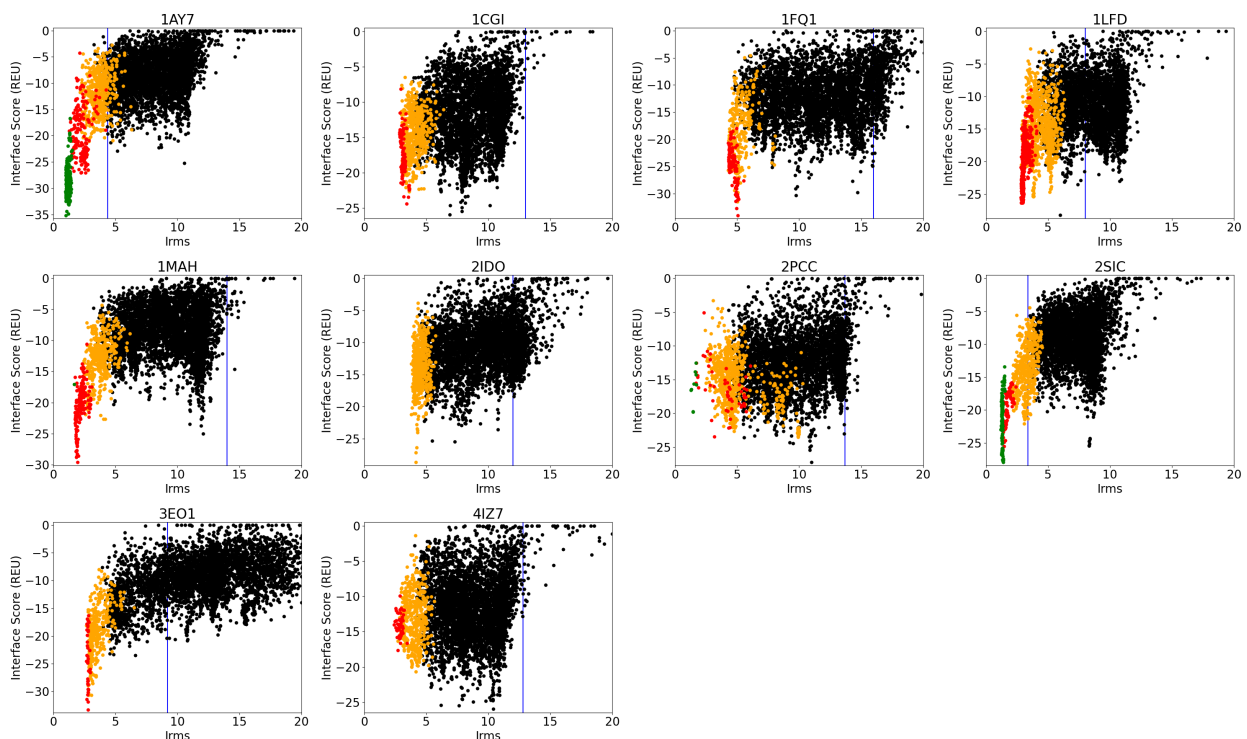


# Scientific test: docking

## FAILURES

None

## RESULTS



## ## AUTHOR AND DATE

Adapted for the current benchmarking framework by Shourya S. Roy Burman (ssrburman@gmail.com; Gray Lab) and Ameya Harmalkar (harmalkar.ameya24@gmail.com; Gray Lab), Jan 2021

## ## PURPOSE OF THE TEST

This benchmark is meant to test how well we discriminate native protein-protein binding orientations from decoys based on the interface score term by performing standard protein-protein docking experiments across a diverse set of protein-protein complexes.

## ## BENCHMARK DATASET

The dataset consists of 10 protein-protein complexes extracted from the Docking Benchmark 5.0 (Vreven, T. et al. J. Mol. Biol., 2015). The set contains 4 rigid (conformational change < 1.5 Ang), 4 medium-flexible (conformational change between 1.5 and 2.2 Ang), and 2 difficult (conformational change > 2.2 Ang).

Structure preparation:

Proteins were extracted directly from the PDB according to the PDB ID of the native structure. They were then cleaned to ensure that both the bound and the unbound structures have the same residues. The unbound structures were superimposed on the bound and then the smaller partner (ligand) was moved away by 15 Ang and rotated by 60 degrees to scramble the interface

## **## PROTOCOL**

Protocol (as per the publication below): "RosettaDock is a Monte Carlo-plus-minimization algorithm consisting of a low-resolution stage, which simulates conformer selection during the formation of the encounter complex, followed by a high-resolution stage, which simulates induced fit in the bound complex. To produce a variety of starting states for the different trajectories, the ligand (the smaller protein) is first randomly rotated and translated about the receptor (the larger protein). In the low-resolution stage, side chains are replaced by coarse-grained "pseudoatoms", allowing the ligand to efficiently sample the interface by rigid-body movements in a smoothed energy landscape. These rigid-body moves are coupled with backbone conformation swaps where the current backbone conformations of the ligand and the receptor are swapped with different ones from a pre-generated ensemble of conformations. In the high-resolution stage, the side chains are reintroduced to the putative encounter complex and those at the interface are packed for tight binding. There is minimal rigid-body motion in this second stage."

Publication:

The methodological details of the protocol, RosettaDock 4.0 and the performance on the benchmark have been thoroughly discussed in Marze, N. A., Roy Burman, S. S. et al. [Bioinfo., 2018](#).

CPU hours:

The benchmark takes ~833 CPU hours (10 targets x 5000 decoys x 60s per decoy). The debug mode takes ~4 mins.

## **## PERFORMANCE METRICS**

Usually, to assess the performance of a docking simulation, the number of structures with a CAPRI-acceptable or better ranking are analyzed. CAPRI model rankings are based on a combination of factors like fraction of native contacts, ligand RMSD, and interface RMSD and are described in detail in [Lensink, Wodak et al. 2019 PSFBI](#) - Table 3. The protocol computes the CAPRI rankings for each model (as well as some of the metrics it is based on), which are written into the score file ("CAPRI\_rank"). Rankings are the following:

- 0 - incorrect model (black)
- 1 - acceptable model (yellow)
- 2 - medium quality model (red)

### 3 - high quality model (green)

The output models are resampled via bootstrap to remove possible sampling biases. Docking complexes can also be classified via the N5 metric, classifying  $N5 \geq 3$  as successful.  $N5 \geq 3$  means that at least 3 out of the top 5 scoring models should be acceptable or better according to CAPRI metrics. In this test, we report this metric in the result.txt file but don't use it for a pass/fail criterion because most targets would fail according to it. This scientific test passes if all targets pass the following metrics:

(1) the highest CAPRI ranking sampled for any model should be equal or higher than the cutoff ranking (as computed in the first run) AND

(2) the interface RMSD of the top-scoring model should be equal or lower than the cutoff  $I\_rmsd$  (as computed in the first run + 2A)

## **## KEY RESULTS**

Unbound structures are docked and compared to the bound native structure.

## **## DEFINITIONS AND COMMENTS**

For speed, this test does not use conformational ensembles of unbound proteins. For best results, use ensembles as described in the article.

## **## LIMITATIONS**

This is a small part of a much larger standard docking benchmark used in the docking community (Vreven, T. et al. J. Mol. Biol., 2015). More targets from that benchmark will help.