Viruses (1)

Eukaryotic microorganisms and viruses
(WS 2010/2011)

VIRUS (latin: poison)

General term for all infectious agents!

China 1000 B. C.
Prevention without knowledge of the agent, based on recognition that survivors of smallpox were subsequently protected against disease

Inoculation of healthy individuals with dry material from smallpox pustules (inhale)**.**

Dimitri Iwanowski (1864-1920)

Discovery of the tobacco mosaic disease (1892)

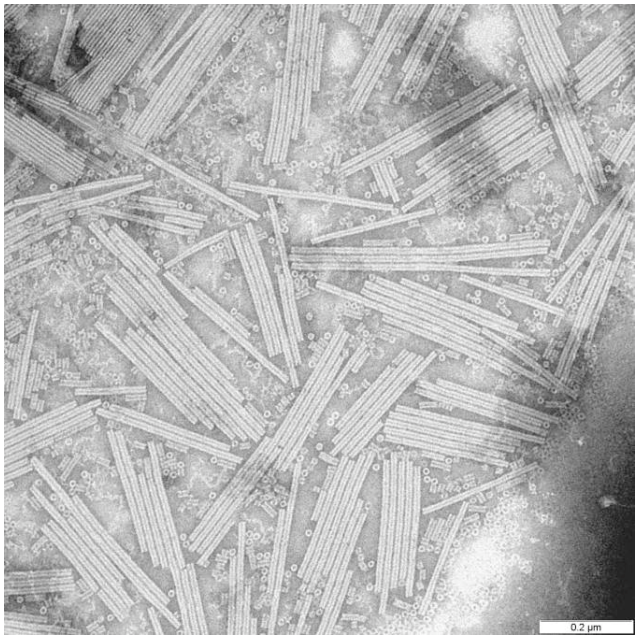
Tobacco mosaic virus

300 x 18 nm

(+) ssRNA

Genus: *Tobamovirus*

Baltimore: class 4



Discovery of the **tobacco mosaic disease** (Iwanowski 1892): Infectous agent of the tobacco mosaic disease passes through filter that retain bacteria.

Contagium vivum fluidum (Beijerink1898): Suggested that the pathogen is a distinct living agent

Agent of **foot and mouth disease** is filterable (Loeffler & Frosch 1898)

Discovery of the first human virus, **yellow fever virus** (Reed 1901)

Discovery of **bacteriophage** (Twort 1915)

Disvory of the first **influenza virus** in pigs (Schope1931)

Significant impact of virology

Medicine

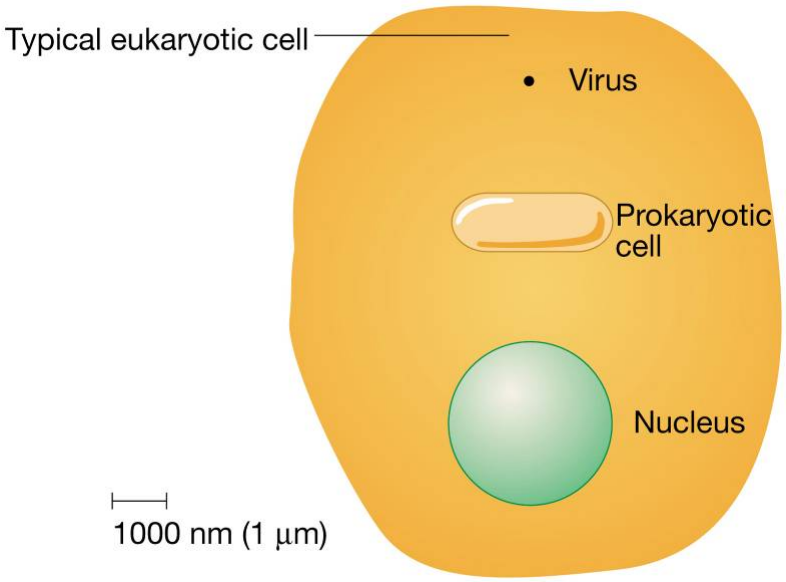
Sociology

Genetic

Biotechnology

Ecology

Size of virus particle (virion) varies between 20-300 nm



Viruses are obligate parasites

They can not perform processes for energy conservation or for biosynthesis

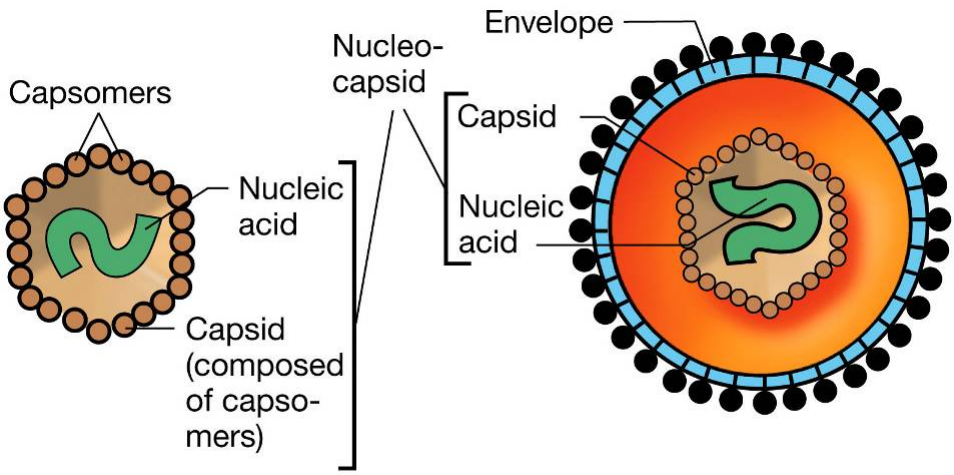
Replication occurs within a host (intracellular)

Occur as nucleic acid in the host (intracelluar) or as virion (extracellular)

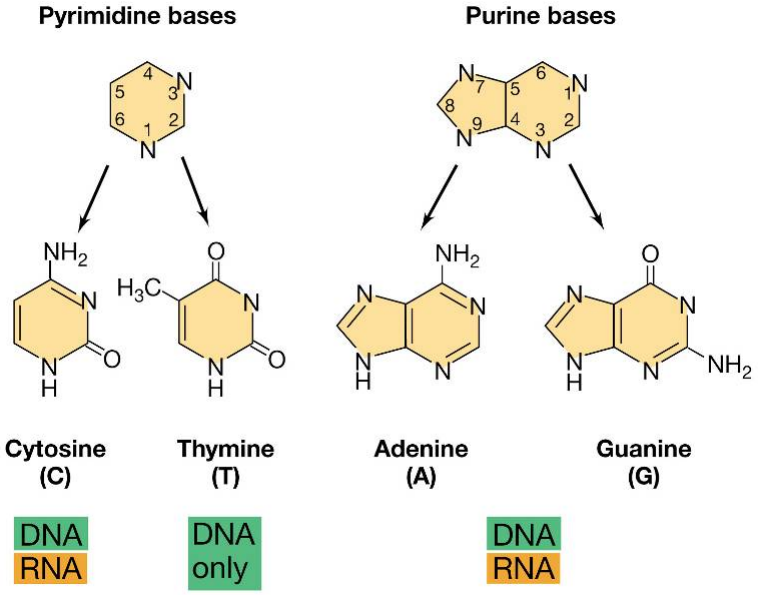
Virions consist of a genome (DNA or RNA), capsid (protein coat), and often virus-specific enzymes

Enveloped viruses are enclosed in a membrane (lipid bilayer)

Structure of virions (extracellular state of viruses)



Nucleic acid can be either DNA or RNA



Classical hierarchical system:

Kingdom

Phylum

Class

Order

Family

Genus

Species

International Committee on Taxonomy of viruses (ICTV)

(http://phene.cpmc.comlumbia.edu)

Yet, 30,000 - 40,000 viruses are known

Viruses are classified in accordance to four main characteristics:

Nature of nucleic acid in virion

Symmetry of protein shell (capsid)

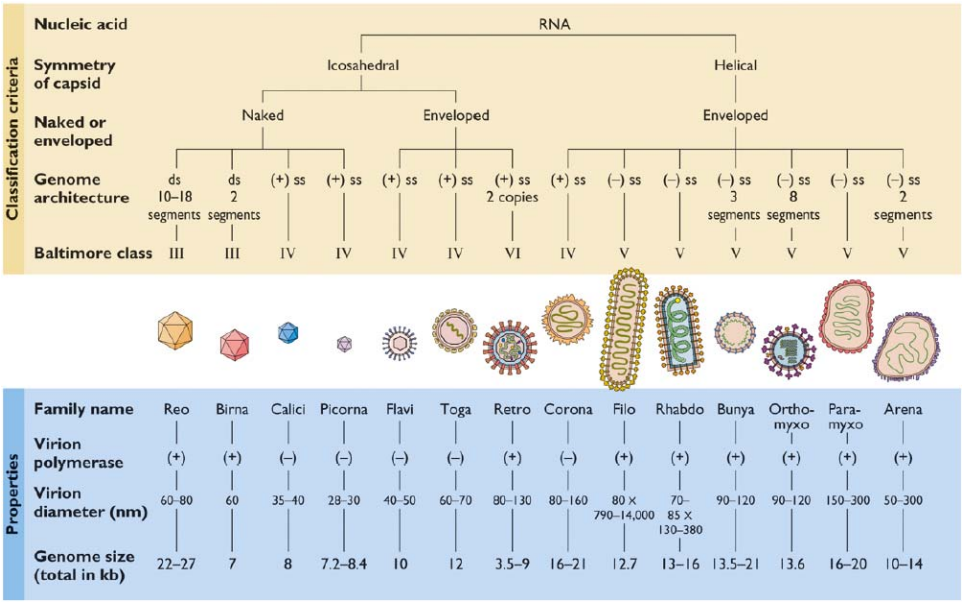
Presence or absence of lipid membrane

Dimension of virion and capsid

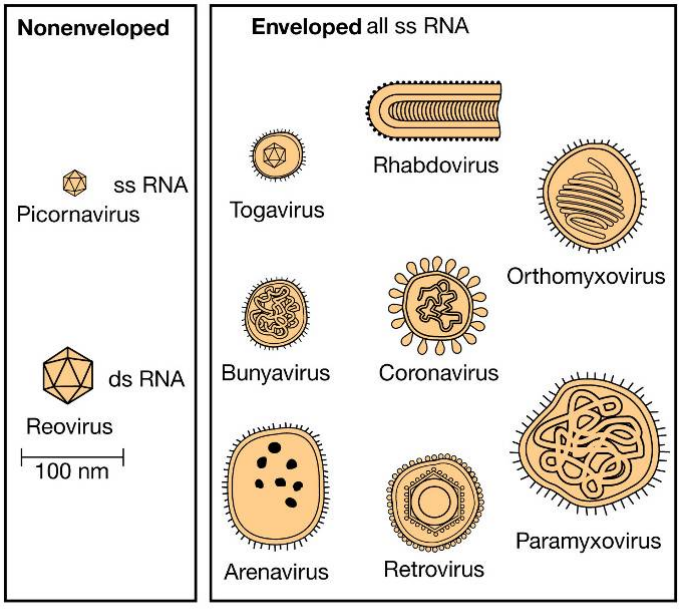
Genomic has also become important

Classification of viruses

RNA viruses



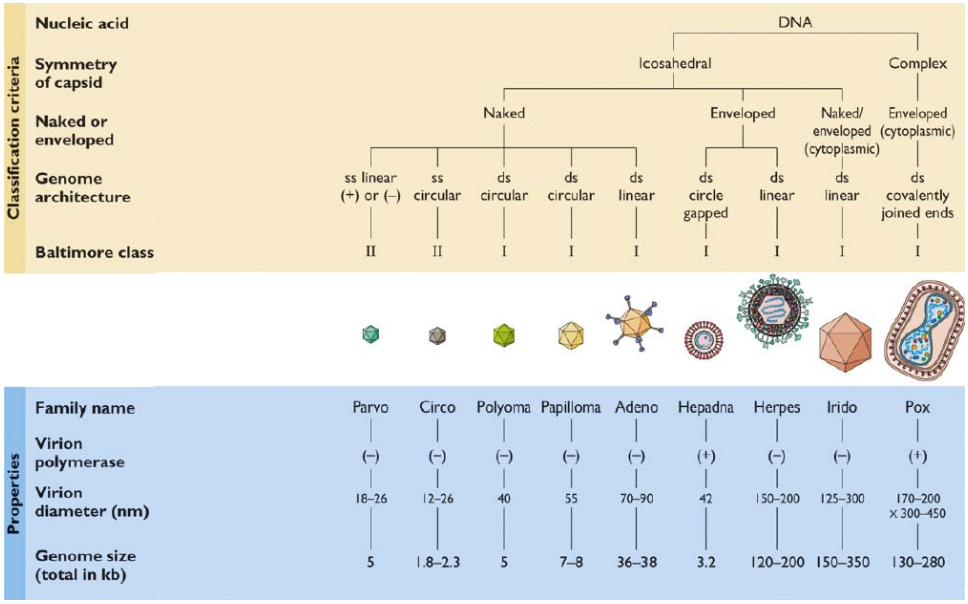
Classification of viruses



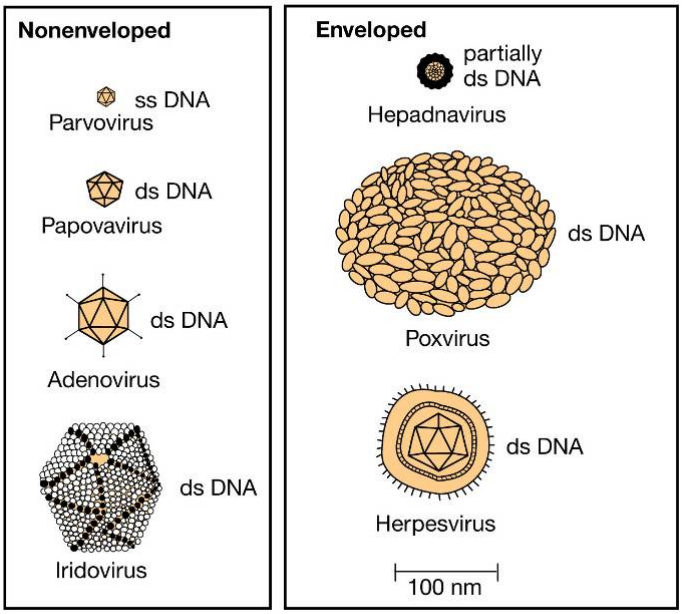
(b) RNA viruses

Classification of viruses

DNA viruses



Classification of viruses



(a) DNA viruses

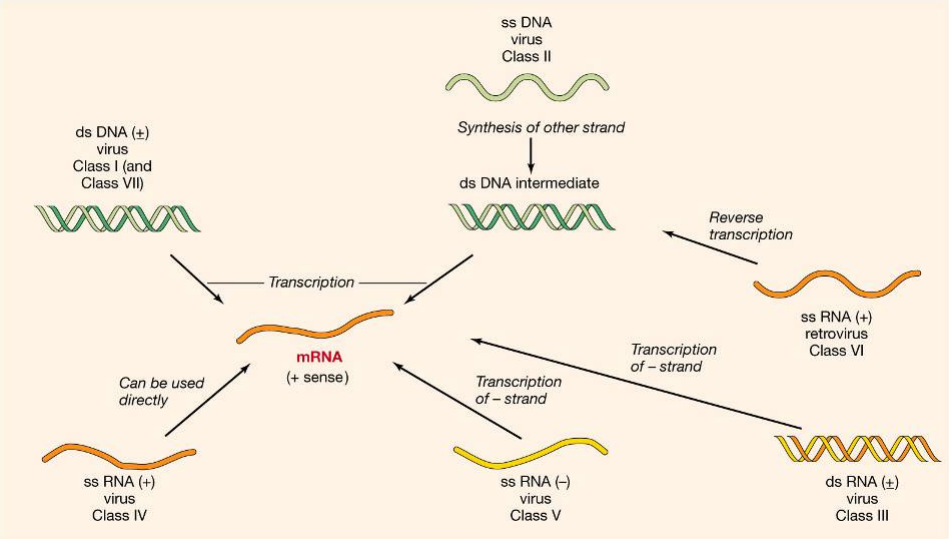
Baltimore classification (focus on synthesis of mRNA)

(+) strand can be directly translated
(-) strand cannot be translated

Combination of
a) type of viral genome and
b) information about genome synthesis

Classification into six distinct virus groups

Formation of mRNA after infection of cells by viruses



In general, RNA polymerases use double-stranded DNA!

Structural units of virions

Subunit (single folded polypetide chain)

Protomer (structural unit, one or more subunits)

Capsomer (surface structure)

Capsid (protein coat/shell)

Nucleocapsid (core, nucleic acid-protein assembly within virion)

Envelope (viral membrane, host-derived lipid bilayer)

Virion (extracellular infectious viral particle)

Function of virion proteins

Protection of the genome
Self assembly of a stable, protective protein shell
Specific recognition and packaging of the genome
Interaction with host cell membranes to form envelope

Delivery of the genome
Binding to host cell receptors
Transmission of signals that induce uncoating of the genome
Induction of fusion with host cell membranes
Interaction with cell components to direct transport of genome to appropiate site
Protection of the genome

Other interaction with host

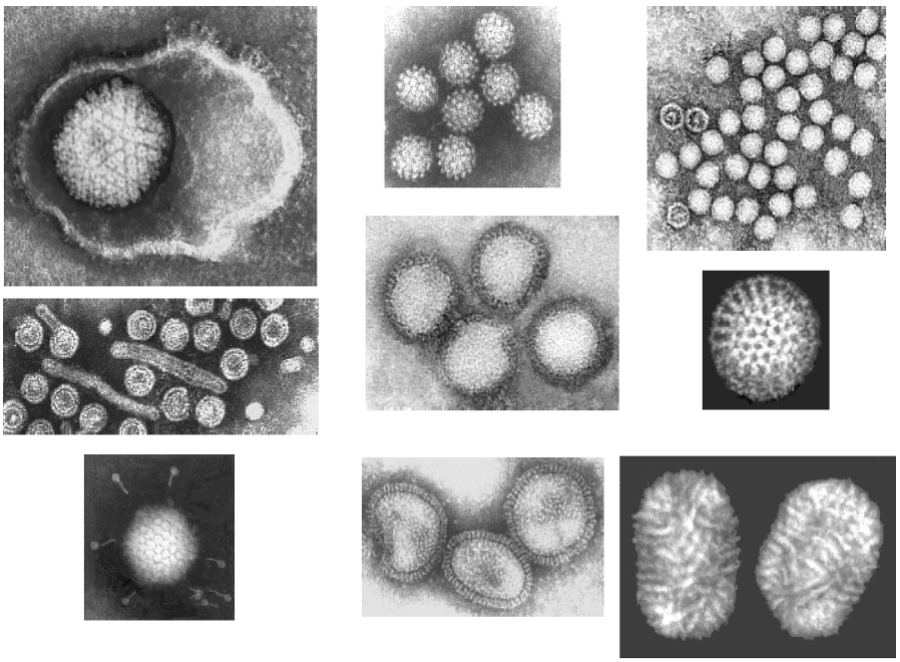
Electron microscopy (50-75 Å)
(Ruska 1940, First picture of virus particles:
Sichtbarmachung der Bakterienlyse im Übermikroskop,
Naturwissenschaften 28)

Biological materials have only little inherent contrast;
staining necessary.
Negative staining with electron-dense material (uranyl acetate, phosphotungstate)
But, detailed structural interpretation impossible

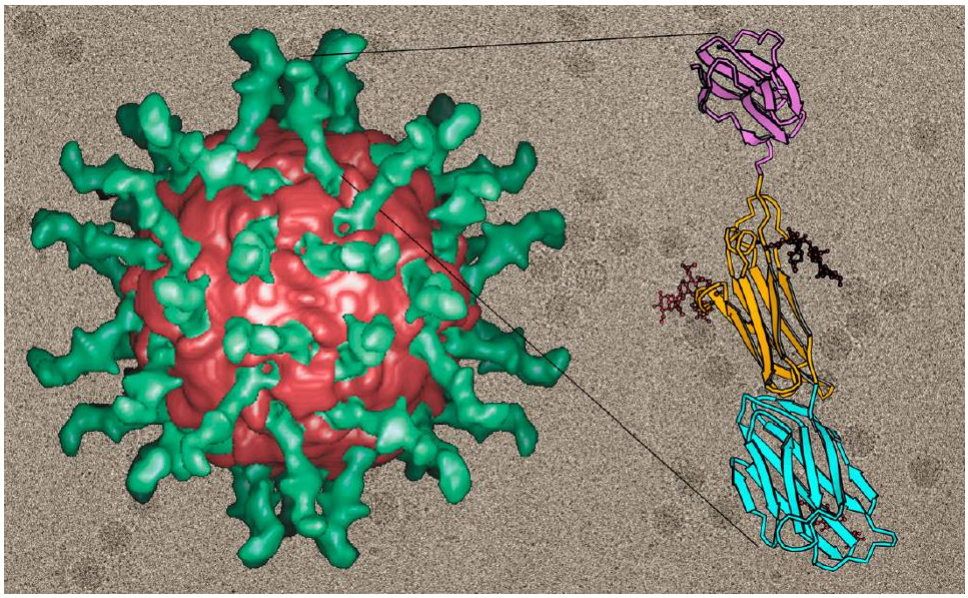
Cryo electron microscopy (8-20 Å)

X-ray crystallography (2-3 Å)
3 dimensional structures

Structure of viruses



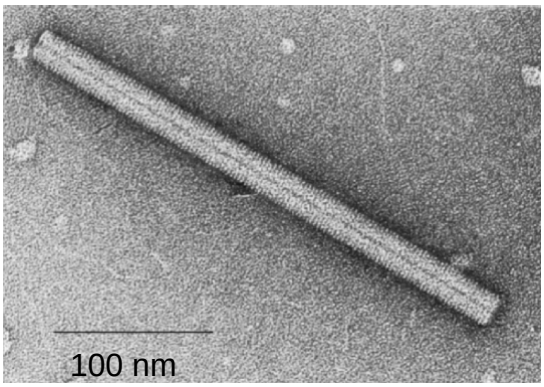
Structure of viruses

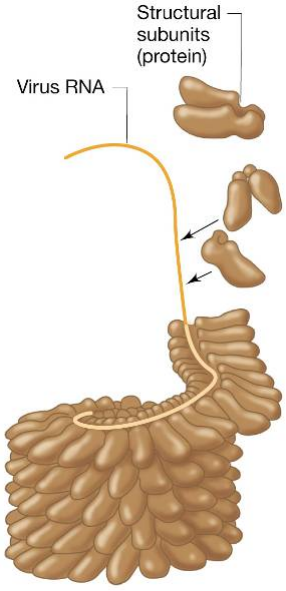


Structure of viruses

Helical structure of the Tobacco mosaic virus (Genus *Tobamovirus*)

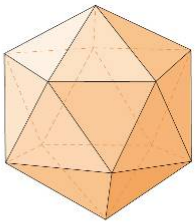
Arrangement of ss RNA and capsid by self-assembly





Structure of viruses

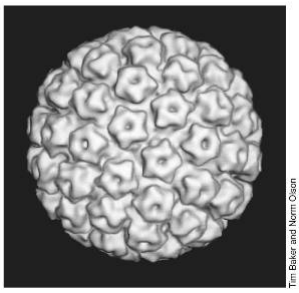
Icosahedral structure of a human papilloma virus (HPV) (Genus *Papillopma virus*)



(a)

ds circular DNA

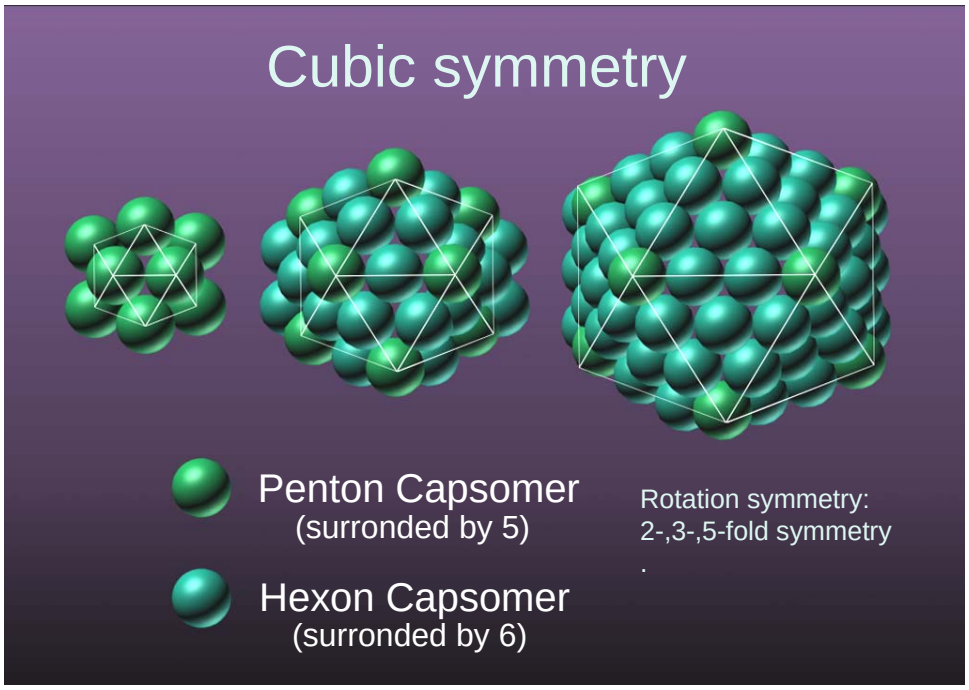
Common infection disease, transmitted by sexual contact.



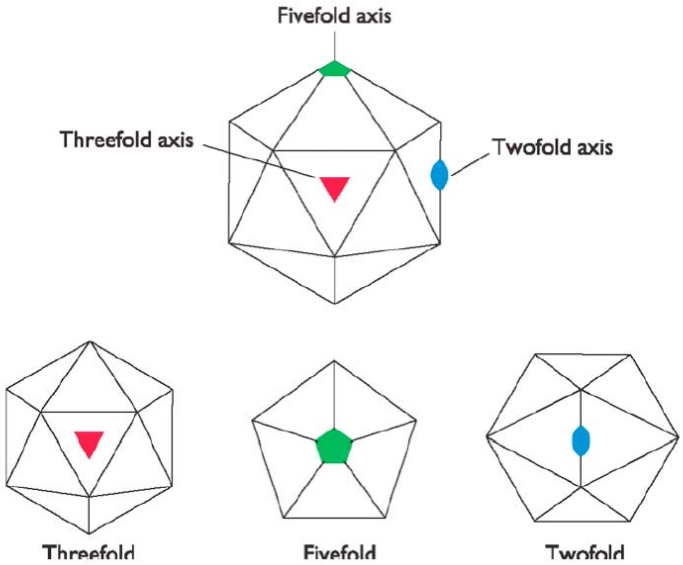
Tim Baker and Norm Olsen

(c)

55 nm in diameter

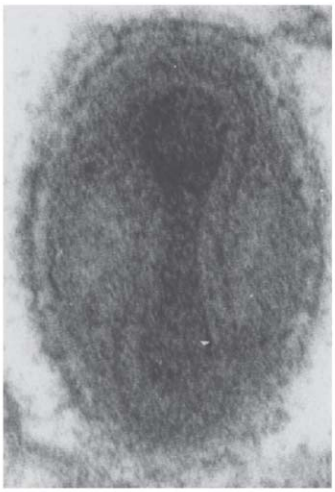


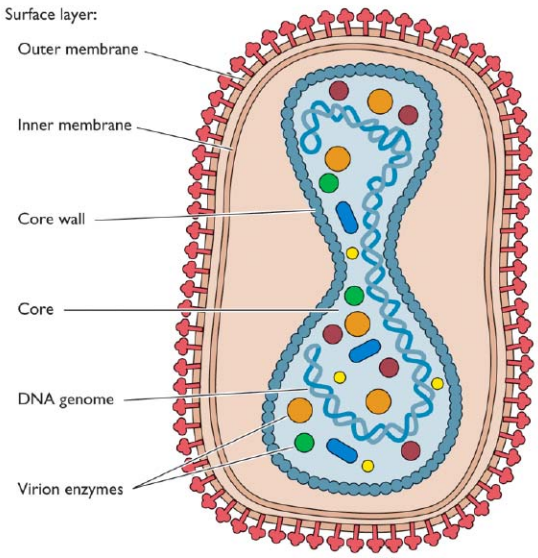
Structure of viruses



Structure of viruses

Complex structure of a vaccinia virus (poxvirus, ds DNA)
Replication in host cytoplasm



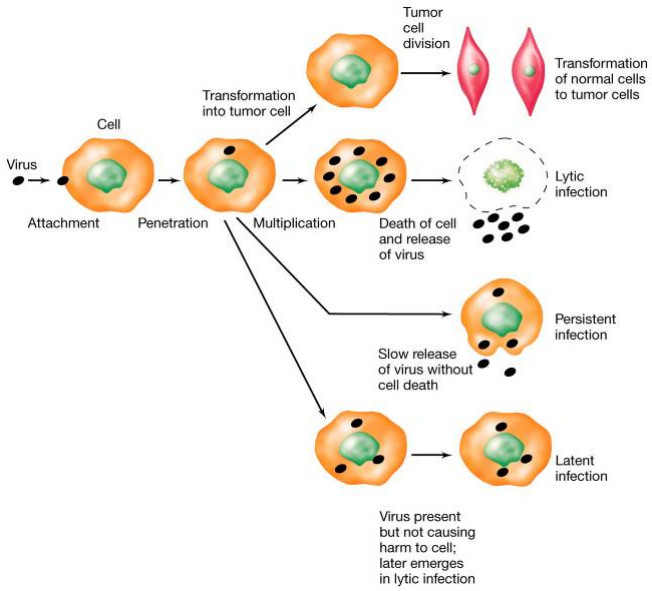


Virus multiplication

- **Attachement (adsorption)** of the virion to susceptible host cell
- **Penetration (injection)** of the virion or its nucleic acid into the host
- **Control of host cell biosynthetic machinery**
- **Replication** of virus nucleic acid
- **Synthesis of viral protein and morphogenesis (assembling and packaging)**
- **Release** of mature virions from the host cell (lysis)

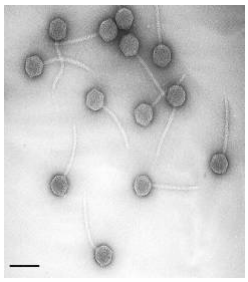
Virus multiplication

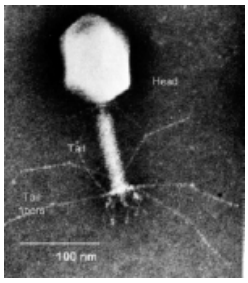
Possible effect of animal viruses on infected cells

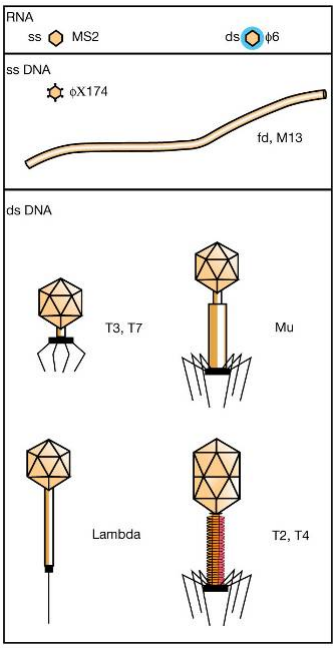


Classification of viruses

Main types of prokaryotic viruses

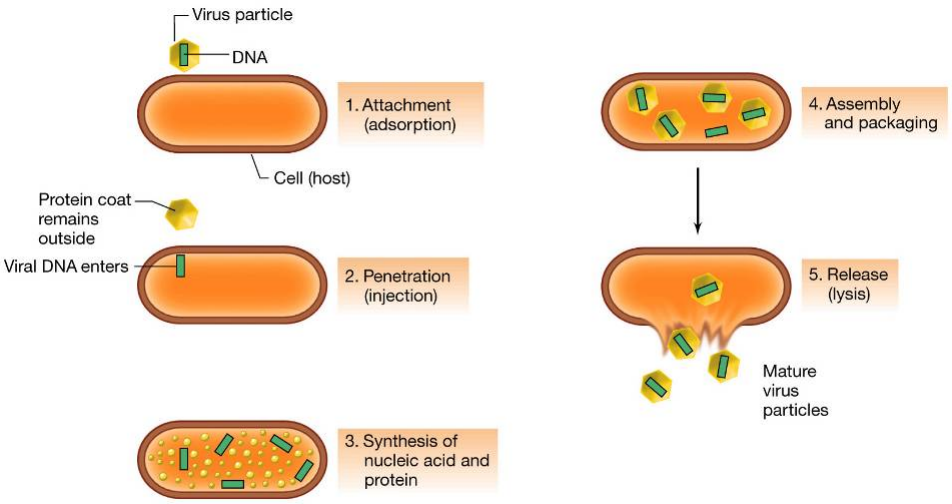




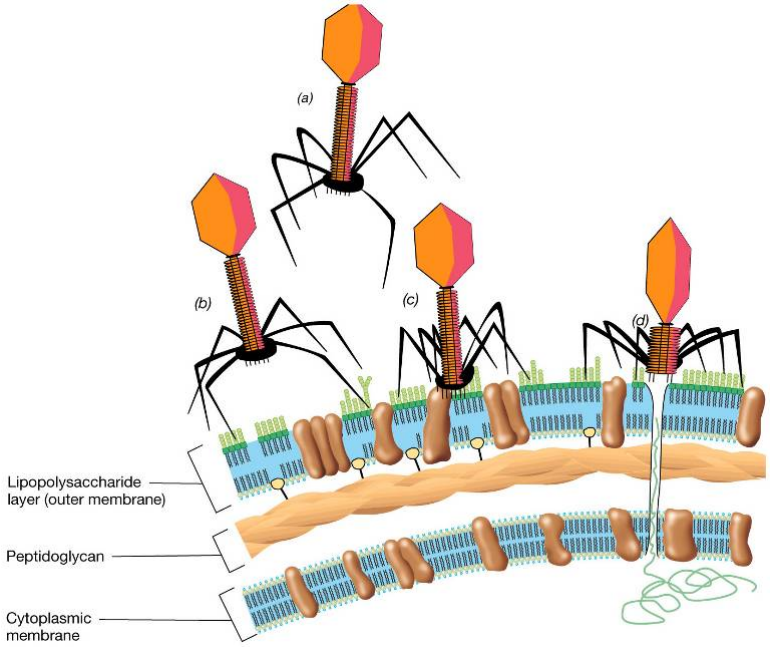


Virus multiplication

Principal replication cycle of a bacterial virus

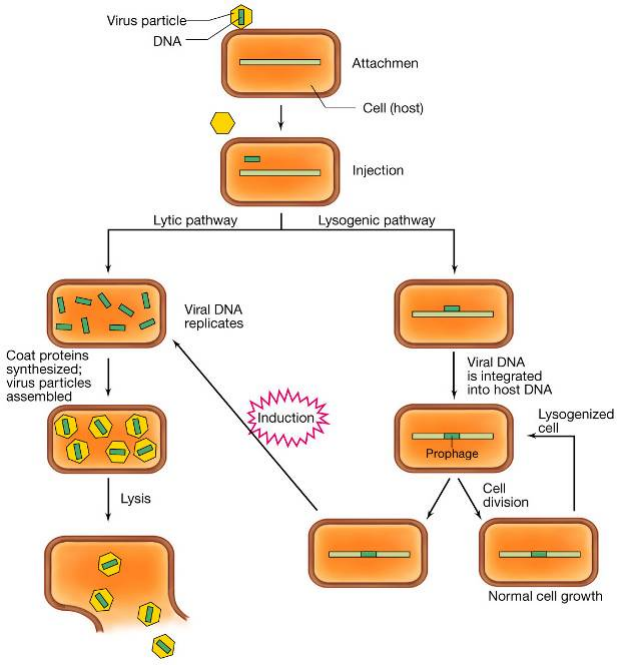


Virus multiplication: Attachment of T4 bacteriophage to the cell wall



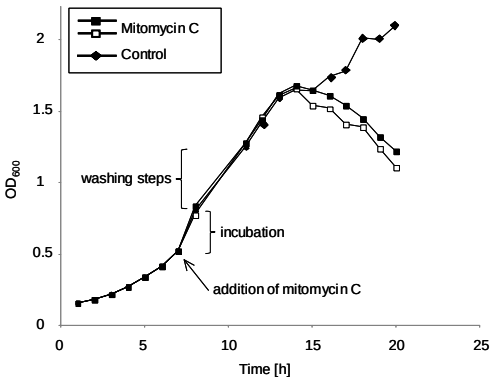
Virus multiplication

Infection by a temperate Bacteriophage (e.g. lambda)



Phage Induction Experiments

- DNA damage via the antibiotics "Mitomycin C" induces the assembly of phages



Rhizobium radiobacter strain P007

ODP Site 1225, depth: 198 mbsf

- 19 hours
  Control: no counts of VLPs
  Mitomycin C: 1.2 x 10^{10} VLPs/ml

Phage Gallery

a **Phage heads** inside a cell of *R. radiobacter*

b **Phage attached** to the cell surface of *R. radiobacter*

c **Free phage particles** induced from *Rho. capsulatus*

Myoviruses from

d1/2 *R. radiobacter*

e *V. diazotrophicus* A

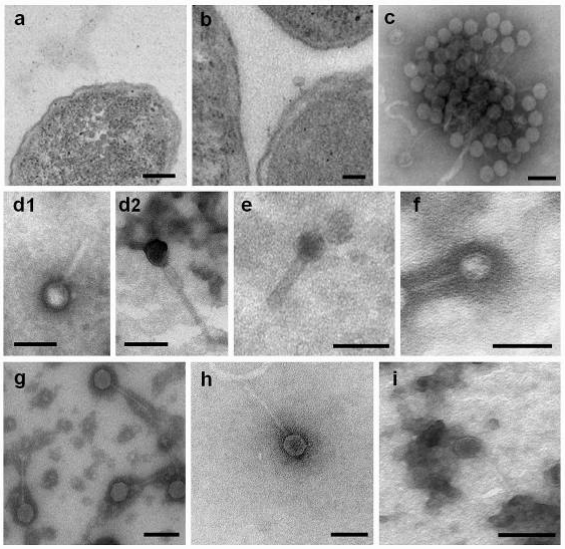
f *V. diazotrophicus* B

Siphoviruses from

g *P. glucanolyticus*

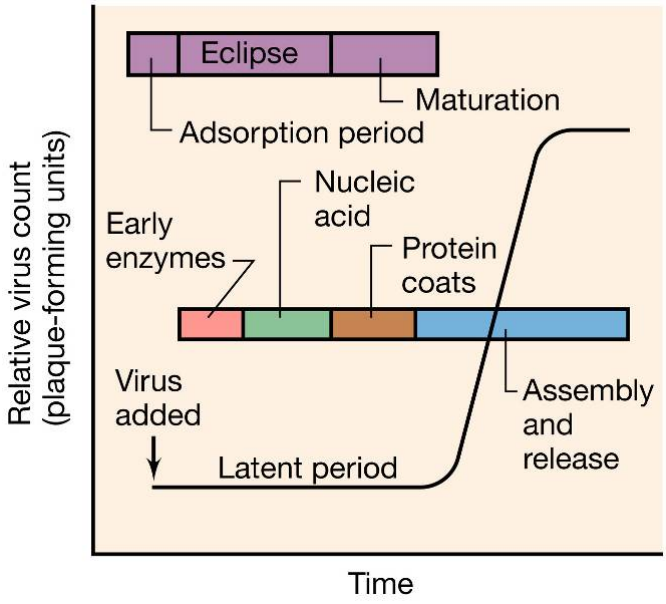
h *Rhb. capsulatus*

i *Rhv. sulfidophilum*

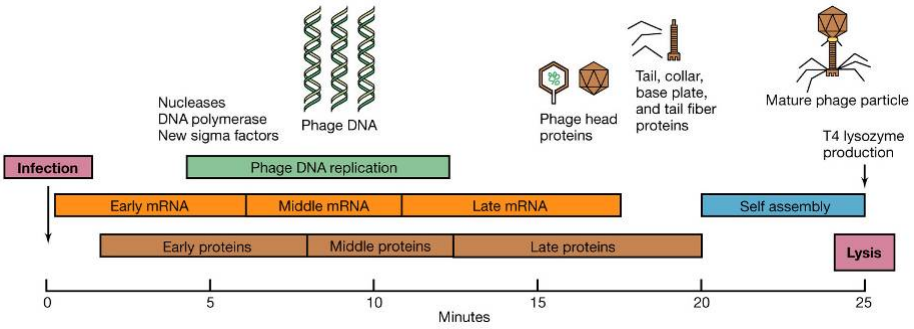


bars 100 nm

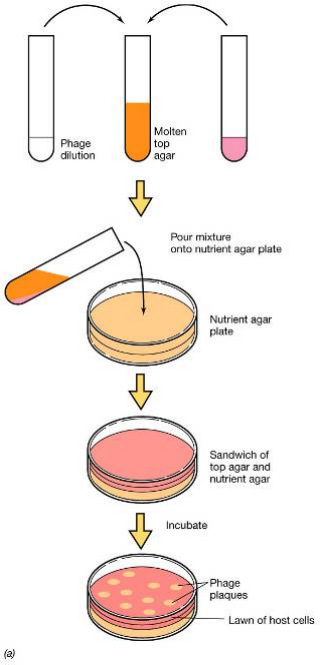
One step growth curve of virus replication

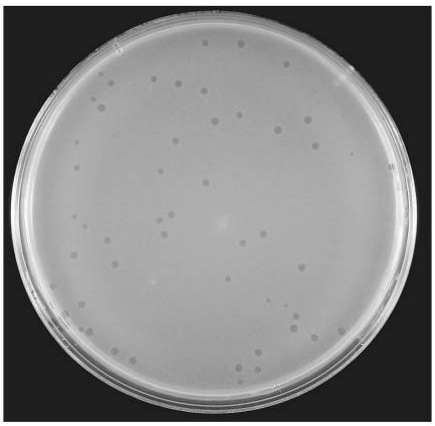


Time course of events after T4 infection



Plaque assay using the agar overlay technique





Plaques are 1-2 mm in diameter

Virus multiplication

Rolling circle replication of phage lambda

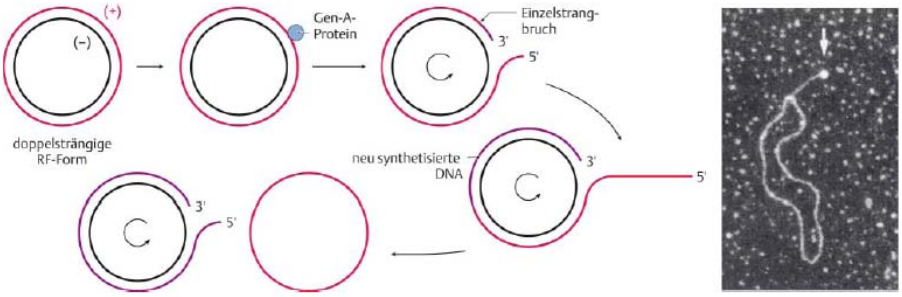


Abb. 4.9 Rolling-Circle-Mechanismus der Virusvermehrung. Nachdem das einzelsträngige minus-DNA-Genom des Phagen in der Zelle in eine doppelsträngige RF-Form transkribiert wurde, führt das Gen-A-Protein (bei ΦX174) in den plus-Strang einen Einzelstrangbruch ein. Am 3'-Ende des aufgebrochenen plus-Strangs beginnt dann die Neusynthese der DNA. Dabei wird das 5'-Ende verdrängt. Beim Phagen ΦX174 wird der neue plus-Strang direkt in die bereits assemblierten neuen Phagenköpfe hineinsynthetisiert. Sobald der neue Strang Genomlänge erreicht hat, wird er durch das Gen-A-Protein abgespalten und wieder zu einer ringförmigen Einzelstrang-DNA ligiert. Die elektronenoptische Aufnahme zeigt ein sich als Rolling Circle replizierendes Genom von ΦX174 mit einem angehefteten Phagenkopf (Pfeil) (aus Kornberg und Baker, 1992).

Viroids

Small, circular, ss RNA molecules

Represent smallest known pathogens (in plants)

Extracellular form has no capsid, just naked RNA

Has been proposed as relict from a “RNA world”

Contain no protein coding sequences

Transmitted by seed or pollen

Prions (Proteinaceous infectious particle)

- Extracellular form consist of protein

- Particles are infectious and cause a variety of diseases in animals: scrapie (in sheep) Creutzfeldt-Jacob disease (human), bovine spongiform encephalopathy (cows,BSE)

- All of those diseases affect brain or neural tissue

- Prions interact with similar host protein resulting in modification of folding and finally loss of function

Still unclear how prions introduce production of the pathogenic protein itself