

Structural Virology

Lecture 3

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NextGenerationEU

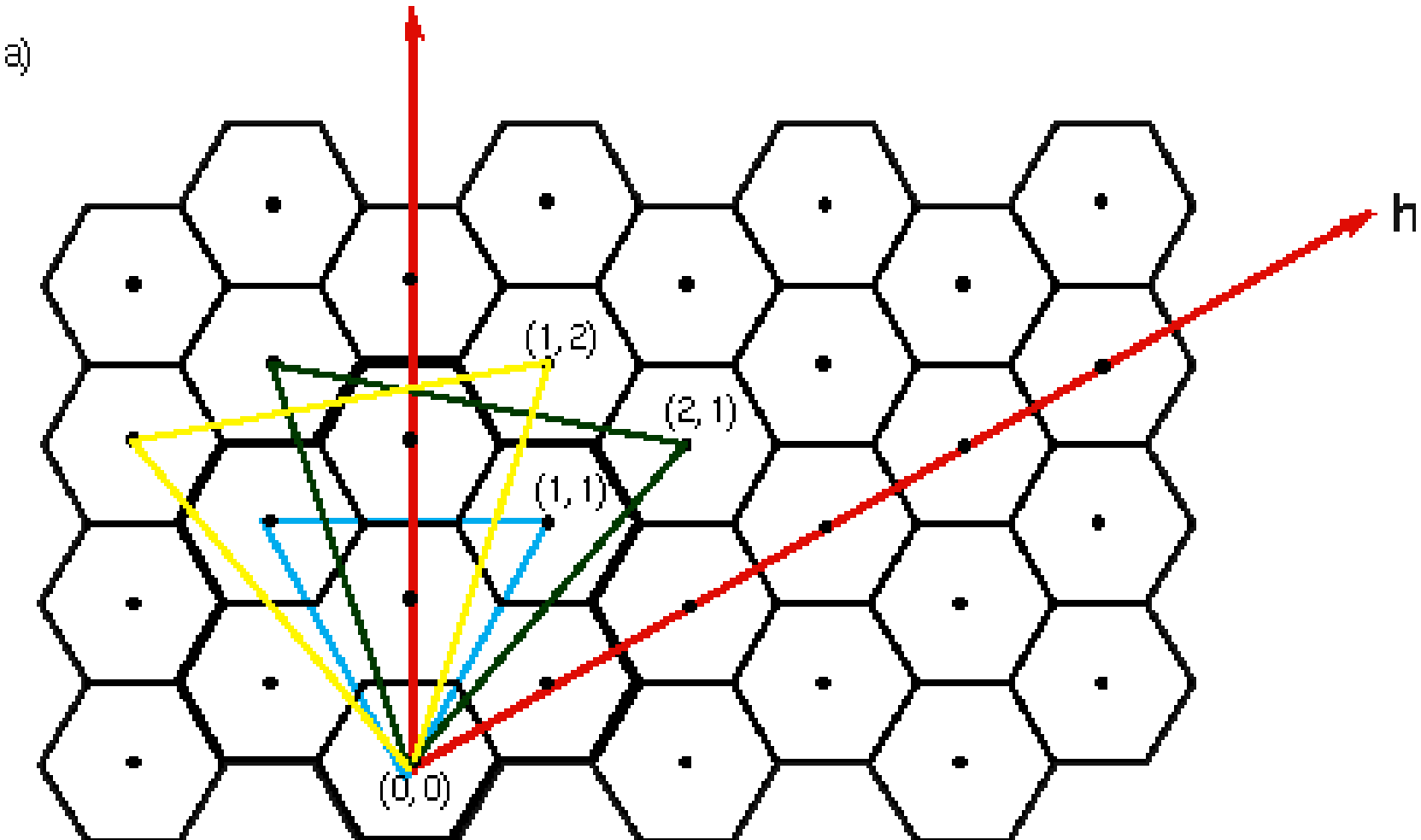


NÁRODNÍ
PLÁN OBNOVY

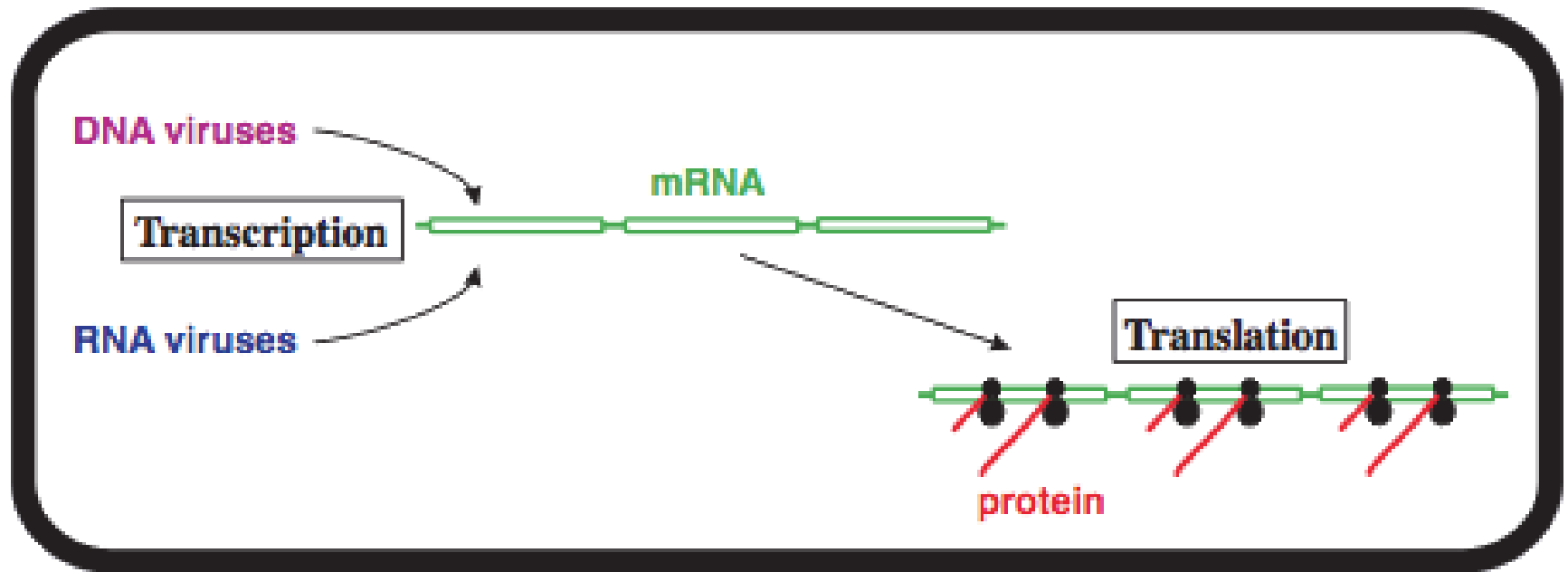
MŠMT
MINISTERSTVO ŠKOLSTVÍ,
MLÁDEŽE A TĚLOVÝCHOVY

Quasi equivalence

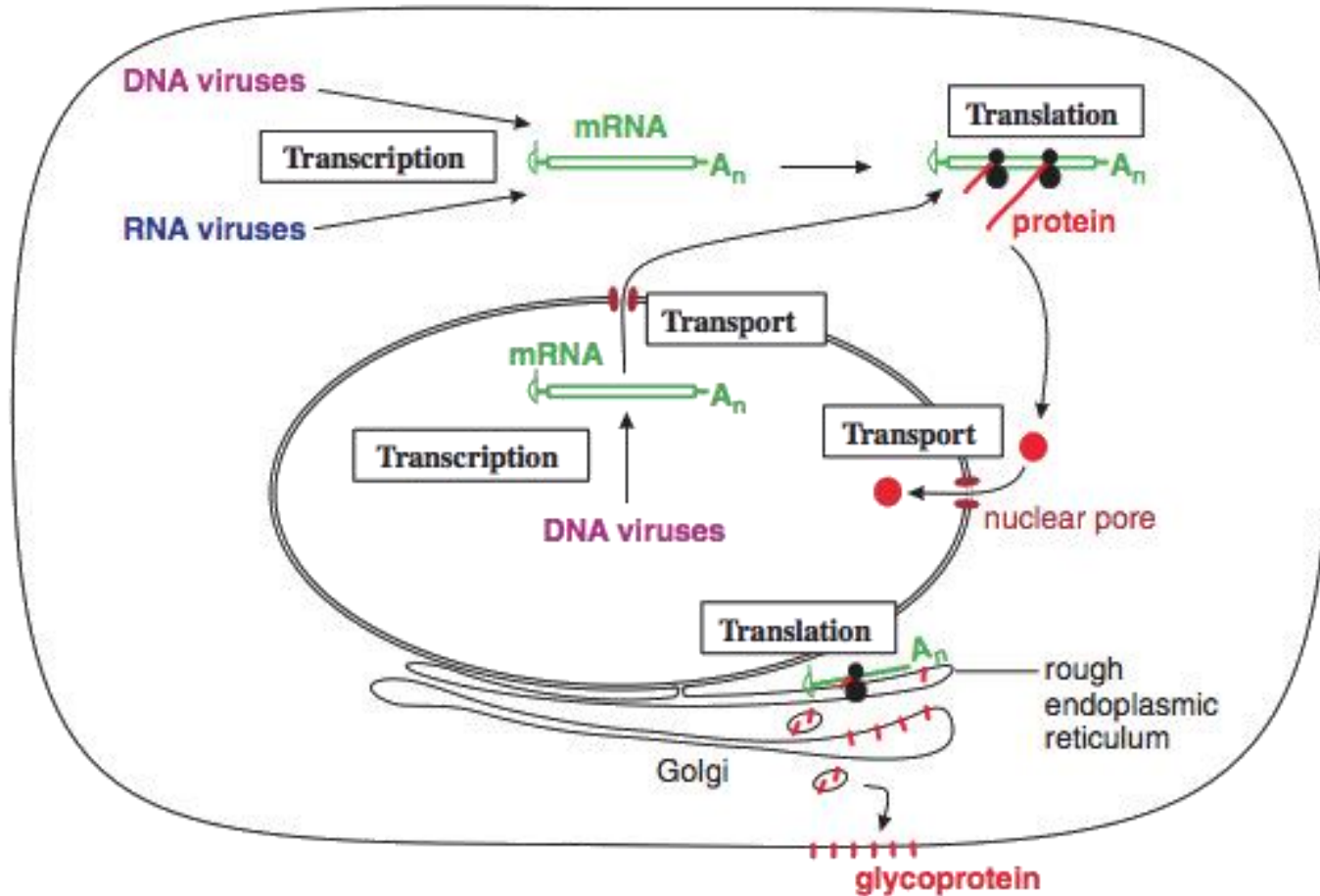
$$T = h^2 + hk + k^2$$



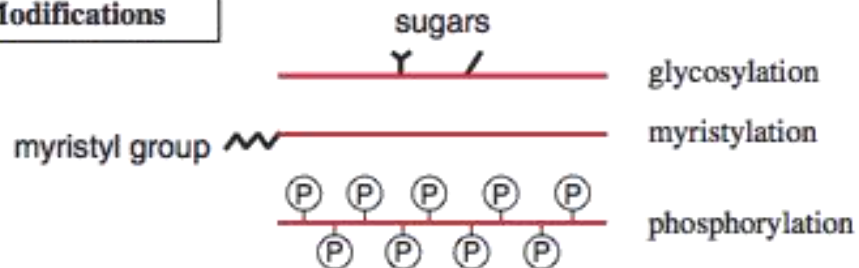
Transcription, Translation, and Transport



Transcription, Translation, and Transport



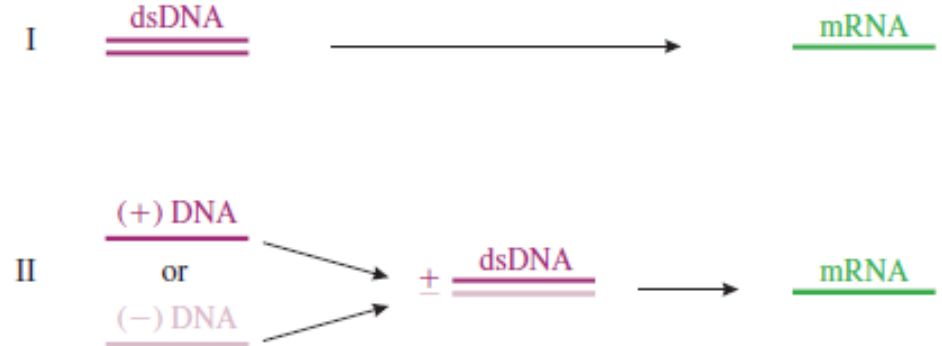
Post-Translational Modifications



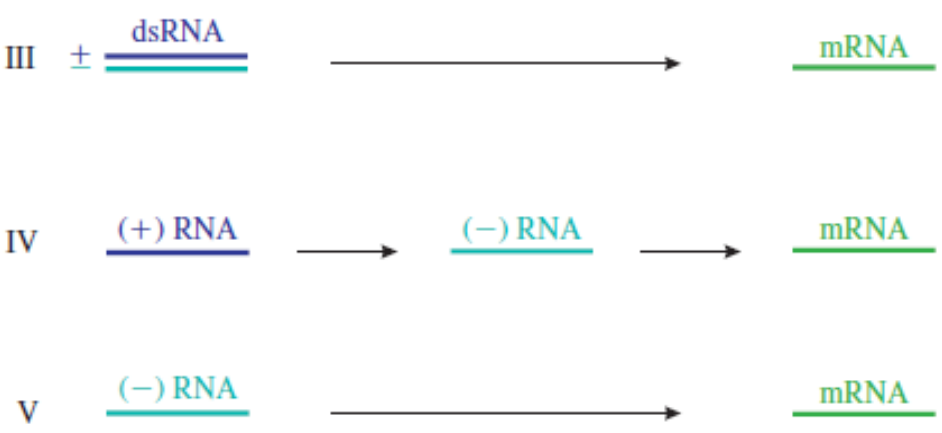
(David) Baltimore virus classification

- genome type
- mode of transcription
- (-) and (+) relative to mRNA
- ambisense viruses (ssDNA - geminiviruses, arenaviruses)

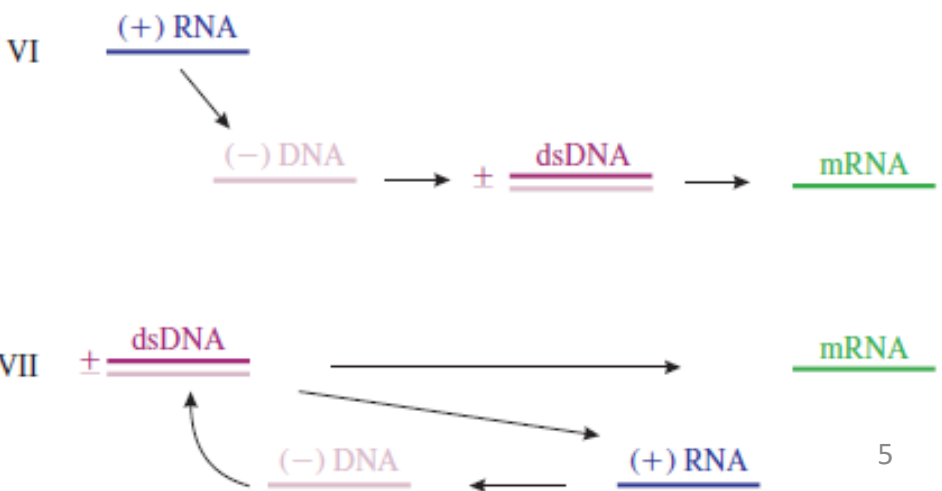
DNA Viruses



RNA Viruses

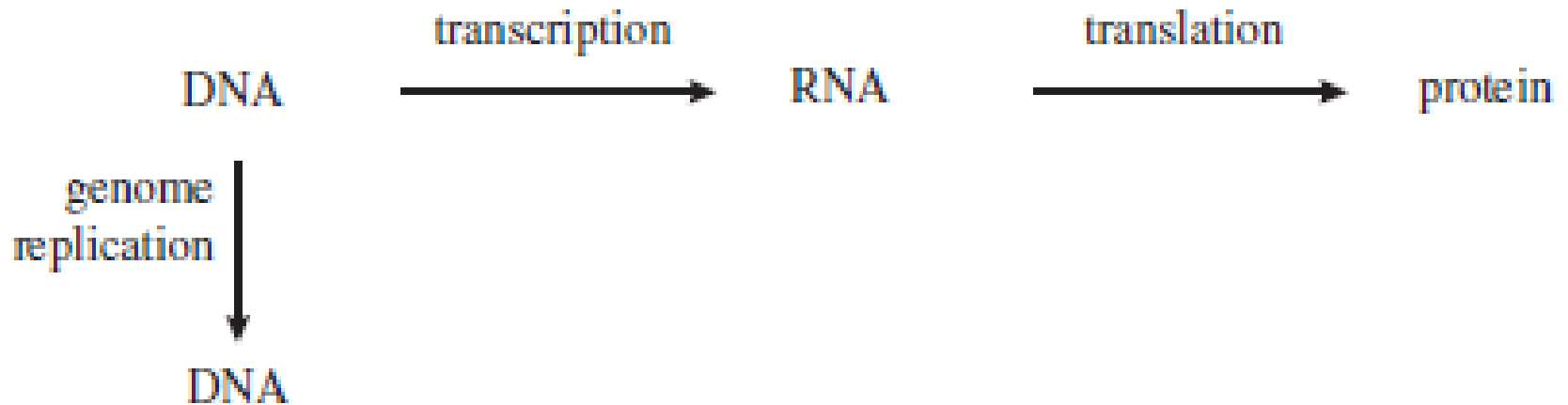


Reverse-Transcribing Viruses

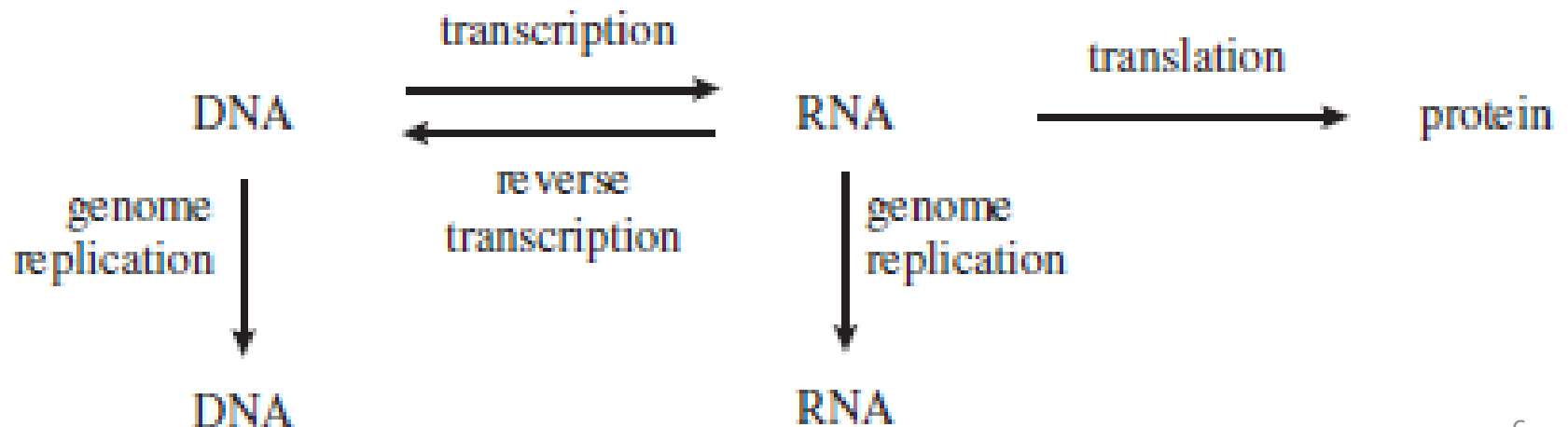


Central Dogma of Molecular Biology

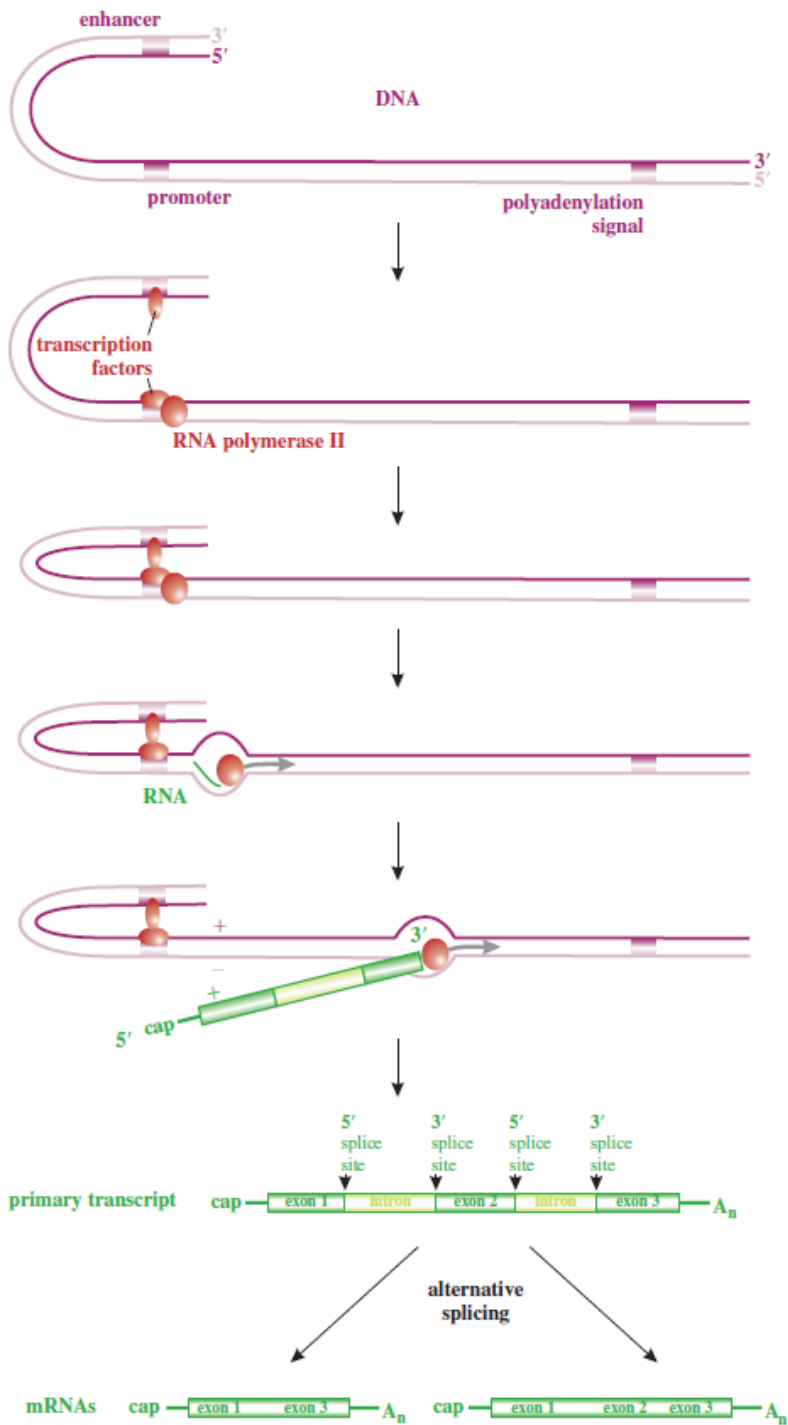
(a) Central Dogma



(b) Modified Central Dogma

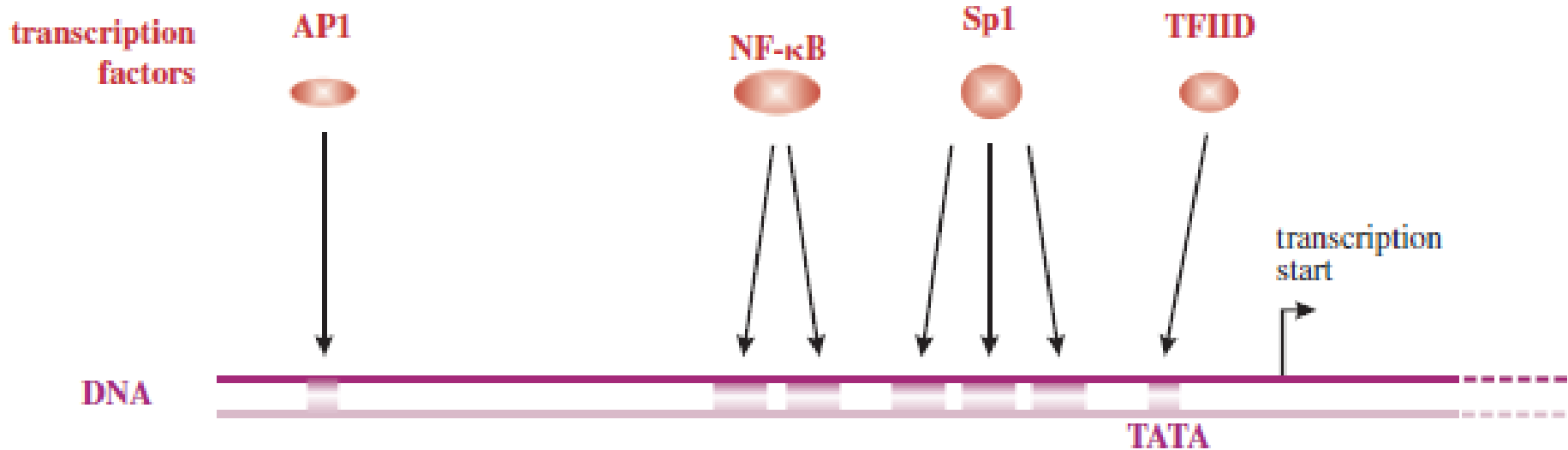


Transcription in Eukaryotes



Promoters, Enhancers, and TATA box

T A T A A/T A A/T A/G



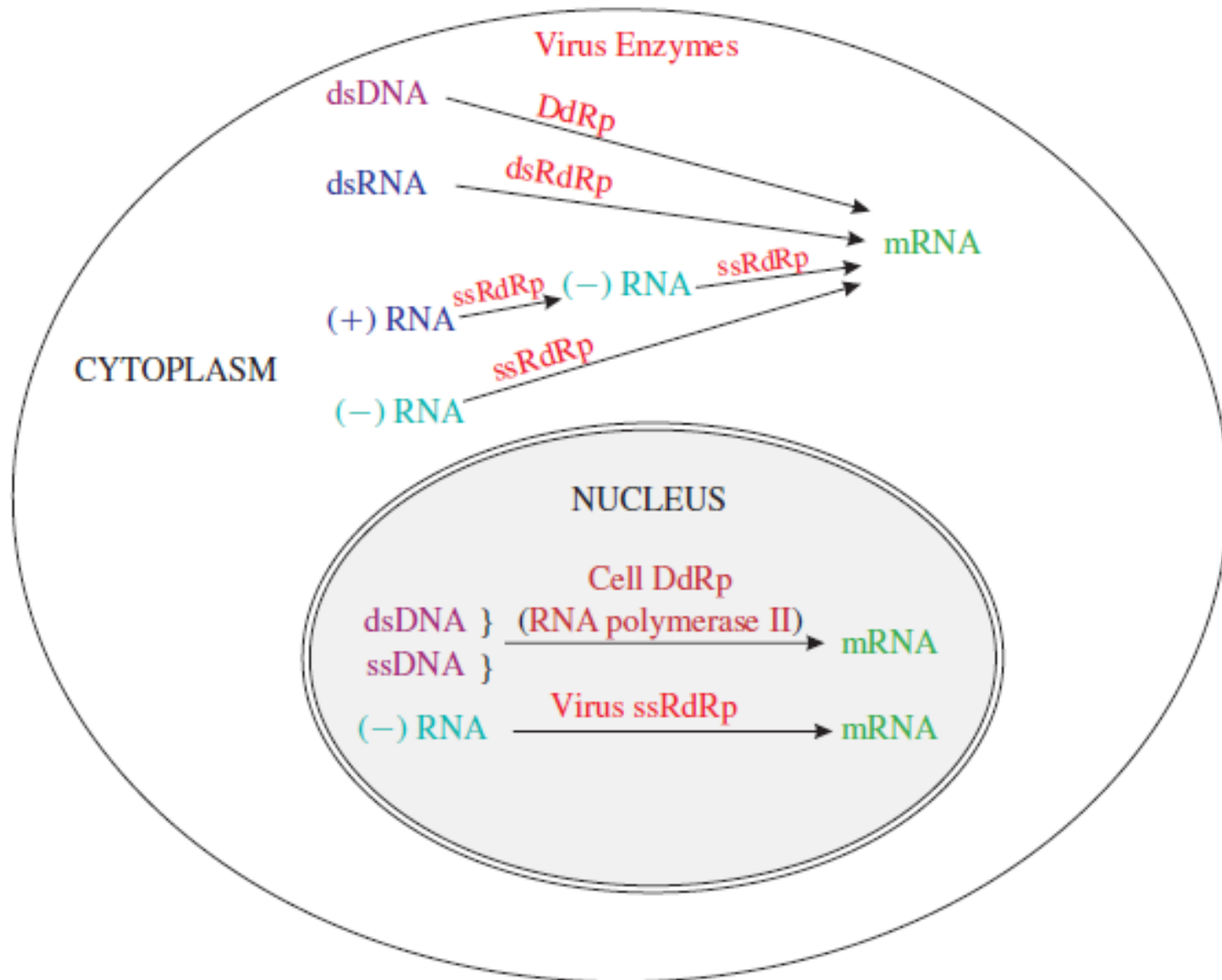
General cellular transcription factors: TFIID

Specific cellular transcription factors.

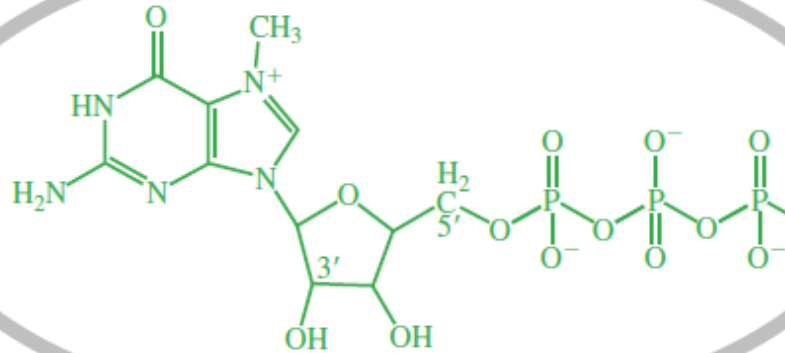
Virus transcription factors: VP16 of herpes simplex virus

- different transcription factors used during different stages of infection

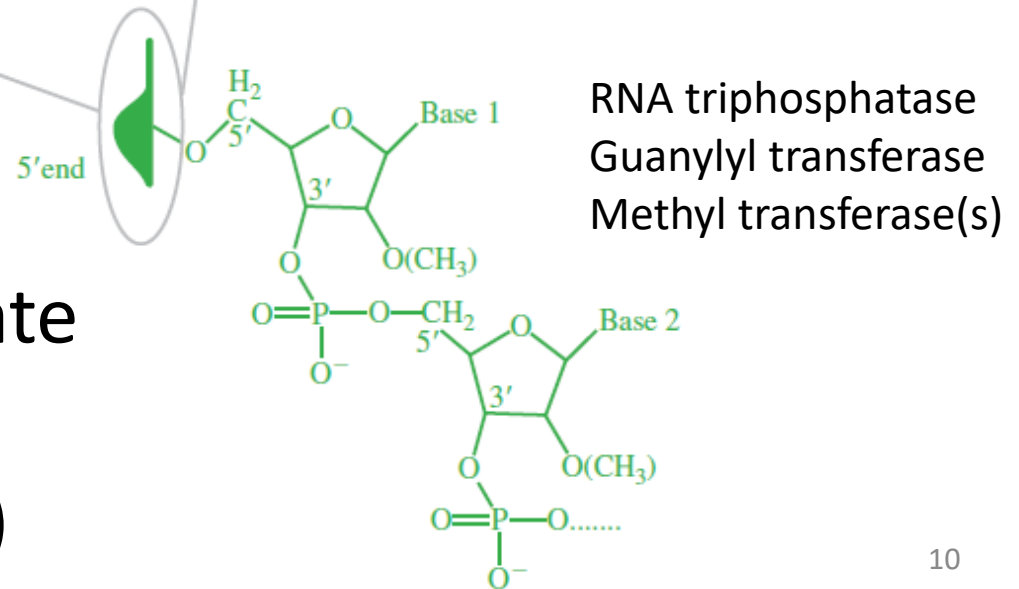
Transcriptases



mRNA cap



- aid mRNA transport from the nucleus to the cytoplasm
- protect the mRNA from degradation by exonucleases
- required for the initiation of translation



Guanosine triphosphate
joined by 5'-5' linkage
(methylated in ribose)

Obtaining mRNA cap

Cell enzymes:

- RNA triphosphatase
- Guanylyl transferase
- Methyl transferase(s)

Influenza virus – cap snatching

Poxviruses, coronaviruses, reoviruses replicate in cytoplasm and encode own capping enzymes.

Cap snatching in cytoplasm – bunyaviruses

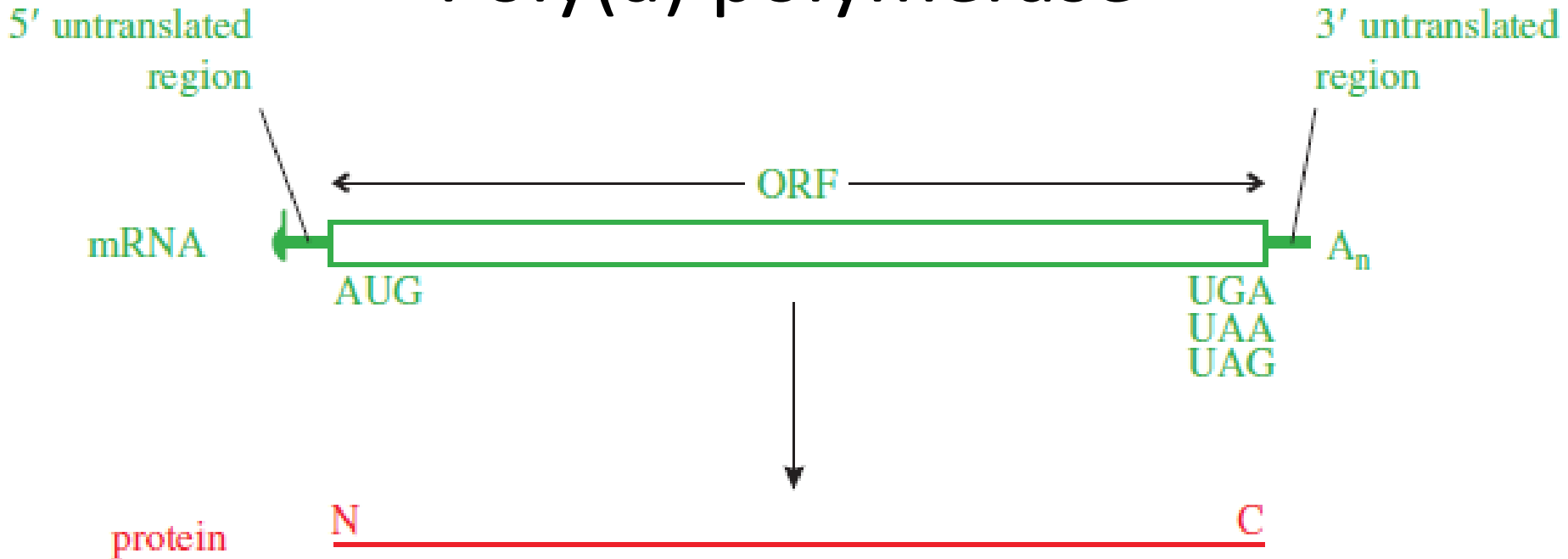
Non-capped mRNAs – picornaviruses

De-capping of host mRNAs – totiviruses

mRNA polyadenylation

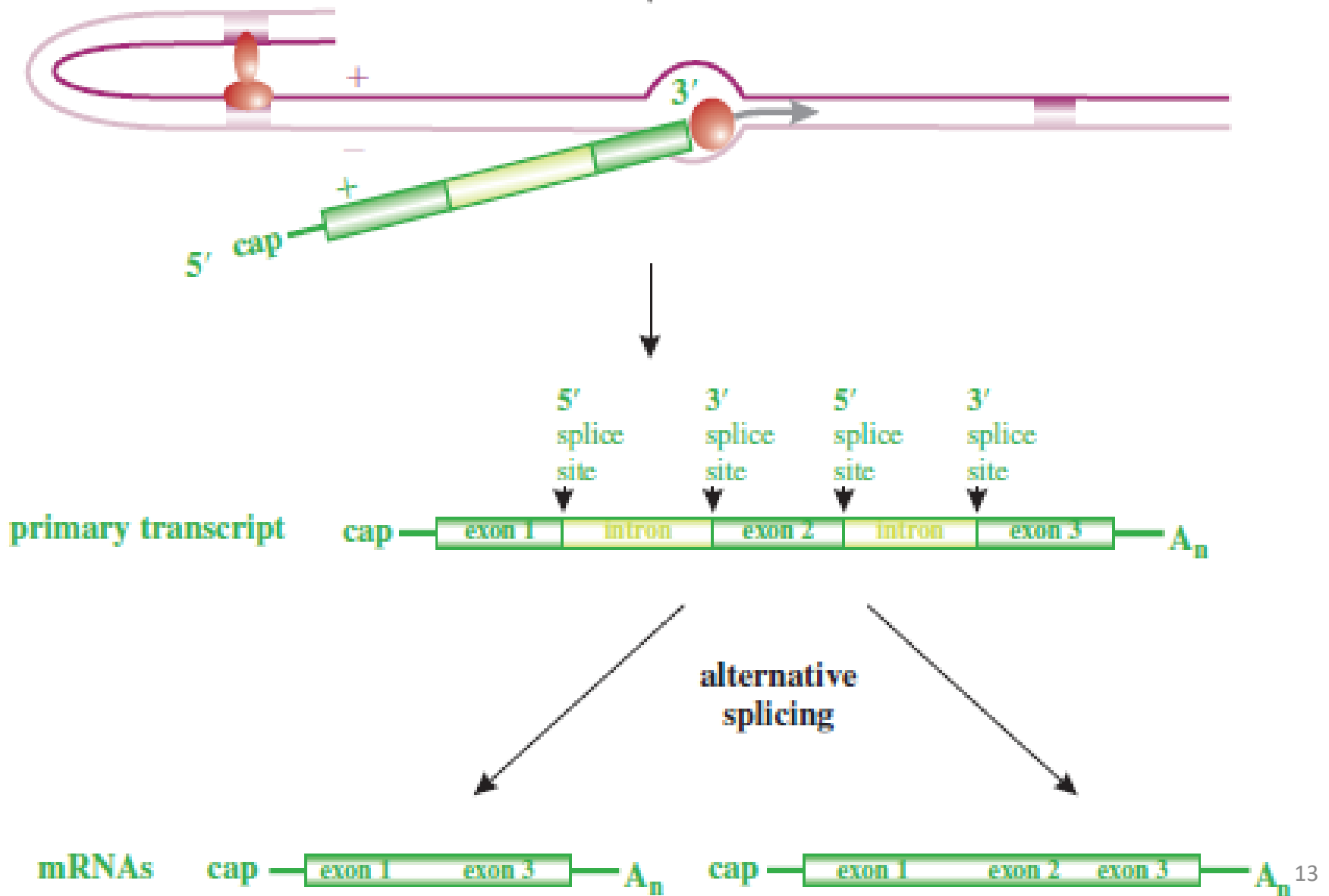
A A T A A A

Poly(a) polymerase

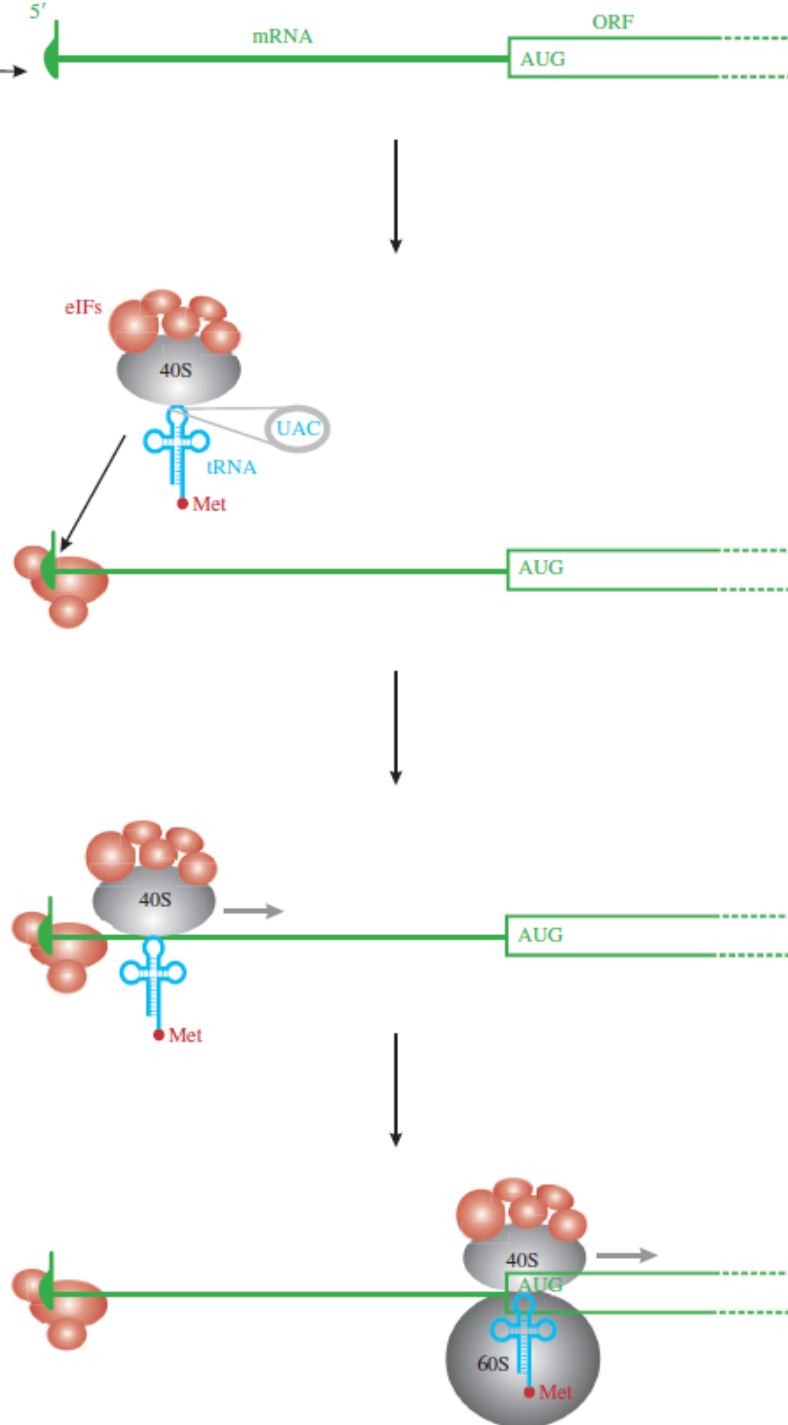


First identified in SV40 transcripts in 1981.

Pre-mRNA splicing

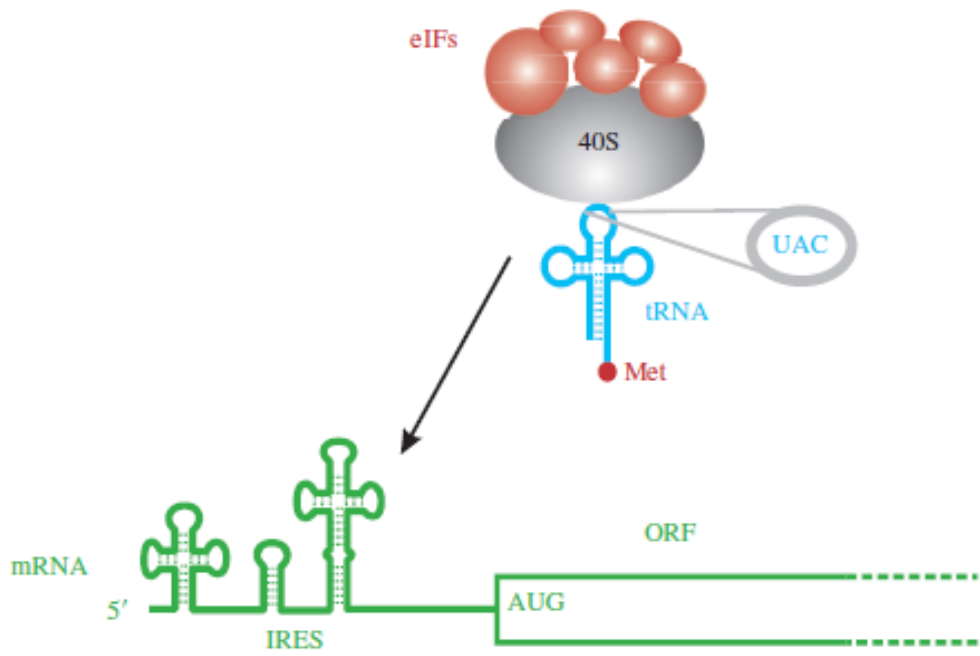


Translation

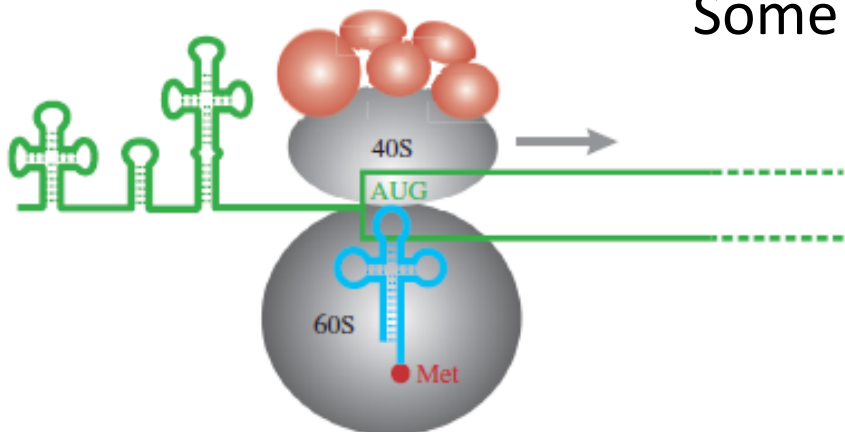


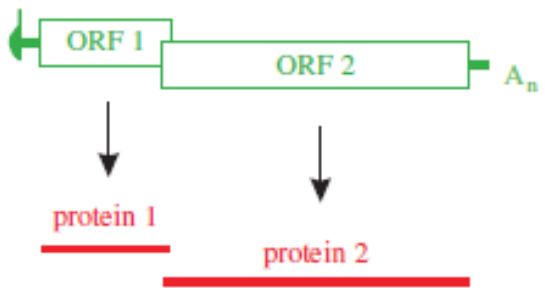
- Most viruses use host translation machinery.
- Mimiviruses encode their own tRNAs.
- eukaryotic Initiation Factors (eIF) (CAP)
- polyA binding proteins
- mRNA circularization
- 5'→3' scanning by 40S subunit (AUG) x Sendai virus (ACG)
- IRES

IRES dependent Translation



Hepatitis C virus
Picornaviruses
Kaposi's sarcoma associated herpesvirus
Some cellular mRNAs

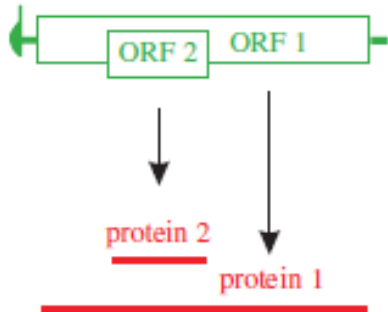




Leaky scanning

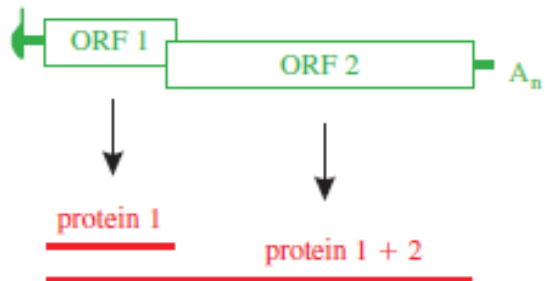
HIV-1 Vpu and Env
(Chapter 18)

Bicistronic mRNAs



Leaky scanning

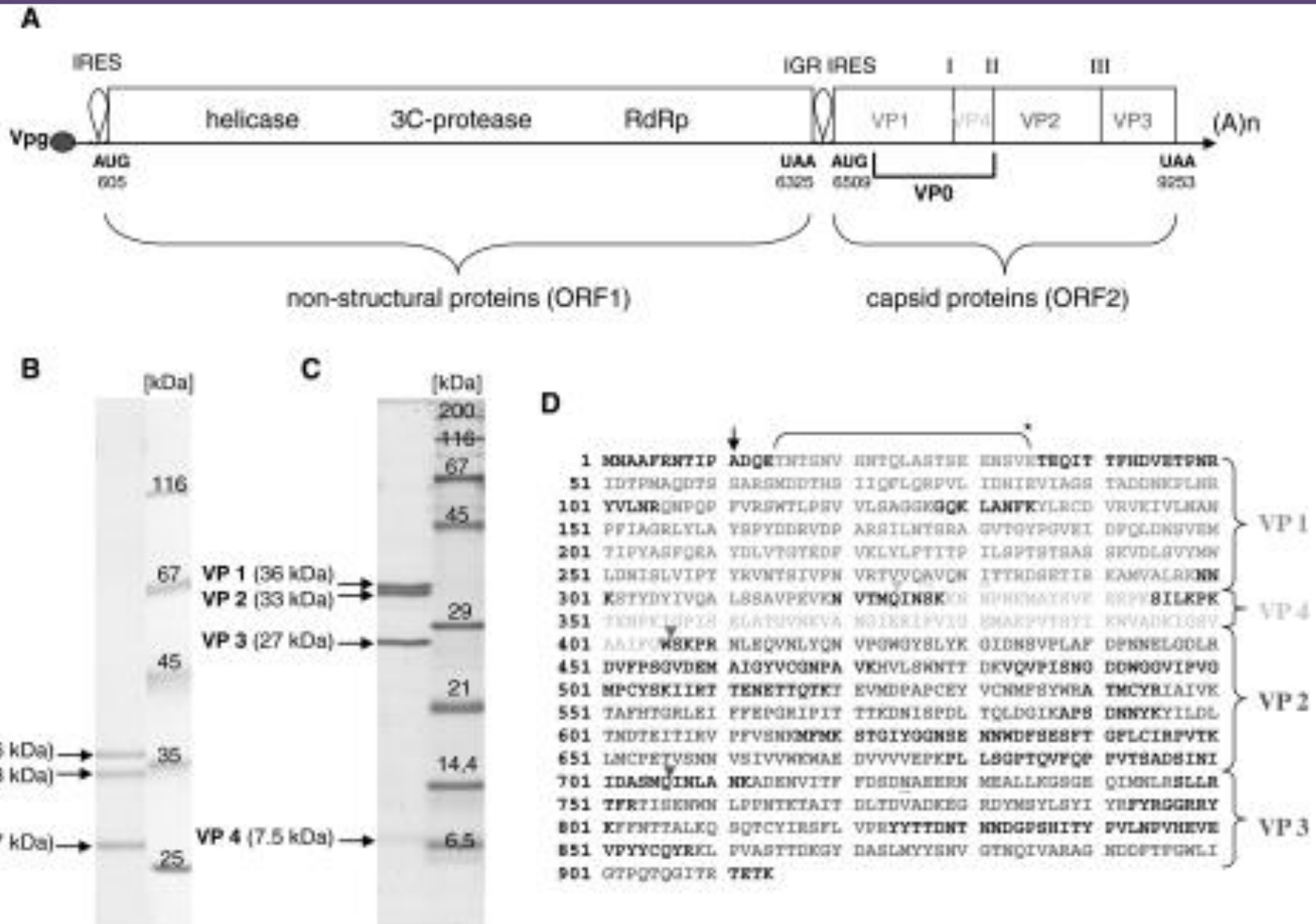
Rotavirus NSP5 and NSP6
(Chapter 13)



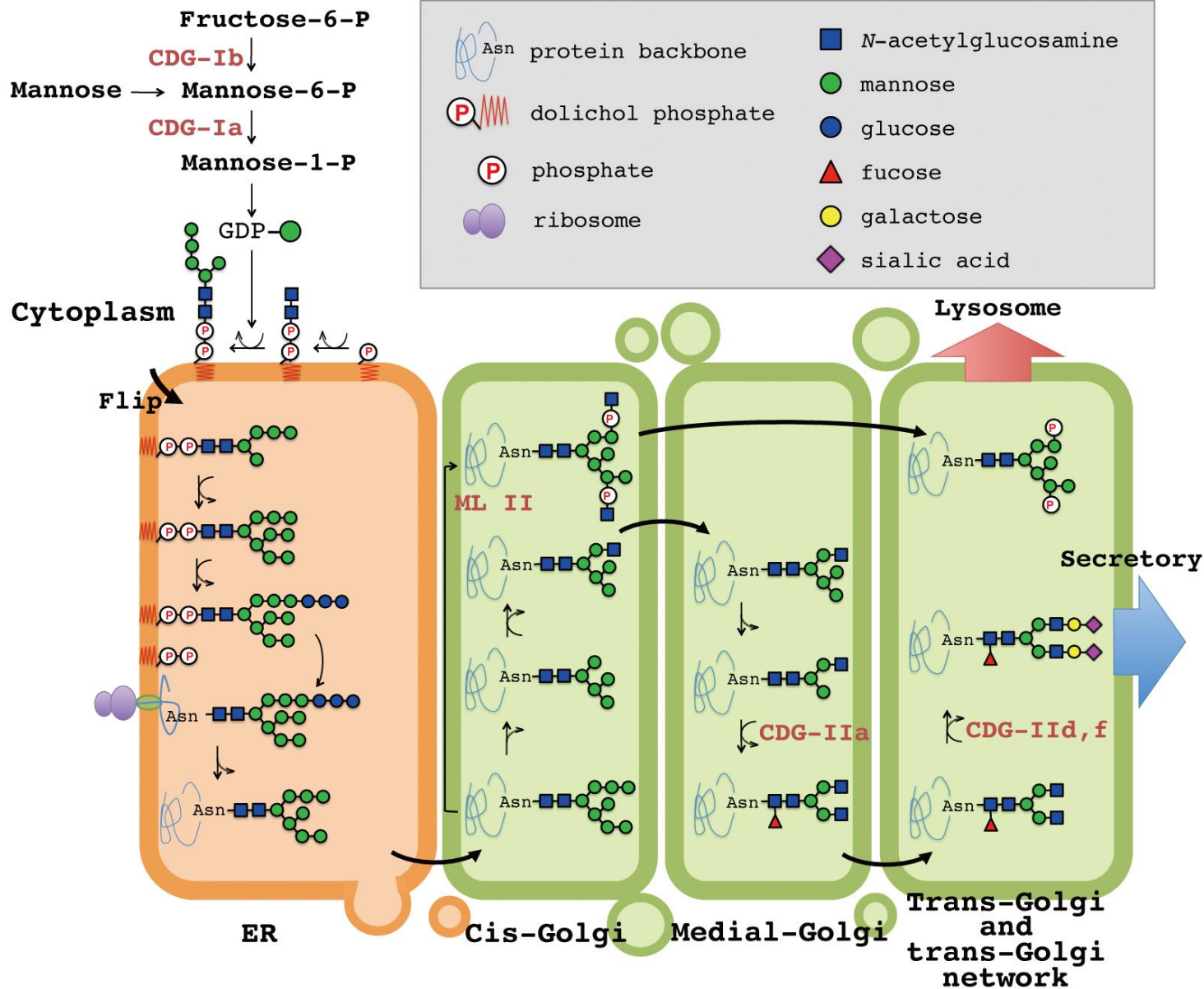
Ribosomal frameshift

HIV-1 Gag and Gag-Pol
(Chapter 18)

Bicistronic mRNAs of dicistroviruses

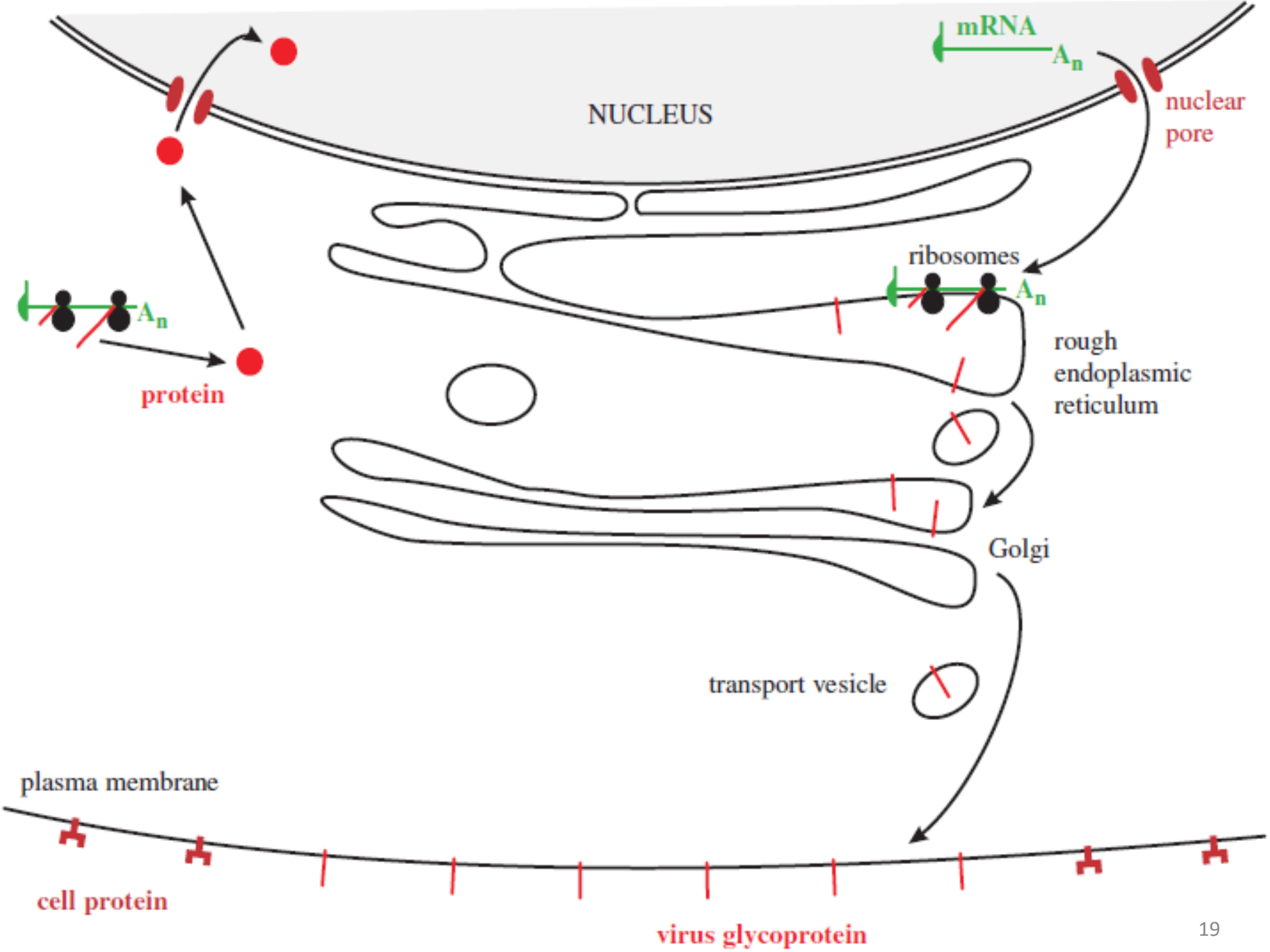


Co- and post translational protein modification



N-glycosylation
(Asn)

O-glycosylation
(Tyr, Ser)



Co- and post translational protein modification

Acylation (addition of Myristic acid)

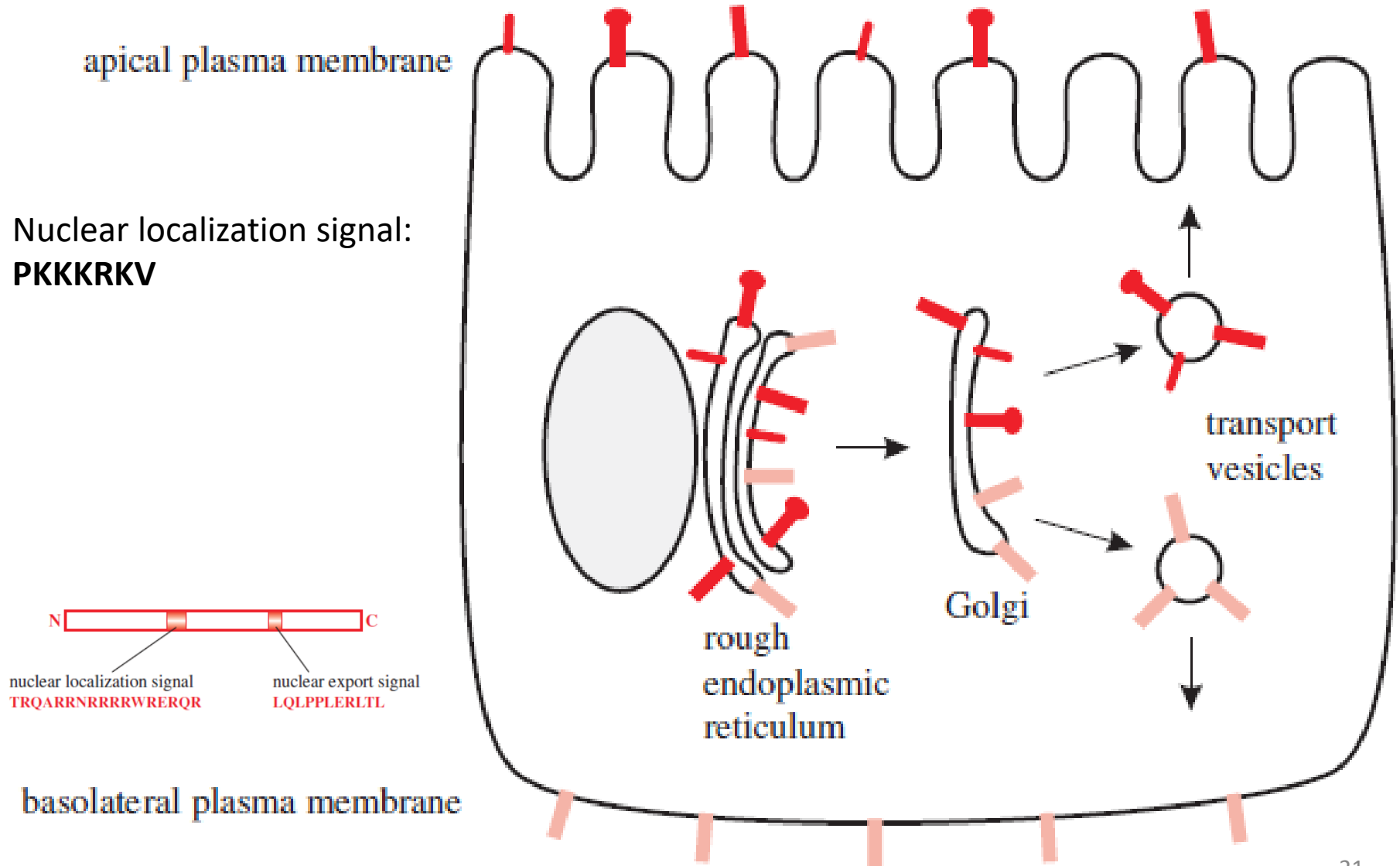
- Gag of HIV
- VP4 of picornaviruses

Phosphorylation

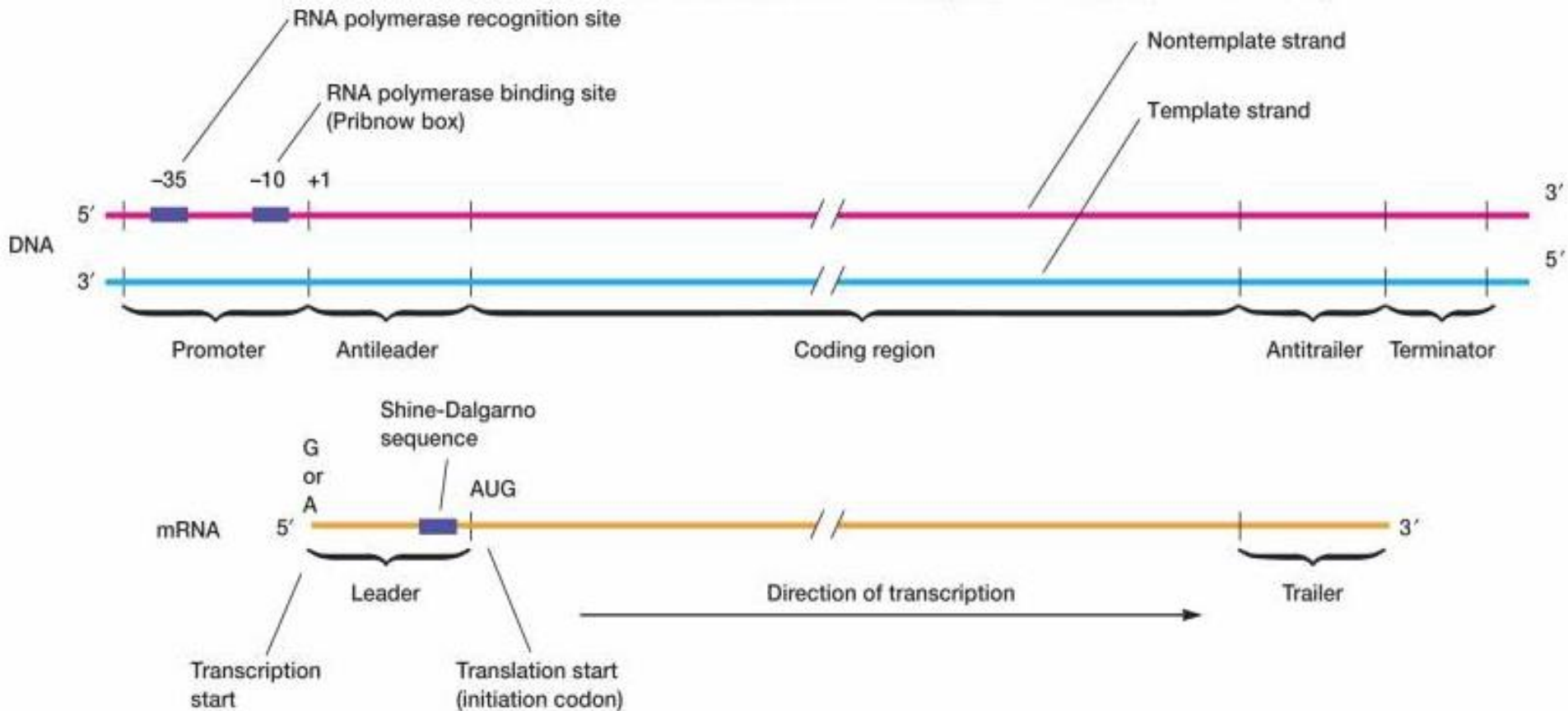
- serine, threonine, tyrosine

Cleavage

Targeting of virus proteins



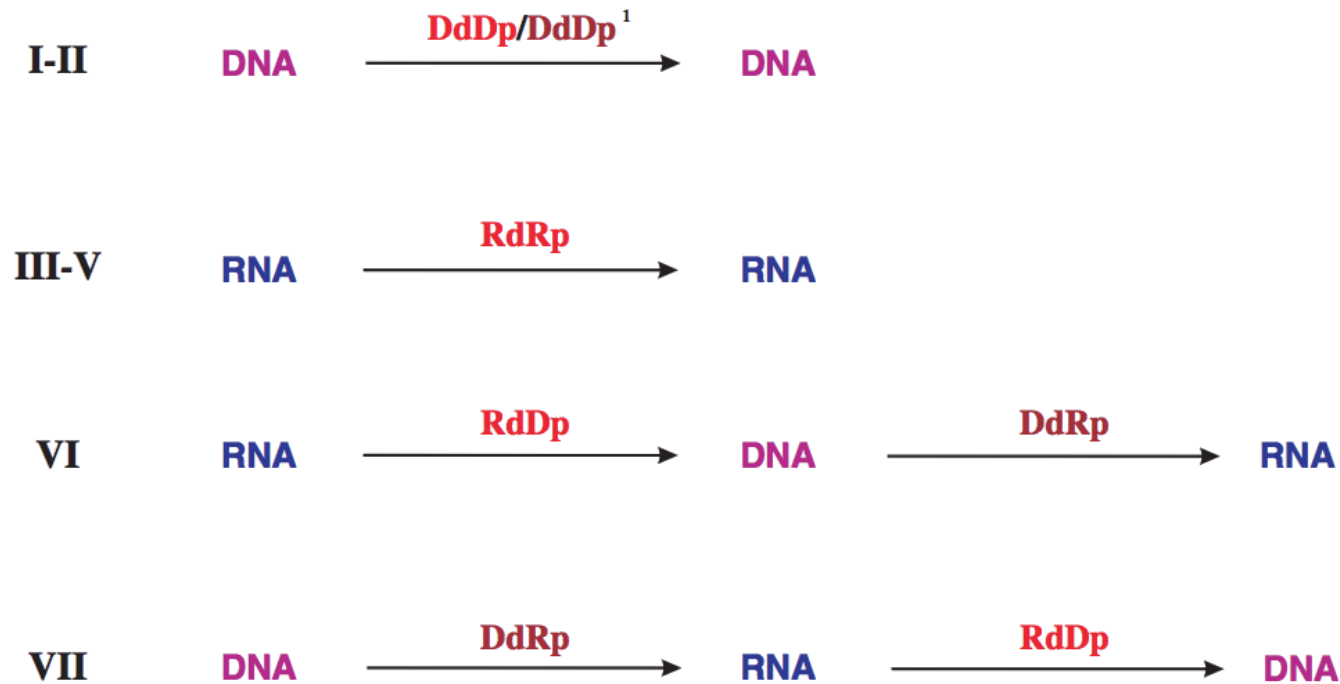
Transcription in bacteria



Learning outcomes

- explain how virus genes are transcribed and translated
- describe the post-translational modifications that some virus proteins undergo
- highlight differences in transcription and translation between prokaryotic and eukaryotic cells
- discuss the transport of virus proteins and RNA within cells

Virus Genome Replication



Virus enzymes: DdDp = DNA-dependent DNA polymerase
RdRp = RNA-dependent RNA polymerase
RdDp = RNA-dependent DNA polymerase (reverse transcriptase)

Cell enzymes: DdDp = DNA-dependent DNA polymerase
DdRp = DNA-dependent RNA polymerase (RNA pol II)

¹ Some dsDNA viruses use a cell DdDp, some encode their own.

CYTOPLASM

some dsDNA viruses

dsRNA viruses

(+) RNA viruses

(-) RNA viruses (non-segmented genomes)

retroviruses & pararetroviruses (RNA → DNA)

NUCLEUS

NUCLEUS

some dsDNA viruses

ssDNA viruses

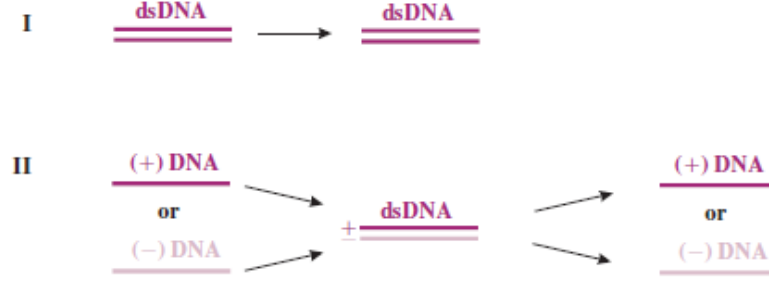
(-) RNA viruses (segmented genomes)

retroviruses & pararetroviruses (DNA → RNA)

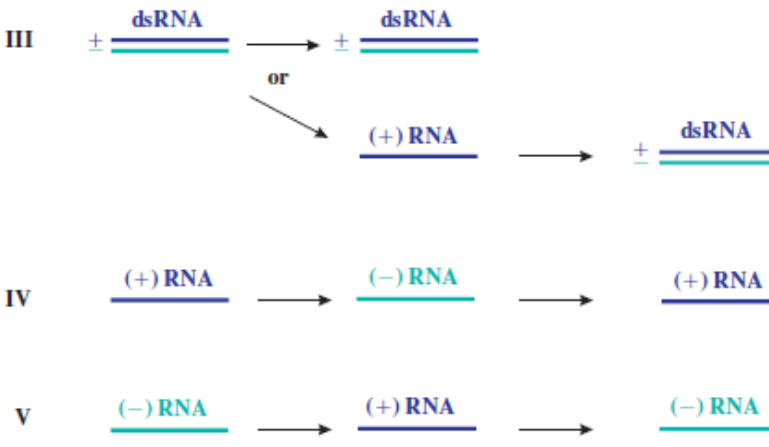
Primers



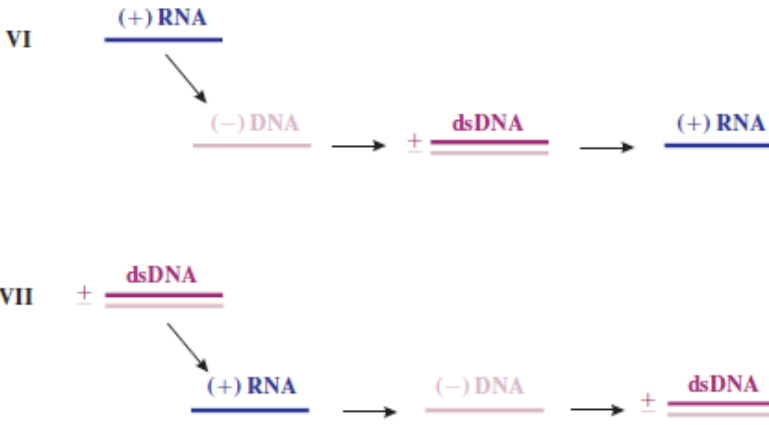
DNA Viruses



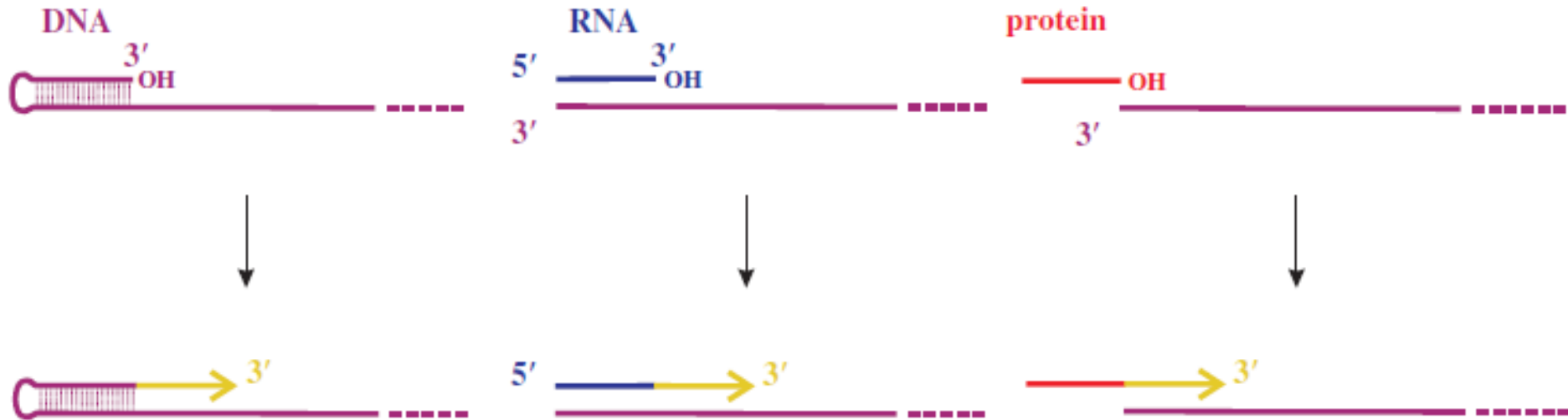
RNA Viruses



Reverse-Transcribing Viruses



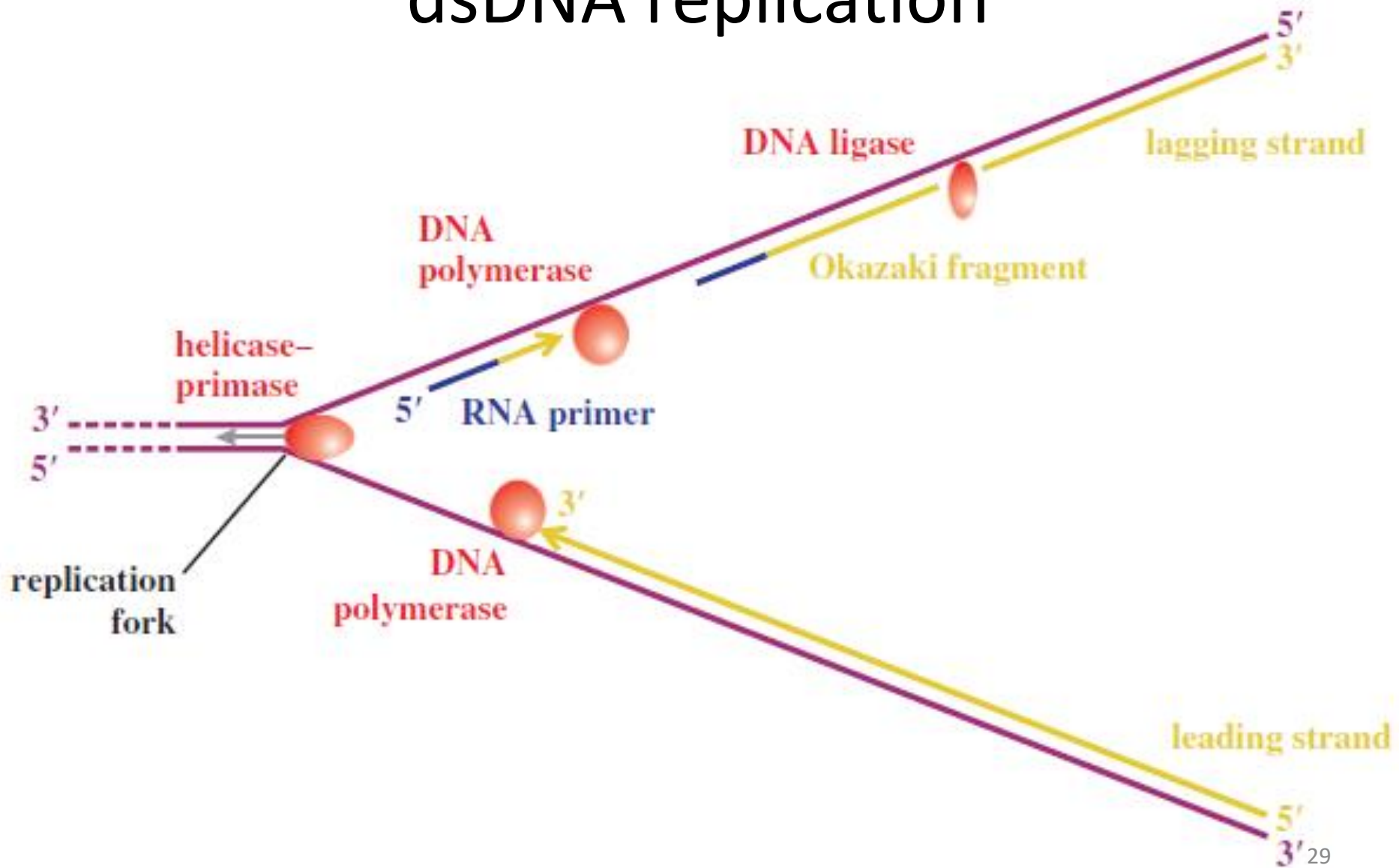
Priming of NA synthesis



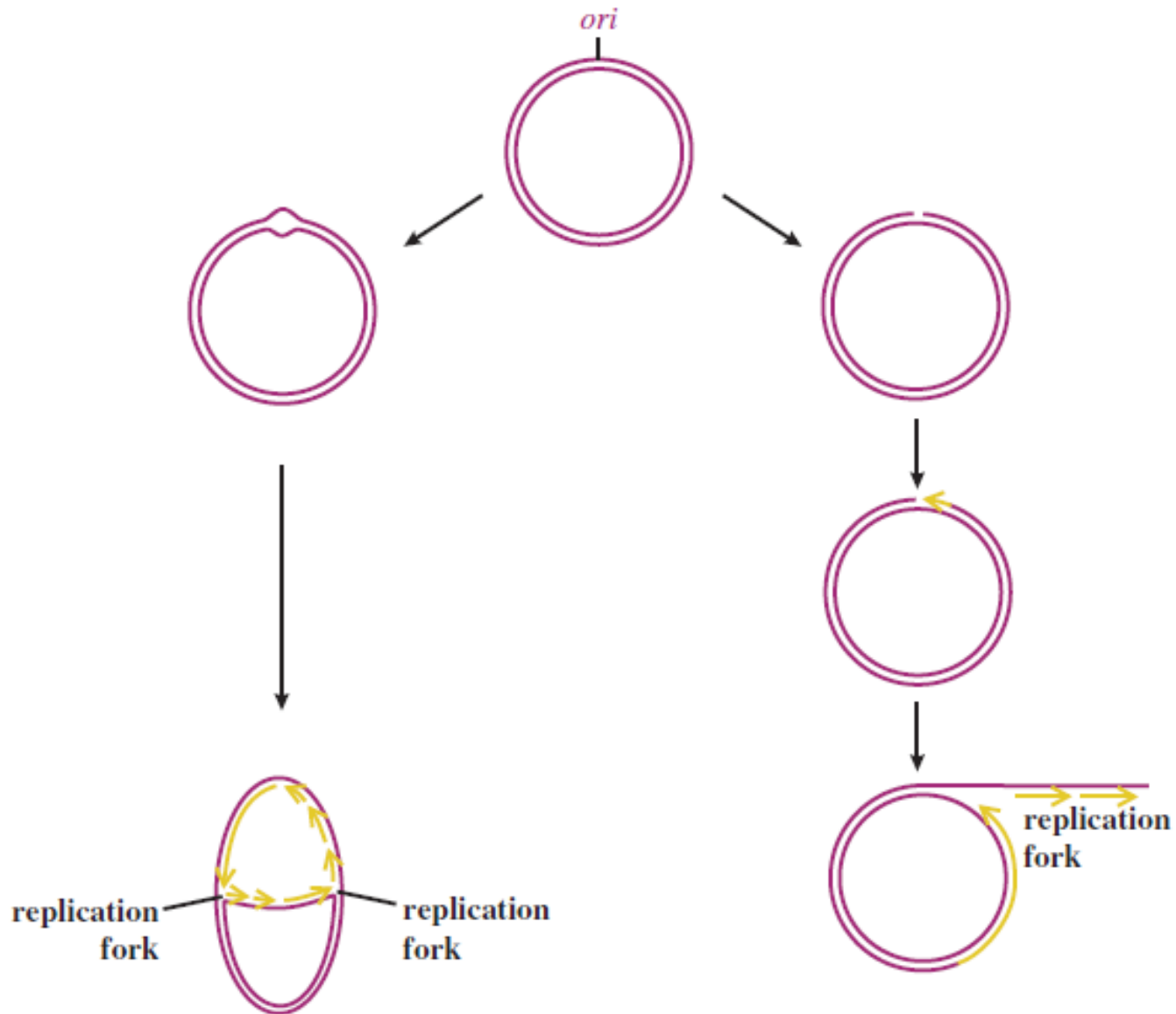
Location of virus replication sites in eucaryotes

Virus genome	Cytoplasm	Nucleus
dsDNA	Some	Some
ssDNA		All
dsRNA	All	
(+) RNA	All	
(-) RNA (non-segmented genome)	All	
(-) RNA (segmented genome)		All
Retroviruses [(+) RNA] } Pararetroviruses [dsDNA] }	ssRNA → dsDNA	dsDNA → ssRNA

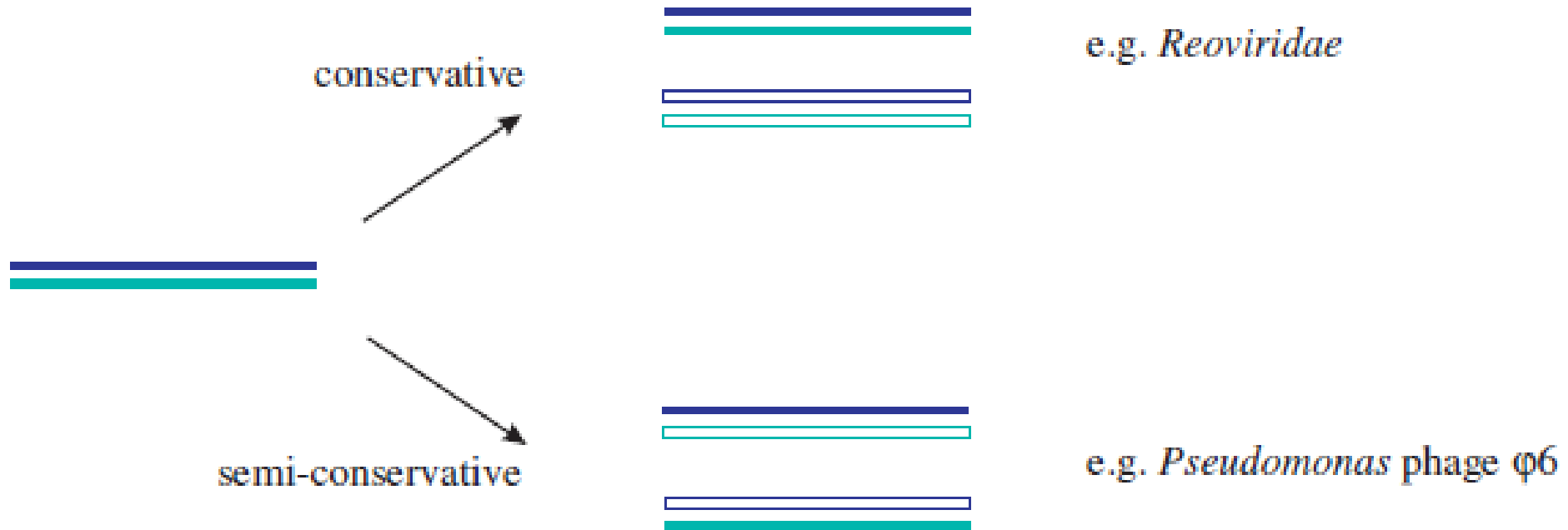
Leading and Lagging strands in dsDNA replication



Rolling circle x “normal” replication



Conservative x semiconservative replication



Replication of retroviruses



Learning outcomes

- state the locations within eukaryotic cells where different categories of virus genome are replicated
- explain the role of primers in virus nucleic acid synthesis
- discuss the roles of virus and host proteins in virus genome replication
- outline the replication mechanisms of virus DNAs and RNAs
- explain the term 'reverse transcription'