Selective Gas-Phase Ion-Vapor Clustering To Enhance Ion Mobility Separation Factors: Deducing Association Energies

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ACKNOWLEDGEMENTS

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Collaborators

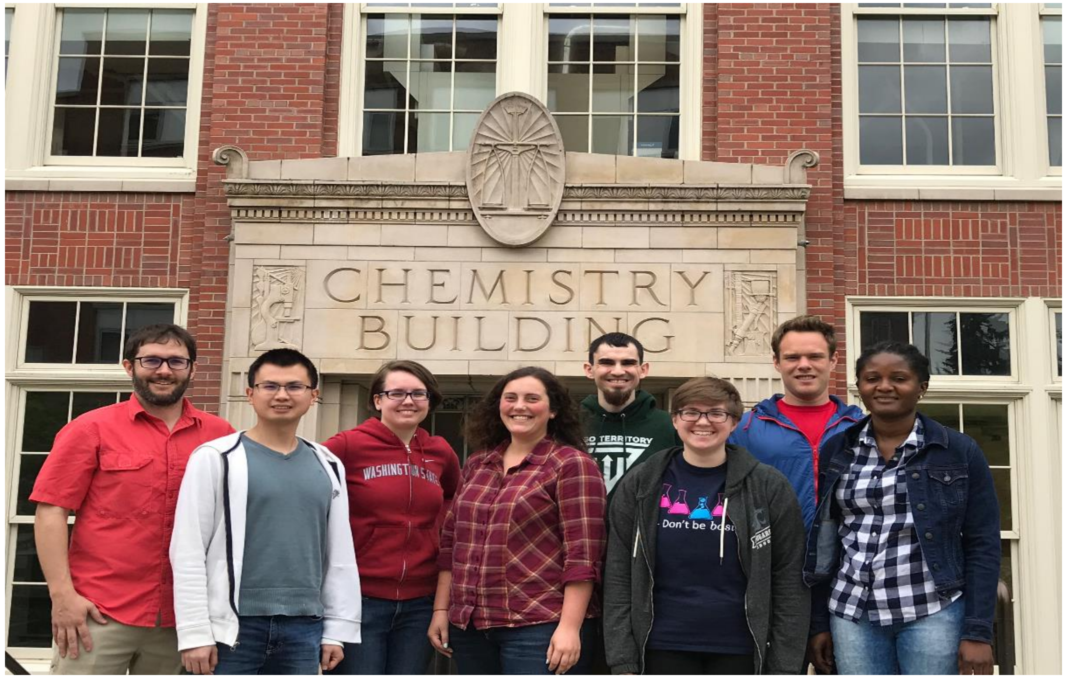
Dr. Christopher Hogan

- University of Minnesota

Dr. Hui Ouyang

- University of Texas-Dallas

Clowers Research Group

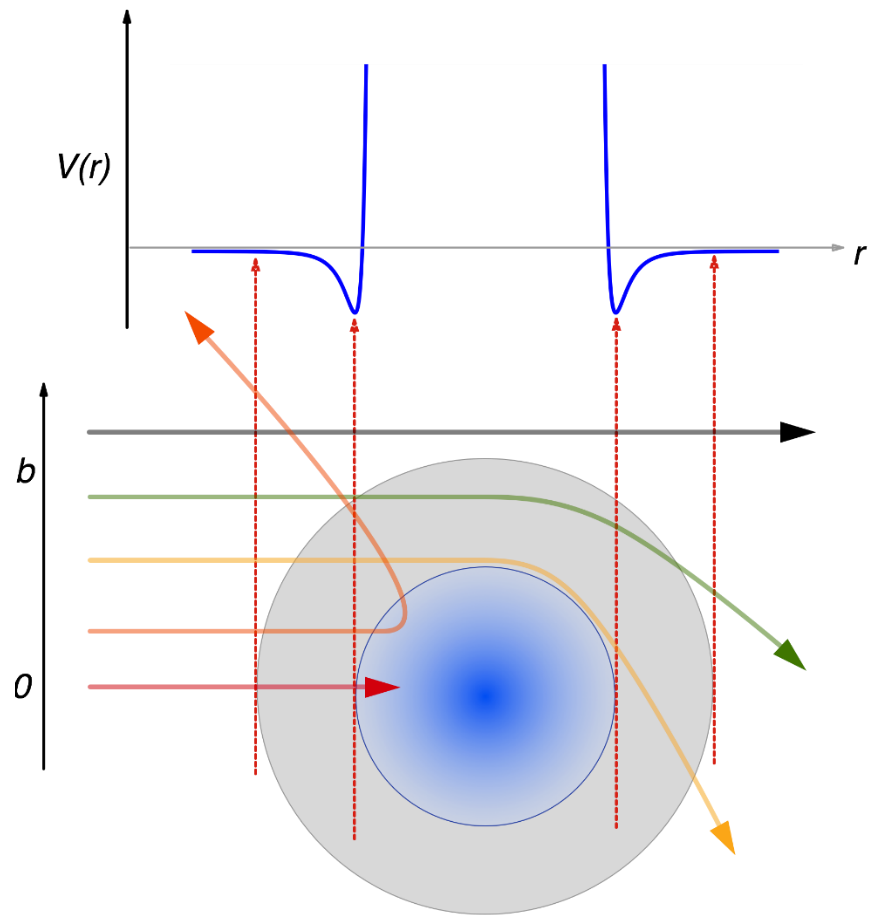


Ion Mobility Spectrometry

$$K = \frac{3qE}{16N}\left[\frac{2\pi}{\mu k \boldsymbol{T_{eff}}}\right]^{1/2}\left[\frac{1}{\Omega}\right]$$

Ion Effective Temperature

Ion-Neutral
Collision Cross Section



- Makes a few assumptions regarding ion-neutral interactions
  - Collisions are instantaneous
  - Ion-ion interactions are negligible
  - There is no ion-neutral clustering
  - Ions are at equilibrium

E. Mason, E. McDaniel. *Transport Properties of Ions in Gases*. Wiley, 1988, ASMS 2010 Reprint

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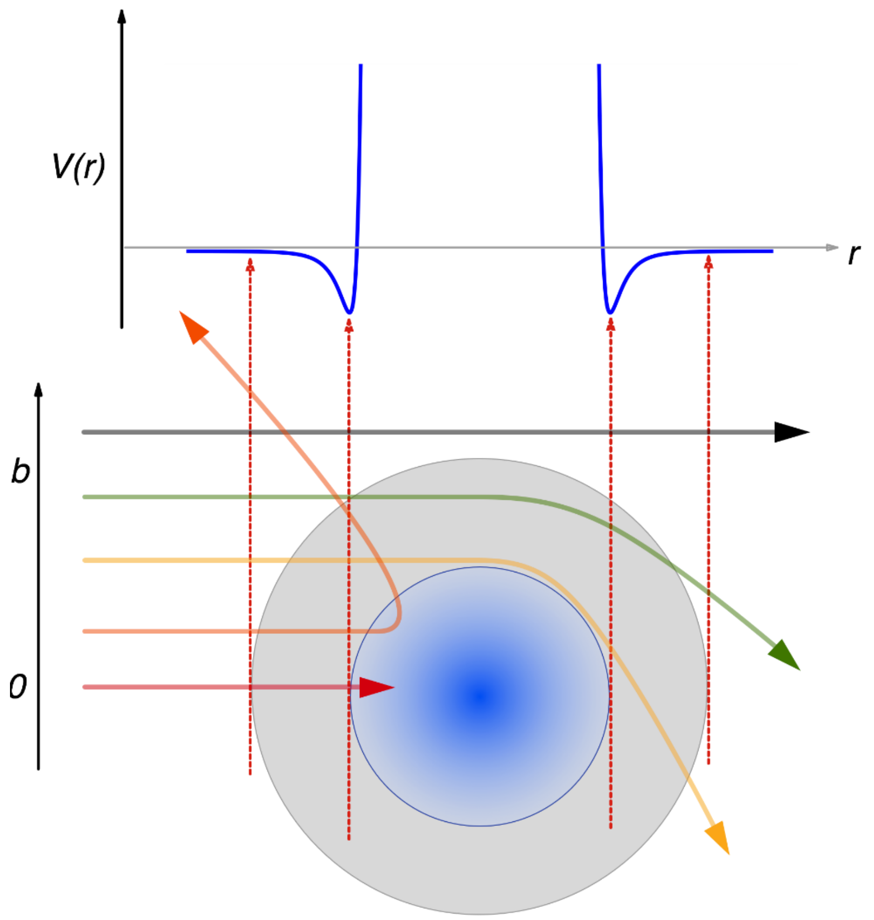

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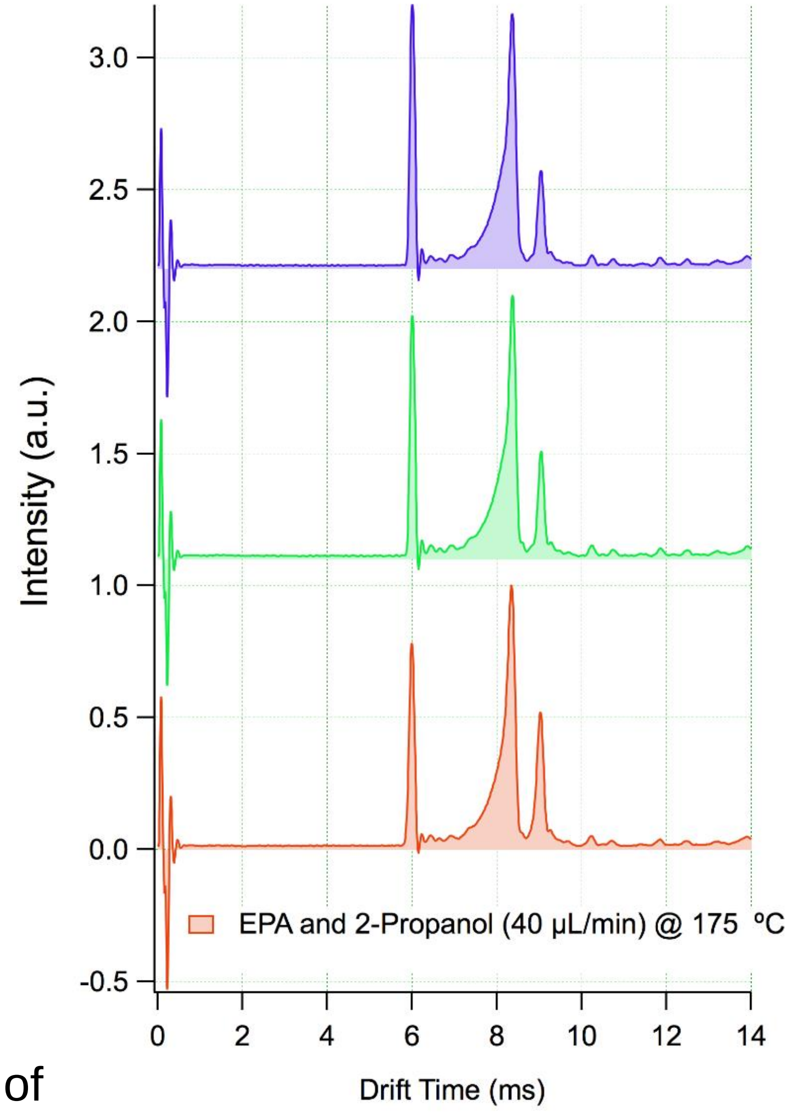
Gas Phase Ion Clustering

- Initial interpretations focused on simplified assumptions related to simple hetero- and homodimers.

- Driven by observations of m/z clusters and peak tailing.
  - Stochastic degradation



This work is aimed at complementing the work at low pressures conducted by Armentrout, Kebarle, Bowers, Castleman, Ervin, Maut-ner, and a range of other researchers making precise gas-phase clustering measurements.

Reaction Quotient > K

The reaction favors the reactants

Reaction Channel

1 $$MH^+ + M \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} MH^+M$$

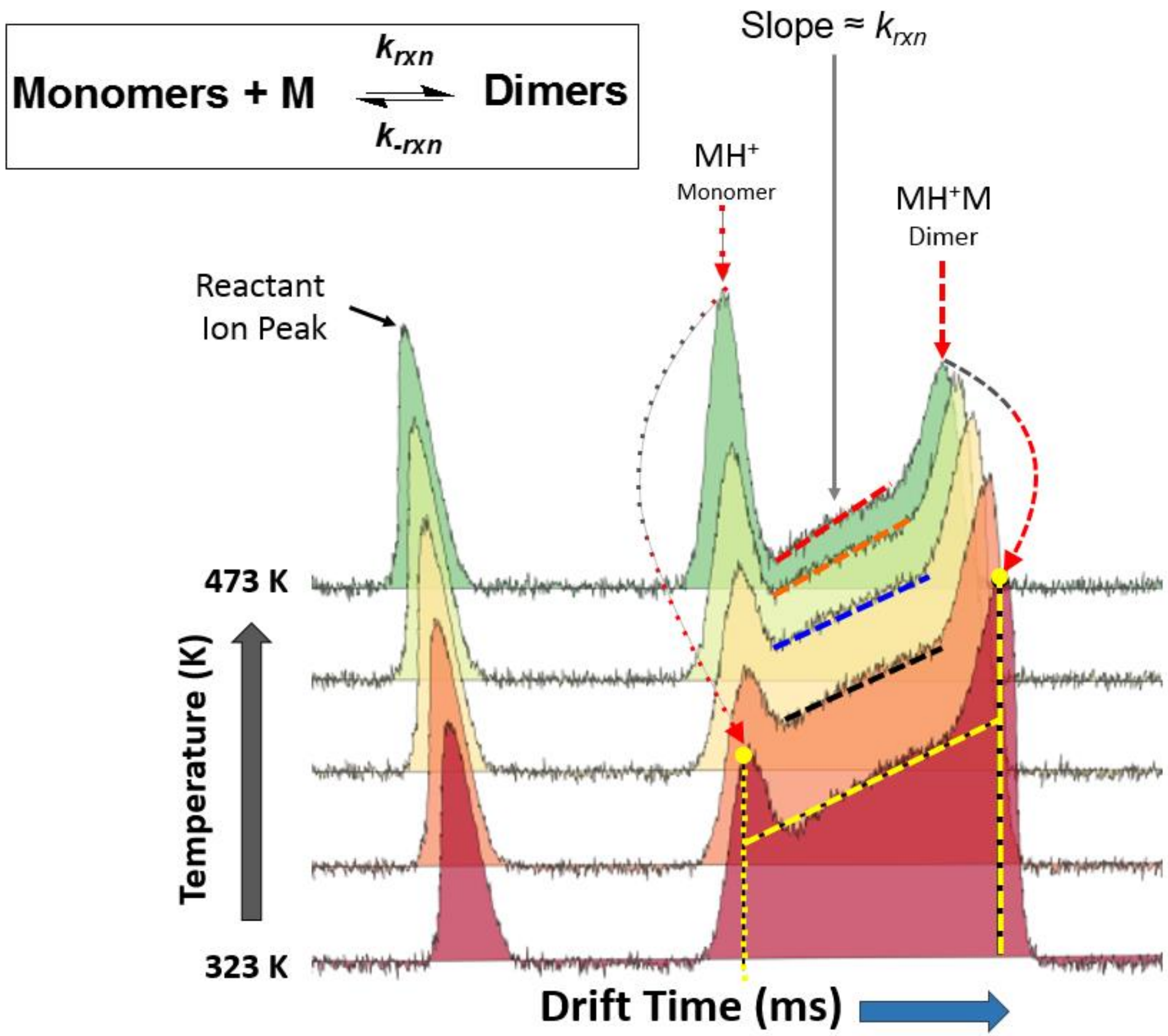
2 $$MH^+(H_2O) + M \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} MH^+M(H_2O)$$

3 $$MH^+(H_2O)_2 + M \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} MH^+M(H_2O)_2$$

⋮

n $$MH^+(H_2O)_n + M \underset{k_{-n}}{\overset{k_n}{\rightleftharpoons}} MH^+M(H_2O)_n$$

$$\textbf{Monomers + M} \underset{k_{-rxn}}{\overset{k_{rxn}}{\rightleftharpoons}} \textbf{Dimers}$$



PEAK FRONTING AND CLUSTER PROPERTIES

- R.G. Ewing et al. determined the rate constants for the decomposition of DMP proton bound dimer.
- Jazan et al. studied the rate constants for the formation of DMP, DMMP and MIBK proton-bound dimer
- Grimsrud probed the clustering interactions with DMP and water using IMS

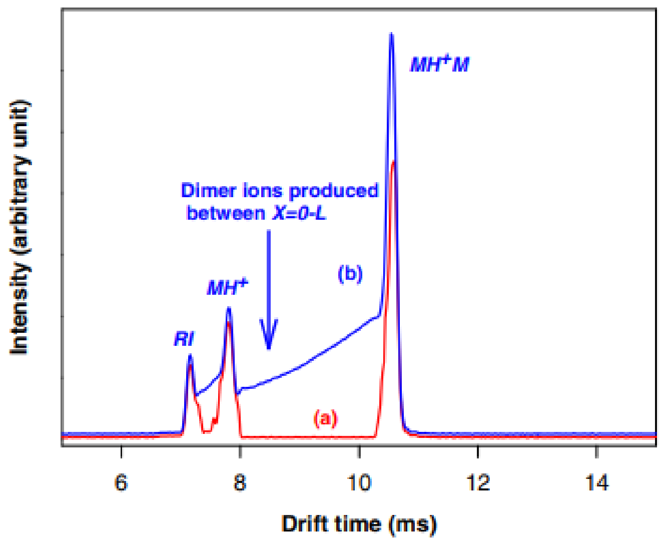
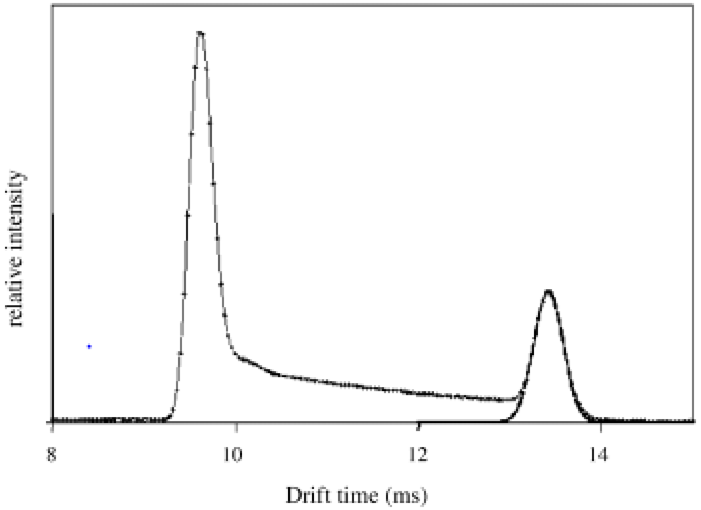


Fig. 2. The ion mobility spectrum of DMP: (a) the sample was introduced into the ionization region, and (b) the sample was introduced into the drift region. RI stands for reactant ions.



Mobility spectra of DMP with 5.0 cm drift length: 353K, 5 ppmv, water vapor. Gaussian functions fitted to the proton bound dimer peak is shown

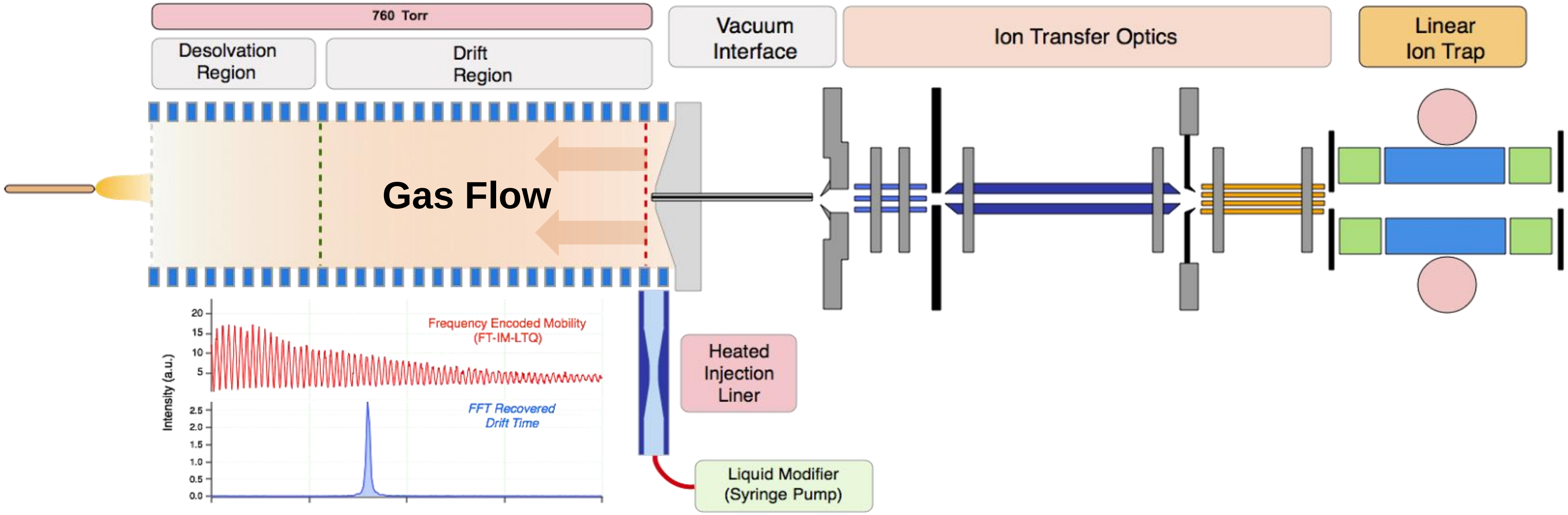
Jazan, E., Tabrizchi, M. *Chem Phys*, **2009**, *355*.
Ewing, R.G., Eiceman, G.A., Harden, C.S. and Stone, J.A. *Int J. Mass Spectrom*, **2006**, 255.

Instead of focusing just on rates of decay…

Can we develop a method that probes gas-phase equilibrium using *peak location*?

IMS-ION TRAP MODIFIER EXPERIMENT

- Integrated Faraday plate for direct ion current measurements.
- Frequency encoded mobility spectra to enhance duty cycle

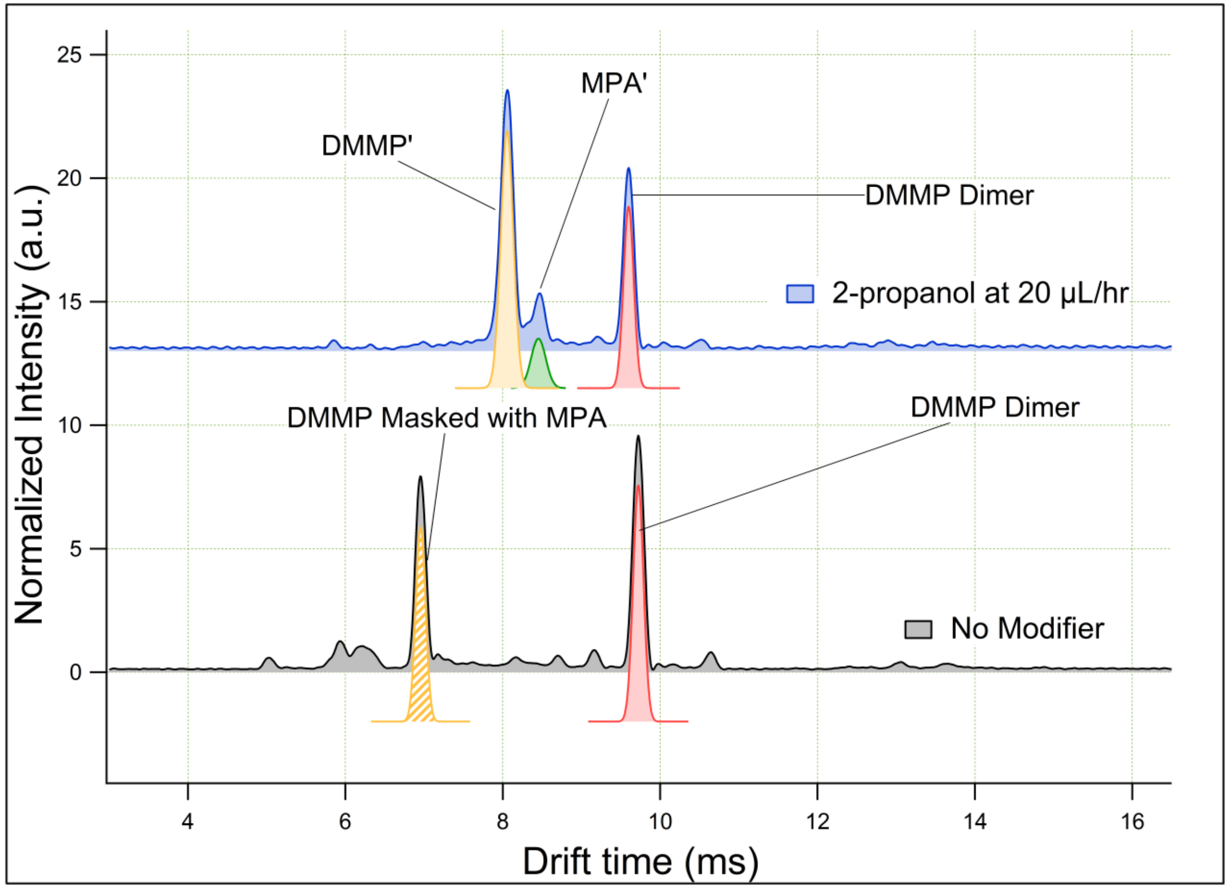


Morrison, K.A., Siems, W.F. and Clowers, B.H. *Anal Chem*, *88*(6), **2016**

ENHANCED SELECTIVITY FOR CWA DEGRADATION PRODUCTS

- Under traditional IMS conditions MPA and DMMP are unresolved in the mobility domain.

The goal is to <u>quantitatively</u> describe the shift and not simply catalog the phenomena.

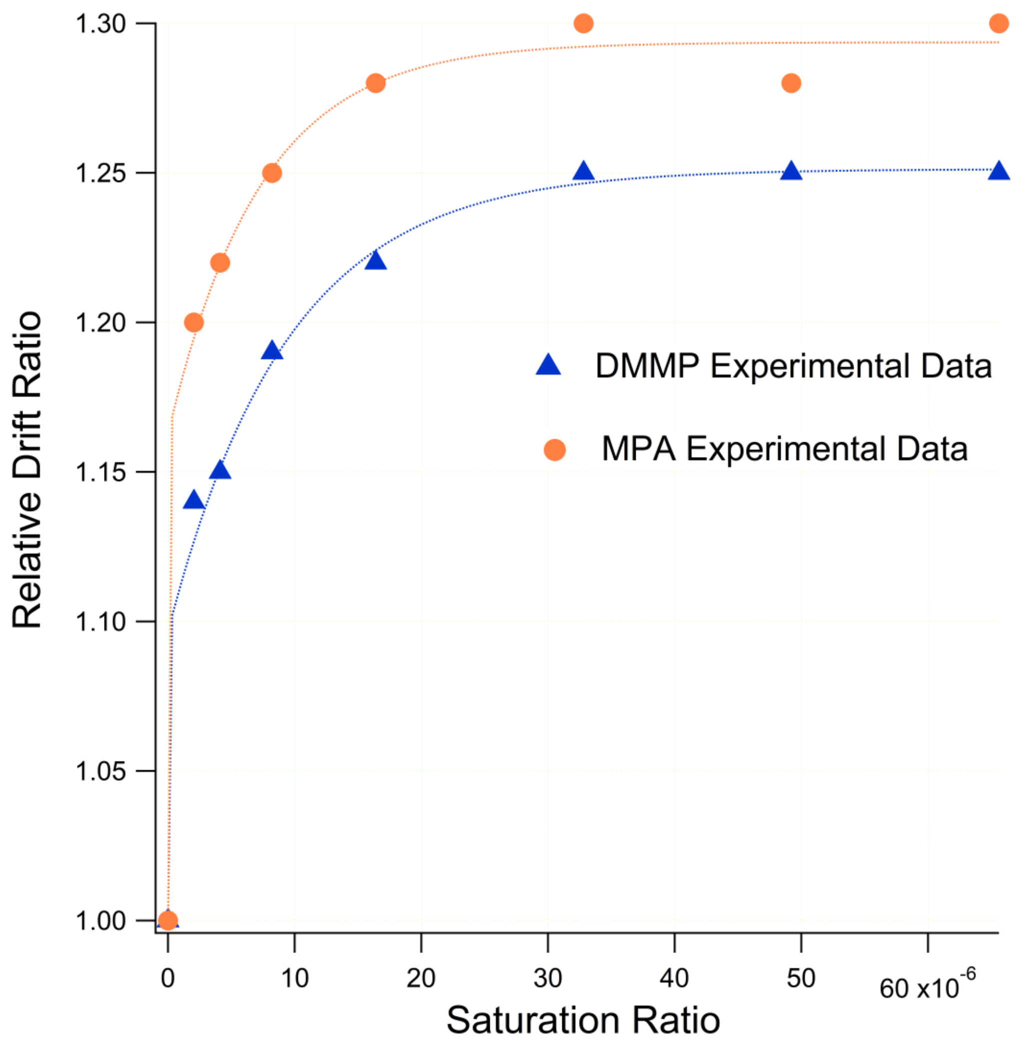


Kwantwi-Barima, P.; Ouyang, H.; Hogan, C. J. Jr.; Clowers, B. H. *Anal Chem*. **2017**

EXPERIMENTAL PROCEDURE

- Vary the gas-phase concentration of the clustering vapor
- Monitor the degree of the shift relative to the homogeneous buffer gas.
- For each desired temperature: repeat

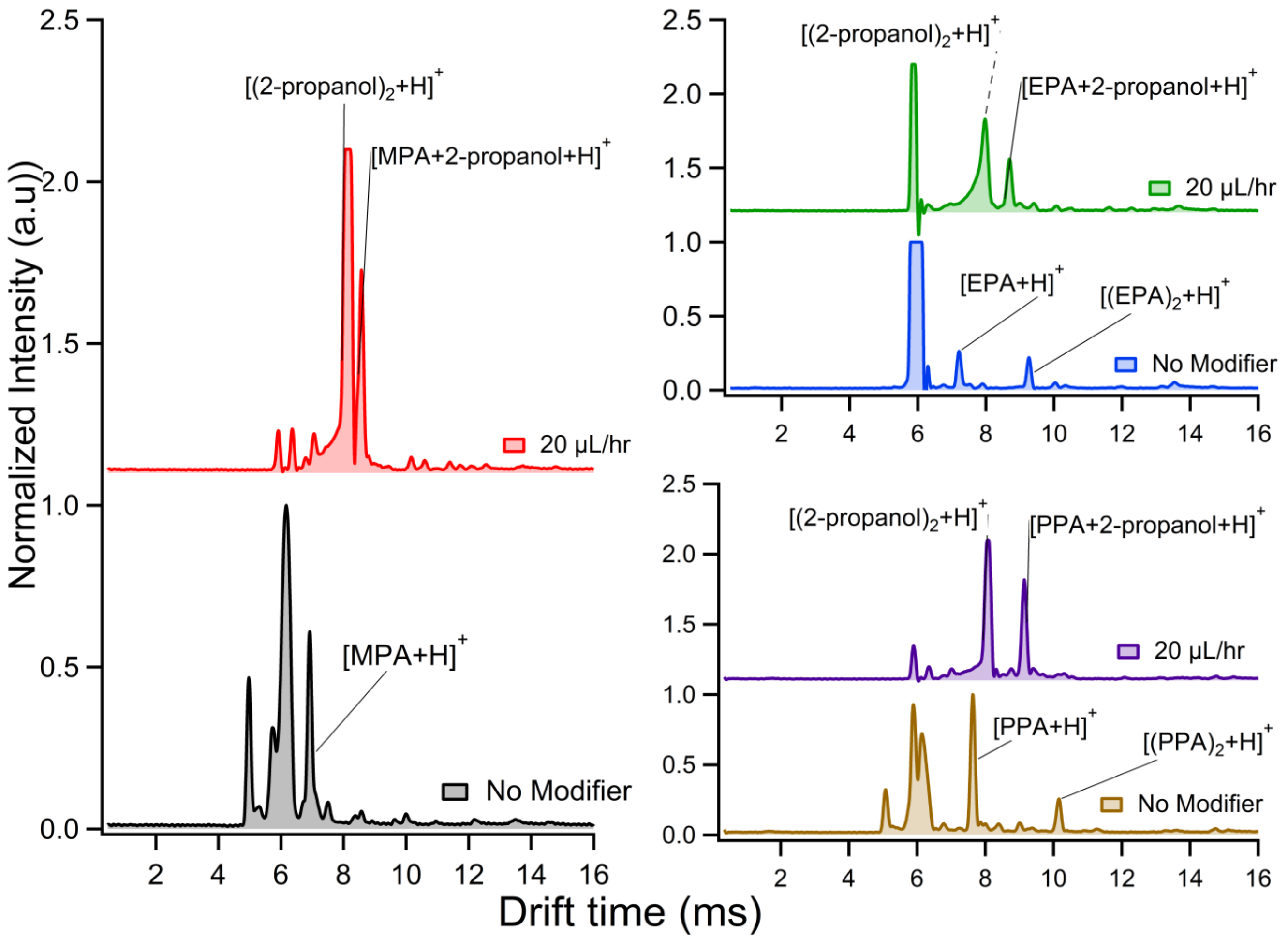
- Given the number of collisions in IMS equilibrium conditions are achieved, however, with respect to the number of vapor molecules, this quantity can be varied.



PHOSPHONIC ACID SHIFTS WITH 2-PROPANOL

- Chemical function groups of both analyte and modifier play an important role

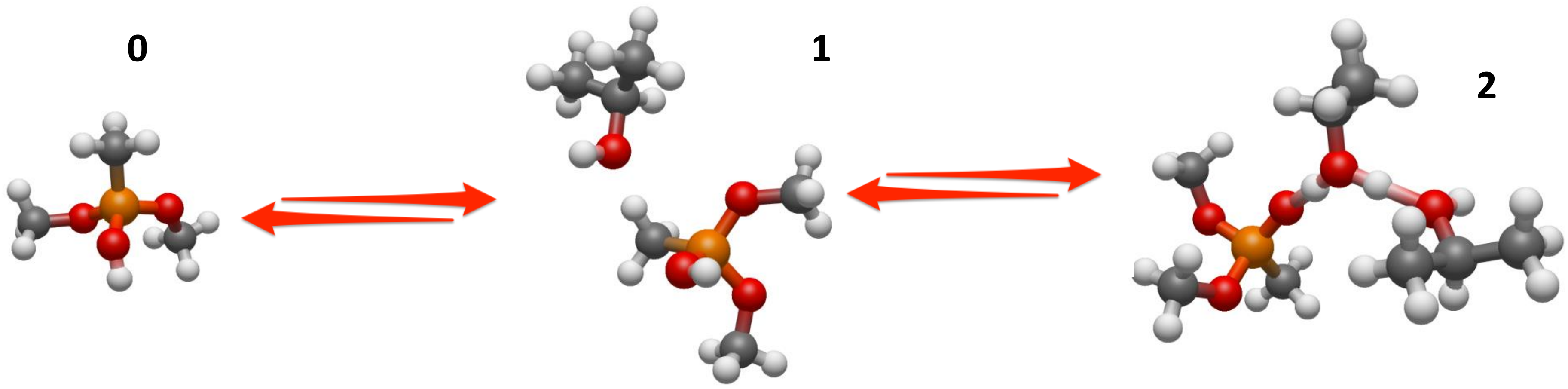
- To what degree are the mobility shifts functional group dependent?



GAS-PHASE CLUSTERING EQUILIBRIA

- At any given time, the number of vapor molecules bound is in a flux.
    - Process of continual sorption and desorption

$$n_0 \leftrightarrow n_1 \leftrightarrow n_2$$



Development of a Quantitative Shift Model

- Ion spends a fraction of time without a vapor molecule bound (t_0) and a fraction with a specific number (g) of vapor molecules bound (t_g) during measurements.

$$t = L/KE \qquad (1)$$

$$L = t_0K_0E + t_1K_1E + t_2K_2E + \ldots + t_gK_gE \qquad (2)$$

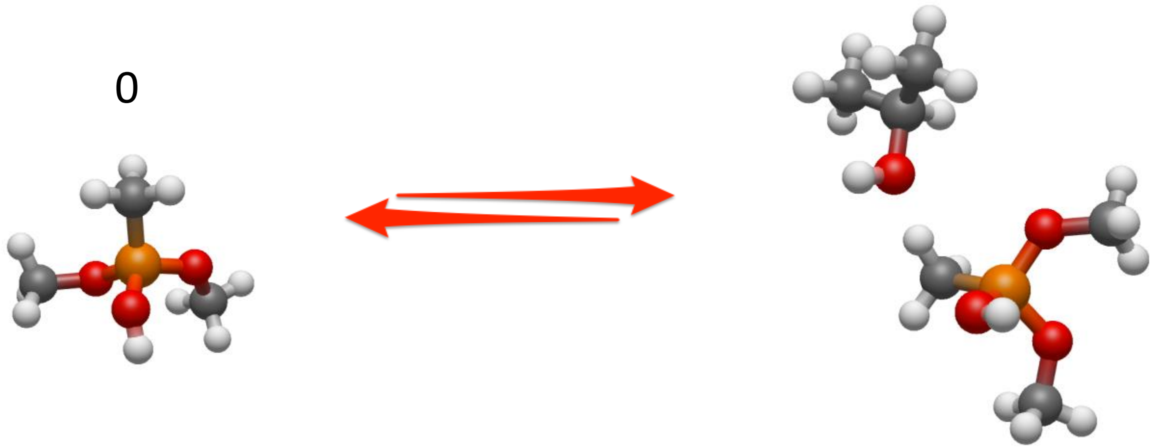
Gas-Phase Clustering Equilibria

$$K_{obs} = \frac{t_0}{t} K_0 + \frac{t_1}{t} K_1 \quad (3)$$

K_{obs} = **Ion Mobility (cm^2 V^{-1} s^{-1})** (Not K_{eq})

Where K_0 and K_1 are the mobilities of the bare ion and the ion plus one (1) vapor molecule complex respectively

0



1

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K_{obs} **= Ion Mobility (cm^2 V^{-1} s^{-1})** **(Not K_{eq})**

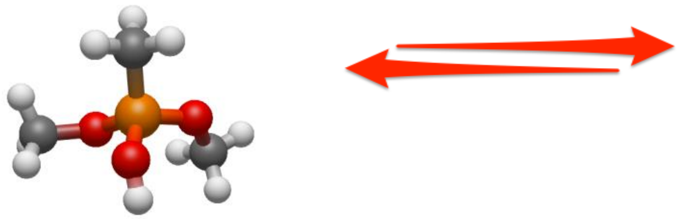
By extension, the ratio of times or mobilities is related to the probability of existence

$$P_0 = \frac{1}{1 + S exp\left(-\frac{\Delta G_1}{kT}\right)}$$

$$P_1 = \frac{exp\left(-\frac{\Delta G_1}{kT}\right)}{1 + S exp\left(-\frac{\Delta G_1}{kT}\right)}$$

$S =$ saturation ratio

0



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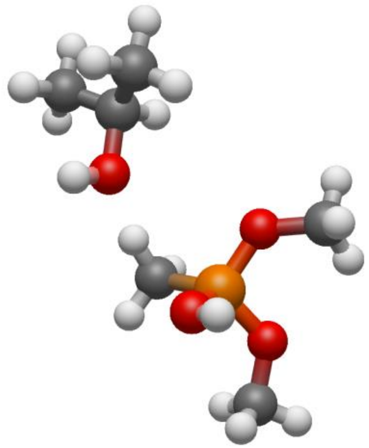

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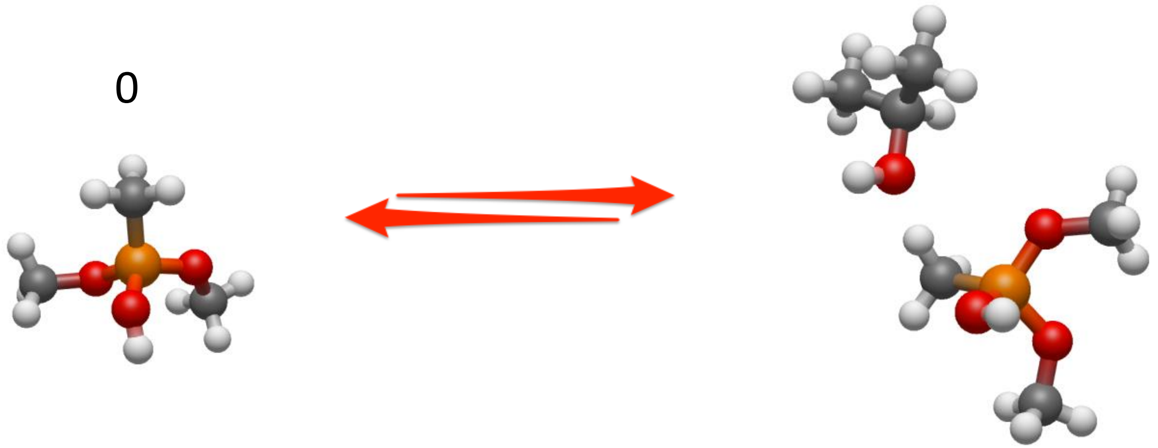
$$\frac{K_{obs}}{K_0} = \frac{1 + \frac{K_1}{K_0} Sexp\left(-\frac{\Delta G_1}{kT}\right)}{1 + Sexp\left(-\frac{\Delta G_1}{kT}\right)} \quad (4)$$

$$\frac{K_1}{K_0} = \frac{\Omega_0 \mu_1^{1/2}}{\Omega_1 \mu_0^{1/2}} \quad (5)$$

$S =$ saturation ratio

0

1



Quantitative Shift Model

- For a linear DTIMS, where **t_i** is the arrival time measured in the absence of vapor modifier, leads to;

$$\frac{t}{t_{\mathrm{i}}} = \frac{1+S exp\left(-\frac{\Delta G_1}{kT}\right)}{1+\frac{\Omega_0 \mu_1^{1/2}}{\Omega_1 \mu_0^{1/2}} S exp\left(-\frac{\Delta G_1}{kT}\right)}$$

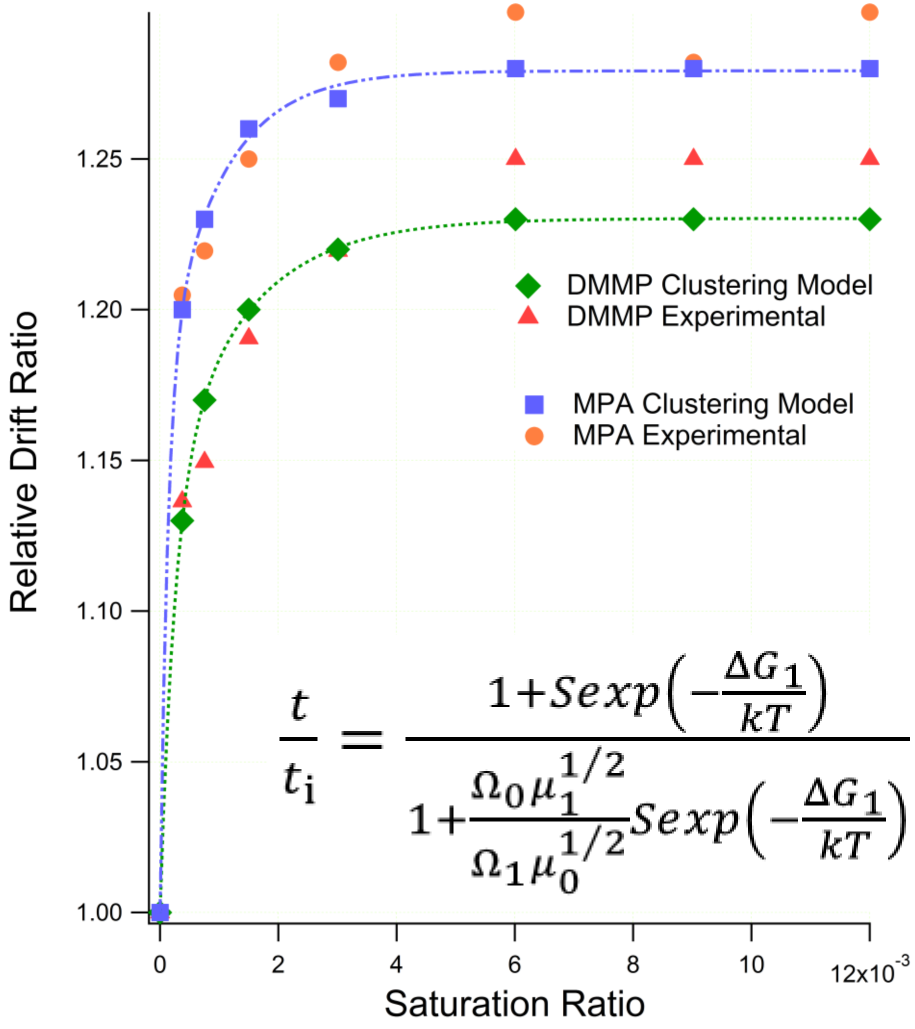
- With $\frac{\Omega_0 \mu_1^{1/2}}{\Omega_1 \mu_0^{1/2}}$ calculated from the model, plots of $\frac{t}{t_{\mathrm{i}}}$ as a function of saturation ratio (S) hence yields, ΔG.

Model Comparison: DMMP and MPA

- Reasonable agreement is achieved using the probabilistic model.

- DMMP is systematically over estimated at higher saturation ratios.
  - Small contributions from higher order clustering (g>1)

Analyte Ion	Experimental CCS	Theoretical CCS	Reduced Mass
$[MPA+H]^+$	91.80 +/- 0.07	91.79	21.73
$[MPA+2\text{-}Propanol+H]^+$	119.12 +/- 0.19	123.57	23.76
$[DMMP+H]^+$	89.10 +/- 0.07	95.05	22.88
$[DMMP+2\text{-}Propanol+H]^+$	112.21 +/- 0.26	121.48	24.32



$$\frac{t}{t_i} = \frac{1+S\exp\left(-\frac{\Delta G_1}{kT}\right)}{1+\frac{\Omega_0 \mu_1^{1/2}}{\Omega_1 \mu_0^{1/2}} S\exp\left(-\frac{\Delta G_1}{kT}\right)}$$

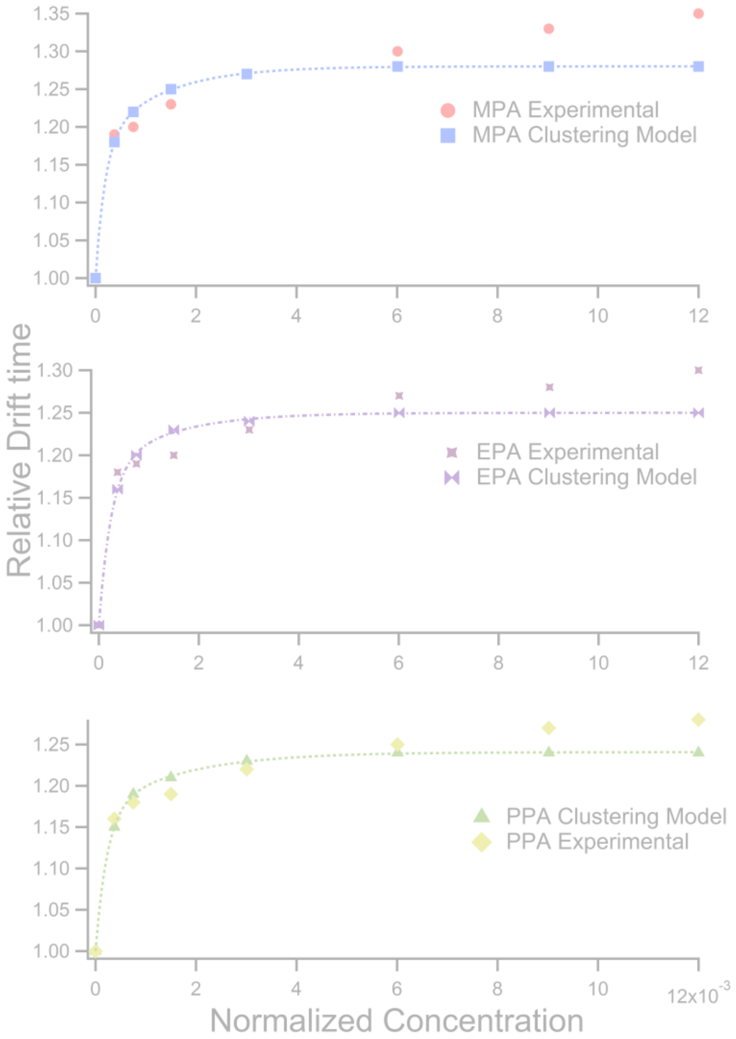
Model Comparison: MPA, EPA and PPA

$$\frac{t}{t_i} = \frac{1+S\exp\left(-\frac{\Delta G_1}{kT}\right)}{1+\frac{\Omega_0 \mu_1^{1/2}}{\Omega_1 \mu_0^{1/2}} S\exp\left(-\frac{\Delta G_1}{kT}\right)}$$

***S** is a relative parameter*

$$\frac{t}{t_i} = \frac{1+n_{(conc)}\exp\left(-\frac{\Delta G_1}{kT}\right)}{1+\frac{\Omega_0 \mu_1^{1/2}}{\Omega_1 \mu_0^{1/2}} n_{(conc)} exp\left(-\frac{\Delta G_1}{kT}\right)}$$

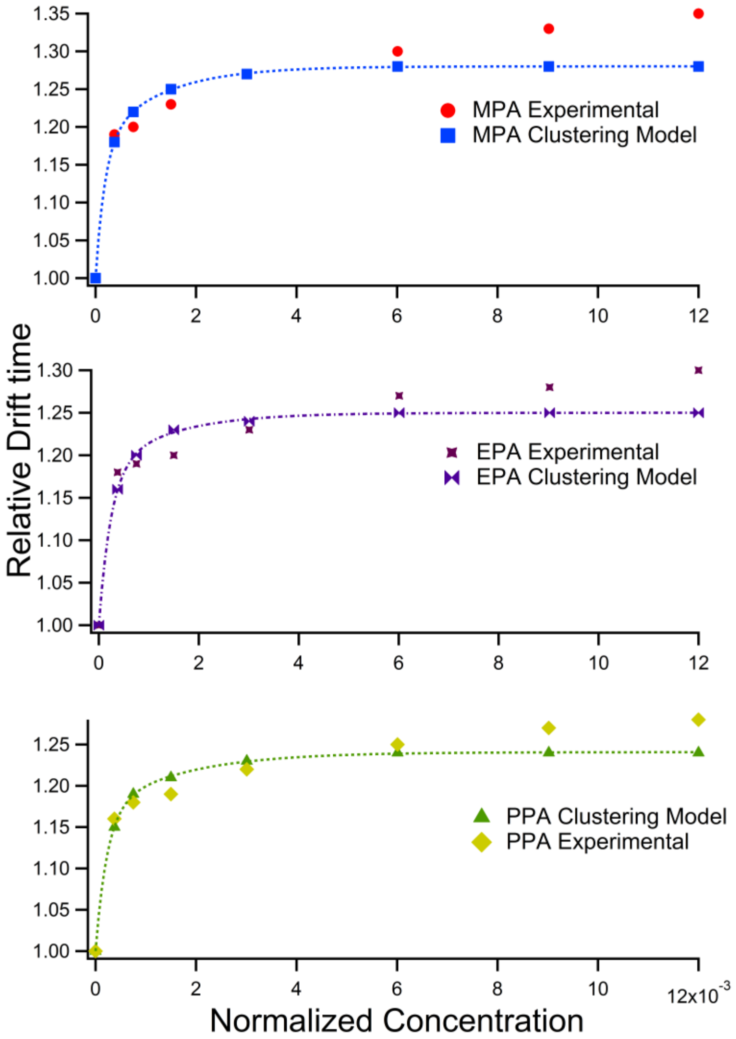
***n** is a reference state*



MODEL COMPARISON: MPA, EPA AND PPA

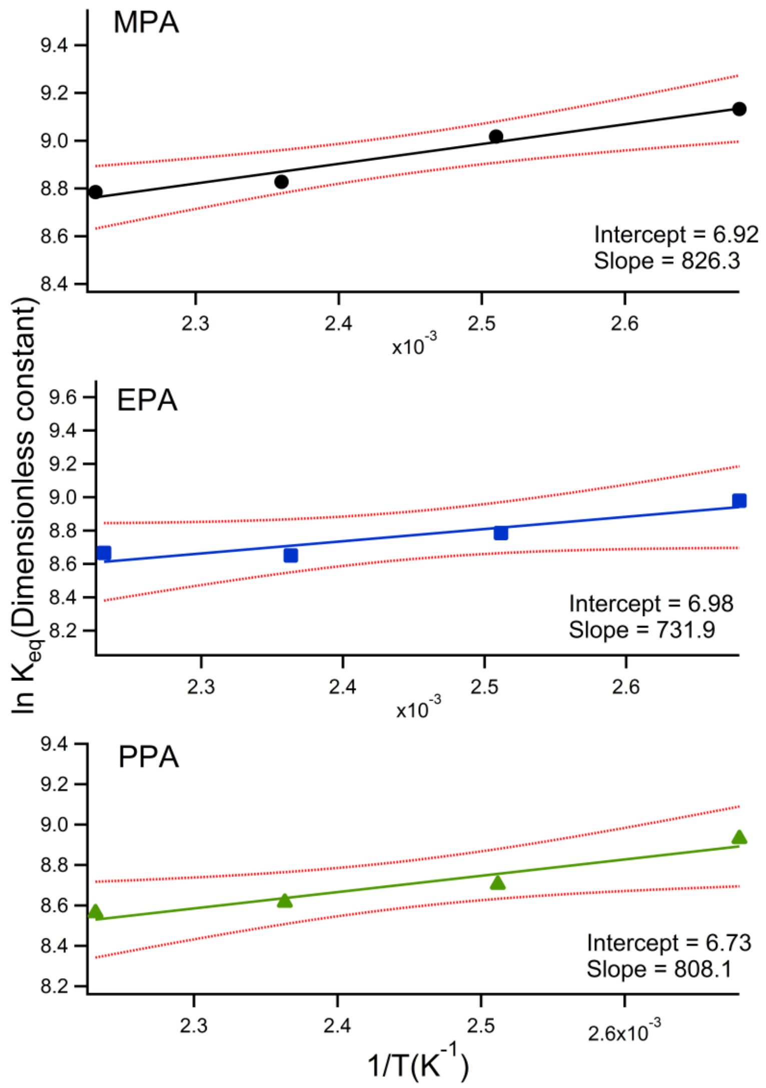
- Deviation at higher saturation (upward trend in experimental curve relative to the clustering model) .
- Suitable agreement between the experimental and clustering model

$$\frac{t}{t_i} = \frac{1+n_{(conc)}\exp\left(-\frac{\Delta G_1}{kT}\right)}{1+\frac{\Omega_0 \mu_1^{1/2}}{\Omega_1 \mu_0^{1/2}} n_{(conc)} exp\left(-\frac{\Delta G_1}{kT}\right)}$$



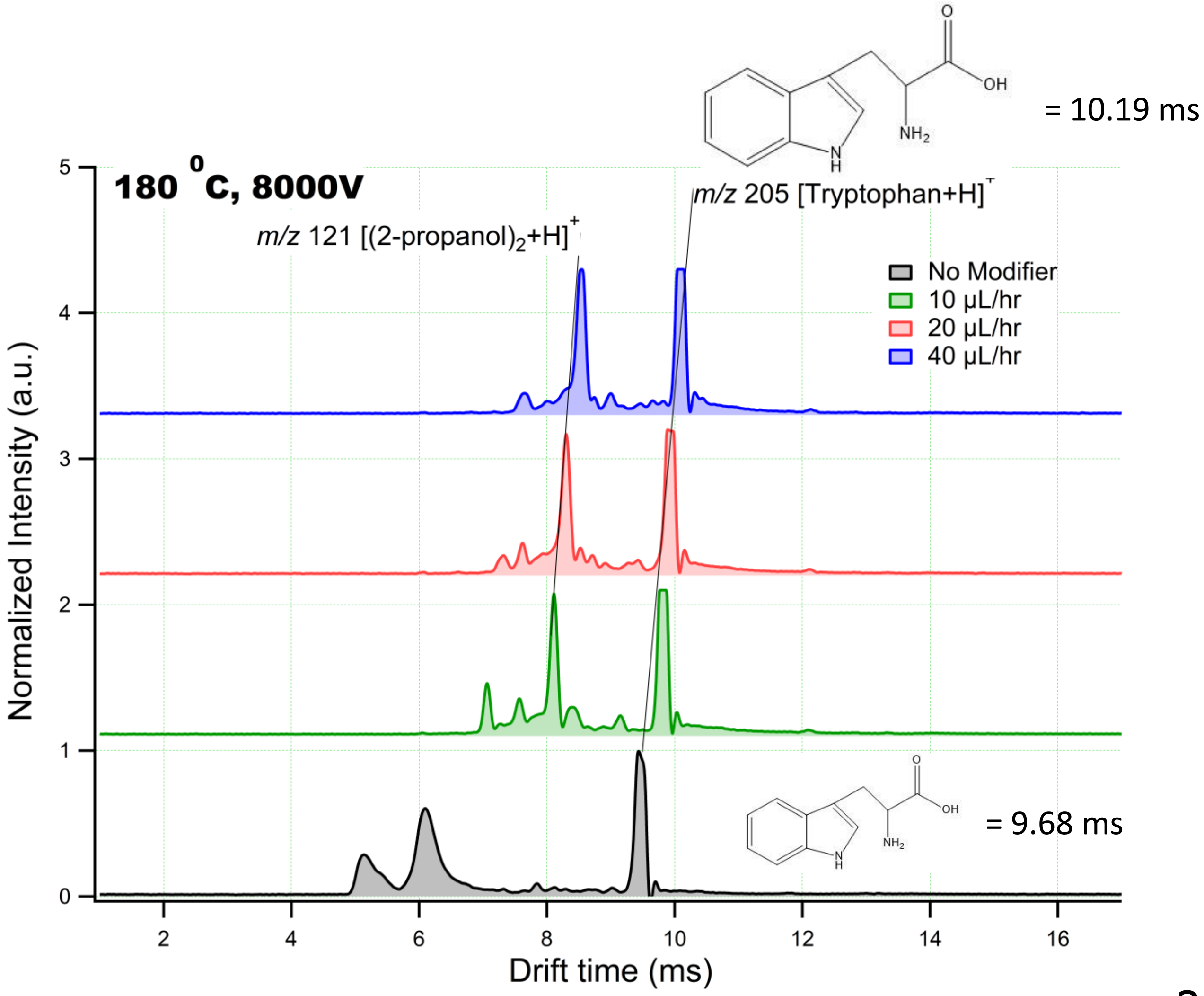
Experimental Thermodynamic Properties

- $\ln(K_{eq})$ increases with a decrease in temperature.
- Enthalpically and entropically favored reaction
- Continued exploration of gas-phase mobility shift of homologous series of analytes



TRYPTOPHAN SHIFT WITH 2-PROPANOL

- The analyte was 100 μM of L-tryptophan
- Significant shift is observed even at 40 μL/hr of the modifier
- Currently, ΔG of association for these clusters is confounded by the large temperature range probed.



Summary and Path Forward

- By establishing conditions that allow for clustering equilibrium to be maintained, thermodynamic properties are readily derived from **shifts in drift times.**
  - **Not fits to decay slopes**
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  - **Sufficient collisions to ensure equilibrium**
- The proposed method can capture information on clusters that may not survive traditional MS interfaces but are amenable to soft ionization sources.
  - **Allows species previously excluded from HPMS to be probed.**
- ΔG indicates that the clustering reactions are favorable
  - **Reemphasize relationship between ΔH and ΔS**
  - **Cast in terms of Castlemann results.**
    - **Examine similar systems**

Will clustering reactions be favorable in the negative mode?

THANK YOU

QUESTIONS?