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Roy R. Lederman*, roy@math.princeton.edu. *Inverse Problems and Unsupervised Learning with applications to Cryo-Electron Microscopy.*

Cryo-Electron Microscopy (cryo-EM) is an imaging technology that is revolutionizing structural biology; the Nobel Prize in Chemistry 2017 was recently awarded "for developing cryo-electron microscopy for the high-resolution structure determination of biomolecules in solution". While some alternative methods, such as x-ray crystallography and NMR, measure ensembles of molecules, cryo-electron microscopes produce images of individual molecules. Therefore, cryo-EM could potentially be used to study mixtures of different conformations of molecules. Current algorithms have been very successful at analyzing homogeneous samples, and can recover some distinct conformations mixed in solutions, but, the determination of multiple conformations, and in particular, continuums of similar conformations (continuous heterogeneity), remains one of the open problems in cryo-EM. I will talk about different components which we are introducing in order to address the problem of continuous heterogeneity in cryo-EM: 1. "hyper-molecules," the mathematical formulation of truly continuously heterogeneous molecules, 2. Computational tools for expressing associated priors, and 3. Bayesian algorithms for inverse problems with an unsupervised-learning component for recovering such hyper-molecules. (Received February 13, 2018)