PowerPoint® Lecture Presentations

CHAPTER 11

Viral Genomics and Diversity

Schema Micro2

Les	Hoofdstuk	Paragraaf
1	7	7.1, 7.2, 7.3, 7.8
2	7	7.5, 7.6, 7.7
3	7	7.9, 7.10, 7.11
4	7	7.12, 7.13, 7.14, 7.15
5	5	5.1, 5.2, 5.3, 5.4, 5.5, 5.6
6	5 en 11	5.7, 5.8, 11.1, 11.2
7	11	11.6, 11.7, 11.8 (MS2 niet)
8	11	11.9, 11.11,
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12	25	25.6, 25.7, 25.8
13	28 en 8	28.10, 28.11, 28.12, 8.10
14	Oefententamen	Alles

NB: Hfdstnrs niet accuraat

I. Viral Genomes and Evolution

- 11.1 Size and Structure of Viral Genomes
- 11.2 Viral Taxonomy and Phylogeny

11.1 Size and Structure of Viral Genomes

- Viral genome size (Figure 11.1)
  - vary ~1000-fold from smallest to largest
  - smallest Circovirus: 1.75-kilobase single strand
  - largest Pandoravirus: 2.5-megabase pairs
    - infects some marine amoebae
    - larger than some bacteria
- RNA genomes
  - typically smaller than DNA viruses

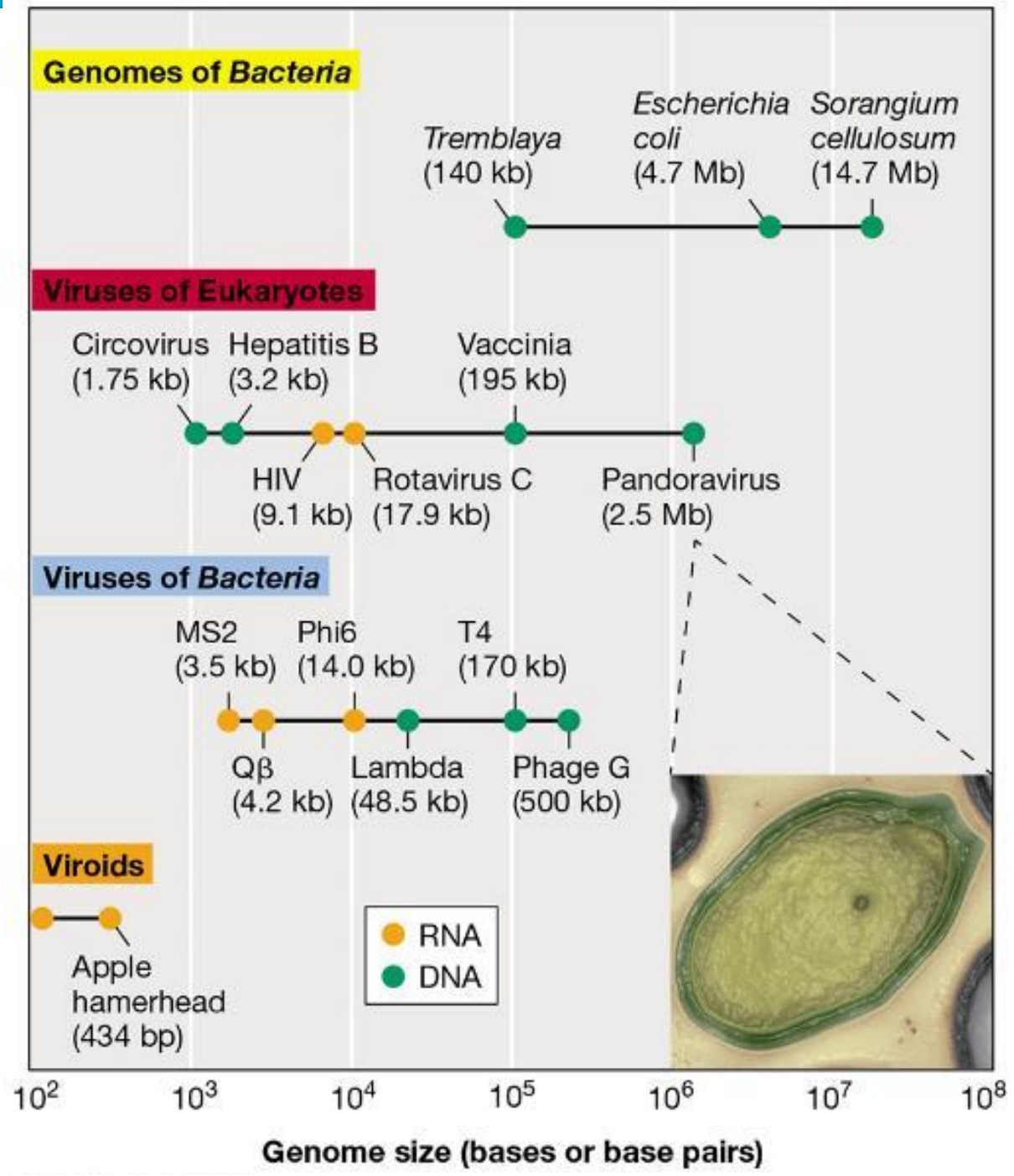

Genomes of Bacteria
Tremblaya (140 kb)
Escherichia coli (4.7 Mb)
Sorangium cellulosum (14.7 Mb)
Viruses of Eukaryotes
Circovirus (1.75 kb)
Hepatitis B (3.2 kb)
Vaccinia (195 kb)
HIV (9.1 kb)
Rotavirus C (17.9 kb)
Pandoravirus (2.5 Mb)
Viruses of Bacteria
MS2 (3.5 kb)
Phi6 (14.0 kb)
T4 (170 kb)
Qβ (4.2 kb)
Lambda (48.5 kb)
Phage G (500 kb)
Viroids
Apple hamerhead (434 bp)
RNA
DNA
10^2
10^3
10^4
10^5
10^6
10^7
10^8
Genome size (bases or base pairs)

Figure 11.1

11.1 Size and Structure of Viral Genomes

- The Baltimore scheme: DNA viruses
  - based on relationship of genome to mRNA, includes seven classes (Figure 11.2)
  - class I: Double-stranded DNA
  - class II: Single-stranded positive- or plus-strand DNA
    - needs replicative form: double-stranded DNA intermediate
    - All but one ssDNA virus are positive-strand viruses.

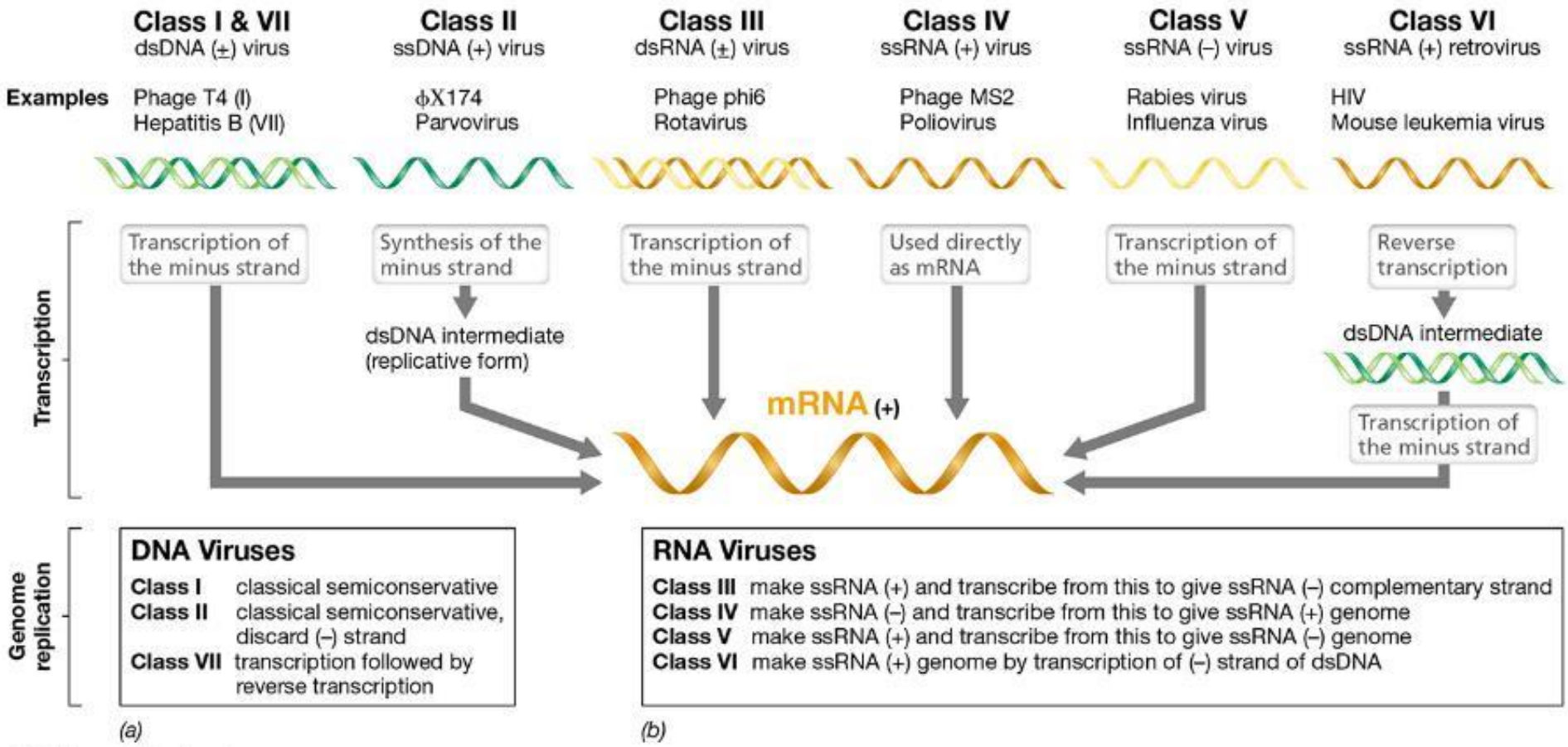


Figure 11.2

11.1 Size and Structure of Viral Genomes

- The Baltimore scheme: RNA viruses
  - RNA viruses must replicate in virion or encode *RNA replicase* (RNA-dependent RNA polymerase).
  - based on relationship of genome to mRNA, includes 7 classes (Figure 11.2)
  - class IV: ss(+) RNA viruses, genome is mRNA
  - class V: ss(–) RNA viruses, RNA replicase makes (+) strand used as mRNA and template for more (–) strand genomes
  - class III: double-stranded RNA, similar replication as class V

11.1 Size and Structure of Viral Genomes

- The Baltimore scheme: RNA viruses
  - class VI (Retroviruses): ss(+) RNA viruses
    - replicate through DNA intermediate
    - *Reverse transcription* copies RNA into DNA, catalyzed by *reverse transcriptase.*
    - example: human immunodeficiency virus (HIV)
  - class VII: ds DNA that replicates through RNA intermediate
    - example: hepatitis B
    - also uses reverse transcriptase

11.1 Size and Structure of Viral Genomes

- Hosts for viruses of each Baltimore class
  - Class I (dsDNA): primarily prokaryotic viruses.
  - Class IV (ss(+)RNA): are primarily eukaryotic viruses.
  - Fungi only infected by classes III and IV
  - Most class I and class V viruses have animal hosts instead of plants.
  - More class II viruses have plant hosts instead of animals.
  - Class VI (Retroviruses) infect only animals.
  - class VII more common in plants than animals

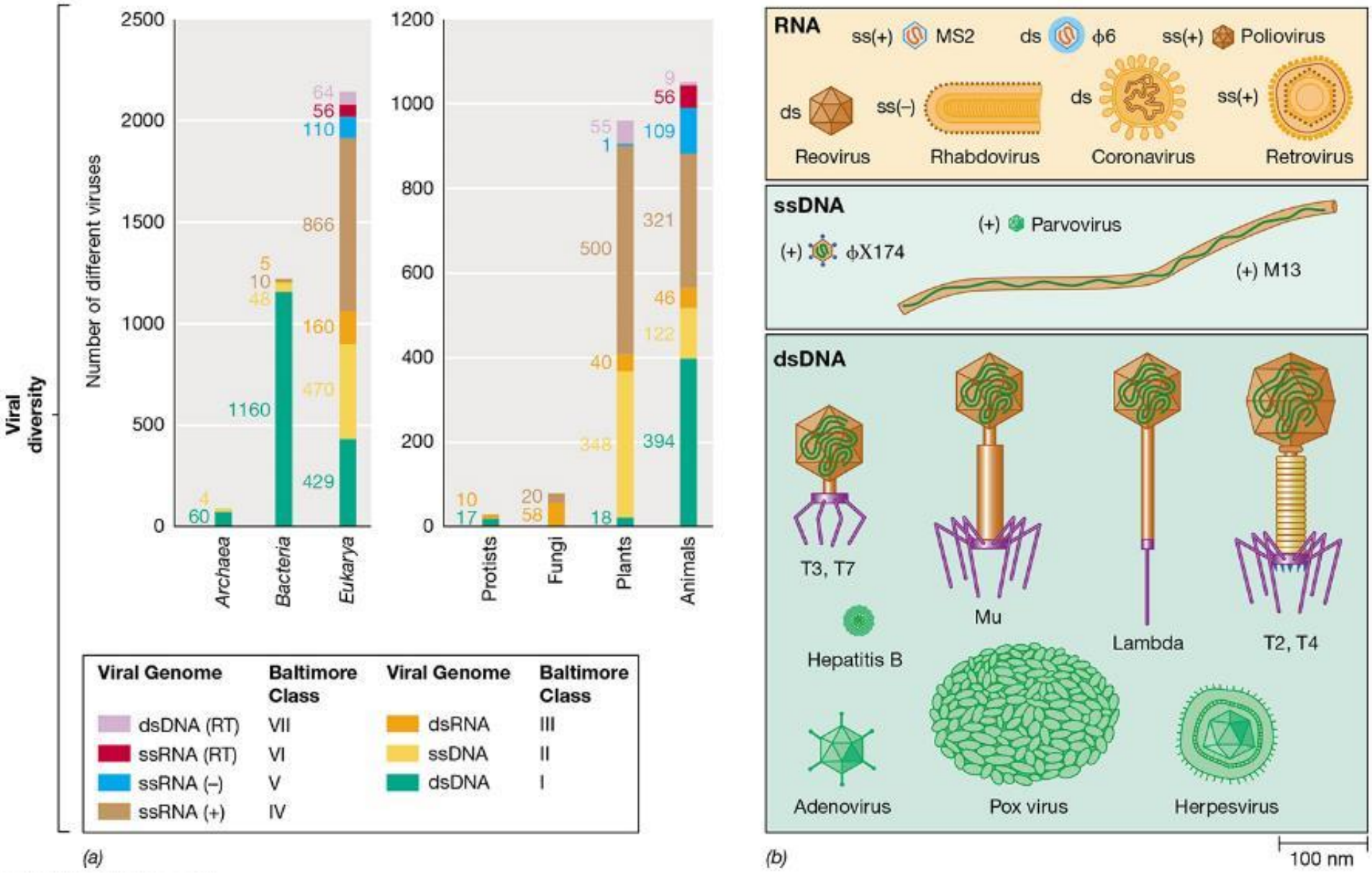


Figure 11.3

11.1 Size and Structure of Viral Genomes

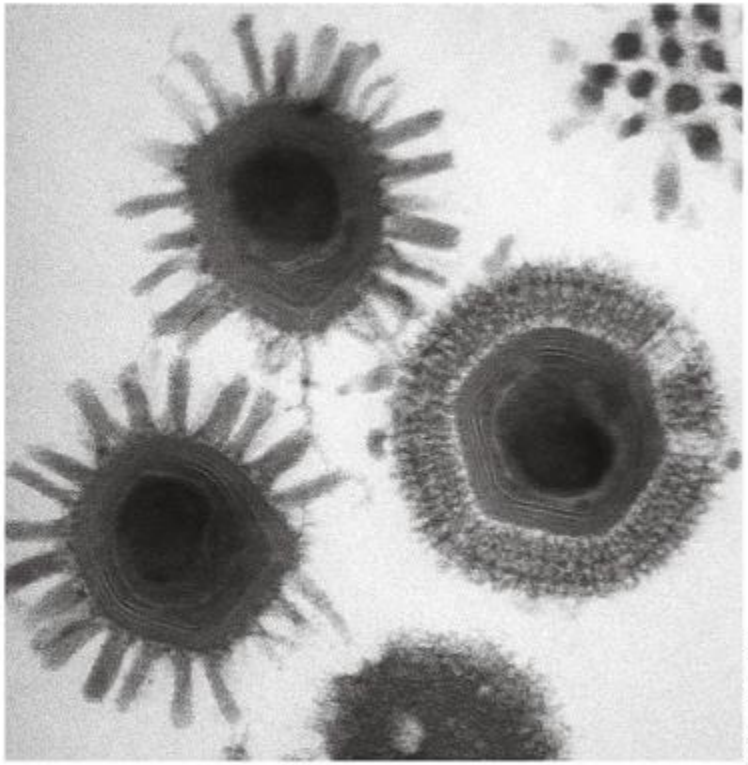
- Viral protein synthesis
  - *early proteins* synthesized soon after infection
    - usually enzymes
    - made in small amounts
    - nucleic acid polymerases, proteins that shut down host transcription and translation
  - *late proteins* synthesized later
    - structural and assembly proteins
    - made in large amounts
  - eventually, new virions assembled and exit by lysis or budding

11.2 Viral Taxonomy and Phylogeny

- Proteomics support an early appearance of viruses.
  - rRNA seq. cannot by used for phylogeny.
  - *proteome* analysis used instead
  - Proteomics suggests viruses originated from ancient cells containing segmented RNA genomes that existed before last universal common ancestor (LUCA).
  - RNA viruses seem to be older than DNA viruses, with dsRNA being oldest of all.

11.2 Viral Taxonomy and Phylogeny

- Viral phylogeny
  - Universal phylogenetic tree constructed from combination of protein sequences and structural features.
  - Most viral genes from nature have no existing homologs, so much of their genomes will be new to biology.
  - Few groups of viruses have trees assembled from sequences of shared/common genes/proteins.
    - example: *nucleocytoplasmic large DNA viruses* (NCLDV): Mimivirus and relatives (Figure 11.5)



Didier Raoult

(a)

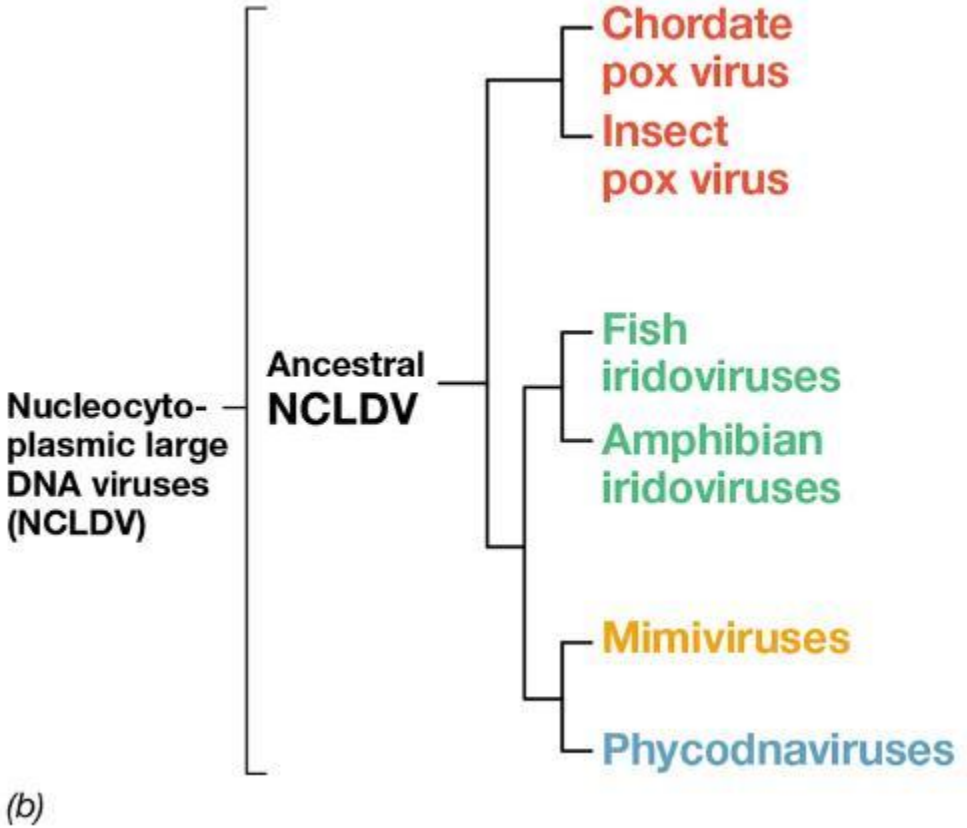


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Figure 11.5

Microbiologie 2: Les 7

II. DNA Viruses

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II. DNA Viruses

- 10.6 Uniquely Replicating DNA Animal Viruses
- 10.7 DNA Tumor Viruses

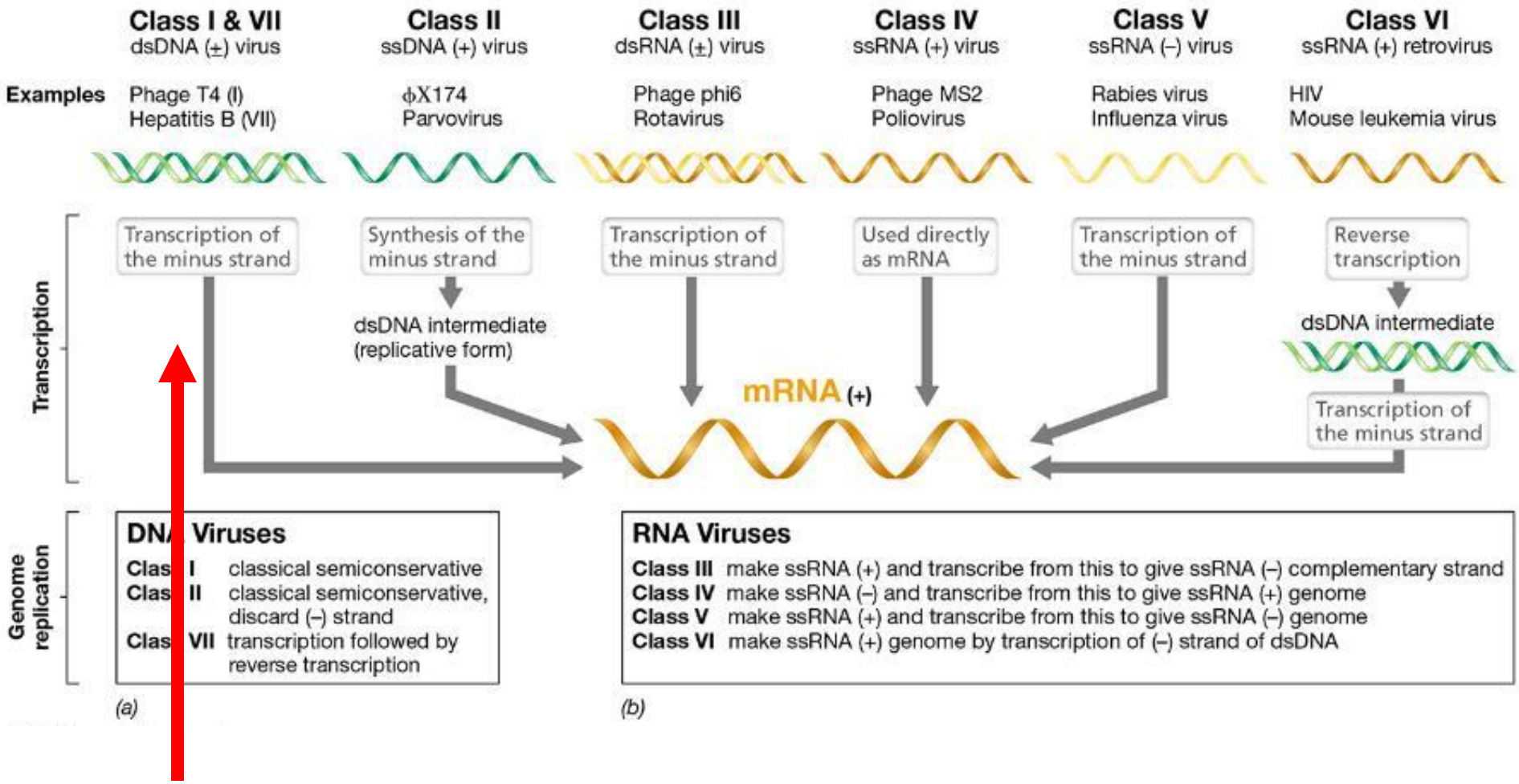


Figure 10.2

11.6 Uniquely Replicating DNA Animal Viruses

- Double-stranded DNA animal viruses that have unusual replication strategies
  - Pox viruses: All replication occurs in cytoplasm.
  - Adenoviruses: DNA replication occurs on both DNA template strands.

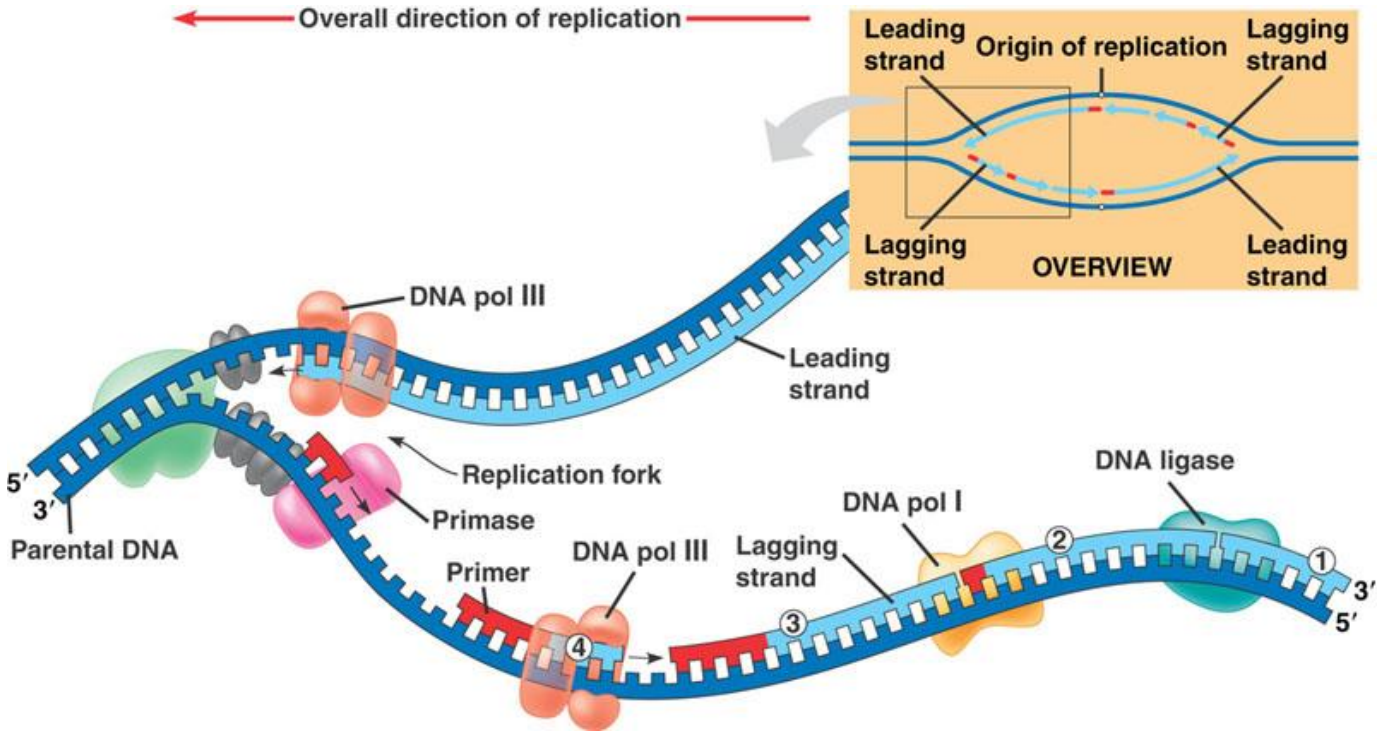
11.6 Uniquely Replicating DNA Animal Viruses

Adenoviruses

- small, naked, icosahedral, double-stranded linear DNA viruses (Figure 11.14*a*)
- mild respiratory infections in humans
- Adenoviral *terminal protein* attaches to 5' end of adenoviral genomic DNA required for genome replication.
- DNA replicates in nucleus.
  - unique because DNA is replication without a lagging strand (Figure ….12)

- virions assembled and released after lysis

Bio3 Flashback



https://www.youtube.com/watch?v=I9ArIJWYZHI

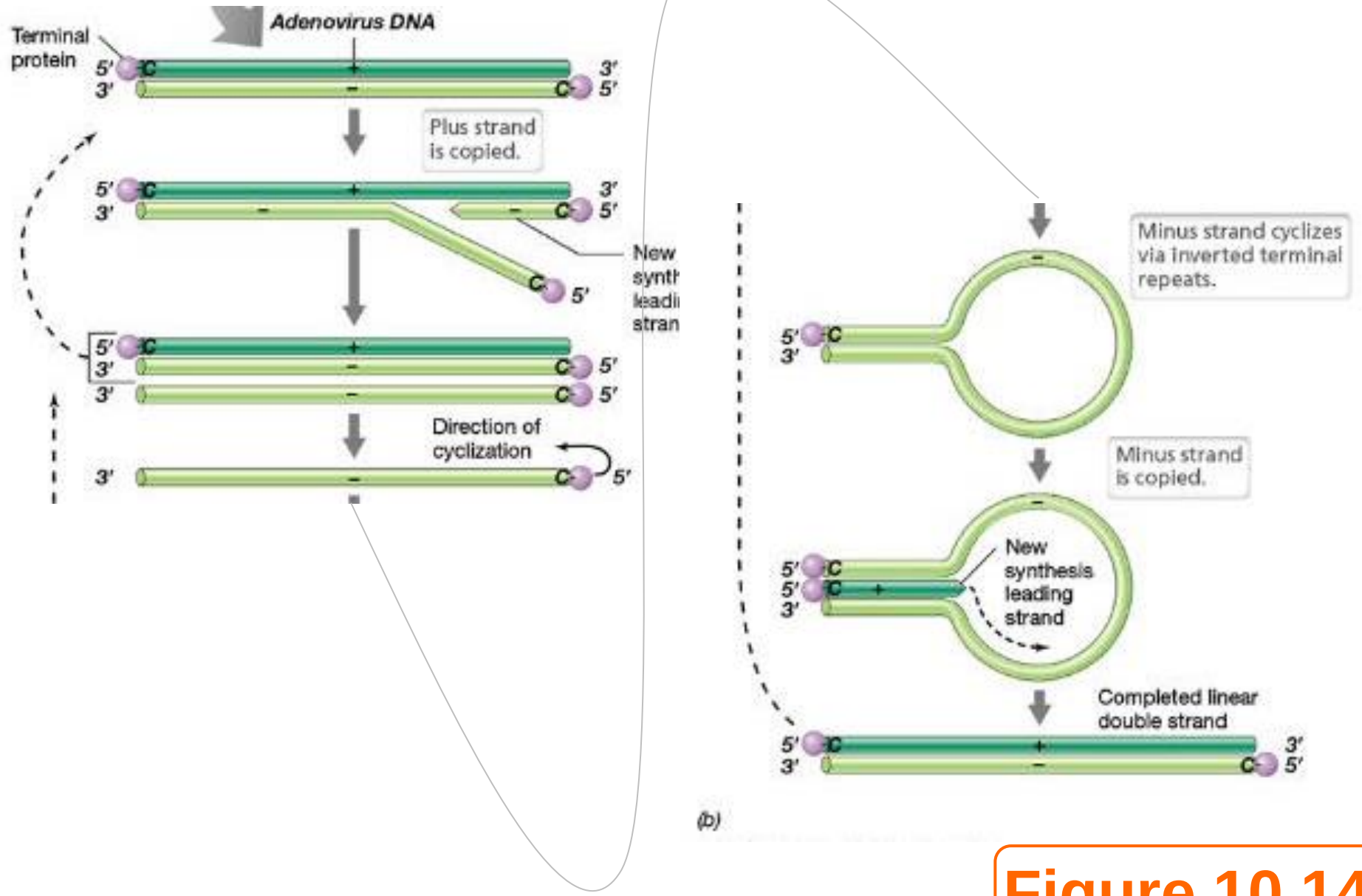


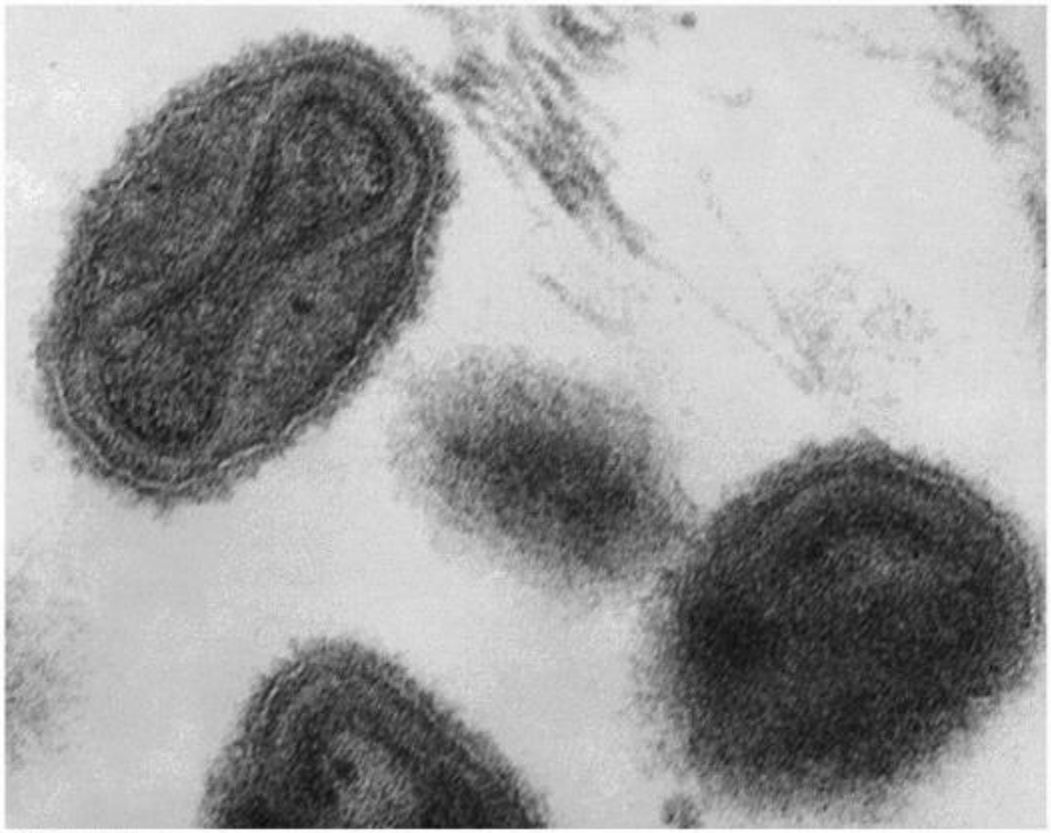
Figure 10.14

11.6 Uniquely Replicating DNA Animal Viruses

Pox viruses

- Smallpox was first to be studied and have a vaccine developed.
- also includes cowpox and vaccinia virus (used as smallpox vaccine and lab model)
- vaccinia
  - Linear dsDNA encoding ~250 genes.
  - Envelopped
  - All replication occurs in cytoplasm.
  - Cell lyses and releases virions.
  - Genetically engineered to make recombinant vaccines (immune response without serious health effects; e.g., influenza, rabies, herpes simplex type 1, hepatitis B)

Linkje: Poxvirus DNA Replication (nih.gov)



CDC/PHIL, Fred Murphy and Sylvia Whitfield

0,35µM lang

Figure 11.16

11.7 DNA Tumor Viruses

- Herpesviruses
  - enveloped dsDNA viruses that cause *e.g.,* cold sores, venereal herpes, chicken pox, shingles
  - An important group causes clinical forms of cancer (*e.g.,* Epstein-Barr virus and Burkitt's lymphoma).
  - able to remain latent for extended periods of time
  - reactivate under stress or weakened immune system

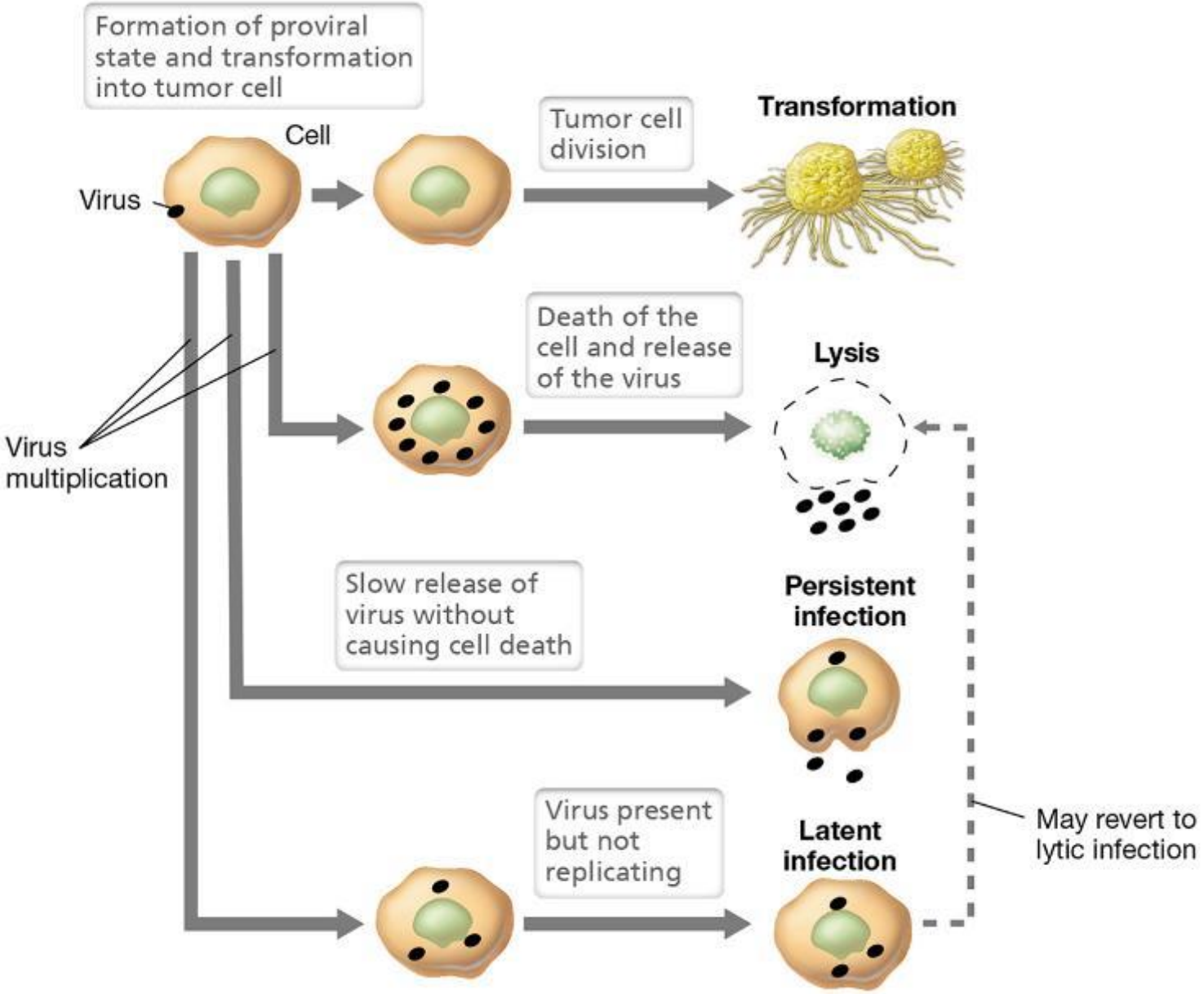
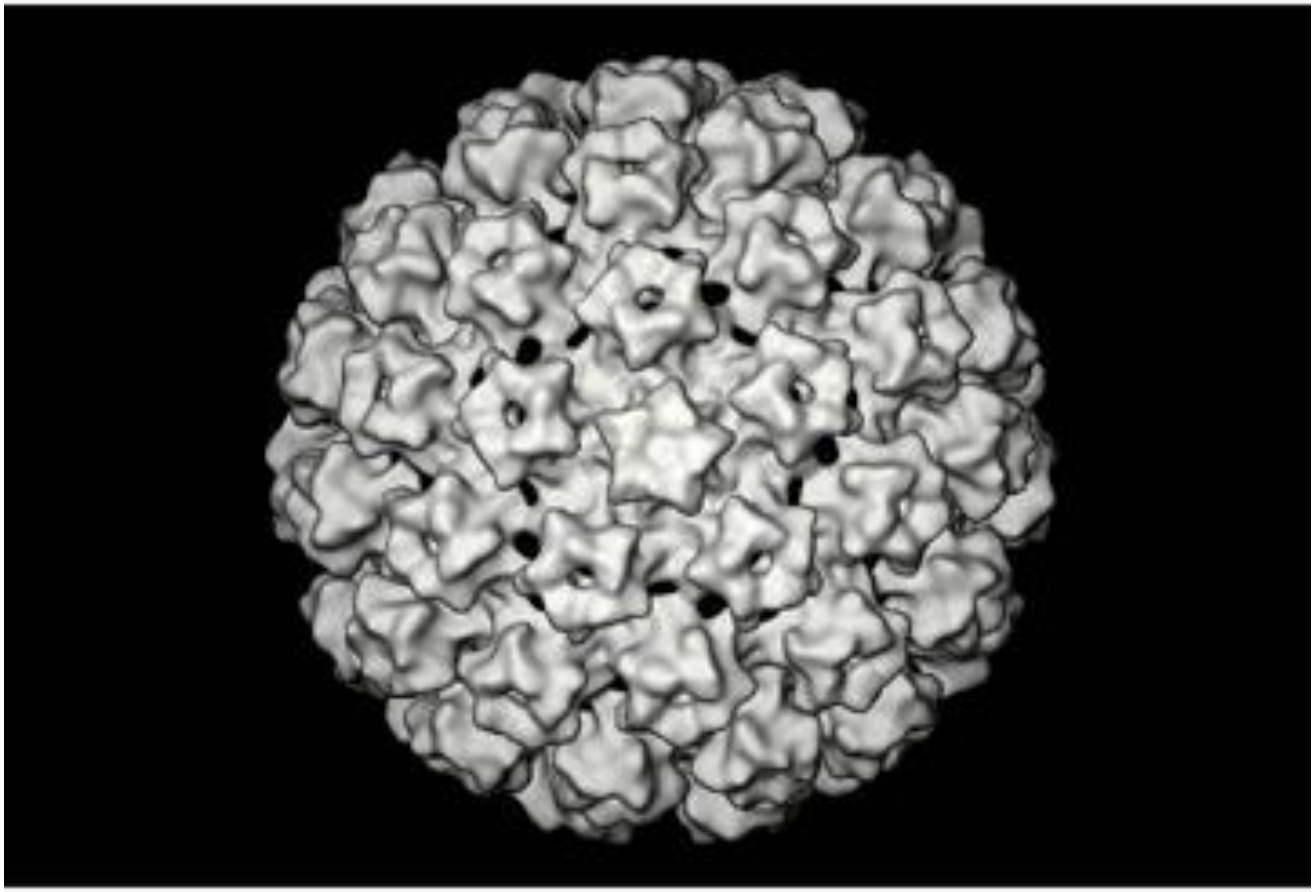


Figure 5.22

dsDNA: HPV (humaan papillomavirus)

- Wratten, baarmoeder-halskanker
- Kunnen passief (latent) of actief voorkomen als episoom.
- Kunnen geïntegreerd voorkomen



Heeft voor replicatie DNA-polymerase nodig van de host, kan daarvoor cel richting celdeling ‘duwen’ => Voorkomt apoptose en geeft telomerase-activiteit.

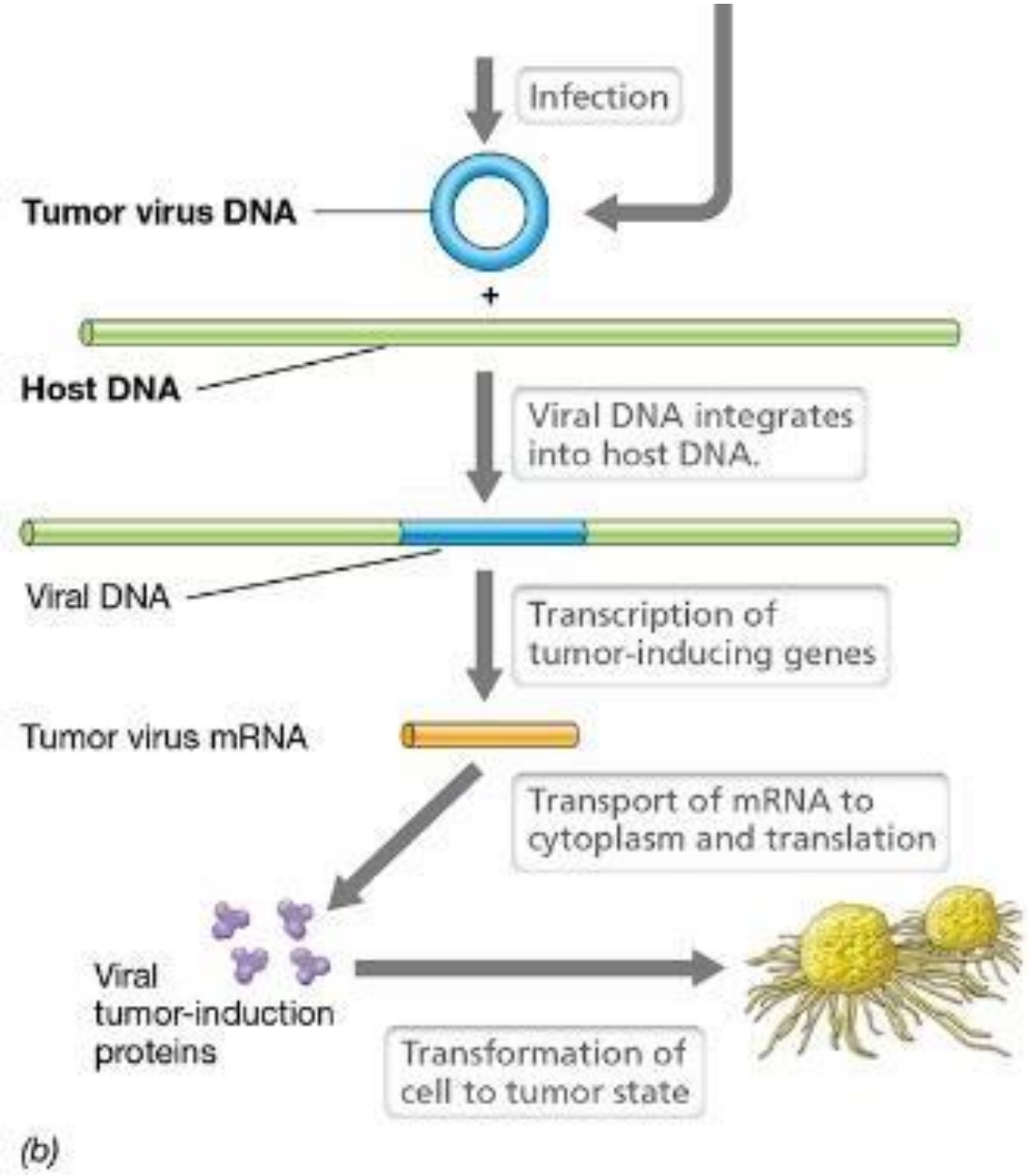


Figure 11.18

11.7 DNA Tumor Viruses

- Herpesviruses
  - After attachment, cytoplasmic membrane and viral envelope fuse, releasing nucleocapsid into cell.
  - In nucleus, viral DNA uncoated, and three classes of mRNA are produced.
    - *immediate early:* encodes regulatory proteins
    - *delayed early:* encodes DNA replication proteins
    - *late:* encodes structural proteins
  - Replication: rolling circle
  - nucleocapsids assembled in nucleus
  - envelope added through budding
  - Release occurs via endoplasmic reticulum.

Remember
Fig. 11.11

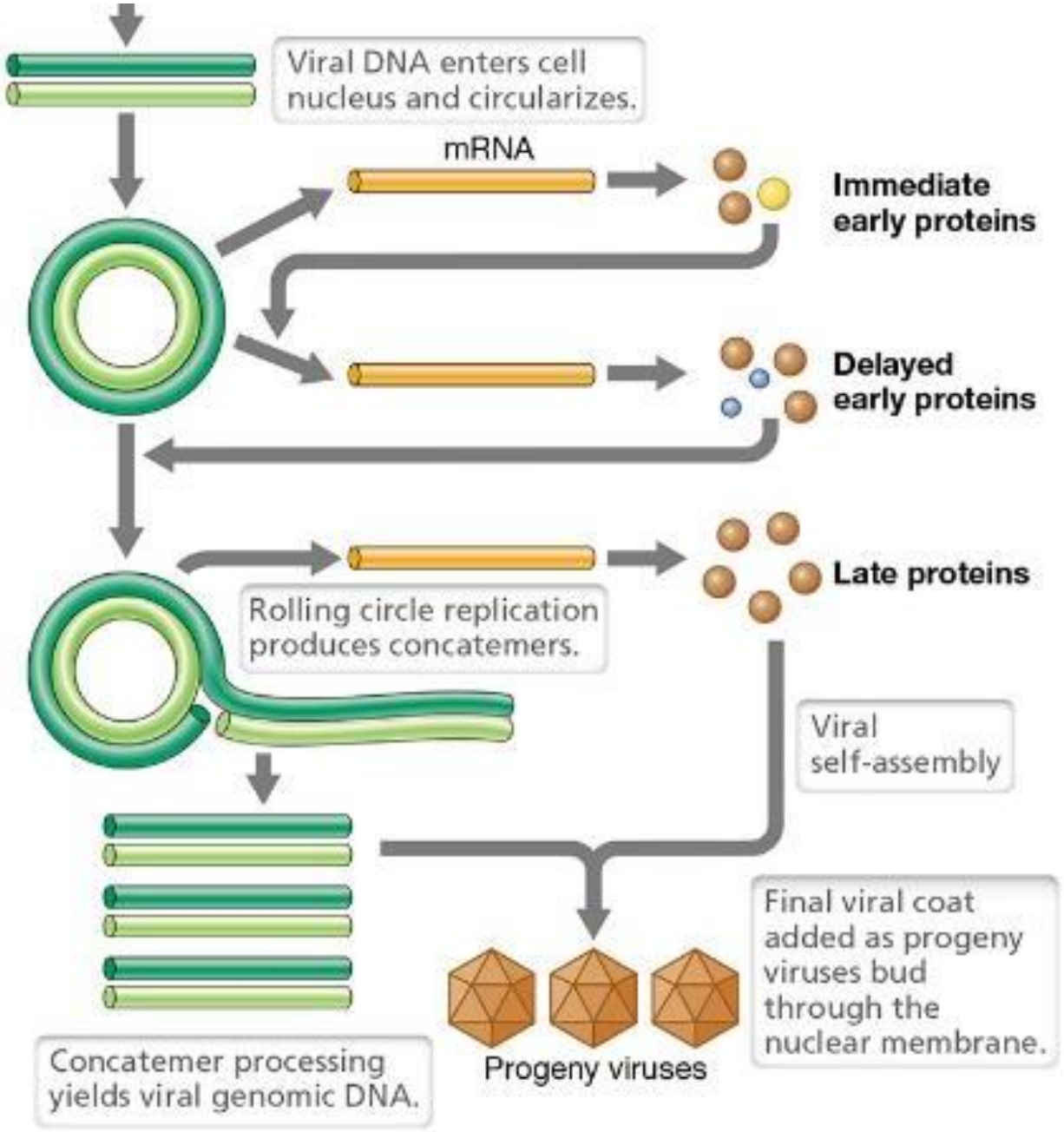
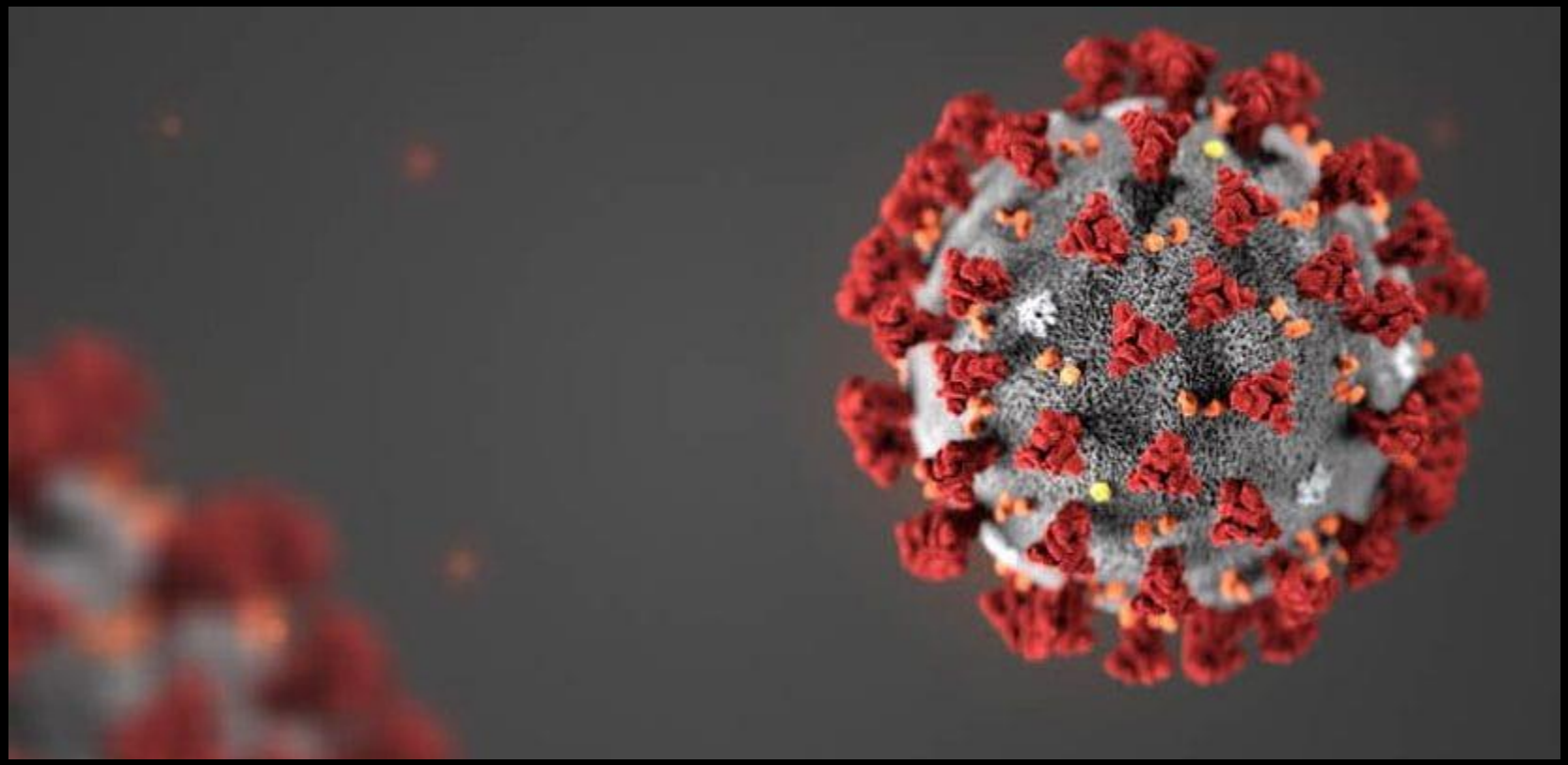


Figure 11.19

Microbiologie 2

II. RNA Viruses



III. Viruses with RNA Genomes

- 11.8 Positive-Strand RNA Viruses
- 11.9 Negative-Strand RNA Animal Viruses
- 11.11 Viruses That Use Reverse Transcriptase

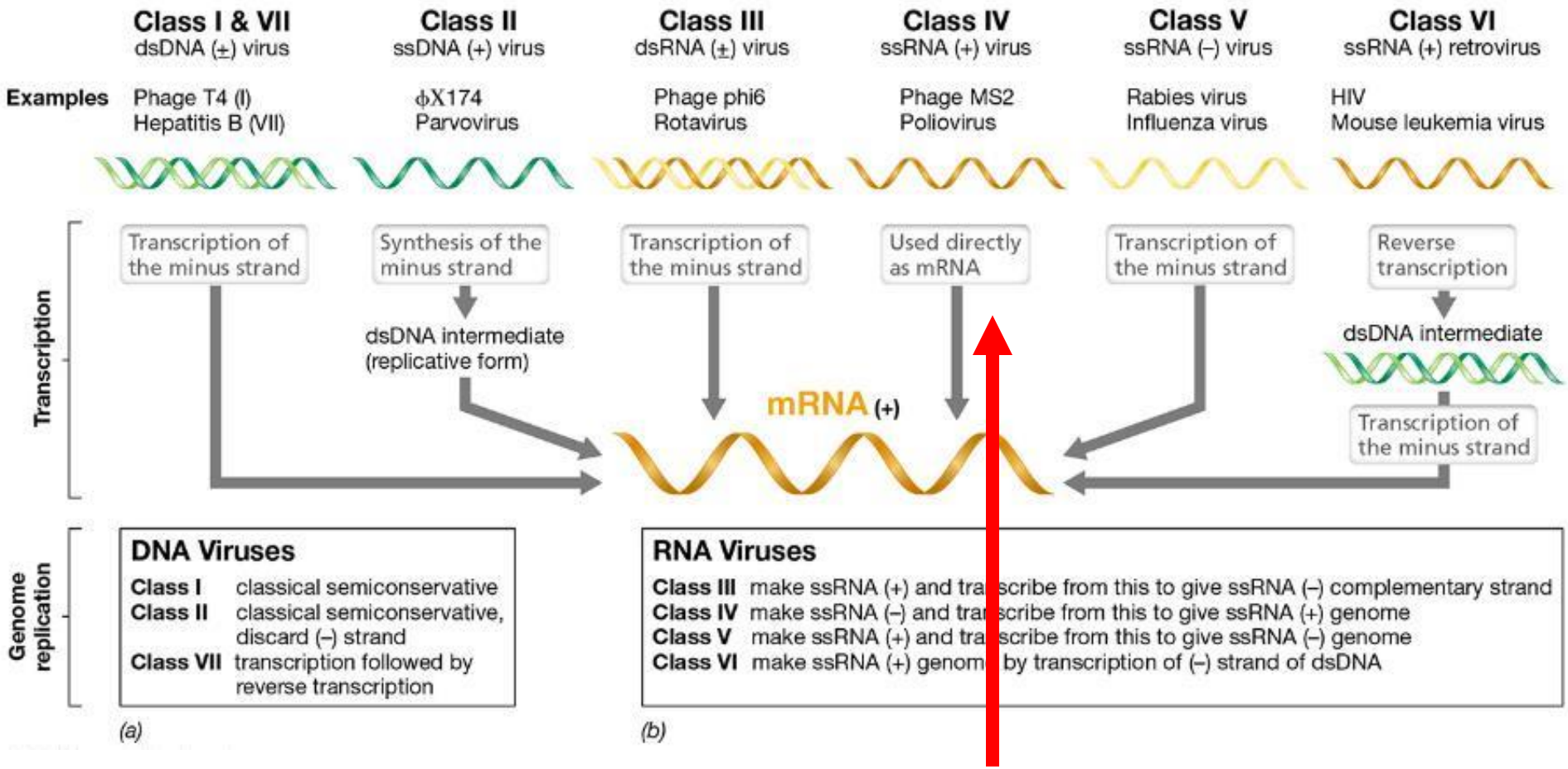
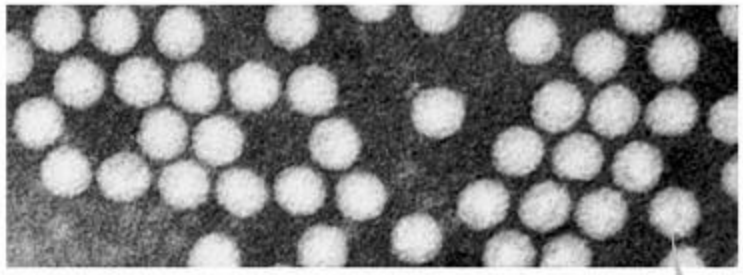


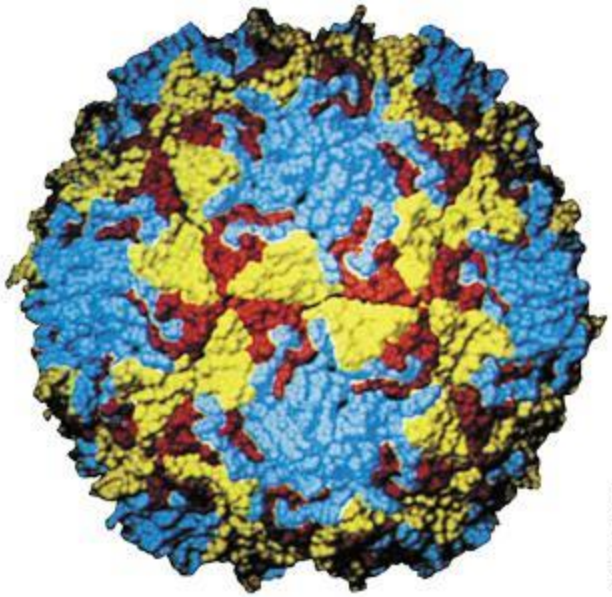
Figure 11.2

11.8 Positive-Strand RNA Viruses

- Poliovirus (Figure 11.21)
  - small icosahedral virus
  - 5'-terminus of RNA covalently bound to *VPg protein* that facilitates binding to ribosomes, 3'-terminus has poly(A) tail
  - Translation yields a single long, giant protein (polyprotein) that undergoes self-cleavage (*post-translational cleavage*) to generate ~20 smaller proteins necessary for nucleic acid replication and virus assembly.
  - Replication occurs in cytoplasm.
  - Lysis occurs, releasing new virions.



(a)



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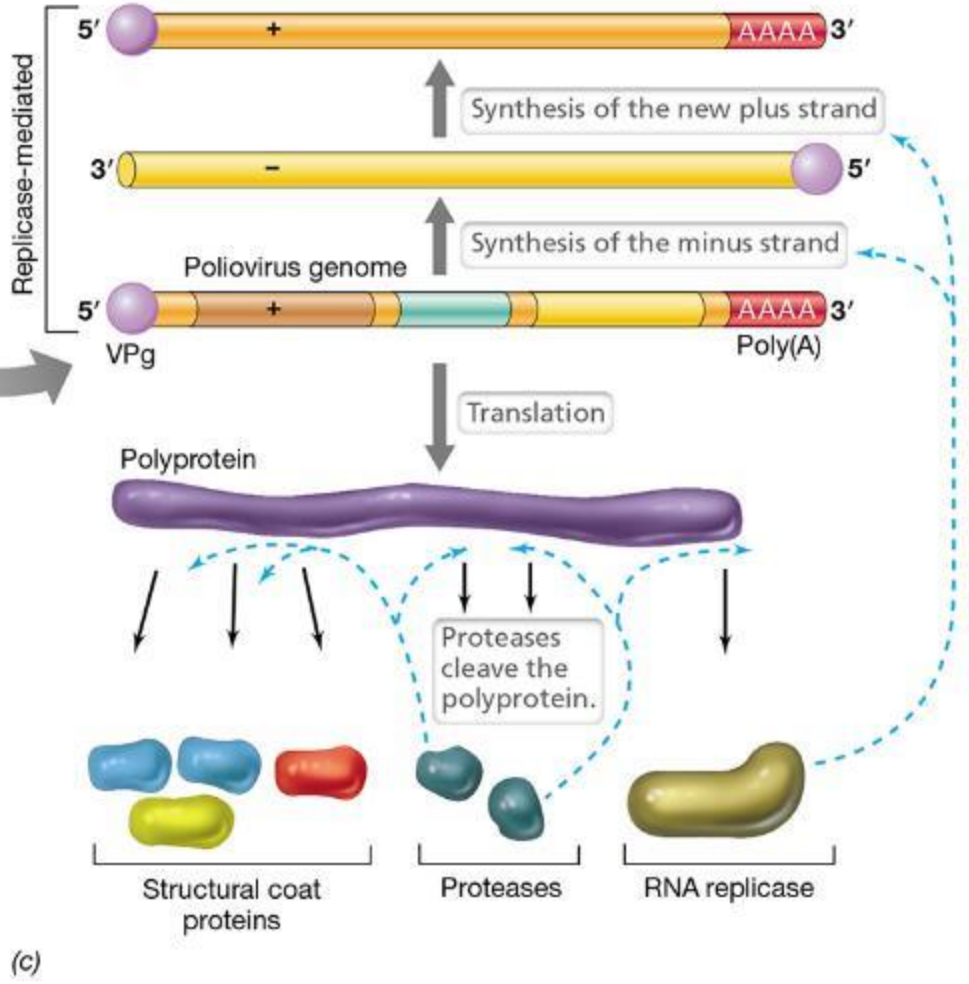


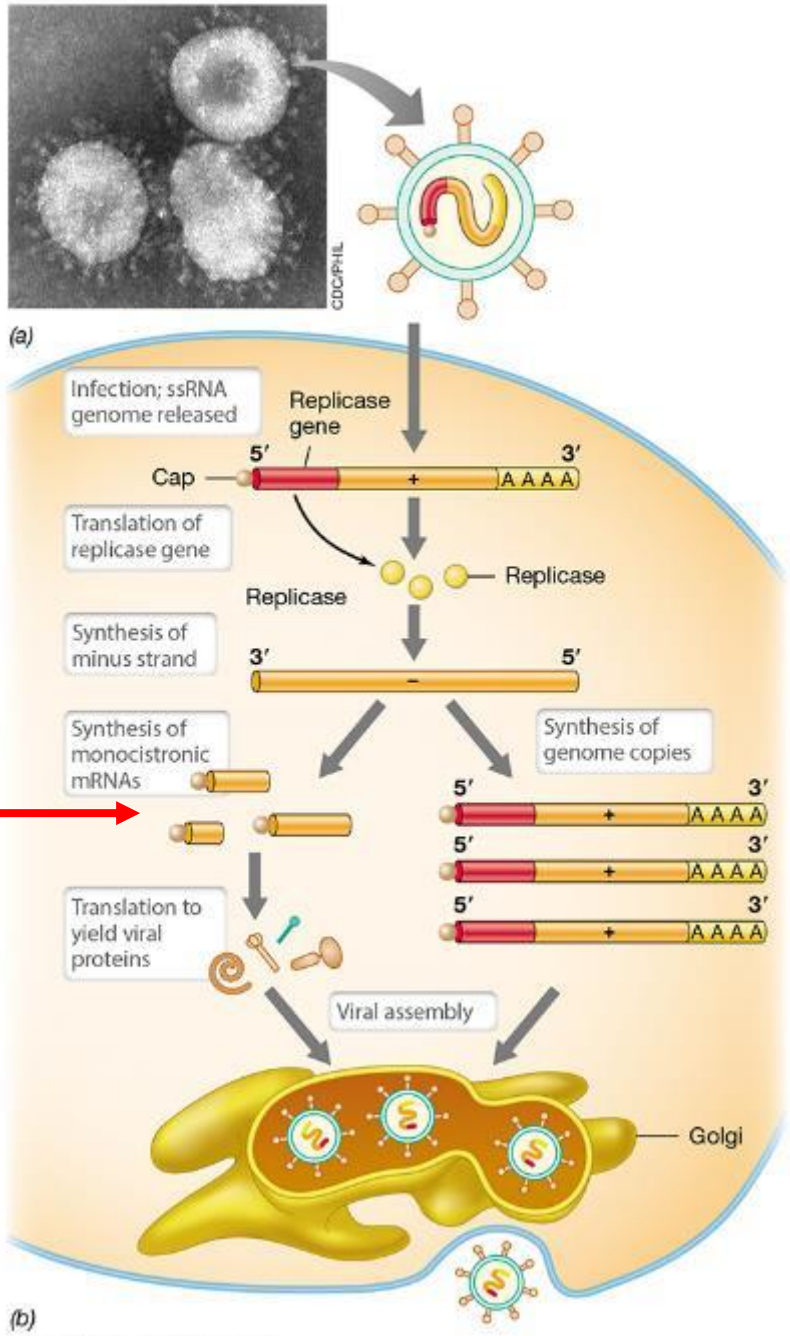
(c)

Figure 11.21

- DNA template > DNA product = DNA polymerase
- DNA template > RNA product = RNA polymerase (transcriptie)
- RNA template > DNA product = Reverse transcriptase
- RNA template > RNA product = RNA replicase

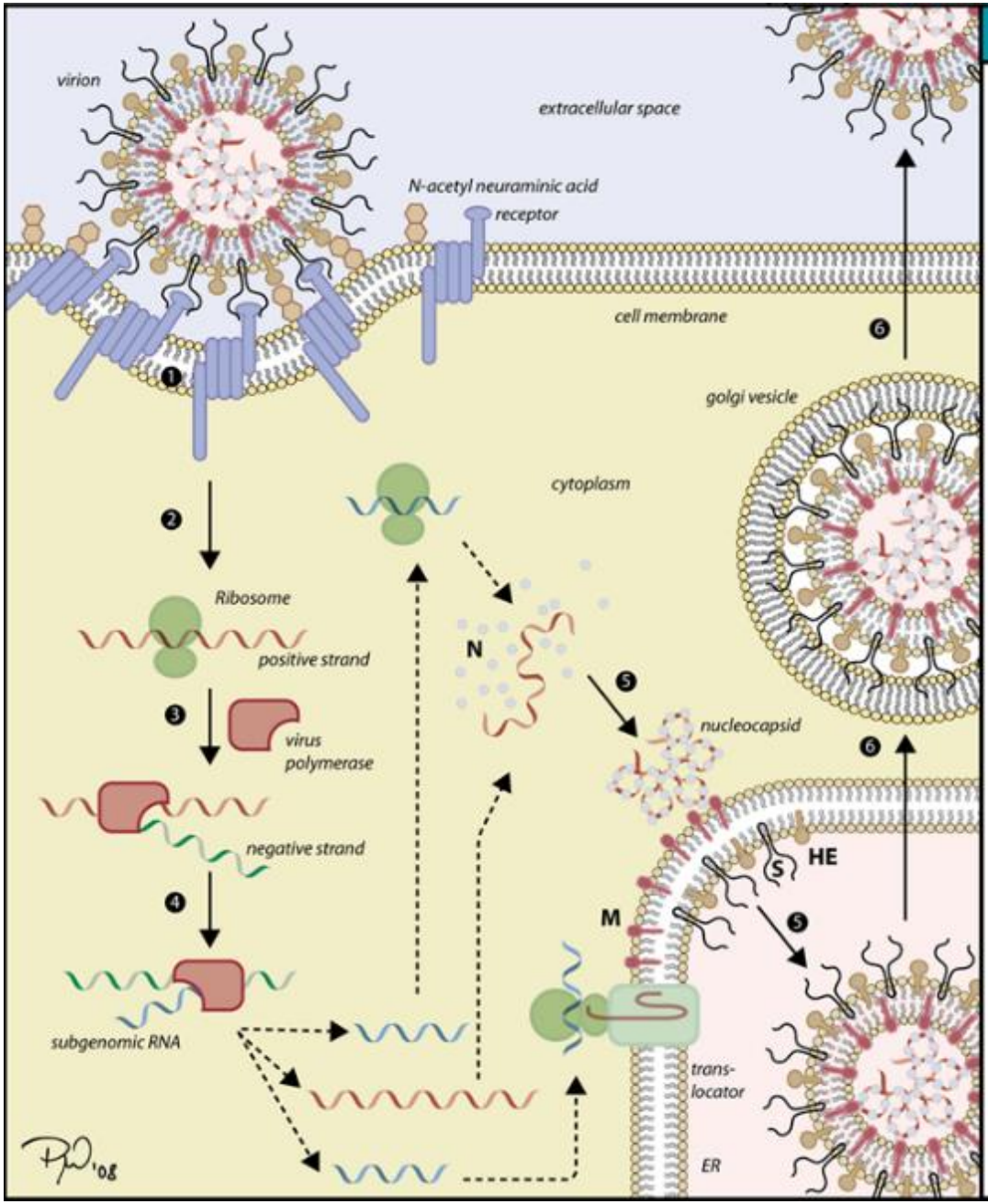
11.8 Positive-Strand RNA Viruses

- Coronaviruses
  - larger virus that replicates in cytoplasm
  - cause respiratory infections, including SARS en covid-19, in humans and other animals
  - enveloped with glycoprotein spikes on surfaces (Figure 11.22*a*)
  - Only part of genome encoding RNA replicase is translated.
  - Genomic RNA used as template to produce (–) strands from which mRNA is produced and translated.
  - Virions assembled in Golgi complex.
  - released from cell surface



NB: +RNA

Figure 11.22



Replication of Coronavirus

1 With their S-protein, coronaviruses bind on cell surface molecules such as the metalloprotease »amino-peptidase N«. Viruses, which accessorily have the HE-protein, can also bind on N-acetyl neuraminic acid that serves as a co-receptor.

2 So far, it is not clear whether the virus get into the host cell by fusion of viral and cell membrane or by receptor mediated endocytosis in that the virus is in-corporated via an endosome, which is subsequently acidified by proton pumps. In that case, the virus have to escape destruction and transport to the lysosome.

3 Since coronaviruses have a single positive stranded RNA genome, they can directly produce their proteins and new genomes in the cytoplasm. At first, the virus synthesize its RNA polymerase that only recognizes and produces viral RNAs. This enzyme synthesize the minus strand using the positive strand as template.

4 Subsequently, this negative strand serves as template to transcribe smaller subgenomic positive RNAs which are used to synthesize all other proteins. Furthermore, this negative strand serves for replication of new positive stranded RNA genomes.

5 The protein N binds genomic RNA and the protein M is integrated into the membrane of the endoplasmatic reticulum (ER) like the envelope proteins S and HE. After binding, assembled nucleocapsids with helical twisted RNA budd into the ER lumen and are encased with its membrane.

6 These viral progeny are finally transported by golgi vesicles to the cell membrane and are exocytosed into the extracellular space.

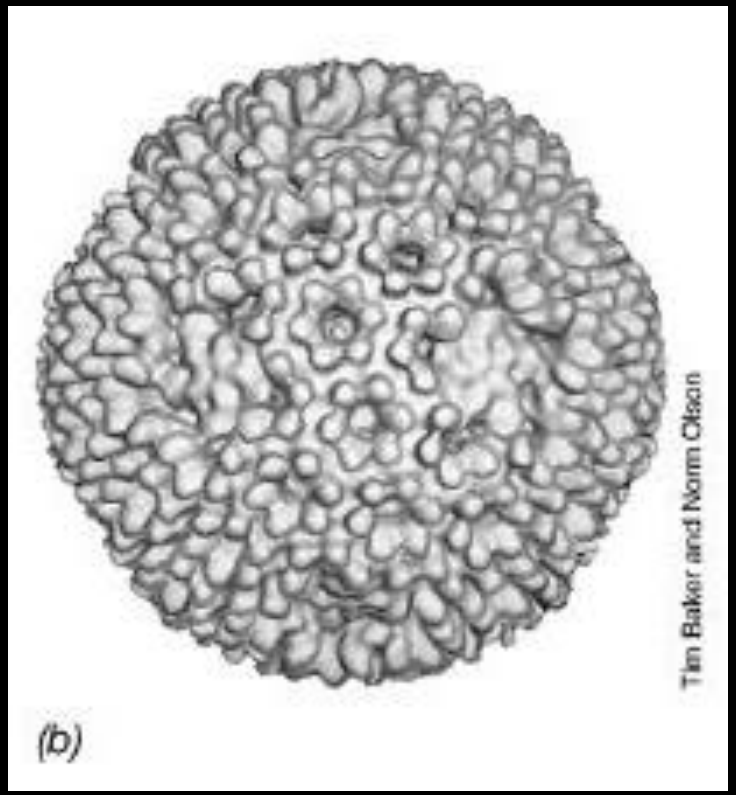
Not drawn to scale! Not all cellular compartments and enzymes are shown. Colors: positive strand RNA (red), negative strand RNA (green), subgenomic RNAs (blue).
Based on: Lai MM, Cavanagh D (1997). The molecular biology of coronavirus. Adv. Virus Res (48) 1-100.

Wiki

EINDE LES 8

Microbiologie 2: Les 8

III. Viruses with RNA Genomes



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III. Viruses with RNA Genomes

- 11.8 Positive-Strand RNA Viruses
- 11.9 Negative-Strand RNA Animal Viruses
- 11.11 Viruses That Use Reverse Transcriptase

11.9 Negative-Strand RNA Animal Viruses

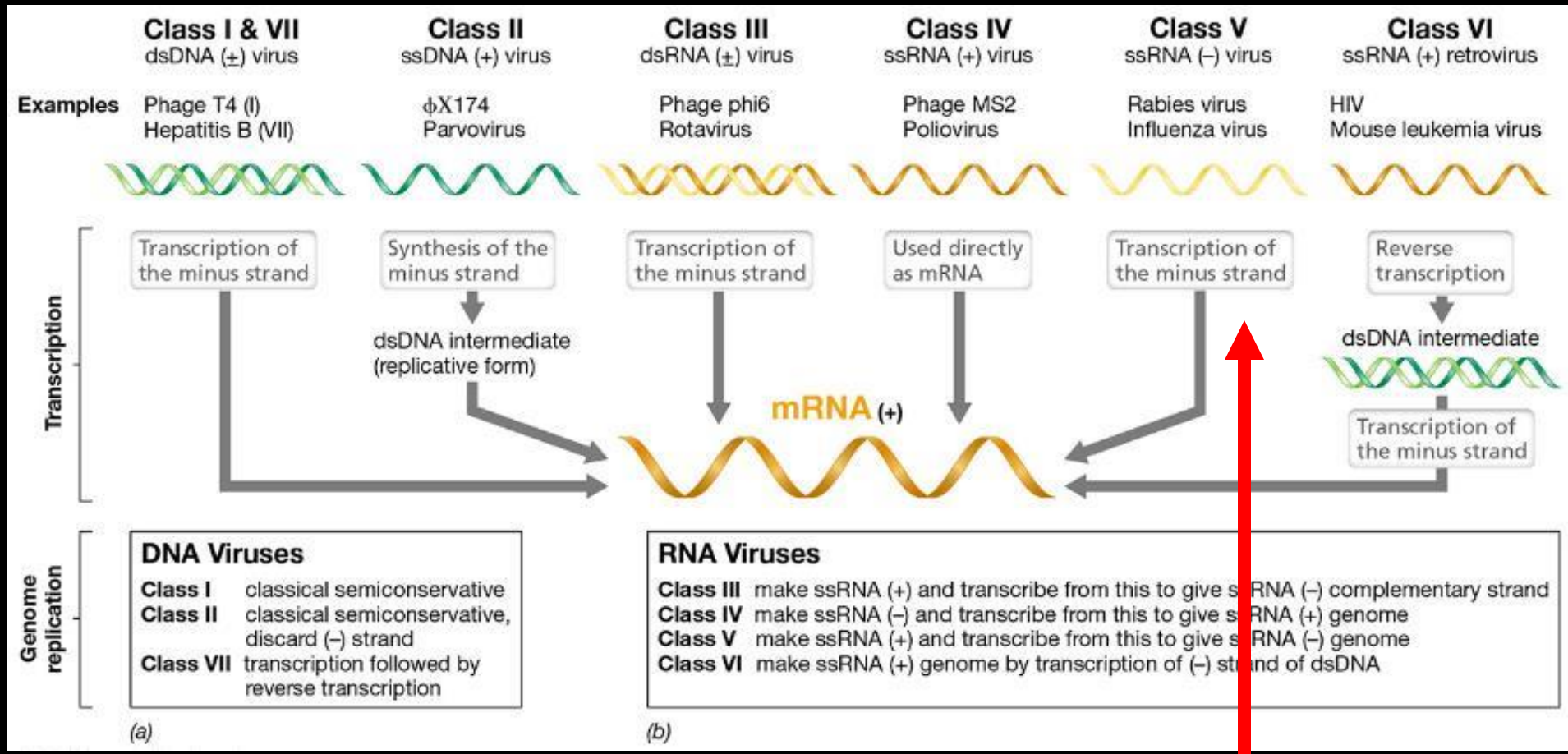
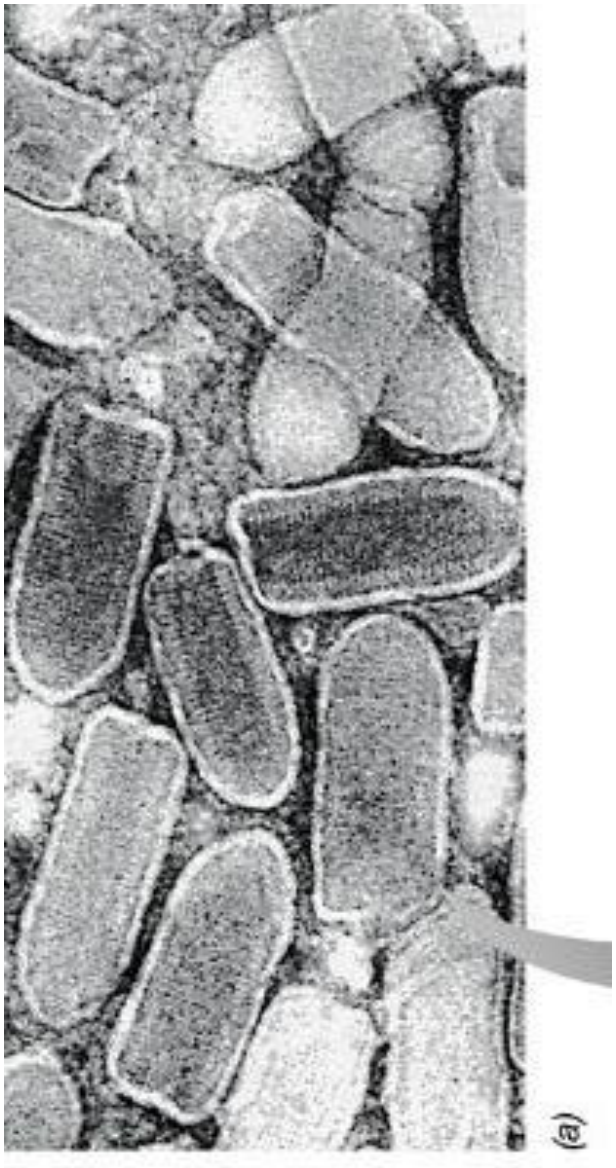


Figure 11.2

11.9 Negative-Strand RNA Animal Viruses

- No known prokaryotic ss(–)RNA viruses
- Rabies virus
  - rhabdovirus: bullet-shaped, enveloped, helical nucleocapsid containing several enzymes (Figure 11.23)
  - Transcription via viral RNA replicase in host cytoplasm into two distinct classes
    - mRNAs encoding structural genes of the virus
    - positive-strand RNA copy of the complete viral genome (template for genomic RNA)
  - release by budding



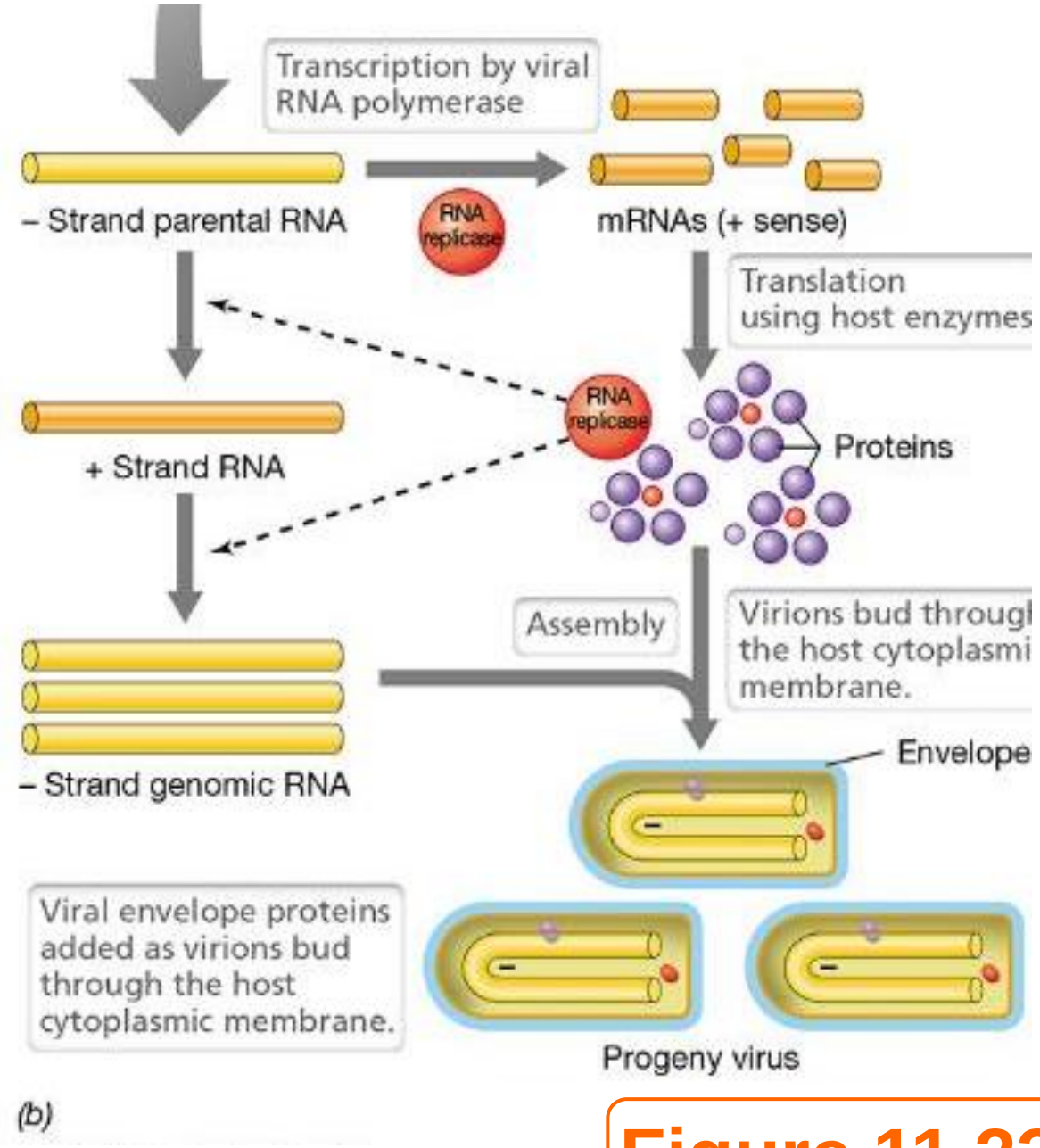
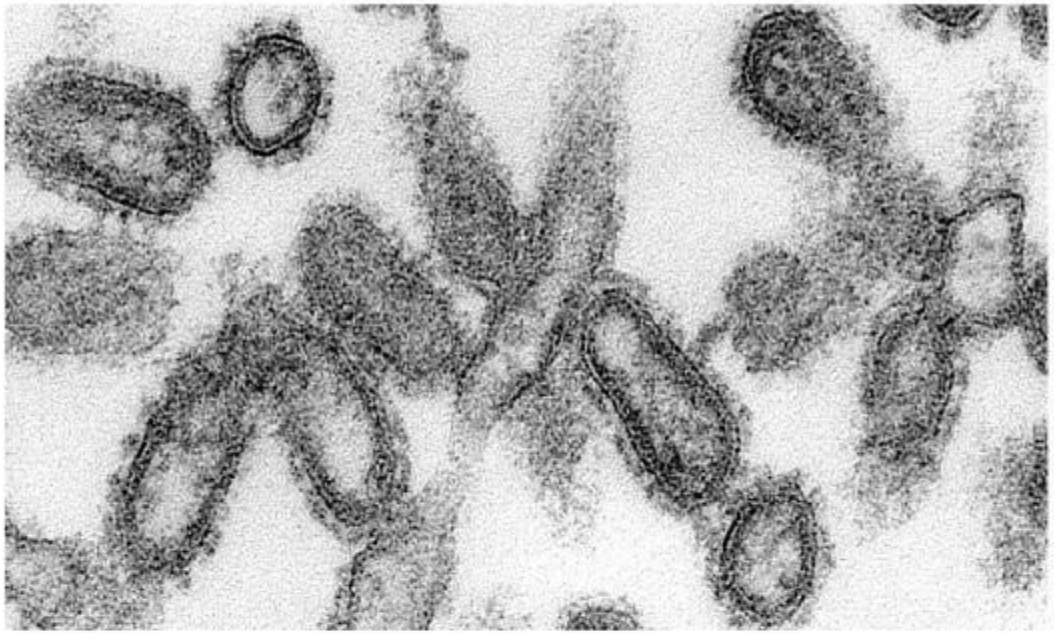


Figure 11.23

11.9 Negative-Strand RNA Animal Viruses

- Influenza virus
  - enveloped, pleomorphic (non-uniform), budding virus with *segmented genome* (separate pieces) (Figure 11.24)
  - surface proteins interact with host cell surface
    - *Hemagglutinin* docks to host cell. Anti-hemagglutinin antibodies prevent infection (immunization).
    - *Neuraminidase* breaks down sialic acid component of host cytoplasmic membrane, functions in virus assembly.
  - has RNA replicase and RNA endonuclease (nuclease removes 5'cap host cell mRNA)
  - Nucleocapsid goes to nucleus for transcription.
  - Enveloped virion forms by budding.



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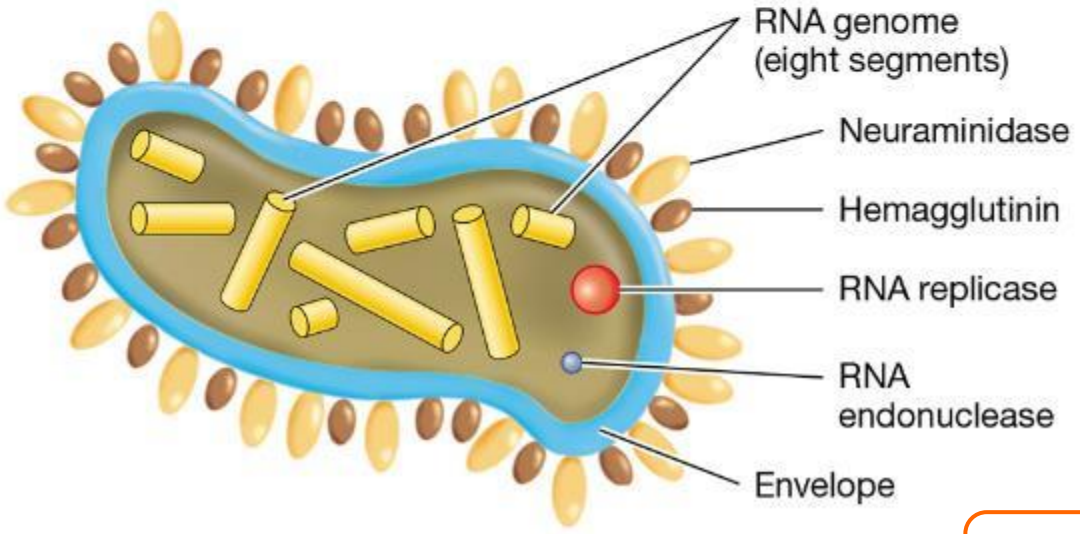


(b)

Figure 11.24

11.9 Negative-Strand RNA Animal Viruses

- Influenza virus
  - Segmented genome results in *antigenic shift.*
    - Segments of the RNA genome from two genetically distinct strains of virus infecting the same cell are reasserted.
    - generates hybrid virions that express a unique set of surface proteins unrecognized by immune system
    - triggers major outbreaks because immunity to new forms absent from population

Negative-strand RNA virussen: Influenza

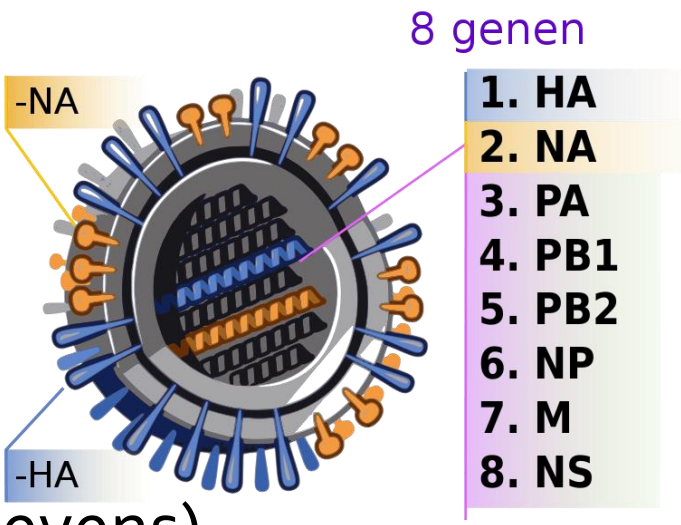
Ontwijken van het immuunsysteem

- *Antigenic drift*
  - Structuur van neuraminidase en hemagglutinin eiwitten veranderen geleidelijk (Geen RNA proofreading)
- *Antigenic shift*
  - Twee verschillende stammen infecteren samen een gastheercel
  - RNA wordt herverdeeld
  - De nieuwe virusdeeltjes hebben een unieke set oppervlakteeiwitten

Influenza A: van soort naar soort

- Influenza B en C infecteren alleen mensen
- Influenza A infecteert vogels, varkens, paarden, mensen (vogels grootste reservoir)
- Influenza A heeft bekende epidemieën veroorzaakt

Influenza A:



Oppervlakte-eiwitten
neuramidinase en hemagglutinine
H1N1: Spanish flu (1918) (40 miljoen levens)
H2N2: Asian flu (1957)
H3N2: Hong Kong flu (1968)
H5N1: Bird flu (2003-2007) (only 160 deaths but mortality 50%)
H1N1: Mexicaanse griep (2009)

Er zijn
18 HA-varianten beschreven en
11 NA-subtypen

11.11 Viruses That Use Reverse Transcriptase

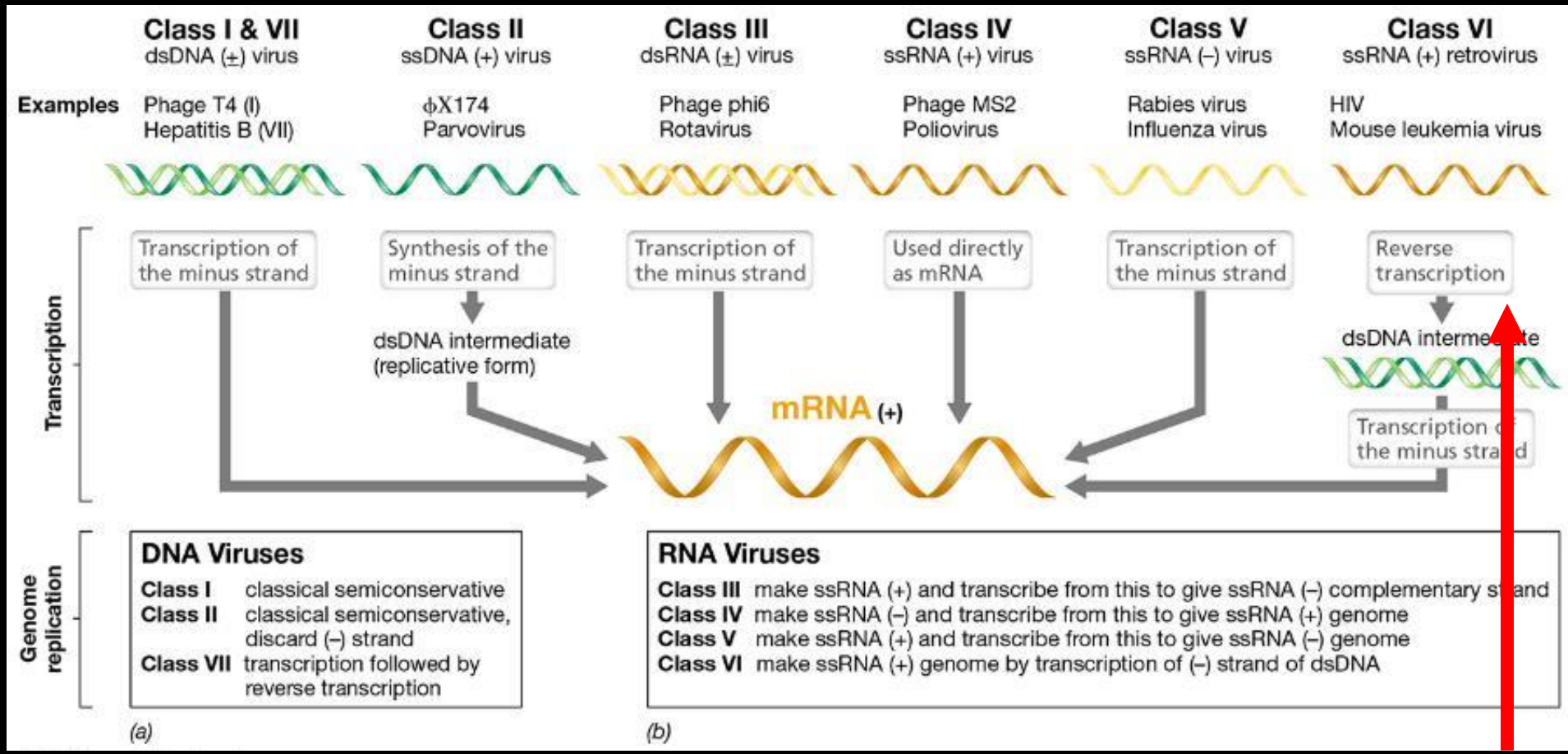


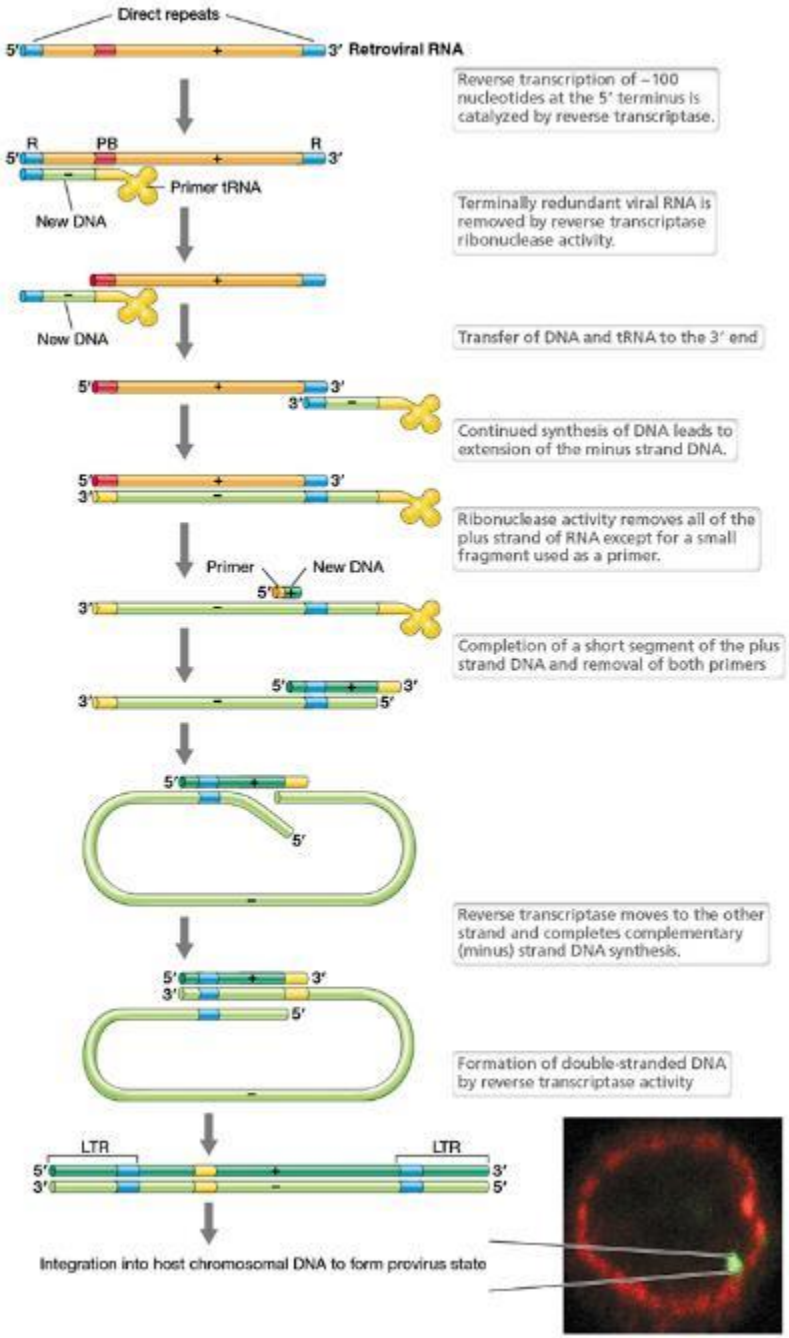
Figure 11.2

11.11 Viruses That Use Reverse Transcriptase

- Retroviruses: integration of viral genes into the host genome
  - enveloped virions that contain two identical copies of the RNA genome
  - Virion contains several enzymes, including reverse transcriptase, and viral tRNA.
  - Retroviral genome is not used as mRNA; converted to DNA by reverse transcriptase and integrated into genome.
  - Example: HIV

11.11 Viruses That Use Reverse Transcriptase

- Retroviruses: integration of viral genes into the host genome
  - reverse transcriptase => 3 activities
    - *Reverse transcriptase activity:* DNA from RNA template => RNA:DNA hybrid
    - *Ribonuclease activity* degrades RNA strand of RNA:DNA hybrid.
    - *DNA polymerase* to make dsDNA from ssDNA
    - Viral tRNA serves as primer.
    - The *gag* encodes several small viral structural proteins.
  - dsDNA with long terminal repeats forms; repeats assist in integration into genome.



NB: polymerases werken 5'=> 3'

Figure 11.27

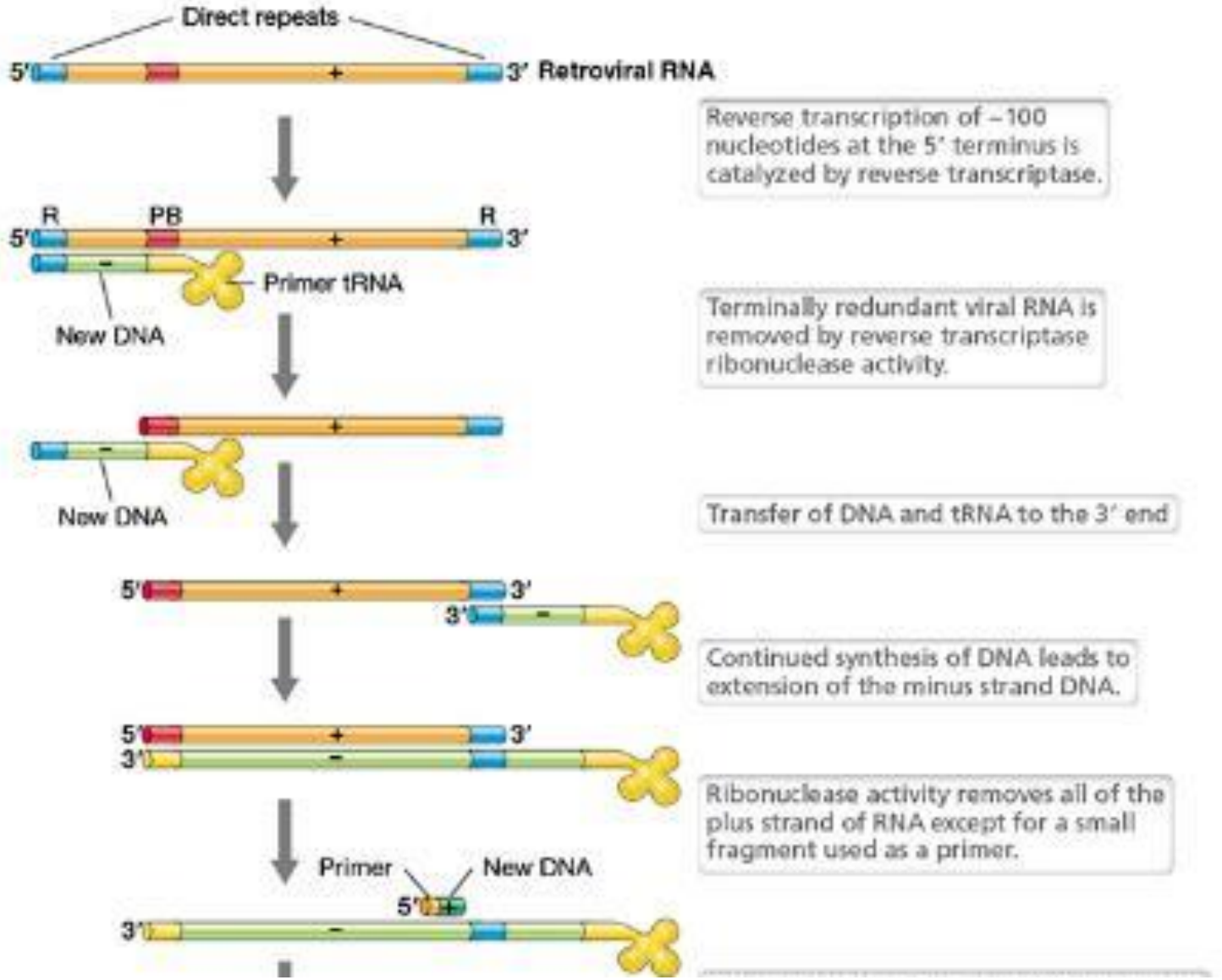


Figure 11.27

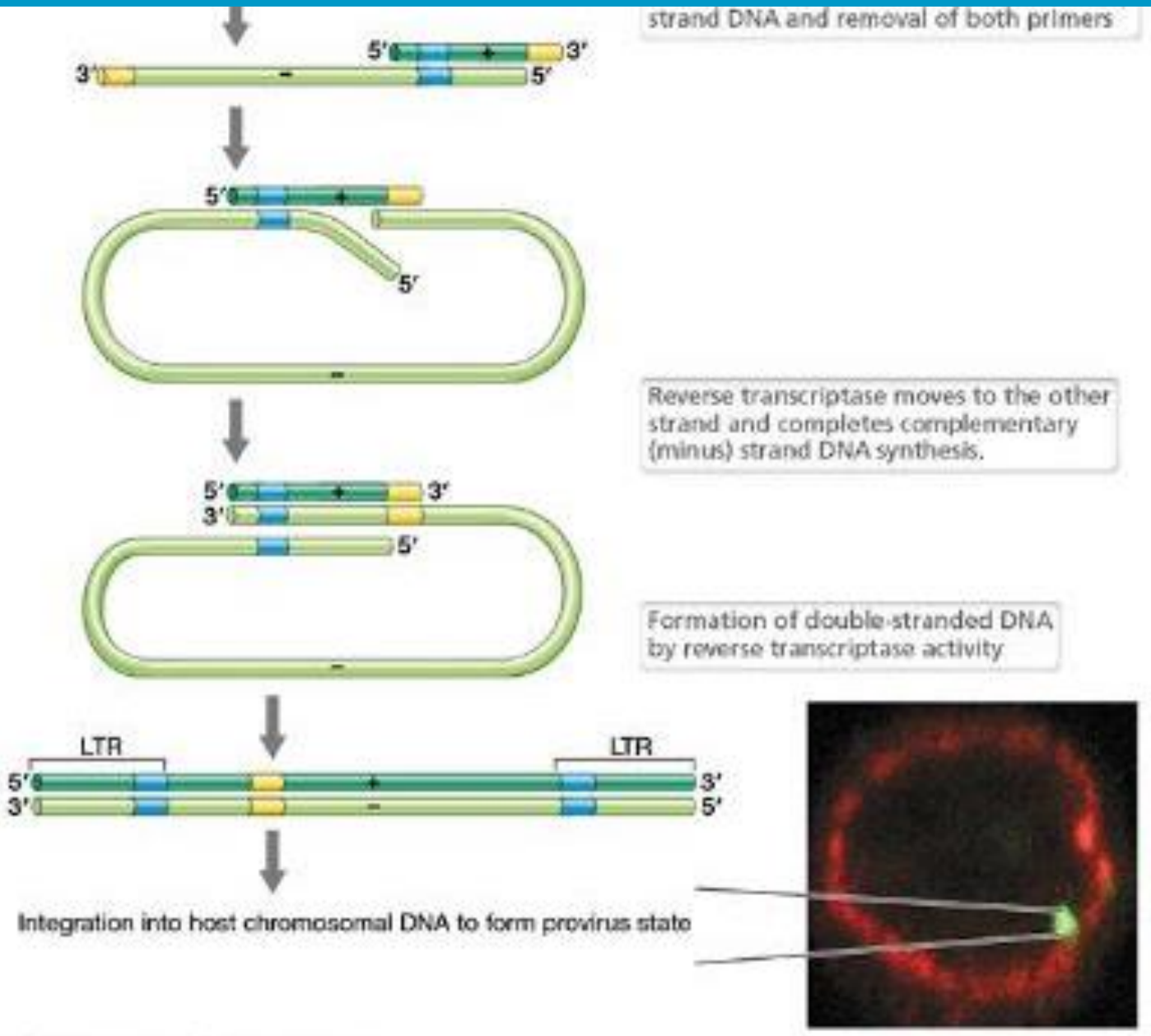


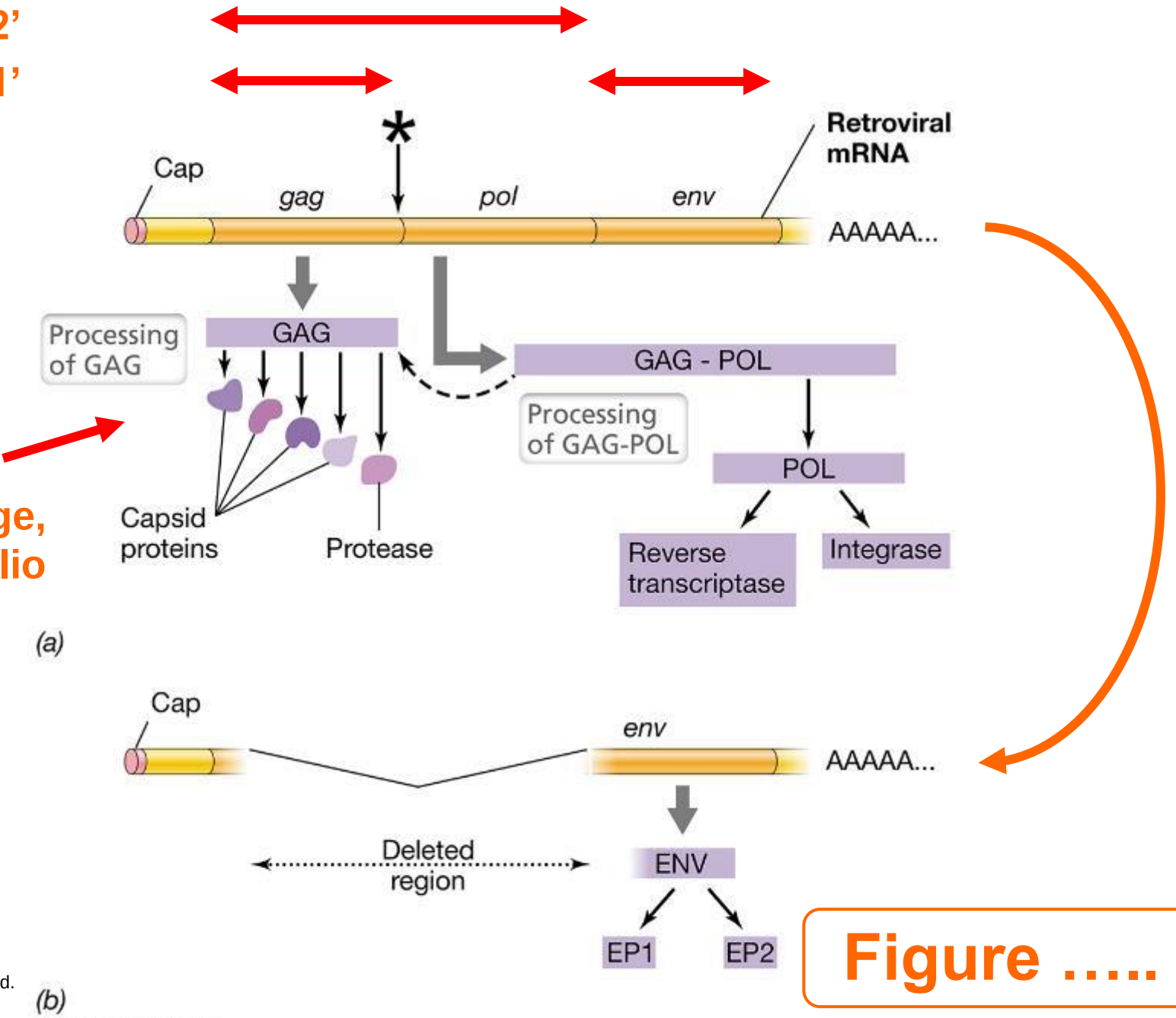
Figure 11.27

11.11 Viruses That Use Reverse Transcriptase

- Retroviruses: induction to form new retrovirus virions
  - Retroviral DNA becomes permanent part of host chromosome.
  - Genes may be expressed or remain latent indefinitely.
  - If induced, retroviral DNA is transcribed; RNA can be packaged into virions or translated. (Figure 10.24)
  - All retroviruses have the three "*genes*"
    - The *gag* encodes several small viral structural proteins.
    - The *pol* is translated into a large polyprotein.
    - The *env* is processed into two distinct envelope proteins.
  - Assembly occurs in cytoplasm; virions released by budding.

ORF ‘2’

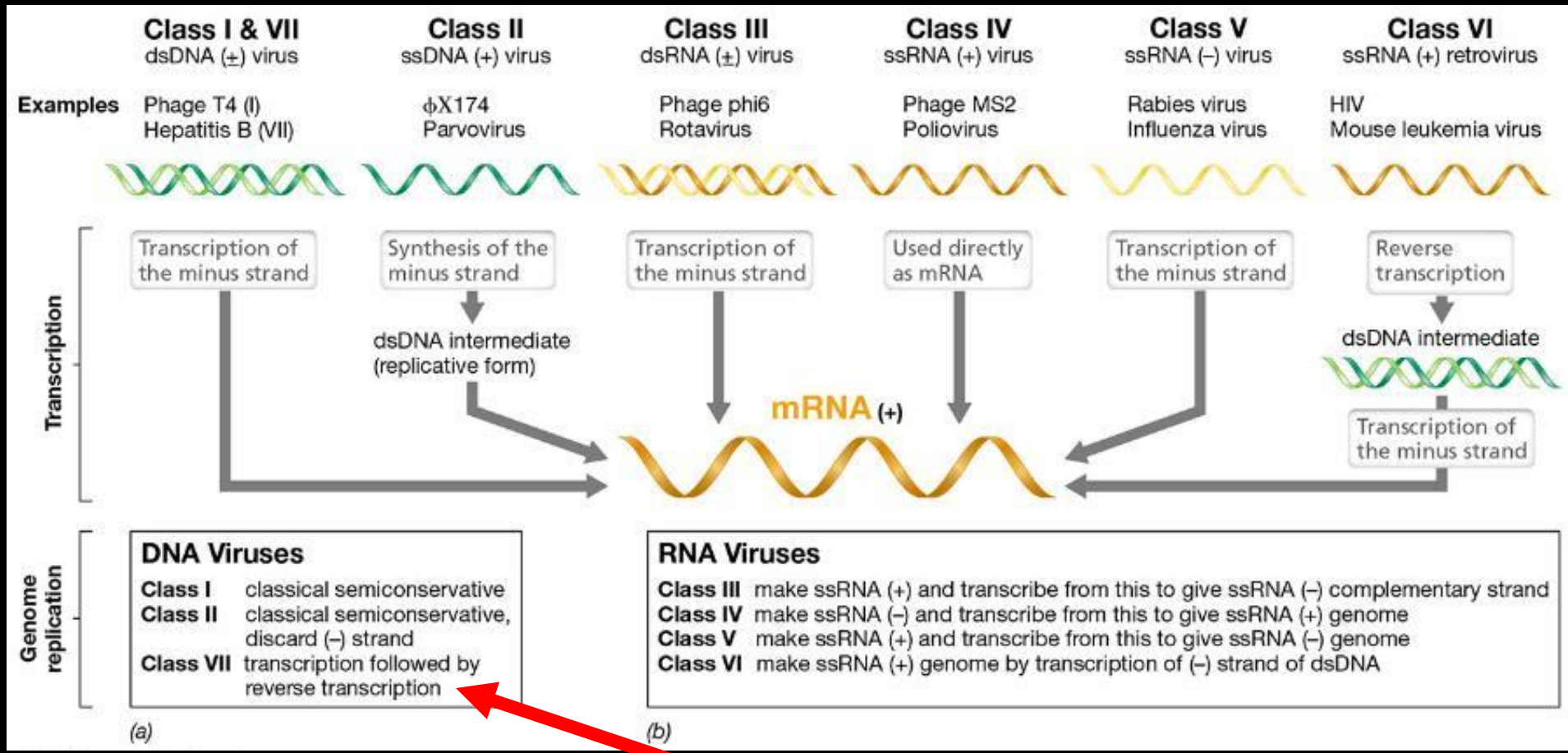
ORF ‘1’



Self cleavage, zoals bij polio

Figure …..

11.11 Viruses That Use Reverse Transcriptase

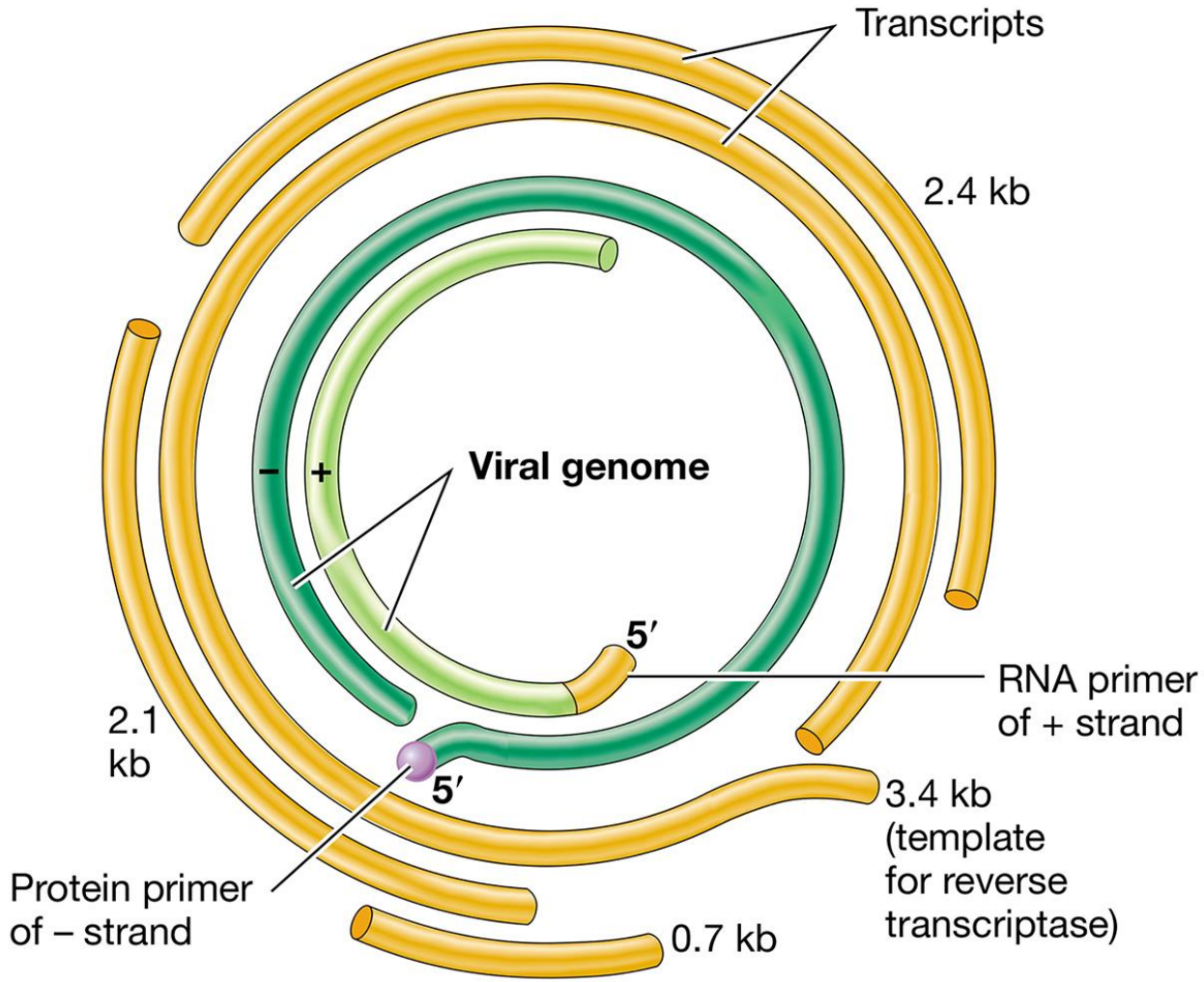


Hepadnavirus

Figure 11.2

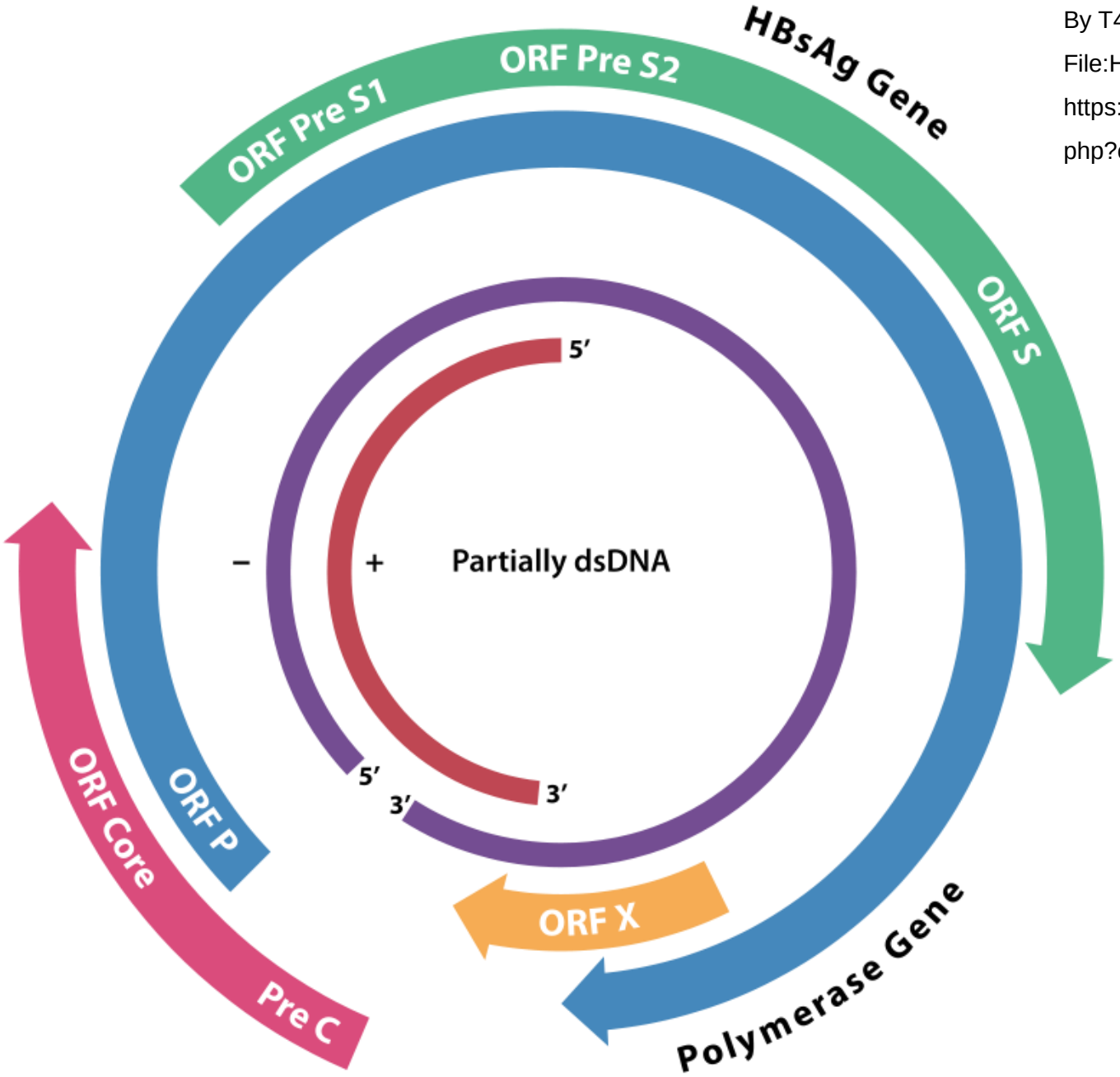
11.11 Viruses That Use Reverse Transcriptase

- Hepadnaviruses
  - include hepatitis B (Figure 11.28)
  - unusual tiny, partially double-stranded genomes
  - overlapping genes
  - Hepadnaviral reverse transcriptase also functions as protein primer for DNA synthesis.
  - Viral replication occurs through an RNA intermediate.



(b)

Figure 11.28



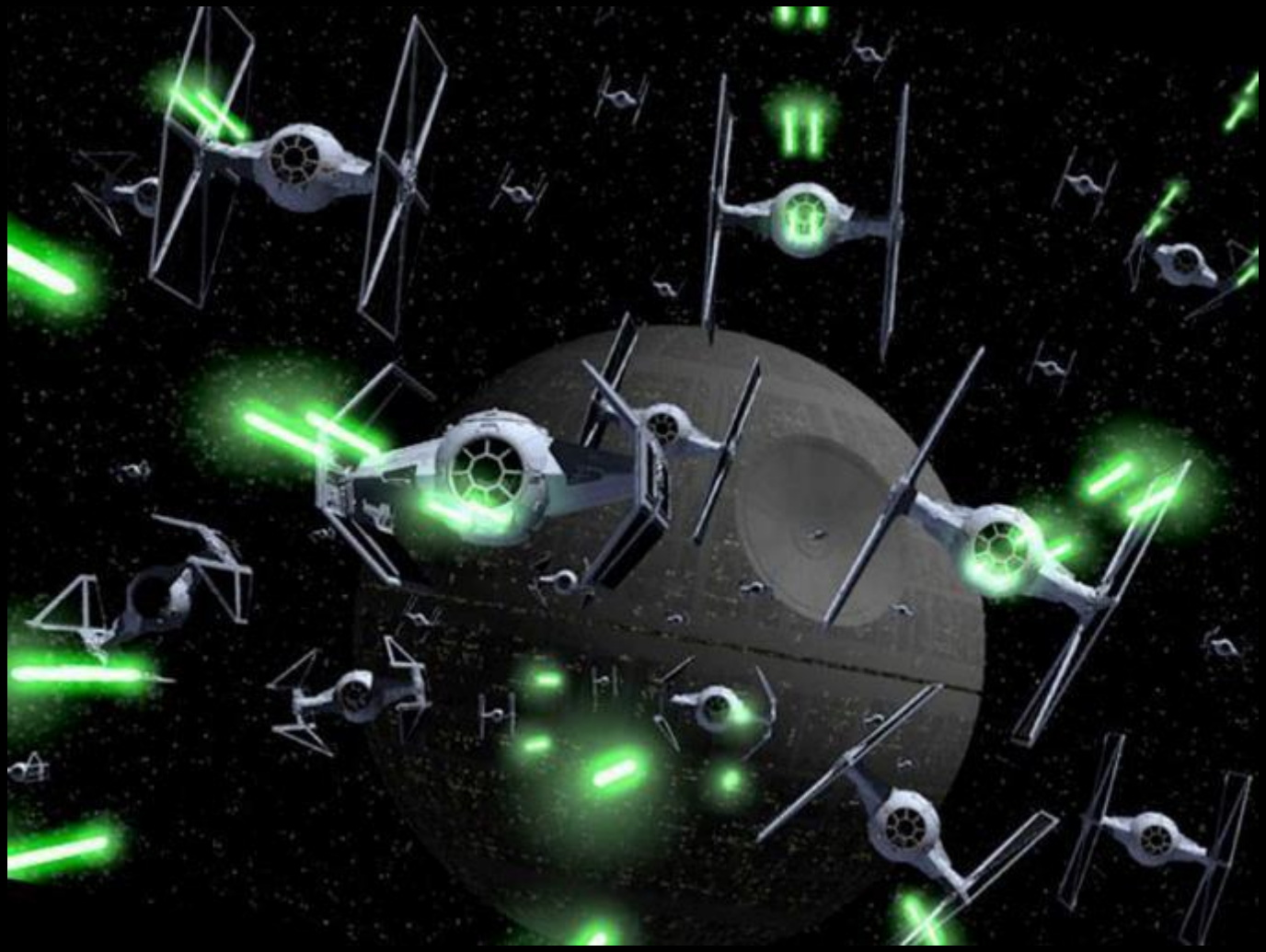
By T4taylor - Own work based on File:HBV_genome.png, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=10687476

11.11 Viruses That Use Reverse Transcriptase

- Hepadnaviruses
  - nucleocapsid enters host nucleus
  - Partial genomic DNA strand is completed to form dsDNA.
  - mature virions exported by budding

EINDE LES 8

Microbiologie 2: Les 9
Microbial Arms Race



Schema Micro2

Les	Hoofdstuk	Paragraaf
1	7	7.1, 7.2, 7.3, 7.8
2	7	7.5, 7.6, 7.7
3	7	7.9, 7.10, 7.11
4	7	7.12, 7.13, 7.14, 7.15
5	5	5.1, 5.2, 5.3, 5.4, 5.5, 5.6
6	5 en 11	5.7, 5.8, 11.1, 11.2
7	11	11.6, 11.7, 11.8 (MS2 niet)
8	11	11.9, 11.11,
9	11	11.13, 11.15, 11.16
10	24	24.1, 24.2, 24.5
11	25	25.1, 25.2, 25.3, 25.5
12	25	25.6, 25.7, 25.8
13	28 en 8	28.10, 28.11, 28.12, 8.10
14	Oefententamen	Alles

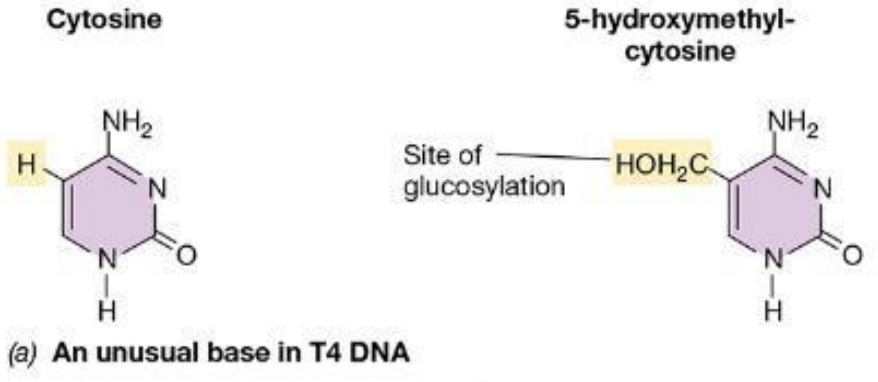
NB: Hfdstnrs niet accuraat

Microbial Arms Race

- 9.12 Preserving Genomic Integrity and CRISPR

9.12 Preserving Genomic Integrity and CRISPR

- The microbial arms race
  1. Bacteria produce restriction endonucleases;
  2. Bacteriophage T4 substitutes cytosine for 5-hydroxymethylcytosine in genome.
  3. *E. coli* evolves altered restriction enzymes for 5-hydroxymethylcytosine T4 DNA.
  4. T4 phages modify DNA by glycosylation.
  5. *E. coli* evolved altered restriction enzymes for glycosylated T4 DNA.
  6. T4 inhibits these modified restriction enzymes.
  7. *E. coli* evolved uninhibited endonucleases.



(a) An unusual base in T4 DNA

9.12 Preserving Genomic Integrity and CRISPR

- The microbial arms race
  - dynamic relationship between bacteriophages and hosts
    - alterations in viral receptor sites: modification of receptor or protection with a shield such as a capsule
    - Viruses can mutate or degrade capsule.
    - See Fig. 9.36

9.12 Preserving Genomic Integrity and CRISPR

- The antiviral system of *Bacteria* and *Archaea*: CRISPR
  - CRISPR: Clustered Regularly Interspaced Short Palindromic Repeats. Protect from bacteriophage infection
    - Regions contain short repeats of constant DNA sequences alternating with short variable *spacers* corresponding to "memory" of viral or other foreign DNA. (Figure 10.28)

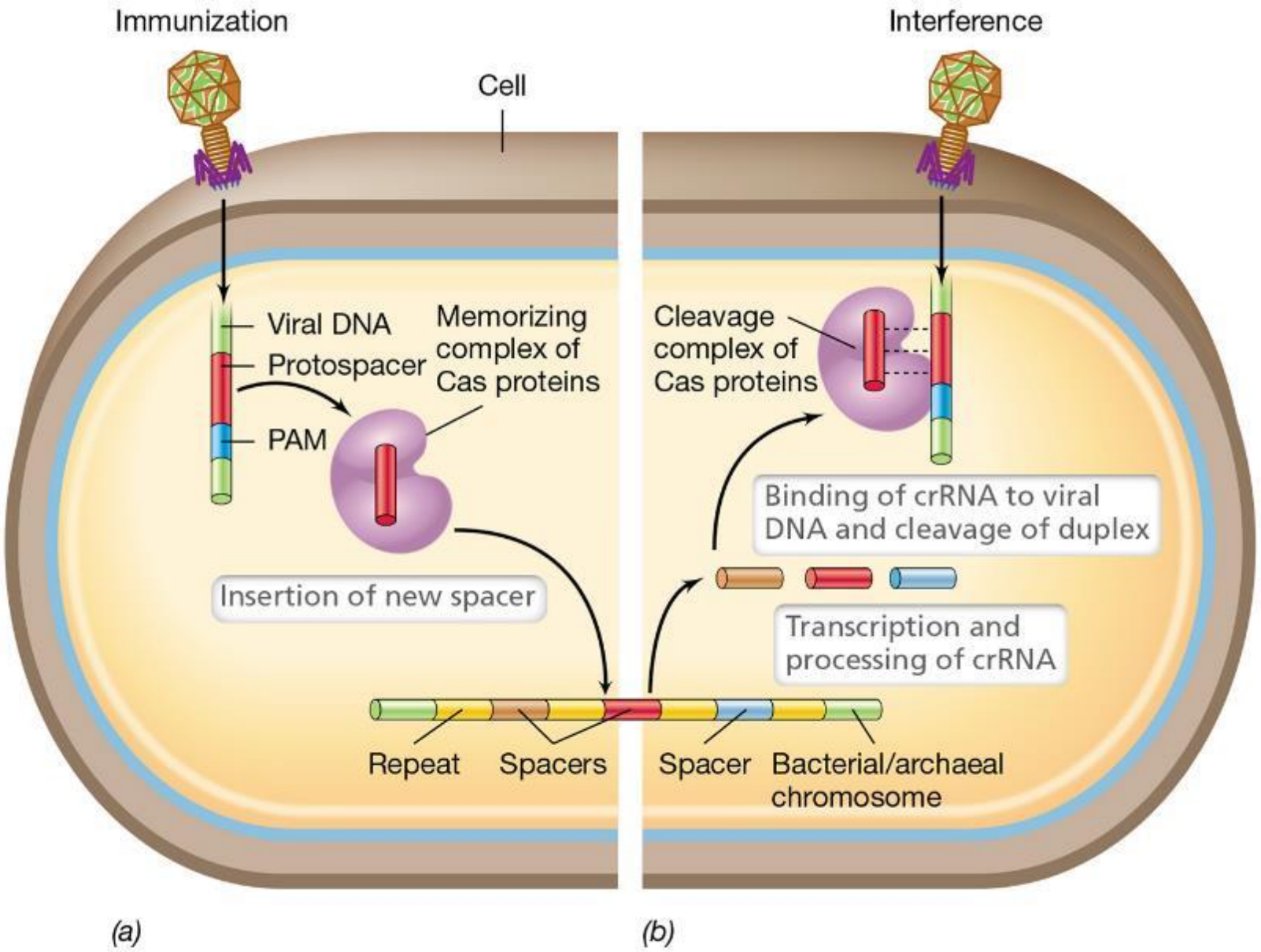


Figure 9.37

9.12 Preserving Genomic Integrity and CRISPR

- CRISPR
  - *Cas* (CRISPR-associated) *proteins*
    - endonuclease activity
    - When virus attaches to host cell, Cas proteins may recognize specific *p*rotospacer *a*djacent *m*otifs (PAMs) in DNA sequences.
    - Cas cleaves viral DNA near PAM and inserts short DNA into the CRISPR region as a spacer, “immunizing” cell.
    - Regions contain short repeats of constant DNA sequences alternating with short variable *spacers* corresponding to “memory” of viral or other foreign DNA. (Figure 10.28)

9.12 Preserving Genomic Integrity and CRISPR

- Immune memory and other aspects of CRISPR
  - When immunized cell encounters same virus, Cas proteins destroy incoming DNA.
  - *Pre-CRISPR RNA* (pre-crRNA) is transcript of CRISPR region containing RNA sequences complementary to repeats and spacers.
  - Viral DNA: crRNA duplexes are cleaved by Cas endonucleases.
  - *Interference* destroys viral genome.

9.12 Preserving Genomic Integrity and CRISPR

- Immune memory and other aspects of CRISPR
  - How does host survive initial invasion long enough to be immunized?
    - probably occurs when incoming virus is inactivated by environment or when restriction enzymes cleave invading DNA
  - Viruses have evolved to avoid CRISPR.
    - mutation of PAM regions
    - production of Cas inhibitors
    - phage-encoded CRISPR in a phage that infects *Vibrio cholerae*

Microbiologie 2: Les 9

IV. Subviral Agents: Viroids

V. Subviral Agents

- 11.12 Viroids
- 11.13 Prions

11.12 Viroids

- Viroids: infectious RNA molecules that lack a protein component
  - small, circular, ssRNA molecules (Figure 11.30)
  - smallest known pathogens (246–399 bp)
  - cause a number of important plant diseases (Figure 11.29)
  - do not infect animals or microorganisms

Potato spindle tuber viroid

Figure 11.29

11.12 Viroids

- Viroid structure and function
  - forms hairpin-shaped ds molecule with closed ends (Figure 11.30), providing stability outside host cell
  - enters plant through wound (*e.g.,* insect, mechanical damage)
  - move between cells through plasmodesmata (thin cytoplasmic strands; Figure 11.31)
  - completely dependent on plant RNA polymerases for replication
  - Catalytic self-cleaving activity releases individual viroids after replication.

Figure 11.30

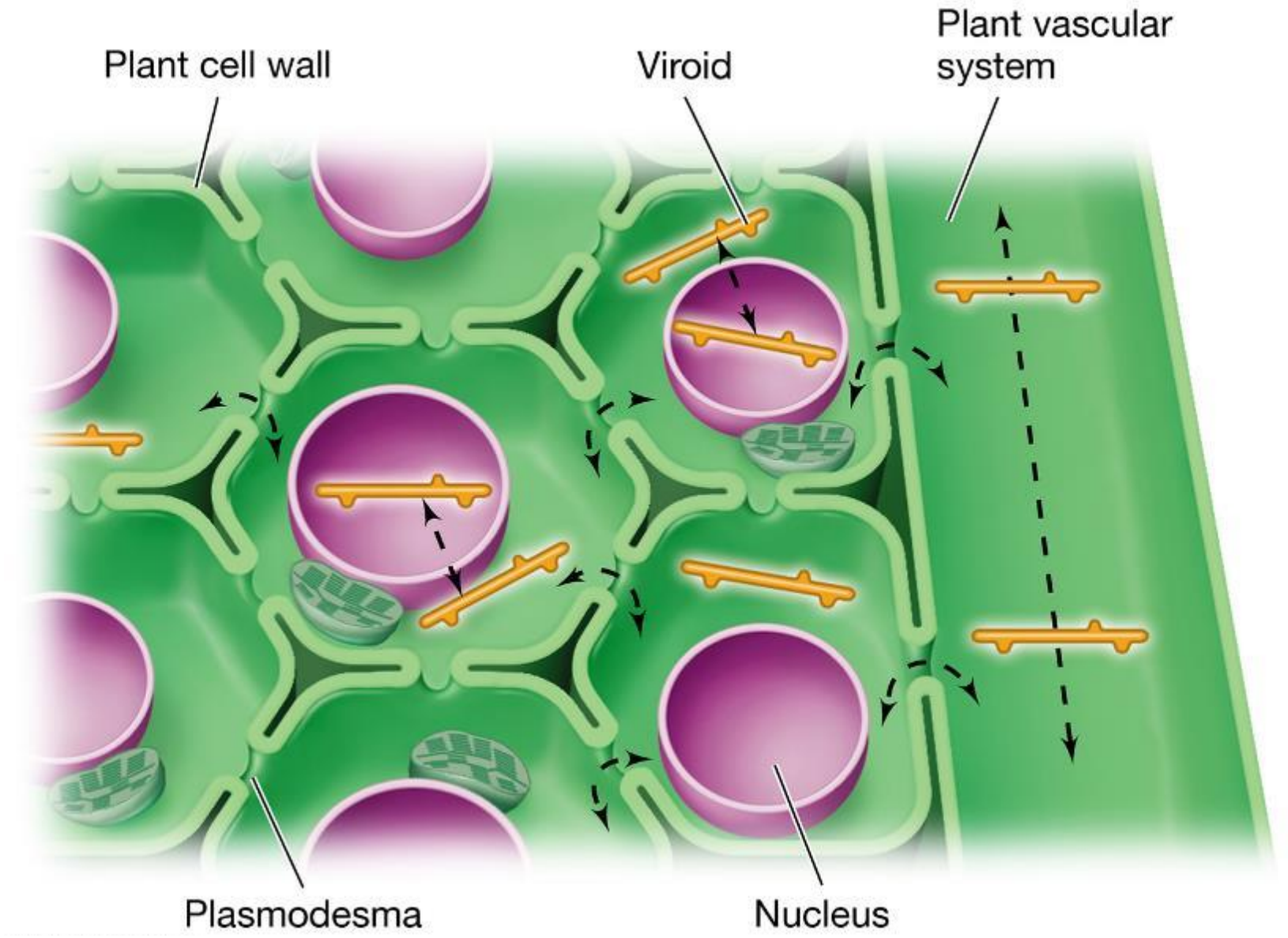


Figure 11.31

11.12 Viroids

- Viroid disease
  - Plants may be asymptomatic or show mild to lethal symptoms.
  - Most symptoms are growth-related.
  - Viroids may mimic or interfere with plant small regulatory RNA.
  - known to yield small interfering RNAs (siRNAs) during replication, may silence/suppress plant genes

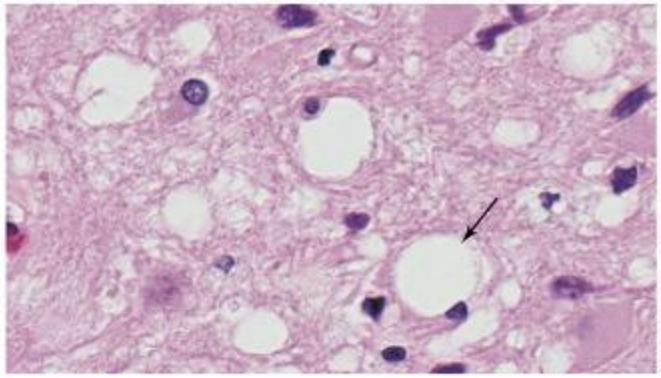
Microbiologie 2: Les 9
IV. Subviral Agents: Prions

11.13 Prions

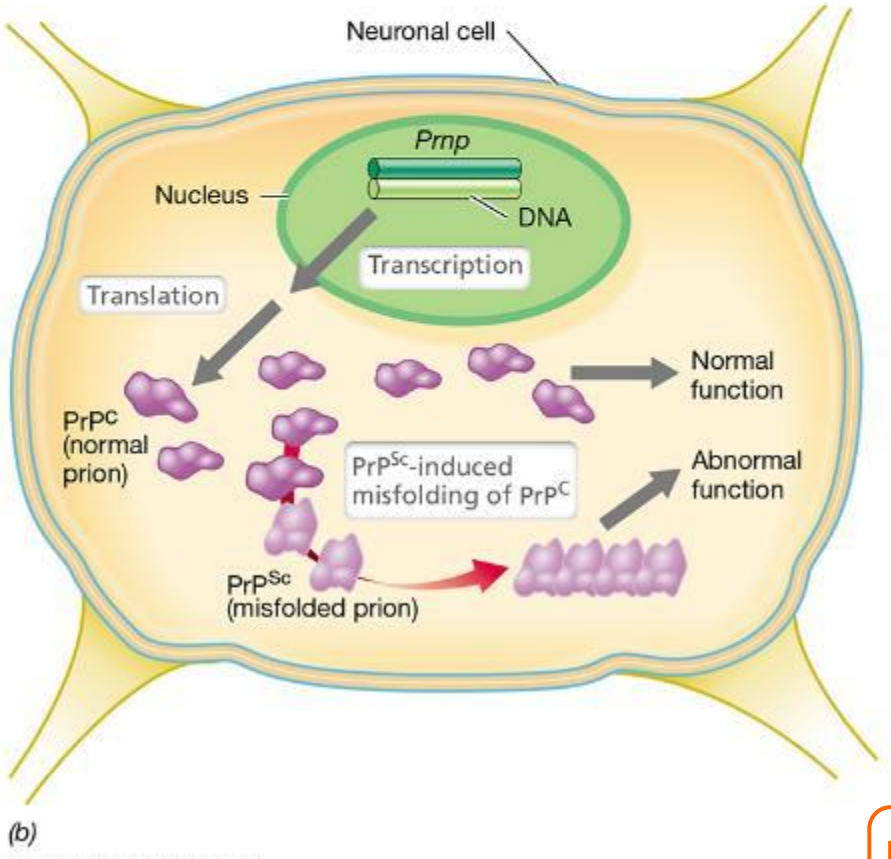
- Infectious proteins whose extracellular form contains no nucleic acid
  - known to cause disease in animals (*transmissible spongiform encephalopathies*), such as scrapie, bovine spongiform encephalopathy/mad cow, chronic wasting disease, kuru, and Creutzfeldt-Jakob disease

11.13 Prions

- Prion proteins and the prion infection cycle
  - Host cell contains gene (*Prnp*) that encodes native form of prion protein (PrP^{C}; prion protein cellular) that is found in neurons/brains of healthy animals. (Figure 10.33*a*)
  - PrP^{Sc} (prion protein scrapie) is pathogenic form with different conformation.
  - Prion proteins are similar but not identical in amino acid sequence.
  - Host range is linked to sequence.
  - PrP^{Sc} promotes conversion of PrP^{C} into pathogenic form.
  - Accumulation and aggregation form insoluble amyloids.
  - destroys brain and other nervous tissue
  - Other amyloid diseases include Alzheimer's, Huntington's, Parkinson's, type 2 diabetes—may or may not be prion diseases.



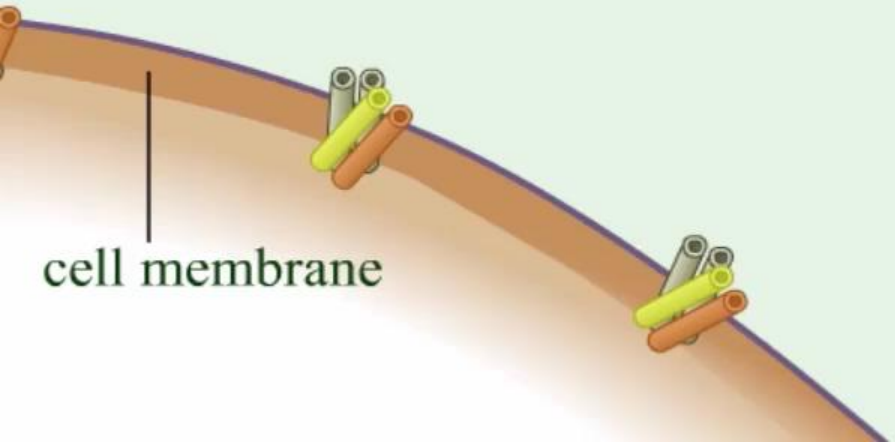
(a)



(b)

Figure 11.32

Prions: Characteristics



11.13 Prions

- Nonpathogenic prions
  - Some fungi have “prions” that do not cause disease and instead adapt to environmental conditions (*e.g.,* altered nutrient utilization, antibiotic resistance, biofilm formation).
  - Example: Yeast URE3 normally represses nitrogen-metabolism genes; URE3 prion allows nitrogen sources to be metabolized.
  - Example: MAVS aggregation upon viral infection in humans triggers interferon production.

EINDE LES 9