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EROS-DOCK for Pairwise and Multi-body Protein-Protein Docking

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Protein-protein docking algorithms aim to predict the 3D structure of a complex using the structures of the individual proteins. For binary complexes, this involves searching and scoring in a six-dimensional space. Many docking algorithms use FFT techniques to exhaustively cover the search space and to accelerate the scoring calculation. However, the results often depend on the initial protein orientations with respect to the Fourier sampling grid. Furthermore, Fourier-transforming a physics-based force field can involve a serious loss of precision.

Here, we present a novel docking algorithm called EROS-DOCK (Exhaustive Rotational Search based Docking) [1] to rigidly dock two proteins using a series of exhaustive 3D rotational searches in which non-clashing orientations are scored using ATTRACT coarse-grained force field (ff) [2]. Initial positions are defined by putting each attractive pair of surface pseudo-atoms at their optimal distance in the ff. Thus, EROS-DOCK retains the exhaustive nature of FFT-based search algorithms while using a sensitive physics-based scoring function. Rather than calculating an $O(N*M)$ interaction energy explicitly at every grid point, we use a quaternion “ π -ball” to represent the space of all possible 3D Euler angle rotations [3], and we recursively sub-divide the π -ball in order to cover the rotational space systematically, from each initial position. An associated tree-like data structure allows rotations that give steric clashes to be pruned efficiently using a “branch-and-bound” technique. To our knowledge, this is the first time that such a branch-and-bound pruning technique has been applied to the rigid-body protein docking problem.

The EROS-DOCK algorithm was tested on 173 target complexes from the Protein Docking Benchmark (v4) [4], and results were compared with those of ATTRACT and ZDOCK [5]. Overall, EROS-DOCK was able to find local minima that were not explored by the ATTRACT gradient-driven atom-based search. After refinement by a short coarse-grained minimization, the EROS-DOCK results were generally better than those of ATTRACT and ZDOCK, according to the standard CAPRI criteria.

EROS-DOCK can use contact restraints as an additional pruning criteria. Our results show that using even just one residue-residue restraint in each interaction interface is sufficient to increase the number of cases with acceptable solutions within the top 10 from 51 to 121 out of 173 pairwise docking cases. We used EROS-DOCK with restraints to dock trimeric complexes by combinatorial assembly of pairwise solutions. We expected that all interfaces in a multi-body docking solution should be similar to at least one interface in each lists of pairwise docking solutions. Thus, we used a new fast technique to calculate the RMSD between pairs of transformation matrices [6], and an adaptation of the branch-and-bound rotational search algorithm to accelerate the search for low RMSD docking solutions. By test on a home-made benchmark of 11 three-body cases, 7 obtained at least one acceptable quality solution in the top 50 solutions.

References

- [1] EROS-DOCK: Protein-protein docking using exhaustive branch-and-bound rotational search. M.-E. Ruiz-Echartea, I. Chauvo de Beauchene, D. W. Ritchie, *Bioinformatics* (2019), pii: btz434
- [2] Binding site prediction and improved scoring during flexible protein-protein docking with ATTRACT. S Fiorucci & M Zacharias. *Proteins* (2010), 78:3131-3139.
- [3] Global Optimization through Rotation Space Search. RI Hartley & F Kahl. *Int. J. Comp. Vis.* (2009), 82:64-79.
- [4] Protein-protein docking benchmark version 4.0. H Hwang et al. *Proteins* (2010), 78:3111-3114.
- [5] Accelerating protein docking in ZDOCK using an advanced 3D convolution library. BG Pierce, Y Hourai & Z Weng. *PLoS One* (2011), 6(9):e24657.
- [6] Rapid determination of RMSDs corresponding to macromolecular rigid body motions. P. Popov, S. Grudinin. *J. Comp. Chem.* (2014), 35(12):950-956.