

Information Dependent Acquisition (IDA): the Way to Go for LC-MS(/MS) Based General Unknown Screening (GUS)

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Introduction (1)

- GUS in (forensic) toxicology:
 - ✂ no foreknowledge → screen for as broad a range of compounds as possible

→ GC-MS

→ LC-MS

👉 Target component analysis

👉 Screening



Introduction (2)

- GUS ~ LC-MS(/MS)
 - Single MS using in-source CID
 - ✖ interfering ions complicate interpretation
 - MS/MS MRM
 - ✖ pre-experiment required
 - IDA (information dependent acquisition)
 - ✔ no foreknowledge required
 - ✔ clean MS/MS spectra obtained

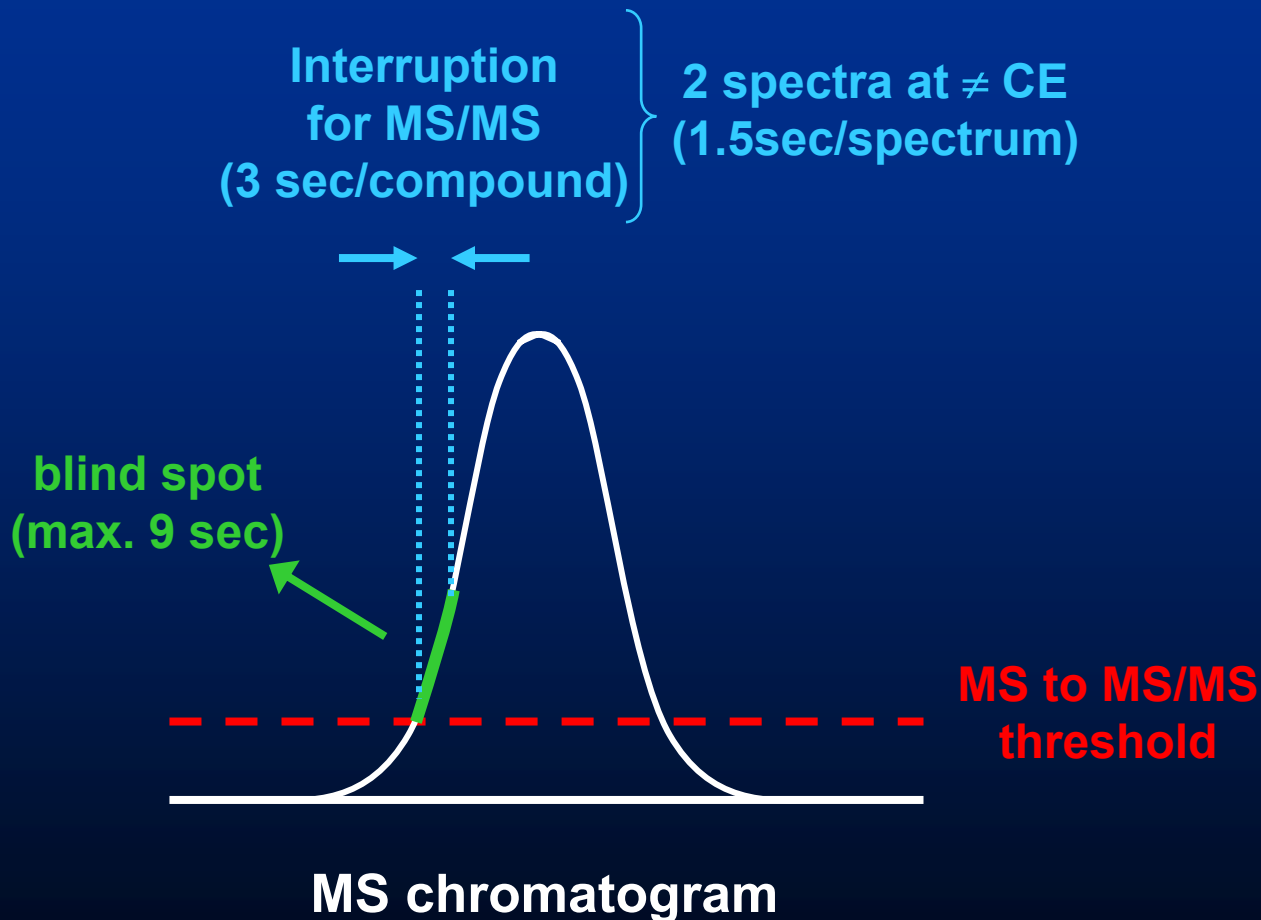


IDA – fundamentals (1)

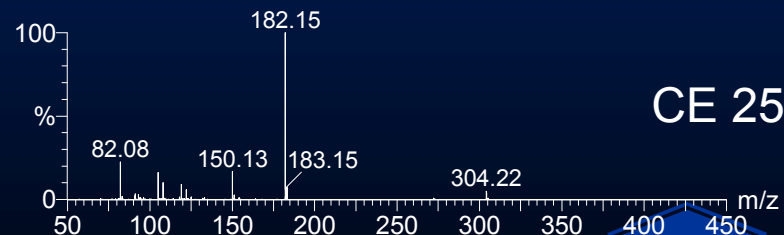
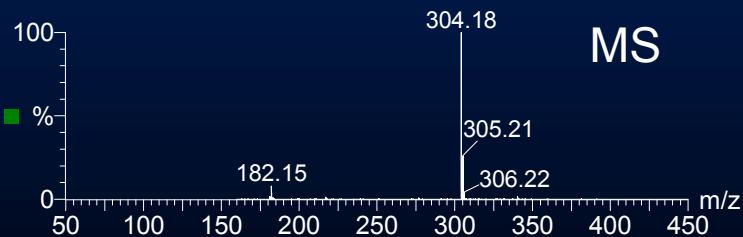
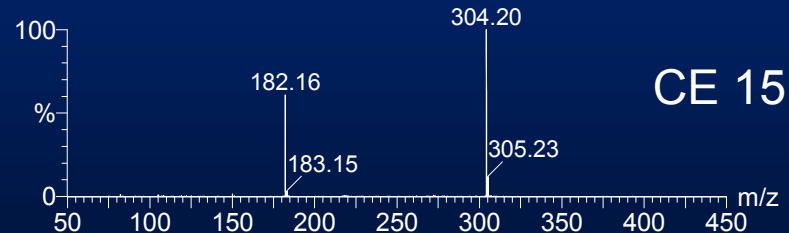
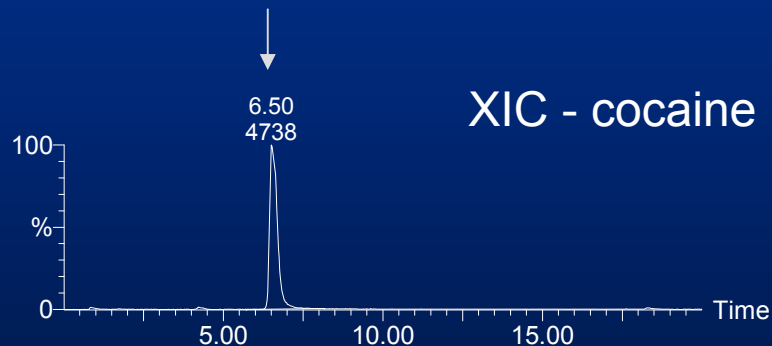
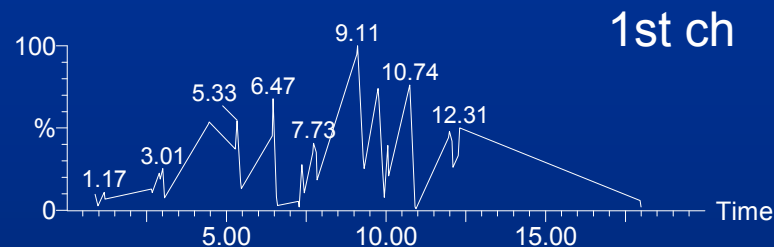
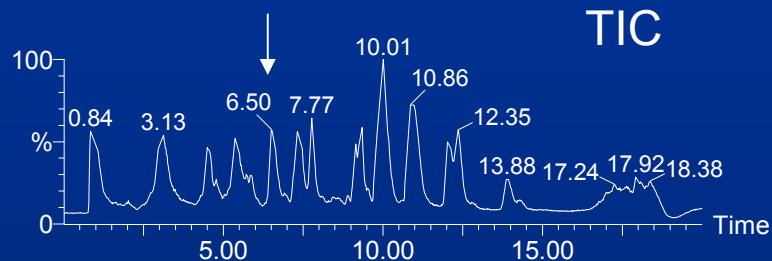
- Initially: QUAD = wide band-pass filter
 - ◆ precursor ion(s) $>$ MS threshold
 - ⇒ switch to MS/MS
 - product ions ⇒ TOF
 - ◆ product ion(s) $<$ MS/MS threshold
 - ⇒ switch back to MS



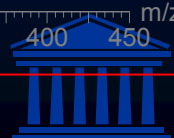
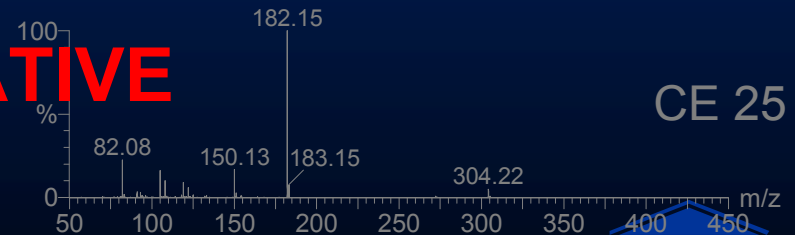
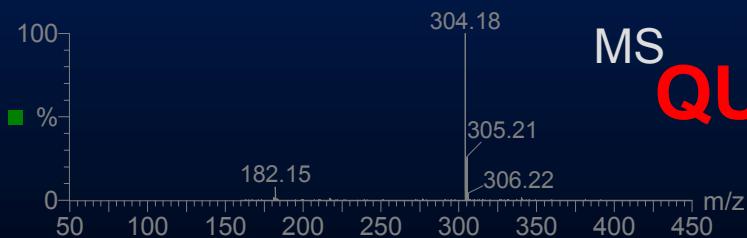
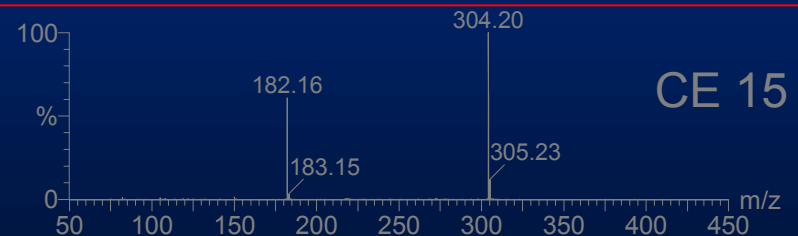
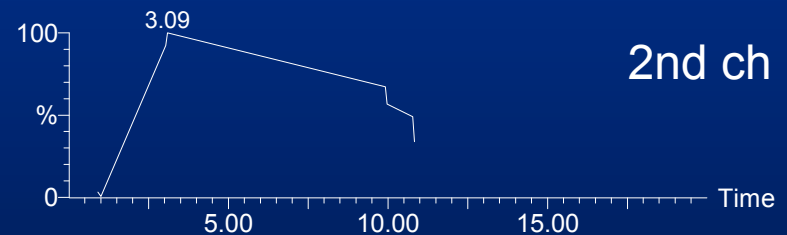
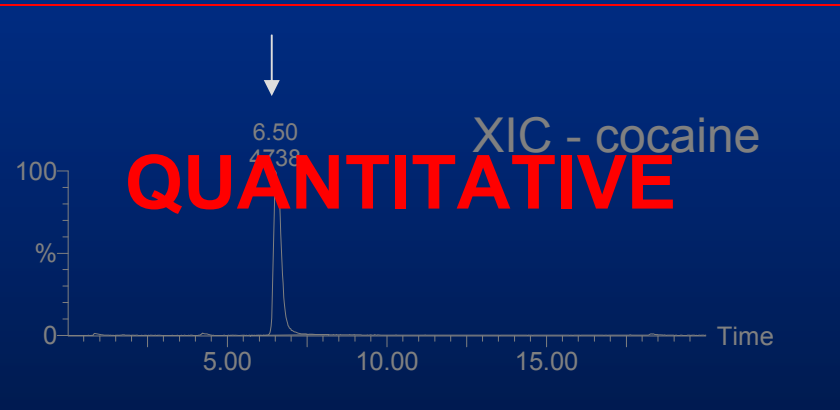
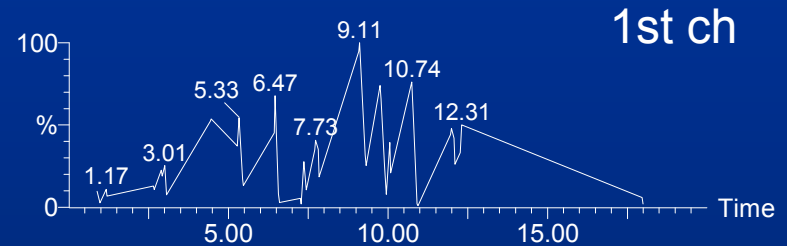
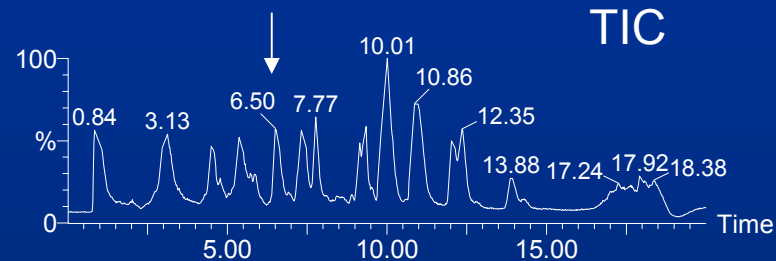
IDA – fundamentals (2)



IDA – fundamentals (3)



IDA – fundamentals (3)



IDA – past, present & future

- Not suitable
 - Triple quadrupole
- Suitable
 - Q-TOF (thanks to the high acquisition speed of the TOF)
 - Quadrupole/ion-trap (QTRAP)*
 - Maybe a future for recently developed fast scanning ion-traps

*P. Marquet et al., J. Chromatogr. B 789 (2003) 9-18



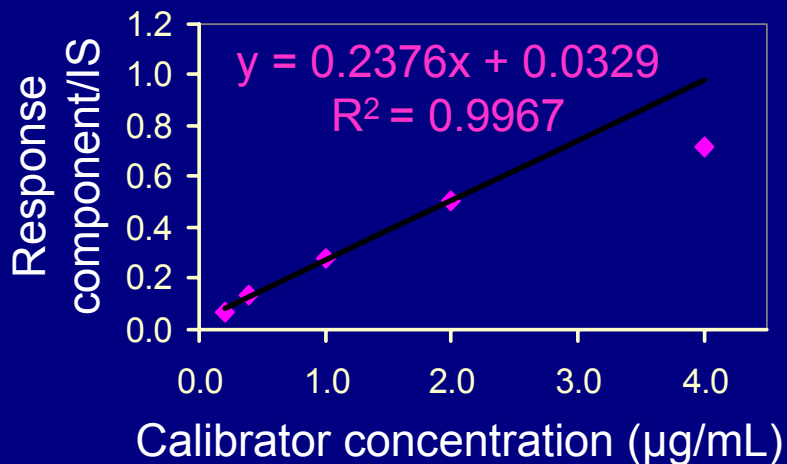
IDA – pro's & con's

- Pro's:
 - Selectivity ↑ & sensitivity ↑
 - No foreknowledge required
- Con's:
 - Difficult setting of MS threshold ~ variable background noise

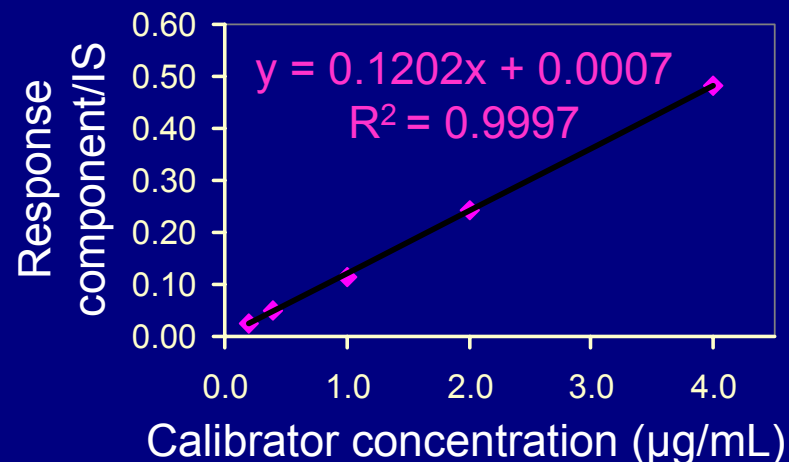


Quantitation results

HALOPERIDOL



NALORPHINE



⇒ Sometimes deviation from linearity due to linear dynamic range constraints

Ref.: K. Clauwaert et al., *Rapid Commun. Mass Spectrom* **13**, 1540 (1999)



Benchmarking of our technique

⇒ Based on the analysis of real samples, e.g.

ROUTINE METHOD		LC-MS
EMIT	HPLC-DAD ¹	
Morphine		Morphine (0.28 µg/mL)
Caffeine		Caffeine (0.38 µg/mL)
	Codeine (4.40 µg/mL)	Codeine (5.20 µg/mL)
	Bromazepam (hy) ²	Bromazepam (0.24 µg/mL)

¹ Ref. method on which quantitation is based

² Bromazepam benzophenone



Conclusions

- LC-MS(/MS) for GUS: yes, it is an option
- IDA could be the way to go
- Wealth of information obtained in 1 run
- Instrument cost
 - Relatively high for a standard toxicology lab
 - ✍ limits routine application so far

