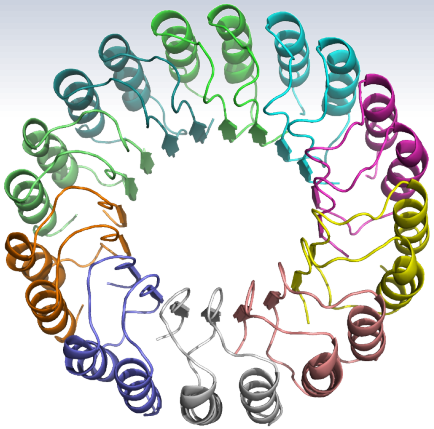
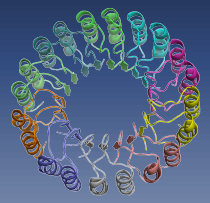


Computational Protein Design

André Lab, Biochemistry & Structural Biology

Sebastian Rämisch

COMPUTE-Retreat, 2012-08-21



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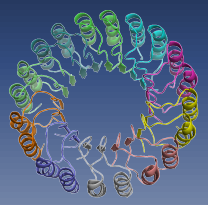


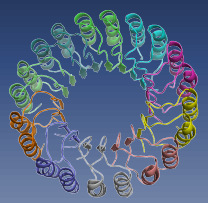
What do proteins do?

Macromolecules

- DNA → information
- Lipids → borders
- Sugars ...many functions
- Proteins → **DO** stuff

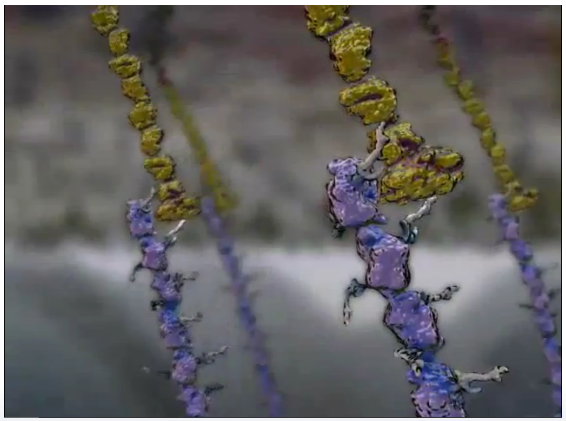
Protein Functions

- Adhesion
- Structure (Stiffness)
- Enzymes
- Receptors
- Signaling

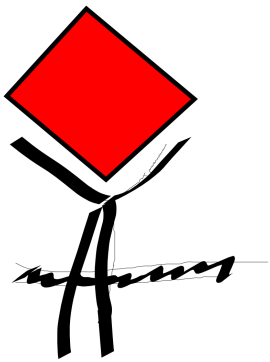


Protein Interactions - Why?

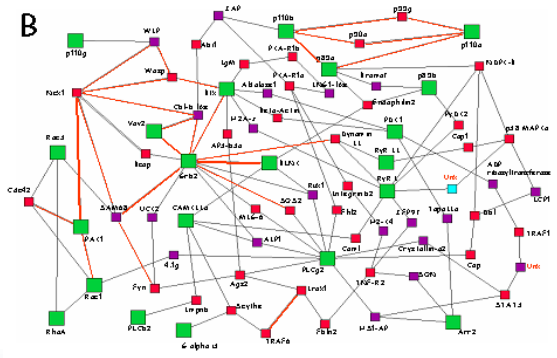
Adhesion

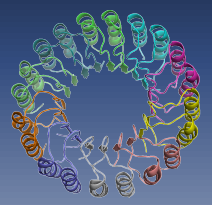


Receptors



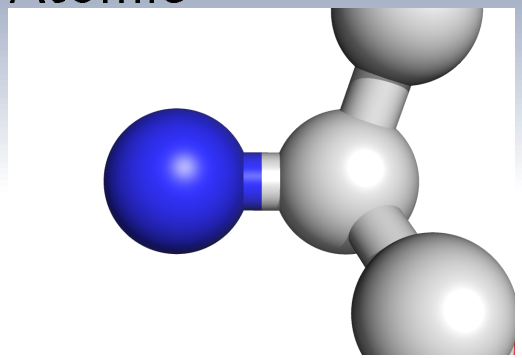
Signaling



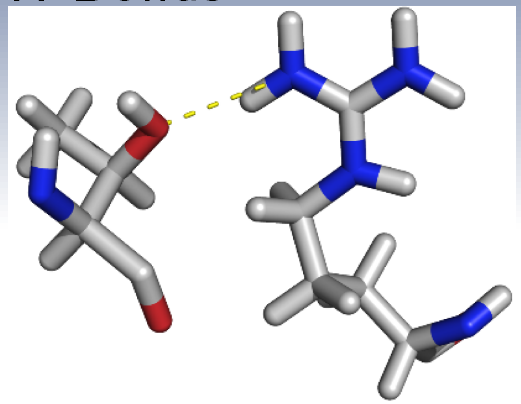


The essential forces

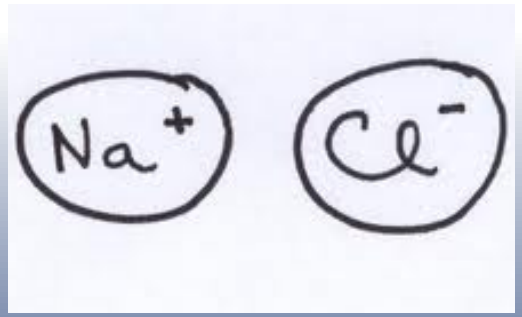
Atomic



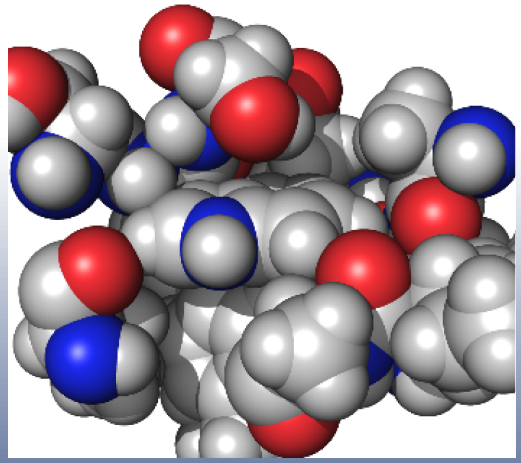
H-Bonds

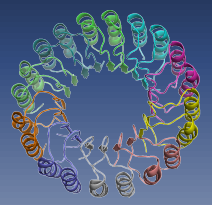


Ionic



Van der Waals





Simualations

How to calculate these interactions?

Ideal:

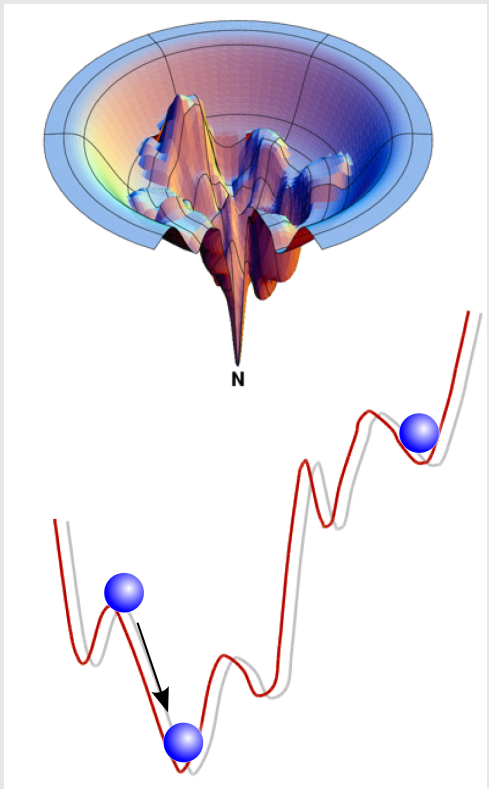
- Calculate all forces between all atoms

Less ideal, but possible:

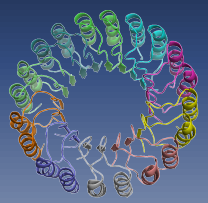
- Calculate pairwise interaction
- Include statistics

Many Monte Carlo Simulations

Find the “energy“ minimum



→ Force Fields



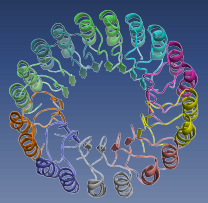
Rosetta "Force Field"

kind of physical terms

- van der Waals (6/12 leonnard-jones)
- H-Bond potential

some statistical terms

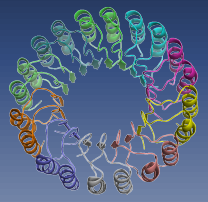
- Electrostatics
- Ramachandran term
- Packing density
- Secondary structure for amino acid
- ...



Protein Design

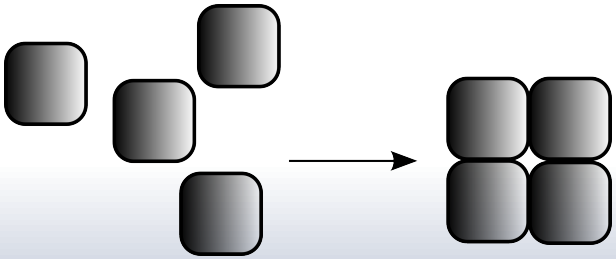
Now ... what again is protein design?

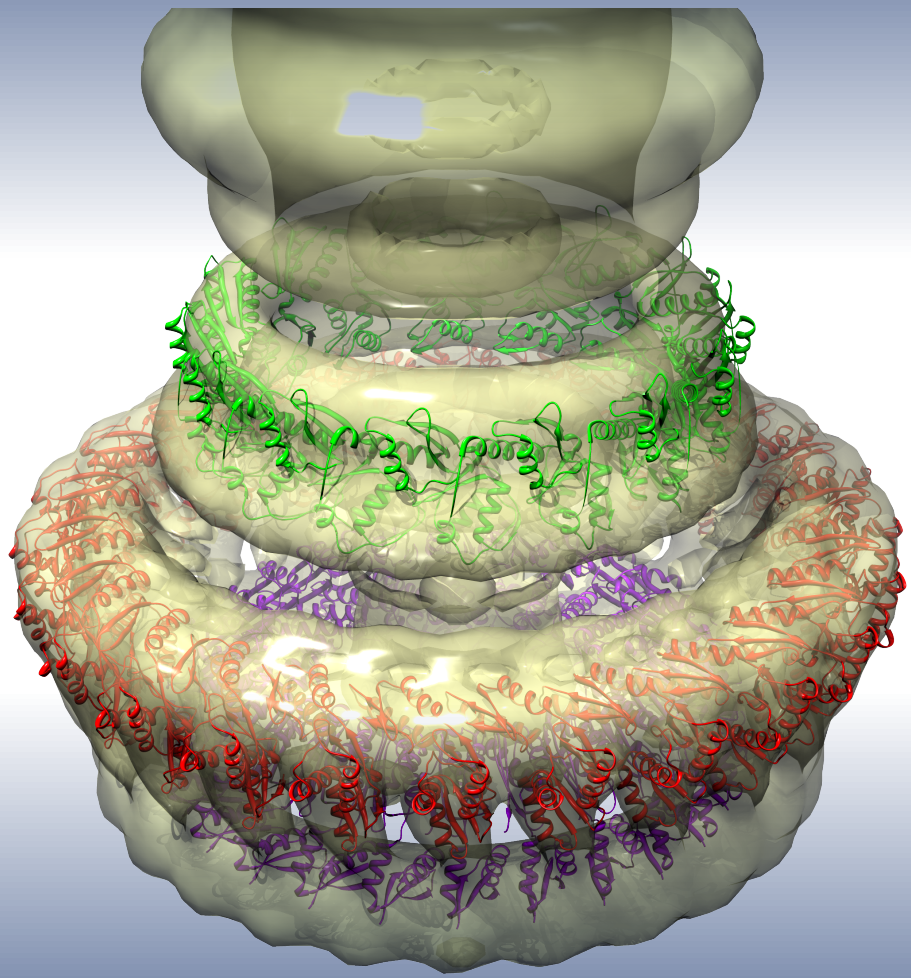
or: where is the white board here?

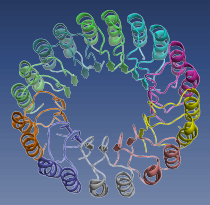


Self Assembly

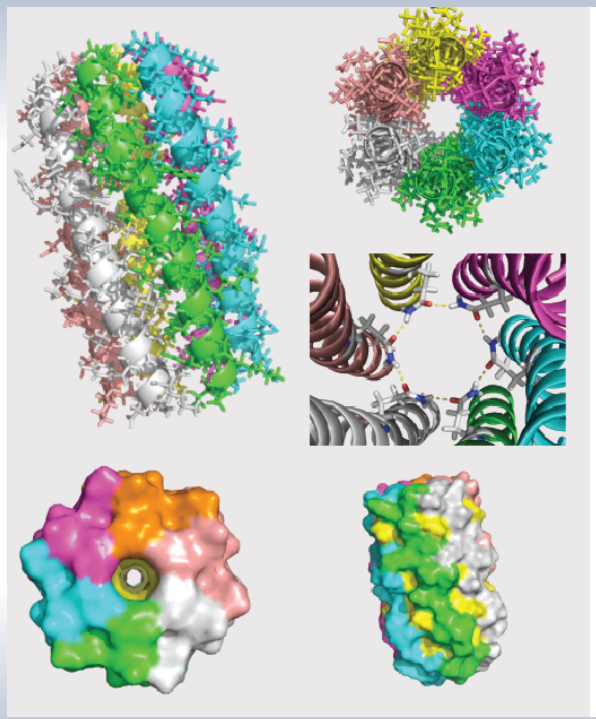
... more applied
... less method
developement (Ingemar)

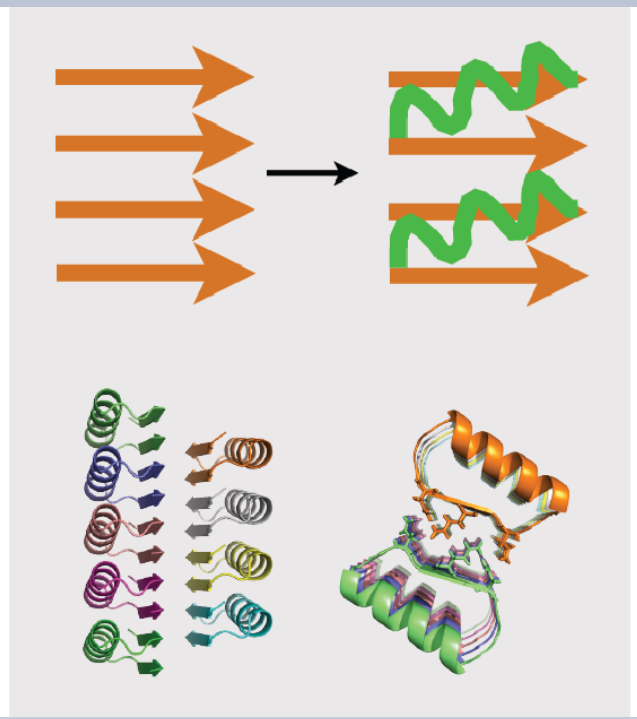


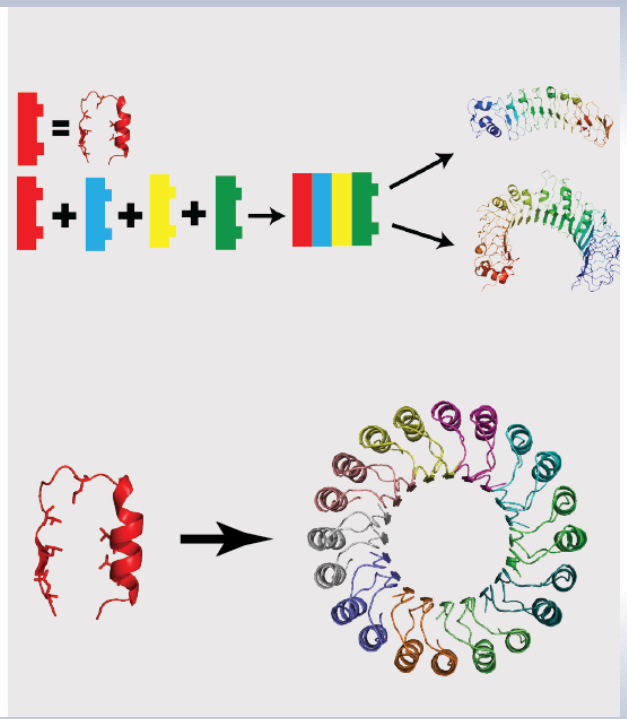


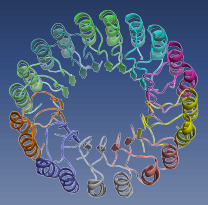


Protein Design Projects









What we hope to learn

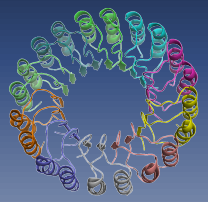
First of all:

We learn about the current caveats of current protein design methods.

Problems are:

- these guys don't fold
- they don't perform their function

There is not very much experience with protein design



What will people use it for?

Peptide Drugs

Biotechnology

Research Tools

Energy Production