

Protein-Biomaterial Interaction



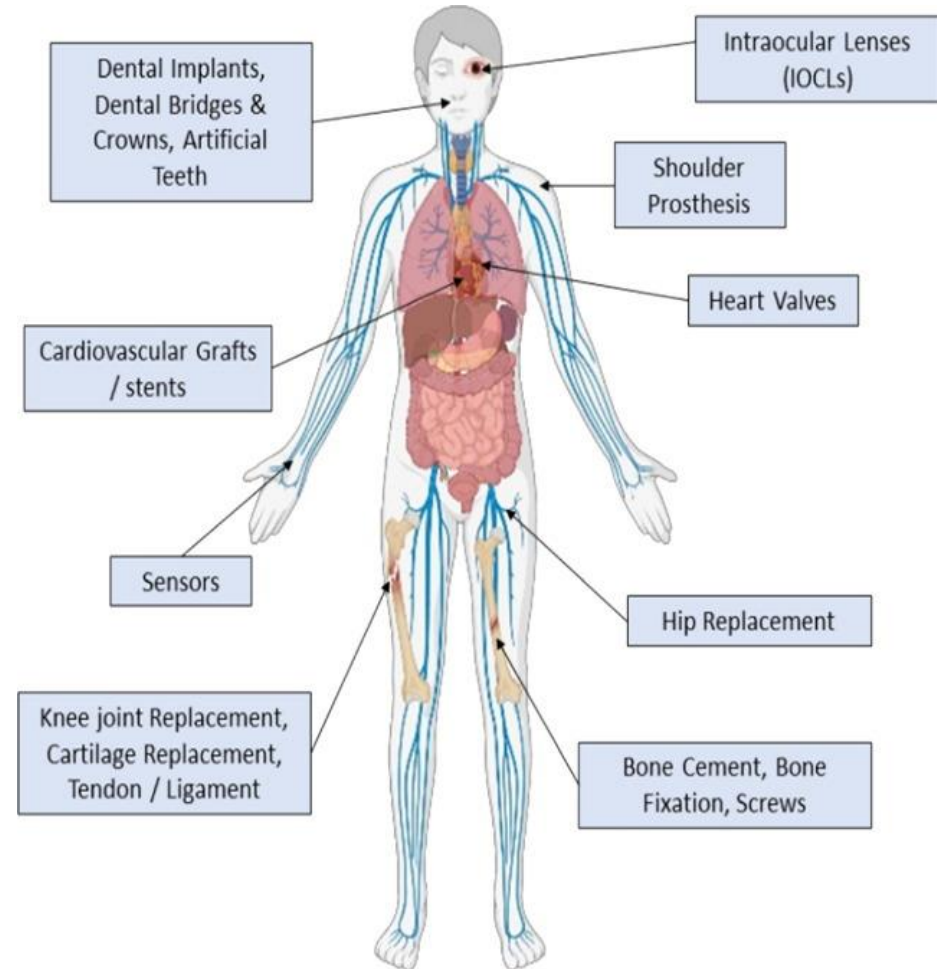
Neeraj Dhandia
MSE, IIT KANPUR

Biomaterials

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

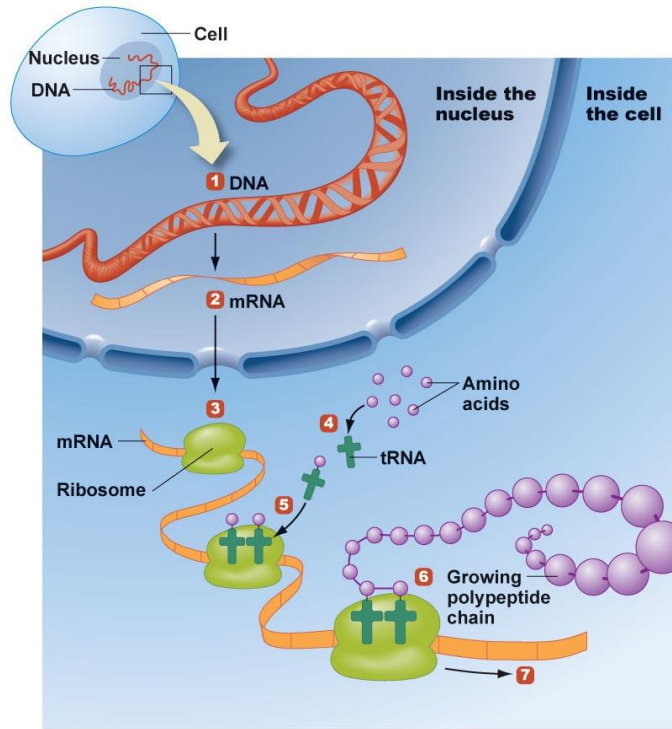
Characteristic property

- **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.



1 Each strand of DNA holds the code to create specific proteins. Because the DNA can't leave the nucleus of the cell, a copy of the code, called messenger RNA (mRNA), is made. This is called transcription.

2 The mRNA takes this information outside the nucleus and brings it to the ribosome.

3 The ribosome moves along the mRNA, reading the code. This is the phase called translation.

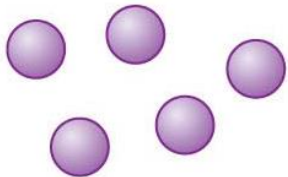
4 Another type of RNA called transfer RNA (tRNA) collects the specific amino acids that are needed to make the protein. There are 20 different tRNAs, one for each amino acid.

5 The tRNA brings the amino acid to the ribosome.

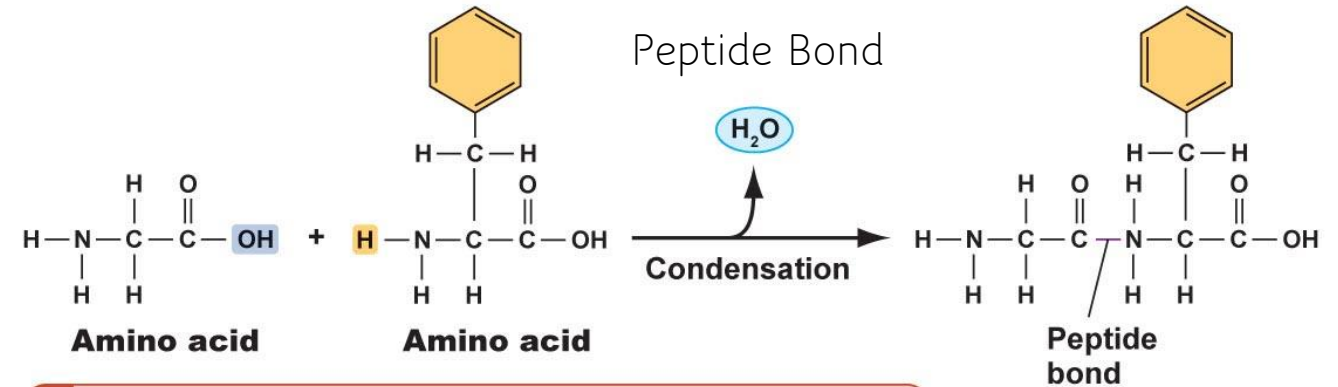
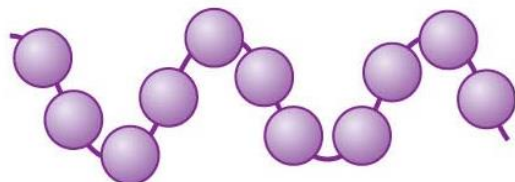
6 The ribosome then builds a chain of amino acids (the protein) in the proper sequence, based on the code in the mRNA, called elongation.

7 The ribosome continues to move down the mRNA strand until all the appropriate amino acids are added and the protein is complete.

Amino acids



Amino acids



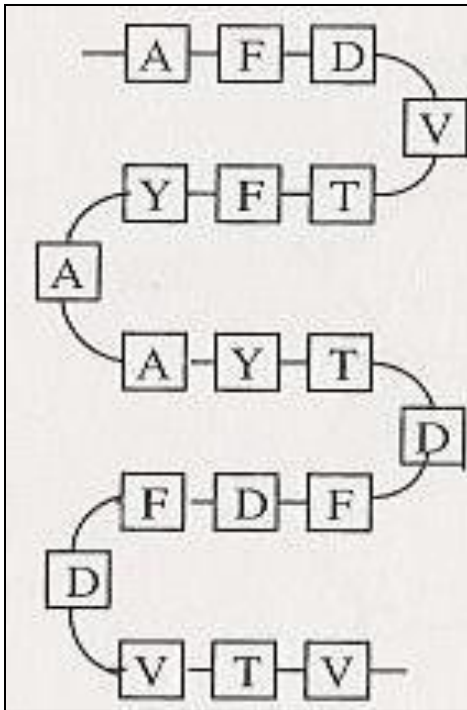
a A peptide bond forms by condensation when the acid group (COOH) and amine group of two different amino acids join and release a molecule of water.

Amino acid side chain heterogeneity manifests:

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

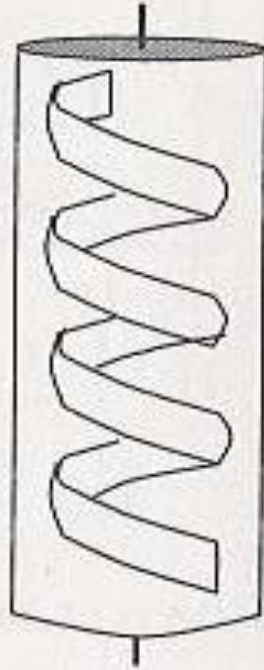
Protein Structures

Primary



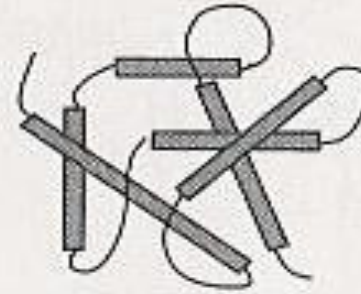
Amino acid sequence.

Secondary



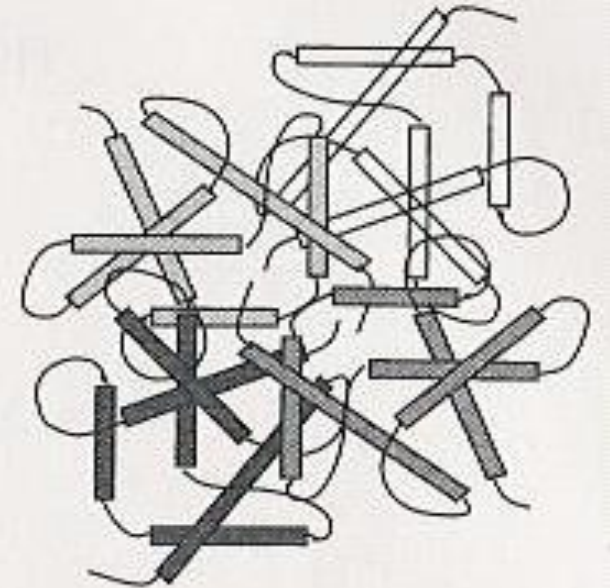
Alpha helices & Beta sheets, Loops.

Tertiary



Arrangement of secondary elements in 3D space.

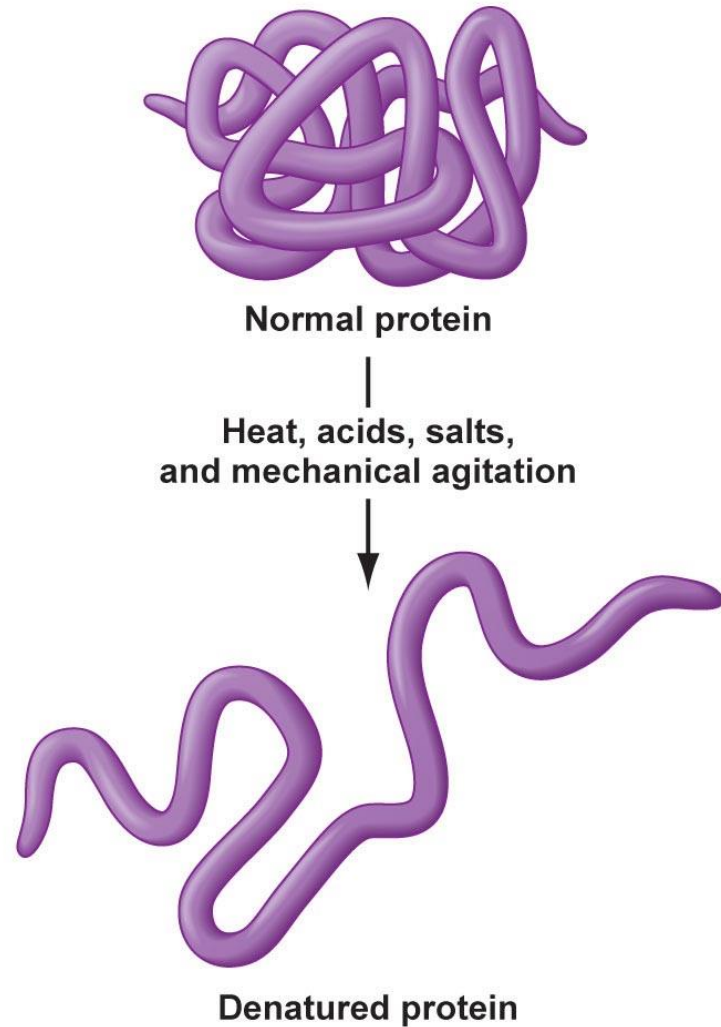
Quaternary



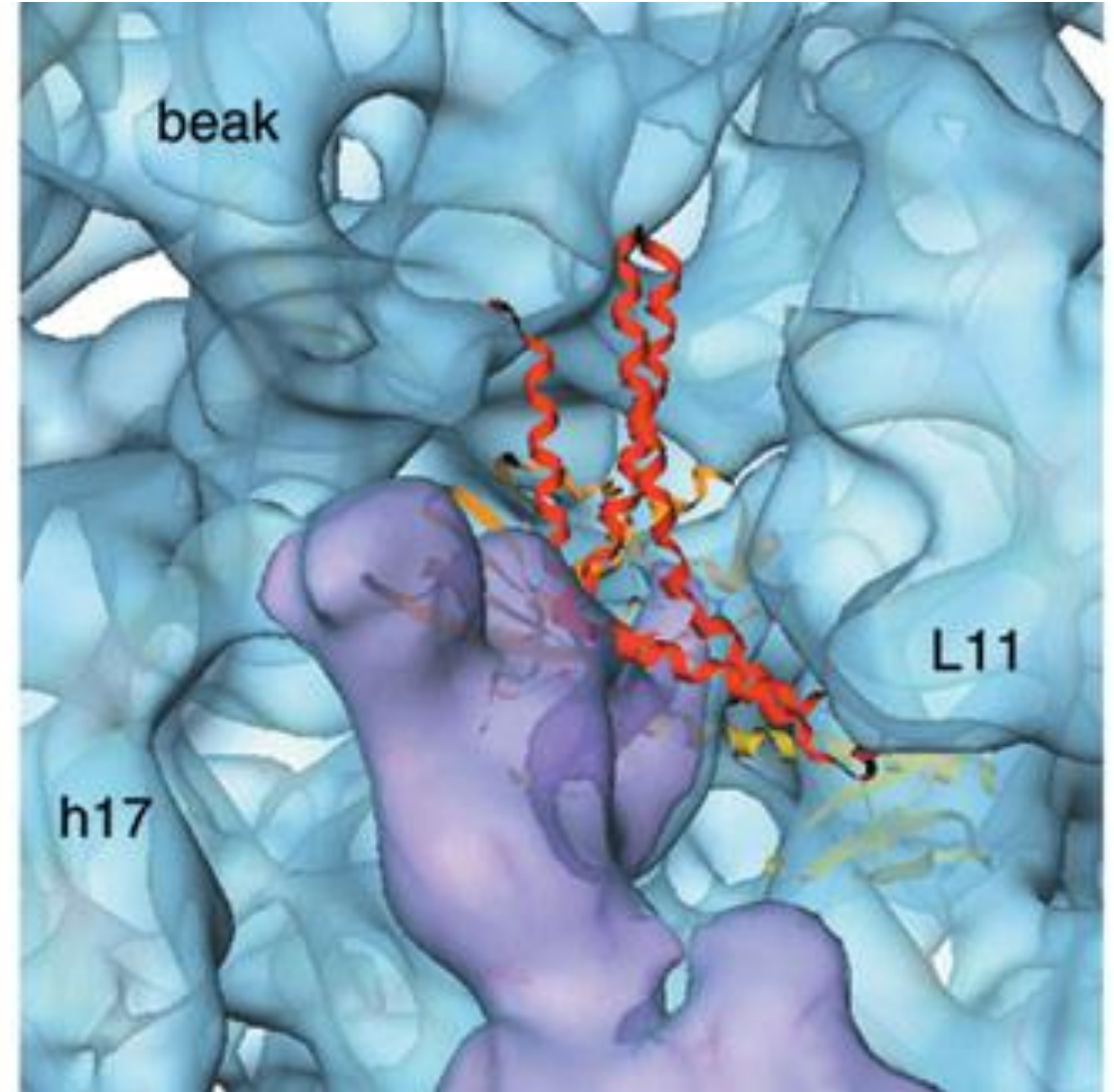
Packing of several polypeptide chains.

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

Sequence→Structure→Function

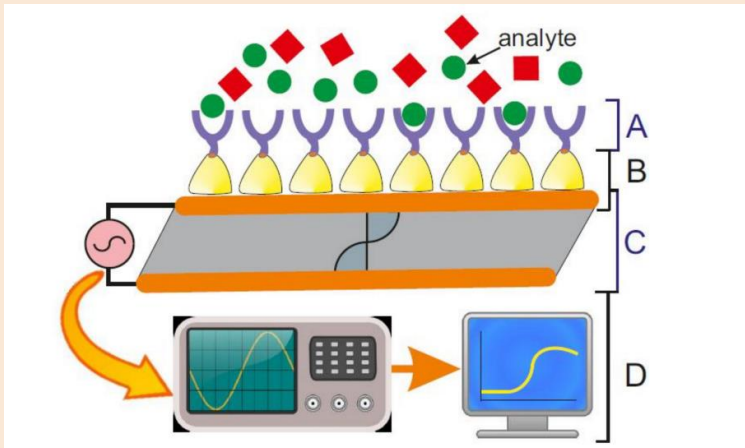


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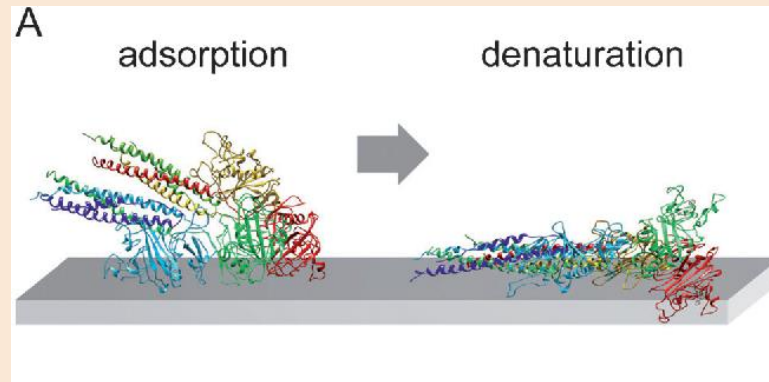
Various Application

Biosensors



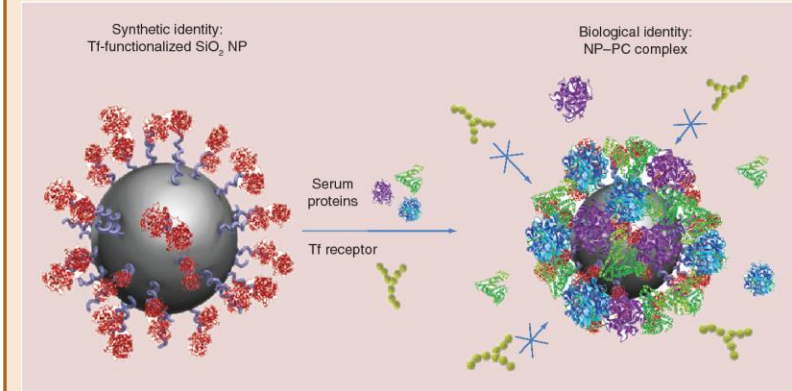
- Amount of protein adsorbed
- Specificity

Biocompatible material



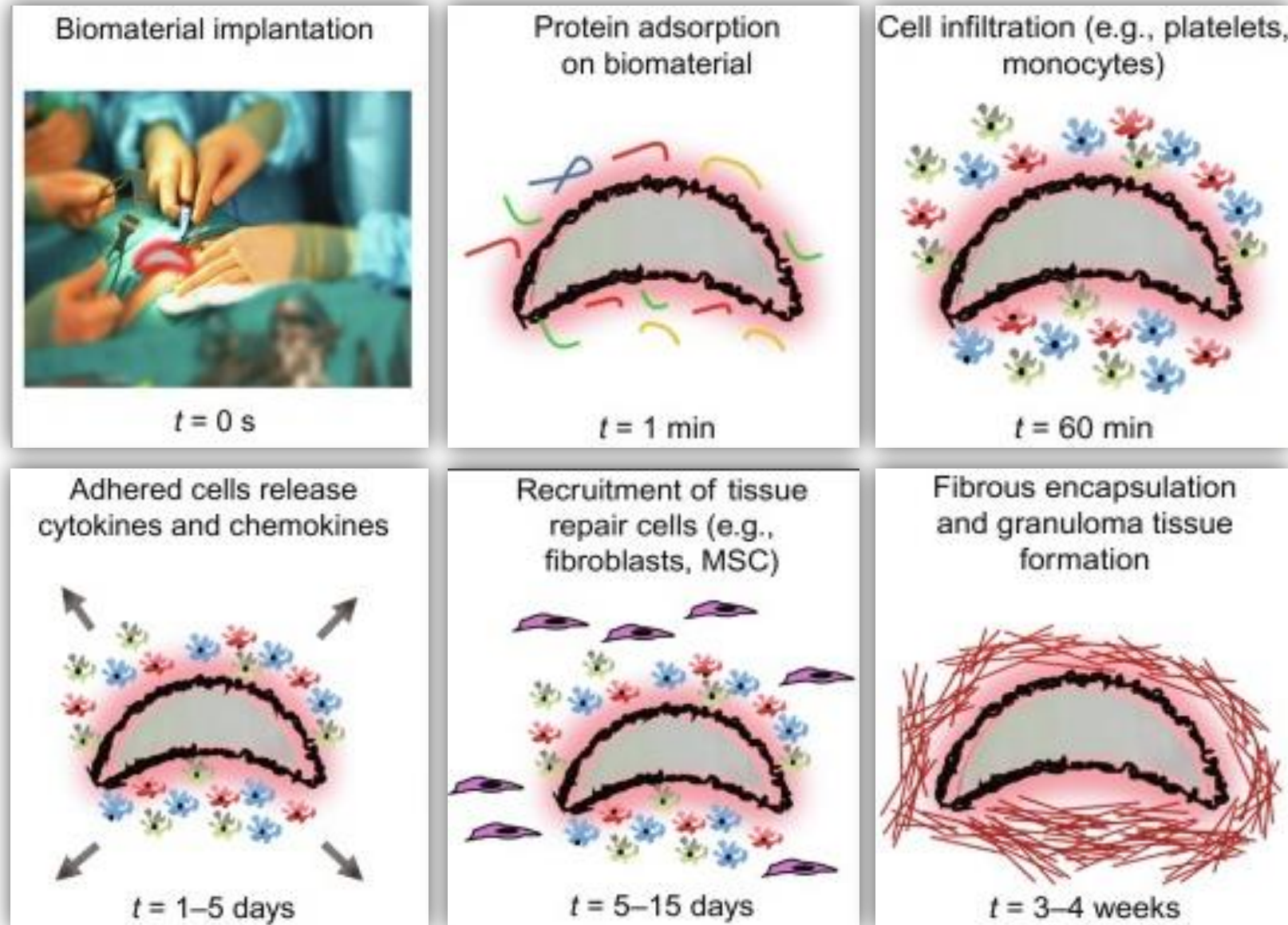
- Inflammation
- Rejection by the body

Drug Delivery



- Drug release rate

Biomaterial In-Vivo Interaction [4]



Graft Failure

- Mechanical failure
- Structural Failure
- Fibrosis
- Bacterial Infection

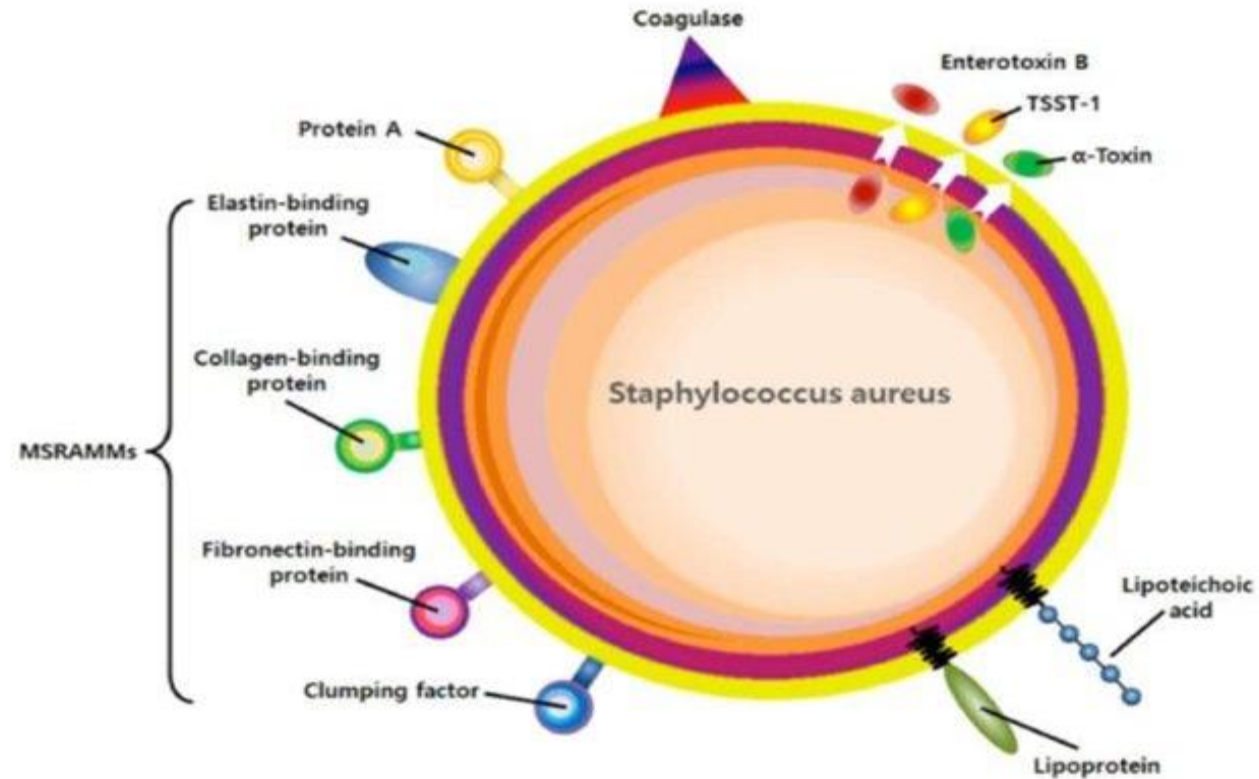
Structure of S. Aureus [5]

Adhesins:

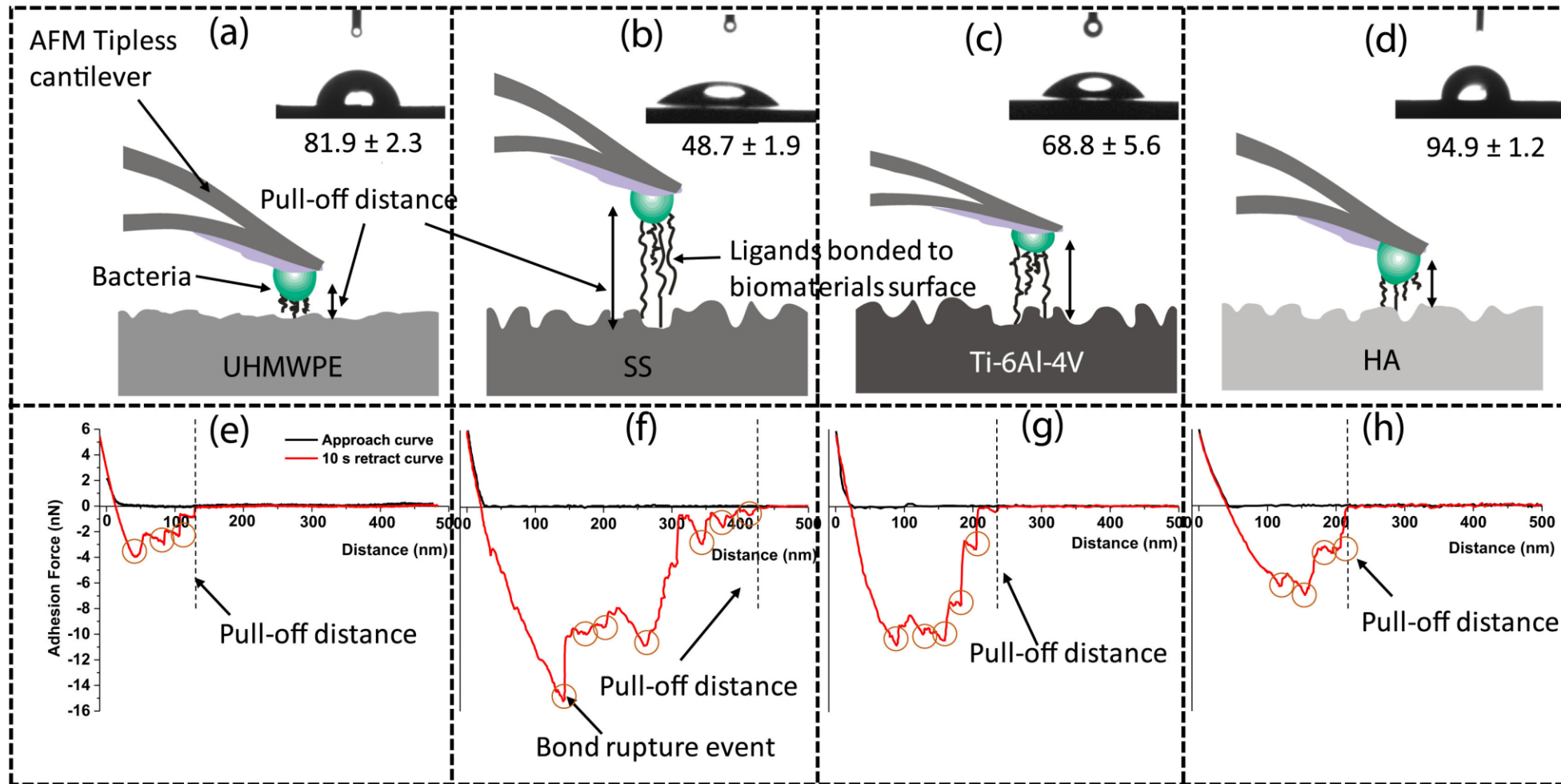
Group of proteins in bacteria involved in attachment or colonization of these bacteria to abiotic (plastic or steel etc) and biological surfaces (found in Bovine or Human Intestine).

Proteins on surface of S. Aureus:

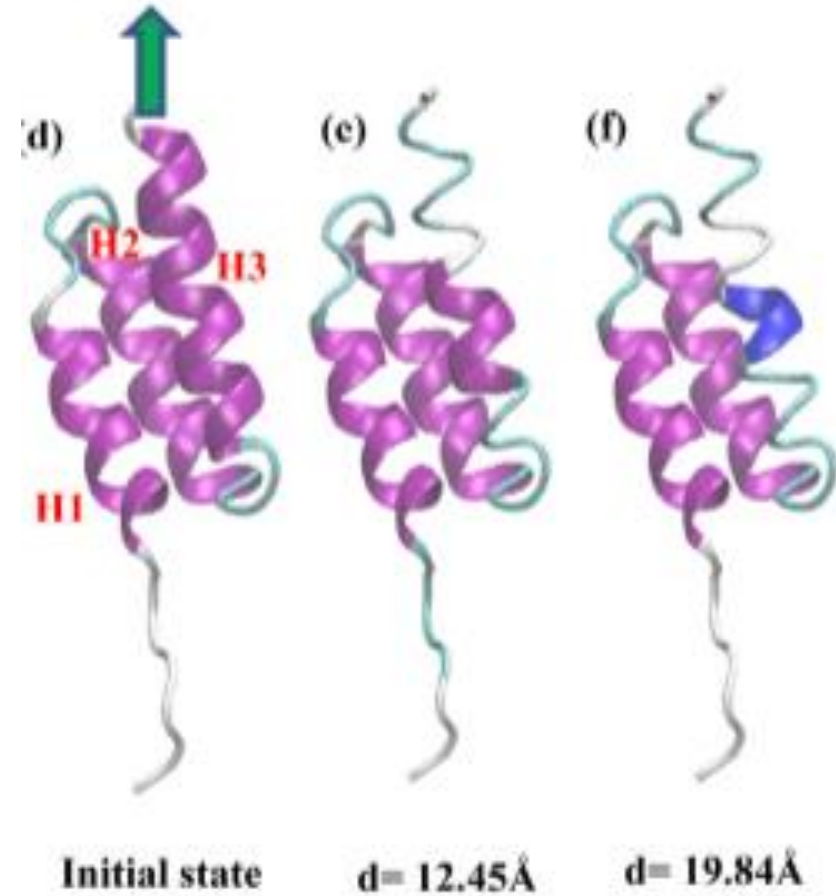
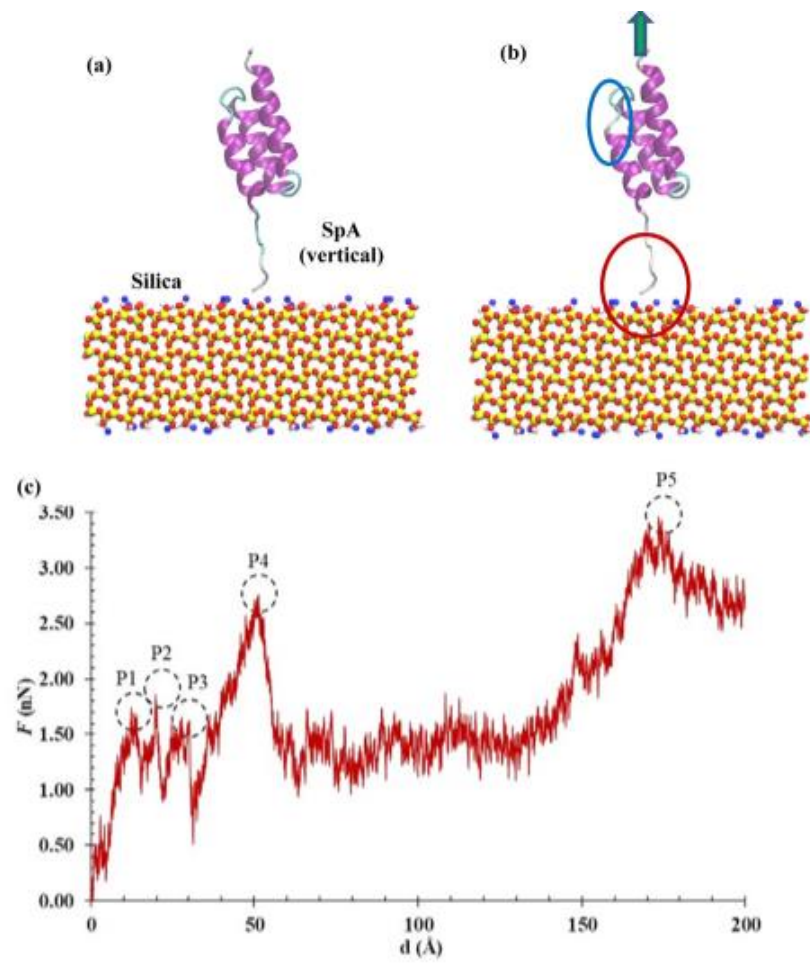
- Collagen-binding protein (eg. CnA)
- Clumping factor (eg. ClfA and ClfB)
- Fibronectin-binding protein
- Elastin binding protein etc



Quantify Adhesin Interaction



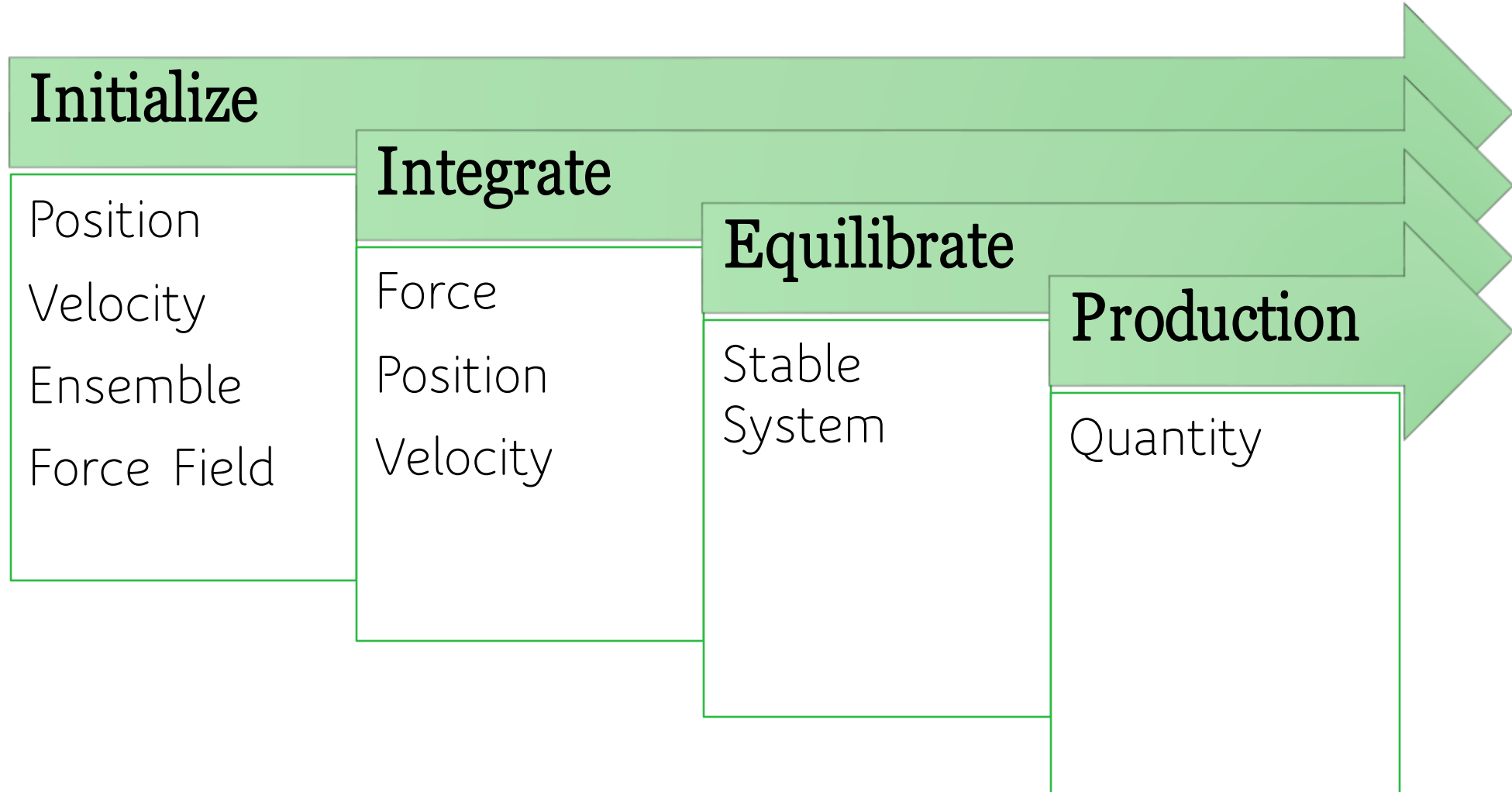
AFM Experiment [6]



MD Simulation [7]

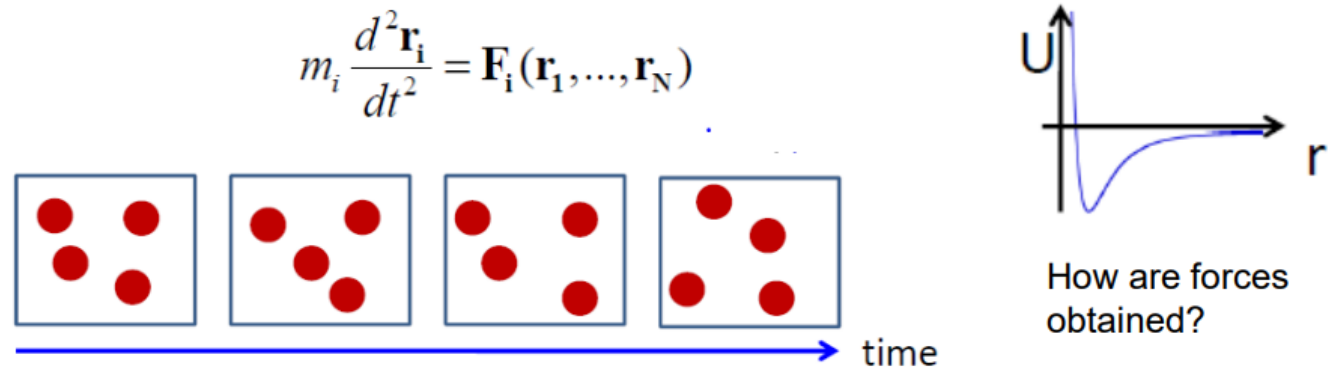
Computational Experiment

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:

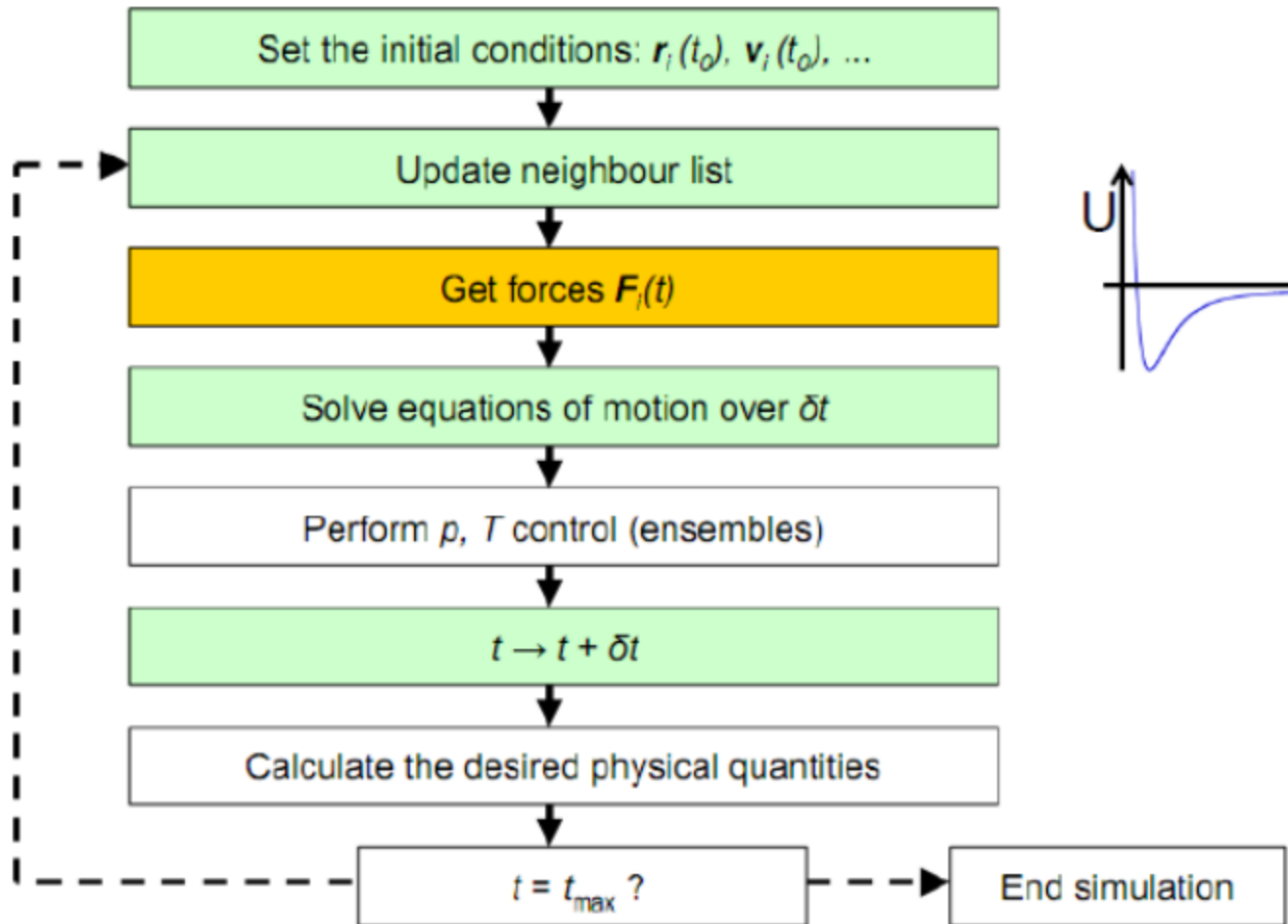
$$m_i \frac{d^2 \mathbf{r}_i}{dt^2} = \mathbf{F}_i(\mathbf{r}_1, \dots, \mathbf{r}_N)$$


The diagram illustrates the simulation of particle dynamics. On the left, four sequential boxes show the positions of four red particles (atoms) at different time steps, with a blue arrow labeled 'time' pointing to the right. Above the boxes is the equation of motion. To the right, a graph shows potential energy U versus distance r , with a curve that has a deep well and then levels off. Below the graph is the text '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.

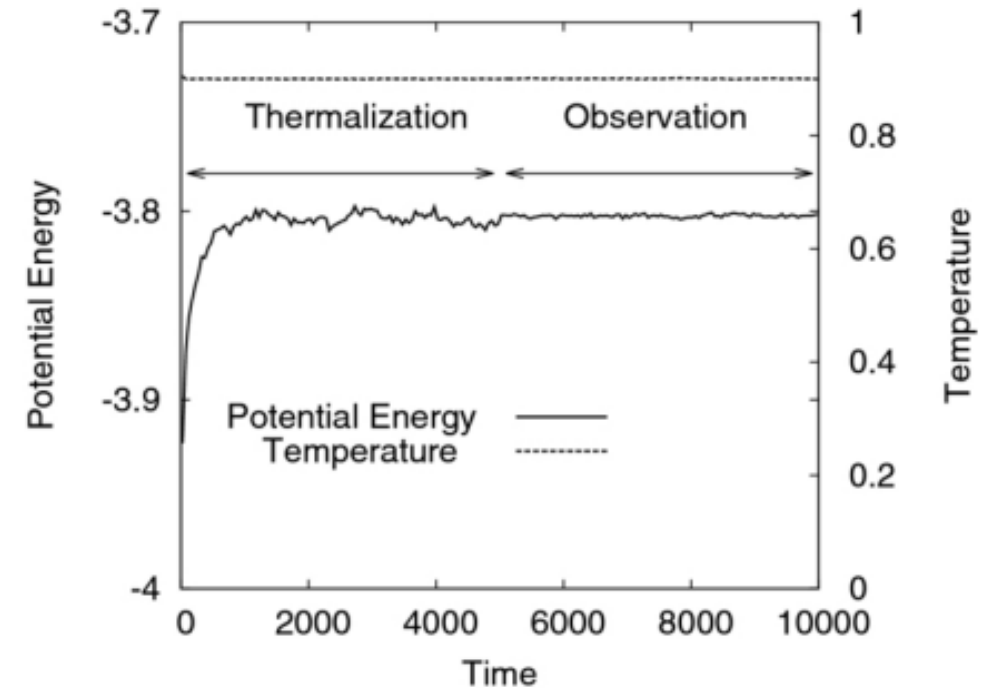
Molecular Dynamics (MD) Simulation

Solve Newton's Equation of motion iteratively



Properties obtained by statistical averaging

Computation of simulation quantities



<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

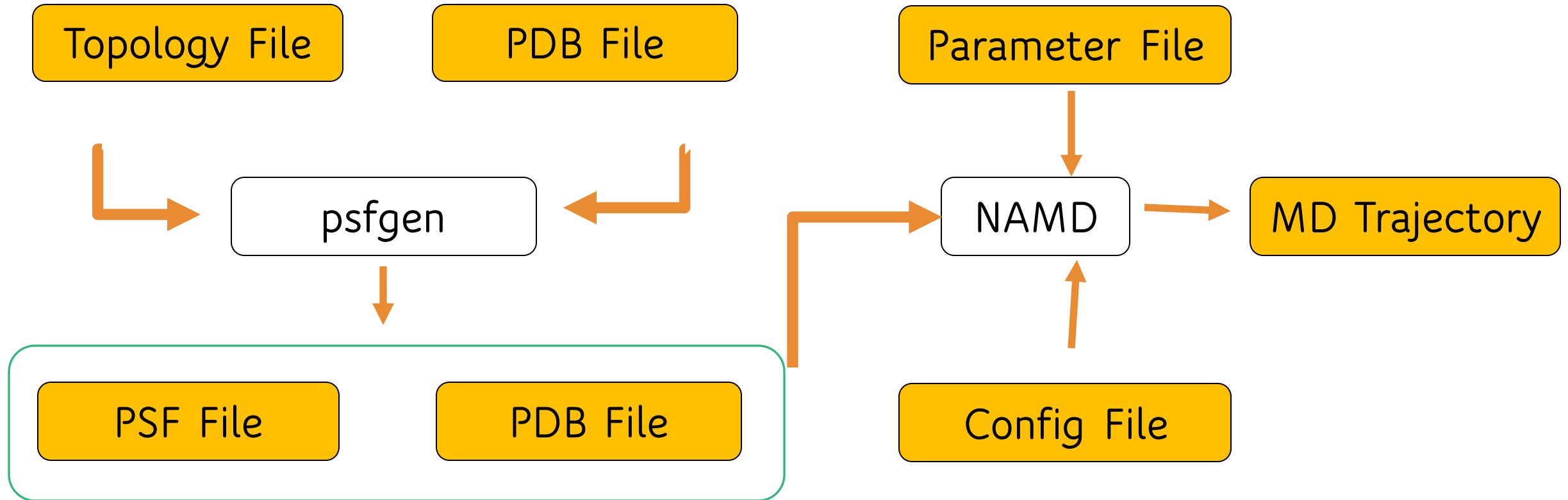
TOPOLOGY FILE

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



A detailed molecular dynamics simulation of a protein in an aqueous environment. The protein is shown as a yellow ribbon structure, with its backbone and side chains clearly visible. It is surrounded by a dense network of water molecules, represented by small red and white spheres. The background is a light beige color with a subtle pattern of small, dark, irregular shapes. The text "THANK YOU" is overlaid in the center in a large, red, serif font.

THANK YOU