# VIROLOGY

## The infectious cycle

## Strategies for expression and replication of viral genomes

# Viral replication

## transcription, translation and genome replication

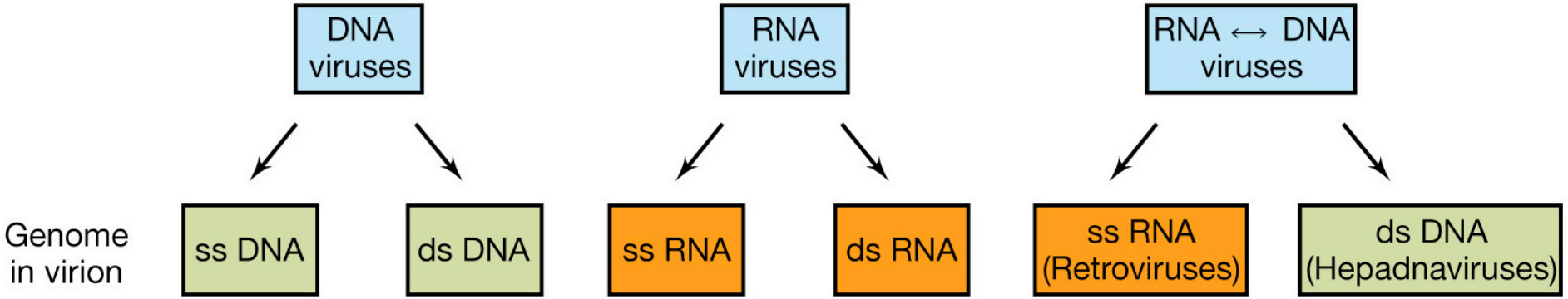
# Synthesis of viral macromolecules

The diversity of viral transcription strategies

The diversity of viral translation strategies

The diversity of viral genome replication strategies

# The diversity of viral genomes architecture



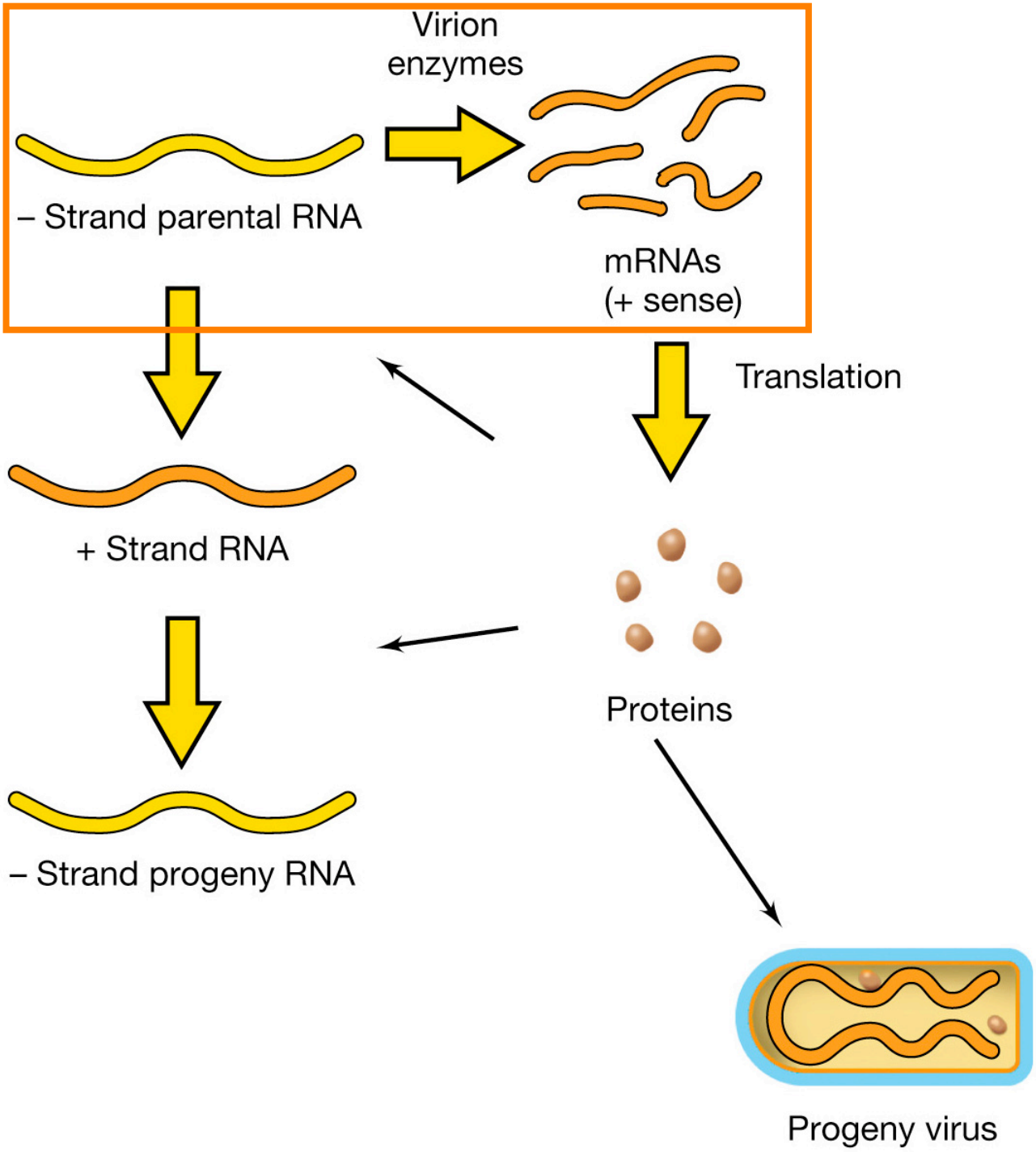

## Genomes of DNA viruses

- 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

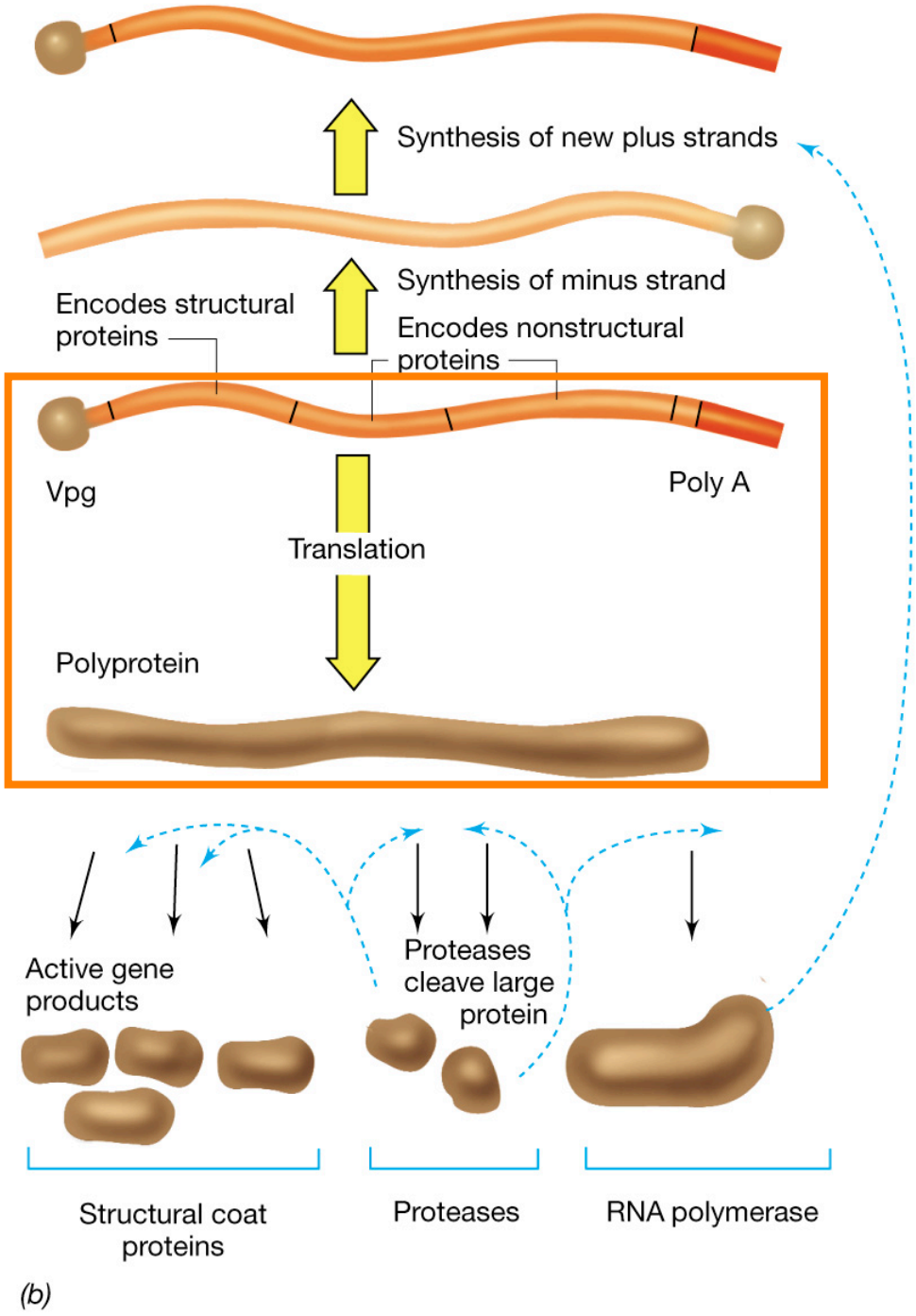
The diversity of viral transcription and translation strategies:
**Rhabdoviruses**
**(-) ssRNA**



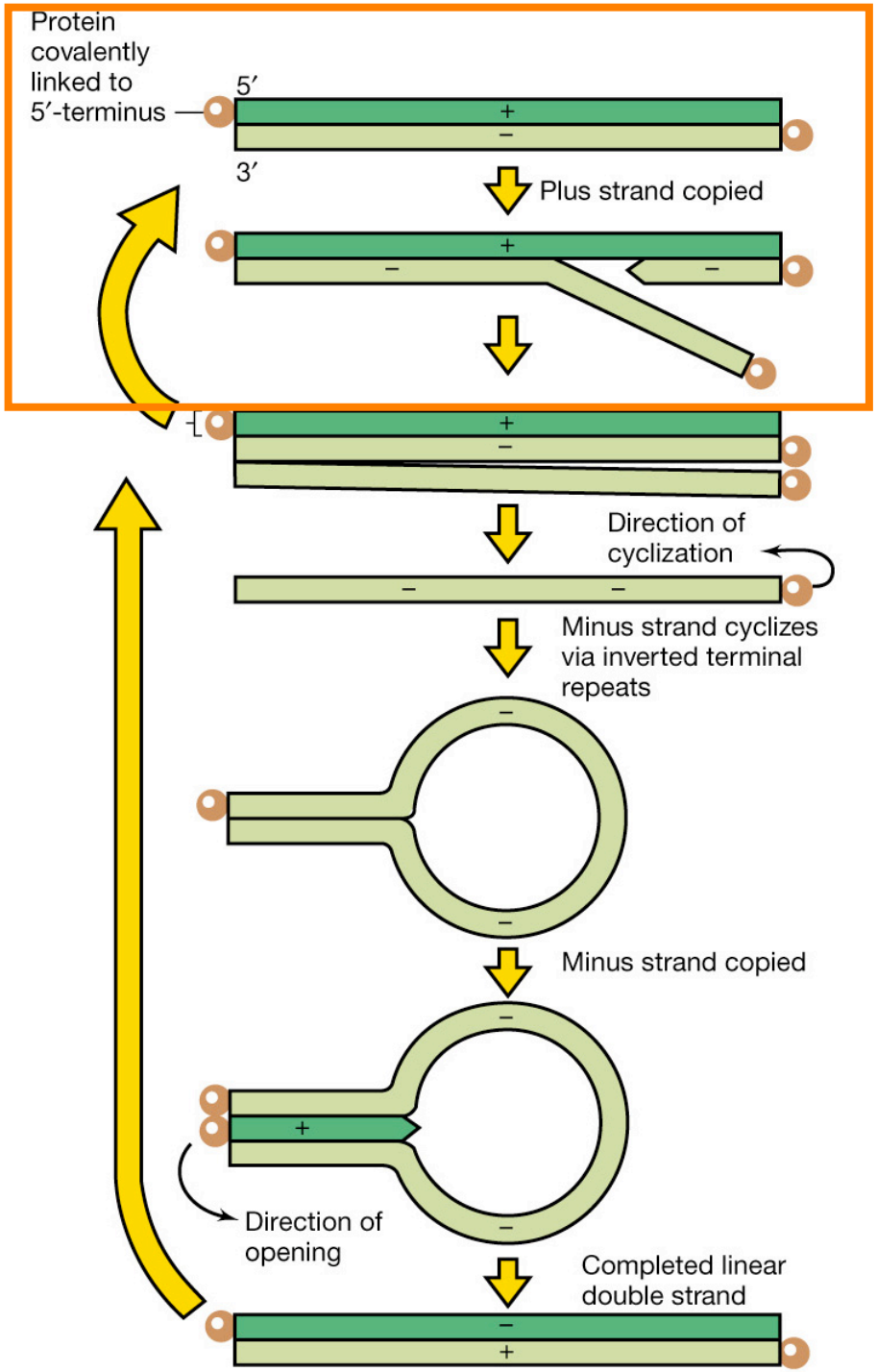
The diversity of viral translation strategies:

**Picornaviruses**

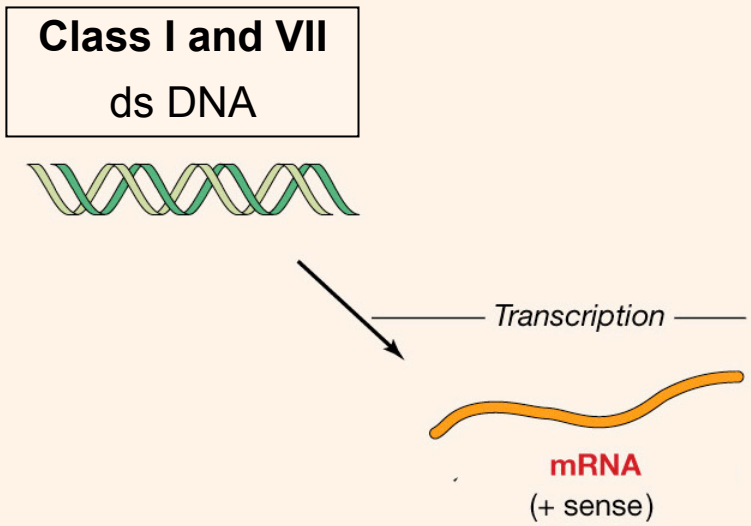
polyprotein synthesis



# The diversity of viral genome replication strategies: adenovirus DNA replication



# The Baltimore classification system



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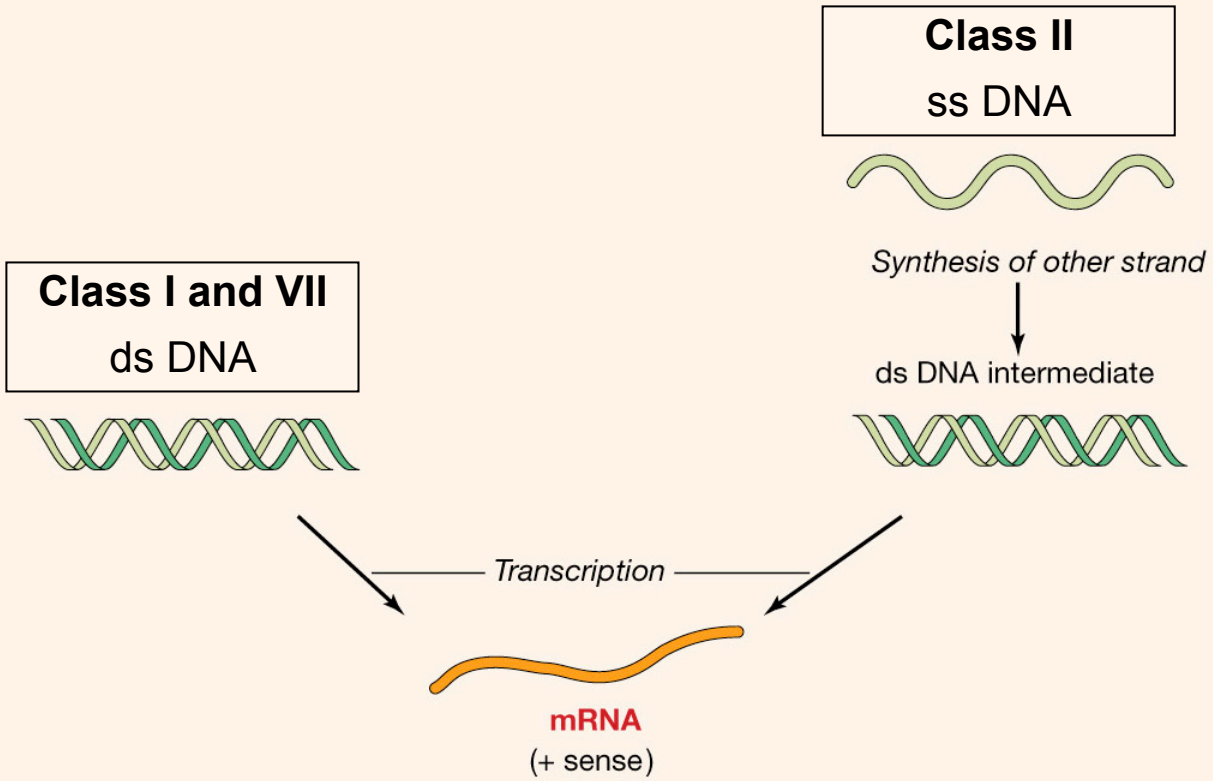

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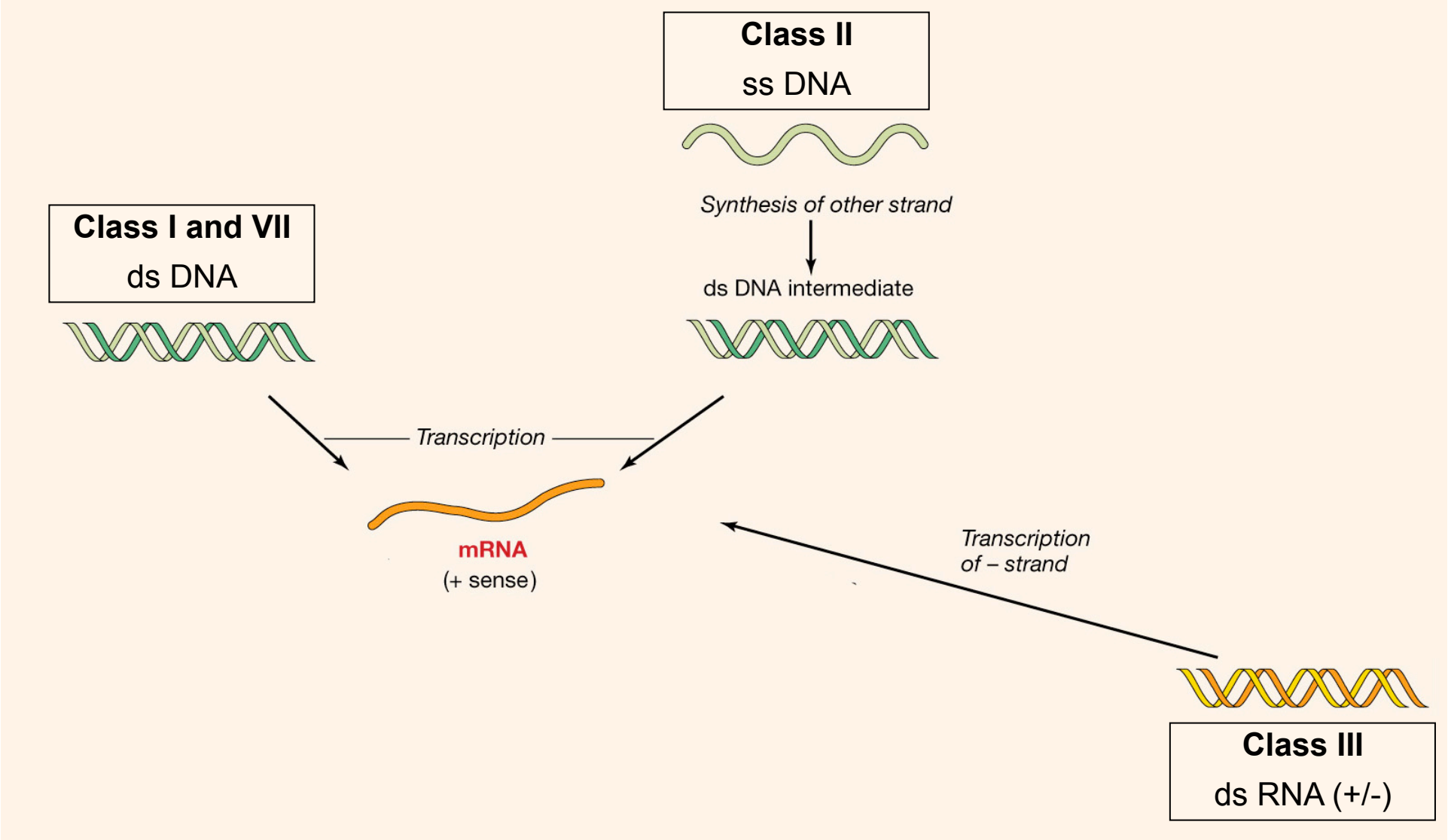

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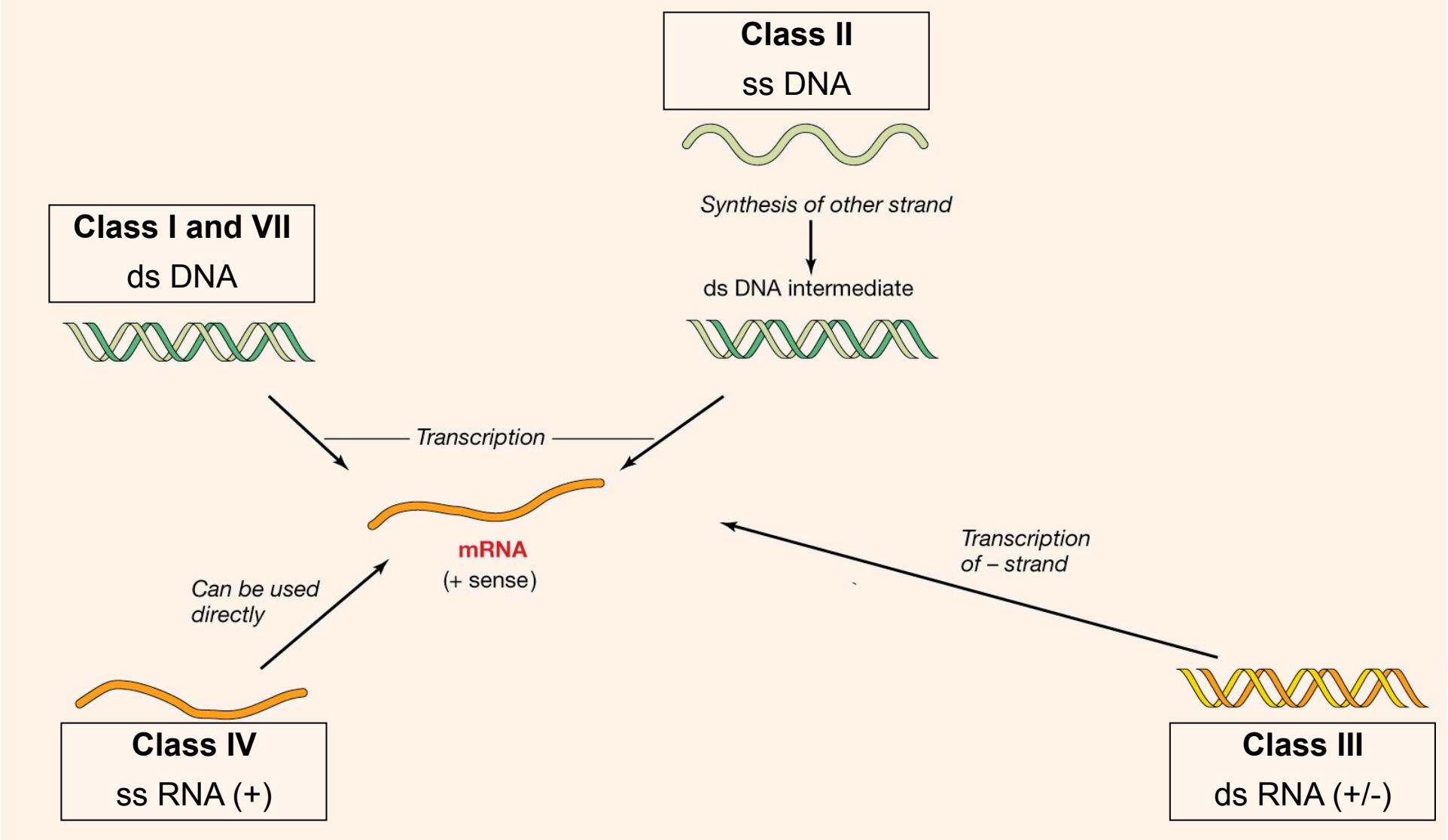
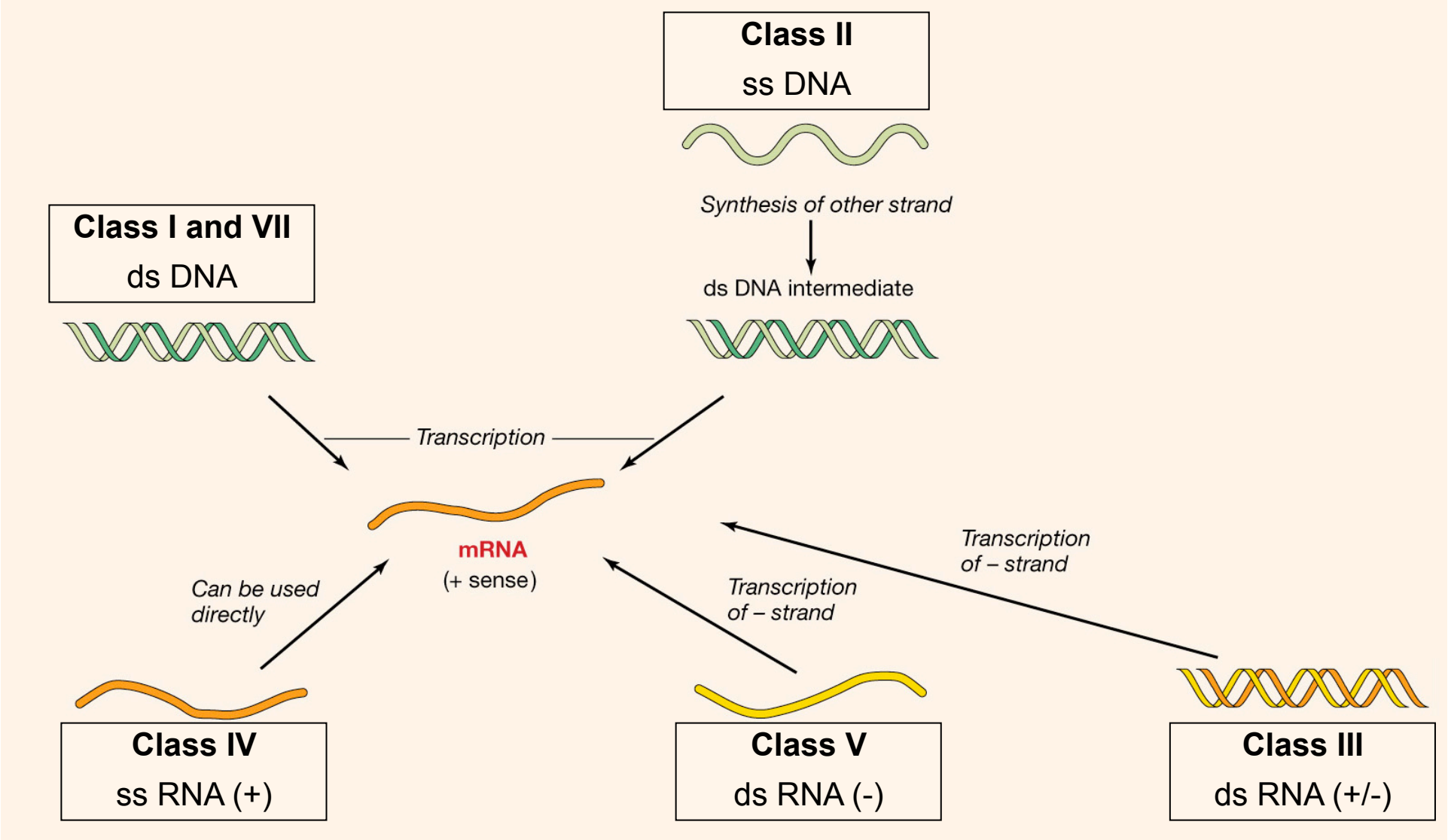


# The Baltimore classification system



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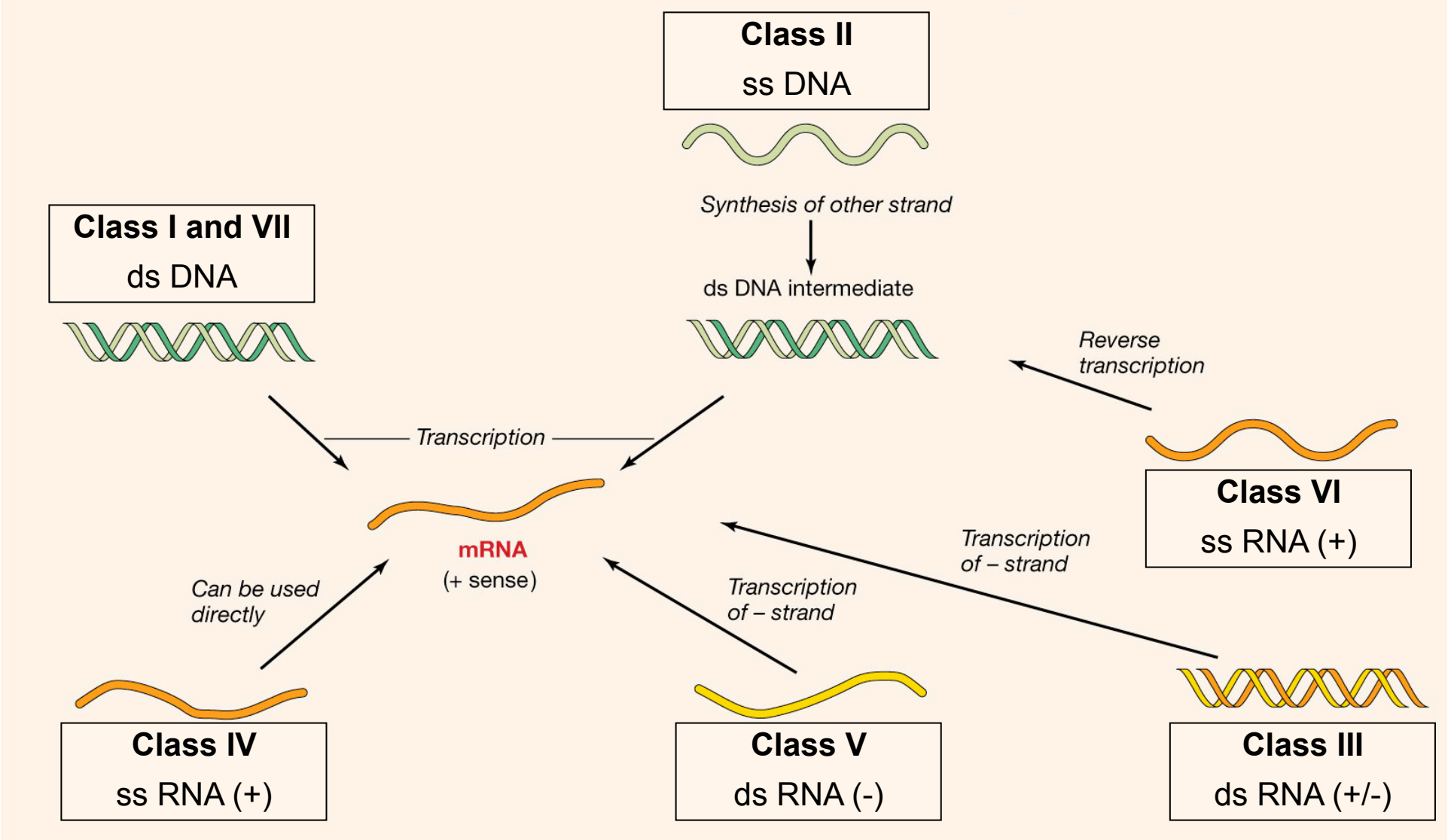
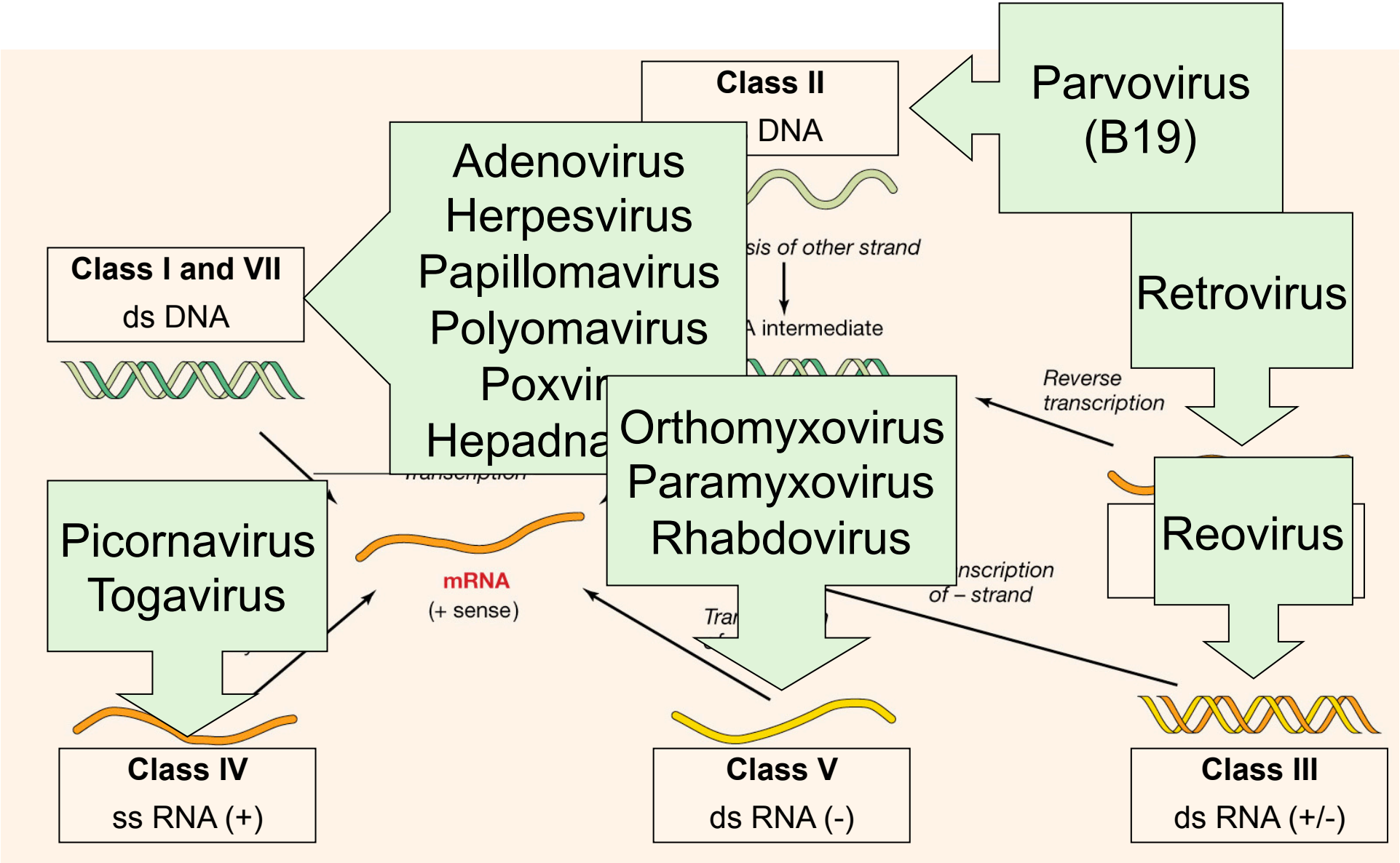


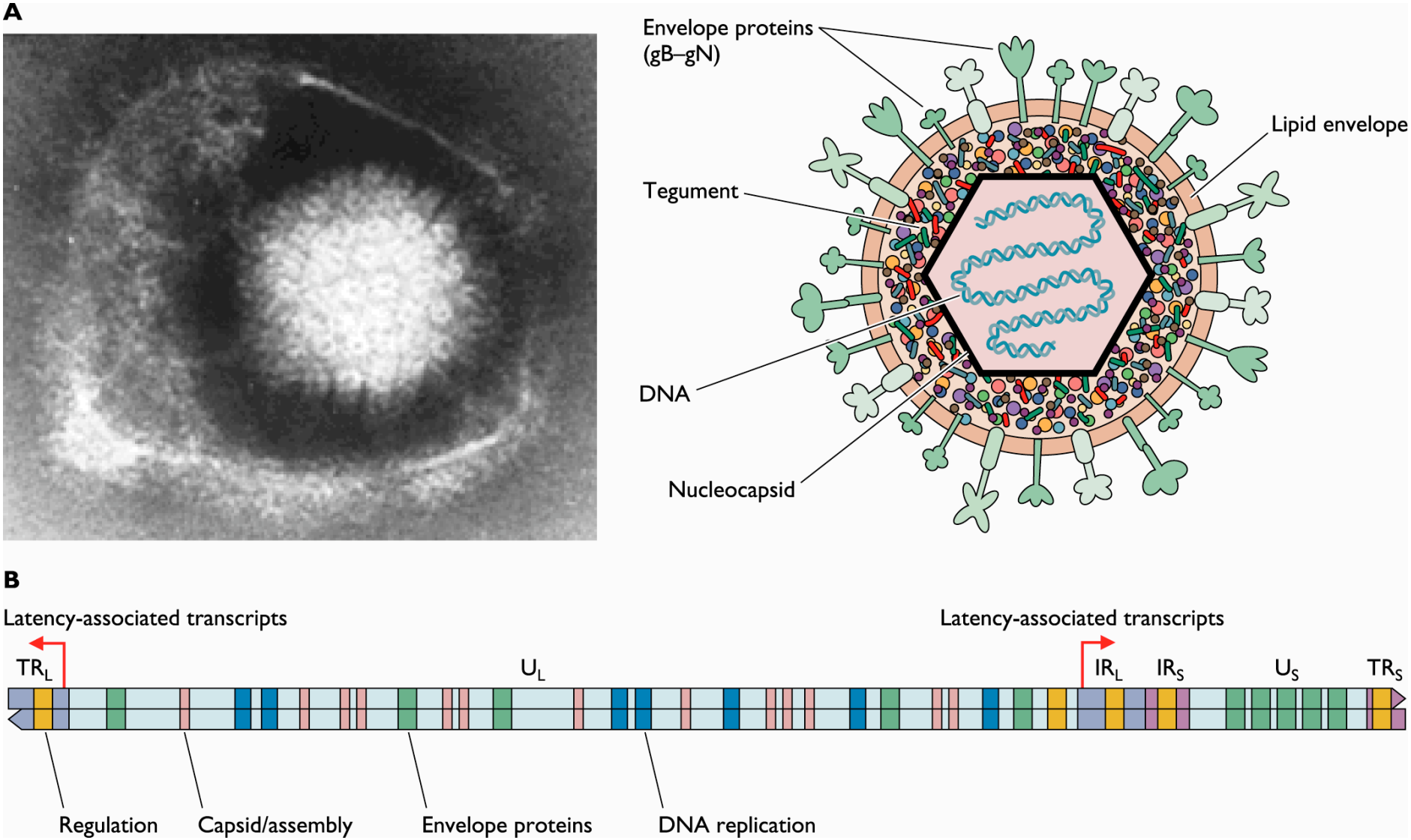
# The Baltimore classification system



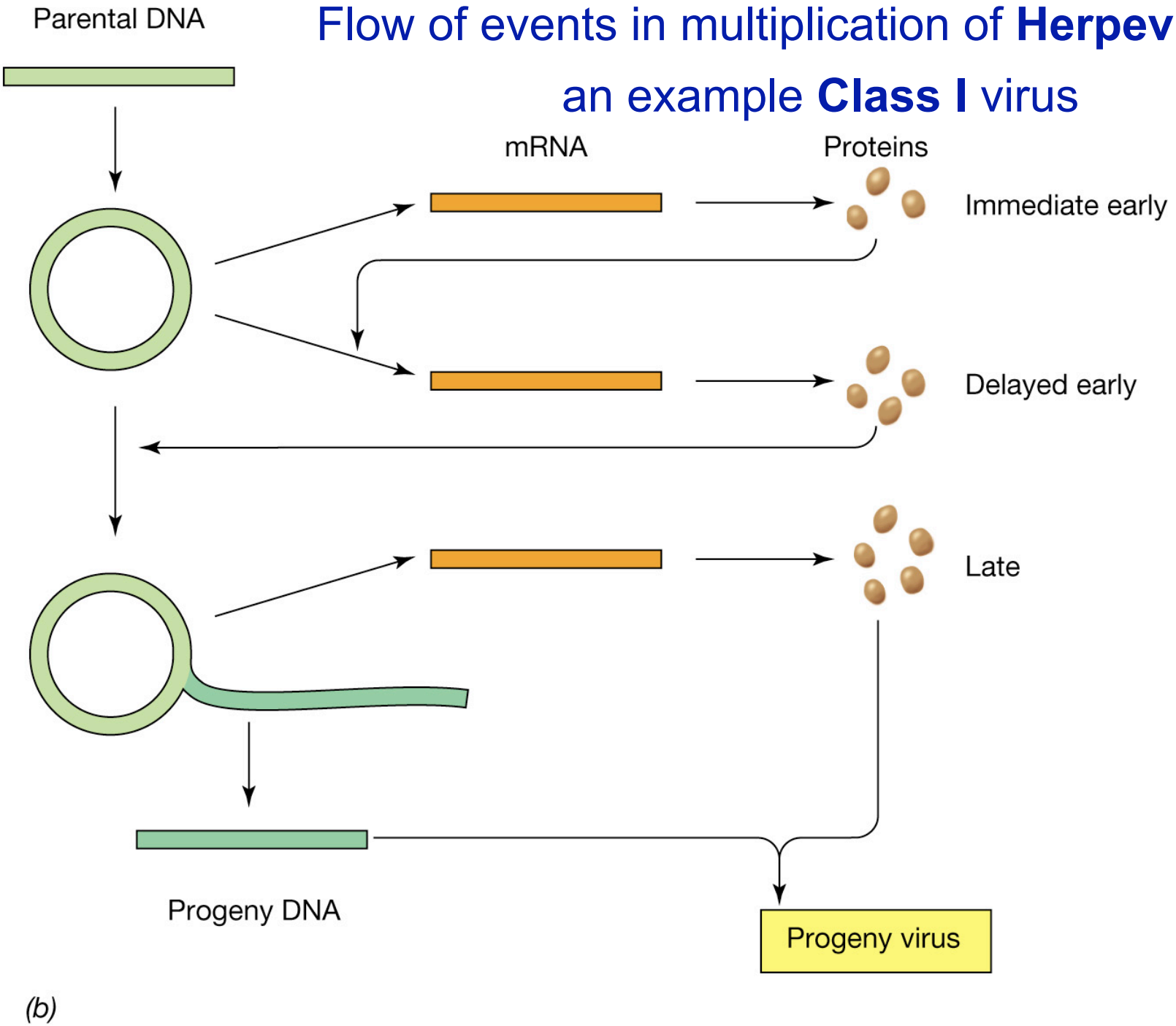
# Viral replication

## transcription, translation and genome replication of DNA viruses

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



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

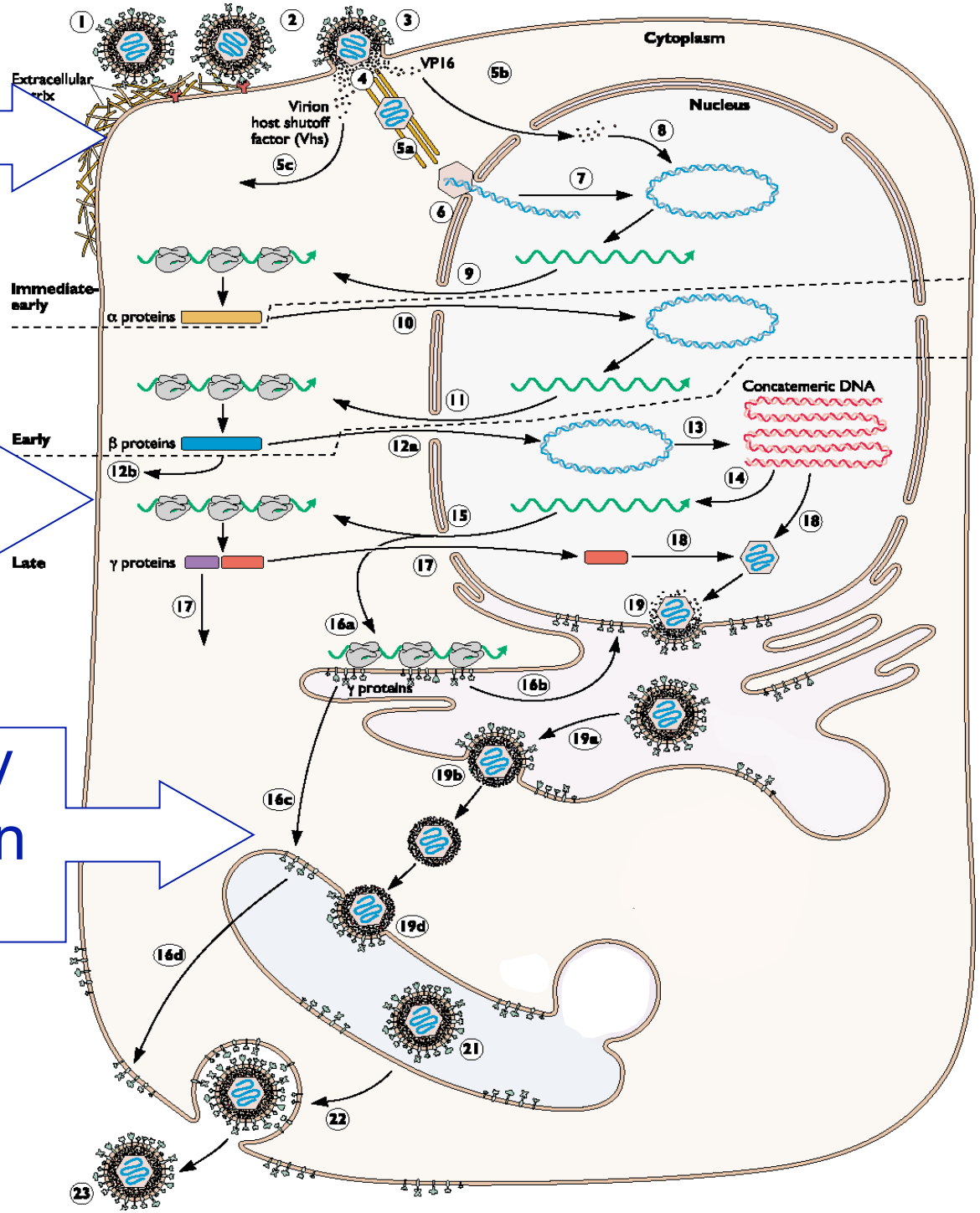



(b)

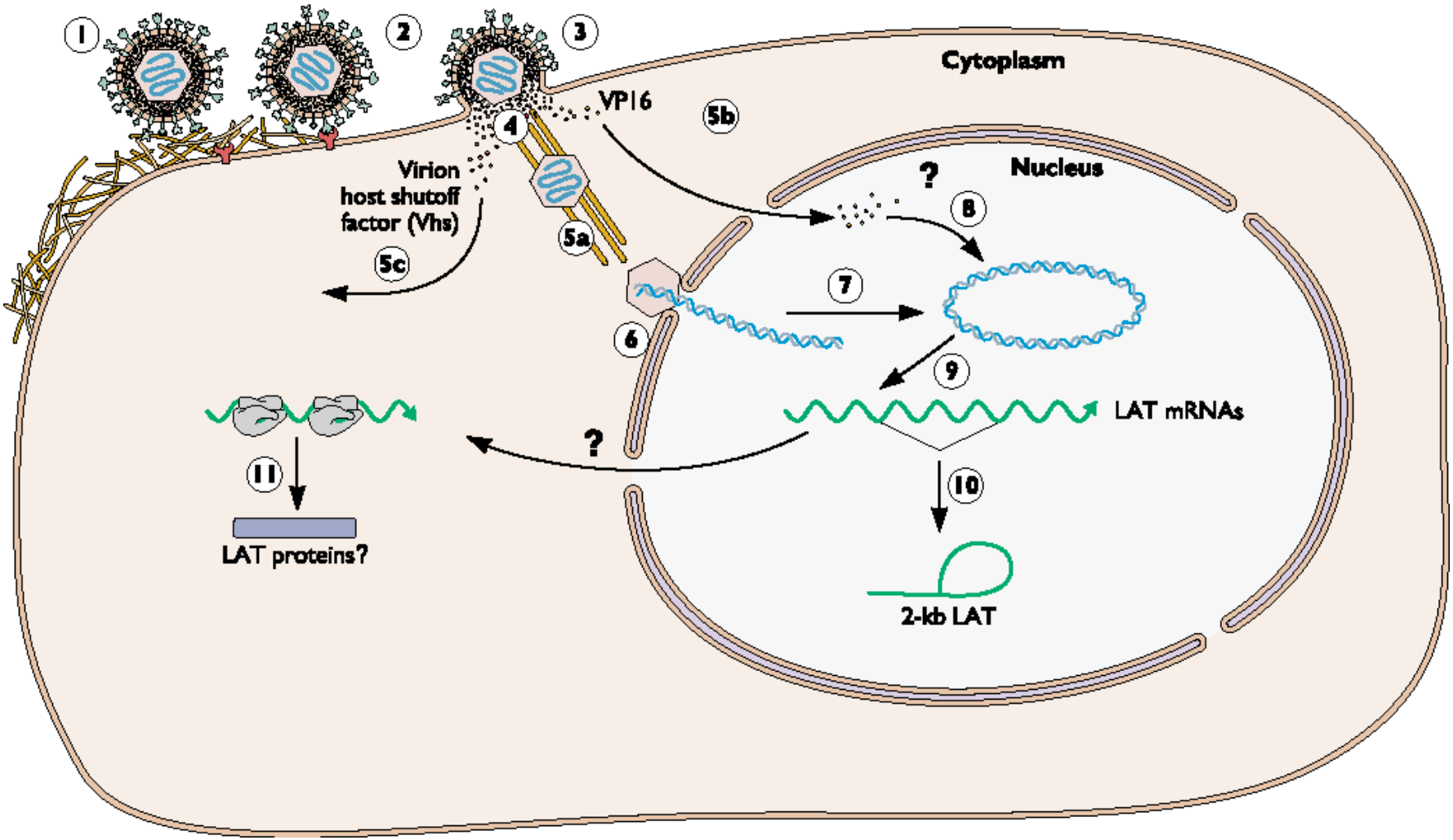
Attachment
Entry
Uncoating

Viral
Synthesis

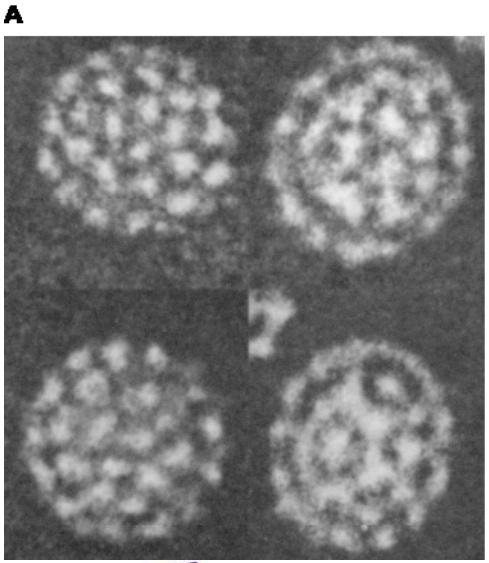
Assembly
Maturation
Exit

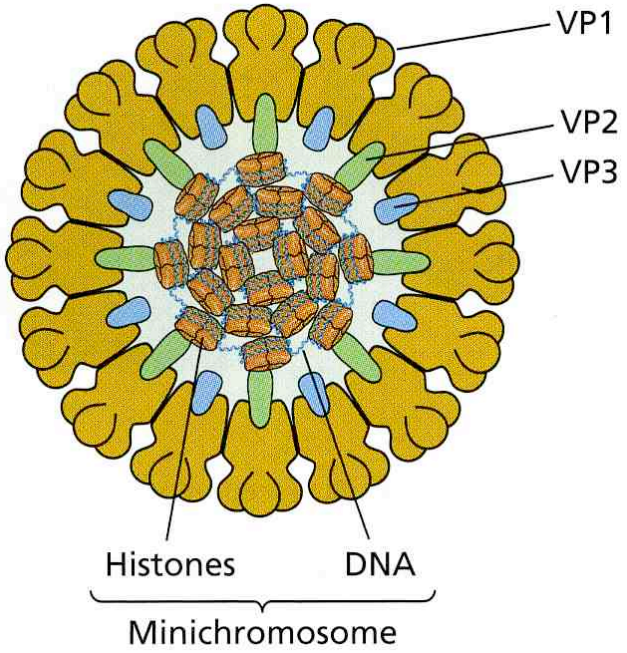


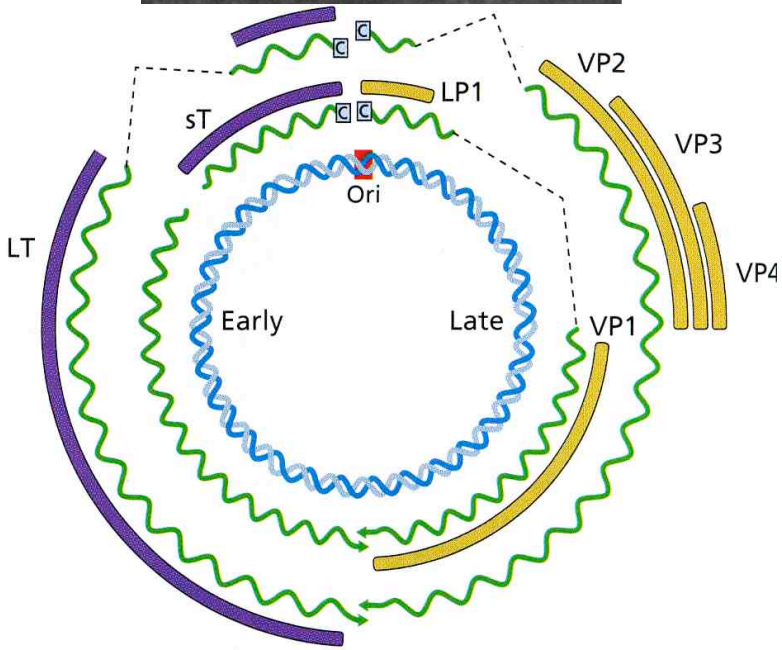
# Herpes simplex virus latent infection in neurons

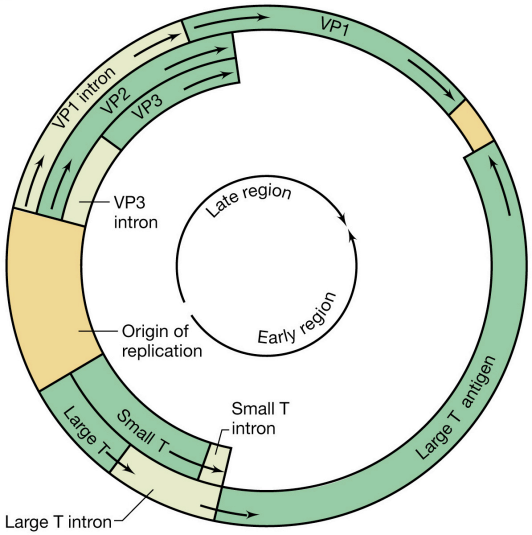


# Structure and genome organization of the **Polyomavirus** **S**imian **V**irus **40**: an example of **Class I** tumoral virus



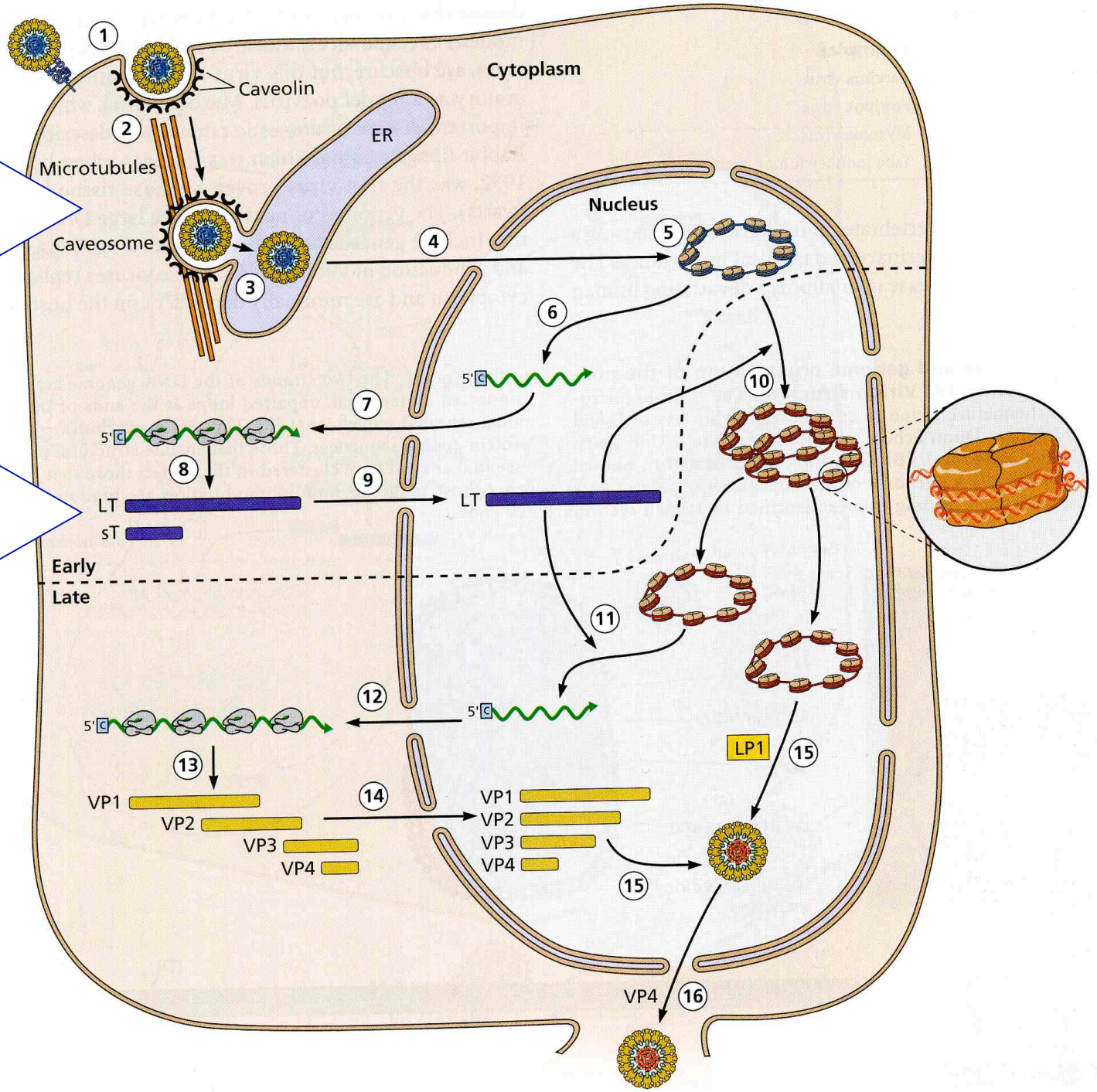



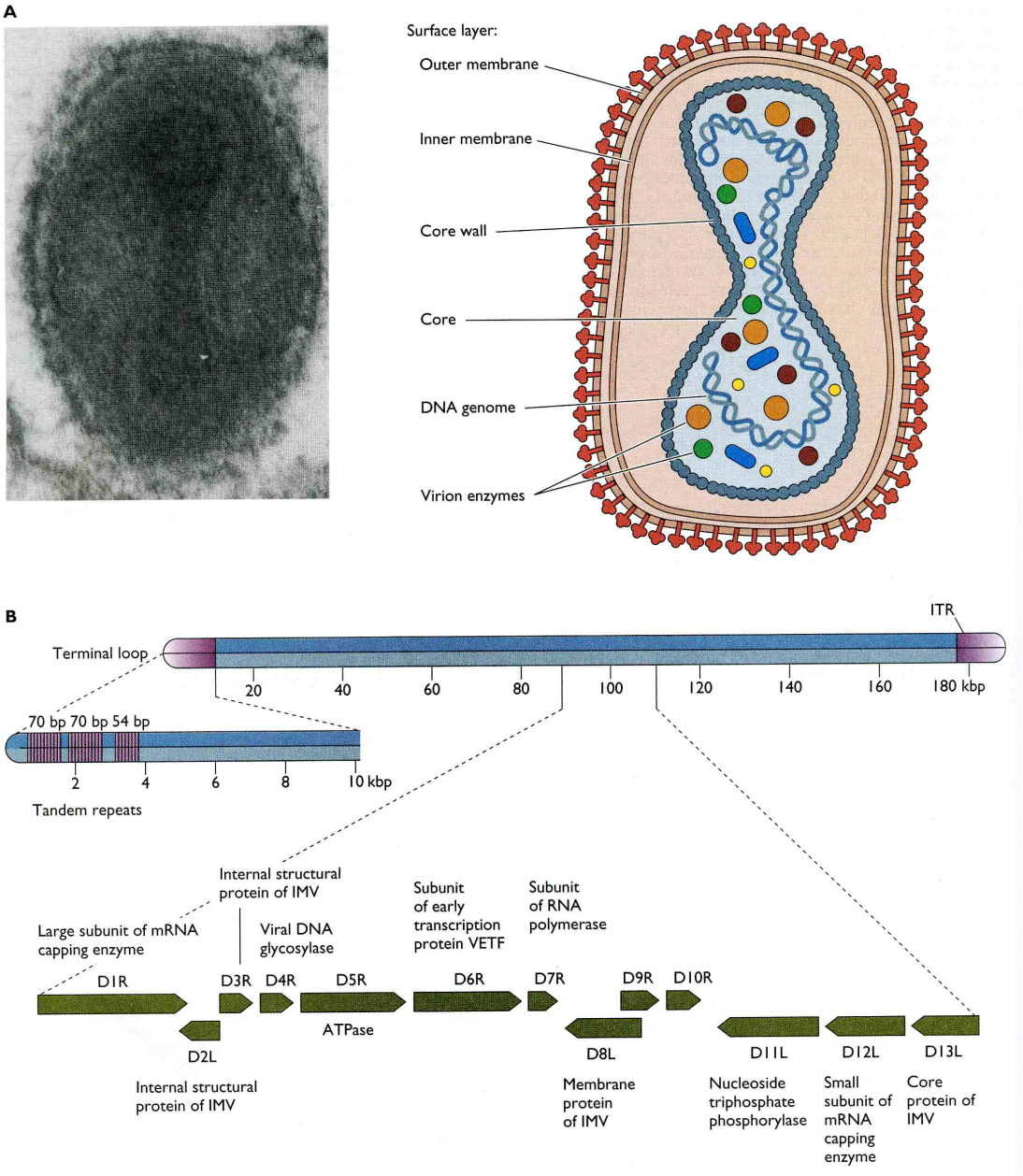



Attachment
Entry
Uncoating

Viral
Synthesis



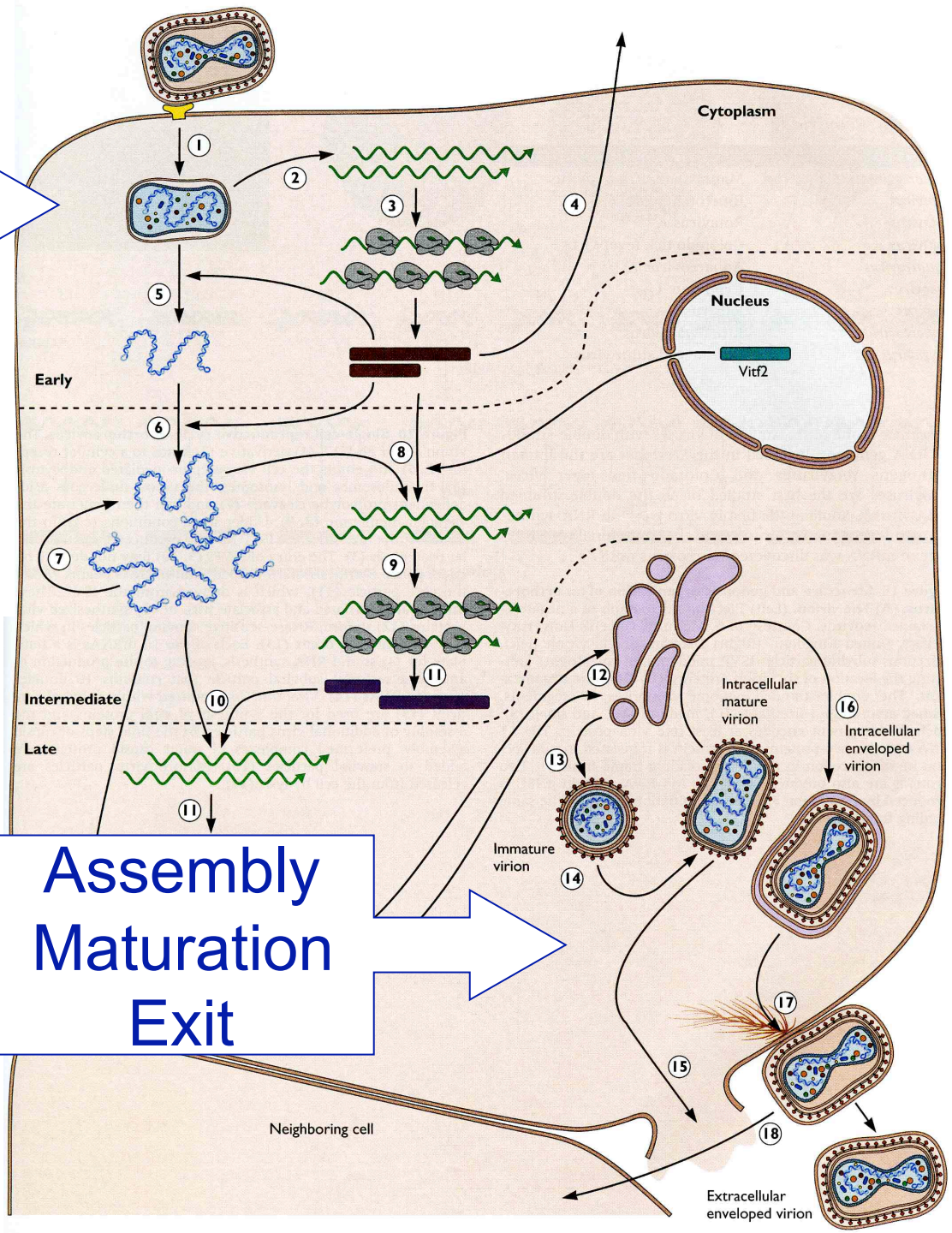
# Structure and genome organization of the **Poxvirus** Vaccinia virus: an example of **Class I** virus that replicates in the cytoplasm



Attachment
Entry
Uncoating

Viral
Synthesis

Assembly
Maturation
Exit

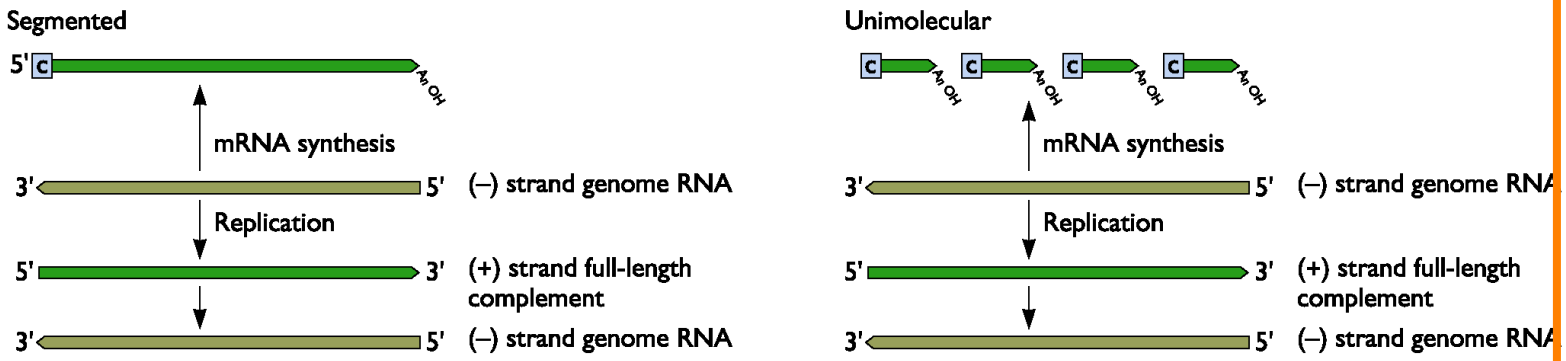


# Viral replication

## transcription, translation and genome replication of RNA viruses

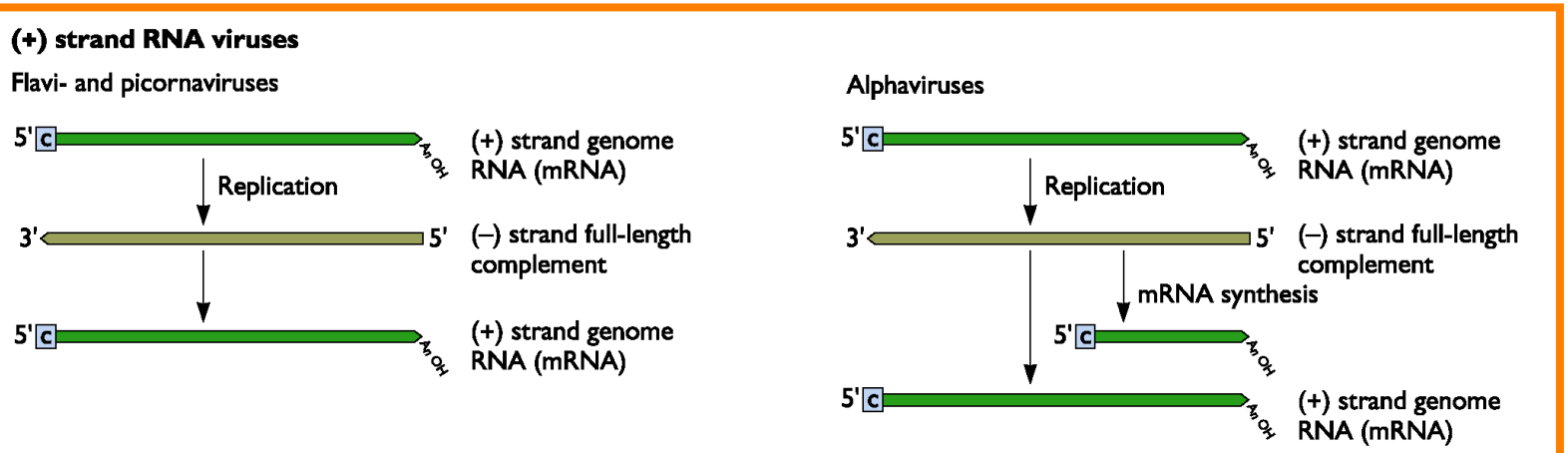
V

## (–) strand RNA viruses

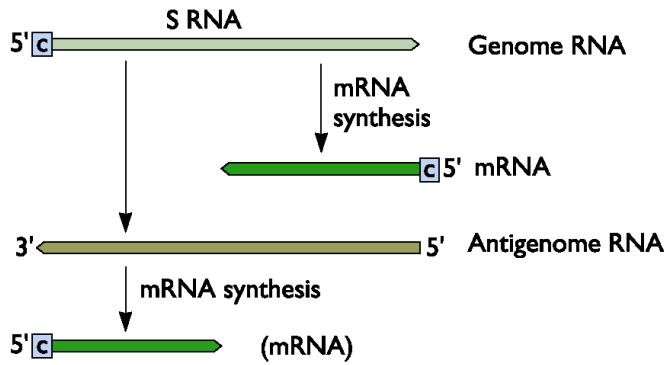



IV

## (+) strand RNA viruses

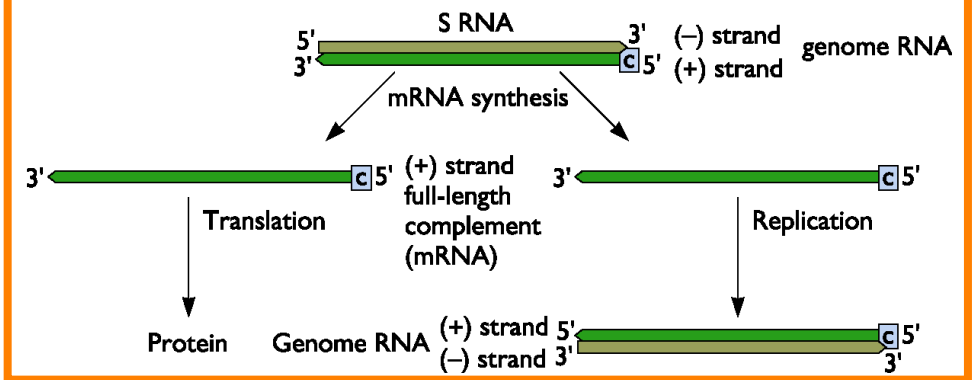



## Ambisense RNA viruses

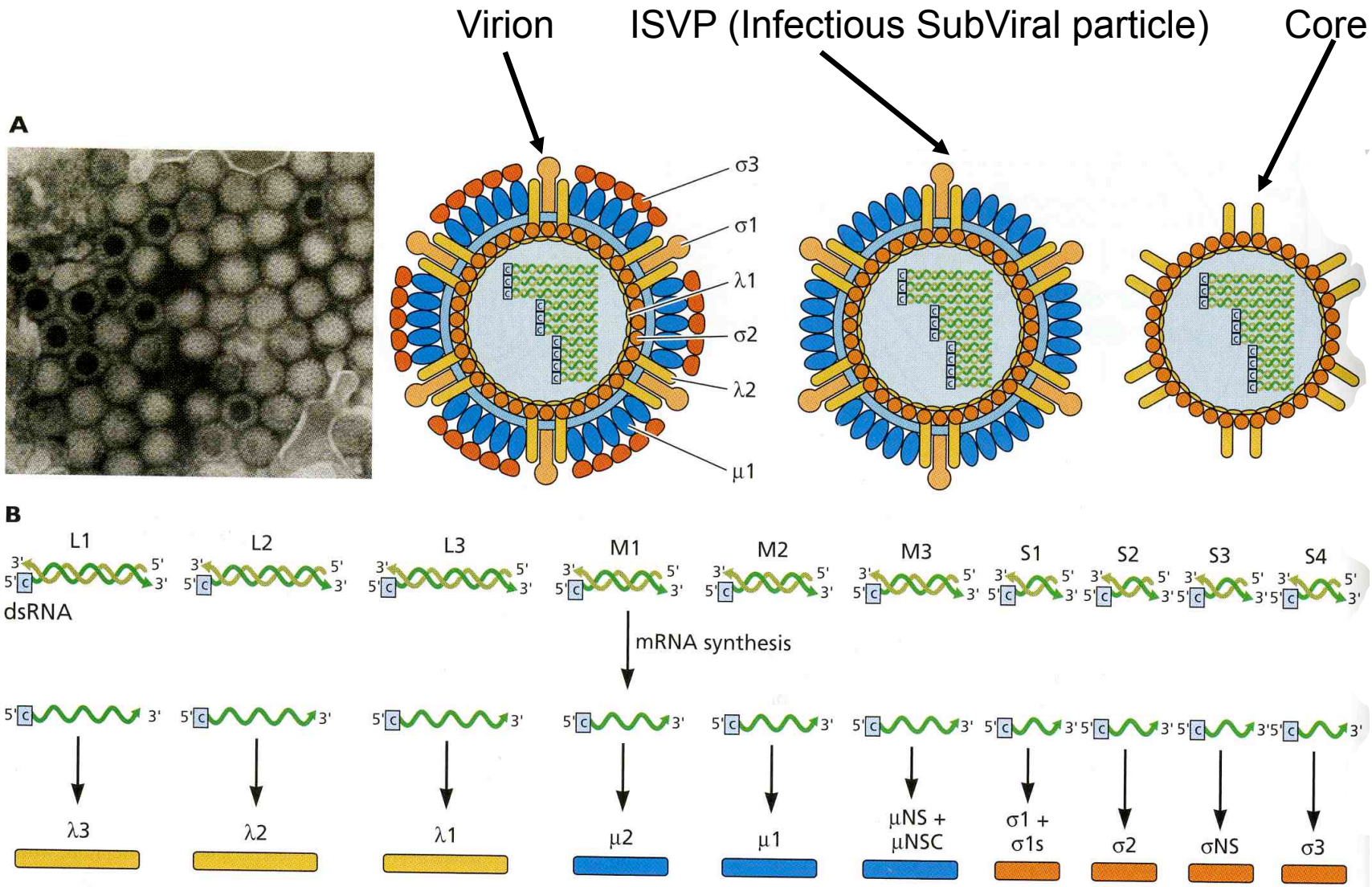



III

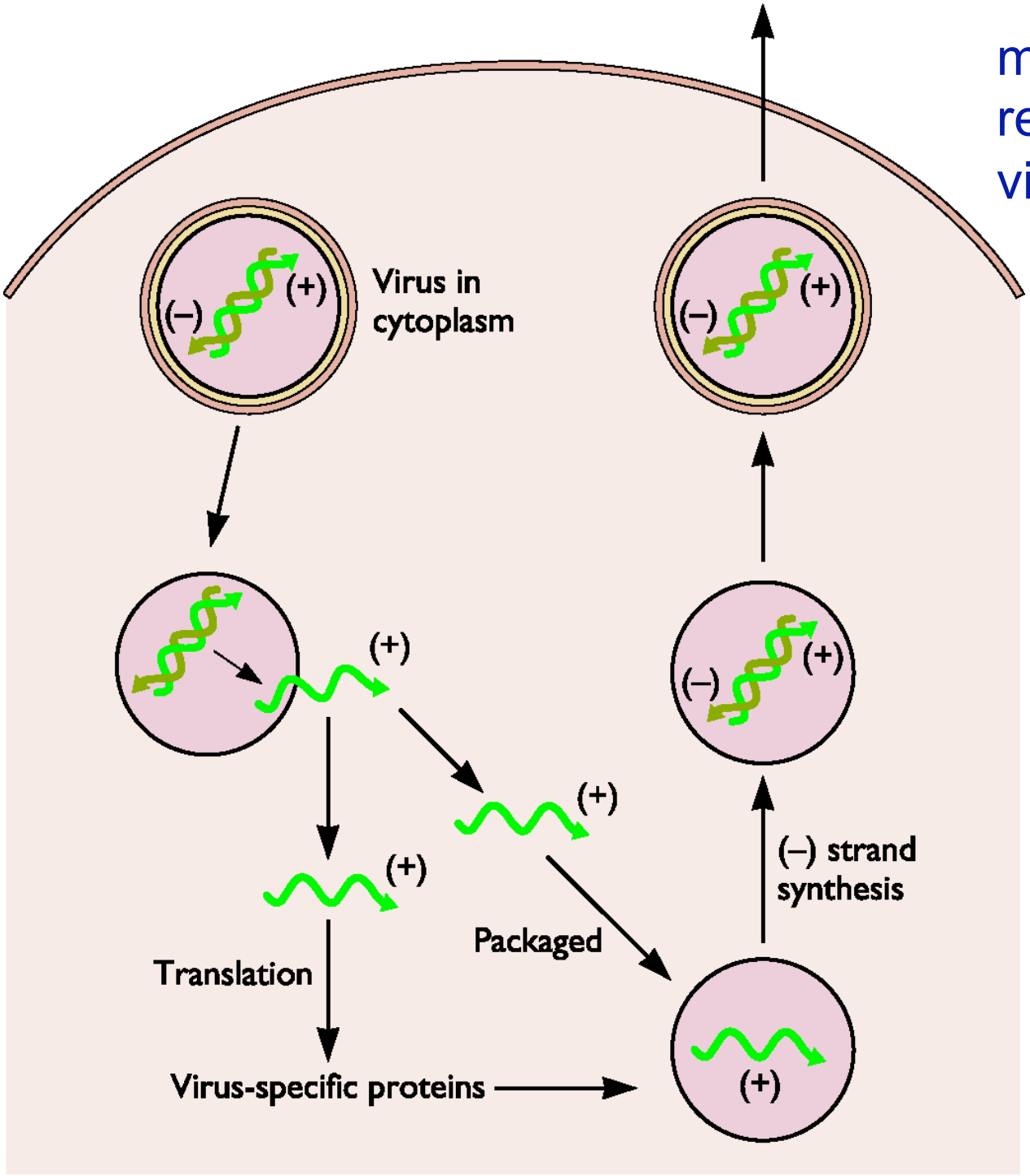
## Double-stranded RNA viruses



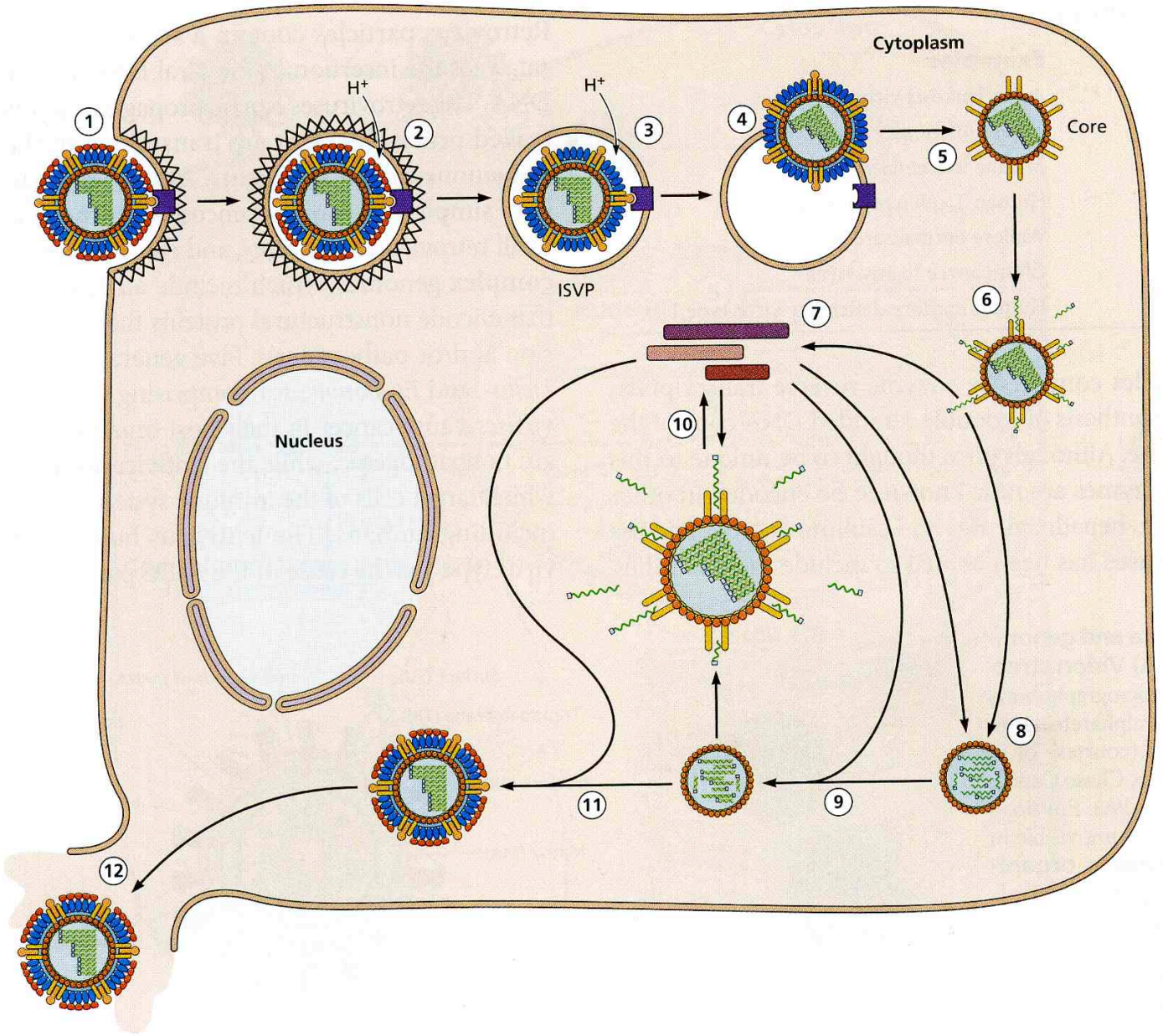
# Structure and genomic organization of a Reovirus



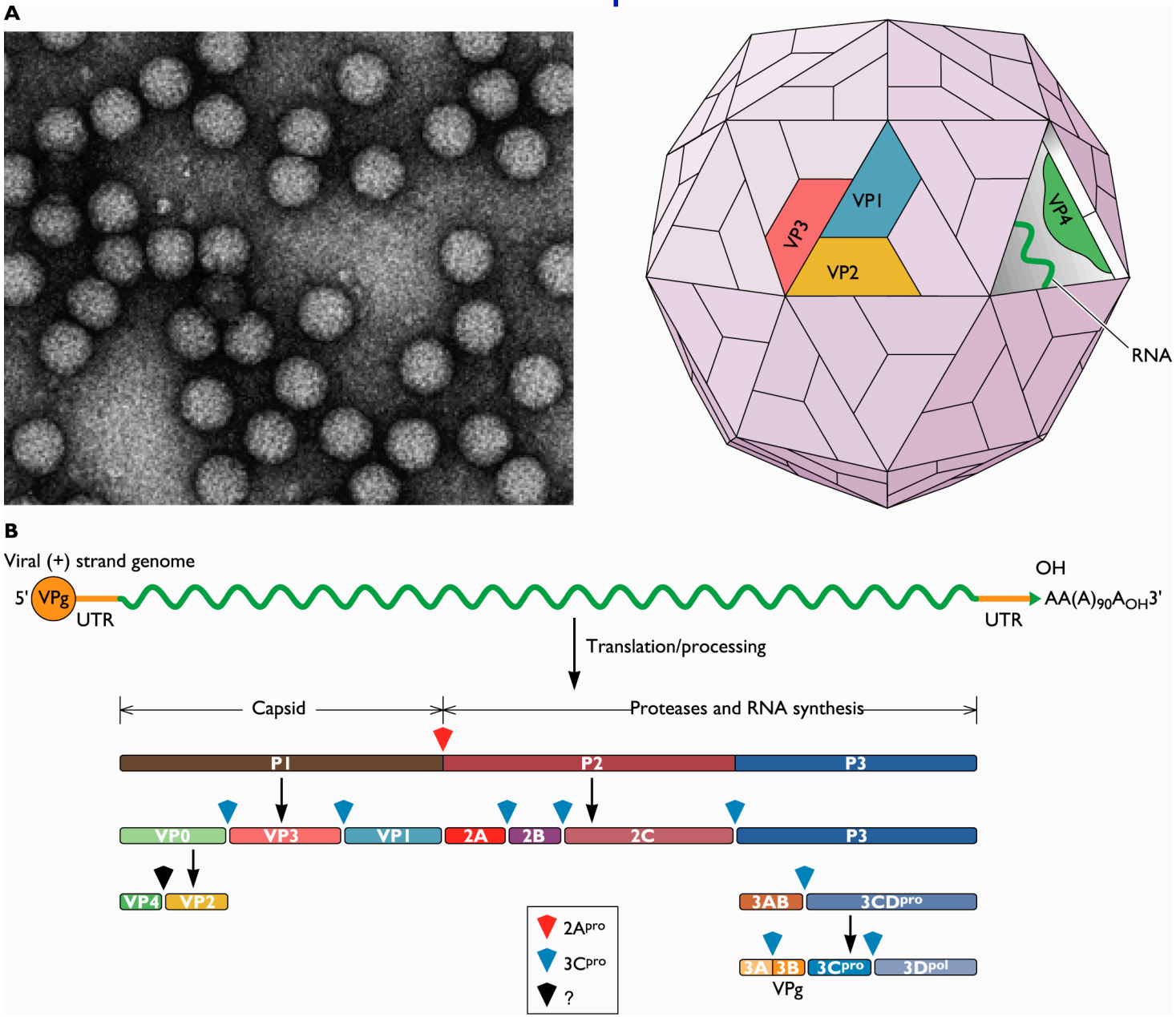
mRNA synthesis and replication of **Class III** virus: the **Reoviruses**



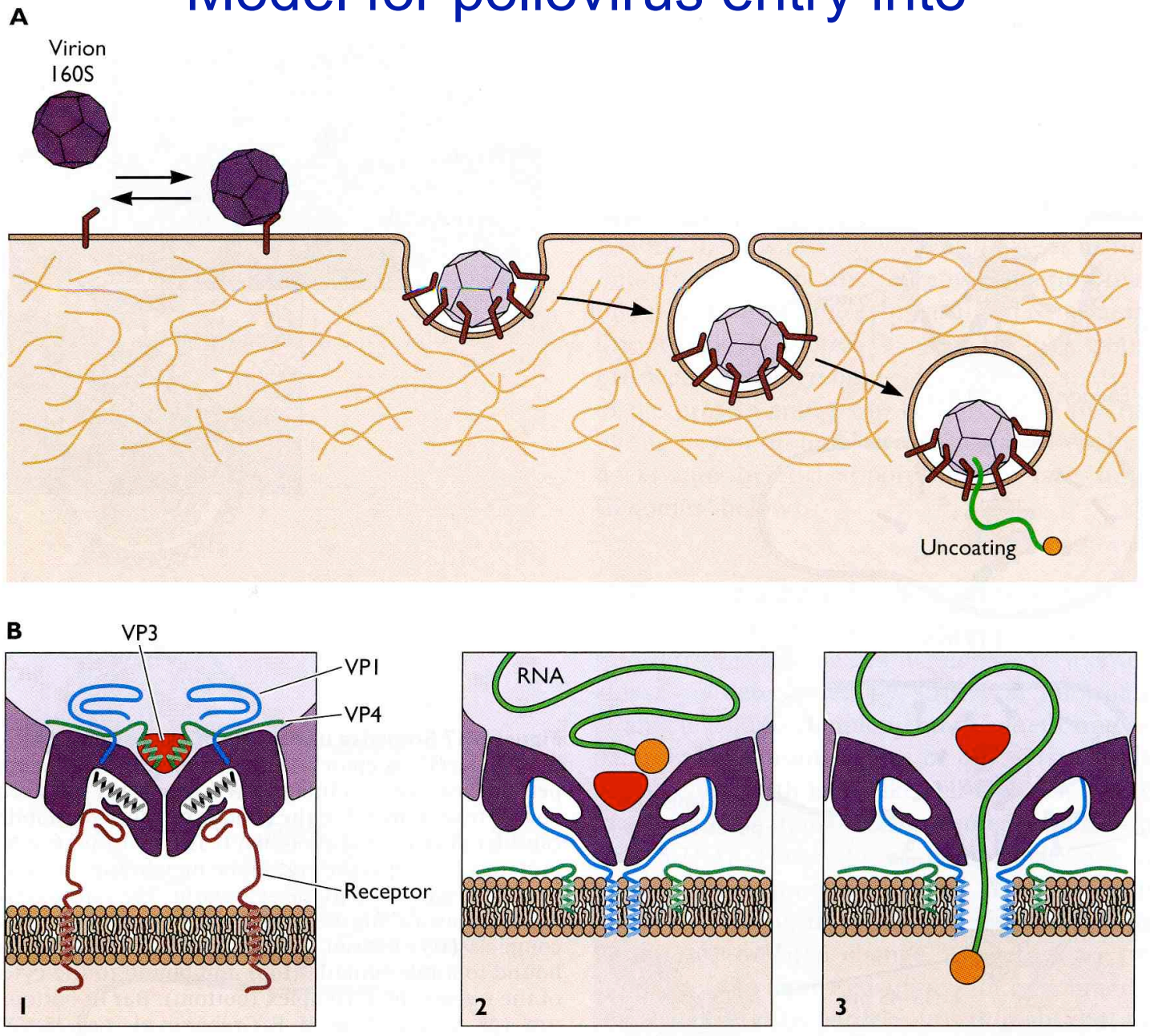
# Reproductive cycle of a Reovirus



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



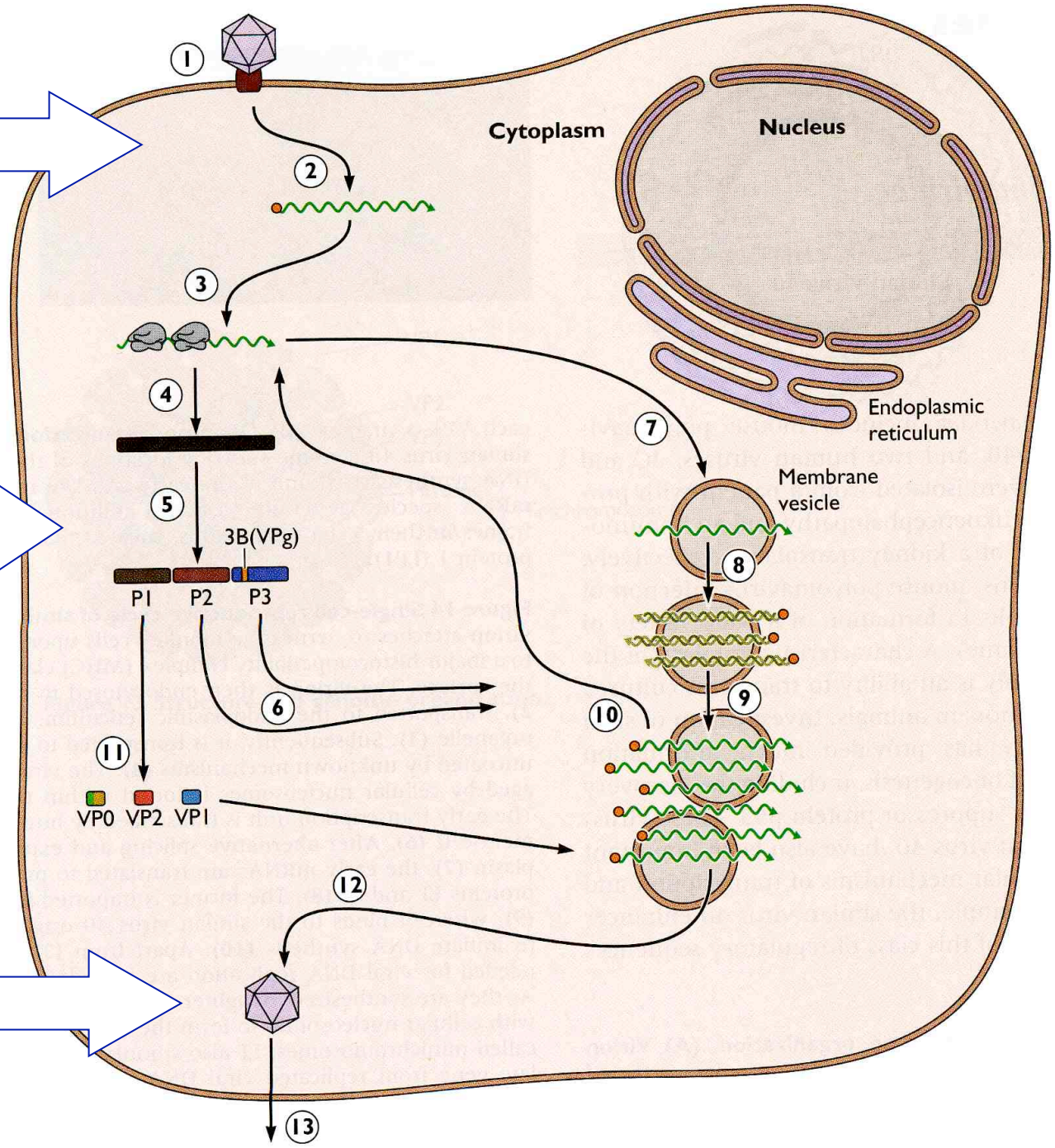
# Model for poliovirus entry into



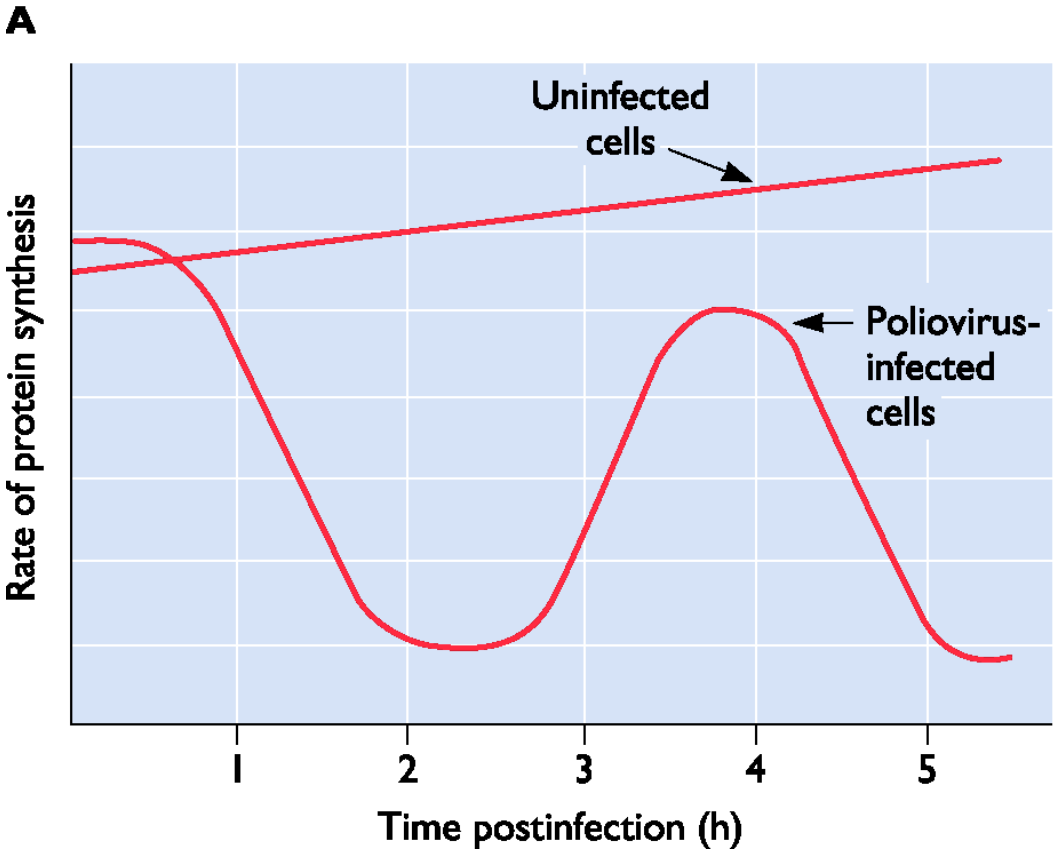
Attachment
Entry
Uncoating

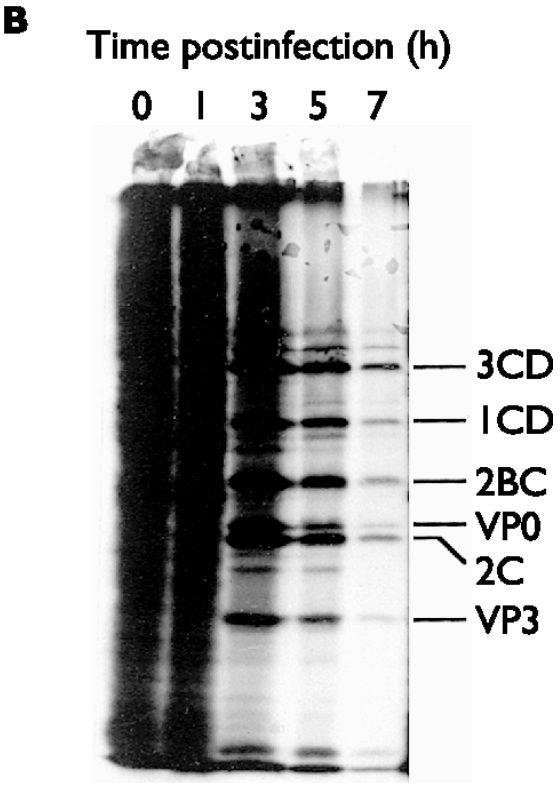
Viral
Synthesis

Assembly
Maturation
Exit

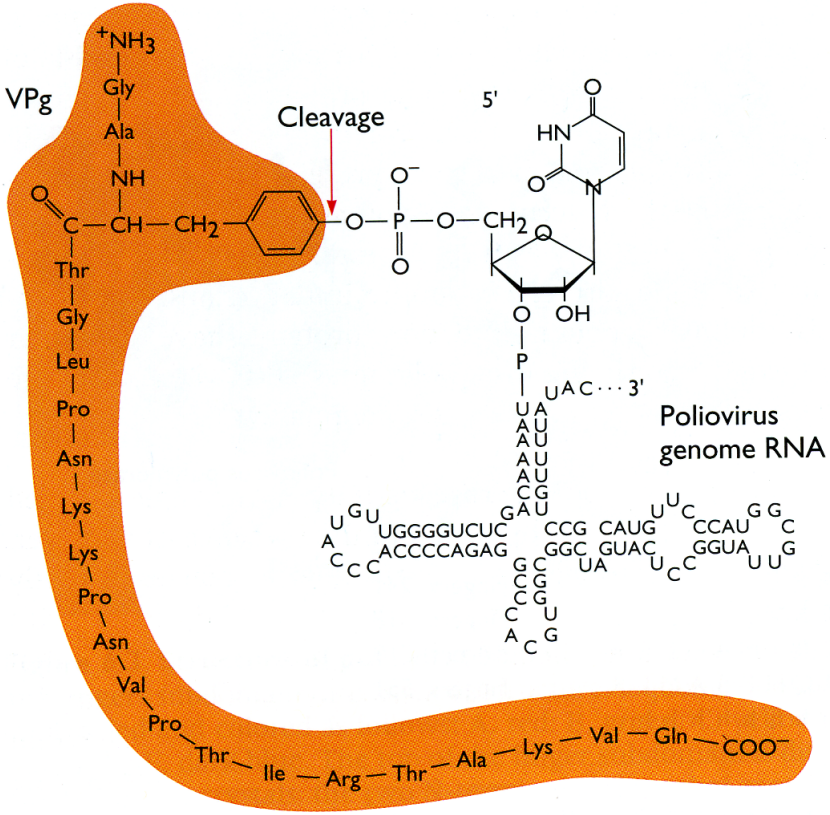


# Inhibition of translation in poliovirus-infected cells

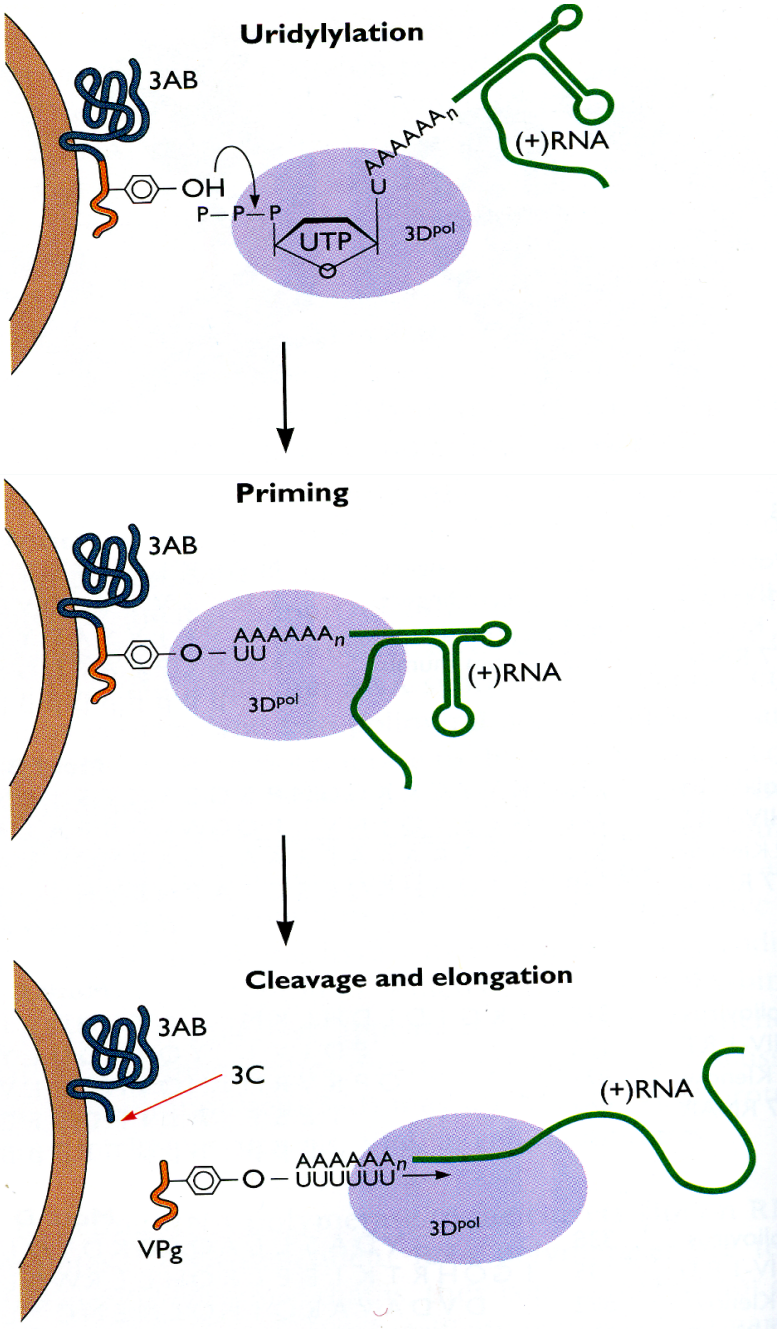


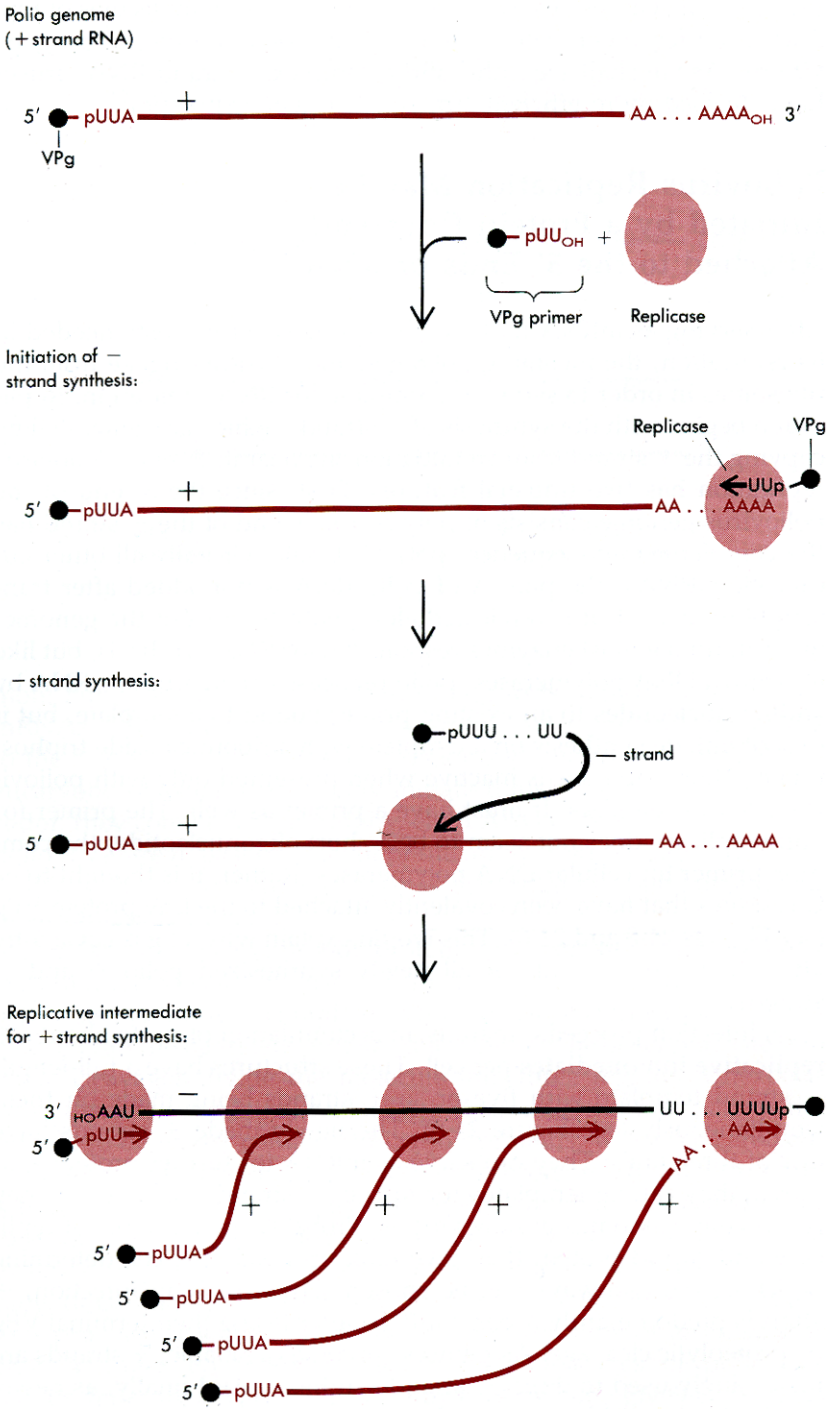
# Poliovirus RNA replication



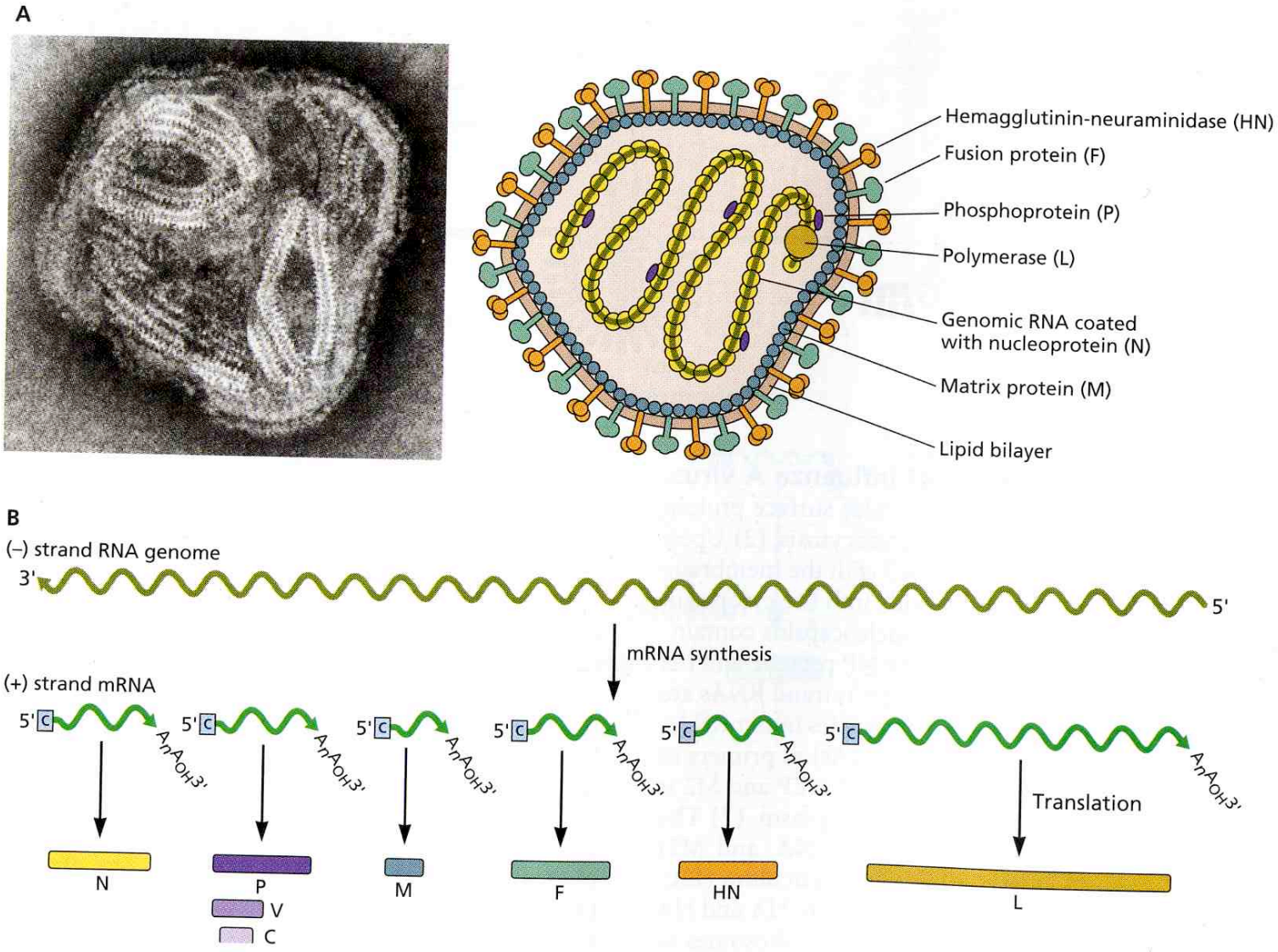

Linkage of VPg to polioviral genomic RNA

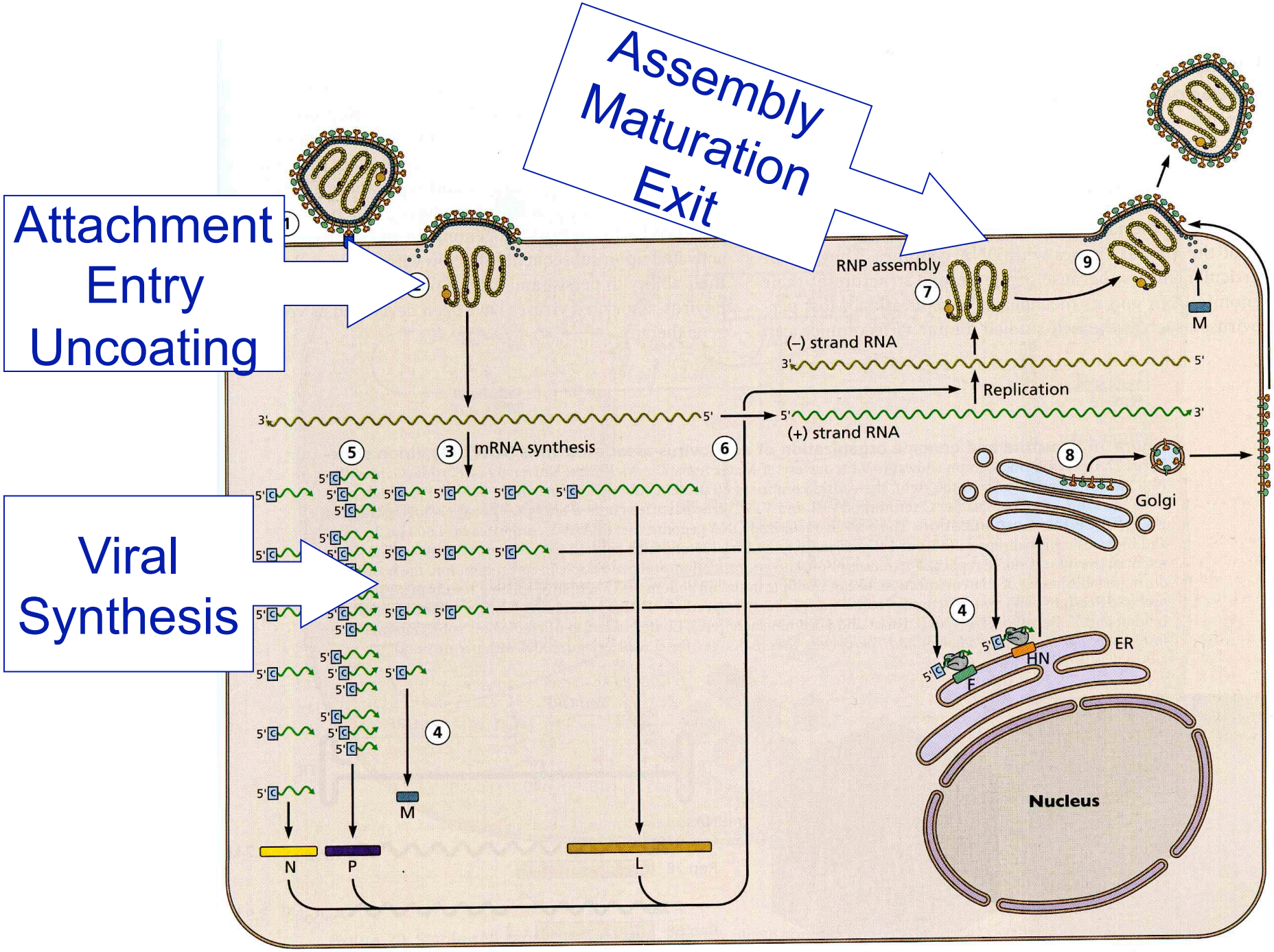


# Poliovirus RNA replication

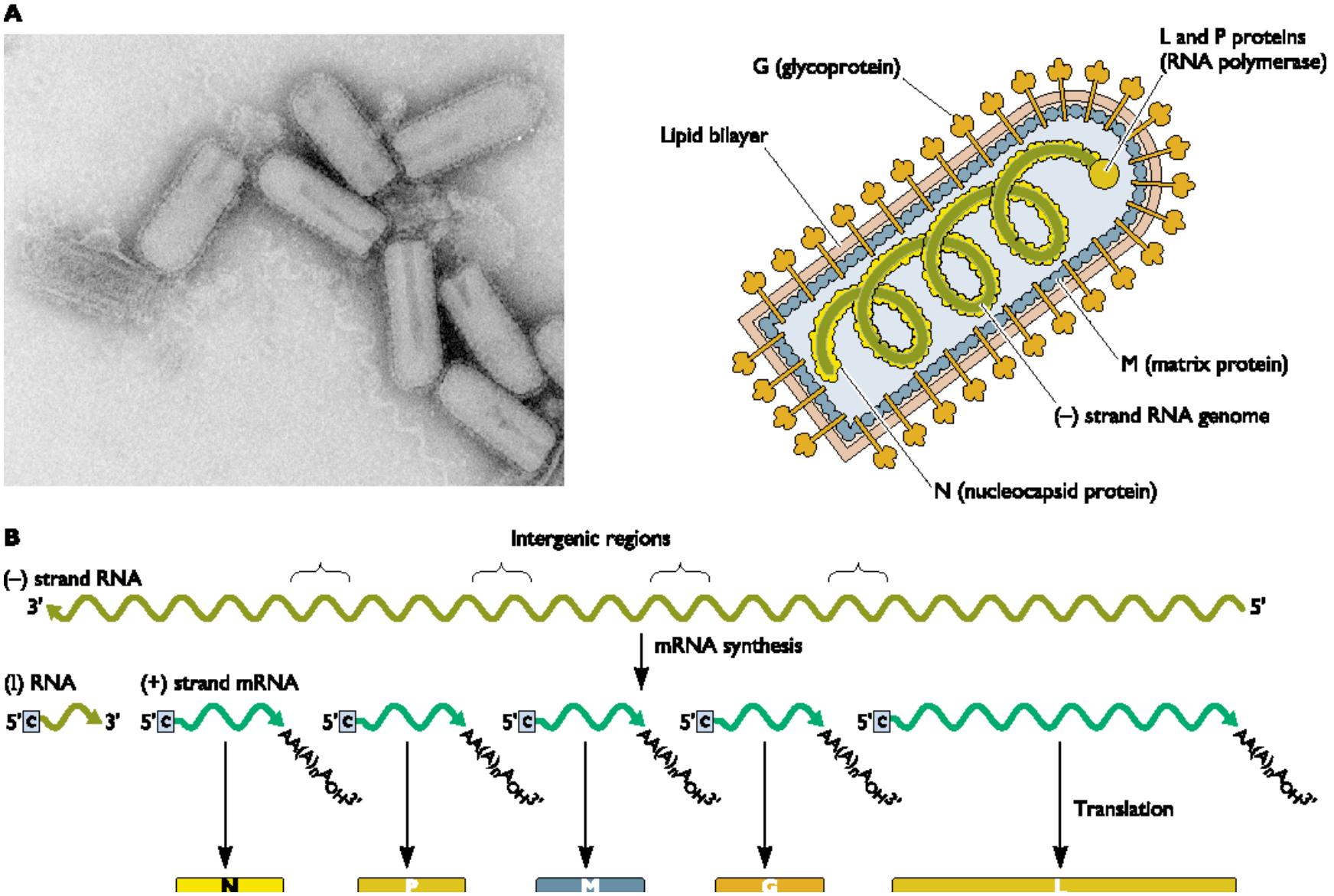


# Structure and genome organization of a **Paramyxovirus**: an example of **Class V virus**

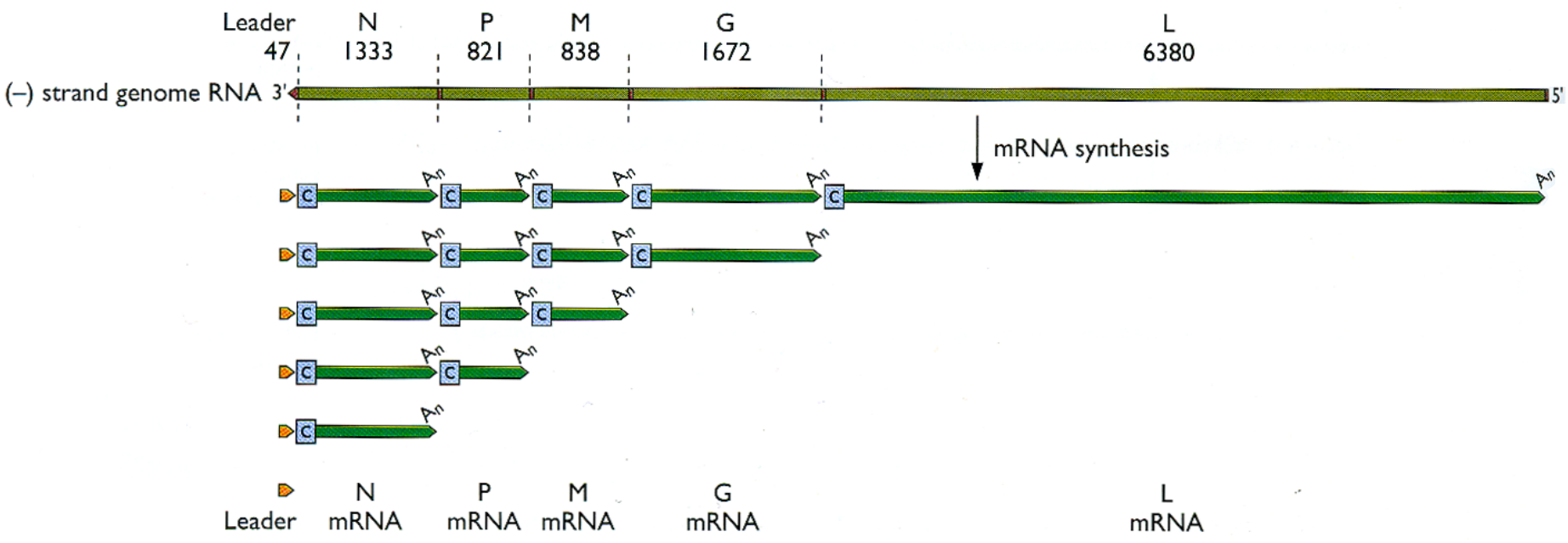



Assembly
Maturation
Exit
Attachment
Entry
Uncoating
Viral
Synthesis
RNP assembly
(–) strand RNA
Replication
(+) strand RNA
mRNA synthesis
Golgi
ER
HN
F
M
N
P
L
Nucleus

# 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
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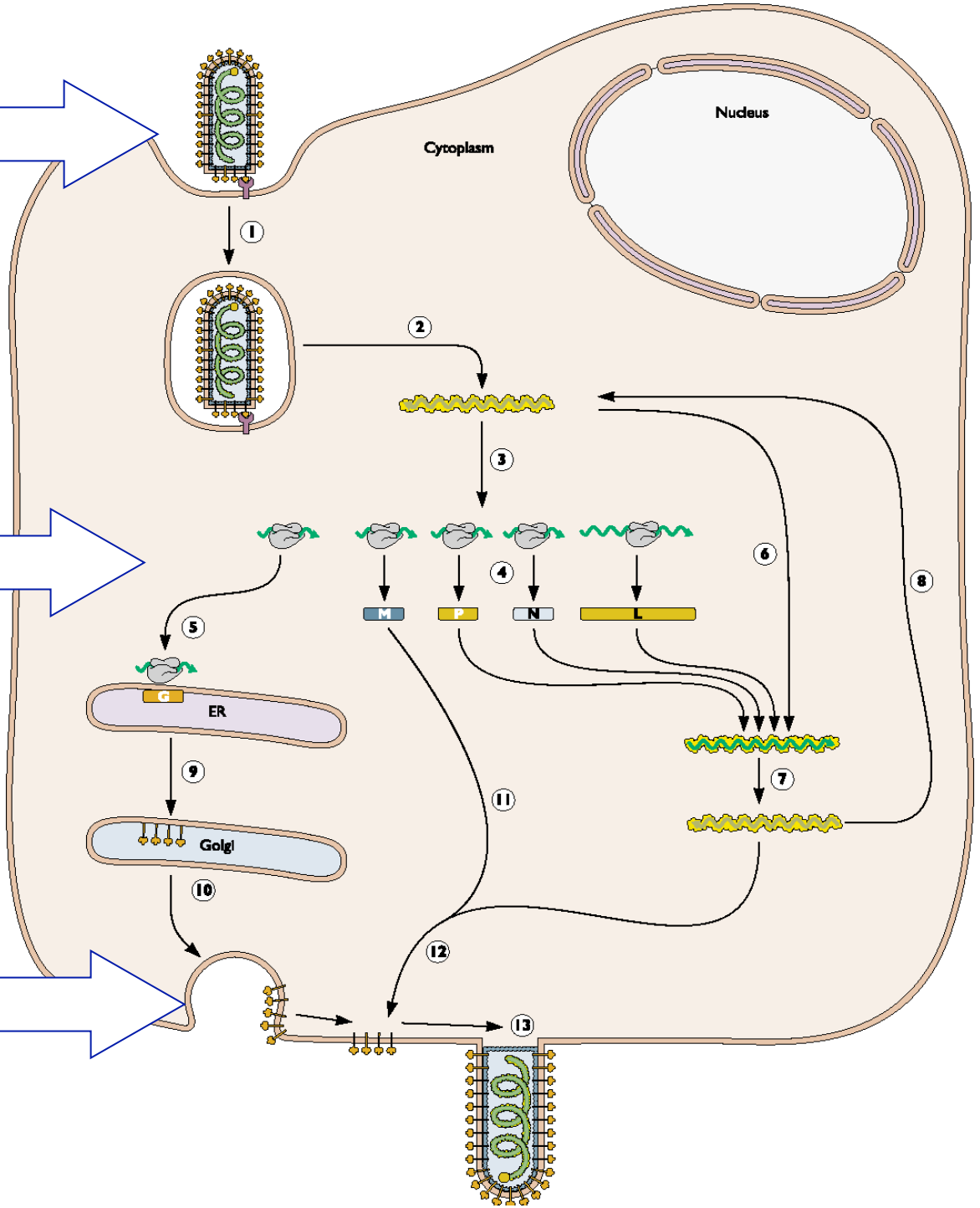
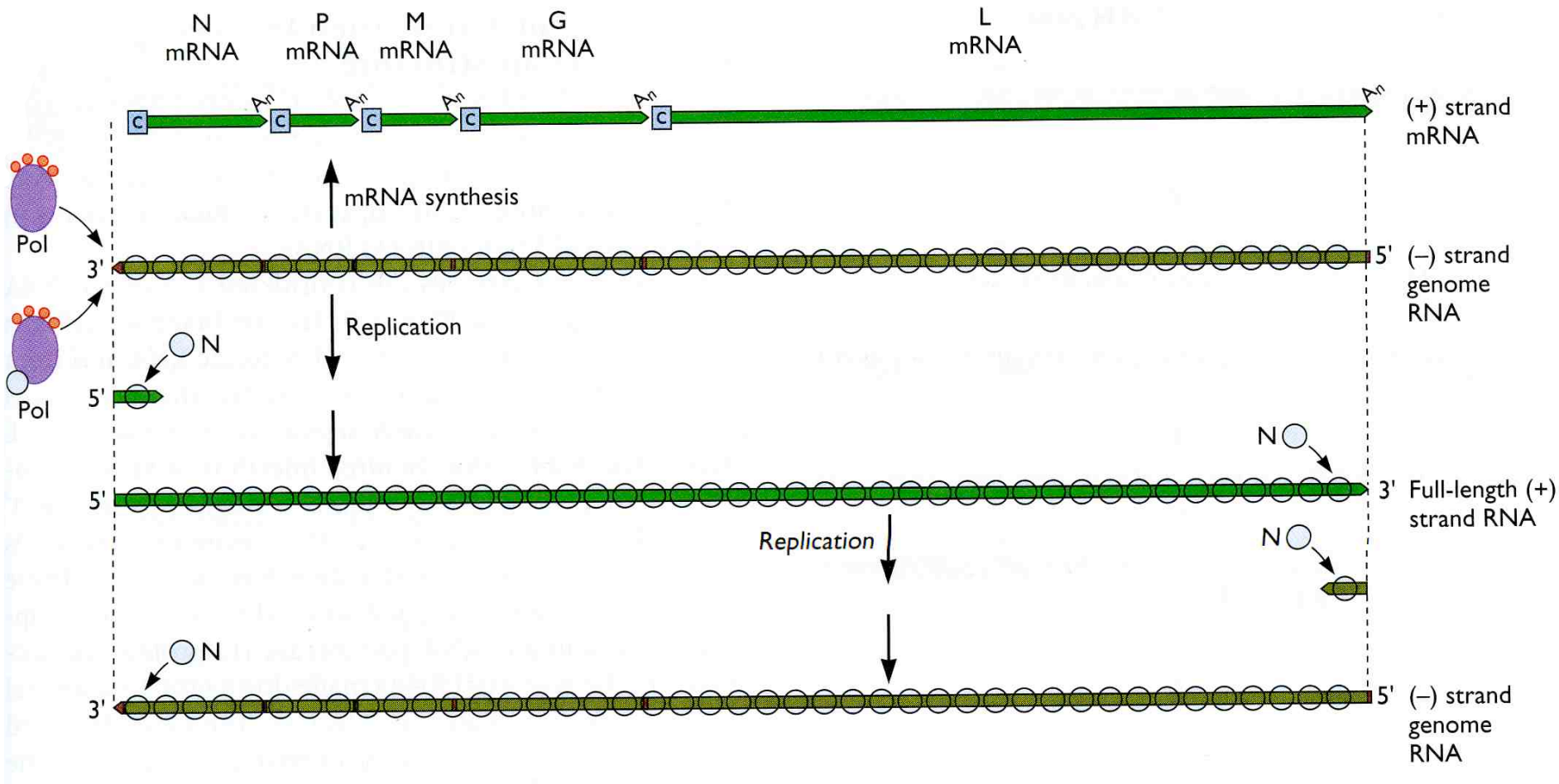
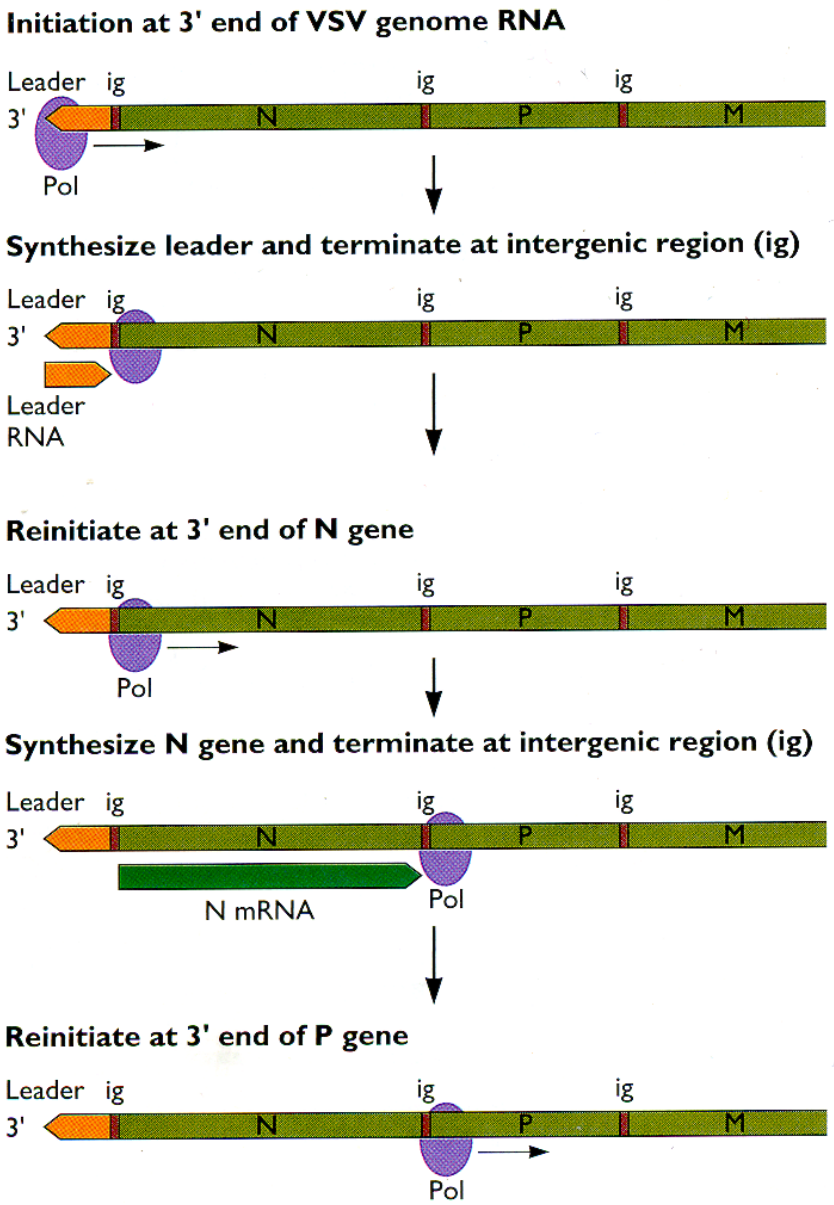
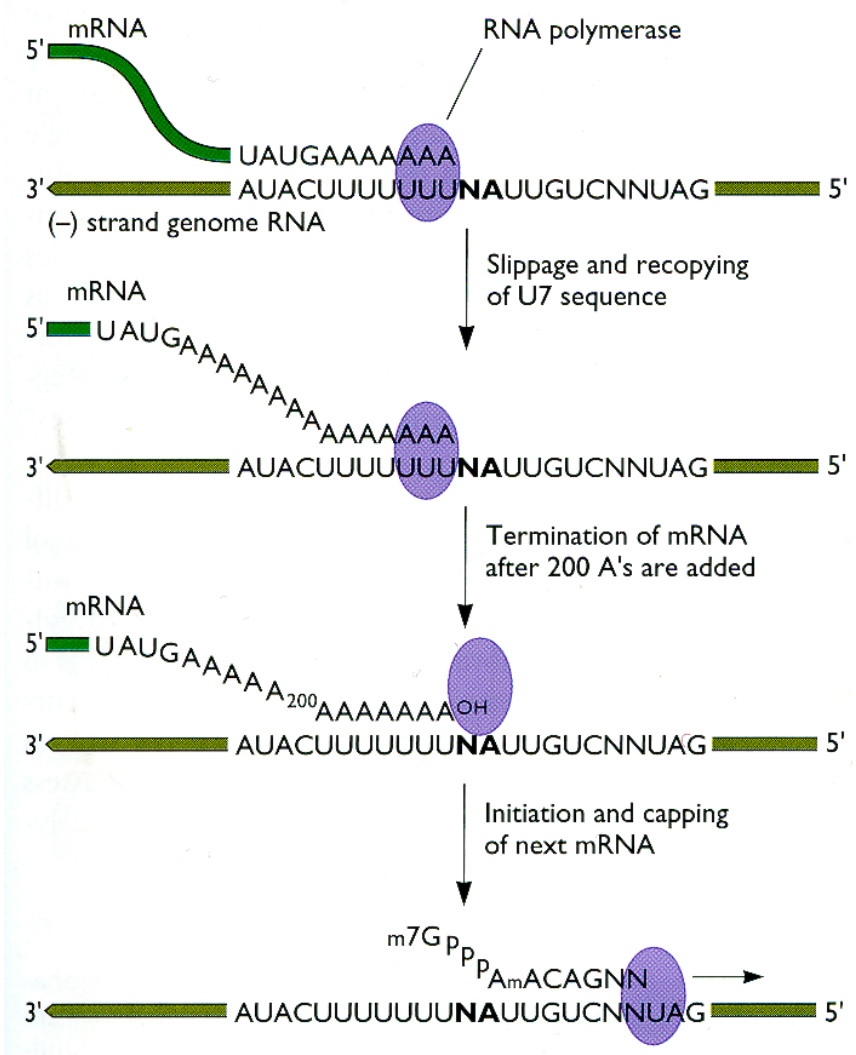


# mRNA synthesis and replication of the VSV genome

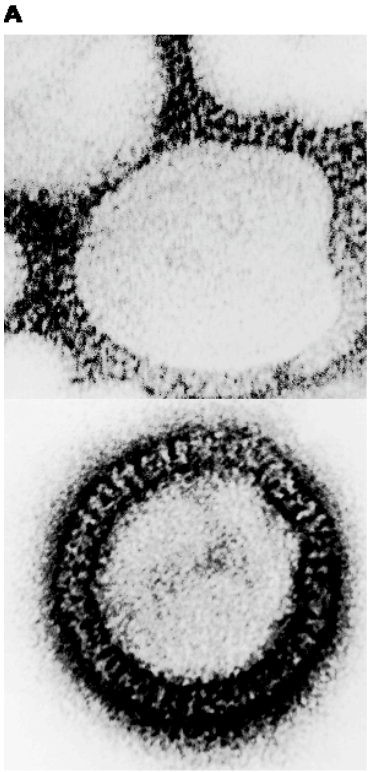


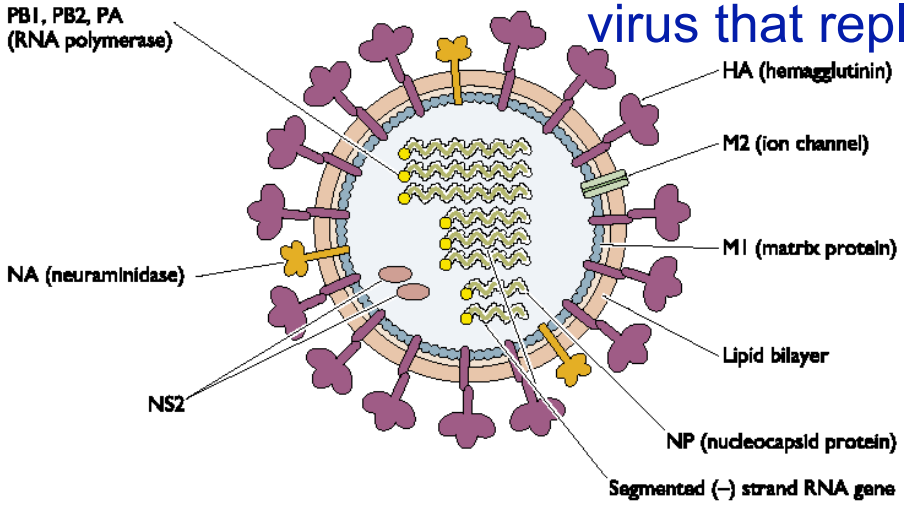
# VSV mRNA synthesis and function of RNA pol at an intergenic region

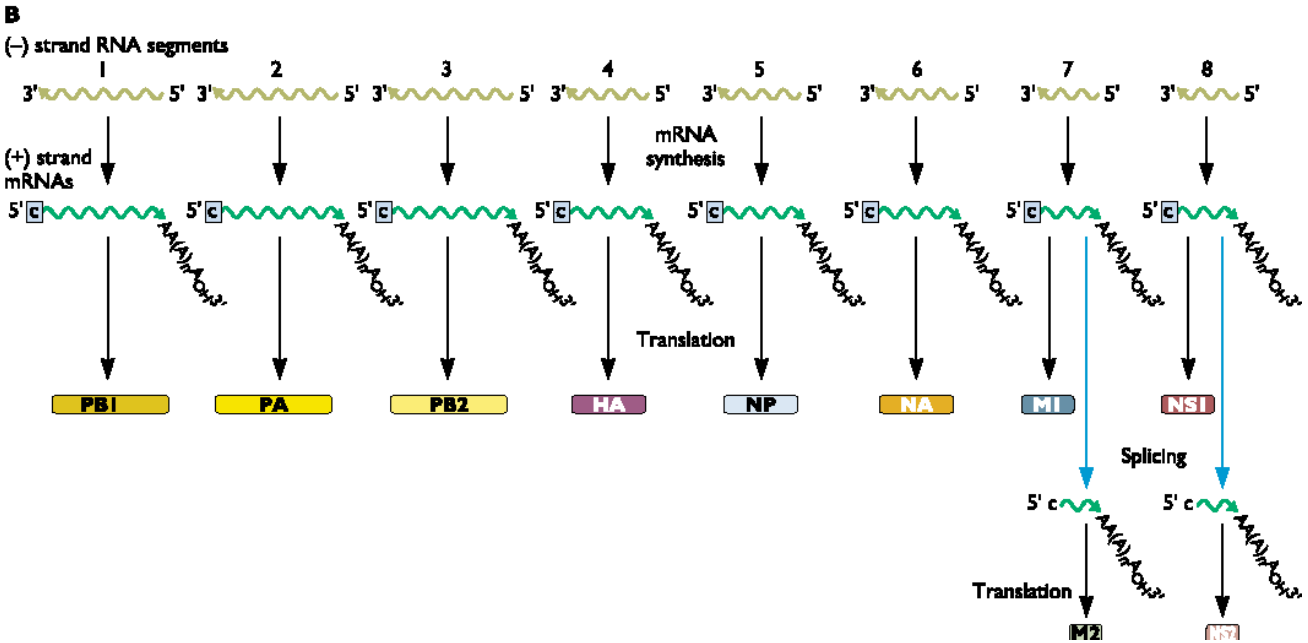


# The **Orthomyxovirus** Influenza A virus: an example of **Class V** virus that replicates in the nucleus



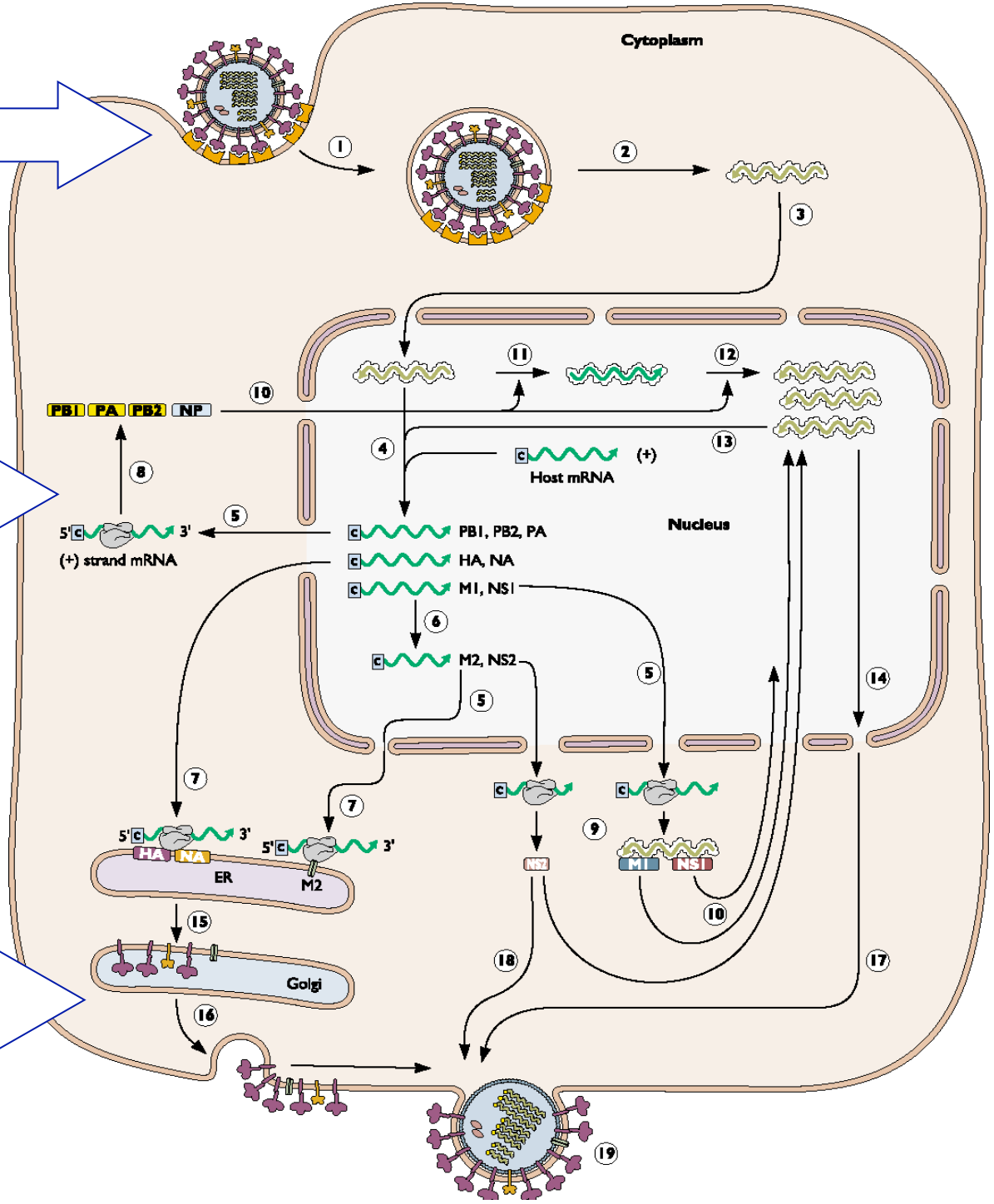



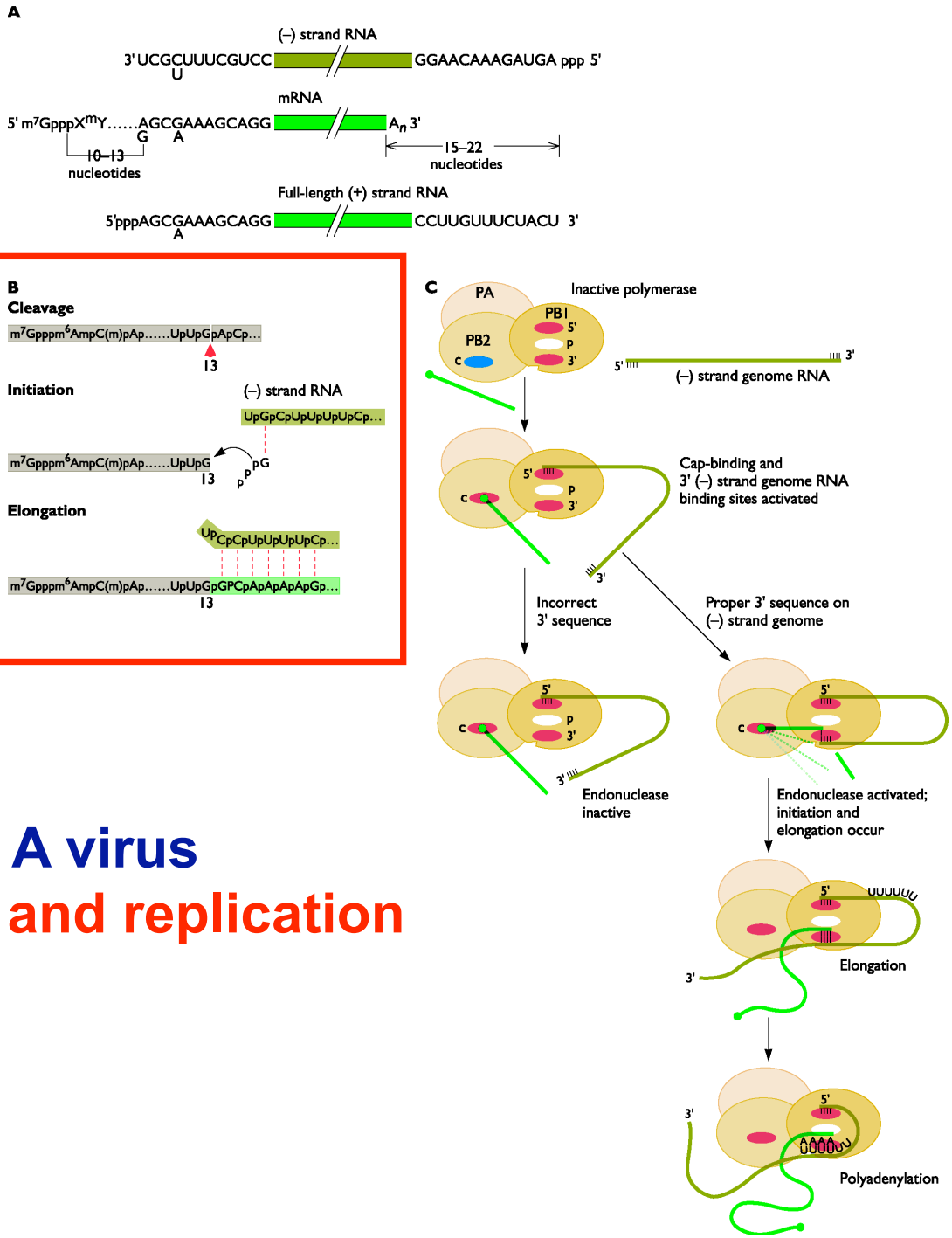
Attachment
Entry
Uncoating

Viral
Synthesis

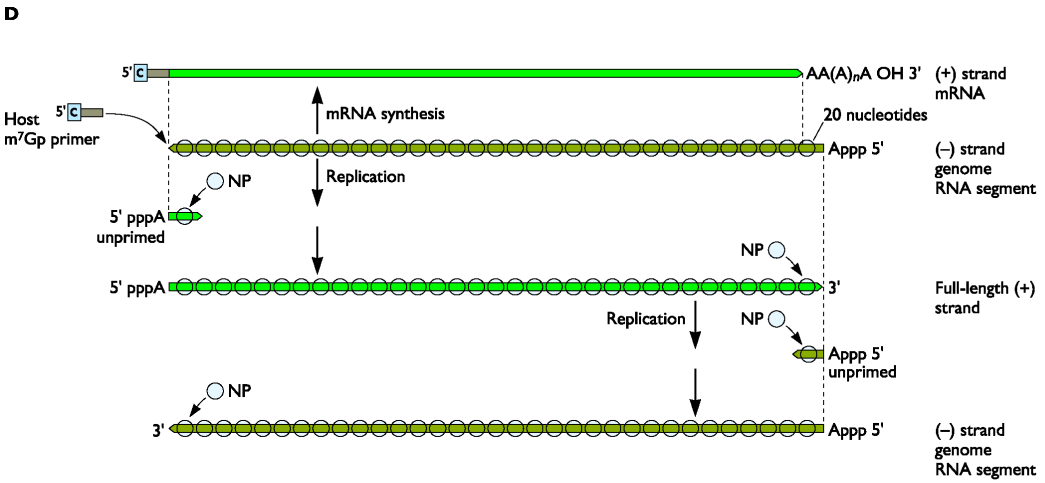
Assembly
Maturation
Exit

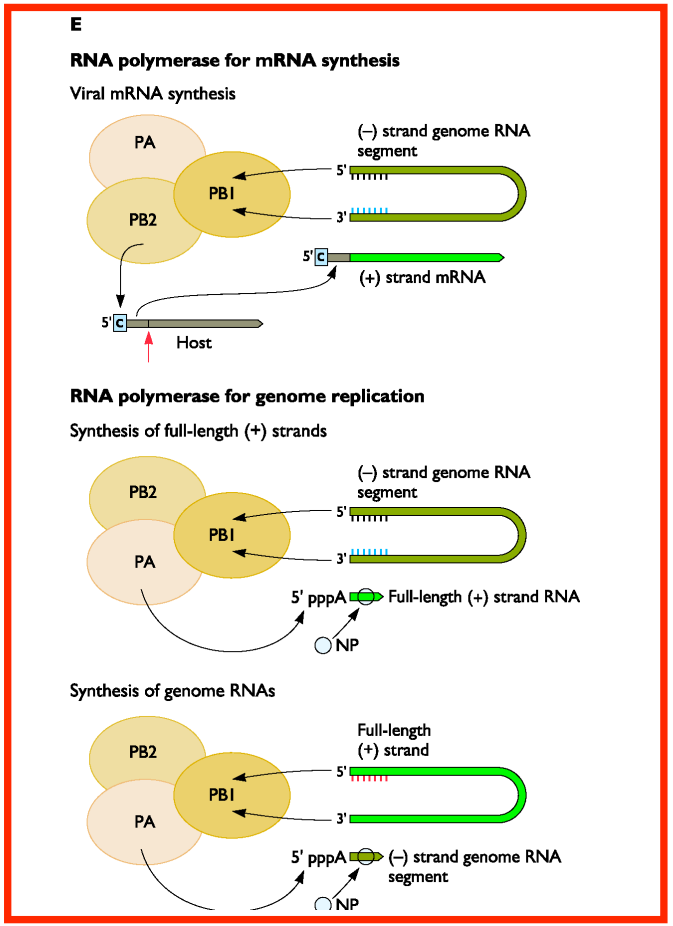


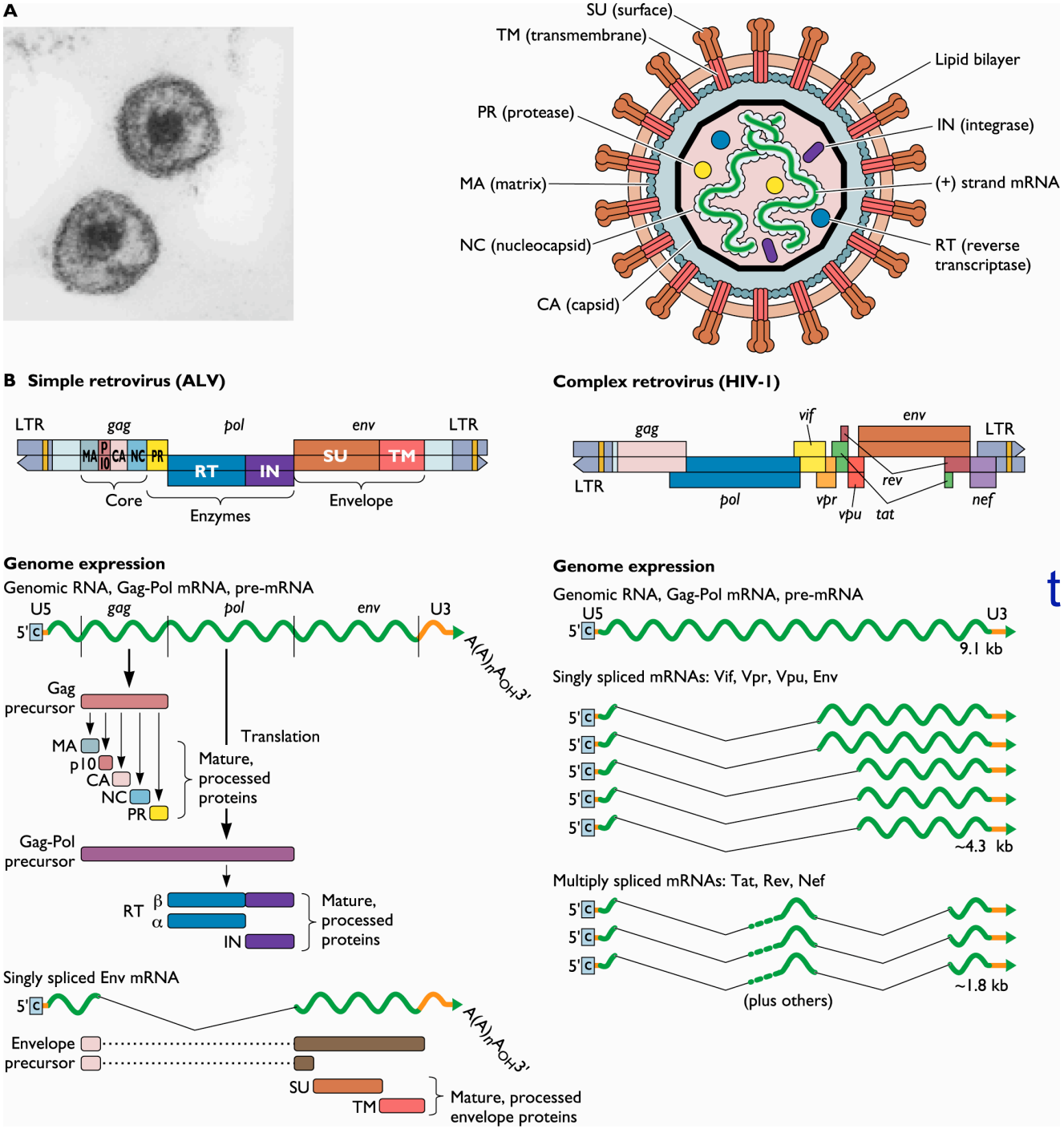
# Influenza A virus
## mRNA synthesis and replication



# Influenza A virus
## mRNA synthesis and replication



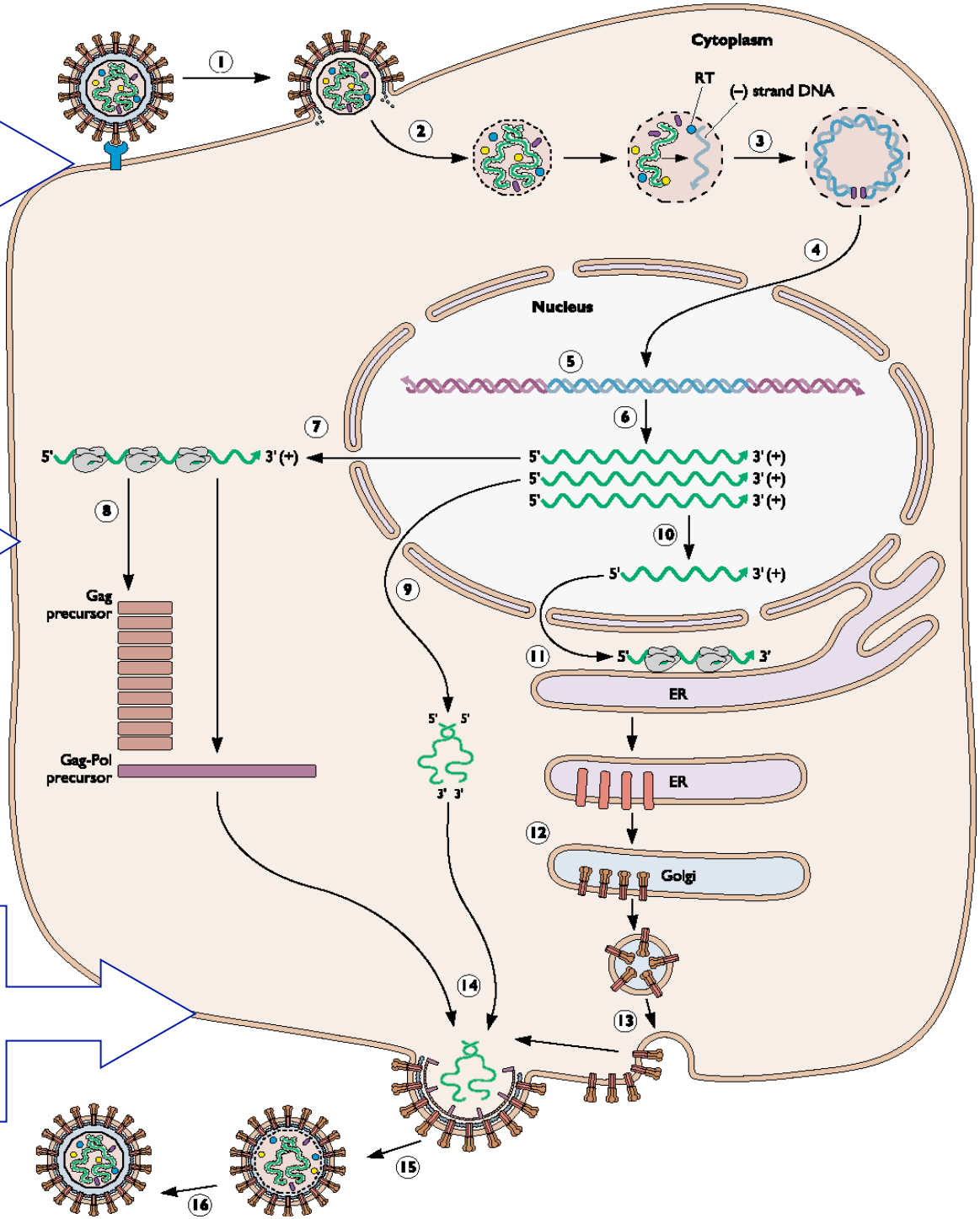



**Class VI** virus:
the **Retroviruses**

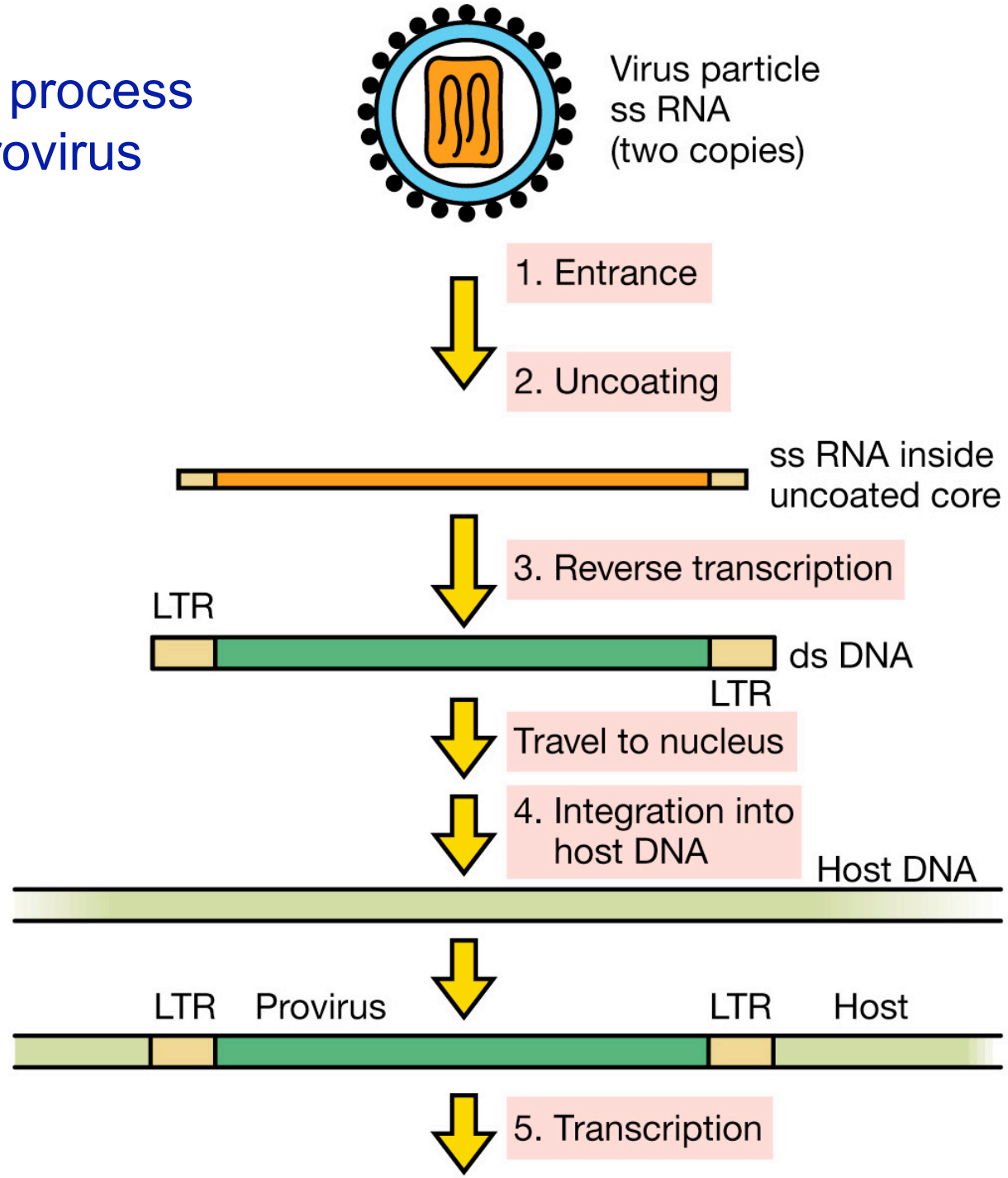
Attachment
Entry
Uncoating

Viral
Synthesis

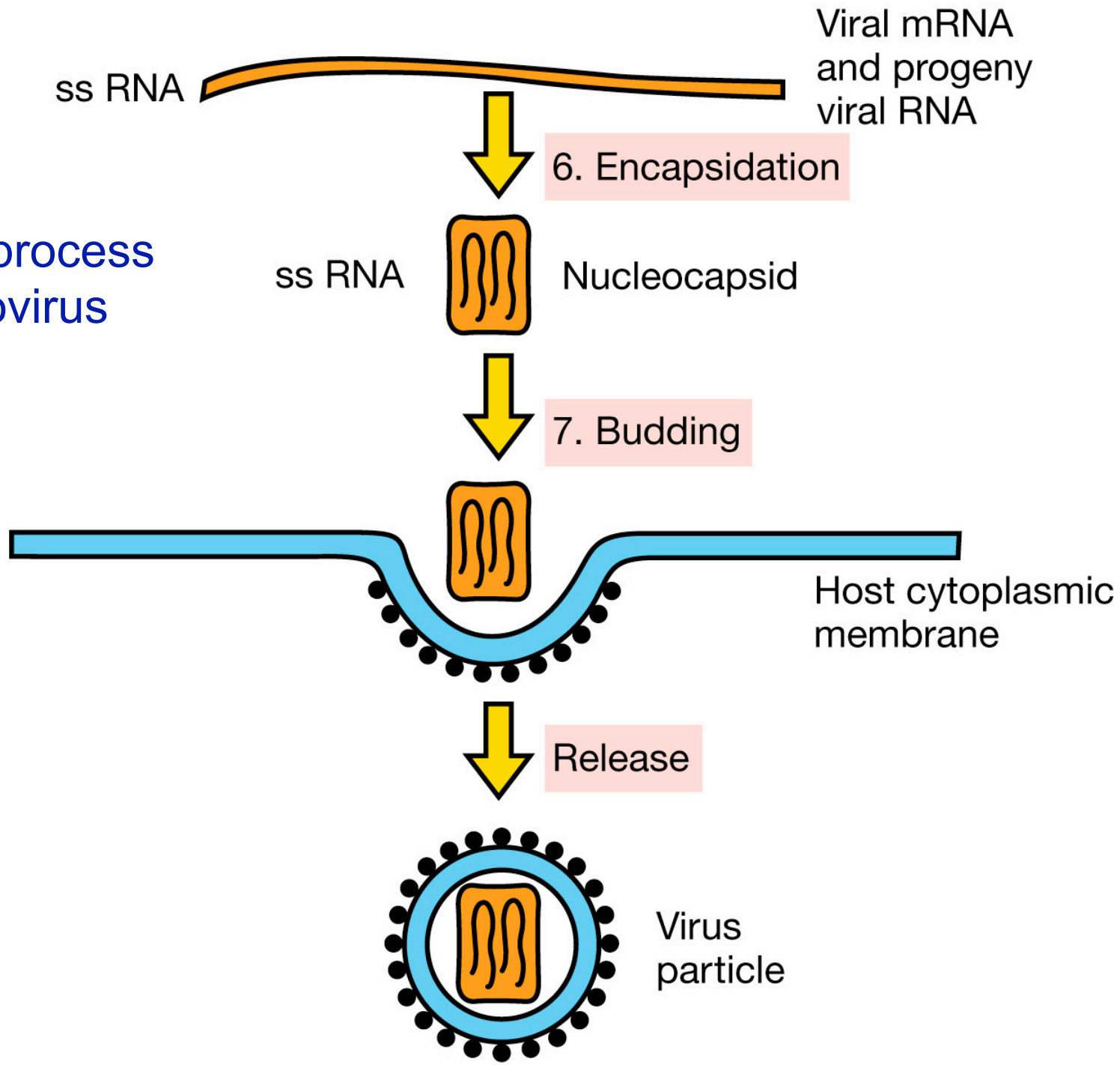
Assembly
Maturation
Exit



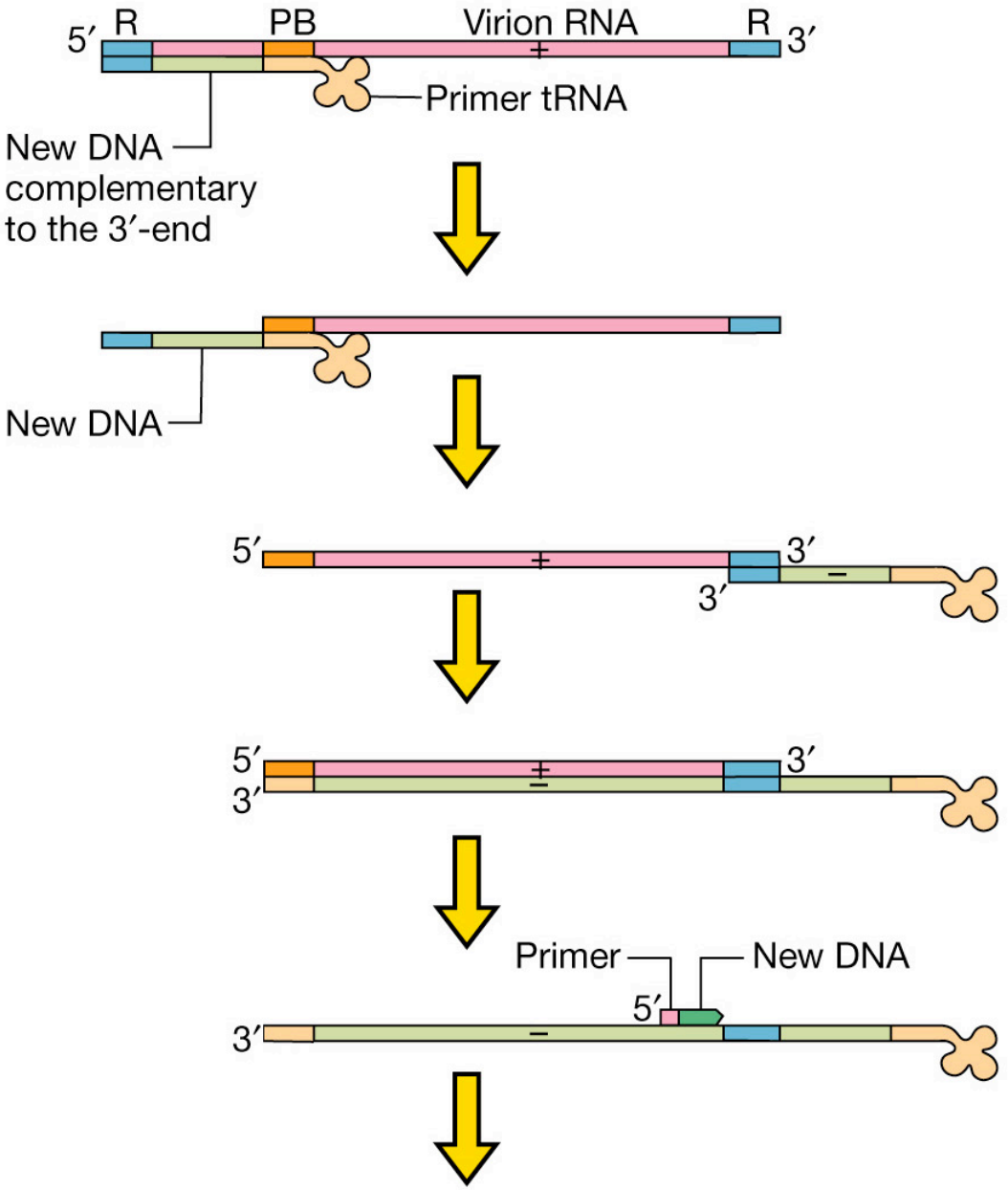
# Replication process of a Retrovirus



# Replication process of a Retrovirus



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



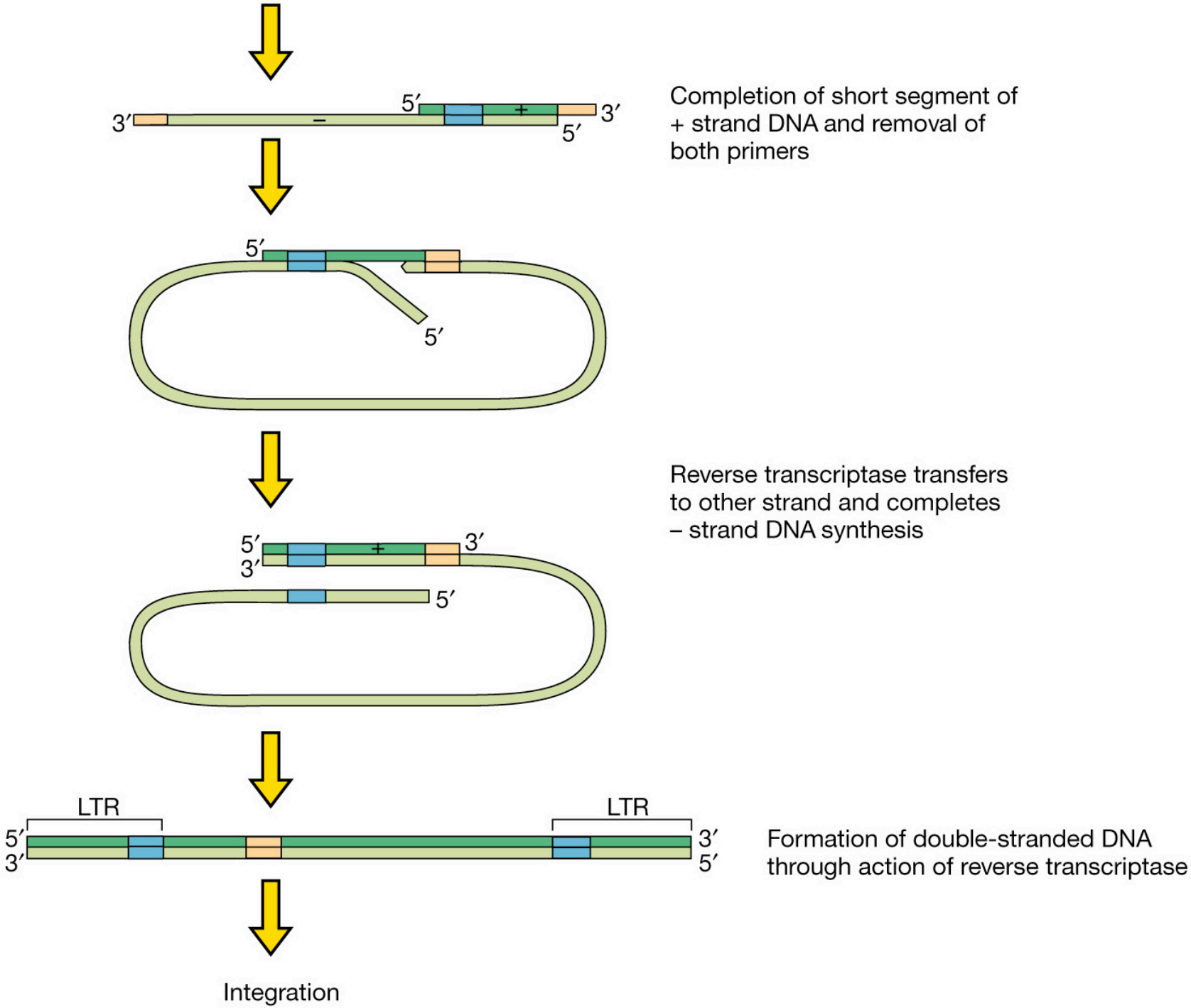

Reverse transcription into DNA of 100 or so nucleotides at the 5′-terminus by reverse transcriptase

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

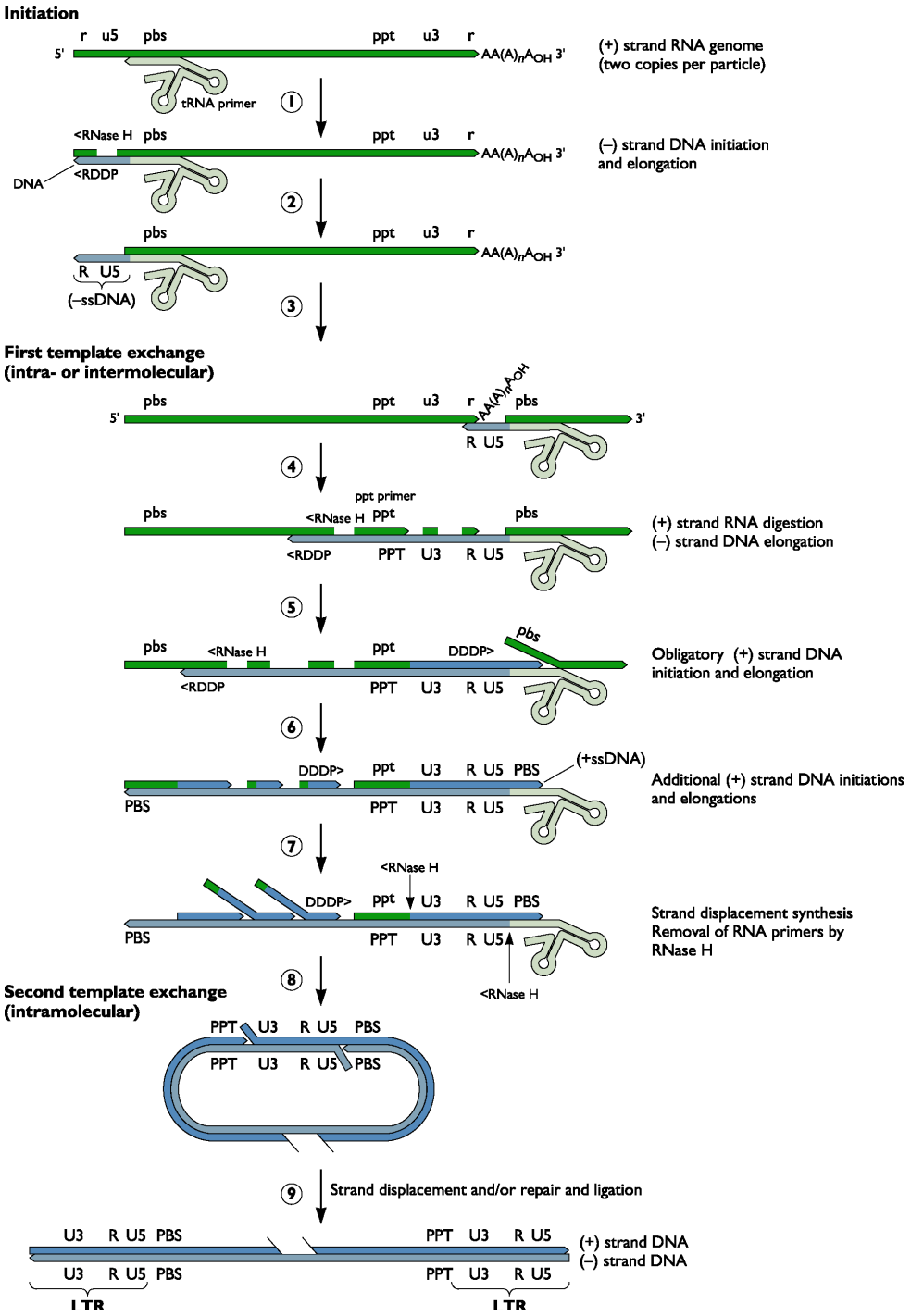



Completion of short segment of + strand DNA and removal of both primers

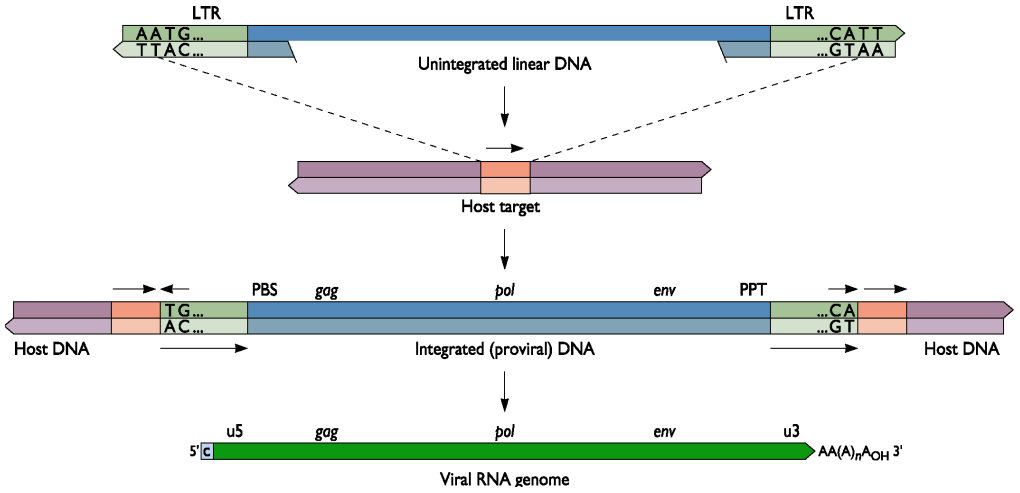
Reverse transcriptase transfers to other strand and completes – strand DNA synthesis

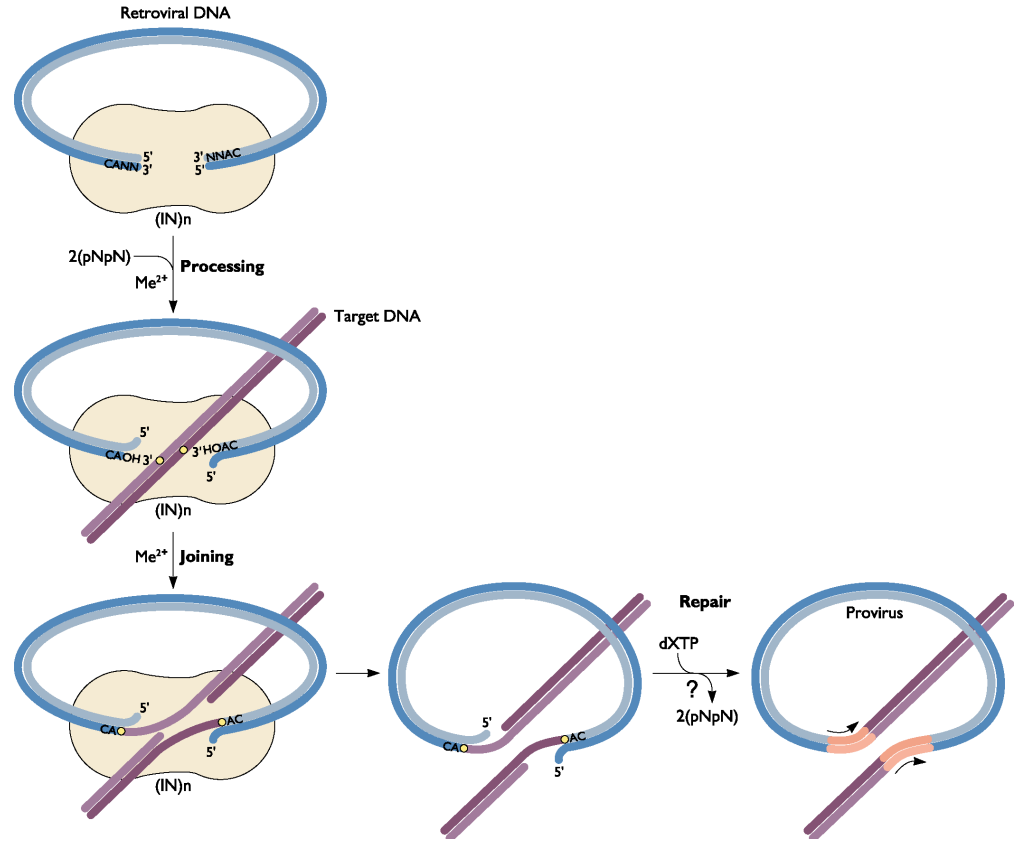
Formation of double-stranded DNA through action of reverse transcriptase

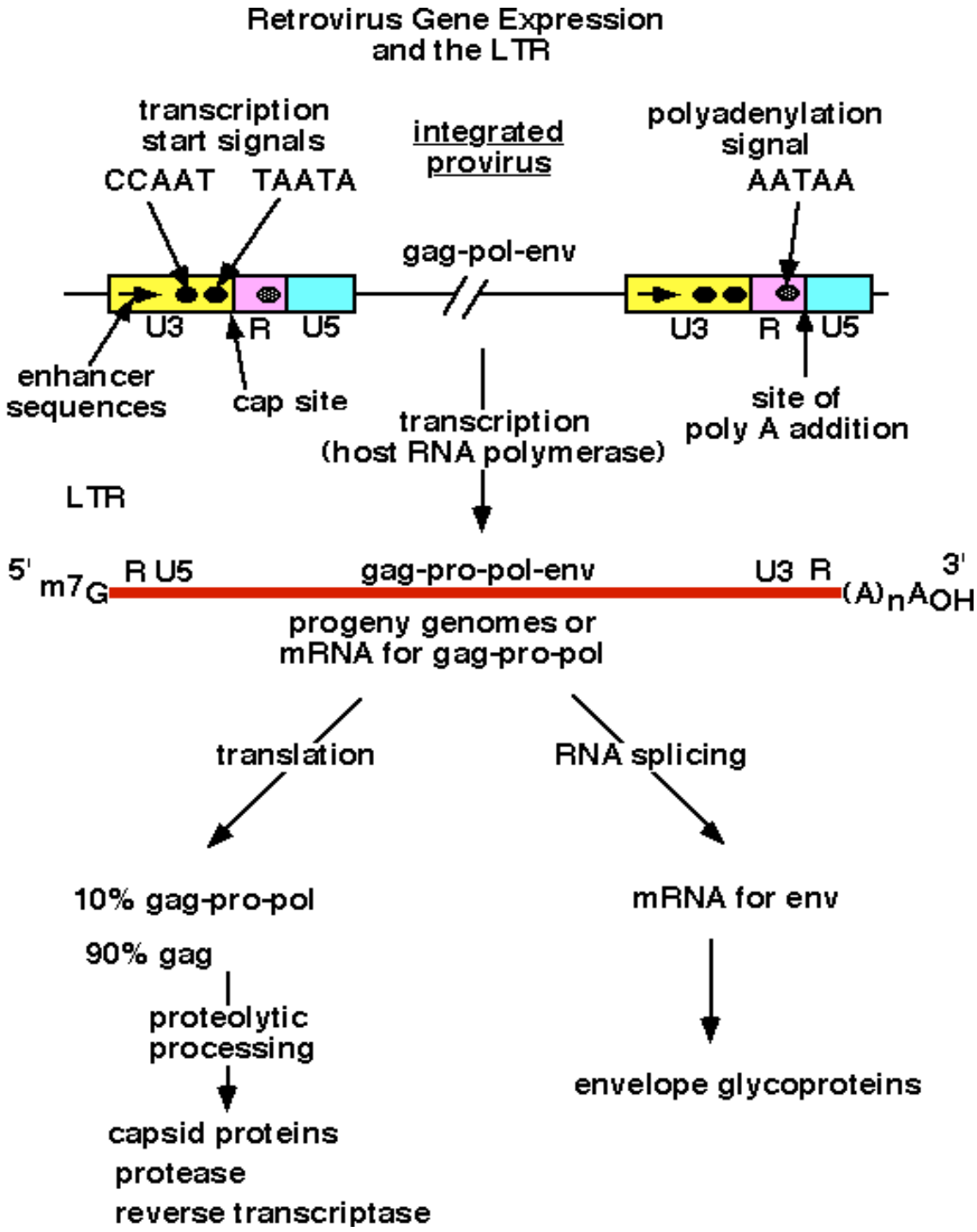
# Reverse transcription process

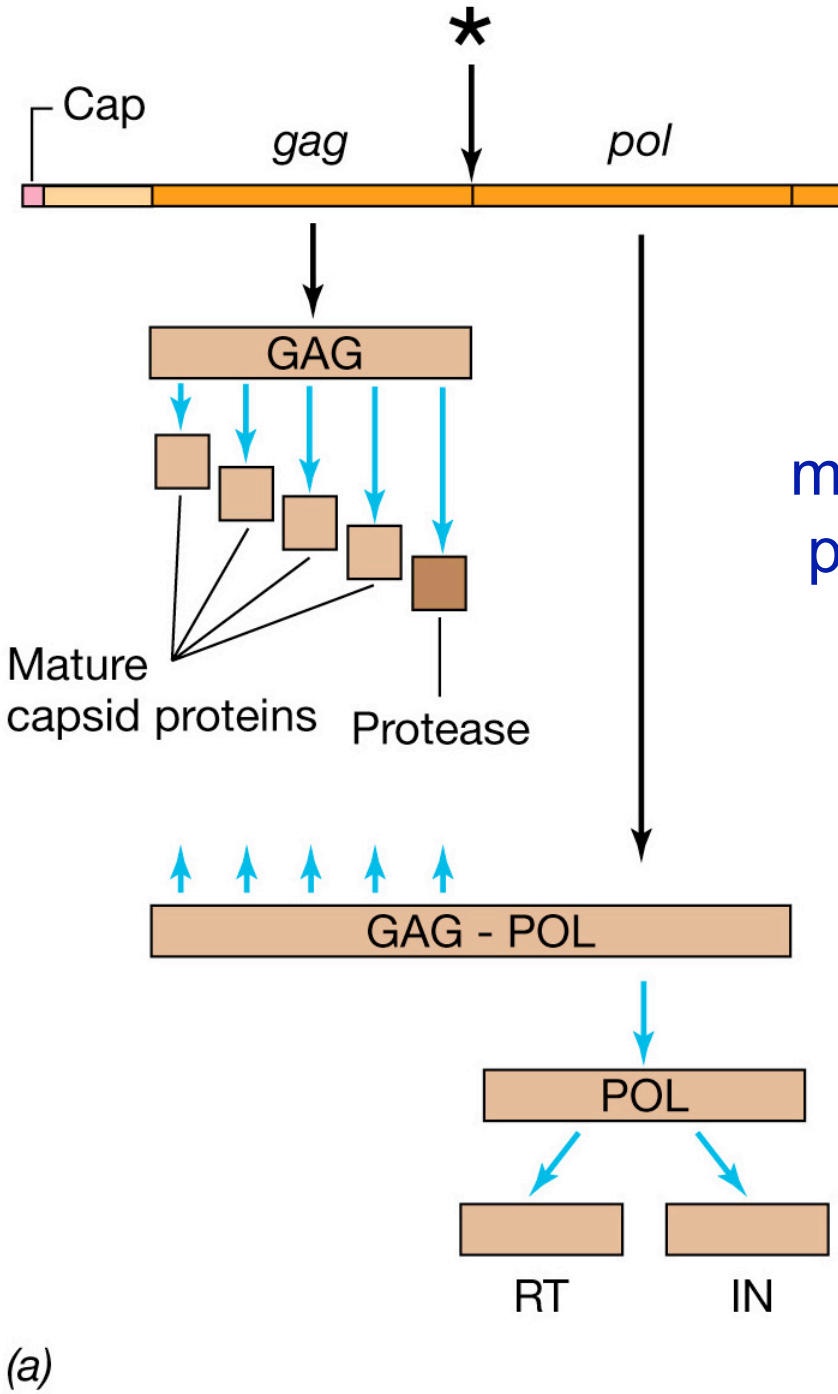


# Retroviral DNA integration

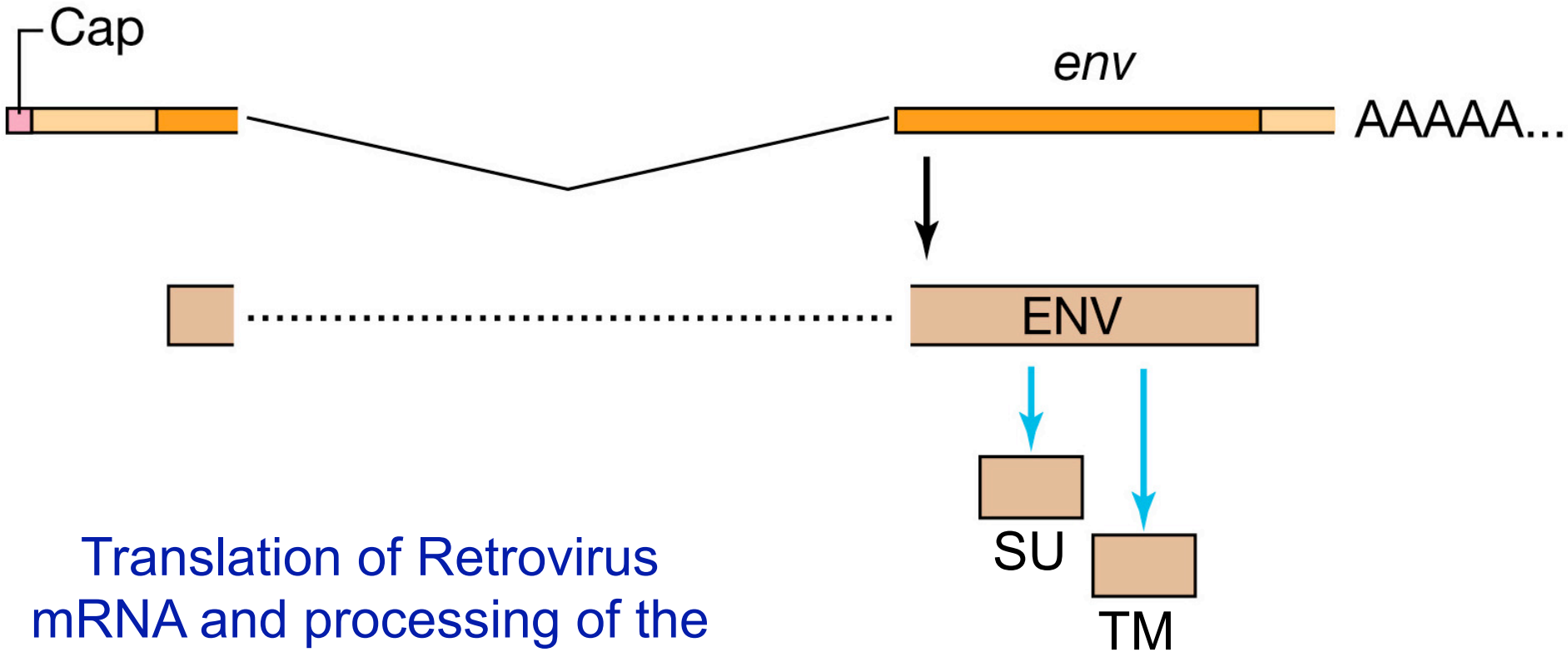



Retrovirus Gene Expression
and the LTR
transcription
start signals
CCAAT
TAATA
integrated
provirus
polyadenylation
signal
AATAA
gag-pol-env
U3
R
U5
U3
R
U5
enhancer
sequences
cap site
transcription
(host RNA polymerase)
site of
poly A addition
LTR
5'
m7G
R U5
gag-pro-pol-env
U3 R
(A)nAOH
3'
progeny genomes or
mRNA for gag-pro-pol
translation
RNA splicing
10% gag-pro-pol
90% gag
proteolytic
processing
capsid proteins
protease
reverse transcriptase
mRNA for env
envelope glycoproteins




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



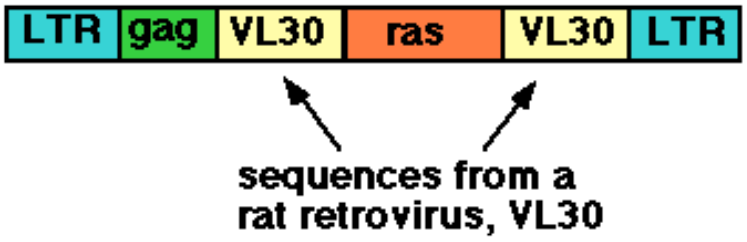

Translation of Retrovirus mRNA and processing of the proteins: the ENV proteins

## Most Transforming Retrovirus are Defective and Cannot Replicate without Helper Virus

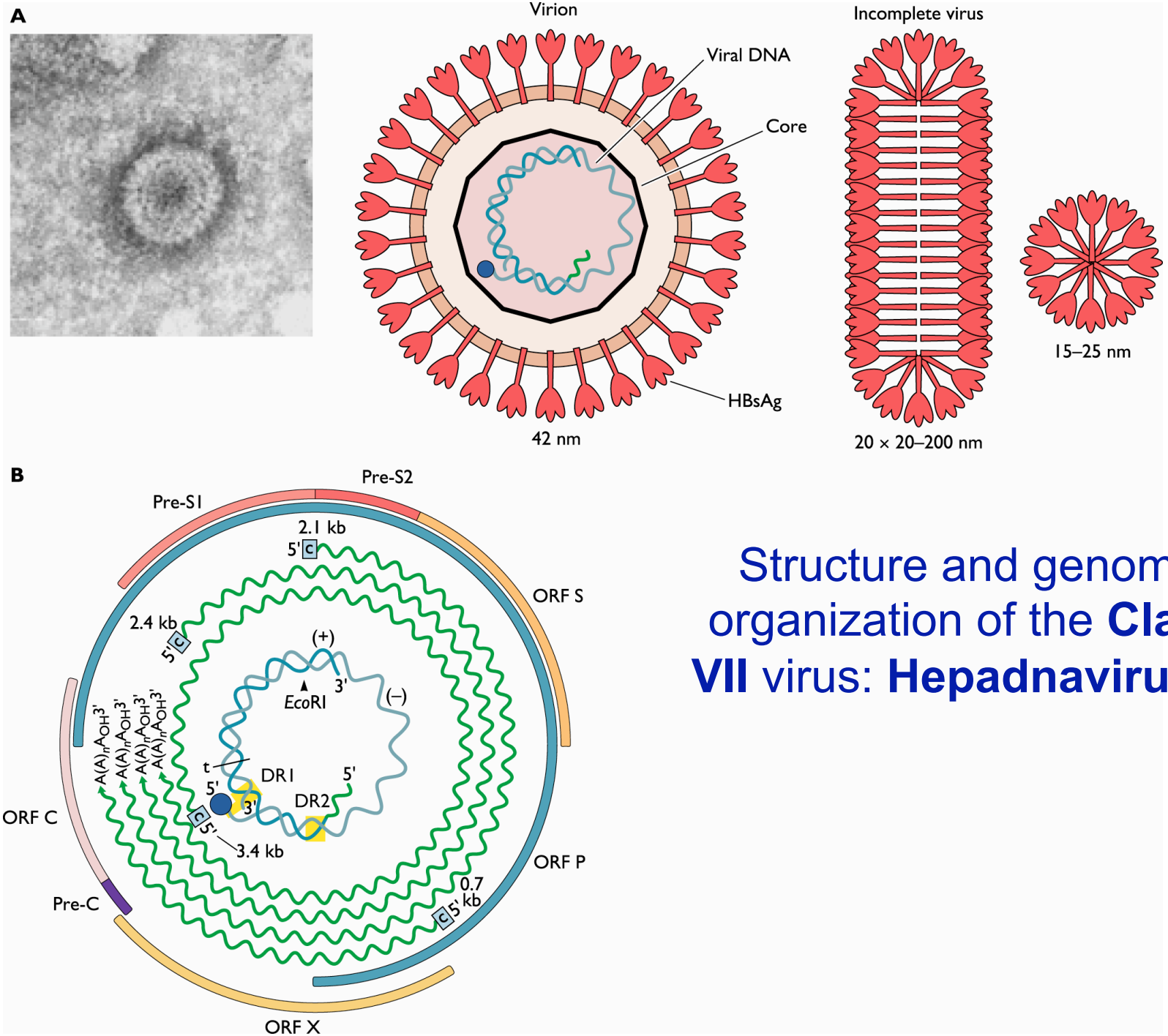
Rous sarcoma virus
(a non-defective, transforming avian virus)


Abelson murine
Leukemia virus
(defective)

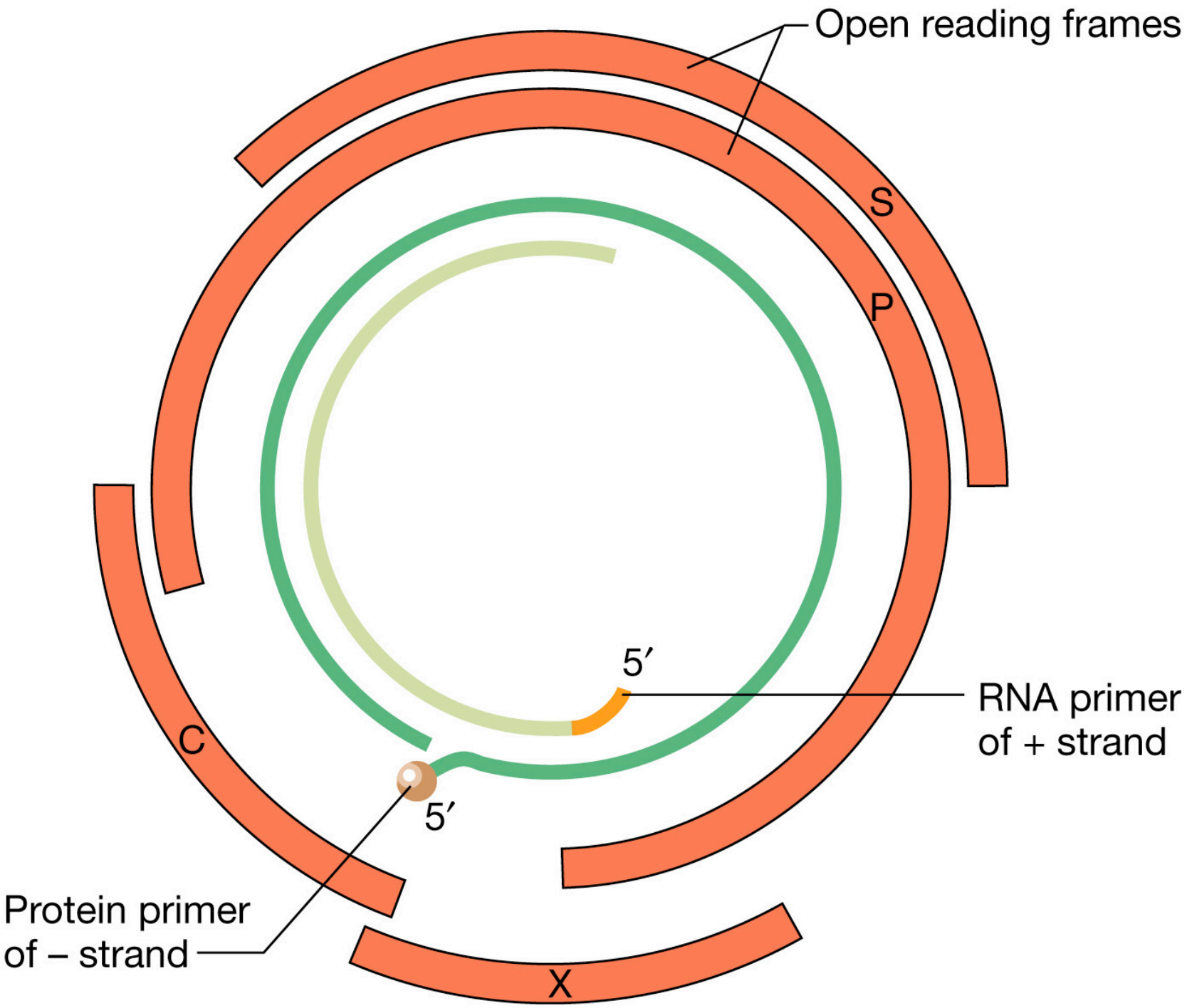

Harvey sarcoma virus
(a defective murine virus)




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

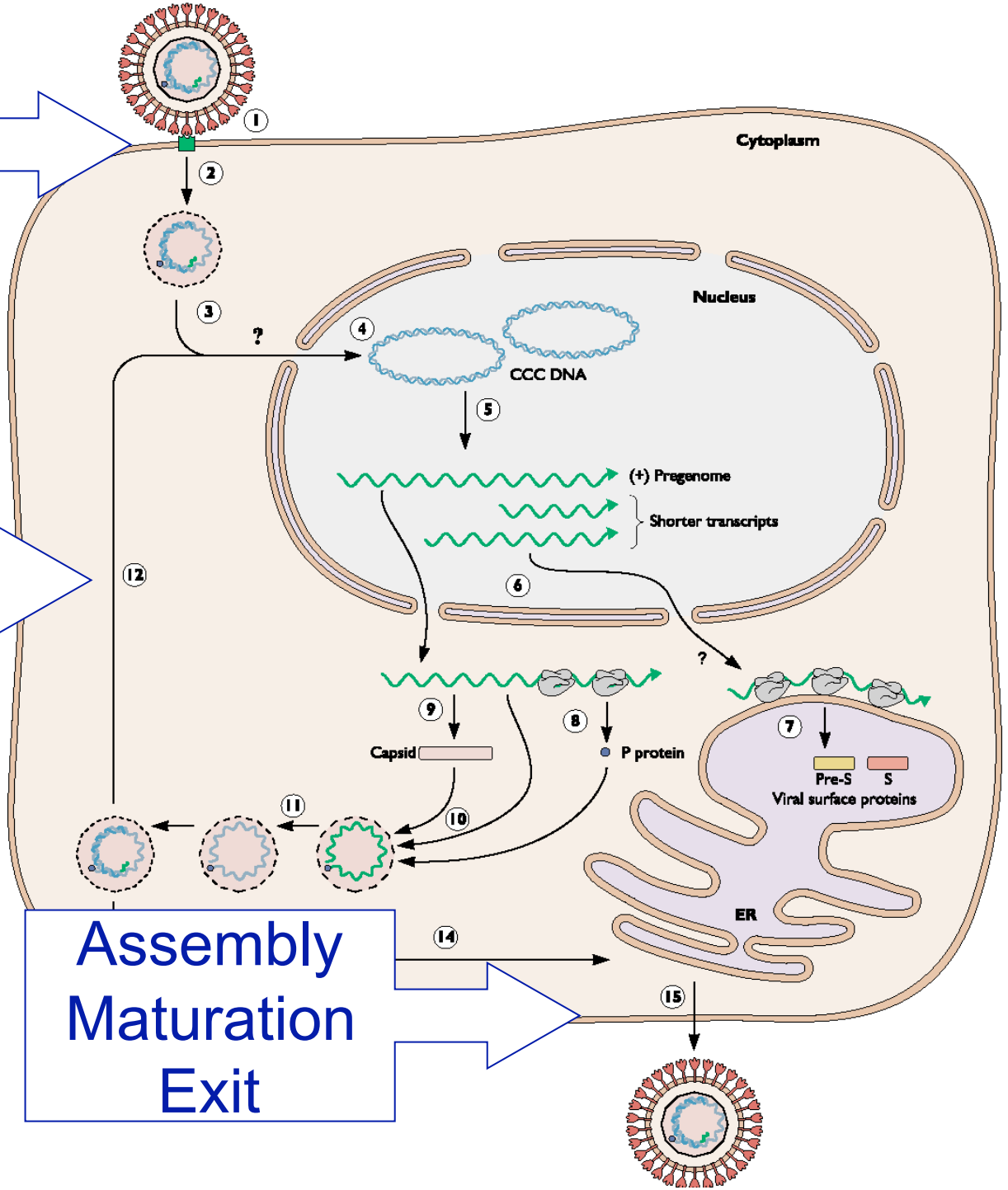



# Structure and genome organization of the **Class VII** virus: **Hepadnaviruses**


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

Attachment
Entry
Uncoating

Viral
Synthesis

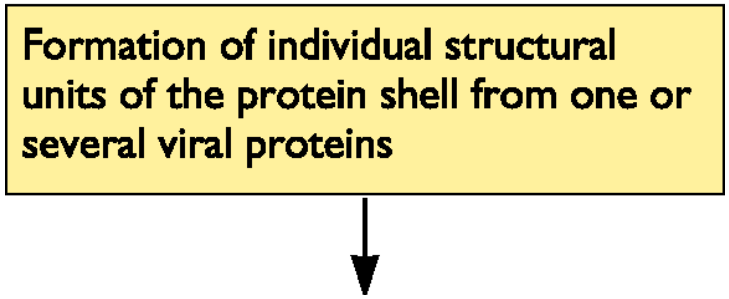


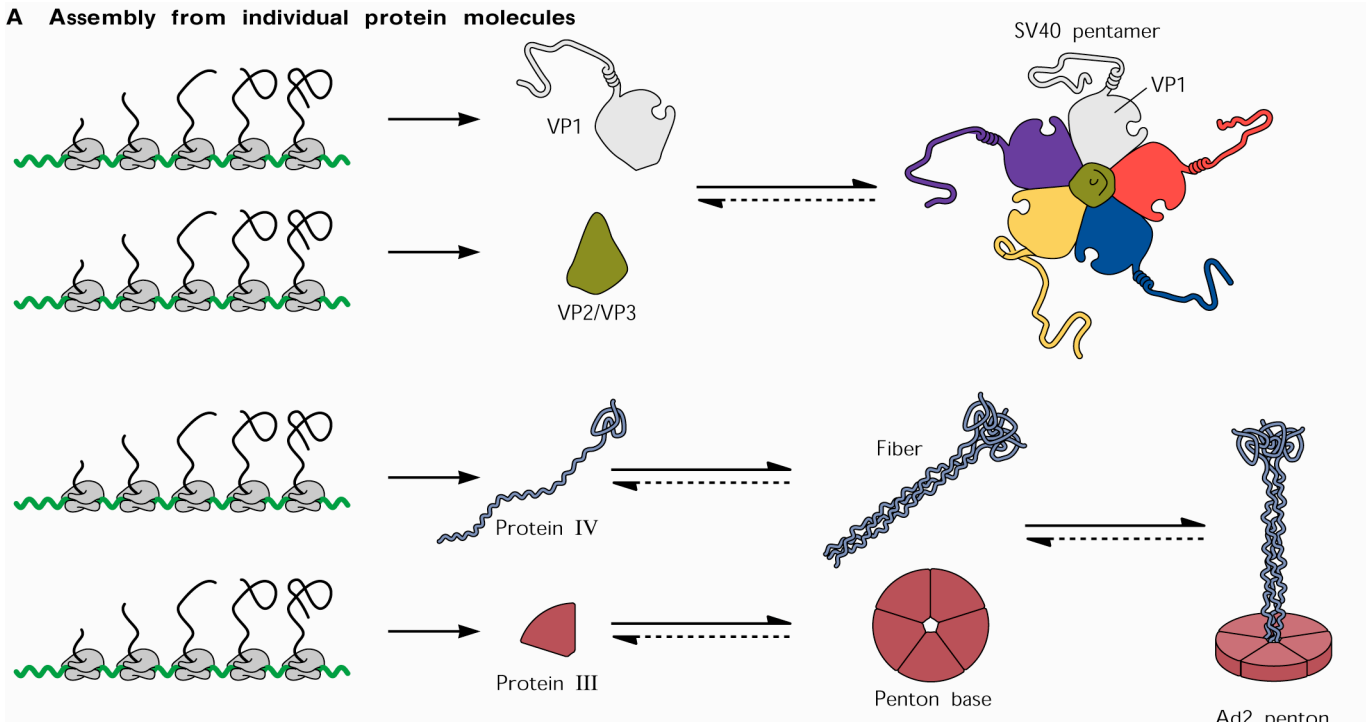

Assembly
Maturation
Exit

# Viral replication

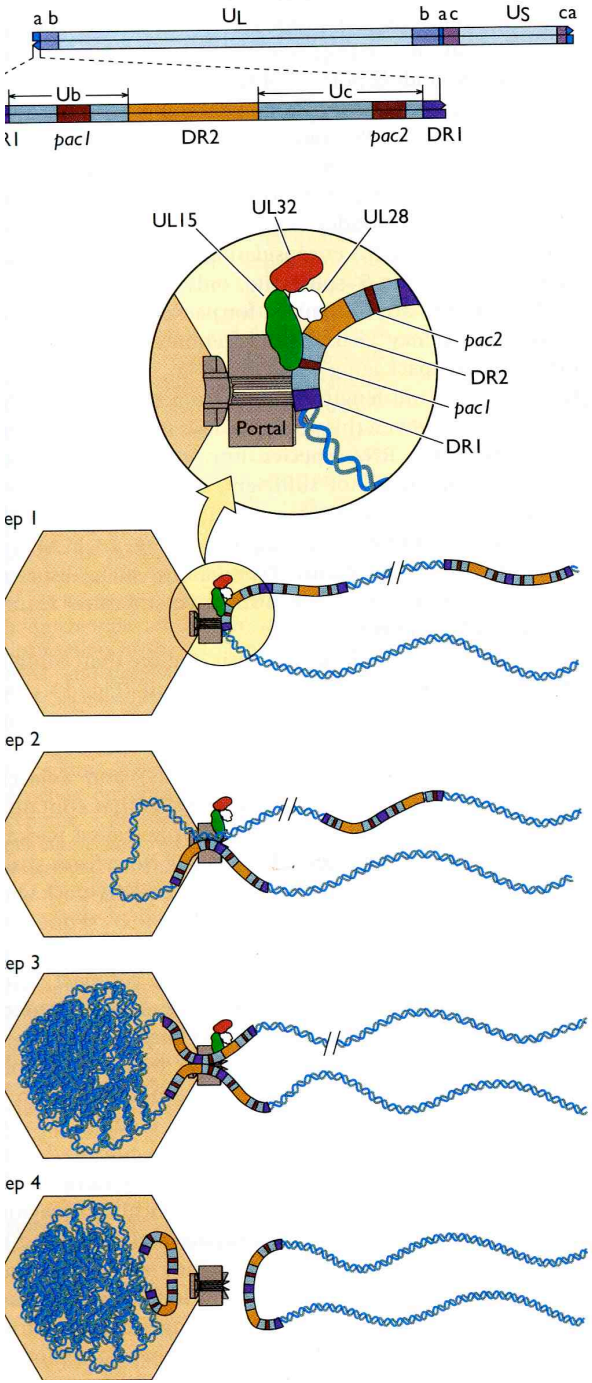
## assembly, exit and maturation of progeny virions

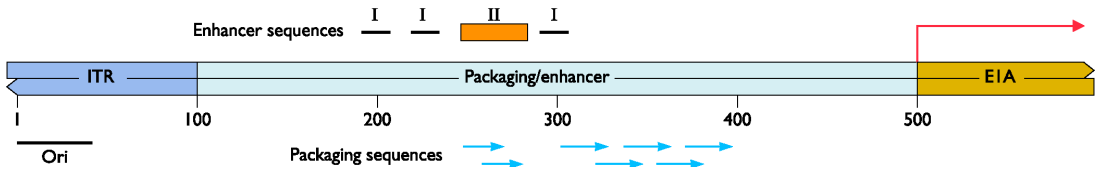
# Hypothetical pathway of virion assembly and release



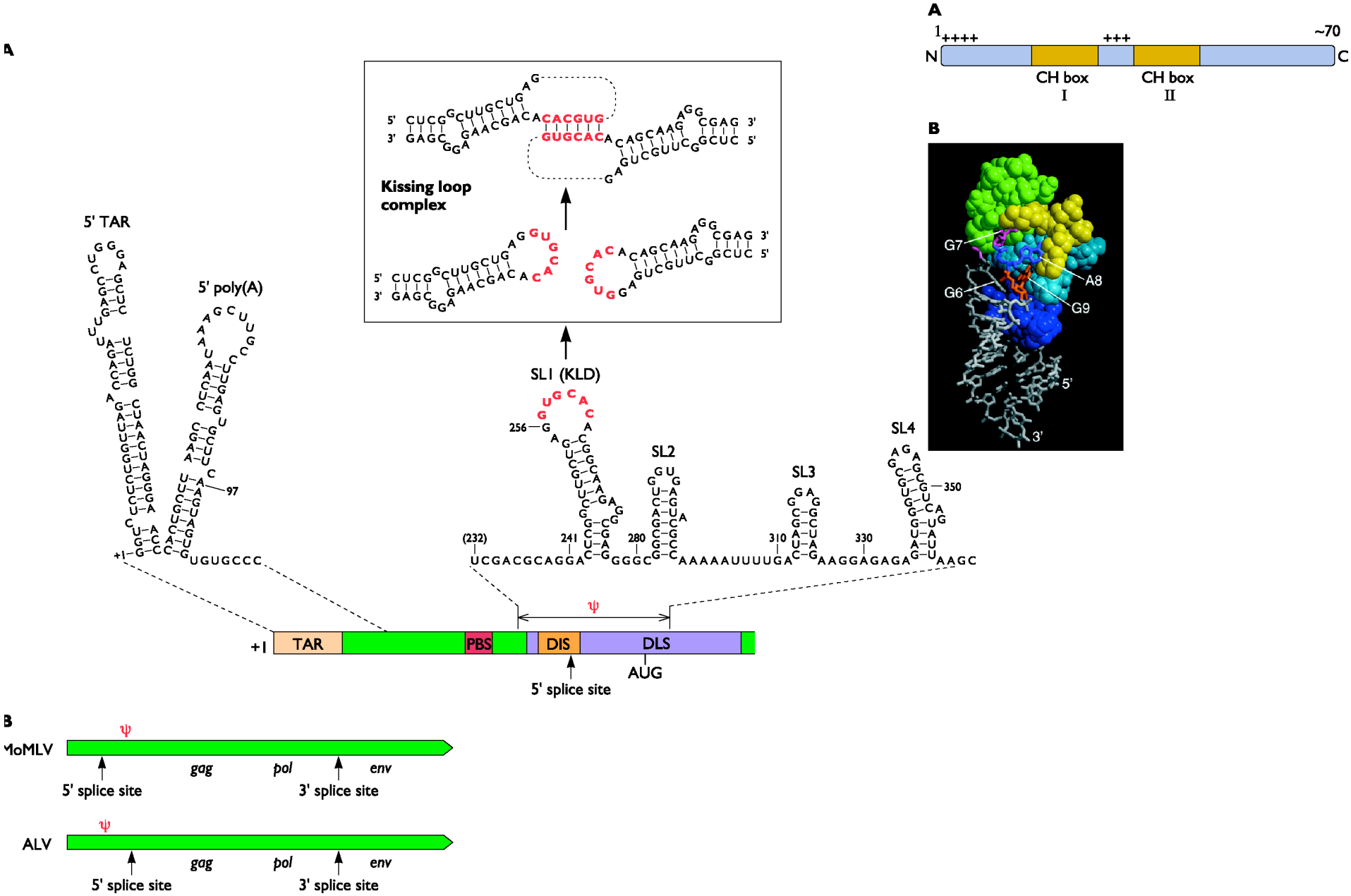

A Assembly from individual protein molecules
SV40 pentamer
VP1
VP1
VP2/VP3
Fiber
Protein IV
Protein III
Penton base
Ad2 penton

# Recognition and packaging of the nucleid acid genome

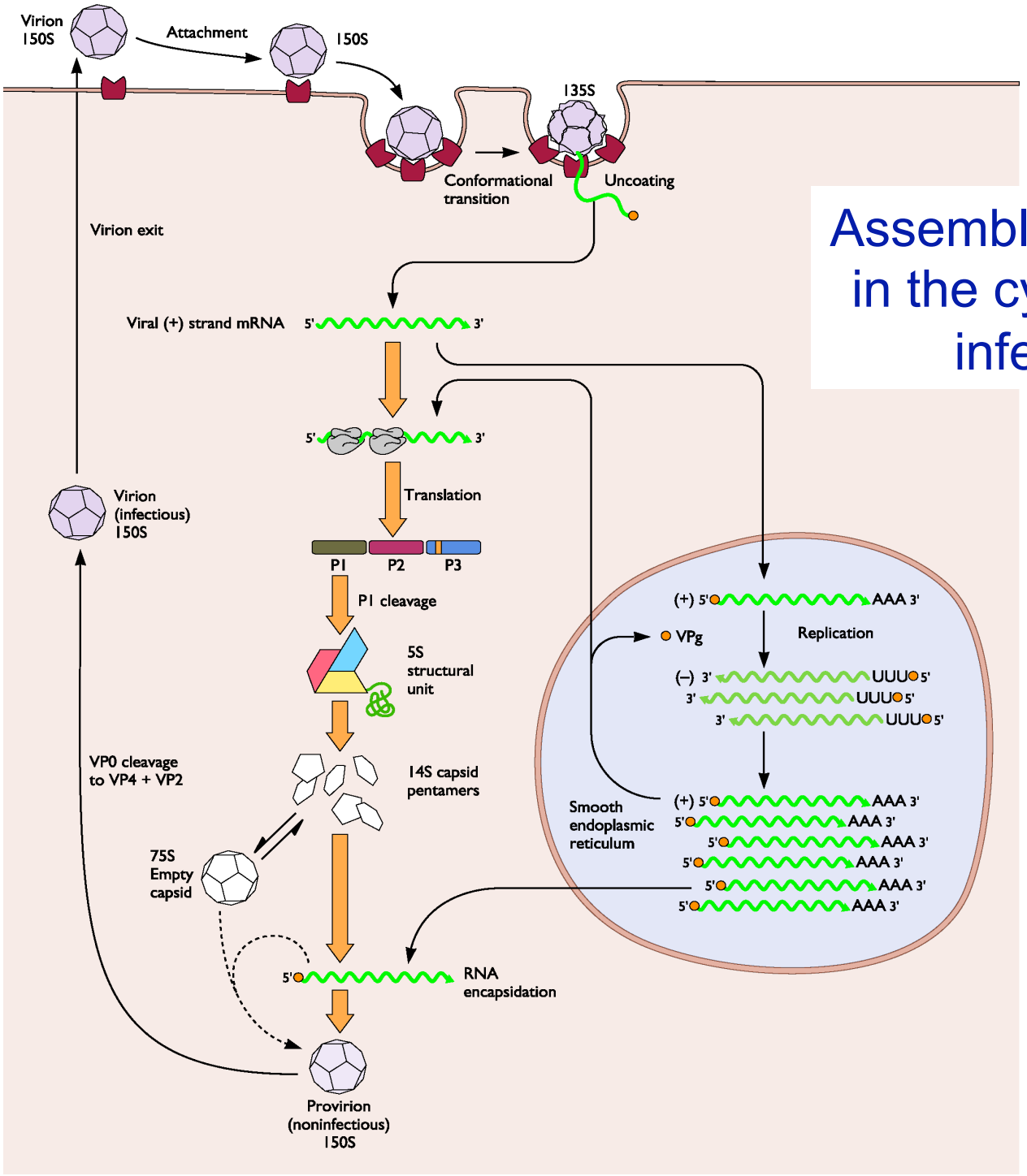


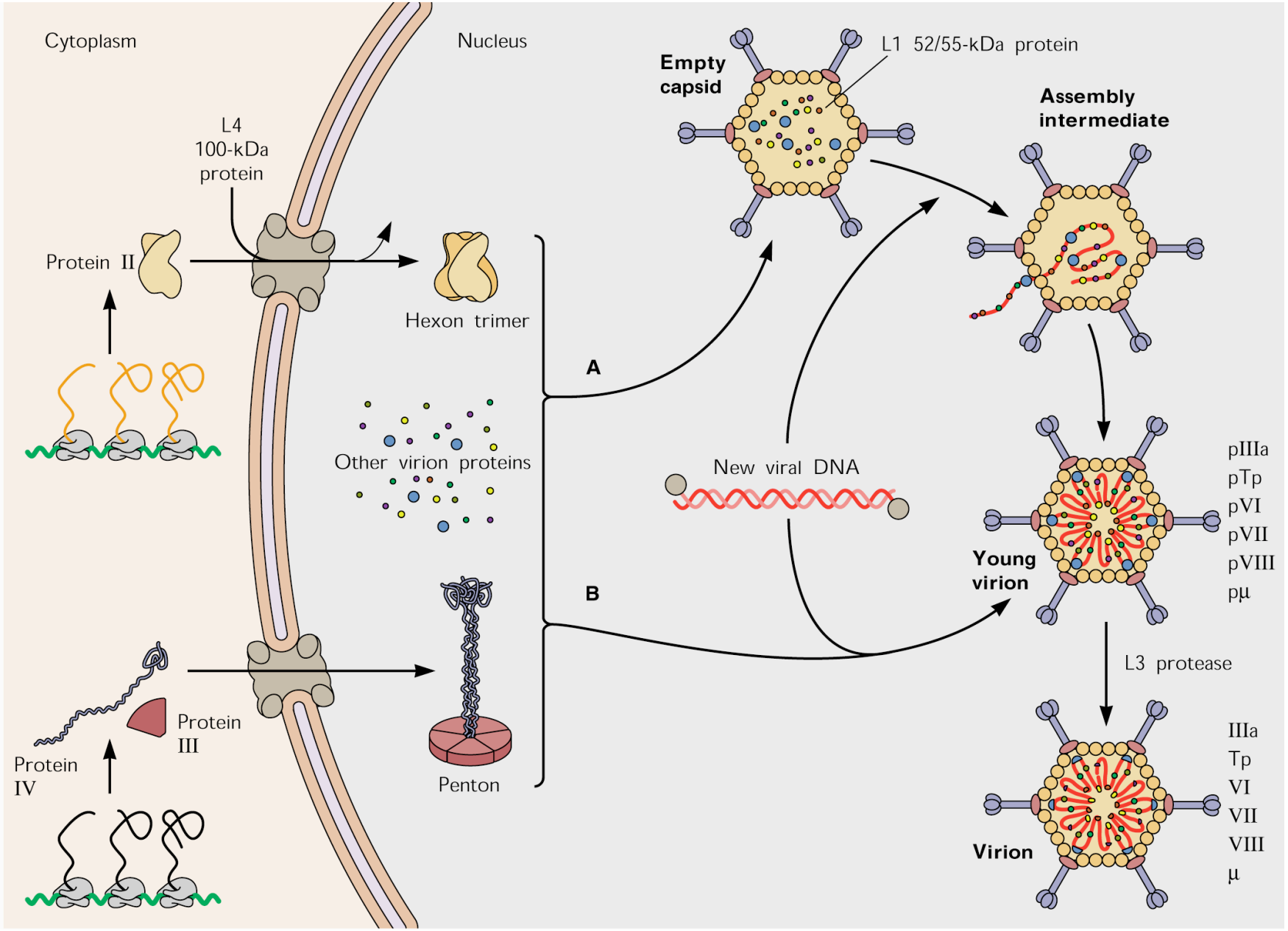
# Recognition and packaging of the nucleid acid genome



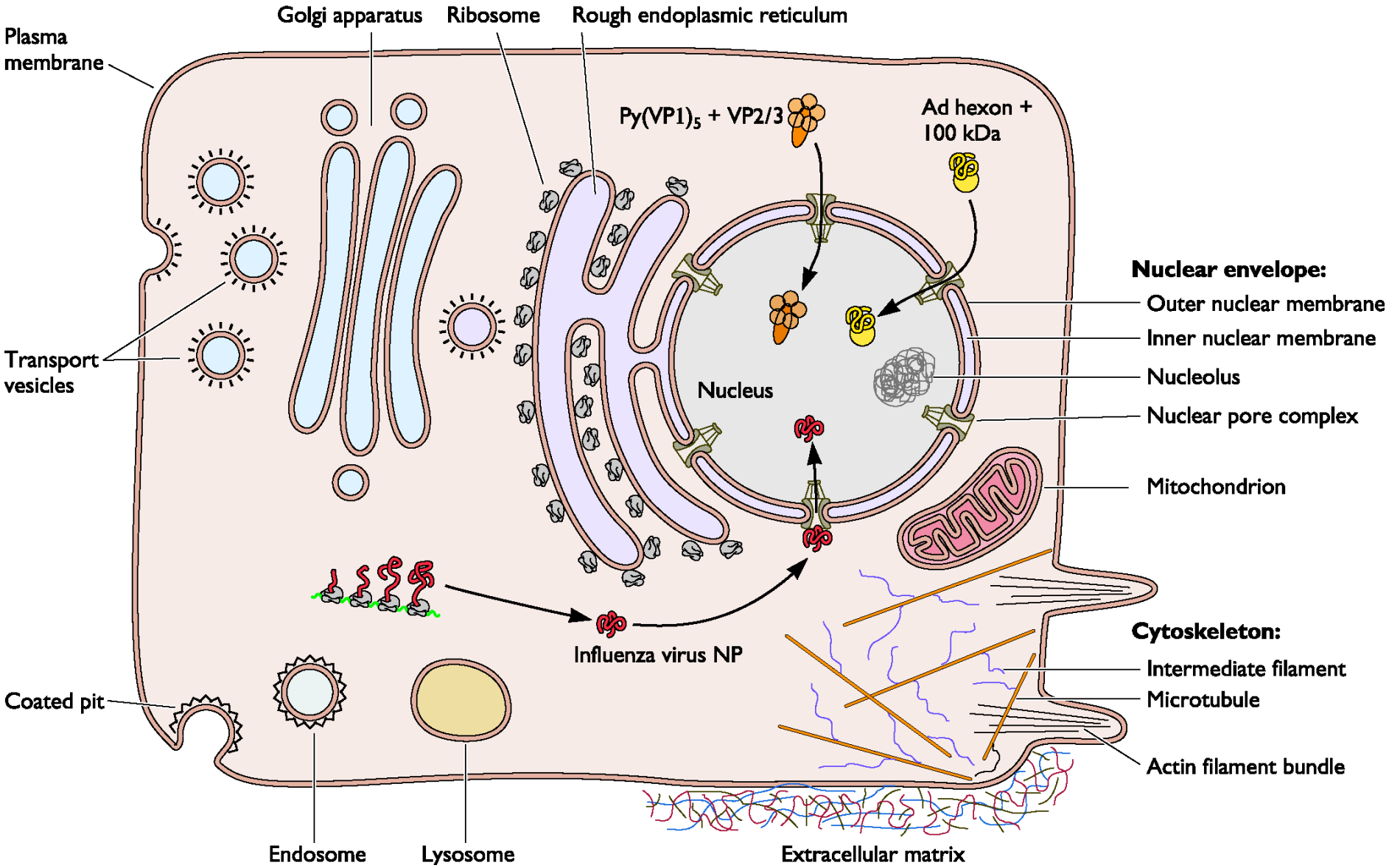
# Assembly of Poliovirus in the cytoplam of an infected cell



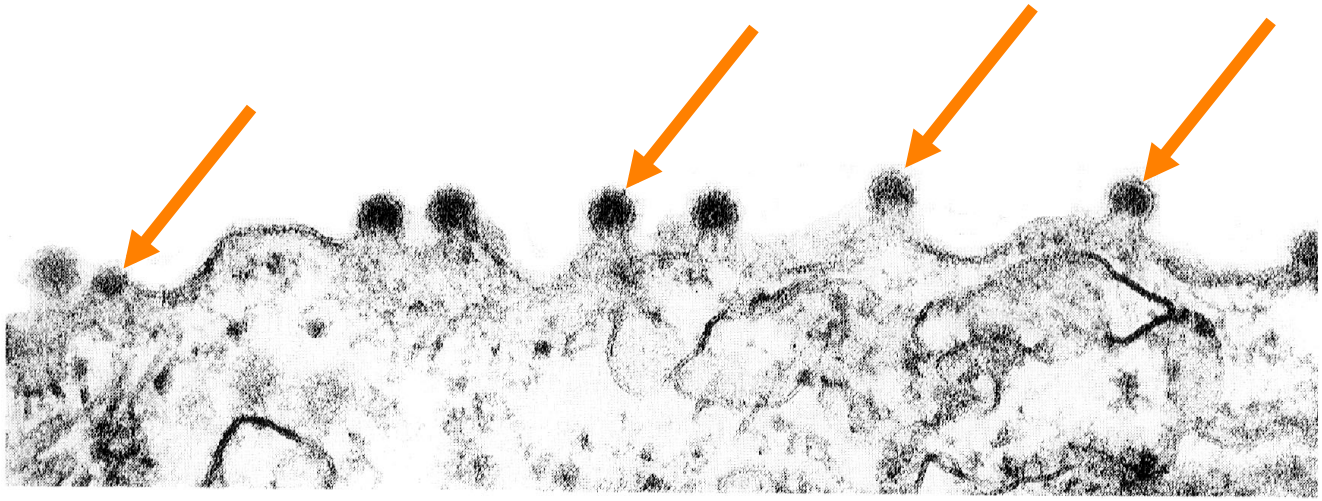
# Assembly of Adenovirus in the nucleus of an infected cell

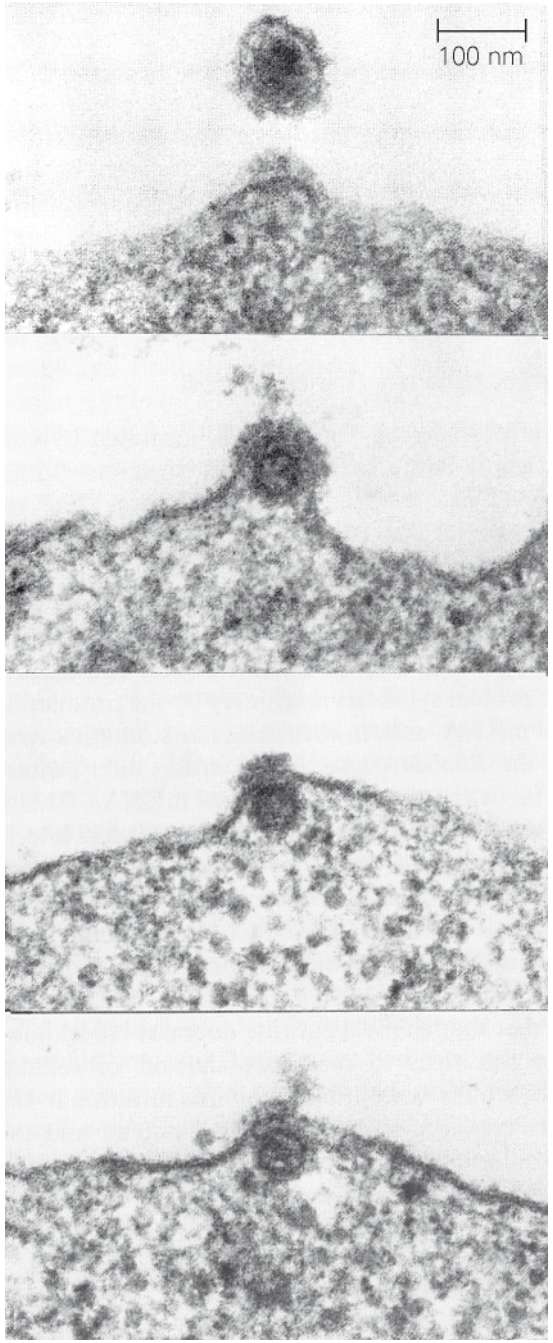


# Localization of viral proteins to the plasma membrane

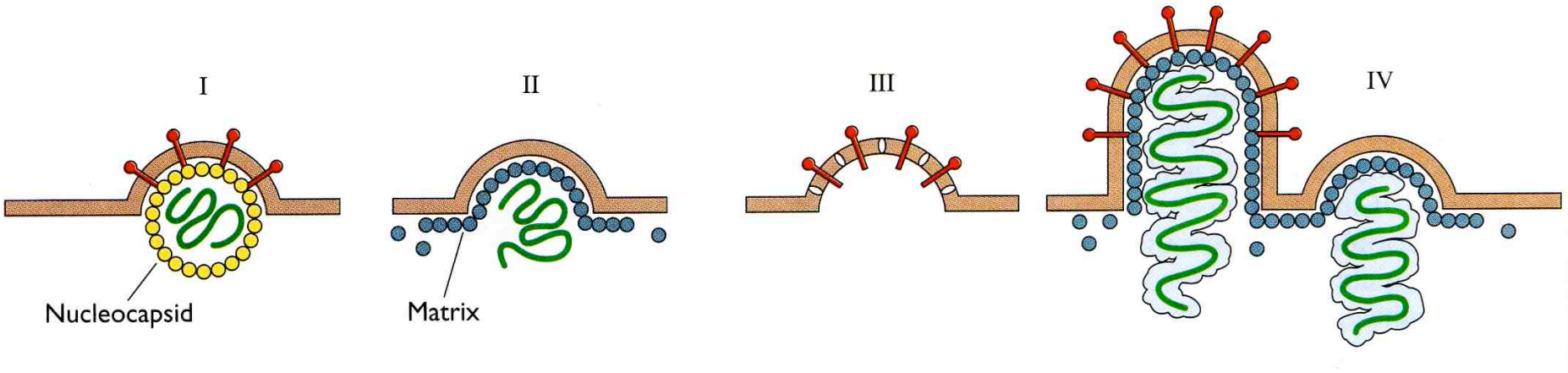


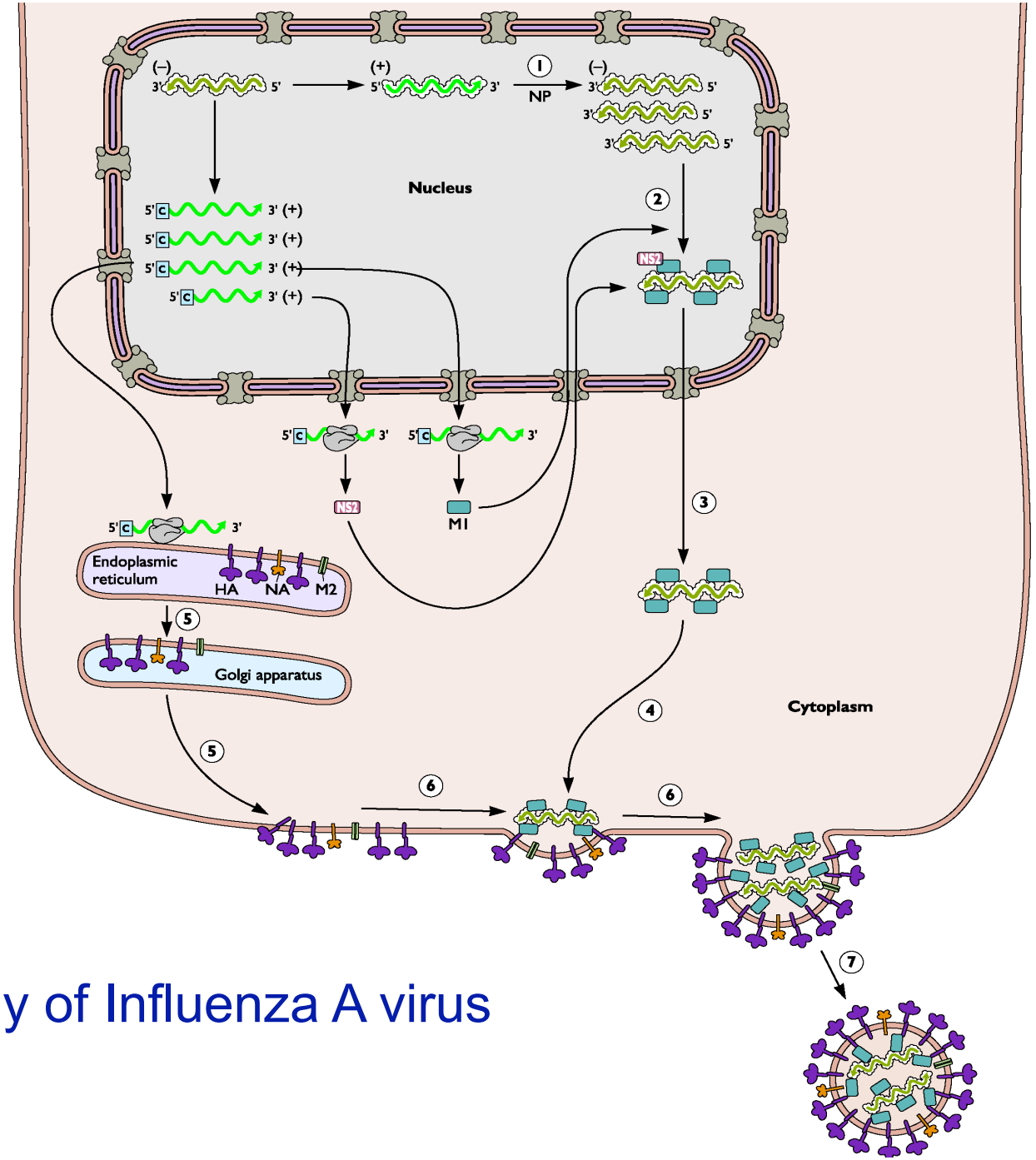
# Mechanism of budding of enveloped viruses




100 nm

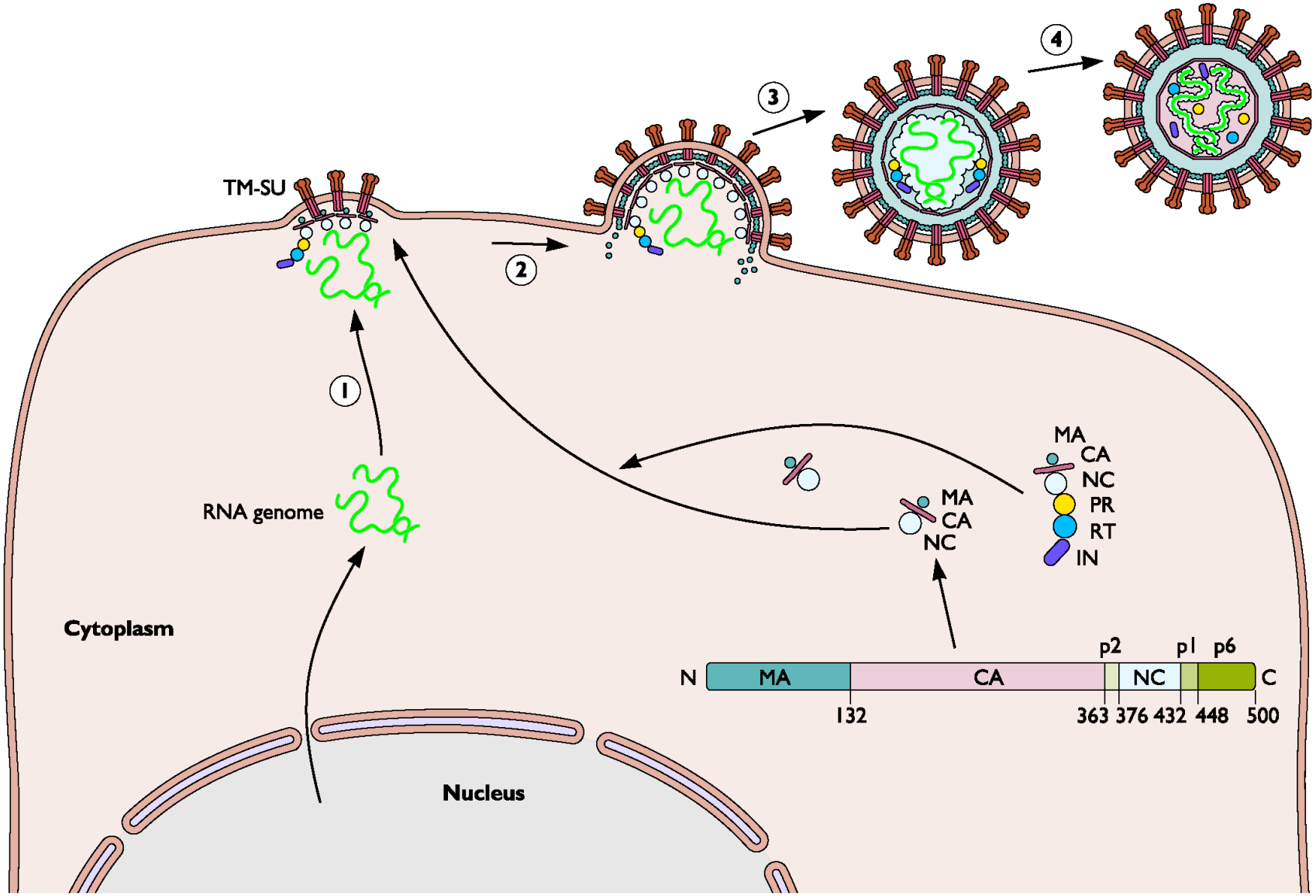
# Interaction of viral proteins responsible for budding at the plasma membrane



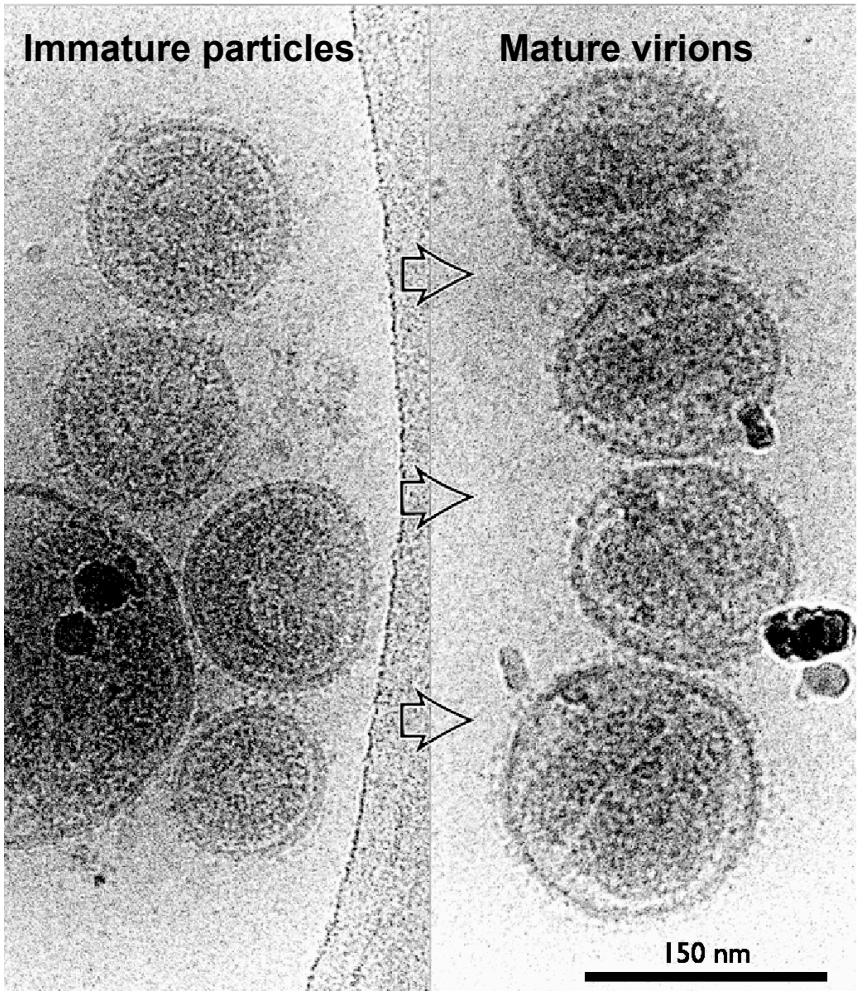


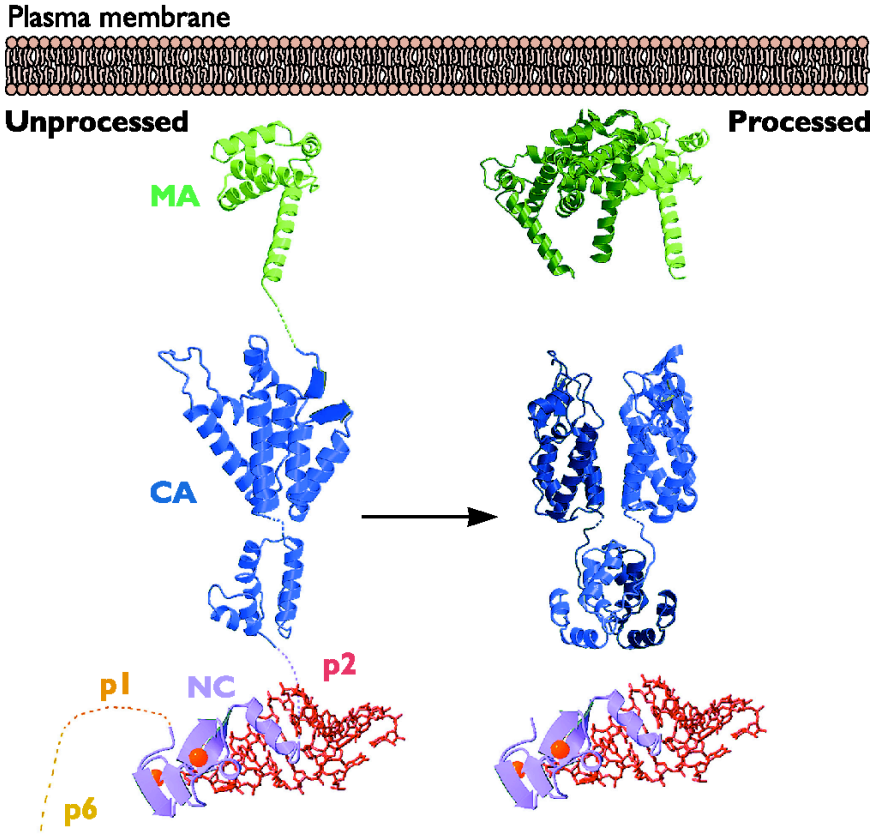

# Assembly of Influenza A virus

# Assembly of a Retrovirus from polyprotein precursors

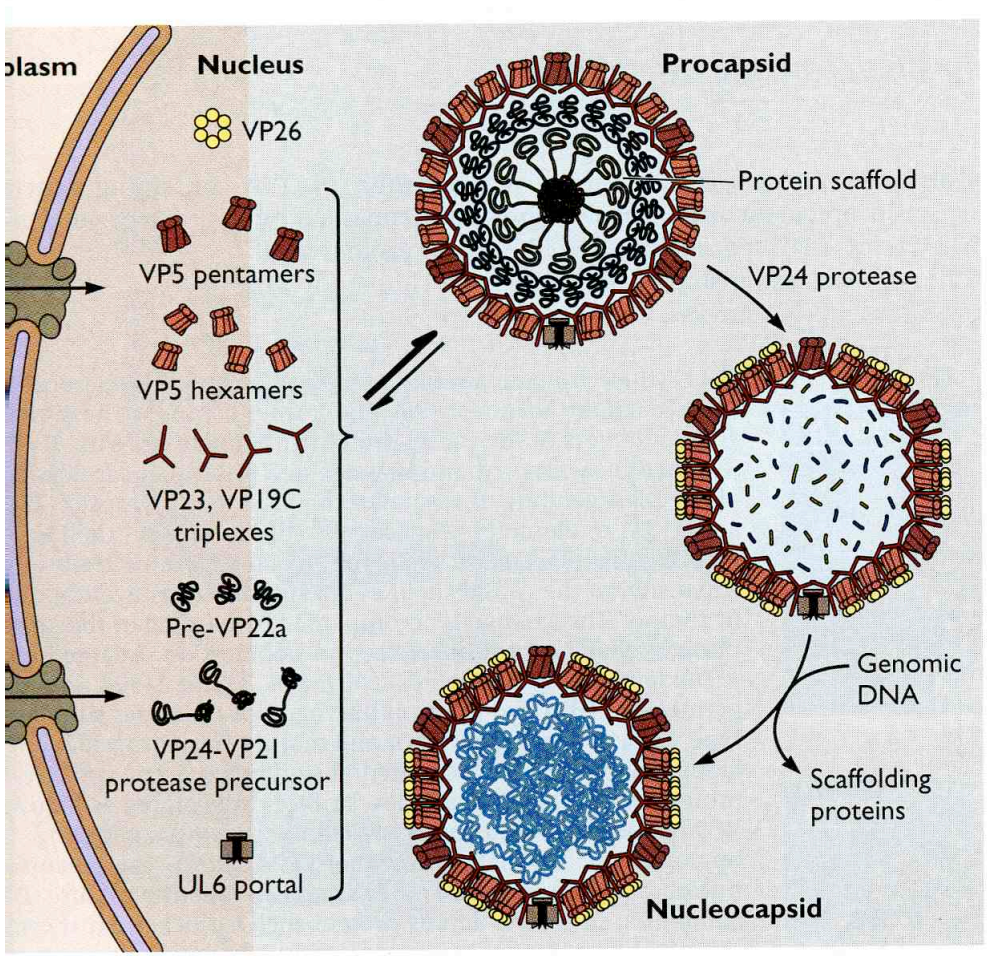


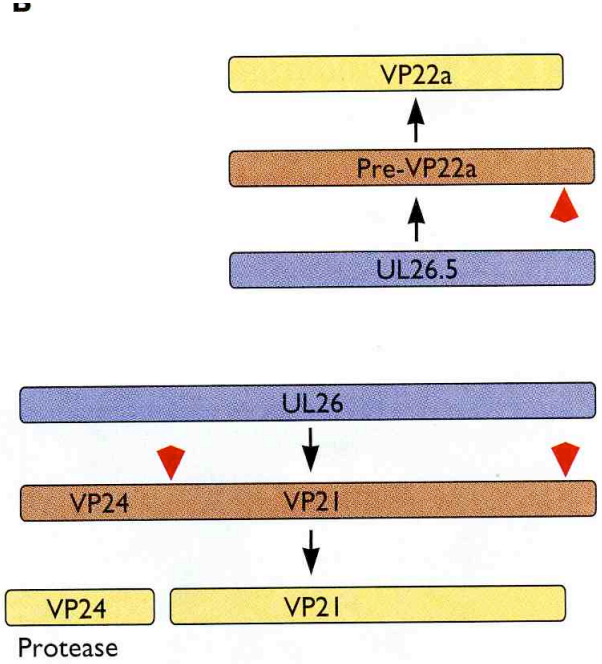
# Morphological rearrangement of the HIV-1 particle upon proteolytic processing of the Gag polyprotein



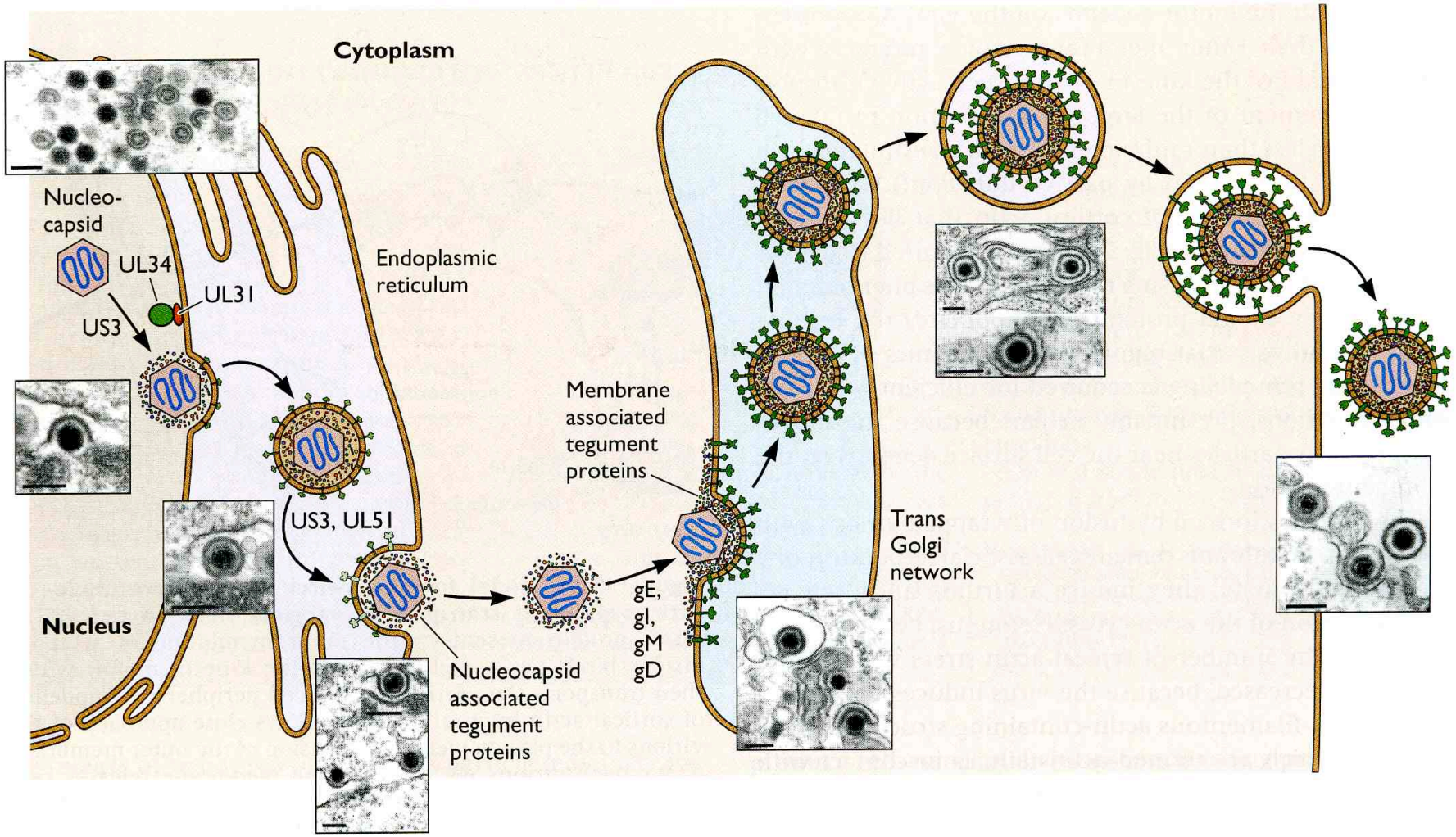



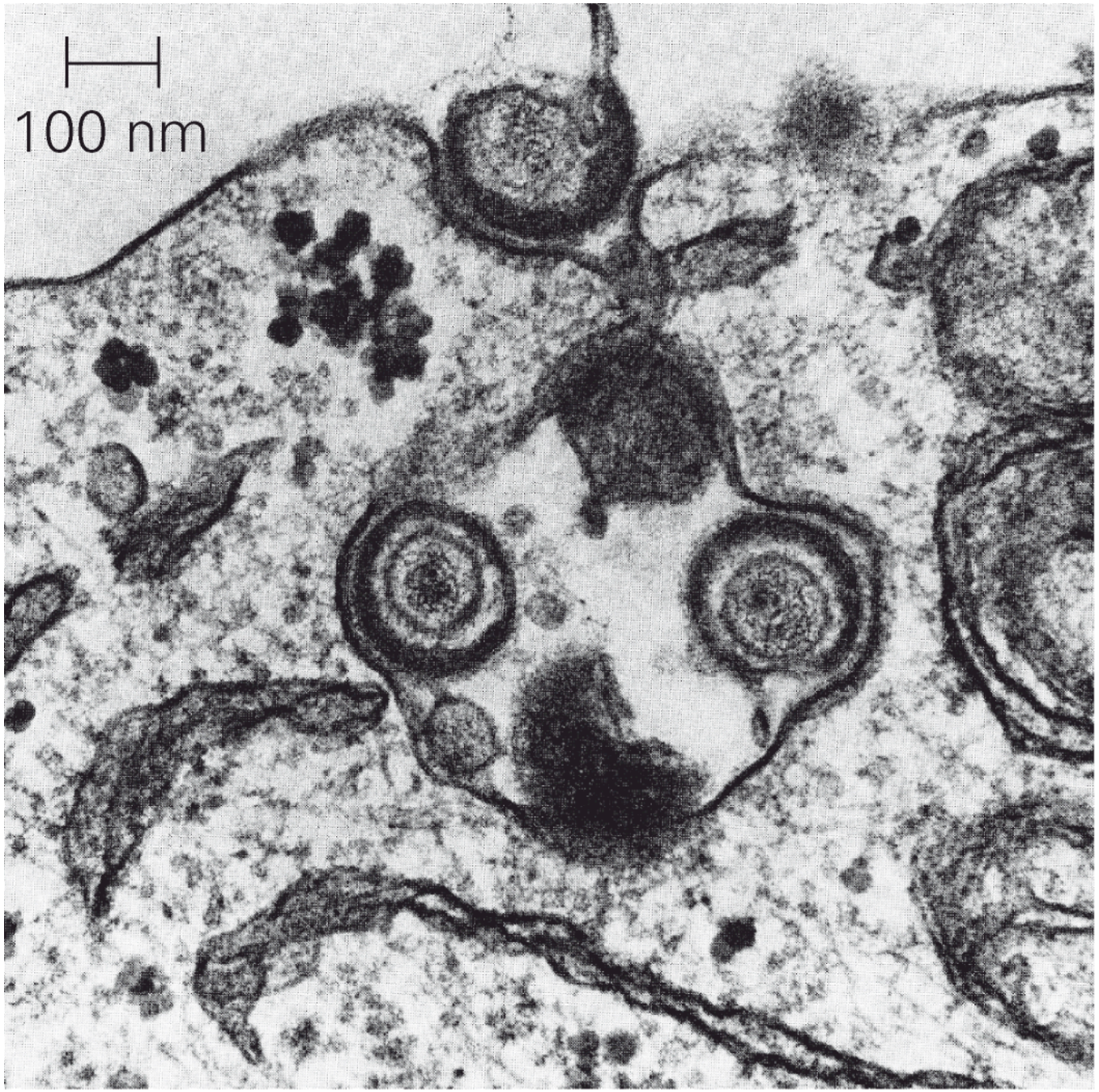
# Assembly of HSV-1 nucleocapsids and the pathway proposed for the virus exit from an infected cell



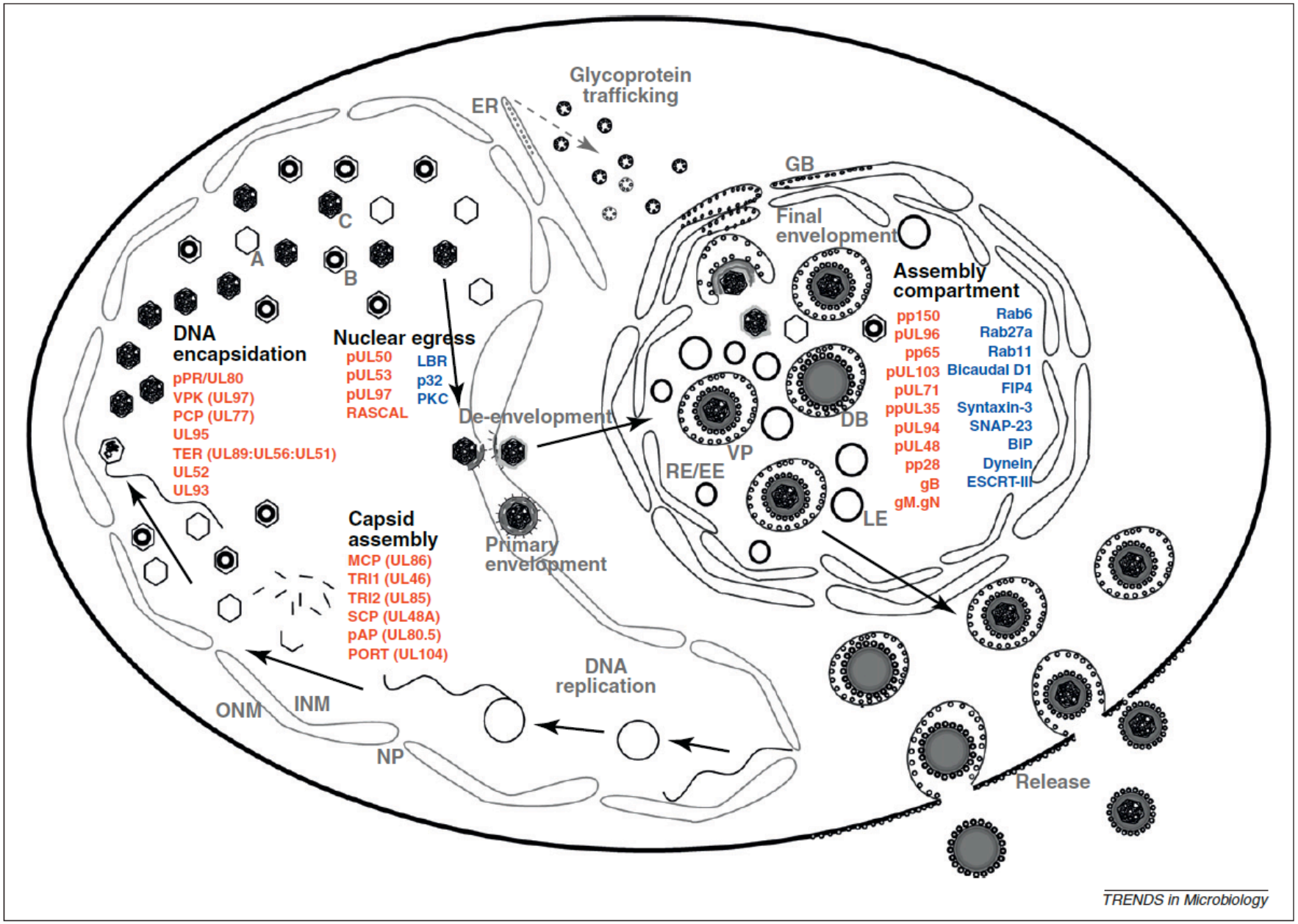



# Assembly of HSV-1 nucleocapsids and the pathway proposed for the virus exit from an infected cell

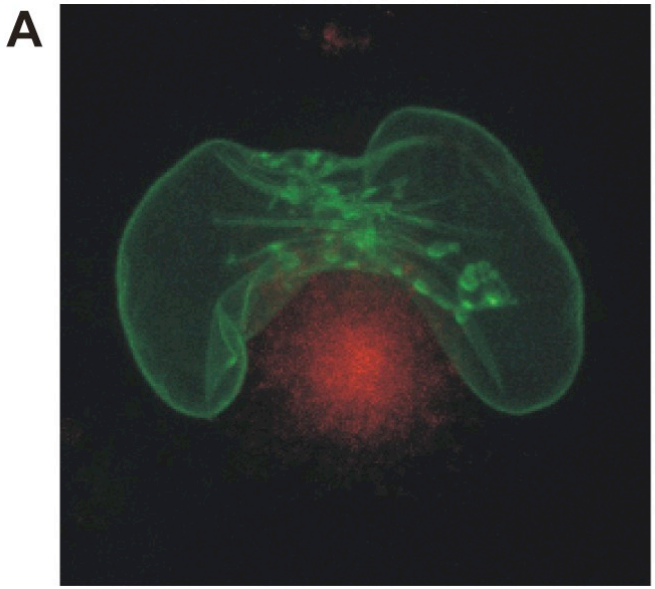


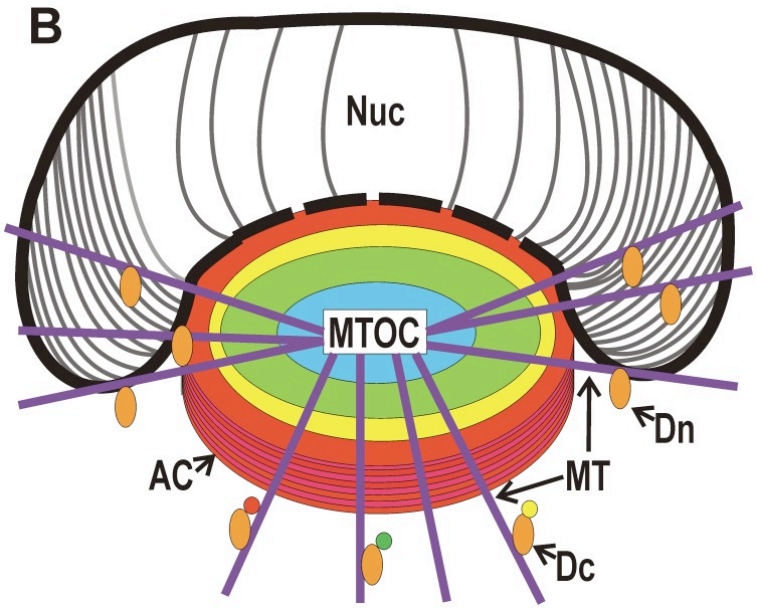

100 nm

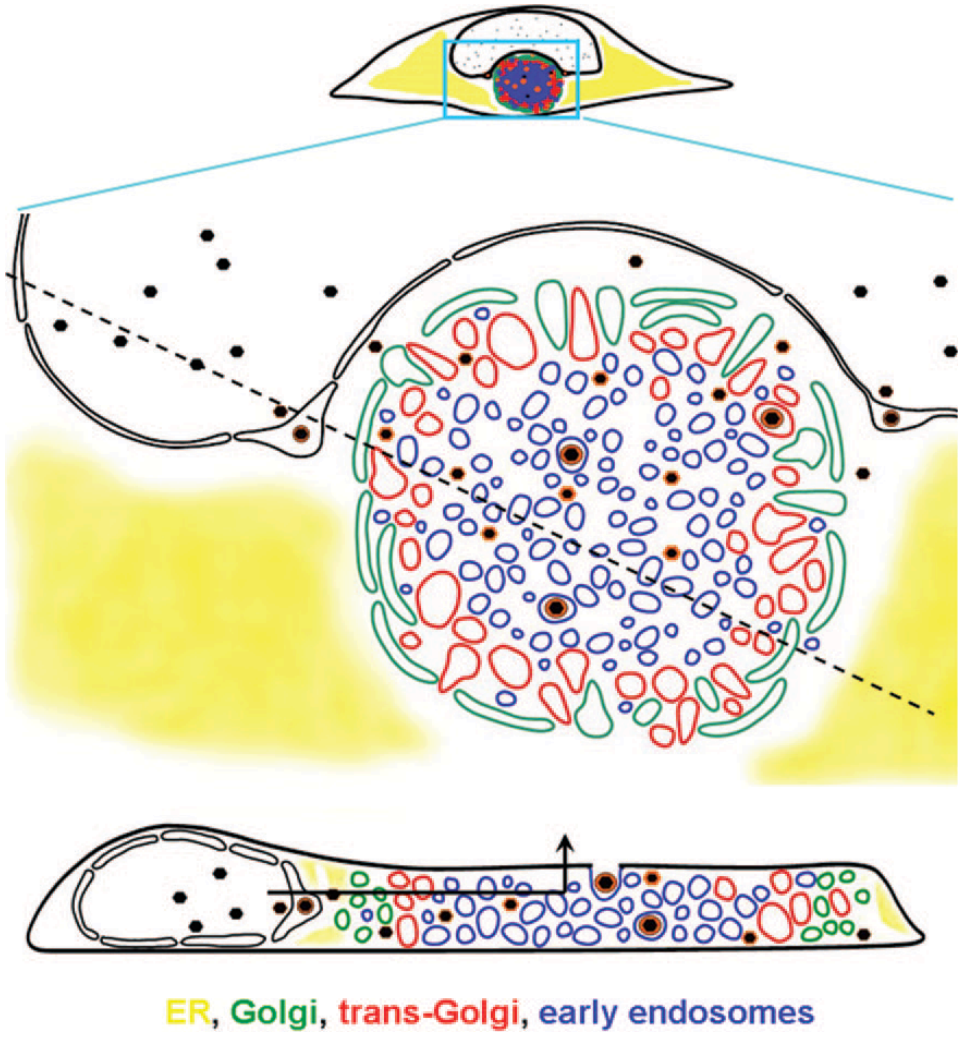
# Summary of human cytomegalovirus (HCMV) maturation.



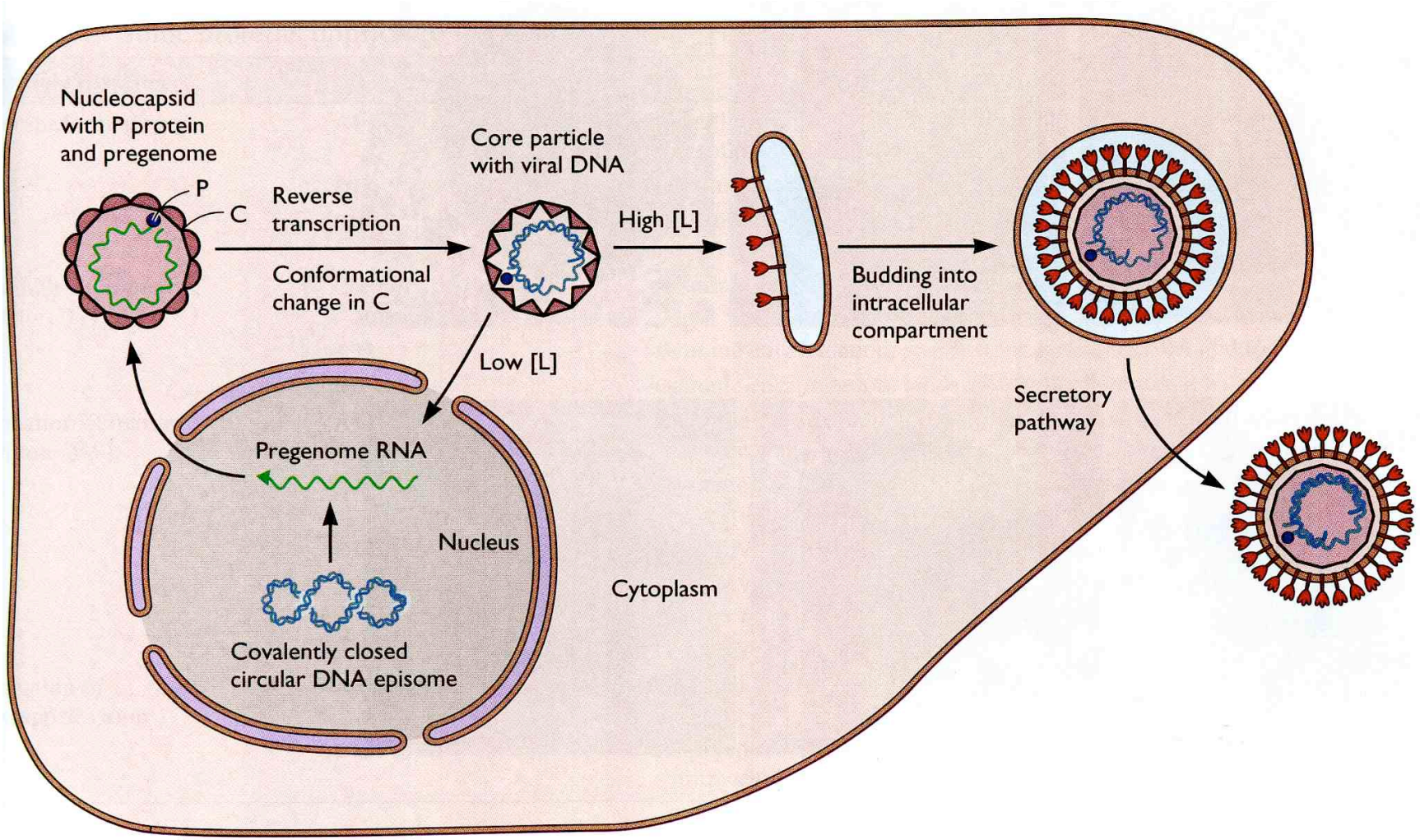
# Microscopic and diagrammatic representations of the assembly compartment and nucleus in an HCMV-infected cell.



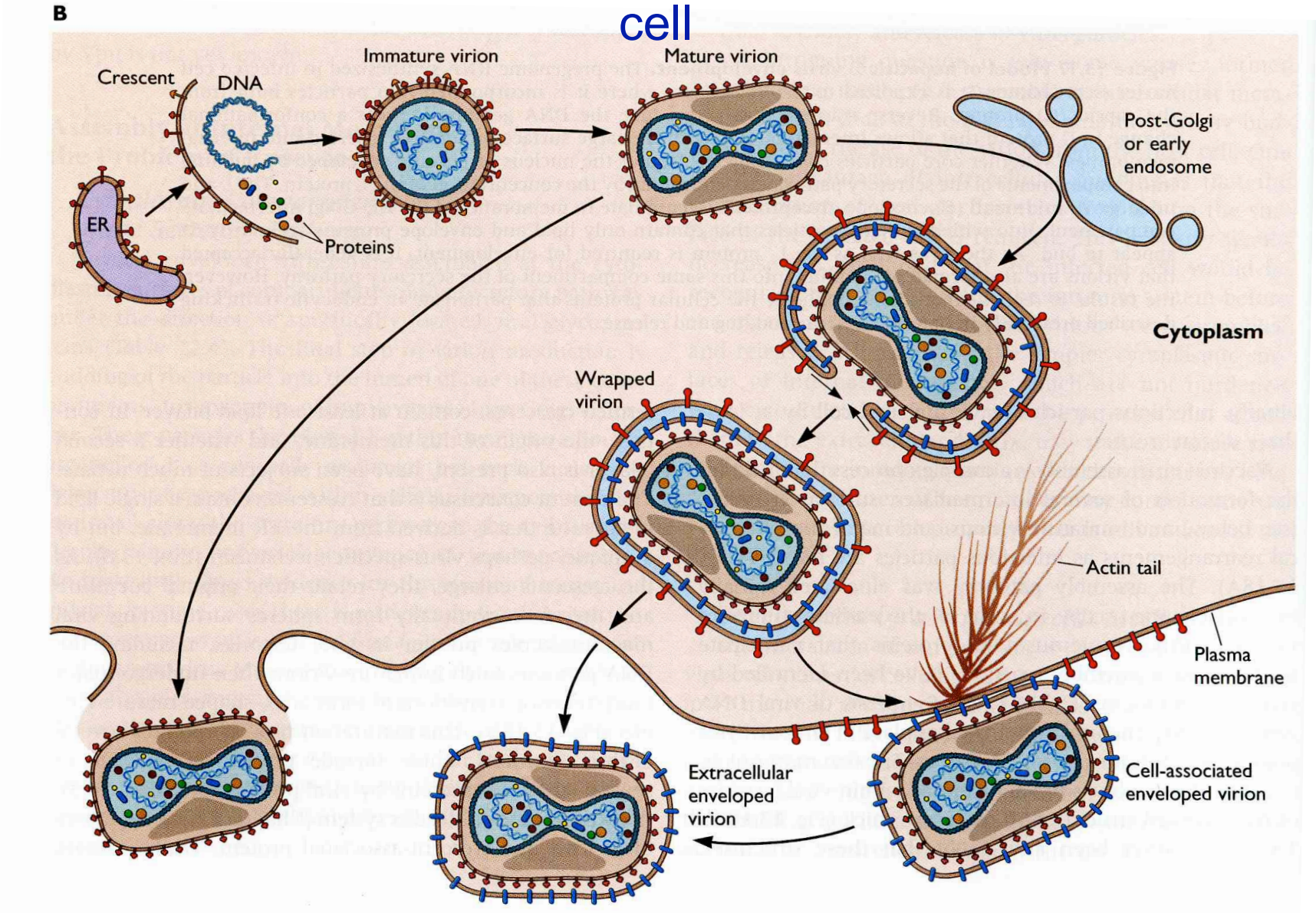



# Assembly of HBV nucleocapsids and the pathway proposed for the virus exit from an infected cell



# 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)**.