An Attempt to Unite Homology Modeling and *Ab Initio* Structure Prediction

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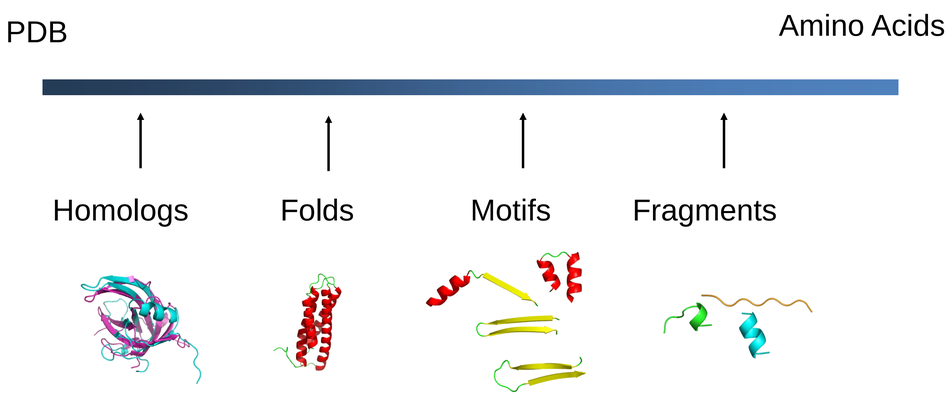
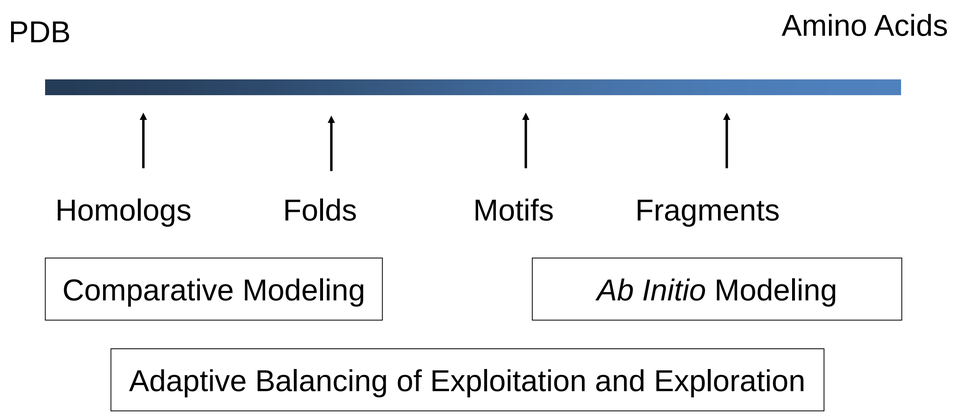
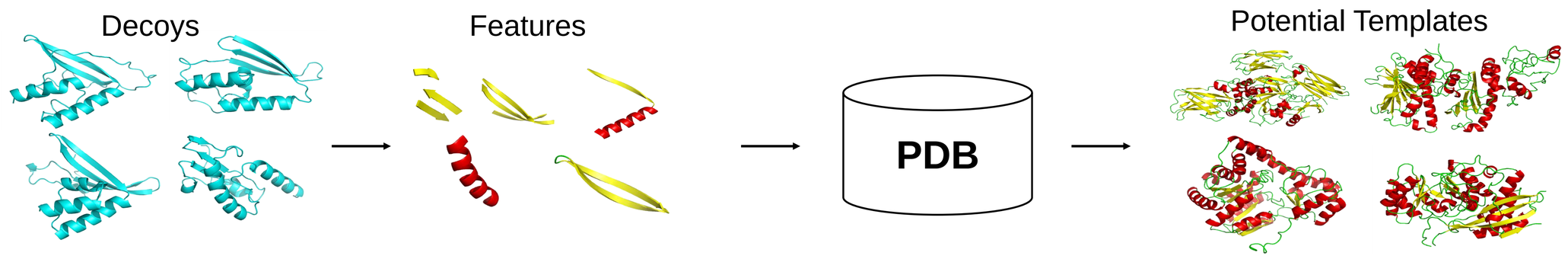
The Challenge and an Opportunity





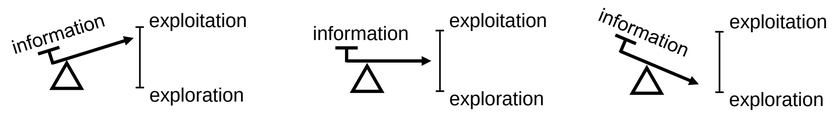
BEETS Strategy – Adaptive Balancing of Exploitation and Exploration

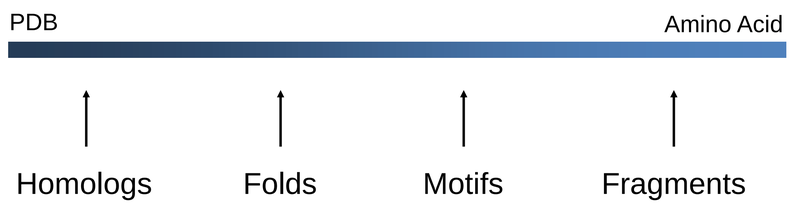
1. Features from decoys to exploit PDB information



2. Optimization tries to identify template utility for guided search

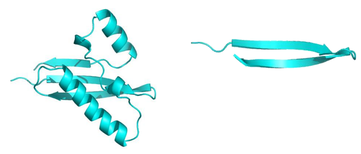
Exploitation and Exploration for Protein Structure Prediction

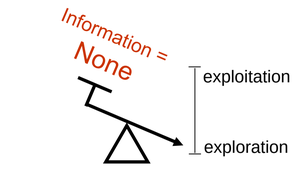




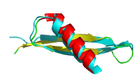
Adaptive Balancing of Exploitation and Exploration

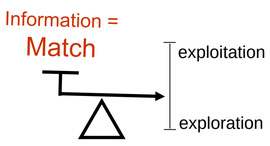
Initial search is pure exploration.



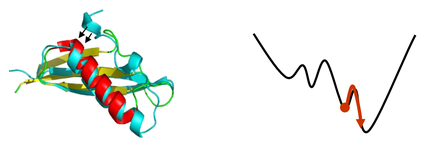


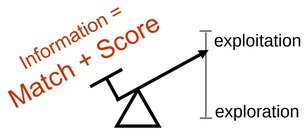
Match with potential template protein leads to increased exploitation.



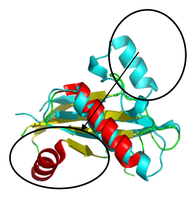


The template protein is used to guide search. If this lowers the energy, exploitation of this specific template is increased.



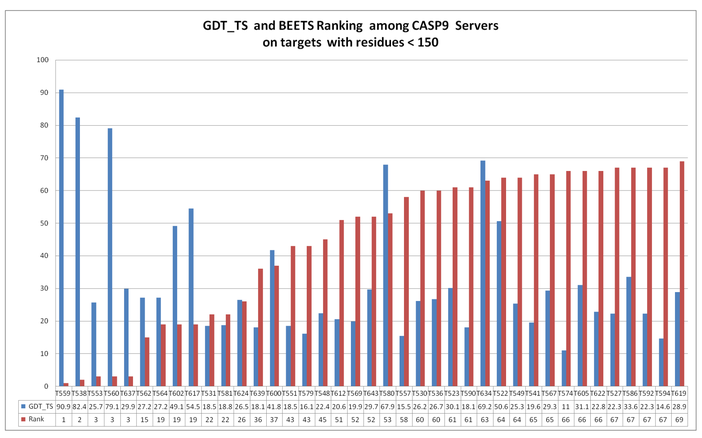


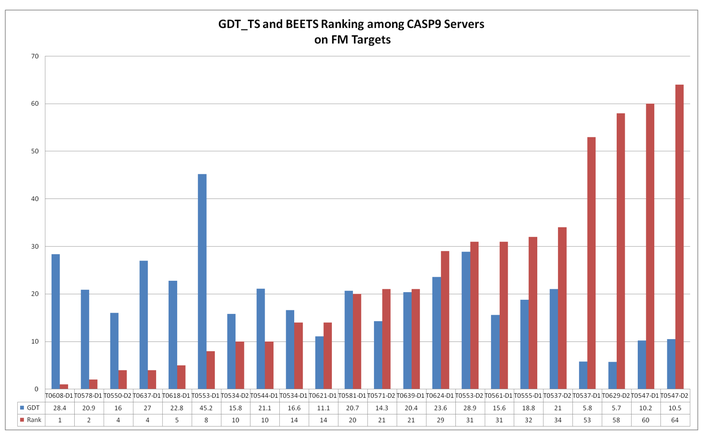
The template will continue to be used until it is no longer useful. Then exploration will be increased.



Results

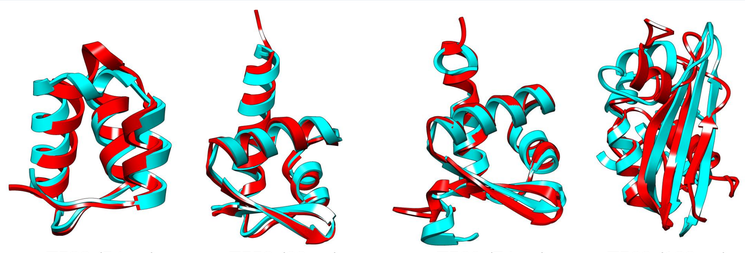
Note: In fact, our CASP9 experiment has been a disaster due to a terrible bug. Therefore, the following results came out of CASP rerun experiment after the bug was removed.



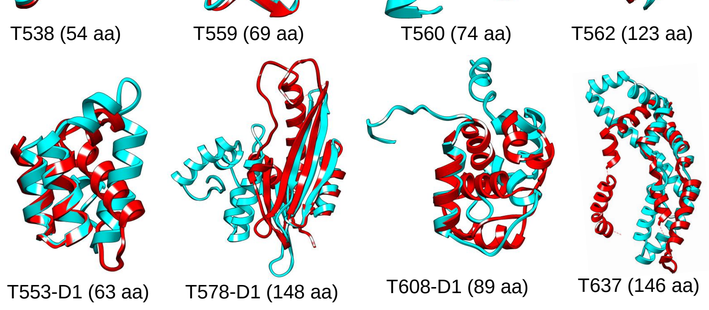


Predictions
Red: native
Cyan: model

TBM



FM



Analysis

BEETS made some good predictions on smaller template-based modeling targets. Though it lowered energy free-modeling (FM) models more than our previous approach, but the sampling problem remains in absence of good templates. On FM targets, BEETS's exploitation criterion is too simplistic to explore while exploiting meaningful regions of weaker templates.

Outlook

Currently BEETS uses a simple (secondary structure-based) matching criterion to find templates. In future, we have plans: 1) to extend the matching criterion by using multi-feature descriptors to identify distantly related homologs or sub-structures candidates, and 2) to improve our adaptive exploration-exploitation mechanism.