



WG 2 Tutorial:

Ions and Biomolecular Interactions

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Overview

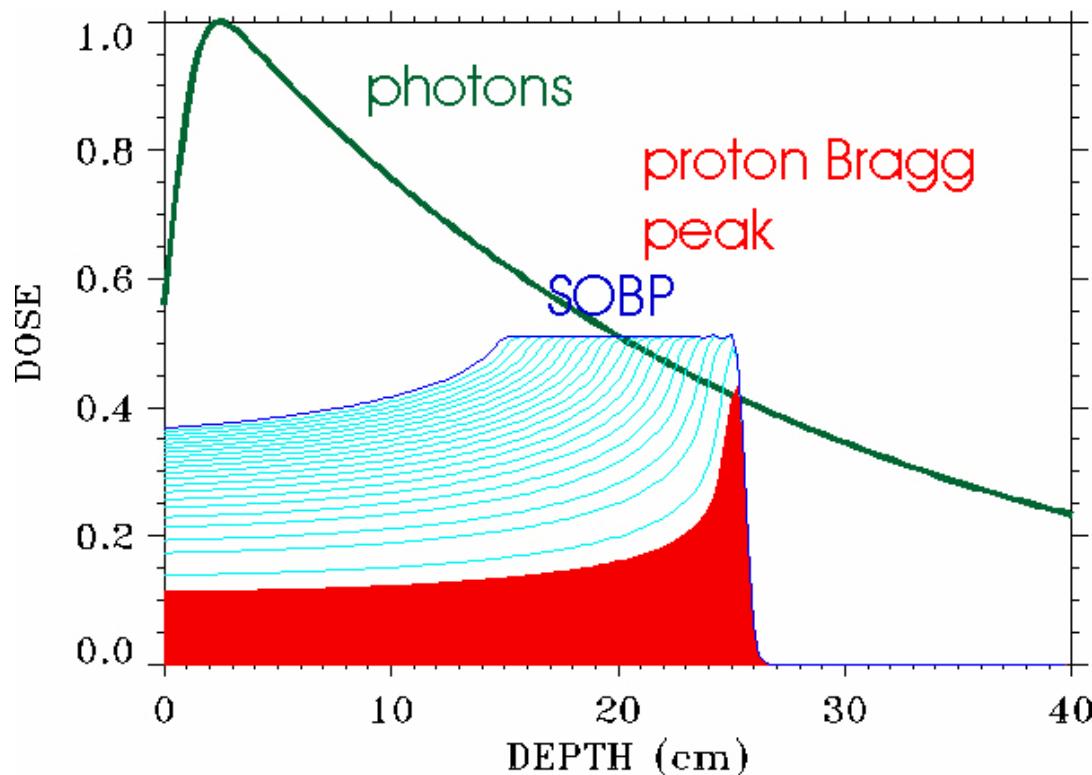
- Introduction
- Ion sources and accelerators
- Gas phase experiments
- Condensed phase experiments
- Large biomolecules and clusters
- Conclusion / outlook

Why look at ion interactions with biomolecules?

- Cancer therapies utilizing ion beams
(Impact from ~ 200 MeV / amu down to 0)
- Cosmic rays
($\sim 90\%$ protons, energies up to 10^{20} eV, $\sim 13\%$ of ambient radiation dose on the Earth's surface, much greater doses in space)
www.arpansa.gov.au/baseline.htm
- Secondary ions
(e.g. H^+ , OH^+ , O^{2+} released in water fragmentation, up to ~ 30 eV... or more following multi-charged ion impact)
Seredyuk et al. *Phys. Rev. A* **71** (2005) 022705
Sobociński et al. *J. Phys. B* **39** (2006) 927
- Analytical techniques
(e.g. utilizing the strong fields around multi-charged ions)

Proton therapy

- **Bragg peak** maximum for energy deposition by incident ions
~ 100 keV / amu
→ localized dose of ionizing radiation
- Healthy cells repair after exposure to ionizing radiation more effectively than cancerous ones
<http://www.proton-therapy.org/>



http://radmed.web.psi.ch/asm/gantry/gantry_master.html

Heavy ion therapies

- Same principle but using larger incident ions (typically C⁺)
- Improved ratio of Bragg peak dose / plateau dose

Jäkel et al. *Nucl. Instr. and Meth. in Phys. Res. B* **241** (2005) 717

WG2 motivations re. these treatments

To understand the *molecular* processes initiated by ion impact:

- At *pre-Bragg peak* velocities (damage to healthy tissue)
- At *Bragg peak* velocities (damage to cancerous tissue)
- At *lower* velocities (incident ions just before the *stopping depth*, neutrals which can penetrate further, secondary ions)

Ion interactions with bound electrons

→ The dominant interactions in this velocity range

- *Direct excitation and ionization*: promotion of an electron in the **target molecule** to an excited state or the continuum
 - ... can lead to the emission of high-energy electrons, notably due to the *Auger effect* or multiple electron scattering (*Fermi-shuttle effect*)
- *Electron loss* by (or electronic excitation of) the **projectile**
- *Electron capture* by the **projectile ion**

The interplay of these energy deposition and charge transfer processes as an incident ion slows down in an absorbing medium is central to the occurrence of the Bragg peak

see Biaggi et al. *Nucl. Instr. And Meth. Phys. Res. B* **159** (1999) 89

Ion impact experiments in relation to the dose

Large cross sections for interactions with bound electrons at ion impact velocities \sim the Bragg peak and stopping depth...

- Highly efficient mechanism to deposit energy in a (bio)molecular system
- Excellent conditions to probe energy deposition and repartition (i.e. the radiation dose) both from the molecular and statistical physics standpoints

Electronic excitation & ionization

(in the target or the projectile)

- Ideal conditions
→ **impact velocity close to that of the bound e⁻**
- Greatest cross sections (σ) for largest orbitals
→ valence e⁻ ($\sim 1-2 v_0 = 50-200$ keV / amu)
- Promotion of more strongly bound e⁻
(faster, smaller orbitals → lower σ)
- Complicated by *competition* with electron capture
- Even more complex when projectile also has e⁻ structure
- Higher impact velocities ($\gtrsim 400$ keV / amu) → *Bethe-Born approximation* applies, simplifying cross section calculations

**Difficult
processes
to model**

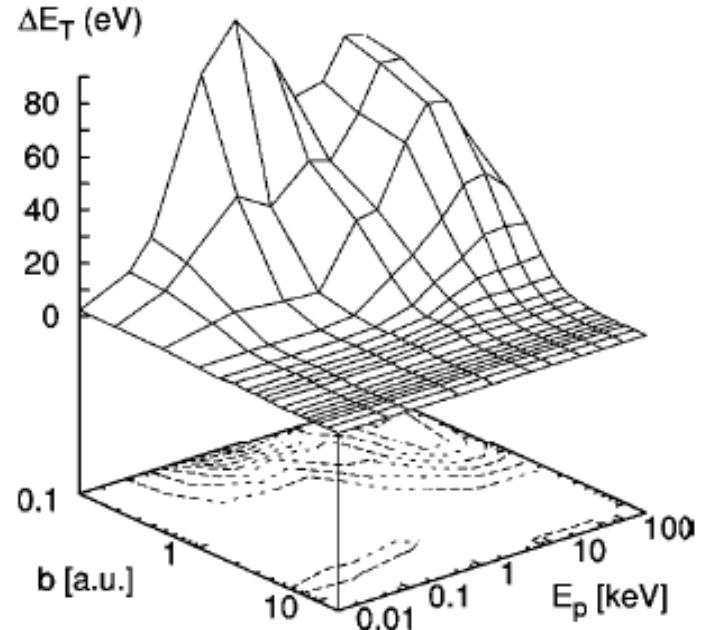
e.g. Miller et al. *Phys. Rev. A* 27 (1983) 1137

Electron Capture

- Cross sections generally peak $\sim 0.5 - 10$ keV / amu
... and fall off sharply above ~ 150 keV / amu
- Multiply charged ion impact \rightarrow increased multiple e^- capture
- Electron capture processes will eventually neutralize an incident ion
 \rightarrow **neutral collisions** with molecules in an exposed medium are essential to understand the effects of ion irradiation
- Neutral impact experiments also carried out in WG2 using ion beams
 - ... *Charge required to accelerate the projectiles*
 - ... *Ions neutralized in a gas cell (electron capture!)*
 - ... *Remaining ions deviated in an E field*
 \rightarrow Pure mono-energetic neutral beam

Energy transfer

- Smaller impact parameters generally → greater energy transfer
 - ... Interactions with more strongly bound electrons, often leading to fragmentation*
- Energy transfer in a collision does not necessarily increase with impact energy
 - (above the obvious $E_P > \Delta E_T$ threshold!)*
- Strong fields around multi-charged ions allow longer-range interactions, with larger impact parameters and lower energy transfer
 - *excellent conditions to probe potential surfaces etc.*



Calculated energy transfer against impact parameter and impact energy for proton collisions with atomic oxygen

Cabrera-Trujillo et al.
Phys. Rev. A **62** (2000) 052714

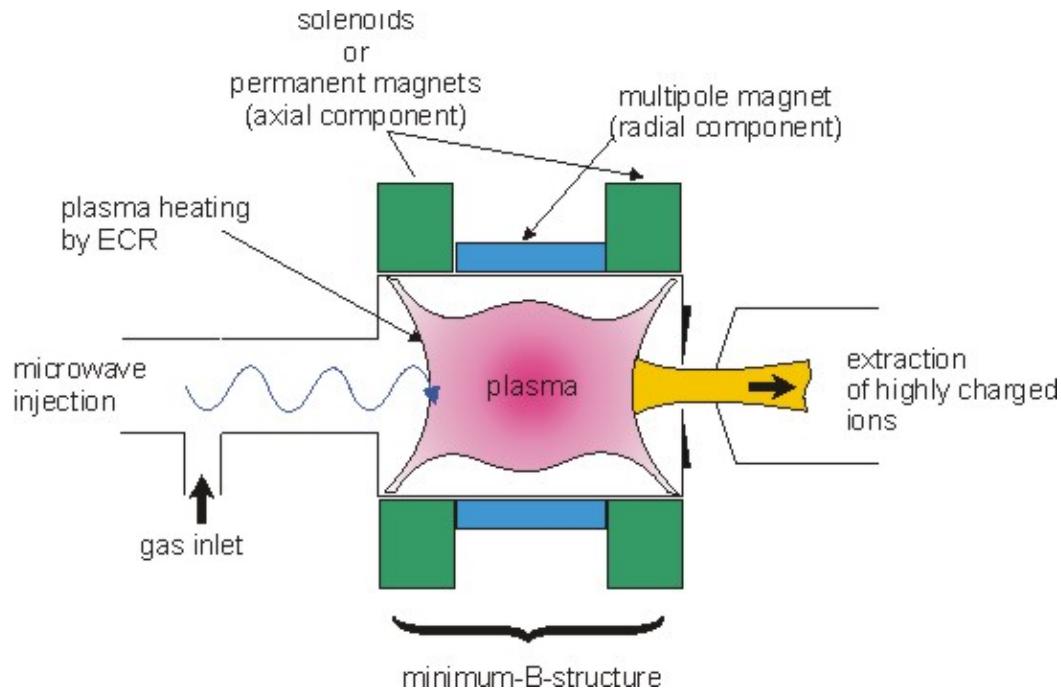
Some ion beams in WG2

- *High accelerating voltages, low charge states (H⁺, He⁺, He²⁺, N⁺, N₂⁺...)*
 - 0.7-5 MV, ATOMKI Debrecen
 - 15-100 kV, Queen's Univ. Belfast
 - 25-100 kV, Univ. Paul Sabatier Toulouse
 - 20-150 kV, IPN Lyon (up to 2005, replacement under construction)
- *Lower accelerating voltages, multiply charged ions*
 - 1-25 kV, up to 25+, KVI Groningen
 - 0.5-5 kV, up to 5+, Queen's Univ. Belfast
 - 3-25 kV, up to 30+, GANIL Caen
 - 1-20 kV, up to 7+, HMI Berlin
- *Biomolecular ion (and cluster ion) sources*
 - 50 kV, Univ. Aarhus
 - 5-40 kV, IPN Lyon (under construction)
 - ELISA storage ring, Univ. Aarhus

ECR sources

Electron-cyclotron resonance

- e^- gyrate around B field lines at *cyclotron frequency*
- Microwaves at this freq. → **resonant acceleration**
- e^- confined in axial and radial B fields → acquire ionization energies
- Ions confined due to high e^- density → multiple e^- impact → **high q states**
- Confinement not perfect... suitable geometry and extraction voltage → ion beam
- ***Ions of practically any element, high plasma efficiency, no filaments...***

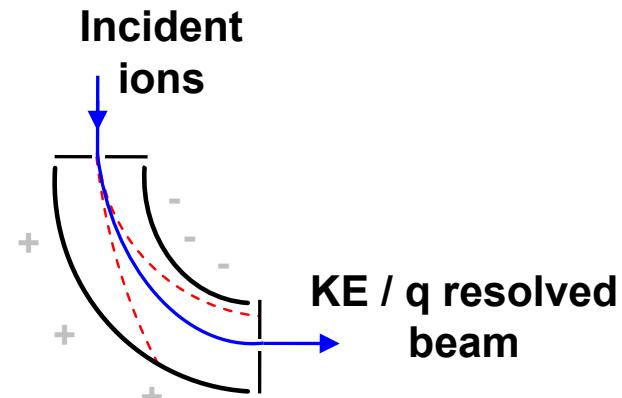


<http://www.strz.uni-giessen.de/~ezr/english/intro.html>

Acceleration & ion selection

- Typically, sources floated at HV
→ acceleration to ground

(KE / q resolution can be improved
by electrostatic deflection)



- Subsequent **magnetic deflection** → **enables m / q selection**
- Can then be accelerated or decelerated using cylindrical electrostatic lens systems
 - ... Particularly useful for low-energy beams (< 1 keV)

e.g. Kearns et al. *J. Phys. B* 35 (2002) 4335

Gas phase experiments

Why study ion impact with isolated biomolecules?

Rather distant approximation of *in vivo*...

... But enables the products of individual excitation, ionisation, and fragmentation processes to be observed directly, revealing detail which cannot be extracted from surface or solution experiments

Bringing biomolecules into the gas phase:

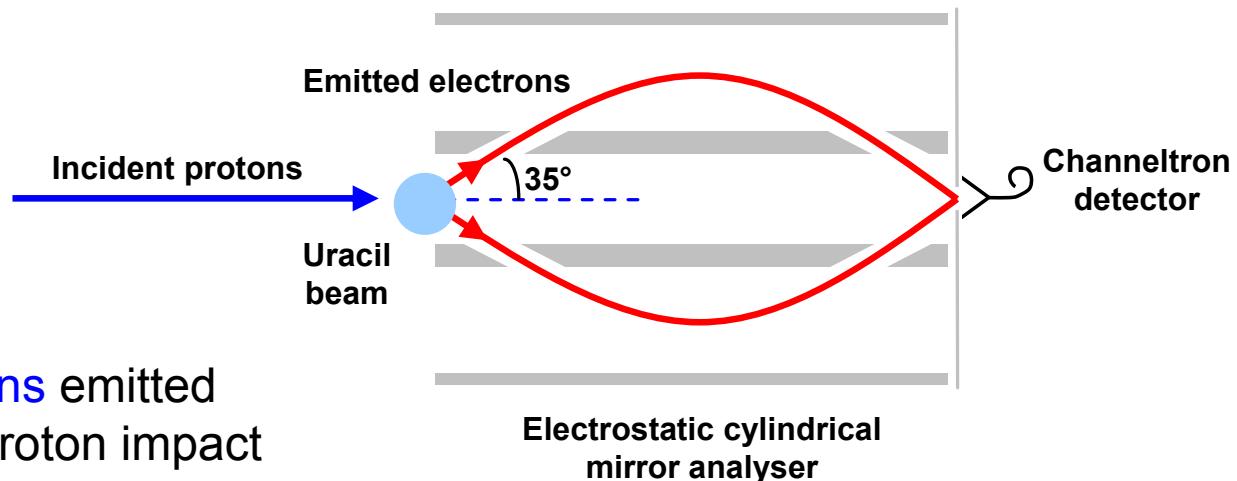
- Easy for high vapour pressure species (e.g. water)
- Various important *small* biomolecules (notably DNA and RNA bases, deoxyribose...) → up to $\sim 200^\circ\text{C}$
- More sophisticated techniques required for biomolecules which are damaged by heating

Example: electron emission following ion impact

- Fast e^- can initiate further ionizations and dissociations → **track patterns**
- Low-energy (< ionization threshold) e^- impact experiments have demonstrated single and double strand breaks in DNA...
 - ... dissociative electron attachment (DEA)
- So all processes which involve e^- release – either by the *target molecule* or by the projectile – are important for modelling radiation damage
- KE analysis of emitted electrons → key information to understand the ion-molecule interaction

Sanche, Physica Scripta 68 (2003) C108

Proton impact upon uracil



- KE analysis of electrons emitted from uracil following proton impact at 25 – 100 keV / amu
- Normalization using proton elastic scattering measurements for the same jet conditions → absolute cross sections

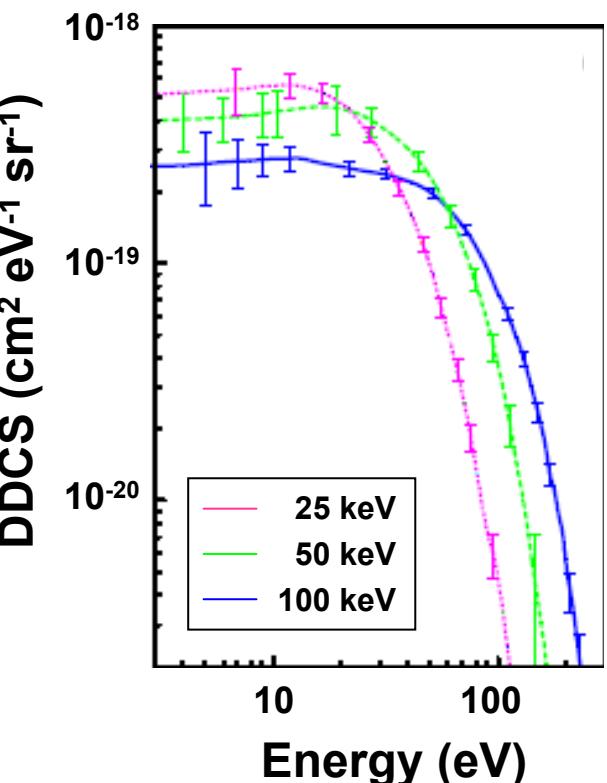
Moretto-Capelle and Le Padellec, *Phys. Rev. A* **74** (2006) 062705



Proton impact upon uracil (... continued)

- High emission cross sections both for slow and ionizing ($\gtrsim 10$ eV) electrons
- No clear peaks for Auger electrons
- Very weak emission of electrons > 100 eV → *expect short tracks from these collisions*

Absolute electron emission cross sections against electron energy



Moretto-Capelle and Le Padellec, *Phys. Rev. A* **74** (2006) 062705



Example: product ion mass spectrometry

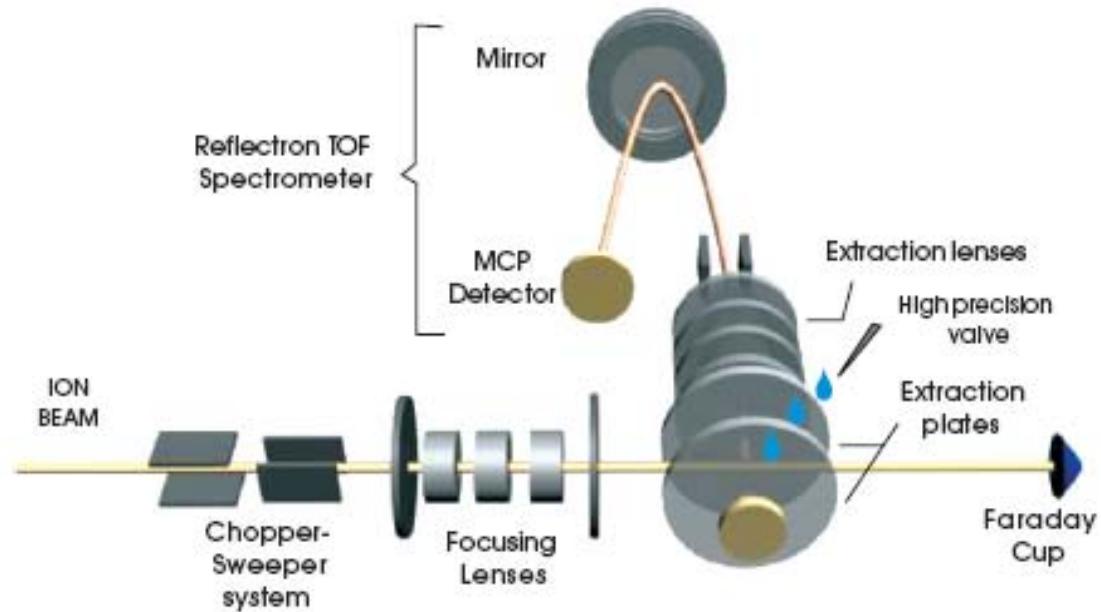
- Biomolecule (particularly DNA and its constituents) fragmentation patterns and cross sections are invaluable to model ion irradiation damage
- Increased strand breaks for hydrated DNA...
Could be due to secondary electrons and / or ions and radicals
- OH capturer in a DNA solution reduces strand breaks
→ *so fragmentation of H_2O is also important*

Folkard et al. *J. Phys. B: At. Mol. Opt. Phys.* **32** (1999) 2753

H^+ and He^{q+} impact upon H_2O

- 1-20 keV / amu ion impact

- Pulsed beam for time-of-flight (TOF) identification of product ions (m / q)



- **Coincidence detection of multiple ions produced in a single collision**

Alvarado et al., *J. Phys. B* **38** (2005) 4085

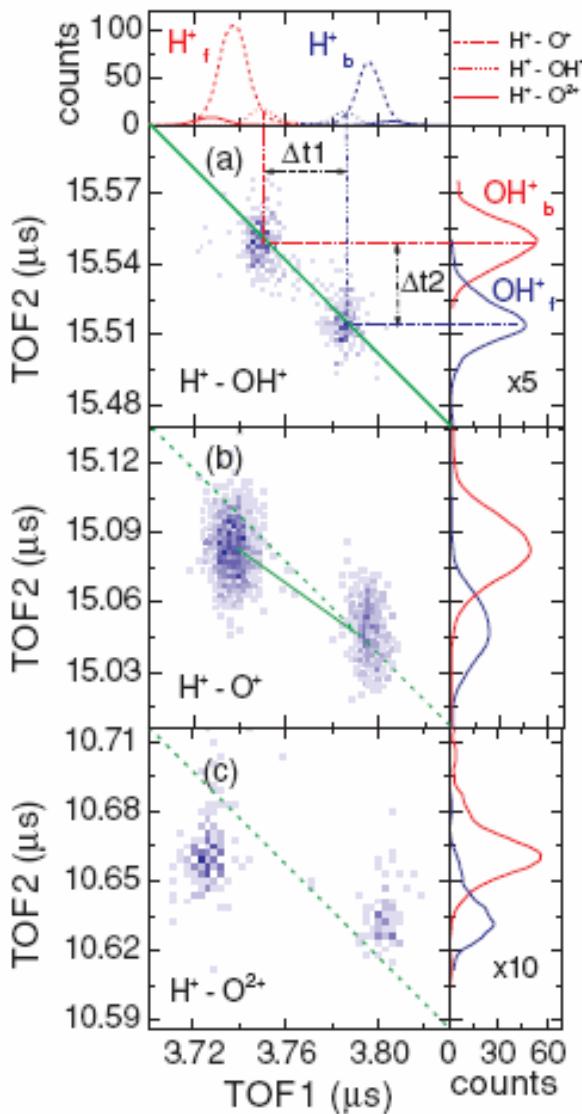


H^+ and He^{q+} impact upon H_2O (... continued)

- Plotted TOF of 1st against 2nd ion
- Islands* → *forwards and backwards* ions w.r.t spectrometer axis (experimental geometry)
... **TOF difference** → **initial velocities** due to kinetic energy release (KER) in fragmentation

(Deviation of islands from negative 1 gradient due to momentum of a 3rd fragment)

Double ion production in 4 keV / amu He^{2+} impact

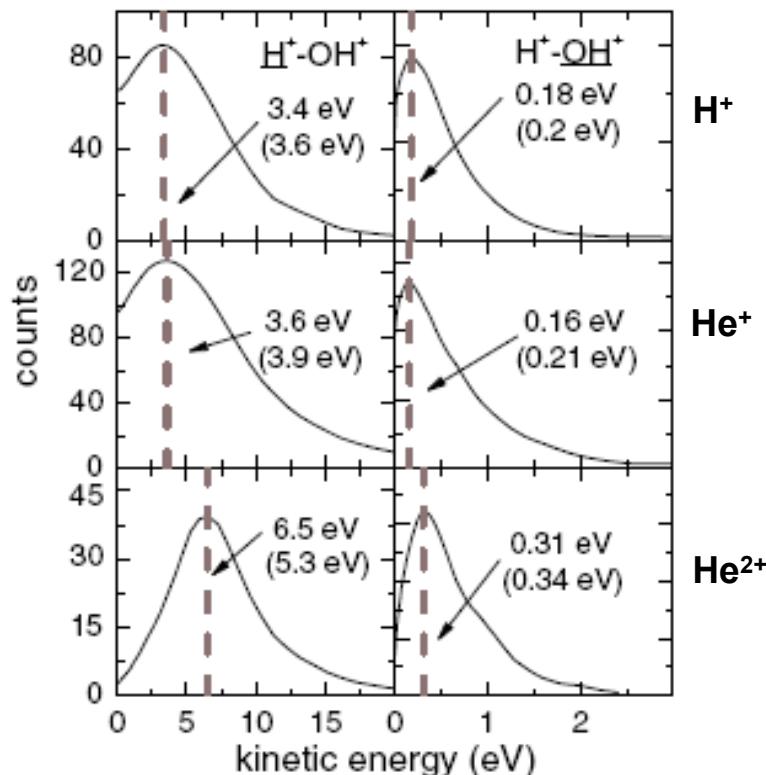


H^+ and He^{q+} impact upon H_2O (... continued)

KER provides key information to elucidate the **excited states** accessed in a collision...

... And to model **secondary processes**

Double ion production KER upon 6 keV impact



Alvarado et al., *J. Phys. B* **38** (2005) 4085

Summary of first part:

- WG focus on impact velocities ~ the Bragg peak and down to the stopping depth in ion radiation exposure (inc. cancer therapies...)
- Interactions with bound electrons dominate
- Difficult theoretical treatment of energy deposition and charge exchange processes
- Gas phase experiments enable the products of individual collisions to be observed and analysed...
... including key secondary species (electrons, radical ions...)

Acknowledgements:

Patrick Moretto-Capelle & Thomas Schlathölter