

1. Q: Is this numerical integration or a different kind? [Page 2]

A: I think it is numerical, let me explain in details. In biological macromolecule crystallography data processing, the integration step refers to the process of integrating the recorded diffraction images from a crystal into a three-dimensional electron density map. The data reduction involves several key procedures: (1) spot finding: to identify and locate the diffraction spots in the recorded images, (2) indexing: to determine the crystal lattice parameters and orientation, **(3) integration:** after the indexing step, the recorded diffraction images are integrated, which involves summing up the intensities of the diffraction spots within each image. This integration process takes into account factors such as spot shape, background noise, and correction for detector imperfections. I will omit further steps here.

2. Q: Is there a reference for this? [Page 3]

A: A contribution highlighting the Daisy project has been presented at CHEP2023 [<https://indico.jlab.org/event/459/contributions/11400/>]. Additionally, there exists an article [<https://arxiv.org/abs/2103.00786>] that may be considered somewhat outdated. We are currently in the process of preparing a new paper to provide the latest updates and advancements in this continuously evolving project.

3. Q: Is there a reference for this? [Page 4]

A: When searching for protein structures in online databases such as those provided by AlphaFold, it is often noted that this method is fast but may not be as suitable for unconventional sequences. The reason for this remark lies in the nature of unconventional sequences, which typically deviate from the standard protein structure patterns and may possess unique structural features or modifications.

AlphaFold and similar methods rely on machine learning algorithms trained on a vast amount of known protein structures. These algorithms excel at predicting the structures of proteins that follow conventional folding patterns. However, unconventional sequences that exhibit non-standard folding behaviors or contain atypical structural elements may pose challenges for these algorithms and thus these models may struggle to accurately predict their structures due to the lack of sufficient training data representing such sequences.