

Viruses with dsDNA genomes (2):

Order *Herpesvirales*



More than 100 viruses of

mammals, birds, fishes, reptiles, amphibians and shellfish.

Commonalities: genome type and size, virion type, viral cycle (infection types)

Herpesviridae - mammals, birds, reptiles

Subfamilies: α -, β -, γ -*herpesvirinae*

Eight human viruses from three subfamilies.

•HHV-1 (*Human herpesvirus 1*) = HSV-1 (Herpes simplex virus), contact transmission, mucosa, skin, cornea infections (epithelial cells), transport to the neuron nuclei.

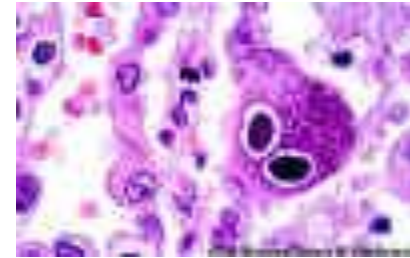
Persistent , latent infection, symptoms during productive (acute) infection.

HHV-2 = HSV-2, genital herpes, sexually transmitted, epithelial cells, infant mortality is 54% !

HHV-3 = VZV (varicella-zoster), chickenpox and shingles, aerosol (droplet) transmission usually in childhood, latent in neurons of head and torso.

HHV-4 = EBV (Epstein-Barr), infects epithelial and B-cells (latent in B-cells), infectious mononucleosis (a kissing disease – transmitted by saliva), Burkitt's lymphomas (endemic, sporadic, AIDS related), nasopharynx carcinoma, Hodgkin lymphoma, non-Hodgkin lymphoma in AIDS patients, lympho-proliferative disturbance in transplanted patients.

- HHV-5 = (h)CMV (Human cytomegalovirus) – mild or symptomless infections in monocytes and epithelia, dangerous for fetus, newborn children (brain, liver, spleen, mental illness, deafness, death), immunocompromised patients (lungs, liver). Transmission-saliva, urogenital excretions, placenta, milk



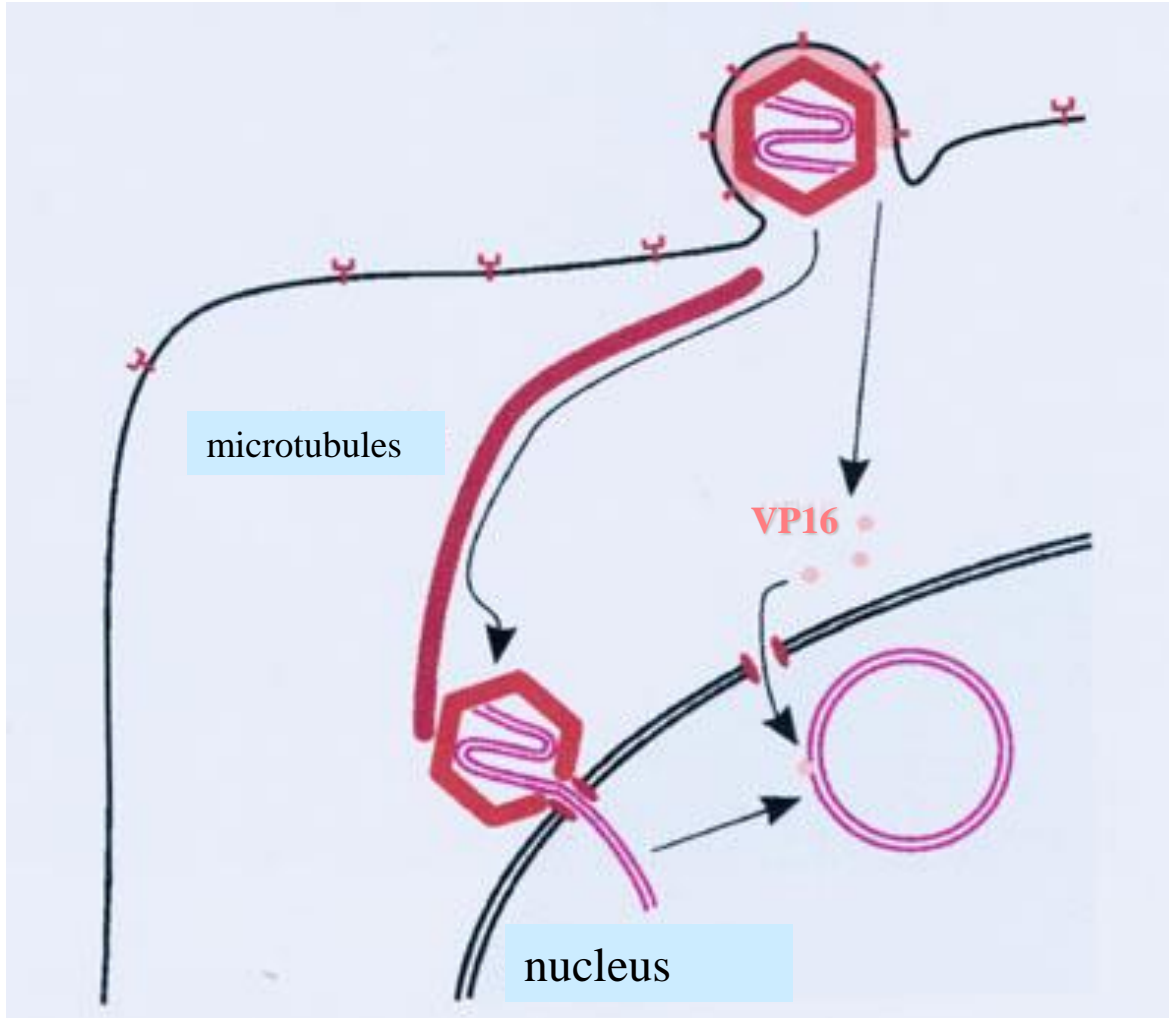
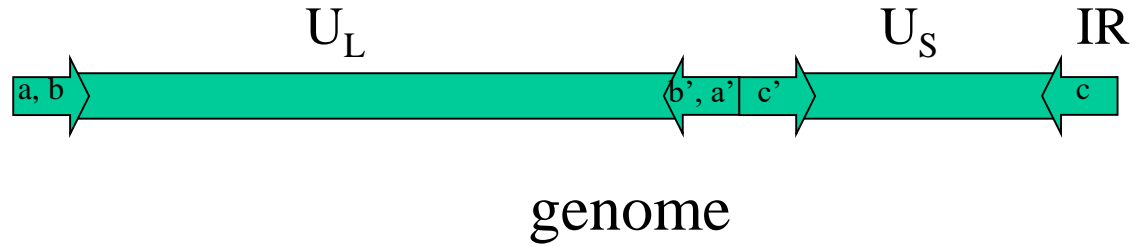
<http://pathmicro.med.sc.edu/virol/herpes.htm>

- HHV-6 – children, fever and rash – *Exanthem subitum (roseola infantum)*, MS?, chronic fatigue? Transmission by saliva, contact, episome integrates, T-cells and?
- HHV-7 - from CD4 T-cell culture of a healthy person, in saliva, urogenital excretions.
- HHV-8 - Kaposi's sarcoma, isolated in 1994 from tumor tissue, in lymphocytes and other cell types.





HHV-1
virion

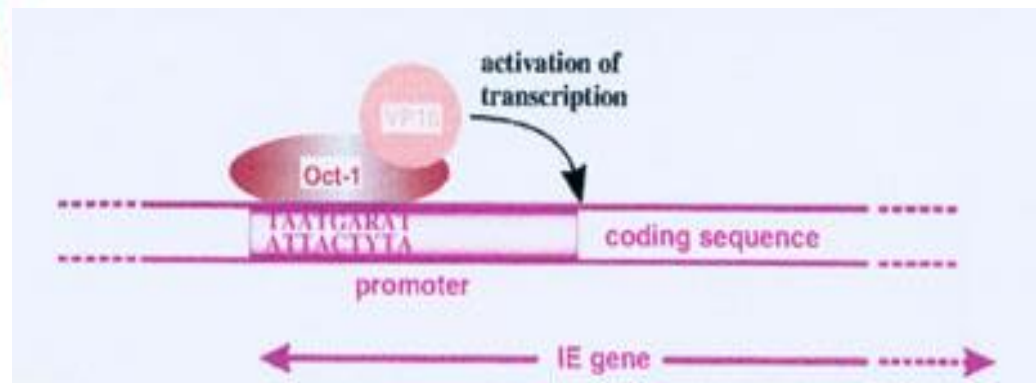
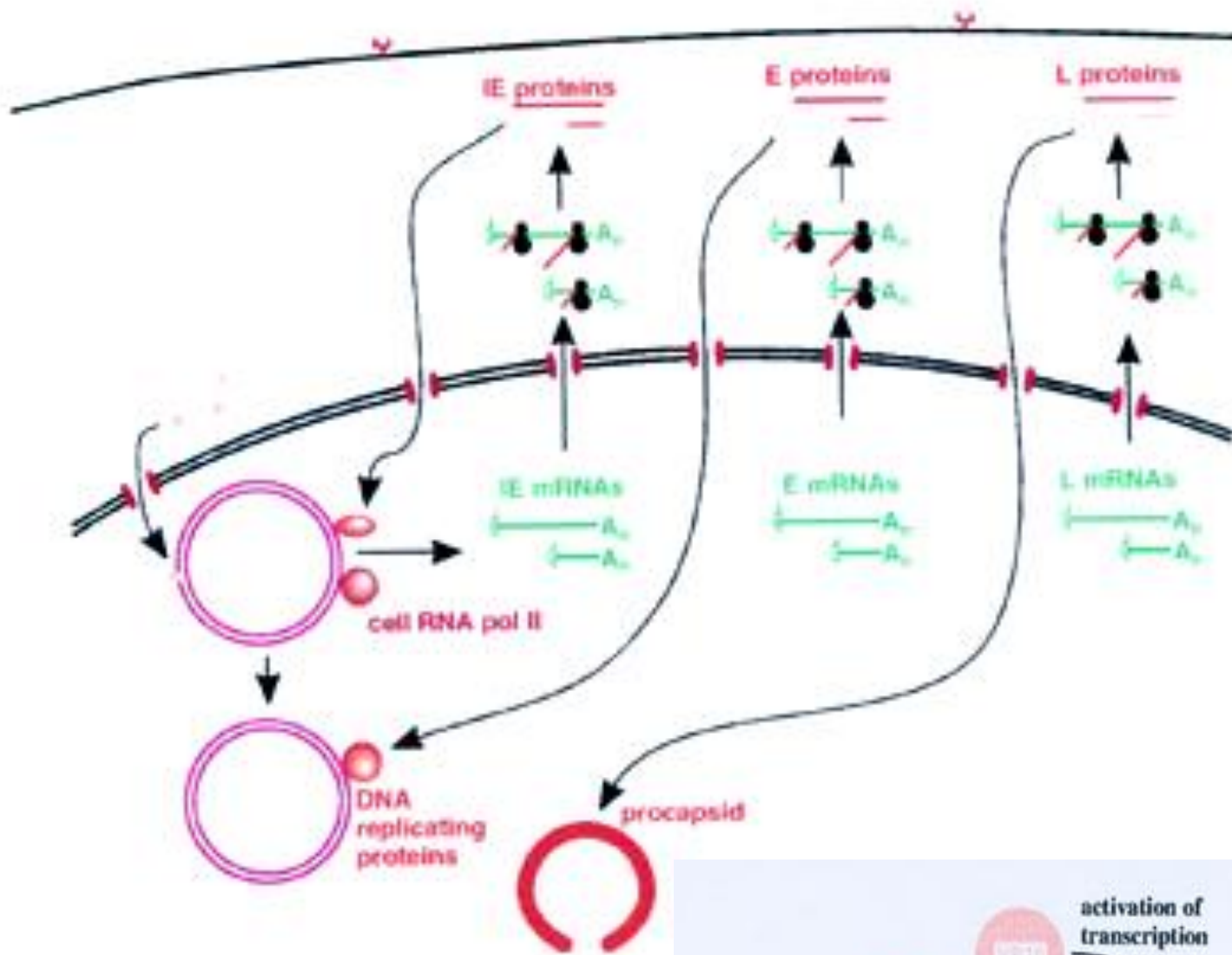


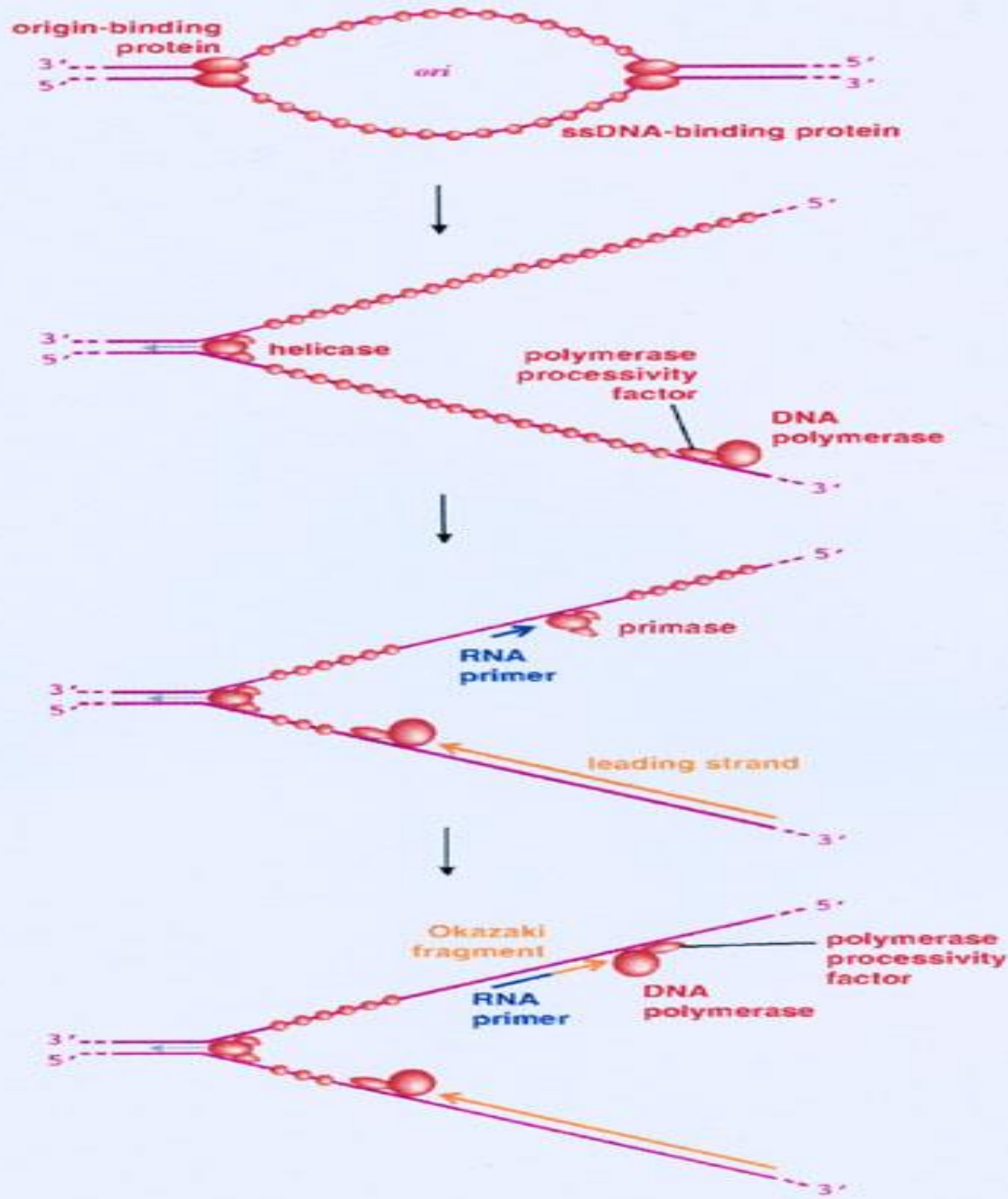
Linear genome
circularizes!

Encodes about 70 proteins.

Virion proteins:

- tegument – min. 15 proteins (VP16) + viral mRNAs
- (nucleo)capsid - VP5
- envelope with at least 12 glycoproteins (gB, gC, gD)





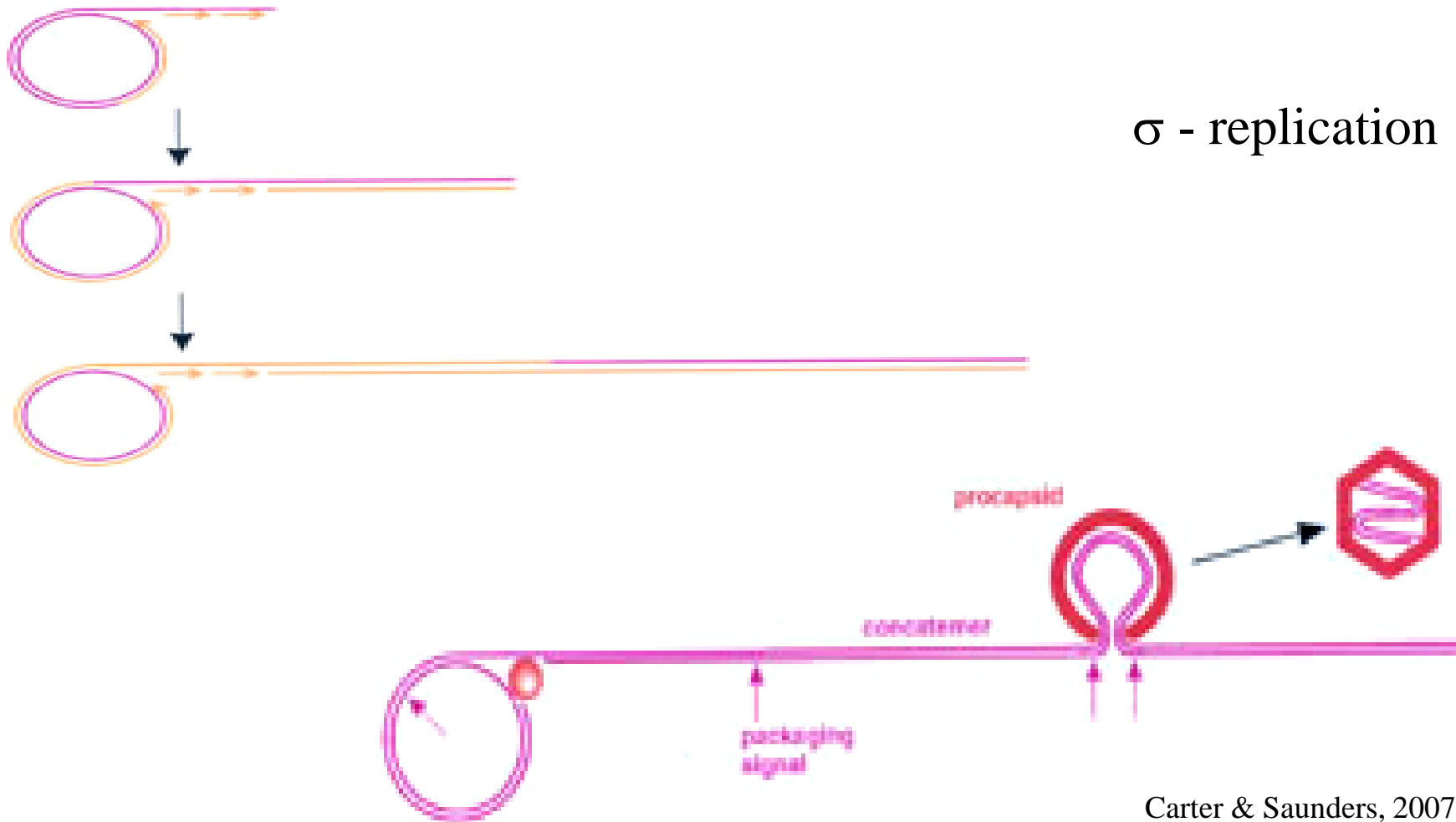
θ – replication

- proteins bind to 1/3 origins of replication.

-seven E proteins essential

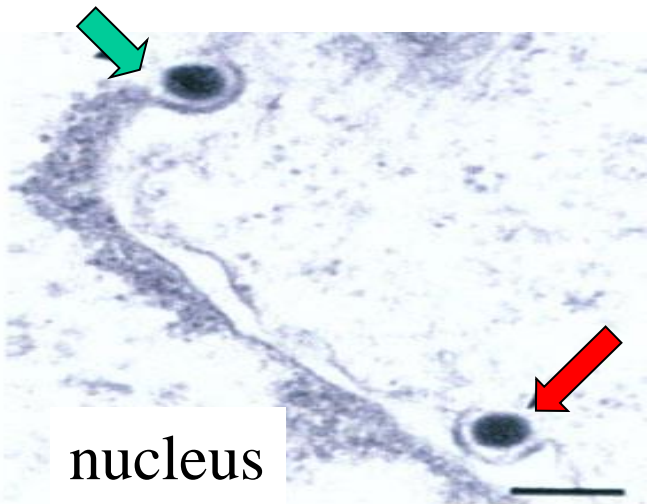
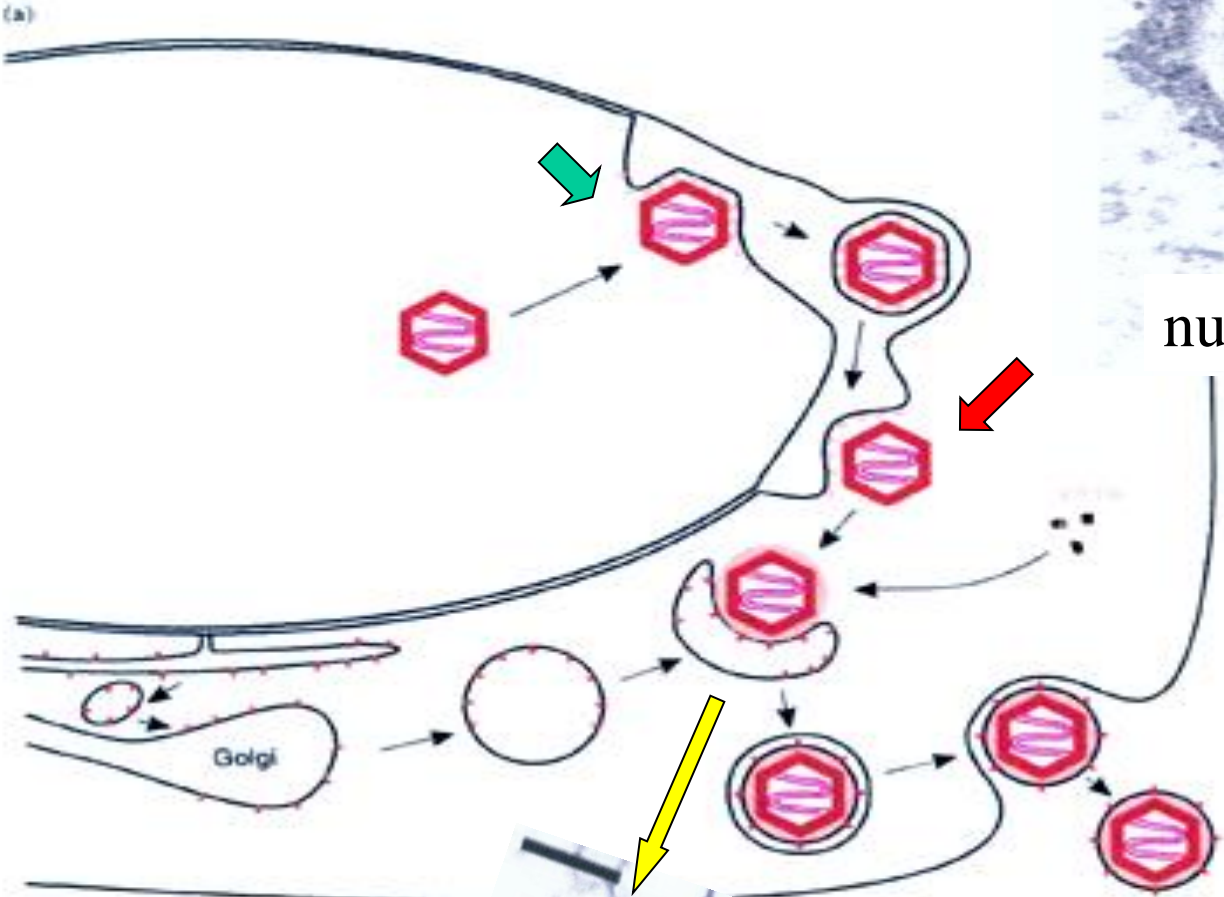


Strauss & Strauss, 2002.

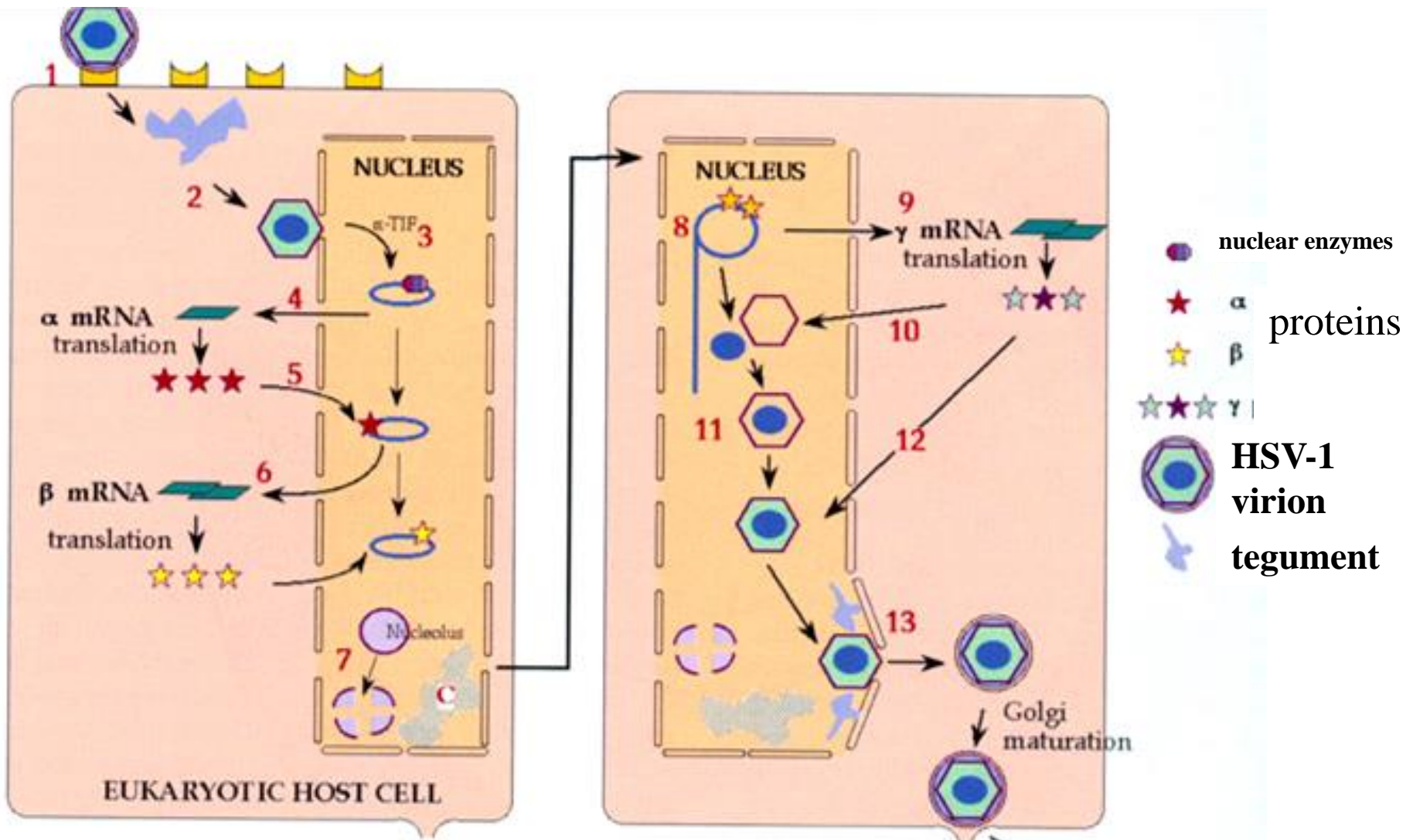


Carter & Saunders, 2007.

HHV-1 exit



Adapted from Carter & Saunders, 2007.



- HHV-1 replication cycle (transcriptome regulation)
- vegetative (“lytic”) and latent infection

How does a herpesvirus maintains latency?

HHV LATs – Latency Associated Transcripts

DNA HHV-1 genome region called Latency Associated Transcript Region is in the terminal repeats.

A set of micro RNAs (miRNAs) important for latency is also transcribed from the same locus.

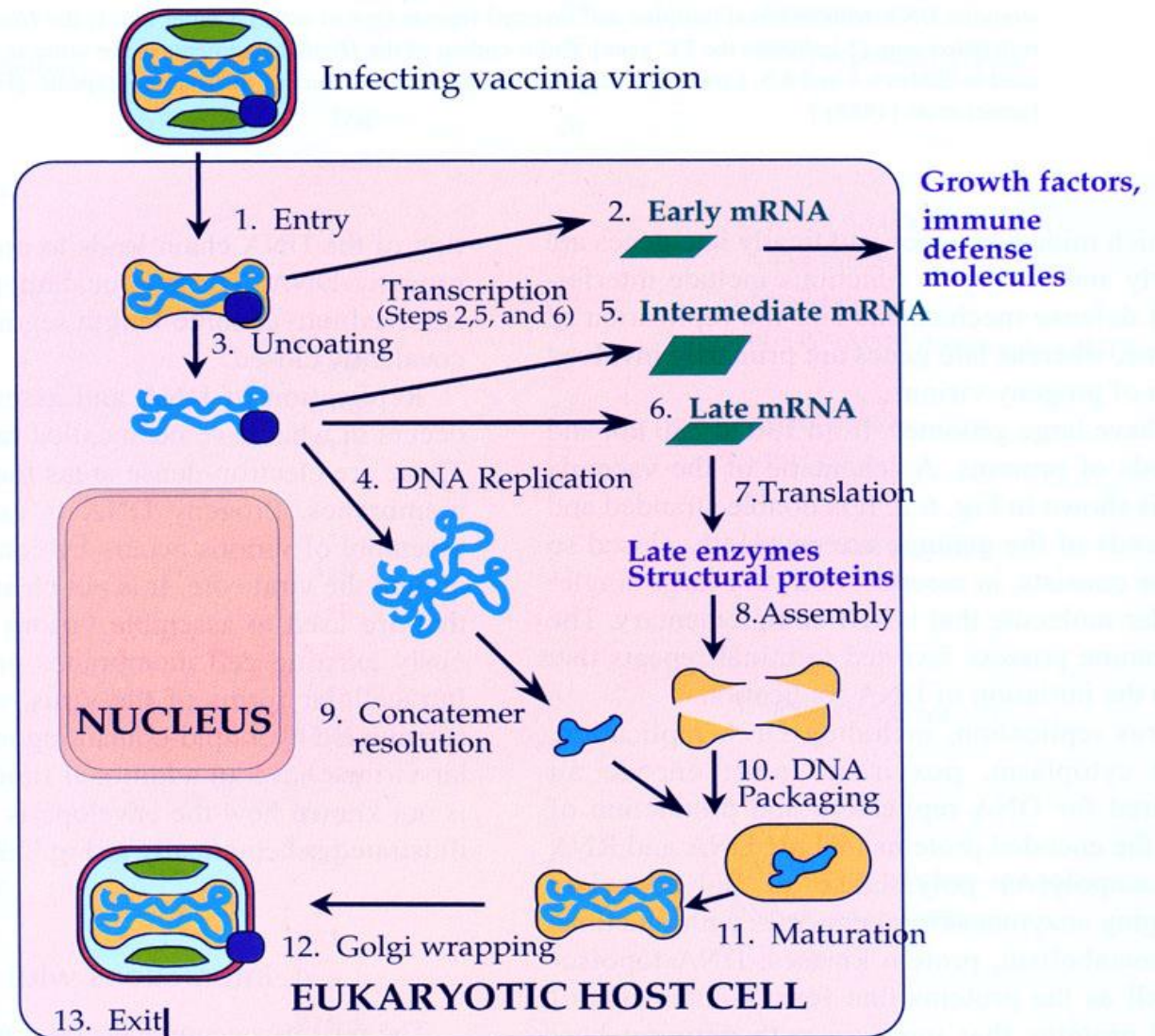
Farrell et al. 1991. Herpes simplex virus latency-associated transcript is a stable intron. *Proceedings of the National Academy of Science (USA)* 88: 790–794.

Phelan D, Barrozo ER, Bloom DC. 2017. HSV1 latent transcription and non-coding RNA: a critical retrospective. *J Neuroimmunol* 308:65–101. <https://doi.org/10.1016/j.jneuroim.2017.03.002>.

Singh N, Tschärke DC. 2020. Herpes simplex virus latency is noisier the closer we look. *J Virol* 94:e01701-19. <https://doi.org/10.1128/JVI.01701-19>.

Family	Subfamily	Genus	Species (virus)
<i>Poxviridae</i>			
	<i>Chordopoxvirinae</i>	<i>Avipoxvirus</i>	fowlpox
		<i>Capripoxvirus</i>	sheeppox
		<i>Leporipoxvirus</i>	myxoma
		<i>Molluscipoxvirus</i>	<i>Molluscum contagiosum</i>
		<i>Orthopoxvirus</i>	vaccinia
			variola (major, minor)
		<i>Parapoxvirus</i>	orf,
			pseudocowpox (pseudovaccinia)
		<i>Suipoxvirus</i>	swinepox
		<i>Yatapoxvirus</i>	Yaba monkey tumorvirus
			Tanapox monkey virus
	<i>Entomopoxvirinae</i>	<i>Entomopoxvirus A</i>	<i>Melolontha melolontha</i> entomopoxvirus
		<i>Entomopoxvirus B</i>	<i>Amsacta moorei</i> entomopoxvirus
		<i>Entomopoxvirus C</i>	<i>Chironomus luridus</i> entomopoxvirus

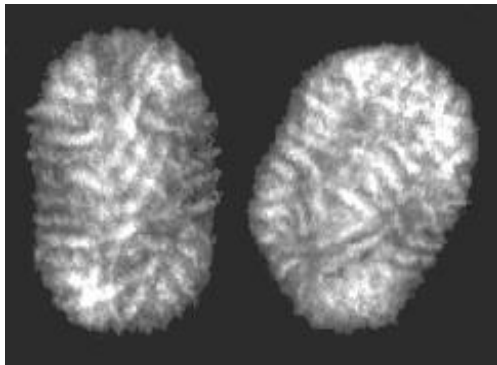
Linear dsDNA-genome with covalently closed ends, 130-300 kbp. More than 200 genes, about 100 proteins, complex structure, complete cycle in the cytoplasm.



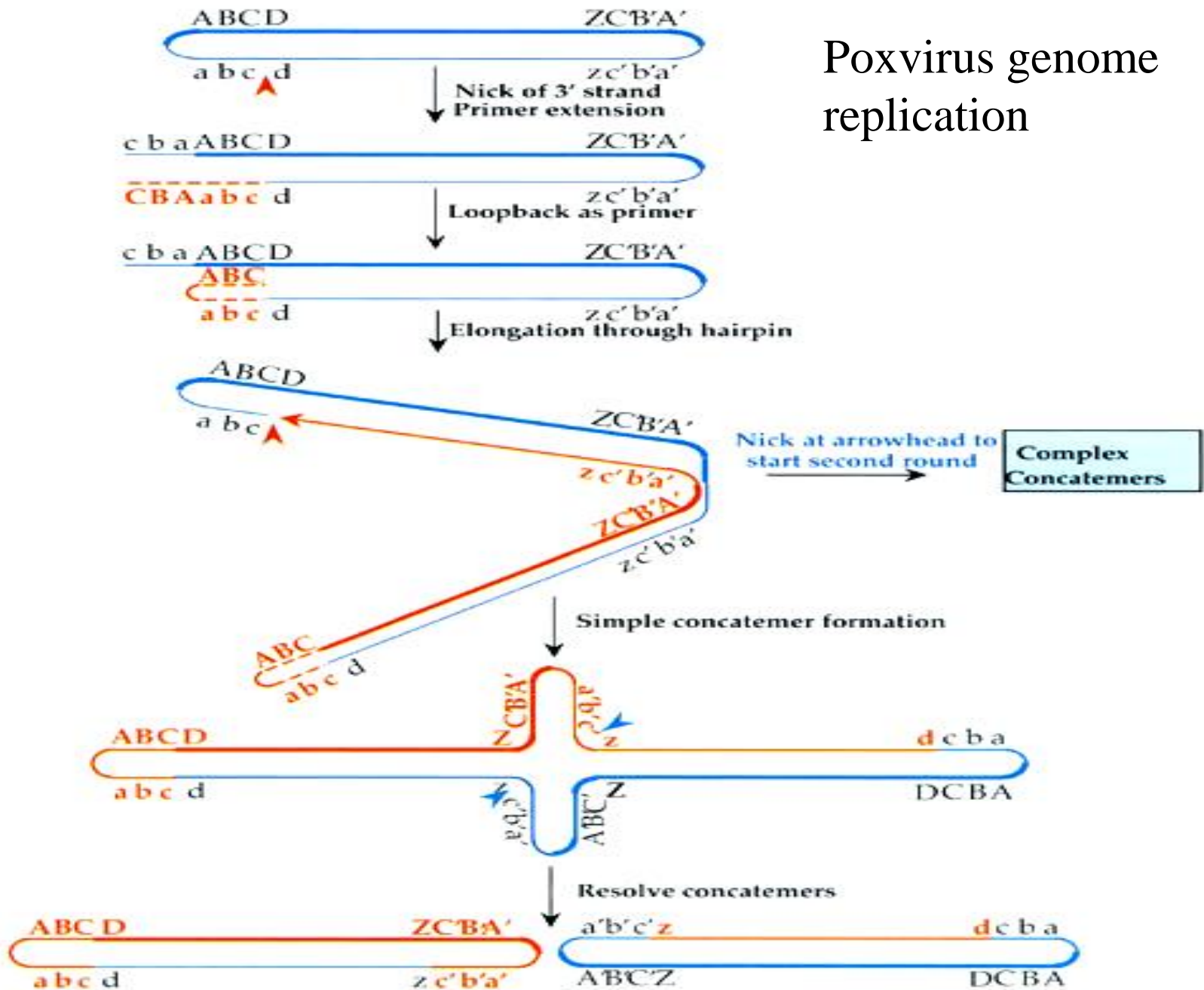
Virion associated enzymes

- RNA polymerase
- Transcription factors
- Capping enzyme
- Poly(A) polymerase

Strauss & Strauss, 2002.



Poxvirus genome replication



Baculoviridae – 90-160 kbp genome, big but not in the NCLDV group in literature, may be a seminar topic.

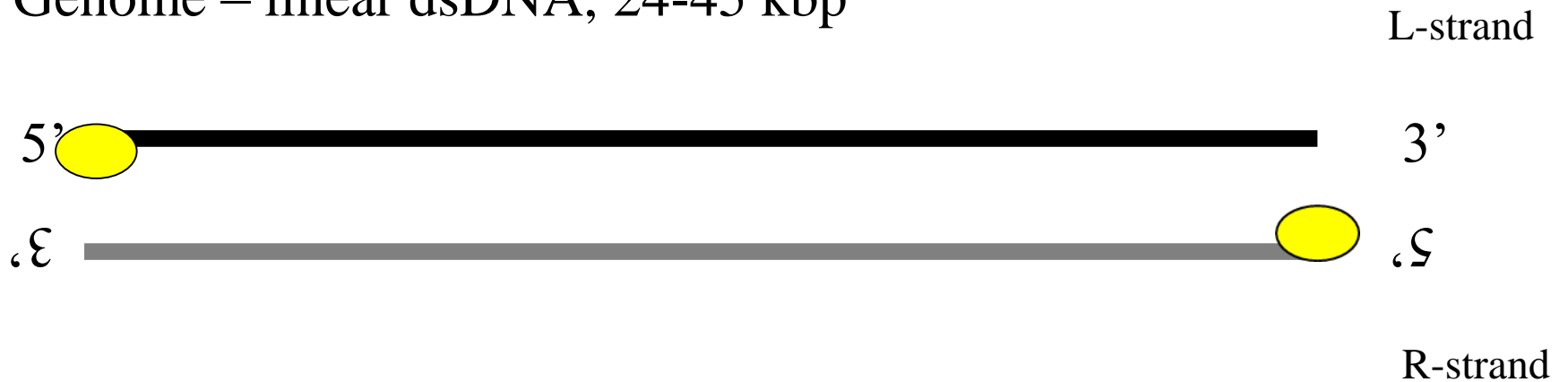
Main features for viruses with big dsDNA genomes :

- complex,
- genes in both DNA strands,
- linear genomes or linear that can circularize (**Herpes** and **Pox**)
- not found in plant hosts,
- may cause tumors,
- important cloning vectors,
- important in gene therapy.

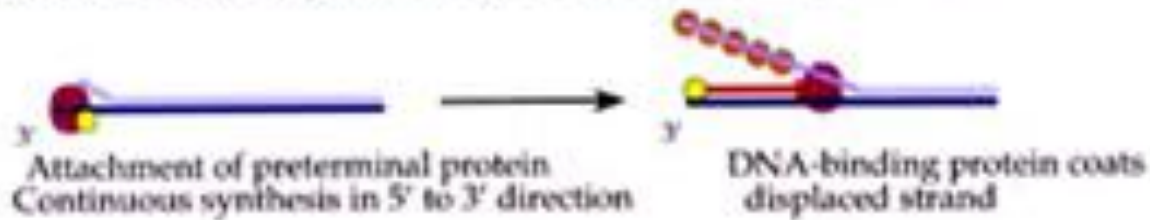
Adenoviridae

70-100 nm, preterminal protein -  primer for DNA synthesis .

Genome – linear dsDNA, 24-45 kbp

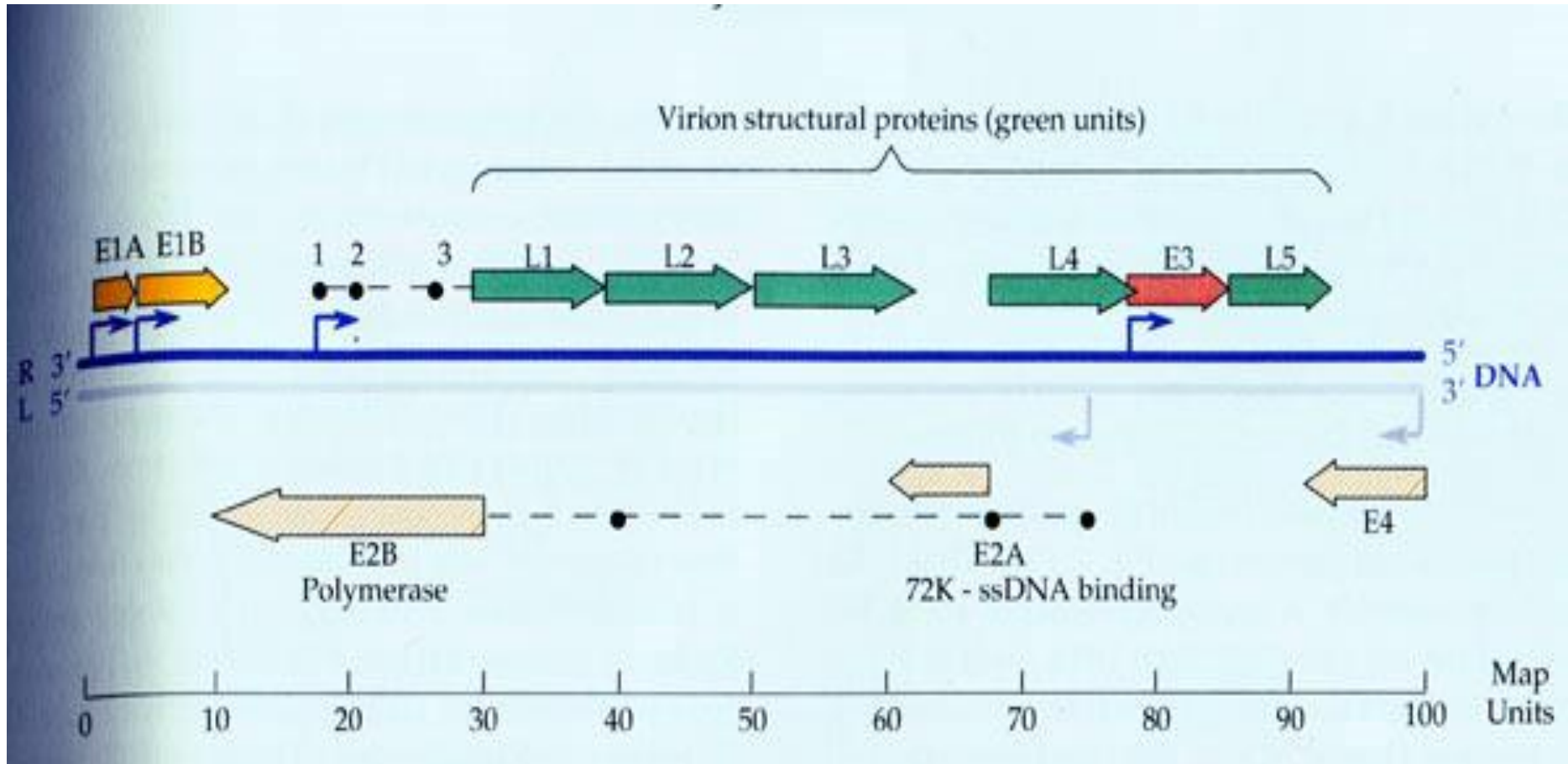


○ Adenovirus DNA Replication by Displacement Synthesis



Human adenovirus type 2 – genome organization and transcription

(36 kbp)



Adenoviral oncogenic proteins (E1A, E1B) interact with cellular proteins

