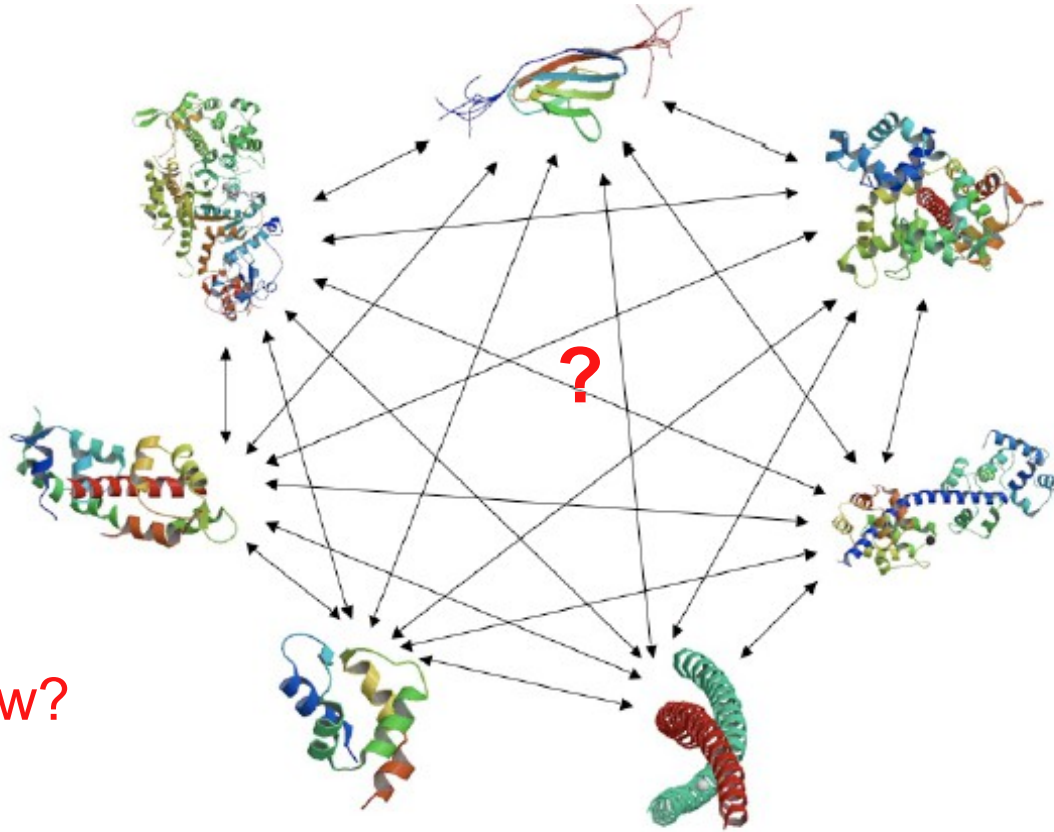
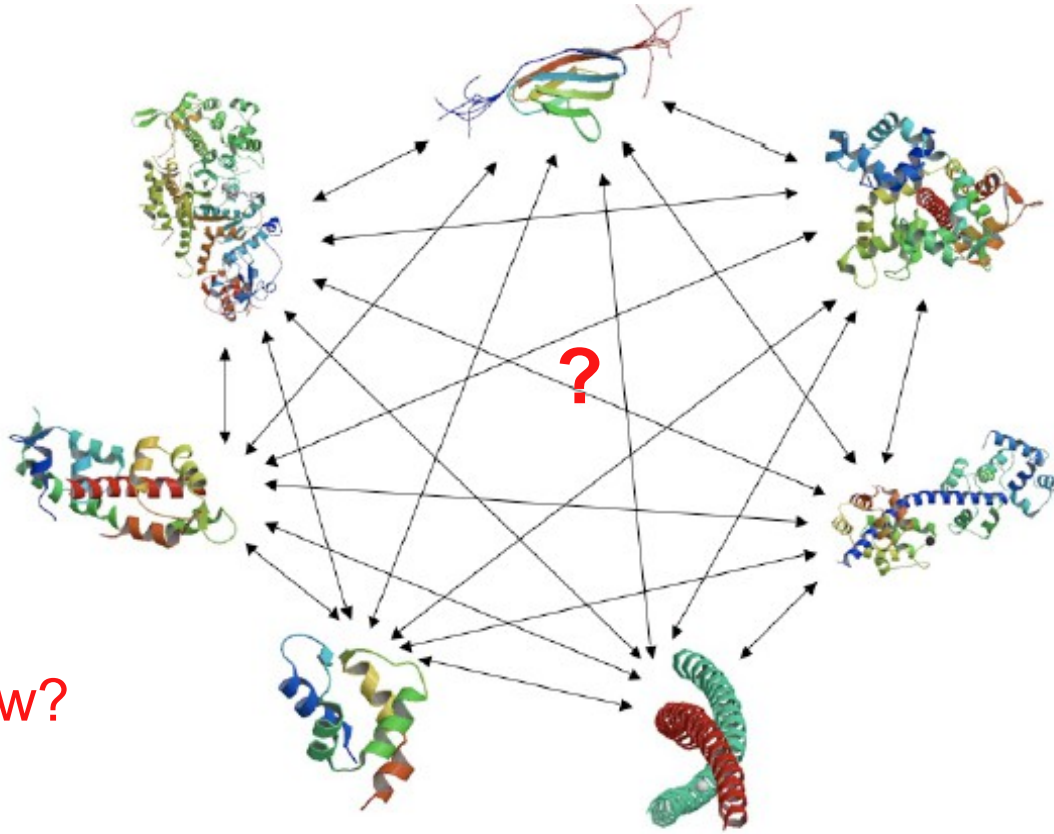


## Protein partner prediction at a molecular scale



who and how?

# Protein partner prediction at a molecular scale



who and how?

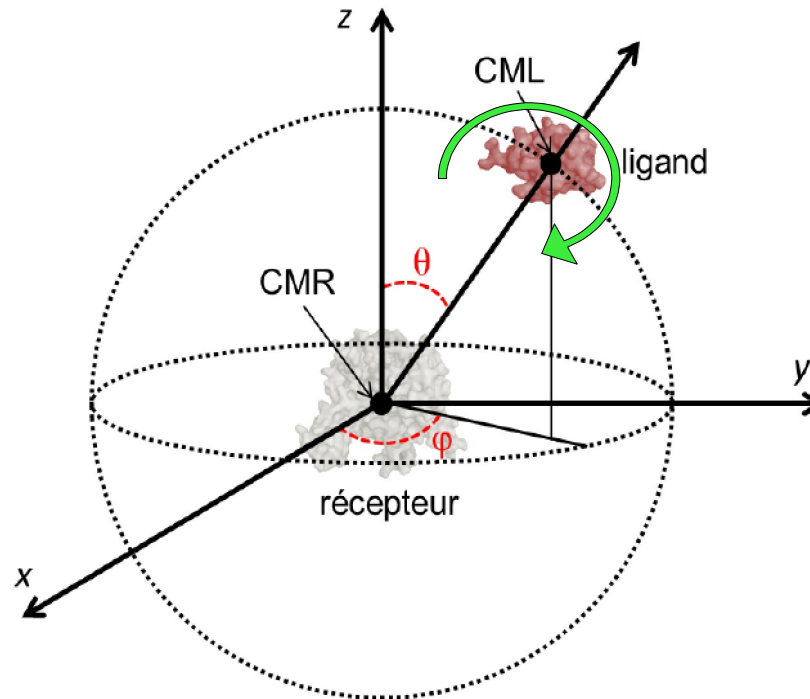
- answering these questions:  
docking (HOW) OR cross-docking calculations (WHO)

# building protein networks: *in silico* approaches

- protein docking

. Many success for protein assembly prediction : **how? OK!**

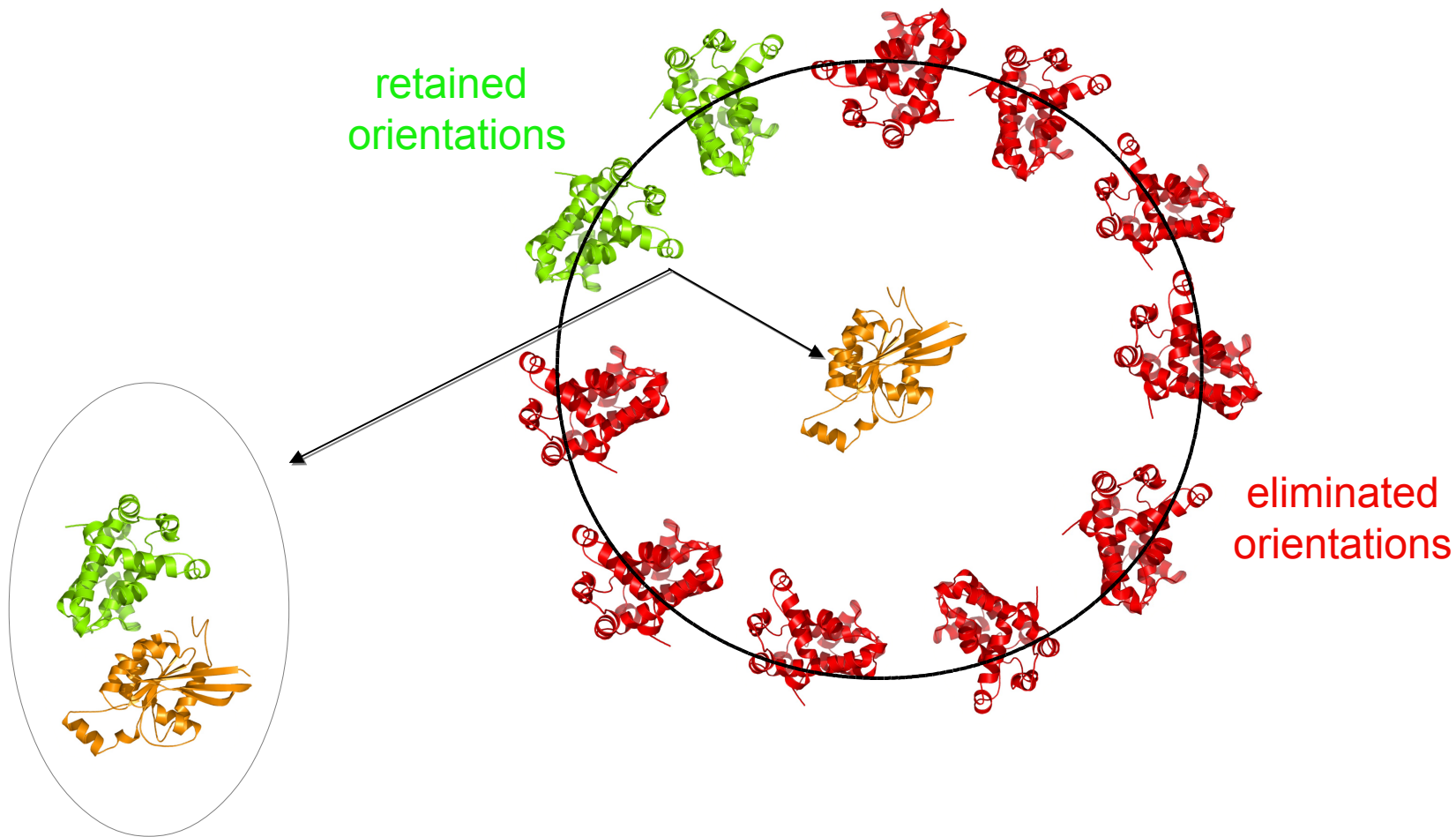
(Méndez et al, *PROTEINS* 2005, Pons et al, *PROTEINS* 2010)



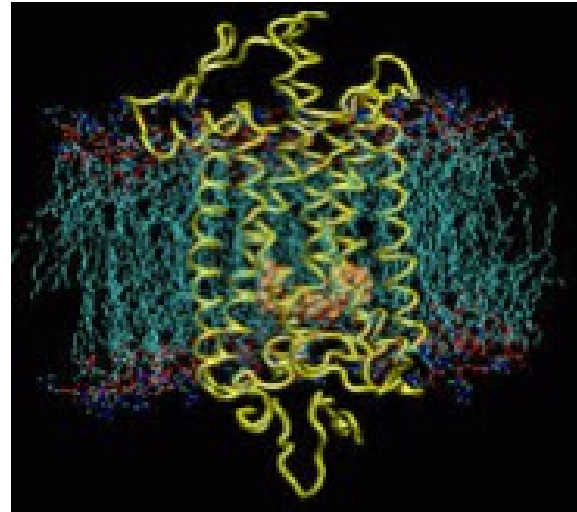
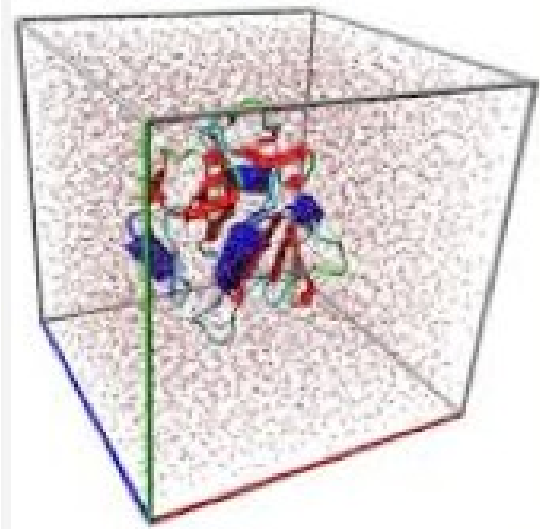
Sacquin-Mora et al, *JMB* 2008

## Identification of the best solution(s)

- Scoring function (energy, evolutionary information...)

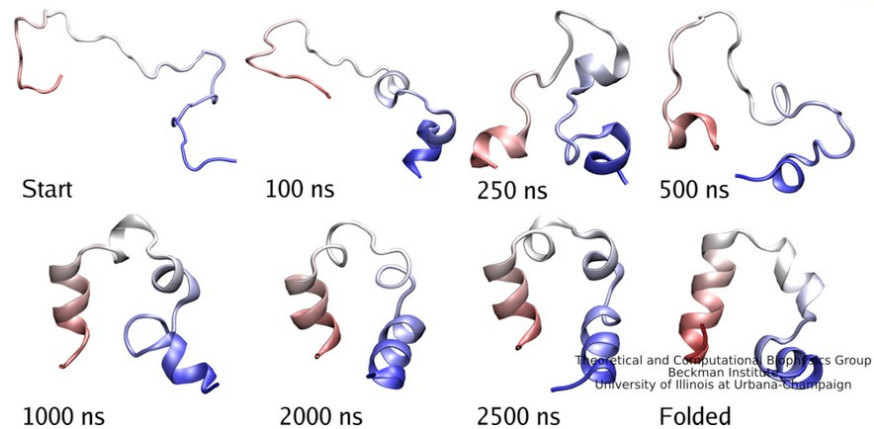
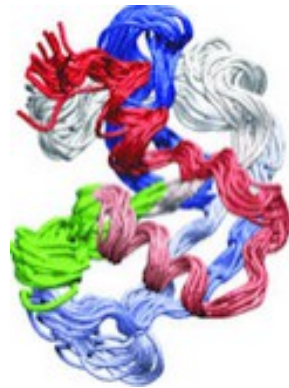


# différentes échelles de temps



dynamique moléculaire

# différentes échelles de temps

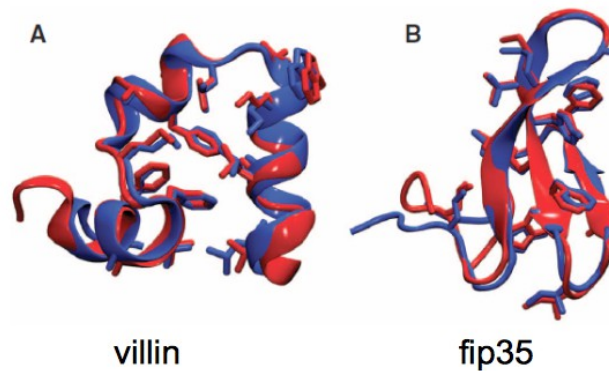


*Peter et al, Biophysical Journal 2008*

# différentes échelles de temps

## Atomic-Level Characterization of the Structural Dynamics of Proteins

David E. Shaw,<sup>1,2\*</sup> Paul Maragakis,<sup>1†</sup> Kresten Lindorff-Larsen,<sup>1†</sup> Stefano Piana,<sup>1†</sup>  
Ron O. Dror,<sup>1</sup> Michael P. Eastwood,<sup>1</sup> Joseph A. Bank,<sup>1</sup> John M. Jumper,<sup>1</sup> John K. Salmon,<sup>1</sup>  
Yibing Shan,<sup>1</sup> Willy Griggers<sup>1</sup>



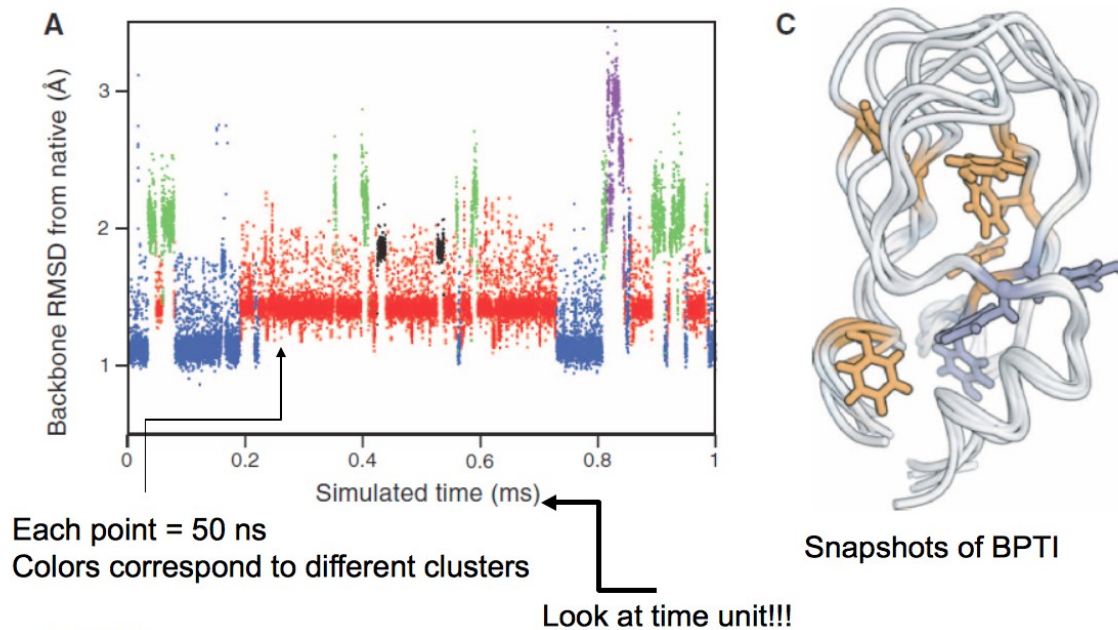
blue: Xray structure

red: final MD structure

Source: Shaw et al., *Science*, 2010<sup>9</sup>

# différentes échelles de temps

## Explicit MD of BPTI (D.E. Shaw)

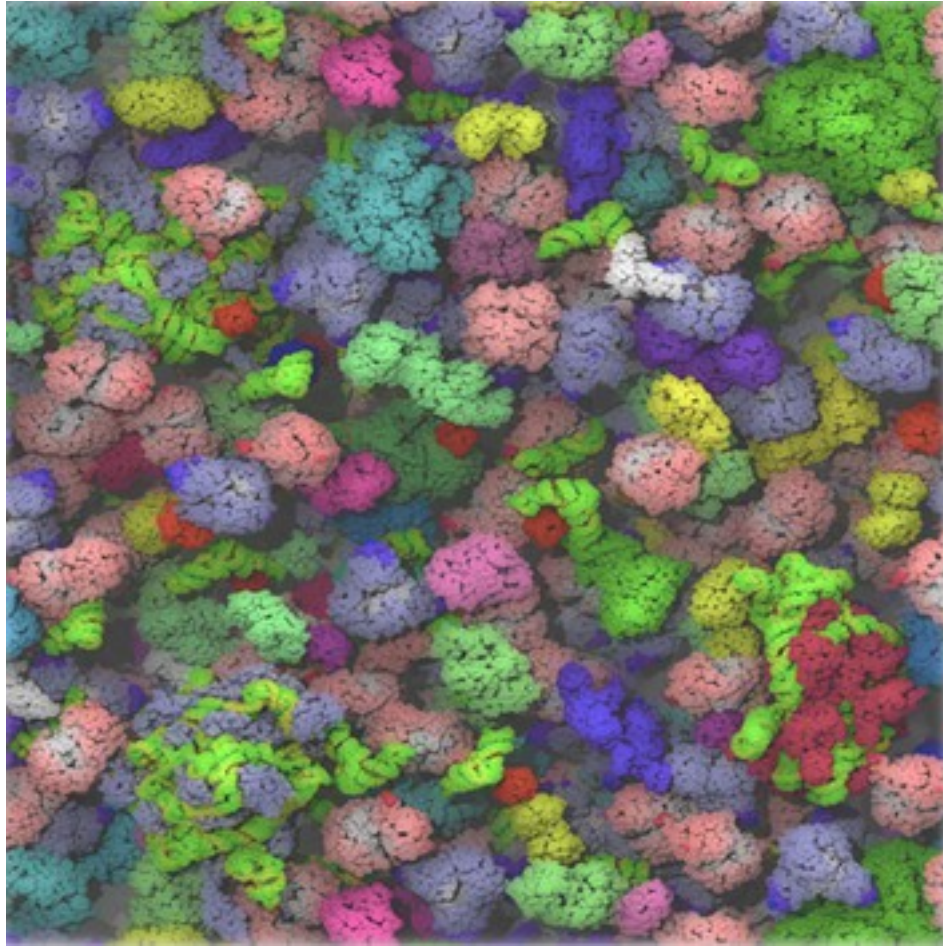


PF 10/2014

10  
Source: Shaw et al., Science, 2010



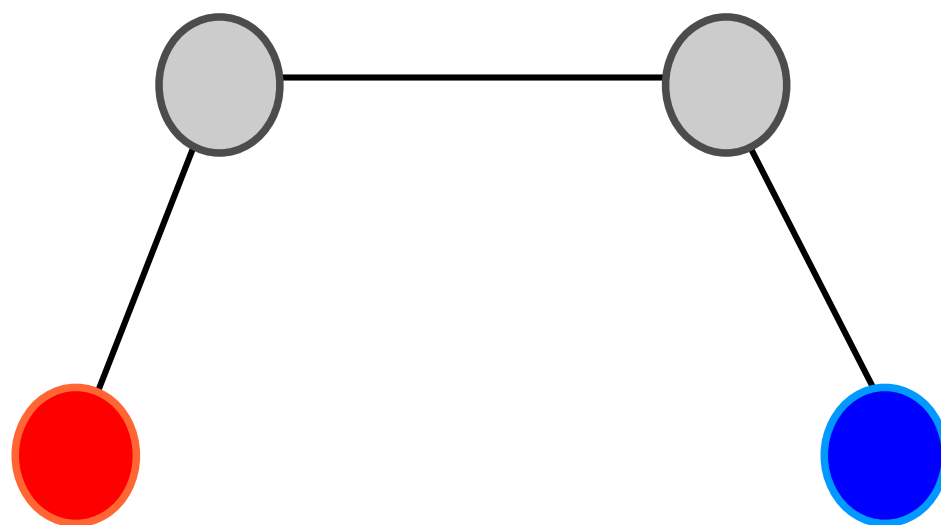
# différentes échelles de temps



*McGuffee & Elcock, PLOS CB 2010*

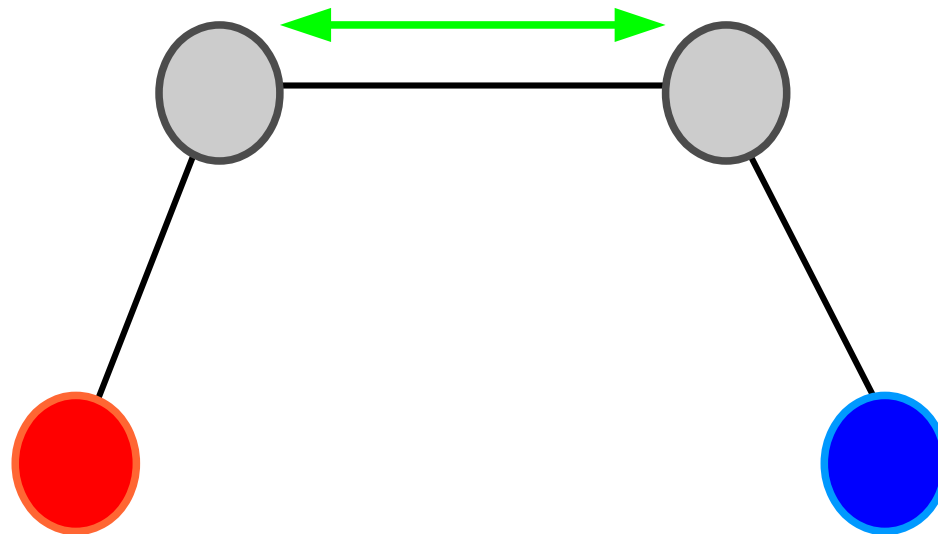
$$E_{\text{total}} = \sum_{\text{bonds}} K_r (r - r_{\text{eq}})^2 + \sum_{\text{angles}} K_{\theta} (\theta - \theta_{\text{eq}})^2 +$$

$$\sum_{\text{dihedrals}} \frac{V_n}{2} [1 + \cos(n\phi - \gamma)] + \sum_{i < j} \left[ \frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^6} + \frac{q_i q_j}{\epsilon R_{ij}} \right]$$



$$E_{\text{total}} = \sum_{\text{bonds}} K_r (r - r_{\text{eq}})^2 + \sum_{\text{angles}} K_{\theta} (\theta - \theta_{\text{eq}})^2 +$$

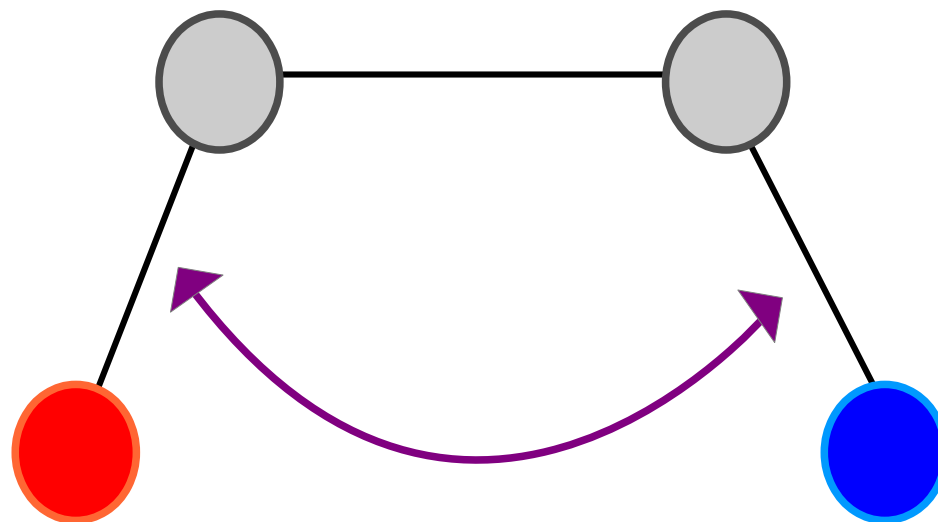
$$\sum_{\text{dihedrals}} \frac{V_n}{2} [1 + \cos(n\phi - \gamma)] + \sum_{i < j} \left[ \frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^6} + \frac{q_i q_j}{\epsilon R_{ij}} \right]$$



termes liés

$$E_{\text{total}} = \sum_{\text{bonds}} K_r (r - r_{\text{eq}})^2 + \sum_{\text{angles}} K_{\theta} (\theta - \theta_{\text{eq}})^2 +$$

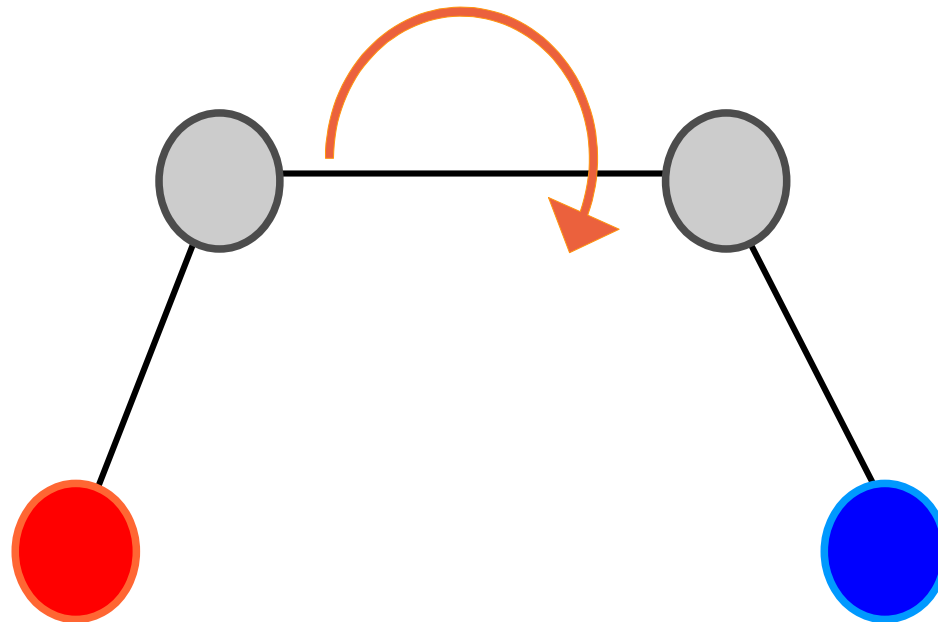
$$\sum_{\text{dihedrals}} \frac{V_n}{2} [1 + \cos(n\phi - \gamma)] + \sum_{i < j} \left[ \frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^6} + \frac{q_i q_j}{\epsilon R_{ij}} \right]$$



termes liés

$$E_{\text{total}} = \sum_{\text{bonds}} K_r (r - r_{\text{eq}})^2 + \sum_{\text{angles}} K_{\theta} (\theta - \theta_{\text{eq}})^2 +$$

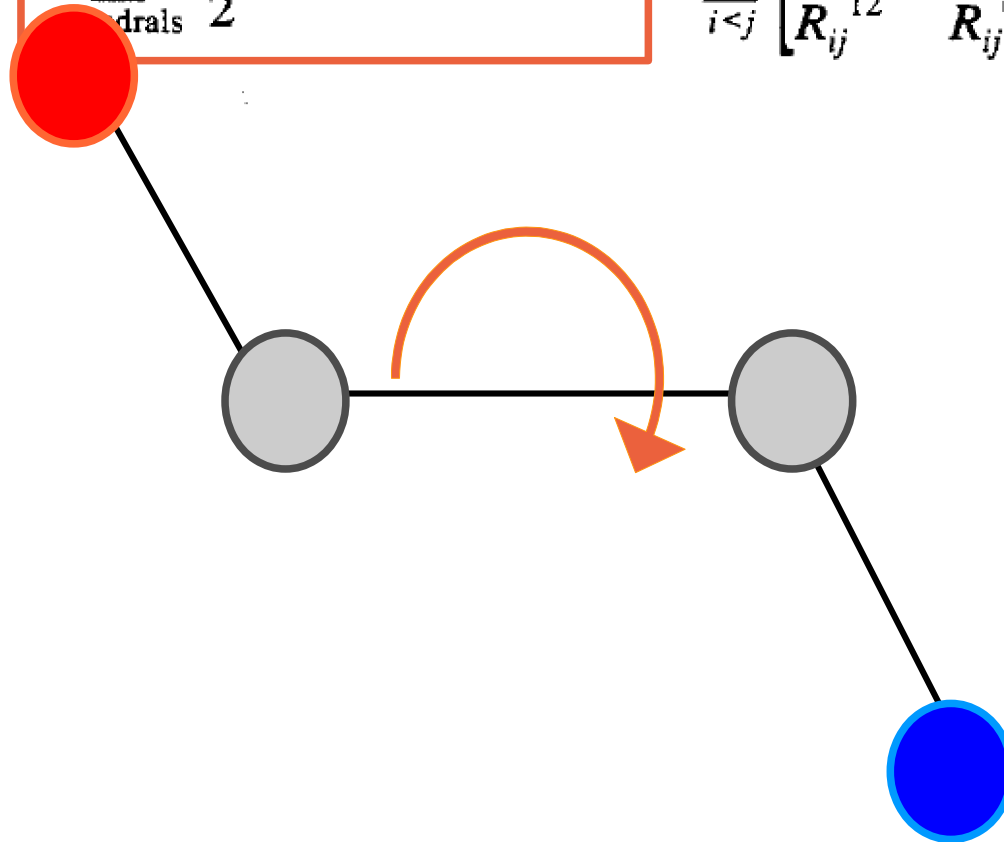
$$\sum_{\text{dihedrals}} \frac{V_n}{2} [1 + \cos(n\phi - \gamma)] + \sum_{i < j} \left[ \frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^6} + \frac{q_i q_j}{\epsilon R_{ij}} \right]$$



termes liés

$$E_{\text{total}} = \sum_{\text{bonds}} K_r (r - r_{\text{eq}})^2 + \sum_{\text{angles}} K_{\theta} (\theta - \theta_{\text{eq}})^2 +$$

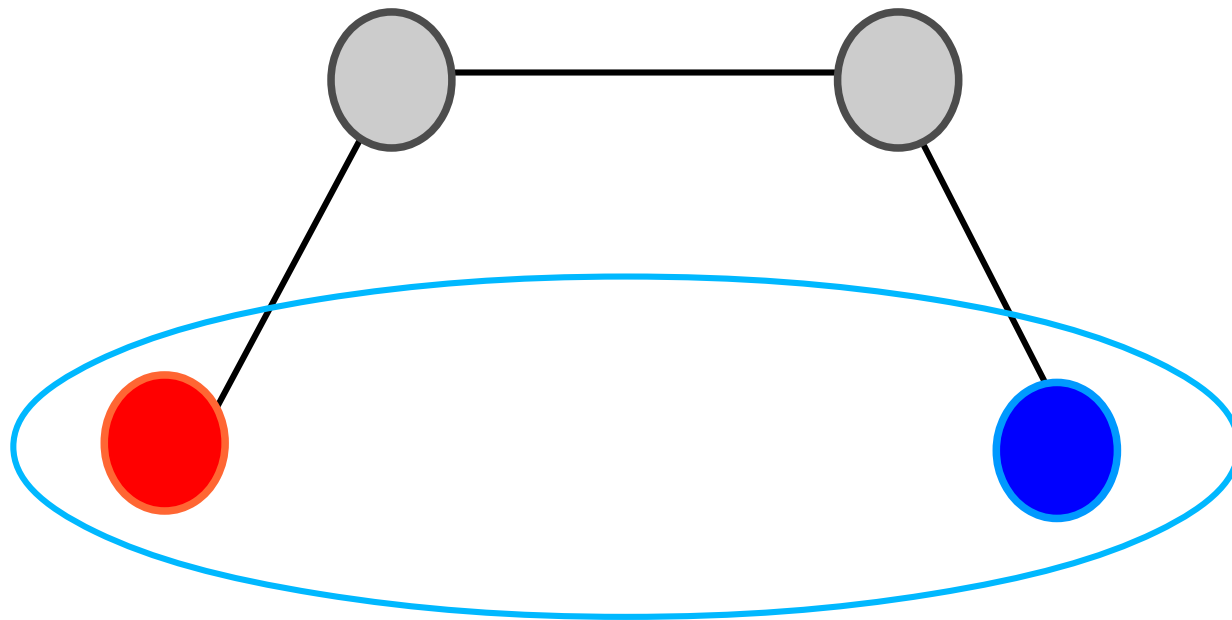
$$\sum_{\text{dihedrals}} \frac{V_n}{2} [1 + \cos(n\phi - \gamma)] + \sum_{i < j} \left[ \frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^6} + \frac{q_i q_j}{\epsilon R_{ij}} \right]$$



termes liés

$$E_{\text{total}} = \sum_{\text{bonds}} K_r (r - r_{\text{eq}})^2 + \sum_{\text{angles}} K_{\theta} (\theta - \theta_{\text{eq}})^2 +$$

$$\sum_{\text{dihedrals}} \frac{V_n}{2} [1 + \cos(n\phi - \gamma)] + \sum_{i < j} \left[ \frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^6} + \frac{q_i q_j}{\epsilon R_{ij}} \right]$$



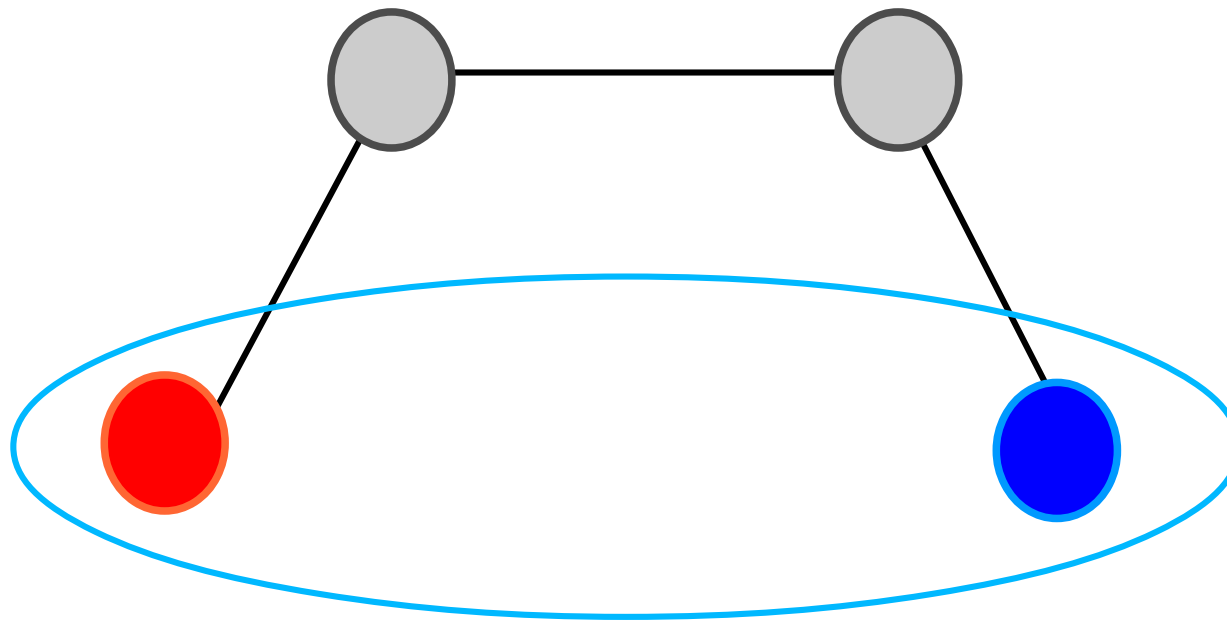
**termes non liés**

$$E_{\text{total}} = \sum_{\text{bonds}} K_r (r - r_{\text{eq}})^2 + \sum_{\text{angles}} K_{\theta} (\theta - \theta_{\text{eq}})^2 +$$

$$\sum_{\text{dihedrals}} \frac{V_n}{2} [1 + \cos(n\phi - \gamma)] + \sum_{i < j} \left[ \frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^6} + \frac{q_i q_j}{\epsilon R_{ij}} \right]$$

LJ ou VdW

électrostatique



termes non liés



$$E_{\text{total}} = \sum_{\text{bonds}} K_r (r - r_{\text{eq}})^2 + \sum_{\text{angles}} K_{\theta} (\theta - \theta_{\text{eq}})^2 + \sum_{\text{dihedrals}} \frac{V_n}{2} [1 + \cos(n\phi - \gamma)] + \sum_{i < j} \left[ \frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^6} + \frac{q_i q_j}{\epsilon R_{ij}} \right]$$

**termes liés**

**termes non liés**

$$E_{\text{tot}} = \text{termes liés} + \text{termes non liés}$$

$$E_{\text{total}} = \sum_{\text{bonds}} K_r (r - r_{\text{eq}})^2 + \sum_{\text{angles}} K_{\theta} (\theta - \theta_{\text{eq}})^2 +$$

$$\sum_{\text{dihedrals}} \frac{V_n}{2} [1 + \cos(n\phi - \gamma)] + \sum_{i < j} \left[ \frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^6} + \frac{q_i q_j}{\epsilon R_{ij}} \right]$$

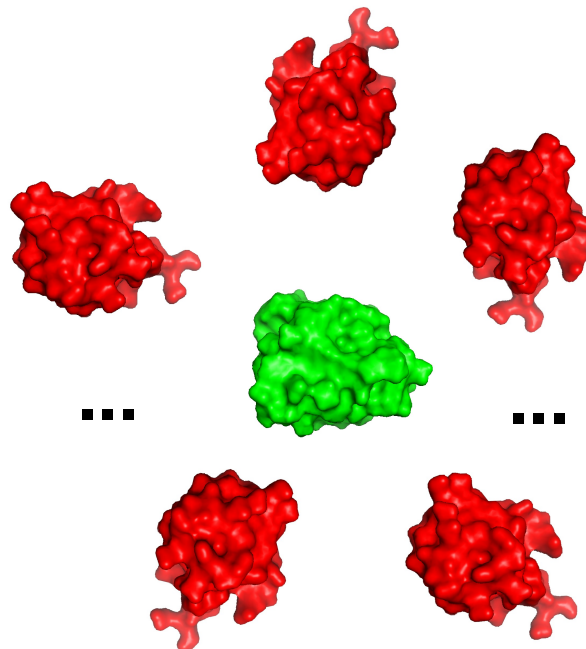
termes liés

termes non liés

docking





vs









$$E_{\text{total}} = \sum_{\text{bonds}} K_r (r - r_{\text{eq}})^2 + \sum_{\text{angles}} K_{\theta} (\theta - \theta_{\text{eq}})^2 +$$

$$\sum_{\text{dihedrals}} \frac{V_n}{2} [1 + \cos(n\phi - \gamma)] + \sum_{i < j} \left[ \frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^6} + \frac{q_i q_j}{\epsilon R_{ij}} \right]$$

termes liés

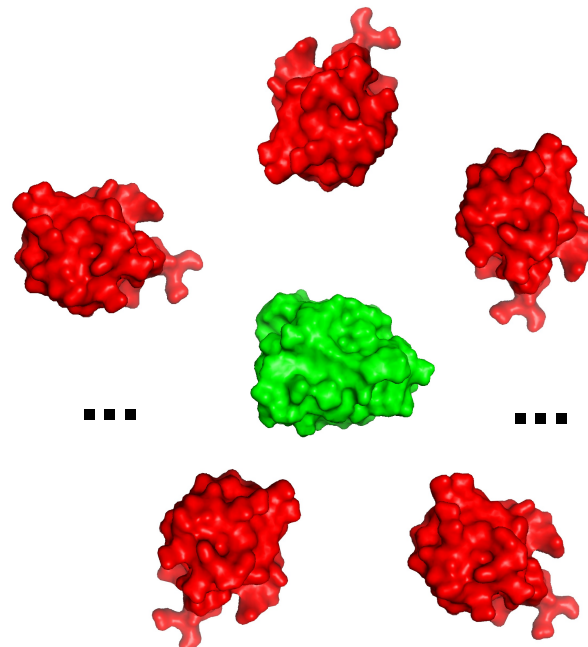
liés  + liés 

termes non liés

non liés  —  + non liés  —   
+ non liés  — 

docking

VS



D'une solution de docking à l'autre :

- les termes liés sont toujours les mêmes
- les termes non liés **intra** protéine sont toujours les mêmes
- seuls les termes non liés **inter** protéines différent d'une conformation à l'autre

