# Advances in heterogeneous reconstruction with cryoDRGN

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Technological advances in cryo-electron microscopy (cryo-EM) have produced new opportunities to study the structural heterogeneity and dynamics of macromolecular complexes. However, this structural heterogeneity complicates 3D reconstruction and is traditionally addressed with discrete clustering approaches that fail to capture the full range of biomolecular dynamics. In this talk, I will overview cryoDRGN, a heterogeneous reconstruction algorithm that leverages the expressive representation power of deep neural networks to reconstruct continuous distributions of cryo-EM density maps. Trained on single particle cryo-EM images, cryoDRGN is capable of reconstructing complex distributions including both discrete compositional and continuous conformational changes. The openly available cryoDRGN software contains automated and interactive tools to inspect the volume ensemble, segment the dataset for further refinement in traditional tools, and filter impurities from datasets. Through a series of vignettes, I will highlight advantages and disadvantages of this approach, extensions, and new opportunities to extract the full spectrum of functionally relevant macromolecular states with single particle cryo-EM.