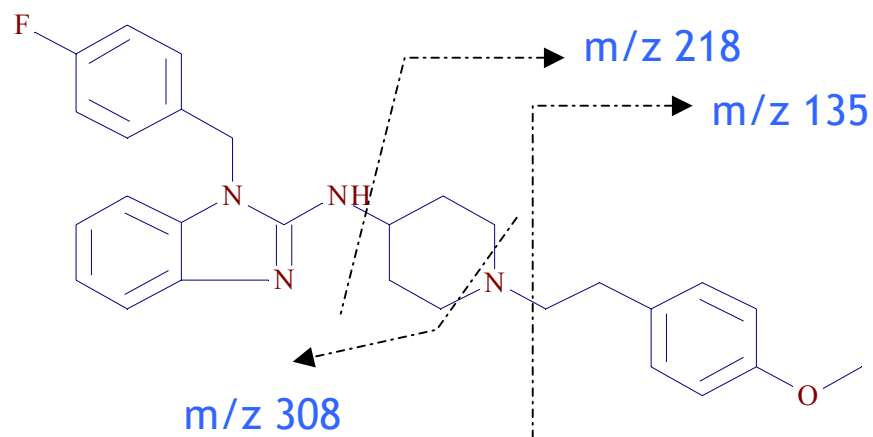




LC/API/MS vs. LC/API/MS/MS
Selectivity

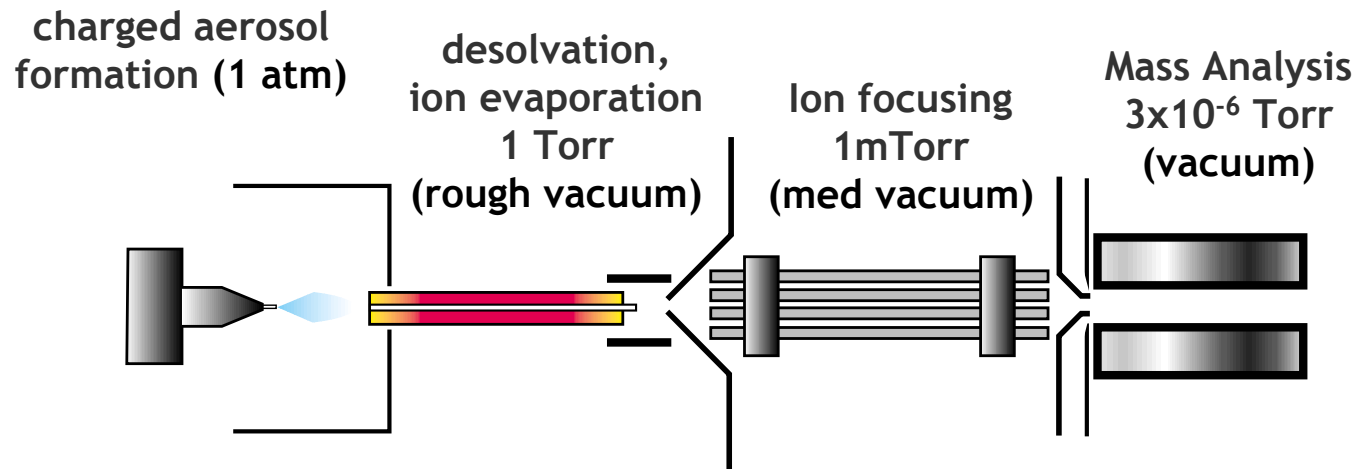
MS/MS Selectivity Example

- Astemizole (antihistamine)
- Source CID (collision-induced dissociation) vs. MS/MS
- SIM vs. SRM
- Direct analysis in rat plasma



Ways to impart energy to ions in API interface

- Interface temp (heated cap.)
- Interface voltage (capillary-skimmer voltage)
- Q_0 offset (*if Q_0 is increased, must offset the rest of the ion path, ions don't go up hill!*)
- With these parameters you can affect fragmentation via source CID (collision-induced dissociation)

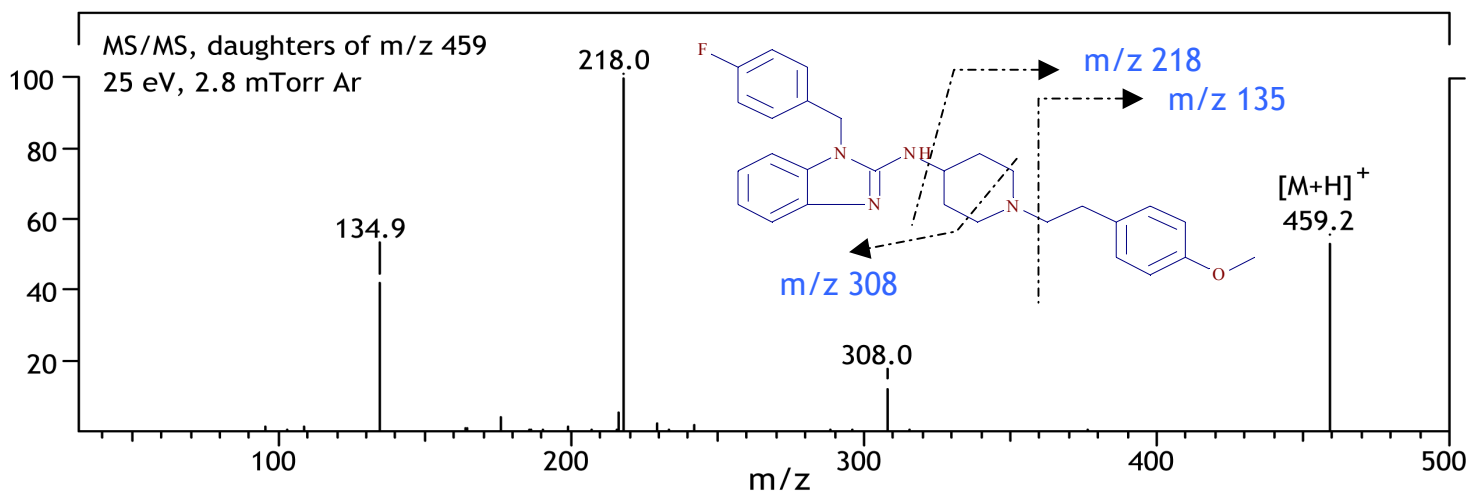
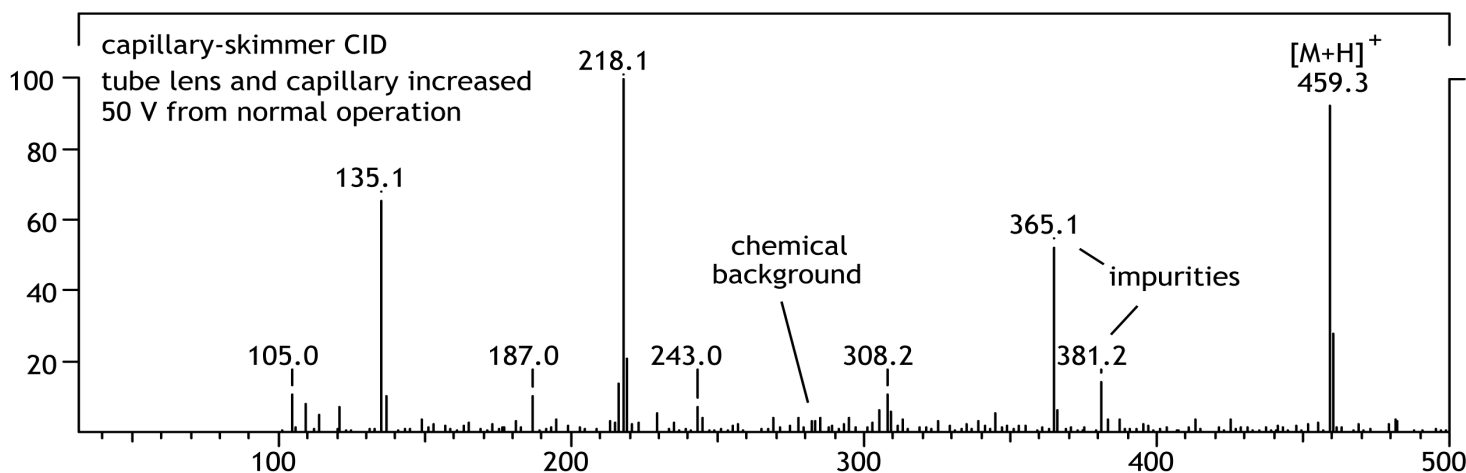


Caution: in-source CID IS NOT MS/MS!

source CID:
no mass
selection
some ions
due to
chemical
background

true
MS/MS:
all frag-
ments are
related to
analyte

Comparison of In-source CID and MS/MS
Astemizole, 1 ng injections, FIA @ 400 uL/min

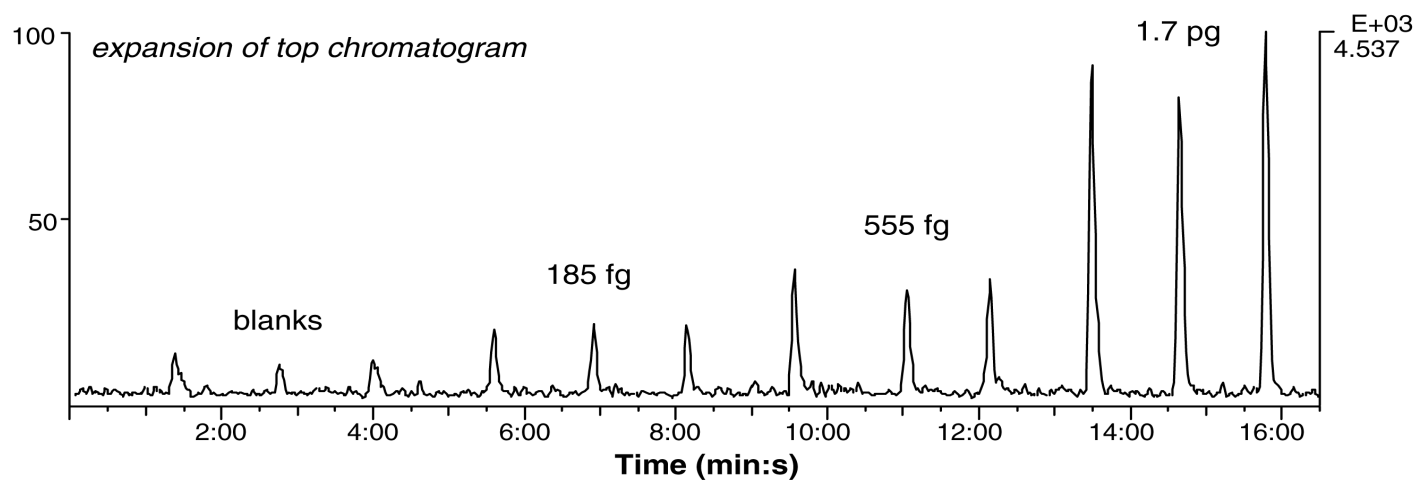
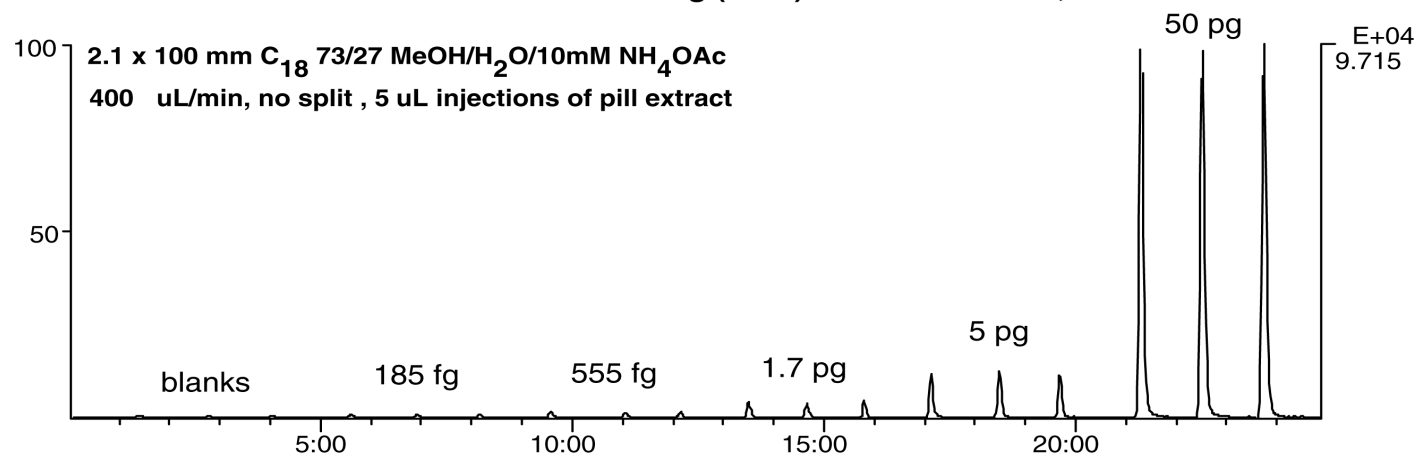


Example of MS/MS Sensitivity

TSQ w/API-1 ESI

Low-Level Detection of Astemizole by LC/ESI/MS/MS

Selected Reaction Monitoring (SRM) of m/z 459 \rightarrow 135, 218



ThermoFinnigan

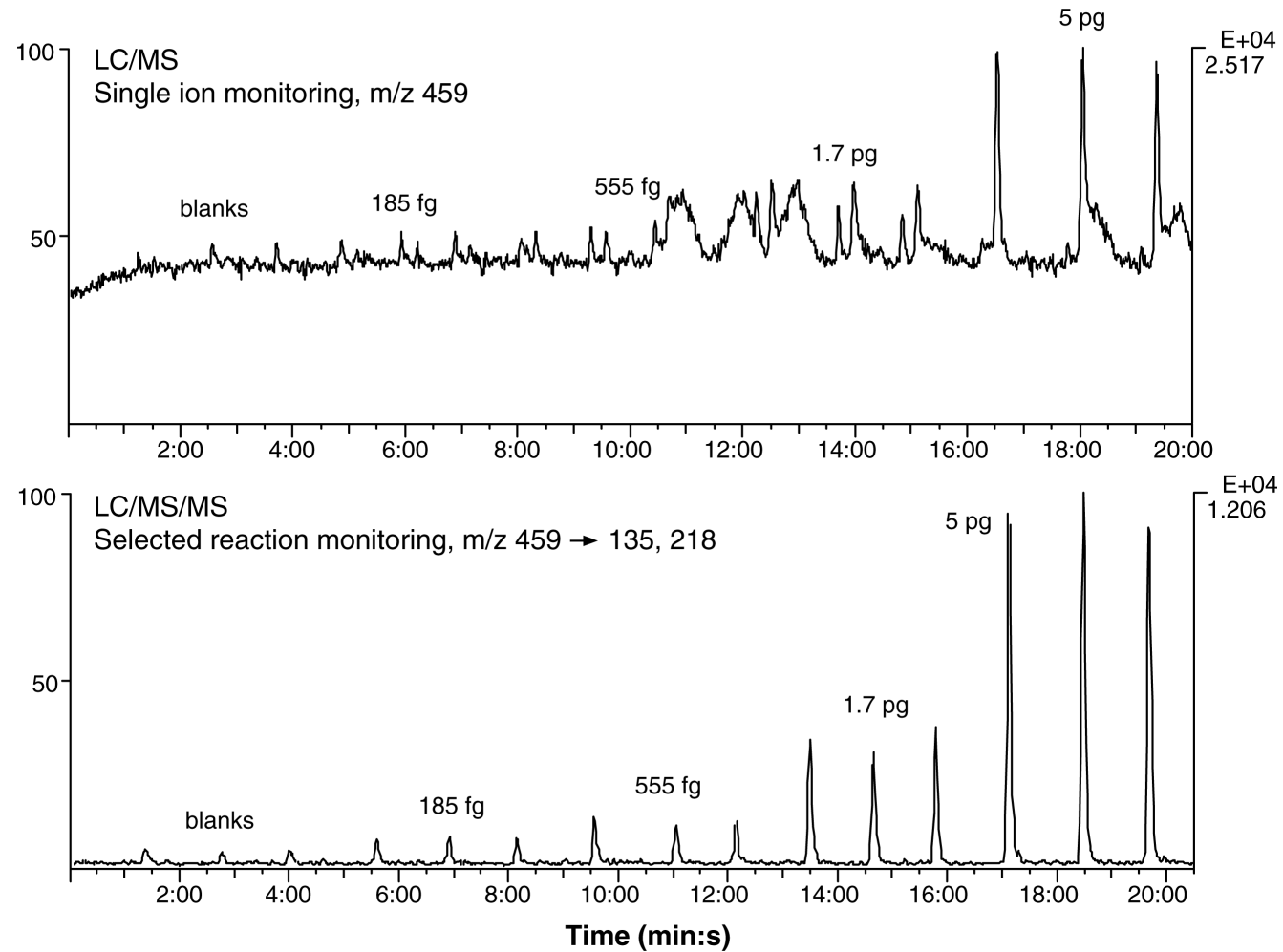
LC/MS SIM vs. LC/MS/MS SRM Sensitivity/Selectivity

TSQ
w/API-1
ESI
SIM

TSQ
w/API-1
ESI
SRM

Comparison of LC/MS and LC/MS/MS for detection of astemizole from a pill extract

2.1 x 100 mm C₁₈ 73/27 MeOH/H₂O/10 mM NH₄OAc @ 400 μ L/min, no split, 5 μ L injections of pill extract



MS/MS selectivity in complex matrices

Comparison of LC/MS and LC/MS/MS for detection of astemizole in rat plasma

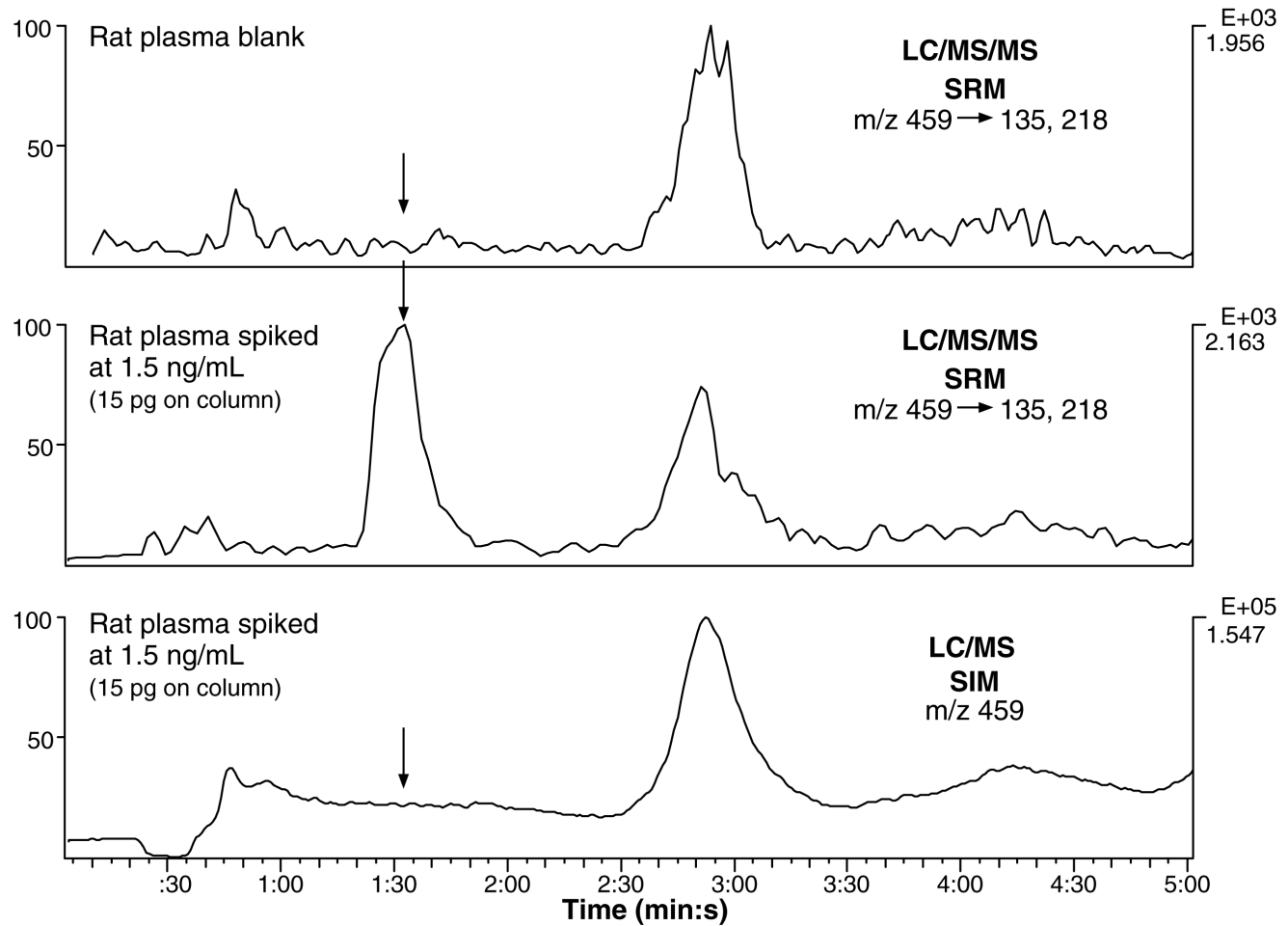
2.1 x 100 mm C₁₈ 65/35 MeOH/H₂O/10 mM NH₄OAc @ 400 μ L/min, no split, 10 μ L injections

TSQ
W/API-1
ESI

Blank
SRM

SRM
spiked

SIM
Spiked



MS/MS Selectivity Summary

- Fact: Signal is lower in MS/MS vs. MS due to transmission losses in mass filters (except in ion trap)
- However, MS/MS selectivity gains S/N over MS due to dramatic reduction in chemical noise
- Use MS/MS to gain selectivity for quantitating in complex matrices
- Use sample cleanup to minimize signal suppression
- Source CID (used mainly on single quads and ESI-ToF) can be useful in providing structural information, **if compound is pure**. On triple quads can use source CID + MS/MS as a form of pseudo-MS³