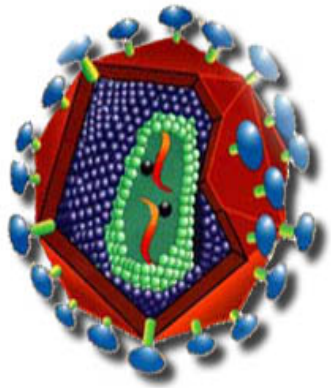


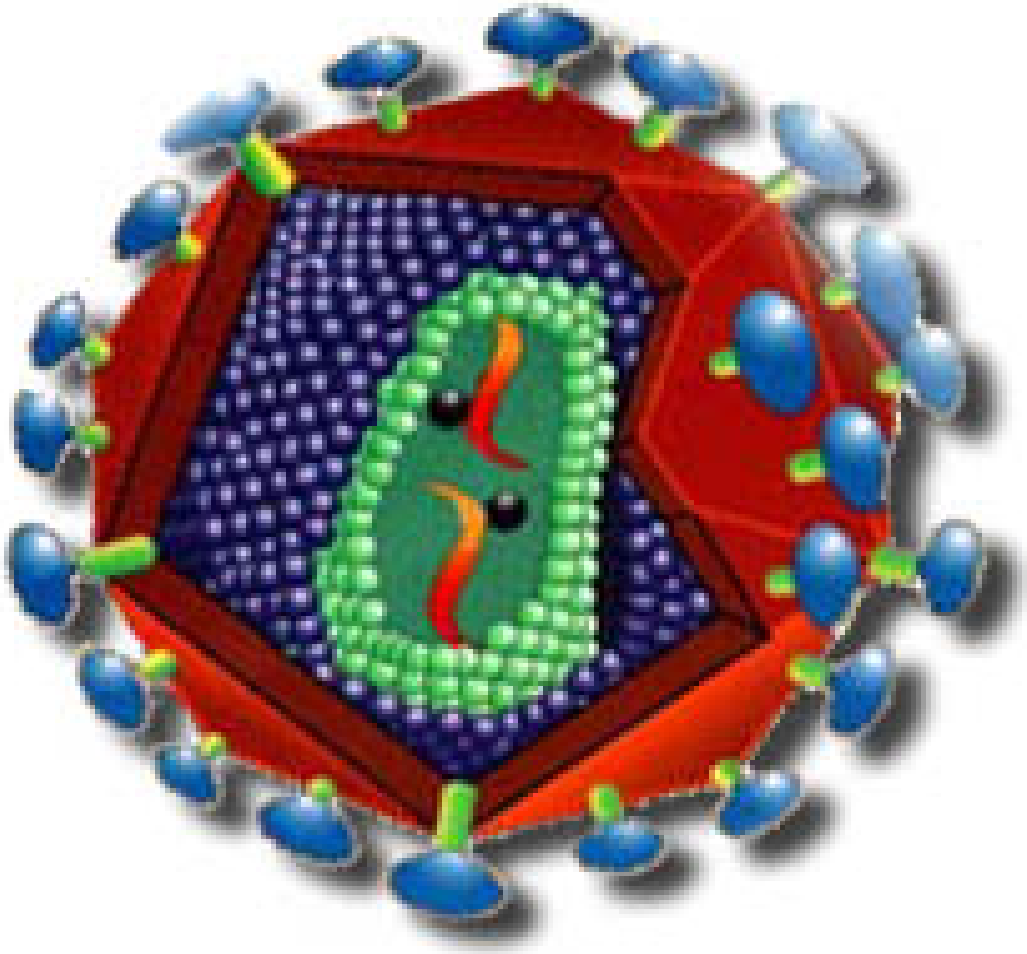
PART III Basic Virology


Basic Concepts of
Viruses

Viruses : non-cellular organisms

General Characteristics of Viruses :

- 1. Smallest: 20 – 300 nm, most were too small to be seen with the light microscope ;
- 2. Simplest: non-cellular entity, contain DNA or RNA and protein.
- 3. Obligate intracellular parasites: growing only within the living cells.
- 4. Self-replication :Once it has invaded a cell it is able to direct the host cell machinery to synthesize new intact infectious virus particles.



Significance of Studing Virology for Life Science

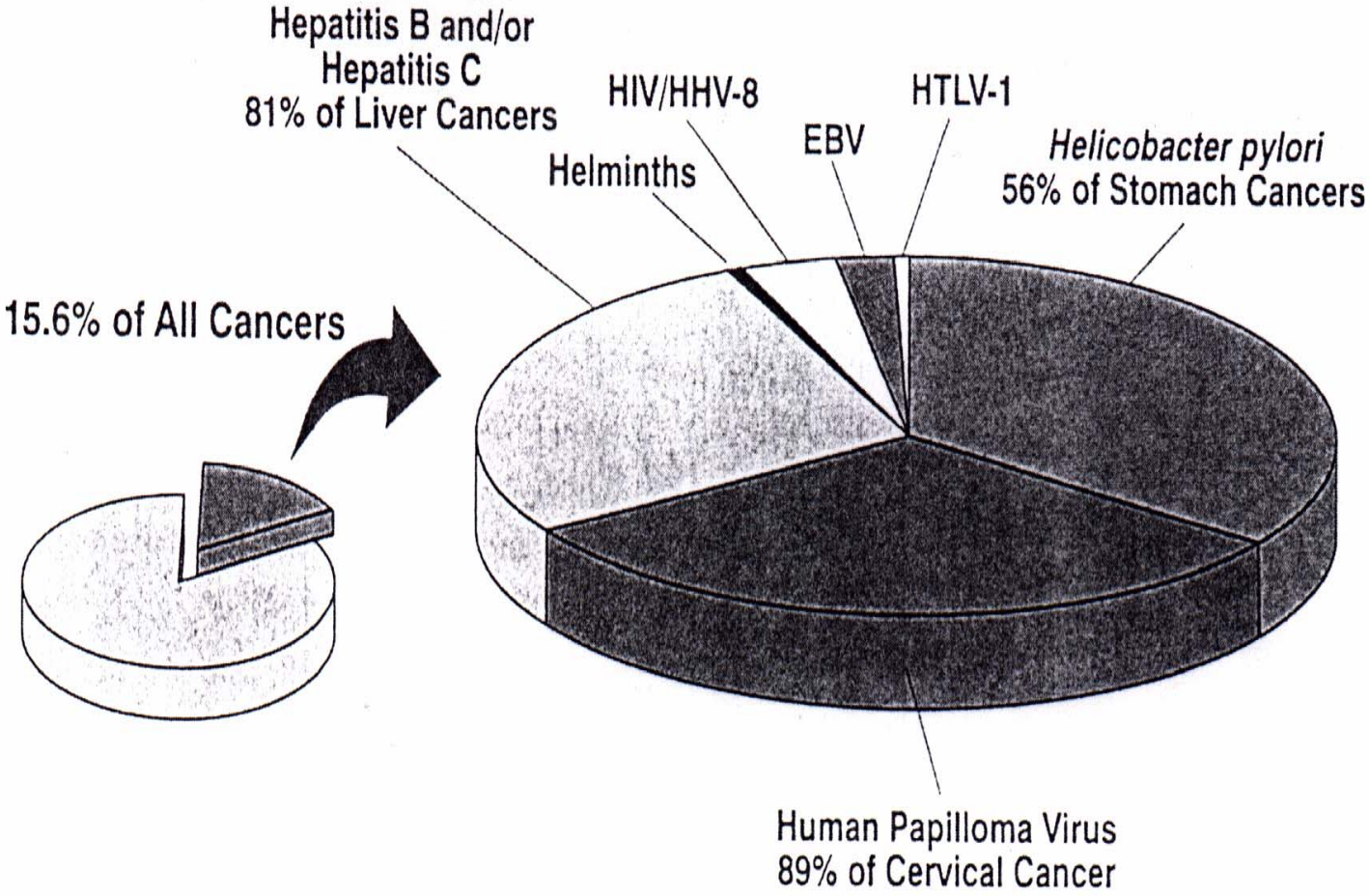
I. Viruses and infectious diseases

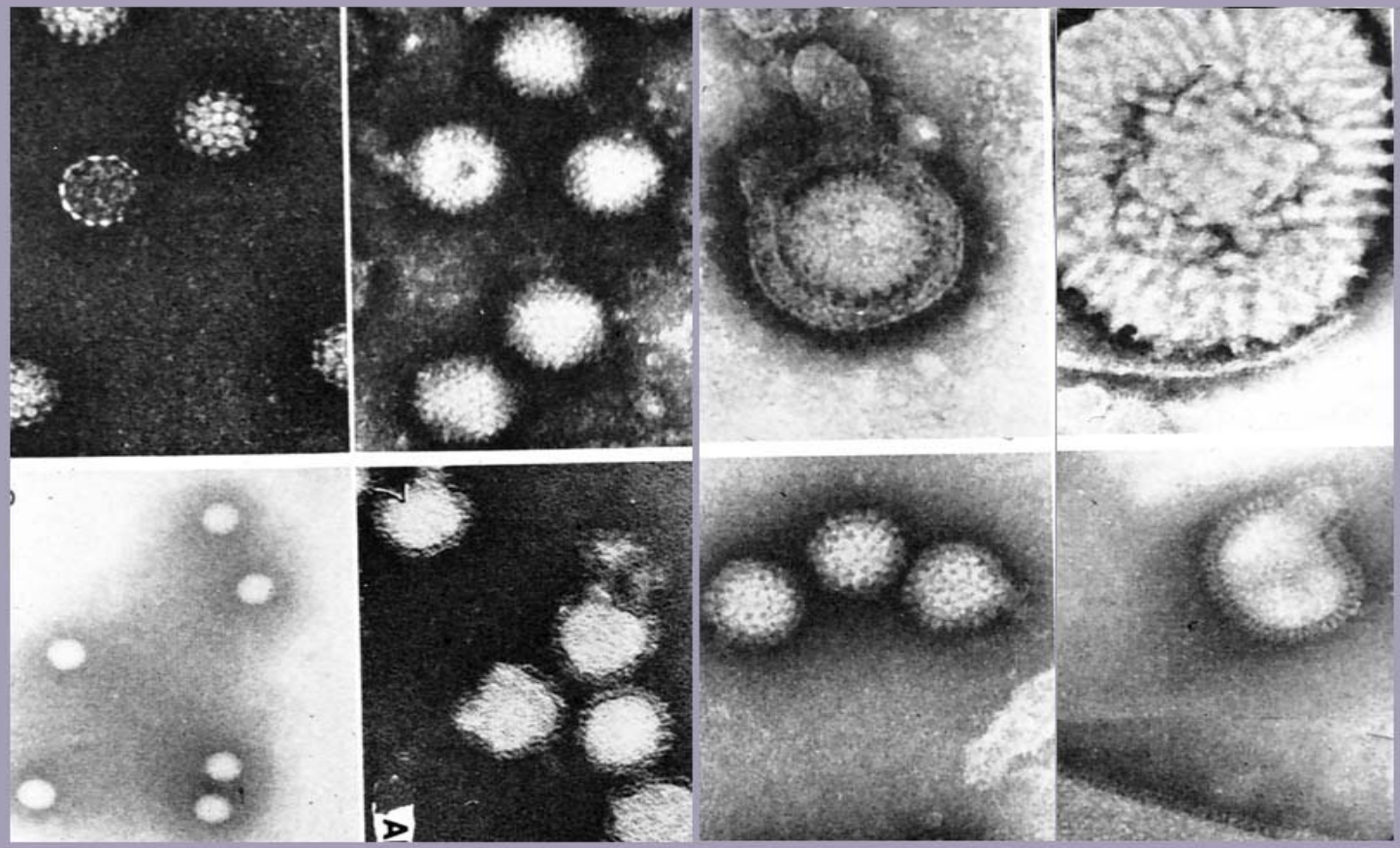
- **New presented viruses and viral infection still harm people's health**

AIDS,
HBV infection,
Influenza ,
SARS

Virus and Cancer

Infections Cause of Cancer





- **Size ： 20 -- 300 nm(the most virus＜150 nm);**
- **Shape: The commonest sape ---- small spherical virus**
- **Others ----- filamentous, brick, bullet**

Size and Shape

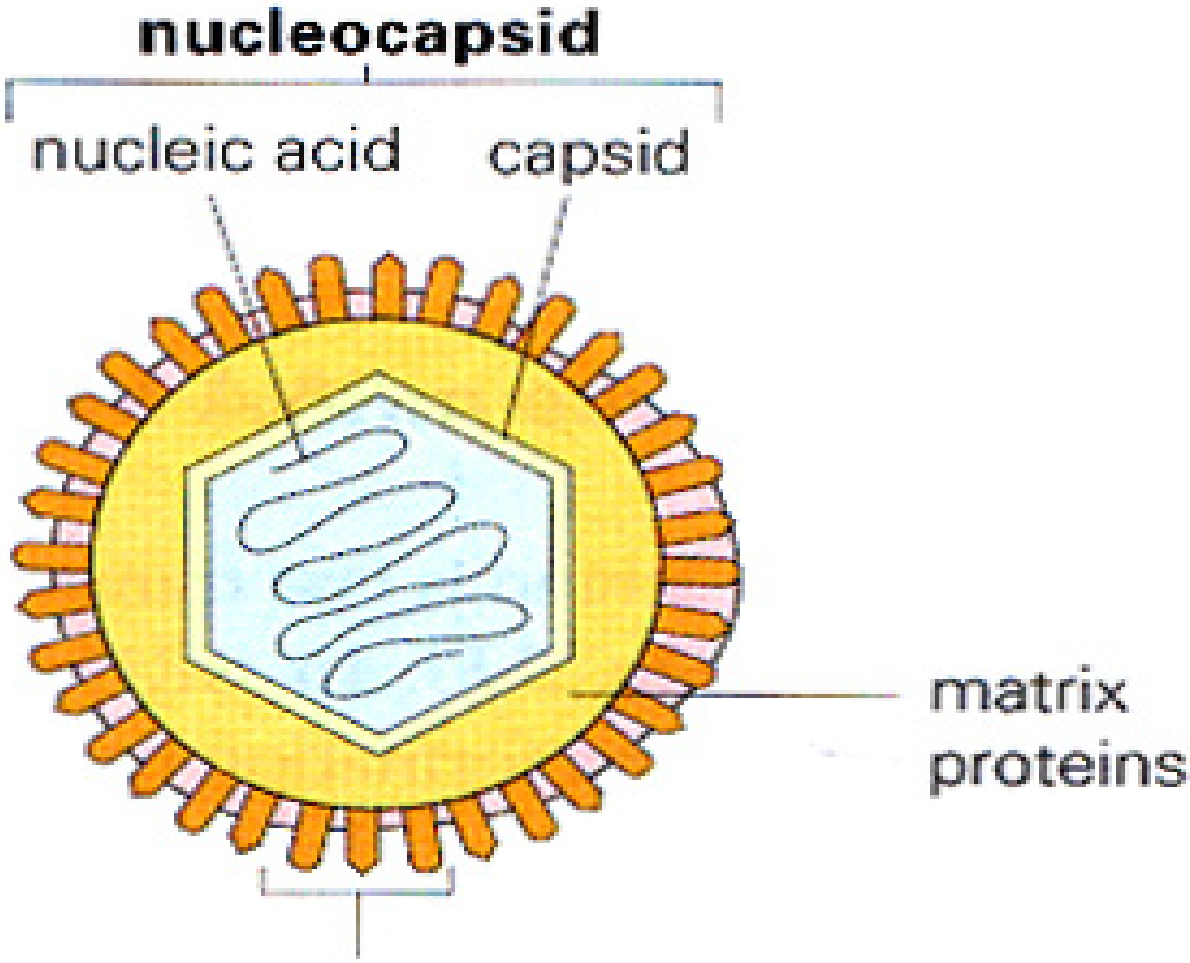
- **Virion**: **The basic infectious particle of a virus is known as the virion.**

Simple virion (naked virus):

a nucleic acid and capsid

Complex virion (enveloped virus):

nucleic acid , capsid, and envelope



derived from host cell
membranes (surface, internal, nuclear)
with inserted viral glycoproteins

Structure

- **Viruses contain:**
- nucleic acid genome (RNA or DNA)
- protective protein coat (called the capsid)
- viral envelope(enveloped virus)
- Non-structural protein

(I) Nucleic acid

1. Single kind: consist of DNA or RNA (never both).

1) DNA :

- single-stranded DNA (ssDNA) :
- double-stranded DNA (dsDNA): --- the commonest type of nucleic acid in viruses of human.

2) RNA:

- double-stranded RNA (dsRNA) :
- single-stranded RNA (ssRNA):

--- the commonest type of nucleic acid in viruses of human..

＋ssRNA : is the same as the viral mRNA , can direct as viral mRNA 。

-ssRNA : as a template transcribe complementary mRNA

2. Function:

1). viral genome （基因组）: viral nucleic acid conteins all genetic information of the virus.

2). possess infectiousness

-- infectious nucleic acid

infectious nucleic acid ：

- Infectious nucleic acid is purified viral DNA or RNA(without any protein) that can carry out the entite viral growth cycle and result in the production of complete virus particles. such as the genomes of dsDNA viruses and +ssRNA viruses.

such as: DNA virus （dsDNA）;

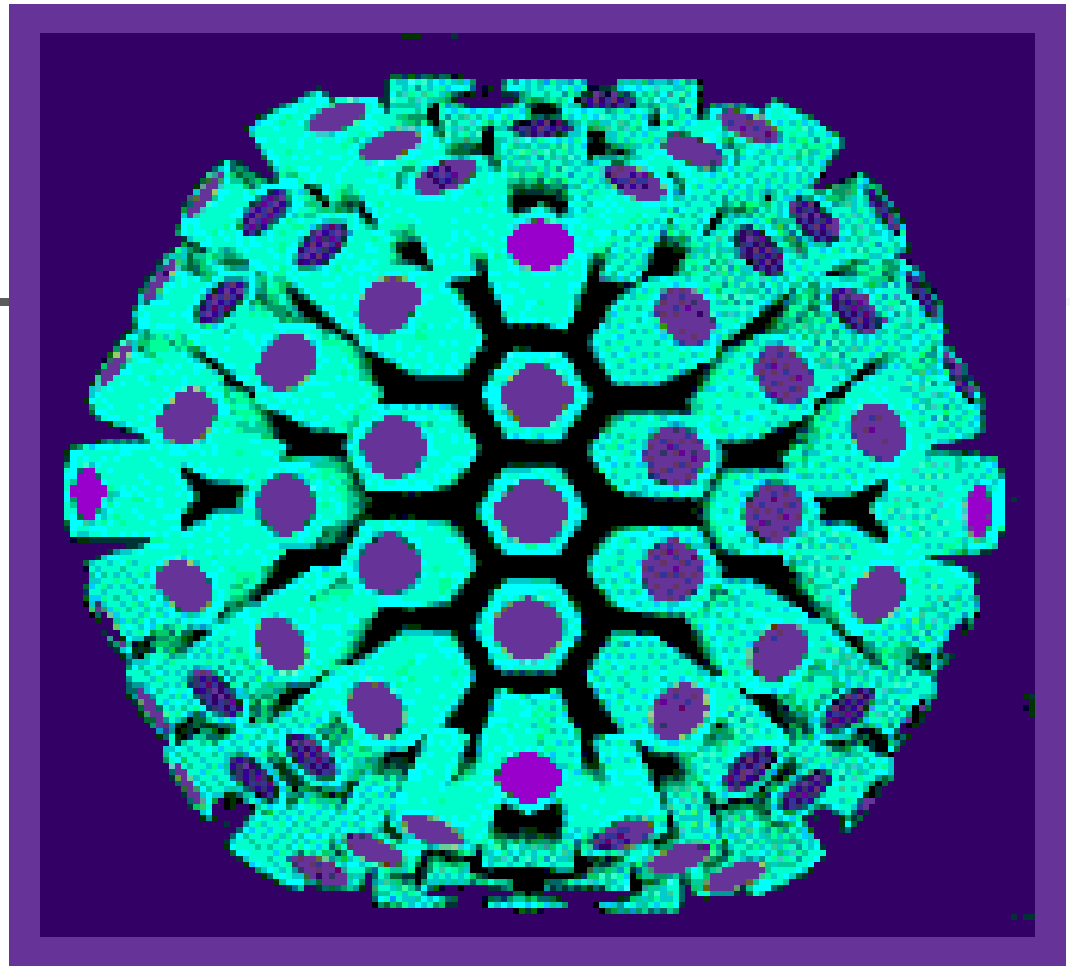
RNA virus (+ssRNA) ;

(II) . Capsid （衣壳）：

protein coat ,

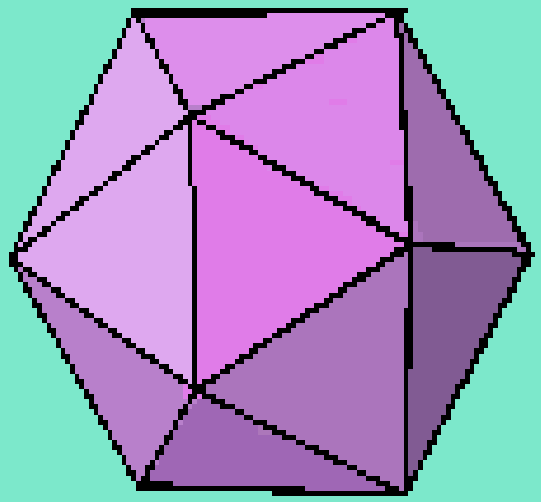
1. capsid is composed of distinct morphologic units---- **capsomeres**

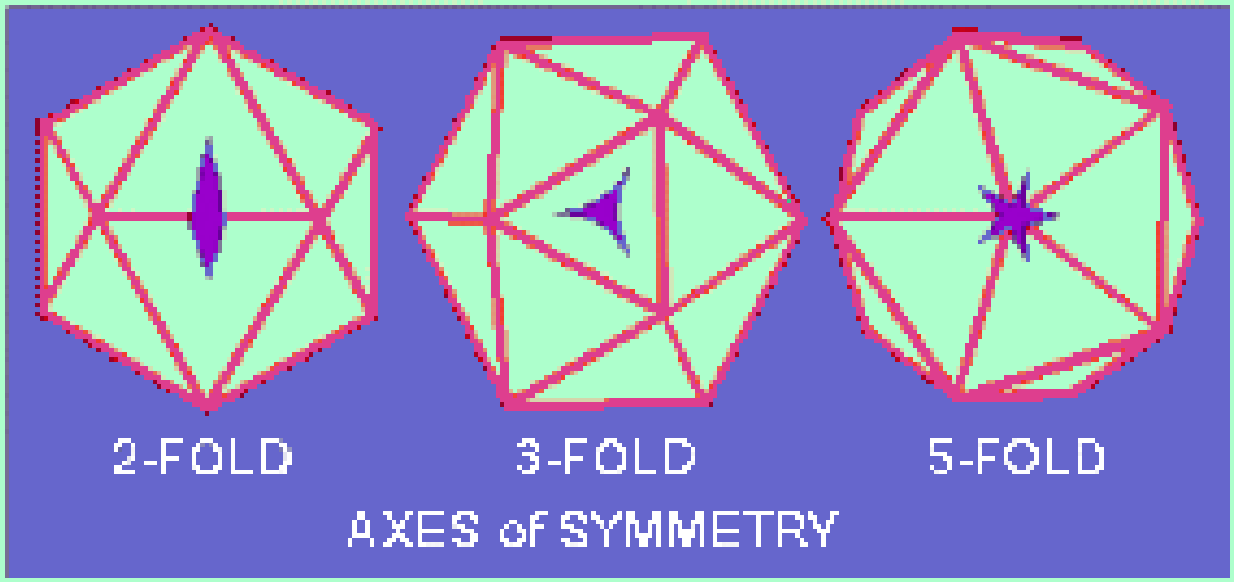
- --- icosahedral symmetry:
- --- helical symmetry:
- --- complex symmetry:



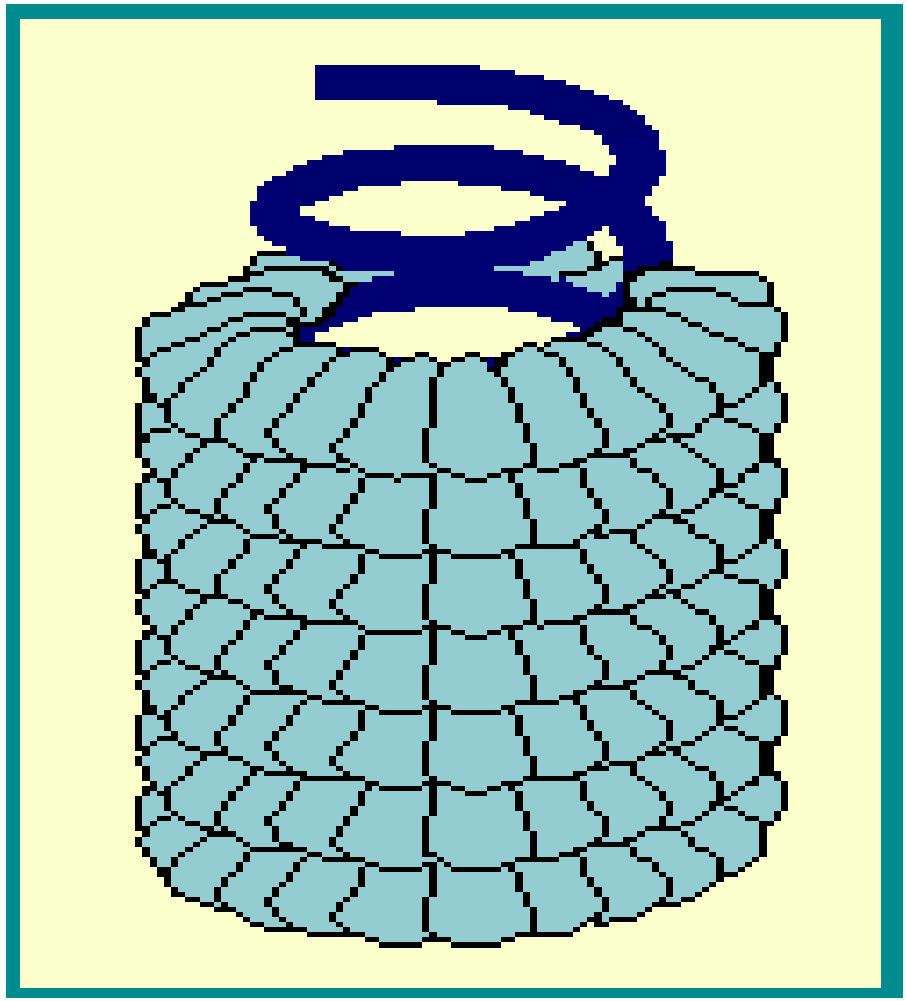
Capsomeres

Icosahedron and symmetry





helical symmetry



2. Function:

- 1) protection --- protect viral nucleic acid from enzymic action.
- specific binding sites --- mediate the viral attachment
- antigenicity ---- important antigens

(III). Envelope (包膜):

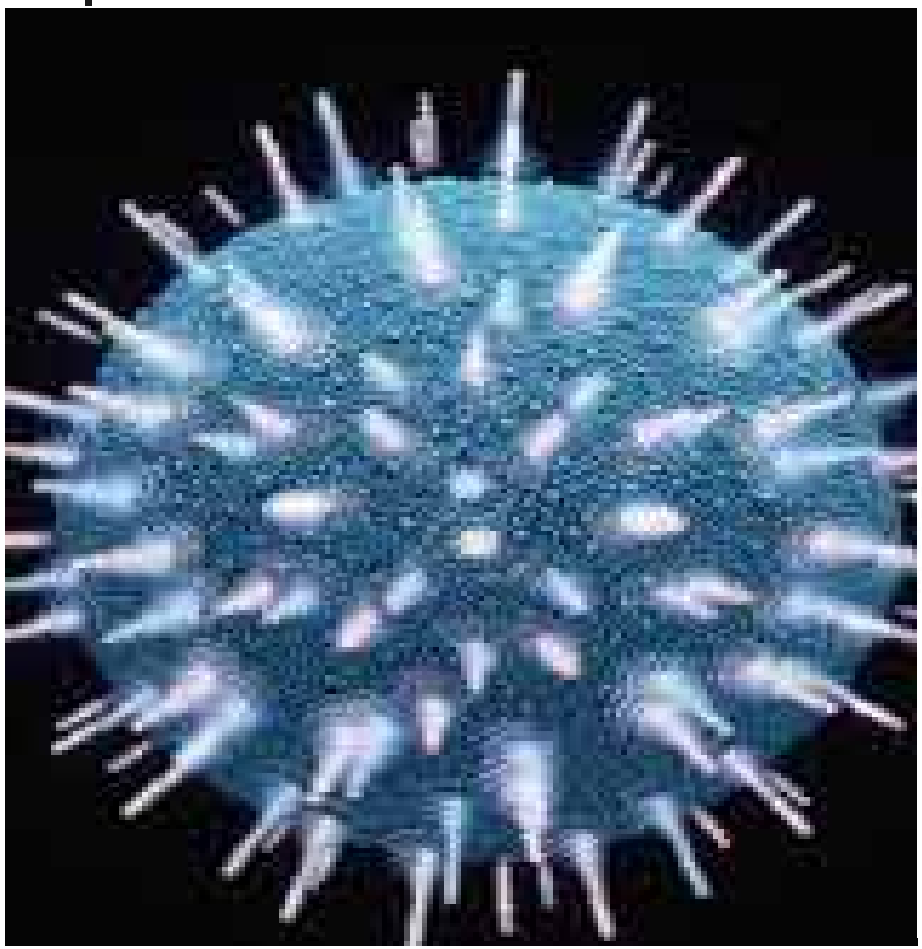
- 1. Consists of lipid bilayer and glycoprotein:

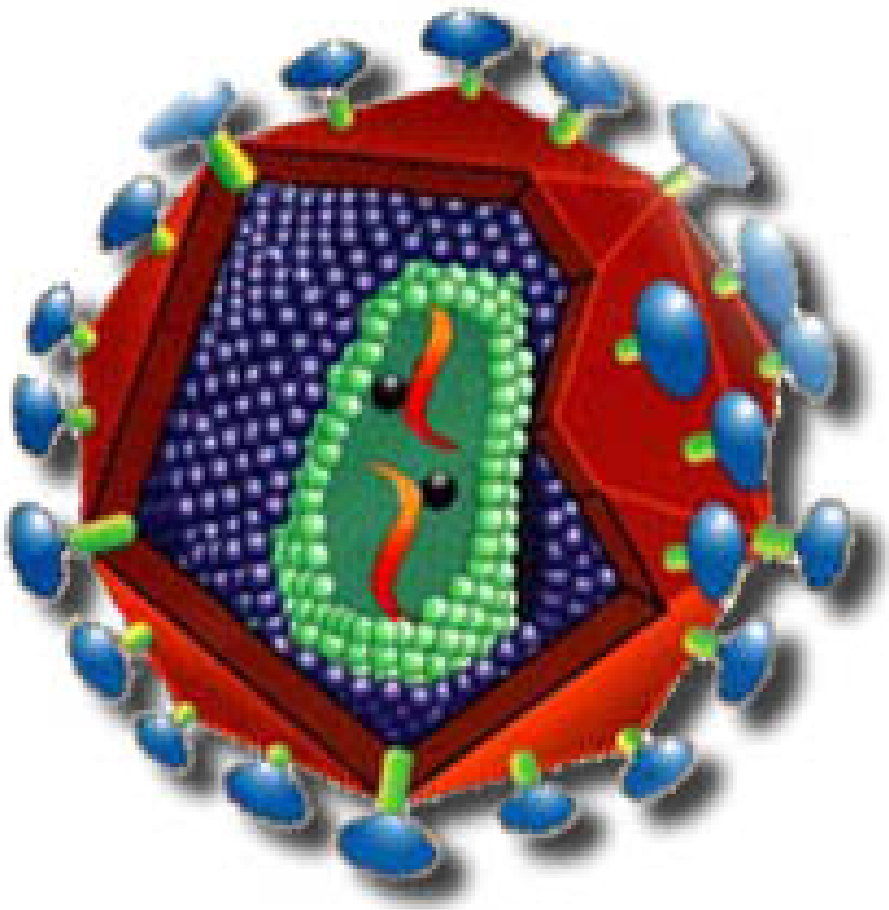
- lipid --- derived from host cell membrane.
- Glycoprotein --- coded by the viral genome.

- **Spikes(刺突)** --- virus-encoded glycoprotein protruding from lipid bilayer, which are important for adsorption and entry into the host cell.

- **2. Functions:**
- 1) as the binding sites -- the spikes of enveloped virus attach to host cell receptors
- 2) have antigenicity ---- envelope glycoproteins are also important antigens
- 3) confers instability on the virus--- enveloped viruses are more sensitive to heat and lipid solvents.

Spikes（刺突）





(IV) . Non-structural protein:

Code by virus; it is not the composition of virion. It can exist in virion and infected cell.

- (1) viral enzymes:

  such as： RNA-dependent RNA polymerase or transcriptase .

- (2) specific viral protein:

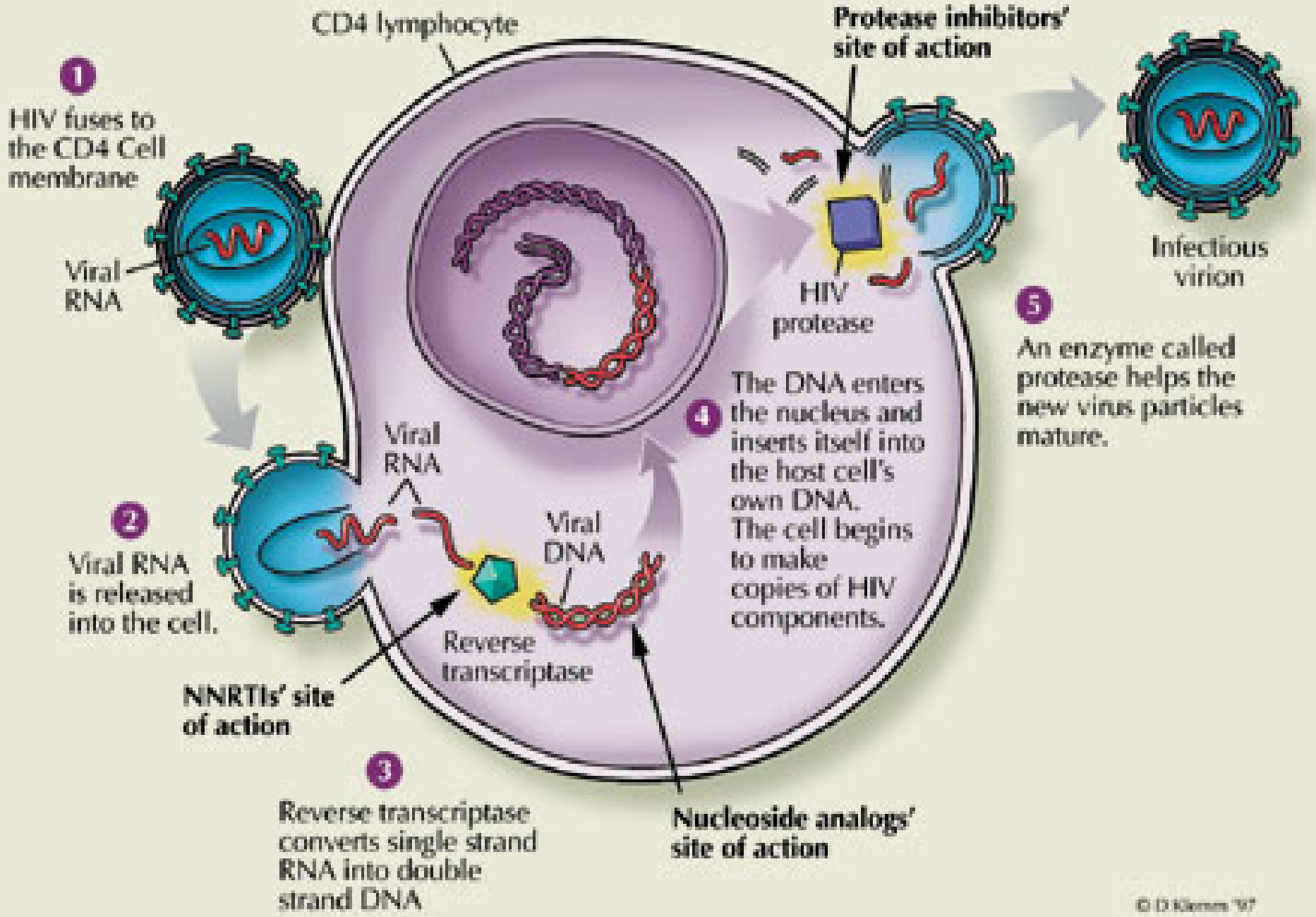
  such as : transformation protein of tumor virus.

III. Viral Multiplication

Replication: The process of intracellular viral multiplication, consisting of the synthesis of PROTEINS; NUCLEIC ACIDS; and their assembly into a new infectious.

- **I. Replication cycle**（复制周期）:

- adsorption—penetration—uncoating—biosynthesis—assembly and release

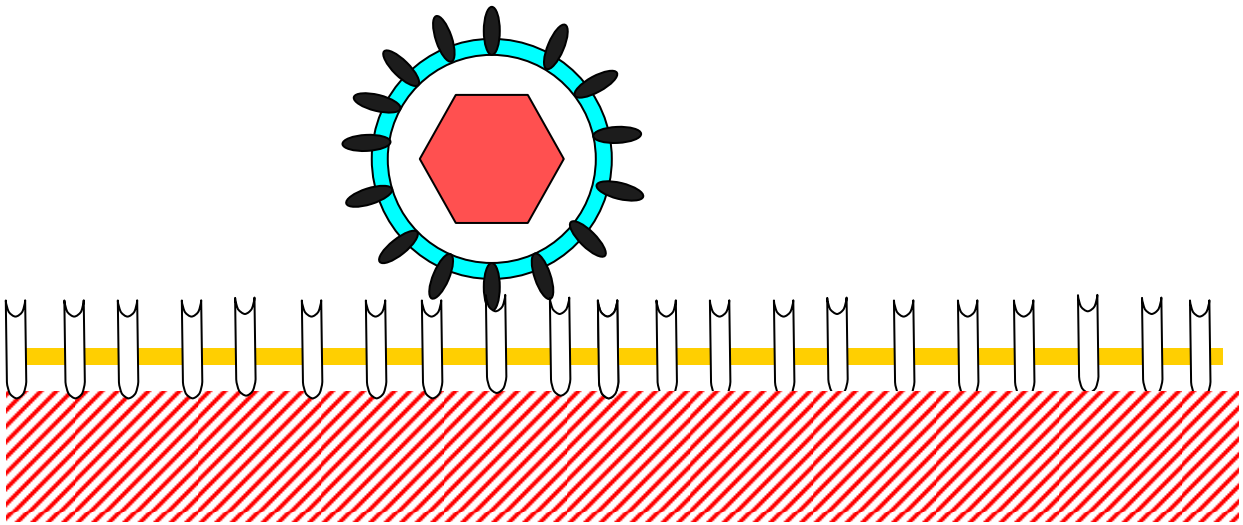

CD4 lymphocyte
Protease inhibitors' site of action
1
HIV fuses to the CD4 Cell membrane
Viral RNA
HIV protease
Infectious virion
5
An enzyme called protease helps the new virus particles mature.
4
The DNA enters the nucleus and inserts itself into the host cell's own DNA. The cell begins to make copies of HIV components.
Viral RNA
2
Viral RNA is released into the cell.
Viral DNA
Reverse transcriptase
NNRTIs' site of action
3
Reverse transcriptase converts single strand RNA into double strand DNA
Nucleoside analogs' site of action
© D Klemm '97

(I) Replication cycle（复制周期）:

1. adsorption (吸附):

The proteins on the suface of the virion (called **virion attachment proteins, VAP**) attach to specific receptors on the host cell surface.

Such as: HIV(gp120) --- Helper T lymphocytes(CD4 protein)



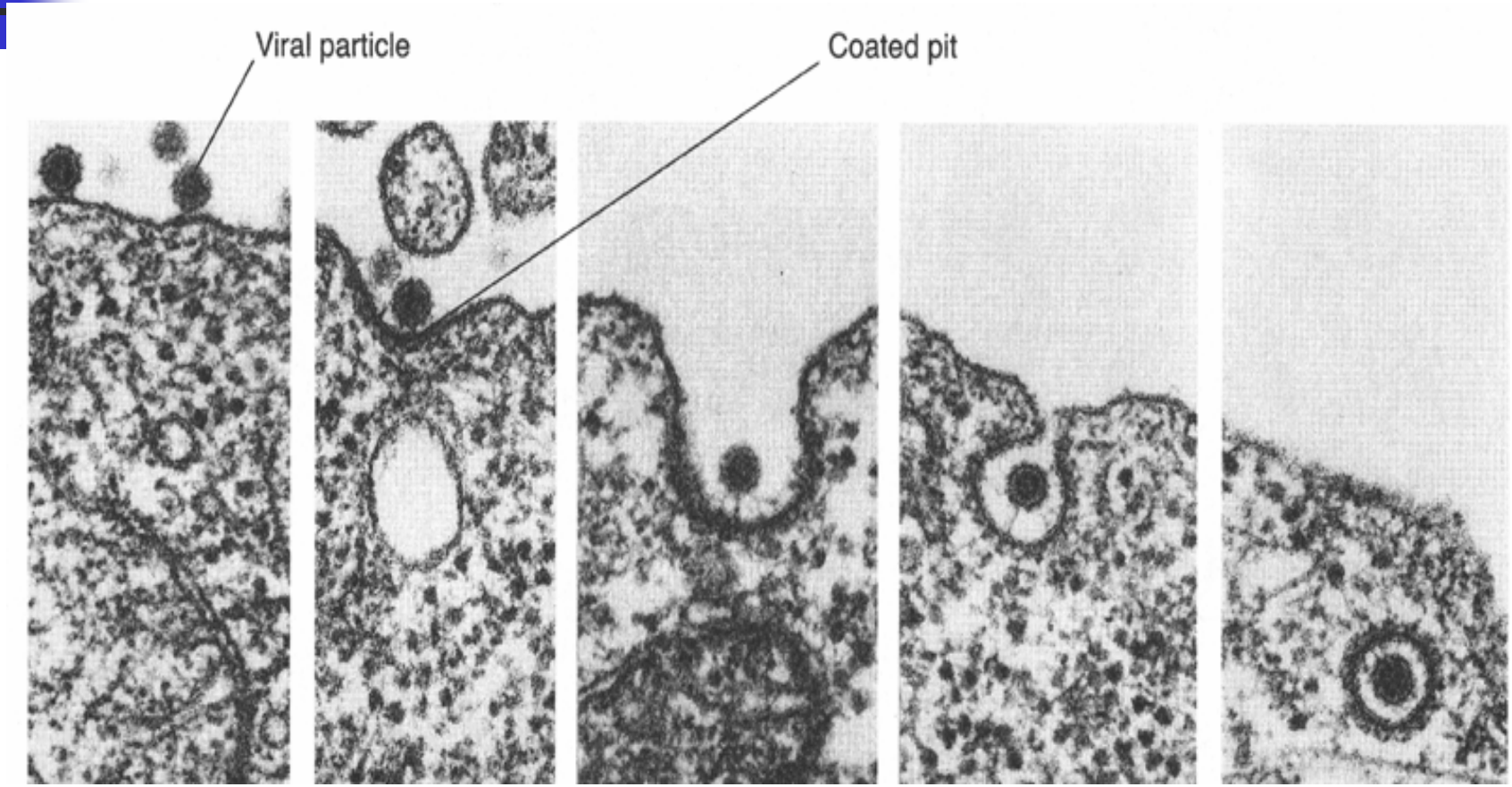
- **2. penetration（穿入）：**

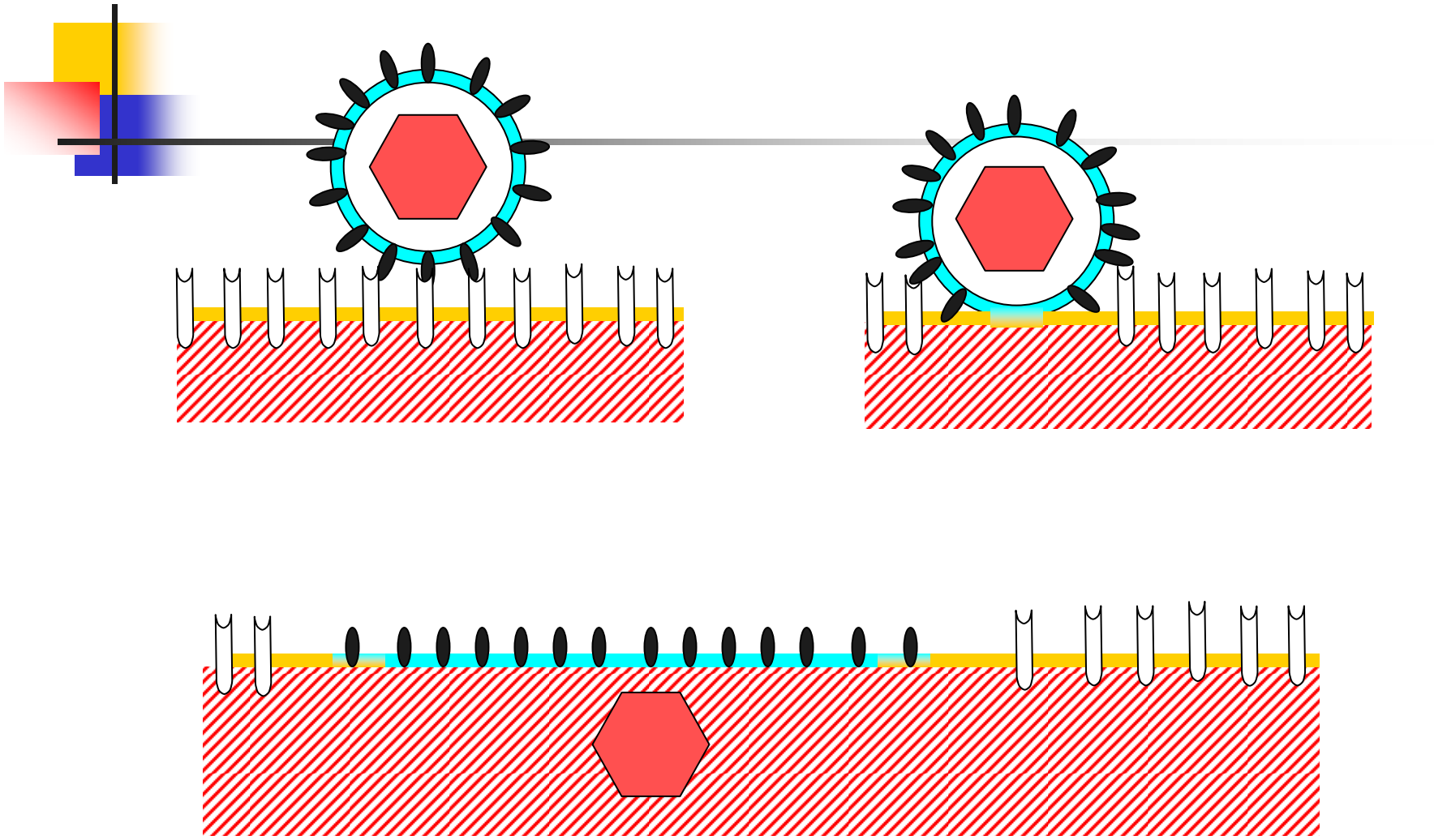
virus enter the cells.

☞ **Entry of Naked viruses:** endocytosis

☞ **Entry of enveloped virus** :

simple fusion of membranes –


Viral particle
Coated pit



- **3. uncoating（脱壳）：**
- Rapid change from stable structure to release of genome

4. Biosynthesis（生物合成）：Gene expression & Genome Replication

Synthsis of viral proteins

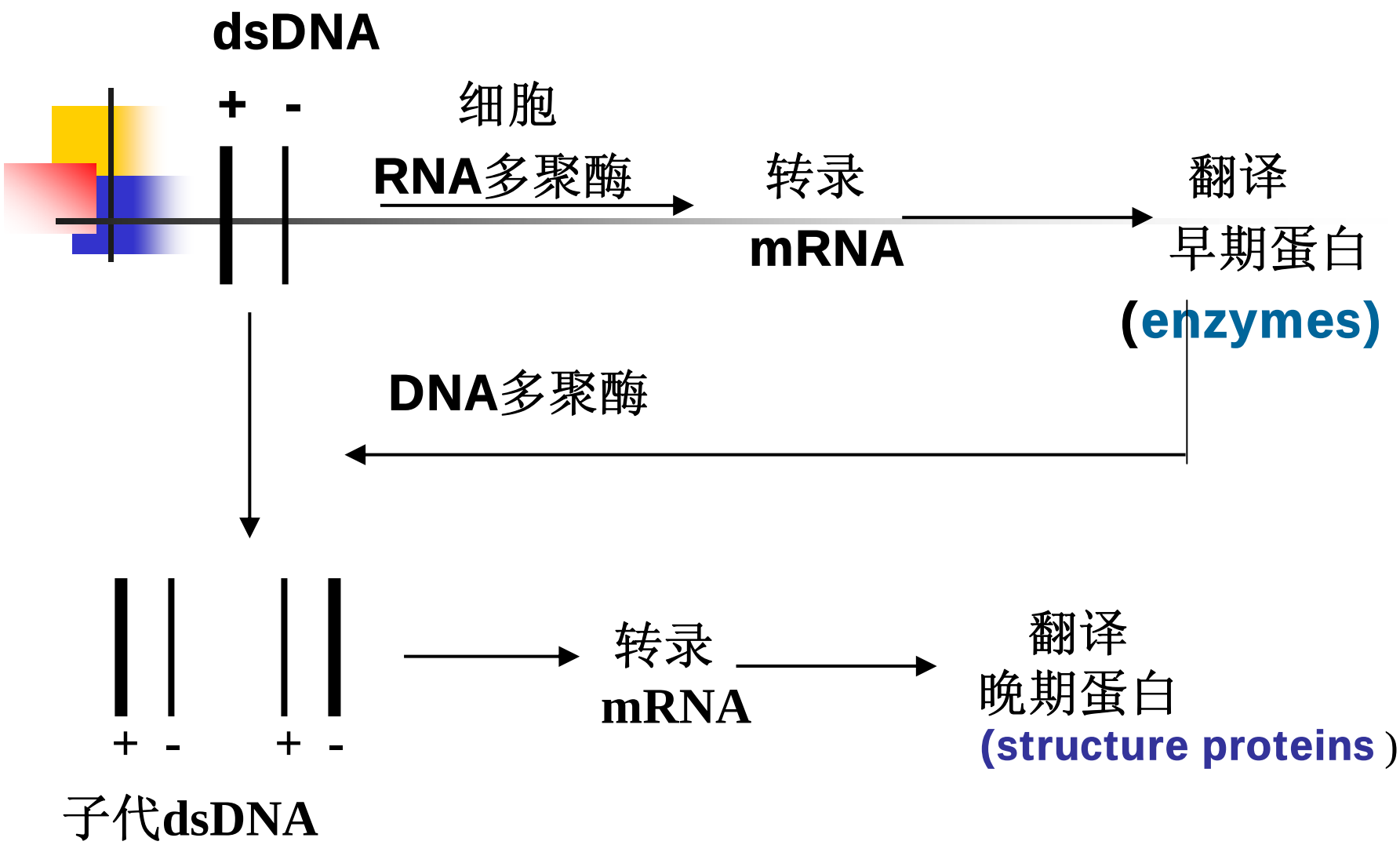
Synthsis of viral nucleic acid

4.1 dsDNA viruses:

Replicate in the nucleus, use the host cell DNA dependent RNA polymerase to synthesize their mRNA

- **4.1 dsDNA viruses:**
- replicate in the nucleus
- use the host cell DNA dependent RNA polymerase to synthesize their mRNA
- (1) early transcription and translation:
- early mRNA (use cell RNA polymerase)
- early proteins (non-structural proteins):
- --- enzyme which is necessary for viral replication.
- --- specific viral proteins: regulation protein (调节蛋白)、transformation protein.
- .

- (2) viral DNA replication :
- (3) late transcription and translation :
- late proteins (structural proteins):
- ---- capsid protein and envelope protein

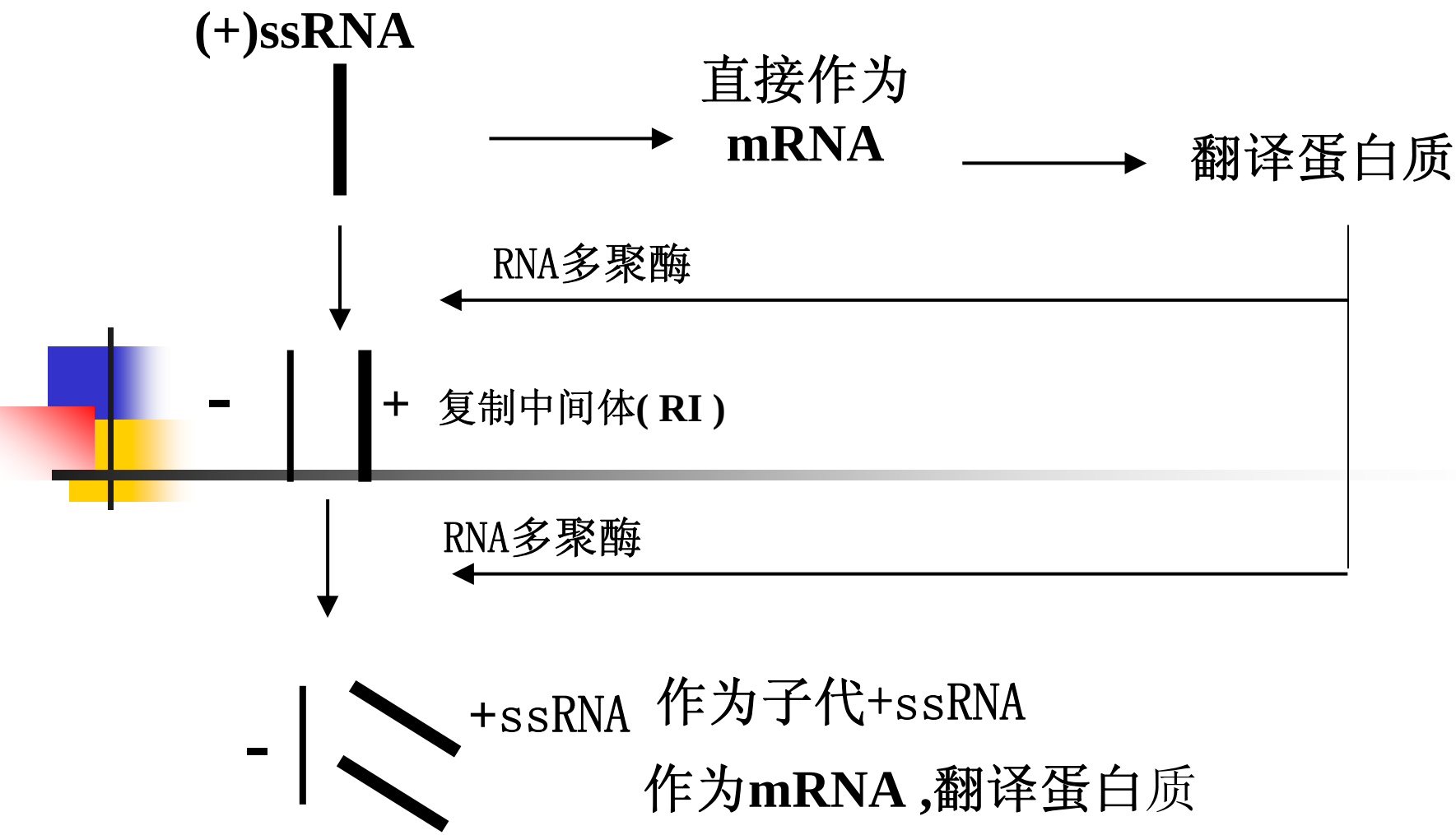


双链DNA病毒复制模式图

4.2 RNA viruses (three kinds) :

- **(1)+ssRNA viruses:**

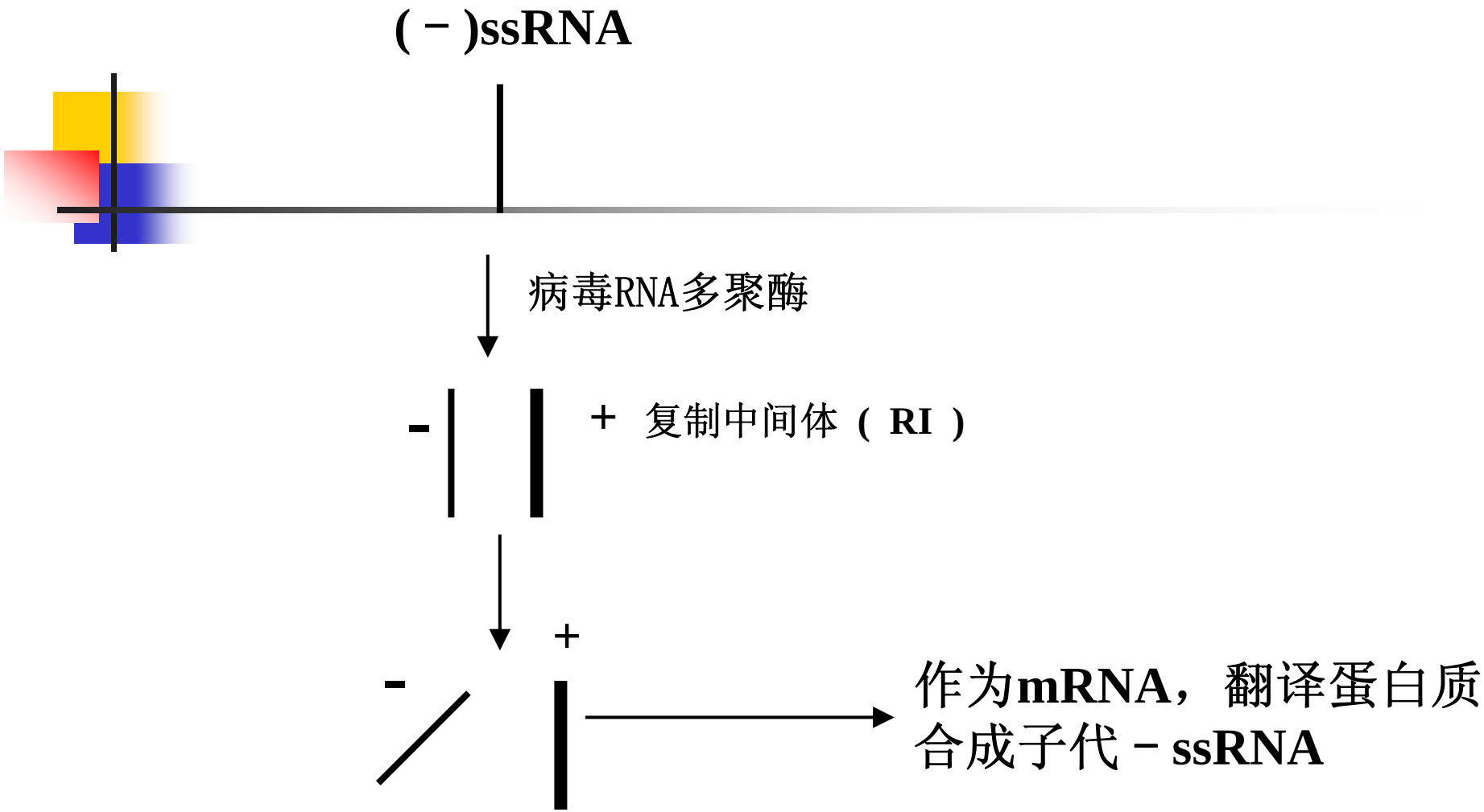
  The +ssRNA itself can direct as viral mRNA .



单正链RNA病毒复制模式图

(2) -ssRNA viruses:

Use the virion RNA polymerase to synthesize viral mRNA.

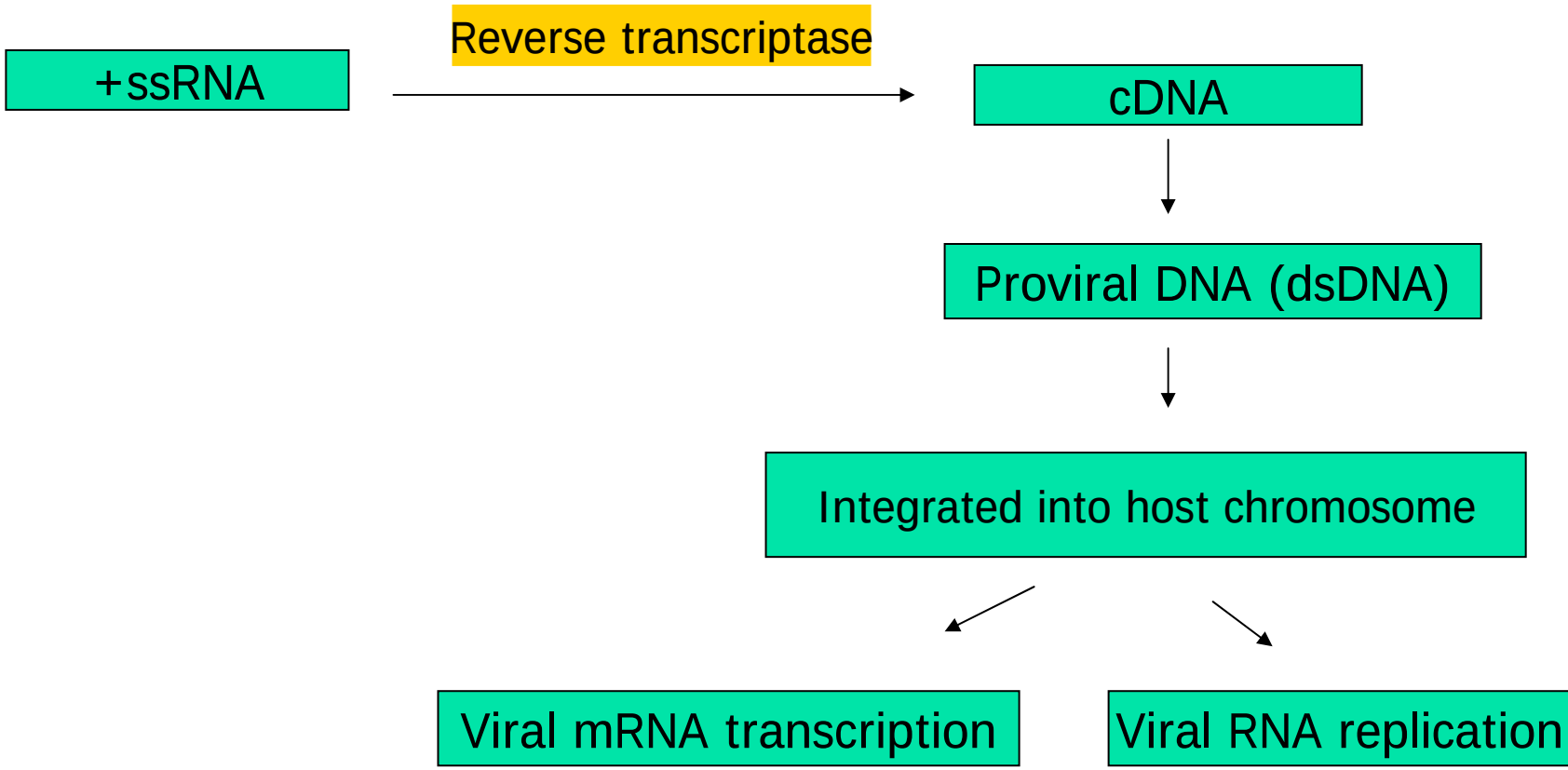


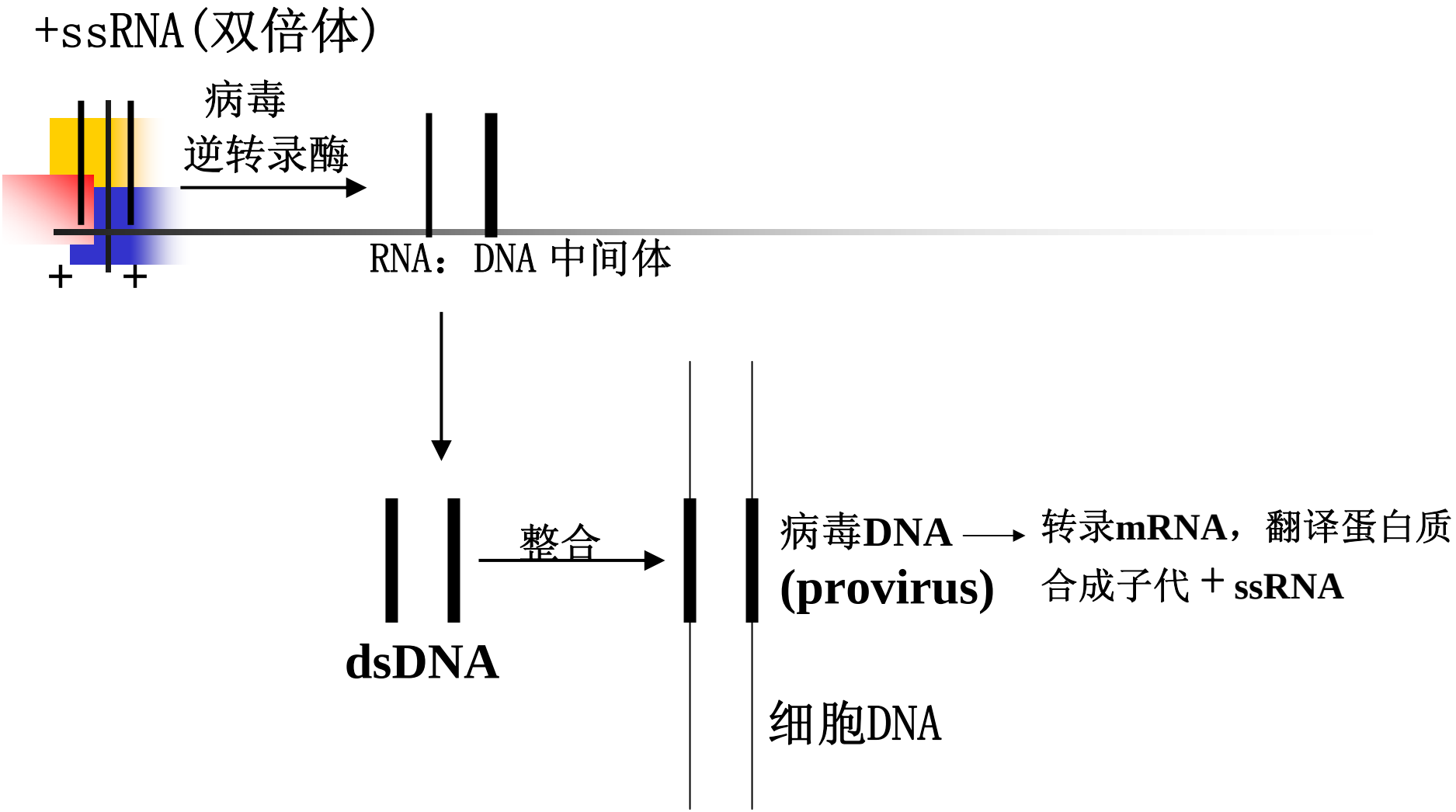
单负链RNA病毒复制模式图

(3) Retroviruses:

- use the virion **reverse transcriptase** to synthesize a DNA cope of the viral RNA genome;
- use the host cell RNA polymerase to synthesize the viral mRNA

(3) Retroviruses:




+ssRNA(双倍体)
病毒
逆转录酶
+ +
RNA：DNA 中间体
整合
dsDNA
病毒DNA
(provirus)
转录mRNA，翻译蛋白质
合成子代＋ssRNA
细胞DNA

反转录病毒复制模式图

RNA Virus:

- The mRNA is translated into a single polypeptide (polyprotein), which is cleaved.
- Be cleaved by a virus-coded protease into various proteins.

DNA Virus:

- **(1) Early gene expression:**
- **----before Viral DNA replication**
- **----enzyme**
- **(2) Late gene expression**
- **----after Viral DNA replication**
- **----structure proteins**

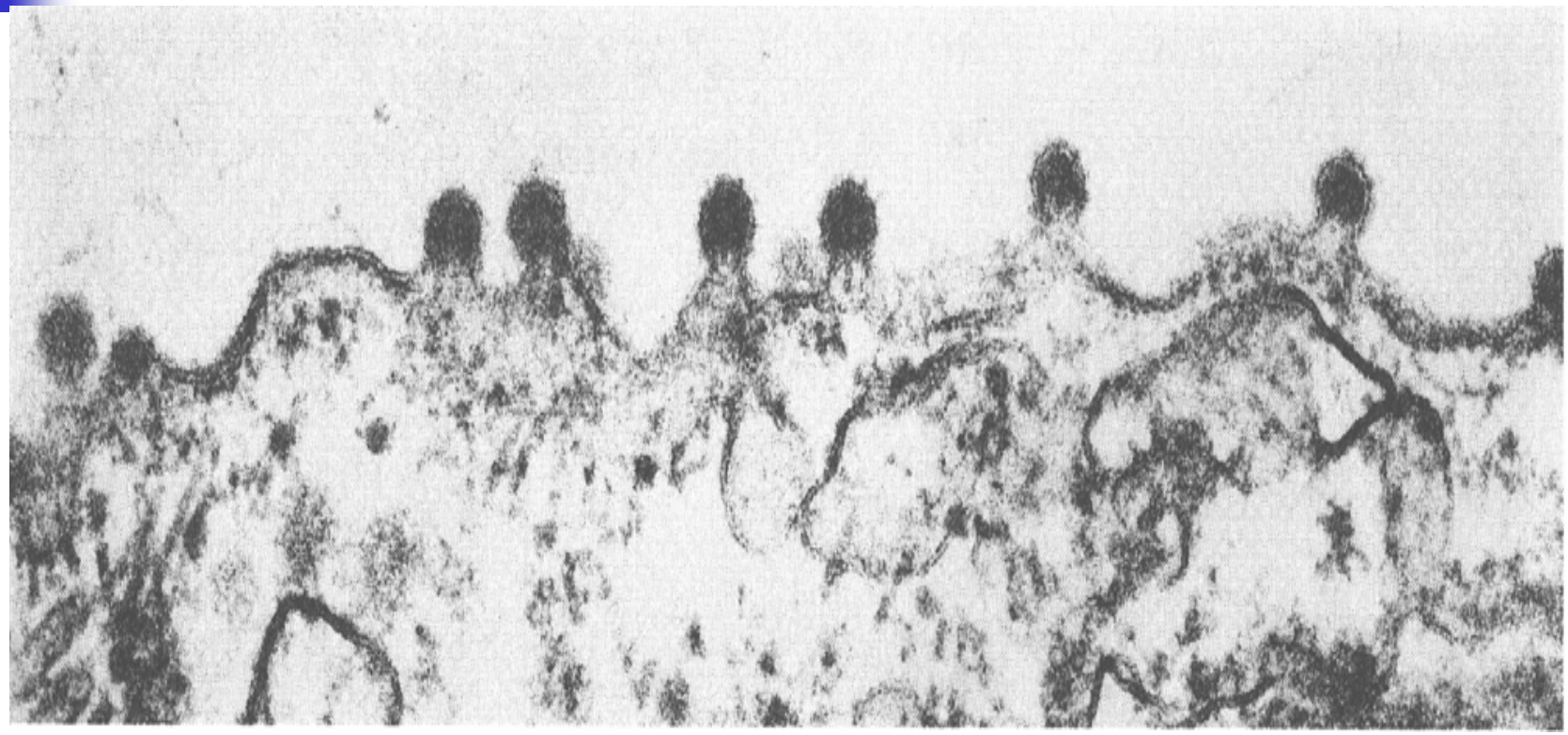
5. assembly and release（装配和释放）：

- **Assembly:**
- --- Assembly of DNA virus occurs in the nucleus
- --- Assembly of RNA virus occurs in the cytoplasm

release：

- --- by lysis of the host cell (naked viruses).
- --- by budding through cell membrane (enveloped viruses).

Virus budding



(II.) Unnormal multiplication:

1. Abortive infection:

virus infects a cell (non-permissive cell), but cannot complete the full replication cycle,

i.e. a non-productive infection.

2. Defective virus（缺陷病毒）:

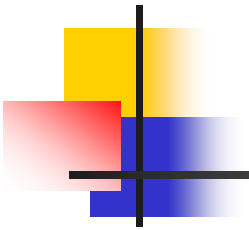
A defective virus is one that lacks one or more functional genes required for virus replication. defective virus cannot replicate without a “helper” virus , which provides the missing function

e.g.: HDV (defective virus)/ HBV(helper virus)

(II.) Unnormal multiplication:

3. Interference（干扰现象）：

The infection of cell by a virus results in that cell becoming resistant to infection by other viruses.



Section 3
Viral heredity and variation

Viral genome

hereditary substance:

DNA ; or RNA

Mutation

Mutation in viral DNA or RNA occur by the processes of base substitution, deletion and frame shift.

- ORIGIN
  (1) Spontaneous mutations
  (2) Mutations that are induced by physical or chemical means

EXAMPLES of Mutant

Mutant(突变株)

--- temperature sensitive mutant, ts突变株

--- drug-resistant mutant，耐药突变株

Temperature-sensitive mutant (ts):

permissive temperature: 28℃~35 ℃

non permissive temperature: 36℃~40 ℃

ts mutant -- attenuated mutant (vaccine mutant)

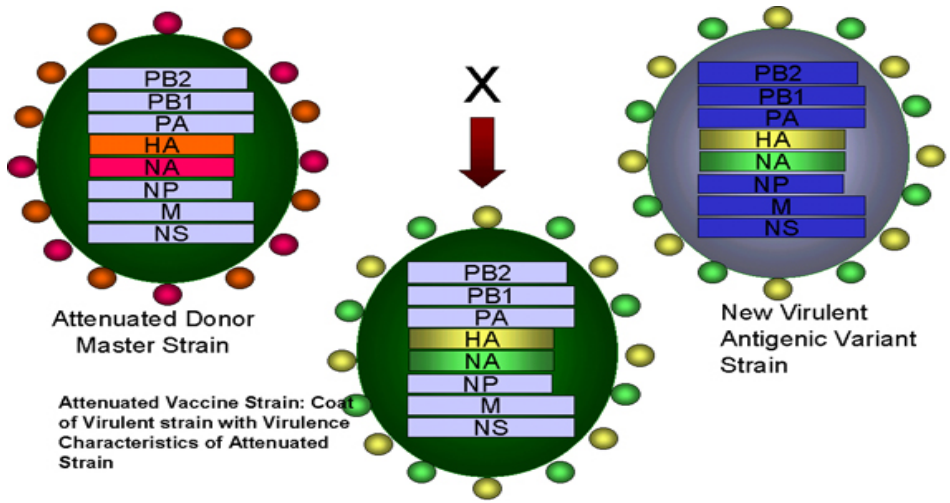
Recombination &Reassortment

Recombination:

the exchange of genes between two related viruses which infected the same cell. (active virus-active virus; active virus-inactive virus).

Reassortment

exchange of genetic material between two segmented viruses which infected the same cell.



Gene integration

Viral genome insert into host cell genome

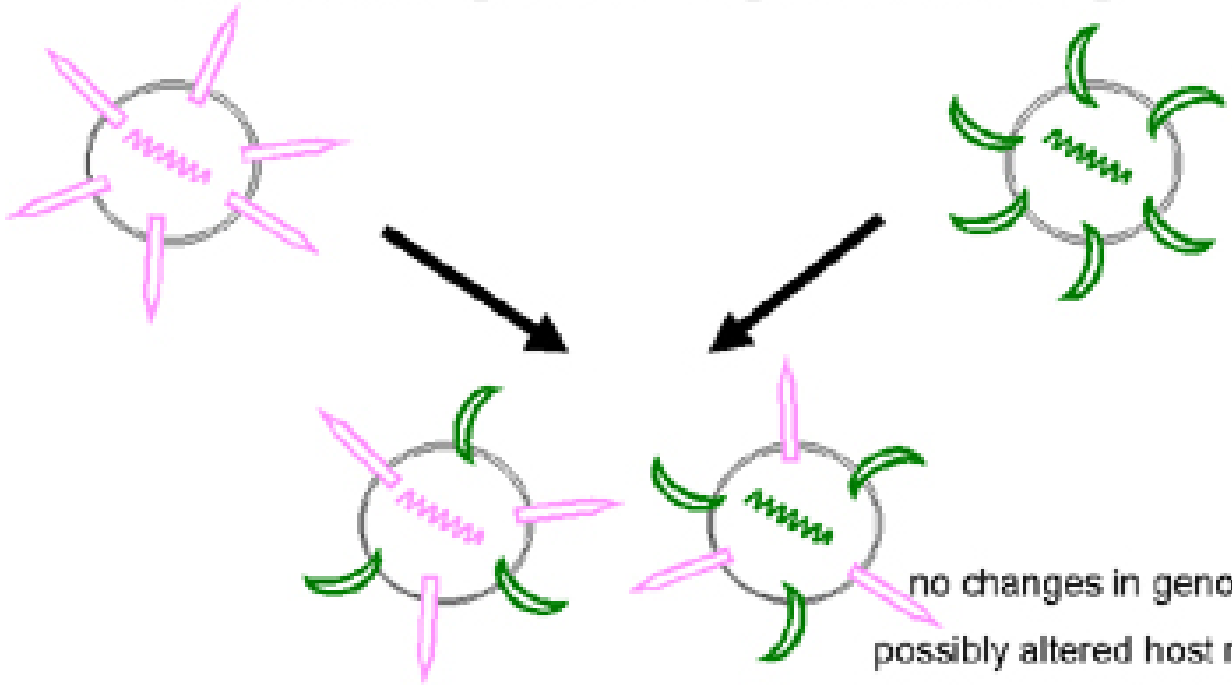
e.g. tumor viruses

Interaction of viral genetic Products

---- nongenetic

- **Complementation：(互补作用)：** genetic production reactivation between two viruses (one or both of which may be defective)
- **Phenotypic mixing(表型混合)：** If two different viruses infect a cell, progeny viruses may contain coat components derived from both parents and so they will have coat properties of both parents.

PHENOTYPIC MIXING

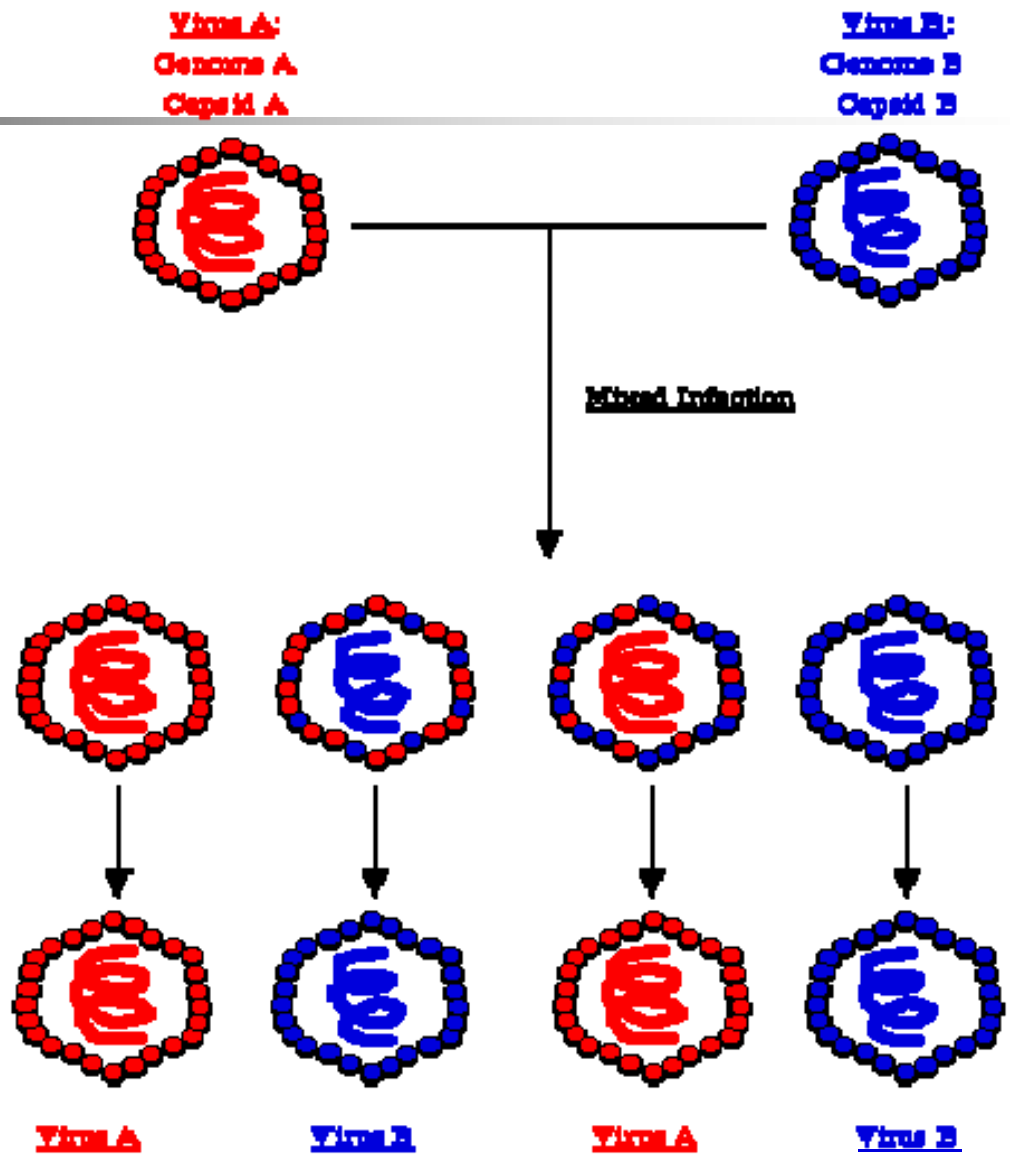


no changes in genome

possibly altered host range

possibly resistant to antibody neutralization

表型混合


Virus A:
Genome A
Capsid A
Virus B:
Genome B
Capsid B
Mixed Infection
Virus A
Virus B
Virus A
Virus B

Section 4

Effects of Physical and Chemical Agents on Viruses

Inactivation :

the virus lose their infections when they are affected by some factors, such as physical or chemical factors .

Lose their infections --- the virus cannot produce infectious virion。

Resistance:

low temperature： - 196℃

pH： 5～9

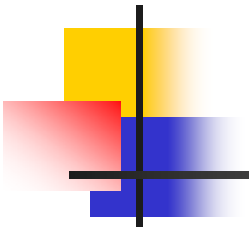
antibiotic

Sensitivity：

high temperature: >50 ℃

radiation and UV

lipo-solvent : enveloped virus



Section 5
Classification of Animal Viruses

Classification

International Committee on Taxonomy of Viruses (ICTV):

- DNA viruses
- RNA viruses
- DNA and RNA Retroviruses

UNCONVENTIONAL AGENTS

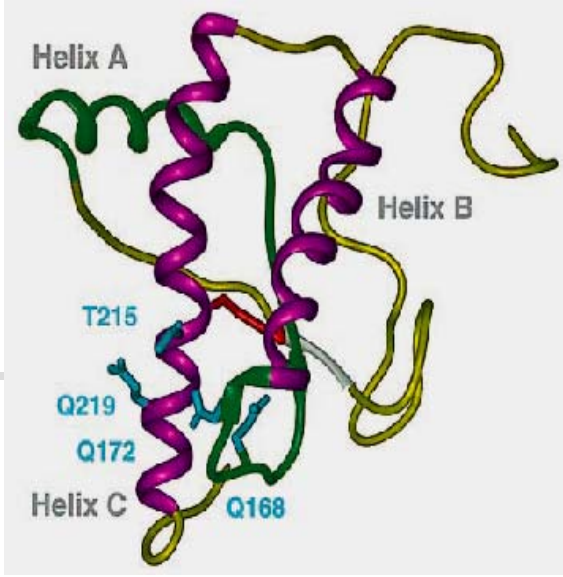
Subvirus：refer to the kind of infectious factor which is smaller than virus.

1. viroid(类病毒) and virusoid(拟病毒)：

- --To contain RNA only
- --To have only been shown to be associated with plant disease.

2. prion (朊粒)：

- prions are infectious particles encoded by gene of normal host cells , they are composed solely of protein; they are implicated as the cause of certain “slow virus disease called transmisslble apongiform encephalopathies(TSEs)” in animals and human.



cellular PrP，PrPc
(细胞朊蛋白)
---- normal

未知因素

scrapie prion protine,
PrPsc (羊瘙痒病朊蛋白)
---- pathogenic