భారతీయ సాంకేతిక విజ్ఞాన సంస్థ హైదరాబాద్
भारतीय प्रौद्योगिकी संस्थान हैदराबाद
Indian Institute of Technology Hyderabad

Introduction of Bio-nanotechnolgy

BT1110

Lecture 10 : Interaction of nanomaterials with biological systems

Himanshu Joshi 23 November, 2023

भारतीय सांकेतिक विज्ञान संस्थ हैदराबाद
भारतीय प्रौद्योगिकी संस्थान हैदराबाद
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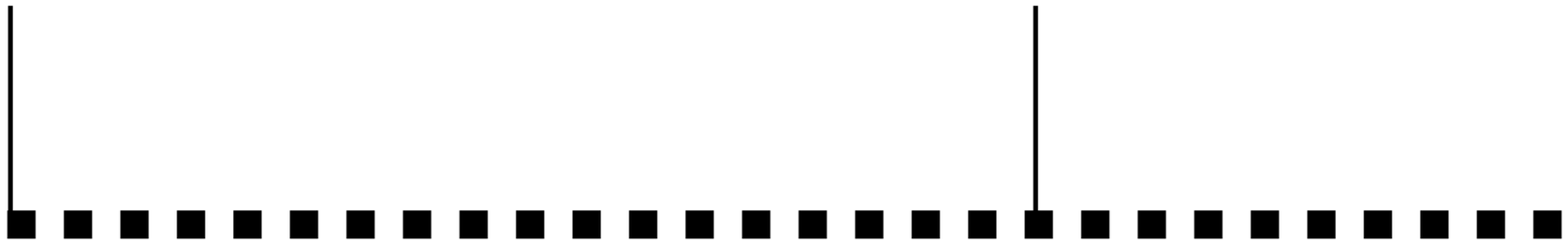
Course contents

- Introduction to nanotechnology and bionanotechnology,
- Biological self-assembly
- Biologically inspired nanostructures - introduction to biomimetics
- Nucleic acid nanotechnology
- DNA origami
- Protein engineering
- Lipid nanotechnology
- Chirality in biological systems
- **Interaction of nanomaterials with biological systems**
- Virology: viruses and vaccines

Journey of universe

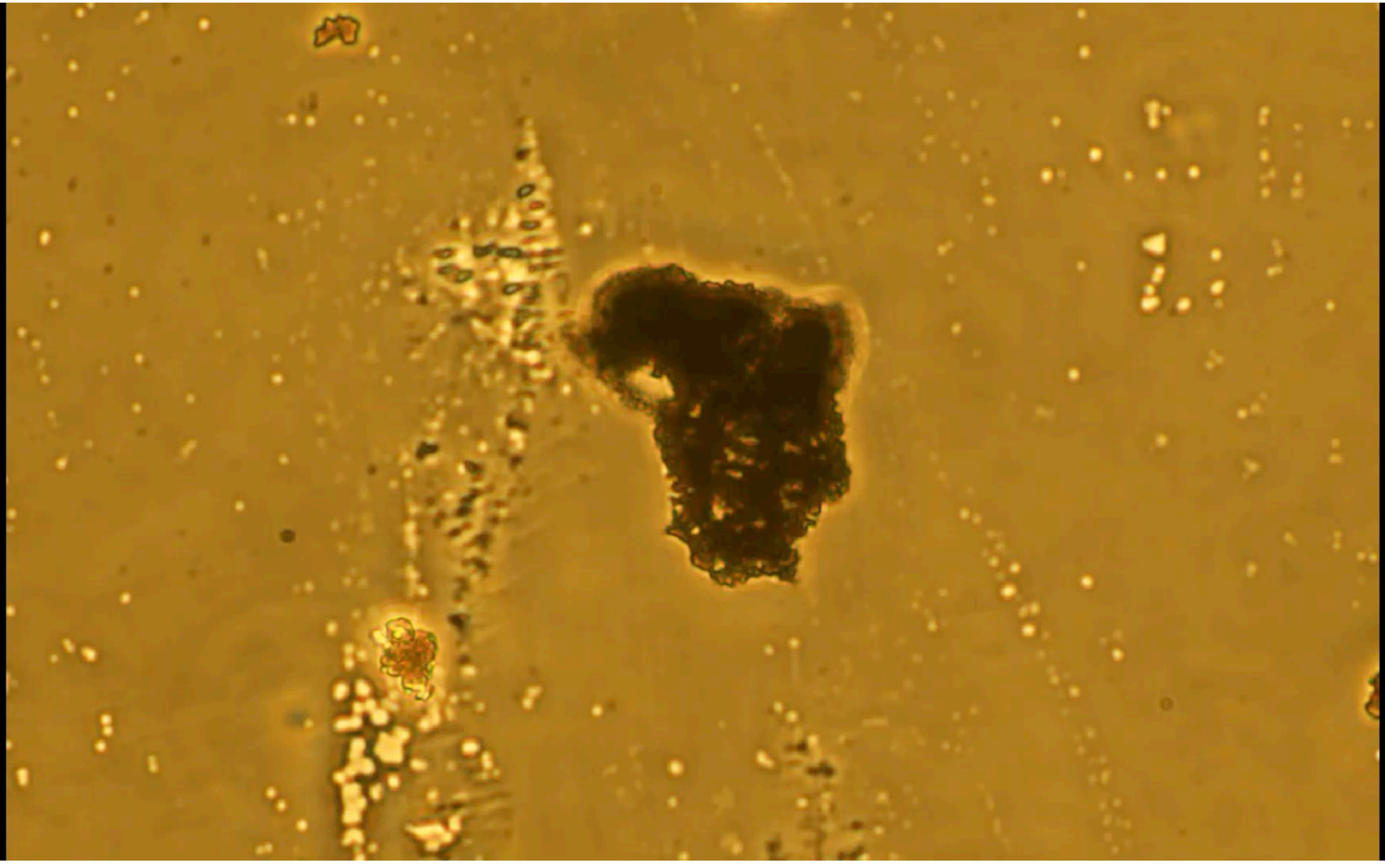


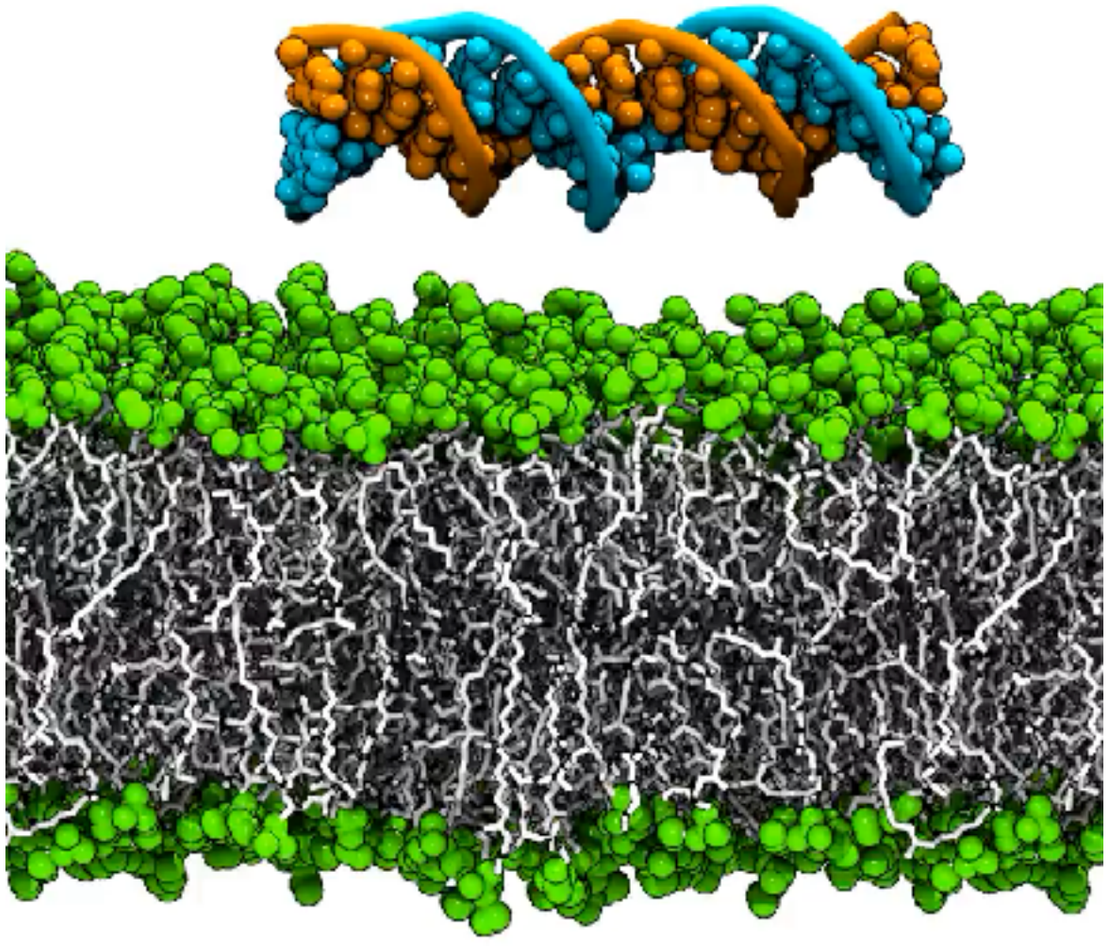
13.8 Billion Years

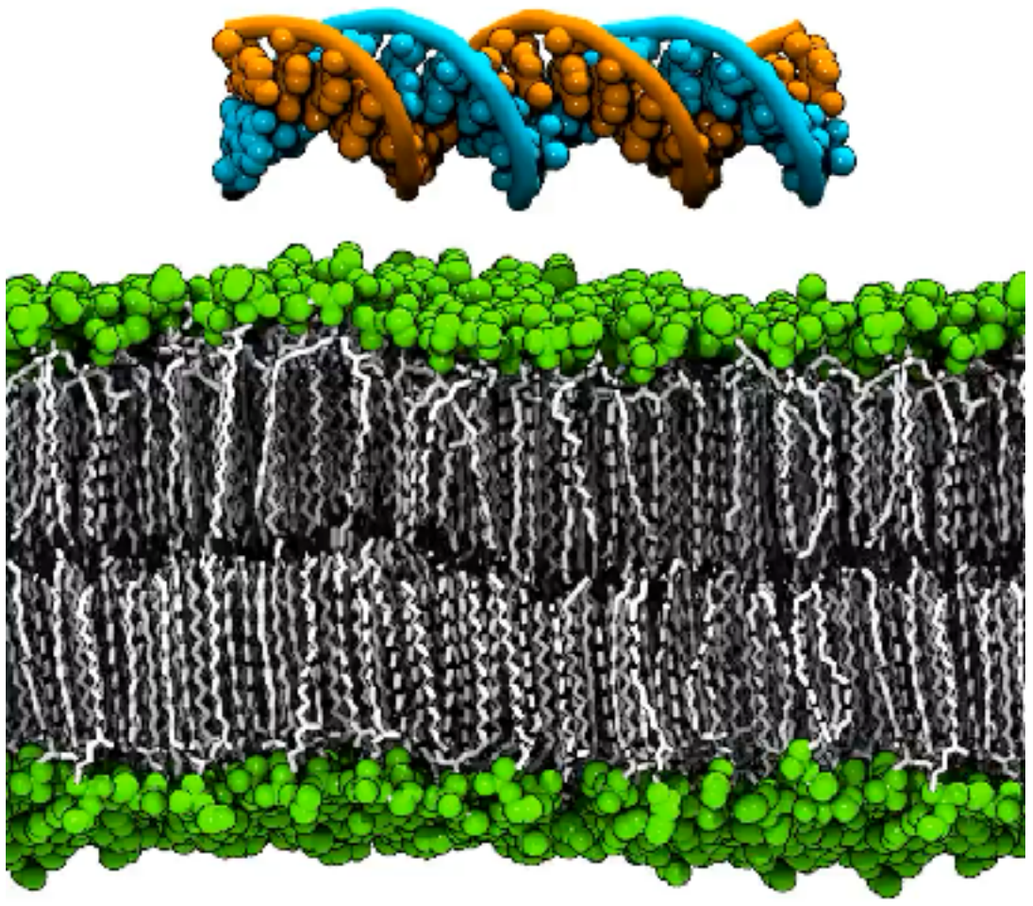
Temperature 10^9 K
Quarks, leptons etc

3.7 Billion Years

Reference https://www.space.com/how-did-universe-elements-form







Energy functional

$$U = U_{\text{bonded}} + U_{\text{non-bonded}} + U_{\text{external}}$$

$$\begin{aligned} U = & \sum_{\text{bonded}} \Big\{ \quad k(r_{ij} - r_0)^2 \\ & \qquad + k_\theta(\theta - \theta_0)^2 \\ & \qquad + k(1 + \cos(n\psi + \phi)) \Big\} \\ + & \sum_{i>j} \Big\{ \quad -U_{\min} \left[\left(\frac{R_{\min}}{r_{ij}} \right)^{12} - 2 \left(\frac{R_{\min}}{r_{ij}} \right)^{6} \right] \\ & \qquad + \frac{C q_i q_j}{\epsilon_0 r_{ij}} \Big\} \end{aligned}$$

$$+ q_i V + m_i . B$$

Non-covalent interactions

Strength 1-5 Kcal/mol

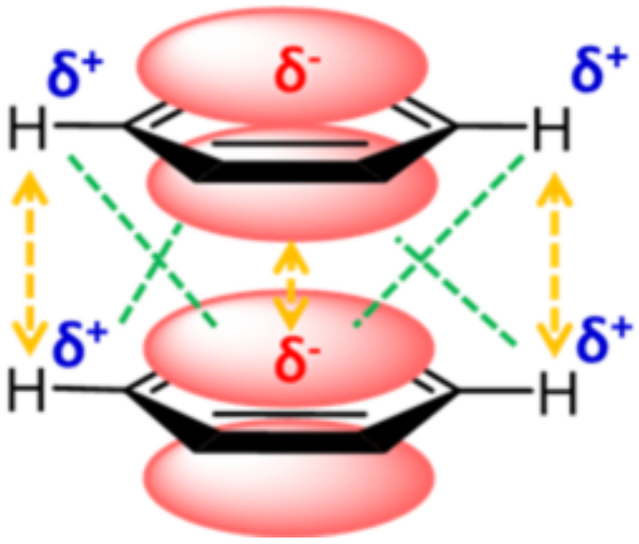
- *pi - pi* stacking.
- Hydrogen bonding
- Cation-pi interactions,
- Hydrophobic interactions

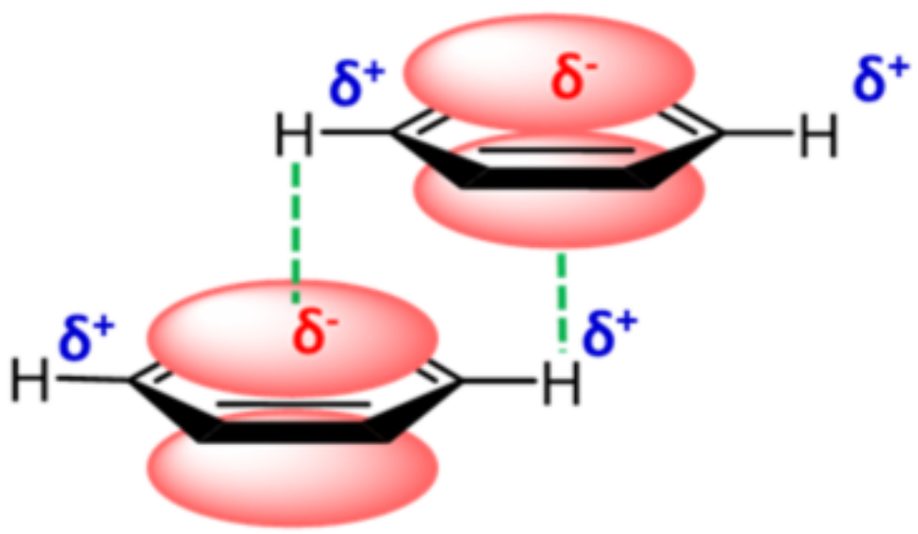
Calorie

a unit of energy equivalent to the heat energy needed to raise the temperature of 1 gram of water by 1 °C

π -π Stacking interactions

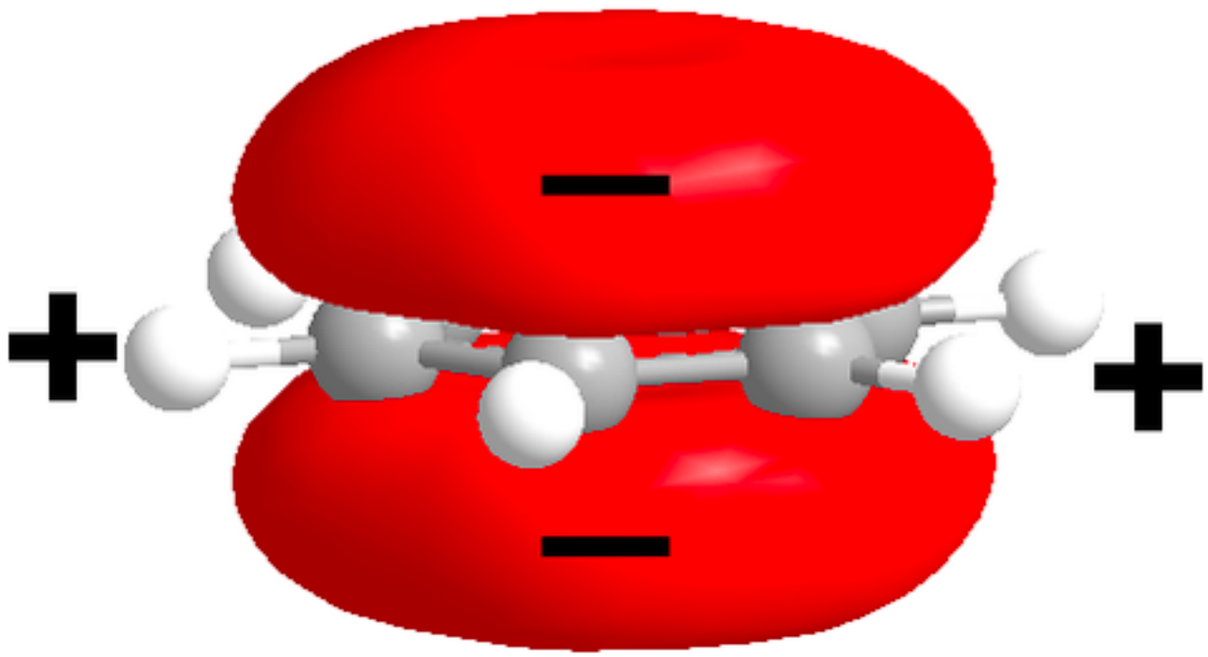
The aromatic π systems bind face to face with one another and involve a combination of dispersion and dipole-induced dipole interactions.

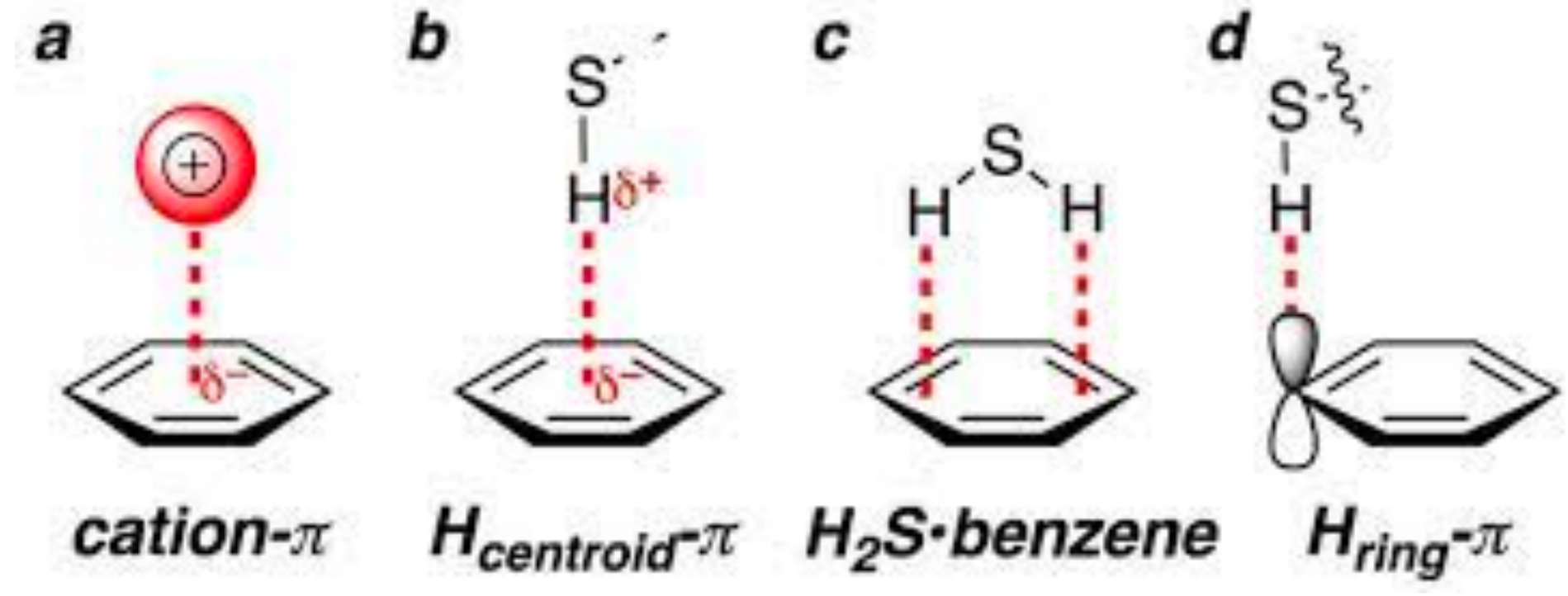




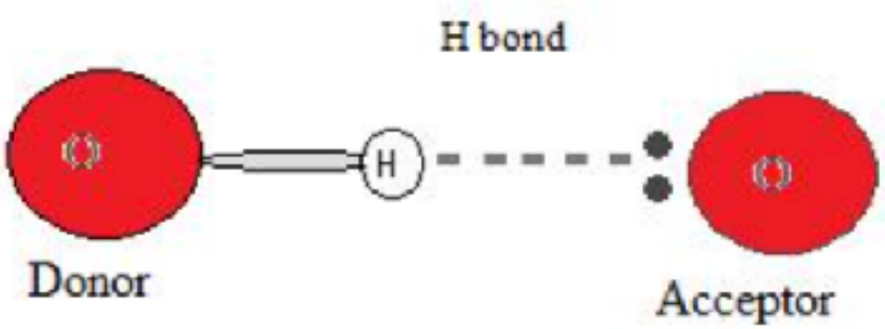
Referene:
https://chem.libretexts.org/

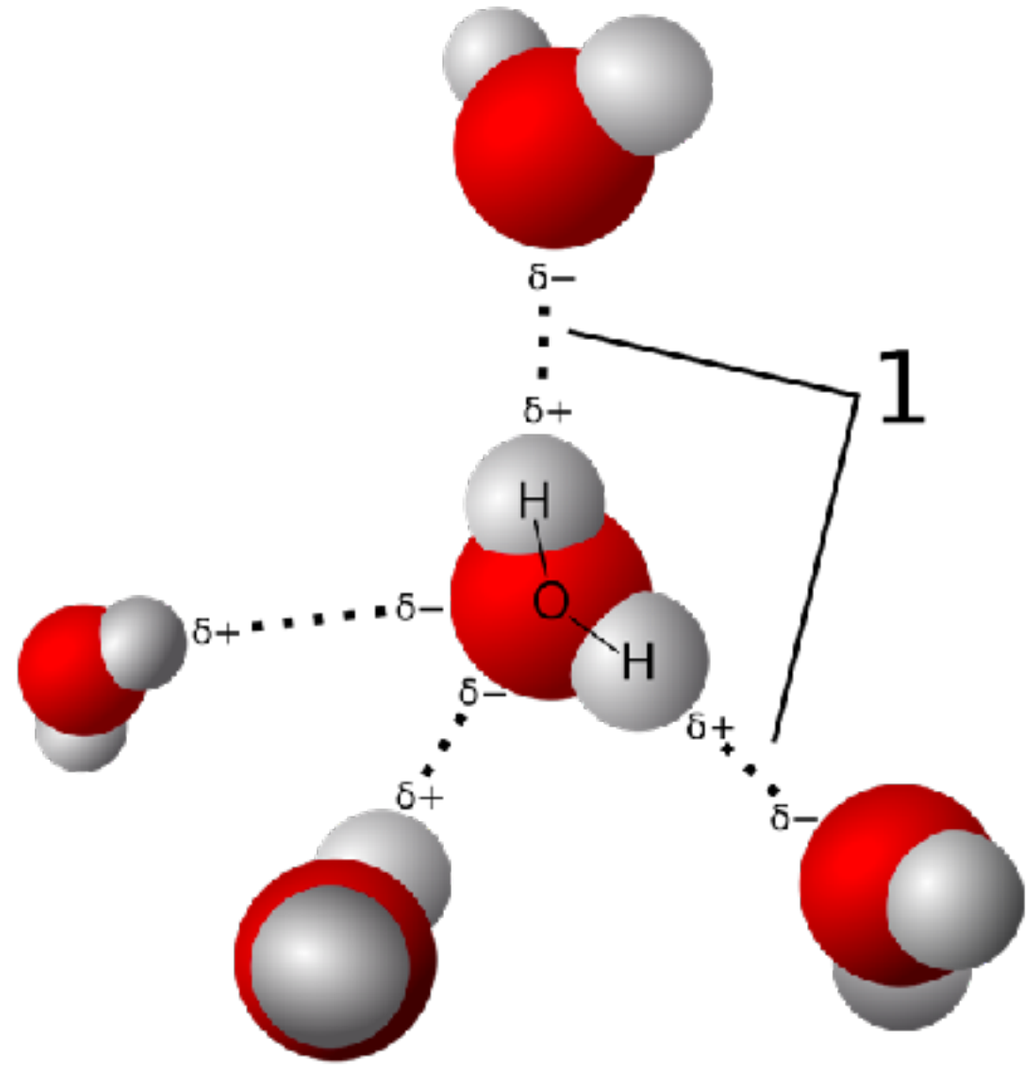
cation-π interactions





Hydrogen bonds

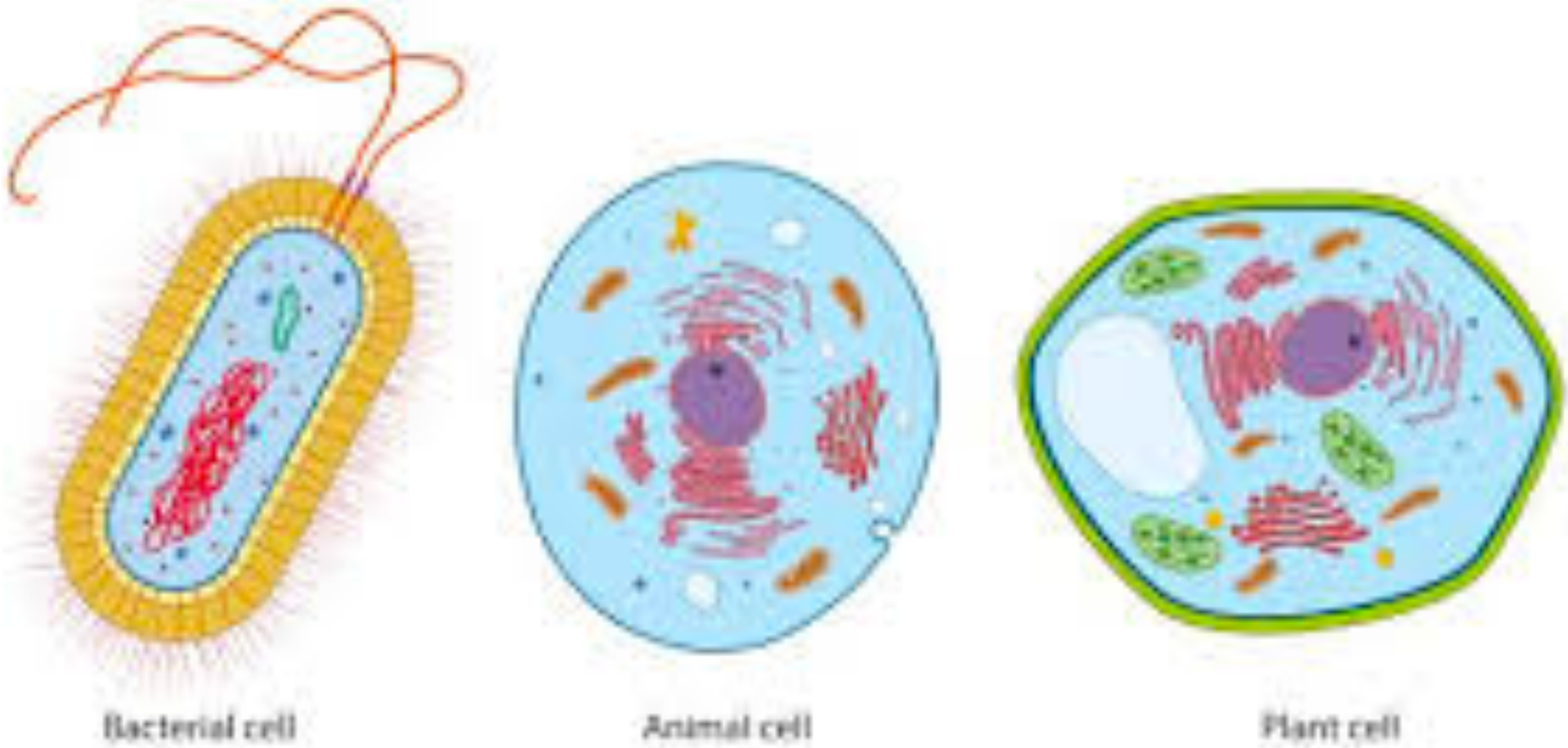




Most hydrogen bonds form between hydrogen (H) and oxygen (O), fluorine (F), or nitrogen (N).

between 1 and 10 kcal/mol
Covalent 50 to 100 kcal/mol

Life
Prokaryotic vs Eukaryotic



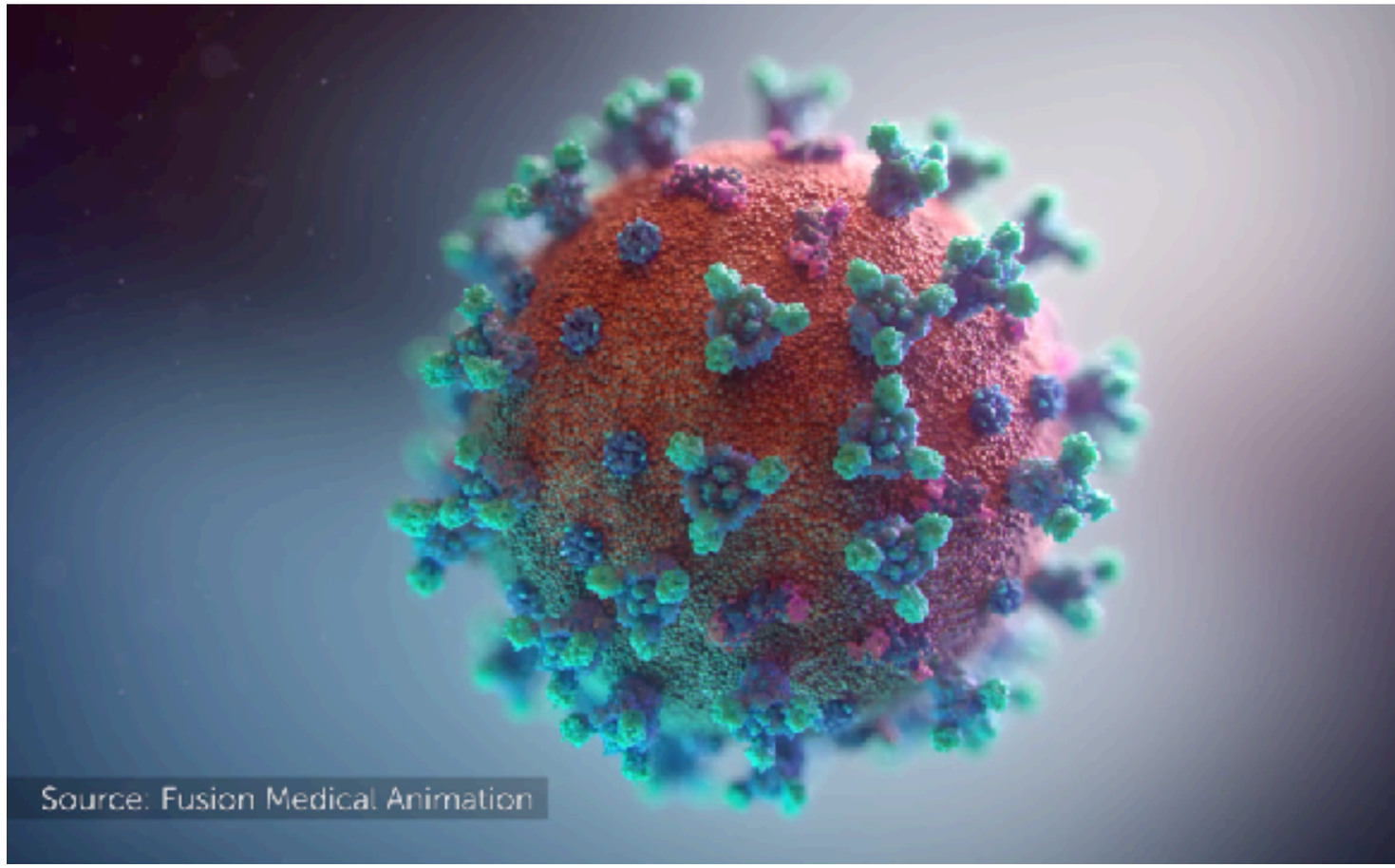
- Eukaryotic contains membrane bound structures, like nucleus, mitochondria etc which Prokaryotic does not have.

- All prokaryotes are unicellular, like Bacteria, Archaea, but all unicellular constructs are not prokaryotes like Yeasts and algae.

Virus

Viruses are smaller and simpler in construction than unicellular microorganisms like bacterial.

Since viruses can not reproduce by themselves, Viruses are in between living and dead, they depends on another species to reproduce.



Viron

- Perhaps millions of virus species are there,
- From 20 nm to 500 nm in diameter,
- Icosahedral Symmetry,
- There are about 219 viruses which are known to infect human,
- Yellow fever virus in 1901 was the first one to be discovered.

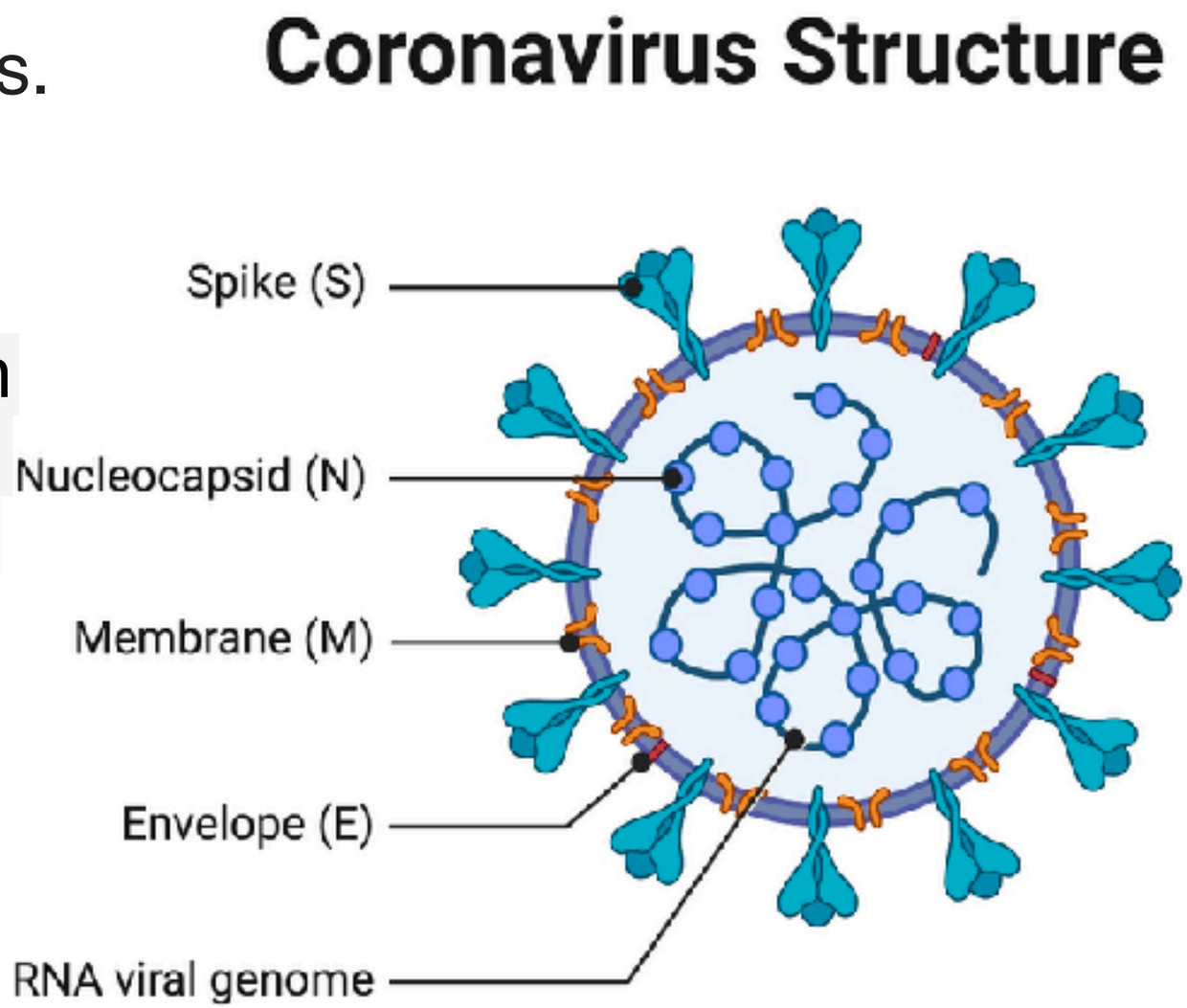
1-100 µM
20-30 µM

(i)the genetic material, i.e., long molecules of DNA or RNA that encode the structure of the proteins by which the virus acts;

(ii) a protein coat, the capsid, which surrounds and protects the genetic material; and in some cases

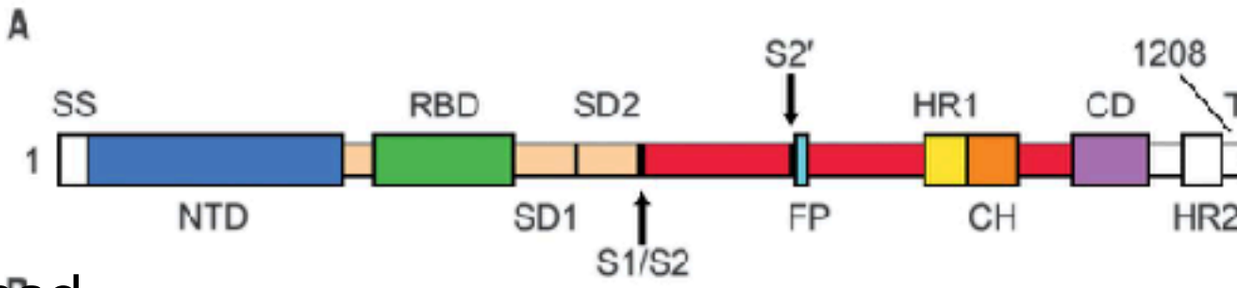
(iii) an outside envelope of lipids.

Similar to many other viral fusion proteins, the SARS-CoV-2 spike utilizes a glycan shield to thwart the host immune response.



Glycosylated spike (S) protein is important for cellular uptake

Ectodomain organization of the protein expression 1 to 1208 residues.

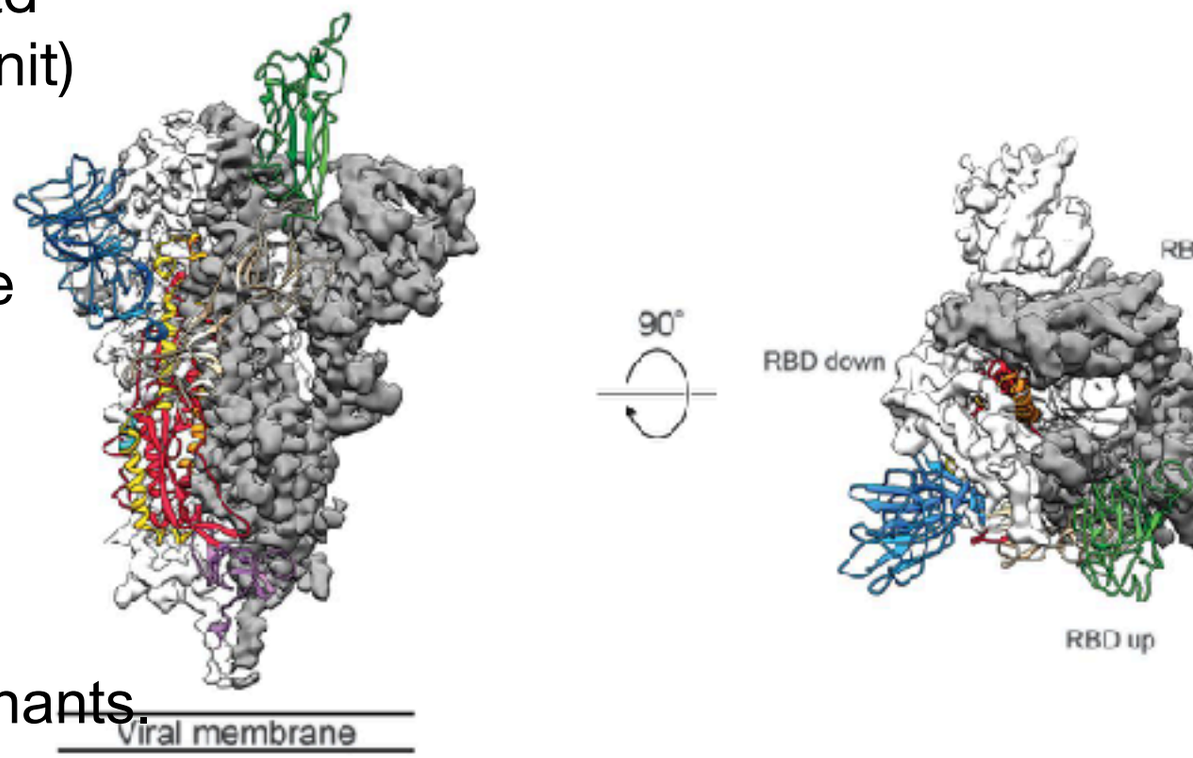


Spike (S) is class 1 trimeric fusion protein which had two functional subunits, S1 (receptor binding subunit) and S2 (membrane fusion subunit).

A metastable state of subunit S1 undergoes a large structural transition after binding to the host cell. Each trimer has 66 N-linked glycosylation sites.

Hinge like conformational movement in S1 subunit either expose (up) or hide (down) the RDB determinants.

There are 66 N-linked glycosylation sites in each trimer of the spike protein of viral envelop.



3D reconstruction of single RBD S1 w
3.5 Å resolution.

Wrapp et al., Science , 367, 1260–1263 2020

Understanding the glycosylation of the viral spikes protiens

SARS-CoV-2 vs SARS-CoV or other coronaviruses spike

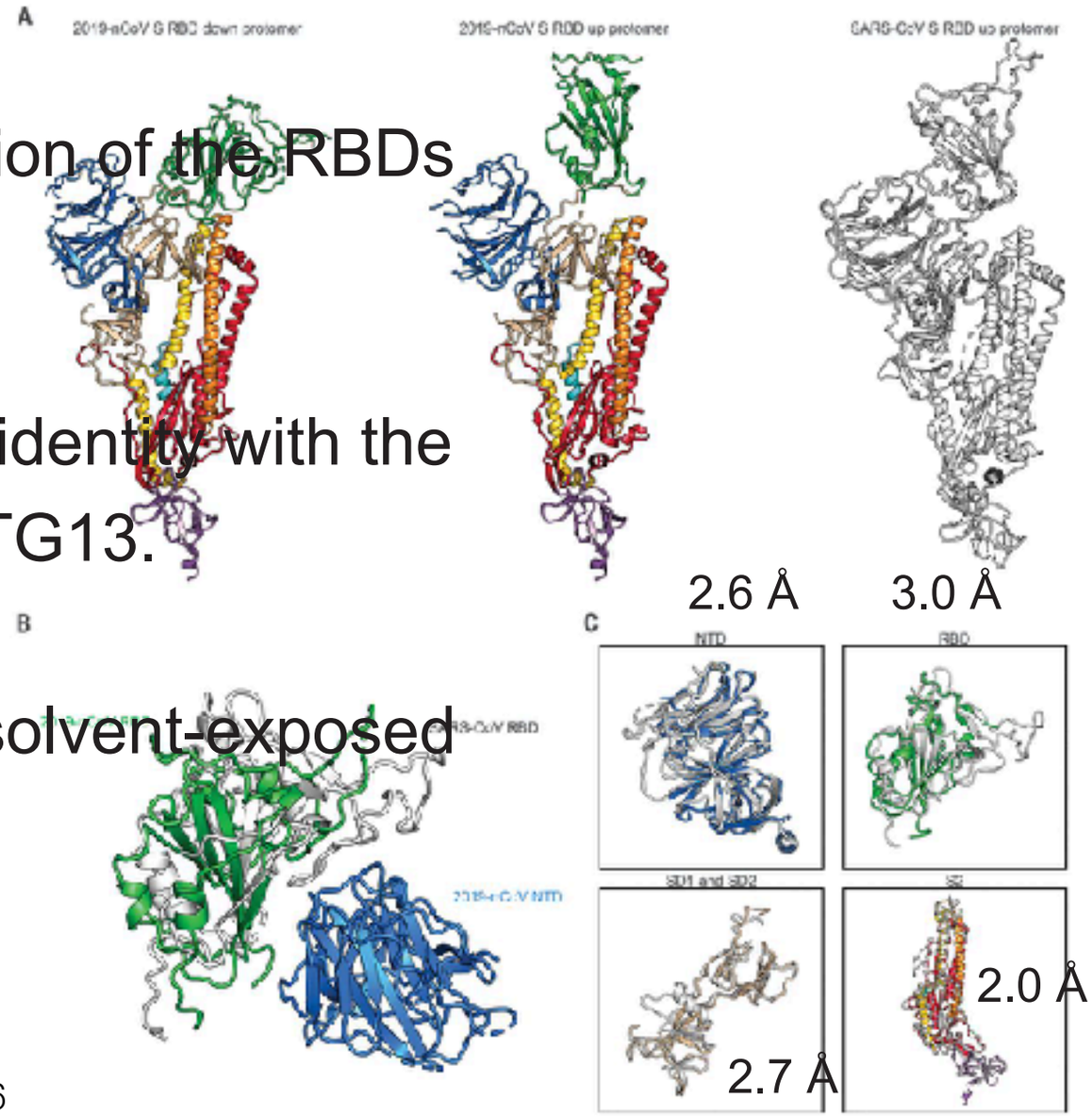
RMSD of SARS-CoV-2 with respect to SARS-CoV turns out to be 3.8 Å over 959 Cα atoms.

PDB ID: 6CRZ

One of the major difference is the position of the RBDs in their respective down conformations.

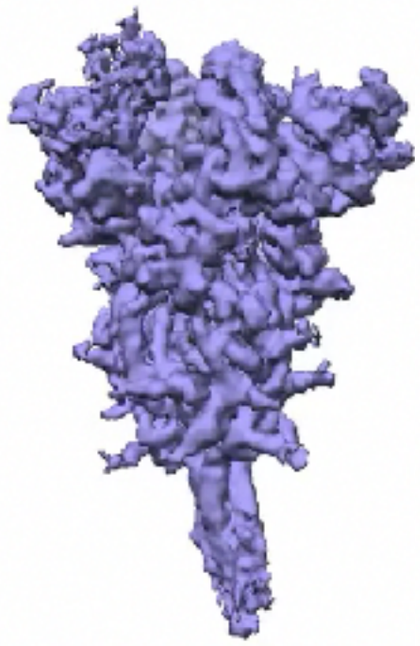
SARS-CoV-2 S shares 98% sequence identity with the S protein from the bat coronavirus RaTG13.

The S1/S2 junction is in a disordered, solvent-exposed loop.

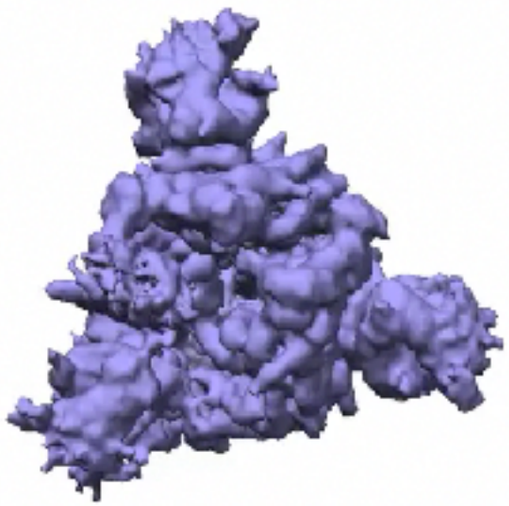


Wrapp et al., Science , 367, 1260–1263 2020

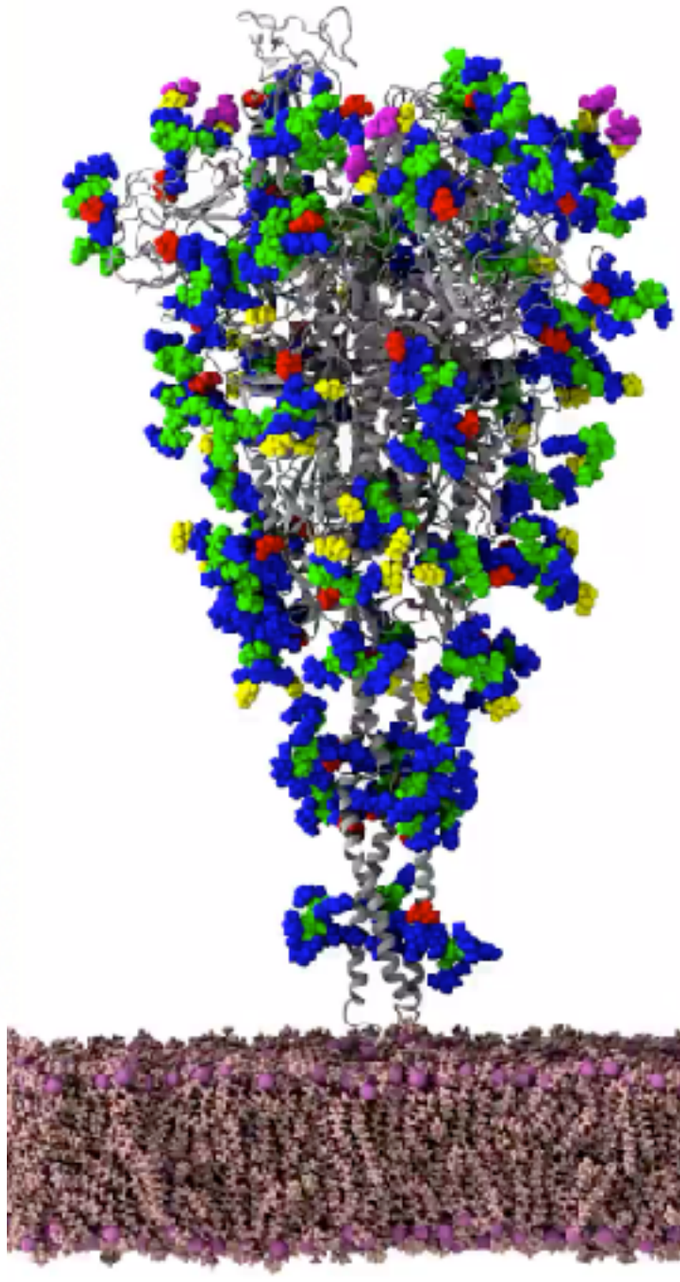
Breathing of S1 subunit as RBD undergoes hinge like motion visualized through CryoSPARC 3D variability analysis



Side View



Top view



This breathing mode could be responsible to the poor resolution of

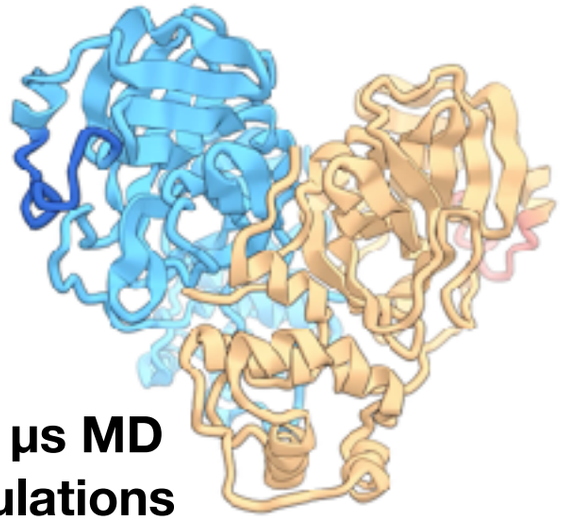
Wrapp et al., Science , 367, 1260–1263 2020

17 MD simulation of 6VSB in POPC

Credit : Rommie Amaro twitter

MD simulation related to SARS-CoV-2 on ANTON2

COVID-19 main protease with unliganded active site



100 μs MD simulations in ANTON2

PDB ID : 6Y84

C.D. Owen et al, 2020.
X-RAY DIFFRACTION 1.38 Å.

0.0 μs

SARS-CoV-2 spike glycoprotein

Walls et al Cell, 2020.

10 μs MD simulations in ANTON2

PDB ID : 6VXX (Open state)

ctron Microscopy 2.8 Å.

PDB ID : 6VYB (Closed state)

Electron Microscopy 2.8 Å.

Credit : D.E. Shaw Research
http://www.deshawresearch.com/resources_sarscov2.html