

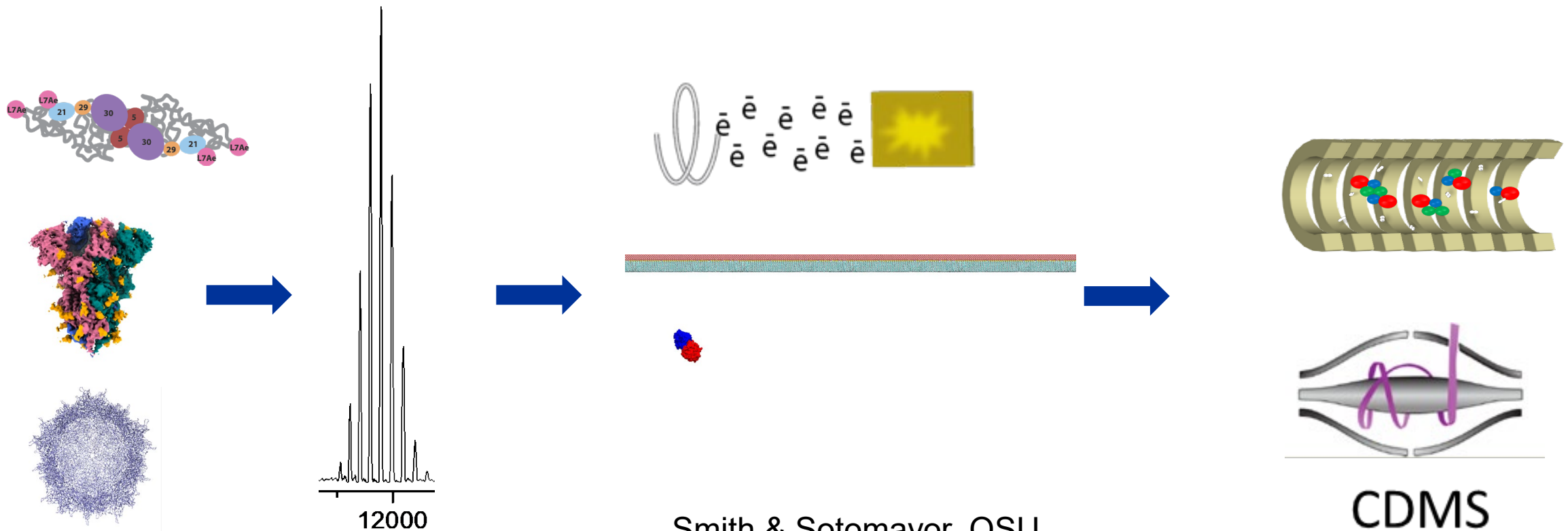
Native MS in Structural Biology

V.H. Wysocki, Georgia Institute of Technology

Sophie Harvey and Steffen Lindert, Ohio State University

Brandon Ruotolo, University of Michigan

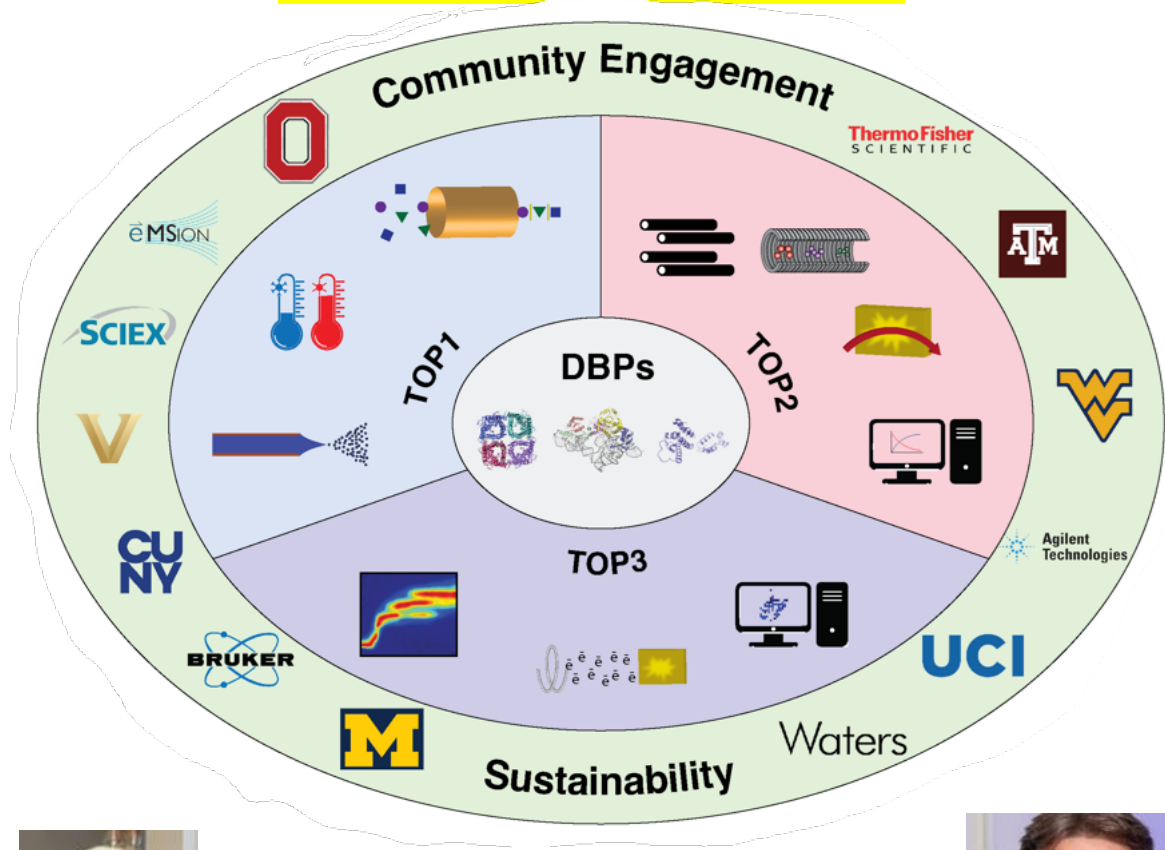
David Russell and Art Laganowsky, Texas A&M University



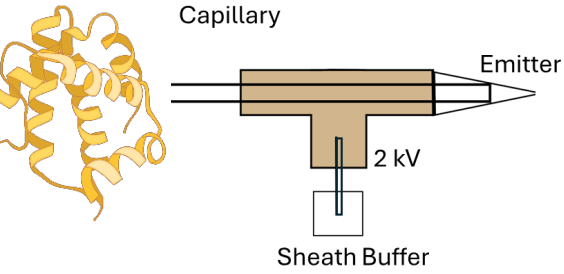
RM1: NIH Biomedical Technology Optimization and Dissemination Center

Native Mass Spectrometry Guided Structural Biology 2023-2028

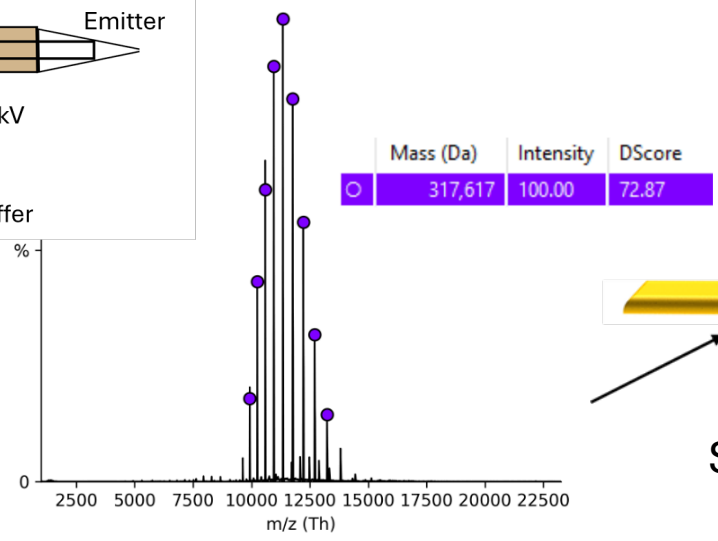
nativems.osu.edu



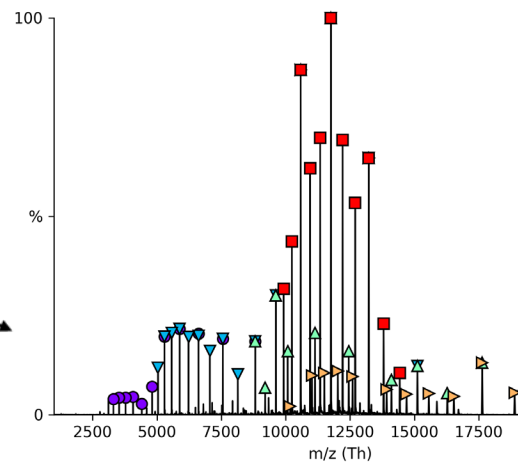
UHMR SID: Online Capillary Electrophoresis E coli Lysate (Sun)



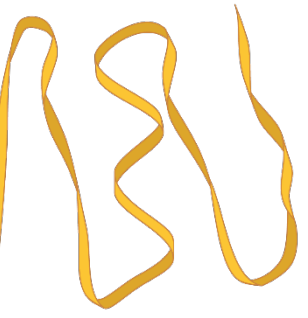
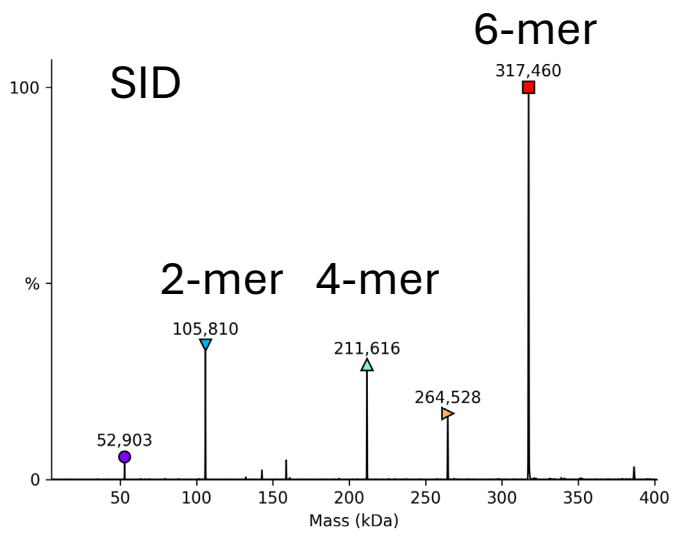
Native MS



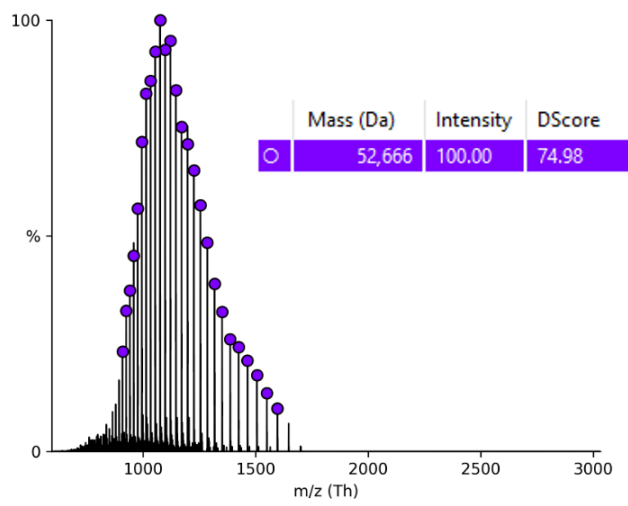
SID



SID

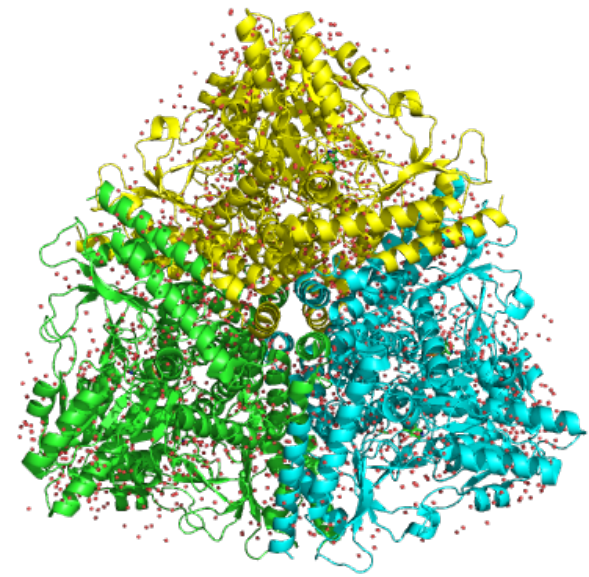


Intact MS



Top-Down

```
N [M]DKKQVTDLRSELLDSRFGAKSIST 25
26 I AESKRFP LHEMRDDVAFQI I I N D E I L 50
51 YLDGNARQNLATF QTWDDENVHKL 75
76 MDLS INKNWIDKEEYPQSA AIDLR 100
101 VNMVADLWHAPAPKNGQAVGTNT I I G 125
126 SSEA M LGGMAMKWRWRKRME AAGK 150
151 PTDKPNLV GGPVQ I WHKFARYWDV 175
176 ELREI PMRPGQLFMDPKRMIEA D E 200
201 NT I G V V P T F G V T Y T G N Y E F P Q P L H D 225
226 A L D K F Q A D T G I D I D M H I D A A S G G F L 250
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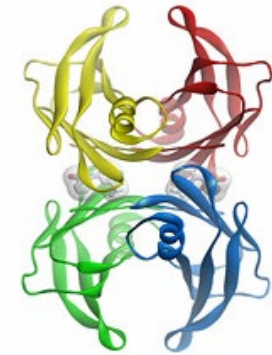


Glutamate decarboxylase β

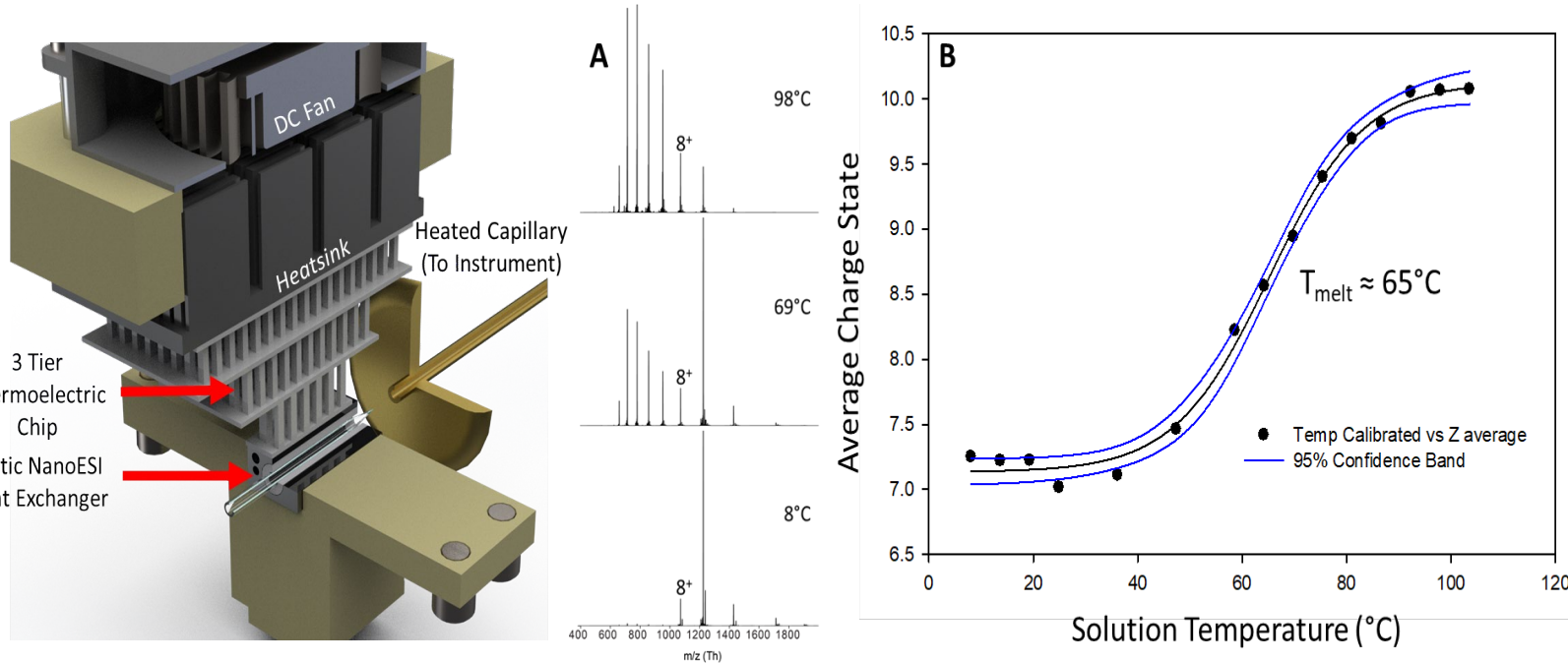
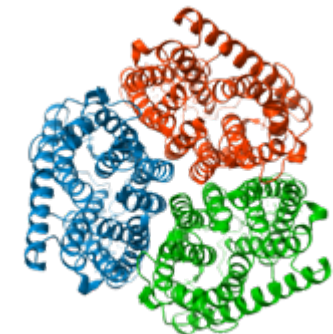
Variable temperature ESI (vT-ESI)

Applications to:

Amyloid disease



Membrane protein lipid interactions

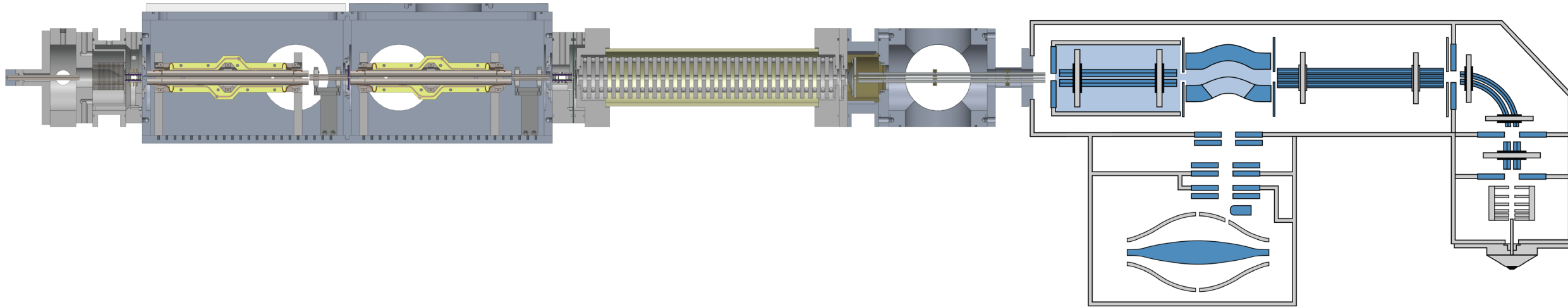


adoption in multiple labs
pharma collaborations
multi-vendor adoption possible

Dissecting the Thermodynamics of ATP Binding to GroEL One Nucleotide at a Time
T. E. Walker et al. ACS Cent Sci 2023, 9, 466-475.

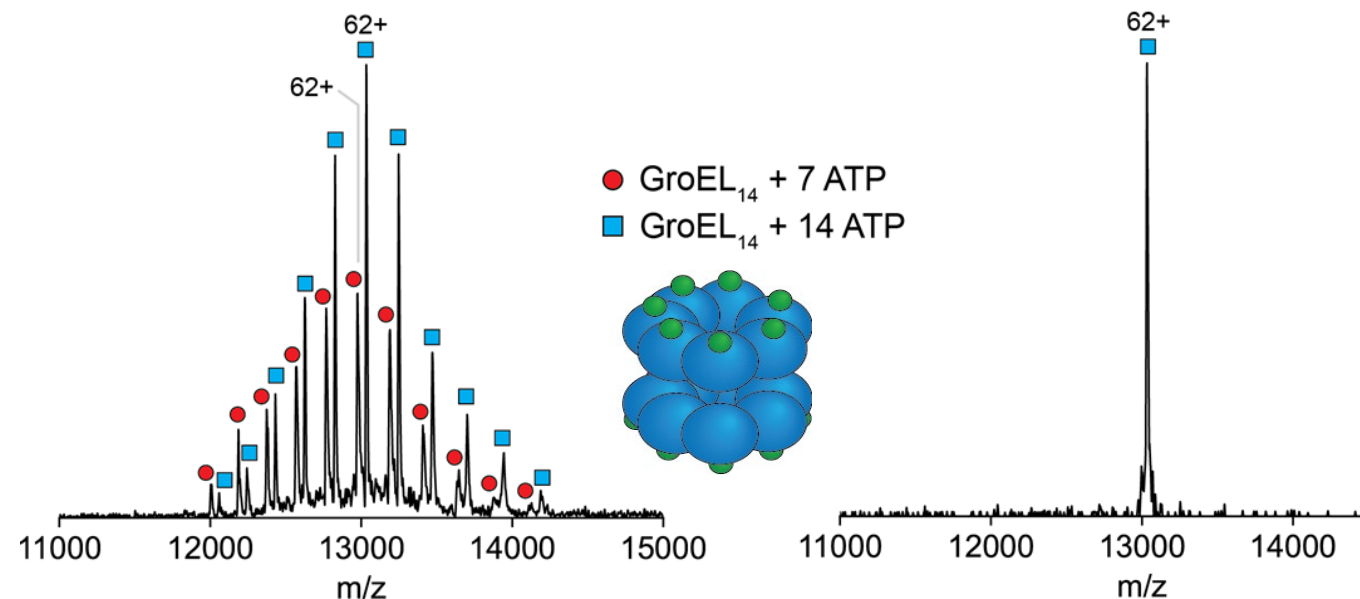
Digital Quadrupole

Orbitrap Exactive Plus EMR

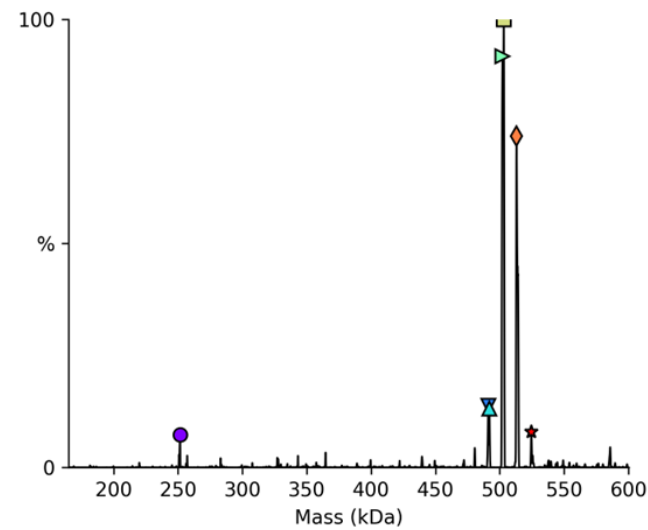
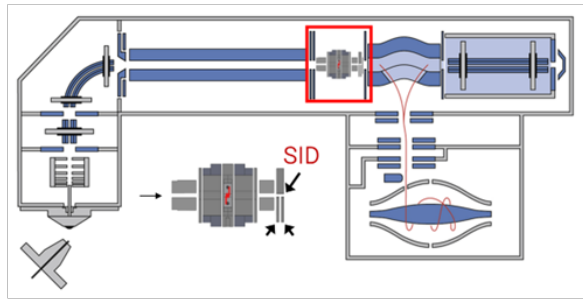
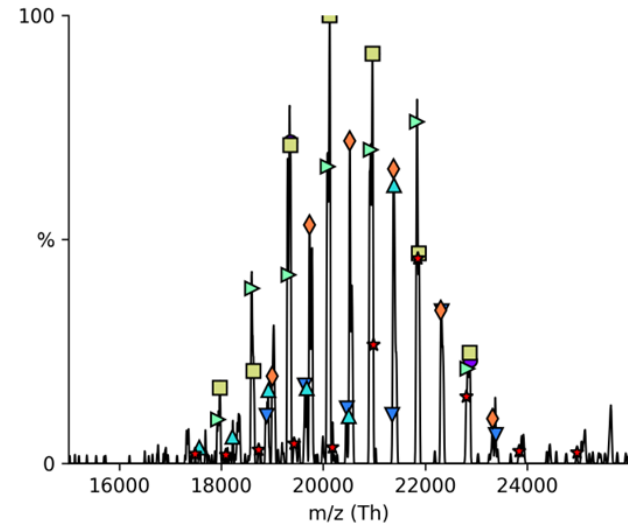
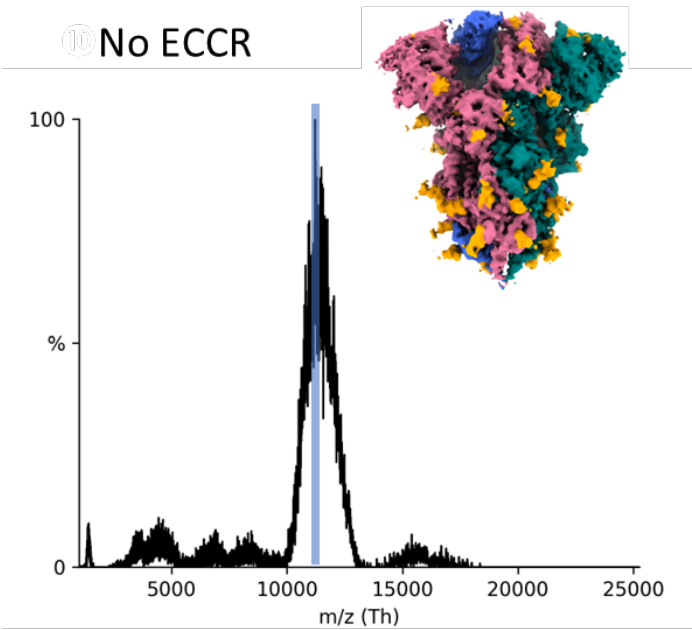


Illustrated at TAMU & OSU
Illustrated in multiple vendors' MS

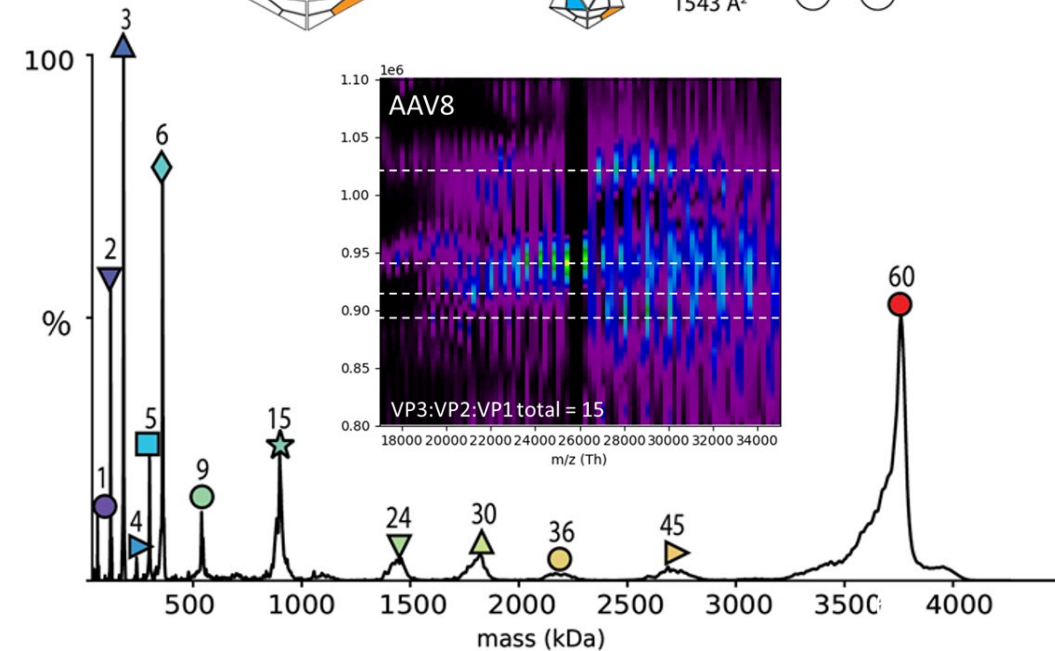
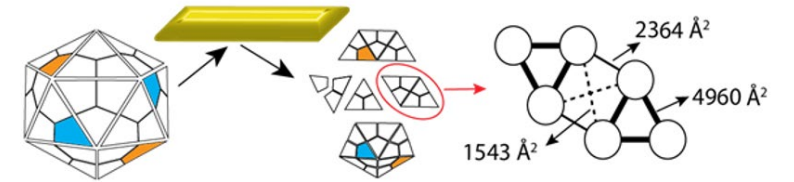
Optimization of a Digital Mass Filter for the Isolation
of Intact Proteins in Stability Zone 1,1
R. L. Schrader et al. *Anal. Chem.* 2023, 95, 3062.



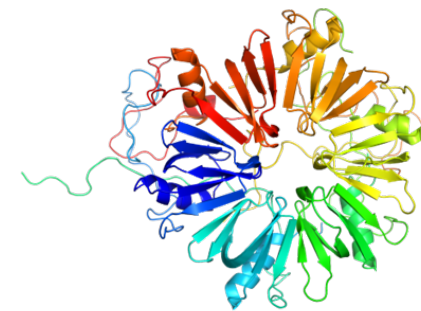
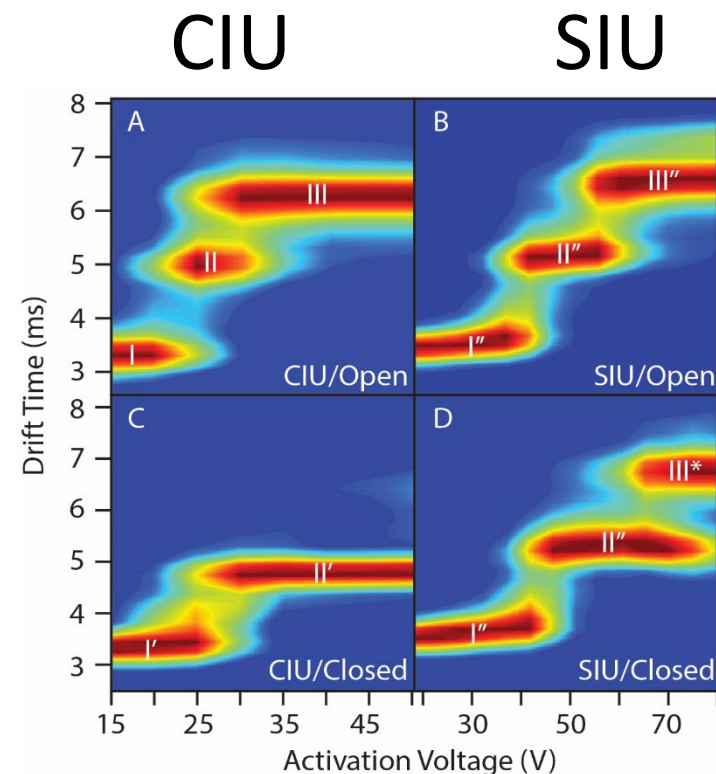
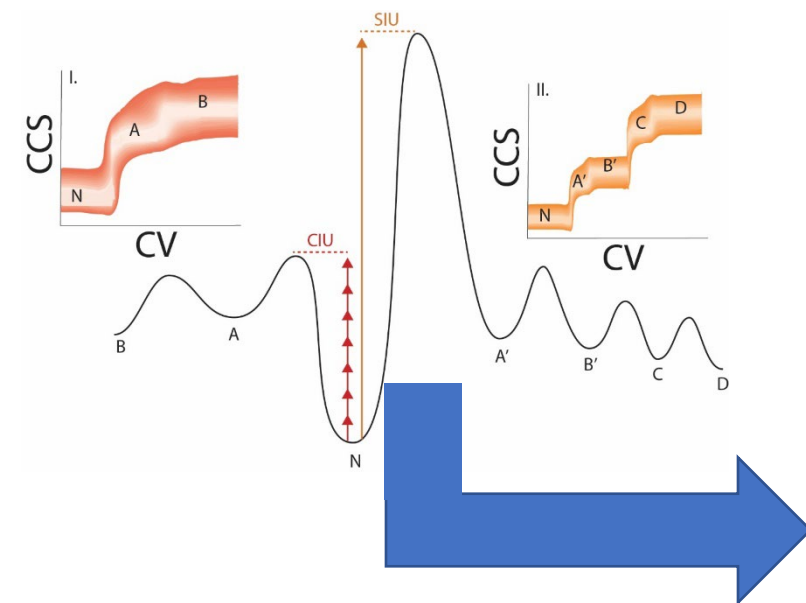
Electron Capture Charge Reduction-Surface Induced Dissociation



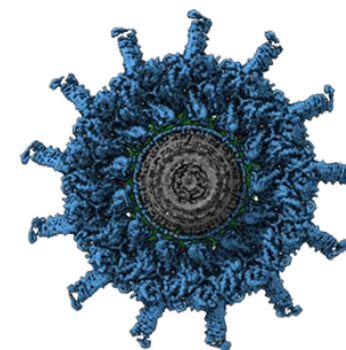
Glycoproteins
AAVs



TOP3, Protein Stability: Collision induced unfolding



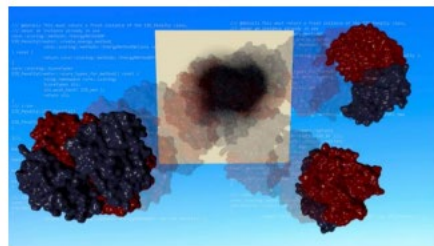
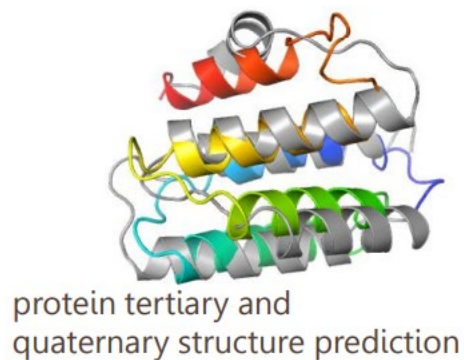
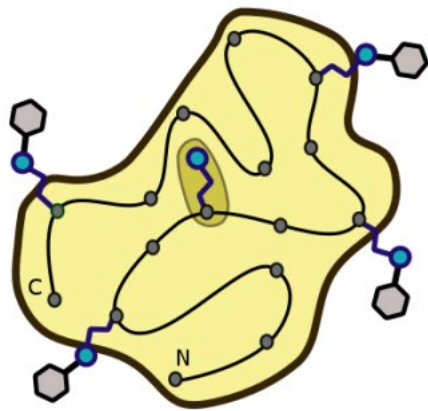
RNA-protein
complexes for
genetic control



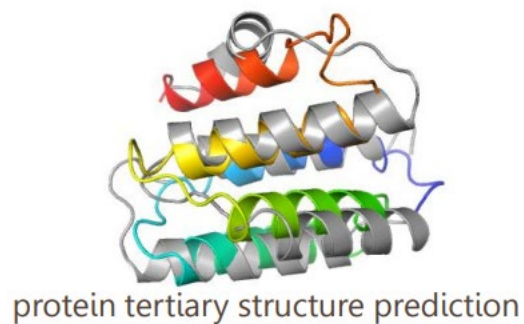
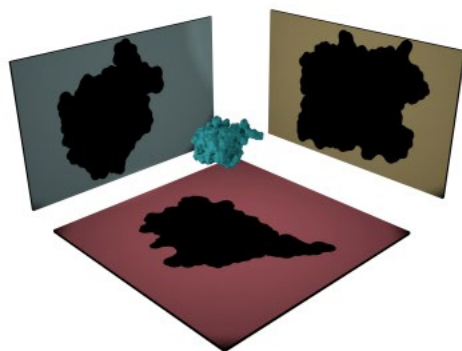
Type IV Protein Secretion

CIU option across dozens of labs worldwide
many pharma collaborations
multi-vendor adoption in progress

Integrative Modeling for Quaternary Structure



protein quaternary structure prediction



Combine MS and/or ion mobility data with complementary low resolution structural data for integrative modeling

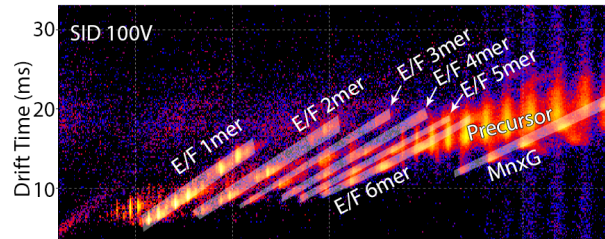
tools are beta tested and provided as developed, extended, and improved (Rosetta or OpenFold)

Complementarity between native MS and cryoEM

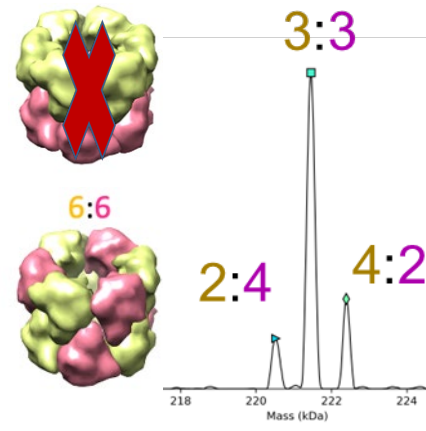
TNH



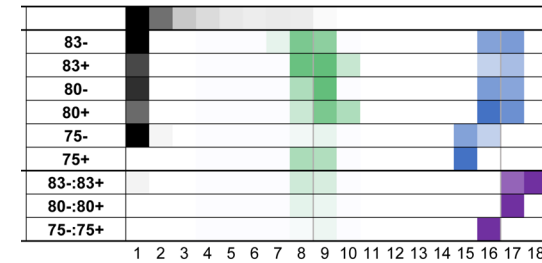
Mnx



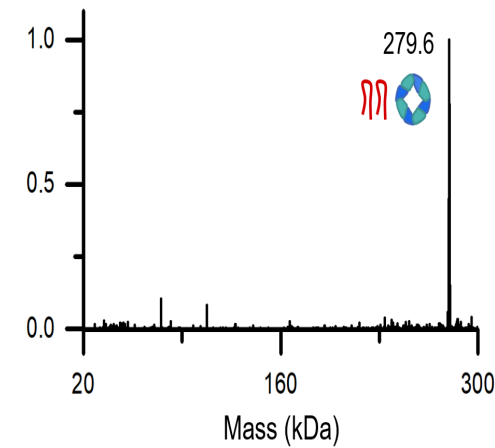
PDX



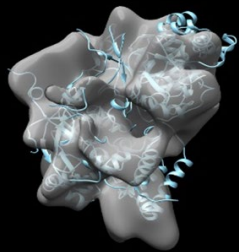
Red beta



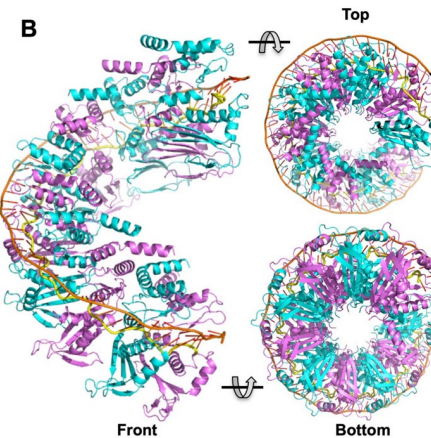
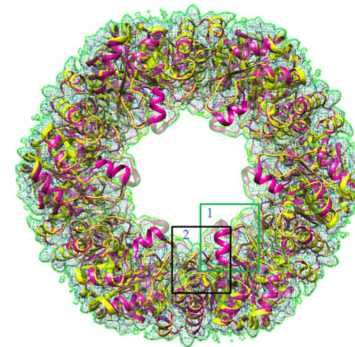
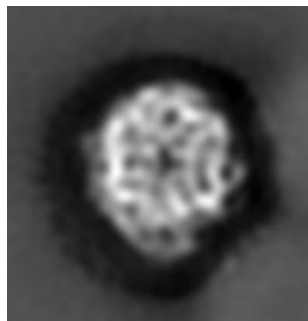
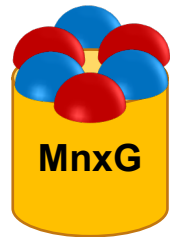
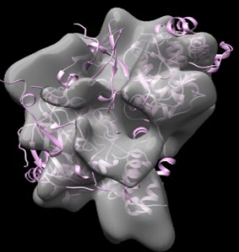
VP40



Complex 1



Complex 2



RNA-generated ring

