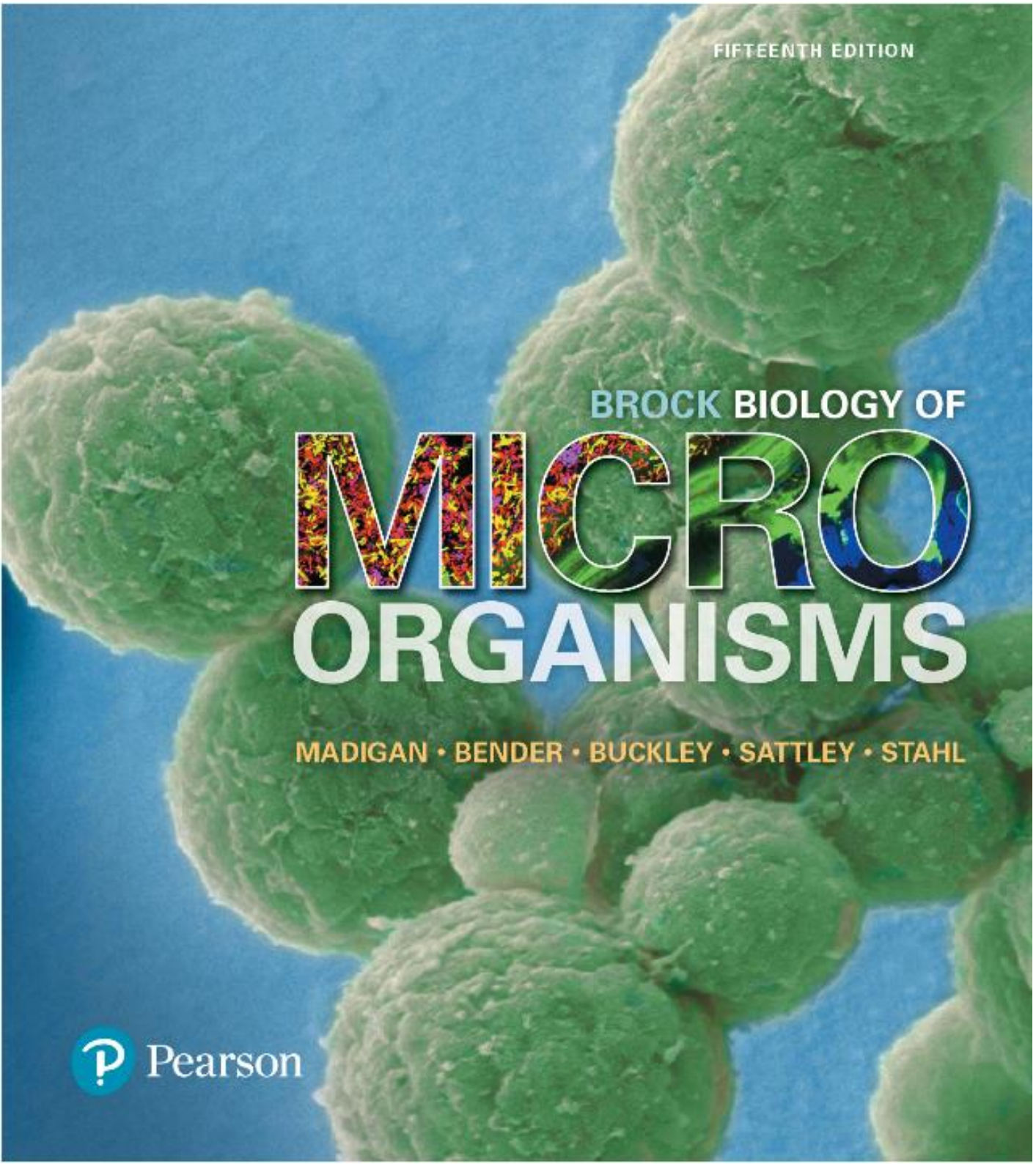


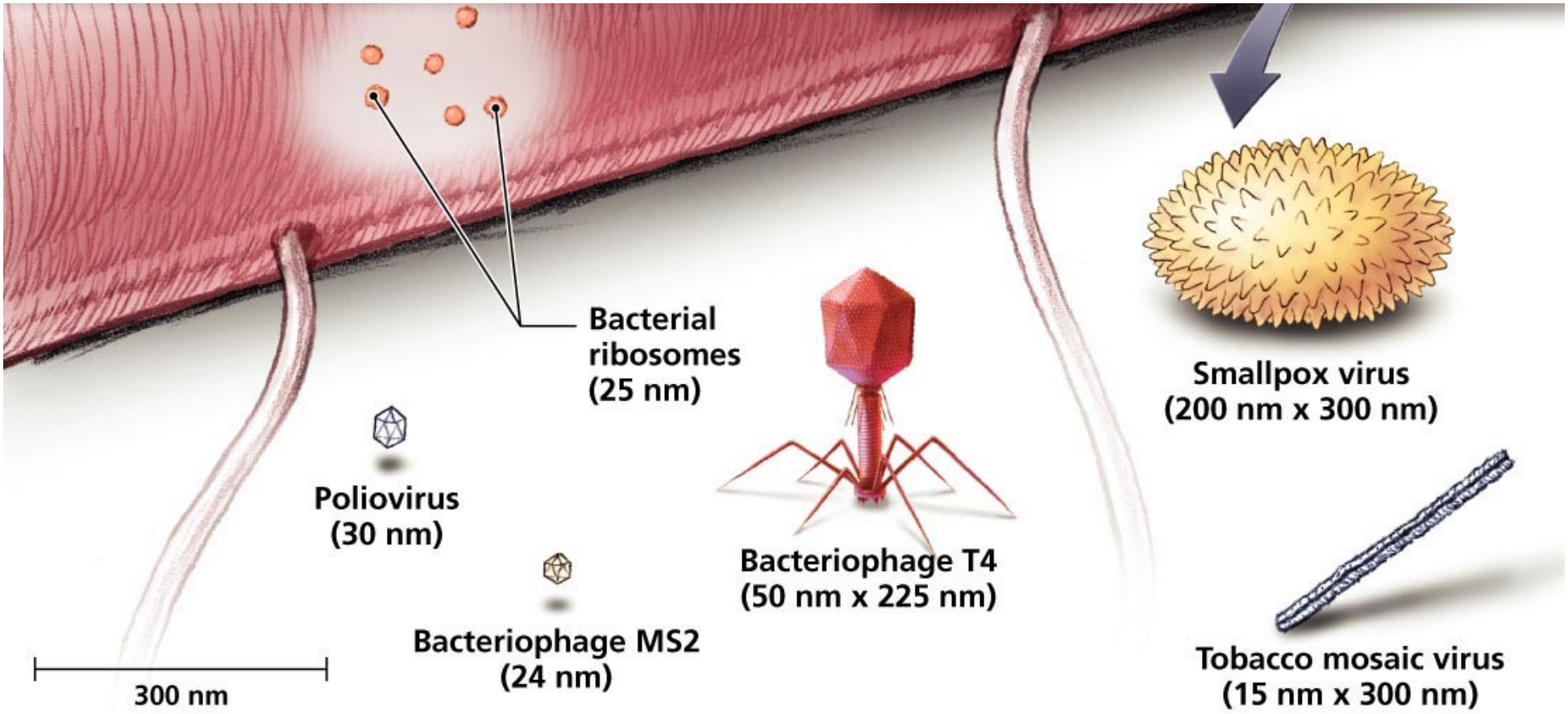
PowerPoint® Lecture Presentations

CHAPTER 8

Viruses and Their Replication

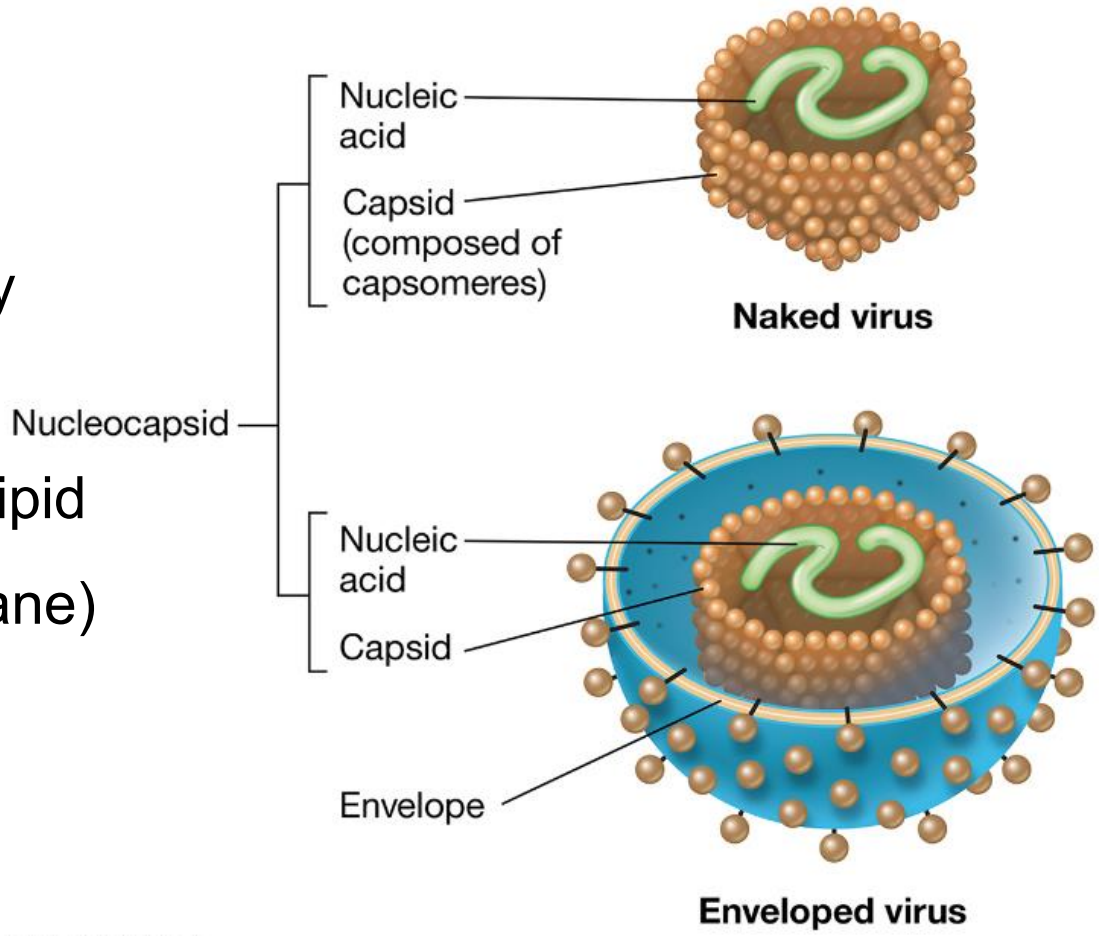
What Is a Virus?

- Virus: genetic element that cannot replicate independently of a living (host) cell
- Virus particle (virion): extracellular form of a virus
  - exists outside host and facilitates transmission from one host cell to another
- Replication/reproduction occurs only upon *infection* (entry into host cell).



Viral Components

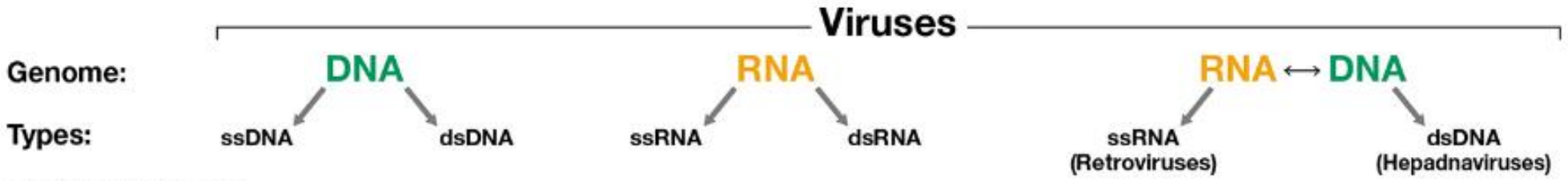
- Capsid:
  - *Naked* viruses (*e.g.*, most bacterial viruses)
  - *Enveloped* viruses (*e.g.*, many animal viruses) have an outer layer consisting of a phospholipid bilayer (from host cell membrane) and viral proteins.



0.02 to 0.3 μm

What Is a Virus?

- Viral genomes
  - either DNA or RNA genomes
  - single-stranded or double-stranded
    - Single-stranded may be *plus sense* (same as mRNA) or *minus sense* (complementary to mRNA).
  - either linear or circular
  - usually smaller than those of cells

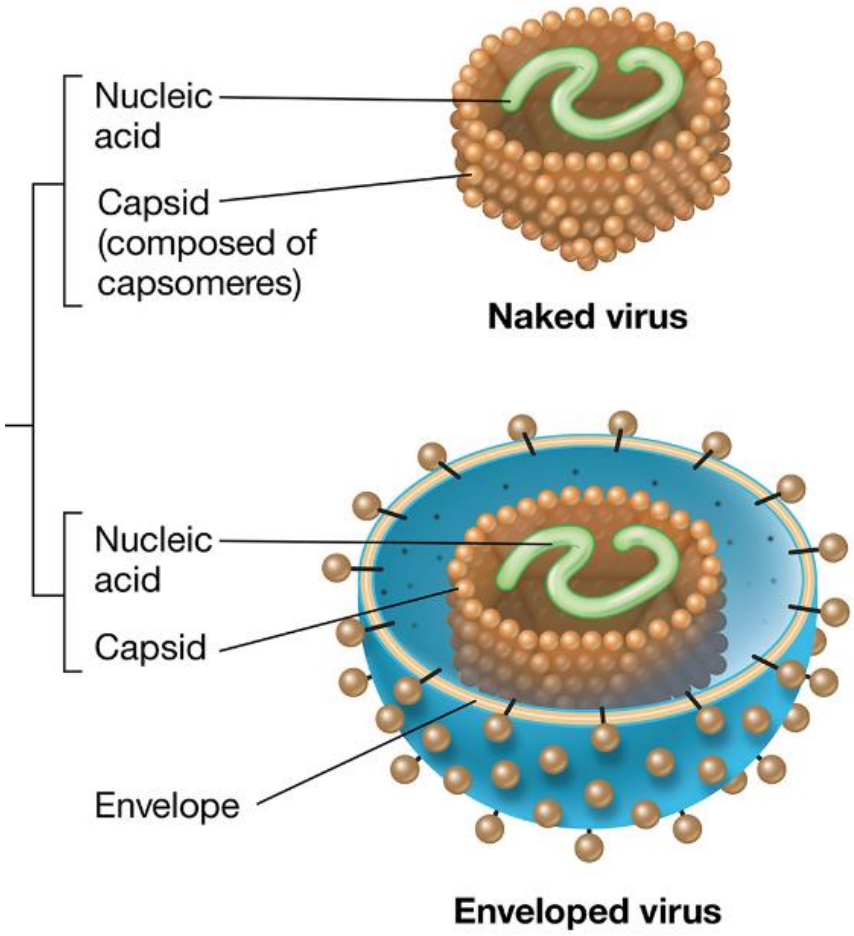


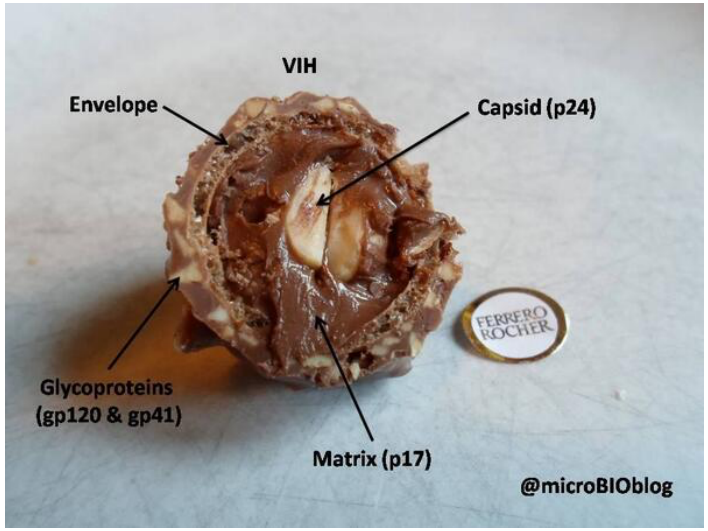
What Is a Virus?

- Viral genomes
  - Viruses can be classified on the basis of the hosts they infect.
    - bacterial viruses (bacteriophages; model systems)
    - archaeal viruses
    - animal viruses (extensively studied)
    - plant viruses (less well studied)
    - other viruses

Structure of the Virion

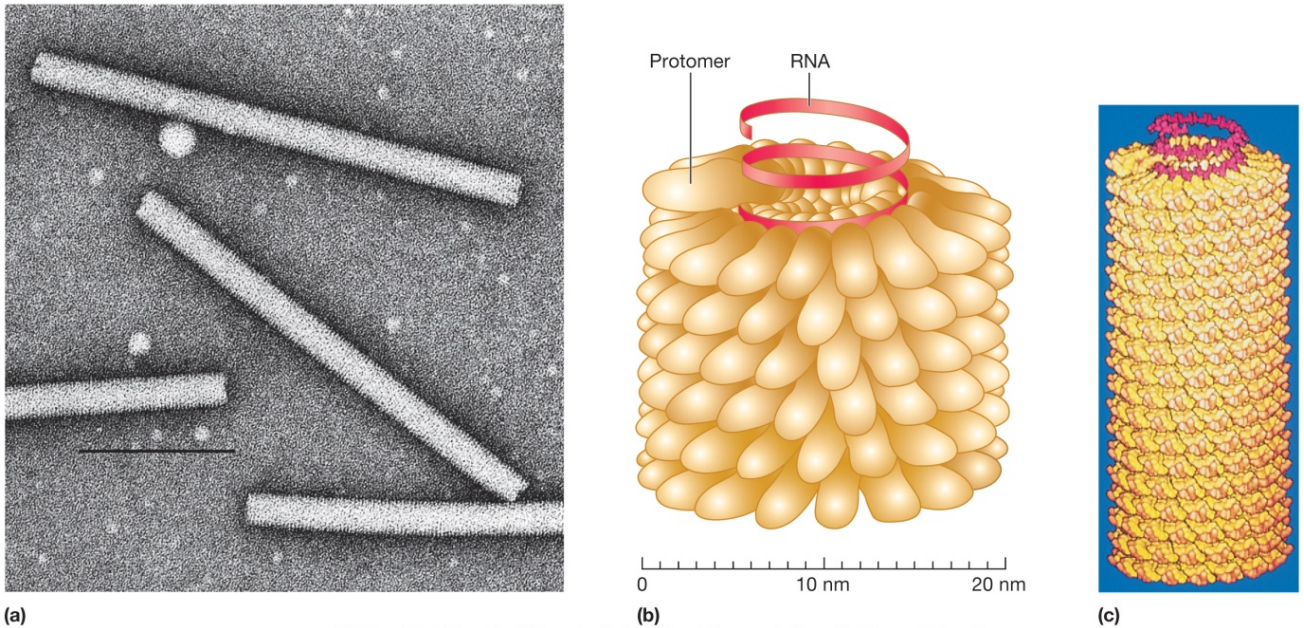
- Virion structure
  - capsomere: individual protein molecules arranged in a precise and highly repetitive pattern around the nucleic acid making up the capsid
    - Capsids can be put together through *self-assembly* (spontaneous) or require host cell folding assistance.





Structure of the Virion

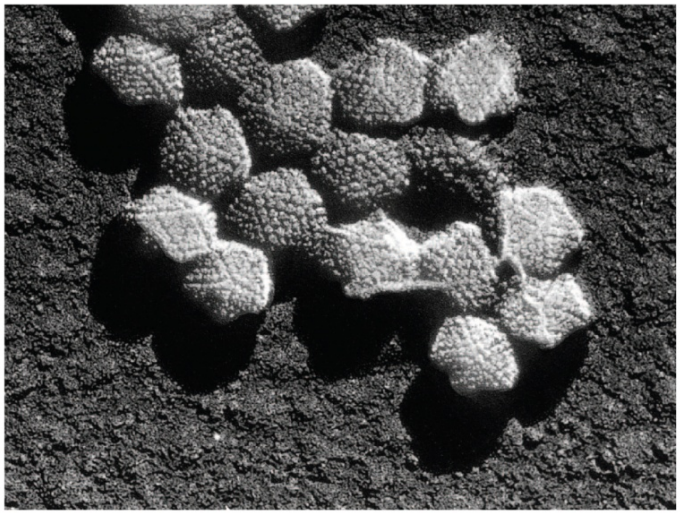
- Virus symmetry
  - *helical* symmetry: rod-shaped viruses (*e.g.*, tobacco mosaic virus or TMV)



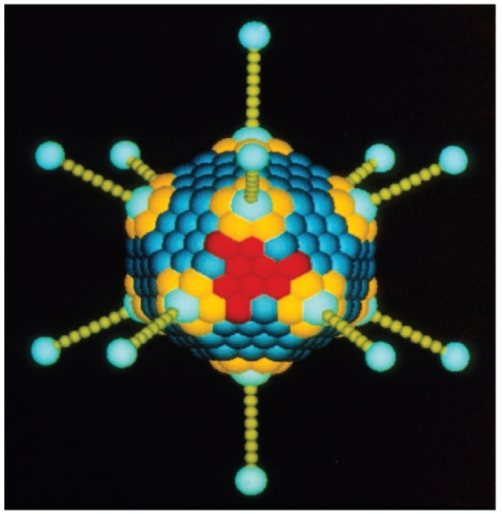
a: © Robert G. Milne, Plant Virus Institute National Research Council, Italy; c: © Gerald Stubbs/Vanderbilt University; Keiichi Namba/Osaka University; and Donald Caspar, Florida State University

Structure of the Virion

- *icosahedral* symmetry: spherical viruses (*e.g.*, human papillomavirus)
  - most efficient arrangement of subunits in a closed shell
  - requires fewest capsomeres



(a)

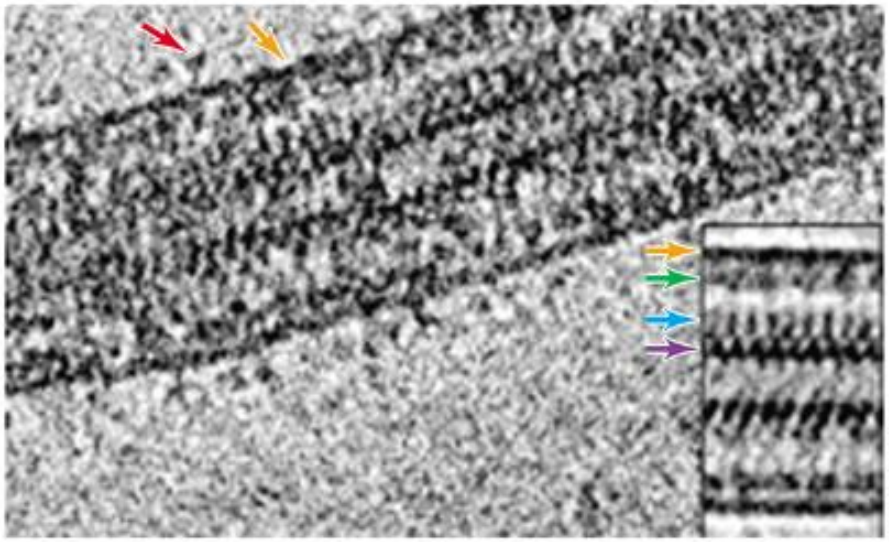


(b)

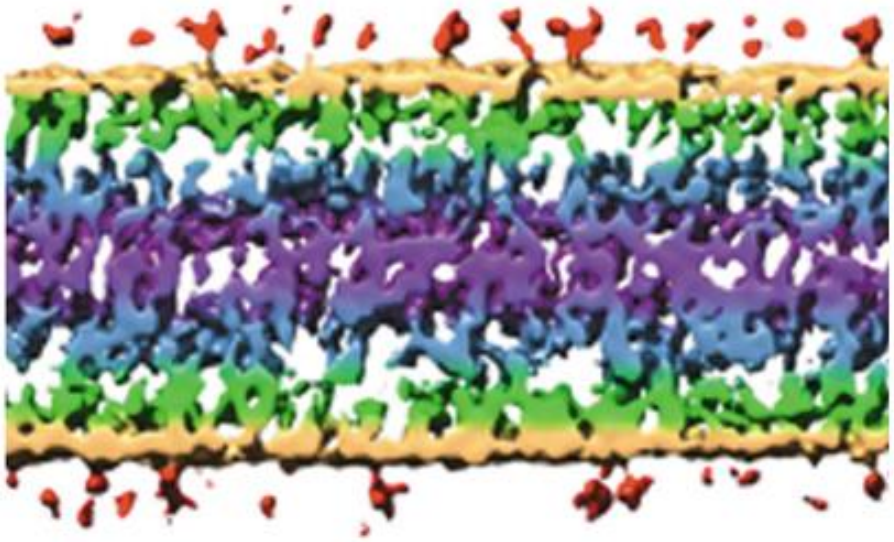
a: © Biophoto Associates/Science Source; b: © Division of Computer Research & Technology, NIH/Science Source

Structure of the Virion

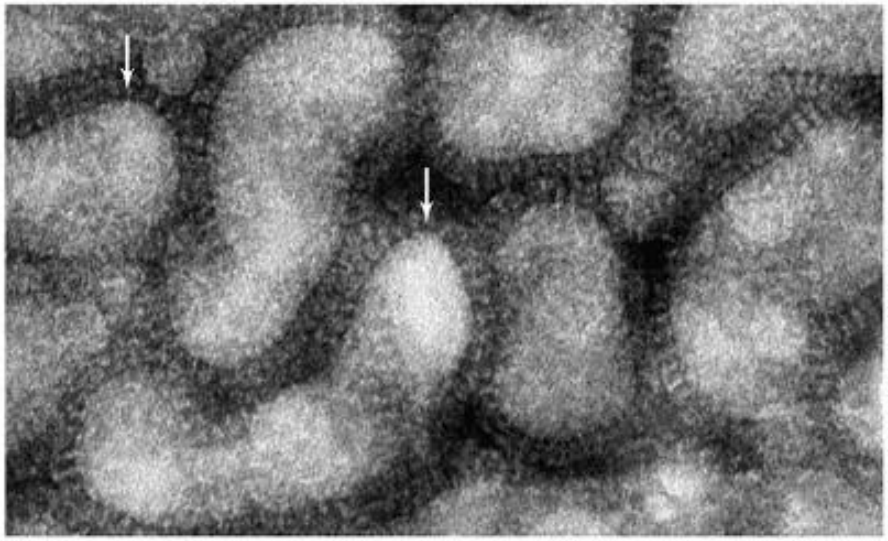
- Enveloped viruses
  - have lipoprotein membrane surrounding nucleocapsid
  - RNA or DNA genomes
  - Envelope proteins attach to and infect animal host cell.
  - relatively few enveloped plant or bacterial viruses because of cell walls surrounding cell membrane
  - Entire virion enters animal cell during infection.
  - Enveloped viruses exit more easily.



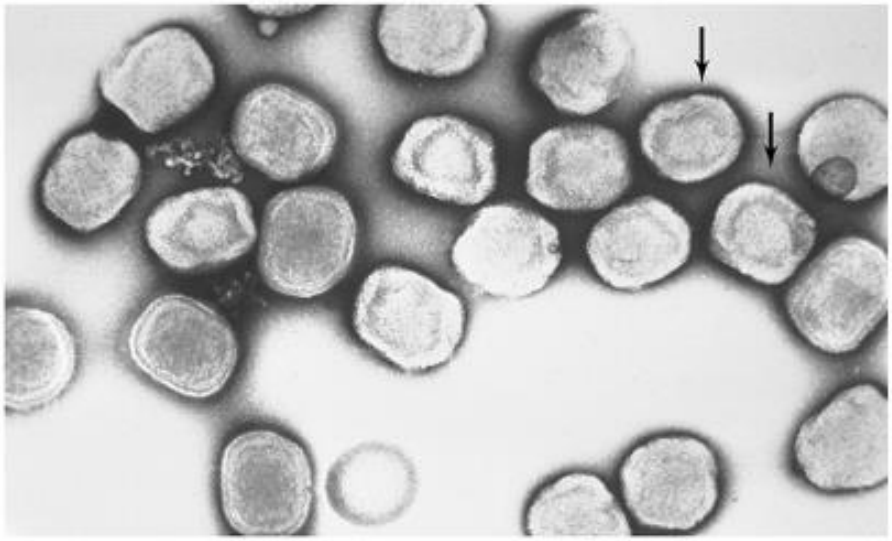
(a)



(b)



(c)



(d)

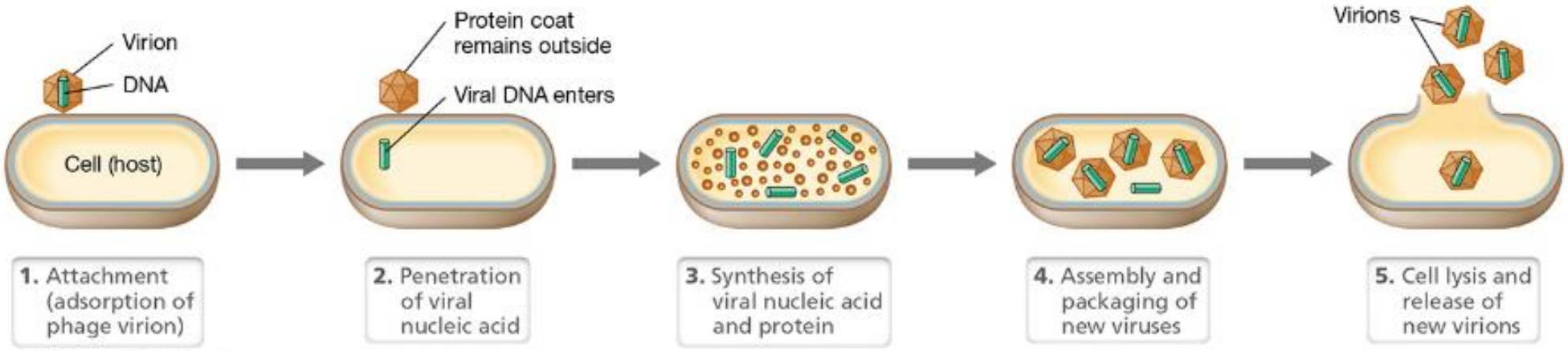
Figure 8.6

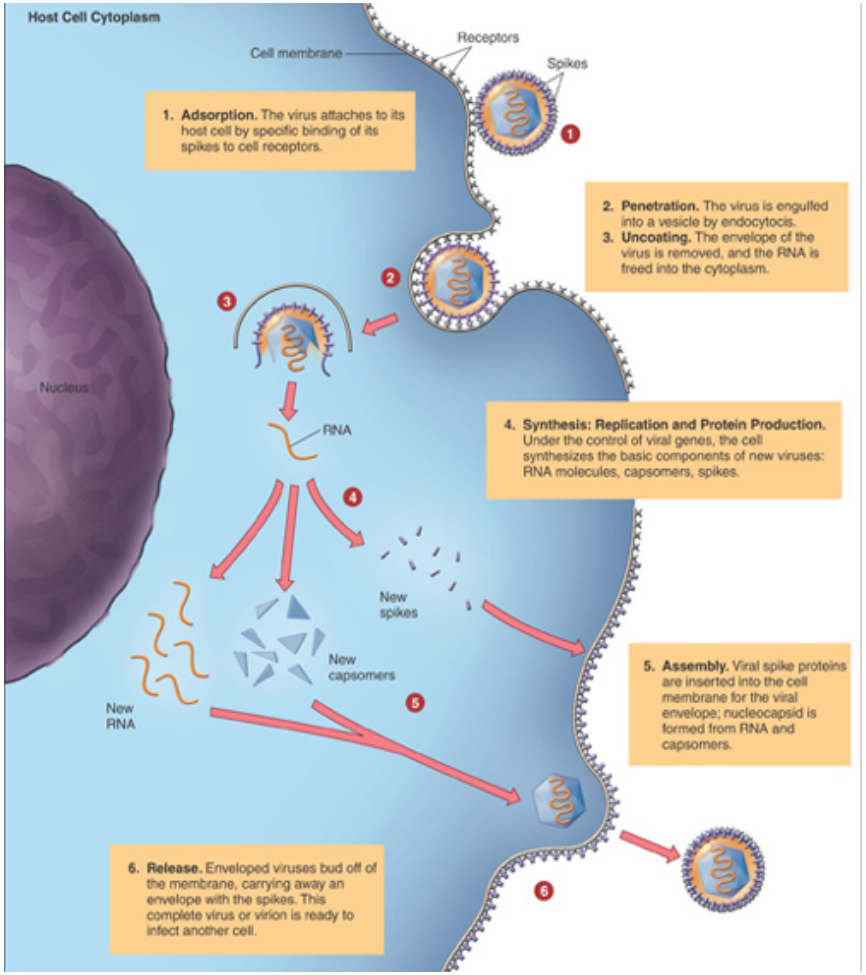
Structure of the Virion

- Enzymes inside virions
  - lysozyme
    - makes hole in cell wall to allow nucleic acid entry
    - also lyses bacterial cell to release new virions
  - *neuraminidases*
    - destroy glycoproteins and glycolipids
    - allows liberation of viruses from cell
  - nucleic acid polymerases (*RNA replicases:* RNA-dependent RNA polymerases)
    - *RNA replicases:* RNA-dependent RNA polymerases
    - *Reverse transcriptase:* RNA-dependent DNA polymerase in retroviruses

Overview of the Virus Life Cycle

- Major difference between phages and animal viruses?
- Phases of viral replication in a *permissive* (supportive) host:
  - *attachment* (adsorption) of the virion
  - *penetration* (entry, injection) of the virion nucleic acid
  - *synthesis* of virus nucleic acid and protein by host cell metabolism as redirected by virus
  - *assembly* of capsids and *packaging* of viral genomes into new virions
  - *release* of mature virions from host cell





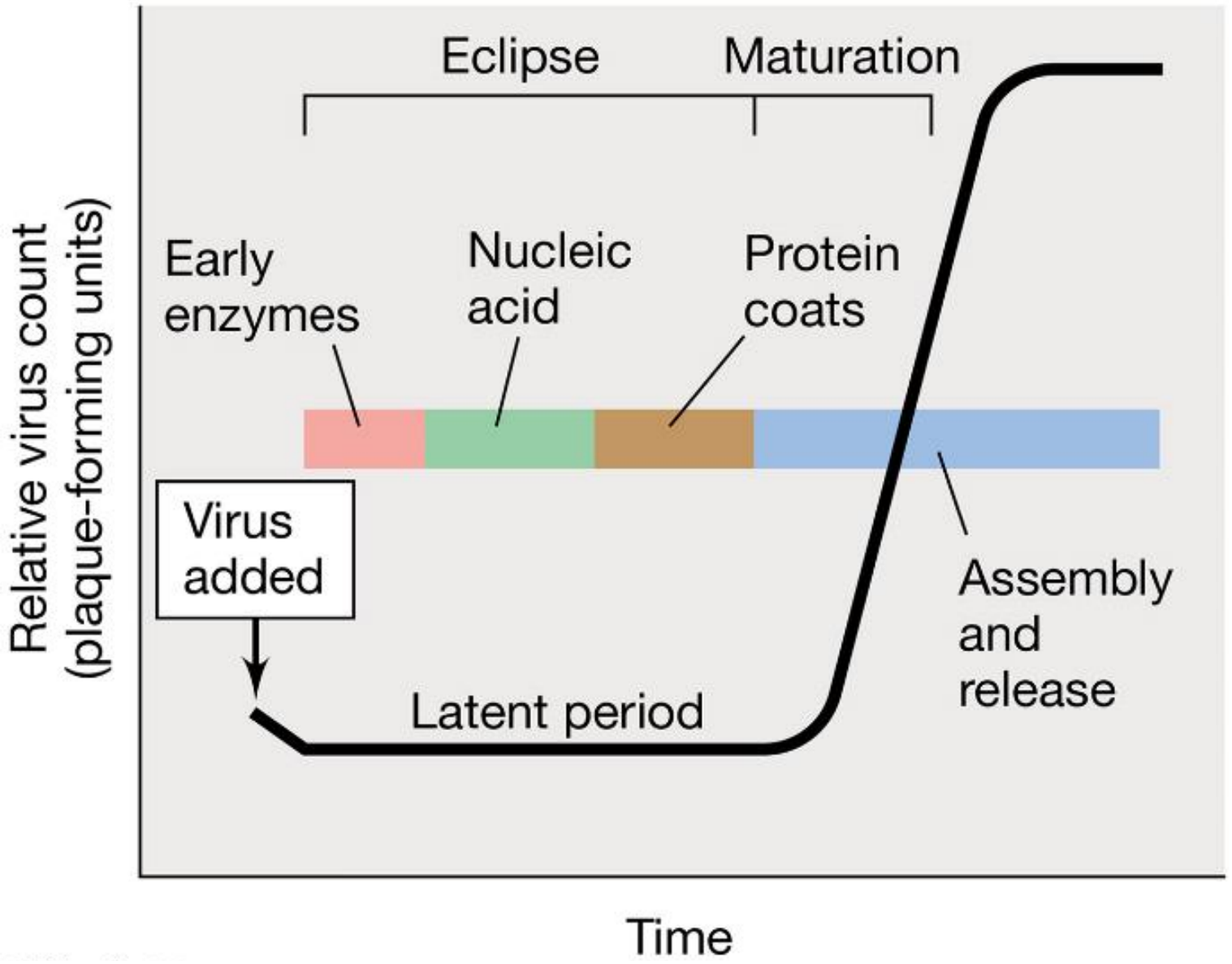


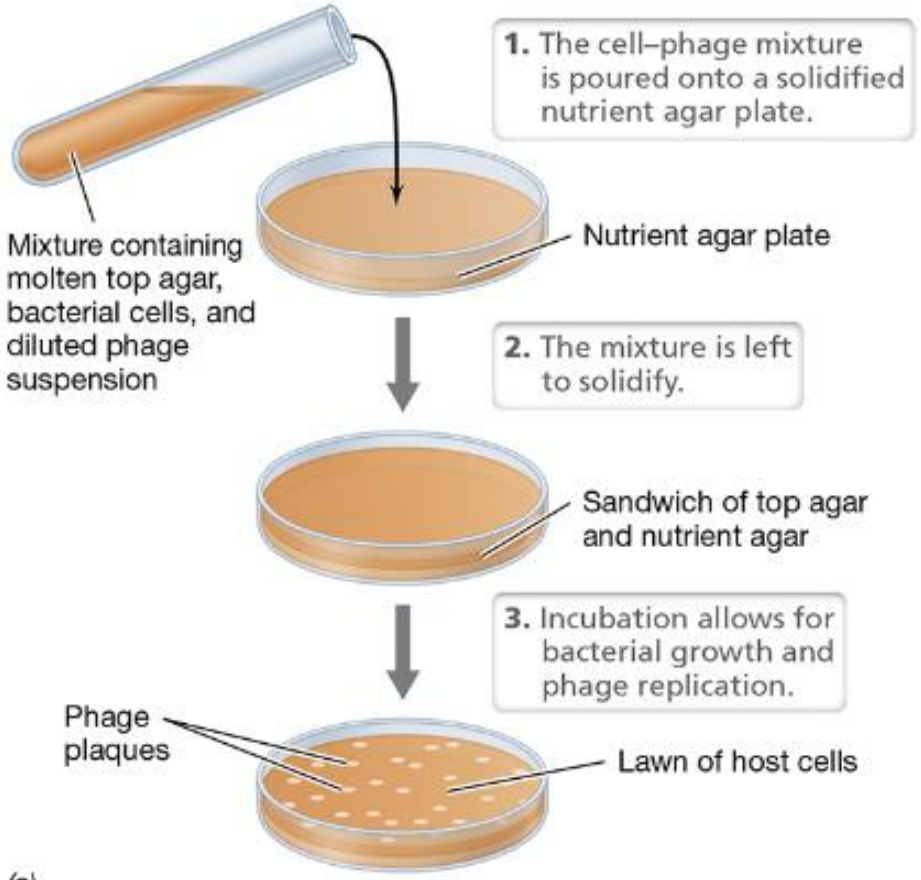
Figure 8.8

Culturing, Detecting, and Counting Viruses

- Bacterial viruses are easiest to grow (hosts in liquid medium or spread as “lawns” on agar and inoculated with virus).
- Animal viruses (and some plant viruses) can be cultivated in *tissue cultures* (from animal organ in culture medium).

Culturing, Detecting, and Counting Viruses

- Detecting and counting viruses: the plaque assay
  - *titer:* number of infectious units per volume of fluid
  - *Plaque assay:* Plaques are clear zones that develop on lawns of host cells where successful viral infection occurs. (Figures 8.9 and 8.10)



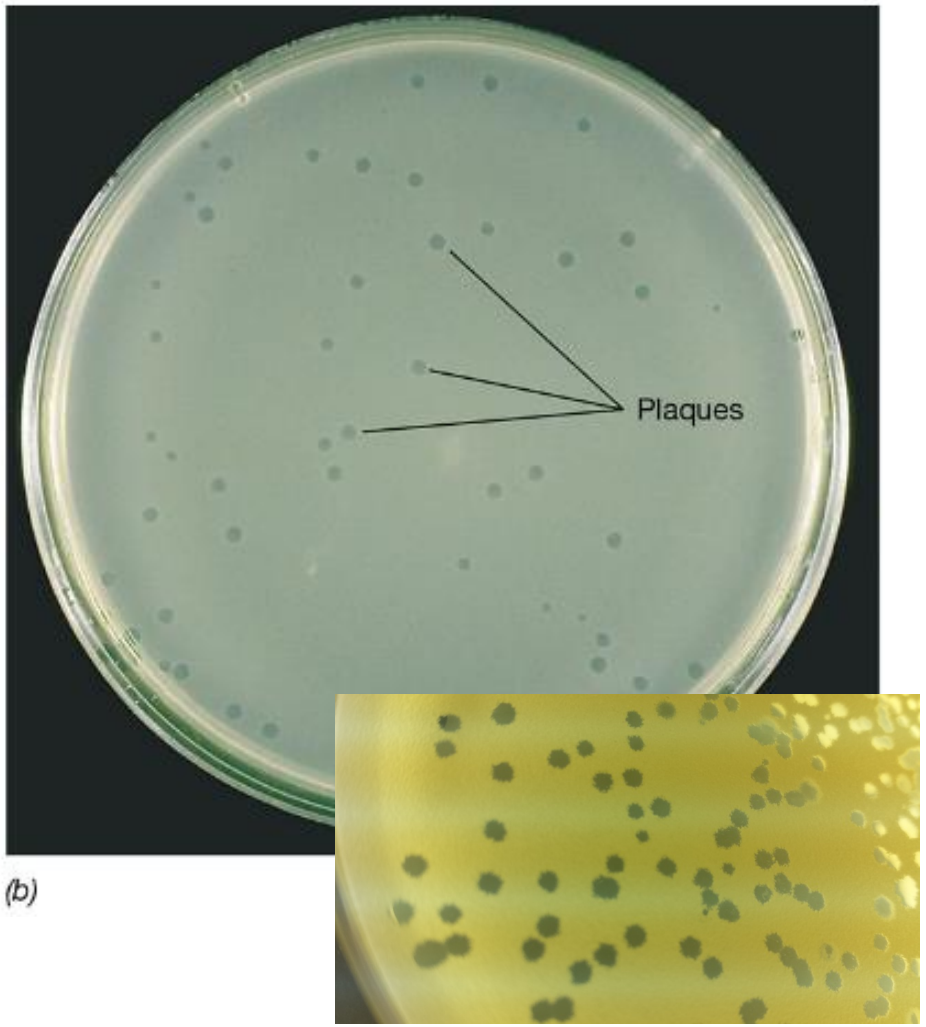
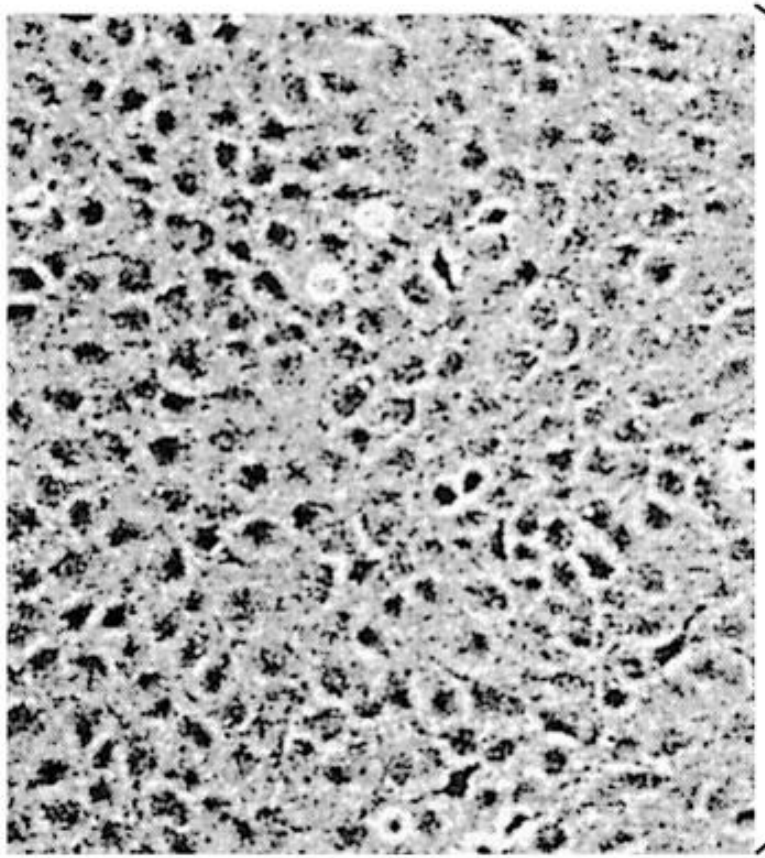
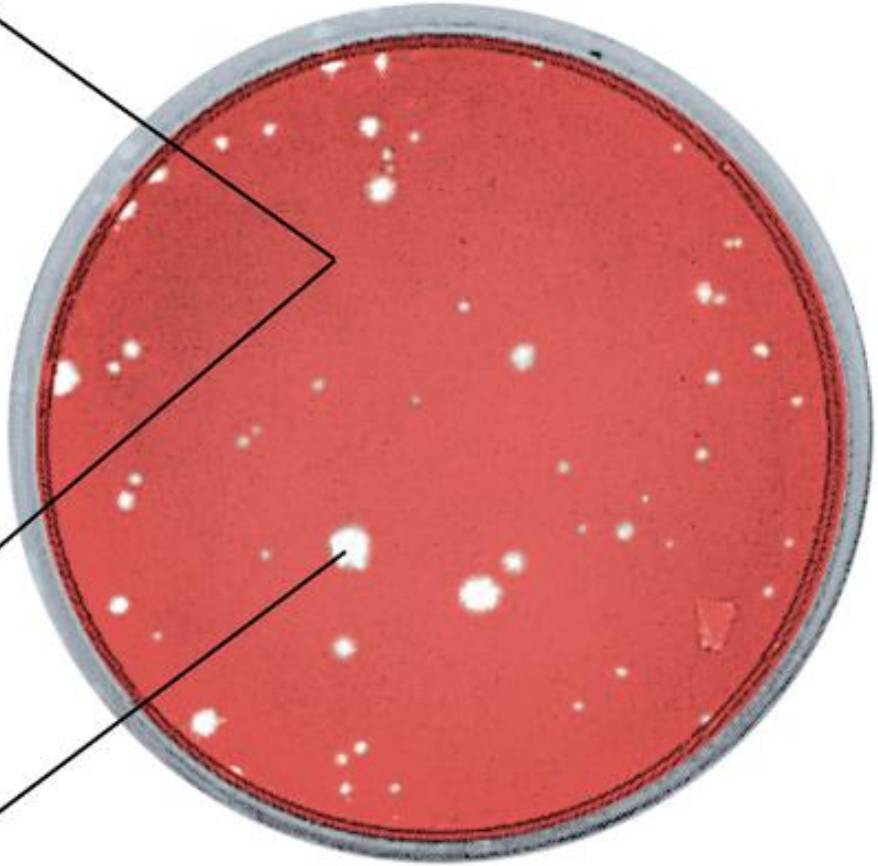


Figure 8.9



Paul Kaplan



T.D. Brock

Confluent monolayer of tissue culture cells

Viral plaques

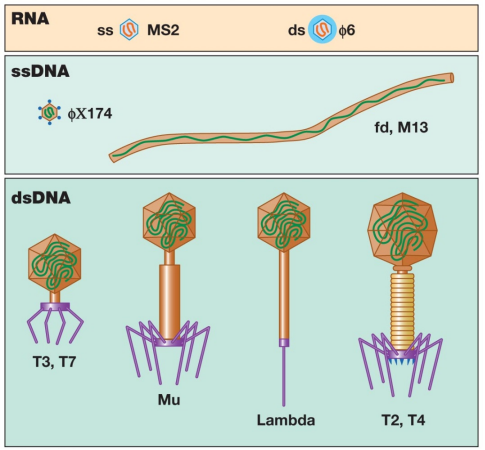
Figure 8.10

The Viral Replication Cycle

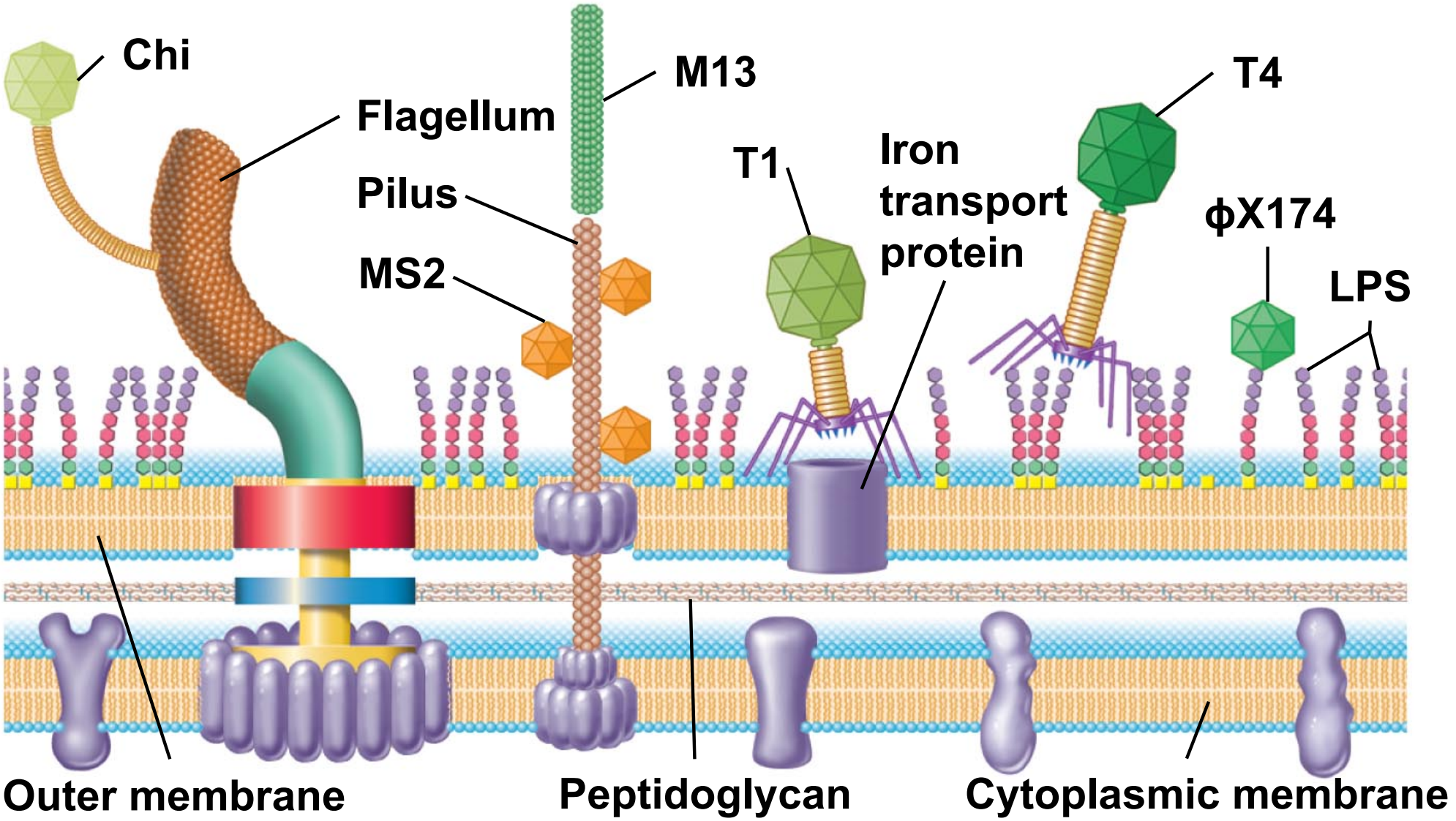
- Attachment, Entry, Replication of Bacteriophage T4
- Temperate Bacteriophages and Lysogeny
- An Overview of Animal Virus Infection

Attachment and Entry of Bacteriophage T4

- Attachment
  - major factor in host specificity
  - requires complementary receptors on the surface of a susceptible host for its infecting virus
    - Receptors include proteins, carbohydrates, glycoproteins, lipids, lipoproteins, or other cell structures.
    - Receptors on host cell carry out normal functions for cell (*e.g.*, uptake proteins, cell-to-cell interaction, flagella, pili).

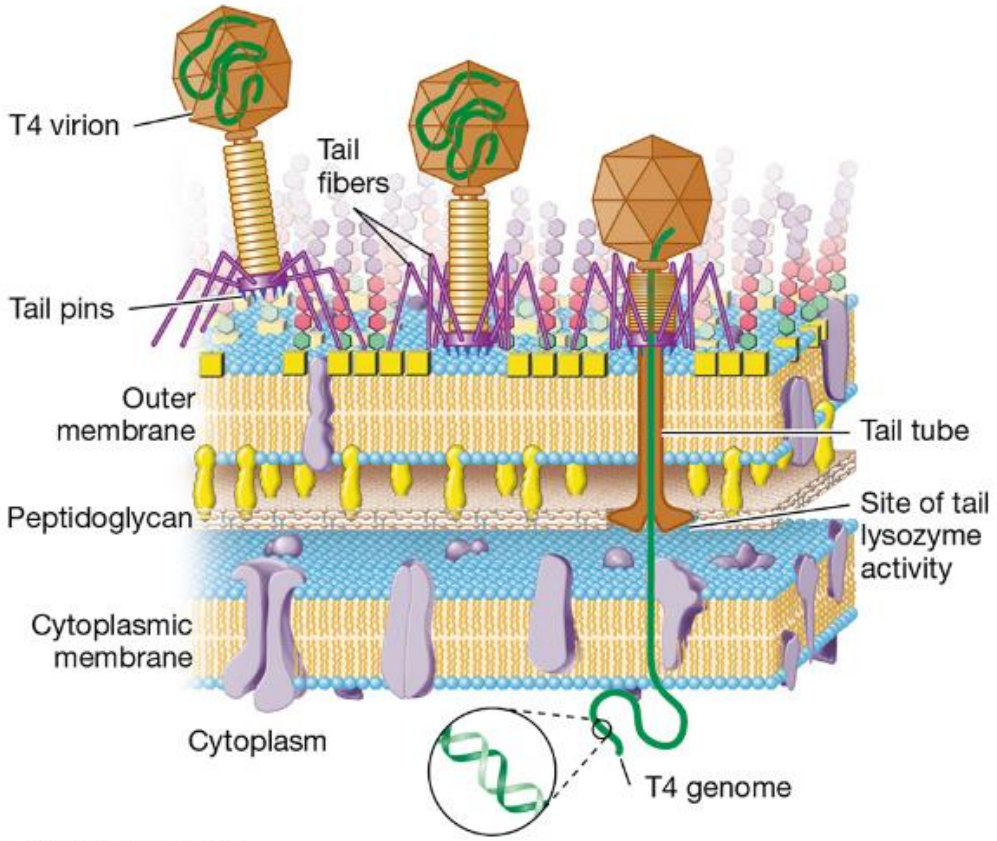


Bacteriophage Attachment



Attachment and Entry of Bacteriophage T4

- Penetration
  - capsid left outside cell
  - Viral genome and viral proteins (for some viruses) enter host cell.

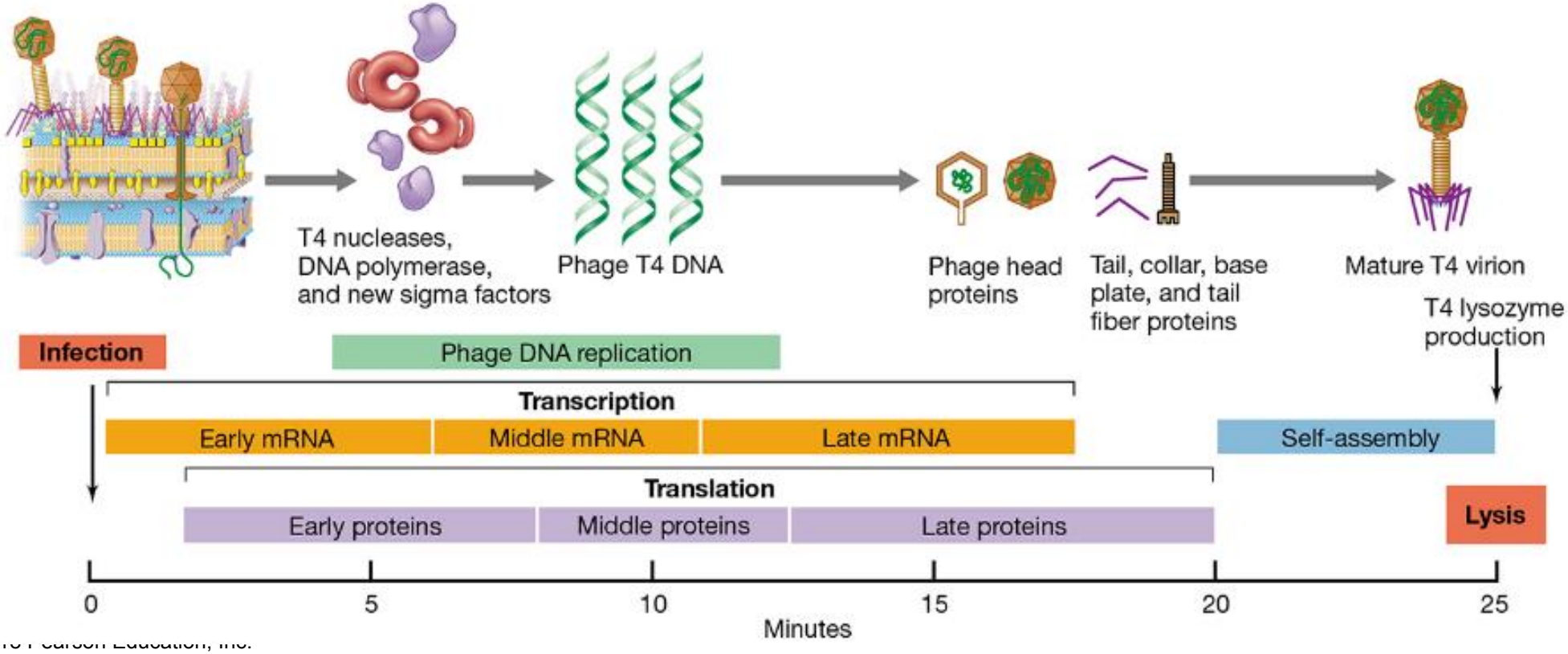


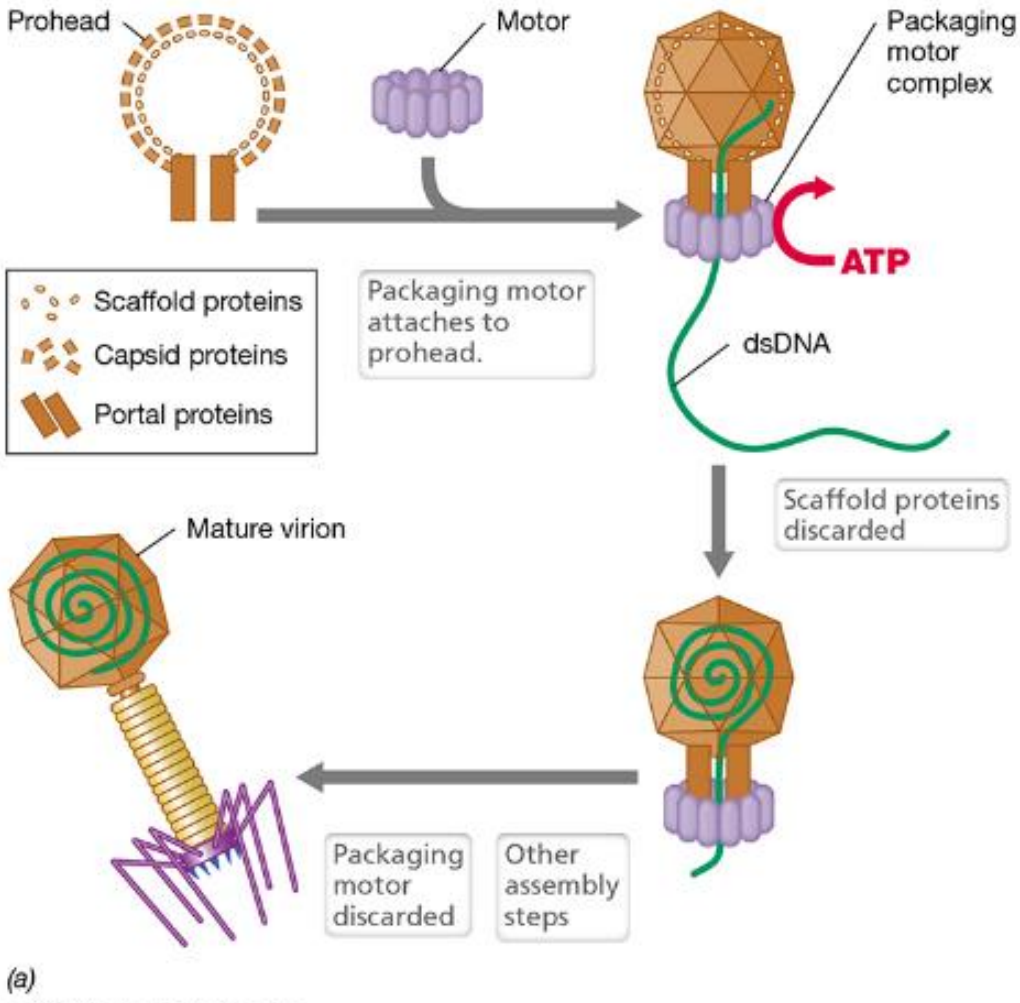
Replication of Bacteriophage T4

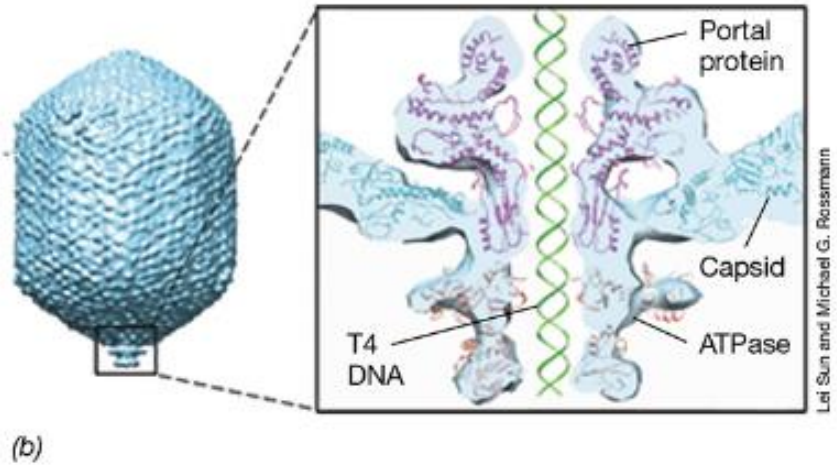
- Genome replication
  - many different schemes for genome replication
  - Small DNA viruses use cell's DNA polymerase.
  - More complex DNA viruses (*e.g.,* T4) encode their own polymerases.
    - T4 also encodes primases, helicases, and 8-protein DNA replisome complex

Replication of Bacteriophage T4

- Transcription and translation
  - Virion synthesis takes ~30 minutes and ends in release of new virions from lysed cell.
  - T4 genome can be divided into three parts: early, middle, and late proteins.







Packaging of DNA into a T4 phage head.

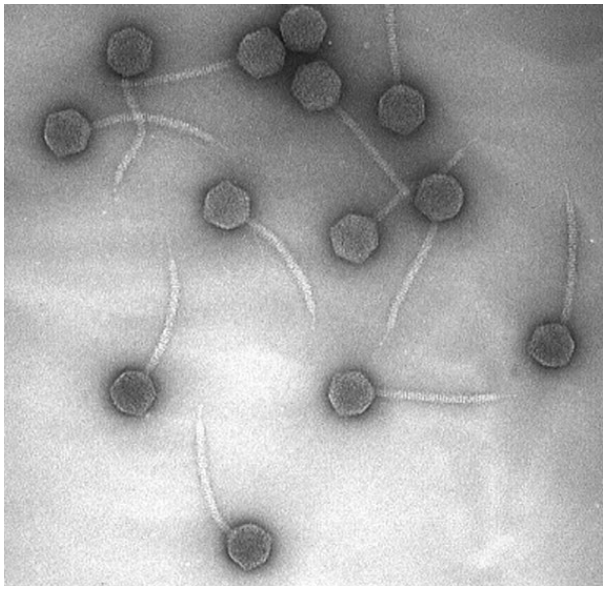
Figure 8.15

Temperate Bacteriophages and Lysogeny

- Viral life cycles
  - Virulent: Viruses always lyse and kill host after infection.
  - Temperate: Viruses replicate their genomes in tandem with host genome and without killing host, establishing long-term, stable relationship.
    - can be lytic/virulent or can enter lysogeny: most viral genes are not transcribed, viral genome is replicated with host chromosome and passed to daughter cells
    - lysogen: host cell that harbors temperate virus
    - can result in *lysogenic conversion* with new properties (*e.g.,* virulence in pathogens)

8.7 Temperate Bacteriophages and Lysogeny

- Replication cycle of a temperate phage
  - examples: lambda phage (λ phage) (linear, dsDNA virus with head and tail)
- In lysogeny, genome is either integrated into bacterial chromosome (lambda) or exists as a plasmid (P1).
- Prophage: viral DNA lysogeny maintained by phage-encoded *repressor protein*
  - Inactivation of repressor induces lytic stage.



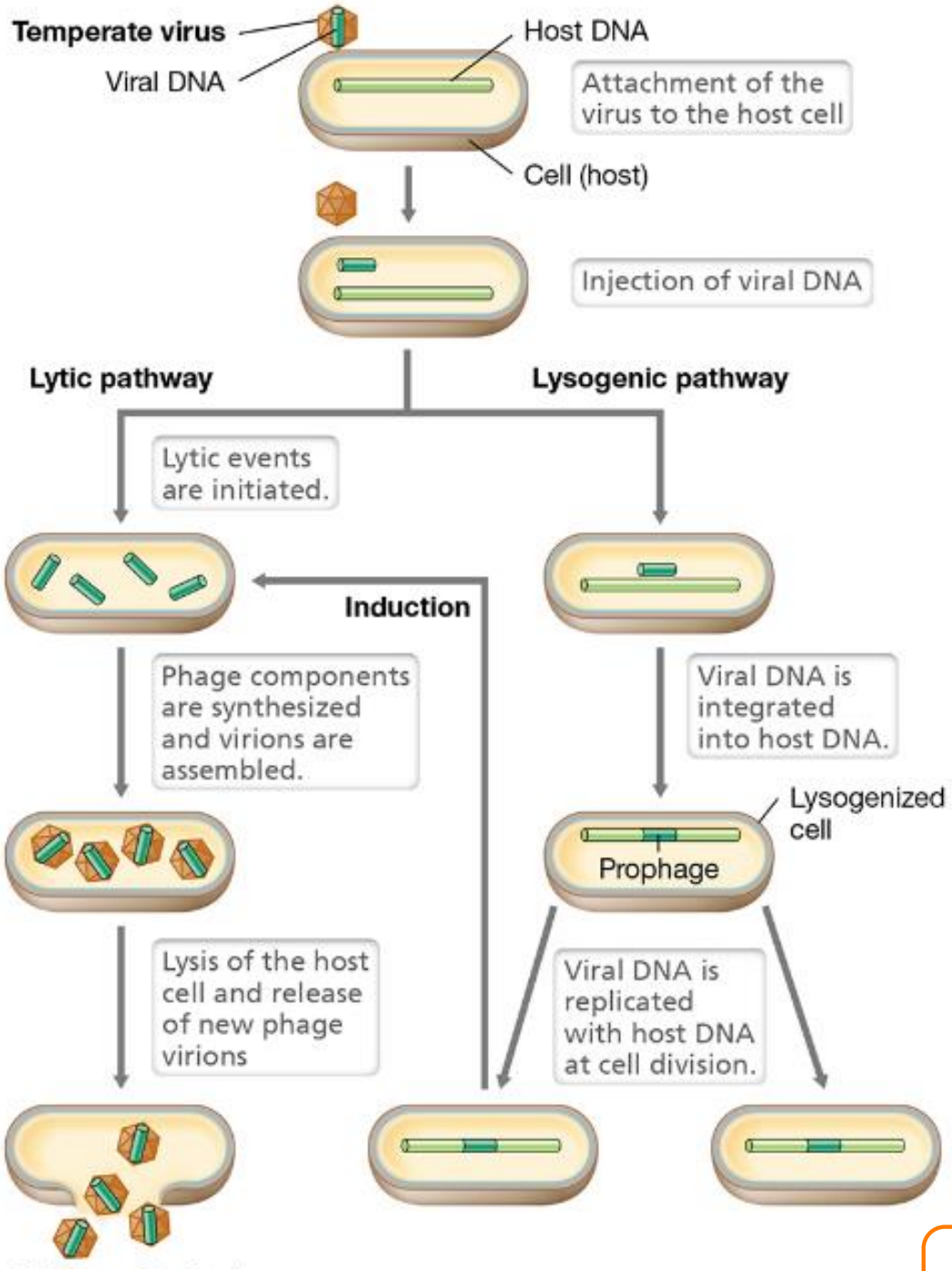


Figure 8.16

Temperate Bacteriophages and Lysogeny

- Lysis or lysogeny: regulation of the lambda lifestyle
  - Key elements are two repressor proteins.
    - the *lambda repressor*: causes repression of lambda lytic events
    - *cro* repressor: controls activation of lytic events
  - First repressor to accumulate controls infection outcome.

8.8 An Overview of Animal Virus Infection

- Major tenets (capsid and DNA/RNA genome, infection and takeover of host, assembly and release) universal
- Classified by genomes
- Most human viral diseases are caused by RNA viruses.
- Two key differences
  - Entire virion enters the animal cell.
  - Eukaryotic nucleus is the site of replication for many animal viruses.

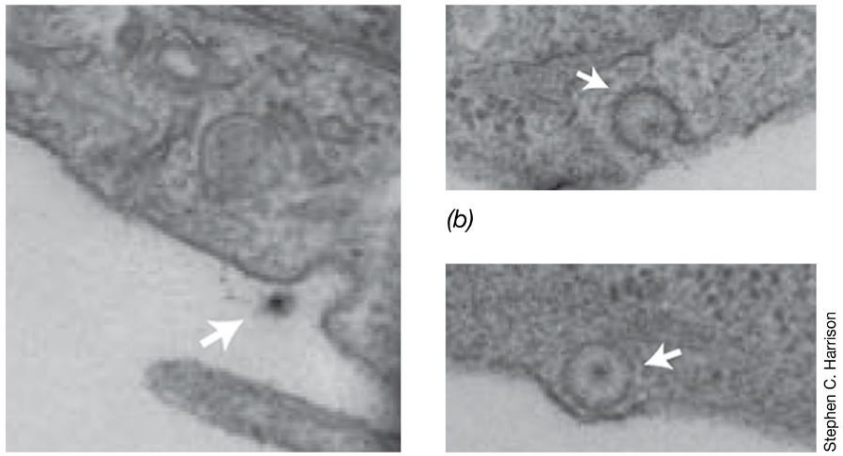
TABLE 8.2 Representative viral diseases of humans

Disease	Virus	Genome DNA or RNA[a]	Size[b]
Cold sores/genital herpes	Herpes simplex	dsDNA	152,000
Smallpox	Variola major	dsDNA	190,000
Polio	Poliovirus	ssRNA (+)	7,500
Rabies	Rabies virus	ssRNA (–)	12,000
Influenza	Influenza A virus	ssRNA (–)	13,600
Measles	Measles virus	ssRNA (–)	15,900
Ebola hemorrhagic fever	Ebola virus	ssRNA (–)	19,000
Severe acute respiratory syndrome (SARS)	SARS virus	ssRNA (+)	29,800
Infant diarrhea	Rotavirus	dsRNA	18,600
Acquired immunodeficiency syndrome (AIDS)	Human immunodeficiency virus (HIV)	ssRNA/dsDNA (a retrovirus) (+)	9,700

[a]ss, single-stranded; ds, double-stranded. +, plus-strand virus; –, negative-strand virus (Section 8.1).
[b]In bases (ss genomes) or base pairs (ds genomes). These viral genomes have been sequenced and thus their lengths are known precisely. However, the sequence and length often vary slightly among different isolates of the same virus. Hence, the genome sizes listed here have been rounded off in all cases.

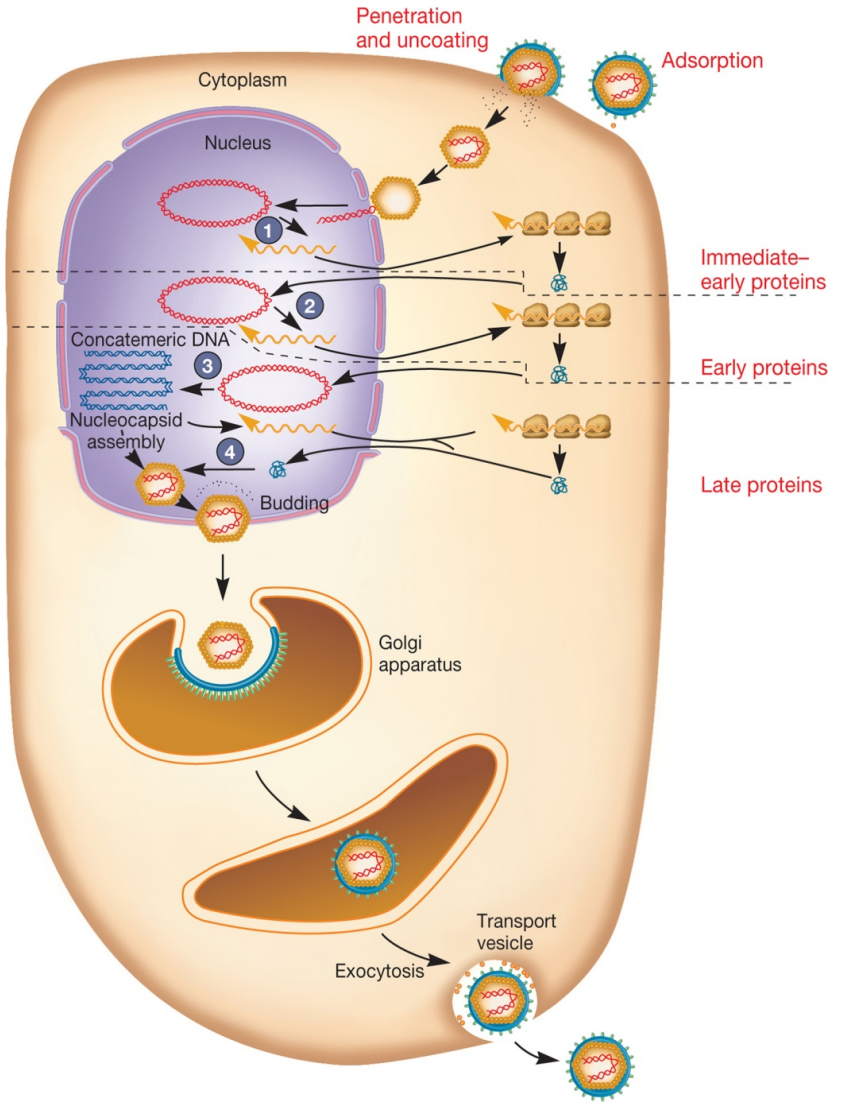
An Overview of Animal Virus Infection

- Viral infection of animal cells
  - bind specific host cell receptors, typically used for cell-cell contact or immune function
  - Different tissues and organs express different cell surface proteins.
    - Often viruses only infect certain tissues.



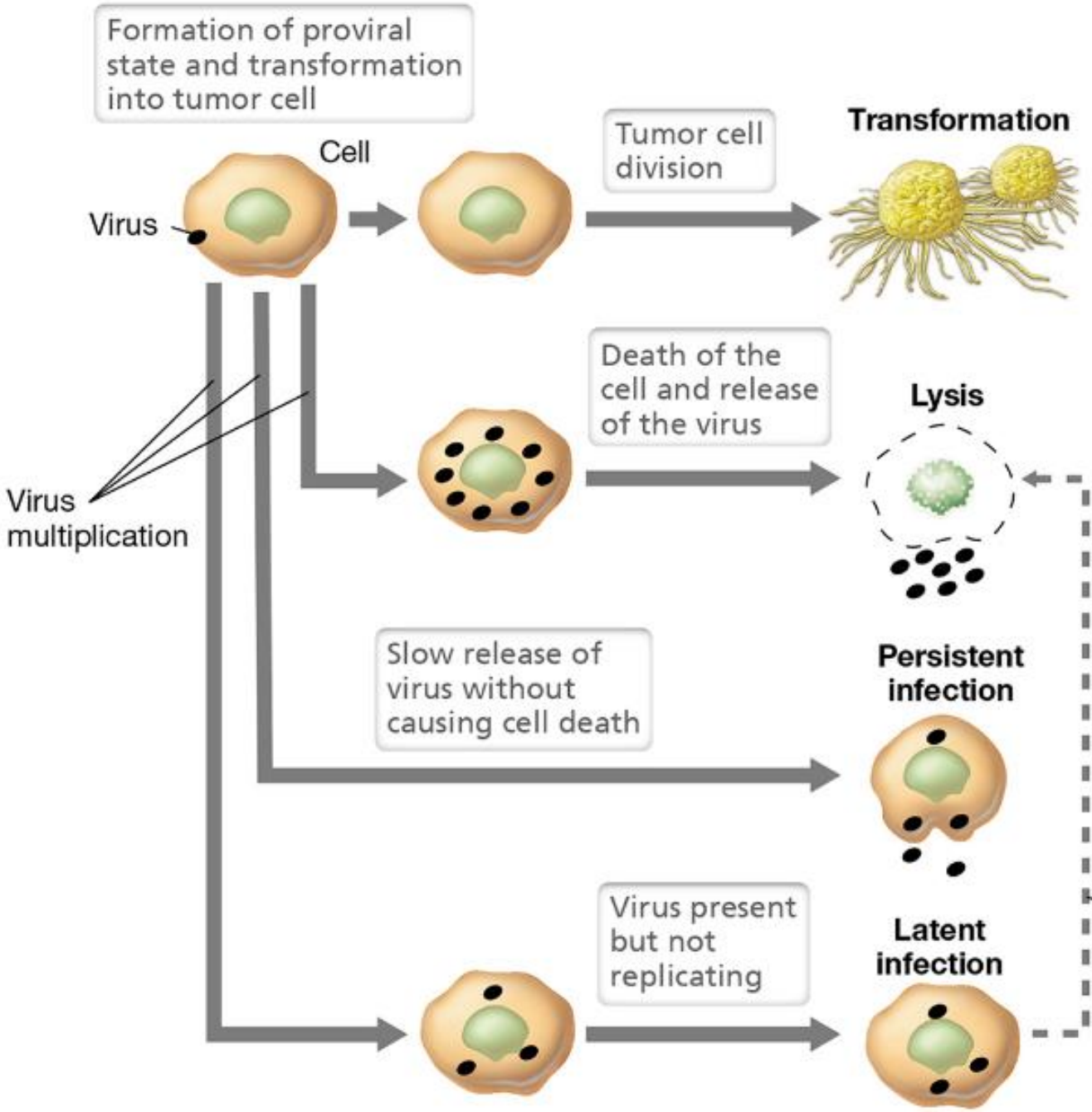
An Overview of Animal Virus Infection

- Viral infection of animal cells
  - Uncoating occurs at cytoplasmic membrane or cytoplasm.
  - Viral DNA genomes enter nucleus, most viral RNA is converted to DNA within nucleocapsid.
    - bind specific host cell receptors, typically used for cell-cell contact or immune function



An Overview of Animal Virus Infection

- Virion assembly and infection outcomes
  - *Virulent infection:* lysis of host cell, most common
  - *Latent infection:* Viral DNA exists in host genome and virions are not produced; host cell is unharmed unless/ until virulence is triggered.
  - *Persistent infections:* Release of virions from host cell by budding does not result in cell lysis.
    - Infected cell remains alive and continues to produce virus
  - *Transformation:* conversion of normal cell into tumor cell



"Oncovirus"
- HPV, HBV

Non-enveloped
Parvovirus

Measles, HCytoM

HSV-1, VSV
(Herpes)

Replication Cycles of Bacteriophage vs. Animal Viruses

Stage	Bacteriophage	Animal Viruses
Attachment	Attach to cell wall structures	Attachment sites are plasma membrane proteins and glycoproteins
Penetration	Viral DNA (RNA) injected into host cell	Capsid enters by endocytosis or fusion
Uncoating	Not required	Enzymatic removal of capsid proteins
Synthesis & Assembly	In cytoplasm	In nucleus or cytoplasm depending on the virus
Chronic infection	Lysogeny	Latency; persistent; cancer
Release	Host cell lysed	Enveloped viruses bud out; non-enveloped viruses rupture plasma membrane