Virology

- Classification
- Characteristics
- Replication
- Viral diseases

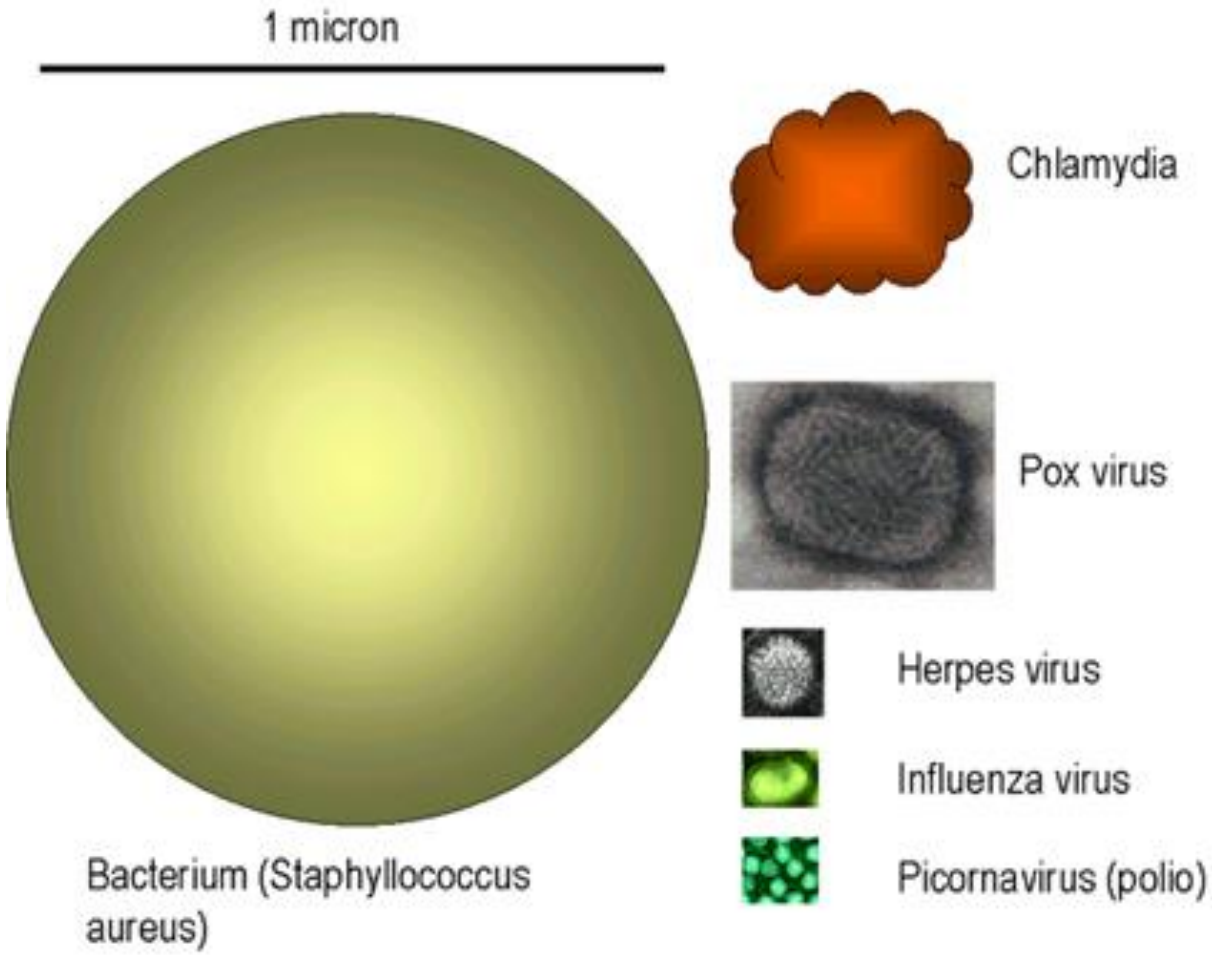
Definition and properties

- Filtrable
- obligately intracellular
- not able of individual metabolic activity – energetic metabolism and proteosynthesis possible only with host cell structures
- replication is not the division but assembly of subparticules
- genome is or RNA or DNA

Consequences of characteristics

- Viruses are not living
- must be infectious to survive
- must be able to use host cell mechanisms to produce self structures or reactions (mRNA, proteins, copies of genome)
- must be able to encode processes not available in host cell
- subparts must be able to assemble

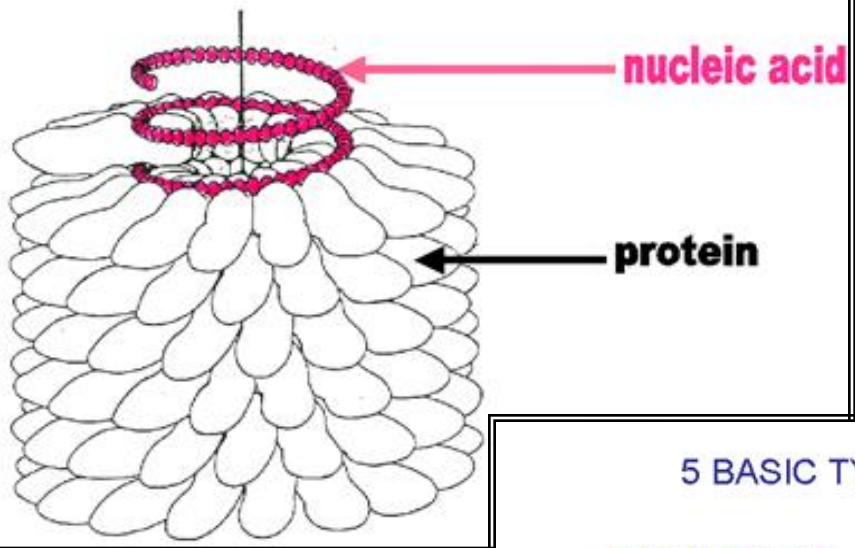
how big are viruses?



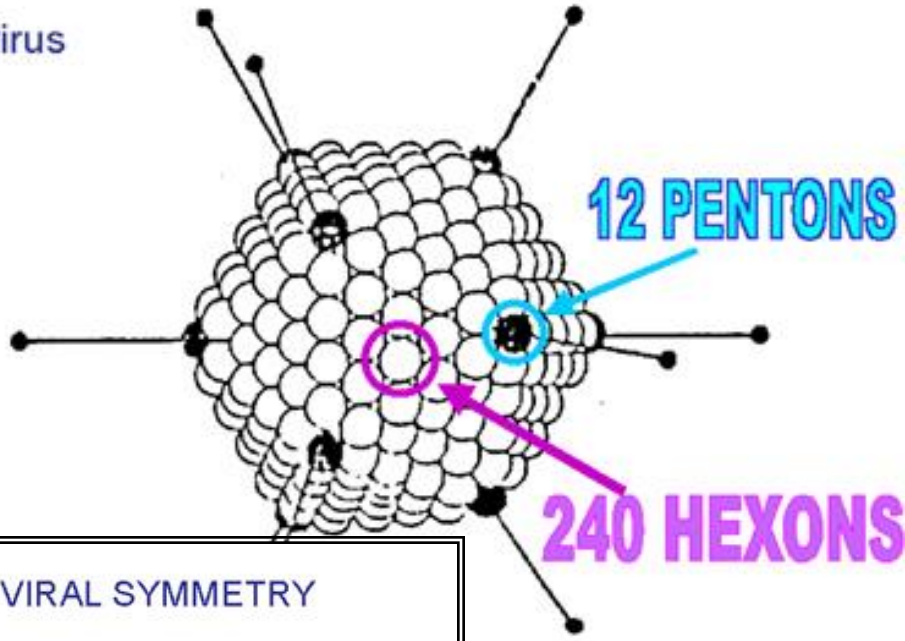
Classification and nomenclature

- Acc.to structure, shape, morfology, ...: picornaviridae,
- **biochemical properties - RNA, DNA**
- disease they cause - VHA – hepatitis A virus
- transmission - arboviruses - artropod-borne
- host cell - HPV, HIV, SIV
- tissue tropisms - adeno, enterov….

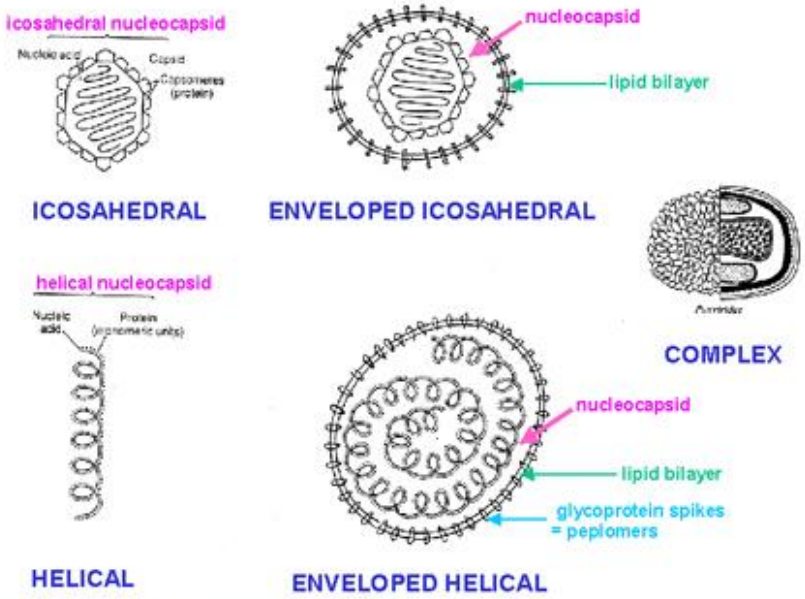
TOBACCO MOSAIC VIRUS



Adenovirus



5 BASIC TYPES OF VIRAL SYMMETRY



Adapted from Schaeler et al., Mechanisms of Microbial Disease

Structure and properties of non encapsulated viruses

- Protein
- Properties
  -stable against temperature, acids. proteases, detergents, drying
  -leaves host cell by its lysis
- Consequencies:
  spread by stool, dirty hands, dust, small droplets, after drying they are infectious, surviving in unfavorable conditions in colon, resistent to detergents, stimulise production of antibodies – humoral immunity

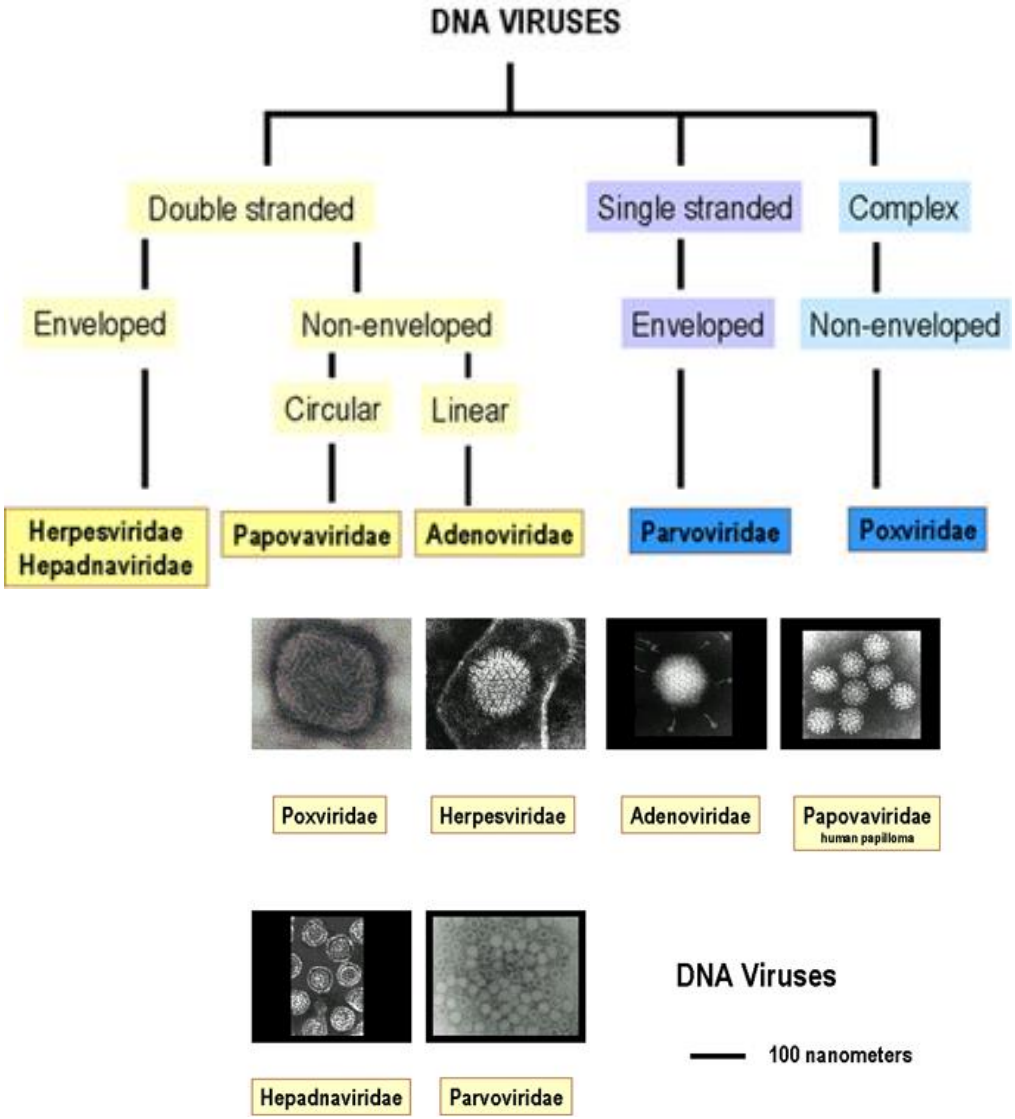
Structure and characteristics of encapsulated viruses

- Membrane: lipid, protein, glycoprotein
- Properties:
  -lability against outside conditions
  -mody cell membrane during replication
  -leaving cells by budding from host cell
- Consequencies:
  require humide environment, do not survive in GIT, spreading by big droplets, blood way, secretions,., stimulise cell immunity, sometimes hypersensitivity a imunopathological concequencies

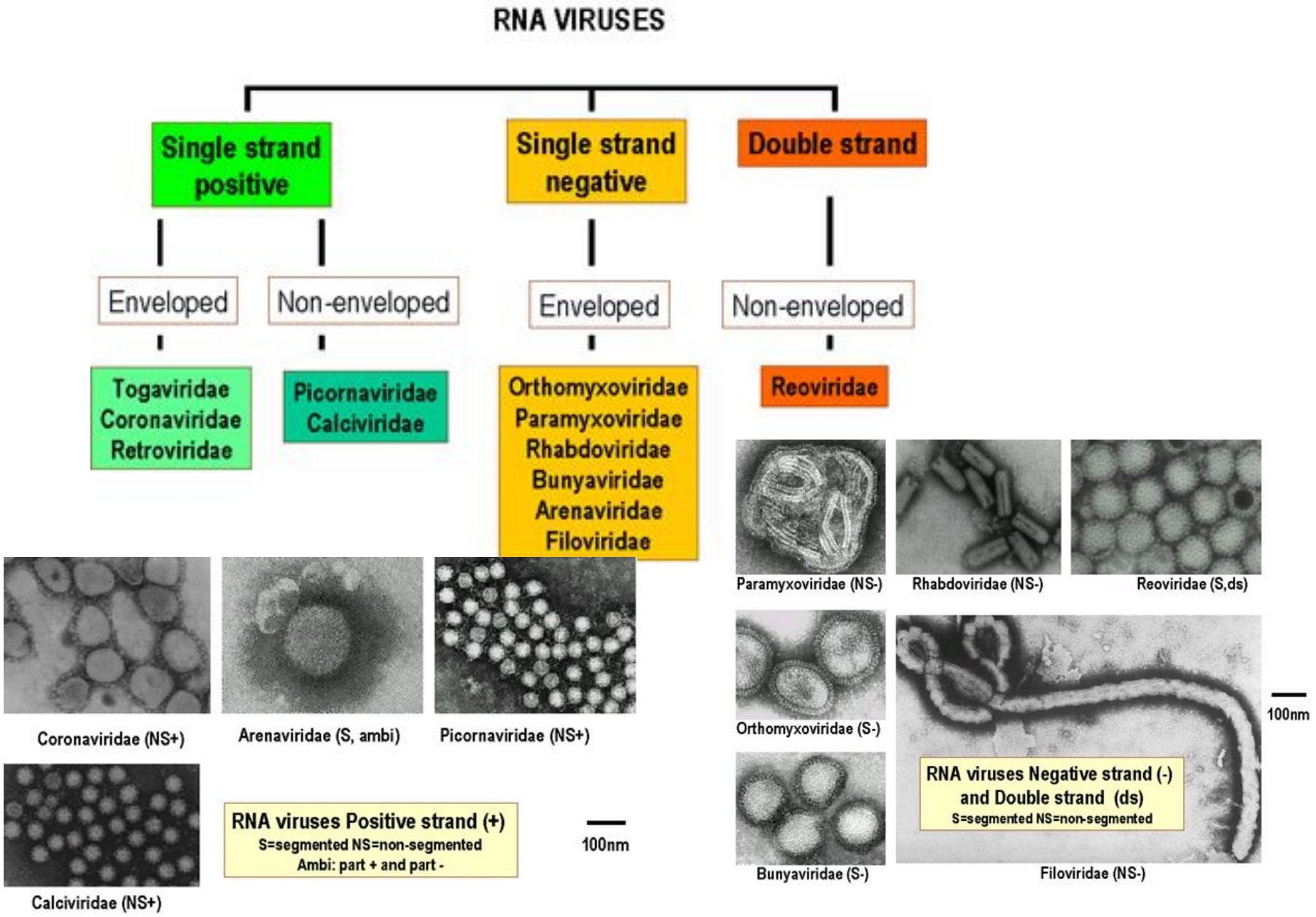
Primary classification

- Acc.to structure of virion and nucleic acid
  -RNA or DNA,
  -ss or ds
  -segmented or nonsegmented genome
  -lineare or circular
  -symetry - icosahedral, helical, complex
  -encapsulated or non encapsulated
  -number of capsomers
- Nonconvential viruses

DNA viruses

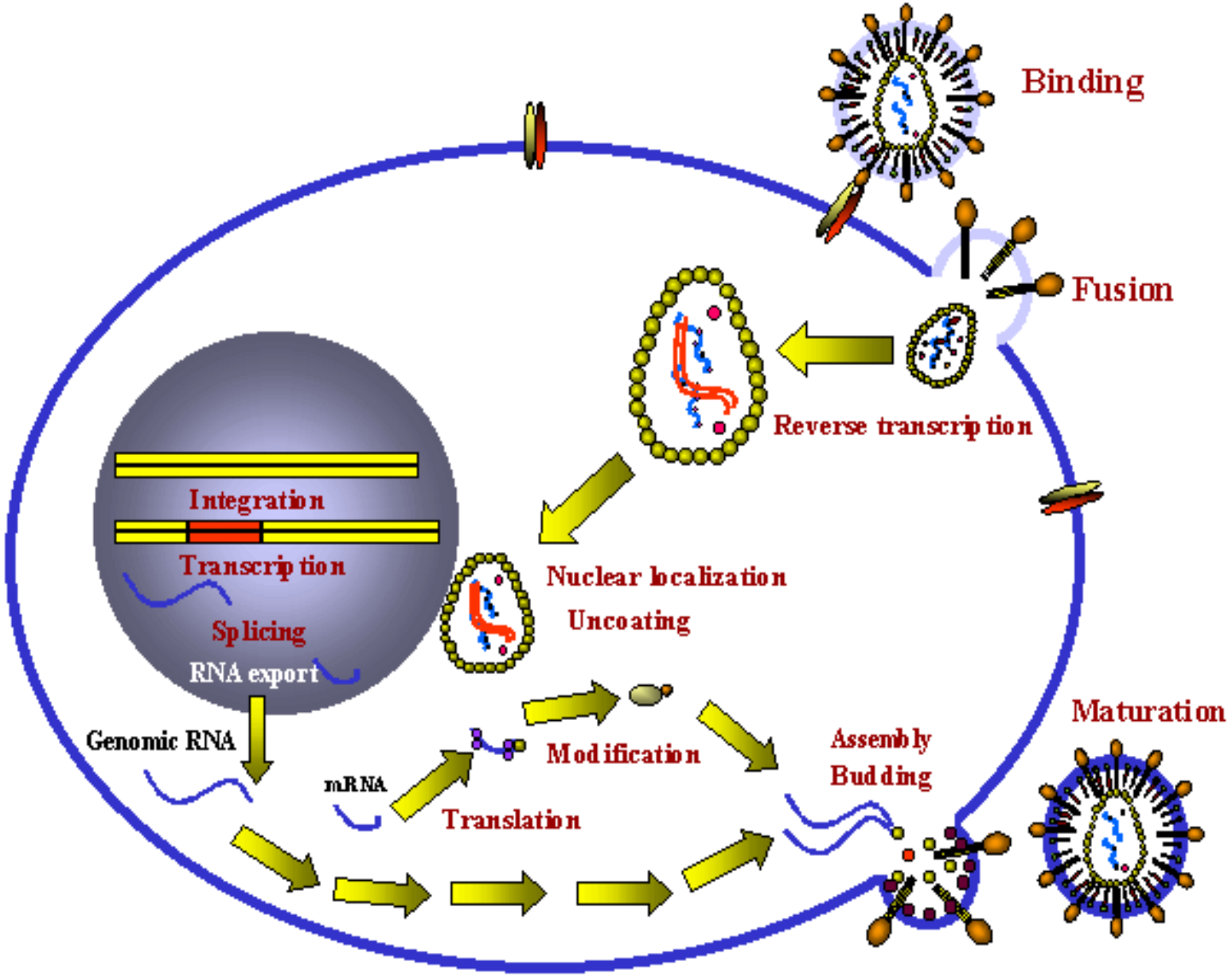

DNA VIRUSES
Double stranded
Single stranded
Complex
Enveloped
Non-enveloped
Enveloped
Non-enveloped
Circular
Linear
Herpesviridae
Hepadnaviridae
Papovaviridae
Adenoviridae
Parvoviridae
Poxviridae
Poxviridae
Herpesviridae
Adenoviridae
Papovaviridae
human papilloma
Hepadnaviridae
Parvoviridae
DNA Viruses
100 nanometers

RNA viruses


RNA VIRUSES
Single strand positive
Single strand negative
Double strand
Enveloped
Non-enveloped
Enveloped
Non-enveloped
Togaviridae
Coronaviridae
Retroviridae
Picornaviridae
Calciviridae
Orthomyxoviridae
Paramyxoviridae
Rhabdoviridae
Bunyaviridae
Arenaviridae
Filoviridae
Reoviridae
Paramyxoviridae (NS-)
Rhabdoviridae (NS-)
Reoviridae (S,ds)
Coronaviridae (NS+)
Arenaviridae (S, ambi)
Picornaviridae (NS+)
Orthomyxoviridae (S-)
100nm
Calciviridae (NS+)
RNA viruses Positive strand (+)
S=segmented NS=non-segmented
Ambi: part + and part -
100nm
RNA viruses Negative strand (-)
and Double strand (ds)
S=segmented NS=non-segmented
Bunyaviridae (S-)
Filoviridae (NS-)

Replication of viruses - stages (fig.1)

- 1. Recognition of target cell
- 2. Attachment
- 3. Penetration
- 4. Uncoating
- 5. Synthesis
  -of early mRNA and nonstructural proteins
  -replication of genome
  -of late mRNA and structureal proteins
- Assembly of parts, budding of nonencapsulated viruses, release from cell


Binding
Fusion
Reverse transcription
Integration
Transcription
Splicing
RNA export
Nuclear localization
Uncoating
Genomic RNA
mRNA
Translation
Modification
Assembly
Budding
Maturation

Replication of viruses (fig.2)

- *Host cell is the source of subtrates, energy and parts important for synthesis of viral proteins and replication of genome. Struggle for energy and sources.*
  What cell will not give as a source, that must be produced in place – must be encoded in the genom of virus.
- Replication cycle:
  - early phase of infection - *recognition, attachement, penetration, uncoating, release of the genome from the nucleus*
  - late phase – *replication of the genome, macromolecules, assembly, release*
  - phase of eclipsia – *from uncoating of the genome – (loss of infectiousity) untill the assembly and appearence of new virions*
  - latent phase – *from eclipsia till release of virions*

Recognition and attachement

- Interaction of viral surface proteins VAP - virus attachment proteins – with receptors on host cell – identify target host, specificity of virus and target tropismus
- VAP- of encapsulated viruses - glycoproteins - gp120HIV - in nonencapsulated – parts of capsid
- **Entry -** penetration – interaction of VAP and receptors starts internalisation

- *non encapsulated* - endocytosis,
- *encapsulated*- endocytosis or fusion

Uncoating

- After internalisation - genome must enter to the place of replication *(DNA – exc. poxviruses in nucleus, RNA are in cytoplasma)* endosomes, lysosomes, production of enzymes

Synthesis of macromolecules

- *Virus must produce mRNA, proteins and generate identical copy of own genom*
- Transcription, translation and replication
- Genome is usefull if it is transcribed to functional mRNA, that is able to bind ribosomes and translate information to proteins – this depends on the structure of genome and on the place of replication

Clasification acc. to replication strategy

- - DNA viruses – replicating in the nucleus – they use DNA dependent RNA polymerase of the host cell
- - DNA viruses - replicating in cytoplasma - poxviruses- produce important ensymes for transcription and replication and production of mRNA
- - mRNA for RNA viruses:
  some viruses of resemblable structure have different ways of replication

DNA viruse

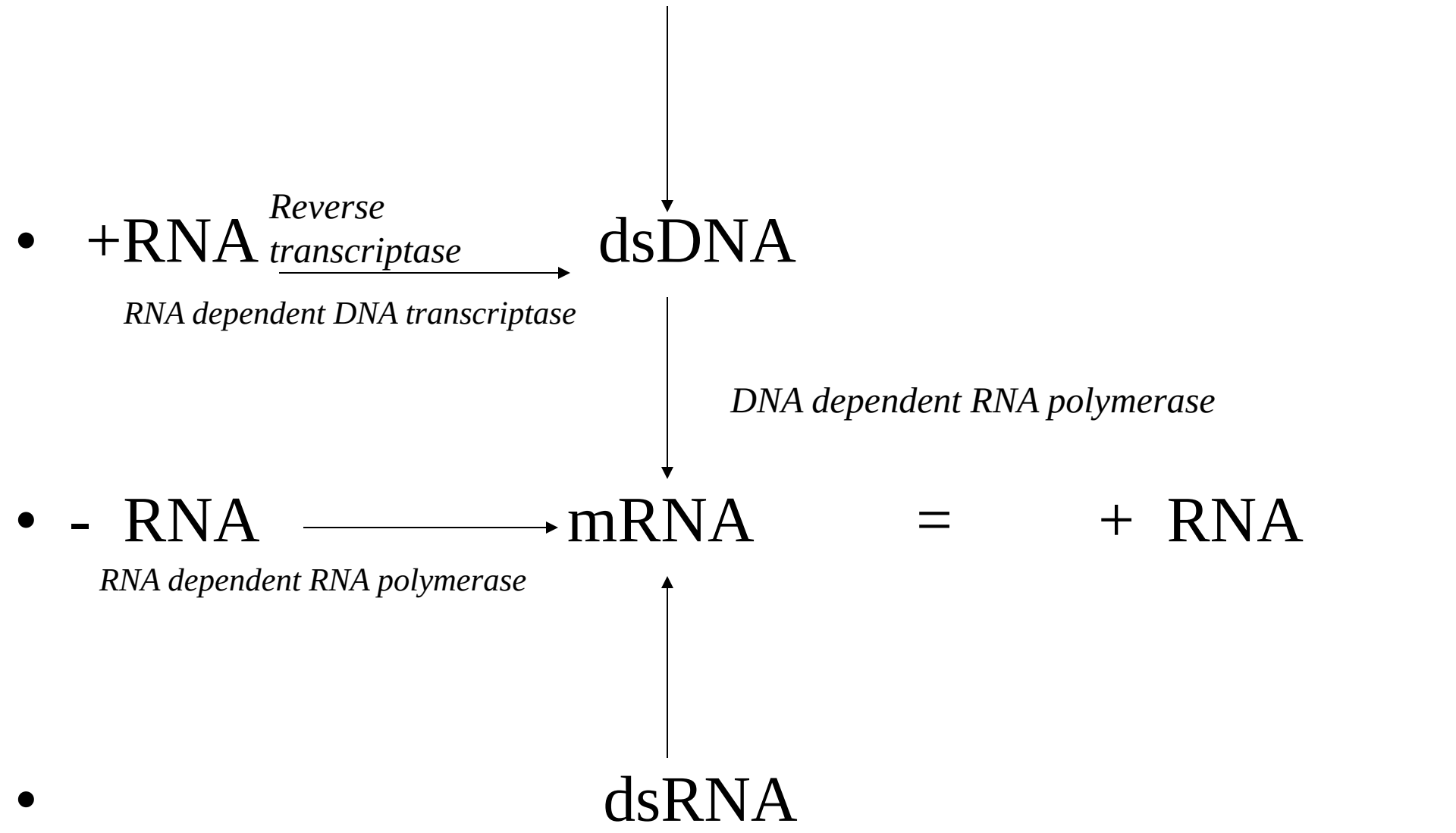
- **Transcription of** DNA in nucleus (excl. pox)
  - viral DNA is similar to host cell DNA.
  - DNA is labil, genome stays in infected cell
  - produce commonly persistent infection
  *early genes – nonstructural proteins - ensymes needed for proteosynthesis (polymerase)
  *late genes – encodes structural proteins needed for assembly
- **Regulation** – availability of DNA polymerase, substrates

RNA viruses

- Replication and transcription is similar – viral genome is or is like mRNA (+RNA) or is the template for mRNA (-RNA)
- dsRNA is produced - structure that does not exist normally in noninfected cells.
- Encoding of RNA dependent RNA polymerase – rapidly degradable - are present in active stage after uncoating or encodes early ensymes
- are labile, replicating in cytoplasma, easily mutate

- **+RNA**
- acts as mRNA, binds on ribosomes and proteosynthesis starts directly - RNA dependent RNA polymerase is synthetised that enables production of (-)RNA copy = (dsRNA)
- **-RNA**
- is not infectious, polymerase must get into the host cell so that the mRNA can be produced. Replication is done in cytoplasma (excl. influenza virus)
- **dsRNA**
- **retrovírusy**: cannot produce mRNA in cytoplasma, contains RNA dependent DNA polymerase

- Host cell gives substrate for nucleotides and polymerase
- ssDNA



Synthesis of viral proteins

- Viruses are dependent on host cells ribosomes, tRNA and production of proteins.
- Eucaryotic ribosomes bind on mRNA and produce continual protein - polyprotein – that is changed by proteases to functional proteins - *posttranslation modification* - fosforylation, glycosylation, acylation...

Assembly

- Unique parts of virions assemble like three dimensional puzzles
- DNA (excl.poxviruses) in nucleus, proteins must be transported from cytoplasma to nucleus
- RNA viruses and poxviruses assemble in cytoplasma
- Nonencapsulated viruses – empty procapside will be filled with genome or capsomers are added one by the other around genome
- Encapsulated viruses – gain capsule during budding throught the membrane of ER, nucleus or cell

Releasing from cell

- after the lysis from the cell – nonencapsulated viruses
- exocytosis, budding from plasmatic membrane – encapsulated

Released viruses are usually responsible for new infection, sometimes for production of multinuclear giant syncytia, or vertical transmission of infection

Genetics of viruses

- **Mutation** – changes of characteristics of daughter viruse in comparision of wild type
- Mutation of general genes – inactivation of virus – lethal mutations
- Mutation of other genes – changes of properties – deletion, atenuation of properties, changes in the host cell or target tissue, resistance to temperatur.....
- Induced chemically, by radiation
- In nature they are caused by insufficiency of viral polymerase
- More common in RNA than in DNA

Genetics of viruses 2

- **Recombination** – coinfection of 2 similar viruses -viruses with segmented genome/reassortment – assembly of defect virus with wild virus/complementation

- Selection pressure on new strains or mutants – possibility to survive in the host cell.

Viral diseases

- Transfer via natural barieres, avoidance of immunity control, killing of important cells or production of destructive immunity or inflamation reaction
- Immunity reaction is the best therapy of viral infection and also the most powerfull factor of pathogenensis of viral infection
- tissue tropismus – different diseases can be caused by the same virus
- one virus can produce different diseases

Infection of target tissue

- Entry to organism throught skin or mucous barrieres protected by tears, mucous, epitelium, stomac acid, IgA,
- Inhalation – most common way of transmission of infection
- Replication in infected cells where it
- – remains or spread – by blood stream, by MFS cells, by lymphatic ways, by neurones
  Viraemia primary, secundary

Pathogenesis of viral infections

Depends on virus and on cell

- Abortive infection - *nonpermisive cell, viral mutants not able to multiply*
- Lytical - *permisive cell, virus able to divide*
- Persistent - chronical, latent, recurent, transformating - *semipermissive cell* – enable only some stages of replication

*Replication leads to cytolysis or alteration of the cell

Types of viral infections on the cell level

Type	production of virus	fate of the cell
• Abortive	-	no effect
• Cytolytical	+	death
• Persistent		
*productive	+	damage
*latent	-	no effect
• Transformating		
*DNA virus	-	immortalisation
*RNA virus	+	immortalisation

Onkogennic viruses

- Some DNA viruses and retroviruses start persistent infection, that enable stimulation of uncontrolled growth of cells – *transformation or immortalisation*
- Continuating growth, loss of contact intercellular inhibition of the growth, ability to grow in suspension or on semisolide agar
- Different mechanism of inhibition of programmed death of the cell - apoptosis
- Viral transformation is the first stage, usually is not enought for oncogenesis or tumorgenesis. But cell are more prone for oncogenesis

Immunity mechanism

- Nonspecific

  Interferon - alfa, beta, gama
- Antigen specific

  humoral immunity,

  T cell immunity
- Immunity reaction

  primary

  secundary
- Mechanism how viruses evade immunity
- Immunopathological processes - hypersensitivity and inflamation

Viral diseases

- Acute infection - prodromal stage, clinical stage, reconvalescence: influenza
- Acute infection with late complication: SSPE
- Latent infection: VZV
- Chronical infection: chronical VHB
- Chronical infection with late onset of the disease: HTLV
- Slow infection: unconvential viruses

Types of viral infection