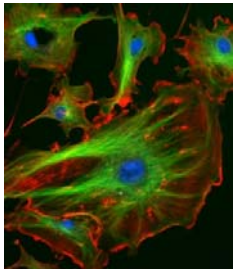
# Lecture 6: In Different Operating Systems

## Section A: From Nature to Concepts

## Genes & Society
## LSM3201 / GEK 1527



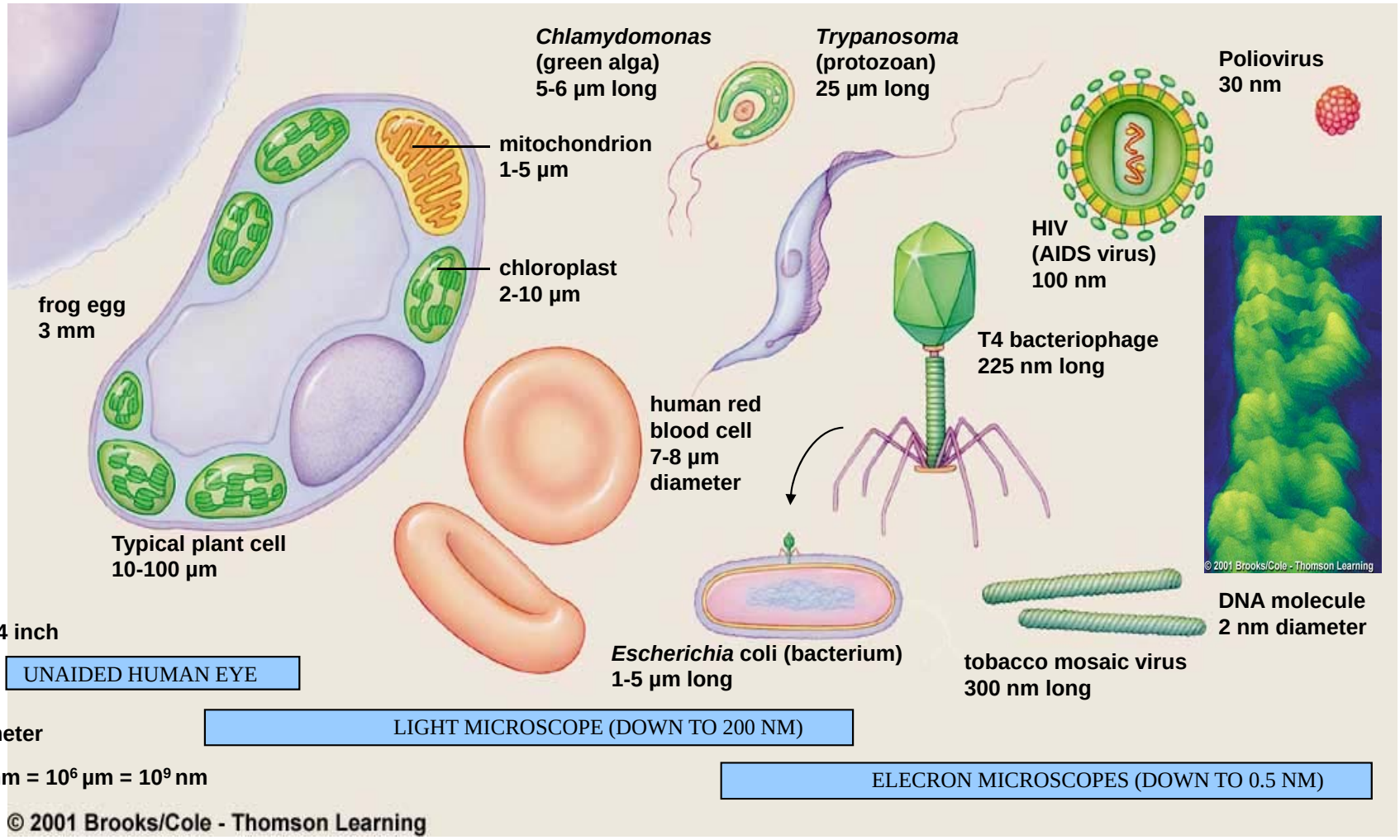
**We are machines built by DNA whose purpose is to make more copies of the same DNA. This is exactly what we are for. We are machines for propagating DNA, and the propagation of DNA is a self-sustaining process. It is every living object's sole reason for living.**

**- Richards Dawkins (ethologist; evolutionary biologist)**

# Overview

- **Comparing Sizes**
- **Viruses**
- **Prokaryotic Cell (Bacteria)**
- **Eukaryotic Cell**
- **Comparative Summary**

***The aim is to appreciate the major differences of how genetic material operates between organisms.*** **Once you know how they work, you will know how to work with them.**




1 cm = 1/100 meter, or 0.4 inch

1 mm = 1/1,000 meter

1 µm = 1/1,000,000 meter

1 nm = 1/1,000,000,000 meter

1 meter = $10^2$ cm = $10^3$ mm = $10^6$ µm = $10^9$ nm

UNAIDED HUMAN EYE

LIGHT MICROSCOPE (DOWN TO 200 NM)

ELECRON MICROSCOPES (DOWN TO 0.5 NM)

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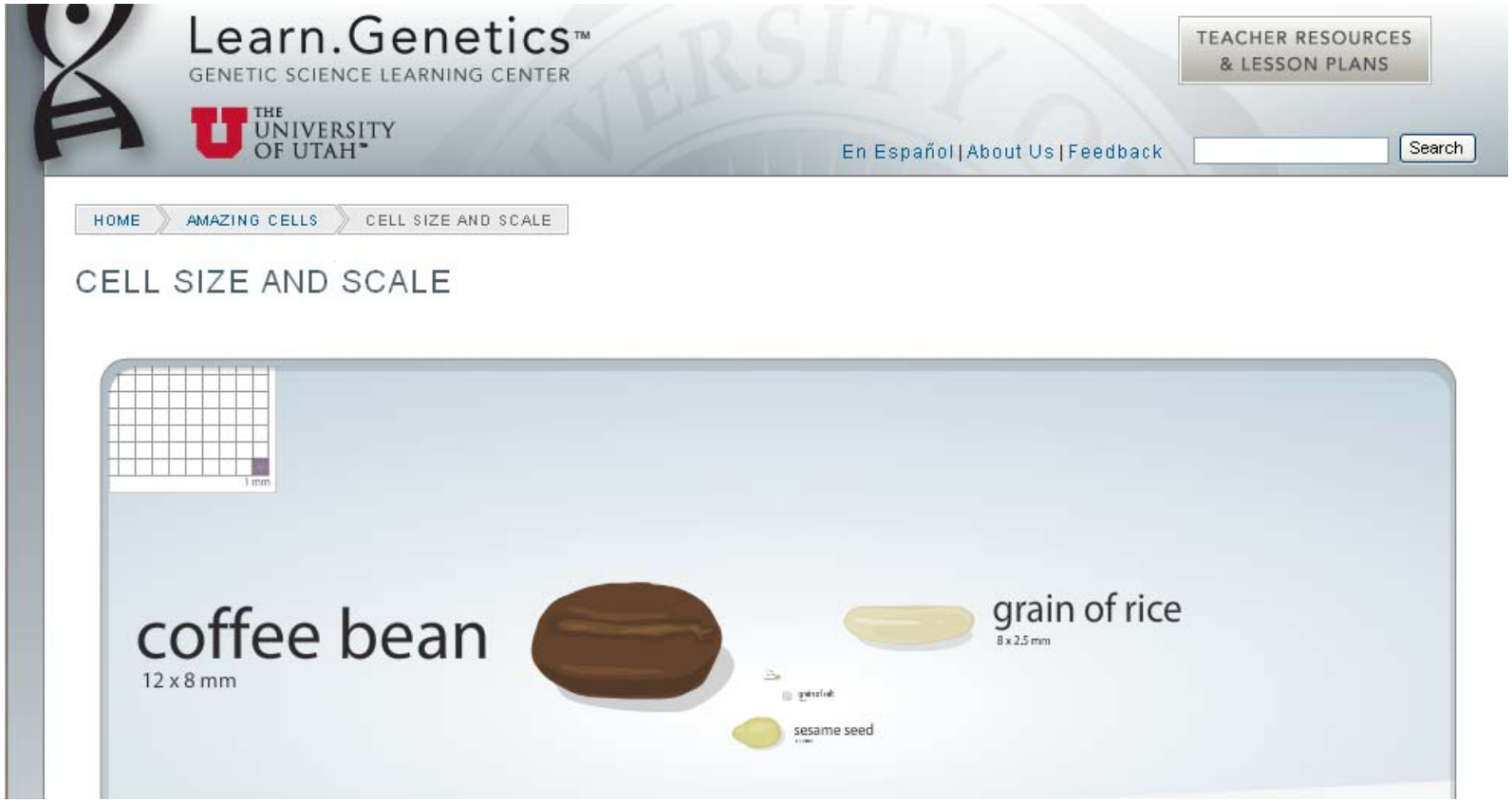
1mm | 100 µm | 10 µm | 1 µm | 100 nm | 10 nm | 1 nm | 0.5 nm

# Check this out:

Learn Genetics>Amazing Cell>Cell Size and Scale




http://learn.genetics.utah.edu/content/cells/scale/

# Viruses

- Smaller than bacteria (~3-30X smaller)
- Proliferate by infecting specific host cells
- Genetic material can be DNA or RNA (can be single or double stranded)
- Small genome with overlapping protein coding regions.

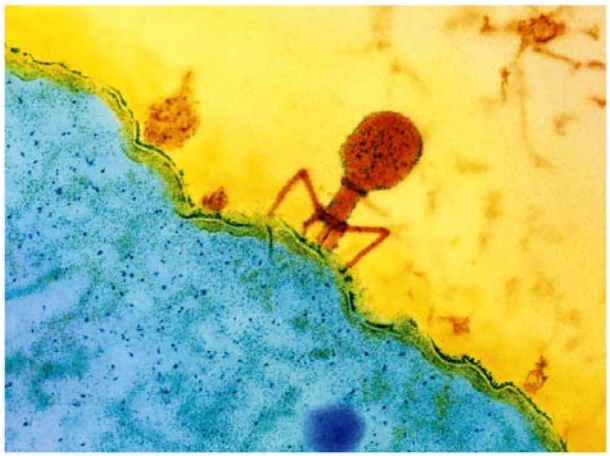


Figure 1-7 Essentials of Genetics, 6/e
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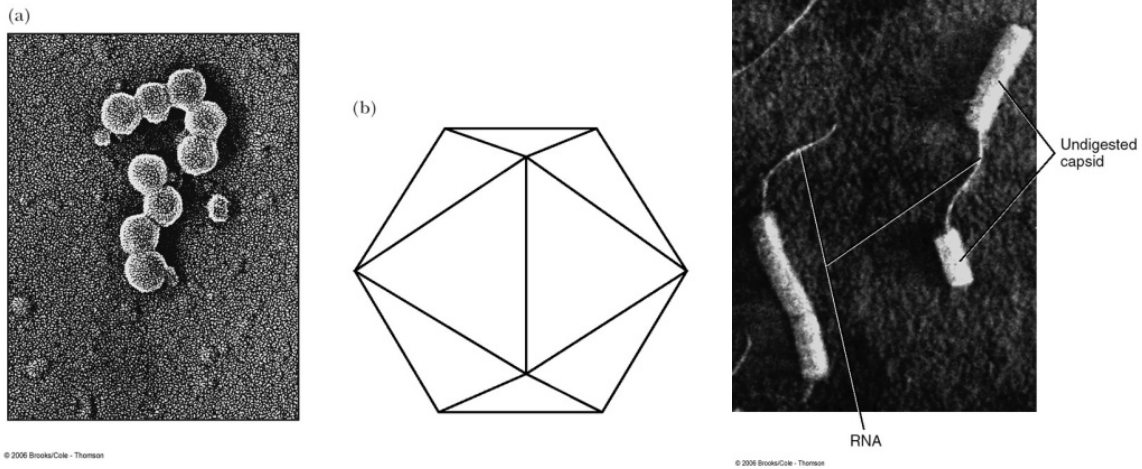


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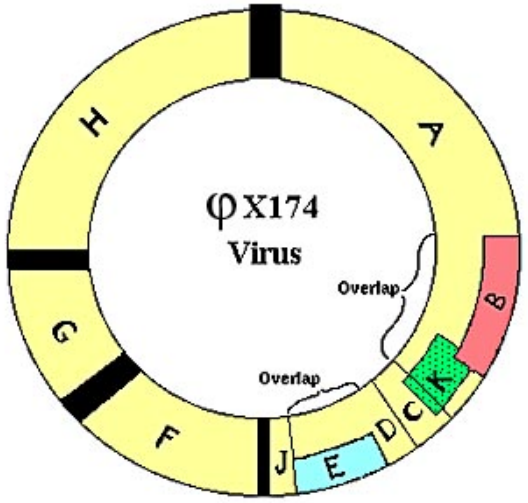
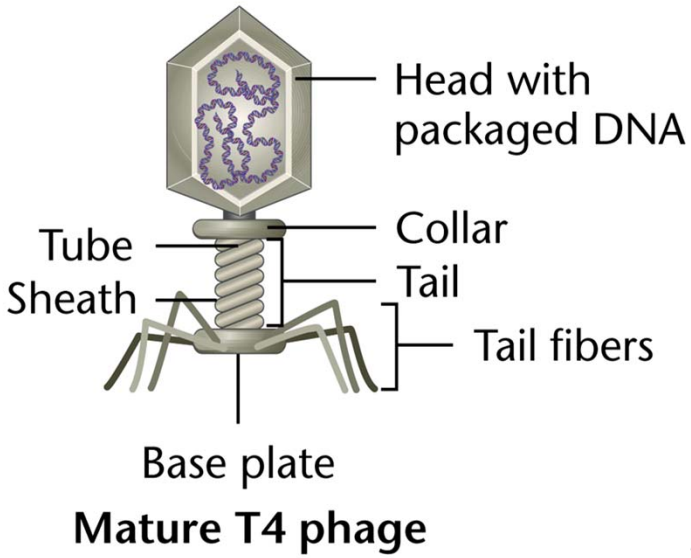
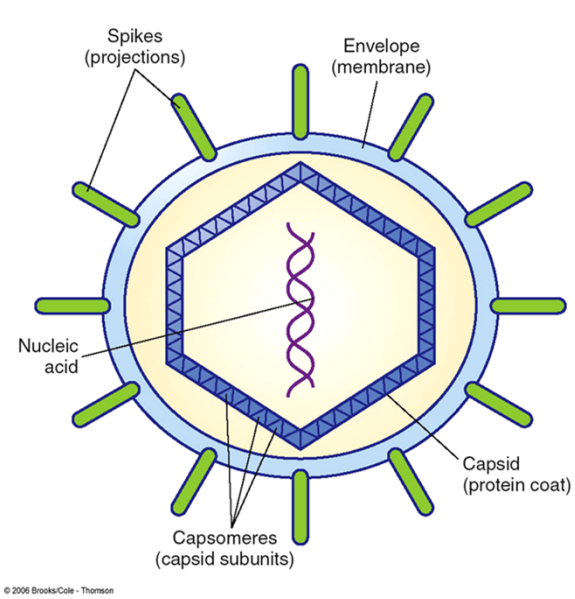



Overlapping Protein Codes

# Different sizes (20-300nm) and shapes

**Basic organization: Nucleic acid (ss or ds RNA or DNA) surrounded by a protein coat (known as capsid).**
**Some virus has a lipid envelope studded with carbohydrate obtained from the host cell.**
**Some can have proteins studded envelope essential for entrance into host cells.**



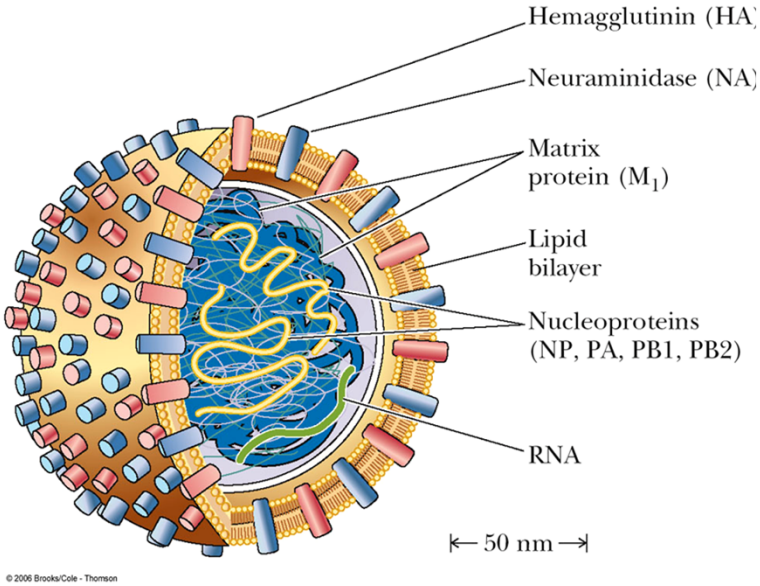




Figure 8-14 part 2 Essentials of Genetics, 6/e
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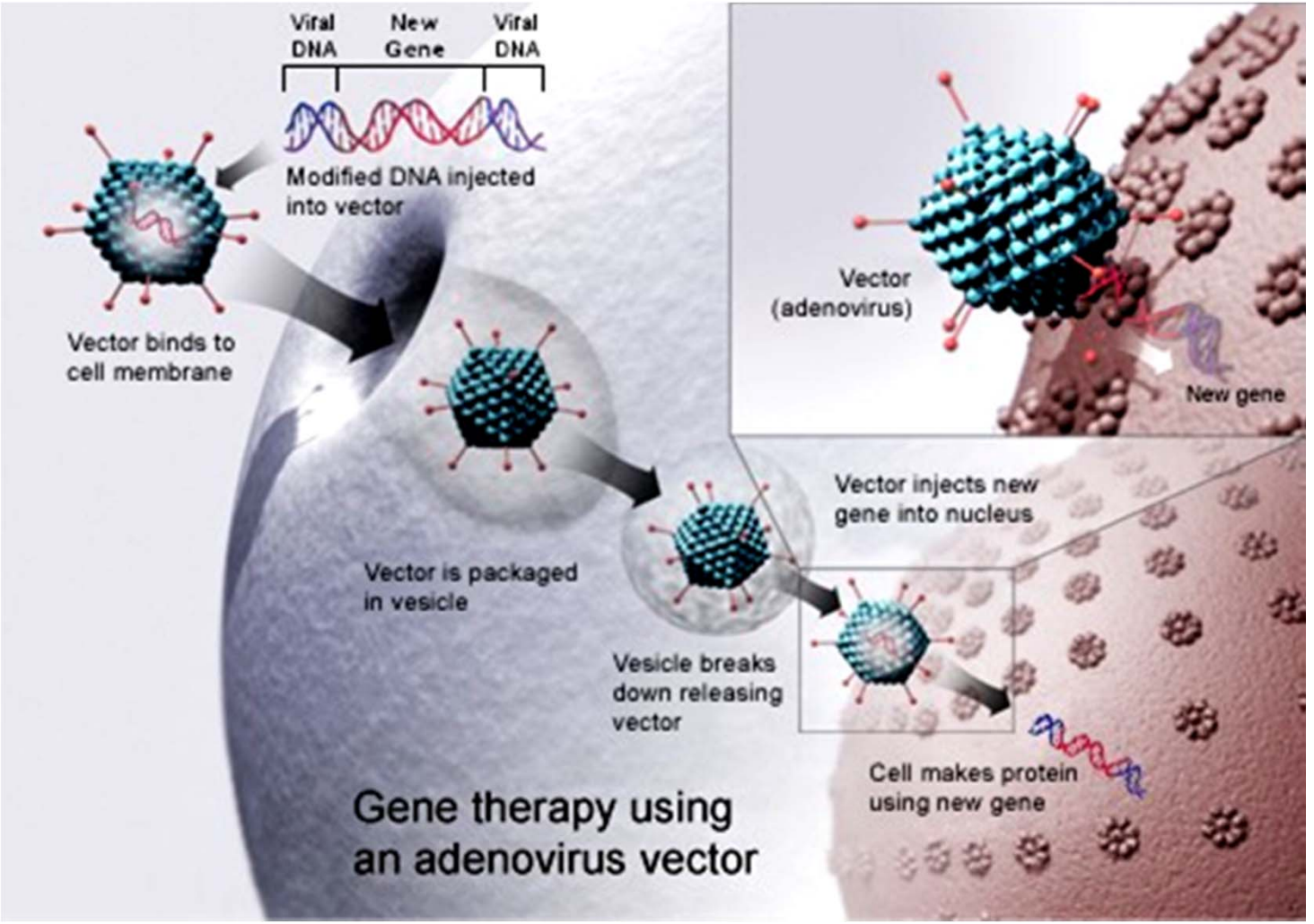
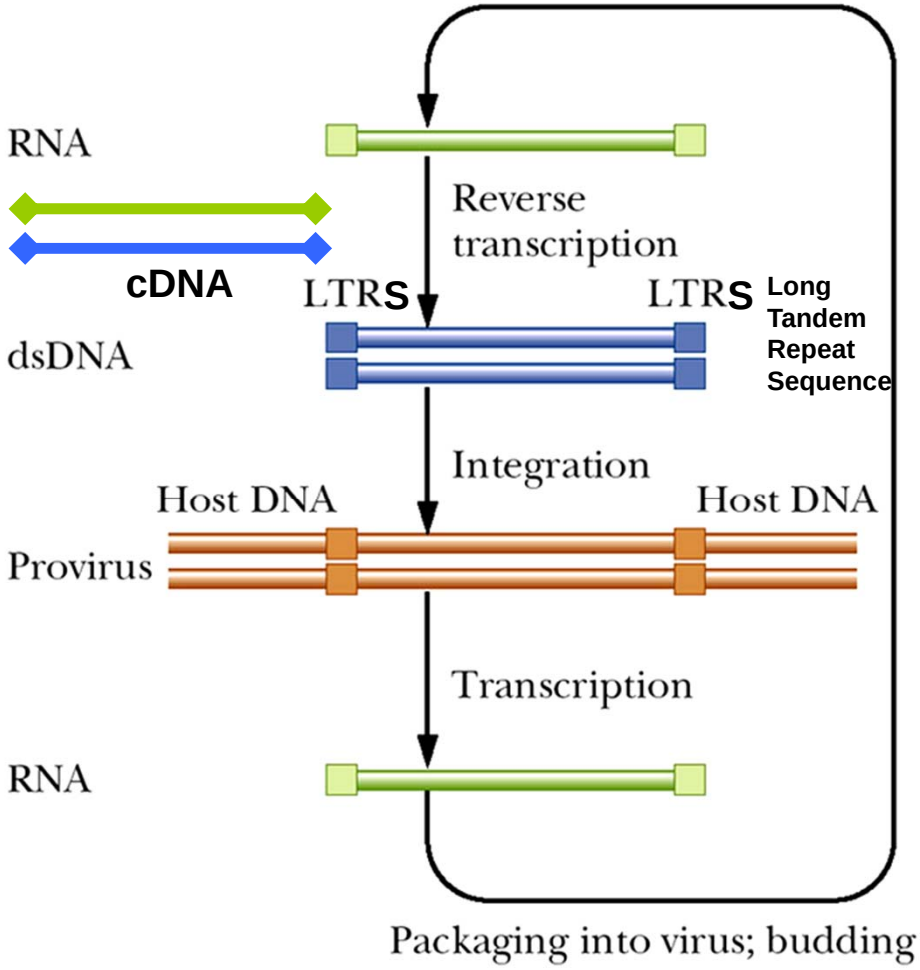
**The ability of virus to infect specific host cells with its nucleic acid make certain viruses a good candidate as a ‘gene delivery boy’ (vector) in Gene Therapy.**



# How RNA Virus Genome is Replicated?

**Viral RNA is released into the host cell, where the viral reverse transcriptase (RT) synthesizes double-stranded DNA from it. Three enzyme activities found in RT:**
**1. RNA-directed DNA polymerase (primer required to synthesize cDNA)**
**2. RNase H activity - degrades RNA in the DNA:RNA hybrids**
**3. DNA-directed DNA polymerase - which makes a DNA duplex after RNase H activity destroys the viral genome**
**DNA is integrated into host's genome and transcribed to RNA, and packaged into new virus particles.**

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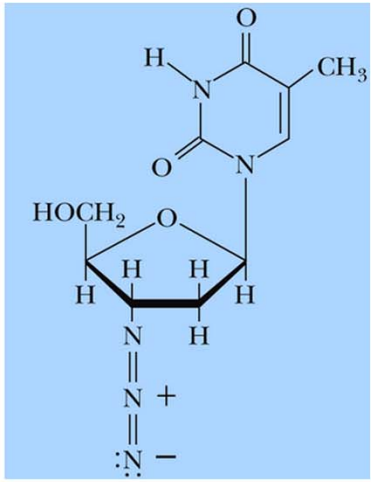
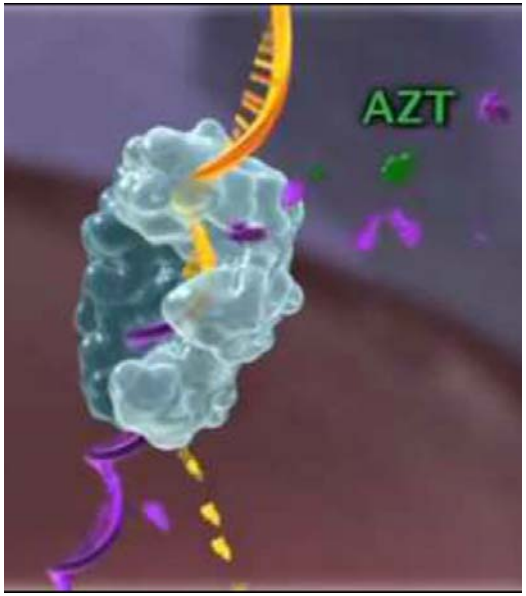
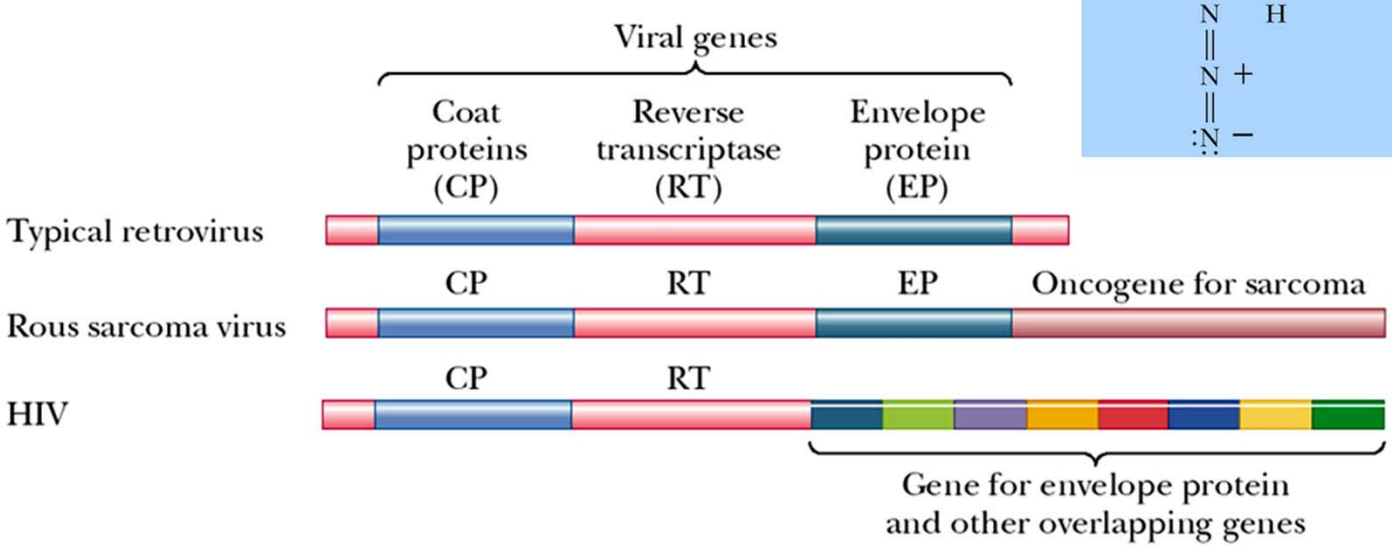
**Watch HIV Life Cycle at**
**http://www.hhmi.org/biointeractive/disease/hiv_life_cycle.html**

# Drug targeting reverse transcriptase of retroviruses

**The structures of AZT (3'-azido-2',3'-dideoxythymidine). the first approved drug for treatment of AIDS. HIV reverse transcriptase incorporates the thymidine analog into growing DNA chains in place of dTTP. Incorporated AZTMP blocks further chain elongation because its 3'-azido group cannot form a phosphodiester bond with an incoming nucleotide. Host cell DNA polymerases have little affinity for AZTTP.**



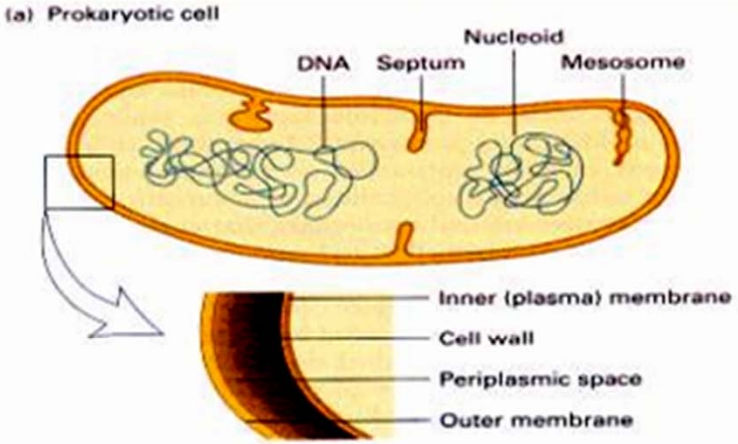


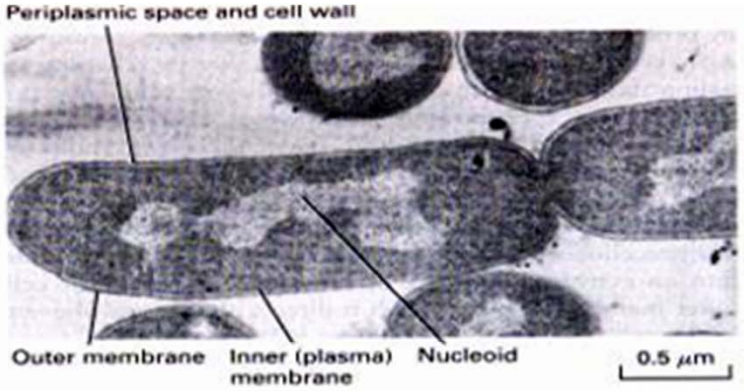



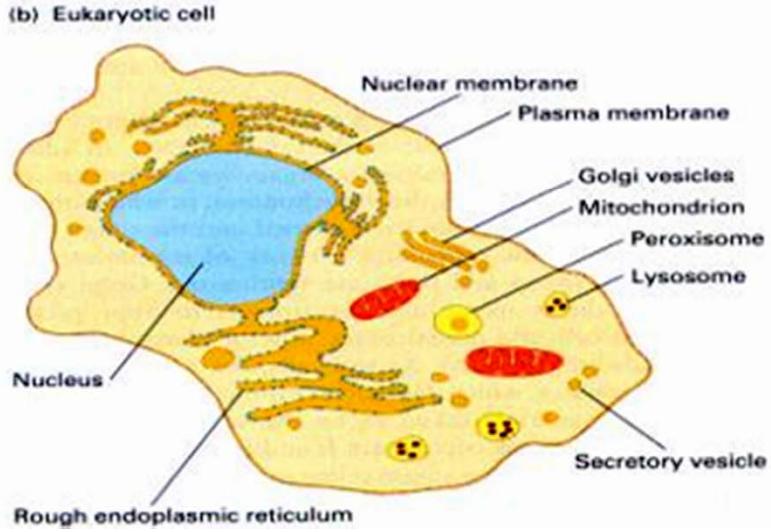

**Check out**
**http://www.hhmi.org/biointeractive/disease/reverse_trans.html**

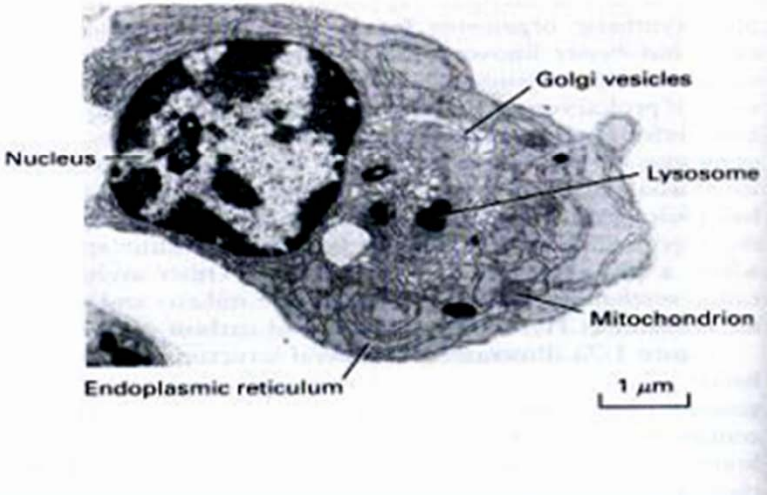
**The RNA genomes of all retroviruses have genes for coat proteins (CP), for reverse transcriptase (RT), for envelope protein (EP) and other proteins.**

# Prokaryotic versus Eukaryotic Cells



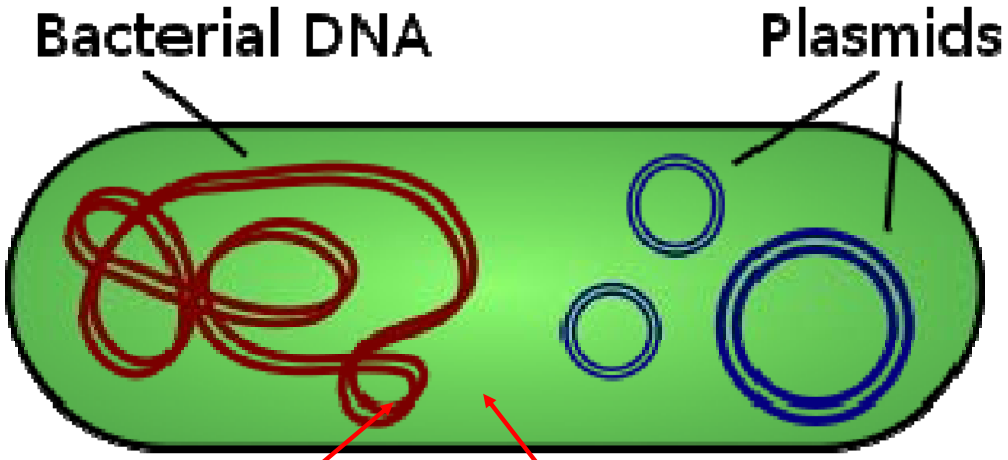

**Prokaryote**

- **Bacteria and archaea**
- **Lack membrane-limited nucleus and other organelles**

**Eukaryote:**

- **All organisms except viruses and bacteria.**
- **Membrane-enclosed nucleus and other organelles**

# Genetic organization in a prokaryote



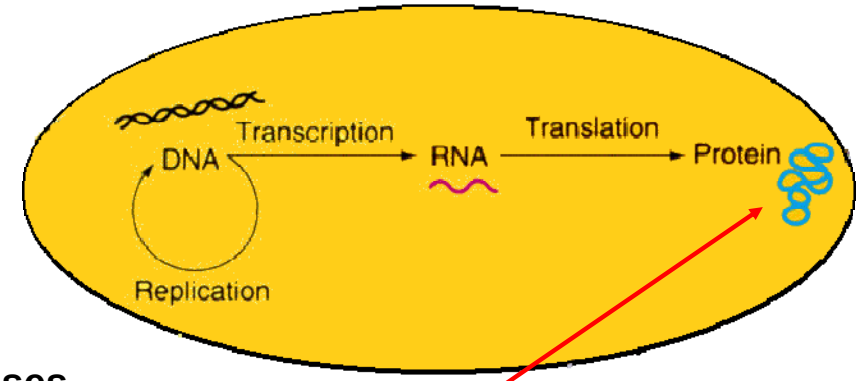

http://en.wikipedia.org/wiki/Plasmid

One circular 'Chromosome' (but DNA is not associated with histones) and not envelope by a nuclear membrane (hence no nucleus)

Cytoplasm (cellular processes & metabolism takes place)

**Plasmid is a small circular extra chromosomal DNA which:**
**(i) can be replicated**
**(ii) can be transferred to different cells**
**(iii) Carries accessory genes (e.g. antibiotic resistance; enzyme that breaks down unusual compounds)**

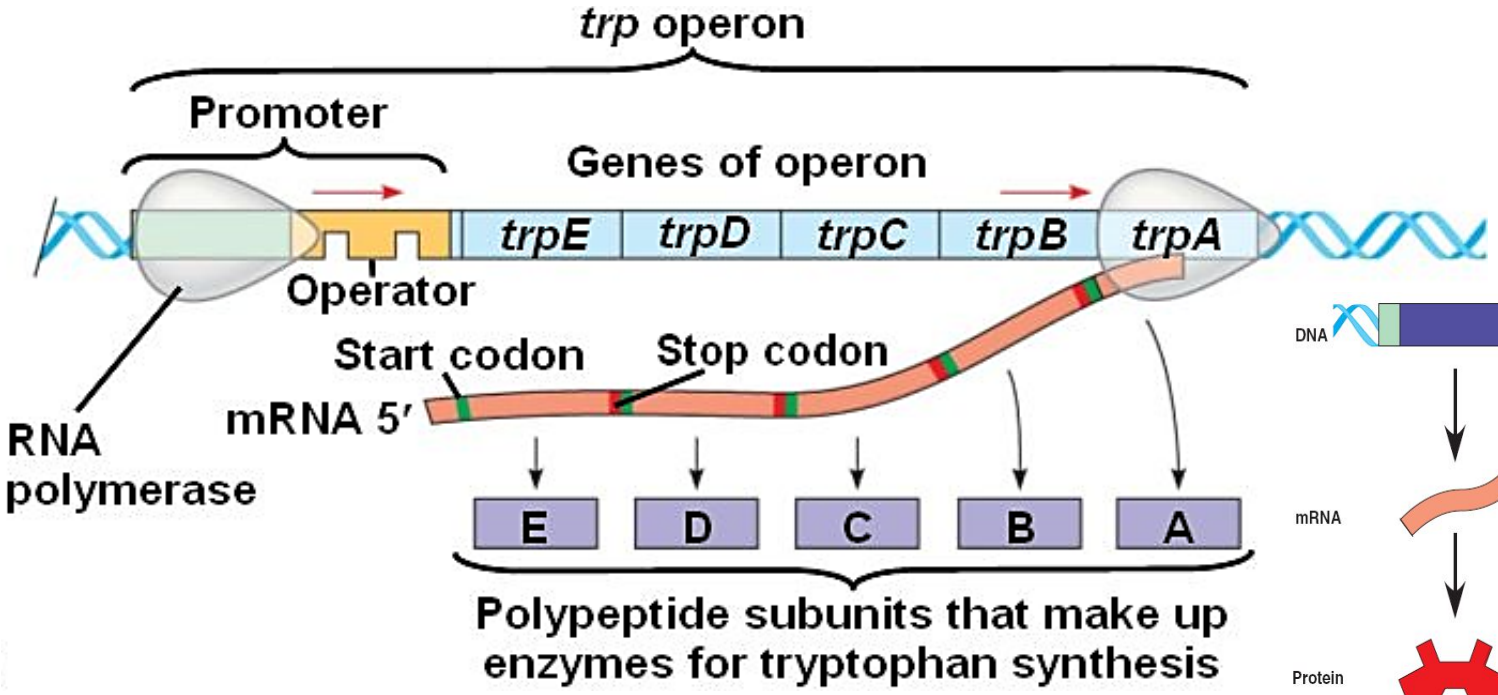
The "Central Dogma" in prokaryotic cells

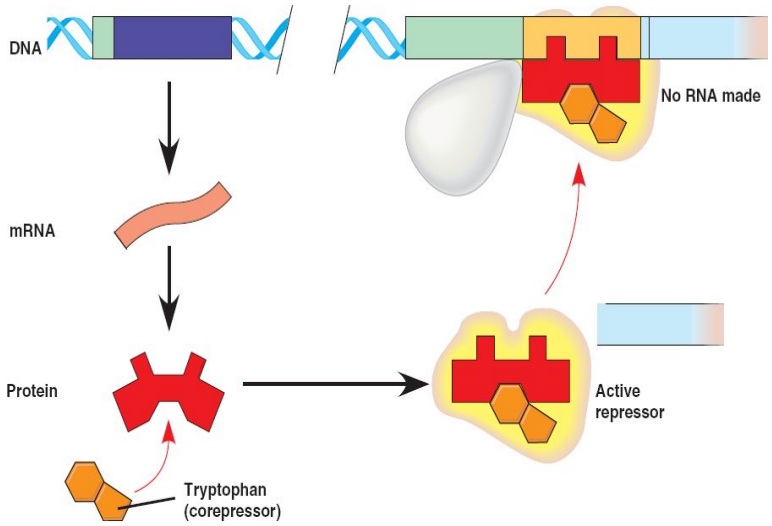



(after Griffiths et al. 1996)

Proteins undergo no or minimal post-translational modification

**Operons are found mostly in prokaryotic cells (rarer in eukaryotic cells, why?) An operon is a group of functionally related genes under the control by a single on-off "switch" within the promoter (regulatory region).**

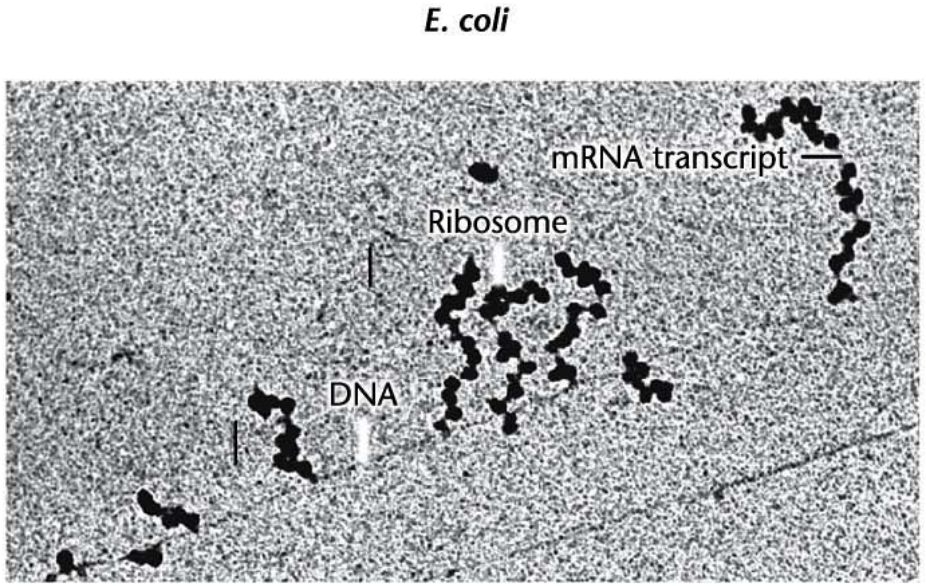


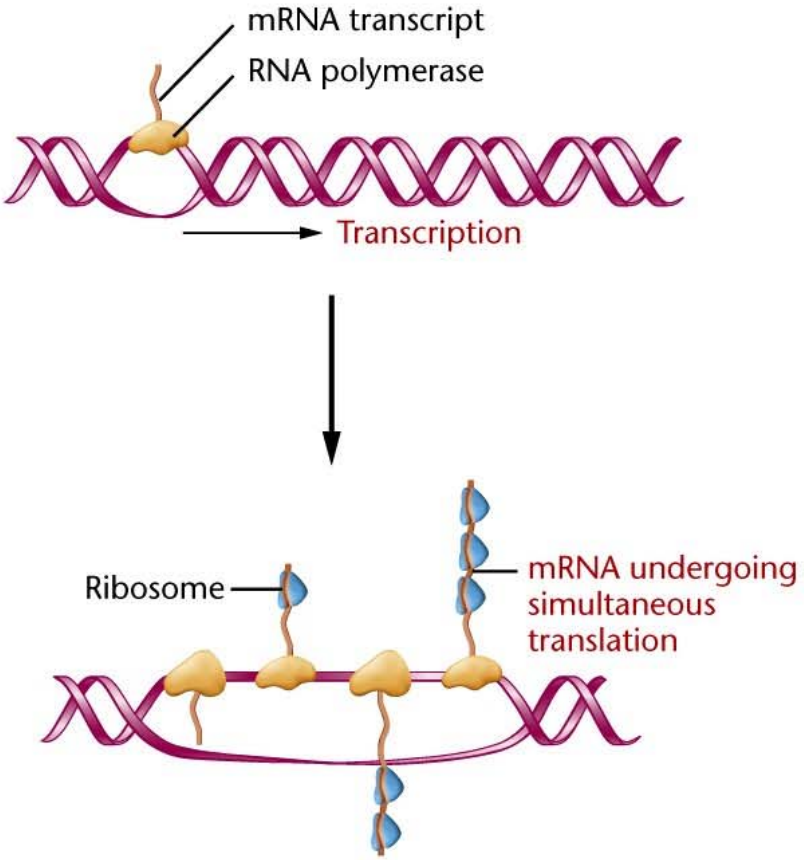




**The operon system allow efficient regulation (rapid turning on & off) of several related genes.**

http://bio1151.nicerweb.com/Locked/media/ch18/trp_operon.html

**An electron micrograph and interpretive drawing of simultaneous transcription of a gene in *E. coli*. As each transcript is forming, ribosomes attach, initiating simultaneous translation along each strand.**




**Watch polyribosome and simultaneous transcription and translation on IVLE**

**Figure 12-14 Essentials of Genetics, 6/e**
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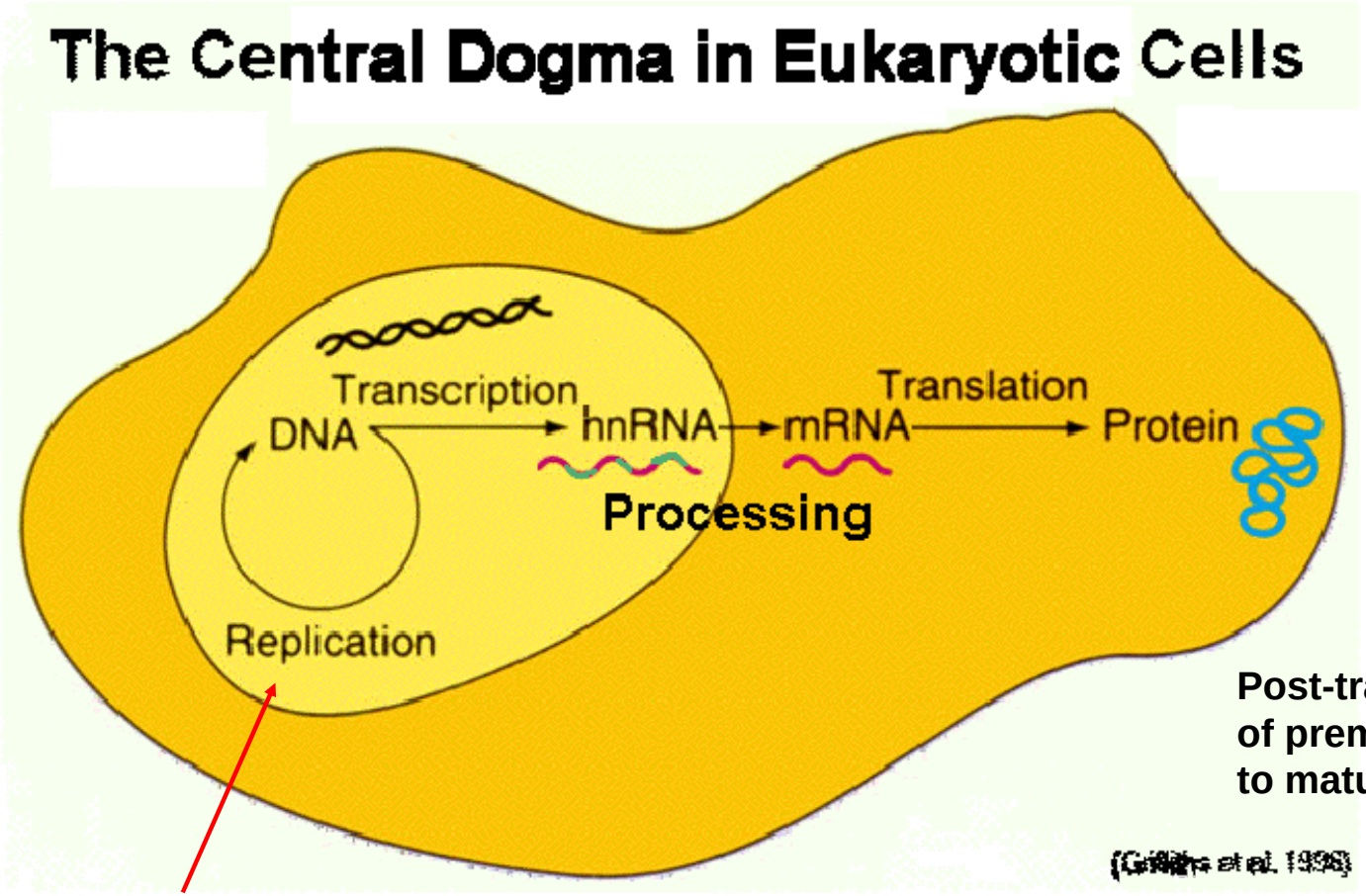



**Proteins undergo post-translational modification**

**Post-transcriptional processing of premature (hetero-nuclear) mRNA to mature mRNA**

**Contain several chromosomes (DNA is packaged with histones) envelope by a nuclear membrane (hence there is nucleus) that separates from the cytoplasm.**

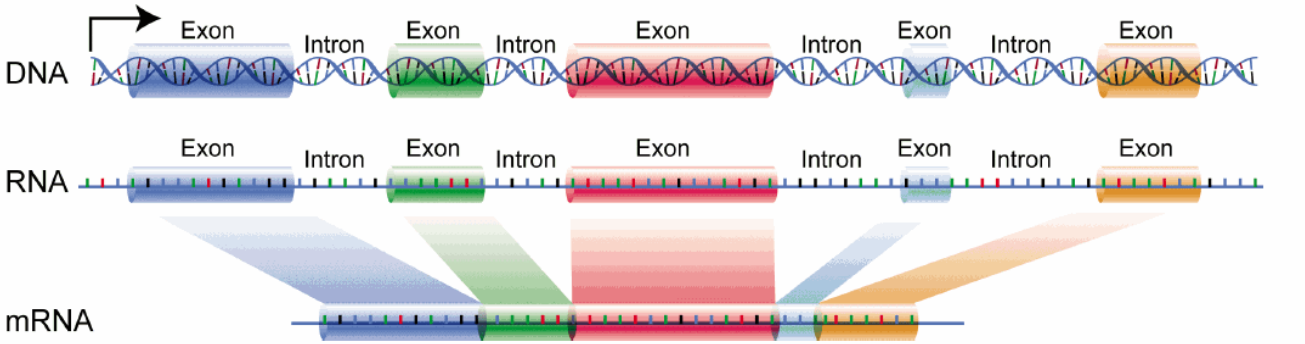
http://www.mun.ca/biology/scarr/Fig13-02_eukaryotic.html

# Post-transcriptional Processing of mRNA in Eukaryotes

- **Translation closely follows transcription in prokaryotes**
- **In eukaryotes, these processes are separated - transcription in nucleus, translation in cytoplasm**
- **On the way from nucleus to cytoplasm, the mRNA is converted from “premature heteronuclear mRNA" to "mature mRNA“**

**Three post-transcriptional processing takes place:**

1. **Capping of G residue (adding of guanylyl group) and methylation at 5’ end.**
2. **Polyadenylating (adding of poly-A sequence to) 3’ end.**
3. **Splicing of coding sequences and removal of non-coding sequences (eukaryotic genes are split into coding (exons) and non-coding regions (introns).**




http://de.wikipedia.org/wiki/Splei%C3%9Fen_(Biologie)#mediaviewer/File:DNA_exons_introns.gif

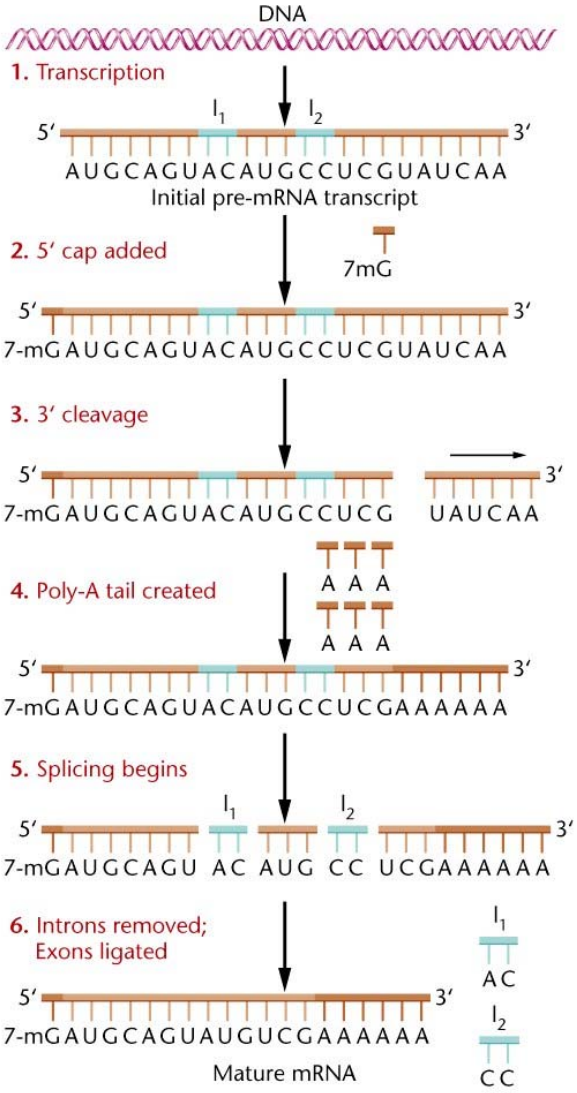



**Figure 12-9 Essentials of Genetics, 6/e**
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# Three post-transcriptional processing:

**Capping of G residue (adding of guanylyl group) and methylation at 5' end. Capped mRNA are resistant to 5'-exonucleolytic degradation and also help ribosome binding during translation initiation.**

**Polyadenylating (adding of poly-A sequence to) 3' end. Poly-A tails are bound by poly(A)-binding proteins that protect mRNA from rapid degradation, thus increasing life-span to hours or days (<30 min for mRNA lacking poly(A) tail).**

**Splicing of coding sequences (eukaryotic genes are split). Gene splicing permits a single gene to encode several proteins with different functions and is an agent for rapid protein evolution**

**See Post-transcriptional Processing on IVLE Animation**

**Interestingly, not all exons are spliced together to form the mature mRNA transcript: Alternative Splicing**

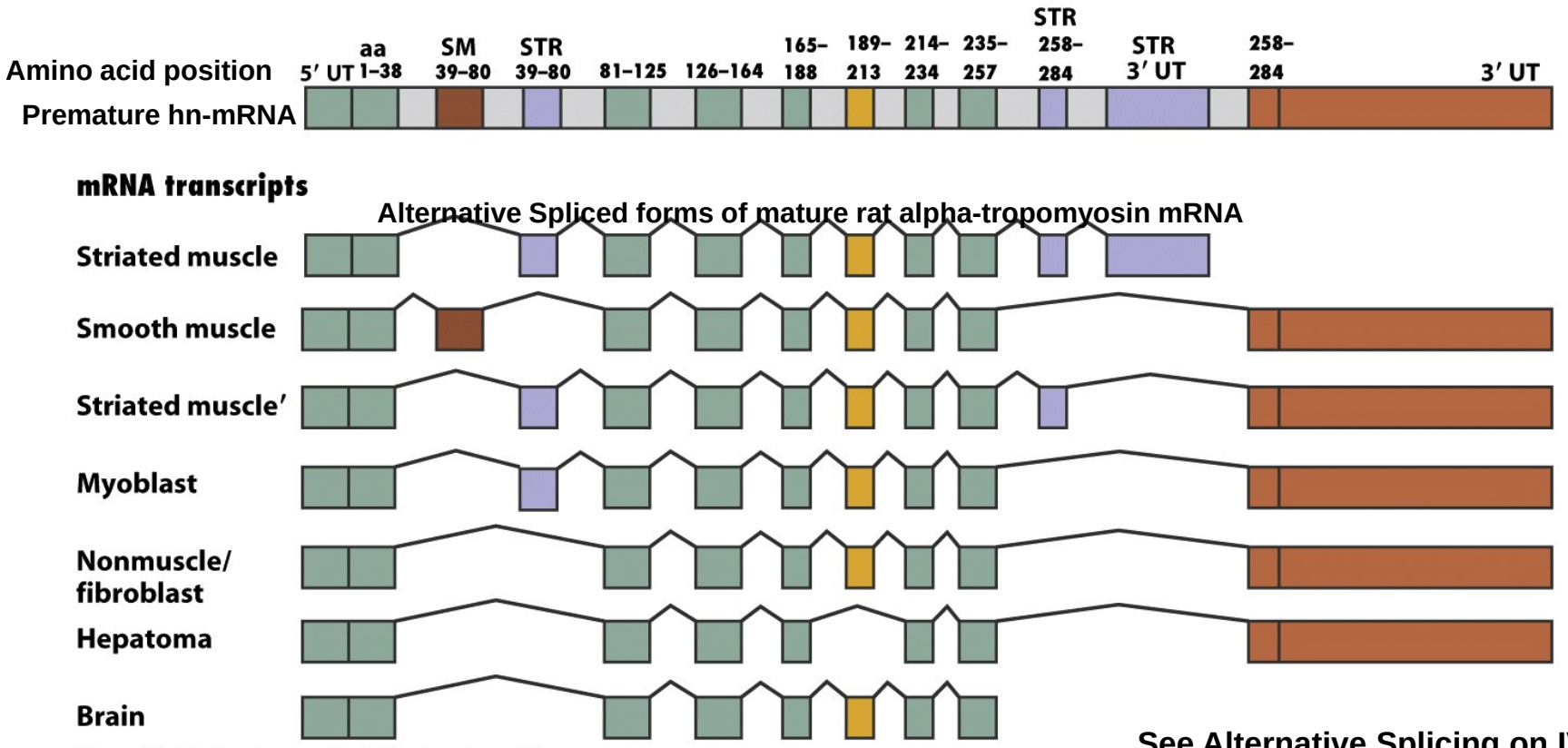


Figure 25-25 Fundamentals of Biochemistry, 2/e
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**See Alternative Splicing on IVLE**

**The alternative spliced form produced in a cell would depend on RNA binding proteins and processing factors present that could bind on splice sites (intron-exon junction) and promote processing of specific alternate spliced form of an mRNA.**

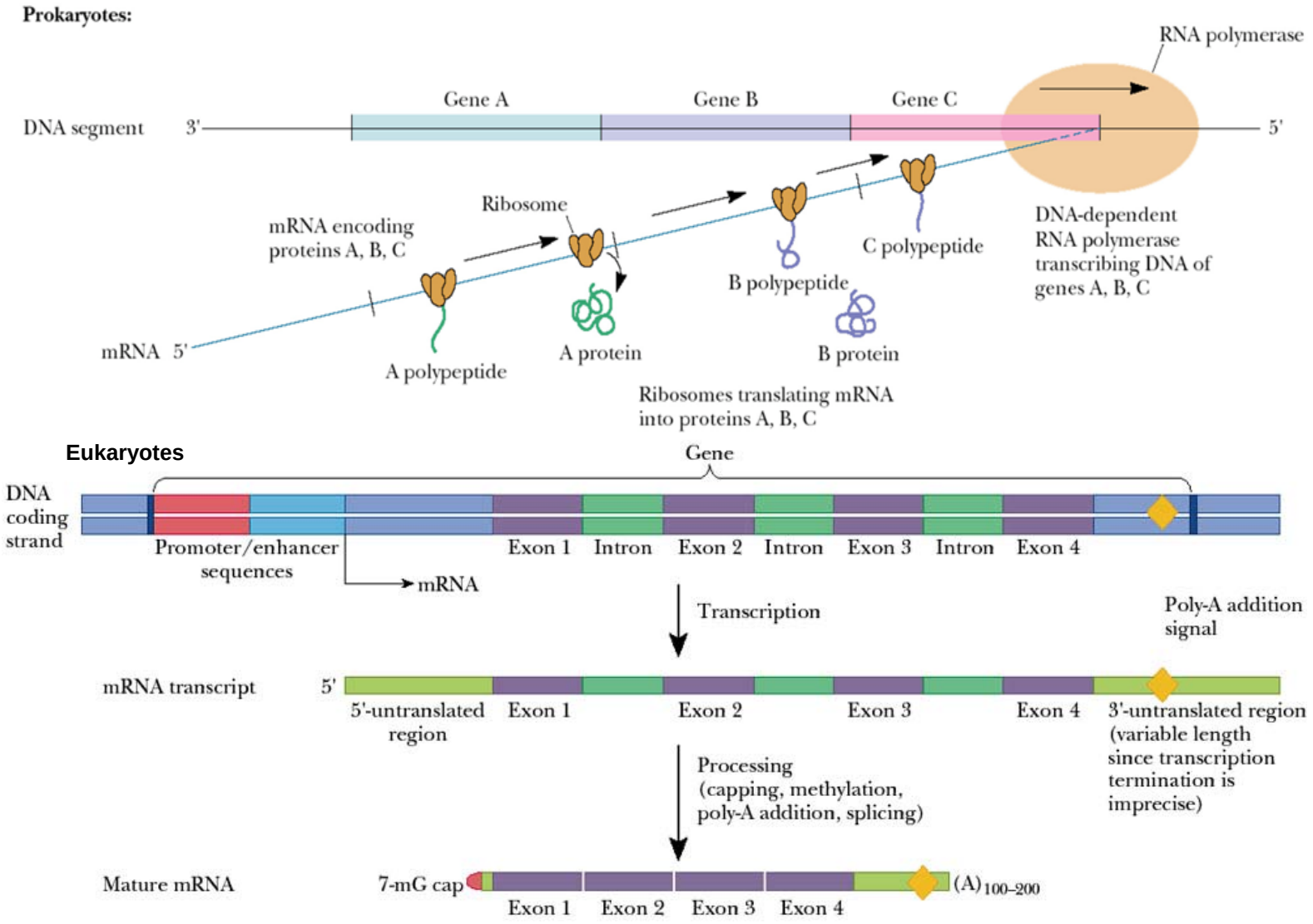
# Why have genes split by introns?

- Gene splicing is a rapid agent for protein evolution. Different exonal regions coding for different functional domains can be combine to give a protein with different functions without the need to ‘reinvent the wheel’ for protein with ‘minor’ differences.

- It allows for **alternative splicing (post-transcriptional processing)**, where a single gene containing multiple **exons** may give rise to transcripts containing mutually exclusive exons translated to different protein properties and functions. Thus ~20,000 genes can give rise to more than 250,000 proteins (also contributed by post-translational modification), hence allowing complexity with lesser number of genes (lower the burden of gene maintenance) .

- Introns (non-coding regions within a gene) and intergenic regions (non-coding regions between two genes) can act as regions for buffering mutation. Only ~1.5 % of our genome are coding regions (greater than 98% of our genome are non-coding regions).

**Watch coding sequences in DNA**
**http://www.hhmi.org/biointeractive/coding-sequences-dna**

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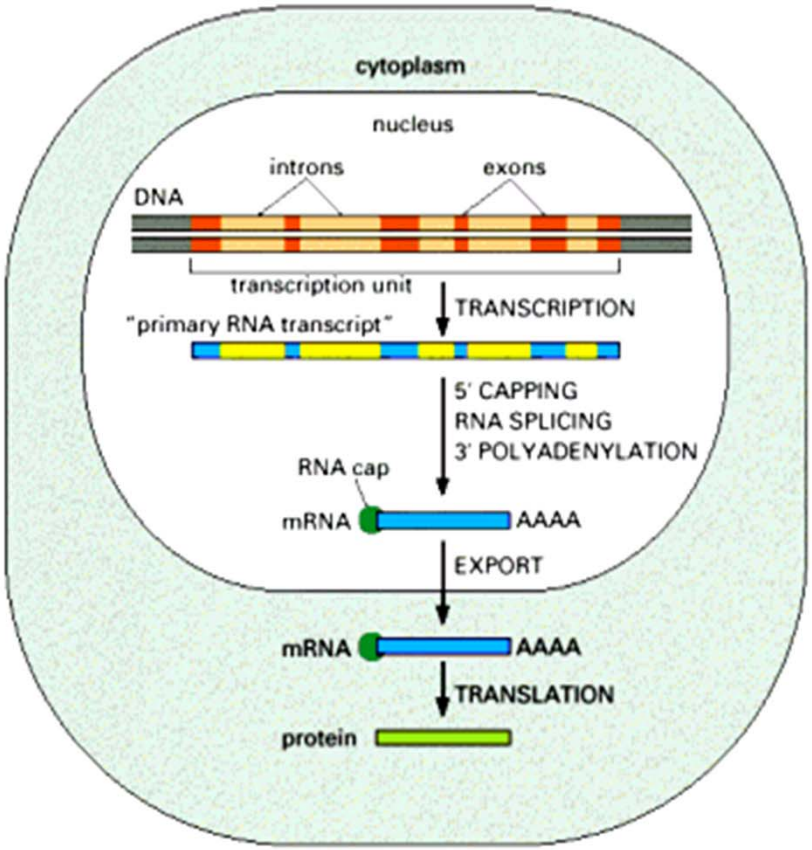
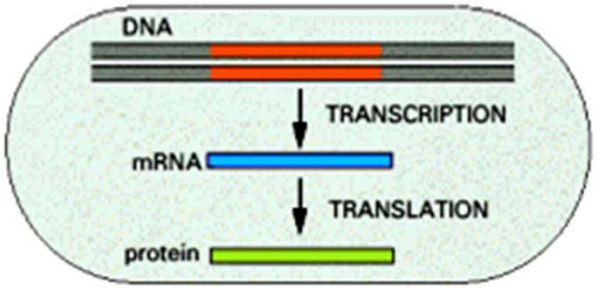
# Summary of the steps leading from gene to protein in eukaryote and prokaryote.

**Eukaryote**




**Prokaryote**




**Although these steps are depicted as occurring one at a time, in a sequence, in reality they are coupled and different steps can occur simultaneously. The final level of a protein in the cell depends on the efficiency of each step and on the rates of degradation of the RNA and protein molecules.**

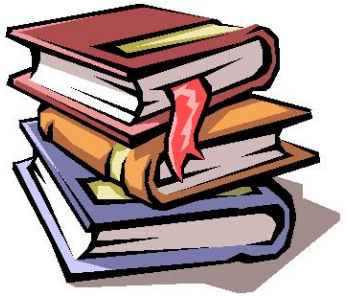
# Summary & Conclusion

- **All viruses are obligate parasites (requiring host cells to propagate). Some have RNA or DNA as genetic material and genome are relatively small with overlapping protein-coding regions. Retroviruses use own reverse transcriptase to replicate genome before integrating into genome of host-cell.**

- **Prokaryotes usually have single circular DNA chromosome not enclosed by nuclear membrane, containing operons and extra-chromosomal DNA (plasmids). Transcription and translation occur simultaneously and their proteins do not undergo, if any minimal, post-translational modification.**

- **Eukaryotes have multiple chromosomes and genes are organized into introns and exons. Premature heteronucler mRNA need to be post-transcriptional processed (alternatively spliced) into mature mRNA in the nucleus before translated into protein in the cytoplasm. Proteins can undergo substantial post-translational modification.**

# Additional Enrichment Materials



- **IVLE Animations: Prokaryote transcription and translation; Post-transcriptional RNA Processing; RNA splicing, Alternative splicing.**
- **Useful Weblinks:**
- **Learn Genetics Cell-Molecules size and scale:**
- http://learn.genetics.utah.edu/content/cells/scale/
- **Watch HIV Life Cycle & AZT inhibition at:**
- **http://www.hhmi.org/biointeractive/disease/hiv_life_cycle.html**
- **http://www.hhmi.org/biointeractive/disease/reverse_trans.html**
- **Watch coding sequences in DNA**
- **http://www.hhmi.org/biointeractive/coding-sequences-dna**