University of California
San Francisco

Selecting and planning for the right mass spectrometer

MSACL US 2018
Palm Springs, CA

Wednesday, January 24th

Deborah French Ph.D., DABCC, FACB

University of California San Francisco

Learning Objectives

After this presentation, you should be able to:

- explain what specifications are important to consider when selecting a mass spectrometer
- explain what ancillary components are required for installation of a mass spectrometry system

Overview

- factors to consider when choosing instrumentation
- which type of instrument do you require?
- what else do you need?
- what resources are available?

Audience Poll

Have you used mass spectrometry before?

A. yes

B. no

Audience Poll

Are you

A. considering mass spectrometry for your lab?

B. in the process of bringing in mass spectrometry?

C. expanding existing mass spectrometry testing?

Initial factors to consider when choosing instrumentation

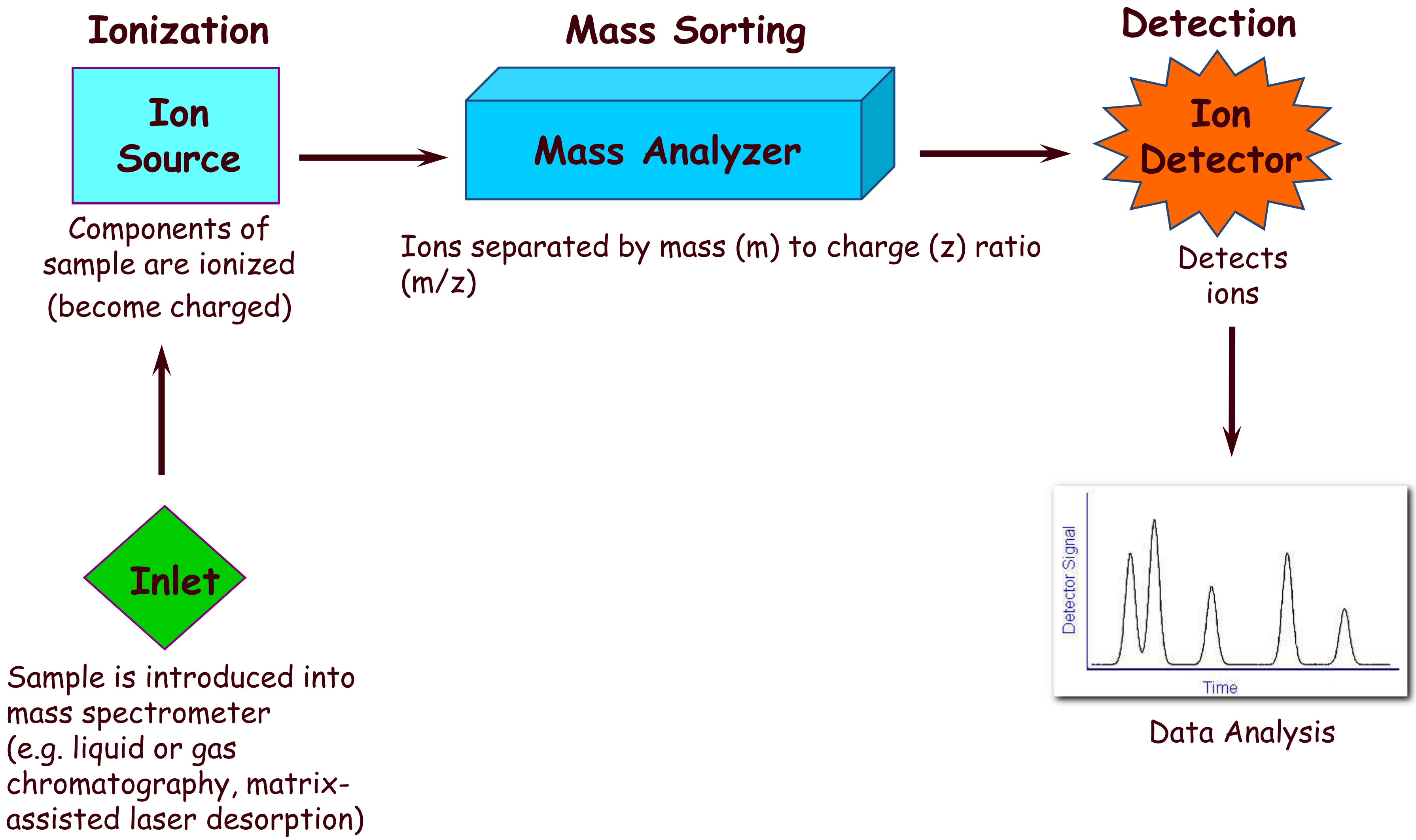
- what do you actually need for the applications you wish to implement?
  - analytes you wish to measure
  - quantitative vs qualitative methods
  - targeted vs untargeted methods
  - accurate mass determination required
  - sensitivity
  - throughput
  - robustness requirements

Initial factors to consider when choosing instrumentation (cont)

- what expertise do your technologists possess?
    - mass spectrometer has to be optimized for every single analyte you want to measure
    - not a “plug and play” technology

- what is the cost – direct and indirect – of implementation?

What are the components of a mass spectrometry system?

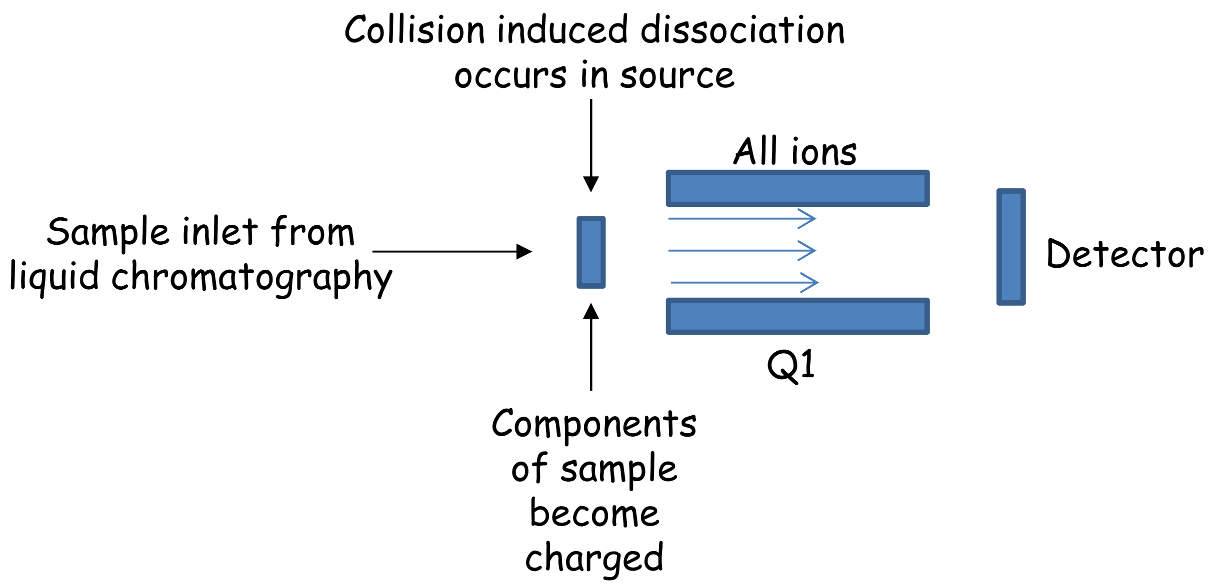


Mass Analyzers

Types of mass analyzers:

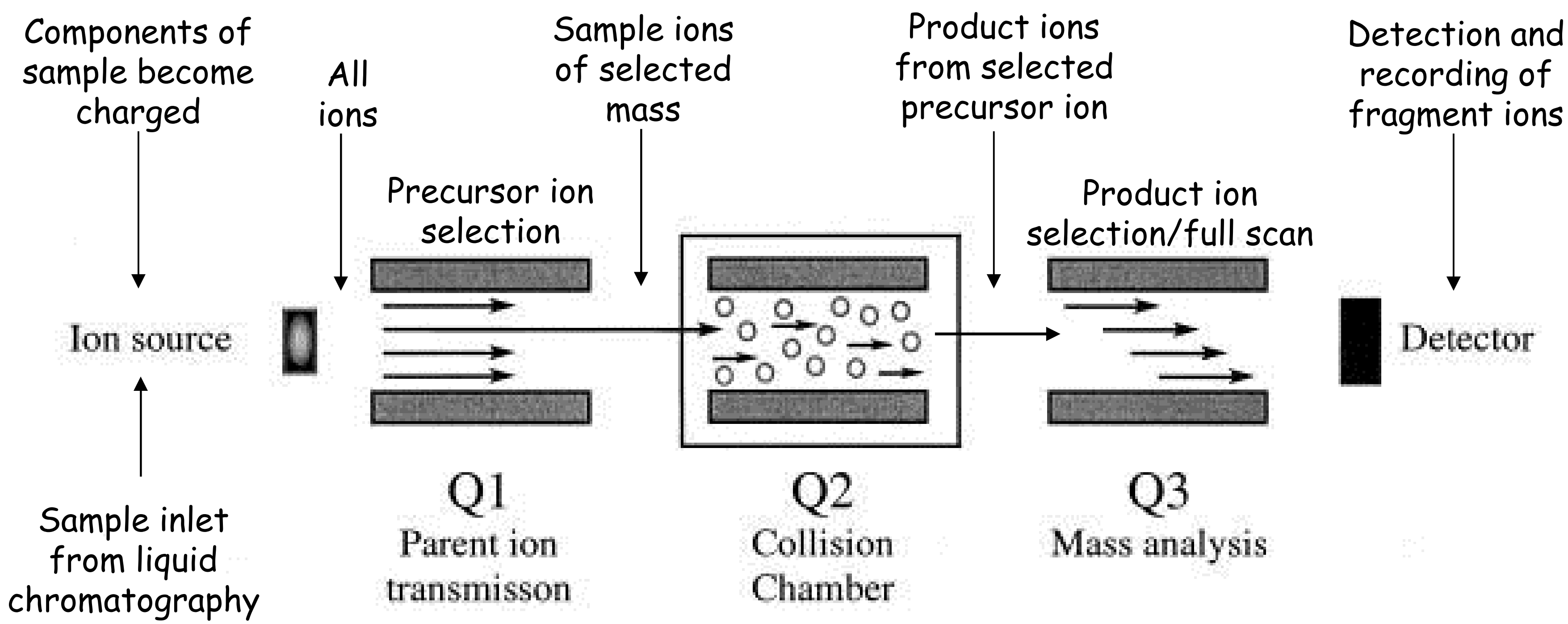
- single quadrupole
- triple quadrupole
- quadrupole ion trap
- time of flight/quadrupole time of flight
- fourier transform ion cyclotron resonance (FTICR)

Single quadrupole mass spectrometer



- only ions of desired mass to charge ratio reach detector when using optimized voltages for analyte of interest
- all analytes with that mass will be detected
- can also scan across a mass range by varying voltages
- not as specific as other instruments

Triple quadrupole mass spectrometer



Q1. Ions of interest are selected (precursor/parent ions)
Q2. Fragmented into smaller product ions
Q3. Product ions separated by mass (m) to charge (z) ratio (m/z)

- also known as a tandem mass spectrometer (MS/MS)
- very selective so best for quantitative analysis
- poor scanning capabilities

Quadrupole Ion trap mass spectrometer

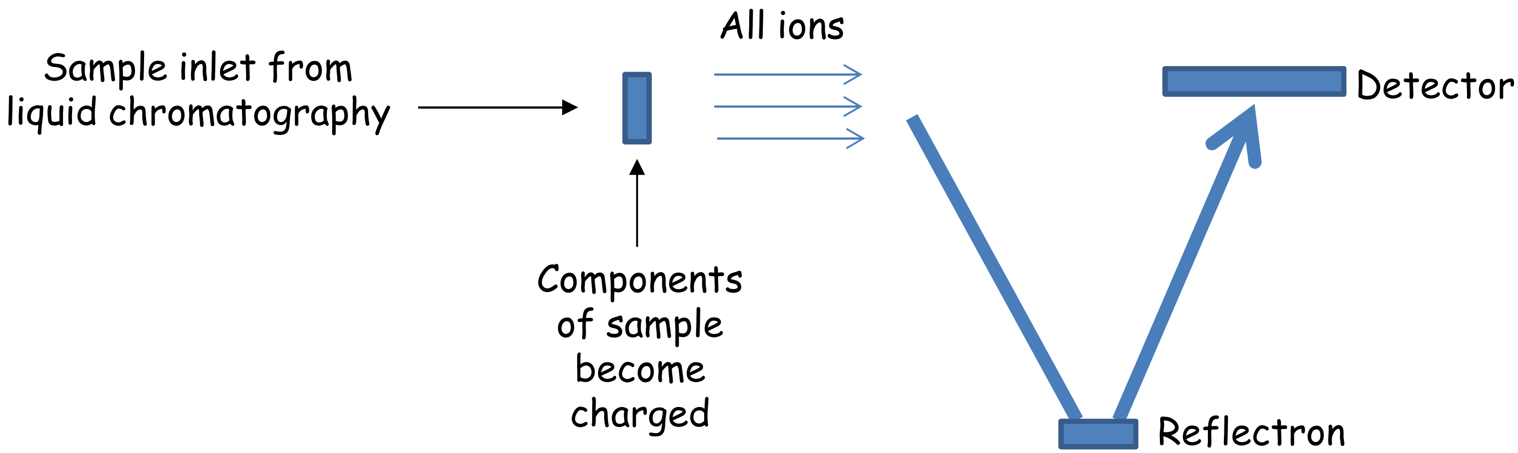
- quadrupole used to generate a field that functions to "trap" ions without destroying them
- ideal for qualitative analysis and elucidation of ion structure
- not as useful for quantitative analysis due to capacity limitations of the trap
- can be used to produce product ion spectra if used with MS/MS
    - an extra layer of selectivity

How is triple quadrupole mass spectrometry commonly used in the clinical laboratory?

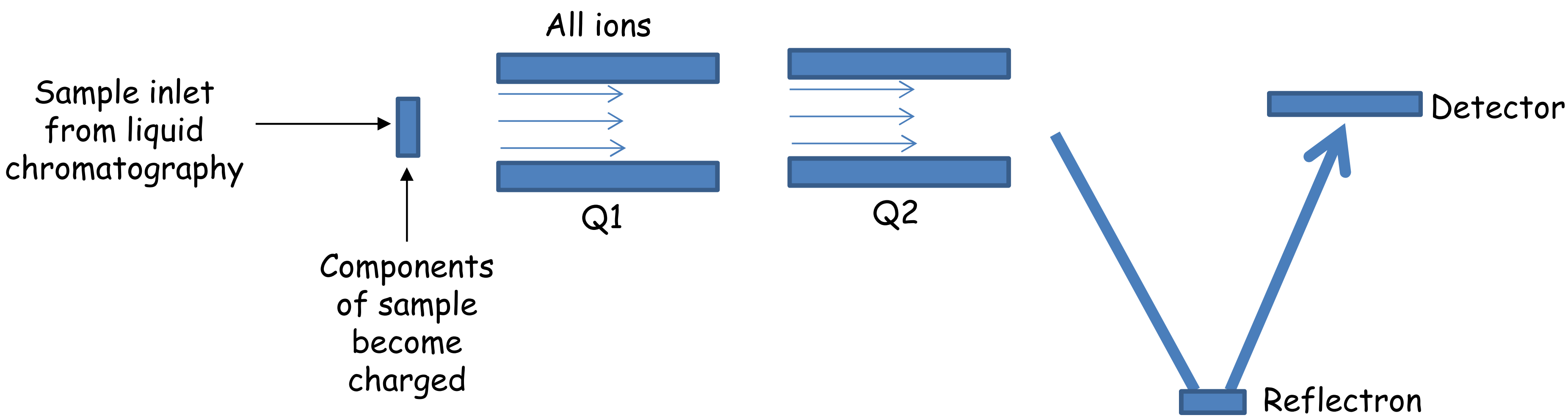
- small molecules
  - steroid hormones
    - testosterone, estradiol, 25-hydroxyvitamin D
  - thyroid hormones
    - free T4, free T3, T4, T3
  - therapeutic drug monitoring
    - cyclosporine, tacrolimus, sirolimus, busulfan, voriconazole, posaconazole, ketoconazole, itraconazole
  - toxicology
    - drug confirmations (opioids, amphetamines, cocaine metabolite etc), comprehensive drug screens
- proteins/peptides
  - thyroglobulin, insulin-like growth factor 1 (IGF-1)

High resolution mass analyzers

Time of flight MS (TOF-MS)

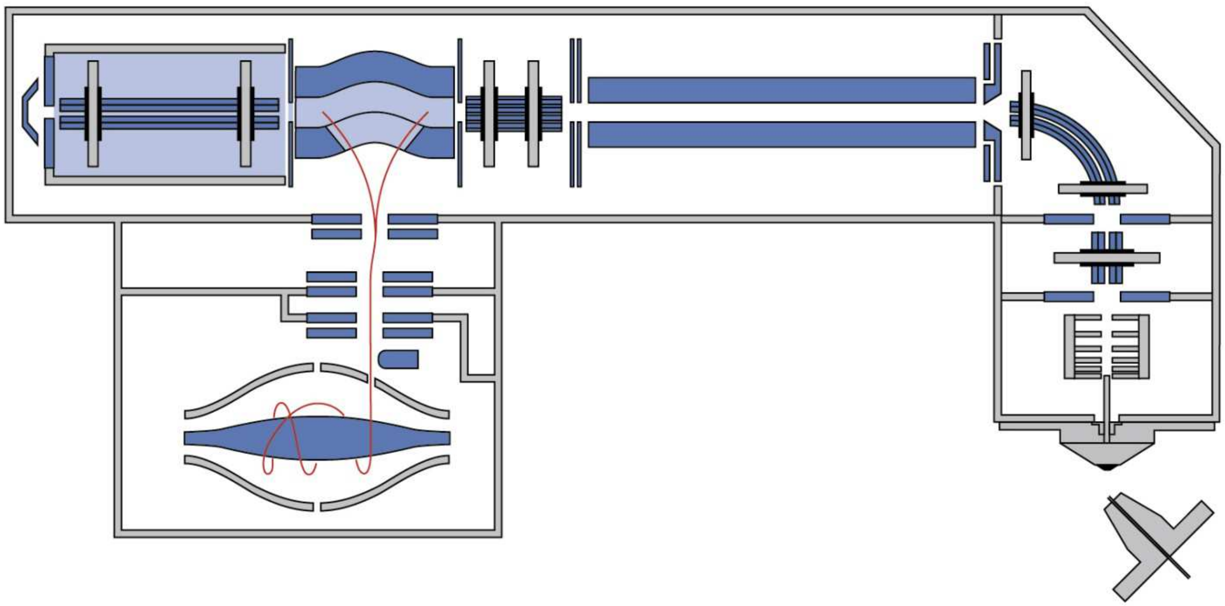


Quadrupole time of flight MS (QTOF-MS)



Fourier transform ion cyclotron resonance MS

- FTICR-MS (Orbitrap technology uses similar principles)



- ions trapped in a cell inside a strong magnetic field and move in circular orbits in a plane perpendicular to magnetic field
- RF electrical potential is applied to transmitter plates causing trapped ions to be excited into larger circular orbits
- frequency of motion of ion is inversely proportional to its mass

How is high resolution mass spectrometry commonly used in the clinical laboratory?

- toxicology
  - comprehensive drug screens
- microbiology (with MALDI ionization source)
  - identification of bacteria, fungi and mycobacteria
- proteins/peptides
  - thyroglobulin, insulin-like growth factor 1 (IGF-1)

Which type of instrument do you require?

	LC-MS	LC-MS/MS	LC-TOF-MS	LC-QTOF-MS	FTICR
Specificity	++	+++	++	+++	+++
Sensitivity	++	+++	++	+++	+++
Resolution	Low	Low	High	High	Highest
Mass Accuracy	~0.1 units	~0.1 units	~0.01 units	~0.01 units	~0.0001 units
Operational difficulty	++	+++	+++	++++	++++
Suited for which Applications?	Targeted Quant	Targeted Quant	Targeted or untargeted Qual	Targeted or untargeted Quant	Targeted or untargeted Quant
Cost	$$	$$$-$$$$	$$	$$$$	$$$$$

DO NOT FORGET THE COST OF A SERVICE CONTRACT – SIGNIFICANT $$$

(Quant: quantitative analysis; Qual: qualitative analysis)

Problem solving

Your lab manager has asked you to develop a method to quantify total testosterone by mass spectrometry in pediatric and female patients.

What type of mass spectrometer would be best suited for this application?

A. TOF

B. FTICR

C. MS

D. MS/MS

Other considerations for implementing mass spectrometry

- mass specs are heavy! and large!
- and they generate heat

- need to move cabinets?
- electrical supply
- gas supply – nitrogen, argon
- exhaust
- UPS or back up power
- roughing pump and oil (and disposing of oil)

Other considerations for implementing mass spectrometry (cont)

- mass spectrometry vendor should be able to give you a site guide documenting the requirements for the instrument

- optional (but really nice!) - interface between mass spectrometer and laboratory information system

All of these components can add $$$ to the cost of implementation!

What resources are available?

- colleagues already running mass spectrometry methods
  - invaluable resource
  - can give you "real world" experience with instrumentation
- mass spectrometry vendors
- attend conferences specializing in mass spectrometry
  - e.g. MSACL, ASMS, AACC/MSSS
- literature search
  - can see what instrumentation other clinical laboratories use to measure specific analytes in clinically relevant concentration ranges

Conclusions

- make a list of what your laboratory needs ahead of time with regards to sensitivity, robustness, throughput etc
- mass analyzers vary in specificity, sensitivity, cost and ease of use – should be chosen wisely in terms of desired applications
- don't forget the "extras" such as gas and electrical supply, exhaust, service contract etc as the cost is significant

References/Resources

- Clinical and Laboratory Standards Institute (CLSI). *Mass Spectrometry in the Clinical Laboratory: General Principles and Guidance; Approved Guideline.* CLSI document C50-A
- Clinical and Laboratory Standards Institute (CLSI). *Liquid-Chromatography-Mass Spectrometry Methods; Approved* Guideline. CLSI document C62-A
- Wu AH, Gerona RR, Armenian P, French D, Petrie M, Lynch KL. *Role of liquid-chromatography-high-resolution mass spectrometry (LC-HR/MS) in clinical toxicology*. Clin Toxicol. 2012. 50(8):733-742
- SelectScience Mass Spectrometers Buying Guide. http://www.selectscience.net/mass_spectrometry_buying_guide.aspx (Accessed November 7th 2017)
- French D, Terrazas E. *The successful implementation of a licensed data management interface between a Sunquest laboratory information system and an AB SCIEX mass spectrometer.* J. Pathol. Inform. 2013. 4:1
- https://www.aacc.org/publications/cln/articles/2015/february/implementing-mass-spec-part-one
- https://www.aacc.org/publications/cln/articles/2015/may/implementing-mass-spectrometry-in-the-clinical-lab

University of California
San Francisco

Deborah French

University of California San Francisco

Email: deborah.french@ucsf.edu