

# Computational Tools Aiding Helical Indexing for Helical Reconstruction with Cryo-EM

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## Abstract

Helical structures are a common form of many biological macromolecules, many of which are known to play important roles in different biological processes. The symmetrical nature of the helical filaments is utilized in Cryo-EM to increase the signal to noise ratio and many solved structures yield near-atomic resolution reconstructions. However, challenges still occur in accurately determining the helical parameters, which are the twist and the rise. Here, we introduce a set of tools we developed to comprehensively index the helical parameters from 2D particle classifications yield from RELION or CryoSPARC, including an open-source Web app, HILL, which features the side-by-side display of power spectrum and phase difference plot with synchronized mouse hovering, making it more feasible to assess the Bessel order of the layer lines and the point group symmetry, and the out-of-plane tilt of the 2D average image. In addition, to enhance helical indexing scenarios having curved filaments, we also embedded a helical segment straightening tool (also with a stand-alone script) in HILL that computationally find the curved helical axis from the curved filament segments and use interpolation to generate the straightened filament. Such support will make it more feasible to perform indexing with longer straightened helical segments which could show sharper layer line features and give better estimation of the helical pitch.

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