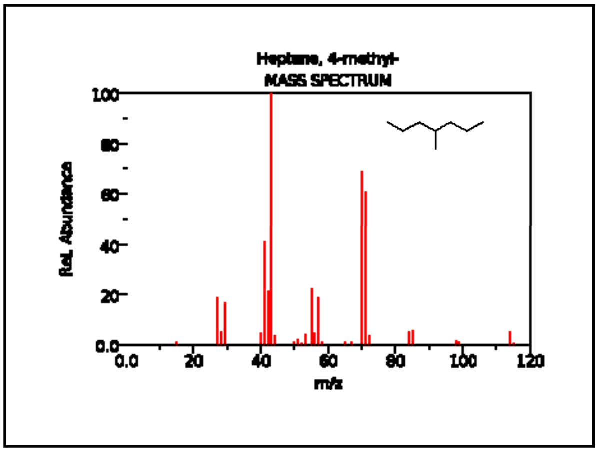
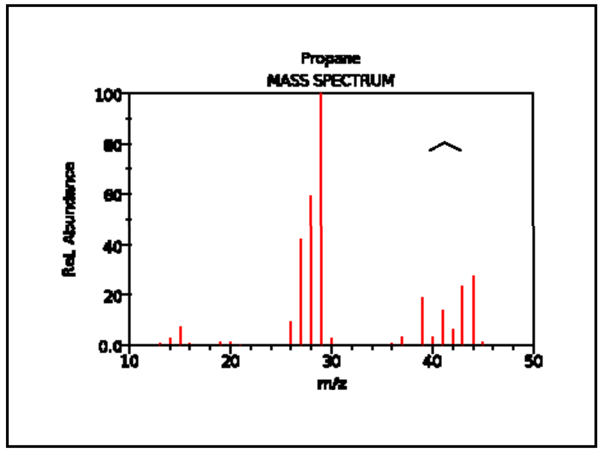
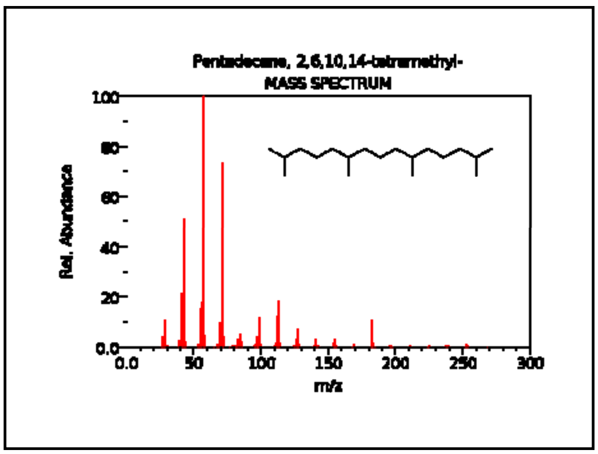
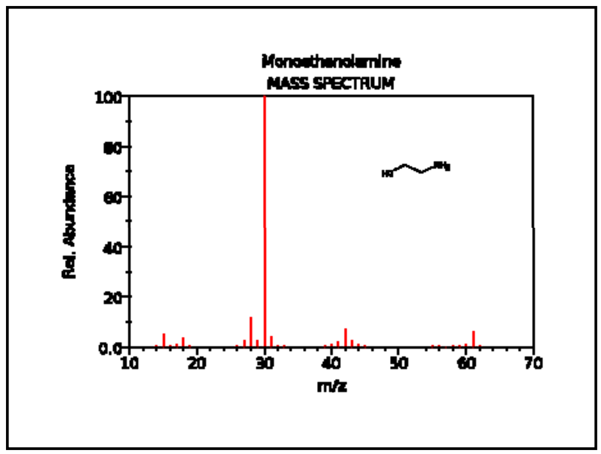
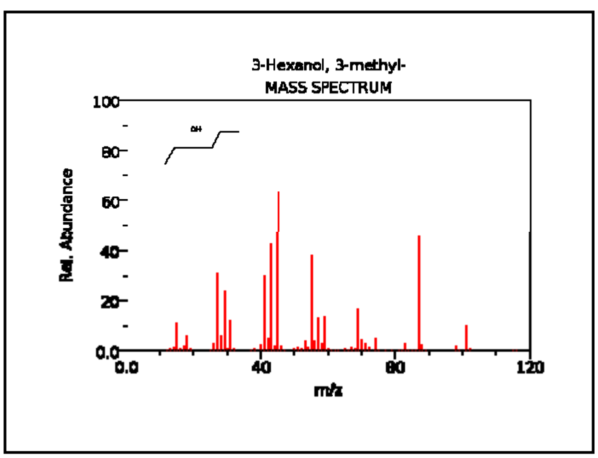
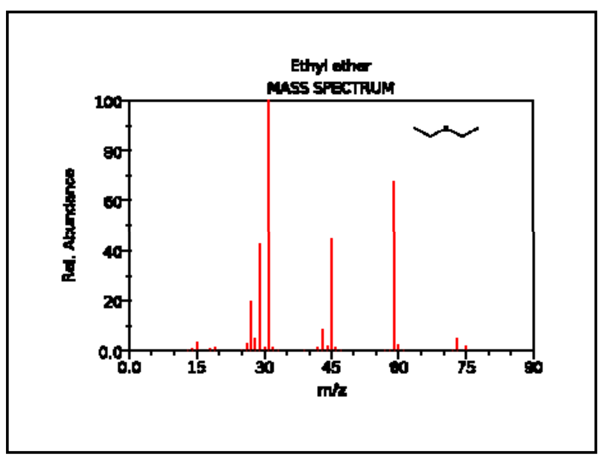

Heptane, 4-methyl-
MASS SPECTRUM
Rel. Abundance
m/z

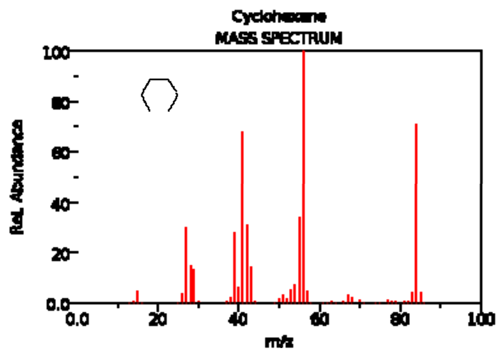

Propane
MASS SPECTRUM
Rel. Abundance
m/z

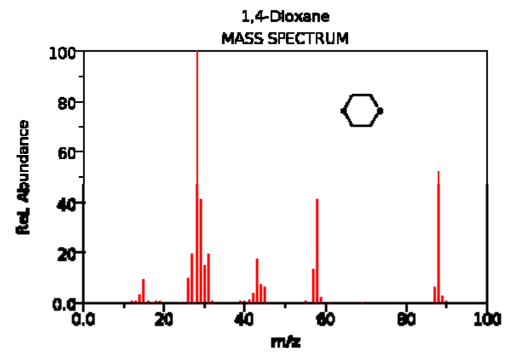

Pentadecane, 2,6,10,14-tetramethyl-
MASS SPECTRUM
Rel. Abundance
m/z

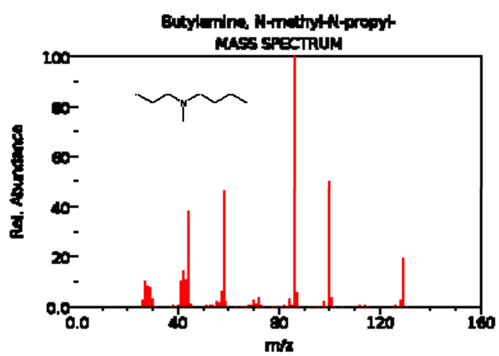

Monoethanolamine
MASS SPECTRUM
Rel. Abundance
m/z


3-Hexanol, 3-methyl-
MASS SPECTRUM
Rel. Abundance
m/z

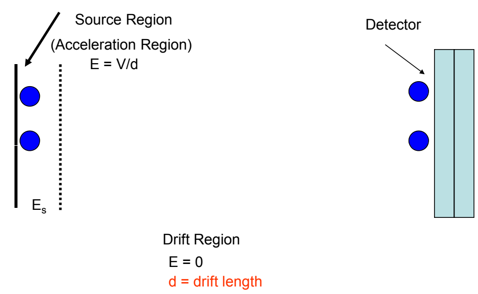

Ethyl ether
MASS SPECTRUM
Rel. Abundance
m/z







Time-of-Flight (TOF)



Time-of-Flight (TOF)

$eV = \frac{1}{2}mv^2$ Kinetic Energy given to the Ion in the Source Region

$v = \left(\frac{2eV}{m}\right)^{\frac{1}{2}}$ Solving for Velocity

$v = \frac{d}{t}$ Solve for Flight Time $t = \left(\frac{m}{2eV}\right)^{\frac{1}{2}} d$

So, with a constant acceleration voltage and a known drift length, the drift time is proportional to the square root of the mass to charge ratio (m/e).

Time-of-Flight (TOF)

Mass spectrometrists define resolution as: $\frac{m}{\Delta m}$

In TOF we start from the drift time equation:

$m = \left(\frac{2eV}{d^2}\right)t^2$ And the derivative is: $dm = \left(\frac{2eV}{d^2}\right)2tdt$

So,

$\frac{m}{dm} = \frac{t}{2dt}$

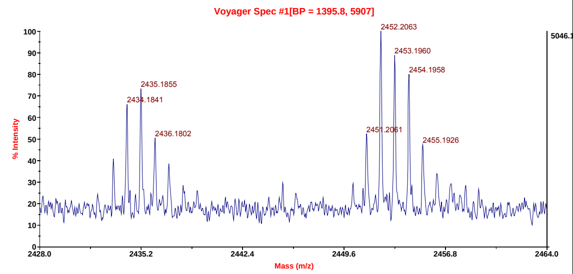
So time-of-flight resolution is defined by:

$R = \frac{m}{\Delta m} = \frac{t}{2\Delta t}$ $R \propto \frac{L}{E_z}$

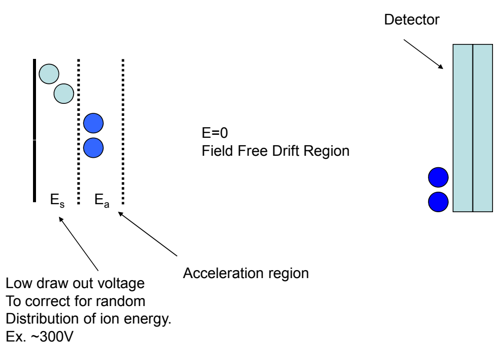
Δt is usually defined a peak width at half height.

Why is resolution so important?

Z	Name	Symbol	Mass of Atom (u)	% Abundance
1	Hydrogen	^{1}H	1.007825	99.9885
	Deuterium	^{2}H	2.014102	0.115
	Tritium	^{3}H	3.016049	*
6	Carbon	^{12}C	12.000000	98.93
		^{13}C	13.003355	1.07
		^{14}C	14.003242	*
7	Nitrogen	^{14}N	14.003074	99.632
		^{15}N	15.000109	0.368
8	Oxygen	^{16}O	15.994915	99.757
		^{17}O	16.999132	0.038
		^{18}O	17.999160	0.205



Time-Lag Focusing



The Quadrupole Field

The potential at any point (x,y,z) is defined as:

$$\phi = \frac{\phi_o}{r_o^2}(\lambda x^2 + \sigma y^2 + \gamma z^2)$$

Where,

ϕ_o= the applied field

λ, σ, γ are weighing constants for their coordinate

r_o= constant for the device

The applied field is the combination of a RF and DC (U) field:

$$\phi_o = U - V\cos(\Omega t)$$

V= 0 to Peak
Ω (rad/s) = 2πf(Hz)

Linear Quads

$$\phi = \frac{\phi_o}{r_o^2}(\lambda x^2 + \sigma y^2 + \gamma z^2)$$

We remember the constraints from the Laplace eq.:

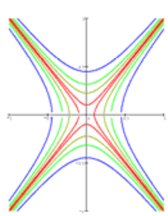
$$\lambda + \sigma + \gamma = 0$$

If we are only interested in quadrupole MS (x,y) then:

$$\gamma = 0$$
$$\lambda = -\sigma$$

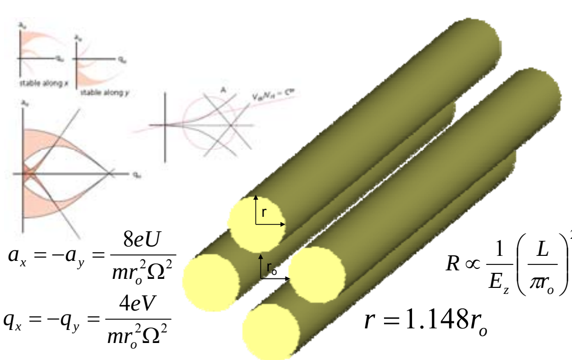
If we set λ=1, then:

$$\phi = \frac{\phi_o}{r_o^2}(x^2 - y^2)$$



The equipotential field plot

Linear Quads



$$a_x = -a_y = \frac{8eU}{mr_o^2\Omega^2}$$

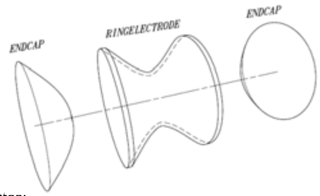
$$q_x = -q_y = \frac{4eV}{mr_o^2\Omega^2}$$

$$R \propto \frac{1}{E_z}\left(\frac{L}{\pi r_o}\right)^2$$

$$r = 1.148 r_o$$

Quad Ion Traps

$$\lambda + \sigma + \gamma = 0$$
$$\lambda = \sigma = 1$$
$$\gamma = -2$$



$$\phi = \frac{\phi_o}{r_o^2}(x^2 + y^2 - 2z^2)$$

Transform into cylindrical coordinates:

$$\phi = \frac{\phi_o}{r_o^2}(r^2\cos^2\theta + r^2\sin^2\theta - 2z^2) \qquad (\cos^2\theta + \sin^2\theta = 1)$$

$$\phi = \frac{\phi_o}{r_o^2}(r^2 - 2z^2)$$

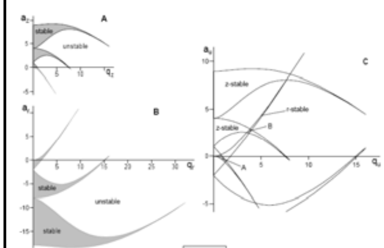
Geometrical constraints:

$$r_o^{\ 2} = 2z_o^{\ 2}$$

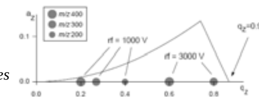
Quad Ion Traps

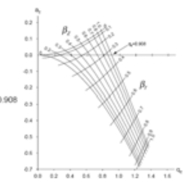
$$a_z = -2a_r = \frac{-16eU}{mr_o^2\Omega^2}$$

$$q_z = -2q_r = \frac{-8eV}{mr_o^2\Omega^2}$$

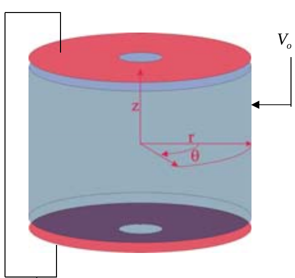


$R \propto t_{trap} \approx \# RFcycles$

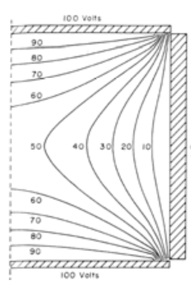




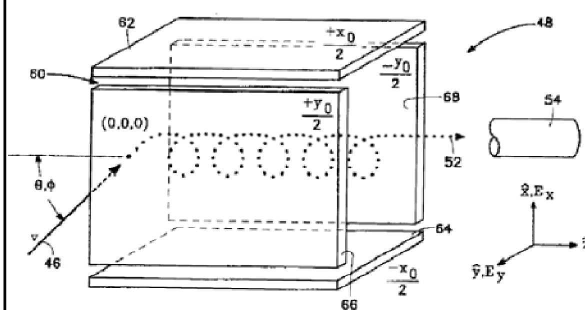
Cylindrical Ion Traps



$$V_o = -(V_{dc} - V_{ac}\cos(\Omega t))$$



V_T $\quad R \propto t_{trap} \approx \# RFcycles$



Ion Motion in a Static Magnetic Field:

Lorentzian Force:

$$\vec{F} = q(\vec{v} \times \vec{B}) \qquad (1.1)$$

$$m\vec{a} = q(\vec{v} \times \vec{B}) \qquad (1.2)$$

- The cross product states that the particles acceleration is always orthonormal to the direction of the magnetic field.
- This will be true even if B varies with position (r), but will change if B varies with time (t).

Lets take a constant magnetic field in the direction z:

$$\vec{B} = \vec{k}B_o \quad \text{Unit vector in the z-direction (k).} \qquad (1.3)$$

$$m\vec{a} = q(\vec{v} \times \vec{k}B_o) = qB\begin{vmatrix} i & j & k \\ v_x & v_y & v_z \\ 0 & 0 & 1 \end{vmatrix} \qquad (1.4)$$

Cyclotron Motion:

$$\omega = \frac{v_{xy}}{r} \quad \text{Angular velocity} \qquad (2.5)$$

Substitute angular velocity:

$$m\omega^2 r = qB_o\omega r \qquad (2.6)$$

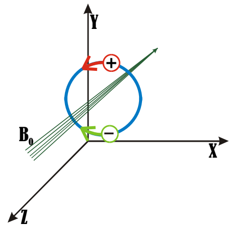
Simplify into the celebrated "ion cyclotron equation":

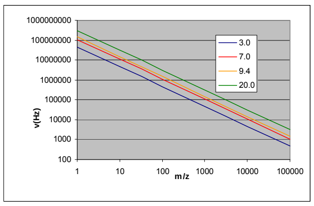
$$\omega = \frac{qB_o}{m} \qquad (2.7)$$

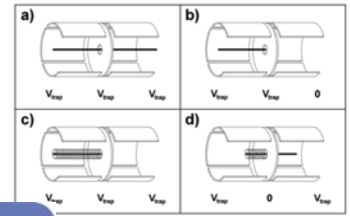
•This equation is the heart of ICR. It tells us that the cyclotron frequency is independent of the ions initial velocity, and all ions with the same mass/charge (m/q) will have the same frequency.

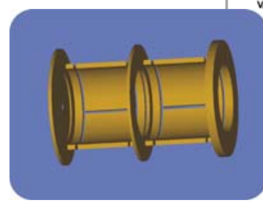
Cyclotron Motion:

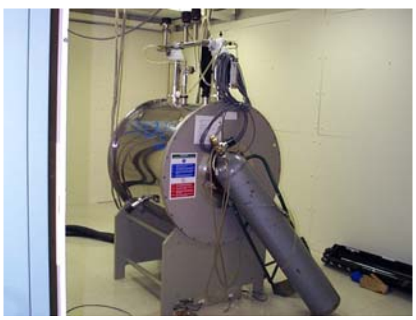
•We can see from our equations that cations will cyclotron counter-clockwise to the in-the-plane magnetic field direction, while anions will cyclotron clockwise











Cyclotron Motion: Other Useful Equations of Cyclotron Motion:

From Eq. 2.4, we can set up the relationship between cyclotron radius and angular velocity:

$$r = \frac{mv_{xy}}{qB_o} \qquad (2.8)$$

2 useful equations can be derived from 2.8;

1. Calculated velocity of a ion with a specific radius:

$$v_{xy} = \frac{qB_o r}{m} \qquad (2.9)$$

2. Calculated translational energy of an ion with a specific radius:

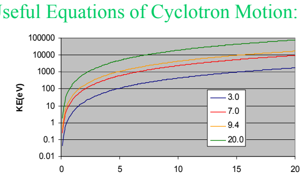
$$E = \frac{mv_{xy}^2}{2} \qquad E_{trans} = \frac{q^2 B_o^2 r^2}{2m} \qquad (2.10)$$

Cyclotron Motion: Other Useful Equations of Cyclotron Motion:

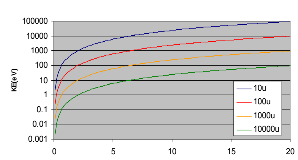
•Translational energy of the ion as a function of cyclotron radius at differing magnet fields (Eq. 2.10) with a mass of 100u.

$$E_{trans} = \frac{48.243 z^2 B_o^2 r^2}{m}$$

•From the simplified equation above, E(eV),B(T),r(mm), m(g/mol).



•Translational energy of the ion at differing masses as a function of radius in a 7.0 Tesla field.



Cyclotron Motion: Other Useful Equations of Cyclotron Motion:

One of the most useful derivations of cyclotron motion is finding the radius at specific temperatures. To do this we use the Boltzman equation and solve:

We assume: $$\frac{m < v_{xy}^2 >}{2} \cong kT$$

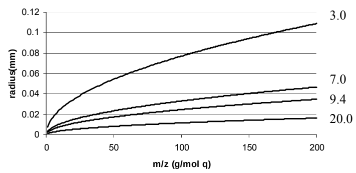
$$r = \frac{\sqrt{2mkT}}{qB_o} \qquad (2.11)$$

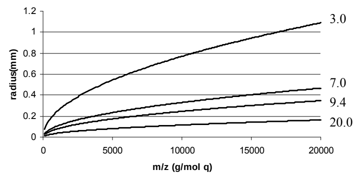
Cyclotron Motion: Other Useful Equations of Cyclotron Motion:

•Here we displayed the cyclotron radius of the conventional cryomagnets as a function of m/z at room temperature. (Eq. 2.11)

$$r = \frac{1.3365\times10^{-3}\sqrt{mT}}{zB_o}$$

•For the above simplified equation; r(mm), m(g/mole), B(T), T(K).





Mass Resolving Power in FT-ICR MS:

Start with the cyclotron equation:

$$\omega = \frac{qB_o}{m}$$

Take the first derivative with respect to mass (m):

$$\frac{d\omega}{dm} = -\frac{qB}{m^2}$$

Rearrange to the resolution equation:

$$\frac{m}{\Delta m} = \frac{qB}{m\Delta\omega}$$

Though from first glance the field has a direct effect on resolution, remember that ion velocity will also increase as a function of B, so collision frequency (therefore $\Delta\omega$) will increase making resolution independent of B.

Upper Mass Limit in FT-ICR MS:

Rewriting the cyclotron equation:

$$m = \frac{qBr}{v_c}$$

For thermalized ions the cyclotron velocity becomes the rms average velocity:

$$v_c(thermal) = \sqrt{\frac{2kT}{m}}$$

Substituting in we get:

$$m(thermal) = \frac{q^2B^2r^2}{2kT}$$

So in a 7T field with a 2cm radius cell the max mass will be 9114 kD. However there is no room to excite and magnetron and axial motion is not included into this equation.

Upper Mass Limit in FT-ICR MS:

Note: Magnetron motion and cell shapes:

$$\frac{m}{q} = \frac{a^2B^2}{4\alpha V_T}$$

So in a 7T field in a cylindrical trap of 2cm radius the mass limit will be about 250 kD.

Collision Cross Section:

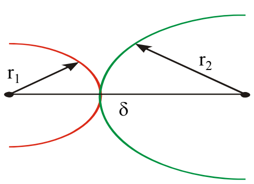
Ideal elastic hard sphere collision:

$$\Omega = \pi(r_1 + r_2)^2$$

Where Ω is the collision cross-section

$$\delta = r_1 + r_2 = \left(\frac{\Omega}{\pi}\right)^{\frac{1}{2}}$$

Where δ is the collision distance



These equations negate potential interactions between the two molecules (atoms), attractive and repulsive, and assume spherical geometry.

Mean Free Path (λ):

#collisions per unit time:

$$Z_1 = \pi d^2 \langle v \rangle N$$

Mean free path (length b/w collisions)

$$\lambda = \frac{\langle v \rangle}{Z_1} = \frac{\langle v \rangle}{\pi(r_1 + r_2)^2\sqrt{2}\langle v \rangle N}$$

$$\lambda = \frac{1}{\pi(r_1 + r_2)^2\sqrt{2}N}$$

Motion in an Applied Field

(Maxwellian ions)

$$v_d = KE$$

v_d=drift velocity(cm/sec)

K=mobility(cm^2/Vsec)

E=applied field (V/cm)

Langevin Equation:

$$K = \frac{e\lambda}{m\,v}$$

e=ionic charge(Volts)

λ=mean free path(m)

Assumptions: ignoring coulombic interaction, Low field limit, close to thermal equilibrium.

Deriving the Nernst-Townsend-Einstein Relation (Einstein Relation):

At equilibrium, the space distributions of ions is given by the Boltzman distribution:

$$n = n_o e^{\frac{eEr}{kT}}$$

Differentiating yields:

$$\frac{1}{n}\nabla n = \frac{eE}{kT}$$

Substitution into the linear transport equation and setting J=0 gives the Einstein relation:

$$K = \frac{eD}{kT}$$

Particle Parameters:

B = Mechanical mobility

D = Diffusion coefficent

K = Electric mobility

Relation:

$$D = kTB$$

$$K = qB$$

Nernst-Townsend-Einstein Relation:

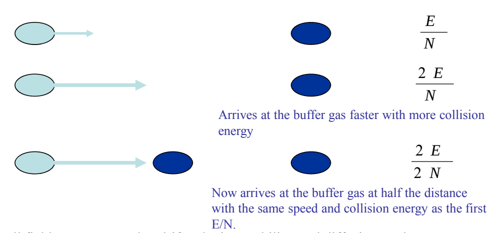
$$K=eD/kT$$

Once again, this only holds true at low fields. We make the assumption that ion's temperature is thermal.

Number Density (N) and Applied Field (E) Dependency:

Both K and D are inversely proportional to N at these low fields.

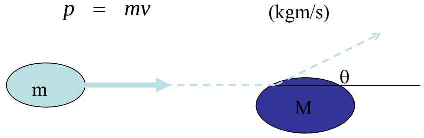
However, at higher applied fields, E is now a factor.



At all fields, we can see that drift velocity, mobility, and diffusion are better characterized with the E/N ratio.

Momentum:

$$p = mv \qquad \text{(kgm/s)}$$



$$\delta = \mu v_{rel}\,(1 - \cos(\theta))$$

Where, δ is the momentum transferred, v_{rel} is the relative velocity b/w collision bodies, and θ is deflection angle.

$$\mu = \frac{mM}{m + M}$$

Where, μ is the reduced mass.

Collision Frequency:

Spherical:

$$Z_{12}=\pi b^2_{max}\langle v_r\rangle N$$

Adding Momentum Transfer:

$$Z_{12}=Q_D(\varepsilon)\langle v_r\rangle N$$

At low fields this is an easy calculation because the velocity of the ion (v) and the bath gas (V) are thermal. However, the field contributes to the velocity of the ion at higher fields.

Wannier equations for Diffusion in high E/N:

Weak Field D(0):

Einstein Relation:

$$K = \frac{eD}{kT}$$

Mobility Equation:

$$v_d = KE$$

So,

$$D(0) = \frac{v_d kT}{eE}$$

Wannier equations for Diffusion in high E/N:

High Field D:

$$D_{T,L}(E) = D(0) + \xi_{T,L}\left(\frac{mM}{m+M}\right)\frac{v_d^3}{eE}$$

$$\xi_T = \frac{1}{3}\frac{(M+m)^2}{m(M+2m)}$$

$$\xi_L = \frac{1}{3}\frac{(M+m)(M+4m)}{m(M+2m)}$$

Representative Mobility Equations

$$v_d = KE_o \longleftarrow$$ Mobility is Defined As:

$$K_o = \frac{p}{760}\frac{273.15}{T}K \longleftarrow$$ Where the reduced mobility is:

$$K = \frac{e}{N}\left(\frac{1}{3\mu k_b T}\right)^{\frac{1}{2}}\frac{1}{\Omega} \longleftarrow$$ The celebrated mobility Equation:

Representative Mobility Equations

$$v_{rel}^2 >> \frac{3kT}{\mu} \longleftarrow$$ What happens when the relative velocity is greater than thermal?

$$v_{rel}^2 = \frac{eE_o}{N\mu\Omega}\left(\frac{2m}{\lambda\mu}\right)^{\frac{1}{2}} \longleftarrow$$ Field induced relative velocity.

Where λ is the relative energy loss for the collision event.

$$K = \left[\frac{e}{E_o N\Omega}\frac{M+m}{M^2}\right] \longleftarrow$$ High field mobility equation:

Resolution

So the variance is:

$$\sigma = \sqrt{2Dt_d}$$

HWHM (half width at half max) is 1.17σ, and FWHM (full width at half max) is 2.35σ.

$$FWHM = W_{1/2} = 2.35\sigma = 3.32\sqrt{Dt_d}$$

Resolution is defined as the ratio of the traveled distance (L) to the peak width at half height ($W_{1/2}$).

$$R = \frac{L}{W_{1/2}}$$

Resolution

Using the drift velocity equation:

$$v_d = KE_o = \frac{L}{t_d}$$

Substituting in the resolution equation for L:

$$R = \frac{t_d KE_o}{3.32\sqrt{Dt_d}}$$

And simplify:

$$R = \frac{KE_o t_d^{\frac{1}{2}}}{3.32D^{\frac{1}{2}}}$$

Resolution

We then arrive at the Nernst-Townsend-Einstein Equation, sometimes referred to as the Einstein relation:

$$K = \frac{qD}{k_b T}$$

The main assumption of the Einstein relation is that mobility theory (motion acting on one species, but not the other) and diffusion theory are at equilibrium. Wannier no longer assumed that the applied field was weak and the ion mass was small.

$$D_{\perp} = K\frac{k_b T}{q} + \frac{m}{3}\frac{m+M}{m+1.908M}\frac{E^2K^3}{q}$$

$$D_{\parallel} = K\frac{k_b T}{q} + \frac{m}{3}\frac{m+3.72M}{m+1.908M}\frac{E^2K^3}{q}$$

Resolution

At this point we can solve the resolution using either the Einstein relation or Wannier's relation. We will see from some of the future results that the maximum resolution is attained from systems that fit the Einstein relation. So, if we solve the resolution equation in terms of the Nernst-Townsend-Einstein equation:

$$R = \frac{L}{3.32\sqrt{\frac{Kk_bT}{q}\frac{L}{KE_o}}} \qquad (2.8)$$

Simplifies to for single charges ions:

$$R = 32.33\sqrt{\frac{LE_o}{T}} \qquad (2.9)$$

Resolution

Taking Wannier's relation in the z direction:

$$D_z = K\frac{k_b T}{q} + \frac{m}{3}\frac{m+3.72M}{m+1.908M}\frac{E^2K^3}{q}$$

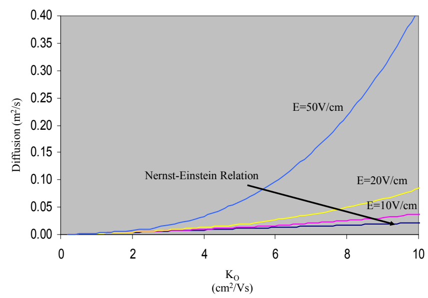
Simplify the mass term in the relation:

$$\mu_w = \frac{m}{3}\frac{m+3.2M}{m+1.908M}$$

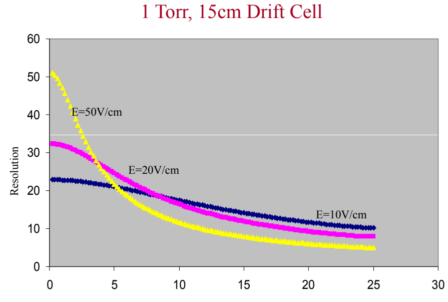
Resolution for a broader range of fields:

$$R = \frac{E}{3.32}\sqrt{\frac{qKt_d}{k_bT + \mu_w E^2K^2}}$$

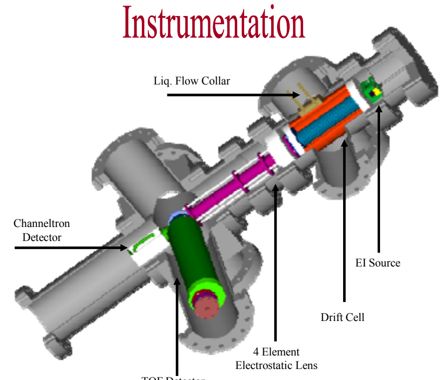
Wannier Relation, 15cm Drift Cell
1 Torr

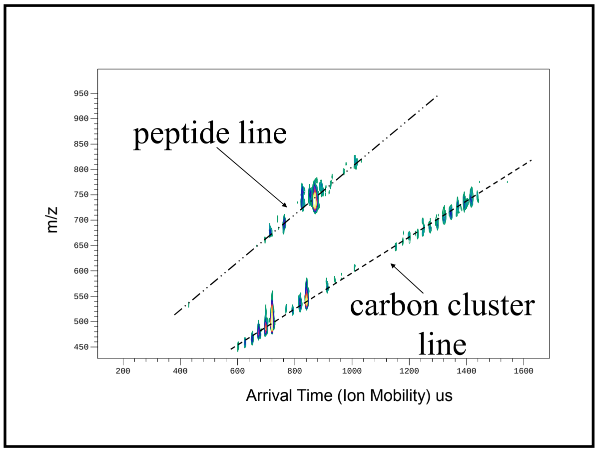


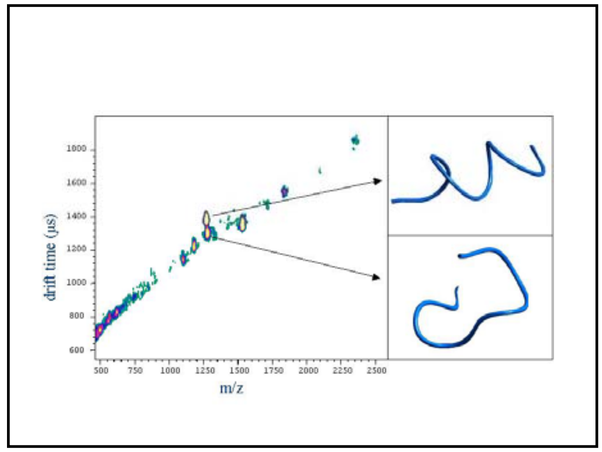
Comparison of Reduced Mobility vs. Resolution
1 Torr, 15cm Drift Cell

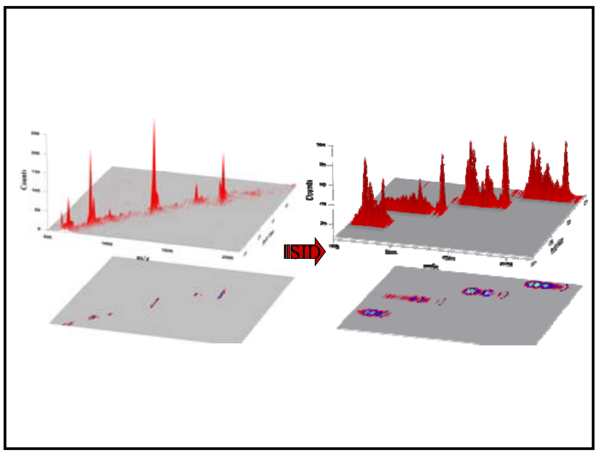


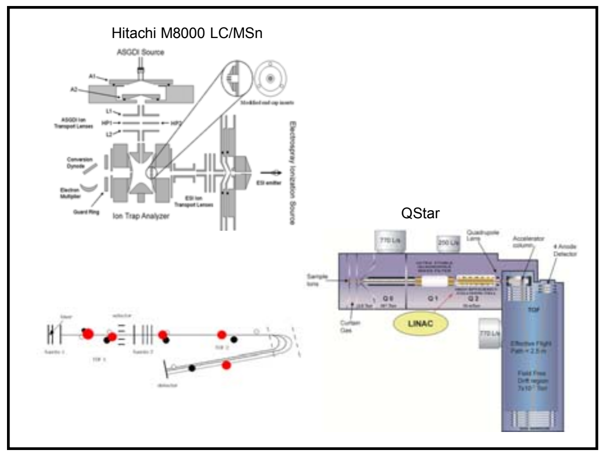
Instrumentation

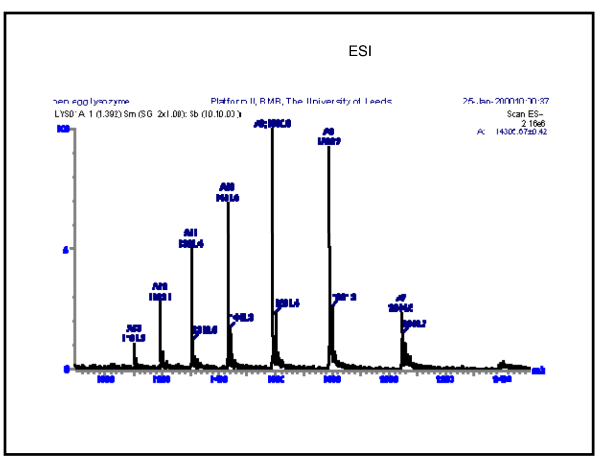


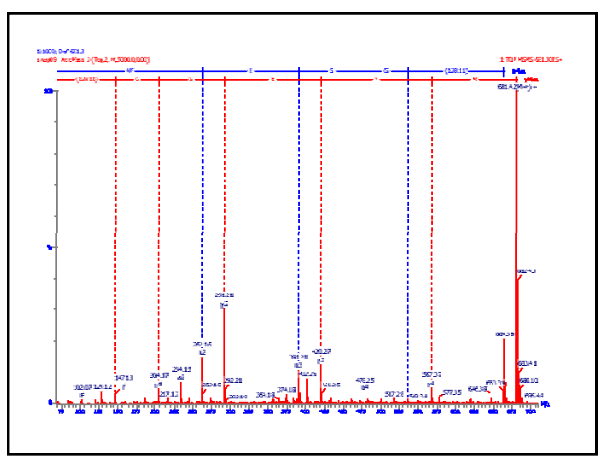

peptide line
carbon cluster line
m/z
Arrival Time (Ion Mobility) us


drift time (μs)
m/z



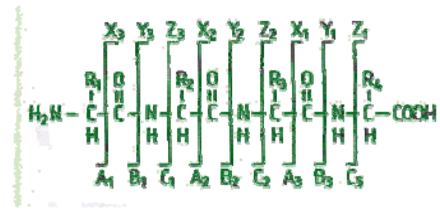

Hitachi M8000 LC/MSn
ASGDI Source
Ion Trap Analyzer
Electrospray Ionization Source
QStar
LINAC


ESI
hen egg lysozyme
Platform II, BMB, The University of Leeds

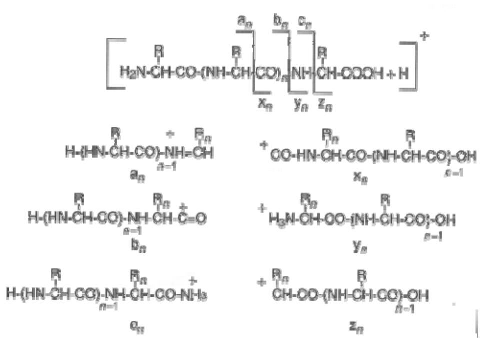


Amino Acid	3 Letter Code	Single Letter Code		Residue Mass	
				Monoisotopic	Average
Glycine	Gly	G		57.02147	57.052
Alanine	Ala	A		71.03712	71.079
Serine	Ser	S		87.03203	87.078
Proline	Pro	P		97.05277	97.117
Valine	Val	V		99.06842	99.133
Threonine	Thr	T		101.04768	101.105
Cysteine	Cys	C		103.00919	103.144
Isoleucine	Ile	I		113.08407	113.160
Leucine	Leu	L		113.08407	113.160
Asparagine	Asn	N		114.04293	114.104
Aspartic Acid	Asp	D		115.02695	115.089
Glutamine	Gln	Q		128.05858	128.131
Lysine	Lys	K		128.09497	128.174
Glutamic Acid	Glu	E		129.04260	129.116
Methionine	Met	M		131.04049	131.198
Histidine	His	H		137.05891	137.142
Phenylalanine	Phe	F		147.06842	147.177
Arginine	Arg	R		156.10112	156.188
Tyrosine	Tyr	Y		163.06333	163.170
Tryptophan	Try	W		186.07932	186.213
Homoserine Lactone				83.03712	83.090
Homoserine				101.04768	101.105
Pyroglutamic acid				111.03203	111.100
Carboxyamidomethyl Cysteine				160.03065	160.197
Carboxymethylcysteine				161.01466	161.181
Pyridylethylcysteine				208.06703	208.284

Peptide Fragmentation



Peptide Fragmentation



Sample MS/MS Spectrum acquired on the 4700 TOF-TOF of a Digested Protein from Industry