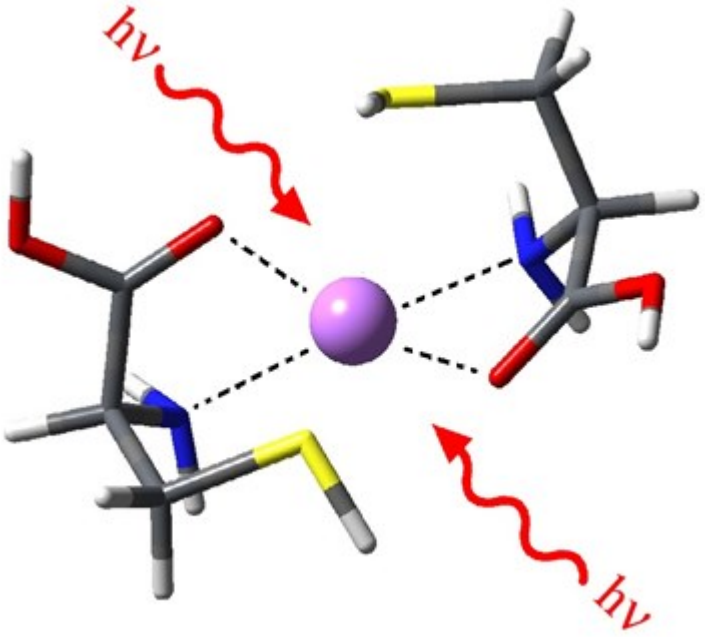
Structural Characterization of Alkali Metal Cationized Cysteine Complexes



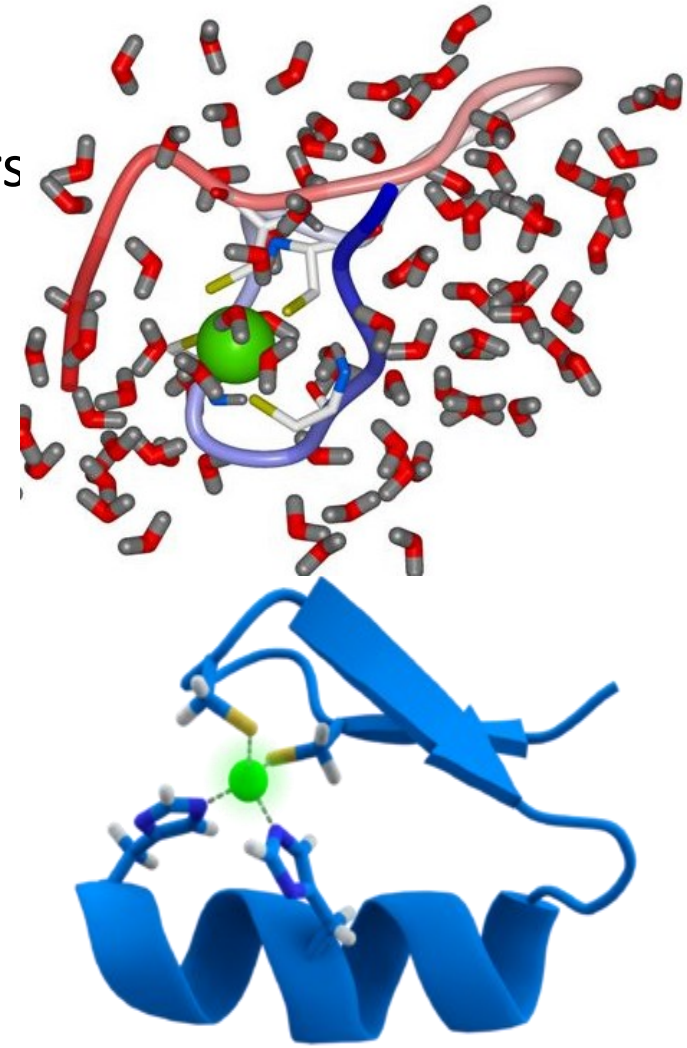
Christian Ieritano, Moaraj Hasan, Michael Burt, Richard Marta, Terry McMahon, W. Scott Hopkins

Biochemical Relevance

- Sulphide source in iron-sulphur clusters & nitrogenase

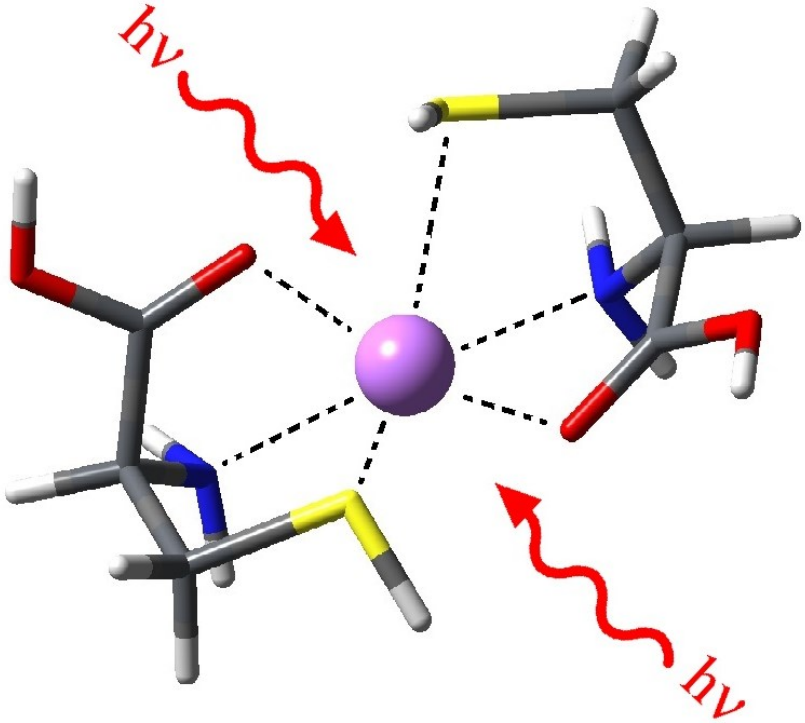
- **Residues in Enzymes**
  - Alcohol dehydrogenase
  - Zinc Fingers
  - Thiol affinity for heavy metals
    - Metallothionein

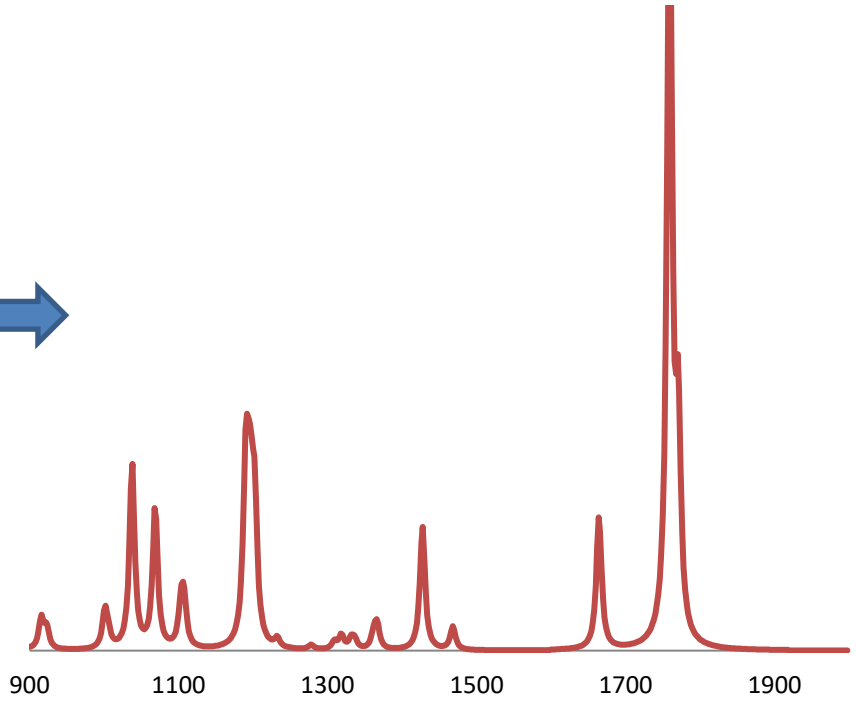
- **Main interest:**
  - Evolution of amino acid structure from solution to gas phase



Mcdowell, J. (2007). *Zinc Protein Binding Motifs*.

Methods
Experimental and Computational





Electrospray Ionization (ESI)

Alkali bound cysteine clusters produced in the gas phase:

1:1 H_2O:MeOH containing:

0.1 mM Cysteine and 0.1 mM **M^+Cl^-**

M^+ = Li, Na, K, Rb

Also Cu^{2+}, Fe^{2+}, Ni^{2+}, Ag^+, Au^{3+}

Soft Ionization technique

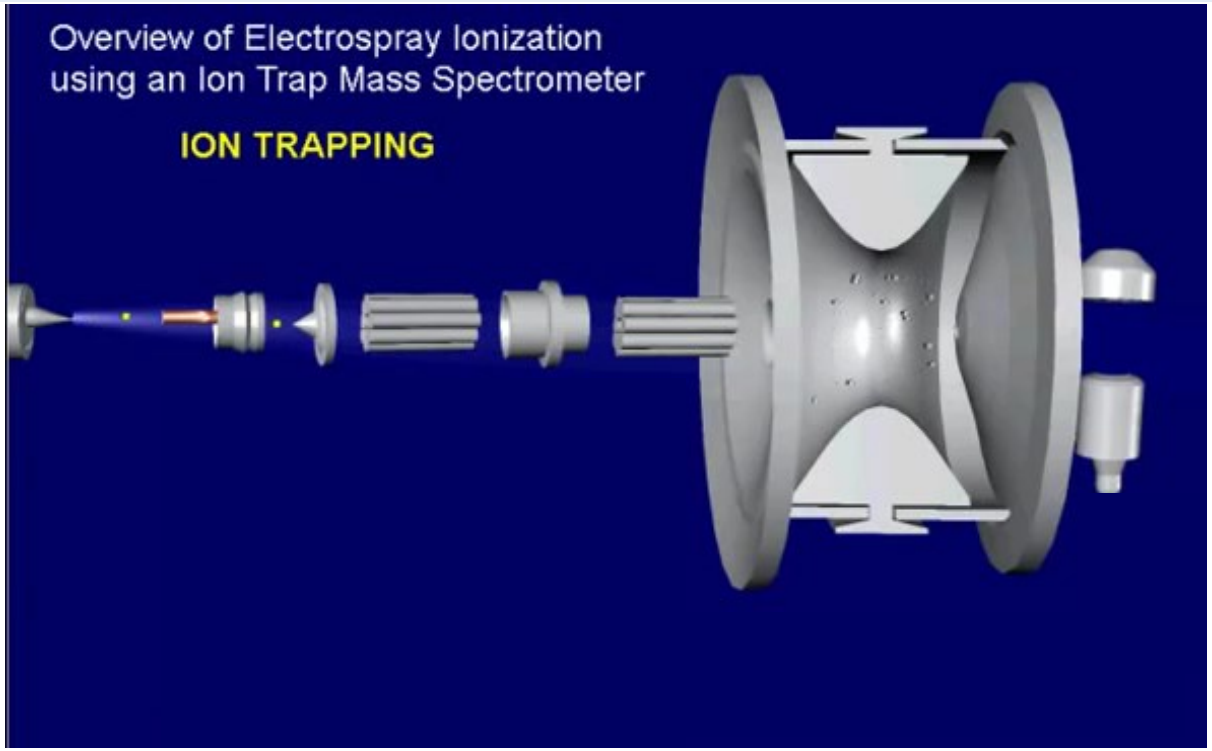
Solution phase structure often conserved

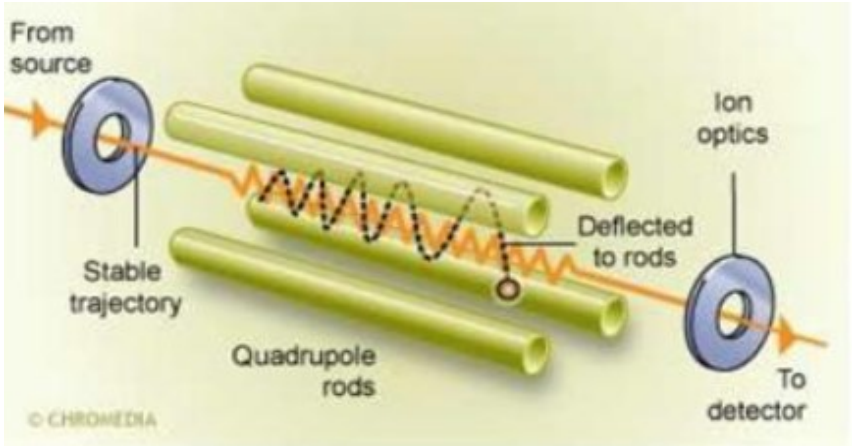
Net Result:

Isolation of ions of interest from solvent

Evaporation into gas phase

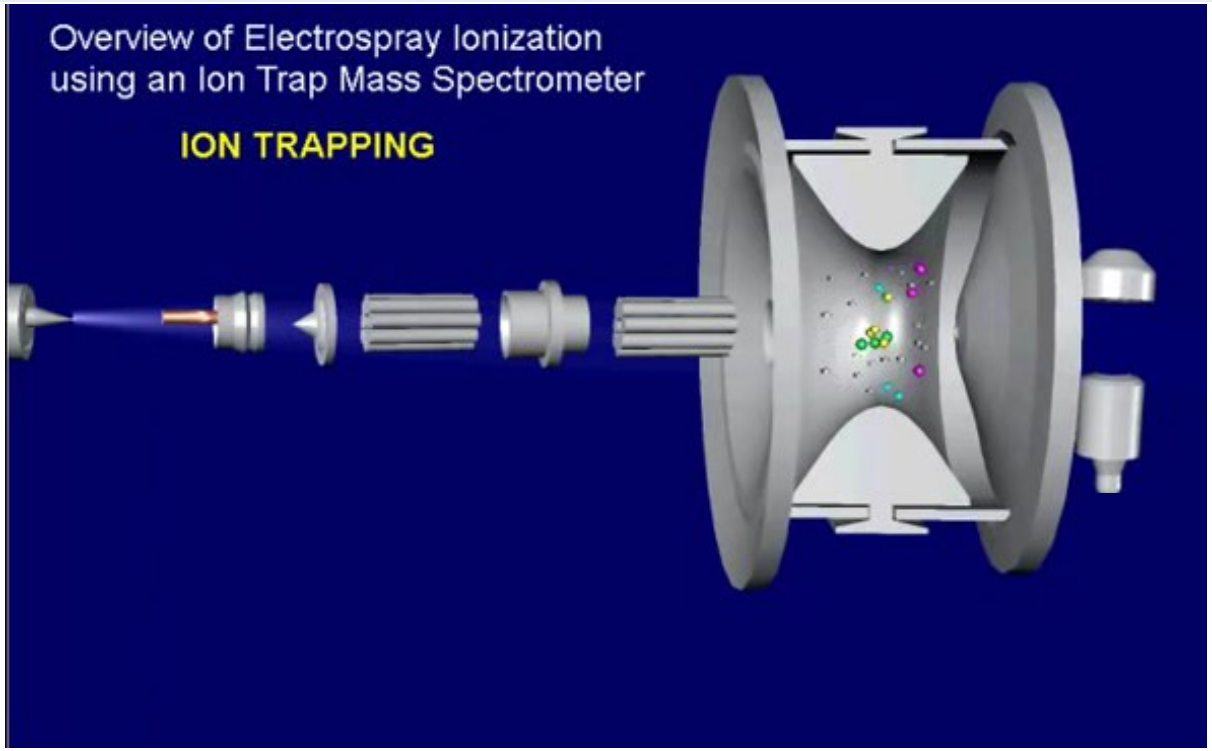
Octapole Mass Filter

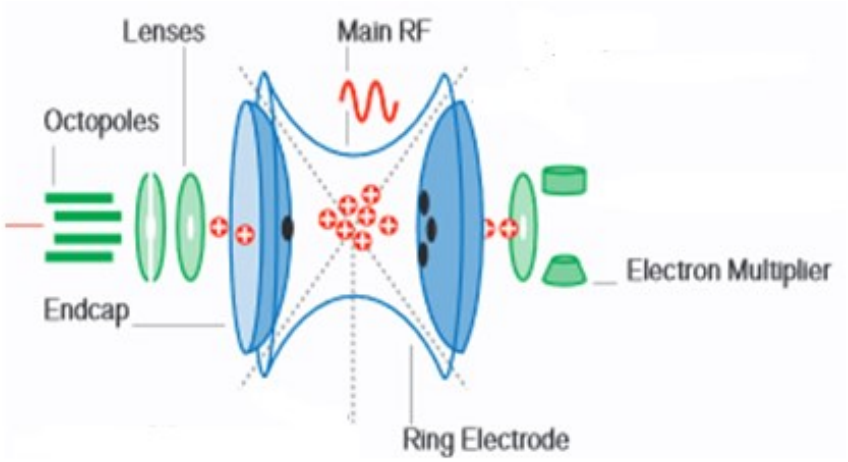




Miller, P., Denton, M. (1986). Octapole Mass Filtering. *Journal of Chemical Education.*
Chromatography Knowledge Base. (2010). Quadrupole Ion Trap.

Quadrupole Ion-trap





Miller, P., Denton, M. (1986). Paul Traps. *Journal of Chemical Education.*

Chromatography Knowledge Base. (2010). Quadrupole Ion Trap.

Infrared Multiphoton Dissociation (IRMPD)

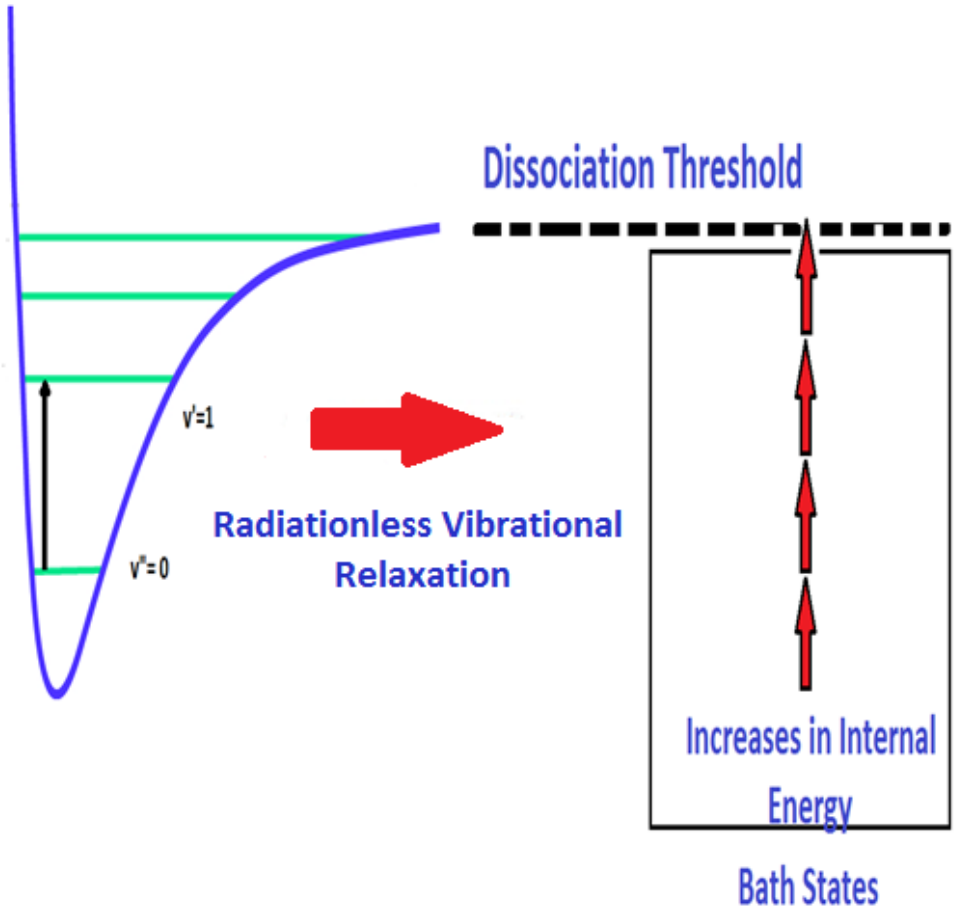
I. IR photon absorption for one normal mode & excitation

II. Energy redistributed via vibrational relaxations into ‘bath states’.

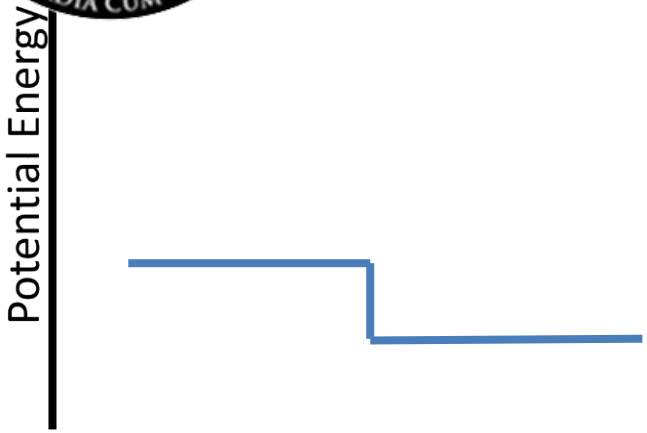
III. Multiple photons induce further excitations and relaxations into bath states.

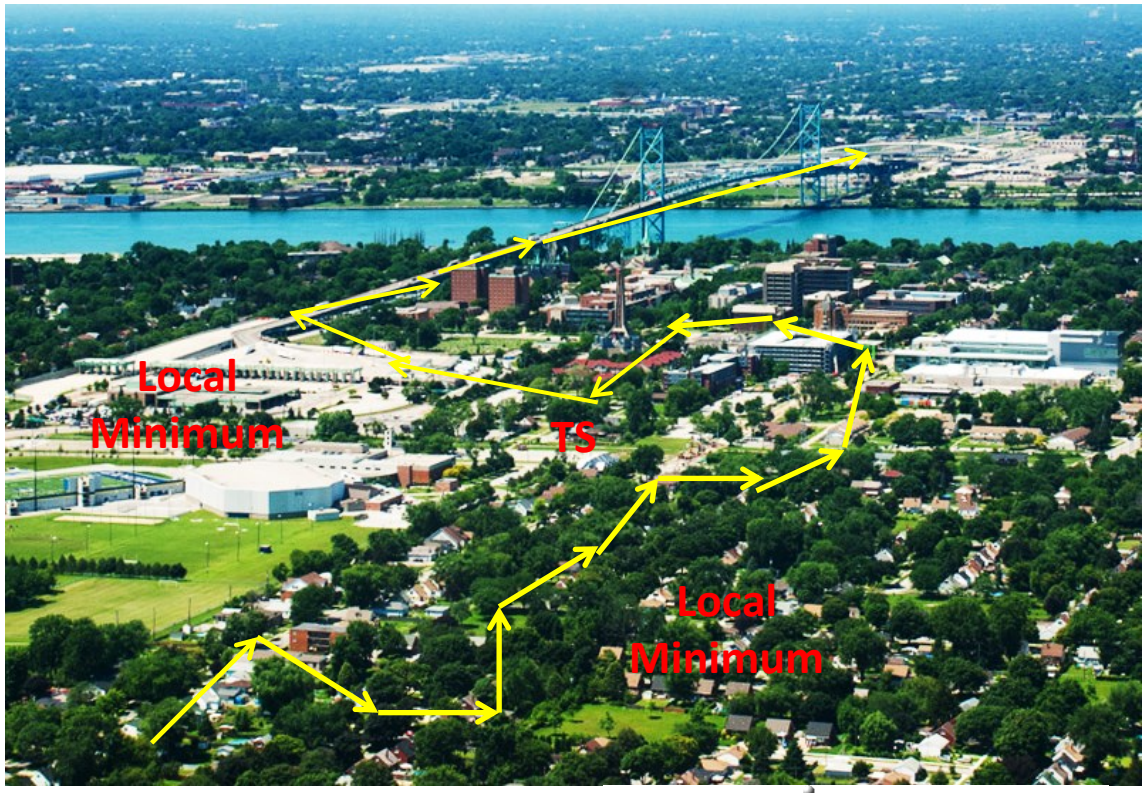
IV. Internal energy is increased; dissociation threshold is passed

V. Spectra generated by monitoring fragmentation as function of cm^{-1}

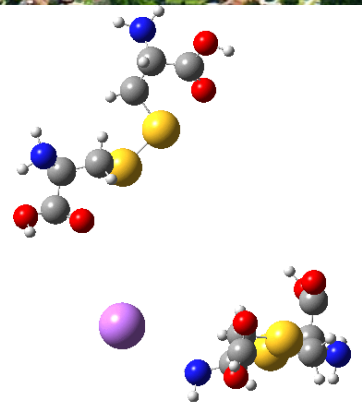


Basin Hopping Routine

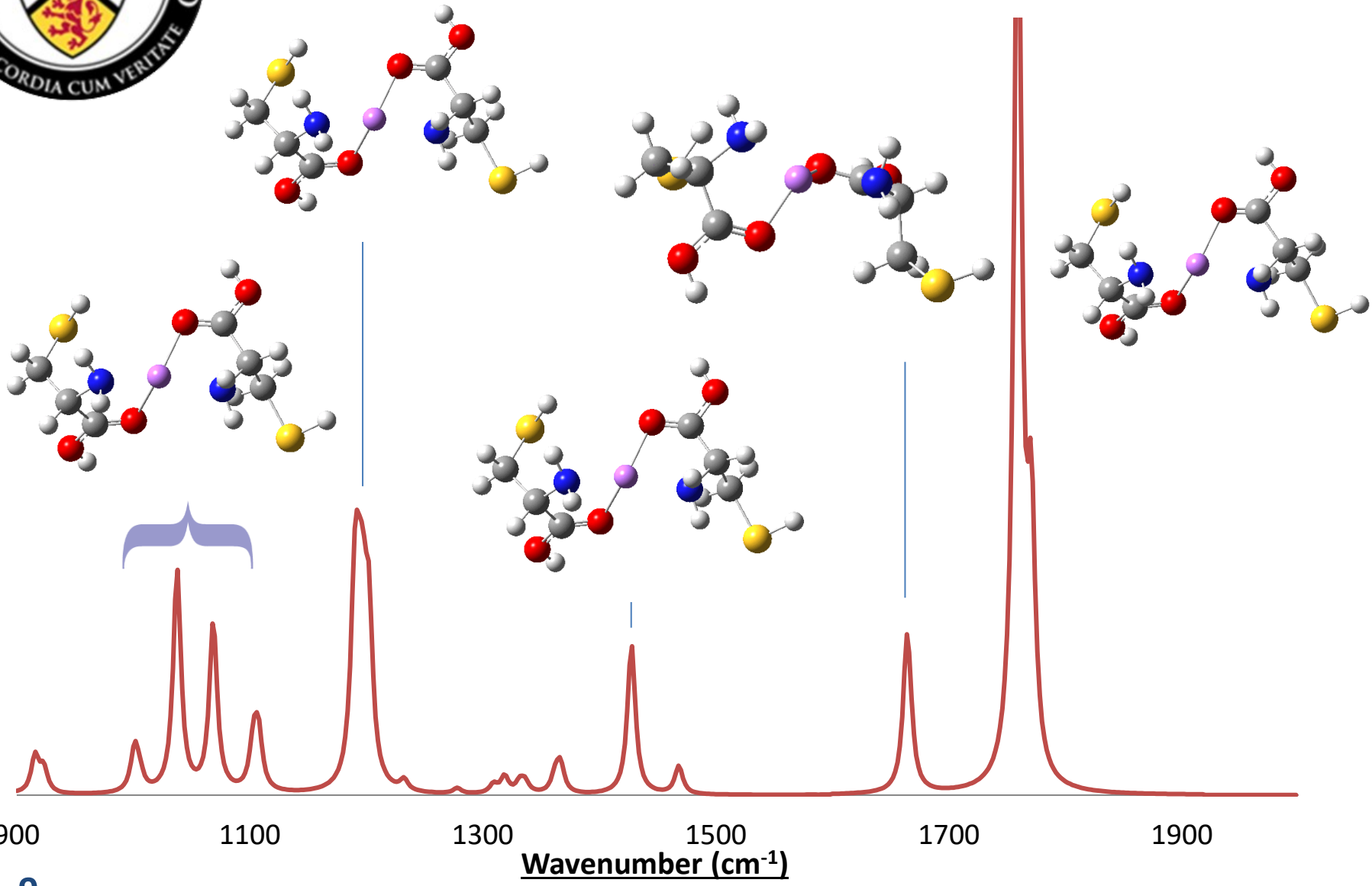




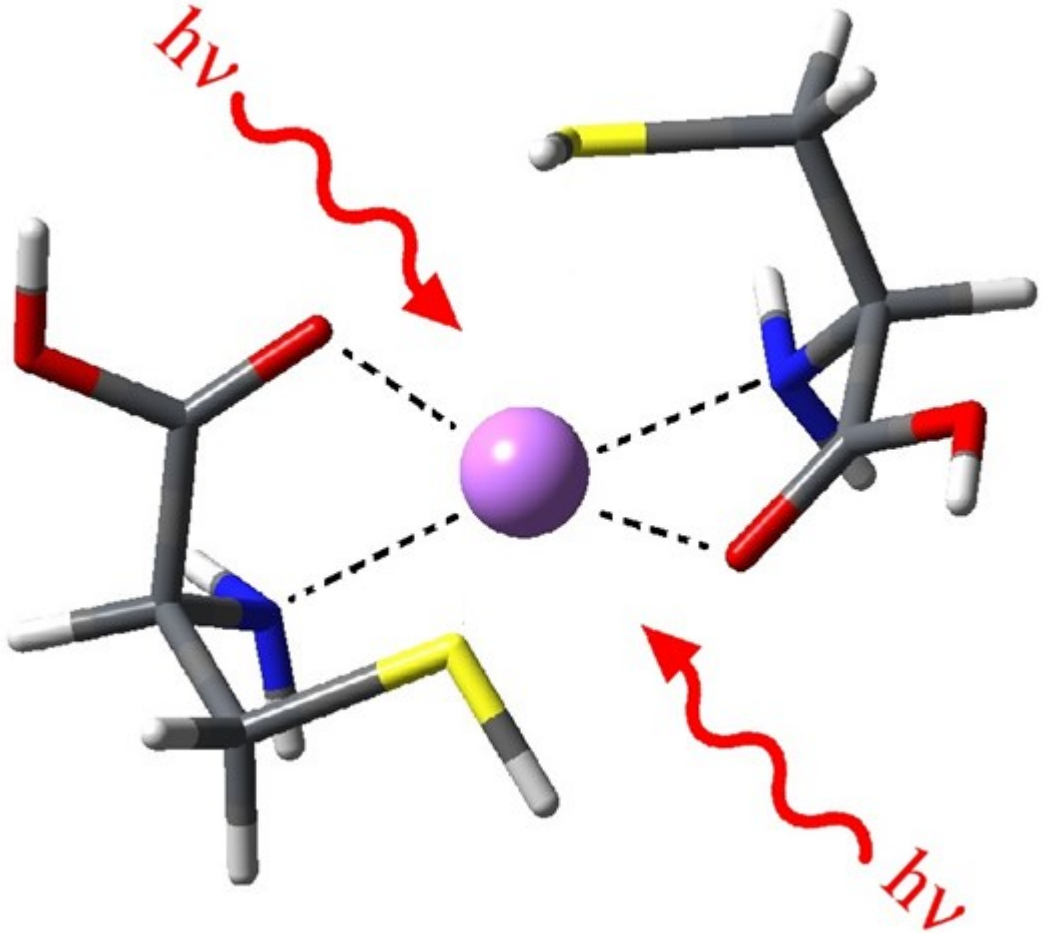
- Exploration of molecular potential energy surface
- Geometry optimizations identify stationary, stable conformations through random contortions of geometry (Monte Carlo)
- Unique conformers carried into DFT optimizations
  - B3LYP functional, 6-311++g(d,p)



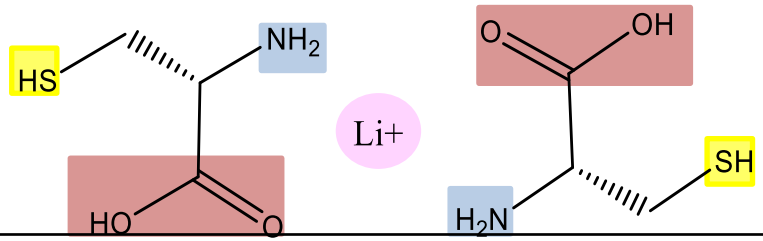
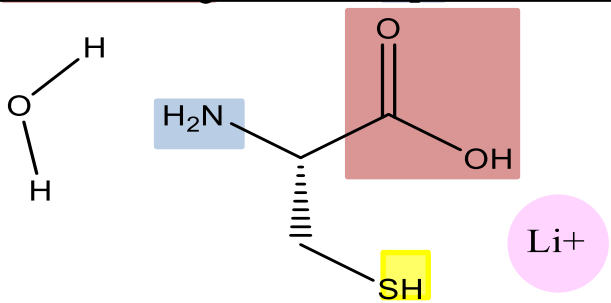
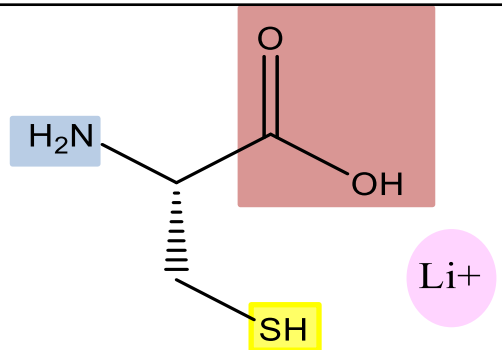
Pertinent Vibrational Motions



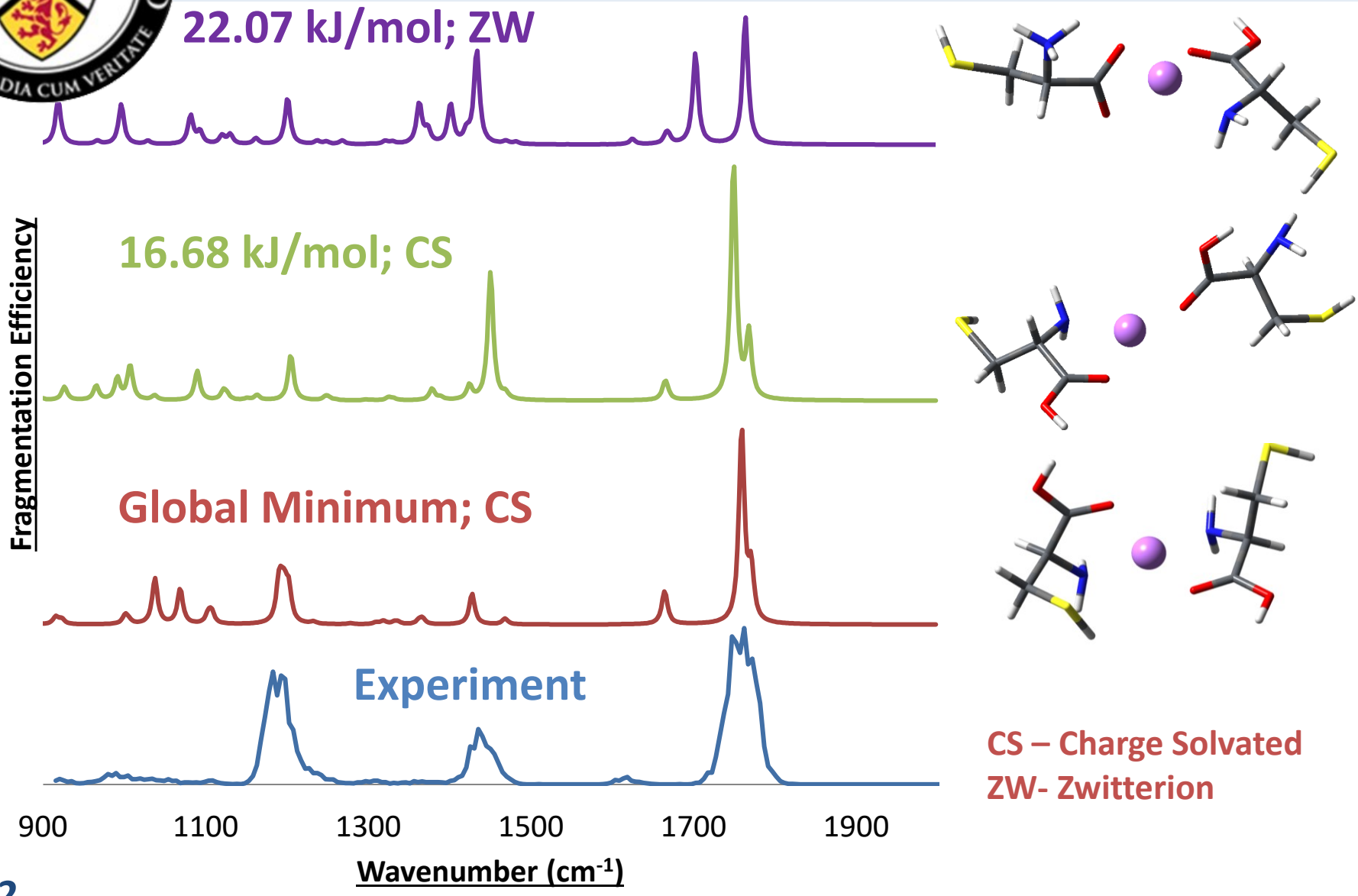
Lithium Cysteine Clusters



Fragmentation Analysis

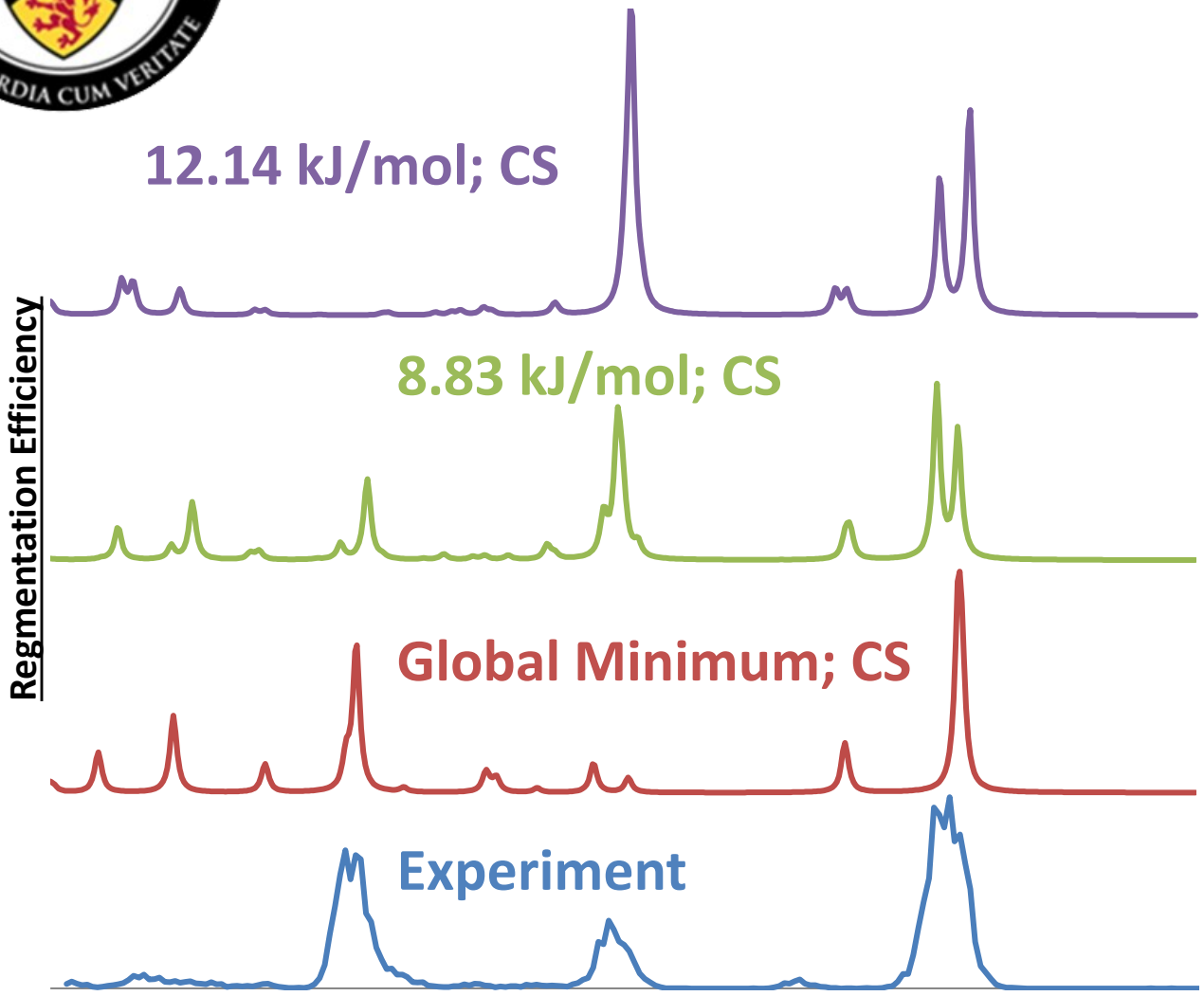
Identity	Structure	m/z	Cys Binding Energies
Parent Ion		249	N/A
Fragment 1		146	83 kJ/mol
Fragment 2		128	82 kJ/mol

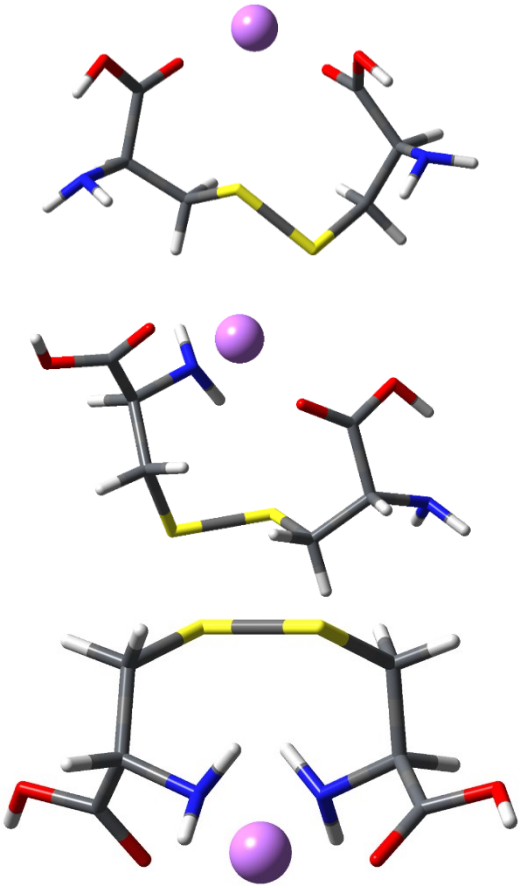
$Li^+ \bullet Cysteine_2$ Spectrum



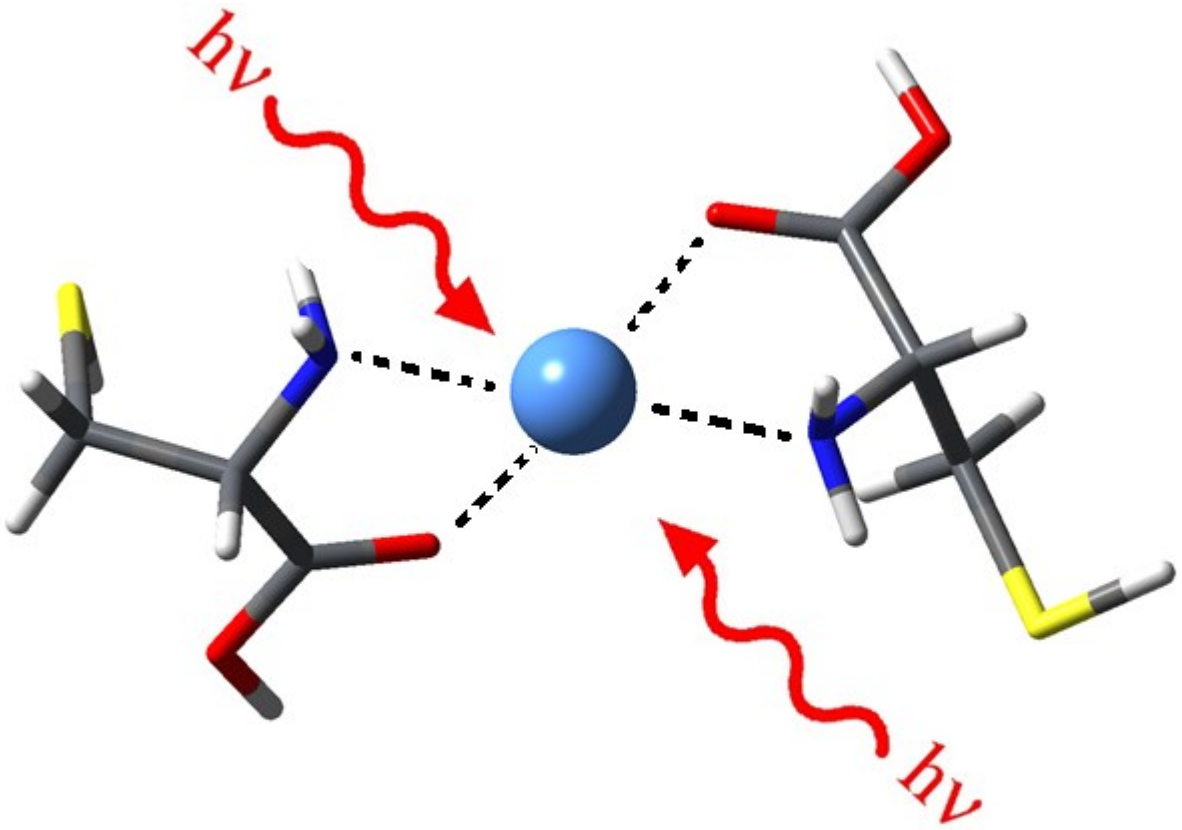
CS – Charge Solvated
ZW- Zwitterion

Li^+•Cystine Spectrum

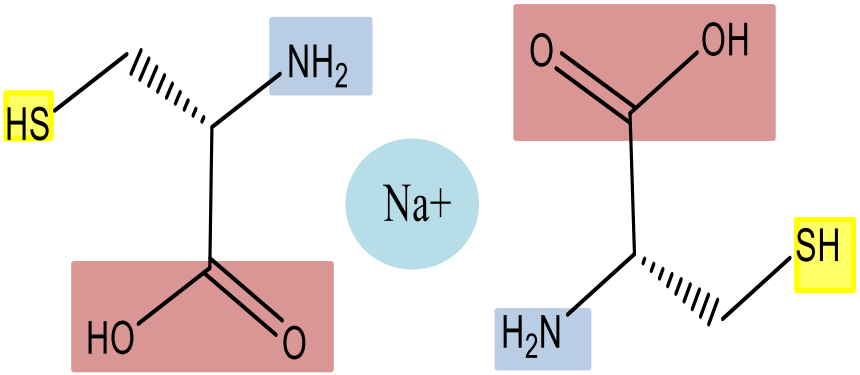
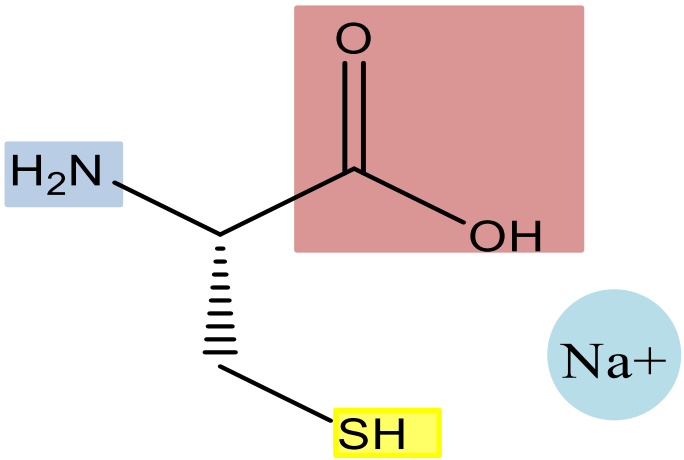




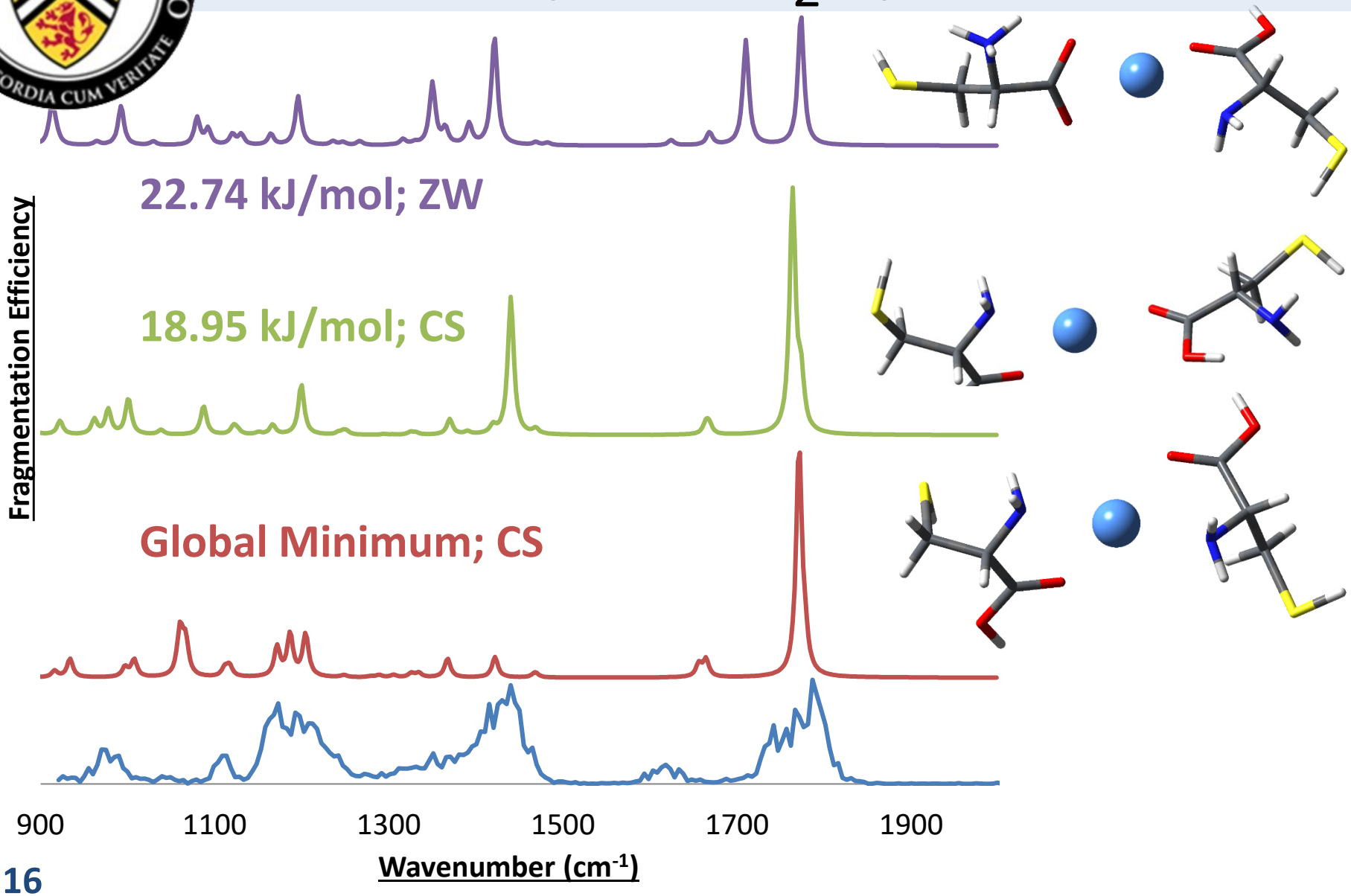
Sodium Cysteine Clusters



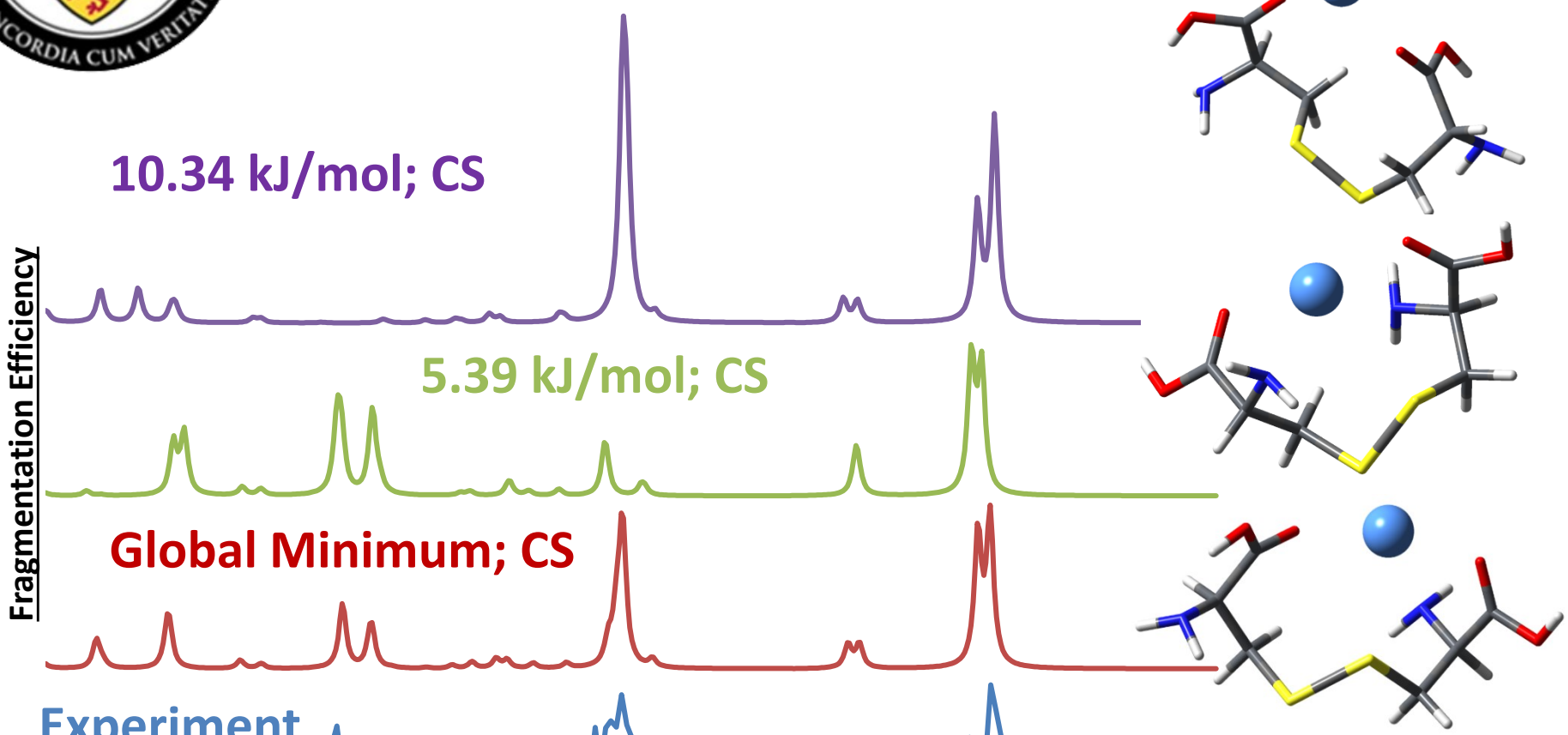
Fragmentation Analysis

Identity	Structure	m/z	Cys Binding Energies
Parent Ion		265	N/A
Fragment 1		144	41 kJ/mol

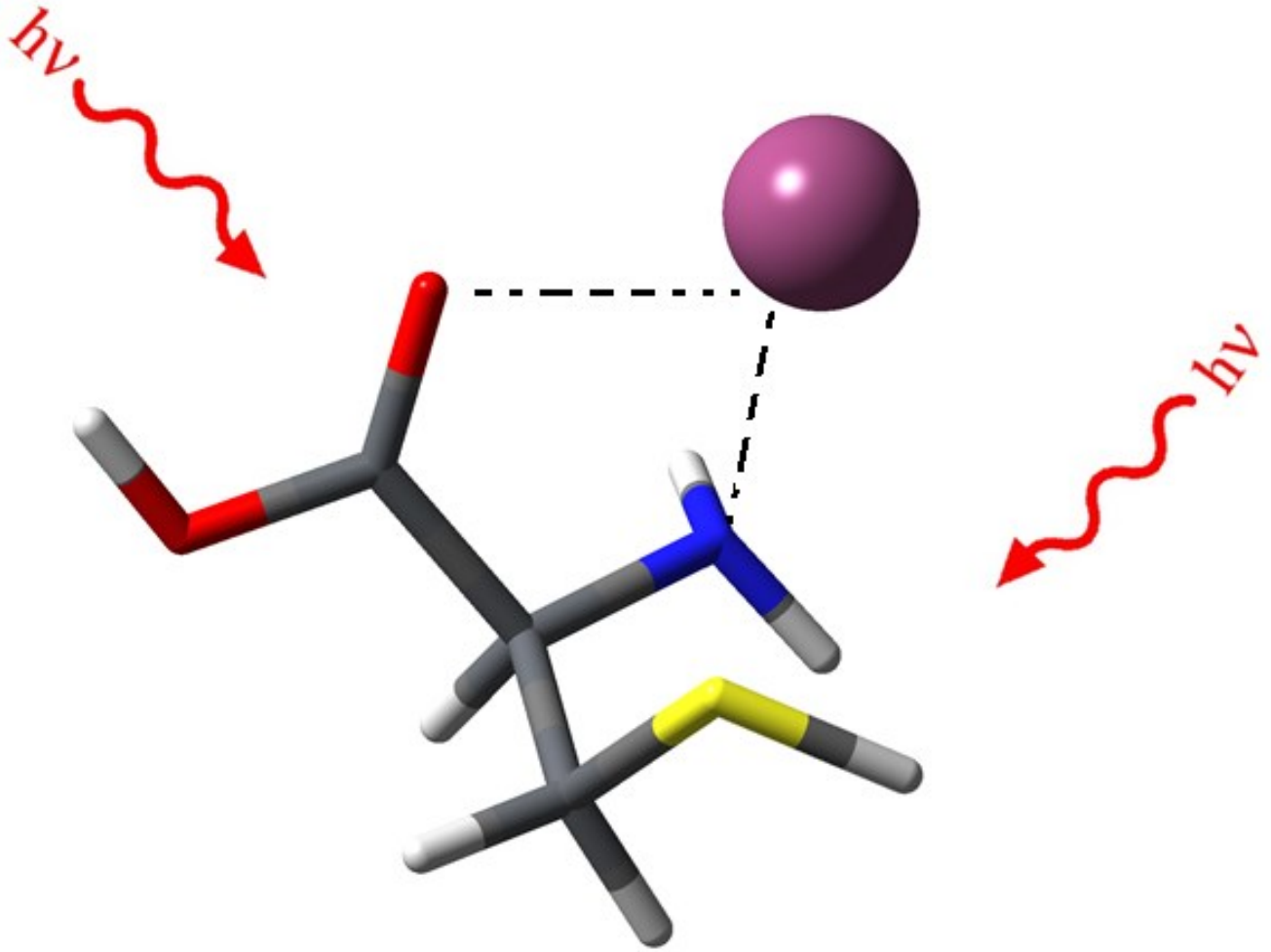
$Na^+ \bullet Cysteine_2$ Spectrum



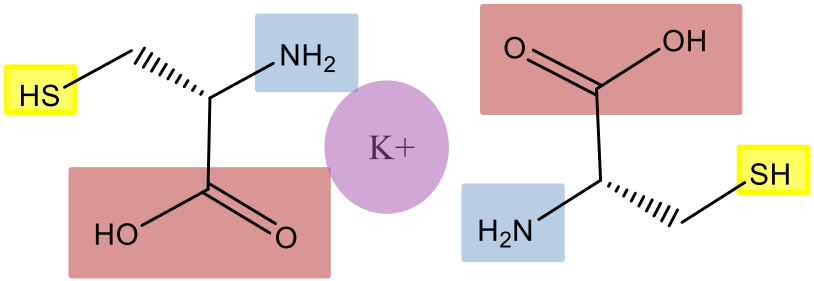
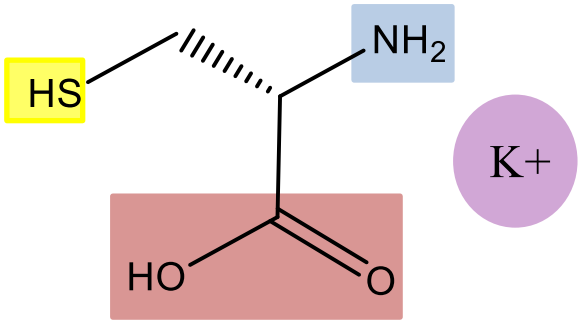
Na^+•Cystine Spectrum



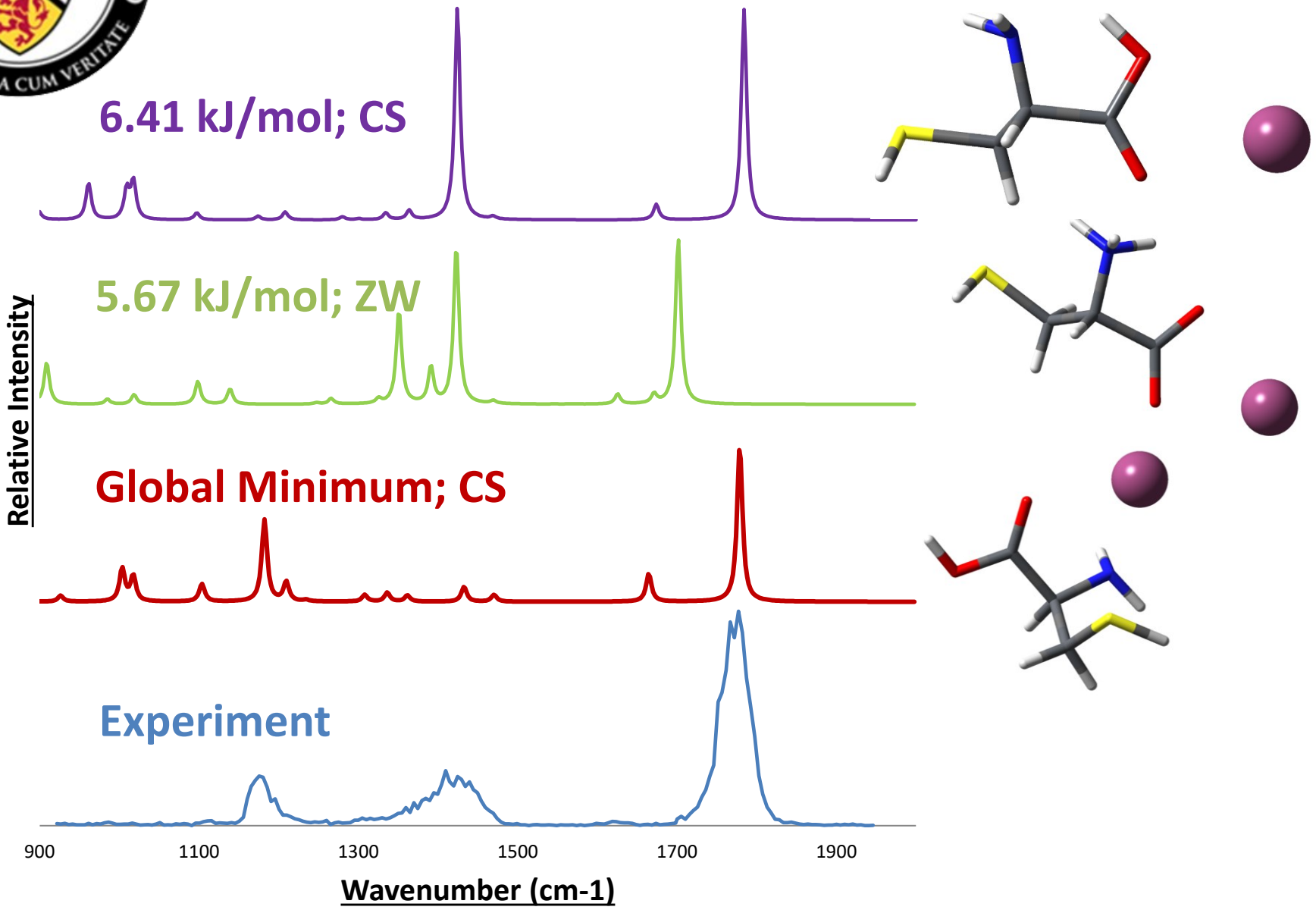
Potassium Cysteine Clusters



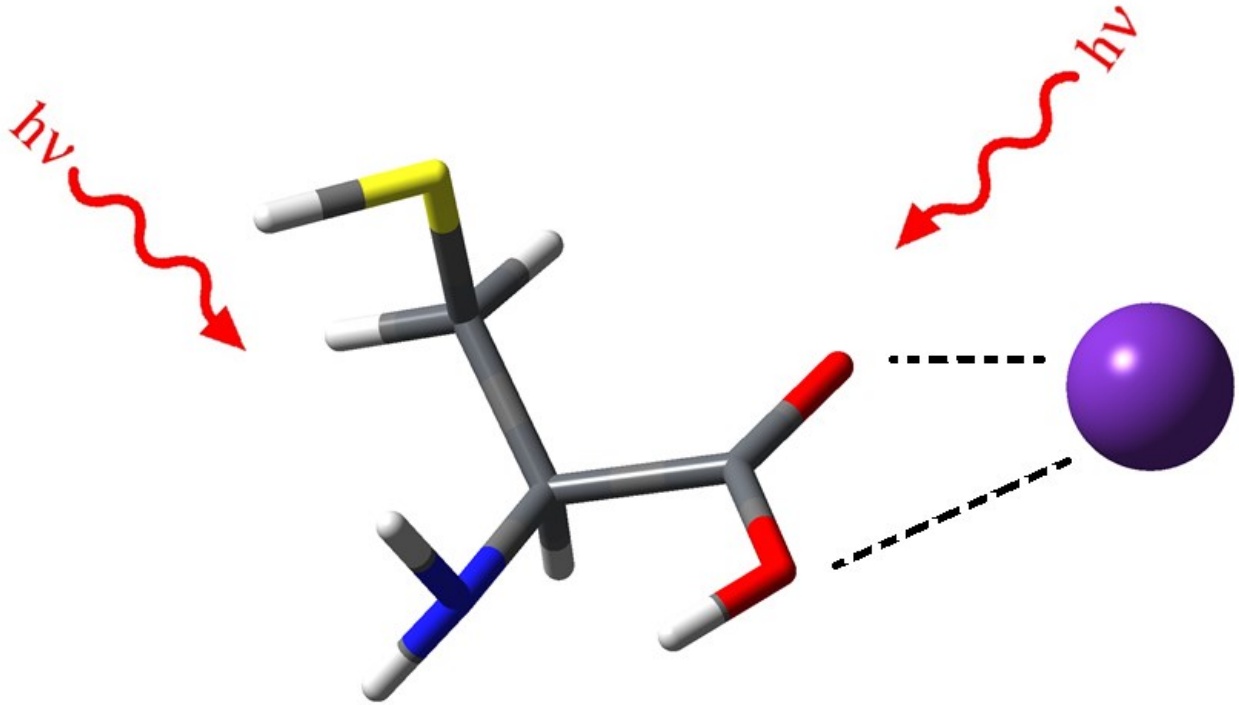
Fragmentation Analysis

Identity	Structure	m/z	Cysteine Binding Energies
Dimer			46 kJ/mol
Parent Ion		160	N/A
Fragment 1		40	85 kJ/mol

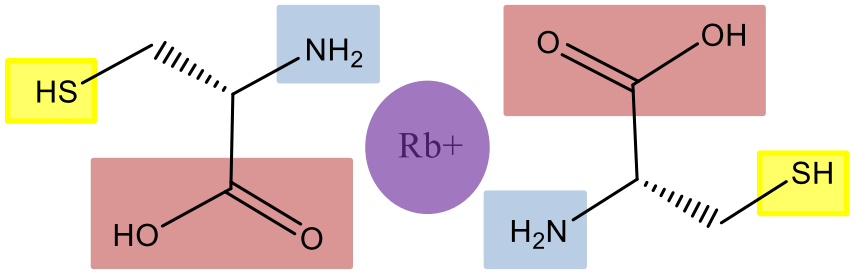
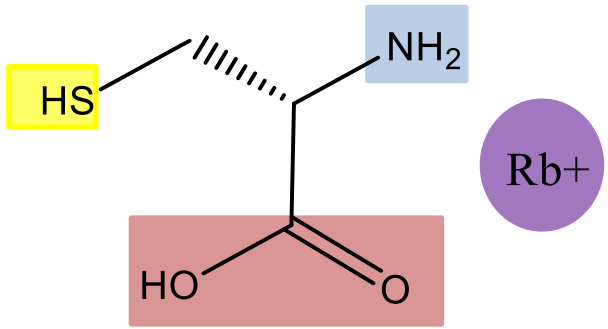
K^+•Cysteine Spectrum



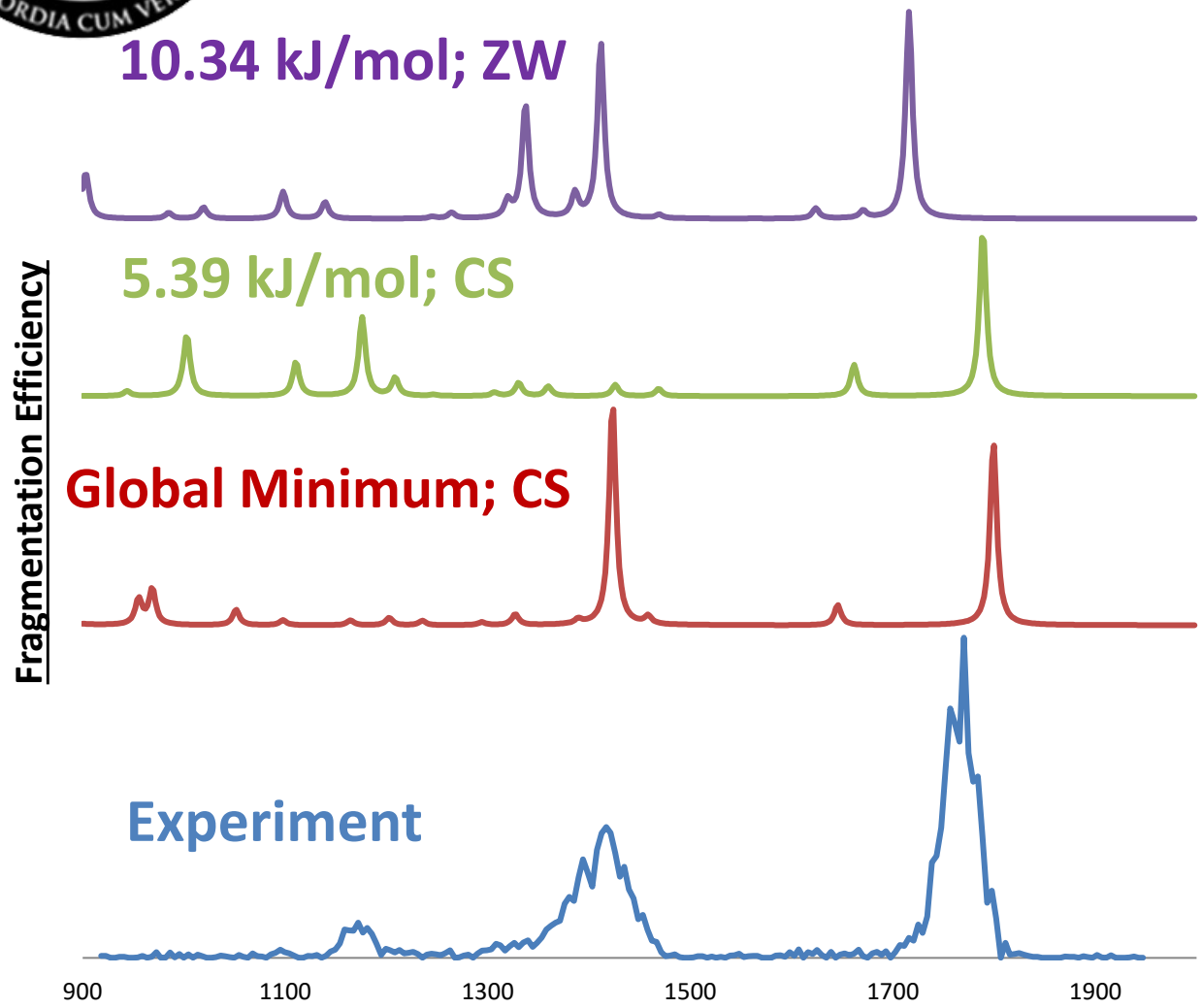
Rubidium Cysteine Clusters

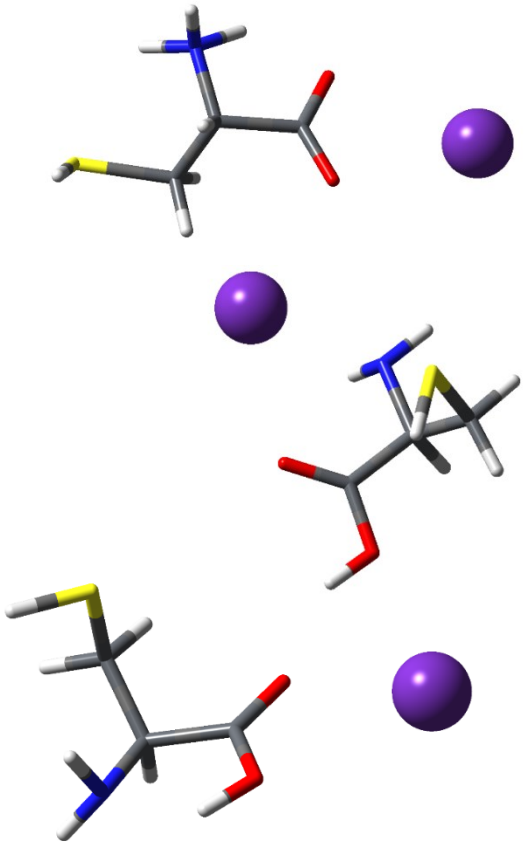


Fragmentation Analysis

Identity	Structure	m/z	Cysteine Binding Energies
Dimer			13 kJ/mol
Parent Ion		146	N/A
Fragment 1		128	68 kJ/mol

Rb^+•Cysteine Spectrum





Conclusion and Acknowledgements

Computational Summary:

- Computational spectra generated with B3LYP 6-311++G(d,p)
- Binding energies of fragments determined

Computational Future Work:

- Basin Hop Zwitterions
- Anharmonic Calculations
- MP2 binding Energies
- Continued work with coinage metals

Acknowledgements

M. Lecours

compute • calcul CANADA

NSERC CRSNG

SHARCNET™

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HOPKINS LABORATORY

6-311++(d,p)

number of primitive Gaussians comprising each core atomic orbital basis function

Composition of valence orbitals, combined with particular number of primitive Gaussian functions

Diffuse Functions
Model tail of atomic orbitals (distant from nuclei)

Polarizabilty Functions
Important when considering bonding between atoms