Cryo-electron microscopy (cryo-EM) has become a tool of fundamental importance in structural biology, helping us visualize the shape and motion of isolated biomolecules in ever increasing details. A challenge that reconstruction algorithms are facing is the rapidly growing size of cryo-EM datasets, leading to high computational and memory costs. The algorithmic challenge of cryo-EM is to jointly estimate the unknown 3D poses and the 3D electron scattering potential of a biomolecule from millions of extremely noisy 2D images. Traditionally, this task is performed through some variant of orientation matching, which scales poorly with dataset size. I will present cryoAI, an ab initio algorithm for homogeneous reconstruction that uses direct gradient-based optimization of particle poses and the electron scattering potential from single-particle cryo-EM data. CryoAI combines a learned encoder that predicts the poses of each particle image with a physics-based decoder to aggregate each particle image into a neural representation of the scattering potential volume. I will show how this inference approach opens a way to tackle arbitrarily large datasets.