Novel Platform for Quantitative Subcellular Resolution Imaging of Human Tissues Using Mass Spectrometry


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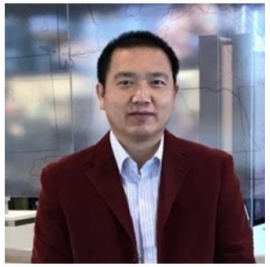
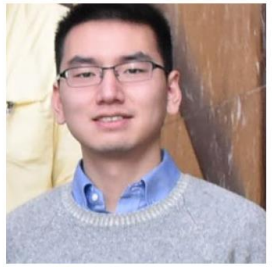
Charles Ansong


Paul Piehowski


Xiangtang Li


Hang Hu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Experts in instrument development, bioanalytical mass spectrometry, omics, microfluidics, computer science, machine learning, compressed sensing, biochemistry

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2019 HuBMAP Meeting

Enabling Quantitative Imaging of Hundreds of Biomolecules with High Resolution and Throughput

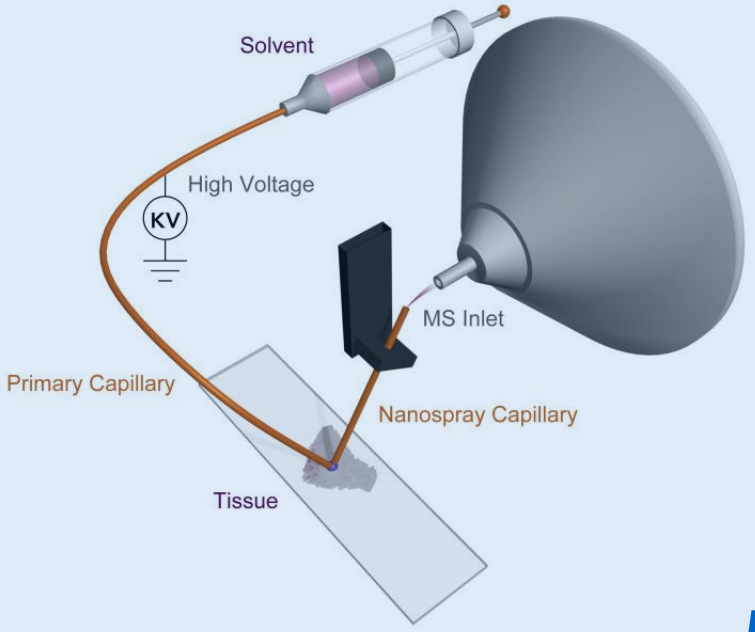
No sample pretreatment

High spatial resolution (~10 um)

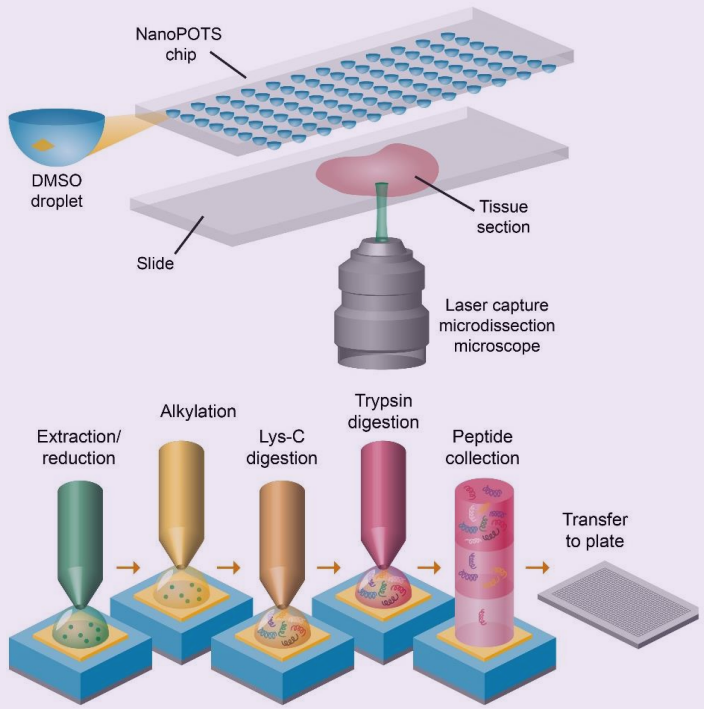
Quantification

Hundreds of lipid/metabolite images in a single experiment

Nano-DESI Imaging (lipids/metabolites)



nanoPOTS Imaging (proteins)



Minimizes analyte losses in sample processing

Thousands of proteins in each voxel

Spatial resolution of ~50 um

Image DB/ Prior Knowledge

Supervised Learning

Sparse Sampling
Throughput Enhancement

Next Year's Deliverable in 1 slide

What resources / data do you expect to make available in 2020?

- An integrated microfluidic chip for nano-DESI imaging
- First experimental implementation of sparse sampling (SLADS) coupled with nano-DESI MSI
- Data sets: Mouse uterine nano-DESI and nanoPOTS data (already available as test sets)
- Human kidney tissue imaging data will be acquired and shared once sample transfer becomes possible (collaboration with Vanderbilt)

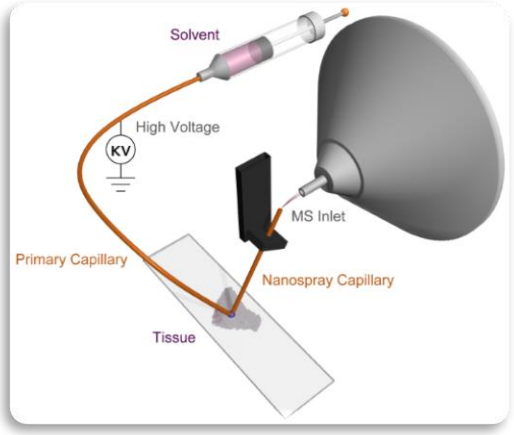
What do you need to do in order to be able to share?

- We are working with Jeff Spraggins on the data and metadata format

Collaborations in 1 slide: Correlative Imaging

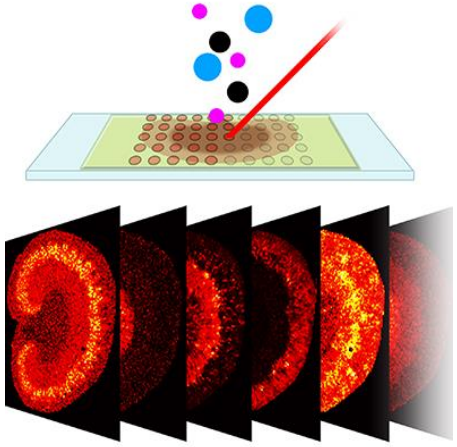
Nano-DESI Imaging

Purdue TTD
Julia Laskin



MALDI Imaging

Vanderbilt TMC
Jeff Spraggins/Ralf Van de Plas



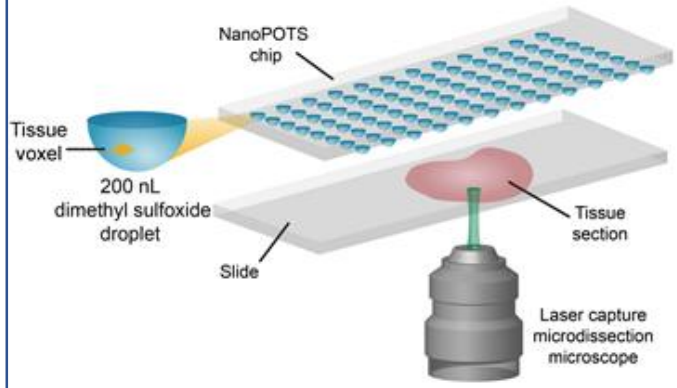
Awaiting the MTA agreement

<u>Goal</u>: obtain best molecular coverage for the analysis of human kidney tissue by fusing nano-DESI and MALDI imaging

- Use autofluorescence microscopy to guide both nano-DESI and MALDI imaging
- Develop advanced algorithms for data registration and data-driven image fusion
- Identify molecular classes that are enhanced in each modality

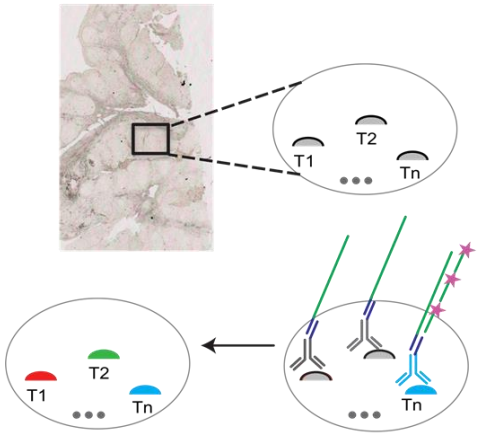
nanoPOTS Imaging

Purdue TTD
Julia Laskin/Kristin Burnum-Johnson



Multiplexed Immuno-SABER Imaging

Harvard TTD
Peng Yin/ Sinem Saka



Targets have been identified

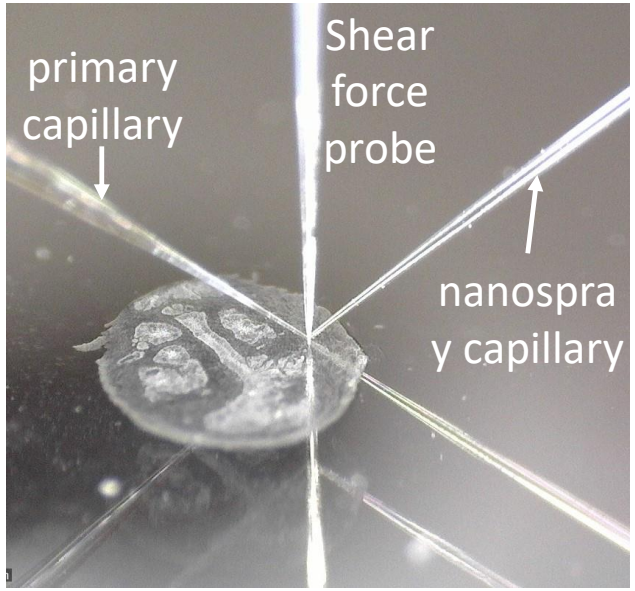
Multiplexed imaging

<u>Goal</u>: obtain a detailed spatial map of proteins, lipids, and metabolites by combining nanoPOTS, Immuno-SABER, and nano-DESI imaging

- use nanoPOTS to uncover global proteomic changes across a heterogeneous tissue sections
- use Immuno-SABER to provide cellular resolution and sensitivity for targets of interest.

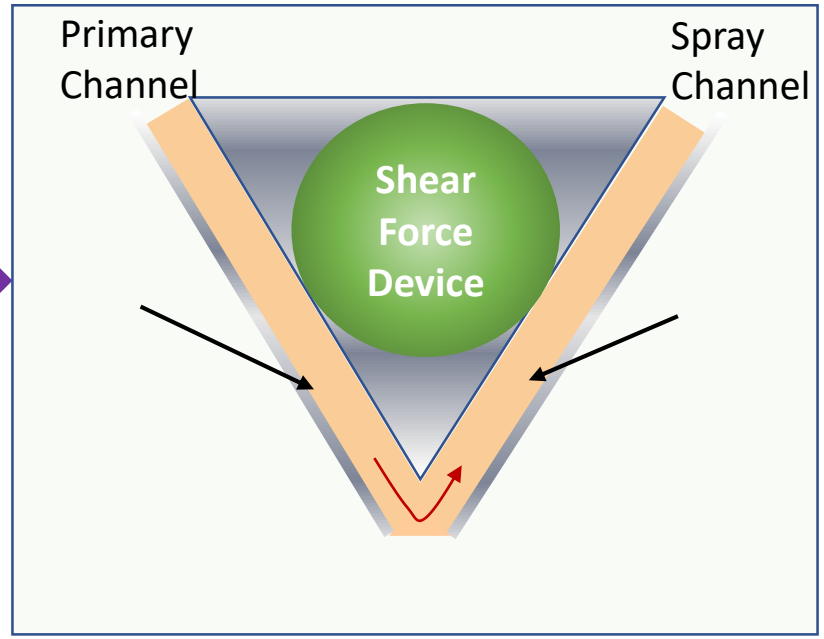
Development of an Integrated Nano-DESI Imaging Probe

Capillaries Setup: Spatial resolution better than 10 um

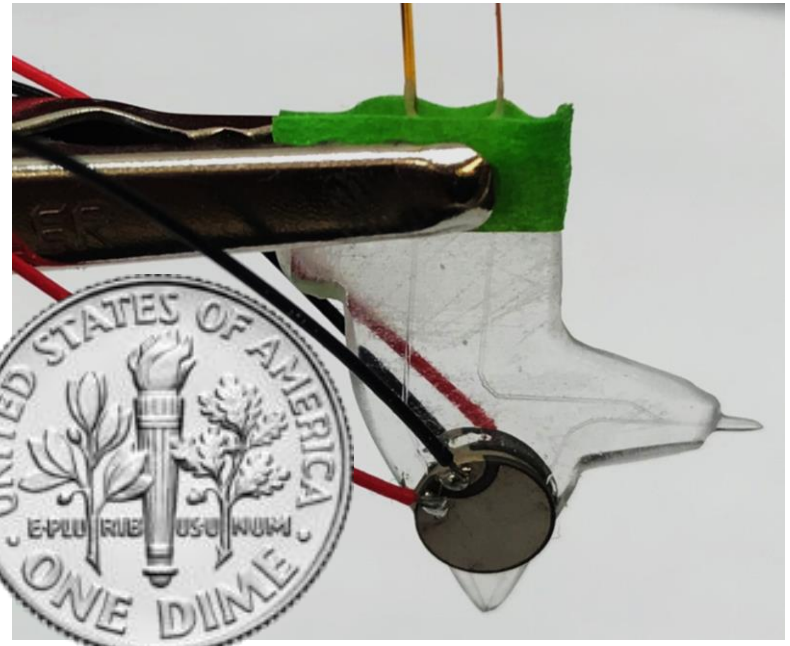


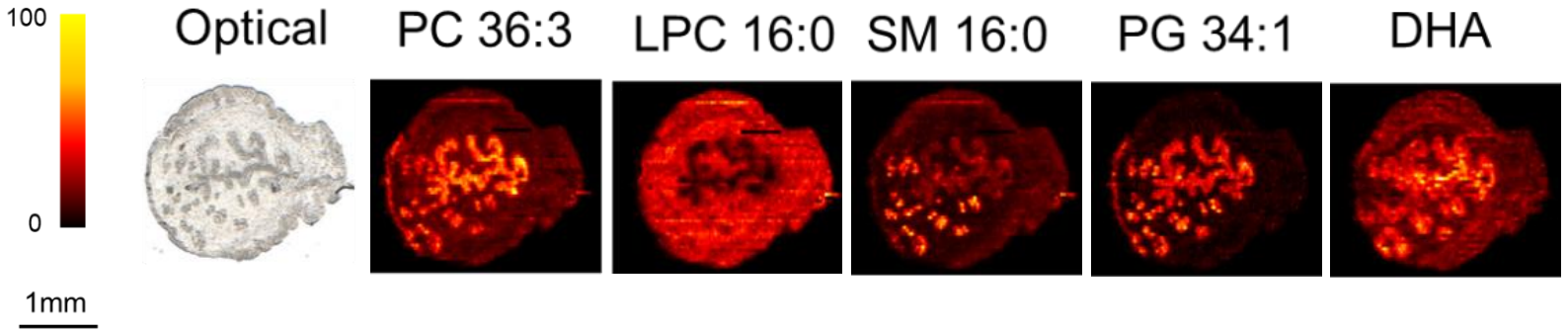
Nat Protocols, 2019, in press

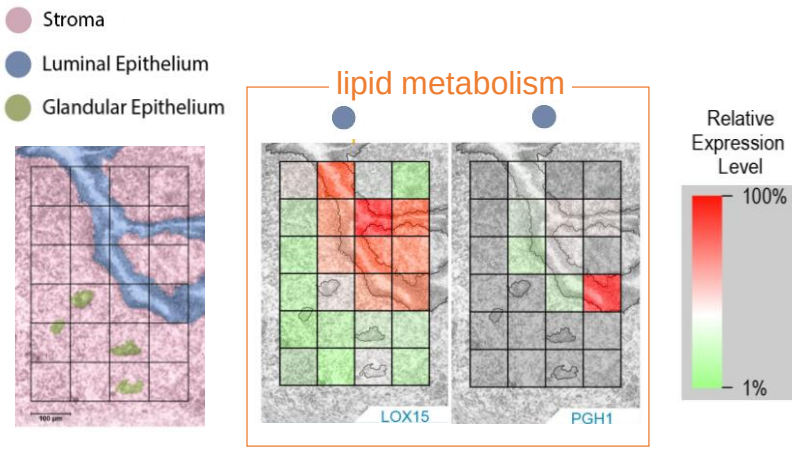
Microfludic Device: Easy operation, spatial resolution better than 20 um



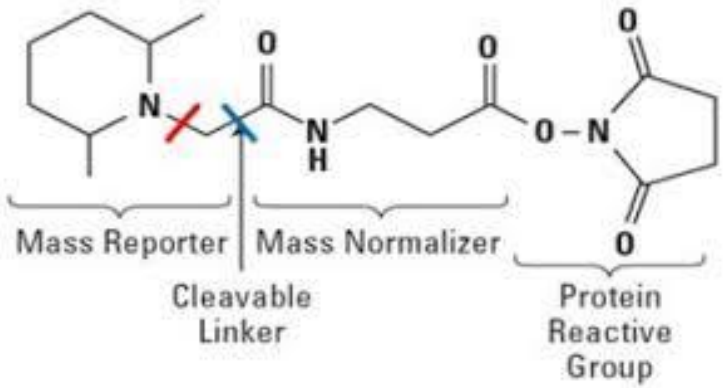
Patent submitted in May 2019



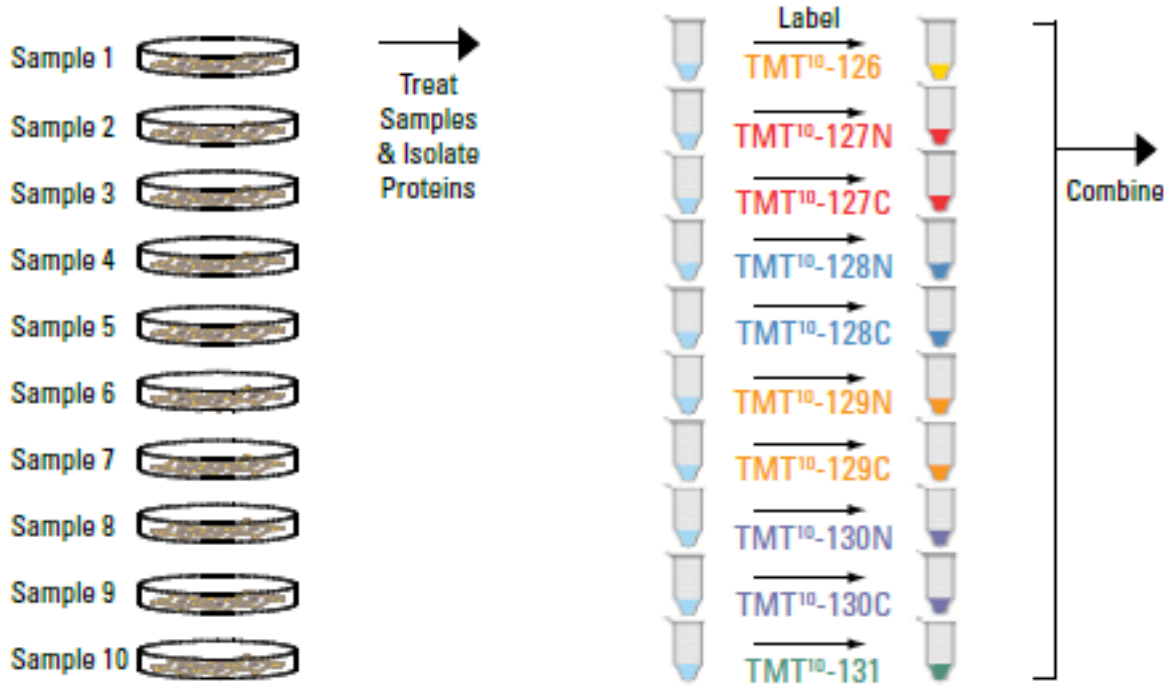


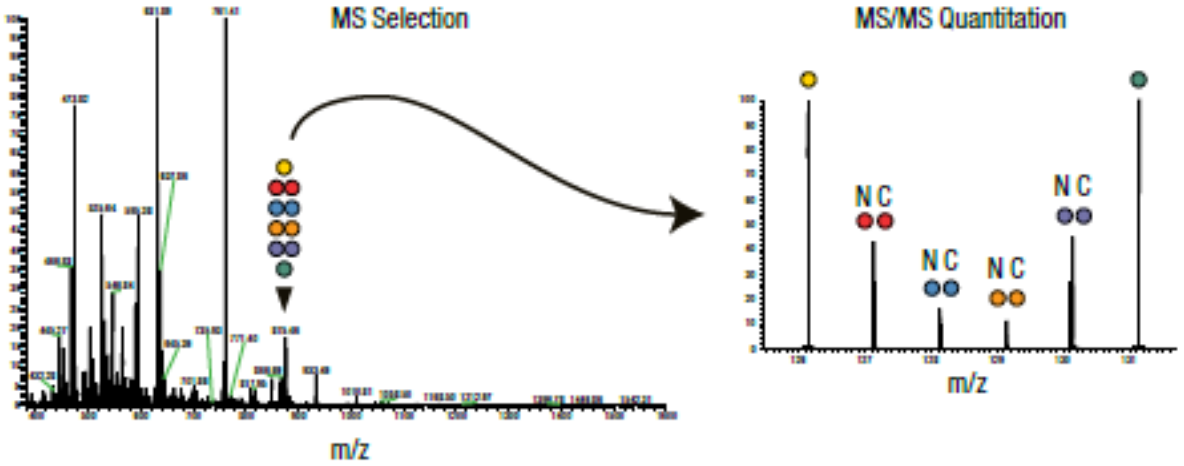


Improving Throughput of nanoPOTS Imaging: TMT concept

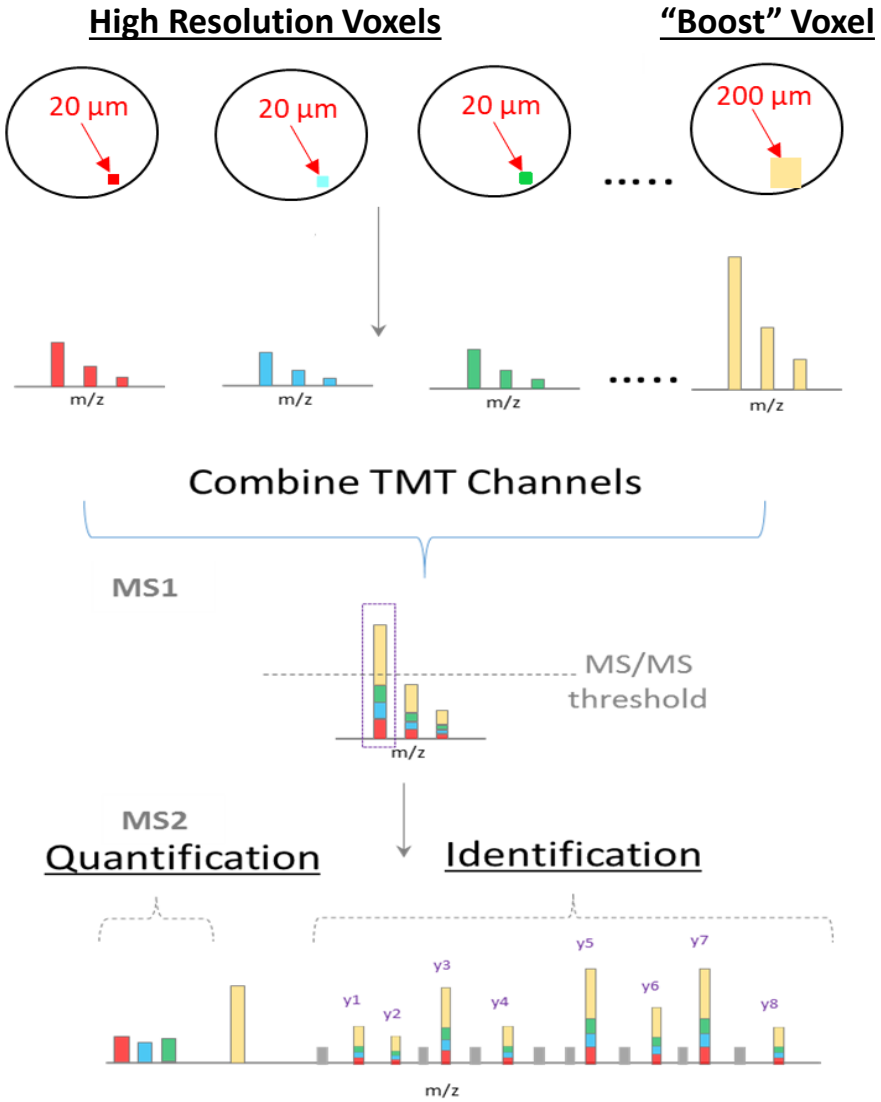


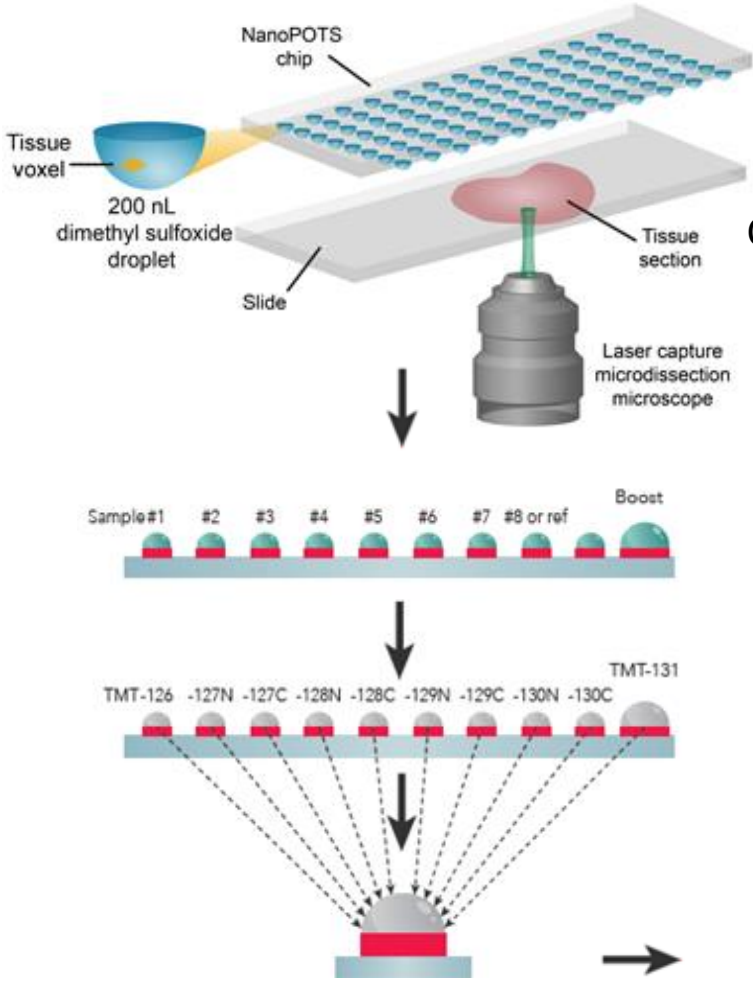
TMT reagent





TMT “Boost” multiplexing increases sensitivity and throughput of nanoPOTS





Collect voxels directly into nanoPOTS using LCM

Digest into peptides

Label voxels with TMT

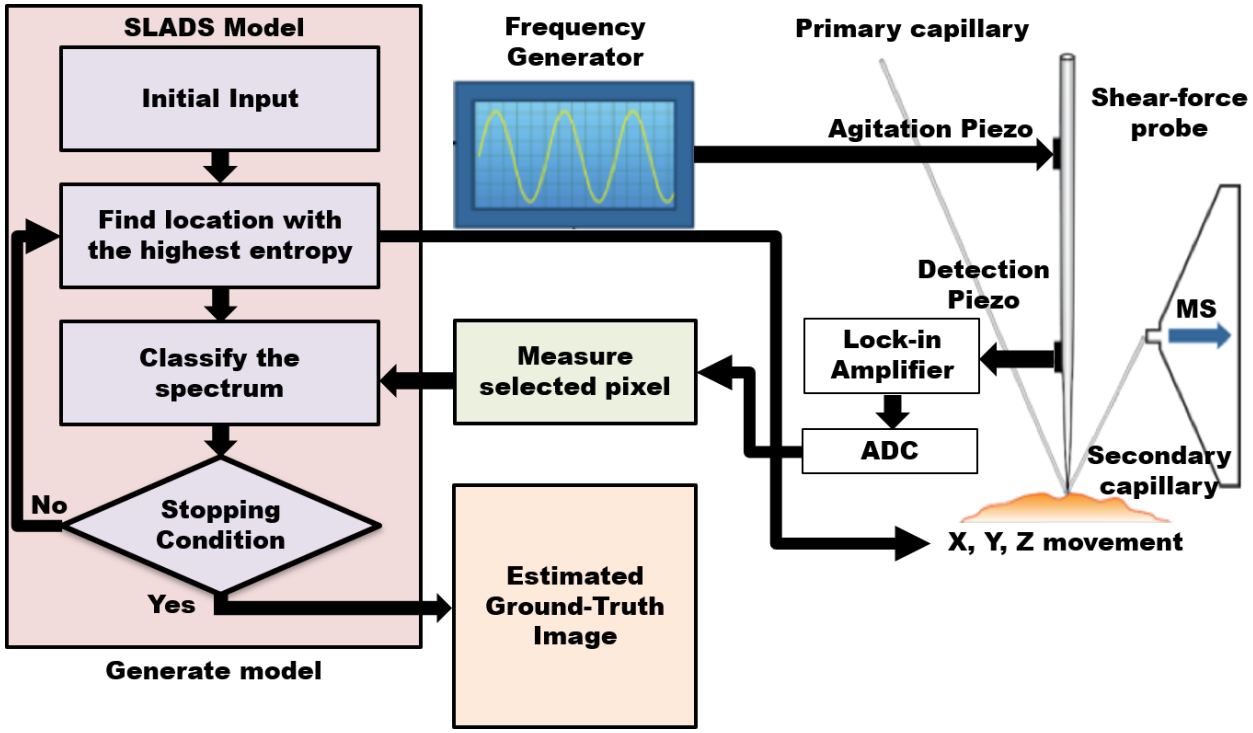
Combine voxels & Boost

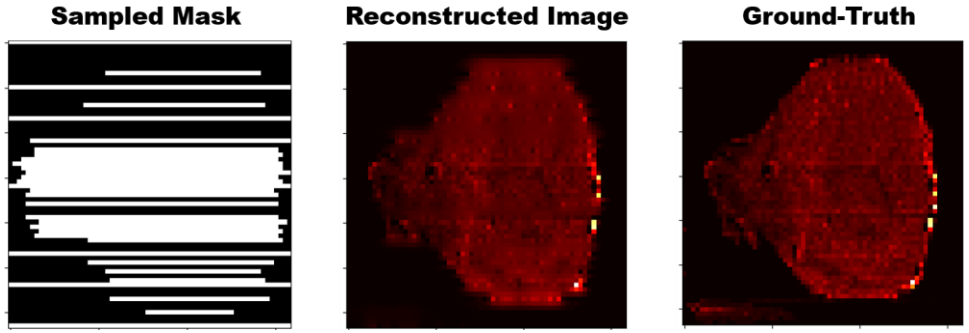
Single LC-MS/MS run

M. Dou *et al.*, *Analytical Chemistry* 10.1021/acs.analchem.9b03349 (2019).

Supervised Learning Approach for Dynamic Sampling (SLADS) for Nano-DESI Imaging

- AI-based Compressed Sensing for High-Throughput Nano-DESI





- **59.38 % of Line Measurements / 50.51 % of Pixel Measurements required for reconstructed image comparable with fully measured ground-truth**
- **Two-fold throughput increase**