

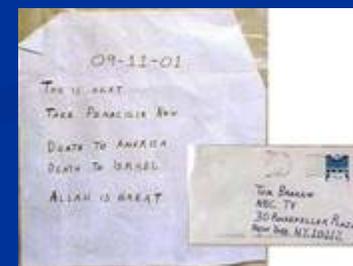
μ ChemLab™: Hand-Portable Microanalytical Instrument for BioAnalysis



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Livermore, California

Sandia's interest started in biodetection with our national security mission

- Objective: Develop miniature, low cost chemical analysis systems for national security applications
 - First responders
 - Facilities monitoring
- Target is the full spectrum of CB agents
- Requirements:
 - Rapid detection for detect-to-warn
 - Low power for field use
 - Low false alarm rate
 - Little or no consumables
 - Adaptable to new threat agents
- Funding start: Internal Sandia LDRD (1996)
- Major program sponsors: DOE Chemical and Biological National Security Program and Dept. of Homeland Security



The μ ChemLab Program has seen tremendous growth over 8 years

**Start
(1996)**



SNL LDRD
Chem-explosives
Detector



DOE CBNP

- Proof of concept device
- Biotoxins



- Second generation device
- Viruses

Tenix/CH2M Hill
Biotoxin detection in
water

DHS
Biotoxin & Virus
Detector

DoD
Modular Chem-Bio Detector
• Bacteria

NIH
Oral Diagnostics

**Today
(2005)**



Instrumentation for chemical analysis is built for the lab not the field

Agilent Capillary
Electrophoresis
System



Caliper Chip-Based System



Waters Capillary
Liquid Chromatography
System



Portable biodetectors are now becoming commercially available

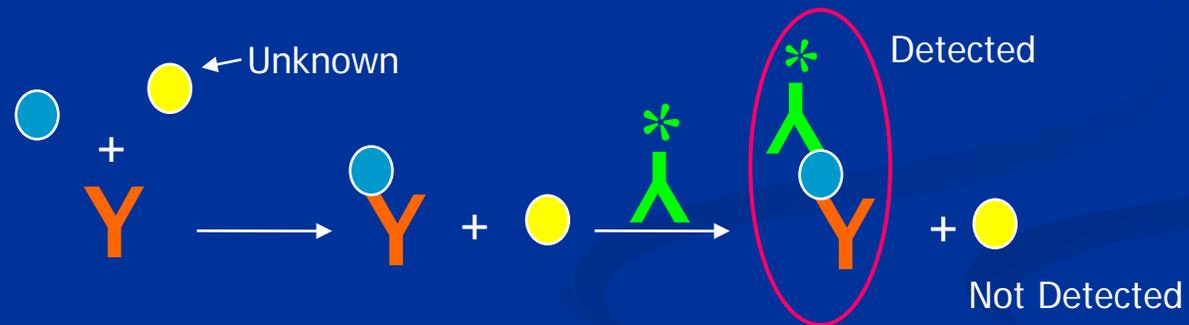
Example Systems	Detection Technology	Advantages	Disadvantages
RAZOR (Idaho Technologies) Bio-Seeq (Smiths Detection)	PCR	<ul style="list-style-type: none"> ■ Hand-held, 6-9 lbs ■ Very sensitive ■ 6-12 samples/30 min ■ Can detect viruses & bacteria 	<ul style="list-style-type: none"> ■ Cannot detect toxins ■ Expensive reagents ■ Manual sample prep (kit or cartridge) ■ 30 min cycle time ■ 5 runs/battery
RAPTOR (Research International)	Antibody	<ul style="list-style-type: none"> ■ Can detect toxins, viruses, bact. ■ Hand-portable, 14 lbs ■ Sensitive ■ 10-15 min ■ No sample prep 	<ul style="list-style-type: none"> ■ Expensive reagents ■ Must replace coupon after positive result or fouling ■ 8 hr continuous use/battery ■ 4 simultaneous assays ■
μChemLab (SNL prototype)	Chemical Separations	<ul style="list-style-type: none"> ■ Can detect toxins, viruses, bact. ■ Hand-held ■ No expensive reagents ■ Sensitivity (w/ preconcentration) comparable to Ab assay ■ 10-15 min 	<ul style="list-style-type: none"> ■ Sensitivity, specificity still unknown in real samples



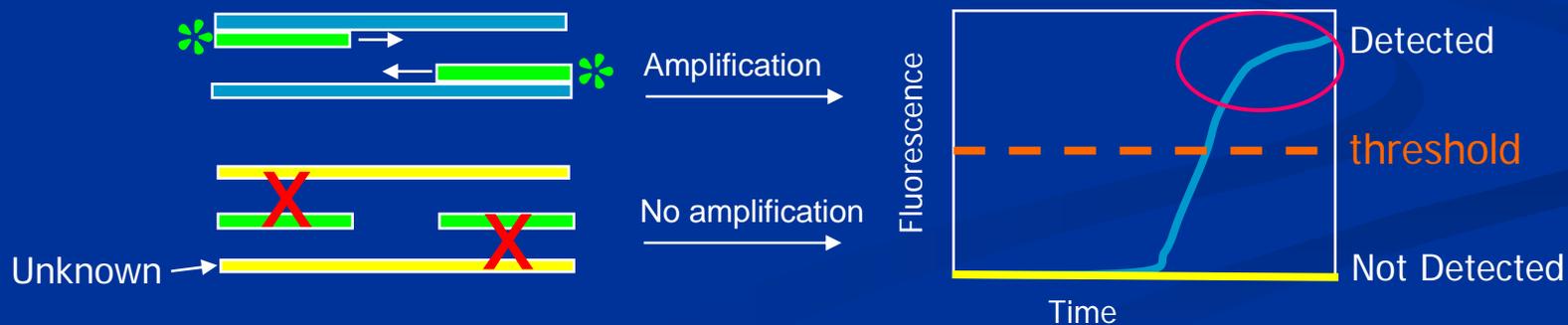
Ab and PCR methods require molecular recognition event for detection

- Only see what you have primers or antibodies for
- These reagents can be expensive

Antibody-based detection (sandwich assay):

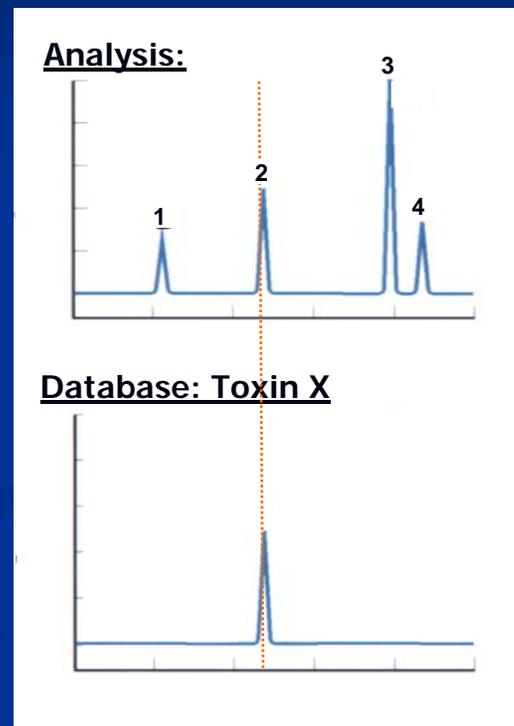


PCR detection:



Chemical separations enable detection of unknowns

- Unique signatures are created from a pattern of separation times
- Signals are matched to a database
- Even if the signature isn't in the database, may still be able to gain useful information
 - e.g., molecular weight, charge, hydrophobicity
 - What it is like
 - What it is not like



Identification:

- 1: no match
- 2: match = Toxin X
- 3: no match
- 4: no match

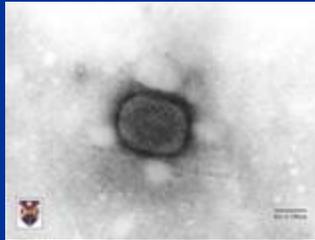


μChemLab uses a proteomics-based approach for bio agent detection



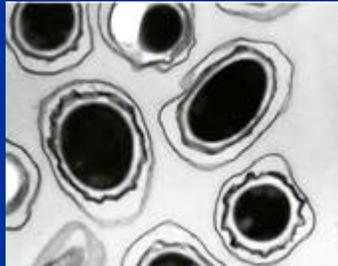
Toxins

- 1-10 nm
- Protein or small molecule
- May have variants



Viruses

- 50-200 nm
- 1-50 proteins
- May have host specific proteins



Spores

- 1 μm
- 50+ proteins
- Vary in copy number



Bacteria

- 1-3 μm
- 2000-5000 proteins
- Protein content dependent on growth conditions

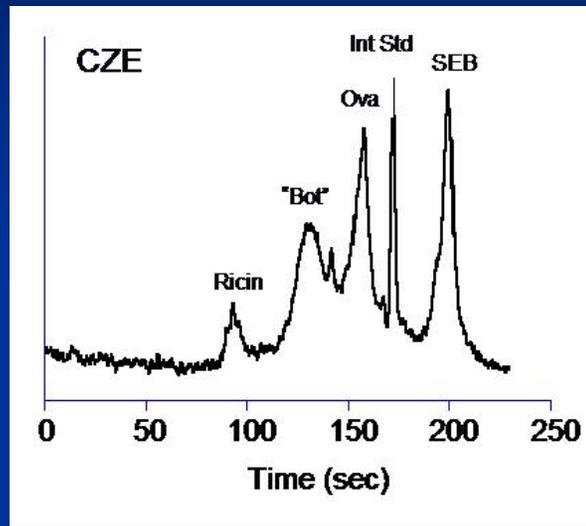
Approach:

- Direct detection of protein toxins
- Detection of pathogens by their protein signatures

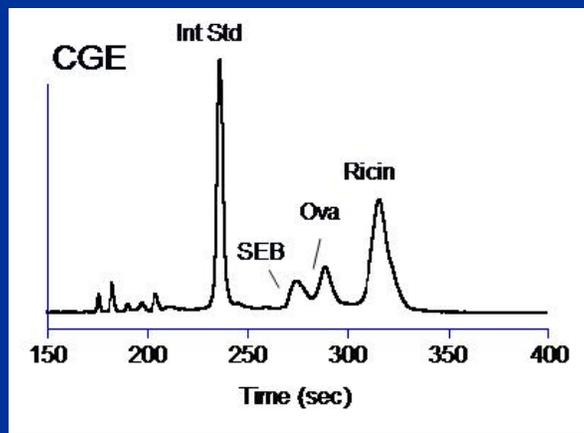
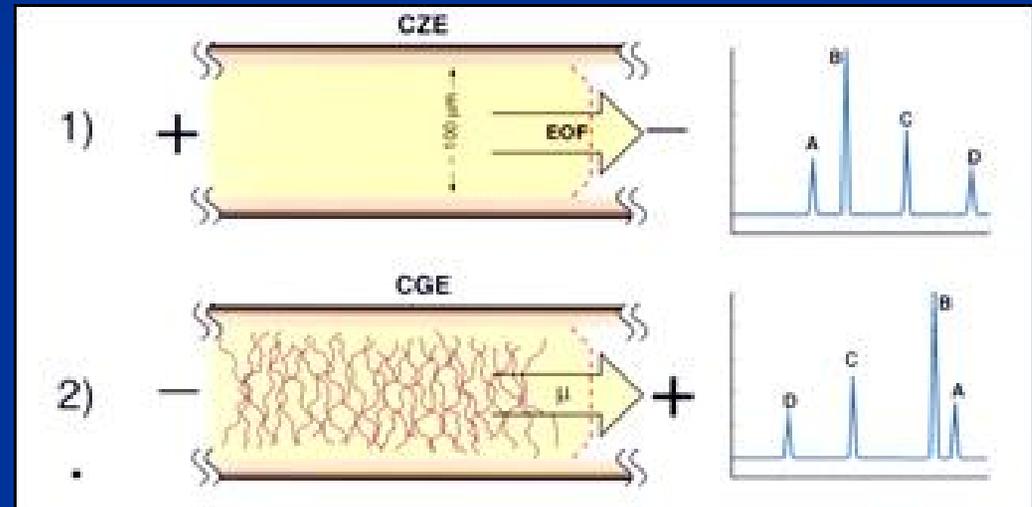
Increasing complexity



Protein detection uses two separation methods for improved detection reliability

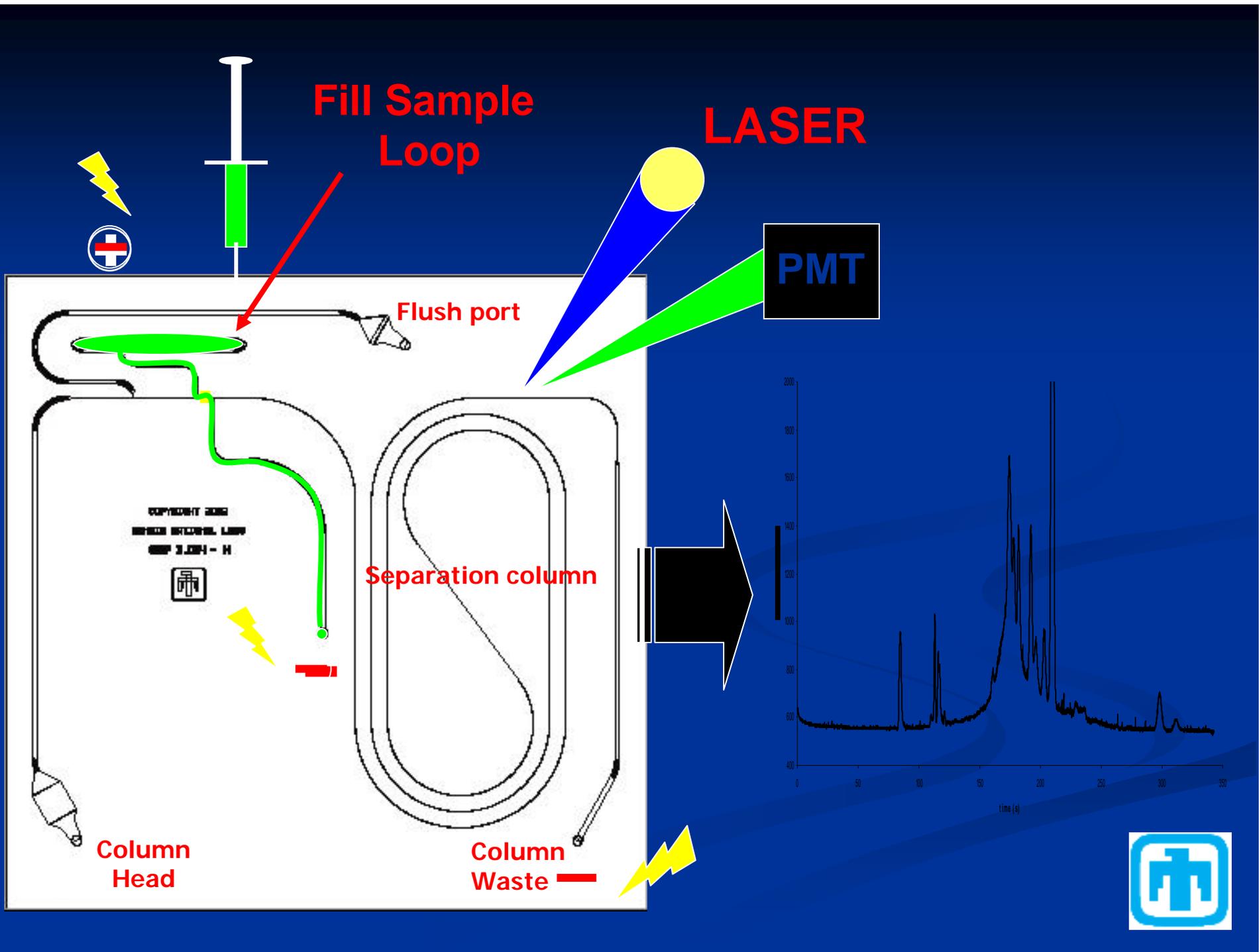


Separation based on charge/mass ratio

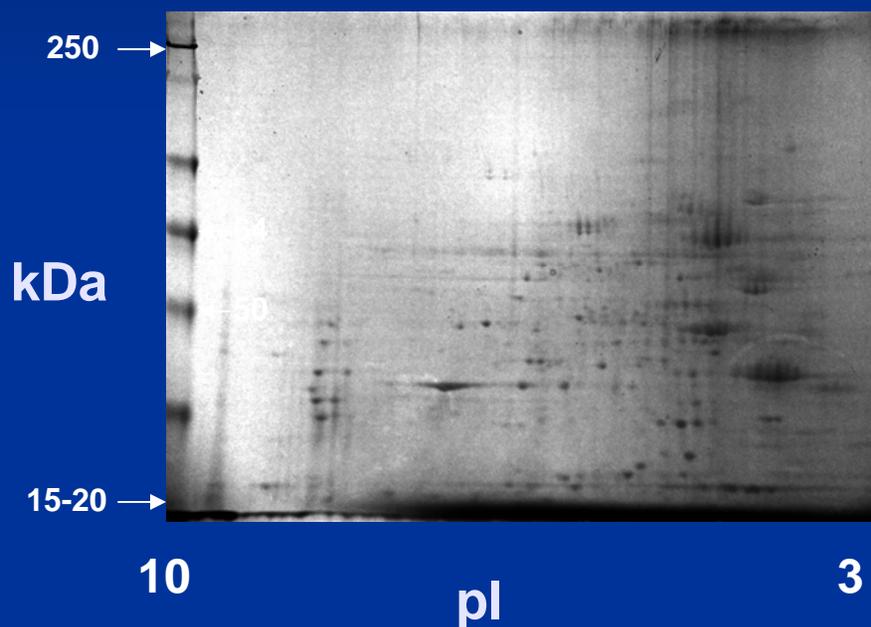


Separation based on mass



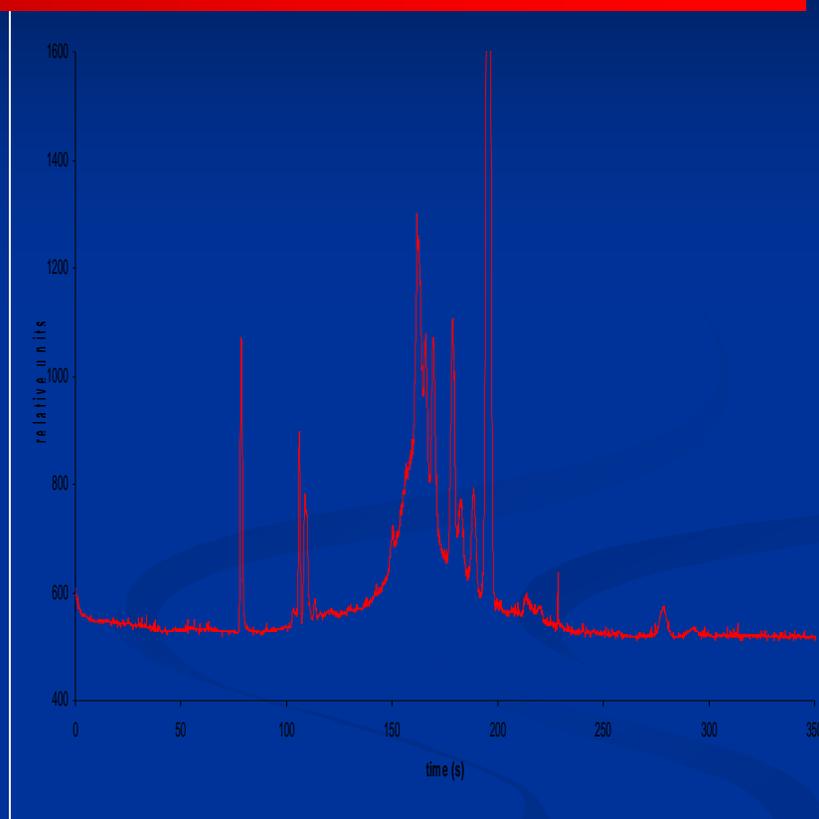


Microfluidic methods are much faster than traditional protein separation/detection methods



2 D Gel (SDS/PAGE)

- Informative
- Time Consuming (Hrs to Days)
- Difficult To Reproduce

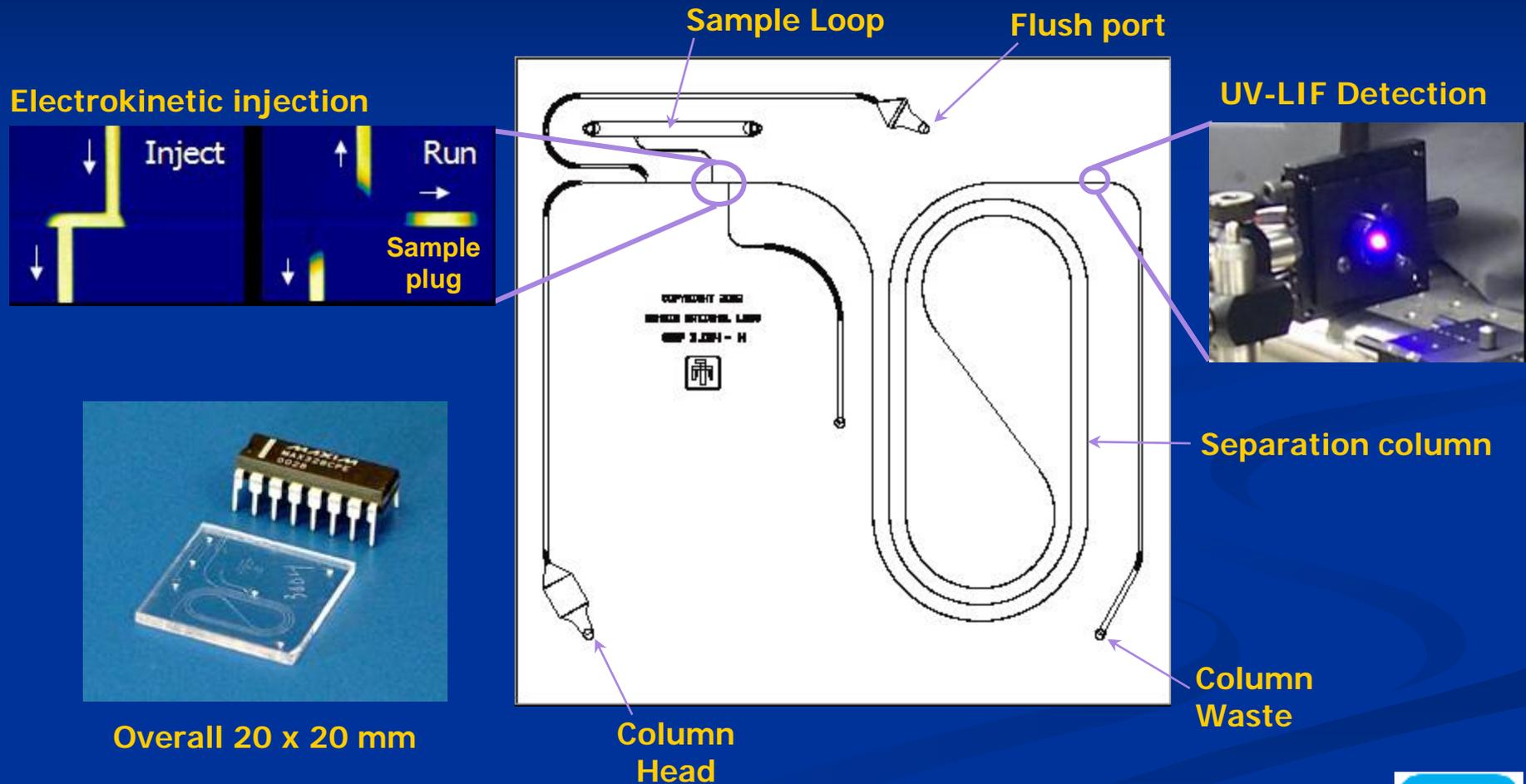


CZE or CGE

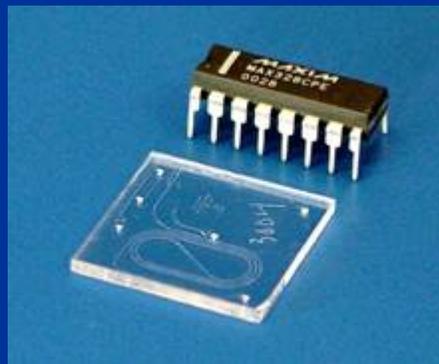
- Not as Informative as 2D
- Fast (less than 10 minutes)
- More Reproducible



Microfluidic chip performs nanoliter sample analysis in 5-10 minutes



Electrokinetic injection

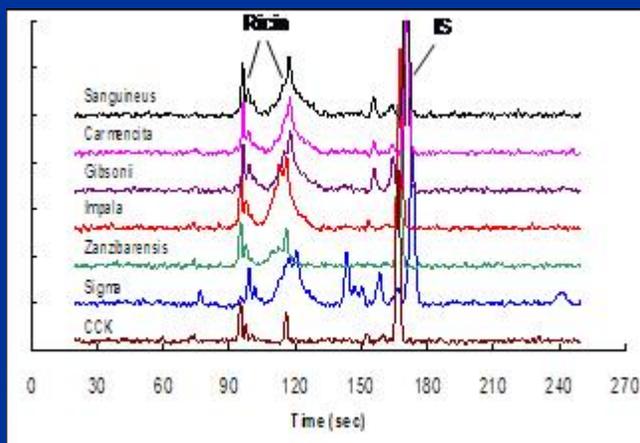
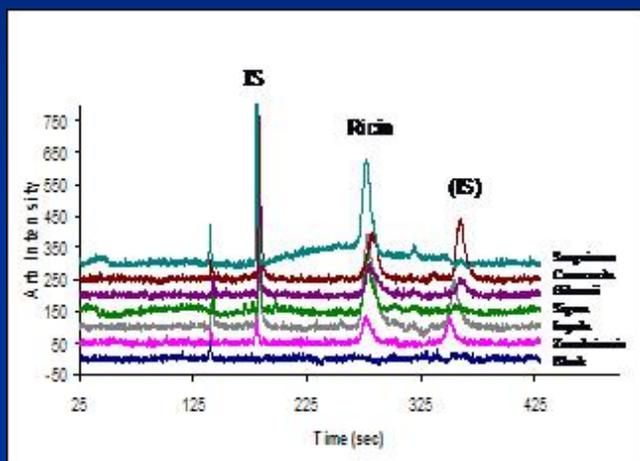


Overall 20 x 20 mm

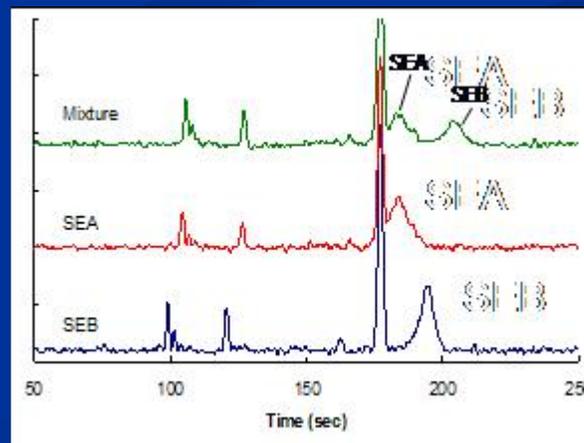
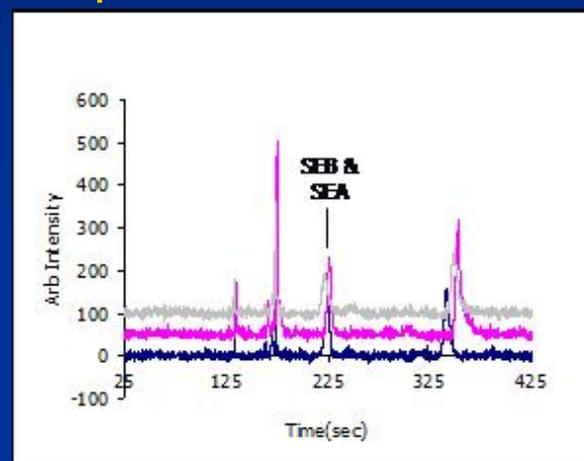


The MicroChemLab instrument has the ability to detect and distinguish toxin variants

Ricin variants



Staph enterotoxin variants



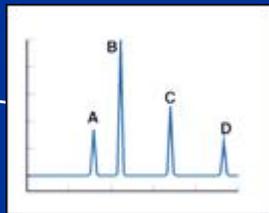
Analyses performed at Defense Science and Technology Laboratory, Porton Down, UK



Sandia's approach: Think about the whole system

Application Space

- Solution is broadly applicable



User Requirements

- Low power
- Semi-continuous operation

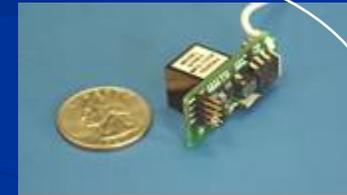
Control Software



High Sensitivity Detection



Miniature Power Supplies



MicroFluidics

- Optimized chip designs
- Fluid delivery



We cover the full spectrum: from fundamental microfluidics to biochemistry to engineered solutions



μ ChemLab contains everything necessary to perform an analysis

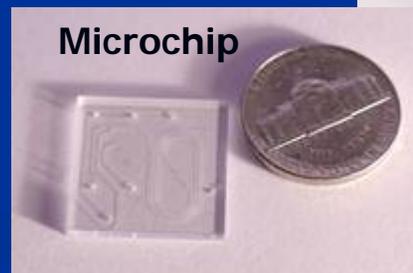
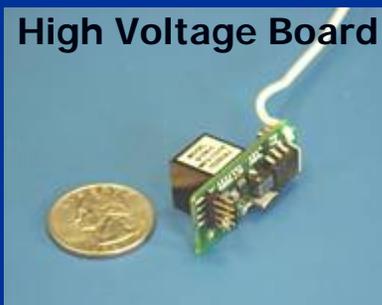
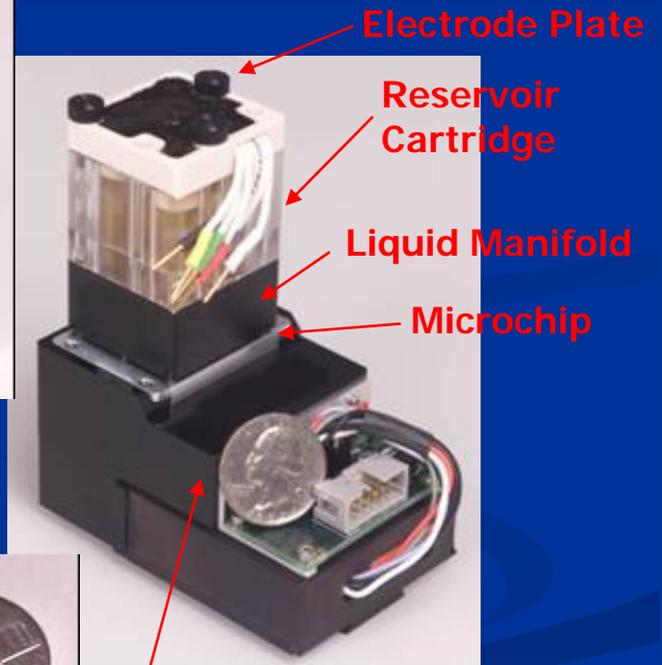
We use this instruments now as flexible, reliable platforms for routine laboratory R&D



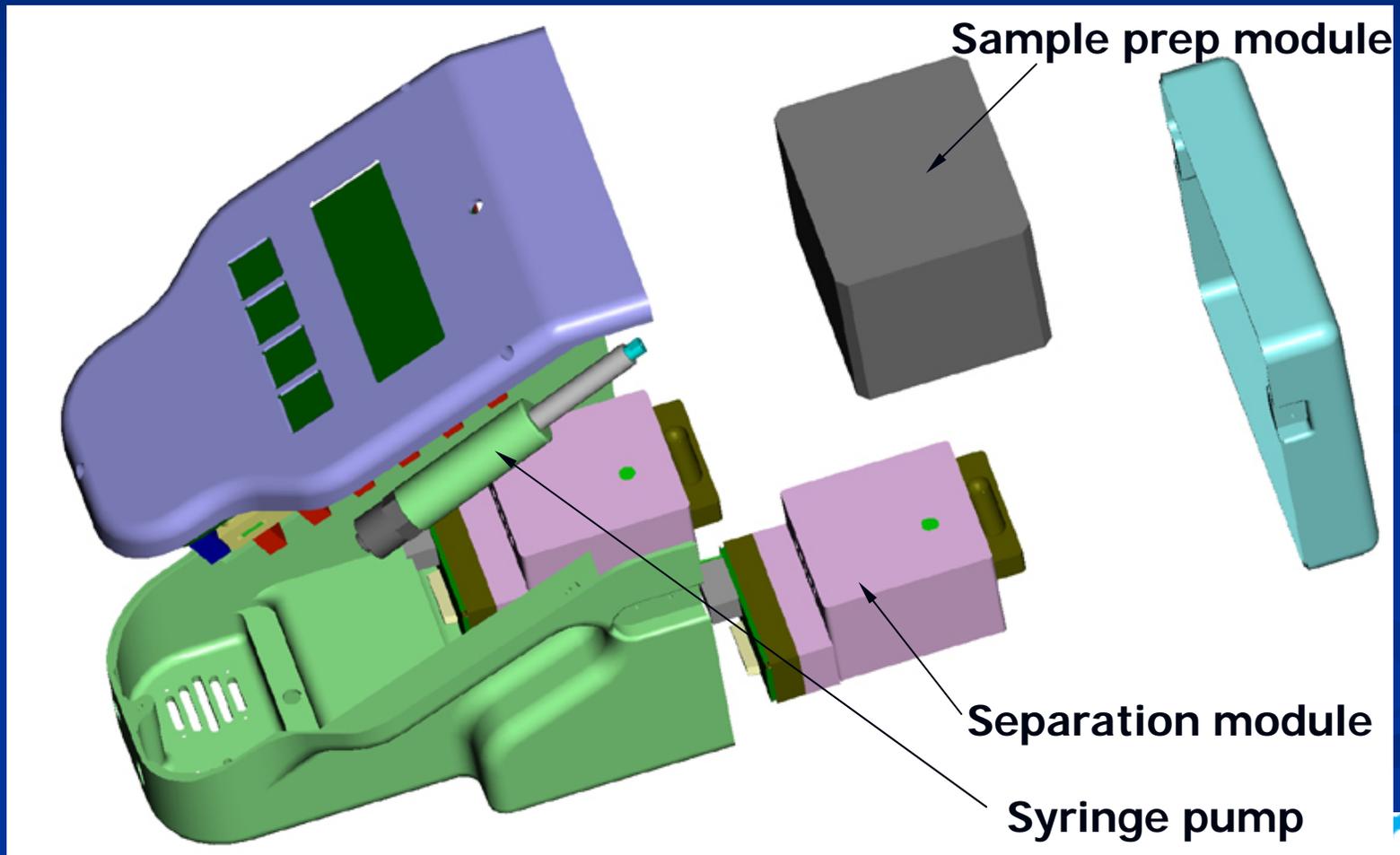
- Hand portable
- Battery operated
- On-board data analysis



- Modular packaging
- Two analysis modules



Modular design enables straightforward component replacement & upgrades

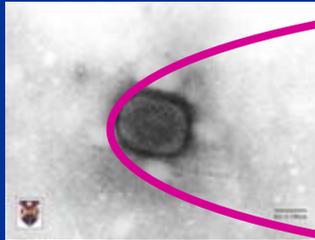


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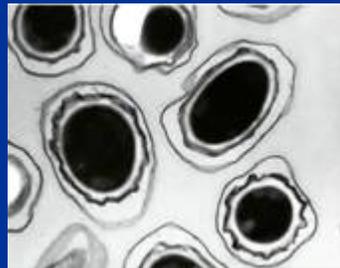
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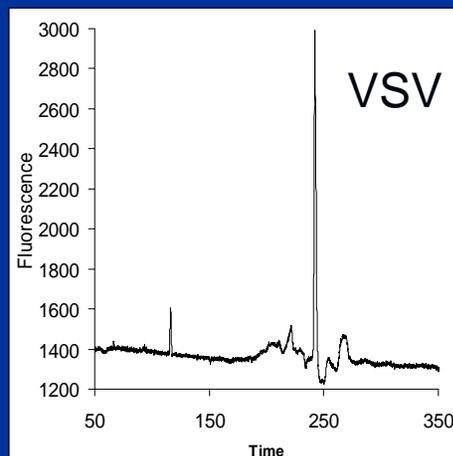
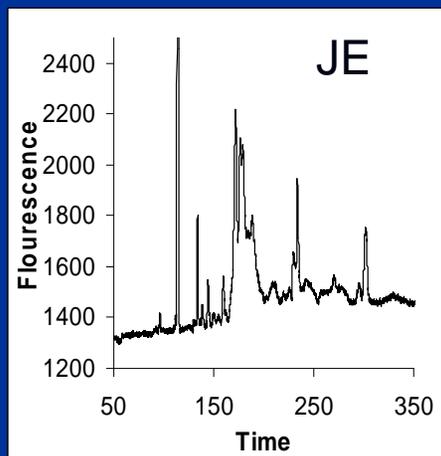
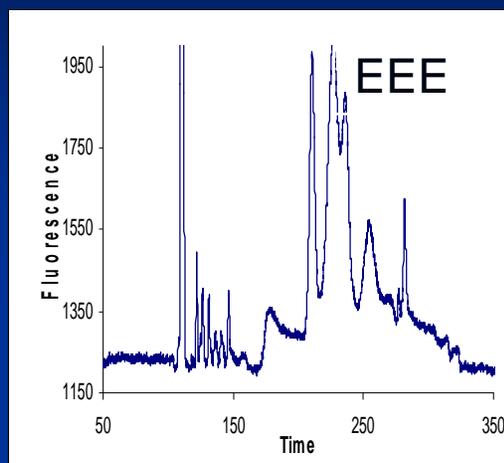
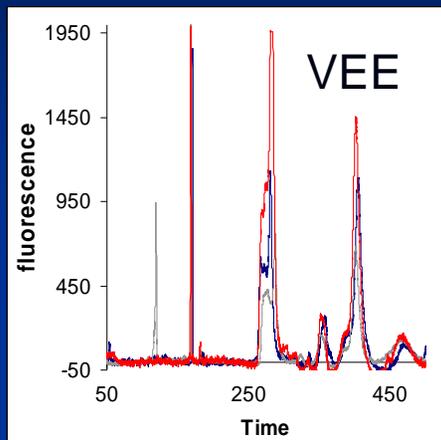
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Increasing complexity



Signatures for a broad range of viruses demonstrates the ability of μ ChemLab to identify these pathogens



- Testing at USAMRIID and SNL
- Related pathogens exhibit distinct signatures

Alphaviruses

VEE- Venezuelan equine encephalitis

EEE- Eastern equine encephalitis

WEE- Western equine encephalitis

Flavivirus

JE- Japanese encephalitis virus

Bunyavirus

VSV- Vesicular Stomatitis virus

Other viruses

Vaccinia

RSV

Epstein-Barr

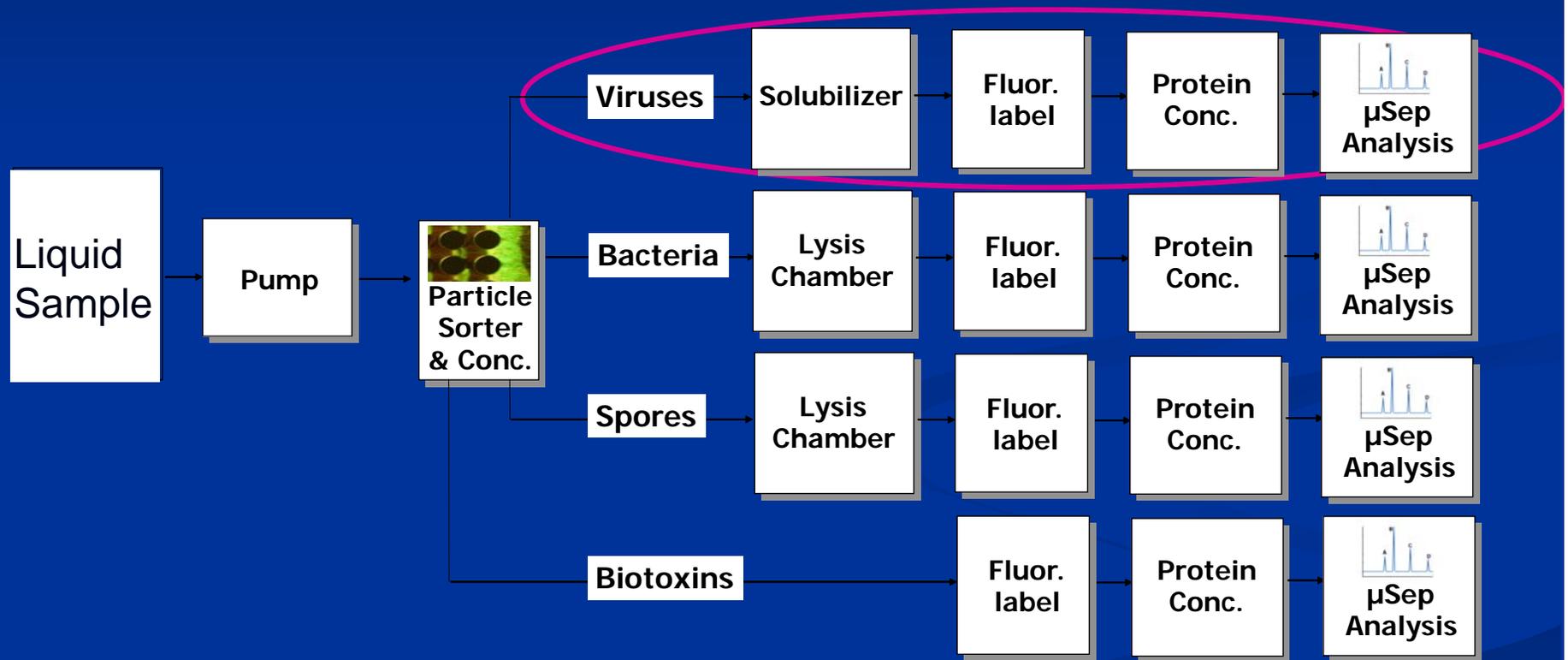
T2, T4, T6

MS2

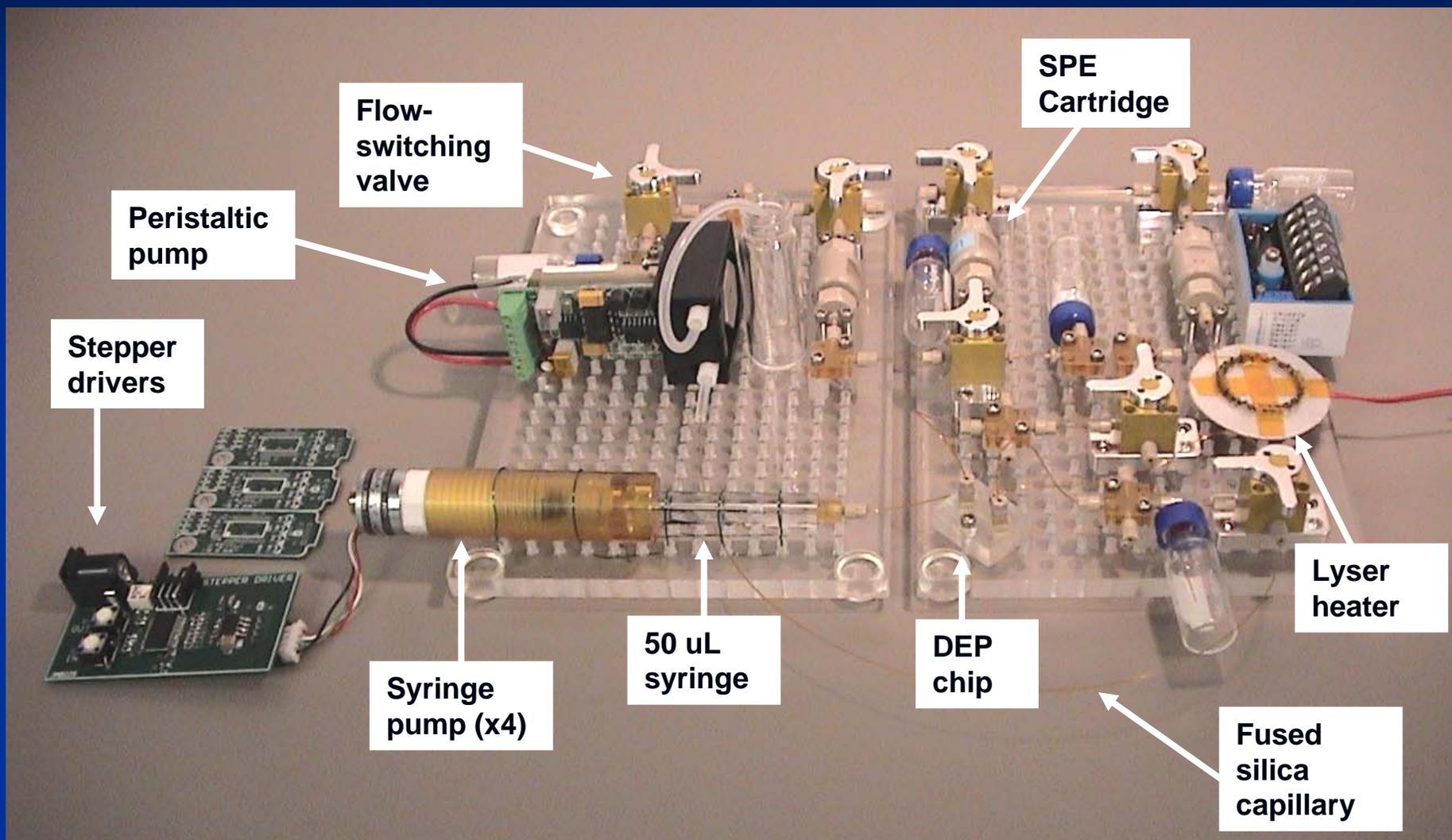
*CGE data



Viral analysis requires more sample prep than for biotoxins



Sample Prep Breadboard Hardware

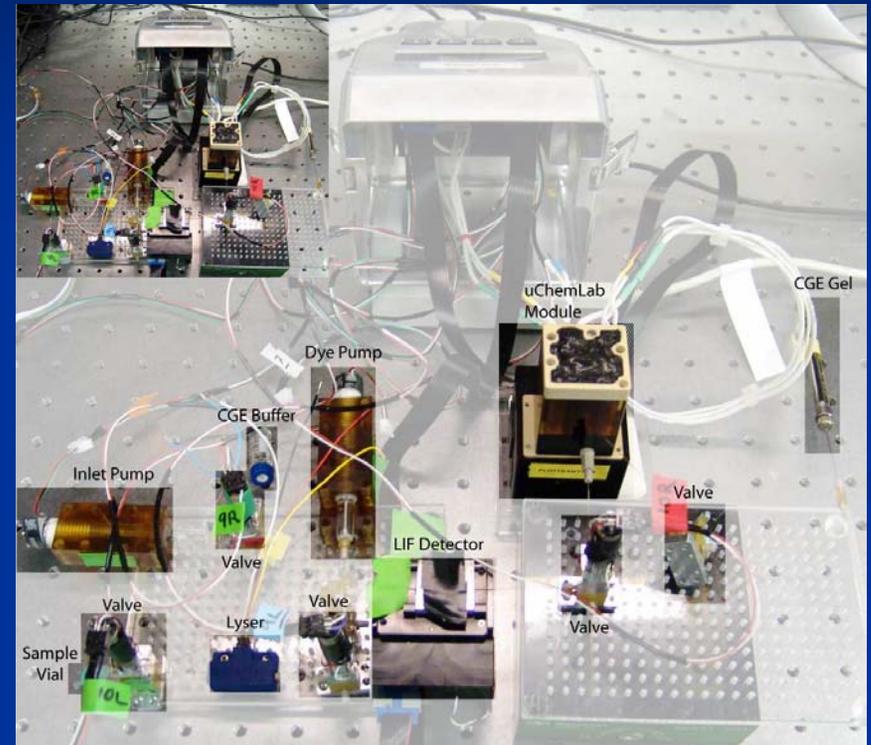
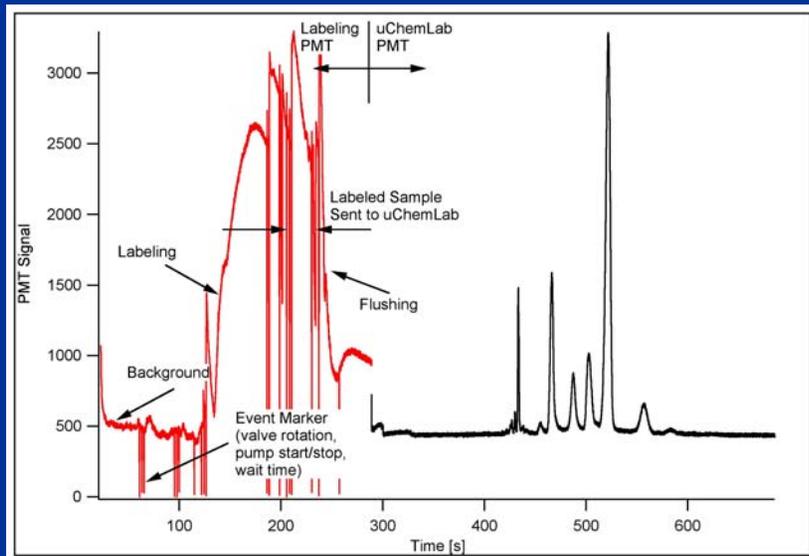


Approximate size: 8 inches x 12 inches



Automated, modular “front-end” sample processing system for μ ChemLab demonstrated

- Integrated system functions:
 - Uptake from sample vial
 - Mixing with buffer
 - Particle lysing to release proteins
 - Protein labeling w/ fluorescent dye
 - Injection into μ ChemLab followed by analysis and detection
 - System purging/prep for next sample



Red: Fluorescence from sample as it moves through system
Black: Fluorescence signature of detected proteins

