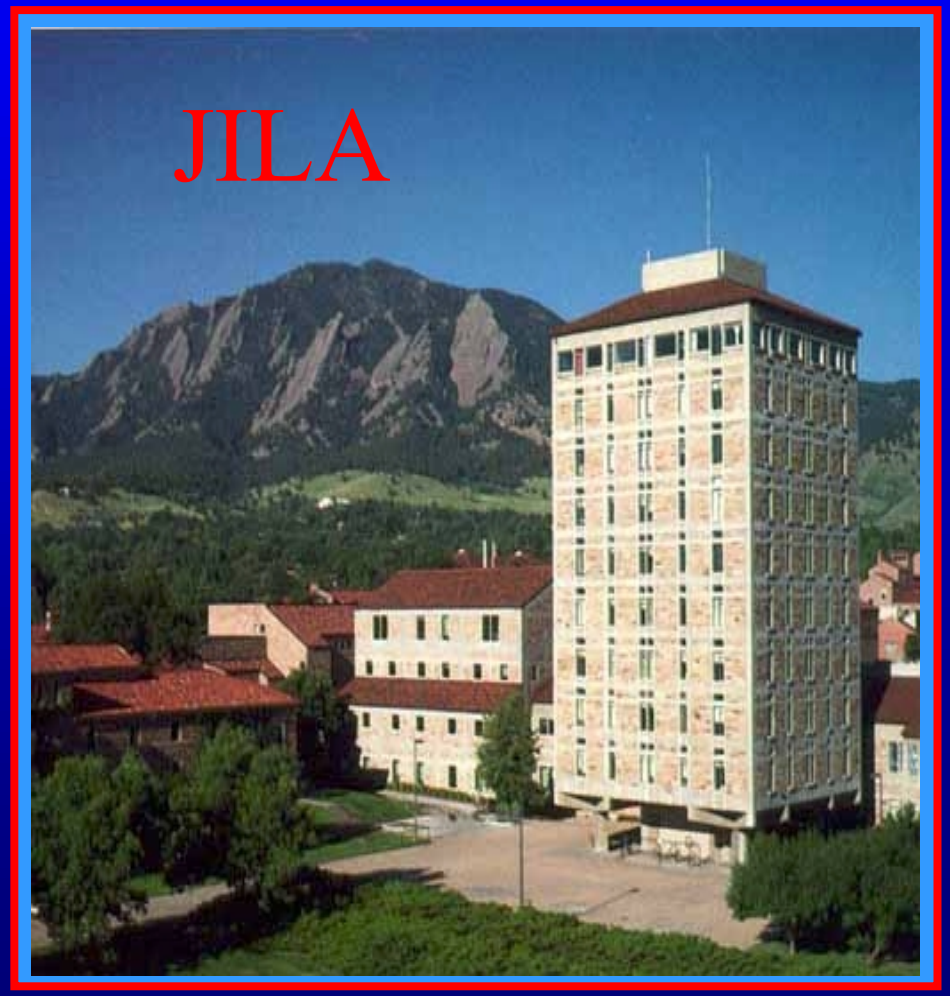
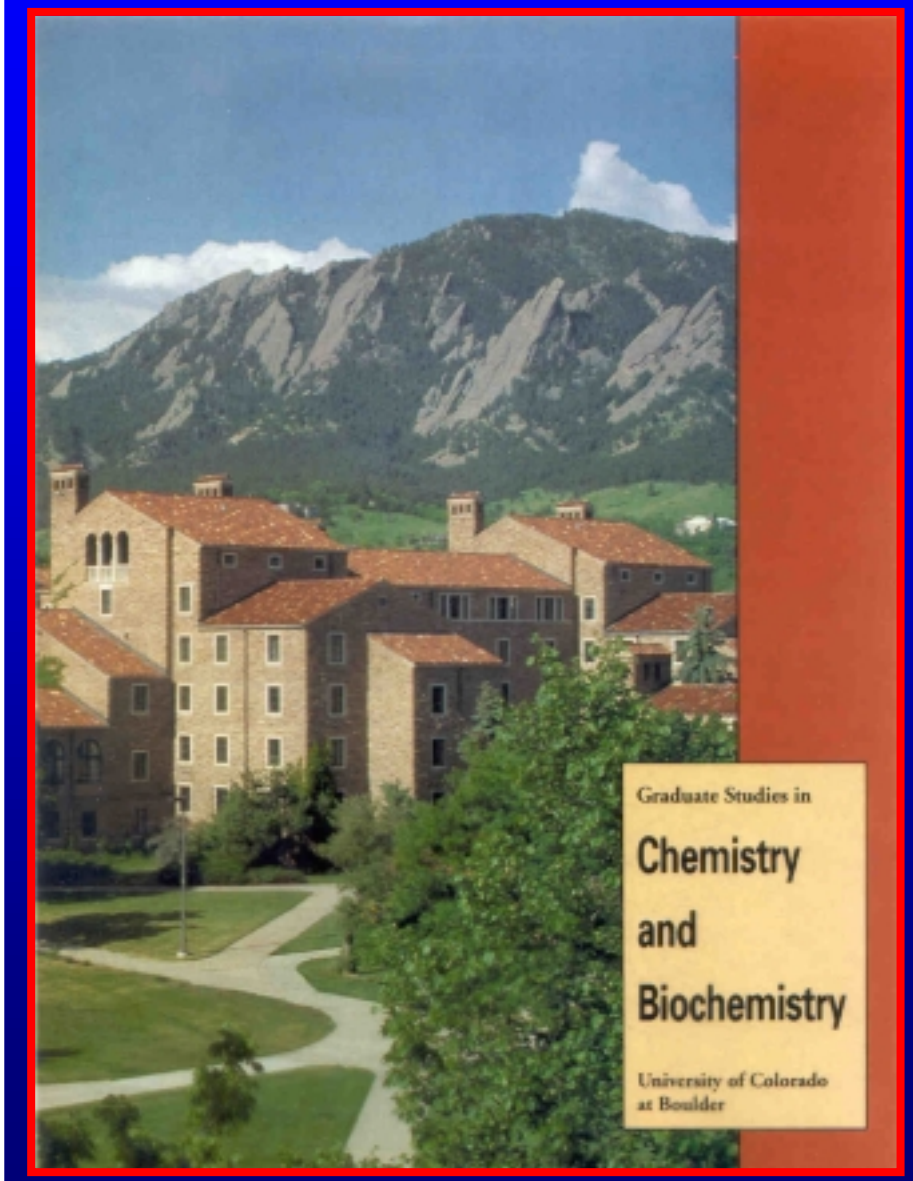
Hydrogen Bond Dynamics: From Simple to Complex



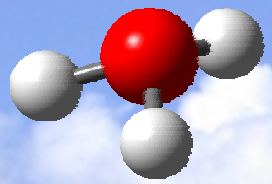
IUPAC Workshop
"Hydrogen Bonding and Other Molecular Interactions"
Pisa, Italy
September 7, 2005

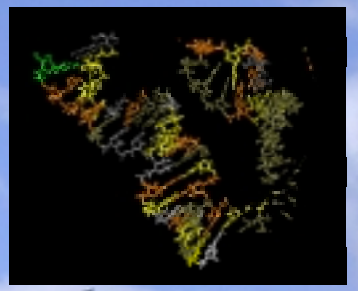
Work done at
JILA/Department of Chemistry and Biochemistry
National Institute for Standards and Technology
University of Colorado
Boulder, CO



Thanks in advance to Nesbitt group and collaborators!

Today's Topics
From simple to complex

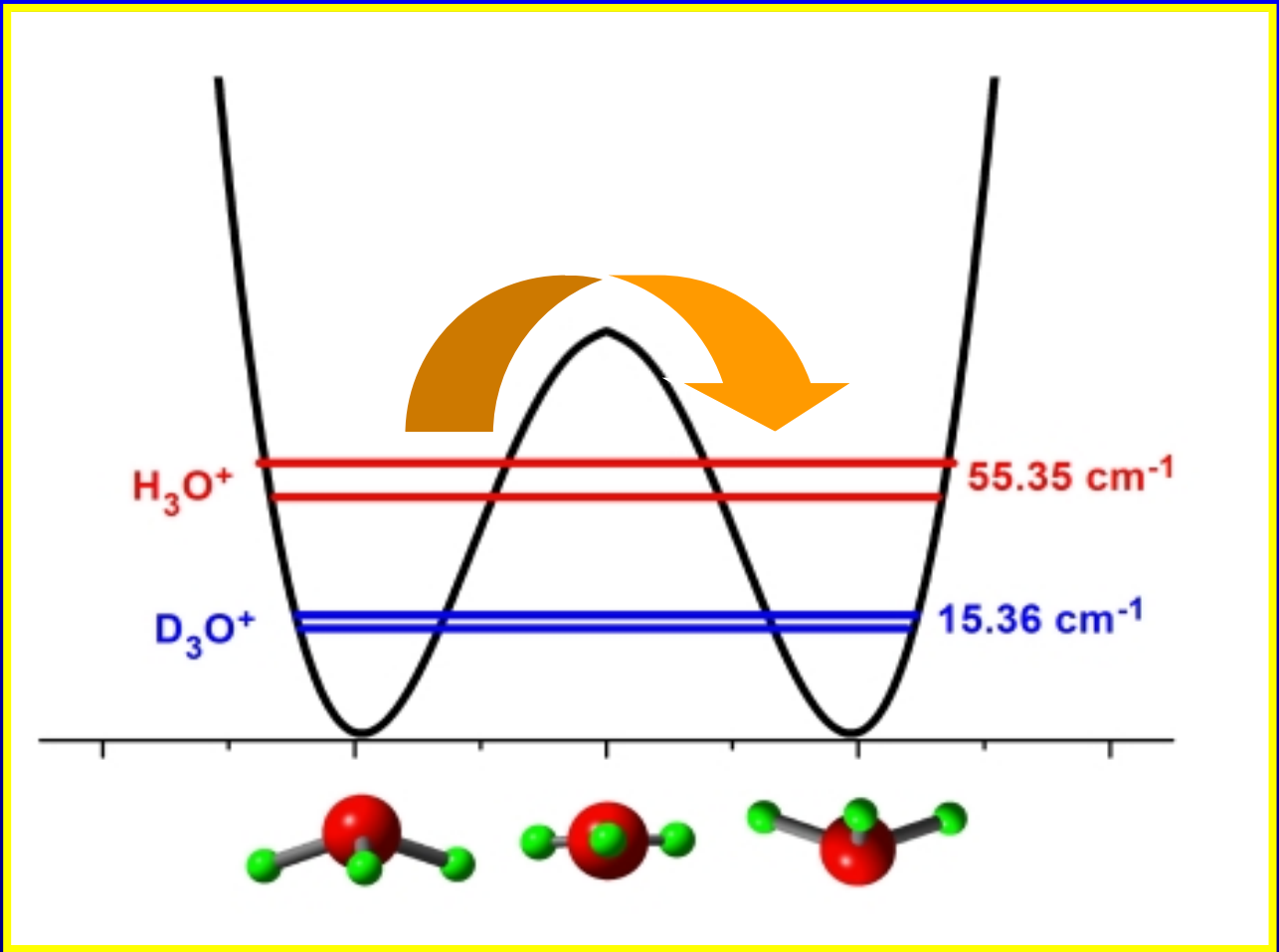




Hydronium tunneling…

…to RNA folding

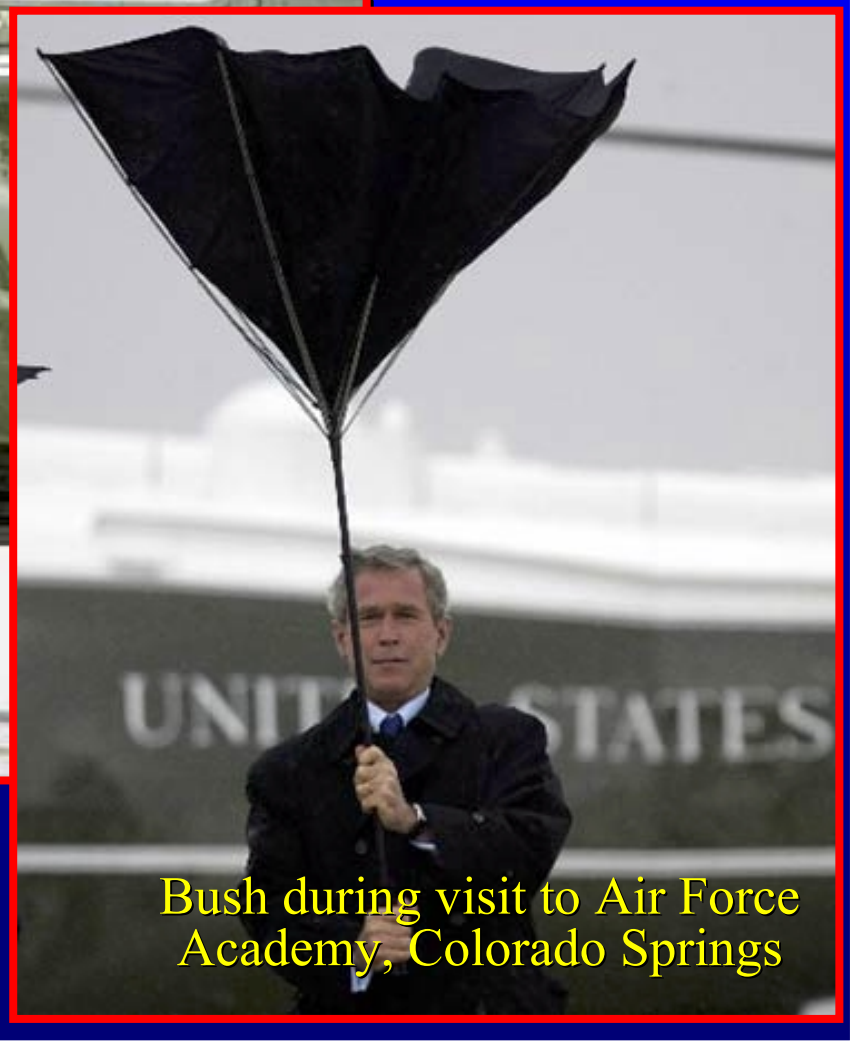
I) From the Simple… (H_3O^+)



- Arguably the simplest (and strongest) hydrogen bond!
- Ubiquitous role in aqueous chemistry and biology.
- Likely abundant polyatomic ion species in interstellar dust clouds
- Large amplitude floppy QM tunneling in “umbrella” mode

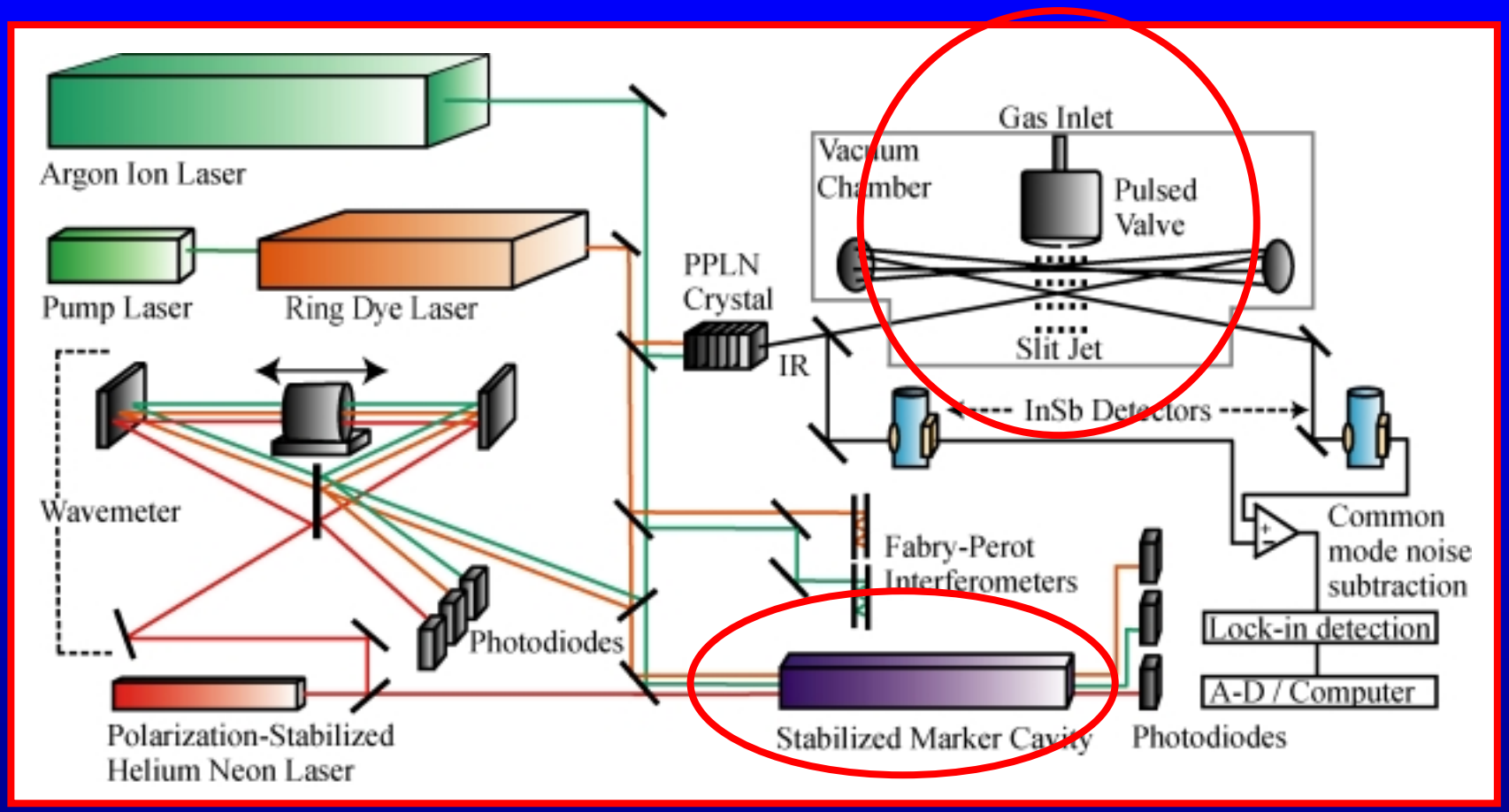
Begemann, and Saykally, PRL 1983; Liu & Oka, PRL 1985; Verhoeve and Dymanus, CPL 1989; Araki and Saito, JCP 1998.

World Le g with Large A tum Inve



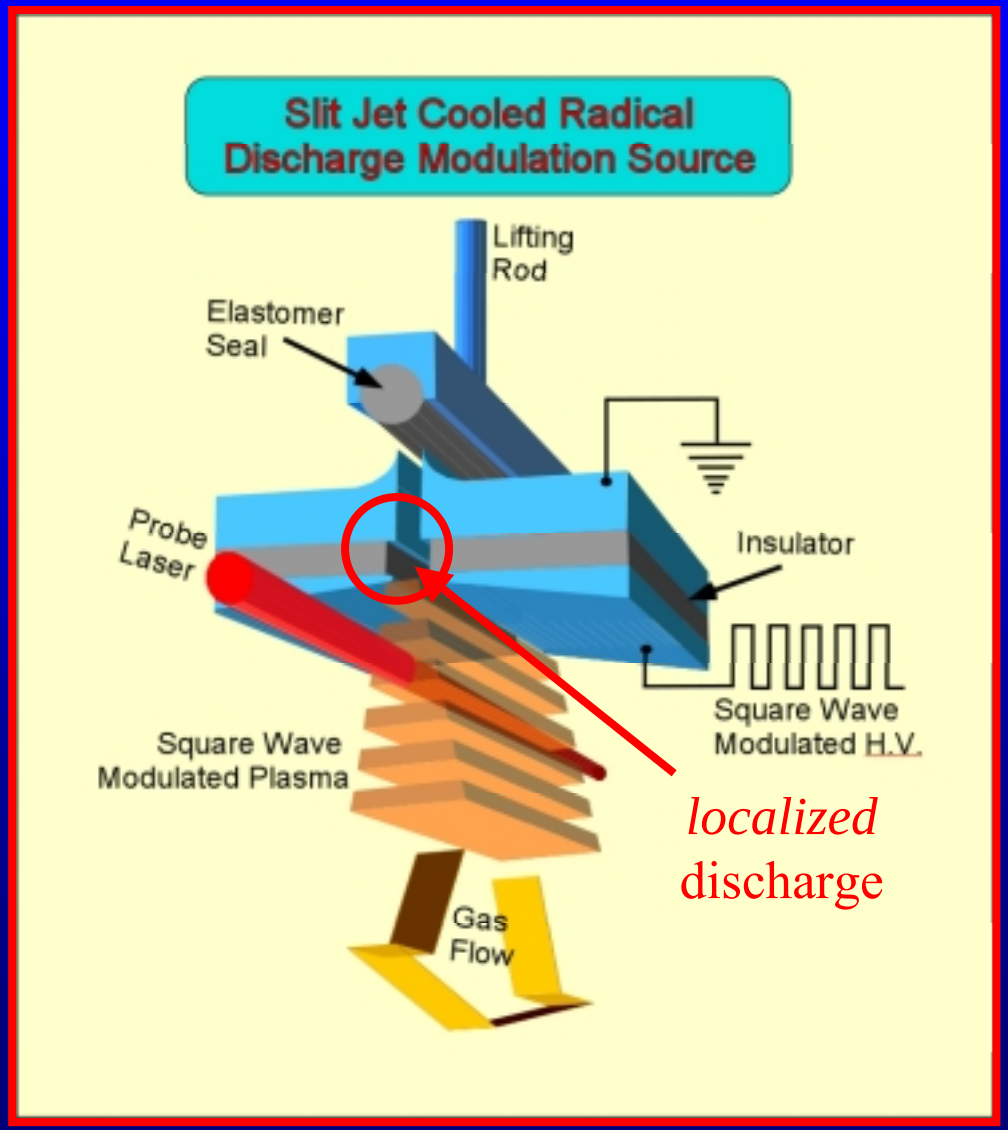
Bush during visit to Air Force Academy, Colorado Springs

Experimental

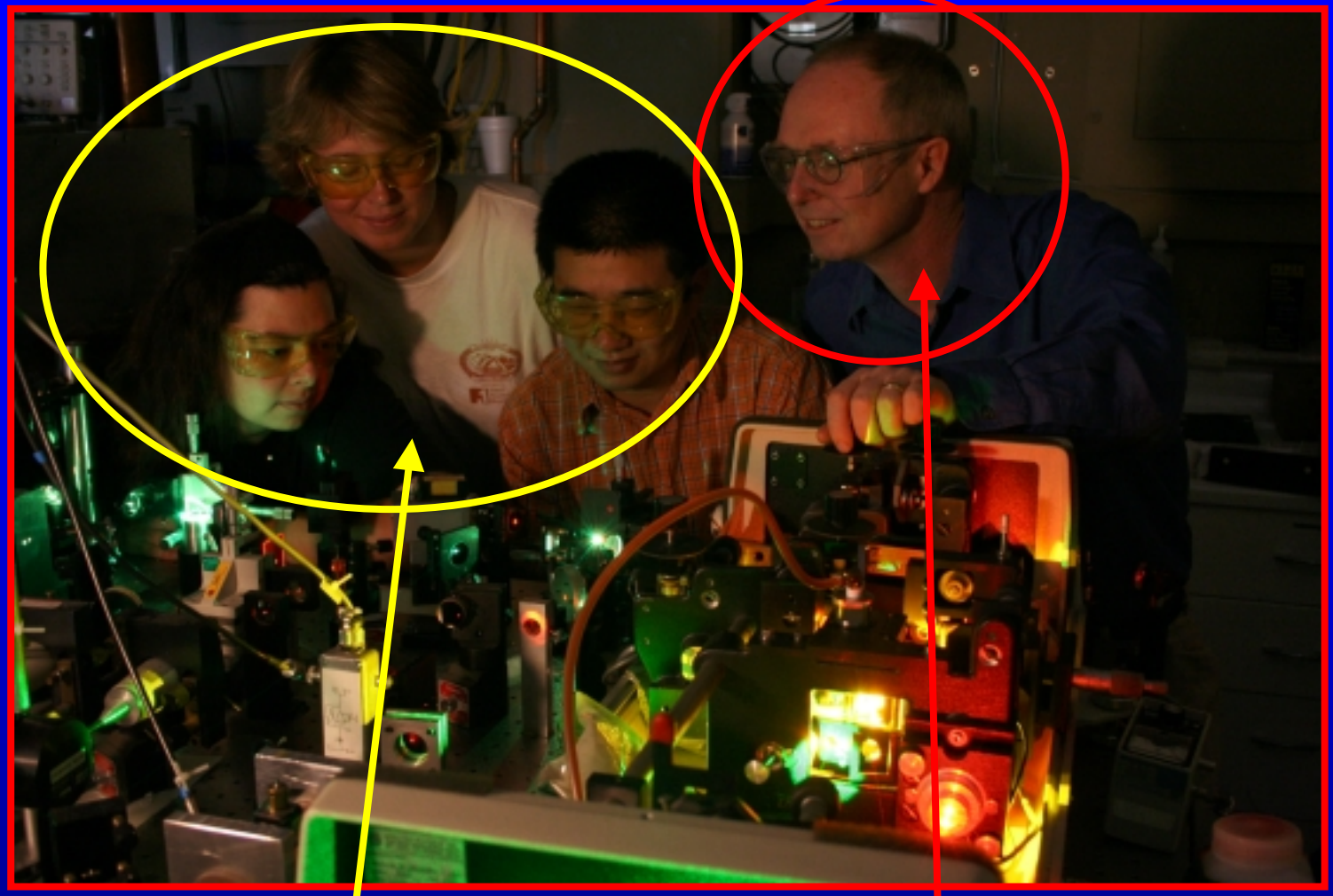


- Sub-Doppler molecular linewidths (≈40 MHz in Ne expansion)
- Servoloop locked optical transfer cavities for high frequency precision (≈20 MHz)
- Shot noise limited detection sensitivity: 1.5 x 10^{-5} (N_{min} ≈10^{7}#/cm^{3}/qs)

Jet Cooled Radical/Ions



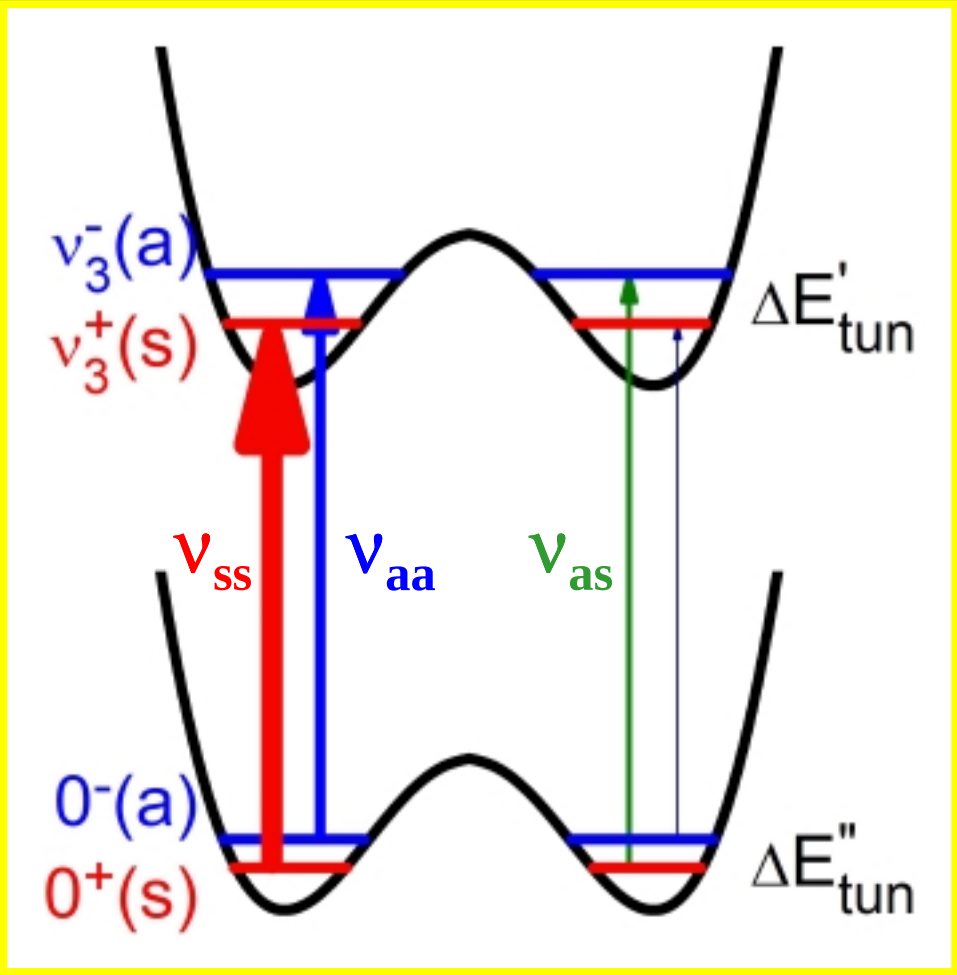
- High resolution spectroscopy of highly reactive chemical transients…
- …under maximally simplified low T conditions



- Post docs and grad students eager for "hot" experimental tips from their research advisor…

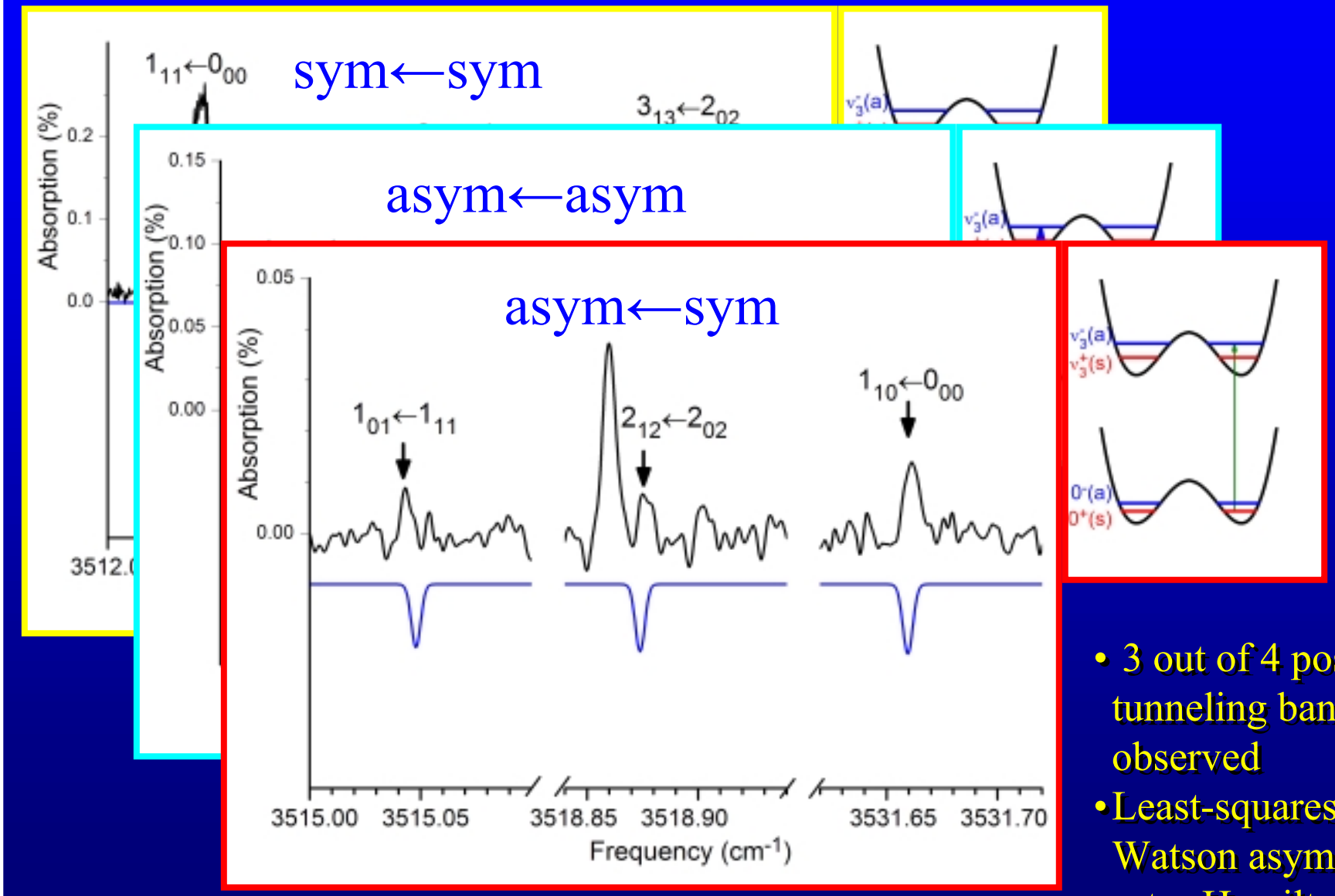
- …research advisor ruining several days of careful alignment

Tunneling Dynamics in H_3O^+ Isotopomers?



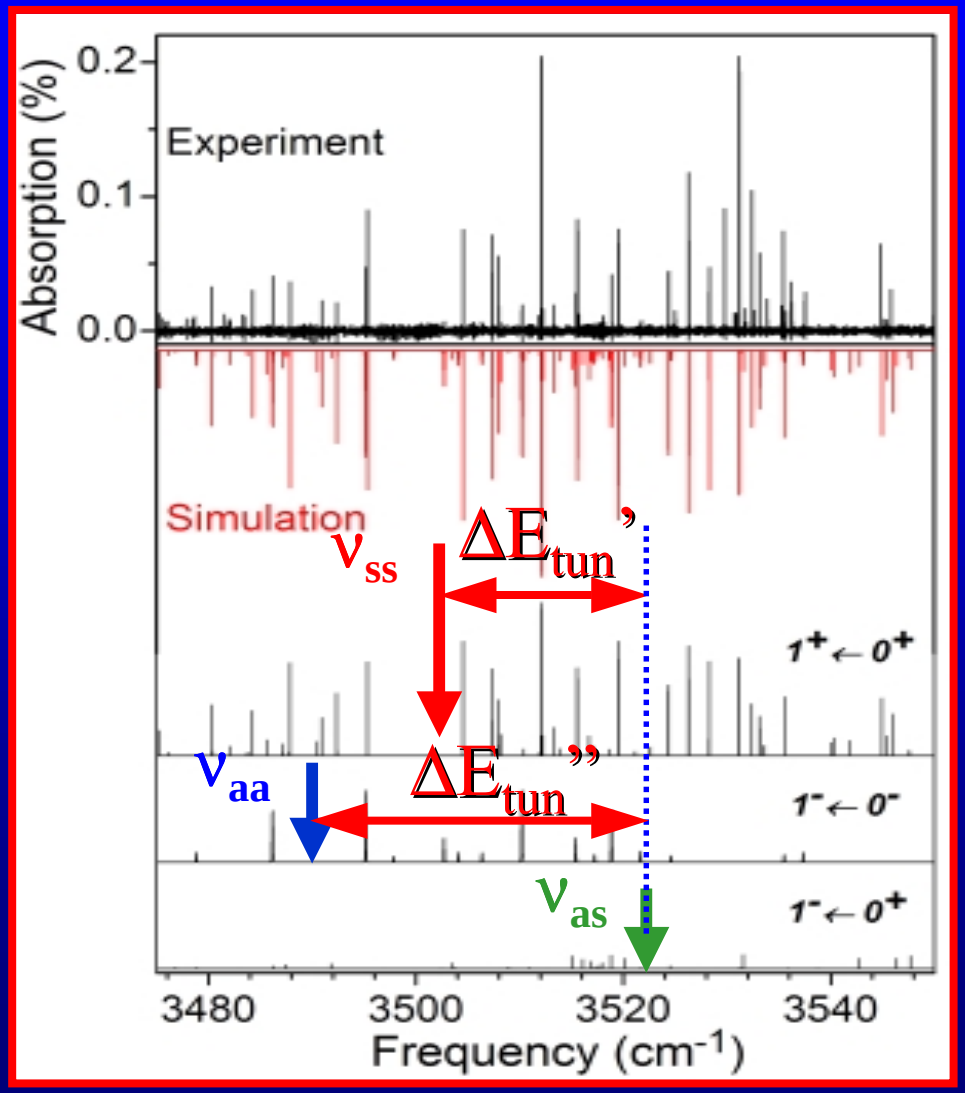
- H_3O^+ vs HD_2O^+ and H_2DO^+
- $\Rightarrow$ *Symmetry breaking* from C_{3v} to C_s (tunneling through a C_{2v} trans state)
- Makes *all four* stretch tunneling transitions allowed in HD_2O^+ and H_2DO^+
- Permits direct tunneling splitting measurements in a *single* IR vibrational band
- $\Rightarrow$ Map out inversion barrier by systematic "tuning" of tunneling masses from H_3O^+ to H_2DO^+ to HD_2O^+ to D_3O^+

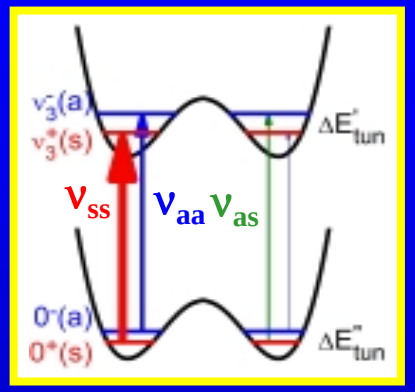
Sample HD_2O^+ Spectral Data



- 3 out of 4 possible tunneling bands observed
- Least-squares fit to Watson asymmetric rotor Hamiltonian

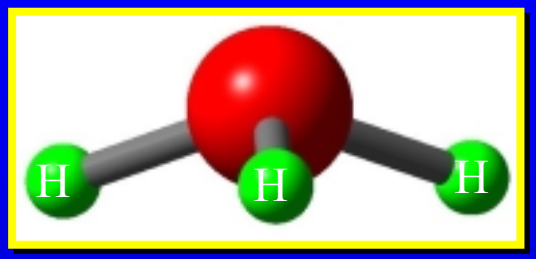
Global Infrared Spectrum of HD_2O^+



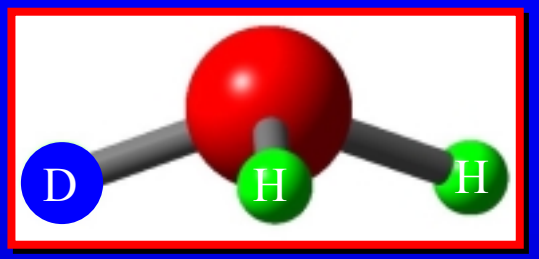


- Direct tunneling splittings in a single vibrational band
  - ΔE_{tun}" = 27.032 cm^{-1}
  - ΔE_{tun}' = 17.761 cm^{-1}
- Large difference between ground and excited state tunneling splittings

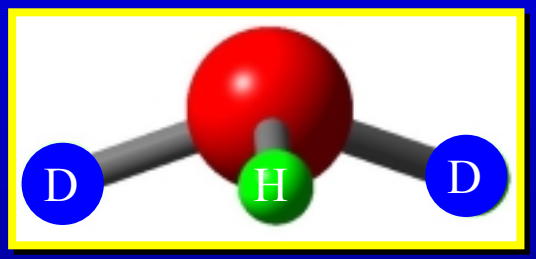
Completing the "Isotopomer Quartet"?



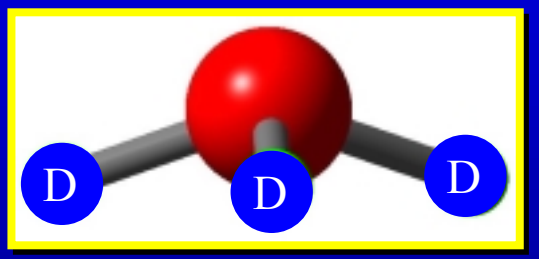
ΔE_{tun}" = 55.35 cm^{-1}



ΔE_{tun}" = ?? cm^{-1}



ΔE_{tun}" = 27.03 cm^{-1}



ΔE_{tun}" = 15.36 cm^{-1}

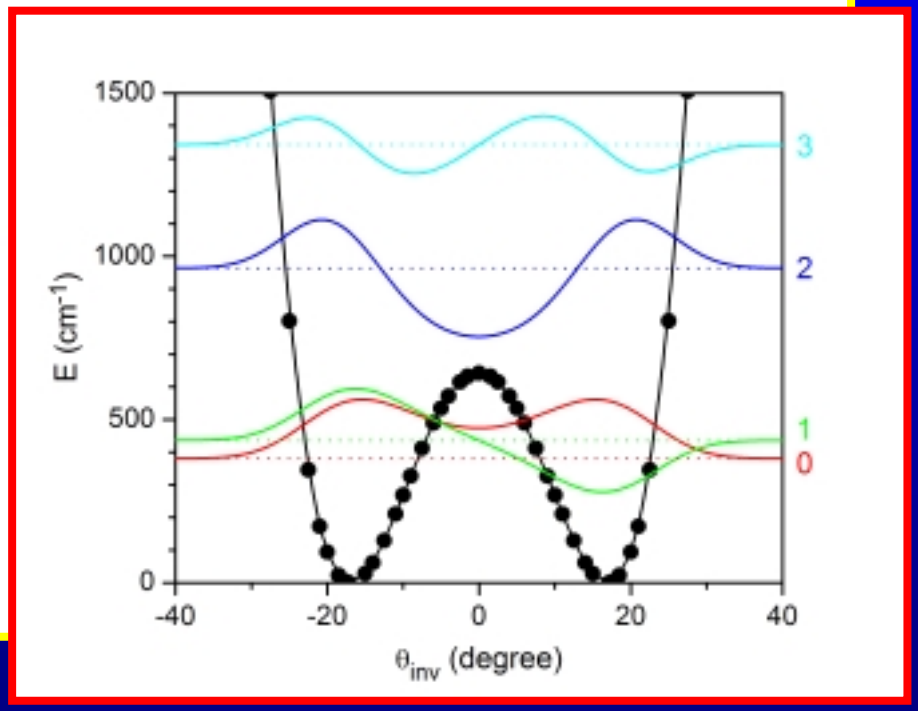
Isotope Dependent Tunneling

	Bowman's	*Halonen's*	*Expt*
		Ground state	
H_3O^+	46	56.02	**55.346 (6)** [a]
H_2DO^+	33	41.14	**41.4 (26)**
HD_2O^+	22	27.49	**27.032 (7)**
D_3O^+	12	15.79	**15.355504 (4)** [c]
V_0	690	650	??
		Excited State	
H_3O^+	32	39.08	**38.747 (6)** [b]
H_2DO^+	21	26.74	**26.3 (26)**
HD_2O^+	13	18.02	**17.761 (5)**
D_3O^+	7	10.23	**9.942 (6)** [d]

[a] Liu & Oka, PRL 1985; [b] Tang & Oka, JMS 1999; [c] Araki & Saito, JCP 1998; [d] Petek et al. JCP 1989.
All units in cm^{-1}.

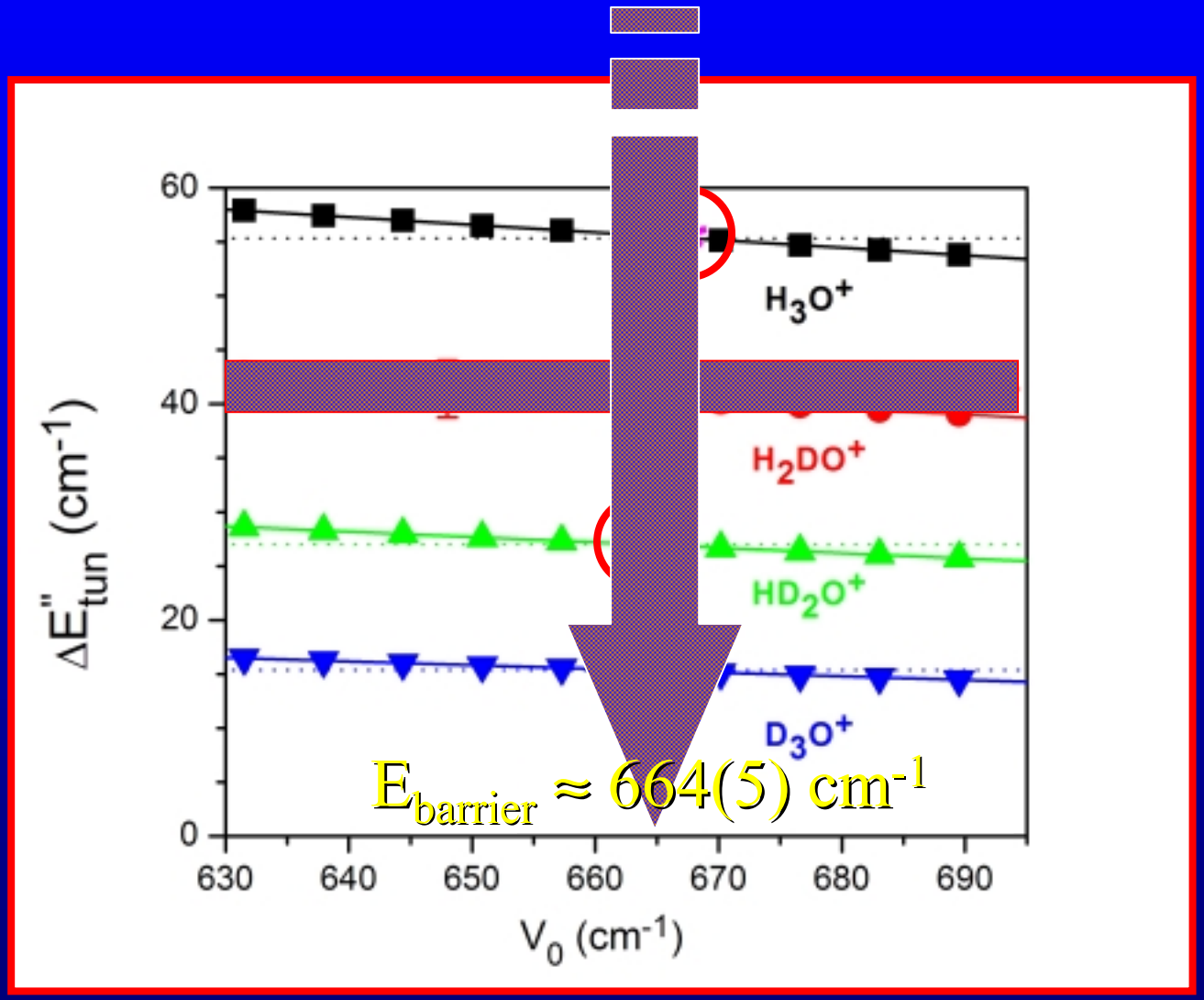
Rush-Wiberg (HBJ) Approach

$$\left[\frac{d^2}{dq^2}+\left[2\mu(q)/\hbar^2\right]\left[E-V(q)\right]\right]\psi(q)=0$$



- Geometry optimization and frequency calculations at CCSD(T)/AVTZ along the tunneling path
- CBS energies extrapolated from CCSD(T), AVnZ (n=D,T,Q)
- ZPE corrections for all other vibrational modes
- Reduced mass μ(q) from the vibration-rotation G-matrix coupling (Rush and Wiberg, Hougen-Bunker-Johns)
- 1D tunneling eigenvalues/ eigenfunctions solved on vertically scaled CCSD(T) PES to extract barrier height

Tunneling Barrier Height



- $E_{barrier} \approx 664$ cm^{-1} estimate for tunneling in H_3O^+ isotopomers
- In quite good agreement with *ab initio* calculations of Halonen et al

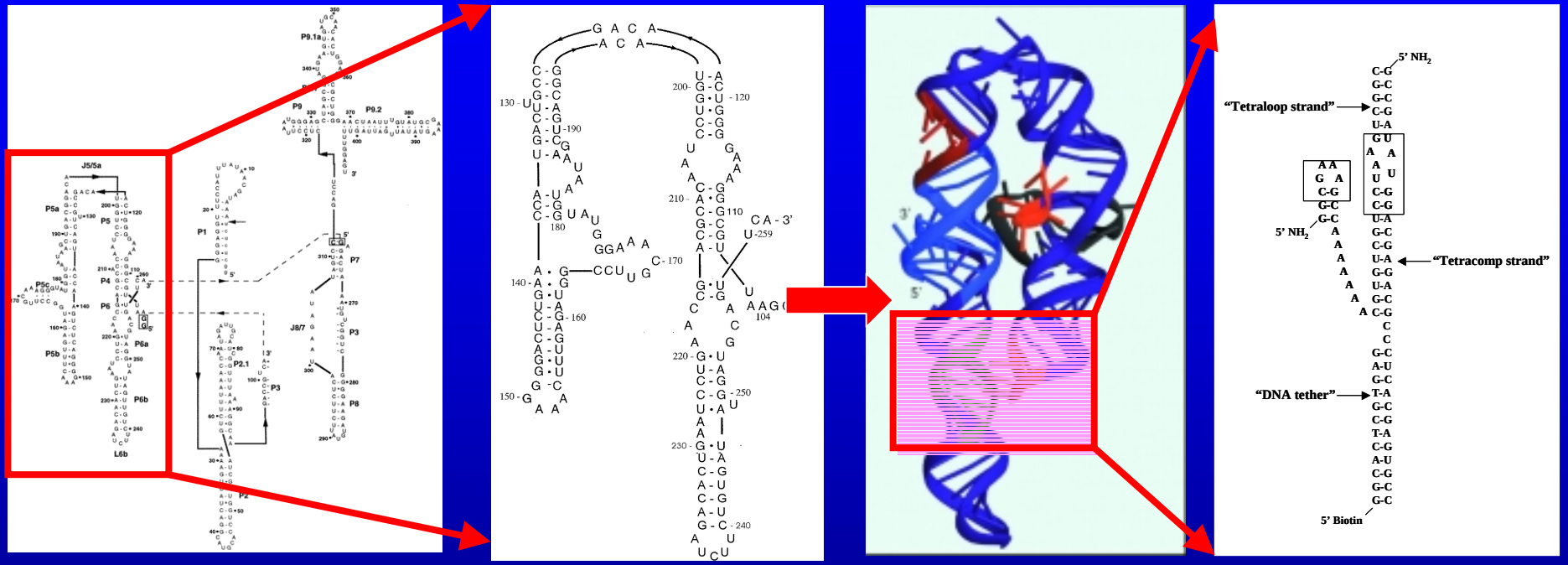
II) …to Complex (RNA folding)

- Conformational change *crucial* to biological activity (the earliest enzymes ("ribozymes") made from self folding RNA)
- Hierarchical RNA folding stabilized by specific *H-bonding tertiary interactions* (e.g. tetraloop-receptor, A-rich bulge, etc)
- Structural information alone is not enough!

Structure + *Dynamics* ⇒ Function

Tertiary Interactions

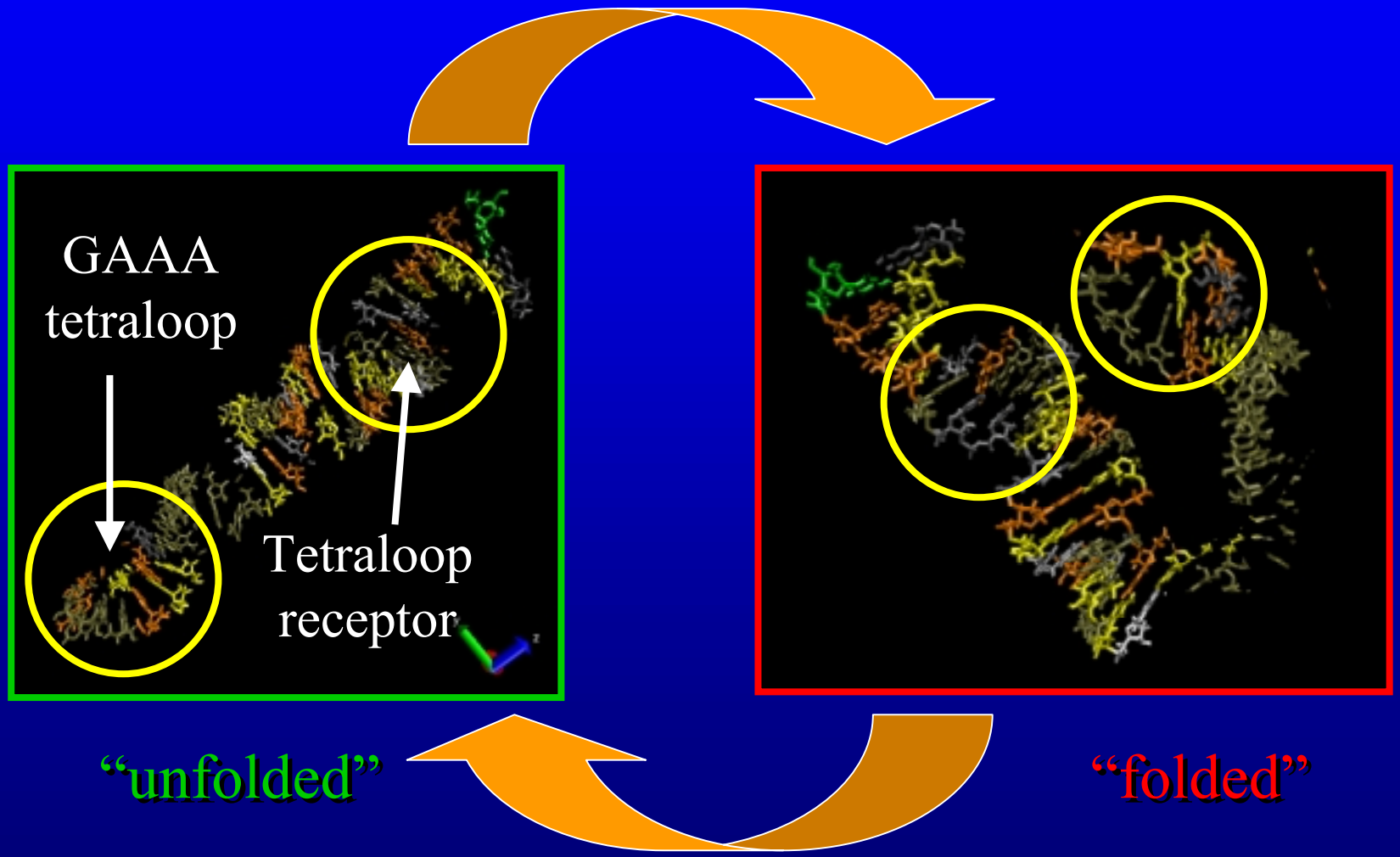
(P4-P6 Domain: *Tetrahymena* Group I Ribozyme)



Cate, J.H, et al.
***Science*, 1996**

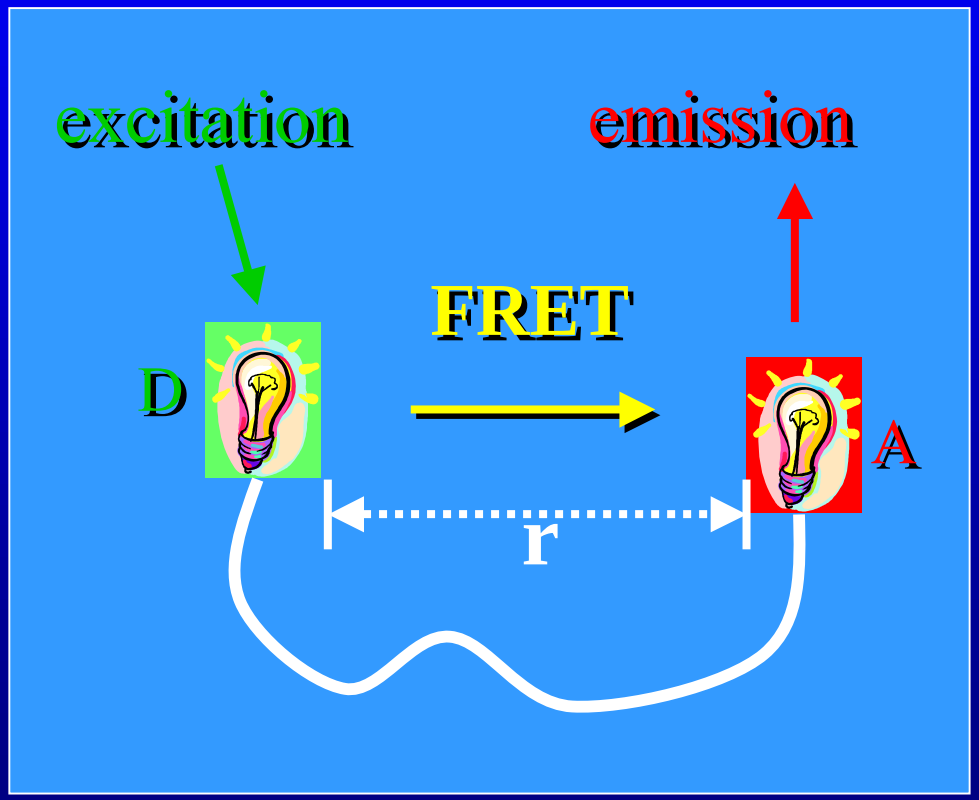
- Ubiquitous RNA "tetraloop- receptor" binding interaction
- Driven by [Mg^{++}] (shielding of repulsive phosphate backbone interactions)
- Responsible for folding complete ribozyme into enzymatically active form

Single RNA Constructs



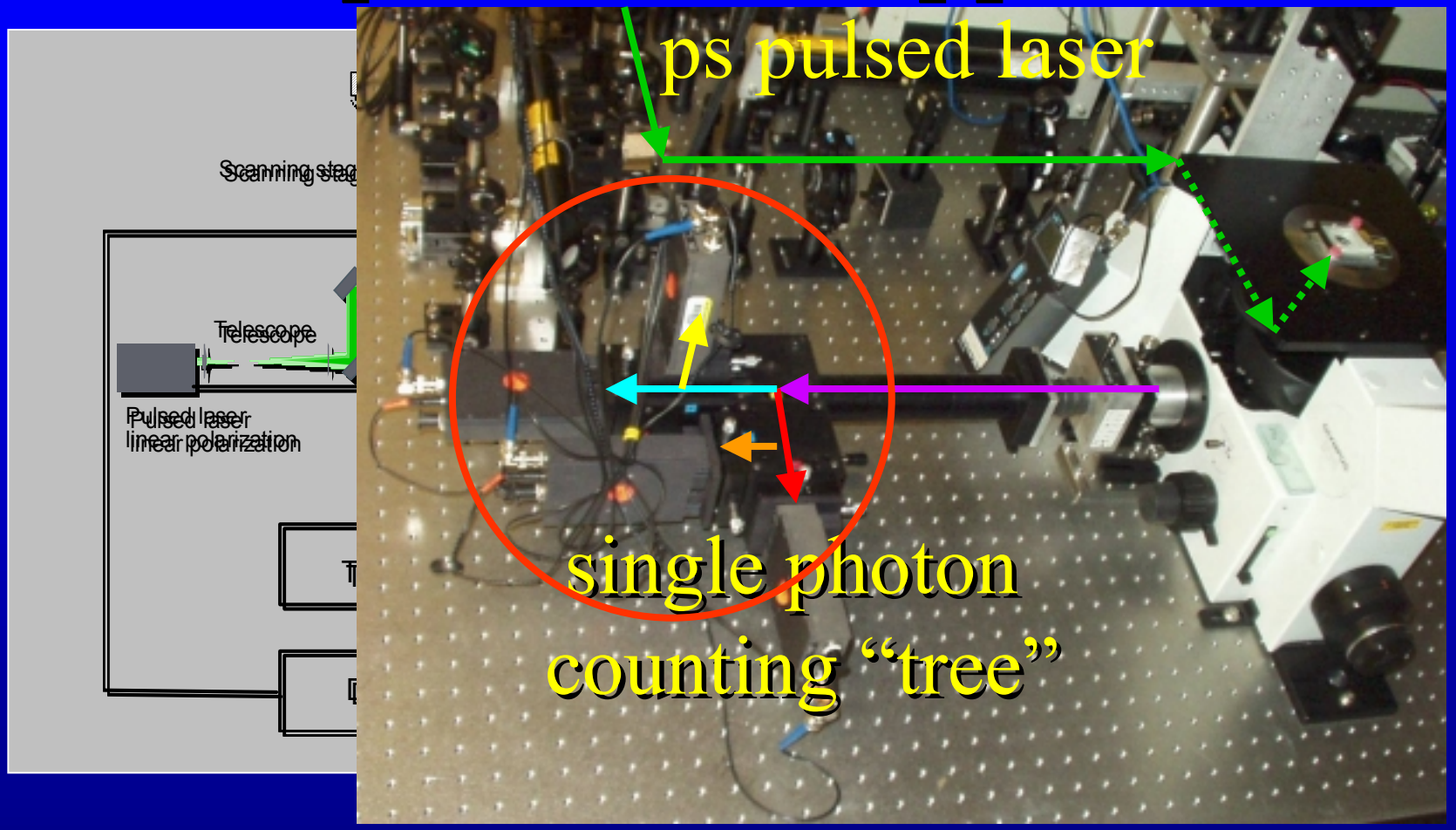
Watching Single RNA Molecules Fold?

(*F*luorescence *R*esonance *E*nergy *T*ransfer)



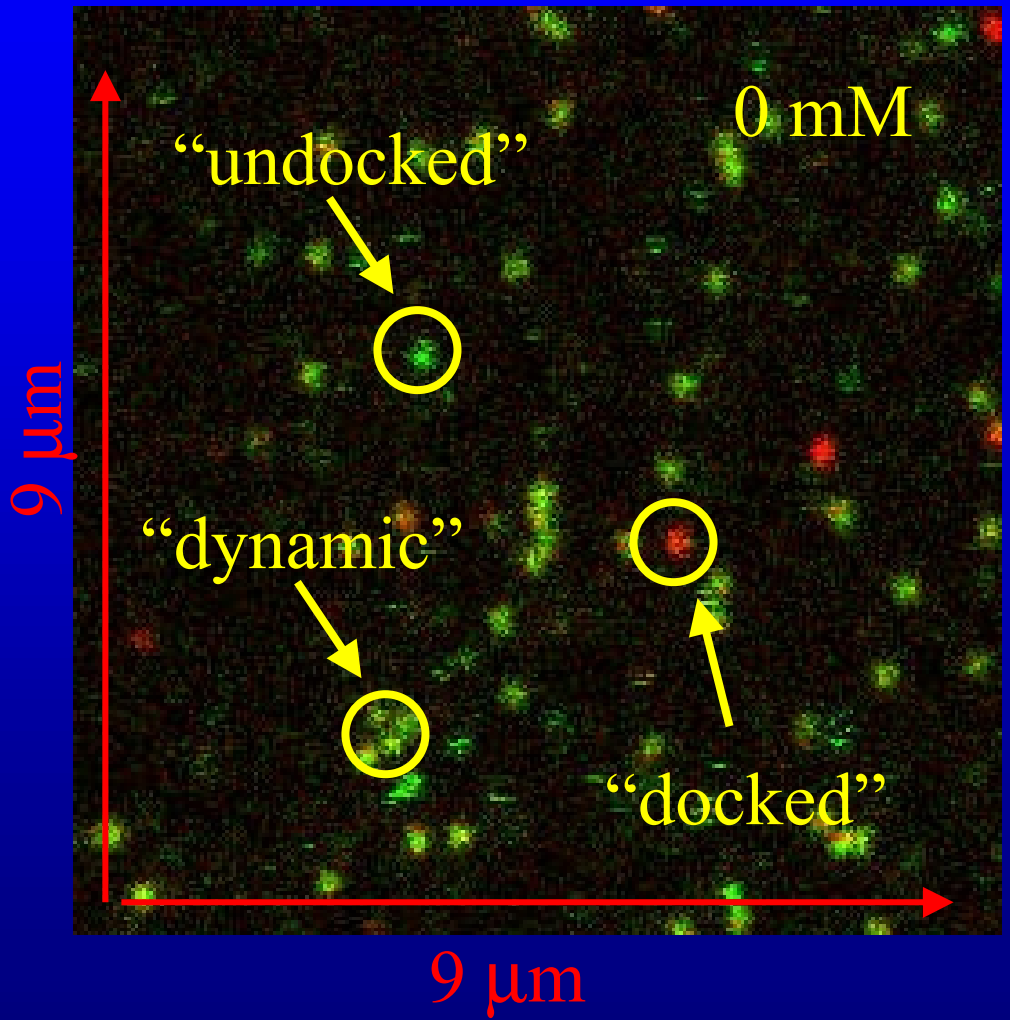
- Excitation transfer from "donor" (I_D) to "acceptor" (I_A) which fluoresces at a *different* color
- Folding detected by *changes* in FRET efficiency $\approx I_A/(I_D + I_A) \propto 1/[1+(r/r_0)^6]$
- "Molecular ruler" on the 10 Å - 100 Å length scale

Experimental Apparatus



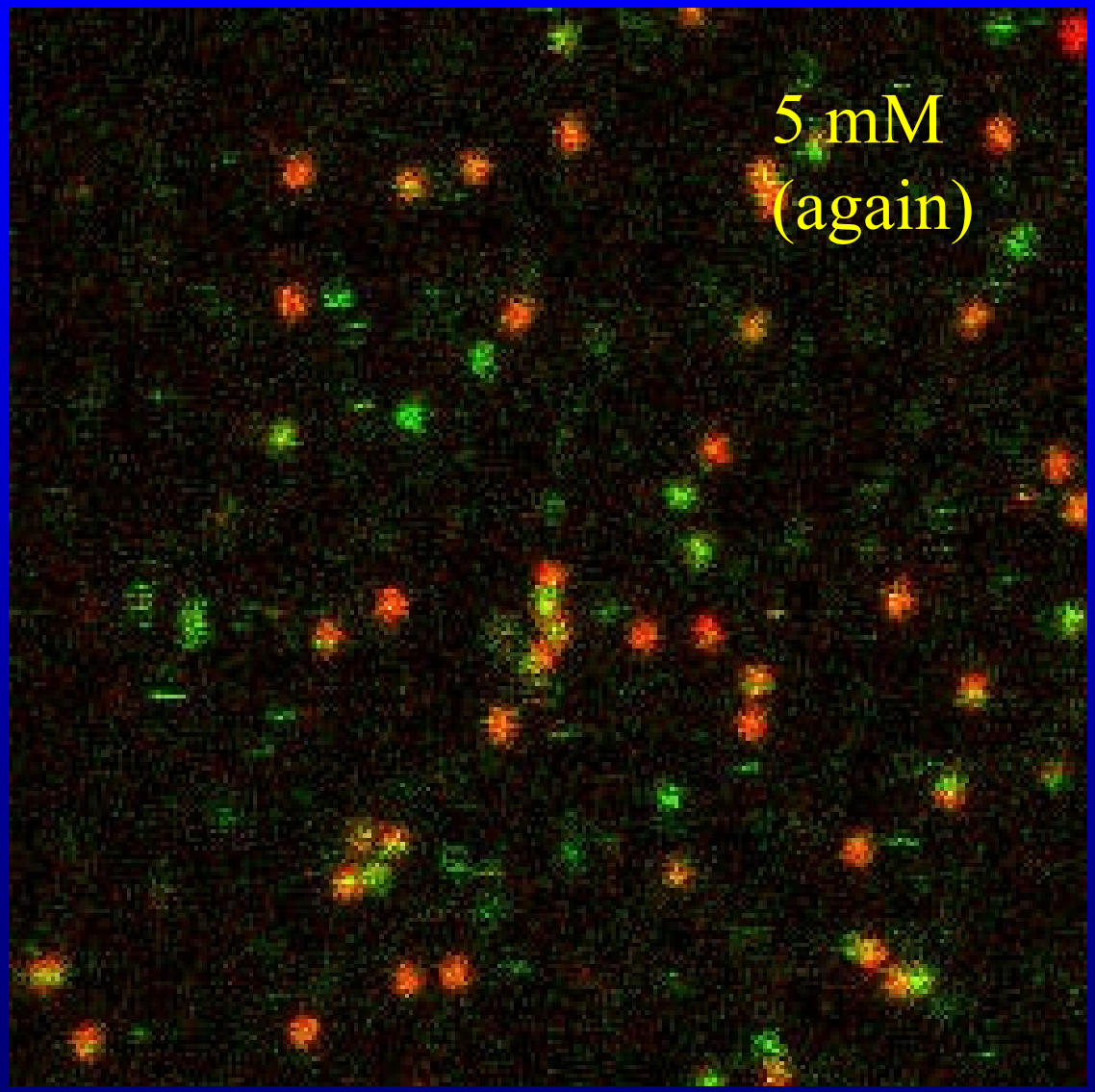
- Time stamped detection (color, polarization, macro and microtime)
- Explicit FRET correction for crosstalk, direct excitation, and background
- Fluorescence/folding/orientation dynamics on time scales from $< 10^{-9}$ sec to $> 10^{3}$ sec!

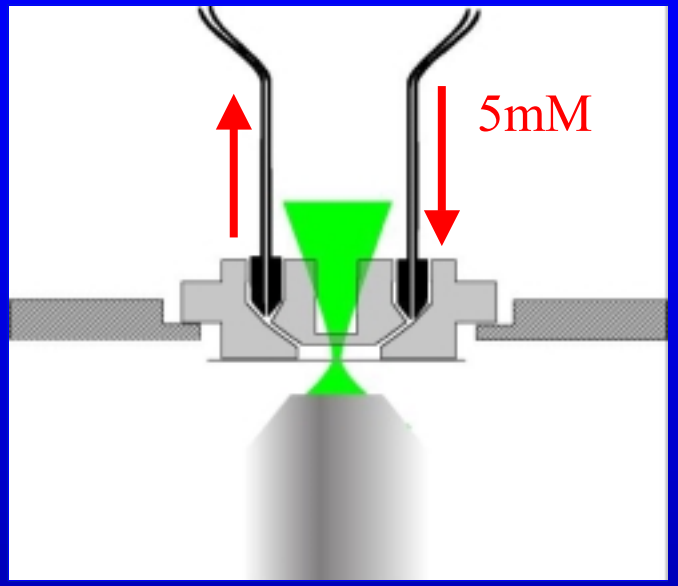
Single RNA FRET Imaging



- FRET identification of docked/undocked constructs
- Heterogeneity at the single molecule level ("average" behavior not the whole story!)

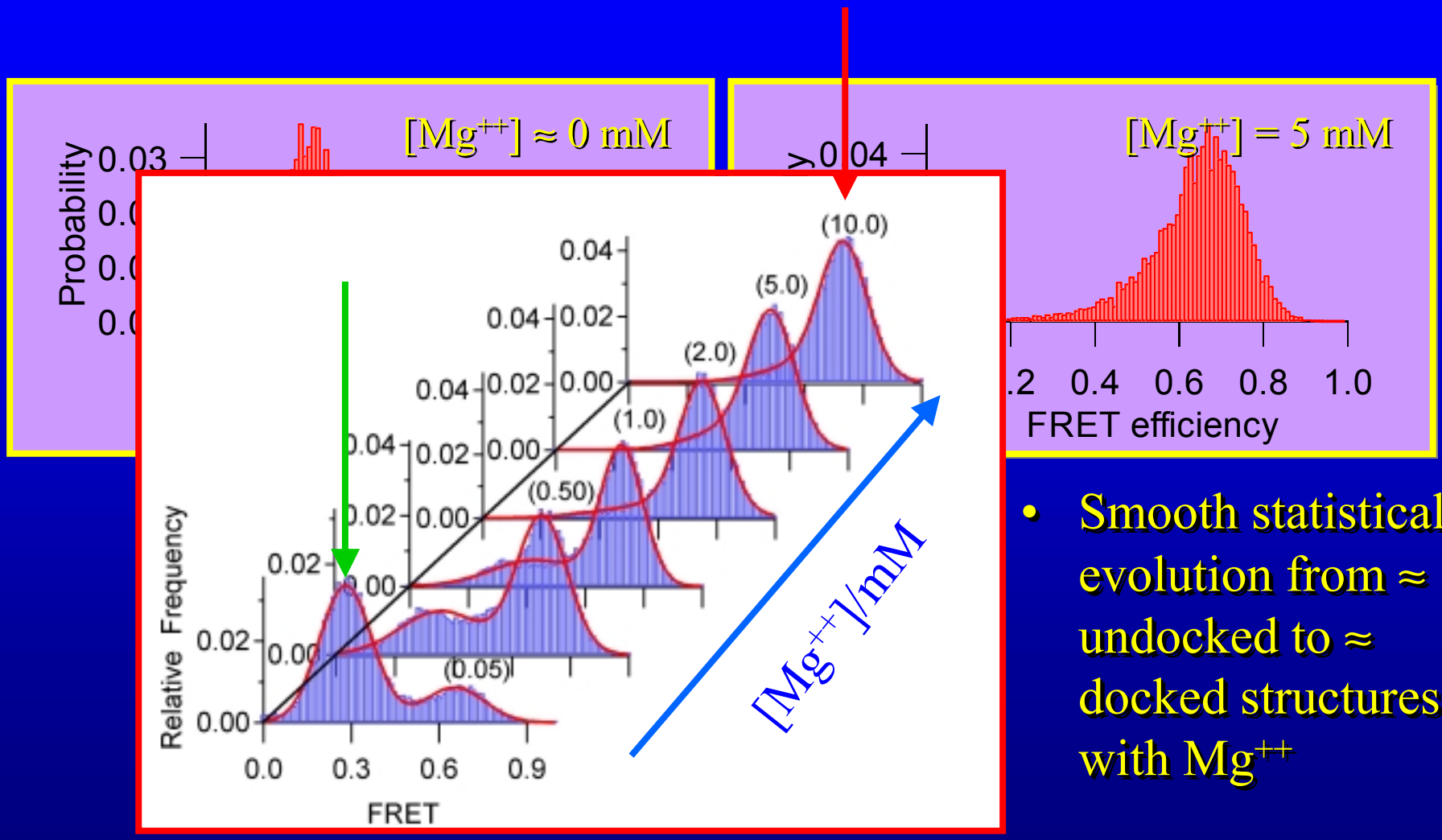
Effects of [Mg^{++}]





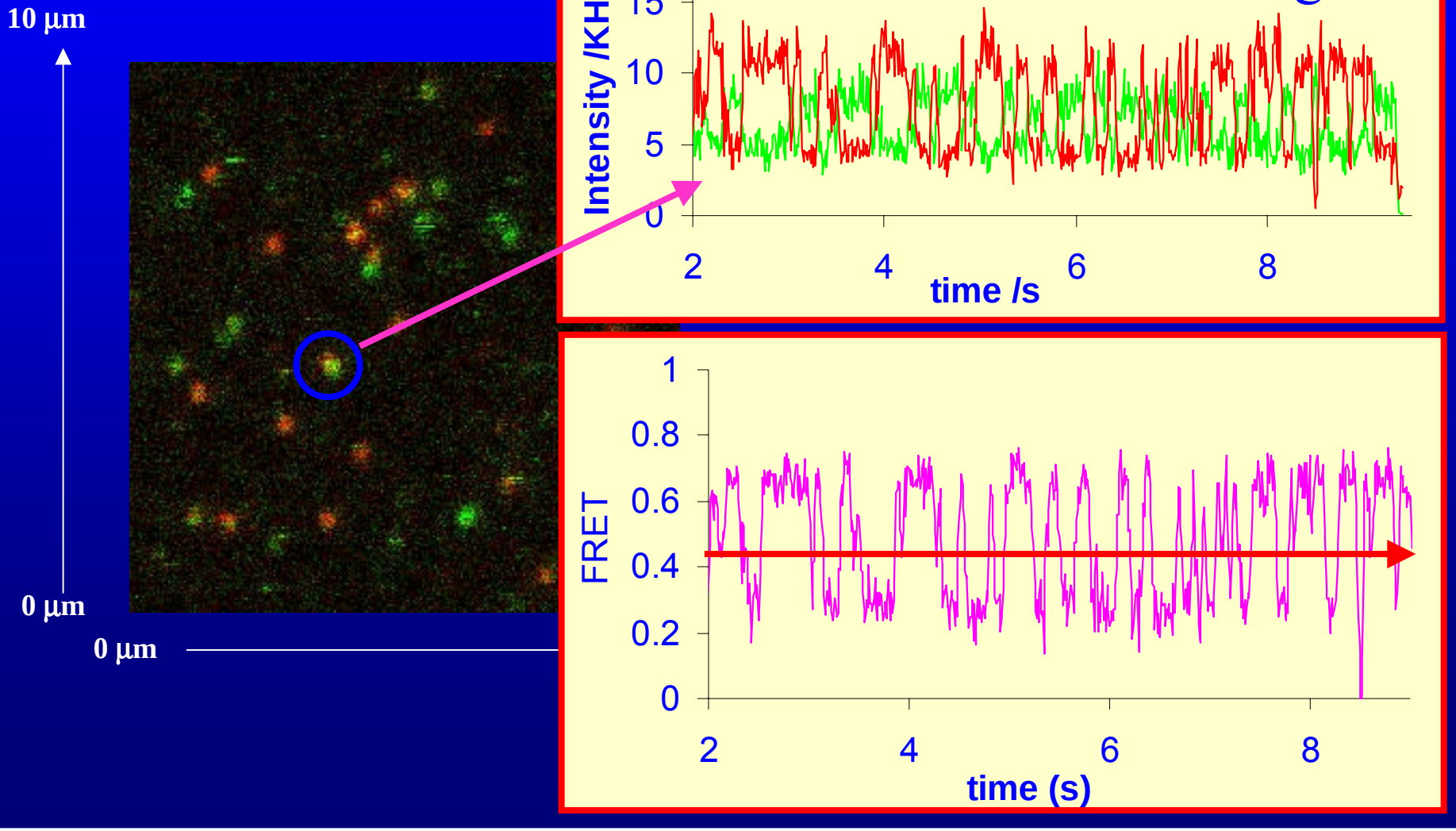
- Reversible folding for majority of single RNA constructs (65%)
- Heterogeneous presence of “nondockers” (34%) and “superdockers” (1%) with no folding dynamics on experimental time scale

FRET Titrations

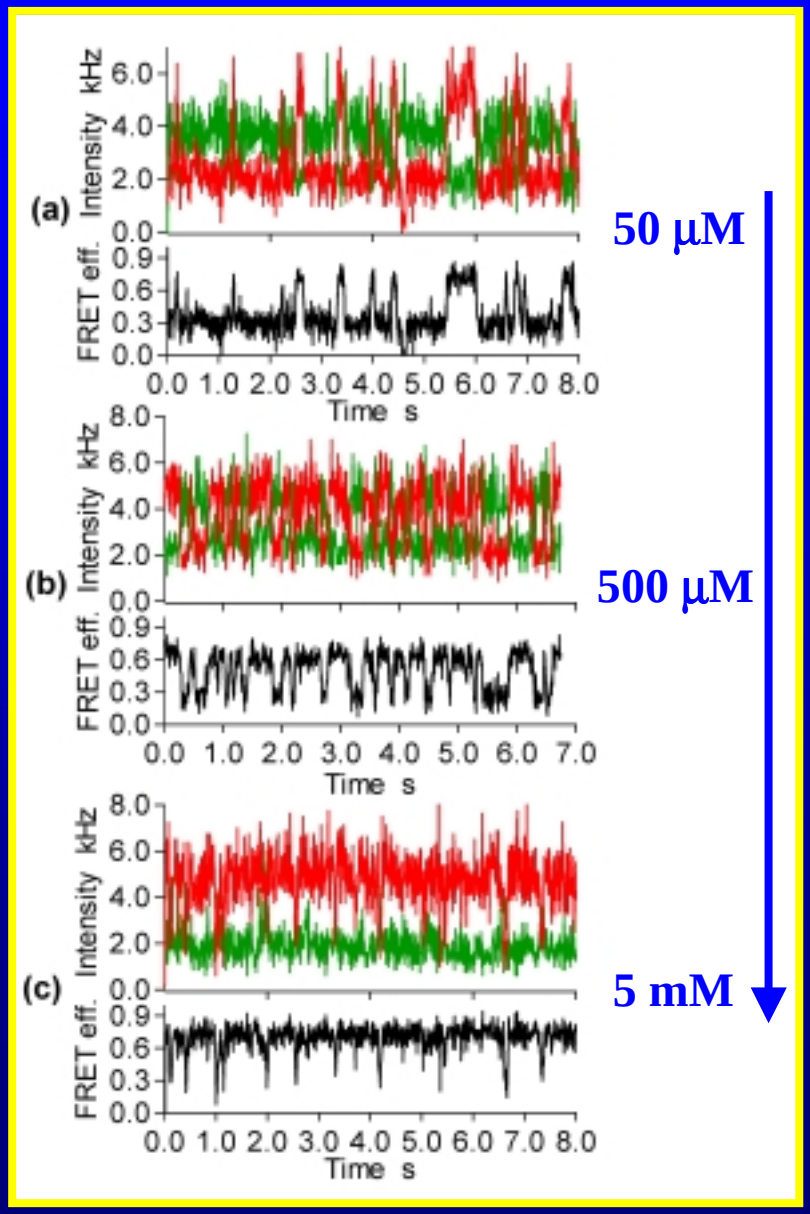


- Smooth statistical evolution from ≈ undocked to ≈ docked structures with Mg^{++}

Real Time Docking/Undocking



Mg^{++} Dependence



- Rapid increase in docked vs. undocked conformations with $[Mg^{++}]$…
- …but dominated by *increase* of k_{dock} with $[Mg^{++}]$
- Docking kinetics *not* rate limited by entropic folding effects
- Mg^{++} mediated "pre-folding" of tetraloop receptor to achieve stable docking interaction

Single Molecule Kinetics…

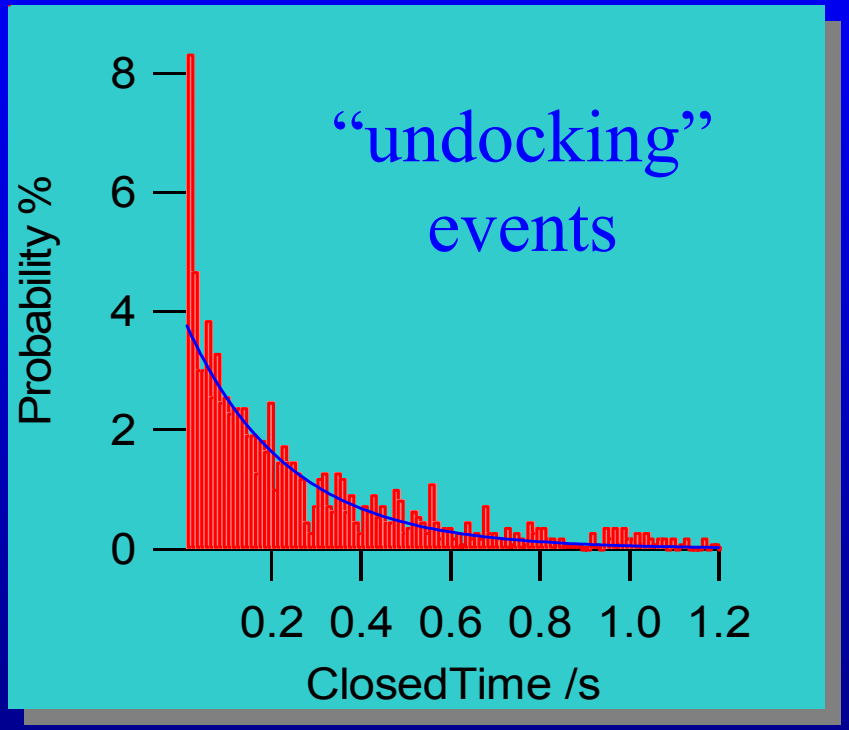
- "Concentration" ill defined – molecule A is either there or isn't!
- Think in terms of *probability* of A if definitely present at t=0, i.e. $N(t) \approx [A(t)]/A_0 = \exp(-kt)$ from ensemble kinetics
- More useful concept "Survival probability", $P(\tau)$

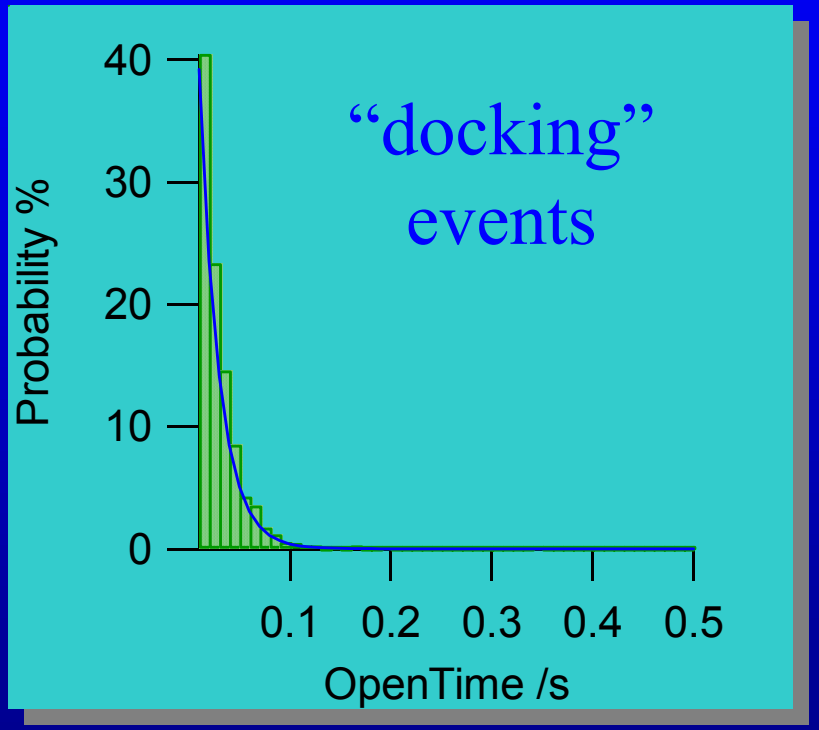
$$N(t) = 1 - \int_0^t d\tau\, P(\tau)$$

$$\Rightarrow P(\tau) = -dN(\tau)/dt \approx k \exp(-k\tau)$$

- $P(\tau)$ *exponentially distributed* in τ (for simple 2-state kinetic systems)

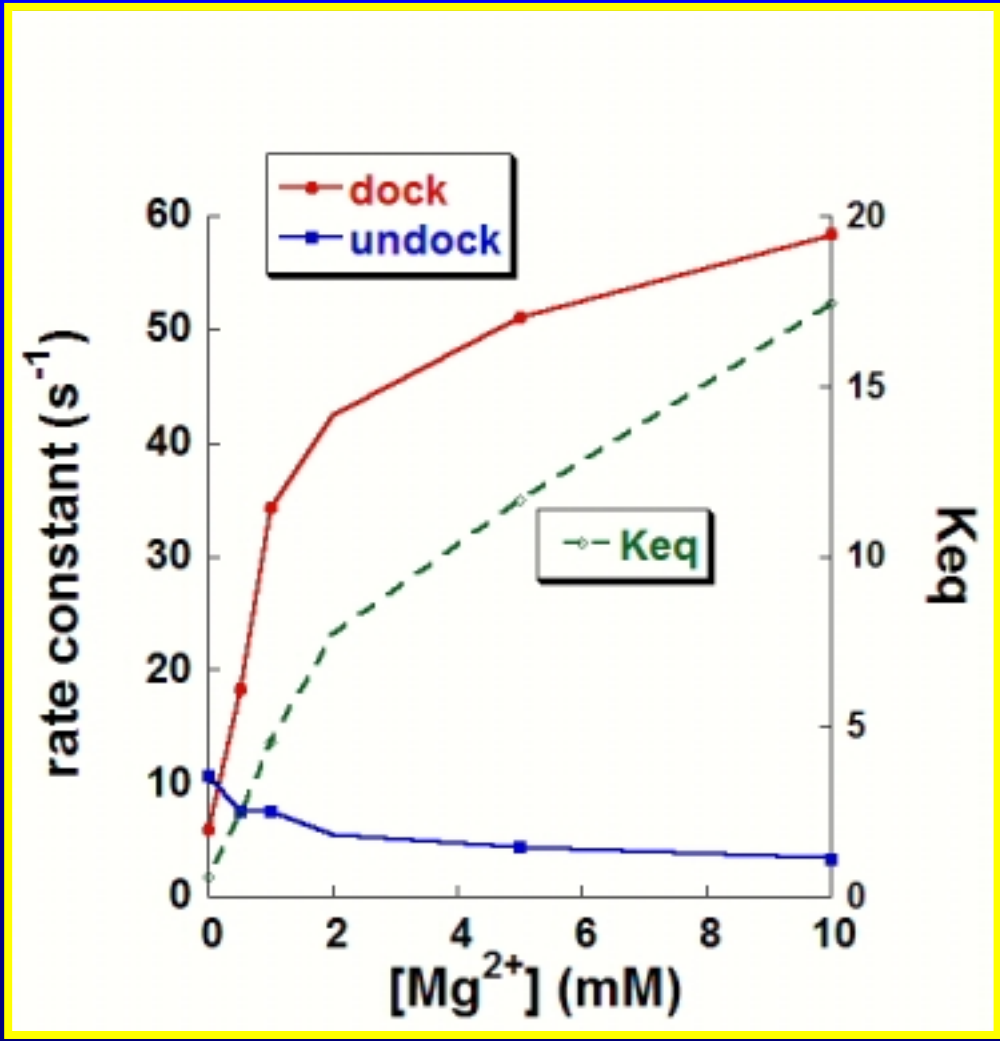
Sample Kinetic Histograms





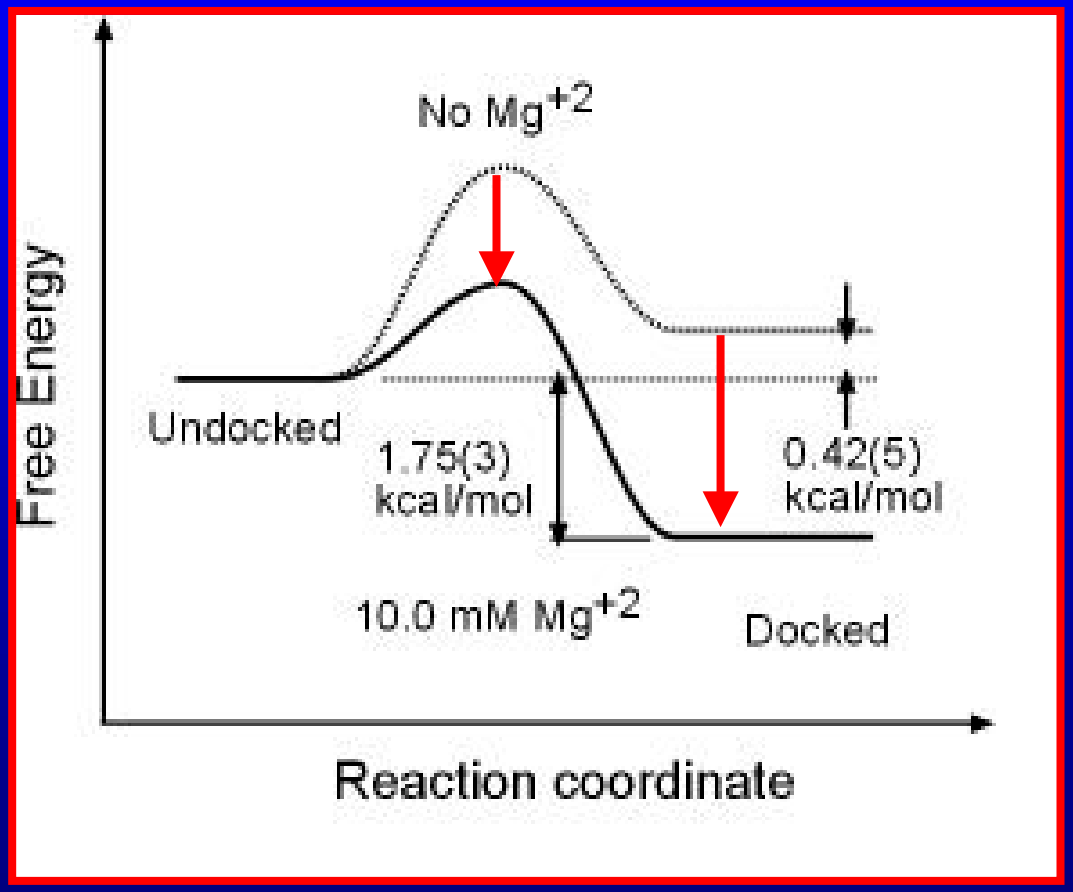
- Survival probability predicts exponential distribution of open(closed) event durations
- Rate constants from semi-log plots of histograms of open/closed time durations

Stern-Volmer Analysis



- k_{dock}, k_{undock} and $K_{eq} = k_{dock}/k_{undock}$ as function of $[Mg^{++}]$
- Rapid increase in K_{eq} with $[Mg^{++}]$ (as expected)…
- …but dominated by *increase* of k_{dock} with $[Mg^{++}]$ (Walter et al)
- Docking kinetics *not* rate limited by entropic effects

Free Energy Landscape (Dependence on Mg^{++})



- ΔG's from k_{docked}, $k_{undocked}$ at low and high Mg^{++}
- Decrease in k_{undock} with Mg^{++} implies ΔG_{docked} drops *faster* than forward activation barrier $\Delta G^{\neq}$ with Mg^{++}

Acknowledgement

Feng Dong
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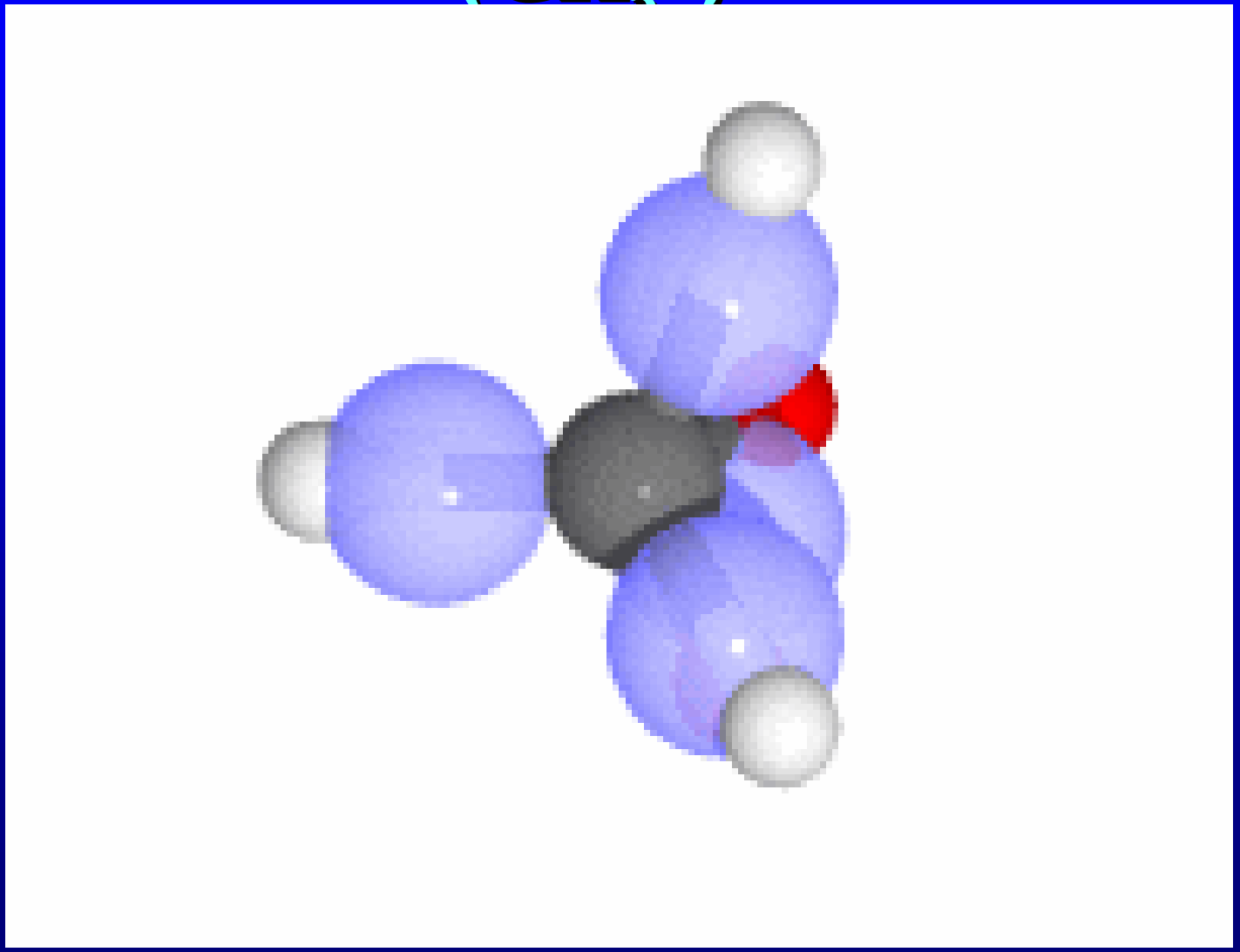
Joel Bowman
Lauri Halonen
Art Pardi

Large Amplitude Quantum Effects (CH_5^+)



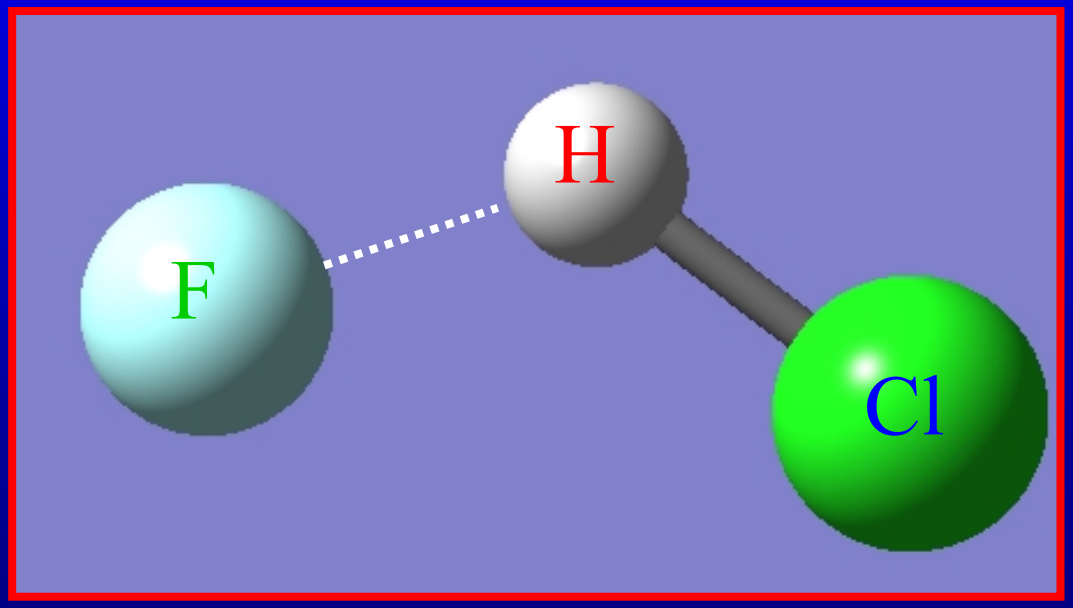
Summary (I)

- First high resolution IR spectra of H_2DO^+
- Boltzmann tunneling analysis for ground and ν_3 excited states (41.4±2.6 cm^{-1} and 26.3±2.6 cm^{-1})
- Good agreement with high level *ab initio*

Summary (II)

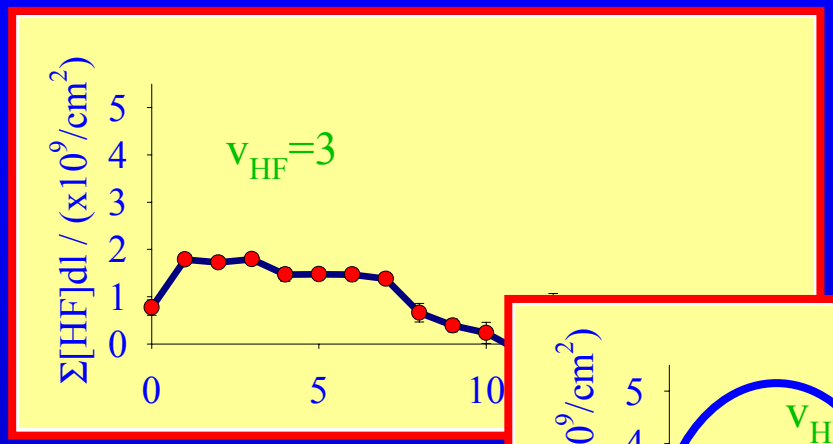
- Kinetic studies of isolated tertiary interactions at the single RNA level by spatial- and time-resolved FRET
- Clear RNA subpopulation heterogeneity in the single molecule dynamics
- Free energies for docking in absence ($\Delta G = 0.42$ kcal/mol) and presence ($\Delta G = -1.75$ kcal/mol) of saturating Mg^{++}

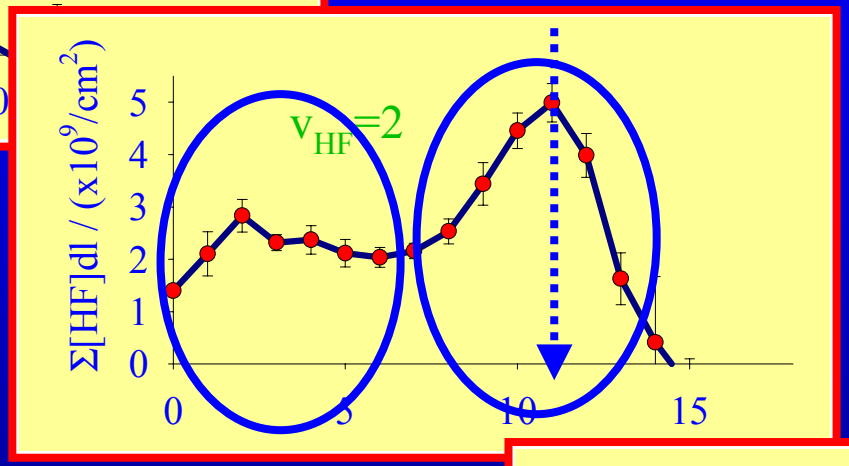
Molecular Interactions in Reaction Dynamics

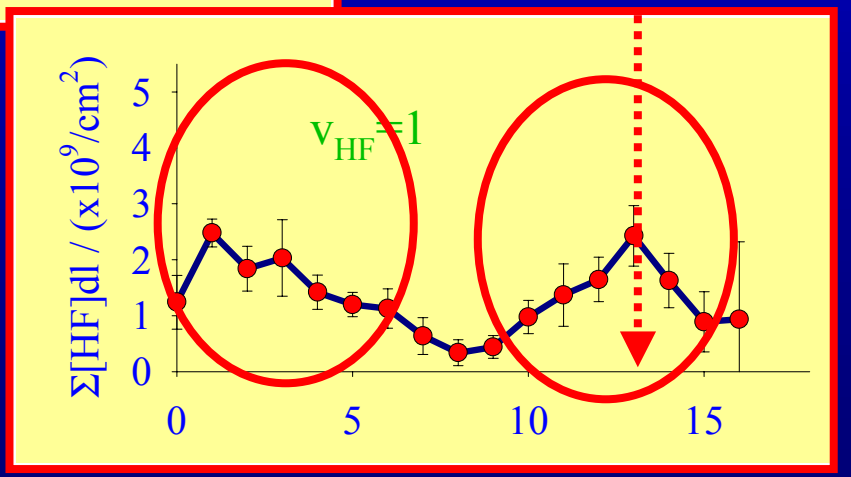


- Classic "H + LH" system (Polanyi et al)
- Non-Arrhenius kinetic behavior (Houston et al)
- Smaller N=3 permits explicit PES grid sampling in full 3D (MCSCF/MRCI+Q, spin orbit, derivative coupling)…
- …and extrapolation to complete basis set limit

What Does Experiment Say?

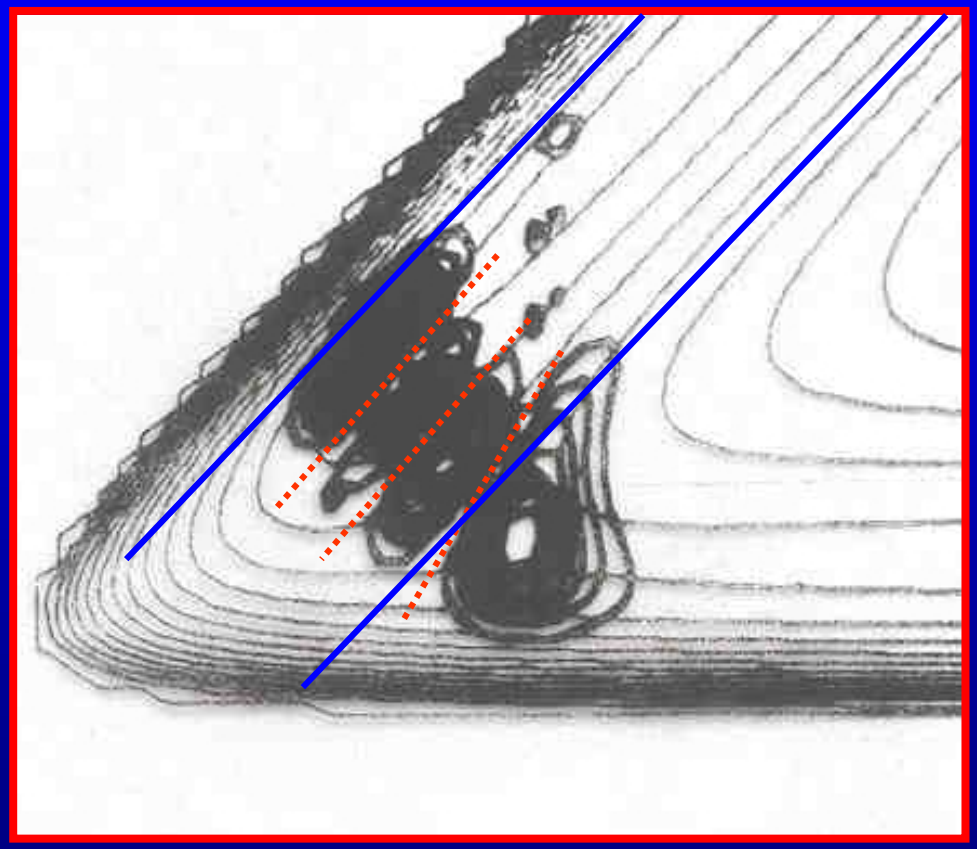






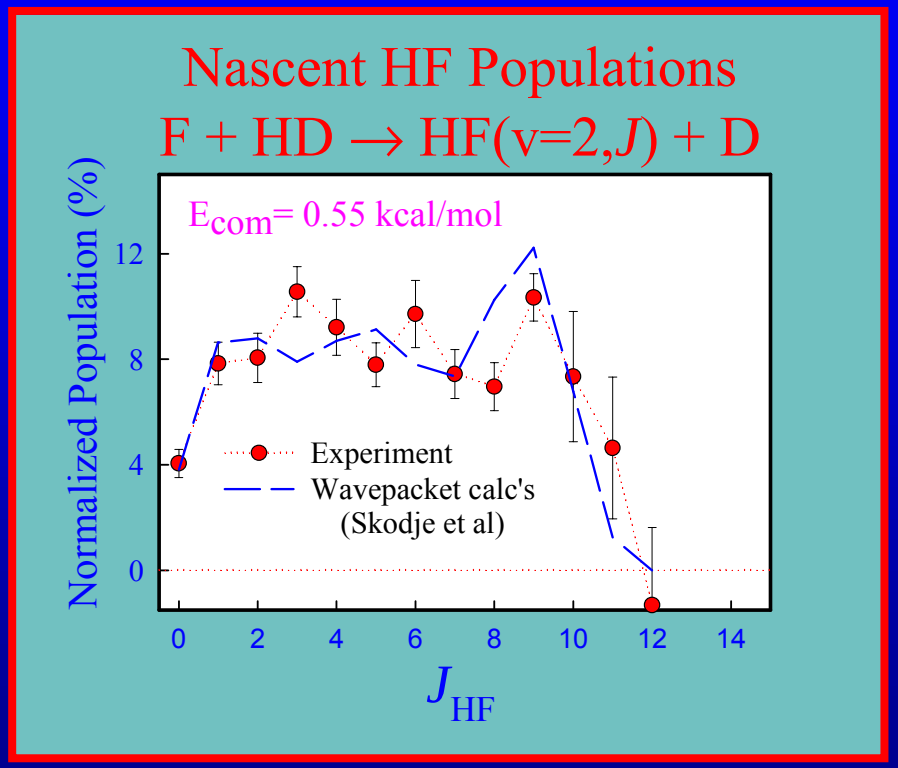
- *Rotationally bimodal* HF(v) distributions quite uncharacteristic of *direct* reaction dynamics
- Strong rotational peaking in HF(v, high J) states corresponding to HF(v+1,J≈0) states in transition region

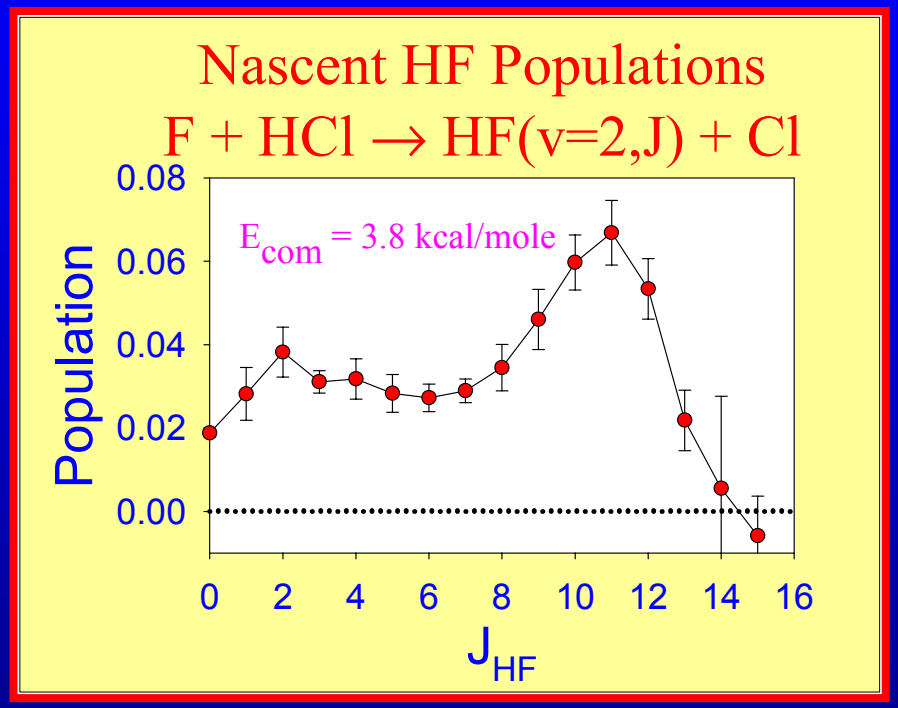
Transition State Resonances (in F--H--D)



- Quasibound resonance wave functions (high "skew angle" due to H-L-H dynamics)
- "Quantum chattering" of H between D and F atoms (Liu, Skodje et al)
- Resonance "signature" predicted in HF(v_{HF}=2,J) rotational quantum state distributions

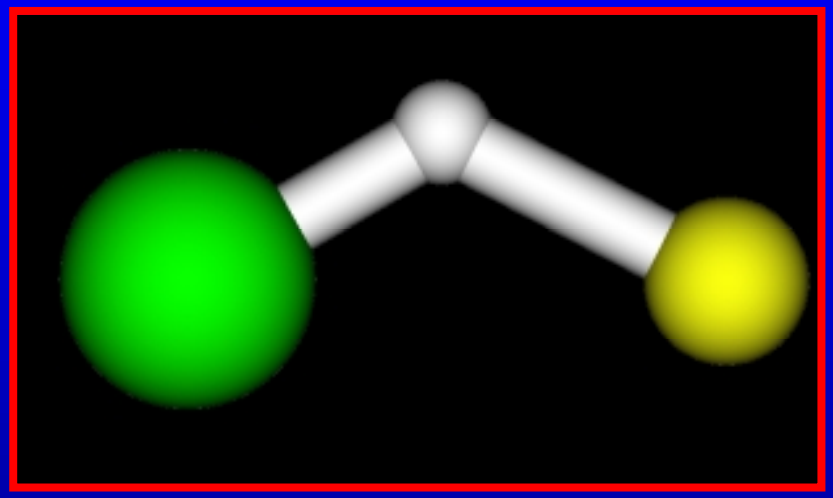
Resonance "Signature" in Nascent Product States





- Near quantitative agreement for F+HD with predictions from exact QM dynamics calculations on state-of-the-art potential surface (Stark-Werner)
- Similar contributions from transition state resonance dynamics in F+HCl?

F + HCl Transition State



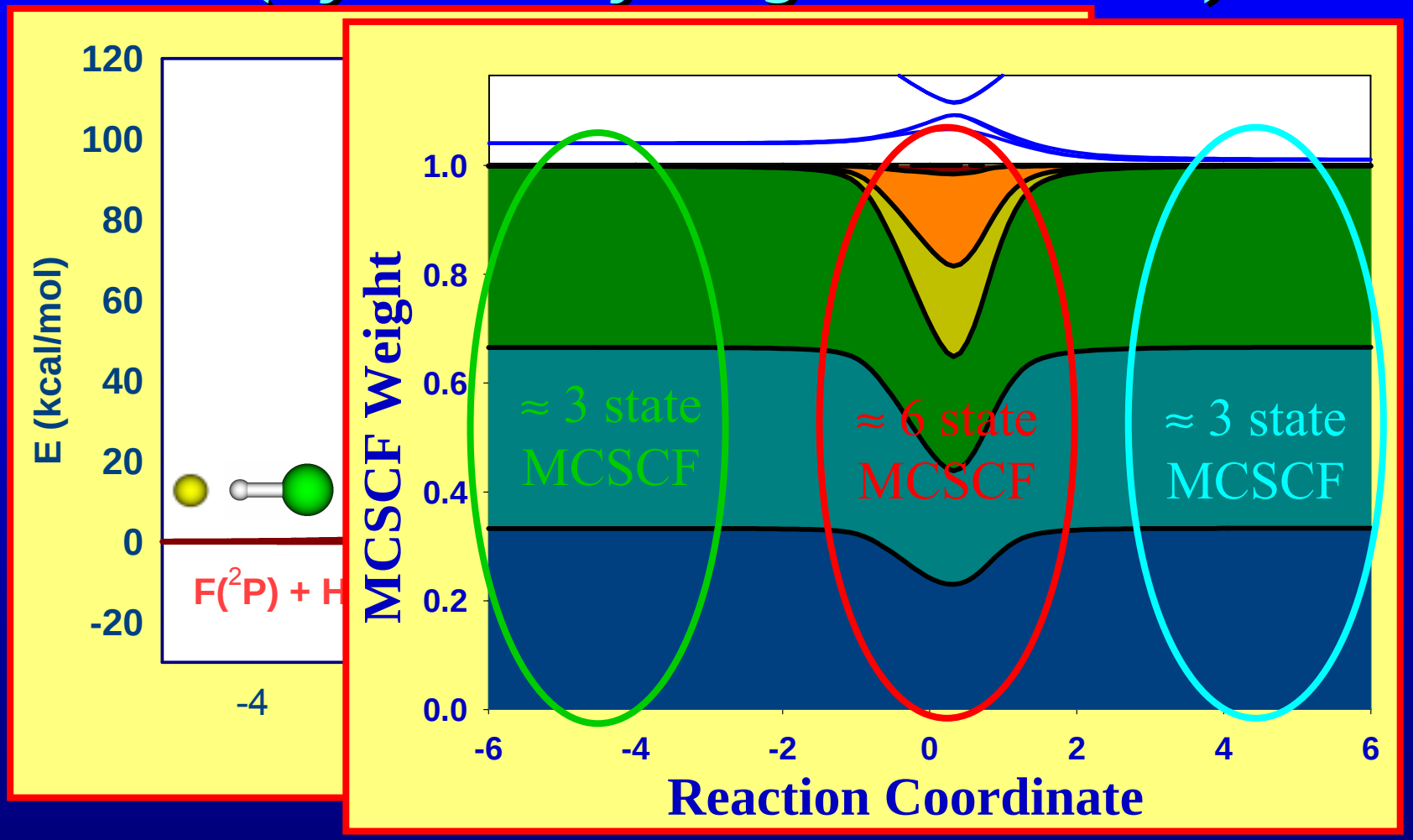
Method	Basis	Bend Angle (degree)	$\Delta E^{\ddagger}$ (kcal/mol)
UMP2*	6-311G(3d2f,3p2d)	137.4	6.2
PUMP2*	6-311G(3d2f,3p2d)	137.4	4.7
PUMP4*	6-311G(3d2f,3p2d)	137.4	4.0
CCSD(T)	AVQZ	118.0	2.2
MRCI+Q	AVDZ	126.2	4.2
	AVTZ	126.4	4.2
	AVQZ	125.9	4.2
	CBS	125.7	4.2
	Scaled	123.5	3.8

*Sayos, et. al. PCCP 1 (6): 947-956 MAR 15 1999

- Similar exothermicity to F + HD (≈ 33 kcal/mol)
- Somewhat higher reaction barrier (≈ 4 kcal/mol)
- *Strongly bent* F-H-Cl transition state ($\theta \approx 123^{o}$)

F + HCl Reaction Path

(Dynamically weighted MCSCF)



- Continuously weighted # of states in MCSCF ⇒ smooth reaction path and PES's (no spurious "root flipping")

Exothermicity Benchmarks

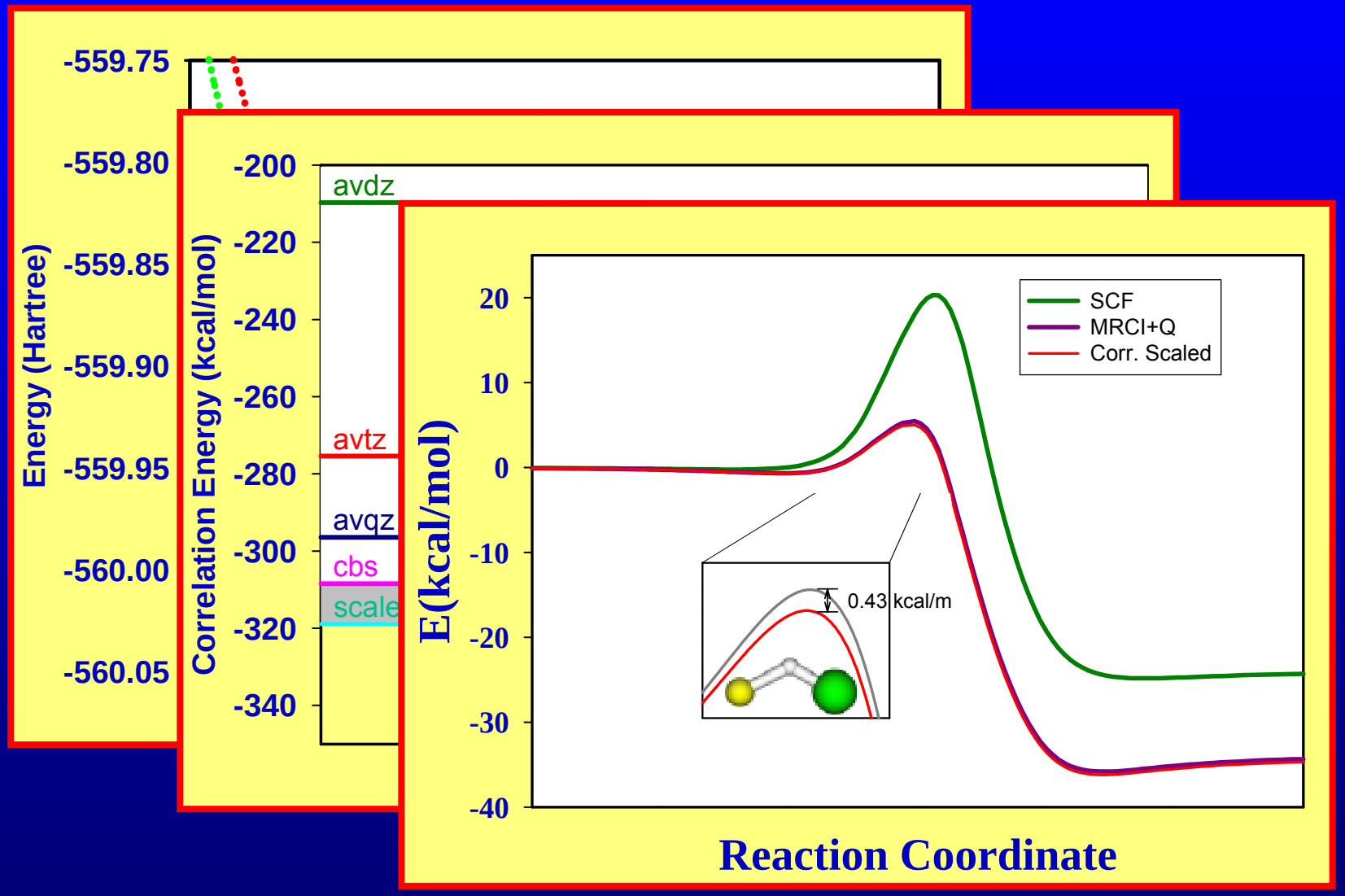
Method	avdz	avtz	avqz	cbs	Error
HF	-19.3	-18.83	-18.67	-18.57	-14.49
MCSCF	-23.1	-22.87	-22.75	-22.68	-10.38
MRCI	-30.41	-29.98	-29.91	-29.87	-3.19
MRCI+Q	-31.33	-31.04	-30.94	-30.88	-2.18
MP2	-37.17	-37.52	-37.78	-37.95	4.89
CCSD	-32.27	-32.5	-32.62	-32.69	-0.37
CCSD(T)	-32.41	-33.1	-33.29	-33.39	0.33

- CBS extrapolation (AVnZ, n=D,T,Q,5…) converges nicely, but still missing some (core) correlation energy (few kcal/mol)

Correlation Scaling

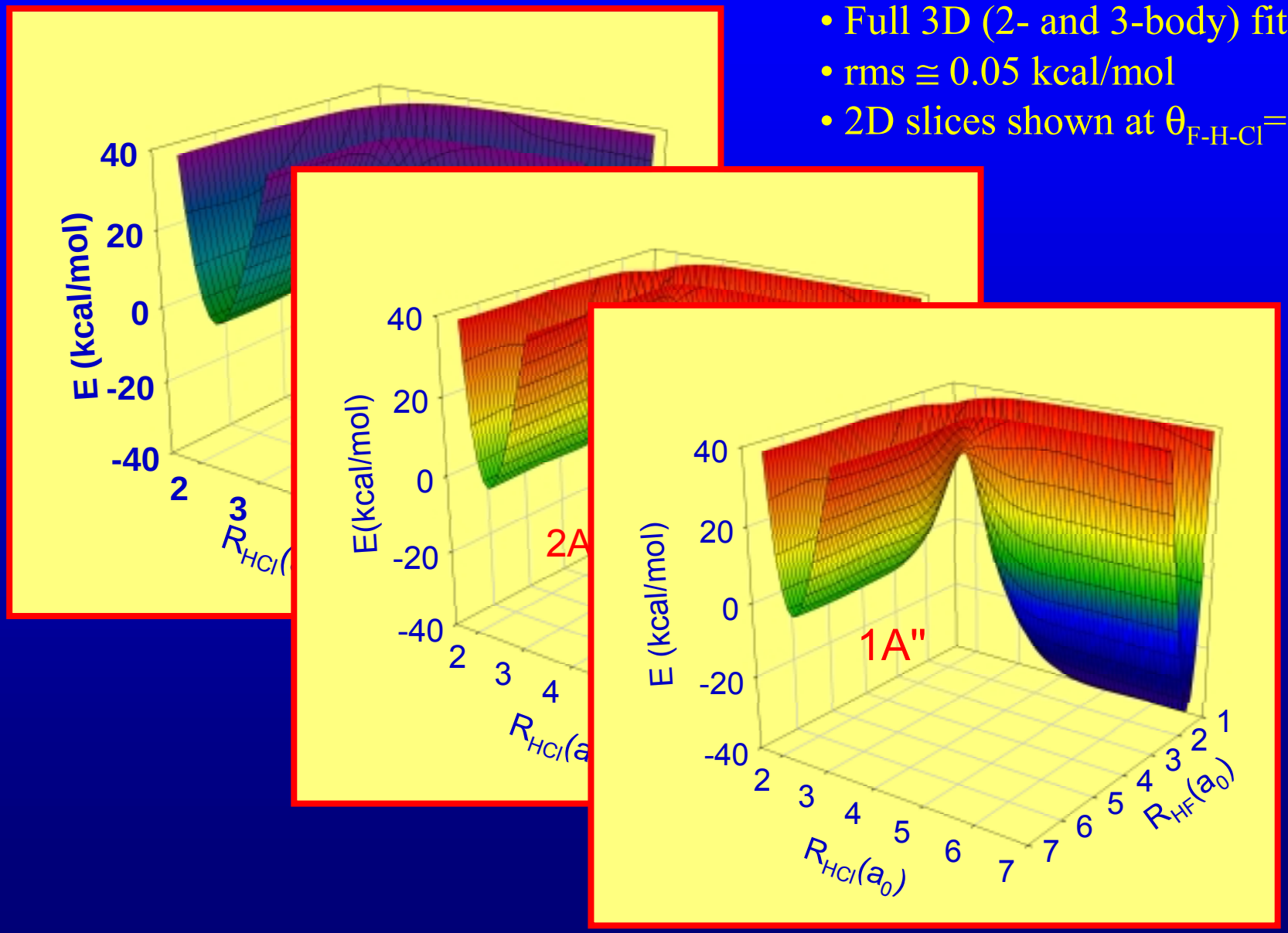
- $E_{corr} = E_{MRCI} - E_{MCSCF}$
- Define $E_{true} = E_{MCSCF} + \gamma E_{corr}$
- Empirically calibrate γ *once* based on experimental reaction exothermicity
- Use *same* γ for all points on PES (Peterson et al)

In Practice…

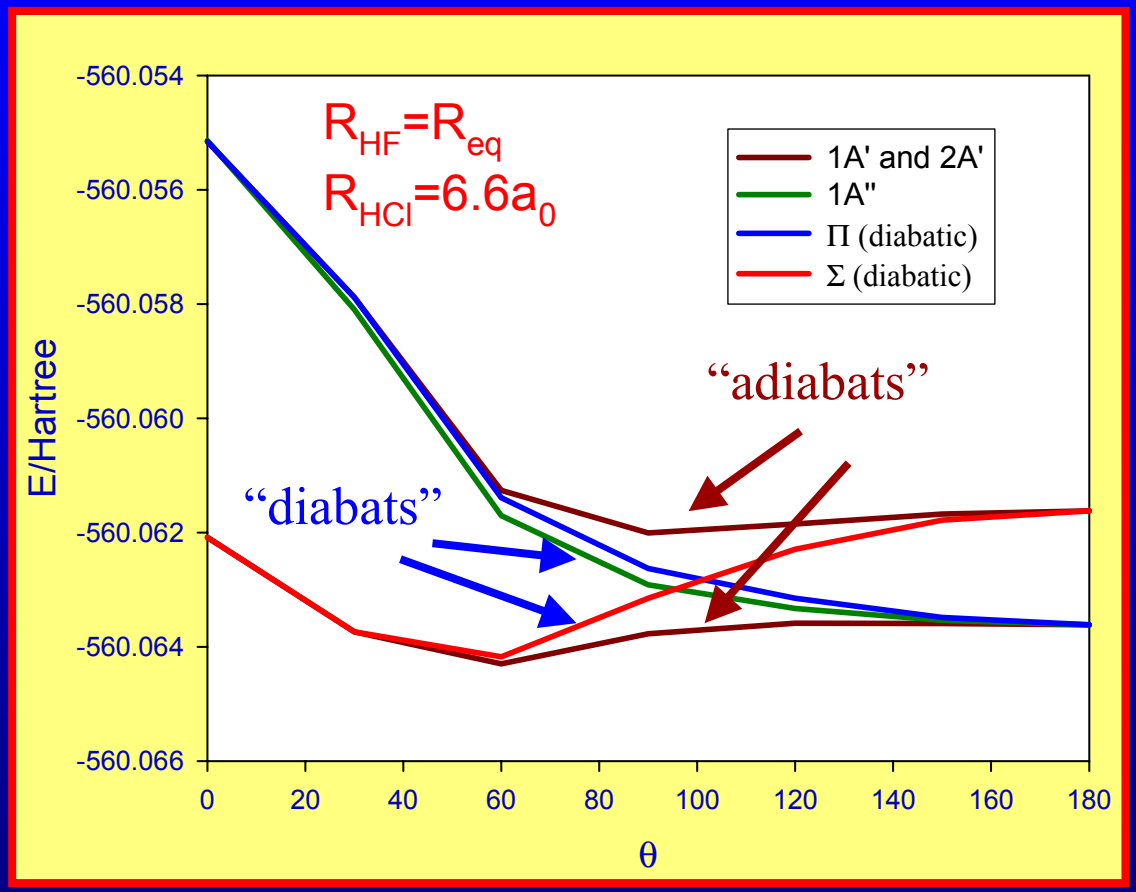

-559.75
-559.80
-559.85
-559.90
-559.95
-560.00
-560.05
Energy (Hartree)
-200
-220
-240
-260
-280
-300
-320
-340
Correlation Energy (kcal/mol)
avdz
avtz
avqz
cbs
scale
20
10
0
-10
-20
-30
-40
E(kcal/mol)
SCF
MRCI+Q
Corr. Scaled
0.43 kcal/m
Reaction Coordinate

Adiabatic Potential Surface(s)

- Full 3D (2- and 3-body) fits
- rms ≅ 0.05 kcal/mol
- 2D slices shown at $\theta_{F\text{-}H\text{-}Cl} = 123^{o}$

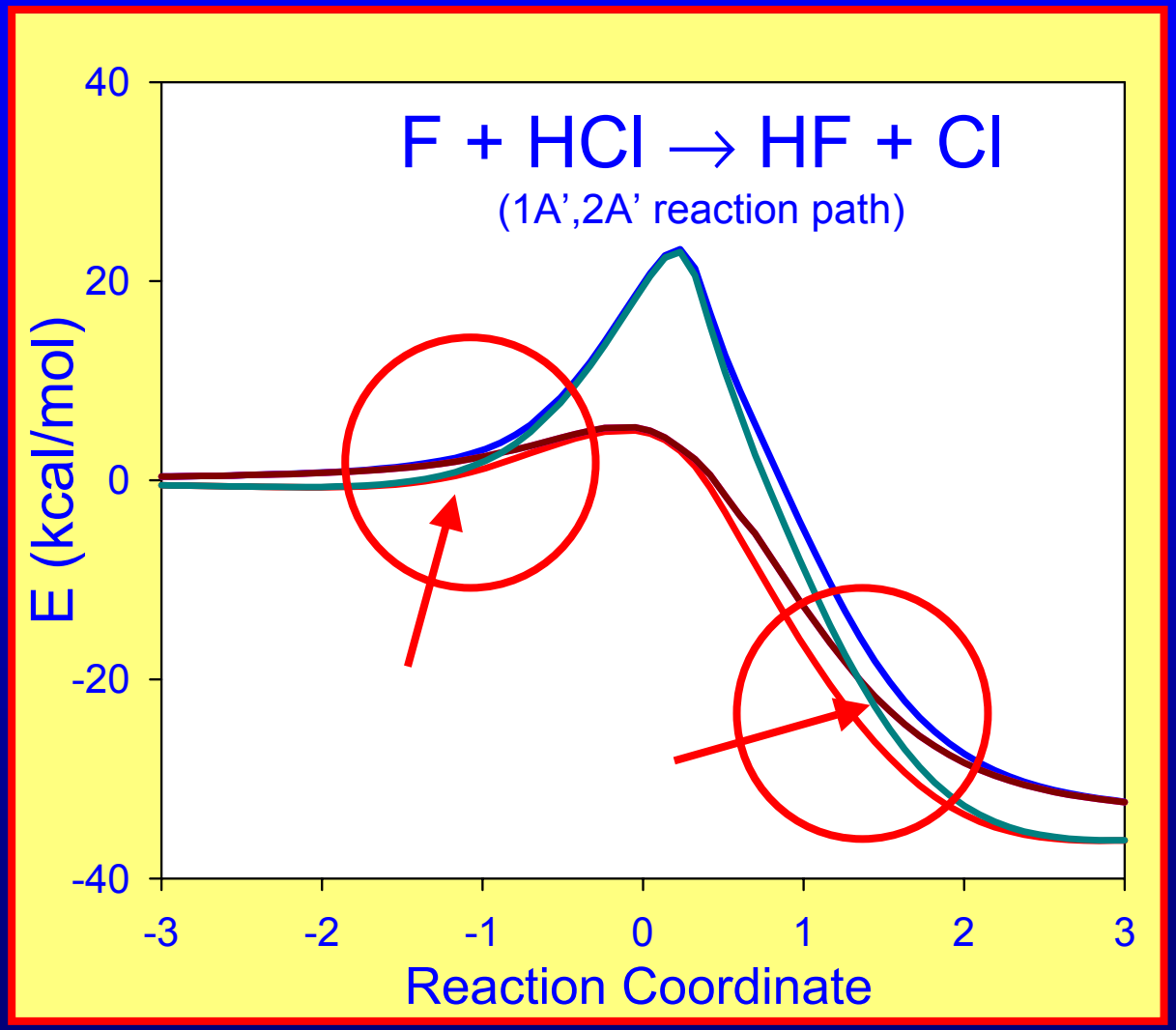


Obtaining *Diabatic* Surfaces



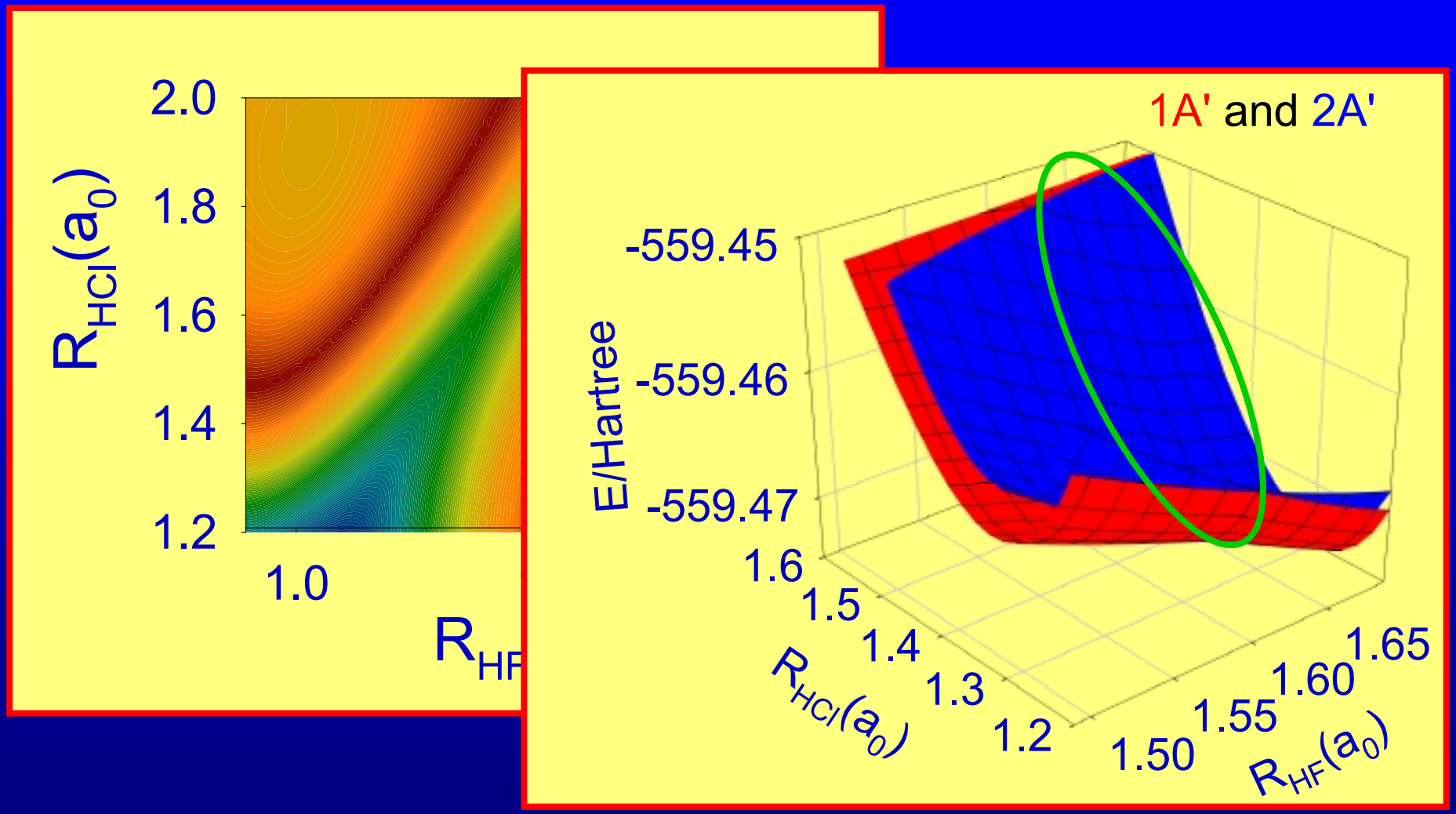
- 1A', 2A', 1A" *diabatic* surfaces built up from "θ scans" at constant r_{HCl}, r_{HF}
- Match *adiabatic* surfaces at θ = 0, 180 (i.e. zero coupling)
- Analytical fits to full 3D diabatic surfaces and non-adiabatic couplings

Interesting Potential Landscapes?



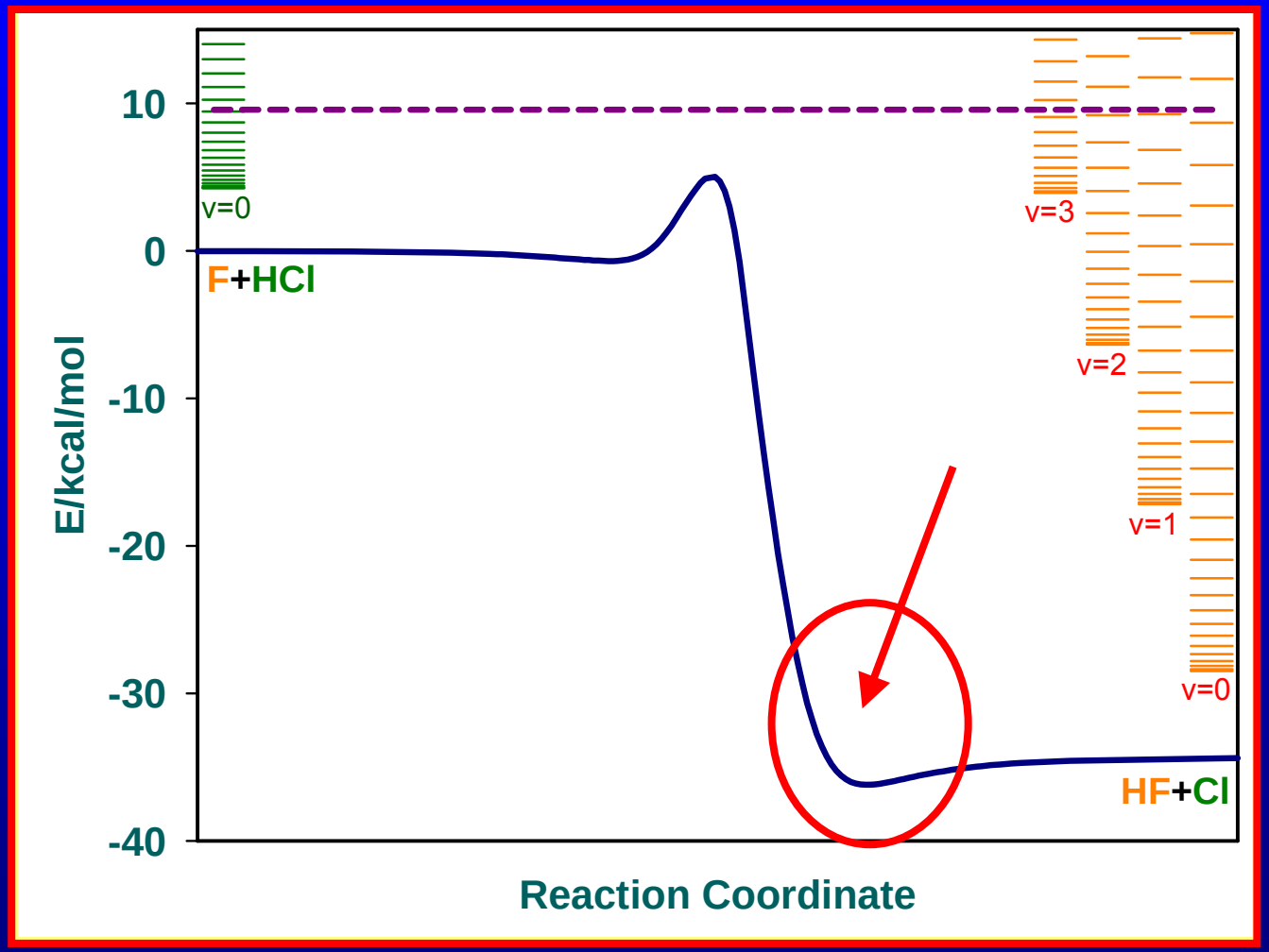
- $E_\Sigma > E_\Pi$ at large distances, $E_\Sigma < E_\Pi$ in chemical region
- Implies Σ, Π *crossing* surfaces for *collinear* F-HCl geometry…
- …but 1A', 2A' *non-crossing* surfaces for *bent* geometry
- Conical intersection seam!!!

Conical Intersection Seams…



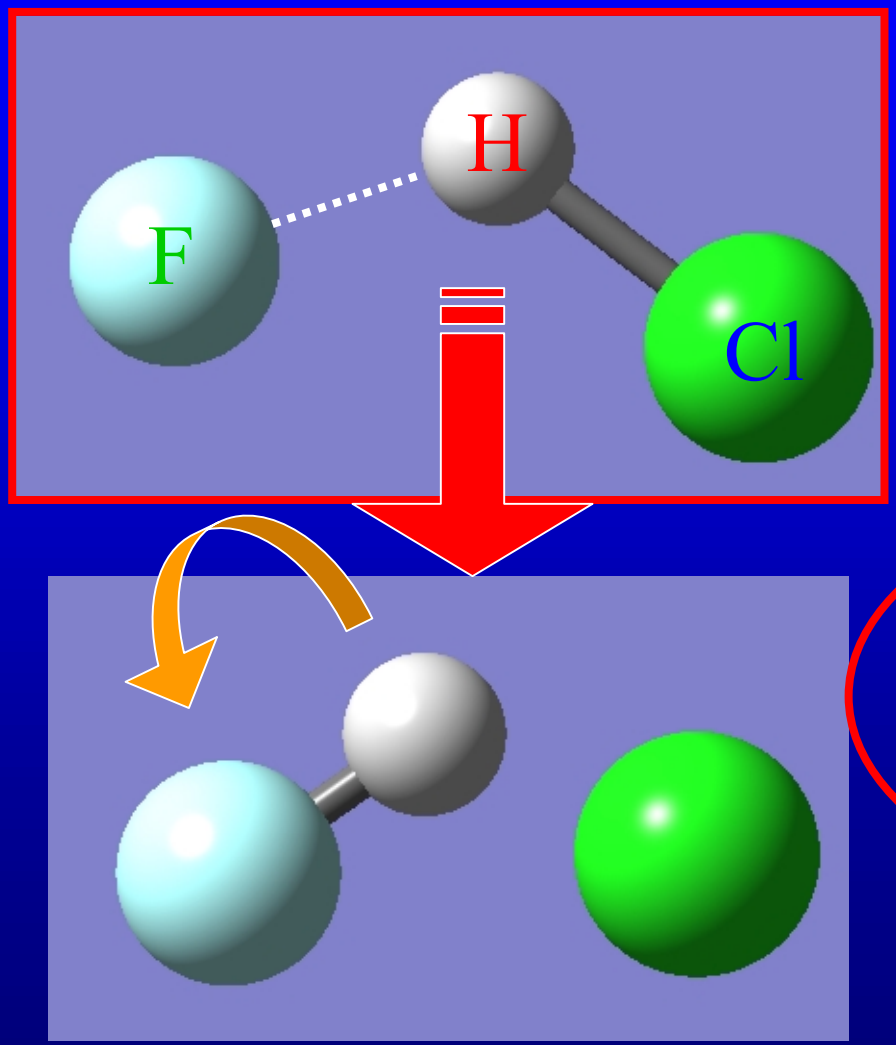
- Conical seam regions accessible at energies < E_{TS}

… and Van der Waals Wells



- Dipole-induced dipole “trap” for nascent HF(v)--Cl products!

High J States? A Physical Picture



- "Franck-Condon" projection of resonance wf onto asymptotic HF states
- ⇒ structured HF(v=2,J) distributions due to bend resonance wave function (e.g. H_2O photolysis studies by Andresen, Schinke, Crim)
- Vibrational predissociation of dipole bound "HF(v=3)--Cl" van der Waals complex
- ⇒ peaking in HF($\Delta v = -1$, $J \approx 11$) (e.g. VdW's fragmentation studies by Miller, Klemperer and others)