Folding with Coevolution

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Bonneau Lab

RosettaCon X

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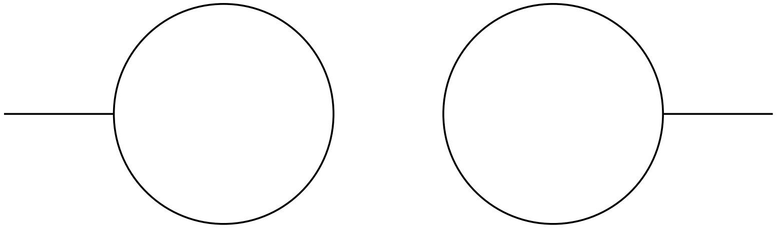

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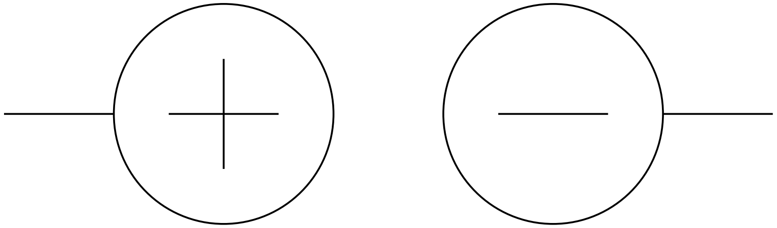

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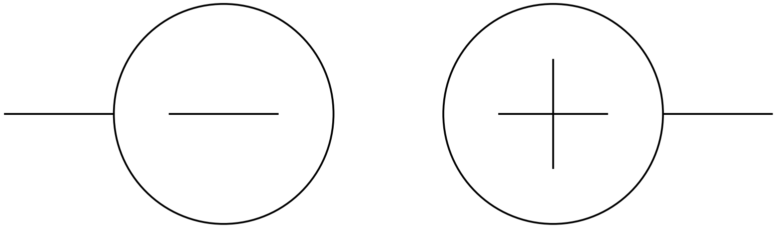

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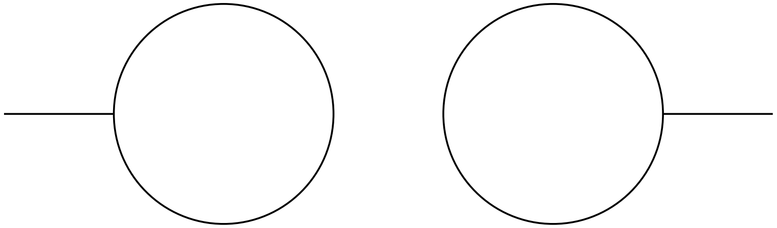

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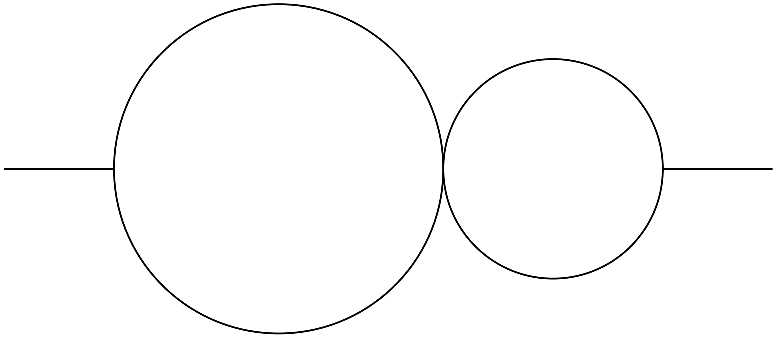

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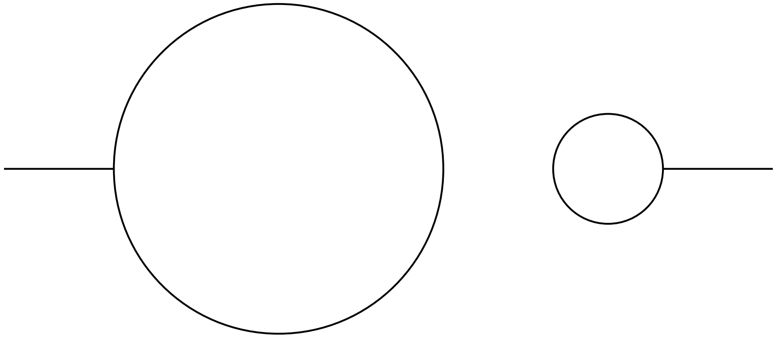

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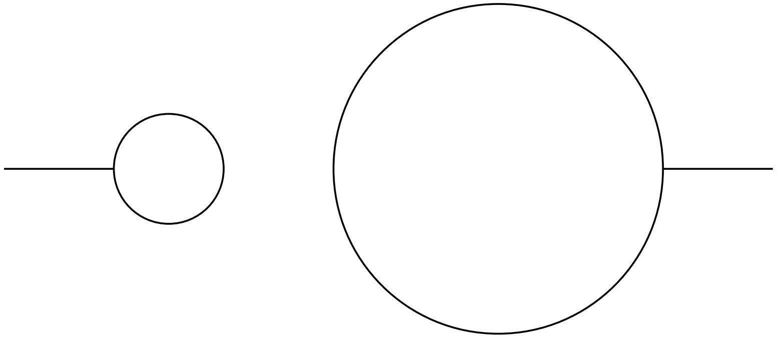

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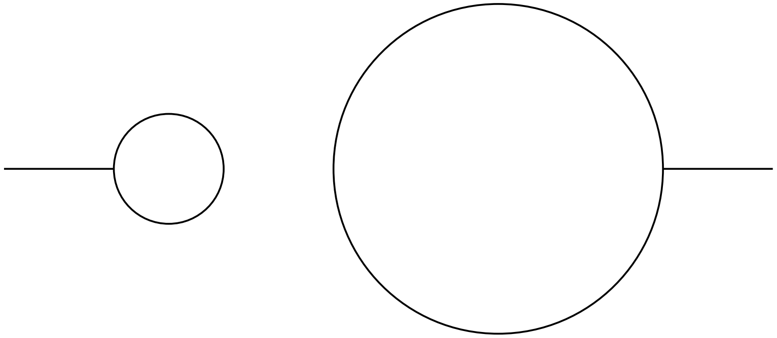

- which correlations are meaningful?

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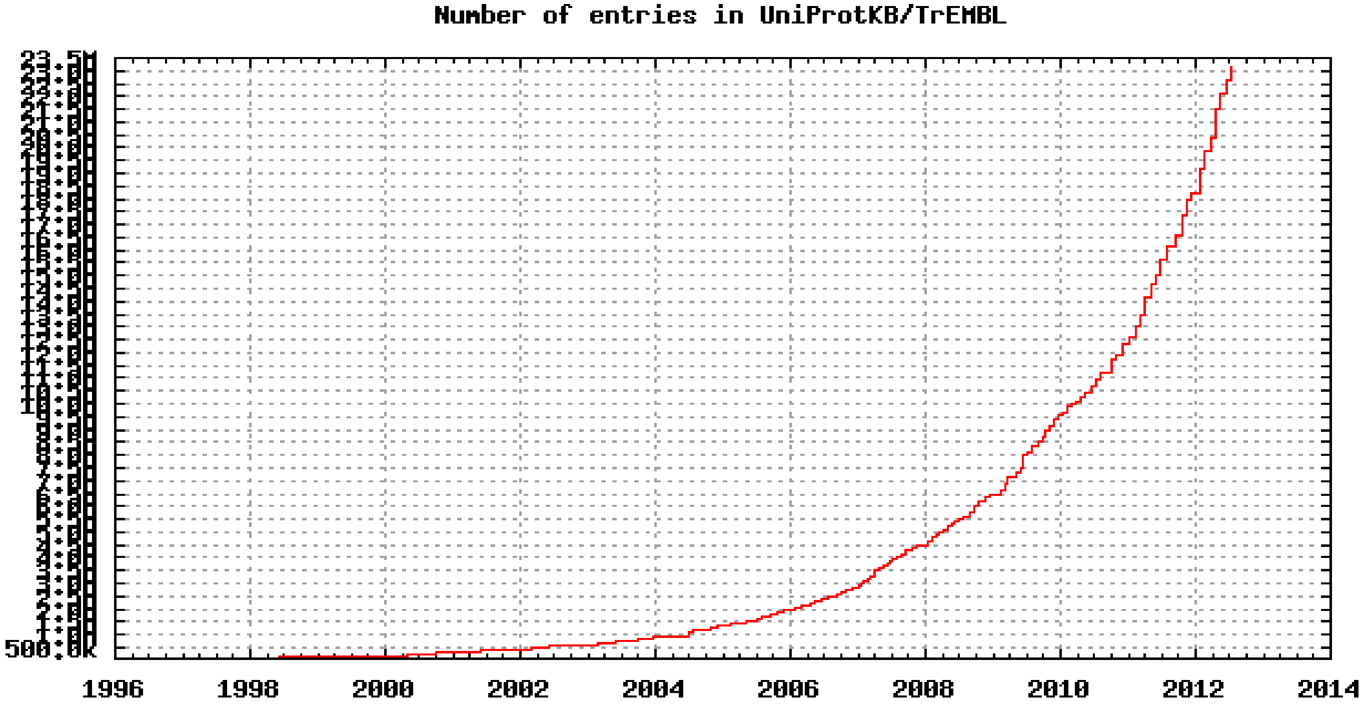

http://www.ebi.ac.uk/uniprot/TrEMBLstats/relstat.html

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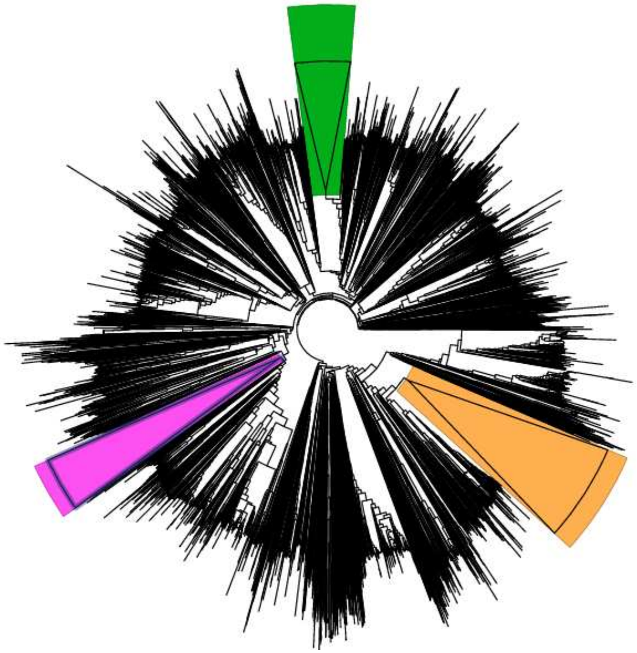

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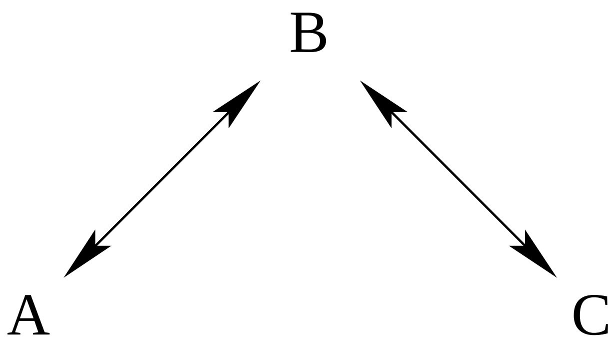

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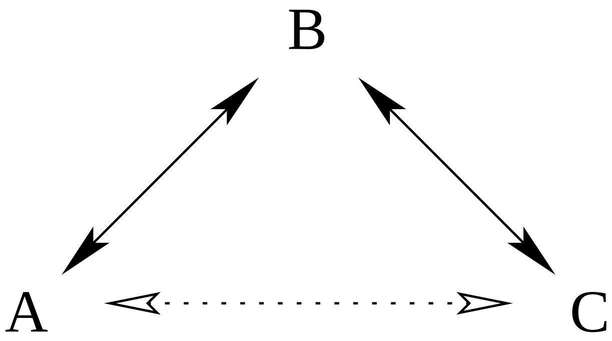

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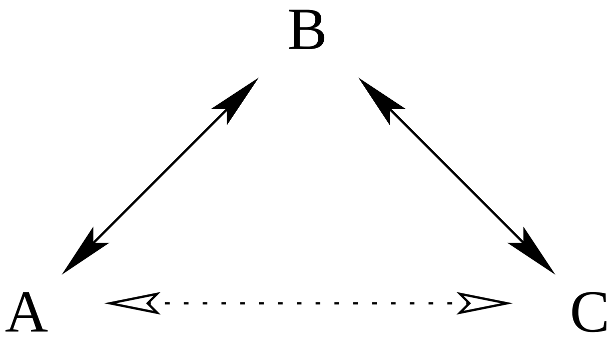

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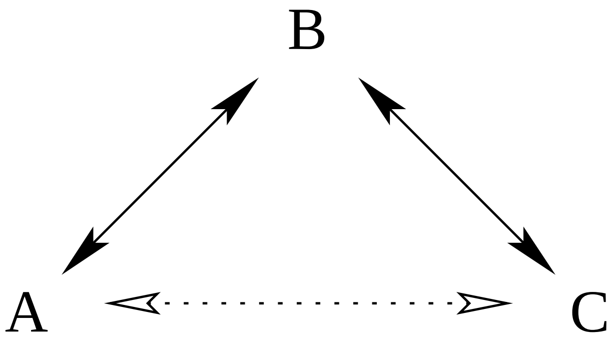

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- new method: “Direct Information”

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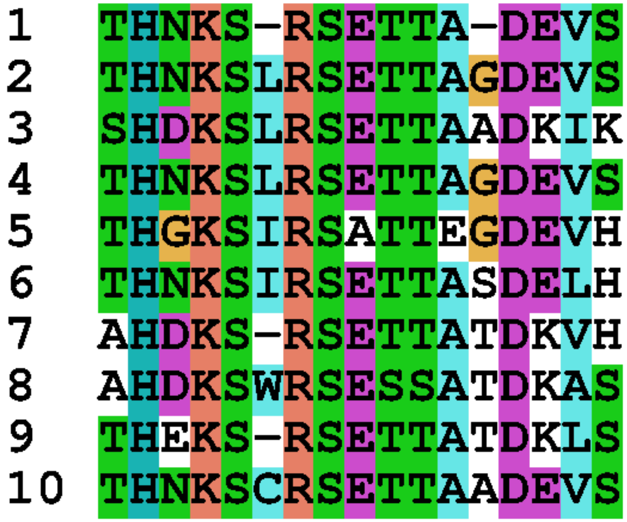

```
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9    THEKS-RSETTATDKLS
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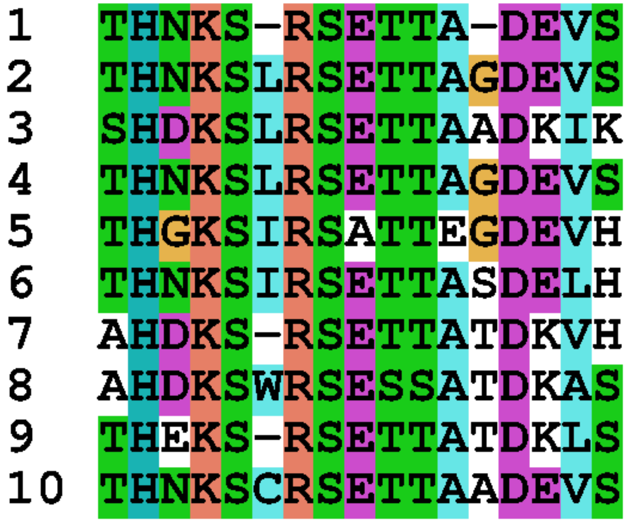

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- DI is the mutual information of a MSA specific distribution

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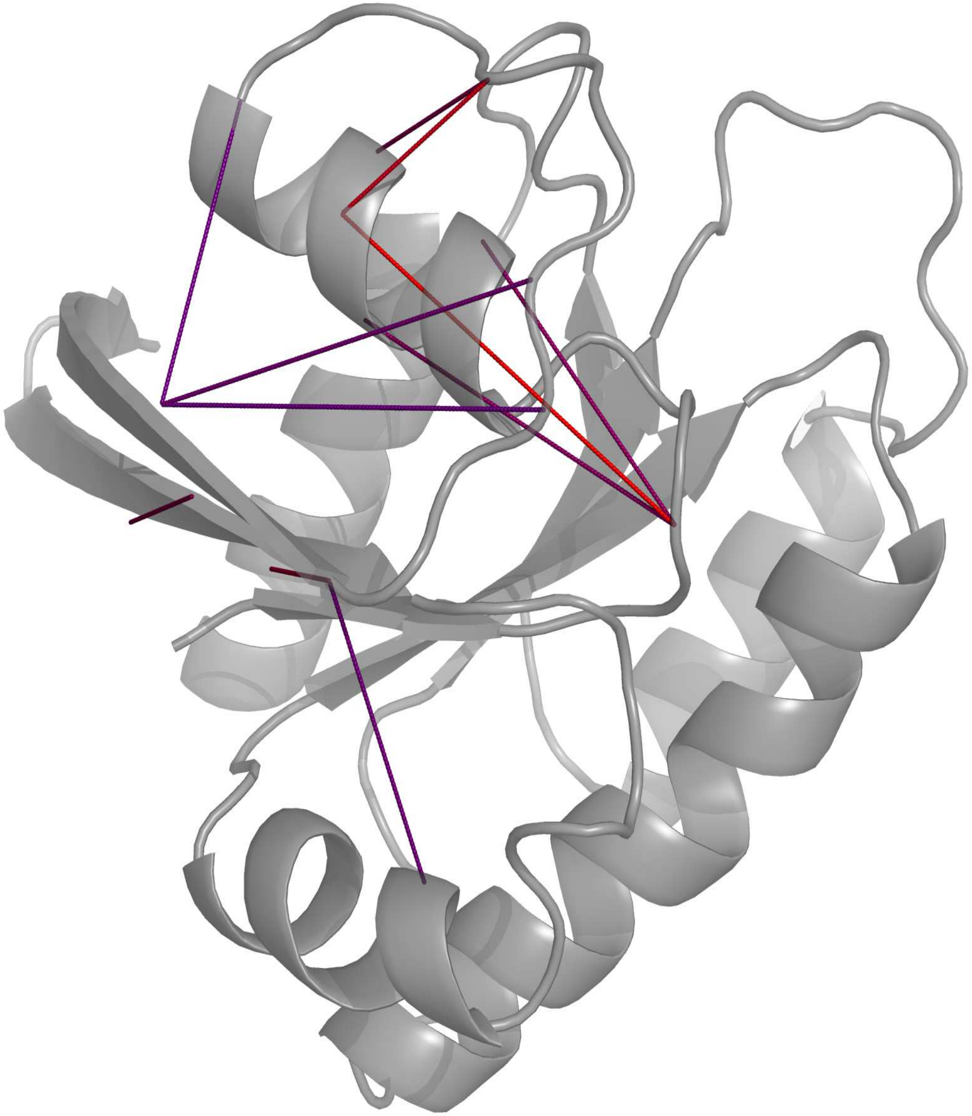
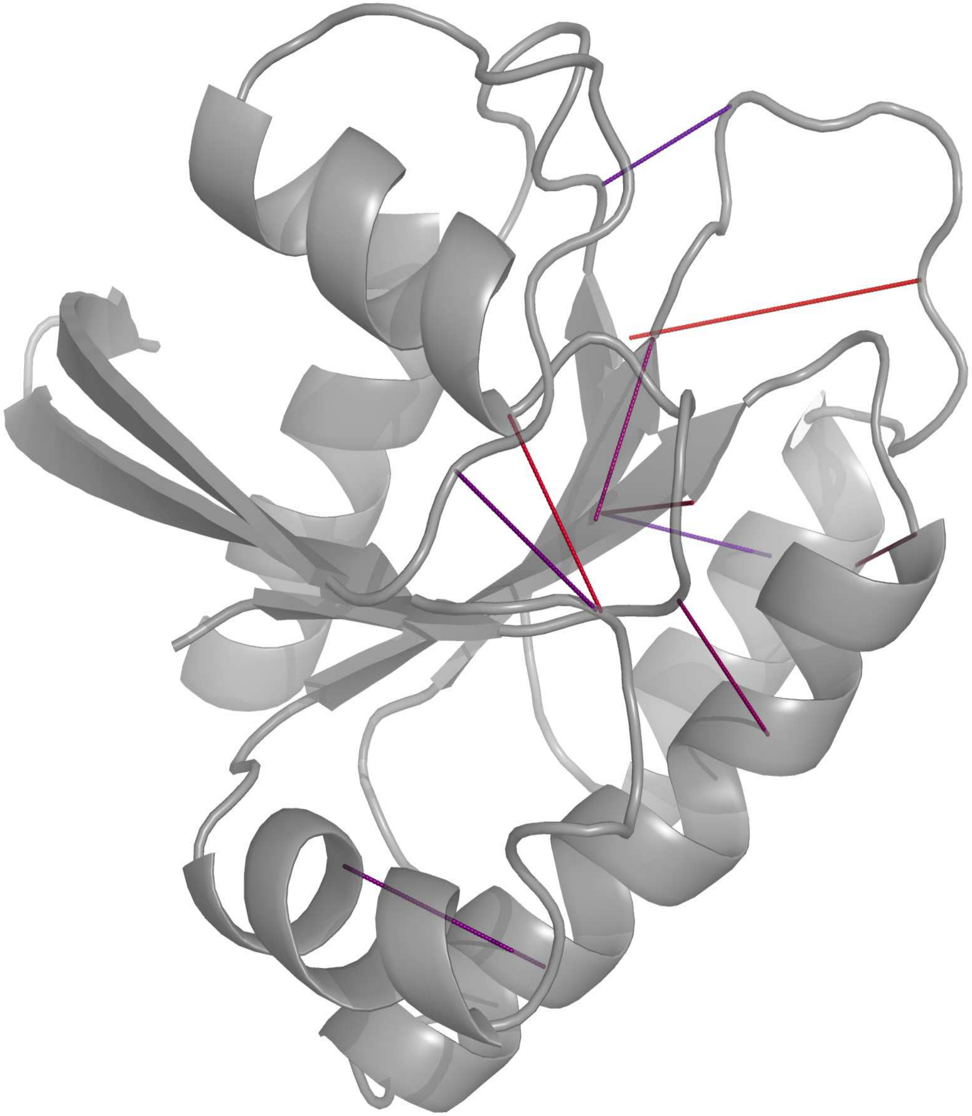
$$\text{MSA} \rightarrow \text{frequencies} \rightarrow P^{(dir)} \rightarrow \text{DI} \rightarrow \text{pairs}$$

MI



DI



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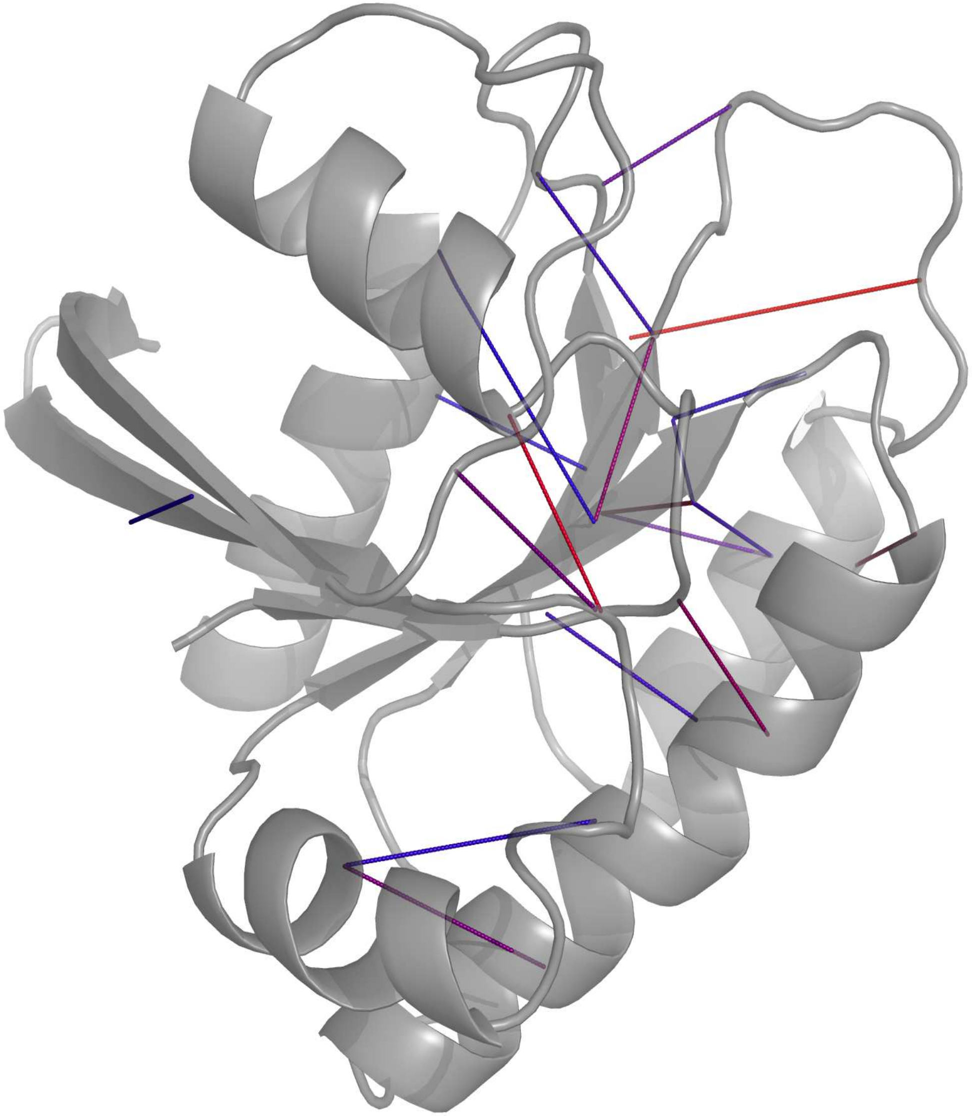

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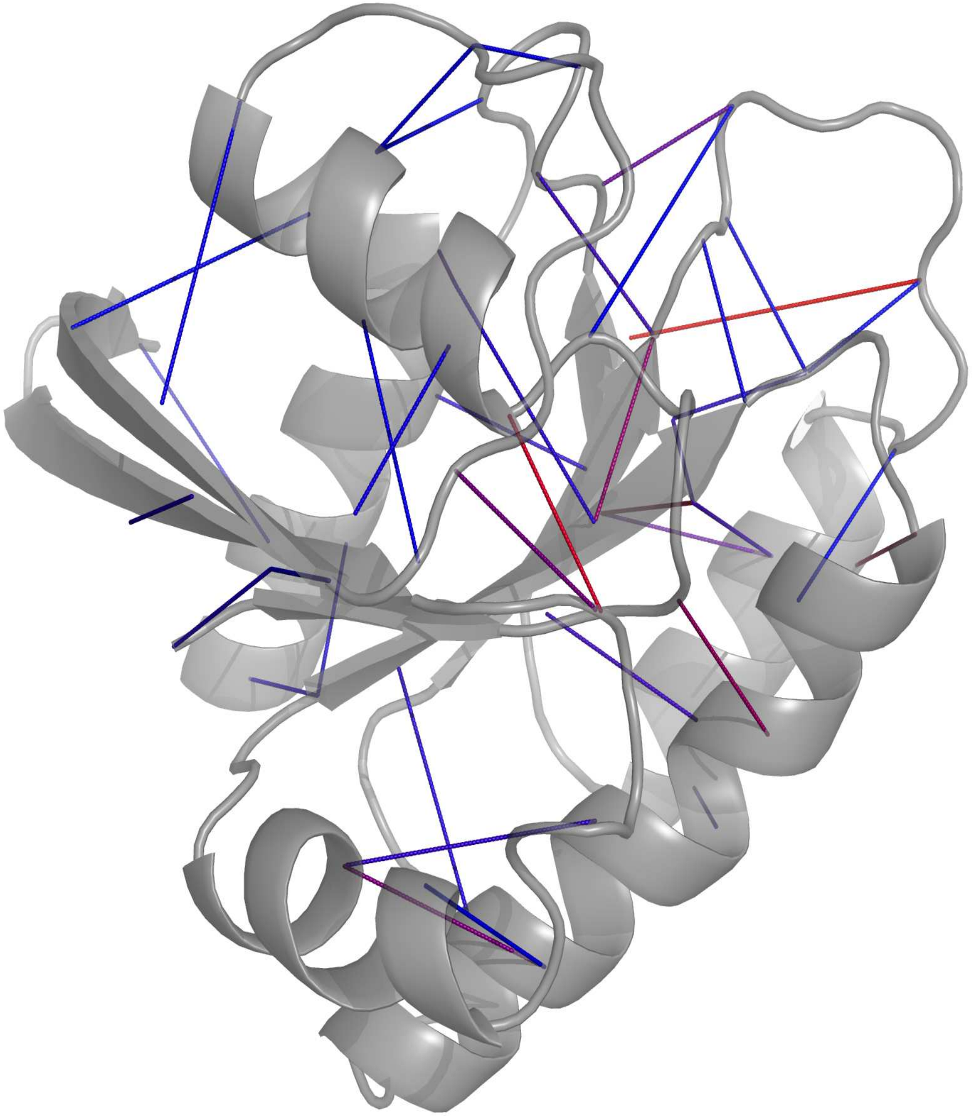

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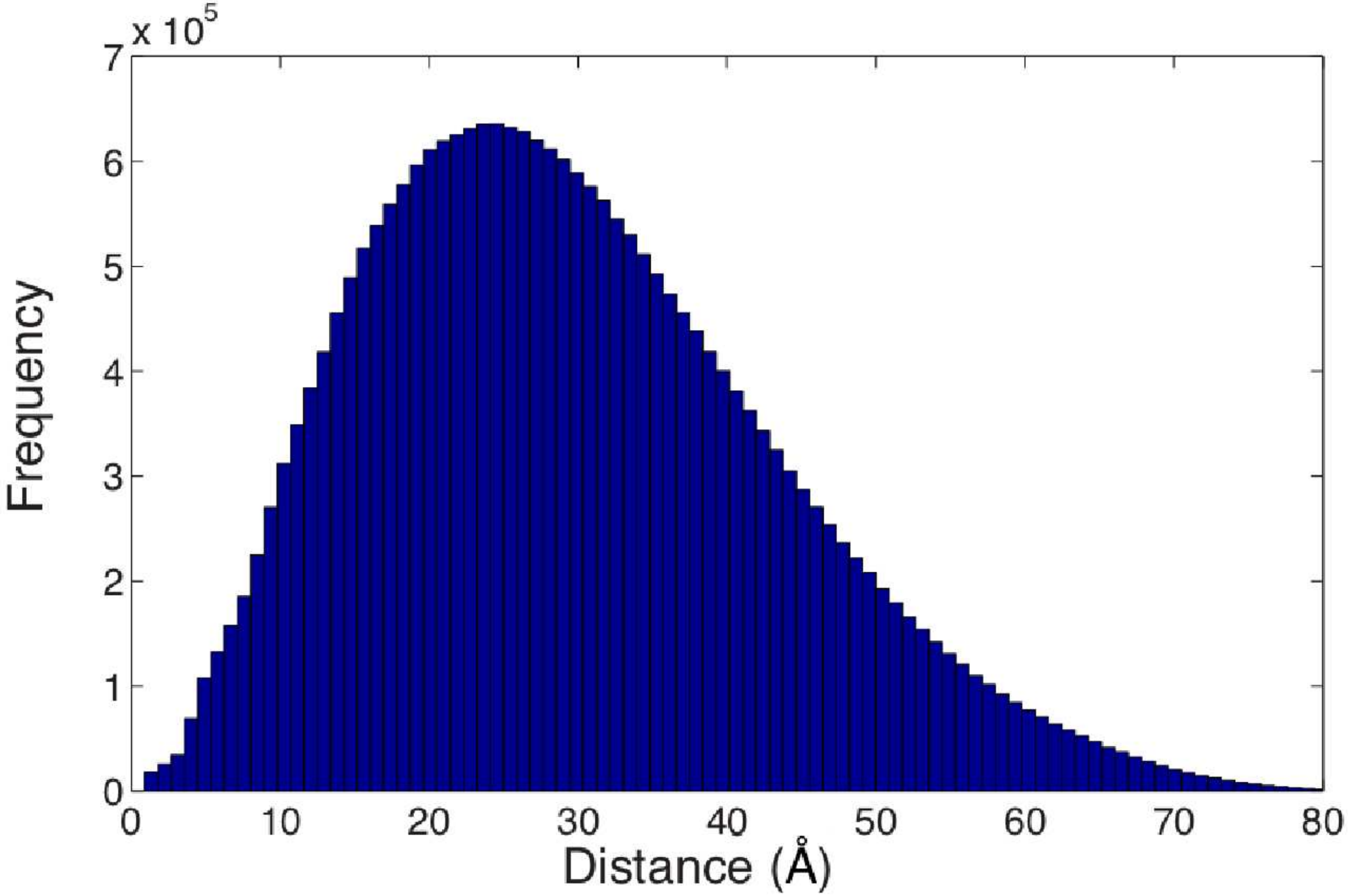

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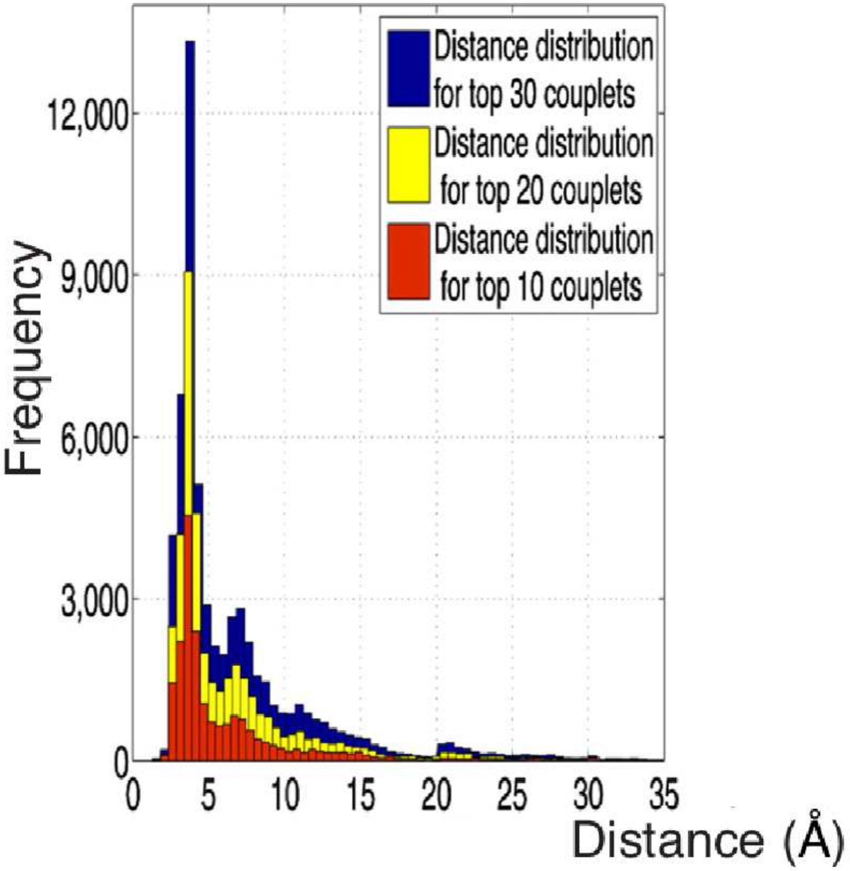

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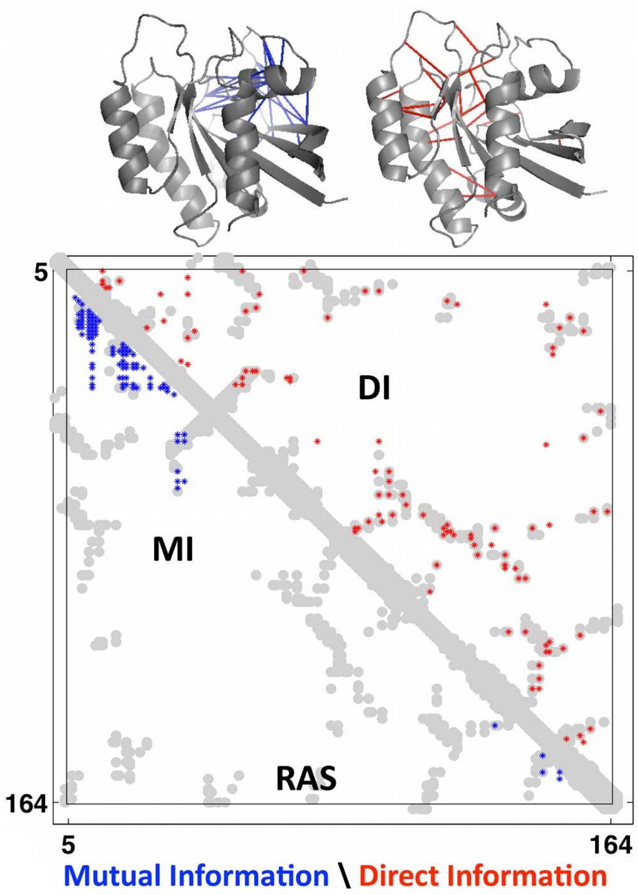

Marks *et al.* 2011, PDB 1NY6, 1JE8, 3C3W – p. 9

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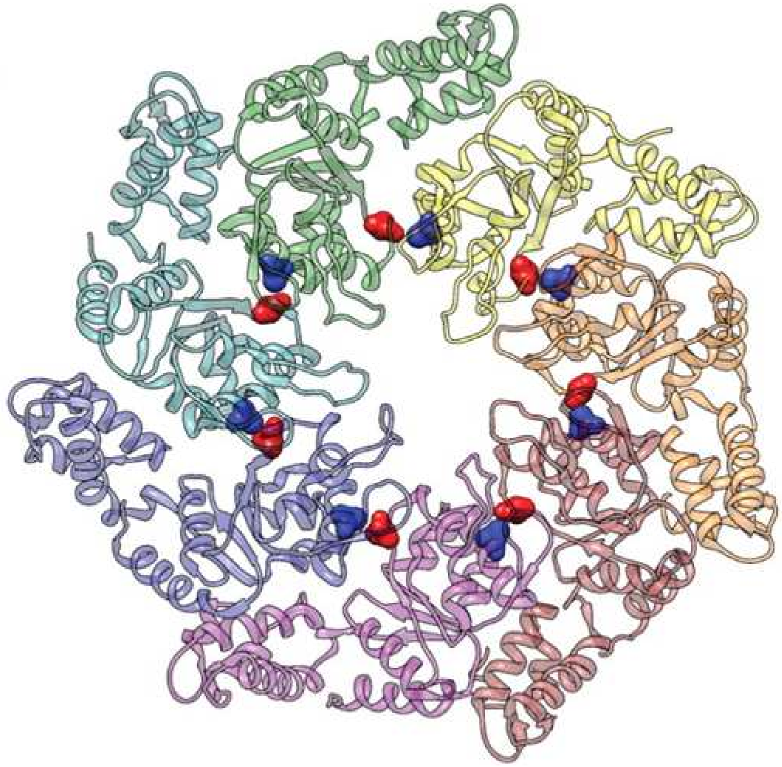

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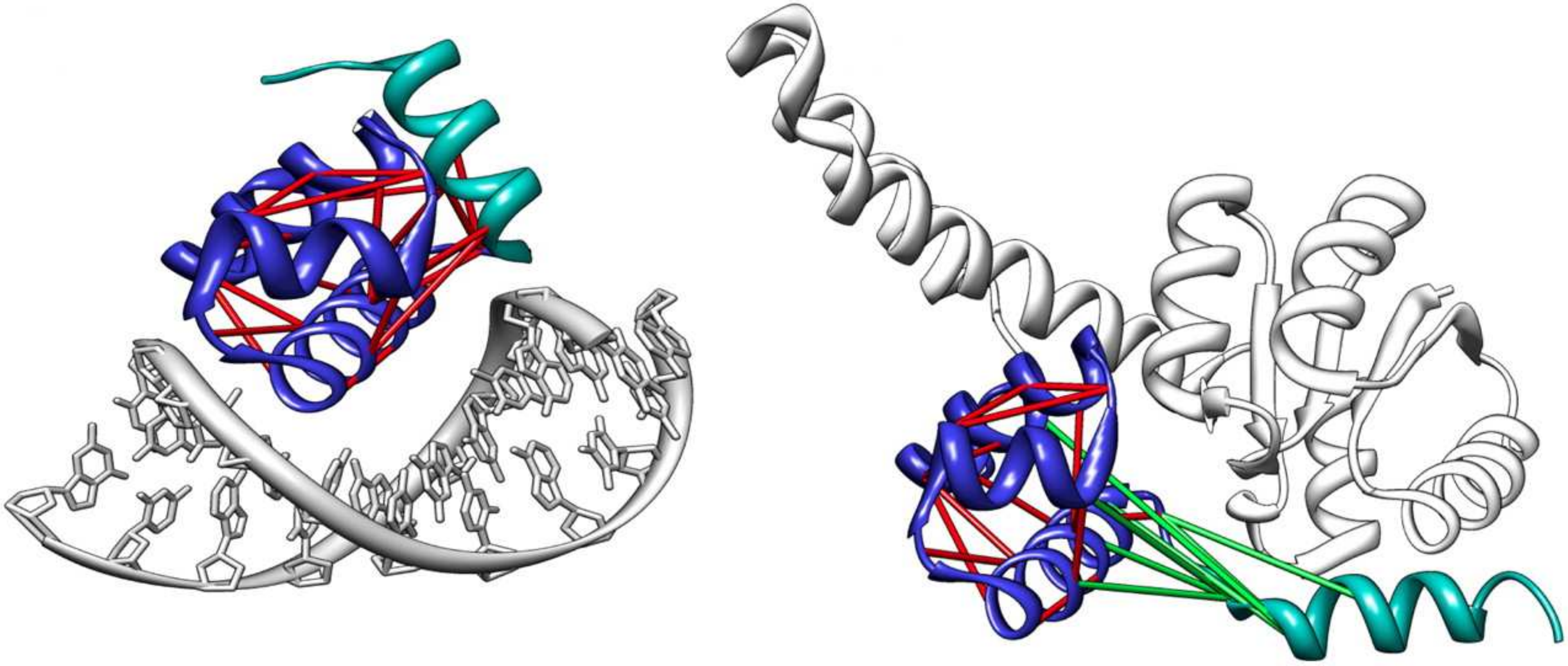

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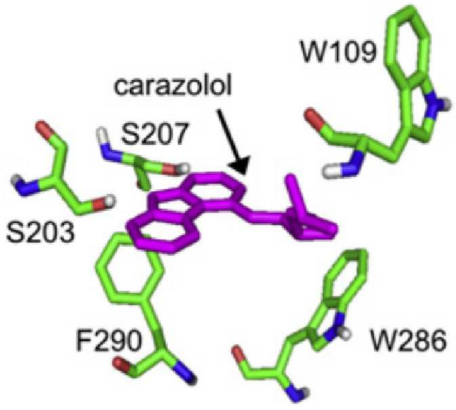

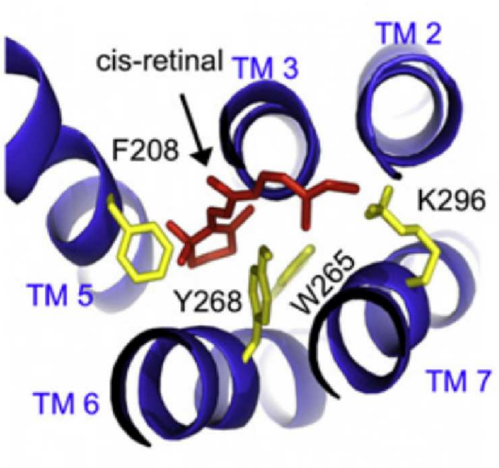

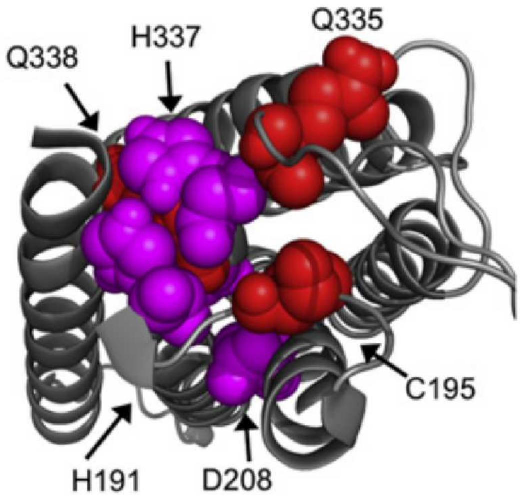

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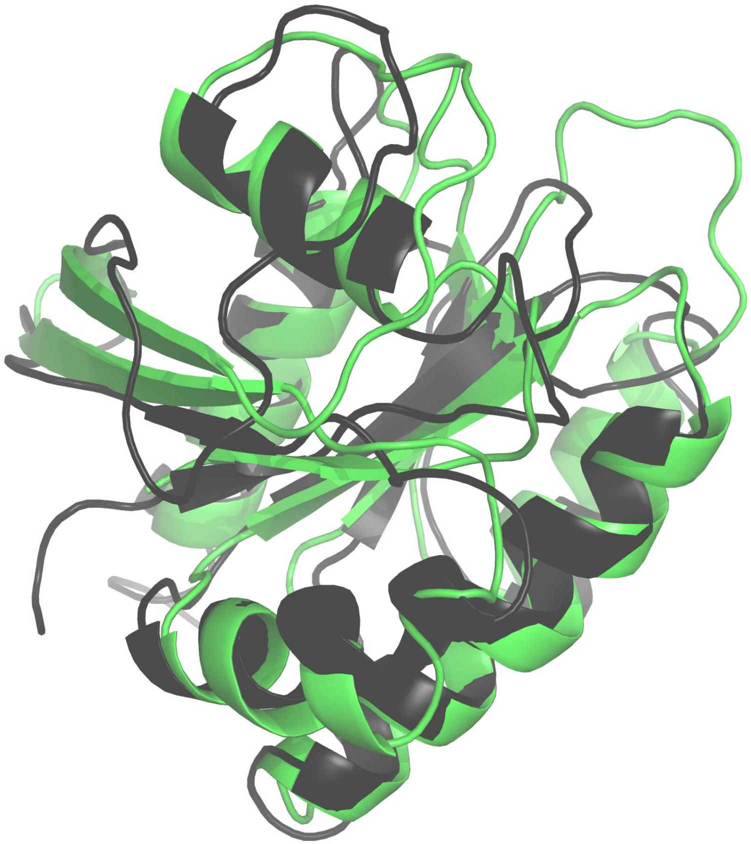

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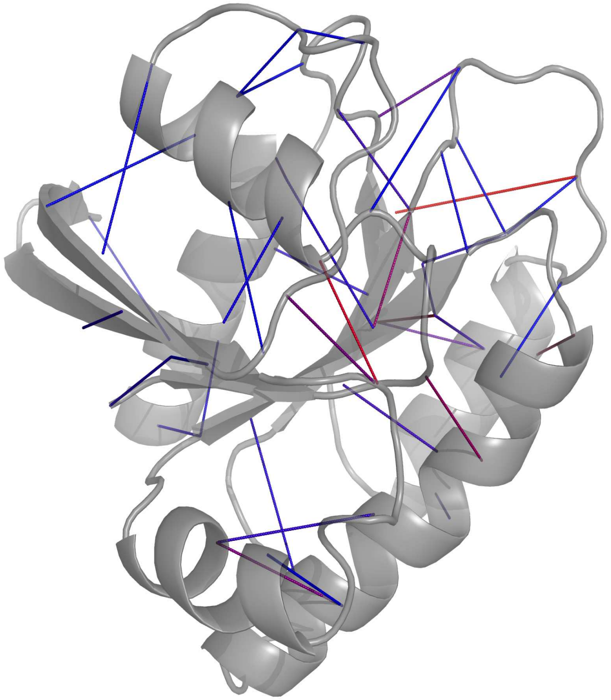

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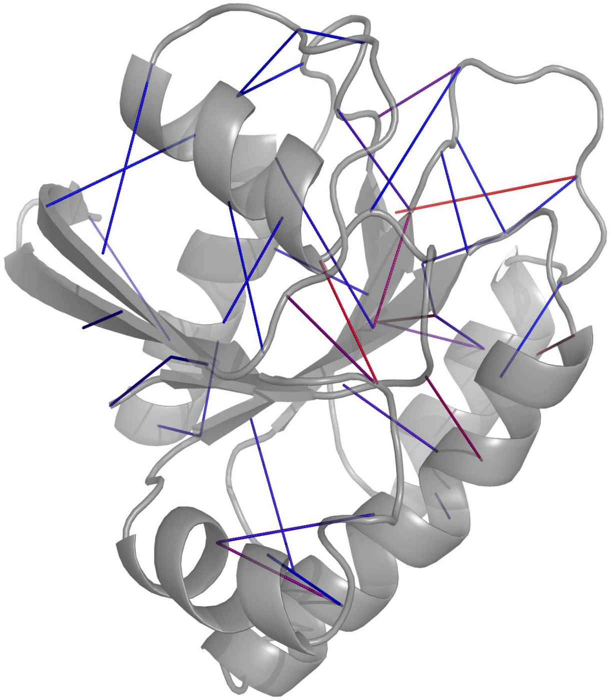

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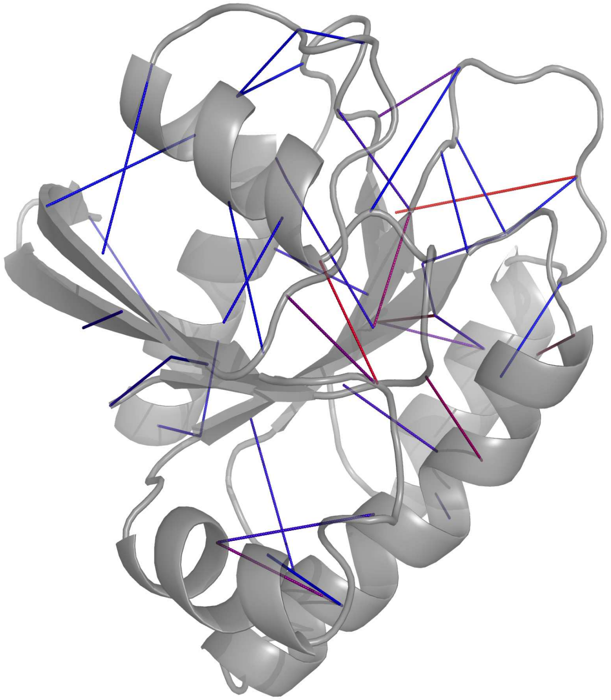

- challenge: may require many constraints

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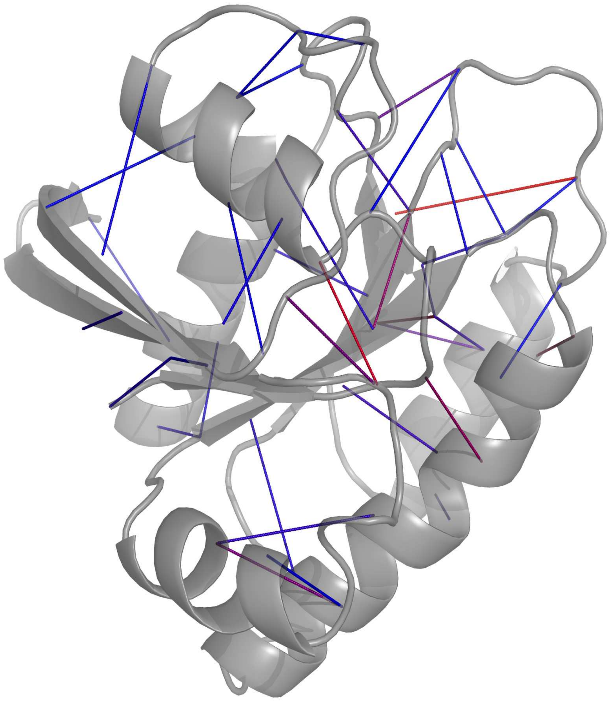

- challenge: undetermined weight in Rosetta scoring

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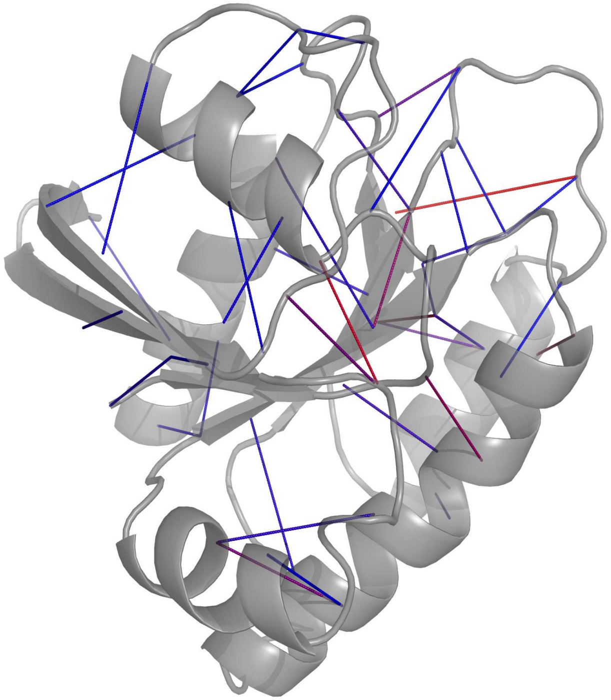

- challenge: many constraint scores are quadratic

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- try 10 best scoring DI pairs using the Rosetta HARMONIC scoring
- apply constraints during centroid stages of AbinitioRelax (20000 decoys)
- compare the score v. RMSD plots with and without constraints for cluster centers of the lowest 400 scoring decoys

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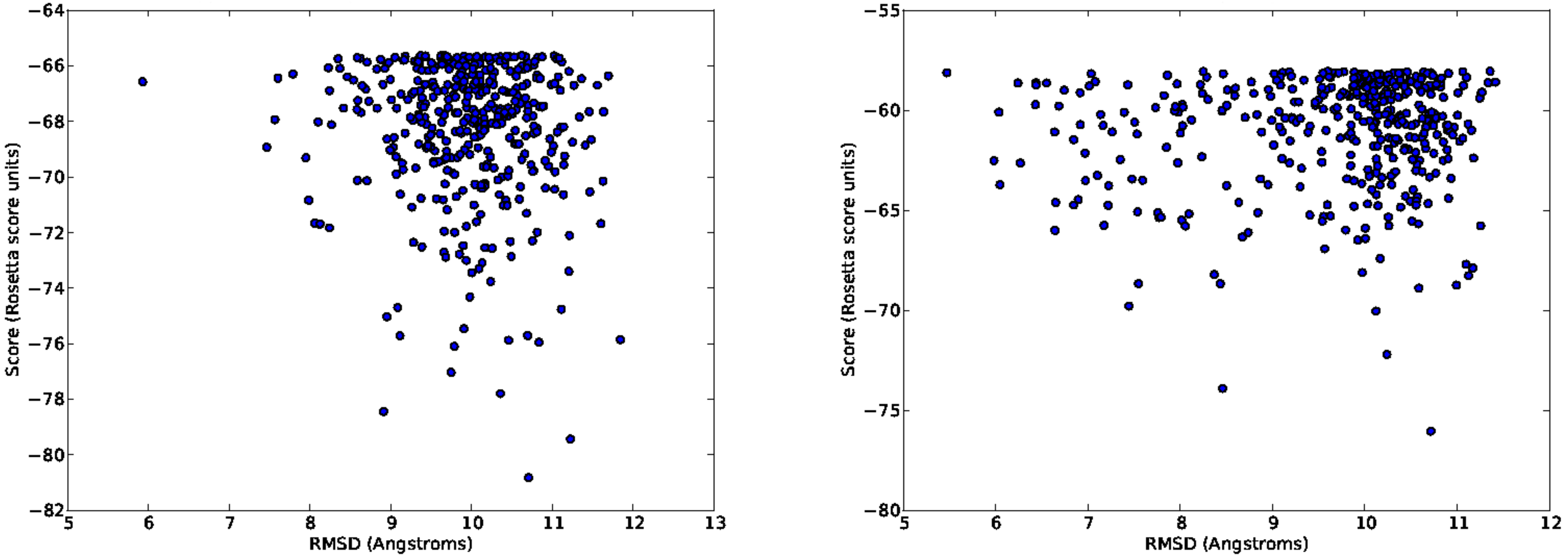

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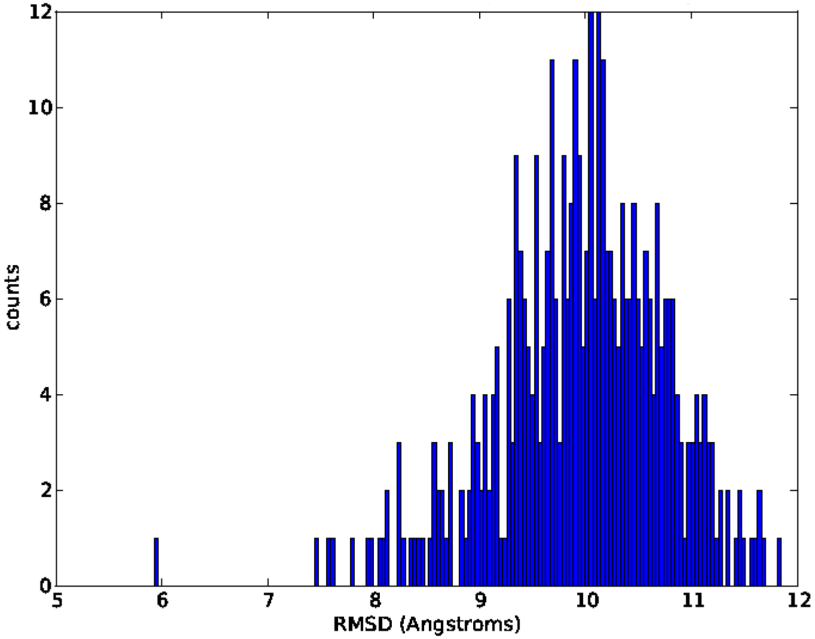

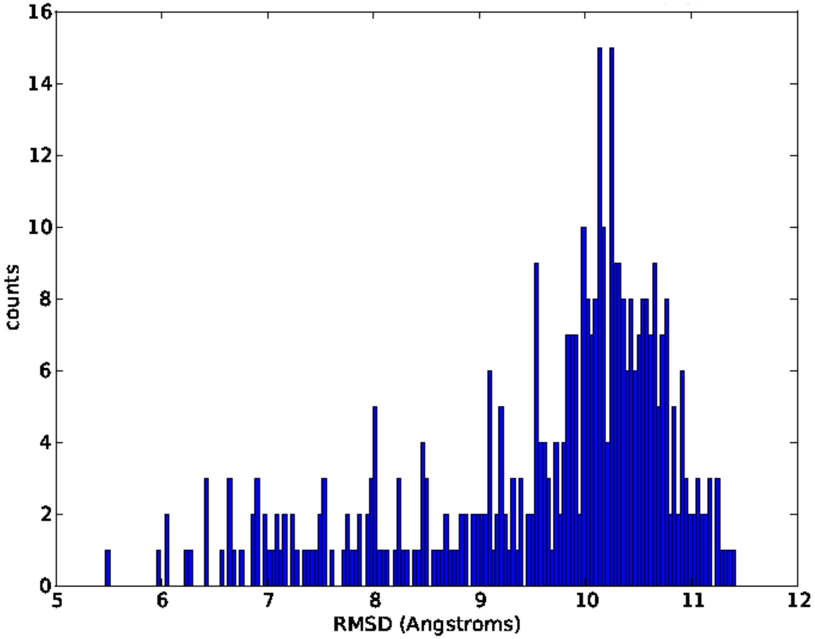

Where are we now?

- how do we properly score these constraints?
- can we classify the interactions identified by DI?
- can DI pairs indicate near-native decoys?
- do DI constraints improve AbinitioRelax?
- can DI constraints improve other protocols?

Thanks for listening!

Rich Bonneau

Kevin Drew

Doug Renfrew

Noah Youngs

Duncan Penfold-Brown

Glenn Butterfoss

Timothy Craven

Abba Leffler

Rebecca Alford

Leif Halvorson

Chris Poultney

The Bonneau Lab

Debora Marks - Harvard Medical School, Dept. of Systems Biology

Chris Sanders - Memorial Sloan-Kettering Cancer Center

Lucy Colwell - MRC Laboratory of Molecular Biology

The Rosetta Community

PyRosetta Team