Reaction dynamics of small bio-molecular ions with electronically excited singlet molecular oxygen using guided-ion beam scattering and direct dynamics simulations

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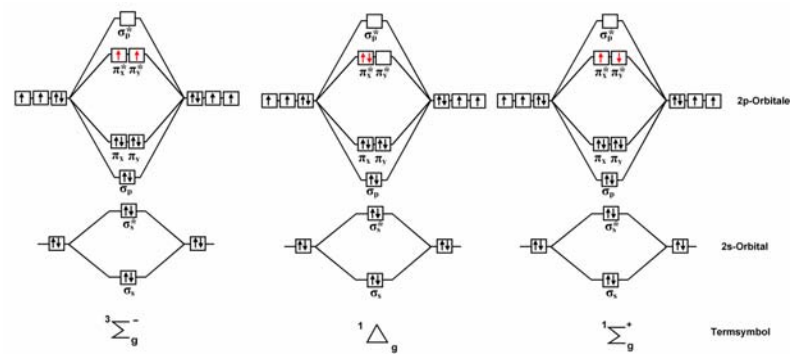
Significance of $^1O_2$ in biological milieux & atmospheric chemistry

$^1O_2$



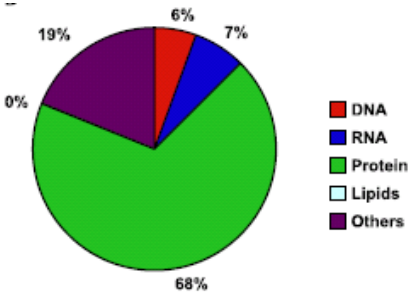
$$O_2(^1\Delta_g) + Q \xrightarrow{\text{quenching}} O_2(^3\Sigma_g^-) + Q$$

spin - fobidden unless Q has multiplicity > 1, thus long - lived

$$O_2(^1\Sigma_g^+) + Q \xrightarrow{\text{quenching}} O_2(^1\Delta_g) + Q$$

not spin - fobidden, 10^5 times faster than $O_2(^1\Delta_g)$

Biological systems: $^1O_2$-mediated damage and cell death



Calculated consumption of $^1O_2$ by various cellular components with a typical leukocyte cell.

M. Davies, *Biochim. Biophys. Acta*, **2005**, 1703, 93

Air Environment:

$^1O_2$ can be produced under sunlight and plays an important role in natural and polluted troposphere

$^1O_2$-mediated oxidation is one of major sinks for amino acids loss in the troposphere, and accounts for one route of aerosol formation over remote marine area.

P.R. Ogilby, *Chem. Soc. Rev.* **2010**, 39, 3181.

Study of $^1O_2$-mediated oxidation in solution

Amino acids susceptible to $^1O_2$-oxidation: Tyr, Met, Cys, Trp and His

Experimental techniques used for most $^1O_2$-oxidation studies:

Photo-sensitized oxidation in the presence of light and sensitizers in solution

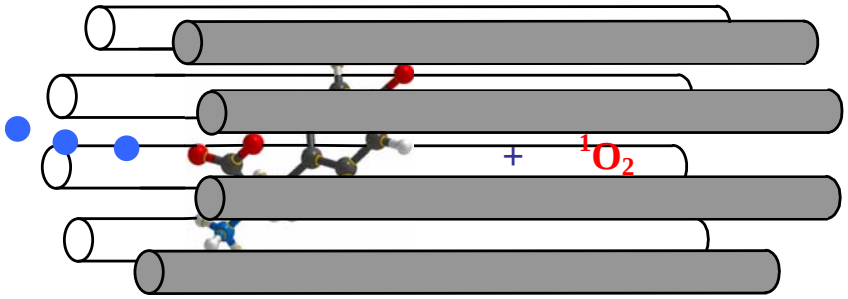
(*since the discovery of photodynamic actions in 1900s*)

$$sensitizer \xrightarrow{h\upsilon} sensitizer^*$$

$$sensitizer^* + {}^3O_2 \xrightarrow{\text{Energy Transfer (TypeII)}} sensitizer + {}^1O_2$$

Other species (e.g. radicals via Type I process) may generate during photosensitization and contribute to reaction.

Reaction dynamics of bio-molecular ions with $^1O_2$ in the gas phase



Guided-ion beam techniques to investigate reactions of amino acid ions with an external clean source of $^1O_2$, aimed at achieving a molecular level understanding of reaction mechanisms

- Reaction thermochemistry & energy dependence (*guided-ion beam scattering*)
- Effects of hydration and charge (*electrospray ionization*)
- Benchmark systems for quantum chemistry and dynamics simulations

In conjunction with solution-phase study

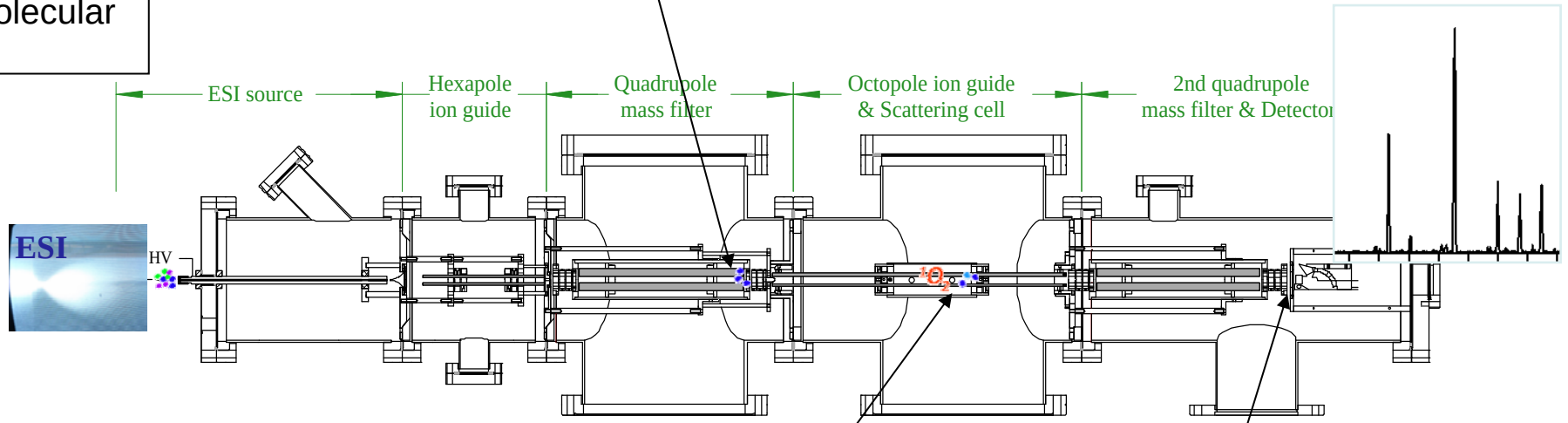
- Revealing intrinsic properties of biomolecules
- Biogenesis
- Better understanding of intrinsic *vs.* external imposed properties in biological systems

Experimental setup for biomolecular ions + $^1O_2$

Step 1. ESI generation of biomolecular ions

2: Ions are passed into a quadrupole for mass selection.

$$\sigma = k / v_{rel} = \frac{I_{product} k_B T}{I_{reactant} P_{cell} l_{cell}}$$



3. Mass-selected ions are guided into an octopole surrounded by a collision cell, and scattered from $^1O_2$ contained within.

4. Product ions are mass analyzed & counted.

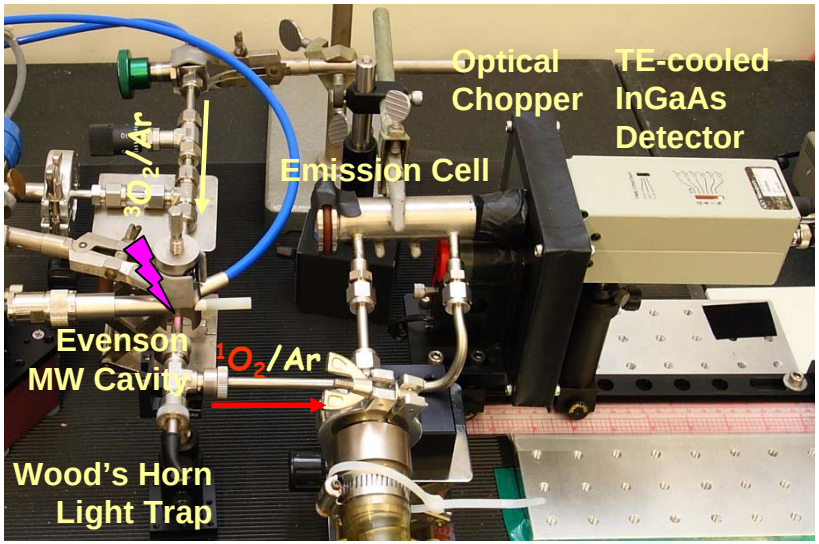
Y. Fang and J. Liu, ***J Phys Chem*** A, 2009, **113**, 11250

Generation and detection of $^1O_2$

Micro-wave discharge

$$^3O_2 \xrightarrow{Microwave\ Discharge} {}^1O_2(^1\Delta_g)$$

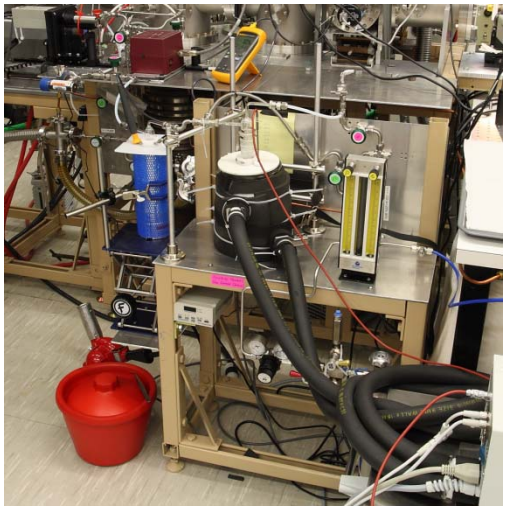
$$O_2(^1\Delta_g) \xrightarrow{Emission} O_2(^3\Sigma_g^-) + 1270\ nm$$



Chemical $^1O_2$ generator

$$2H_2O_2 + Cl_2 + 2KOH \xrightarrow{-21°C} {}^1O_2/{}^3O_2 + 2KCl + 2H_2O$$

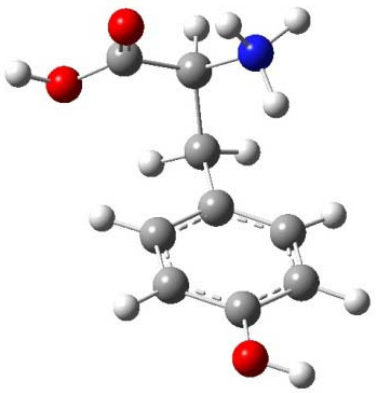
High yield, w/o O atom and O_3 contaminants



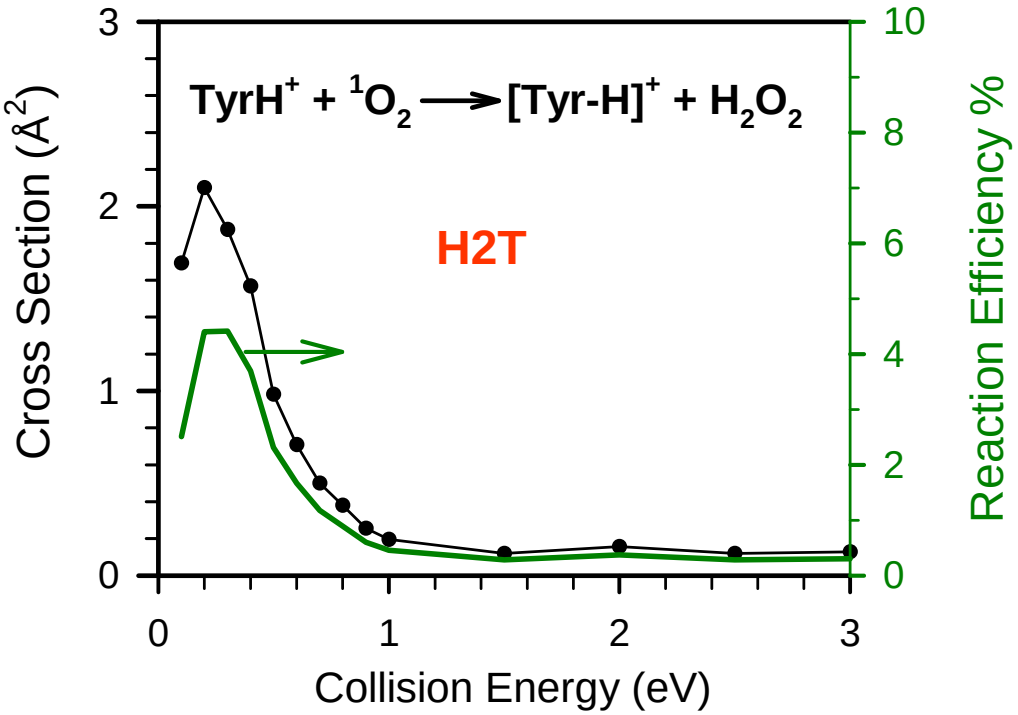
A. Midey, I. Dotan, J. Seeley and A. Viggiano, ***IJMS***, 2009, **280**, 6.

Y. Fang, F. Liu, A. Bennett, S. Ara and J. Liu, ***J Phys Chem B***, 2011, 10.1021/jp11223yy

I. Reaction of protonated tyrosine with $^1O_2$



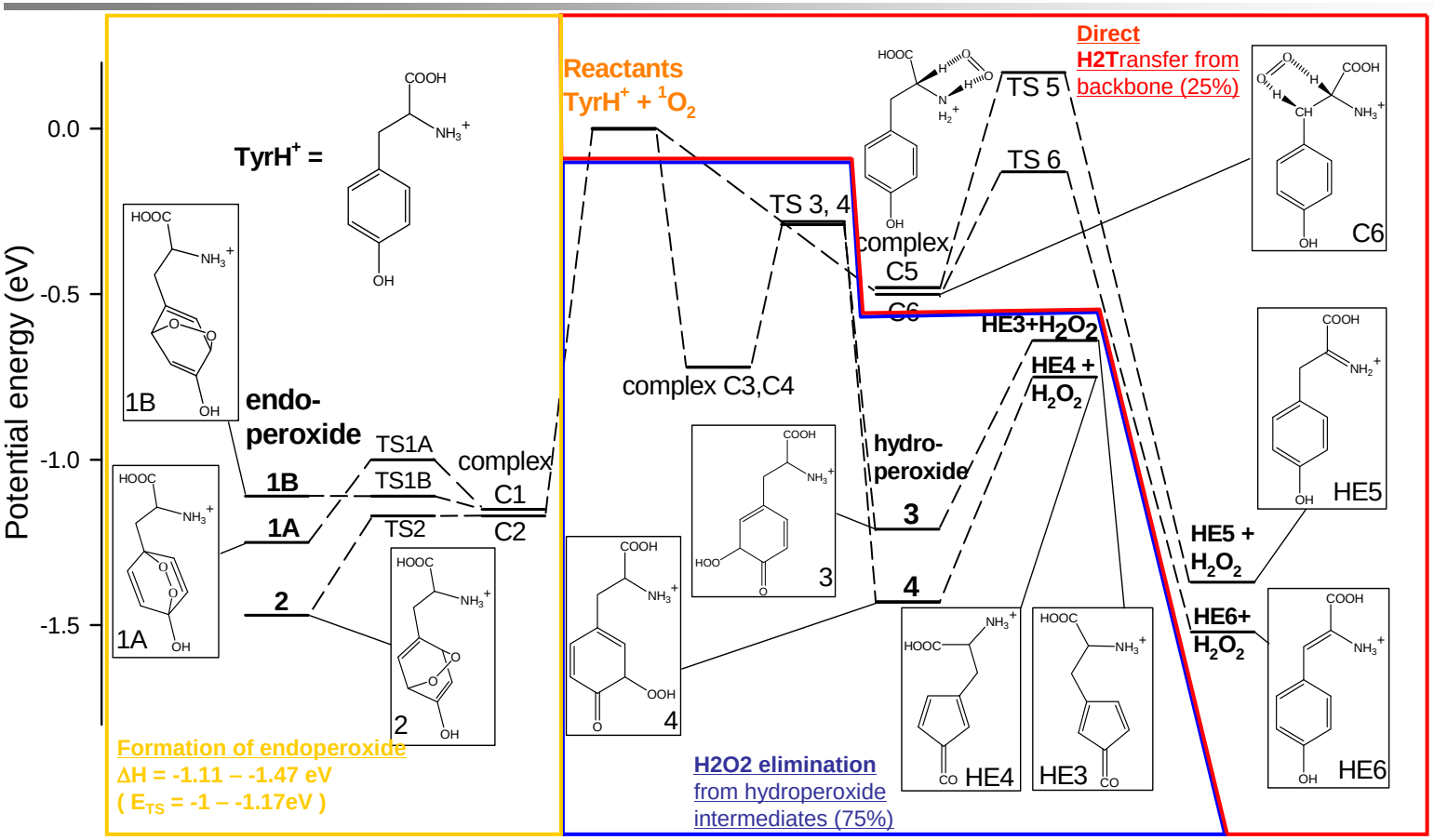
[TyrH]$^+$



Only one product channel is observed, corresponding to generation of H_2O_2 via transfer of two H atoms from TyrH$^+$ to O_2 (**H2T**).

At low E_{col}, the reaction shows strong inhibition by collision energy;
At high E_{col}, the reaction efficiency drops to 1% and starts to have contribution from a direct mechanism.

Reaction coordinate and statistical modeling at low E_{col}

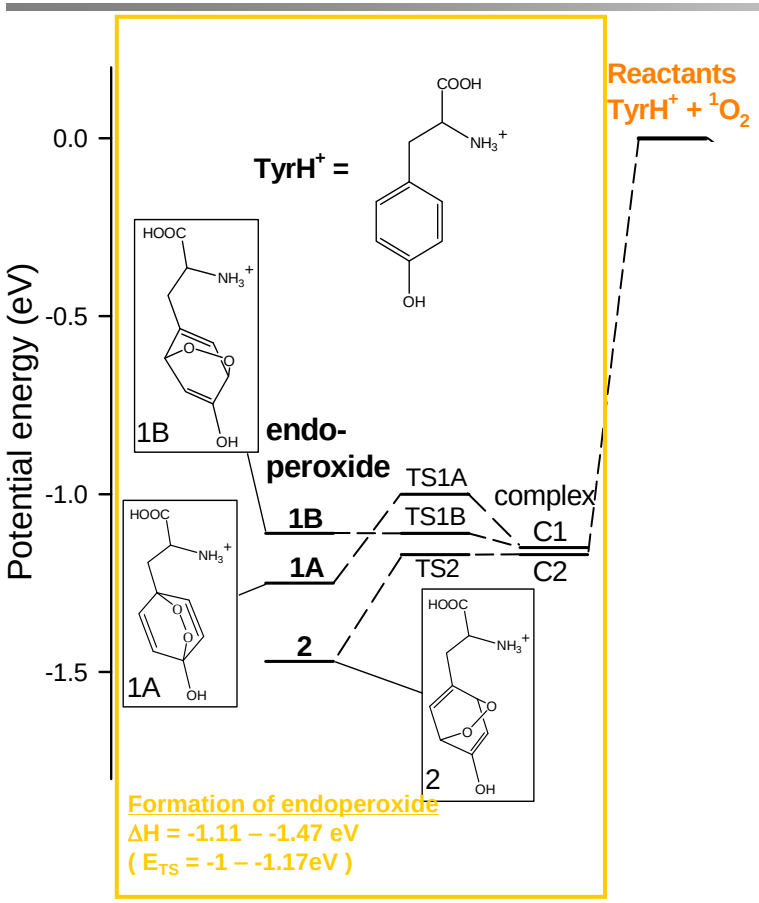


- Intermediate complexes $\tau \geq 10$ ps, able to mediate reactions at low E_{col}.
- RRKM predicted H2T% close to experimental values, i.e., 2-2.4% at E_{col} = 0.1- 0.2 eV, 0.5 % at 0.5 eV.

RRKM

$$k(E.J) = \frac{d}{h}\frac{\sum_{k=-J}^{J} G[E - E_0 - E_r^+(J,K)]}{\sum_{k=-J}^{J} N[E - E_r(J,K)]}$$

Potential energy surface and statistical modeling at low E_{col}



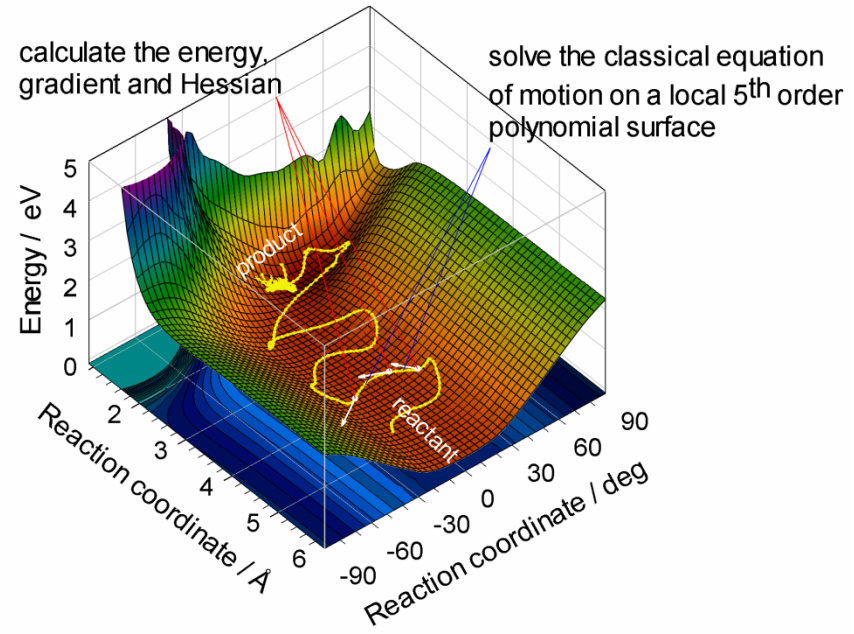
- RRKM predicted formation of endoperoxides overwhelms at low E_{col} (> 90%).
  Their fate?

$$TyrH^{+} + {}^{1}O_2 \rightarrow [{}^{\delta+}TyrH^{+} \cdots {}^{1}O_2{}^{\delta-}] \rightarrow$$
$$[{}^{3}TyrH^{+} \cdots {}^{3}O_2{}^{\delta-}] \rightarrow {}^{3}TyrH^{+} + {}^{3}O_2$$

Direct dynamics trajectory simulations

- Based on **Born-Oppenheimer approach**

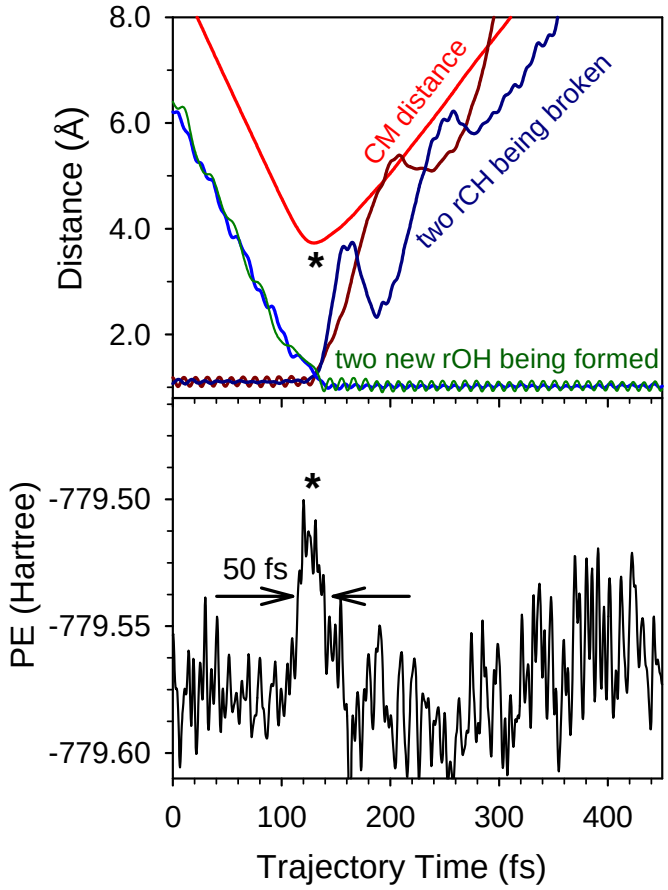
- **Trajectory initial conditions generated using Hase's Venus**
  (representing experimental conditions)
  batches of trajectories (125 each) at
  b = 0.1, 0.5, 1.0,1.5,2.0,2.5,3.0, and 4.0 Å

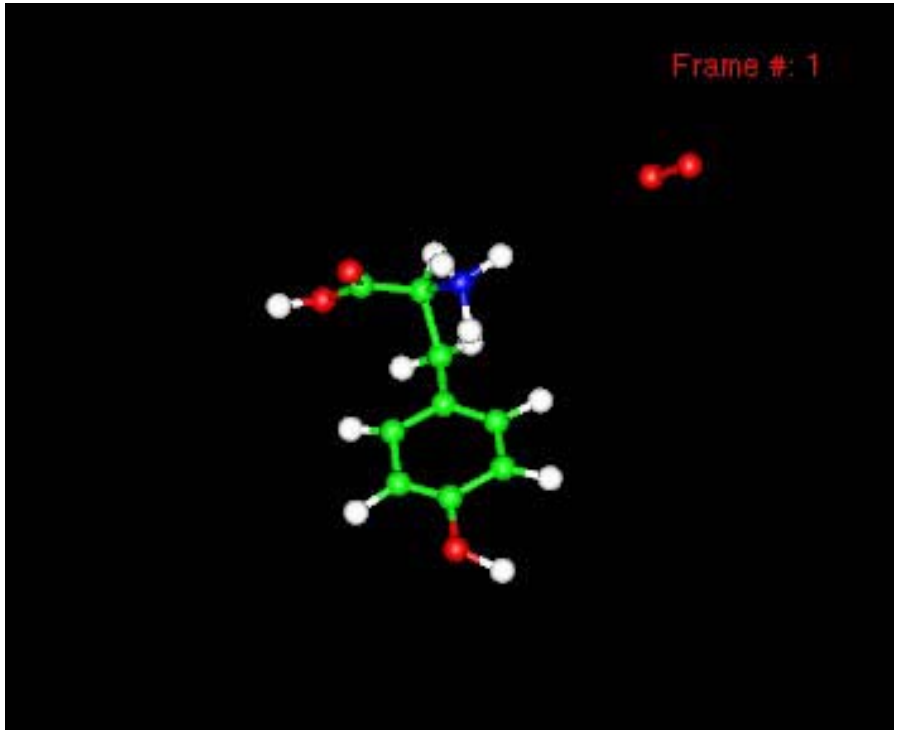


- **Trajectory integration using G03**
  - B3LYP/6-21G

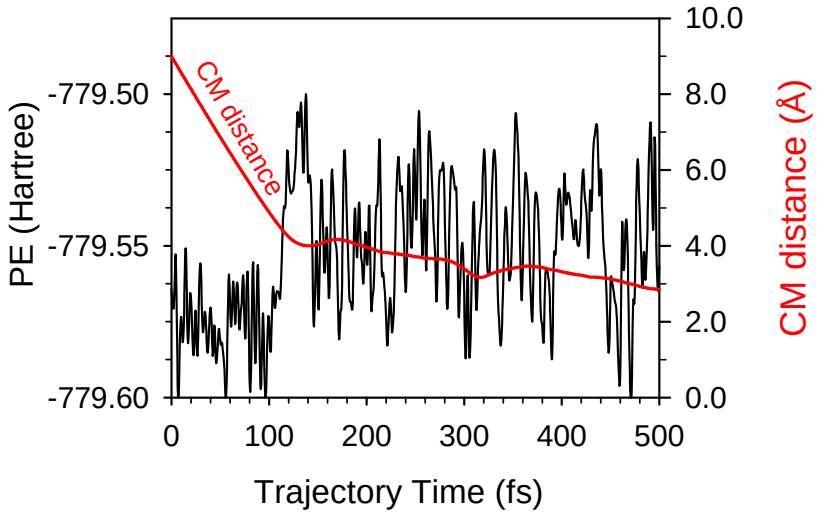
- **Linux-based computer cluster**

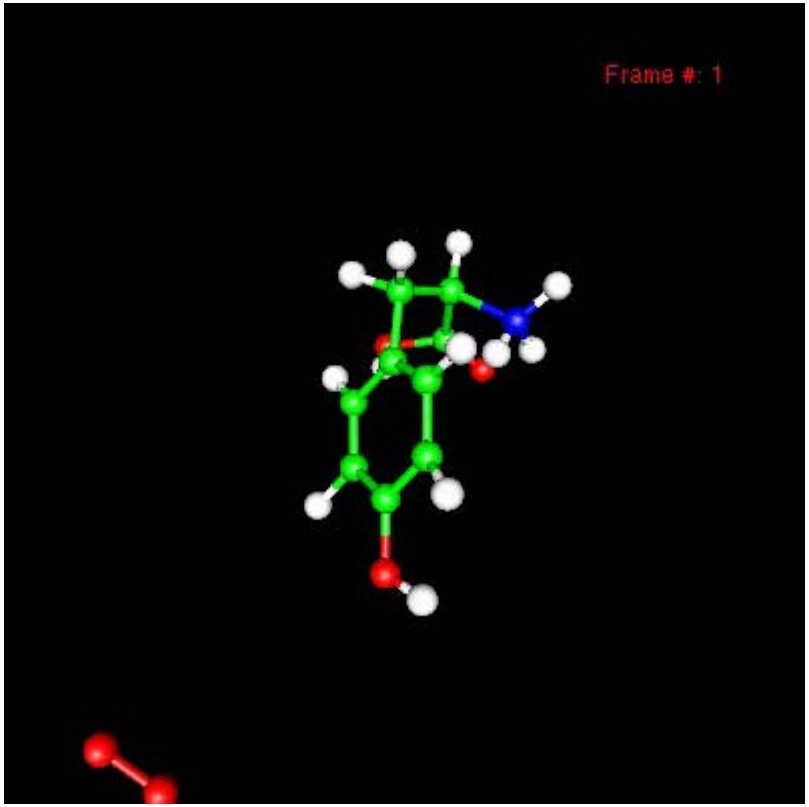
A direct H2T trajectory



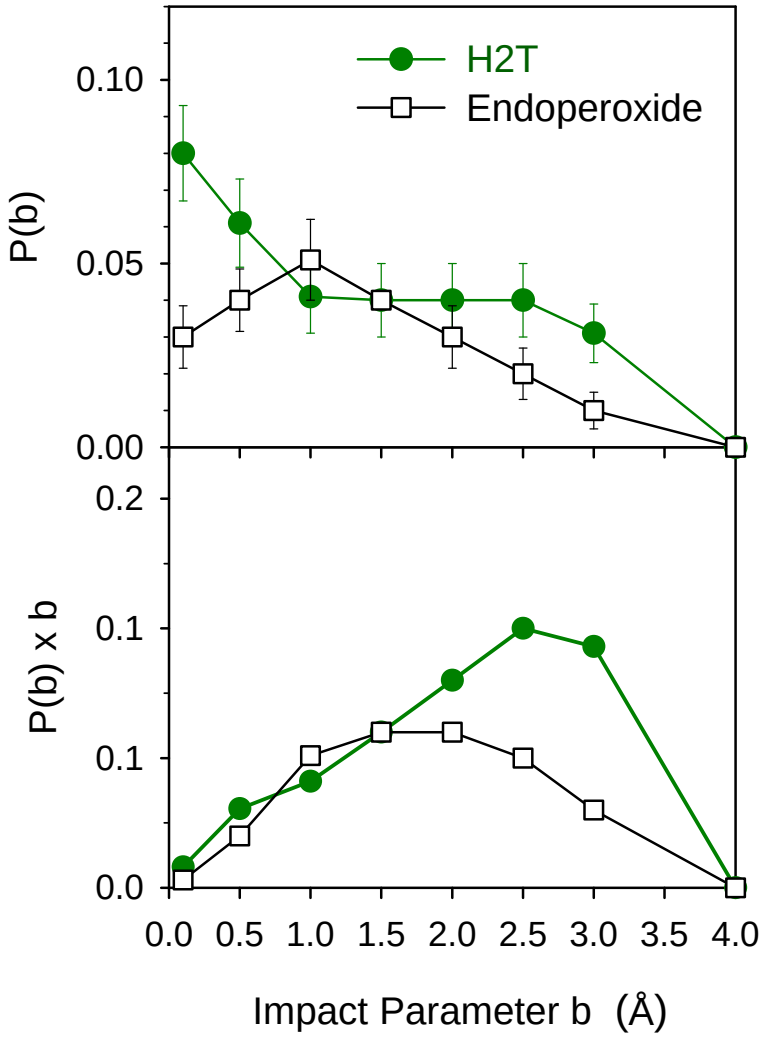


H2T following formation of hydroperoxide





Dependence on impact parameter & collision orientation



$$\sigma = 2\pi \int_0^{b_{max}} P(b) b db$$

$$\approx \pi \sum_{b_{min}=0}^{b_{max}} [P(b_i) \times b_i + P(b_{i+1}) \times b_{i+1}] \times (b_{i+1} - b_i)$$

Contribution of different mechanism *vs.* orientation dependence:

25% H2T via direct H2T

— only in collisions where orientation allows simultaneous rupture of two C-H bonds in backbone while forming two O-H bonds in H_2O_2.

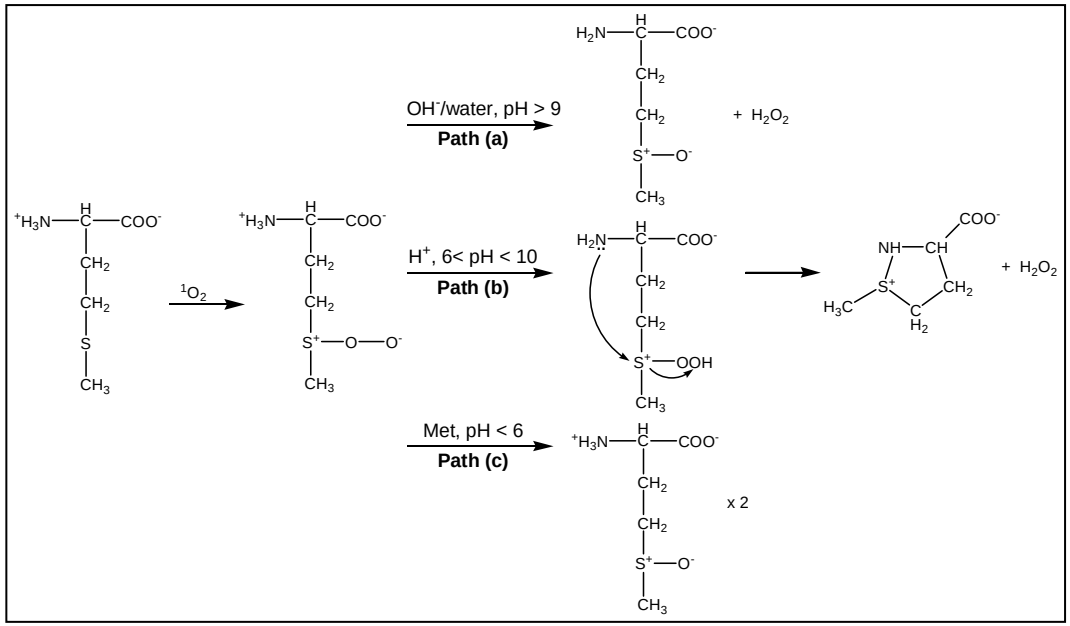
8% of collisions have "O_2 in parallel to two H atoms being abstracted", and 10% of those reactive.

75% H2T via decomposition of hydroperoxide

— 13% of collisions have "O_2 close to the phenolic group", and 30% eventually forms hydroperoxide.

II. Reaction of protonated methionine with $^1O_2$

Summary of photo-oxidation results



Biological significance of Met oxidation

ELSEVIER
Available online at www.sciencedirect.com
SCIENCE DIRECT
Biochimica et Biophysica Acta 1703 (2005) 135–140
BBA
http://www.elsevier.com/locate/bba

Review

Methionine oxidation and aging

Earl R. Stadtman[a,*], Holly Van Remmen[b], Arlan Richardson[b], Nancy B. Wehr[a], Rodney L. Levine[a]

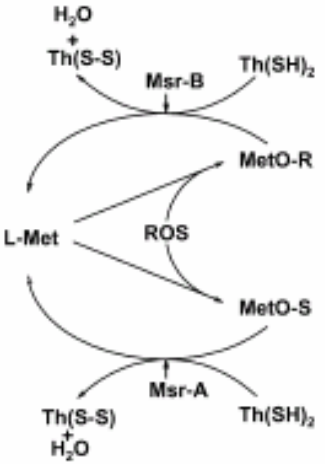
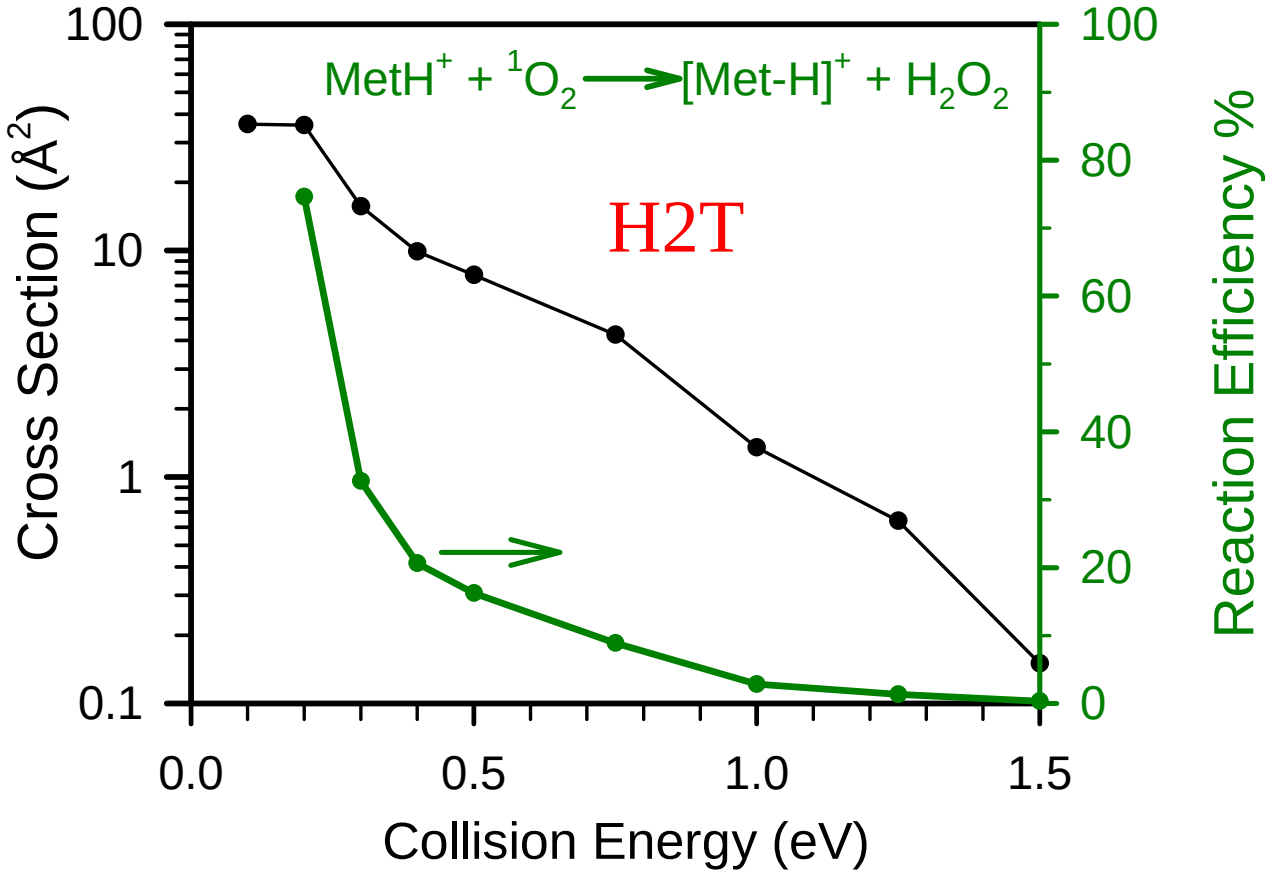
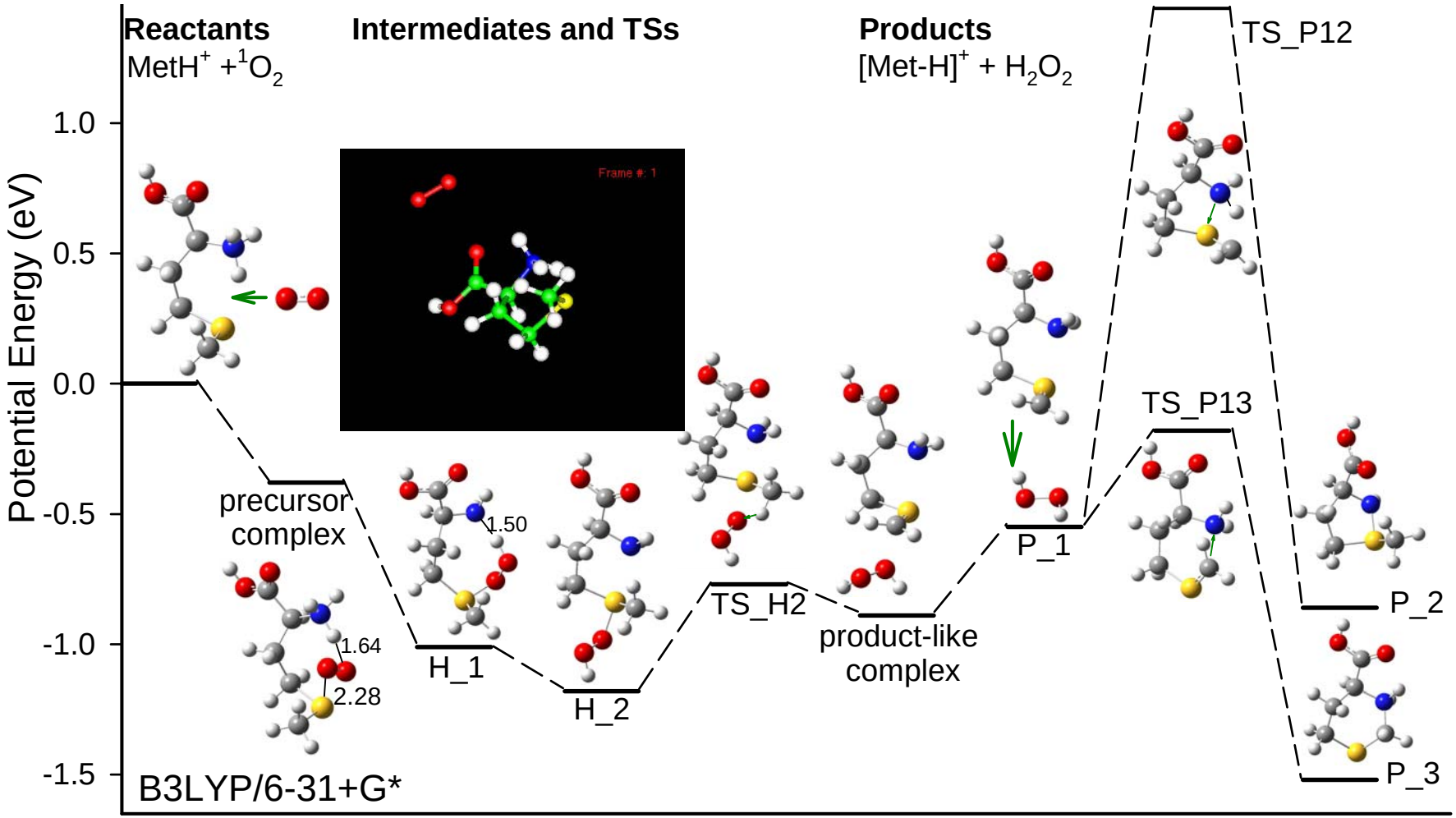


Fig. 1. Cyclic interconversion of Met and the R- and S-isomers of MetO. L-Met, L-isomer of Met; MetO-R and MetO-S, R- and S-isomers of MetO, respectively; MsrA and MsrB refer to the methionine sulfoxide reductases that are specific for reduction of the S- and R-isomers of MetO, respectively; $Th(SH)_2$ and Th(S-S) refer to the reduced and oxidized forms of thioredoxin, respectively.

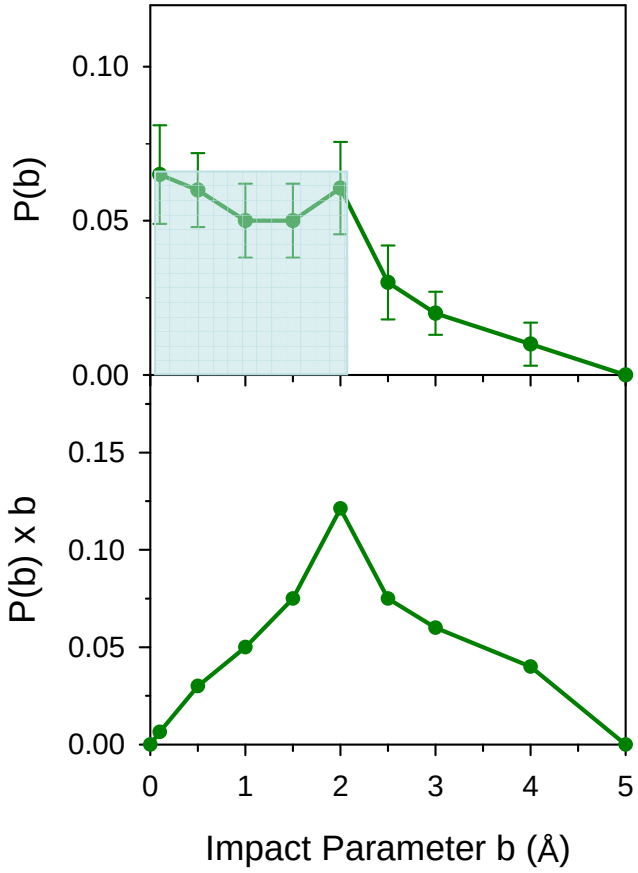
Reaction cross section and efficiency



Potential Energy Surface



Trajectory results for $MetH^+ + {}^1O_2$



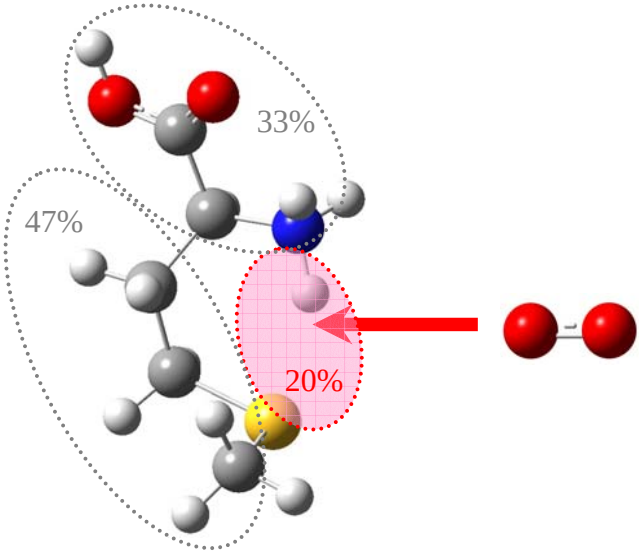
At E_{col} = 1.0 eV

σ_{traj} = 2.0 Å^2 vs. σ_{exp} =1.5 Å^2

Nature of dynamical bottleneck at E_{col} = 1.0 eV

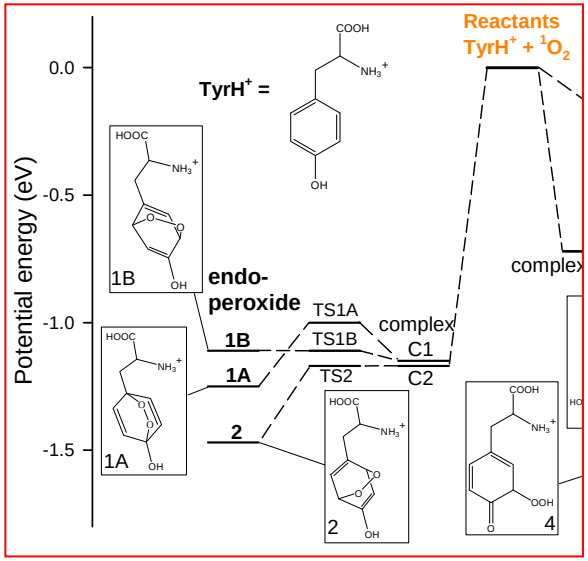
Strong orientation-dependence:

20% collisions have favorable orientation at the time of collision, and less than half eventually lead to reaction.

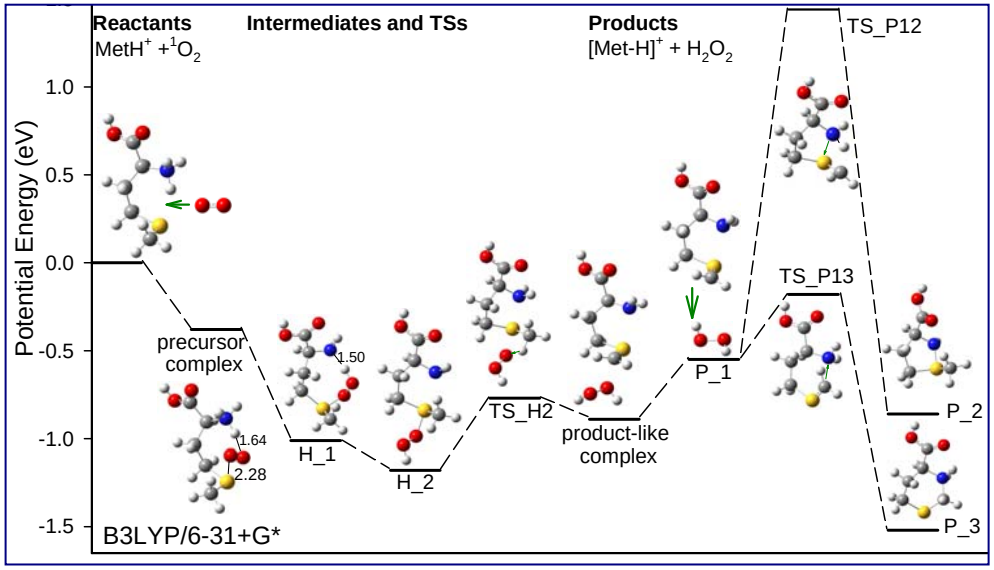


$TyrH^+ + {}^1O_2$ vs. $MetH^+ + {}^1O_2$

- Reaction efficiency of $TyrH^+$ is significantly lower than that of $MetH^+$, presumably due to the formation of endoperoxides which eventually leads to physical quenching of $^1O_2$.

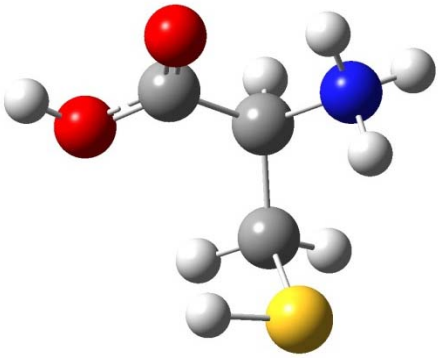


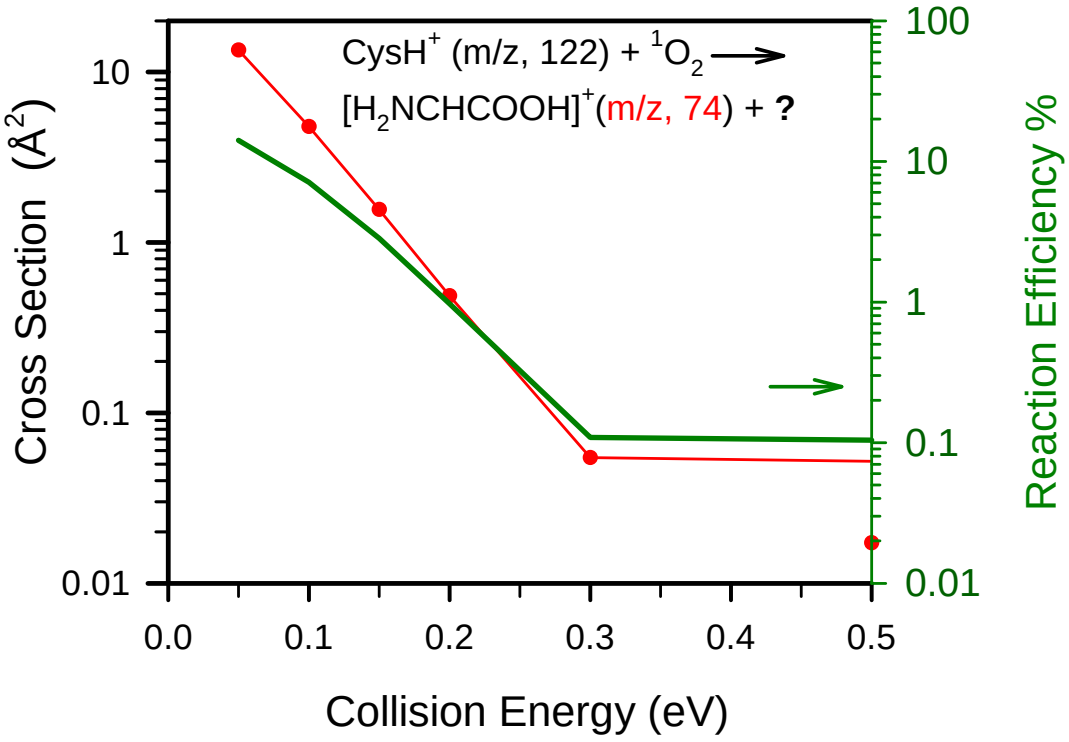
vs.



- Biological implication: locally produced $^1O_2$ with a short lifetime converts to H_2O_2 that has a much longer lifetime and can diffuse to distant targets in biological systems.

III. Reaction of protonated cysteine with $^1O_2$



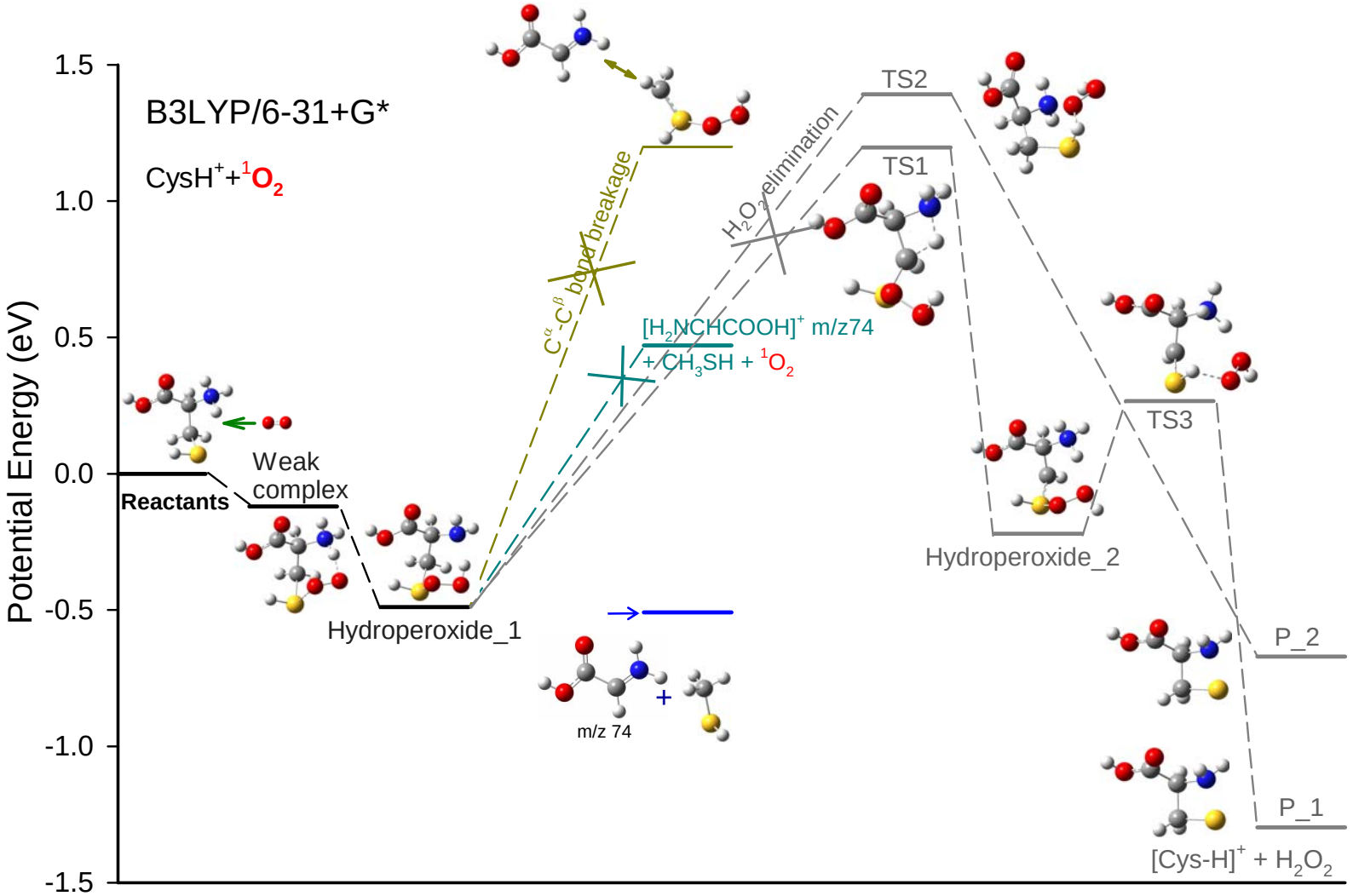


NO H2 elimination (m/z 120) was observed for

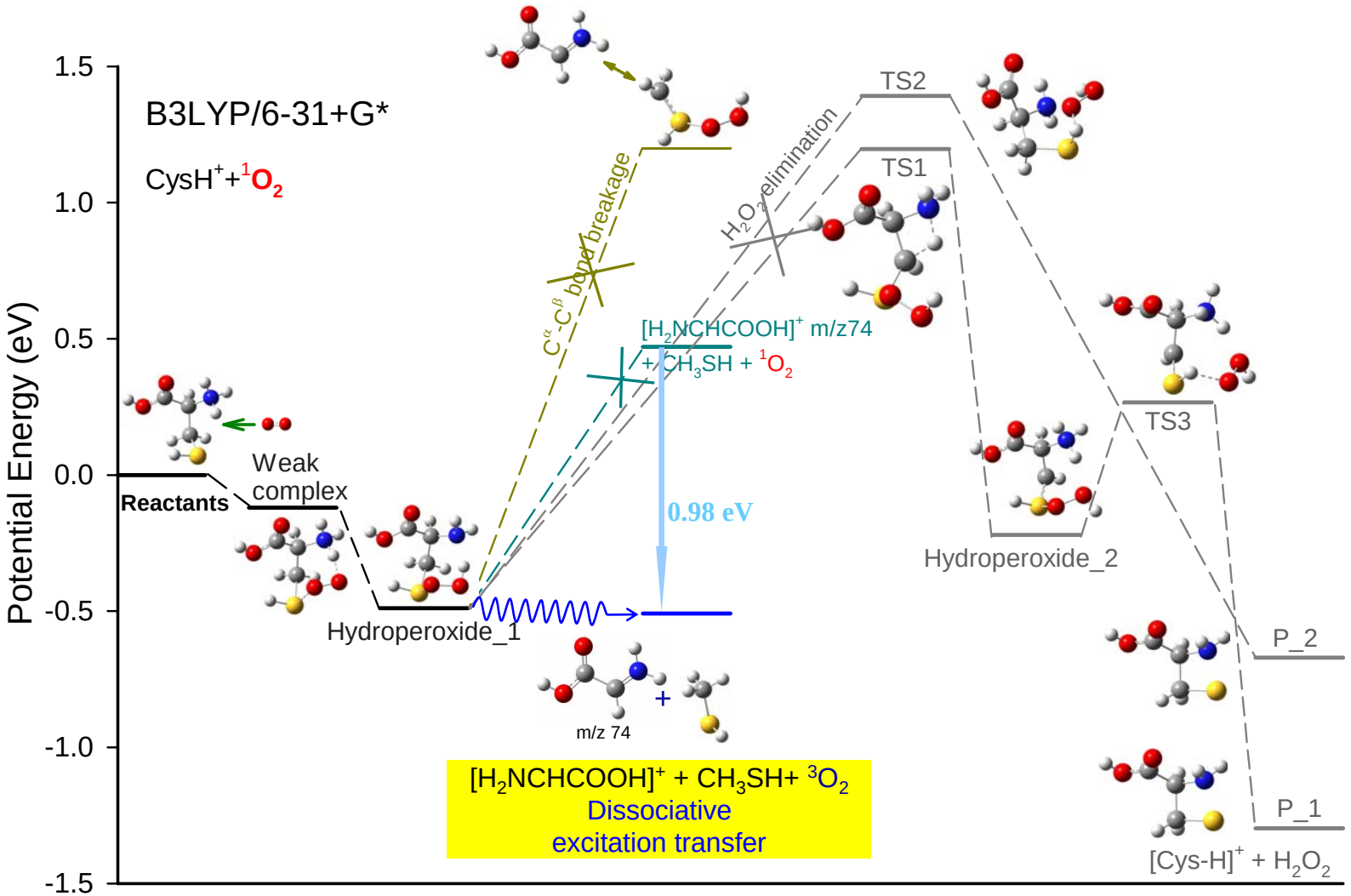
$CysH^+$ (m/z 122) + $^1O_2$

- Exothermic
- No activation barriers above the reactants

Dissociative excitation transfer in $CysH^+ + {}^1O_2$



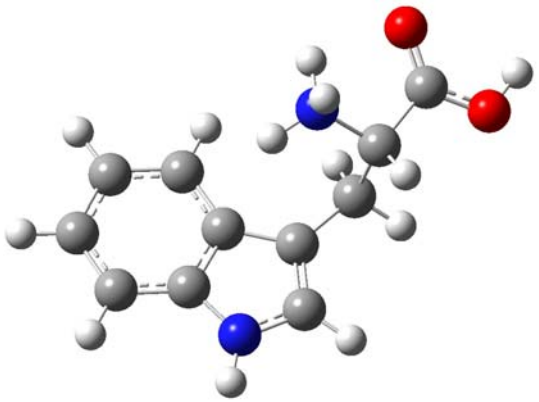
Dissociative excitation transfer in $CysH^+ + {}^1O_2$



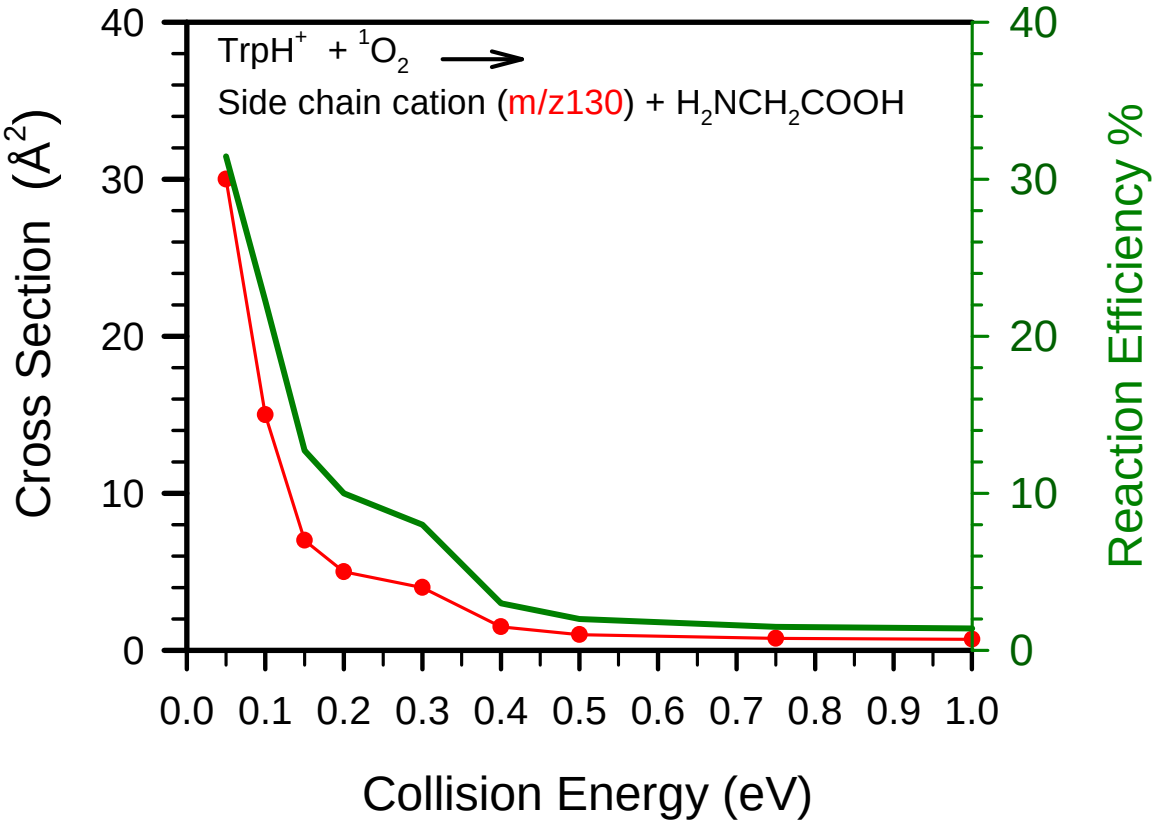
Previous report on dissociative excitation transfer: $OH^-(H_2O) + {}^1O_2 \rightarrow OH^- + H_2O + O_2(X^3\Sigma_g^-)$

A. Viggiano, et al. JCP, 2009, **131**, 094303

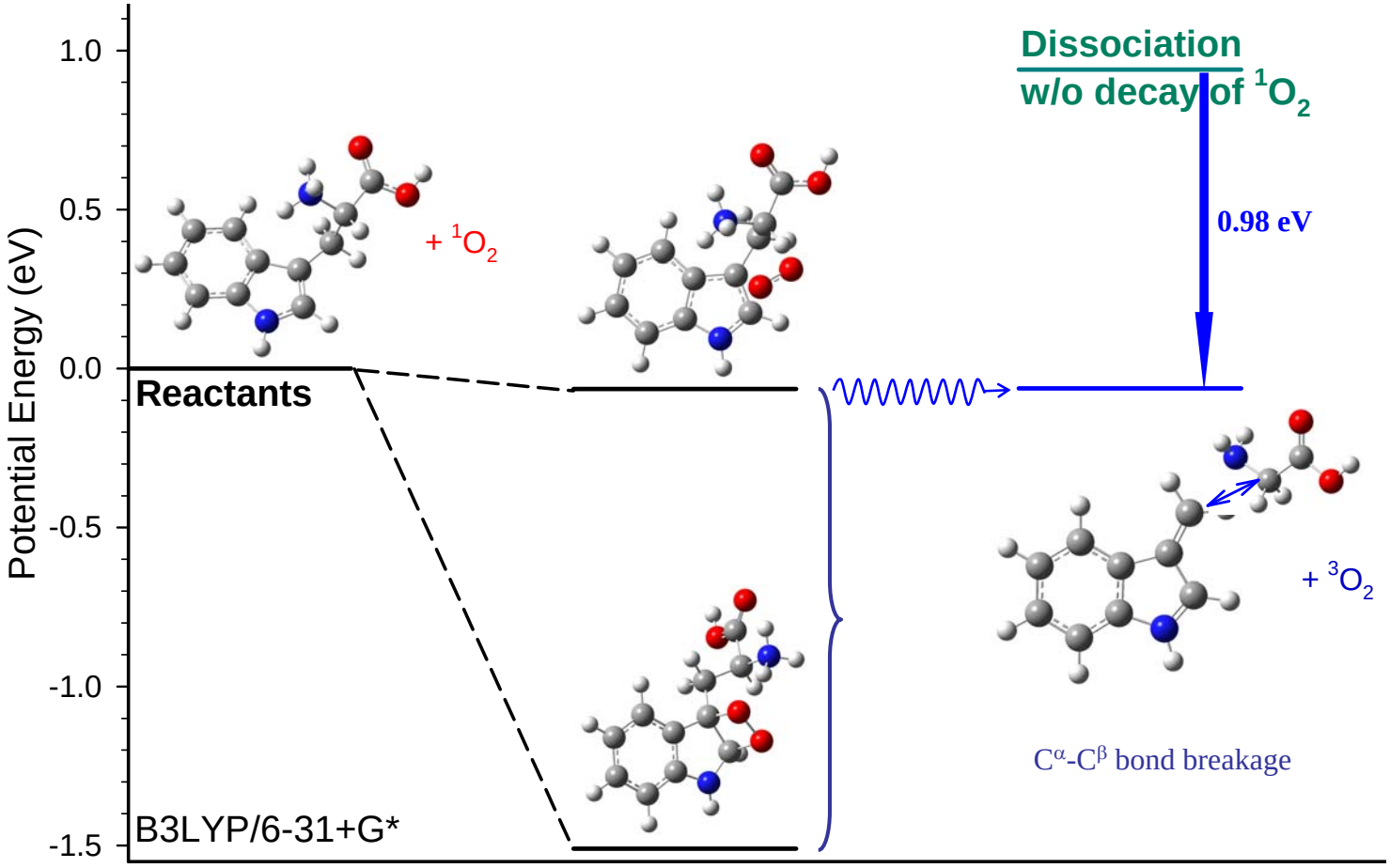
Another example of dissociative excitation transfer: $TrpH^+ + {}^1O_2$



$TrpH^+$

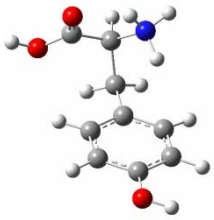
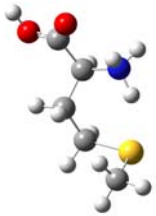
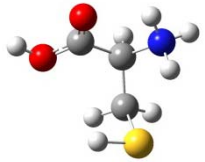
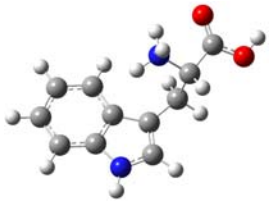
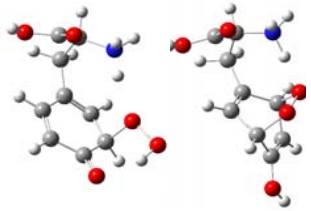
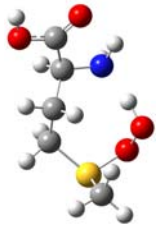
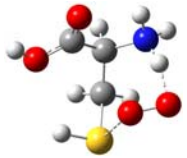
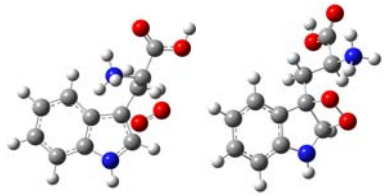
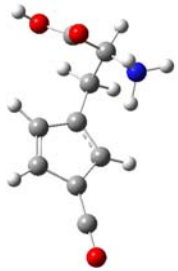
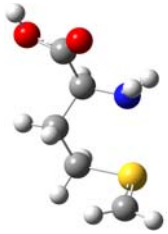
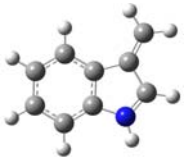
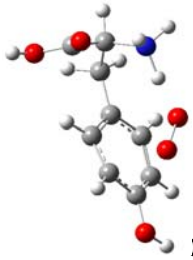


Dissociative excitation transfer in $TrpH^+ + {}^1O_2$



$$\Delta H(c^{\alpha}\text{-}c^{\beta}) \approx E^*({}^1O_2)$$

Conclusions

Protonated amino acids	 $TyrH^+$	 $MetH^+$	 $CysH^+$	 $TrpH^+$
Most probable Intermediate complexes	 (L) Hydroperoxide (R) endoperoxide	 Hydroperoxide	 Hydroperoxide	 endoperoxide
Reaction mechanisms, product ions and reaction efficiencies	 H_2O_2 eli. from hydro-peroxide < 3%	 H_2O_2 eli. from ydroperoxide > 84%	 Dissociative excitation transfer < 15% (spin-forbidden process)	 Dissociative excitation transfer < 25% (spin-forbidden process
Other paths	 Endo-peroxides decay to reactants, quench $^1O_2$	No physical quenching at low E_{col}	No H_2O_2 elimination or other oxidation reactions observed, due to high TSs.	No H_2O_2 elimination or other oxidation reactions observed.

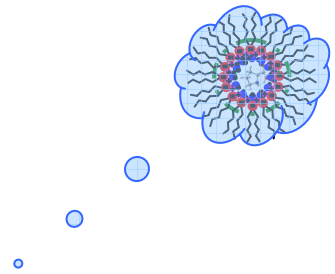
Creating a biologically relevant gas-phase environment for bio-molecules

Gas-phase reverse micelles

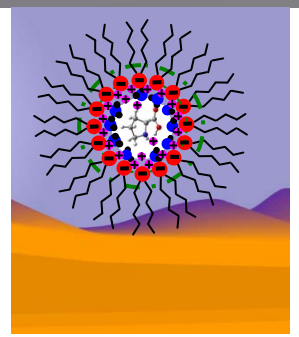
In Nature

(marine aerosols)

1. Formation of aerosol particles at the sea surface



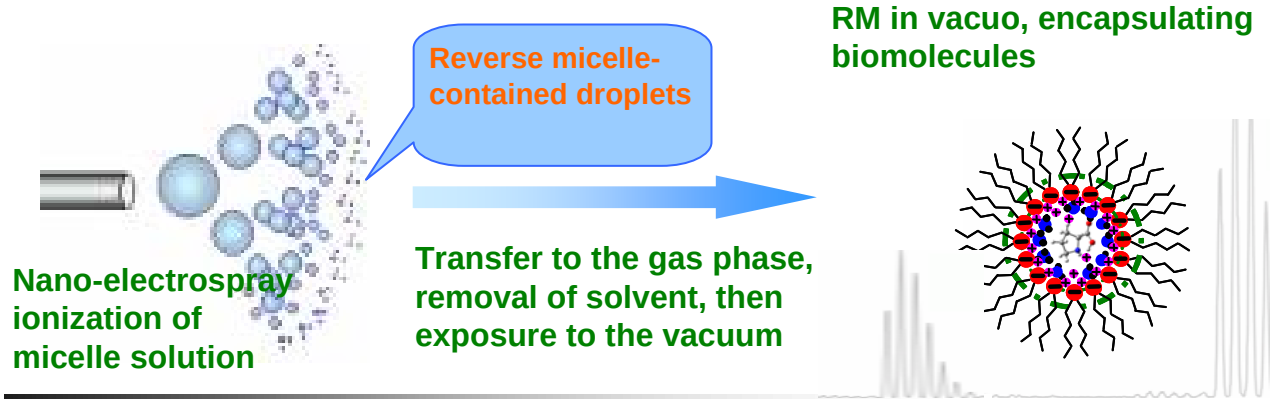
2. Transfer of micelle-contained droplets to the gas phase, evaporation of water



3. RM in the gas-phase, maintaining encapsulated minerals and small organics

C. M. Dobson, G. B. Ellison, A. F. Tuck, V. Vaida. *PNAS*, **97**, 11864 (2000)

In Laboratory

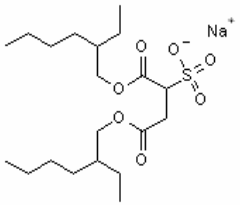


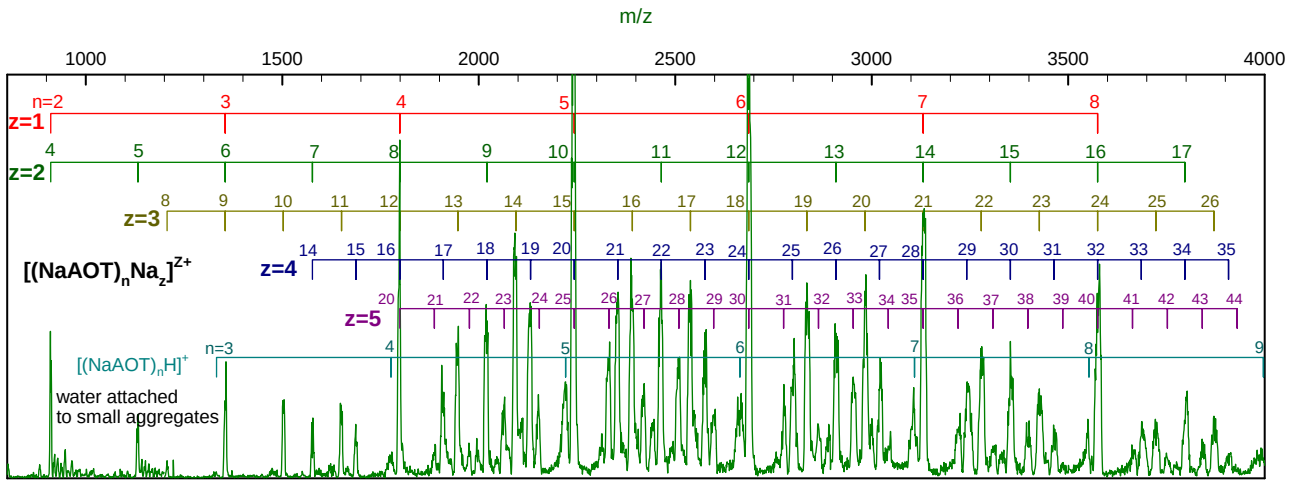
Formation of gas-phase AOT reverse micelles, and encapsulation of biomolecules

Multiply charged, gas-phase AOT reverse micelles, obtained by ESI of AOT solution.

NaAOT:

bis(2-ethylhexyl) sulfosuccinate





Y. Fang, A. Bennett and J. Liu, ***IJMS***, 2010, **293**,12;

PCCP, 2011, **13**, 1466

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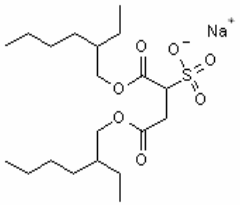
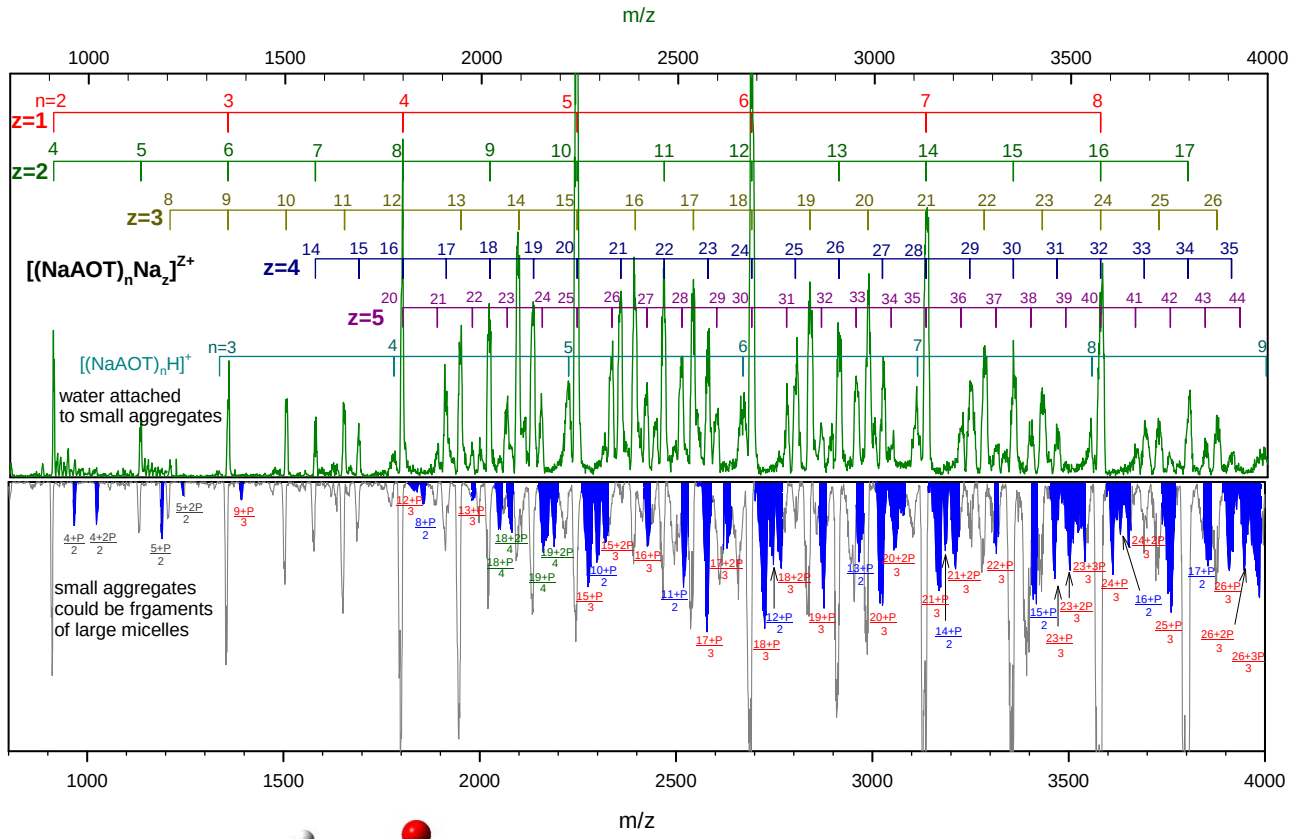
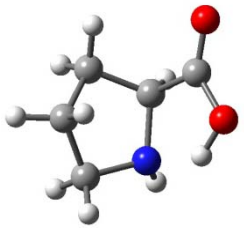


Encapsulation of proline into the micellar internal core, indicated in shaded peaks as

$$\frac{n + mP}{Z} = [(NaAOT)_n\, Na_z\, (Proline)_m]^{z+}$$



Proline:



Y. Fang, A. Bennett and J. Liu, ***IJMS***, 2010, **293**,12;

PCCP, 2011, **13**, 1466

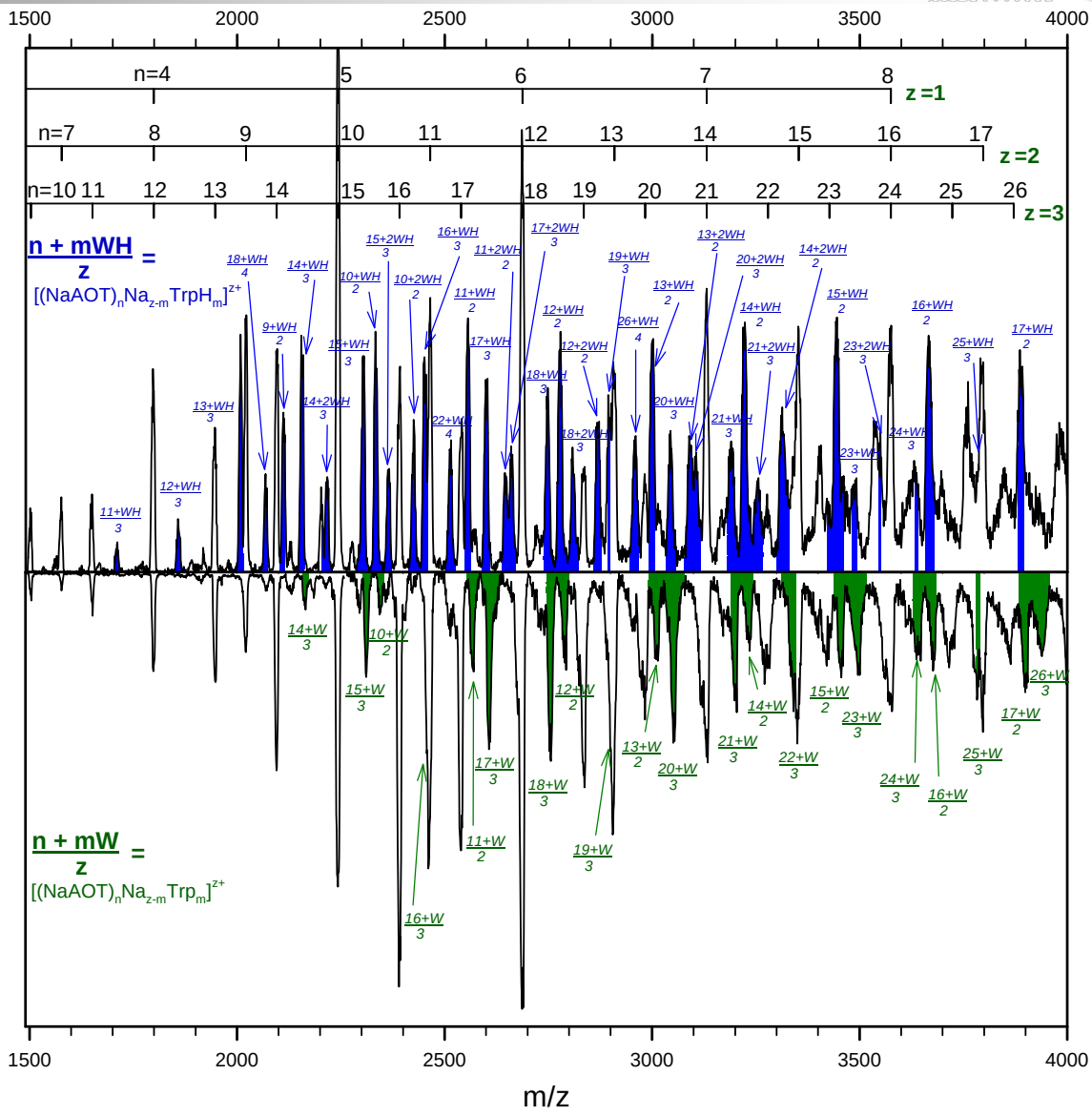
Driving force for solubilization in gas-Phase RM?

Top:

RM occupied with protonated $TrpH^+$ (hydrophilic)

Bottom:

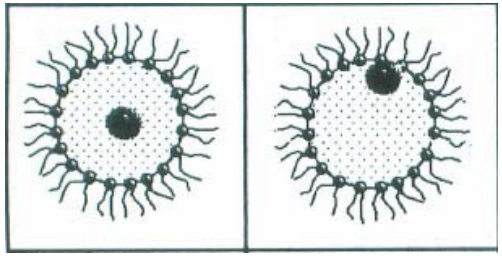
RM occupied with neutral Trp (hydrophilic)



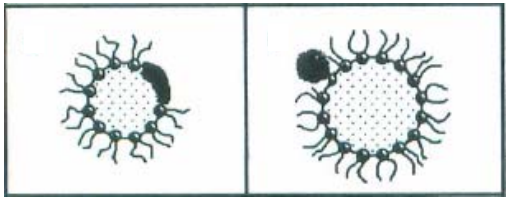
Encapsulation in solution-phase reverse micelles

In Solution-Phase RM

Hydrophilic biomolecule (e.g. Gly, $TrpH^+$) located in the internal core
— electrostatic interaction

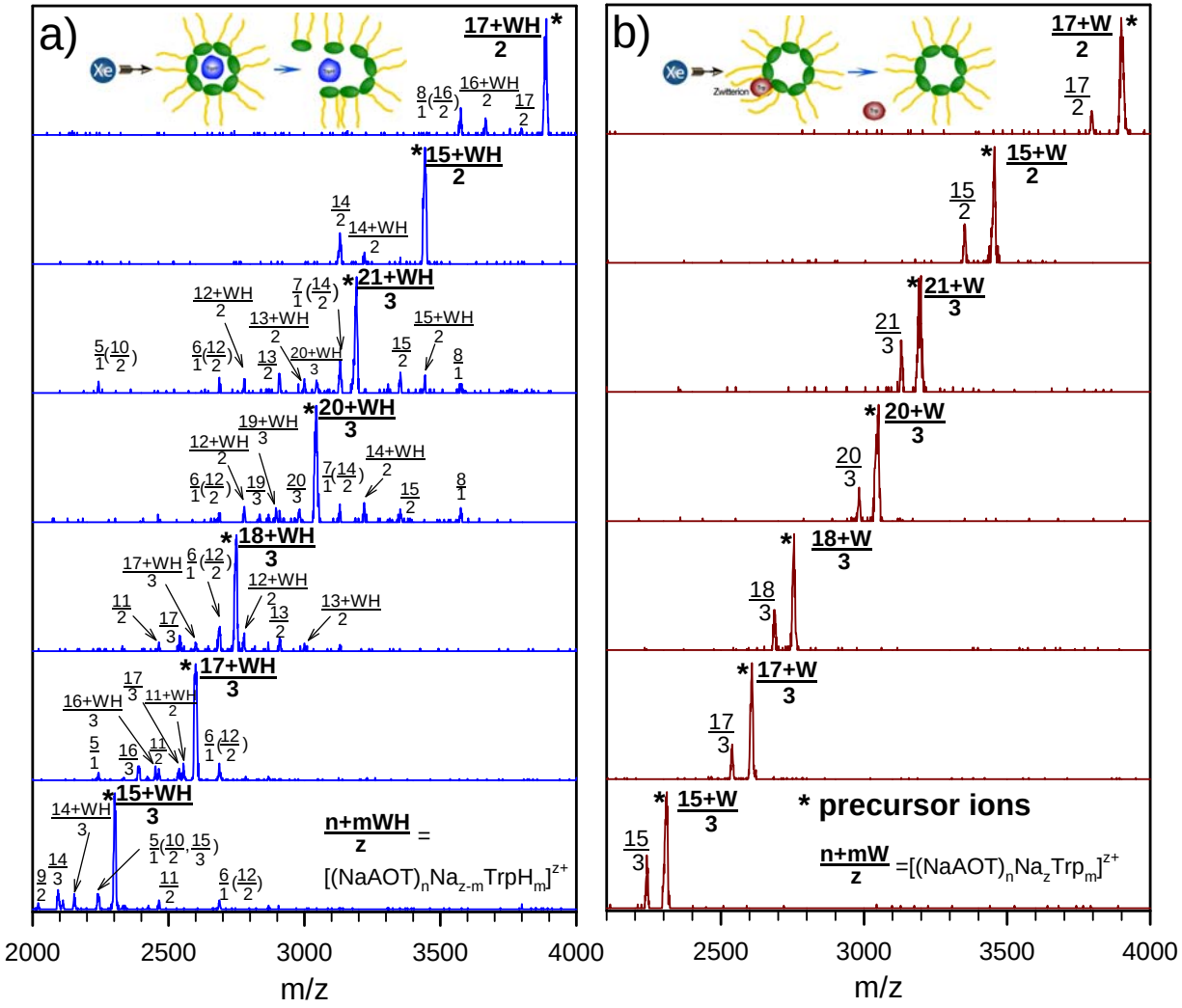


Hydrophobic biomolecule (e.g. neutral Trp) located at the interface
— hydrophobic interaction



P. L. Luisi, M. Giomini, M. P. Pileni, B. H. Robinson, *Biochimica et Biophysica Acta*, **947,** 209(1988)

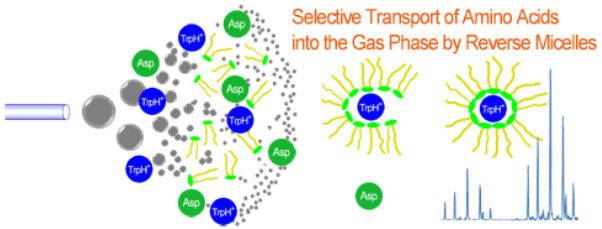
Structures of gas-phase reverse micelles

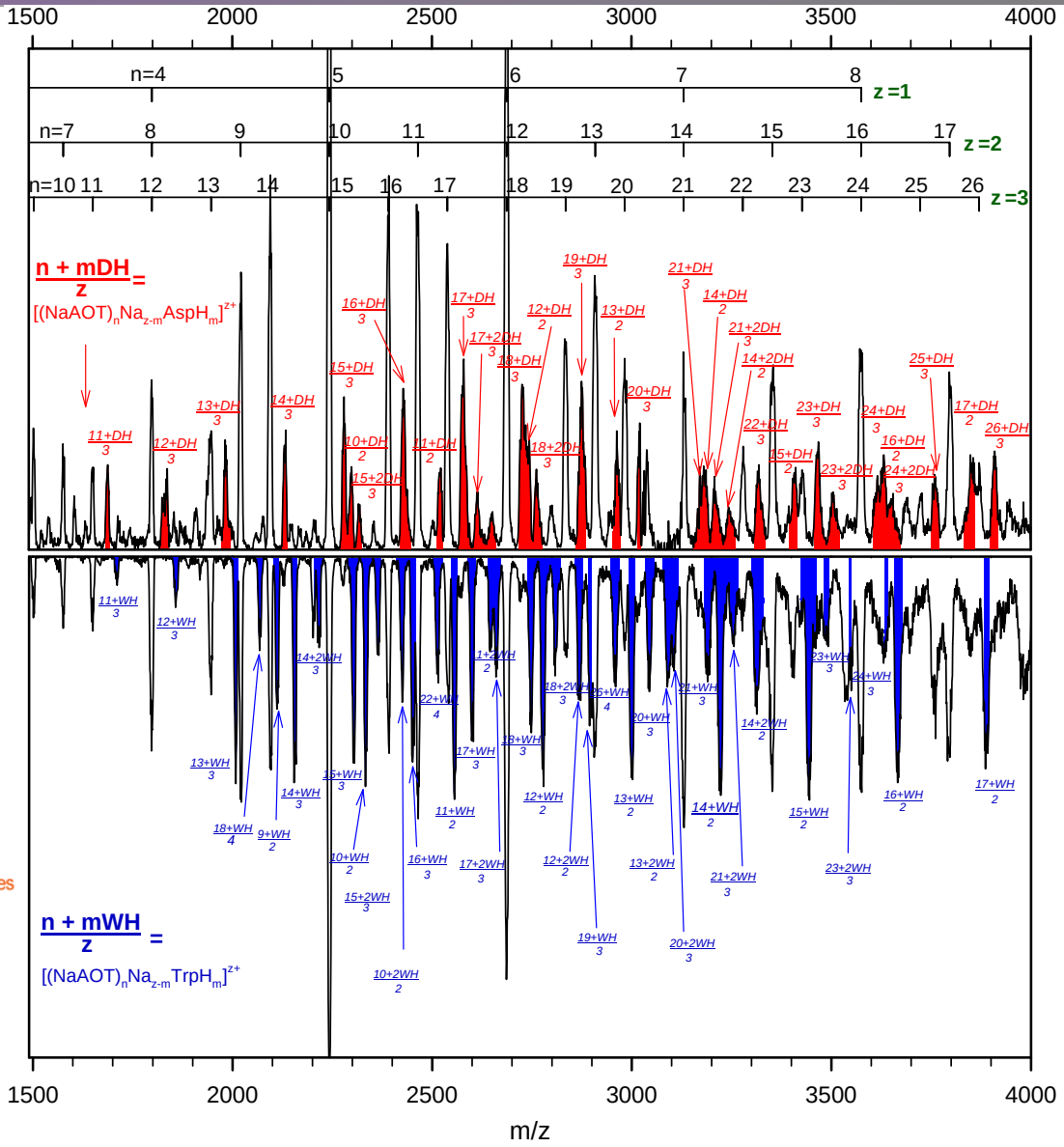


Selectivity between different amino acids

ESI of AOT/Asp

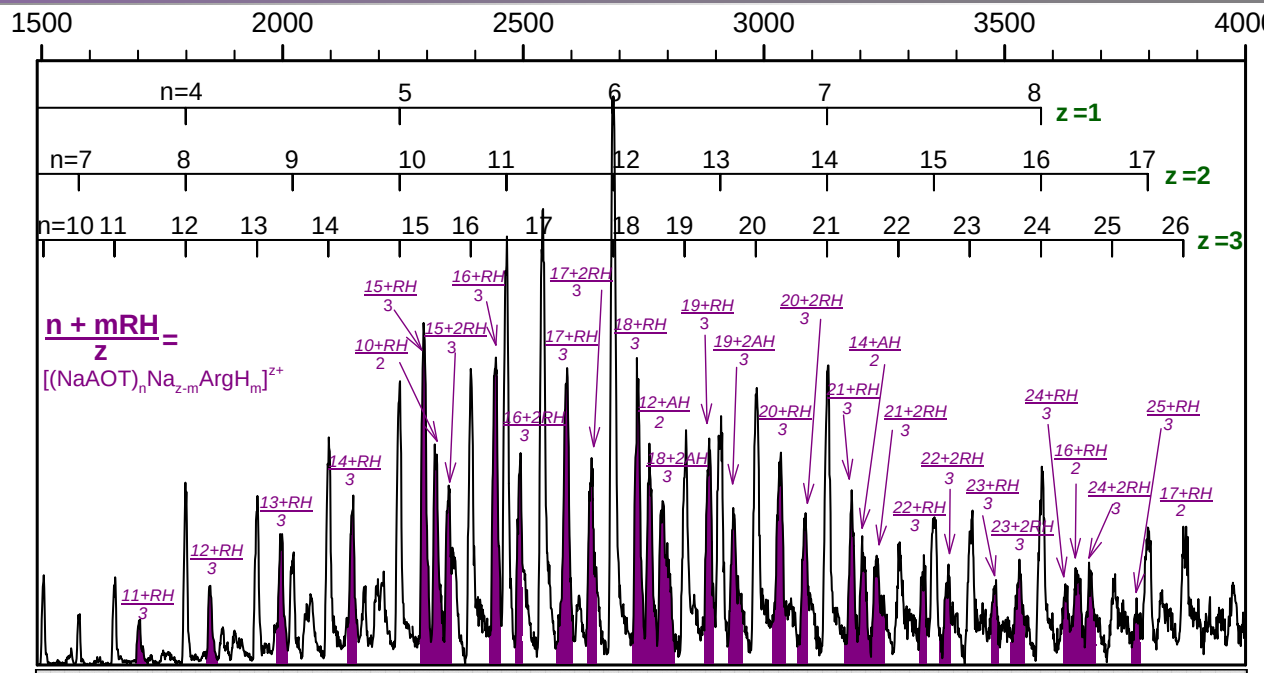
ESI of AOT/Asp+Trp





Selectivity between different amino acids

ESI of AOT/Arg



ESI of AOT/Arg+Trp

No changes when mixed with Trp !

Only Arg detected,

no encapsulation of Trp

Fundamentals of selectivity

	Aspartic acid (D)	Tryptophan (W)	Proline (P)	Arginine (R)
pK_a of α-COOH	1.9	2.8	2.0	2.2
pK_a of α-NH_3^+	9.6	9.4	10.6	9.0
pK_a of acidic R	3.7	-	-	12.5
pI	2.8	5.9	6.3	10.8

***pH* of ESI solution of AOT/(Trp+Asp) in methanol/water = 5.1**

***pH* of ESI solution of AOT/(Trp+Arg) in methanol/water = 7.4**

Transport selectivity between different AAs?

• Selectivity reflects a competition between electrostatic & hydrophobic forces, which can be tuned up by changing the pH of ESI solution.

• Amino acid with a higher ***pI*** exists in protonated form and has a larger affinity with AOT^-.

(i.e., Arg > Trp > Asp)

Conclusions

- Gas-phase NaAOT reverse micelles can act as nanometer-sized vehicle for the selective transport of non-volatile biomolecules into the gas phase.

- Site locations and driving forces for solubilization in gas-phase reverse micelles (.. more in Yigang Fang's poster).

Future Directions

- $^1O_2$-mediated oxidation of bio-molecule encapsulated in gas-phase gas phase
- Modeling of bio-molecule encapsulating gas-phase reverse micellar structure and reactivity

Acknowledgements

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