Protein-Biomaterial Interaction

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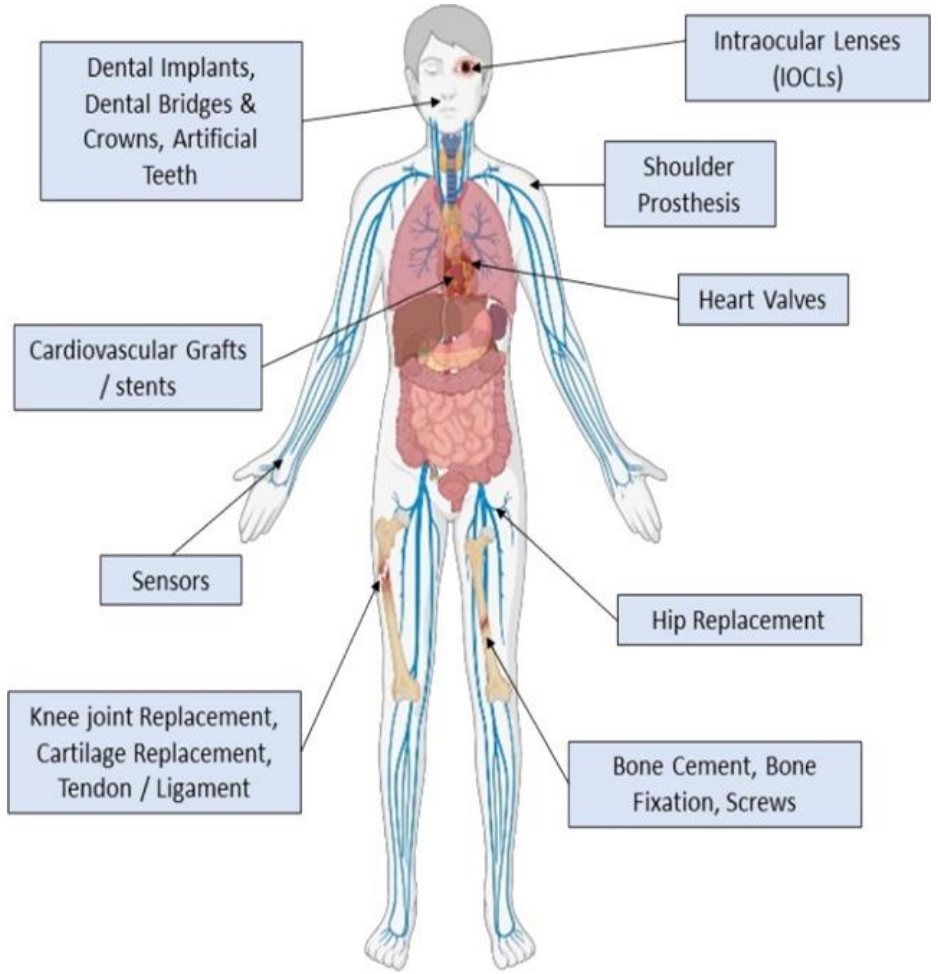
Biomaterials

Non viable materials used in a medical device intended to interact with biological system [1]

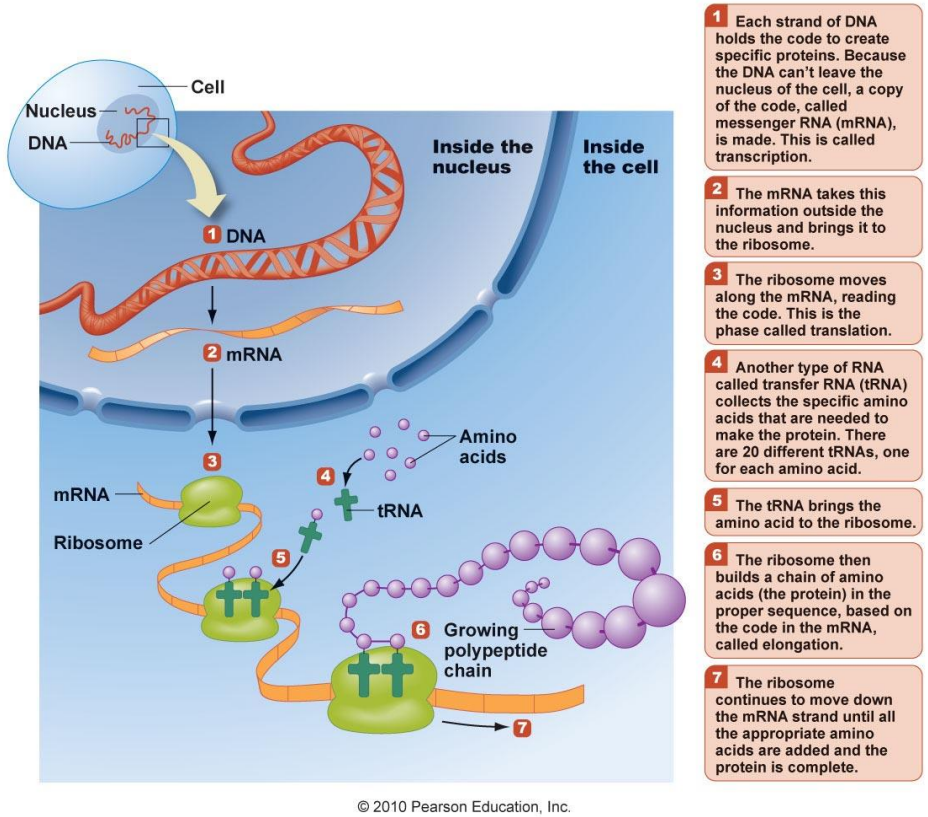
Characteristic property

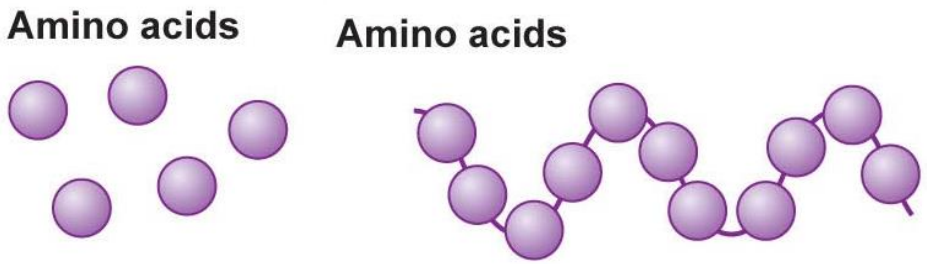
- **Biocompatibility**: Perform with an appropriate host response in a specific application
- **Host response**: The reaction of material inside the body with local milieu.

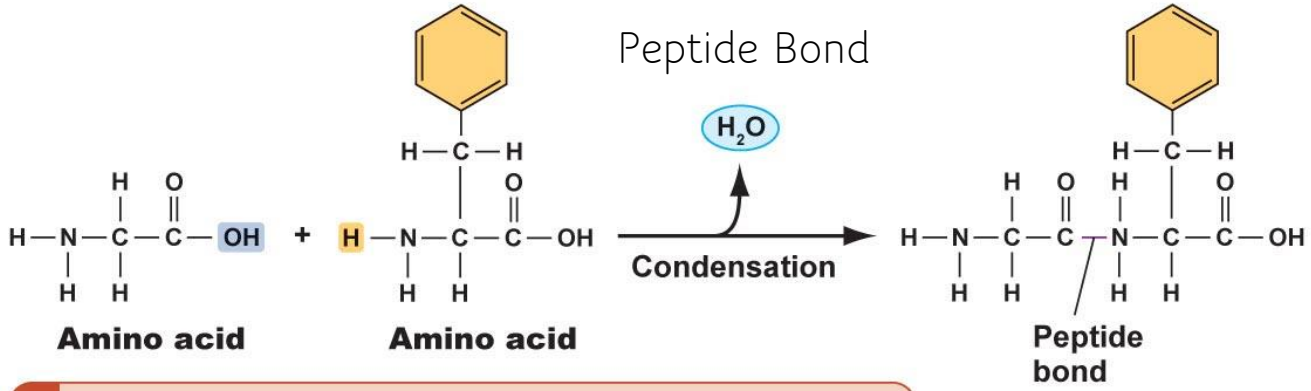


Proteins

Proteins are comprised of discrete building blocks (amino acids) assembled into hierarchical structures.



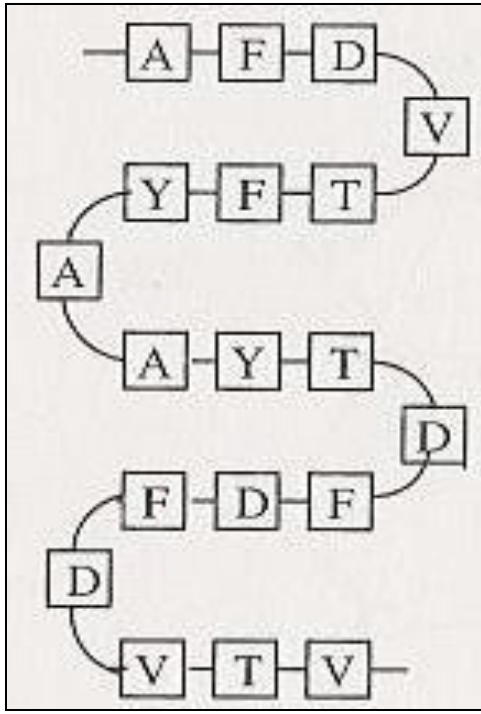
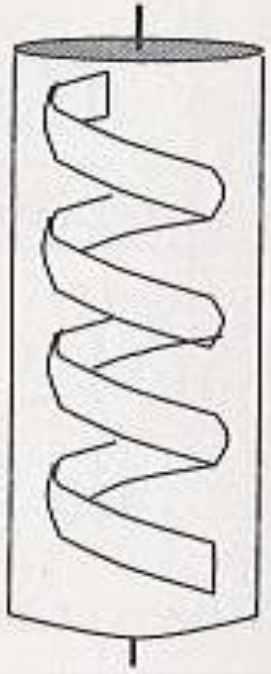
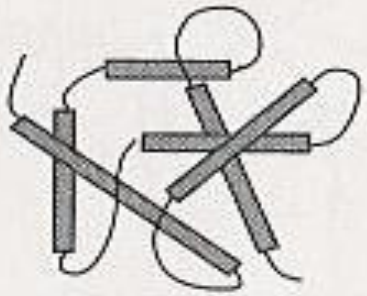
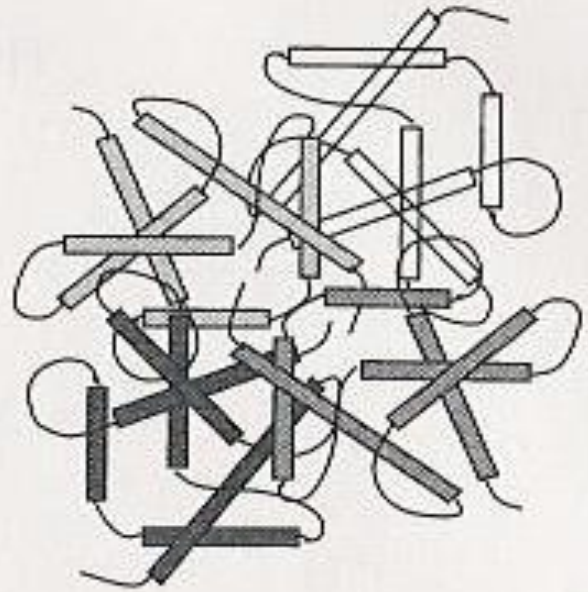




Amino acid side chain heterogeneity manifests:

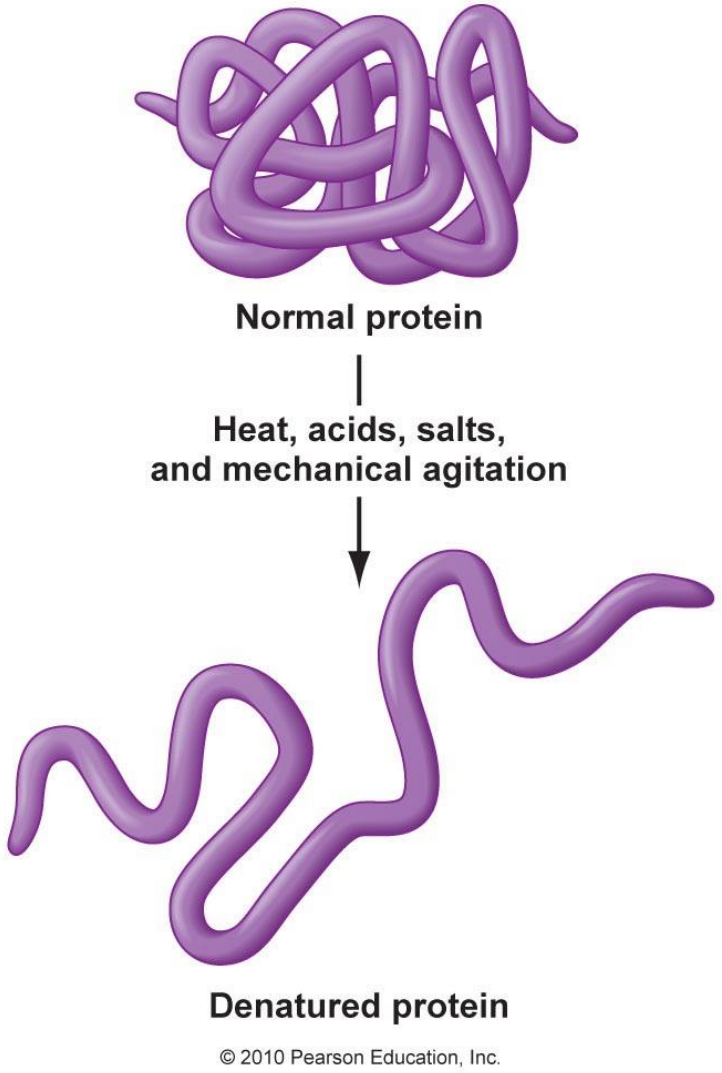
- charged (acidic / basic)
- non-charged polar } "hydrophilic"
- non-charged, non-polar } "hydrophobic"

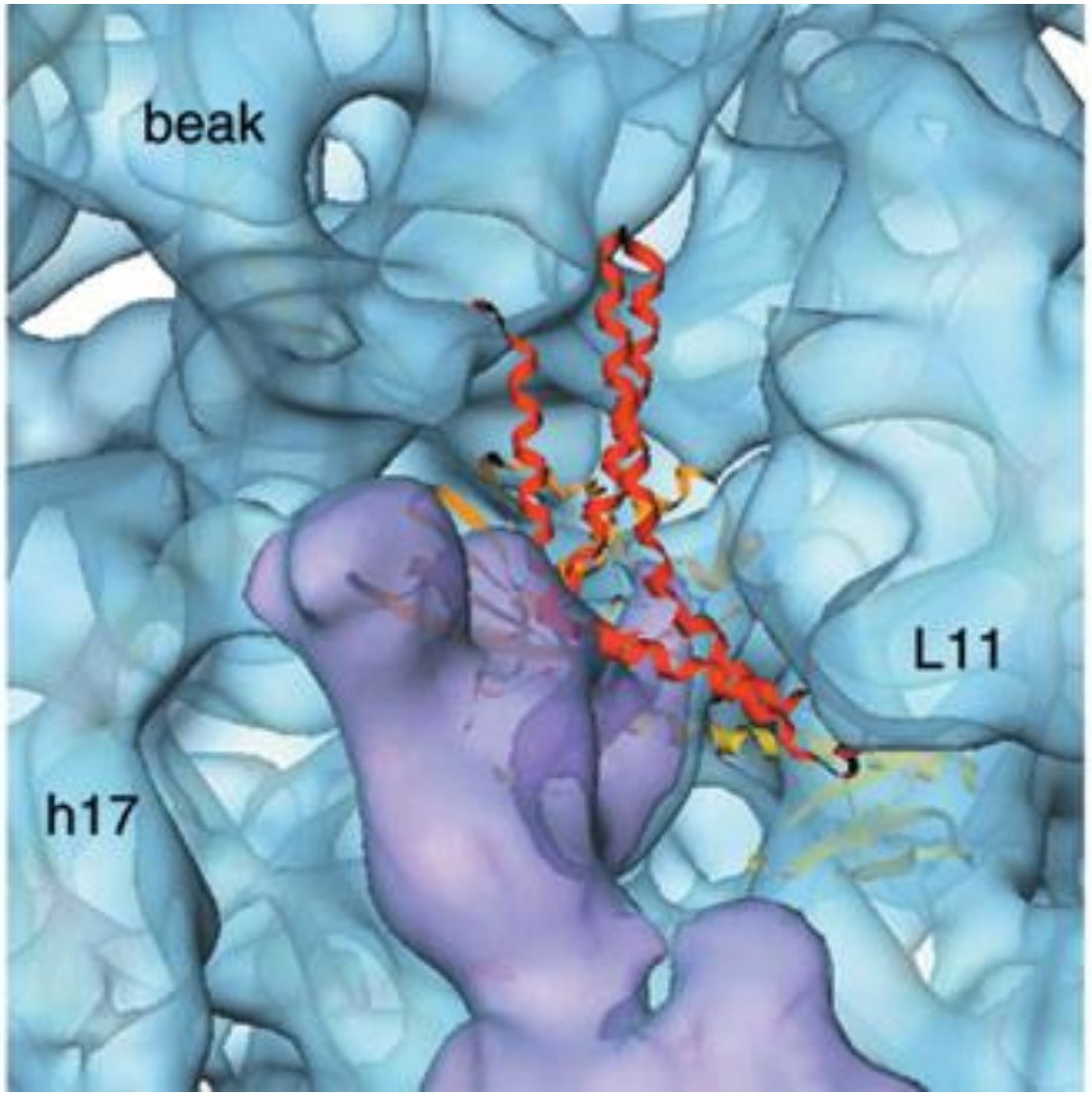
Protein Structures

Primary	Secondary	Tertiary	Quaternary
			
Amino acid sequence.	Alpha helices & Beta sheets, Loops.	Arrangement of secondary elements in 3D space.	Packing of several polypeptide chains.

Given an amino acid sequence, we are interested in its secondary structures, and how they are arranged in higher structures.

Sequence→Structure→Function

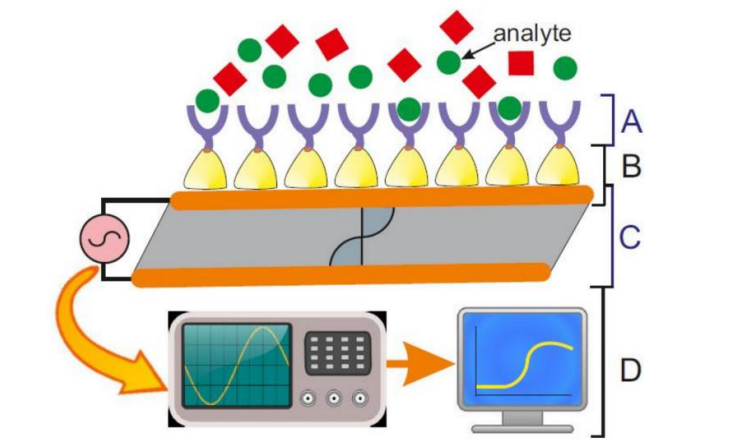




Stereo pair: Release factor 2/3 Klaholz et al, Nature (2004) 427:862

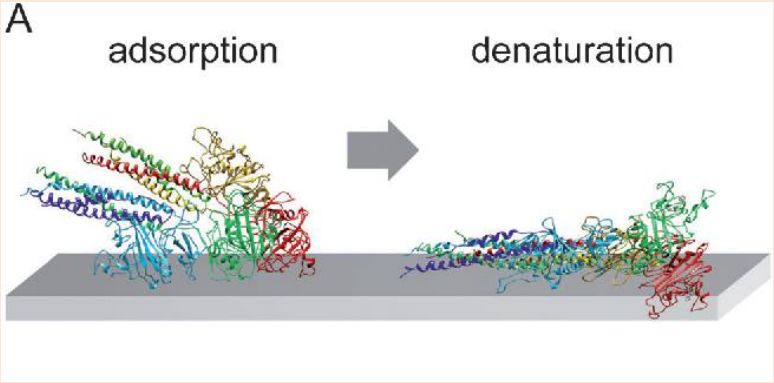
Various Application

Biosensors



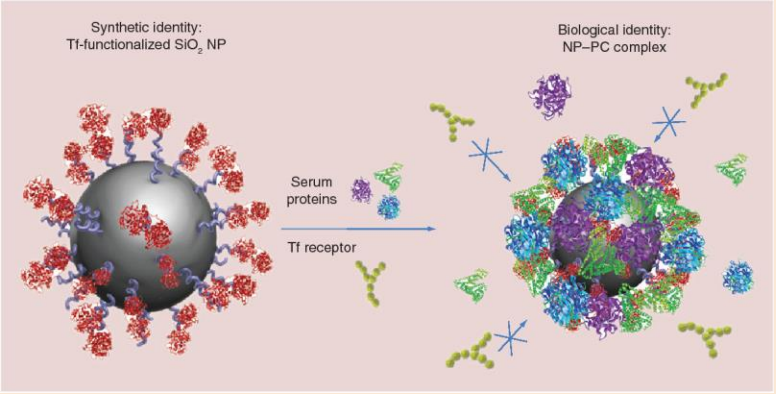
- Amount of protein adsorbed
- Specificity

Biocompatible material



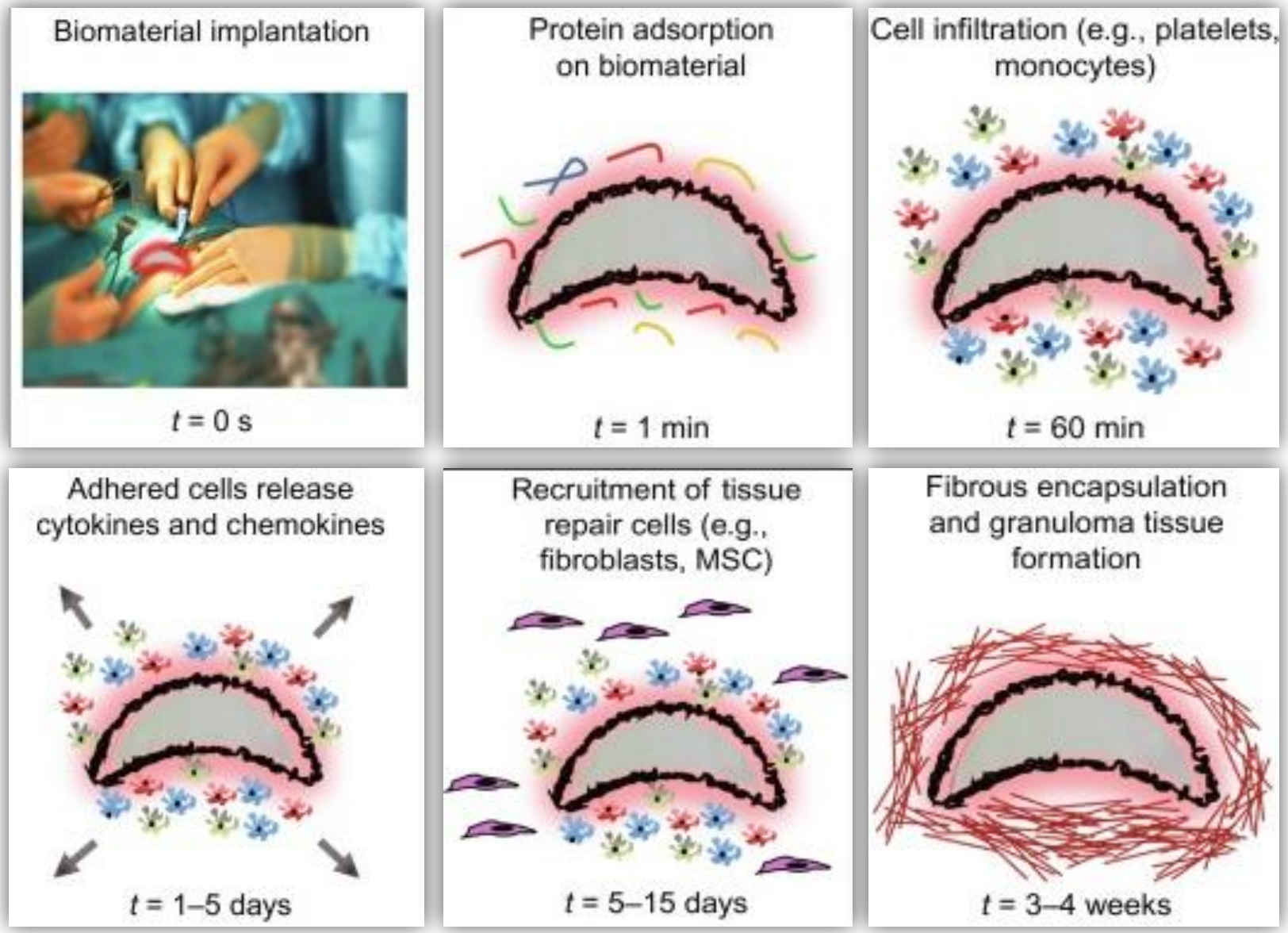
- Inflammation
- Rejection by the body

Drug Delivery



- Drug release rate

Biomaterial In-Vivo Interaction [4]



Graft Failure

- Mechanical failure
- Structural Failure
- Fibrosis
- Bacterial Infection

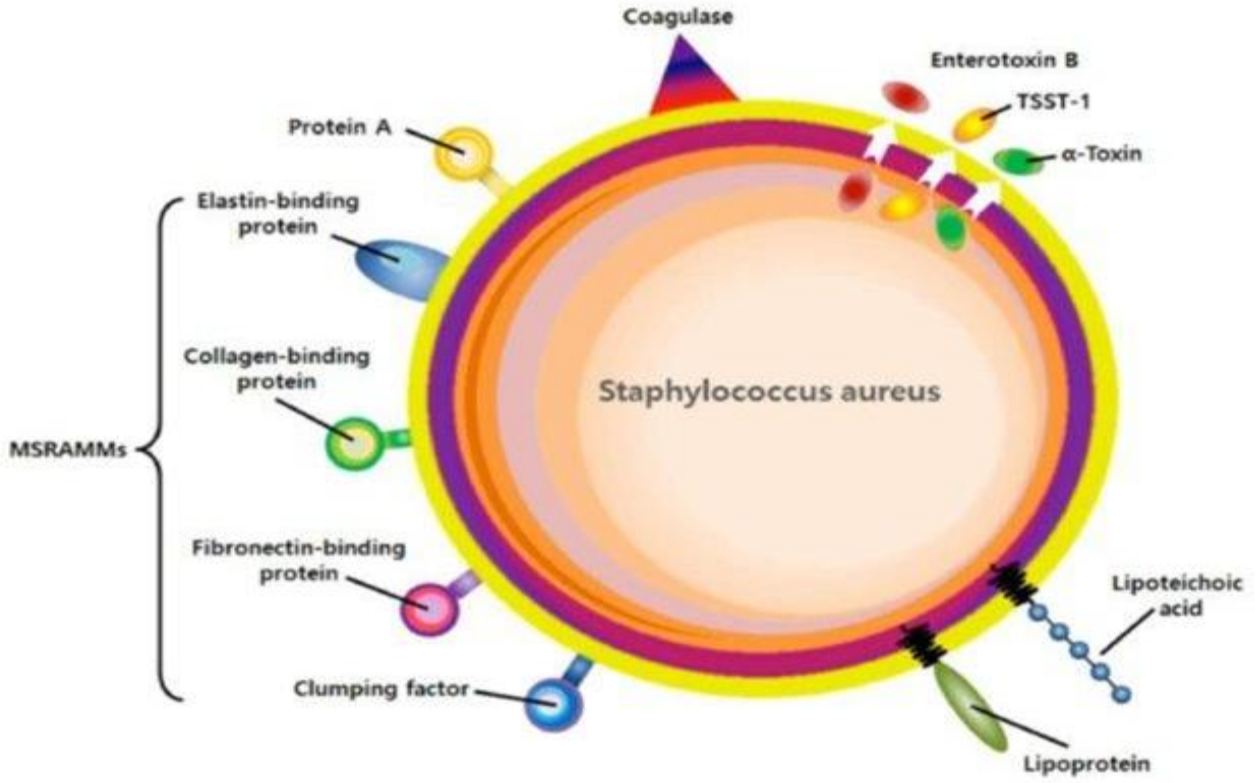
Structure of S. Aureus [5]

Adhesins:

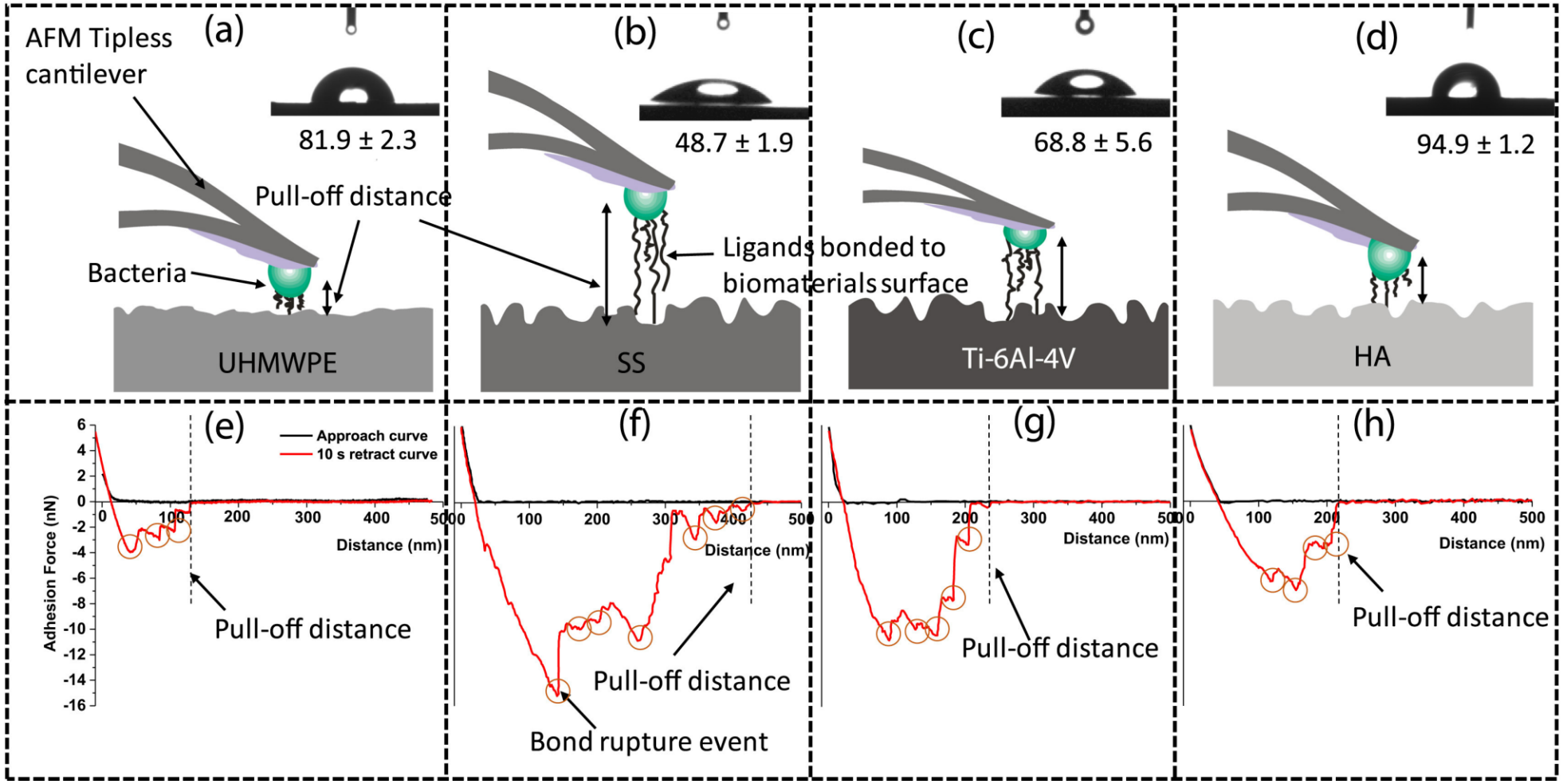
Group of proteins in bacteria involved in attachment or colonization of these bacteria to abiotic (plastic or steel etc) and biological surfaces (found in Bovine or Human Intestine).

Proteins on surface of S. Aureus:

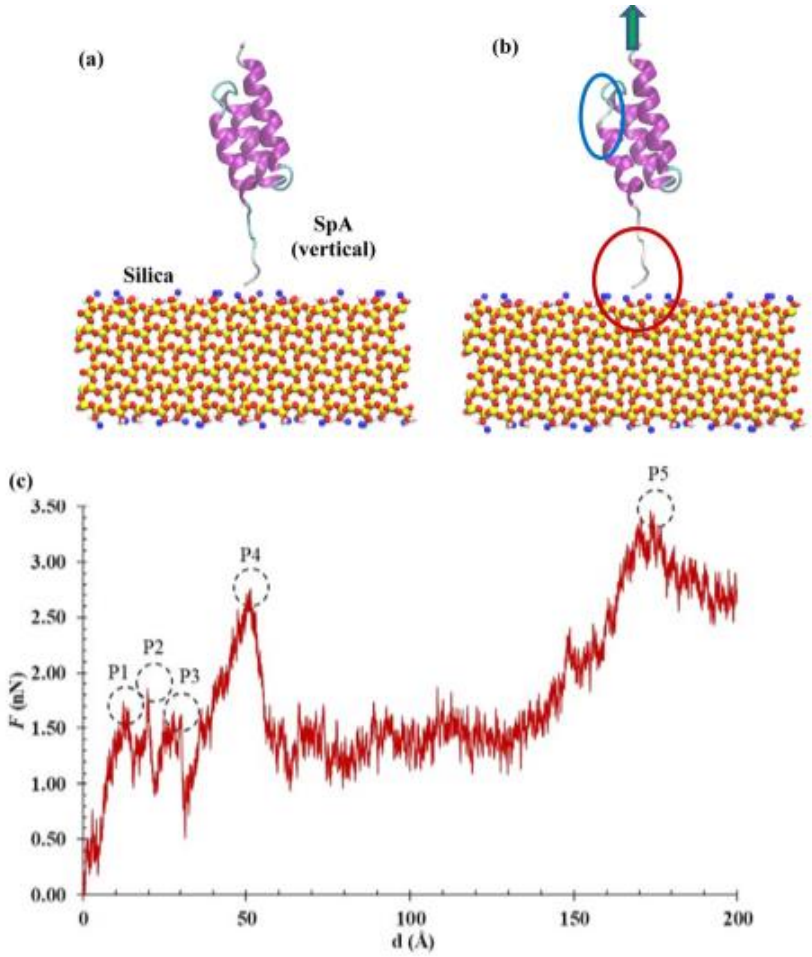
- Collagen-binding protein (eg. CnA)
- Clumping factor (eg. ClfA and ClfB)
- Fibronectin-binding protein
- Elastin binding protein etc

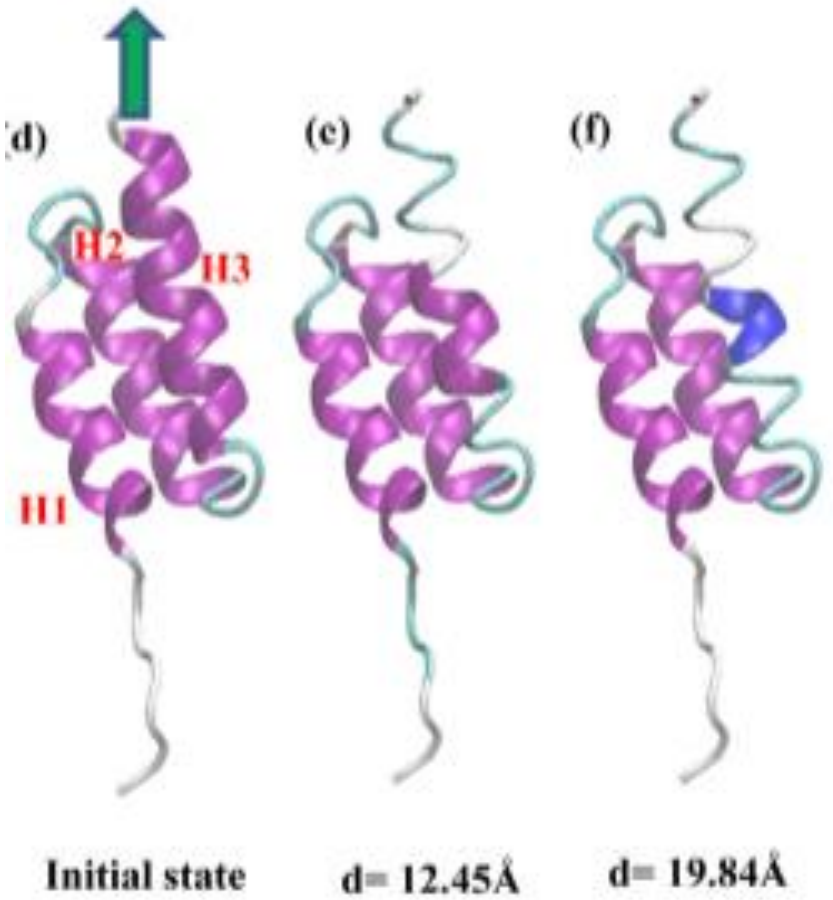


Quantify Adhesin Interaction



AFM Experiment [6]

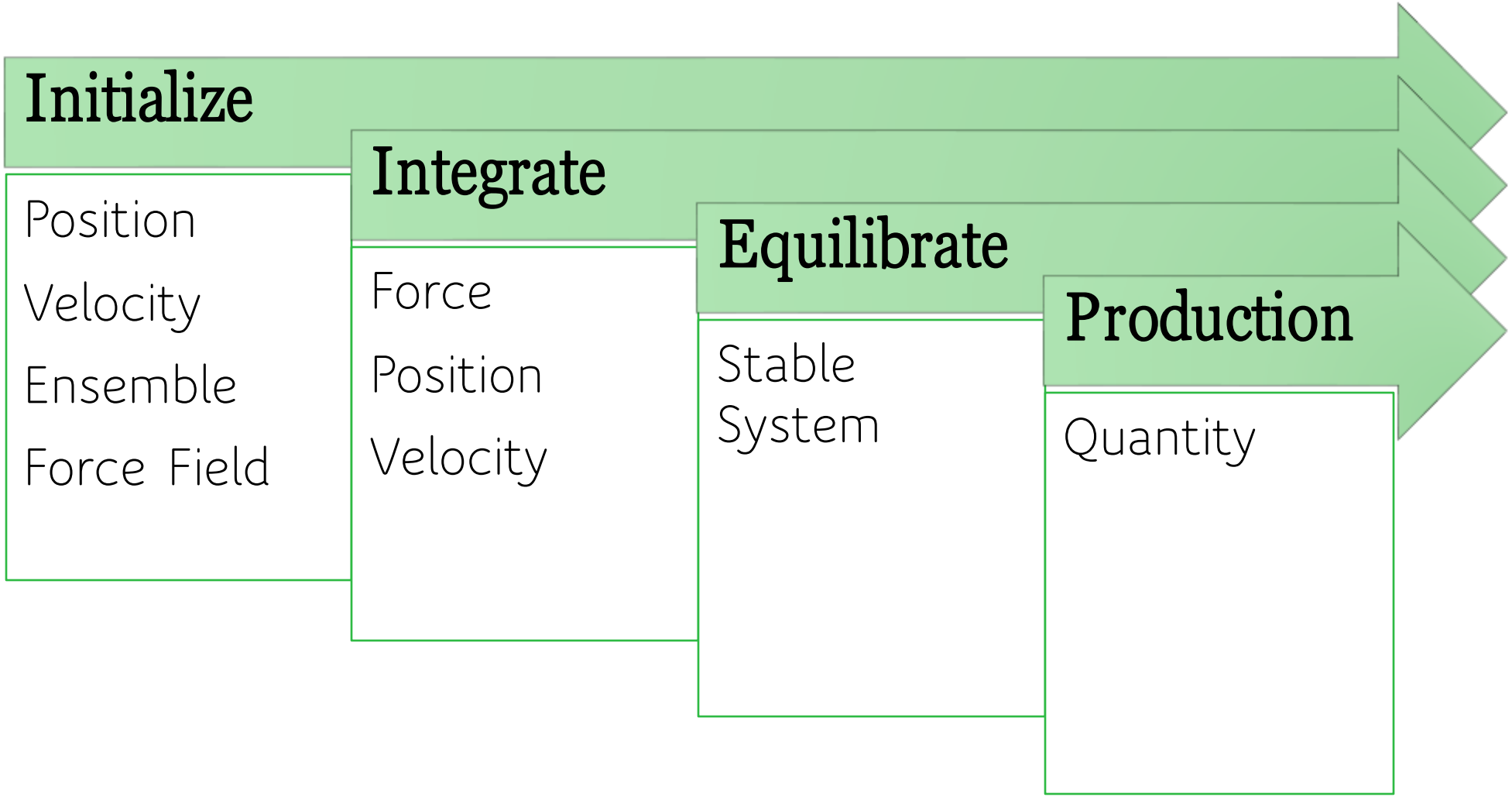




MD Simulation [7]

Computational Experiment

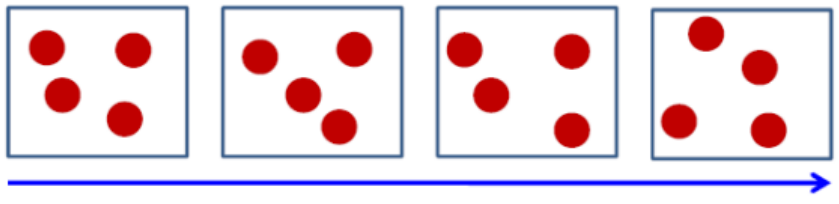
Performing MD simulation is akin to the following computational experiment

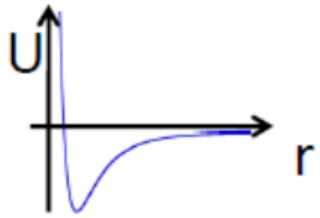


Molecular Dynamics (MD) Simulation

- Simulates the "real" dynamics of a collection of particles (atoms, molecules, No electrons!)
- Solves Newton's equation of motion for every particle in the system:

$$m_i \frac{d^2\mathbf{r}_i}{dt^2} = \mathbf{F}_i(\mathbf{r}_1, \ldots, \mathbf{r}_N)$$



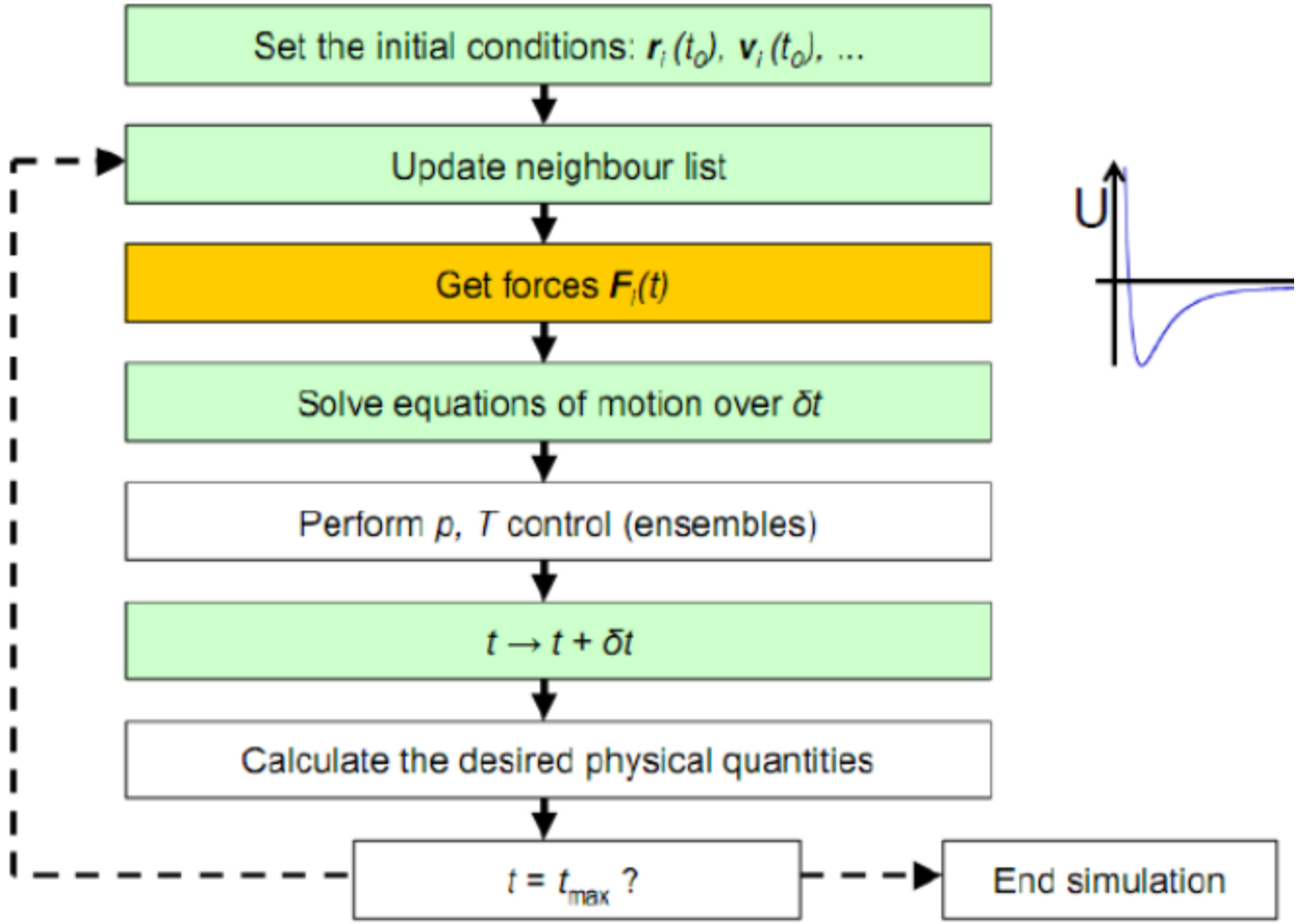


How are forces obtained?

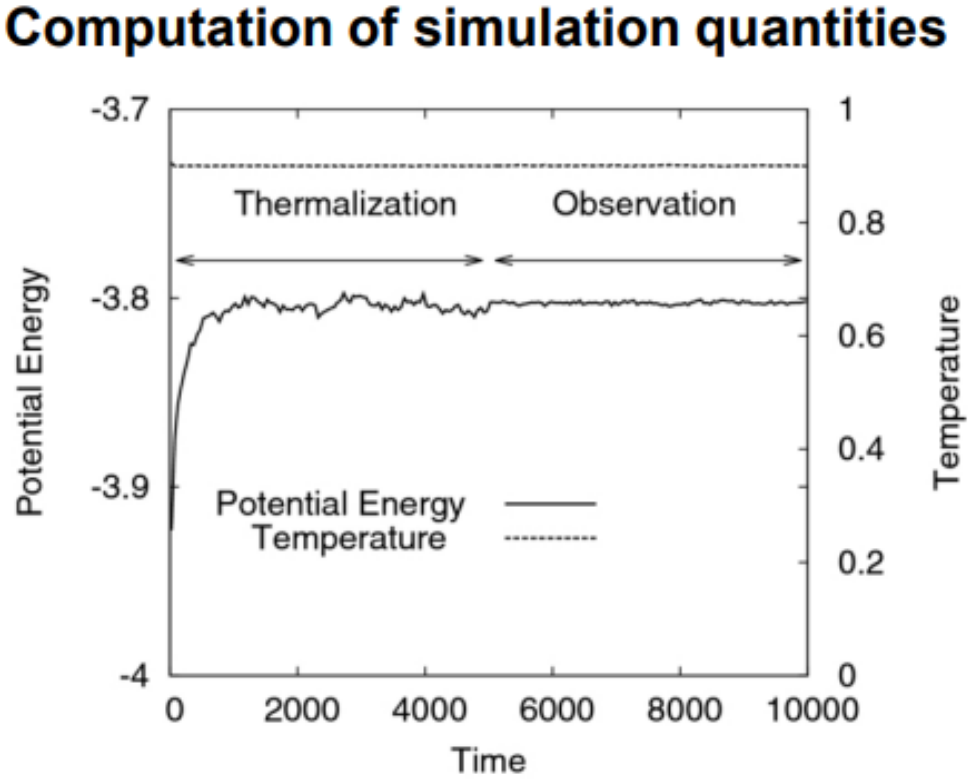
- MD is a deterministic method: The state of the system at any future time can be predicted from its current state
- Result: a trajectory that shows how positions and velocities of atoms change with time, from which, structural, dynamical, thermodynamic and statistical properties may be calculated.

Molecular Dynamics (MD) Simulation

Solve Newton's Equation of motion iteratively



Properties obtained by statistical averaging



http://physics.weber.edu/schroeder/md/

HANDS-ON TUTORIAL

Input files

PDB

A Protein Data Bank (pdb) file stores atomic coordinates and/or velocities for the system, not connectivity information (from RCSPDB)

PSF

A Protein Structure File (psf) which stores structural information of the protein, such as various types of bonding interactions.

CONFIGURATION FILE

It tells NAMD how the simulation is to be run, all the options that NAMD should adopt in running a simulation

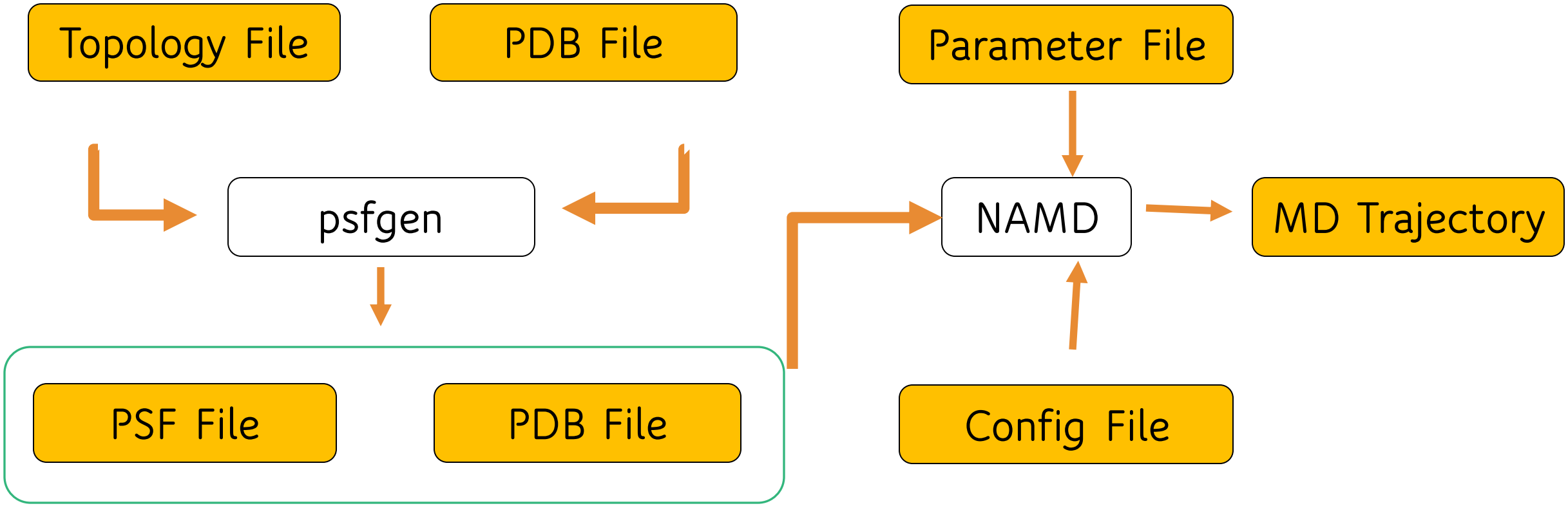
TOPOLOGY FILE

It stores the information on atom types, charges, and how the atoms are connected in a molecule.

FORCE FIELD PARAMETER FILE

The parameter file defines bond strengths, equilibrium lengths, etc.

Flowchart for running MD




THANK YOU