KINARI-BioAssembly Case Study: 1HHP

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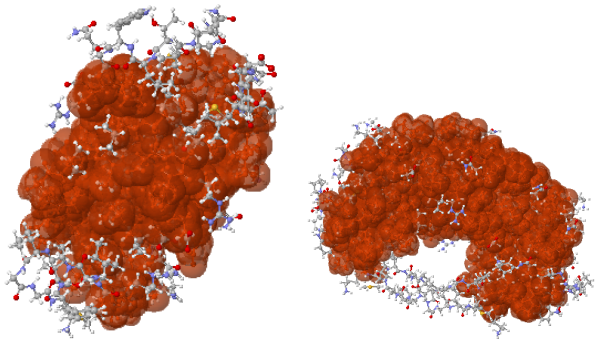

(a) 1HHP Asymmetric Unit (b) 1HHP Biological Assembly (2 copies of Asymmetric Unit)

Figure 1: Visualization of rigidity analysis results of 1HHP from KINARI. The asymmetric unit (a) has one large rigid cluster. When two asymmetric units are combined to for the biological unit (b), the rigid clusters of the two individual clusters in each asymmetric unit combines to form one even larger rigid cluster.

1HHP is the aspartyl protease from HIV-1 isolate BRU. HIV-1 protease is the human immunodeficiency virus, which has no known cure. HIV-1 isolate BRU is a recombinant protein, meaning that it is formed with recombinant DNA, or DNA sequences that derive from laboratory methods such as molecular cloning [2]. HIV-1 isolate BRU is known to be the most widely used strain in the study of potential drugs against this virus [2]. The protein is composed of two identical chains, and each chain contains 99 residues. The

PDB file for 1HHP contains only one of the two chains as the asymmetric unit. Using the integrated version of KINARI BioAssembly with KINARI Curation and Rigidity Analysis, we can see the evolution of the rigidity of 1HHP from its asymmetric unit form to its functional (biological assembly) form (Table 1).

Table 1: Rigidity results for 1HHP - the number of each type of rigid cluster is listed for the asymmetric and biological unit. The asymmetric unit contains one copy of chain A, and the biological unit contains two copies of chain A (AU = Asymmetric Unit, BU = Biological Unit).

Size	**AU**	**BU**
3	23	38
4	8	12
5	199	336
6	34	44
11	3	4
12	2	2
15	1	0
16	2	2
19	1	2
710	1	0
1802	0	1

From the KINARI Rigidity Analysis results, we see that the asymmetric unit of 1HHP (Fig. 1a) has one large rigid cluster of 710 atoms. All other clusters have 19 or fewer atoms. When the biological assembly of 1HHP (Fig. 1b) is analyzed, we see that the two chains combine to form one large rigid cluster of 1802 atoms with two flexible protein flaps. This indicates that the chemical interactions between the two chains that make up the biological assembly has an effect on the rigidity of the structure. These results are consistent with the studies on the protein's function. When the virus is in action, its flaps open to wrap around the host protein. The host protein is then held tightly inside the tunnel formed by the rigid part of the virus, where the virus then breaks down the host protein [1].

References

[1] D. Goodsell. HIV-1 protease. *RSCB PDB Molecule of the Month*, 2000.

[2] E. A. Semenova, N. Gashnikova, T. V. Il'ina, T. R. Pronyaeva, and A. G. Pokrovsky. Characterization of recombinant integrase of human immunodeficiency virus type 1 (isolate Bru). *Biochemistry*, 68(9):988–993, 2003.