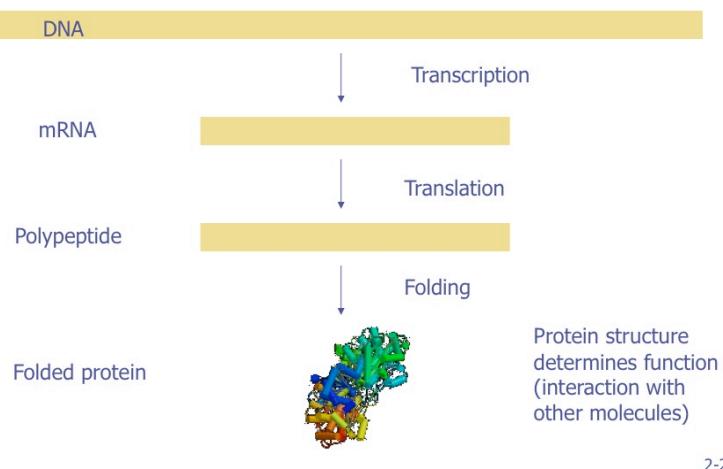




Part 2

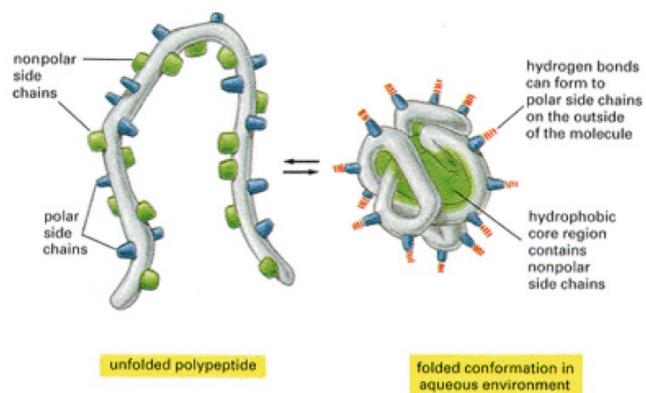
Structures and Proteins

Gene to proteins



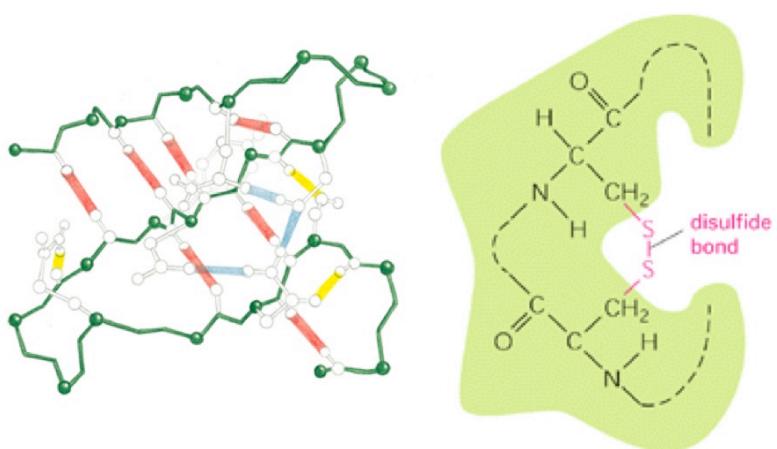
2-2

Protein folding



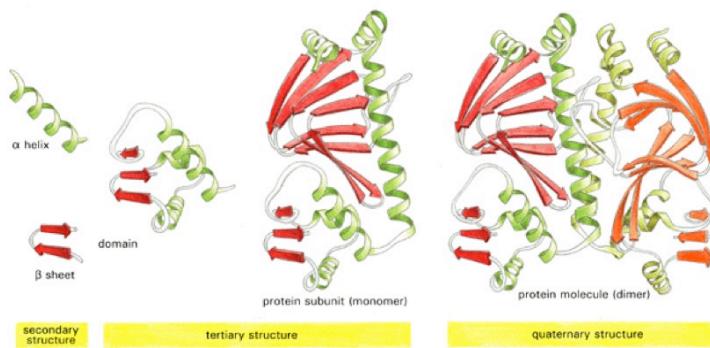
2-3

Hydrogen bonds/Disulfide bonds



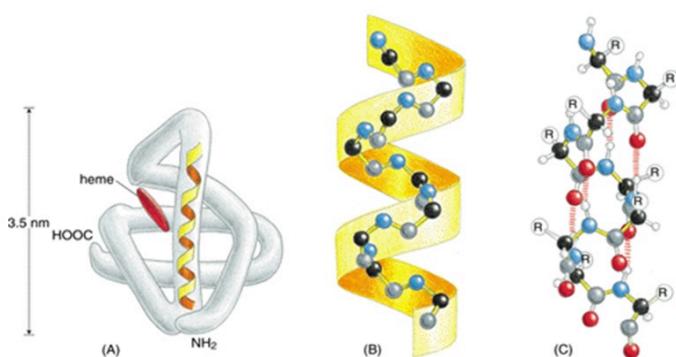
2-4

Protein structure levels



2-5

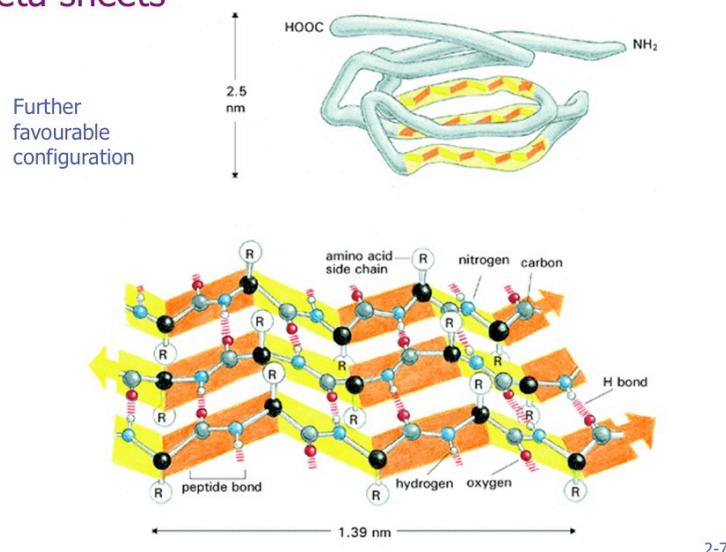
Alpha helices



Energetically favourable configuration of the bond between amino acids

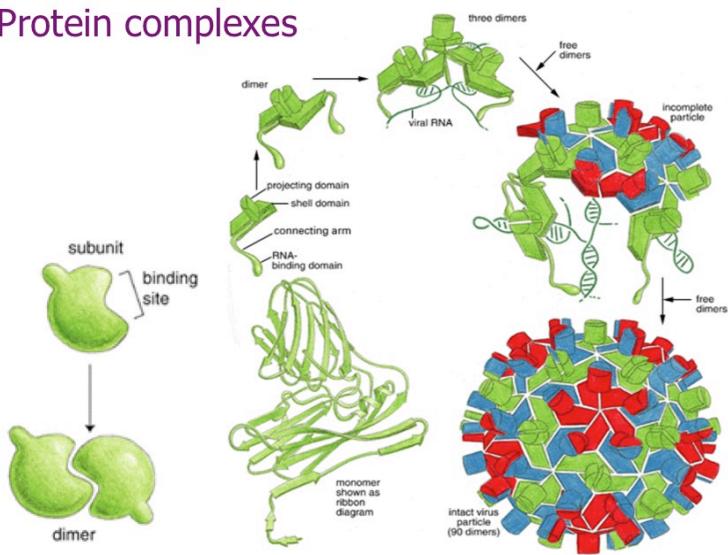
2-6

Beta sheets



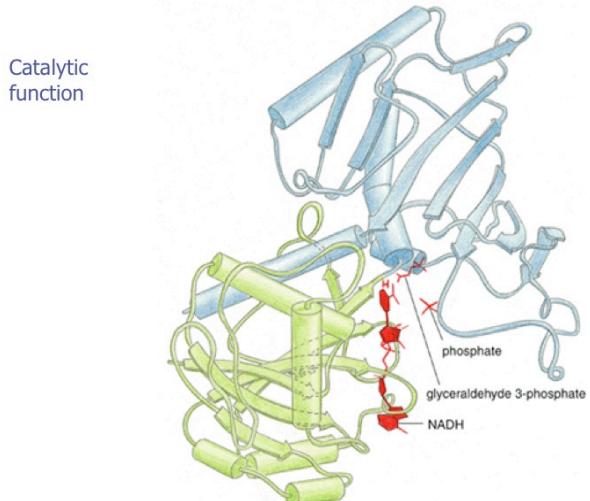
2-7

Protein complexes



2-8

Ligand binding between two domains



2-9



2.1

Protein structure determination

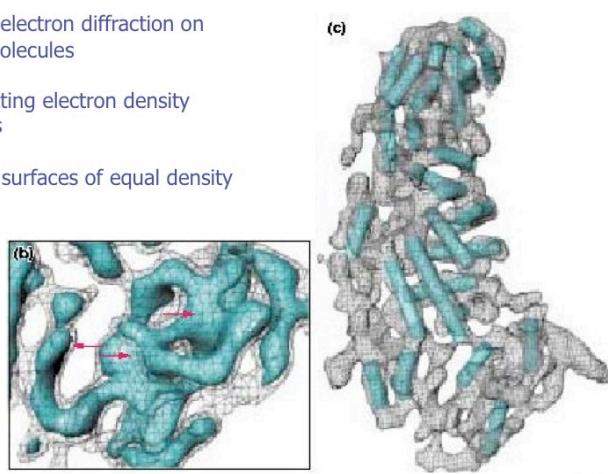
10

Transmission electron microscopy

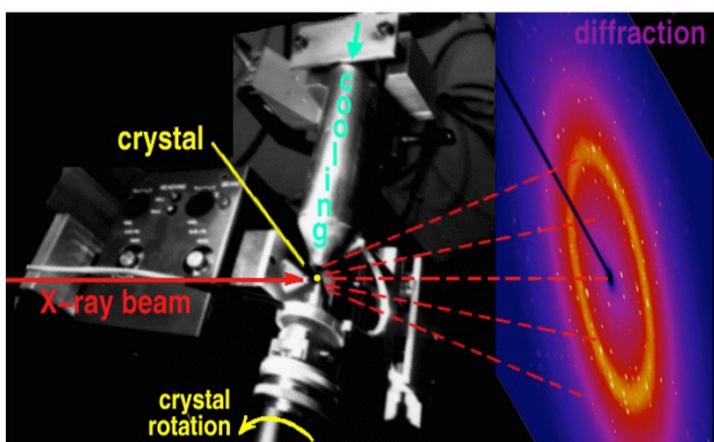
1. Measuring electron diffraction on cryofixed molecules

2. Reconstructing electron density around atoms

3. Visualizing surfaces of equal density (isosurfaces)



X-ray diffraction analysis



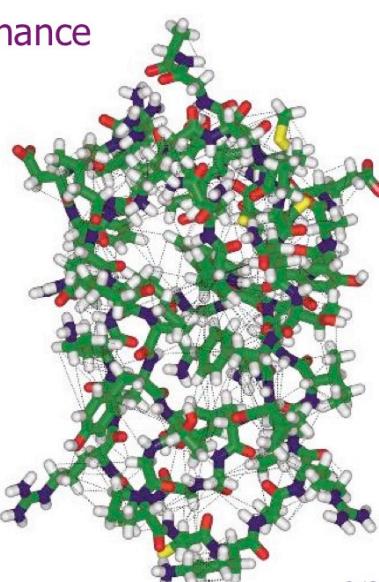
Most exact, but proteins have to be crystallized

Nuclear magnetic resonance

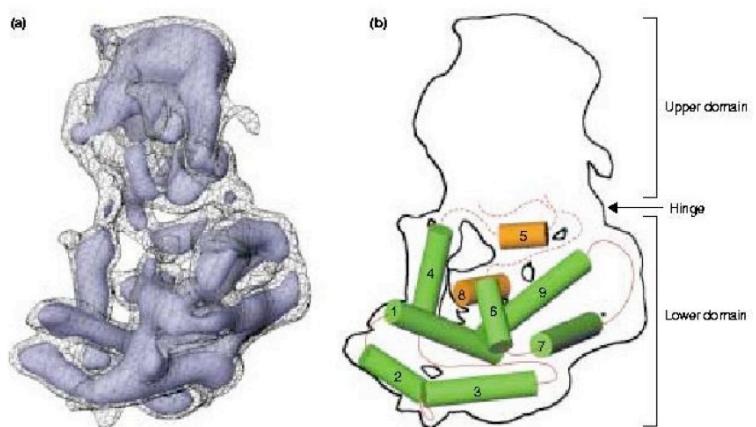
Gives information about hydrogen bonds (spin of electrons)

Proteins in solution

Poor resolution



Determining structure model



2-14

Example: EM density slice of ribosome



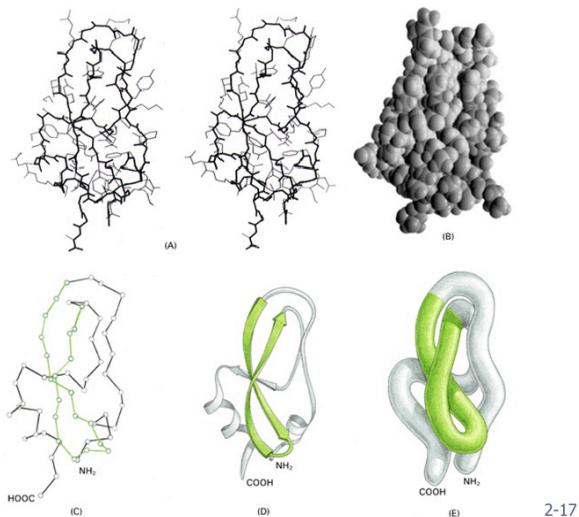
2-15

2.2

Protein structure visualization

16

Different visualizations



2-17

Representations of 3-D structure

(1) Volume datasets

- Capture electron density directly from imaging methods
- Experimental data
- Direct visualization (volume rendering) difficult

(2) Surface representations

- Isosurfaces of equal density
- Allow better visualization (detail removed, natural appearance with lighting)

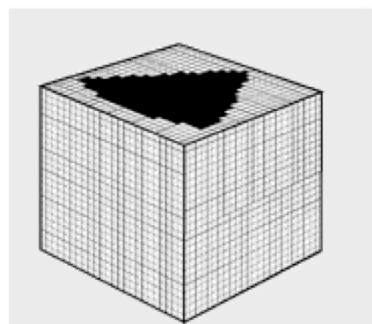
(3) Structure files

- Give direct information about atom positions and secondary structures
- Can be visualized as surfaces or more abstract graphics

2-18

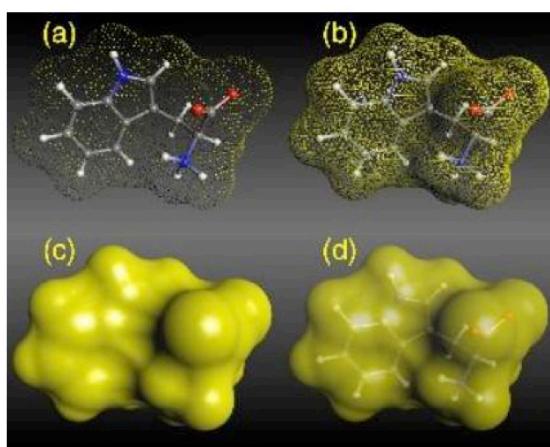
Volume dataset

- (1) Voxel: (cubic) volume element
- (2) Density: scalar value assigned to voxel (grey value)
- (3) Three-dimensional array



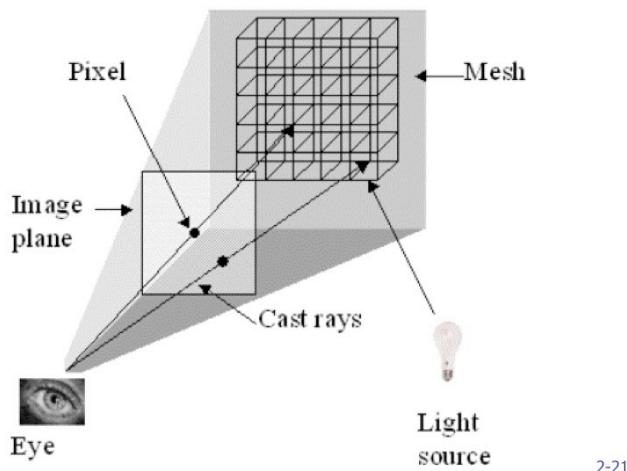
2-19

Surfaces and Structure Models



2-20

Rendering: Ray casting



2-21

Ray casting: how to determine pixel

(1) Colour and opacity as integral

- over all voxels along the ray

$$\int e^{-\int_0^x \sigma(t) dt} \cdot I(x) dx$$

(2) Problem: opacity

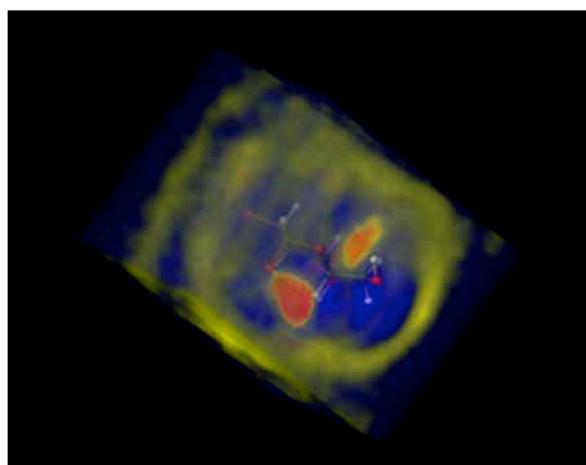
- Without opacity you can see only the outside
- Opacity proportional to density: high density regions stick out
- Opacity above a certain threshold: clear surfaces

(3) Simpler mechanisms

- Maximum intensity projection: maximum along ray

2-22

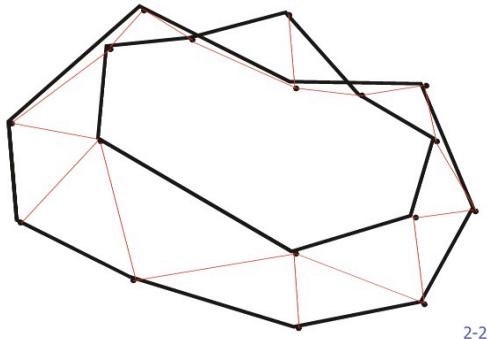
Volume rendering



2-23

Triangulation

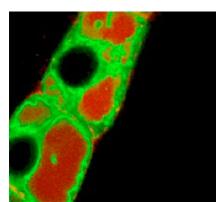
- (1) Surfaces are composed of triangles in 3D
 - Rendering uses projection and hidden surface removal plus lighting (angle of triangle to light source)
- (2) Can be computed from boundaries in a plane connected with triangles



2-24

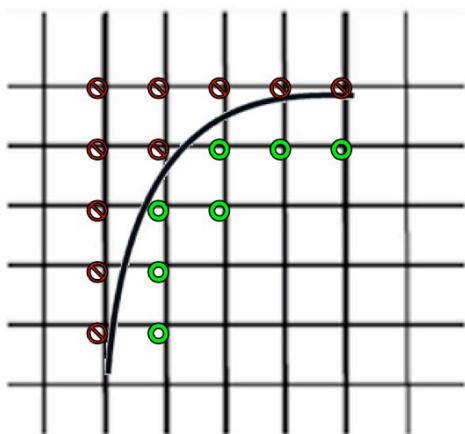
Segmentation

- (1) Assignment of each voxel to one of several classes (e.g. object and background)
 - E.g., based on a simple threshold
 - Or by manual delineation
 - Or based on threshold plus connectivity (seedpoints)
 - Or based on complex attributes calculated from the environment of a voxel (texture measures)
- (2) Needed to identify objects within volume datasets



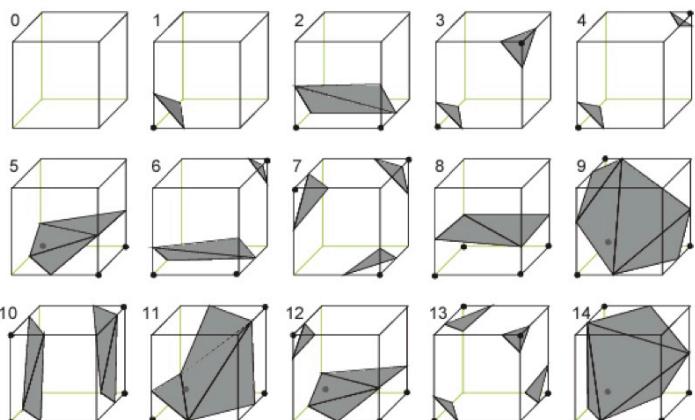
2-25

Marching cubes: Surface detection



2-26

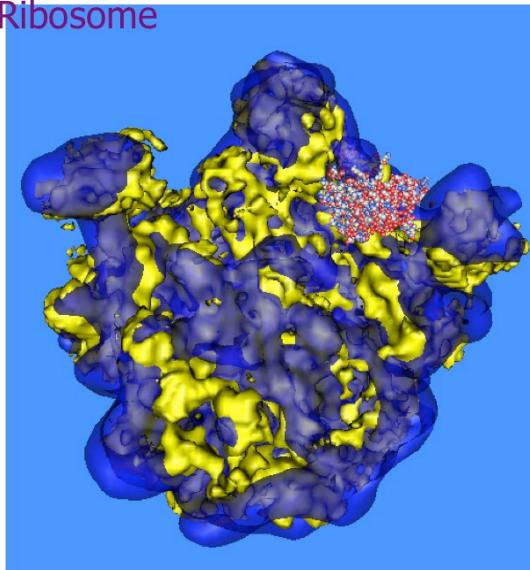
Marching cubes: Surface generation



Surfaces are generated between voxels from different segments

2-27

Example: Ribosome



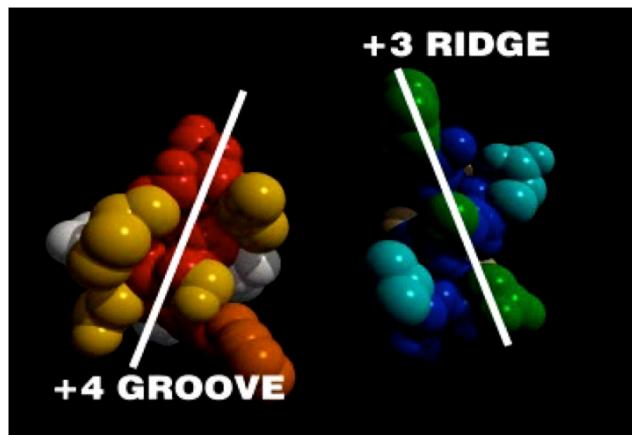
2-28

PDB (structure) files

- (1) A 3-D coordinate (x,y,z) and binding length for each atom
 - Type of binding has to be reconstructed by software („chemistry rules“)
- (2) „Residue dictionaries“ simplify software
 - In MMDB (molecular modeling database) type files
 - Contains chemical structure of each residue
- (3) Are available in protein databases
 - Swissprot, MMDB, etc.
- (4) Visualized as surface graphics by rendering applications
 - Such as Chime, RasMol, Swiss PdbViewer

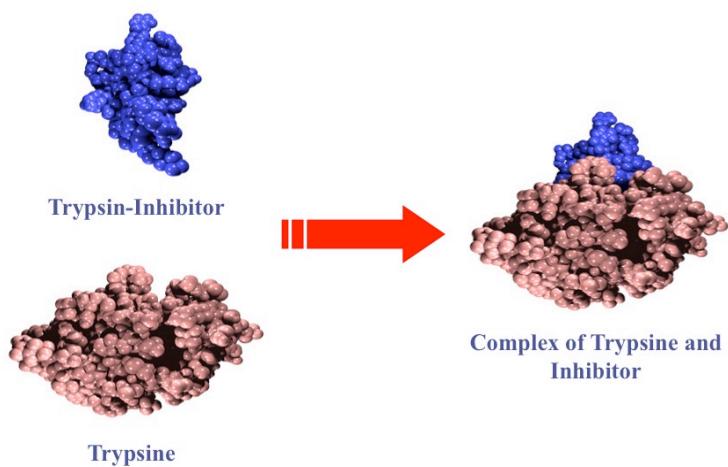
2-29

Docking



2-30

Docking simulation



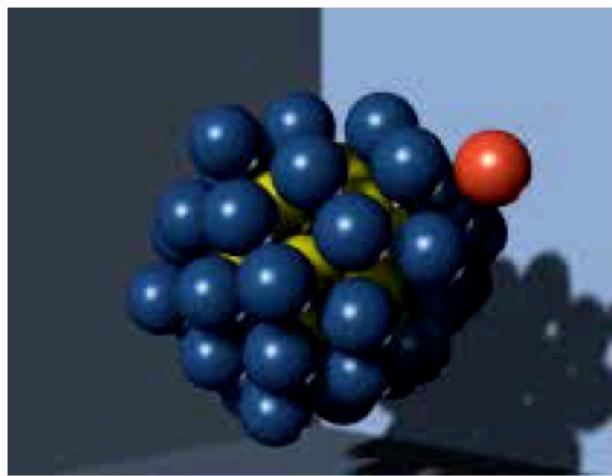
2-31

Docking prediction

- (1) Generation of candidates
 - Rigid structure assumed (simplification)
- (2) Calculating fitness function between protein and candidate
 - Geometric alignment (collision detection)
 - E.g., counting number of van der Waals contacts

2-32

Molecular Dynamics



2-33