AccuTOF DART : a new technology for fast screening and characterization

Int. Symposium HPTLC

Berlin, October 11th 2006.

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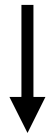
“AccuTOF” ?

- **Accu**rate **T**ime-**o**f-**F**light Mass Spectrometer



- What is “Accurate”?
  - Accurate mass
    - **Exact mass measurement**
  - Accurate ion intensity
    - **Wide dynamic range**

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Feature (1)

- Easy operation for exact mass
  - One known ion is enough for internal reference
- High sensitivity
  - An order of magnitude of higher sensitivity in spectrum measurement in comparison with conventional sector MS and QMS
- It is possible to obtain exact masses of trace components
  - TOF MS is always running with high mass resolution
  - Not necessary to trade off resolution and sensitivity

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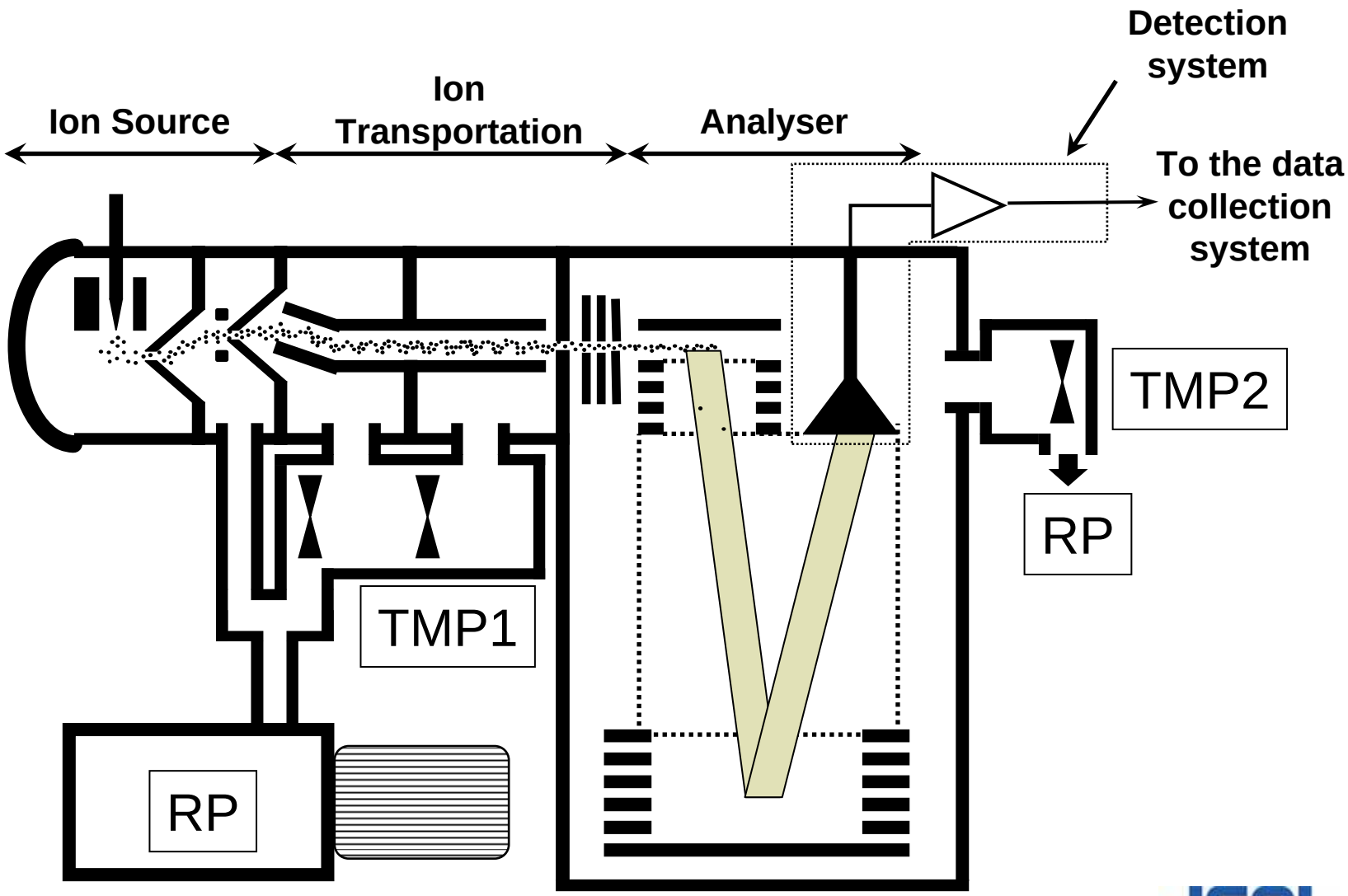
Feature (2)

- Quantitative analysis
  - Wide dynamic range comparable to sector MS and QMS ⇒ **Continuous Averager**
  - Possible to get good selectivity comparable to high-resolution SIM analysis by sector MS
- In LC-MS version a new orthogonal ESI ion source was developped with
  - Excellent durability
  - Various optional ion sources:

    APCI, nanoESI, ***DART***, MALDI,etc.

JMS-T100LC “AccuTOF”



DART on AccuTOF

DART

Feature of TOF MS

- There is no upper limit in the measured mass range in principle.
- TOF can a full-range mass spectrum in a very short time(<1ms).
- High ion transmission results in very high sensitivity .

Specifications

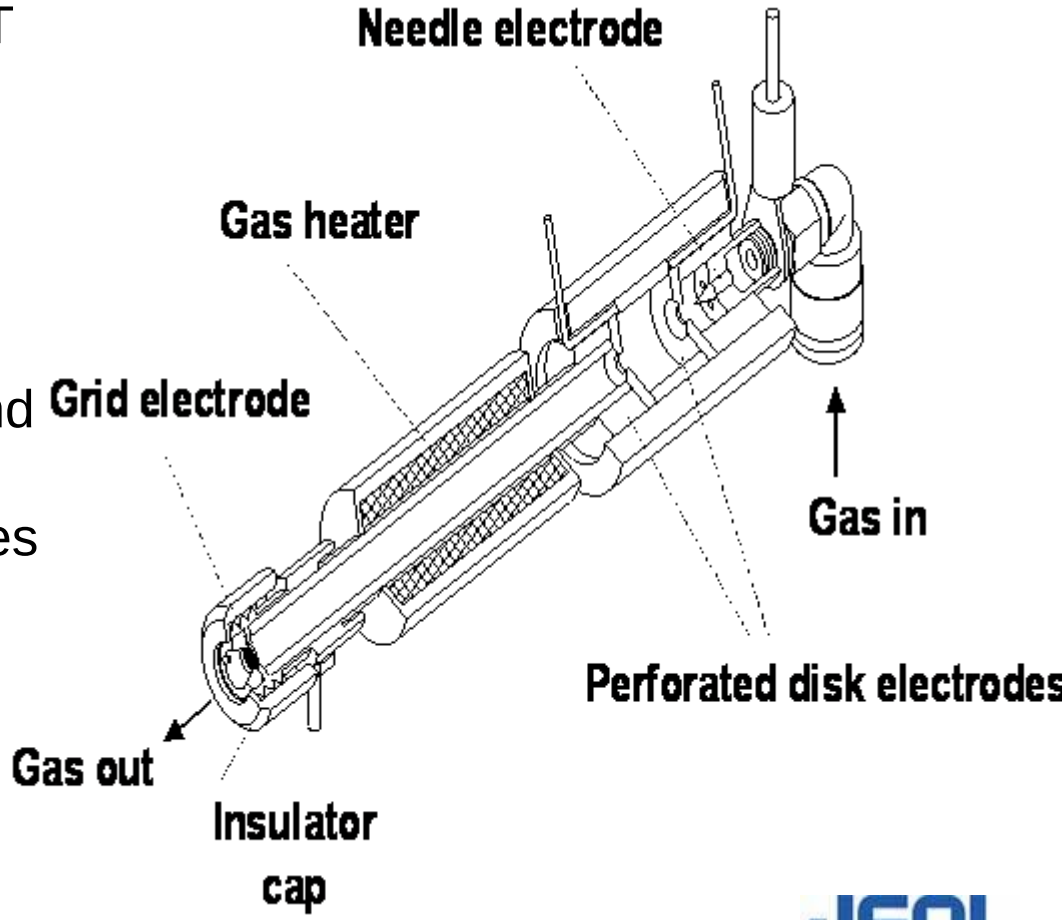
- Mass resolution： > 6,000
  - FWHM、Reserpine m/z 609
- Sensitivity： Reserpine 10pg S/N>10
  - LC-ESI [Flow rate: 0.2mL/min]
  - Mass chromatogram of m/z 609 RMS
- Mass accuracy： < 2ppm RMS
- Dynamic Range： > 10^5 (10 pg - 100 ng)

What is DART?

- DART is a new non-contact surface sampling technique for mass spectrometry or ion mobility spectrometry at atmospheric pressures.
- DART can be used to analyze gases, liquid, solids and materials on surfaces.
- Developed by J. Laramee and R. Cody at JEOL USA, Inc.

DART Schematic

- Gas flows through DART
- Electrical discharge creates a plasma
- Lenses remove charged particles
- Grid prevents ion-ion recombination at exit, and other functions
- No exposed high voltages
- Operated at ambient pressure in open air



Context of DART as an Ion Source

- Does not require reduced-pressure operation
- Operates in open air: no exposed high voltages or laser beams
- Analyte not exposed to electrical discharge
- Gas, liquid, or solid-phase samples
- Direct analysis of materials on surfaces
- Can ionize both polar and nonpolar materials
- Very low vapor pressure analytes

Not a separation technique

- Rely on high resolution
- Exact masses / elemental compositions
- Fragmentation

Significance of DART™

- Like “direct probe” at atmospheric pressure
- Fast instantaneous response
- Non-contact surface sampling and identification
- No solvents & no waste
- Non-volatile chemicals can now be sampled
  - RDX (vapor pressure $<10^{-15}$ torr), HMX
  - Cocaine on currency
  - GHB sodium salt
  - VX, EA2192

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Significance of AccuTOF: High-resolution MS detector

- All elemental composition assignments shown in this presentation were confirmed by exact mass measurements
- This allows us to discriminate between analyte and interferences
- Example: TNT $M^{+\cdot}$ ($C_7H_5N_3O_6$)= 227.0178
  Myristic acid $[M-H]^-$ ($C_{14}H_{27}O_2$) = 227.2011
- Fragmentation can be controlled to provide specificity

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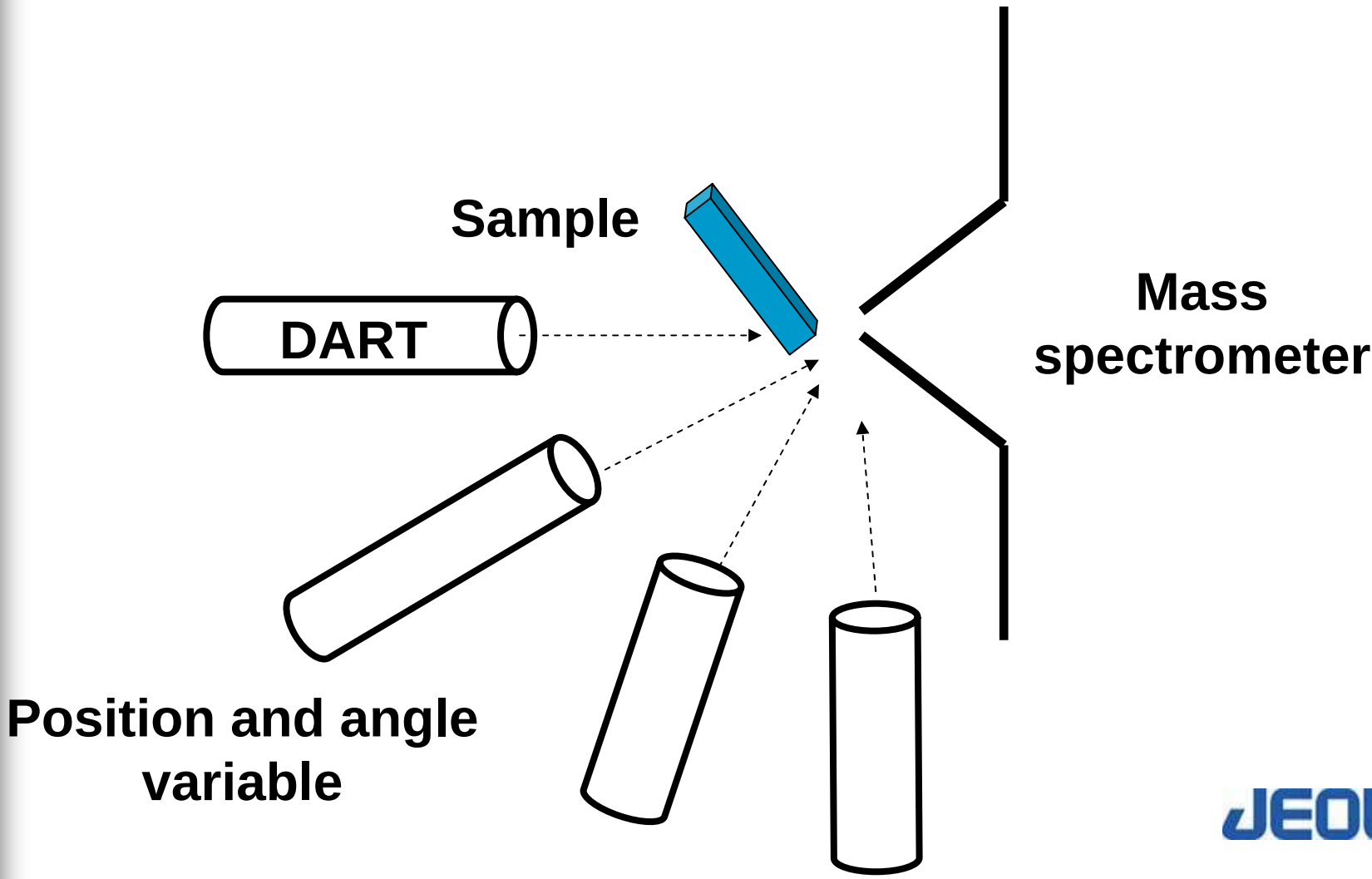
DART versus Mass Spectrometer Sampling Orifice



Operating Principle

- Excited-state atoms or molecules interact with sample and atmosphere
- Several modes of operation possible depending on carrier gas, polarity, addition of dopants, etc.

Proton Transfer

$$He(2^3S) + H_2O \rightarrow H_2O^{+\bullet} + He(1^1S) + electron$$

$$H_2O^{+\bullet} + H_2O \rightarrow H_3O^+ + OH^\bullet$$

$$H_3O^+ + nH_2O \rightarrow [(H_2O)_nH]^+$$

$$[(H_2O)_nH]^+ + M \rightarrow MH^+ + nH_2O$$

- Metastable atoms react with atmospheric water to produce ionized water clusters
- Dominant reaction mechanism when helium carrier used: He(2^3S) energy = 19.8 eV
- Huge reaction cross section: 100 A^2

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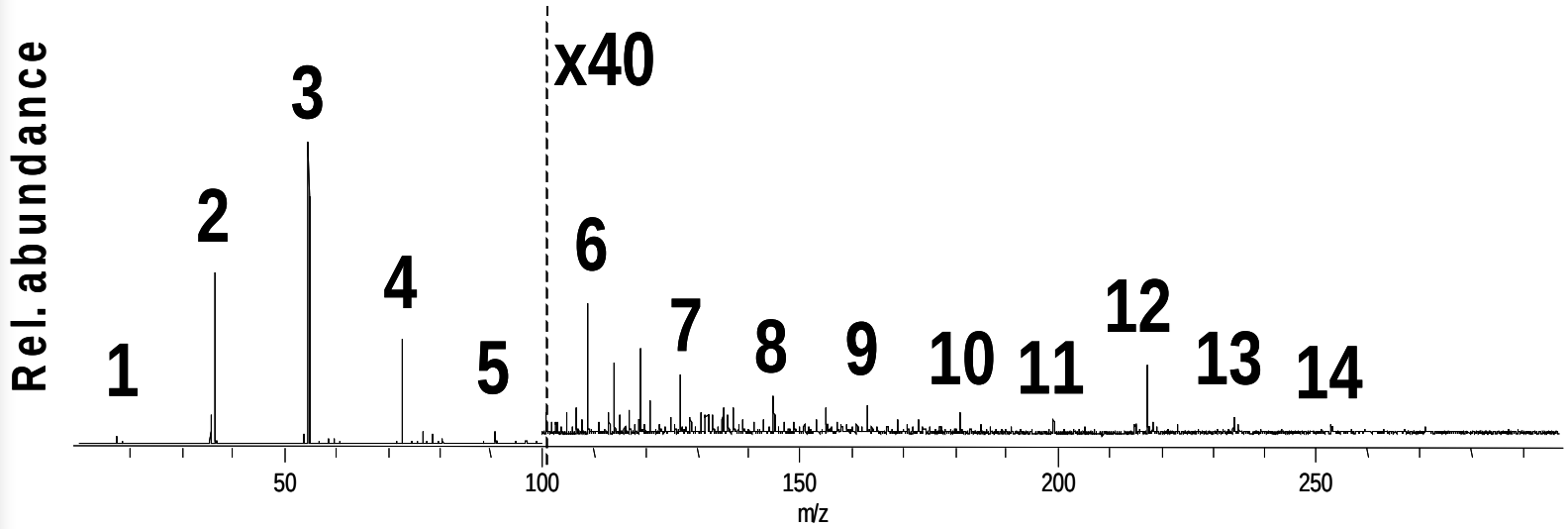
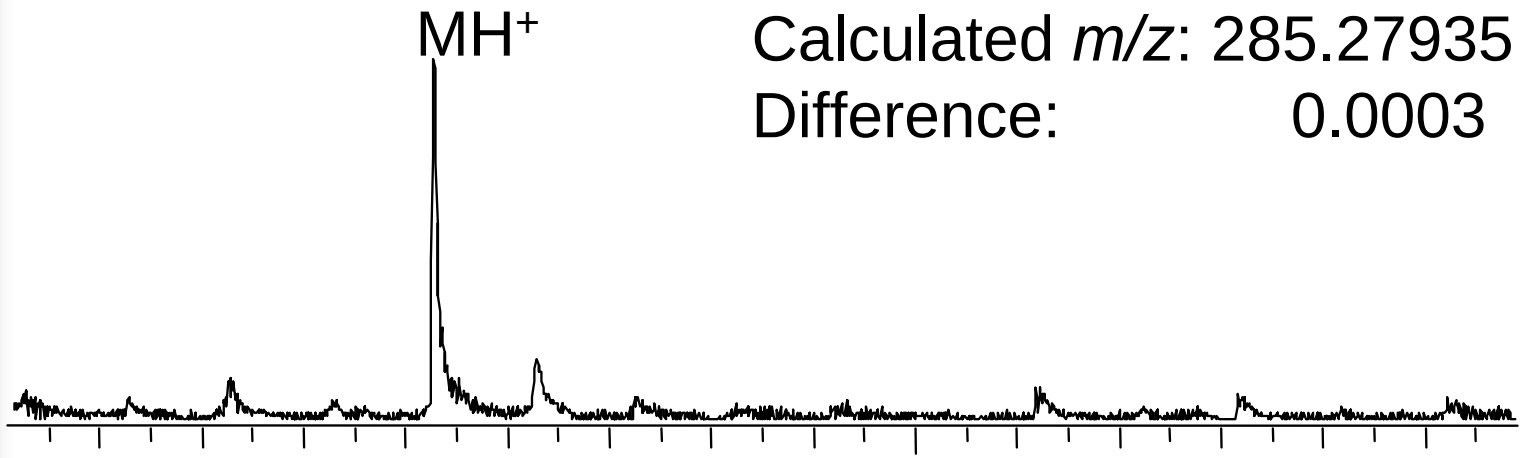
Ionized Water Clusters $[(H_2O)_nH]^+$ Produced by DART (He carrier) in Room Air



Sensitivity for a “difficult” compound: Ethyl palmitate (2 pg applied to glass rod)



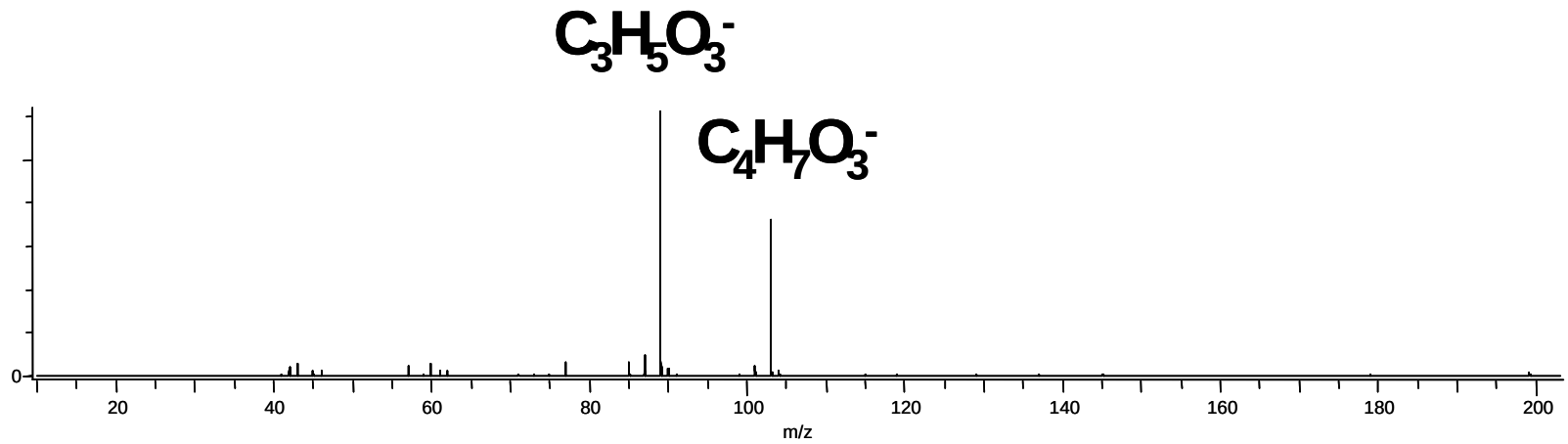
Measured *m/z*: 285.27995
Calculated *m/z*: 285.27935
Difference: 0.0003

Fatty acid esters are not readily ionized by ESI or APCI

Desorption from Surfaces

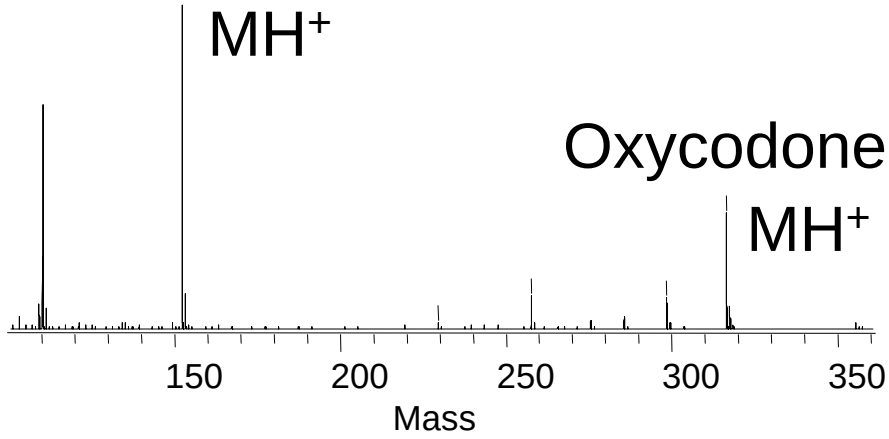
- Heating the gas assists in desorbing some materials
- Substances with minuscule vapor pressures that cannot be desorbed by heat alone are readily detected
- Other mechanisms must play a role

Date-rape drug:
Sodium g-Hydroxybutyrate
100 ng deposited on rim of a cocktail glass

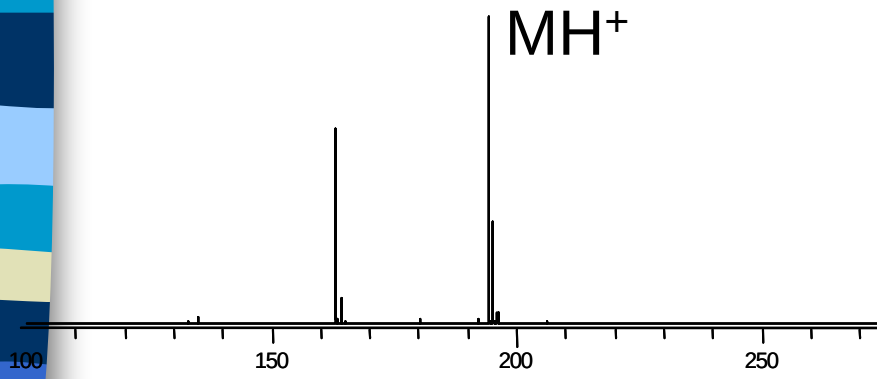


Direct Detection of Drugs in Pill Form

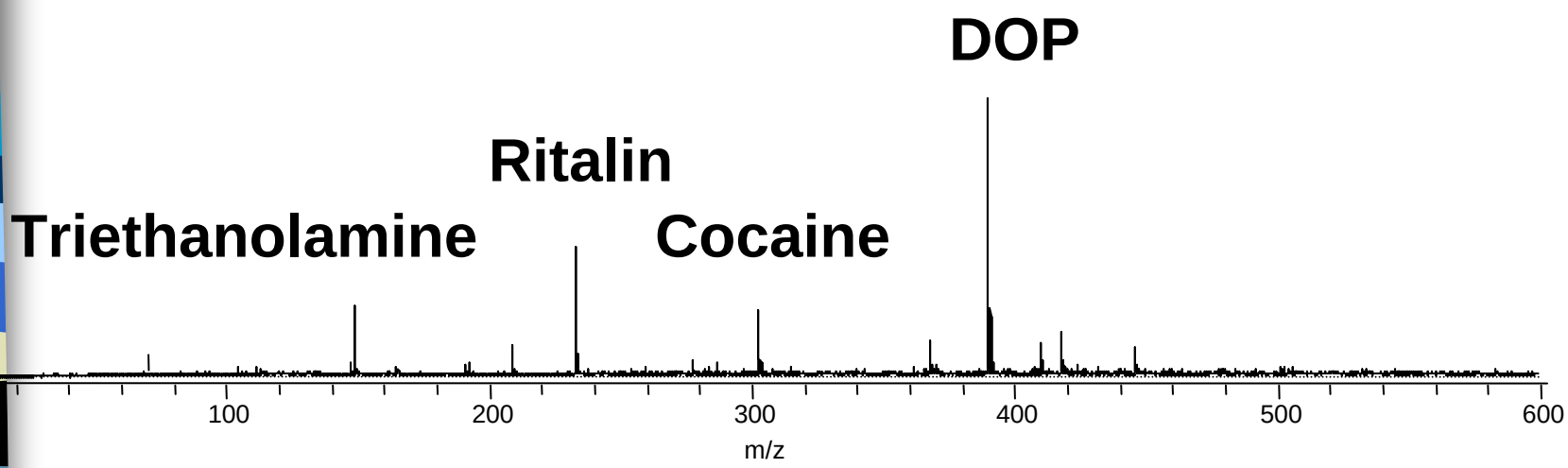
Acetaminophen



“Ecstasy” (MDMA)



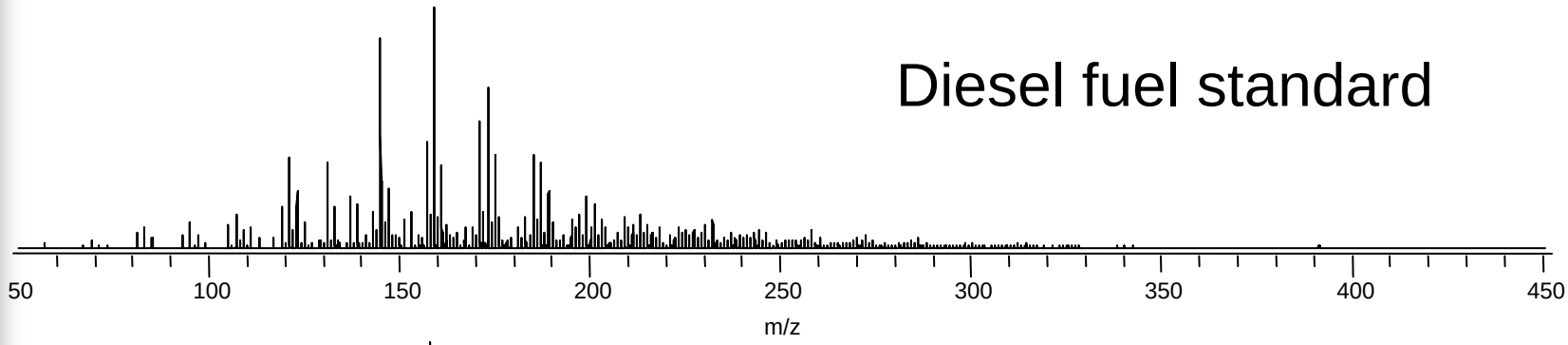
One-Dollar Bill



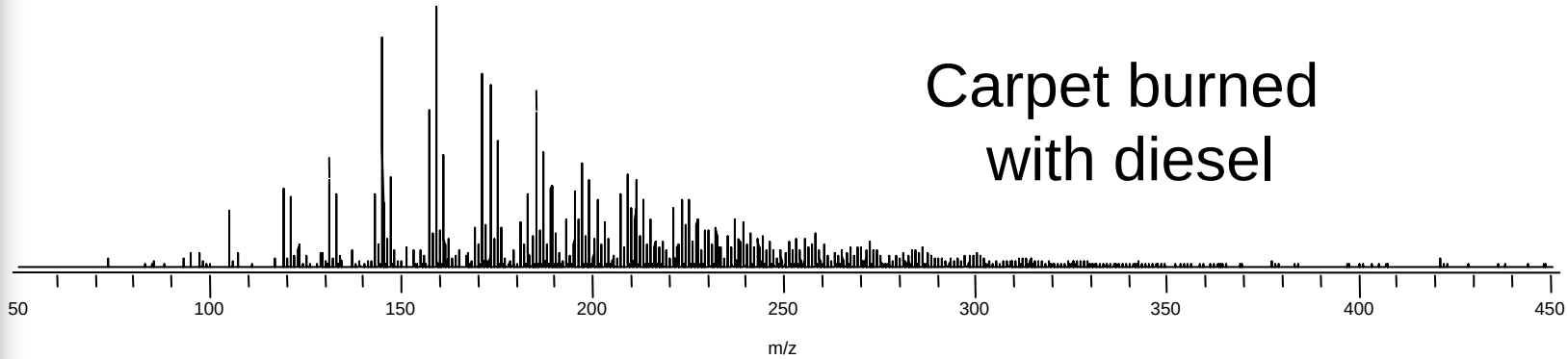
1. Triethanolamine is a pH-adjuster used in cosmetics
2. All labeled compounds are detected as MH^+
3. Common on bills: sunscreen, DEET, nicotine, glycerol and polyglycols (from printing process?)

Accelerants: Carpet Burned with Diesel Fuel

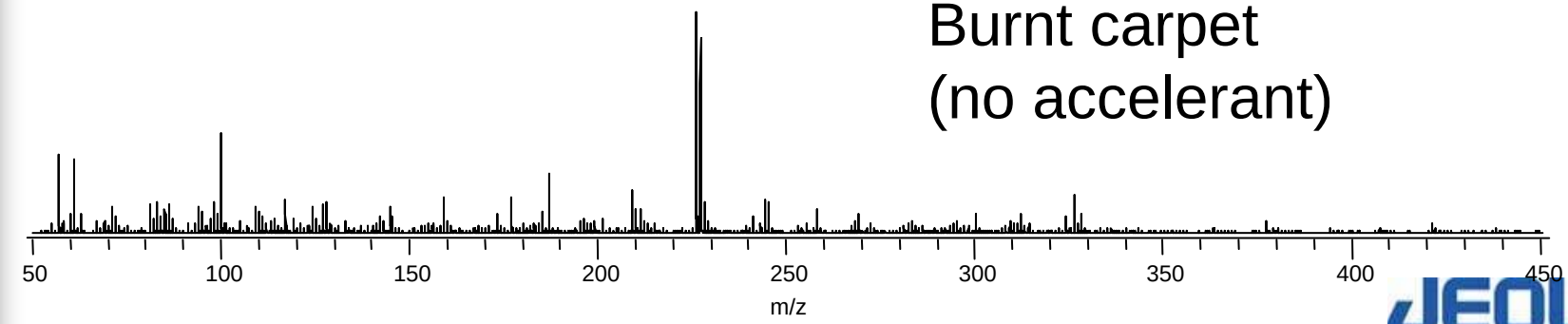
Diesel fuel standard



Carpet burned with diesel



Burnt carpet (no accelerant)



DART applications:

- Forensics
- Drugs (medicinal, herbal, illicit, counterfeit)
- Powders, extracts
- Metabolites
- Waste control, cleaning check etc
- Explosives
- Synthetic organics and organometallics
- Foods and beverages
- Pesticides
- Toxic industrial materials

DART for High-Throughput Analysis of Small Molecules

- **Fast analysis**
  - Analysis complete in seconds
- **Simple**
  - No vacuum, solvents, plumbing
- **No carryover**
  - Tolerates large sample quantities
- **Polar and nonpolar compounds**

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DART for High-Throughput Analysis of Small Molecules (2)

- **Simple mass spectra**
  - No adducts or multiple charges
- **“Green”**
  - No solvents → no solvent disposal
- **Less susceptible to suppression**
  - Tolerant of high levels of salts
  - Analyzes salts with sub-millitorr vapor pressures

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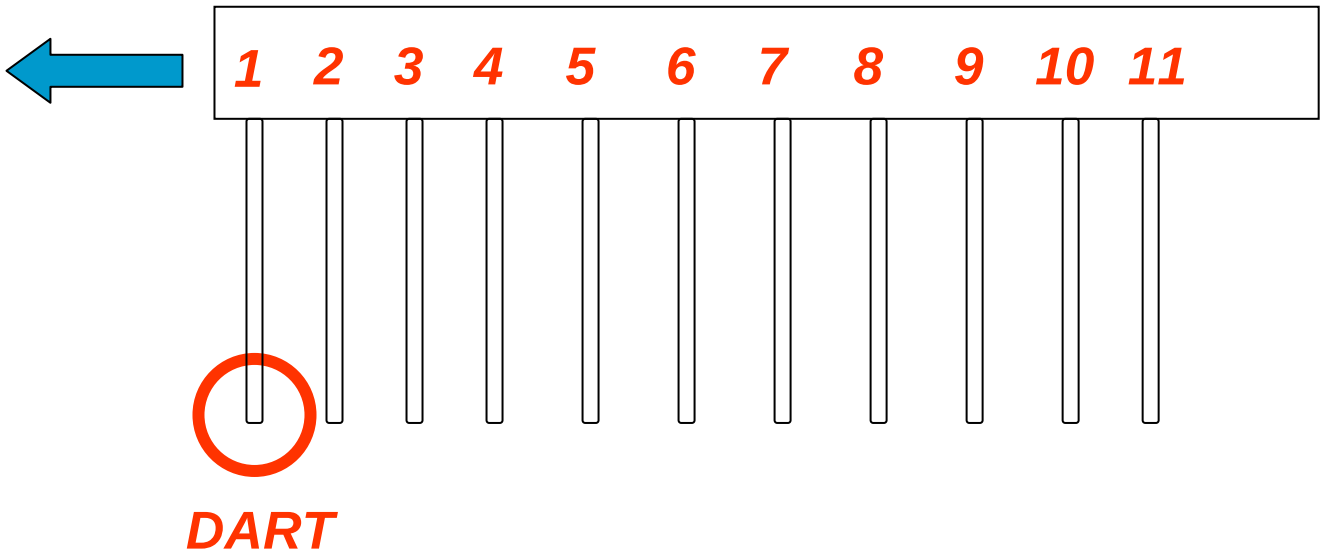
High-throughput test

- Measure 11 small drug compounds in under 40 seconds
- Determine unique elemental compositions from exact-mass measurements and isotope abundances

Experiment



- Samples deposited on melting point tubes
- Pass tubes quickly through DART source
- Acquire 5-10 spectra per second
- Post-calibration with PEG 600 on filter paper

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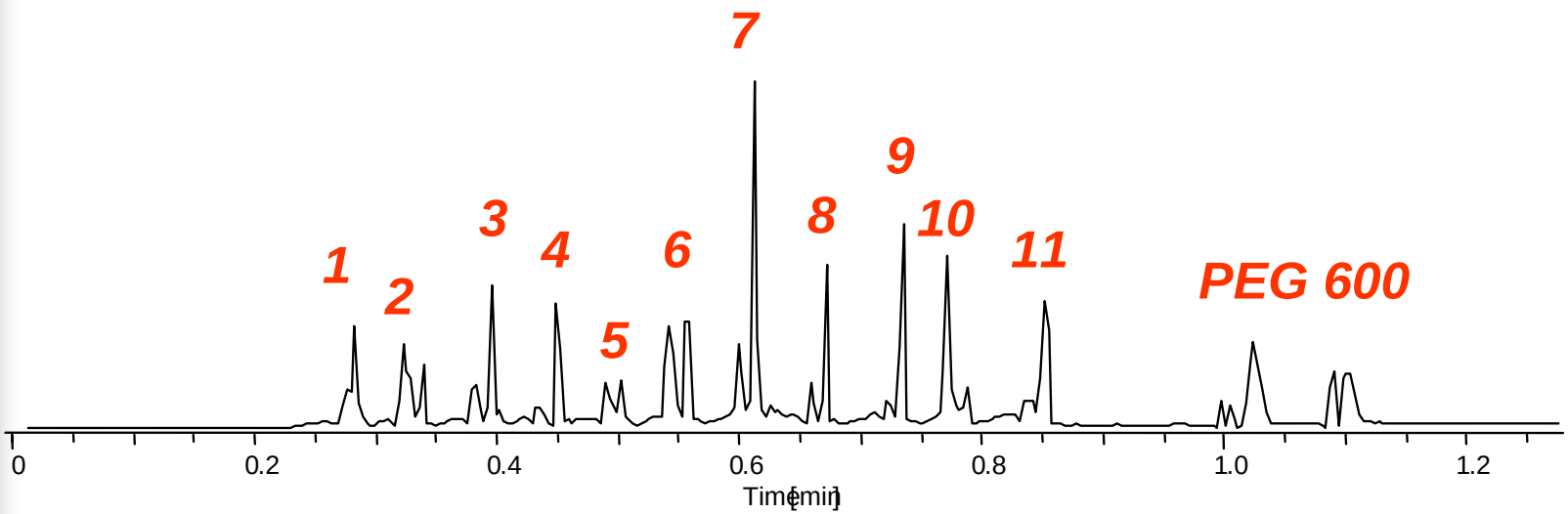
TIC for high-throughput trial

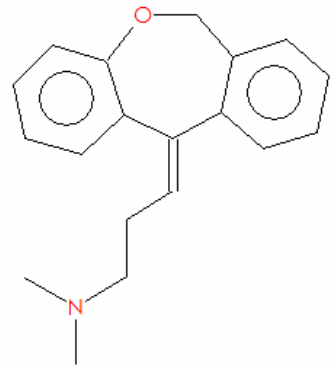


0.58 min

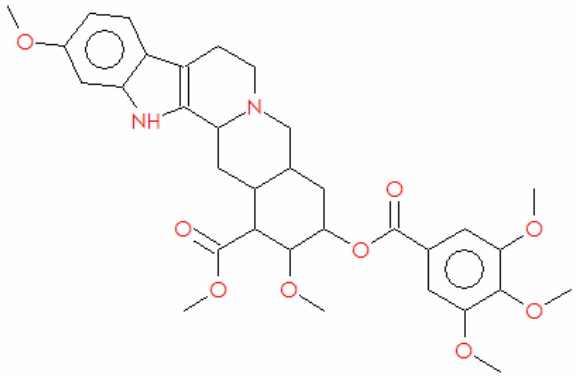
~3 seconds per compound

Example mass spectra

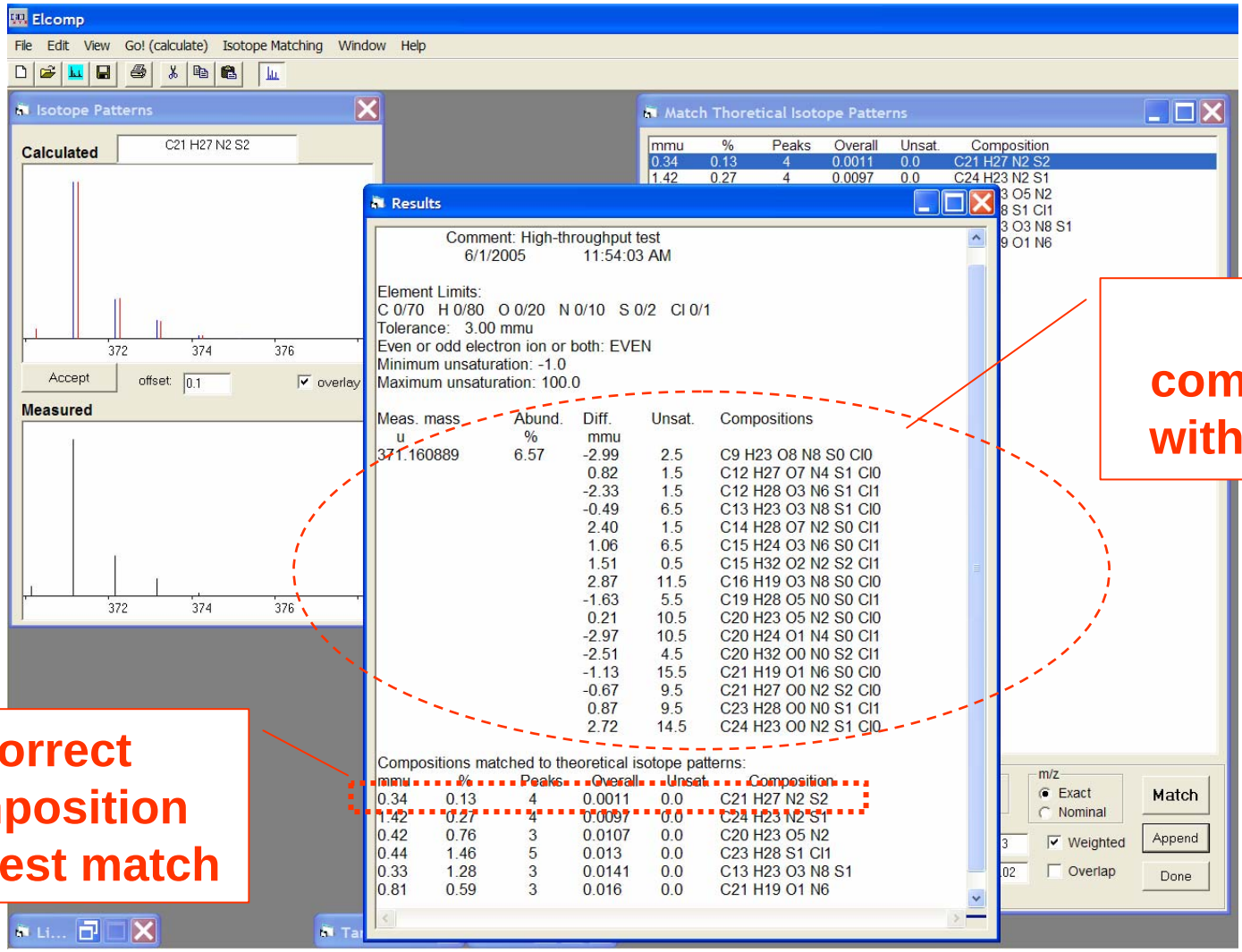
Doxepin [M+H]+



Reserpine [M+H]+



Automated isotope matching software



16 compositions within 0.003 u

Correct composition has best match

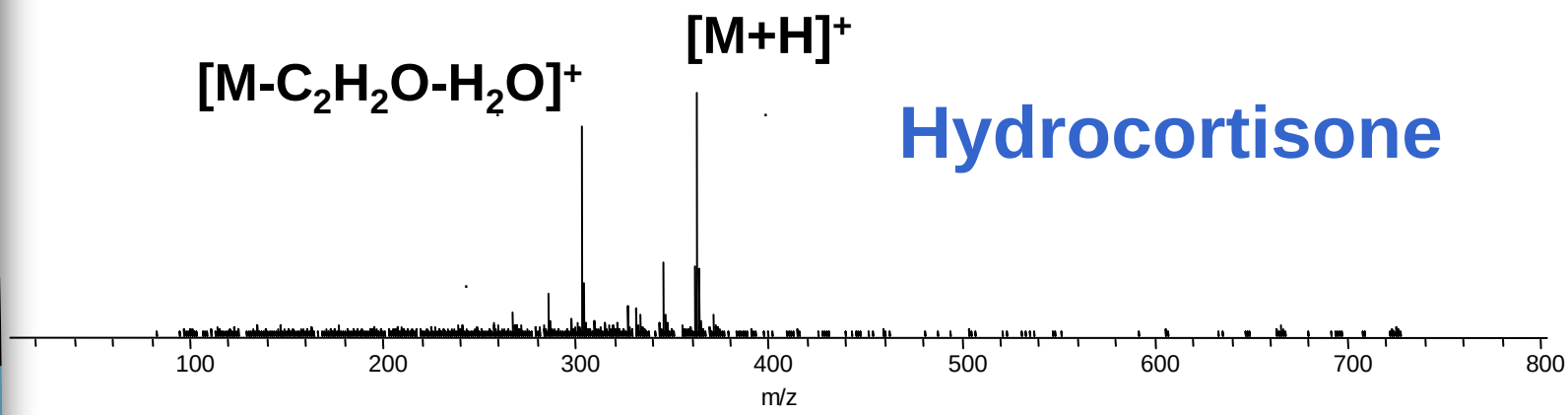
Elemental Compositions

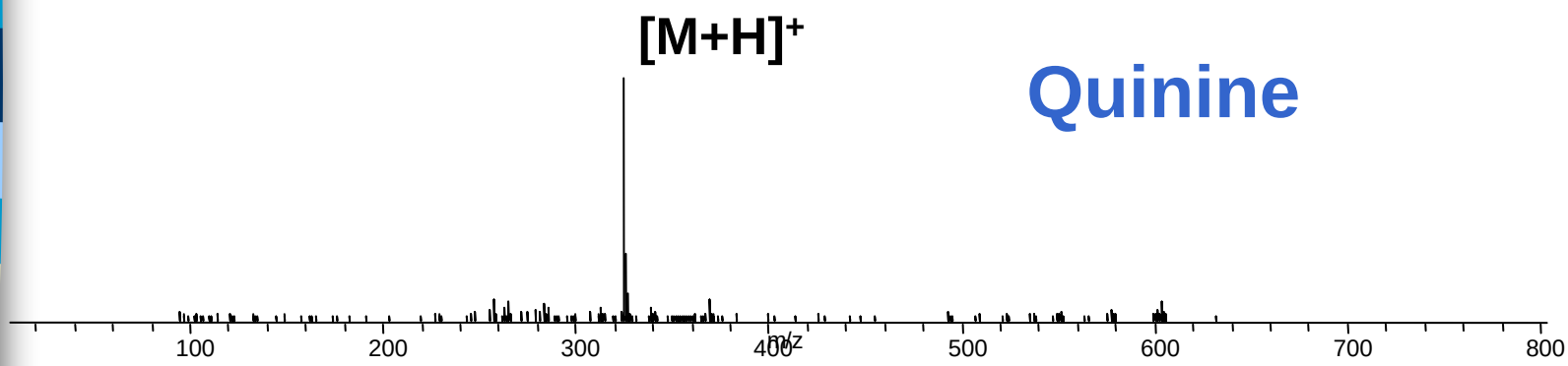
Limits: C 0/70 H 0/80 O 0/20 N 0/10 S 0/2 Cl 0/1
Tolerance: 3mmu, even-electron ions

Compound	Composition	Calculated *m/z*	#Compositions	Rank
Phenolphthalein	C20H15O4	319.097035	18	1
Promazine	C17H21N2S	285.142544	11	1
Quinine	C20H25N2O2	325.191603	8	1
Nortrityplene	C19H22N	264.175224	5	1
hioridazine	C21H27N2S2	371.161565	16	1
Chlorpromazine	C17H20N2SCl	319.103572	18	1
Doxepin	C19H22NO	280.170139	5	1
Hydrocortisone	C21H31O5	363.21715	9	1
Reserpine	C33H41N2O9	609.281208	30	1
Caffeine	C8H11N4O2	195.088201	7	1
Erythromycin	C37H68NO13	734.469069	22	1

All compositions correctly identified, r.m.s. error = 2.2 ppm

Analytes can be detected in saturated KCl solution: no K^+ adducts, no suppression

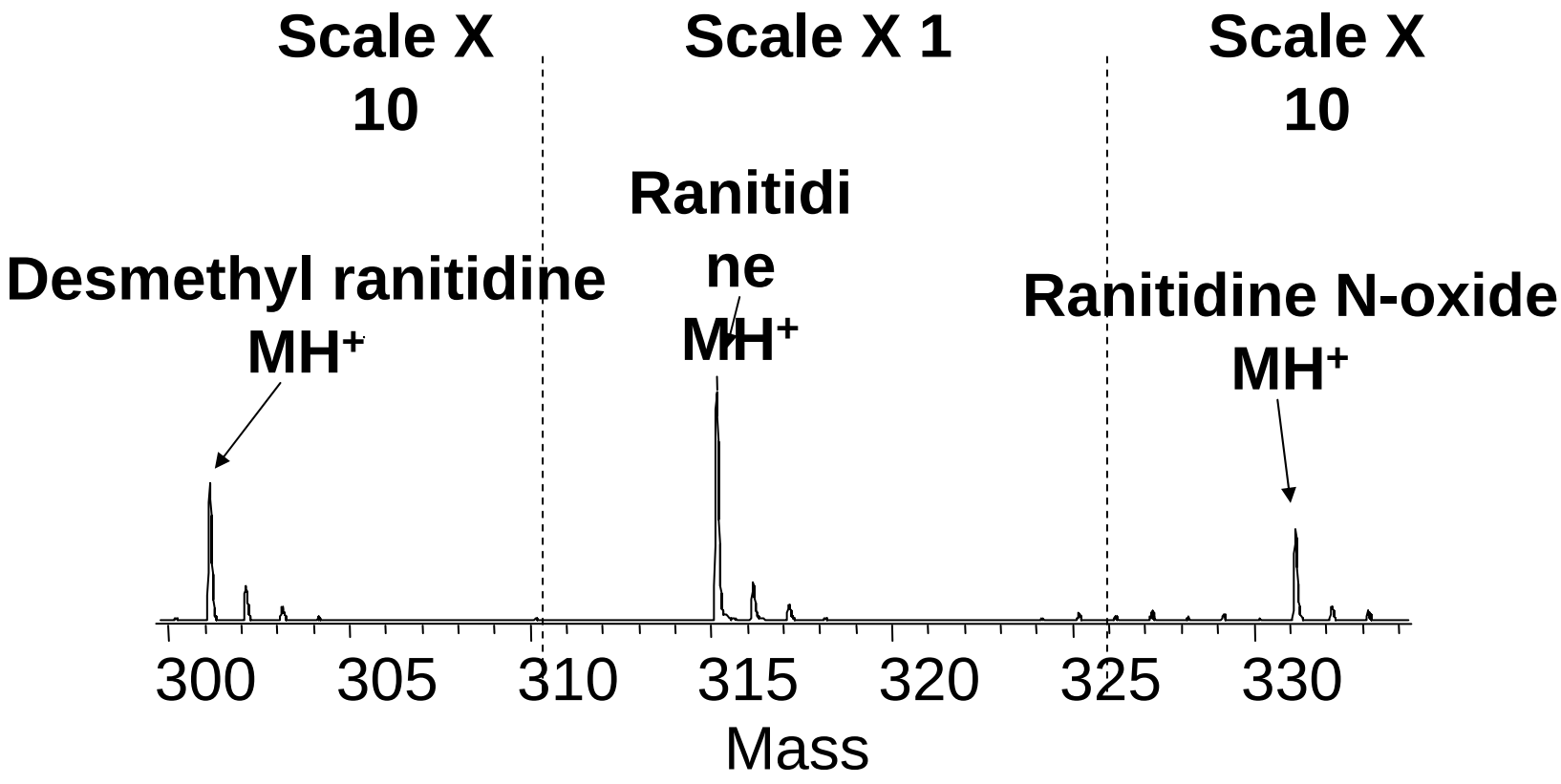




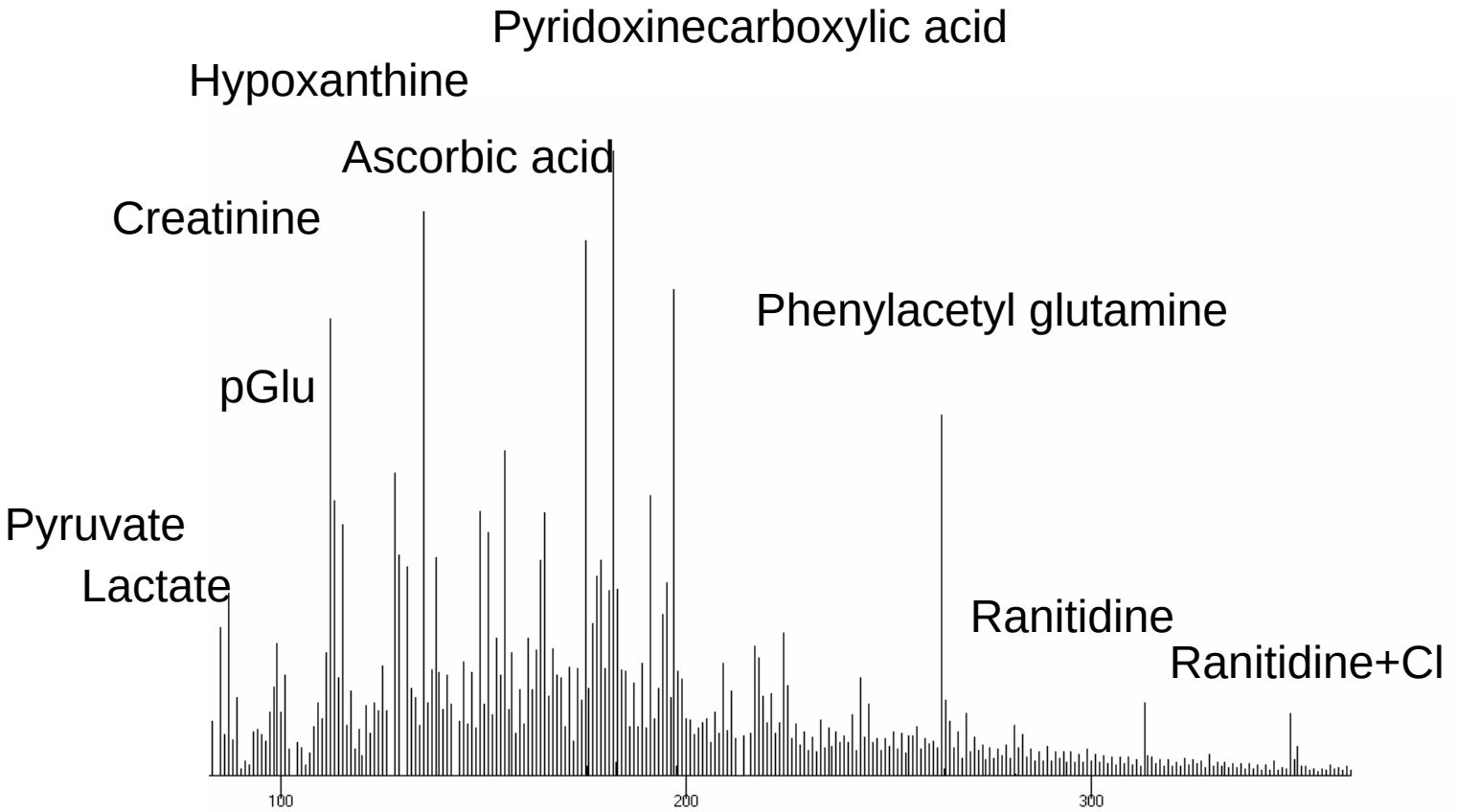
DART Analysis of Body Fluids

- DART is fast!
- Blood, urine or saliva deposited onto glass rod
- Results obtained within seconds

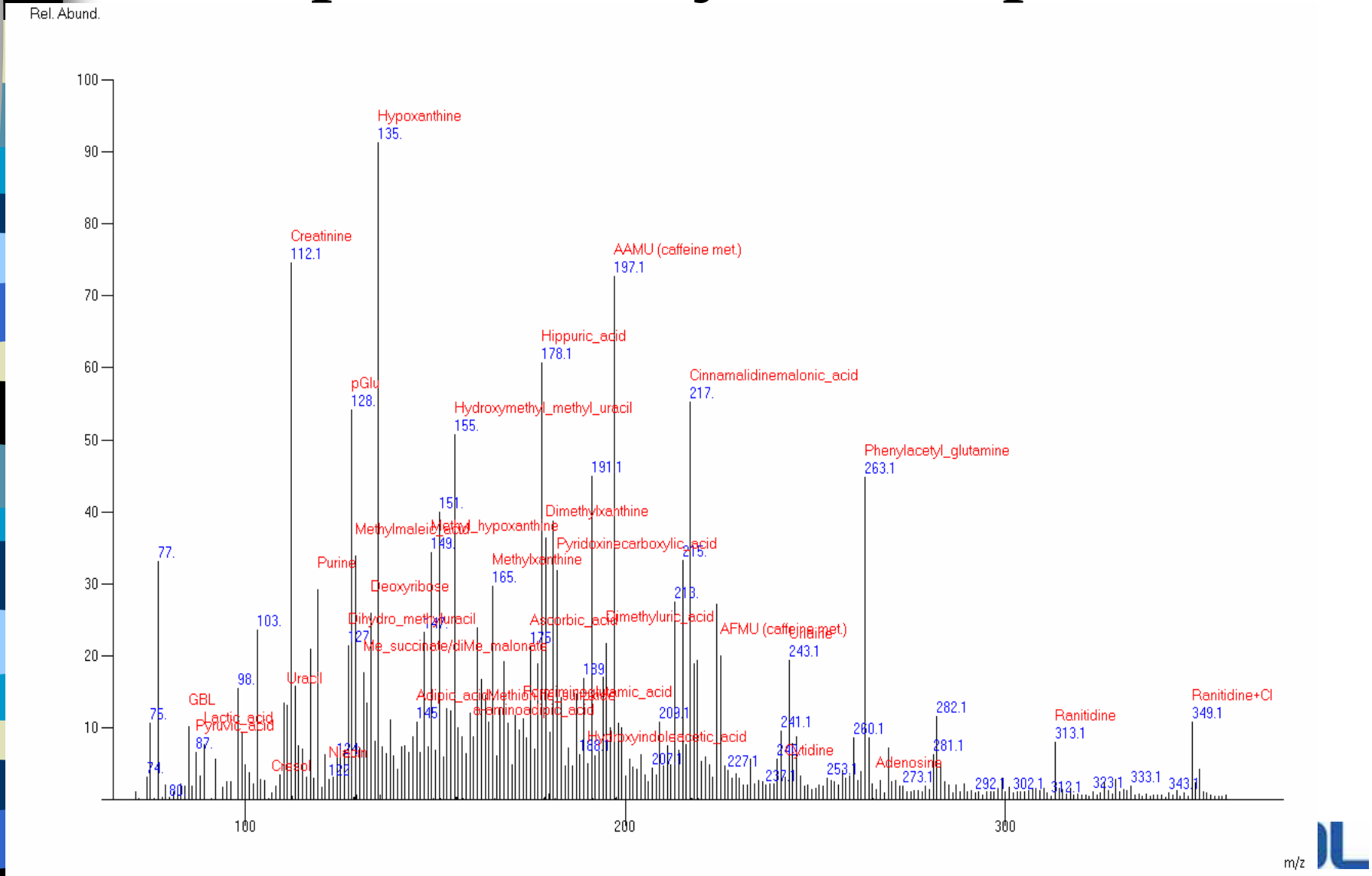
Zantac^{tm} (Ranitidine) Metabolites in Urine



Urine


Pyridoxinecarboxylic acid
Hypoxanthine
Ascorbic acid
Creatinine
Phenylacetyl glutamine
pGlu
Pyruvate
Lactate
Ranitidine
Ranitidine+Cl
100
200
300

Computer Analysis of Spectrum



Name	Meas.	Calc.	Diff(u)	Abund.
GBL	85.0295	85.0290	0.0006	11.0317
Pyruvic_acid	87.0084	87.0082	0.0002	7.1700
Lactic_acid	89.0236	89.0239	-0.0002	8.3658
Cresol	107.0492	107.0497	-0.0004	.9294
Uracil	111.0153	111.0195	-0.0041	14.3328
Creatinine	112.0513	112.0511	0.0002	81.6851
Purine	119.0354	119.0358	-0.0004	31.9510
Niacin	122.0277	122.0242	0.0035	3.1489
Dihydro_methyluracil	127.0486	127.0508	-0.0021	23.3773
pGlu	128.0353	128.0348	0.0006	59.2337
Methylmaleic_acid	129.0212	129.0188	0.0024	37.1191
Me_succinate/diMe_malonate	131.0368	131.0358	0.0010	19.3593
Deoxyribose	133.0489	133.0501	-0.0012	28.3521
Hypoxanthine	135.0306	135.0307	-0.0001	100.0000
Adipic_acid	145.0469	145.0501	-0.0032	11.7389
Methyl_hypoxanthine	149.0454	149.0463	-0.0009	37.5243
Hydroxymethyl_methyl_uracil	155.0453	155.0457	-0.0003	55.5832
a-aminoadipic_acid	160.0568	160.0610	-0.0042	9.5885
Methionine_sulfoxide	164.0419	164.0381	0.0037	11.7609
Methylxanthine	165.0408	165.0412	-0.0004	32.4341
Formiminoglutamic_acid	173.0536	173.0562	-0.0027	12.3531
Ascorbic_acid	175.0285	175.0243	0.0042	23.1998
Hippuric_acid	178.0513	178.0504	0.0009	66.4487
Glucose	179.0552	179.0556	-0.0004	39.7499
Dimethylxanthine	179.0552	179.0569	-0.0017	39.7499
Pyridoxinecarboxylic_acid	182.0479	182.0453	0.0026	34.7913
Hydroxyindoleacetic_acid	190.0542	190.0504	0.0037	5.4133
Dimethyluric_acid	195.0527	195.0518	0.0009	23.7577
AAMU (caffeine met.)	197.0667	197.0675	-0.0007	79.6617
Cinnamalidinemalonic_acid	217.0483	217.0501	-0.0017	60.5399
AFMU (caffeine met.)	225.0643	225.0624	0.0019	21.9092
Cytidine	242.0801	242.0777	0.0024	3.4545
Uridine	243.0641	243.0617	0.0024	21.1156
Phenylacetyl_glutamine	263.1033	263.1032	0.0001	48.9665
Adenosine	266.0861	266.0889	-0.0028	1.4869
Ranitidine	313.1321	313.1334	-0.0013	8.7459
Ranitidine+Cl	349.1113	349.1101	0.0011	11.7296

Urine (-)

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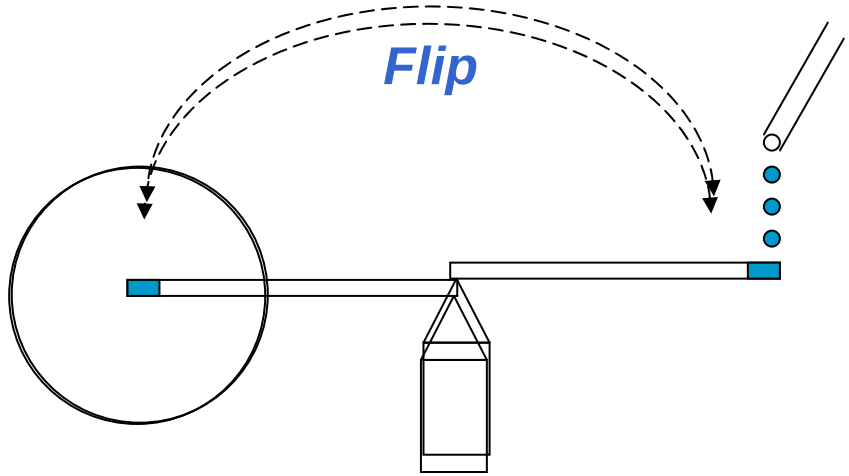
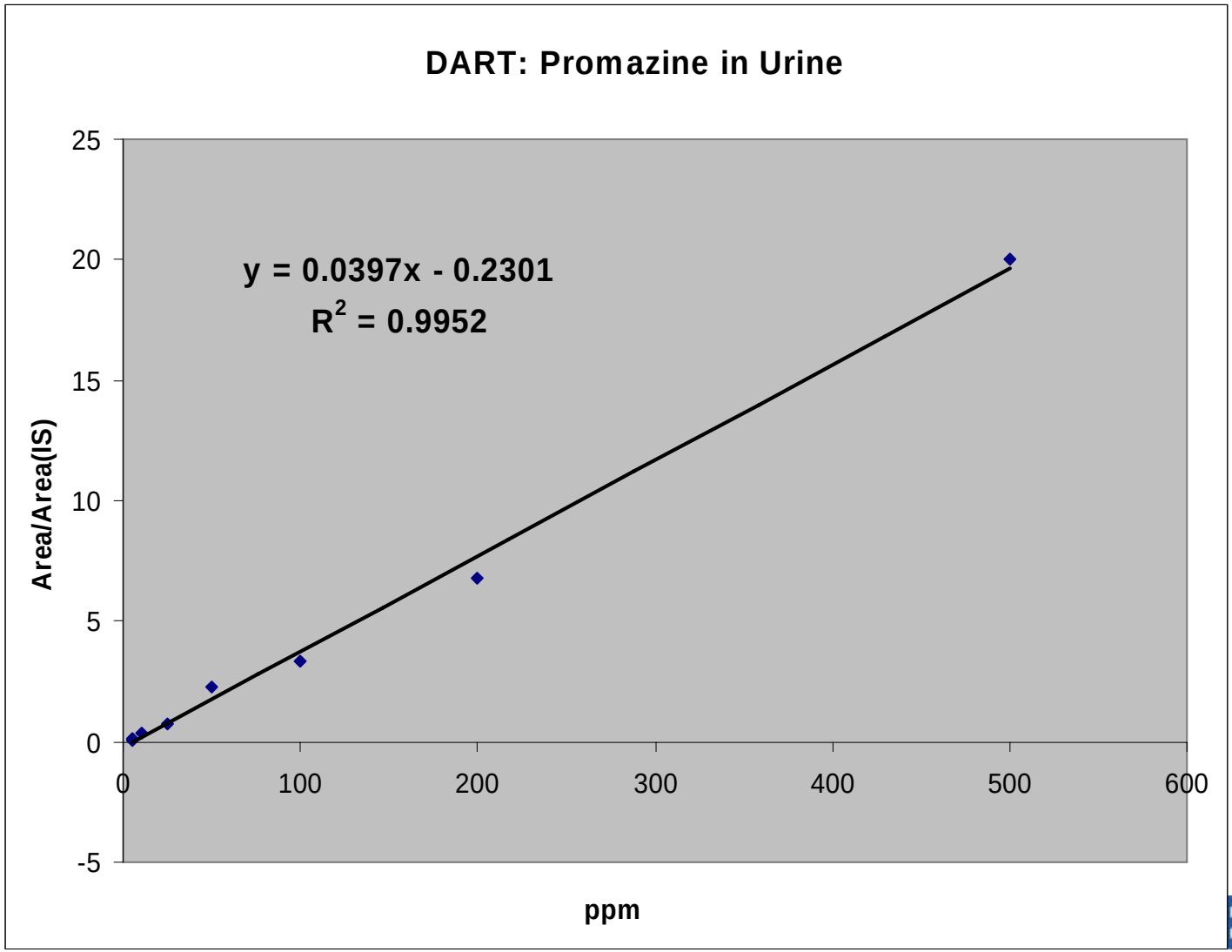
Drugs in Urine and Plasma



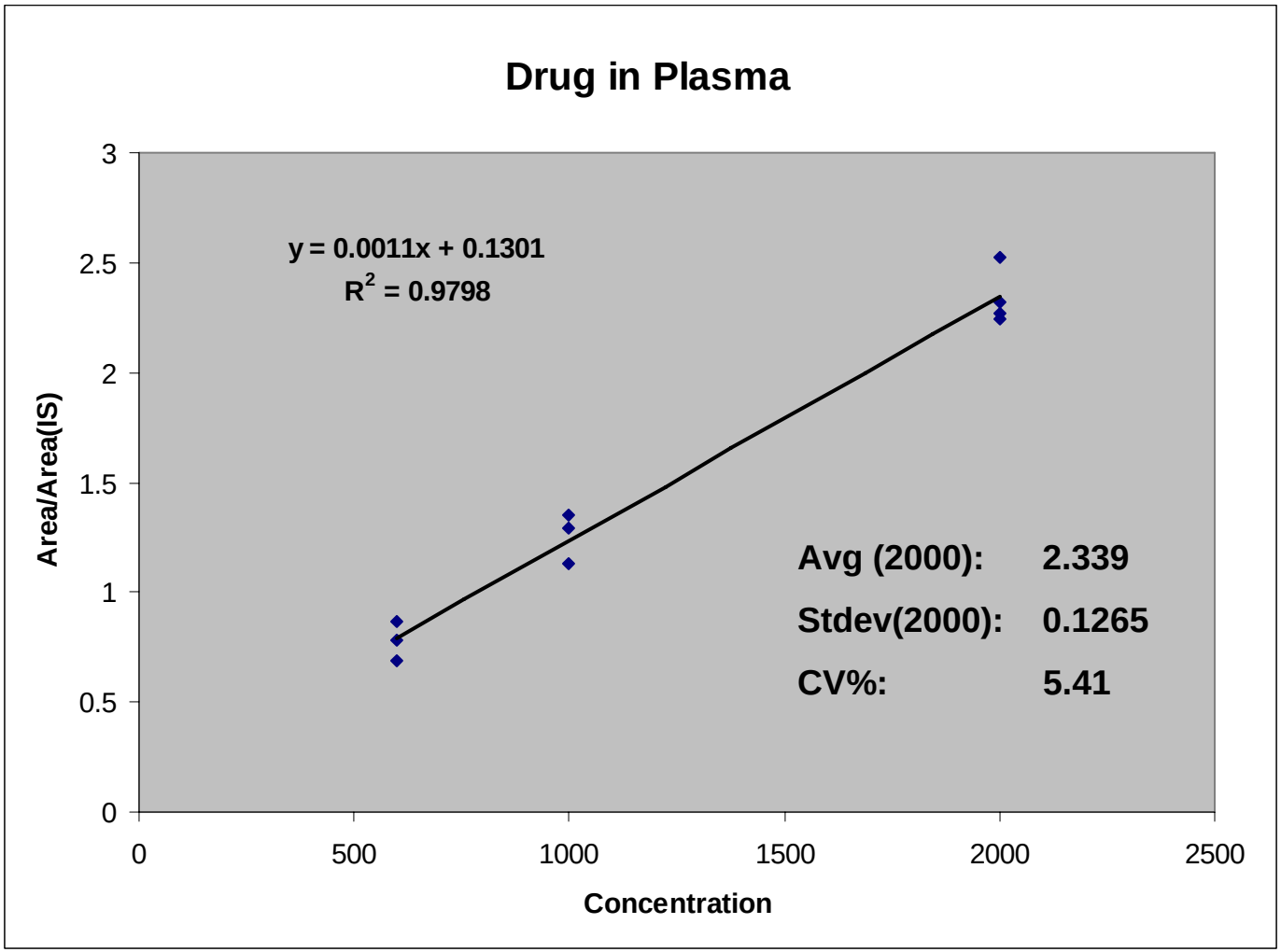
- Pipette a few microliters onto glass rod
- Swing into position
- See spectrum within seconds
- Remove, rinse, repeat

Promazine in Urine

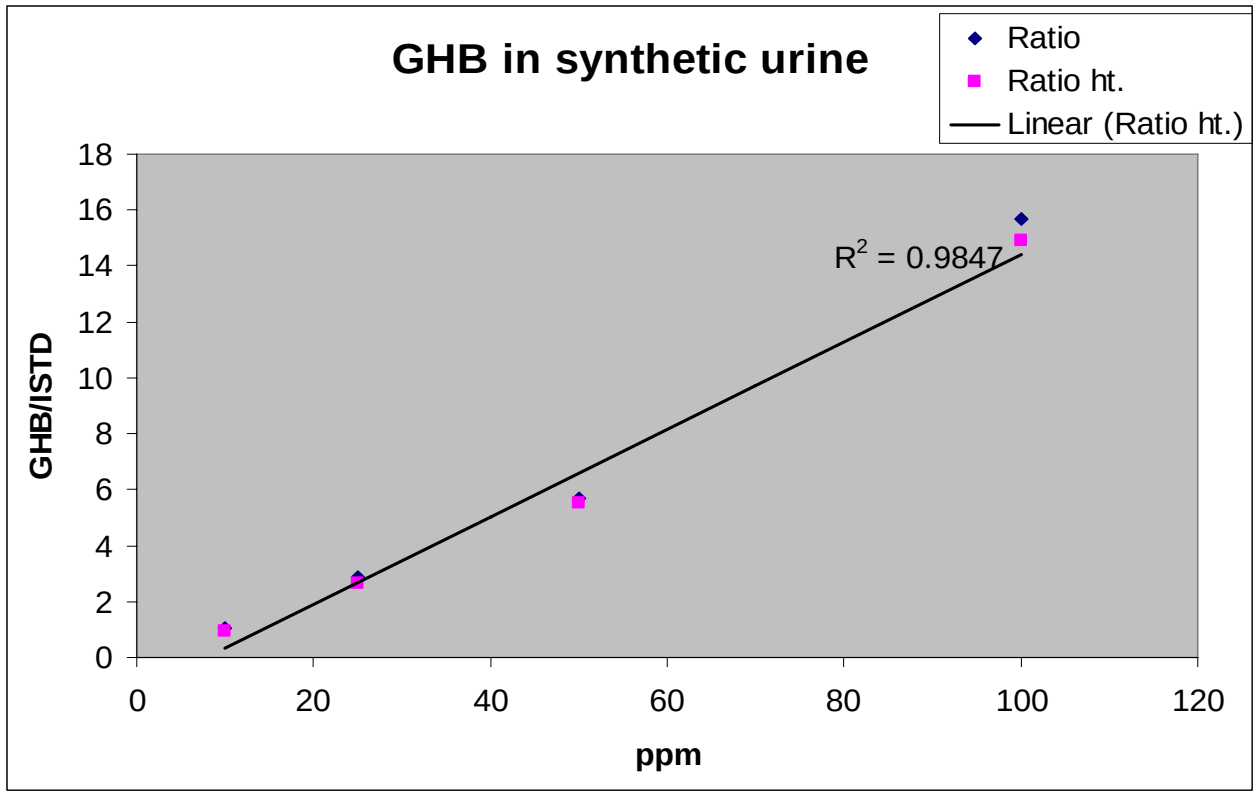
Chlorpromazine internal standard



Developmental Drug in Plasma



Gamma Hydroxybutyrate (GHB) in Urine (Deuterated I.S.)



Thanks to Eshwar Jagerdeo and Roman Karas, FBI Laboratory, Quantico VA

Conclusion

- DART provides a means for rapid analysis of samples with no solvents or sample preparation
- The TOF provides fast high-quality analysis that allow us to take advantage of the DART ion source

“AccuTOF GC”

“AccuTOF DART”

“AccuTOF LC-plus”

“AccuTOF CS”

More Information

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