

MOLECULAR VIROLOGY

Introduction

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Literature

Bernard N. Fields, David M. Knipe, Peter M. Howley (1996)
"Virology"
Lippincott Williams & Wilkins Publishers.

Susanne Modrow, Dietrich Falke (1997)
"Molekulare Virologie"
Spektrum Verlag

John M. Coffin, Stephen H. Hughes, Harold E. Varmus. (1997).
"Retroviruses".
Cold Spring Harbor Laboratory Press.

Internet

<http://www.virology.net/>



Virus lat. poison /slime

Causative agent of infectious diseases of man, animals, plants and bacteria.

Historical: “Ultra-filterable infectious agent ”
(▲ size 20-300 nm)

Modern: intracellular parasit
no independent metabolism (no ribosomes
and mitochondria)

First description of viral infection



Ruma

1.500 B.C.

Viruses as tools for molecular biology

1952: T4 bacteriophage

DNA is infectious = DNA carries genetic

1970: polyadenylation (Vaccinia virus)

1970: reverse transcriptase (Rous sarcoma virus)

1977: RNA splicing (SV40)

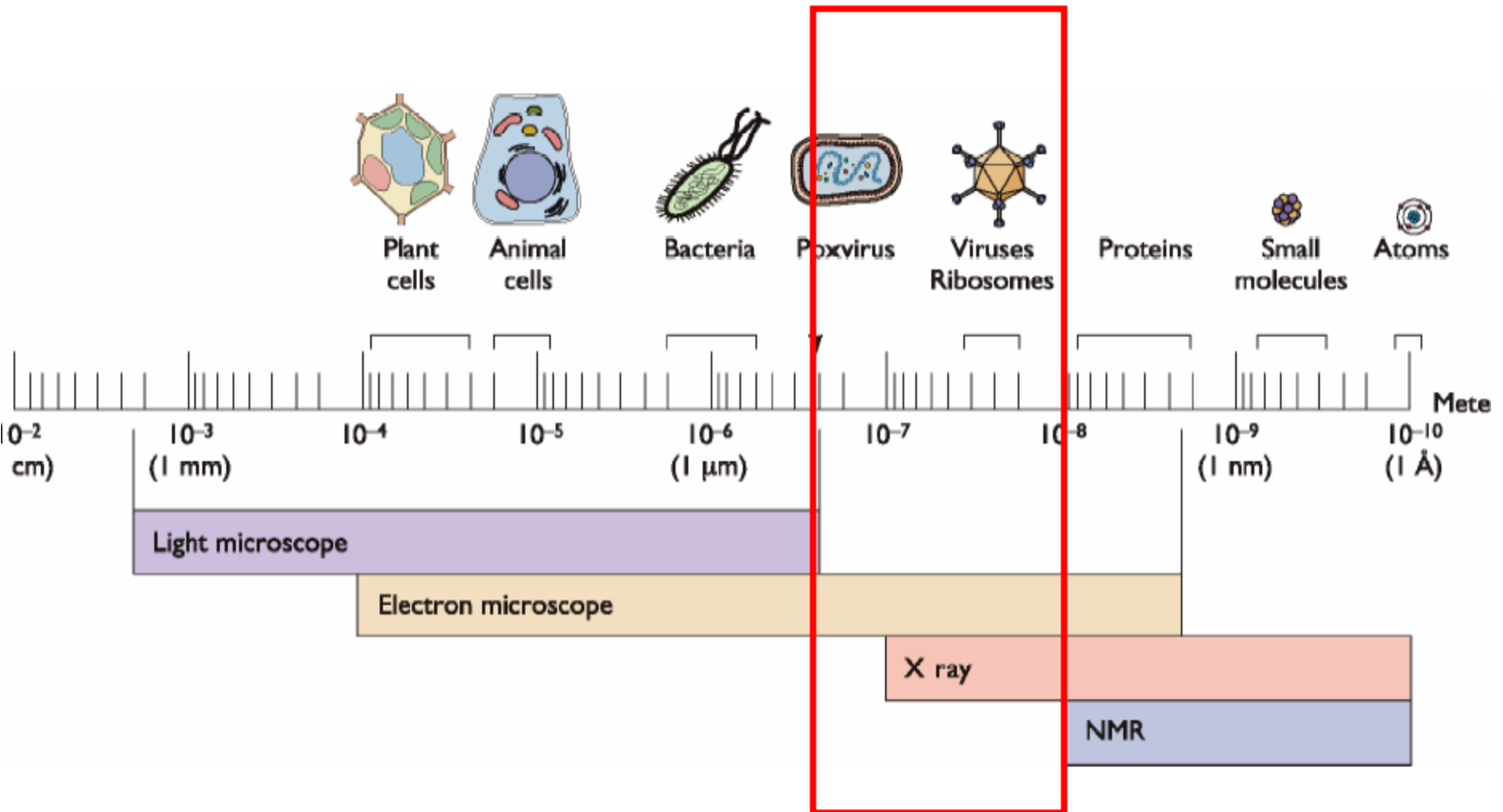
1981: Enhancer elements (SV40)

1983: Histone-nucleosome structure of DNA
Transcription factors (SV40)

Viruses, Bacteriophages, Viroids u. Prion

Agent	genetic material	size	number of proteins
Virus Bacteriophages	DNA/RNA	10-330nm	1-200
Viroids (plants)	RNA	<10nm	non
Prion	none	3-5nm	1

Dimensions I



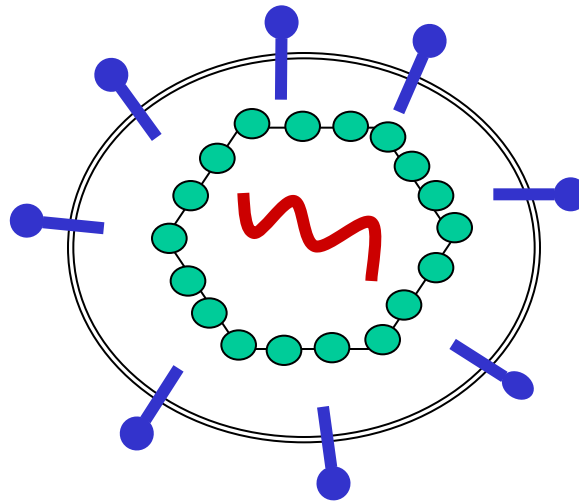
Dimensions II

Humans ca. 30,000 Gene
(5 x 10⁹ Bp)

E. Coli ca. 2,000 Gene
(4 x 10⁶ Bp)

Viruses 1 – ca. 250 Gene
(ab ca. 2,000 Nukleotide)

VIRUS STRUCTURE

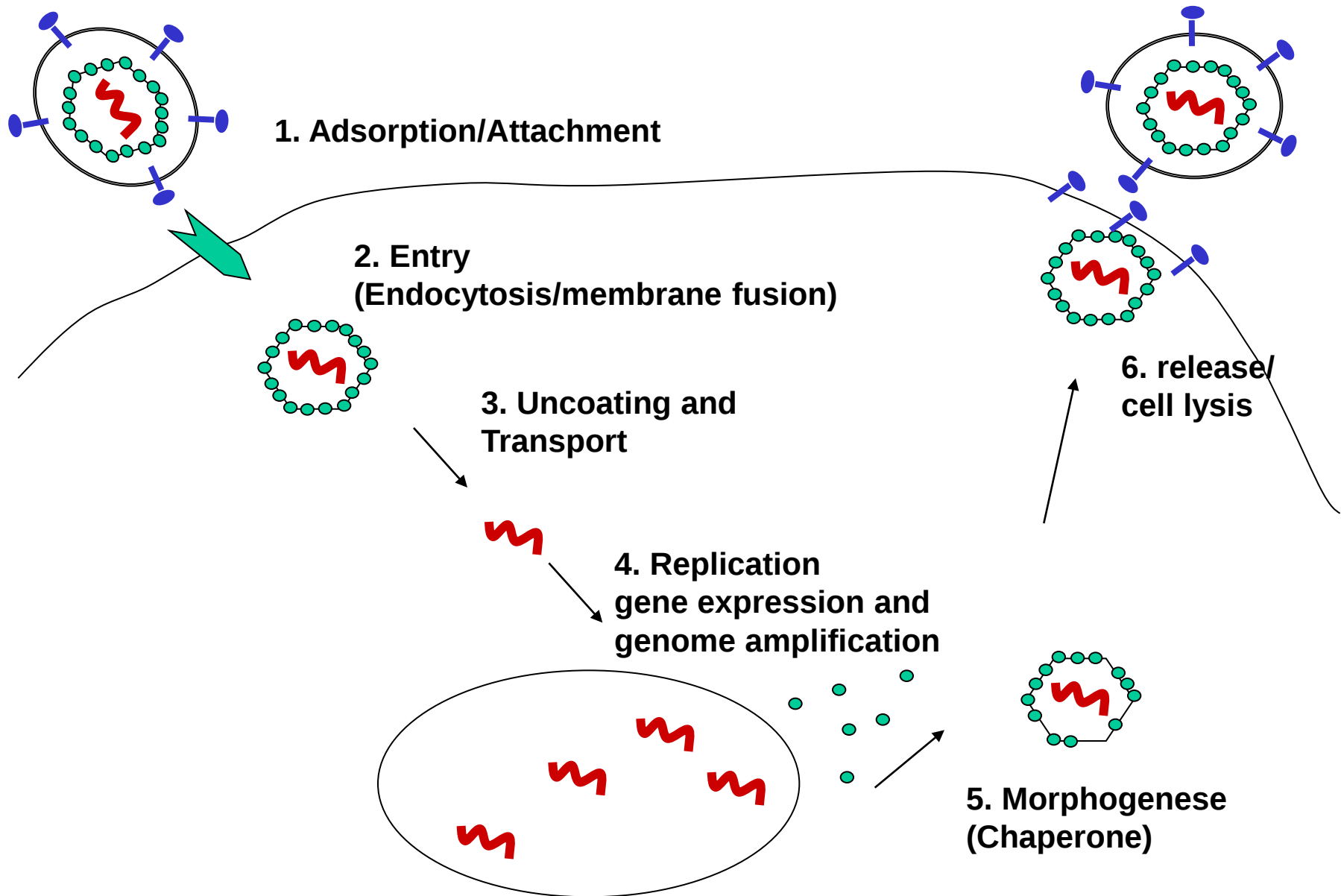


**Genome:
DNA/RNA**

**protection:
protein**

cover (Envelope)

VIRUS REPRODUCTION



Virus families

1. type of genome: RNA/DNA, +/- strand, ss/ds, segmented/continuous
2. Symmetry of the capsid
3. Presence of envelope

Further subdivision in **Genera** and **Virustypes** is based on serology and genome sequence.

<u>Virus family</u>	<u>Genus</u>	<u>example</u>	<u>envelope</u>	<u>Capsidform</u>	<u>Genom</u>
Picorna viridae	Entero virus	Polio	no	Ikosaeder	+ssRNA
Retro- Viridae	Lenti- virus	HIV	yes	conus	+ssRNA, dsDNA

Virus Types

+ssRNA genome

Picornavirus	(Polivirus, Hepatitis A, Rhinovirus)
Flavivirus	(Gelbfieber, Denguevirus, Hep C)
Togavirus	(Rötelnvirus)
Coronavirus	(HCV)
Calicivirus	(Hep E, Norwalkvirus)

-ssRNA continuous genome

Rhabdovirus	(Tollwut)
Paramyxovirus	(Parainfluenza, Masern, Mumps)
Filovirus	(Marburg-, Ebolavirus)
Bornavirus	(Bornavirus (Pferd))

dsDNA

Hepadnavirus	(Hepatitis B)
Papovavirus	(Polyoma-, Papilloma)
Adenovirus	(Adenoviruses)
Herpesvirus	(Simplex, Varicella, CMV)
Poxvirus	(Variola, Vaccinia)

-ssRNA segmented genome

Orthomyxovirus	(Influenza A, B)
Bunyavirus	(La-Crosse Virus, Hantaanvirus)
Arenavirus	(LCMV, Lassavirus)

ssDNA

Parvovirus	(Parvovirus, AAV)
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dsRNA

Reovirus	(Reo-, Rotavirus)
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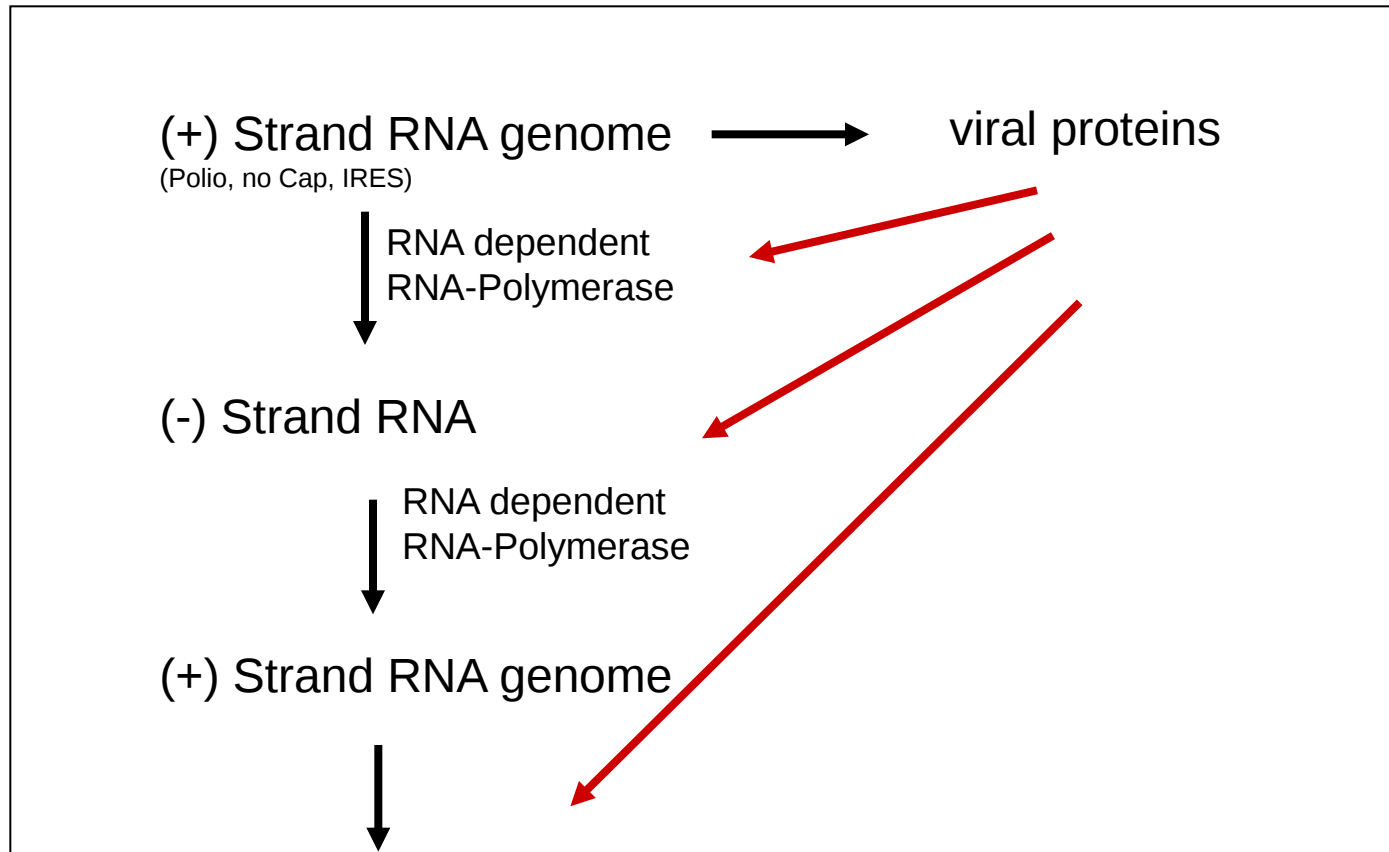
ssRNA with dsDNA

Retrovirus	(Onco-, Lenti-, Spumaviruses)
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Viral replication strategy

(+) ssRNA Virus

Virus particle

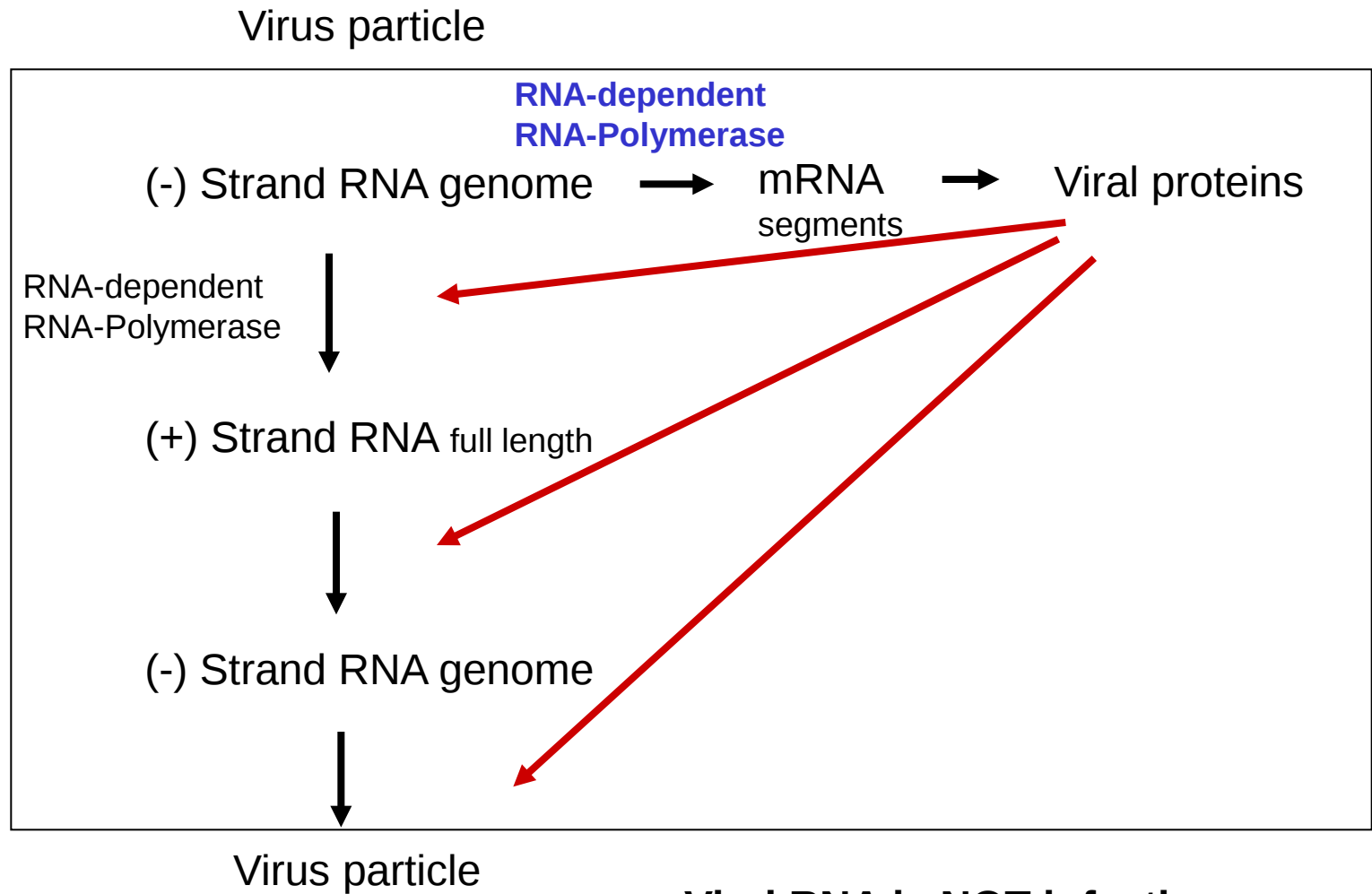


Virus particle

Picornavirus
(Poliovirus, Kinderlähmung)

Viral RNA is infectious
Virus particle without essential enzymes

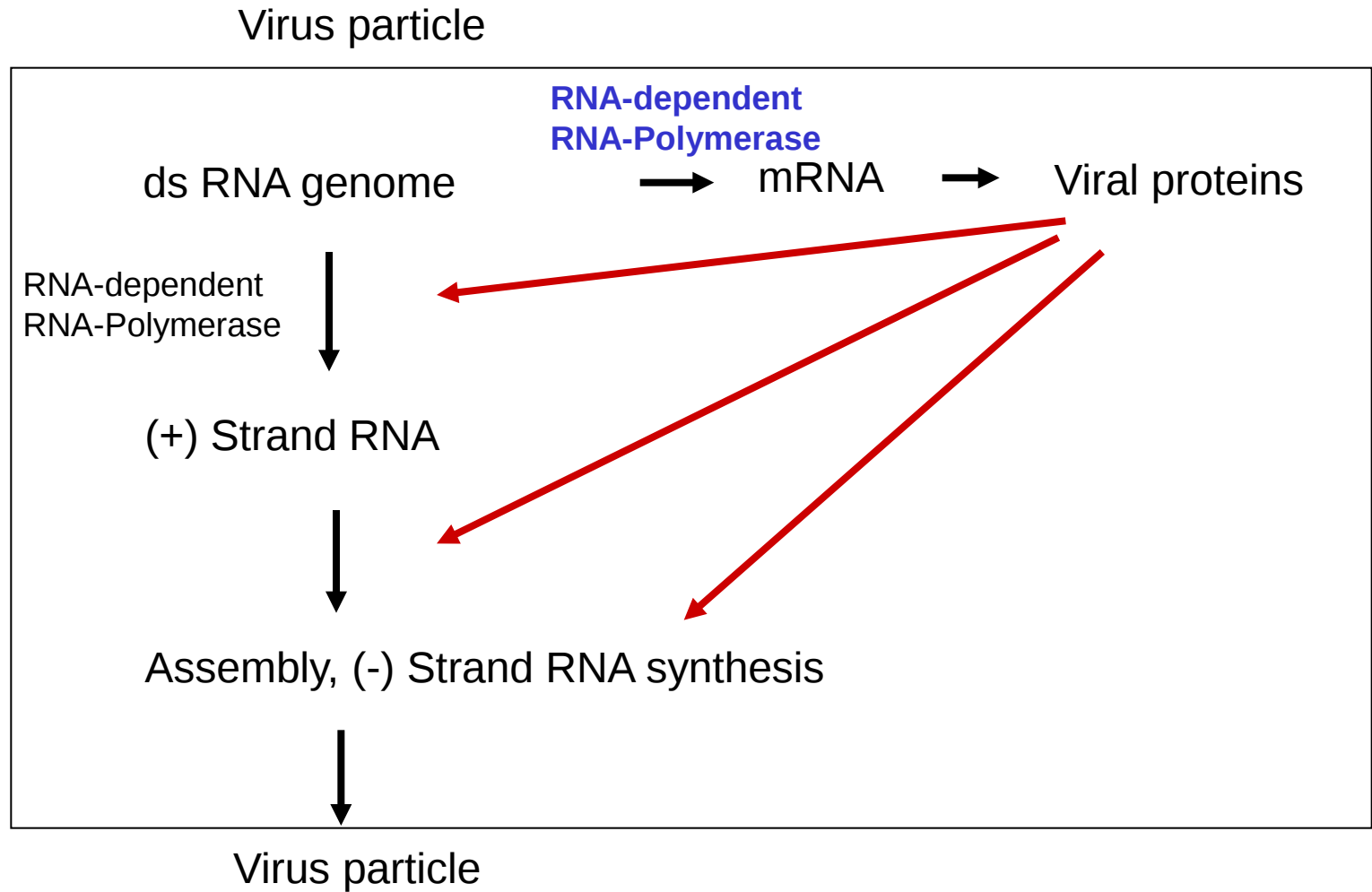
(-) ssRNA Virus



Rhabdo viruses
VSV, Rabies (Tollwut)

Viral RNA is NOT infectious
Virus particle contains RNA-dependent RNA-Polymerase

ds RNA Virus



Reoviren

(mostly asymptomatic)

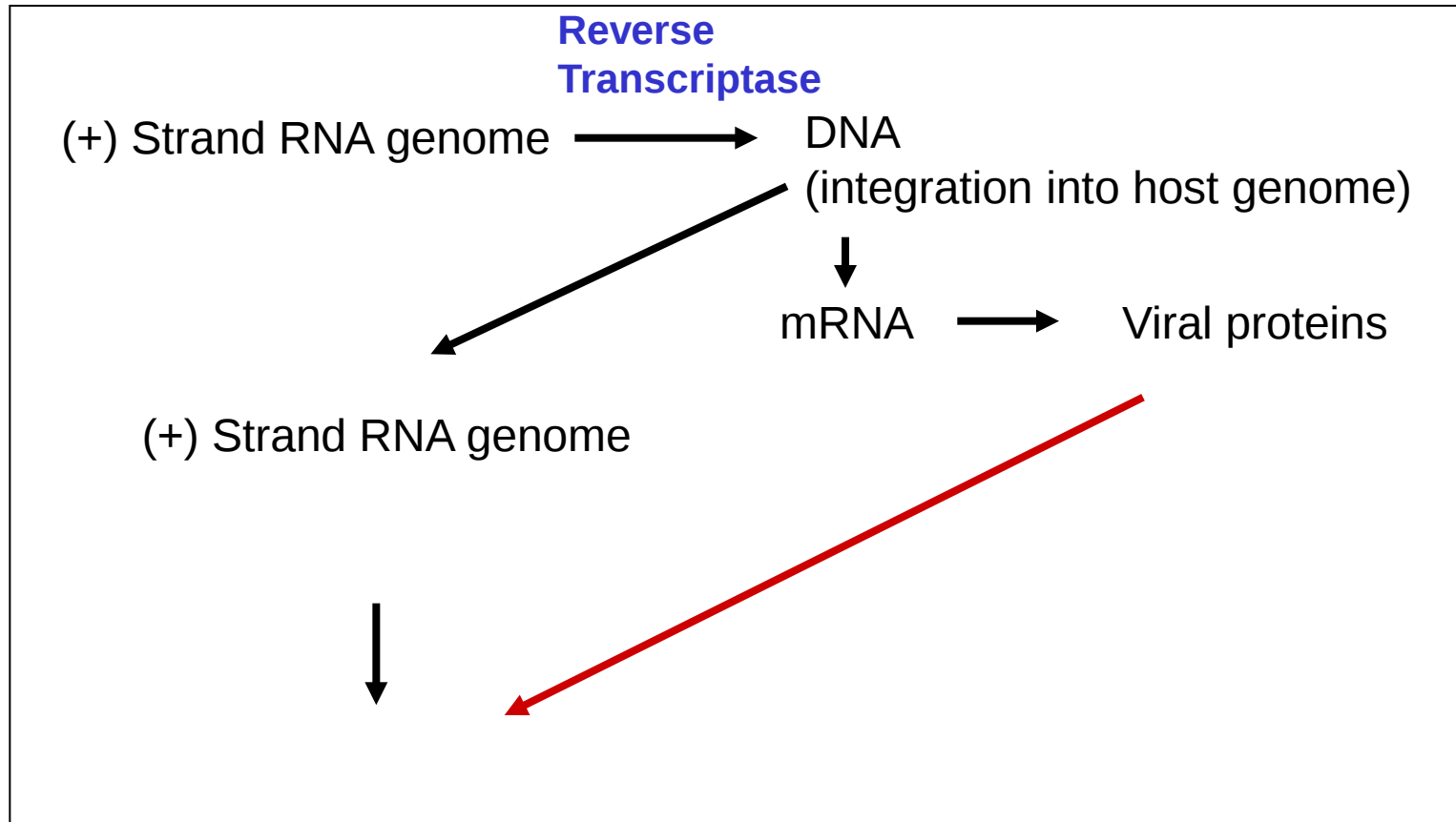
Rotavirus (Gastroenteritis)

Viral RNA is NOT infectious

Viral particle contains polymerase

Retroviruses

Virus particle

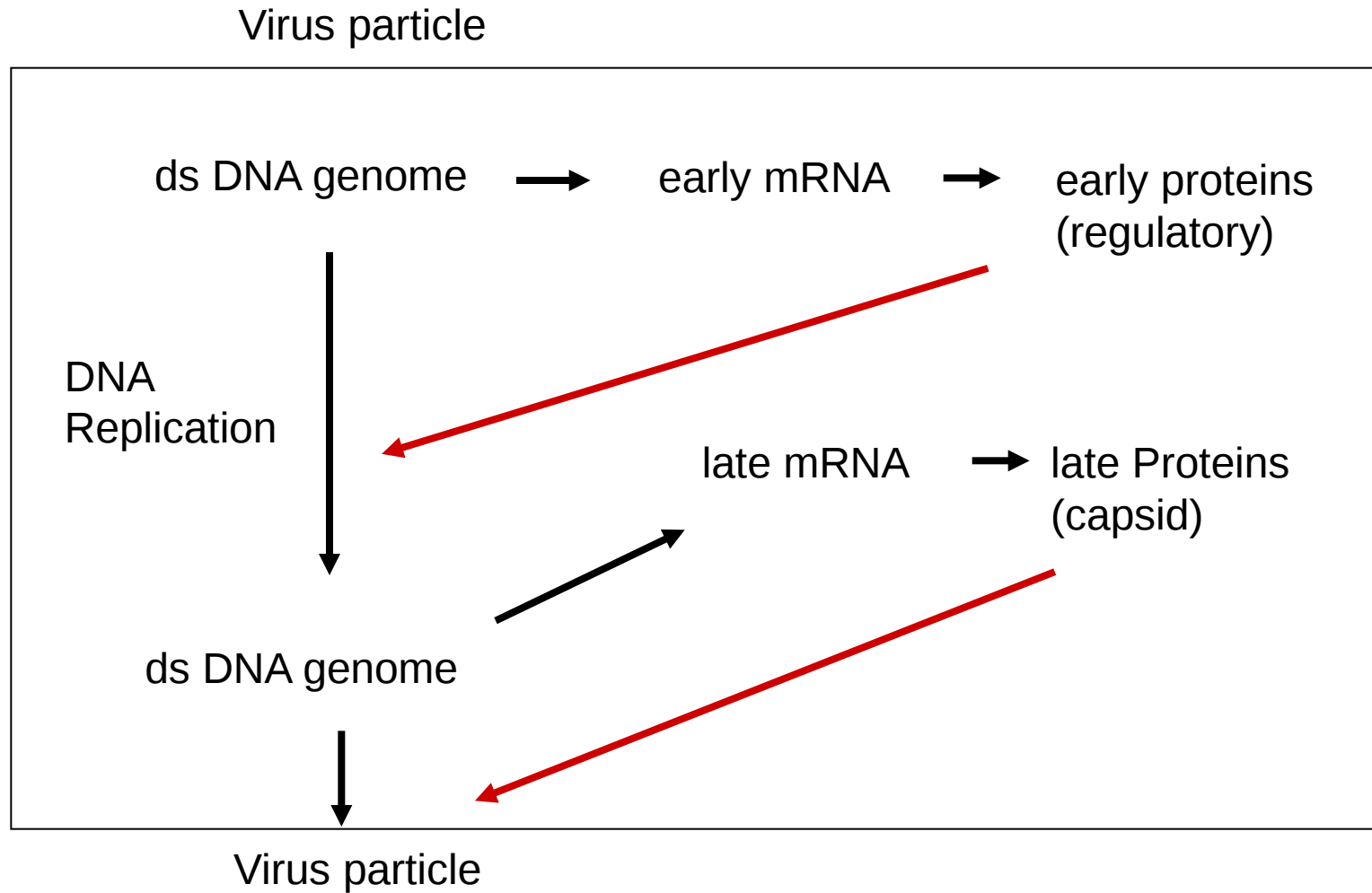


Virus particle

Retroviruses
HIV (AIDS)

Viral RNA is NOT infectious
Viral particle contains reverse transcriptase and primer RNA

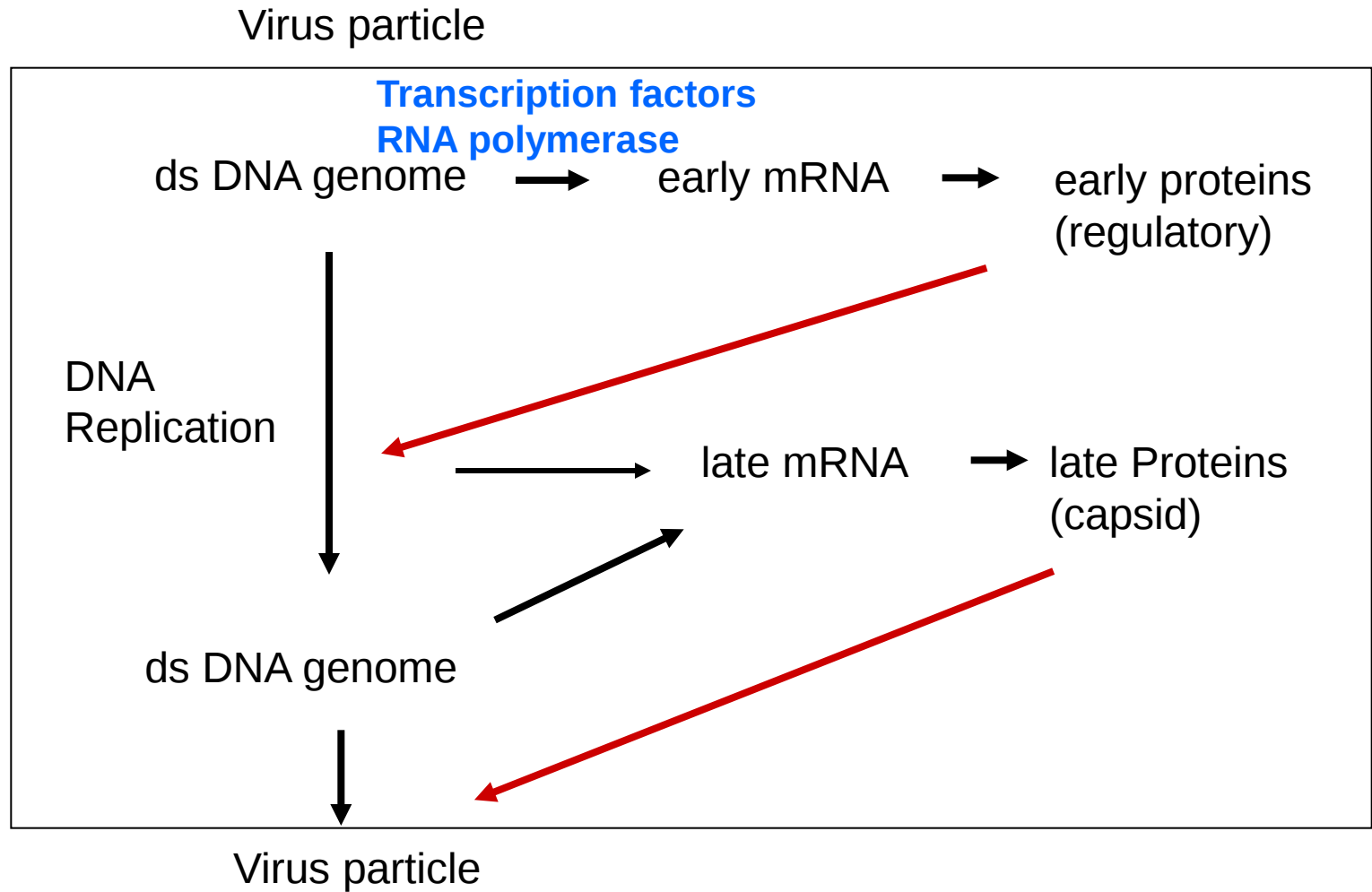
ds DNA Virus



Polyoma-(SV40), Papillomvirus (HPV1-17)
Adeno-, Herpesvirus

Viral DNA infectious

ds DNA Virus

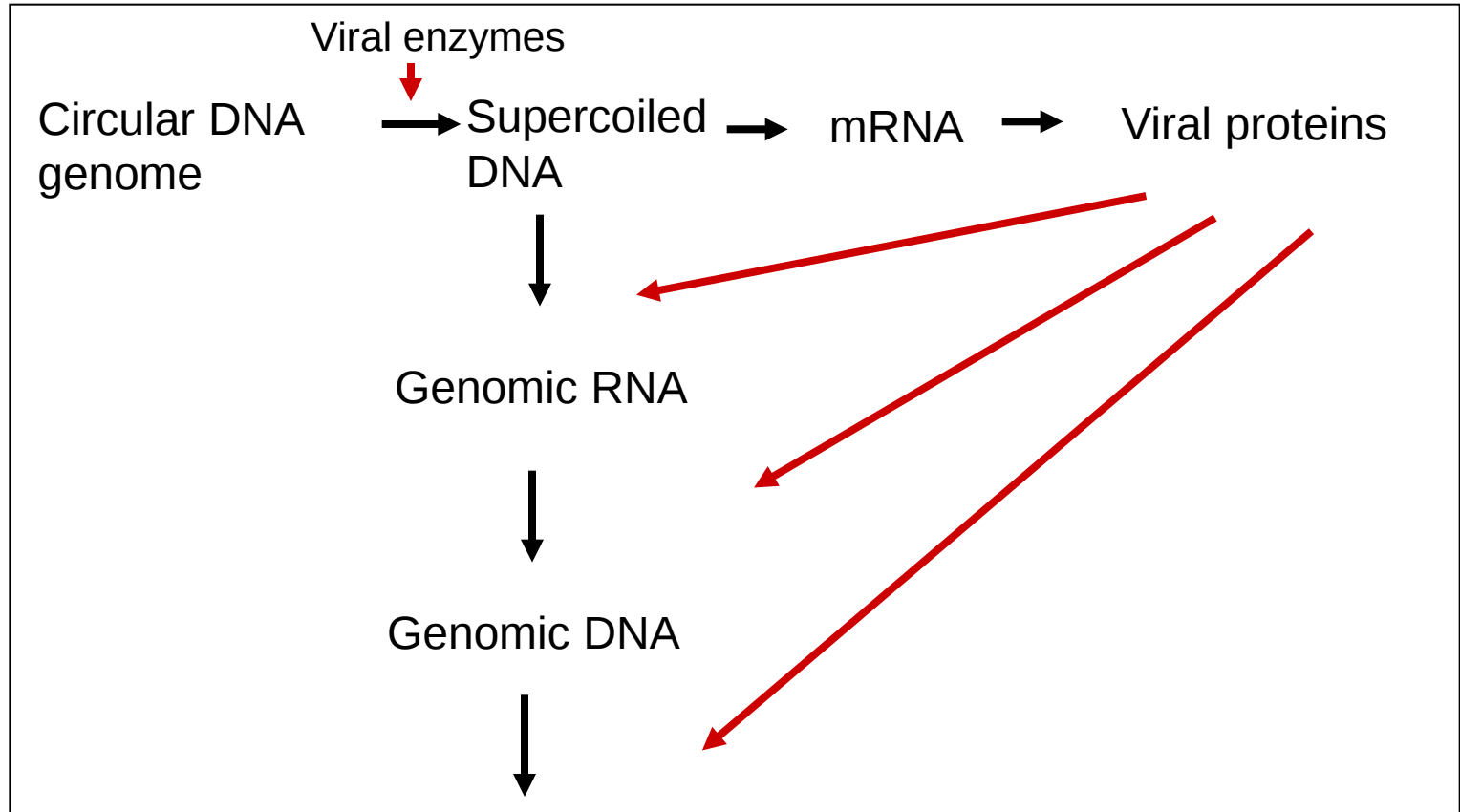


Poxviruses
(cytoplasmic replication)

Viral DNA **not** infectious

Hepadna Virus

Viral particle

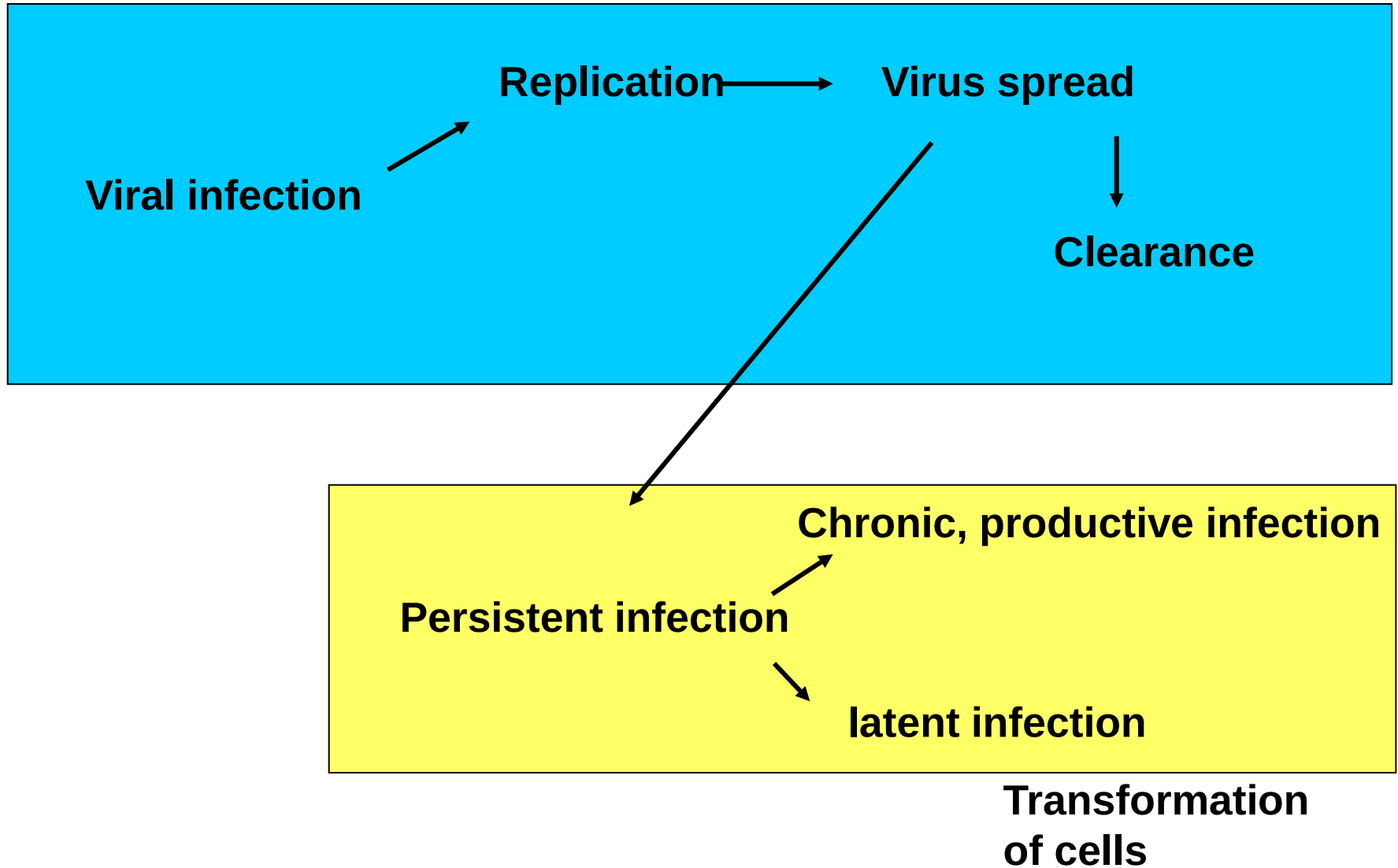


Viral particle

Hepatitis B Virus
(Leberentzündung)

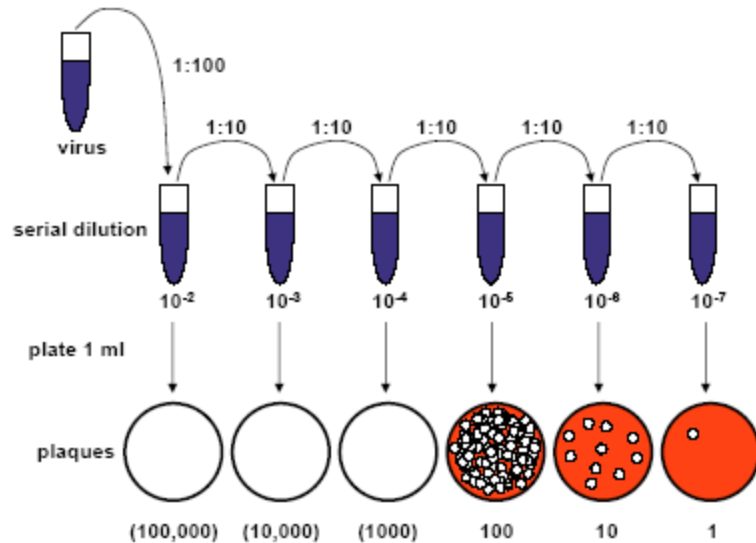
Viral DNA NOT infectious

Types of viral infection



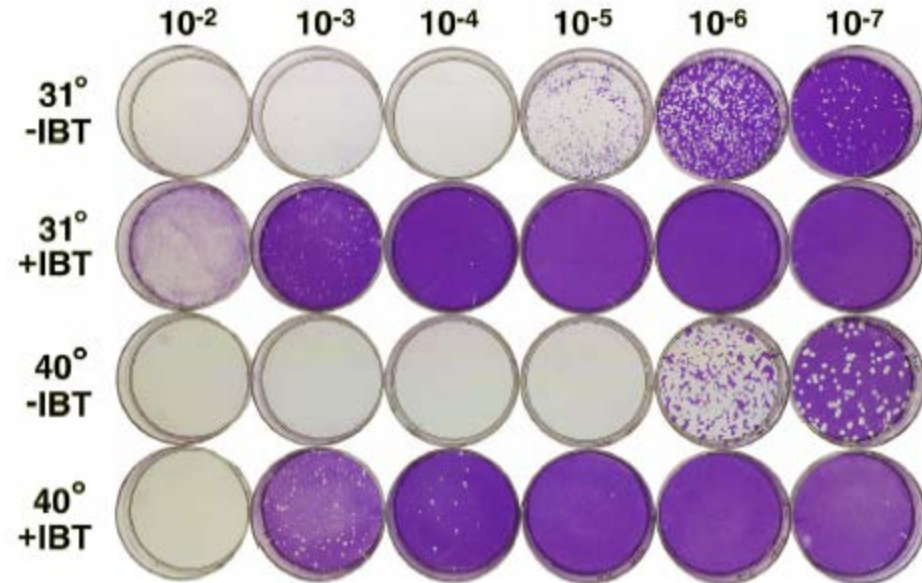
How can we measure the amount of virus (titer)?

Plaque assay: method

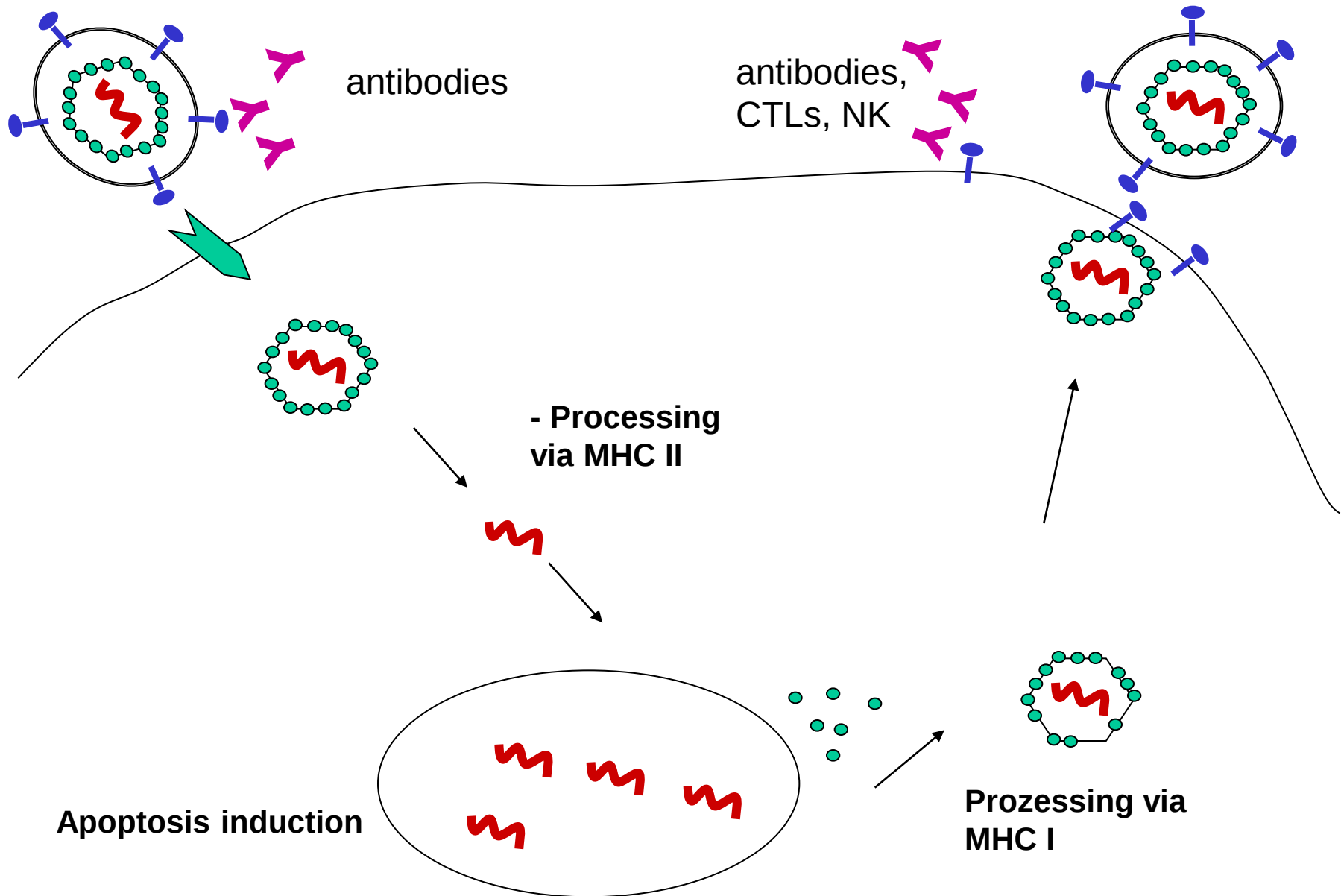


Titer = 1×10^7 pfu/ml

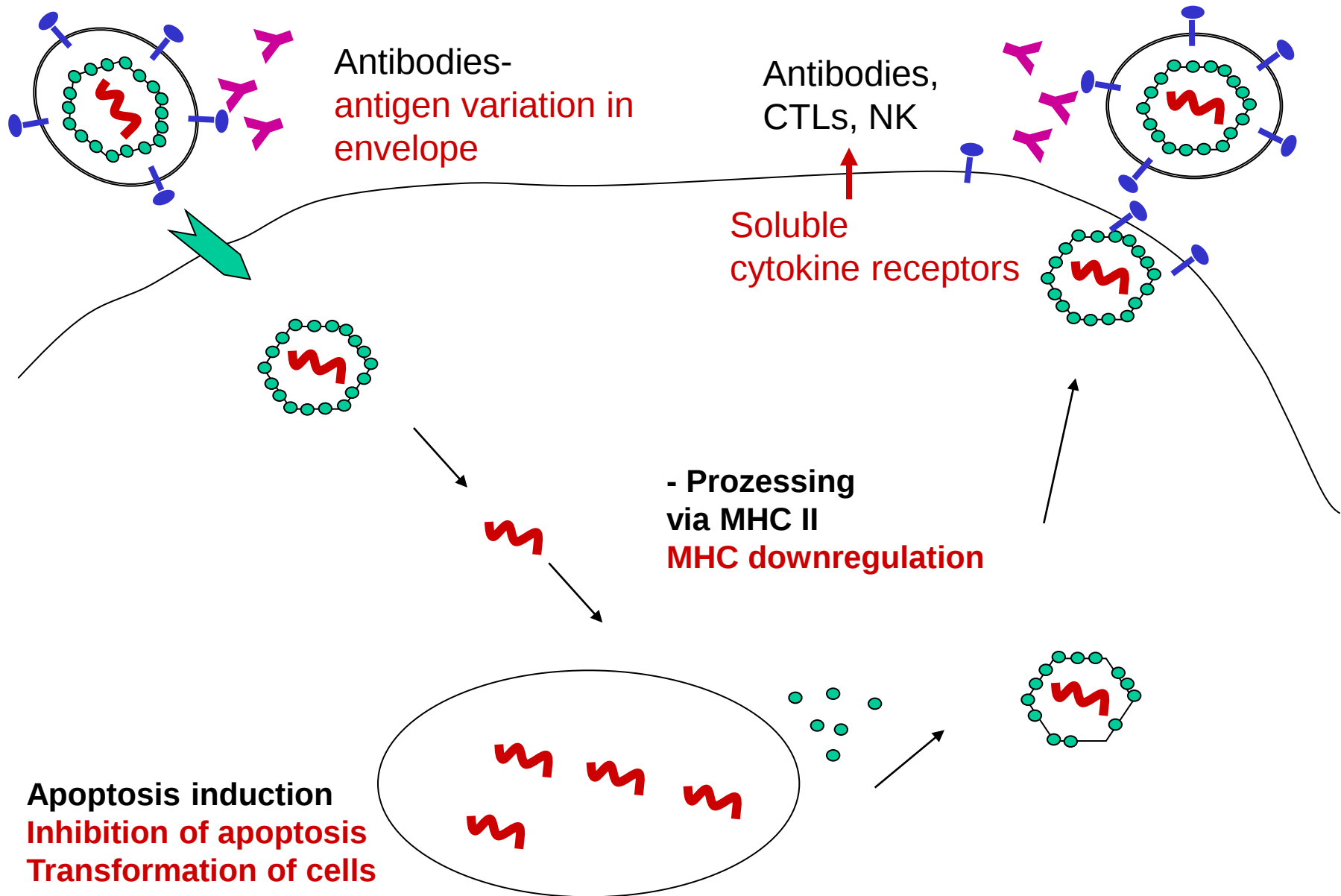
Plaque assay (the real thing) vaccinia



CELLULAR RESPONSE TO VIRAL INFECTION



VIRAL ESCAPE MECHANISMS



CELL DAMAGE BY VIRUSES

Direct cell damage:

Cytopathogenicity (rounding of cells, *in vitro*)

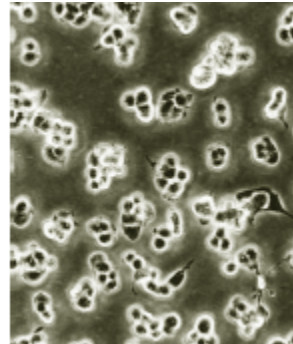
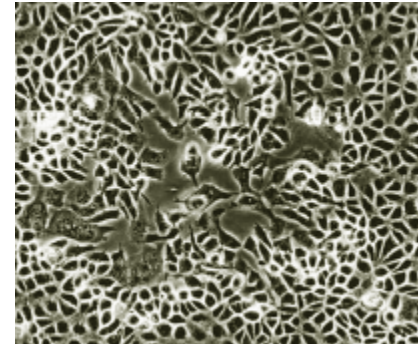
Inhibition of cellular protein synthesis

(Cap-independent protein synthesis) (Poliovirus)

Inhibition of DNA, RNA and protein synthesis (Poxvirus)

Inhibition of RNA Transport (Adenovirus)

→ Damage of microfilament (rounding)

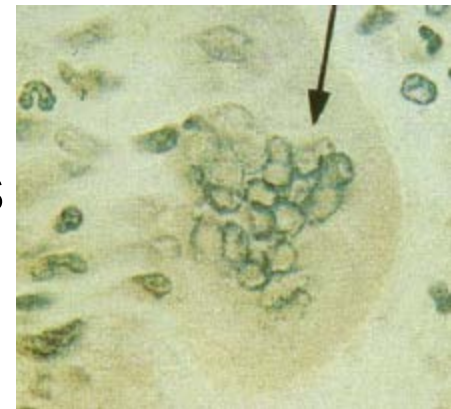


Syncytia

Cell fusions of inf. and uninfected cells (Measles, HIV)

Immunologically caused cell damage:

Hepatitis B infection, damage of liver cells by CTLs



VIRUS SPREAD IN ORGANISMS

entry:

-mucosa, mouth, nose, throat
(Adeno-, Para-Orthomyxoviren)

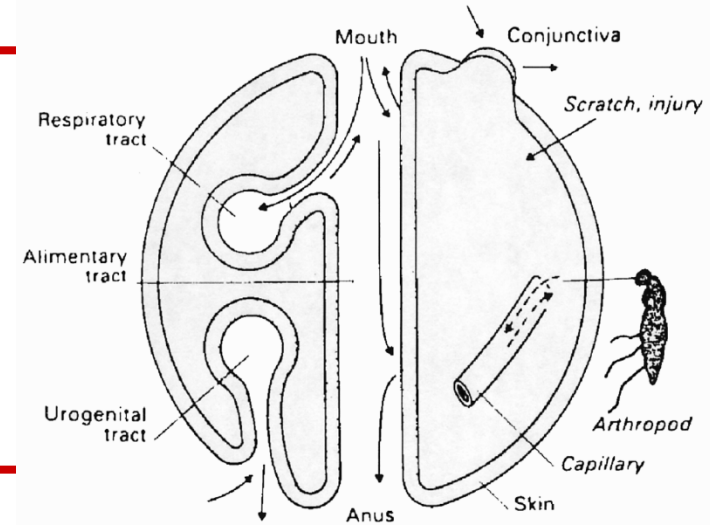
-Genital mucous membrane
-(HIV, Papillon, HSV 2)

- stomach, intestine
(acid resistant Enterovirus, Polio, HepA)

- bites, stings
(Flavi, Bunyaviren (Insekten), rabies)

-Skin injury
(Hep B, Papillom-, Herpesviren)

Virus Uptake into the Body

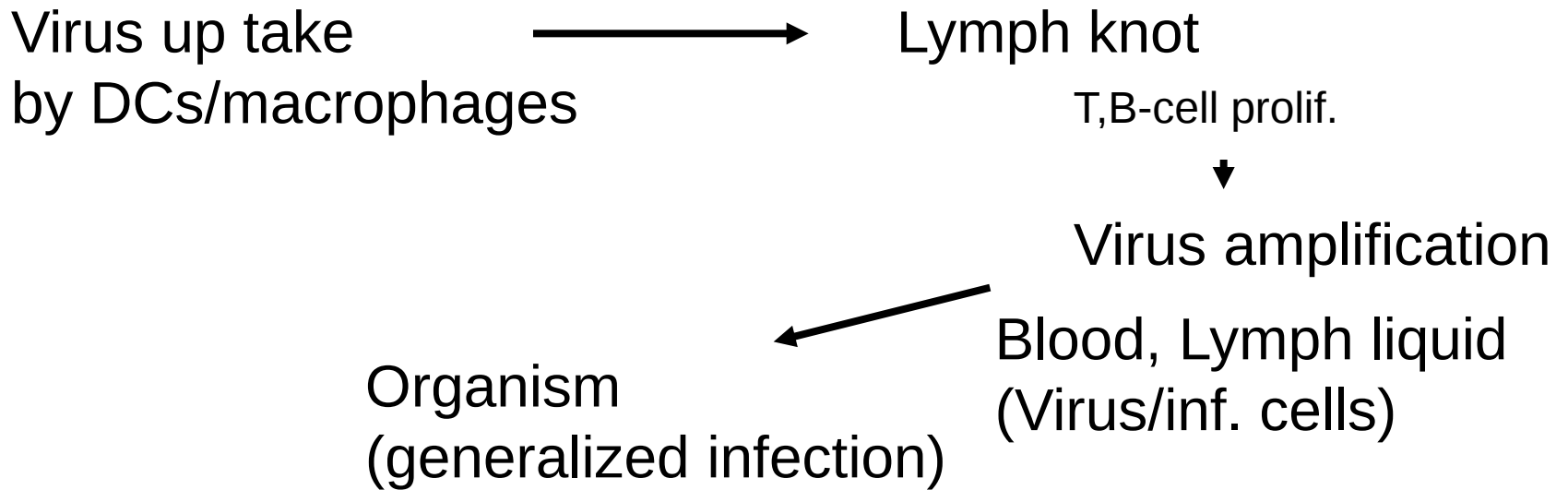


**Langerhans cells
(DCs, macrophages)**

VIRUS SPREAD

1. Lokal infection (Papilloma virus, wart)

2. Lympho-hematogenic spread



3. Neurogenic spread (Herpesvirus)
along nerve fibers,
peripheric nerve, spinal cord, brain

MOLECULAR VIROLOGY

Thursday 1.12.2011: GSH (Bredesaal, 9:00 - ca.13:00)

Friday 2.12.2011: PEI Hörsaal (9– ca. 13:00)

General introduction: Structure and replication strategies of viruses

Barbara Schnierle

(PEI) 9-9:45

Simple retroviruses: Structure, replication, receptors, oncogenes, vectors

Barbara Schnierle

(PEI) 9:45-10:30

Complex retroviruses I: HIV, receptors, regulatory proteins, HTLV-I

Ursula Dietrich

(GSH) 10:45-11:30

Complex retroviruses II: AIDS, chemotherapy, novel therapeutics, gene therapy, vaccines, animal models

Ursula Dietrich

(GSH) 11:30-12:15

Viruses as gene transfer vehicles and expression system:

Retroviral vectors, adenovirus vectors, clinical studies,

Expression systems; Semliki Forest Virus

Stephan Stein

(GSH) 12:15-13

2.12.2011

Immune reaction to viral infections and their inhibition: Humoral und cellular immunity, INF resistance, anti-apoptotic genes, IRES, growth factors

Renate König

(PEI) 9-9:45

Vaccinia Virus: Structure and replication strategies, vectors

Barbara Schnierle

(PEI) 9:45-10:30

Hepadna Viruses:

Structure and replication strategies

Matthias Schweizer (PEI)

10:45-11:30

Herpesvirus:

Structure and replication strategies, vectors

Christian Buchholz

(PEI) 11:30-12:15

Modeling of virus evolution: constraints of viral viability in the quasispecies model

Christel Kamp

(PEI) 12:15-13