厦门大学
生命科学学院
SCHOOL OF LIFE SCIENCES XIAMEN UNIVERSITY

MICROBIOLOGY

Lecture 4

Chapter 6

Viruses and Other Acellular Infectious Agents

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Review or recall

4. Provide two examples that illustrate the similarity of archaea to bacteria; list two examples of their similarity to eukaryotes.

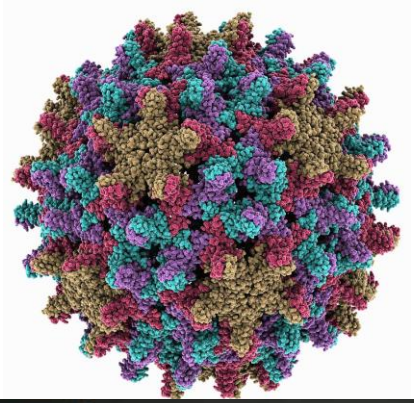
5. Identify two other molecules that could be used to determine if a microbe having a typical prokaryotic architecture is a bacterium or an archaeon.

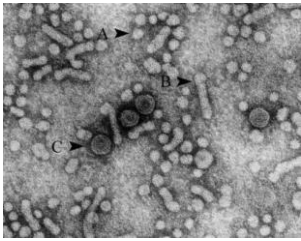
6. Compare and contrast nutrient uptake mechanisms observed in bacteria and archaea

Virus is bad or good?

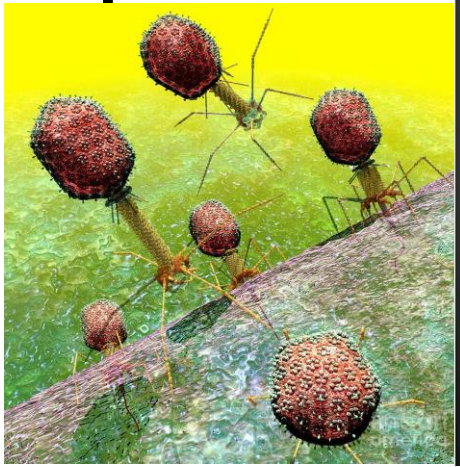
- **Typically we think of them as major causes of disease.**
- **Viruses as agents of good will come as a surprise to many.**
- **Important members of aquatic world(move organic matter from particulate to dissolved)**
- **Important in evolution transfer genes between bacteria, others**
- **Important model systems in molecular biology(vector)**
- **Bacterial viruses are being used in some European countries to treat infections caused by bacteria.**

Outline





- Discovery
- General features
- The structure of virus
- Types of virus
- Viral multiplication

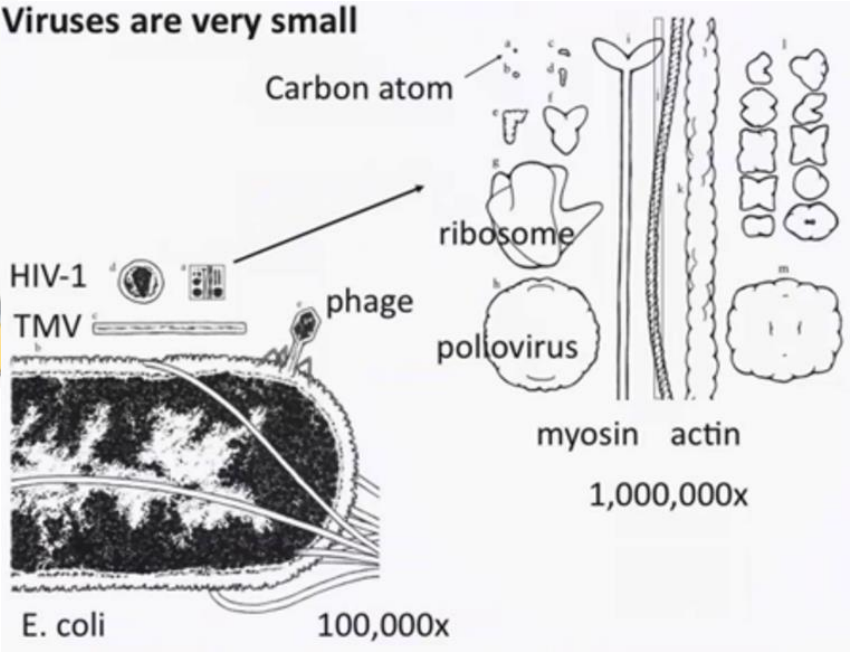


Discovery Virus

Virus discovery - filterable agents

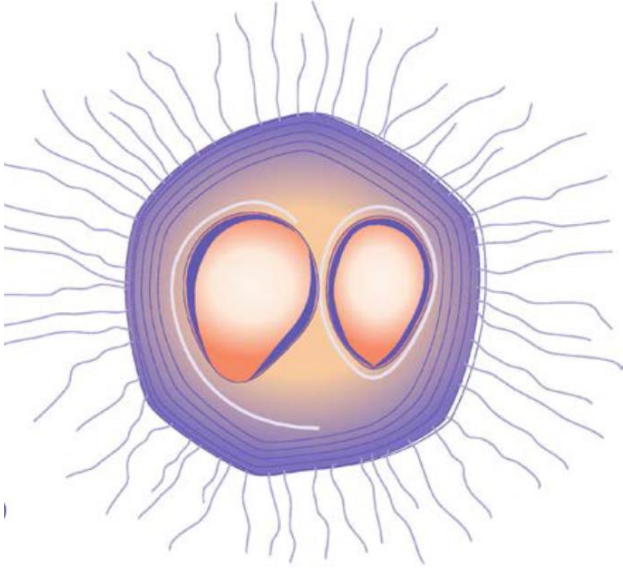
- 1892 - Ivanovsky - found the agent of tobacco mosaic disease passes through filters that retain bacteria

Viruses are very small



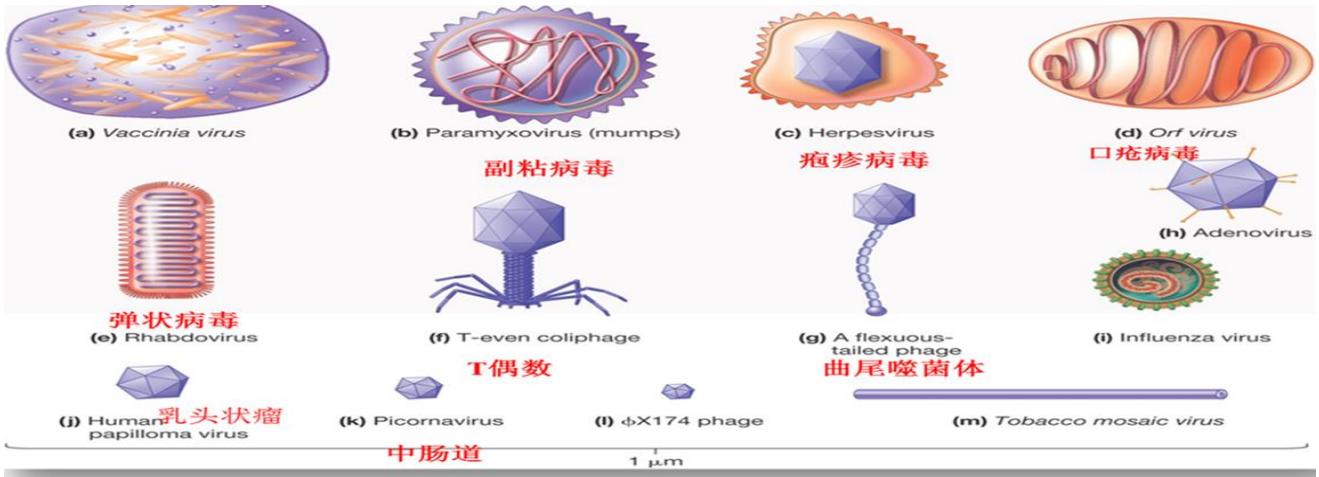
6.1 Viruses Concept

- **A unique group of infectious agents whose distinctiveness resides in their simple, acellular organization and pattern of multiplication.**
- **Despite this simplicity, viruses are major causes of disease.**
- **Viruses can exist either extracellularly(inactive) or intracellularly(active).**



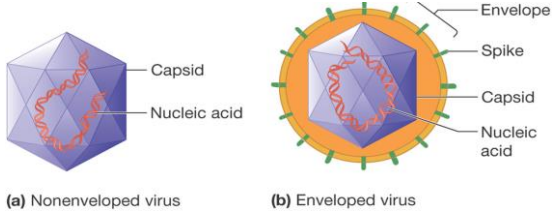
6.1 Viruses Types

- Viruses can infect **all cell types**.
- Bacterial viruses called bacteriophages (phages)
- Few archaeal viruses. Most are eukaryotic viruses:plants, animals, protists, and fungi
- Viruses have been classified into numerous families based primarily on genome structure, life cycle, morphology, and genetic relatedness (ICTV)



6.2 Virion Structure

What does virus look like?

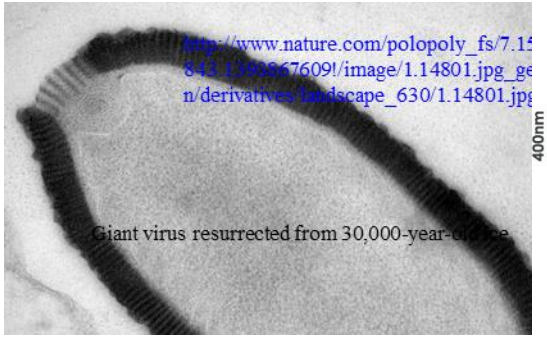


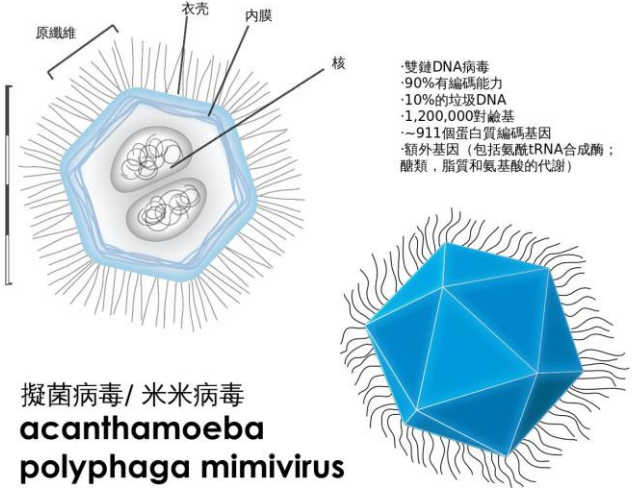
How to study the virus?

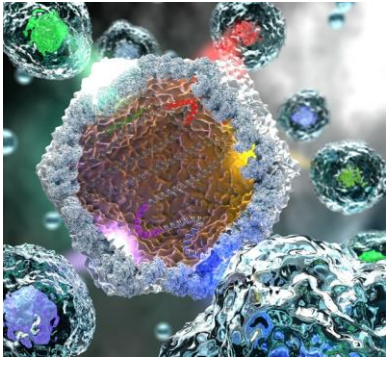
Electron microscopy,
X-ray diffraction,
Biochemical analysis,
Immunology

6.2.1 General Structural Properties

- **A complete virus particle is called a virion**
- **Virions range in size from about 10 to 400 nm in diameter.**
- **The smallest are a little larger than ribosomes,**
- **Whereas mimiviruses, the largest viruses known, can be seen in the light microscope.**

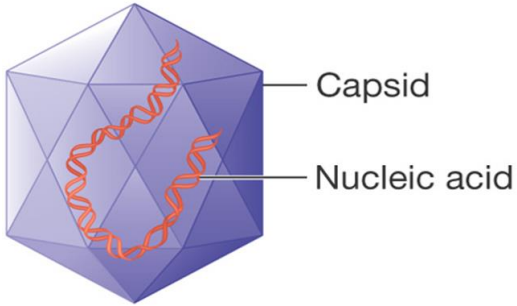




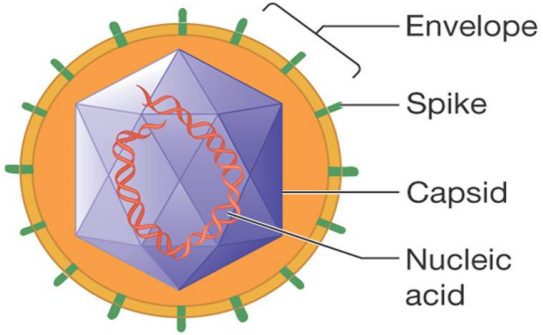


6.2.1 General Structural Properties

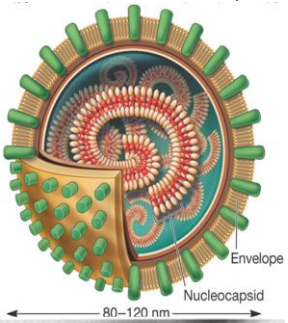
- **Virions lacking envelopes- Naked viruses**(a)
- **Virions having envelopes-Enveloped viruses**(b)
- **The simplest virions are constructed of a nucleocapsid.**
- **Nucleocapsid= genome+ capsid (protein coat, coded by viral genome)**
- **Envelopes-outside of capsid**

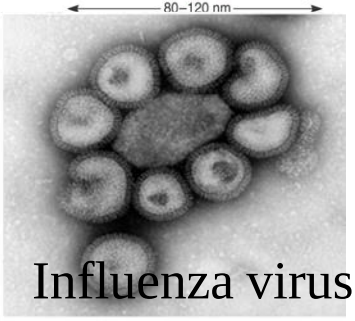


(a) Nonenveloped virus



(b) Enveloped virus





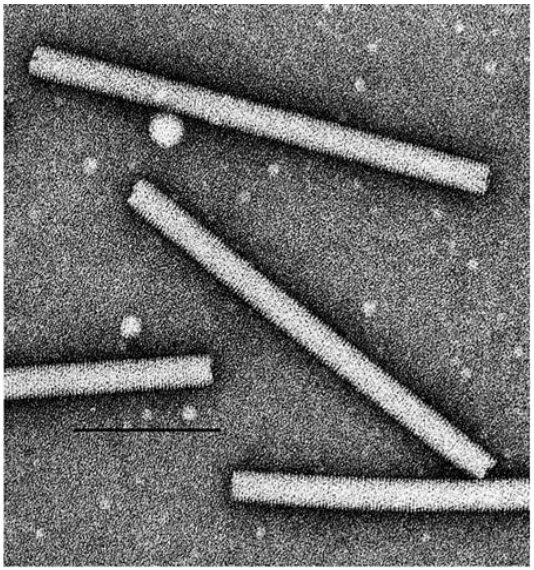
Influenza virus

6.2.1 General Structural Properties-Capsids 衣壳

- **Components: protein, are coded by the viral genome.**
- **Function: protect viral genetic material and aids in its transfer between host cells**
- **Arrange: several protomers (protein subunits)-capsomer壳体-capsomers(ring or knob shape)-capside**
- **Virion morphology: capsids are helical, icosahedral二十面体病毒, or complex, result from capsid symmetry with the presence or absence of an envelope.**

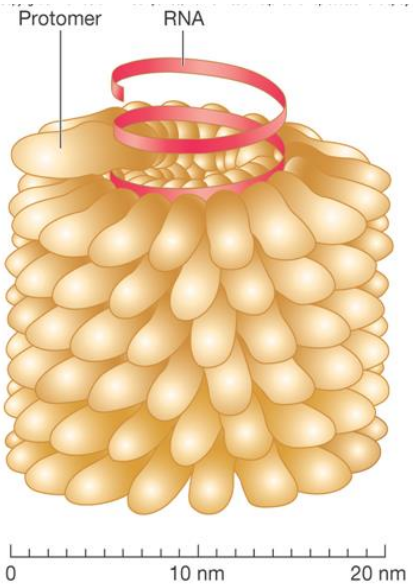
6.2.2 Helical Capsids

Helical capsids are shaped like hollow tubes with protein walls. The capsid encloses an RNA genome, which is wound in a spiral and lies within a groove formed by the protein subunits.

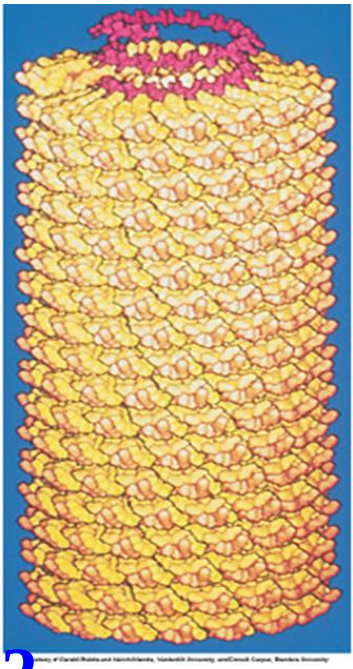


(a)

Robert G. Milne, Plant Virus Institute, National Research Council, Italy



(b)



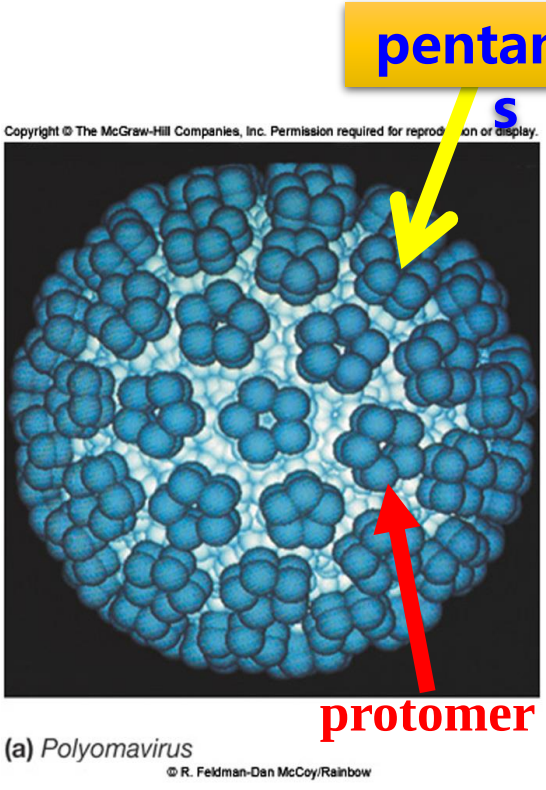
Who decided the length and diameter?

6.2.3 Icosahedral(20) capsids

- An icosahedron is a regular polyhedron正多面体 with 20 equilateral faces and 12 vertices顶点
- They are constructed from ring- or knob-shaped units called capsomers, each usually made of five or six protomers.
- Capsomer壳体
  - Pentamers (pentons) – 5 protomers(vertices)
  - Hexamers (hexons) – 6 protomers(faces)

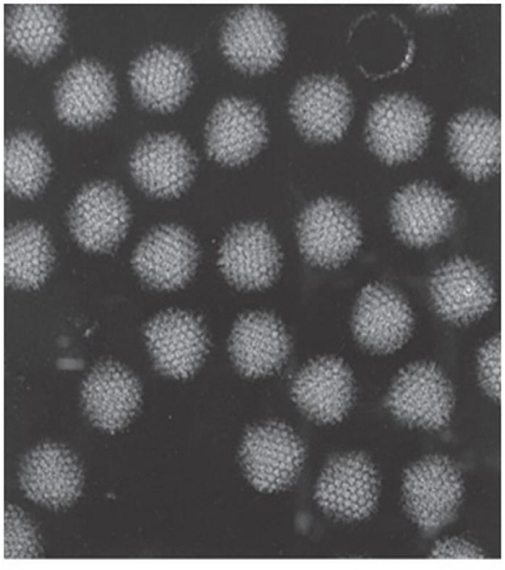
Icosahedral capsids are the most efficient way to enclose a space. Why ?

6.2.3 Icosahedral(20) capsids



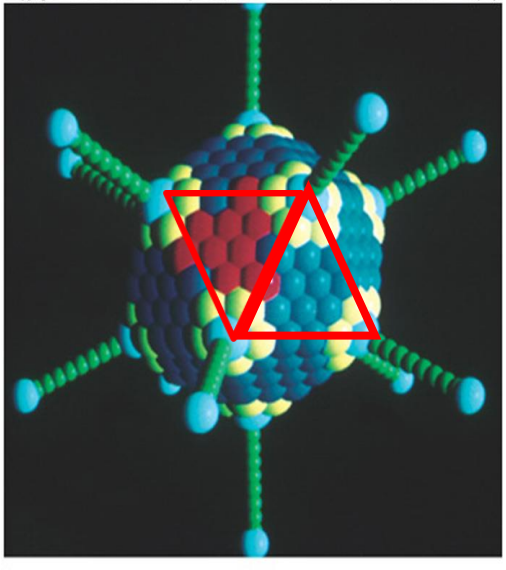
(a) *Polyomavirus*

72capsomers



(b) Adenovirus

252capsomers

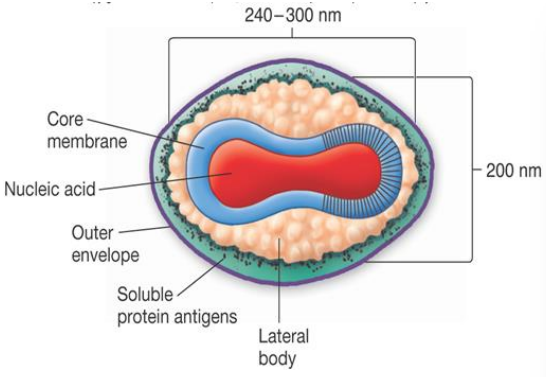


(c) Adenovirus

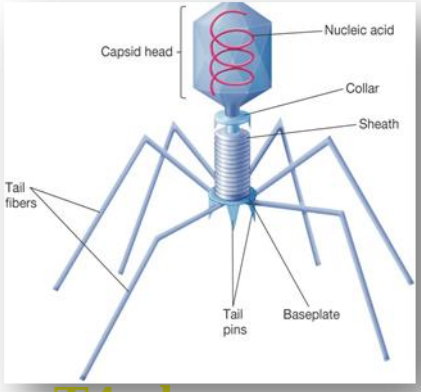
mimic

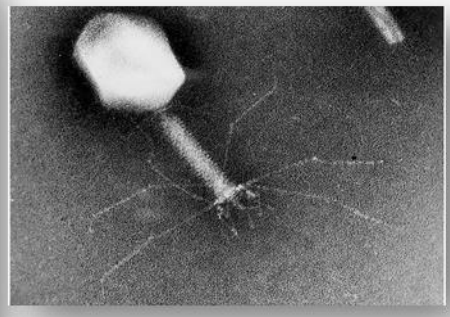
6.2.4 Capsids of Complex Symmetry

- Some viruses do not fit into the category of having helical or icosahedral capsids
- Examples
  - Poxviruses – largest animal virus
  - Large bacteriophages – binal symmetry head resembles icosahedral, tail is helical



Vaccinia virus

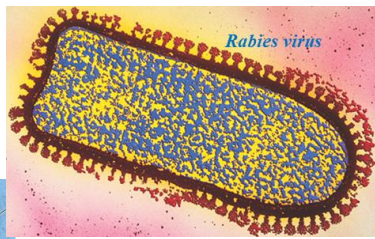




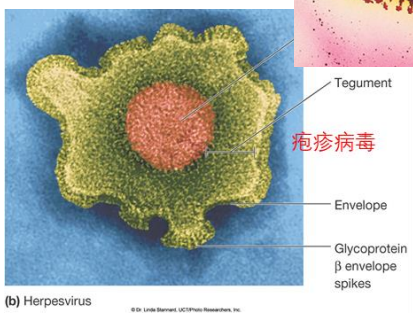
T4 phage

6.2.5 Viral Envelopes and Enzymes

- **Many viruses are bound by an outer, flexible, membranous layer called the envelope**
- **Animal virus envelopes (lipids and carbohydrate usually arise from host cell plasma or nuclear membranes.**
- **Many enveloped viruses are pleomorphic(a). However, the bullet-shaped rabies viruses(b) are a constant, characteristic shape.**



- **Where from of the protein?**



6.2.5 Viral Envelopes and Enzymes

- **Envelope proteins are coded for by viral genes and may even project from the envelope surface as spikes or peplomers棒状包膜粒**
- **Most of its envelope proteins are glycoproteins. A nonglycosylated protein, the M (matrix) protein, on the inner surface of the envelope and helps stabilize influenza virus.**
- **Spikes are involved in viral attachment to host cell**
  - **e.g., hemagglutin(HA) of influenza virus**
  - **Used for identification of virus.**

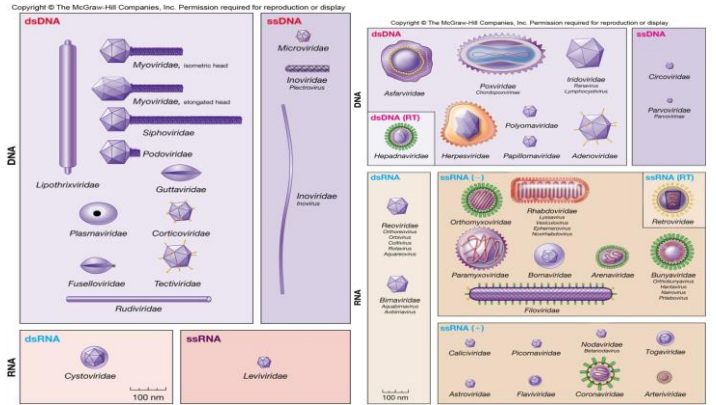
6.2.5 Viral Envelopes and Enzymes

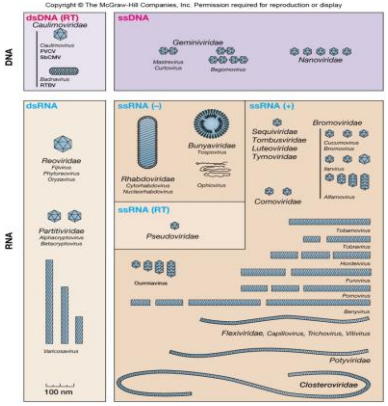
Virion enzymes

- It was first erroneously thought that all virions lacked enzymes
- A variety of virions have enzymes
  - some are associated with the envelope or capsid but most are within the capsid
  - Influnza virus carry an enzyme that synthesizes RNA
  - Can you give an example?

6.2.6 Viral genome

- **Cellular genomes are always double-stranded (ds) DNA.**
- **A virus may have single or double stranded DNA or RNA(ds, ss)(how many?)**
- **The size of the nucleic acid also varies from virus to virus(4Knt)**
- **Genomes can be segmented or circular**





6.2.6 Viral genome and classification

- **Focuses on viral genome and process used to synthesize viral mRNA**

- **(ds) DNA**
- **(ss) DNA**
- **dsRNA**
- **ssRNA (+/-)**
- **Retrovirus**
- **Gapped dsDNA**

Table 25.1 The Baltimore System

Group	Description
I	Double-stranded DNA genome *genome replication: dsDNA → dsDNA* *mRNA synthesis: dsDNA → mRNA*
II	Single-stranded DNA genome *genome replication: ssDNA → dsDNA → ssDNA* *mRNA synthesis: ssDNA → dsDNA → mRNA*
III	Double-stranded RNA genome *replication: dsRNA → ssRNA → dsRNA* *mRNA synthesis: dsRNA → mRNA*
IV	Plus-strand RNA genome *replication: +RNA → −RNA → +RNA* *mRNA synthesis: +RNA = mRNA*
V	Negative-strand RNA genome *replication: −RNA → +RNA → −RNA* *mRNA synthesis: −RNA → mRNA*
VI	Single-stranded RNA genome *replication: ssRNA → dsDNA → ssRNA* *mRNA synthesis: ssRNA → dsDNA → mRNA*
VII	Double-stranded gapped DNA genome *replication: gapped dsDNA → dsDNA → +RNA → −DNA → gapped dsDNA* *mRNA synthesis: gapped dsDNA → dsDNA → mRNA*

T4phage

Bacteriaphages ϕx174

Rotavirus

Poliovirus

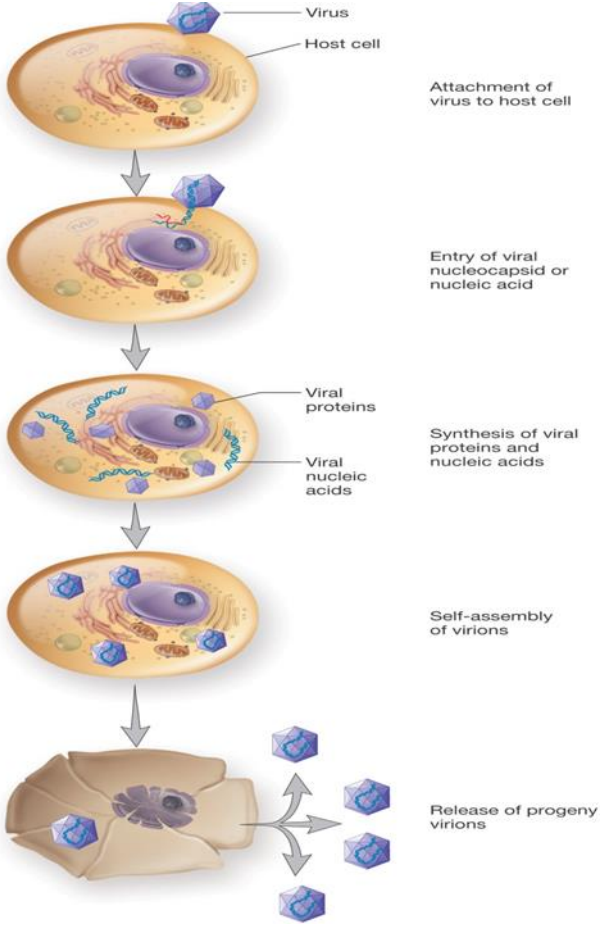
Influenza

Retroviruses(HIV)

HBV

6.3 Viral multiplication繁殖

- **Mechanism used depends on viral structure and genome**
- **Steps are similar**
- **Attachment to host cell**
- **Entry into host cell**
- **Synthesis stage**
- **Assembly**
- **Release**



6.3.1 Attachment (adsorption)

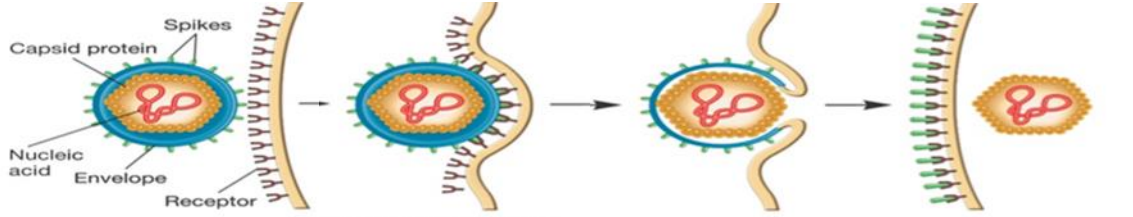
- All viruses, must associate with a potential host cell long enough to gain entry into the cell (exception of plant viruses).(How?)
- Attachment to the host specific receptor(?).
- Bacteriophages attach to the LPS or TA of host.
- Receptor determines host preference
  - May be specific tissue (tropism - 向性)
  - May be more than one host (rabies virus)
  - May be more than one receptor(CD4, CCR5)
  - May be in vital protein for cellular function(stable)
  - May be in lipid rafts providing entry of virus

  (HIV and Ebola are concentrated in lipid rafts)

How about of plant viruses?

6.3.2 Entry into the Host

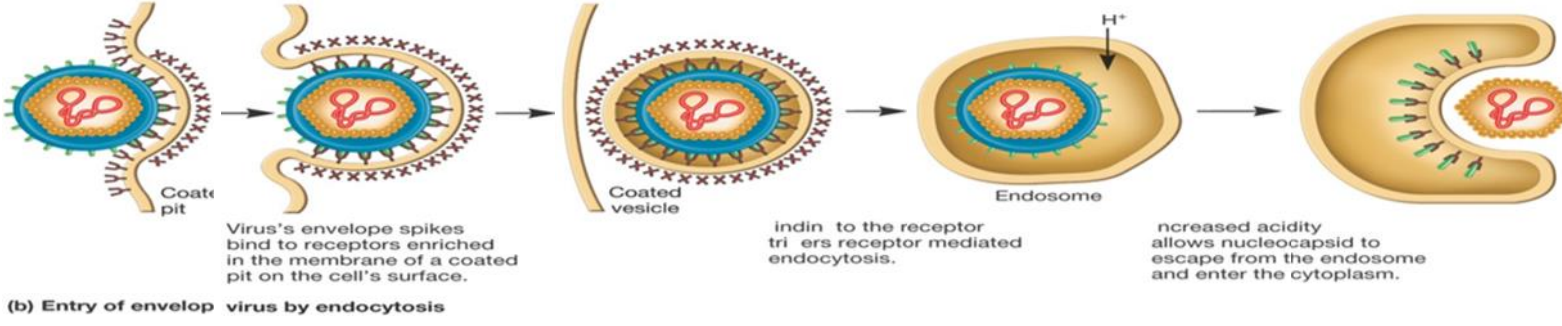
- **The virus's genome or the entire nucleocapsid enters the cytoplasm.**
- **Three methods used**
- **1)Fusion of the viral envelope with host membrane; nucleocapsid enters**



(a) Entry of enveloped virus by fusion with plasma membrane

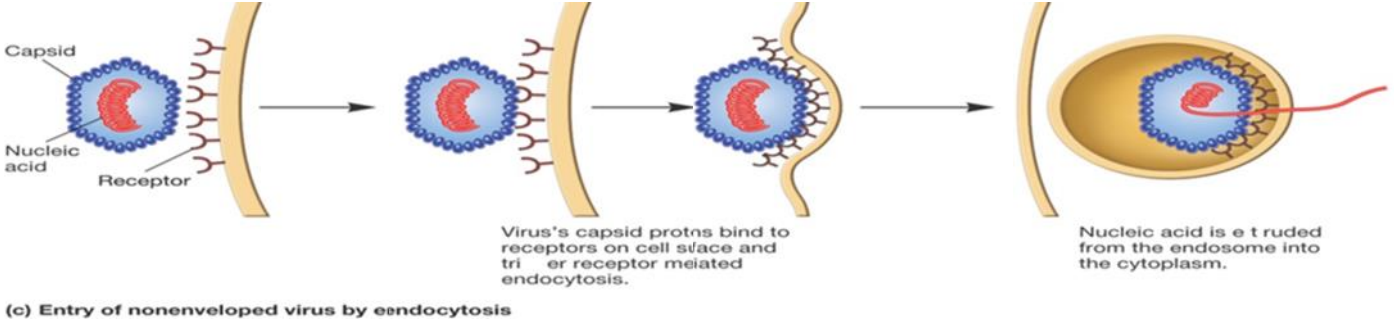
6.3.2 Entry into the Host

- **2) Endocytosis in vesicle; endosome aids in viral uncoating.(acidity)** low pH



(b) Entry of envelop virus by endocytosis

- **3) Injection of nucleic acid(phage)**



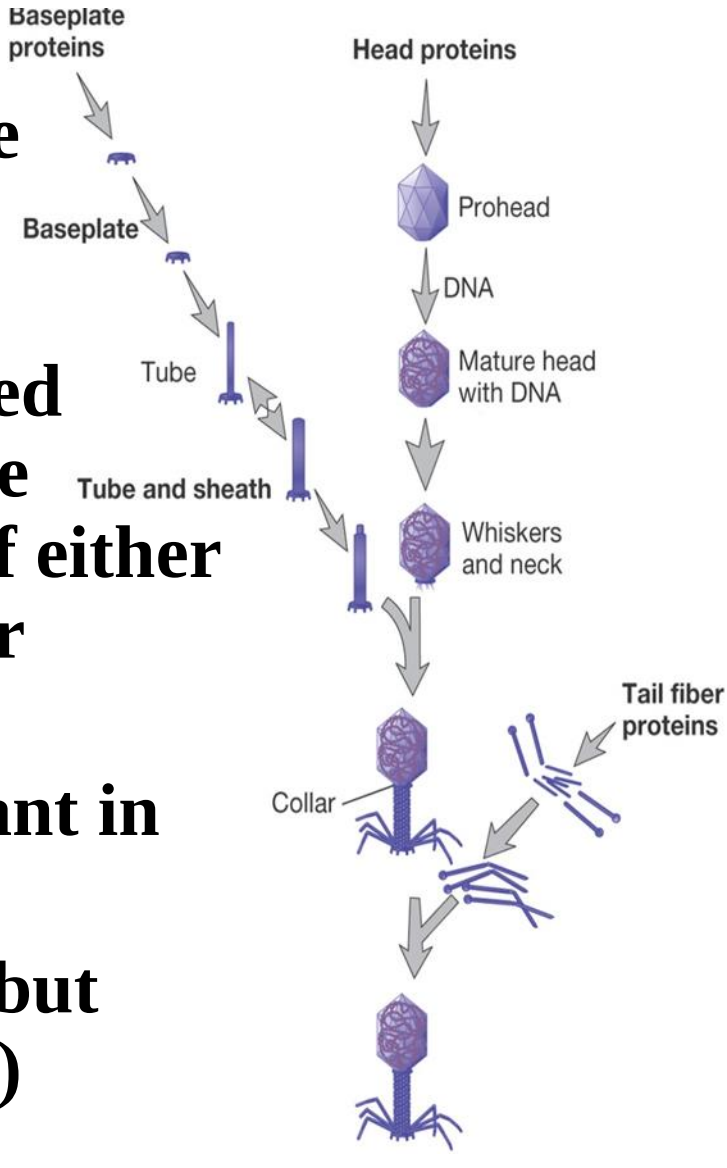
(c) Entry of nonenveloped virus by eendocytosis

6.3.3 Synthesis stage

- **This stage differs dramatically among viruses because the genome of a virus dictates the events that occur.**
- **DNA(ds) typical flow(transcription-translation)**
- **RNA viruses(+/-RNA)-mRNA**
  - **Virus must carry in or synthesize the proteins during the infection process.**
- **Regardless of genome structure, synthesis of vira proteins is tightly regulated.**
- **Early proteins are synthesized early (**taking over the host cell)**;**
- **Late proteins are synthesized later(**capsid and assemble,release)

6.3.4 Assembly

- **Most are assembled in the cytoplasm, and some are assembled in the nucleus.**
- **For many viruses, so-called "virus factories" are large paracrystalline clusters of either complete nucleocapsids or procapsids.**
- **Late proteins are important in assembly.**
- **Assembly is complicated but varies(e.g.bacteriophages)**

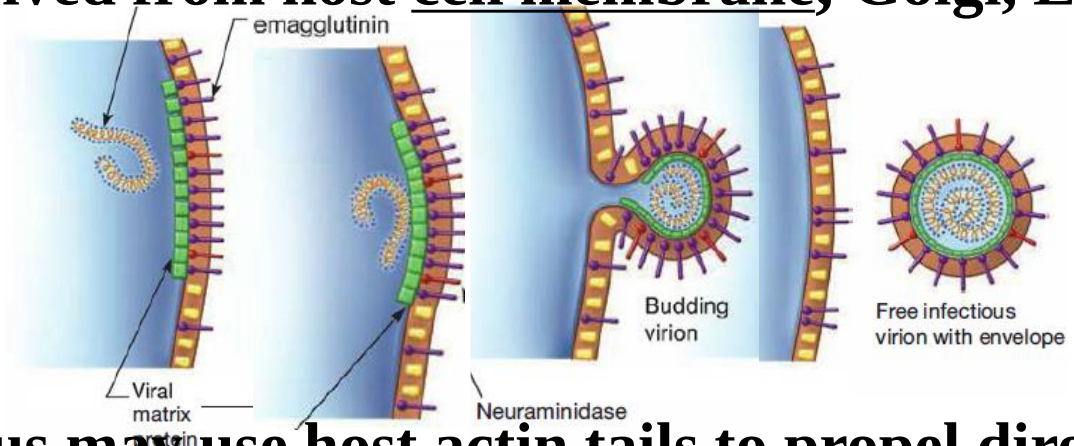


6.3.5 Virion release.

- **Naked viruses lyse the host cell(lysozyme, holin)**
  - **T4 phage may attack peptidoglycan(?) or membrane(holin)**

6.3.5 Virion release. How about of host?

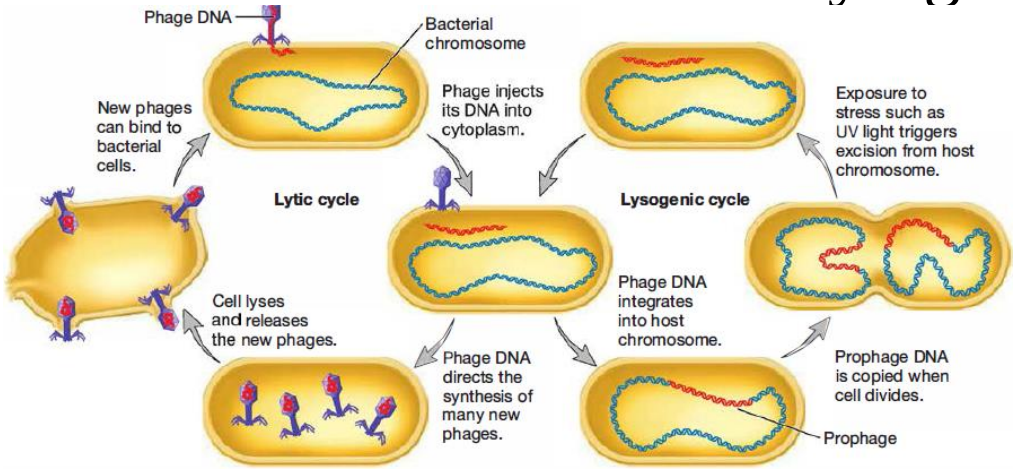
- **Enveloped viruses use budding**
  - Envelope formation and virion release are usually concurrent processes
- **Virus-encoded proteins are incorporated into the membrane.**
- **Nucleocapsid is simultaneously released and the envelope formed by membrane budding**
- **Envelop derived from host cell membrane, Golgi, ER, or other**



- **Vaccinia virus may use host actin tails to propel directly into an adjacent cell(escape defense).**

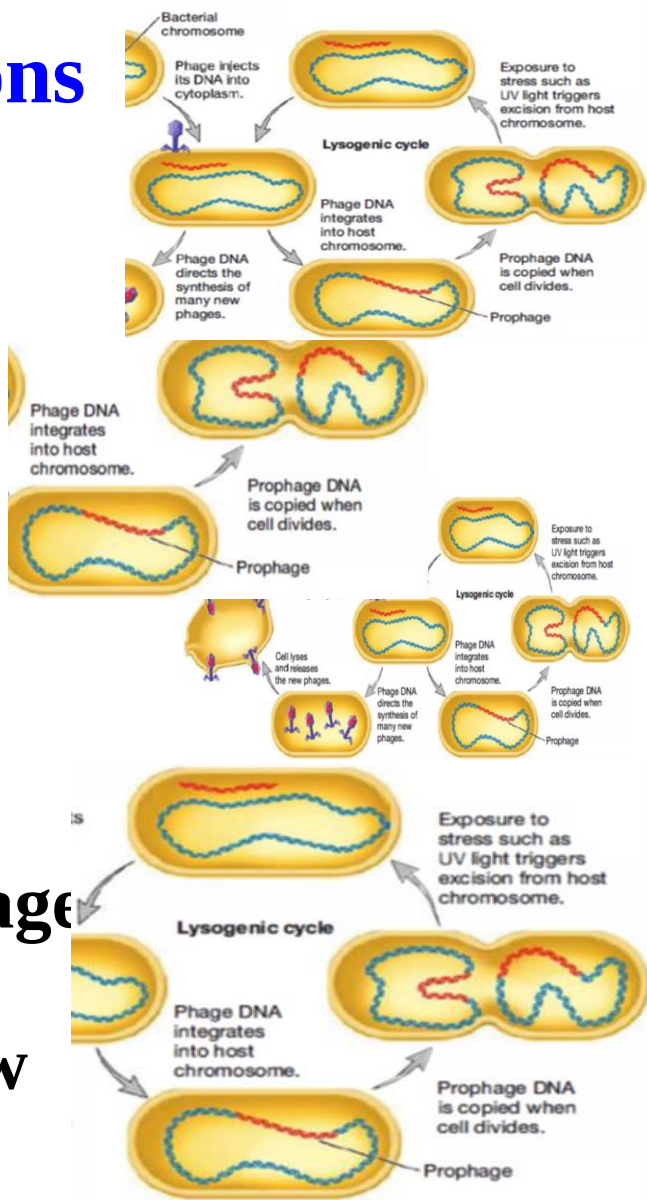
6.4 Types of Viral Infections

- **Lysis and Lysogeny(bacteria and archaea):**
- **A virulent phage**: to begin multiplying immediately upon entering its bacterial host, followed by release from the host by lysis.
- **Temperate phages** : upon entry into the host, they can multiply and lyse the host cell, or they can remain within the host without destroying it.



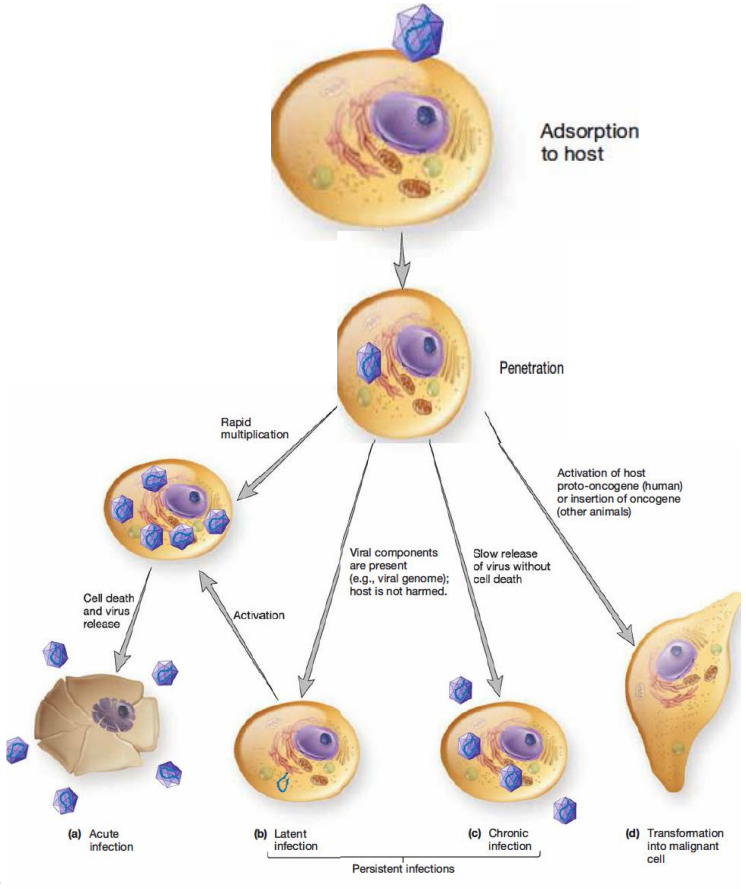
6.4 Types of Viral Infections

- **Lysogeny: The relationship between a temperate phage and its host.**
- **Prophage: The form of the virus that remains within its host.**
- **Lysogens: The infected bacteria.**
- **Induction: Cause the prophage to initiate synthesis of phage proteins and to assemble new virions.**



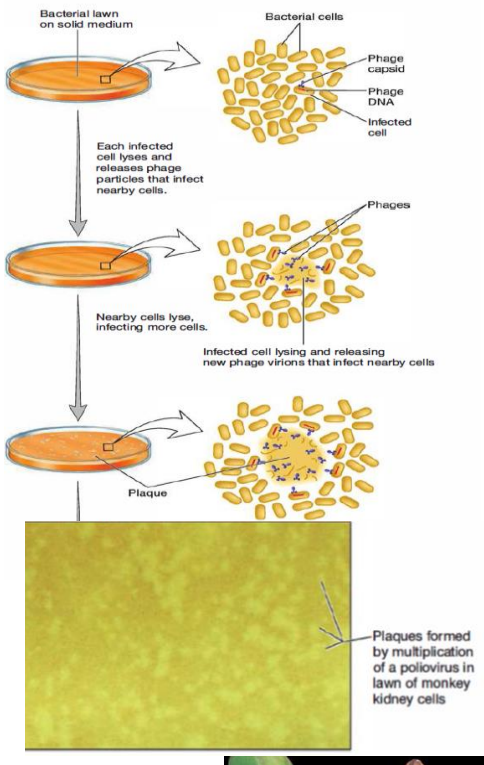
6.4 Types of Viral Infections(Eukaryotic Cells)

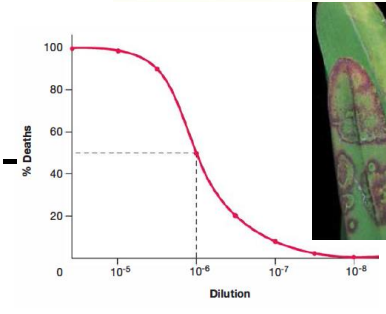
- **Cytocidal infection: An infection that results in cell death.**
- **Cytopathic effects: Eukaryotic viruses can cause degenerative changes or abnormalities in host cells that are distinct from lysis.**
- **Outcome: is the transformation of normal host cells into malignant or cancerous cells.**

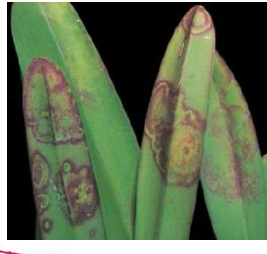


6.5 Cultivation and Enumeration of Viruses

- **1)Viruses are cultivated (using tissue cultures, embryonated eggs, bacterial cultures, and other living hosts).**
- **To observe: plaques(bacterial); or pocks and plaques; localized necrotic lesions (plant).**
- **2)Virions can be counted directly with the transmission electron microscope or indirectly by hemagglutination and plaque assays.**
- **3)Infectivity assays can be used to estimate virion numbers in terms of plaque-forming units, lethal dose (LD50), or infectious dose (ID50)**

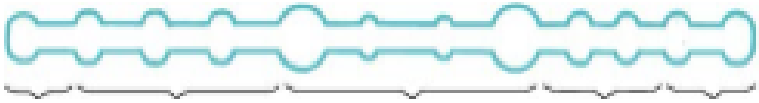






6.6 Viroids and Satellites

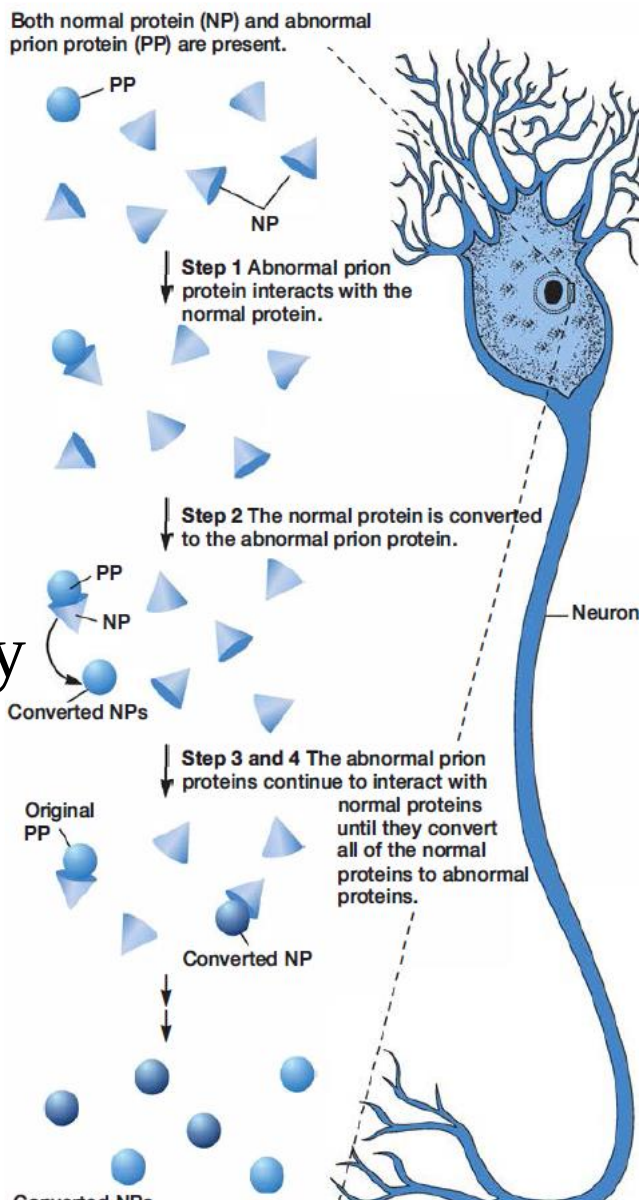
- **Viroids** are infectious agents that consist only of RNA.



- Viroids are covalently closed, circular ssRNAs, about 250 to 370 nucleotides long, which forms double-stranded regions with single stranded loops.
- Infection mechanism: replication (DNAdependent RNA polymerase and DsRNA silencing).
- **Satellites** are similar to viroids in that they also consist only of a **nucleic acid** (either DNA or RNA). Need a helper virus to replicate and infect host cells.
- Imagination: nc**RNA** as a **viroids** in cell(?)

6.7 Prions

- **Prions** are small **proteinaceous agents** associated with at least six **degenerative nervous system disorders**.
- **Hypothesis: prion proteins** exist in **two forms**: abnormally folded form and a normal cellular form.
- The interaction between the **PP** and the **NP converts the PP into** the **NP.**
- **?**



Summary

Virion structure and components
The structure of viruses
Types of virus
Viral multiplication (lysogeny)

Discussion!

1. Discuss whether you think viruses evolved before the first cell or whether they have coevolved and are perhaps still coevolving with their hosts.

2. Discuss the ways that viruses can be cultivated.

3. What advantages might a phage gain by being capable of lysogeny?

4. Explain why the receptors that viruses have evolved to use are host surface proteins that serve very important, and sometimes essential, functions for the host cell?

5. Consider the origin of viral envelopes and suggest why enveloped viruses that infect plants and bacteria are rare.

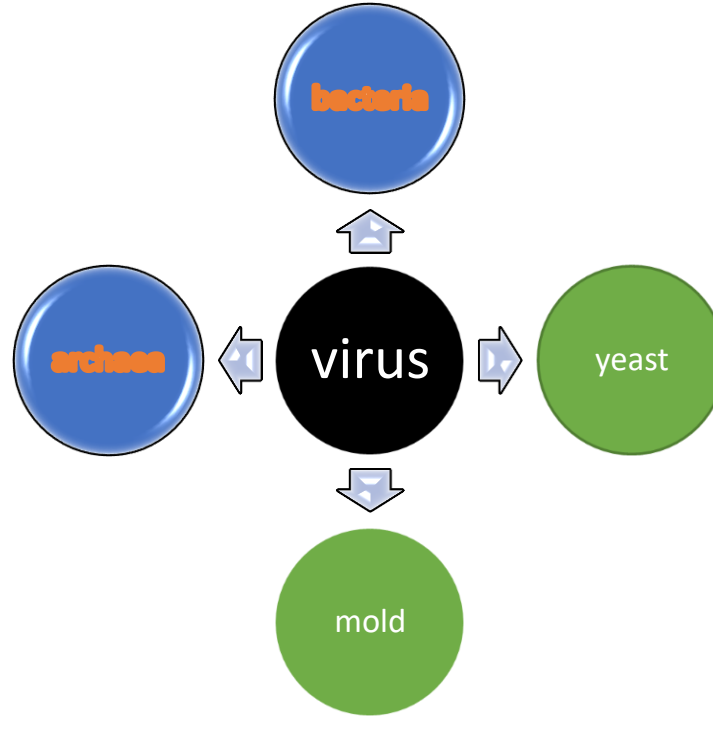
6. Compare and contrast in general terms viruses, viroids, satellites, and prions

作业和练习

- 1.请用任意一种文体，介绍细菌的相关知识（形态特征、结构及其功能等）。引力波会对细菌的结构有影响吗？
- 2.您认为细菌、古菌和真菌最主要的差别是什么？它们的细胞膜的组成或结构有什么异同？您能否举例说明2017年诺贝尔化学奖中的技术用于细胞膜蛋白质的研究，有何显著的特点？
- 3.根据病毒的组成及结构以及繁殖特点，以乙肝病毒为例设想病毒病的几种治疗策略。
- 同学间互评的翻译练习（不需要交）：第3章（星期二班）；第4章（星期五班）；第6章（星期三班）
- 说明：请在期中考试的前2周前提交作业；请在期中考试前完成翻译练习。

Summary

- Bacteria, Archaea, Fungi and virus
- Components, Structure and reproduction
- The difference between them
- The significant of them.
- The relative diseases and benefits



Thanks!

Next chapter 7