Viral Adsorption/Entry/Penetration MIC 204

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Viral Life Cycle: 5 major stages

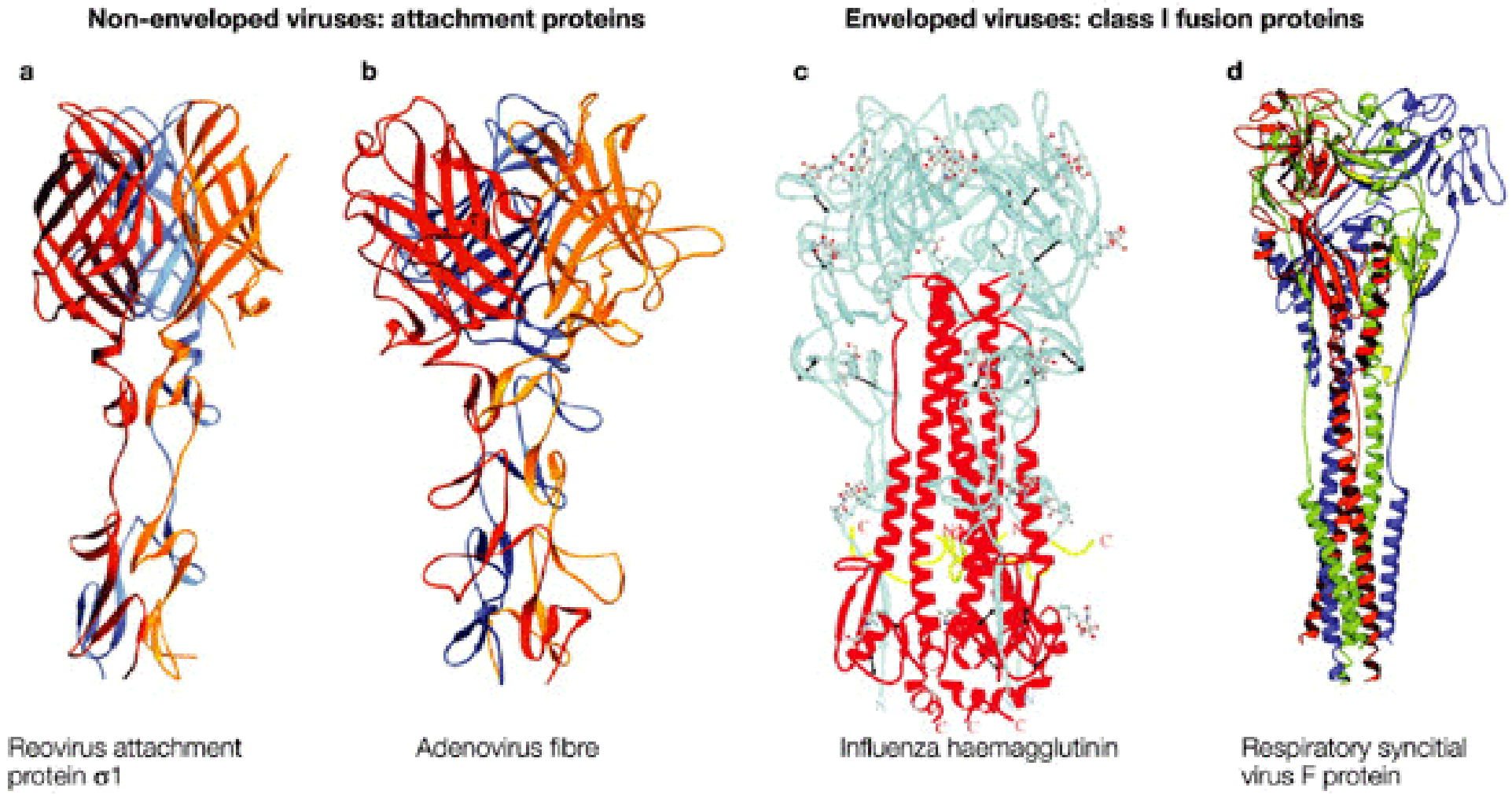
- Attachment
- Entry
- Uncoating
- Replication
- Assembly
- Release

Viral Adsorption/Attachment

- Viral adsorption is defined as the specific binding of a **virus** to a cellular (host) receptor. It is a receptor to ligand interaction in which **viruses** function as specific ligands and **bind** to the receptors present on the cell **surface**.
- Virus–receptor interactions play a key regulatory role in
  - viral host range
  - tissue tropism, and
  - viral pathogenesis
  - Diagnosis
  - Vaccine and antiviral drug
- Lock and Key model

Viral entry proteins

- Diverse structure, amino acid sequence and functions
- Viral attachment proteins: 10 nm protusions/spikes/canyons
- Non enveloped viruses- small and stable oligomers(several XRD structures)
- Enveloped Virus entry proteins are divided depending on several criteria, including
  - mechanism of action,
  - whether the entry protein is cleaved and
  - whether the entry protein is complexed with other viral proteins.



Dimitrov, D. Virus entry: molecular mechanisms and biomedical applications. *Nat Rev Microbiol* **2,** 109–122 (2004). https://doi.org/10.1038/nrmicro817

Viral attachment proteins

- Non-enveloped viruses; the viral proteins that are exposed to the environment and recognize receptor molecules from several plant, insect and mammalian viruses contain the same basic core structure, which consists of an 8-stranded β-barrel with a jelly-roll motif
- Enveloped Viruses: Glycoprotein spikes homo or heteromers (external or transmembrane proteins. Structure is usually β-strands are packed in sheets, including a six-stranded β-barrel in the second domain, and an immunoglobulin-like β-barrel fold in the third domain
- CLASS I FUSION PROTEIN: Coiled-coils proteins, such as influenza HA, paramyxovirus fusion protein F and HIV glycoprotein 160 (gp160
- CLASS II FUSION PROTEIN: Envs proteins of alphaviruses and flaviviruses have been designated class II fusion proteins.
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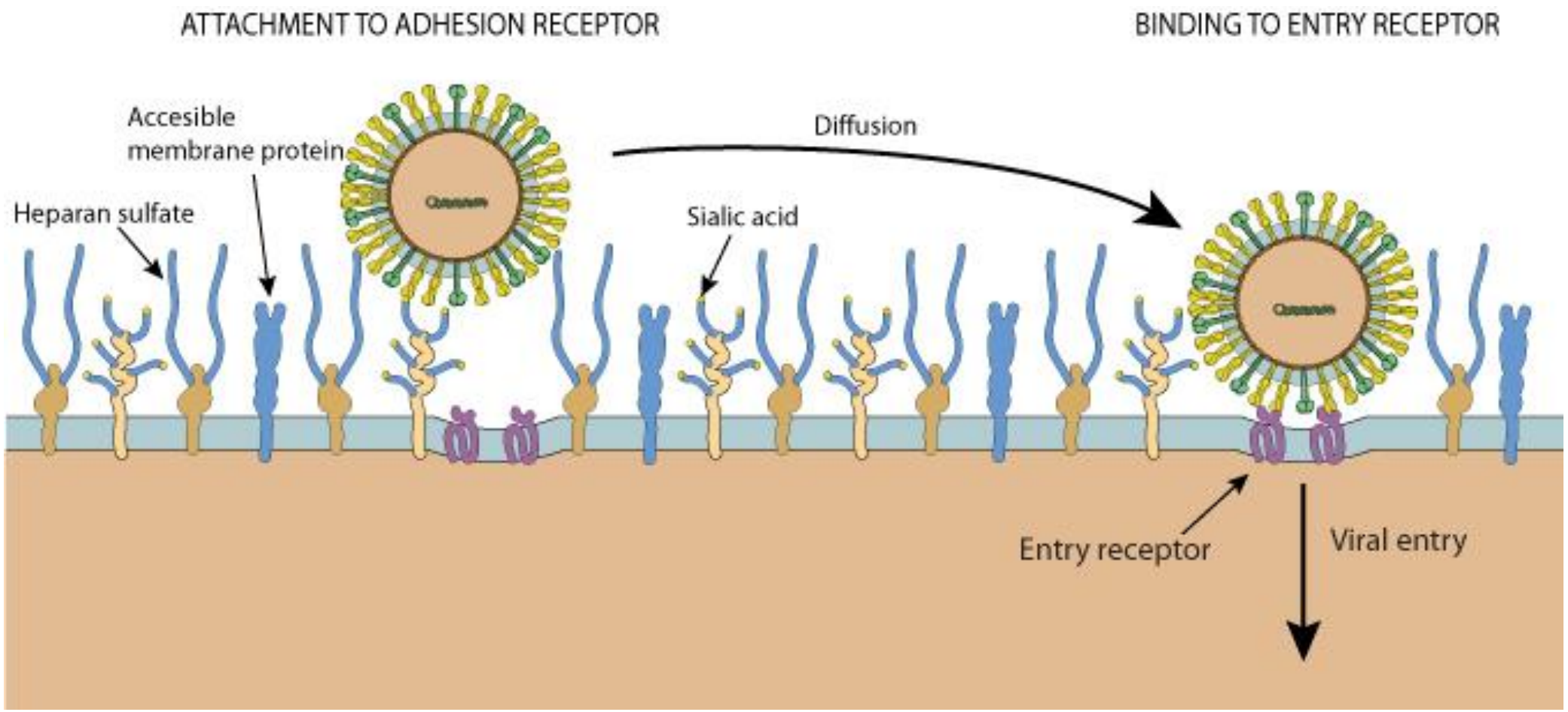
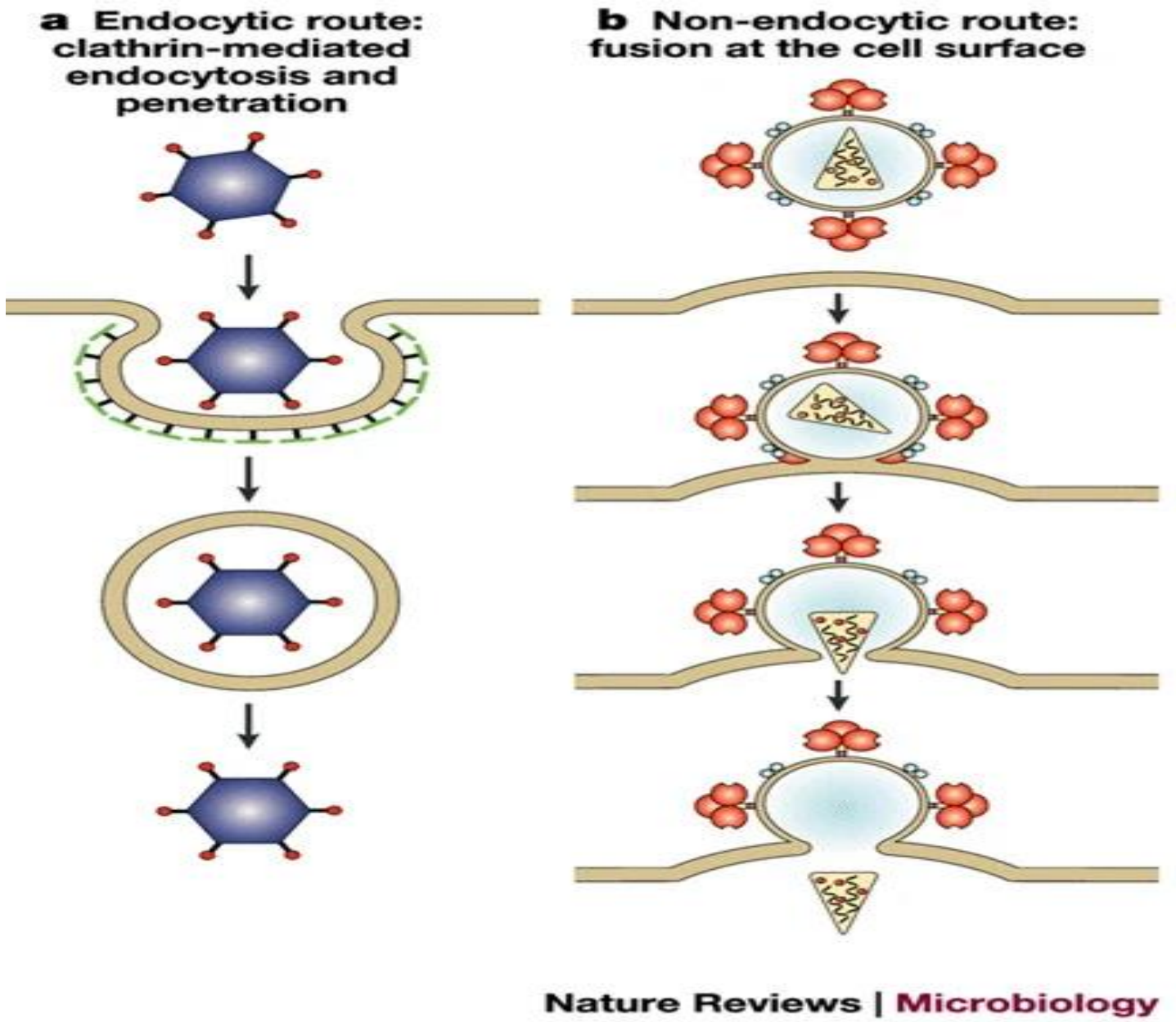
Viral receptor-Host Cell Receptors

- Cell receptors to virus can be classified in two classes: adhesion receptors are attaching the virus in a reversible manner to target cells or organs. This adhesion is not mandatory for virus entry, and alone do not trigger entry. Nonetheless it enhances significantly infectivity by concentrating the virus in the vicinity of it's entry receptors. These receptors are triggering virus entry by endocytosis/pinocytosis or by inducing fusion/penetration, and the consequences of this binding are irreversible. They have often be named "co-receptors".
- **Virus attachment to target cells can involve different partners:**
  -Viral proteins that bind host glycans, receptor proteins, adhesion proteins or peptidases.
  -Viral glycans that bind host lectins.
  -Viral lipids that bind host receptor proteins.
- https://viralzone.expasy.org/956

Cell surface receptors





a | Clathrin-mediated endocytosis, for example, adenovirus. Endocytosis by caveolae can also occur, for example, SV40. **b** | Fusion at the cell membrane, for example, HIV.Fusion can also occur from inside an endosome, for example, influenza.

https://www.youtube.com/watch?v=D9OtJU3F6eQ

Table 2 | **Human viruses and host cell receptors**

Virus	Entry protein*	Receptor‡	Co-receptor	Alternative receptor§	Notes
Influenza A	Haemagglutinin	Sialic acid (mM)	Unknown	unknown	There are no indications that influenza needs co-receptor(s) for entry
HIV-1	gp160 (gp120)	CD4 (nM)	CCR5, CXCR4, other (nM–μM)	Galactosyl ceramide (μM)	Some HIV-1 isolates are CD4-independent and can use CCR5 or CXCR4 as receptors; affinities for co-receptors are higher in the presence of CD4; entry in the absence of CD4 is typically much less efficient.
SARS-CoV	S (S1)	ACE2 (nM)	Unknown	Unknown	
Herpes simplex virus 1 (HSV-1)	Glycoprotein D (gD)	HveA (μM)	Unknown	Unknown	Several other viral (gB, gC, and the heterodimer gH/gL) and cellular (heparin sulphate, nectin-1) receptors are implicated in the complex entry mechanism; a truncated form of gD exhibits 100-fold higher affinity for HveA
Poliovirus 1	Capsid shell (VP1, VP2, VP3)	CD155 (nM–μM)	Unknown	Unknown	CD155 is the receptor for all three serotypes; affinities forcell surface receptors significantly differ from those for soluble receptors and are also temperature-dependent.
Rhinovirus 3 (HRV3)	Capsid shell (VP1, VP2, VP3)	ICAM-1 (μM range)	Unknown	Unknown	Minor-group human rhinoviruses use VLDL-R as a receptor; there are structural similarities between ICAM-1 binding to capsid shell and CD4 binding to gp120.
Adenovirus 2	Fibre, penton base	CAR (nM)	αv integrins	Sialic acid and heparin sulphate proteoglycans	Adenovirus fibre attaches to the CAR and integrins interact with the penton base, leading to internalization.
Reovirus 1	σ1	JAM-1 (nM)	Unknown	Sialic acid	There are structural similarities between adenovirus fibre and σ1, and between CAR and JAM-1. All serotypes bind JAM-1.

*Attachment proteins that are subunits of the respective entry proteins and bind to receptors are shown in parentheses. ‡Approximate affinities (equilibrium dissociation constants) are shown in parentheses. §For most viruses, co-receptors and alternative receptors are not known, or it is unclear if a molecule that has a role in entry is a co-receptor, a receptor or an alternative receptor. ACE2, angiotensin-converting enzyme 2; CAR, coxsackievirus-adenovirus receptor; HveA, herpesvirus entry mediator A; ICAM-1, intercellular adhesion molecule 1; JAM-1, junctional adhesion molecule 1.

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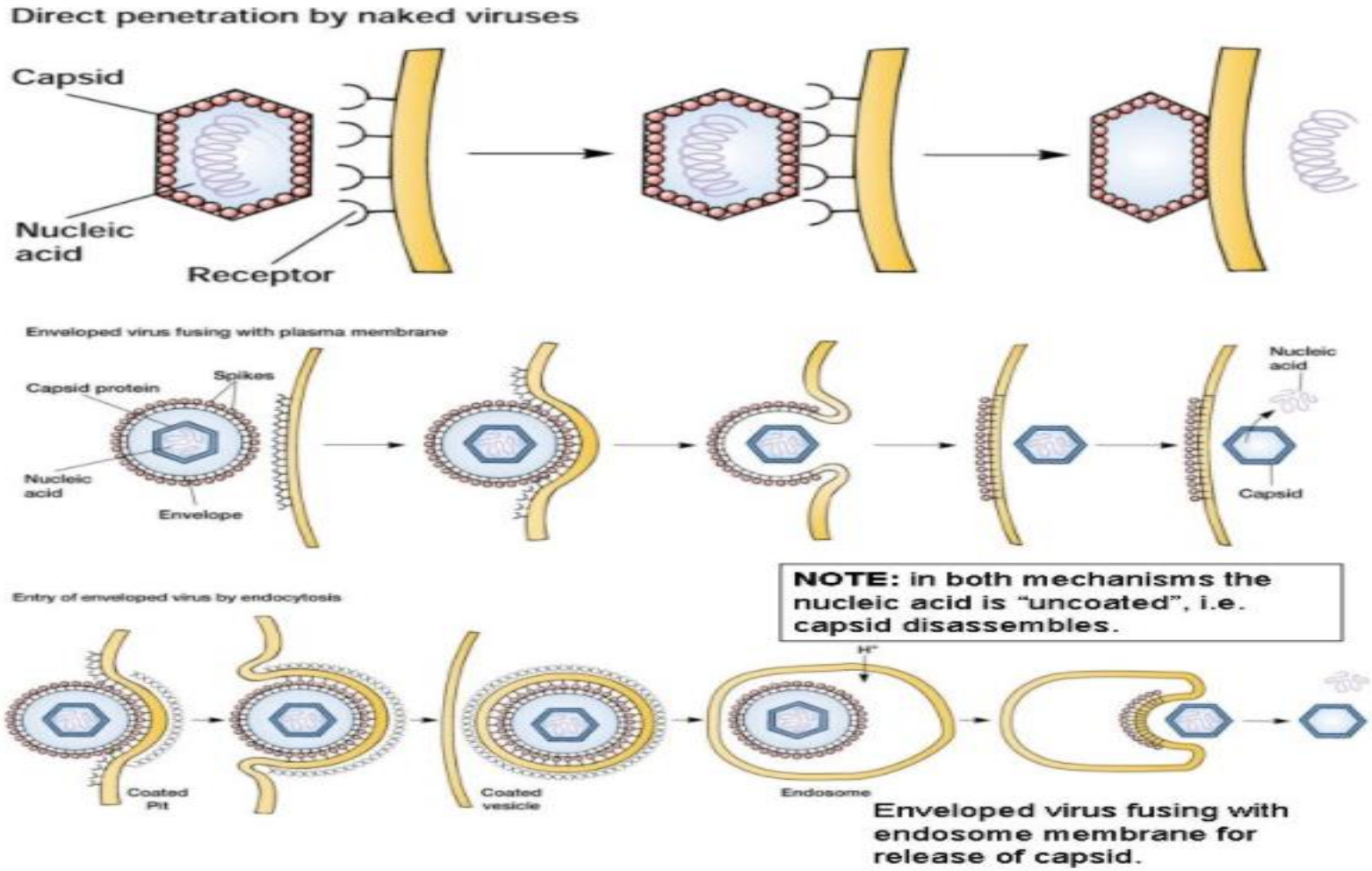
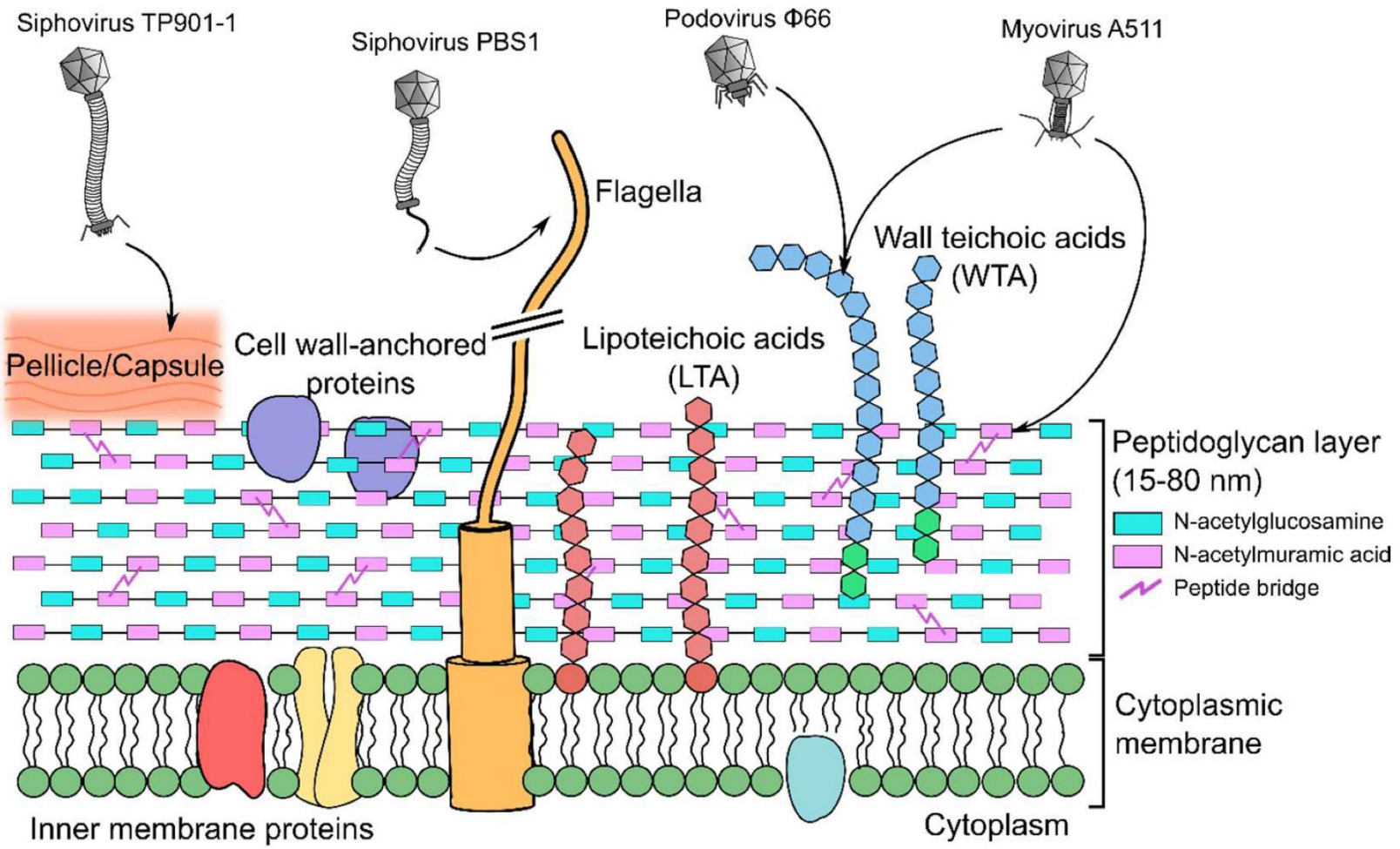
Membrane Penetration



Bacteriophage Entry- 3 steps

- The first step involves random collisions between phage and host caused by Brownian motion, dispersion, diffusion or flow
- Second Step: Reversible binding to bacterial surface components is not definitive and the phage can desorb from the host
- Third Step: Irreversible binding that is a specific connection between bacterial receptor and phage-binding domains, sometimes mediated by an enzymatic cleavage. This step triggers conformational rearrangements in other phage molecules that allow the insertion of the genetic material into the host

Bacterial Host cell receptor



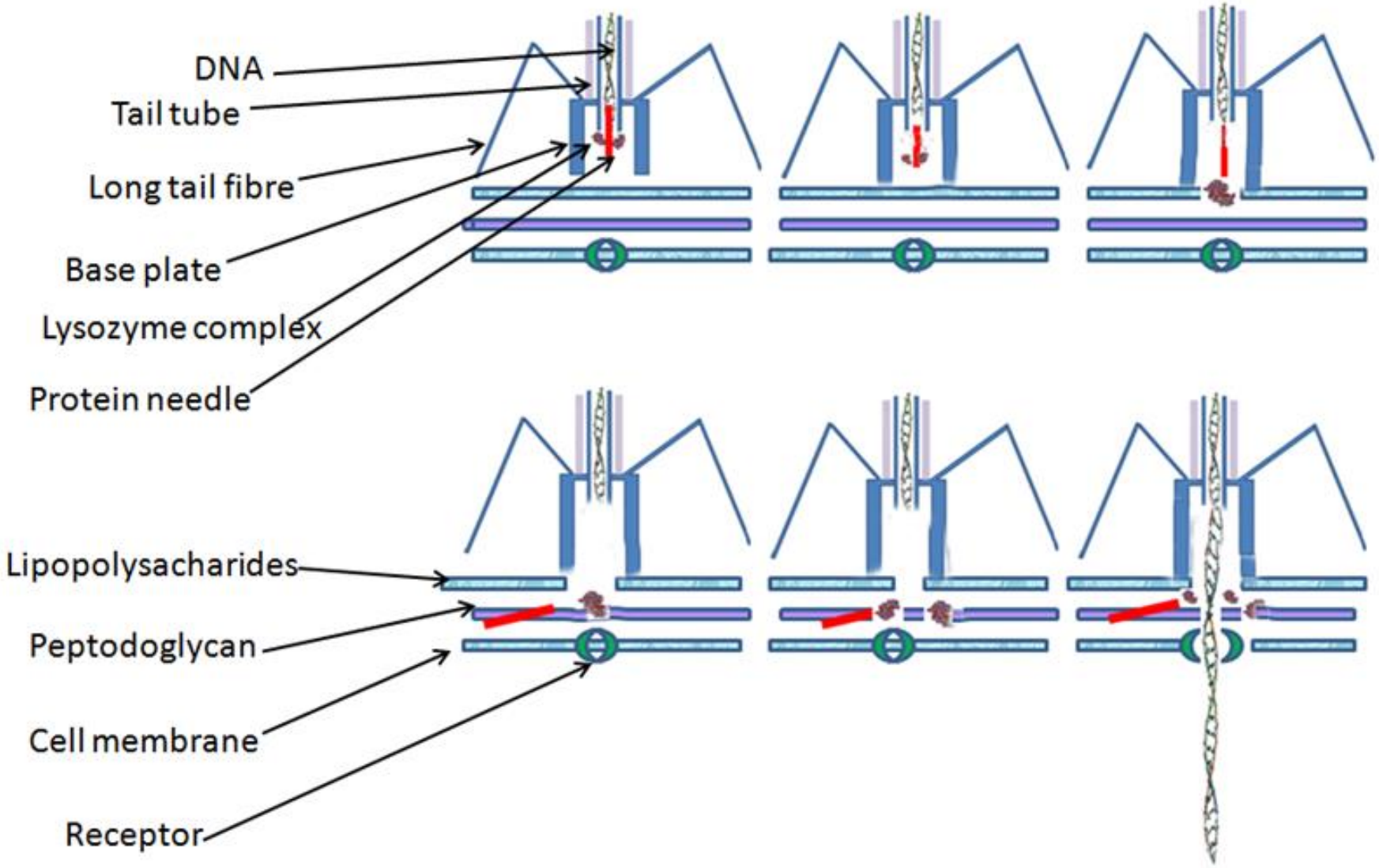
Viruses **2018**, *10*(8), 397; https://doi.org/10.3390/v10080397

- Gram positive bacteria: Peptidoglycan, or murein/ Teichoic acid residues, is an important component of the bacterial cell wall and is often involved in bacteriophage adsorption.
- Gram Negative bacteria: Lipo polysaccharide and sugar moieties

Bacteriophage penetration

- Polysaccharide-degrading enzymes, like endolysins are virion-associated proteins to enzymatically degrade the capsular outer layer of their hosts, at the initial step of a tightly programmed phage infection process.
- Myovirus bacteriophages use a hypodermic syringe-like motion to inject their genetic material into the cell. After contacting the appropriate receptor, the tail fibers flex to bring the base plate closer to the surface of the cell. This is known as reversible binding.
- Once attached completely, irreversible binding is initiated and the tail contracts, possibly with the help of ATP, present in the tail injecting genetic material through the bacterial membrane. The injection is accomplished through a sort of bending motion in the shaft by going to the side, contracting closer to the cell and pushing back up.
- Podoviruses lack an elongated tail sheath, they use their small, tooth-like tail fibers enzymatically to degrade a portion of the cell membrane before inserting their genetic material.

Bacteriophage penetration



https://en.wikipedia.org/wiki/Bacteriophage#/media/File:Phage_injection.png