Fragment-based modeling of protein-bound ssRNA
Isaure Chauvot de Beauchêne, Sjoerd J de Vries, Martin Zacharias

To cite this version:
Isaure Chauvot de Beauchêne, Sjoerd J de Vries, Martin Zacharias. Fragment-based modeling of protein-bound ssRNA. ECCB 2016: The 15th European Conference on Computational Biology, Sep 2016, Den Haag, Netherlands. 2016. hal-01573352

HAL Id: hal-01573352
https://hal.science/hal-01573352
Submitted on 9 Aug 2017

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.
**BIOLGICAL CONTEXT**

The structure of an RNA-protein complex is a key to:
(i) understand its function or malfunction (ii) modulate or create it, for medicine or biotechnology

**RATIONALLE**

Docking MODEL versus

**RESULTS**

**METHODS**

ATRACT docking engine [1,2]

1) Random string generation (position * orientation * conformation) 
2) Energy minimization of bead-bead interactions in an empirical force field 
3) Elimination of redundant poses (converged on same local minima) 
4) Ranking of poses by score (pseudo-energy)

**STRATEGY**

**CONCLUSION**

**Achievements**

Our fragment-based approach to model protein-bound ssRNA proved effective to sample fragment poses at the surface of the protein. This permits to predict the RNA binding site with some sensitivity and specificity than all other binding site prediction methods based on protein structure [3].

We can predict the orientation of nucleotides binding to RNA-protein conserved contacts, in the most abundant RNA-binding domains of proteins (RBM and PUF) [4].

With those anchoring nucleotides, we could model bind ssRNA up to 12-nucleotides long, with a resolution comparable to X-ray structures [4].

**Perspectives**

We considered so far that we know which part of our RNA is single-stranded (ss) and binds the protein. In many real cases, the RNA is partially structured (e.g. double-stranded, ds) or parts of it occlude between ss and ds RNA. However, the ss part binds the protein by only some of the nucleotides. Therefore, we will include RNA secondary structure prediction methods together with in vitro data (e.g. SHAPE) to evaluate the likelihood of protein-binding for each nucleotide in the RNA, of interest, before or within the docking process.

**METHODS**

Docking

**RANKING**

1-10 random string generation (position * orientation * conformation) 
2- Energy minimization of bead-bead interactions in an empirical force field 
3- Elimination of redundant poses (converged on same local minima) 
4- Ranking of poses by score (pseudo-energy)

**ASSEMBLING**

**Structural**

**RANKING**

**METHODS**

ATRACT docking engine [1,2]

1) Random string generation (position * orientation * conformation) 
2) Energy minimization of bead-bead interactions in an empirical force field 
3) Elimination of redundant poses (converged on same local minima) 
4) Ranking of poses by score (pseudo-energy)

**APPLICATION**

**METHODS**

**Docking**

**ASSEMBLING**

**Scoring**

**RESULTS**

**CONCLUSION**

**Achievements**

Our fragment-based approach to model protein-bound ssRNA proved effective to sample fragment poses at the surface of the protein. This permits to predict the RNA binding site with some sensitivity and specificity than all other binding site prediction methods based on protein structure [3].

We can predict the orientation of nucleotides binding to RNA-protein conserved contacts, in the most abundant RNA-binding domains of proteins (RBM and PUF) [4].

With those anchoring nucleotides, we could model bind ssRNA up to 12-nucleotides long, with a resolution comparable to X-ray structures [4].

**Perspectives**

We considered so far that we know which part of our RNA is single-stranded (ss) and binds the protein. In many real cases, the RNA is partially structured (e.g. double-stranded, ds) or parts of it occlude between ss and ds RNA. However, the ss part binds the protein by only some of the nucleotides. Therefore, we will include RNA secondary structure prediction methods together with in vitro data (e.g. SHAPE) to evaluate the likelihood of protein-binding for each nucleotide in the RNA, of interest, before or within the docking process.