

MDQ: A Symmetric Metric for MD-Based Protein Complex Analysis

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Monitoring protein–protein interface evolution during molecular dynamics (MD) simulations is essential to determine whether complexes converge toward similar conformations, undergo interface rearrangements, or sample multiple structural states. Clustering MD trajectories can therefore help identify distinct interface conformations based on structural descriptors and shared interface residue contacts.

However, conventional docking score is not adapted for this purpose, as it was designed to compare docking models against native reference structures. In MD simulations, only frames from the same trajectory are compared, resulting in score asymmetry.

To address this limitation, we developed MDQ (Molecular Dynamic DockQ), a symmetric and reference-free scoring framework inspired by DockQ. MDQ combines three complementary metrics: Fraction of Shared Contacts (FSC) to quantify shared interface residue pairs, interface RMSD (iRMSD) to measure interface structural deviations, and ligand RMSD (LRMSD) to evaluate ligand displacement relative to the receptor interface.

The resulting MDQ score enables clustering and monitoring of interface evolution throughout MD simulations. MDQ was applied to two protein complexes and complemented by interaction profiling analyses, allowing validation of conformational clusters through comparison of interaction patterns and interface rearrangements.

Bibliography :

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