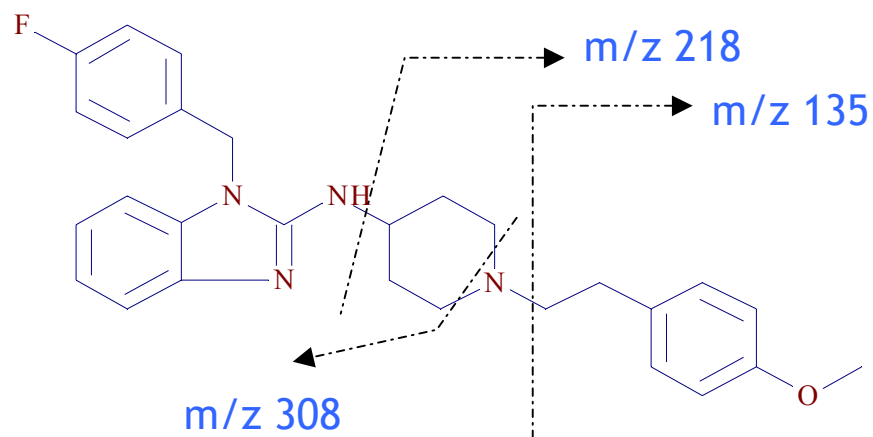


A vertical bar on the left side of the slide with a gradient from red at the top to dark blue at the bottom.

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

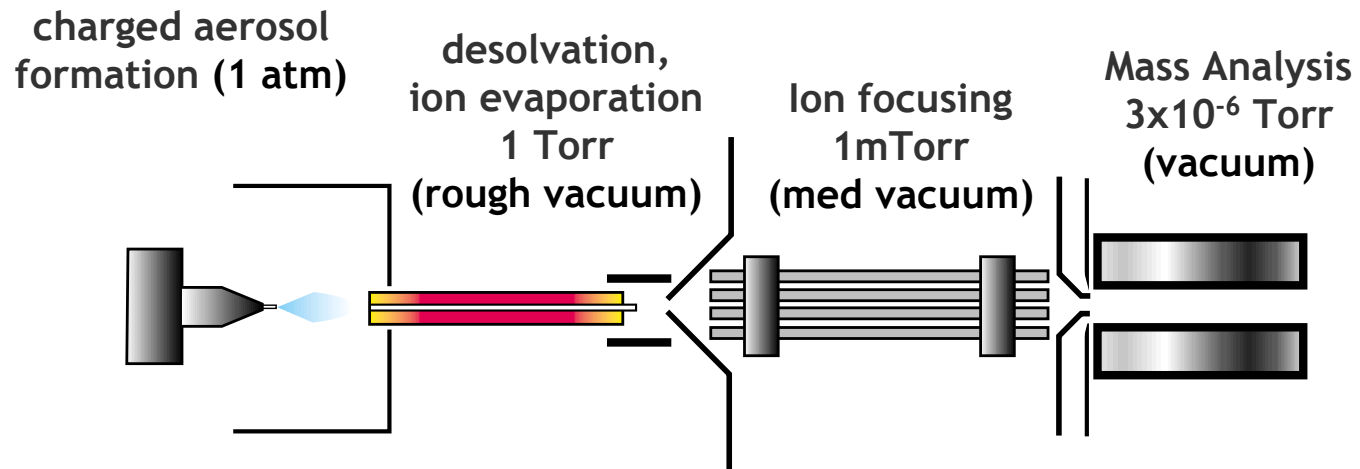
# MS/MS Selectivity Example

- 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)

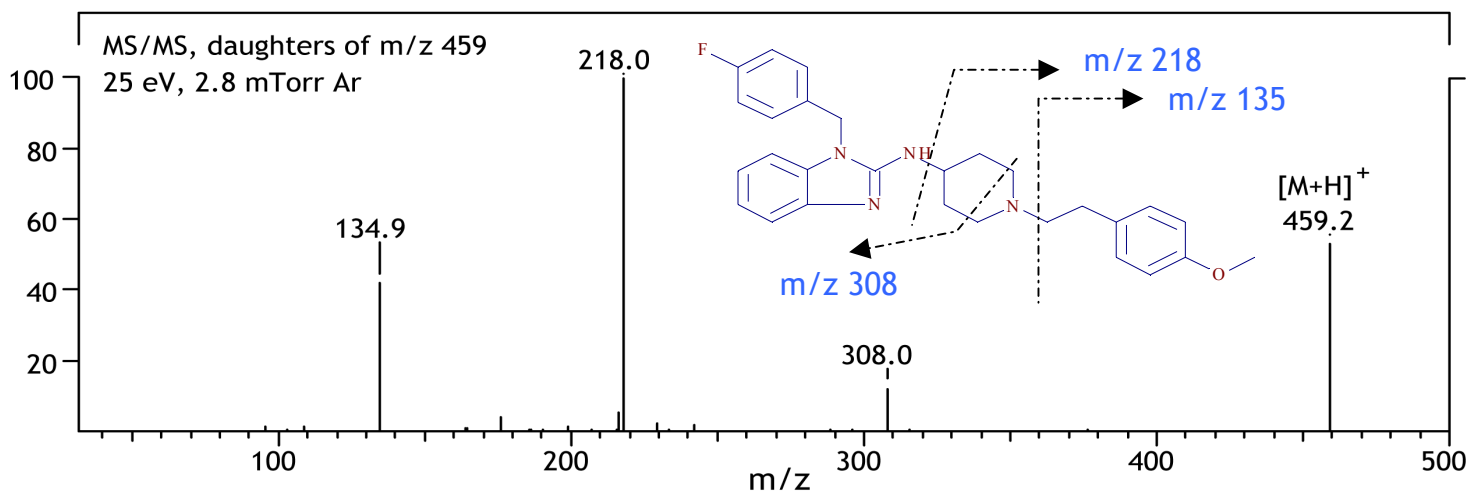
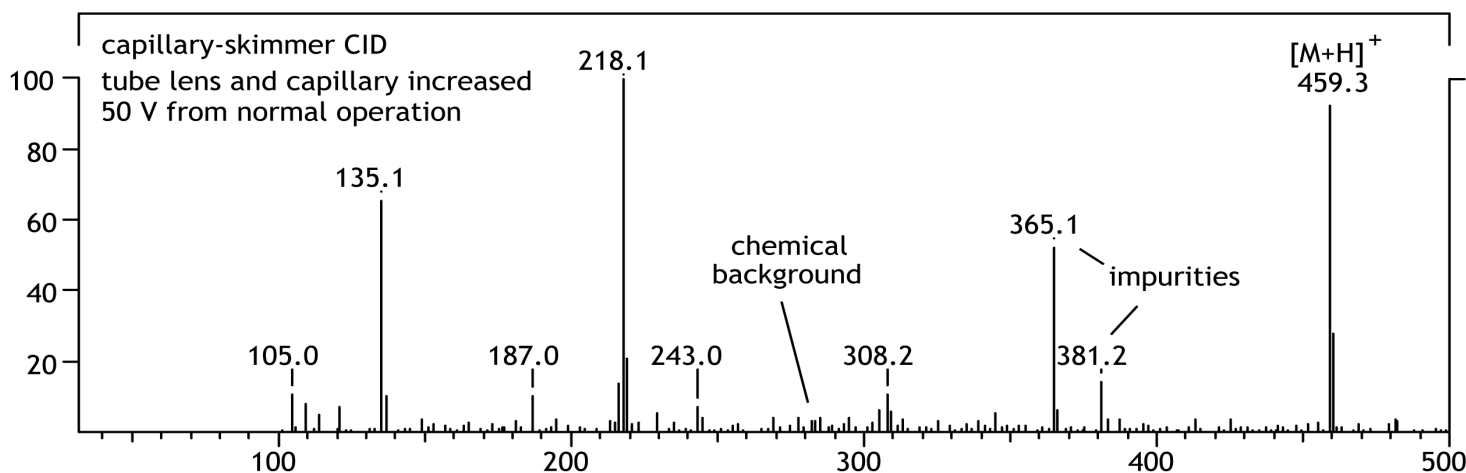


# Caution: in-source CID IS NOT MS/MS!

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

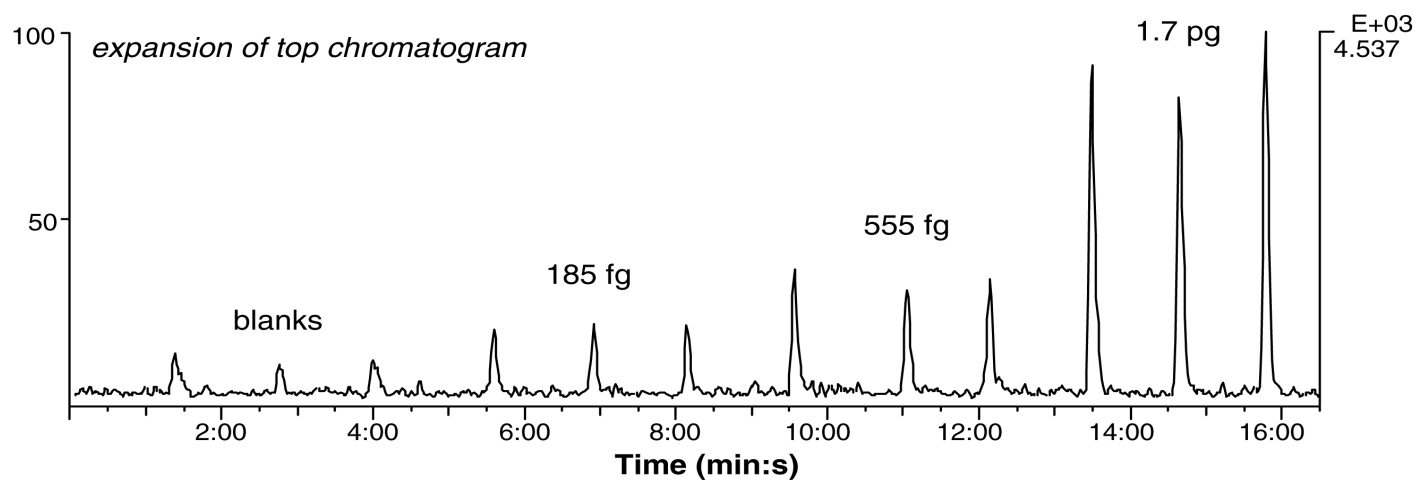
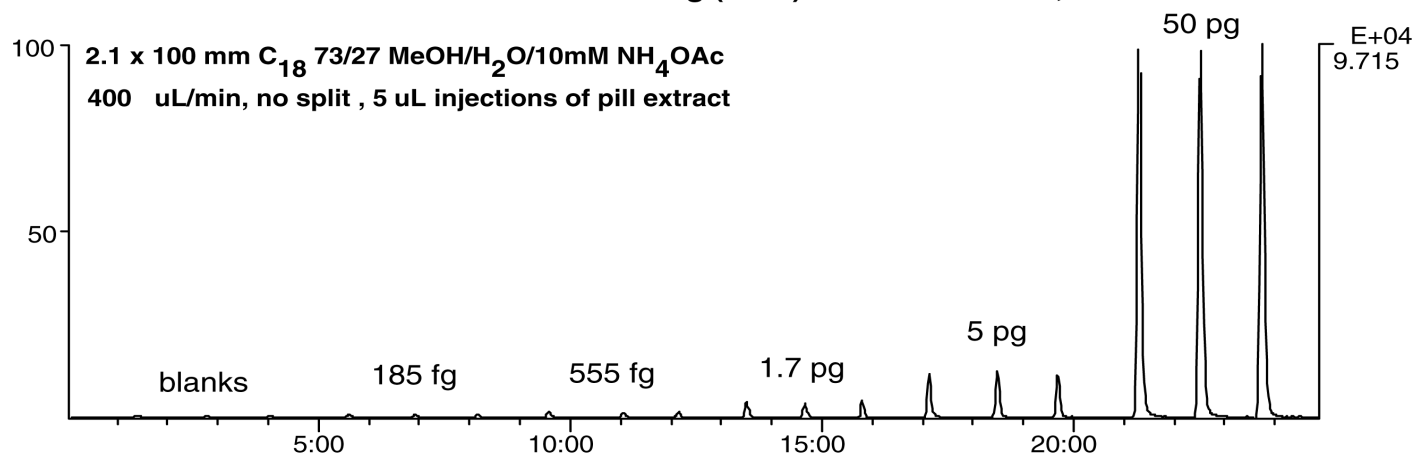


# Example of MS/MS Sensitivity

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

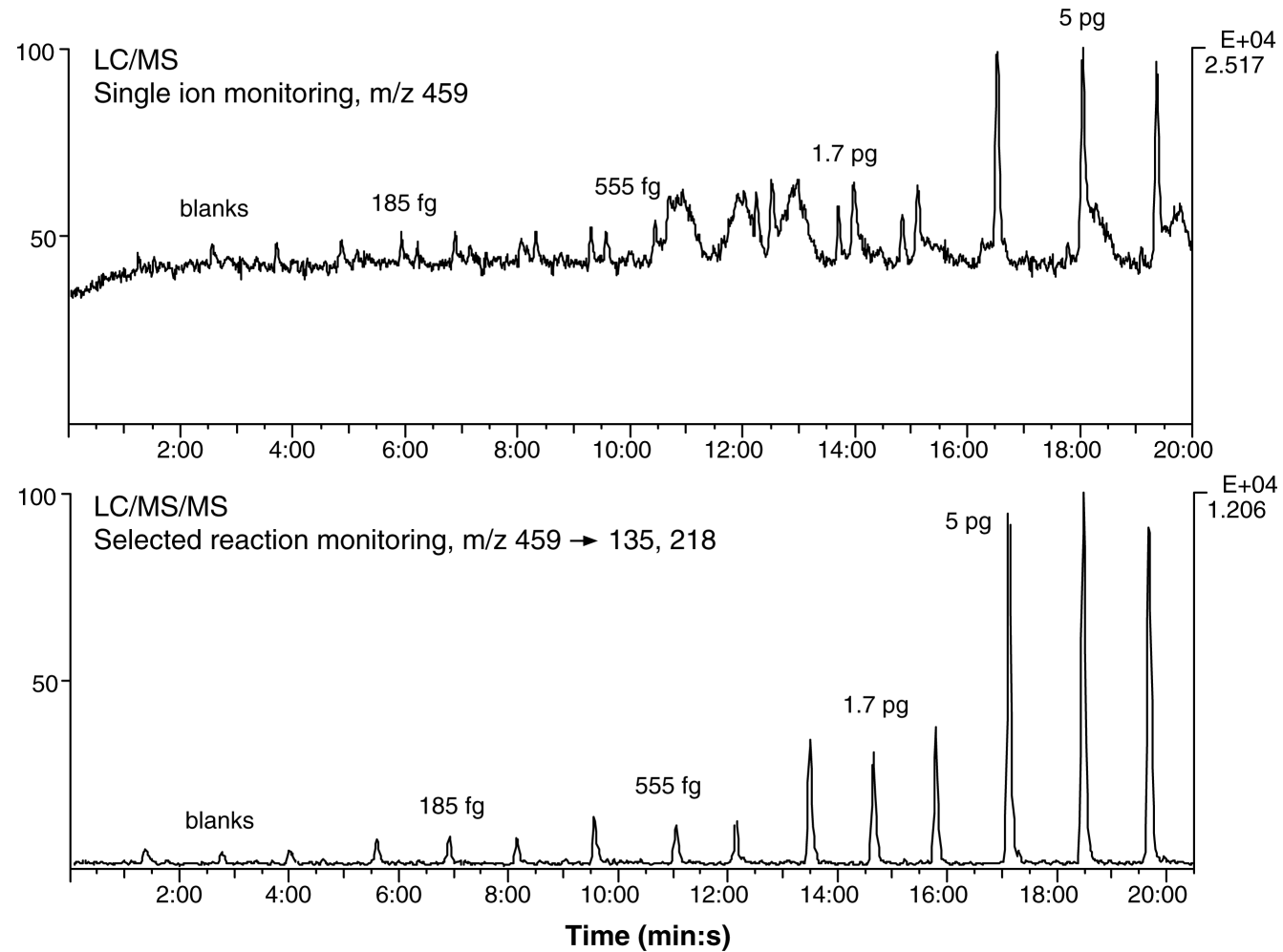
# LC/MS SIM vs. LC/MS/MS SRM Sensitivity/Selectivity

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 C<sub>18</sub> 73/27 MeOH/H<sub>2</sub>O/10 mM NH<sub>4</sub>OAc @ 400  $\mu$ L/min, no split, 5  $\mu$ 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

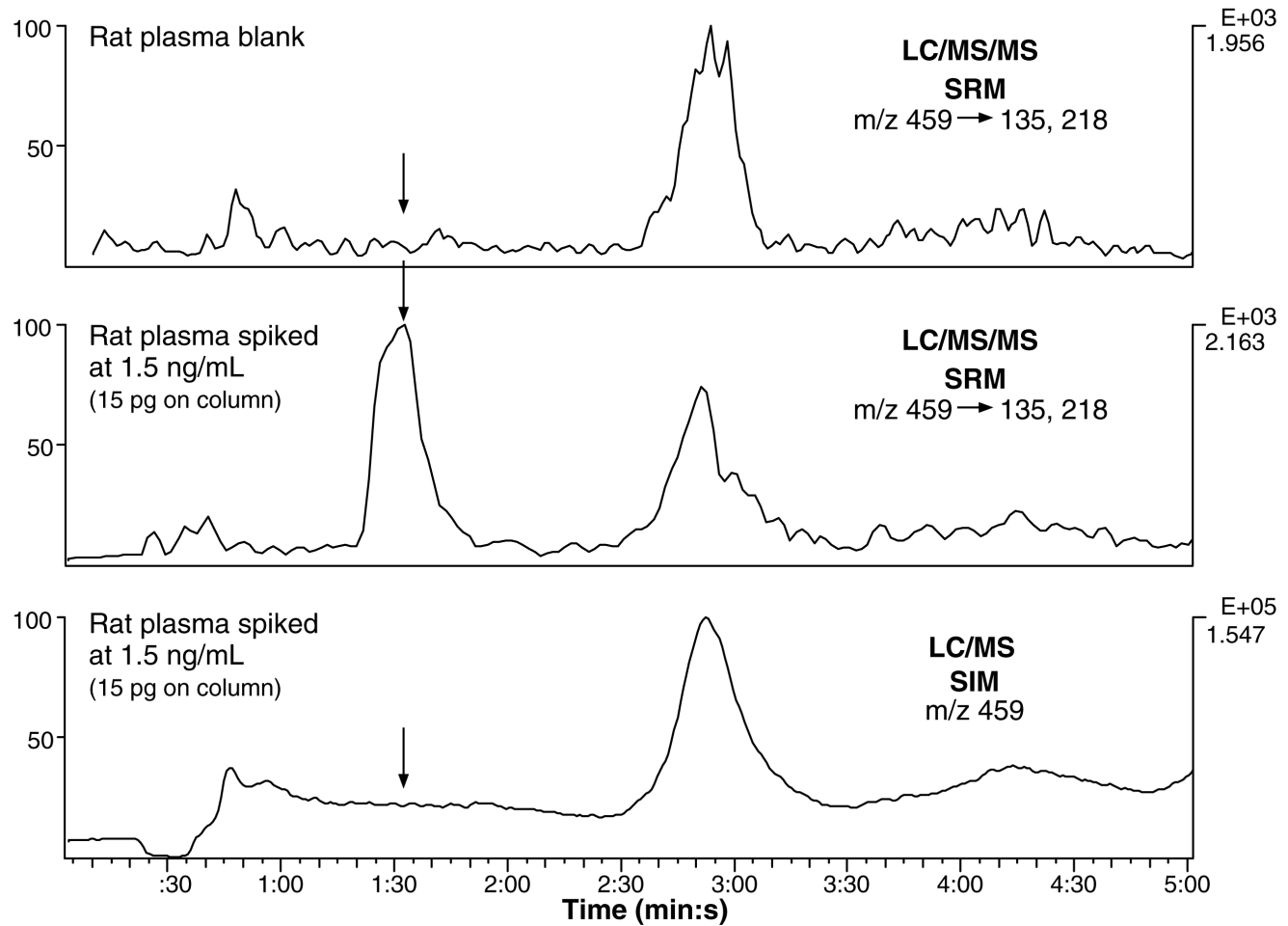
2.1 x 100 mm C<sub>18</sub> 65/35 MeOH/H<sub>2</sub>O/10 mM NH<sub>4</sub>OAc @ 400  $\mu$ L/min, no split, 10  $\mu$ L injections

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-MS<sup>3</sup>