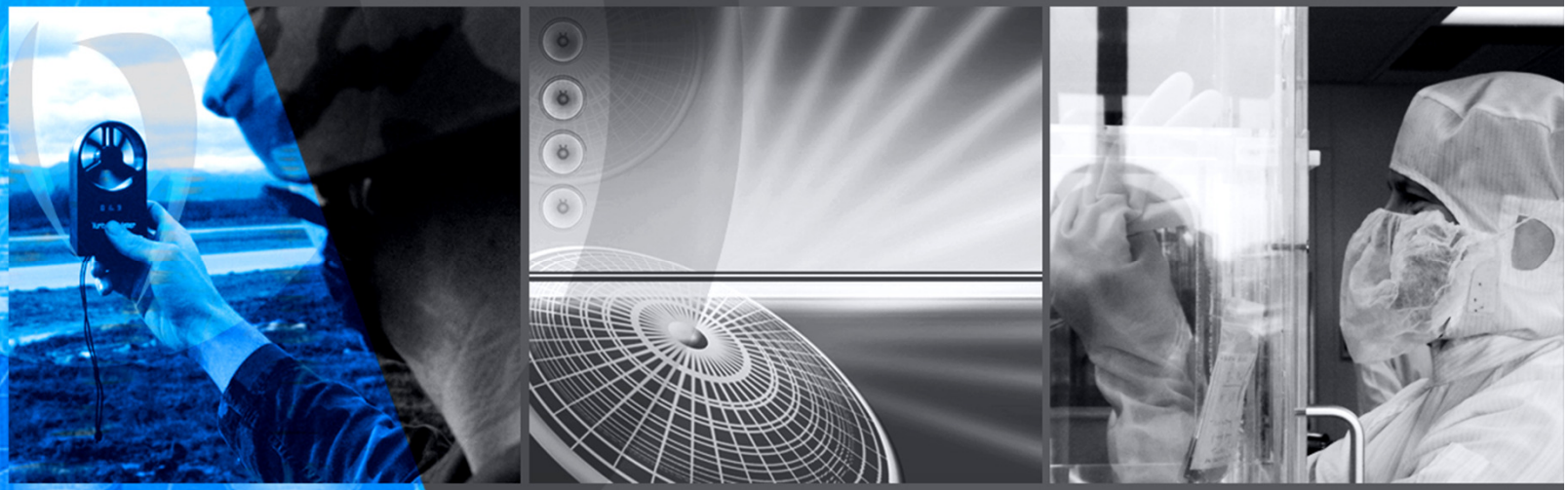
Monday March 12 2012

600-5

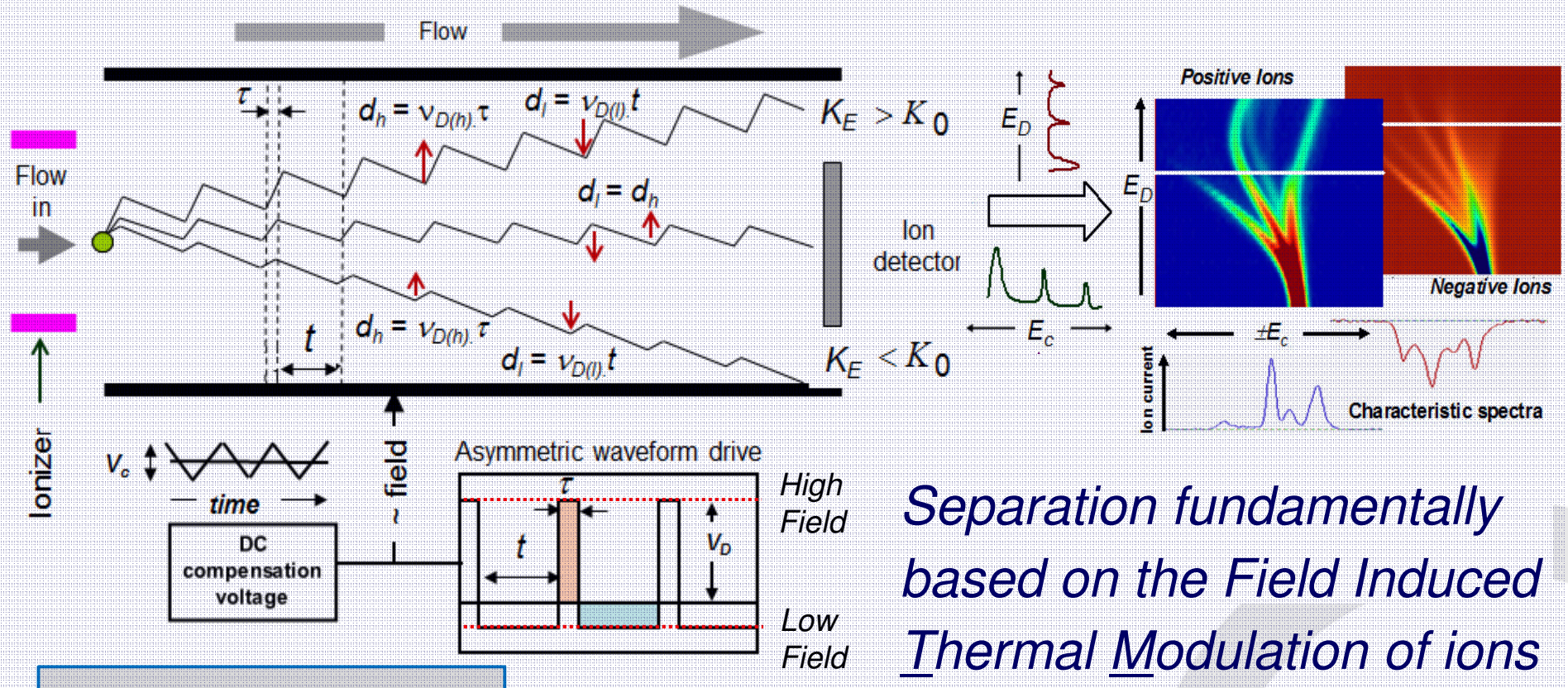
ASHLEY T WILKS & Billy Boyle



Pittcon 2012
Orange County
Convention Center
Orlando, Fl

Developments in Ultra FAIMS Instrumentation for Standalone and Hyphenated Applications

Principles in 30 seconds



Separation fundamentally based on the Field Induced Thermal Modulation of ions ***in the Ion Separator***

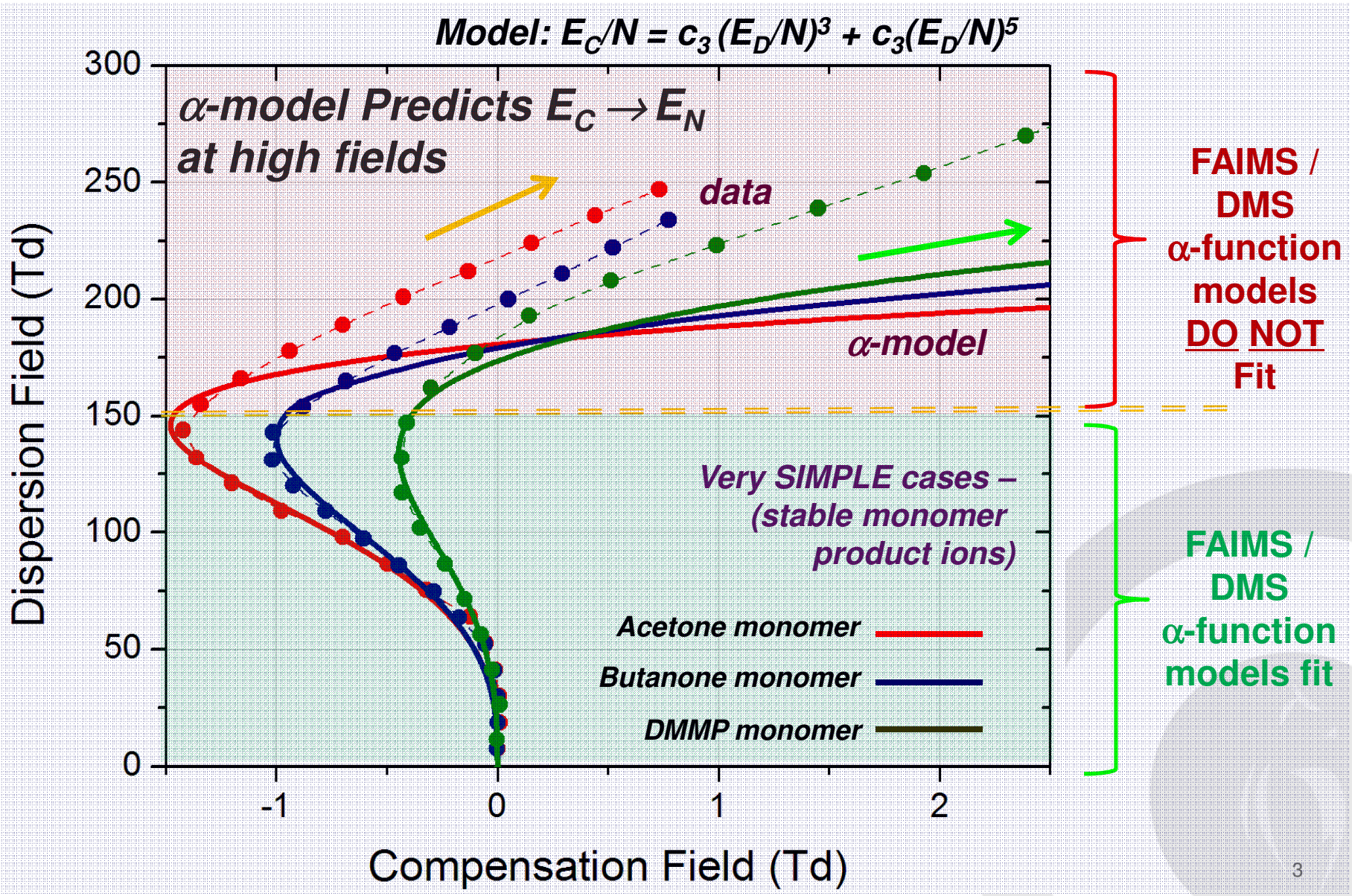
Classical model

~~$v_{D(h)} = K(E).E(\tau)$~~

$v_{D(l)} = K(0).E(t)$

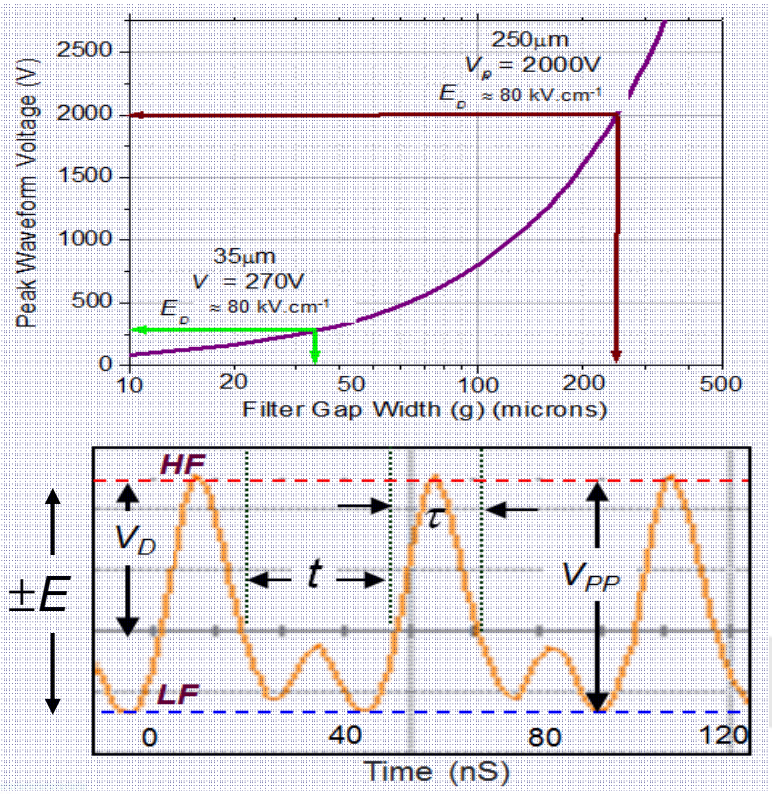
$K(E) / K(0) \approx 1 + \alpha_2 E^2 + \alpha_4 E^4 \ldots + \alpha_n E^{2n}$

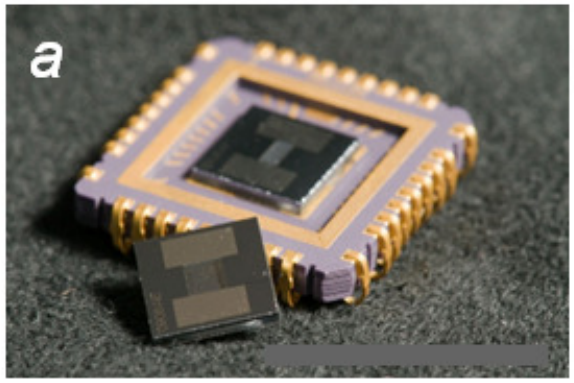
α-model breakdown

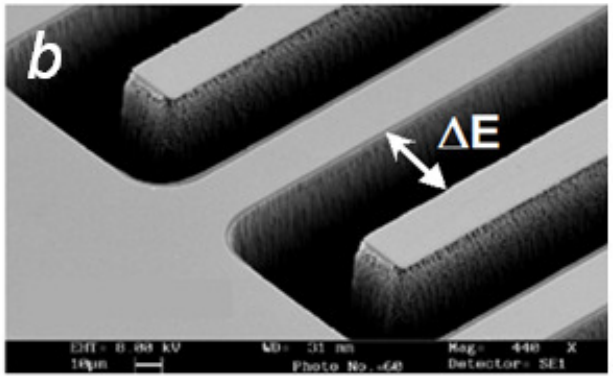


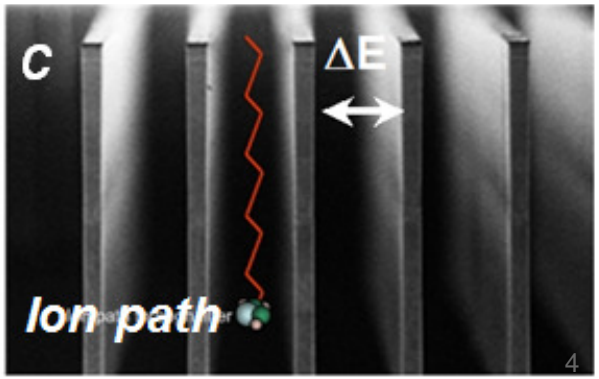
Micro-Design / High Voltage & High Frequency separation waveform

- Ion separator employs multiple *serpentine* arranged *micro-gap* spaced electrodes (*g* = **35µm** standard)
- The length (*l*) of the filter channel can be varied (**300µm** standard)
- Asymmetric Waveform frequency = **27MHz**
- Typical ion residence times of ~**30µs**
- Peak operational field is >**75kV.cm^{-1}** (**~320Td** at 1 atmosphere)



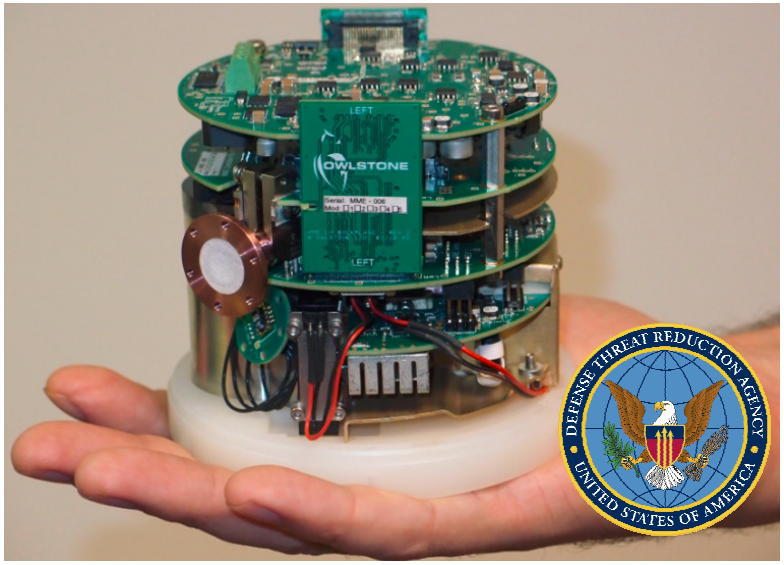




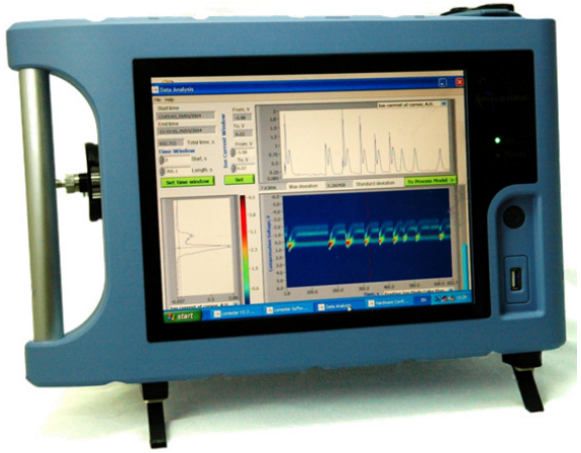


UH-FAIMS Platforms

MCD Static Chemical Monitor



LoneStar

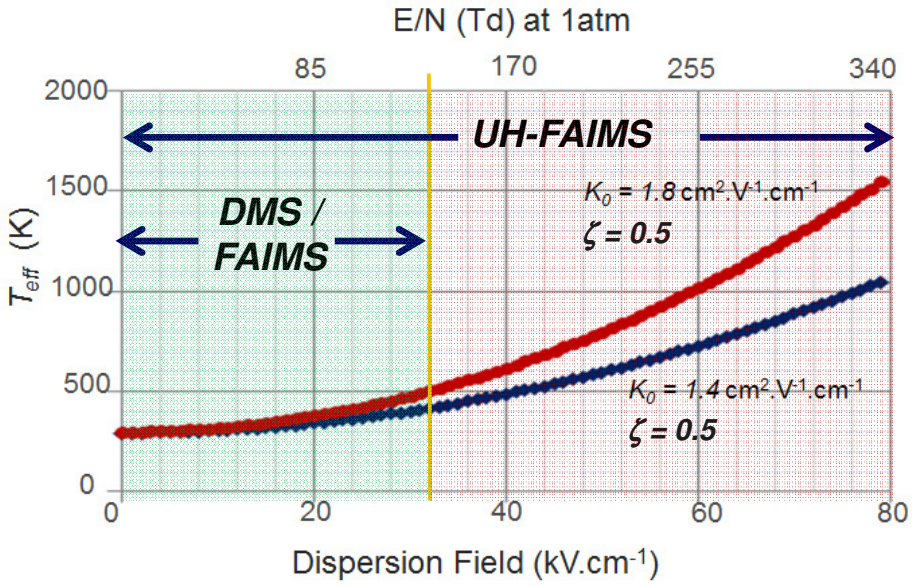


Electrospray UltraFAIMS-MS

Key Aspect relating Extreme Field operation
- *Effective Ion Temperature (T_{eff})*

$$T_{eff} = T + \zeta . M . K_{(E/N)}{}^{2} . (E_D/N)^2 / (3k_b)$$

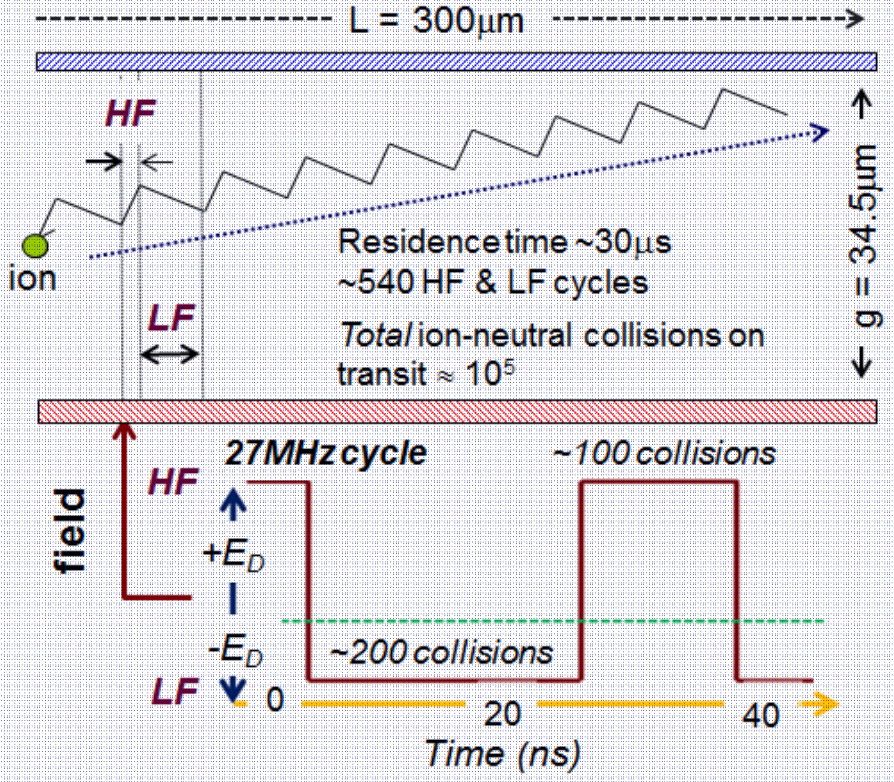
T	=	Drift gas temperature (K)
ζ	=	Energy transfer (collisional) efficiency factor
M	=	Av. MW of carrier gas
$K_{(E/N)}$	=	Field specific Ion Mobility ($m^2.V.s^{-1}$)
E_D/N	=	Field / number density ($V.m^2$)
k_b	=	Boltzmann constant ($J.K^{-1}$)



Features of use of High Field & High Frequency -

Ion-neutral collision frequency -

≈ **5GHz** at **1atm**



Features

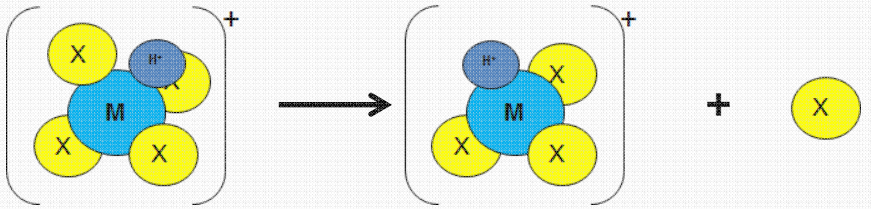
- Ultra-High Peak Field
  - = *much higher **"peak"** Effective Ion Temperatures*
- Low field not "negligible"
  - = *much higher **"average"** Effective Ion Temperatures*
- High Frequency
  - = *fewer ion-neutral **collisions** in **high** and **low** field portion of applied waveform*

Ultra-High Field Operation - **Impacts**

"*In filter*" ion transformations/ reactions…

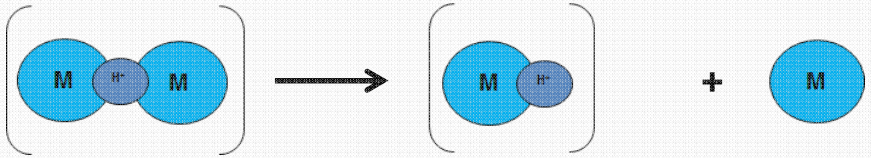
- ***Desolvation*** – loss of ion-dipole /ion-induced-dipole species

  $M(X_n)^{+/-} \rightarrow M(X_{n-1})^{+/-} + X$



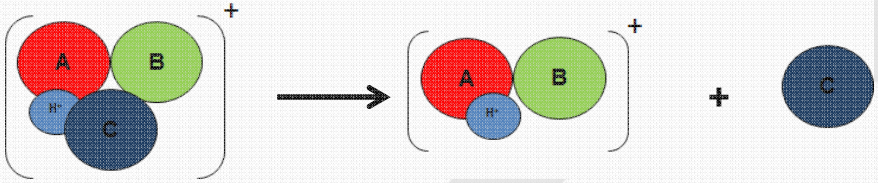
- ***Adduct dissociation*** (*e.g.*, ionic H bond cleavage)

  $(M_2H)^+ \rightarrow (MH)^+ + M$



- ***Fragmentation*** (covalent site)

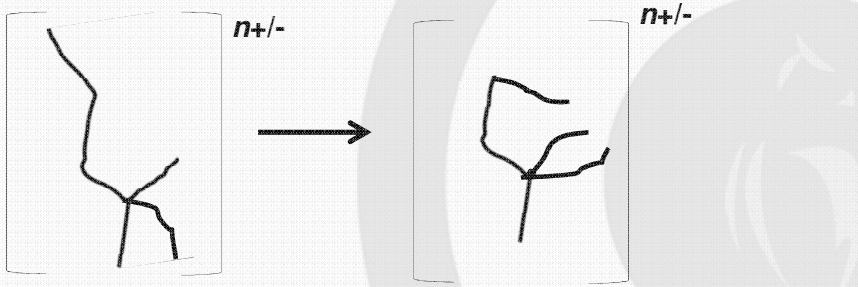
  $(ABC)^{+/-} \rightarrow (AB)^{+/-} + C$



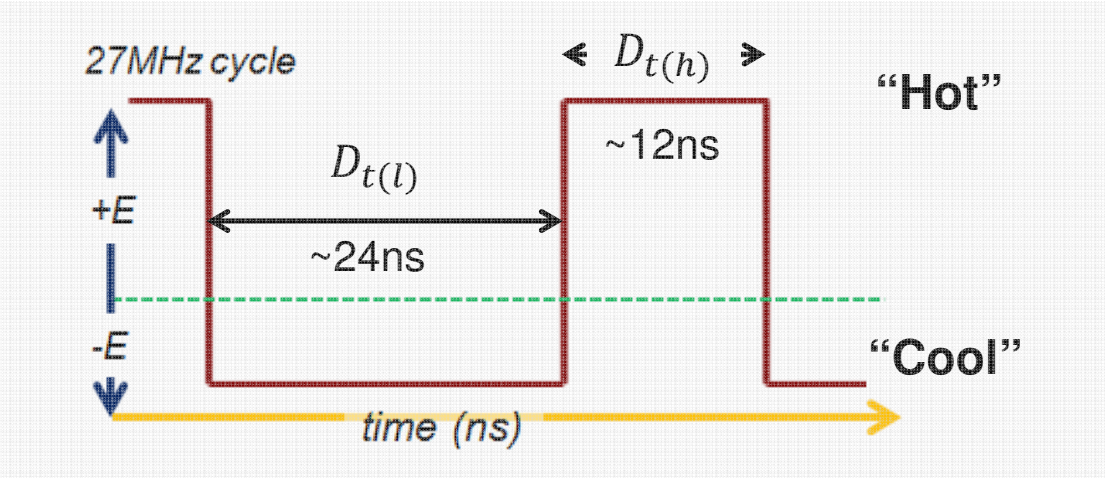
- ***Conformational*** (*geometric*), *e.g.*

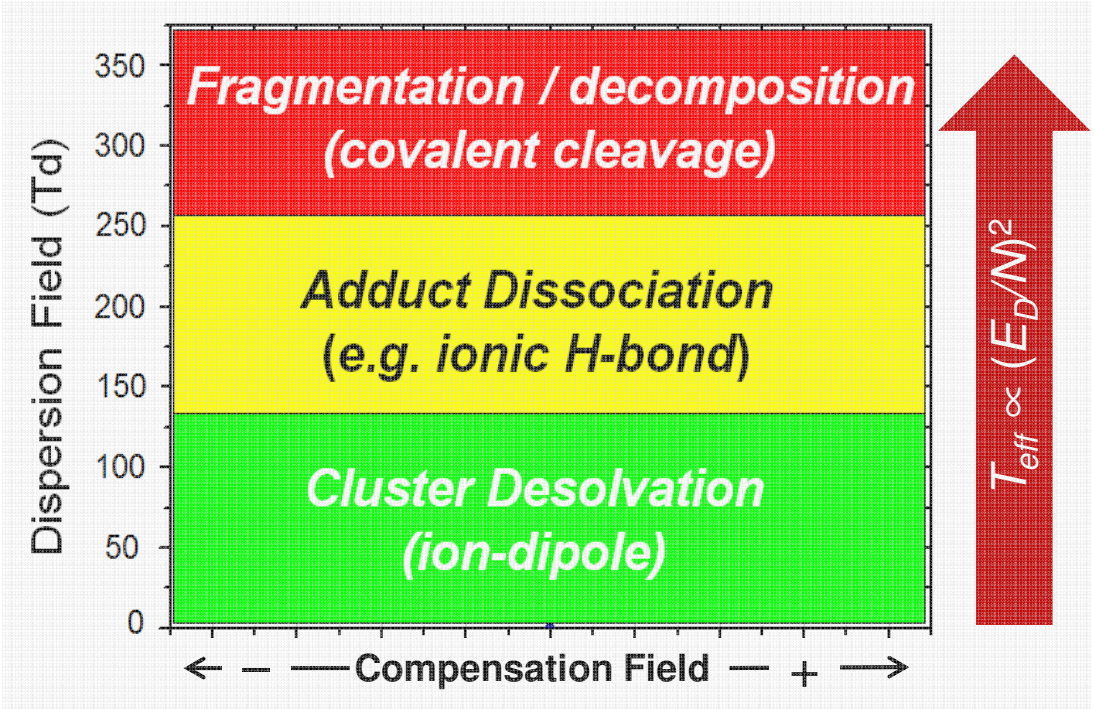
  Barrier to internal rotation

  Folding (high MW *multi-charged* molecular ions (peptides, proteins)



Ion dissociation processes





For hypothetical ion dissociation process -

$$MA^+ \xrightarrow{k} M^+ + A$$

$$E_A = \Delta H - RT$$

E_A = Association energy

ΔH = enthalpy of Association

$$k(T_{eff}) = A.\ exp - (E_A / R.T_{eff})$$

"In filter" Dissociation when -

$$1/k(T_{eff}) < \sum D_{t(h)}$$

Ion Transmission; model breakdown

Field Dependent Diffusion Losses

$$D_{II}\left(\frac{E_D}{N}\right) = D\left[1 + \frac{f.M.K_0{}^2 N_0{}^2 (E_D/N)^2}{3k_bT}\right]$$

$$D = \left[\frac{k_bTK_0N_0}{qN}\right]$$

From Einstein Relationship

M = Drift gas MW t_{res} *= ion residence time*

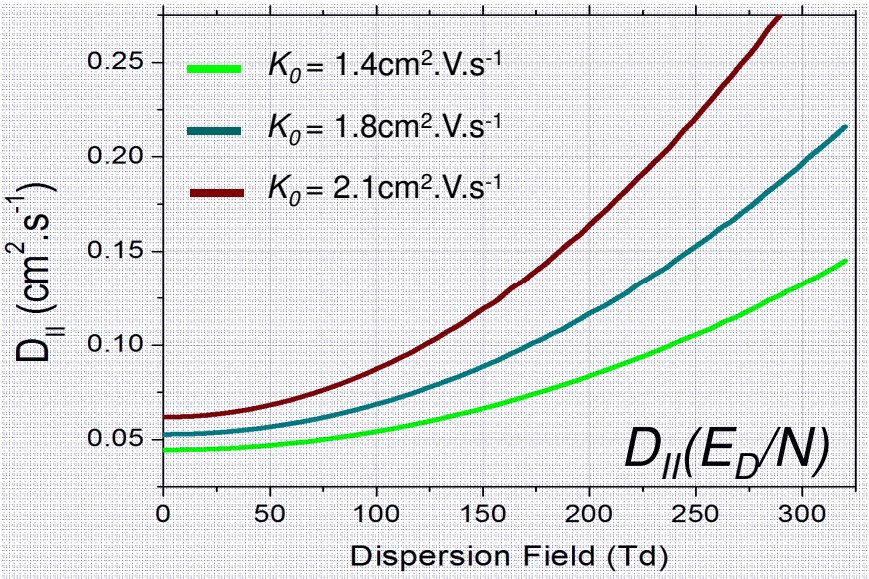
T = Drift gas temp. g_{eff} *= effective gap size*

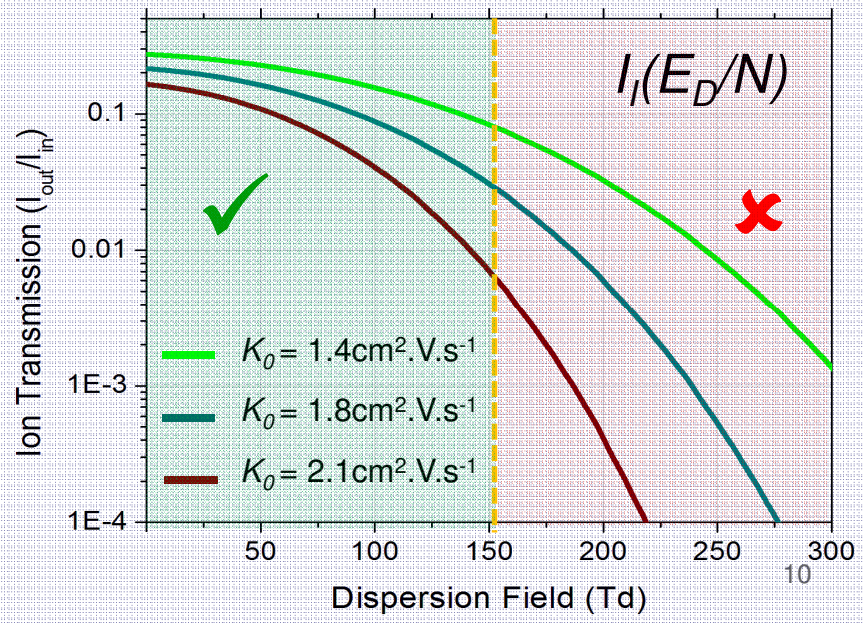
$f = \langle F_2 \rangle \times F_{II}$

(*molecular ion potential* x *waveform property*)

Transmission function -

$$I(E_D/N) = \exp\left[-t^2.D_{II}(E_D/N).\left(\frac{t_{res}}{g_{eff}\,2}\right)\right]$$





Ion Kinetics - *EXAMPLE; A SIMPLE CASE* (Dimer Dissociation)

Dimer → Monomer + Neutral

$M_2H^+ \rightarrow MH^+ + M$

Pseudo first order (monomers and neutral can't recombine at low field) -

$$r = -d[M_2H^+]/dt = k[M_2H^+]$$

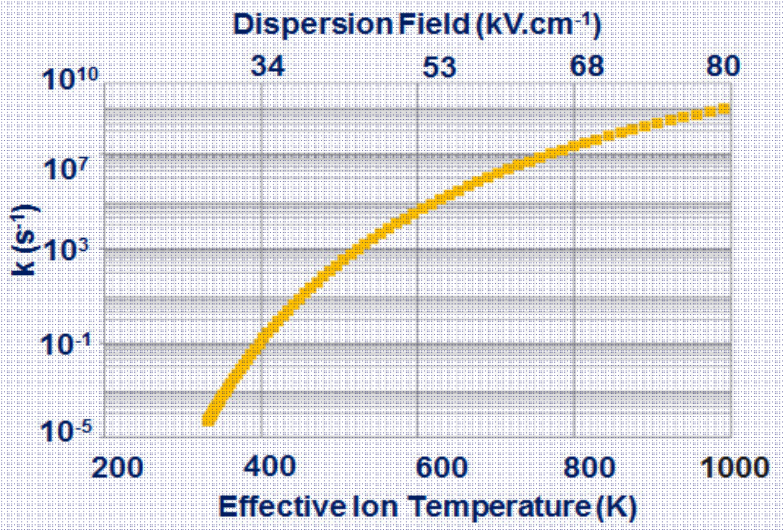
$$[M_2H^+]_t = [M_2H^+]_0 \exp -kt$$

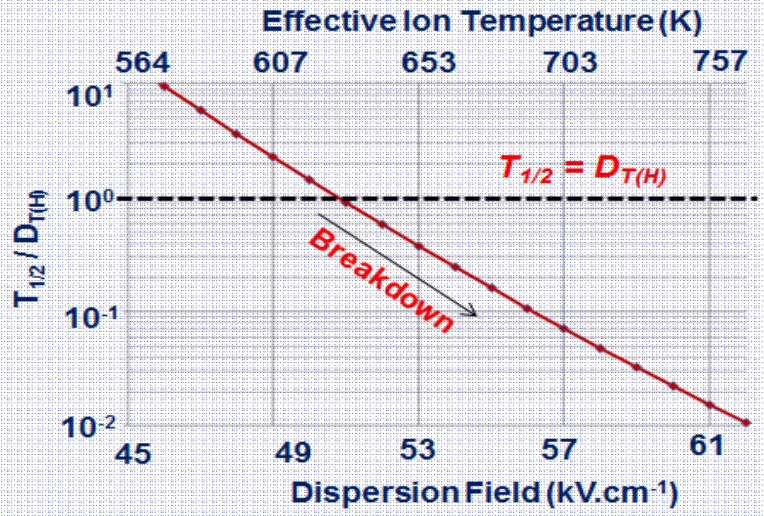
$$t_{1/2} = \ln 2 / k$$

$$k(T_{eff}) = A.\, exp - (E_A / R.T_{eff})$$

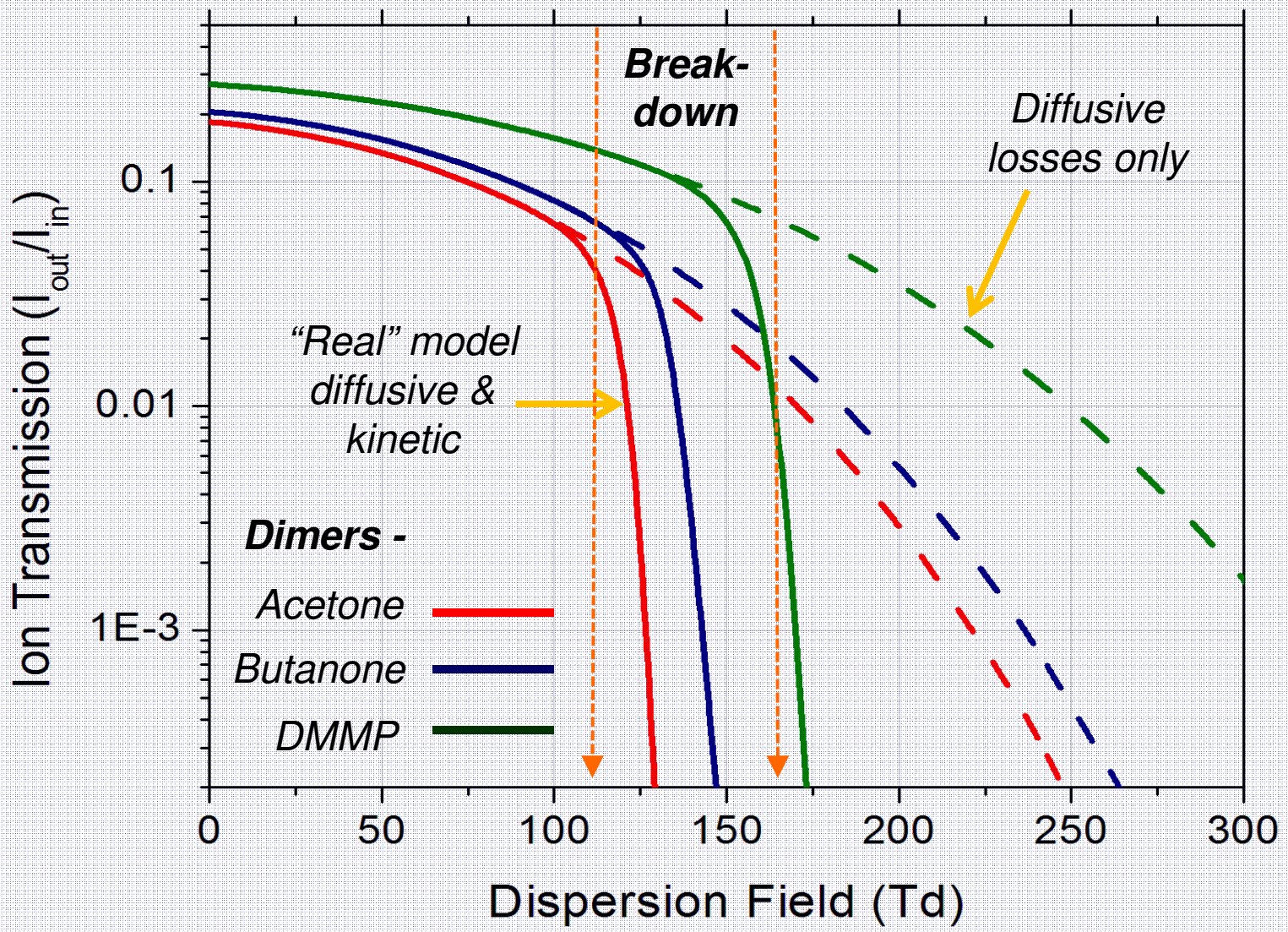
In Ion Separator

$$[M_2H^+]_t / [M_2H^+]_0 = \exp -k(T_{eff}).D_{\tau(h)}$$

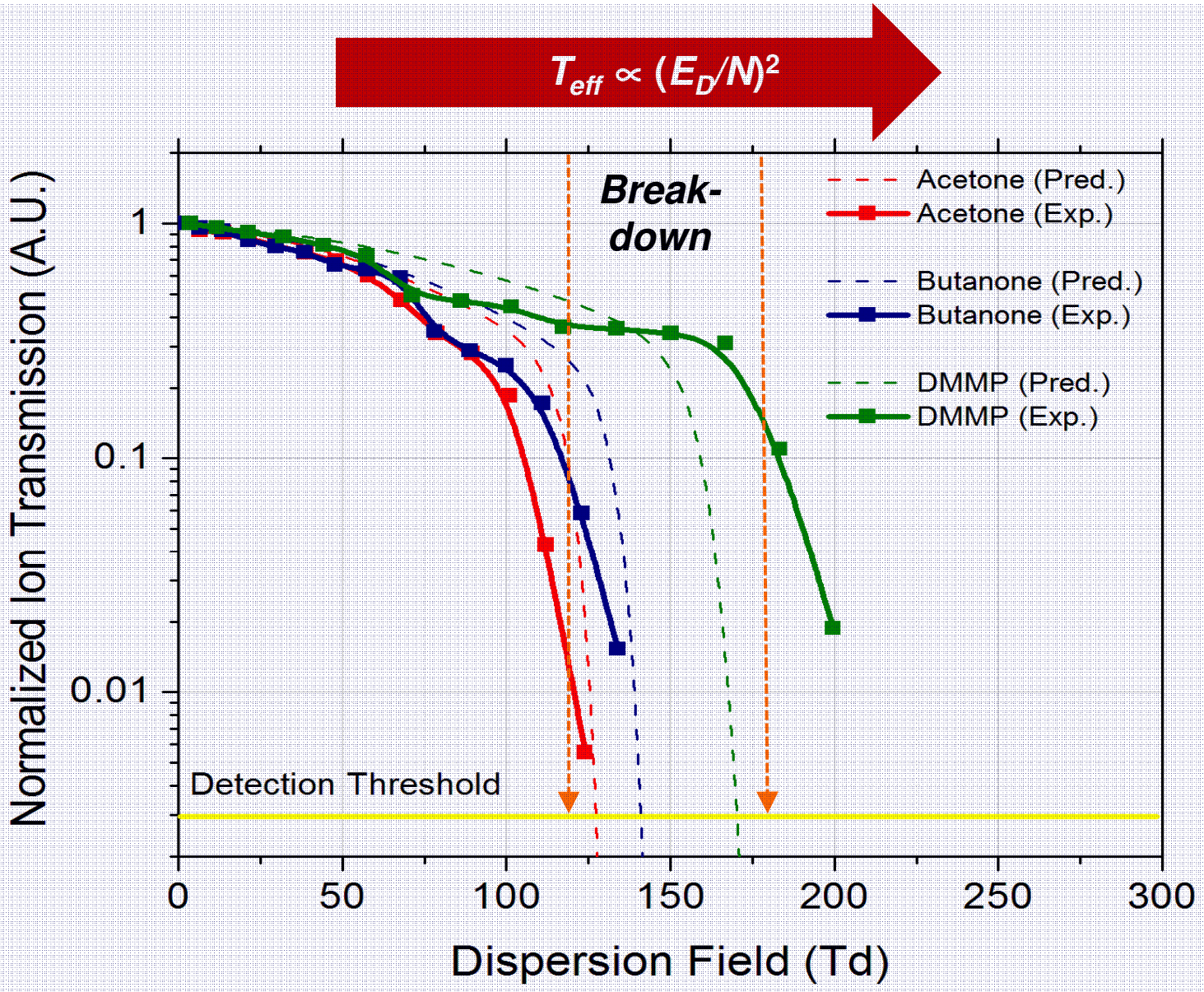




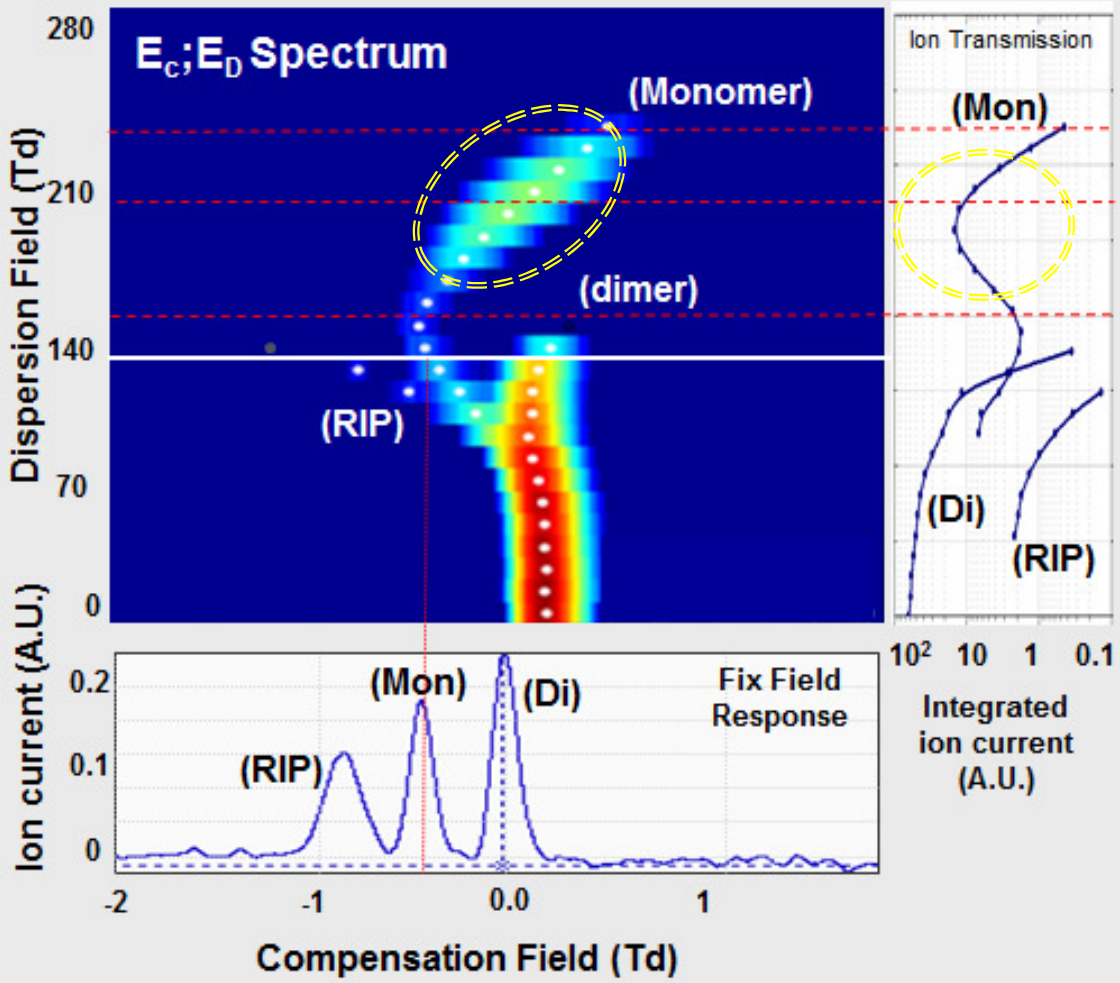
Kinetic “losses” dominate



Experiment *vs.* Theory



In filter monomer formation



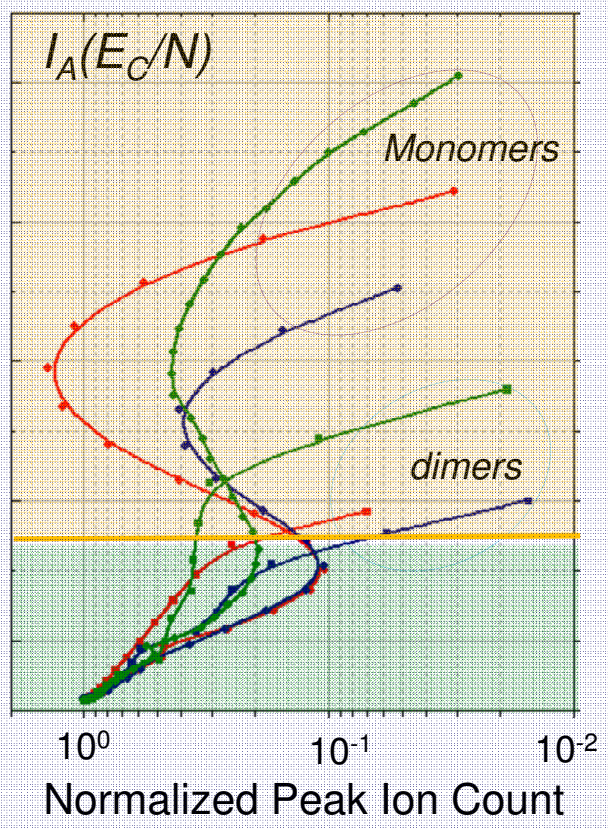
$$M_2H^+ \rightarrow MH^+ + M$$

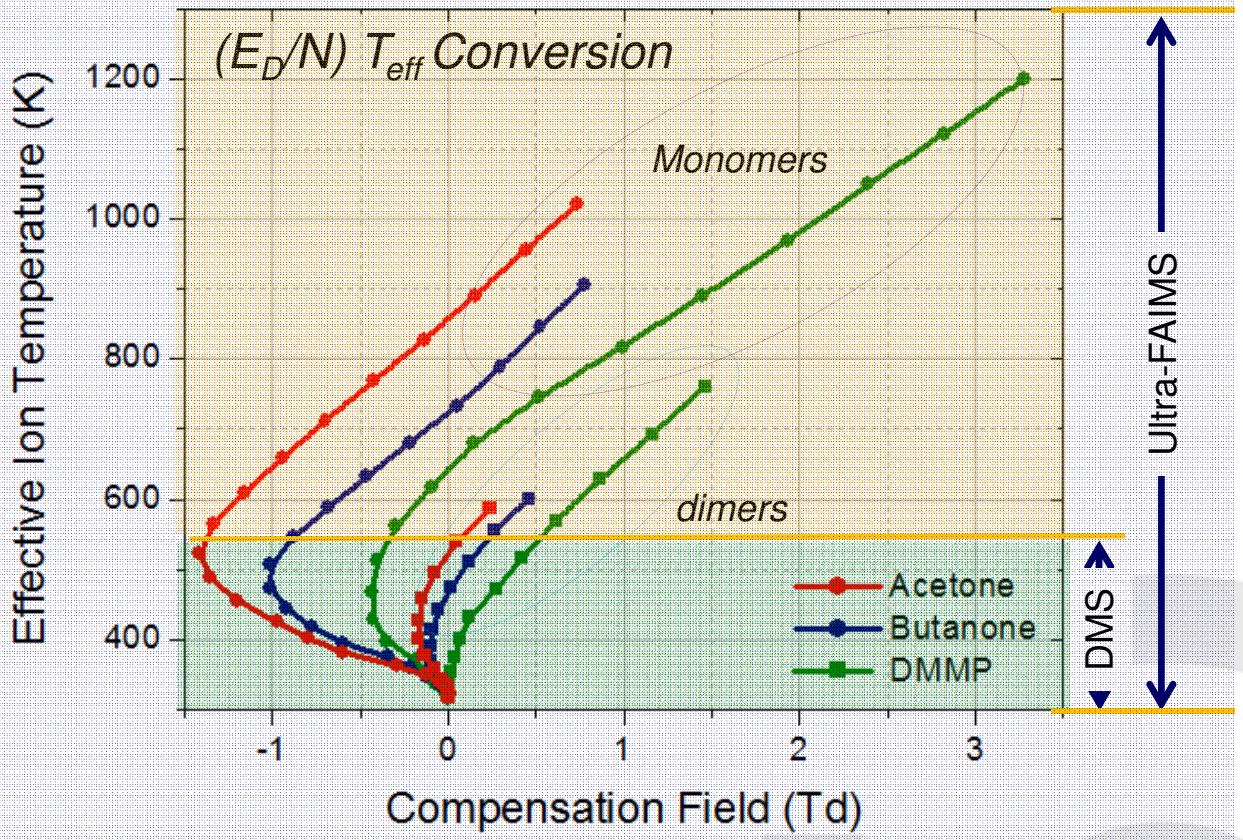
Dimer may be predominant at low Field since dimer formation is kinetically / thermodynamically favorable

But at higher fields one observes breakdown and dimer re-association cannot occur in the Ion-filter

Monomer “resurges”

Effective Ion Temperature; *a FAIMS vs. UH-FAIMS perspective*

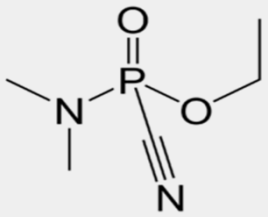


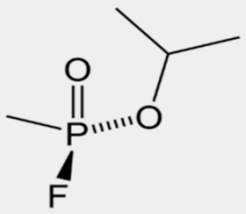


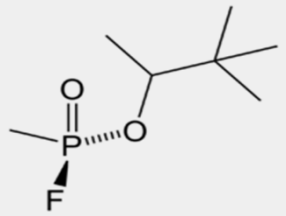
Linear scanning of E_D/N ?

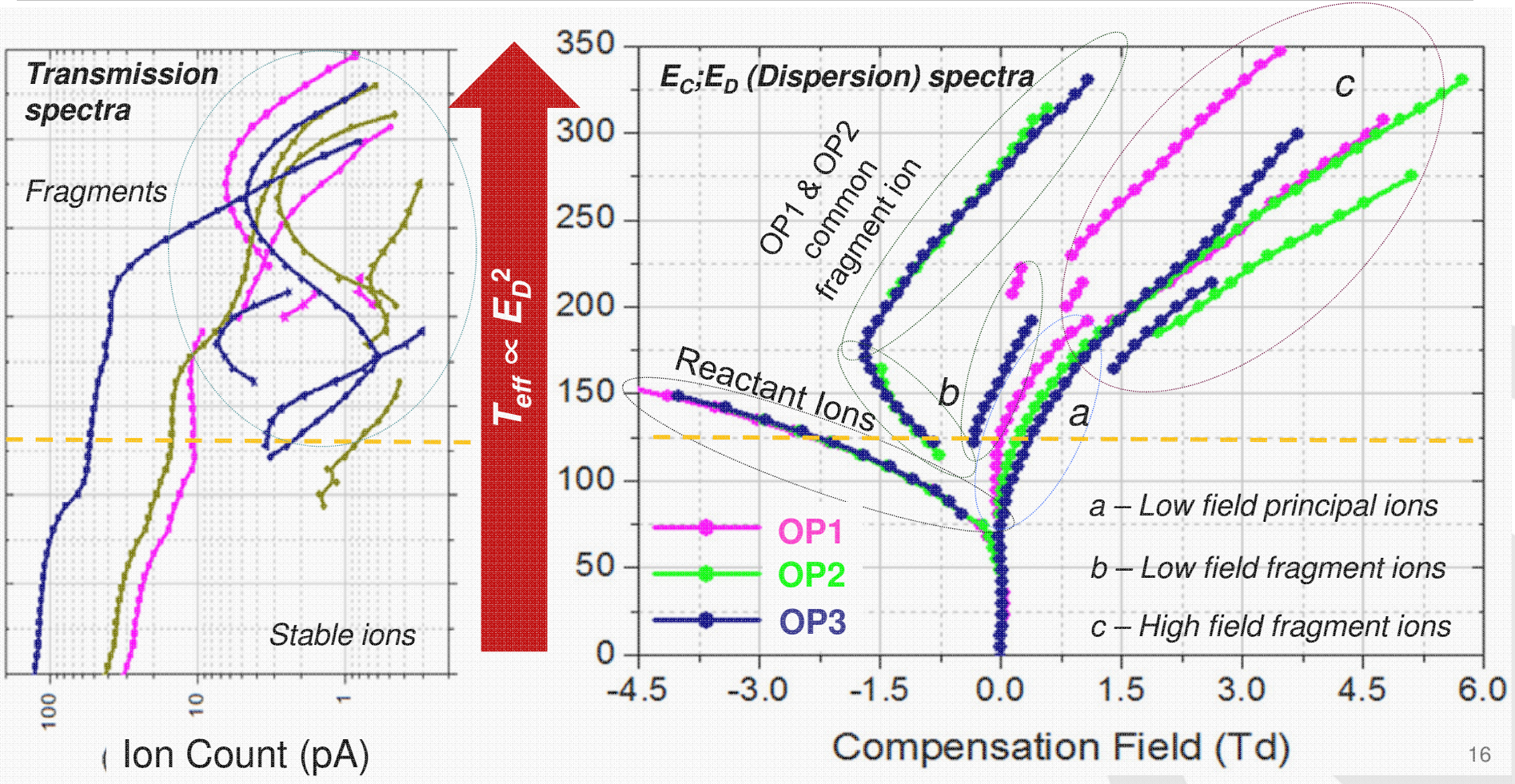
*Yes – need data through wide "effective ion temperature range" (**Low** & **High** Field)*

"Functional" molecules

OP1 

OP2 

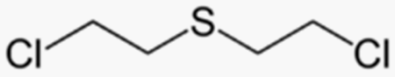
OP3 



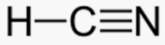
Negative Ions –

CICN

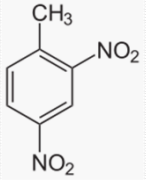
B(2-CES):



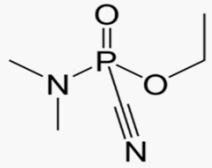
HCN

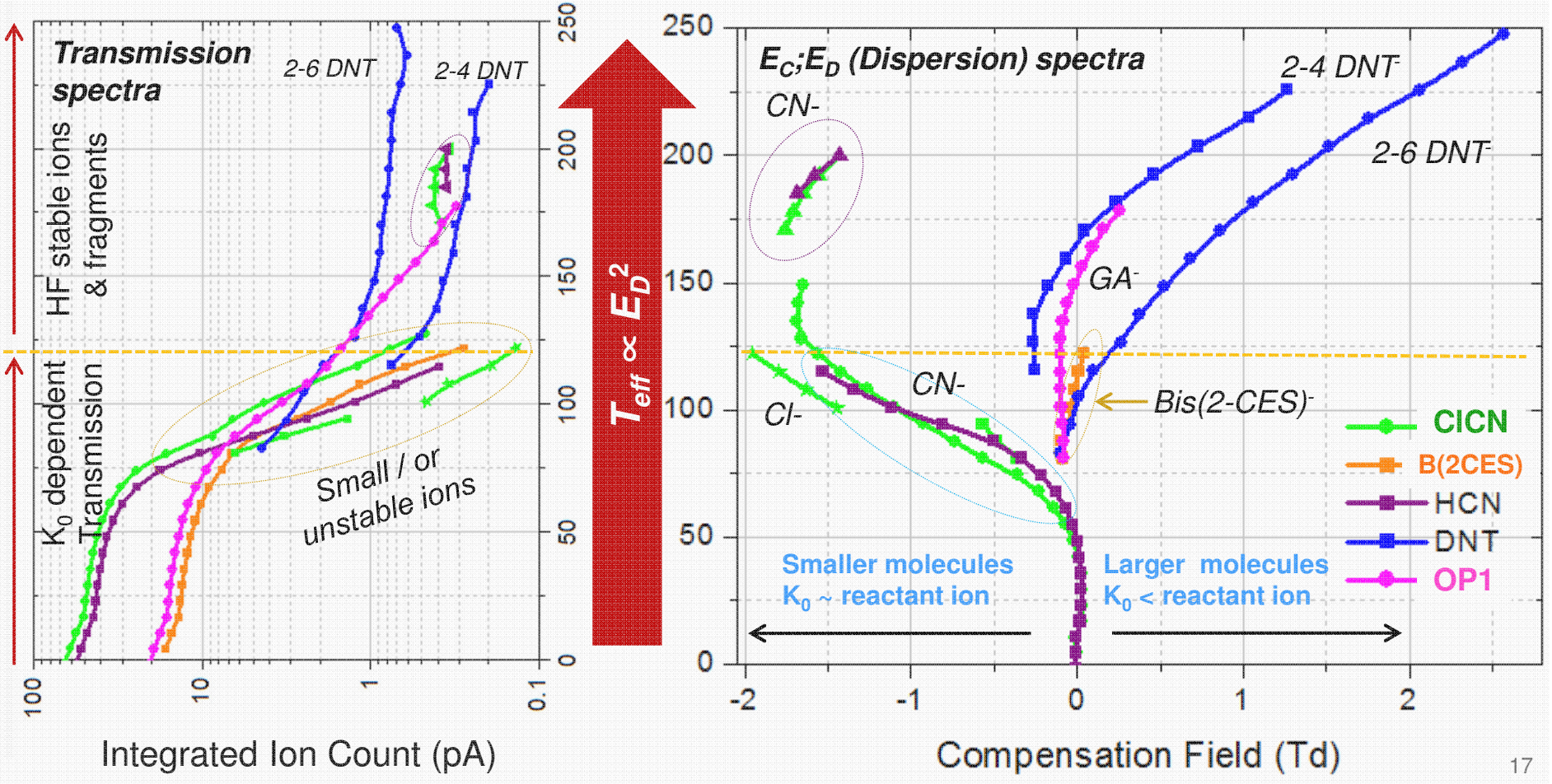


DNT



OP1





Mining the $E_C;E_D$ Spectrum…

Large amount of information generated and processed extremely rapidly (*second timescales*)

Gaussian parameters -

→ **Peak Width**

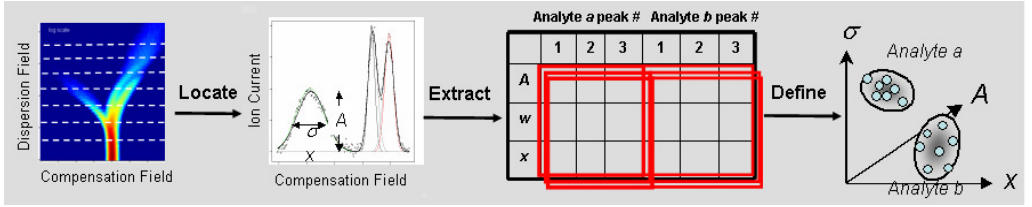
→ **Peak Area**

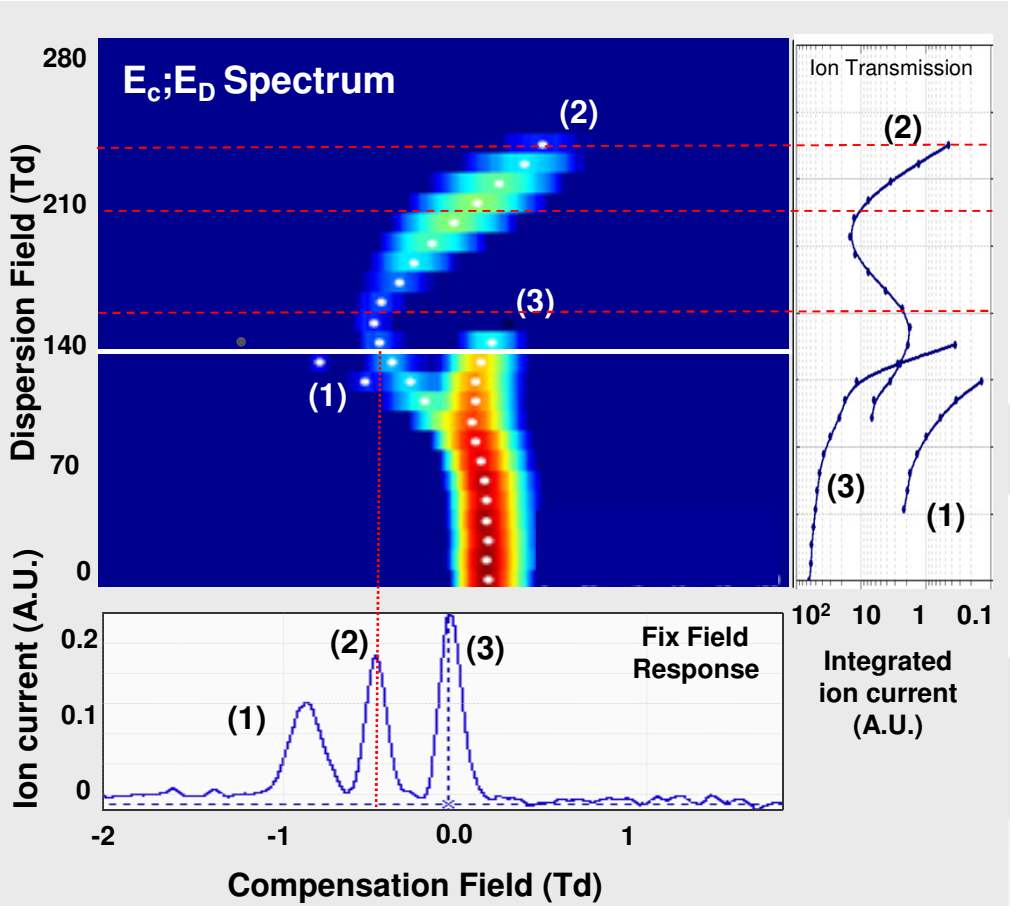
→ **Peak Location**

…….as a <u>function</u> of Dispersion Field

Key Information

Parameter	Information
Peak Width $W_{1/2}(E_D/N)$	Low field mobility Field specific Ion behavior
Ion Transmission $I_{A(}(E_D/N)$	Agent level Field specific Ion behavior (*e.g.* Ion cluster breakdown)
Peak location $E_C(E_D/N)$	Ion (agent) identity





Additional information; Peak width – $W_{1/2}(E_D/N)$

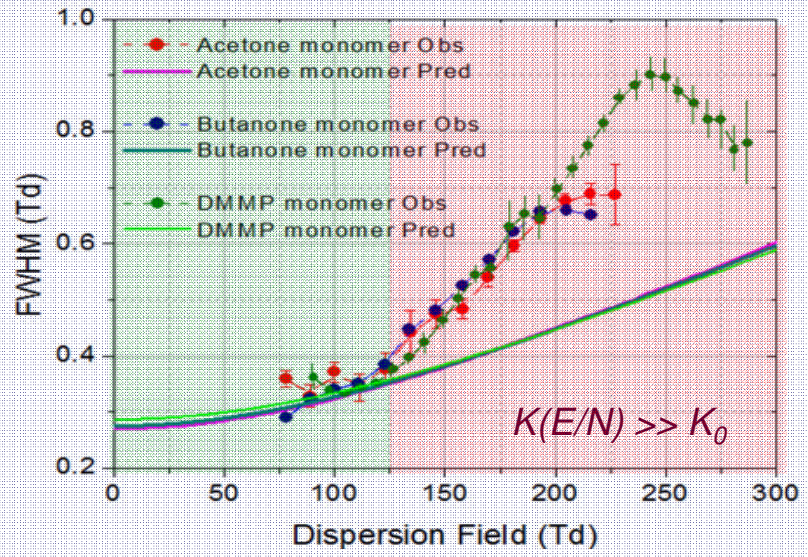
FWHM ($W_{1/2}$) -

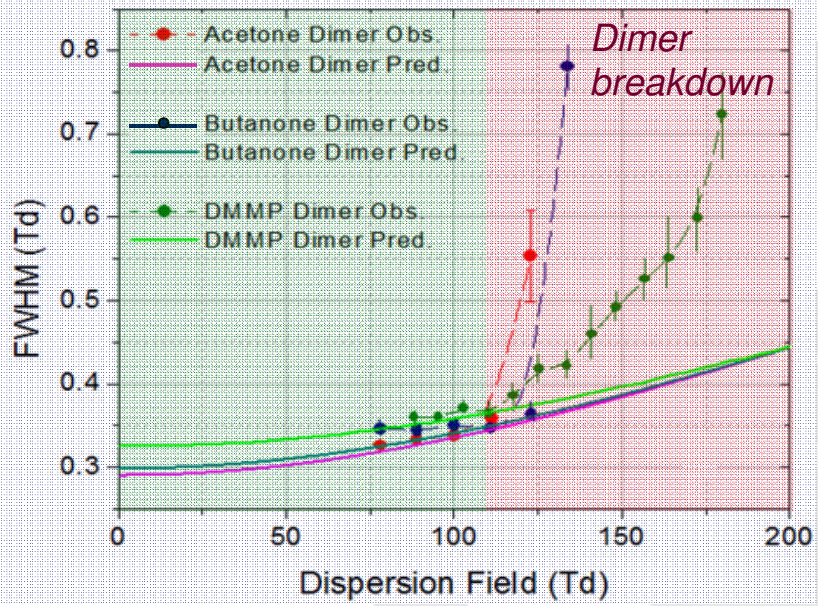
$$W_{1/2} = \left(\frac{4N}{K_0 N_0}\right)\left(\frac{D_{II}\, ln2}{t_{res}}\right)^{1/2}$$

At $E_D/N = 0$, $D_{II} = D$

$$D = \frac{k_b T K_0 N_0}{qN}$$

$$K_0 = \frac{16 N ln2 . k_b T}{N_0 . q t_{res} . {W_{1/2}}^2}$$





Ultra-High Fields - Summary

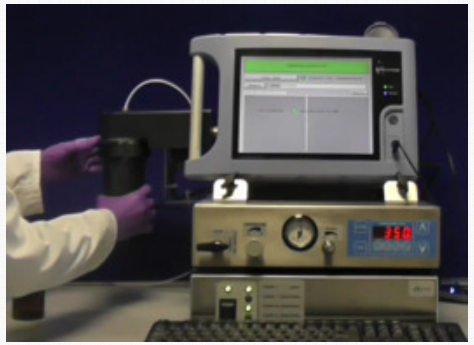
Differentiators	Enablers	Yields
Ultra high field operation (> 80kV.cm^{-1}), *high effective ion temp*.	Narrow separation electrode gaps (35μm) combined with RF-drivers	Data – *e.g.* ion kinetics (fragmentation at *high effective ion temp*.)
Very high frequency separation field (27MHz) – *pulse time scales on order of ion collision frequency*	State-of-the-Art high field drivers combined with narrow, precision engineered electrode gaps (35μm)	Separation not dependant solely on conventional ion cluster / de-cluster model – *additional information*
Very short ion residence time (~30μS)	Short length (300μm) ion separation channels	Fast separation – E_c;E_D scans on *few second* timescale
Atmospheric pressure operation	Ultra high fields & short separation Channels	Extreme Sensitivity - ($ppb_{(v)}$)

Applications

Real time gas and vapor detection –

- VOCs, toxic gases / vapors
- Oil & Gas
- Food & Beverage
- Head space sampling

Fast response combined with extreme sensitivity



LC-*Ultra*FAIMS MS

- Pharma
- Proteomics
- Metabolomics

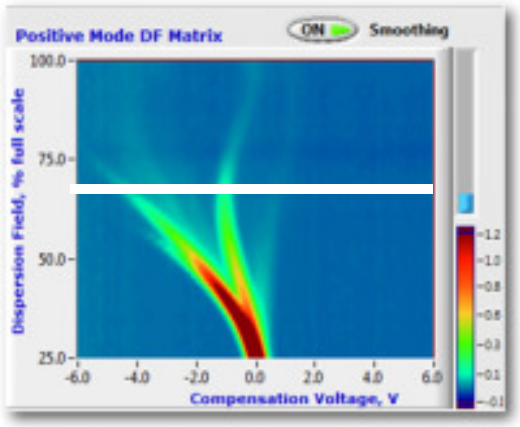
Enhanced selectivity

Faster separations (reduced chromatographic time)

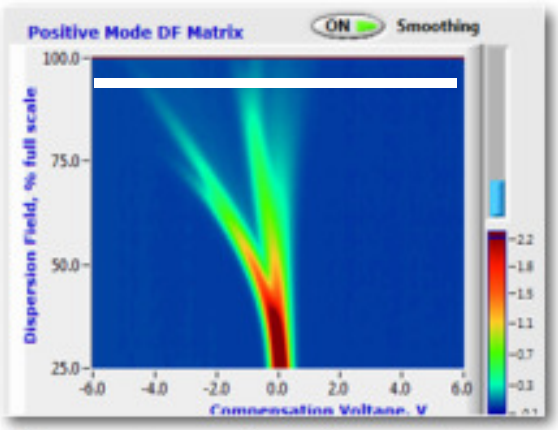
MS sensitivity enhancement

Food, beverage and Pharma QC – direct headspace sampling (complex matrices)

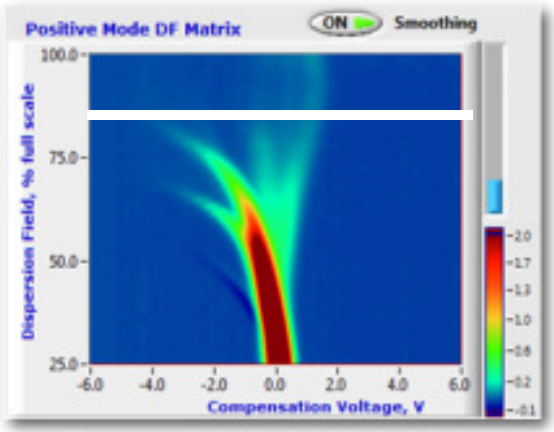
*Tune system to the separation "**Sweet Spot**"*



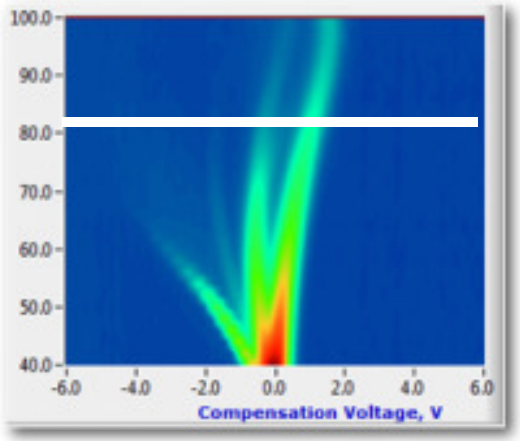
Biogenic amines in milk



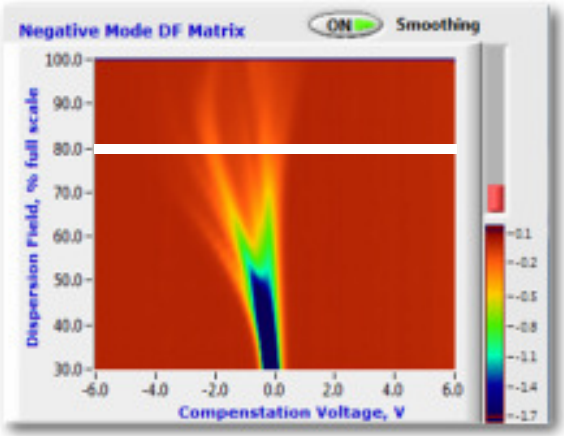
10ppm trace cleaning product



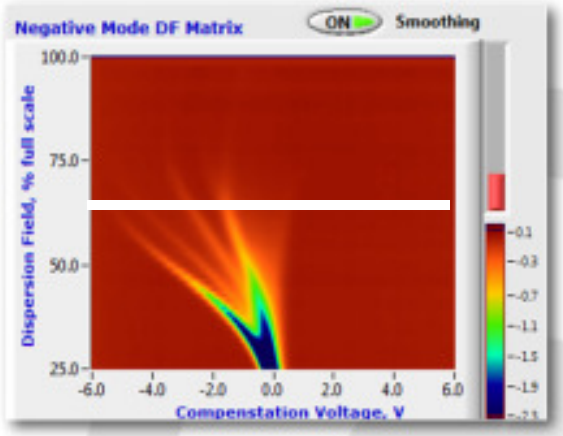
Pharma solvent mixture



Chloroform

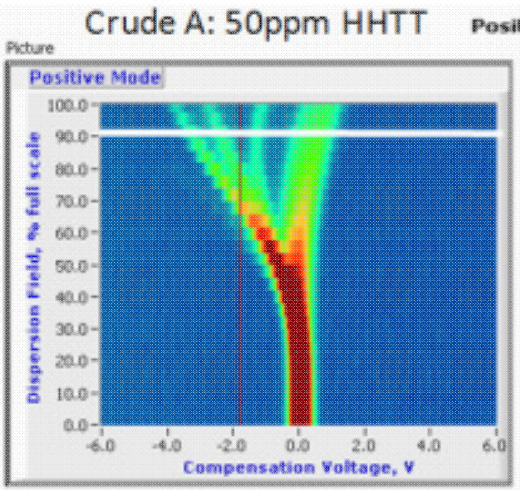


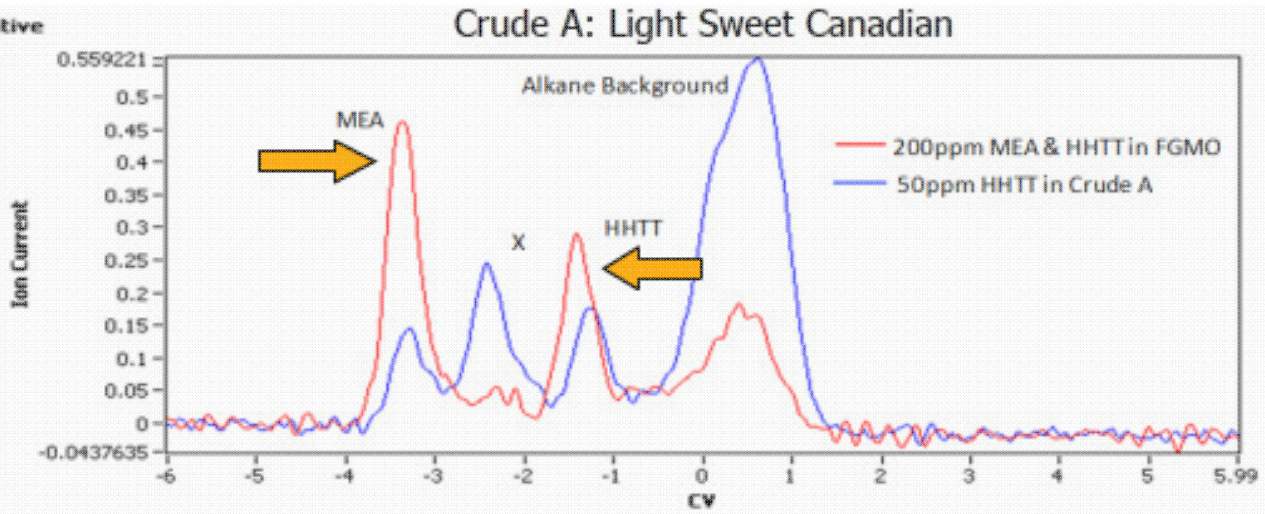
Sulphides, acids, diaceytl in beer

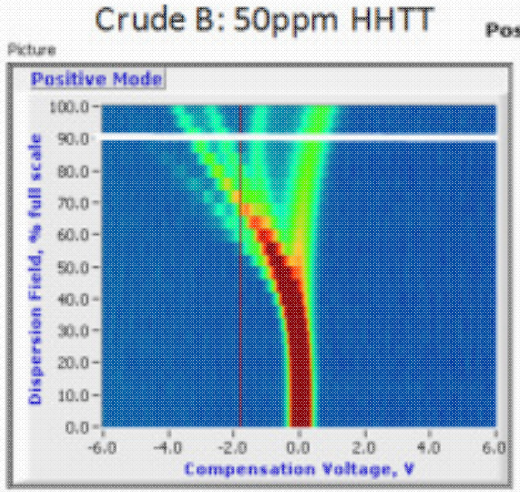


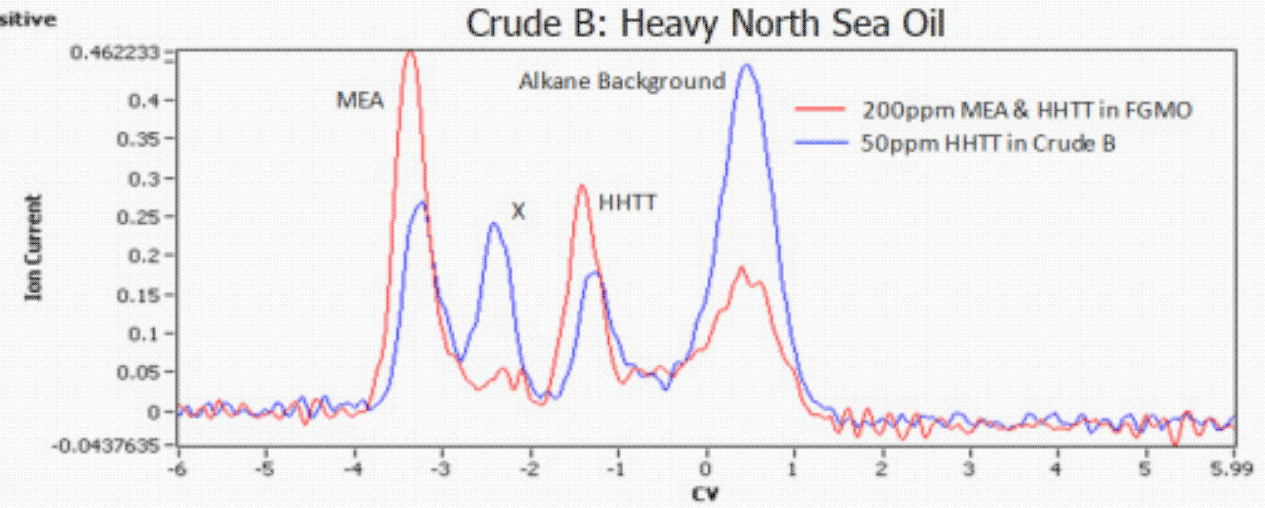
Halogenated organics & lactic acid

Direct headspace analysis of Crude Oil

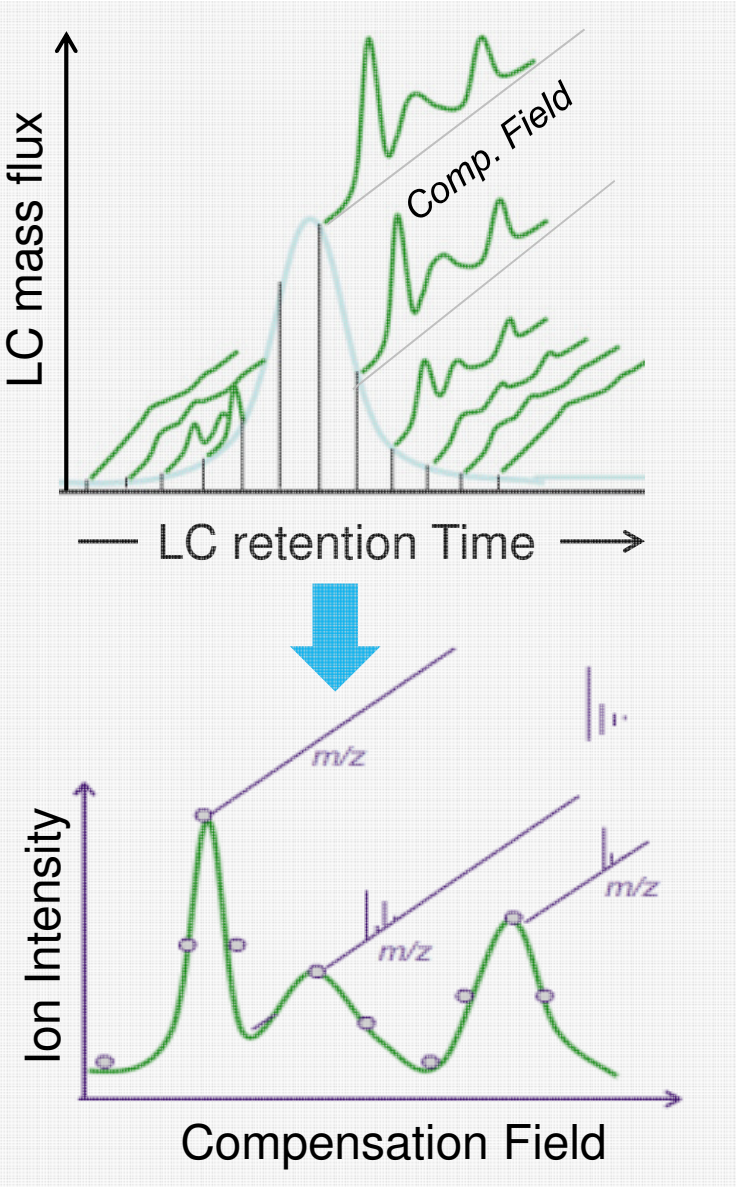




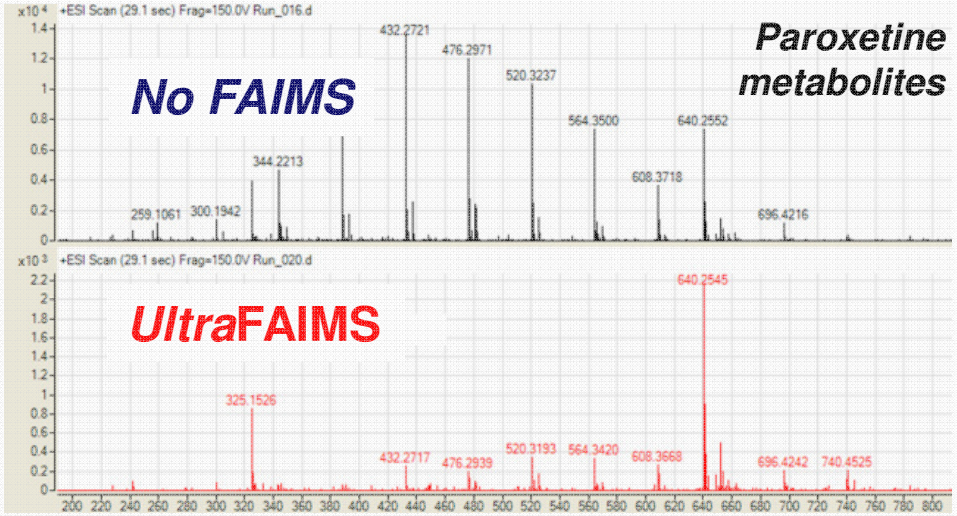




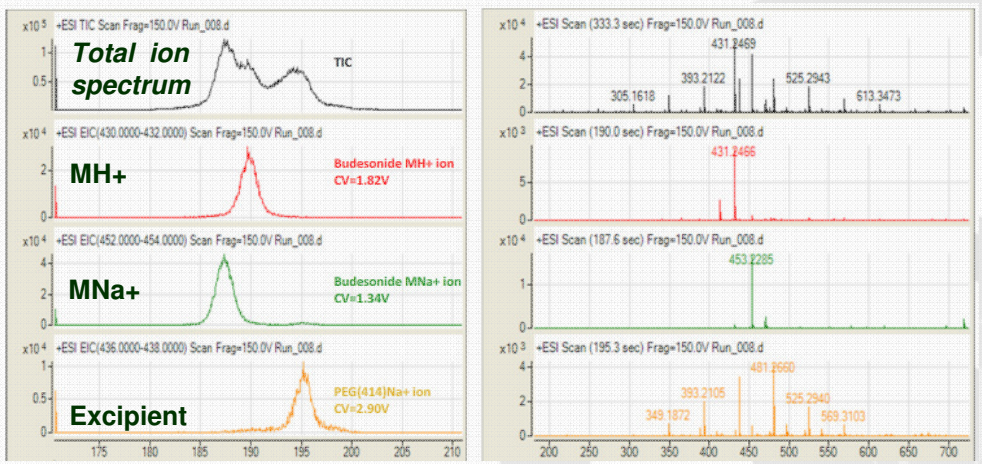
(LC)-*ultra*FAIMS-Electrospray-MS



e.g. Metabolite separation



Budesonide assay (without LC)



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