# Bridging in situ Structural Biology and Multiscale Modelling: Mapping Human Chromatin 3D Architecture and Condensate Material States in Intact Cells

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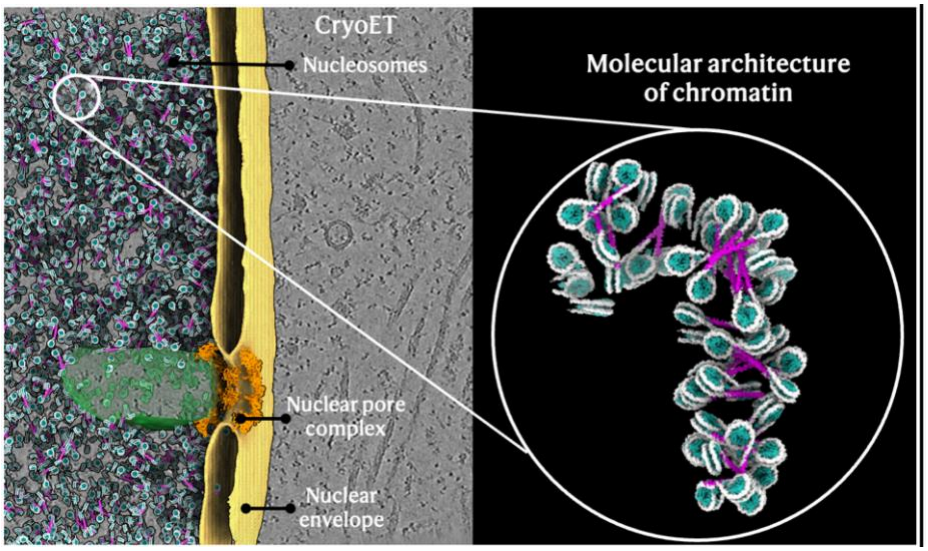
Cells are densely packed with molecular machines whose structure, localization, and dynamics shape cellular function. Cryo-electron tomography (cryoET) captures 3D snapshots of intact cells at near molecular resolution. However, extracting reliable molecular identities and interactions from tomographic data remains challenging.

In this talk, I will present how we combine high-confidence 3D template matching (hcTM) [1], a robust computational method for in situ feature detection, with multiscale molecular simulations to identify, model, and simulate subcellular environments directly from cryoET data [1-3]. This approach enables the localization of diverse complexes, including nuclear pores, HIV building blocks, vaults, ribosomes, proteasomes, lipid membranes, and cytoskeletal elements inside crowded eukaryotic cells. Combined with machine learning, hcTM also resolves subunits and functional states in situ. The resulting spatial maps form the basis for building simulation-ready models of subcellular environments. We applied this framework to study molecular transport [1], viral nuclear entry [2], chromatin organization [3], and the biophysical properties of biomolecular condensates inside cells [4].

By bridging experimental imaging and simulation, this integrative strategy advances in situ structural modeling across scales and opens new avenues for visual proteomics and the mechanistic understanding of cellular functions in their native context.




**Keywords**: Visual proteomics, cryoET, high-confidence template matching, multi-scale simulations, chromatin, biomolecular condensates.

[1] Cruz-León, et al., *Nat. Comm.*, 2024
[2] Kreysing*, Heidari*, Zila*, et al., *Cell,* 2025
[3] Kreysing*, Cruz-León*, Betz*, et al., *BioRxiv*, 2025
[4] Boyle*, Cruz-León*, Lizarrondo*, Brenner*, et al, BioRxiv, 2026