A differentiable representation of solvent-solute interface

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Abstract

The biophysical processes of protein, include ligand binding, protein folding, have attracted lots of interest for decades. Implicit solvent models are widely used to research these processes in silico, as the explicitly solvated protein model is too expensive to be simulated. A critical step of constituting an effective implicit solvent model is representing the solvent-solute interface properly. However, most current representations are based on specific geometric criteria, making the interface derivative hard to calculate. To overcome this difficulty, we introduced a Transformer-like neural network to represent the solvent-solute interface. This network is trained on a dataset containing 8000 all-atom solvated protein models and has a good generalization ability for the untrained protein structure.

1 Introduction

Since Max Perutz and John Kendrew resolved the Myoglobin's structure in 1960[1;2;3], the native structure of protein has attracted many scientists for over six decades, as this knowledge is germane for the advanced research in many area, for example: pharmaceutics[4;5;6], enzyme catalysis mechanism[7;8;9;10],

2 Method

2.1 Dataset constitution

2.2 Model architecture

3 Result

4 Conclusion

References

[1] J. C. Kendrew, G. Bodo, H. M. Dintzis, R. G. Parrish, H. Wyckoff, and D. C. Phillips. A Three-Dimensional Model of the Myoglobin Molecule Obtained by X-Ray Analysis. Nature,

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181(4610):662–666, 1958.

[2] J. C. Kendrew, R. E. Dicerson, B. E. Strandberg, R. G. Hart, D. R. Davies, D. C. Phillips, and V. C. Shore. Structure of Myoglobin: A Three-Dimensional Fourier Synthesis at 2 Å. Resolution. Nature, 185(4711):422–427, 1960.

[3] Hilary Muirhead and M. F. Perutz. Structure Of Hæmoglobin: A Three-Dimensional Fourier Synthesis of Reduced Human Haemoglobin at 5.5 Å Resolution. Nature, 199(4894):633–638, 1963.

[4] Simon J. Teague. Implications of protein flexibility for drug discovery. Nature Reviews Drug Discovery, 2(7):527–541, 2003.

[5] Adriano Aguzzi and Tracy O'Connor. Protein aggregation diseases: pathogenicity and therapeutic perspectives. Nature Reviews Drug Discovery, 9(3):237–248, 2010.

[6] Jacob D Durrant and J Andrew McCammon. Molecular dynamics simulations and drug discovery. BMC Biology, 9(1):71, 2011.

[7] Greg Winter, Alan R. Fersht, Anthony J. Wilkinson, Mark Zoller, and Michael Smith. Redesigning enzyme structure by site-directed mutagenesis: tyrosyl tRNA synthetase and ATP binding. Nature, 299(5885):756–758, 1982.

[8] Elan Zohar Eisenmesser, Daryl A. Bosco, Mikael Akke, and Dorothee Kern. Enzyme Dynamics During Catalysis. Science, 295(5559):1520–1523, 2002.

[9] David D. Boehr, Dan McElheny, H. Jane Dyson, and Peter E. Wright. The Dynamic Energy Landscape of Dihydrofolate Reductase Catalysis. Science, 313(5793):1638–1642, 2006.

[10] David Hess, Veronika Dockalova, Piia Kokkonen, David Bednar, Jiri Damborsky, Andrew deMello, Zbynek Prokop, and Stavros Stavrakis. Exploring mechanism of enzyme catalysis by on-chip transient kinetics coupled with global data analysis and molecular modeling. Chem, 7(4):1066–1079, 2021.