Using machine learning and fast conformational space exploration techniques for some problems in structural bioinformatics

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Computer simulations in structural biology have become an integral part of current research activities. To elucidate some structure or function of biological systems, most often researchers use molecular dynamics simulations with classical forcefields. However, the application of these methods to large biomolecules still faces important practical difficulties due to the combinatorial explosion of possible interactions involved. There have been numerous attempts to reduce the size of the conformational space of a system under study that would increase the efficiency of the simulations. Consequently, the reduced conformational space would require the adapted potential functions.
I my talk will demonstrate how machine learning and optimization in general can be used to design interaction potentials adapted to specific conformational space exploration problems. More precisely, I will present our recent results on the prediction of properties of small molecules [1], on the prediction of protein-protein [2, 3, 4] and protein-drug interactions [5, 6], as well as individual protein folds at atomic level. I will also present some methods for efficient space exploration including FFT-accelerated techniques [2, 6]. Some relevant publications can be also found on our website at https://team.inria.fr/nano-d/publications/.

Références

[1] Maria Kadukova & Sergei Grudinin, *Knodle: A Support Vector Machines-Based Automatic Perception of Organic Molecules from 3D Coordinates*, Journal of Chemical Information and Modeling, 2016, 56 (8), pp.1410-1419.

[2] Emilie Neveu, David Ritchie, Petr Popov & Sergei Grudinin, *PEPSI-Dock: a detailed data-driven proteinprotein interaction potential accelerated by polar Fourier correlation*, Bioinformatics, 2016, 32 (7), pp.i693-i701.

[3] Petr Popov & Sergei Grudinin, *Knowledge of Native ProteinProtein Interfaces Is Sufficient To Construct Predictive Models for the Selection of Binding Candidates*, Journal of Chemical Information and Modeling, 2015, 55 (10), pp.2242-2255.

[4] Marc F. Lensink et al., *Prediction of homo- and hetero-protein complexes by protein docking and template-based modeling: a CASP-CAPRI experiment*, Proteins, 2016, 84 (S1), pp.323-348.

[5] Sergei Grudinin, Maria Kadukova, Andreas Eisenbarth, Simon Marillet & Frdric Cazals, *Predicting binding poses and affinities for protein-ligand complexes in the 2015 D3R Grand Challenge using a physical model with a statistical parameter estimation*, Journal of Computer-Aided Molecular Design, 2016, 30 (9), pp.791-804.

[6] Sergei Grudinin, Petr Popov, Emilie Neveu & Georgy Cheremovskiy, *Predicting Binding Poses and Affinities in the CSAR 20132014 Docking Exercises Using the Knowledge-Based Convex-PL Potential*, Journal of Chemical Information and Modeling, 2016, 56 (6), pp.1053-1062.

[7] David W. Ritchie & Sergei Grudinin, *Spherical polar Fourier assembly of protein complexes with arbitrary point group symmetry*, Journal of Applied Crystallography, 2016, 49 (1), pp.158-167.

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