PHYSICAL CHEMISTRY SEMINAR

New cryoEM approaches to protein and nucleic acid structures in cellular milieu

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219 BRL

We have developed an integrative proteomics cryoEM method to determine atomic structures of native cellular complexes. Of particular note, our cryoID method allows determination of atomic structures of endogenous complexes in cellular milieu, capturing their multiple states, including those in their catalytic or metabolic actions.1 Applications of cryoID has enabled atomic structure determination of previously intractable protein and nucleic acid complexes from cellular milieu and membrane.2-4 While the cryoID approach works well for isolated macromolecular complexes at atomic resolution by averaging hundreds of thousands of particles, the biological functions of these complexes, however, are carried out through their interactions and often depend on their spatial arrangements within cells or sub-cellular organelles. Such molecular sociology information requires the use of cryogenic electron tomography (cryoET), which has another limitation, known as the “missing-wedge” problem. Anisotropic resolution arising from the intrinsic “missing-wedge” problem has presented major challenges in visualization and interpretation of tomograms. Towards this end, we have developed IsoNet,5 a deep learning-based software package that iteratively reconstructs the missing-wedge information and increases signal-to-noise ratio, using the knowledge learned from raw tomograms. Applications of IsoNet to processing cryoET data have allowed direct interpretation of molecular sociology of native complexes in cells.