



Multidimensional Portable Mass Spectrometry for Biological Detection

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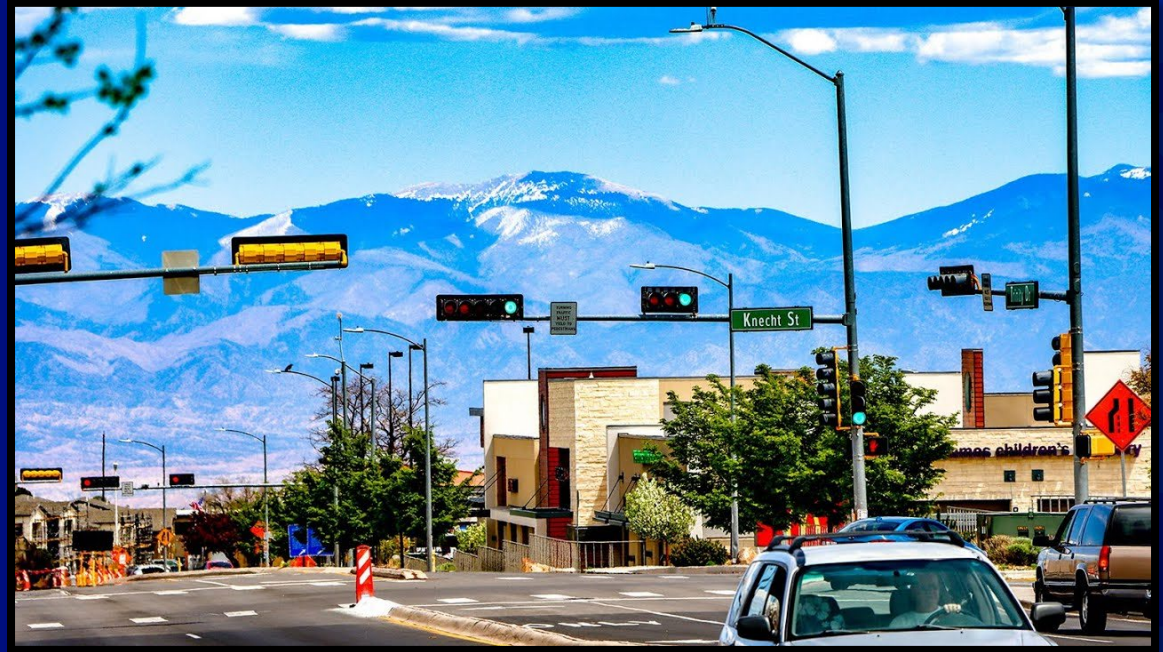
September 27th, 2022

LA-UR-22-29901

Los Alamos, New Mexico



Population: 13,200 (2020)
Elevation: 7320'
Average High: 82.5°F (July)



Los Alamos National Laboratory (LANL)



\$4B budget

40 square miles,
47 technical areas

897 bldgs.,
8.4M sq ft.

13 nuclear facilities

15,000
workers

~10,000 career
employees

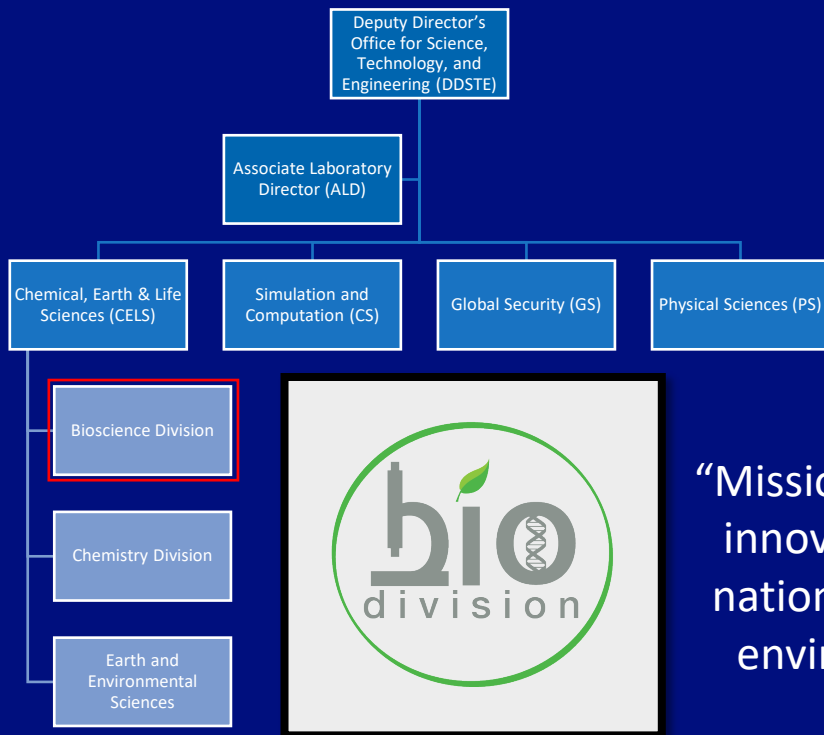
1,850 students,
462 postdocs

Employee
average age: 43

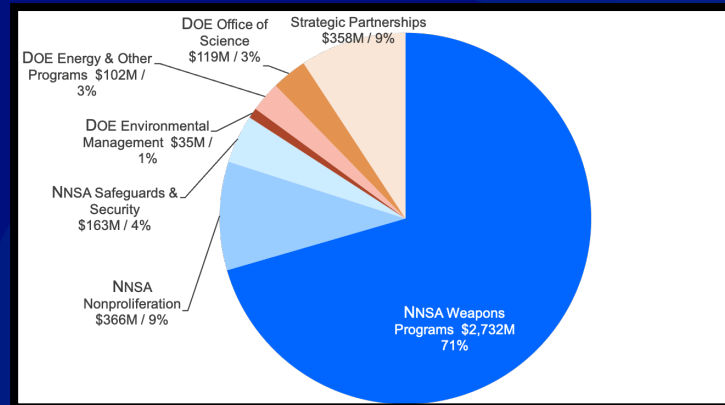
67% male;
33% female
49% minorities

40.2% of
employees are
native New
Mexicans

LANL Organization-STE

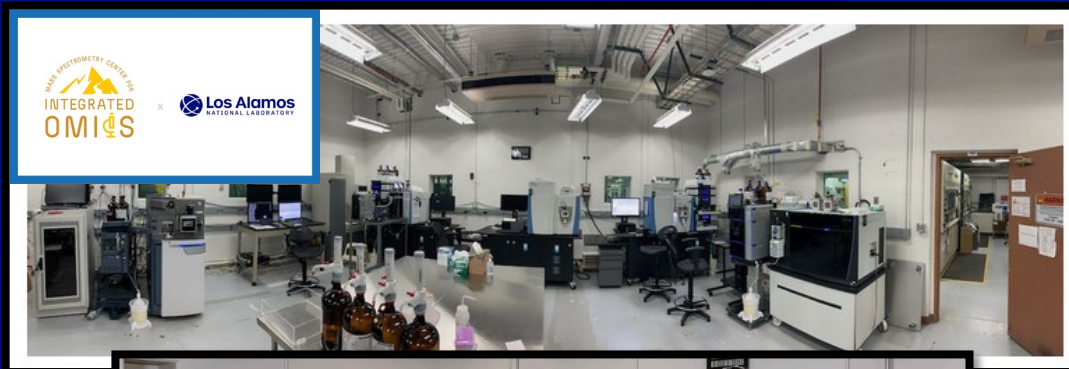


FY22 Budget



“Mission-driven science and innovation to protect the nation from biological and environmental threats.”

Mass Spectrometry Center for Integrated –Omics (MSCIO)



Portable MS Biological Detection

- Modern portable MS have achieved mass range capable of biological discrimination
- However, resolution for mass fingerprinting still presents a significant challenge for portable instruments
- Solving this problem is critical to implement these instruments at point of care and field-forward locations

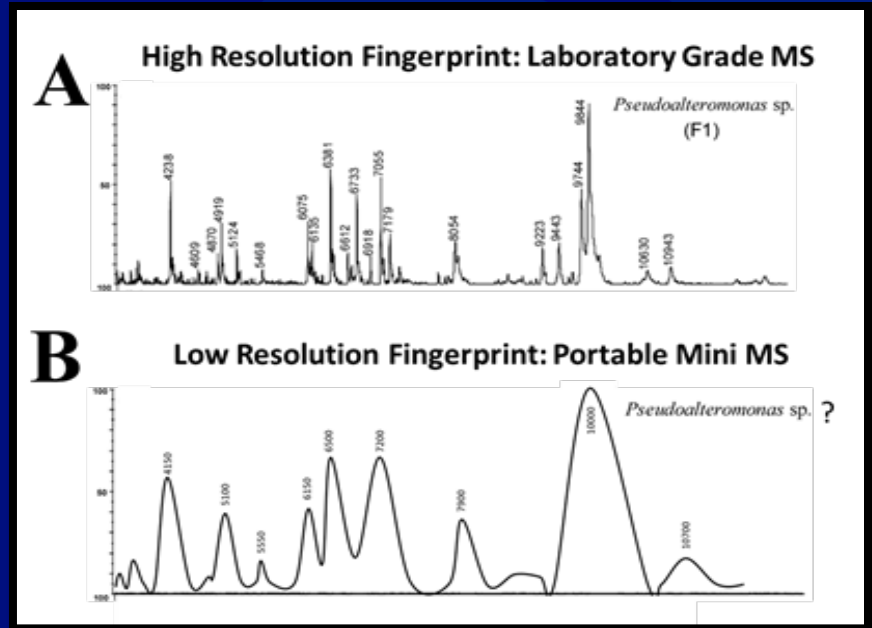
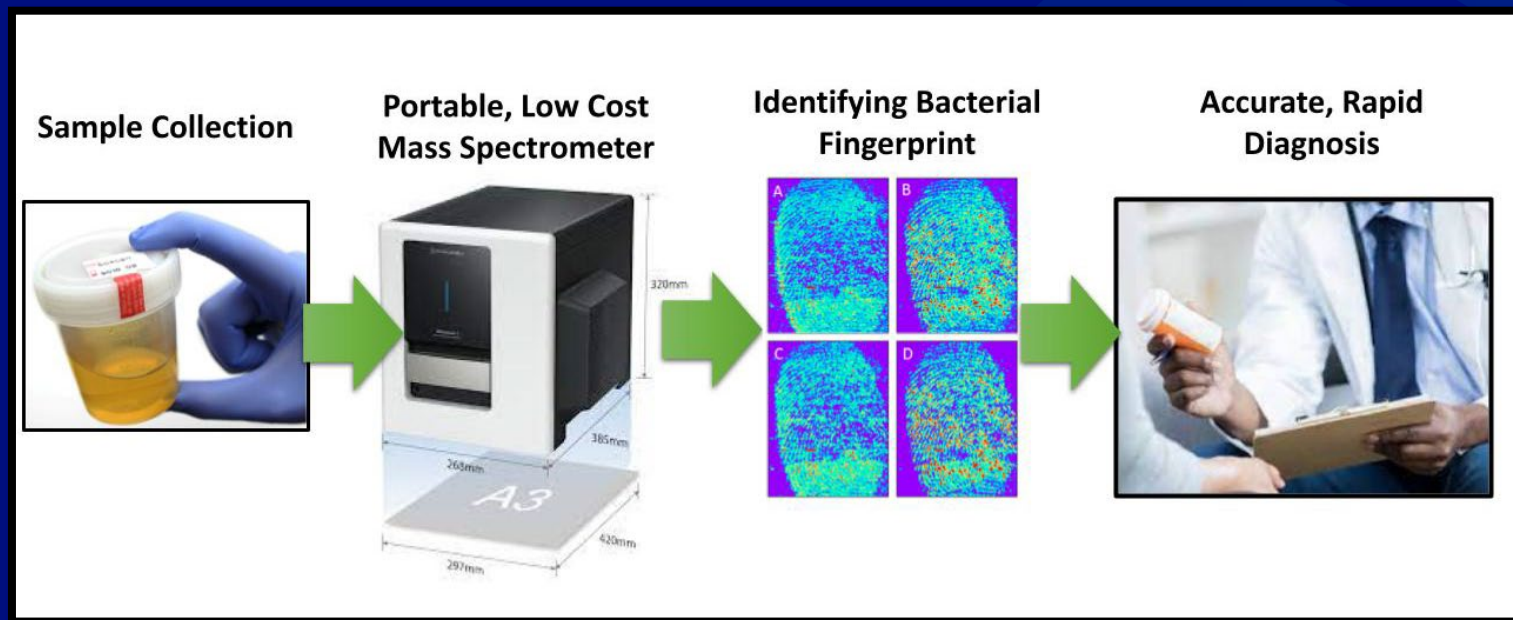


Image adapted from: Dieckmann, R., *et al.* Rapid screening and dereplication of bacterial isolates from marine sponges of the Sula Ridge by Intact-Cell-MALDI-TOF mass spectrometry (ICM-MS). *App. Microbio. Biotech.*, 67(4), 539-548.

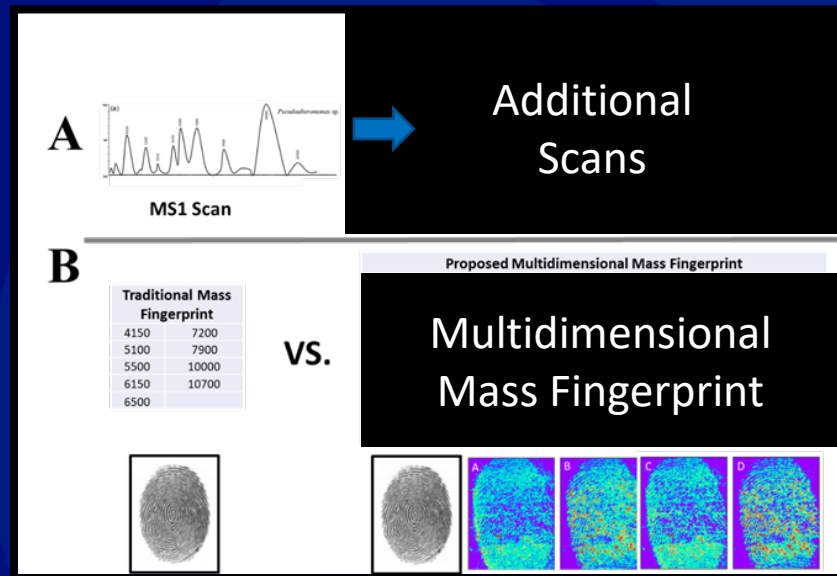
From Sample Collection to Diagnosis



Days → Hours

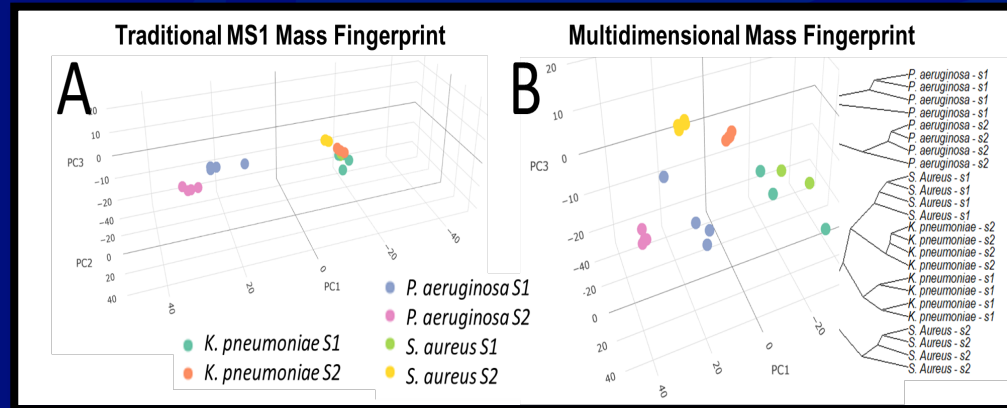
Multidimensional Mass Spectrometry Overview

- Obtain a parent mass scan (first dimension)
- Perform additional scans in addition to the initial scan
- The combination of these scans produces our mass “fingerprint”



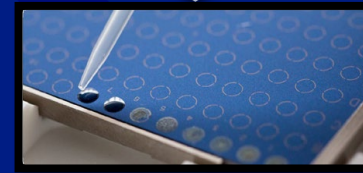
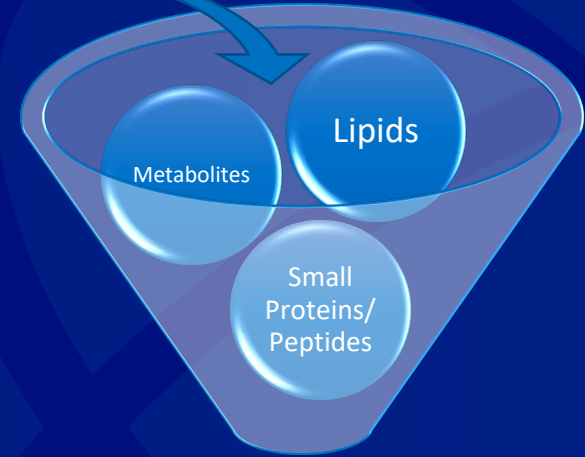
Workflow

- Bacteria (Gram positive/negative) are cultured and then extracted
- Bacterial extractions are spotted onto MALDI plates with matrix and analysis is performed
- Post-analysis scans are combined
- Biological replicates provide a means of discriminating between species and/or strain



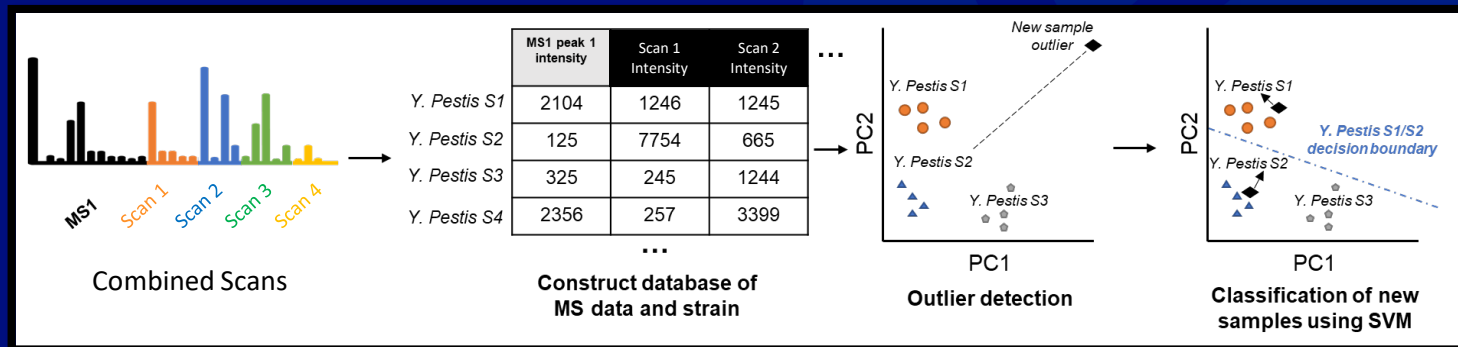
1. Universal Sample Preparation

- Currently experimenting with various sample-agnostic extraction procedures from culture
- Goal is to extract many different classes of compounds, rather than targeting a specific compound class (e.g., lipids)



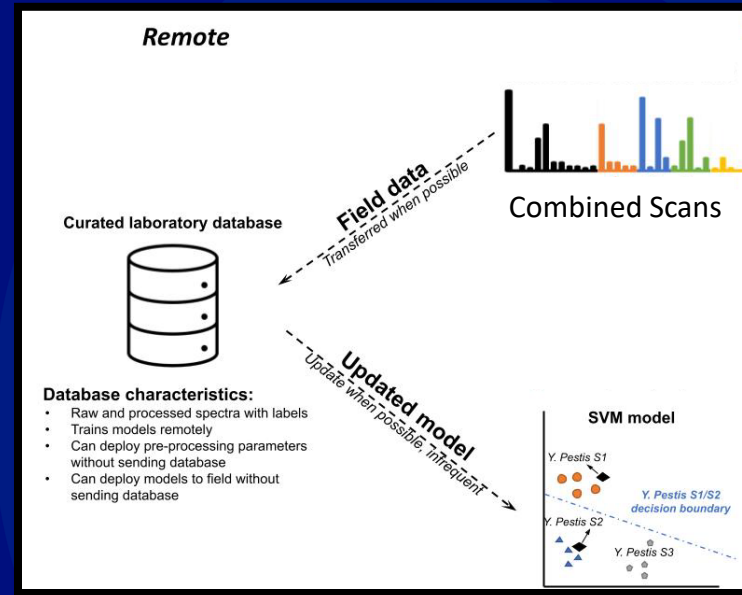
2. Mass Fingerprinting

- MS1 and additional scans will be “stitched” together to form the full multidimensional spectrum for each species
- Stitched data collection can be performed in minutes.

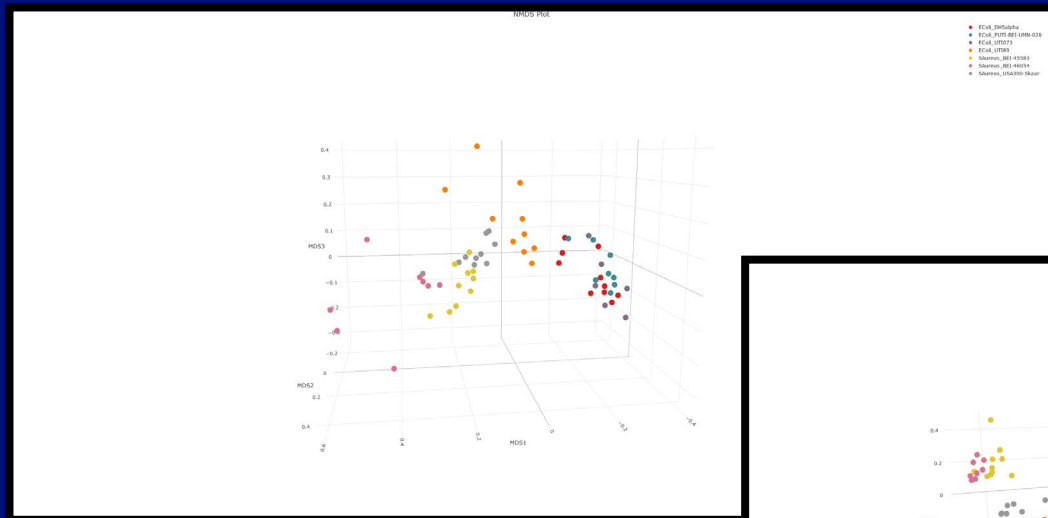


3. Data Processing Approach

- Data will be curated throughout the process, including pre-processing, to improve database construction
- Final model construction will be critical to ensure smooth transition to portable instrumentation with low SWaP requirements
- Models will ideally be continuously updated with field data

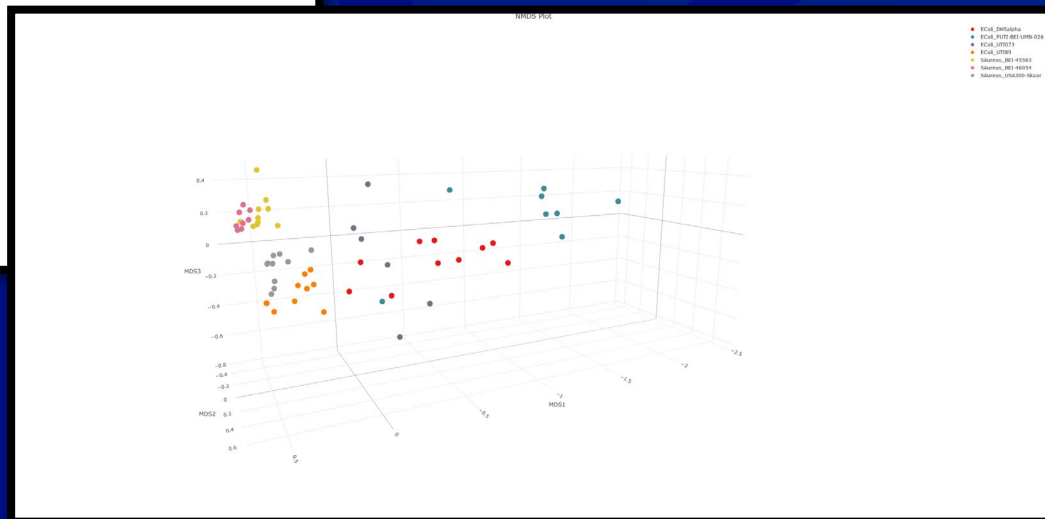


Preliminary Data – MS1 vs. Additional Scans, Strain Level

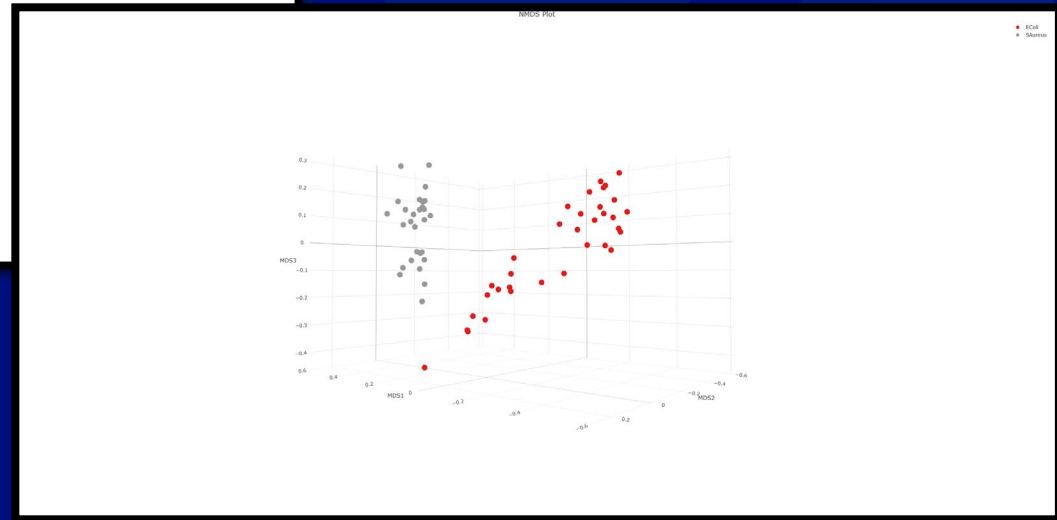
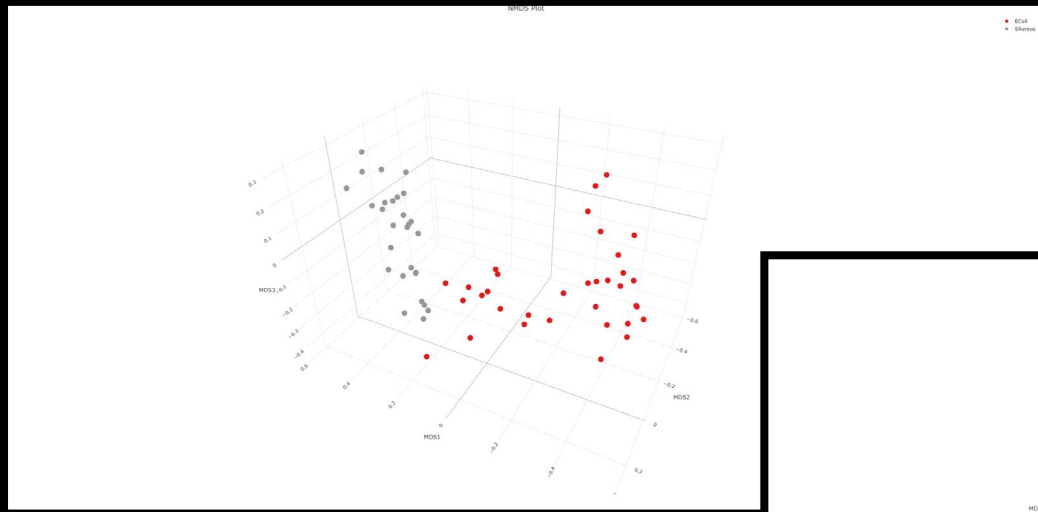


MS1

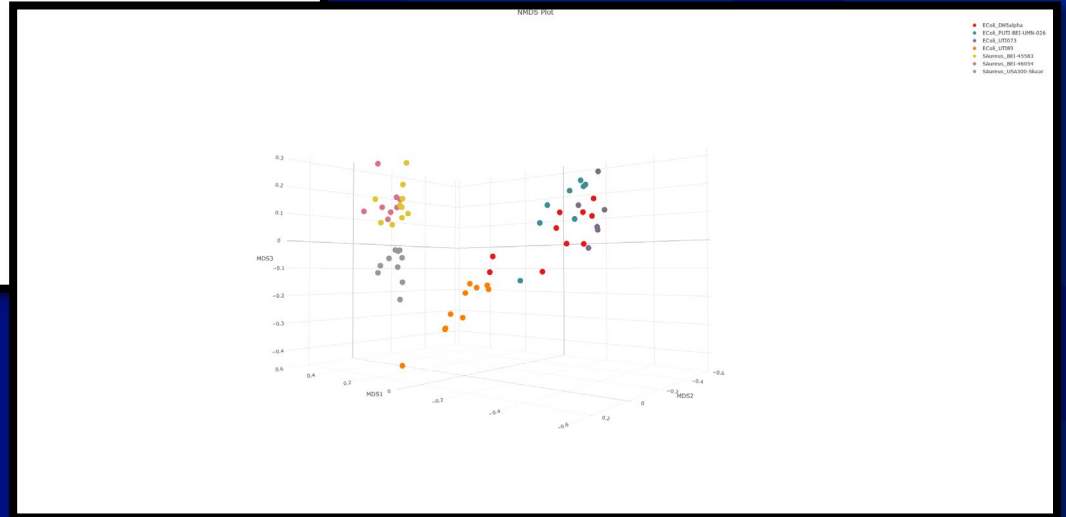
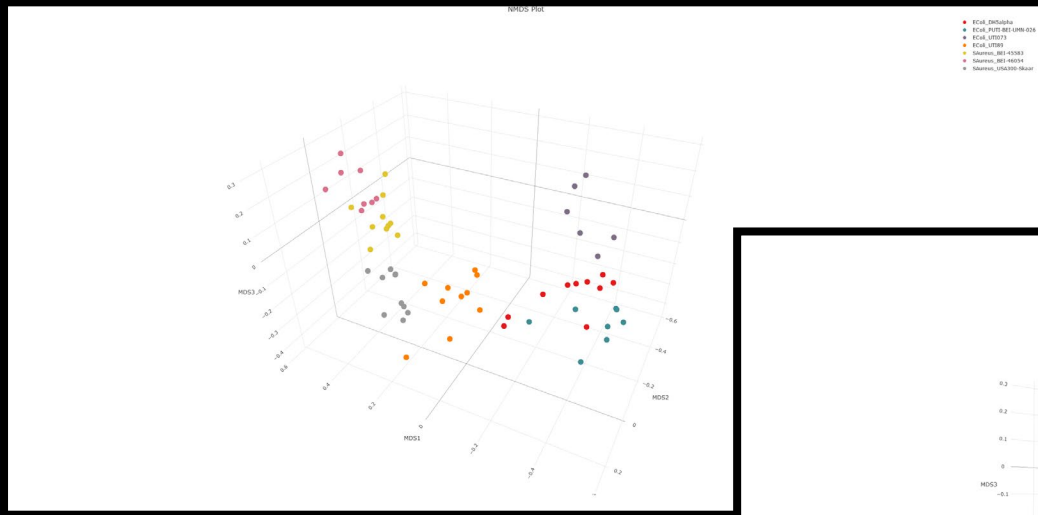
Additional Scans



Preliminary Combined Data – Species Level



Preliminary Combined Data – Strain Level



From Benchtop to Portable

- Our current plan involves preliminary data on a benchtop “high” resolution instrument, followed by work on a lower resolution, portable instrument for comparison
- Concurrent work involves the modification of scan parameters to meet our needs



Low SWaP MALDI-MS – “Portable Biological”

- For the first time, there are several commercially-available portable MALDI systems capable of being used for biological detection
- Aside from SWaP, considerations include:
 - Sample type
 - Mass range
 - Sample introduction
 - Ease of use

Shimadzu
MALDImini-1



BioFlyte BioTOF™
z200

Next Steps

- Currently expanding to new species/strains
- Incorporation of portable system for comparison testing
- Comparing positive/negative mode, as well as extraction protocol

Acknowledgements

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Questions?

