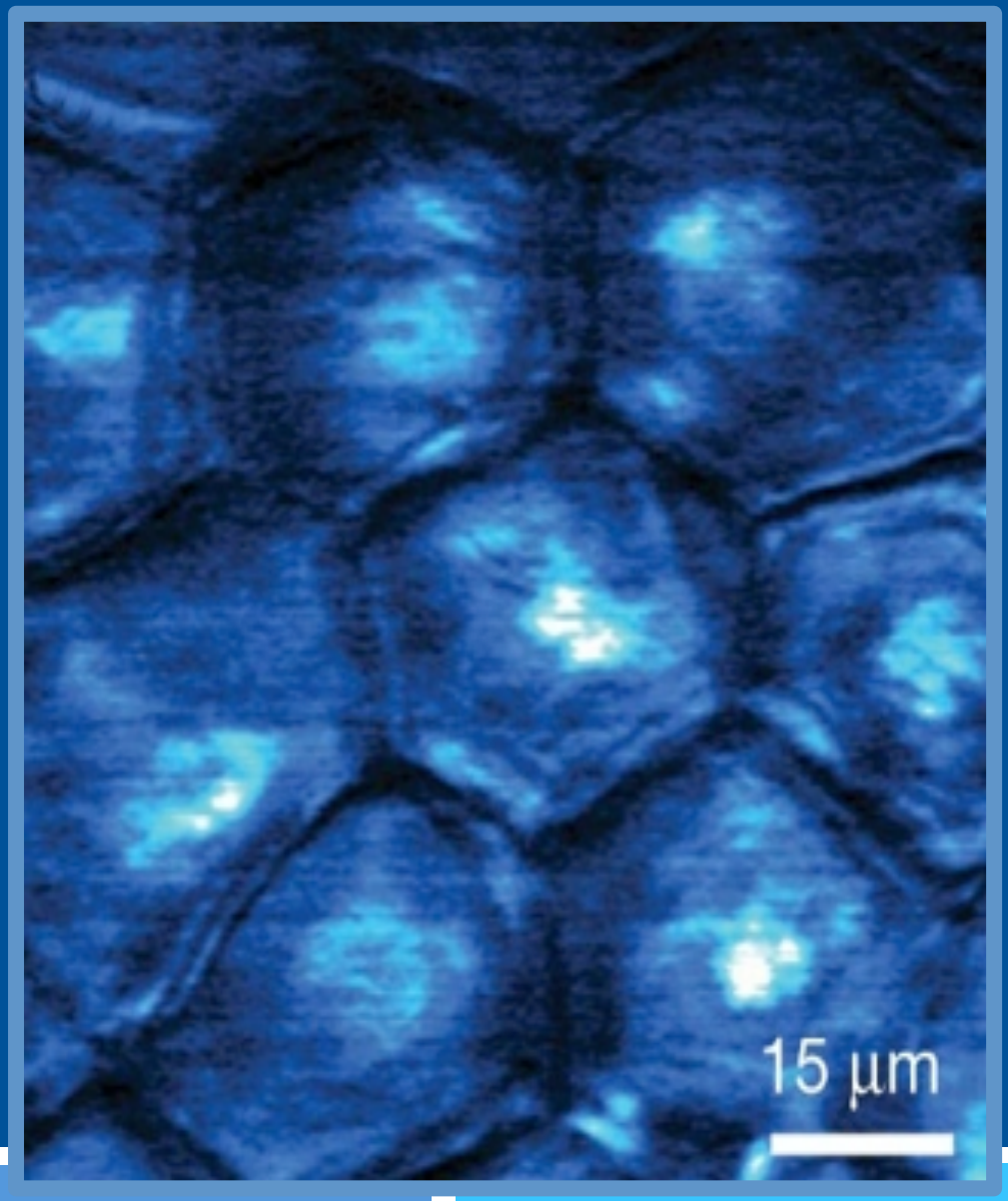


GENES AND CHROMOSOMES III

Lecture 5

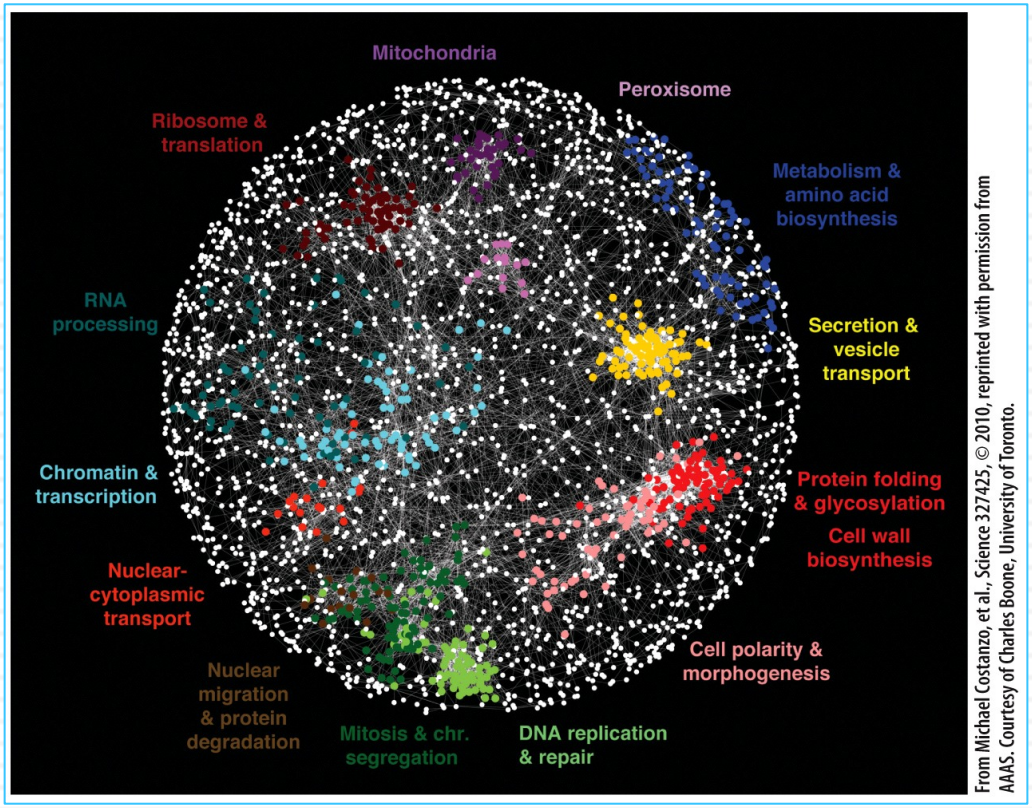
BIOL 266/4

2014-15

Dr. S. Azam

Biology Department
Concordia University

CELL NUCLEUS AND THE CONTROL OF GENE EXPRESSION

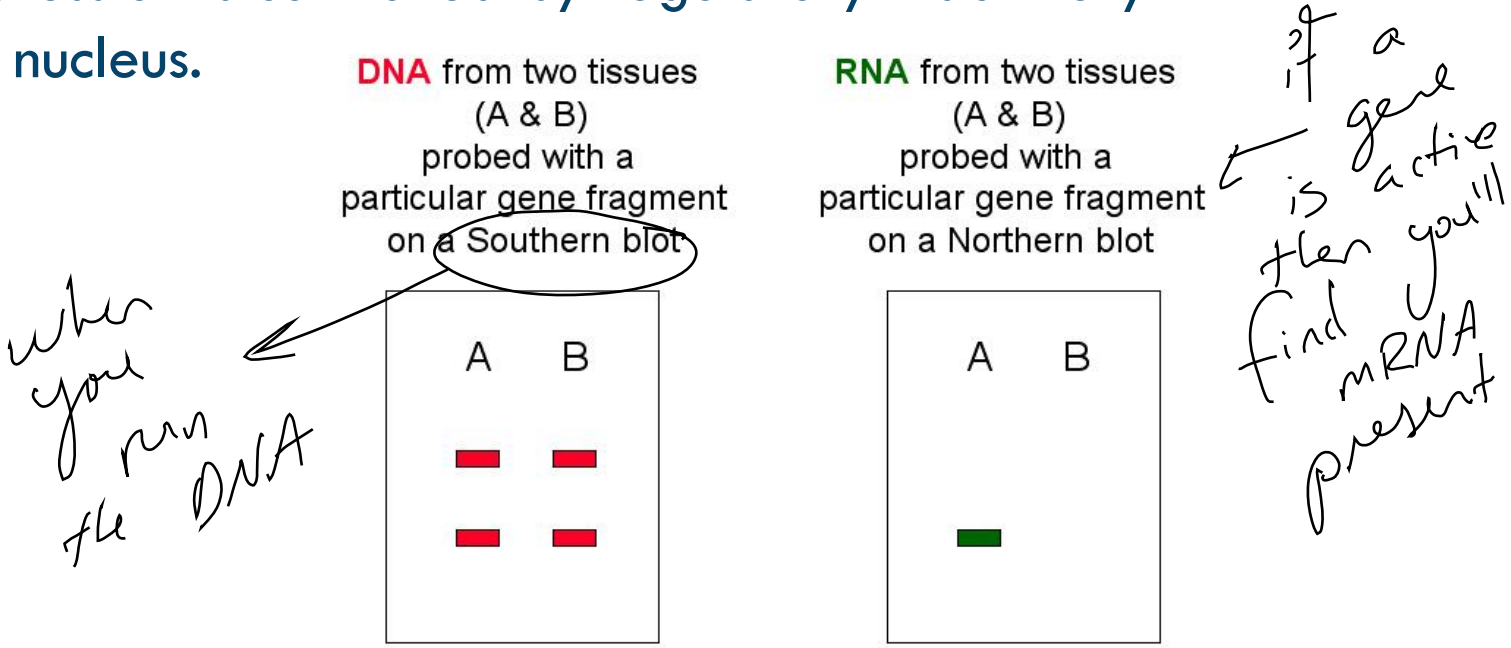


From Michael Costanzo, et al., Science 327425, © 2010, reprinted with permission from AAAS. Courtesy of Charles Boone, University of Toronto.

OPERONS

Introduction

- All cells in a multi-cellular organism contain the same complement of genes.
- Cells express their genetic information selectively.
- Gene expression is controlled by regulatory machinery in the cell nucleus.



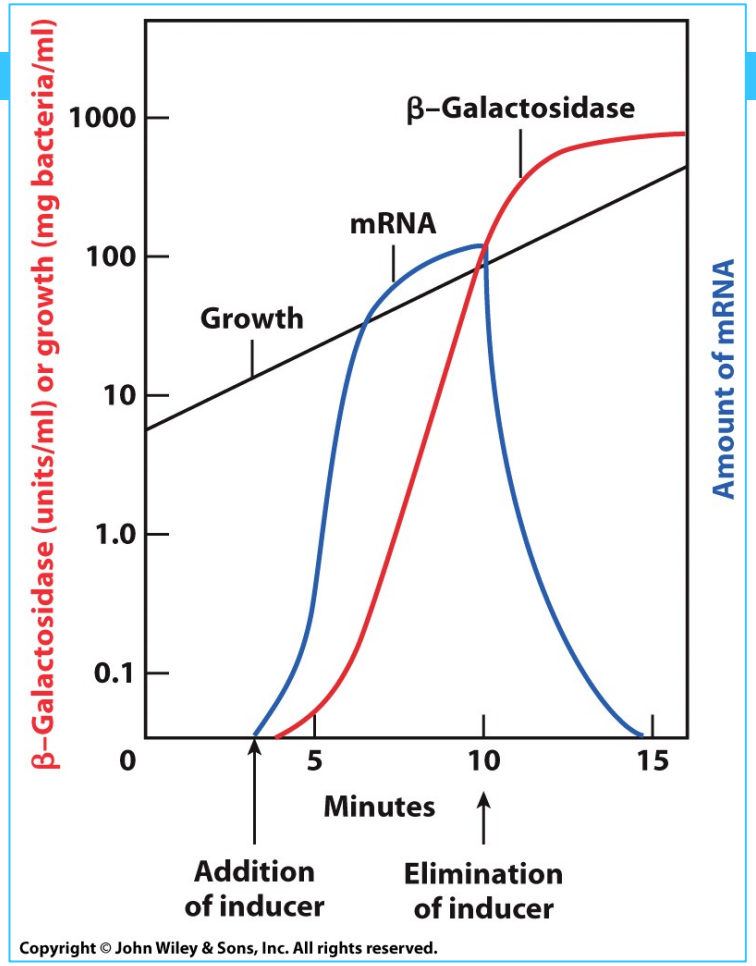
Control of Gene Expression in Bacteria

Bacterial cells selectively express genes to use the available resources effectively.

1. The presence of lactose in the medium induces the synthesis of the enzyme β-galactosidase.
2. The presence of tryptophan in the medium represses the genes that encode enzymes for tryptophan synthesis.

a matter of digestion

a matter of synthesis



The kinetics of β-galactosidase induction in *E. coli*: mRNA and protein induction

Control of Gene Expression in Bacteria

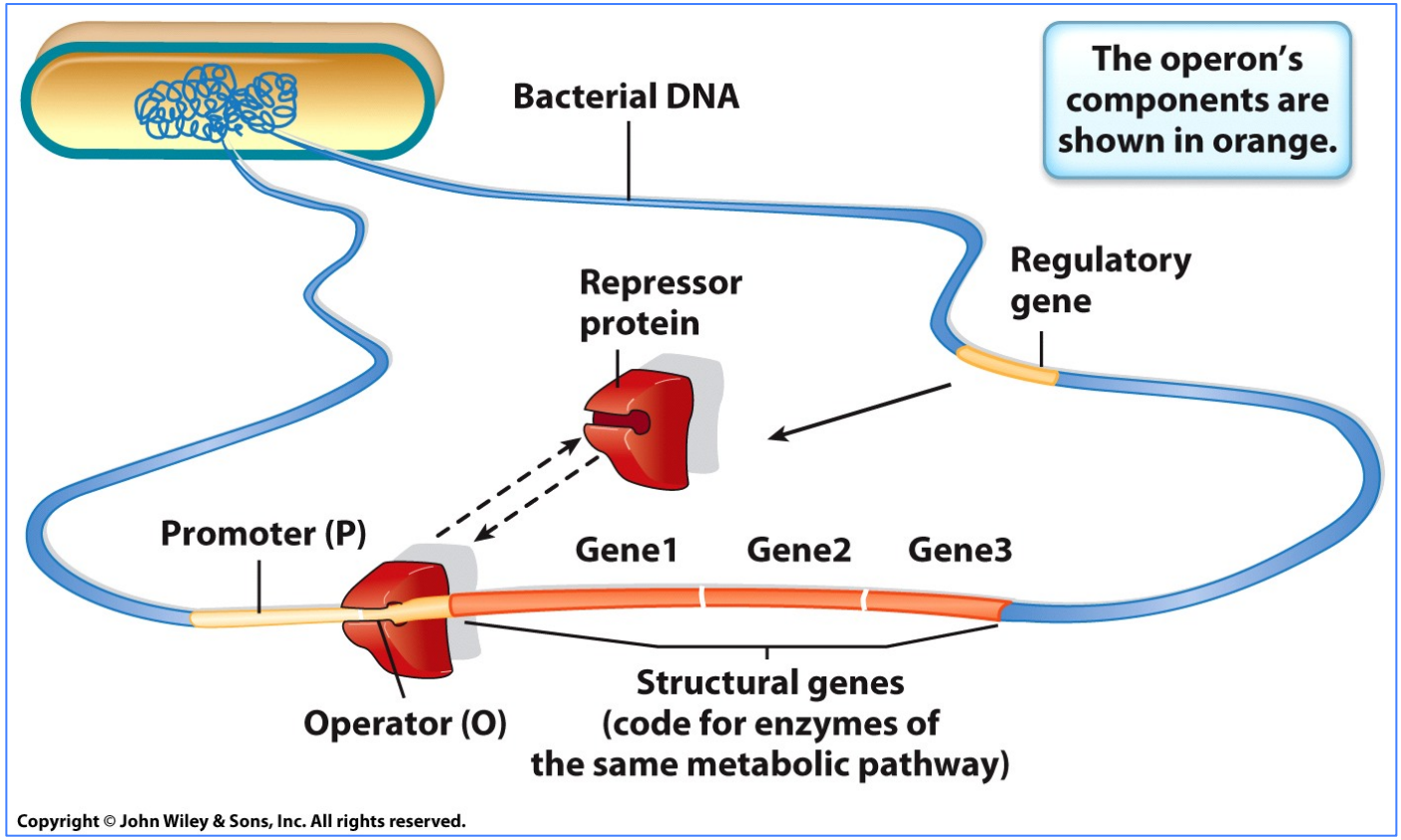
The Bacterial Operon

An operon is a functional complex of genes containing the information for enzymes of a metabolic pathway. It includes:

- ***Structural genes*** – code for the enzymes and are translated from a single mRNA that is usually polycistronic (encodes for more than one protein).
- ***Promoter*** – where the RNA polymerase binds.
- ***Operator*** – site next to promoter where the regulatory protein can bind.

Control of Gene Expression in Bacteria

The Bacterial Operon

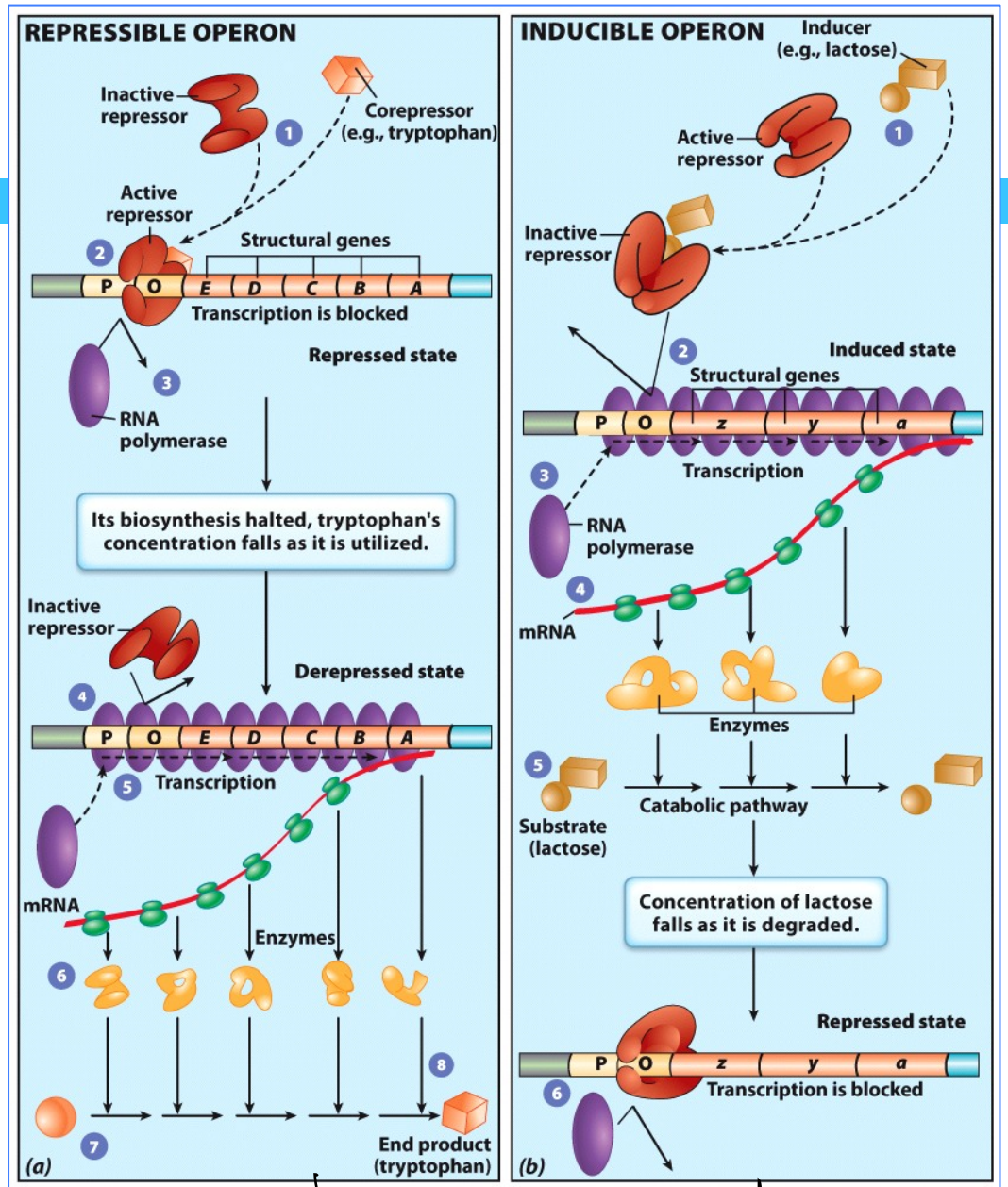


Organization of a bacterial operon. Enzymes in a metabolic pathway are encoded by a series of structural genes that reside in a contiguous array within the bacterial chromosome.

Gene regulation by operons

Two types of operons

1. Repressible Operon
   (Tryptophan)
2. Inducible Operon
   (Lactose)
   What are they?



negative feedback

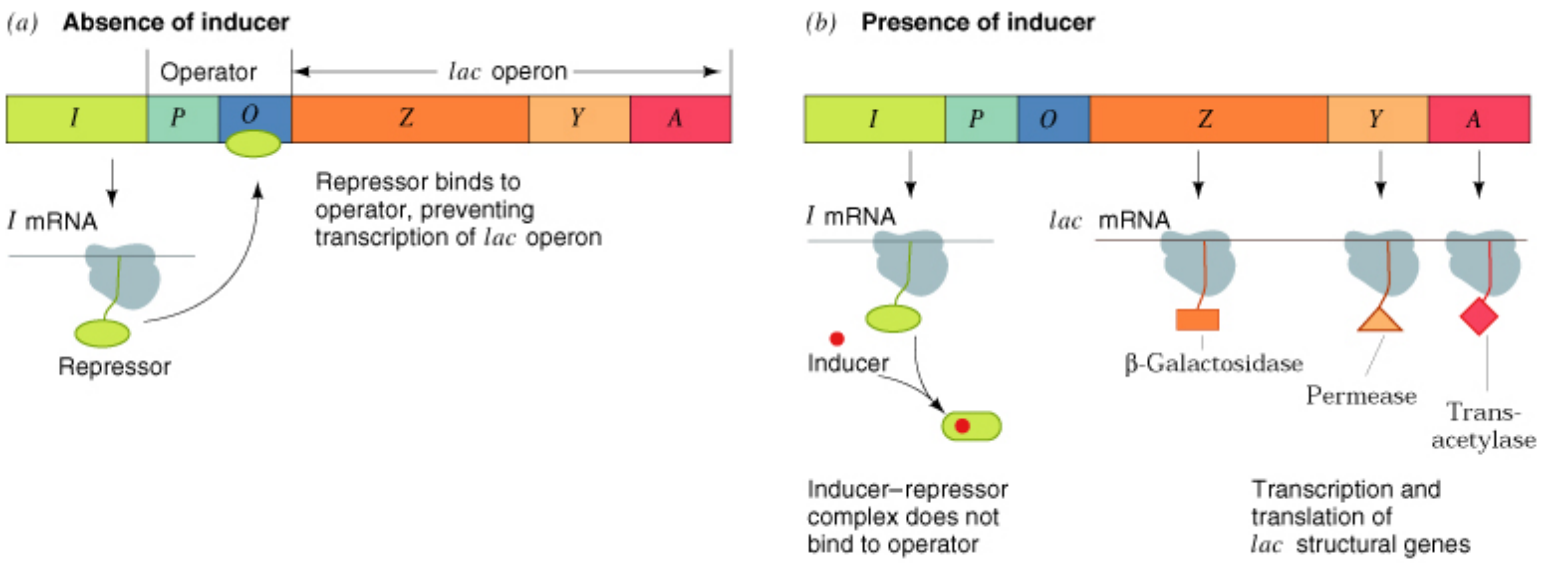
positive feedback

Gene regulation by operons: *lac* Operon

Inducible operon: which is turned on in the presence of lactose (**inducer**)

- Lac operon contains three structural genes; β - galactosidase, Permease, Transacetylase
- Lactose binds to the repressor, changing its conformation and making it unable to bind to the operator.
- A **repressor** which binds to a specific DNA sequence to determine whether or not a particular gene is transcribed.
  - RNA polymerase is unable to bind to the promoter if the repressor is bound.

Gene regulation by operons: *lac* Operon

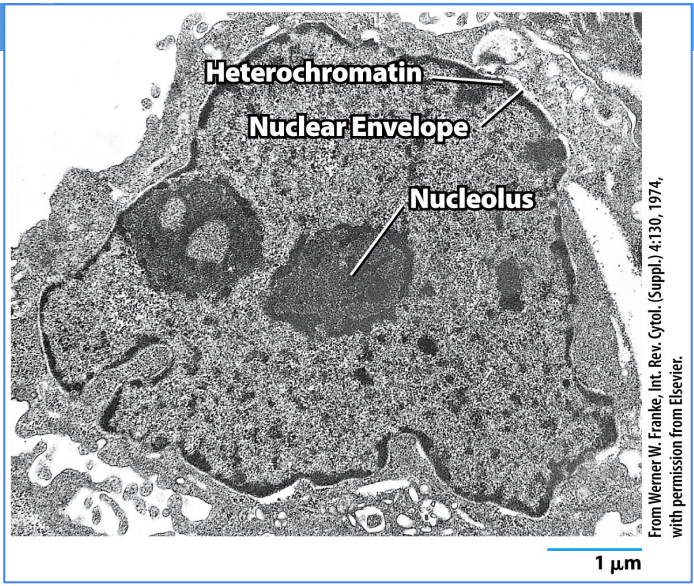


- β - galactosidase→ enzyme cleaves lactose into glucose and galactose
- Permease→ proteins insert in the plasma membrane and allow more lactose molecules to move in

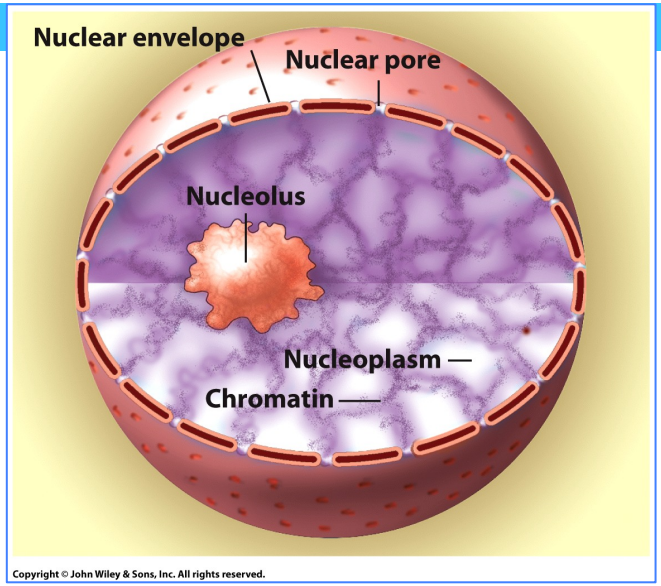
NUCLEUS AND NUCLEAR MEMBRANE

Control of Gene Expression in Eukaryotes

Structure and Function of the Cell Nucleus



The cell nucleus. EM of an interphase HeLa cell nucleus (left) and schematic drawing of major components (right).



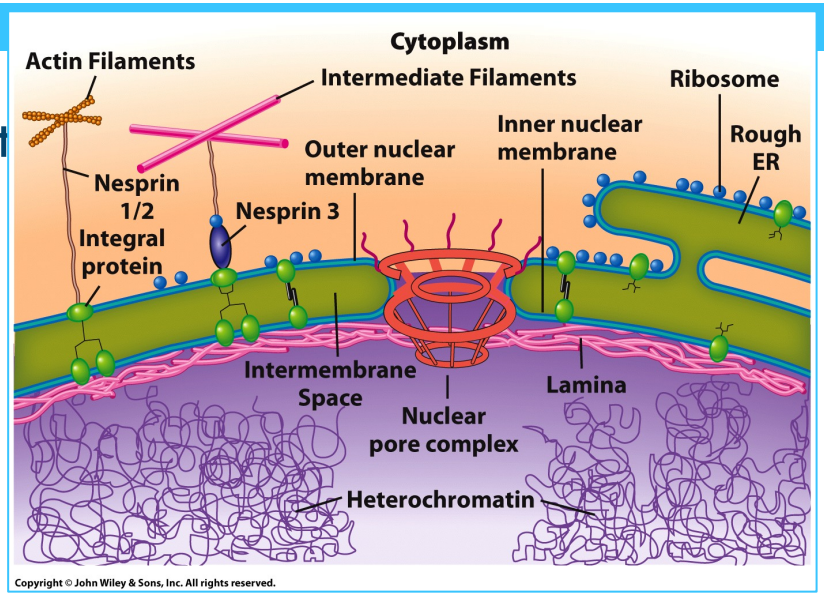
- The contents of the nucleus are enclosed by the *nuclear envelope*.
- A typical nondividing nucleus includes:
  - Chromosomes as extended fibers of *chromatin*.
  - *Nucleoli* for rRNA synthesis.
  - *Nucleoplasm* as the fluid where solutes are dissolved.

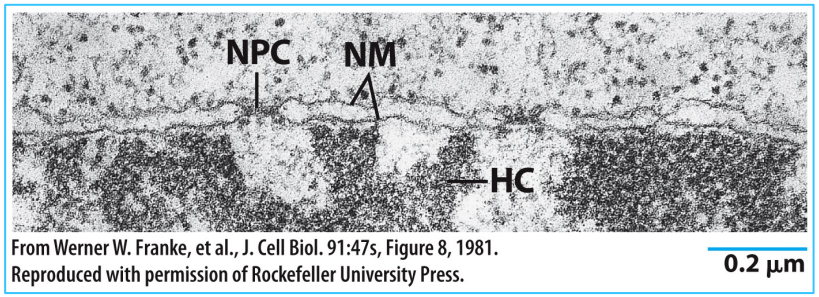
Control of Gene Expression in Eukaryotes:

Nuclear Envelope

The **nuclear envelope** is a structure that divides the nucleus from its cytoplasm.

- Consists of two membranes separated by a inter-membrane space.
- The two membranes fuse at sites forming a nuclear pore.
- The inner surface of the nuclear envelope is lined by the **nuclear lamina**.
- Contains around 60 distinct transmembrane proteins.



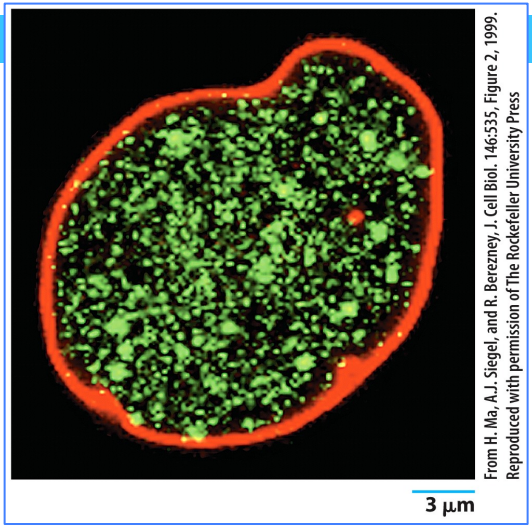


The nuclear envelope. Schematic drawing (top) and EM of the nuclear envelope of an onion root tip cell (bottom)

Control of Gene Expression in Eukaryotes

Nuclear Pore Complex

Nucleus stained for nuclear lamina (R) and nuclear matrix (G)



The nuclear lamina

- Supports the nuclear envelope and it is composed of lamins.
- Integrity of nuclear lamina regulated by phosphorylation/ dephosphorylation.
- Human conditions:
  - lamin A/C mutation gives Hutchinson-Gilford Progeria syndrome
  - lamin B mutation causes leukodystrophy (loss of myelin)

extremely quick aging

found on axons

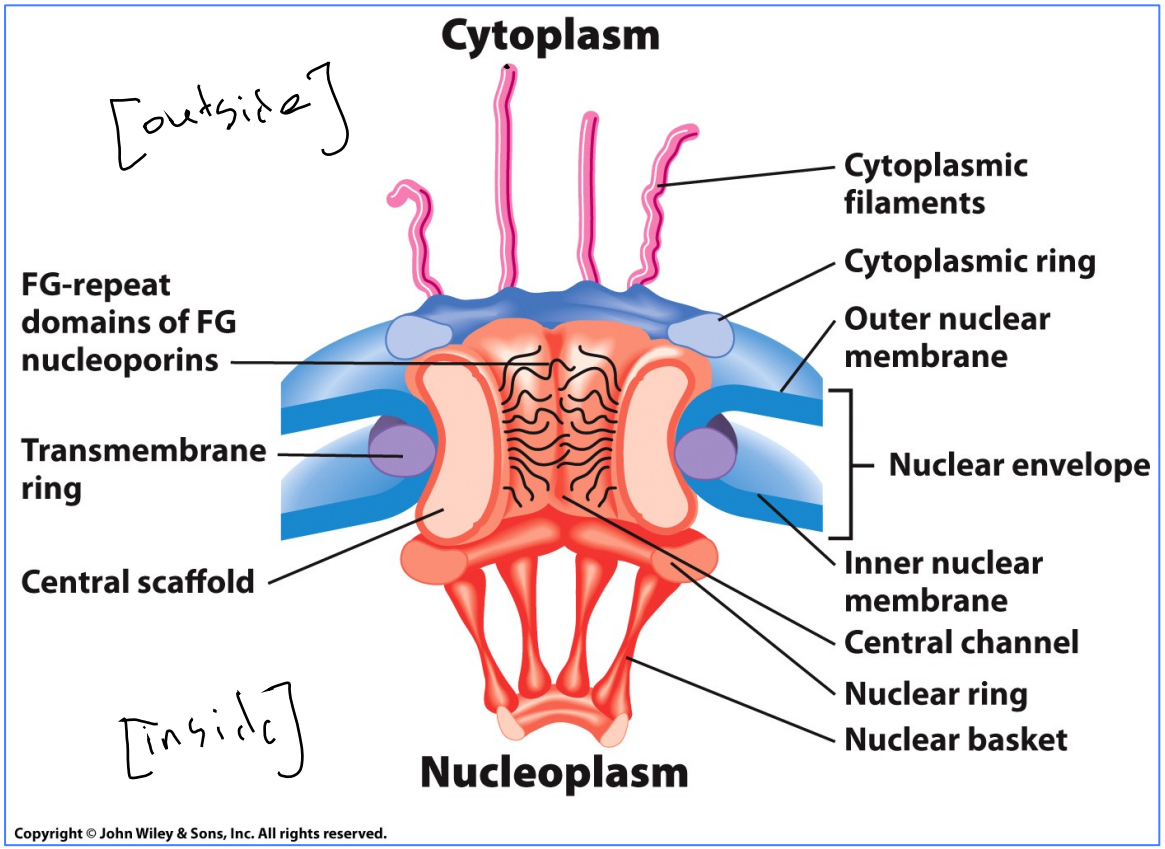
Control of Gene Expression in Eukaryotes

The Nuclear Pore Complex

- Nuclear pores contain the nuclear pore complex (NPC) that appears to fill the pore like a stopper.
- Nuclear Pore Complex plays an important role in Nucleo-cytoplasmic Trafficking
- Proteins and RNA are transported in and out of the nucleus.
- NPC is composed of ~30 proteins called *nucleoporins*.

Control of Gene Expression in Eukaryotes

The Nuclear Pore Complex



Model of a vertebrate nuclear pore complex (NPC). The structure consists of several parts, including a scaffold that anchors the complex to the nuclear envelope, a cytoplasmic and a nuclear ring, a nuclear basket, and eight cytoplasmic filaments.

FG (phenylalanine-glycine) domains form a hydrophobic sieve that blocks the diffusion of larger macromolecules (greater than about 40,000 Daltons).

Control of Gene Expression in Eukaryotes

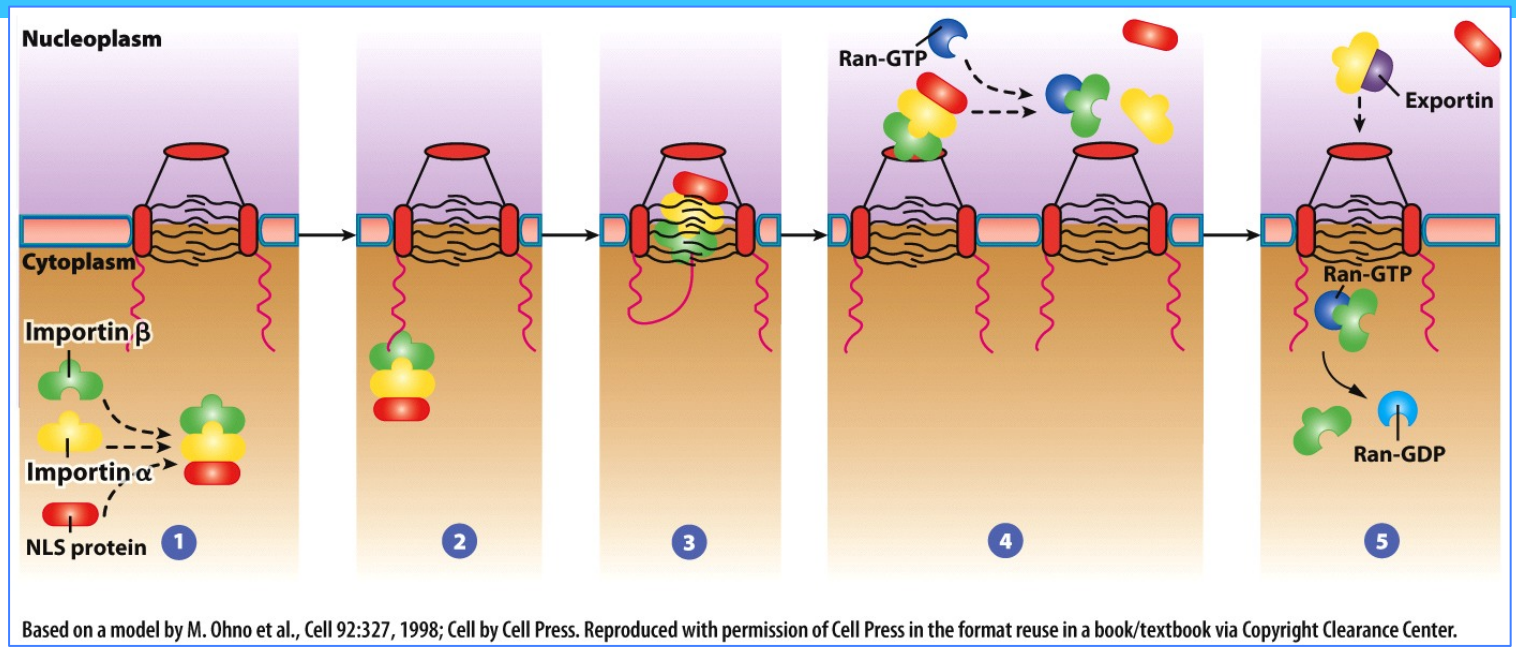
Importing Proteins

Proteins synthesized in the cytoplasm are targeted for the nucleus by the **nuclear localization signal** (**NLS**), e.g. **P-K-K-K-R-K-V**

- Proteins with an NLS stretch bind to an NLS receptor (*importin*)
- Conformation of the nuclear pore complex (NPC) changes as the protein passes through.
- RNAs move through NPCs as ribonucleoprotein and carry *NES* (*nuclear export signals*) to pass through

Control of Gene Expression in Eukaryotes

Importing Proteins



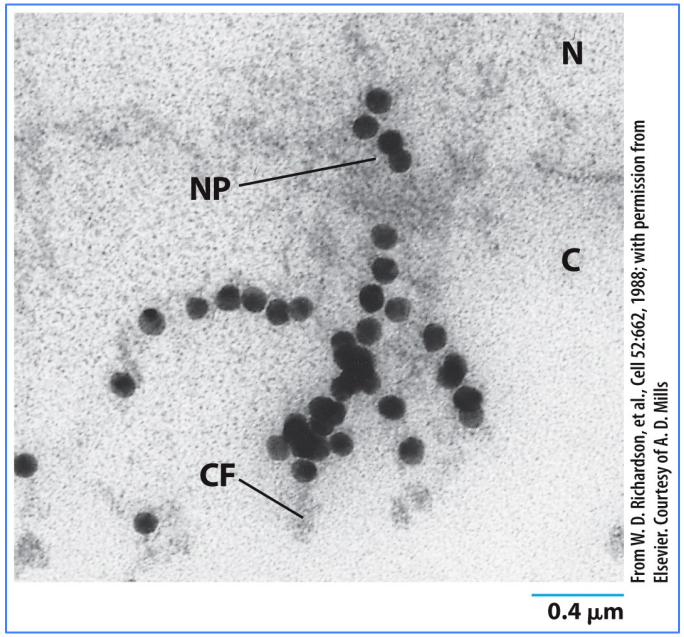
Based on a model by M. Ohno et al., Cell 92:327, 1998; Cell by Cell Press. Reproduced with permission of Cell Press in the format reuse in a book/textbook via Copyright Clearance Center.

Importing proteins into the nucleus. Steps in nuclear protein import (left).

- NLS containing cargo protein
- NLS receptor importin α/β (resides in the cytoplasm)
- Ran-GDP is exported back to the nucleoplasm

Control of Gene Expression in Eukaryotes

Importing Proteins



Gold particle-nucleoplasmin injection into frog oocytes shows binding to cytoplasmic filaments (right)