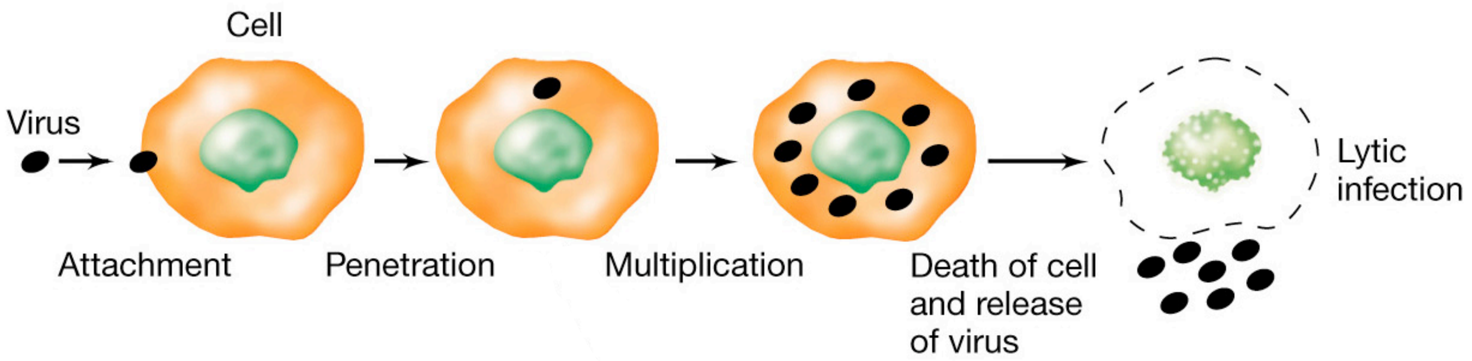
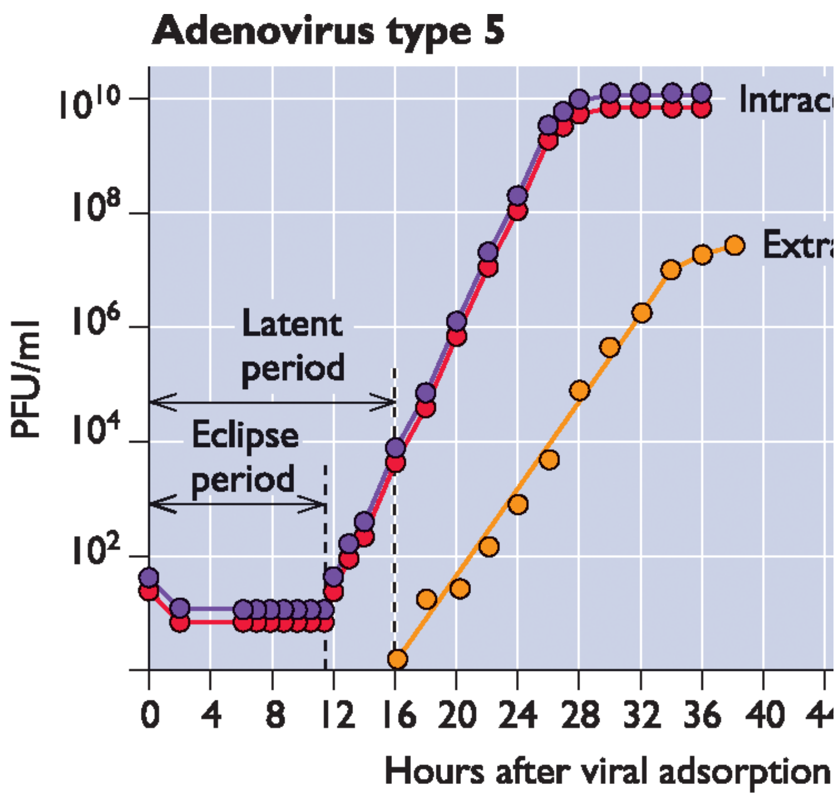
VIROLOGY

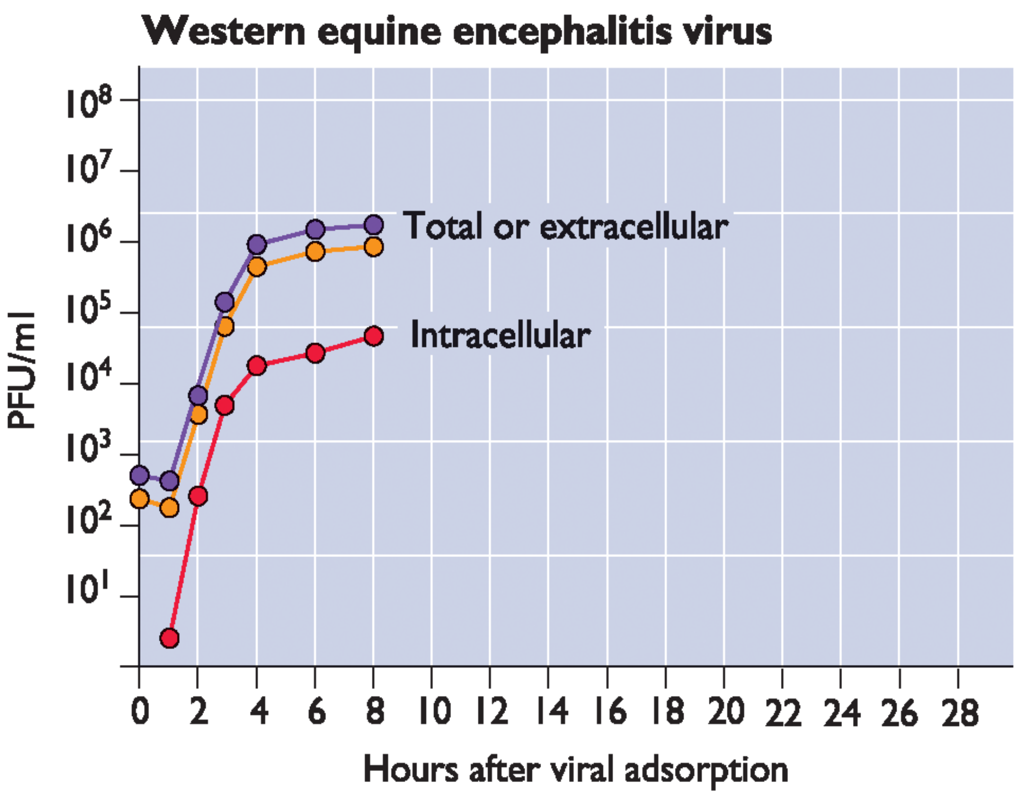
Viral replication



Possible cytopathogenesis of cells
infected with animal viruses

The one-step growth curve is a fundamental feature of a virus



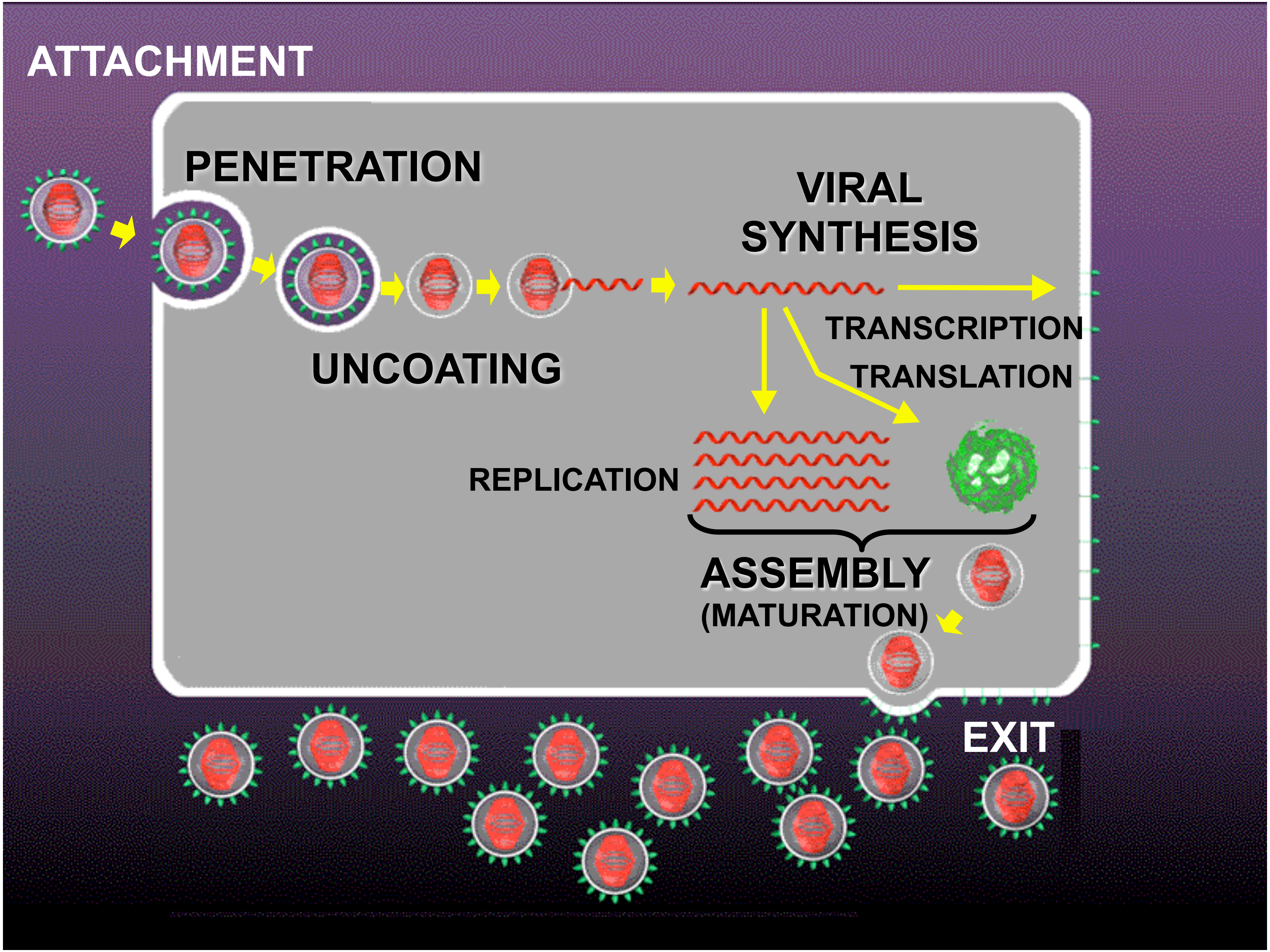


The time interval from infection to plateau represents the time required for a single cycle of growth.

The yield of virus at plateau shows the amount of virus produced per cell during a single round of infection .

The reproductive cycle of animal viruses

- Virus attachment to host cell
- Virus entry into cells
- Transcription, translation and genome replication
- Assembly, exit and maturation of progeny virions


ATTACHMENT
PENETRATION
UNCOATING
VIRAL
SYNTHESIS
TRANSCRIPTION
TRANSLATION
REPLICATION
ASSEMBLY
(MATURATION)
EXIT

Viral replication

virus attachment to host cells

Viral receptors and coreceptors

Table 4.1 Viral receptors and coreceptors[a]

Virus	Receptor	Type of molecule	Coreceptor
Picornaviridae			
Foot-and-mouth disease virus (cell culture adapted)	Heparan sulfate	Glycosaminoglycan	
Foot-and-mouth disease virus	$\alpha_v\beta_3$ (vitronectin receptor)	Integrin	
Encephalomyocarditis virus	Vcam-1	Ig-like	
	Sialylated glycophorin A (for hemagglutination only)	Carbohydrate	
Poliovirus type 1 to 3	Pvr	Ig-like	
Coxsackieviruses A13, A18, A21	Icam-1	Ig-like	
Coxsackievirus A21	Decay-accelerating protein (CD55)	SCR-like (complement cascade)	Icam-1
Coxsackievirus A9	$\alpha_v\beta_3$	Integrin	
Coxsackieviruses B1 to B6	Car (coxsackievirus-adenovirus receptor)	Ig-like	
Coxsackieviruses B1, B3, B5	CD55	SCR-like (complement cascade)	$\alpha_v\beta_6$ integrin
Echoviruses 1 and 8	$\alpha_2\beta_1$ integrin (Vla-2)	Integrin	β_2 microglobulin
Echovirus 22	$\alpha_v\beta_3$ (vitronectin receptor)	Integrin	
Echoviruses 3, 6, 7, 11 to 13, 20, 21, 24, 29, 33	CD55	SCR-like (complement cascade)	β_2 microglobulin
Enterovirus 70	CD55	SCR-like (complement cascade)	
Bovine enterovirus	Sialic acid	Carbohydrate	
Hepatitis A virus	HAVCr-1	Ig-like, mucin-like	
Major group rhinoviruses (91 serotypes)	Icam-1	Ig-like	
Minor group rhinovirus (10 serotypes)	Low-density lipoprotein receptor protein family	Signaling receptor	
Rhinovirus 87	Sialic acid	Carbohydrate	
Coronaviridae			
Mouse hepatitis virus	Bgp (biliary glycoprotein)	Ig-like	
Human coronavirus 229E	Aminopeptidase N	Protease	
Transmissible gastroenteritis virus	Aminopeptidase N	Protease	
Human coronavirus OC43	Sialic acid	Carbohydrate	
Bovine coronavirus	Sialic acid	Carbohydrate	
Togaviridae			
Semliki Forest virus	Major histocompatibility class I molecule	Ig-like	
Sindbis virus	High-affinity laminin receptor	Integrin	
	Heparan sulfate	Glycosaminoglycan	
Dengue virus	Heparan sulfate	Glycosaminoglycan	
Rhabdoviridae			
Rabies virus	Nicotinic acetylcholine receptor	Neurotransmitter receptor	
	Neural cell adhesion molecule CD56	Ig-like	
	Low-affinity nerve growth factor receptor	Tnf receptor protein superfamily	
Paramyxoviridae			
Measles virus	Membrane cofactor protein, CD46	Complement-regulating protein	
Sendai virus	Sialic acid	Carbohydrate	
	Asialoglycoprotein receptor Gp-2	Transport protein (receptor-mediated endocytosis)	
Orthomyxoviridae			
Influenza A and B viruses	Sialic acids (*N*-acetyl neuraminic acid)	Carbohydrate	
Influenza C virus	Sialic acids (9-*O*-acetyl neuraminic acid)	Carbohydrate	
Arenaviridae			
Lymphocytic choriomeningitis virus	α-Dystroglycan	Laminin receptor	
Lassa virus	α-Dystroglycan	Laminin receptor	

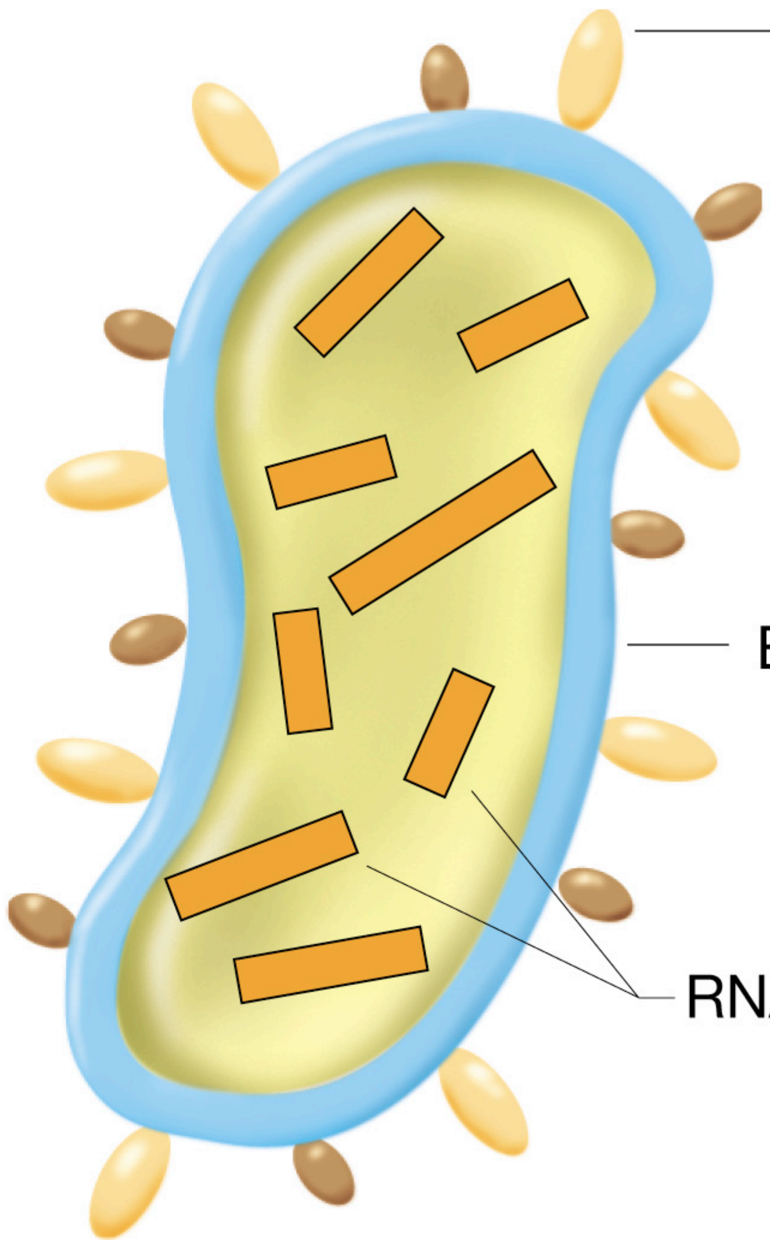
(contin

Table 4.1 Viral receptors and coreceptors[a] *(continued)*

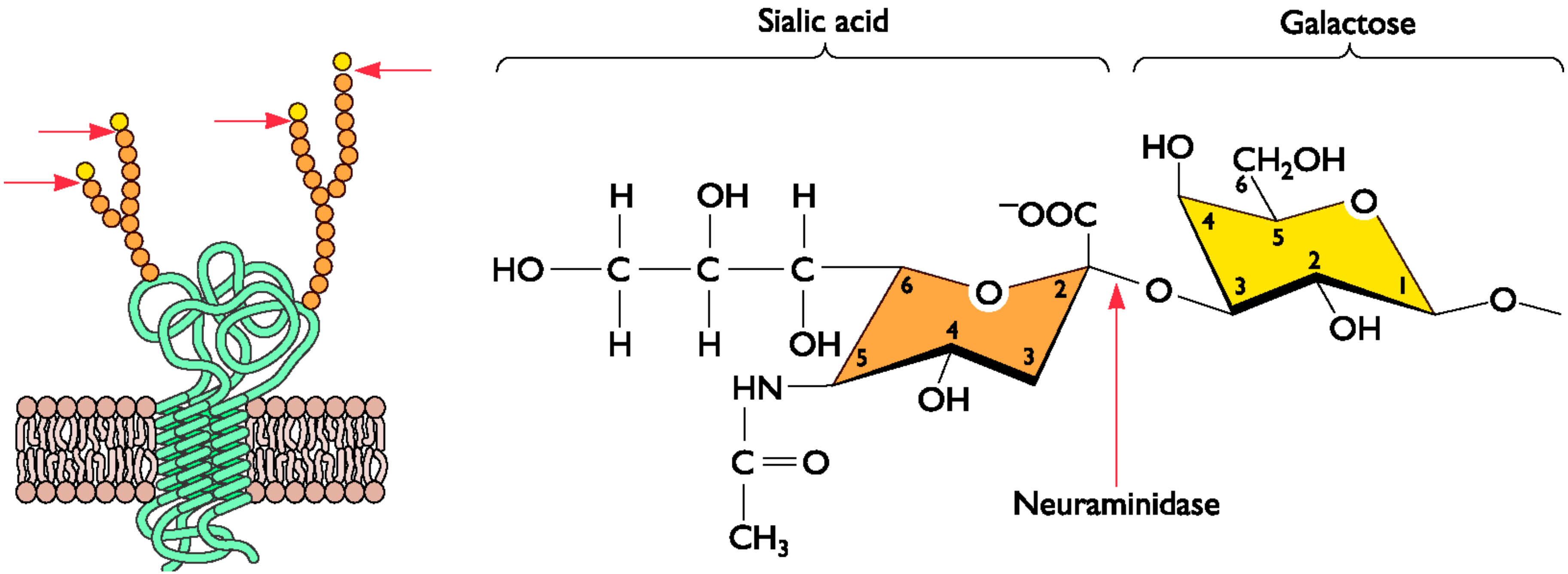
Virus	Receptor	Type of molecule	Coreceptor
Reoviridae			
Reovirus	Sialic acids	Carbohydrate	
Group A porcine rotavirus	Sialic acids	Carbohydrate	
Retroviridae			
Human immunodeficiency virus type 1	CD4	Ig-like	Chemokine receptors (Ccr5, Cxcr4, Ccr3)
	Galactosylceramide	Glycolipid	
Human immunodeficiency virus type 2	CD4	Ig-like	Chemokine receptors
	Cxcr4	7-transmembrane superfamily	
Simian immunodeficiency virus	CD4	Ig-like	Chemokine receptors
Gibbon ape leukemia virus	Glvr1	Sodium-dependent phosphate transport protein	
Feline leukemia virus B	Glvr1	Sodium-dependent phosphate transport protein	
Amphotropic murine leukemia virus	Ram-1	Sodium-dependent phosphate transport protein	
Ecotropic murine leukemia virus	Cat	Cationic amino acid transport protein	
Subgroup A avian leukosis and sarcoma virus	Tva	Low-density lipoprotein receptor protein family	
Subgroup B and D avian leukosis and sarcoma viruses	Car1	Tnf receptor family protein superfamily	
Bovine leukemia virus	BLVRcp 1	Unknown	
Feline immunodeficiency virus	Cxcr4	7-transmembrane superfamily	
Visna virus	Major histocompatibility complex class II molecule	Ig-like	
Parvoviridae			
Bovine parvovirus	Sialic acids	Carbohydrate	
Adeno-associated virus type 2	Heparan sulfate	Glycosaminoglycan	$\alpha_v\beta_5$ integrin
Papovaviridae			
Simian virus 40	Major histocompatibility class I molecule	Ig-like	
Adenoviridae			
Adenovirus subgroups A, C, D, E, F	Car	Ig-like	α_v integrins
Adenovirus type 5 (subgroup C)	Major histocompatibility class II molecule	Ig-like	α_v integrins
Adenovirus type 2 (subgroup C)	$\alpha_M\beta_2$	Integrin	α_v integrins
Adenovirus type 9 (subgroup D)	α_v integrins	Integrin	
Herpesviridae			
Herpes simplex type 1	Heparan sulfate	Glycosaminoglycan	HveA, Prr1
Herpes simplex type 2	Heparan sulfate	Glycosaminoglycan	HveA, Prr1, Prr2
Pseudorabies virus	Heparan sulfate	Glycosaminoglycan	Pvr, Prr1, Prr2
Bovine herpesvirus 1	Heparan sulfate	Glycosaminoglycan	Pvr, Prr1
Human herpesvirus 7	CD4	Ig-like	
Epstein-Barr virus	Complement receptor Cr2 (CD21)	SCR-like (complement cascade)	
Human cytomegalovirus	Heparan sulfate	Glycosaminoglycan	Aminopeptidase N (CD13)
Poxviridae			
Vaccinia virus	Heparan sulfate	Glycosaminoglycan	
	Epidermal growth factor receptor	Signaling receptor	

[a]The name of the receptor and the type of molecule are listed for selected viruses. When coreceptors have been identified, they are listed; a blank in the coreceptor column indicates that none have been identified to date. Abbreviations: Vcam, vascular cell adhesion molecule; Prr1, Prr2, Pvr-related proteins 1 and 2; SCR, short consensus repeat; Ig, immunoglobulin; Tnf, tumor necrosis factor; Car1, cytopathic avian leukosis and sarcoma virus receptor; Car, coxsackievirus and adenovirus receptor; HveA, herpesvirus entry mediator.

Influenza virus structure



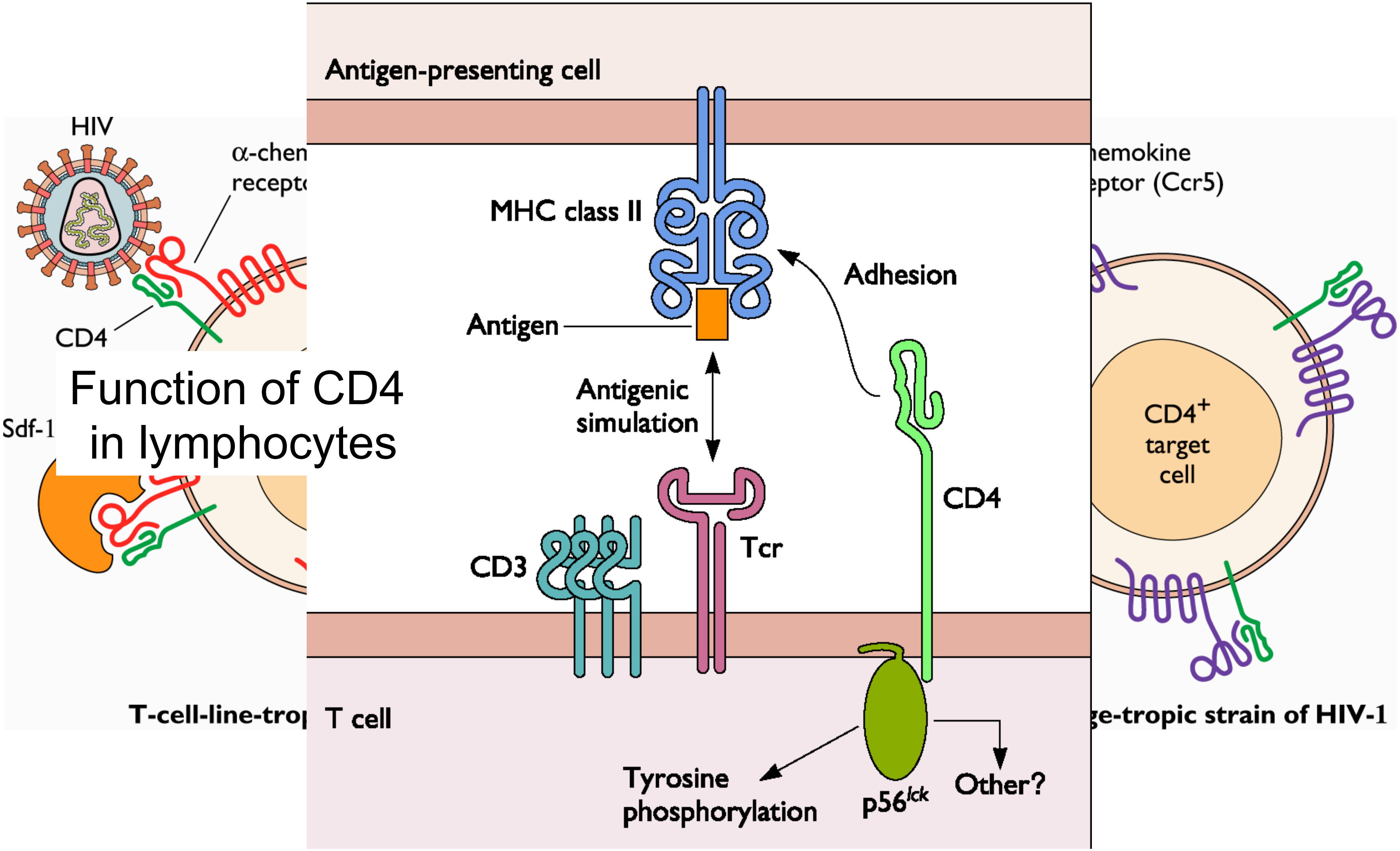
Sialic acid receptors for influenza virus



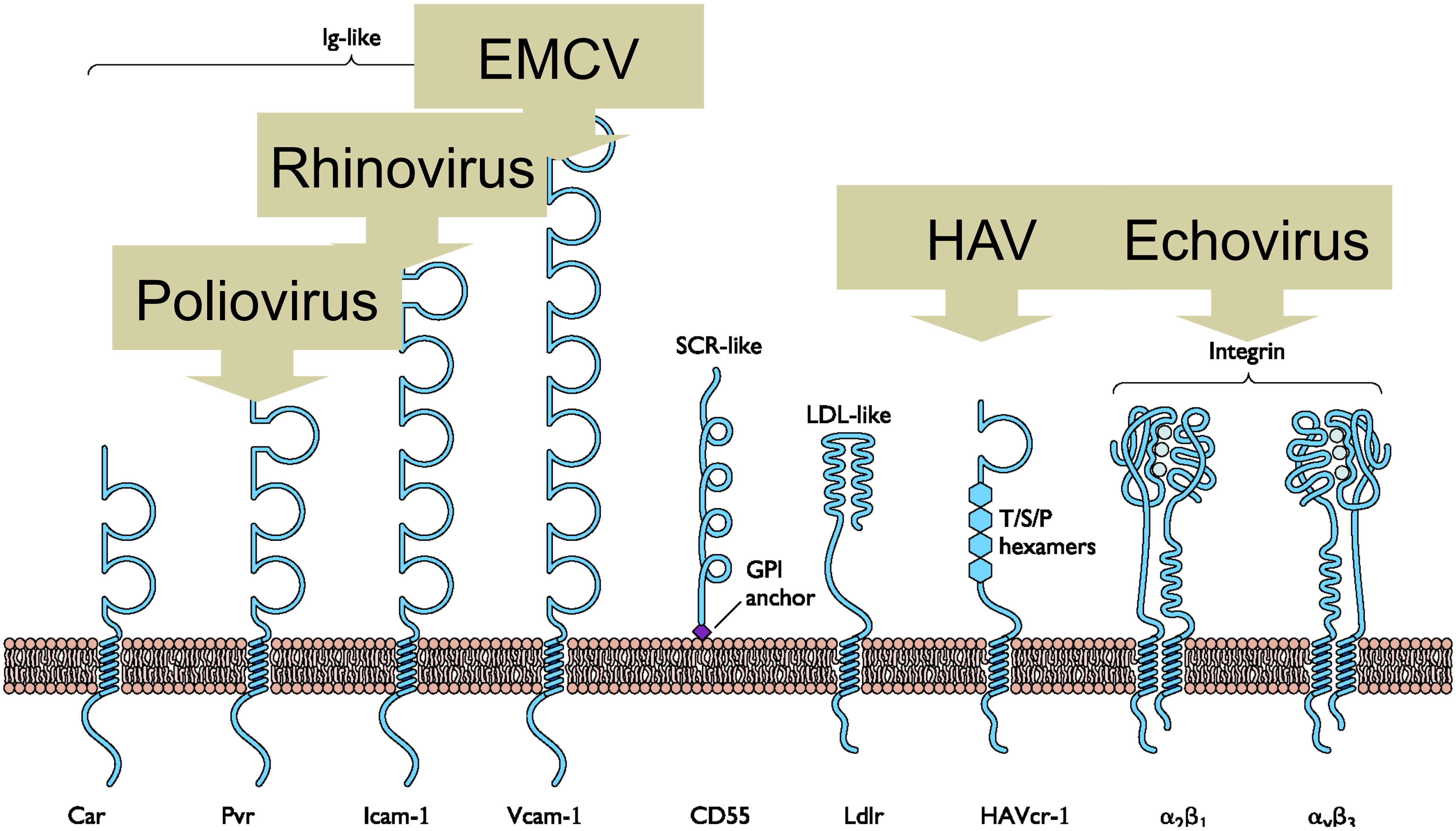
The interaction of influenza virus with sialic acid moieties is mediated by the viral surface glycoprotein **hemagglutinin** (**HA**)

Receptor and coreceptors for macrophage/monocyte- and T-cell- tropic strains of HIV-1

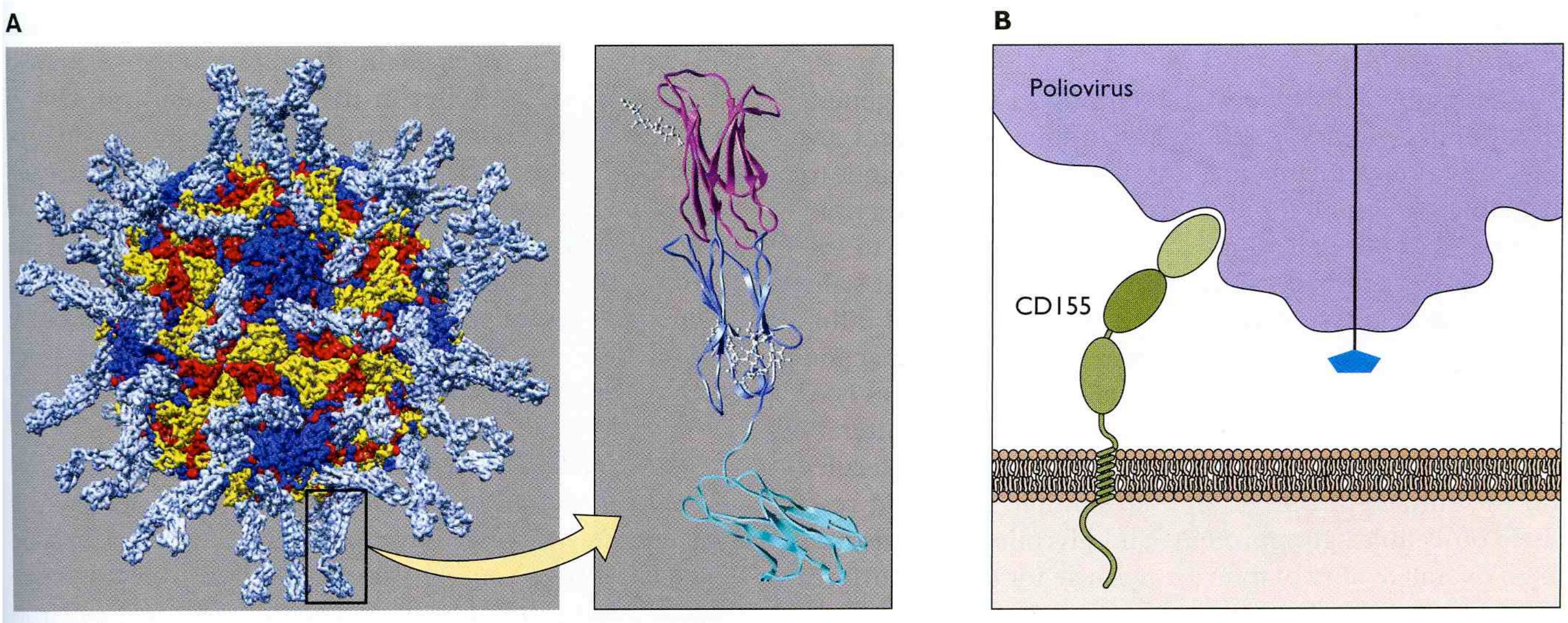
Function of CD4 in lymphocytes



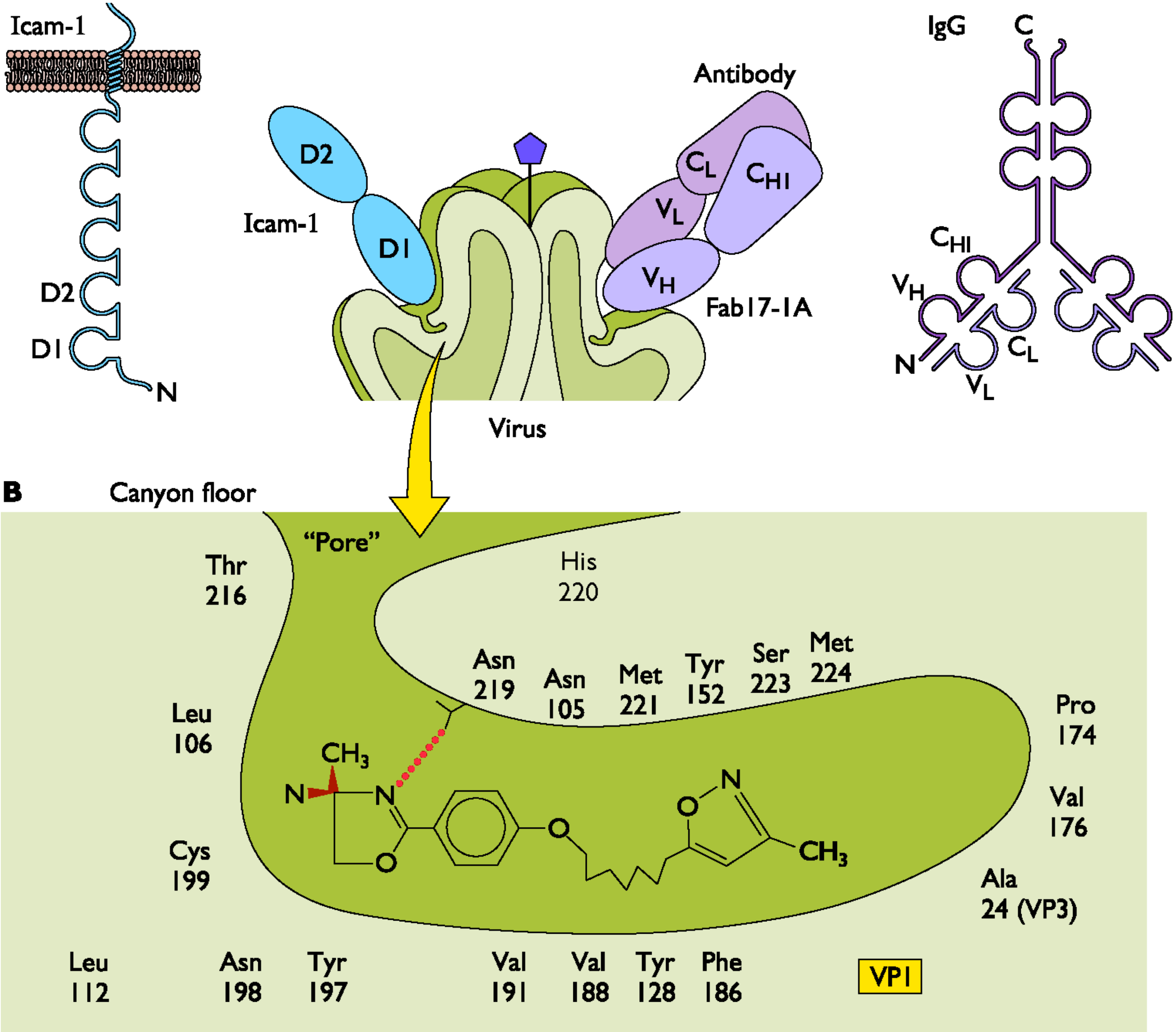
Cell receptors for picornaviruses

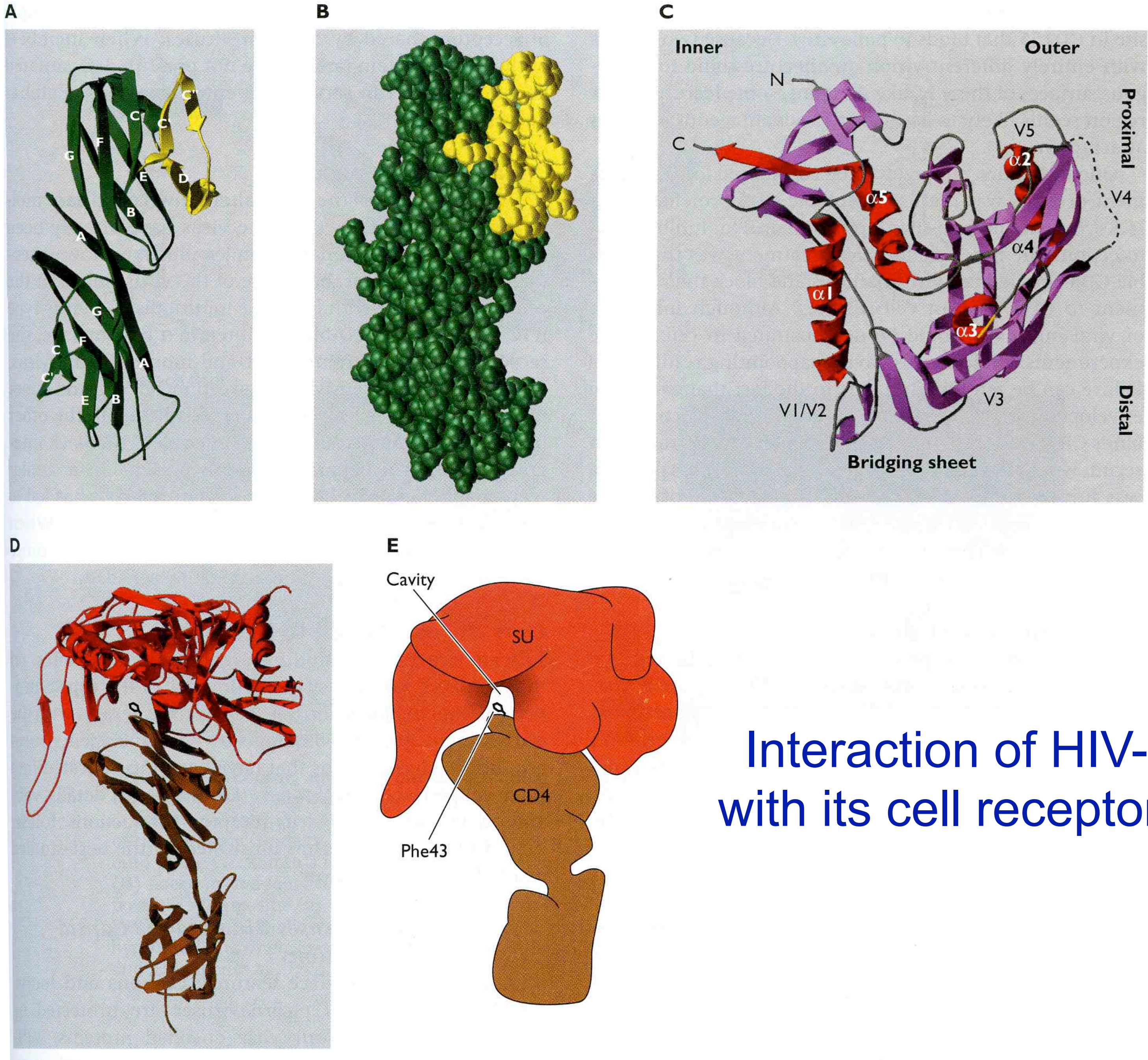


Poliovirus-receptor interactions



Receptor, antibody, and drug binding to the rhinovirus capsid



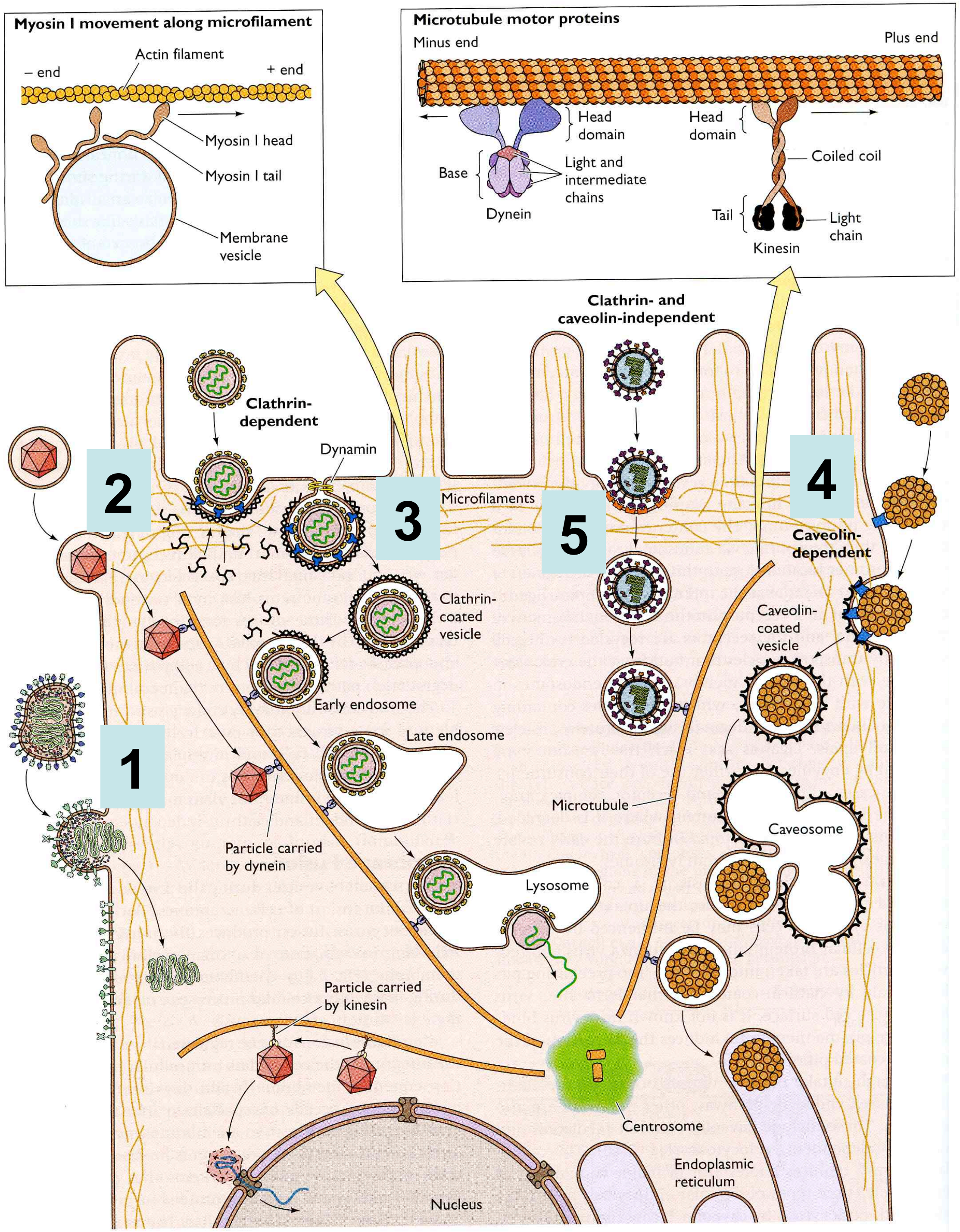


Interaction of HIV-1 SU with its cell receptor, CD4

Viral replication

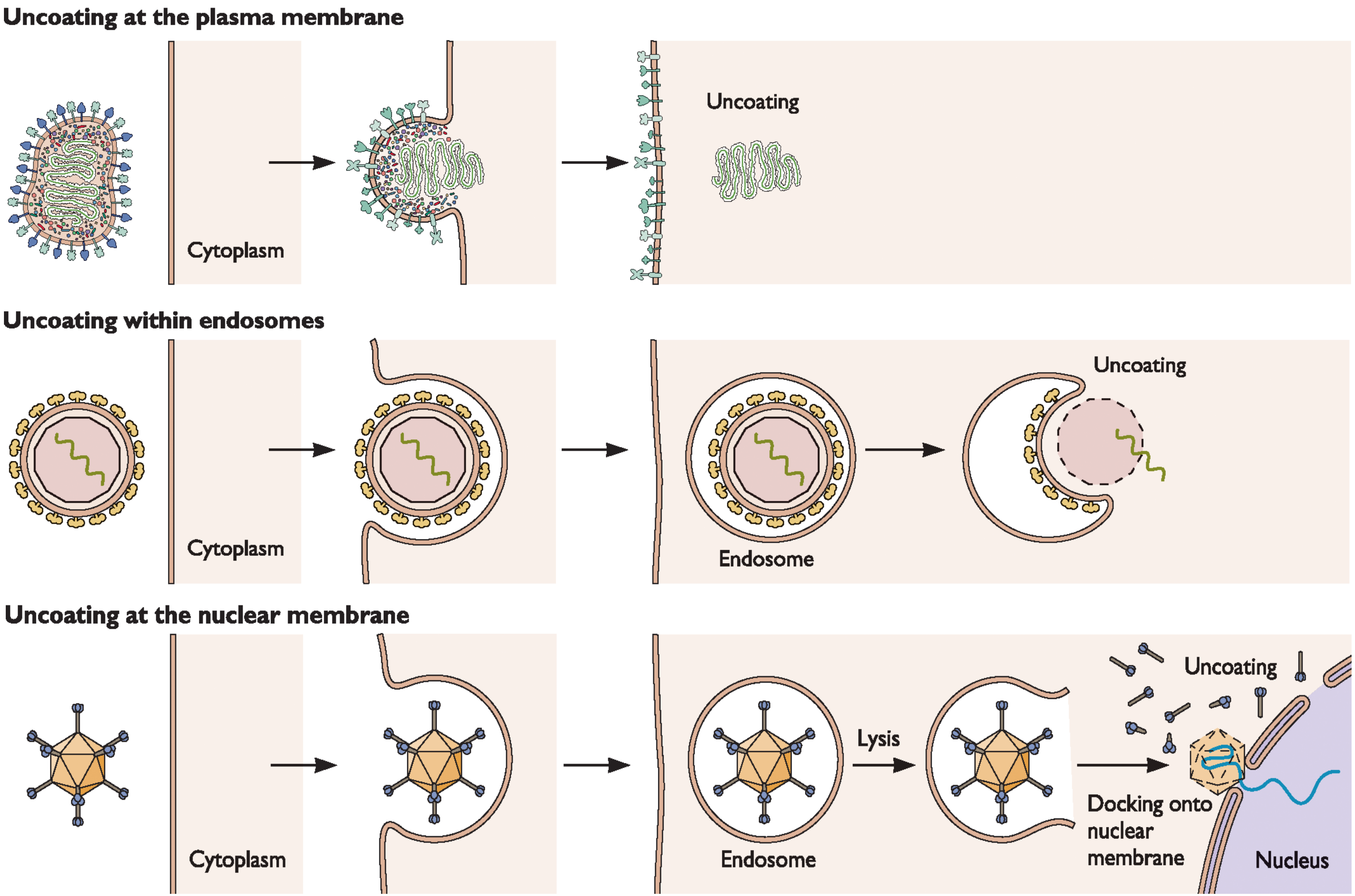
virus entry into host cells

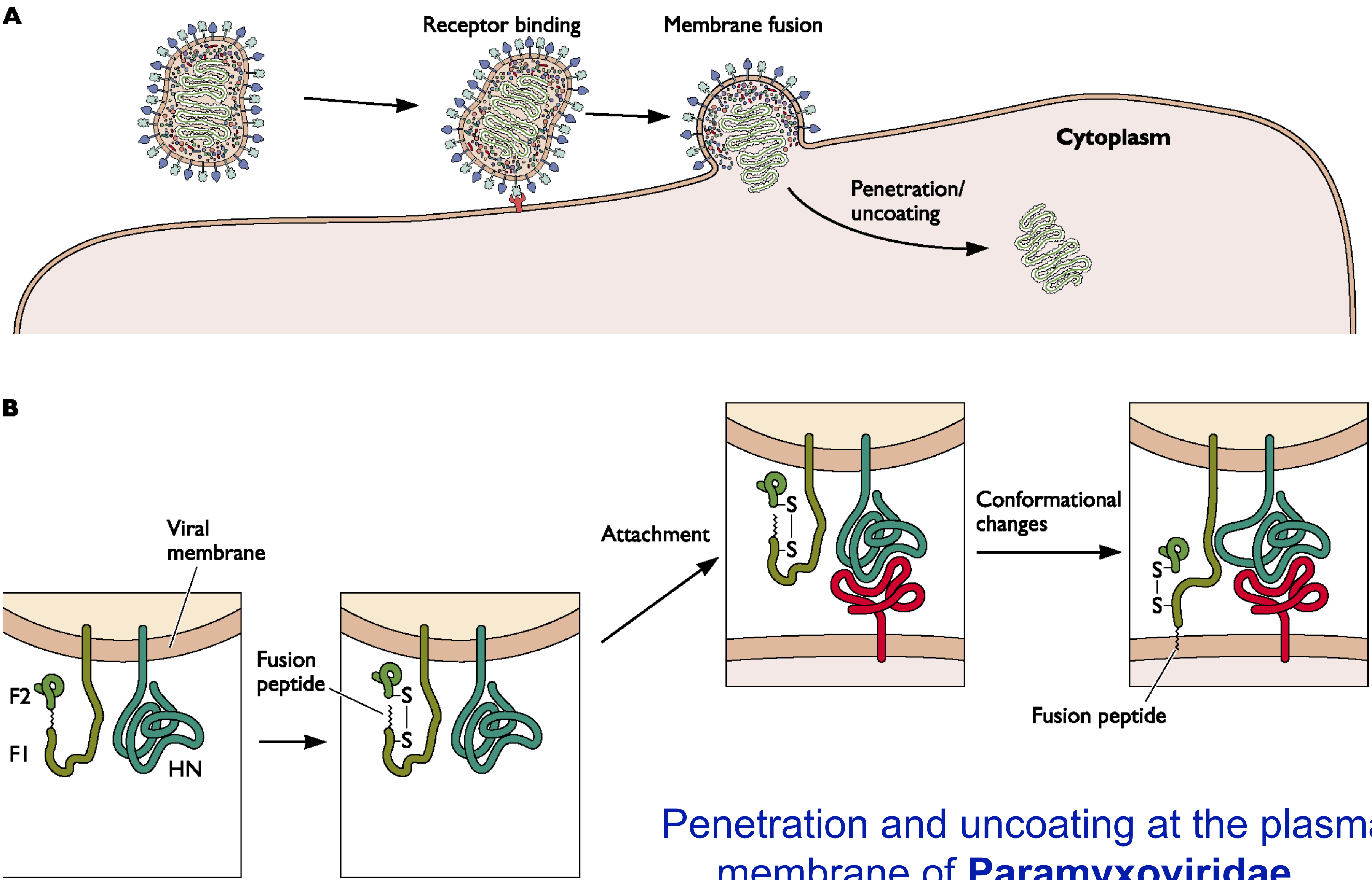
Virus entry strategies



1. Entry and uncoating at the **plasma membrane**
2. Entry at the **plasma membrane** and uncoating at the **nuclear membrane**
3. Entry by **clathrin-dependent** endocytosis
4. Entry by **caveolin-dependent** endocytosis (raft-mediated)
5. Entry **clathrin- and caveolin-independent** endocytosis

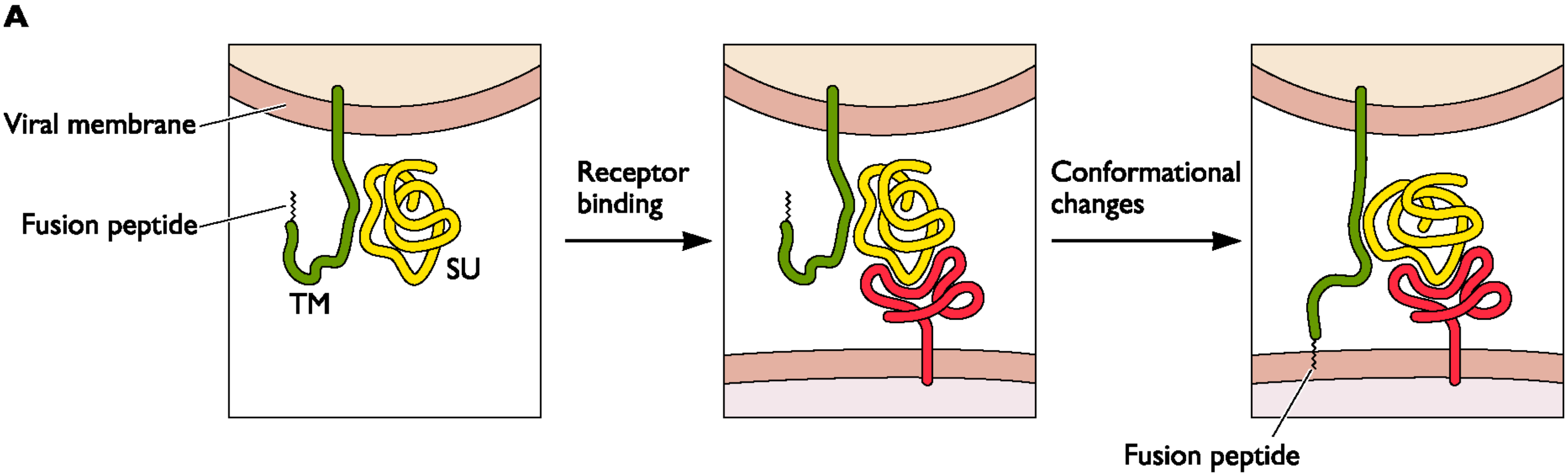
Three entry and uncoating strategies



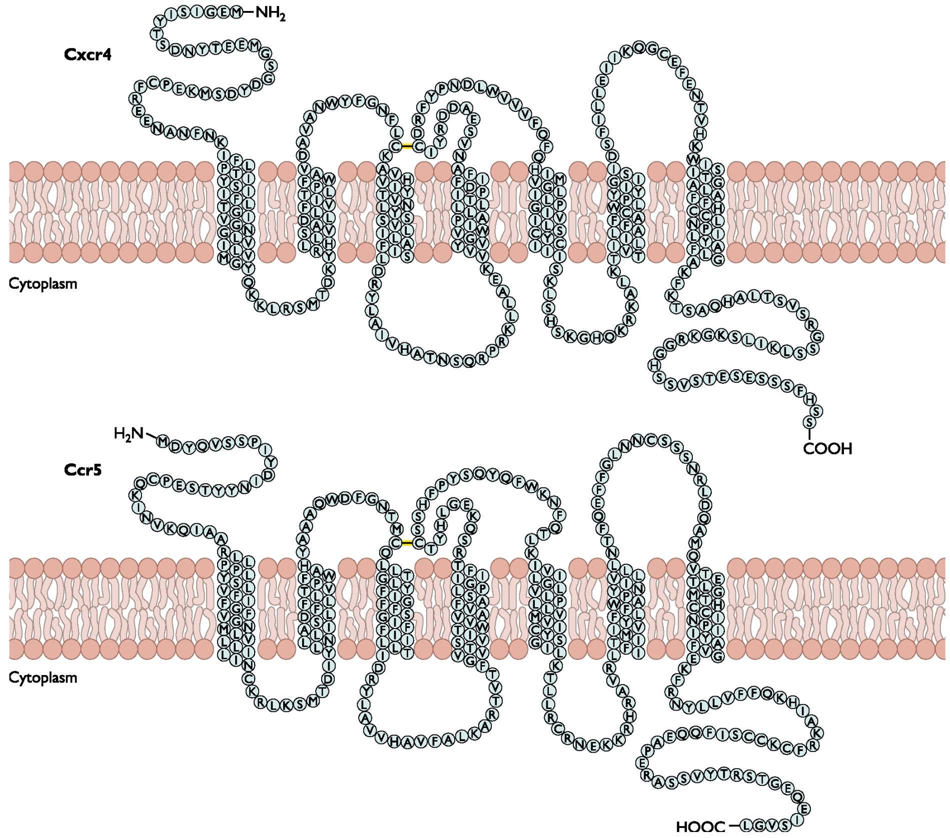


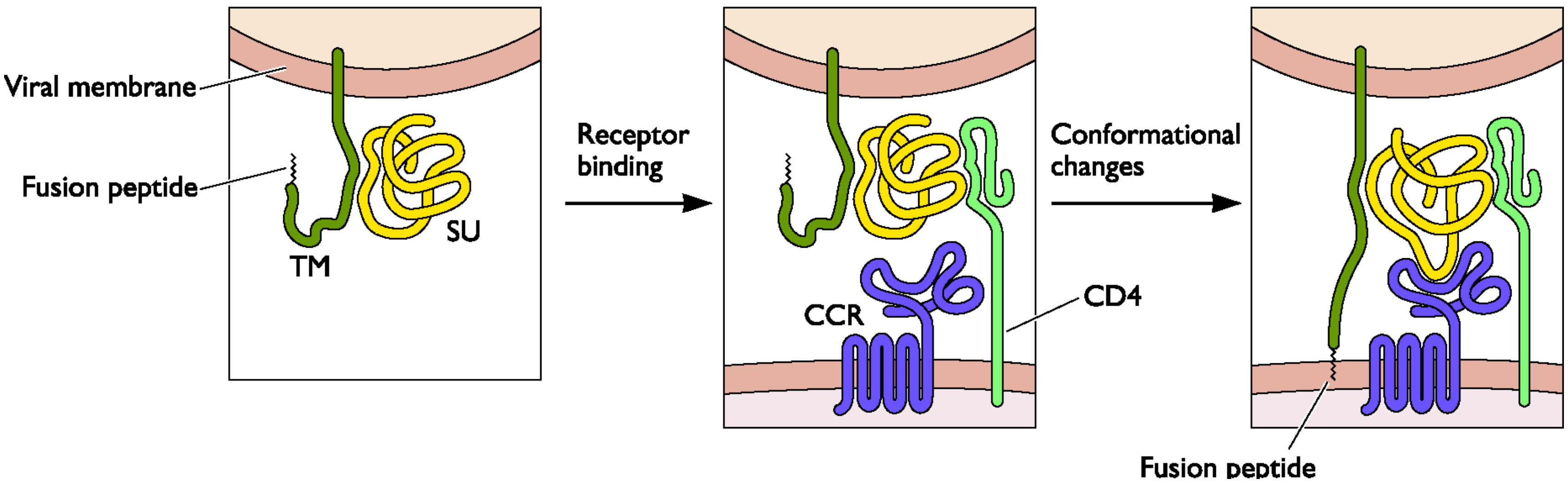
Penetration and uncoating at the plasma membrane of **Paramyxoviridae**

Mechanism of retroviral fusion with the plasma membrane

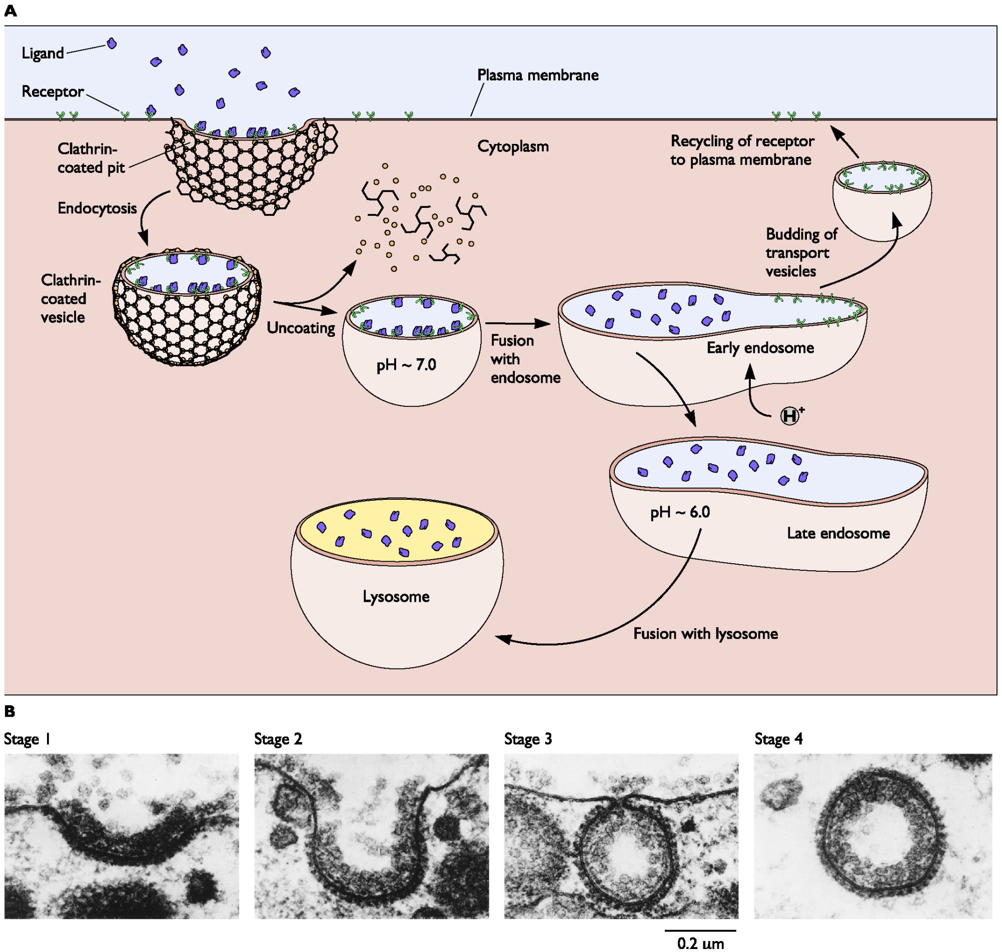


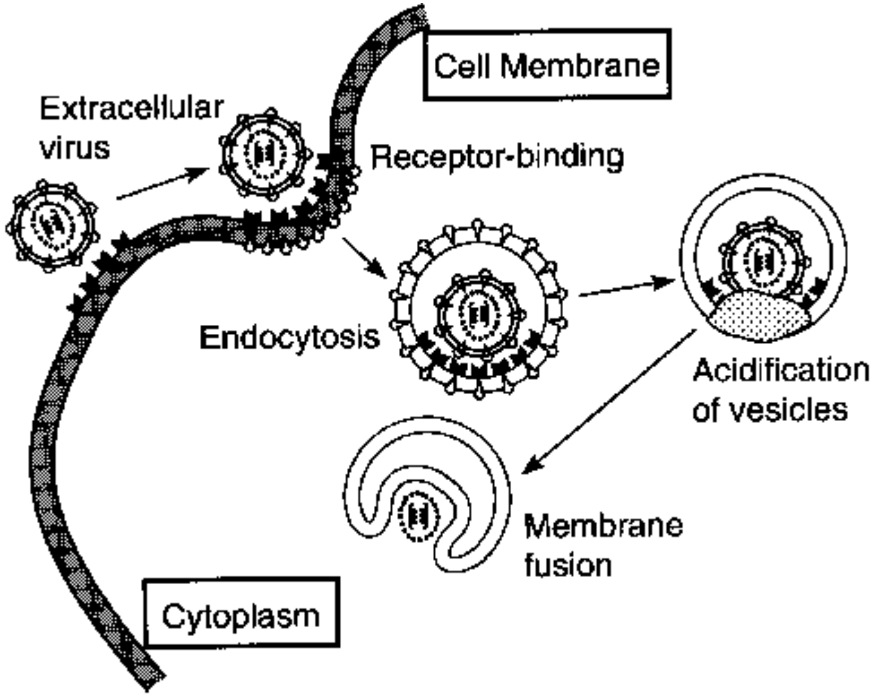
Mechanism of HIV-1 fusion with the plasma membrane



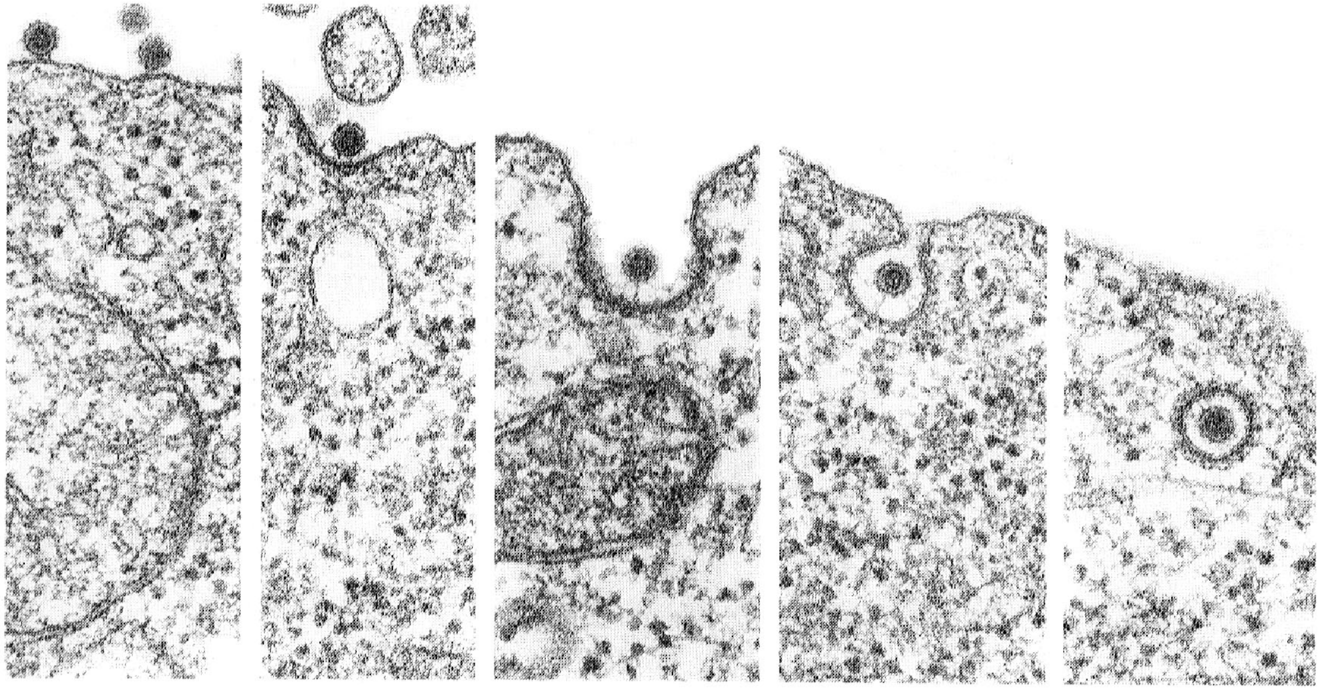


Mechanism of uncoating within endosomes

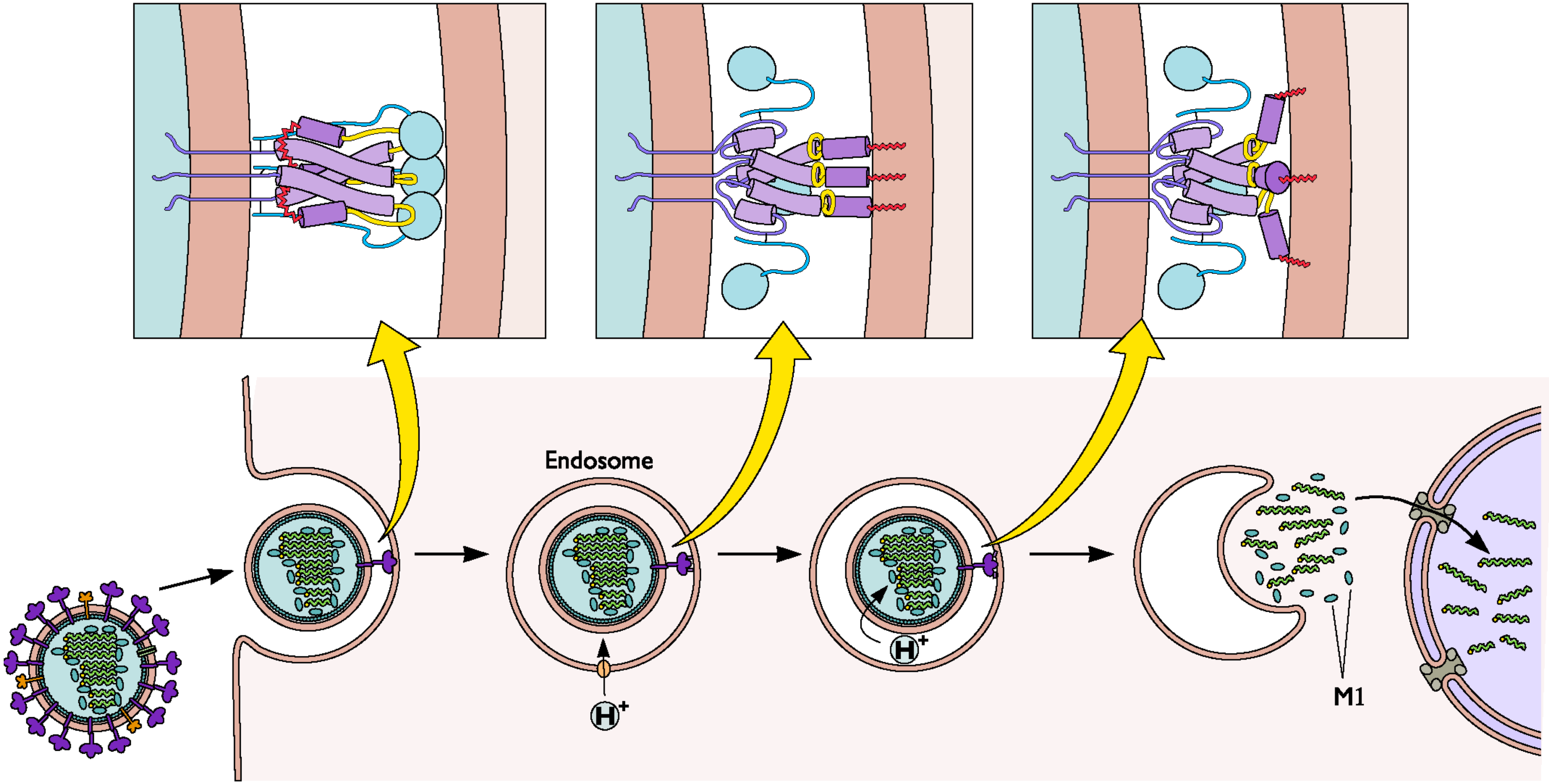




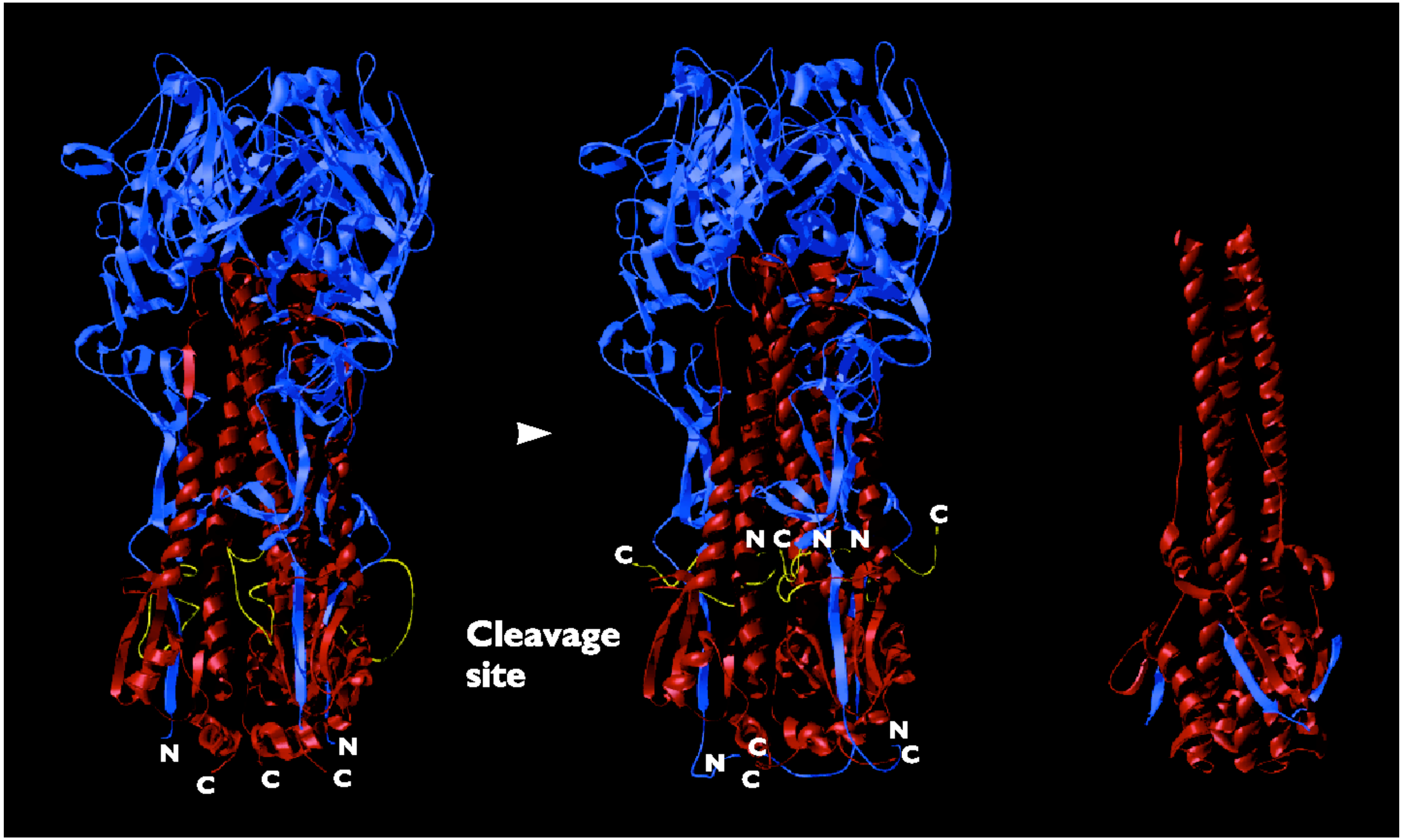
Virus entry via receptor-mediated endocytosis



Influenza virus: an example of virus entry via the clathrin-dependent receptor-mediated endocytic pathway



Cleavage- and low-pH-induced structural changes in the Influenza virus HA

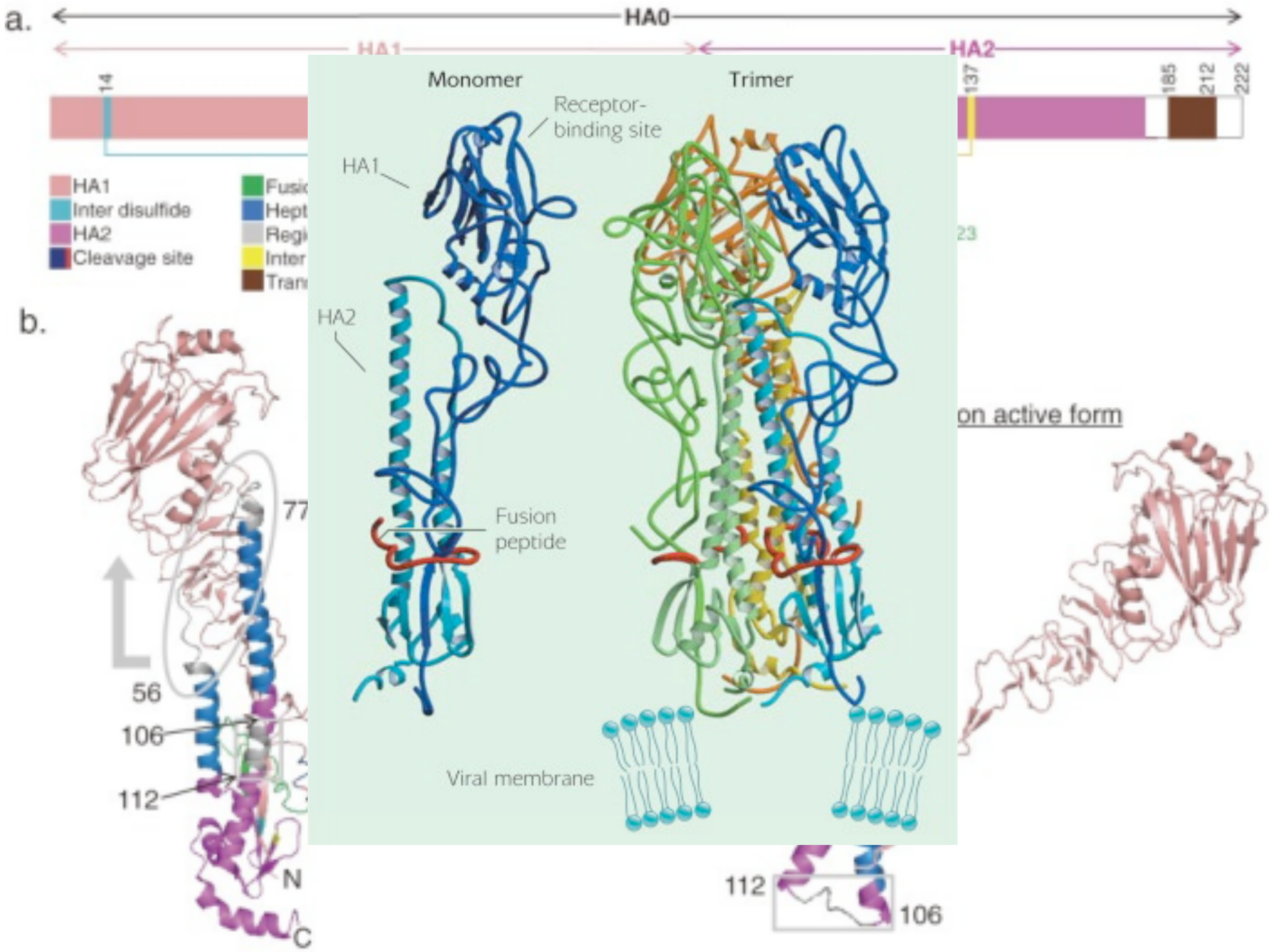


Uncleaved HAO precursor

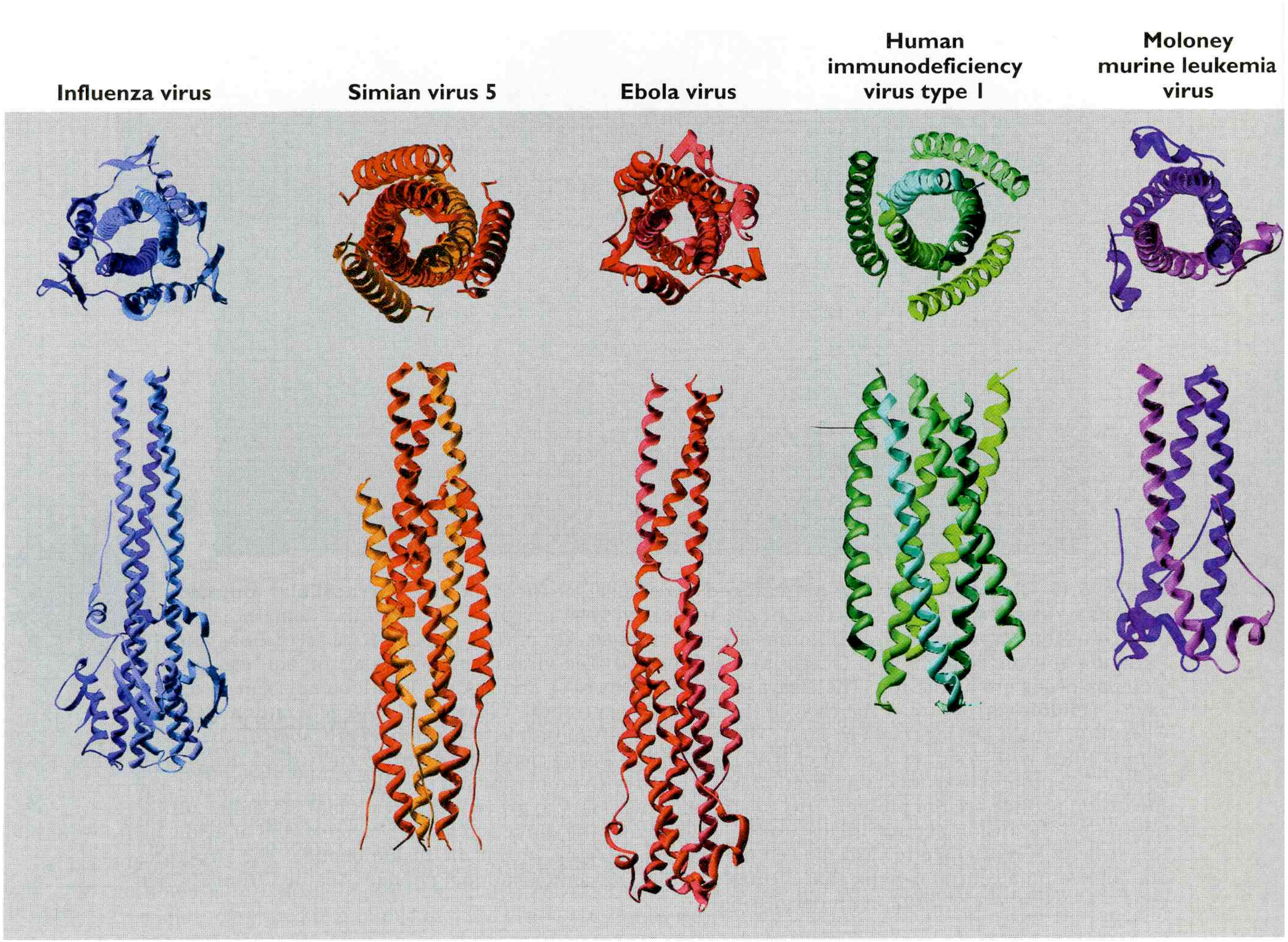
Structure of the HA trimer at neutral pH

Structure of the low pH trimer (only HA2 is shown)

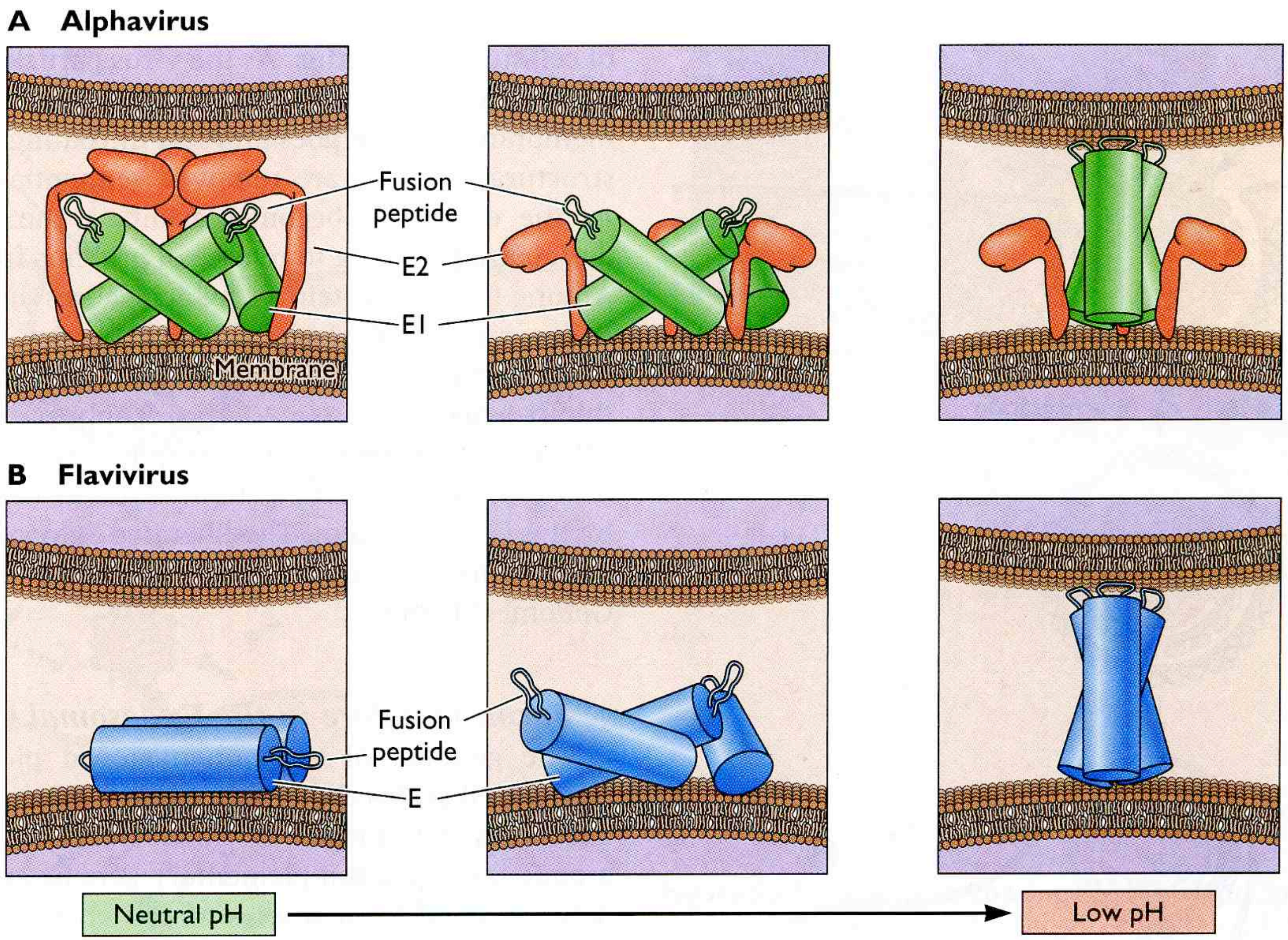
Conformational changes of HA at the pH of membrane fusion



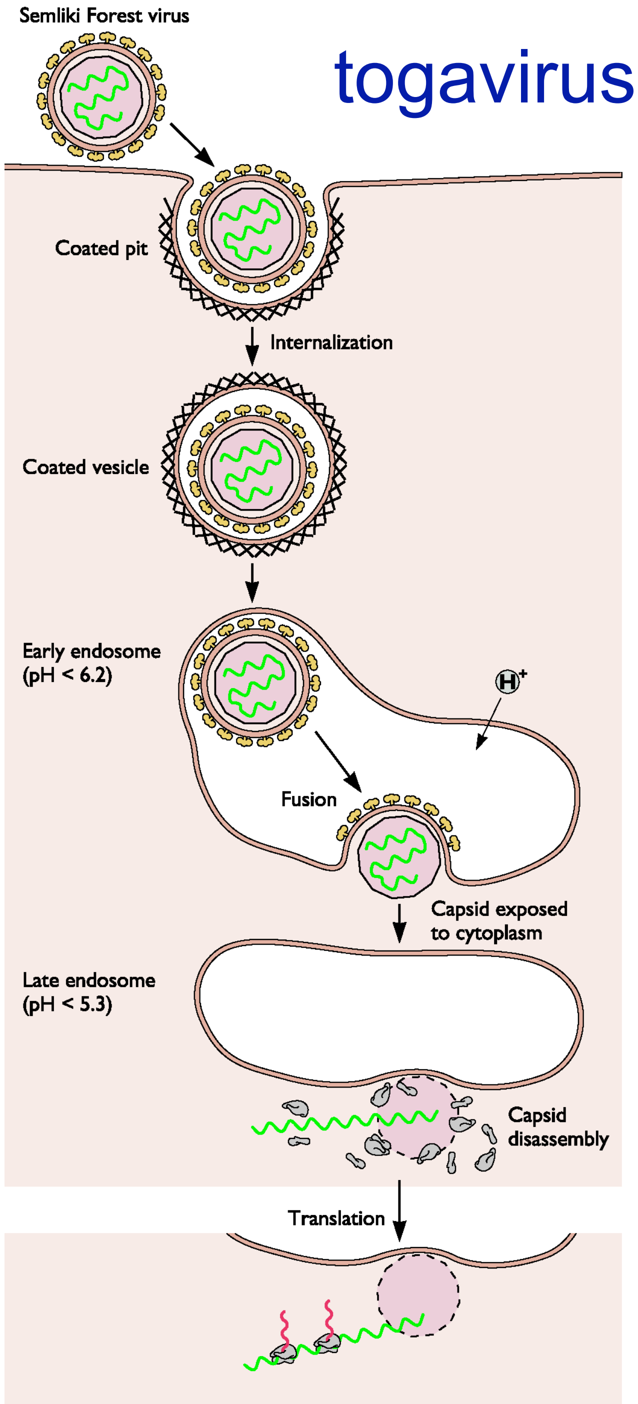
Similarities among five viral fusion protein



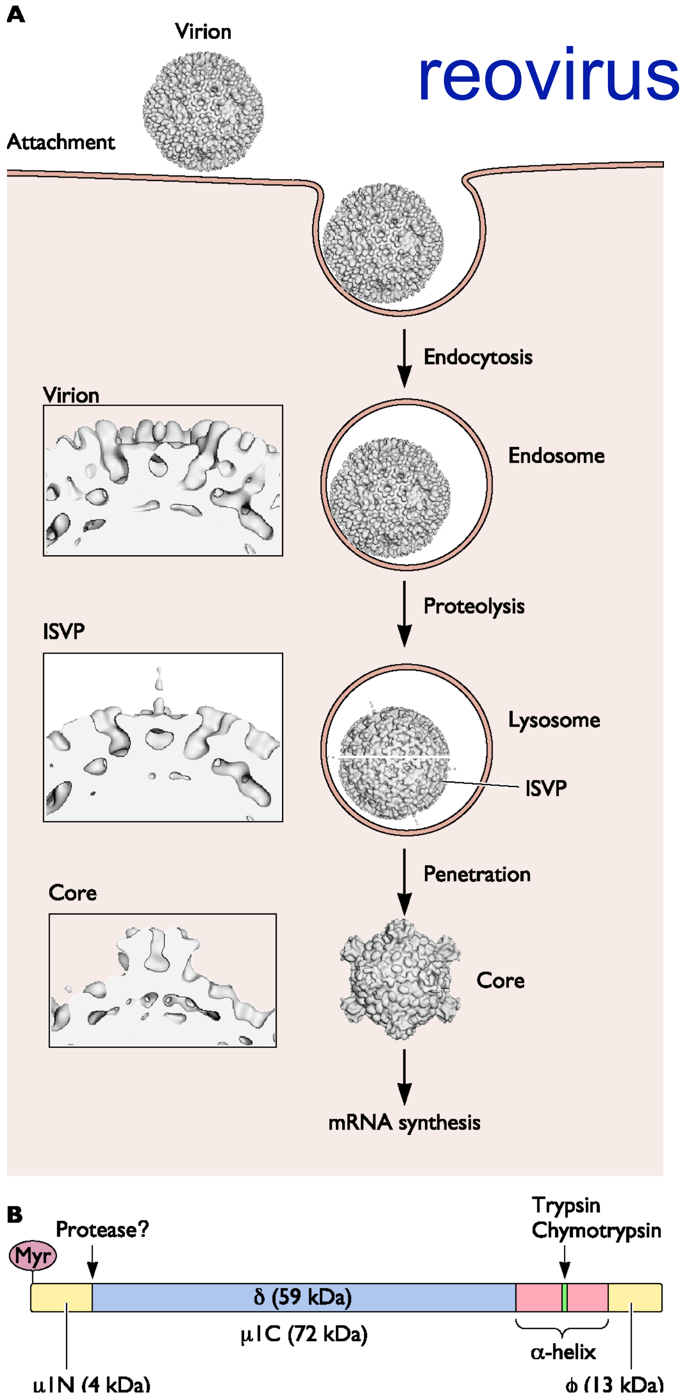
Model for low-pH-induced movement of alphavirus and flavivirus glycoproteins

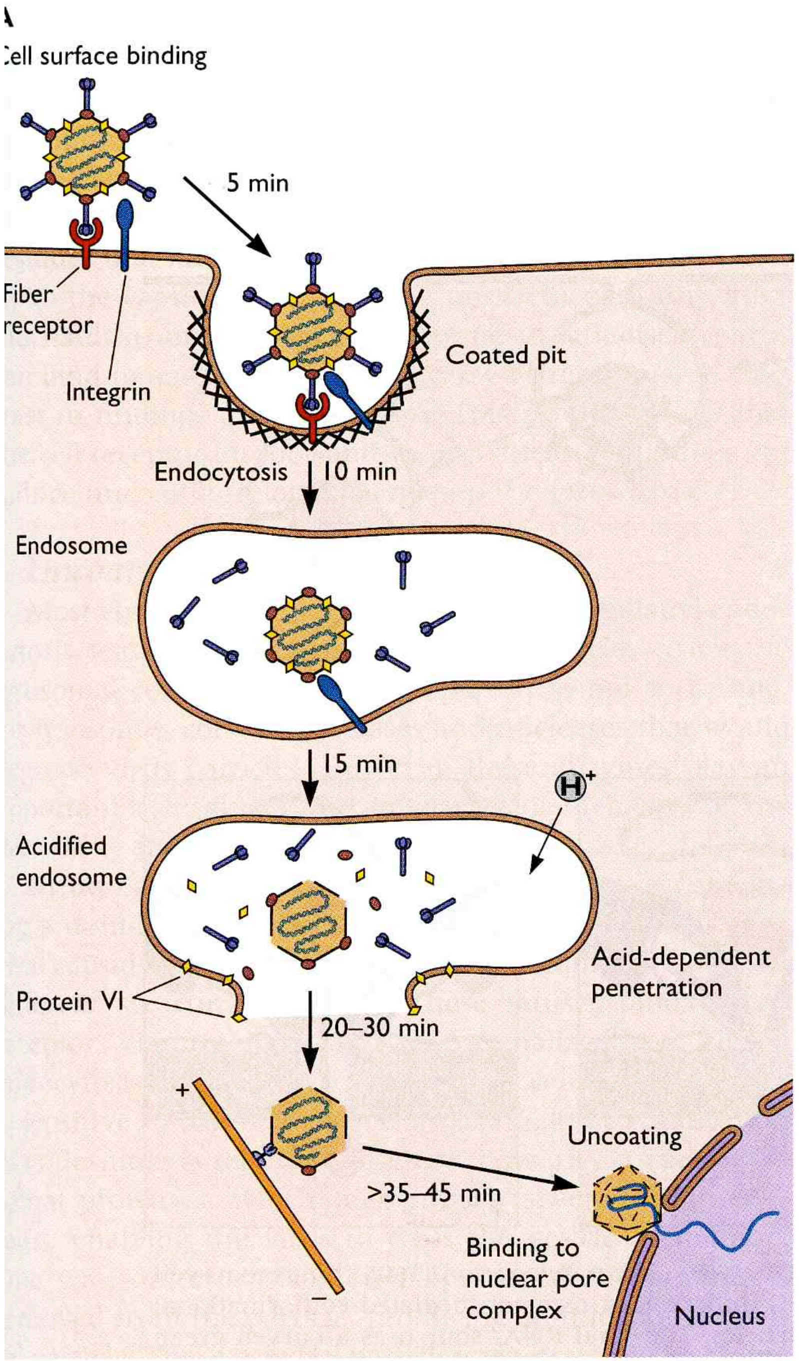


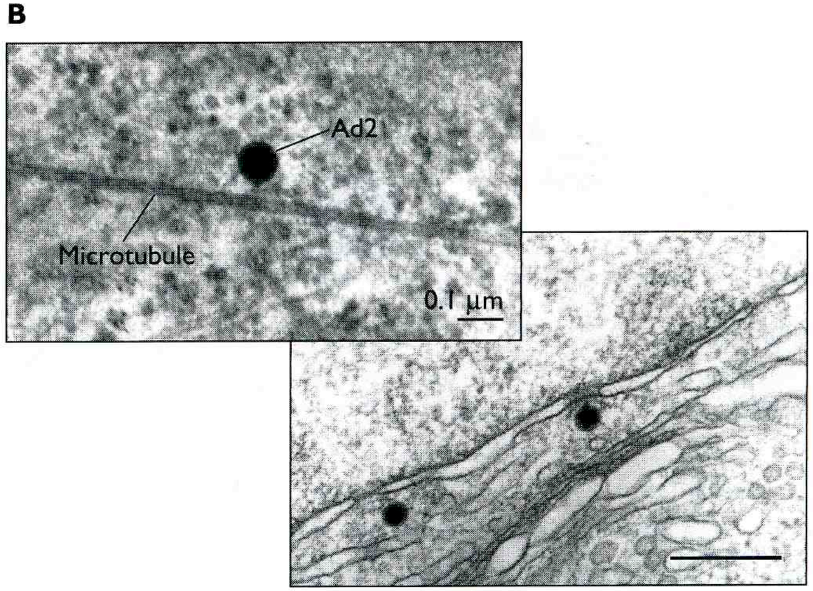
togavirus



reovirus

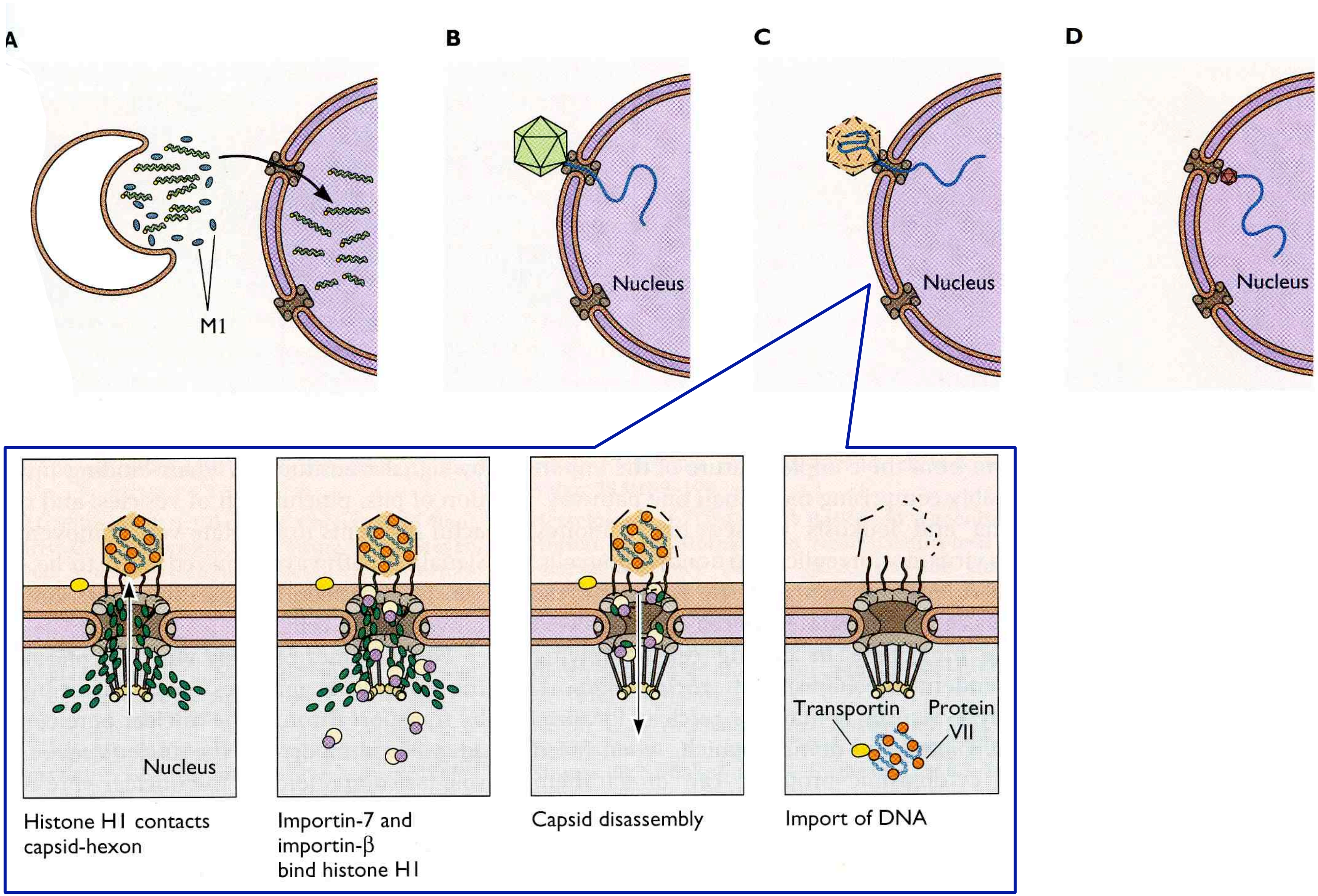




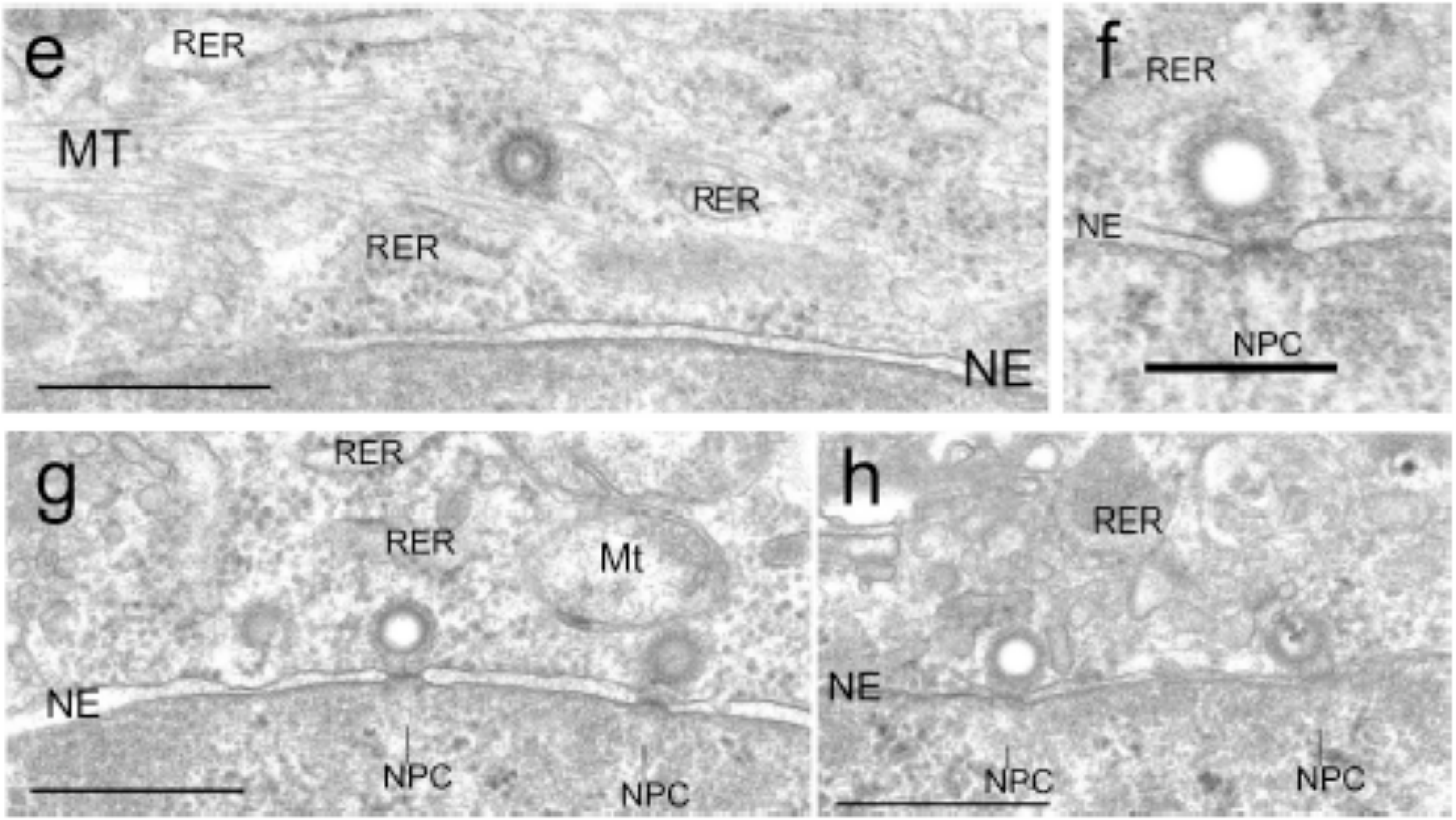


Adenovirus: an example of virus entry via the clathrin-dependent receptor-mediated endocytic pathway and uncoating at the nuclear membrane

Different strategies for entering the nucleus



The microtubule network mediates nuclear targeting of Human Cytomegalovirus capsids



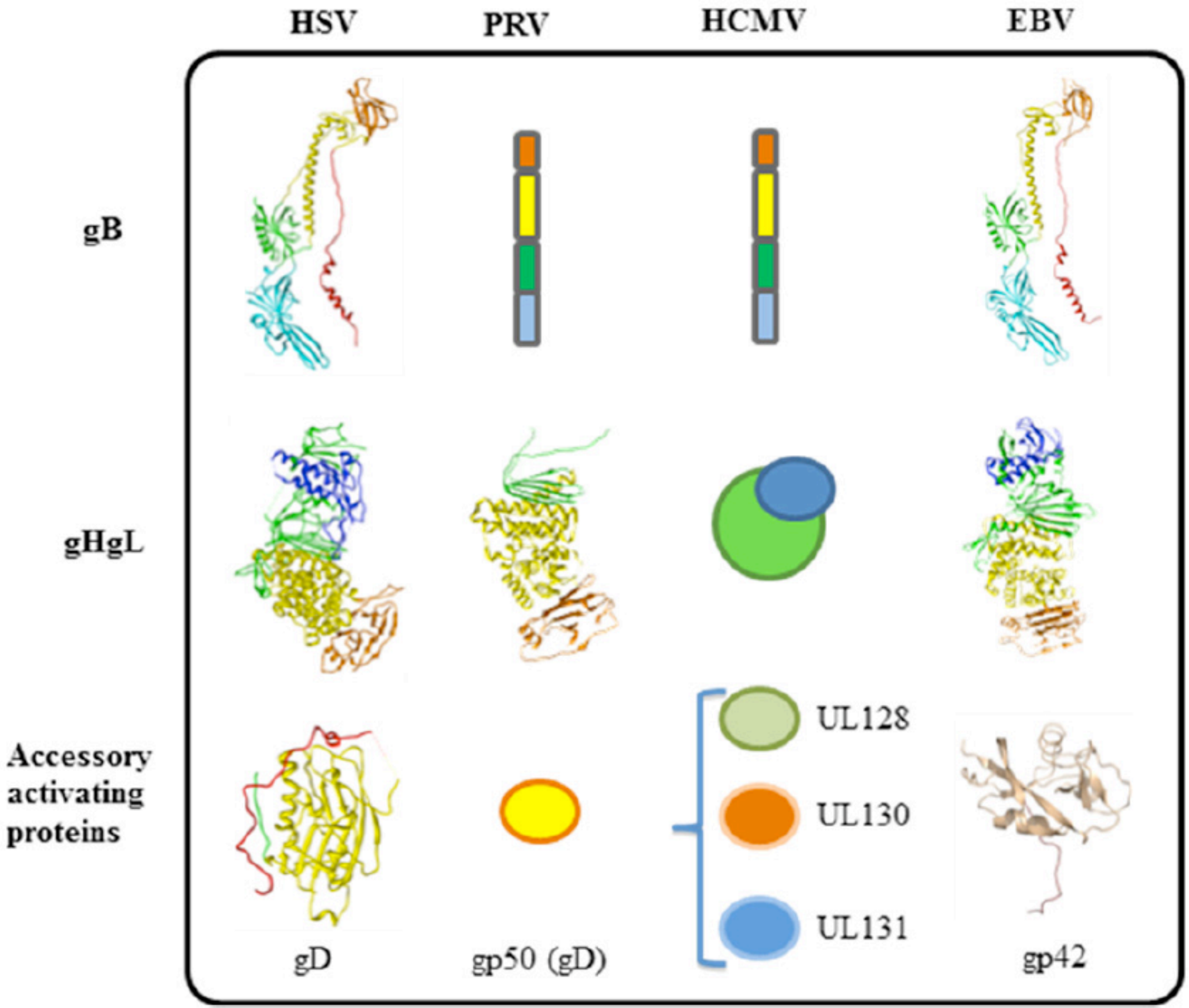
(Ogawa-Goto et al., 2003)

Viral replication

virus entry into host cells:

Herpesvirus entry

Fusion machinery of Herpesviruses



Eisenberg et al., 2012

The basic steps in Herpes simplex virus entry

Herpes simplex virus enter cells via direct fusion with the plasma membrane at neutral pH, or by endocytosis.

The fusion is a process that consists of three basic steps carried out by the virion glycoproteins:

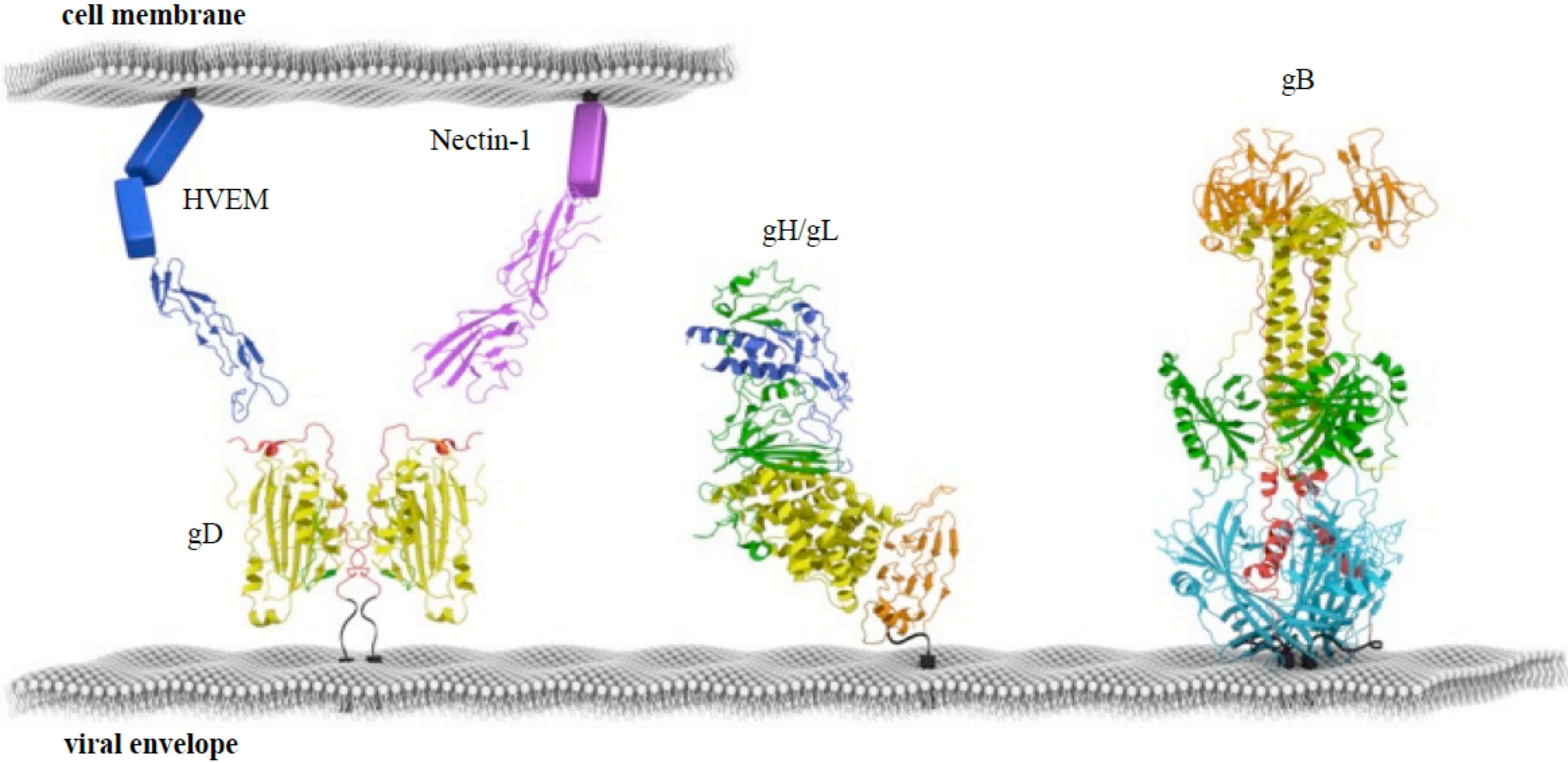
1) **recognition of a cellular receptor by a viral glycoprotein**

2) **triggering of fusion**

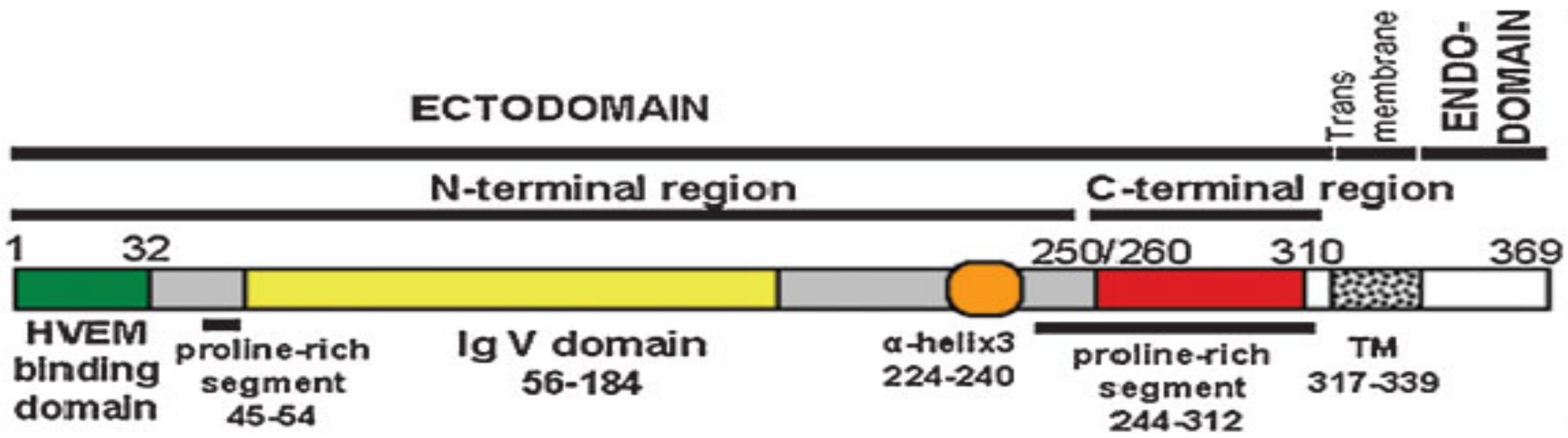
3) **fusion execution**

These steps are carried out by four essential virion glycoproteins: **gB, gD, gH** and **gL.**

Fusion machinery of HSV-1



Structure and function of HSV **gD** glycoprotein



Campadelli *et al.*, 2007

- **369 aa**
- **organized in three domains:**

1) ecto-domain: aa 1-317

N-terminal: aa 1-260
core: aa 56-184;
α-helix, aa 224-240
C-terminal: aa 261-310

2) trans-membrane domain: aa 318-339
3) endo-domain: aa 340-369

gD functions:

1) **receptor recognition**

2) **triggering of fusion**

Functions of HSV **gD**: receptor recognition

The three natural gD receptors:

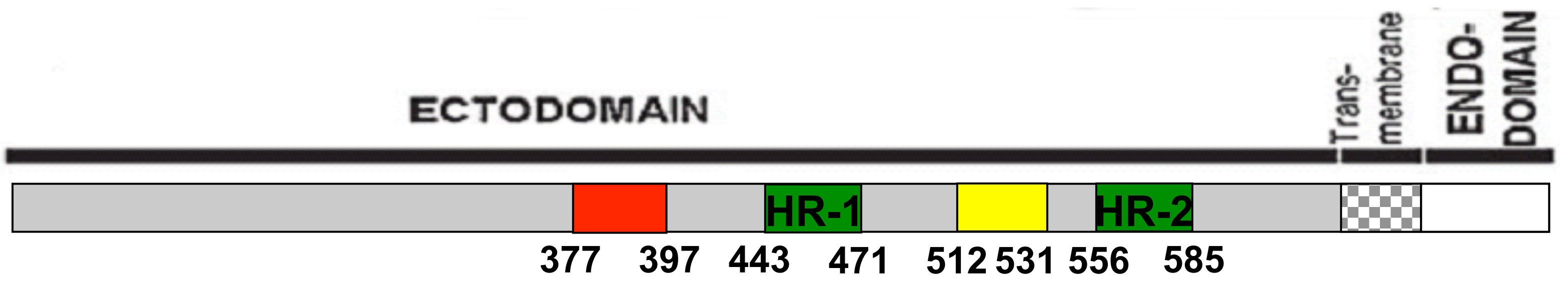
1. **herpesvirus entry mediator (HVME):**
   tumor necrosis factor receptor family;
   in T-lymphocytes or lymphoyd organ.
   HVEM binding-site: aa 1-32 (contact residues between aa 7-15 and 24-32).

2. **nectin 1:**
   intercellular adhesion molecules family;
   in sensory neurons, muco-epithelia or epithelia cells.
   nectin-1 binding-site: critical aa residues (aa 34, 38, 215 and aa 222-223).

3. **O-sulphated HS (heparan sulfate):**
   modified heparan sulfate by enzymes in neuronal and endothelial cells, corneal fibroblasts.

Structure and function of HSV **gH**

HSV-1 gH exibits structural and functional features typical of class I viral fusion gp



- **838 aa**
- **organized in three domains:**

1) ecto-domain
   heptad repeats: HR-1 (aa 443-471)
   HR-2 (aa 556-585);

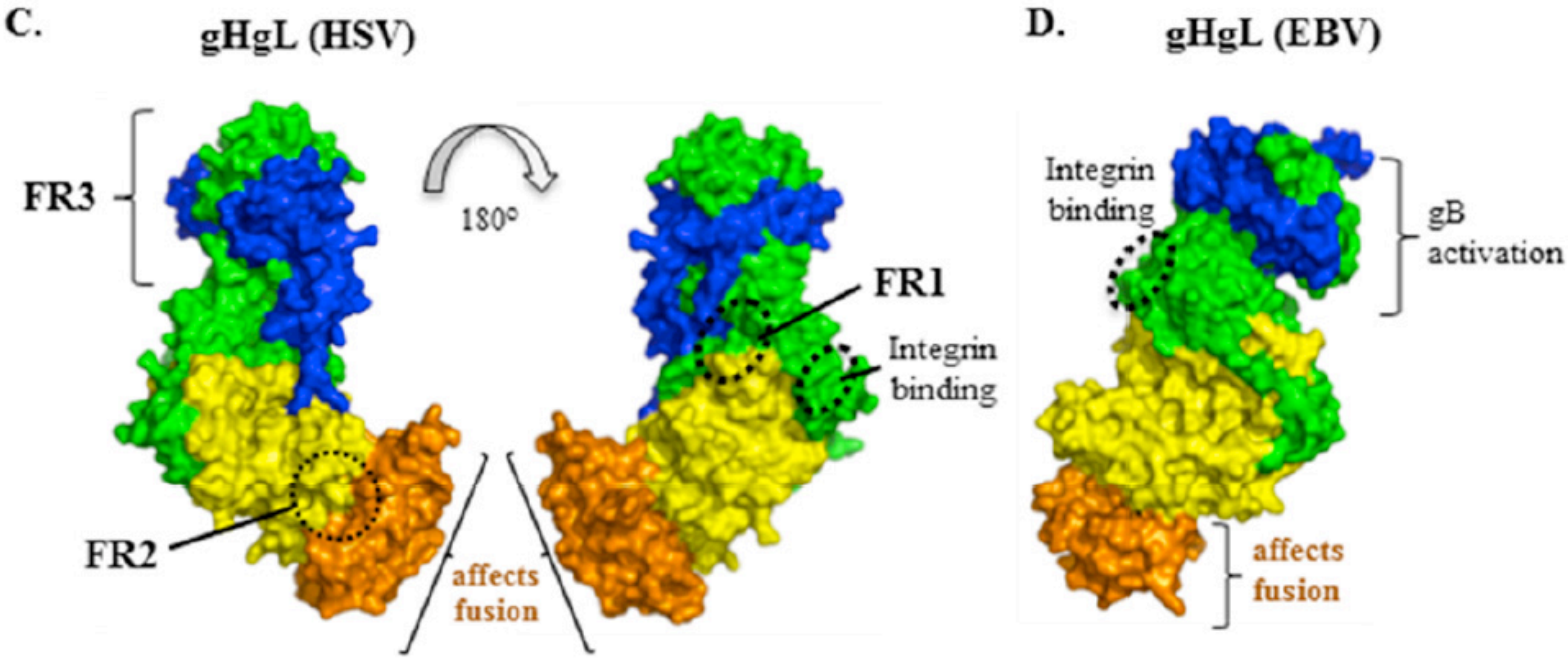
2) trans-membrane domain
3) endo-domain

gH functions:

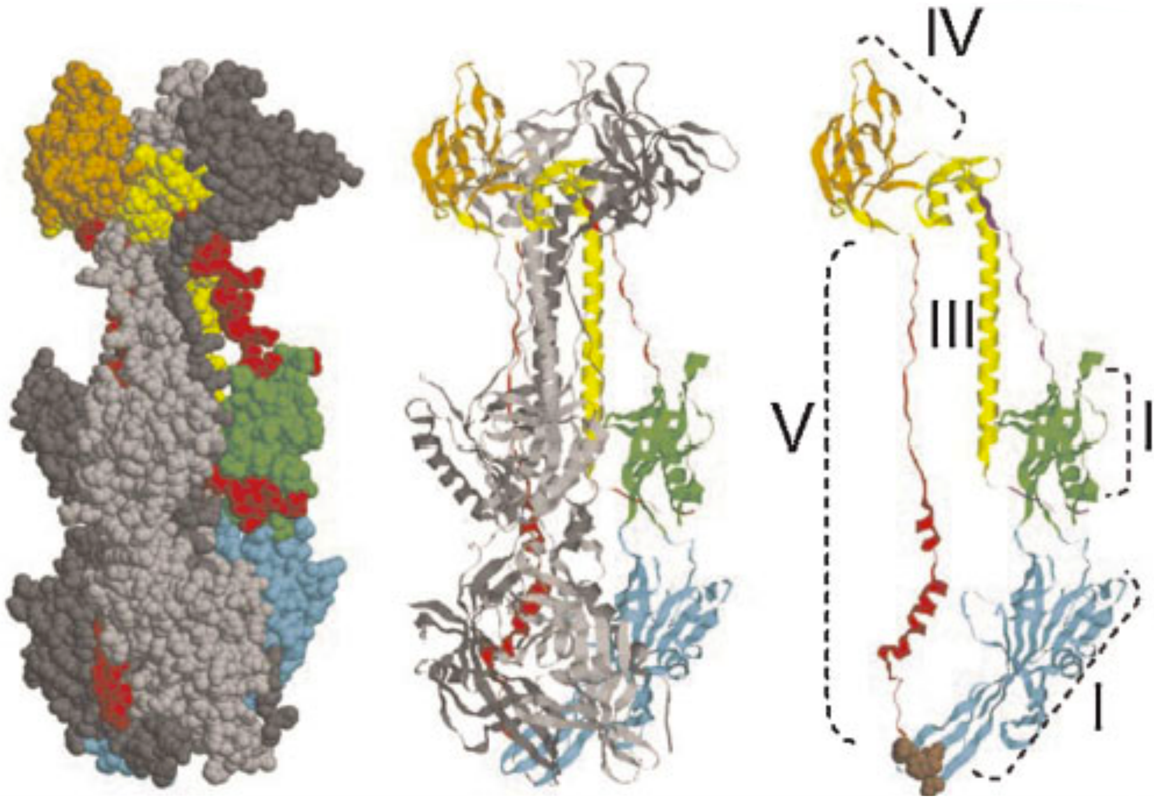
1) interactions with gD and gB

2) triggering of fusion

Structure and function of HSV **gH**



Structure and function of HSV **gB**: an effector of membrane fusion



Campadelli *et al.*, 2007

- **904 aa**
- **trimer with a coiled-coil core**
- **organized in three domains:**
  1) ecto-domain: 696 aa
     α-helix III,
     HR-1 (aa 92-112)
     HR-2 (618-631)

  2) trans-membrane domain:69 aa

  3) endo-domain: 109 aa

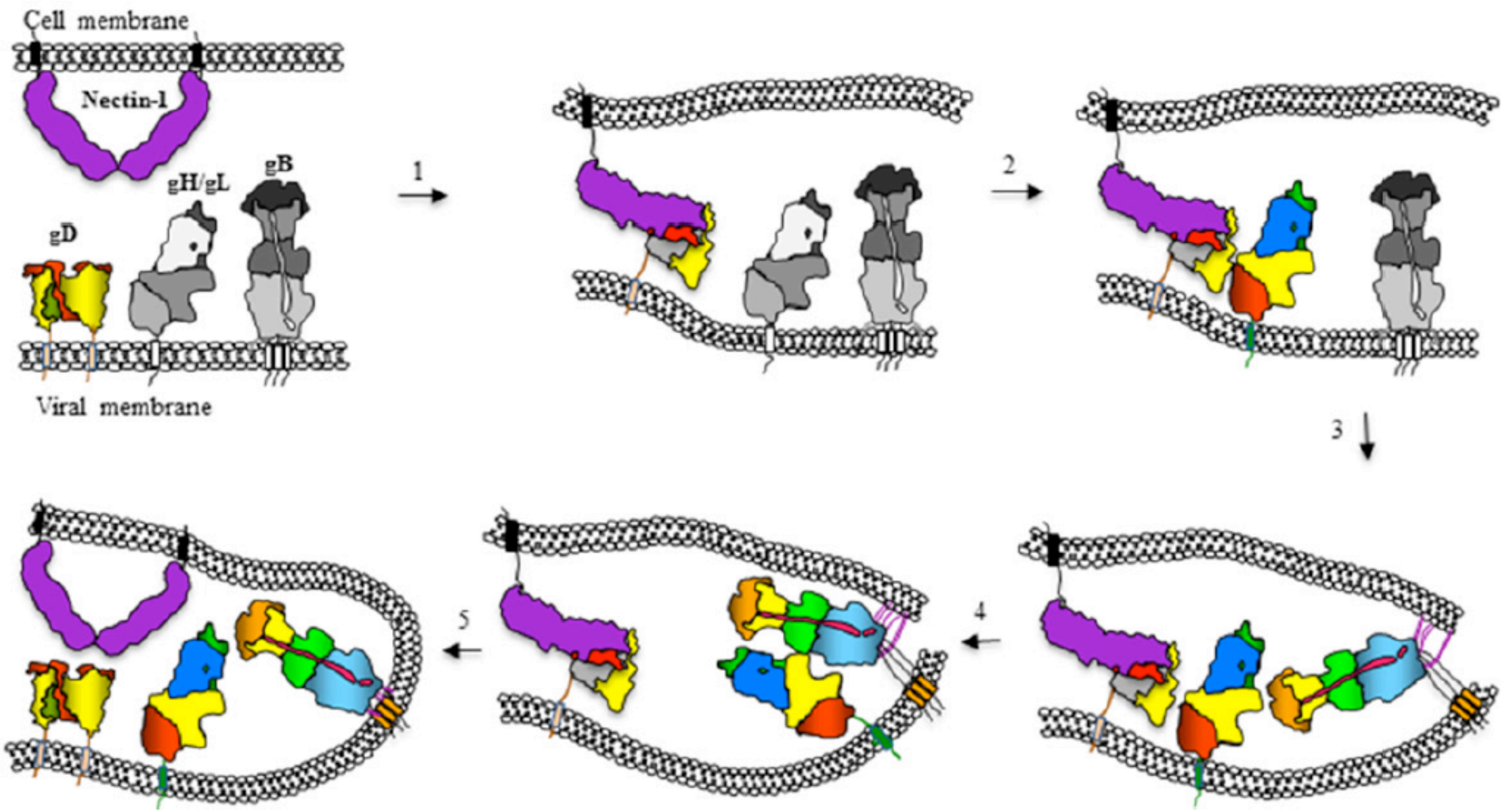
gH functions:

1) Binding to HSPG

2) Fusion execution

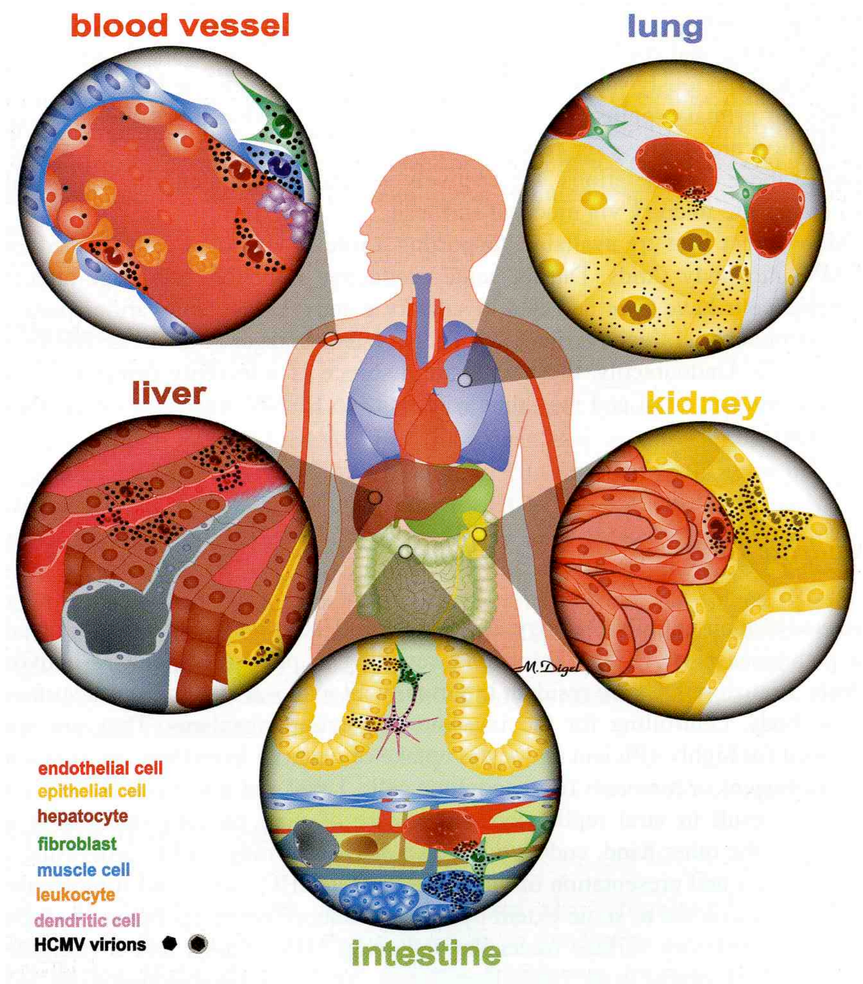
HSV-1 gH exibits structural and functional features typical of Class III viral fusion gp

Working model for HSV entry into cells

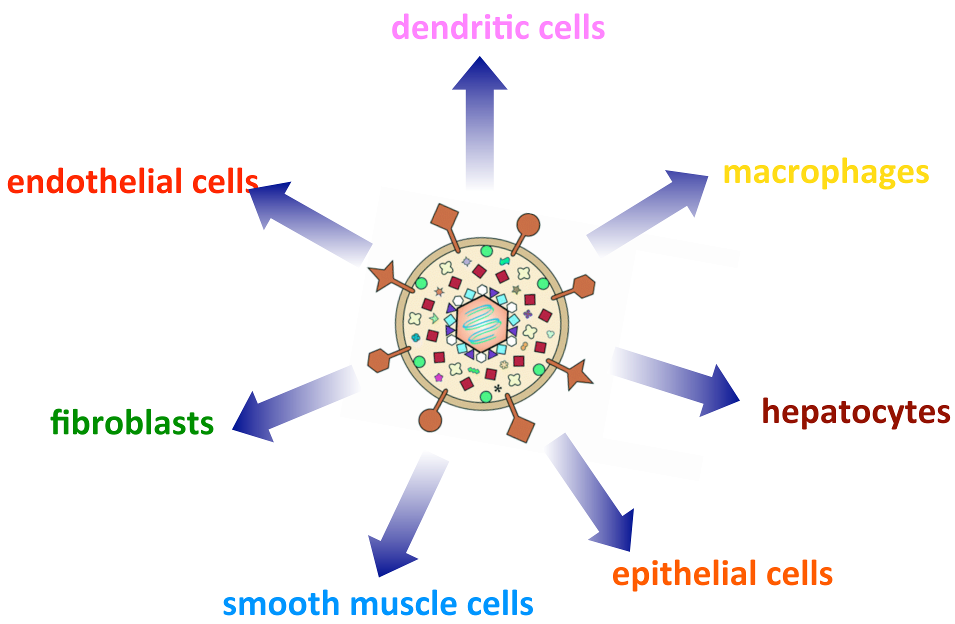


Eisenberg et al., 2012

The broad cell tropism of HCMV

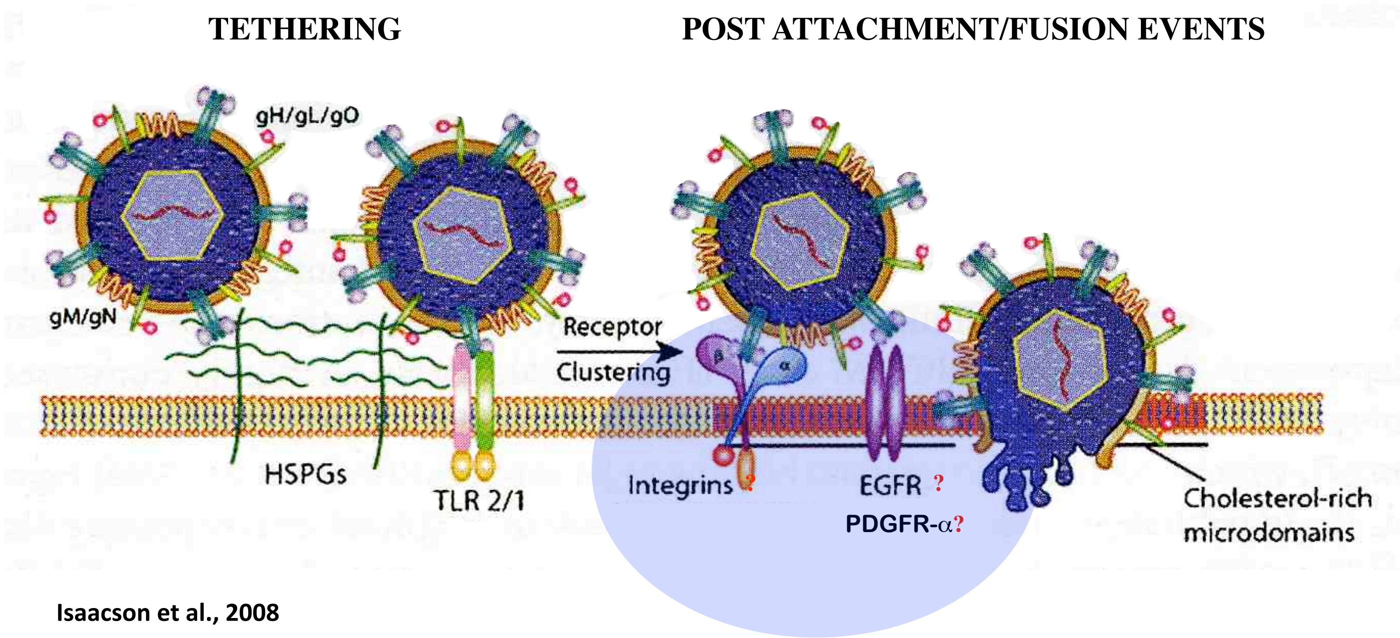


Sinzger et al., 2008



The broad spectrum of cell types infected *in vivo* greatly contributes to the pathogenesis of HCMV diseases

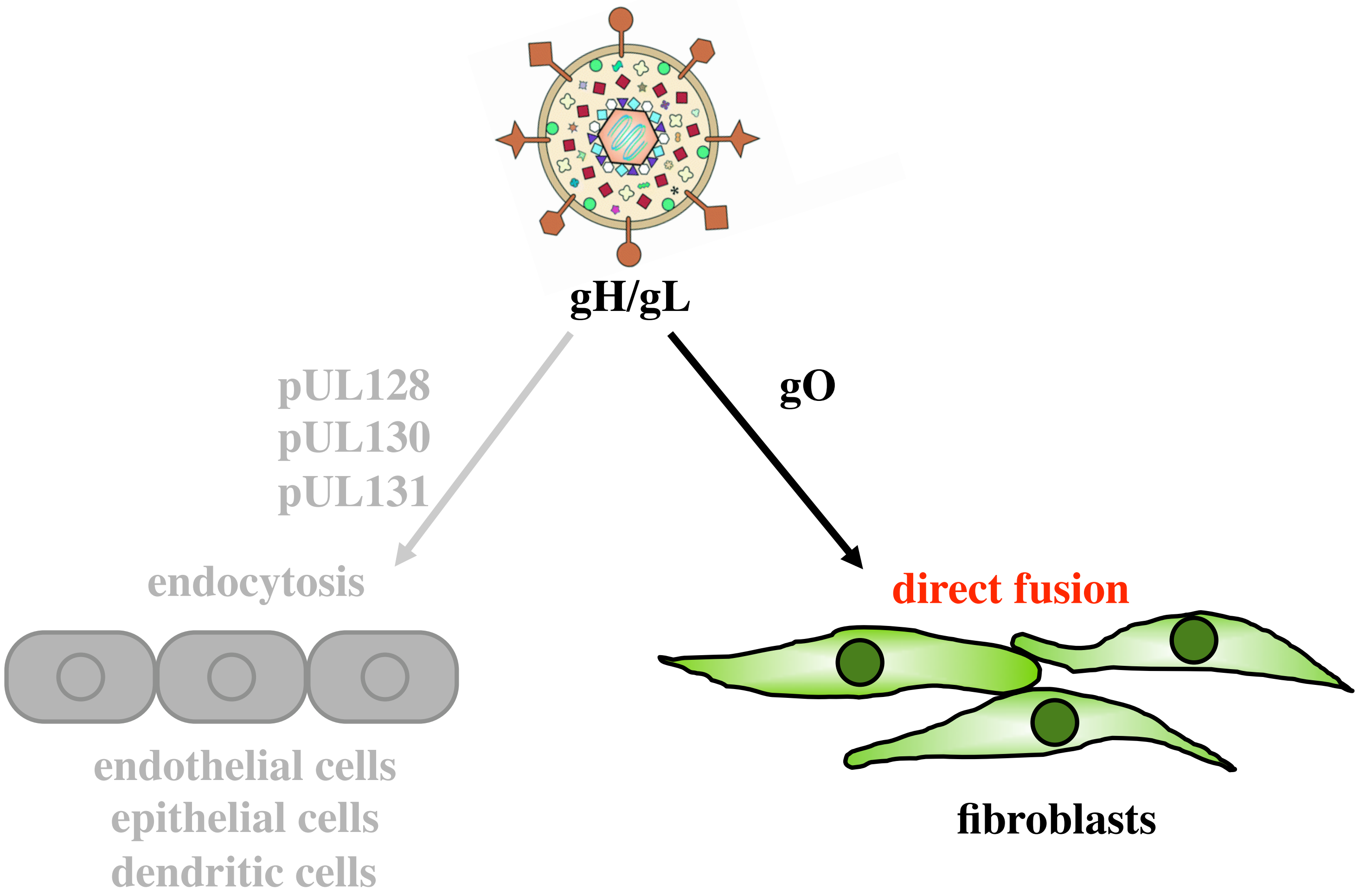
The broad cell tropism of HCMV: different receptor utilization



Isaacson et al., 2008

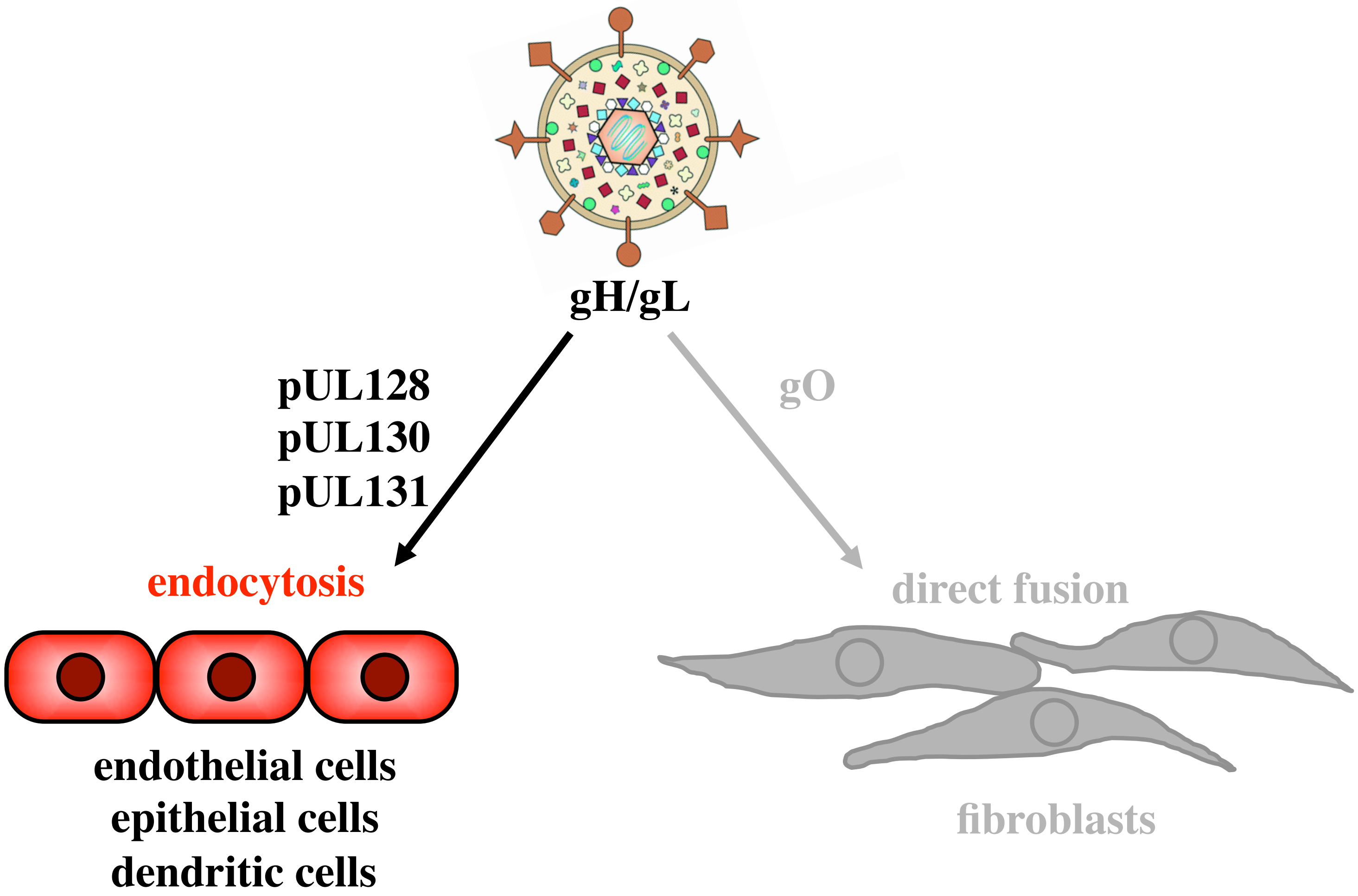
Presence of multiple and/or ubiquitously expressed cellular receptors

The broad cell tropism of HCMV: different envelope glycoproteins and tropism factors requirements



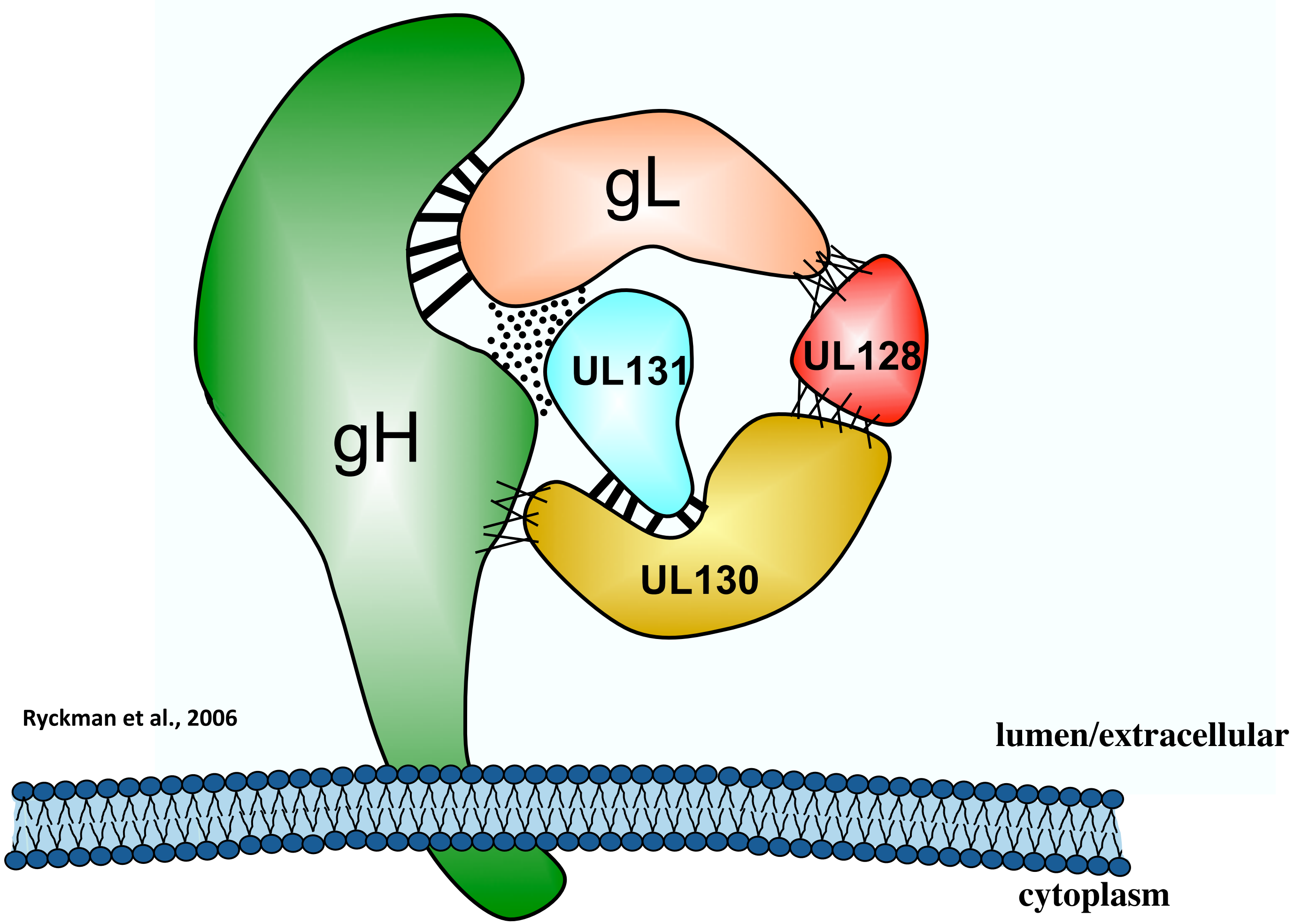
Presence of modular envelope complexes that mediate viral entry in different cell types by different pathways

The broad cell tropism of HCMV: different envelope glycoproteins and tropism factors requirements



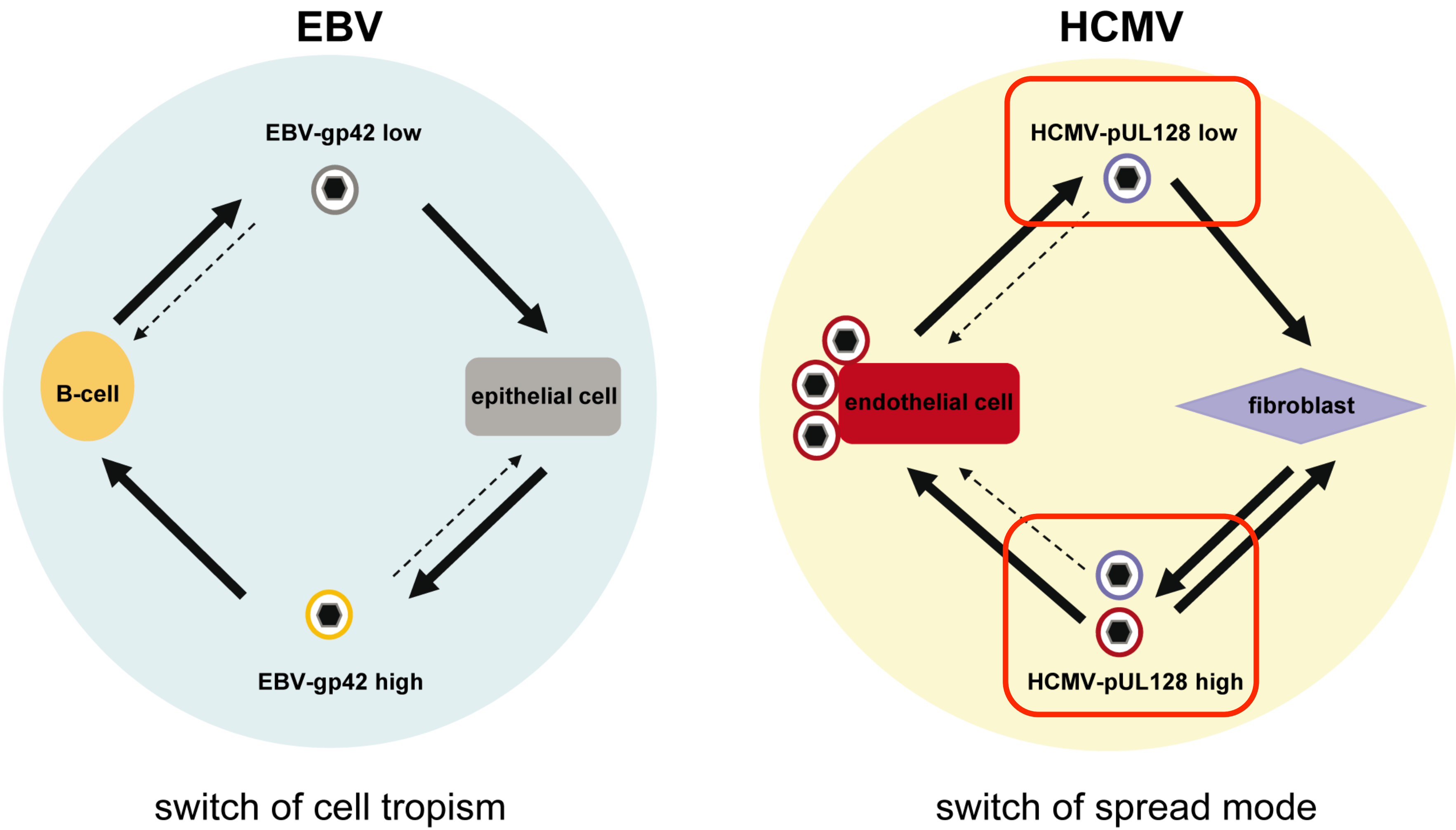
Presence of modular envelope complexes that mediate viral entry in different cell types

The broad cell tropism of HCMV: the role of pUL tropism factors



pUL (UL128, UL130 and UL131) proteins assemble onto a gH/gL scaffold to form a virion complex that mediates entry in epithelial and endothelial cells.

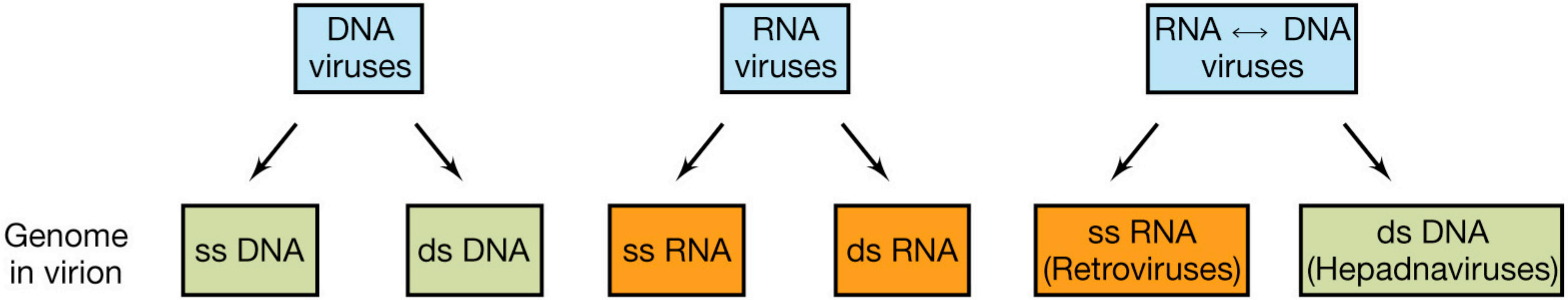
The presence of different Herpesvirus envelope complexes may switch route of infection in vivo



Scrivano et al., 2011

Viral replication

transcription, translation and genome replication



Genomes of DNA viruses

- unimolecular
- ds or ss
- 5-240 kb (1.2 Mb NCLDV)
- linear or circular

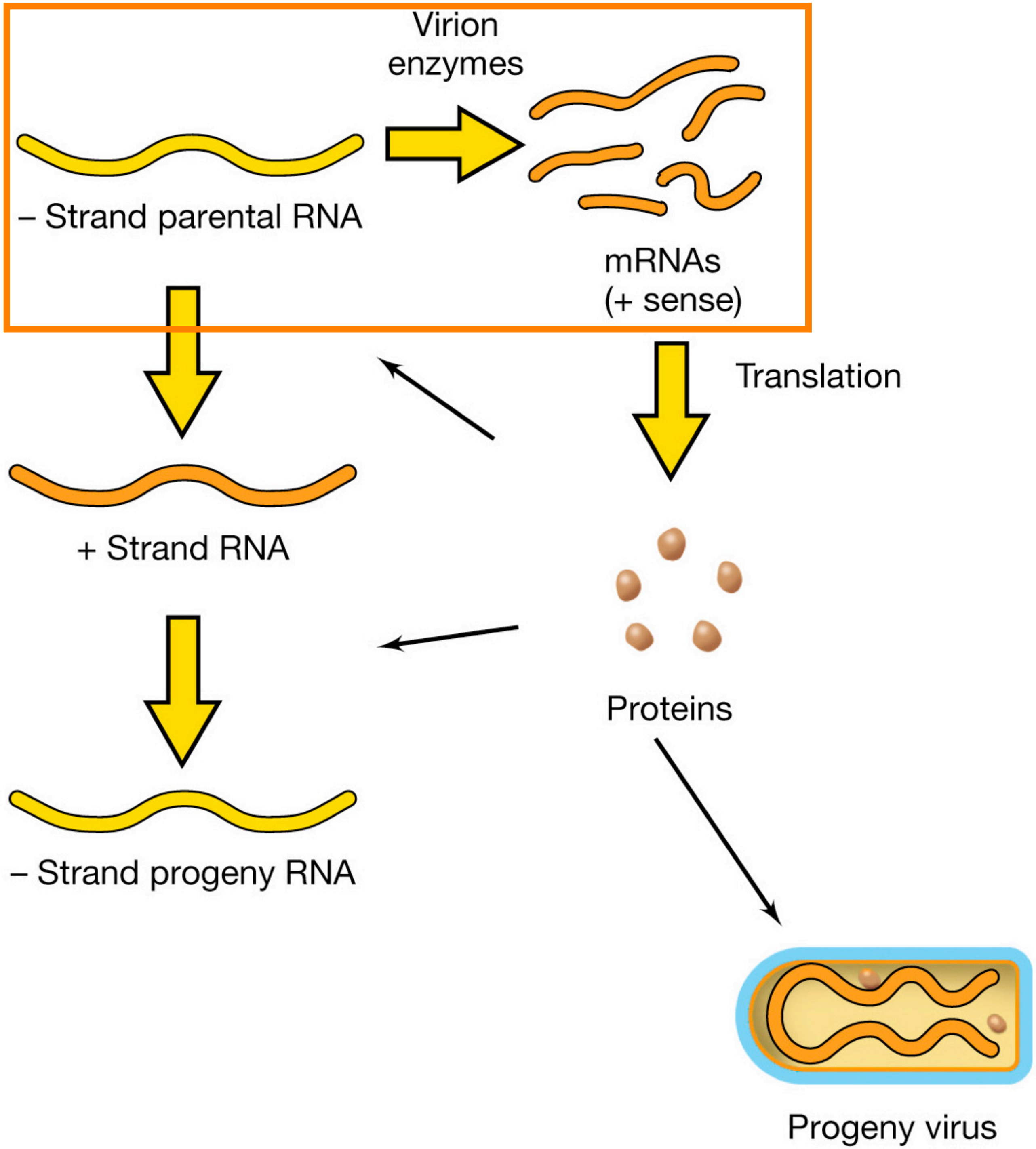
Genomes of RNA viruses

- unimolecular or segmented
- ss or ds
- 1,7-30 kb
- linear or circular
- (+)or (-) polarity

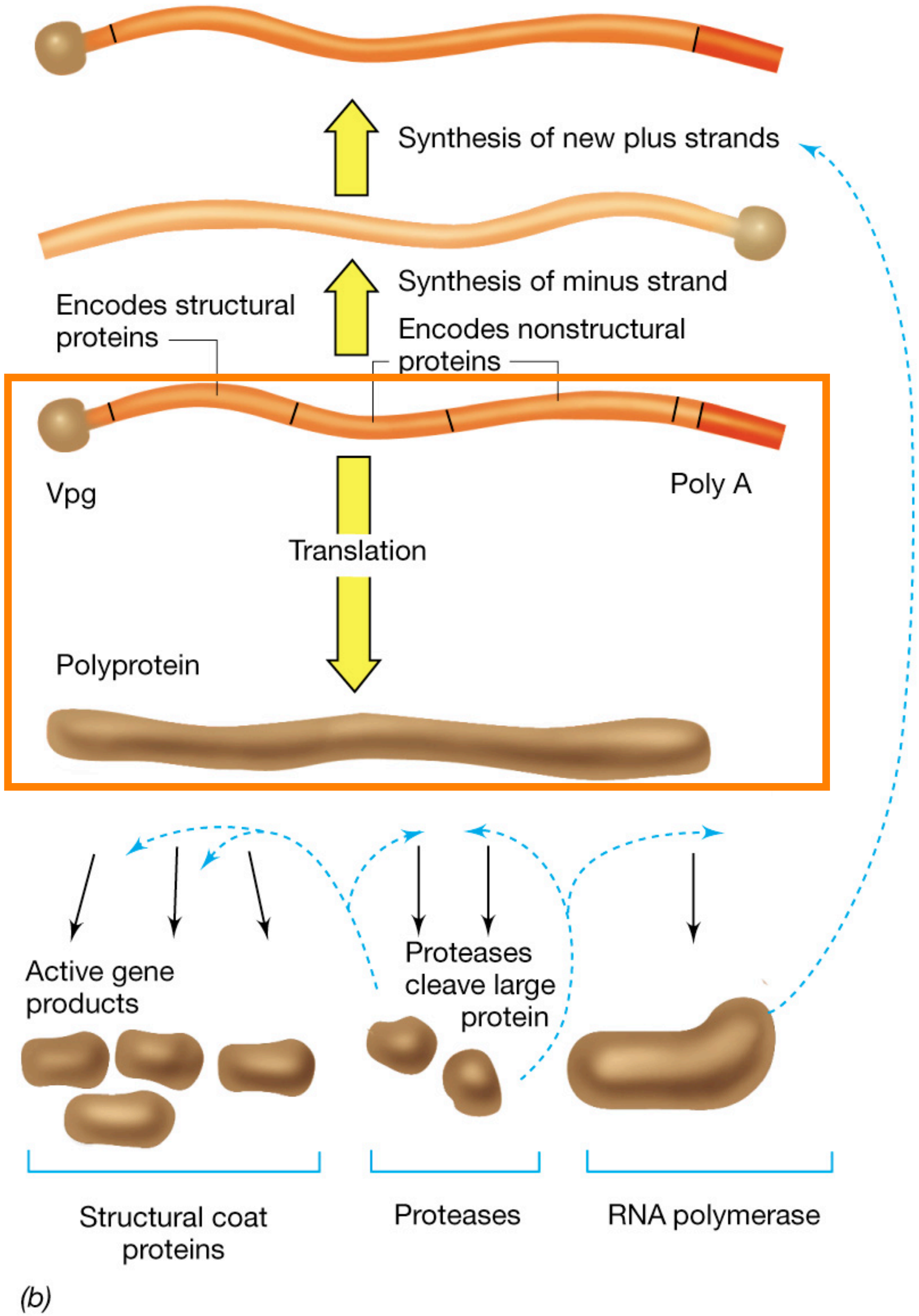
Synthesis of viral macromolecules

- The diversity of viral transcription strategies
- The diversity of viral translation strategies
- The diversity of viral genome replication strategies

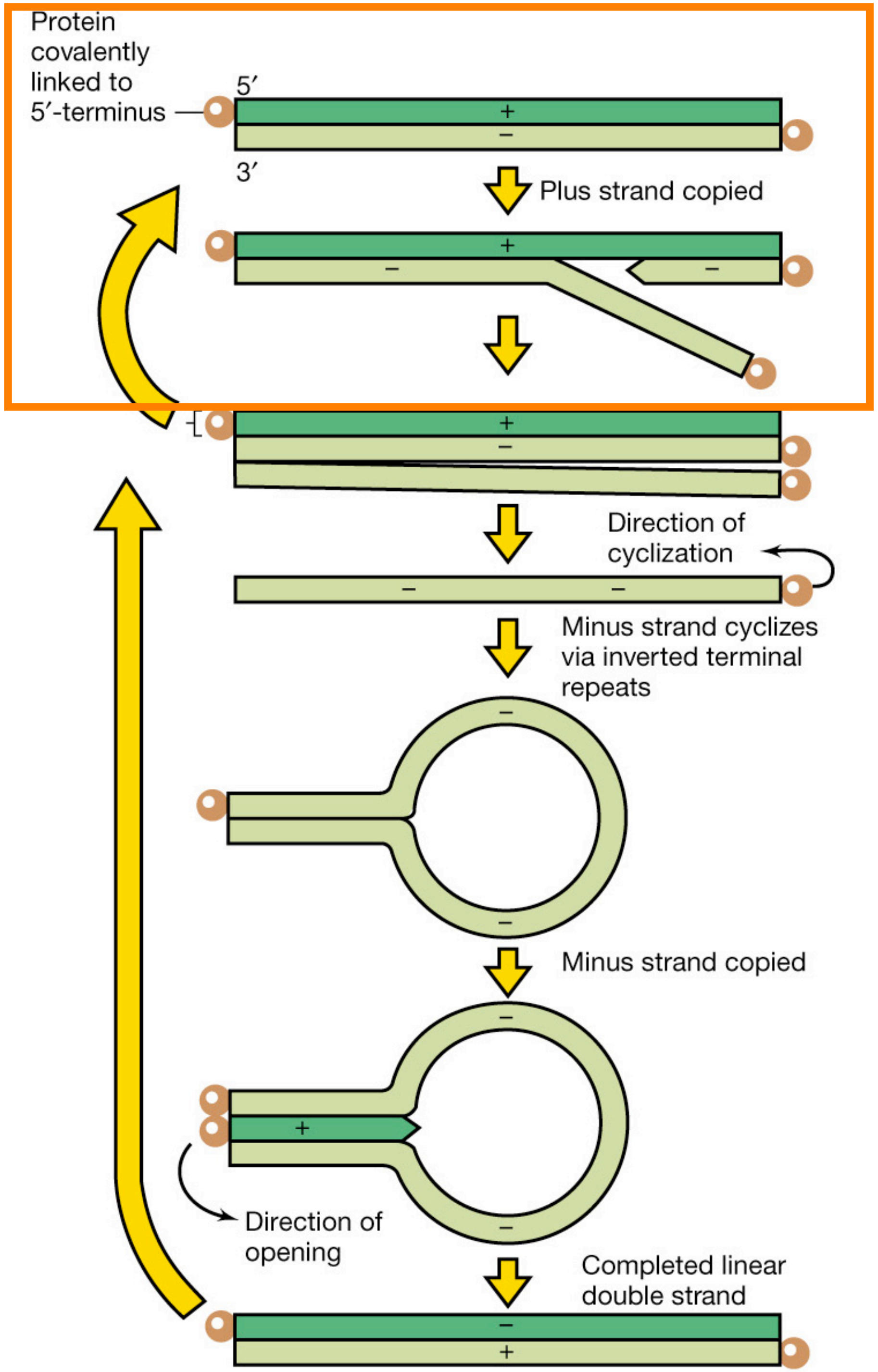
The diversity of viral transcription and translation strategies:
Rhabdoviruses
(-) ssRNA



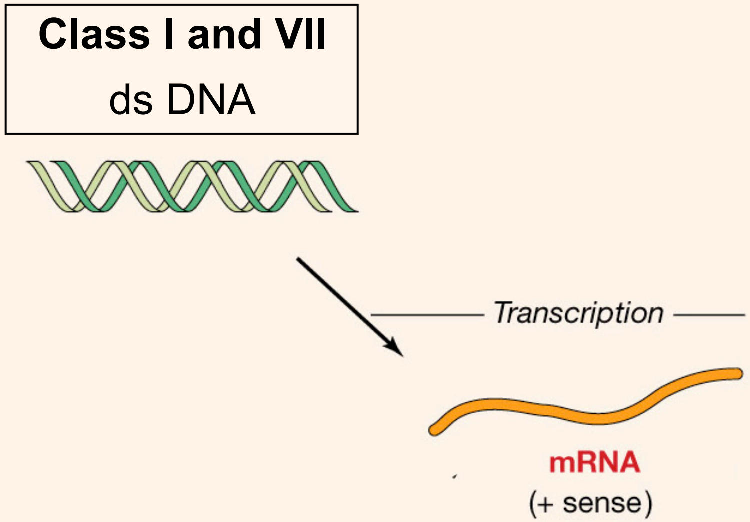
The diversity of viral translation strategies: **Picornaviruses** polyprotein synthesis



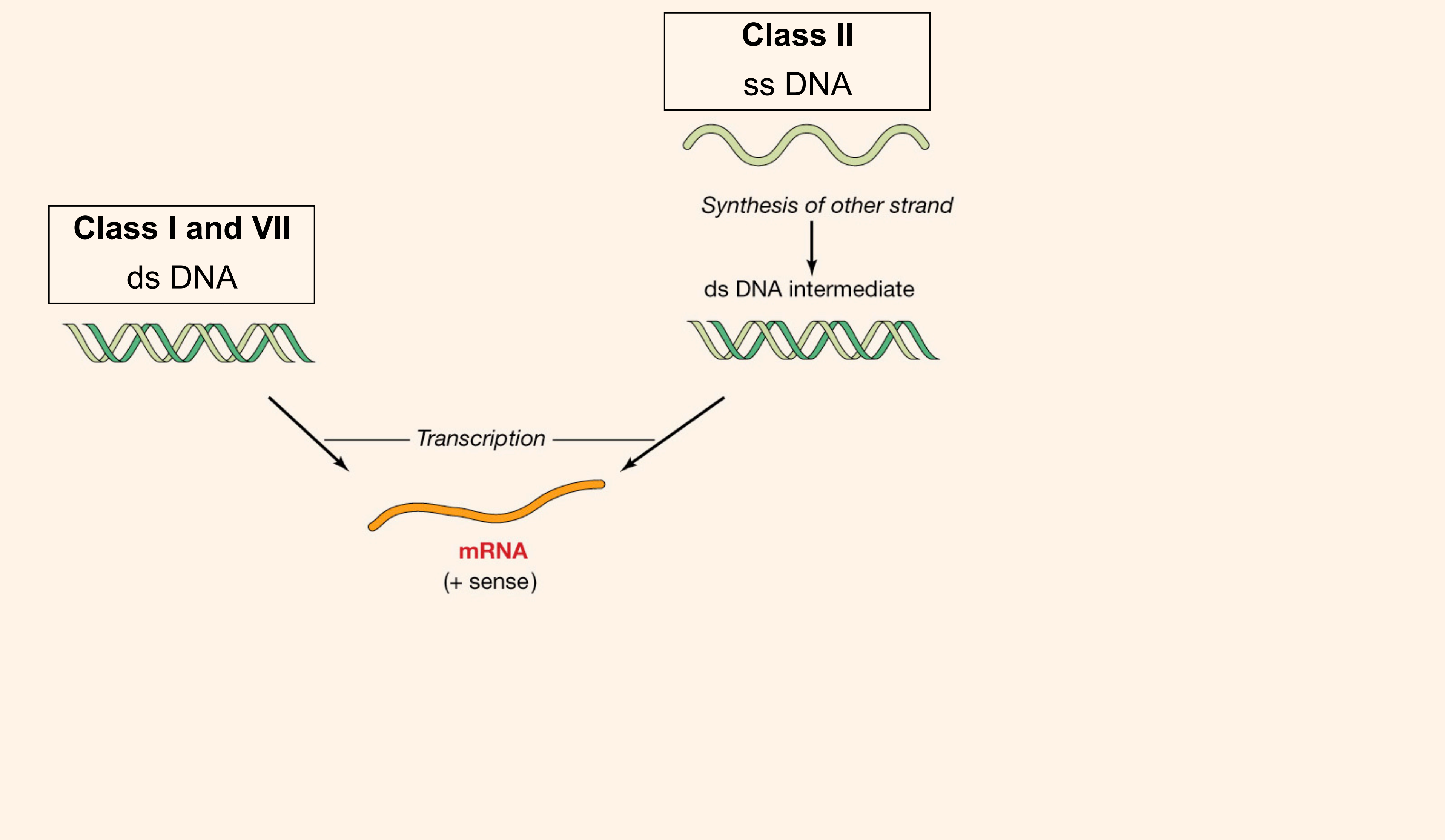
The diversity of viral genome replication strategies: adenovirus DNA replication



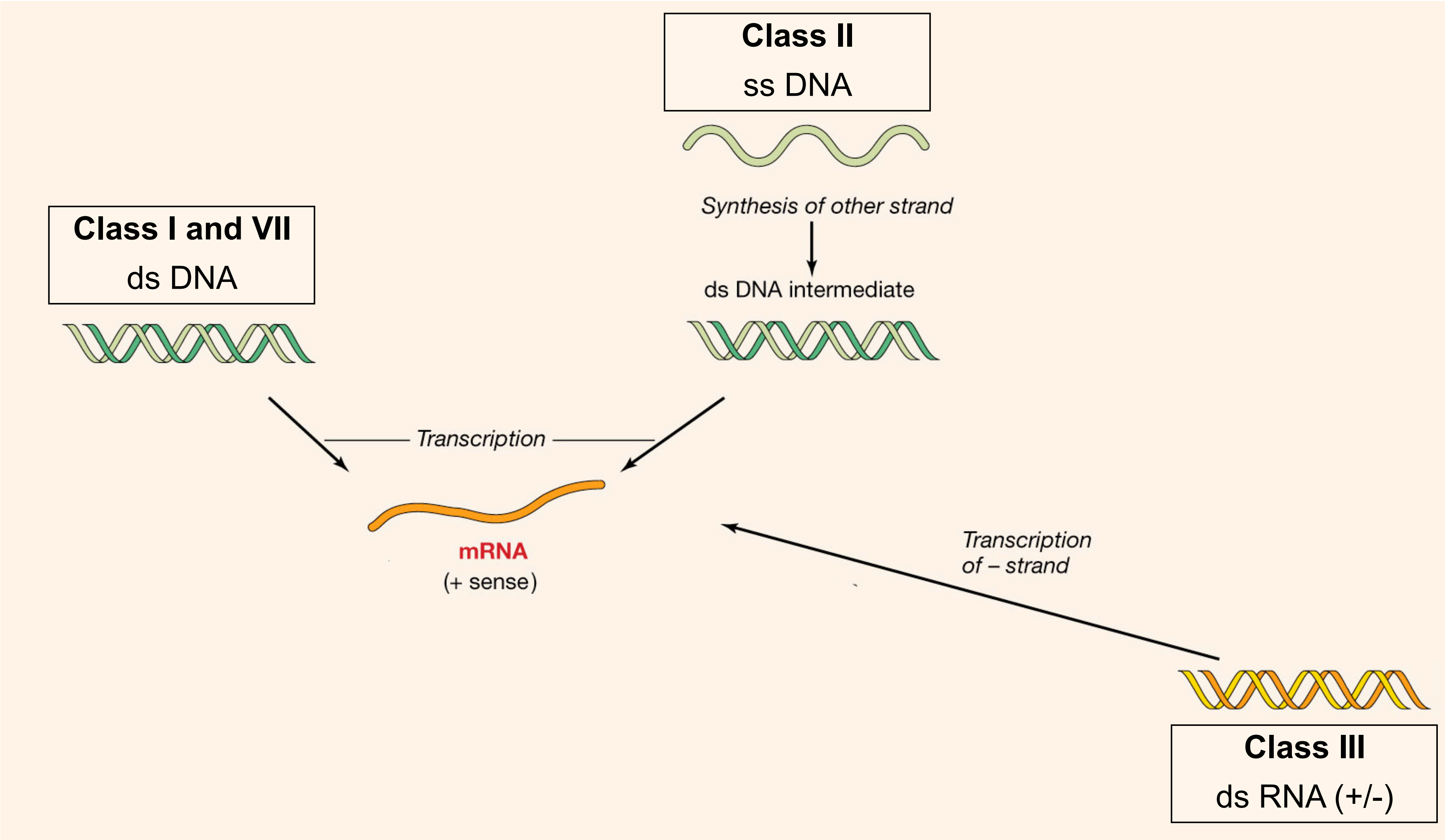
The Baltimore classification system



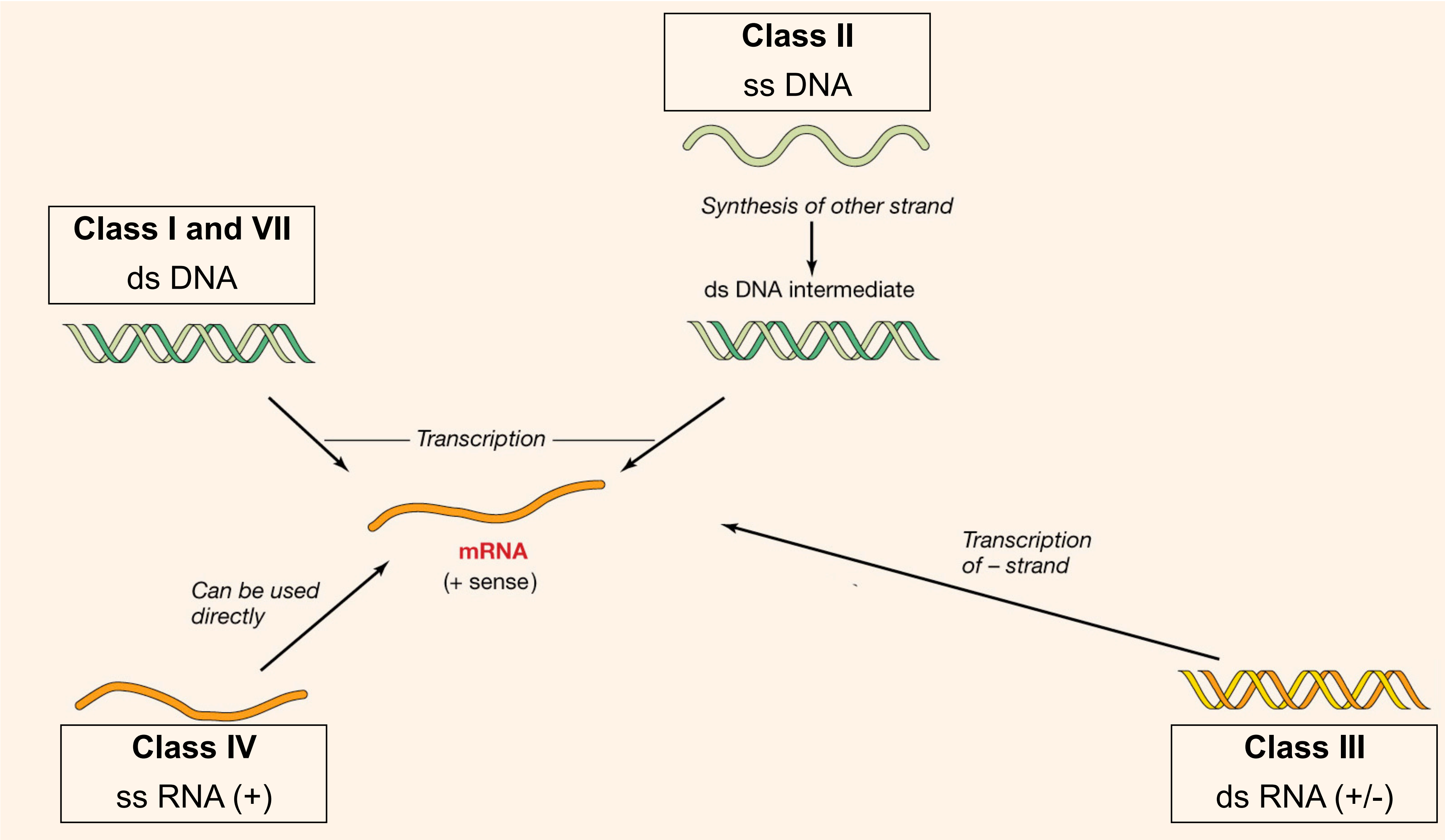
The Baltimore classification system



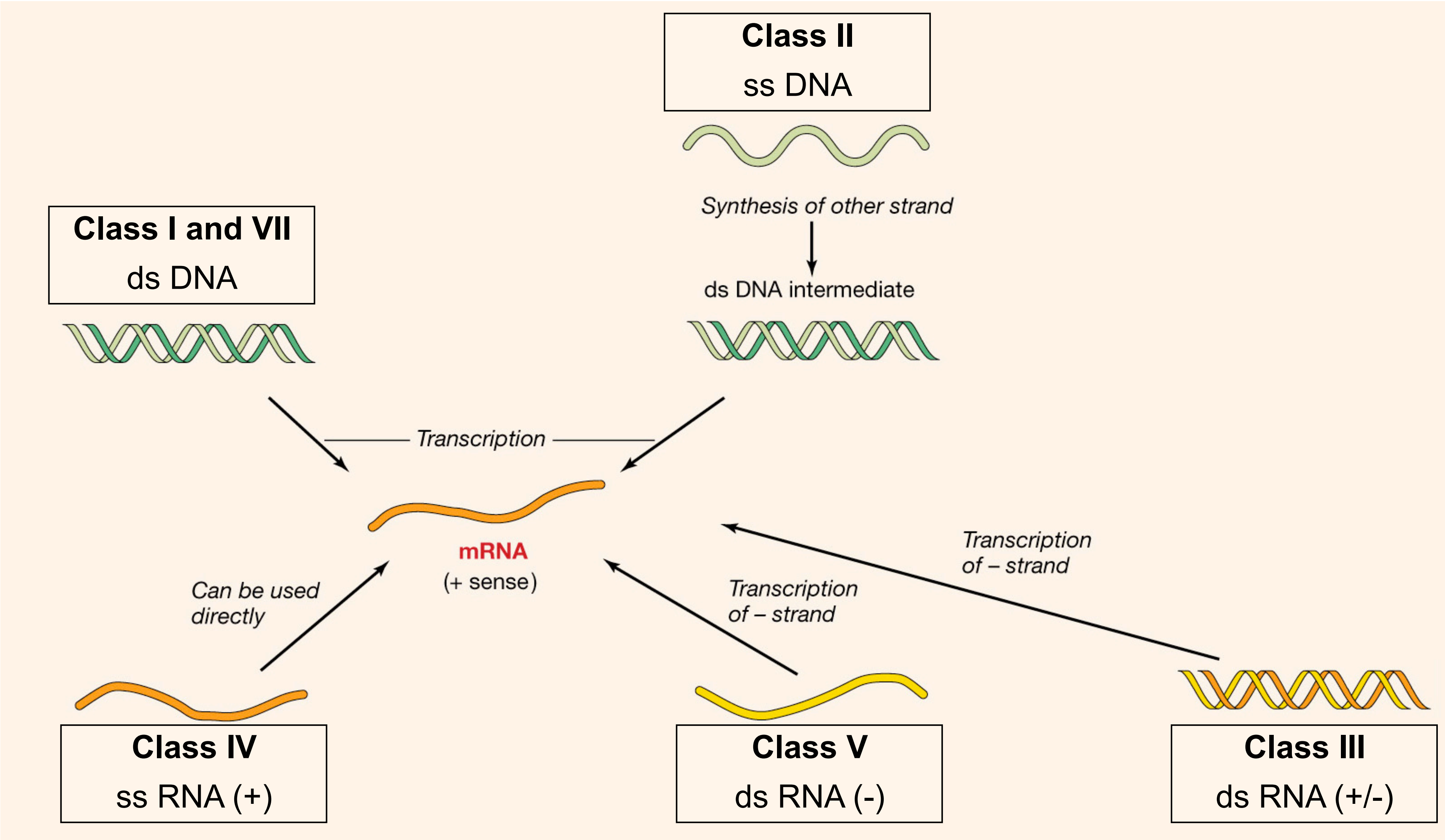
The Baltimore classification system



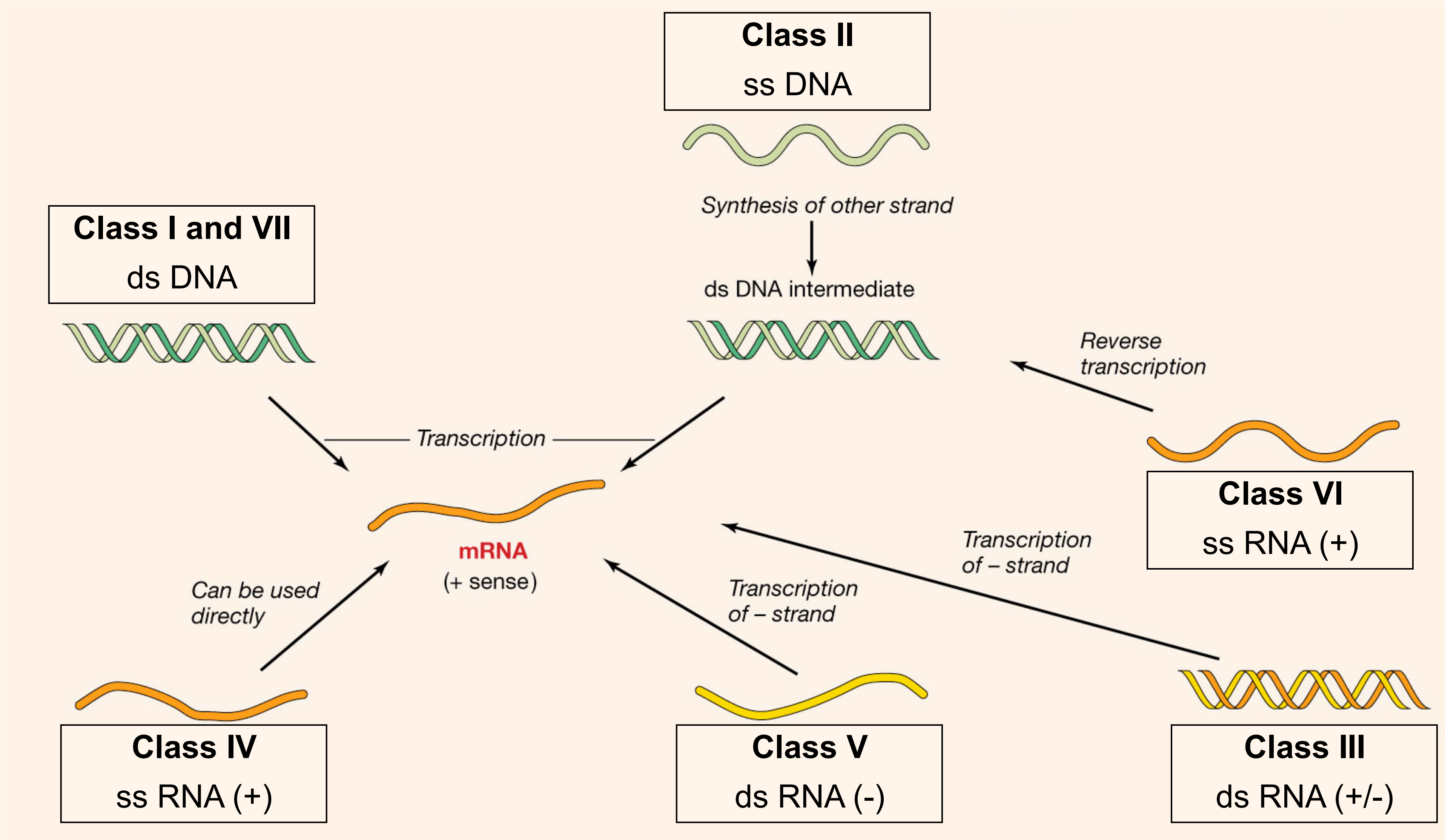
The Baltimore classification system



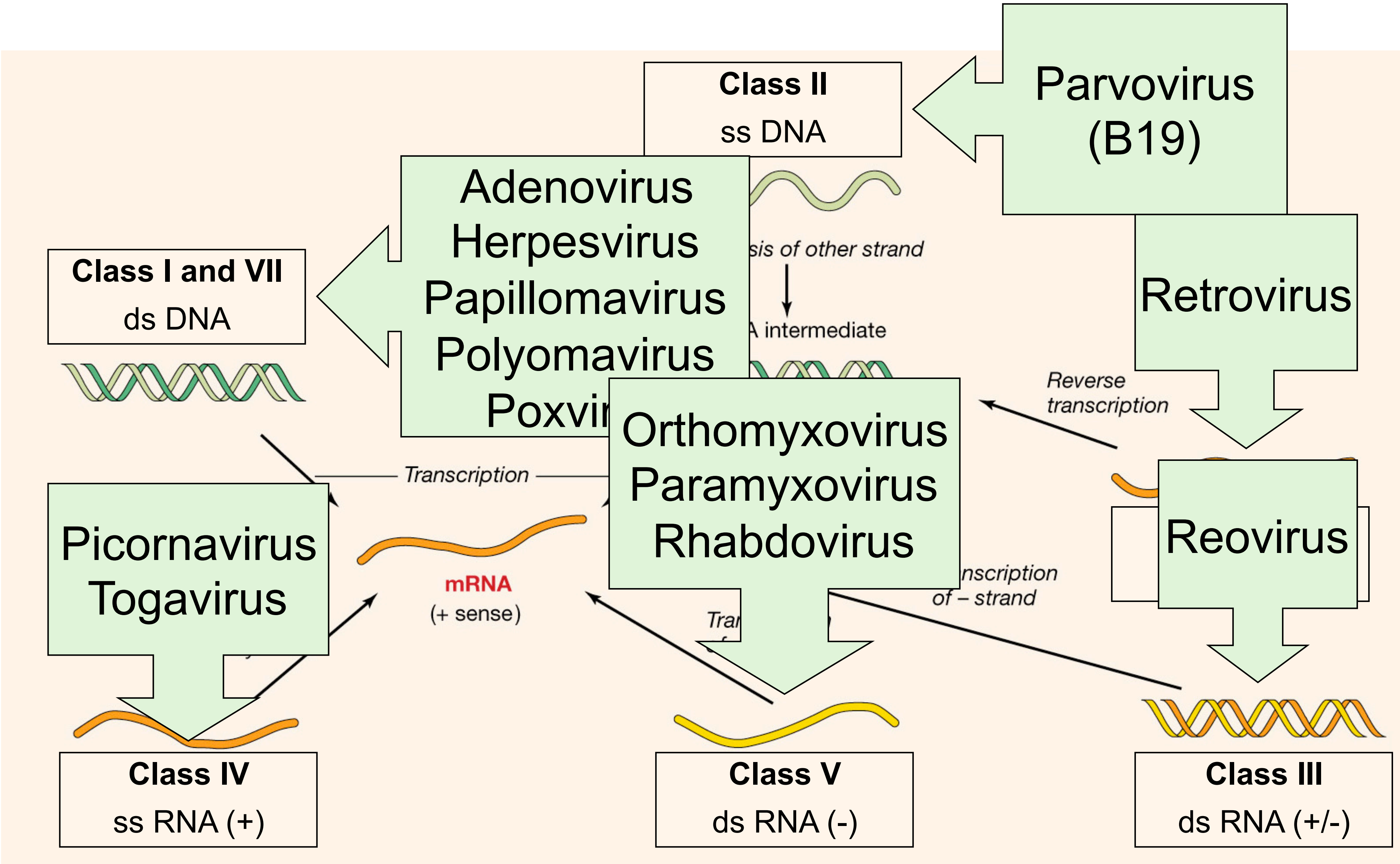
The Baltimore classification system



The Baltimore classification system



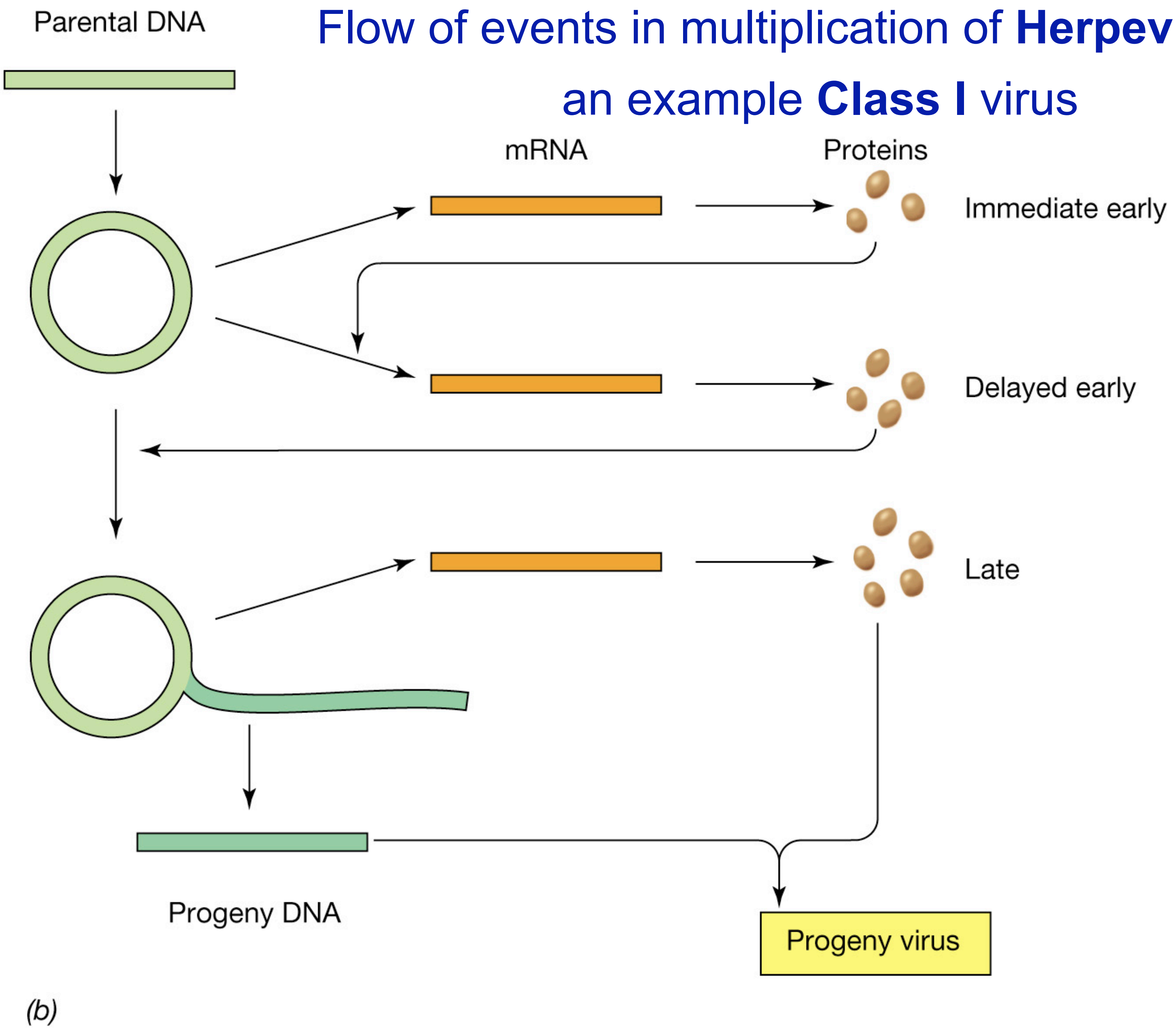
The Baltimore classification system



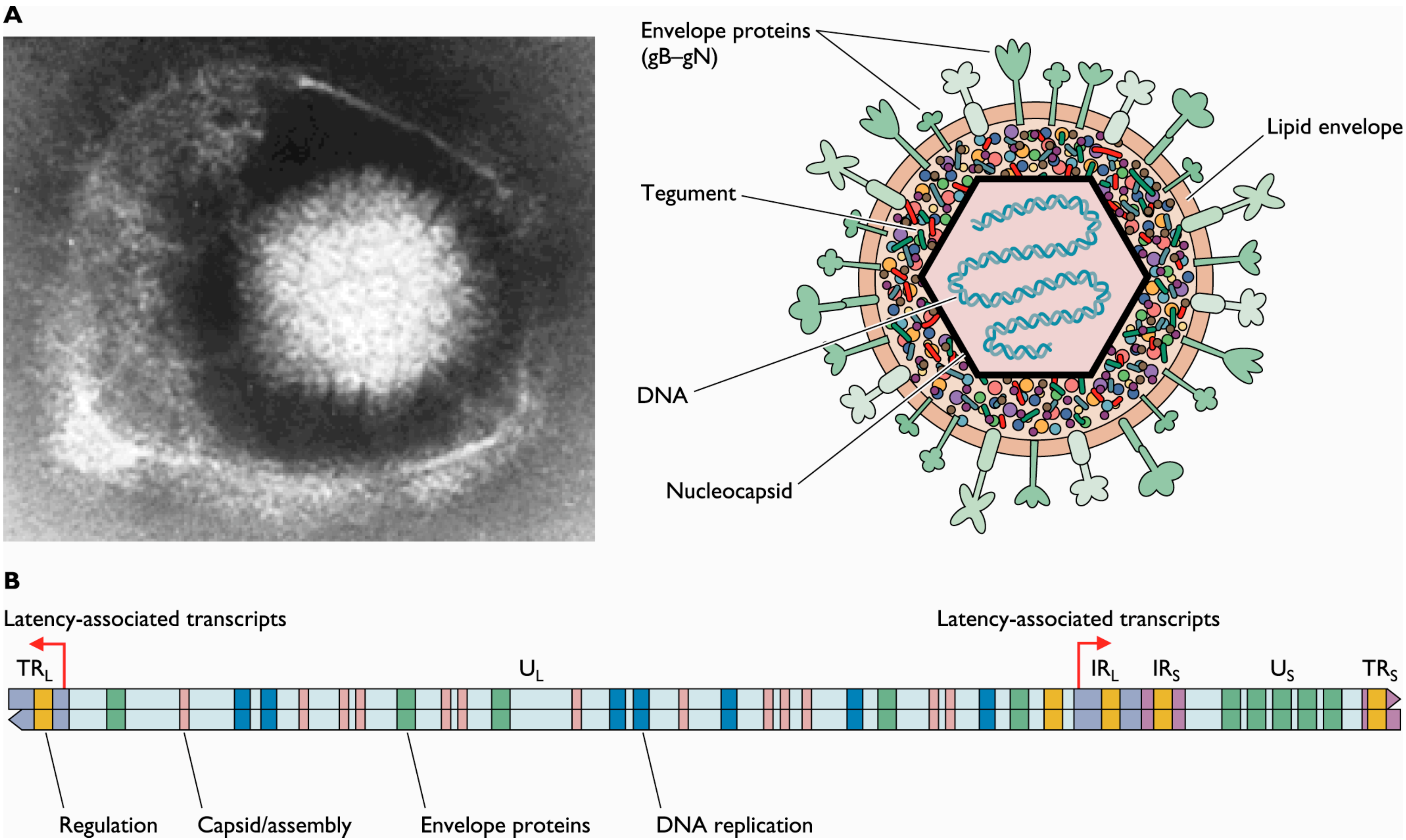
Viral replication

transcription, translation and genome replication of DNA viruses

Flow of events in multiplication of **Herpeviruses**: an example **Class I** virus



Structure and genome organization of Herpes simplex 1 virus (**HSV-1**)



Attachment
Entry
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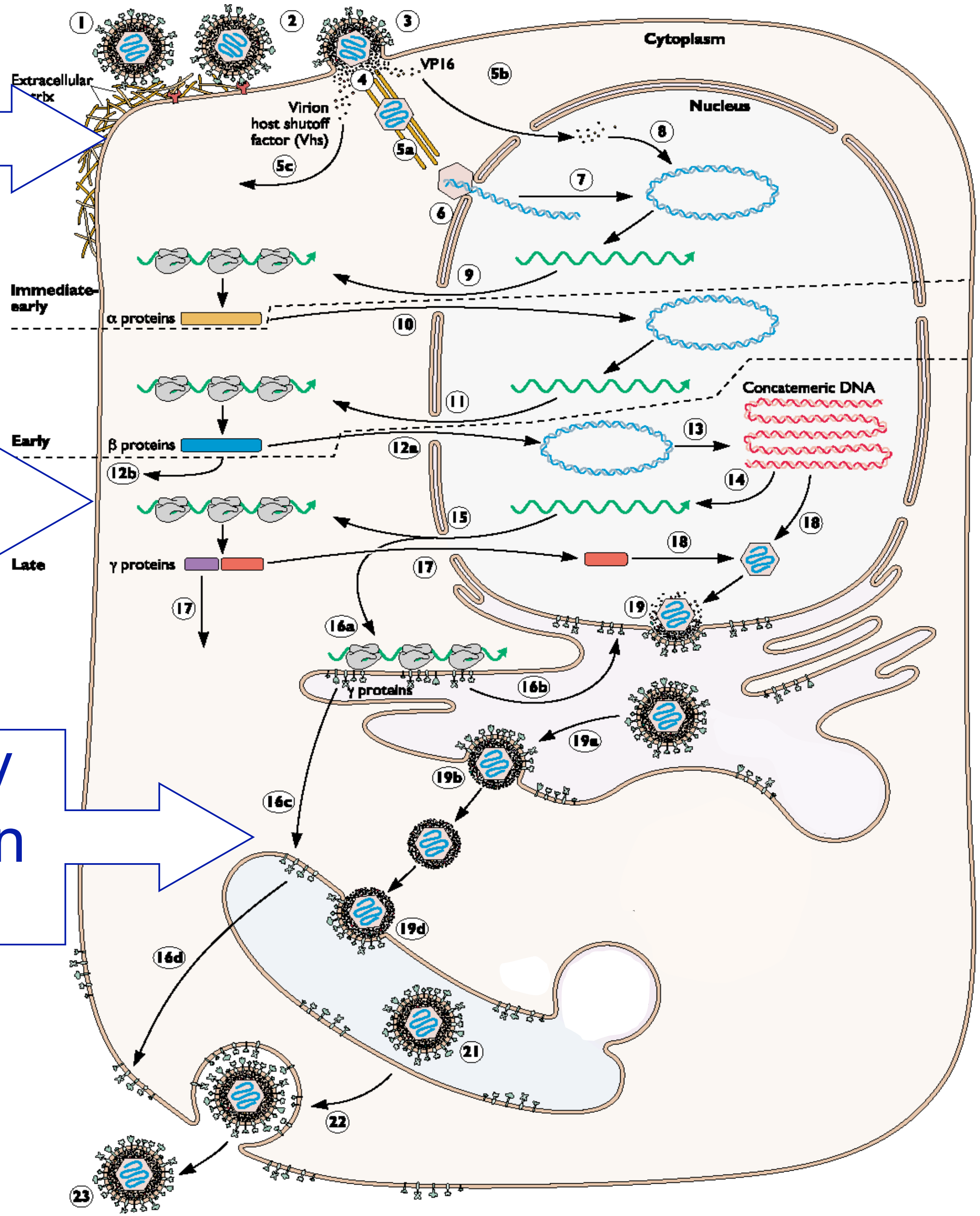
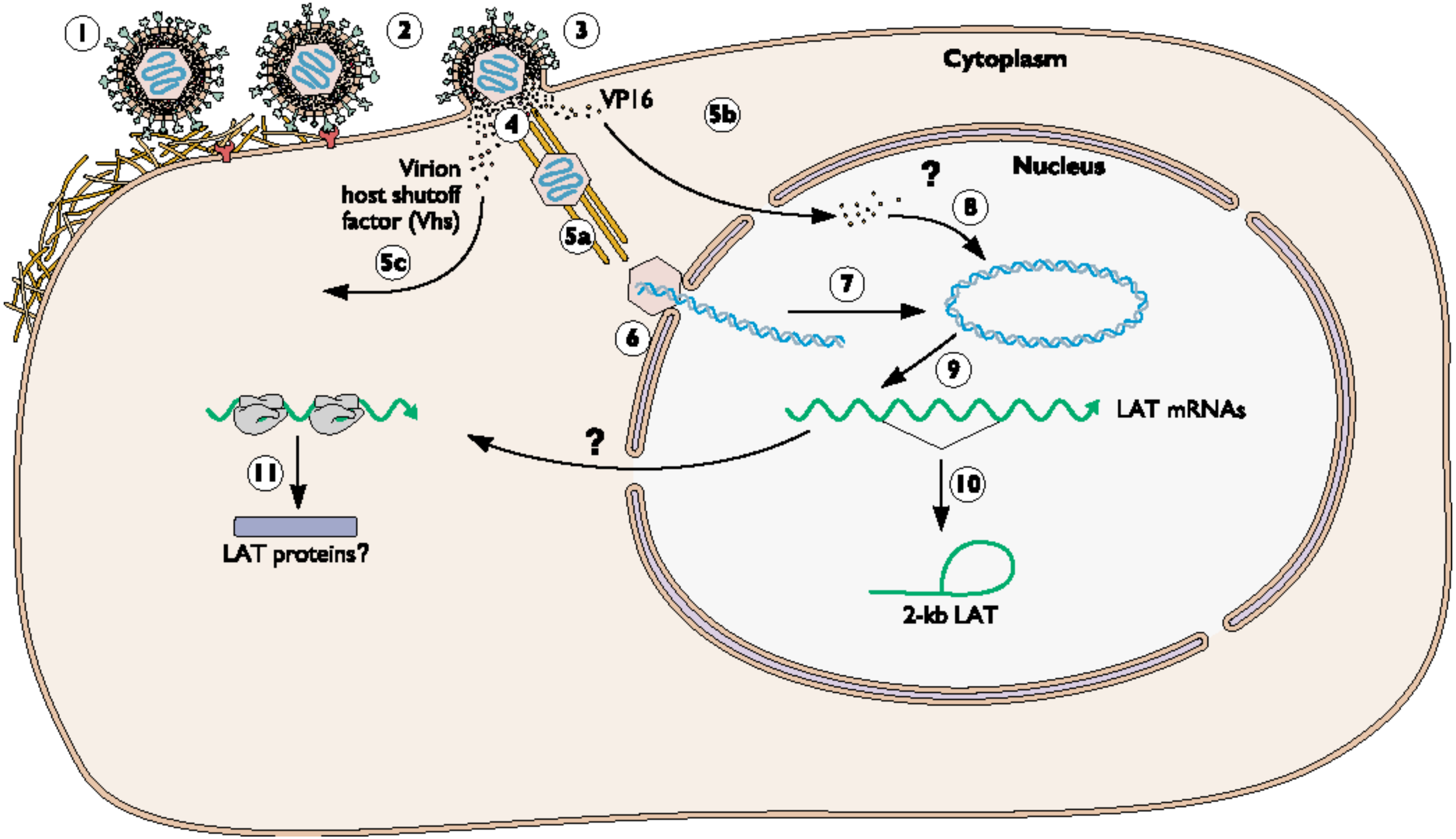
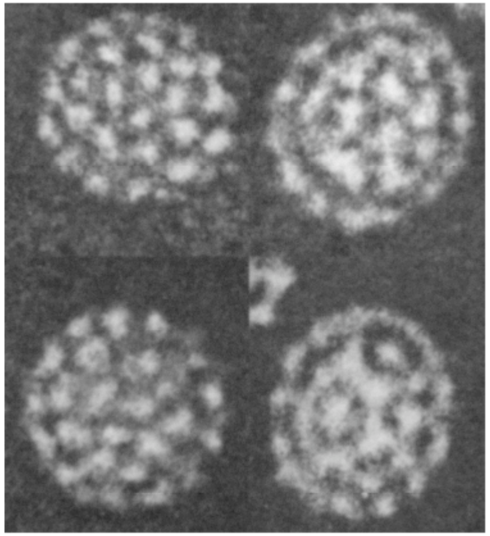


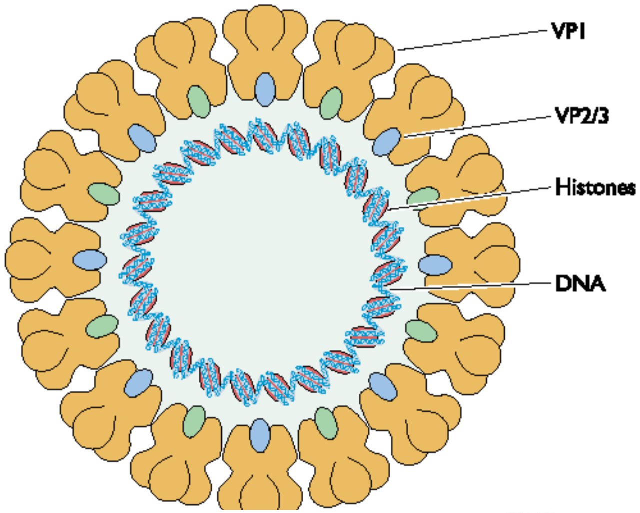
Herpes simplex virus latent infection in neurons



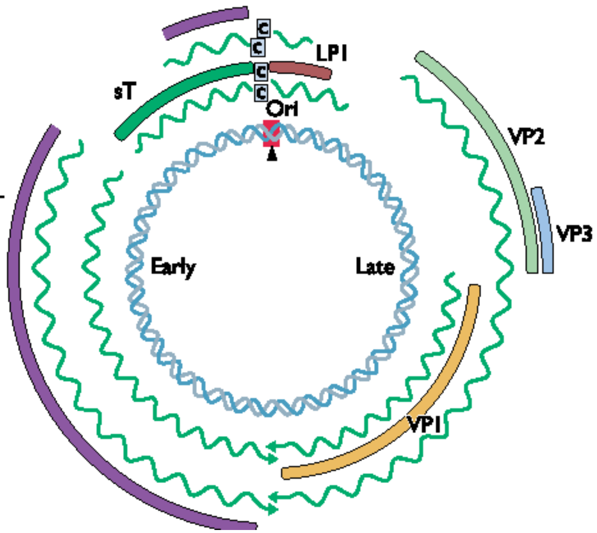
Structure and genome organization of the **Polyomavirus S**imian **V**irus **40**: an example of **Class I** tumoral virus

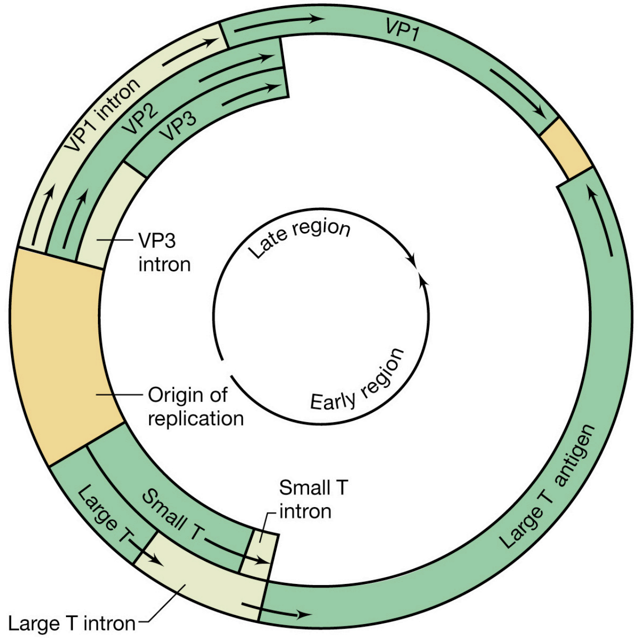
A





B





Attachment
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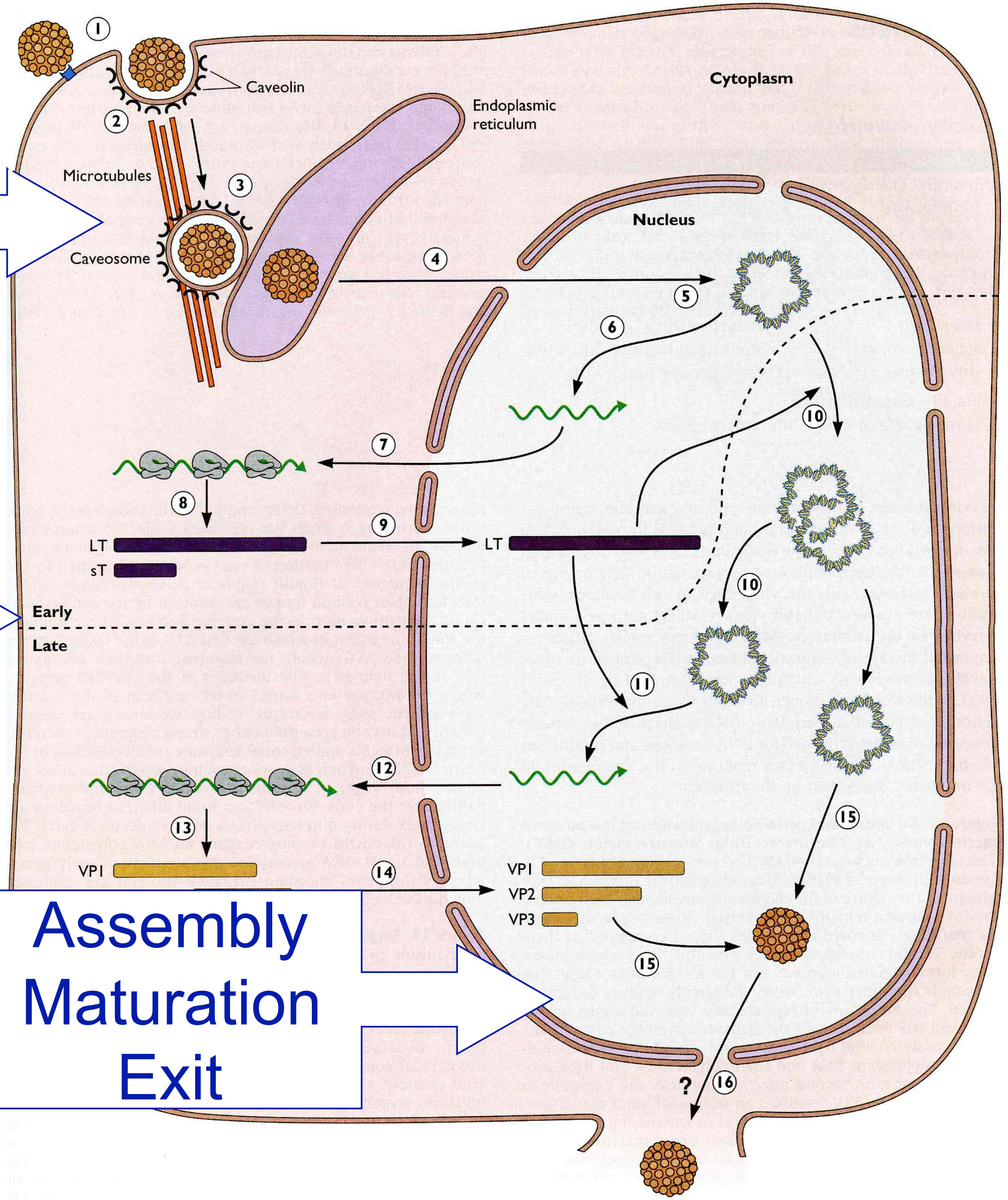
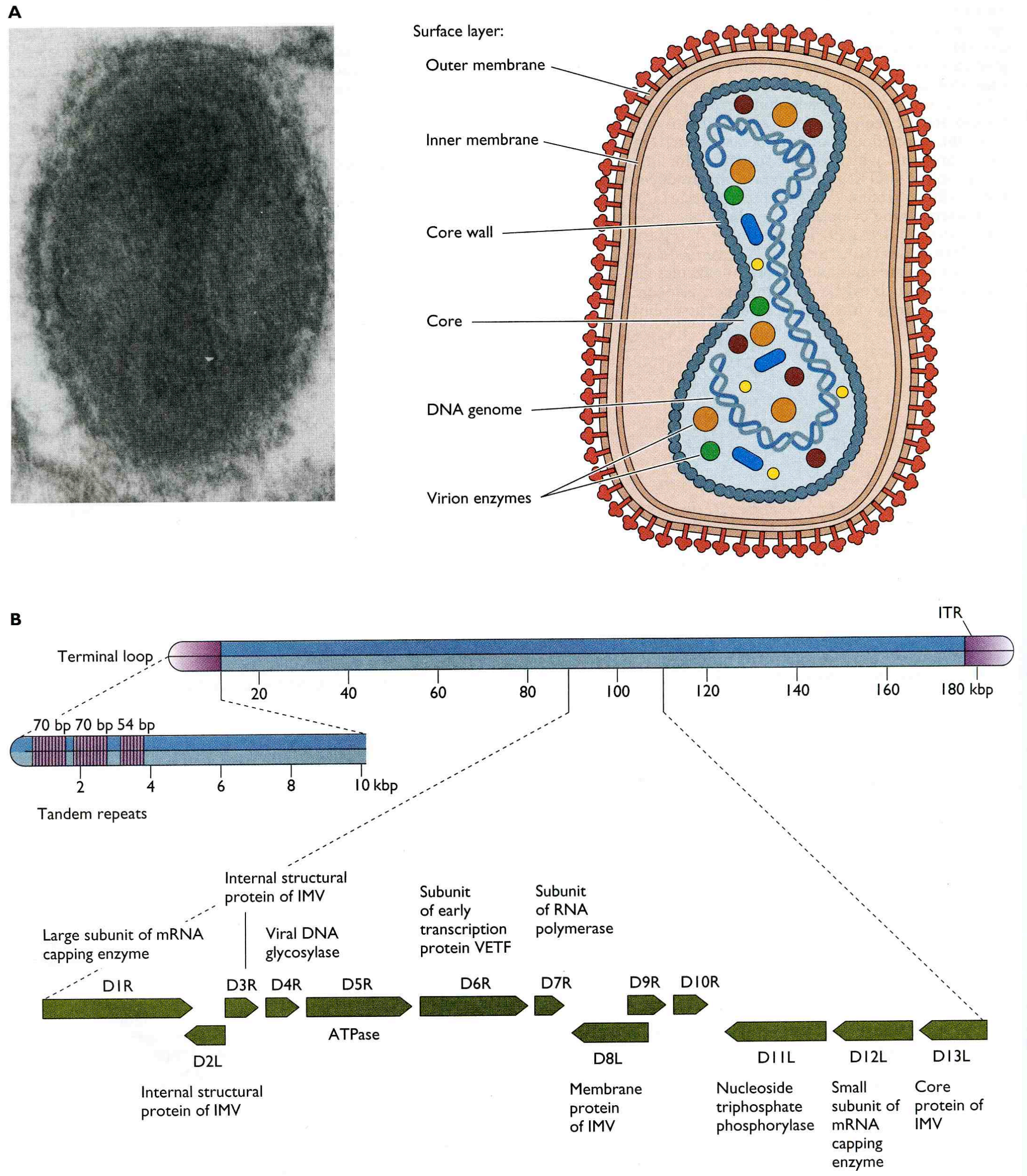


Structure and genome organization of the **Poxvirus** Vaccinia virus: an example of **Class I** virus that replicates in the cytoplasm



Attachment
Entry
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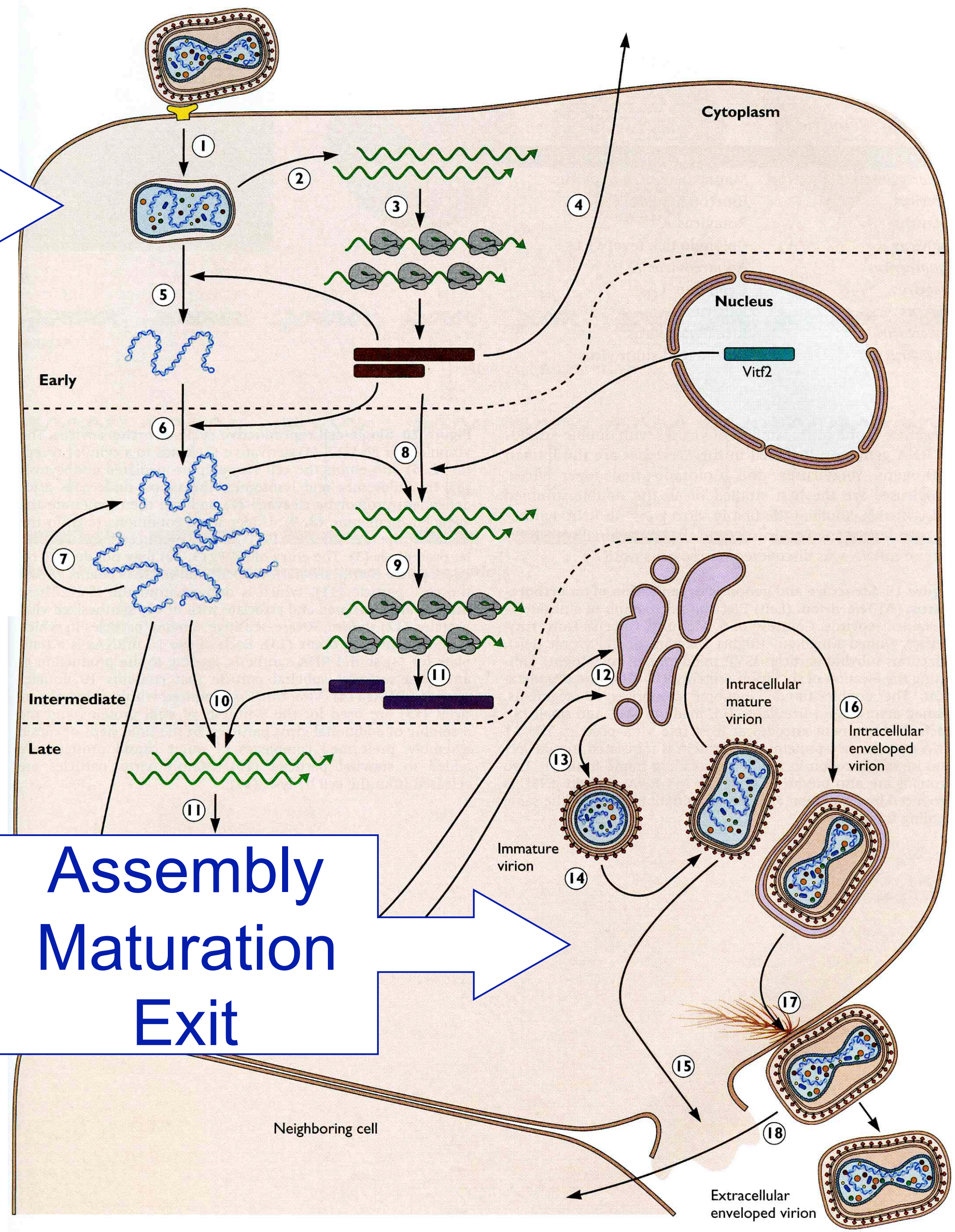
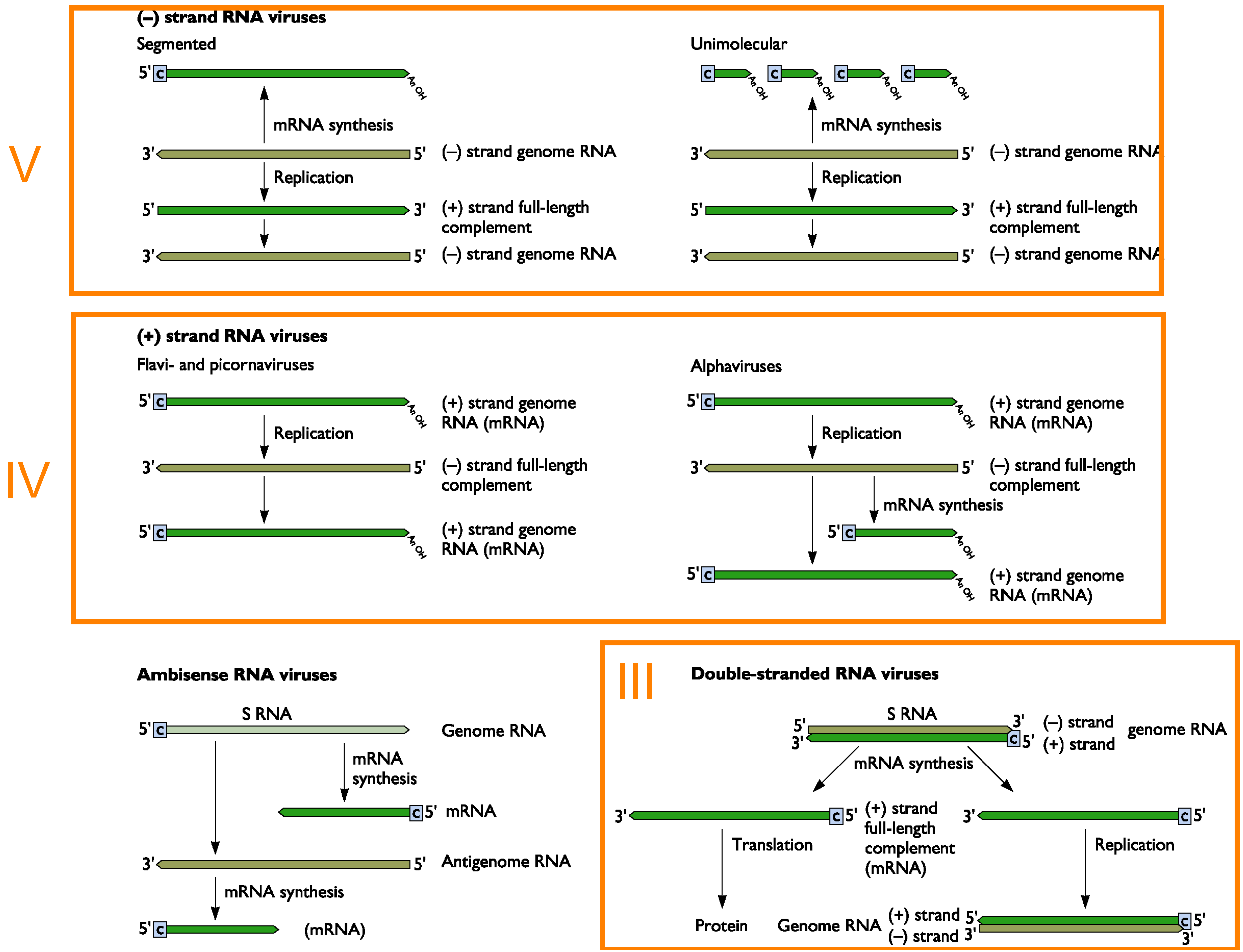


Viral replication

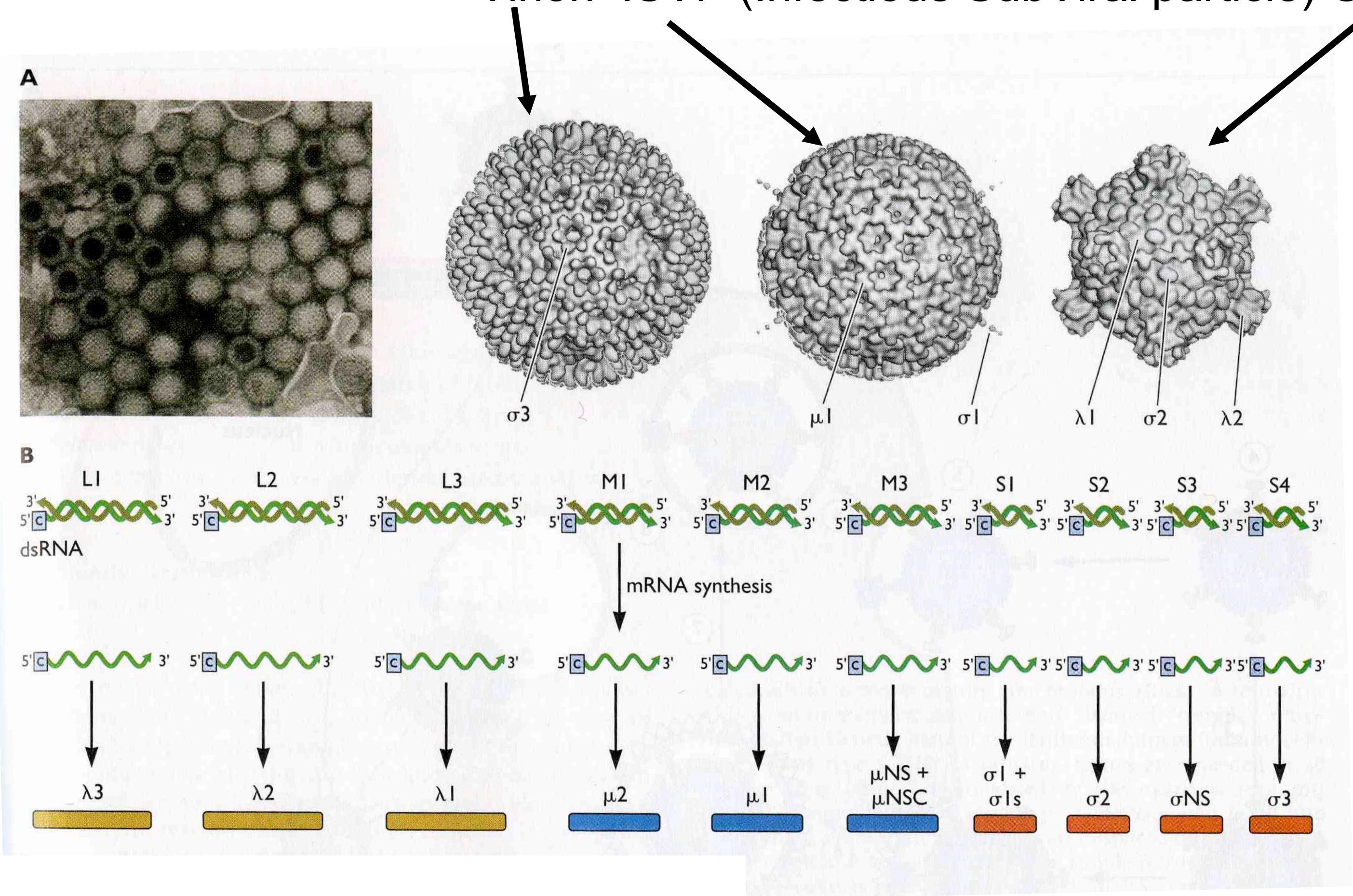
transcription, translation and genome replication of RNA viruses



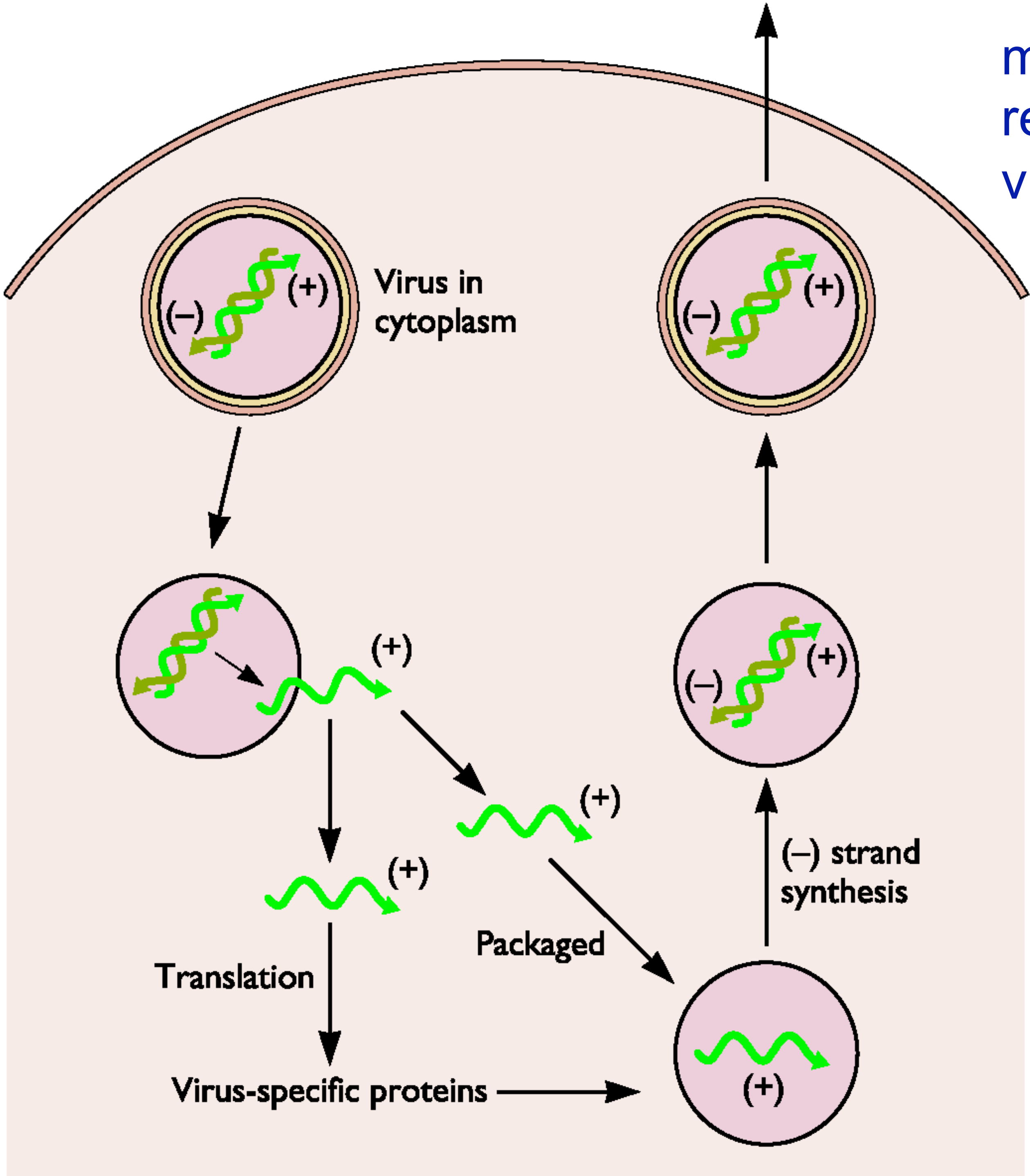
V
(–) strand RNA viruses
Segmented
5' C
An OH
mRNA synthesis
3' 5' (–) strand genome RNA
Replication
5' 3' (+) strand full-length complement
3' 5' (–) strand genome RNA
Unimolecular
C An OH
mRNA synthesis
3' 5' (–) strand genome RNA
Replication
5' 3' (+) strand full-length complement
3' 5' (–) strand genome RNA
IV
(+) strand RNA viruses
Flavi- and picornaviruses
5' C An OH (+) strand genome RNA (mRNA)
Replication
3' 5' (–) strand full-length complement
5' C An OH (+) strand genome RNA (mRNA)
Alphaviruses
5' C An OH (+) strand genome RNA (mRNA)
Replication
3' 5' (–) strand full-length complement
mRNA synthesis
5' C An OH
5' C An OH (+) strand genome RNA (mRNA)
Ambisense RNA viruses
S RNA
5' C Genome RNA
mRNA synthesis
C 5' mRNA
3' 5' Antigenome RNA
mRNA synthesis
5' C (mRNA)
III
Double-stranded RNA viruses
S RNA
5' 3' (–) strand
3' C 5' (+) strand
genome RNA
mRNA synthesis
3' C 5' (+) strand full-length complement (mRNA)
3' C 5'
Translation
Replication
Protein
Genome RNA
(+) strand 5' C 5'
(–) strand 3' 3'

Structure and genomic organization of a Reovirus

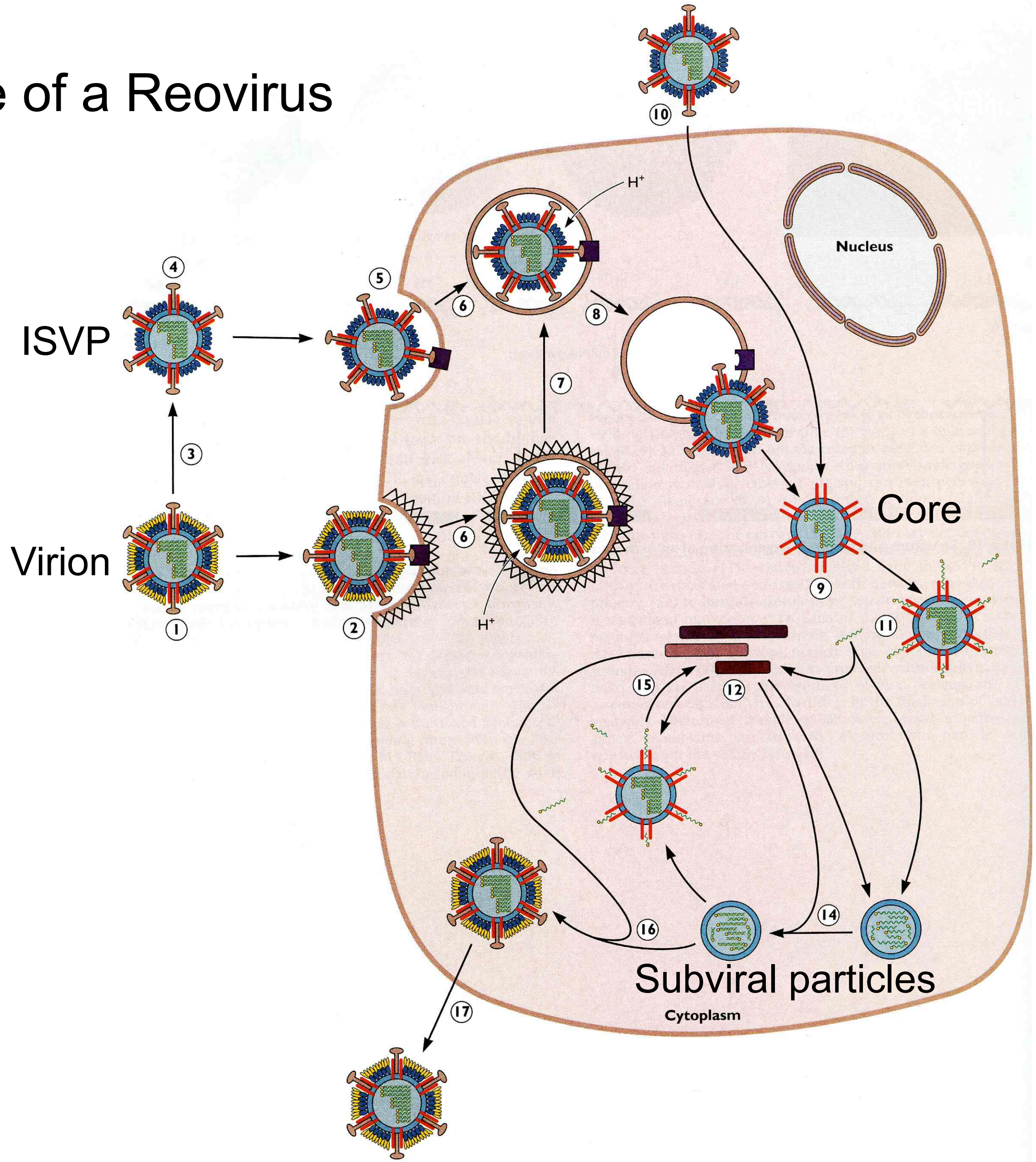
Virion ISVP (Infectious SubViral particle) Core



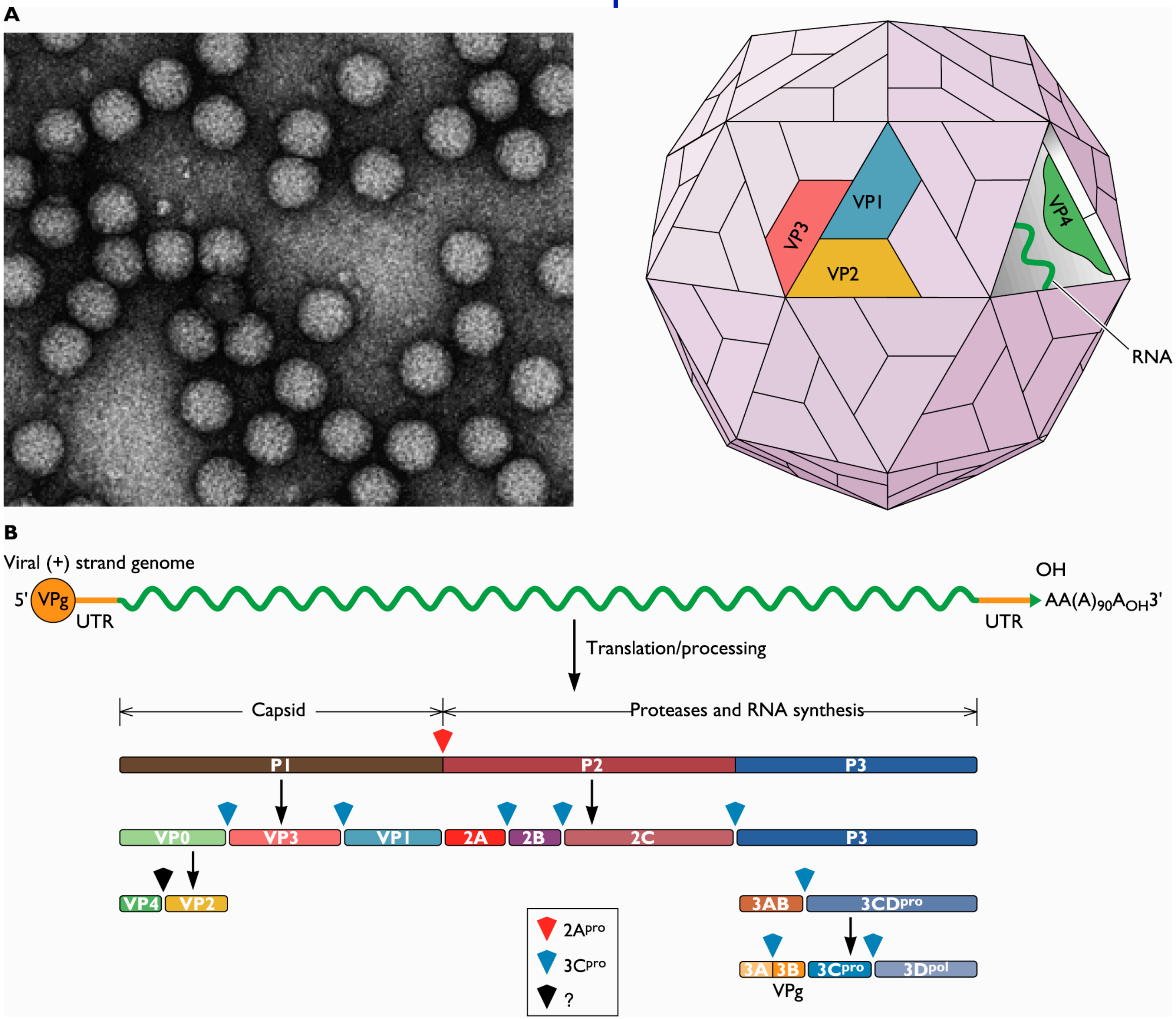
mRNA synthesis and replication of **Class III** virus: the **Reoviruses**



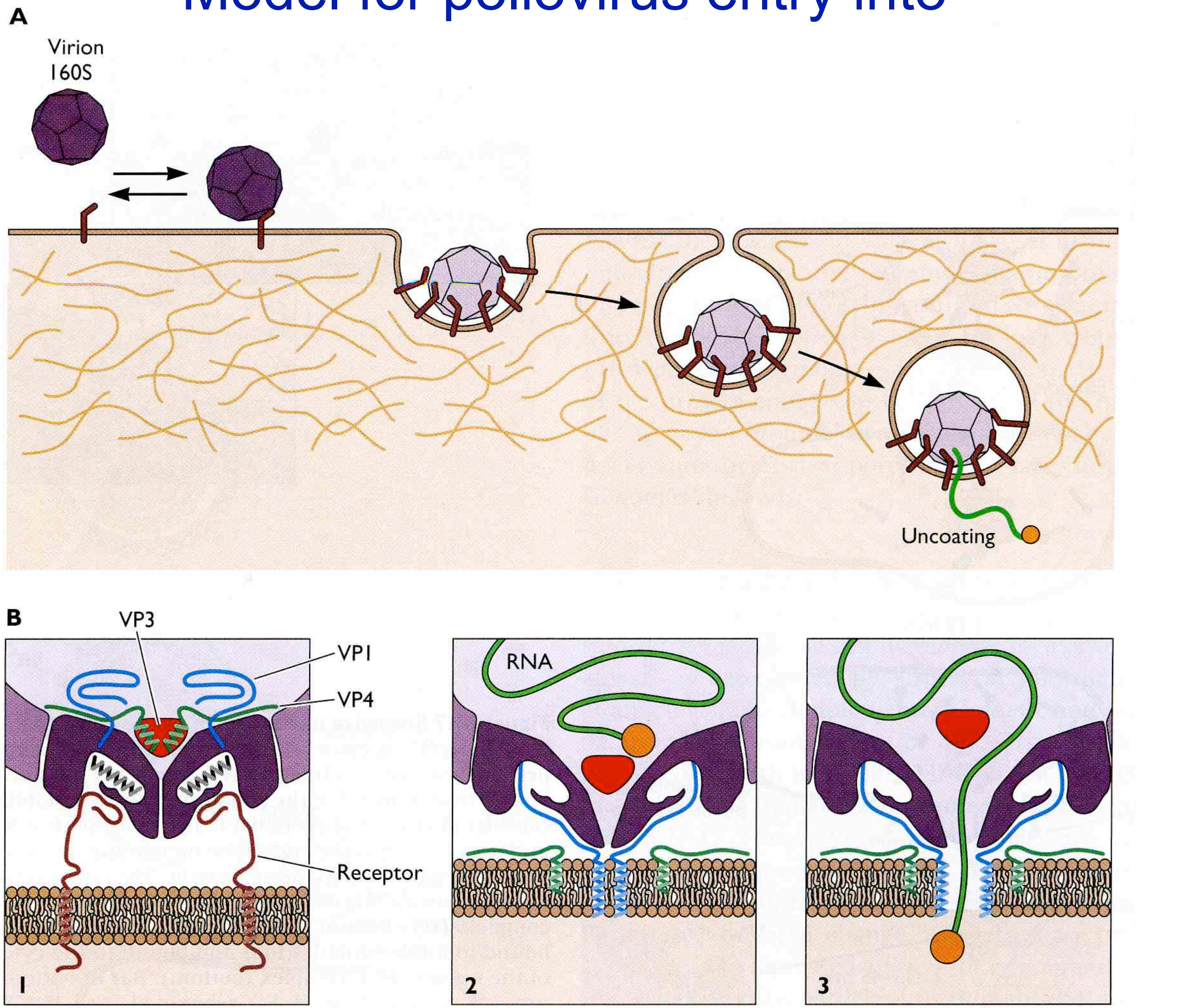
Reproductive cycle of a Reovirus



Structure and genome organization of the **Picornavirus** Poliovirus: an example of **Class IV** virus



Model for poliovirus entry into



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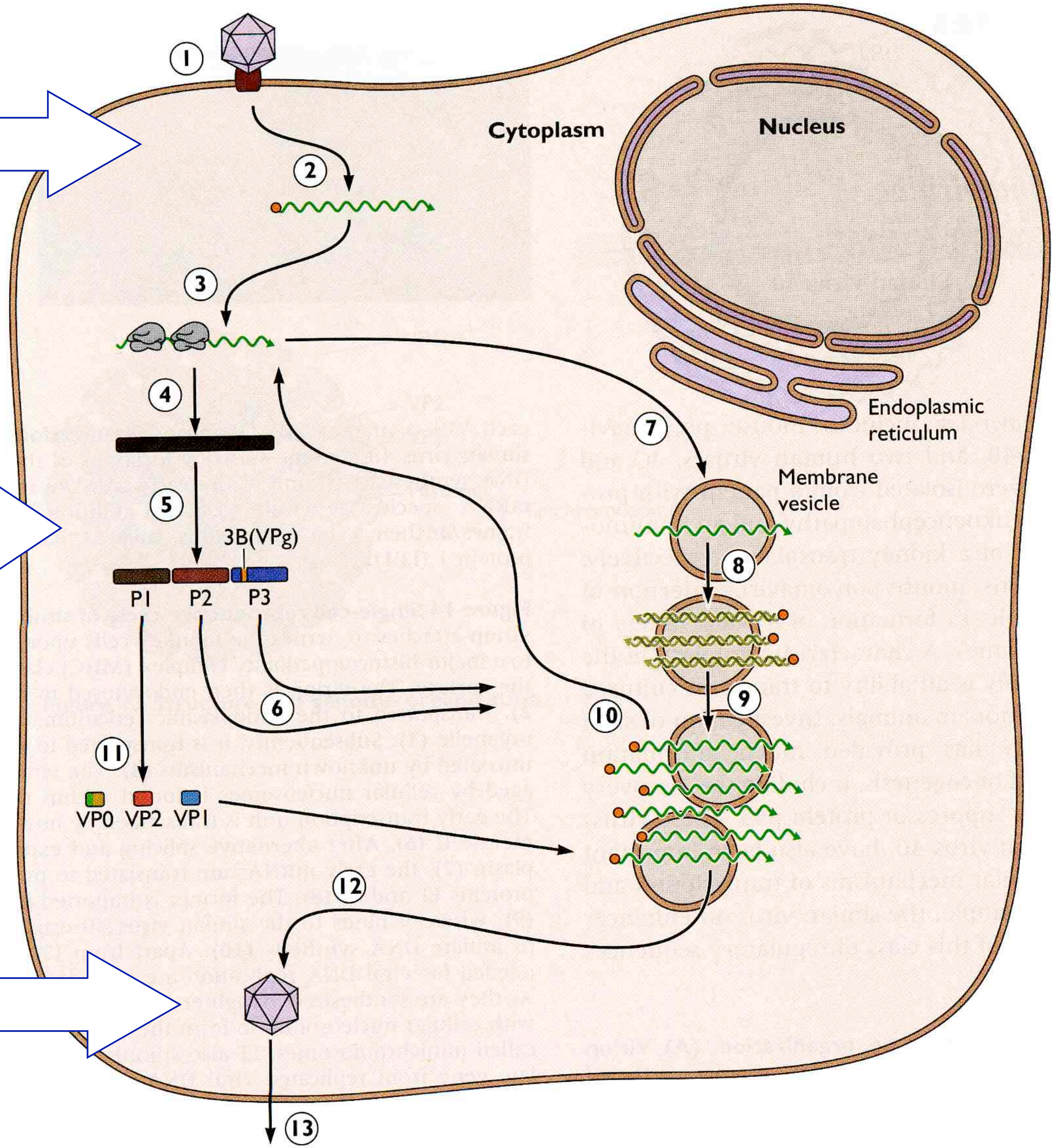
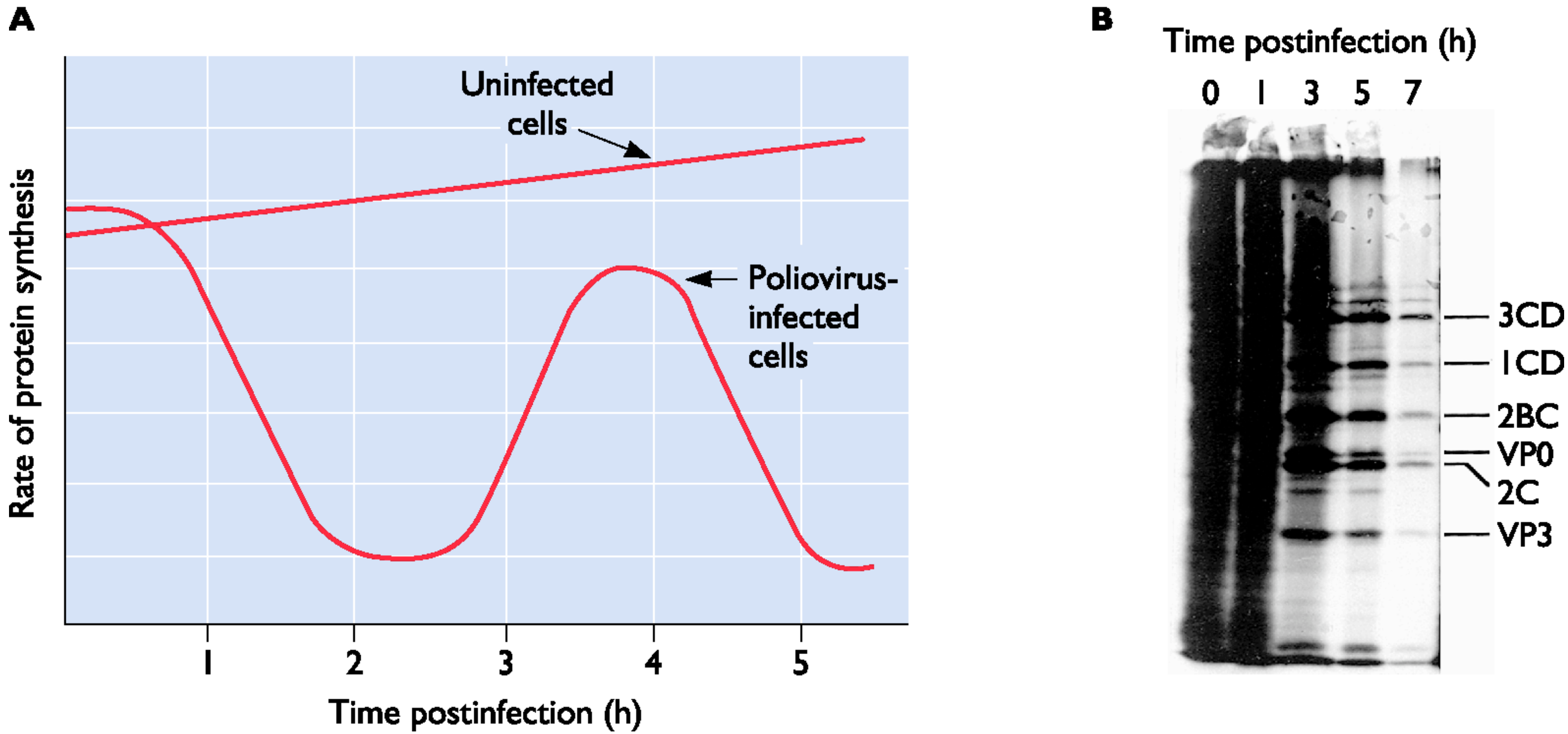
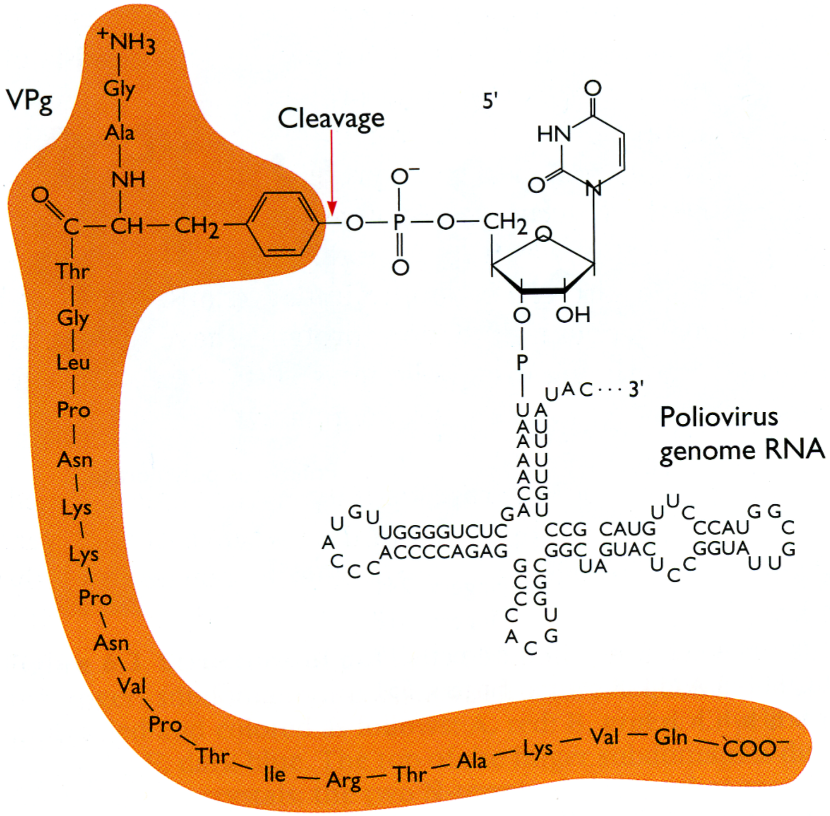


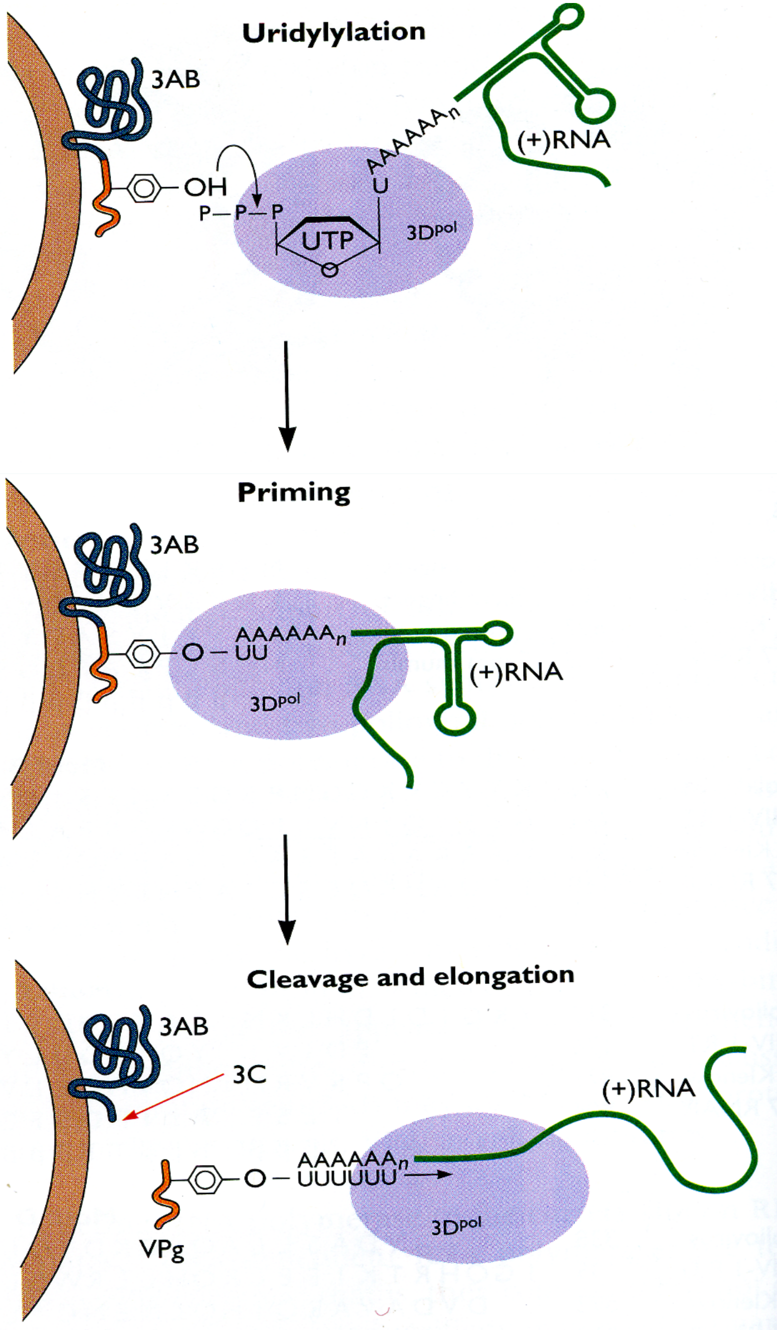
Inhibition of translation in poliovirus-infected cells



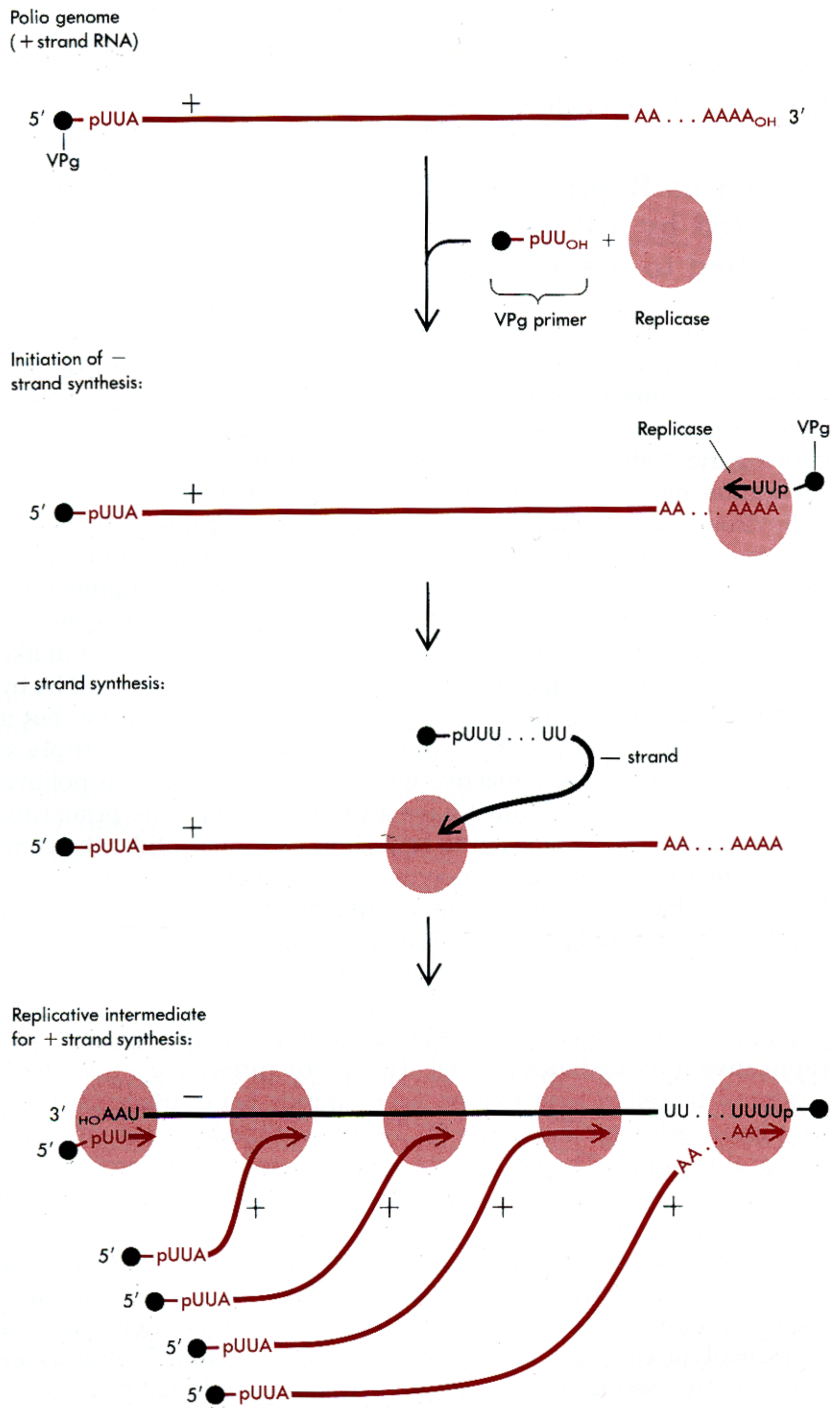
Poliovirus RNA replication



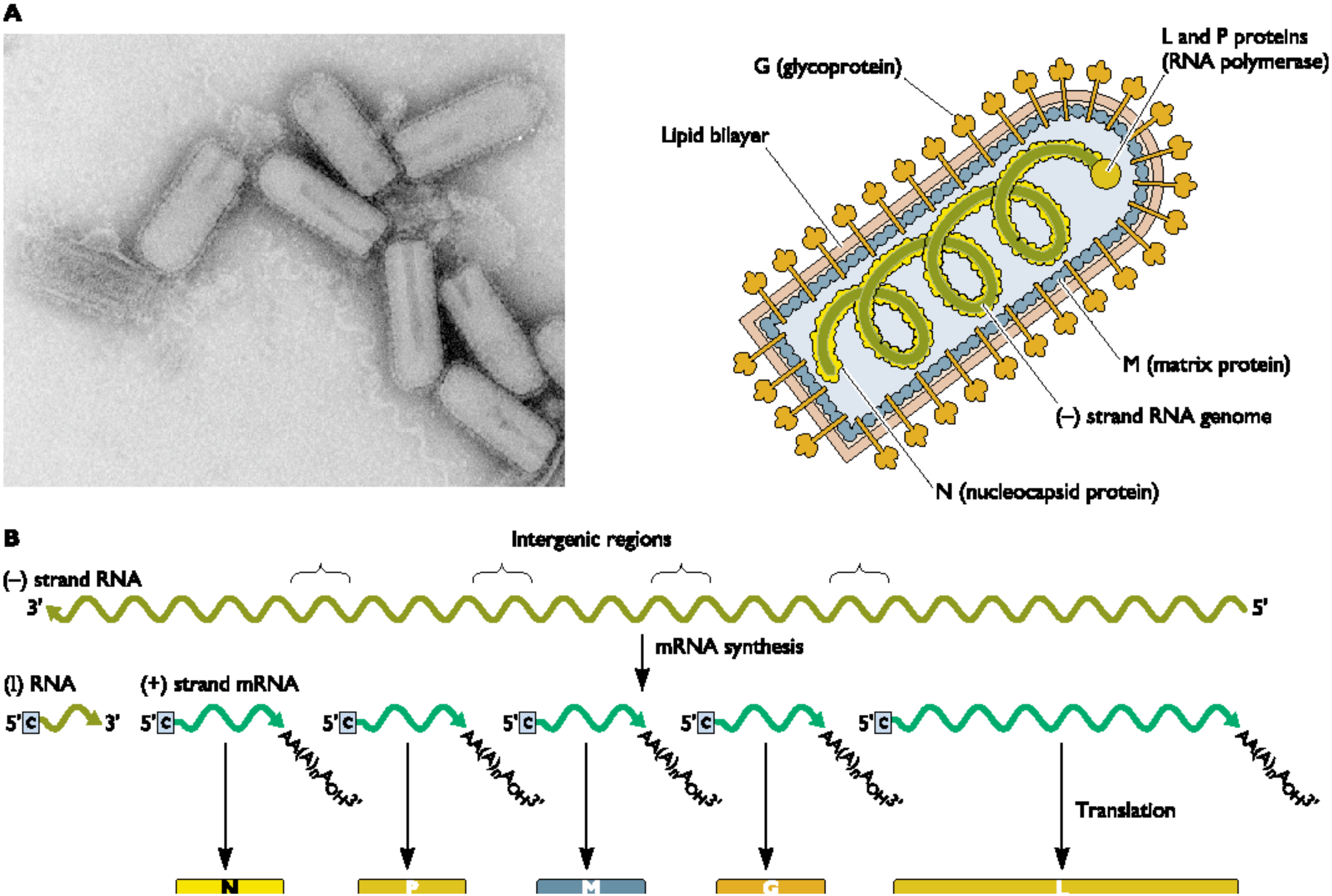
Linkage of VPg to polioviral genomic RNA



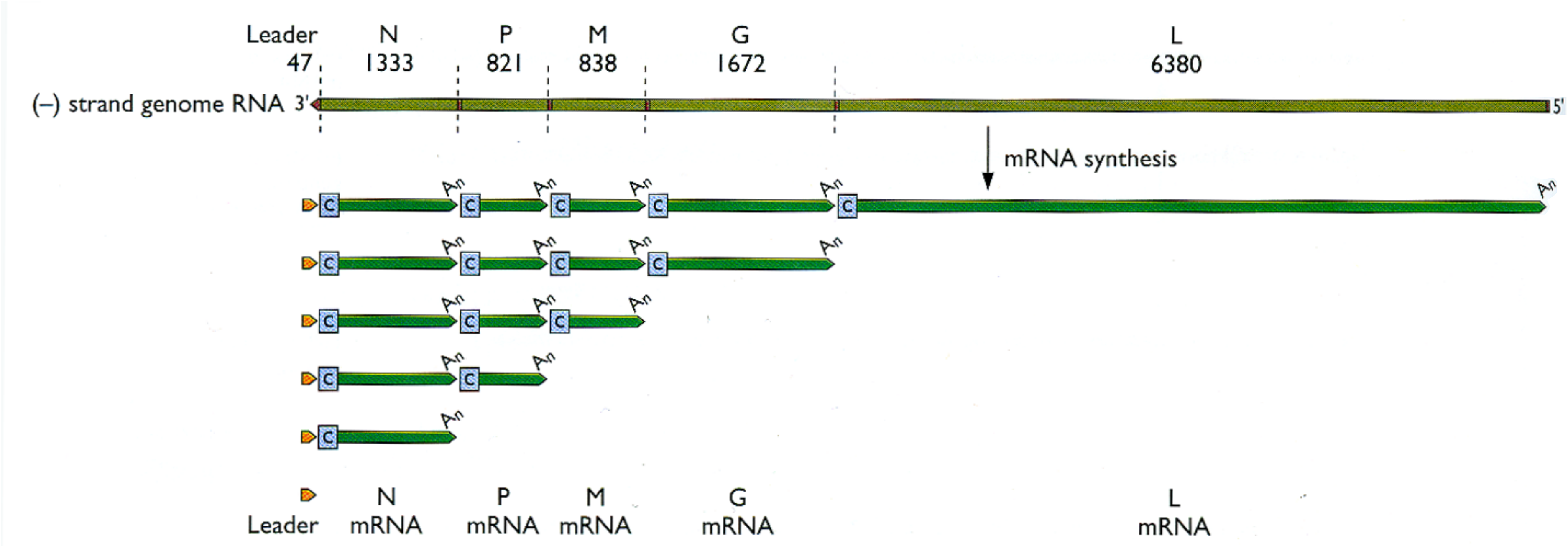
Poliovirus RNA replication



Structure and genome organization of the **Rhabdovirus** **V**esicular **S**tomatitis **V**irus: an example of **Class V virus**



Vesicular stomatitis virus mRNA map



Attachment
Entry
Uncoating

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Synthesis

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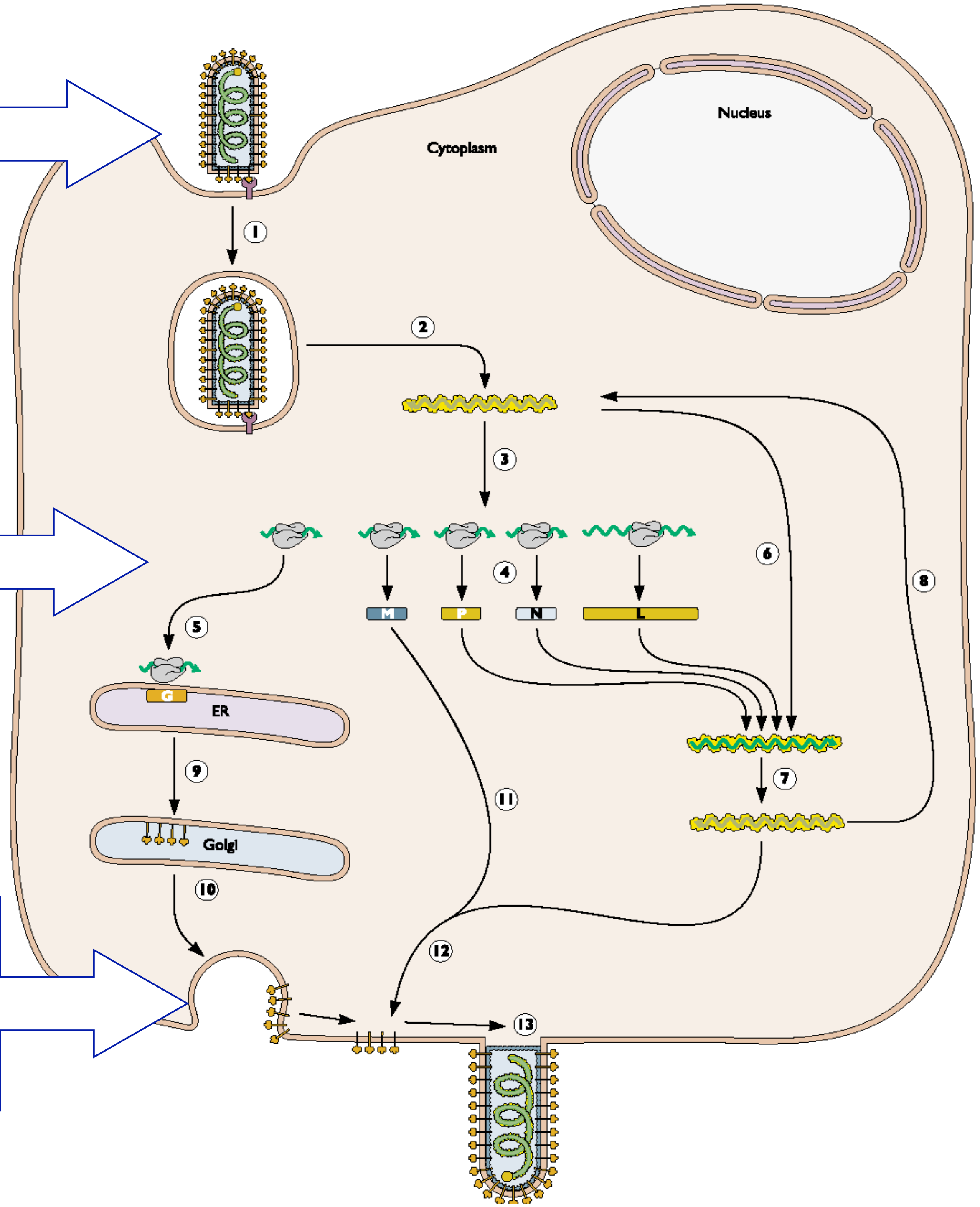
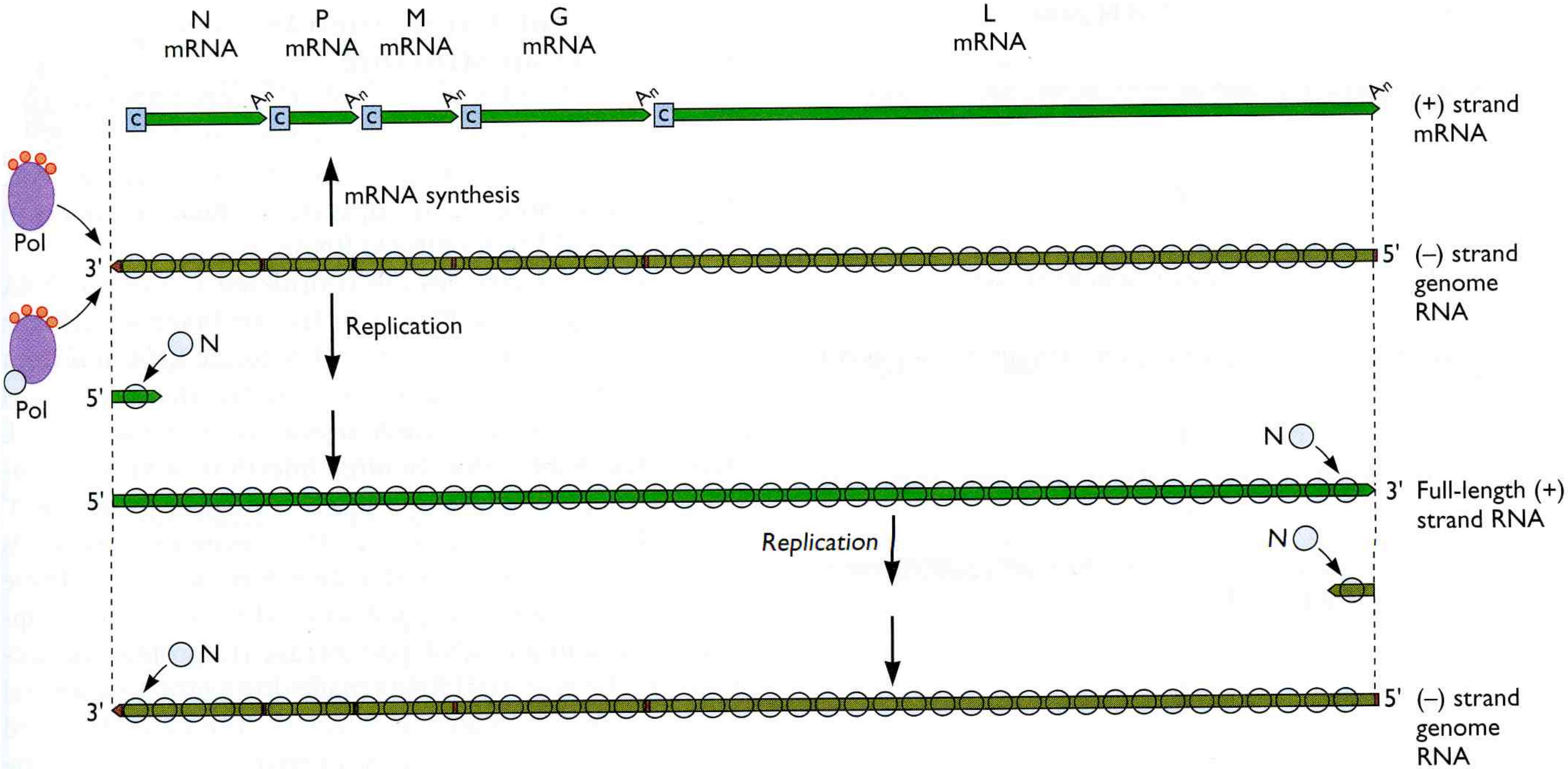
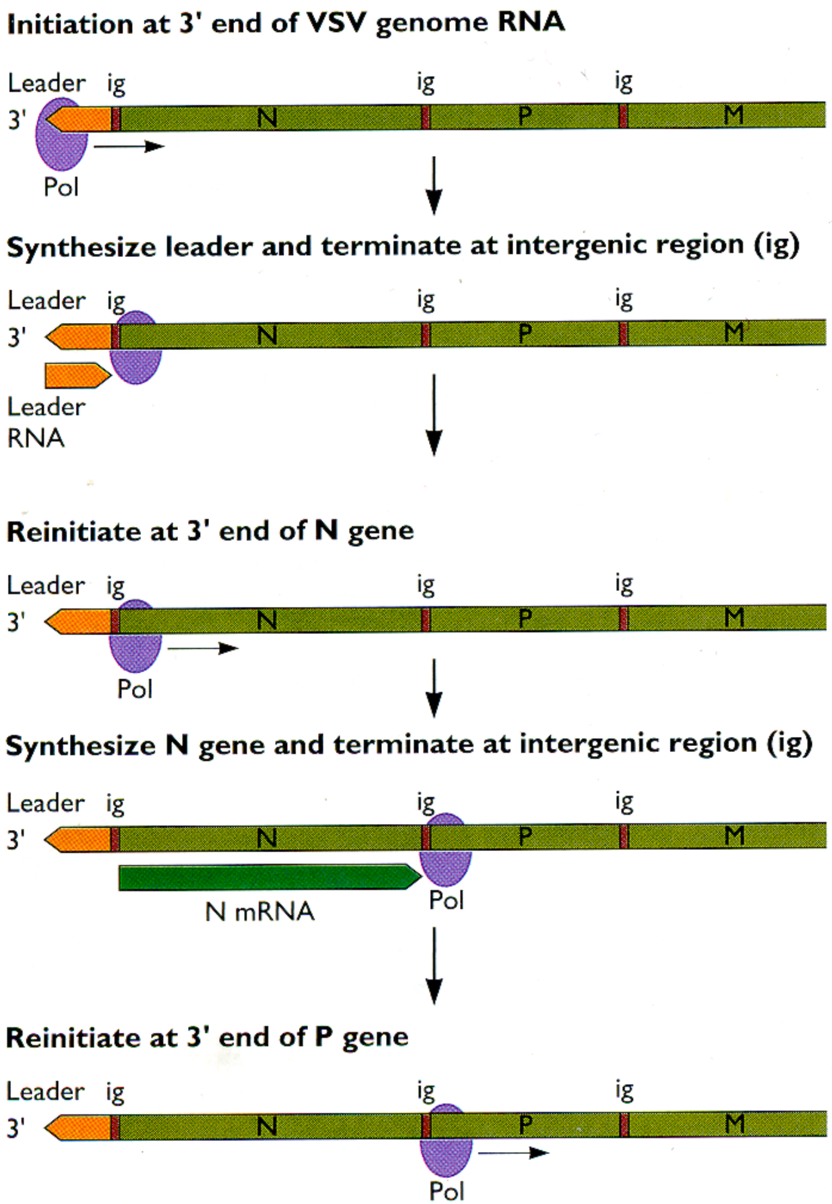
Exit

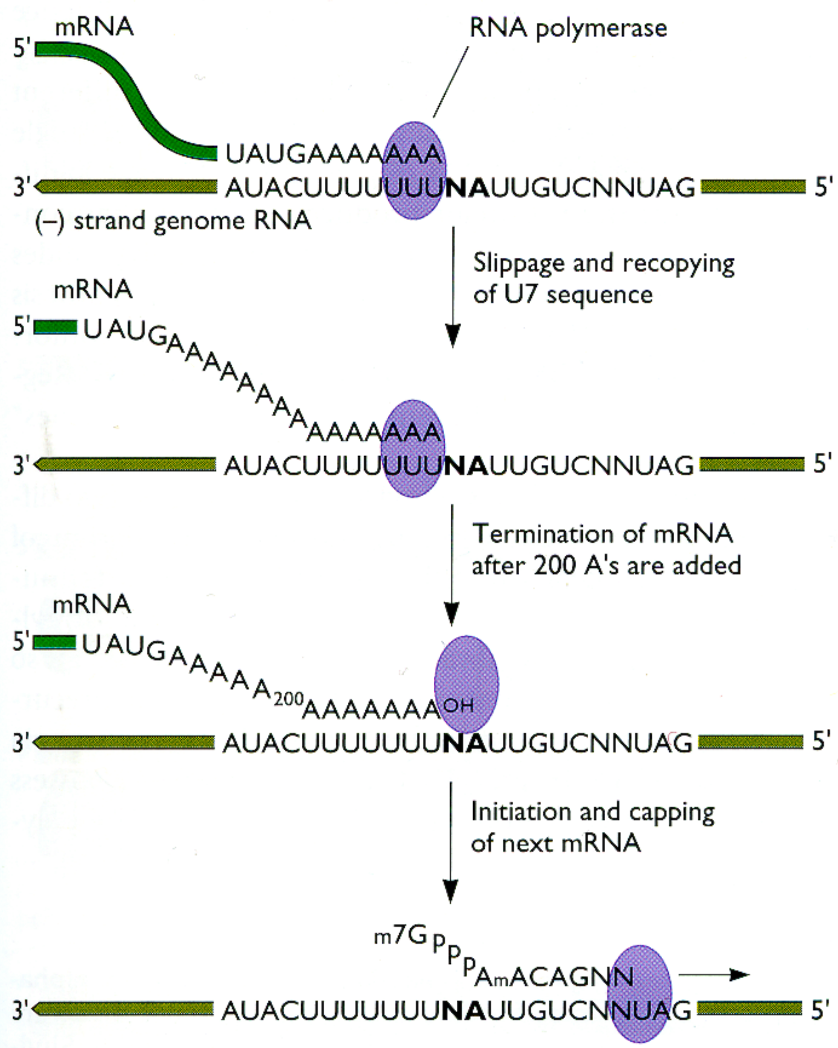


Transcription and replication of the VSV genome



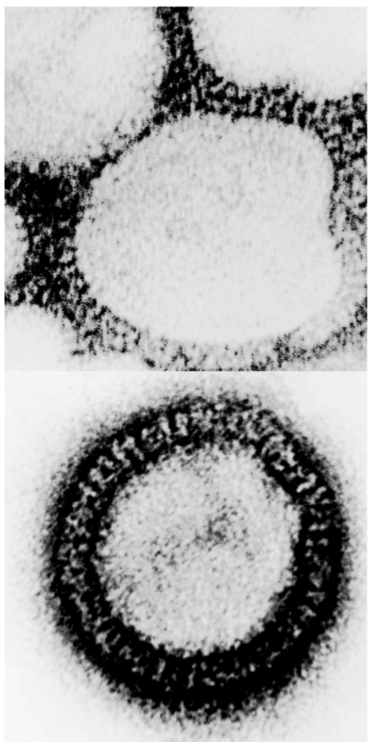
VSV mRNA synthesis and function of RNA pol at an intergenic region

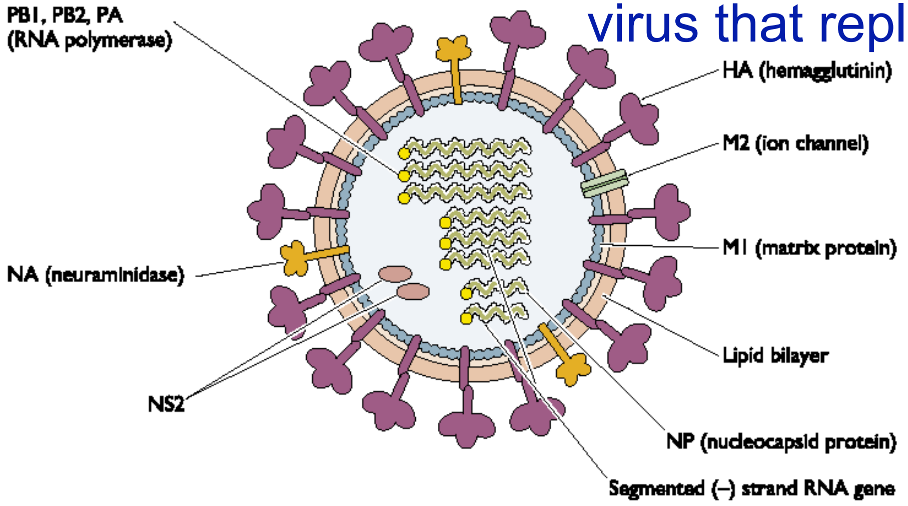




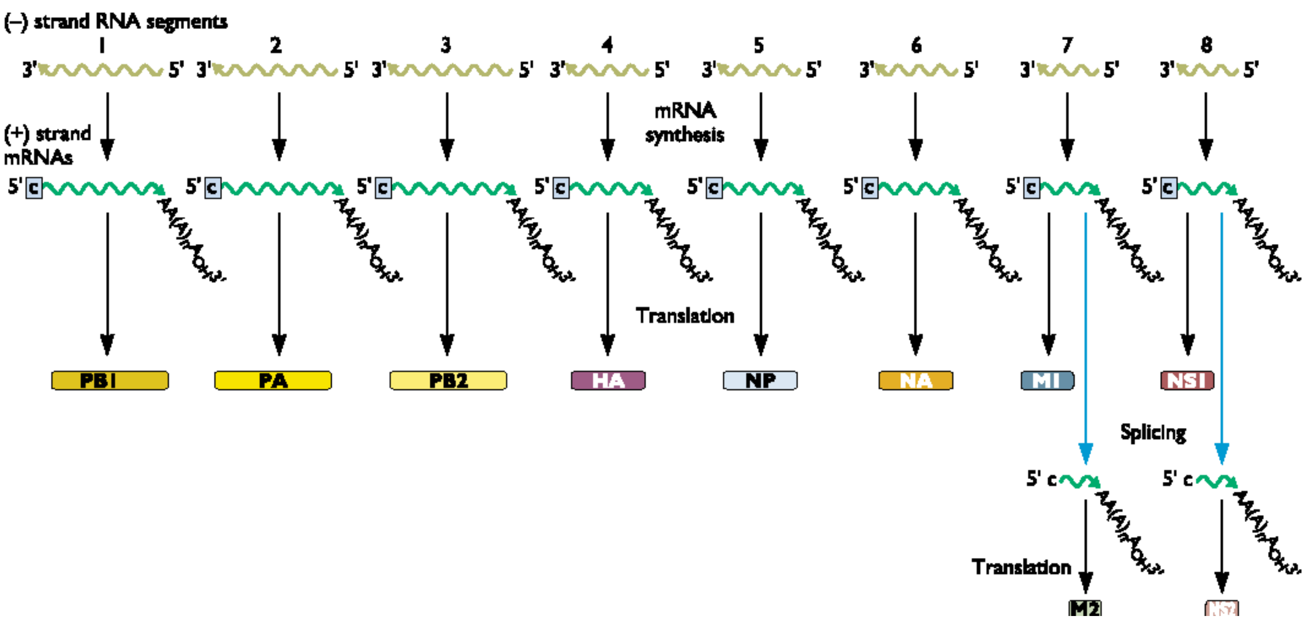
The **Orthomyxovirus** Influenza A virus: an example of **Class V** virus that replicates in the nucleus

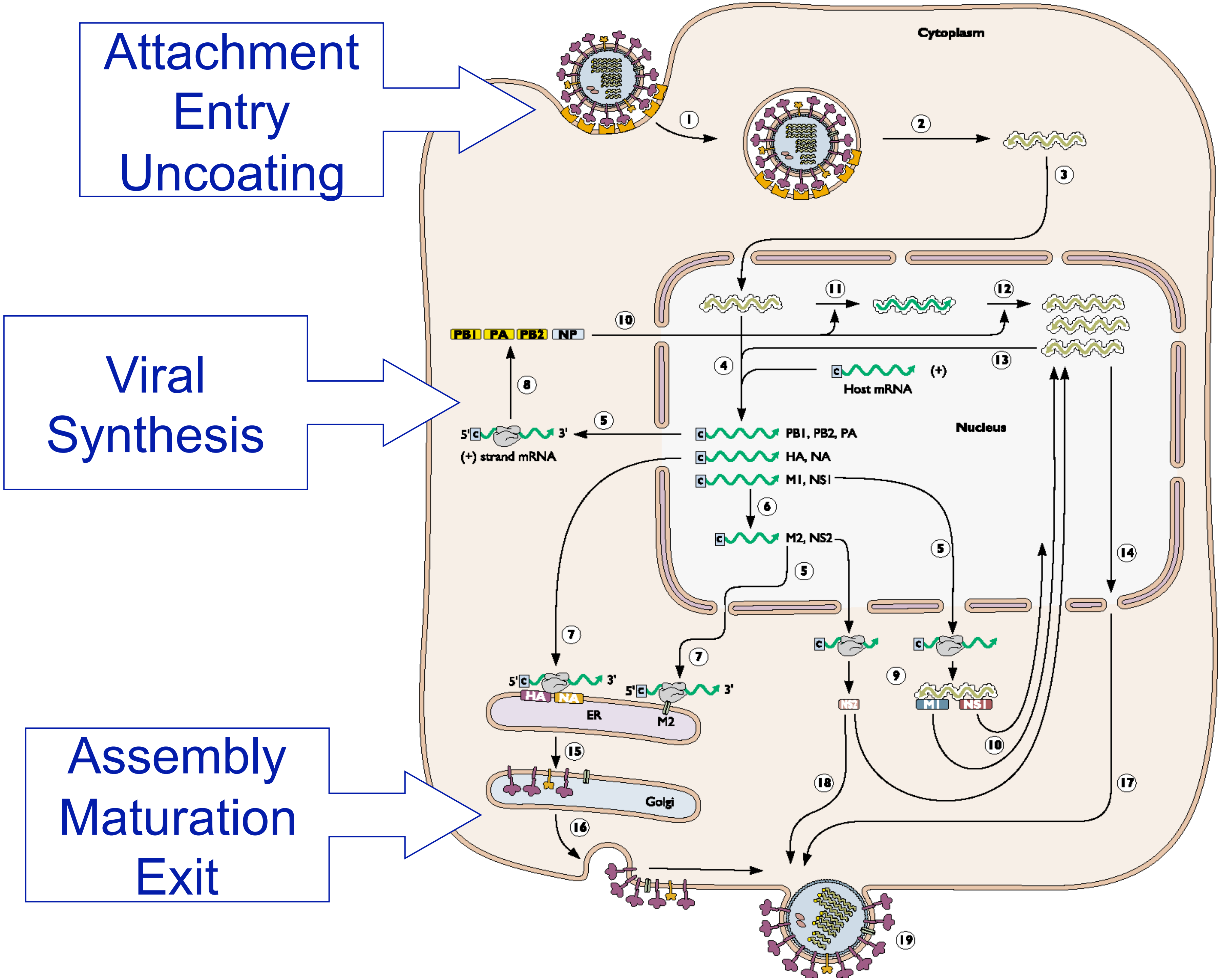
A





B




Attachment
Entry
Uncoating
Viral
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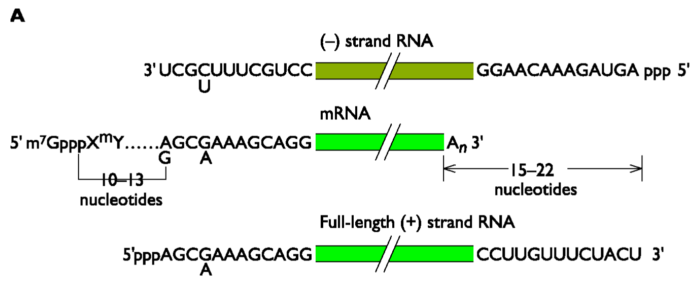
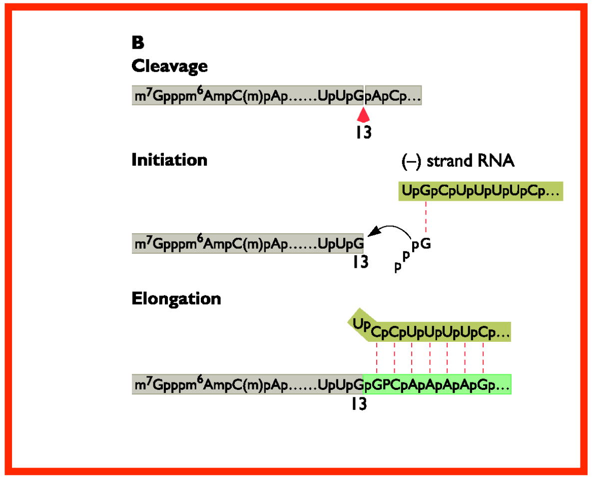
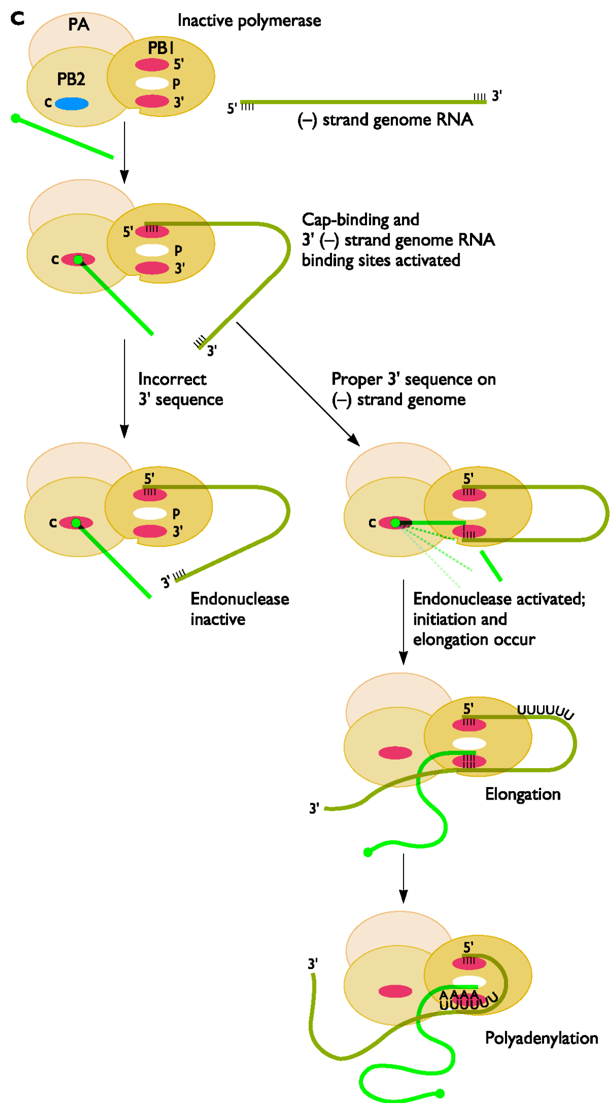
Maturation
Exit
Cytoplasm
Nucleus
PB1 PA PB2 NP
Host mRNA
(+)
PB1, PB2, PA
HA, NA
M1, NS1
M2, NS2
5' C 3'
(+) strand mRNA
HA NA
ER
M2
Golgi
NS2
M1 NS1

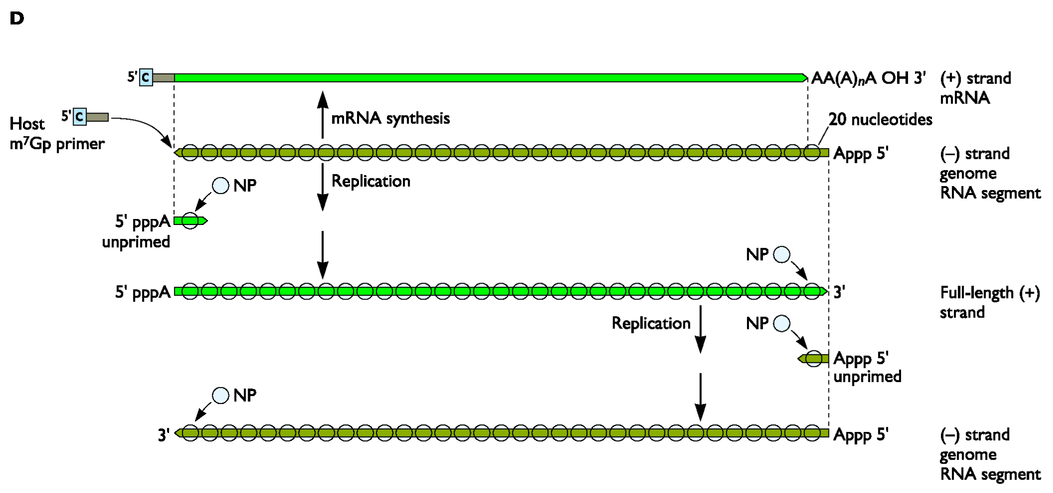




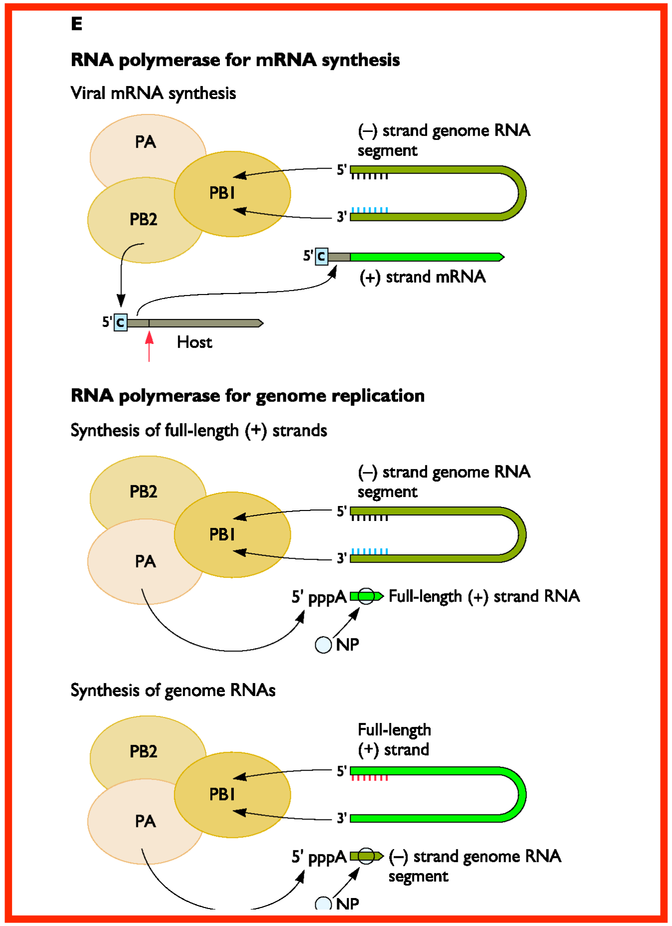


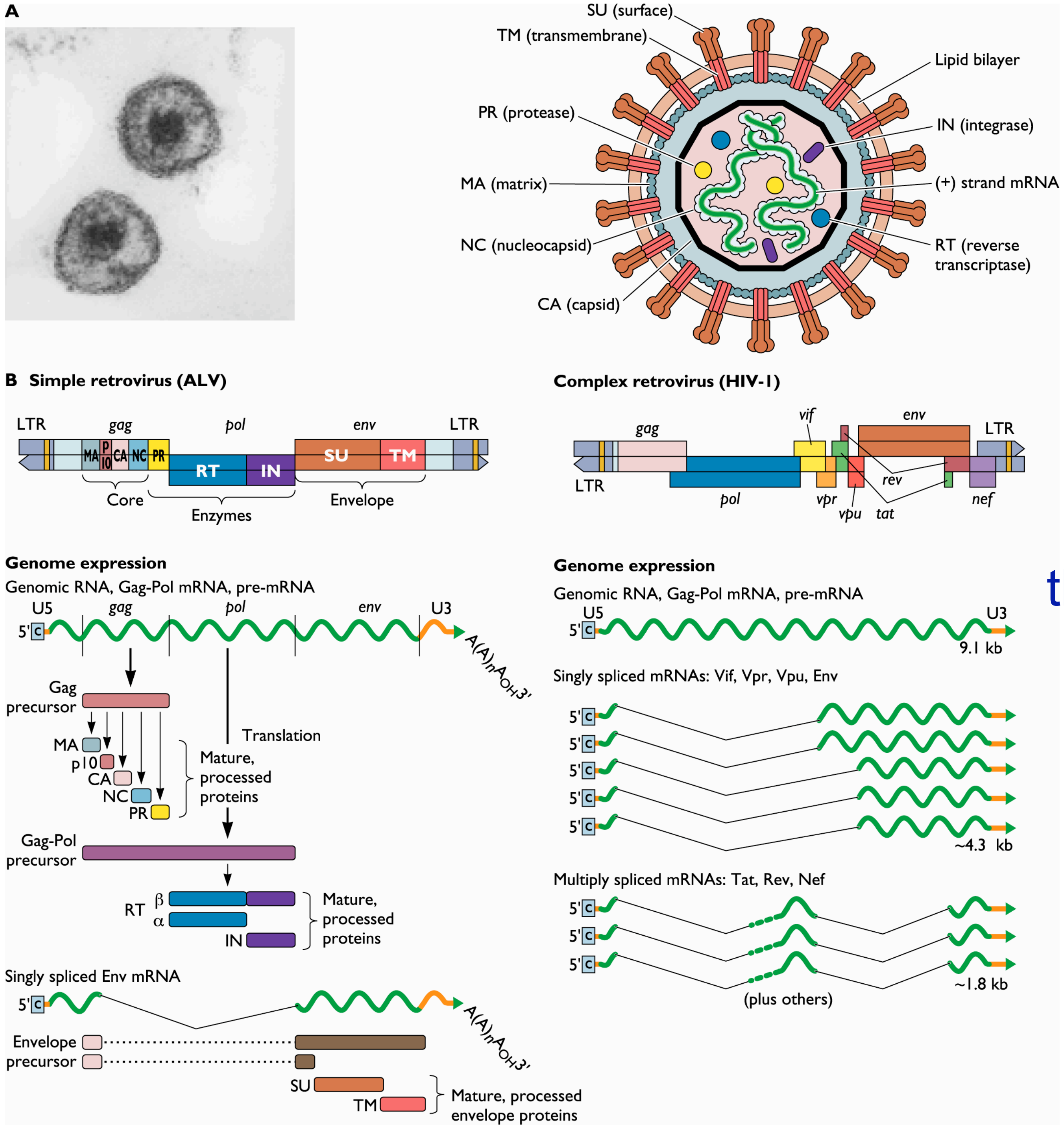
Influenza A virus

transcription and replication



Influenza A virus
transcription and replication





Class VI virus: the **Retroviruses**

Attachment
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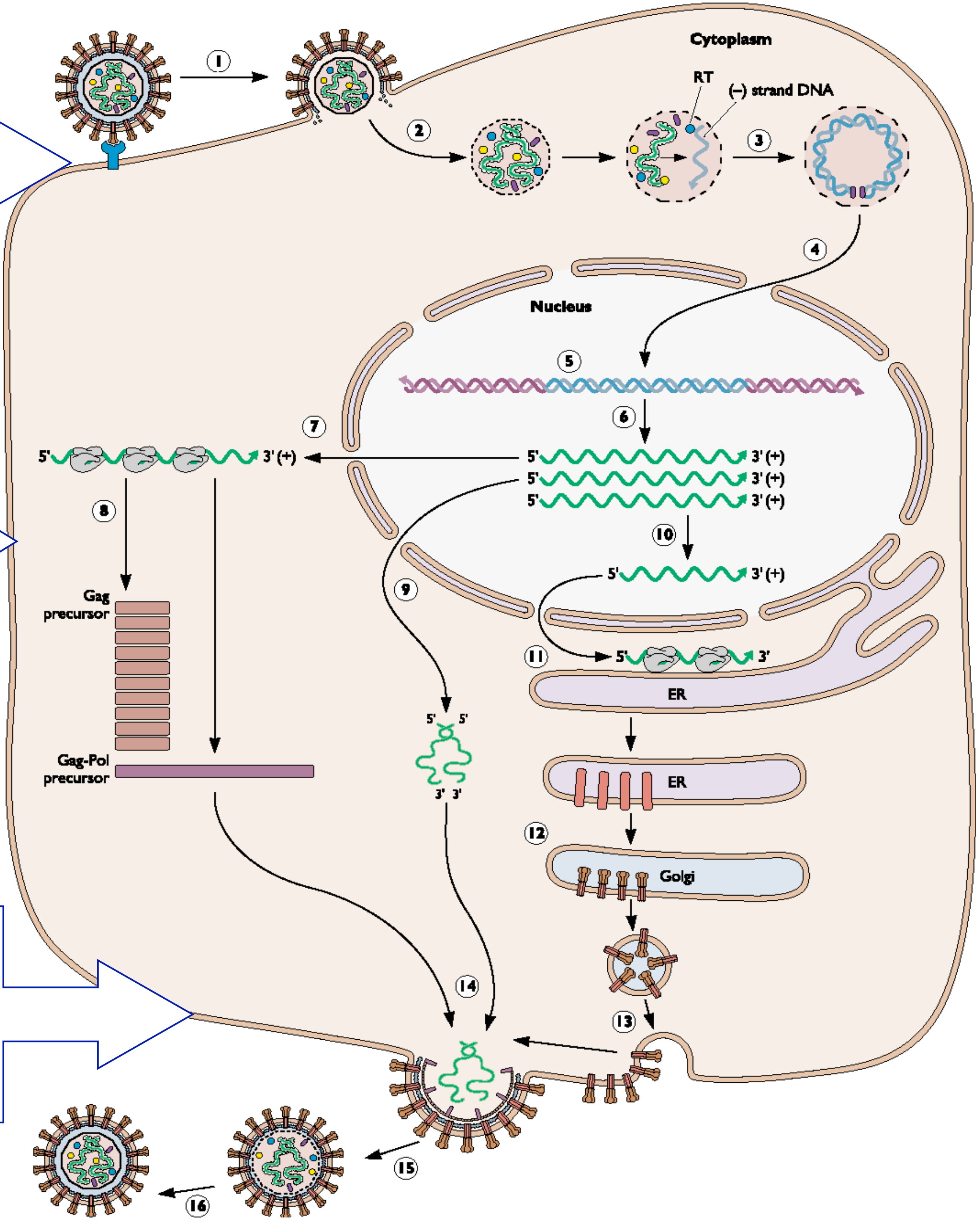
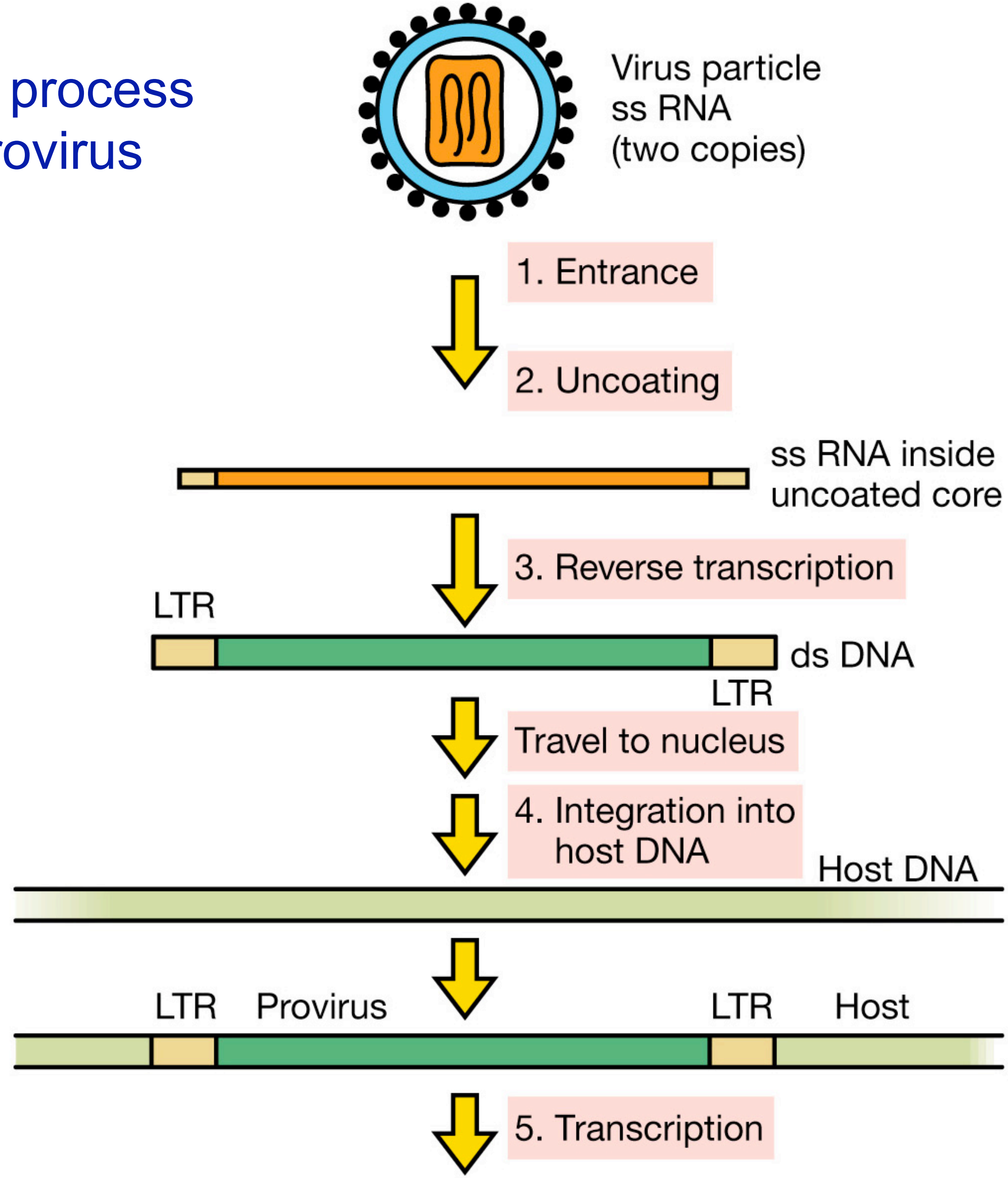
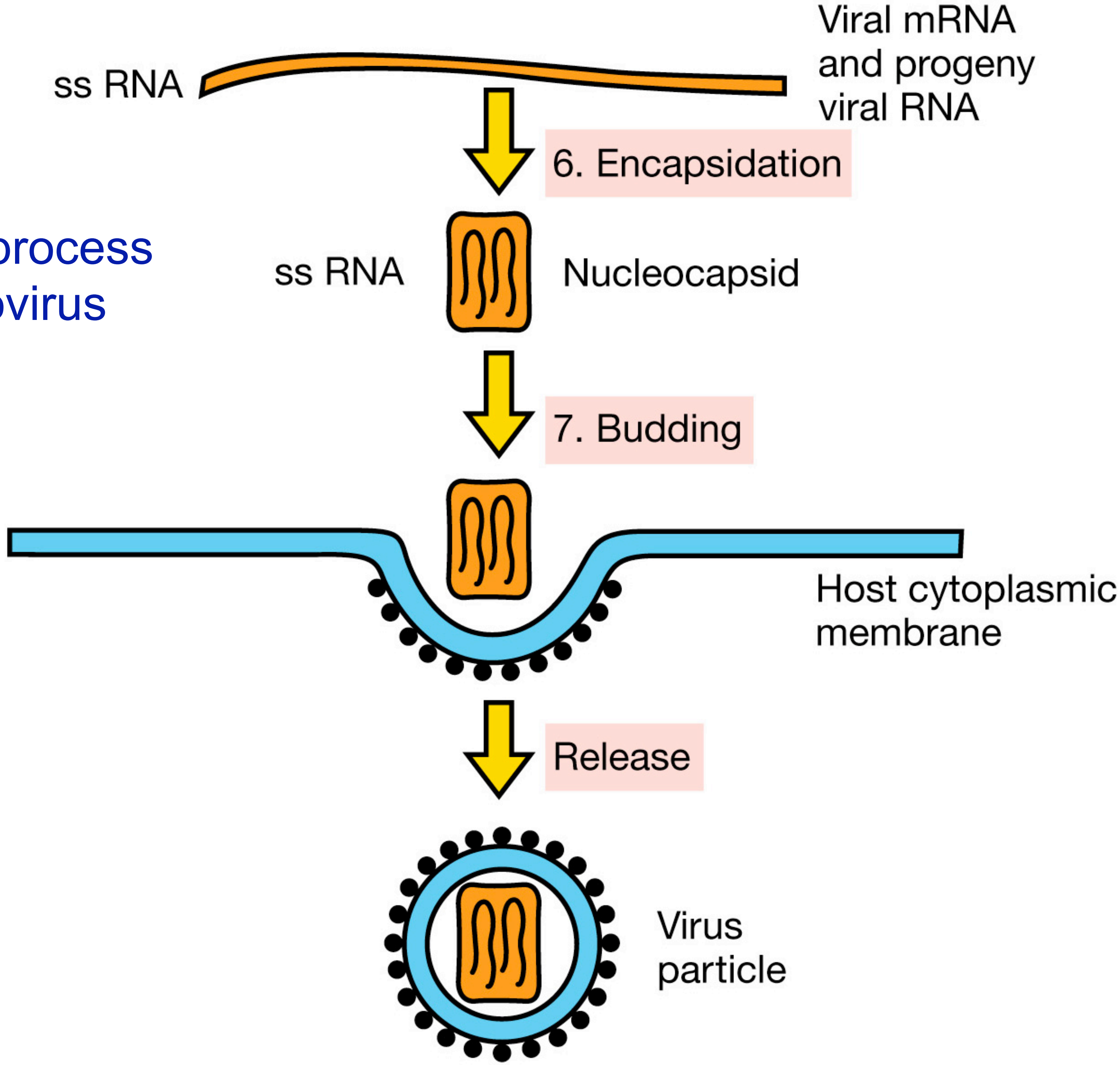


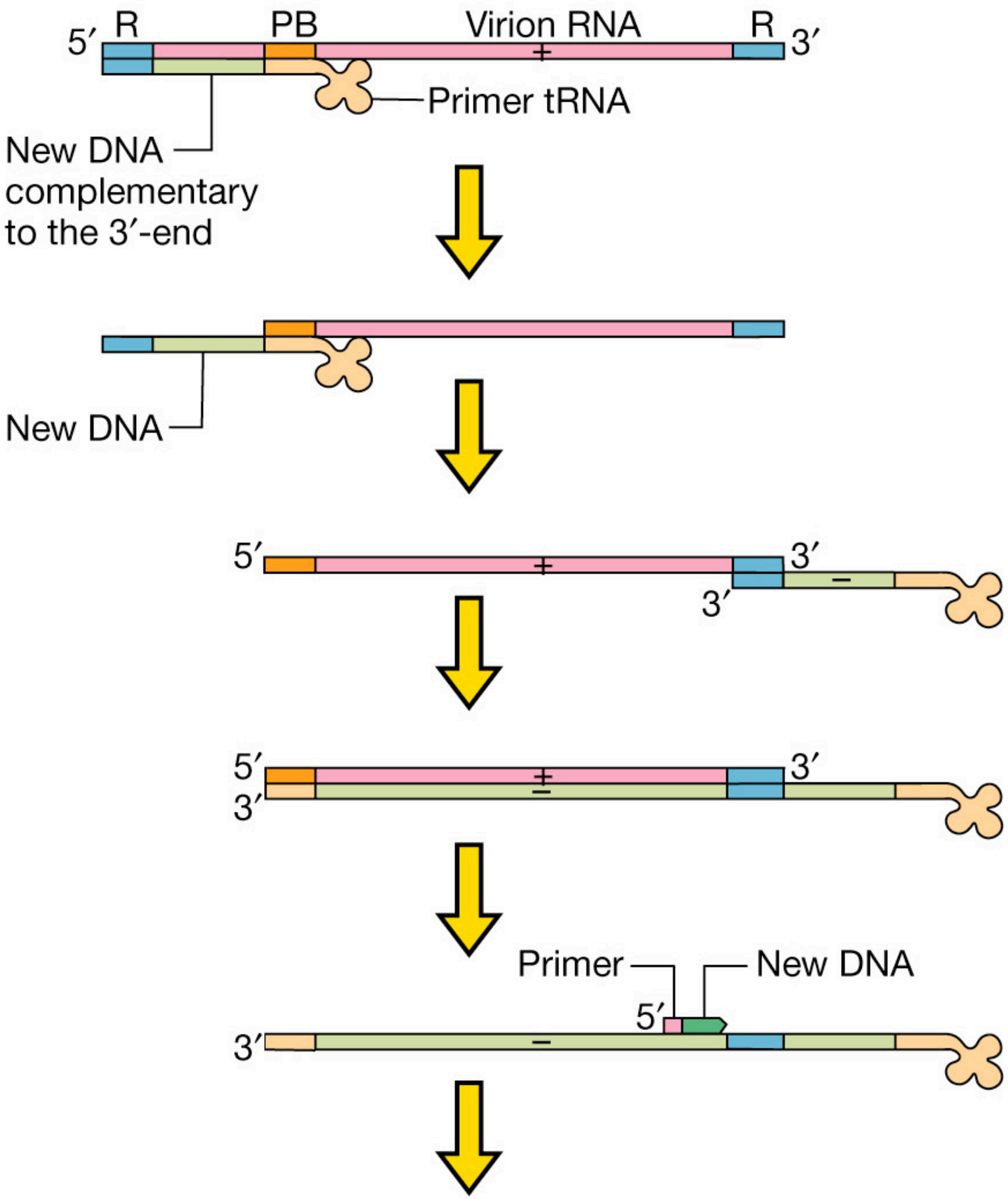
Replication process of a Retrovirus



Replication process of a Retrovirus



Overall steps in the formation of double-stranded DNA from Retrovirus single-stranded RNA



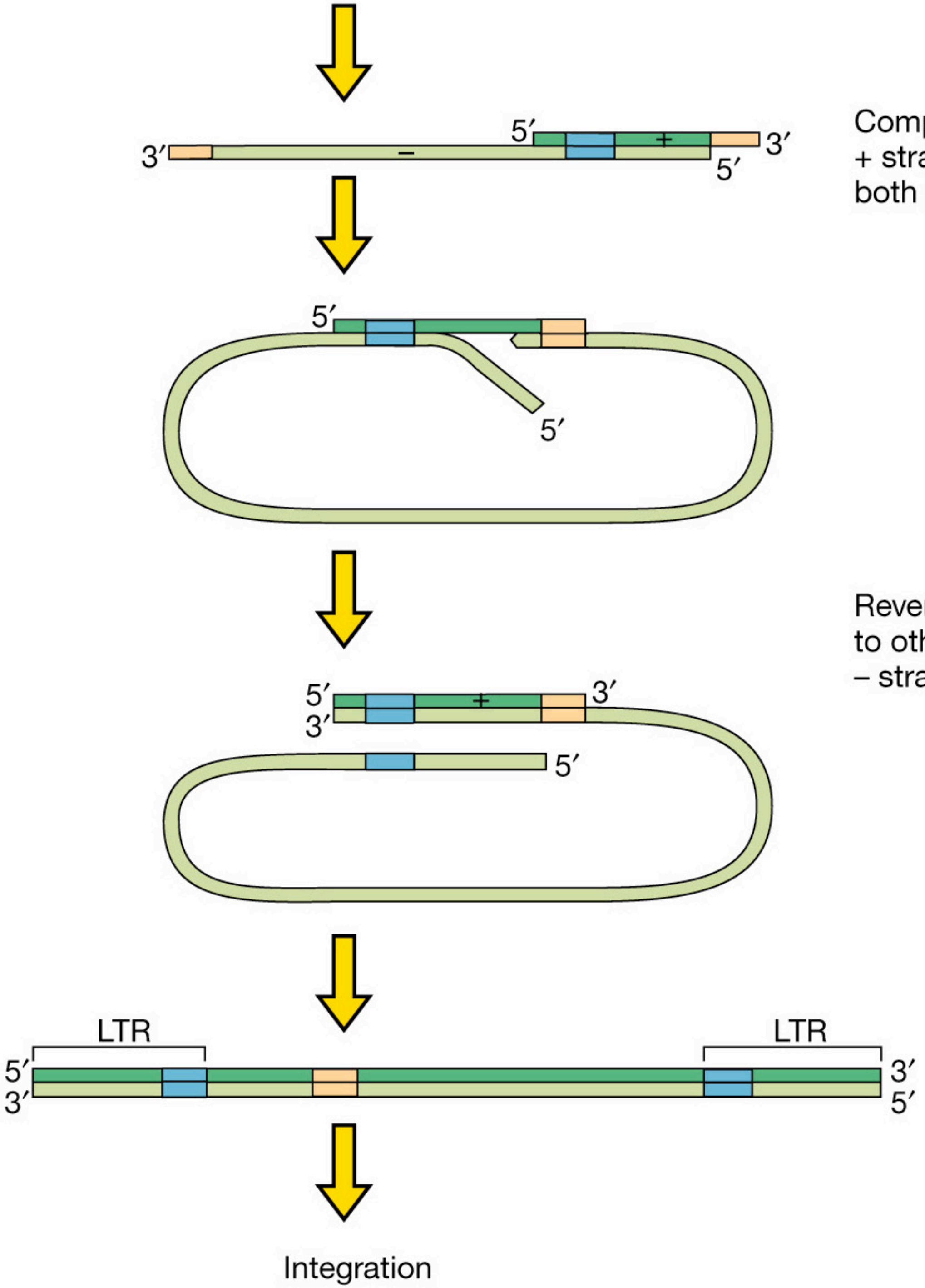
Reverse transcription into DNA of 100 or so nucleotides at the 5′-terminus by reverse transcriptase

Removal of terminally redundant virion RNA by reverse transcriptase ribonuclease H activity

Transfer of DNA and tRNA to 3′-end

Continued synthesis leads to extension of – strand DNA

Ribonuclease H activity removes all of + strand RNA except small fragment used as primer

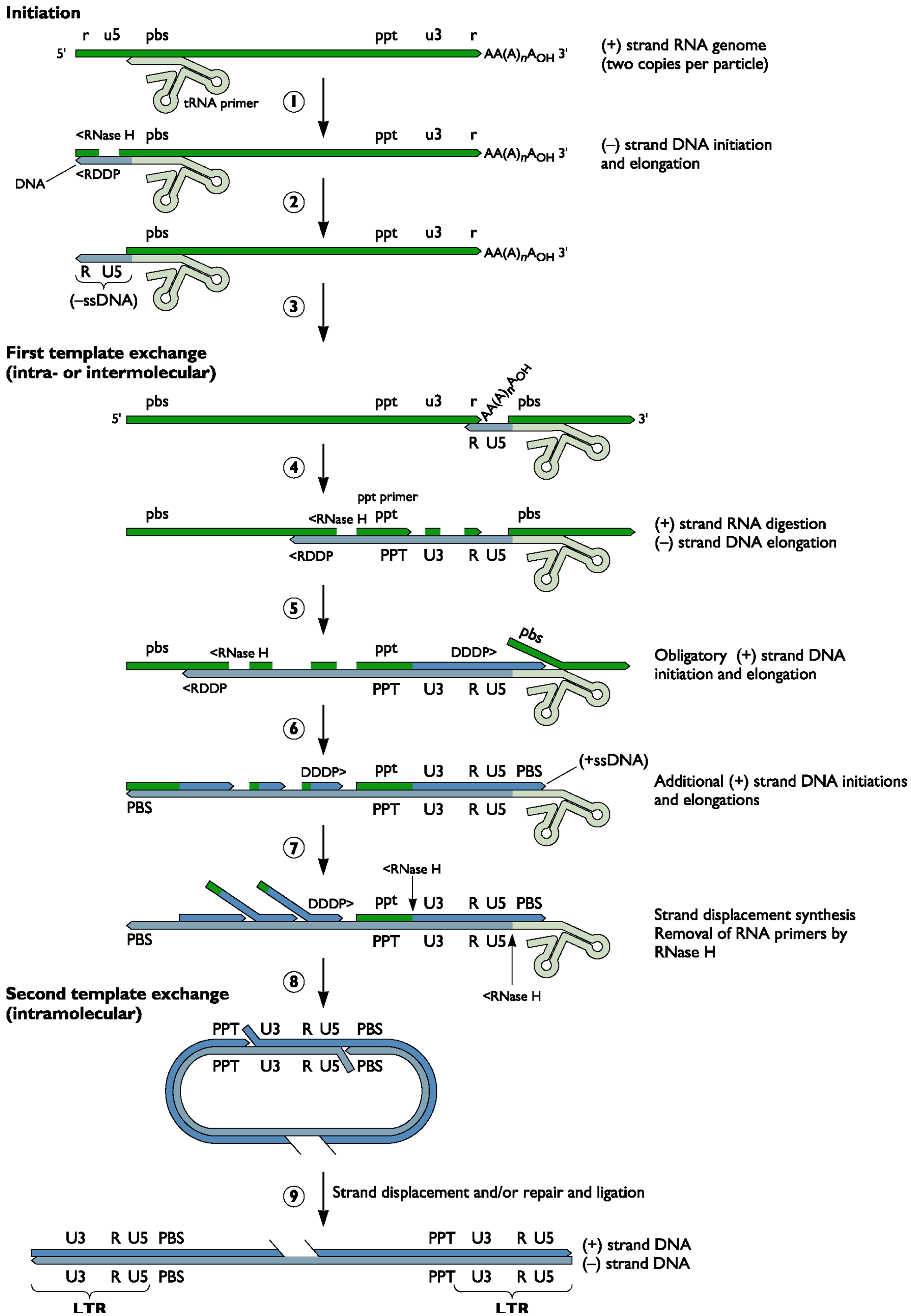


Completion of short segment of + strand DNA and removal of both primers

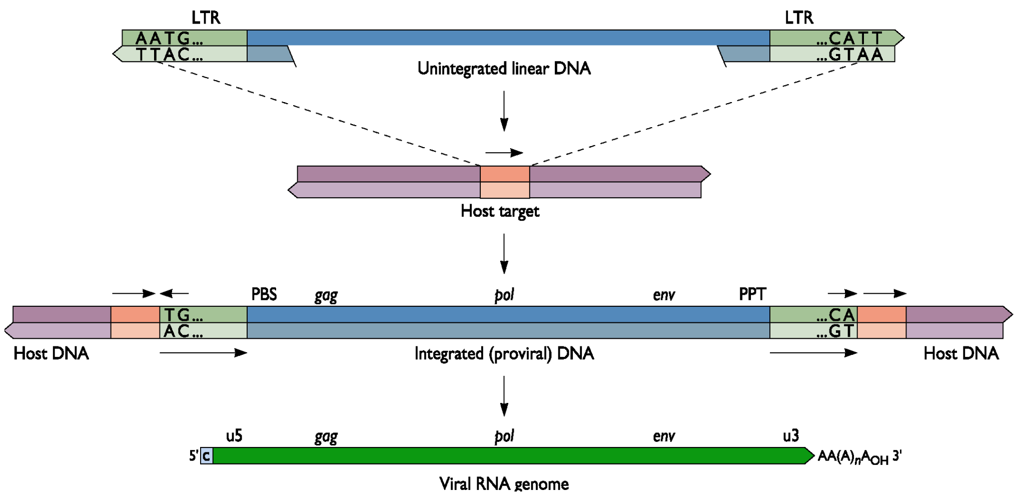
Reverse transcriptase transfers to other strand and completes – strand DNA synthesis

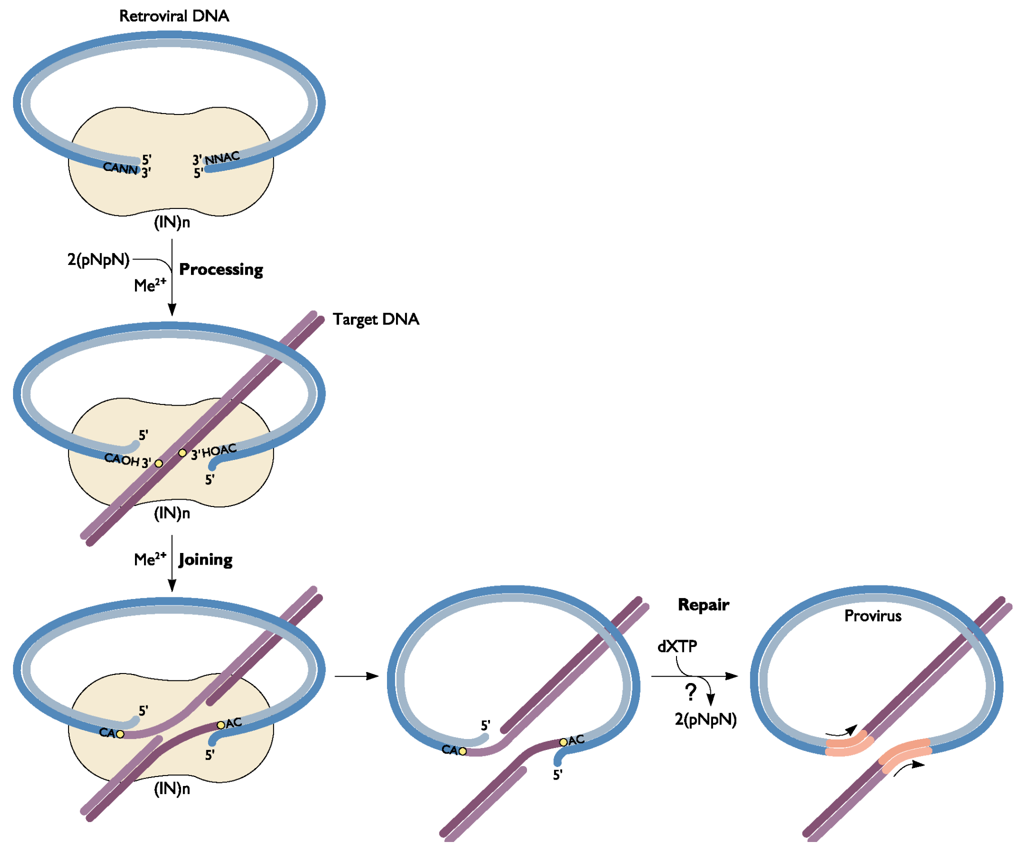
Formation of double-stranded DNA through action of reverse transcriptase

Reverse transcription process

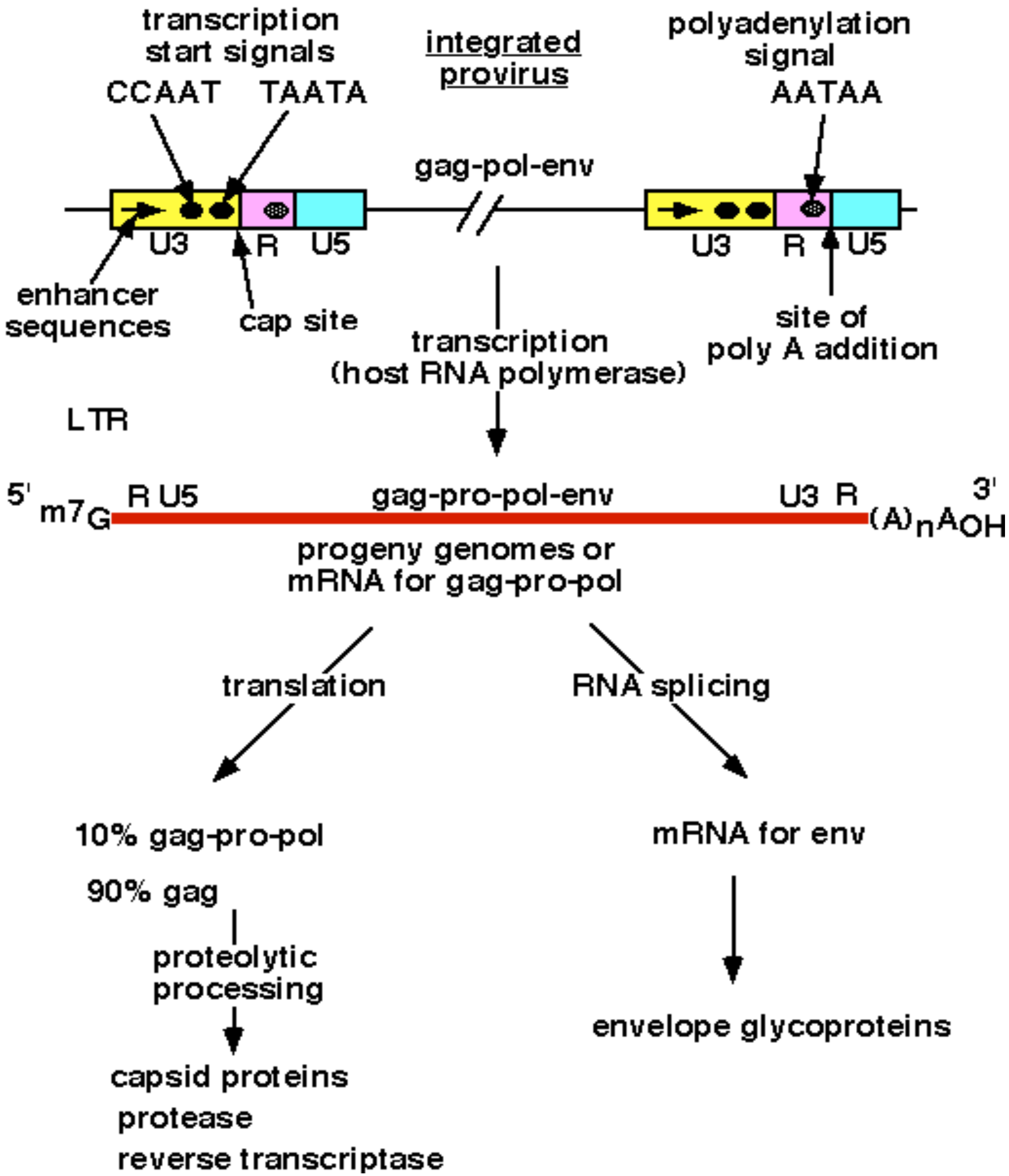


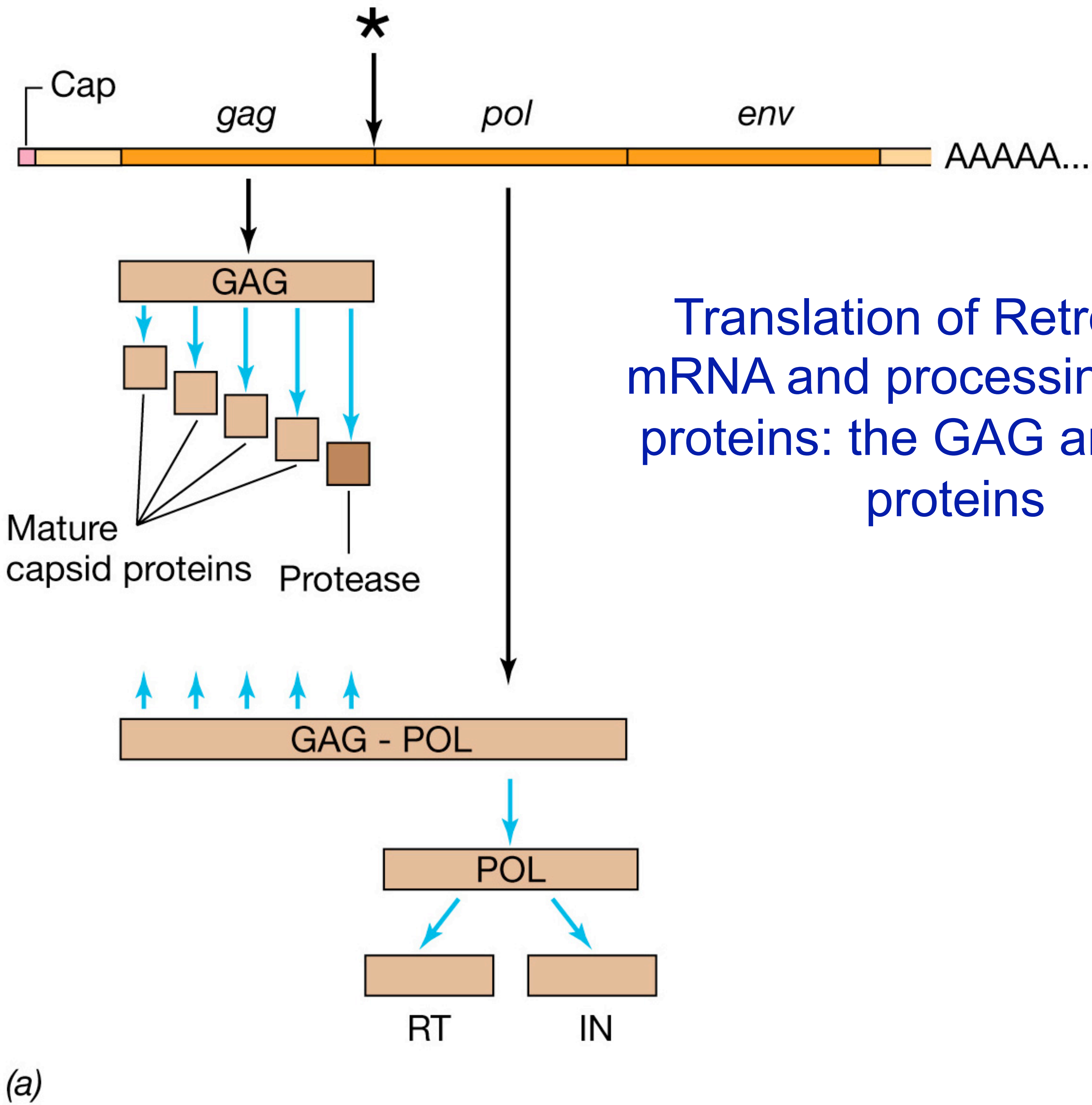
Retroviral DNA integration



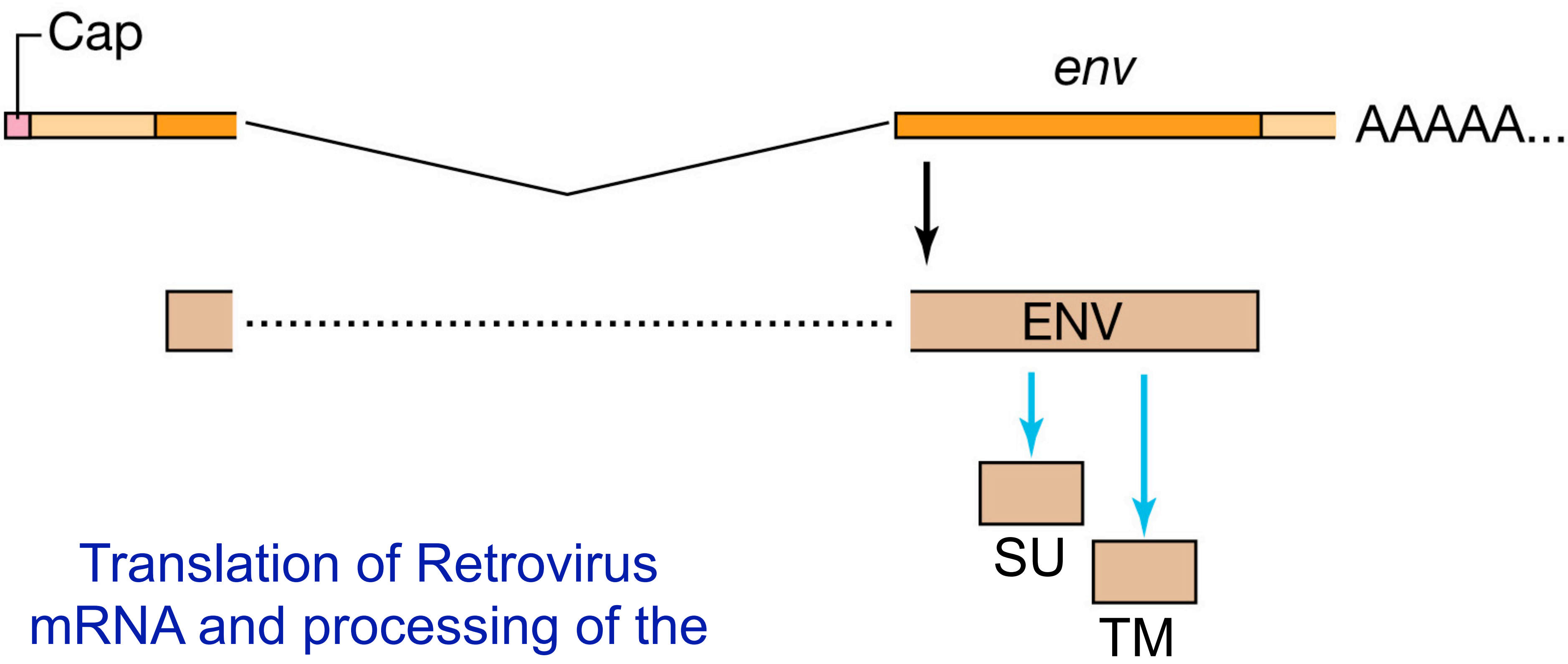


Retrovirus Gene Expression and the LTR





Translation of Retrovirus mRNA and processing of the proteins: the GAG and POL proteins



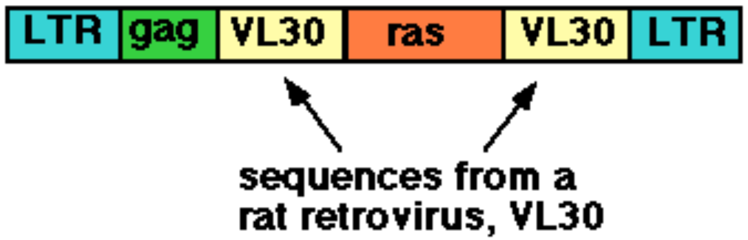
Translation of Retrovirus mRNA and processing of the proteins: the ENV proteins

Most Transforming Retrovirus are Defective and Cannot Replicate without Helper Virus

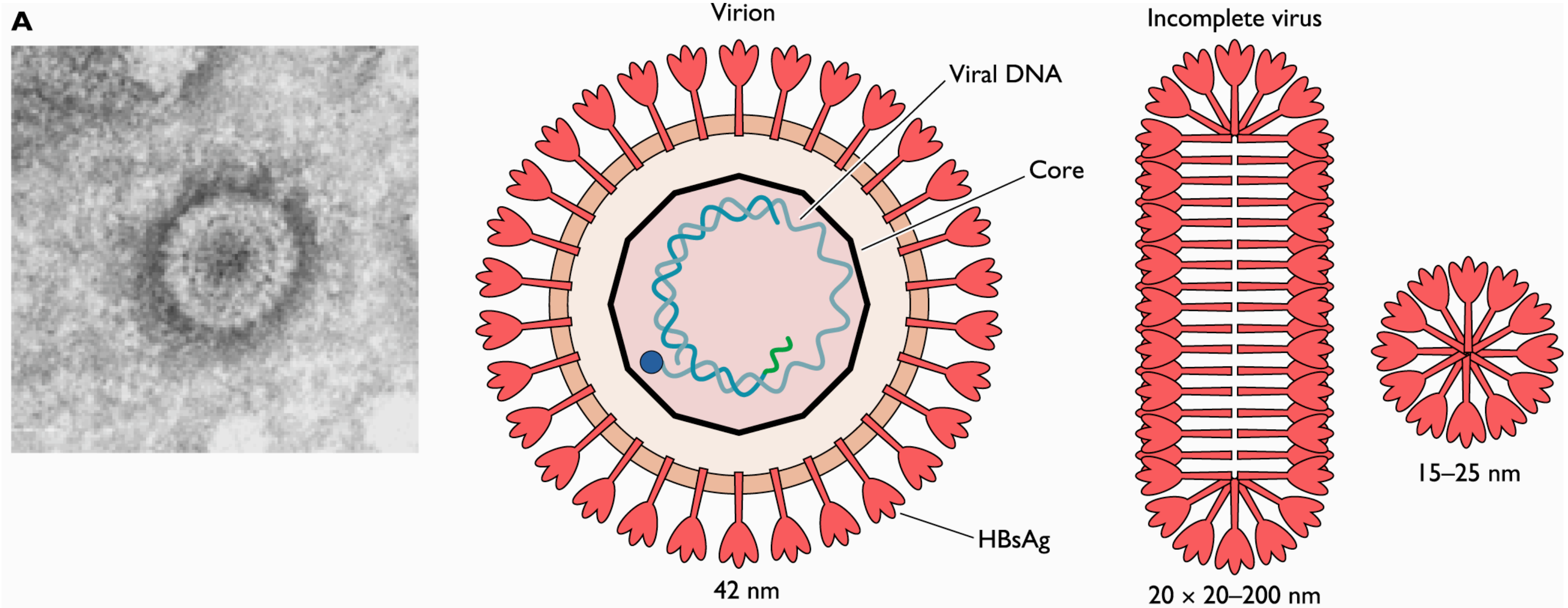
Rous sarcoma virus
(a non-defective, transforming avian virus)

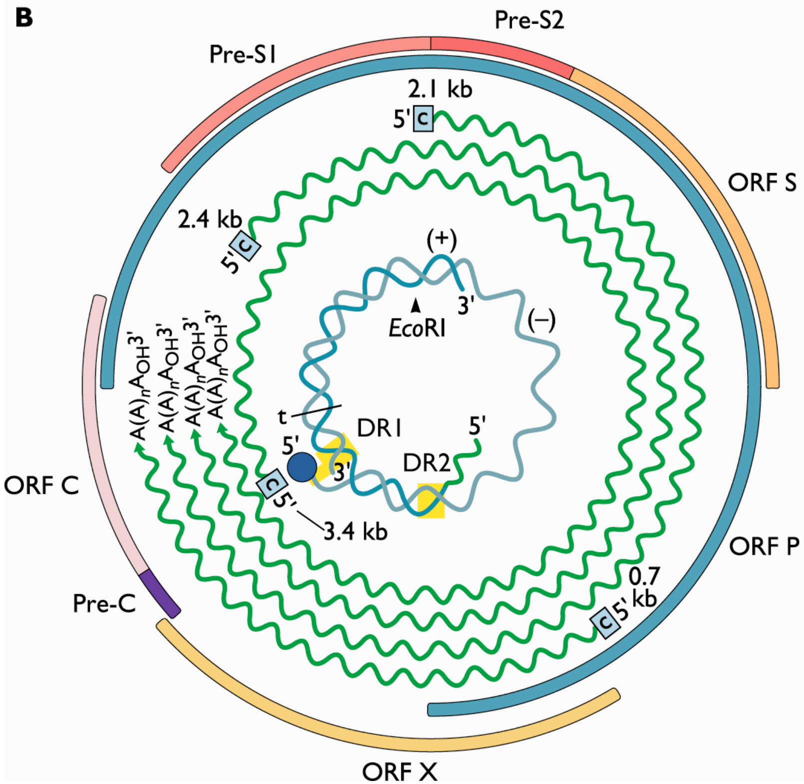
Abelson murine
Leukemia virus
(defective)

Harvey sarcoma virus
(a defective murine virus)

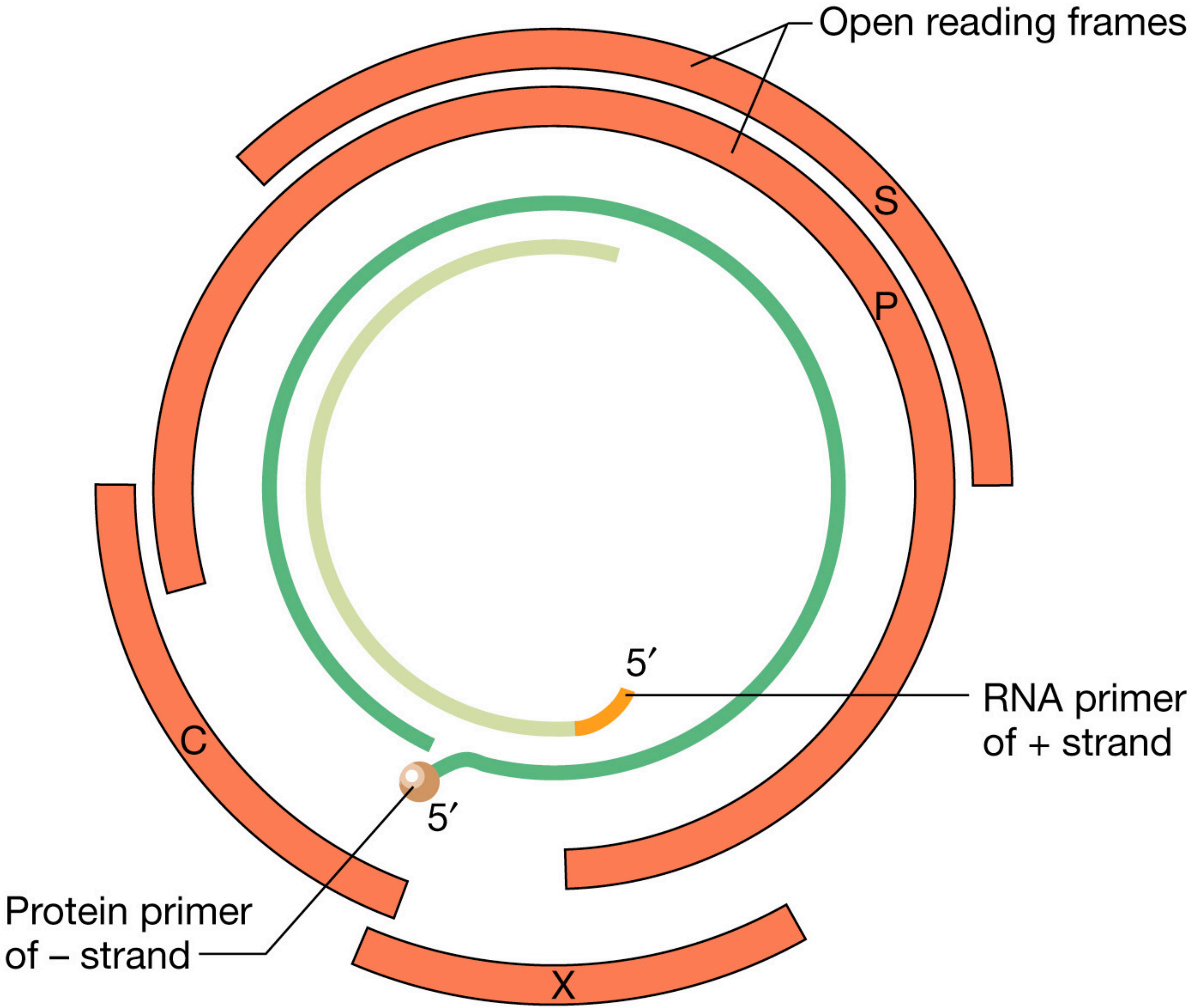


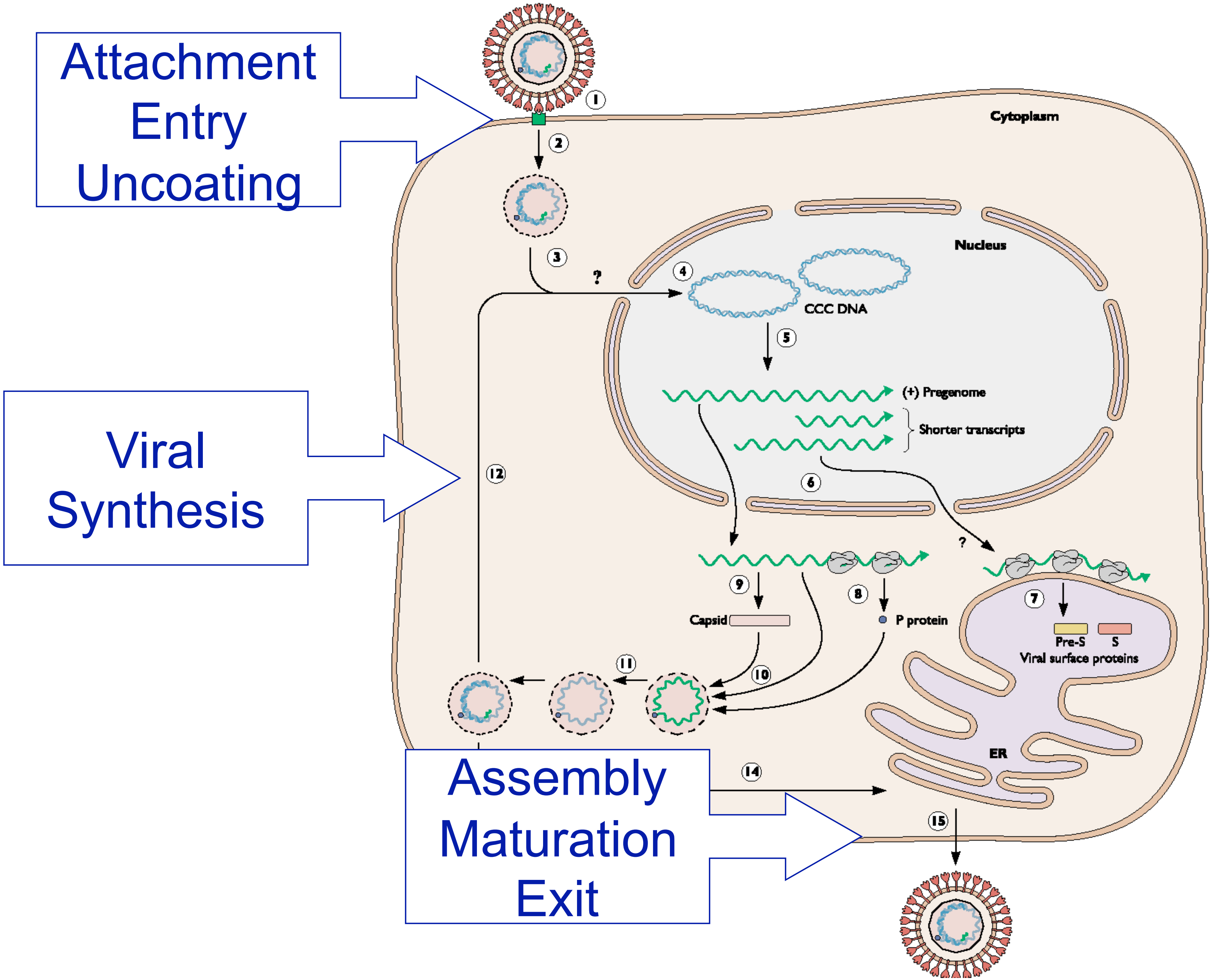
src, abl and *ras* are v-onc sequences which were picked up (probably as processed trancripts) from c-onc sequences in the host.





Structure and genome organization of the **Class VII** virus: **Hepadnaviruses**


Open reading frames
S
P
C
X
5′
RNA primer
of + strand
5′
Protein primer
of – strand



Attachment
Entry
Uncoating
Viral
Synthesis
Assembly
Maturation
Exit
Cytoplasm
Nucleus
CCC DNA
(+) Pregenome
Shorter transcripts
Capsid
P protein
Pre-S
S
Viral surface proteins
ER

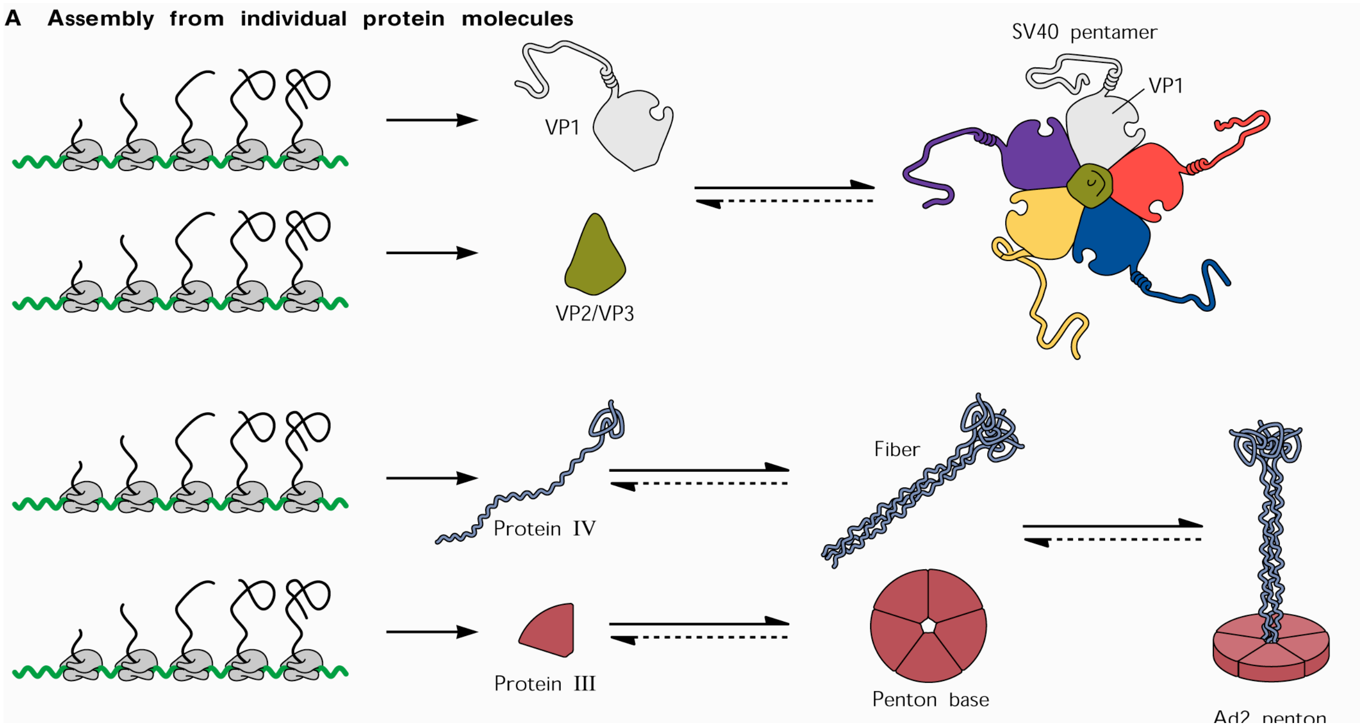
Viral replication

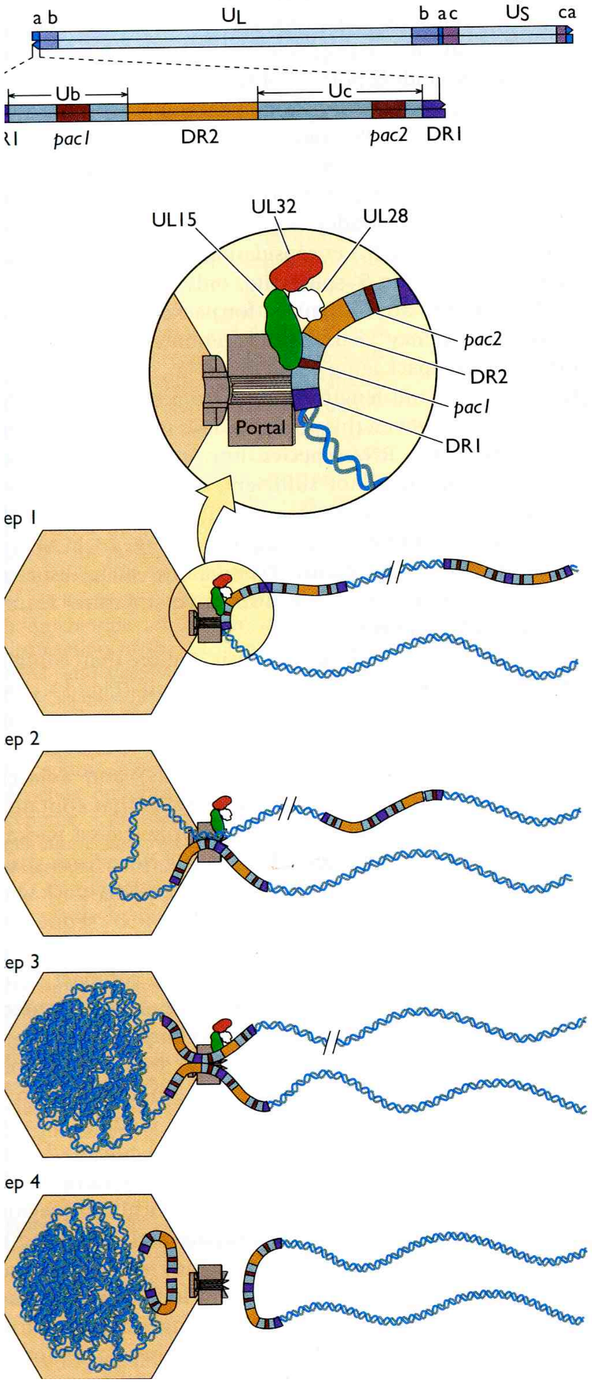
assembly, exit and maturation of progeny virions

Hypothetical pathway of virion assembly and release

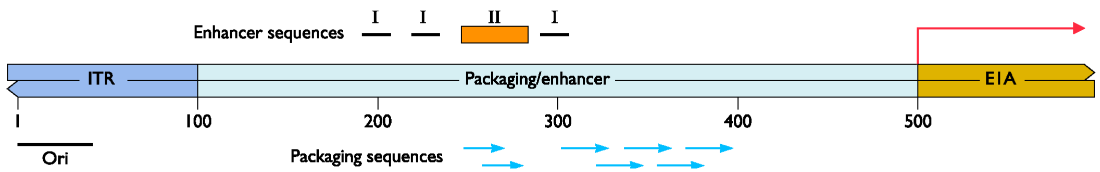
Formation of individual structural units of the protein shell from one or several viral proteins

↓

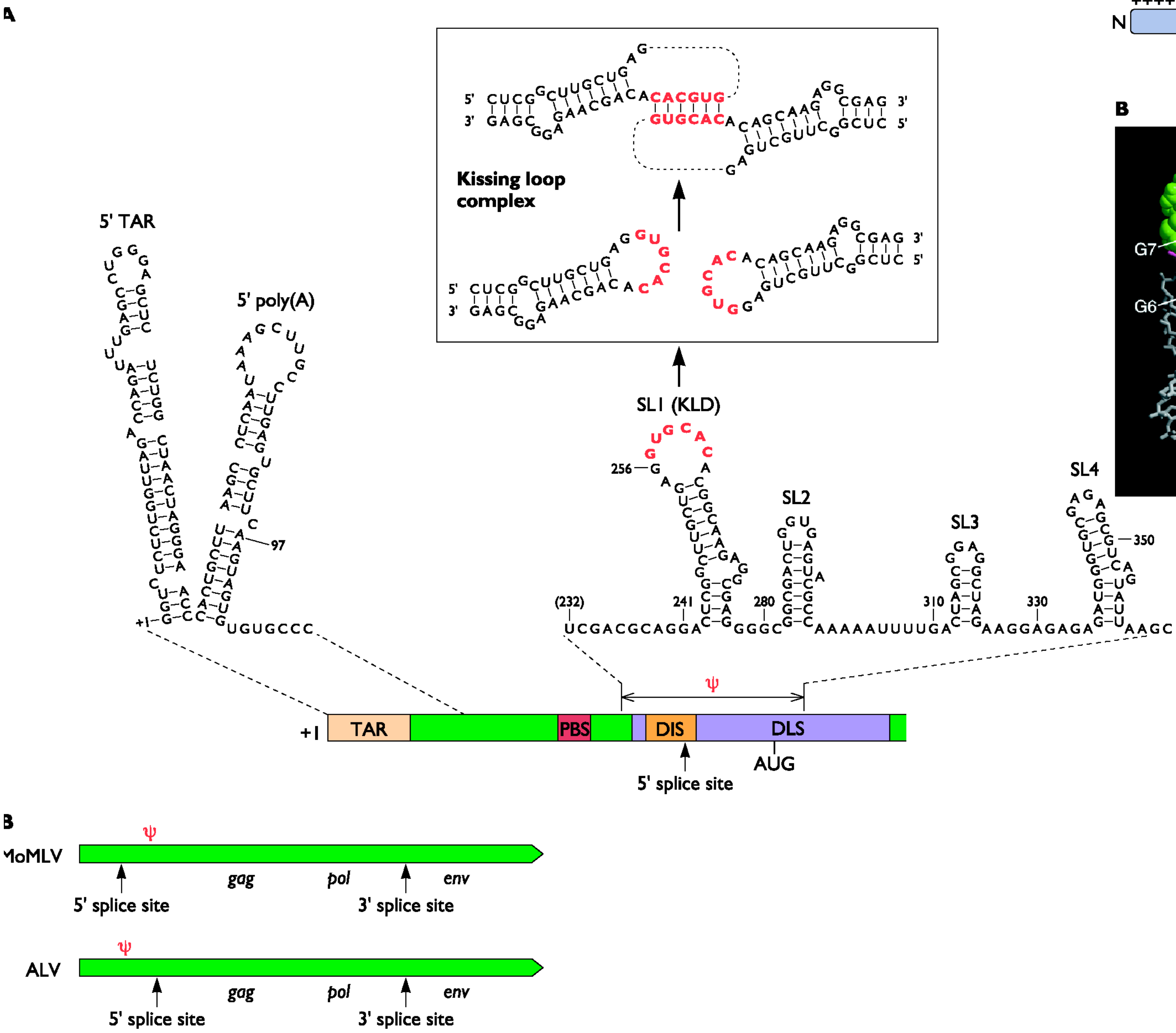

A Assembly from individual protein molecules
VP1
VP2/VP3
SV40 pentamer
VP1
Protein IV
Fiber
Protein III
Penton base
Ad2 penton

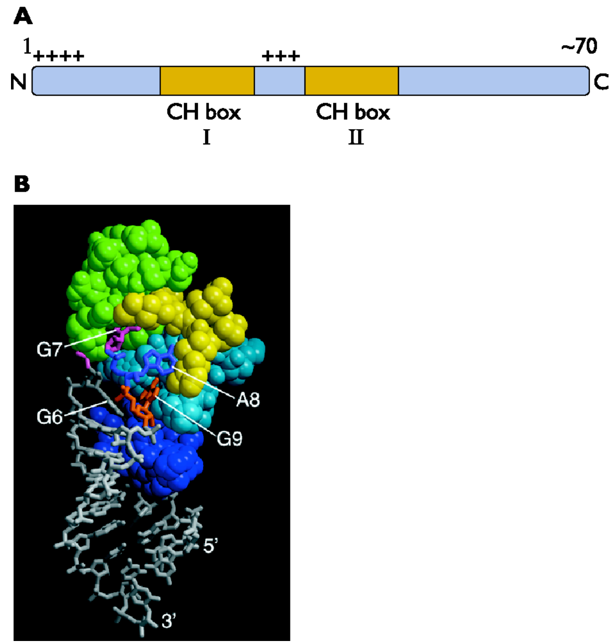


Recognition and packaging of the nucleid acid genome

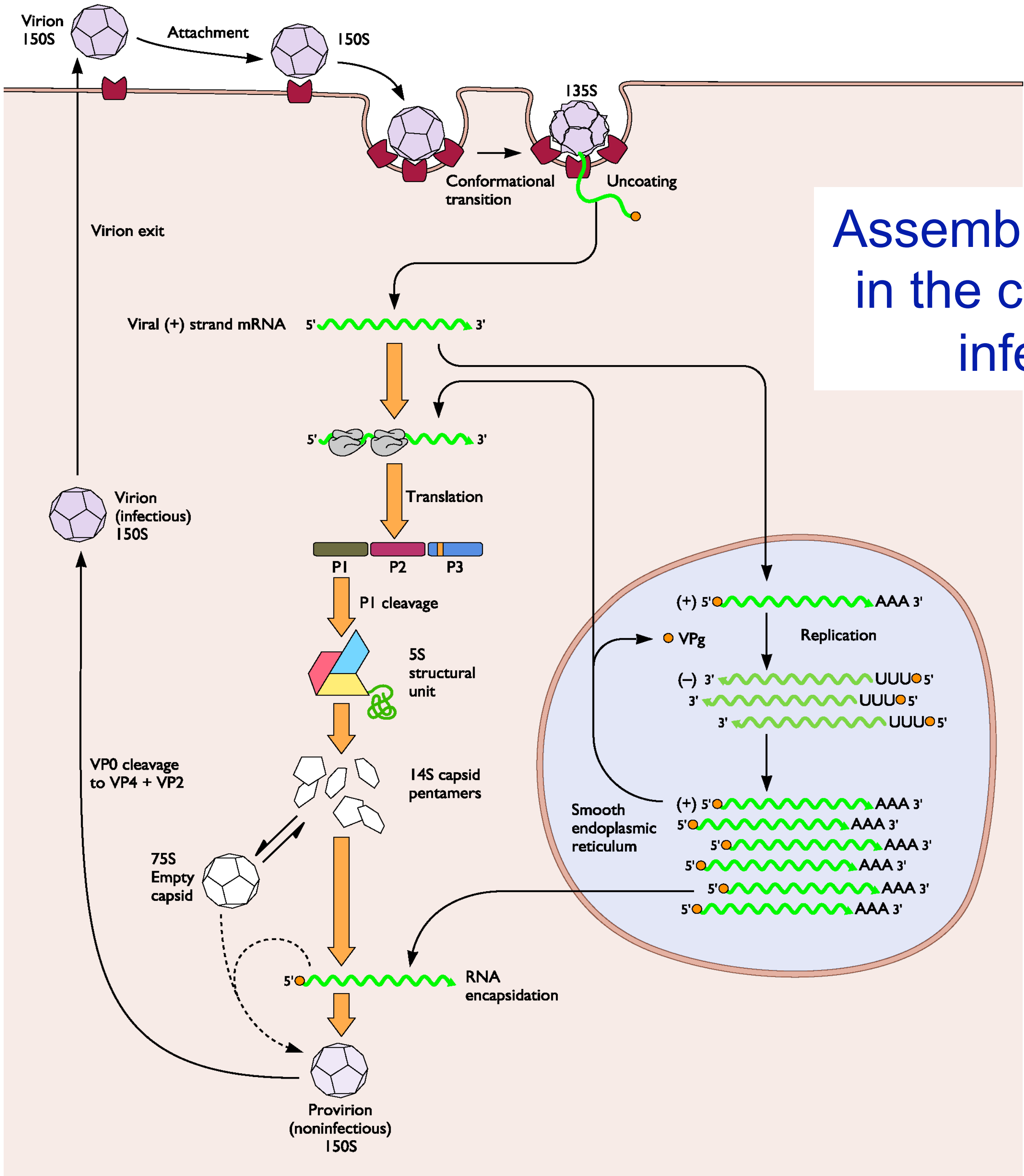


Recognition and packaging of the nucleid acid genome

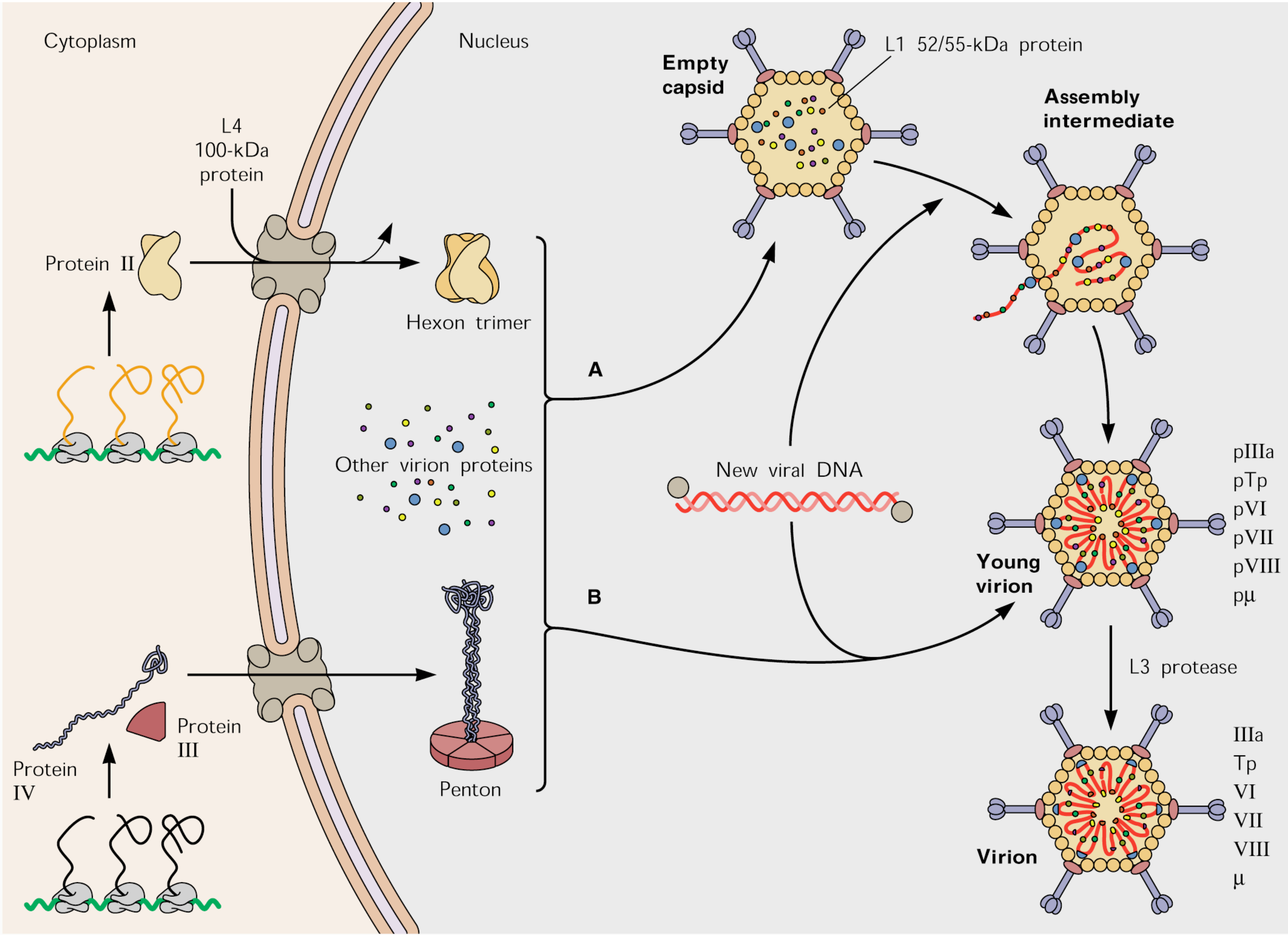




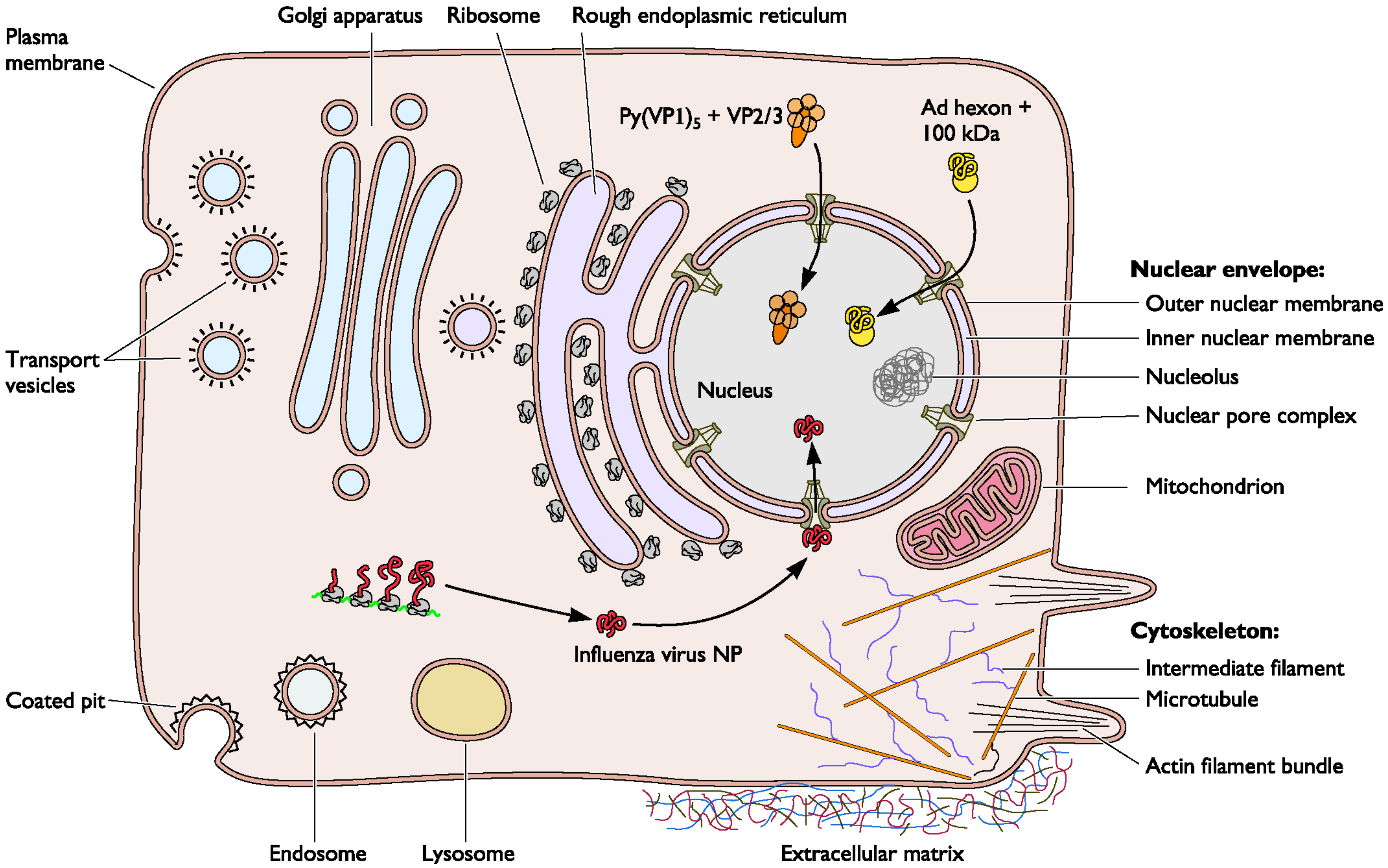
Assembly of Poliovirus in the cytoplam of an infected cell



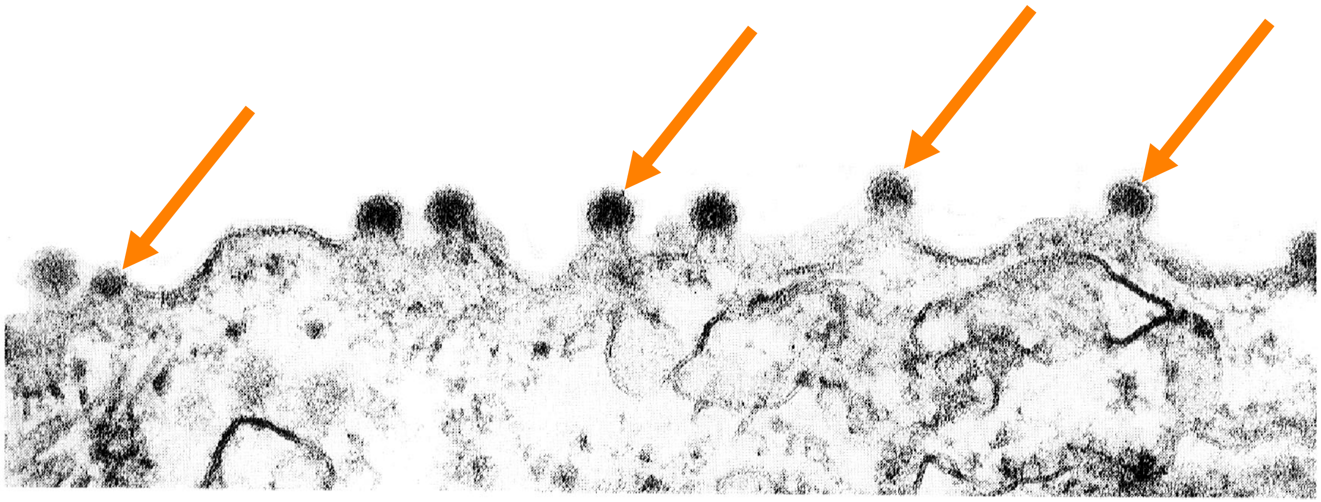
Assembly of Adenovirus in the nucleus of an infected cell

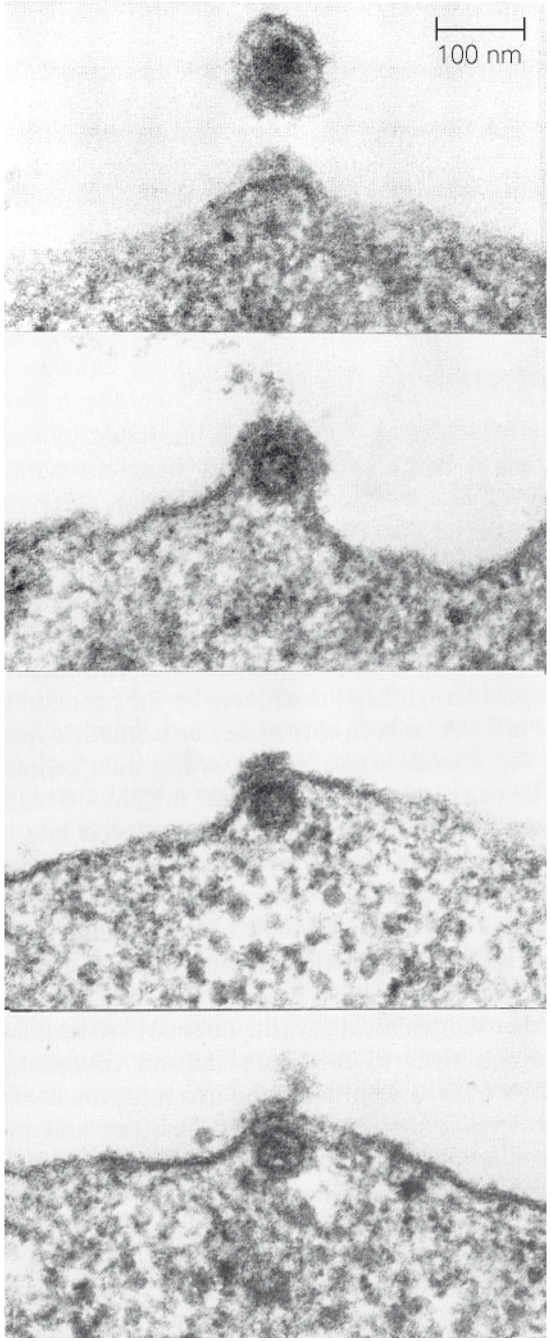


Localization of viral proteins to the plasma membrane

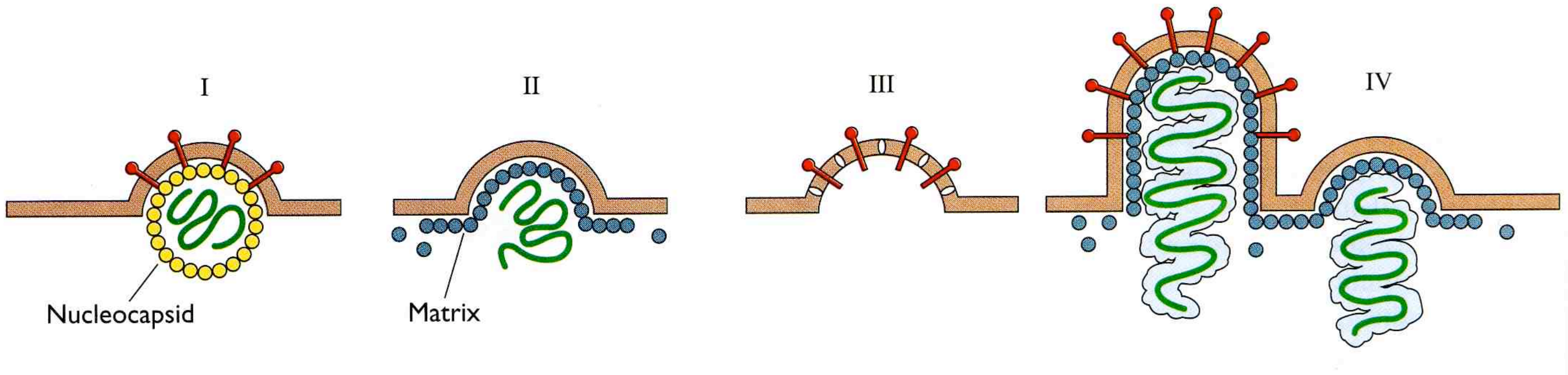


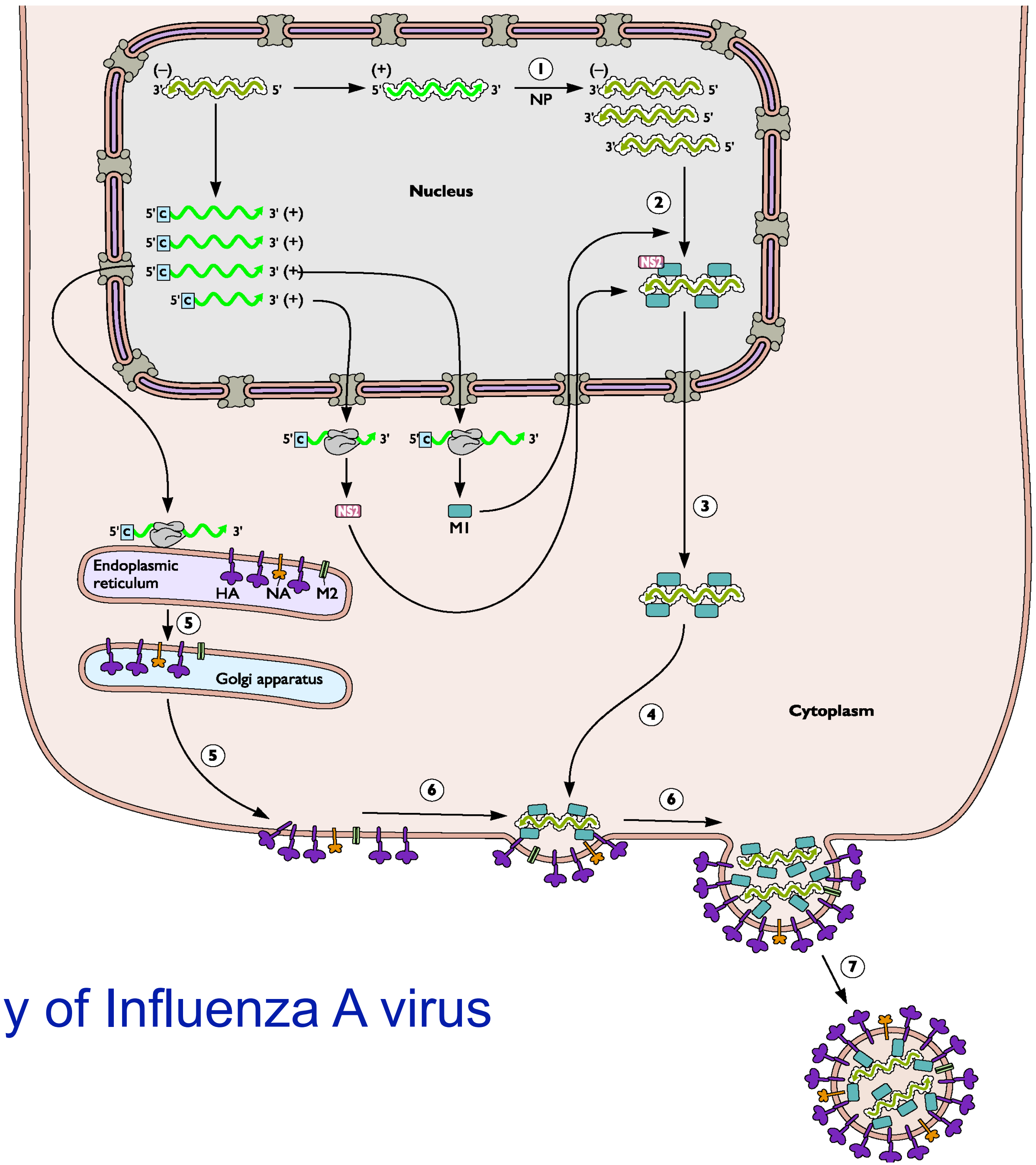
Mechanism of budding of enveloped viruses




100 nm

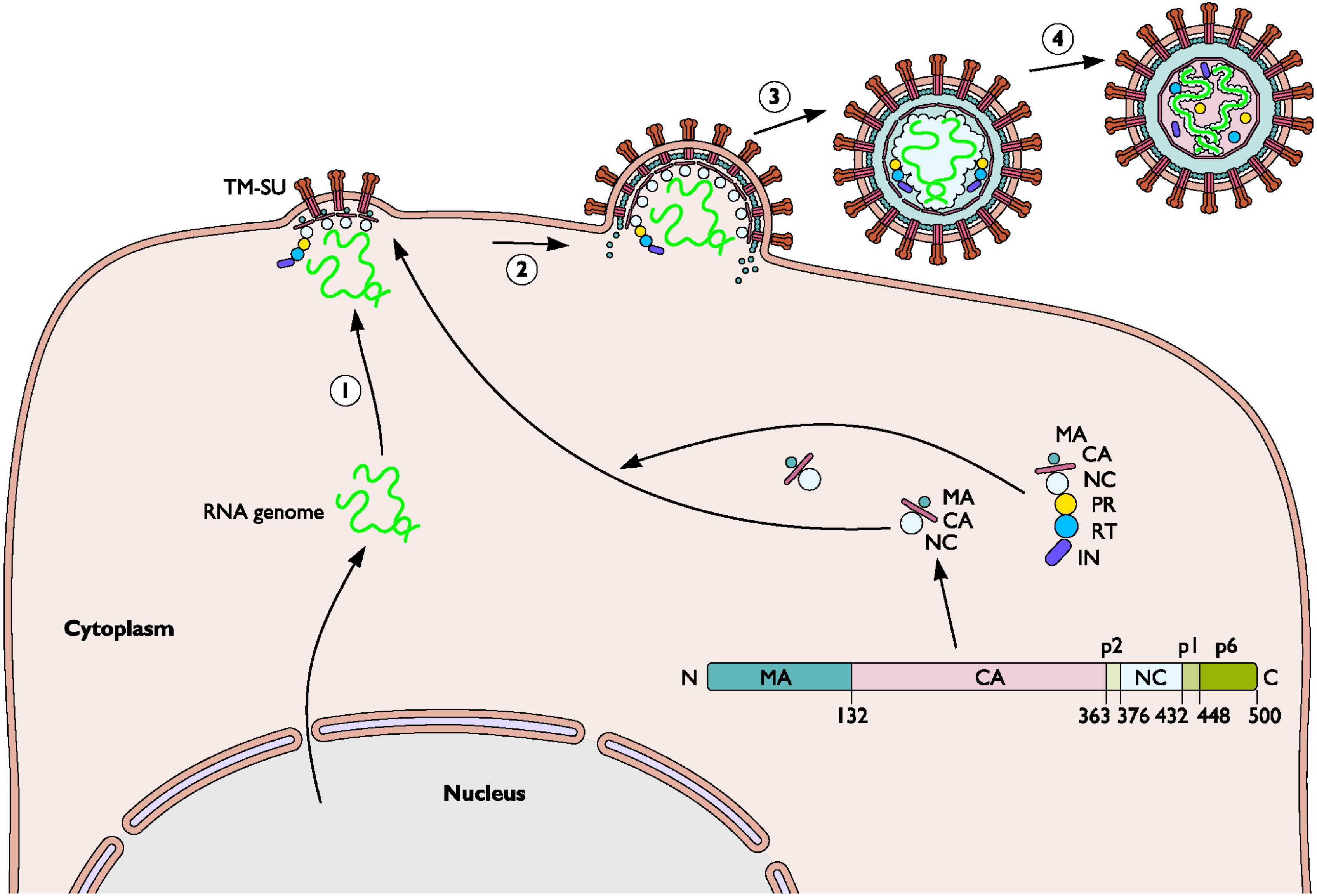
Interaction of viral proteins responsible for budding at the plasma membrane



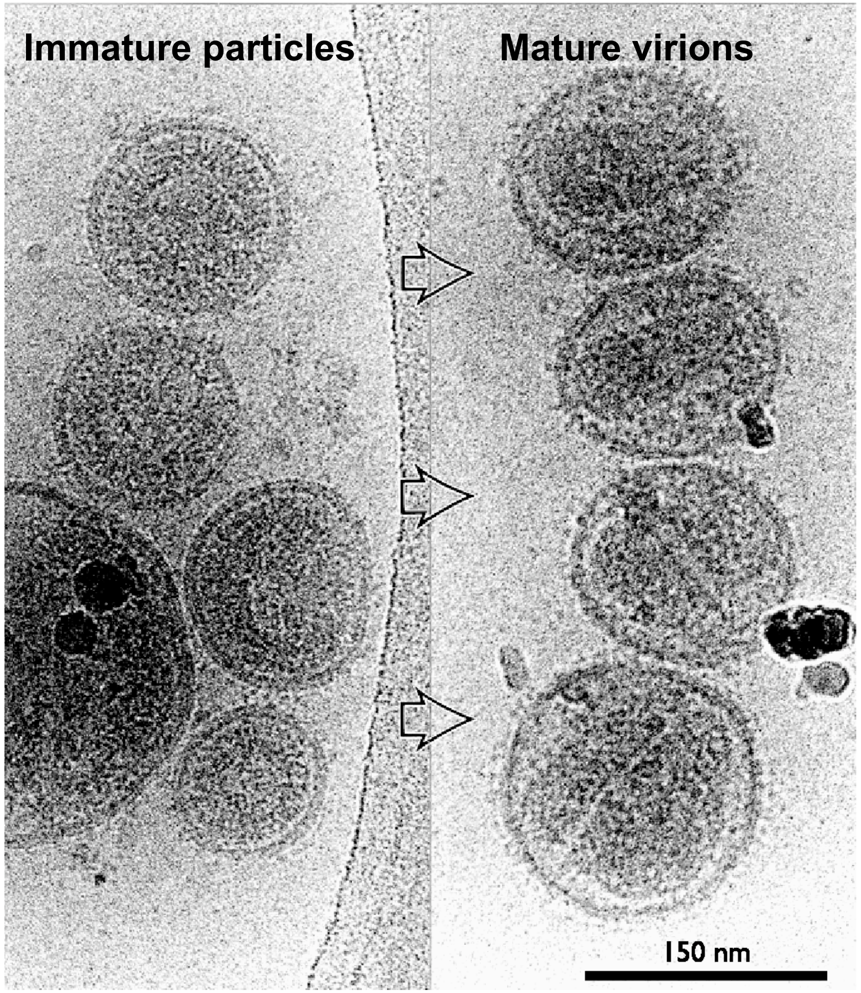


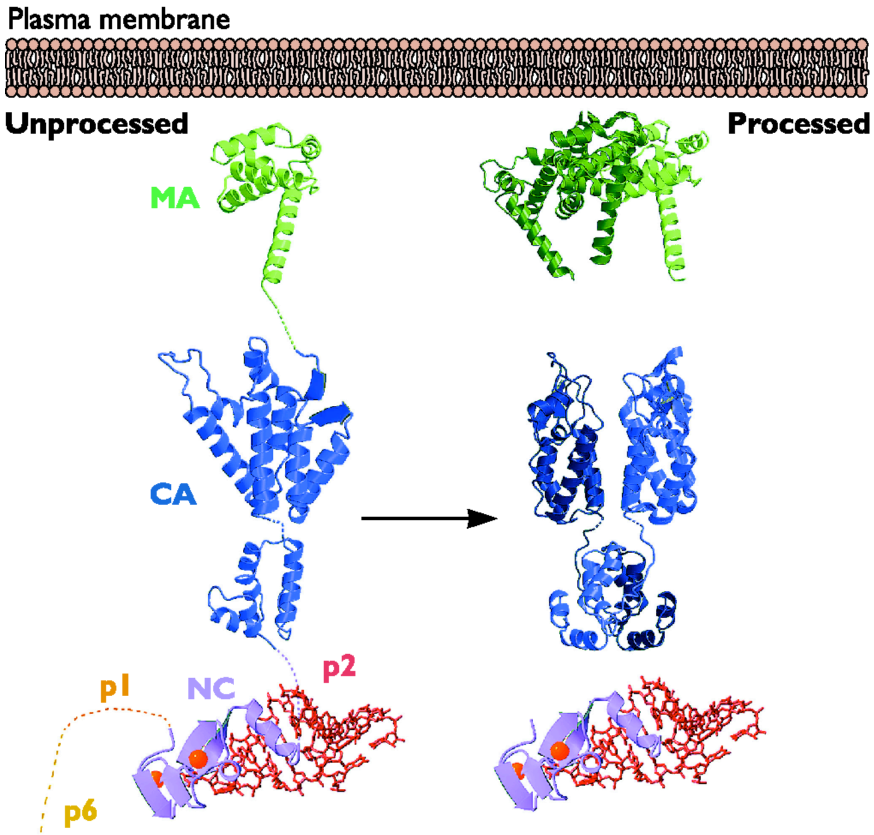
Assembly of Influenza A virus

Assembly of a Retrovirus from polyprotein precursors

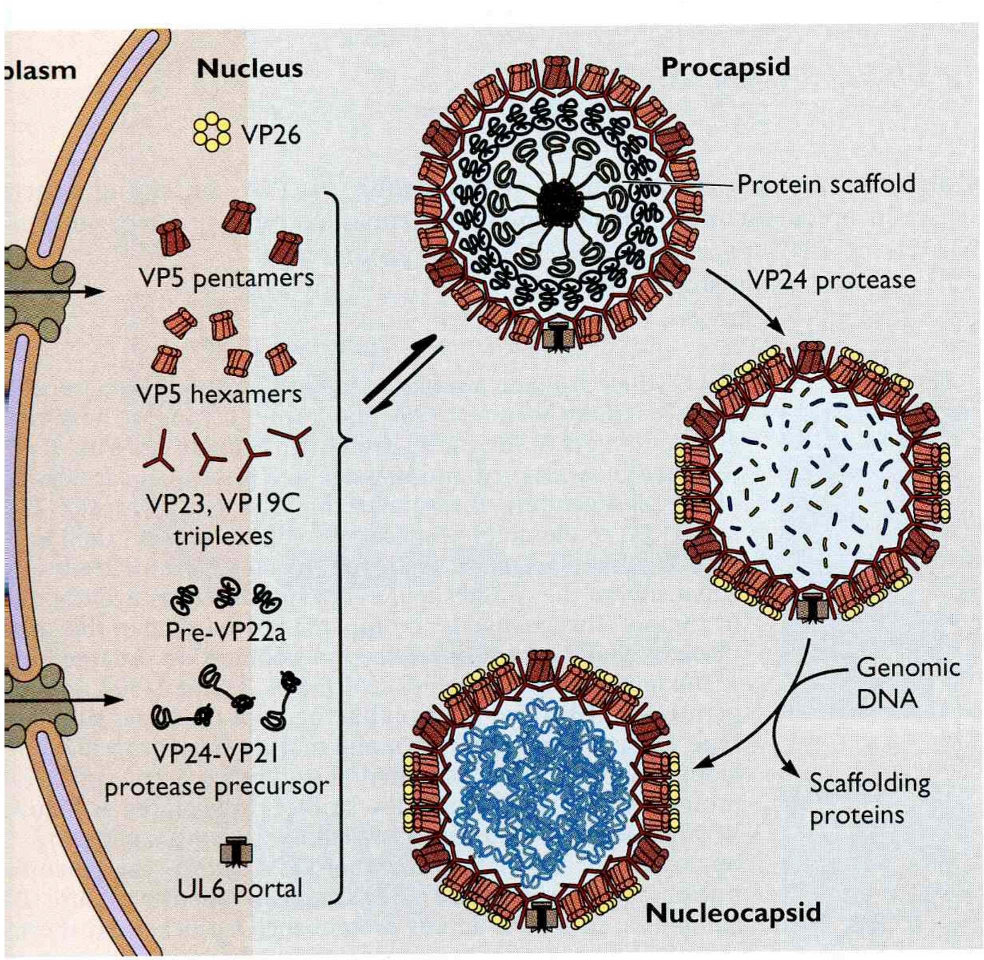


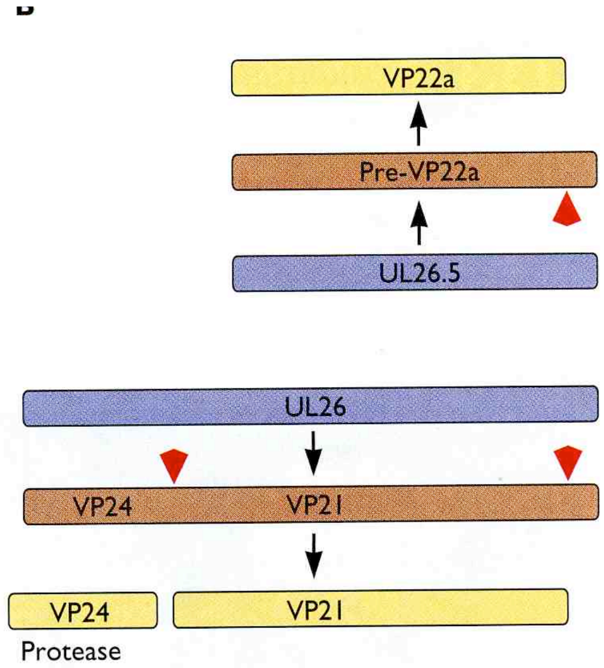
Morphological rearrangement of the HIV-1 particle upon proteolytic processing of the Gag polyprotein



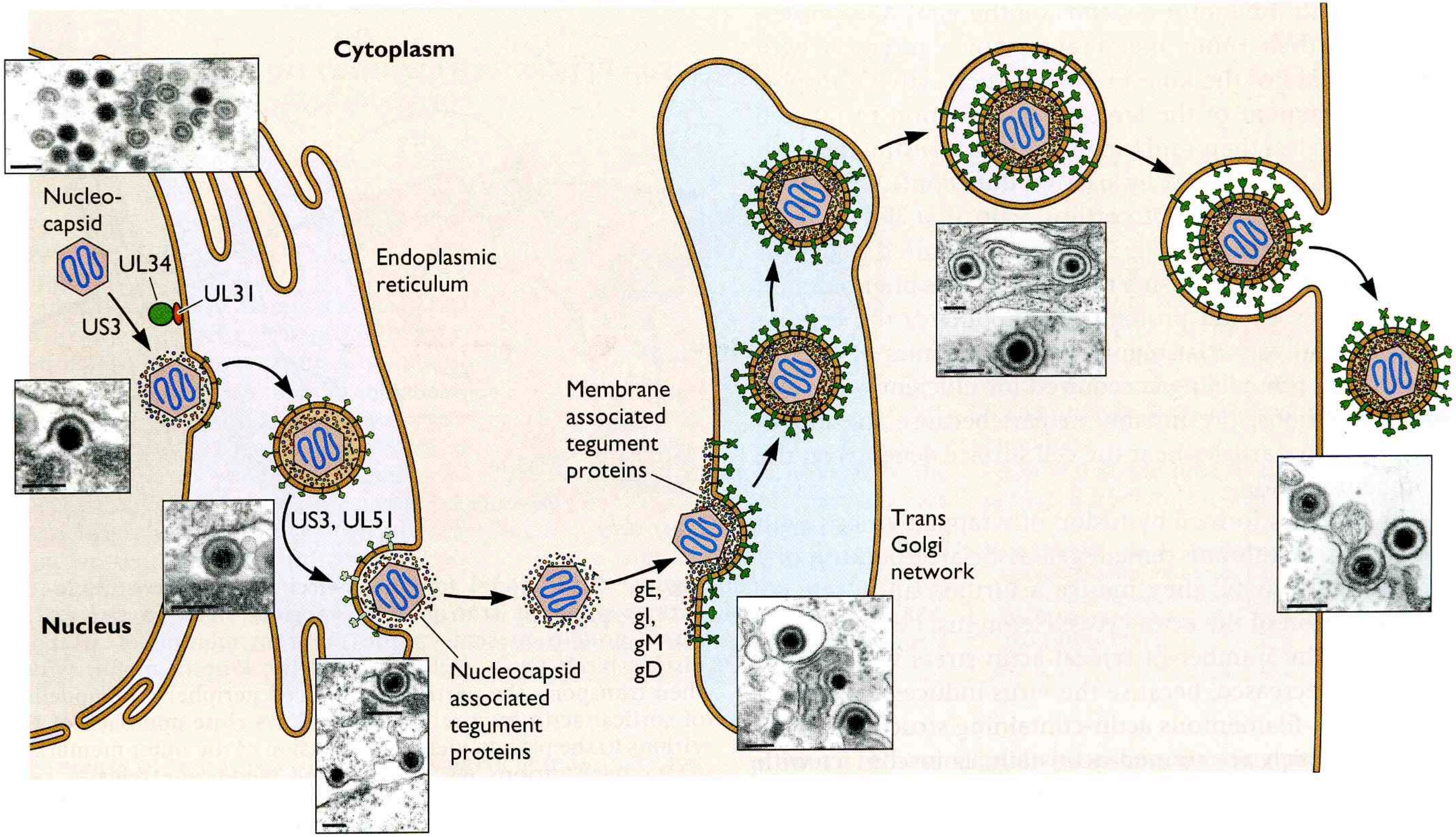


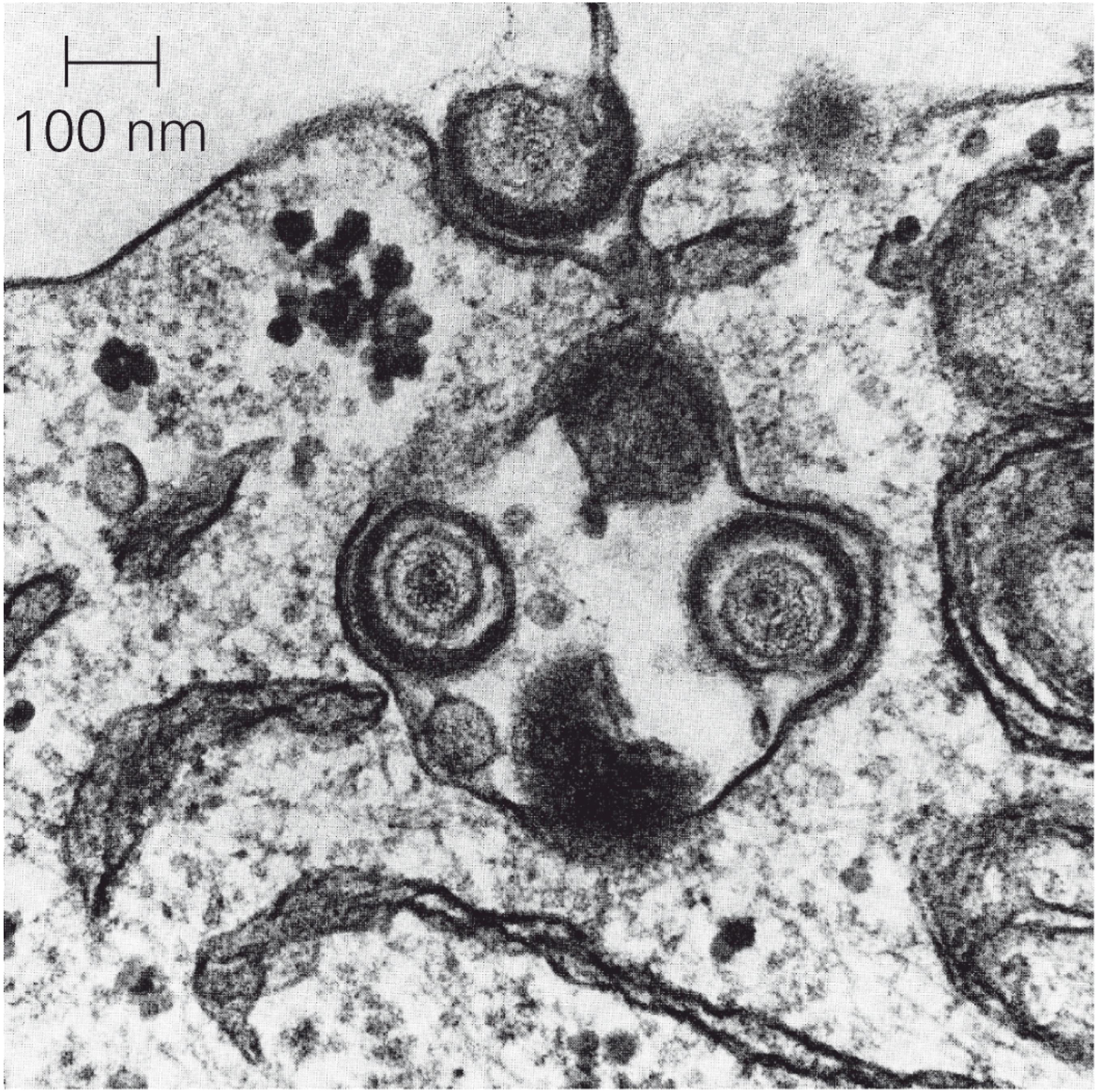
Assembly of HSV-1 nucleocapsids and the pathway proposed for the virus exit from an infected cell



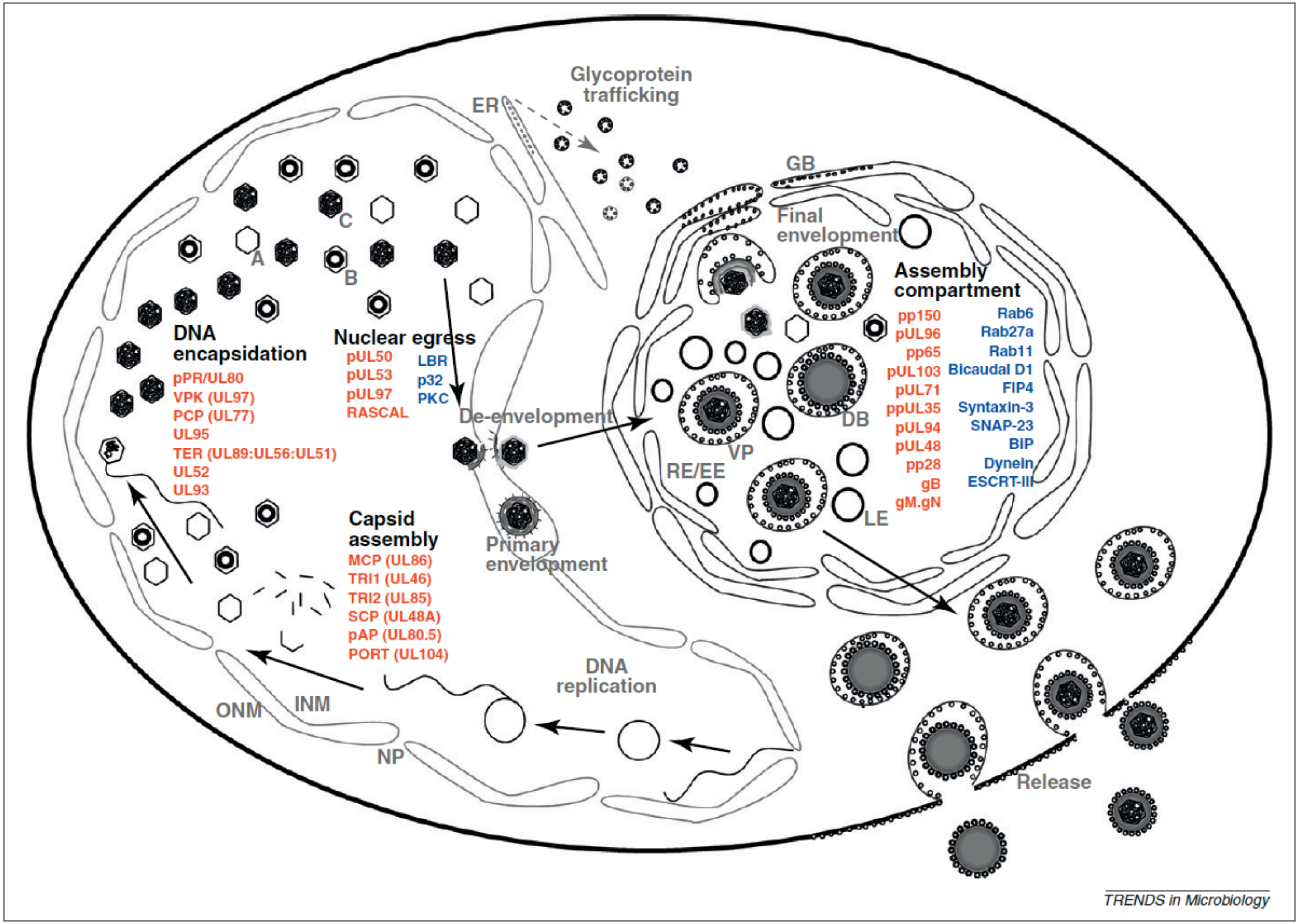


Assembly of HSV-1 nucleocapsids and the pathway proposed for the virus exit from an infected cell

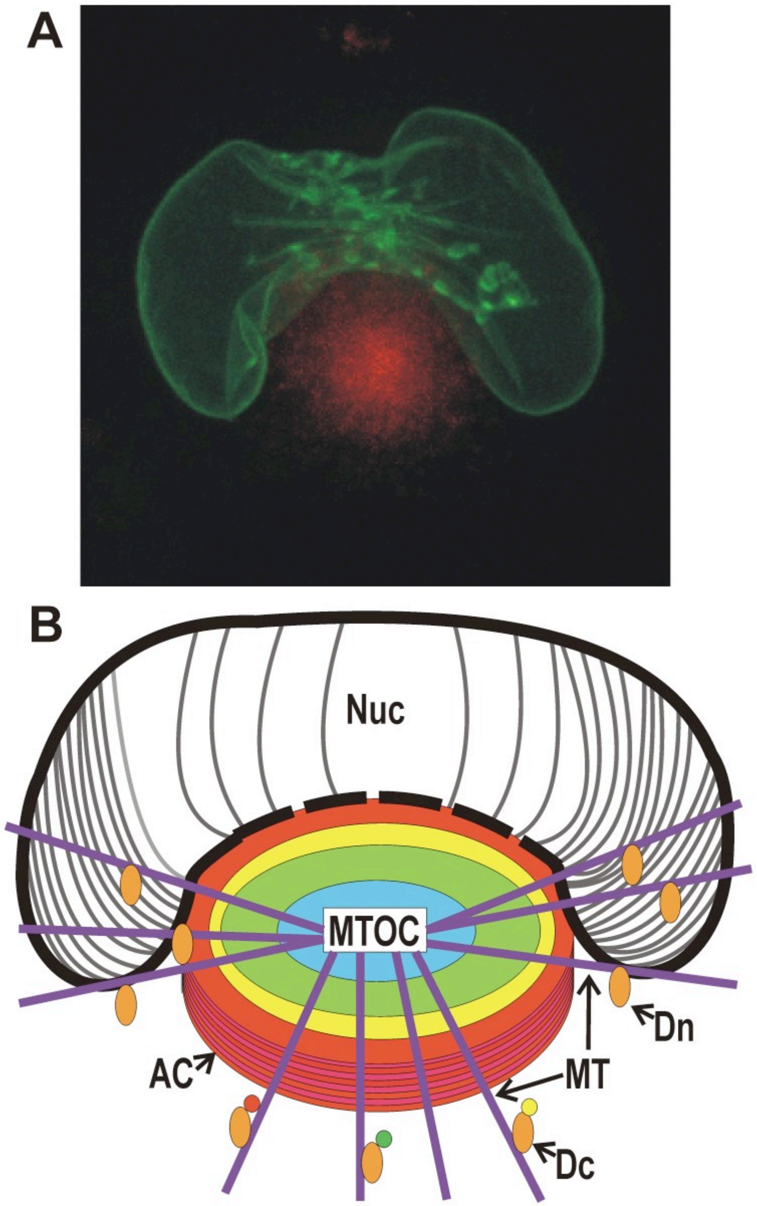


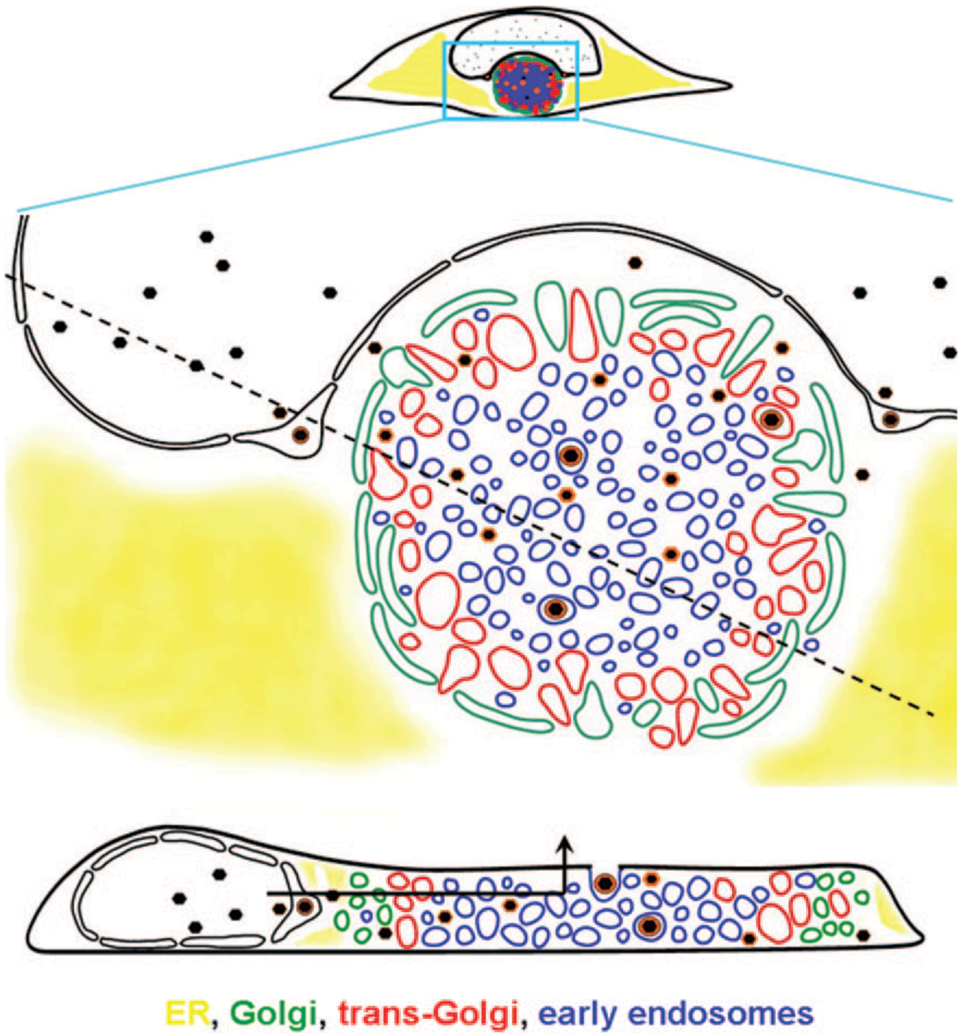

100 nm

Summary of human cytomegalovirus (HCMV) maturation.

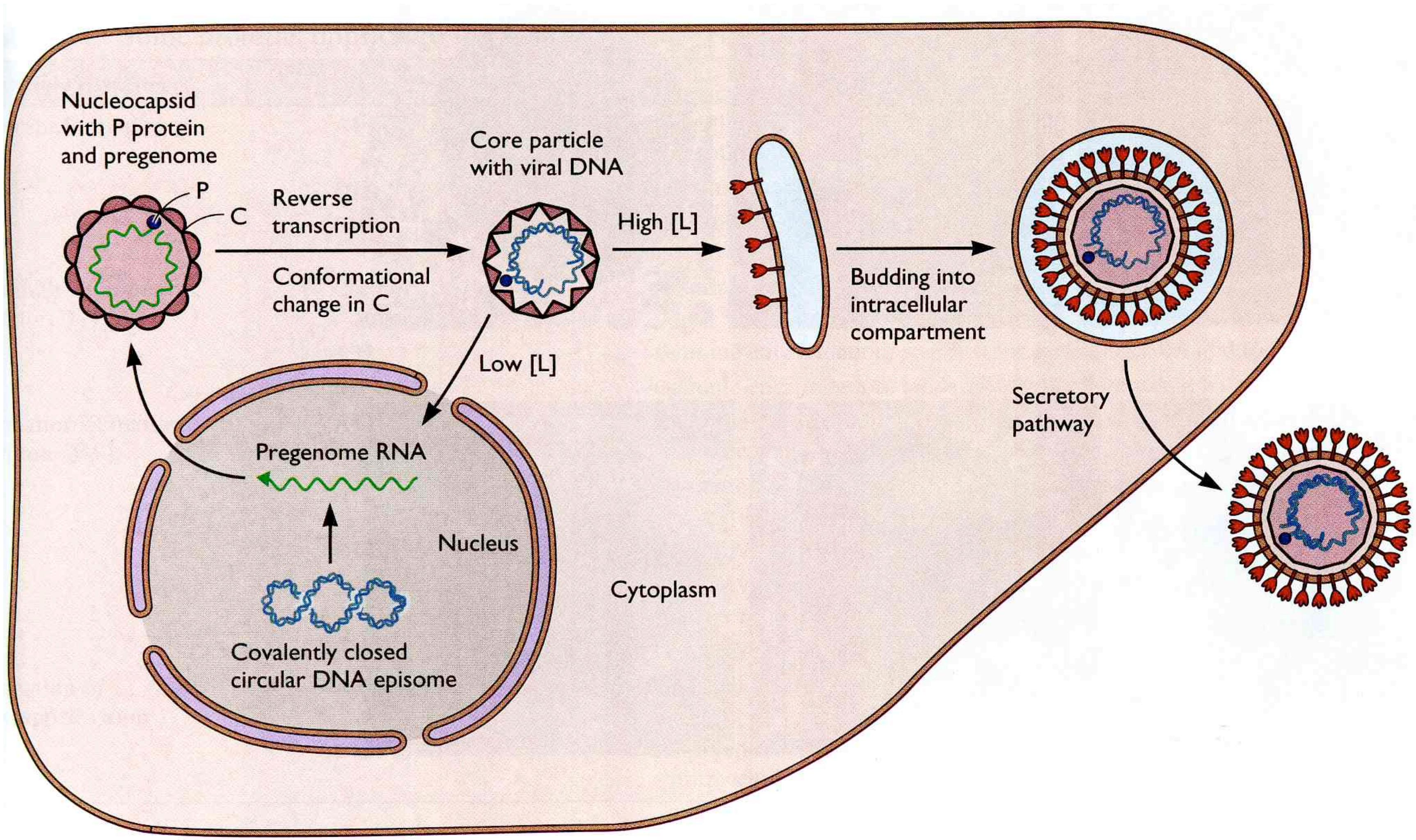


Microscopic and diagrammatic representations of the assembly compartment and nucleus in an HCMV-infected cell.

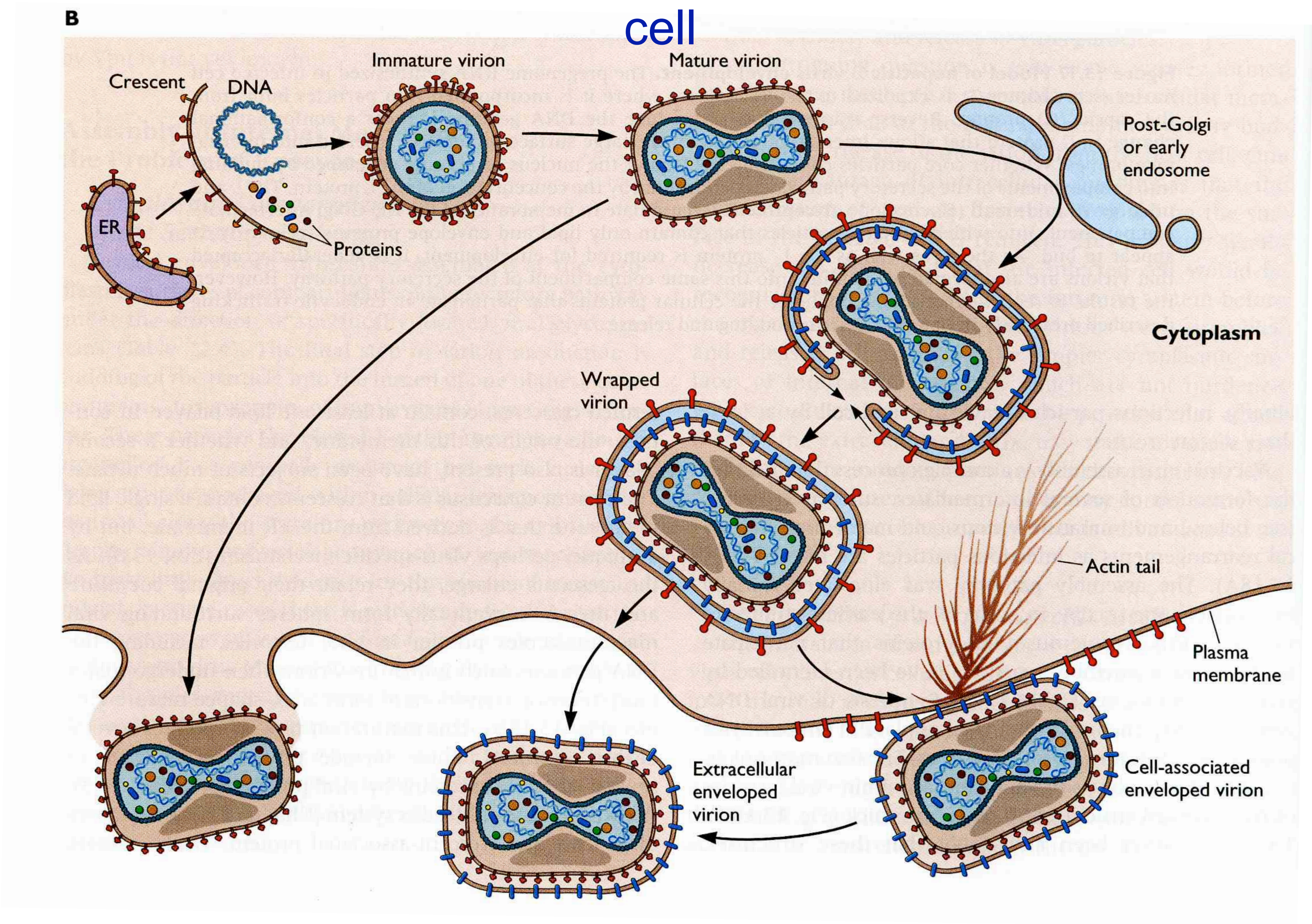




Assembly of HBV nucleocapsids and the pathway proposed for the virus exit from an infected cell



Assembly of Vaccinia virus nucleocapsids and the pathway proposed for the virus exit from an infected cell



BOX 13.11

BACKGROUND

Extracellular and cell-to-cell spread

Many viruses spread from one host cell to another as extracellular virions released from an infected cell **(A)**. Such extracellular dissemination is necessary to infect another naive host. Some viruses, notably alphaherpesviruses and some retroviruses, can also spread from cell to cell without passage through the extracellular environment **(B)** and can therefore spread by both mechanisms **(C)**.