

The viral cycle overview

- 1. Attachment**
- 2. Entry (uncoating)**
- 3. Transcription**
- 4. Translation**
- 5. Genome
Replication**
- 6. Assembly (and
Maturation)**
- 7. Exit (Egress)**

Viral (life?) cycle entails all steps beginning from an entry of a viral particle (virion) into a host cell until the exit of new virions from that cell.

What is the difference between a viral particle and a virion?

Mol. Virology 2 - 2025/6

1. The entry (and attachment) of the virus into the cell is an active process!

Reaching the genome replication site (entry) includes:

endocytosis,

membrane fusion,

movement of vesicles within the cell,

entry into the nucleus for some viruses.

1. **Attachment** (of a virus to the surface of target cells):

On the surface of the virus are attachment structures -virus (glyco) proteins, “antireceptors”, and on the cell surface are receptors that correspond to them in structure and charge.

Capsid or envelope (glyco)proteins (peplomers, spikes, projections) are important for the attachment.

- Phages – host range/specificity of a virus is determined on the level of attachment.
- Phyto- and Mycoviruses regulate host range differently.
- Animal viruses – attachment mostly determines host specificity, but virus tropism too (tissue and cell types where a virus can invade and replicate therein).

Do all viruses attach to the cell surface prior to entry?

- Plant virus specificity is determined at the genome transcription (replication) level.

TMV-A replicates in tomato



RNA TMV-A + capsid TMV-B

TMV-B no replication



RNA TMV-B + capsid TMV-A

- Phytoviruses have a specific problem to solve – virion passage to new host cells inside a plant host. Why?
- Solutions:
 - a) Only a genome is transported (+RNA) aided by a movement protein (MP) through plasmodesmata,
 - b) or a whole virion is trafficked through a tubule inserted into plasmodesmium to enlarge it (enlarging *size exclusion limit*).

Families and Genera of Viruses Infecting Bacteria

+ Archaea

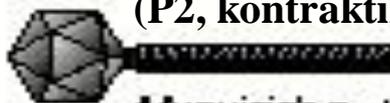
dsDNA

ssDNA

Thermoproteus
virus 1

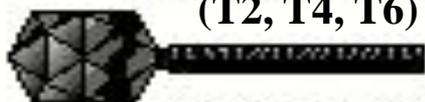


(P2, kontraktilan rep)



Myoviridae, isometric head

(T2, T4, T6)



Myoviridae, elongated head

(λ, T1, T3, T5)



Siphoviridae, rigidan rep



Podoviridae (T7)

Lipothrixviridae



"SNDV-like viruses"

ovojnica,
(MV-L2)



Plasmaviridae



Corticoviridae (PM2)



Fuselloviridae



Tectiviridae



Rudiviridae

(φX 174,
spiroplazma-fag 4)

Microviridae



(MV-L51)

Inoviridae
Plasmavirus

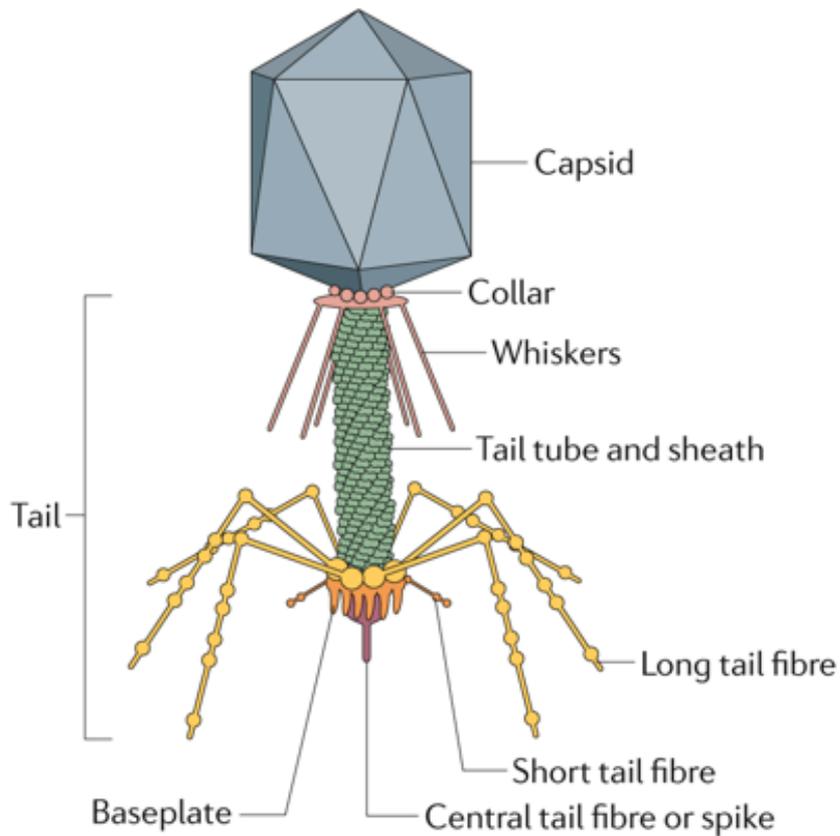


Inoviridae
Inovirus

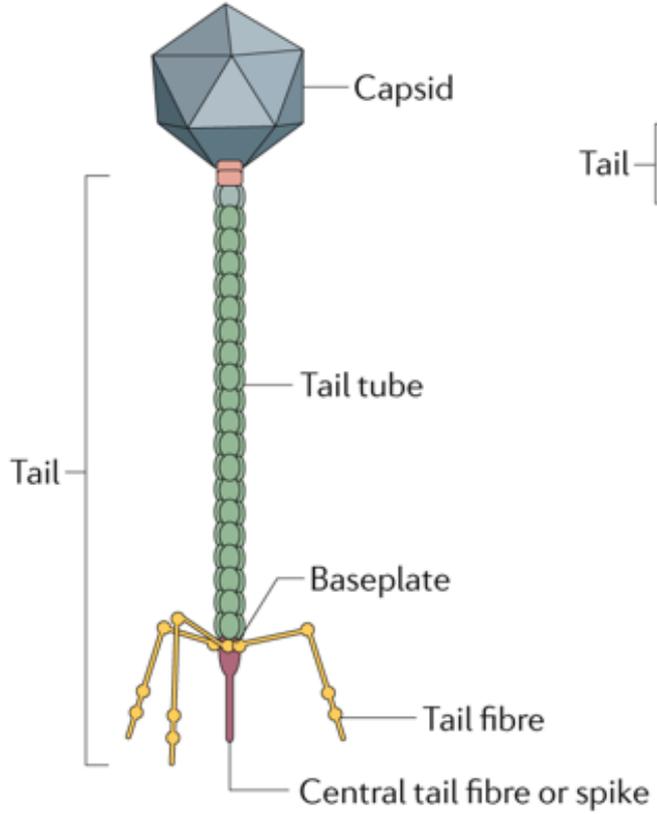
(f1, fd, M13)

DNA

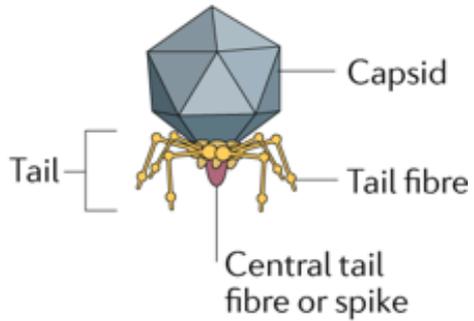
a Myoviridae



b Siphoviridae



c Podoviridae



Families and Genera of Viruses Infecting Bacteria

RNA

dsRNA



Cystoviridae

100 nm

ssRNA



Leviviridae

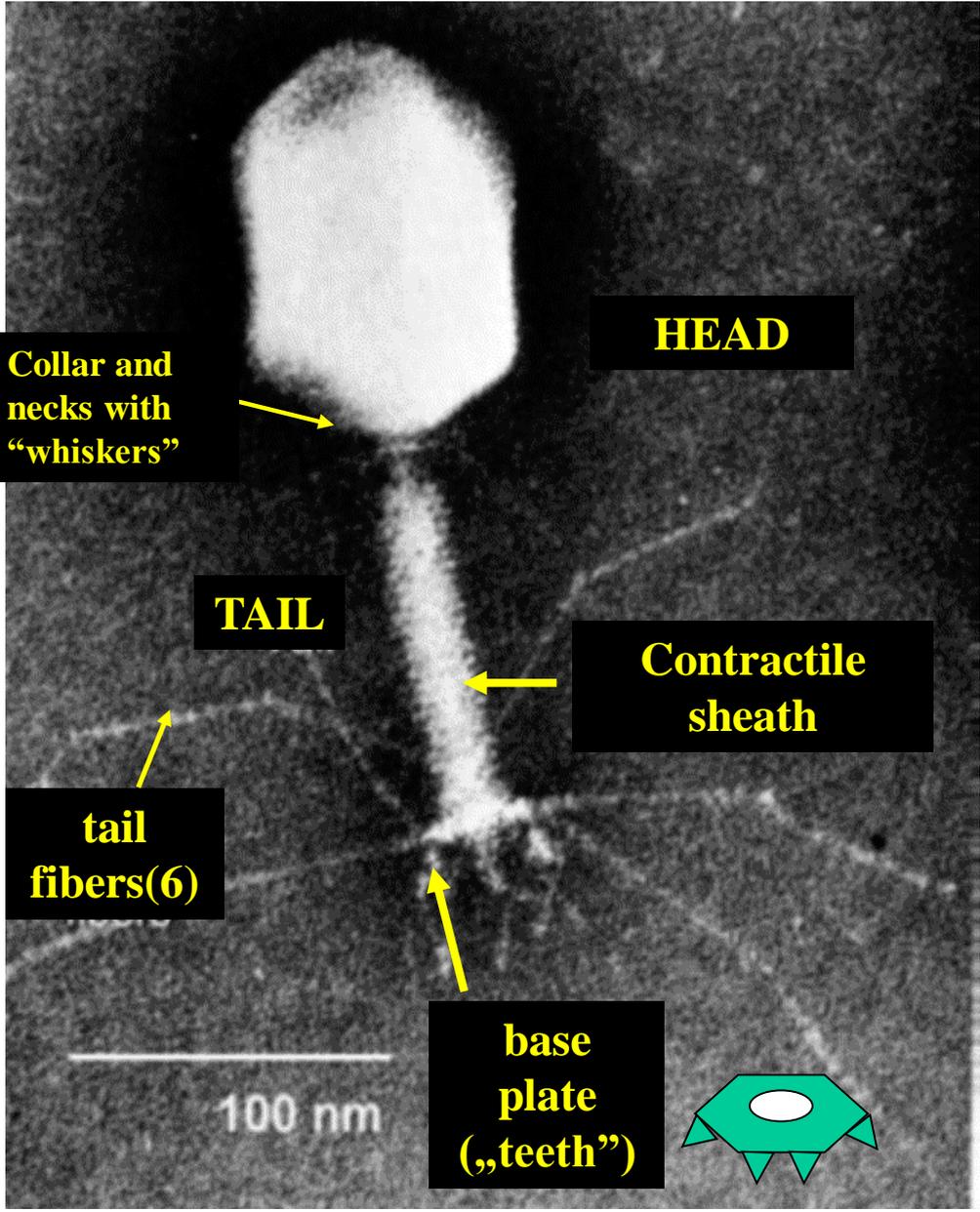
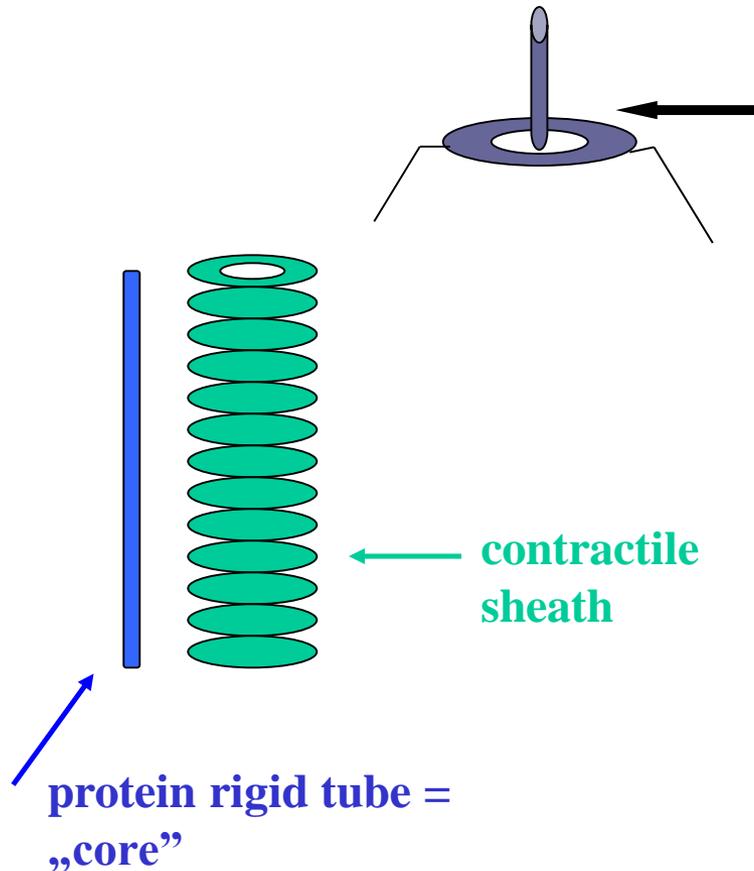
capsid+envelope, $\phi 6$

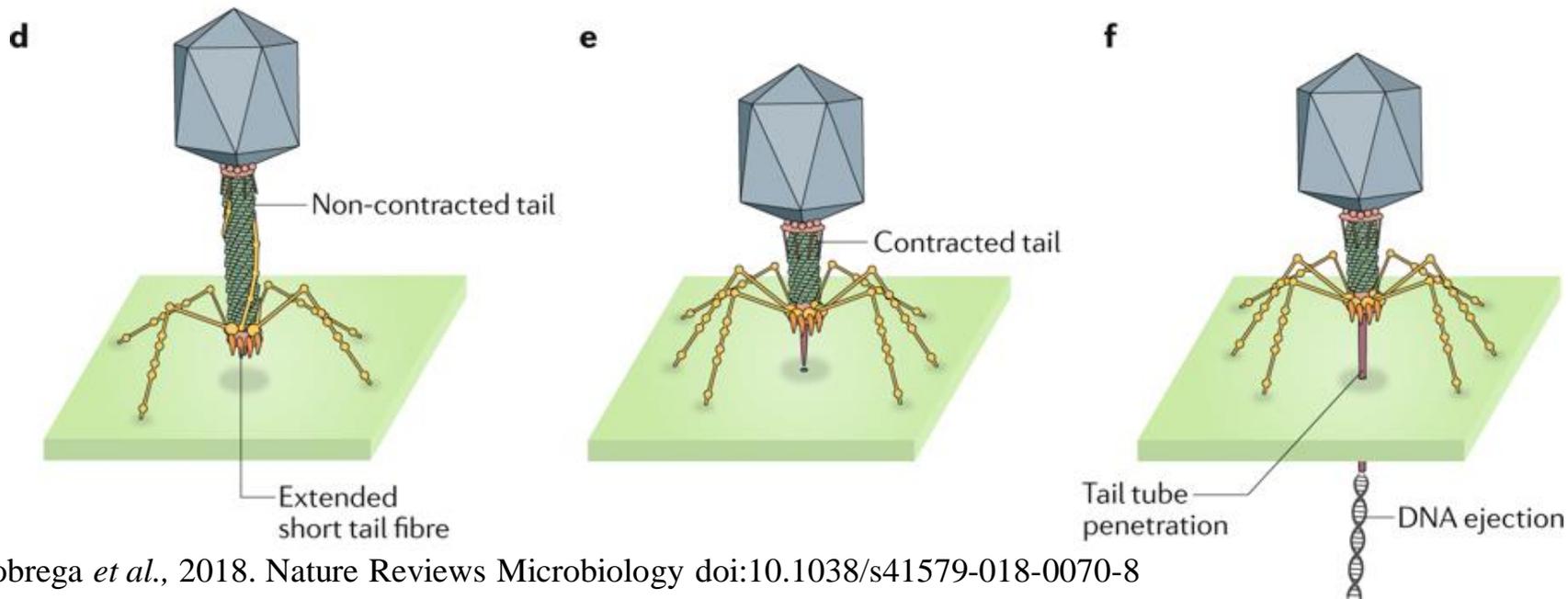
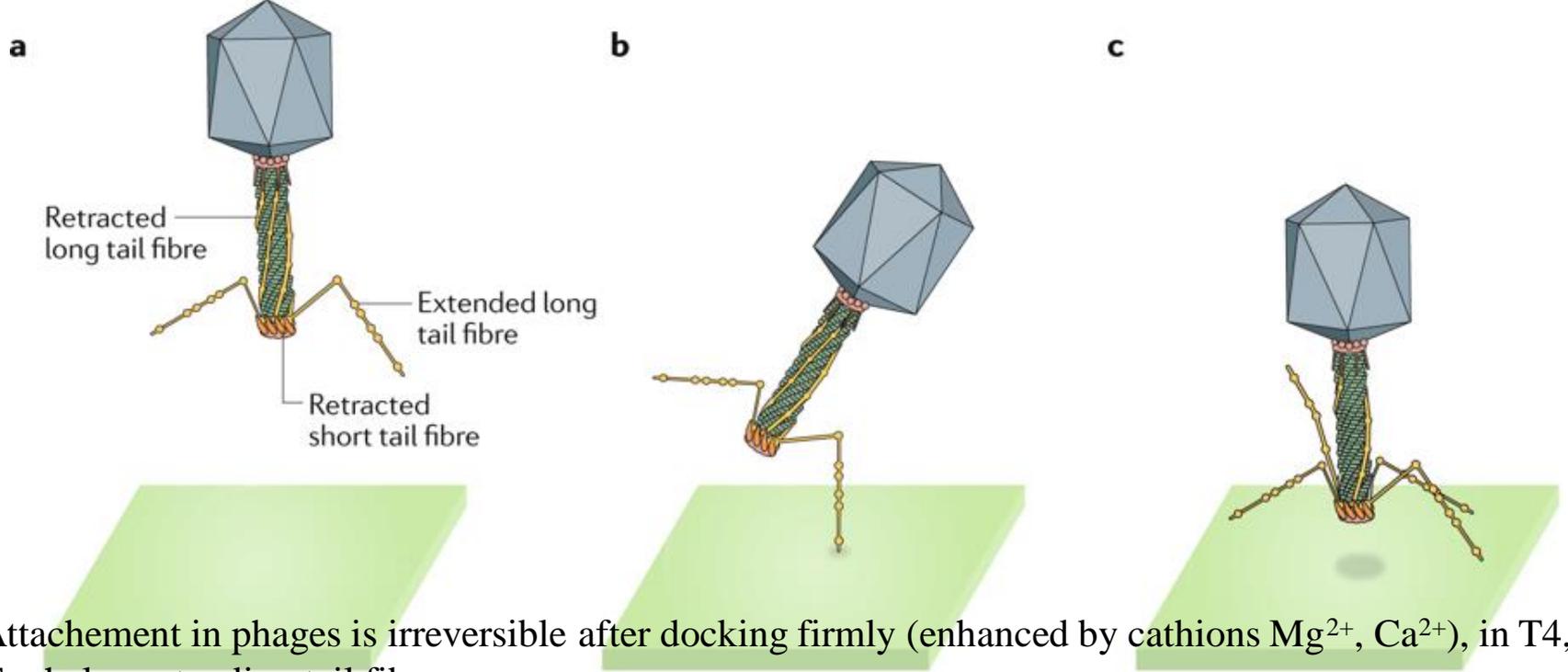
unenveloped, MS2, Q β , f2

• Phage attachment depends on the phage type

T4 coliphage – d = 80 nm, l = 200 nm

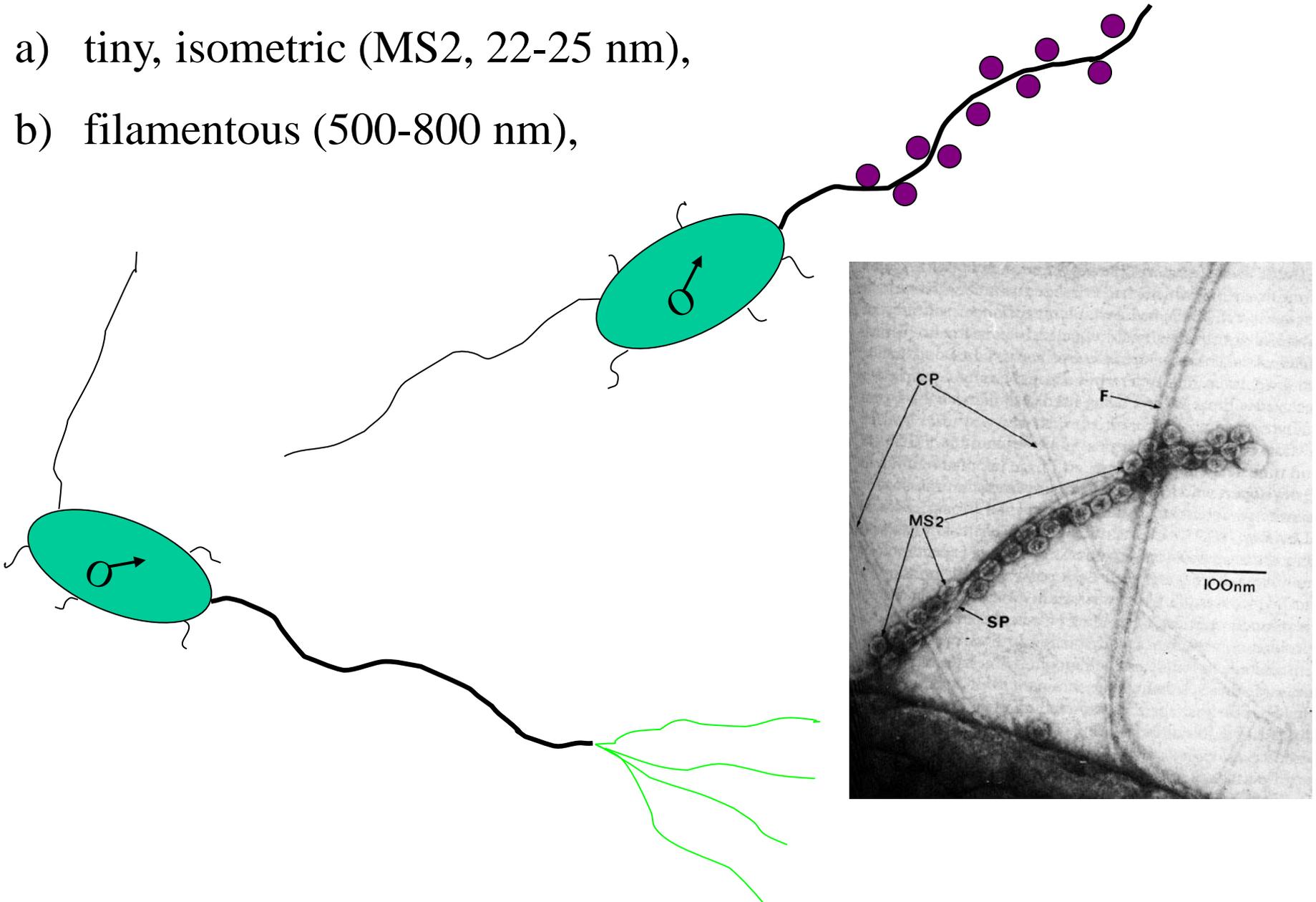
Escherichia coli strain B





Androphage attachment:

- a) tiny, isometric (MS2, 22-25 nm),
- b) filamentous (500-800 nm),



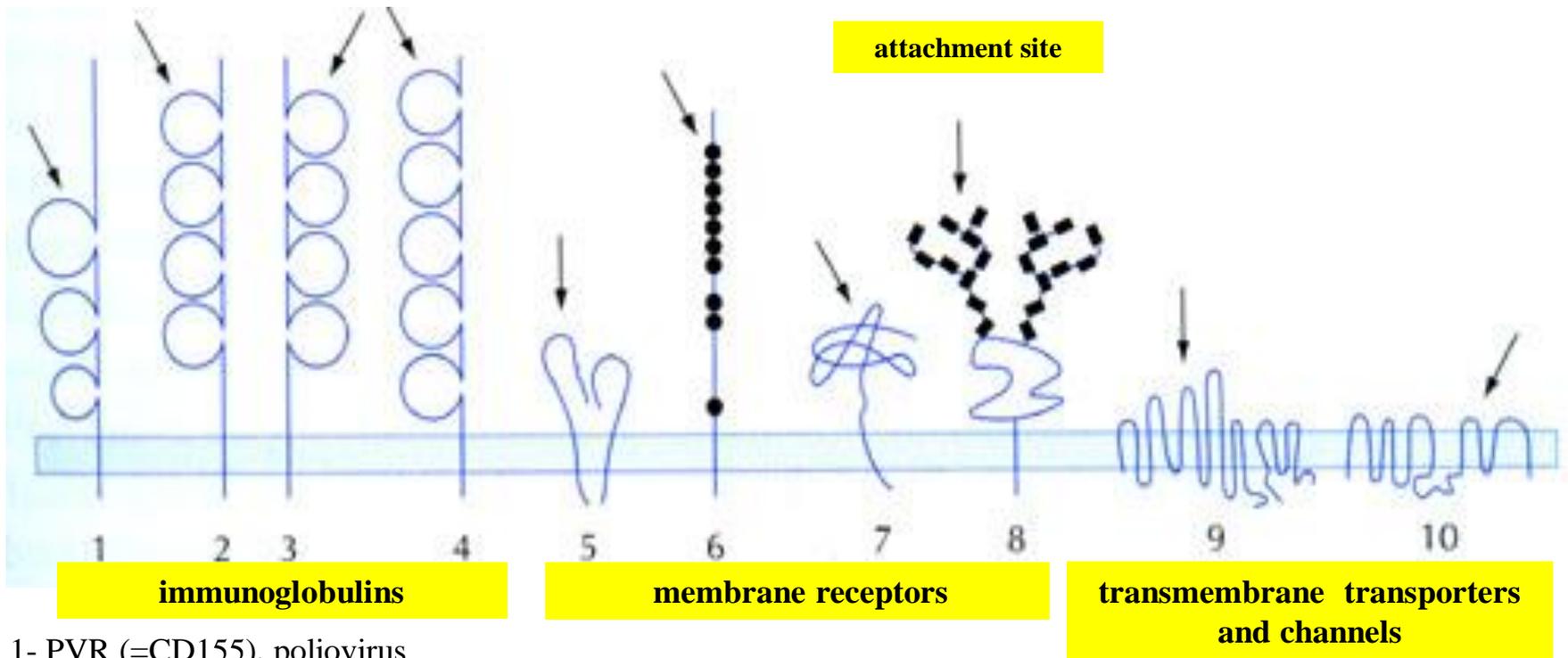
What type of molecules are cell receptors?

Proteins (usually glycoproteins - specific receptors) or carbohydrate components of them or glycolipids (less specific).

One virus species can use more than one receptor (herpes virus).

Different viruses can use the same receptor.

Some viruses need a receptor and a coreceptor (HIV-1).



1- PVR (=CD155), poliovirus

2- CD4, HIV

3- carcinoembriogenic antigens , coronaviruses

4- ICAM-1, rhinoviruses

5- VLA-2 integrin, echoviruses

6- LDL-receptor, rhinoviruses

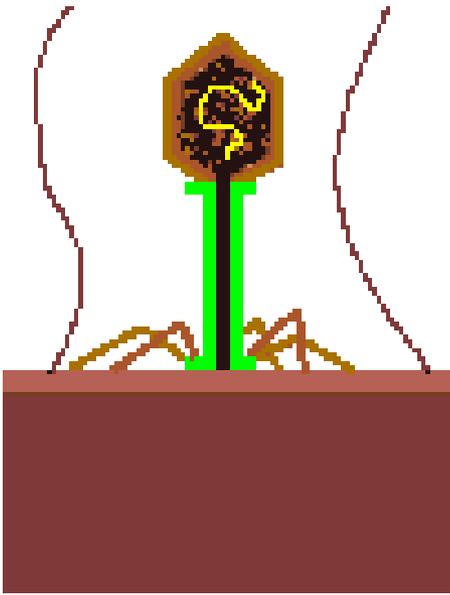
7- aminopeptidase N, coronaviruses

8- sialic acid - influenza, reoviruses, rotaviruses

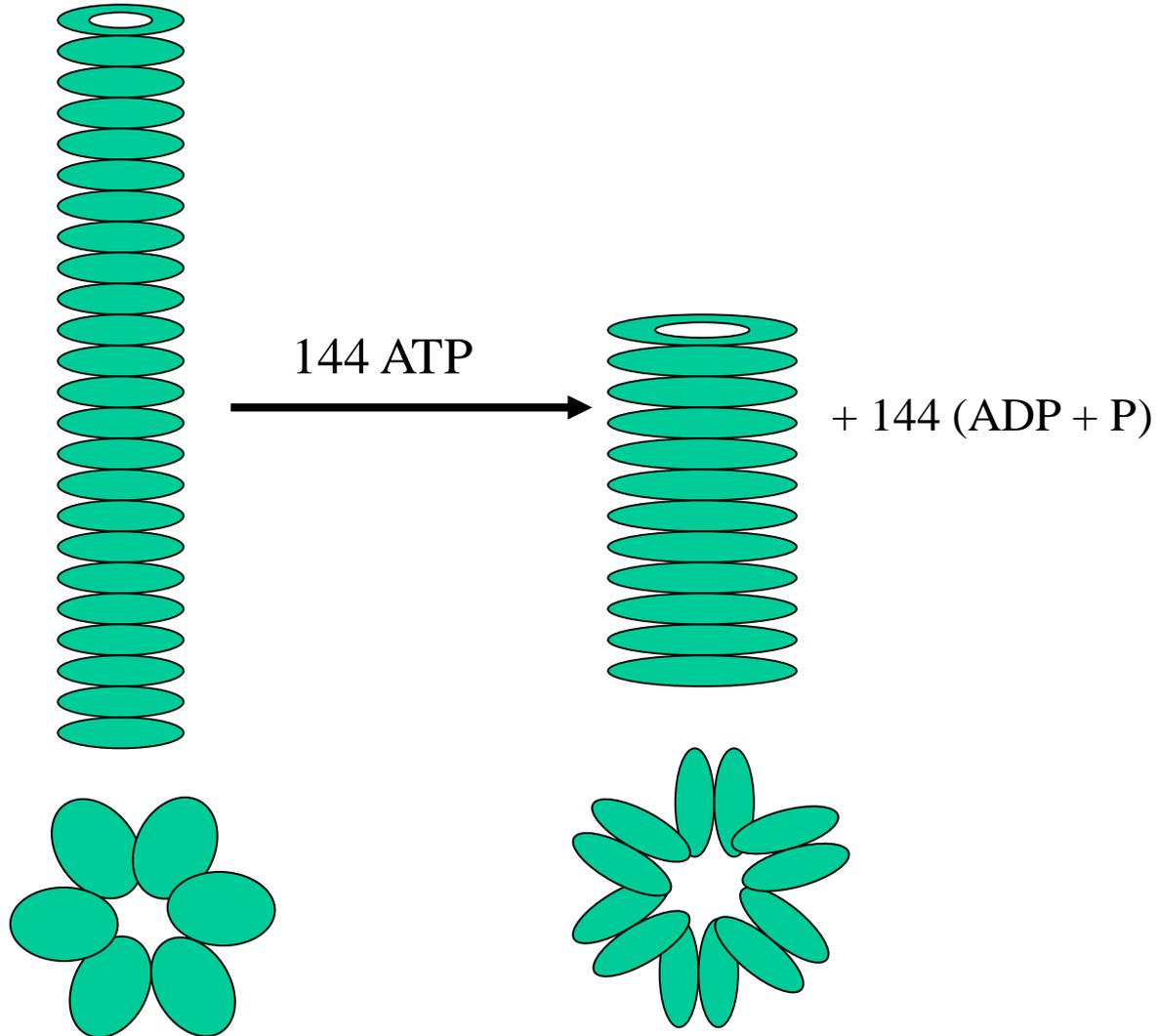
9- cation transporter of amino acid, murine leukemia virus

10- Na- dependent phosphate receptor, gibbon leukemia virus

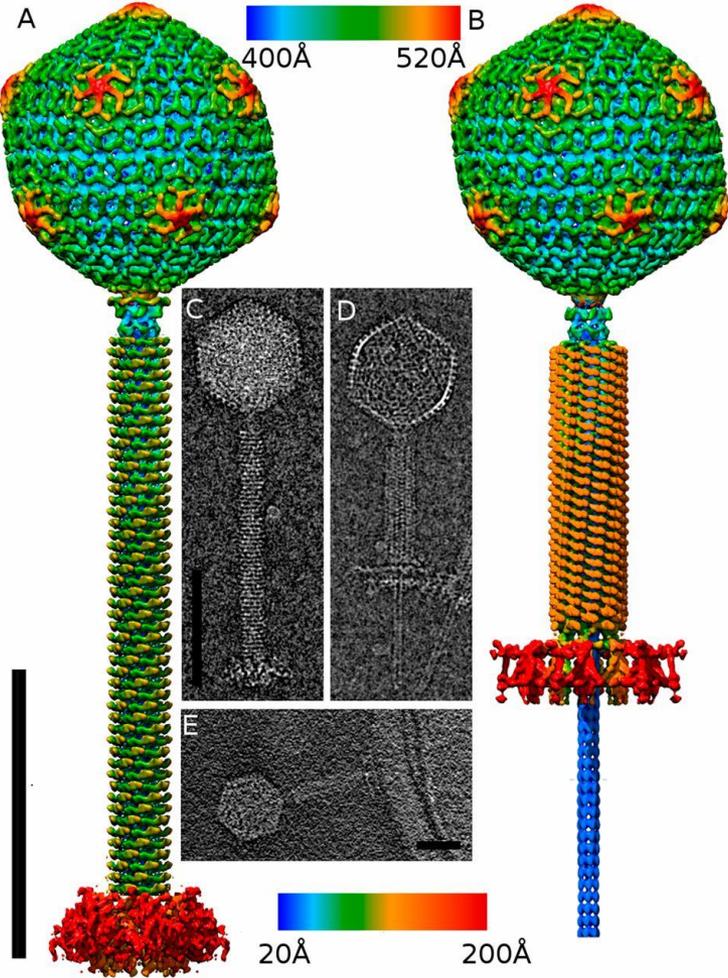
2. Entry (penetration) – a genome enters the cell, immediately after attachment, only in live cells (energy!). Mostly in cytoplasm, but some travel to nucleus or to other places?



Phage chemically and physically disrupts bacterial cell wall (on glycoside bond between N-acetyl muraminic acid and N-acetyl glucosamine).

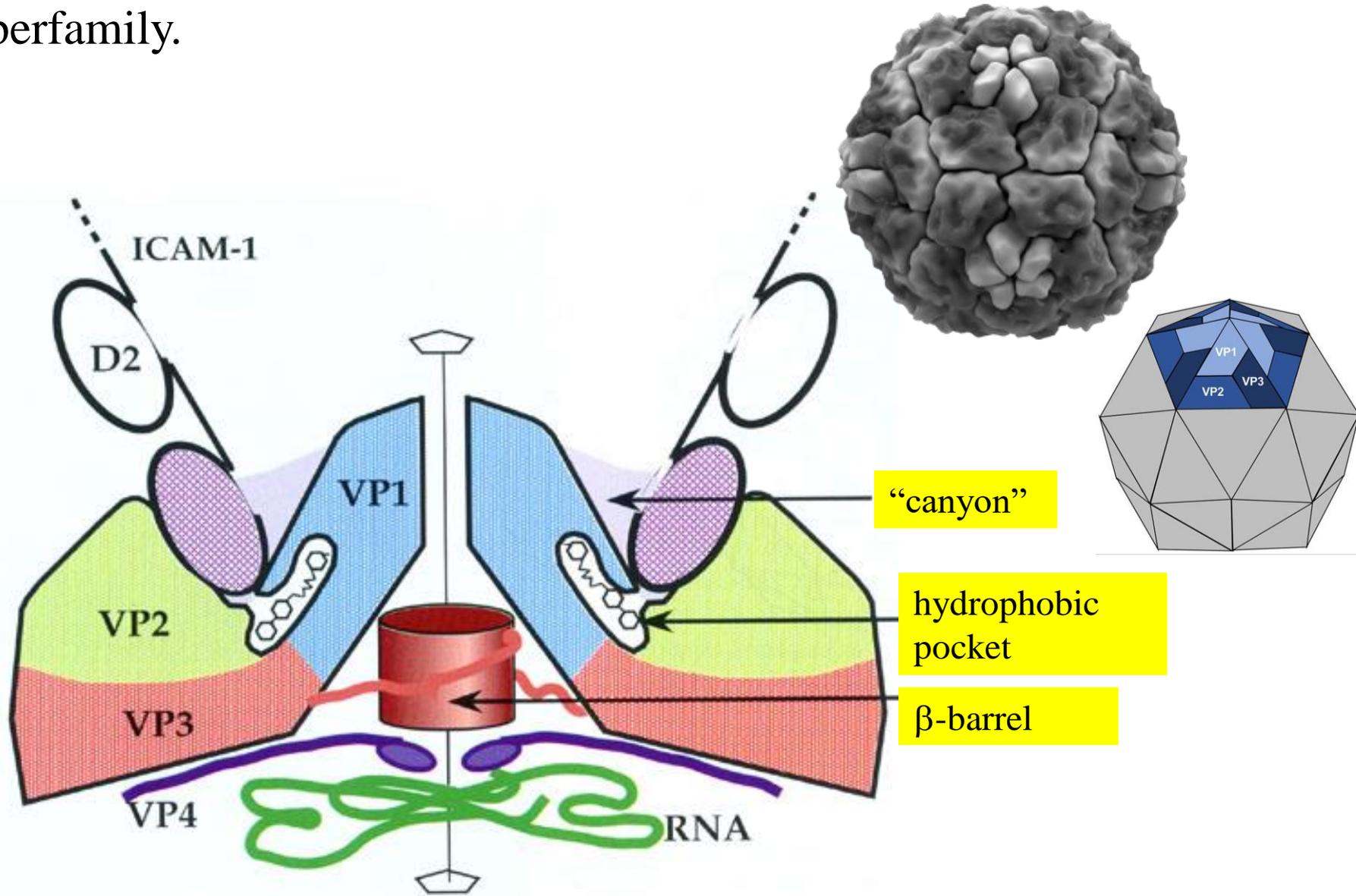


Virions of bacteriophage phi812 in native conformation (A) and after tail contraction (B).



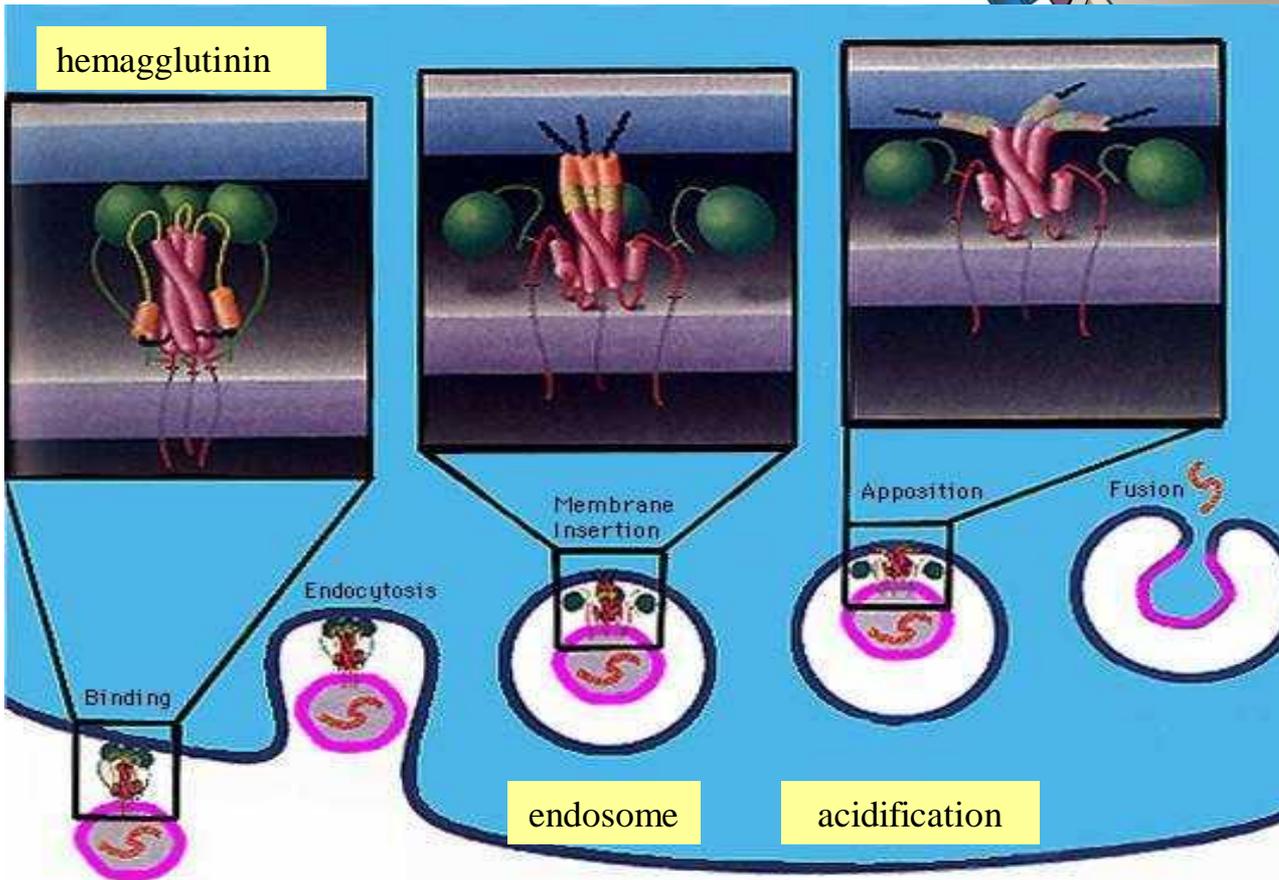
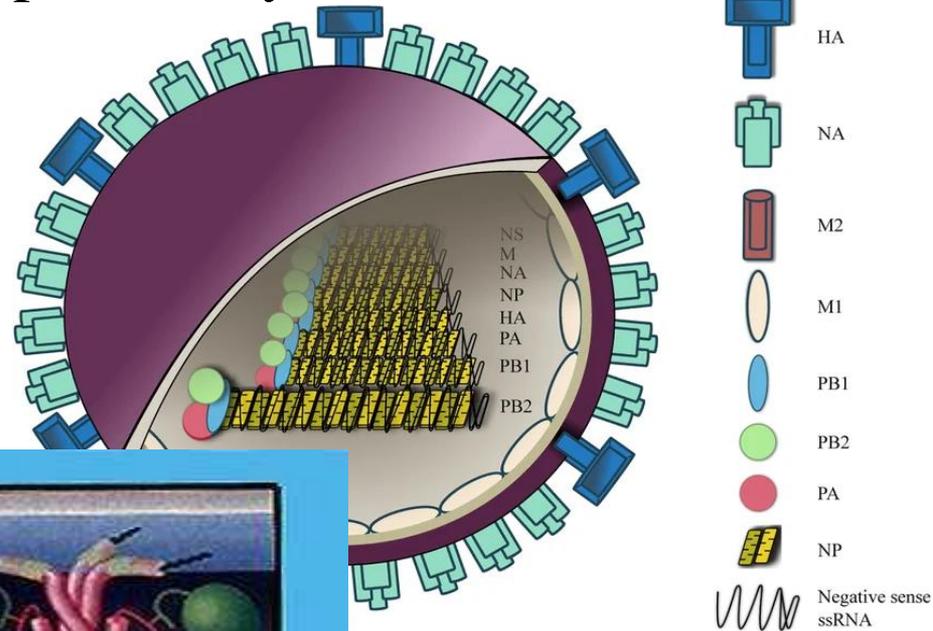
Jiří Nováček et al. PNAS 2016;113:9351-9356

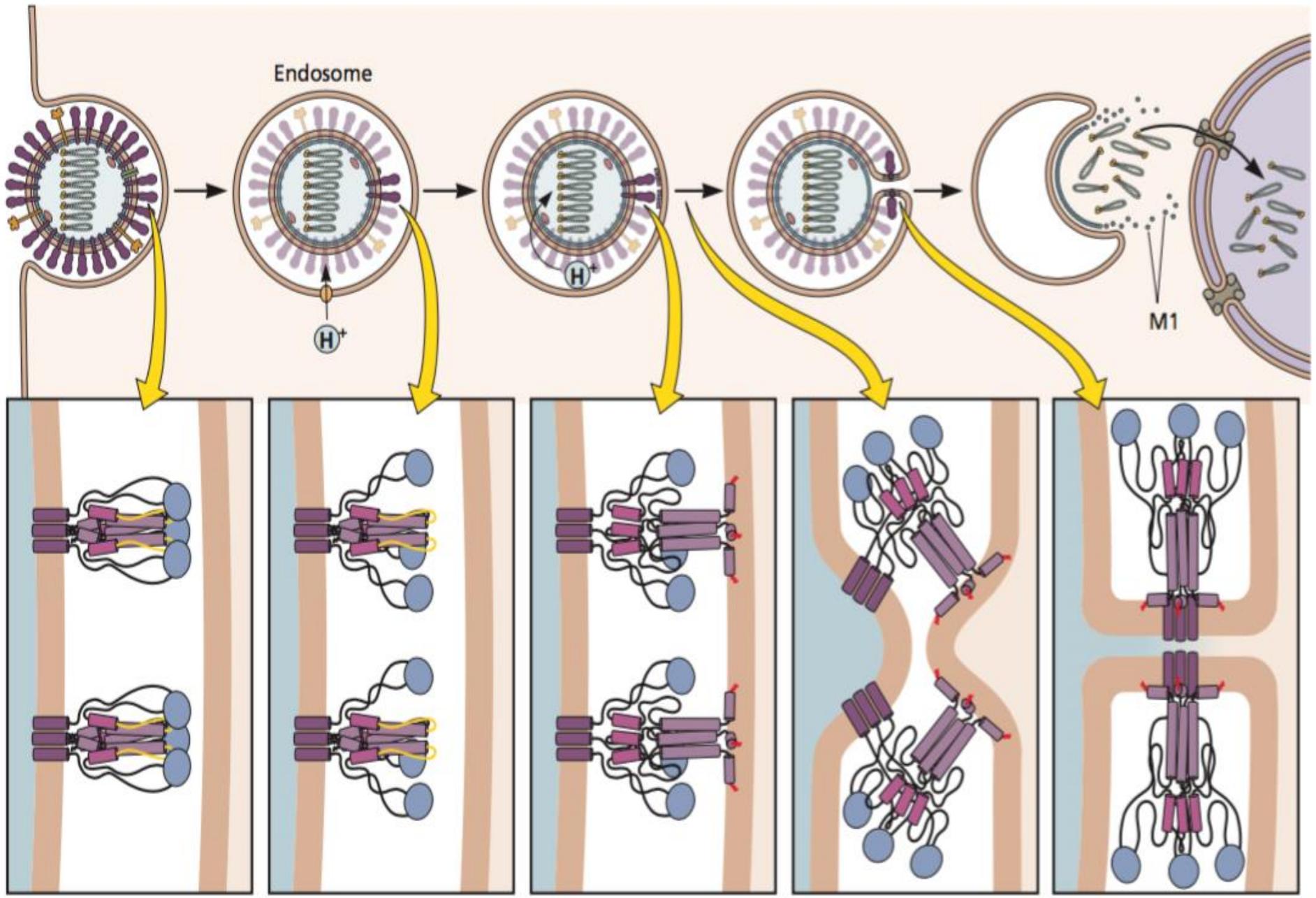
Human rhinovirus entry (HRV, *Picornaviridae*) - ICAM-1 (*intercellular adhesion molecule-1*) receptor, immunoglobulin superfamily.

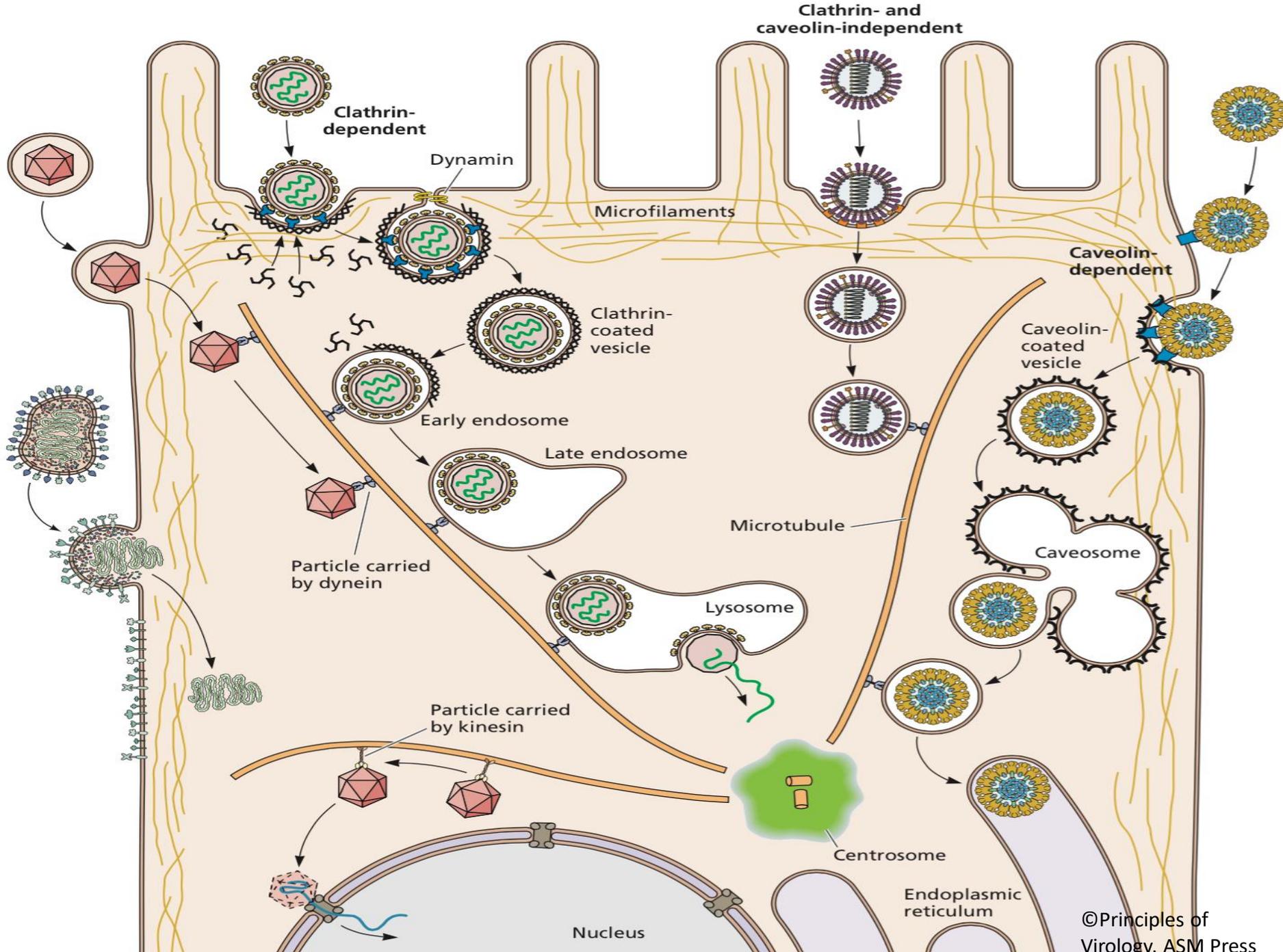


• endocytosis is the most frequent type of entry

– influenza A virus (IAV)







3.-5. Multiplication of the genome and virus proteins

Phages and some animal viruses insert only genome into a cell, most animal viruses enter with nucleocapsid. It needs to be uncoated to start transcription and translation of the genome.

The genome is uncoated and resources of the cell found to do these processes. Where?

Enzymes needed for nucleic acids synthesis: DNA- and RNA-polymerases (which ones?), endonucleases, exonucleases, ligases, topoisomerases...

Most of the viruses discovered before the age of metagenomics change the and organism cell metabolism. Others latently infect their hosts (iceberg effect).

An official website of the United States government [Here's how you know](#) ▼

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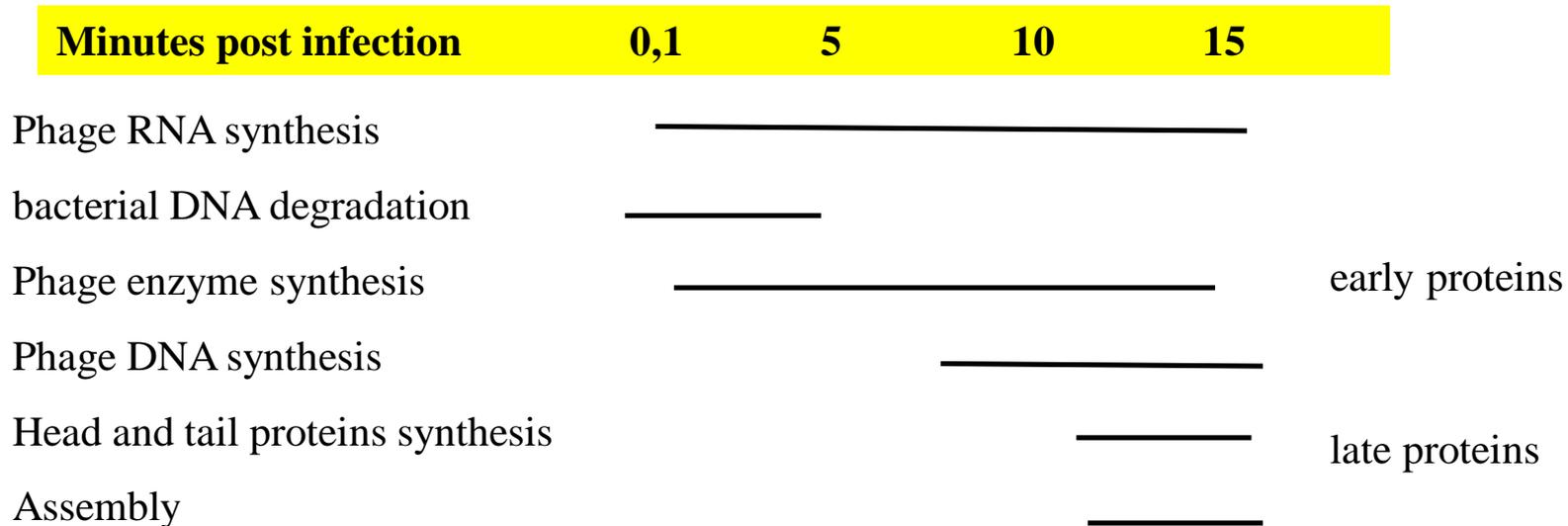
Ninety percent of an iceberg is below the waterline.

By [Water Science School](#)



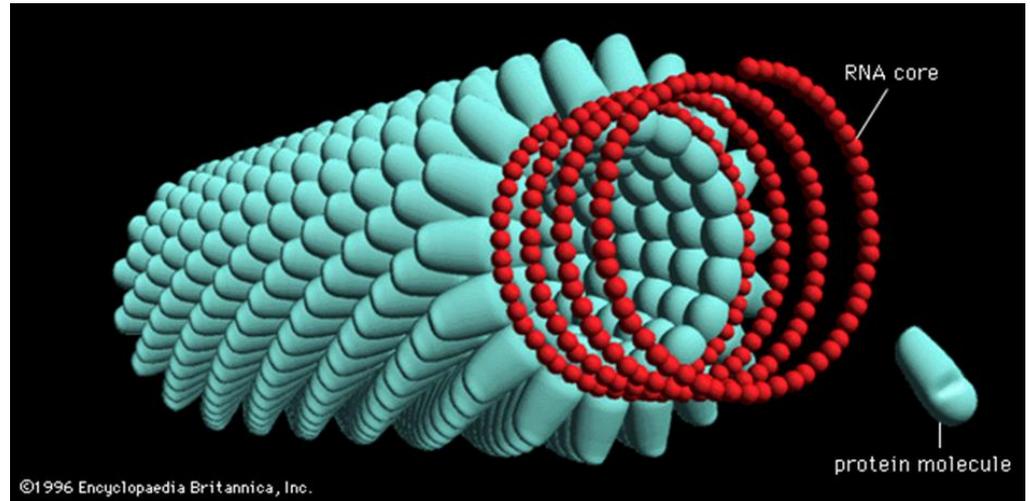
Phage induced changes at the level of cellular nucleic acids:

- 1) Stops or changes host DNA synthesis
- 2) Changes or disrupts host mRNAs
- 3) Stops host mRNA synthesis because it changes RNA polymerase (T4)
- 4) Disintegrates host DNA, phage DNA is tagged and protected (5-methyl cytosine)
- 5) Changes ribosomes – higher affinity for viral mRNAs
- 6) Modifies cell tRNAs and makes those better adapted for the virus



6. Assembly (of virus particles)

Structural components are assembled and basic structure of the virus particle is made. It does not have to be a final one!



The assembly location depends on the virus:

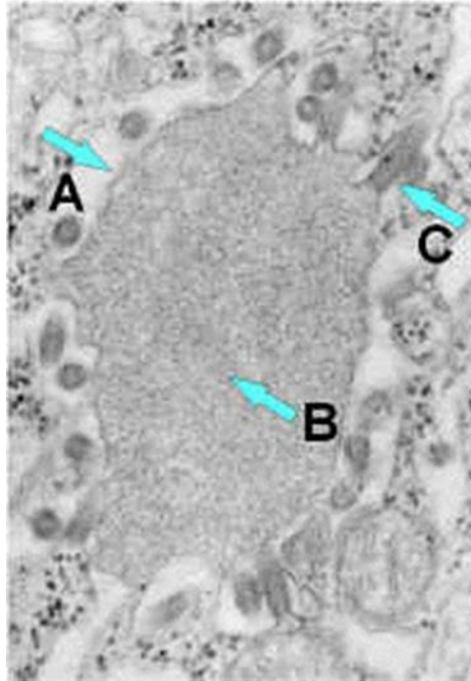
picorna, pox, reoviruses in the cytoplasm,

adeno, polyoma, parvo viruses in nucleus.

Cell membrane – after reaching critical level, viral (glyco)proteins are anchored into the membrane in parallel to viral assembly.

Control of the processes is important, both temporal and spatial.

Some viruses compartmentalize the building blocks into a cell – inclusion bodies – e.g. Negri bodies (rabies virus).



Particle formation is a simple process determined by the rules of symmetry and interactions between capsid proteins in some viruses.

In others, stepwise and complex - viral structural proteins, other v. proteins, cell skeletal proteins participate in the process as “scaffolding” but are not part of the virion.

- **Maturation** – viral particle becomes infectious (virion).

Specific cleavage of capsid proteins and formation of mature products, or conformational changes in the protein during particle constitution.

Picornaviruses - strongly altered antigenicity during maturation.

Condensation of proteins and genomes within the nucleocapsid for many DNA viruses.

Viral proteases may be involved in maturation - very specific peptide bond cleavage reactions.

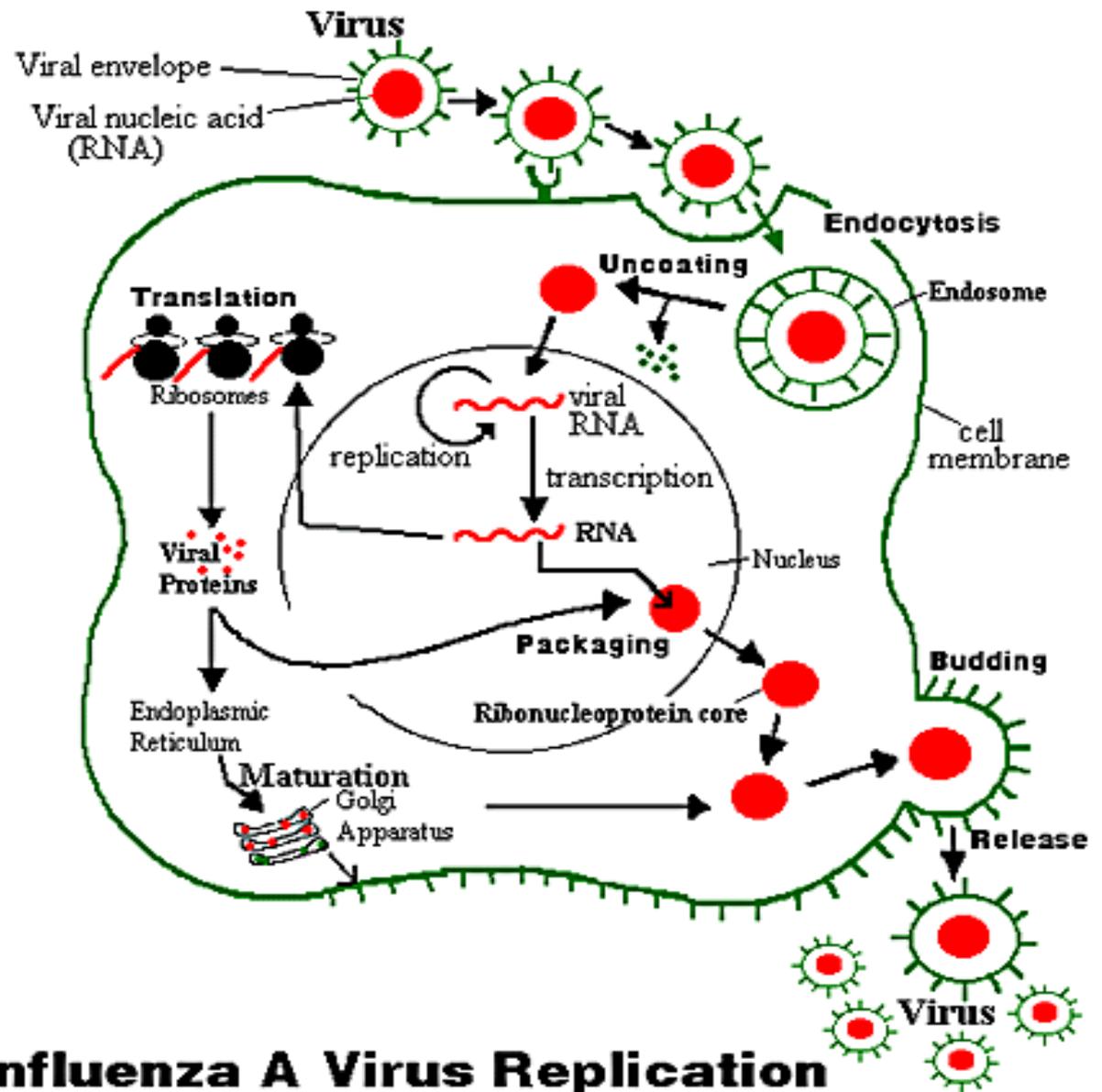
Sometimes cellular enzymes are involved (e.g. furin) or cellular and viral.

7. Exit (Egress)

For most unenveloped viruses, the exit is lytic (phage lipase, lysozyme; poliovirus), and the enveloped bud out through the cell membrane (retro, toga, ortomyxo, paramyxo, bunya, corona, rhabdo, hepadna; f1 and fd-phages, as opposed to endocytosis) or into the intracellular structure (tubules, ER vesicles, intercellular junctions) and then exit out of the cell.

Budding can immediately cause cell damage (paramyxo, rhabdo, toga viruses) or not (retroviruses).

For some viruses the regulation of exit is well studied (neuraminidase - IAV), temporal and spatial regulation must be very precise of all late steps in the cycle (assembly, maturation, exit). These phases often overlap.



Influenza A Virus Replication

Homework:

Is this representation of IAV cycle correct?

Learning outcomes

You should be able to:

- Define a viral cycle
- Differentiate critical steps in a cycle
- Define prerequisites (molecular components of cells and a viruses) for completing each step of the cycle in some viruses of bacteria, plants and humans
- Explain molecular basis for viral specificity and tropism
- Understand in depth influenza A virus entry
- Explain some of the viral effects on host transcription, translation and defense
- Explain the importance of knowing details of a virus cycle for its host range, pathogenicity, and disease prevention

