

Higher precision 3D analysis from structure to function

Combining cryo-electron microscopy with mass spectrometry

Determine how proteins function within the cellular environment by combining the near-atomic resolution of cryo-electron microscopy (cryo-EM) with advanced biomolecular mass spectrometry (MS). Integrating several complementary techniques can help you move beyond protein structure to understand the function and dynamics of large molecular machines.

Below are just a few examples of how various mass spectrometry techniques can be combined with cryo-EM to provide unique insights beyond protein structures. This includes native MS screening of sample quality prior to vitrification, crosslinking MS to increase the resolution of cryo-electron tomography (cryo-ET) structures, and hydrogen-deuterium exchange to provide a dynamic view of static protein structures. Integrative structural biology offers you the solutions to tackle today's most challenging scientific questions.

Accelerated adoption of integrated workflows that use mass spectrometry and cryo-EM.

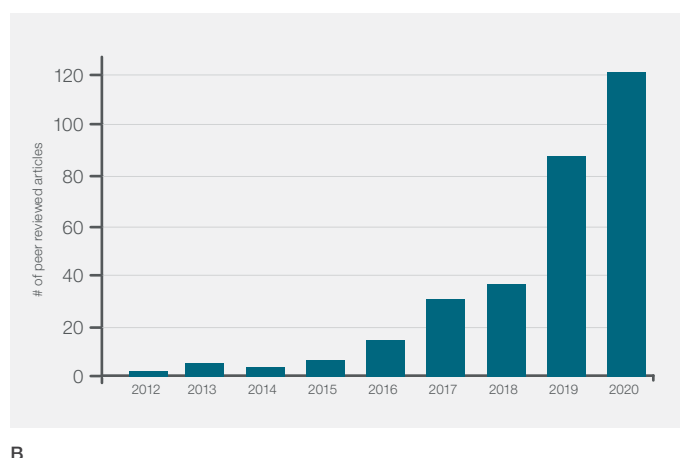
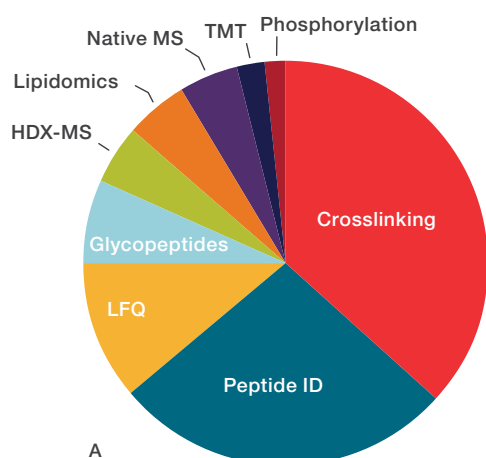


Figure 1. A) the most common mass specification applications that are used to supplement cryo-EM. B) the rapidly growing number of articles that feature Thermo Scientific™ cryo-EM and Orbitrap™ mass spectrometers.

Mass spectrometry toolbox for structural biology

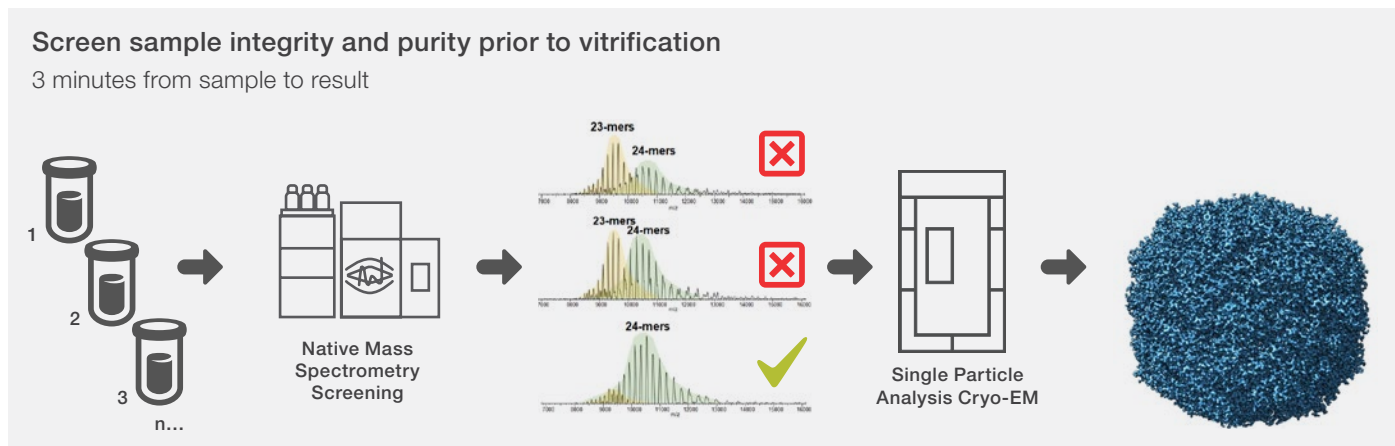


Figure 2. High-throughput native mass spectrometry: from sample to result in just three minutes.¹

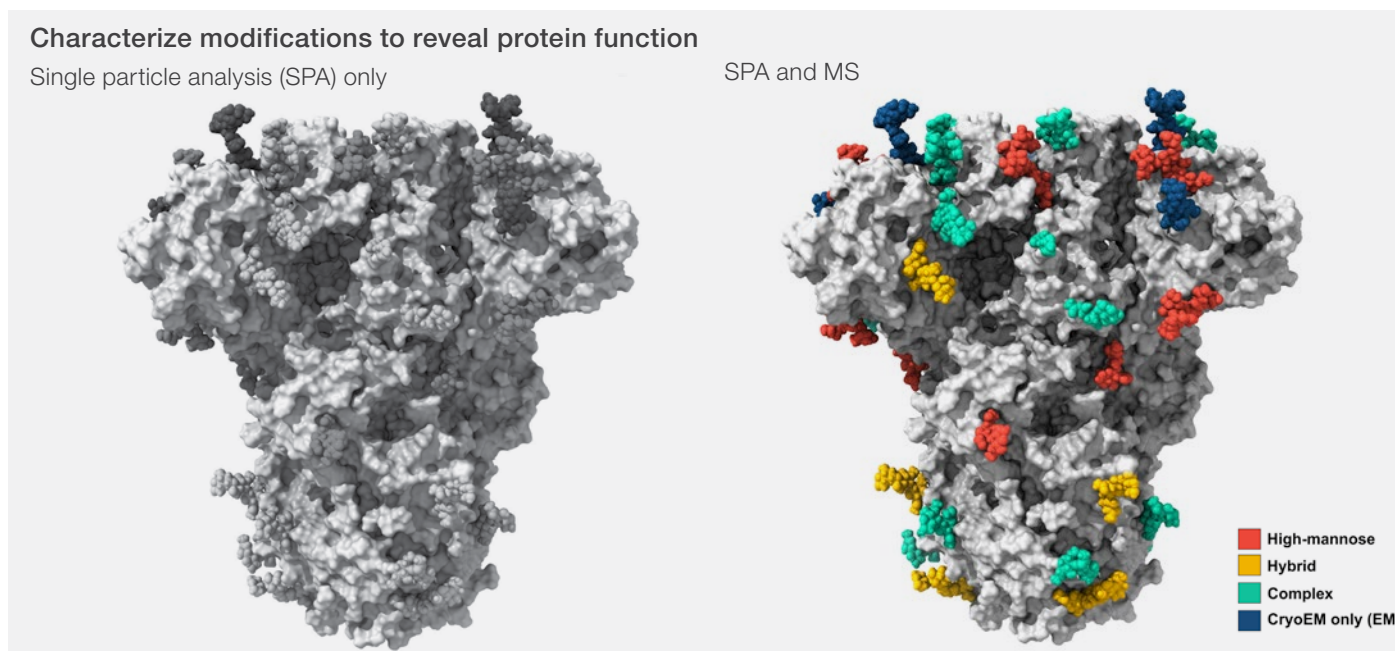


Figure 3. Glycoproteomics: characterization of the 5-glycan shield of coronavirus S glycoproteins (MERS-CoV S).²

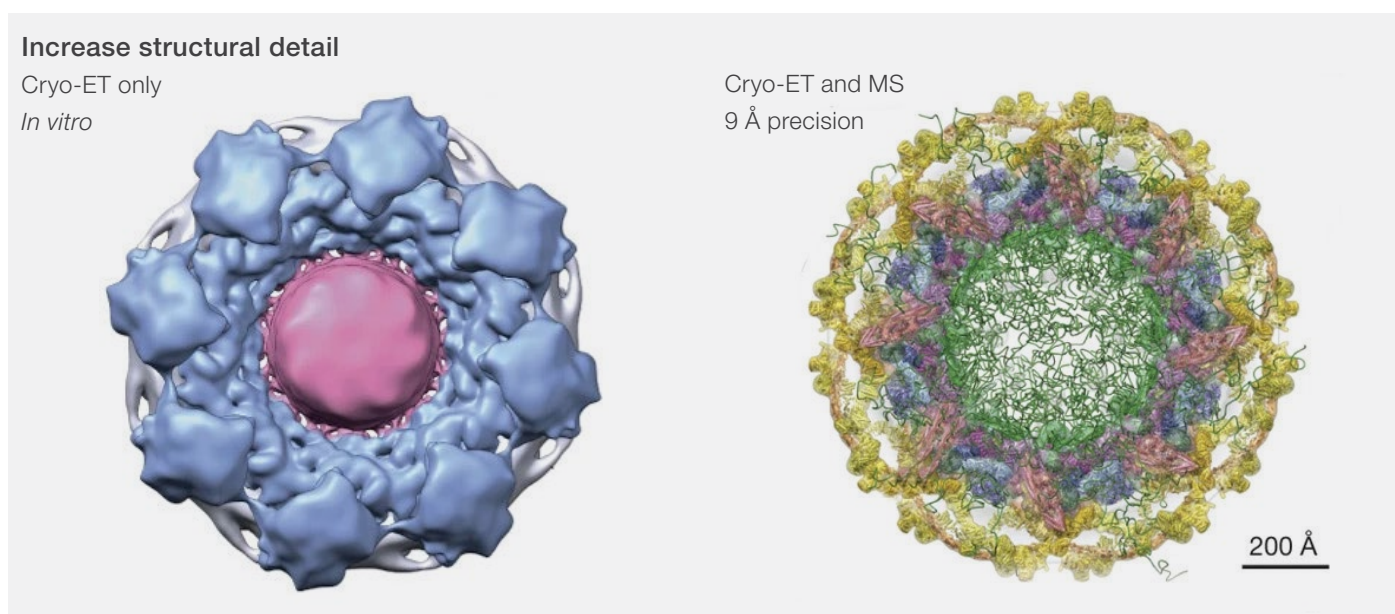


Figure 4. Crosslinking MS (XL-MS) with high-resolution cryo-ET provides detailed structural and functional insights into the nuclear pore complex a nuclear pore complex.³

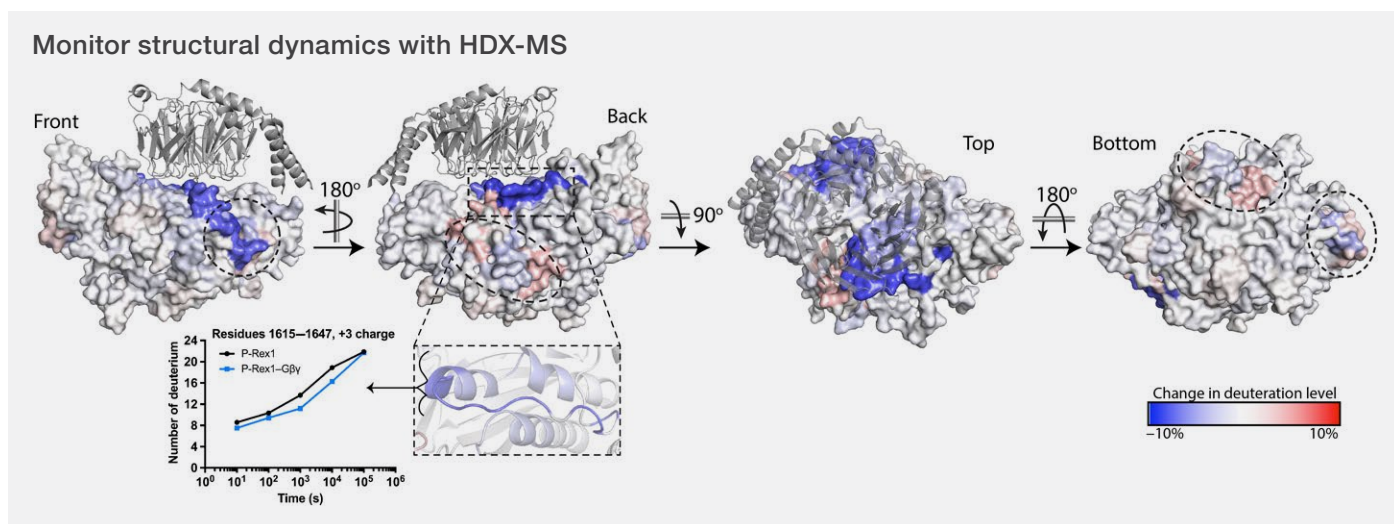


Figure 5. Hydrogen-deuterium exchange mass spectrometry (HDX-MS): ligand-binding dynamic of P-REX1 complex.⁴

Cryo-EM and MS workflow for integrated structural biology

Analytical techniques/workflow steps		MS*	Negative staining	SPA**	Cryo-ET**
Sample	Sample identity	●	○	○	○
	Biochemical optimization	●	●	◐	◐
	Sample quality screening	●	◐	●	◐
	Vitrification	○	○	●	●
Structure	Low resolution or initial model	◐	●	◐	◐
	3D construction or HR model	○	○	●	●
	Cellular information	◐	○	○	●
Function	Subunit connectivity	●	○	◐	○
	Complex dynamics	●	○	◐	○
	Lipids, ligands, modifications	●	○	◐	○

*<https://www.thermofisher.com/us/en/home/industrial/mass-spectrometry/proteomics-mass-spectrometry/protein-structure-analysis-mass-spectrometry.html>

**<https://www.thermofisher.com/us/en/home/electron-microscopy/life-sciences/learning-center.html>

References

1. Image generated by Thermo Fisher Scientific. For more information, please watch our webinar with Dr. Paul Dominic B. Olinares of Rockefeller University: <https://www.thermofisher.com/us/en/home/global/forms/industrial/integrative-structural-biology-webinars.html>
2. Walls AC, Xiaoli X, Park Y-J, et al. (2019) Unexpected receptor functional mimicry elucidates activation of coronavirus fusion. *Cell* 176(5): 1026–1039.
3. Kim SJ, Fernandez-Martinez J, Nudelman I, et al. (2018) Integrative structure and functional anatomy of a nuclear pore complex. *Nature* 555(7697): 475–482.
4. Cash JN, Urata S, Li S, et al. (2019) Cryo-electron microscopy structure and analysis of the P-Rex1-Gβγ signaling scaffold. *Sci Adv* 5(10): eaax8855.

Learn how to **optimize your MS workflows with cryo-EM**

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