Viruses occur universally. It is likely that every living organism on this planet is infected by a species-specific range of viruses.

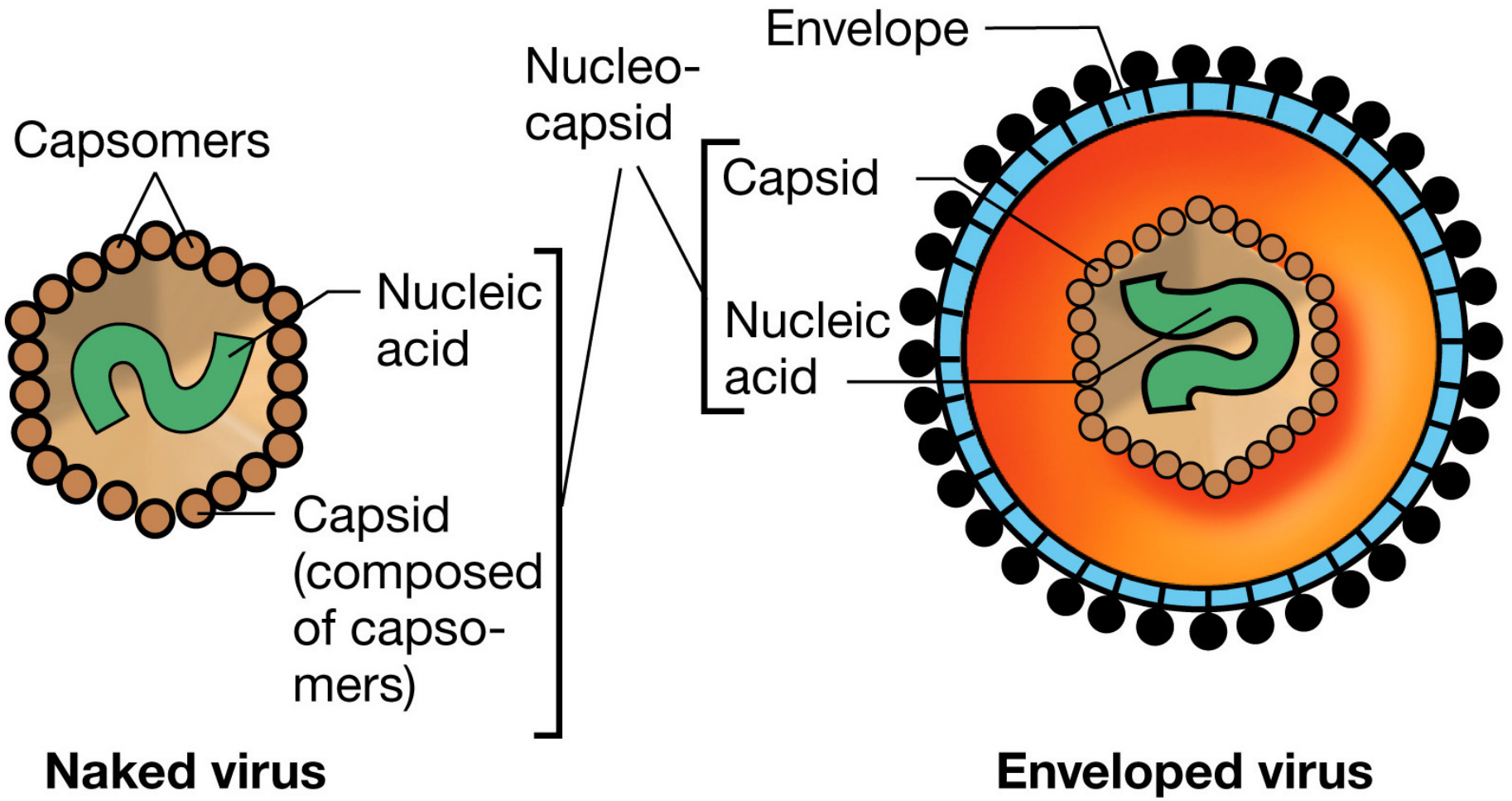
Viruses are obligate intracellular parasites that require a host within which they replicate.

Although they are well known for causing disease, most viruses coexist peacefully with their hosts.

# Properties common to all viruses

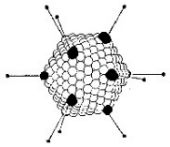
- Viruses have a nucleic acid genome of either DNA or RNA.
- Compared with a cell genome, viral genomes are small, but genomes of different viruses range in size by over 100-fold (ca 3000 nt to 1,200,000 bp)
- Small genomes make small particles – again with a 100-fold size range.
- Viral genomes are associated with protein that at its simplest forms the virus particle, but in some viruses this nucleoprotein is surrounded by further protein or a lipid bilayer.
- The outermost proteins of the virus particle allow the virus to recognise the correct host cell and gain entry.
- Viruses can only reproduce in living cells: they are obligate parasites.

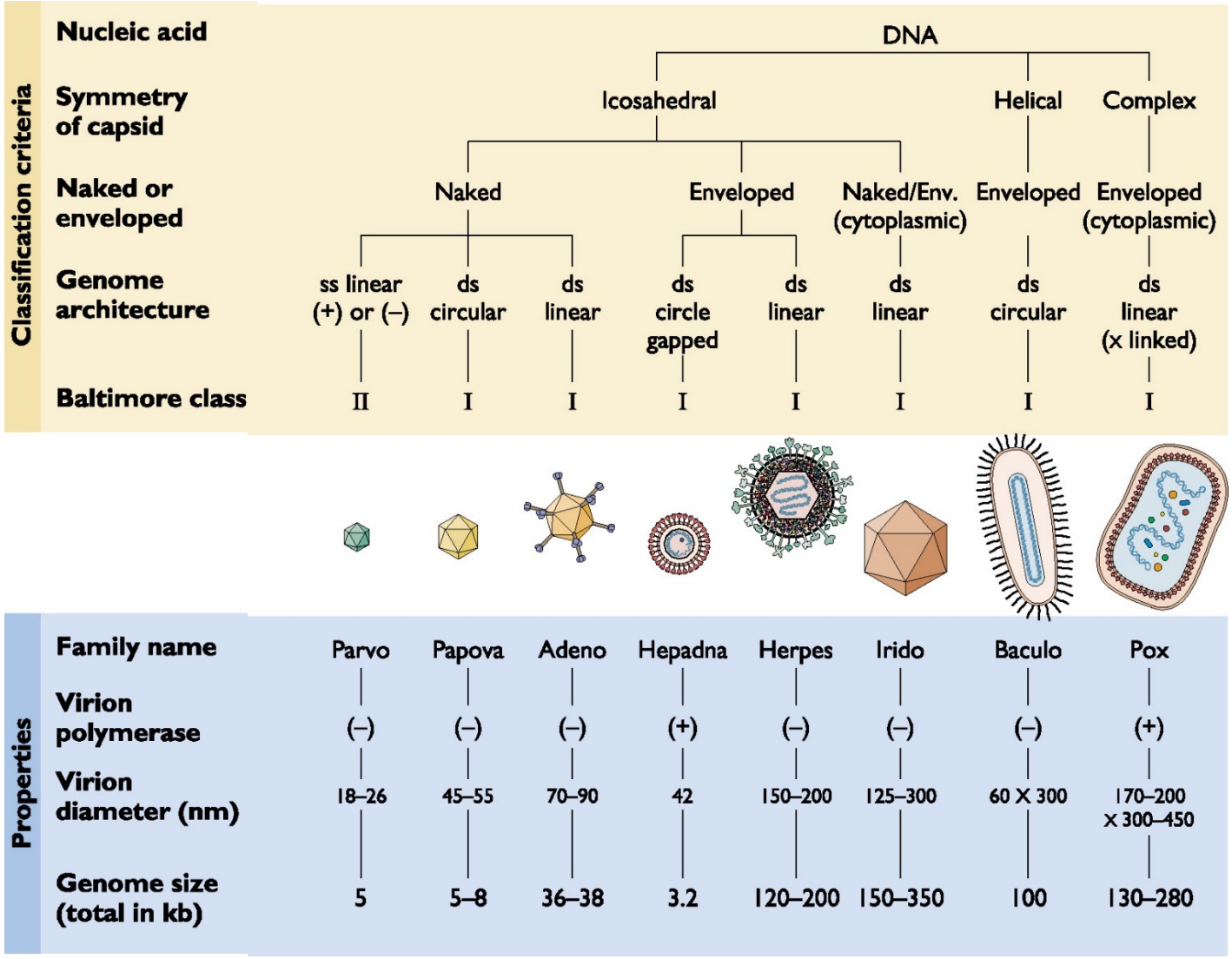
# Diagrammatic structure of virus particles



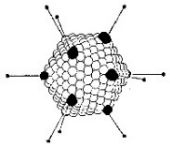
# Classification criteria

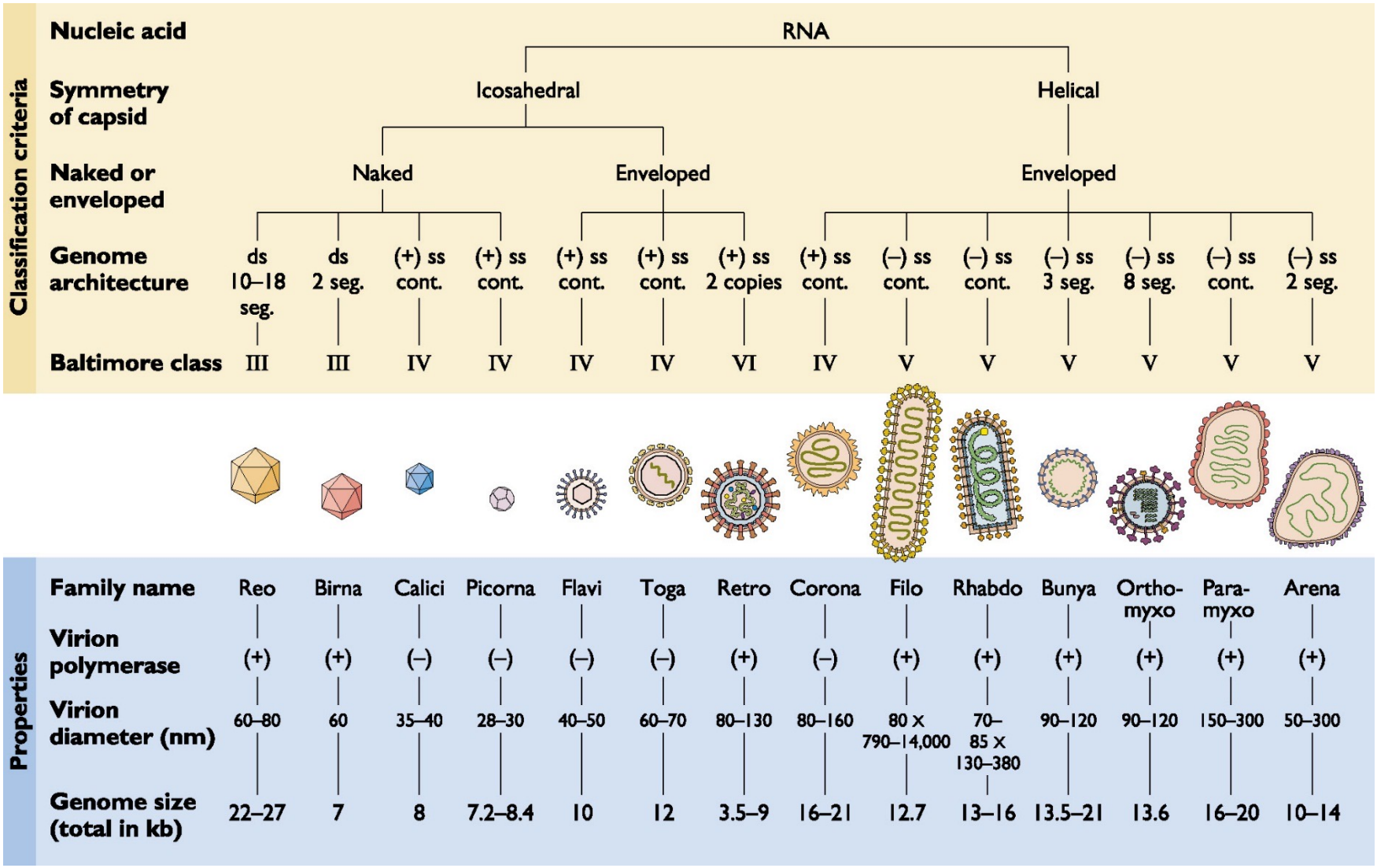
- Nature of the nucleic acid
- Protein coat symmetry (capsid)
- Presence or absence of lipid envelope
- Genome architecture






From Flint et al. *Principles of Virology* (2000), ASM Press

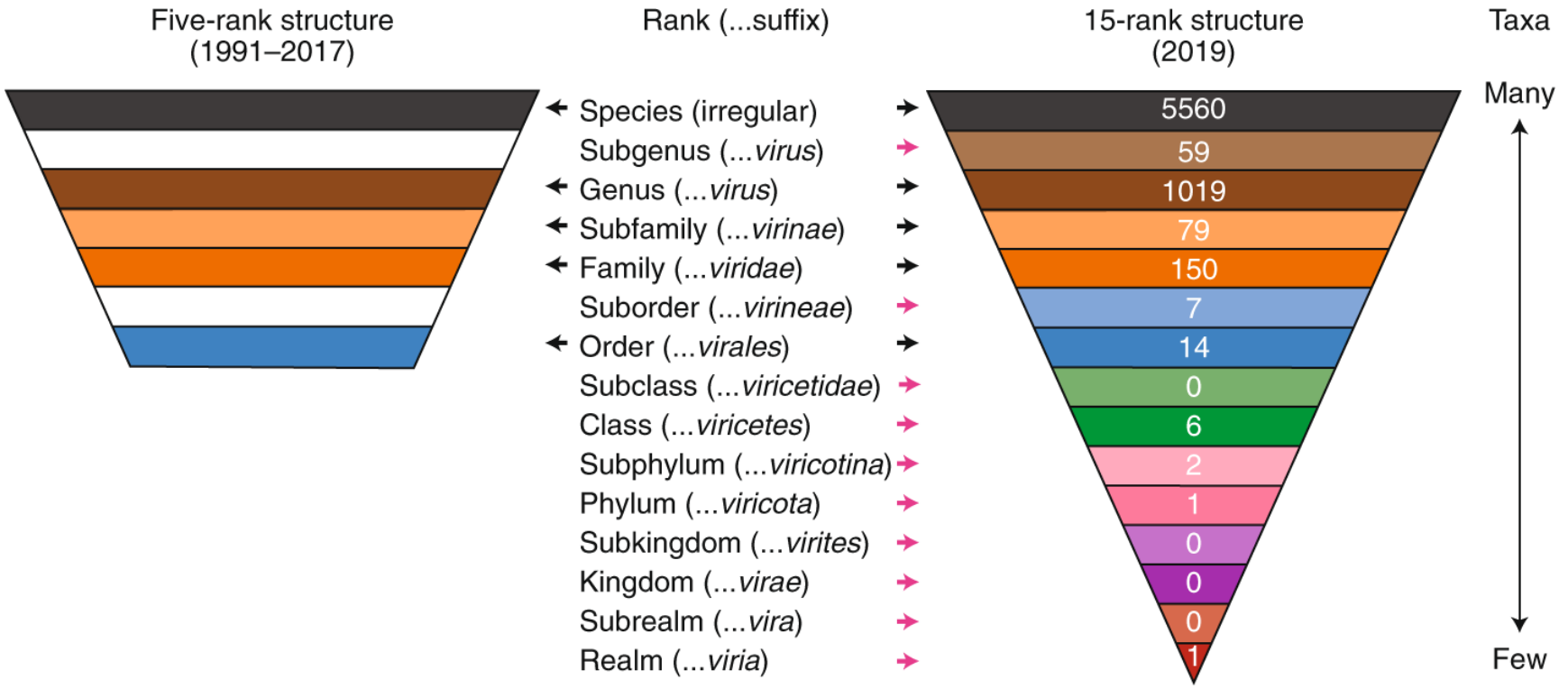





From Flint et al. *Principles of Virology* (2000), ASM Press

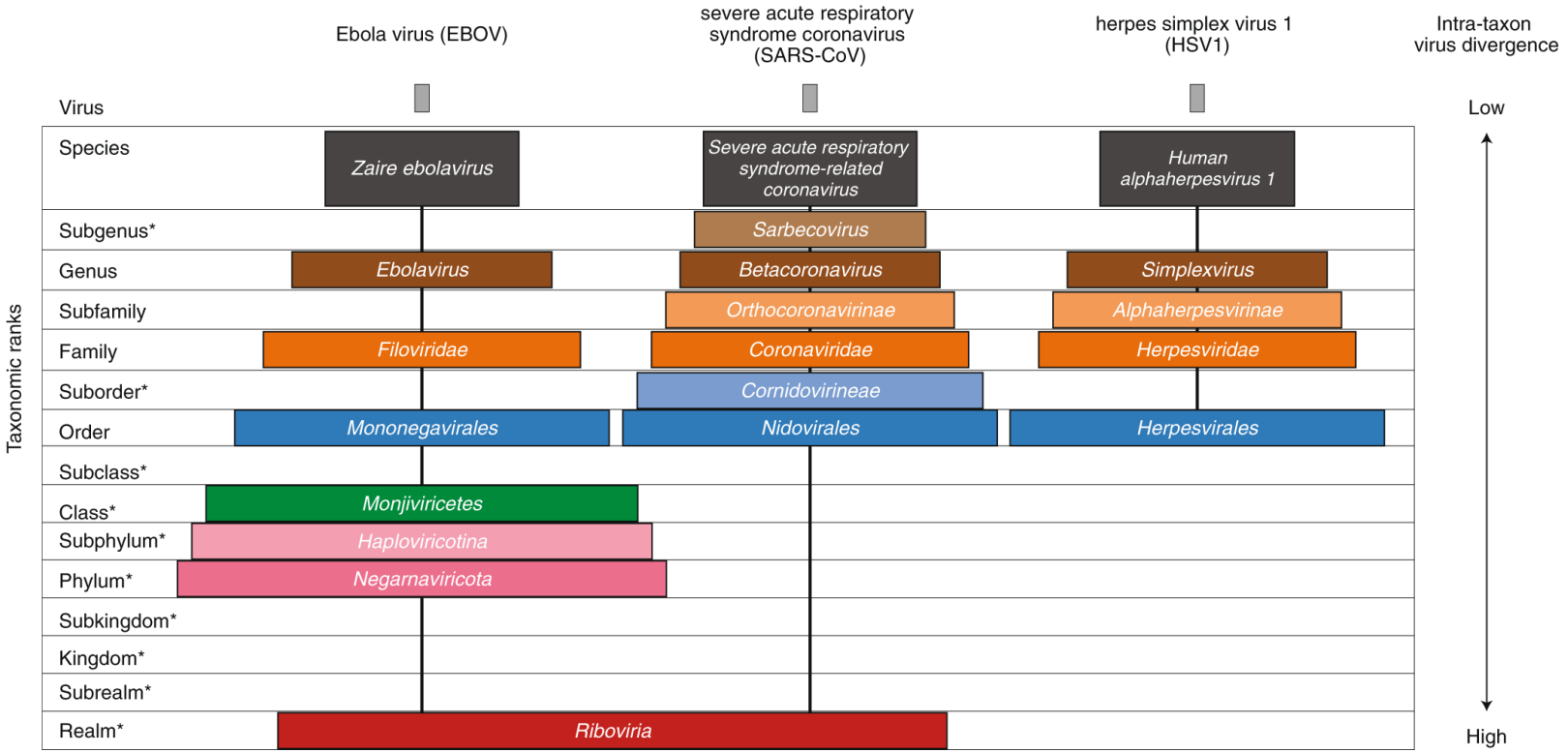
- **A comparison of the ICTV (International Committee on Taxonomy of Viruses) taxonomic rank hierarchy in 1991–2017 and 2019**

Taxonomic ranks are shown in relation to the distribution pattern of taxa. The number of taxa assigned to each rank (as recorded in the current ICTV Master Species List, release 2018b, MSL34) are shown in white font on the 15-rank structure. When the ranks are described as a hierarchy, the species rank is often referred to as the lowest rank and the realm rank as the highest rank. However, when the ranks are used as phylogenetic terms, the realm rank can be described as basal and the species rank as apical or terminal. Both conventions are used in this Consensus Statement. Black arrows, ranks common to the five- and 15-rank structure; pink arrows, ranks introduced in the 15-rank structure




*Nature Microbiology* **volume 5**, pages 668–674 (2020)

# Classification of EBOV, SARS-CoV and herpes simplex virus 1 in the 15-rank taxonomic hierarchy



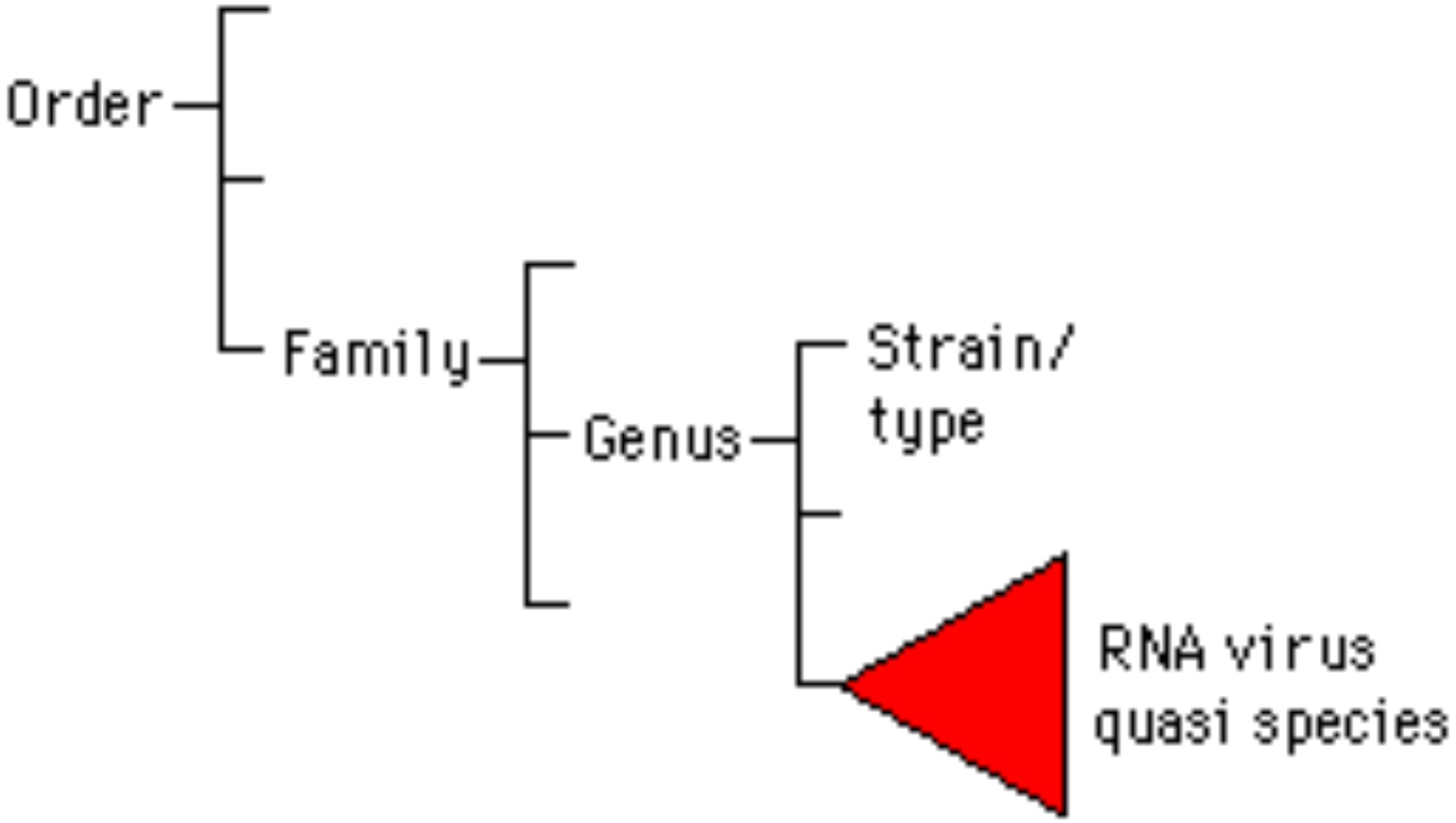

Intra-cluster virus divergence, which increases from the virus species rank to the realm rank, is represented by the increasing width of the respective rectangles, which are not drawn to scale. EBOV is most closely related to, but distinct from, Bombali, Bundibugyo, Reston, Sudan and Taï Forest viruses, which belong to separate species included in the *Ebolavirus*genus. SARS-CoV is one of several closely related coronaviruses isolated from humans and animals, such as palm civets and bats, and are included in the species *Severe acute respiratory syndrome-related coronavirus*. Herpes simplex virus 1 is one of two human herpesviruses belonging to different species in the *Simplexvirus* genus. Ranks that were introduced with the extended rank structure are indicated by an asterisk.

*Nature Microbiology* **volume 5**, pages 668–674 (2020)

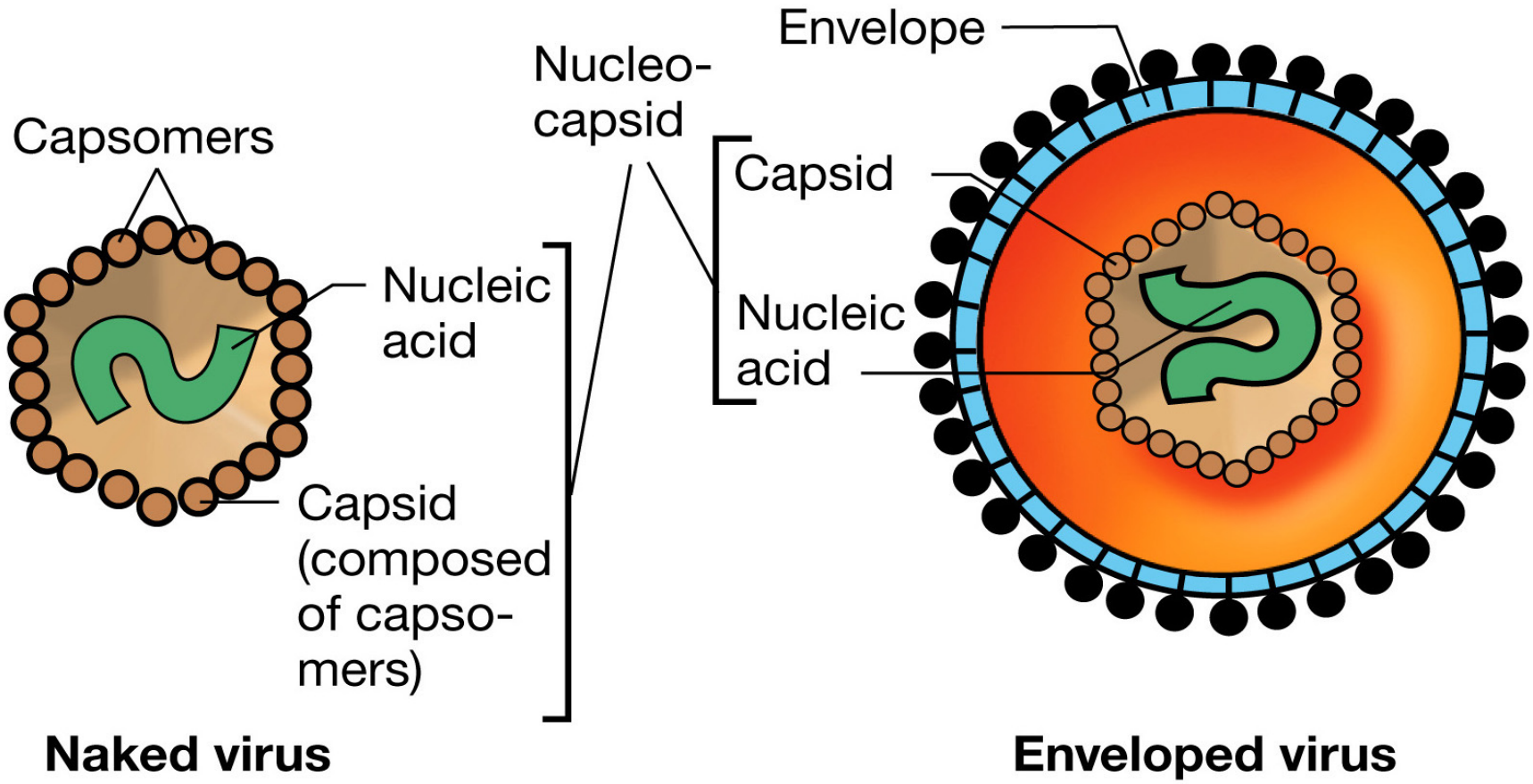
# Virus taxonomy

(ICTV fondato fine anni ‘60)

L’ordine ha suffisso –virales. La famiglia ha suffisso -viridae. La sottofamiglia ha suffisso –virinae. Il genere ha suffisso -virus. La specie?



# Diagrammatic structure of virus particles



# The diversity of viral genomes

## DNA Genomes

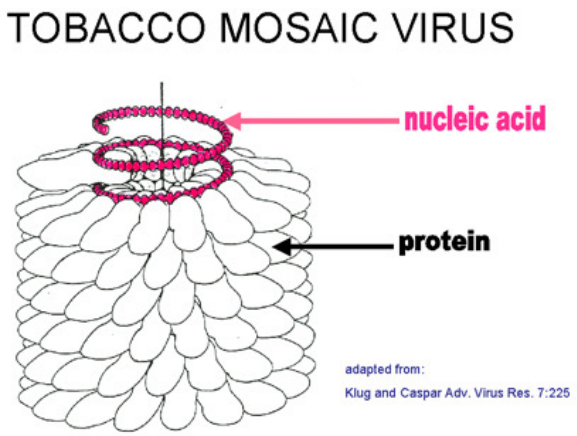
*Double-Stranded DNA (dsDNA)*
*Gapped DNA*
*Single-Stranded DNA (ssDNA)*

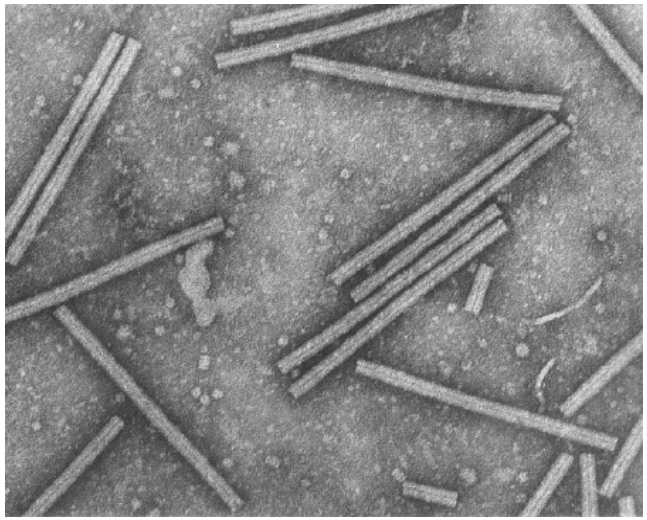
## RNA Genomes

*dsRNA*
*(+) Strand RNA*
*(-) Strand RNA*

# Capsid symmetry

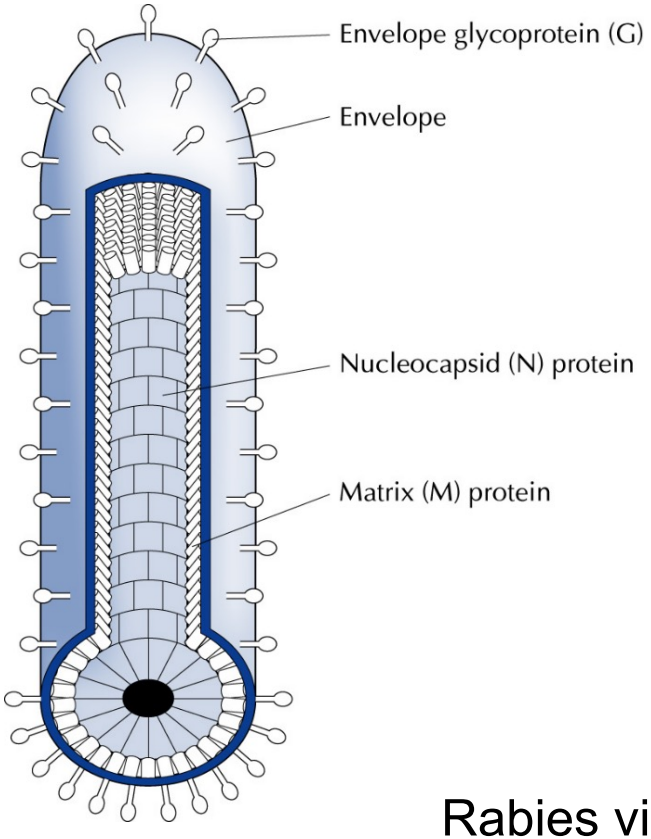
The helical symmetry is very common among plant viruses

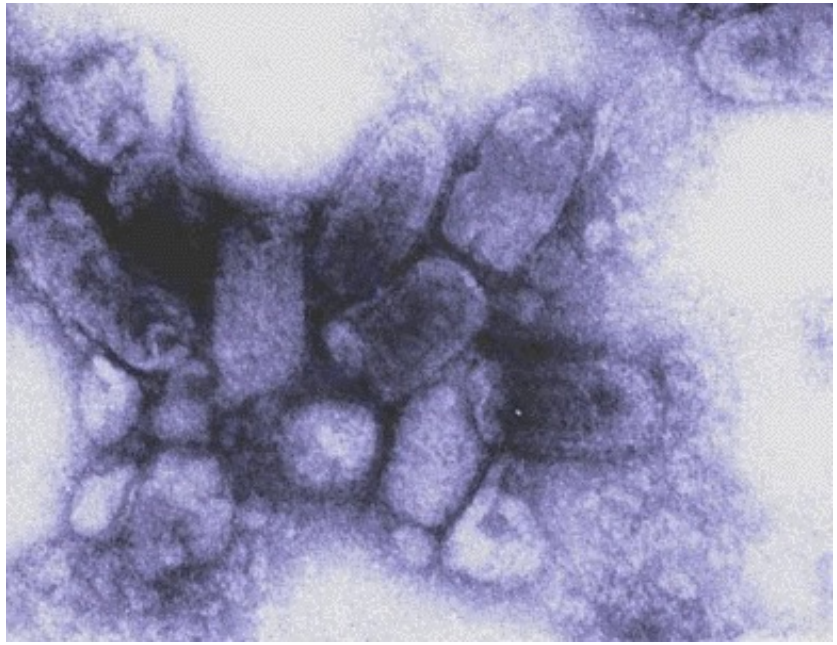


# Capsid symmetry

Helical animal viruses are all enveloped viruses.
Many of them are pathogenic to humans: influenza virus (*Orthomyxoviridae*), viruses that cause measles and mumps (*Paramyxoviridae*), the rabies virus (*Rhabdoviridae*) Ebola and Marburg viruses (*Filoviridae*)



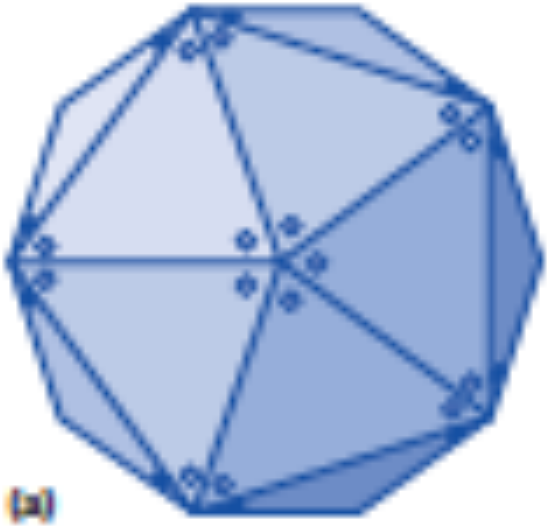



Rabies virus

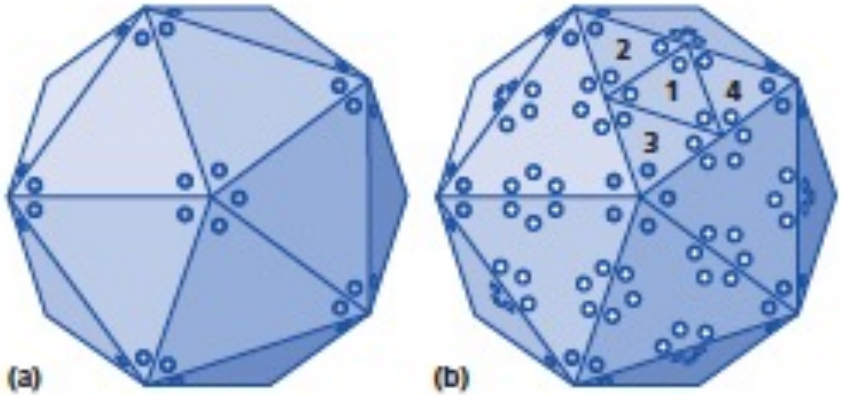
From Cann *Principles of molecular virology* (2001). Academic Press

# Capsid symmetry

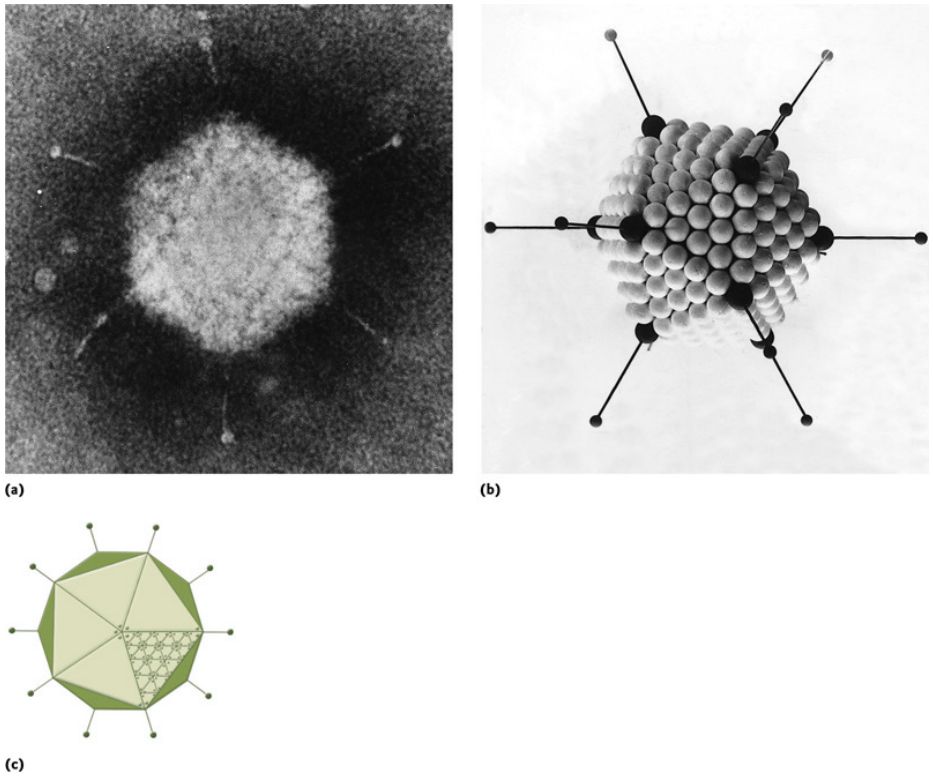
Icosahedral symmetry. The simplest capsids are formed by 60 protomers. They are distributed such that there is one subunit at the vertices of each of the triangular faces. Five protomers around each vertex of the icosahedron form the capsomer, the morphological units (in this case named penton). Icosahedral viruses with capsid consisting of 60 protomers are known, but they are not independently replicating viruses



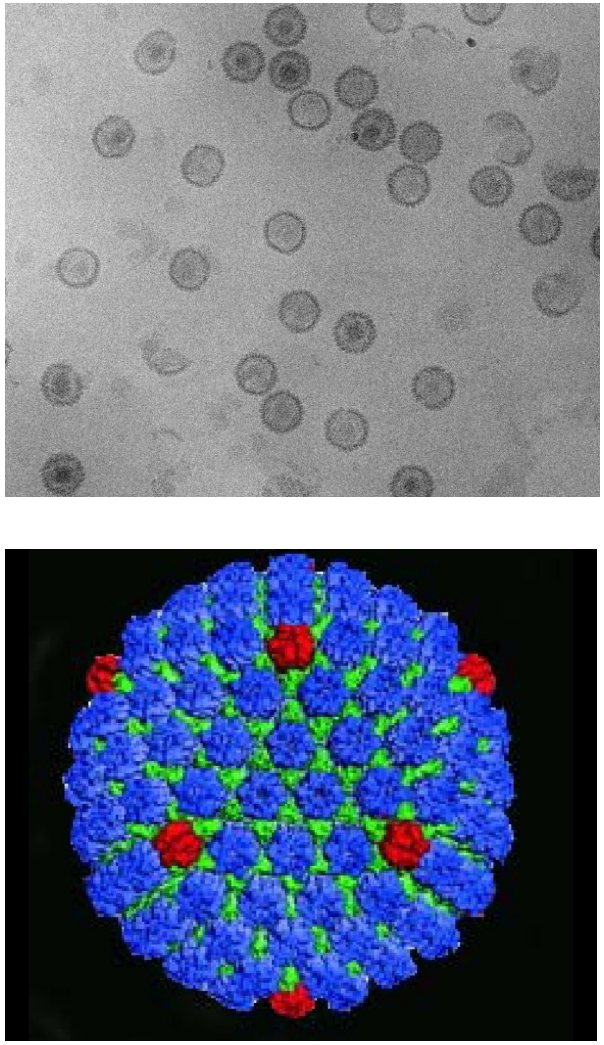
# Capsid simmetry




Arrangement of 60n identical subunits on the surface of an icosahedron. (a) n = 1 and the 60 subunits are distributed such that there is one subunit at the vertices of each of the 20 triangular faces. Note that each subunit has the same arrangement of neighbours and so all the subunits are equivalently related. (b) n = 4. Each triangular face is divided into 4 smaller, but identical, equilateral triangular facets and a subunit is again located at each vertex. In total, there are 240 subunits. Note that each subunit, whether represented by an open or closed circle, has the identical arrangement of neighbours: see the face in which triangles 1–4 have been drawn. However, since some subunits are arranged in pentamers and others in hexamers, the members of each set are quasi-equivalently' related.




Adenovirus T=25



HSV-1 T=16

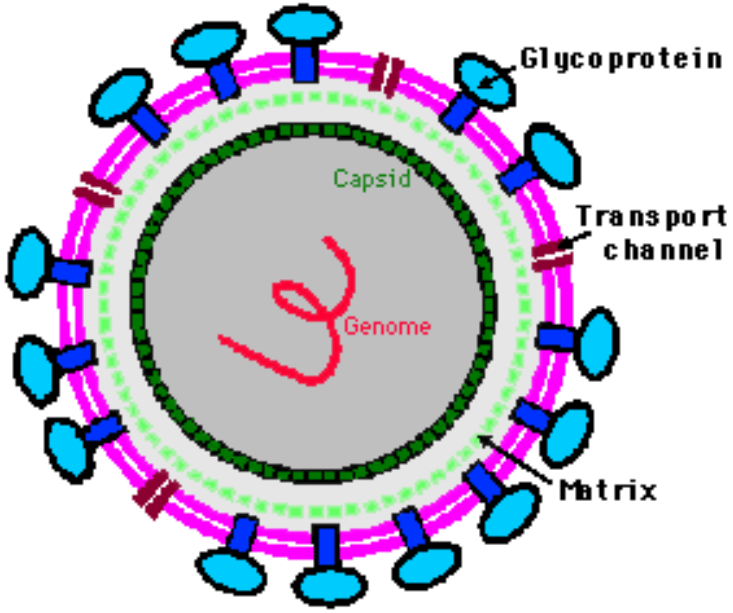
# VIRAL ENVELOPE

The envelope is made up of a **lipid bilayer** that is acquired by budding from the cell membranes and contains virus-specific proteins:

**Surface glycoproteins (all enveloped viruses)**

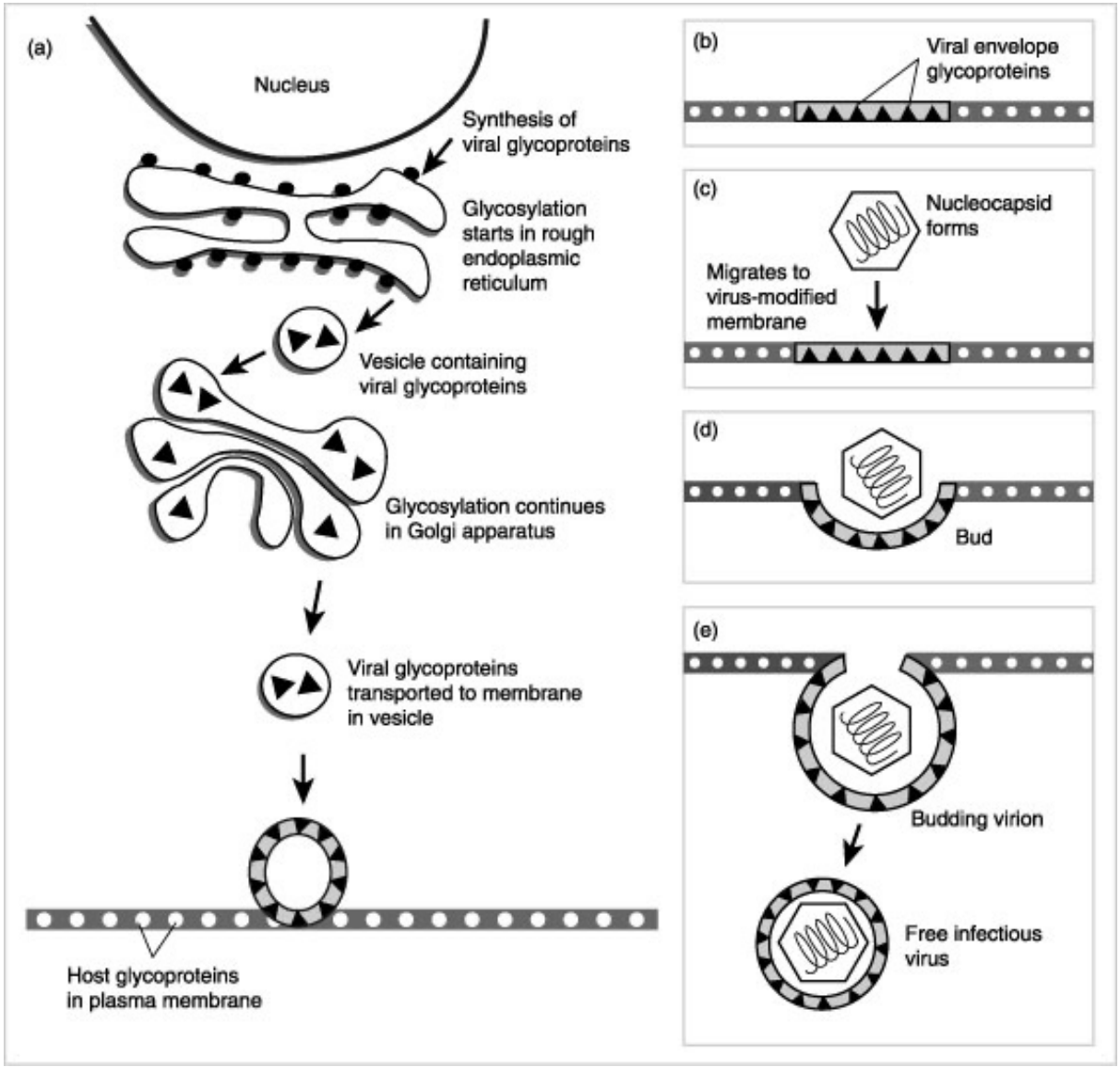
**Transmembrane glycoproteins**

**Transport channel**

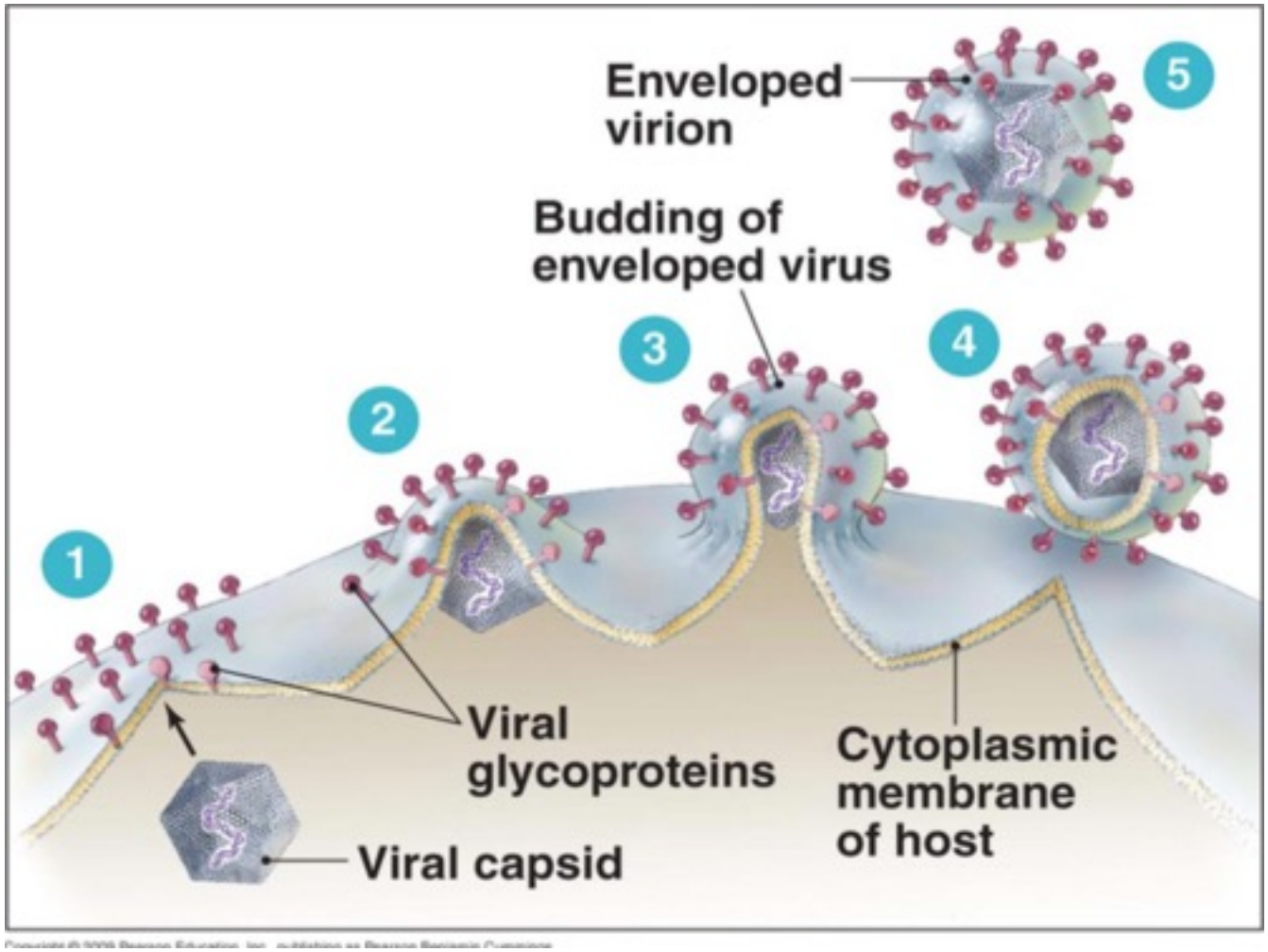



Most enveloped viruses are characterized by the presence of a **matrix** that connects the capsid to the lipid envelope.

# Budding

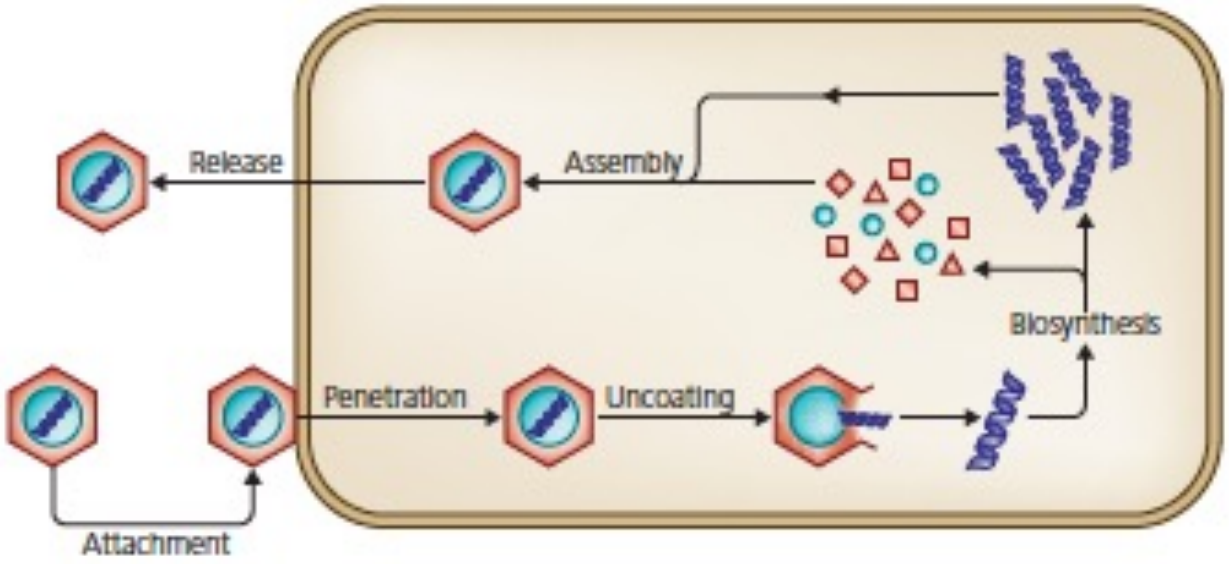

(a)
Nucleus
Synthesis of viral glycoproteins
Glycosylation starts in rough endoplasmic reticulum
Vesicle containing viral glycoproteins
Glycosylation continues in Golgi apparatus
Viral glycoproteins transported to membrane in vesicle
Host glycoproteins in plasma membrane
(b)
Viral envelope glycoproteins
(c)
Nucleocapsid forms
Migrates to virus-modified membrane
(d)
Bud
(e)
Budding virion
Free infectious virus

# Envelope acquisition - Budding



# Virus Multiplication

Viruses multiply by assembling many progeny particles from a pool of virus specified components, whereas cells multiply by binary fission.




*Introduction to Modern Virology*, Seventh Edition. N. J. Dimmock, A. J. Easton and K. N. Leppard.

# Virus Multiplication

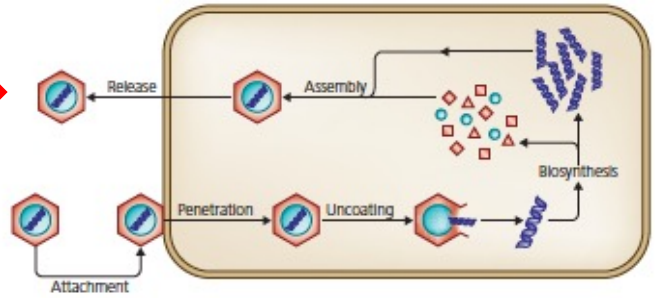
The efficiency of multiplication demonstrated by viruses is such that the infection of a single host can generate more new viruses than there are individuals in the host population. For example, a single human infected with influenza virus can shed sufficient virus particles to be theoretically capable of infecting the entire human population.

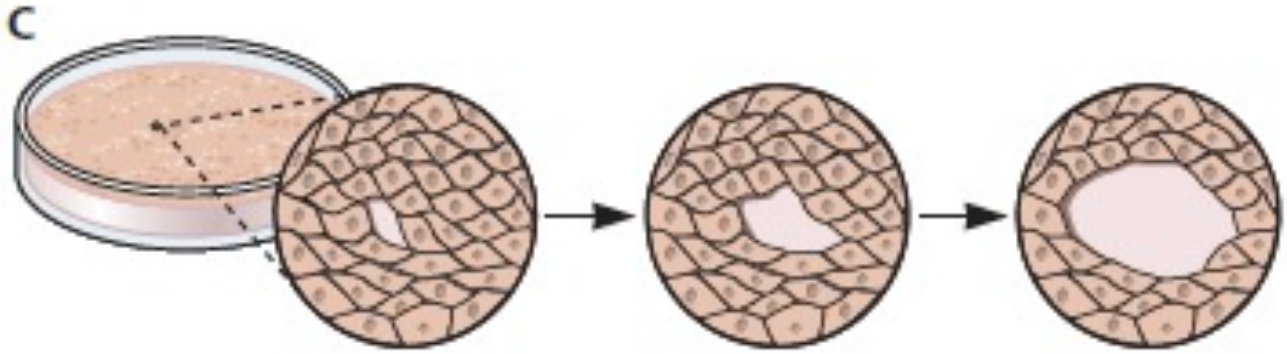
# Particle-to-PFU ratios of some animal viruses

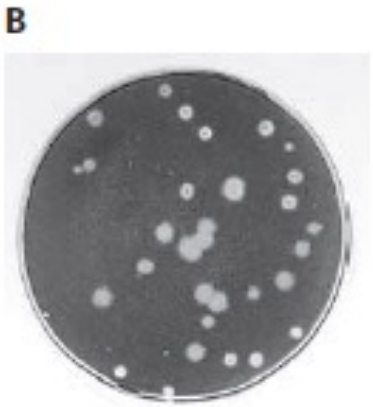
| Virus | Particle/PFU ratio |
|---|---|
| Papillomaviridae | |
| Papillomavirus | 10,000 |
| Picornaviridae | |
| Poliovirus | 30–1,000 |
| Herpesviridae | |
| Herpes simplex virus | 50–200 |
| Polyomaviridae | |
| Polyomavirus | 38–50 |
| Simian virus 40 | 100–200 |
| Adenoviridae | 20–100 |
| Poxviridae | 1–100 |
| Orthomyxoviridae | |
| Influenza virus | 20–50 |
| Reoviridae | |
| Reovirus | 10 |
| Alphaviridae | |
| Semliki Forest virus | 1–2 |

# Counting virus infectious particles by the plaque assay

Many, many new particles →

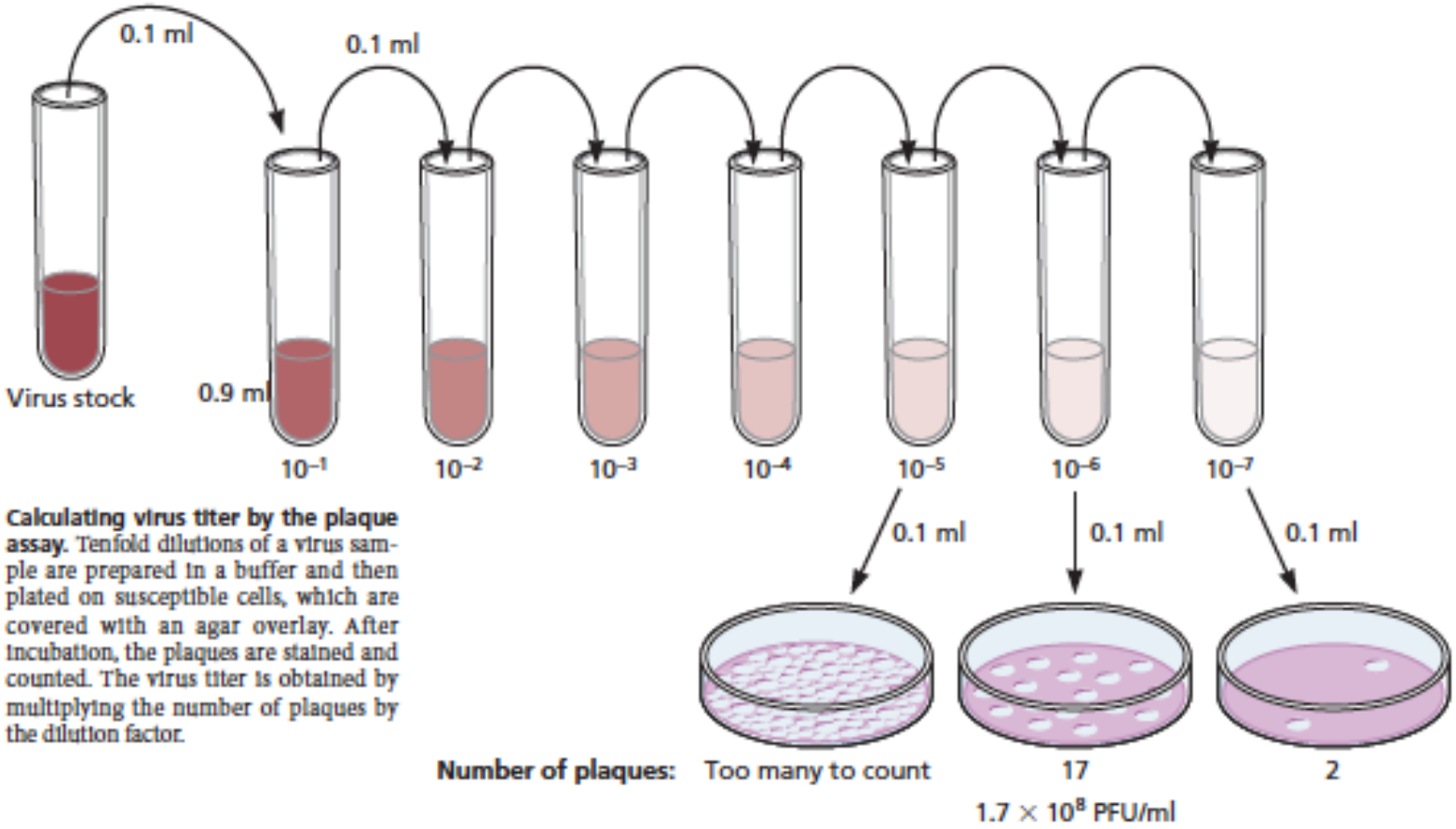



From Flint et al. *Principles of Virology* (2015), ASM Press

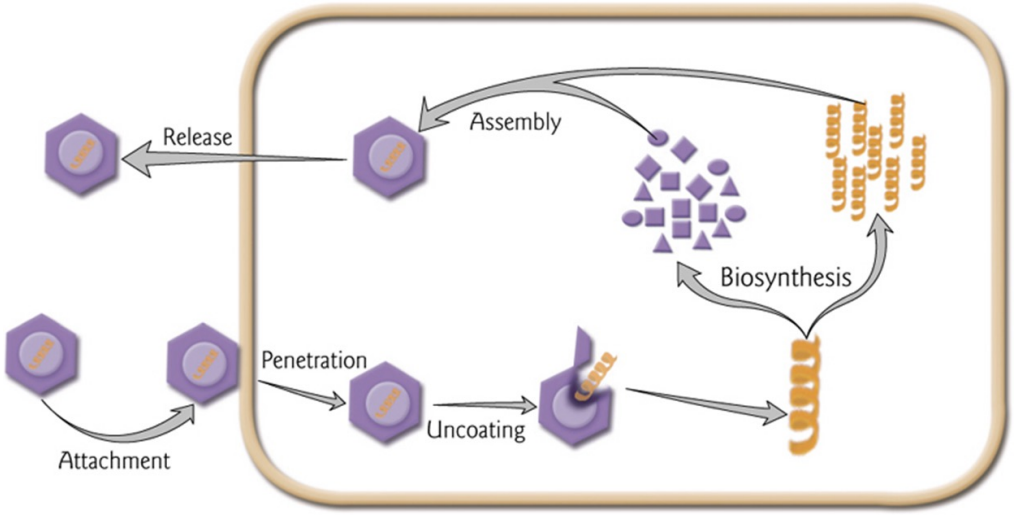
# Calculating virus titre by the plaque assay



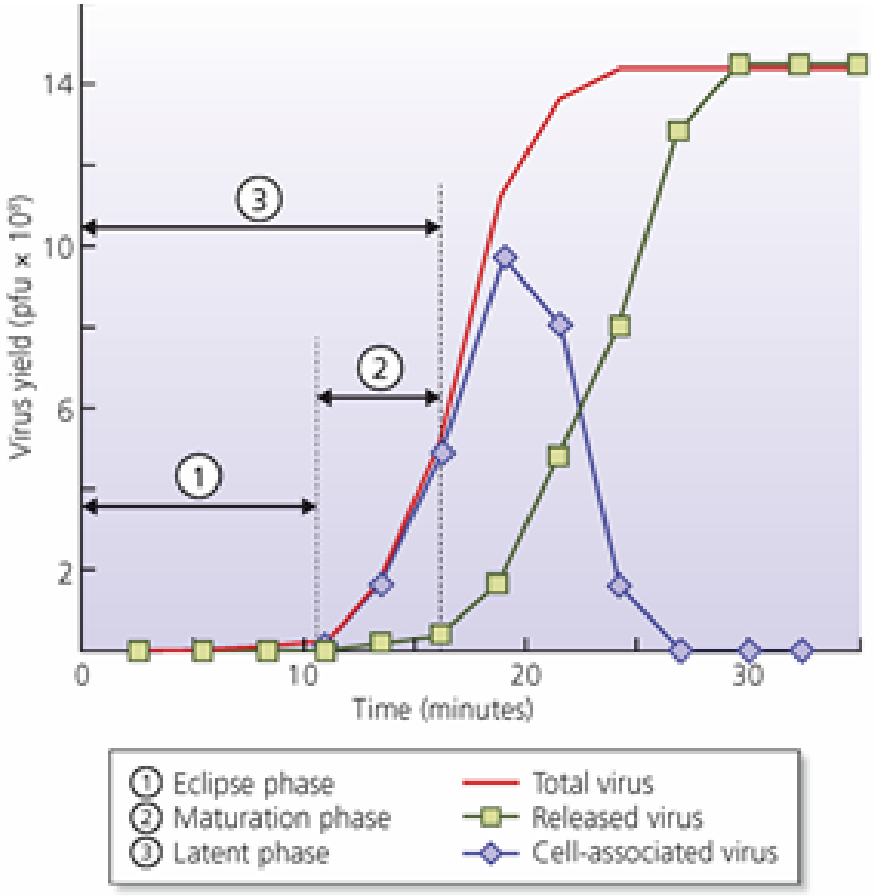

**Calculating virus titer by the plaque assay.** Tenfold dilutions of a virus sample are prepared in a buffer and then plated on susceptible cells, which are covered with an agar overlay. After incubation, the plaques are stained and counted. The virus titer is obtained by multiplying the number of plaques by the dilution factor.

From Flint et al. *Principles of Virology* (2015), ASM Press

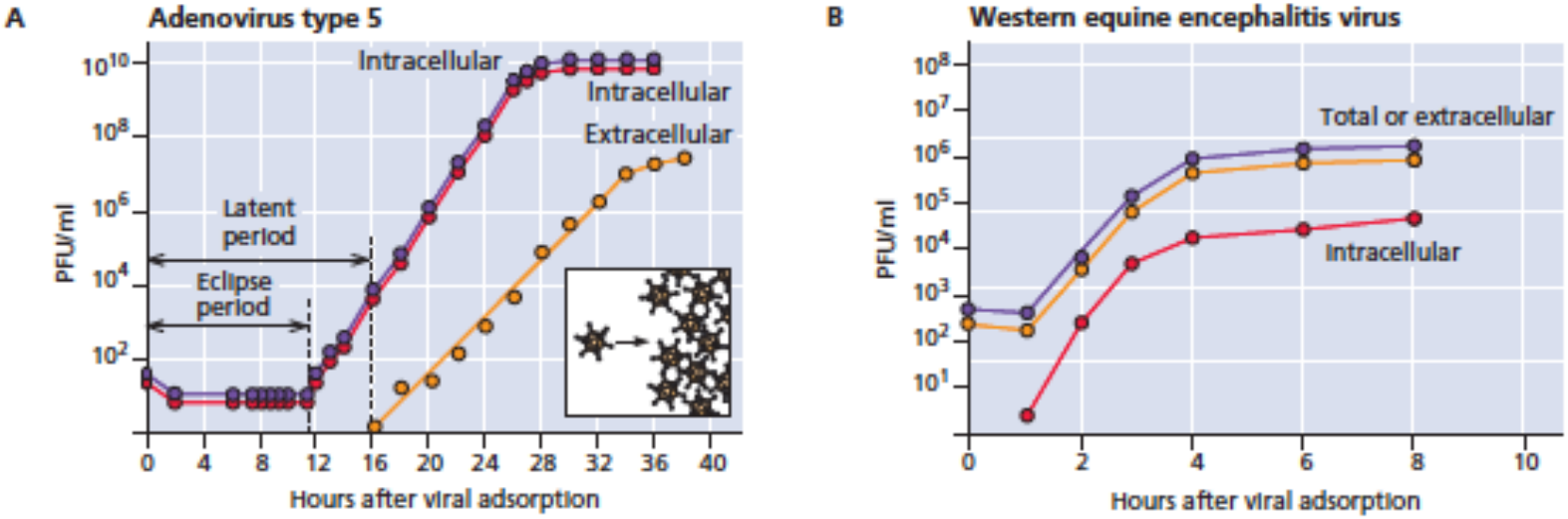
# One-Step Growth Curve
# Ellis and Delbruck (1939)




Viral genome drives the formation of new viral particles which are the result of viral component assembly



# One-Step Growth Curve of animal viruses

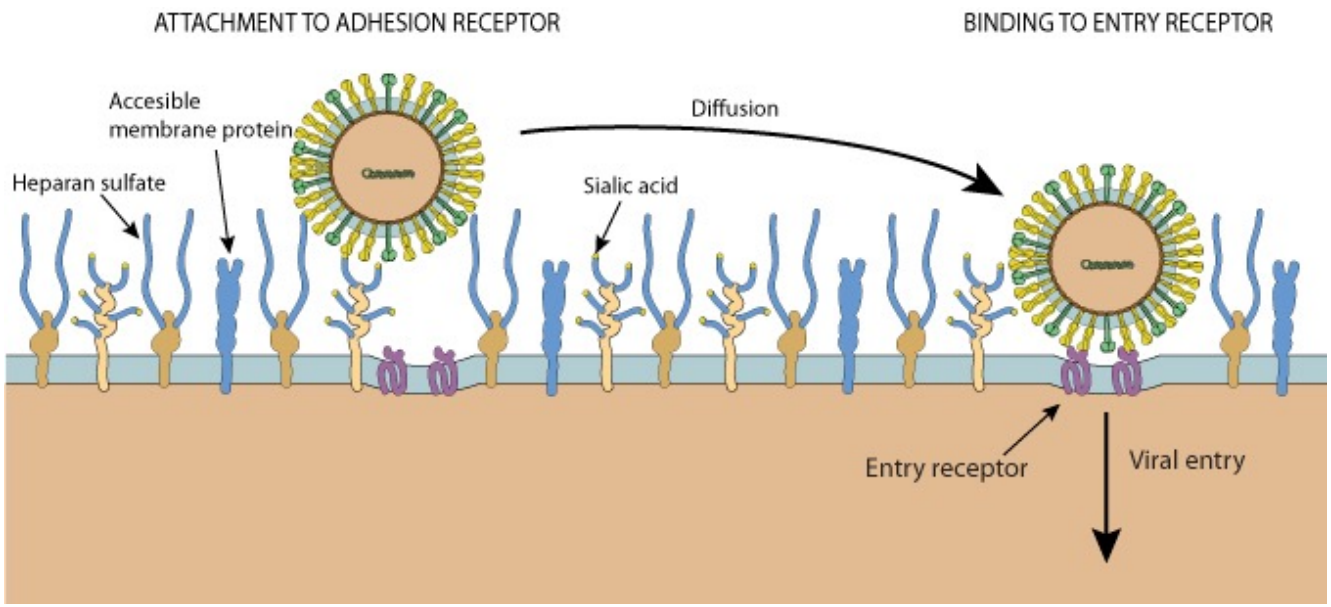



The kinetics of the one-step growth curve can vary dramatically among different viruses. For example, enveloped viruses that mature by budding from the plasma membrane generally become infectious only as they leave the cell, and therefore little intracellular infectious virus can be detected (Fig. B). The curve shown in Fig. A illustrates the pattern observed for a DNA virus with the long latent and synthetic phases typical of many DNA viruses, some retroviruses, and reovirus. For small RNA viruses, the entire growth curve is complete within 6 to 8 h, and the latent and synthetic phases are correspondingly shorter.

One-step growth curve analysis can provide quantitative information about different virus-host systems. It is frequently employed to study mutant viruses to determine what parts of the infectious cycle are affected by a particular genetic lesion. It is also valuable for studying the multiplication of a new virus or viral replication in a new virus-host cell combination.

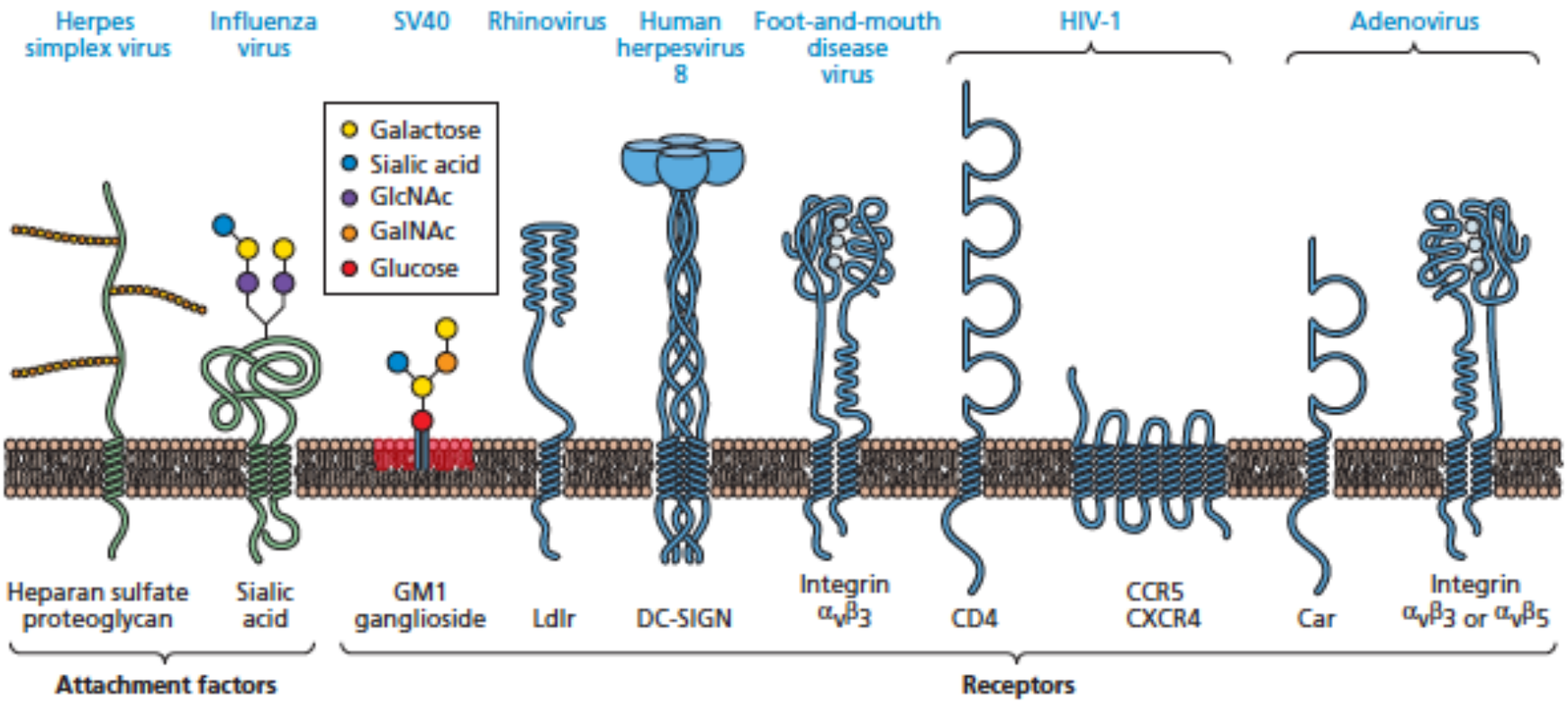
From Flint et al. *Principles of Virology* (2015), ASM Press

# Viral attachment to host cell




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. Entry receptors are often difficult to access for the virion, which circumvents this problem by binding first to adhesion receptors, which increases the probability of binding to the entry receptor.

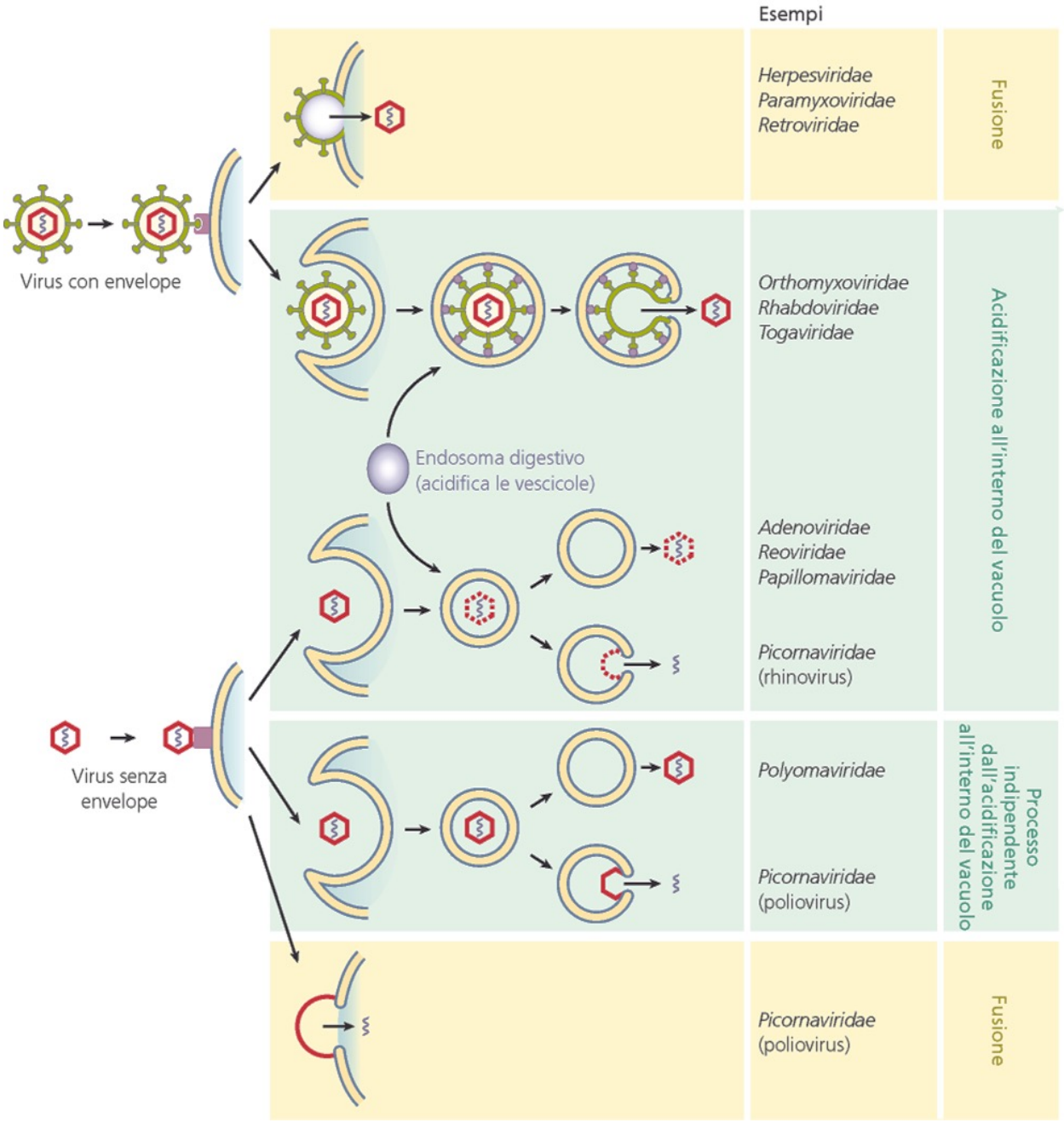
# Cell recognition




Some cell attachment factors and receptors for viruses. Schematic diagrams of cell molecules that function during virus entry. GlcNAc, N-acetylglucosamine; GalNAc, N-acetylgalactosamine; Ldlr, low-density lipoprotein receptor; DC-SIGN, dendritic cell-specific intercellular adhesion molecule-3-grabbing non-integrin; Car, coxsackievirus-adenovirus receptor.

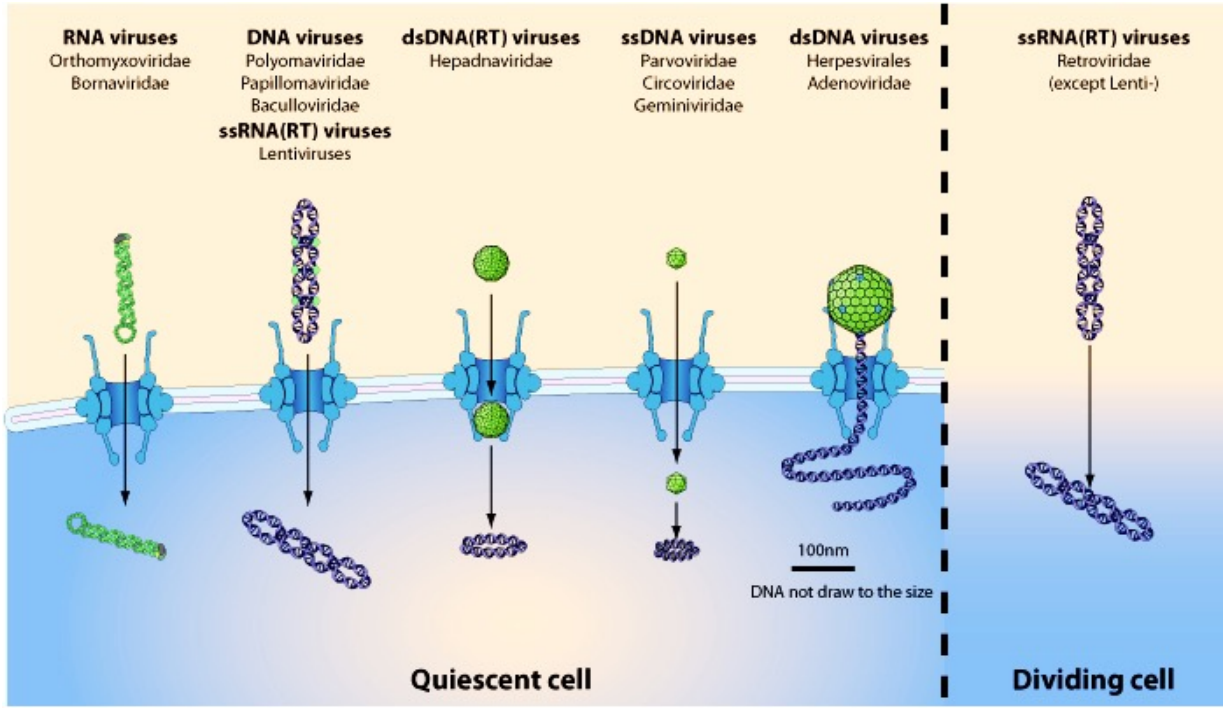
From Flint et al. *Principles of Virology* (2015), ASM Press

# Attachment and entry/uncoating




From Harper D., Virus, Zanichelli 2013

# Viral penetration into host nucleus




Most DNA and few RNA viruses target their genome to the host nucleus. The crossing of nuclear membrane occurs in several ways:

-RNA virus, dsDNA virus and lentivirus genomes enter via the nuclear pore complex (NPC) through the cellular Importin transport.

-ssDNA virus capsid seems to be small enough to cross the NPC and enter the nucleus as an intact capsid.

-Hepadnaviridae capsid would enter the NPC pore, but remains attached to it and releases the viral genomic DNA into the nucleoplasm.

-Herpesvirales capsid is too large to enter the NPC pore, the viral genome is directly injected through the NPC on which the capsid docks.

-All retroviridae except lentivirus would enter the nucleus during mitosis, when the nuclear membrane temporarily disintegrates.