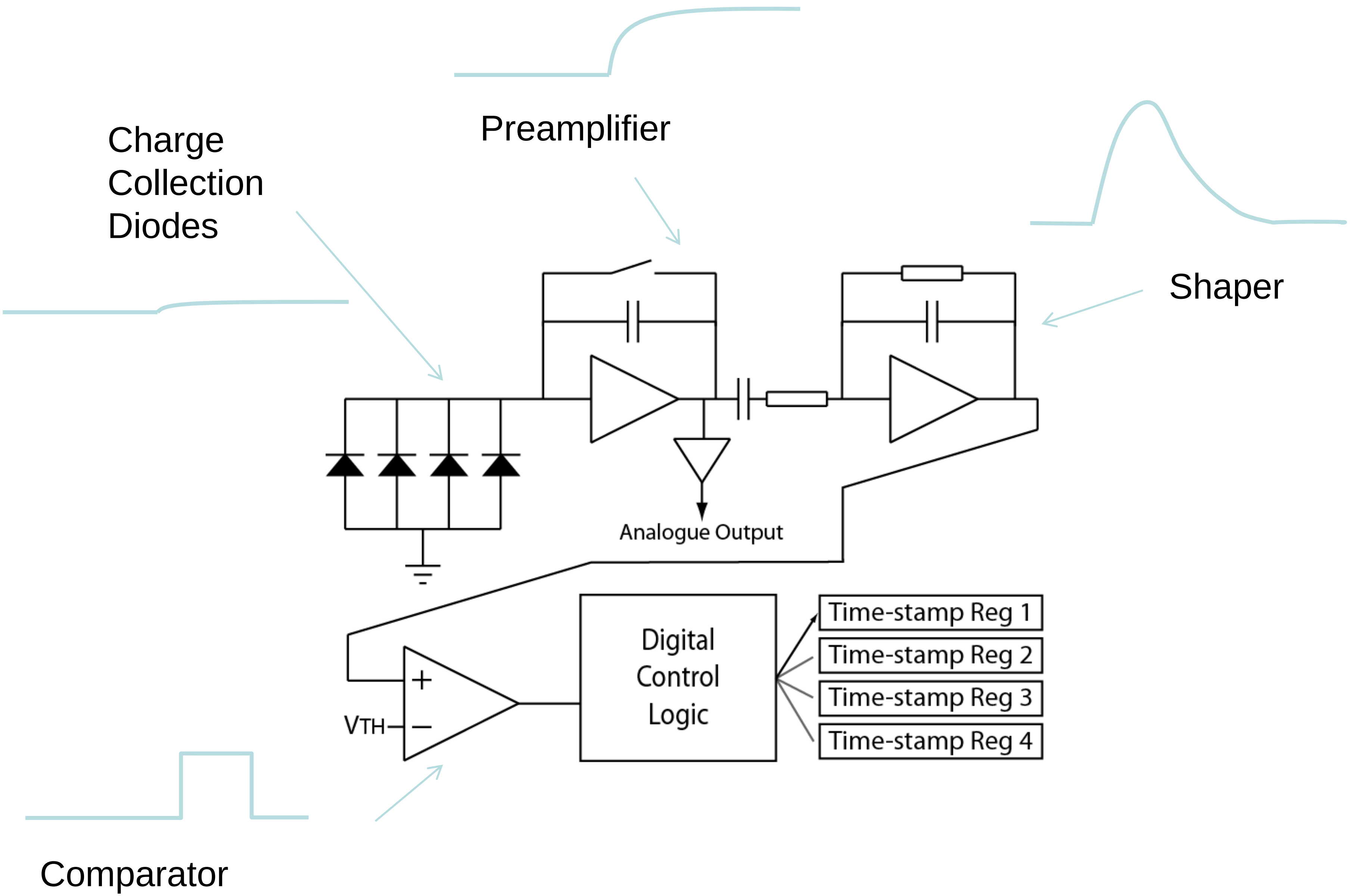


- 0.18 μm INMAPS process
- 615 transistors in every pixel



7.2 mm

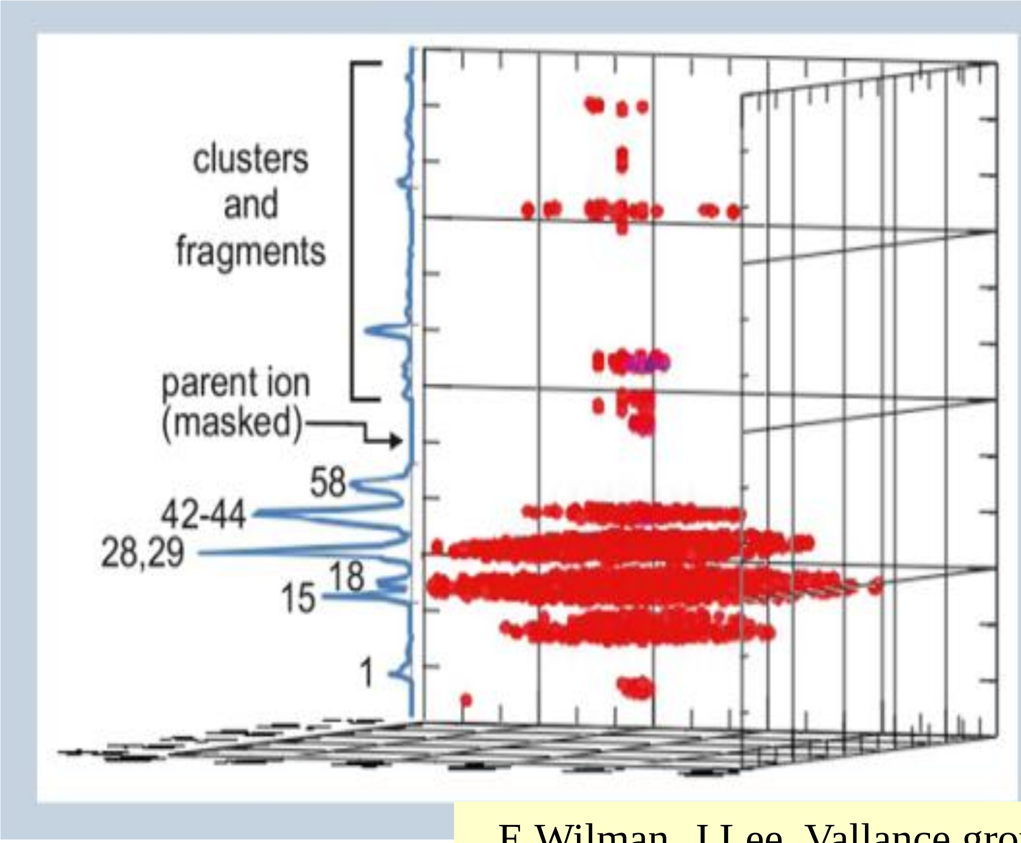
The PImMS Pixel

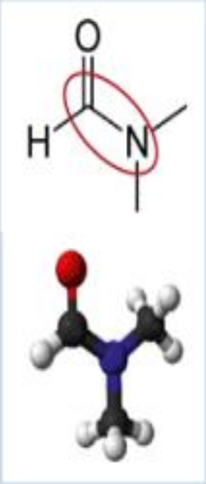


Velocity Mapping with PImMS

Data recorded for 193 nm photolysis of N,N dimethylformamide

good model for studying fragmentation of the peptide bond





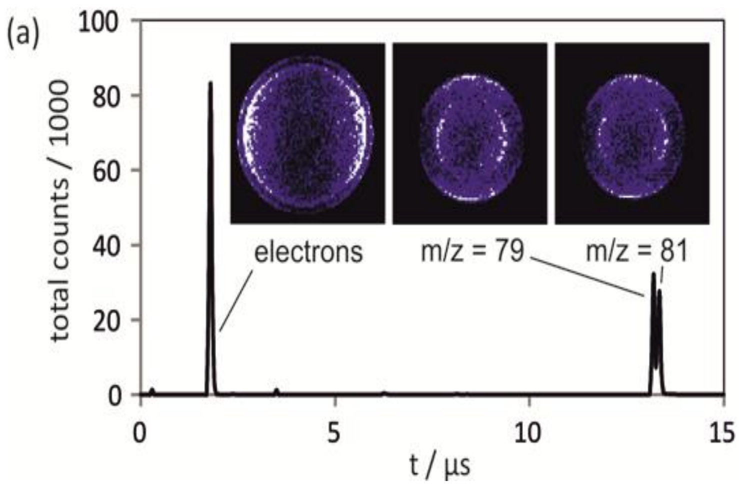
E.Wilman, J.Lee, Vallance group, Oxford Chemistry

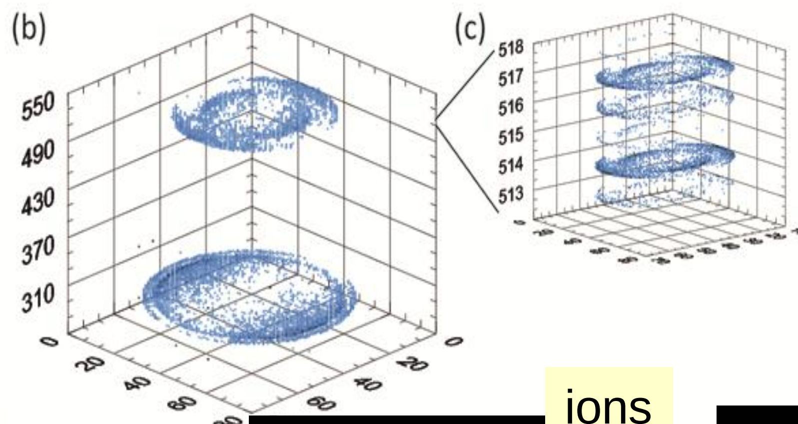
Coincidence Ion Imaging with PImMS

Study dynamics of chemical reactions
First steps: simultaneous imaging on a single detector

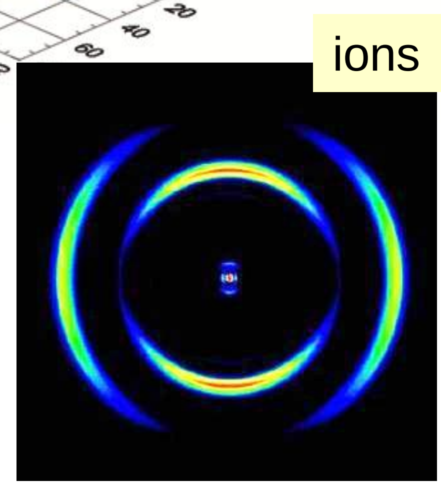
$$Br_2 \longrightarrow Br + Br$$
$$\qquad\quad\; Br + Br^*$$

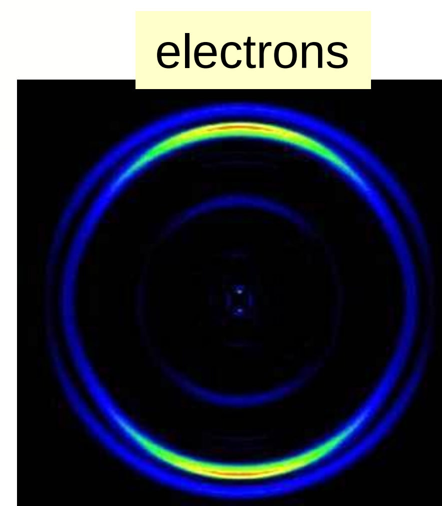
$$Br \longrightarrow Br^+ + e^-$$





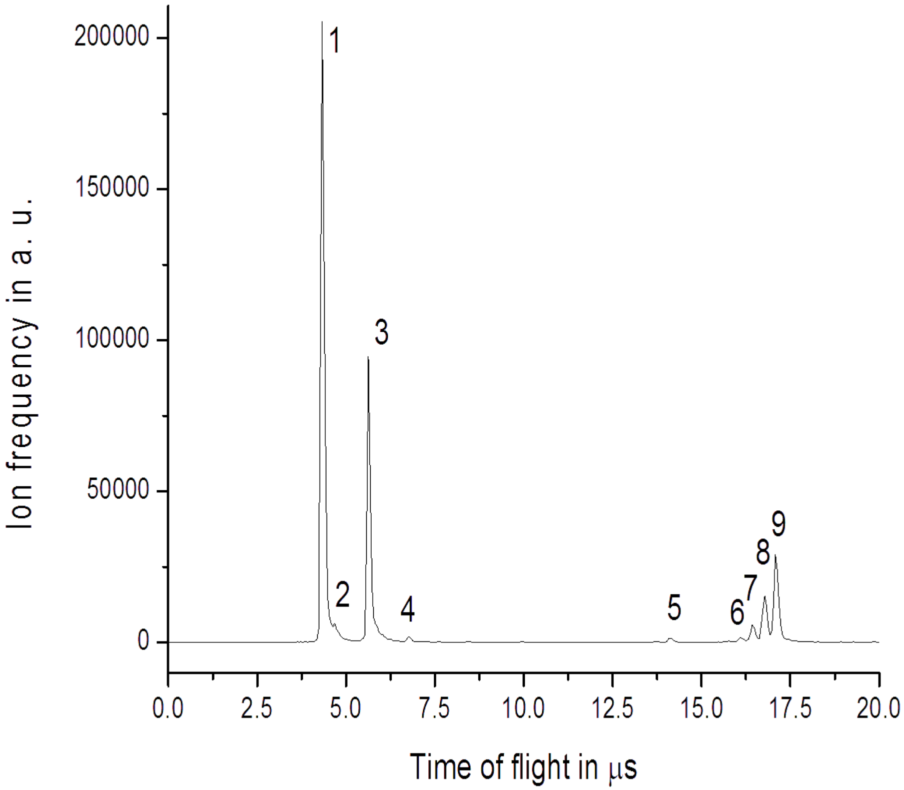
Time-of-flight spectrum of the electrons and ions formed during 446.32 nm photolysis of Br_2

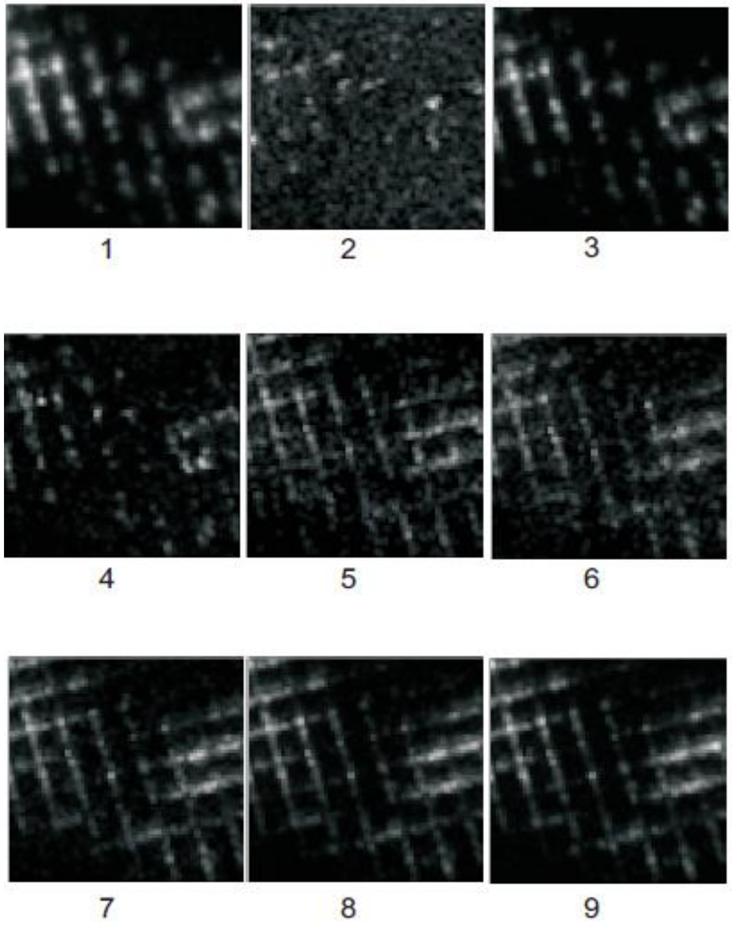




C.Slater, J.Lee, Brouard group, Oxford Chemistry

Surface Imaging with PImMS





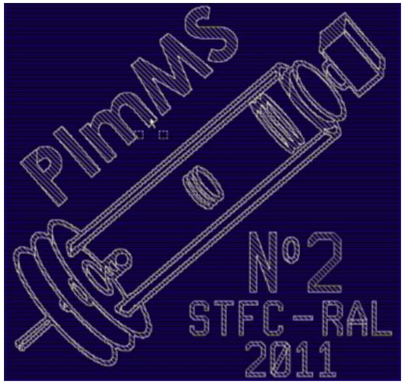
E.Halford, B.Winter, Brouard group

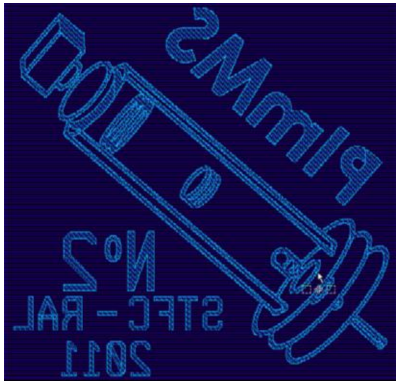
"Chemical" microscopy of crystal violet and CHCA. Target:

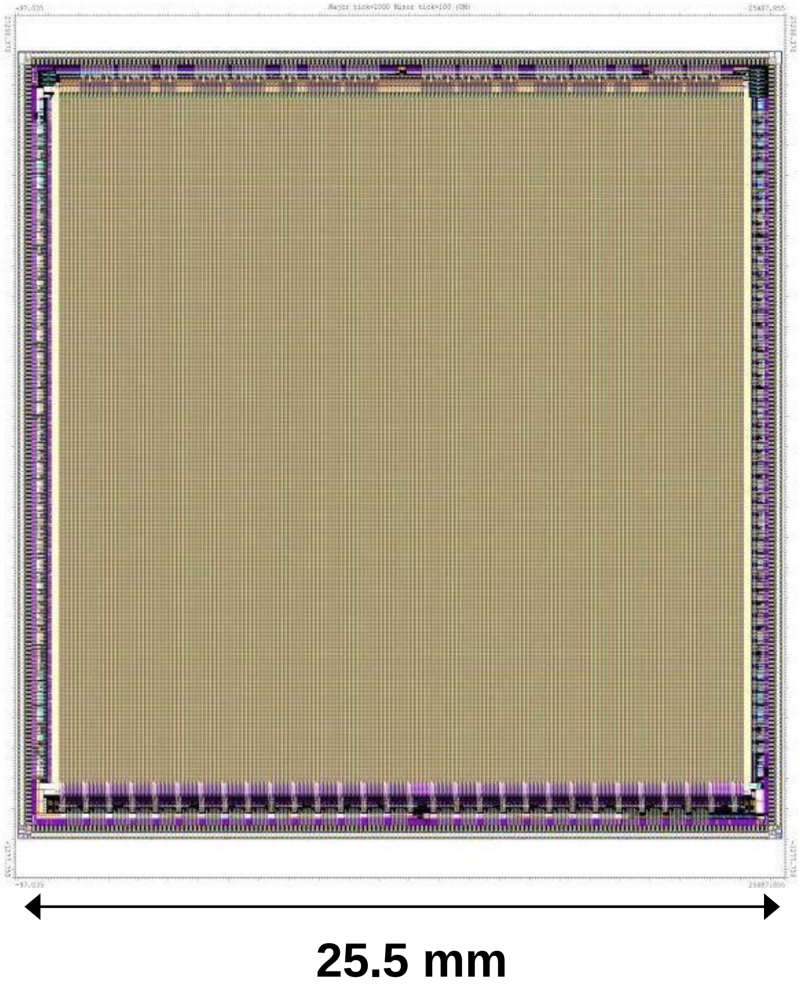
- sample size 4 mm x 4 mm
- 10 micron spatial resolution
- mass resolution m/Δm ~ 2000
- Earlier results: Application of fast sensors to microscope mode spatial imaging mass spectrometry; M Brouard, A J Johnsen, A Nomerotski, C S Slater, C Vallance and W H Yuen, 2011 JINST 6 C01044

Next Step: PImMS2

- Larger array 324 x 324 pixels
- 500 experiments/second
- Submitted in Feb 2012, available in May 2012



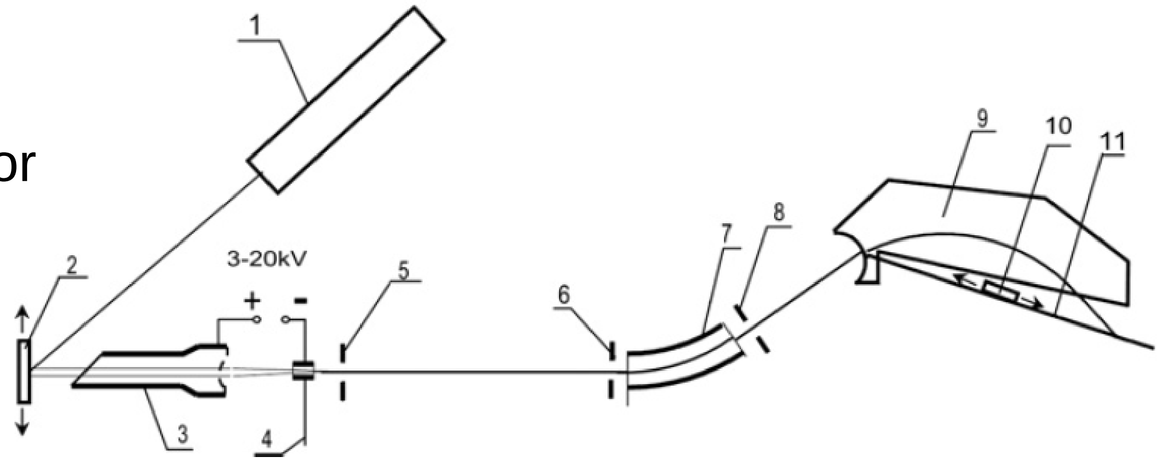




Direct Detection of Low Energy Ions

Mass Spectrometry of Ion Beams

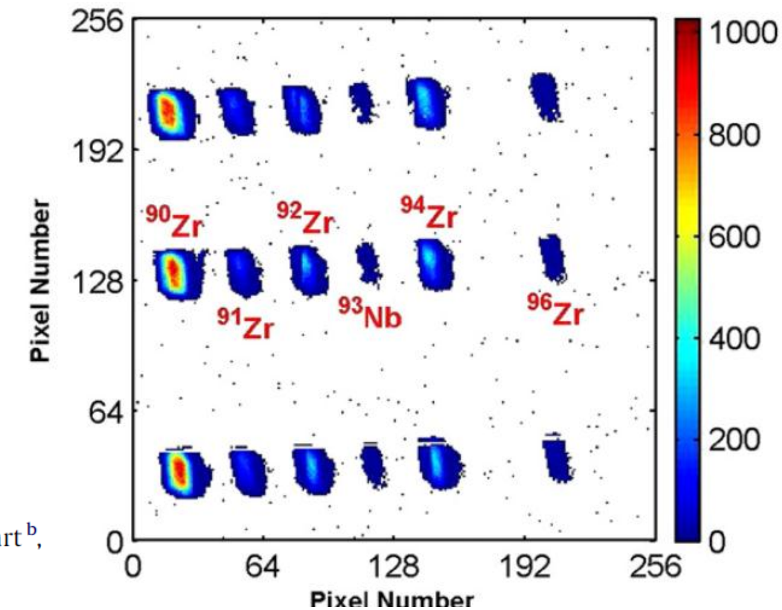
- Double-focusing magnetic mass-spectrometer with Timepix as direct ion detector



- Timepix used in Time-Over-Threshold mode

- Direct detection of 25 keV ions
  - 10 nm range in Si
  - Large number of ions required

- Can resolve isotopes
- Position correlation used to improve mass resolution



Metal and hybrid TimePix detectors imaging beams of particles

V. Pugatch [a,*], M. Campbell [b], A. Chaus [a], V. Eremenko [d], S. Homenko [d], O. Kovalchuk [a], X. Llopart [b], O. Okhrimenko [a], S. Pospisil [c], A. Shelekhov [d], V. Storizhko [d], L. Tlustos [b]

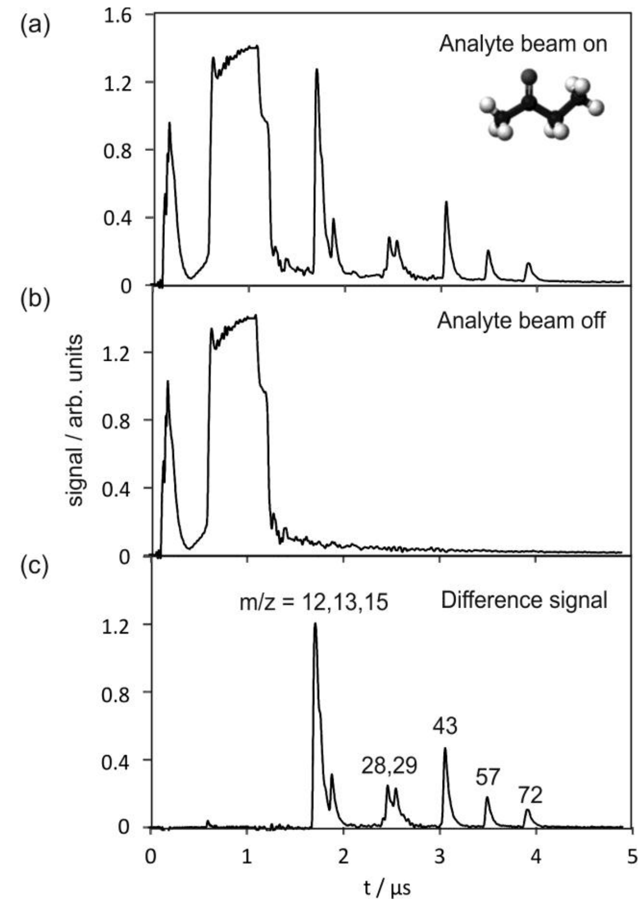
[a] Institute for Nuclear Research, National Academy of Sciences of Ukraine, Kiev, Ukraine
[b] CERN, Geneva, Switzerland
[c] Institute of Experimental and Applied Physics, Prague, Czech Republic
[d] Institute of Applied Physics, National Academy of Sciences of Ukraine, Sumy, Ukraine

Nuclear Instruments and Methods in Physics Research A 650 (2011) 194–197

Direct Detection of Low Energy Ions

- MCP has < 60-70% efficiency, needs vacuum and is expensive
- Major difficulty: 10 keV ions stop in first nm

- First measurements on direct detection of low energy ions using 0.2 mm thin LYSO scintillator and MPPC (Hamamatsu)
- Expect only a handful of photons → need a SiPM



Wilman ES, Gardiner SH, Nomerotski A, Turchetta R, Brouard M, Vallance C
*A new detector for mass spectrometry: Direct detection of low energy ions using a multi-pixel photon counter, Rev Sci Instrum **83**(1):013304 Jan 2012*

First steps towards SPAD ion imager

Summary

- Modern instrumentation is going towards time-resolved measurements in many areas (single photon counting, TOF, coincidences etc) → becomes more and more aligned with PP in fast detection
- Applications in imaging MS is a good example
  - Ideal detector for IMS: each pixel operates as an independent mass spectrometer with 0.1 ns time resolution and small deadtime
  - Many measurements can be done with more relaxed specs
- Fast and intelligent CMOS pixel detectors have a bright future here

Acknowlgements

- Medipix collaboration, in particular M.Campbell and J.Jungmann
- PImMS collaboration