

# Ion Mobility Mass Spectrometry: a Tutorial

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# What is Ion Mobility Mass Spectrometry?

Ion's mobility ( $K$ ) = a physical property of the ion

Ion mobility spectrometry ( $IM$  or  $IMS$ ) = an instrument to  
measure the mobility of ions

$IM-MS$  = an ion mobility spectrometer hyphenated to  
a mass spectrometer

# What is an ion's mobility ( $K$ )?

- Ions have charges ( $q = z.e$ )
- Charges are accelerated in electric fields ( $F = q.E$ )  
→ ions migrate
- Collisions slow down the ions
- At **steady state**, acceleration and deceleration compensate each other → ions migrate at apparent **constant velocity**

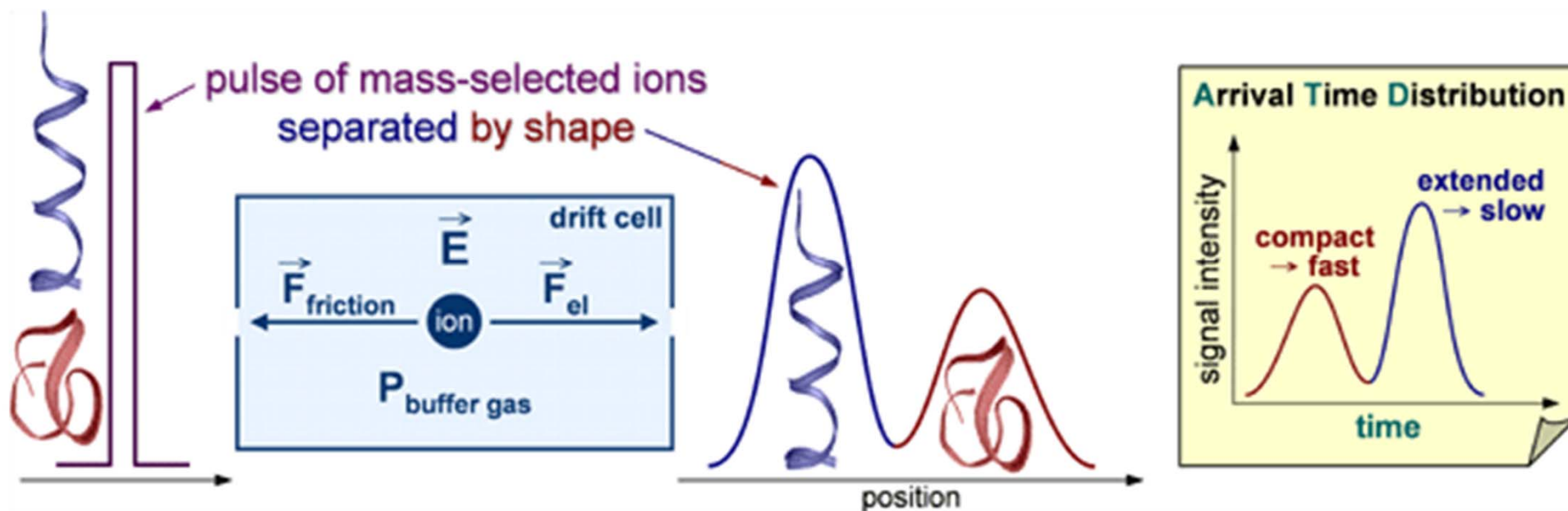
Drift velocity:

$$v_d = K.E$$

$K$  depends on  $z$

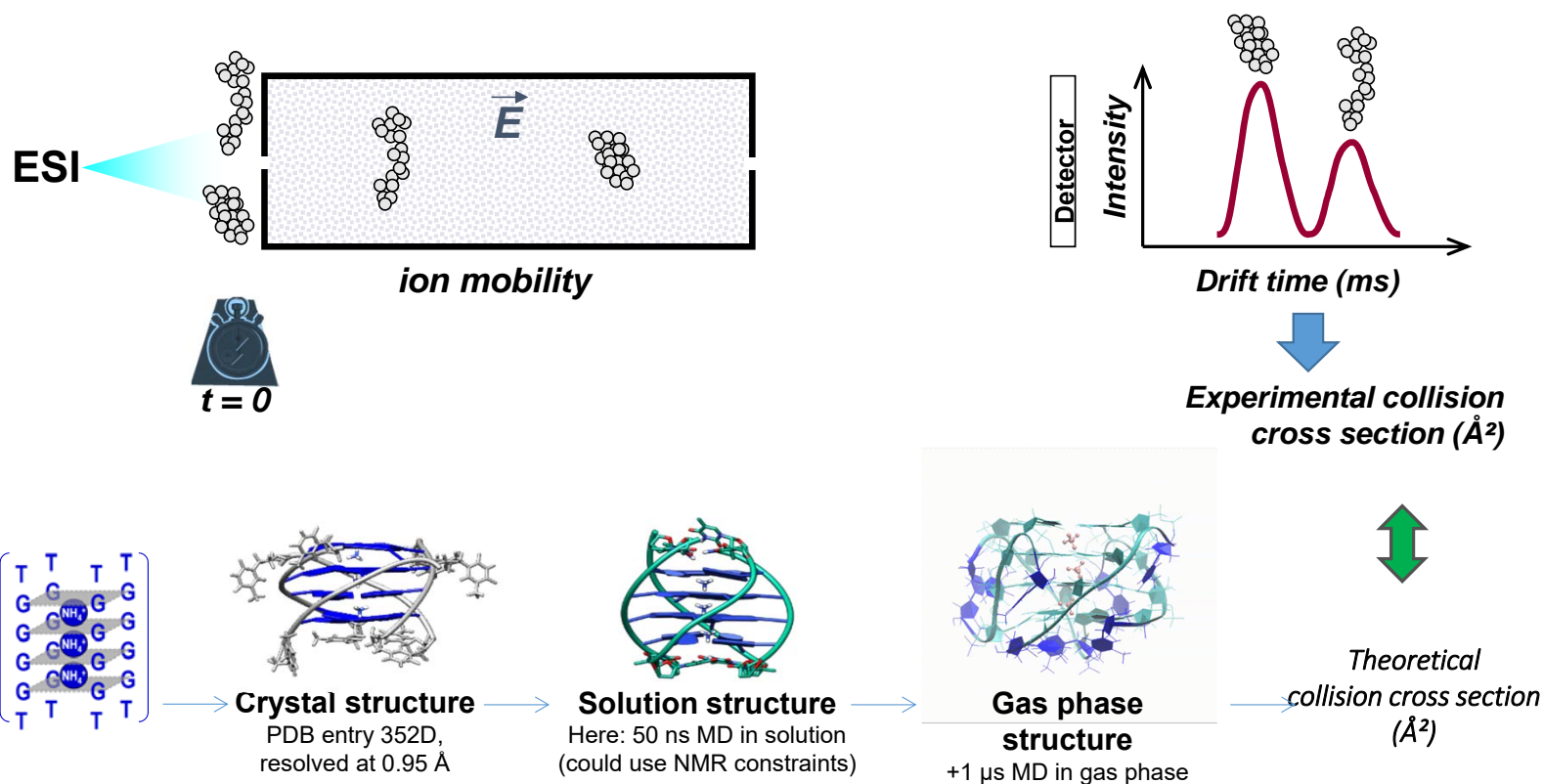
on how collisions slow down the ions,  
=> on charge and **shape**

# What is Ion Mobility Mass Spectrometry?



[https://labs.chem.ucsb.edu/bowers/michael/theory\\_analysis/ion-mobility/index.shtml](https://labs.chem.ucsb.edu/bowers/michael/theory_analysis/ion-mobility/index.shtml)

# What is Ion Mobility Mass Spectrometry?



D'Atri, Porrini, Rosu & Gabelica, *J. Mass Spectrom.* (2015) Tutorial, 50: 711

# Philosophy of the presentation

1. Not "theory" then "practical considerations"  
Will start from practical problems, then explore how they can be understood/solved based on theory
2. Focus on measurement sciences  
**Ion mobility measures mobilities** ( $K$ , in  $\text{m}^2 \text{V}^{-1} \text{s}^{-1}$ ),  
**not collision cross sections** ( $\Omega$  or CCS, in  $\text{m}^2$ )
3. CCS values derived from mobility measurements are useful for structural interpretation, based on the appropriate level of theory (not on simple visualization)

# What is an ion's mobility ( $K$ )?

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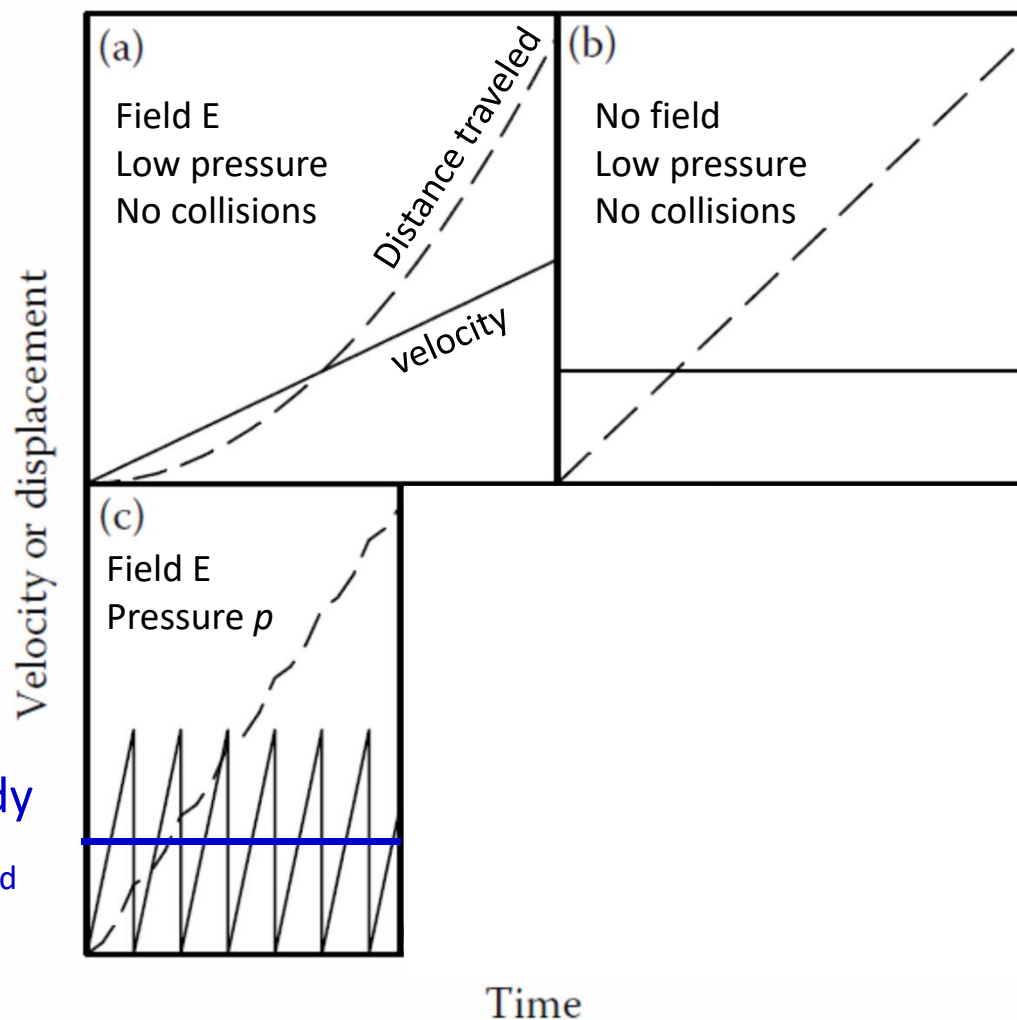
on how collisions slow down the ions,  
=> on charge and **shape**

# Illustration of the steady state in ion mobility

MS:

IMS:

Apparent steady  
state velocity  $v_d$



$$v_d = K.E$$

Figure 1.3 from  
Shvartsburg AA: Differential Ion  
Mobility Spectrometry. Nonlinear Ion  
Transport and Fundamentals of  
FAIMS. Boca Raton: CRC Press; 2009.

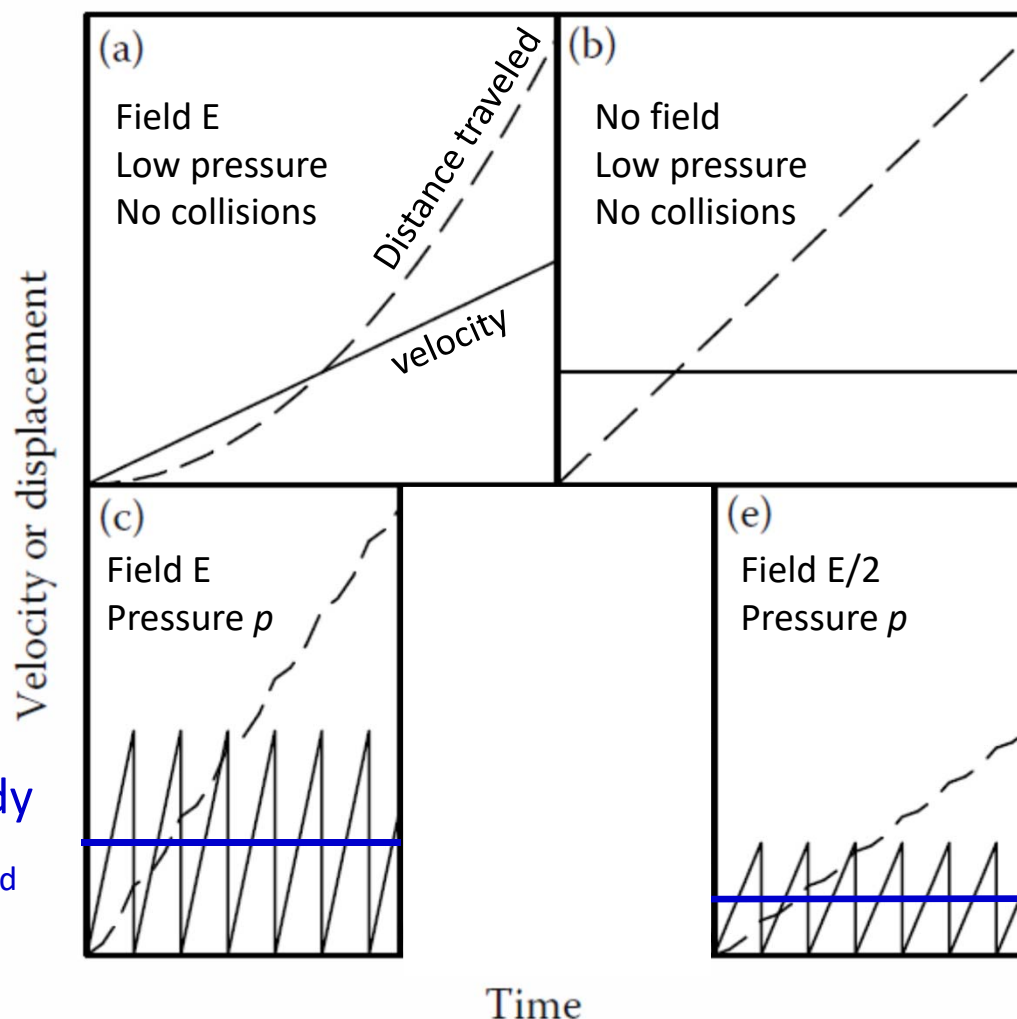


# Influence of electric field $E$ on drift velocity $v_d$

MS:

IMS:

Apparent steady  
state velocity  $v_d$



$$v_d = K.E$$

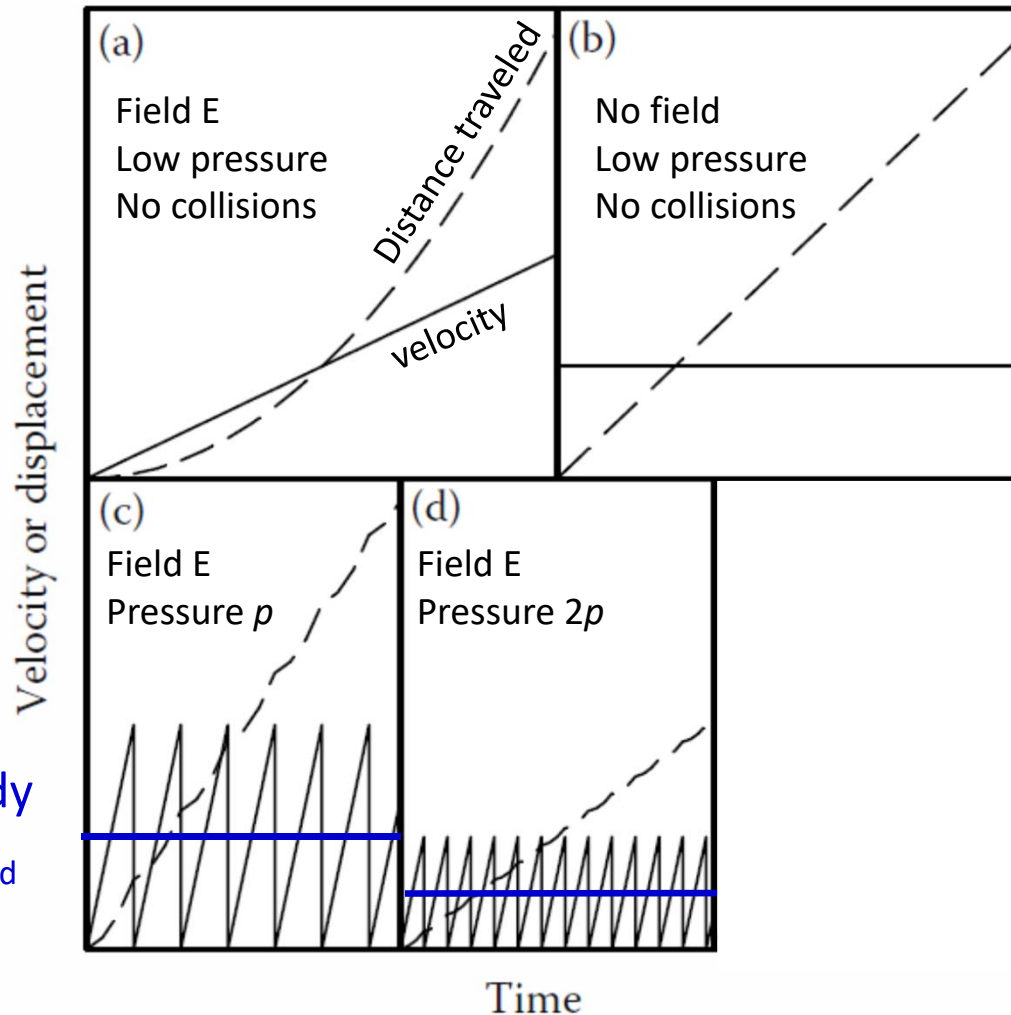
Figure 1.3 from  
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# Influence of collision frequency on ion mobility $K$

MS:

IMS:

Apparent steady  
state velocity  $v_d$



Gas number density  
(perfect gas):

$$N = \frac{n}{V} = \frac{p}{RT}$$

$N$  influences  $K$

$$v_d = K \cdot E$$

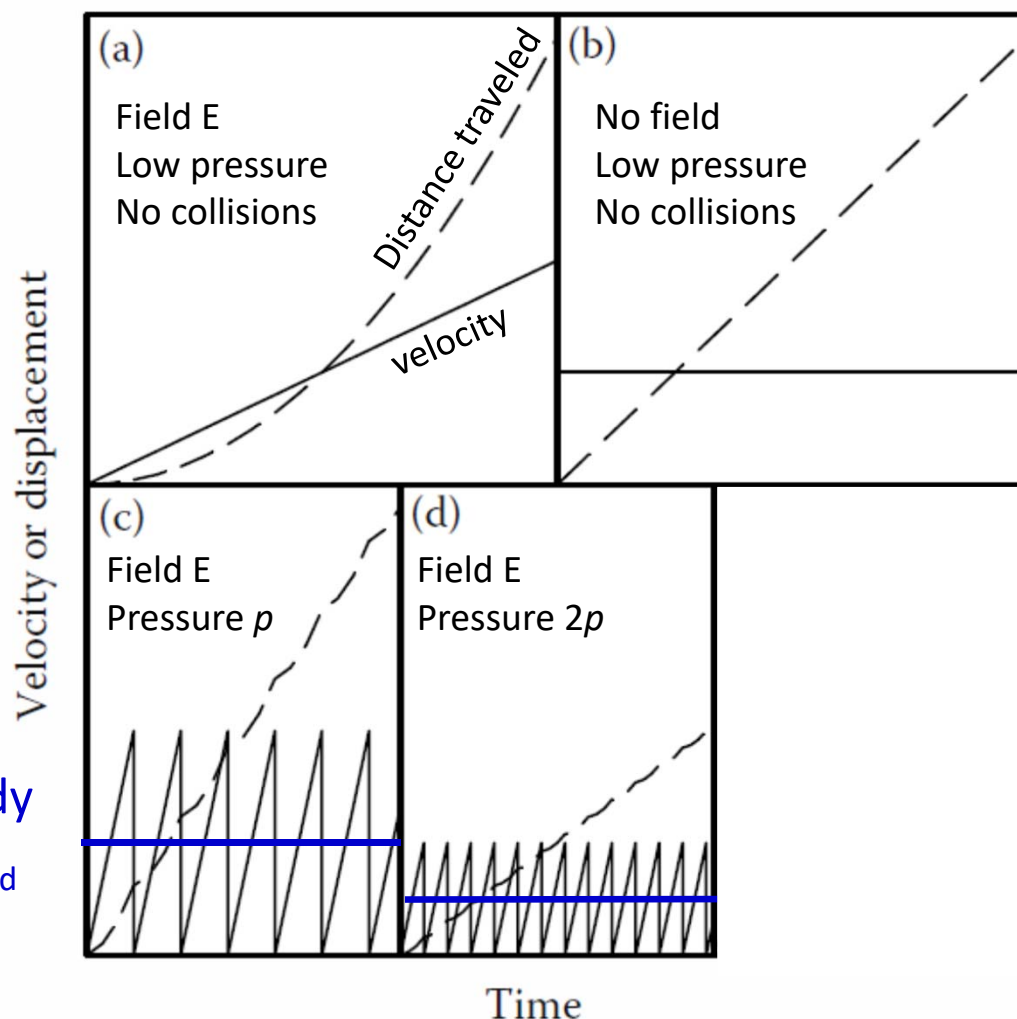
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# Influence of pressure and temperature on $K$

MS:

IMS:

Apparent steady  
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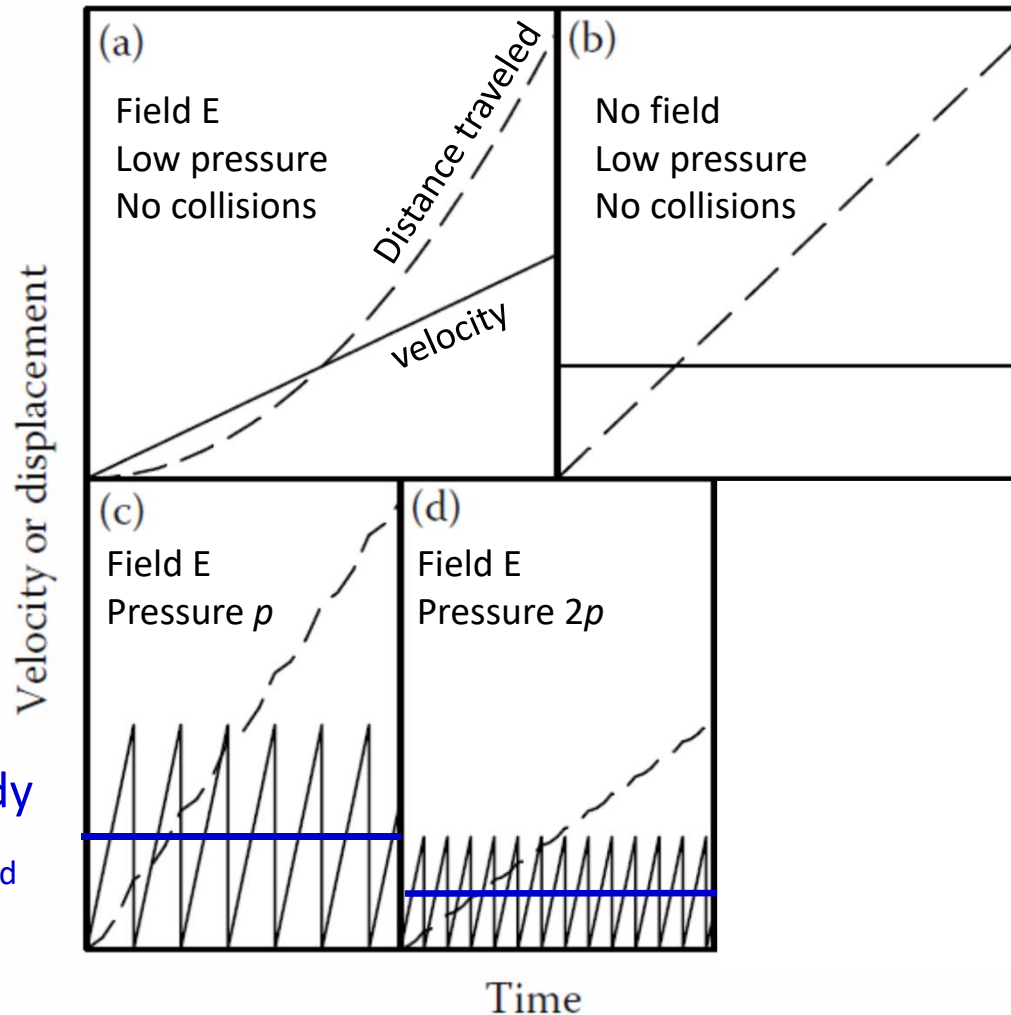
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MS:

IMS:

Apparent steady  
state velocity  $v_d$



Gas number density  
(perfect gas):

$$N = \frac{n}{V} = \frac{p}{RT}$$

$T$  and  $p$  influence  $K$

Reduced mobility  $K_0$

$$K_0 = K \frac{N}{N_0} = K \frac{p T_0}{p_0 T}$$

$$\begin{aligned} T_0 &= 273.15 \text{ K} \\ P_0 &= 1 \text{ atm (STP)} \\ N_0 &= 2.687 \times 10^{25} \text{ m}^{-3} \end{aligned}$$

# Influence of pressure and temperature on $K$

One reason  $T$  and  $p$  influence  $K$  is collision frequency

The reduced mobility  $K_0$  corrects for collision frequency effects

$$K_0 = K \frac{N}{N_0} = K \frac{p T_0}{p_0 T}$$

 The ion's reduced mobility  $K_0$  still depends on  $T$ ,  $p$  and  $E$  for other reasons

# Effect of $E/N$ on $K_0$

Low  $E/N$

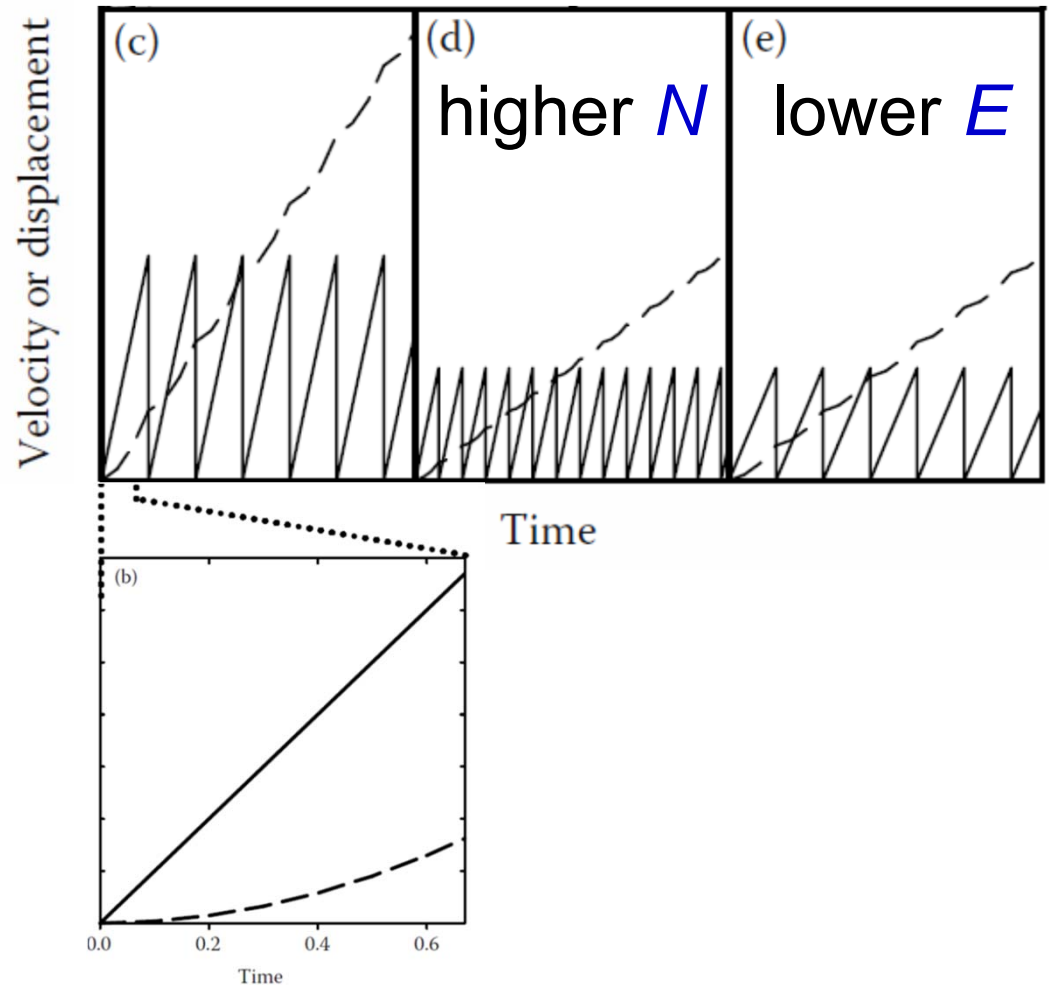
→  $K_0$  independent on  $E/N$

Not too much acceleration between collisions

→ No collisional activation (no energy transfer into internal energy)

→ Elastic collisions

→ Criterion:  $v_d \ll v_{\text{thermal}}$



# Effect of $E/N$ on $K_0$

Low  $E/N$

→  $K_0$  independent on  $E/N$

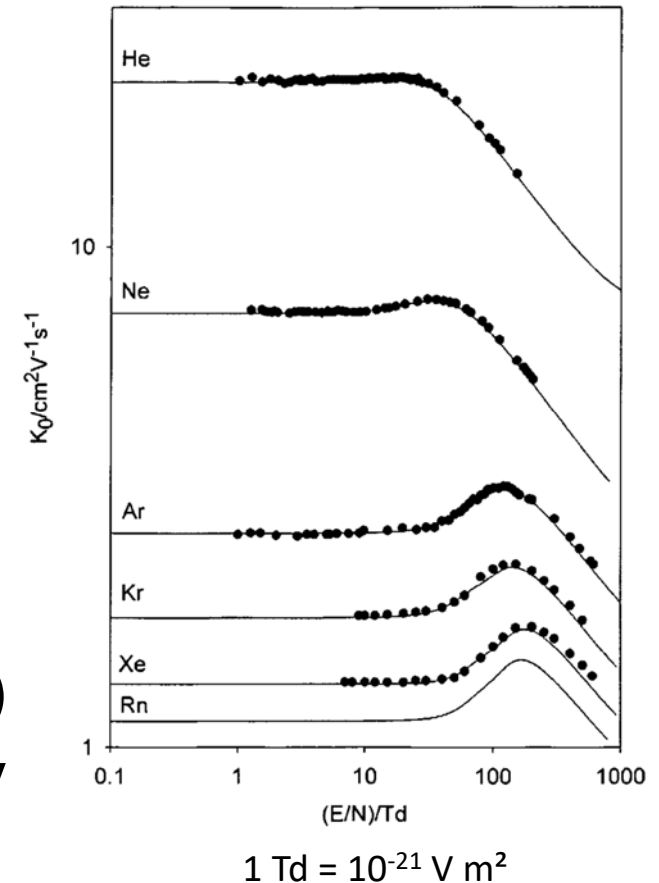
Higher  $E/N$

$$\rightarrow K_0\left(\frac{E}{N}\right) = K_0(0) \left[ 1 + \alpha_2 \left(\frac{E}{N}\right)^2 + \alpha_4 \left(\frac{E}{N}\right)^4 + \dots \right]$$

Linear IMS methods assume "low  $E/N$ "

Nonlinear IMS methods (FAIMS, DIMS,...) exploit the  $E/N$  dependence of the mobility for *separation* purposes

$K^+$  ions in rare gases



## Effect of $E/N$ on $K_0$

Low  $E/N$

→  $K_0$  independent on  $E/N$

Linear IMS methods assume "low  $E/N$ "

- Low-field drift tube IMS (Agilent, ToFwerk)
- Travelling wave IMS (Waters)
- Trapped IMS (Bruker)
- Low-field differential mobility analyzers (SEADM)

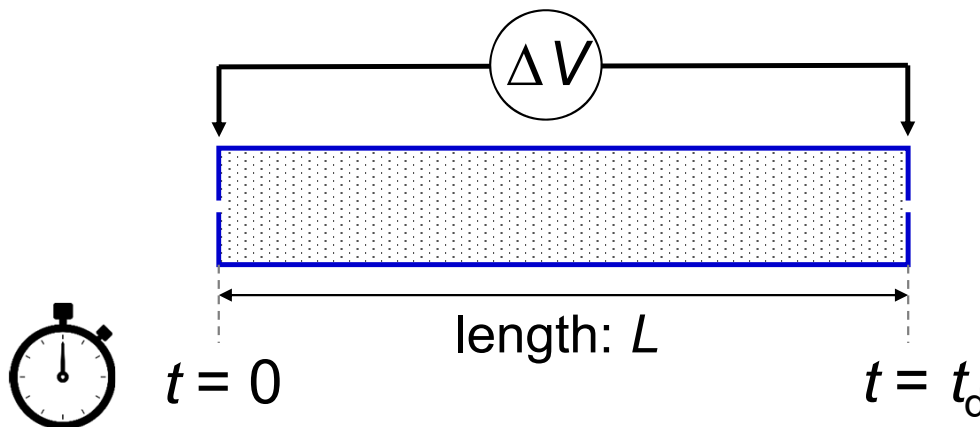
Is the assumption justified?



# How to determine $K$ ?

$$v_d = K \cdot E \quad K = \frac{v_d}{E}$$

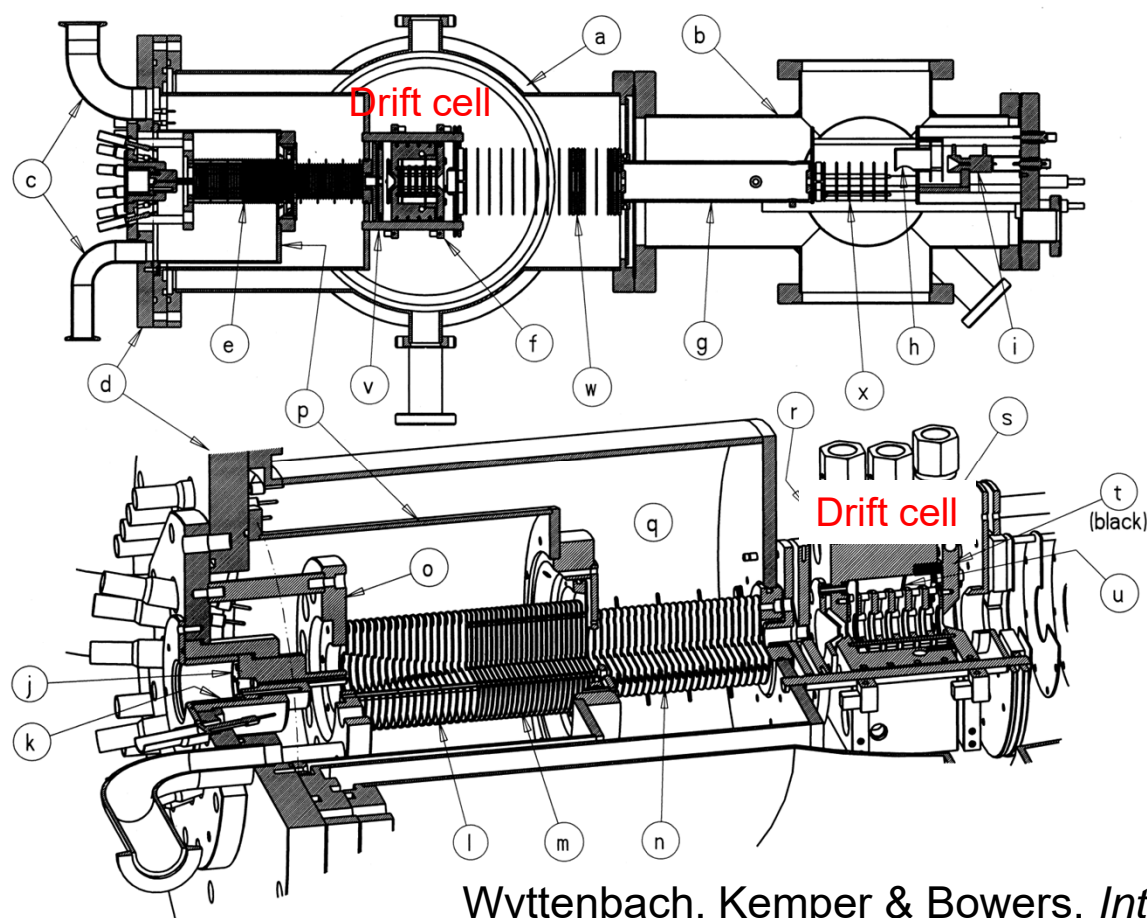
- ➔ Determine  $v_d$  and  $E$
- ➔ Easiest in principle: constant field and linear tube
- ➔ Drift tube ion mobility spectrometry (DTIMS)



$$E = \frac{\Delta V}{L}$$
$$v_d = \frac{L}{t_d}$$
$$K = \frac{L^2}{t_d \cdot \Delta V}$$

# Drift Tube IMS Instruments

## Bowers lab

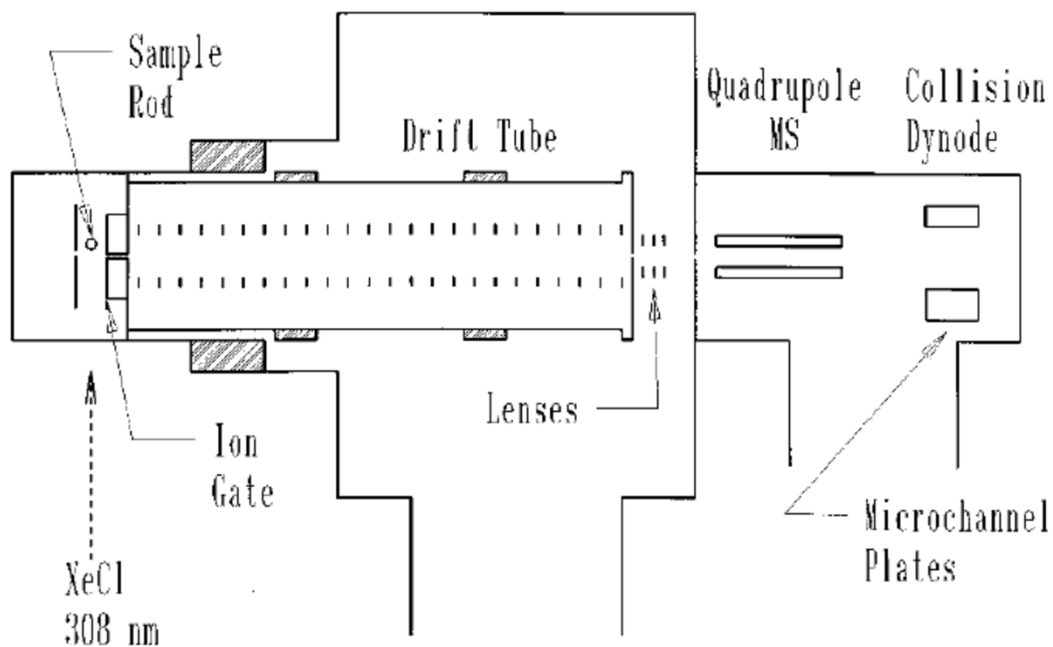


$L = 4.503 \text{ cm}$   
 $\Delta V = 30\text{-}100 \text{ V}$   
 $E = 6\text{-}20 \text{ V/cm}$   
 $p_{\text{He}} = 4\text{-}5 \text{ Torr}$

Wytenbach, Kemper & Bowers, *Int. J. Mass Spectrom.* (2001) 212, 13.

# Drift Tube IMS Instruments

## Jarrold lab

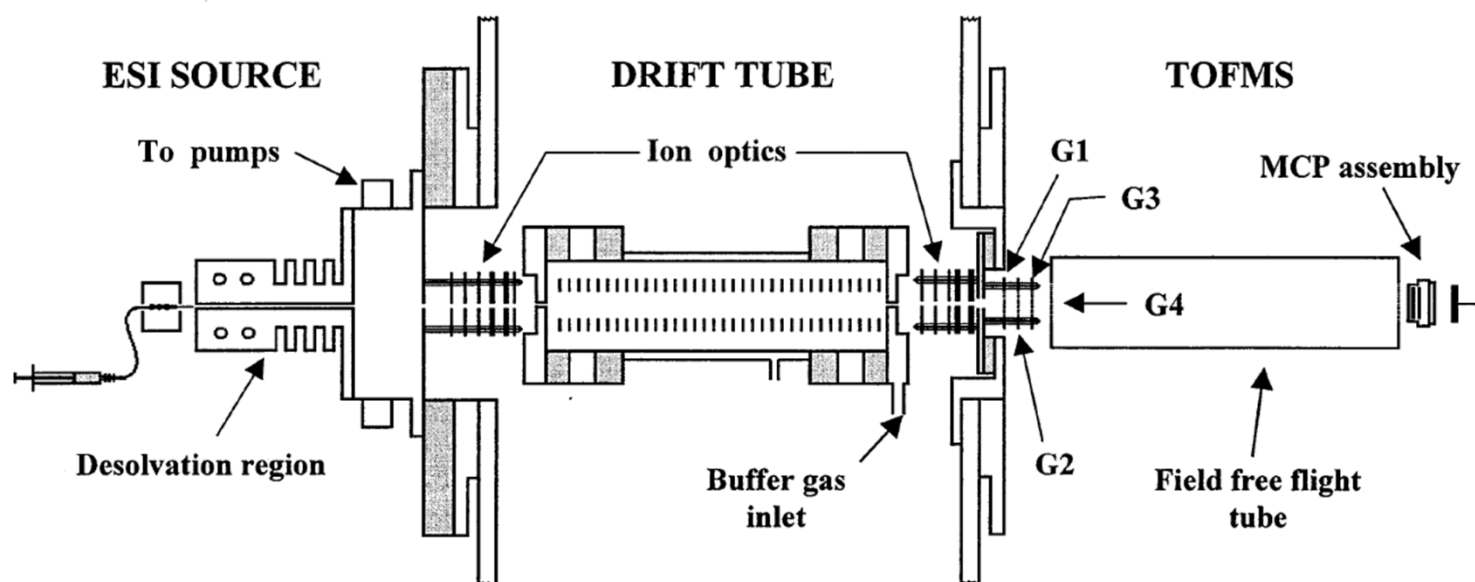


$L = 63 \text{ cm}$   
 $\Delta V = \rightarrow 14000 \text{ V}$   
 $E \rightarrow 220 \text{ V/cm}$   
 $p_{\text{He}} = 500 \text{ Torr}$

Dugourd, Hudgins, Clemmer & Jarrold, *Rev. Sci. Instrum.* (1997) 68, 1122.

# Drift Tube IMS Instruments

## Clemmer lab

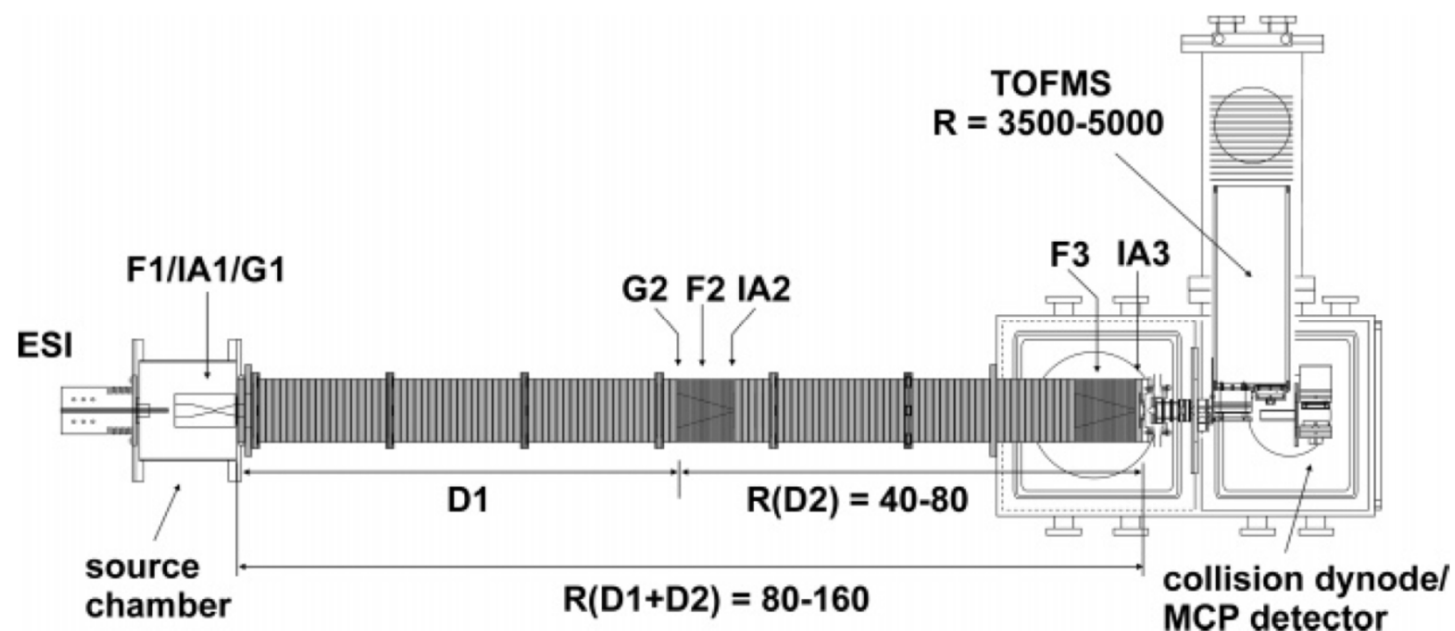


$L = 48.74 \text{ cm}$   
 $\Delta V = 1000\text{-}2000 \text{ V}$   
 $E = 20\text{-}40 \text{ V/cm}$   
 $p_{\text{He}} = 200 \text{ Torr}$

Counterman, Valentine,... & Clemmer, *J. Am. Soc. Mass Spectrom.* (1998) 9, 743.

# Drift Tube IMS Instruments

## Clemmer lab



$$L_1 = 87.1 \text{ cm}$$

$$L_2 = 94.9 \text{ cm}$$

$$\Delta V = 1000-2000 \text{ V}$$

$$p_{\text{He}} = \sim 3 \text{ Torr}$$

Keoniger, Merenbloom, Valentine, Jarrold, Udseth, Smith & Clemmer, *Anal. Chem.* (2006) 78, 4161.

# Determining $K_0$ using DTIMS (primary method)

$$K = \frac{L^2}{t_d \cdot \Delta V}$$

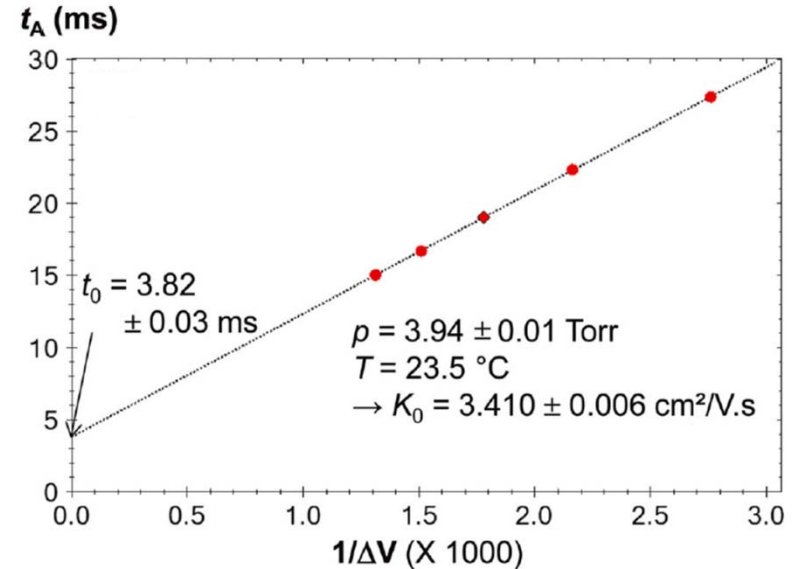
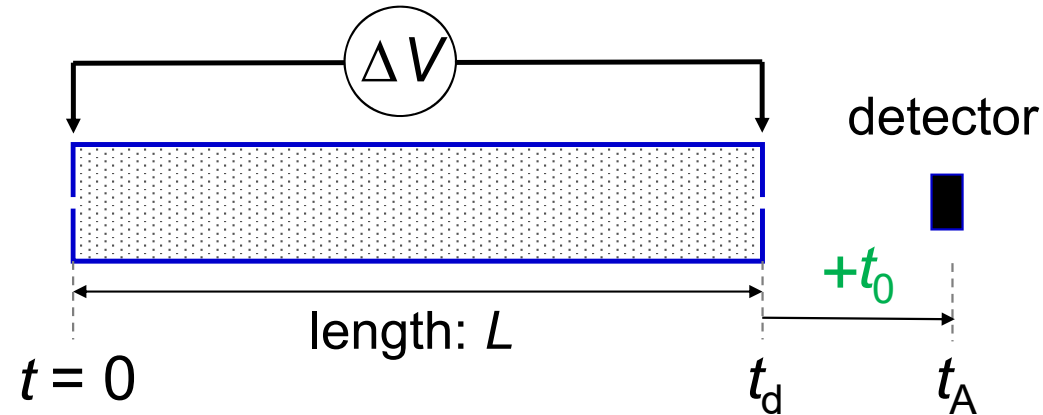
$$K_0 = K \frac{p T_0}{p_0 T} = \frac{L^2 \cdot p \cdot T_0}{t_d \cdot \Delta V \cdot p_0 T}$$

$$t_A = t_0 + t_d = t_0 + \frac{L^2 \cdot p \cdot T_0}{K_0 \cdot \Delta V \cdot p_0 T}$$

2 unknowns

$$t_A = t_0 + t_d = t_0 + \frac{L^2 T_0}{K_0 p_0 T} \cdot \frac{p}{\Delta V}$$

intercept and slope



# Determining $K_0$

## Practical challenges of the primary method

- ➔ Increasing the resolution (longer tube, higher  $p$ , higher  $\Delta V$ )
- ➔ Ensuring gas purity in the whole tube region, and no net gas flow
- ➔ Measuring  $p$  *inside* the tube
- ➔ Measuring  $T$  *inside* the tube
- ➔ Determining the tube length  $L$
- ➔ Measuring the *actual* voltages  $\Delta V$  applied

## Practical solution: calibration (secondary method)

## Calibration with compounds of known $K_0$

Principle of "secondary methods of measurement":

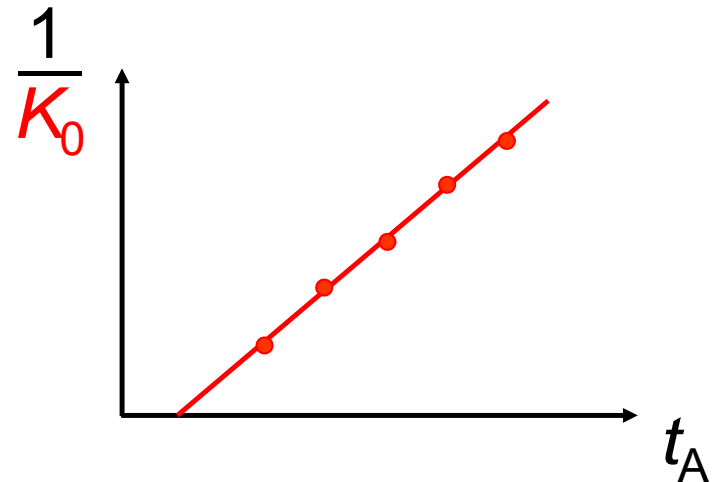
Instead of characterizing perfectly  $p$ ,  $T$ ,  $L$ ,  $\Delta V$ s and gas flows for each mobility measurement

➔ Calibrate instrument with compound(s) of known  $K_0$  value(s) and an appropriate mathematical function

### DTIMS calibration, first order:

$$t_A = t_0 + t_d = t_0 + \frac{L^2 T_0}{K_0 p_0 T} \cdot \frac{p}{\Delta V}$$

$$\text{Approx: } t_A = t_{\text{fix}} + \beta \frac{1}{K_0}$$





# Alternatives to home-made Drift Tube IMS

## Differential Mobility Analyzers (DMA)

J. Fernandez de la Mora (<1998)

SEADM

Aerosol sciences

## Travelling wave IMS (TWIMS)

K. Giles

Waters SYNAPT™ (2006)

Structural biology

## Commercial DTIMS

PNNL designs (R. D. Smith)

Agilent 6560 IMS-Q-TOF (2013)

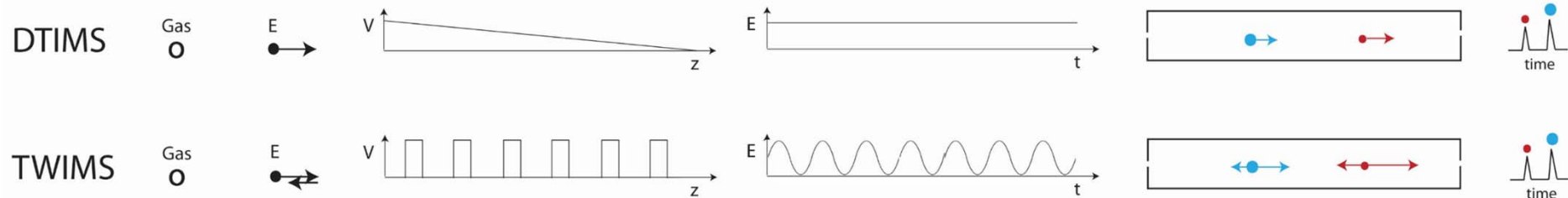
## Trapped ion mobility spectrometry (TIMS)

F. Fernandez-Lima, M. Park

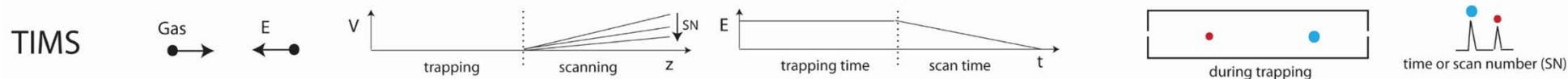
Bruker timsTOF™ (2016)

# Different types of ion mobility spectrometers

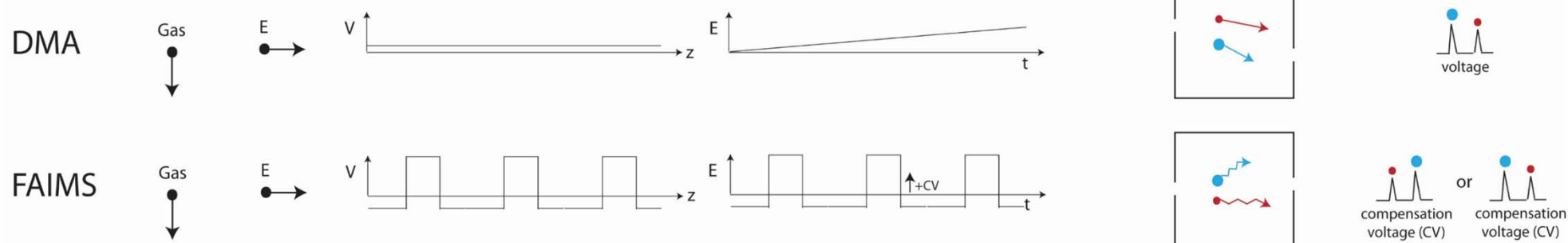
## Time-dispersive



## Mobility-selective instability scan

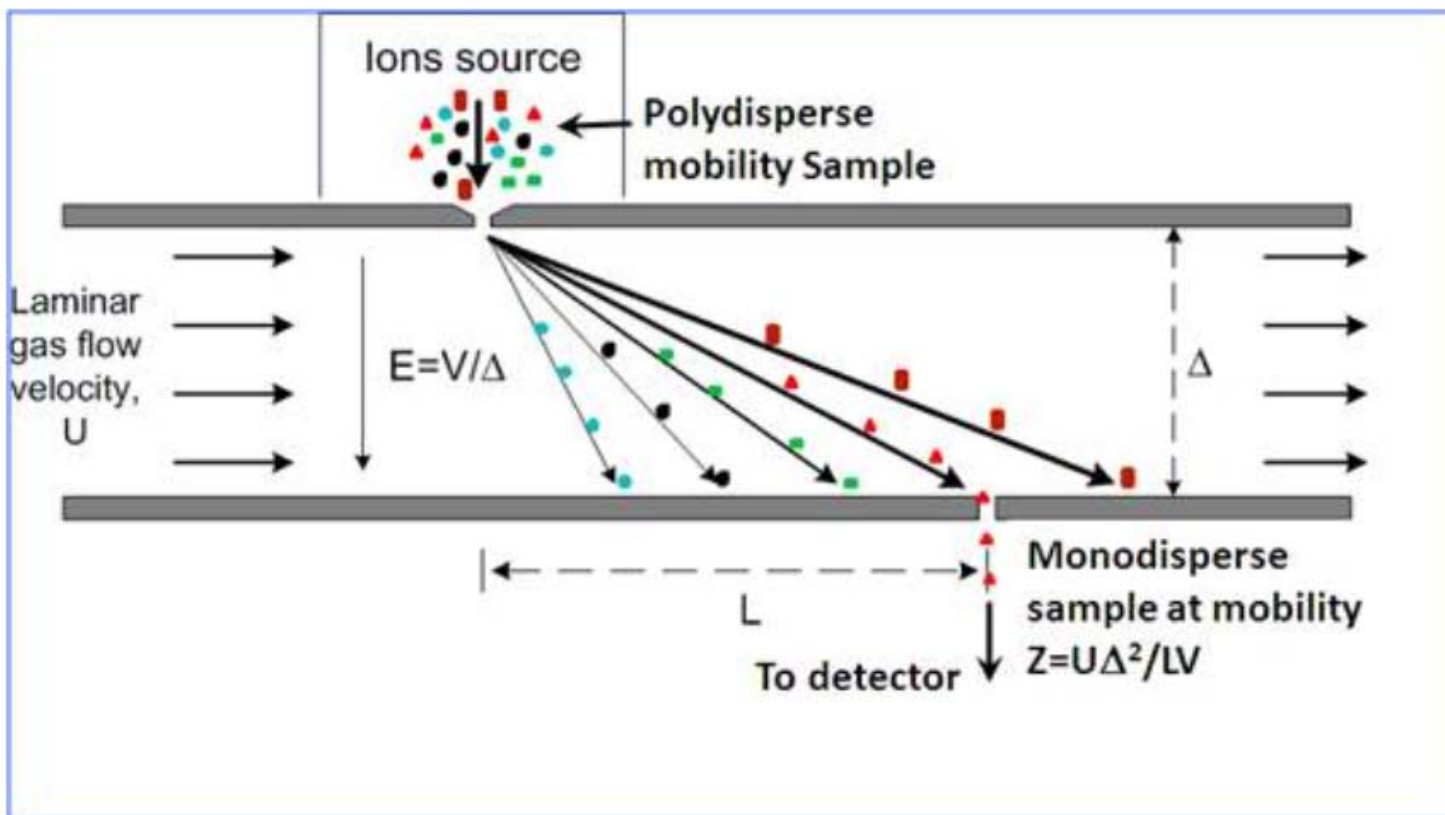


## Spatially dispersive (filter)



# Differential Mobility Analyzer (DMA)

Functions as an ion mobility filter



<https://www.seadm.com/products/mobility-front-end-ion-mobility-filter/>

## Calibration with compounds of known $K_0$

Principle of "secondary methods of measurement":

Instead of characterizing perfectly  $p$ ,  $T$ ,  $L$ ,  $\Delta V$ s and gas flows for each mobility measurement

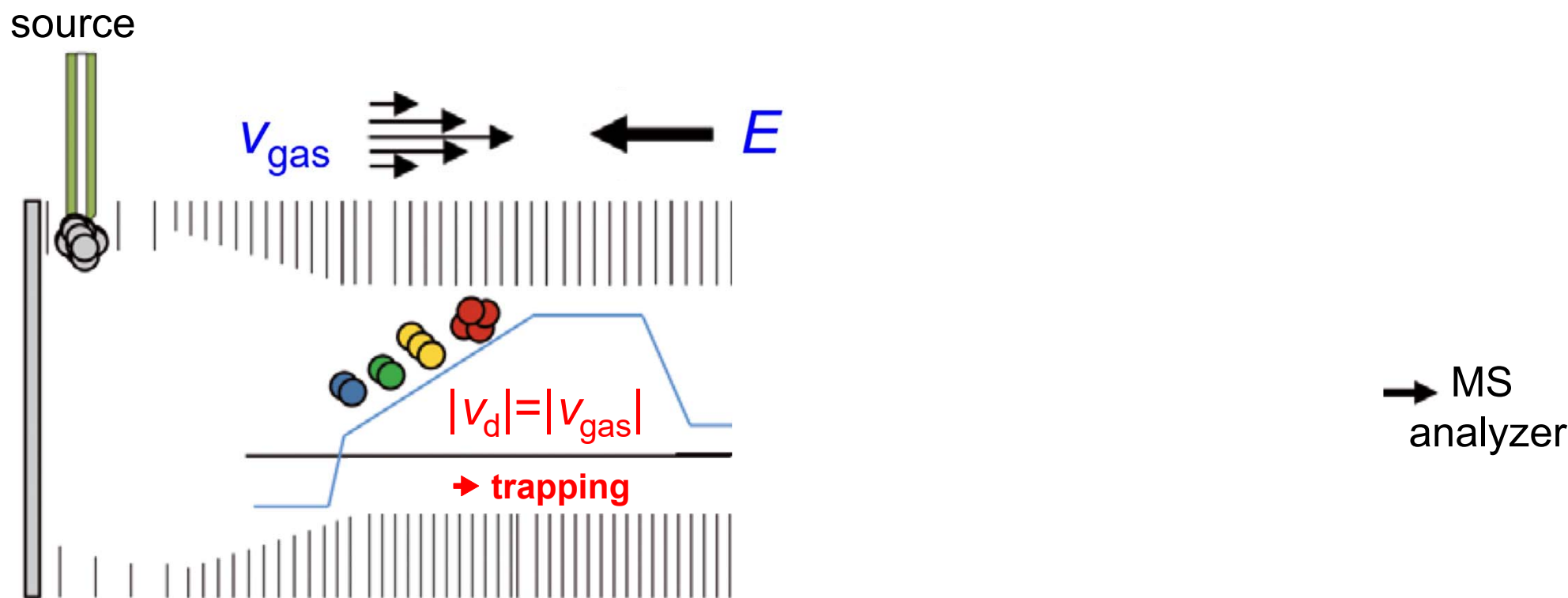
➔ Calibrate instrument with compound(s) of known  $K_0$  value(s) and an appropriate mathematical function

DMA calibration:

$$K_{0(\text{ion})} = K_{0(\text{calibrant})} \frac{V_{\text{calibrant}}}{V_{\text{ion}}}$$

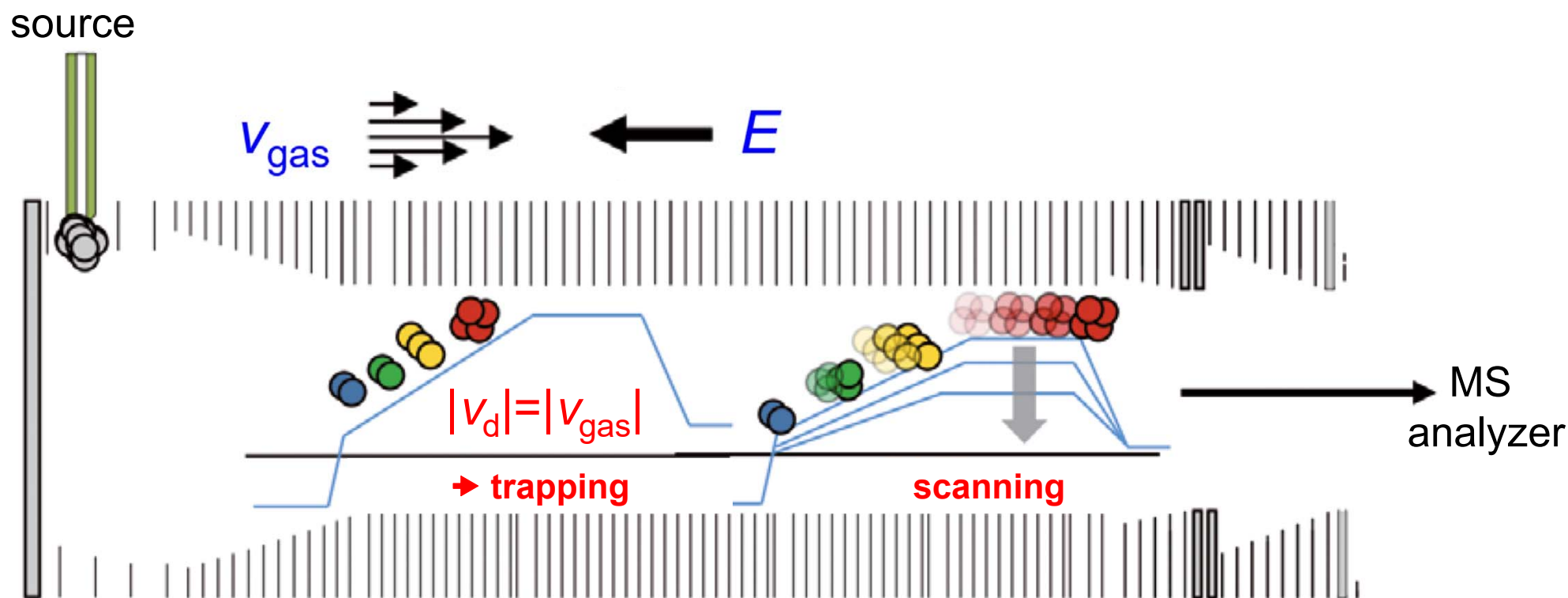
# Trapped Ion Mobility Spectrometry (TIMS)

Functions using an ion mobility-selective instability scan



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Functions using an ion mobility-selective instability scan



## Calibration with compounds of known $K_0$

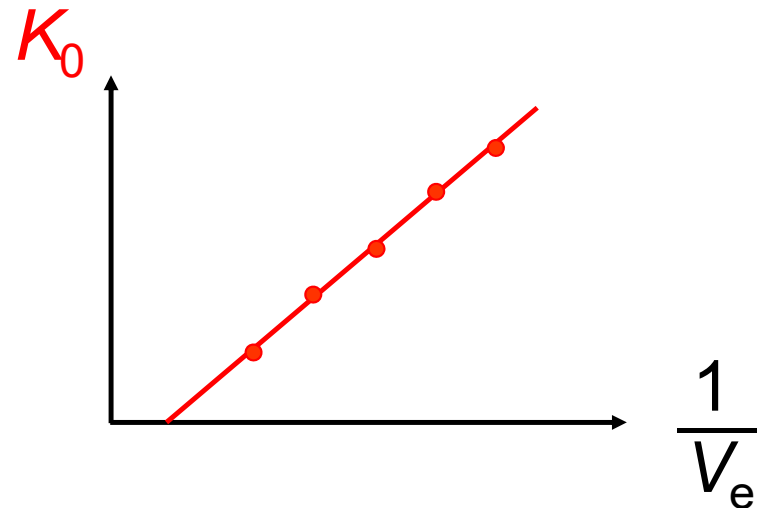
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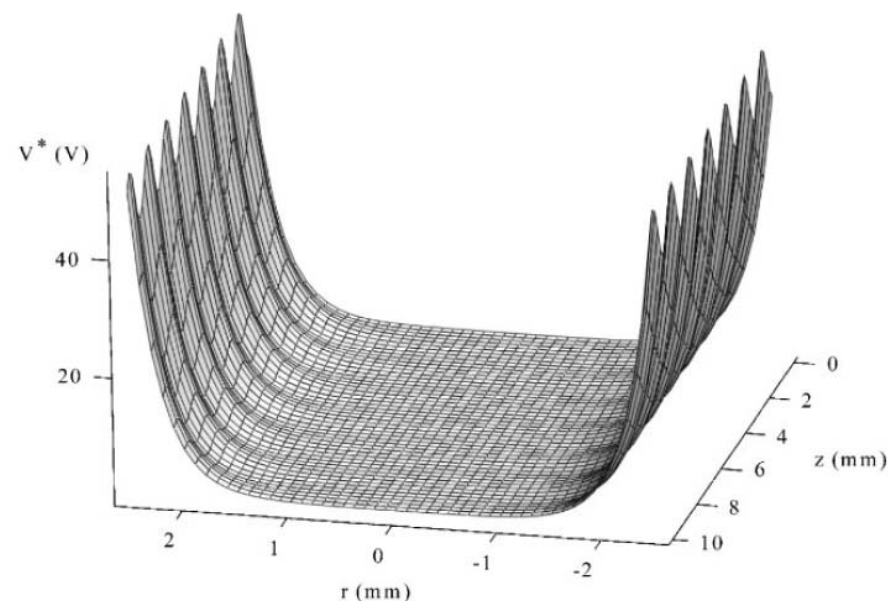
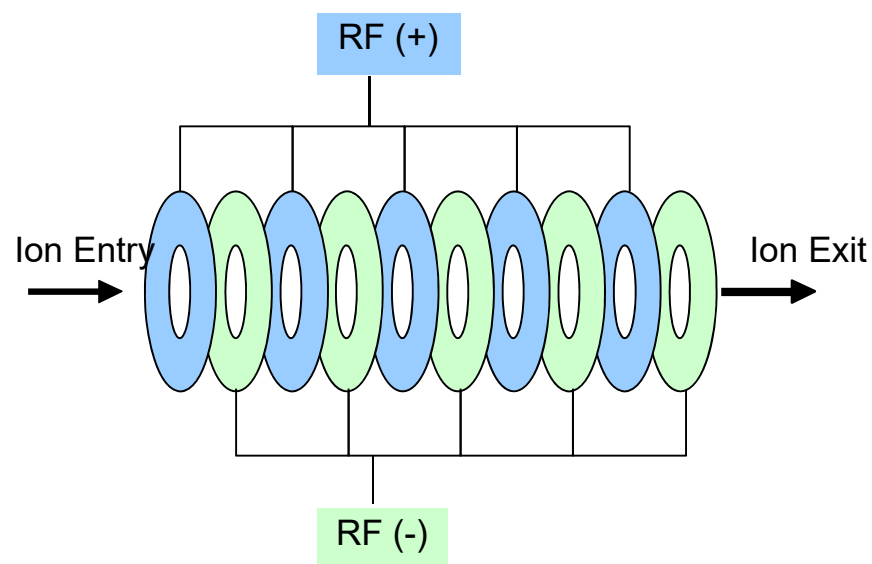
$$\text{Approx: } K_0 = a + b \frac{1}{V_{\text{elution}}}$$



# Travelling Wave Ion Mobility Spectrometry (TWIMS)

RF-only stacked ring ion guide

To confine ions in the center



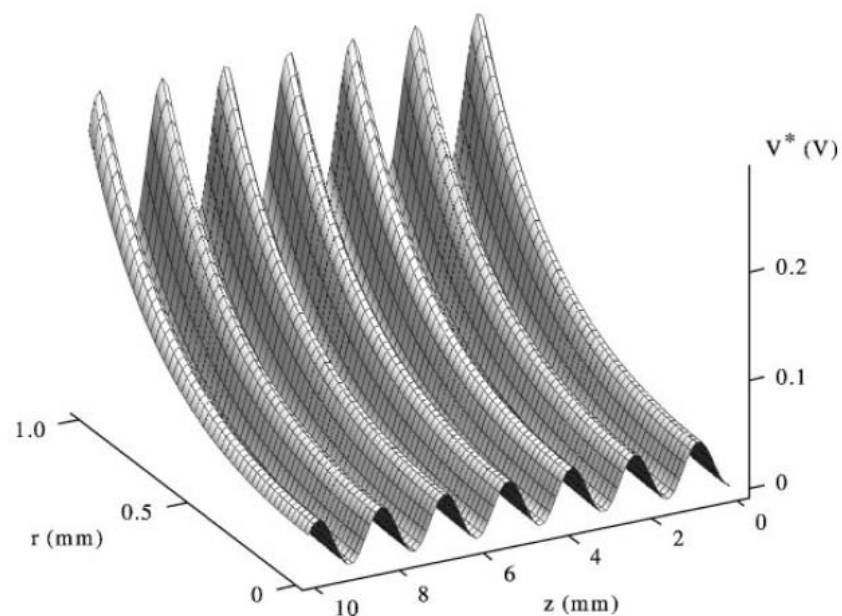
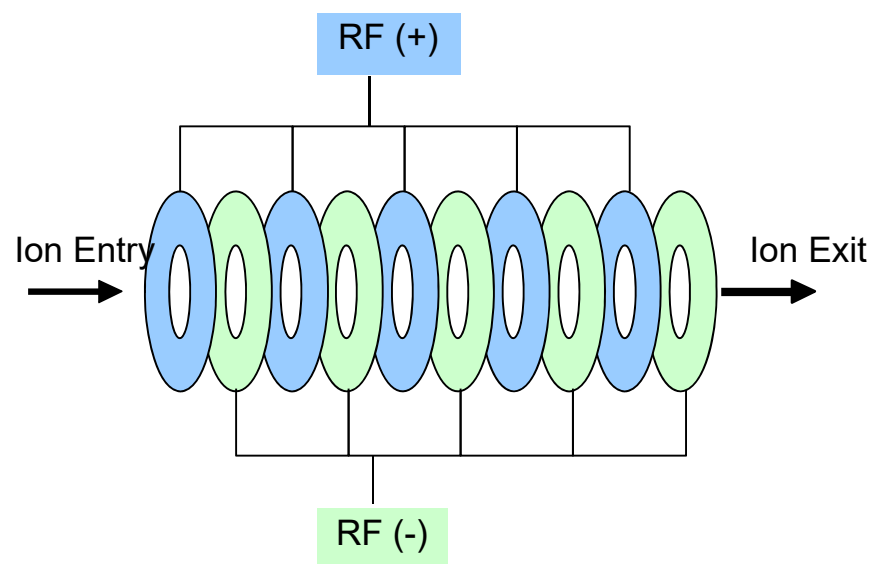
**Figure 2.** The effective potential for a SRIG calculated using Eqn. (1) with an aperture radius  $\rho = 2.5$  mm, ring spacing  $d = 1.5$  mm,  $V_{\text{RF}} = 100$  V at 1 MHz frequency for an ion of mass  $m = 500$  Da and charge  $q = +1e$ .



# Travelling Wave Ion Mobility Spectrometry (TWIMS)

RF-only stacked ring ion guide

To confine ions in the center

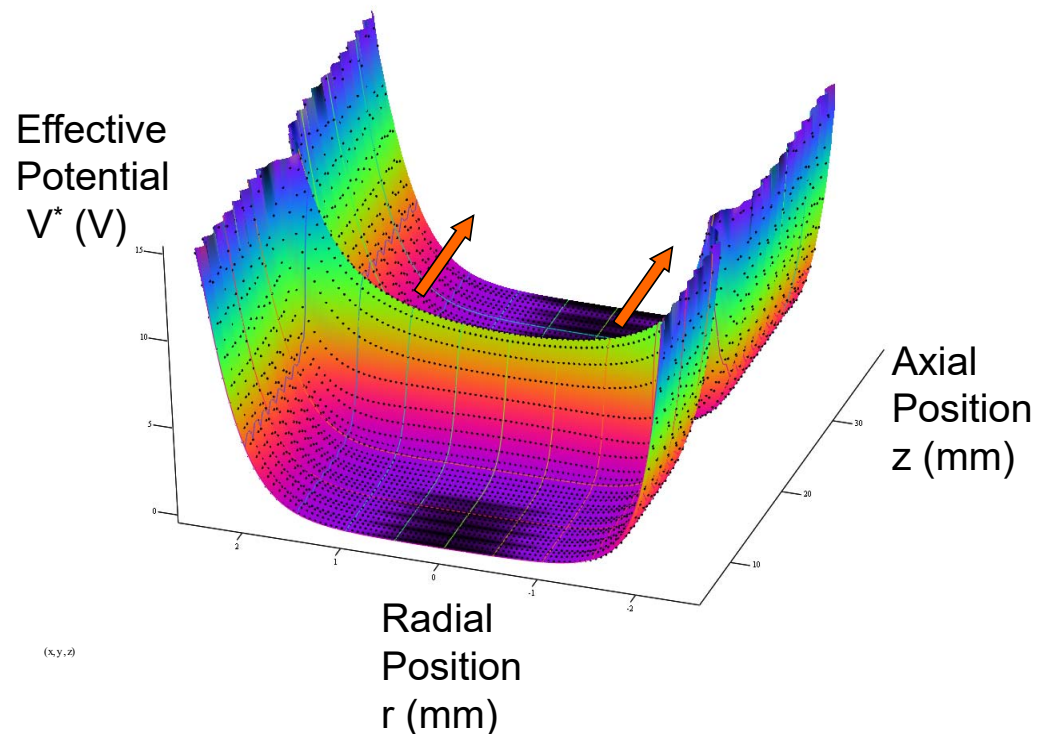
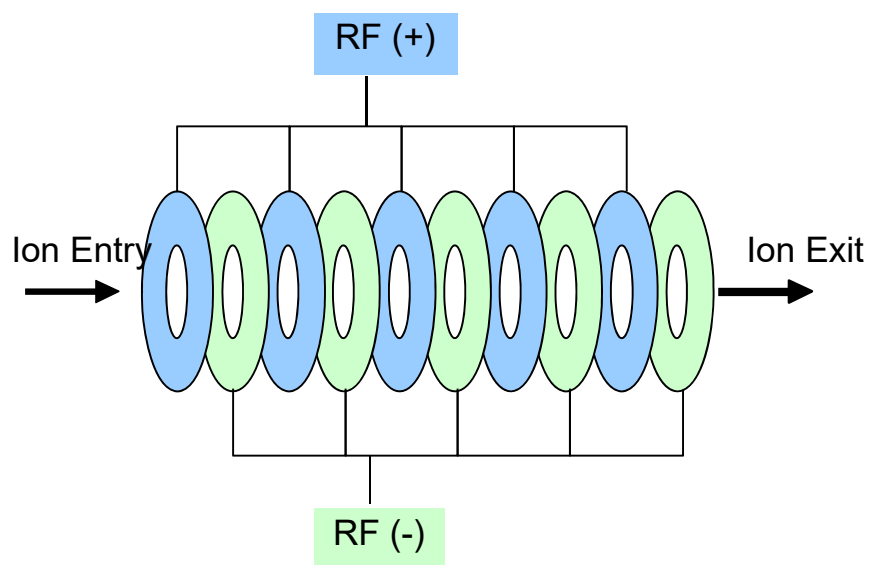


**Figure 3.** Expanded view of the SRIG effective potential shown in Fig. 2 illustrating the 'traps' formed along the  $z$ -axis of the device.

# Travelling Wave Ion Mobility Spectrometry (TWIMS)

RF-only stacked ring ion guide + travelling DC pulse

To confine ions in the center + to move ions towards the exit

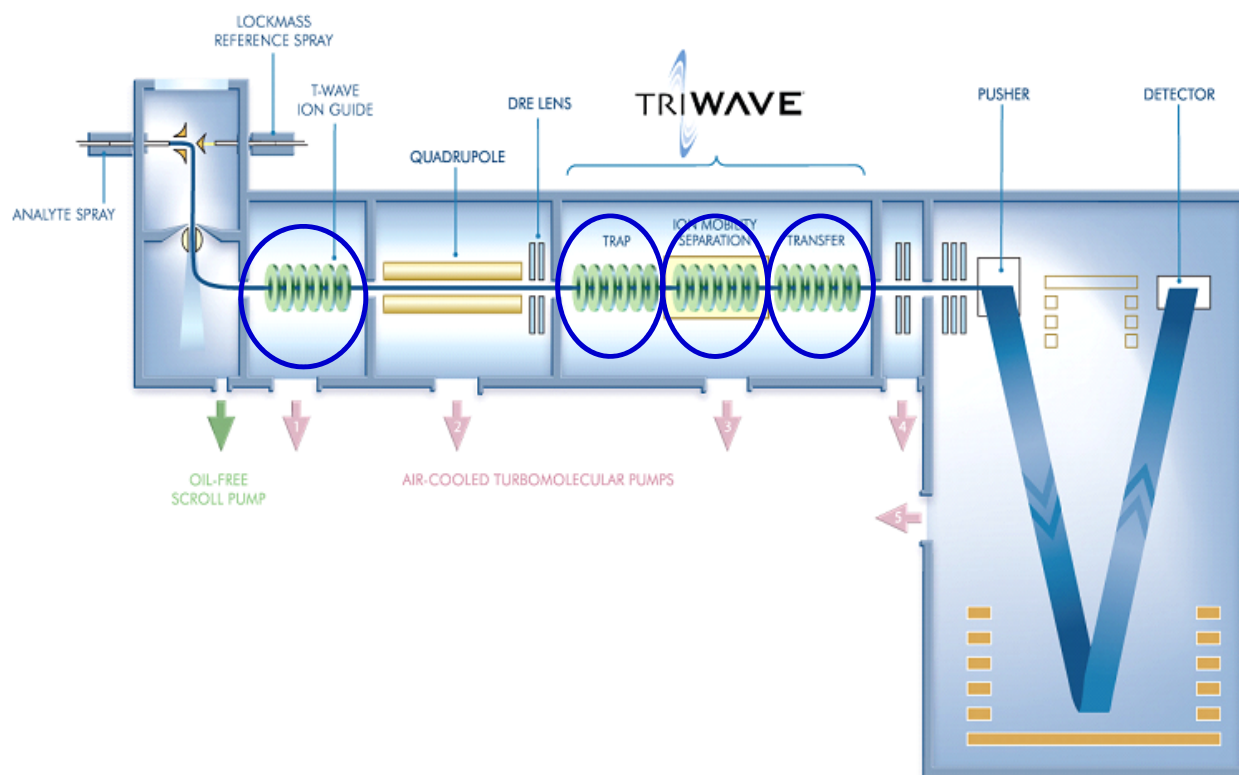


Giles et al., *Rapid Commun. Mass Spectrom.* (2004) 18: 2401

# Travelling Wave Ion Mobility Spectrometry (TWIMS)

## Travelling Wave Stacked Ring Ion Guide

→ for ion transmission



SYNAPT G1 instrument scheme (Waters)

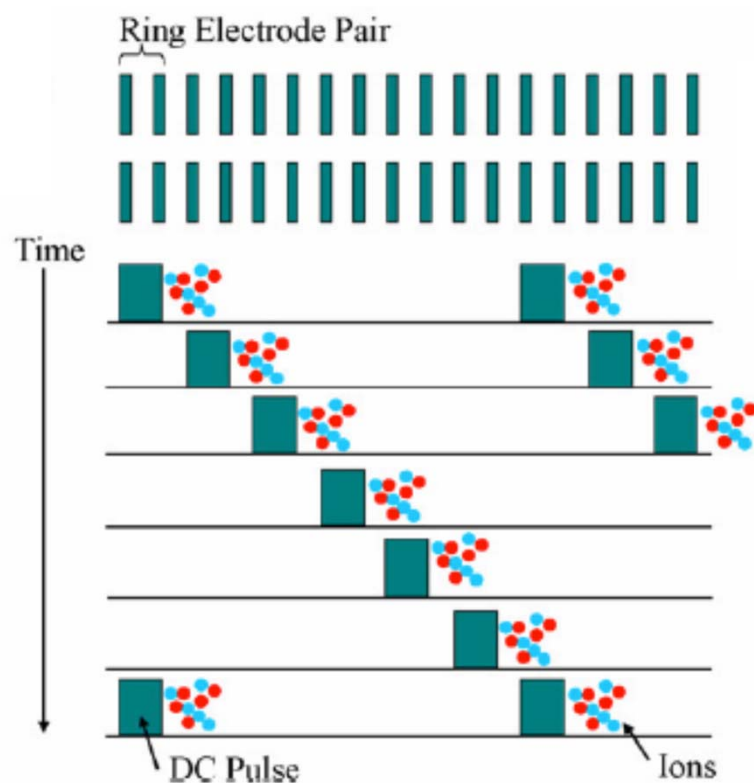
# Travelling Wave Ion Mobility Spectrometry (TWIMS)

## Travelling Wave Stacked Ring Ion Guide

➔ for ion transmission

If **high wave height** and **low pressure**

➔ All ions are pushed at wave speed

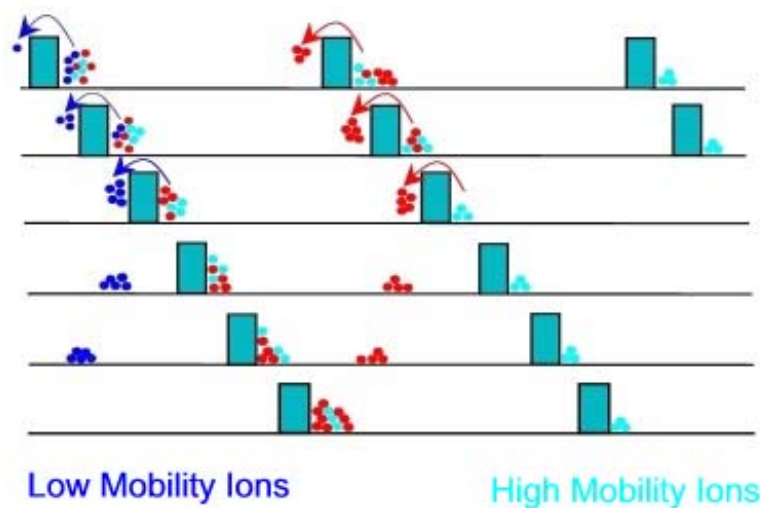


# Travelling Wave Ion Mobility Spectrometry (TWIMS)

## Travelling Wave Stacked Ring Ion Guide

➔ for ion mobility

If **low wave height** and **high pressure**  
➔ Ions are slower than wave speed, because of friction (collisions)

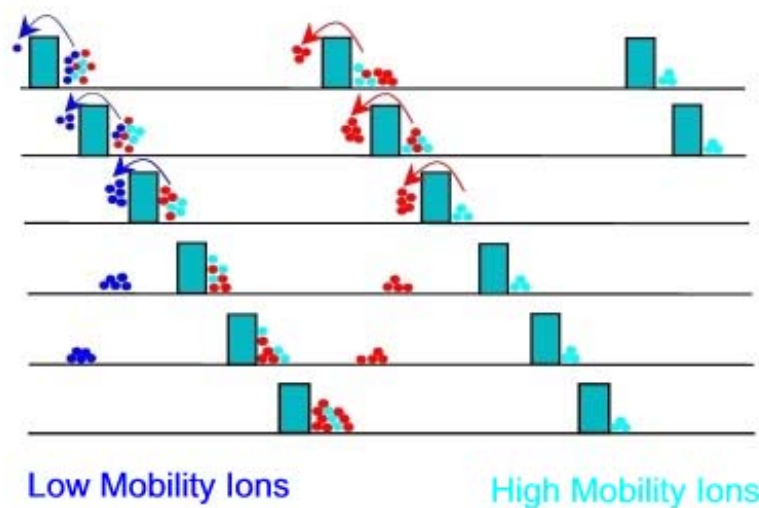


# Travelling Wave Ion Mobility Spectrometry (TWIMS)

## Travelling Wave Stacked Ring Ion Guide

### ➔ for ion mobility

If **low wave height** and **high pressure**  
➔ Ions are slower than wave speed  $s$ ,  
because of friction (collisions)



- ➔ Ion instant speed is dictated by  $v_d = K.E$
- ➔ Time spent by ions in the TW ( $t_d$ )  
is correlated to  $K$



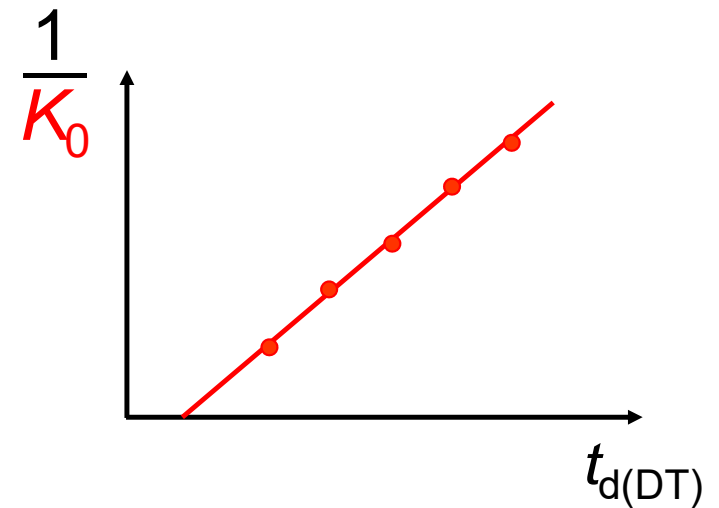
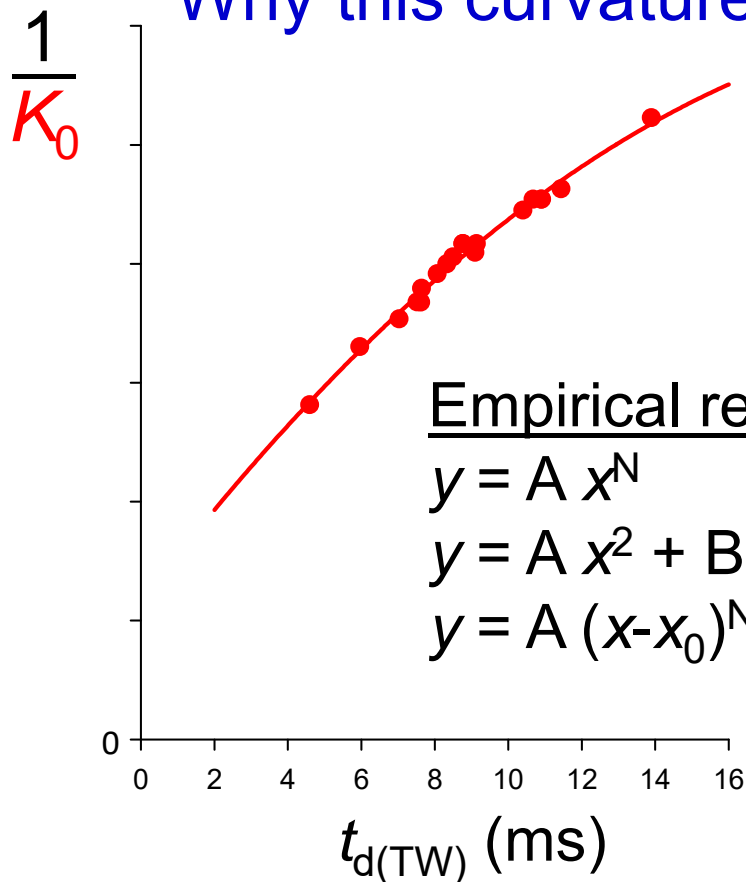
# Calibration with compounds of known $K_0$

**TWIMS**

≠

**DTIMS**

Why this curvature?



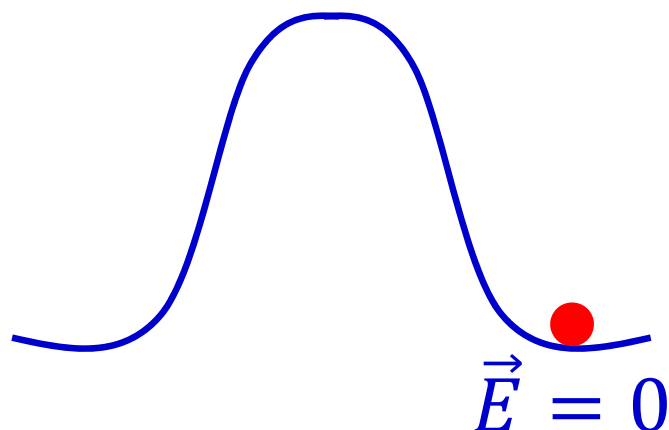
# Travelling Wave Ion Mobility Spectrometry (TWIMS)

## How drift time $t_d$ relates to $K$ in TWIMS

Ions respond to field by reaching a velocity  $\vec{v}_d = K \cdot \vec{E}$

Travelling Wave IMS  $\rightarrow$  the field is constantly changing

$\rightarrow$  ion velocity is constantly changing





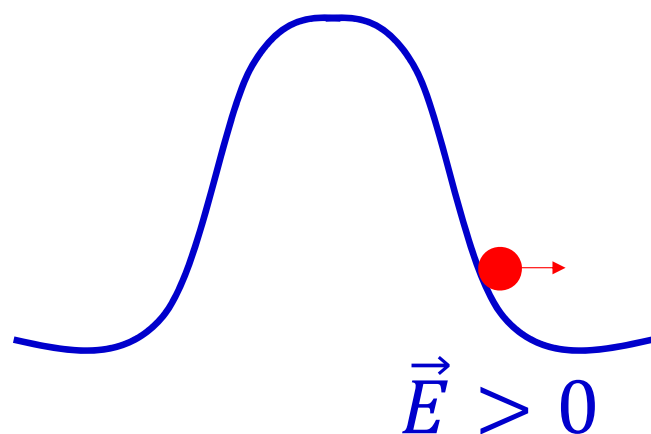
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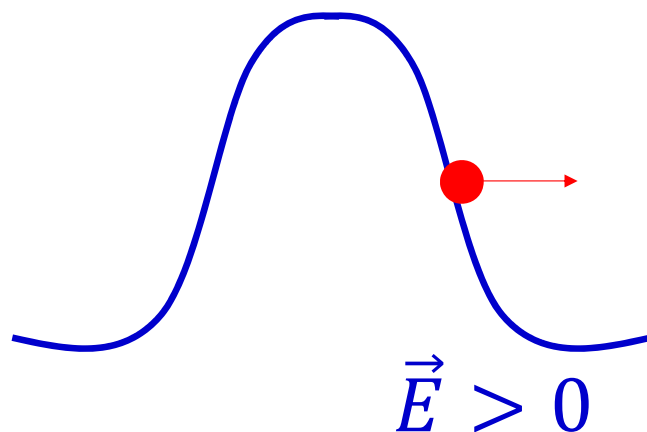
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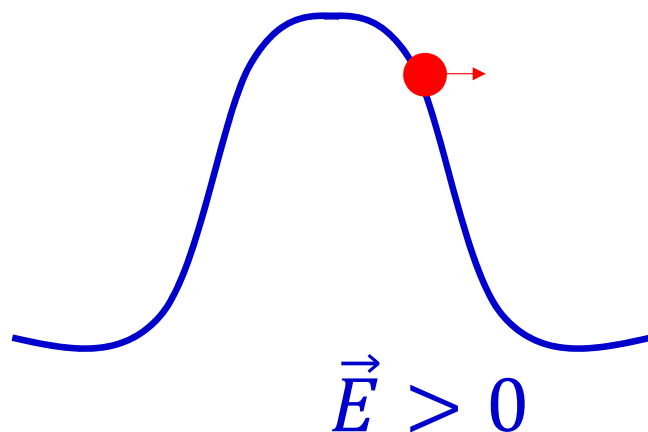
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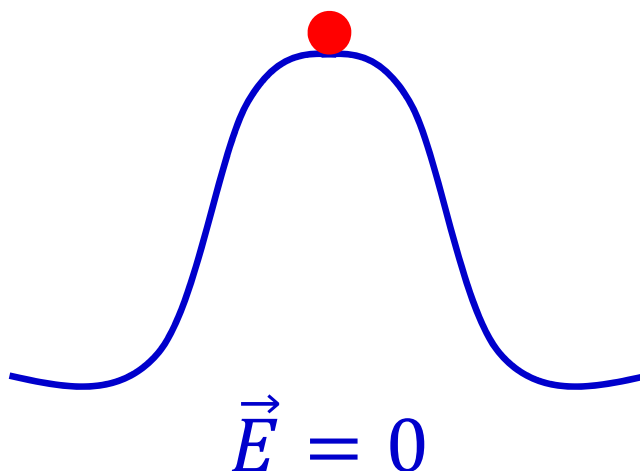
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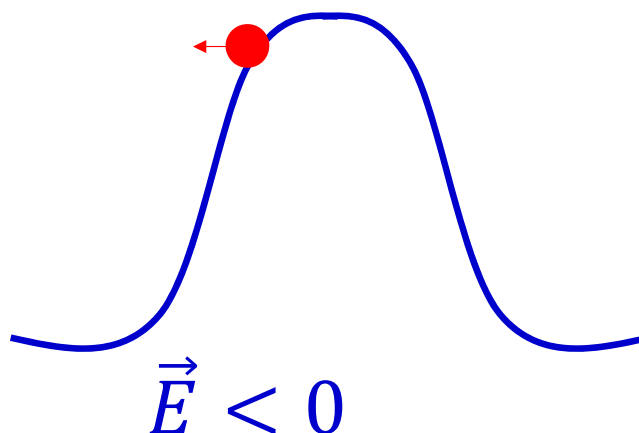
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Ions respond to field by reaching a velocity  $\vec{v}_d = K \cdot \vec{E}$

Travelling Wave IMS  $\rightarrow$  the field is constantly changing

$\rightarrow$  ion velocity is constantly changing



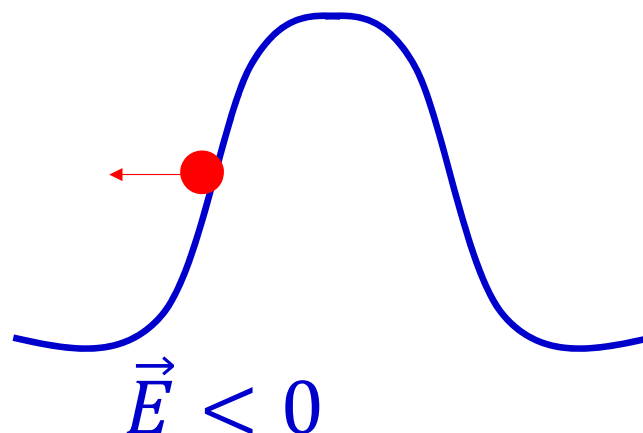
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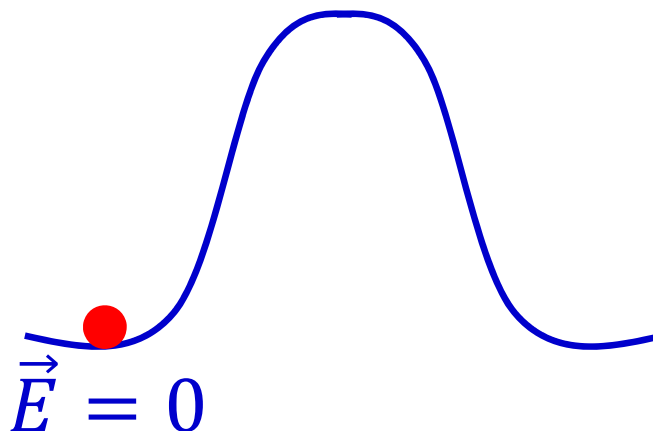
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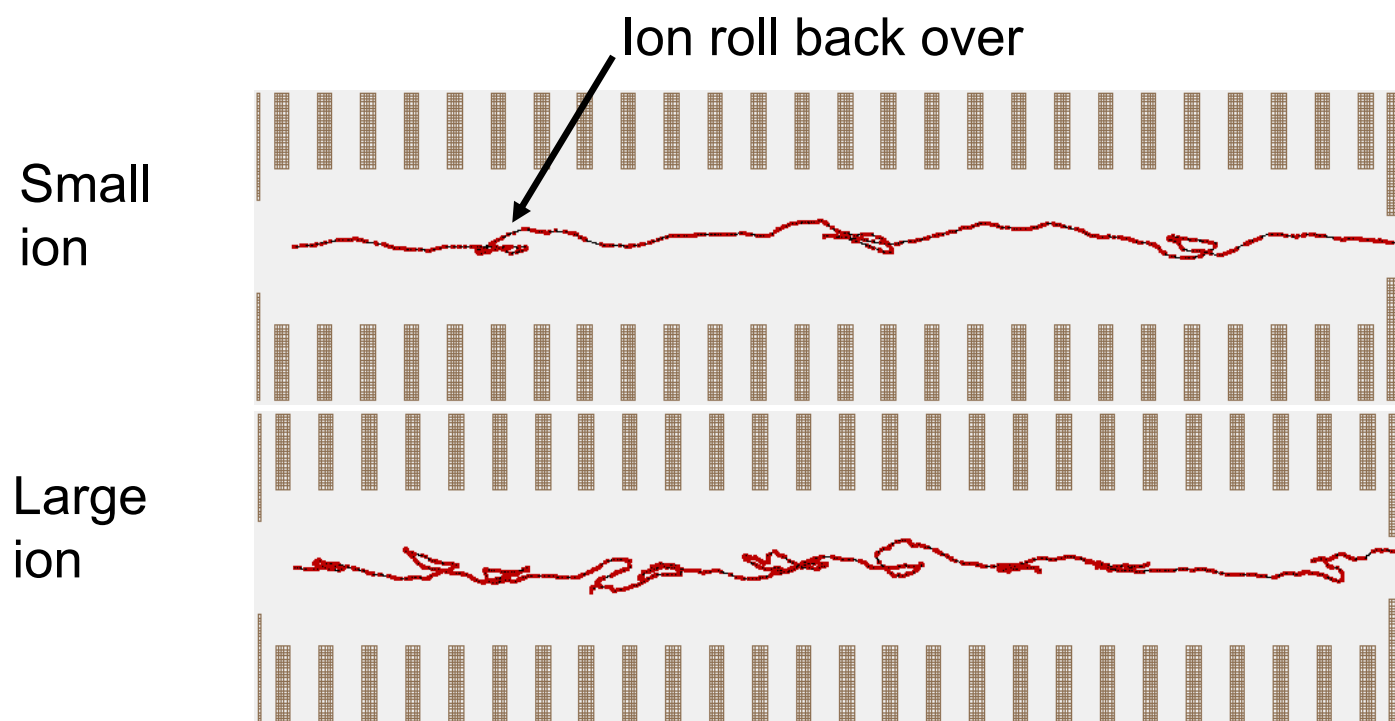
$\rightarrow$  ion velocity is constantly changing



# Travelling Wave Ion Mobility Spectrometry (TWIMS)

How drift time  $t_d$  relates to  $K$  in TWIMS

Simulated ion trajectories:





# Travelling Wave Ion Mobility Spectrometry (TWIMS)

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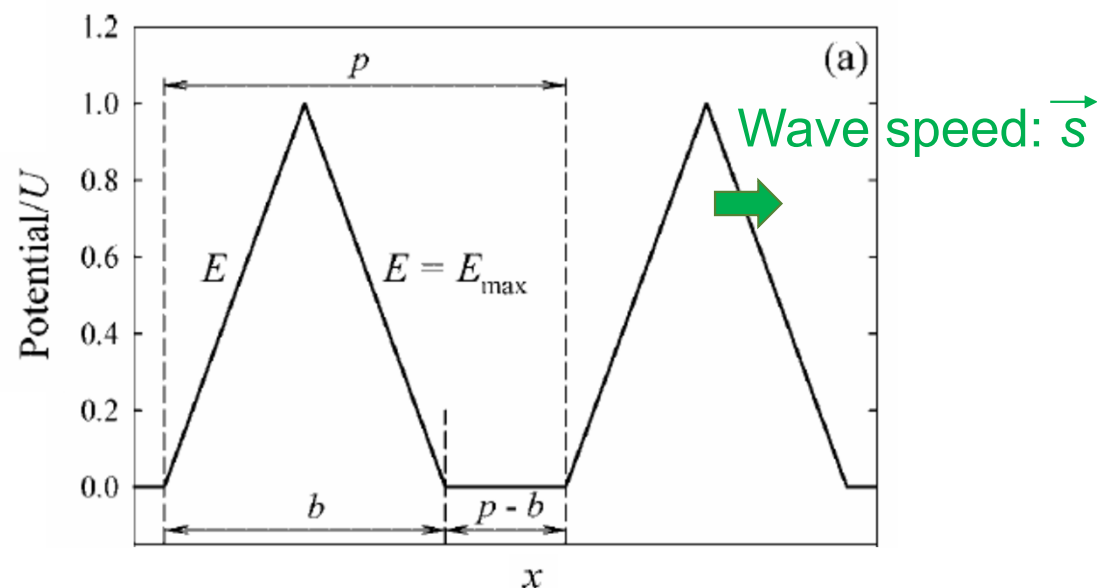
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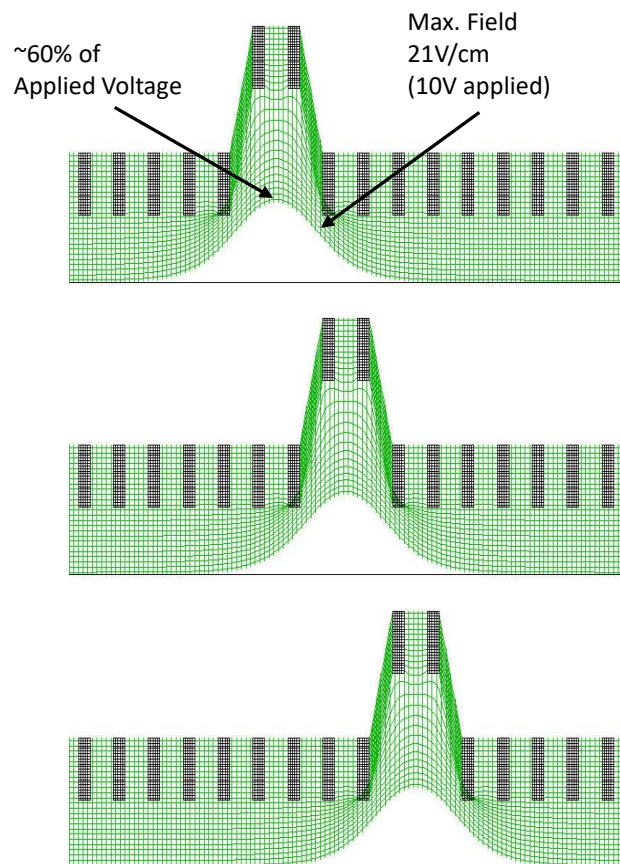
Assuming triangular waves  
and instant response to  $\vec{E}$

$$\frac{L}{t_{d(TW)}} = \frac{b \cdot s \cdot (KE)^2}{ps^2 - (p - b)(KE)^2}$$

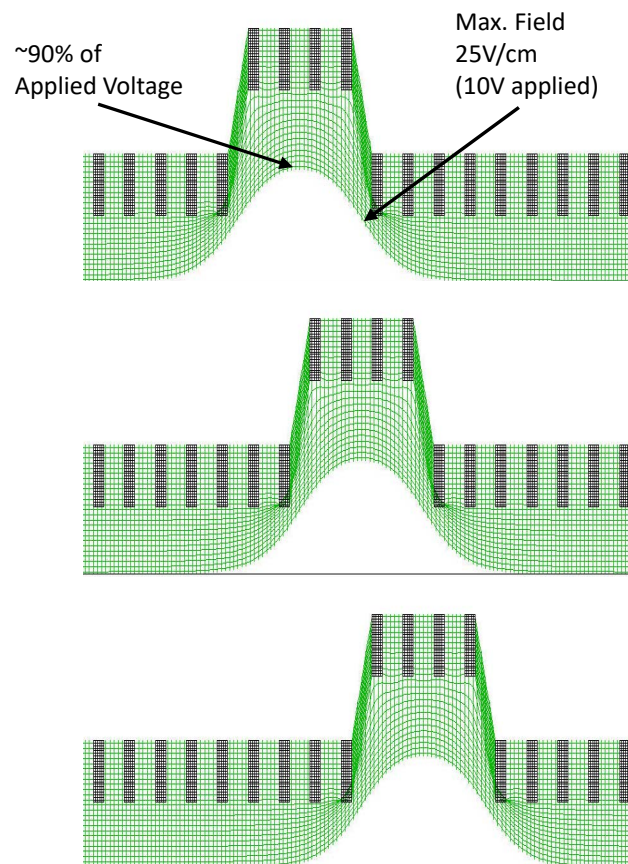


# Travelling Wave Ion Mobility Spectrometry (TWIMS)

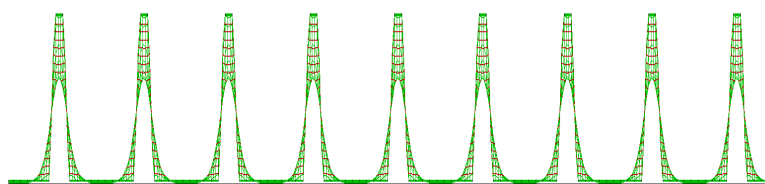
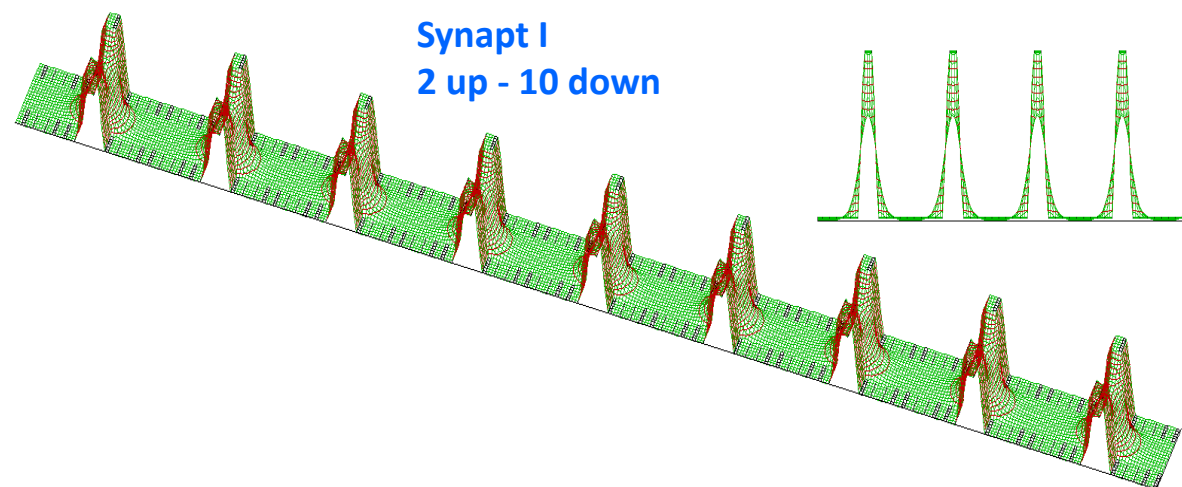
Synapt I



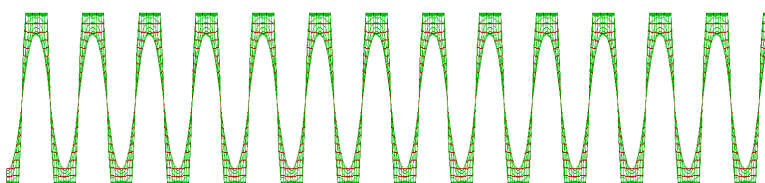
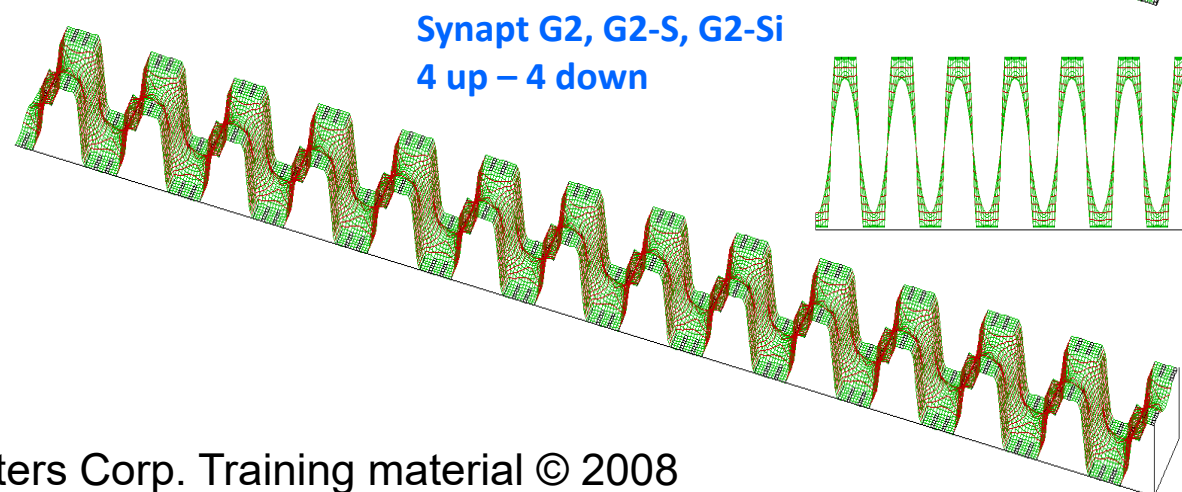
Synapt G2, G2-S, G2-Si



# Travelling Wave Ion Mobility Spectrometry (TWIMS)



~50% of the time  
at  $E=0$  (no wave felt)



Adjacent waves

# Travelling Wave Ion Mobility Spectrometry (TWIMS)

## How drift time $t_d$ relates to $K$ in TWIMS

Ions respond to field by reaching a velocity  $\vec{v}_d = K \cdot \vec{E}$

Travelling Wave IMS  $\rightarrow$  the field is constantly changing

$\rightarrow$  ion velocity is constantly changing

Assuming triangular waves  
and instant response to  $\vec{E}$

Synapt I

$p=2b$

Synapt G2, G2-S, G2-Si

$p=b$

$$\frac{L}{t_{d(TW)}} = \frac{b \cdot s \cdot (KE)^2}{ps^2 - (p - b)(KE)^2}$$

$$t_{d(TW)} \approx \frac{L \cdot s}{(KE)^2}$$

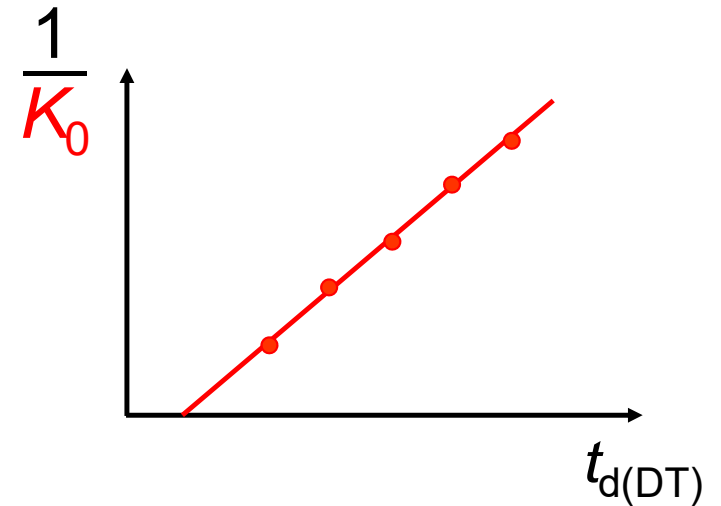
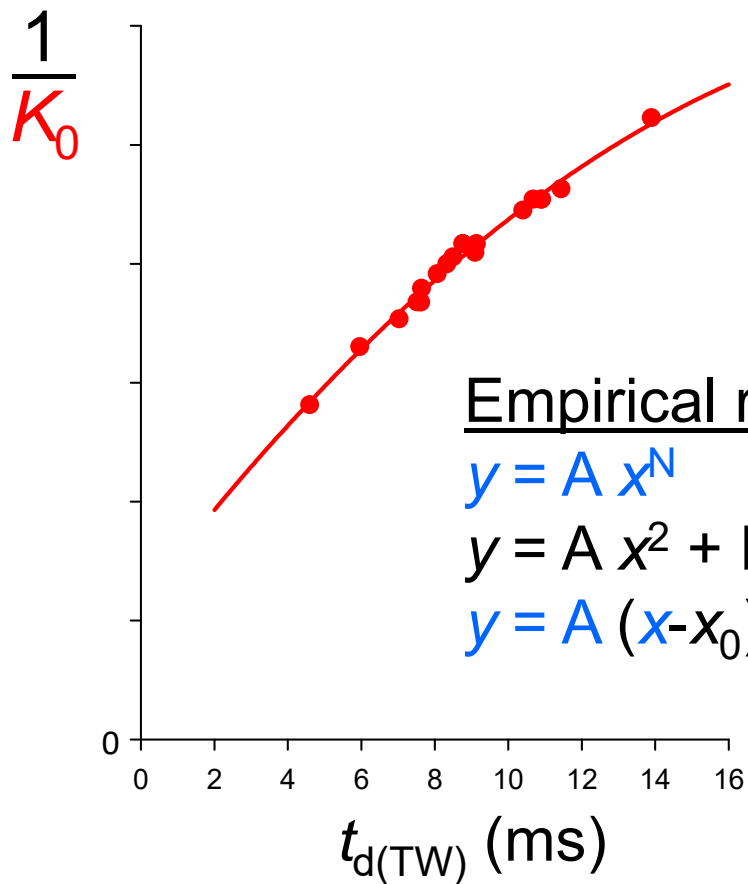
$$\frac{1}{K} \propto A \cdot t_{d(TW)}^{0.5}$$

# Calibration of TWIMS

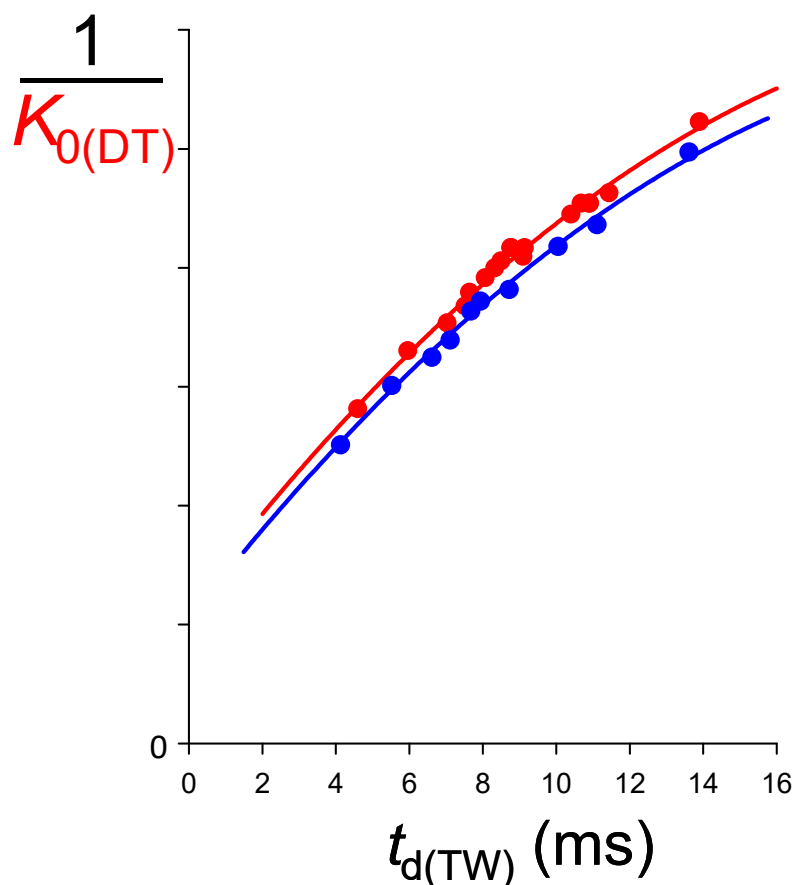
**TWIMS**

≠

**DTIMS**



# TWIMS Calibration Depends on Compound Class



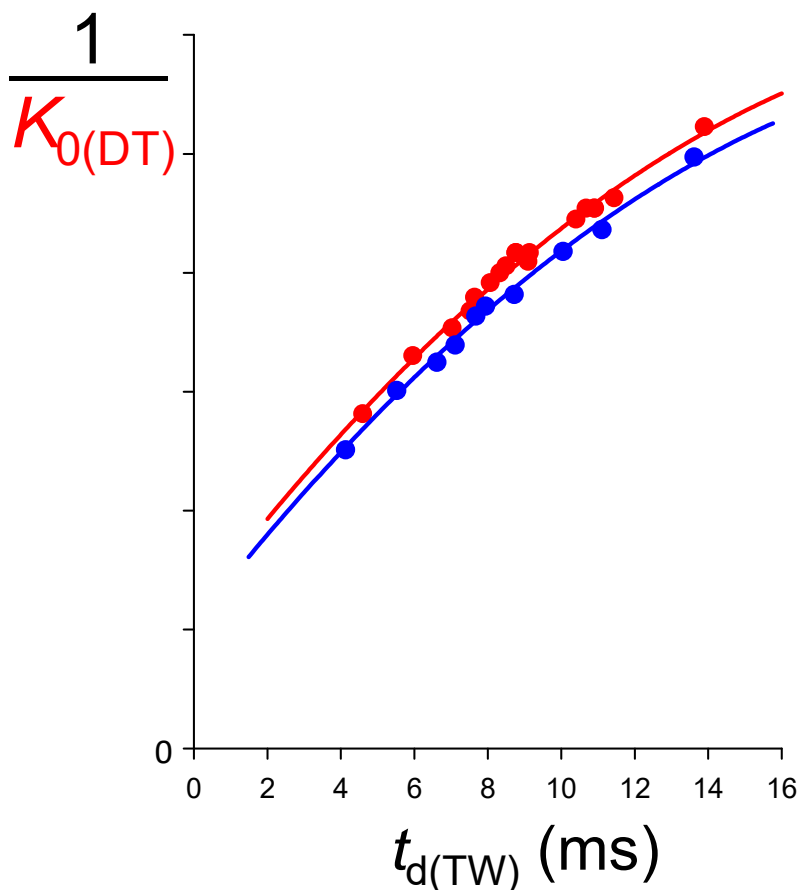
Singly charged  $\neq$  Doubly charged

Lipids  $\neq$  Peptides

Native proteins  $\neq$  Denatured proteins

Soluble proteins  $\neq$  Membrane proteins

# TWIMS Calibration Depends on Compound Class. Why?



A simple explanation in some cases: poor experimental design

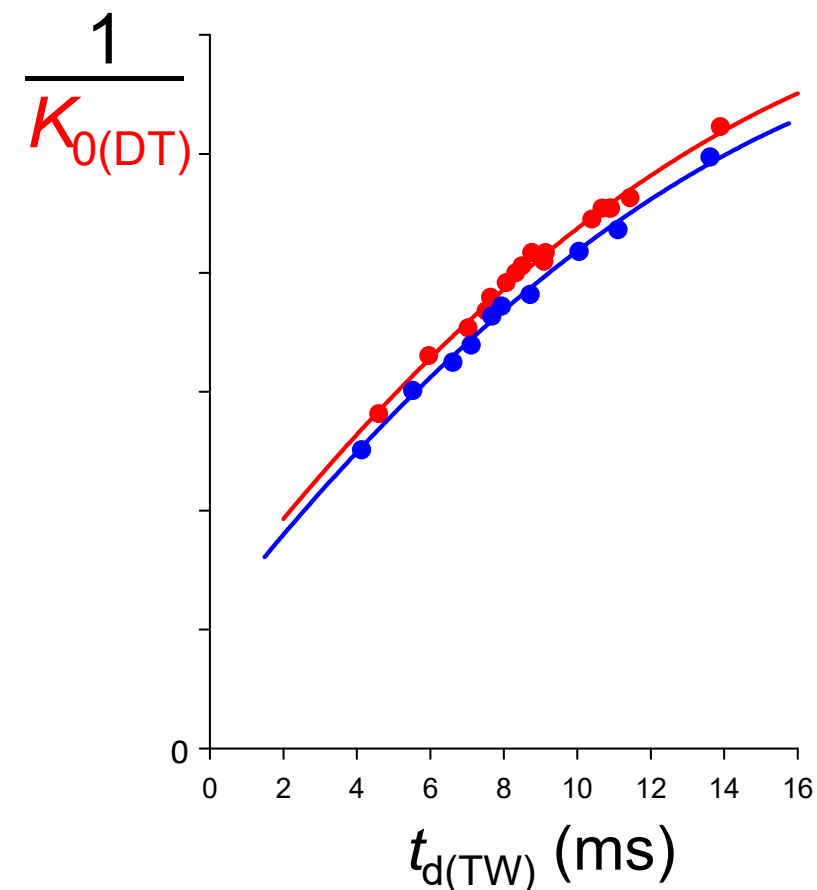
$K_{0(DT)}$  values of series A from lab A

$K_{0(DT)}$  values of series B from lab B

There may be an unrecognized bias between the two labs

➔ If you calibrate using values from lab A, you will reproduce values as measured by lab A

# TWIMS Calibration Depends on Compound Class



Singly charged  $\neq$  Doubly charged

Lipids  $\neq$  Peptides

Native proteins  $\neq$  Denatured proteins

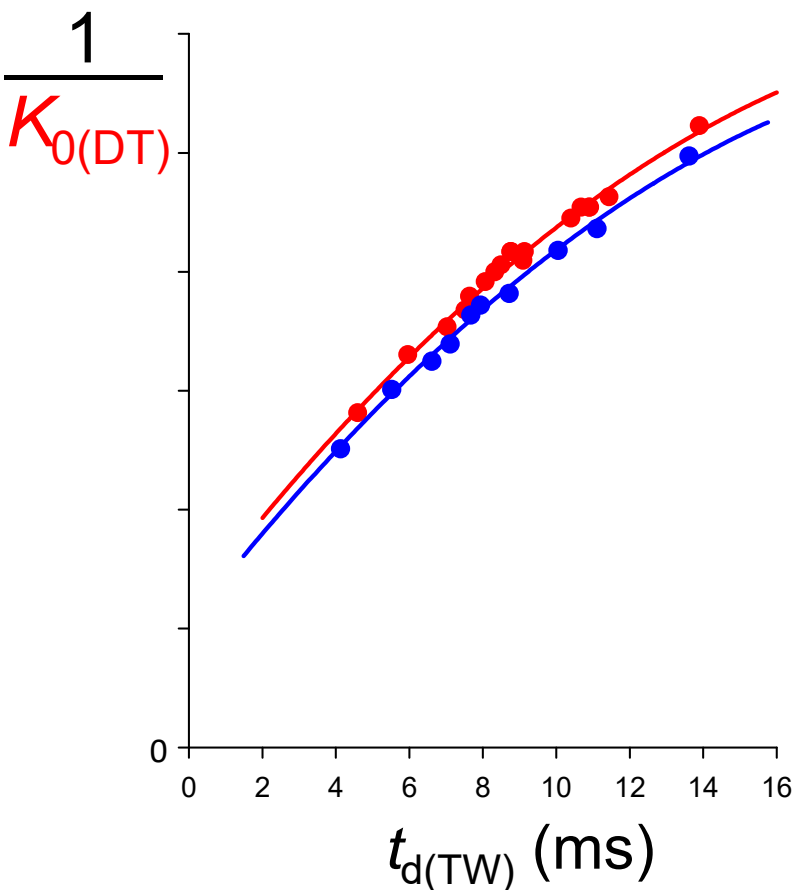
Soluble proteins  $\neq$  Membrane proteins

Even discarding labA/labB effects,  
compound-class effects remain

**Why?**



# TWIMS Calibration Depends on Compound Class. Why?



Hypothesis 1:

$$K_0(TW) \neq K_0(DT)$$

And the relationship depends on compound class

**How could  $K_0$  be different in DT and in TW?**

# Influence of pressure and temperature on $K$

One reason  $T$  and  $p$  influence  $K$  is collision frequency

The reduced mobility  $K_0$  corrects for collision frequency effects

$$K_0 = K \frac{N}{N_0} = K \frac{p T_0}{p_0 T}$$

 The ion's reduced mobility  $K_0$  still depends on  $T$ ,  $p$  and  $E$  for other reasons

## Effect of $E/N$ on $K_0$

Is the "low  $E/N$ " assumption justified?

- The value of the *low field limit* ( $E/N$ , in Td) is unknown  
It depends on
  - the ion
  - the collision gas
  - the measurement precision
- Low-field limit criterion:  $v_d \ll v_{\text{thermal}}$

➔ How much is  $v_{\text{thermal}}$ ? 
$$v_{\text{thermal}} = \sqrt{\frac{8 k_B T}{\pi \mu}}$$
$$\mu = \frac{m_{\text{ion}} m_{\text{gas}}}{(m_{\text{ion}} + m_{\text{gas}})} = \text{reduced mass}$$

# Effect of $E/N$ on $K_0$

$$v_{thermal} = \sqrt{\frac{8 k_B T}{\pi \mu}}$$

$$\mu = \frac{m_{ion} m_{gas}}{(m_{ion} + m_{gas})}$$

$m_{gas}$ (Da)	$m_{ion}$ (Da)	$T$ (K)	$v_{thermal}$ (m/s)
4	200	300	1239
4	2000	300	1228
4	20000	300	1227
4	200000	300	1227
28	200	300	495
28	2000	300	467
28	20000	300	464
28	200000	300	464
28	200000	100	268
28	200000	200	379
28	200000	300	464
28	200000	400	535
28	200000	500	599

He:  
~1230 m/s

N<sub>2</sub>:  
~470 m/s

# Effect of $E/N$ on $K_0$

Criterion:  $v_d \ll v_{\text{thermal}}$

He:  $v_{\text{thermal}} \approx 1230 \text{ m/s}$

N<sub>2</sub>:  $v_{\text{thermal}} \approx 470 \text{ m/s}$

How much is  $v_d$ ?

Table 1

Estimates of typical operating parameters for contemporary commercial instruments

Instrument and manufacturer	Operation principle	$p$ (Torr)	$E$ (V/cm)	Typical $E/N$ (Td)	Typical $v_D$ (m/s)
6560 IMS-Q-TOF, Agilent Technologies	Drift tube	4	9.5–20	7–15 [33]	10–80
Synapt HDMS, Waters	TWIMS	0.4	21 (maximum axial field at wave height = 10 V) [34]	$\leq 160$	200–600 [29]
Synapt G2, G2-S and G2Si HDMS, Waters	TWIMS	2	100 (maximum axial field at wave height = 40 V)	$\leq 155$	200–300 [30]
TIMS-TOF, Bruker	TIMS	2	30–55	45–85	120–170 <sup>a</sup> [35]
IMS-TOF, ToFwerk	Drift tube	570–788	$\sim 400$	1–2 [36]	$\sim 5$

<sup>a</sup> Gas velocity; in TIMS the ion is static.

➔ In TIMS and TWIMS in N<sub>2</sub>, we *may not* be in the "low  $E/N$ " limit

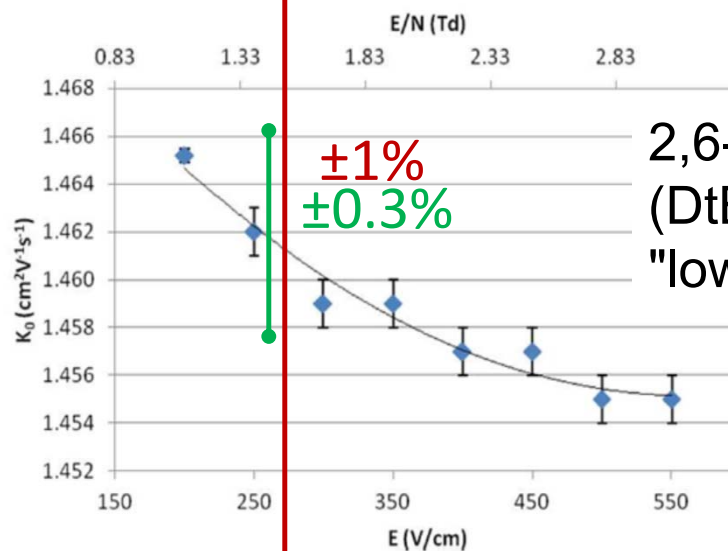
Gabelica & Marklund, *Curr. Op. Chem. Biol.* (2018) 42:51–59

## Effect of $E/N$ on $K_0$

➔ In TIMS and TWIMS in  $N_2$ , we *may not* be in the "low  $E/N$ " limit

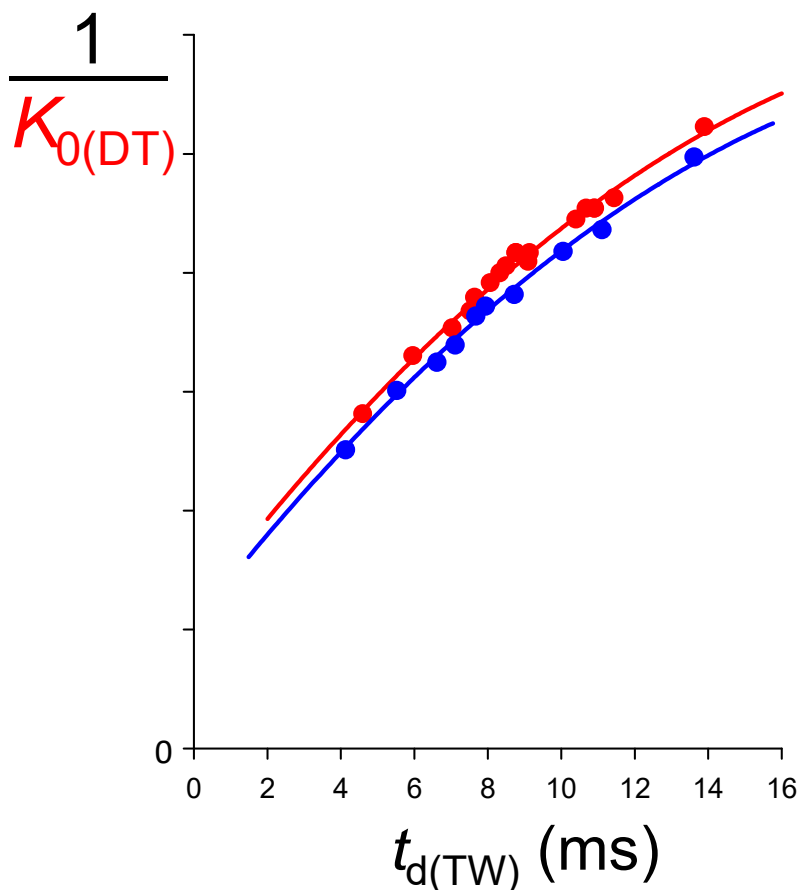
Are the effects significant?

We don't know yet. - It depends on measurement precision  
- Calibration may compensate some effects



Hauck, Siems, Harden, McHugh & Hill, *J. Phys. Chem. A* (2017) 121, 2274

# TWIMS Calibration Depends on Compound Class. Why?



Hypothesis 1:

$$K_0(\text{TW}) \neq K_0(\text{DT})$$

because measurements are done at different  $E/N$

and the relationship  $K_{0(\text{low } E/N)} / K_{0(\text{high } E/N)}$  depends on compound class

However, similar  $E/N$  in TWIMS and TIMS, yet compound-class dependence doesn't arise in TIMS.  
=> Hyp. 1 not the main reason.

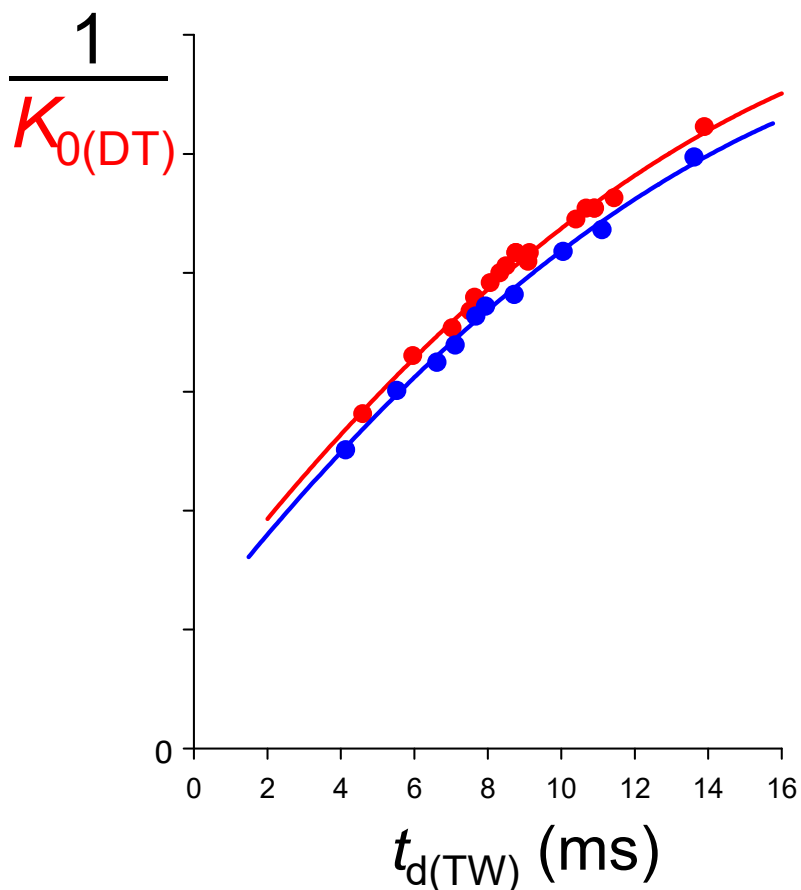
# TWIMS Calibration Depends on Compound Class. Why?

Hypothesis 2:

$$K_0(\text{TW}) \neq K_0(\text{DT})$$

because measurements are done  
in **different gases**

and the relationship  $K_{0(\text{gas1})}/K_{0(\text{gas2})}$   
depends on compound class

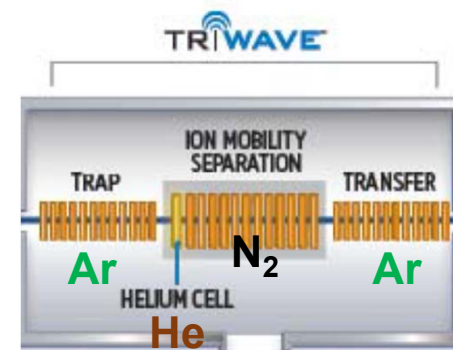




## Gases in TWIMS

Synapt G1       $\text{N}_2$  most common  
He, Ar,  $\text{CO}_2$ ,... possible but rare

Synapt G2       $\text{N}_2$  most common in IM region  
Helium cell right in front  
 $\Rightarrow$  in practice:  $\text{N}_2/\text{He}$  mixture



## Gases in DTIMS

Before 2010: almost only He data were available

2010:  $\text{N}_2$  data available (RF-confining drift cell in a Synapt)

G1: Bush, Hall, Giles, Hoyes, Robinson & Ruotolo, *Anal. Chem.* (2010) 82: 9557.

G2: Allen, Giles, Gilbert & Bush, *Analyst* (2016) 141: 884.

2013: Agilent drift tube: most common is  $\text{N}_2$

## Effect of the collision gas and $T$ on $K_0$

### Actually, what is a collision?

- If ion and gas change trajectory after their encounter, a collision has happened
- Collisions can be elastic or inelastic. Theories discussed here apply only elastic collisions (i.e. only to low-field IMS)
- Elastic collision: conservation of translational energy (momentum is conserved; only momentum transfer)  
no conversion of translation energy into rotation or vibration

# Relationship between $K$ and “Collision Cross Section”

Fundamental low-field limit ion mobility equation:

(abusively called « Mason-Schamp equation »)

$$K = \frac{3}{16} \sqrt{\frac{2\pi}{\mu k_B T}} \frac{ze}{N \Omega} = \frac{3}{16} \sqrt{\frac{2\pi}{\mu k_B T}} \frac{ze}{N_0 \left( \frac{p}{p_0} \cdot \frac{T_0}{T} \right) \Omega} \quad \text{with } \mu = \frac{m_{ion} m_{gas}}{(m_{ion} + m_{gas})}$$
$$K_0 = \frac{3}{16} \sqrt{\frac{2\pi}{\mu k_B T}} \frac{ze}{N_0 \Omega}$$

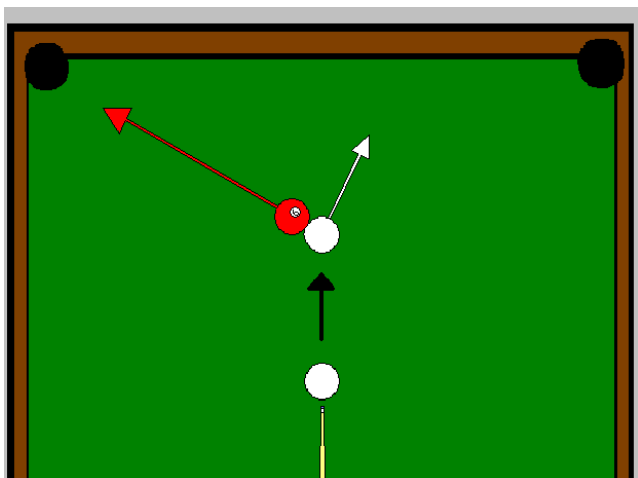
$\Omega$  = momentum transfer cross section, abusively called  
« collision cross section » and abbreviated CCS




Alternative equations based on other physical representations are possible. It's a mathematical model.

## Effect of the collision gas and $T$ on $K_0$

Historically, the term « collision cross section » was used in the context of a hard spheres collision model



 **Atoms are  
not hard spheres!**

Wytttenbach, Bleiholder & Bowers  
*Anal. Chem.* (2013) 85, 2191.

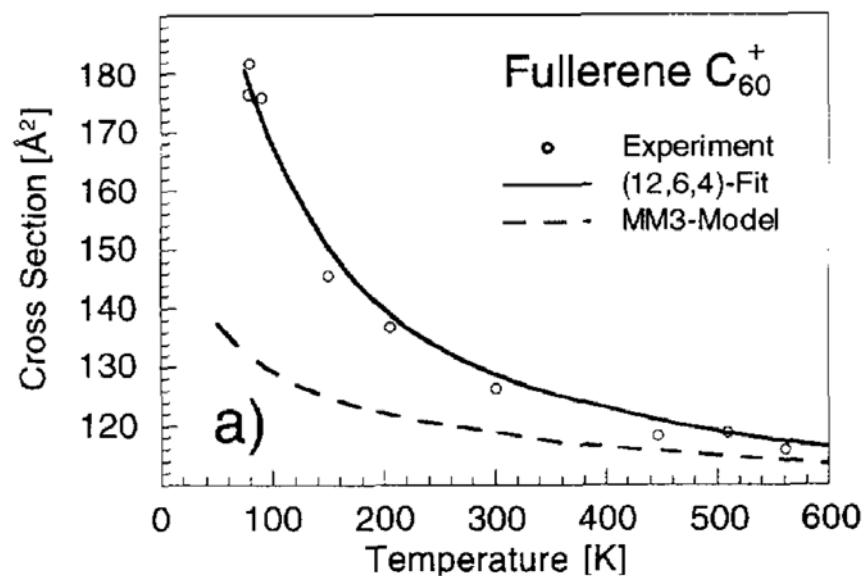
# What is a collision?

## Atoms are not hard spheres

However, the size of helium is not the only factor contributing to the IMS-measured size of an ion. This is demonstrated by a comparison of the  $\Omega_{\text{IMS}}$  values for  $\text{H}^+$  and  $\text{CH}_4^+$  of 37 and 26 Å<sup>2</sup>, respectively (in helium at 300 K).<sup>32</sup> Measured by IMS,  $\text{CH}_4^+$  is smaller than  $\text{H}^+$ . Clearly, the probe

effect (Figure 3a). We noticed this type of inconsistency in the 1990s during the Gly<sub>n</sub> series of ion mobility measurements: atomic radii increase with increasing  $n$ .<sup>28</sup> In other words, a hydrogen atom in glycine appears to be smaller than a hydrogen atom in hexaglycine. This effect is thought to be due to an increase of the well depth in the helium–ion interaction with increasing number of atoms in the ion. The interaction

buffer gas temperature. If the cross section were determined exclusively by the molecular skeleton, its value would not change with temperature for a rigid structure such as, e.g., fullerene C<sub>60</sub> (720 Da). However, the C<sub>60</sub><sup>+</sup> experimental cross section value measured in helium does change from 180 to 126 to 117 Å<sup>2</sup> at 80, 300, and 600 K, respectively.<sup>34</sup> The cross

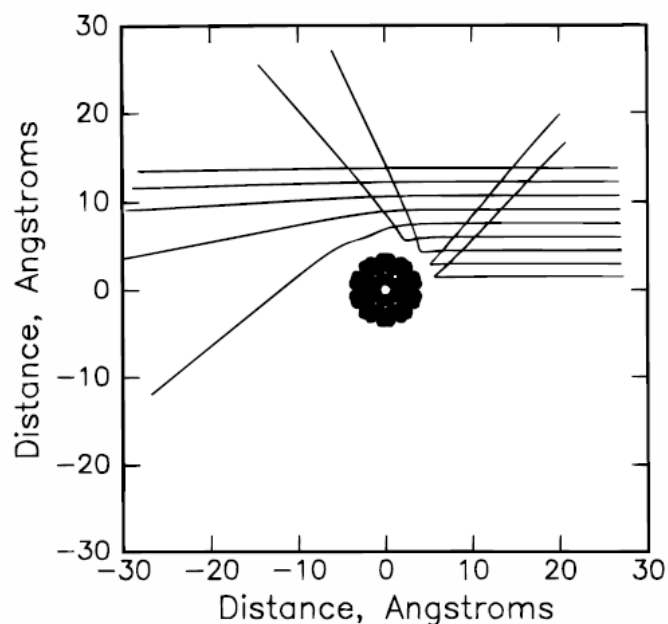


Wytenbach, Bleiholder & Bowers,  
*Anal. Chem.* (2013) 85, 2191.

Wytenbach et al., *JASMS* (1997) 8, 275.

# Effect of the collision gas and $T$ on $K_0$

## Long-range and short-range interactions between gas and ion



### Interaction potentials:

- Repulsive at very short distance
- Attractive at medium distance
- Null at infinite distance

Example:

Lennard-Jones interaction potentials



Wytténbach, Bleiholder & Bowers, *Anal. Chem.* (2013) 85, 2191.

# Effect of the collision gas and $T$ on $K_0$

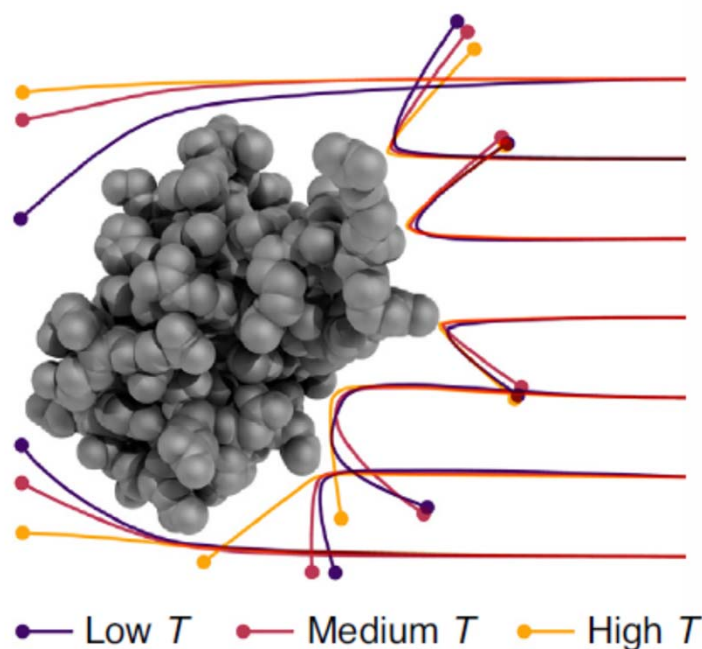
## Trajectory calculations (TM):

### ➔ momentum transfer collision integral

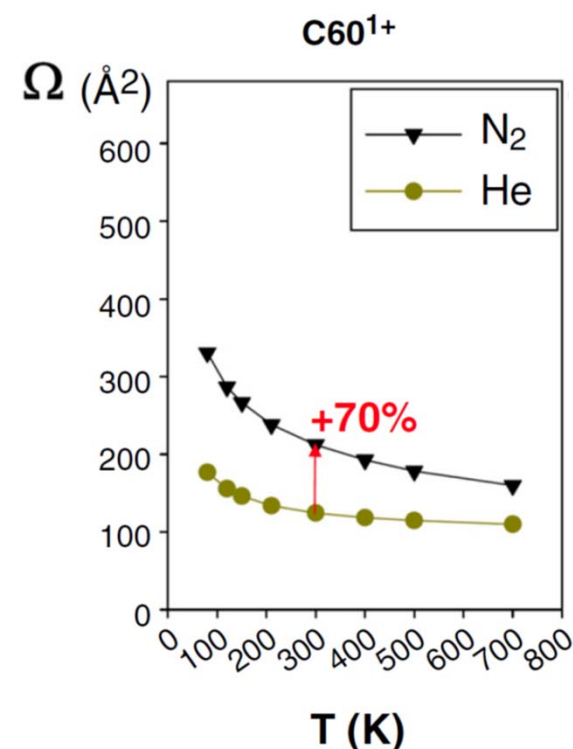
Bleiholder et al.,  
*Anal. Chem.* (2015) 87, 7196

The ion-gas interaction depends on:

- The ion-gas relative velocity ( $T$ )
- The nature of the gas (polarizability)
- The exposure of polar/charged groups



When you report CCS values, specify the gas, e.g.  $^{DT}CCS_{N_2}$



# Effect of the collision gas and $T$ on $K_0$

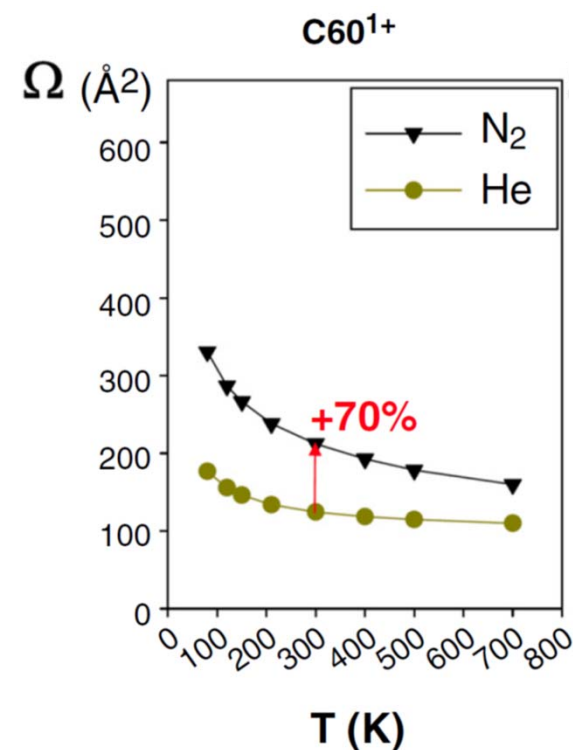
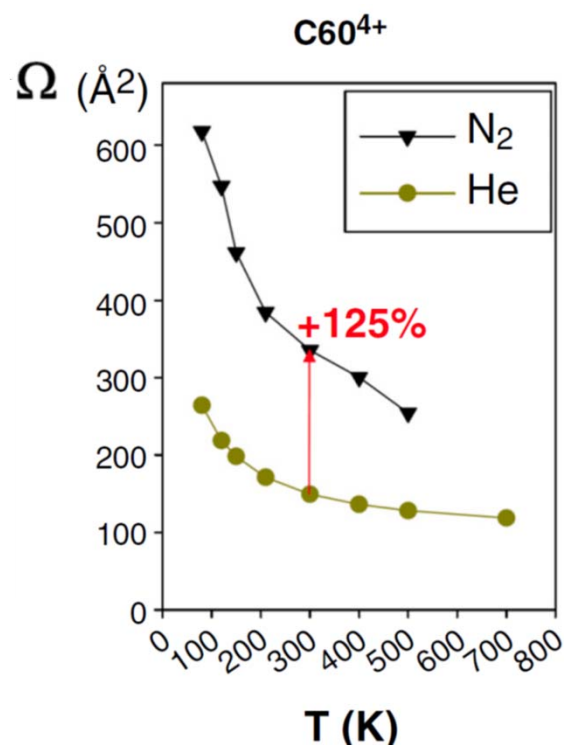
## Trajectory calculations (TM):

### ➔ momentum transfer collision integral

Young & Bleiholder,  
*J. Am. Soc. Mass Spectrom.*  
(2017) 28: 619.

The ion-gas interaction depends on:

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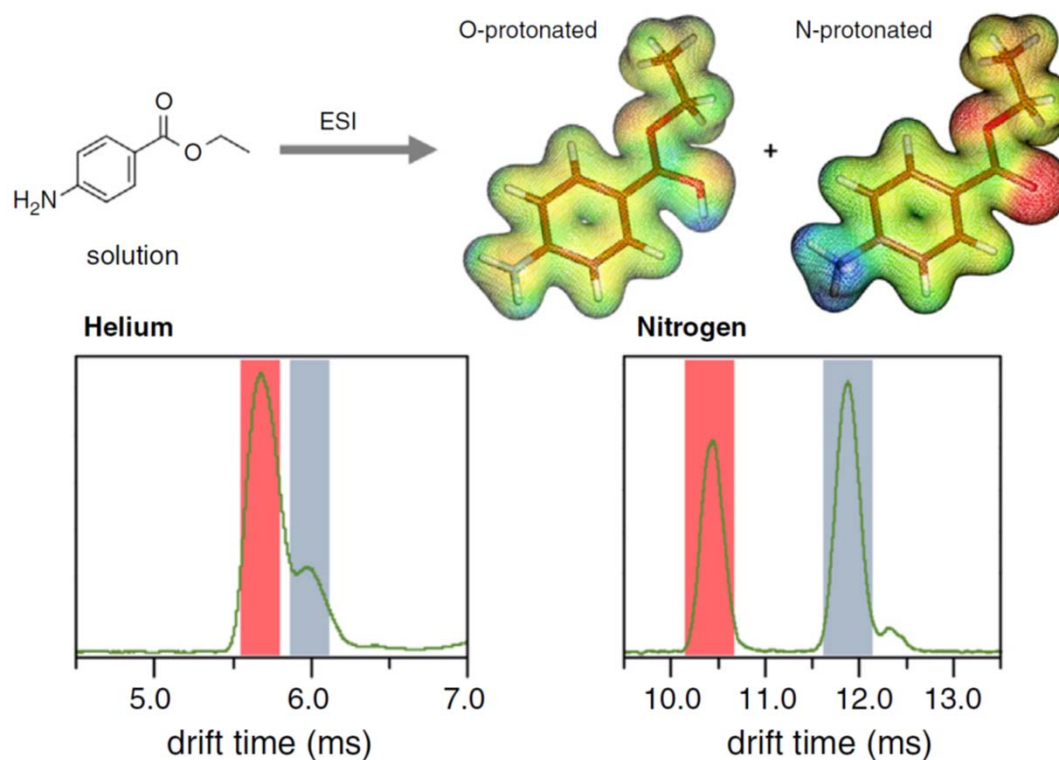




# Effect of the collision gas and $T$ on $K_0$

In polarizable gases ( $N_2$ ), the CCS will depend on the exposure of polar/charged groups  $\rightarrow$  charge location matters

## Benzocaine:

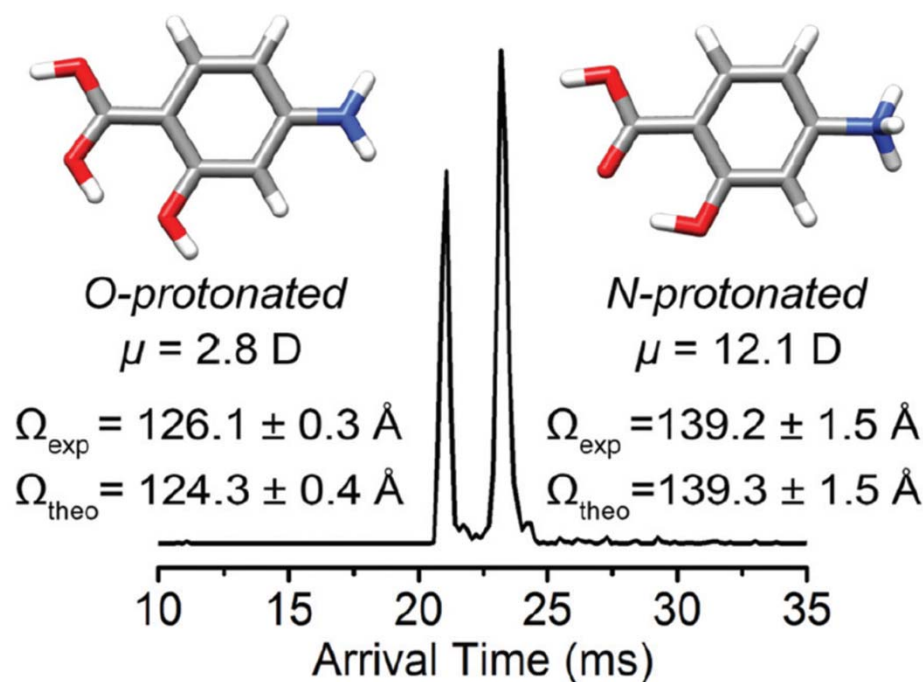


Warnke et al.,  
*J. Am. Chem. Soc.*  
(2015) 137, 4236

## Effect of the collision gas and $T$ on $K_0$

In polarizable gases ( $N_2$ ), the CCS will depend on the exposure of polar/charged groups  $\rightarrow$  charge location matters

4-aminosalicylic acid:

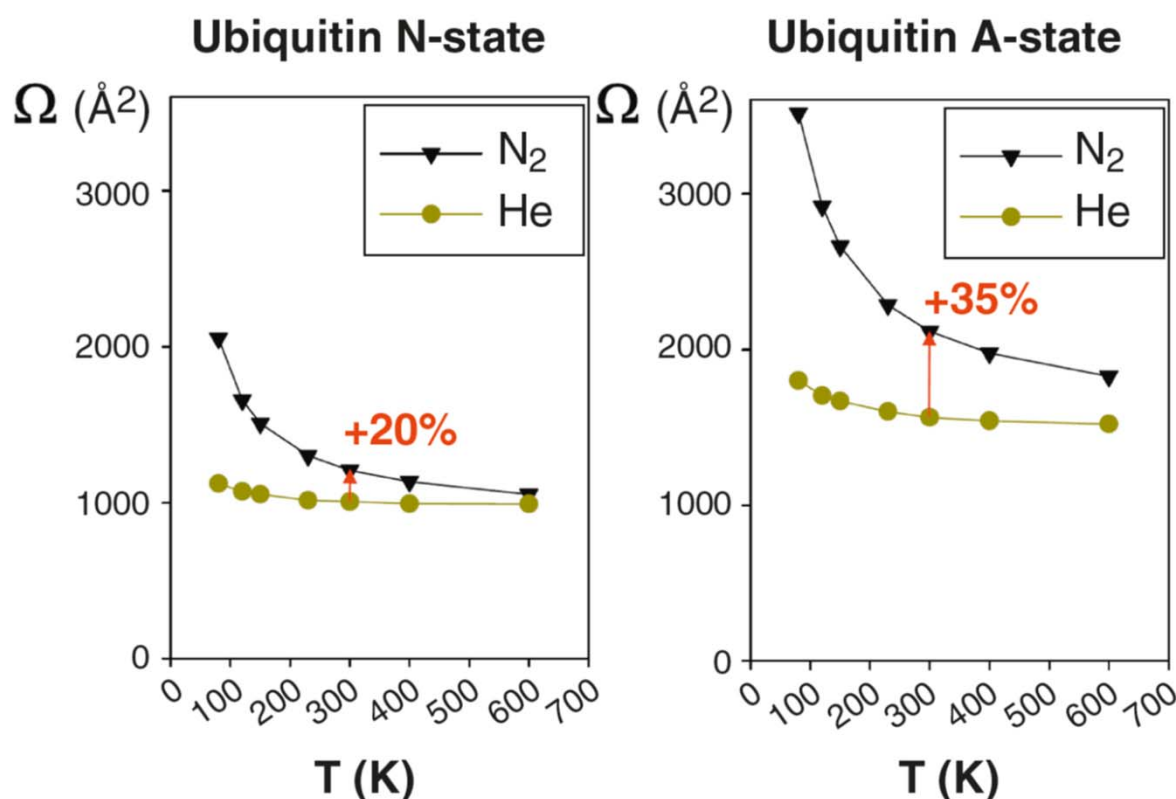


Campbell, Le Blanc & Schneider, Anal. Chem. (2012) 84: 7857

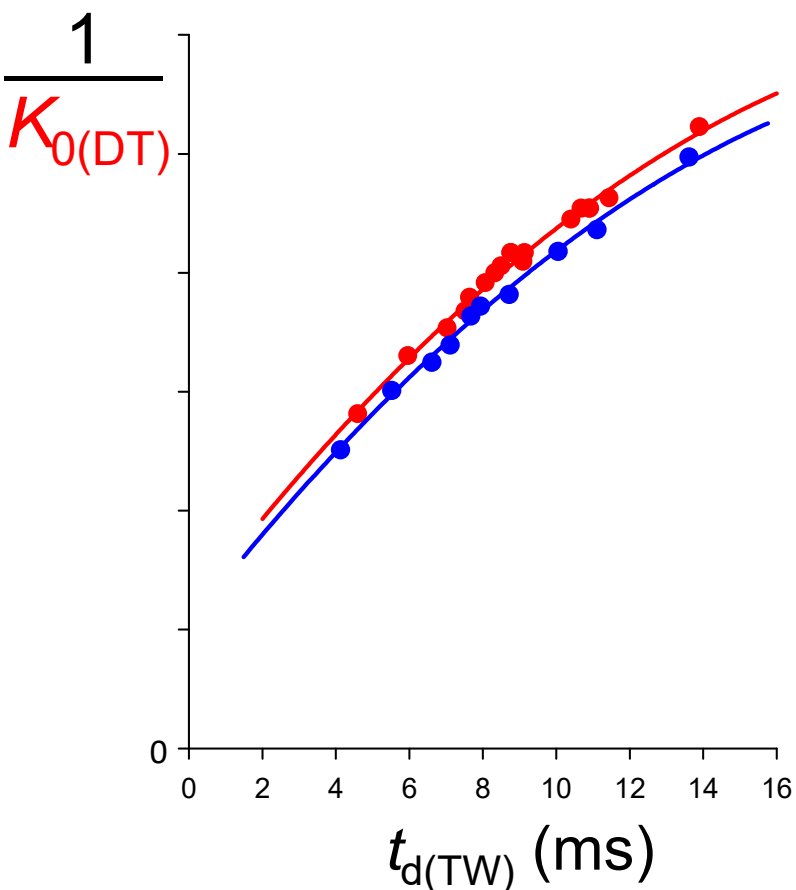
Lee, Lee, Davidson, Bush & Kim, *Analyst* (2018) 143: 1786

## Effect of the collision gas and $T$ on $K_0$

In polarizable gases ( $N_2$ ), the CCS will depend on the exposure of polar/charged groups  $\rightarrow$  conformation matters



# TWIMS Calibration Depends on Compound Class. Why?



Hypothesis 2:

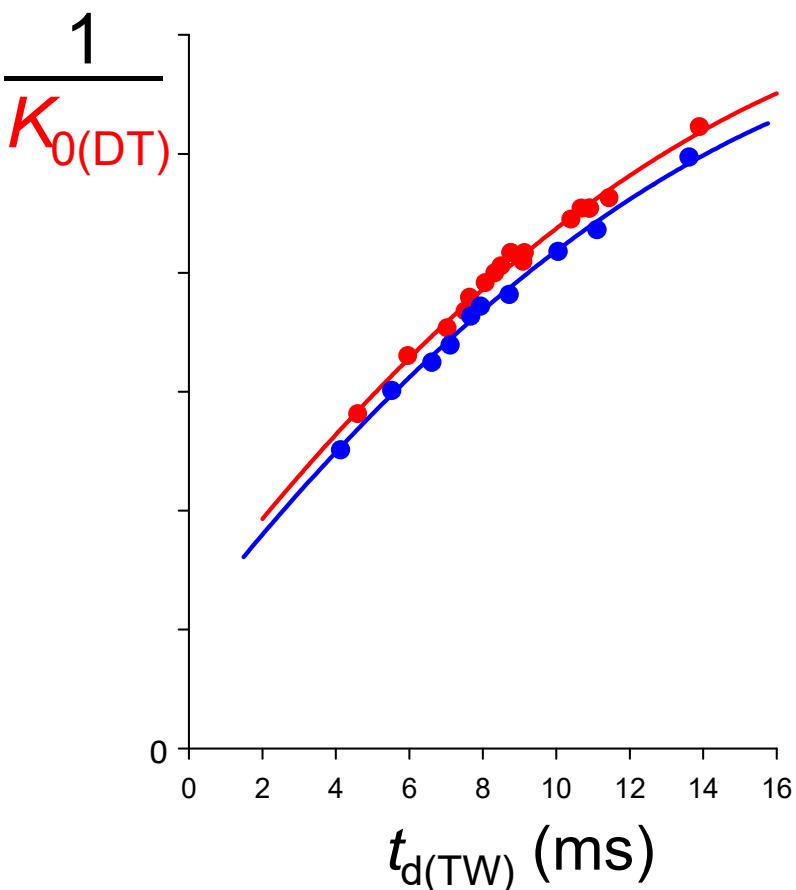
$$K_0(TW) \neq K_0(DT)$$

because measurements are done  
in different gases

and the relationship  $K_{0(gas1)}/K_{0(gas2)}$   
depends on compound class

Conclusion: hyp. 2 is correct when  
using  $^{DT}K_{He}$  values to calibrate TW  
(operating in *mainly*  $N_2$ )

# TWIMS Calibration Depends on Compound Class. Why?



Hypothesis 3:

$$K_0(\text{TW}) \neq K_0(\text{DT})$$

because measurements are done at **different effective temperatures**

and the relationship  $K_{0(T1)}/K_{0(T2)}$  depends on compound class

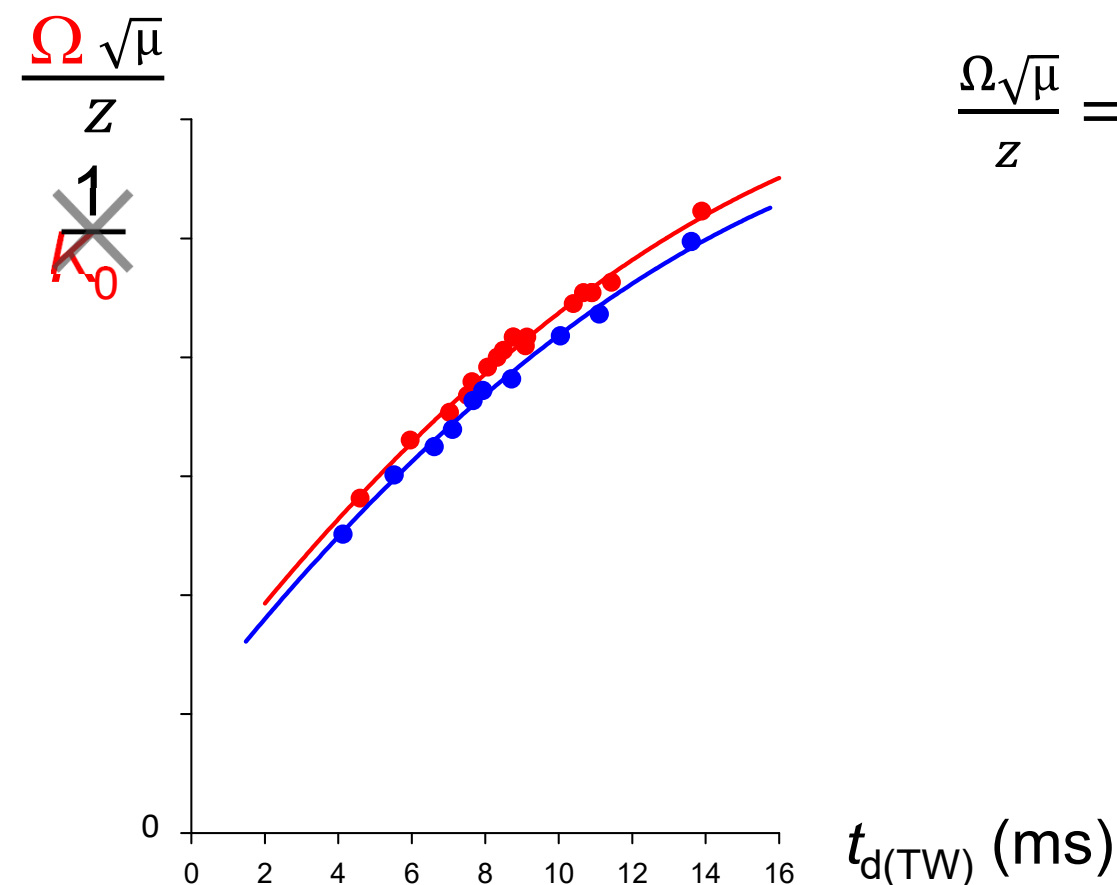
Effective temperature:

temperature characterizing the actual gas/ion relative velocity

$$v_{\text{thermal}} = \sqrt{\frac{8 k_B T}{\pi \mu}} \quad v_{\text{actual}} = \sqrt{\frac{8 k_B T_{\text{eff}}}{\pi \mu}}$$

# TWIMS Calibration Depends on Compound Class

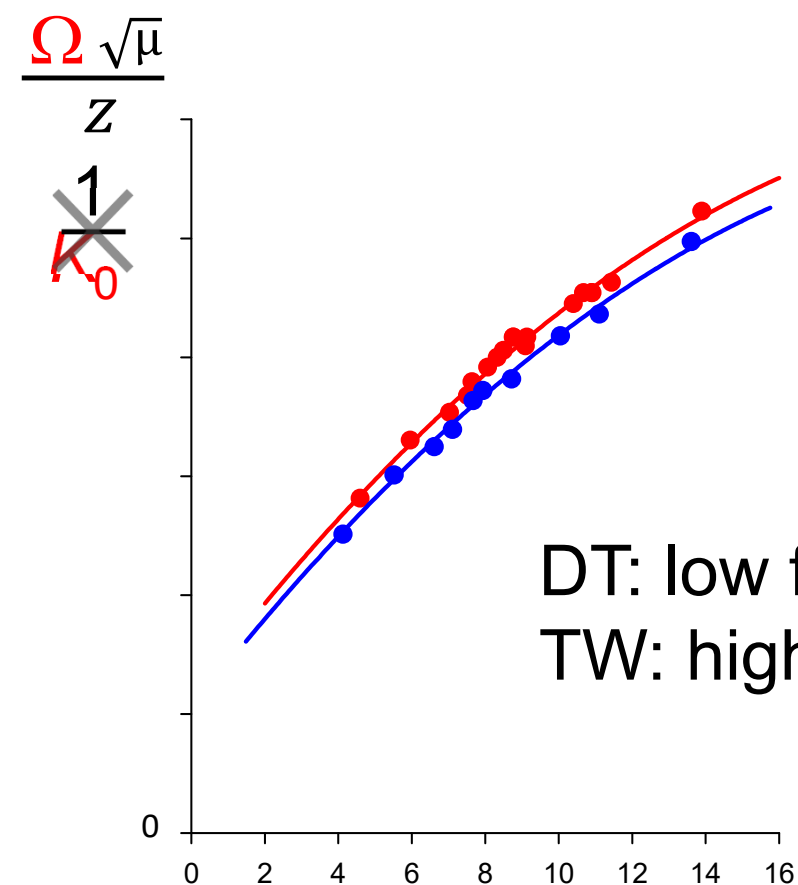
Actually, we use  $\Omega$  values, not  $K_0$  values, to calibrate TWIMS



$$\frac{\Omega \sqrt{\mu}}{z} = \frac{3}{16} \sqrt{\frac{2\pi}{k_b T_{eff}}} \frac{e}{N_0 K_0} = X \frac{1}{K_0}$$

# TWIMS Calibration Depends on Compound Class

Actually, we use  $\Omega$  values, not  $K_0$  values, to calibrate TWIMS



$$\frac{\Omega \sqrt{\mu}}{z} = \frac{3}{16} \sqrt{\frac{2\pi}{k_b T_{eff}}} \frac{e}{N_0 K_0} = X \frac{1}{K_0}$$

Constant **only** if  $T_{eff}$  is the same for all compounds

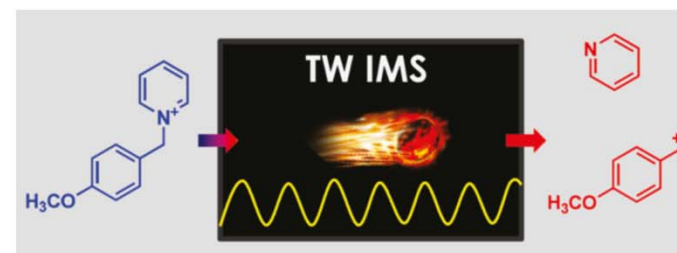
DT: low field limit:  $T_{eff} = T_{gas}$  ( $\Rightarrow X$  is constant)

TW: higher field:  $T_{eff} = T_{gas} + m_{gas} (K_0 N_0 \cdot E/N)^2 / 3k_B$

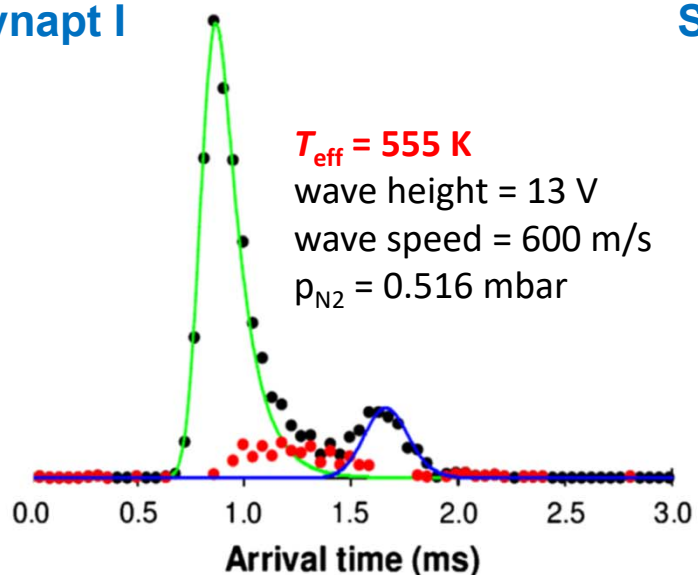
# TWIMS Calibration Depends on Compound Class

Actually, we use  $\Omega$  values, not  $K_0$  values, to calibrate TWIMS  
We don't know  $T_{\text{eff(TW)}}$ , but at  $E_{\text{max}}/N \geq 100$  Td,  $T_{\text{eff}} > T_{\text{gas}}$

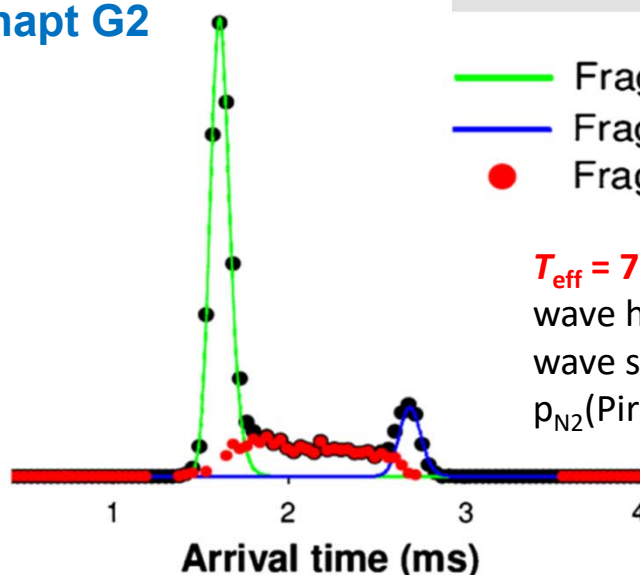
Small molecule fragmentation inside the TWIMS proves that collisions are inelastic



Synapt I



Synapt G2



- Fragmentation before the IMS cell
- Fragmentation after the IMS cell
- Fragmentation inside the IMS cell

$T_{\text{eff}} = 728$  K  
wave height = 40 V  
wave speed = 800 m/s  
 $p_{\text{N}_2}(\text{Pirani}) = 4.5$  mbar

Morsa & al. *Anal. Chem.* (2011)  
Morsa & al. *JASMS* (2014)

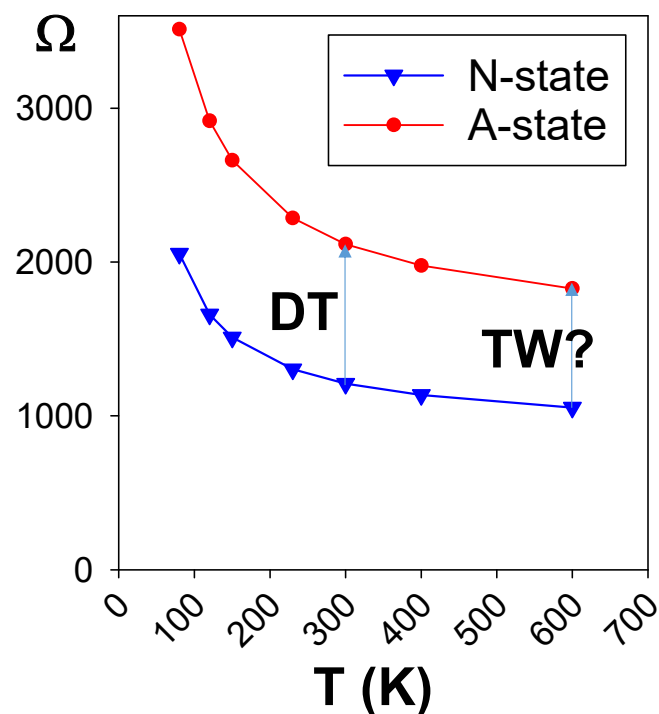


# TWIMS Calibration Depends on Compound Class

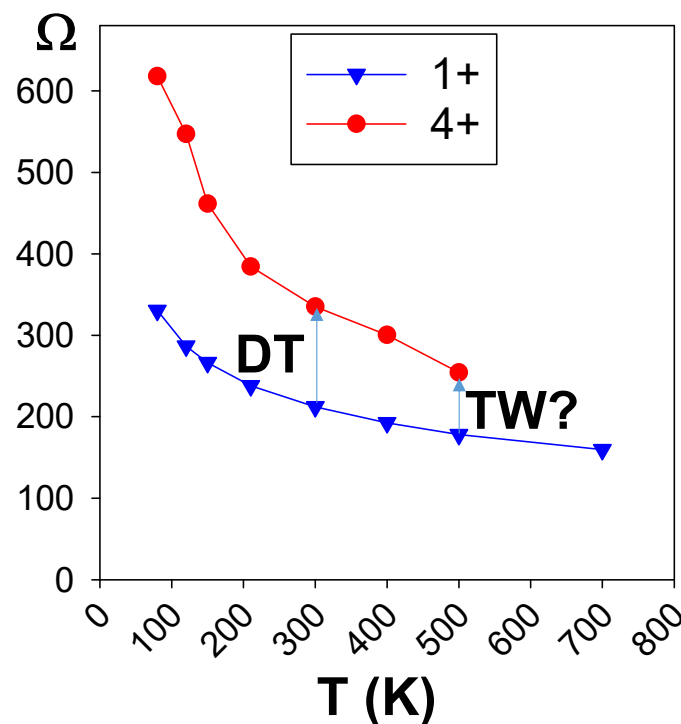
Actually, we use  $\Omega$  values, not  $K_0$  values, to calibrate TWIMS

We don't know  $T_{\text{eff(TW)}}$ , but at  $E_{\text{max}}/N \geq 100$  Td,  $T_{\text{eff}} > T_{\text{gas}}$

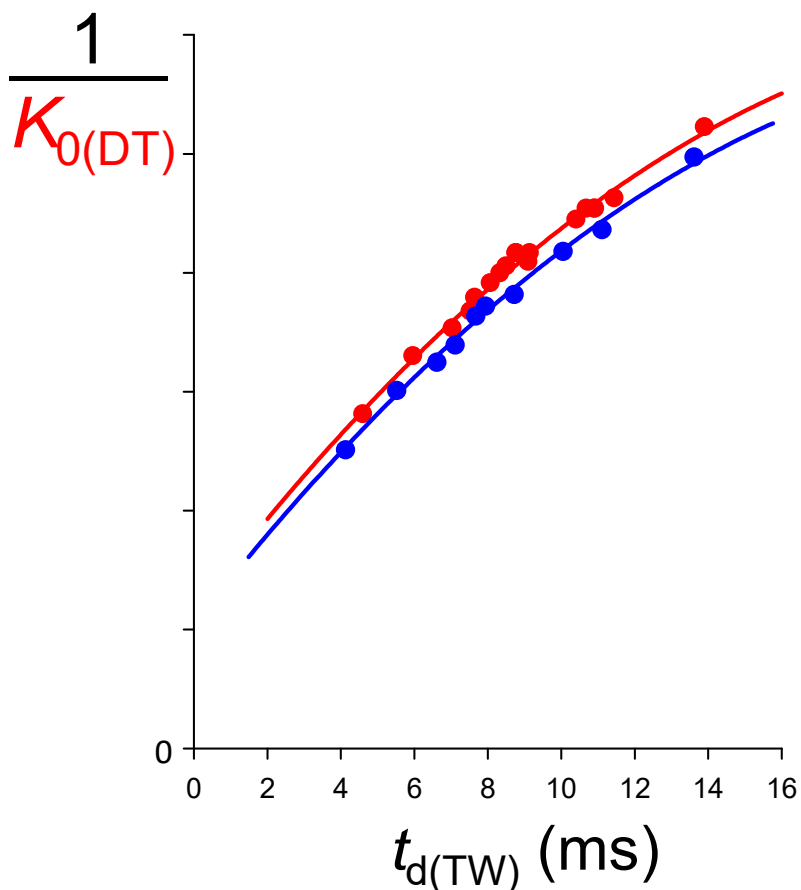
Ubiquitin



C<sub>60</sub>



# TWIMS Calibration Depends on Compound Class. Why?



Hypothesis 3:

$$K_0(\text{TW}) \neq K_0(\text{DT})$$

because measurements are done at different temperatures

and the relationship  $K_{0(T1)}/K_{0(T2)}$  depends on compound class

Conclusion: hyp. 3 is plausible and compound class matching would mean similar  $T$ -dependence of  $\Omega$ .

## TWIMS Calibration Depends on Compound Class

### Hypothesis 4: velocity relaxation effects

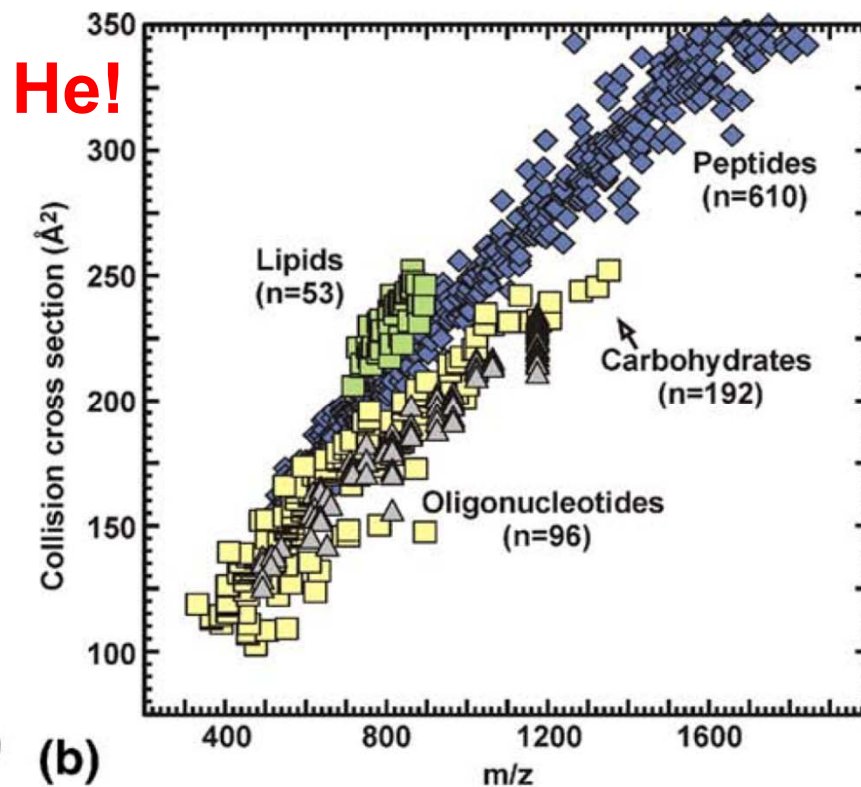
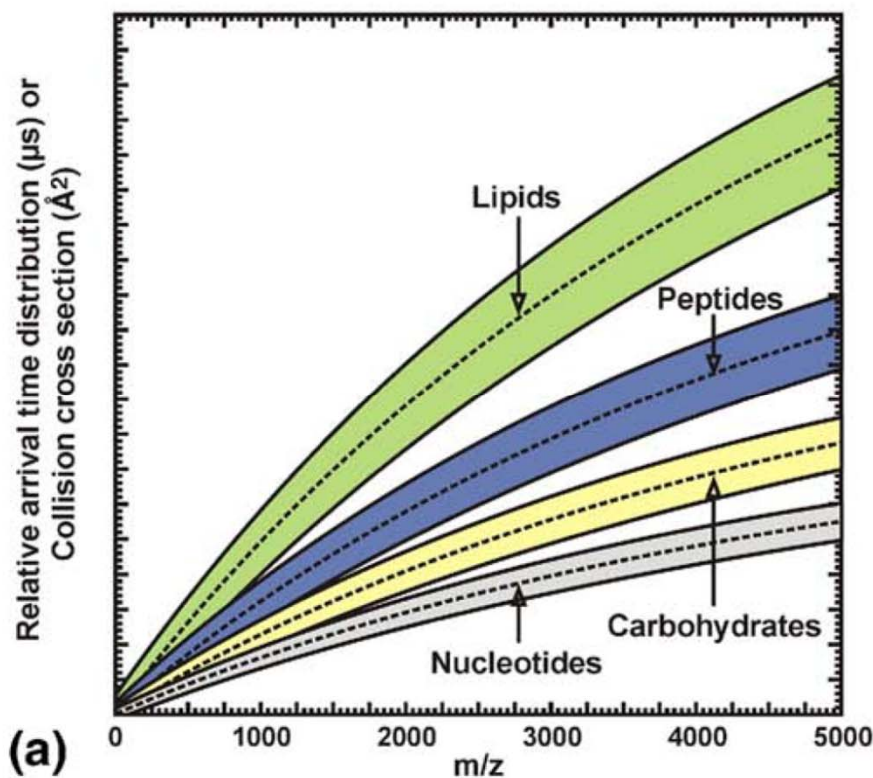
i.e., ions do not respond immediately to field changes

i.e.,  $v_D = K.E$  is not satisfied at all times in TWIMS

- Velocity relaxation depends on  $K$  and  $m/z$
- With the current mathematical model for calibration, analyte and calibrant must have similar velocity relaxation effects
- Must have a similar dependence of  $K_0$  on  $(m/z)$

# TWIMS Calibration Depends on Compound Class. Why?

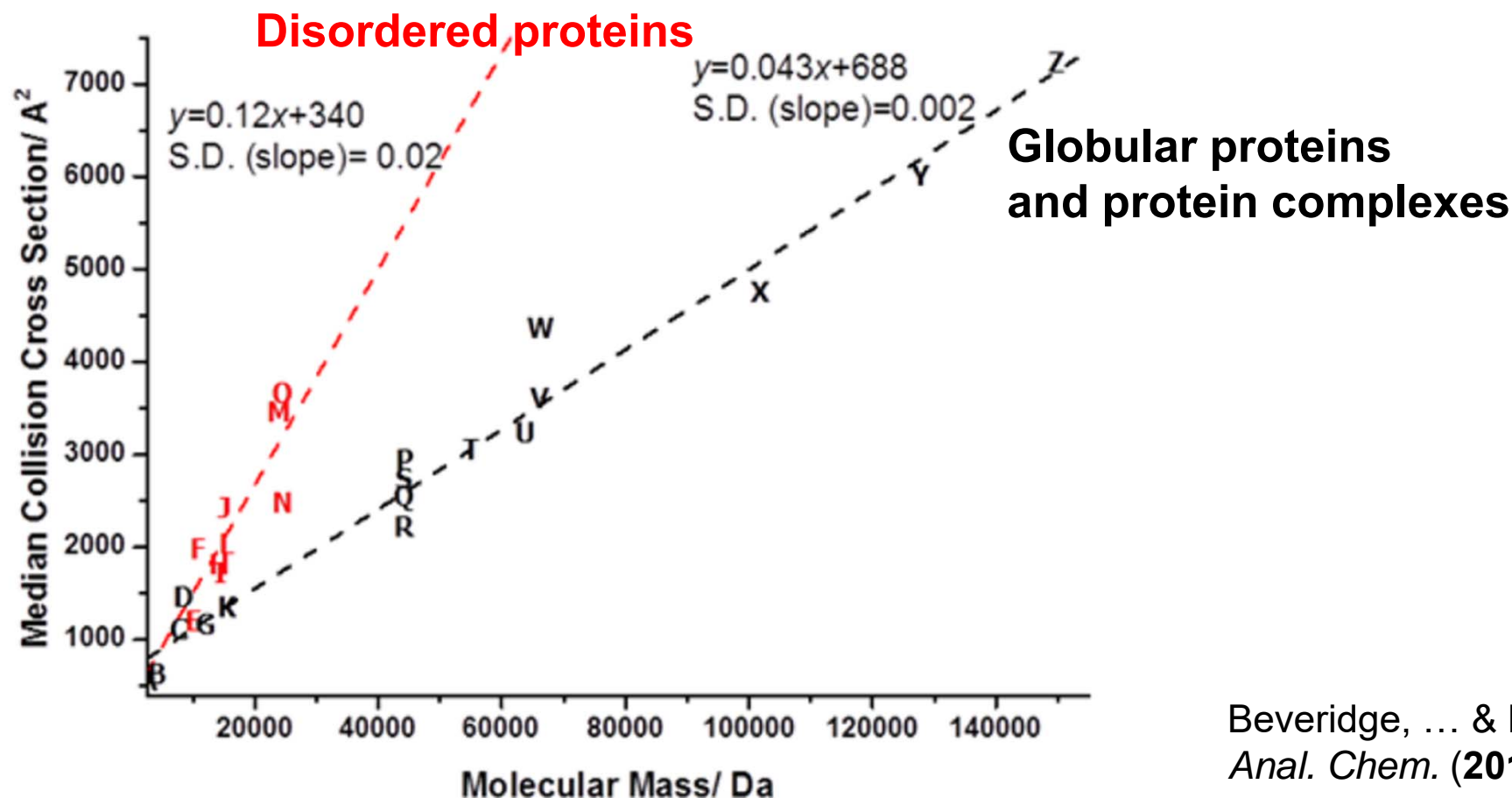
Chemical classes influence  $K_0$  dependence on ( $m/z$ )



McLean, J. Am. Soc. Mass Spectrom. (2009) 20: 1775.

# TWIMS Calibration Depends on Compound Class. Why?

Protein conformation influences  $K_0$  dependence on ( $m/z$ )



Beveridge, ... & Barran,  
*Anal. Chem.* (2014) 86: 10979

# TWIMS Calibration Depends on Compound Class

## Hypothesis 4: velocity relaxation effects

i.e., ions do not respond immediately to field changes

i.e.,  $v_D = K.E$  is not satisfied at all times in TWIMS

- With the current mathematical model for calibration, analyte and calibrant must have similar velocity relaxation effects
- Must have a similar dependence of  $K_0$  on  $(m/z)$
- Meaning to belong to a same class of structures
- Future: new calibrations procedures for TWIMS?

$$\text{i.e.: } \bar{v}_{\text{ion}} = c_2 K^2 + c_4 K^4 + c_{42} K^4 \left( \frac{m}{q} \right)^2 + c_6 K^6$$

## Summary: What Do We Measure In Ion Mobility?

Ion mobility spectrometry measures the **mobility** of **ions**,  
not collision cross sections (deduced afterwards)  
not the mobility of the analyte in solution

The ion's mobility ( $K$ ,  $K_0$ ) depends on:

- The ion's structure (atom positions + electronic structure)
- The temperature
- The nature of the collision gas
- $E/N$

But NOT on the method of measurement (unless the measurement involves different ion structure,  $T$ , gas, or  $E/N$ )

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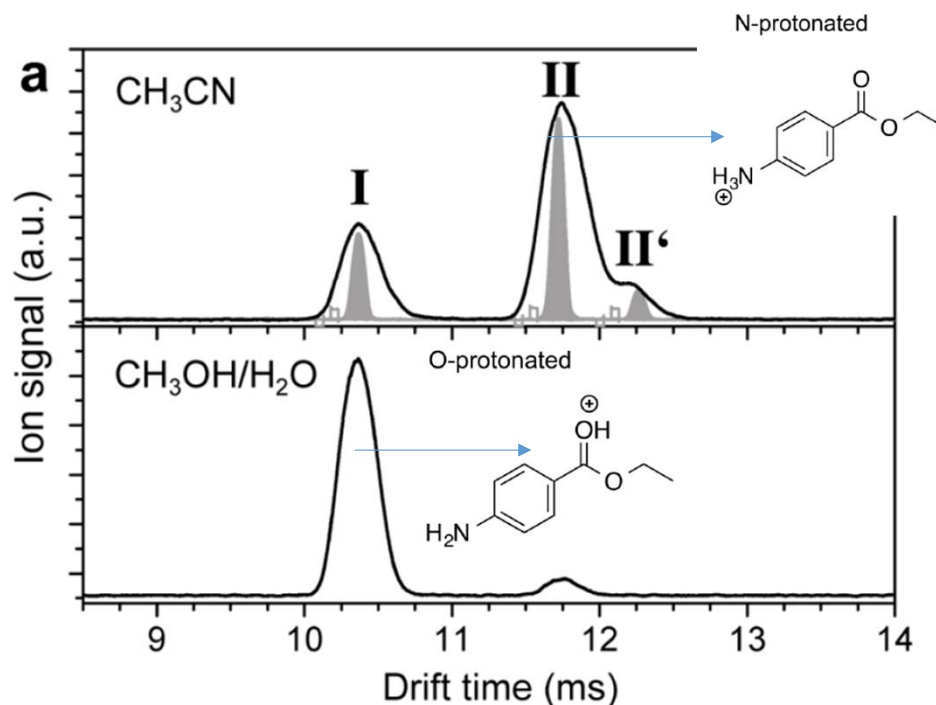
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# How analytes become ions affect the result

Recall: in  $N_2$ , the CCS will depend on the exposure of polar/charged groups  
→ charge location matters  
→ influence of solvent

## Benzocaine:



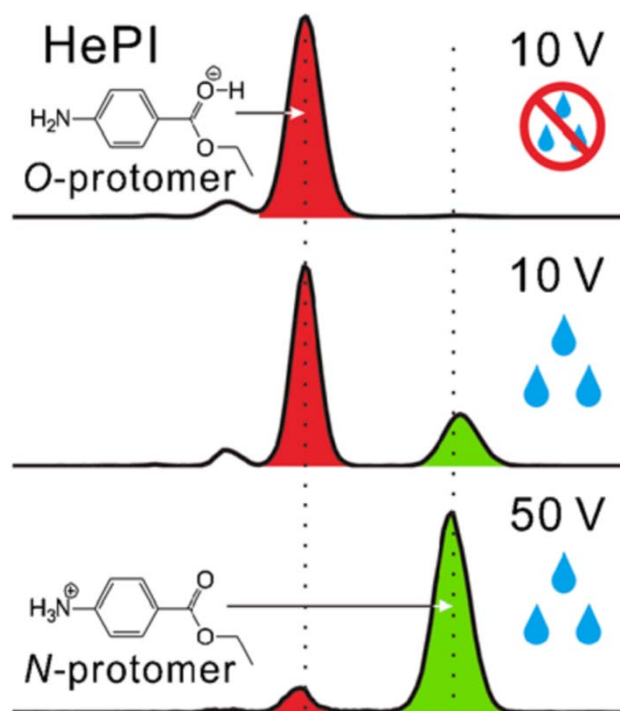
Warnke et al.,  
*J. Am. Chem. Soc.*  
(2015) 137, 4236

# How analytes become ions affect the result

Recall: in  $N_2$ , the CCS will depend on the exposure of polar/charged groups → charge location matters

→ influence of solvent, ionization, vapors in the source, and ion activation

## Benzocaine:



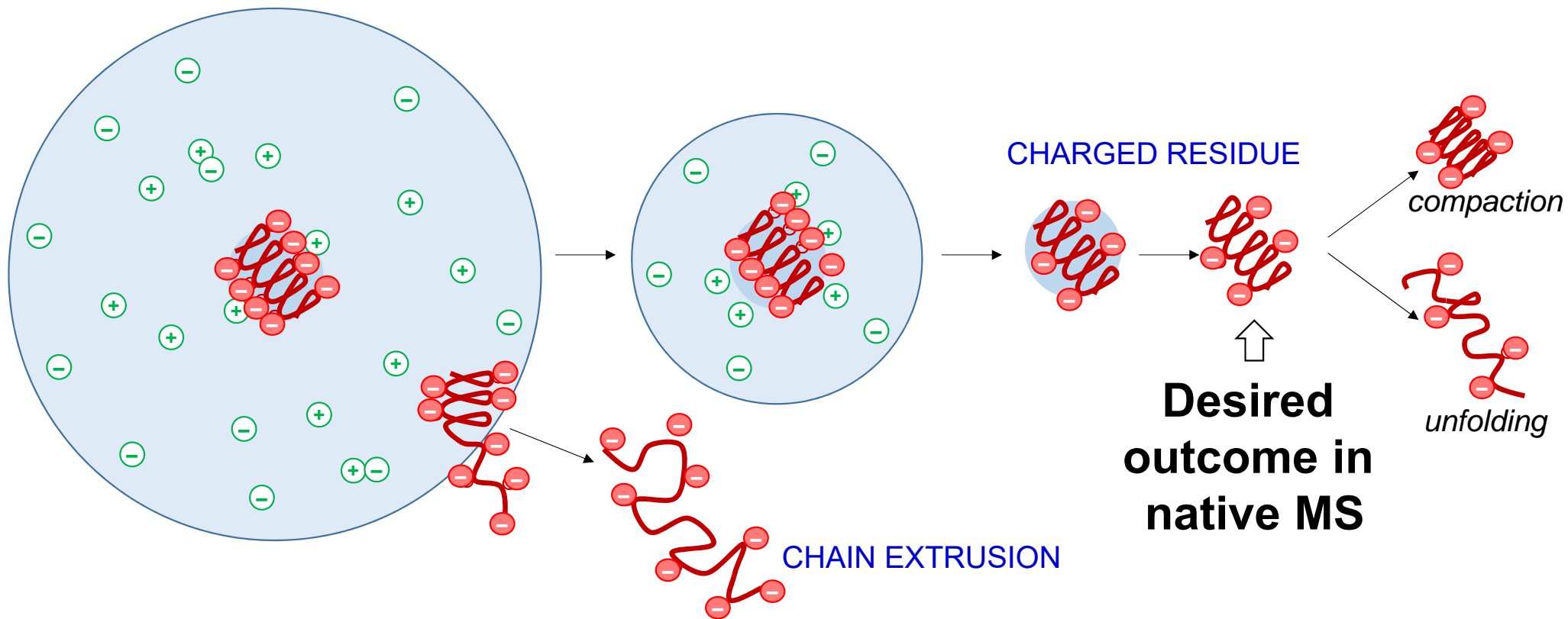
vapors in the source,  
and ion activation

+  $H_2O$  vapor  
in the source

Xia & Attygalle,  
*J. Am. Soc. Mass Spectrom.*  
(2017) 28, 2580

# How analytes become ions affect the result

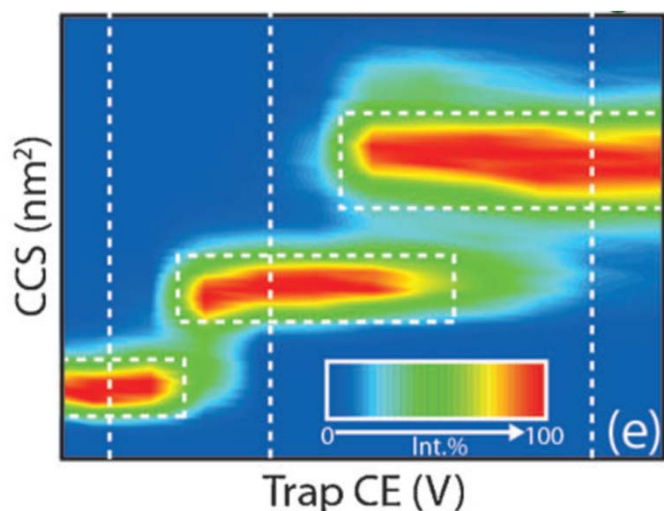
- ➔ Importance of controlling ionization mechanisms, including for native MS



# How analytes become ions affect the result

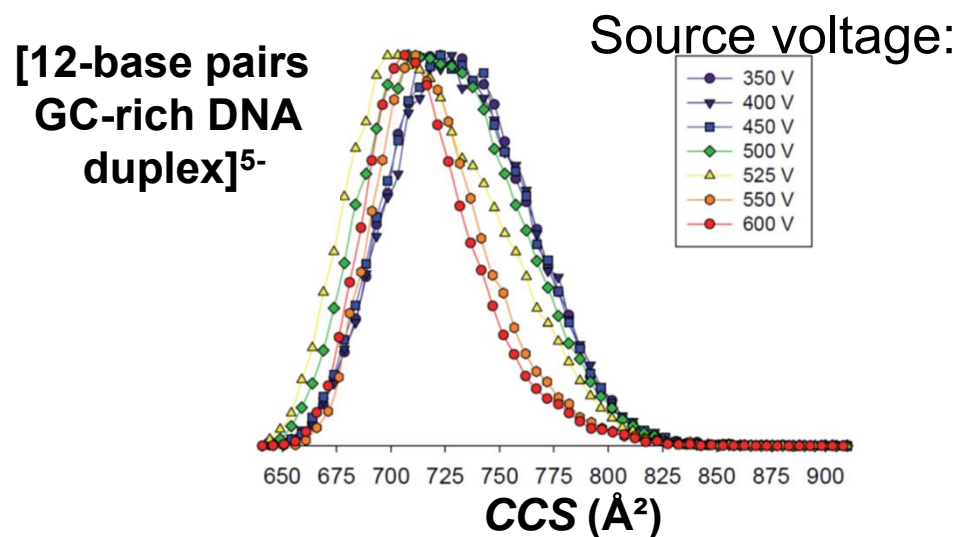
➔ Importance of controlling ionization mechanisms:  
charging level and internal energy

Enough charges  
⇒ collision-induced **unfolding**



Zhong, Han & Ruotolo *Angew. Chem. Int. Ed.* **2014**, 53, 9209.

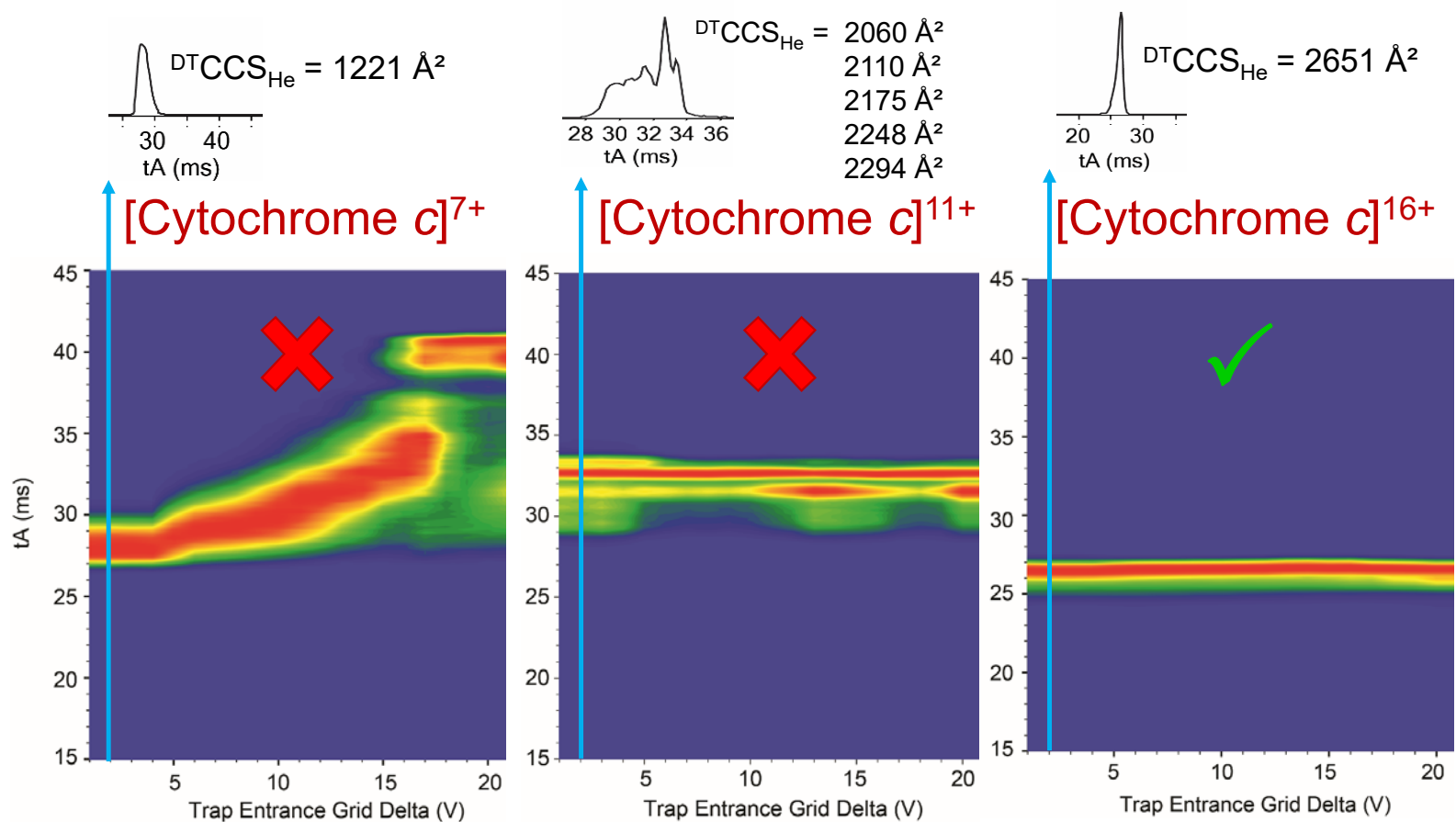
Not enough charges  
⇒ collision-induced **compaction**



Porrini et al., *ACS Cent. Sci.* **2017**, 3: 454.

# Choosing robust calibrants

Sensitive to activation → too risky as calibrant

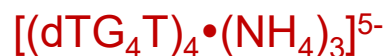


# Choosing robust calibrants

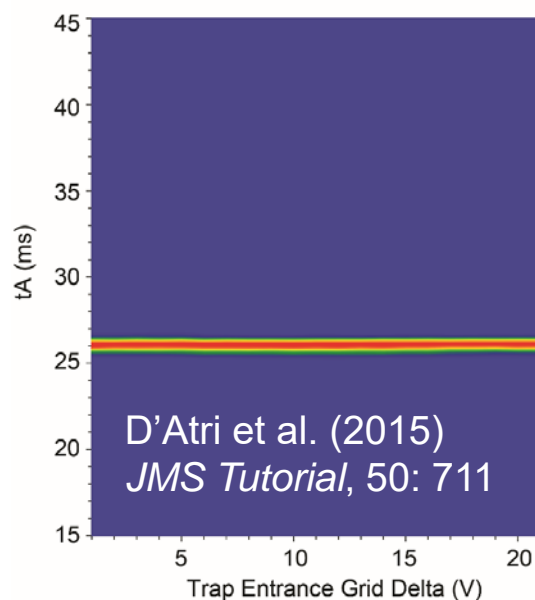
Sensitive to activation → too risky as calibrant

## Negative ion mode calibrants

### Rigid G-quadruplexes



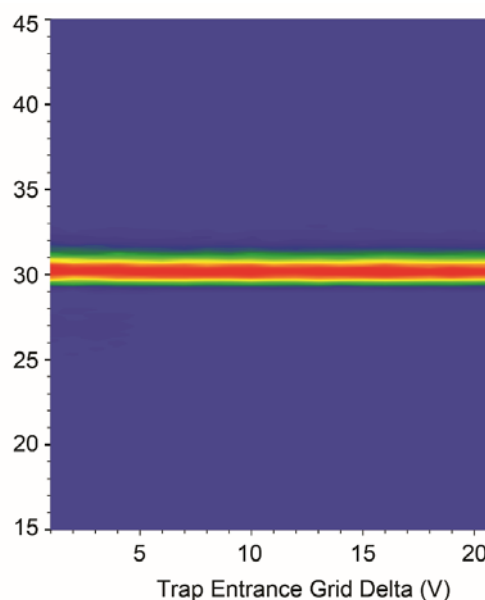
$$^{DT}CCS_{He} = 787.5 \pm 0.7 \text{ \AA}^2$$



### Poly(dT)



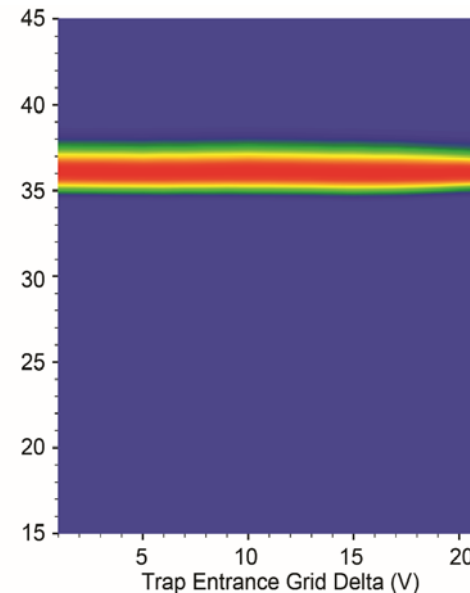
$$^{DT}CCS_{He} = 359.5 \pm 1.3 \text{ \AA}^2$$



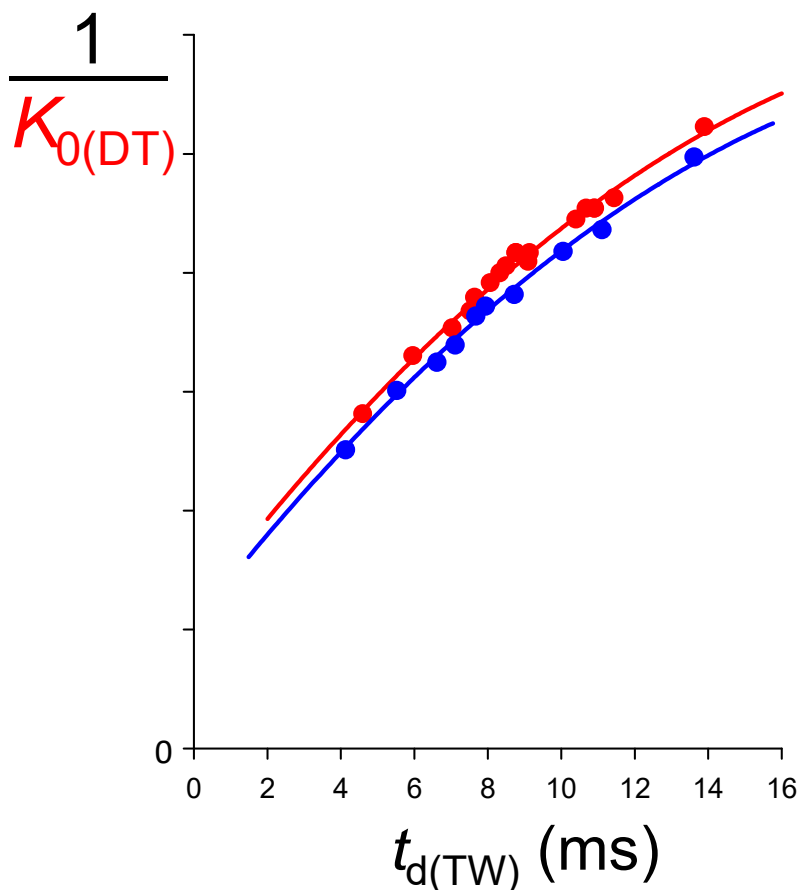
### Agilent/Bruker Tune Mix



$$^{DT}CCS_{He} = 215.5 \pm 1.4 \text{ \AA}^2$$



# TWIMS Calibration Depends on Compound Class. Why?



Hypothesis 5:


$$K_0(\text{TW}) \neq K_0(\text{DT})$$

because measurements are done on **different ion structures**

and the relationship  $K_{0(\text{conf1})}/K_{0(\text{conf2})}$  depends on compound class

RF-only drift cell in Synapt was supposed to solve that, but in pure  $\text{N}_2$ , ion preparation is not as soft as with He cell => Problems persist!

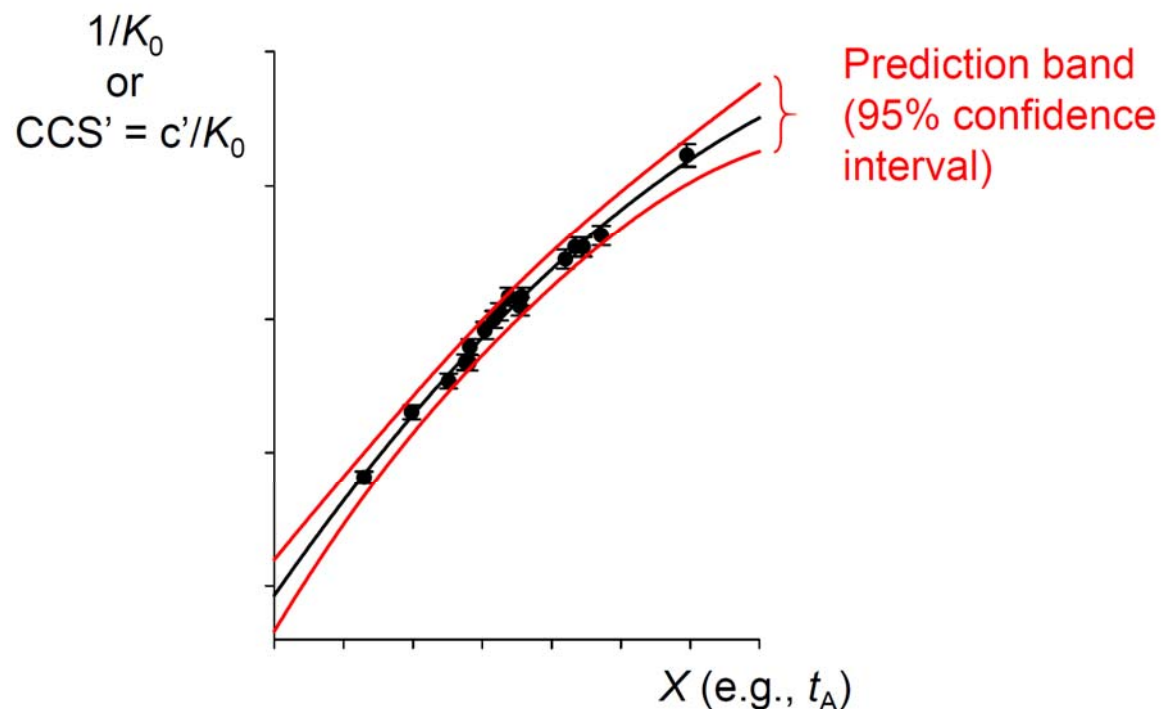
# Important points

- We measure mobilities ( $K = v_d/E$ , in  $\text{cm}^2 \text{V}^{-1} \text{s}^{-1}$ ), not surfaces (in  $\text{m}^2$ )
- The measured property ( $K_0$ ) and the CCS depend only on:
  - The ion structure
  - The gas nature
  - The temperature in the low-field limit
- The ratio between electric field and gas number density ( $E/N$ )
- The measured property does not depend on the method of measurement (DTIMS, TWIMS, TIMS, DMA) as long as the ion structure, gas, temperature and  $E/N$  range are identical



## Important points

Report calibration equations, show the curves, list of calibrants and origin of the values (ion structure preparation, gas and temperature)



# The meaning of ATD peak width

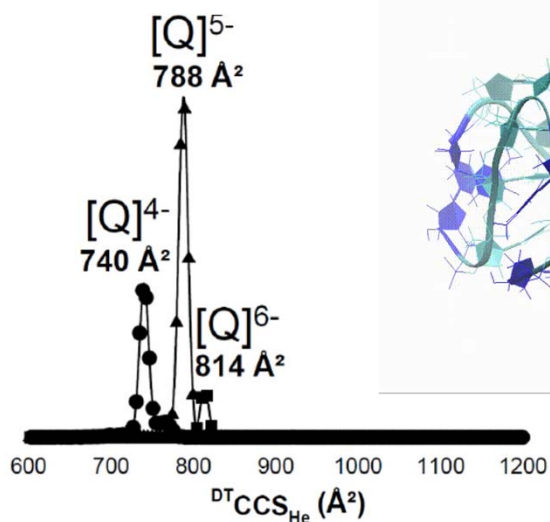
2 narrow peaks => 2 structures

1 broad peak => several structures

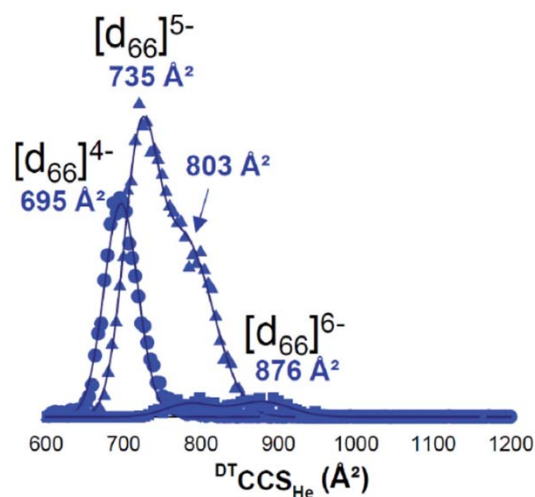
## How to know if a peak is "broad"?

Marchand, Livet, Rosu & Gabelica, *Anal. Chem.* (2017) 89, 12674

G-quadruplex DNA: *JMS* (2015), 50, 711



Duplex DNA: *ACS Cent Sci* (2017), 3, 454



# The meaning of ATD peak width

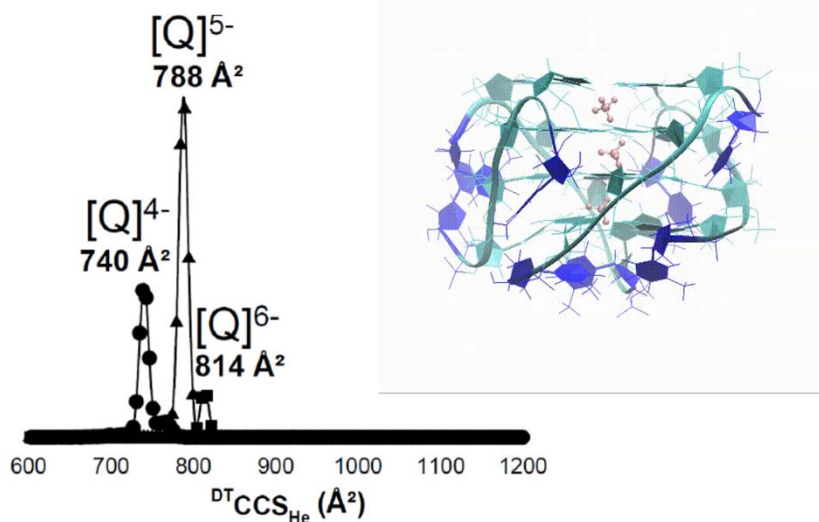
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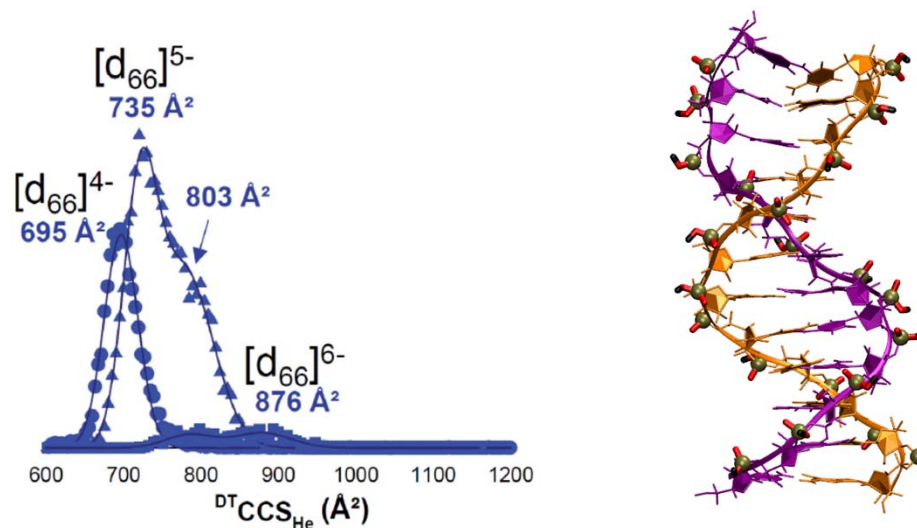
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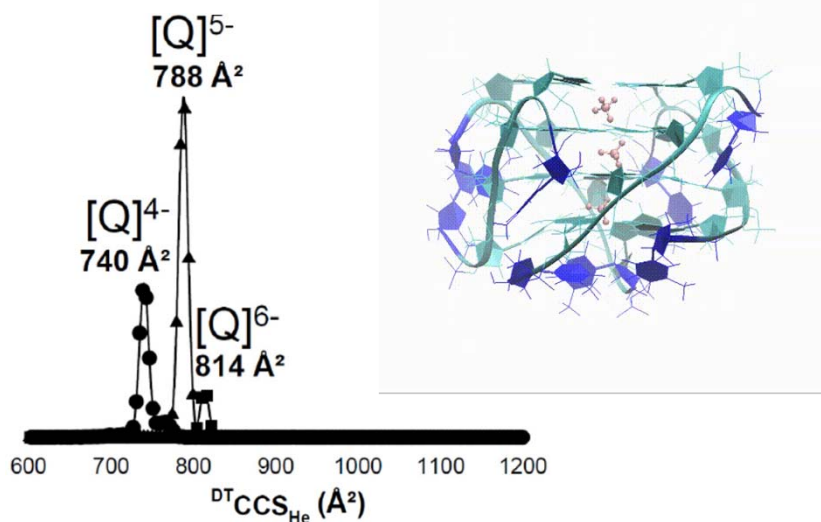
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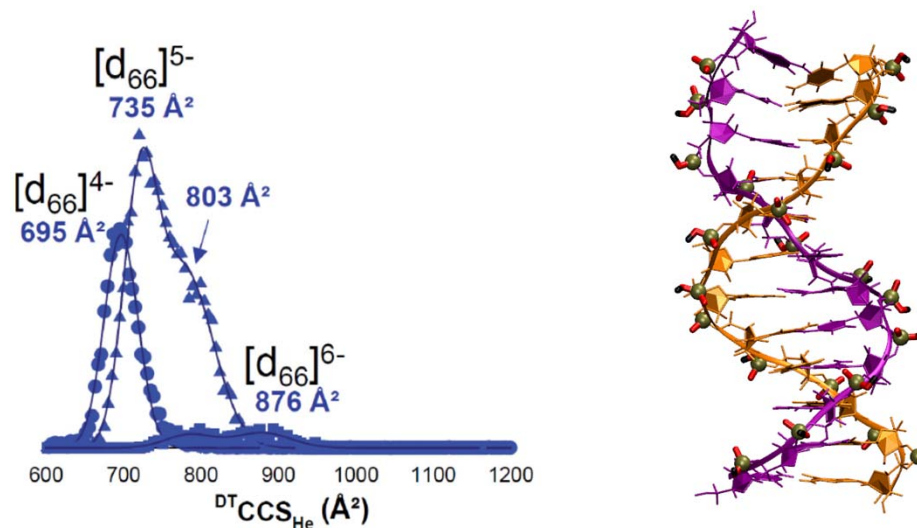
1 broad peak => several structures

Ion mobility peak width reflects the multiplicity of ways ions can rearrange **prior to IMS analysis**

G-quadruplex DNA: *JMS* (2015), 50, 711



Duplex DNA: *ACS Cent Sci* (2017), 3, 454



# The meaning of ATD peak width

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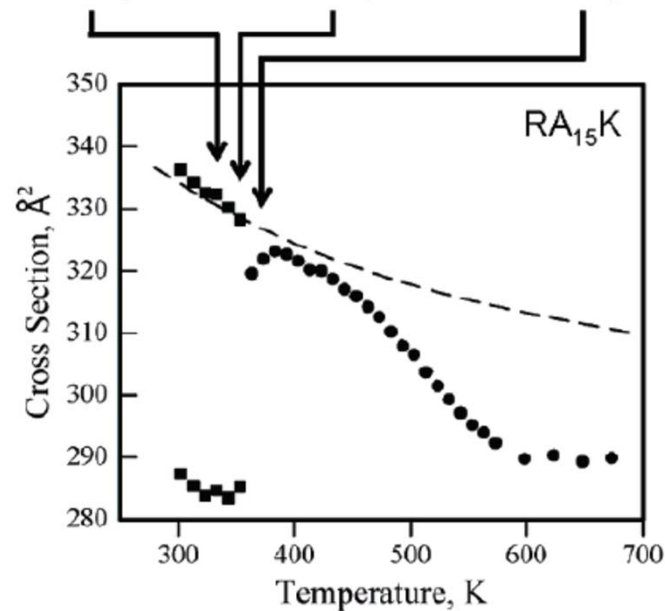
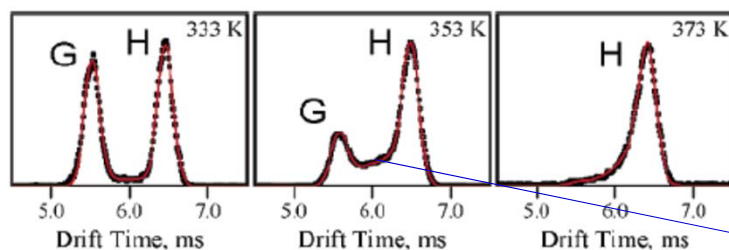
1 narrow peak => 1 structure?

**Not necessarily!**

Narrow peak can also be due to fast structural inter-conversion **inside the IMS**

# Effect of the internal temperature on conformation(s)

Population interconversion depends on the temperature

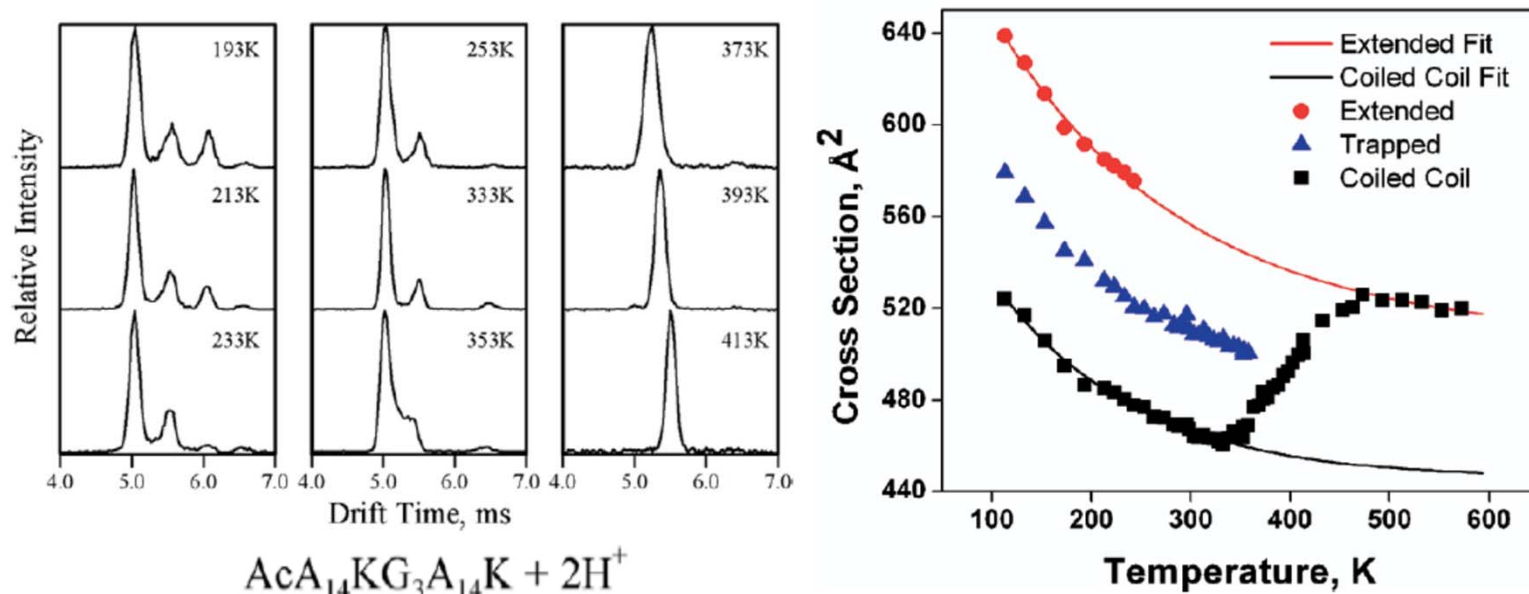


Bridge between peaks:  
in the tube, ions spend  
part of the time as G and  
part of the time as H

# Effect of the internal temperature on conformation(s)

## Population interconversion depends on the temperature

Zilk, Kaleta, Kohtani, Krishnan & Jarrold, *J. Am. Soc. Mass Spectrom.* (2007) 18, 1239



Single peak at average CCS:  
ions spend part of the time as coil  
and part of the time as extended

Single peak => not necessarily a single conformation!

# Effect of the internal temperature on conformation(s)

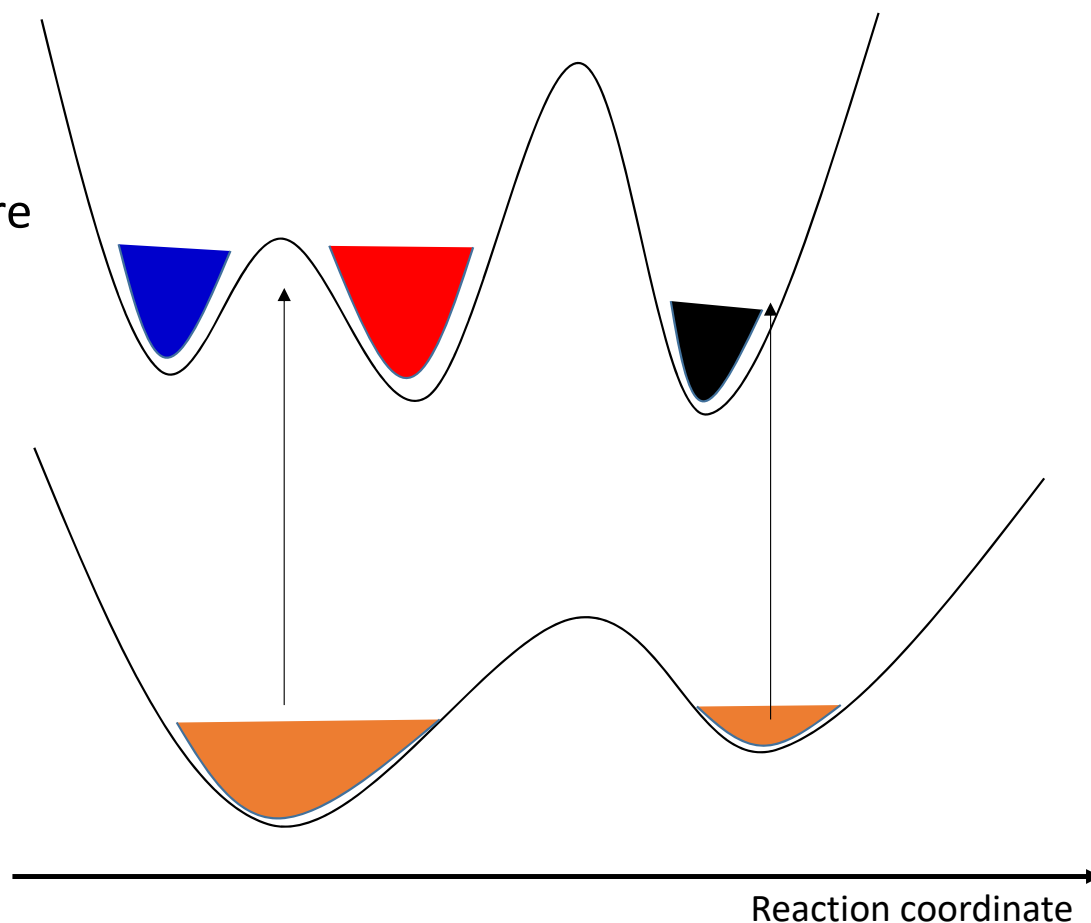
Population interconversion depends on the temperature

**Gas phase**

3 ensembles  
at low temperature

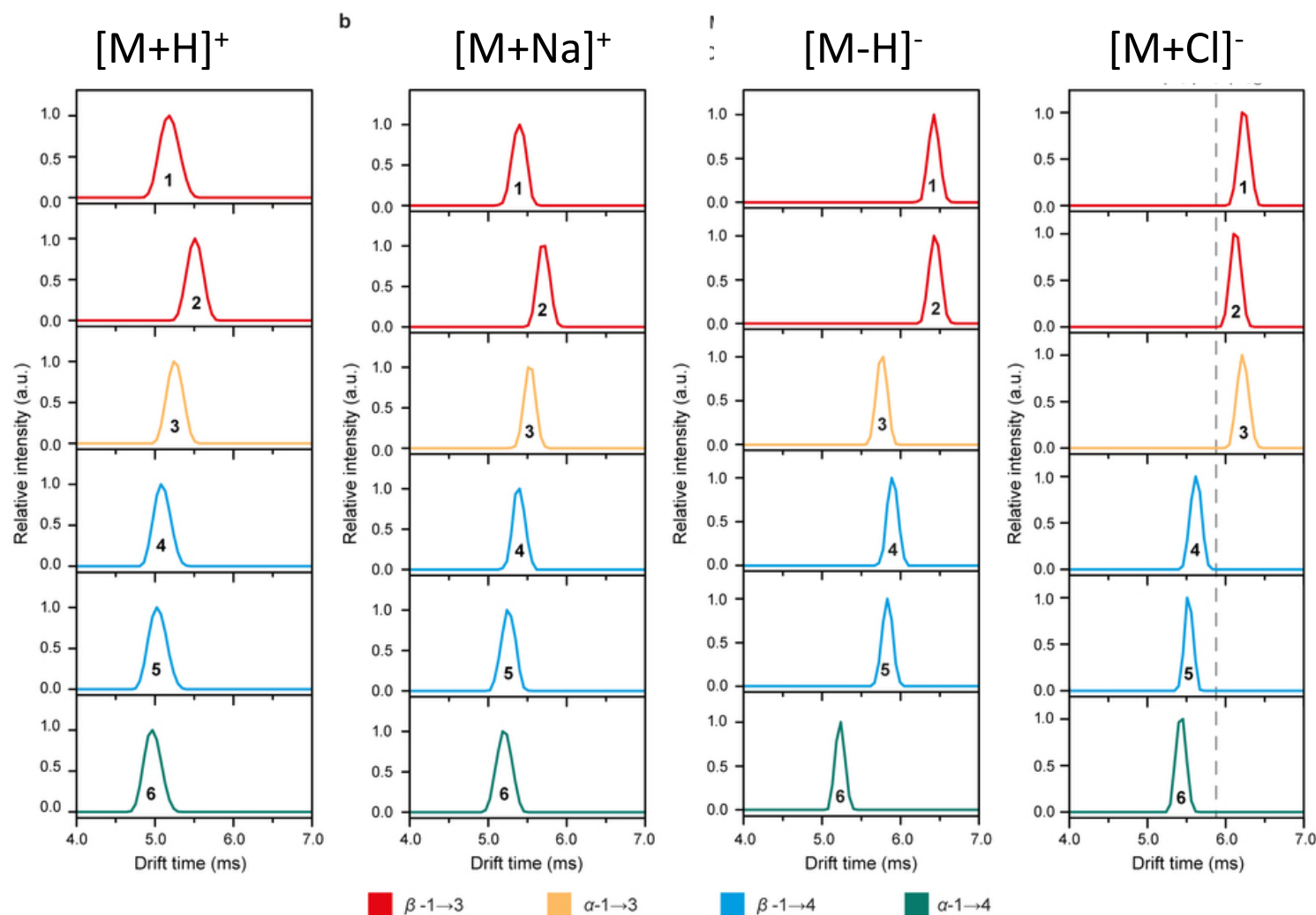
**Solution**

2 ensembles





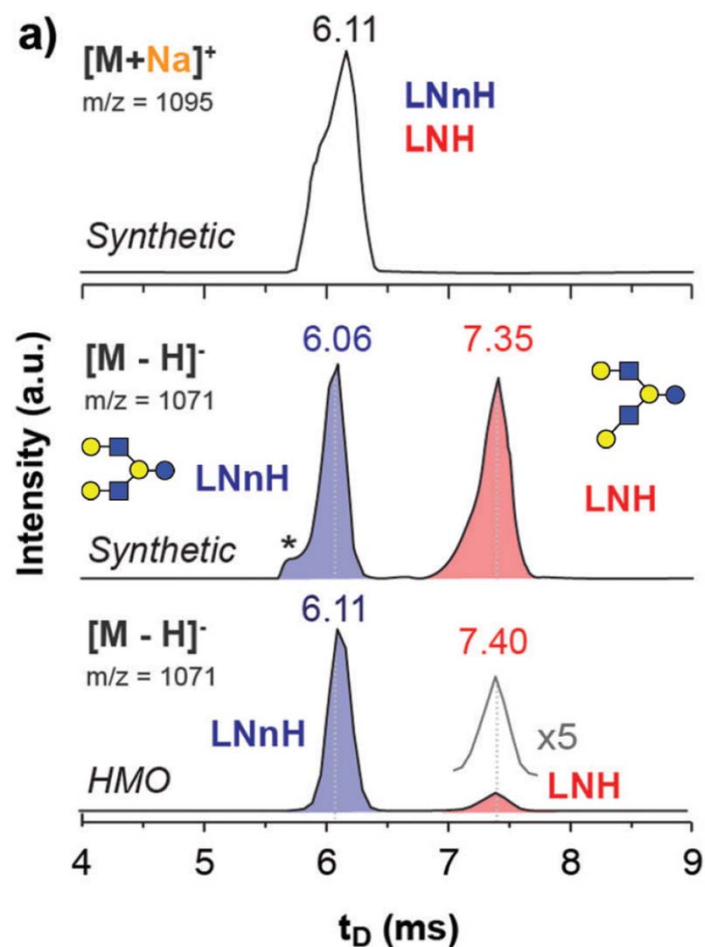
# The meaning of ATD peak width



Trisaccharide  
 $[M-H]^-$ : Narrower  
peaks, larger  
CCS differences  
=> Best  
discrimination  
between isomers

Hofmann, Hahm, Seeberger &  
Pagel, *Nature* (2015) 526, 241

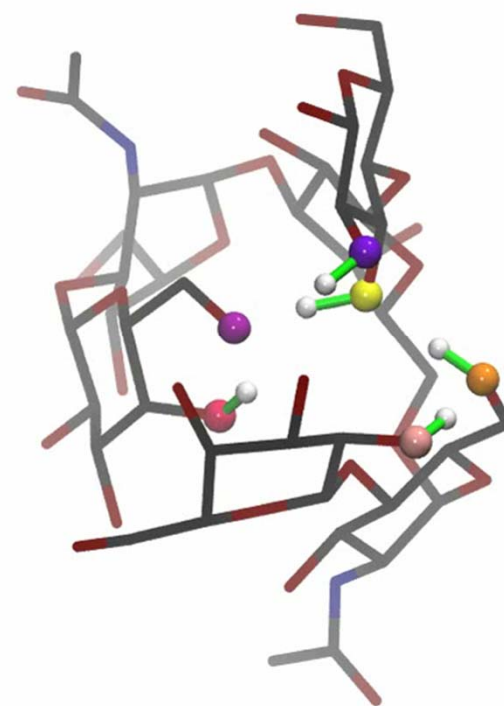
# The meaning of ATD peak width



No single  
optimized structure  
has a CCS  
matching the  
experiment

$t = 0.0$  ps

$[M-H]^-$



See animation in the supporting information of:

Struwe et al. (2015): Ab initio MD simulation of protons hopping in a deprotonated carbohydrate in the gas phase.

Struwe, Baldauf, Hofmann, Ruff & Pagel, *Chem. Commun.* (2016) 52, 12353

# The meaning of ATD peak width

2 narrow peaks => 2 structures

1 broad peak => several structures

Ion mobility peak width reflects the multiplicity of ways ions can rearrange **prior to IMS analysis**

1 narrow peak => 1 structure?


**Not necessarily!**

Narrow peak can also be due to fast structural inter-conversion **inside the IMS**


Again, we measure drift times, not collision cross sections

2 different kinds of « flexibility »

# Structural Interpretation of Ion Mobility Results

1. Measure  $K$
  2. Determine  $\Omega$  (CCS)
  3. Propose putative structures and calculate  $\Omega$  (CCS)
    - A. Generate structural model
    - B. Choose level of theory for CCS calculation
    - C. Choose parameterization of ion/gas interactions
    - D. Choose algorithm/program version
  4. Compare  $\Omega_{\text{theor}}$  and  $\Omega_{\text{exp}}$
  5. If they match, it *may be* the right structure
- 
- $$K = \frac{3}{16} \sqrt{\frac{2\pi}{\mu k_B T}} \frac{ze}{N\Omega}$$

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# Physical models and algorithms

**EHSS, He**

**An exact hard-spheres scattering model**

Chemical Physics Letters 261 (1996) 86–91

**TM, He & N<sub>2</sub>, faster**

**Collidoscope**

J. Am. Soc. Mass Spectrom. (2017) 28:587–596

**PA, TM, He**

**Effects of the Long-Range Potential**

J. Phys. Chem. 1996, 100, 16082–16086

**TM, N<sub>2</sub>**

Anal. Chem. 2012, 84, 1026–1033

**PA, faster**

**IMPACT**

Structure 23, 791–799, April 7, 2015

**SEDI**

**scattering on electronic density isosurfaces**

J. Chem. Phys. 112, 4517 (2000)

J. Phys. Chem. A 2014, 118, 6763–6772 **SEDI, faster**

**DHSS, TDHSS (IMoS)**

**diffuse trajectory methods (DHSS, TDHSS)**

J. Phys. Chem. A 2013, 117, 3887–3901

**PSA (He, N<sub>2</sub>)**

**A projected superposition approximation**

International Journal of Mass Spectrometry 308 (2011) 1–10

**LCPA**

**local collision probability approximation**

Analyst, 2015, 140, 6804

# New parameterizations for CCS calculation in N<sub>2</sub>

Machine learning (input: chemical descriptors, not the structure)

- MetCCS: Zhou, Shen, Tu & Zhu, *Anal. Chem.* **(2016)** 88: 11084
- LipidCCS: Zhou, Tu, Xiong, Shen & Zhu, *Anal. Chem.* **(2017)** 89: 9559

Trajectory method (input: 3D structure from DFT calculations + partial charges)

- Wu, Derrick, Nahin, Chen & [Larriba-Andaluz](#), *J. Chem. Phys.* **(2018)** 148: 074102
- Lee, Lee, Davidson, [Bush & Kim](#), *Analyst* **(2018)** 143: 1786
- Ieritano, Crouse, [Campbell & Hopkins](#), *Analyst* **(2019)** 144: 1660

## Calculation of $\Omega$ for structural models

**Experiments are easier in  $N_2$  than in He**

**BUT**



**Trajectory method is necessary in  $N_2$   
for small molecules**

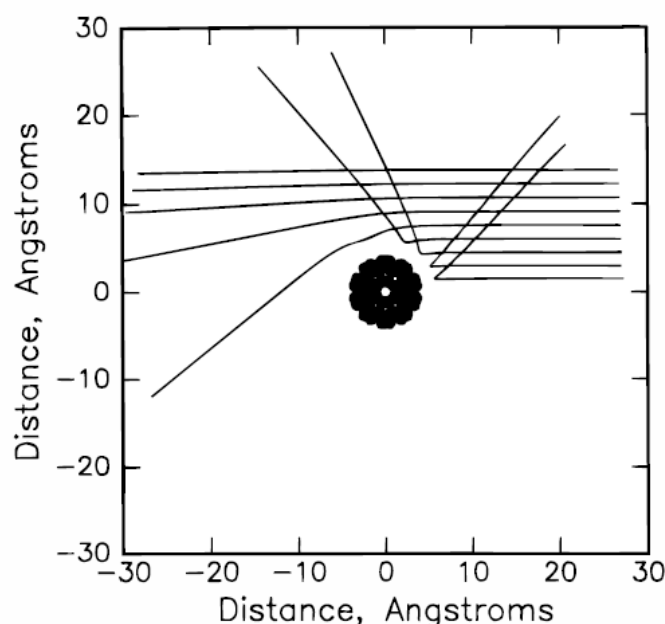
**Calculations are better parameterized in He  
(at 300 K, mostly hard spheres)**



# Calculation of $\Omega$ for structural models

## Trajectory Model (TM)

➔ **Completely captures the collision physics**



### Interaction potentials:

- Repulsive at very short distance
- Attractive at medium distance
- Null at infinite distance

Example:

Lennard-Jones interaction potentials

Parameterized for C, H and Si in He  
(or from old force fields, re-optimized  
based on drugs<sup>exp</sup>CCS at RT)



Mesleh, Hunter, Shvartsburg, Schatz & Jarrold, *J. Phys. Chem.* (1996) 100: 16082.  
Campuzano, Bush et al., *Anal. Chem.* (2012) 84: 1026. re-opt including N<sub>2</sub>

# Calculation of $\Omega$ for structural models

## Projection Approximation (PA)

➔ The "historical" view of collision cross sections

"Hit or miss" model

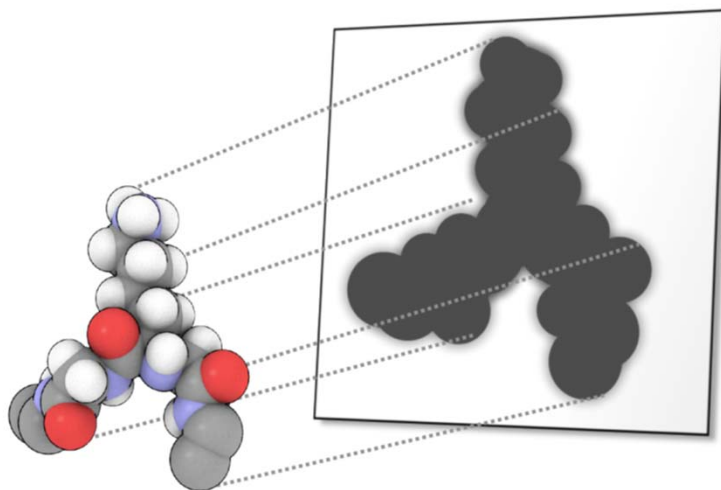
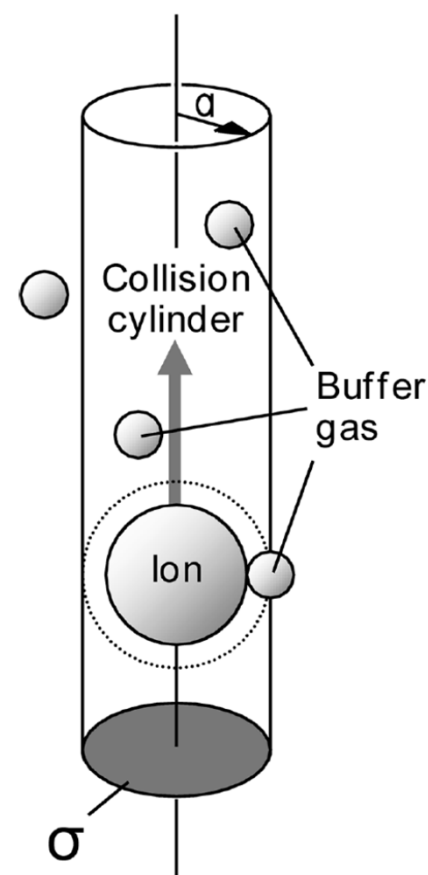


Image: K. Pagel (2015)

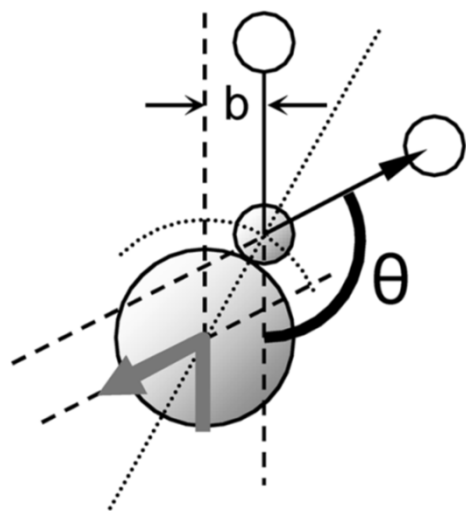


Wytenbach, Bleiholder & Bowers,  
*Anal. Chem.* (2013) 85, 2191.

# Calculation of $\Omega$ for structural models

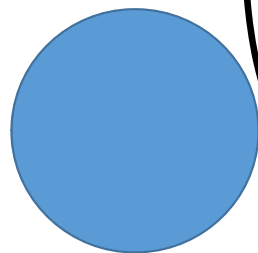
## Elastic hard spheres scattering (EHSS)

### → Momentum transfer cross section



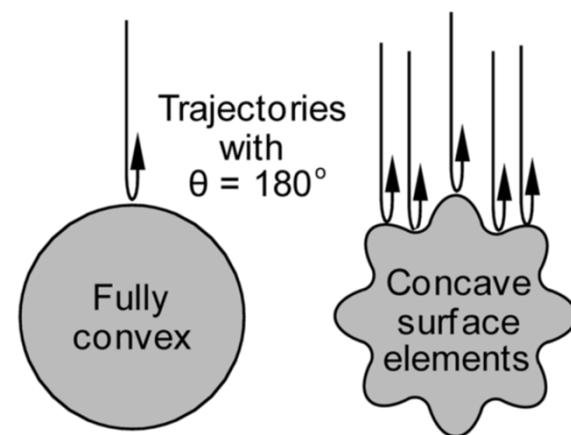
Wytenbach, Bleiholder & Bowers,  
*Anal. Chem.* (2013) 85, 2191.

More  
efficient




Less  
efficient

Surface roughness  
matters



# Structural Interpretation of Ion Mobility Results

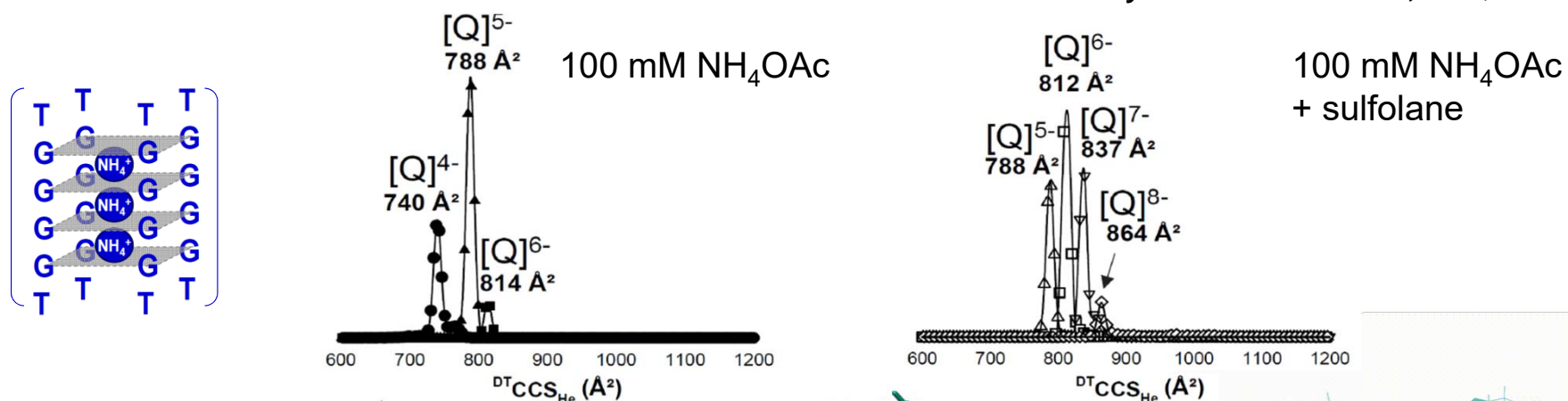
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  5. If they match, it *may be* the right structure
- 
- $$K = \frac{3}{16} \sqrt{\frac{2\pi}{\mu k_B T}} \frac{ze}{N\Omega}$$

# For DNA structures, 10—40 nucleobases

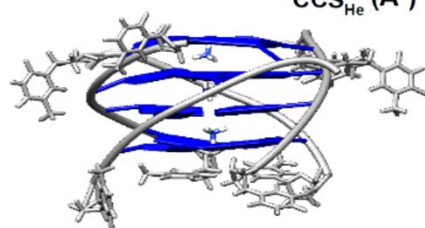
→ Measurements in **Helium**, drift tube, first principles

→ **EHSS** calculations, **reparameterization** from Siu's lab,

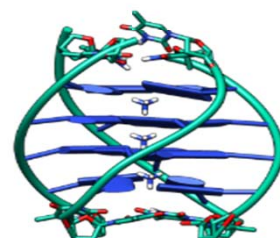
*J. Phys. Chem. B* **2010**, 114, 1204.



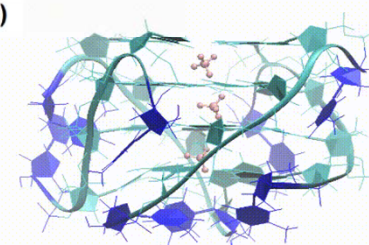
D'Atri, Porrini,  
Rosu & Gabelica,  
*J. Mass Spectrom.*  
(**2015**) 50: 711



**Crystal structure**  
PDB entry 352D,  
resolved at 0.95  $\text{\AA}$



**Solution structure**  
Here: 50 ns MD in solution  
(could use NMR constraints)



**Gas phase structure**  
—+1  $\mu\text{s}$  MD in gas phase—

# Structure of duplex DNA in the gas phase?

(dCGCGAATTCGCG)<sub>2</sub>

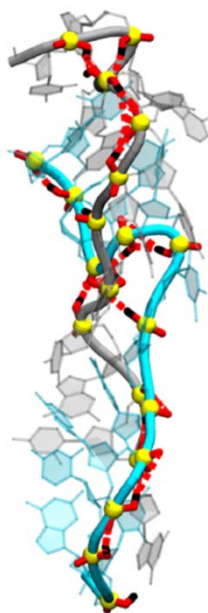
X-ray crystal structure



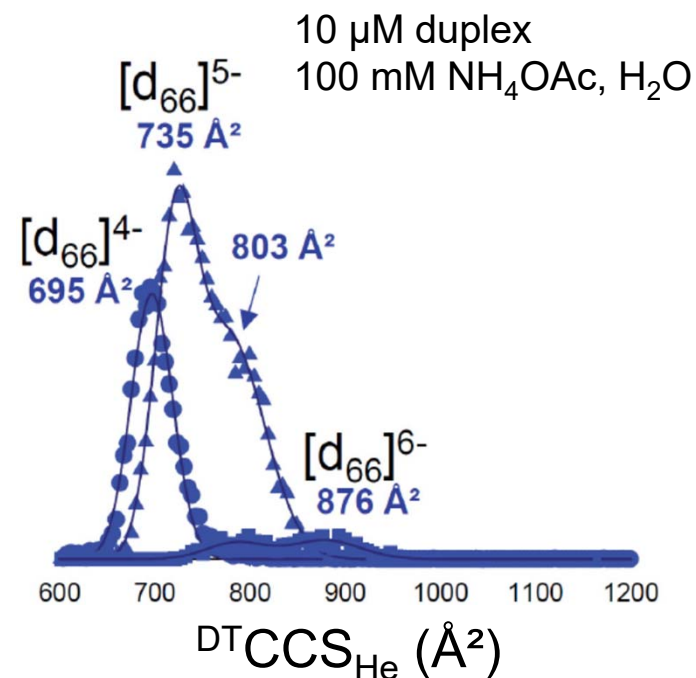
EHSS, SiuCCS<sub>He</sub>  
= 910 Å<sup>2</sup>

Gas-phase structure?

unbiased MD, parmbsc0 ff

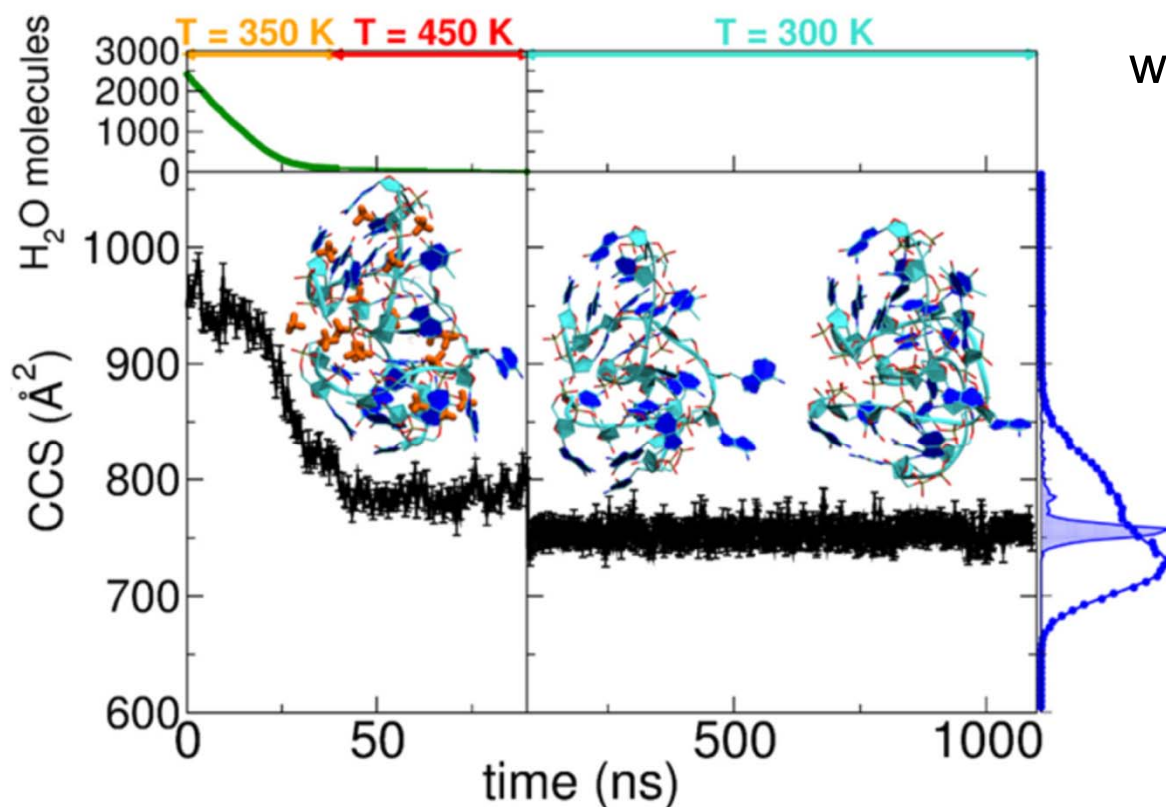
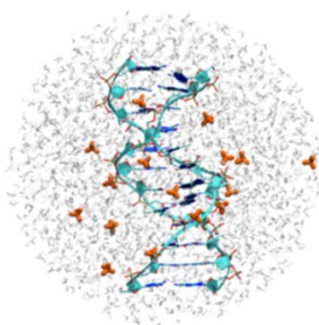


EHSS, SiuCCS<sub>He</sub>  
= 890 Å<sup>2</sup>

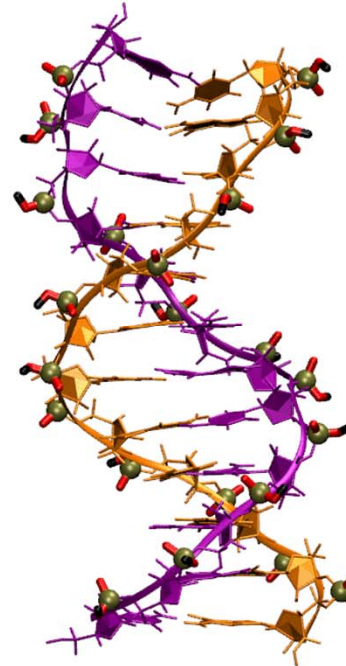


# Structure of duplex DNA in the gas phase?

## How to generate plausible structural models?



Biased ff MD  
with dual groove zipping

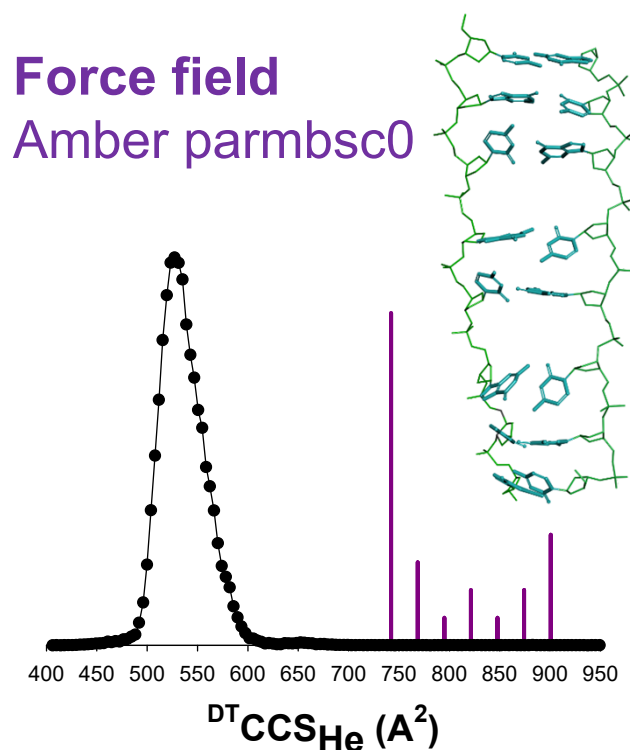




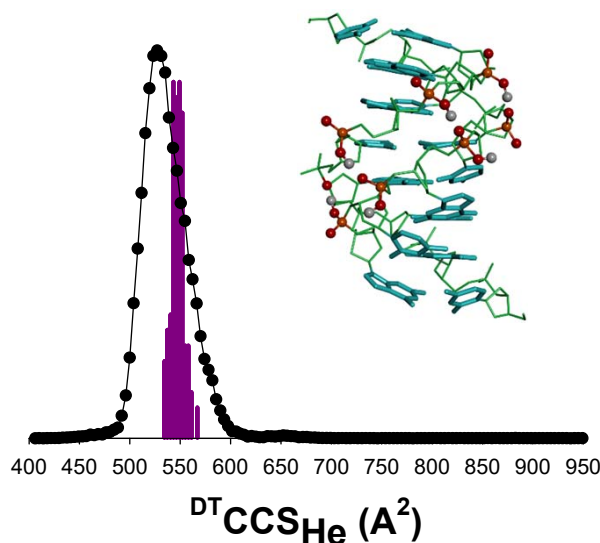
# Structure of duplex DNA in the gas phase?

We would need gas-phase force fields

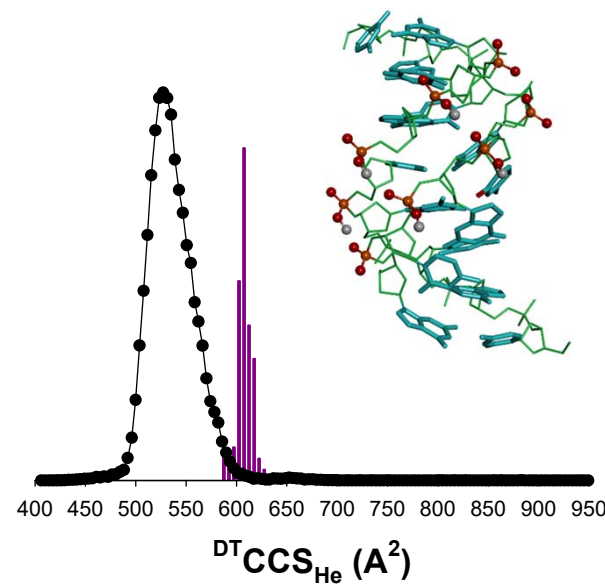
Semi-empirical calculations OK up to 10 kDa structure



**DFT**  
M06-2X, 3-21G\*+GD3



**Semi-empirical**  
PM7



Rosu & Gabelica, unpublished

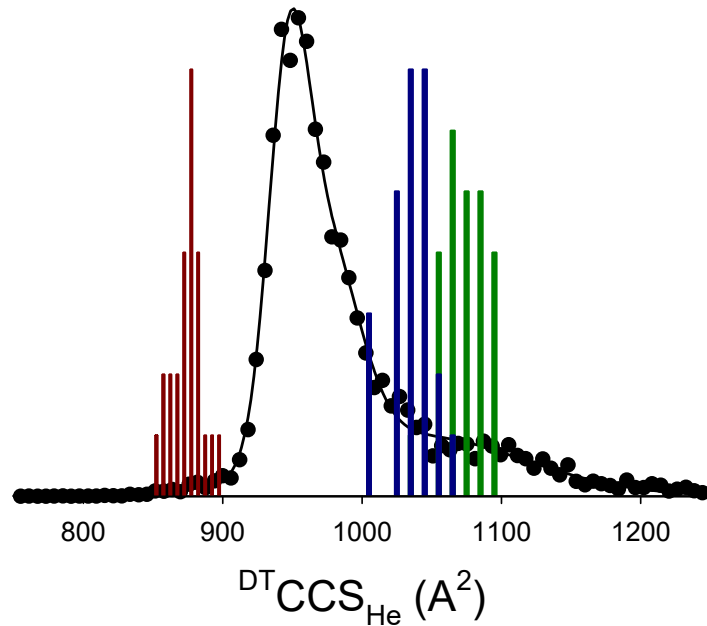


Proteins and DNA obey to the same laws of physics,  
only the balance between forces may differ

## charmm (force field) MD ❌

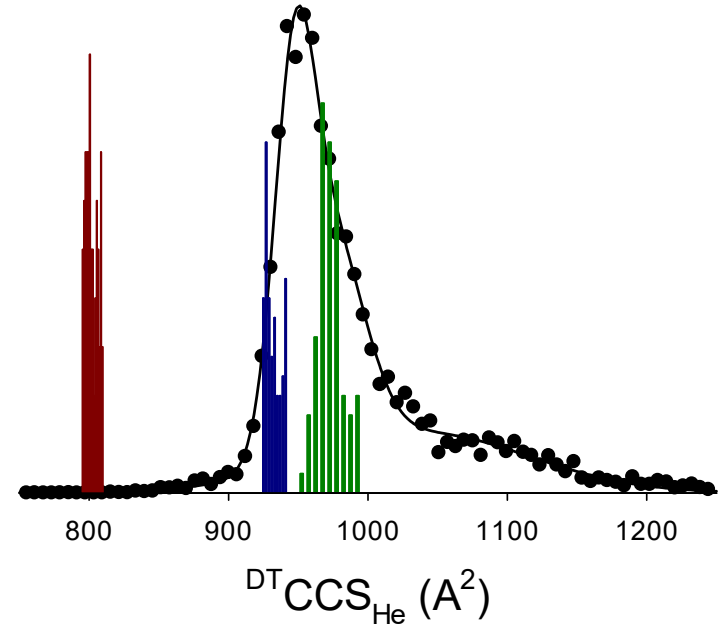
amber  
OPLS

- Ubiquitin<sup>6+</sup>
- TM
- EHSS<sub>rot</sub> Siu
- PA



## PM7 (semi-empirical) MD ✔

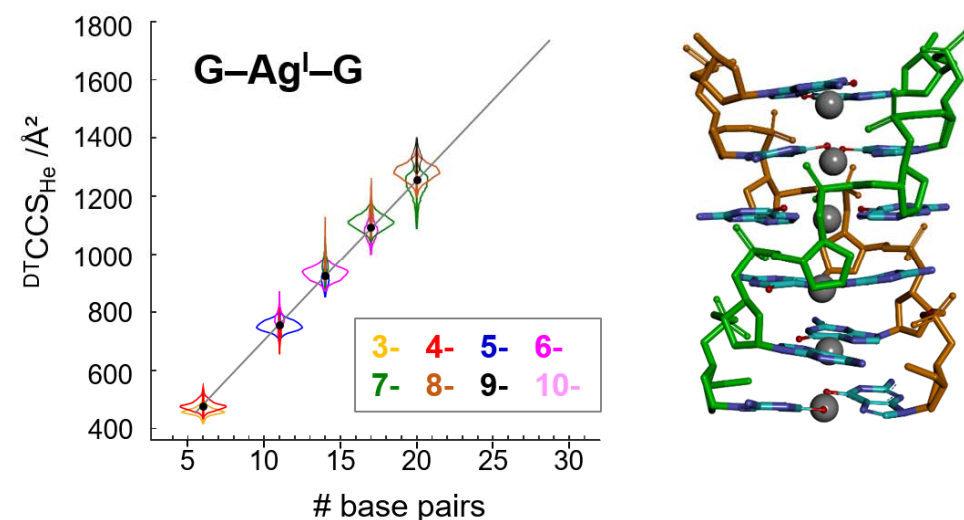
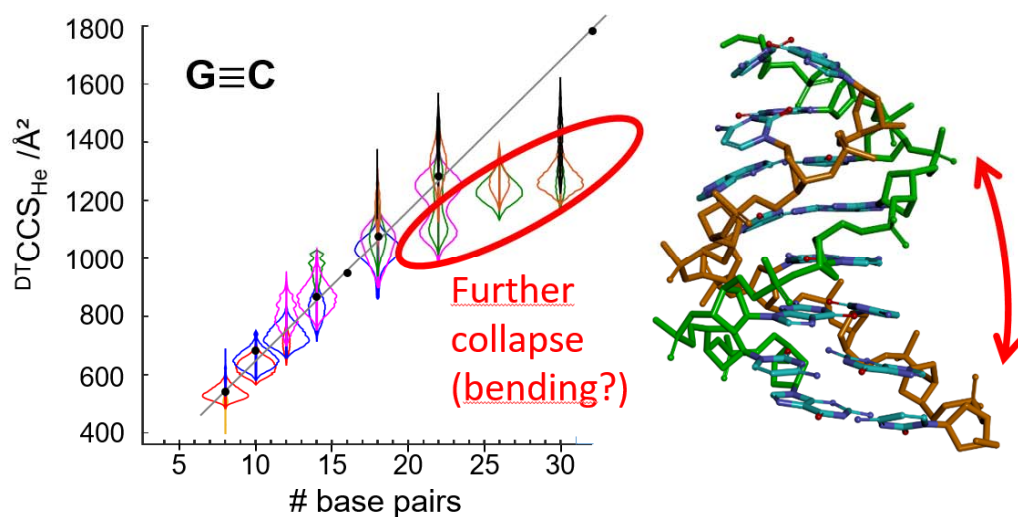
- Ubiquitin<sup>6+</sup>
- TM
- EHSS<sub>rot</sub> Siu
- PA



Rosu & Gabelica, unpublished

# For DNA structures, 10—40 nucleobases

- Structure generation: DFT, or semi-empirical, or concatenate DFT-optimized building blocks
- Force fields are inadequate in the gas-phase



## Take-home messages

The **CCS** is not just a molecular descriptor, it is **a property of the ion-gas pair** (and depends on the temperature)

**N<sub>2</sub>**: more resolute, **more sensitive to electronic structure**, less easy to model (for small molecules: TM is necessary and new parameterizations are available)

**He**: **more directly related to conformation**

Because one determines **CCS of ions in the gas phase**, **ion preparation** is as important as sample preparation

To infer solution structure from gas-phase measurements we must understand **rearrangements caused by electrospray**

## Further reading

1. D'Atri, V.; Porrini, M.; Rosu, F.; Gabelica, V., **Linking molecular models with ion mobility experiments. Illustration with a rigid nucleic acid structure.** *J. Mass. Spectrom.* **2015**, 50 (5), 711-726 ([open access here](#))
2. Gabelica, V.; Marklund, E., **Fundamentals of Ion Mobility Spectrometry.** *Curr. Opin. Chem. Biol.* **2018**, 42, 51-59 ([open access here](#))
3. Gabelica, V.; Shvartsburg, A. A.; Afonso, C.; Barran, P.; Benesch, J. L.; Bleiholder, C.; Bowers, M. T.; Bilbao, A.; Bush, M. F.; Campbell, J. L.; Campuzano, I. D. G.; Causon, T. J.; Clowers, B. H.; Creaser, C.; De Pauw, E.; Far, J.; Fernandez-Lima, F.; Fjeldsted, J. C.; Giles, K.; Groessl, M.; Hogan, C. J., Jr.; Hann, S.; Kim, H. I.; Kurulugama, R. T.; May, J. C.; McLean, J. A.; Pagel, K.; Richardson, K.; Ridgeway, M. E.; Rosu, F.; Sobott, F.; Thalassinos, K.; Valentine, S. J.; Wyttenbach, T., **Recommendations for Reporting Ion Mobility Mass Spectrometry Measurements.** *Mass Spectrom. Rev.* **2019**, 38 (3), 291-320 ([open access here](#))