Neuronal Cell:

Chemical Processing in Steady State

Protein Production

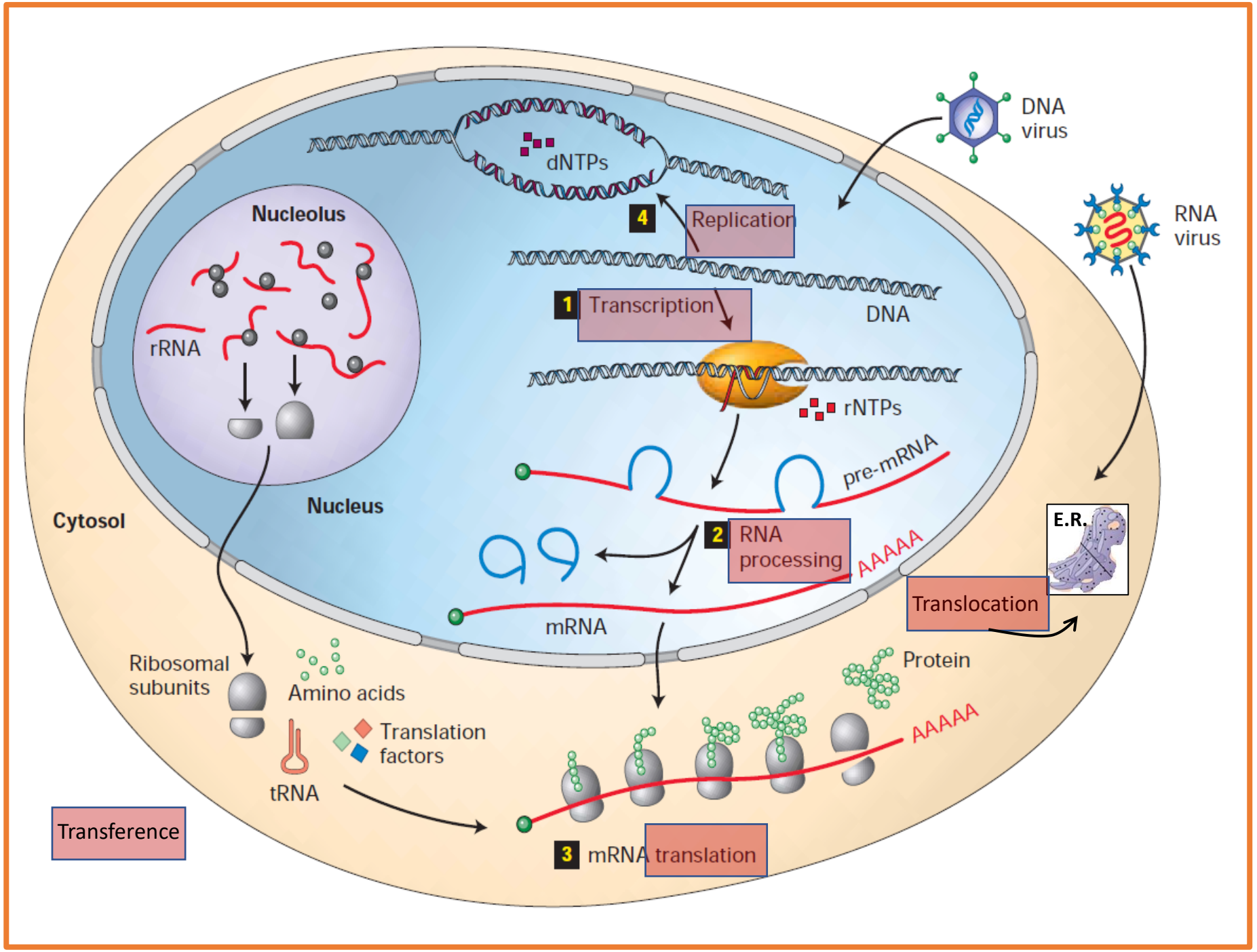
Basic Genetic Processes:

$R^2 T^5$

Replication of DNA
(during Cell Division)

Protein Formation Steps:

- Transcription,
- RNA processing,
- Transference,
- Translation
- Translocation



Protein Destruction/Degradation

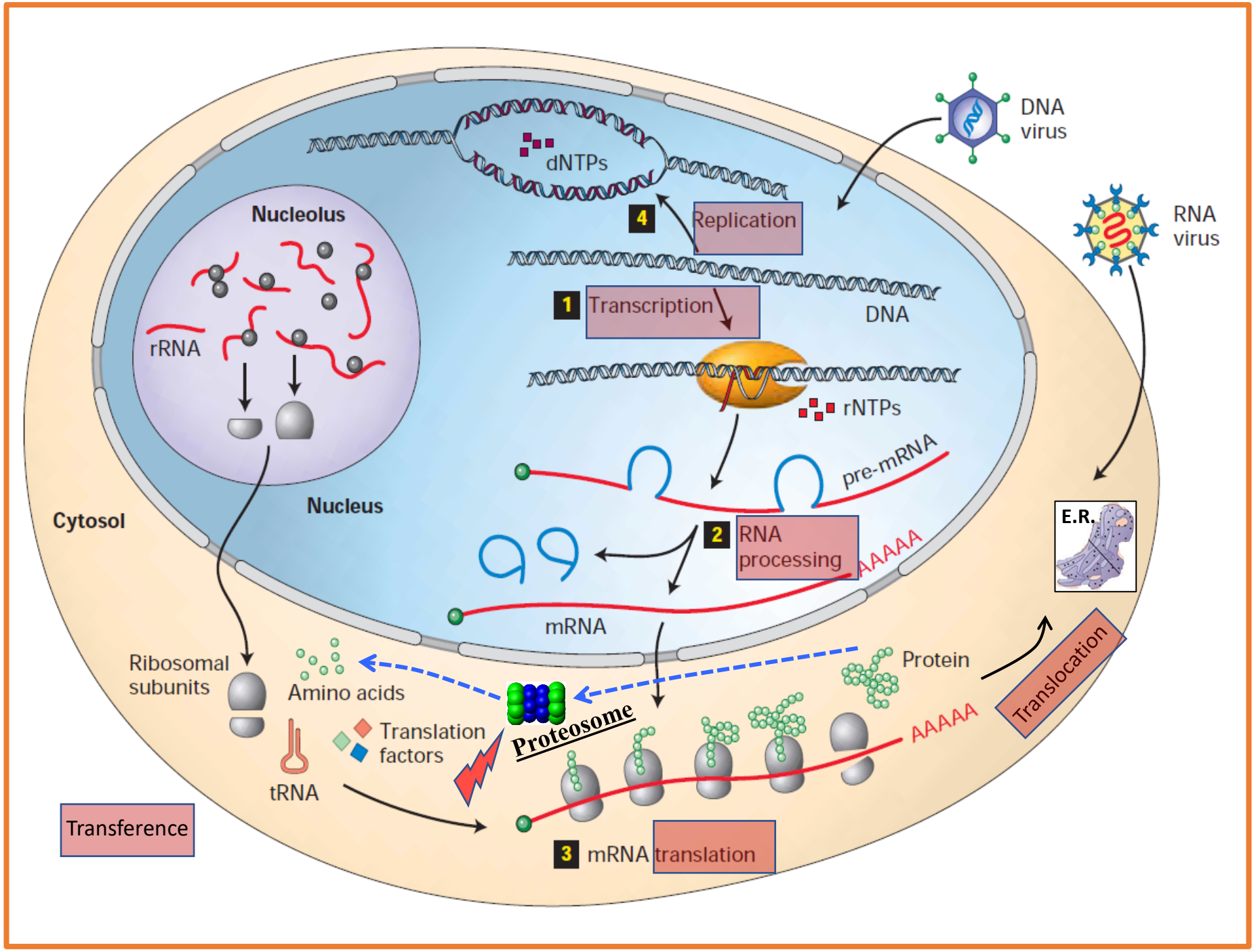
Basic Genetic Processes:

$R^2 T^5$

Replication of DNA
(during Cell Division)

Protein Formation Steps:

- Transcription,
- RNA processing,
- Transference,
- Translation
- Translocation



The Researchers

The Nobel Prize in Chemistry 2004

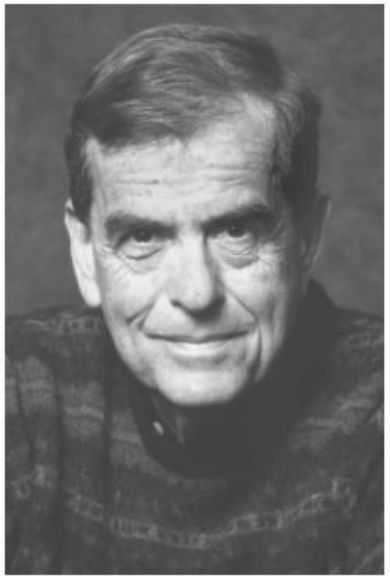


Photo: D. Porges

Aaron Ciechanover

Prize share: 1/3

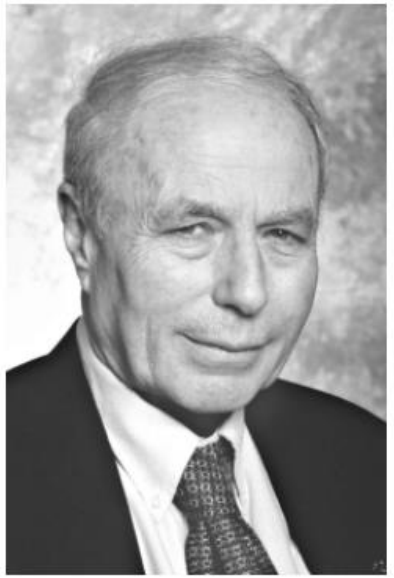


Photo: D. Porges

Avram Hershko

Prize share: 1/3

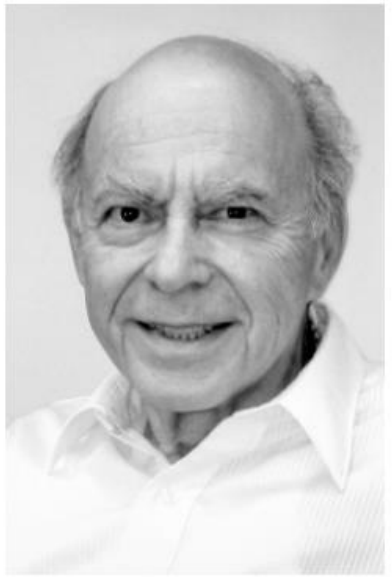


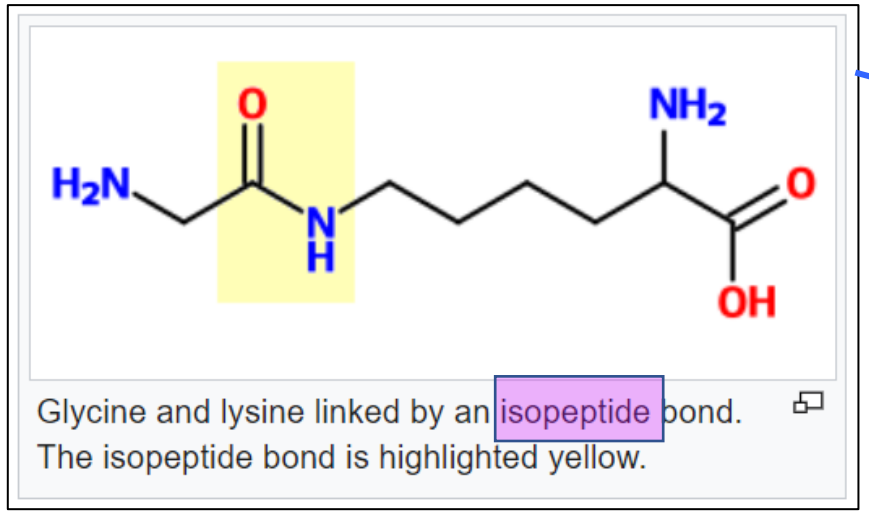
Photo from the Nobel Foundation archive.

Irwin Rose

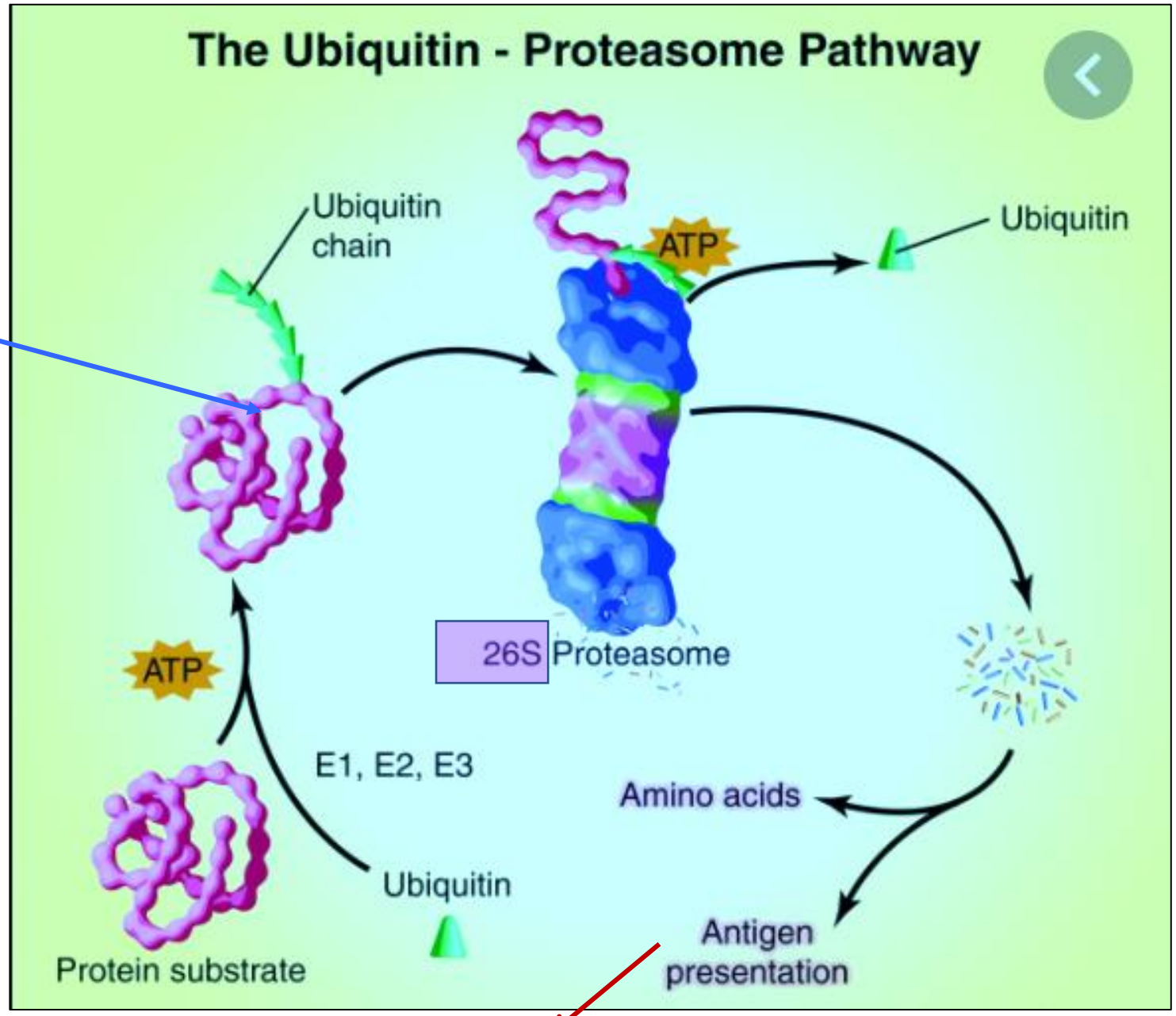
Prize share: 1/3

The Nobel Prize in Chemistry 2004 was awarded jointly to Aaron Ciechanover, Avram Hershko and Irwin Rose "for the discovery of ubiquitin-mediated protein degradation."

Protein Degradation & Destruction



Glycine and lysine linked by an isopeptide bond.
The isopeptide bond is highlighted yellow.



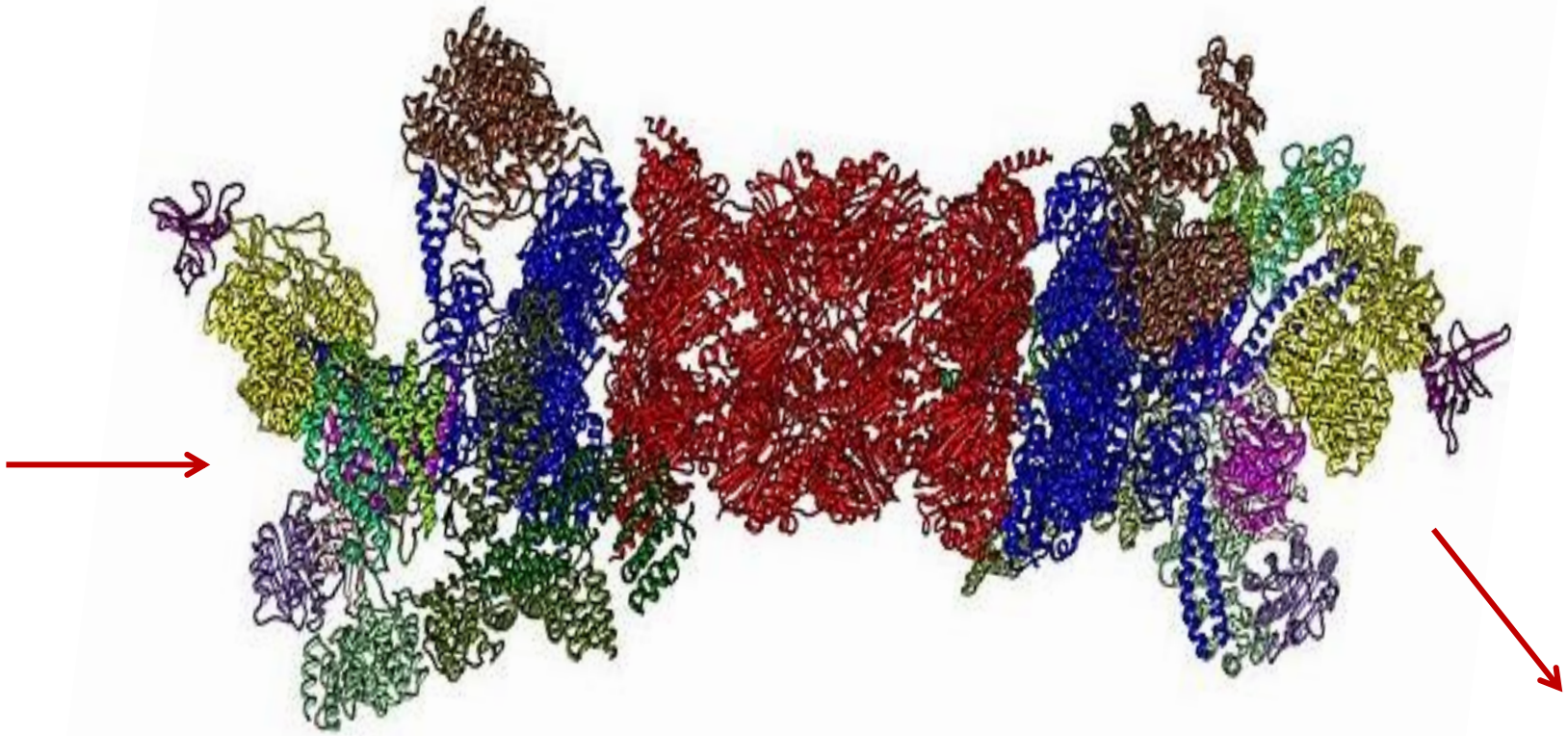
E1: Ubiquitin Activating Enzyme

E2: Ubiquitin Conjugating Enzyme

E3: Ubiquitin Ligating Enzyme

If degraded protein is from invading virus

Proteosome Structure



RNA Operations:

Processes

The Nobel Prize in Physiology or Medicine 1965

François Jacob

André Lwoff

Jacques Monod

The Operon: A Group of Genes Whose Expression is Coordinated by an Operator

By François Jacob, David Perrin, Carmen Sanchez and Jacques Monod

The analysis of different bacterial systems leads to the conclusion that in the synthesis of certain proteins (enzymatic or viral) a double genetic determinism intervenes involving two genes with distinct functions: one (the gene for structure) responsible for the structure of the molecule, and the other (the regulator gene) governing the expression of the former through the intermediary action of a repressor[1]. The regulator genes which have so far been identified show the remarkable property of exercising a *pleiotrophic coordinated effect*, each governing the expression of several genes for structure, closely linked together, and corresponding to protein enzymes belonging to the *same biochemical sequence*. To explain this effect, it seems necessary to invoke a new genetic entity, called "operator," which would be: (a) adjacent to a group of genes and would control their activity; and (b) would be sensitive to the repressor produced by a particular regulator gene[1]. In the presence of the repressor, the expression of the group of genes would be inhibited through the intermediation of the operator. This hypothesis leads to some distinctive predictions concerning the mutations which could affect the structure of the operator. In effect:

(1) Certain mutations affecting an operator would be manifested by the loss of the capacity to synthesize the proteins determined by the group of linked genes "coordinated" by that operator. These simple mutations would behave like physiological deletions, and would not be complemented by any mutant in which one of the genes for structure of the sequence had been altered.

(2) Other mutations, for example involving a loss of sensitivity (affinity) of the operator for the corresponding repressor, would be manifested by the constitutive synthesis of the proteins determined by the coordinated genes. These constitutive mutations, unlike those which result from the inactivation of regulator genes, would be *dominant* in a diploid heterozygote, but their effect would only be manifested for the genes which were in the *cis* position with respect to the mutated operator.

We have studied certain mutations which, affecting the metabolism of lactose in *Escherichia coli* K-12 and acting simultaneously on the synthesis of β-galacto-

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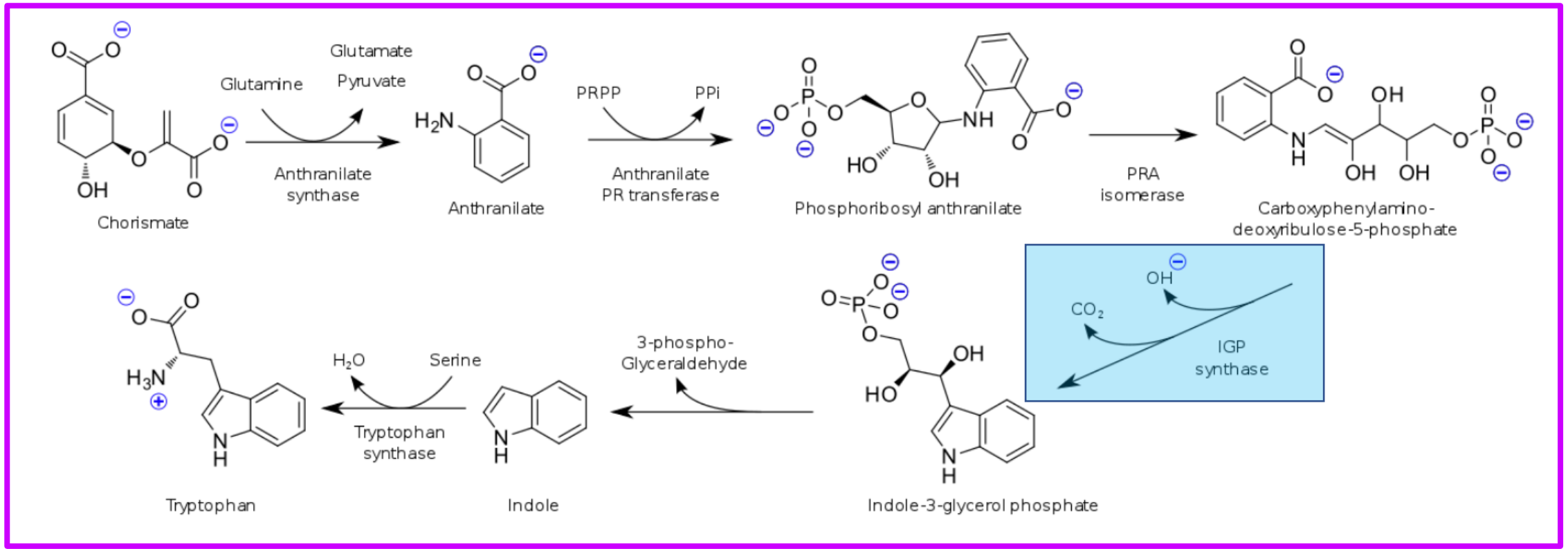
Biosynthesis of Tryptophan (Trp) Amino Acid:

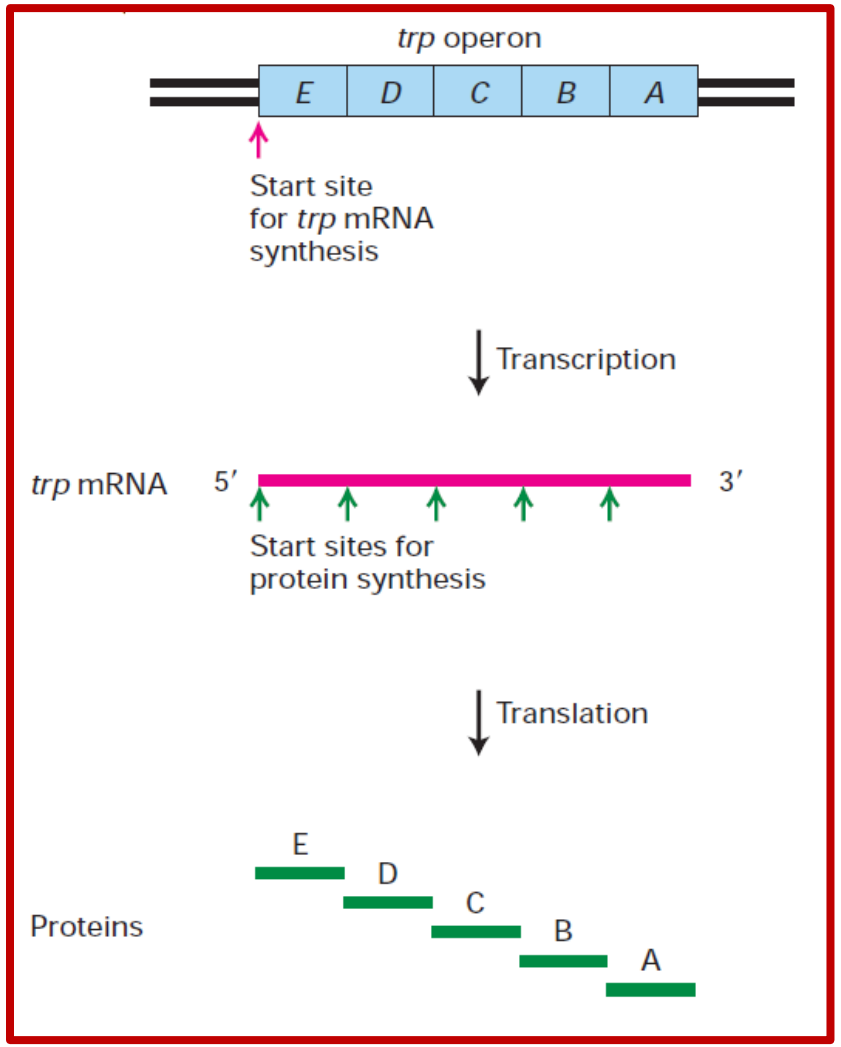
Several Steps by Different Enzymes



Genetic Processing (*Tryptophan Biosynthesis*)

Pro-karyotes (Bacteria, *E. Coli*)

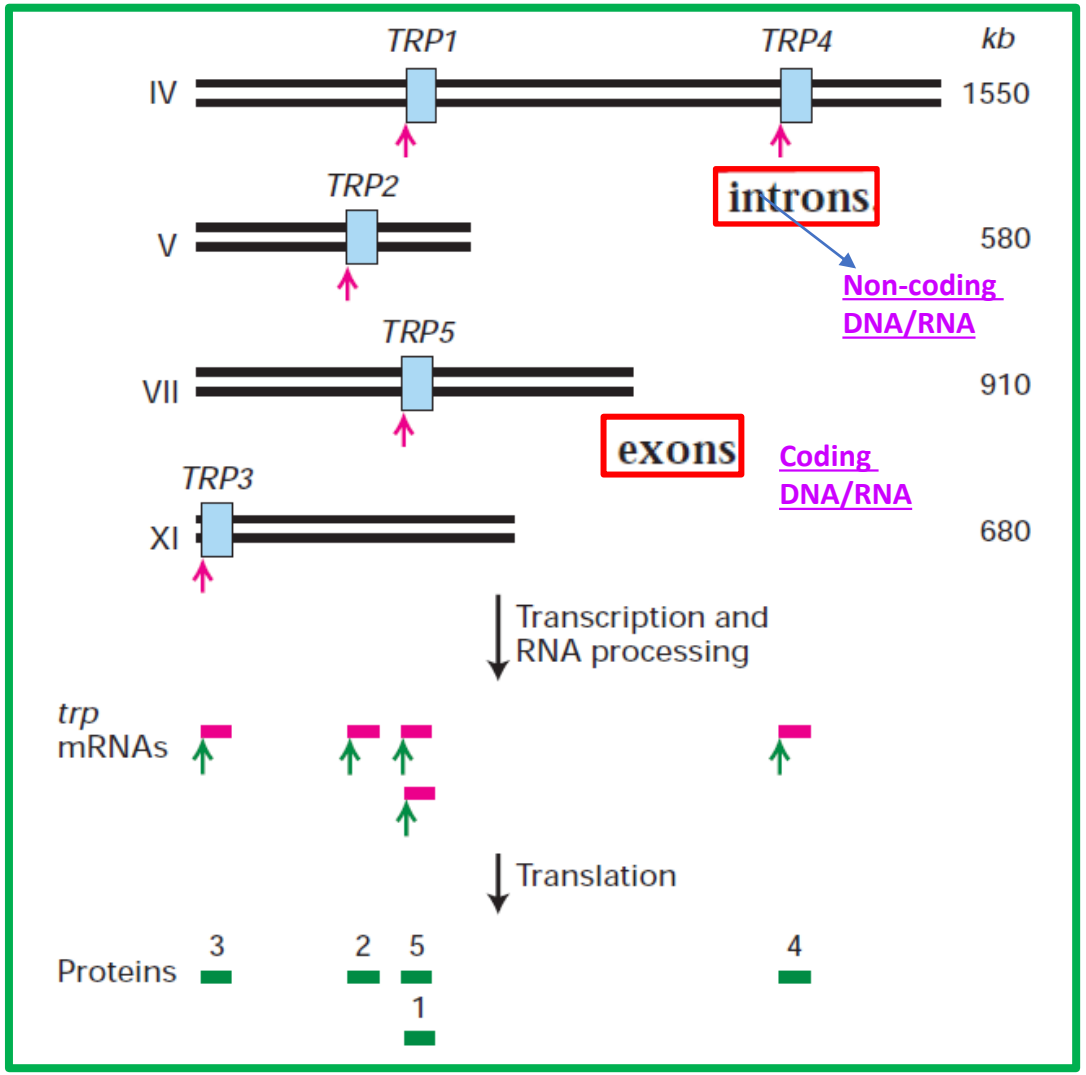
1 DNA Segment operates together: "Operon" (No Chromo.)



1 Billion Years

Eu-karyotes (Yeast, Plants)

Several Chromosomes: Several Genes



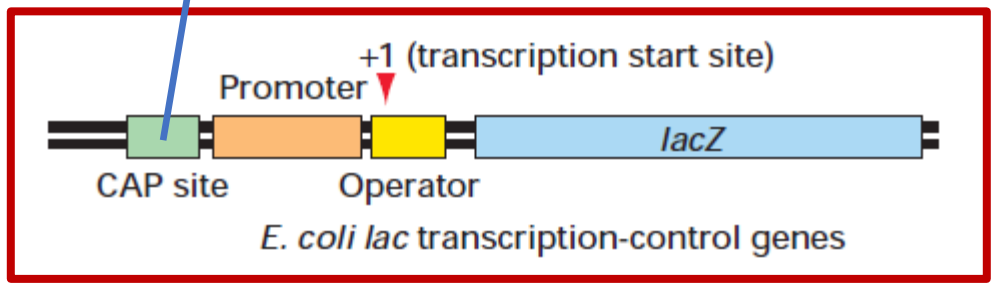
DNA "Operon": Transcription's "Control" Region

Feedback Control of Transcription:

Activation & Inhibition:

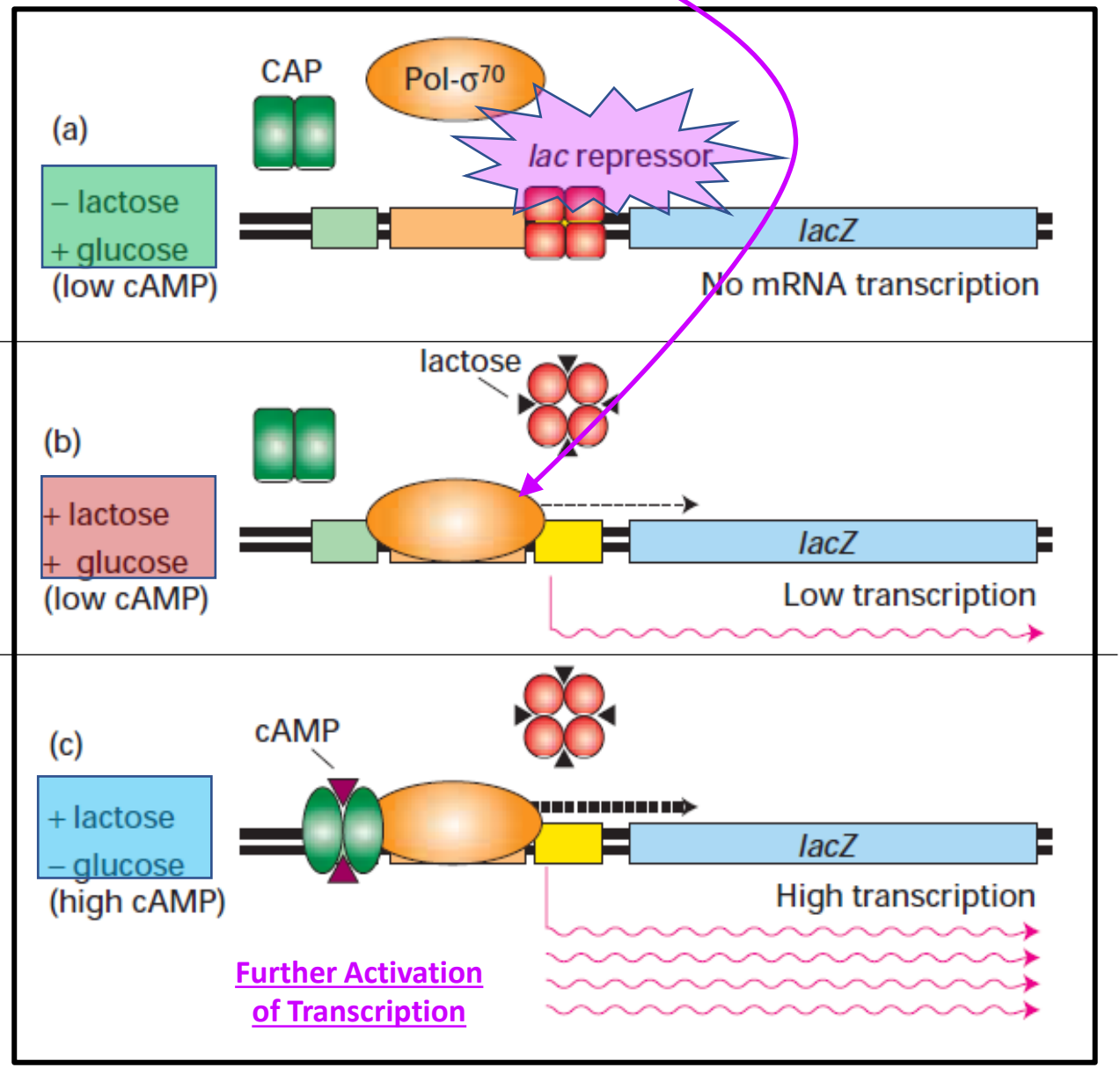
Lactose Metabolism: 'Lac' Operon in *E. Coli* Bacteria

Catabolite "Activator" Protein, CAP



≈ 100 Base Pairs

Protein's Conformation Structural Change



Extra Activation of Transcription's Promoter.

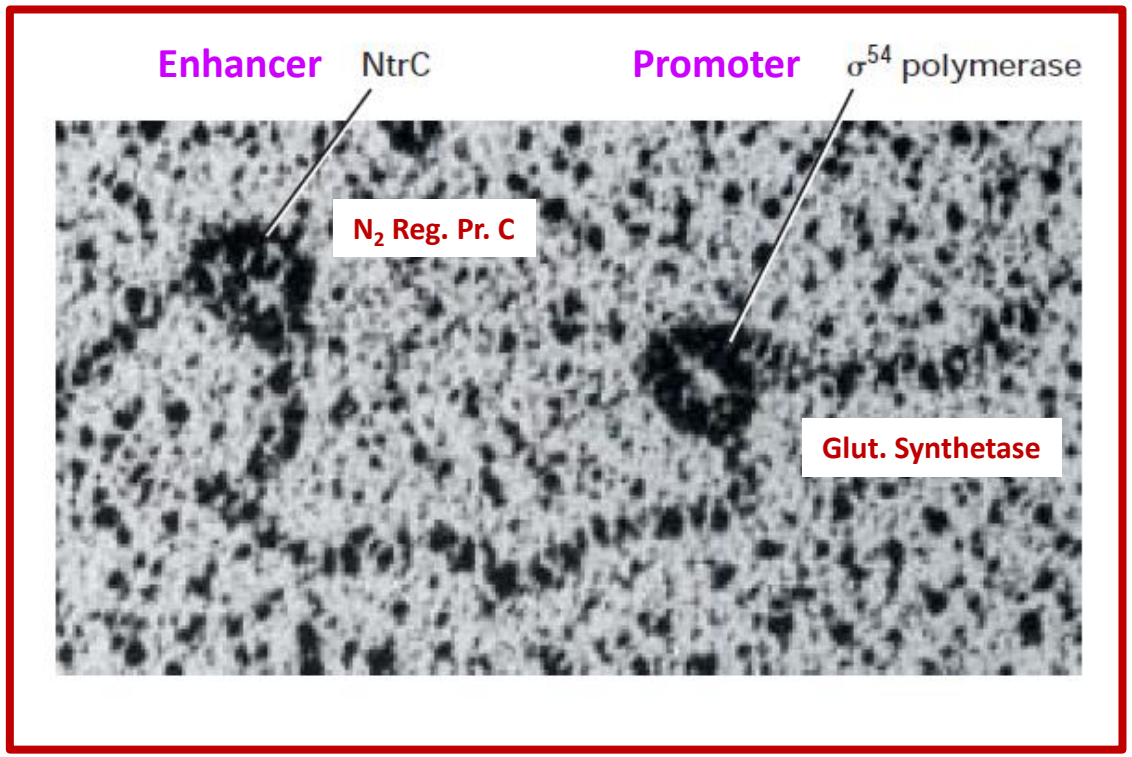
Synthesis of Glutamine A.A. from Glutamic Acid

► "Activator" = a Biochemical → Binds to DNA region ("Enhancer") far from Transcription start site ("Promoter")

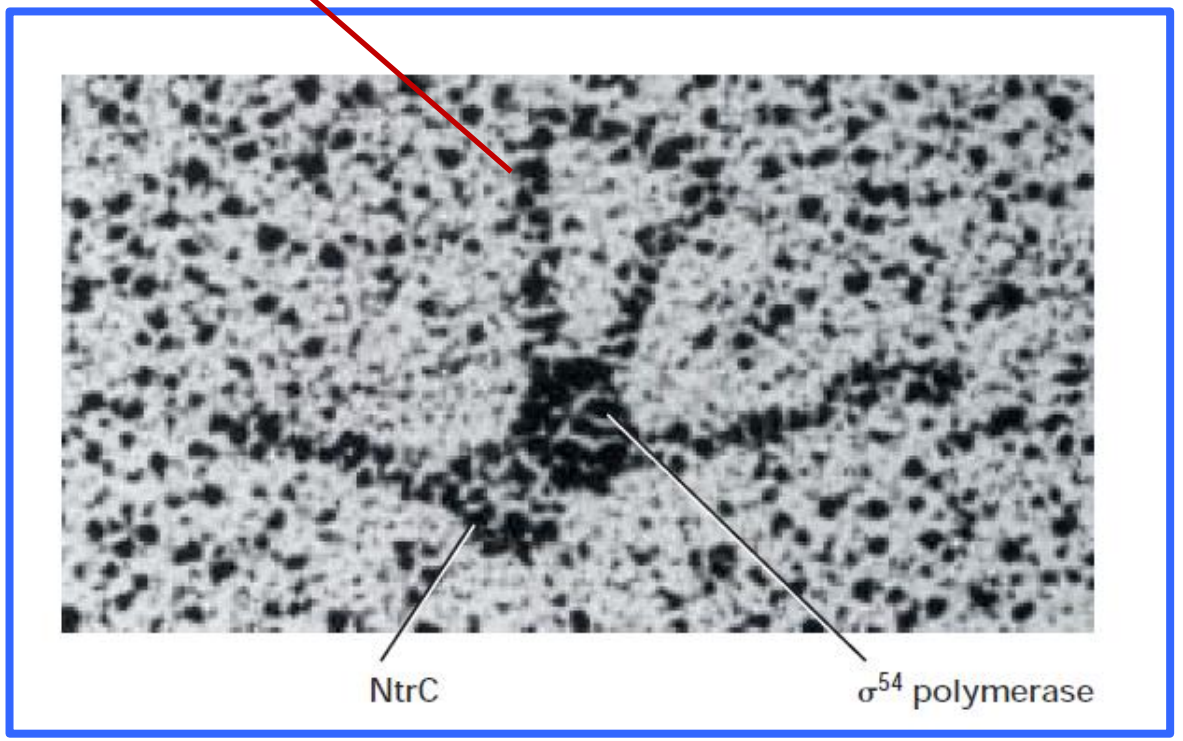
- DNA folding enables Activator to contact Promoter region → DNA Unwinding → transcription by RNA Polymerase

- Activator: "Nitrogen Regulatory Protein C" (NtrC) → Acts on Promoter of Gene of Glutamate Synthetase Enzyme

Electron Microscopy



DNA Folding



2-component Phosphate Regulatory System:

E. Coli Bacteria ("DNA Reflexion")

For Coping with low phosphate environ