



IRSAMC



Collision induced ionization and fragmentation of DNA/RNA bases and Halogen derivatives

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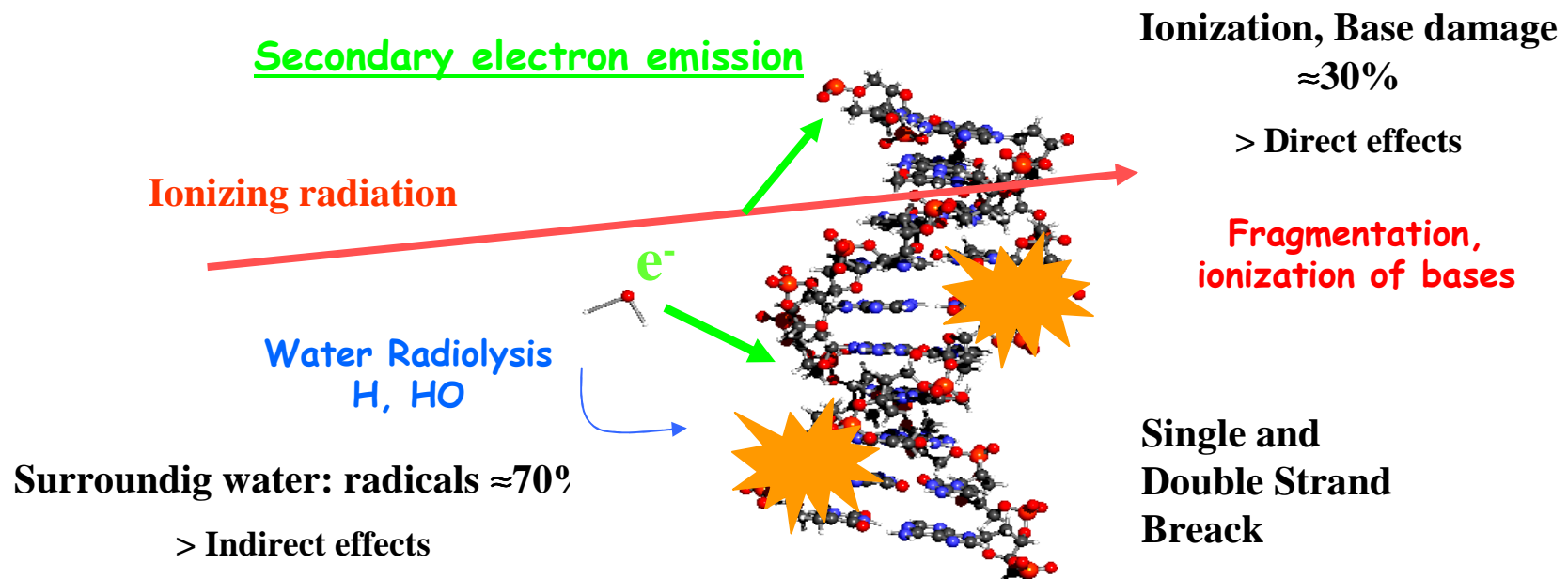
Damage induced by ionizing radiations

Radiobiology:

Ionizing Radiations → Biological effects

Principal Target : DNA Molecule

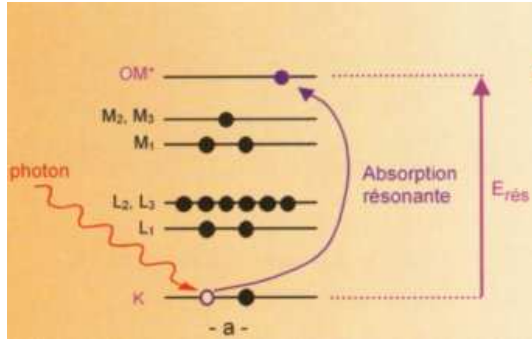
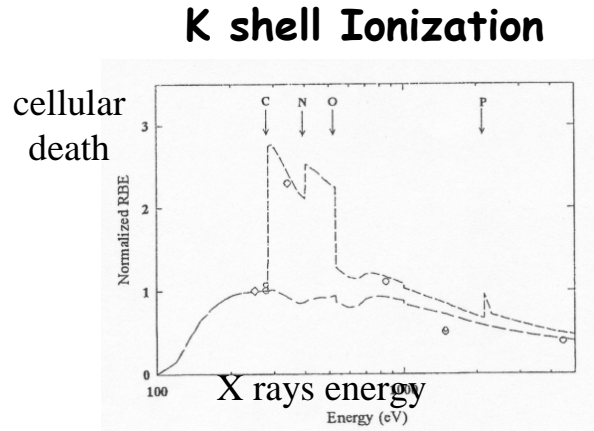
Results: Cellular death, Mutations, Cancer...



Very complicated....

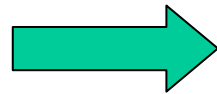
What about Physics ???

atomic physic processes

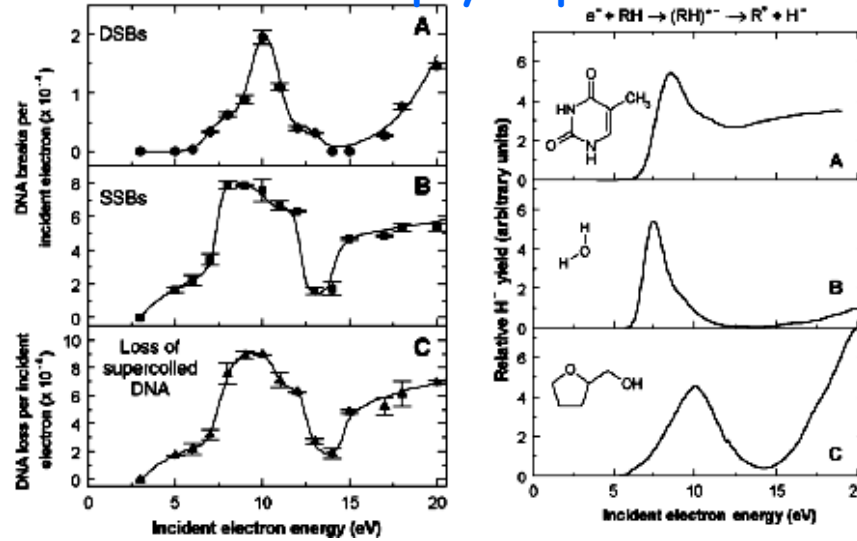


Auger electrons → DAMAGES

A.Chetioui et al
C.Lesech et al



molecular physic processes

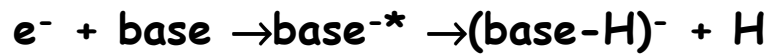


Low energy electron (<I_p) on DNA

Low energy electron on simple molecules such

Thymine

Dissociative Electron Attachment



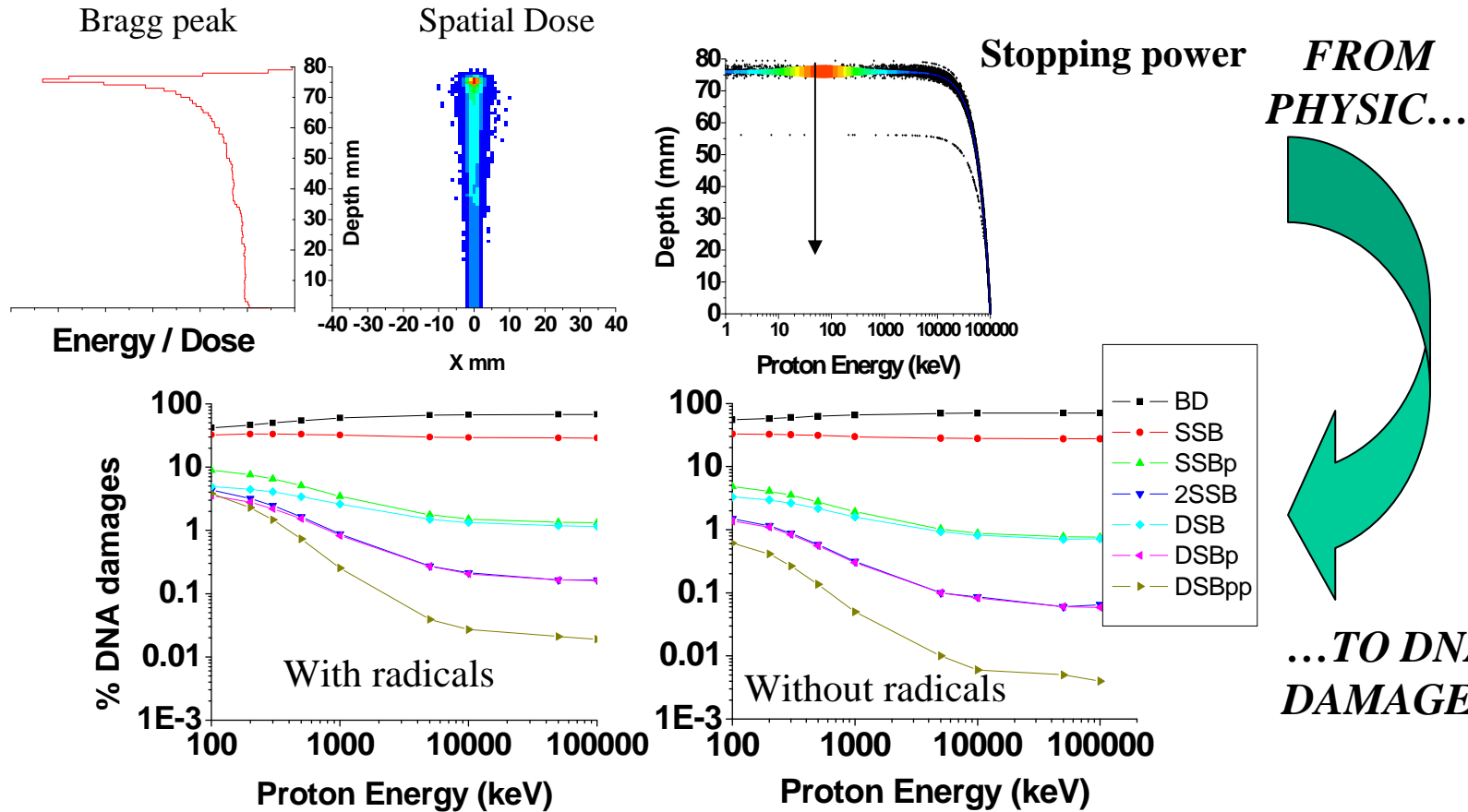
Boudaiffa et al



‘Simple’ elementary physical processes....

Ionizing radiation used in cancer treatment: X rays, electrons ‘diffuse’ dose deposition

BUT :Interaction of **ions with matter**: possibility of strong energy deposition in a well defined region around the **Bragg peak used in Protontherapy**



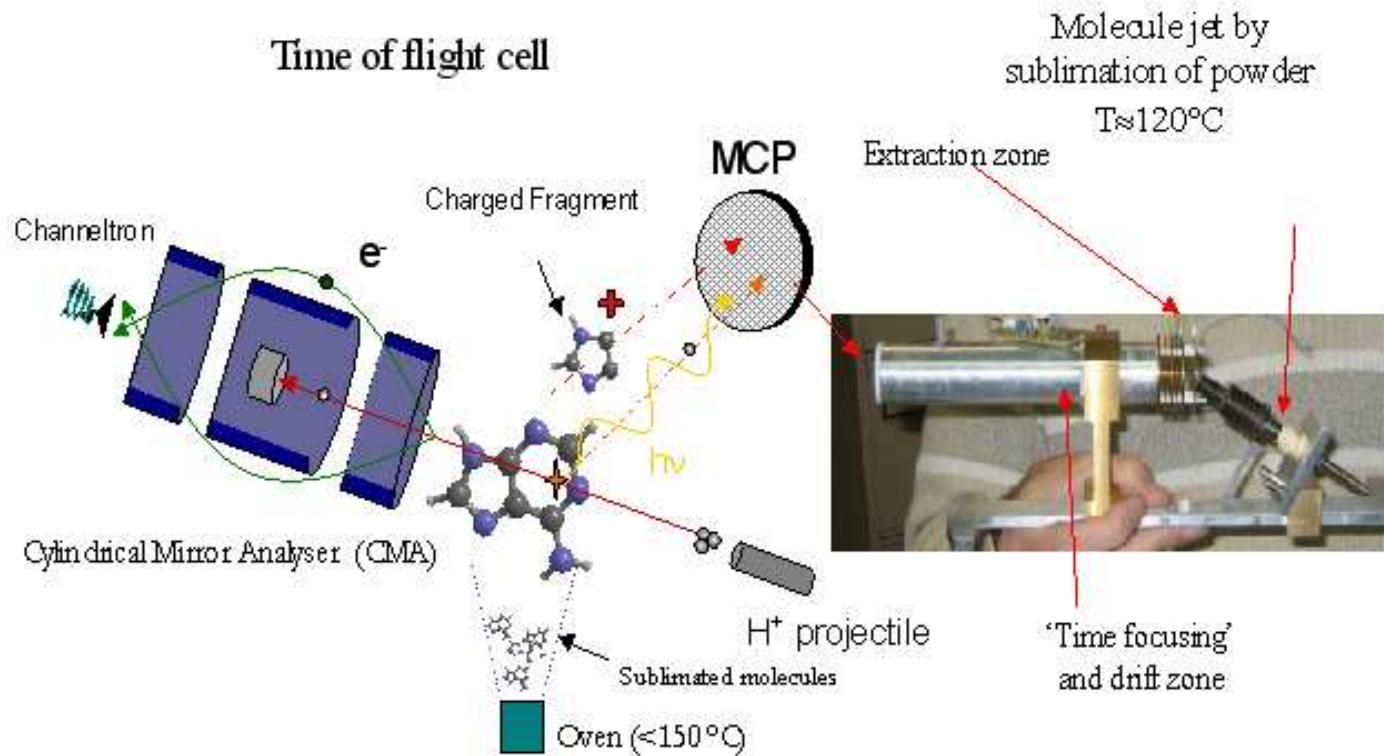
≈100keV → maximum of ionization cross section, electron emission

≈Quantum physic studies : C. Dal Cappello and P.A Hervieux (private communication)

≈Classical studies (CTMC) : I.Abbas et al, Phys.Med.Biol. 53 (2008) /P.Moretto-Capelle et PRA 74, 062705 (2006)

Damages on Molecules... Fragmentation

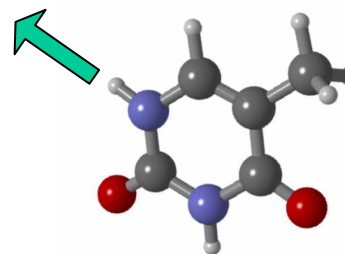
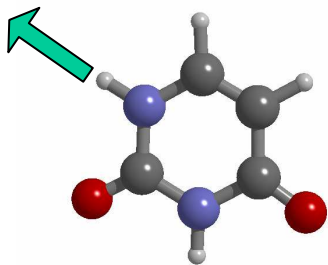
Experimental set up



Pulsed beam , Pulsed extraction (900V rise time 10ns); event by event acquisition mode

Molecules studied...

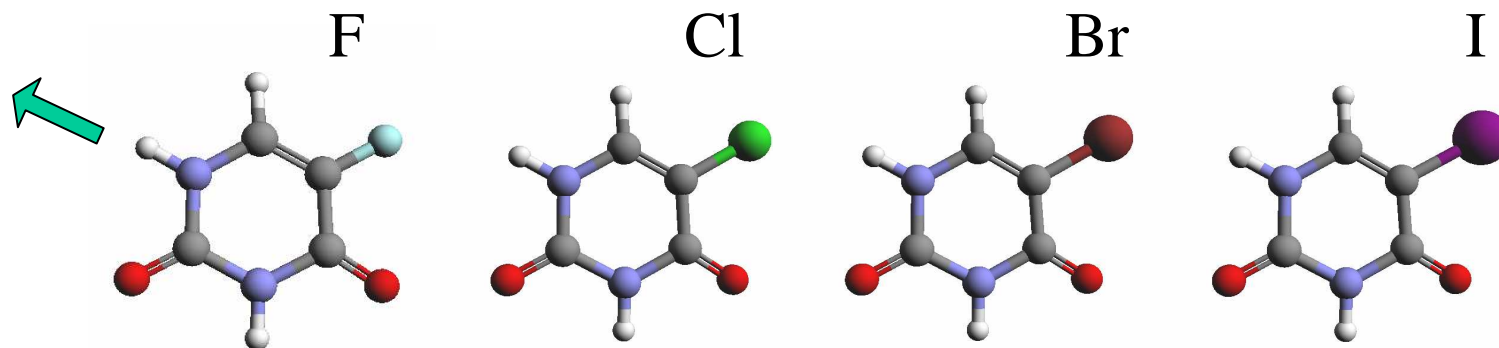
'Natural' molecules RNA/DNA bases ex Uracil Thymine



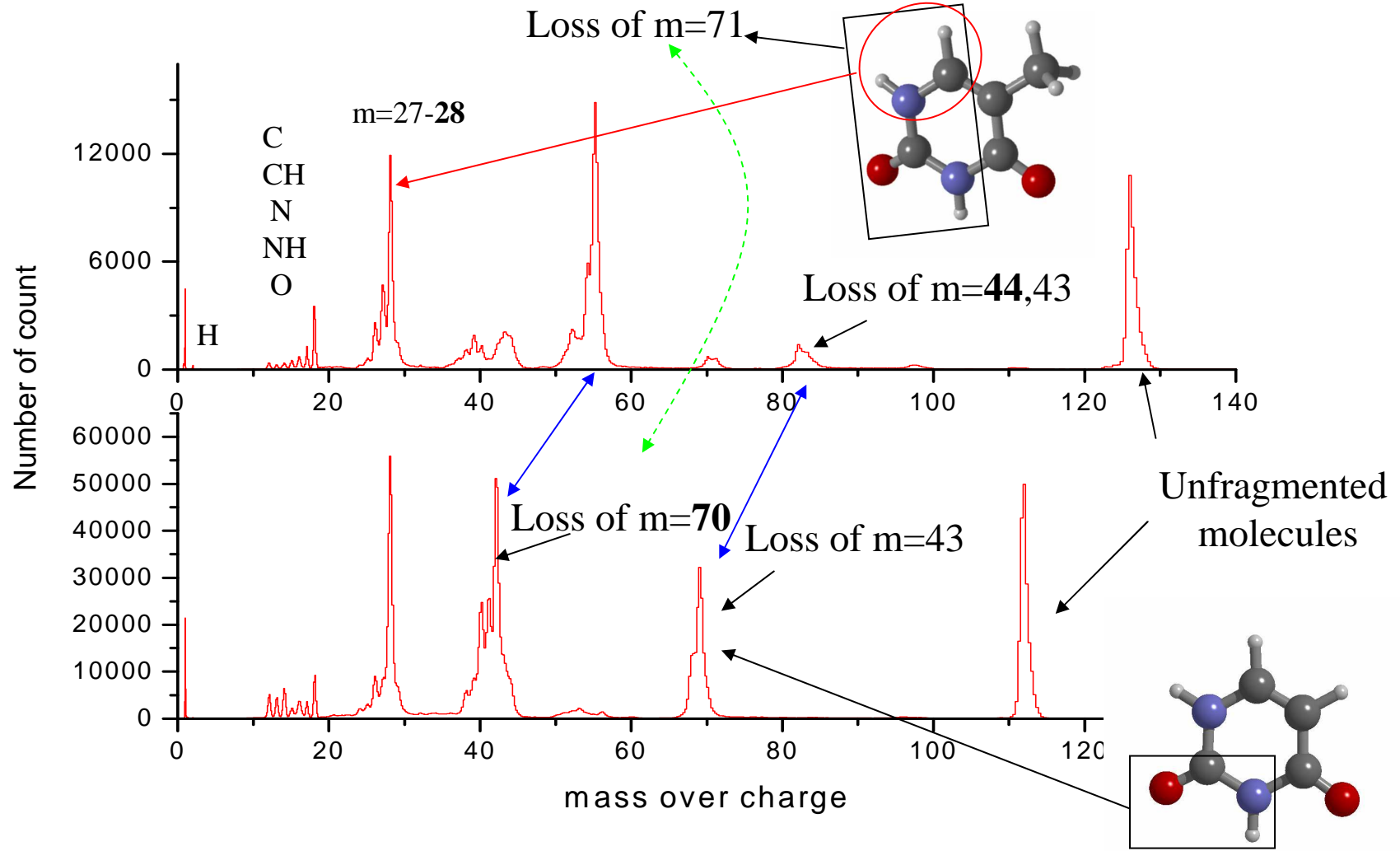
Substitute 'Derivative' of bases: Halo-Uracil

Known to be radiosensitive ie increase of the action of radiation

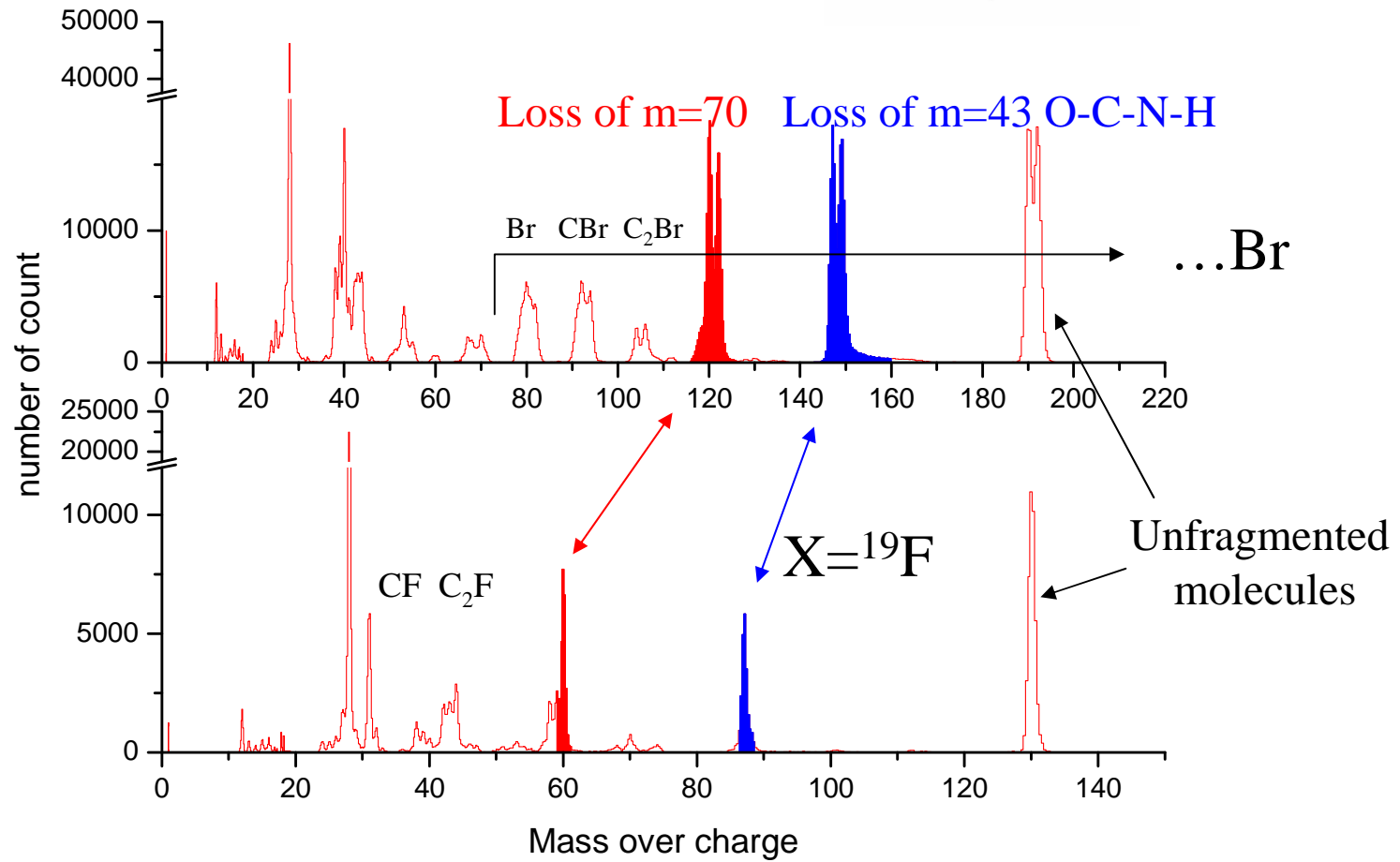
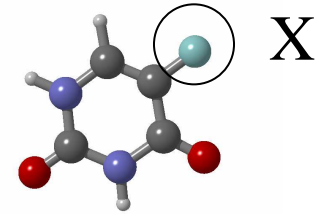
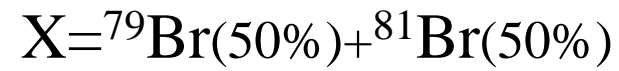
Mechanisms ? -Auger effect (heavy atoms) -DEA

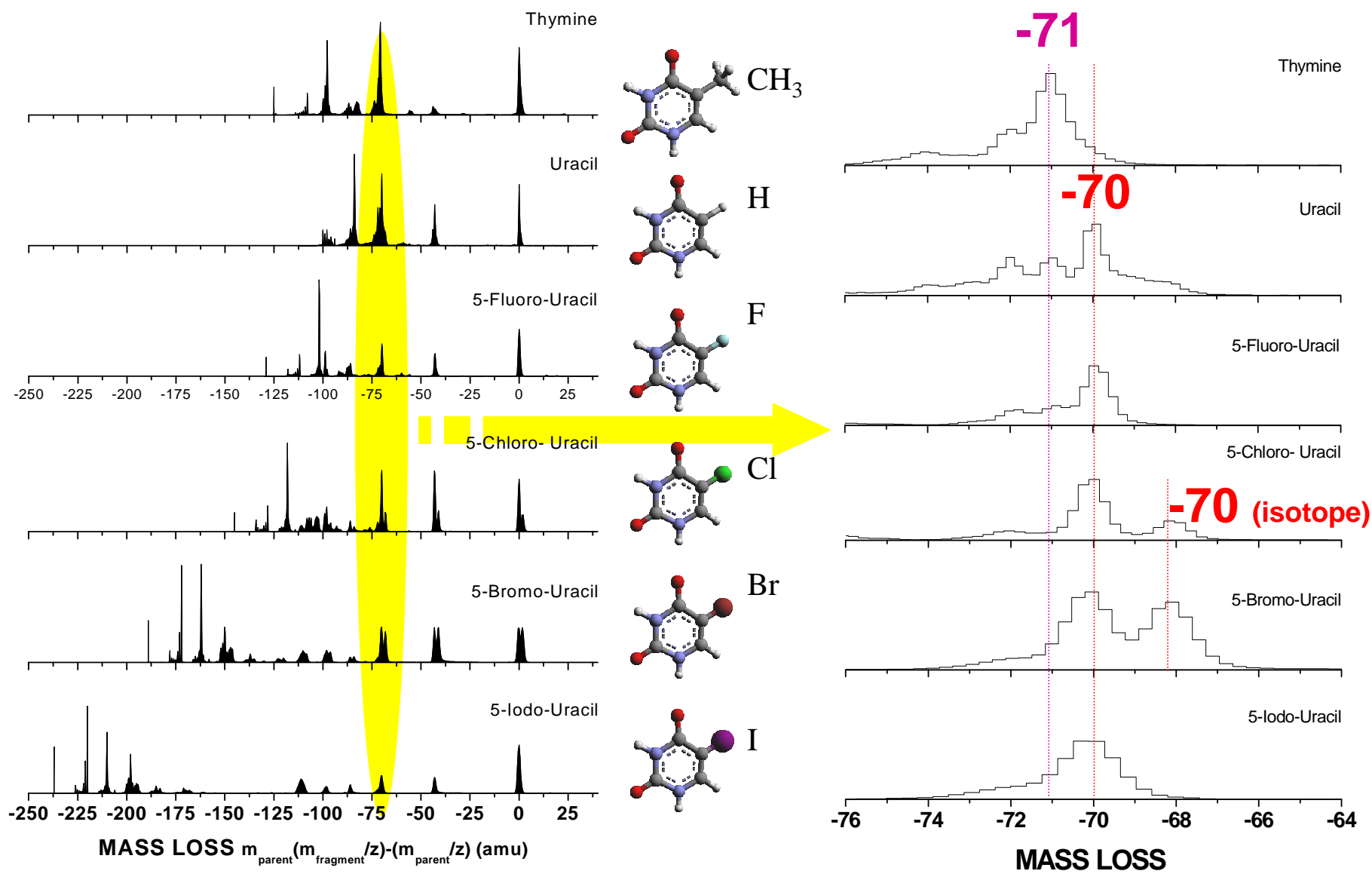


90% events: Single Ionization → Fragmentation of singly charged 'Natural' molecules

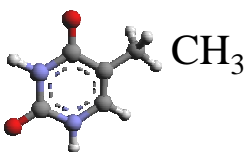


Halo-Uracil

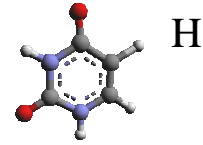




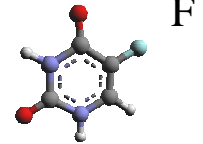
Thymine



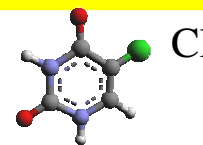
Uracil



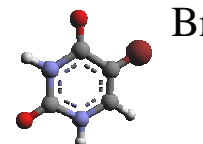
5-Fluoro-Uracil



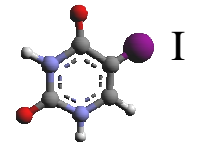
5-Chloro-Uracil



5-Bromo-Uracil



5-Iodo-Uracil



-71

Thymine

-70

Uracil

-70 (isotope)

5-Chloro-Uracil

5-Bromo-Uracil

5-Iodo-Uracil

-250 -225 -200 -175 -150 -125 -100 -75 -50 -25 0 25

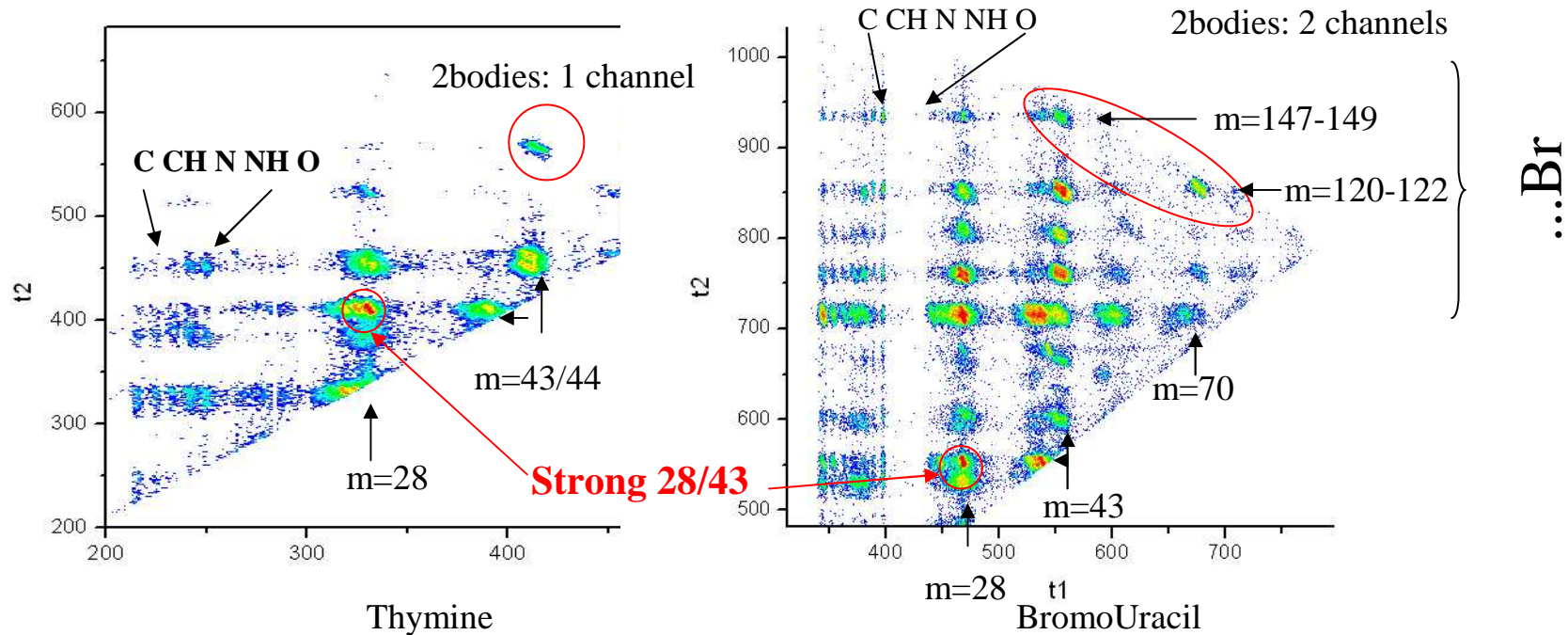
MASS LOSS $m_{\text{parent}}(m_{\text{fragment}}/z)-(m_{\text{parent}}/z)$ (amu)

-76 -74 -72 -70 -68 -66 -64

MASS LOSS

What for the (dissociating) doubly charged molecule?

Correlated between Time of flight of the two charged fragments



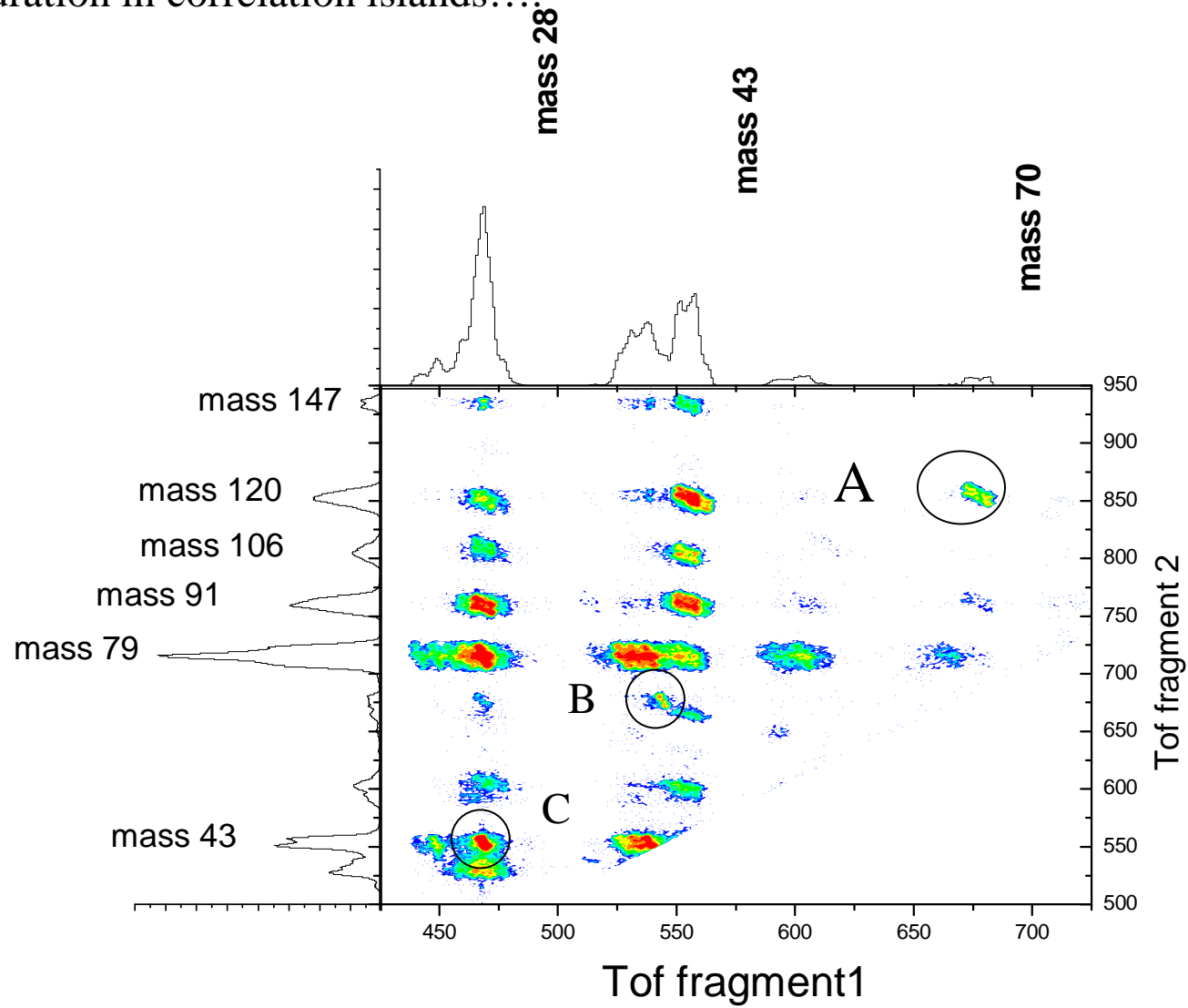
2-bodies fragmentation for

HaloUracil : emission of mass 43 and mass 70

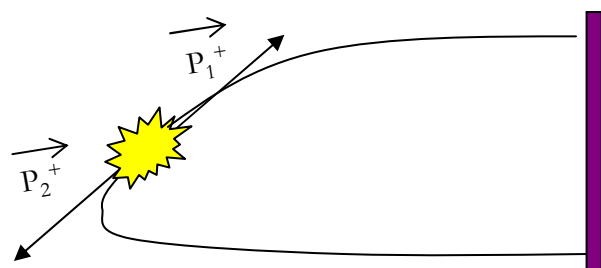
Uracil/ Thymine/Cytosine: emission of 43/44

→Structuration in correlation islands....

....Structuration in correlation islands....



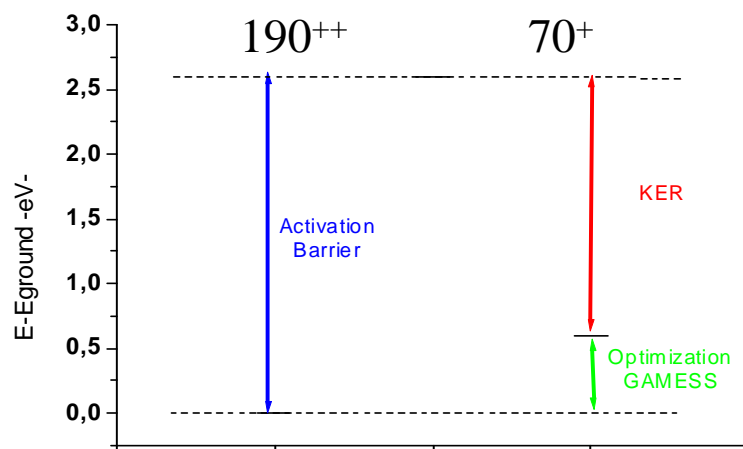
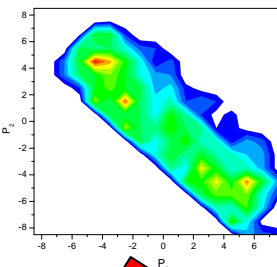
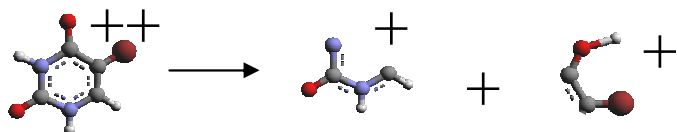
Kinetic Energy Release in the dissociation



$$T = T_0 - P_{//} / qE ;$$

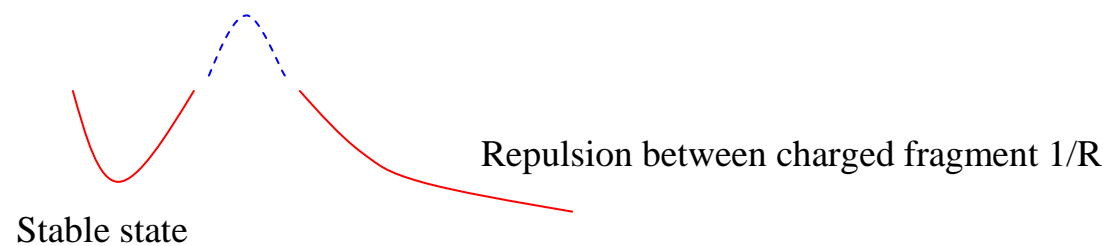
$P_{//}$ momentum,
 q charge, E extraction field

A Two bodies dissociation with charge separation: $p_1 + p_2 = 0$



KER $\approx 2\text{eV}$

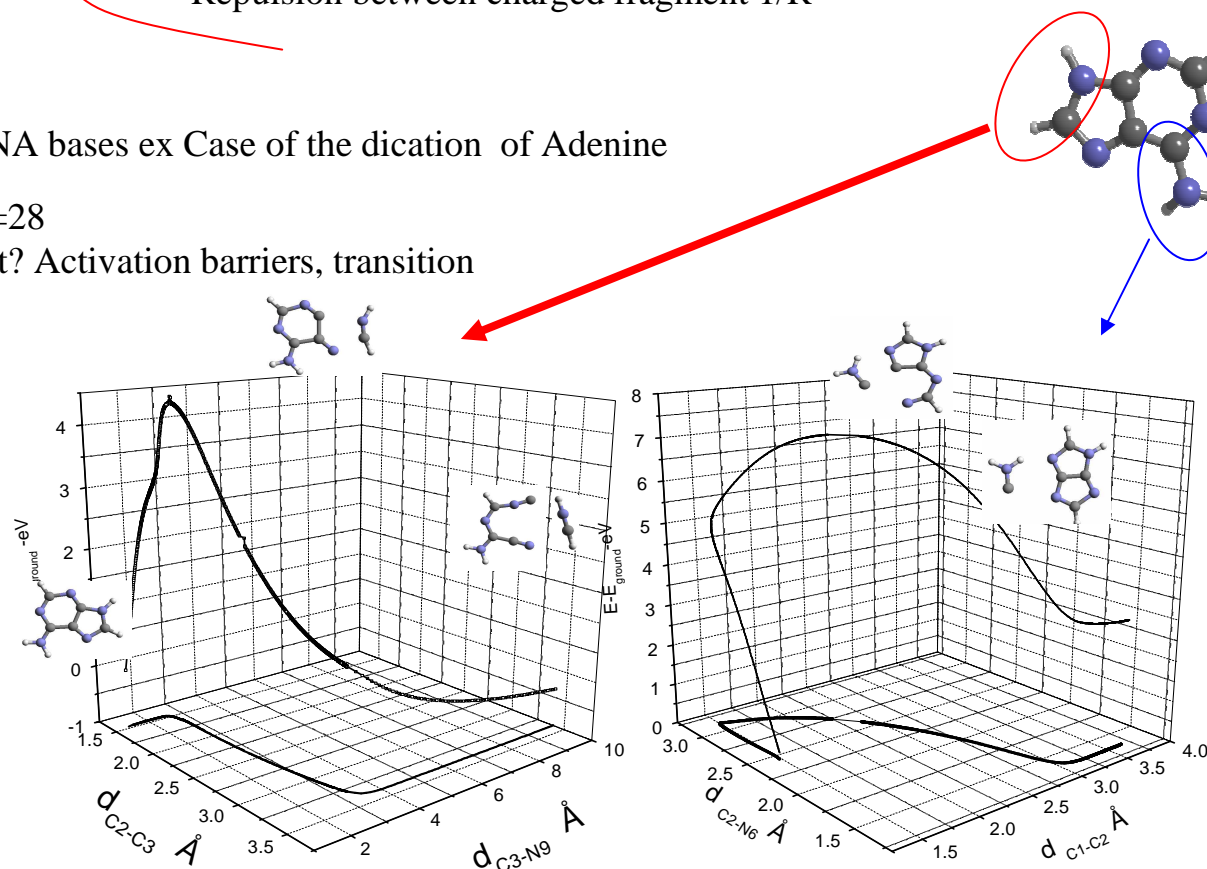
Activation/Dissociation Barrier?



'Natural' molecules DNA bases ex Case of the dication of Adenine

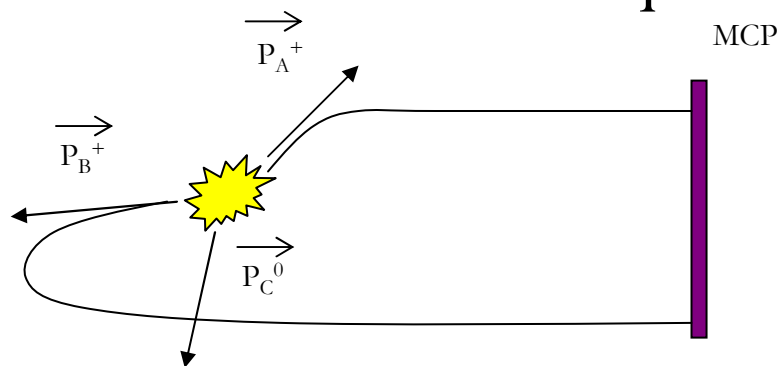
Strong emission of $m=28$

Nature of the fragment? Activation barriers, transition state



Calculation of ground state structure/ Transition State and IRC using GAMESS code at HF level *P.Moretto-Capelle, A. Le Padellec J.Chem.Phys 127 (2007) 234311*

More frequently...Neutral emission



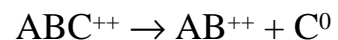
$$P_A + P_B + P_C = 0$$

Dissociation mode:

1) Concerted: pure 3 bodies process

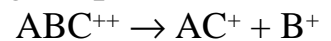
2) Sequential

- deferred charge separation:

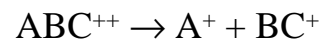


$$\angle A^{++}B^+ \longrightarrow P_A = -P_B$$

-charge separation:



$$\angle A^{++}C^0 \longrightarrow P_{AC} = -P_B$$



$$\angle B^{++}C^0 \longrightarrow P_{BC} = -P_A$$

SUPPOSE That energetic is due to coulomb explosion

$$V_A = V_c$$

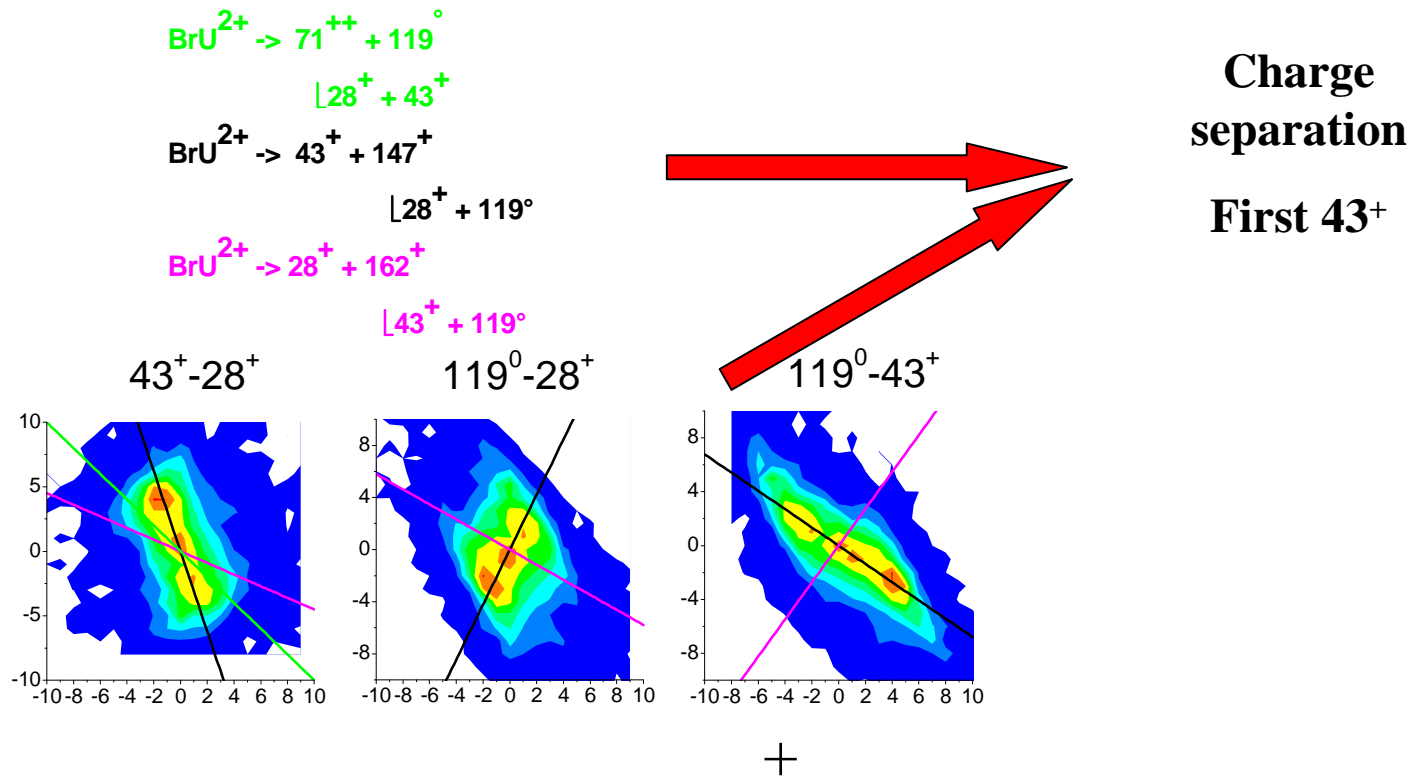
$$P_{BC} = -P_A$$

$$V_B = V_c$$

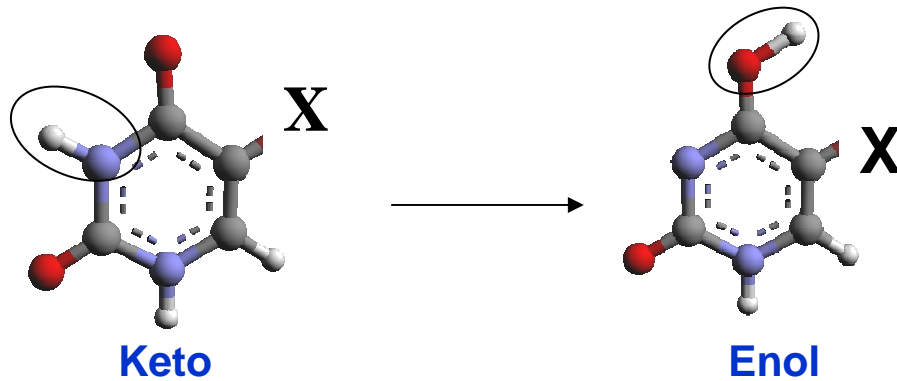
MOST Important channel :Correlation between fragments 28^+ and 43^+

From correlated time of flight \rightarrow correlated Momenta between charged fragments

From momentum conservation and event by event acquisition mode \rightarrow neutral momentum



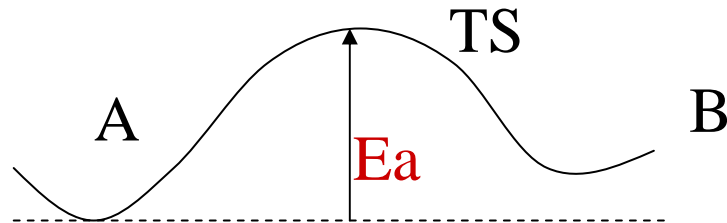
Origin of mass=70? => molecular reorganization: Tautomerization



Energetic of the reaction

Keto Enol Tautomerization in oven?

Need activation barrier E_A of the reaction ie to find the TRANSITION STATE



Reaction rate (TS Theorie):

$$k_{A \rightarrow TS \rightarrow B} = kT/h * Q_{TS}/Q_A * \exp(-Ea/kT)$$

T:temperature

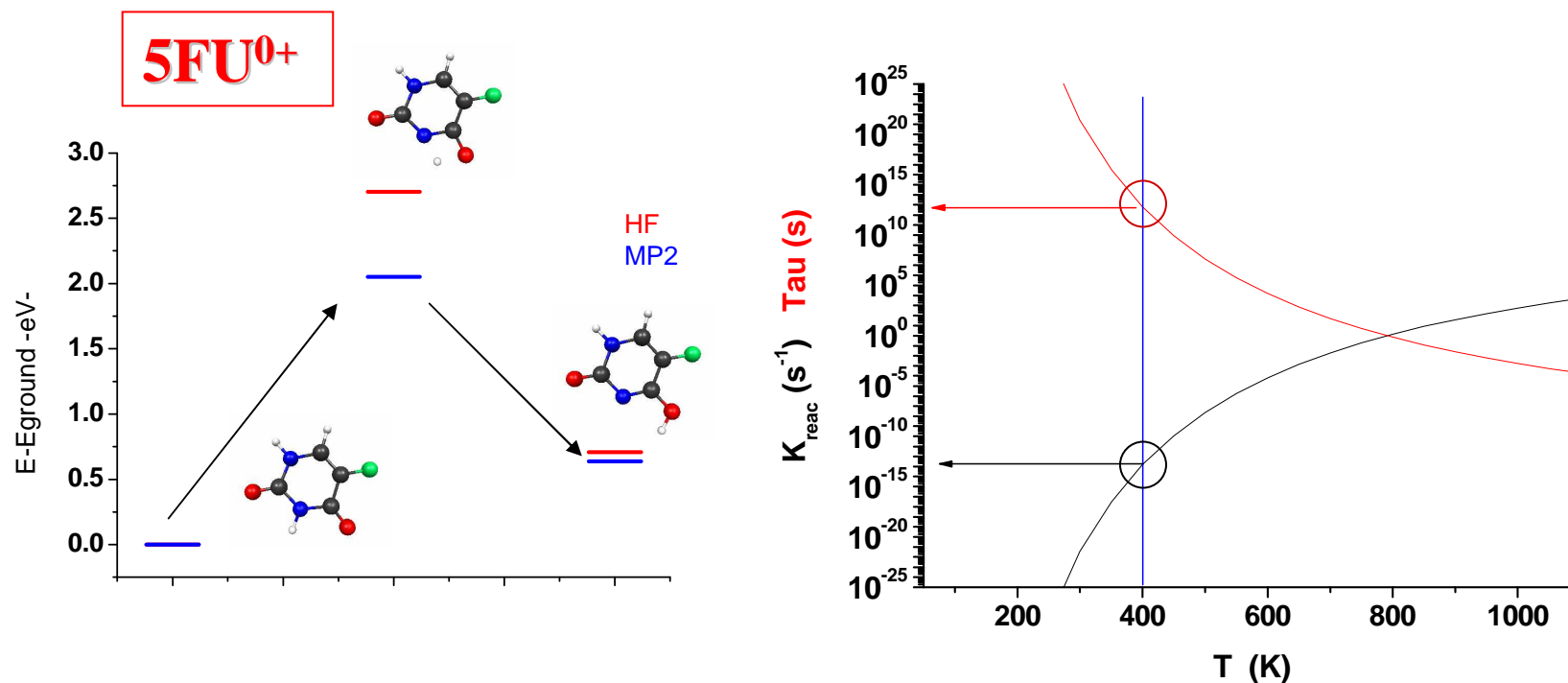
Q_{TS} , Q_A : partition functions

Search for the Transition State:

Quantum chemistry package:

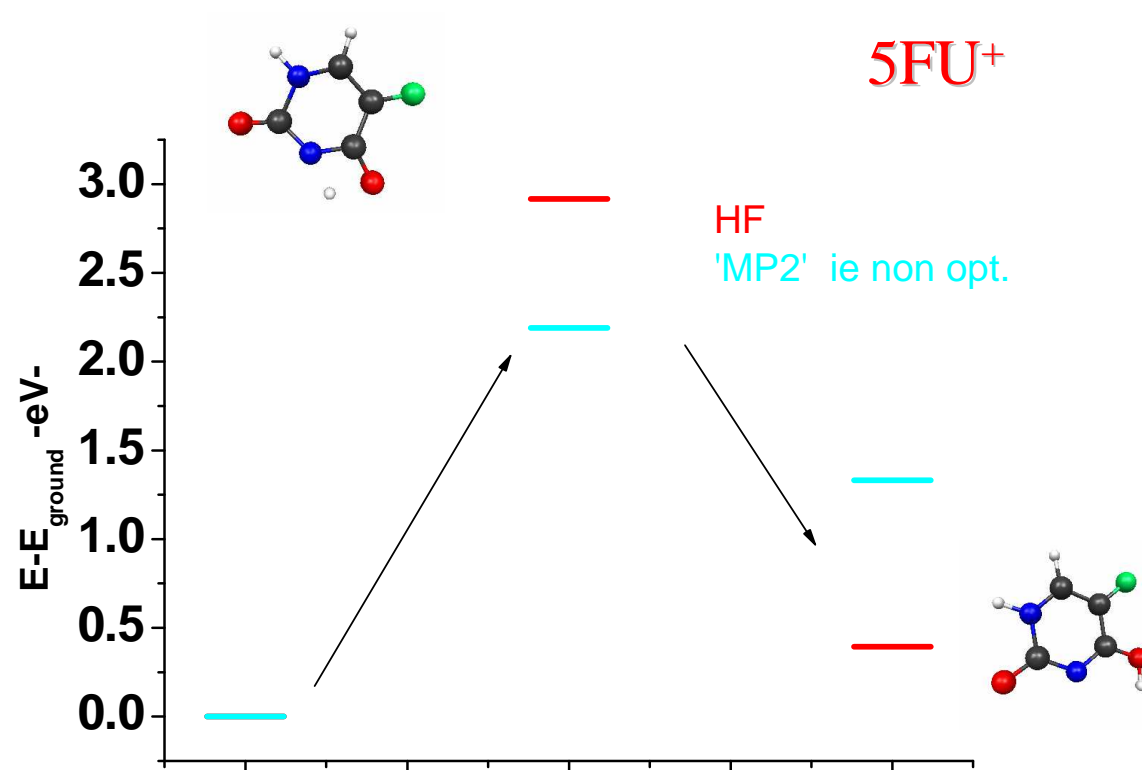
i) initialization of the structure with semi-empirical hamiltonian (MOPAC)

ii) Ab initio calculation with GAMESS (HF 6-31G and HF+MP2 6-31G)

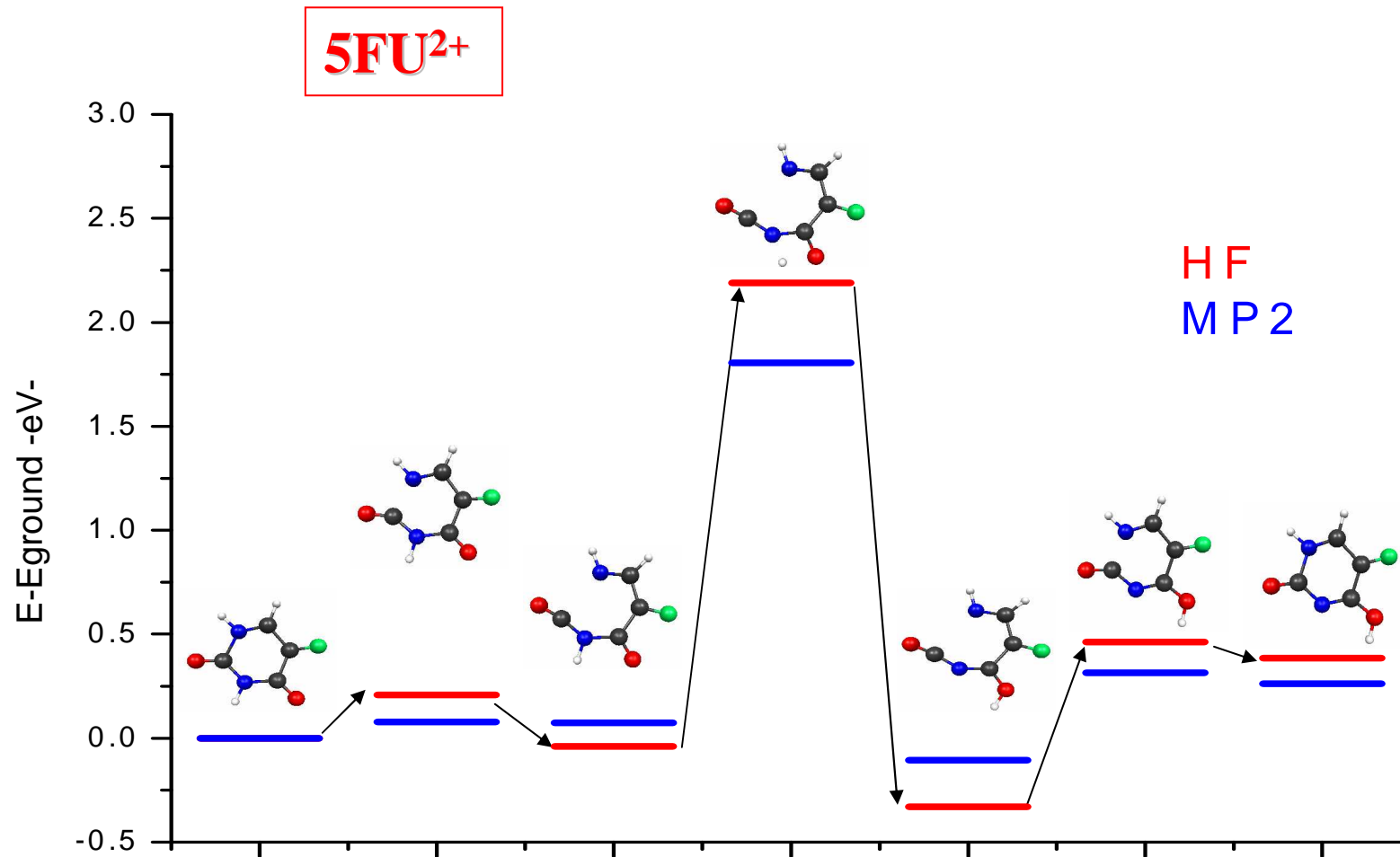


~~Keto → Enol OVEN~~ ⇒ Induced by Collision !

Barriers for charged molecules



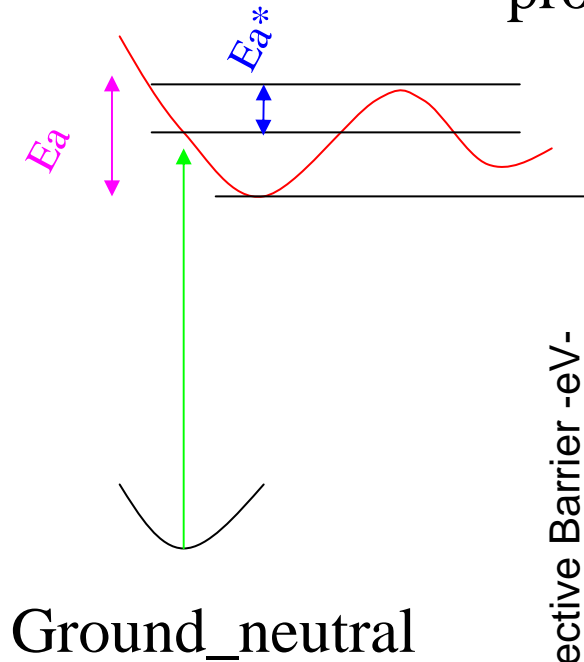
≈ The same as neutral....



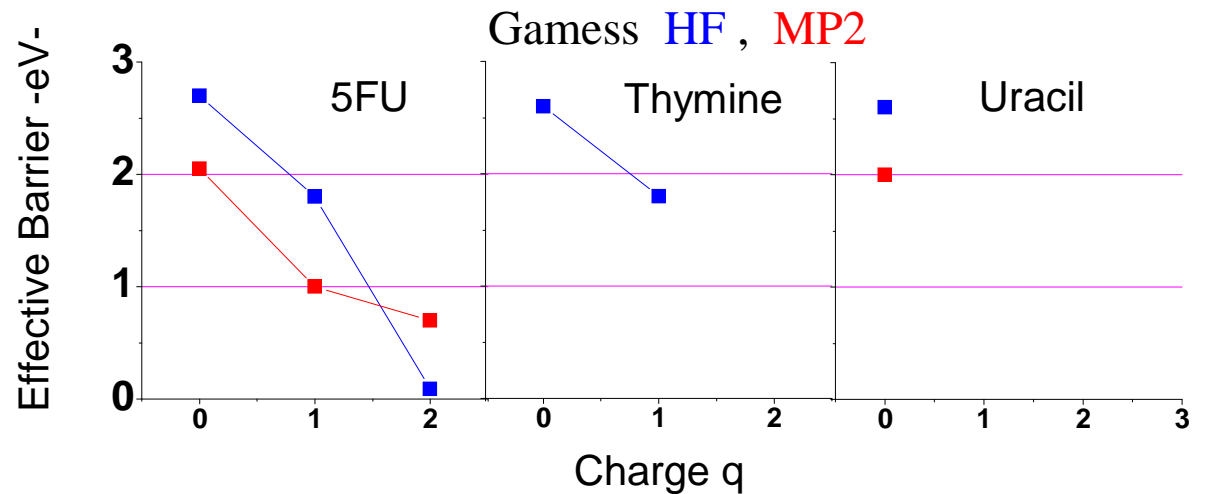
Proton transfer => multi-steps processes, bond breaking C1-N2 (barriers 0.1-0.2 eV)

Opening of the ring

'Effective' activation barriers for proton Transfer



Vertical transition → Excitation

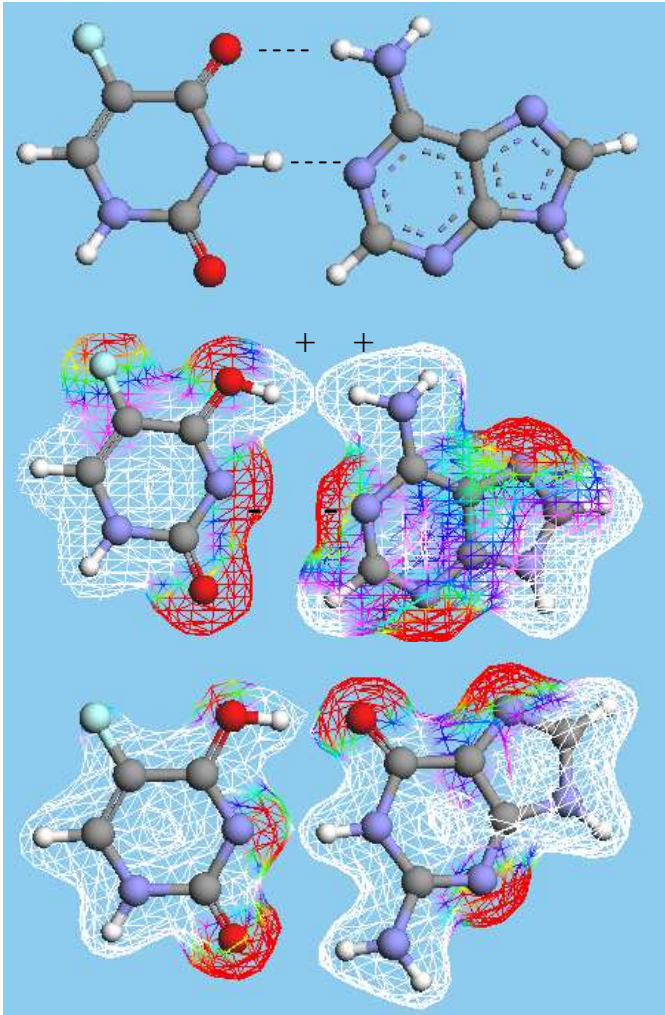


☹️: Ground State calculations: **NO DIFFERENCES BETWEEN THYMINE, URACIL and 5FU !!!**

In progress...

Importance/Consequence of the tautomerization ??

Watson-Crick pair



Keto:

Thymine, Uracil, FU---Adenine

Enol:

Uracil, FU~~---~~Adenine

Enol:

Uracil, FU-----Guanine

MISPAIRING !!

Conclusions and future...

-Investigation of Fragmentation induced by collision of DNA/RNA bases

-Investigation of Radiosensitizer: HaloUracil (substitute of Uracil and Thymine)

-Differences with 'Natural' molecules

tautomerization: Keto→ Enol

- Calculation of proton transfer barrier

-in ground state not satisfactory (same results)

-Need excited states !!

- Need absolute cross sections to compare systems

Other type of rdiosensitizer: molecule containing Platinum

(Carbo,Cis Platin)