Protein-RNA Cross-Docking of Conformational Ensembles

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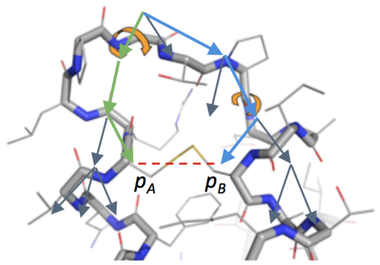
Conformational Sampling

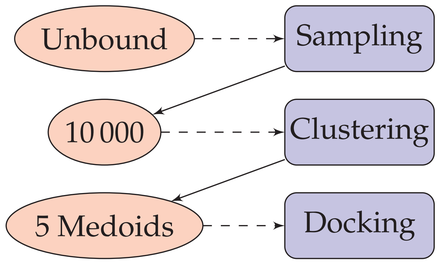
- **Graph** representation of the molecule:
  - rotatable bonds (edges)
  - groups of atoms (vertices)
  - hydrogen bonds (cycles)
- Sampling with **inverse-kinematics** moves [2].



Outline

Objective: Predicting the structure of protein-RNA complexes.

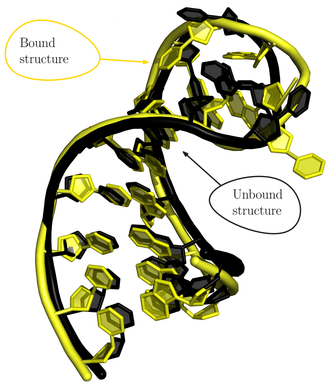
Problem: *Bound* structure to predict differs from available *unbound* structure.



Procedure:

1. Generate 10 000 conformations per partner,
2. *Clustering* to obtain representative conformations,
3. Perform *cross-docking* experiments with RosettaDock [1].

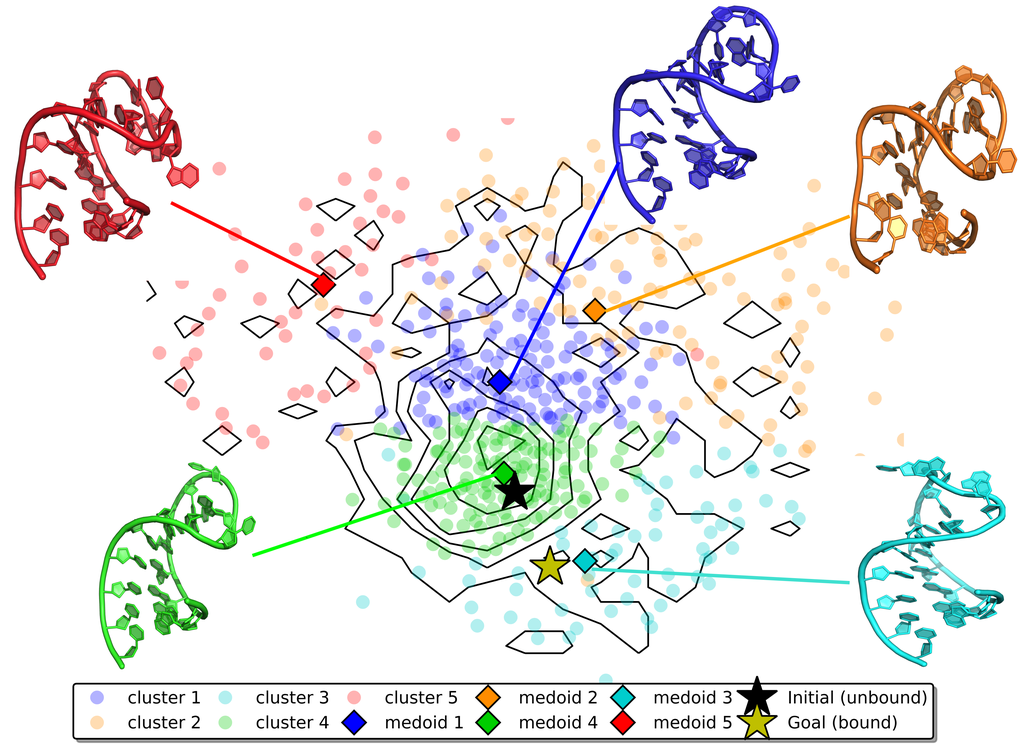
Gaussian Mixture Clustering



Clustering: 10 000 conformations in 5 *gaussian clusters*.

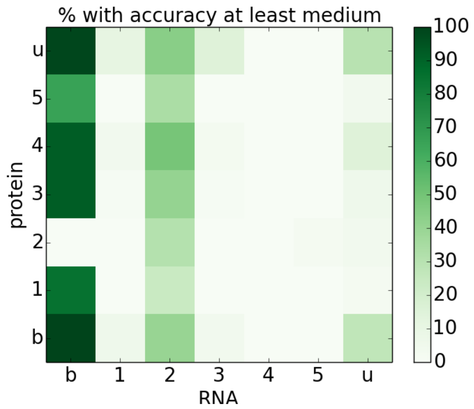
Visualization: 2D projection by global energy minimization.

Output: 5 representative conformations per partner.



Docking

Evaluation: *Pairwise* cross-docking and calculation of accuracy using CAPRI classification (medium).



Result: *Representative conformation #2* is a better starting point than unbound structure with 40% versus 27% of medium accuracy samples.

Conclusion and Perspectives

- The procedure *improves* the semi-rigid docking results and might now be used to address biological problems.
- We want to enlarge the set of protein/RNA complexes for benchmark results.
- We still need to *adjust the number of clusters* and try other clustering algorithms.

References

[1] Jeffrey J. Gray, Stewart Moughon, Chu Wang, Ora Schueler-Furman, Brian Kuhlman, Carol A. Rohl, and David Baker. *J Mol Biol*, 331(1):281–299, Aug 2003.

[2] Rasmus Fonseca, Dimitar V. Pachov, Julie Bernauer, and Henry van den Bedem. *Nucleic Acids Res*, 42(15):9562–9572, 2014.

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