Moc/Bio and Nano/Micro

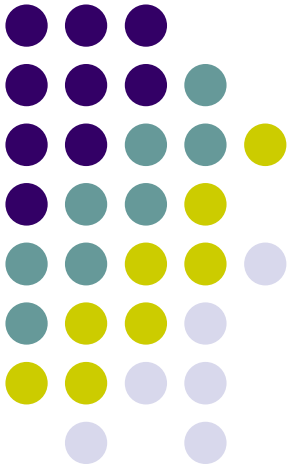
Lee and Stowell

Moc/Bio-Lecture 7

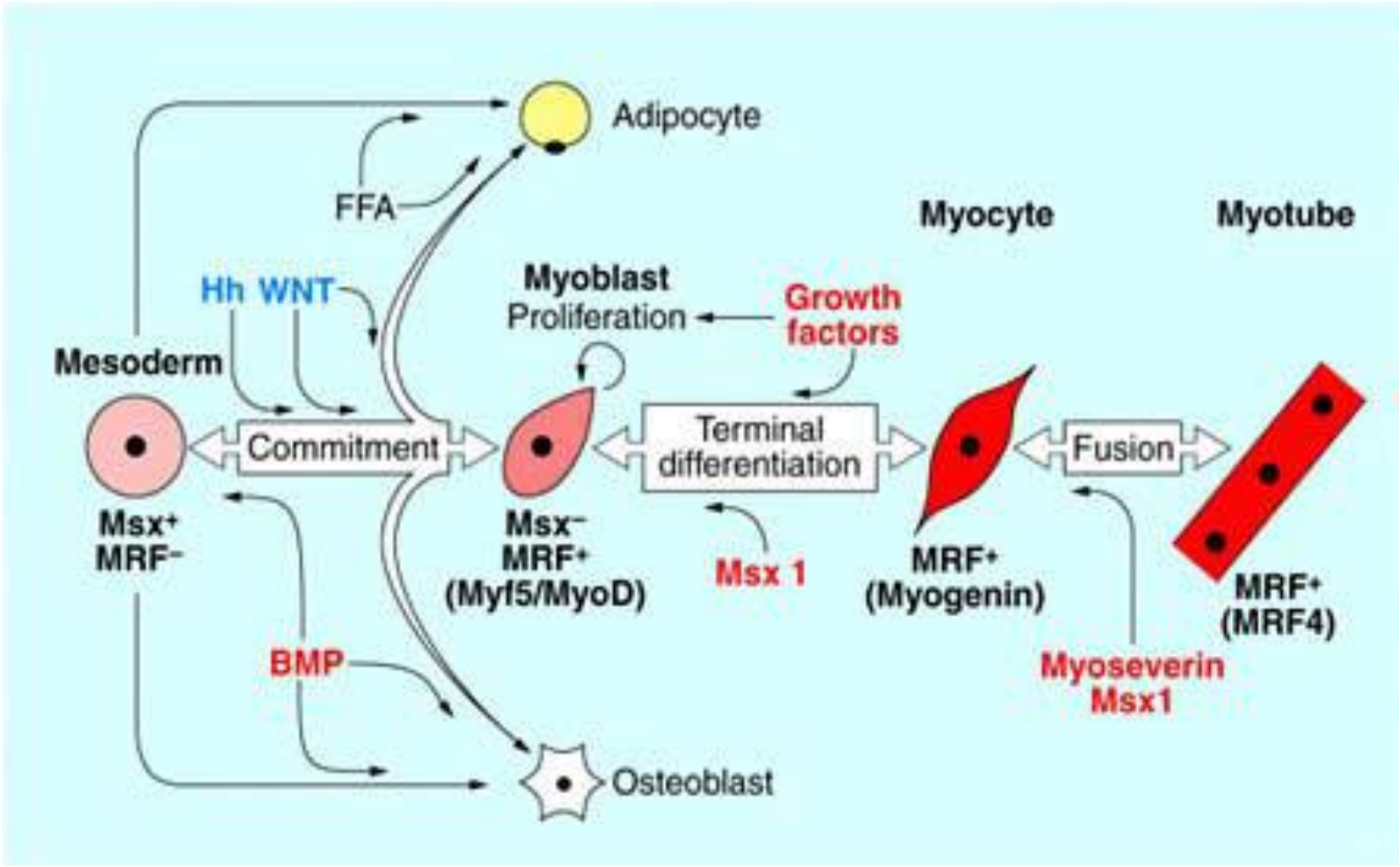
Coordination of Biomolecular functions
- **Gene regulation**
  - **DNA level**
  - **RNA level**
  - **Protein level**

Intercellsignaling (first messengers)
- **Signaling molecules**
- **Receptors**

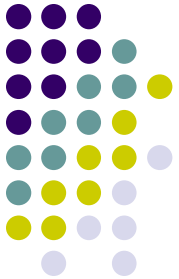
Intracellsignaling (second messengers)
- **cAMP**
- **cGMP**
- **Phospholipids**



One genome many cell types



Biological outcome is under multilayered biochemical control



- Transcriptional control
  - DNA level
- Translational control
  - RNA level
- Post-translational (Activity) control
  - Protein level

Coordination of these controls

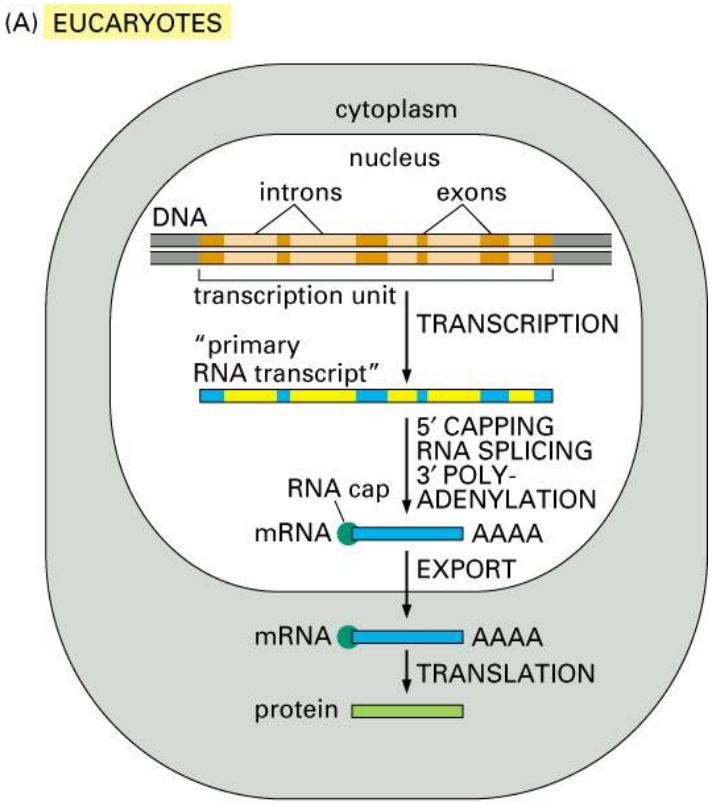


Figure 6–21 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

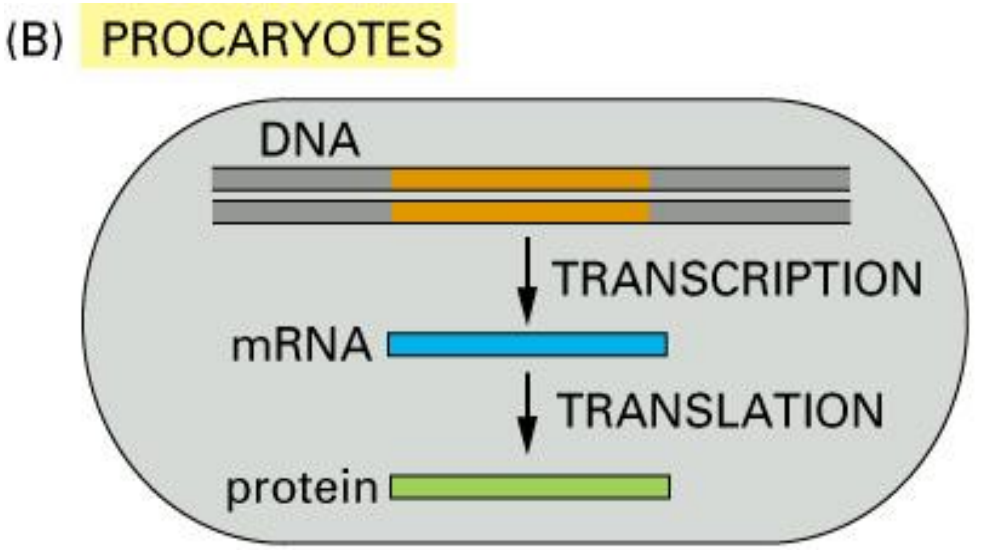


Figure 6–21 part 2 of 2. Molecular Biology of the C

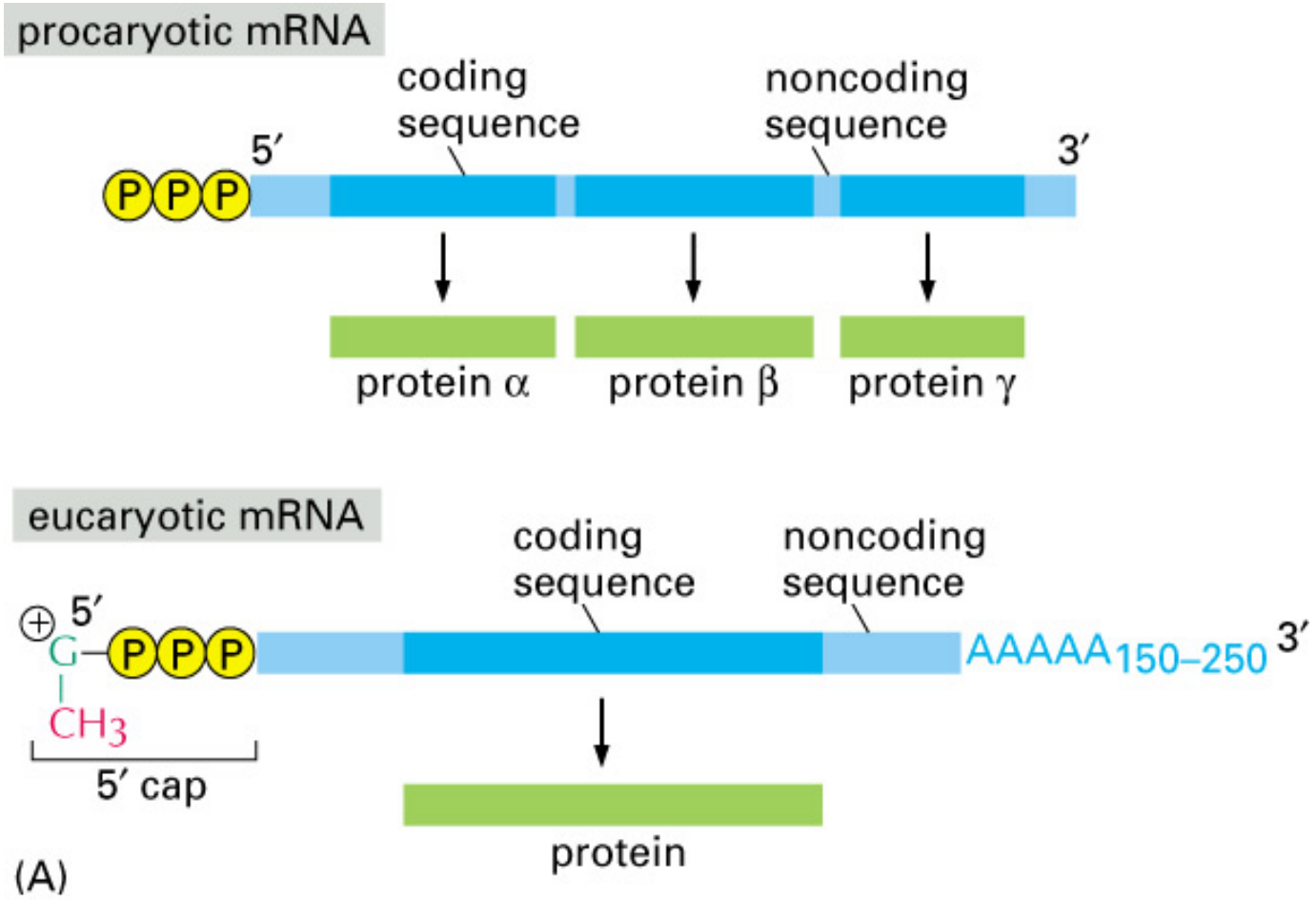
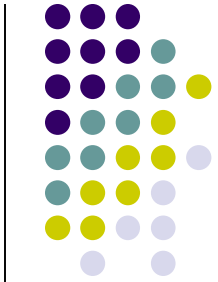
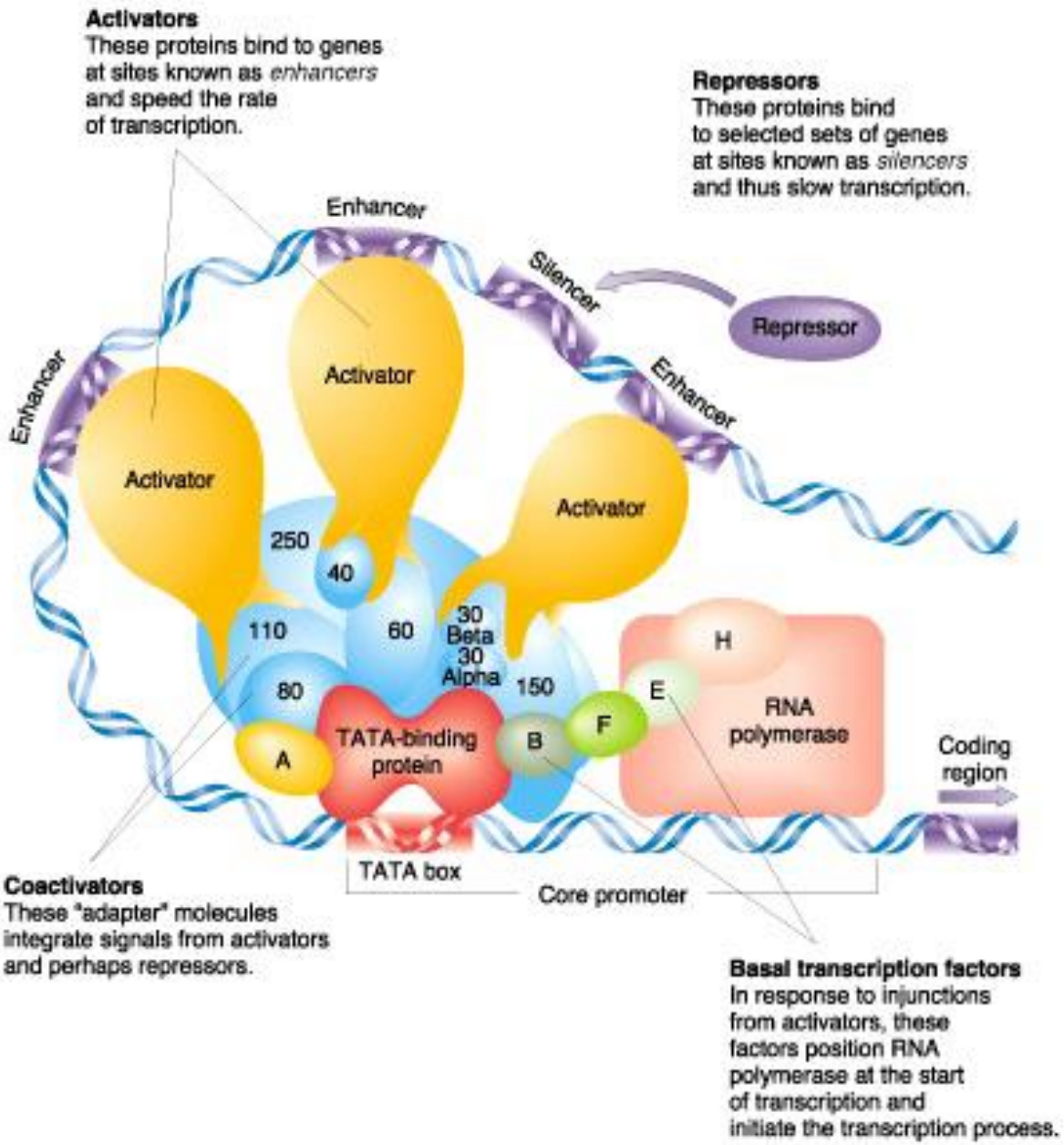


Figure 6–22 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

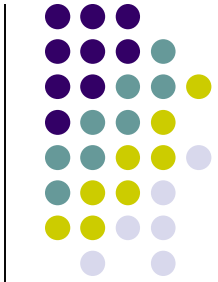
Transcriptional Control



- Key concepts
  - Regulates the number of mRNA molecules produced
  - Can be enhanced and suppressed
  - Encoded by the noncoding5’ upstream region of the gene.


Activators
These proteins bind to genes at sites known as enhancers and speed the rate of transcription.
Repressors
These proteins bind to selected sets of genes at sites known as silencers and thus slow transcription.
Enhancer
Silencer
Repressor
Enhancer
Enhancer
Activator
Activator
Activator
250
40
110
60
30 Beta
30 Alpha
150
80
A
TATA-binding protein
B
F
E
H
RNA polymerase
Coding region
TATA box
Core promoter
Coactivators
These "adapter" molecules integrate signals from activators and perhaps repressors.
Basal transcription factors
In response to injunctions from activators, these factors position RNA polymerase at the start of transcription and initiate the transcription process.

Case study Lac operon

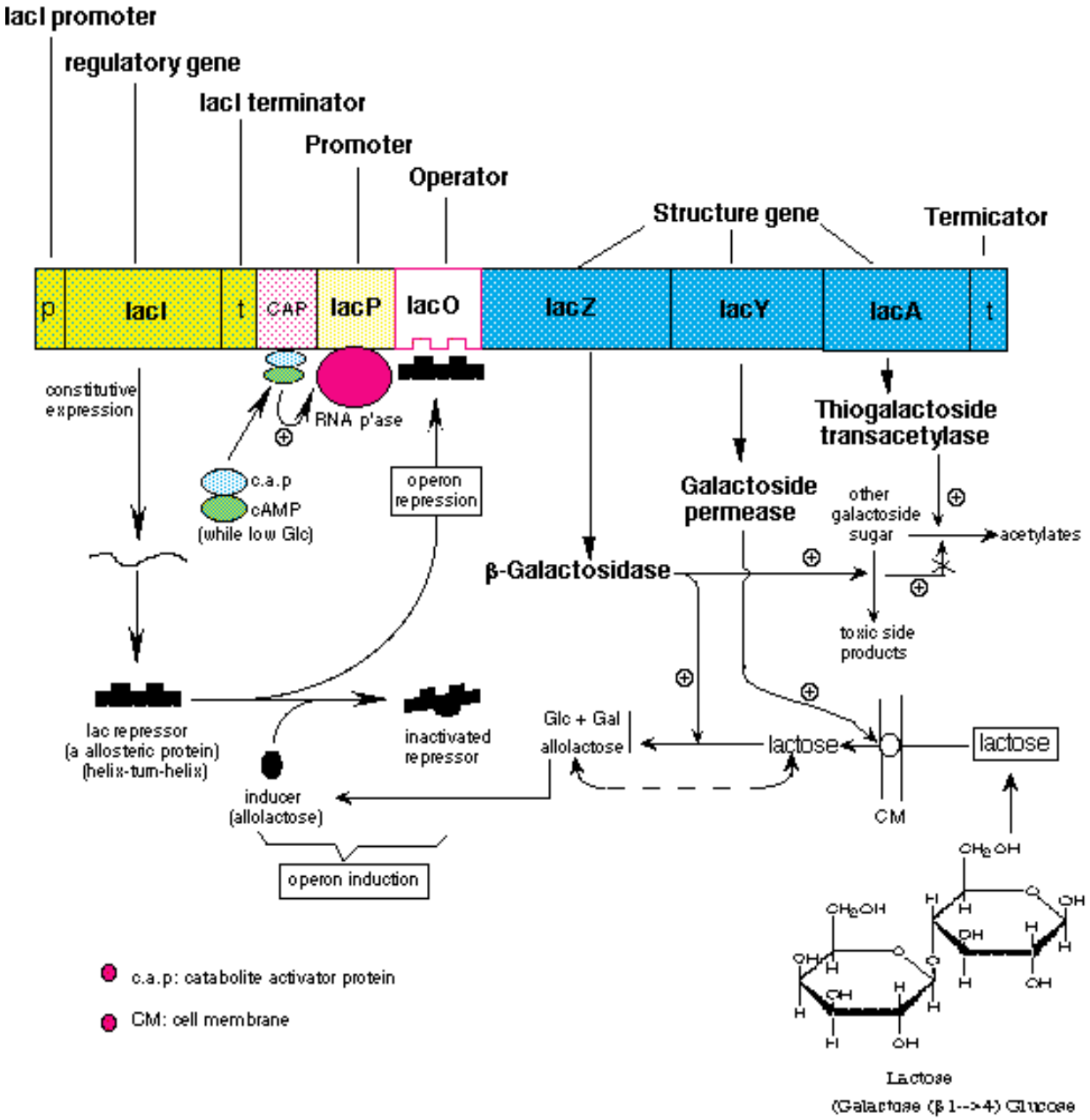


A protein-DNA feedback loop for carbohydrate consumption in bacteria

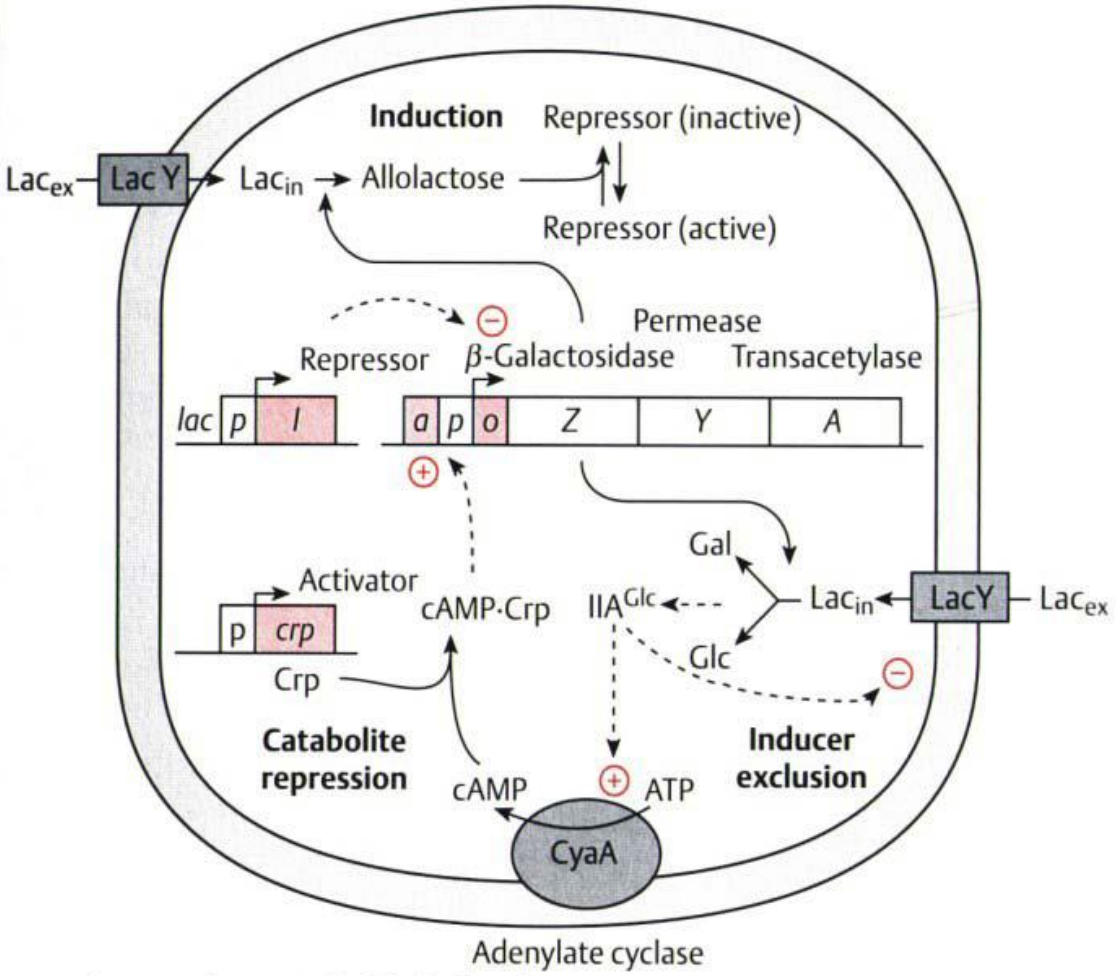
- **3 functional proteins under 1 promoter**
  - **Beta galactosidase(LacZ)**
  - **Transacetylase(Lac A)**
  - **Lactose permease(Lac Y)**

- **1 Repressor protein constitutive expression**
  - **Binds operator (promoter region) blocks transcription**

Lac Operon


lacI promoter
regulatory gene
lacI terminator
Promoter
Operator
Structure gene
Termicator
p
lacI
t
CAP
lacP
lacO
lacZ
lacY
lacA
t
constitutive expression
RNA p'ase
c.a.p
cAMP
(while low Glc)
operon repression
Thiogalactoside transacetylase
Galactoside permease
other galactoside sugar
acetylates
β-Galactosidase
toxic side products
lac repressor
(a allosteric protein)
(helix-turn-helix)
inactivated repressor
Glc + Gal
allolactose
lactose
lactose
inducer
(allolactose)
CM
operon induction
c.a.p: catabolite activator protein
CM: cell membrane
Lactose
(Galactose (β 1-->4) Glucose

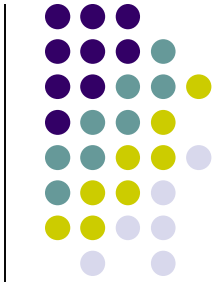
Typische polycistronische Genstruktur am Beispiel lac-Operon von E. coli



aus Lengeler et al: Biol. Prokaryotes

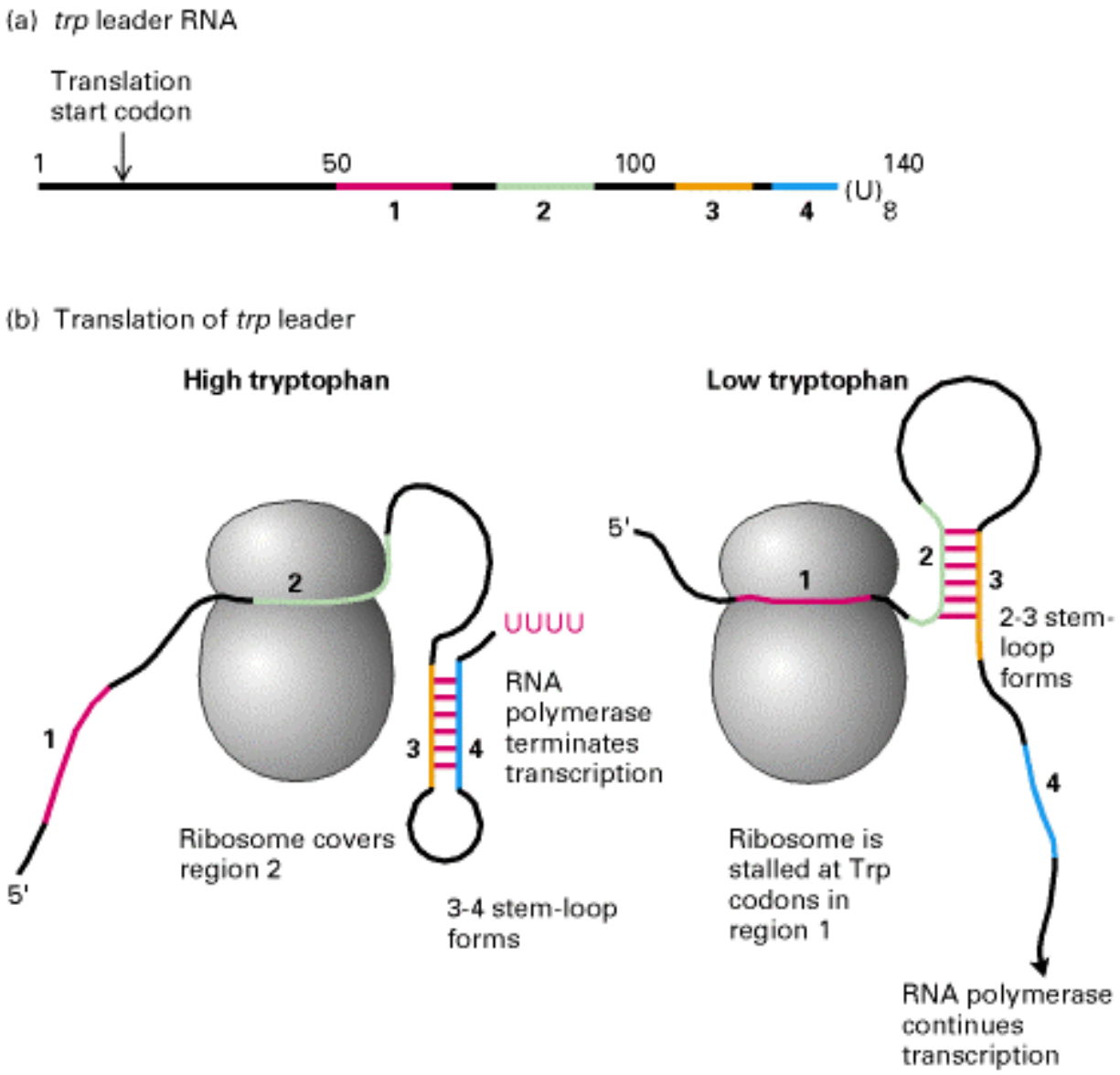
mi4_111.gif

Translational Control

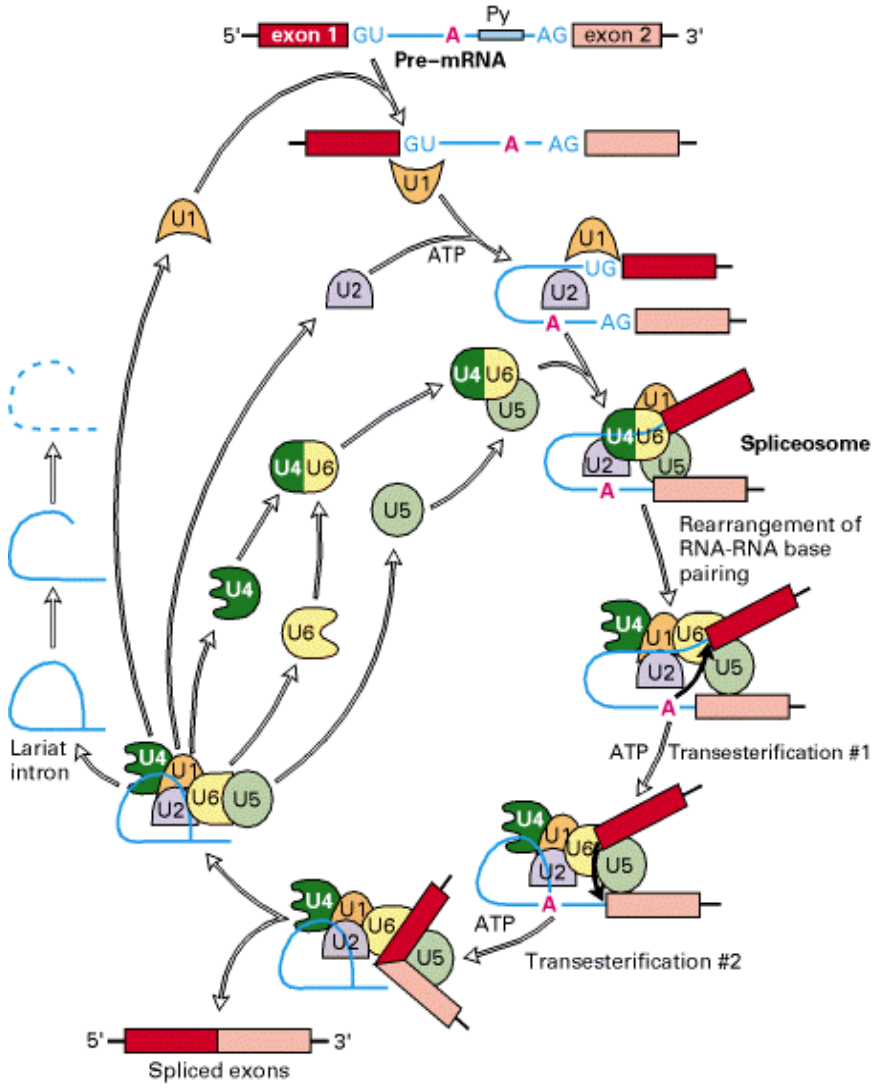


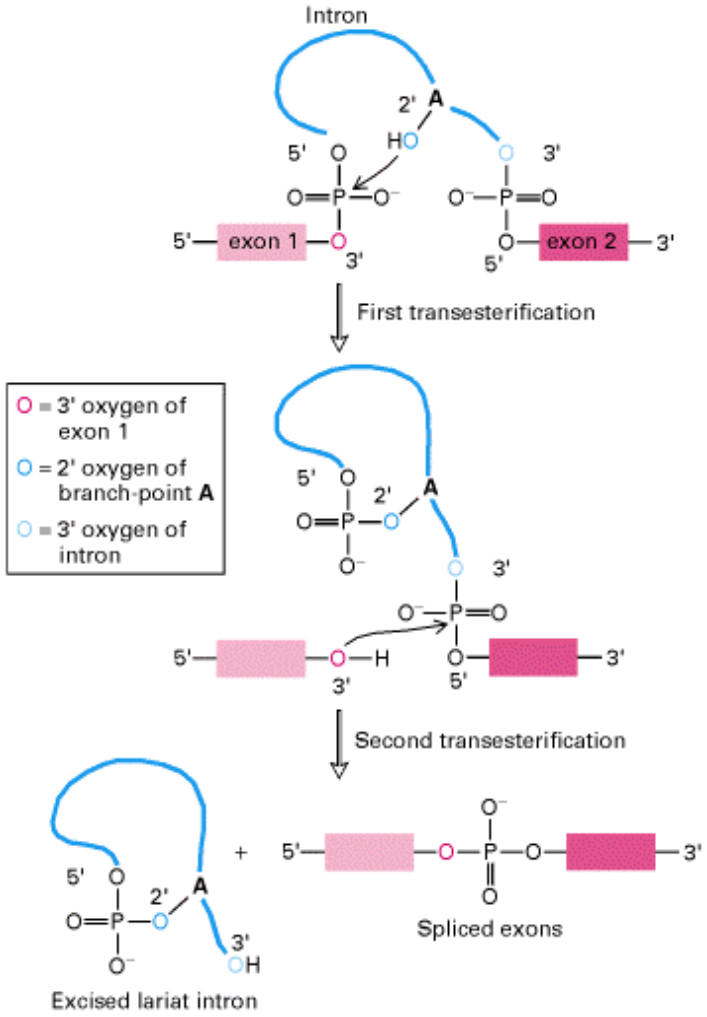
- Translational stalling and transcription termination
- Trp operon
- RNA processing
  - Polyadenylation(mRNA lifetime)
  - Splicing and alternative splicing
  - Transport regulation
- RNA editing

Example Trp operon

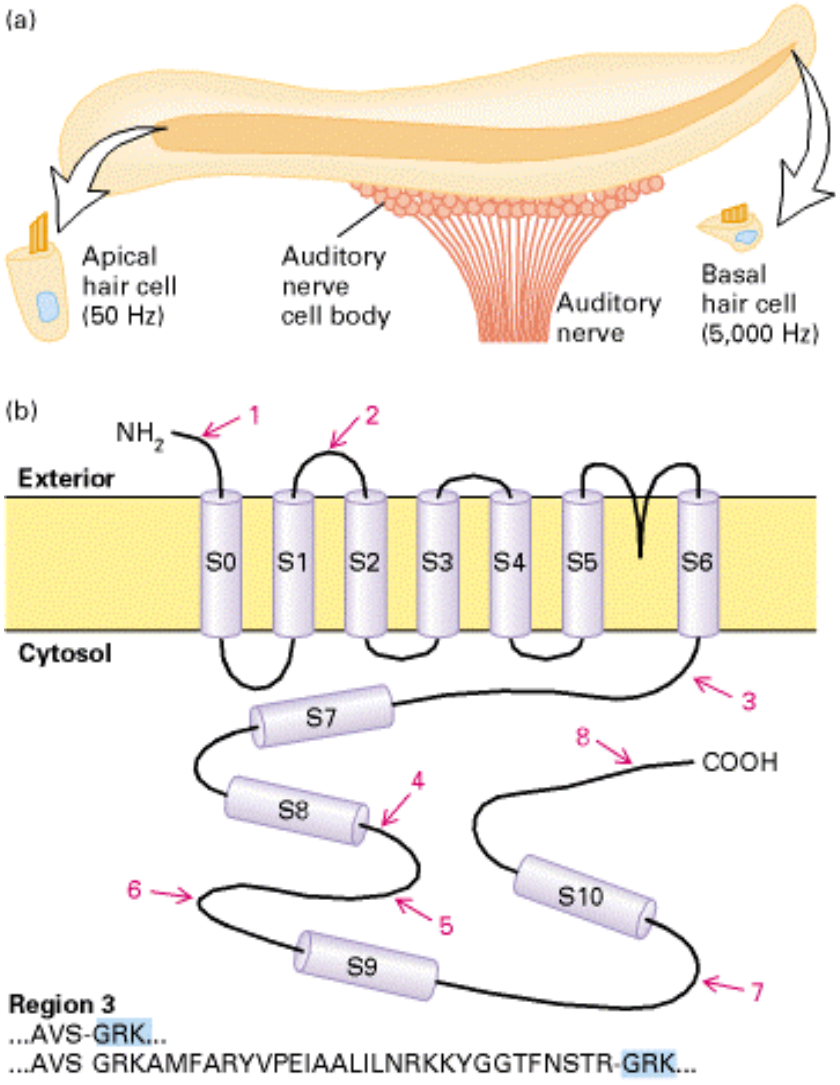


Alternative splicing



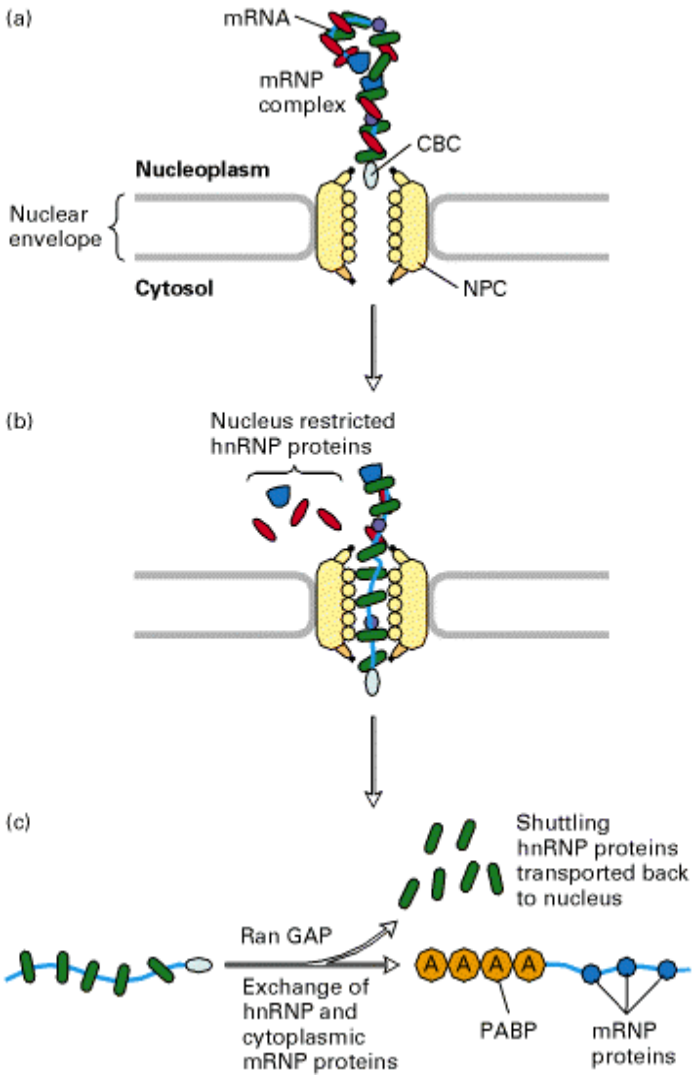


Alternative splicing



576 isoforms

mRNA export regulation



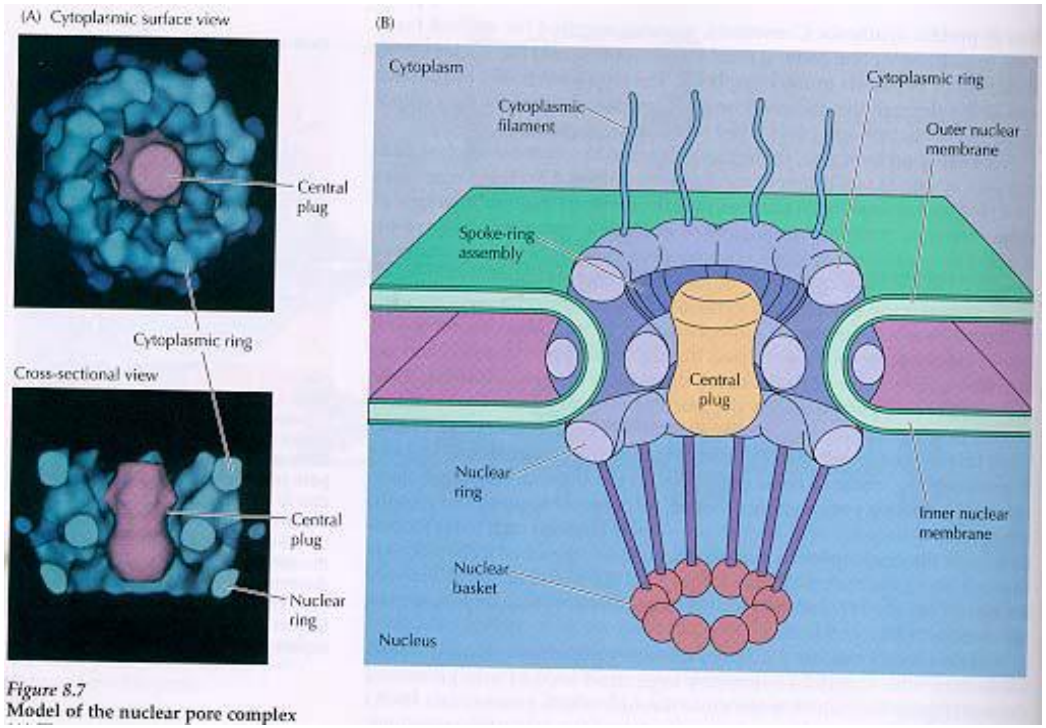
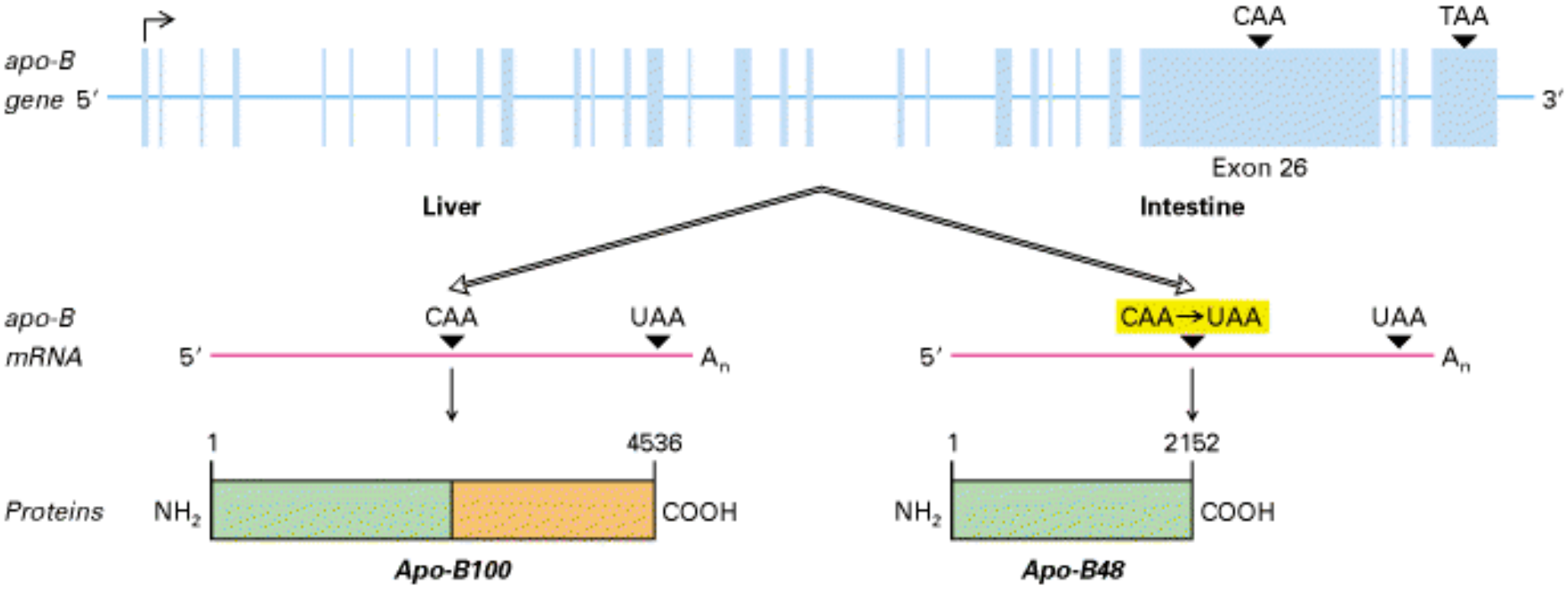
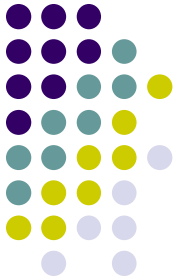


Figure 8.7
Model of the nuclear pore complex

RNA editing

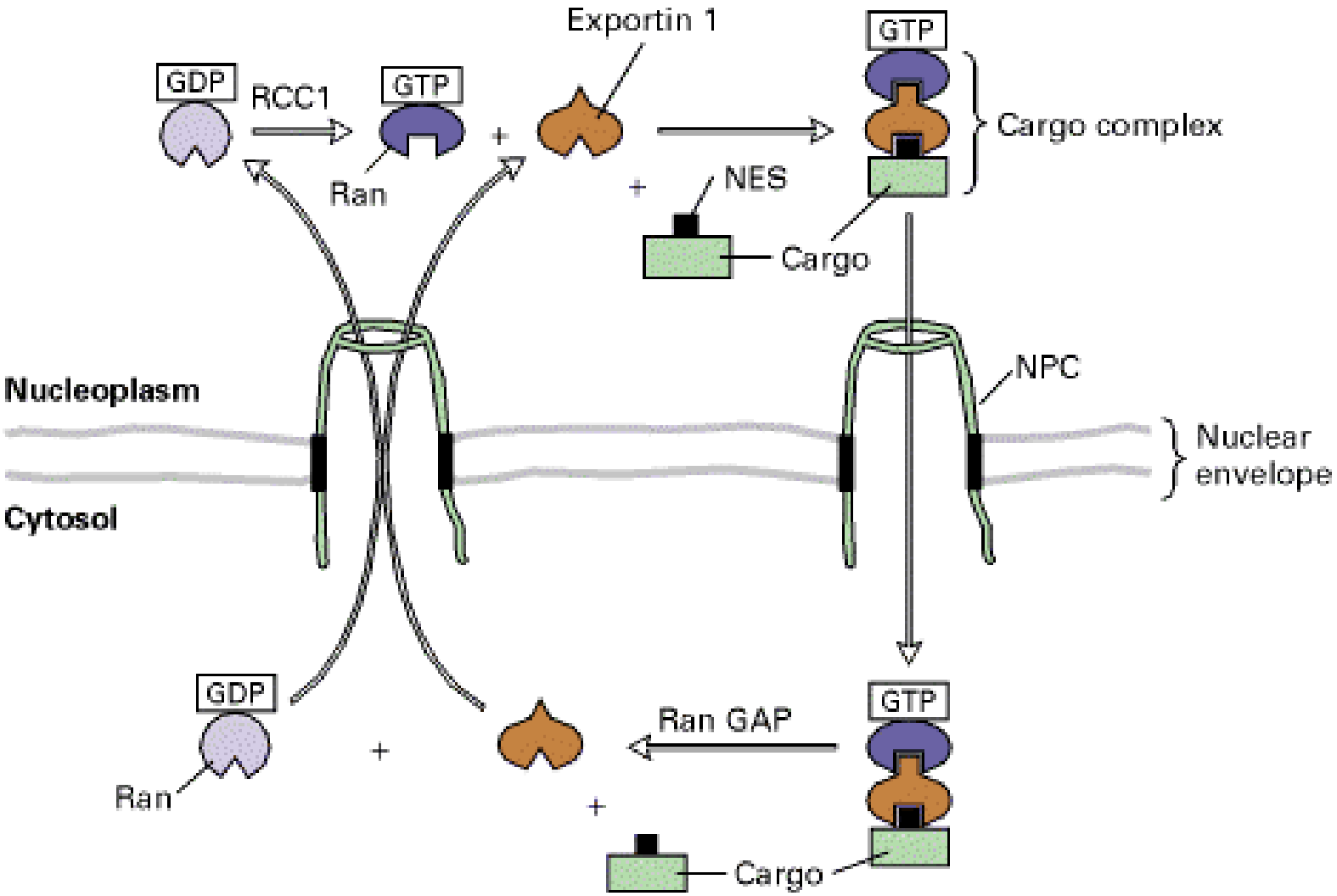

apo-B
gene 5′
CAA
TAA
3′
Exon 26
Liver
Intestine
apo-B
mRNA
5′
CAA
UAA
An
CAA→UAA
UAA
5′
An
1
4536
1
2152
Proteins
NH2
COOH
NH2
COOH
Apo-B100
Apo-B48

Post-translational control

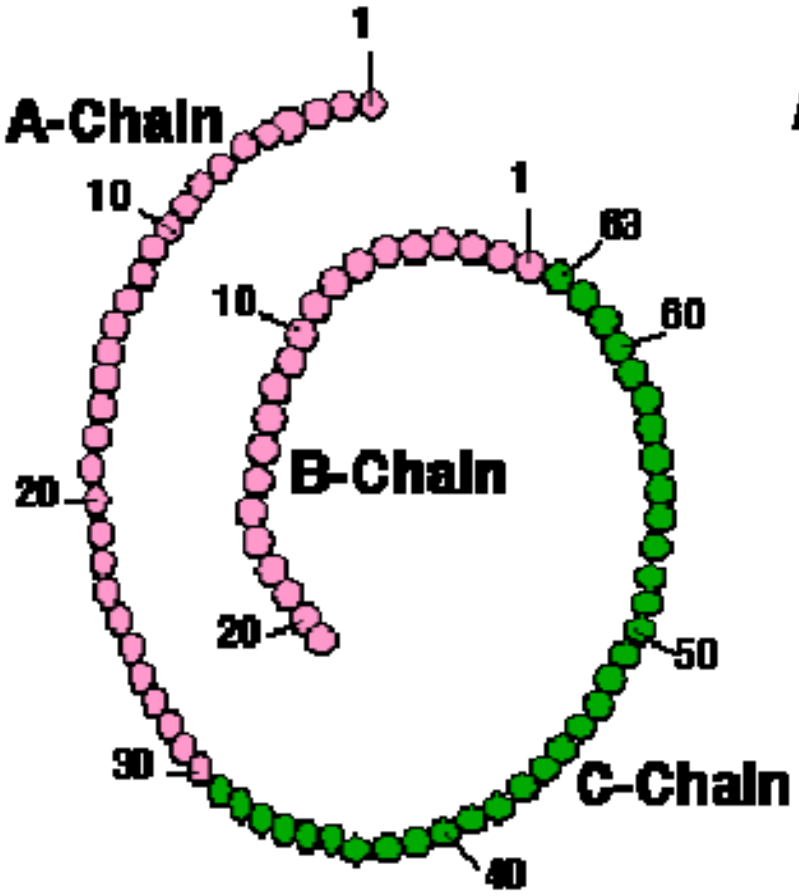


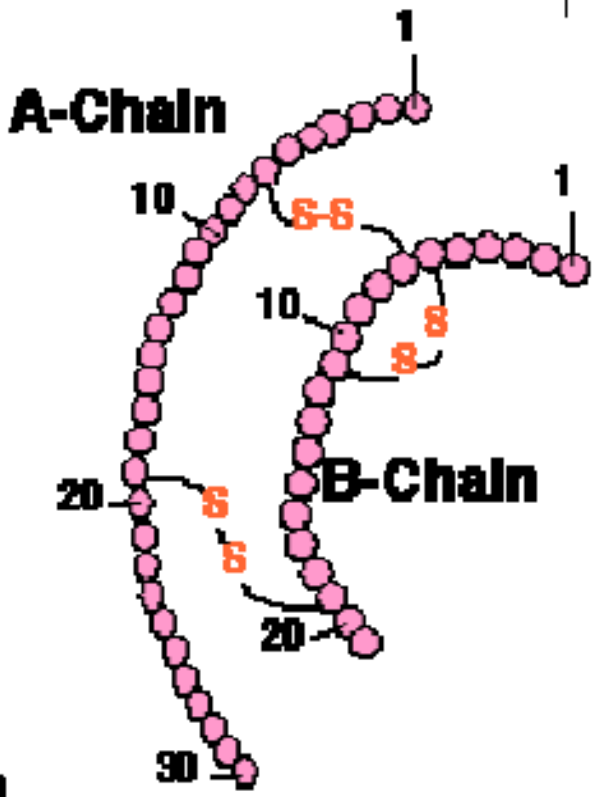
- Protein processing
  - Signal sequences (localization)
  - Preproteinsf olded but not biologically active
- Side chain modification
  - Ser, Thr, Tyrphosphorylation
  - Lysacetylation,ubiquitination
  - Cys, lipidation
  - Glu, methylation, carboxylation

Protein localization

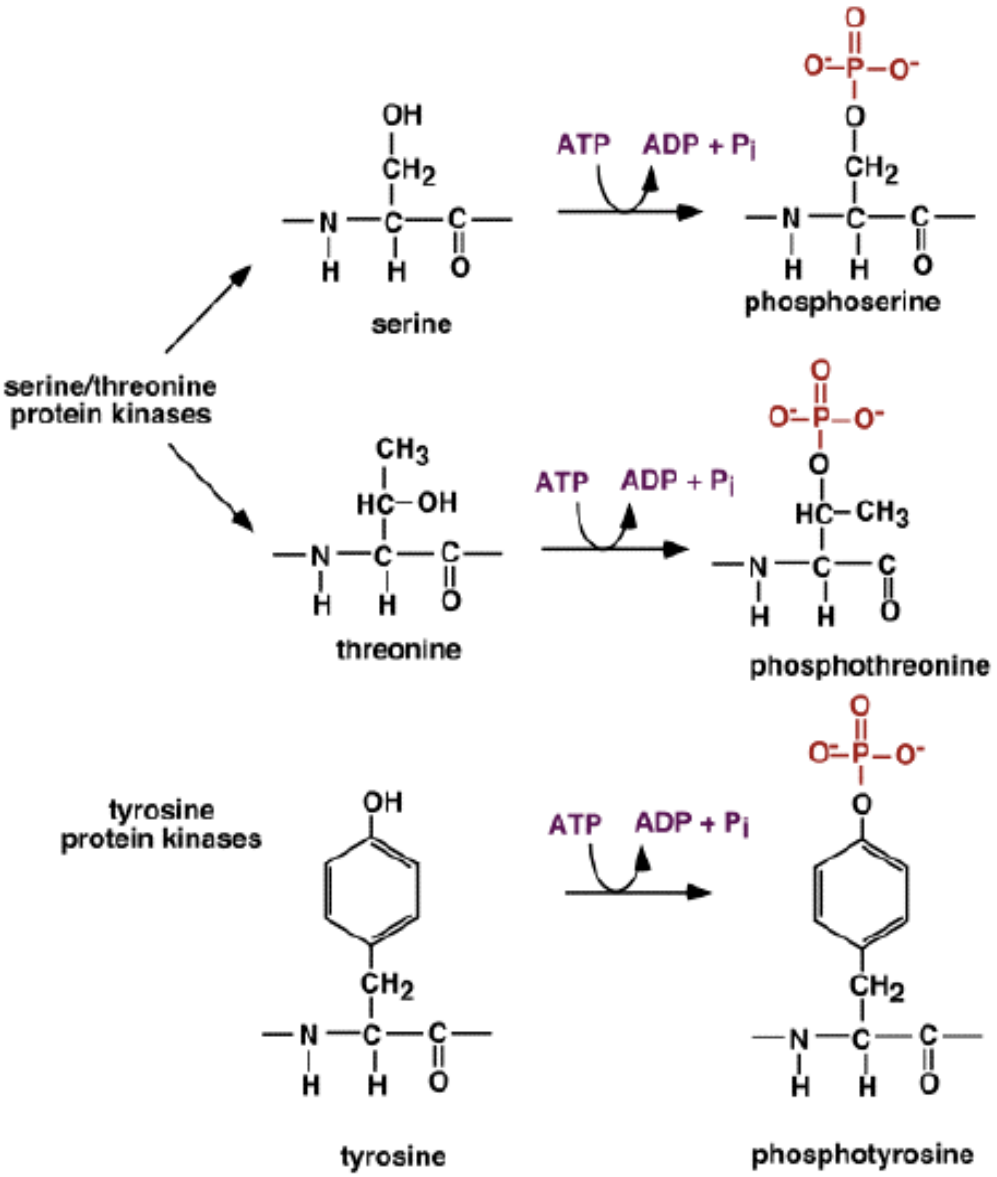


Proteolytic processing Insulin

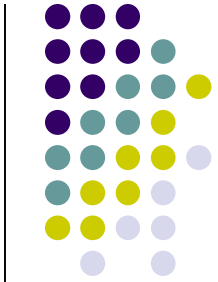




Side chain modifications

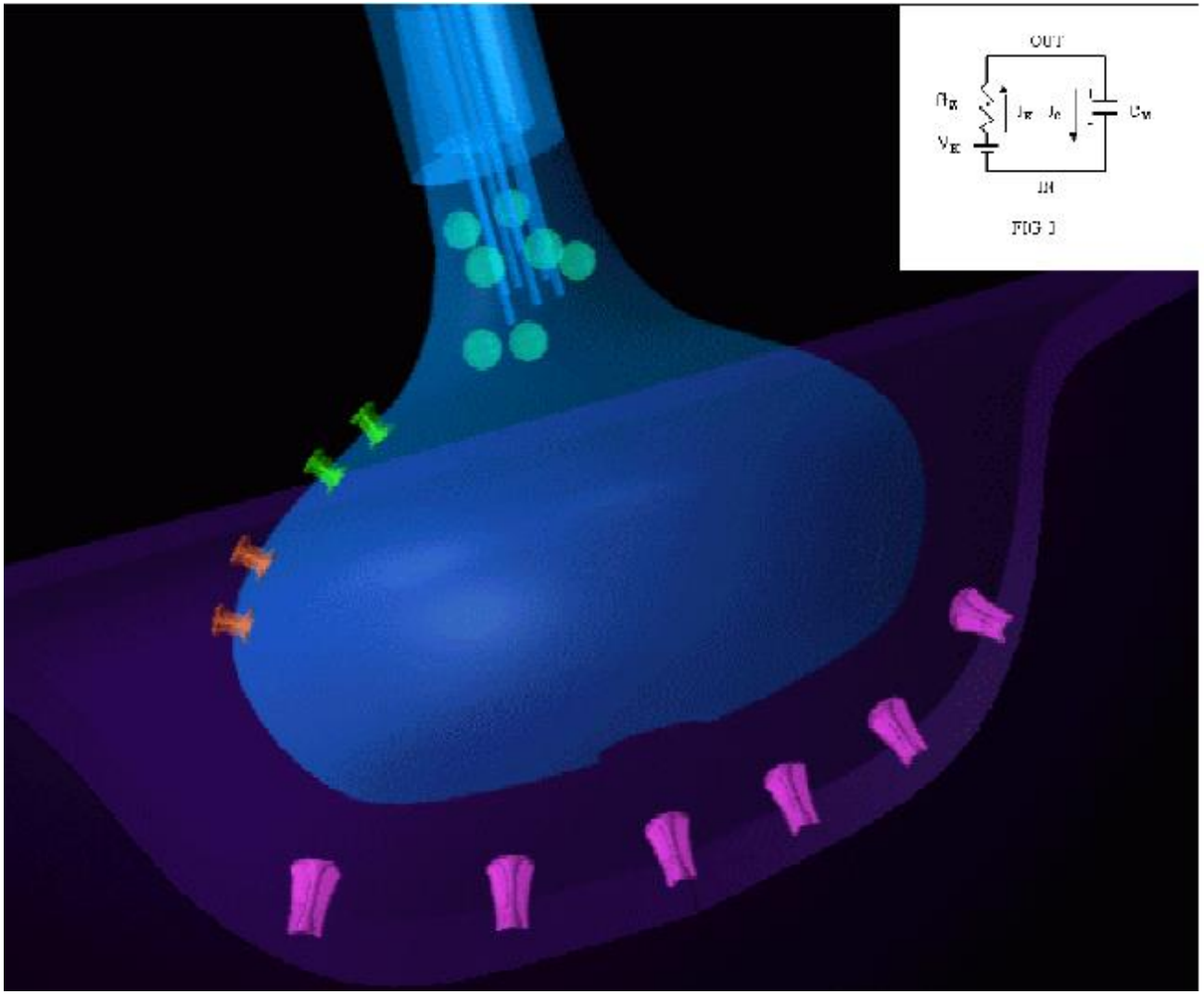


Intercellular signalling

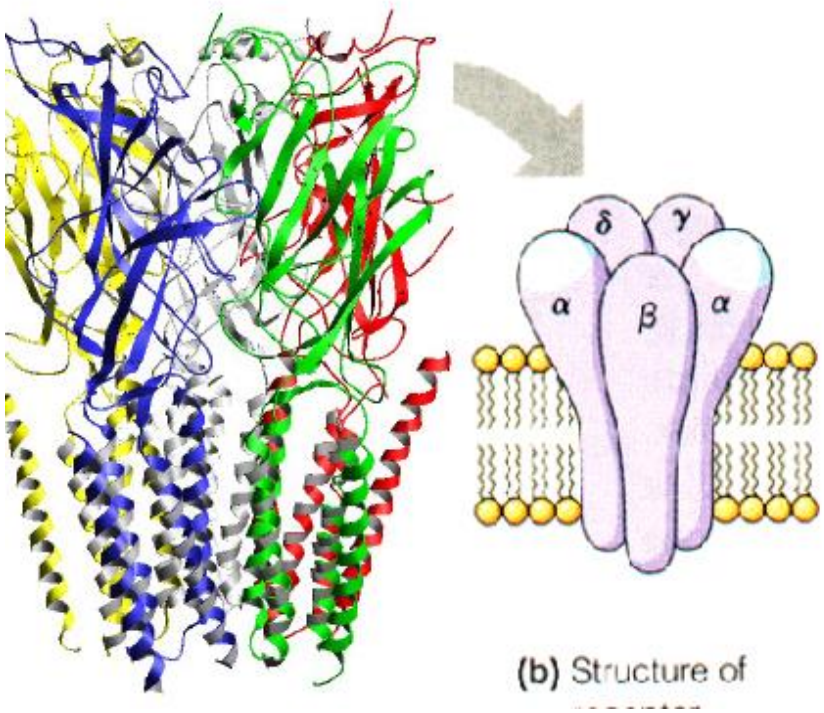


- First messengers
  - Hormones, peptide or otherwise
  - Nitric Oxide
  - Neurotransmitters
  - etc
- Receptors
  - GPCR’s
  - Receptor Protein-tyrosine kinase
  - Ion channel receptors

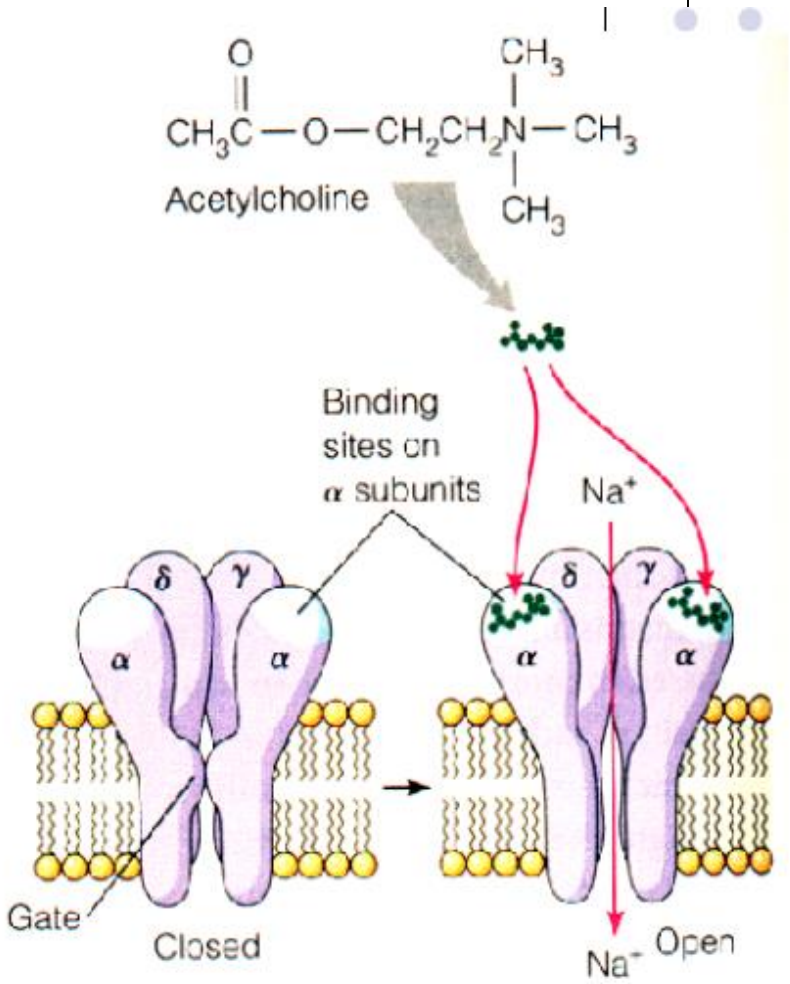
Neurotransmission case study



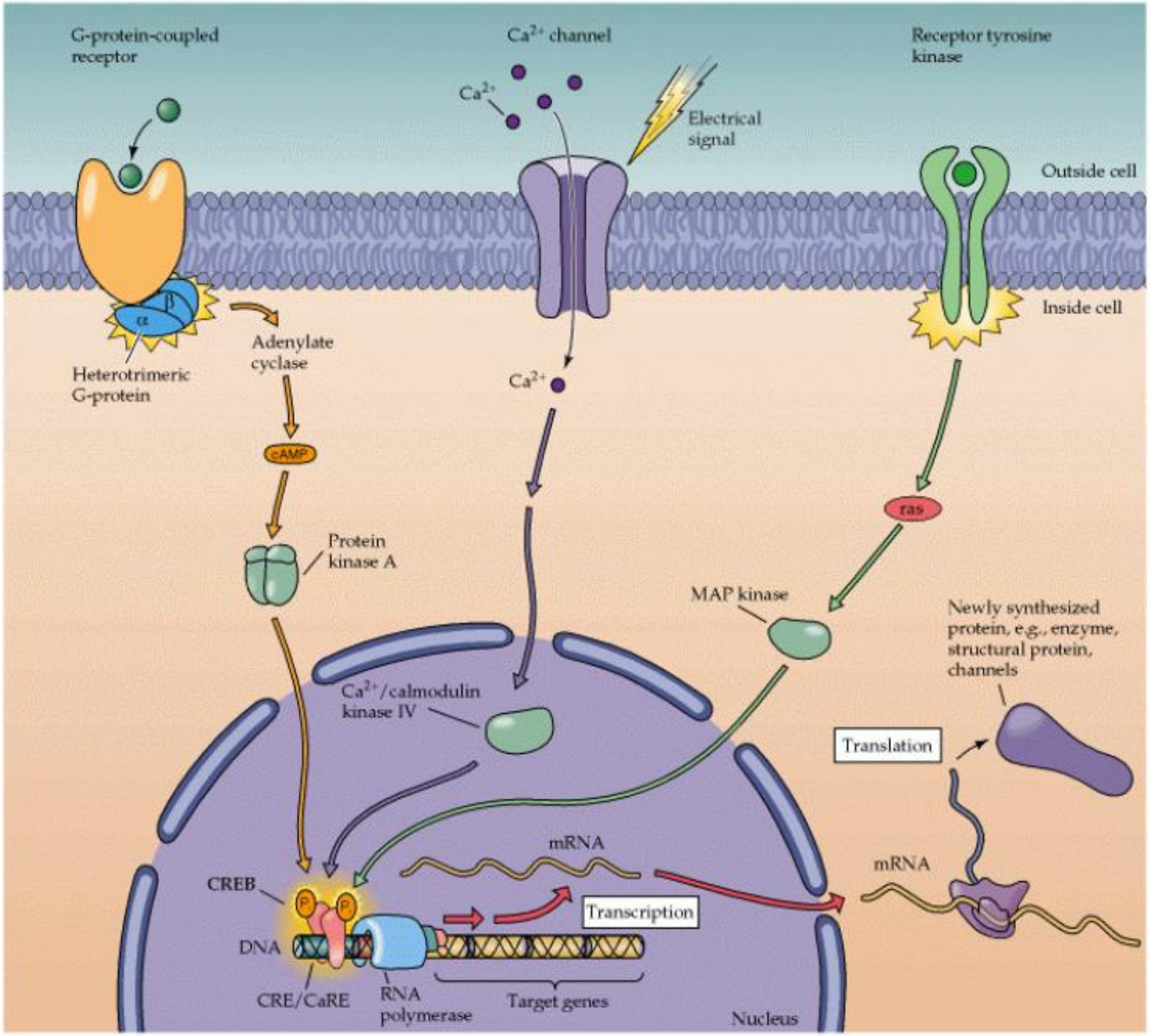
Ion channels



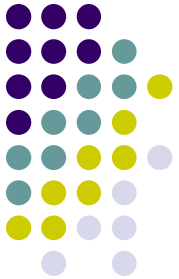
(b) Structure of



(c) Function of receptor

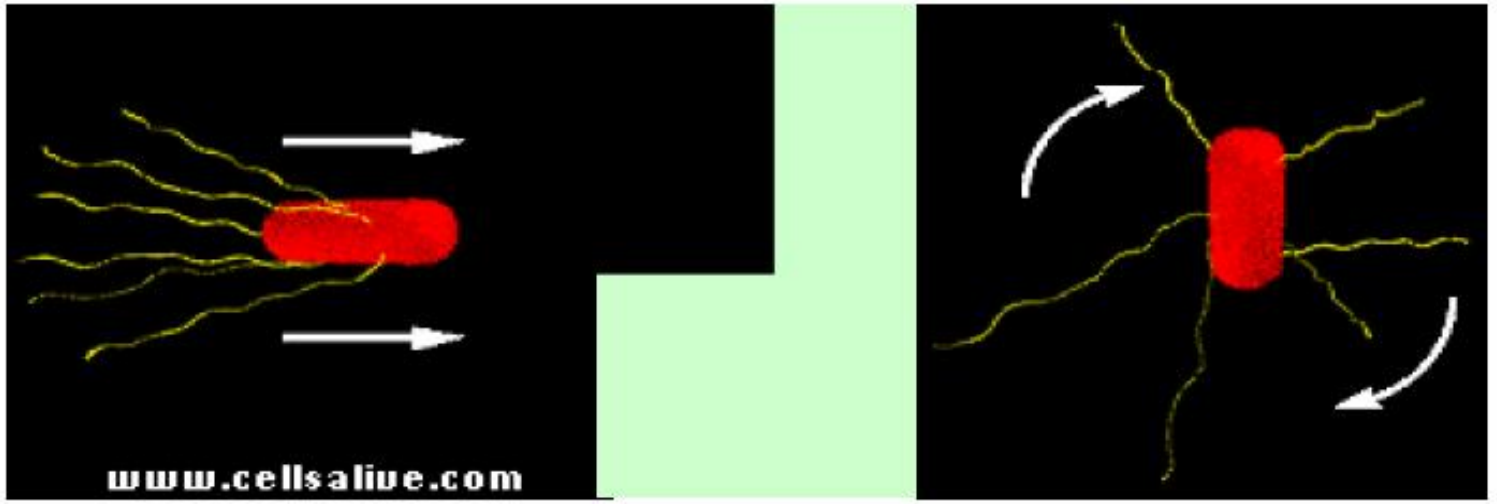

G-protein-coupled receptor
Ca^{2+} channel
Receptor tyrosine kinase
Ca^{2+}
Electrical signal
Outside cell
Inside cell
α
β
Heterotrimeric G-protein
Adenylate cyclase
cAMP
Ca^{2+}
ras
Protein kinase A
MAP kinase
Newly synthesized protein, e.g., enzyme, structural protein, channels
Ca^{2+}/calmodulin kinase IV
Translation
mRNA
mRNA
CREB
P
P
Transcription
DNA
CRE/CaRE
RNA polymerase
Target genes
Nucleus

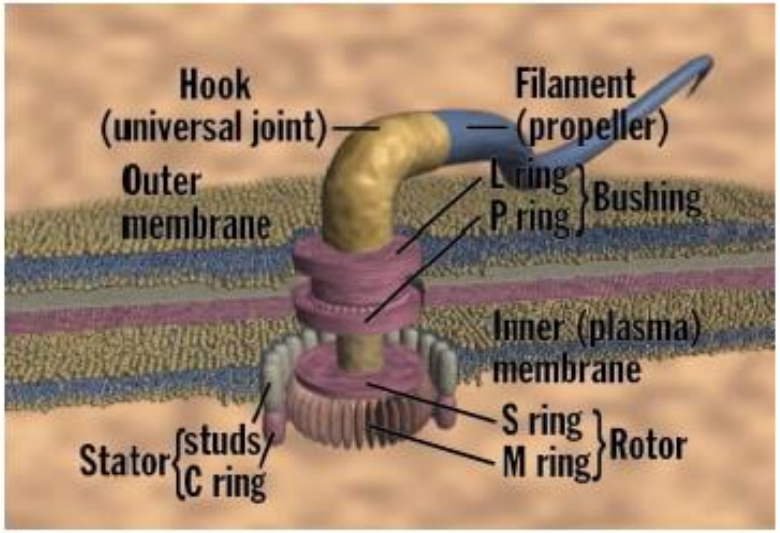
Intracellular signaling



- Second messengers
  - cAMP
  - cGMP
  - Phospholipids
  - Ca++
  - Ras, Raf, MAP kinase

Case study chemotaxis





receptor
CheW
CheW
kinase (CheA)
CheY
phosphatase (CheZ)
CheY-P
CheY-P
switch
motor