Cryo-electron microscopy (cryo-EM) is an imaging technology that is revolutionizing structural biology, enabling reconstruction of molecules at near-atomic resolution. Cryo-EM produces a large number of noisy two-dimensional tomographic projection images of a molecule, taken at unknown viewing directions. The extreme levels of noise make classical tasks in statistics and signal processing, such as alignment, detection and clustering, very challenging.

I will start the talk by studying the multi-reference alignment problem, which can be interpreted as a simplified model for cryo-EM. In multi-reference alignment, we aim to estimate multiple signals from circularly-translated, unlabeled, noisy copies. In high noise regimes, the measurements cannot be aligned or clustered. Nonetheless, accurate and efficient estimation can be achieved via group-invariant representations (invariant polynomials). Furthermore, such estimators achieve the optimal estimation rate.

Then, I will show how this framework can be applied to the problem of 2-D classification in cryo-EM. In the last part of the talk, I will introduce the analog invariants of the cryo-EM problem and discuss how they can be used for ab initio modeling.