

# DOCKING OF SMALL PEPTIDES ON INORGANIC SUBSTRATES



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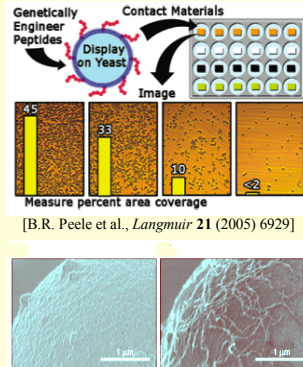
## CAN PEPTIDES RECOGNIZE INORGANIC SURFACES ?

In a number of recent experiments, artificial peptide sequences (expressed, e.g., by phage- or yeast-display) have been deposited on semiconductors (Si, GaAs) and carbon (graphite, nanotubes).

In those experiments it has been demonstrated that specific peptide sequences can exhibit different adhesion strength as a function of the orientation and morphology of the crystal surface.

Such findings open the way to a number of interesting possibilities in the domain of **biomimetic self-assembly of nanostructures**.

Carbon nanotubes binding on the surface of microspheres coated with binding phage clone B1 (non-binding NB2 on the left). [S. Wang et al., *Nature Mat.* 2 (2003) 196]



Running direct Molecular Dynamics simulations on such complex systems, moreover explicitly including the effect of solvent (water molecules) can be **very ineffective**:

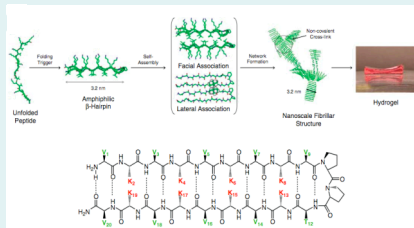
- 1) sensitivity to initial conditions, finite-size sampling, entropic effects etc...
- 2) need to start from a "good" initial configuration to save time (at least...)

## OUR STRATEGY

- Build artificial peptide sequences and perform initial folding "in vacuo" (solvent can be added eventually as a background field) **BALL** software, simple geometric folding based on chemical criteria
- Search docking configurations to the (carbon, Si, metal) surface to maximize the sticking free energy (min energy at const entropy) **AUTODOCK**, configuration search by Lamarckian genetic algorithm
- Perform Molecular Dynamics simulation w empirical force fields and explicit solvent, starting from the best folded+docked configuration(s) **TINKMD** code, AMBER97 parameters + Tersoff potential for C, Si

## SELF-ASSEMBLING $\beta$ -HAIRPIN PEPTIDE SEQUENCE

(R.V.Rughani and J.P.Schneider, *MRS Bulletin* 6 (2008))

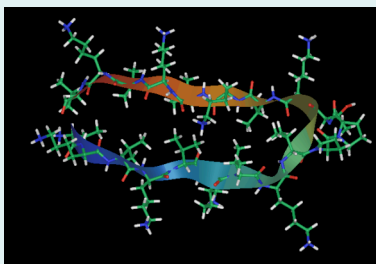


Alternating sequence of Valine (hydrophobic) and Lysine (polar, hydrophilic), with a V<sup>D</sup>PPT "elbow-turning" group to give the "U" (hairpin) shape.

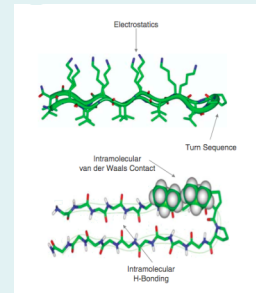
### BALL results:

Initial sequence correctly folds to a "U" shaped hairpin, starting from a linear peptide.

Lysine residues are now arranged on opposite sides of the  $\beta$ -sheet (note the changing color of the ribbon from blue to red).



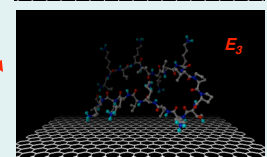
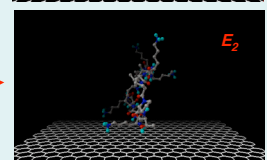
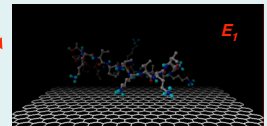
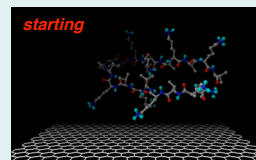
During folding of the artificial peptide sequence into the secondary ( $\beta$ -sheet) structure, **electrostatic** and **van der Waals forces** are the main contributions. Some hydrogen bonds are formed across the two sides of the symmetric chains, and electrostatic repulsion keeps residues away from each other.



The hairpin is **amphiphilic**. Lysine residues point on one side of the  $\beta$ -sheet, while Valine point to the opposite face of the sheet.

### AUTODOCK results:

18 configurations, regrouped into 3 general categories:



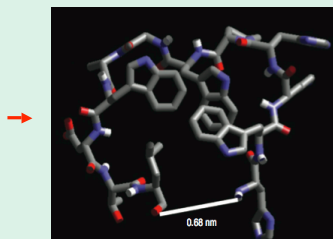
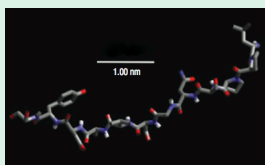
$E_3 = 0$   
 $E_2 = -1.2$  kcal/mole  
 $E_1 = -3.9$  kcal/mole  
 The largest variation is found in the van der Waals energy.

## SELECTION OF SEQUENCES WITH HIGH AFFINITY FOR CARBON

S. Wang et al. (*Nature Mat.* 2 (2003)) identified by phage display, an engineered peptide sequence which binds selectively to carbon SWNT.

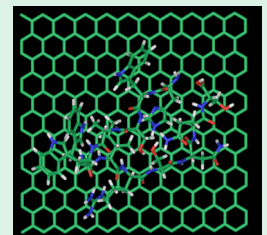
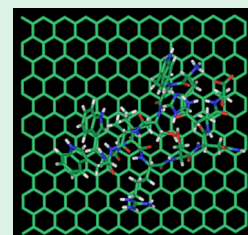
- WPHHPHAAHTIR peptide is experimentally identified as the best candidate

- 1) Test the initial configuration with **BALL** and study folding - solvent is described by a background dielectric constant



- 2) **AUTODOCK** contact to graphite surface +

- 3) **MD without solvent**



Identification of binding specific groups in the peptide:

- Proline are the residues showing the largest contact surface.
- Contact energy depends also on the adjacent residues: WPH is less effective in binding than HPH