Comparing macromolecular complexes - a fully automated benchmarking suite

Supplemental Materials

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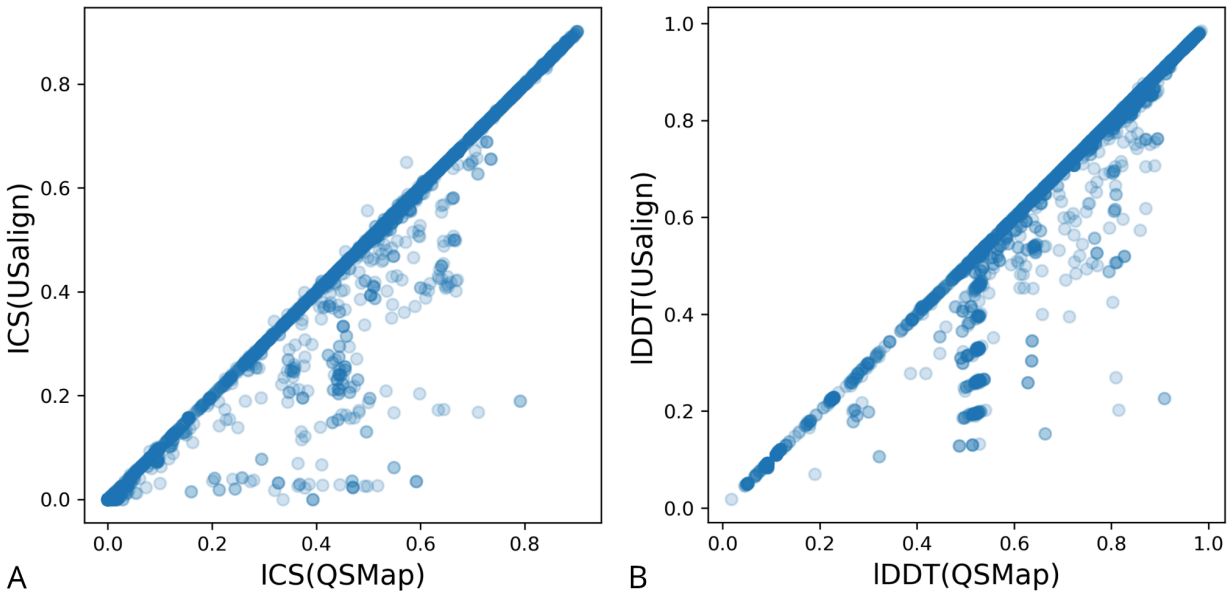

Fig S1: Chain mapping comparison QSMap / USalign. Score differences for interface contact similarity (ICS) (A) and (Cα) LDDT (B) on all models of selected CASP15 prediction targets. Chain mappings from QSMap are better in terms of contact based comparisons.

S1 LDDT summary

For each interatomic distance ≤15 Å in the reference structure, a comparison is made with its corresponding counterpart in the model. LDDT calculates the fraction of distance differences that fall below a threshold *d*. Distances involving atoms that are not present in the model are considered unfulfilled, i.e. above the threshold. The finally reported values are averages of four fractions calculated using thresholds [0.5, 1.0, 2.0, 4.0].

As a preprocessing step, LDDT evaluates stereochemistry, checking the model for significant stereochemical irregularities such as uncommon bond lengths/angles and clashes. Ideal bond lengths and angles, along with their standard deviations, are hardcoded for proteinogenic amino acids according to Engh and Huber [1]. Deviations exceeding 12 standard deviations are considered serious violations. Additionally, interatomic distances between pairs of non-bonded atoms in the model are considered clashing if the distance between them is smaller than the sum of their corresponding atomic van der Waals radii (Allen, 2002), within a predefined tolerance threshold (by default 1.5 Å). LDDT is penalized by removing all sidechain atoms if any of the sidechain atoms is involved by such irregularities or by removing all atoms of the entire residue if the backbone is involved (backbone definition for amino acids: N, CA, C, O, all other atoms are considered sidechain atoms). The latter results in a per-residue LDDT of 0.0.

Some residues are symmetric, i.e. allow different mappings between reference and model that are chemically equivalent. One example are the OD1/OD2 atoms in aspartic acid (ASP). Symmetries in proteinogenic amino acids can additionally be found in glutamic acid (GLU), leucine (LEU), valine (VAL), arginine (ARG), phenylalanine (PHE) and tyrosine (TYR). In LDDT, residues with symmetric atoms are pre-processed by calculating the LDDT score for the symmetric atoms relative to all fixed atoms (i.e., atoms from other residues that are not symmetric). Two computations are performed: LDDT_1 uses the mapping based on the original atom naming and LDDT_2 a swapped mapping (e.g. OD1 and OD2 in ASP are interchanged). The higher scoring mapping is then used in the final LDDT computation.

S2 Comparison to reference implementations

DockQ/ f_{nat}/ iRMS/ LRMS: OpenStructure aims to be an exact clone of these scores which are designed to assess two-body problems, i.e. dimers. We compiled a testset of 6408 models from 23 dimer targets in the CASP15 assembly prediction category [2] to compare the OpenStructure implementations with DockQ v2.1.3 available from https://github.com/bjornwallner/DockQ. Chain mapping derived from QSMap was set as a command line parameter in DockQ. Results from OpenStructure closely match the ones from DockQ v2.1.3 (Fig S2).

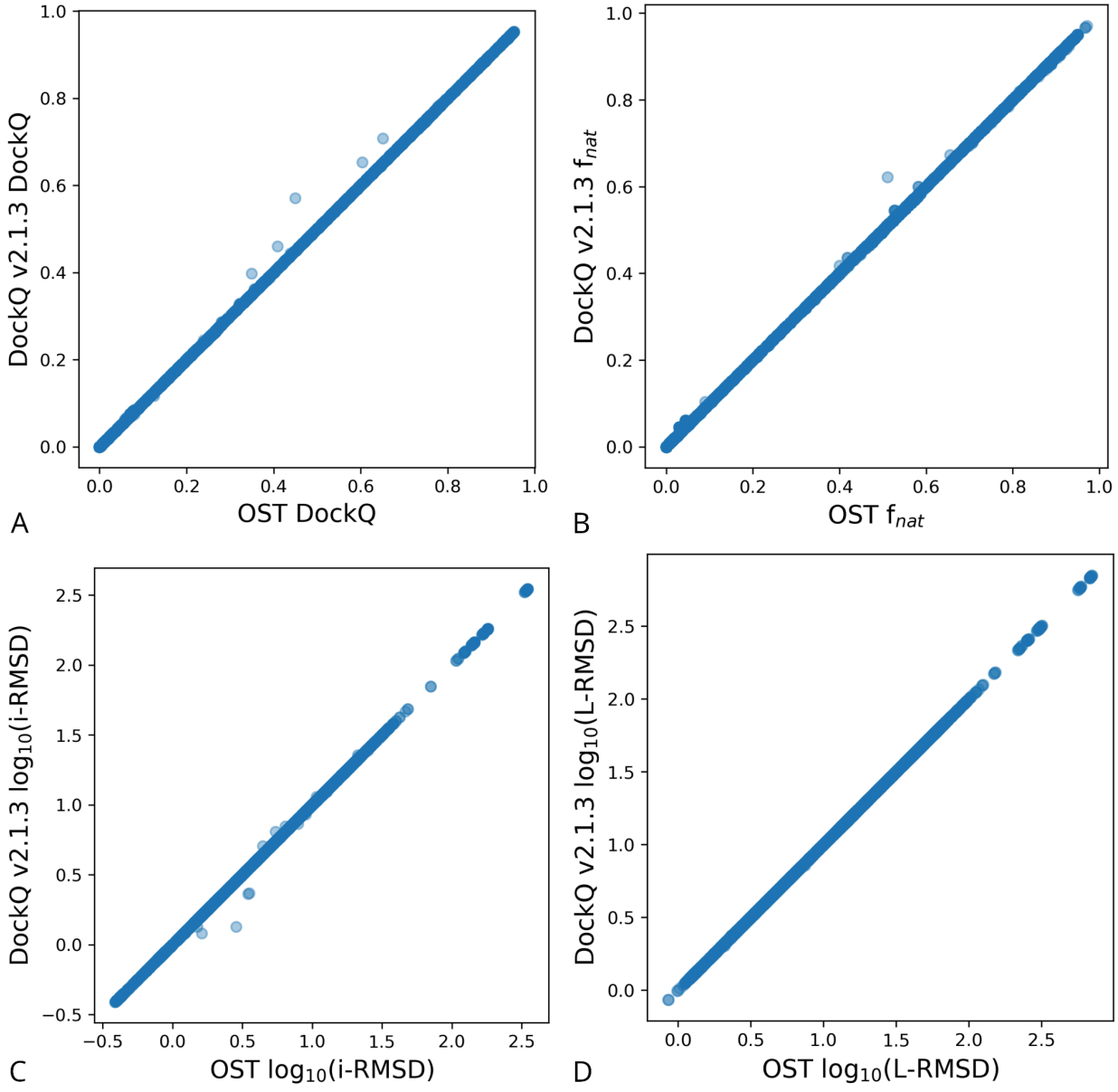

Fig S2: Comparison of DockQ v2.1.3 and OpenStructure (OST) DockQ scores on 6406 CASP15 dimer structure model/reference pairs. Closely matching values for DockQ (A) and all scores contributing to it: f_{nat} (B), iRMSD (C) and lRMSD (D).

ICS/IPS: We compiled a testset of 11122 models from 41 assembly targets in the CASP15 assembly prediction category [2] to compare the OpenStructure implementations with scores reported by the Prediction Center (https://predictioncenter.org/download_area/CASP15/results/tables/oligo.tar.gz). Results from OpenStructure closely match for dimers. Results for higher order assemblies are qualitatively similar, with discrepancies likely due to differences in chain mapping and score aggregation (Fig S3).

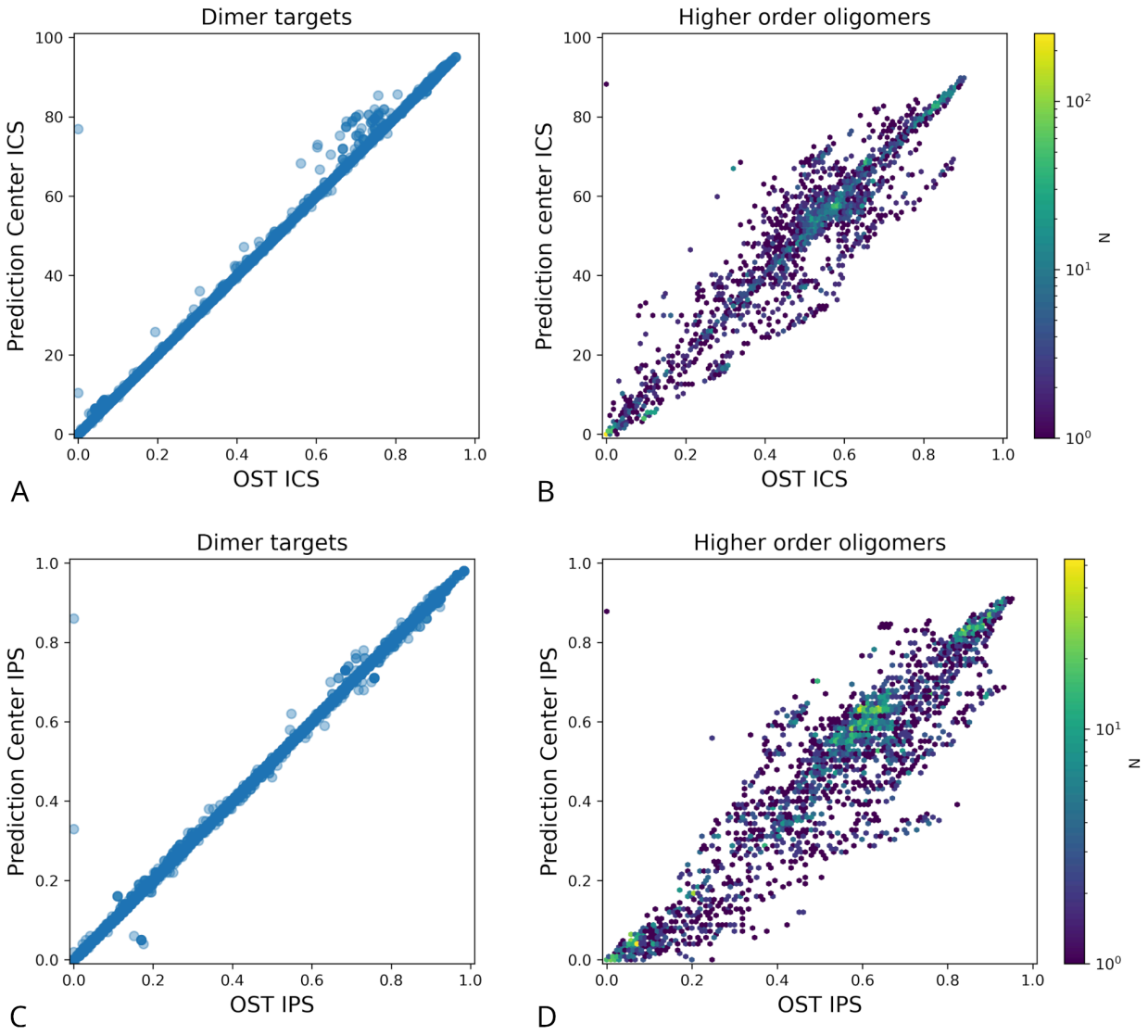

Fig S3: Comparison of ICS/IPS scores from Prediction Center and OpenStructure (OST) on 6323 CASP15 dimer structure model/reference pairs and 4627 higher order oligomer model/reference pairs. Scores for dimers closely match (A/C) and scores for higher order oligomers are qualitatively similar (B/D).

GDT: Since LGA does not support oligomers, we used all CASP15 tertiary structure models with domain-split reference structures as provided by the CASP15 organizers (20644 data points) to compare GDT_TS from OpenStructure with GDT_TS scores reported by the Prediction Center (https://predictioncenter.org/download_area/CASP15/results/sda/). The scores closely match, with 99.5% of the values falling within 2 points of each other on a scale of 0 to 100. On average, GDT_TS scores obtained from the Prediction Center were 0.21 points higher than those from OpenStructure, with the largest discrepancies observed in models with lower GDT_TS scores (Fig. S4).

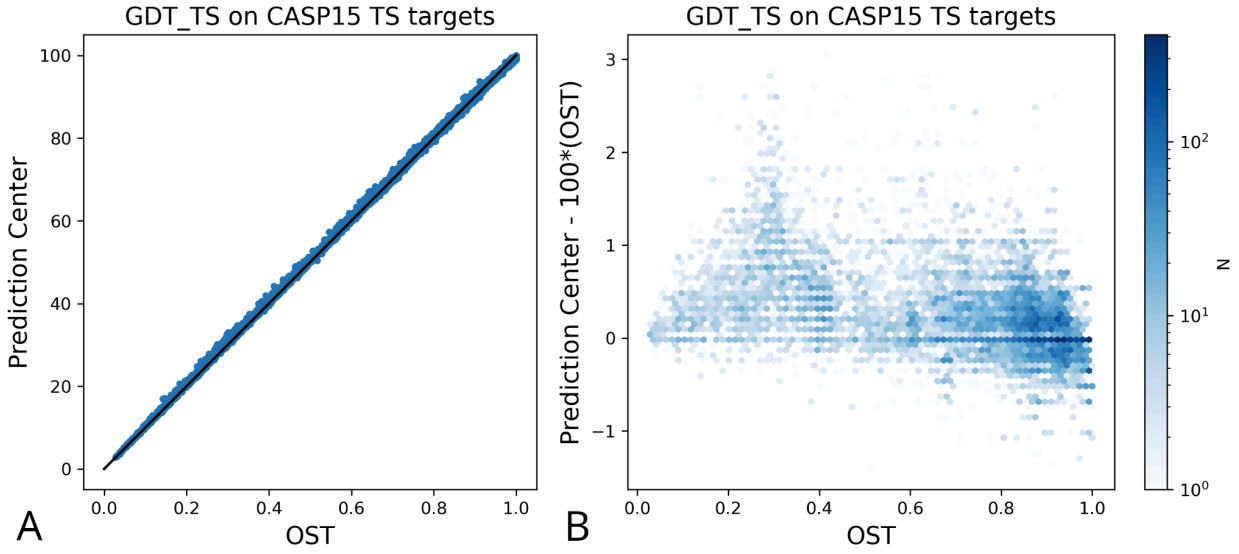

Fig S4: Comparison of GDT_TS scores from Prediction Center and OpenStructure (OST) on 20644 CASP15 tertiary structure model/reference pairs. (A) The scores closely match, with 99.5% of the values falling within 2 points of each other on a scale of 0 to 100. (B) On average, GDT_TS scores obtained from the Prediction Center were 0.21 points higher than those from OpenStructure, with the largest discrepancies observed in models with lower GDT_TS scores.

Supplemental References

1. Engh, R. A. & Huber, R. Accurate bond and angle parameters for X-ray protein structure refinement. *Acta Crystallogr. A* **47**, 392–400 (1991).
2. Ozden, B., Kryshtafovych, A. & Karaca, E. The Impact of AI-Based Modeling on the Accuracy of Protein Assembly Prediction: Insights from CASP15. *bioRxiv* (2023) doi:10.1101/2023.07.10.548341.