Special topics in Bioengineering/Virology

WS 2019/2020

General information

- Student presentations
- Discussions
- Attendance and participation
- One group is presenting
- All others ask questions and discuss (after the presentation)
- All students **must** read a paper for that day!

- All students get all papers and the book!
- Presenting group gets questions and comments from the audience
- All presentations will be uploaded (dashboard)!
- Use it for learning
- Everyone who asks questions (I will take the notes!) and has attendance of at least 85% gets additional 5 % to the final grade

How to prepare presentation about viruses?

- You get a copy of book
- Or download it from **b-ok.org**
- Virology book: Carter/Saunders: Virology-principles and applications, 2007
- Make a presentation by presenting everything what you think is important about the virus group (!)
- Max. 1 hour

How to prepare presentation from paper?

- Start from the title
- Understand the title
- Read the abstract
- Understand the abstract
- Focus on main parts of the paper
- Explain them
- Max. 1 hour

Grading

- Midterm exam 30%
- Presentation and participation 25 %
- Attendance 5%

Groups

- 7 Master students – make 2 presentations about viruses (structure of viruses and virus classification) – 2 groups of students
- 15 undergraduate students – make 7 presentations (groups of 2 students): general information about the virus of interest (book chapter) + paper
- Again Master students make 2 additional presentations from the paper and the book chaper (at the end)

Syllabus

Week	Topic	Students	Material
1	Intro and Syllabus	-	-
2	Intro to Bioengineering and Viruses	-	Presentation
3	Structure of viruses	Music/Smajovic/Ajdina Karic	Chapter 3 (book)
4	Virus classification	Azra Karic/Abdukic/Huseinbegovic/Kurtanovic	Chapter 10 (book)
5	Herpesvirus	Vardic-Kajtazovic/Sezer	Chapter 11 + paper
6	Parvovirus	Sidran/Rudalija/Jusic	Chapter 12 + paper
7	Reovirus	Hrapovic/Šabanovic	Chapter 13 + paper
8	**MIDTERM!**	**-**	**-**
9	Picornavirus	Mezic/Adilovic	Chapter 14 + paper
10	Rhabdovirus	Mahalbasic/Lipjankic	Chapter 15 + paper
11	Retrovirus	Ratkovic/Smajovic	Chapter 16 + paper
12	Adenovirus	Adilce/Fatic	Chapter + paper
13	Bacterial viruses	Music/Huseinbegovic/Ajdina Karic	Chapter 19 + paper
14	Hepadnavirus	Abdukic/Karic/Kurtanovic	Chapter 18 + paper
15	Review and future directions	-	-

Introduction to Bioengineering

The evolution of modern health care system

- Primitive humans – disease “visitors” in form of spirits
- Medical practice – domain of witch doctors
- Healing process – cult
- Herbs and solutions
- Passed on further generations
- Ancient Egypt

- Roman Empire
- Greeks
- The Church
- Renaissance
- England and Henry VIII
- History of modern medicine (Germ Theory)
- Medicine nowadays

Biochemical engineering

- Problems of health professionals
- involve the fundamental aspects of device and systems analysis, design, and practical application
- lie at the heart of processes that are fundamental to engineering practice

- Medically relevant design problems can range from very complex large-scale constructs, such as hospital information systems or
- creation of relatively small and “simple” devices, such as recording electrodes and transducers
- Biomedical engineeres

- involves applying the concepts, knowledge, and approaches of virtually all engineering disciplines
- the opportunities for interaction between engineers and health care professionals are many and varry
- many conflicting opinions concerning the field can be traced to disagreements about its definition

- consider the terms *biomedical engineering, bioengineering, biological engineering, and clinical (or medical) engineer*
- are defined in the Bioengineering Education Directory

- **Bioengineering** - defined as a basic-research oriented activity closely related to biotechnology and genetic engineering:
- that is, the modification of animal or plant cells or parts of cells
- improve plants or animals or to develop new microorganisms for beneficial ends.

- In the food industry - this has meant the improvement of strains of yeast for fermentation
- In agriculture - improvement of crop yields by treatment plants with organisms to reduce frost damage

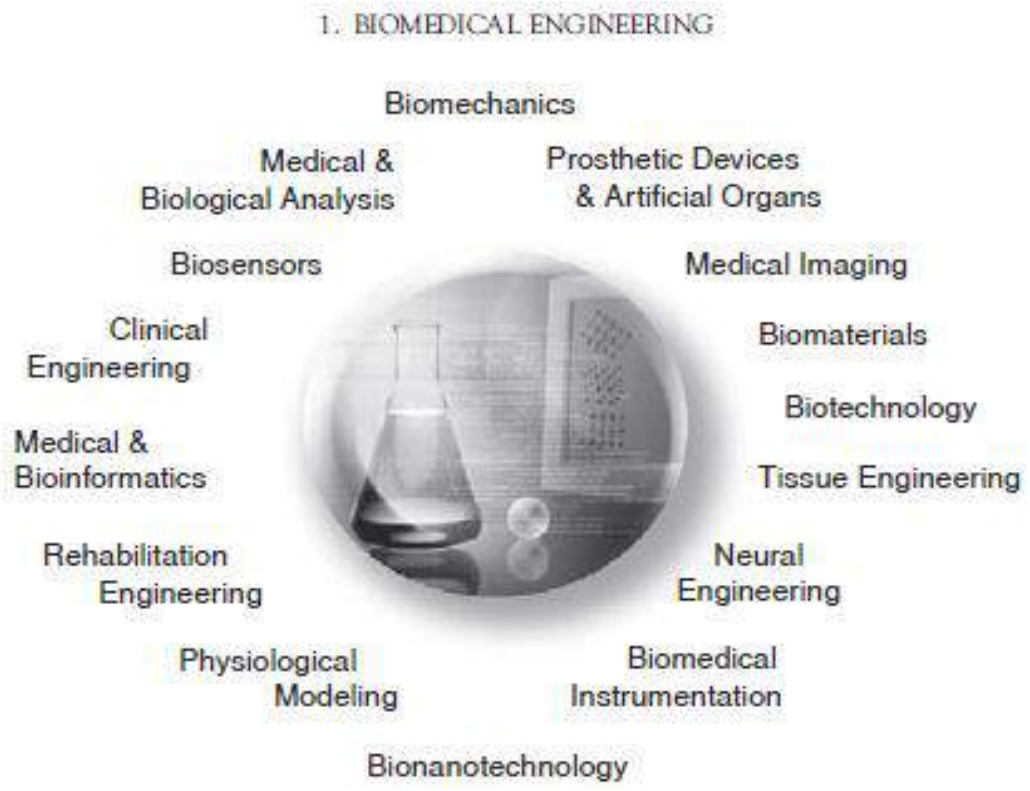
- It is clear that bioengineers for the future will have tremendous impact on the quality of human life
- Typical pursuits include the following:

- The development of improved species of plants and animals for food production
- The invention of new medical diagnostic tests for diseases
- The production of synthetic vaccines from clone cells
- Bioenvironmental engineering to protect human, animal, and plant life from toxicants and pollutants
- The study of protein-surface interactions
- Modeling of the growth kinetics of yeast and hybridoma cells
- Research in immobilized enzyme technology
- The development of therapeutic proteins and monoclonal antibodies

- biomedical engineering appears to have the most comprehensive meaning
- apply electrical, chemical, optical, mechanical, and other engineering principles
- to understand, modify, or control biological (i.e., human and animal) systems
- works within a hospital or clinic, he or she is more properly called a clinical engineer.

- The breadth of activity of biomedical engineers is significant
- The field has moved significantly: from being concerned primarily with the development of medical devices in the 1950s and 1960s
- to include a more wide-ranging set of activities

- now includes many new career areas:



- Many other applications use the talents and skills of the biomedical engineer
- the list of activities of biomedical engineers depends on the medical environment in which they work (especially clinical engineers):

- ❑ essentially responsible for all the high-technology instruments and systems used in hospitals today,
- ❑ the training of medical personnel in equipment safety, and the design,
- ❑ selection, and use of technology to deliver safe and effective health care

- Clinical engineers today provide extensive engineering services for the clinical staff
- serve as a significant resource for the entire hospital

- Biomedical engineering is thus an interdisciplinary branch of engineering heavily based in both engineering and the life sciences
- ranges from theoretical, nonexperimental undertakings to state-of-the-art applications
- can encompass research, development, implementation, and operation

- like medical practice itself, it is unlikely that any single person can acquire expertise that encompasses the entire field
- explosion of biomedical engineering specialties to cover this broad field
- considerable interplay and overlapping of interest and effort between them

- The field of biomedical engineering offers hope in the continuing battle to provide high-quality health care at a reasonable cost

- If properly directed toward solving problems, biomedical engineers can provide the tools and techniques to make our health care system more effective and efficient.

Roles played by Biomedical Engineers

- biomedical engineering involves training essentially three types of individuals:

- the clinical engineer in health care,
- the biomedical design engineer for industry,
- the research scientist

- First type – problem solver:

- Maintains the traditional service relationship with the life scientists who originate a problem that can be solved by applying the specific expertise of the engineer

- Second type - technological entrepreneur

- examine some portion of the biological or medical front and identify areas in which advanced technology might be advantageous
- they pose their own problem and then proceed to provide the solution, at first conceptually and then in the form of hardware or software

- Third type - engineer-scientist

- primarily interested in applying engineering concepts and techniques to the investigation and exploration of biological processes
- most powerful tool at their disposal is the construction of an appropriate physical or mathematical model of the specific biological system under study

Viruses

Viruses

- genetic elements that cannot replicate independently of a living cell (**host cell**)
- possess their own genetic information and are thus independent of the host cell's genome
- rely on the host cell for energy, metabolic intermediates, and protein synthesis
- obligate intracellular parasites that rely on entering a suitable living cell to carry out their replication cycle
- have an extracellular form (the virus particle) that enables them to exist outside the host
- that facilitates transmission from one host cell to another
- To multiply, viruses must enter a cell in which they can replicate, a process called infection

Viruses

- Exists in either extracellular or intracellular forms.
- In its extracellular form: is a microscopic particle containing nucleic acid surrounded by a protein coat and other macromolecules
- Virus particle = **virion**
- metabolically inert and cannot generate energy or carry out biosynthesis
- The virus genome moves from the cell in which it was produced to another cell inside the virion.
- Once in the new cell, the intracellular state begins and the virus replicates.

ALL viruses follow a simple three part general strategy to ensure survival

- All viruses package their genomes inside a particle used for transmission of the genome from host to host.

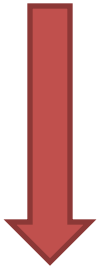
- The viral genome contains the information to initiate and complete an infectious cycle within a susceptible and permissive cell.

- All virus genomes are able to establish themselves in a host population so that viral survival is ensured.

SURVIVAL!!!!

The tactics used to achieve is very diverse

- There are countless virus particles out with big diversity:
  - Size, nature, topology of genomes.
  - Strange particles
  - Different coding strategy



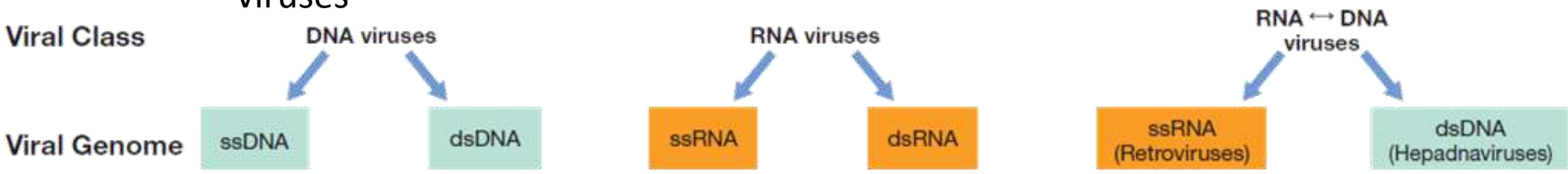
VIROLOGY

General Properties of Viruses

- *Virus*: very small, infectious, obligate intracellular parasites.
- *Virus particle (virion)*: extracellular form of a virus
  - Exists outside host and facilitates transmission from one host cell to another
  - Contains nucleic acid genome surrounded by a protein coat and, in some cases, other layers of material

General Properties of Viruses

- Viral Genomes
  - DNA or RNA genomes (at different stages of their replication cycle both can be used)
  - Some circular, but most linear
  - DNA viruses follow central dogma (DNA->RNA->Protein) but not the RNA viruses



Viral Host and Taxonomy

•Classification: based on their genome and of host they infect!

- Bacterial viruses (bactriophages)
- Archeal
- Plant
- Animal

Nature of the Virion

- Virions come in many sizes and shapes
- Most viruses are smaller than prokaryotic cells.
  - 0.02 to 0.3 µm (20-300 nm)
  - *Smallpox* is one of the biggest, 200nm.
  - *Poliovirus* one of the smallest 28nm.

- Viral genomes are smaller than those of most cells.
  - Bacterial genome are between 100-5000 Kbp
  - Largest know virus genome *Mimivirus* consist of 1.18Mbp
  - Larger than some cellular genomes

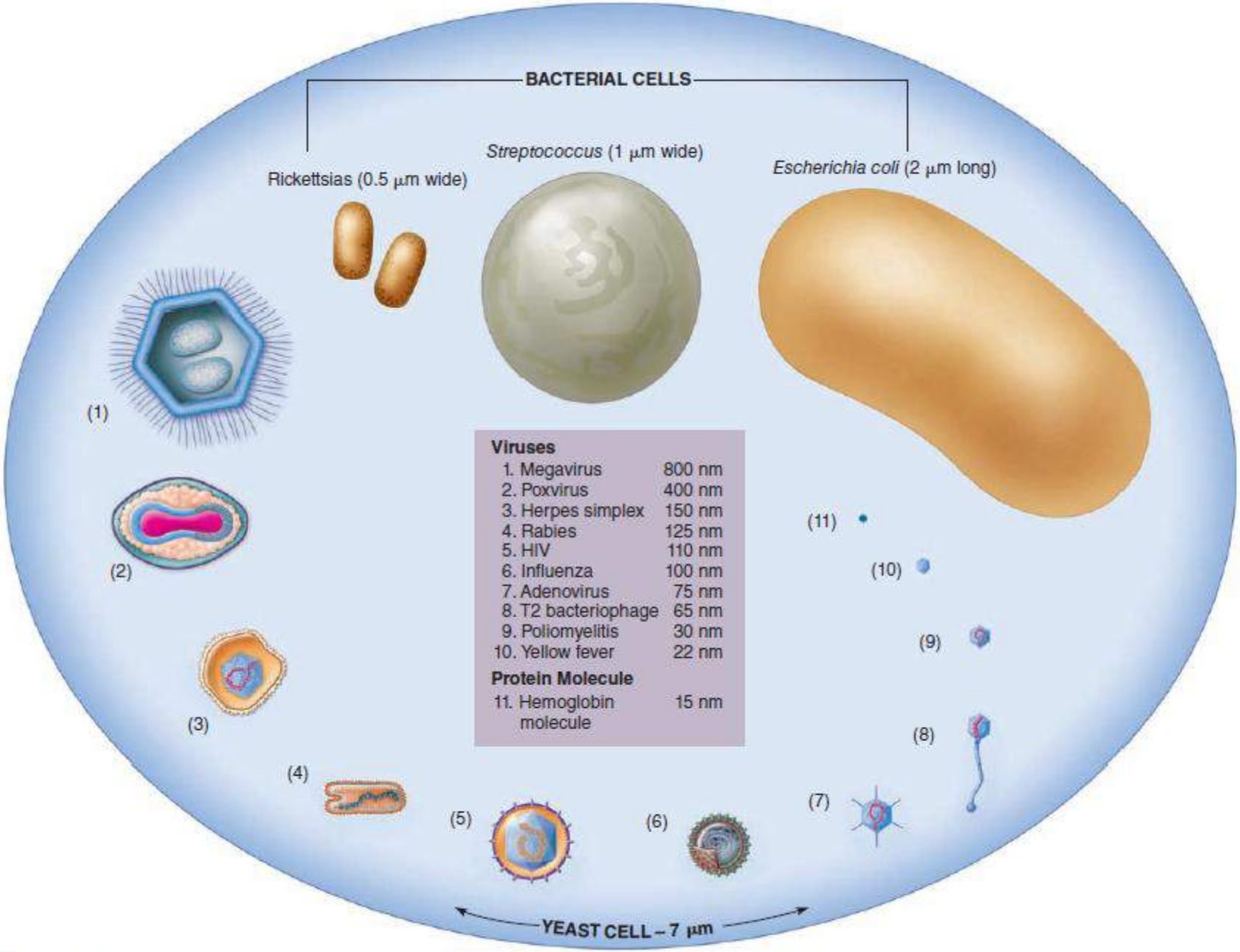


Figure 6.1 **Size comparison of viruses with a yeast cell colored blue (eukaryotic) and various bacteria (prokaryotic).** Viruses range from largest (1) to smallest (10). A molecule of a large protein (11) is included to indicate relative size of macromolecules.

Enzymes in viruses

- Some virions contain enzymes critical to infection
  - *Lysozyme*
    - Makes hole in cell wall (initial stage of infection)
    - Lyses bacterial cell (later stage of infection)
  - *Nucleic acid polymerases*
    - For viral replication and transcription
    - Reverse DNA polymerase
  - *Neuraminidases*
    - Some animal viruses for their release form host!
    - Enzymes that cleave glycosidic bonds of animal connective tissue
    - Allows liberation of viruses from cell

The Virus Host

- Because viruses replicate only inside living cells, the cultivation of viruses requires the use of appropriate hosts!
- Bacterial viruses (bacteriophage) are easiest to grow; model systems
  - Pure cultures are grown in liquid or semisolid (agar) medium
- Animal viruses (and some plant viruses) can be cultivated in tissue or cell cultures
- Plant viruses typically are most difficult because study often requires growth of whole plant

Quantification of Viruses

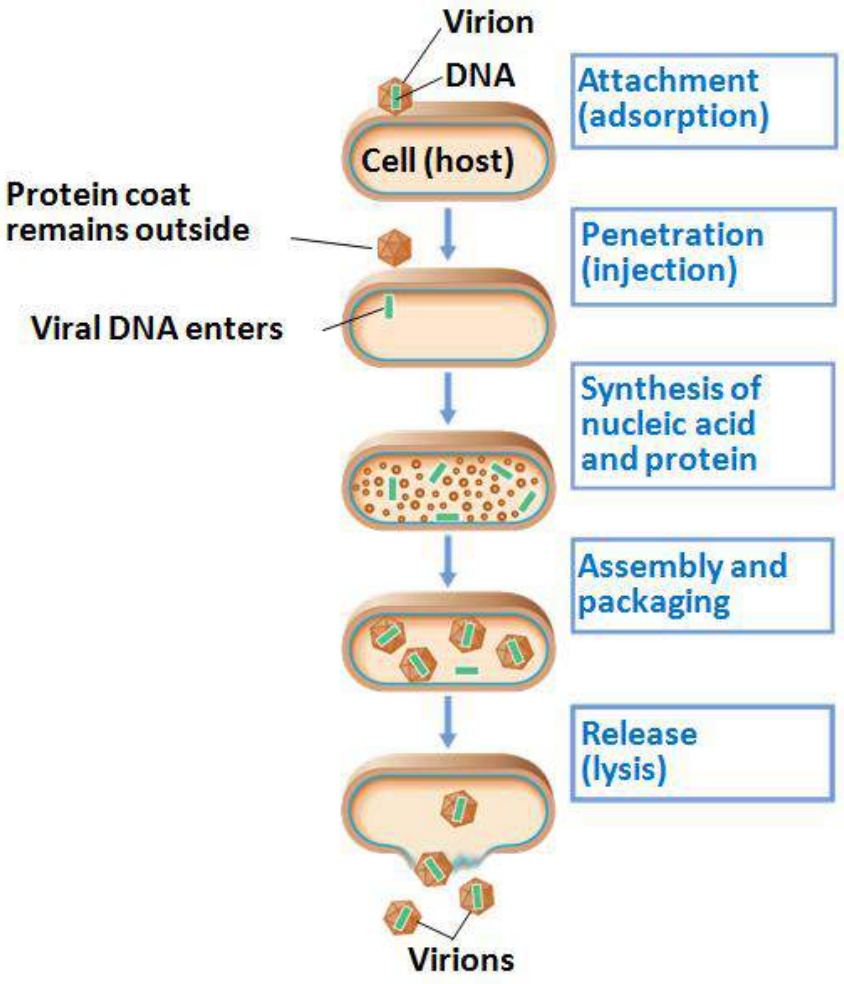
- necessary to quantify the number of virions in a suspension:
  - Counting using electron microscope
  - Measuring of their effects on the host
- By determining the number of infectious units per volume of fluid, a measure of virus quantity, called a **titer**, can be obtained.

Quantification of Viruses

- Traditional Methods
  - Plaque assay
  - 50% Tissue culture Infective Dose
  - Fluorescent Focus Assay
  - Proteins Assay
  - Transmission Electron Microscopy
- Modern Methods
  - Flow cytometry
  - Quantitative Polymerase Chain Reaction (qPCR)
  - Enzyme Linked Immunosorbent Assay (ELISA)

General Features of Virus Replication

- Phases of Viral Replication
  - *Attachment (adsorption)* of the virus to a susceptible host cell
  - *Entry (penetration)* of the virion or its nucleic acid
  - *Synthesis* of virus nucleic acid and protein by cell metabolism as redirected by virus
  - *Assembly* of capsids and packaging of viral genomes into new virions (maturation)
  - *Release* of mature virions from host cell



Viral Proteins

- Production follows synthesis of viral mRNA
  - *Early proteins*
    - synthesized soon after infection
    - necessary for replication of virus nucleic acid
    - typically act catalytically
    - synthesized in smaller amounts

Viral Proteins

– *Late proteins*

- Synthesized later
- Include proteins of virus coat (capsid)
- Typically structural components
- Synthesized in larger amounts

- Virus infection upsets the regulatory mechanisms of the host
- marked overproduction of viral nucleic acid and protein in the infected cell.
- In some cases, virus infection causes a complete shutdown of host macromolecular synthesis
- in other cases, host synthesis proceeds concurrently with virus synthesis.
- In either case, regulation of virus synthesis is under the control of the virus rather than the host.

Viral life cycle

Virulent (or lytic)mode: viruses lyse or kill their hosts after infection (**phage T4)**

Temperate (or lysogenic) mode: viruses replicate their genomes in step with the host genome and without killing their hosts.

Subviral Entities

- There are several infectious agents that resemble viruses but whose properties are at odds with this definition, and are thus not considered viruses:

  - Defective Viruses
  - Viroids
  - Prions

Defective Viruses

- *Defective viruses*: viruses that are parasitic on other viruses
  - Require other virus (*helper virus*) to provide some function
    - Some rely on intact virus of same type
    - *Satellite viruses*: defective viruses for which no intact version exists; rely on unrelated viruses as helpers
  - Example: bacteriophage P4, of *E coli* needs P2 for major capsid proteins.
  - Example: Adeno Associate Virus, Adenovirus

Viroids

- *Viroids*: infectious RNA molecules that lack a protein coat (capsid)
  - Smallest known pathogens (246–399 bp)
  - Cause a number of important plant diseases (not animals or prokaryotes)
  - Small, circular, ssRNA molecules
  - Do not encode proteins; completely dependent on host-encoded enzymes

Prions

- They have distinct extracellular form, which consist entirely of proteins.
- The prion particle contains neither DNA nor RNA.
- Known to cause disease in animals. (scrapie in sheep)

Prions

- animal (cow) prion disease are known as bovine spongiform encephalopathie (BSE).
- The pathogenic form of the prion protein,PrPSc (prion protein Scrapie), because the first prion disease to be discovered was scrapie in sheep.
- PrPSc is identical in amino acid sequence to PrPC from the same species, but has a different conformation.

- Native prions consist largely of α-helical segments,
- whereas pathogenic prions have less α -helix and more β -sheet regions instead.
- This causes the prion protein to lose its normal function, to become partially resistant to proteases, and to become insoluble, leading to aggregation within the neural cell