VIRUSES

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VIRUSES AND VIROLOGY

- Viruses are **genetic elements** (or particle) containing either **DNA or RNA** that replicates in live cells **(host)** but is characterized by having an extracellular state → Not regarded as cell
- For multiplication, viruses must enter live cell in which they can replicate, a process called" infection" → **obligate intracellular parasite**
- Extremely small (0.02 - 0.3 µm)
- Enteric virus: Some are able to cause **enteric** disease through contaminated food consumption
  - Hepatitis
  - A Norwalk-like or Norovirus
  - Poliovirus
  - Adenovirus
  - Echo virus Coxsackie virus

GENERAL PROPERTIES OF VIRUSES

- **A virion**:
  - The extracellular form of a virus and contains either RNA or DNA genome
  - The virus genome is introduced into a new host cell by "infection". The infected virus redirects the host metabolism to support virus replication.
- All viruses use host cell's translation machinery, and so regardless of the genome structure of the virus, mRNA must be generated that can be translated on the host cell ribosome (DNA → RNA → protein).
- Viruses are classified on the basis of the
  - Hosts they infect: animal, plant, bacteria (bacteriophage)
  - Type of genomes : DNA, RNA

GENERAL PROPERTIES OF VIRUSES

The genomes of viruses can be either DNA or RNA, and some use both as their genomic material at different stages in their replication cycle.

- Retrovirus:
  - Animal virus
  - Contain **RNA genome** ("retro" means backward).
  - Replicate through reverse transcription using the enzyme reverse transcriptase (synthesis DNA from RNA template)

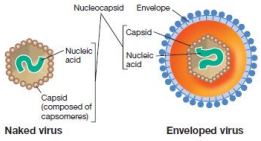
GENERAL PROPERTIES OF VIRUSES

Virus	Host	DNA or RNA	Single- or double-stranded	Viral genome: Structure	Viral genome: Number of molecules	Size (bases or base pairs)[a]
H-1 parvovirus	Animals	DNA	Single-stranded	Linear	1	5,176
ϕX174	*Bacteria*	DNA	Single-stranded	Circular	1	5,386
Simian virus 40 (SV40)	Animals	DNA	Double-stranded	Circular	1	5,243
Poliovirus	Animals	RNA	Single-stranded	Linear	1	7,433
Cauliflower mosaic virus	Plants	DNA	Double-stranded	Circular	1	8,025
Cowpea mosaic virus	Plants	RNA	Single-stranded	Linear	2 different	9,370 (total)
Reovirus type 3	Animals	RNA	Double-stranded	Linear	10 different	23,549 (total)
Bacteriophage lambda	*Bacteria*	DNA	Double-stranded	Linear	1	48,514[b]
Herpes simplex virus type I	Animals	DNA	Double-stranded	Linear	1	152,260
Bacteriophage T4	*Bacteria*	DNA	Double-stranded	Linear	1	168,903
Human cytomegalovirus	Animals	DNA	Double-stranded	Linear	1	229,351

The size is in bases or base pairs depending on whether the virus is single- or double-stranded. The sizes of the viral genomes chosen for this table are known accurately because they have been sequenced. However, this accuracy can be misleading because only a particular strain or isolate of a virus was sequenced. Therefore, the sequence and exact number of bases for other isolates may be slightly different. No attempt has been made to choose the largest and smallest viruses known, but rather to give a fairly representative sampling of the sizes and structures of the genomes of viruses containing both single- and double-stranded RNA and DNA.
bThis includes single-stranded extensions of 12 nucleotides at either end of the linear form of the DNA (see Section 9.10).

STRUCTURE OF THE VIRION

- **Naked virus**
  - Only nucleic acid and protein are present
  - With the nucleic acid on the inside; the whole unit is called the nucleocapsid (Figure).
- **Enveloped virus**
  - One or more lipoprotein layers surround the nucleocapsid is called "envelope" and this determines the specificity of virus infection.
  - Most infect animal cells.



Comparison of naked and enveloped virus particles.

NATURE OF THE VIRION

- **Viral enzymes**: Although viruses are metabolically inert, one or more key enzymes
  - Lysozyme
  - Reverse transcriptase
  - RNA polymerase
  - Neuraminadase

GROWTH AND QUANTIFICATION

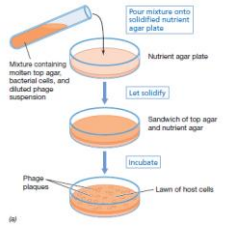
THE VIRUS HOST

- Viruses can replicate only in certain types of living cells or in whole organisms (bacteria, plants, animal).
- **Bacterial viruses (bacteriophages)** have proved useful as model systems because the host cells are easy to grow and manipulate in culture.
- Many animal and plant viruses also can be grown in cultured cells.

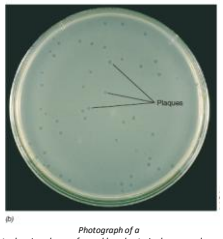
QUANTIFICATION OF VIRUSES

- Plaque: When a virion initiate an infection on a layer of host cell growing on a flat surface, a zone of lysis may be seen as a clear area in the layer of growing host cells.
- It is assumed that each plaque originated from the replication of a single virion
- Plaque forming unit (PFU): tells us the titer or number of virus infectious unit present in virus sample permits the isolation of pure virus strain.
- Comparable to Koch's development of solid media (pure culture)
- Although it requires only a single virion to initiate an infectious cycle, not all virions are equally infectious. The plaque assay is one of the most accurate ways to measure virus infectivity.
- By counting the number of pfu/ml of fluid, a measure of virus quantity, called titer, can be obtained (Figure).

GROWTH AND QUANTIFICATION



A dilution of a suspension containing the virus is mixed in a small amount of melted agar with the sensitive host bacteria.



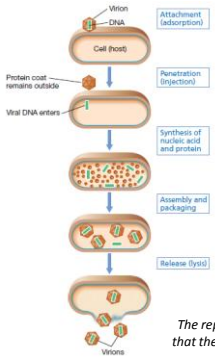
Photograph of a plate showing plaques formed by a bacteriophage on a lawn of sensitive bacteria. The plaques shown are about 1–2 mm in diameter.

VIRAL REPLICATION

GENERAL FEATURES OF VIRUS REPLICATION
REPLICATION CYCLE

- The virus life cycle can be divided into five stages:
  1. attachment (adsorption)
  2. penetration (injection)
  3. protein and nucleic acid synthesis
  4. assembly and packaging
  5. virion release (Figure).

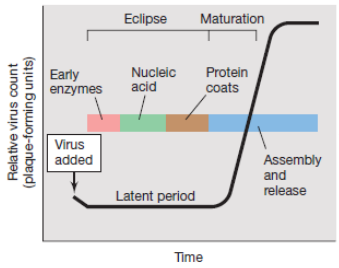
VIRAL REPLICATION



The replication cycle of a bacterial virus. Note that the viruses and cell are not drawn to scale.

VIRAL REPLICATION

ONE STEP GROWTH CURVE



This graph displays the results of a single round of viral replication in a population of cells. Following adsorption, the infectivity of the virus particles disappears, a phenomenon called *eclipse. This is due to the uncoating of* the virus particles. During the latent period, viral nucleic acid replicates and protein synthesis occurs. The maturation period, when virus nucleic acid and protein are assembled into mature virus particles, follows. Finally, the virions are released, either with or without cell lysis.

VIRAL REPLICATION

Latent period

- Eclipse
  - Infectious particles can not be detected in the culture medium
  - Uncoating of virus particle
  - Replication of viral nucleic acid and protein occurs
- Maturation
  - Package of newly synthesized nucleic acid into protein coat
  - Titer rises dramatically
  - However, new virus particles can not be detected in the culture medium

Assembly and release

- The number of virions released, called burst size, varies with the particular virus and particular host cell and can range from a few to a few thousand.
- Duration of replication time
  - Bacteriophage: 20-60 min
  - Animal virus: 8-40 h

VIRAL REPLICATION

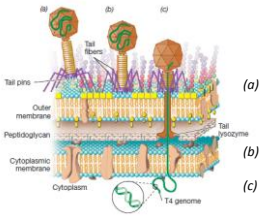
ATTACHMENT

- Attachment of virion to host cell is highly specific
  - Requires complementary receptors on the surface of a susceptible host and its infecting virus
  - Receptors on host cell carry out normal functions for cell (e.g., uptake proteins, cell to cell interaction)
  - Receptors include proteins, carbohydrates, glycoproteins, lipids, lipoproteins, or complexes
- The attachment of a virus to its host cell results in changes to both virus and cell surface that facilitate penetration
- Permissive cell: host cell that allows the complete replication cycle of a virus to occur
  - Absence of receptor on host → no adsorption → no infection
  - Mutation of the host receptor → host become resistant to viral infection
  - However, virus can mutate themselves to the adjust the mutated host
  - Some virus have more than one receptor
  - Host range of virus: determined by availability of suitable receptors that virus can recognize

VIRAL REPLICATION

PENETRATION

- Bacteriophage T4: virus of E. coli: One of the most complex penetration mechanisms (Figure 9.10)
  - Virions attach to cells via tail fibers that interact with core polysaccharides on E. coli cell envelope
  - Tail fibers retract and tail core makes contact with E. coli cell wall
  - Lysozyme-like enzyme forms small pore in peptidoglycan
  - Tail sheath contracts and viral DNA passes into cytoplasm



(a) Attachment of a T4 virion to the cell wall by the long tail fibers interacting with core lipopolysaccharide.
(b) (b) Contact of cell wall by the tail pins.
(c) Contraction of the tail sheath and injection of the T4 genome.

DEFENSE MECHANISM

- Many eukaryotes possess defense mechanisms to diminish viral infections
  - For example, immune defense mechanisms, RNA interference
- Prokaryotes also possess antiviral mechanisms
  - CRISPR (clustered regularly interspaced short palindromic repeat) : Similar to RNA interference (RNAi)
  - Restriction / Modification system
- Restriction modification systems
  - DNA destruction system; only effective against double-stranded DNA viruses
  - Restriction enzymes (restriction endonucleases) cleave DNA at specific sequences
  - Modification of host's own DNA at restriction enzyme recognition sites prevents cleavage of own DNA

DEFENSE MECHANISM

- Viral mechanisms to evade bacterial restriction systems
  - Chemical modification of viral DNA (glycosylation or methylation)
  - Production of proteins that inhibit host cell restriction system
- The gene(s) involved in R/M system is usually located in bacterial plasmid DNA.

DEFENSE MECHANISM

PRODUCTION OF VIRAL NUCLEIC ACID AND PROTEIN

Viral Proteins

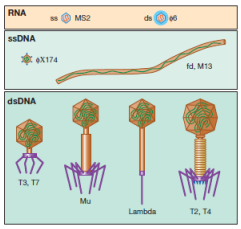
Production follows synthesis of viral mRNA

- Early proteins
  - Synthesized soon after infection
  - Necessary for replication of virus nucleic acid
  - Typically act catalytically
  - Synthesized in smaller amounts
- Late proteins
  - Synthesized later
  - Include proteins of virus coat
  - Typically structural components
  - Synthesized in larger amounts

OVERVIEW OF BACTERIAL VIRUSES

- Phagein: to devour
- Bacteriophages are very diverse (Figure)
- Best-studied bacteriophages infect enteric bacteria
  - Examples of hosts: E. coli, Salmonella enterica
- Most phages contain dsDNA genomes
- Most are naked, but some possess lipid envelopes
- They are structurally complex, containing heads, tails, and other components

OVERVIEW OF BACTERIAL VIRUSES



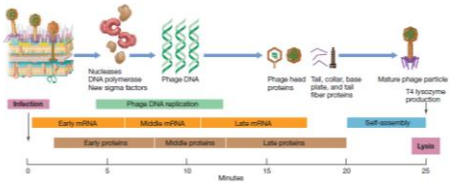
Schematic representations of the main types of bacterial viruses. Sizes are to approximate scale. The nucleocapsid of 6 is surrounded by a membrane.

- Viral Life Cycles Virulent mode:
  - viruses lyse host cells after infection
  - Temperate mode: viruses replicate their genomes in tandem with host genome and without killing host. Virus can also be lytic

OVERVIEW OF BACTERIAL VIRUSES

VIRULENT BACTERIOPHAGES

- First viruses studied in detail contained linear, dsDNA genomes that infect enteric bacteria
- Always kill host cell



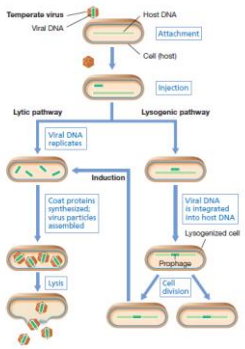
Time course of events in phage T4 infection.

OVERVIEW OF BACTERIAL VIRUSES

TEMPERATE BACTERIOPHAGES, LAMBDA, AND P1

- Temperate viruses: can undergo a stable genetic relationship within the host (Figure)
  - But can also kill cells through lytic cycle
- Two alternative pathways
  - Lysogenic pathway
  - Lytic pathway
- Lysogeny: state where most virus genes are not expressed and virus genome (prophage) is replicated in synchrony with host chromosome
- Lysogen: a bacterium containing a prophage (phage genome integrated in host chromosome)
- Prophage induction: Under certain (UV, mitomycin C, N-nitrosamine) conditions lysogenic viruses may revert to the lytic pathway and begin to produce virions
- Prophages are important agent in 'horizontal gene transfer'

OVERVIEW OF BACTERIAL VIRUSES



The consequences of infection by a temperate bacteriophage. The alternatives upon infection are replication and release of mature virus (lysis) or lysogeny, often by integration of the virus DNA into the host DNA, as shown here. The lysogen can be induced to produce mature virus and lyse.

OVERVIEW OF BACTERIAL VIRUSES

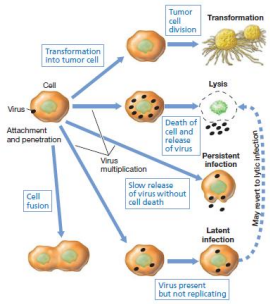
Significance of Lysogeny

- Ecological importance
  - Most bacteria isolated from nature are lysogens for one or more bacteriophages
- Confer new genetic properties on bacterial host cell
  - Some pathogenic bacteria whose virulence depends on the lysogenic bacteriophage they harbor

Application of bacteriophages in food microbiology

- Eradication of harmful bacterial foods (phage therapy)
  - Bacillus cereus in fermented soybean
  - Lactic acid bacteria in kimchi to extend shelf-life

Animal Viruses



- Can result in lytic infection, persistent infection, or latent infection
- Some viruses can transform the host cell

Possible effects that animal viruses may have on cells they infect. Most animal viruses are lytic, and only very few are known to cause cancer.

Subiral Entities : Virus-like agents

- **Viroids are small, circular ss RNA molecules**
- Encode no proteins
- Consist of protein but have no nucleic acid.
- It is infectious and cause bovine spongiform encephalopathy (BSE or mad cow disease), chronic wasting disease (elk and deer), kuru and Creutzfeldt-Jakob Disease (CJD) in humans.
- Linked to improper feeding practices in which protein supplements of their own species are formulated.
- Destruction of brain or related nerve tissue by the self-propagating accumulation of aggregated prion proteins. Cause transmissible spongiform encephalopathies (TSEs)


VIRUSES
THANK YOU
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