

Virus

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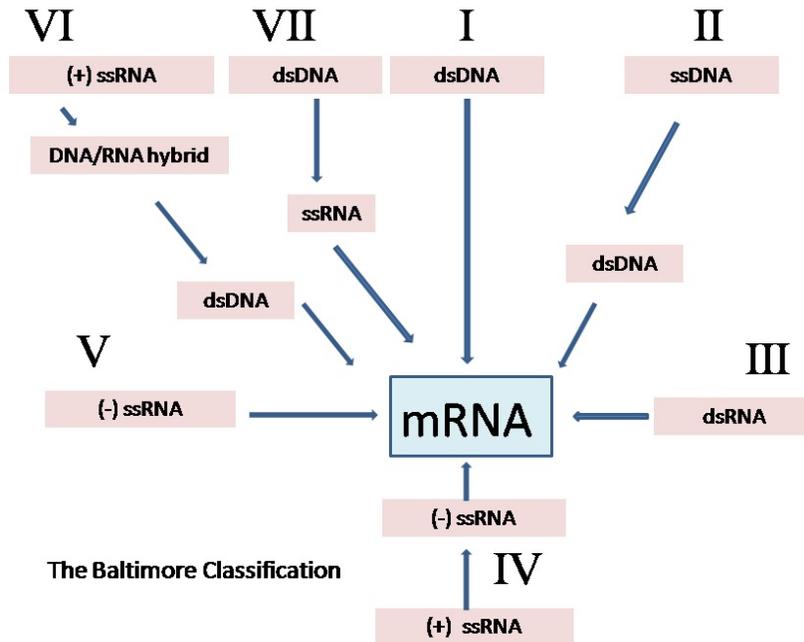
How do viruses differ?

- 1) genetic material within a virus
 - a. DNA or RNA but never both
 - b. Several different configuration of nucleic acids
 - 1) (ds)DNA, (ss)DNA, (ds)RNA, (ss(+))RNA, (ss(-))RNA, RNA retro
 - c. viral genomes are much smaller than genomes of host
- 2) the cells they attack
 - a. viruses infect only particular host's cells
 - b. affinity of viral surface proteins or glycoproteins for surface of host cell
 - 1) HIV attacks only lymphocytic T4 helper and not muscle cells
 - 2) Generalist: Rabies virus infects mammals
- 3) the composition of their capsid coats
 - a. composed of a single or several proteins
 - 1) subunits called capsomeres
- 4) their shape
 - a. shapes used to classify virus
 - 1) Helical
 - 2) Polyhedral
 - a) icosahedron with 20 sides
 - 3) Complex
 - a) many different shapes not readily fitting into either of the two categories
 - 1) small pox virus with several covering layers including a lipid layer
- 5) the presence or absence of an envelope
 - a. Non-enveloped virus: naked virus
 - b. viral envelope may be similar in composition to a cytoplasmic membrane derived from host
 - 1) envelopes's protein and glycoproteins play a role in the recognition of host cell

How are viruses classified?

- 1) Viruses are classified by:
 - a. Nucleic acid
 - b. presence of an envelope,
 - c. shape
 - d. size
- 2) Relationships between virus not well understood
 - a. Only three orders established
 - 1) Virus classified according to Family relationships: *viridae*

How are viruses classified



ICTV classification

The International Committee on Taxonomy of Viruses (ICTV) developed the current classification system and put in place guidelines that put a greater weighting on certain virus properties in order to maintain family uniformity. A universal system for classifying viruses, and a unified taxonomy, has been established since 1966. In determining order, taxonomists should consider the type of nucleic acid present, whether the nucleic acid is single- or double-stranded, and the presence or absence of an envelope. After these three main properties, other characteristics can be considered: the type of host, the capsid shape, immunological properties and the type of disease it causes. The system makes use of a series of ranked taxons. The general structure is as follows:

Order (-virales)

Family (-viridae)

Subfamily (-virinae)

Genus (-virus)

Species (-virus)

The recognition of orders is very recent; to date, only 3 have been named, most families remain unplaced. The committee does not formally distinguish between subspecies, strains, and isolates. In total there are 3 orders, 56 families, 9 subfamilies, 233 genera. ICTV recognizes about 1,550 virus species but about 30,000 virus strains and isolates are being tracked by virologists.[25]

In addition to this classification system, the Nobel Prize-winning biologist David Baltimore devised the Baltimore classification system.[26][27] The ICTV classification system is used in conjunction with the Baltimore classification system in modern virus classification.[28][29][30]

Baltimore Classification

The Baltimore Classification of viruses is based on the method of viral mRNA synthesis

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Baltimore classification Group Contains

I	dsDNA viruses
II	ssDNA viruses
III	dsRNA viruses
IV	(+)ssRNA viruses
V	(-)ssRNA viruses
VI	ssRNA-RT viruses
VII	dsDNA-RT viruses

ss: single-stranded, ds: double stranded

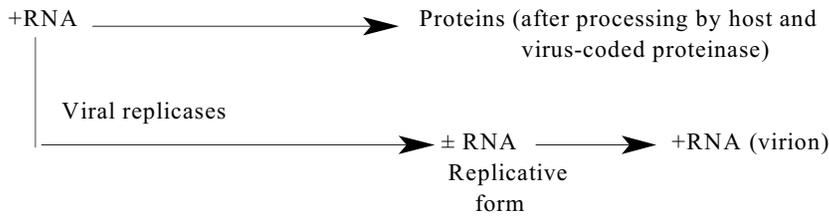
RT: reverse transcribing

The Baltimore classification of viruses is based on the mechanism of mRNA production. All viruses must generate positive strand mRNAs from their genomes, in order to produce proteins and replicate themselves, but different mechanisms are used to achieve this in each virus family. This classification places viruses into seven groups:

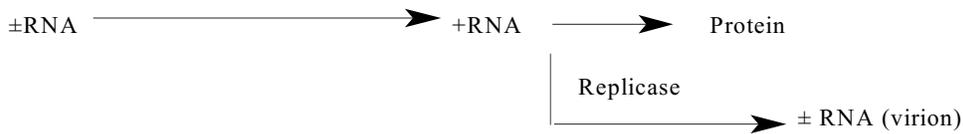
- I: Double-stranded DNA (e.g. Adenoviruses, Herpesviruses, Poxviruses)
- II: Single-stranded (+)sense DNA (e.g. Parvoviruses)
- III: Double-stranded RNA (e.g. Reoviruses)
- IV: Single-stranded (+)sense RNA (e.g. Picornaviruses, Togaviruses)
- V: Single-stranded (-)sense RNA (e.g. Orthomyxoviruses, Rhabdoviruses)
- VI: Single-stranded (+)sense RNA with DNA intermediate in life-cycle (e.g. Retroviruses)
- VII: Double-stranded DNA with RNA intermediate (e.g. Hepadnaviruses)

As an example of viral classification, the chicken pox virus, Varicella zoster (VZV), belongs to family Herpesviridae, subfamily Alphaherpesvirinae and genus Varicellovirus. It remains unranked in terms of order. VZV is in Group I of the Baltimore Classification because it is a dsDNA virus that does not use reverse transcriptase.

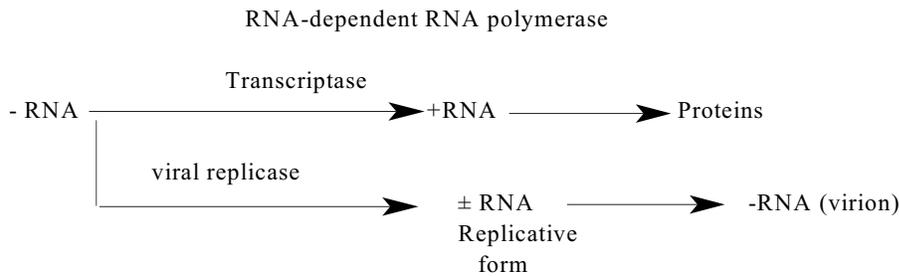
A) Positive single-stranded RNA viruses (picornaviruse)



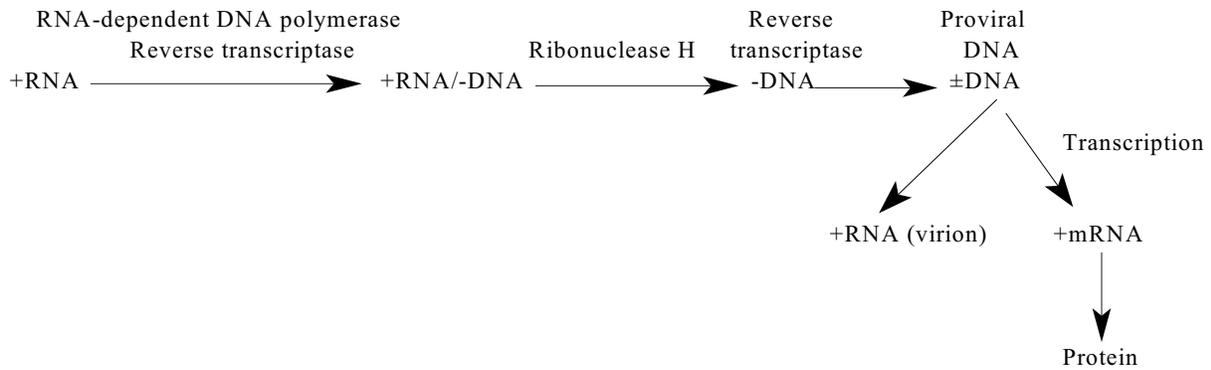
B) Double-stranded RNA viruses (reoviruses)



C) Negative single-stranded RNA viruses (paramyxoviruse - mumps and measles orthomyxoviruses — influenza)



D) Retroviruses (Rous sarcoma virus, HIV)



RNA Reproductive Strategies

Prescott, Harley and Klein. McGraw Hill, Microbiology, pg 379, 4th ed. 1999.

Do different virus attack different tissues//organs systems within the human body?

Localized Infections:		
Virus	Primary Replication:	
Rhinoviruses	Upper respiratory tract	
Rotaviruses	Intestinal epithelium	
Papillomaviruses	Epidermis	
Systemic infections:		
Viruse:	Primary Replication	Secondary Replication:
Enteroviruse (poliovirus)	Intestinal epithelium	Lymphoid tissues, CNS
Herpesvirus (HSV type 1 and 2)	Oropharynx or urogenital tract	Lymphoid cells, peripheral nervous system, CNS
Rabies virus	Muscle cells and connective tissue	CNS

RNA Reproductive Strategies

Prescott, Harley and Klein. McGraw Hill, Microbiology, pg 379, 4th ed. 1999.

What is a Bacteriophage, what is their mode of action (MOA) upon bacteria and how do they differ from animal virus?

Bacteriophages

A. Fine structure

1. Capsid (head), {sheath, tail fiber, baseplate, pin} = Tail

B. Detection and quantification (see lab 15)

C. Life cycle of a lytic phage

1. Molecular events during **5 distinct stages**:

- a. 1- attachment; 2 - penetration; 3 - biosynthesis 4 - maturation 5 - release

2. **Eclipse** period

- a. The period of time is when viral multiplication is complete, yet, infective virions are not present.

3. **Burst time**

- a. averages 20 - 40 minutes
- b. the number of phage particles released from a single cell is referred to burst size
Ranging from 50 to 200 particles

D. Life cycle of a lysogenic phage

Lysogeny is a state of cell chromosome where a bacteriophage genome has been inserted into the bacterial chromosome by nonreciprocal recombination occurring between the phage chromosome and the bacterial chromosome. This insertion occurs at specific locations in each of chromosomes where there is homology of sequences in the two chromosomes.

Lysogenic conversion is the state of a cell that shows new properties like ability to form cytotoxins. The *tox* gene, coding for a toxic protein affecting eukaryotic cells, is on the phage genome that is expressed in the bacterium without causing lysis of the bacterial cell and production of more phage. The *tox* gene that is located in a corynephage chromosome codes for diphtheria toxin that kills susceptible human cells. When this phage chromosome becomes inserted into chromosome of the bacterium *Corynebacterium diphtheriae*, human infection with this microbe leads to formation and release of diphtheria toxin in the human host producing symptoms of diphtheria.

1. Molecular events during replication

- a. Lysogenic phages are also called temperate phages

- (1) may also induce lytic cycle,
- (2) are also capable of incorporating into the host DNA (inserted phage DNA is called a **prophage**)

- b. In lysogeny, the phage remains latent or inactive.

- (1) Host cells are known as **lysogenic** cells.

2. Formation of prophage

- a. 1 - **Penetration**;

- 2 - Original linear phage DNA **forms a circle**;
- 3 - circular DNA **becomes part of the circular bacterial DNA** (the lysogenic cycle);
- 4 - Prophage genes are **repressed** by two repressor proteins products of the prophage virus

3. Relationship to **specialized (restricted) transduction**

- a. When host cell replicates ---- prophage DNA is replicated but prophage remains silent
- b. Spontaneous event or UV light or certain chemicals causes phage to pop out of host DNA becoming active
 - (1) Lytic cycle initiated

4. Important results of lysogeny

First, the lysogenic cell is immune to reinfection by the same phage virus **but** the cell is not immune to other virion attacks.

Second, Phage conversion: The host cell may exhibit new properties.

Example: *Corynebacterium diphtheriae* (causes diphtheria) The organism can produce toxin only when it carries a temperate phage, prophage carries the gene coding for the toxin

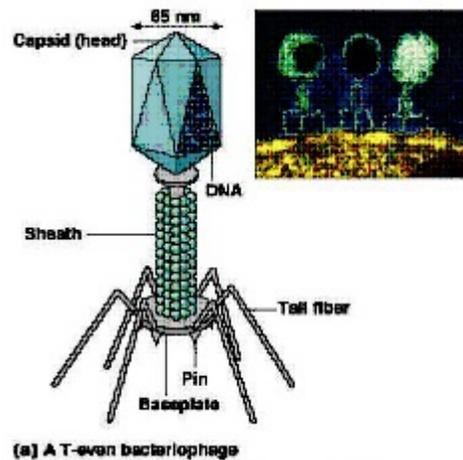
Third, Specialized transduction: Transfer of bacterial DNA from previous to new host. Bacterial DNA is packaged along with prophage DNA in the same capsid.

- (1) Bacteriophage λ picks up the *gal* gene for galactose carrying it to galactose negative cell

How does lysogenic conversion affect a bacteria?

The important outcomes of lysogenic conversion of a bacteria by a bacteriophage are:

- 1) Bacteria become immune to further attack by similar phage virus
- 2) The temperate phage become incorporated into the new host structure along with a viral gene that codes for a protein that suppresses phage expression. This incorporated phage is now called a prophage
- 3) The lysogenic temperate phage may be carrying a gene from a previous host cell that provides a new phenotype expression for the infected host.



How do Animal Viruses Differ from Bacterial type viruses?

A. Replication of animal viruses

1. Multiplication of animal virus follow the basic patter that of bacteriophage with several differences
 - a. mechanism of cellular penetration
 - b. Synthesis and assembly of new viral components differs
 - (1) Animal viruses have different enzymes not found in phages

B. Cultivation

- 1 - **Attachment** to receptor site on cell membrane
 - a. Animal virus do not contain appendages like tail fibers
 - b. Attachment sites of virus may include spikes: *Influenzaviurs*
 - c. Gene variation between animals results in variability of susceptibility of animal host
2. **Penetration** 3 methods of viral penetration into eukaryotic host cell
 - a. **endocytosis**: folding of the cell membrane inward engulfing enveloped virus
 - 1) Enveloped virus uncoats within cytoplasm of host release nucleic acid
 - b. **Fusion**: Envelope of Enveloped viruses fuse with host plasma membrane
 - (1) releasing capsid into cell's cytoplasm HIV works in this manner
 - c. **Direct penetration** of nucleic acid into cytoplasm through membrane of host without capsid entering the cytoplasm
3. **Uncoating**
 - a. Viral nucleic acid separates from its protein coat.
 - b. Enzymes degrade the proteins of the viral capsid releasing the virus nucleic acid
Poliovirus works in this manner

C. Replication & Maturation

Biosynthesis of Nucleic Acid

Virus uses the host system to make new nucleic acid

Proteins and capsid are synthesized in cytoplasm.

Proteins migrate into nucleus and are assembled into active virus.

Released from host cell

DNA viruses

Transcription and translation using host enzymes

Exception is Poxviruses - All component synthesized in cytoplasm. Poxviruses use their own transcriptase enzyme

D. Importance: Interactions with host cells

1. **Active infections** caused by DNA viruses include hepatitis, infectious mononucleosis, Burkitt's lymphoma, chicken pox, and small pox.
2. **Latent infections** caused by DNA viruses include genital herpes and pharyngitis caused by adenoviruses
3. **Oncogenic** (cancer-causing) and potentially oncogenic DNA viruses are common; such viruses cause cancer of the liver and genitourinary tract, as well as lymphoma and papilloma.
4. **Prions:** infectious protein particles:
 - a. the gene of PrP^c is located on chromosome 20 in humans. PrP^c produced by cells is secreted to the cell surface. This type of disease runs in the family line.
 - b. PrP^{sc} reacts with PrP^c on the cell surface converting the PrP^c to PrP^{sc}
 - c. PrP^{sc} is taken in by endocytosis and accumulates in the lysosome.

Animal virus

<http://textbookofbacteriology.net/themicrobialworld/AnimalViruses.html>

HIV

<http://www.youtube.com/watch?v=RO8MP3wMvqg>

PBS NOVA Now: Flu (Avian)

<http://www.pbs.org/wgbh/nova/sciencenow/3318/02.html>

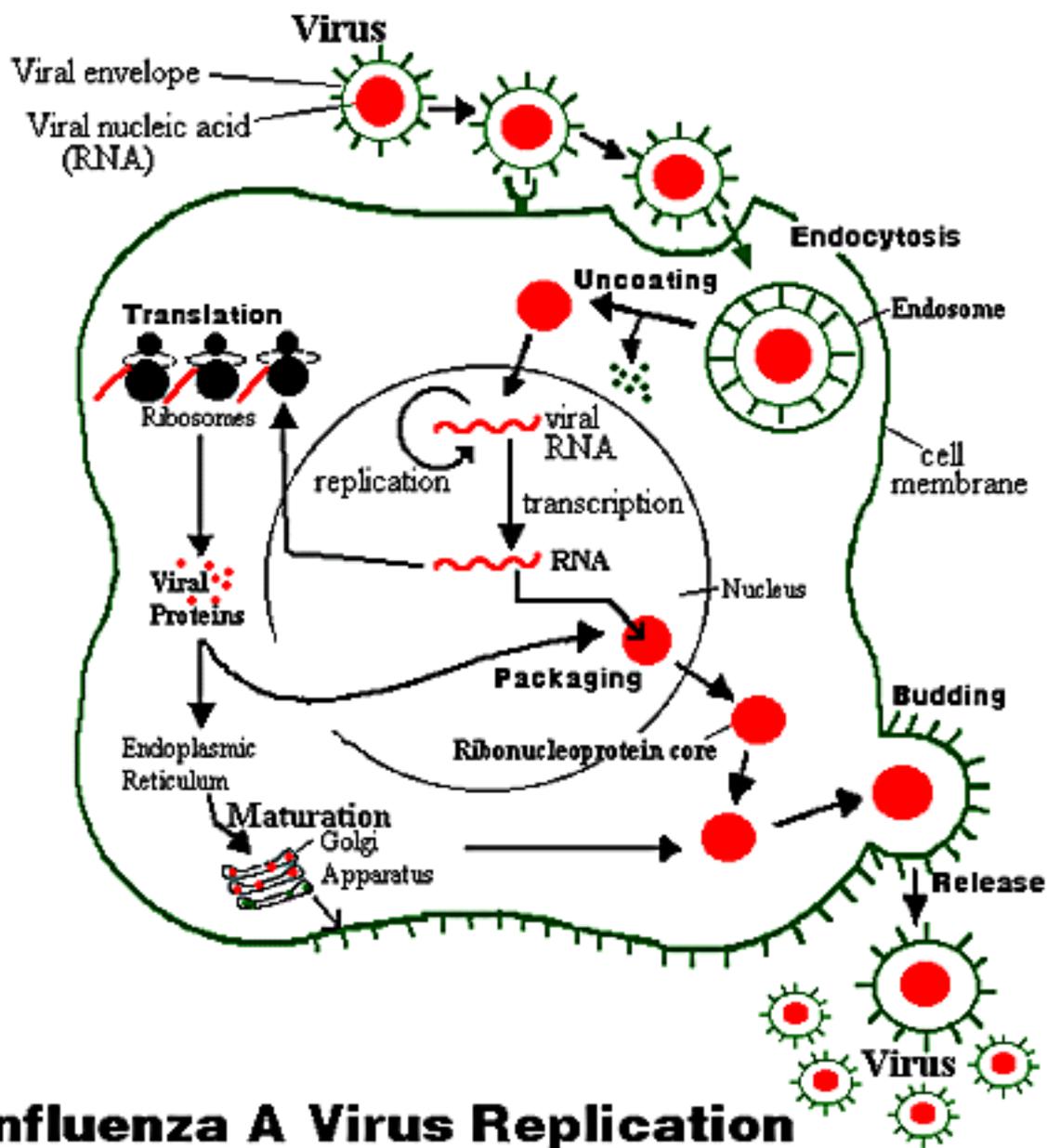
PBS NOVA Now: Flu (Avian) (part 2)

<http://www.pbs.org/wgbh/nova/sciencenow/3302/04.html>

Lysogenic cycle

<http://www.youtube.com/watch?v= J9-xKitsd0>

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Influenza A Virus Replication