
Institut Pasteur





2007 - 2013

# The Operon Model and its Impact on Modern Molecular Biology

## Institut Pasteur, Paris, France

## 17-20, May 2011

### Theme of the conference

**We will attept to trace the influence of this discovery on the way molecular biology has progressed in the last half century.Some of the best world specialists will review our present knowledgeon gene expression control, stem cells and development, cell growth and division and systems biology among others.**

The review article entitled " Genetic Regulatory Mechanisms in the Synthesis of Proteins " or in brief the "Operon model" by François Jacob and Jacques Monod was published in the Journal of Molecular Biology in June 1961 ( J.Mol.Biol. 3, 318-356, 1961).

This review traced the experiments on the regulation of the lacZ gene encoding beta galactosidase in E. coli and of phage lambda lysogeny. It formulated for the first time the hypothesis that genes are regulated at the transcriptional level by specific regulatory proteins (or RNA) and that these regulators respond to metabolic changes, environment etc. This publication can be considered as one of the major milestones in the emergence of Molecular Biology in the second half of the 20th century.

The 50th anniversary of this publication will be celebrated with a special symposium to be held at the Pasteur Institute in Paris between the 17th and the 20th of May 2011.

### Scientifics Sessions

- Historical perspective
- Transcription mechanisms
- Epigenetics
- Stem cells and development
- Transcription and differentiation
- Cell growth and division
- Networks and system biology

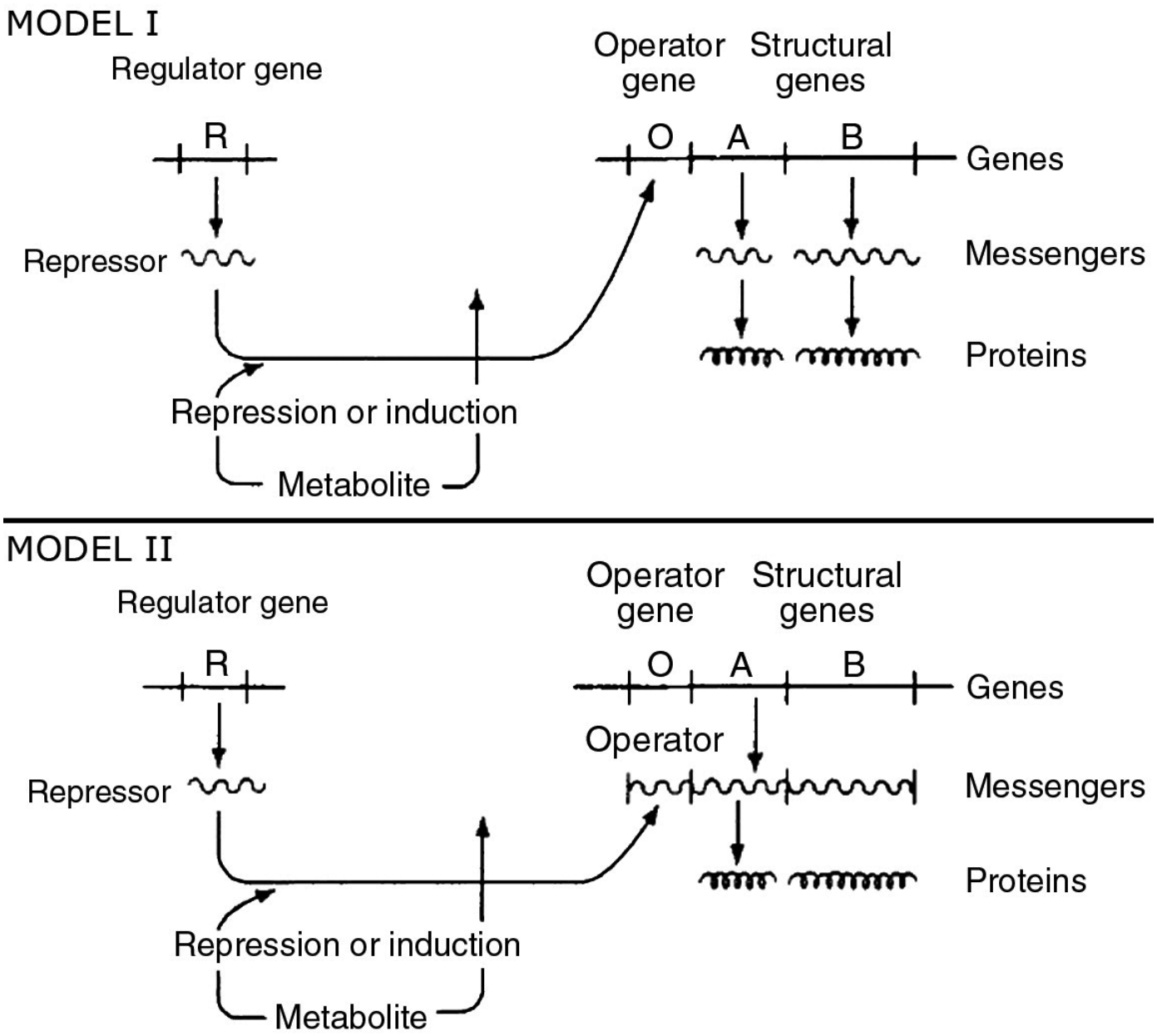
J Mol Biol. 1961 Jun;3:318-56.

# Genetic regulatory mechanisms in the synthesis of proteins

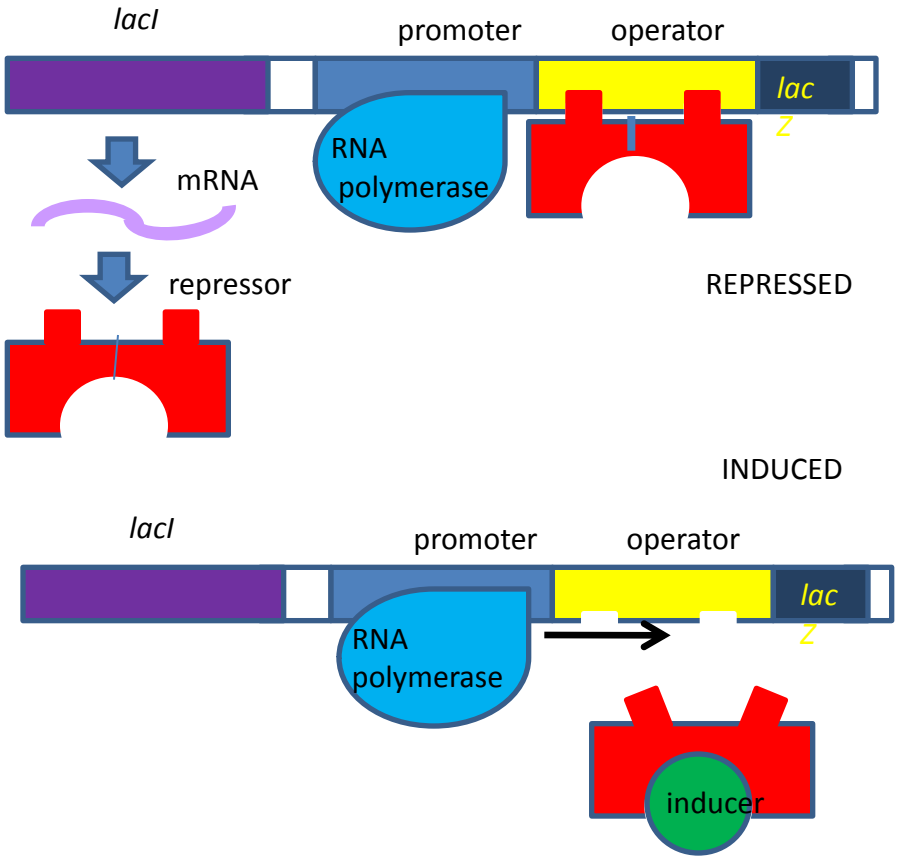
## (Or the Operon Theory)

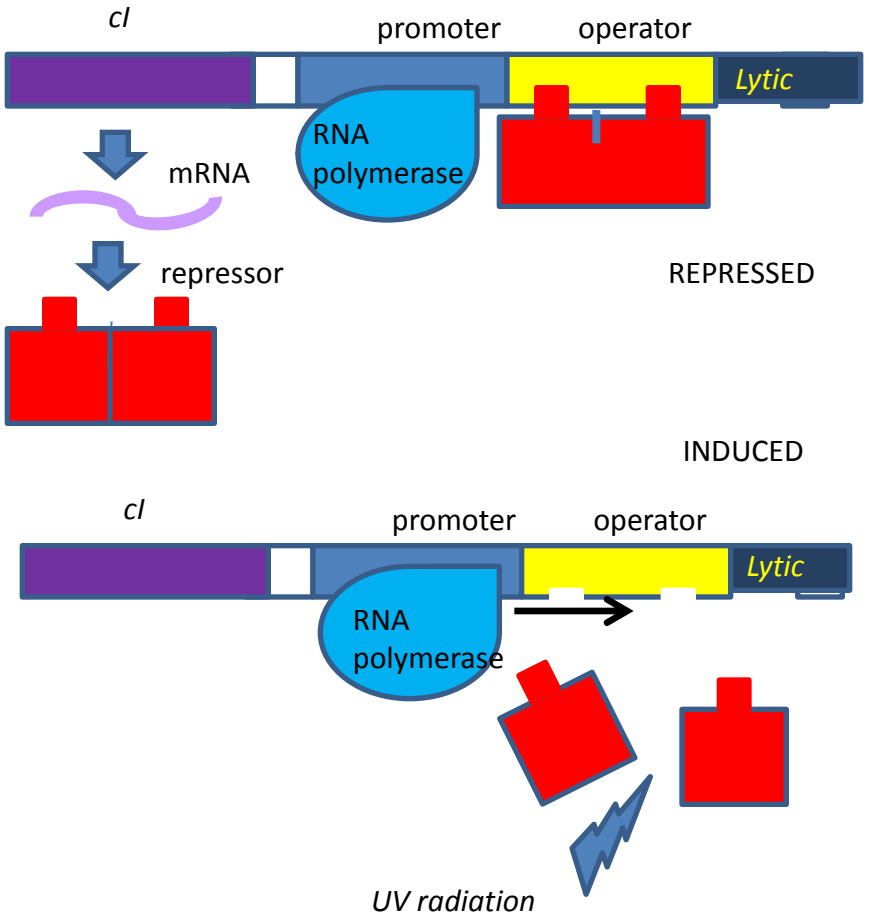
François JACOB & Jacques MONOD

# The Operon Model, Jacob & Monod, 1961



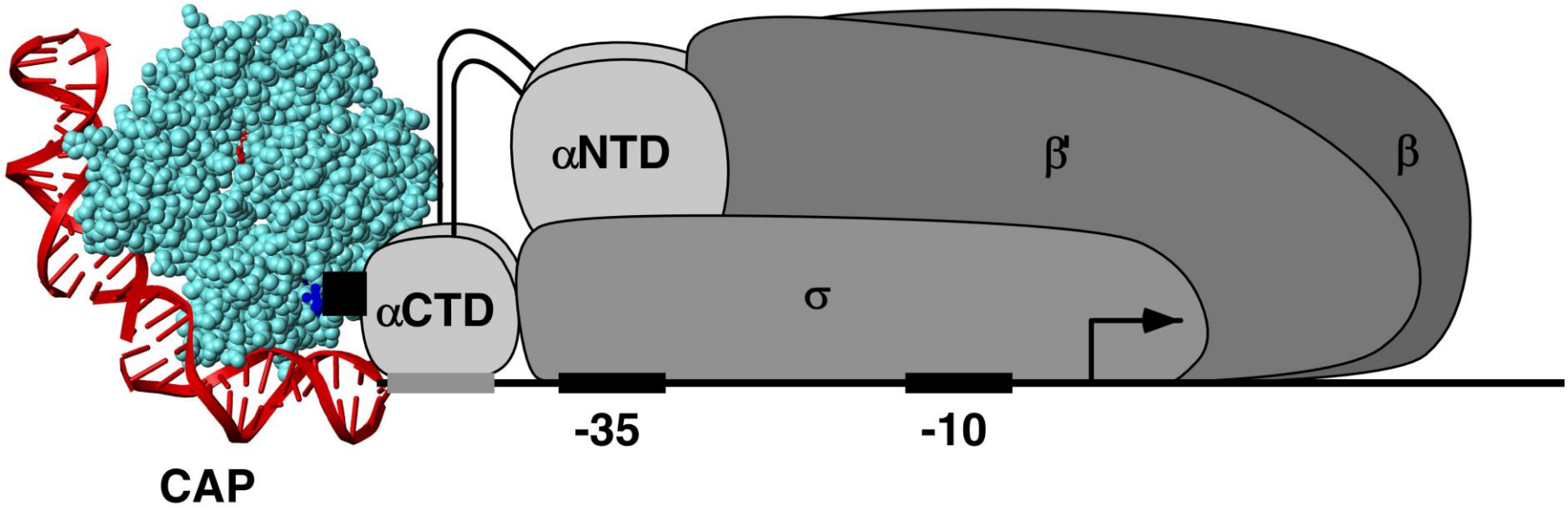
# Lac & bacteriophage lambda induction



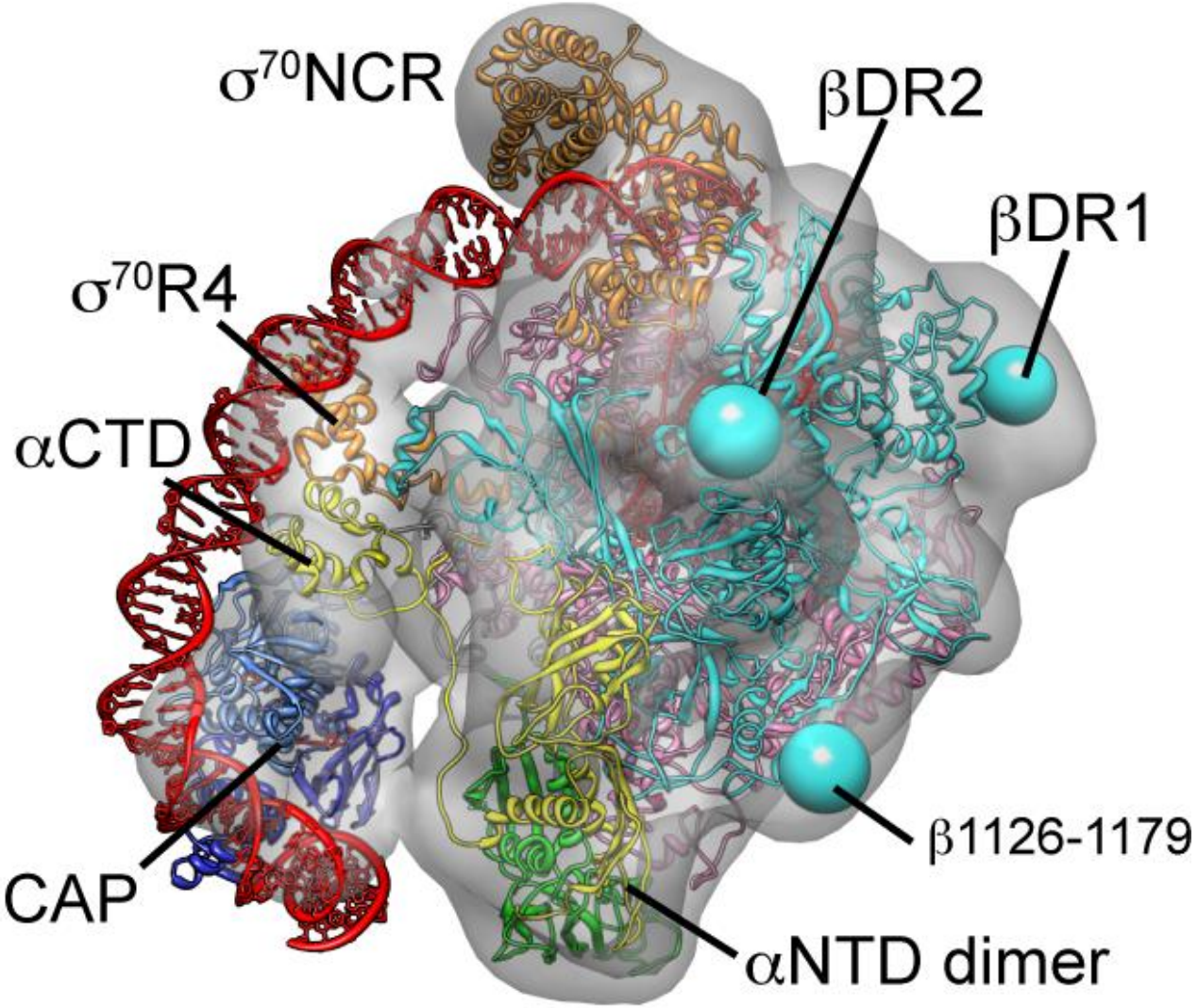
# RNAP α subunit consists of two domains connected by a long, flexible linker.

## The α N-terminal domain (αNTD) interacts with RNAP β and β' subunits.
## The α C-terminal domain (αCTD) interacts with CAP and with DNA.



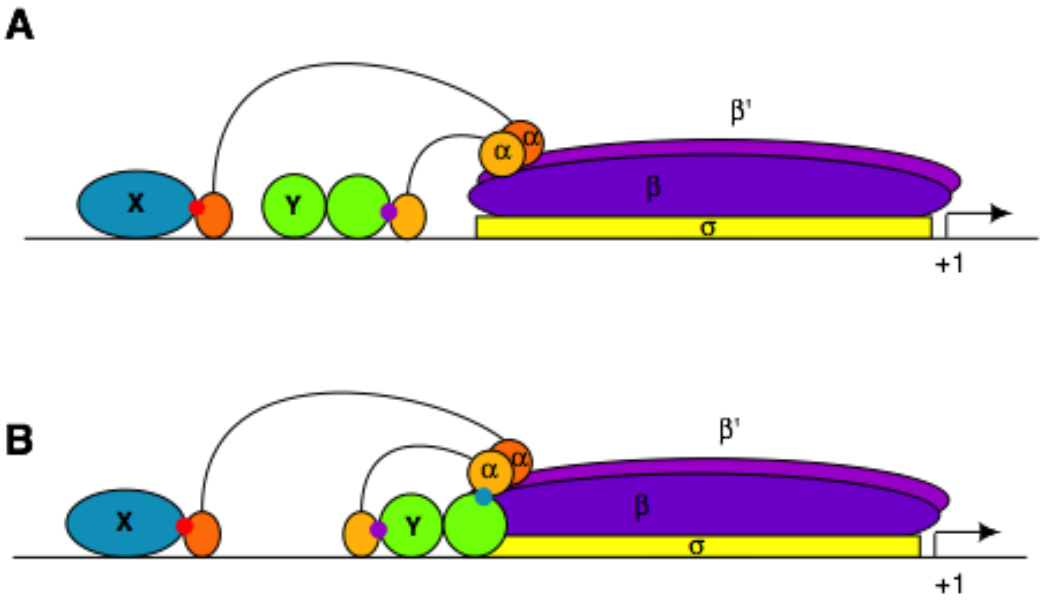

*R.Ebright lab Cell* **78**:889, 1994

# Determination of an EM structure of the intact CAP-RNA Polymerase-promoter complex.




*R. Ebright lab PNAS* **106**:1, 2009

Exemples simples de co-activation avec action indépendante de deux activateurs




Transcription activation by two independent activators

- Transcription regulation in bacteria, extensions

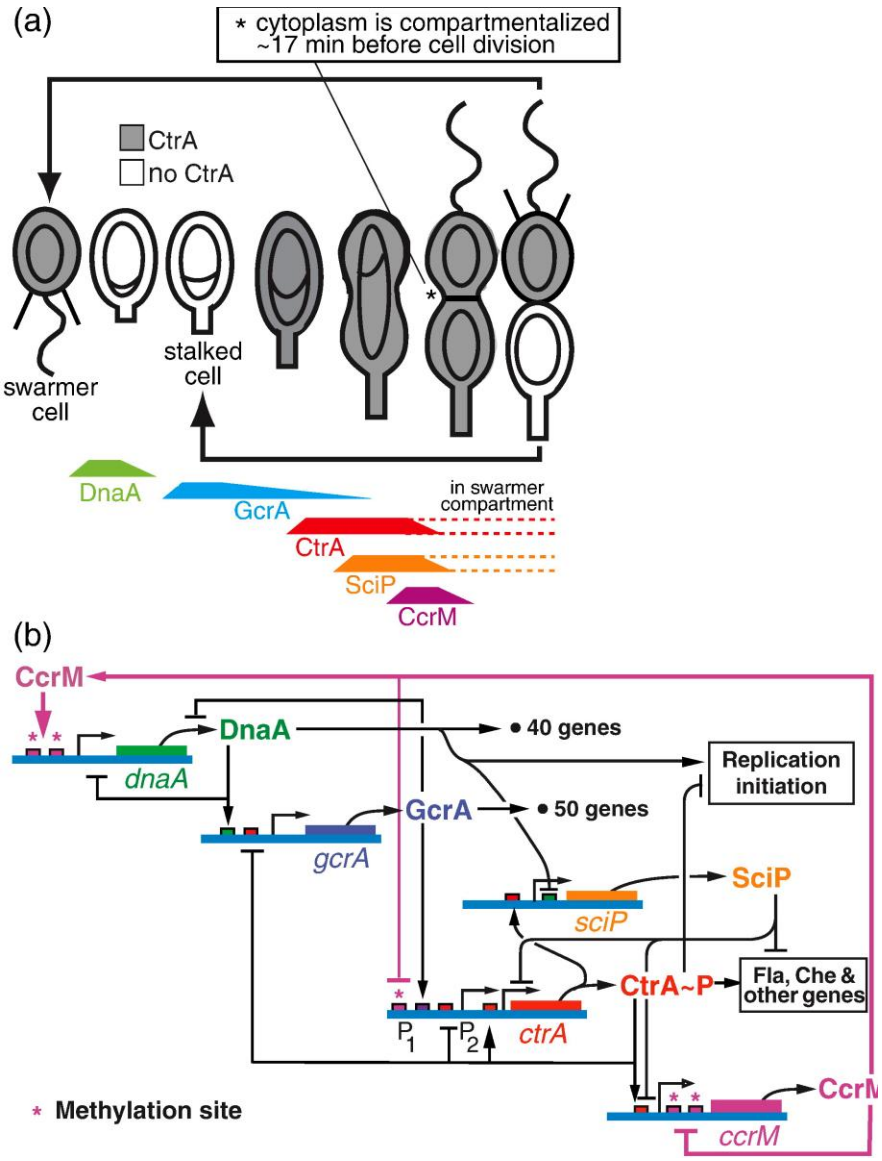
- Negative and positive regulators
- Several regulators for a single gene
- DNA bending to facilitate contacts

# Systems biology in bacteria

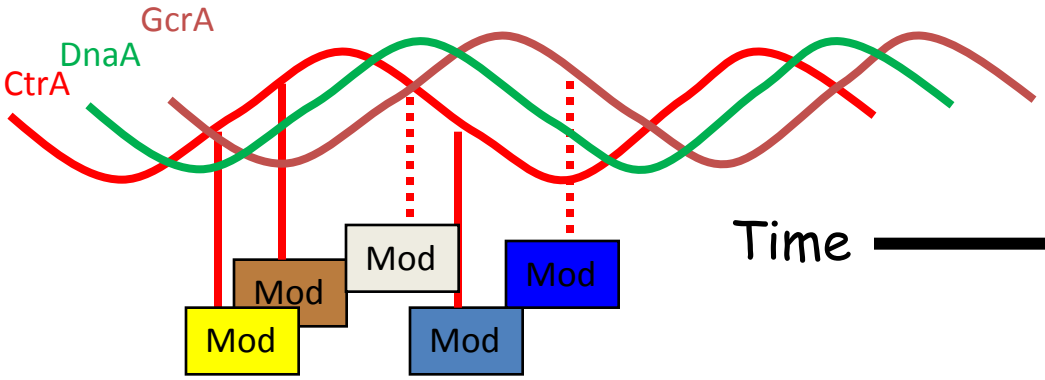
Can we describe a bacterial life cycle?

The caulobacter's asymmetric cell division

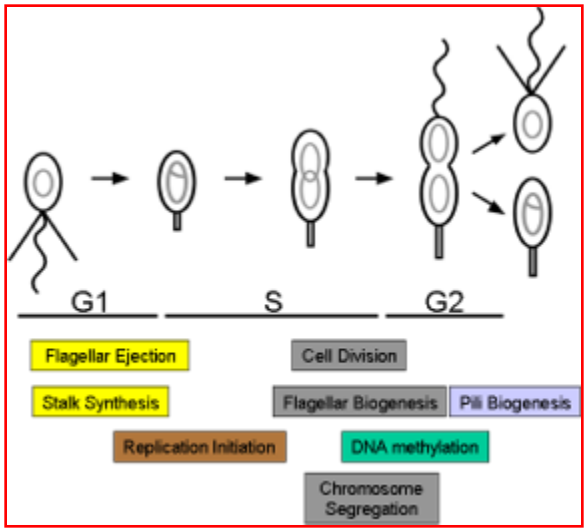
Harley McAdams & Lucy Shapiro


(a)
* cytoplasm is compartmentalized
~17 min before cell division
CtrA
no CtrA
swarmer cell
stalked cell
DnaA
GcrA
CtrA
SciP
CcrM
in swarmer compartment
(b)
CcrM
DnaA
dnaA
• 40 genes
Replication initiation
GcrA
• 50 genes
gcrA
SciP
sciP
CtrA~P
Fla, Che & other genes
P1
P2
ctrA
CcrM
ccrM
* Methylation site

# Flexible design for genetic subsystem control



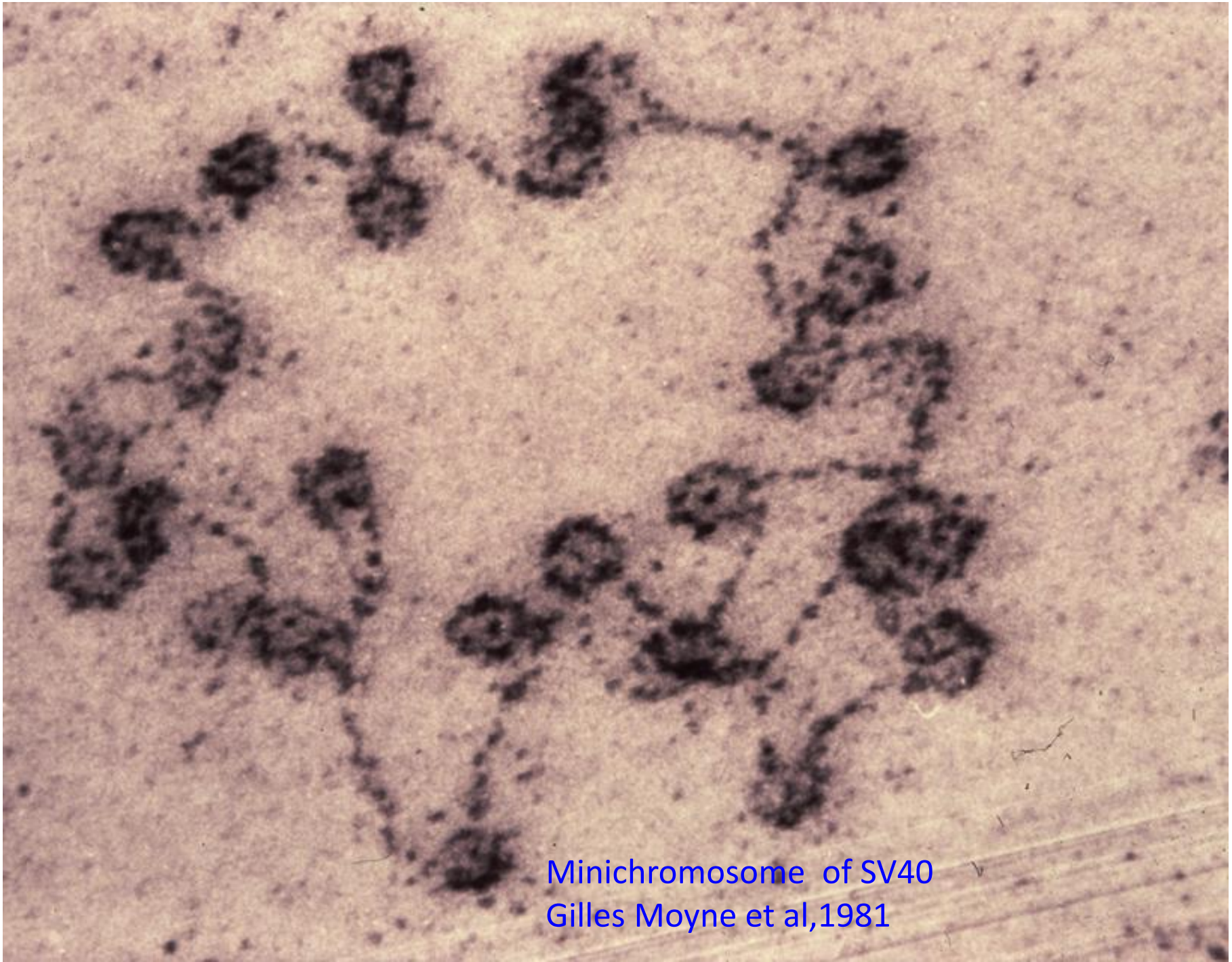

Time



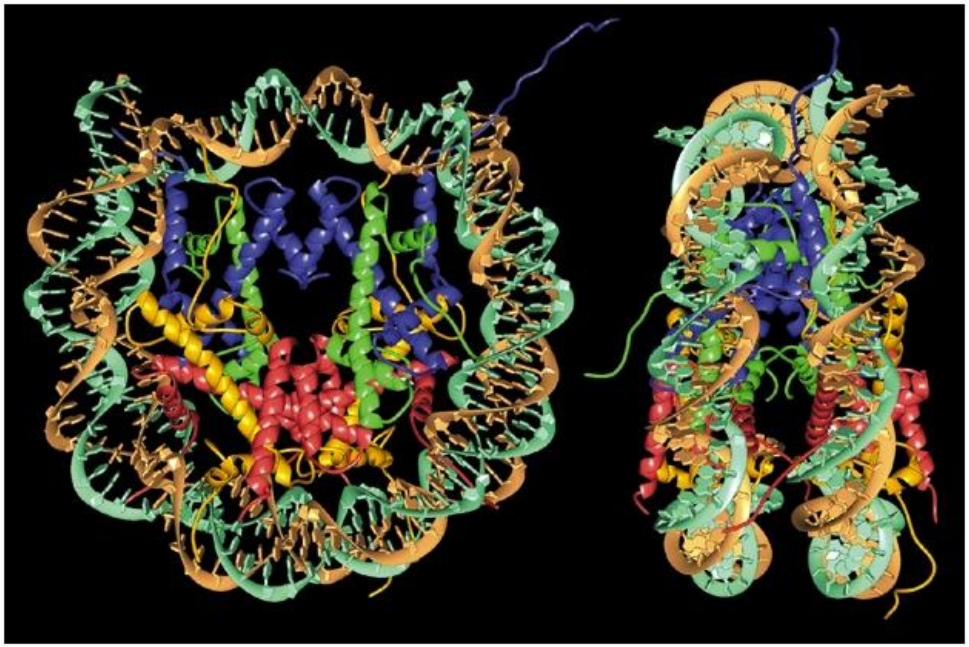

- Cyclical regulatory protein concentrations activate and repress modular subsystems
- Feedback and checkpoints add additional synchronization controls

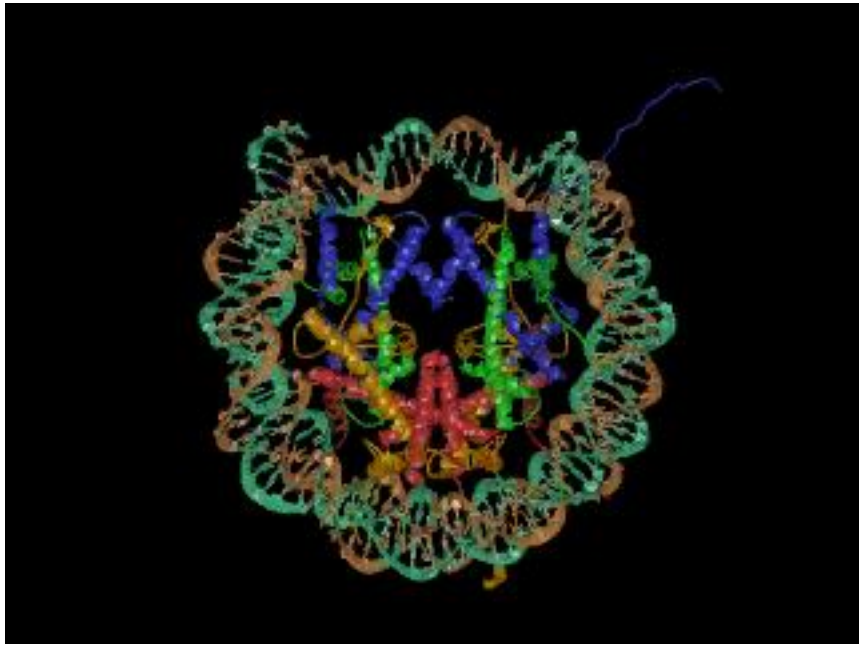
# Going from bacteria to nucleated eucaryotes

- Site of transcription is distinct from that of protein synthesis
- Compaction of DNA in nucleosomes and higher order structures: Chromatin


Minichromosome of SV40
Gilles Moyne et al,1981

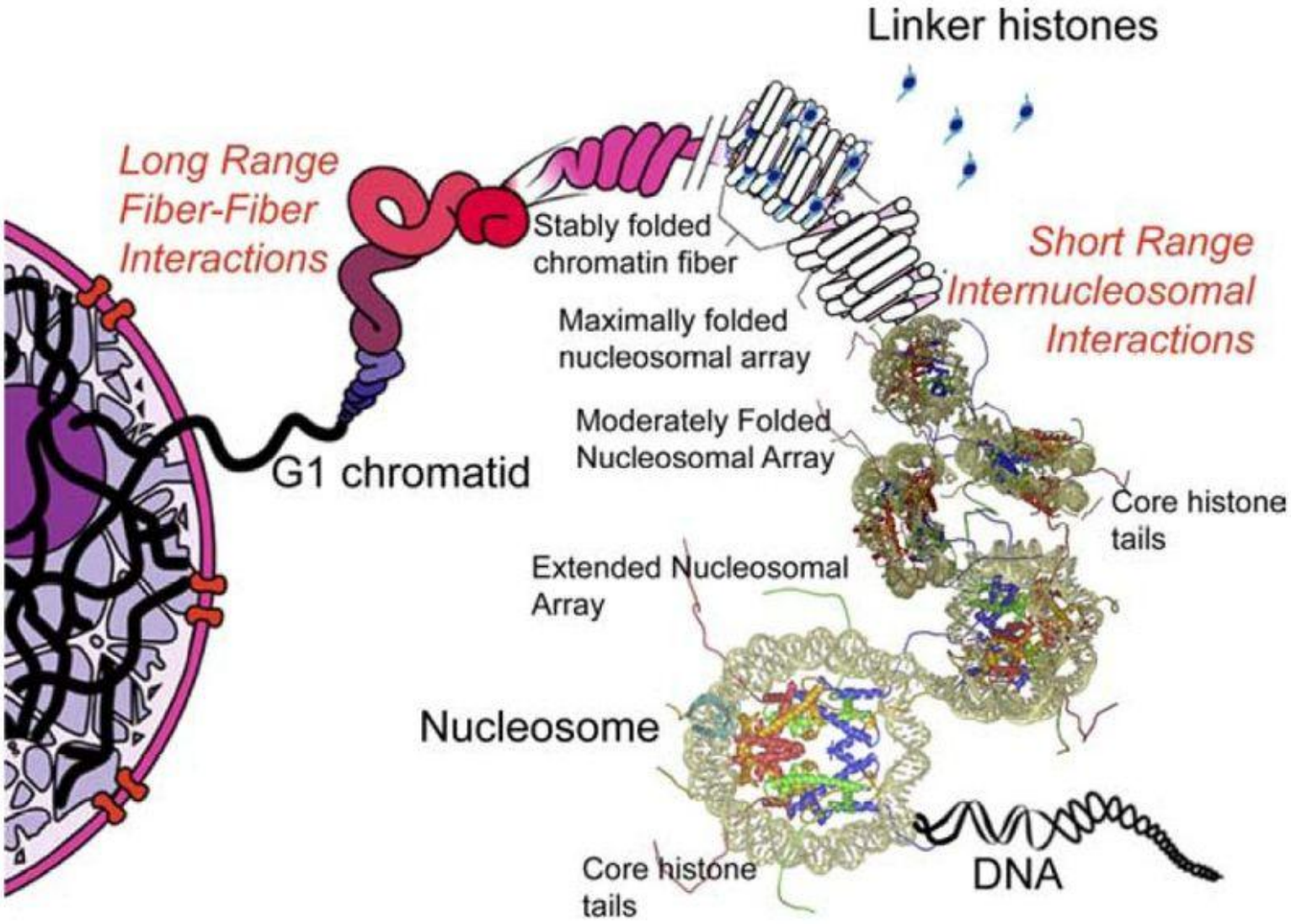
# The nucleosome and the tails of histones



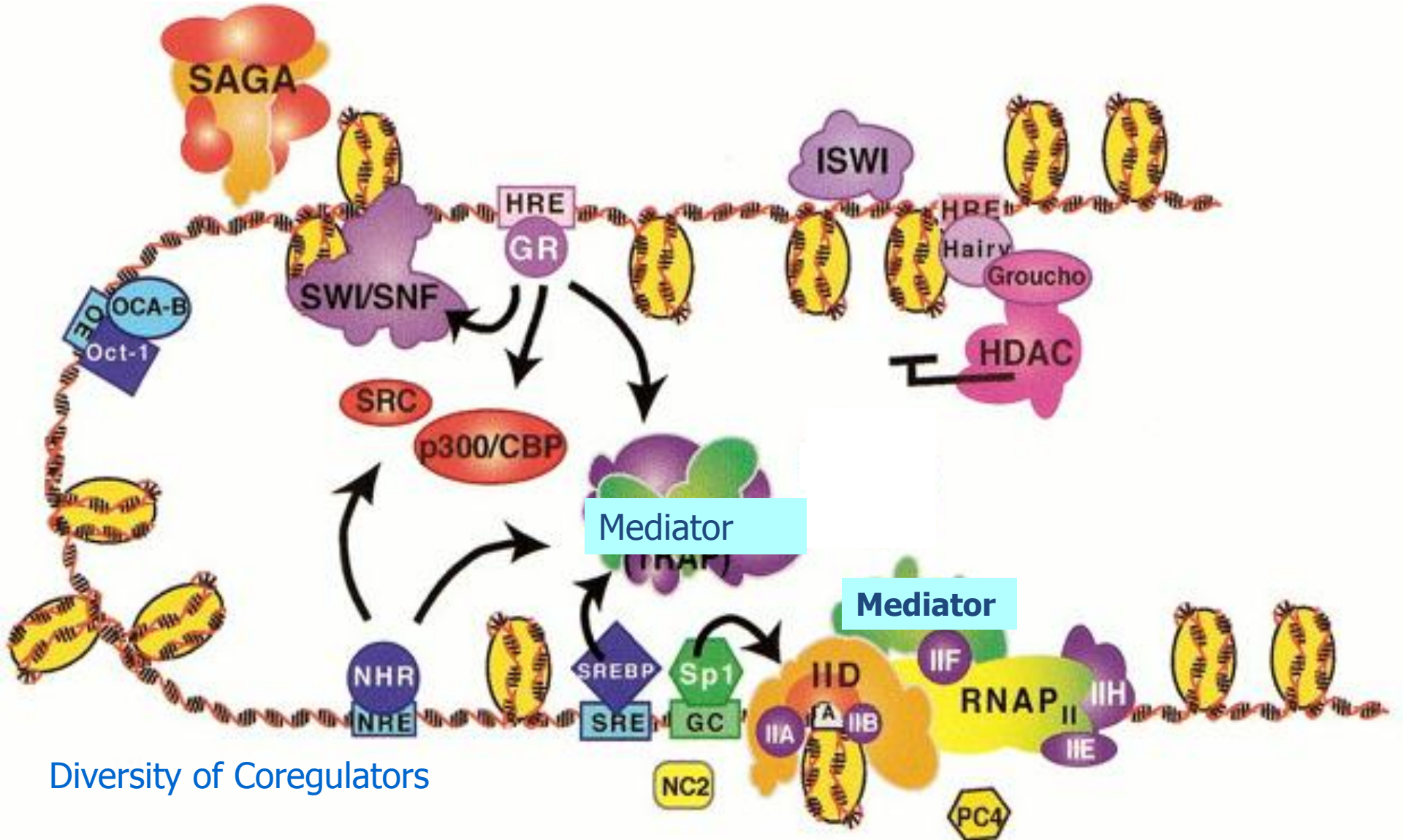


H2A yellow; H2B red; H3 blue; H4  green, T.Richmond et al

# Chromatin, DNA compaction and gene regulation



# Elements of eukaryotic transcriptional control



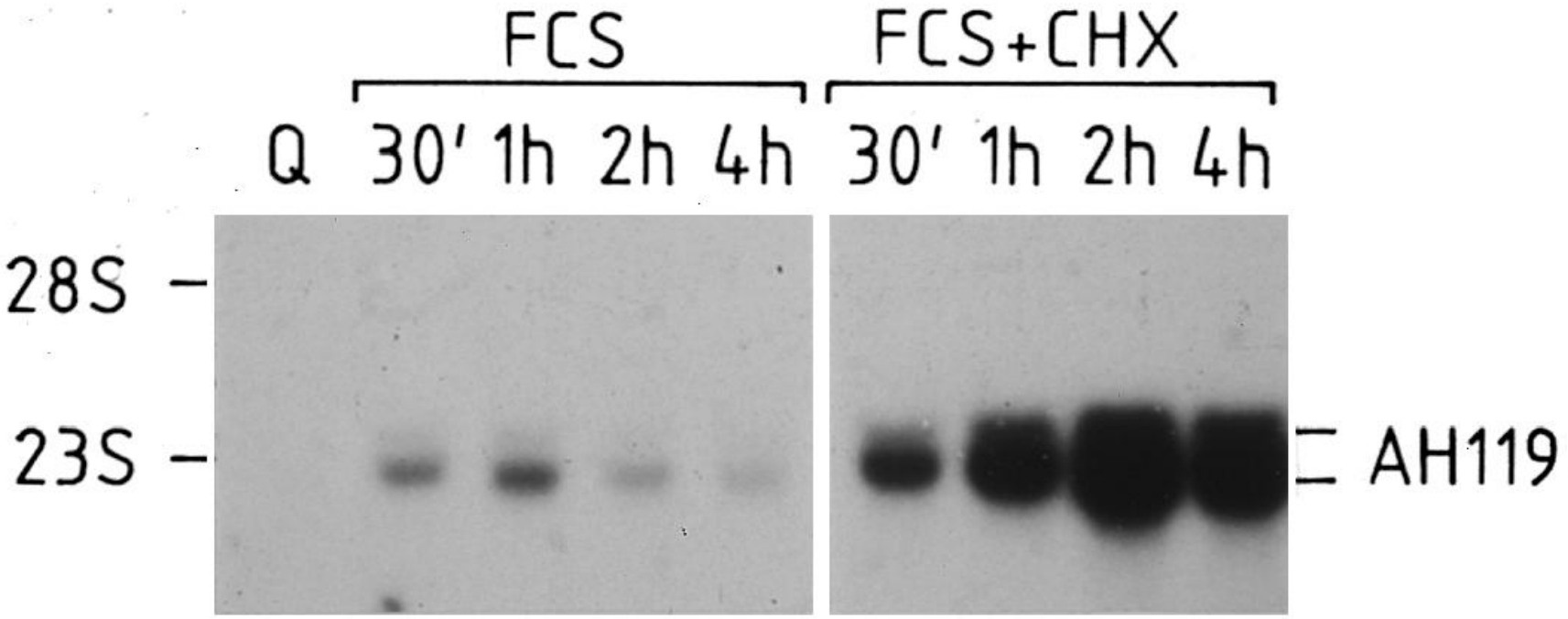

Diversity of Coregulators

# The AP1 transcription factor

A dimer of cJun and cFos

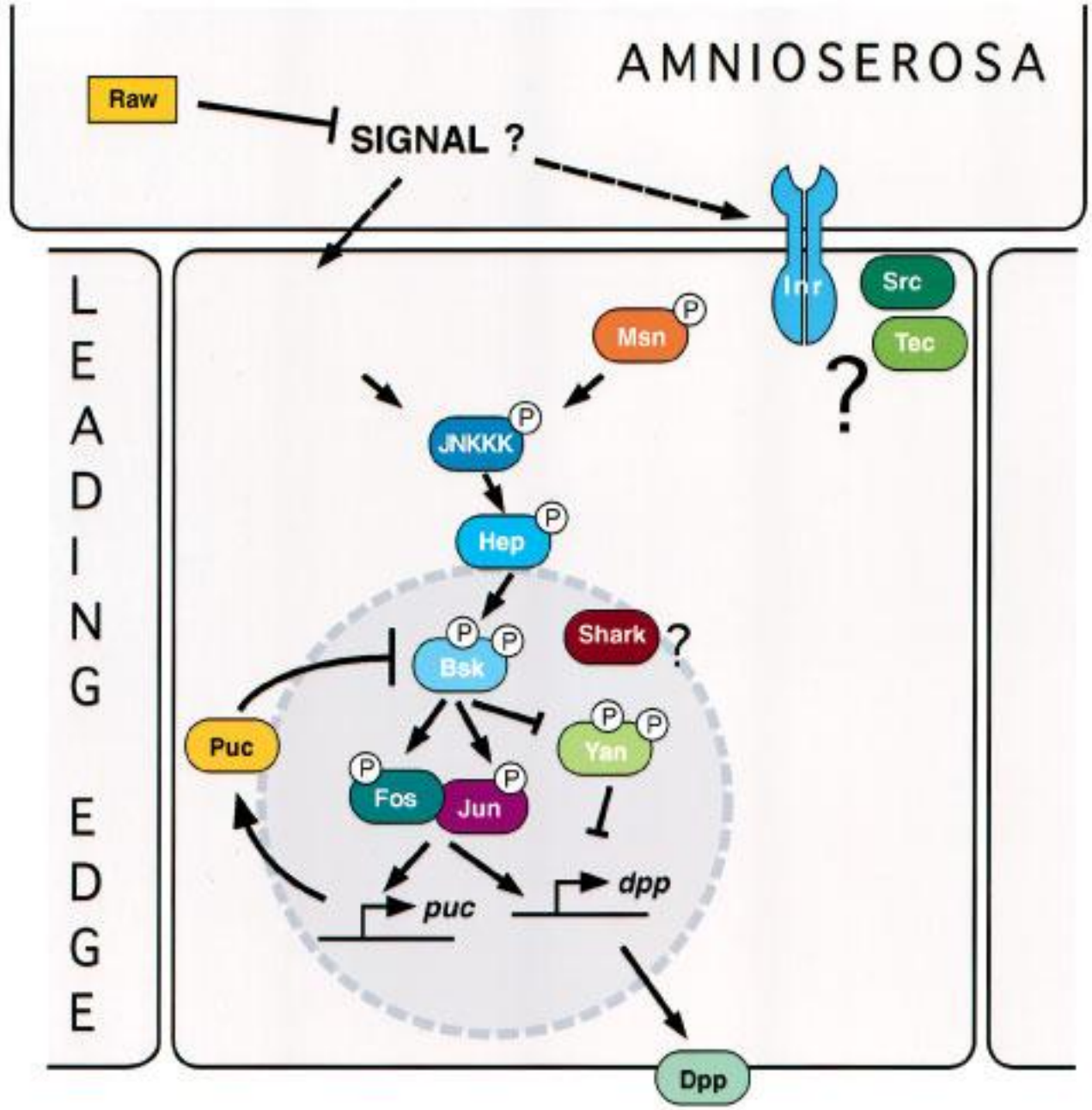
A paradigm for eucaryotic TFs

# Transcriptional induction of cJun mRNA in the absence or presence of protein synthesis inhibitor




Protein induced specifically binds to 5' TGACTCA

# Negative feed back loops in gene activation




D. Bohmann

# Kinetics of Jun proteins induction by serum growth factors