Docking gros grain ADN - protéine

Pierre Poulain

pierre.poulain@univ-paris-diderot.fr

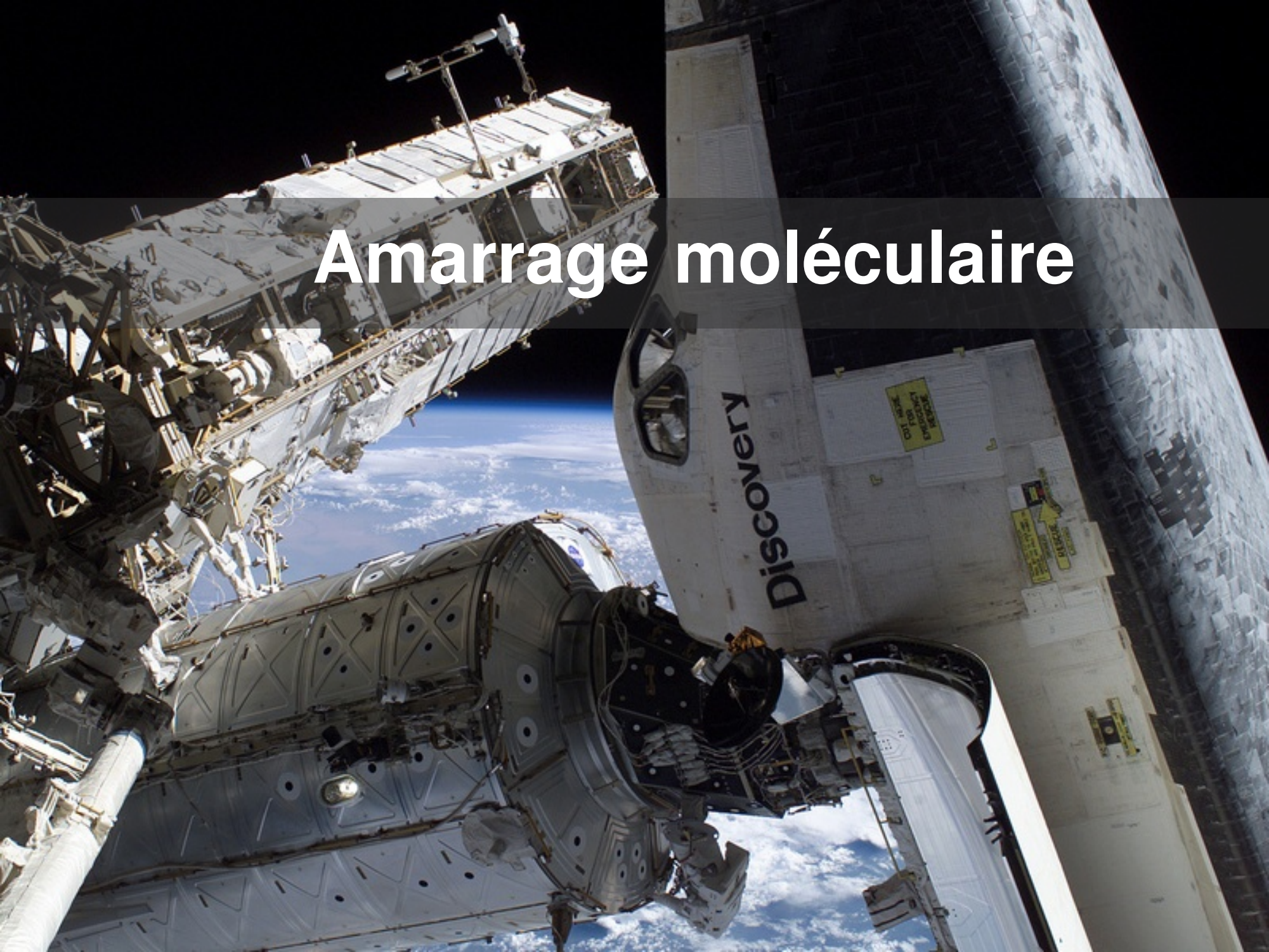
M2 BI – 11/2011

université PARIS DIDEROT PARIS 7

Menu

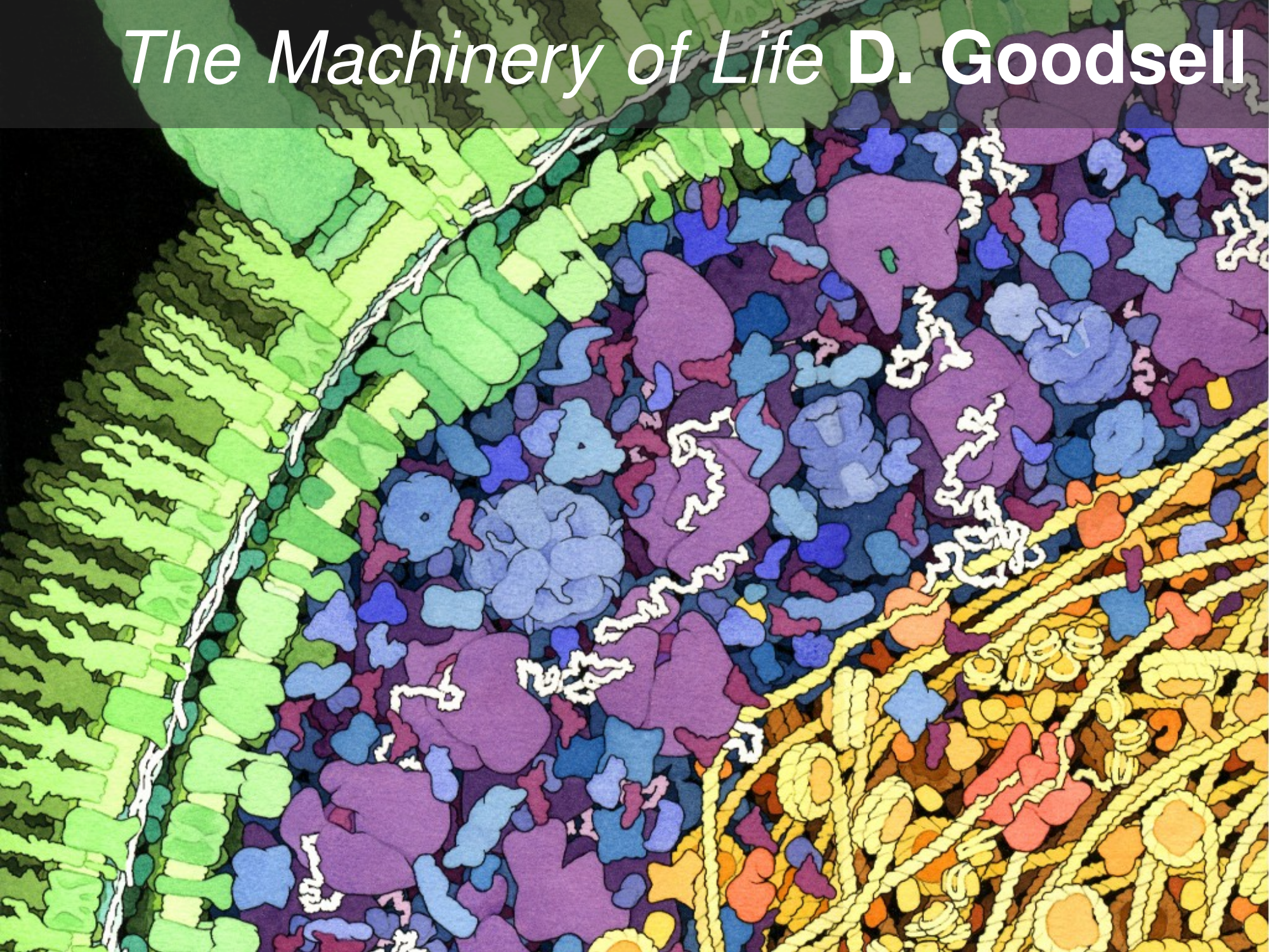
Menu

Docking ?

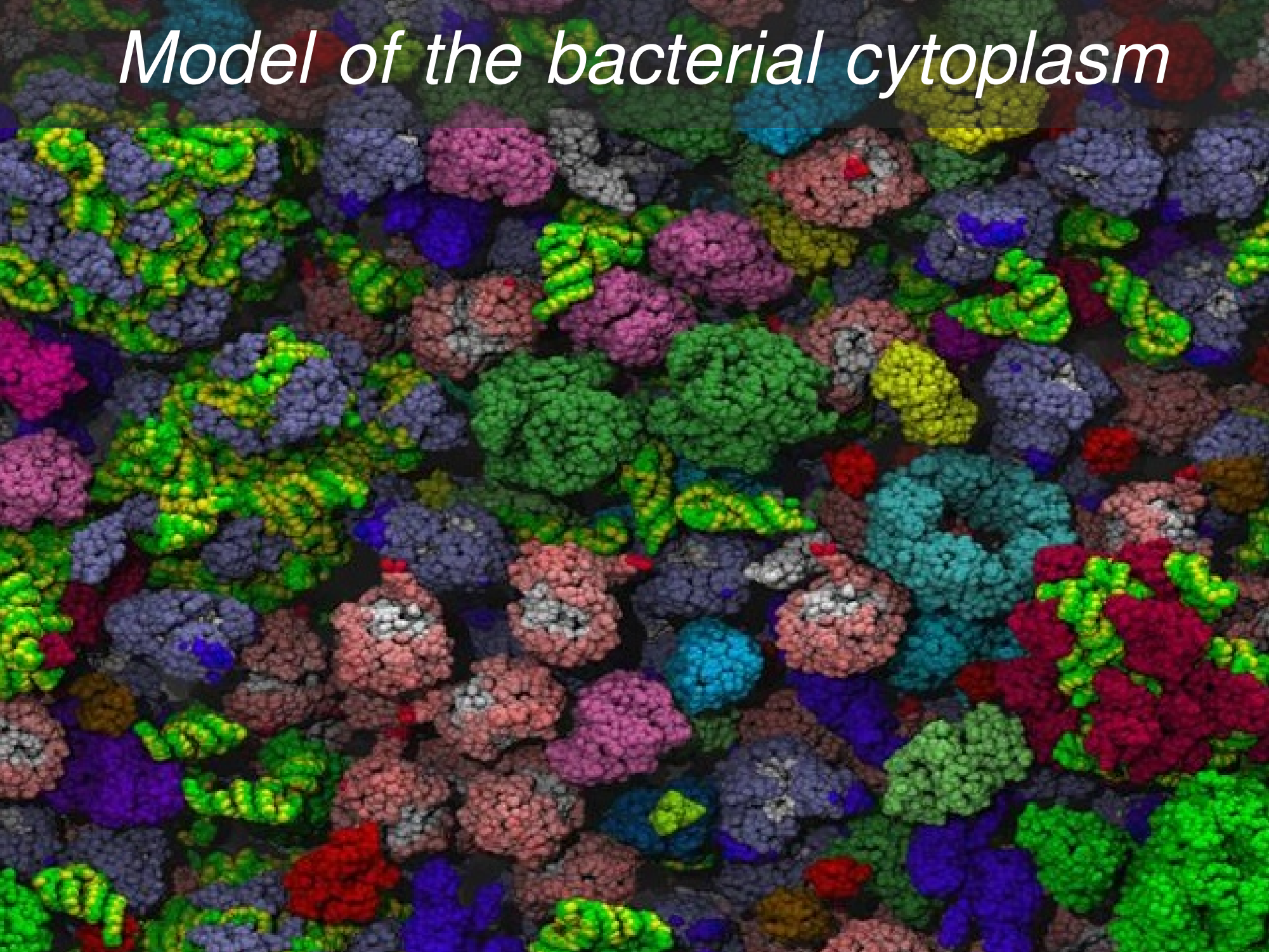


Amarrage moléculaire

The Machinery of Life **D. Goodsell**



Model of the bacterial cytoplasm



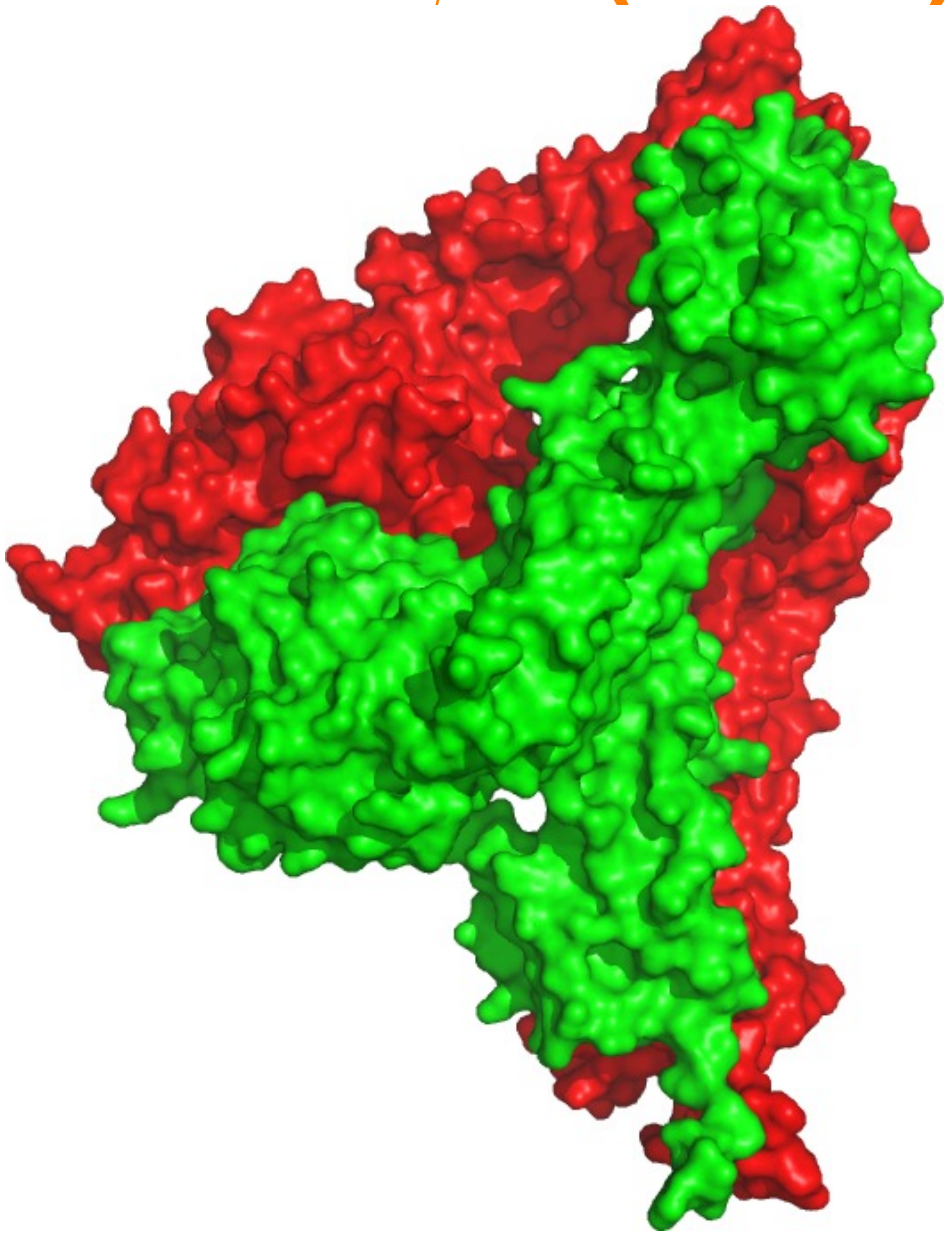
Pourquoi ?

fonction

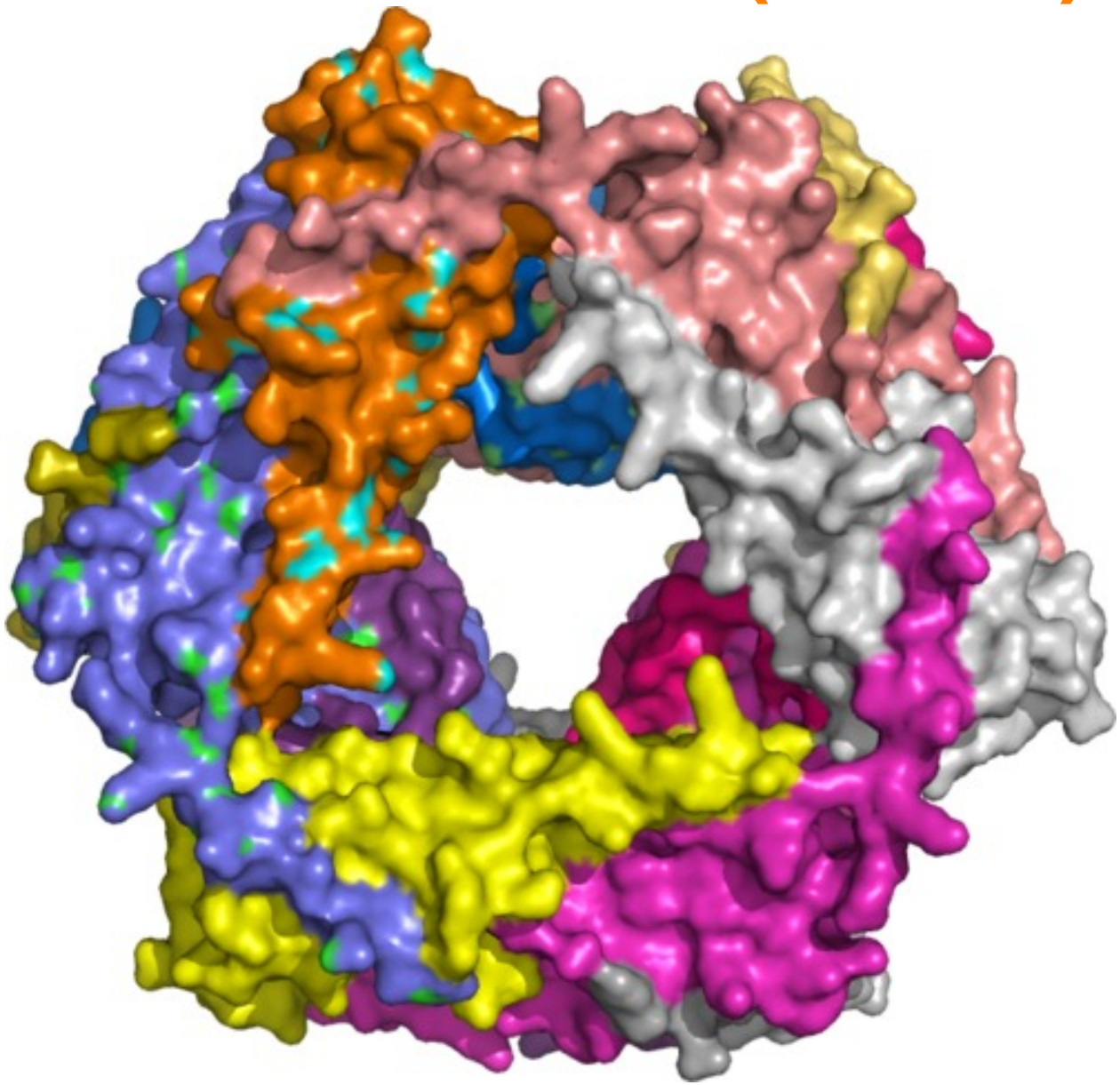
interaction (complexe)

S. cerevisiae $\sim$ 4 000 protéines $\sim$ 2/3 en complexes
Krogan *et al.*, *Nature* **440** : 637 (2006)

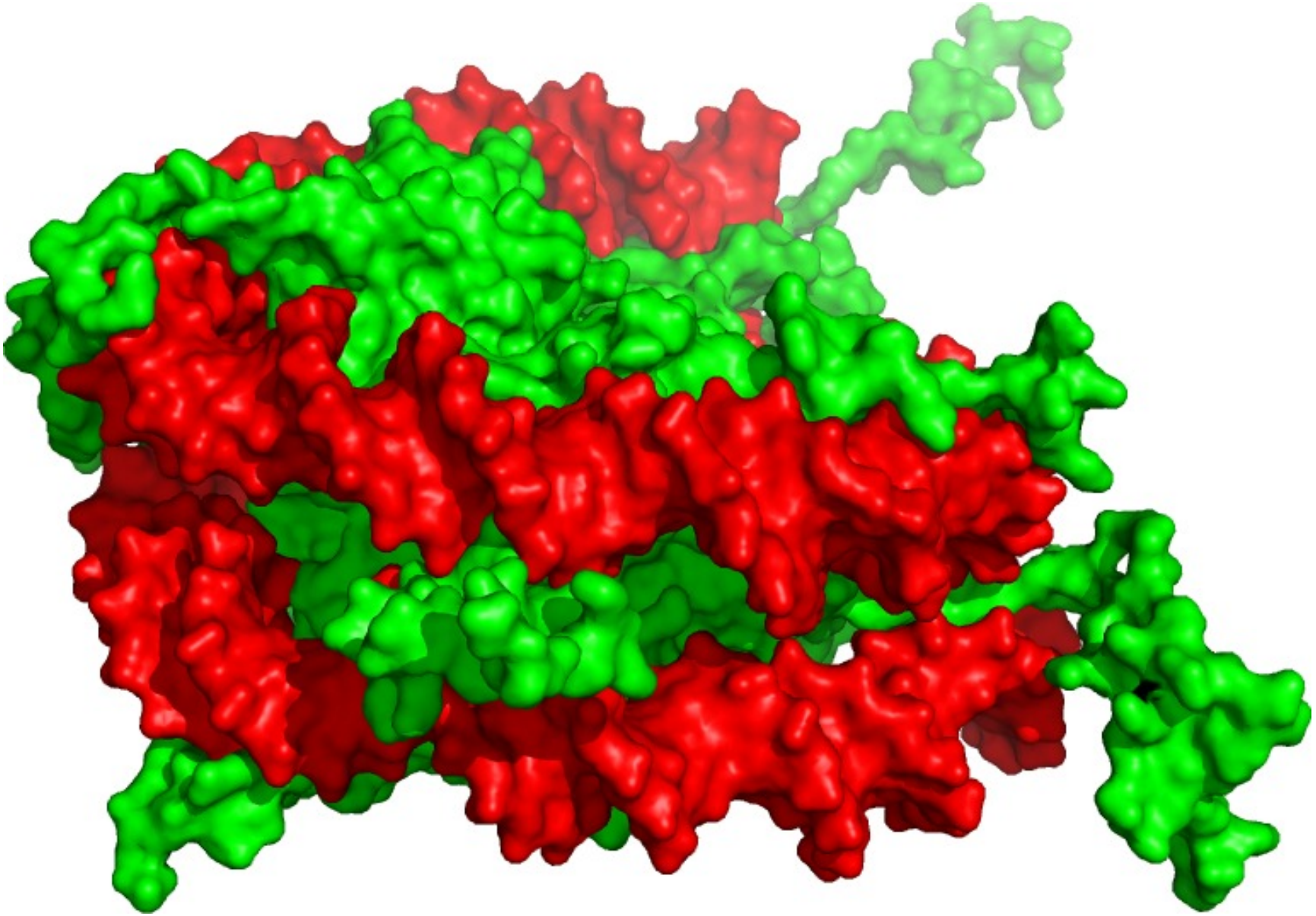
intégrines αIIb + β3 (3FCS)



sHSP 1GME 12-mère (1GME)

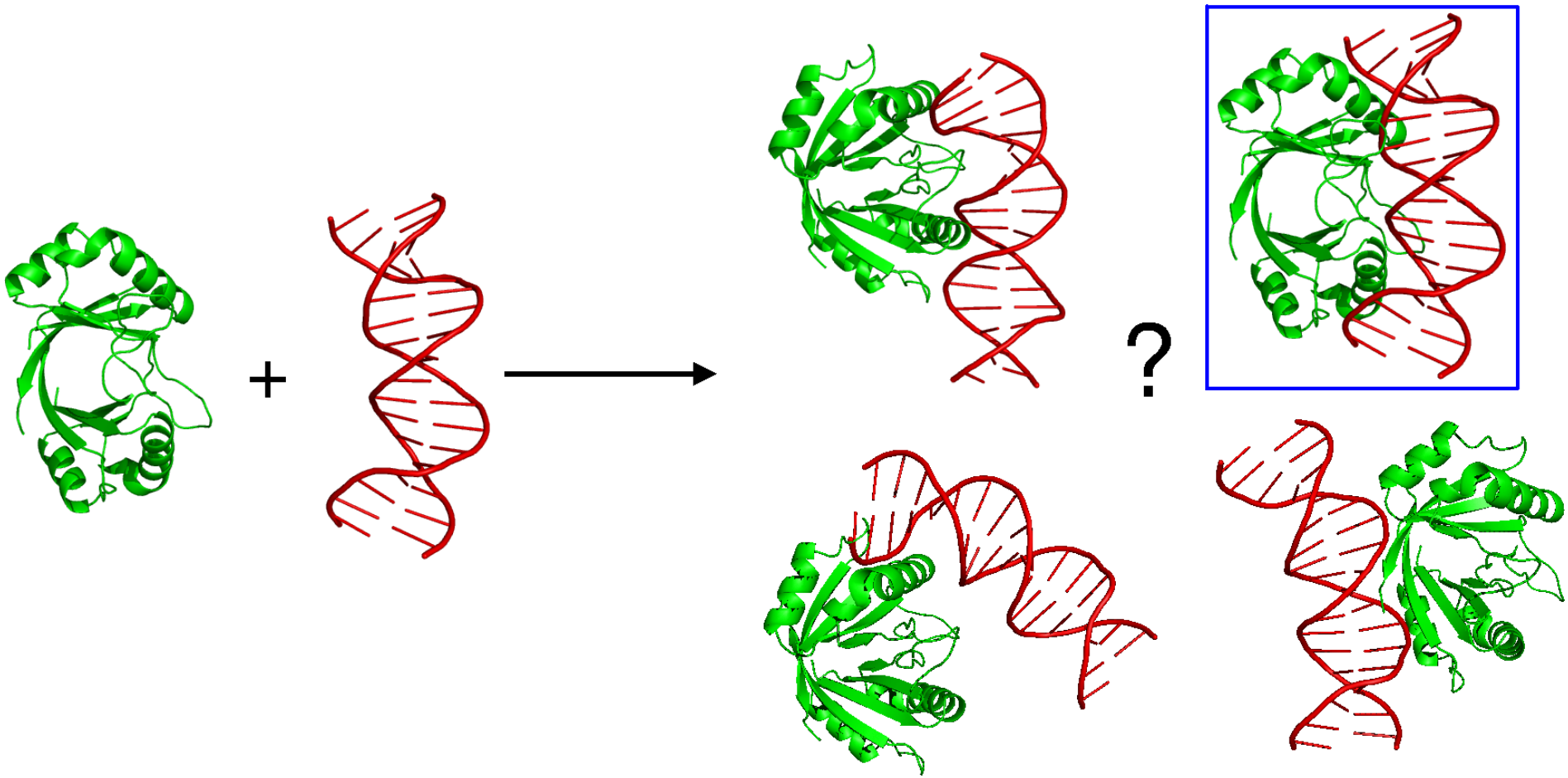


nucléosome (1KX5)



Prédire un complexe (macro)moléculaire

Principe



Principe (2)

Prédire un complexe (macro)moléculaire

1. Exploration

des associations possibles

2. Évaluation

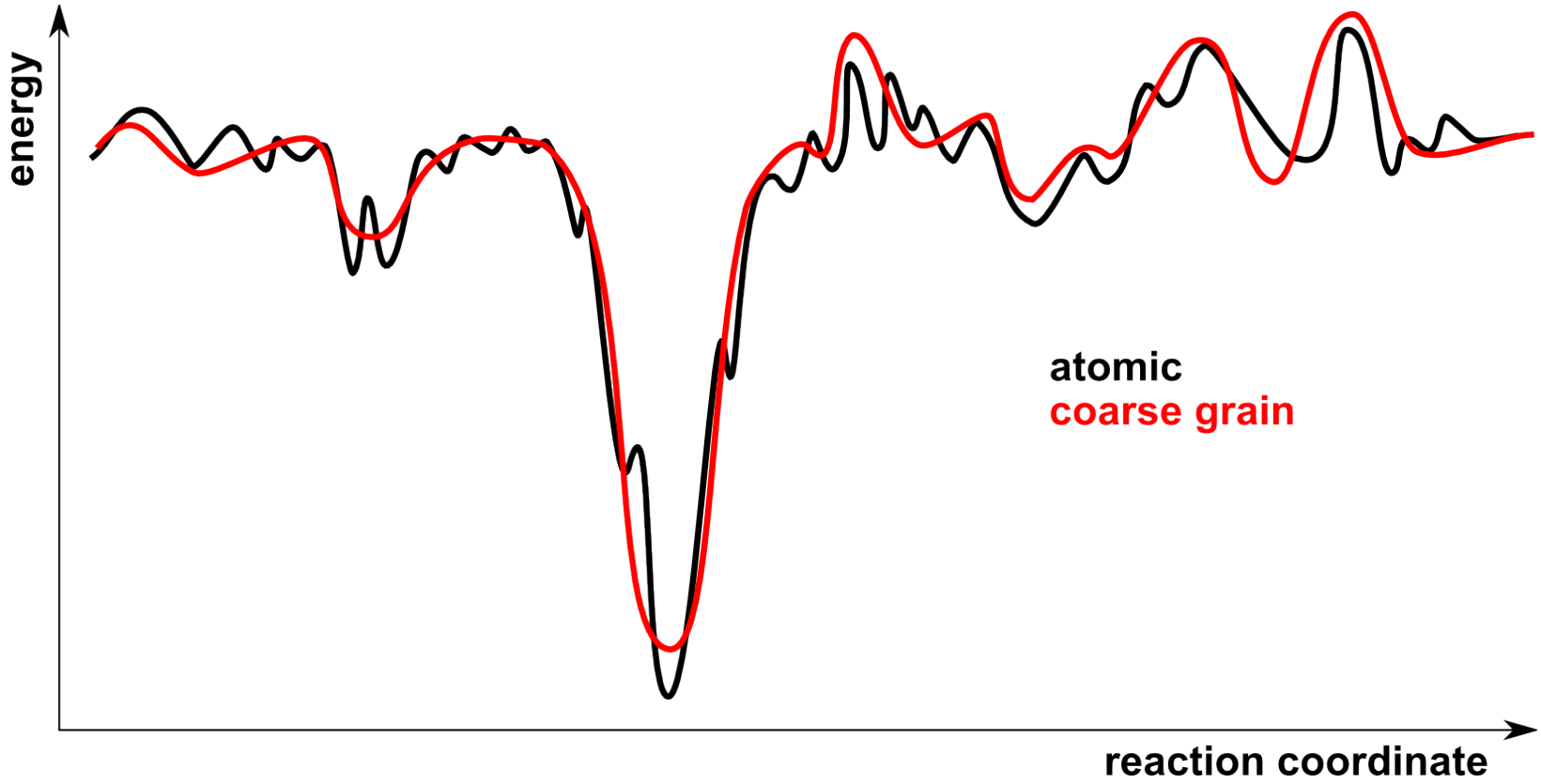
scoring

Menu

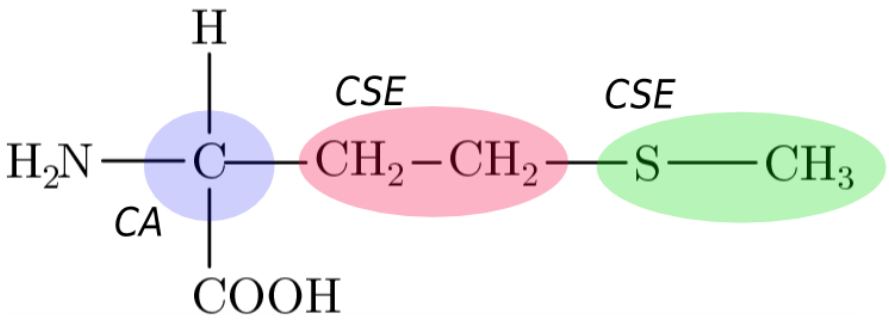
Gros grain

1 bille (grain) = *n* atomes

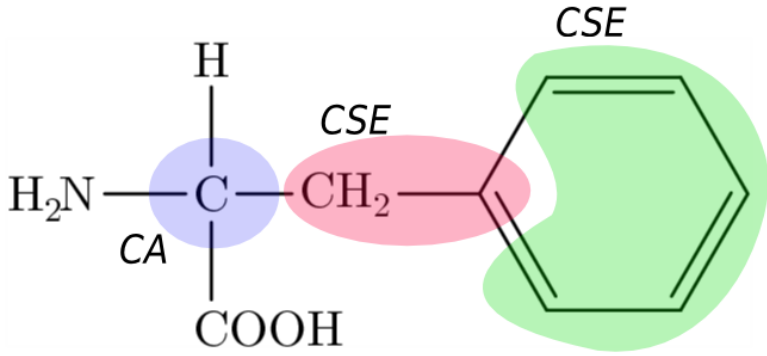
Intérêt principal



Un modèle de protéine



Methionine
Met / M

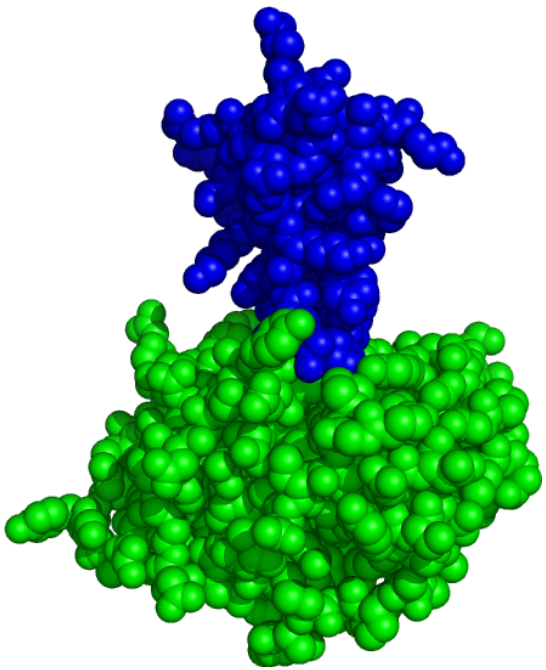


Phenylalanine
Phe / F

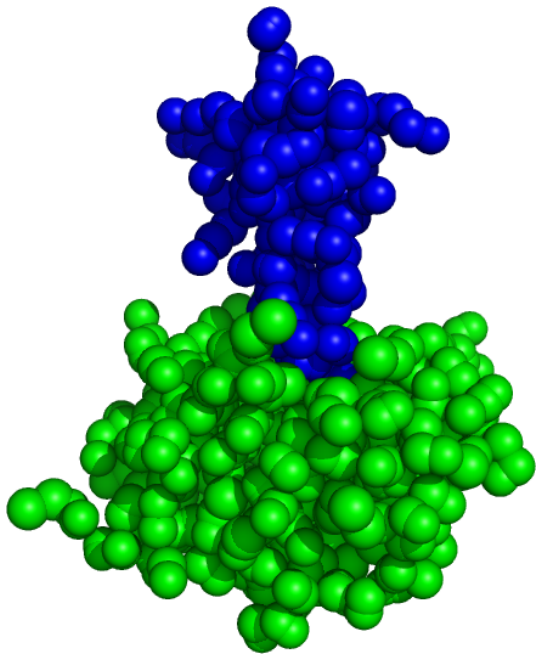
Zacharias, *Protein Sci* **12** : 1271 (2003)

Résolution et modèle gros grain

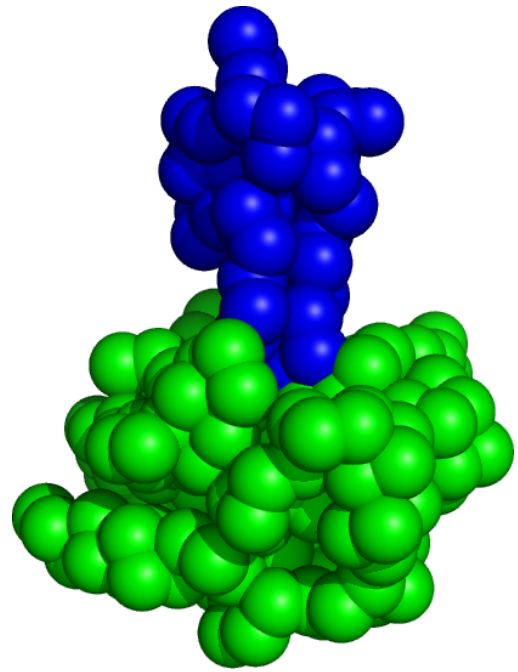
trypsine et son inhibiteur (PDB 1BZX)



tout-atome
(2133 part.)

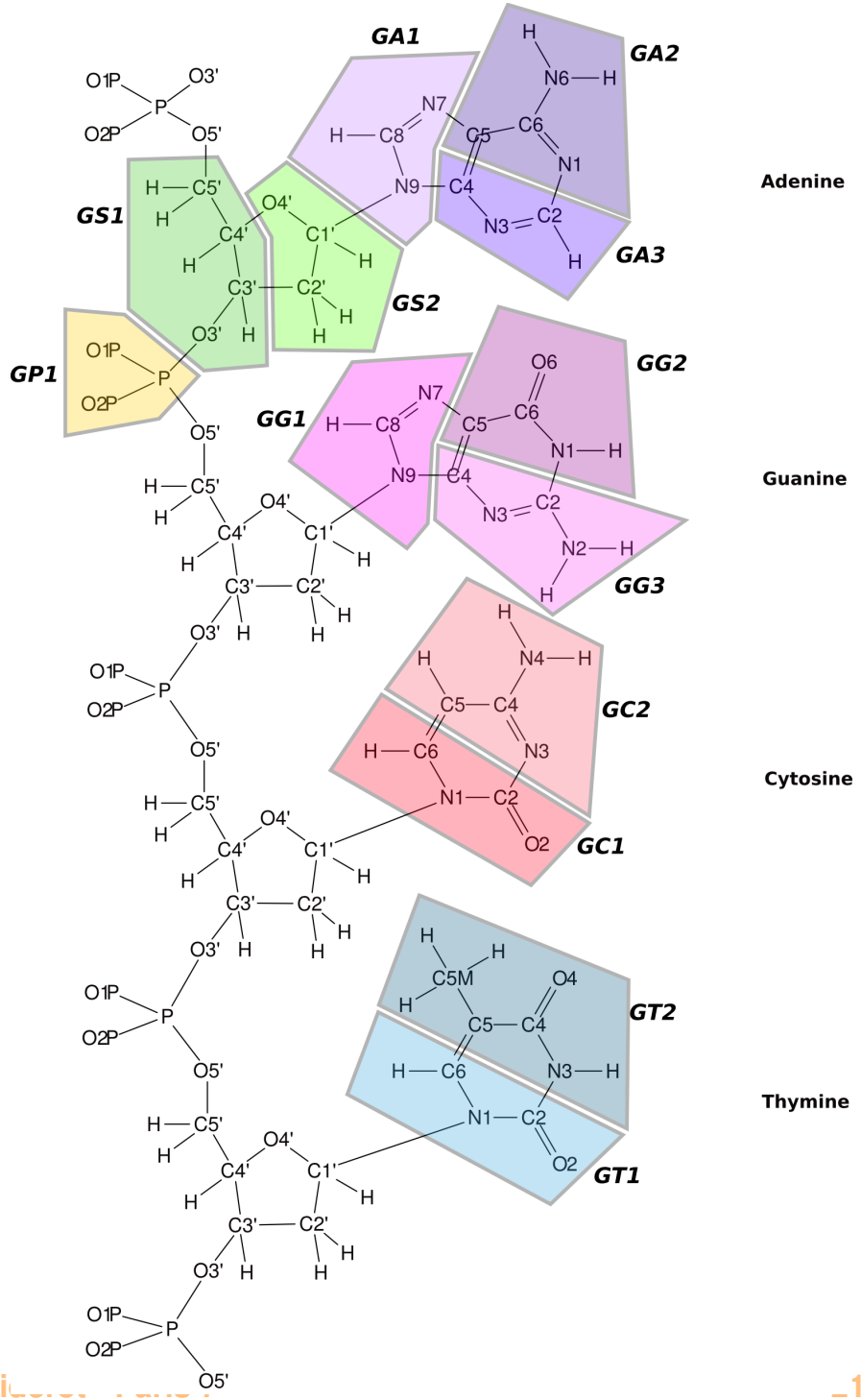


Zacharias
(603 part.)



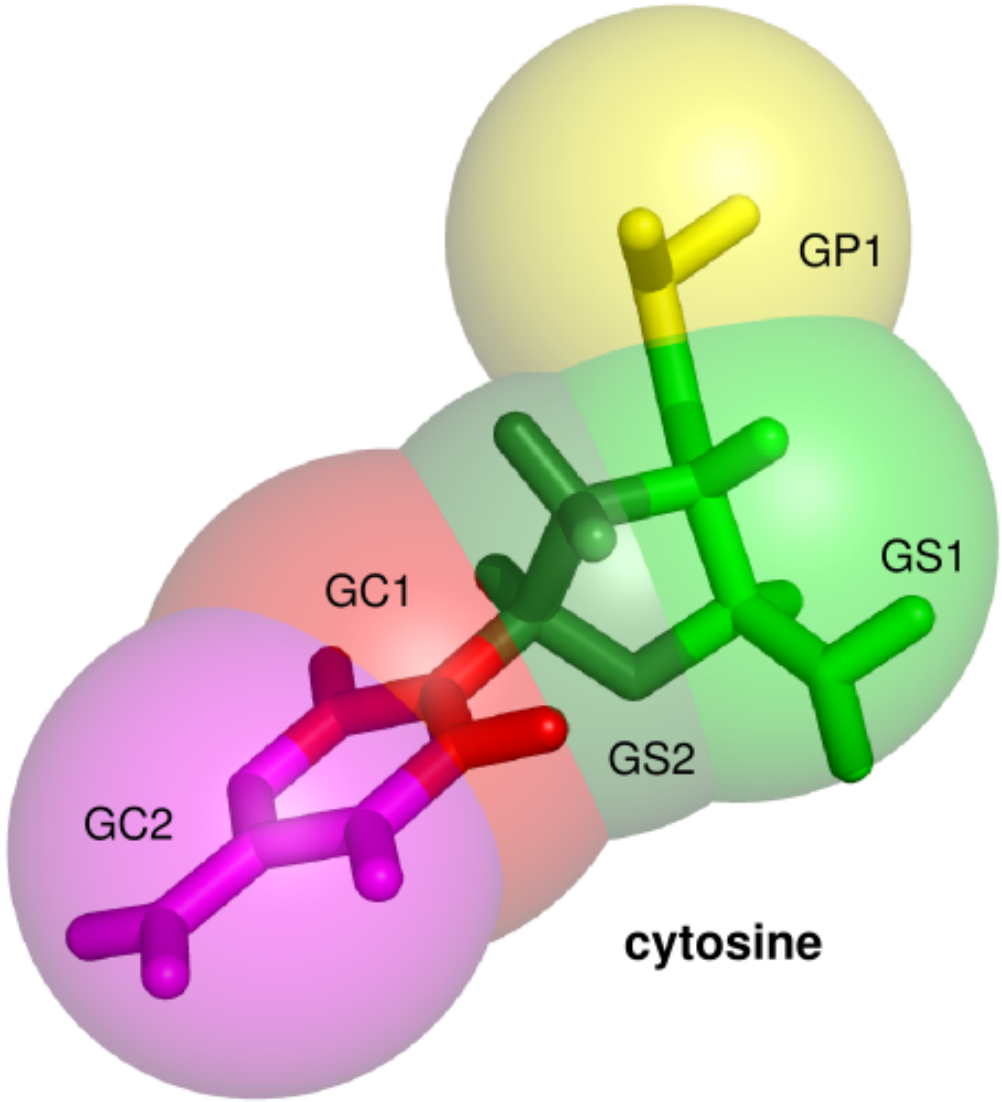
Cα
(280 part.)

Un modèle d'ADN



Poulain *et al.*,
J Comput Chem **39** : 2582 (2008)

Un modèle d'ADN (2)



Menu

PTools

bibliothèque C++/Python [GPL]

protéine – ADN

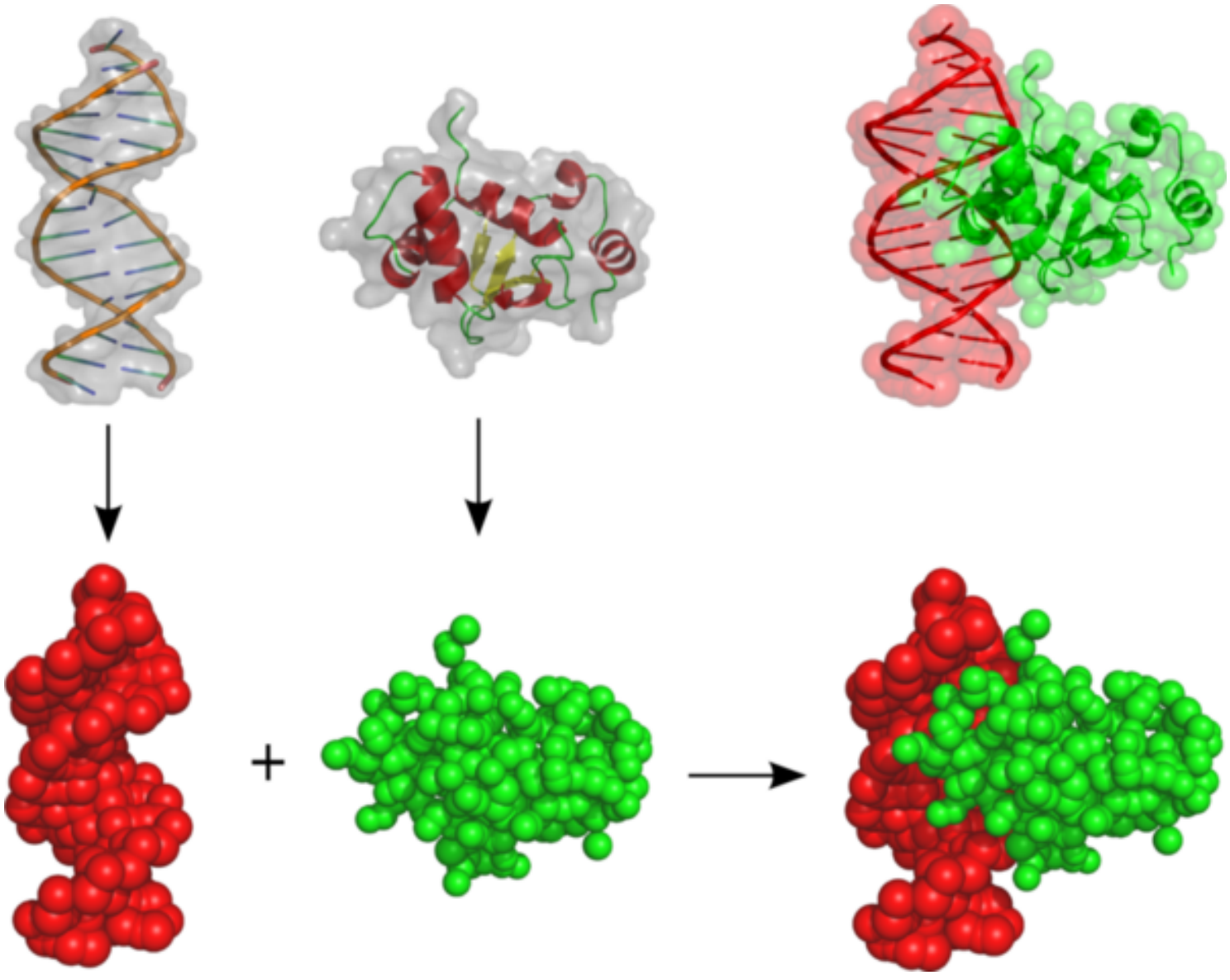
atome – gros grain

`https://launchpad.net/ptools`

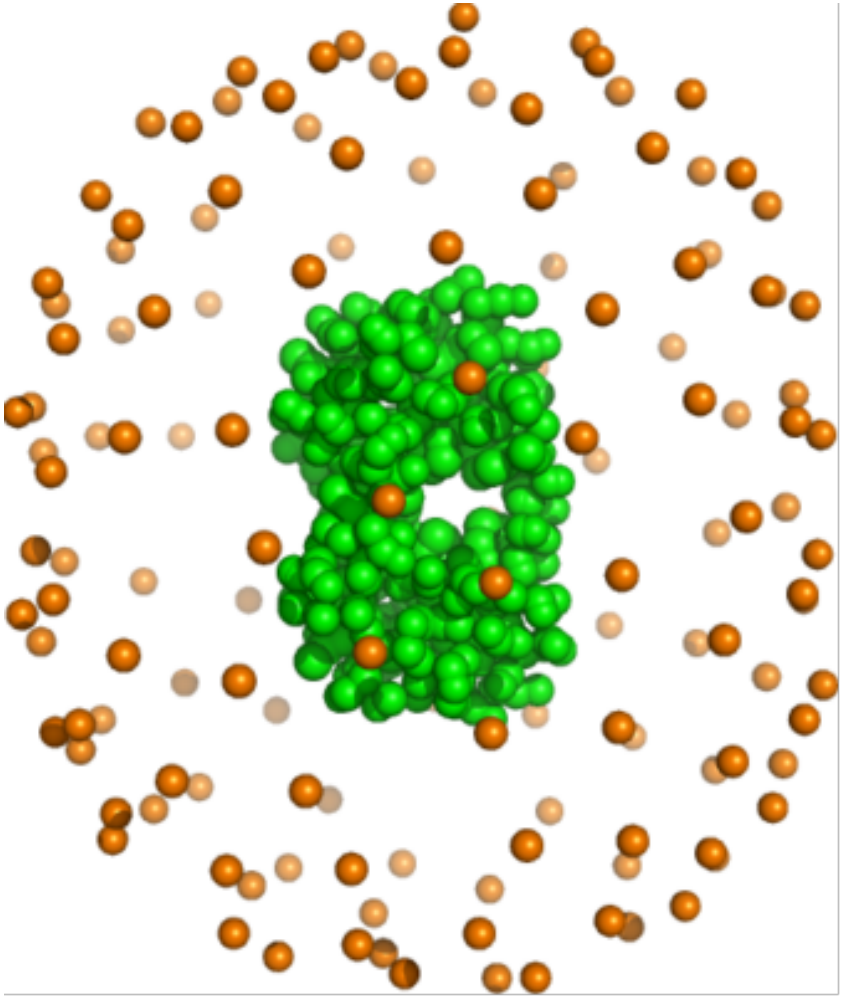
Saladin *et al.*, *BMC Struct Biol* **9** : 27 (2009)

Amarrage gros grain systématique en corps rigides

Amarrage gros grain



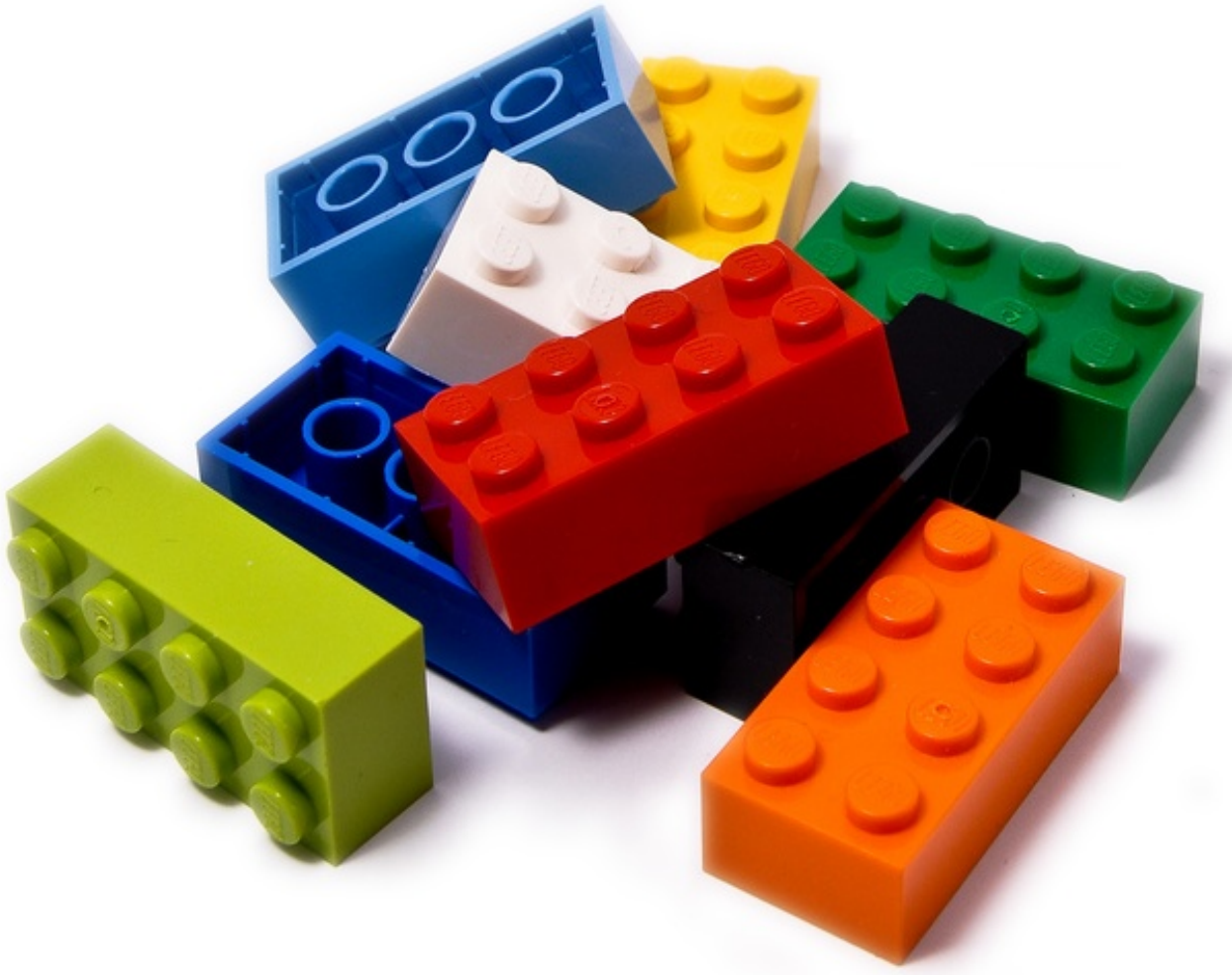
Amarrage systématique



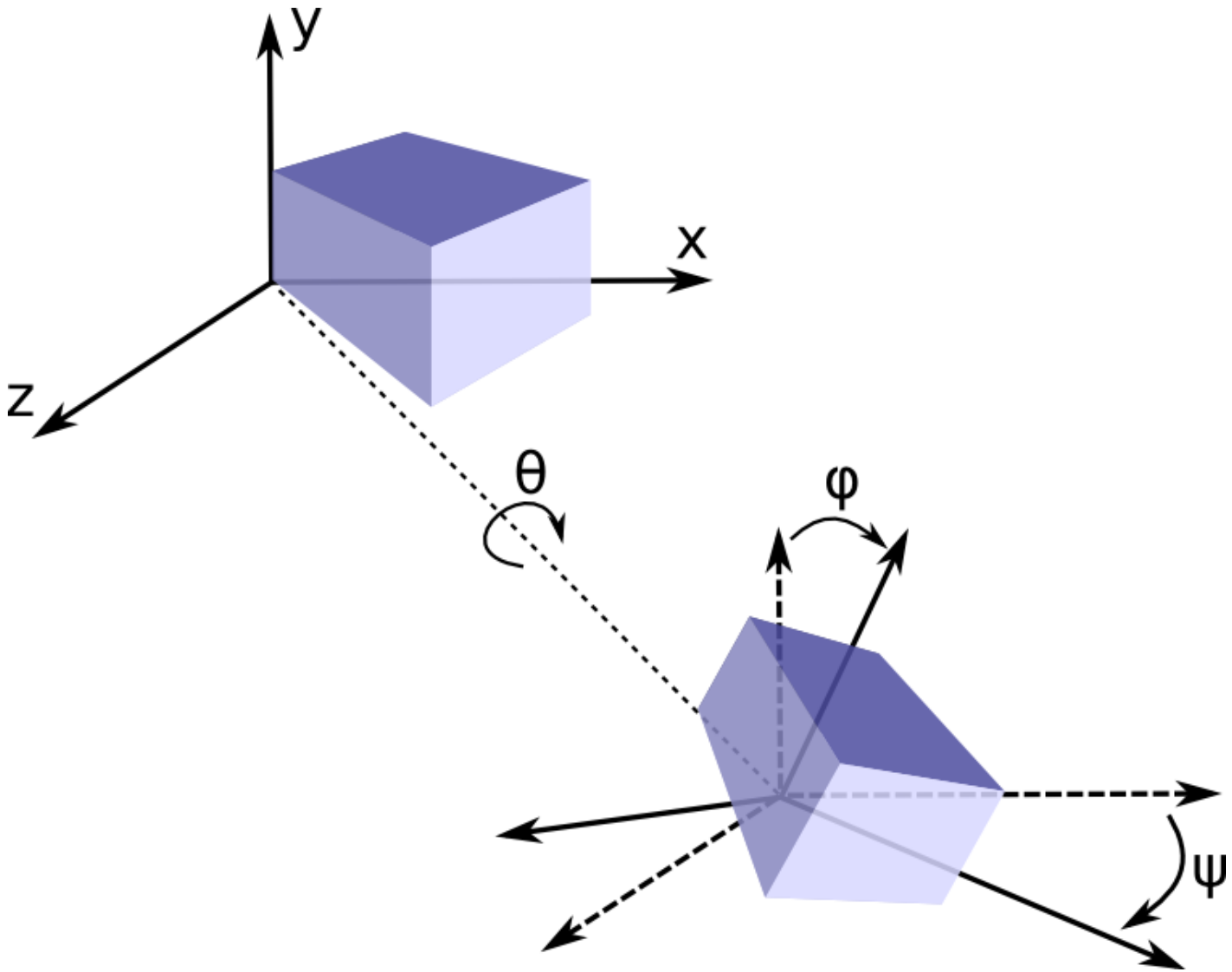
$\sim$ 60 000 positions

Amarrage en corps rigides

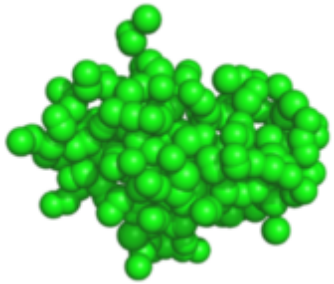
Rigid body docking



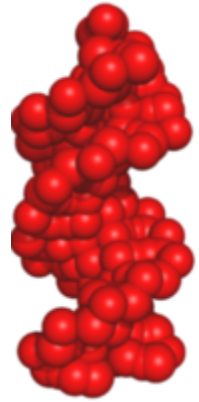
6 degrés de liberté



Énergie d'interaction



I

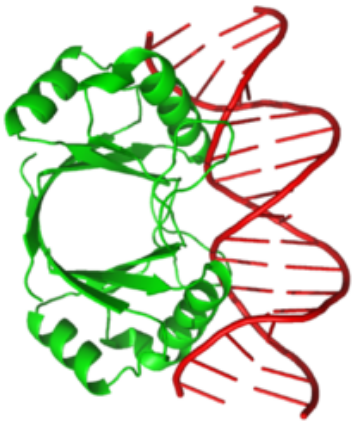


J

$$E = \sum_{i \in I} \sum_{j \in J} \left(\frac{B_{ij}}{r_{ij}^8} - \frac{C_{ij}}{r_{ij}^6} \right) + \sum_{i \in I} \sum_{j \in J} \left(\frac{q_i q_j}{\epsilon r_{ij}} \right)$$

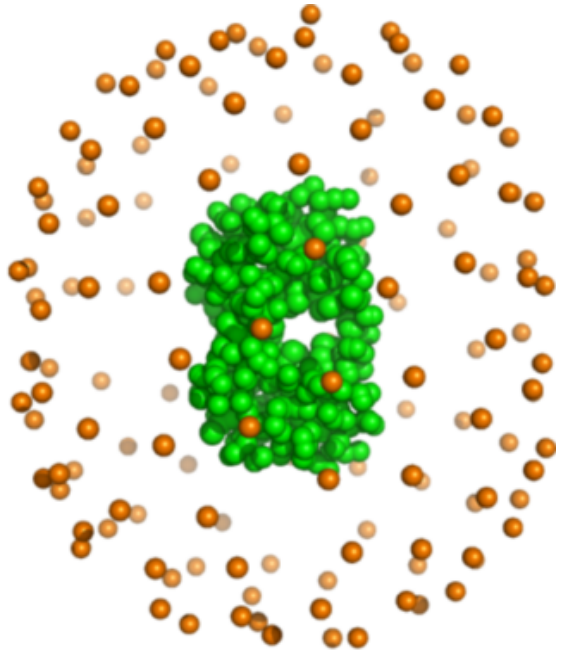
$$\epsilon = 15 r_{ij}$$

Protocole complet



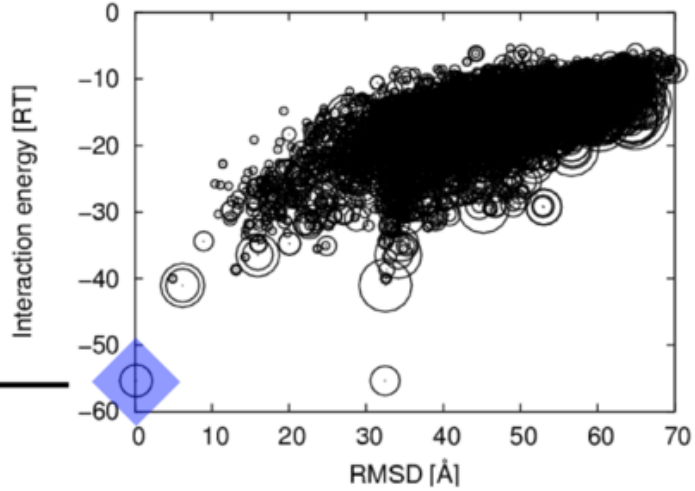
atomic resolution

coarse grain resolution



DNA positions dispatched
all around the protein

systematic docking
ATTRACT



RMSD compared to the native structure
versus interaction energy

lowest energy
close to the native structure

Menu

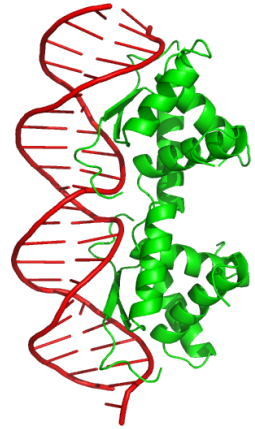
Étude de cas 1

Insights on protein-DNA recognition
by coarse grain modelling

P. Poulain, A. Saladin, B. Hartmann et C. Prévost
J Comput Chem **29** : 2582 (2008)

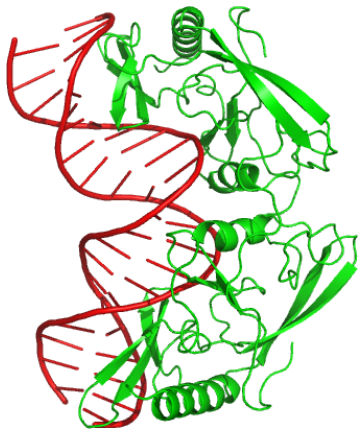
Étude de cas 1

(a) ETS-1/DNA
PDB 1K79

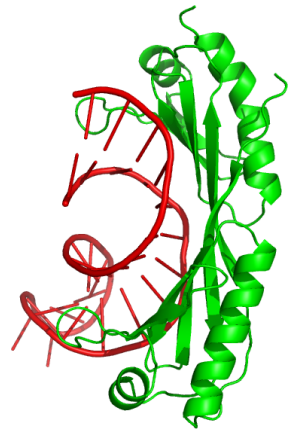


(b) ARC/DNA
PDB 1PAR

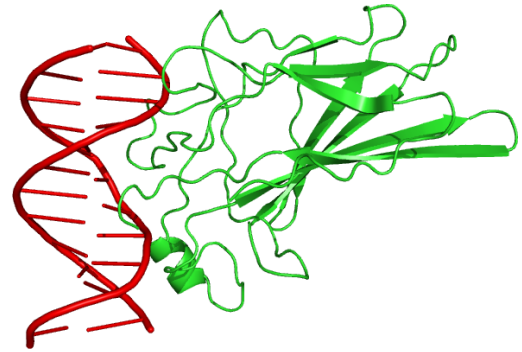
(c) E2/DNA
PDB 2BOP



(d) I-*Ppo*I/DNA
PDB 1A74

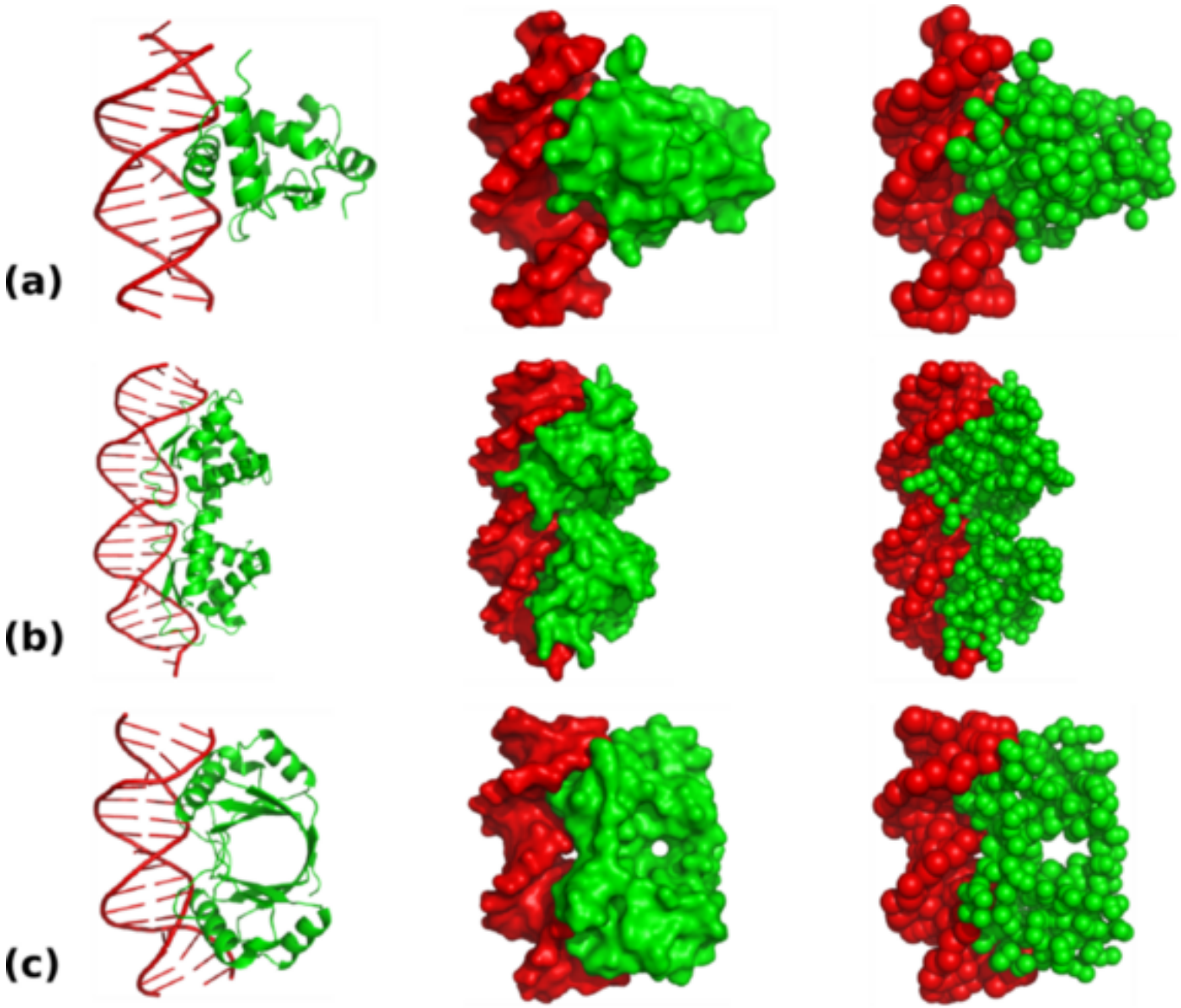


(e) TBP/DNA
PDB 1YTB

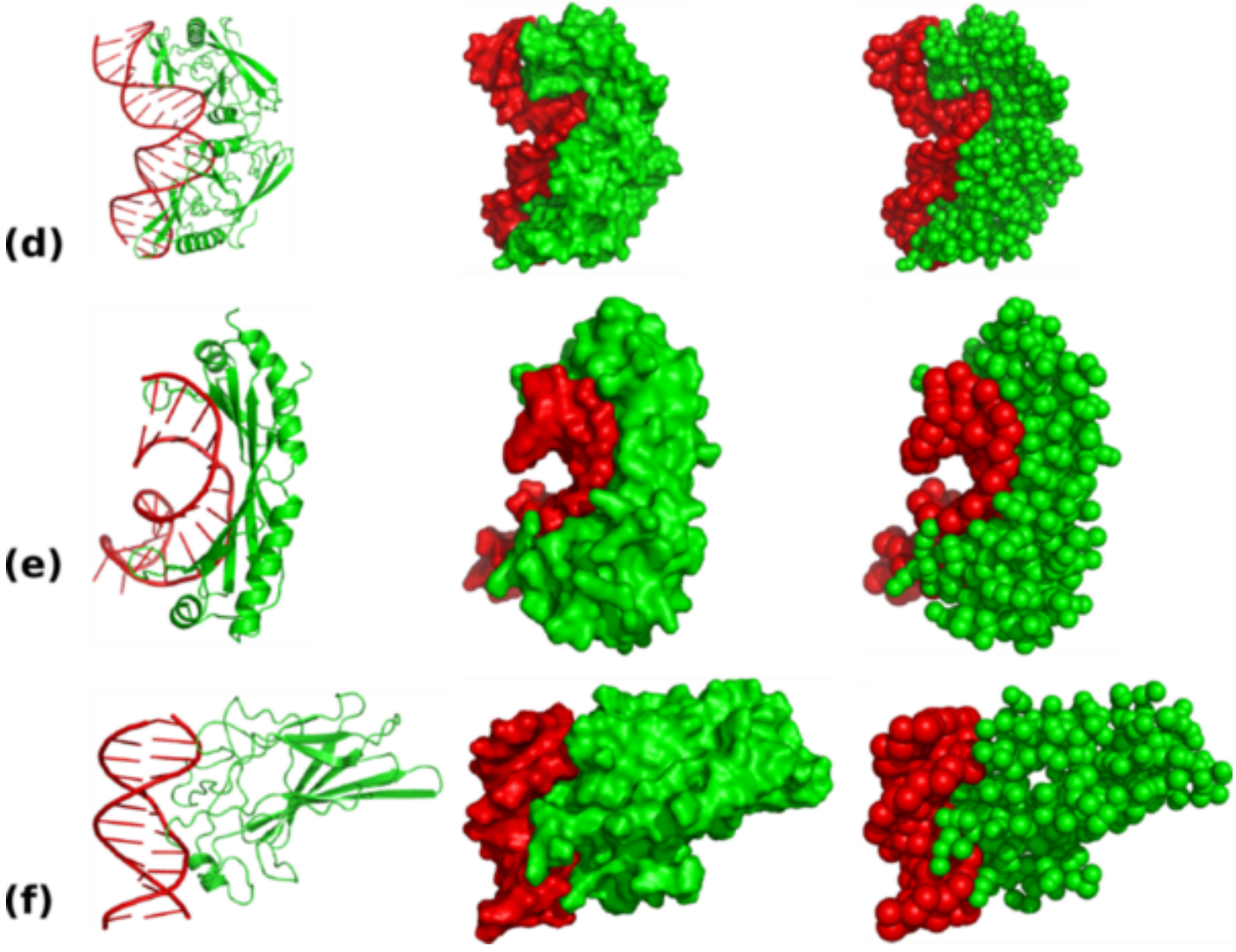


(f) NFATC1/DNA
PDB 1A66

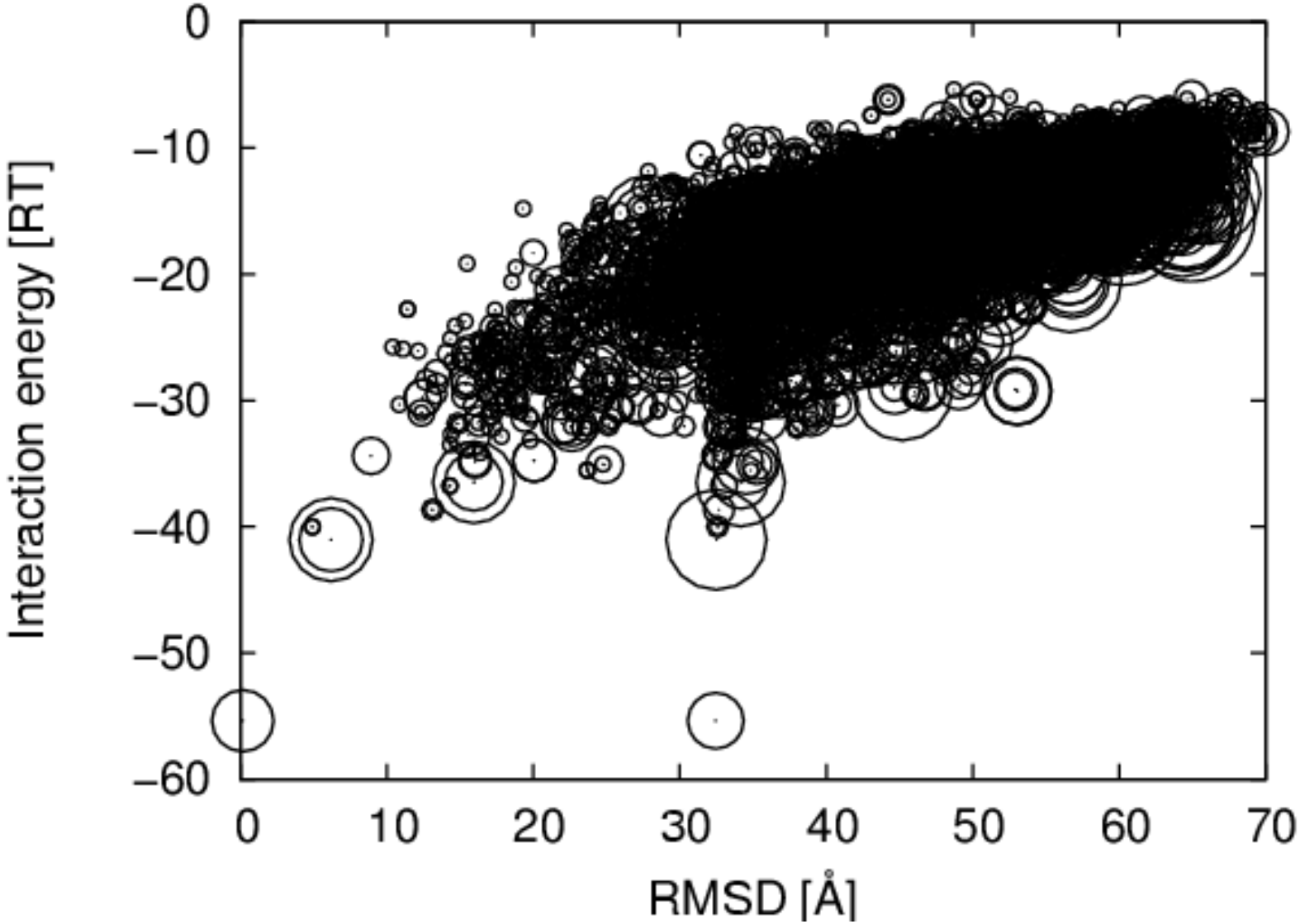
Modélisation gros grain



Modélisation gros grain 2



Résultats

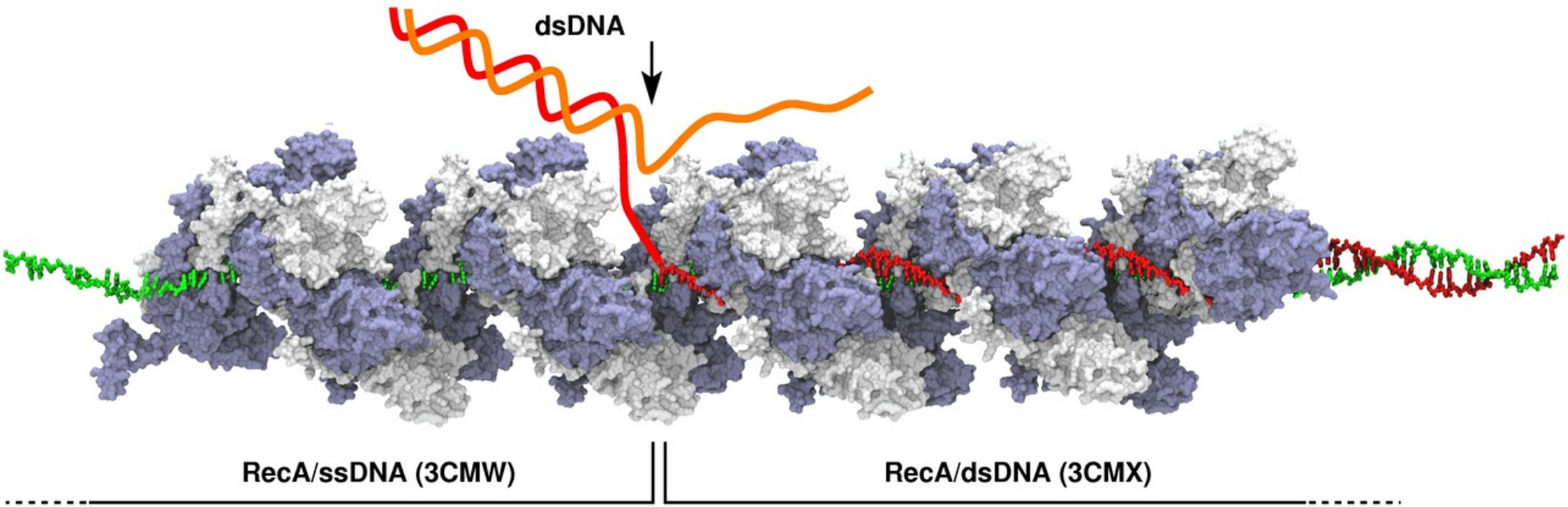

Interaction energy [RT]
0
−10
−20
−30
−40
−50
−60
0
10
20
30
40
50
60
70
RMSD [Å]

Étude de cas 2

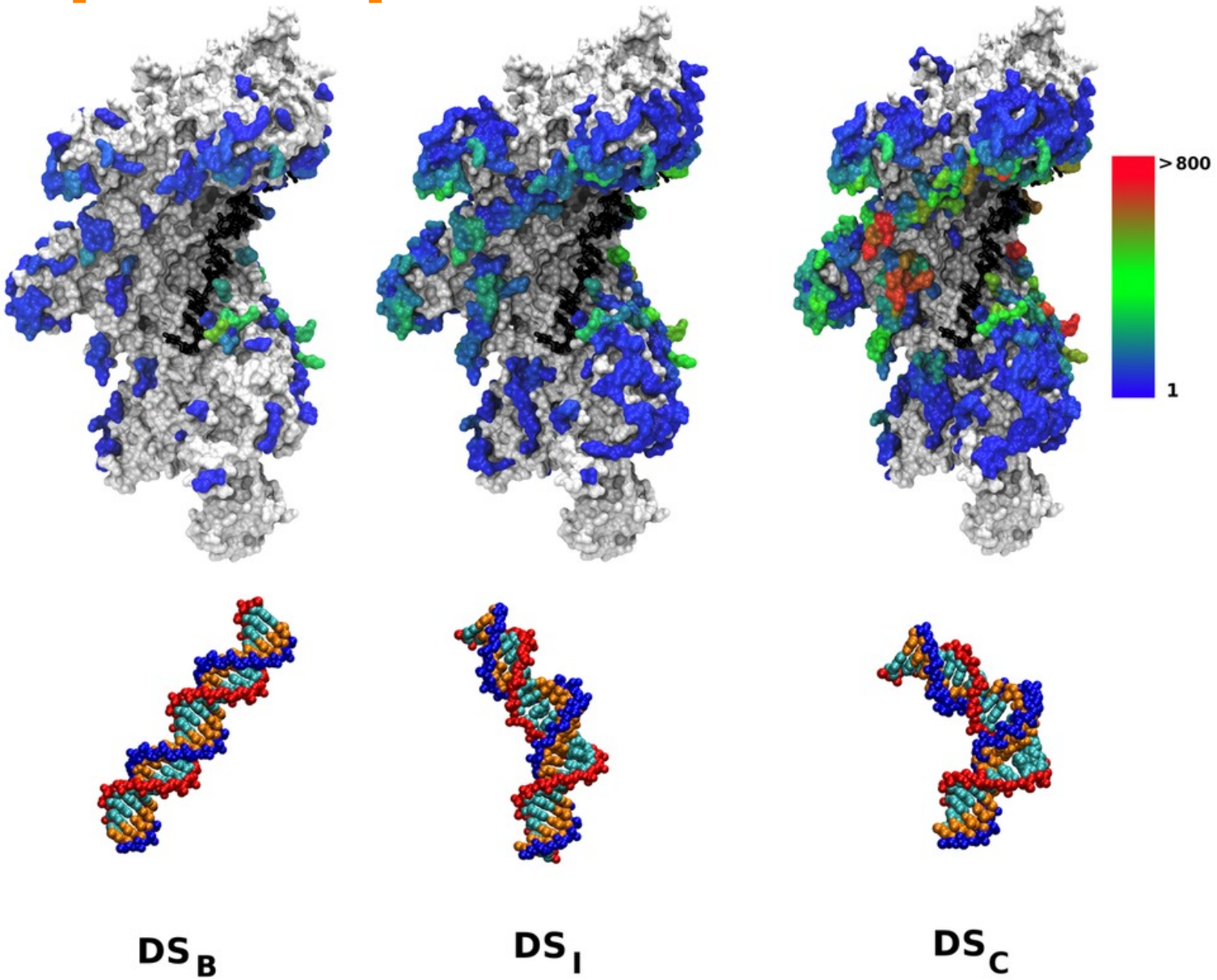
Modeling the early stage
of DNA sequence recognition
within RecA nucleoprotein filaments

A. Saladin, C. Amourda, P. Poulain, N. Férey,
M. Baaden, M. Zacharias, O. Delalande et C. Prévost
Nucleic Acids Res **38** : 6313 (2010)

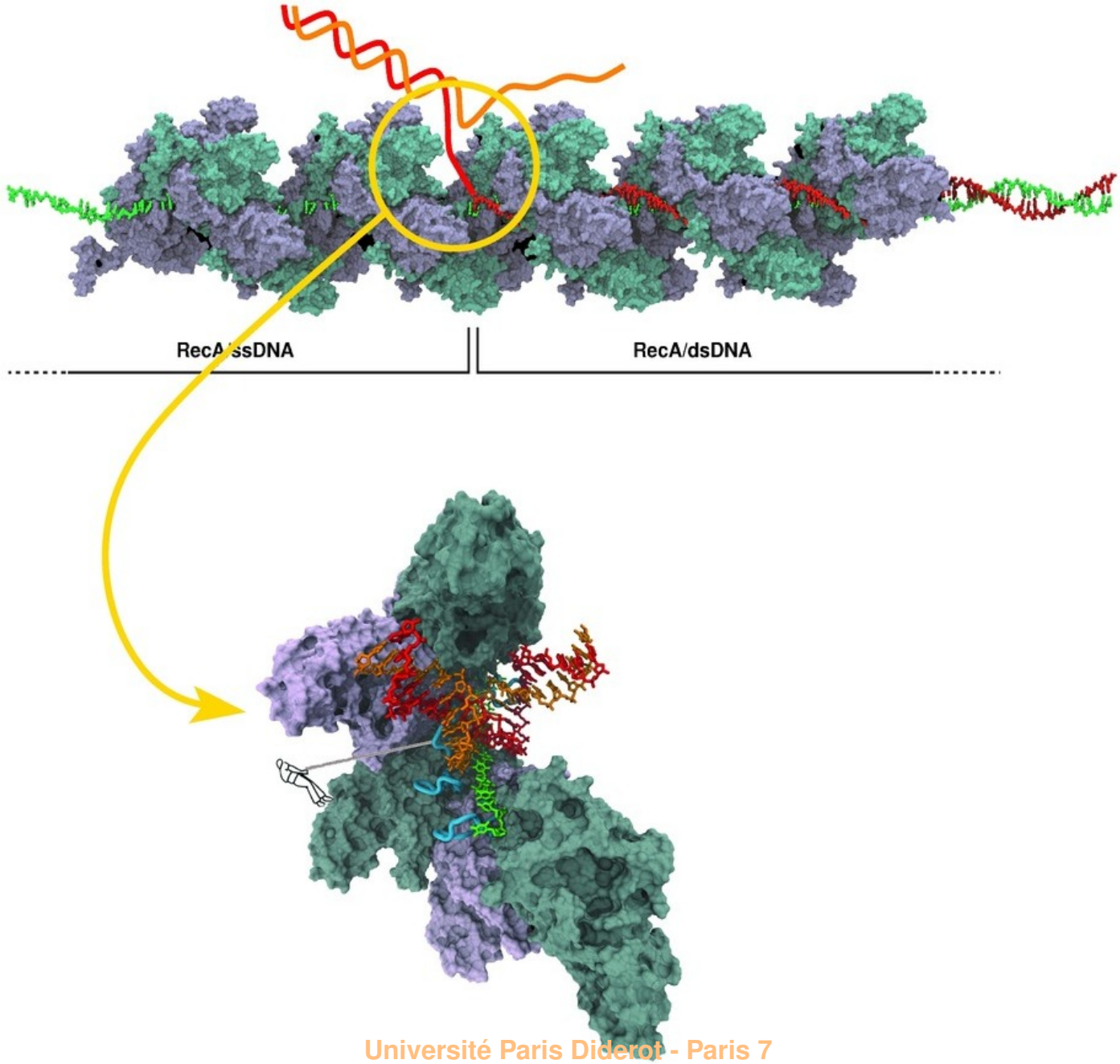
Les questions

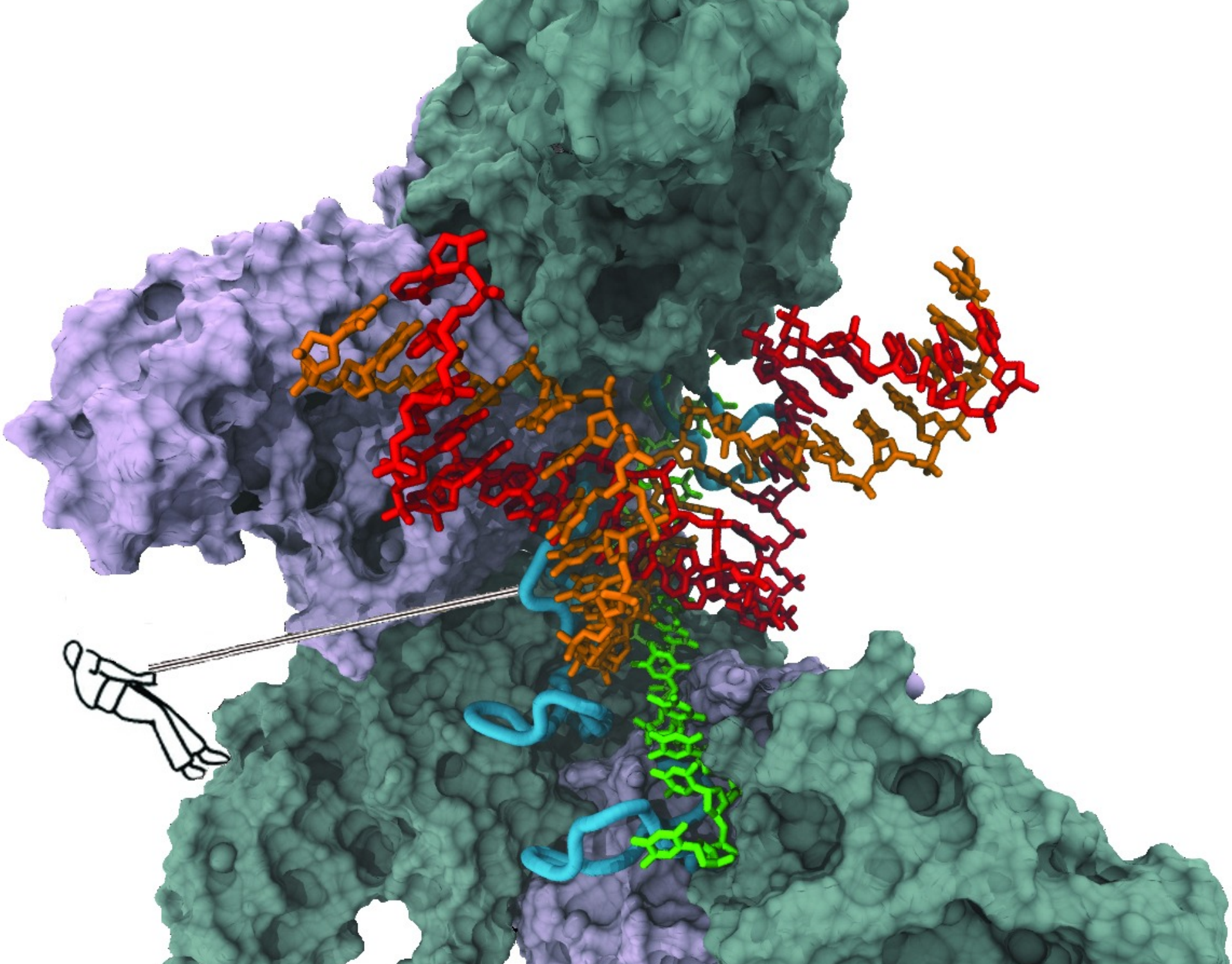


Quelques réponses

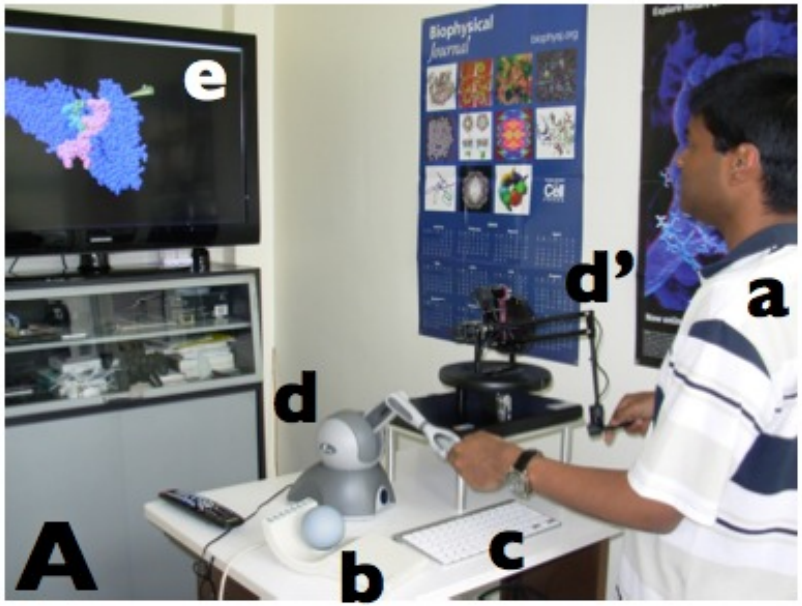


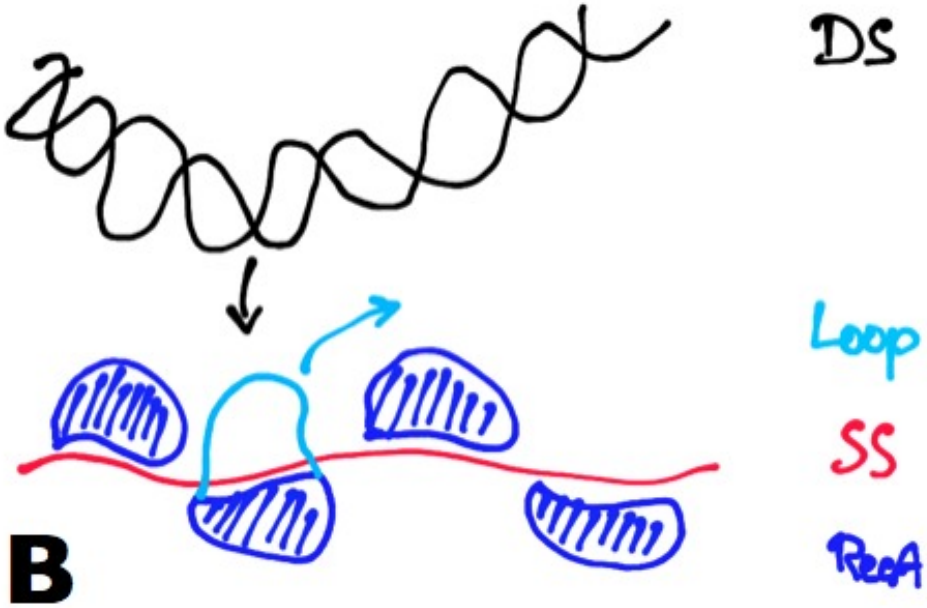
D’autres questions

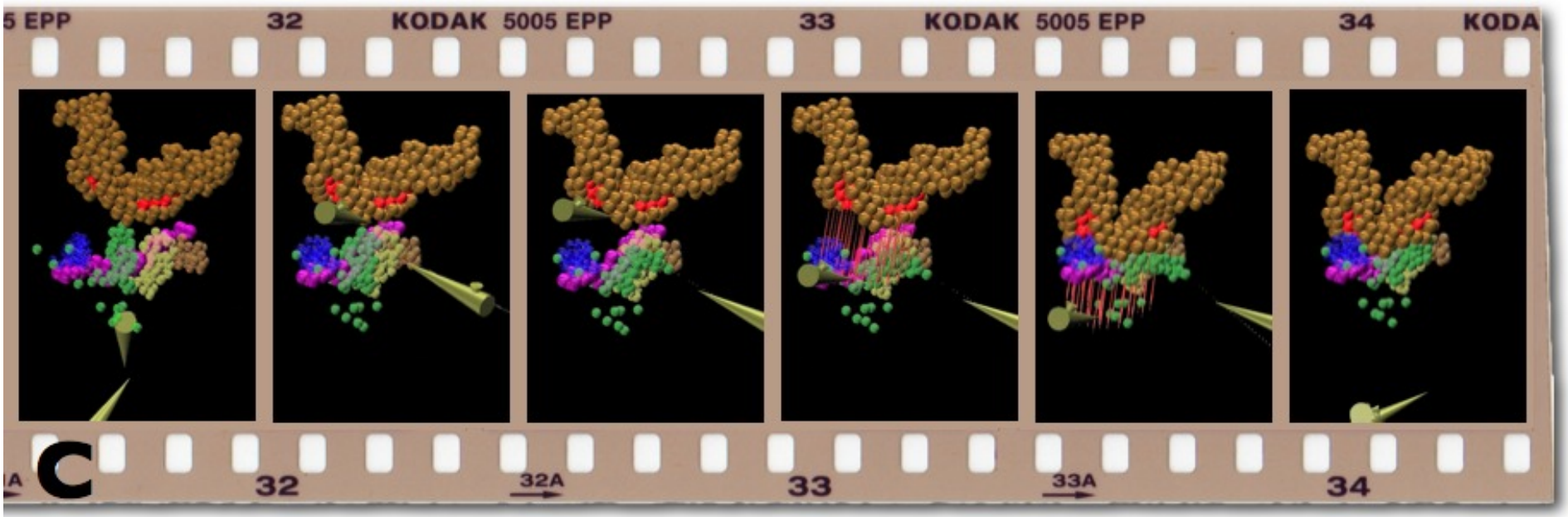




D’autres méthodes







D’autres réponses

`http://www.ibpc.fr/chantal/VR-RecA.m4v`

Menu

ATTRACT et les autres

High Ambiguity Driven biomolecular DOCKing (HADDOCK)
`http://www.nmr.chem.uu.nl/haddock/`
`http://haddock.chem.uu.nl/services/HADDOCK/haddock.php` [server]

RosettaDock
`http://graylab.jhu.edu/docking/rosetta/`
`http://rosettadock.graylab.jhu.edu/` [server]

Hex
`http://hex.loria.fr/`
`http://hexserver.loria.fr/` [server]

DOT
`http://www.sdsc.edu/CCMS/DOT/`

Menu

Complexes (macro)moléculaires

= « machines » du vivant

Comprendre leur organisation

↓

Docking

Complexes (macro)moléculaires 2

= xxxxxxxxx atomes

Simulations

↓

gros grain + corps rigide

Menu

Collaborateurs

DSIMB
Inserm UMR-S 665 et Université Paris Diderot - Paris 7 (Paris)
B. Hartmann

MTi
Inserm UMR-M 973 et Université Paris Diderot - Paris 7 (Paris)
A. Saladin

LBT
IBPC, CNRS UPR 9080 (Paris)
C. Amourda, O. Delalande, N. Férey, M. Baaden, **C. Prévost**

LCMBA
CMRS UMR 6001 et Université de Nice-Sophia Antipolis (Nice)
S. Fiorucci

Physik-Department
Technische Universität München (Munich)
M. Zacharias

Références

Coarse-grained models for proteins
Tozzini V, *Curr Opin Struct Bio* **15 :**144 (2005)
doi 10.1016/j.sbi.2005.02.005

Protein-protein docking with a reduced protein model accounting for side-chain flexibility
Zacharias M, *Protein Sci* **12 :**1271 (2003)
doi 10.1110/ps.0239303

Insights on protein-DNA recognition by coarse grain modelling
Poulain P *et al.*, *J Comput Chem* **29** : 2582 (2008)
doi 10.1002/jcc.21014

PTools : an opensource molecular docking library
Saladin A *et al.*, *BMC Struct Biol* **9** : 27 (2009)
doi 10.1186/1472-6807-9-27

Modeling the early stage of DNA sequence recognition within RecA nucleoprotein filaments
Saladin A *et al.*, *Nucleic Acids Res* **38** : 6313 (2010)
doi 10.1093/nar/gkq459

Références 2

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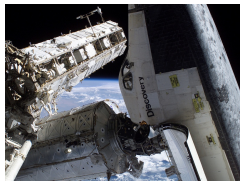
ISBN 978-0387849249
existe en français : La machinerie de la vie, EDP Sciences (2010)

Protein-protein complexes
Zacharias M, *World Scientific* (2010)
ISBN 978-1848163386

Understanding DNA : The Molecule & How It Works
Calladine C R, Drew H R, Luisi B et Travers A, *Academic Press* (2004)
ISBN 978-0121550899

Crédits graphiques



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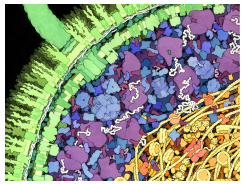
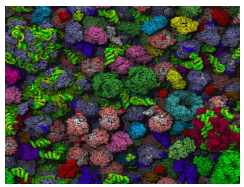


D. Goodsell (copyright)

`http://mgl.scripps.edu/people/goodsell/`



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