

# **BIOMENG 261**

## **TISSUE AND BIOMOLECULAR ENGINEERING**

*Module I: Reaction kinetics and systems biology*

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# MODULE OVERVIEW

Reaction kinetics and systems biology (*Oliver Maclaren*)  
**[11 lectures/3 tutorials/2 labs]**

*1. Basic principles: modelling with reaction kinetics* [4 lectures]

Conservation, directional and constitutive principles. Mass action. Enzyme kinetics. Enzyme regulation. Mathematical/graphical tools for analysis and fitting.

*2. Systems biology I: signalling and metabolic systems* [2 lectures]

Overview of systems biology. Modelling signalling systems using reaction kinetics. Introduction to parameter estimation. Modelling metabolic systems using reaction kinetics. Flux balance analysis and constraint-based methods.

*3. Systems biology II: genetic systems* [3 lectures]

Modelling genes and gene regulation using reaction kinetics. Gene regulatory networks, transcriptomics and analysis of microarray data.

# LECTURE 10: GENE REGULATION CONTINUED

- Example of modelling gene expression/regulation using reaction modelling
  - The lac operon
- Moving to larger systems of gene regulatory networks (GRNs)
  - Gene space
  - Intro to transcriptomics

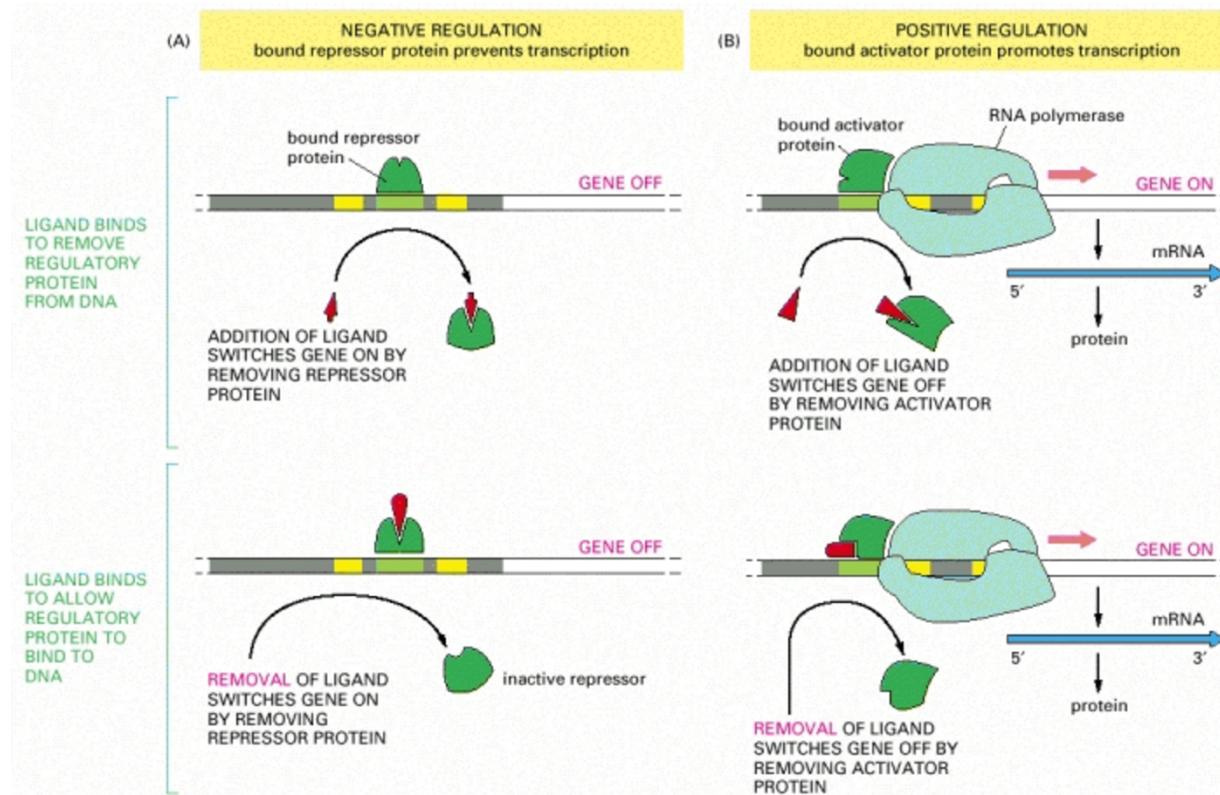
Next time: data analysis for 'transcriptomics'

# SETTING: LACTOSE METABOLISM IN E. COLI

- E. coli '*prefers*' glucose but is capable of metabolising lactose when glucose is not available
- Jacob and Monod (1961) explained this in terms of *changes in gene expression*
  - Proposed a general theory of (prokaryotic) regulation of gene expression
  - Idea: genes are controlled in functional groups via single feedback mechanism: *control of repression*

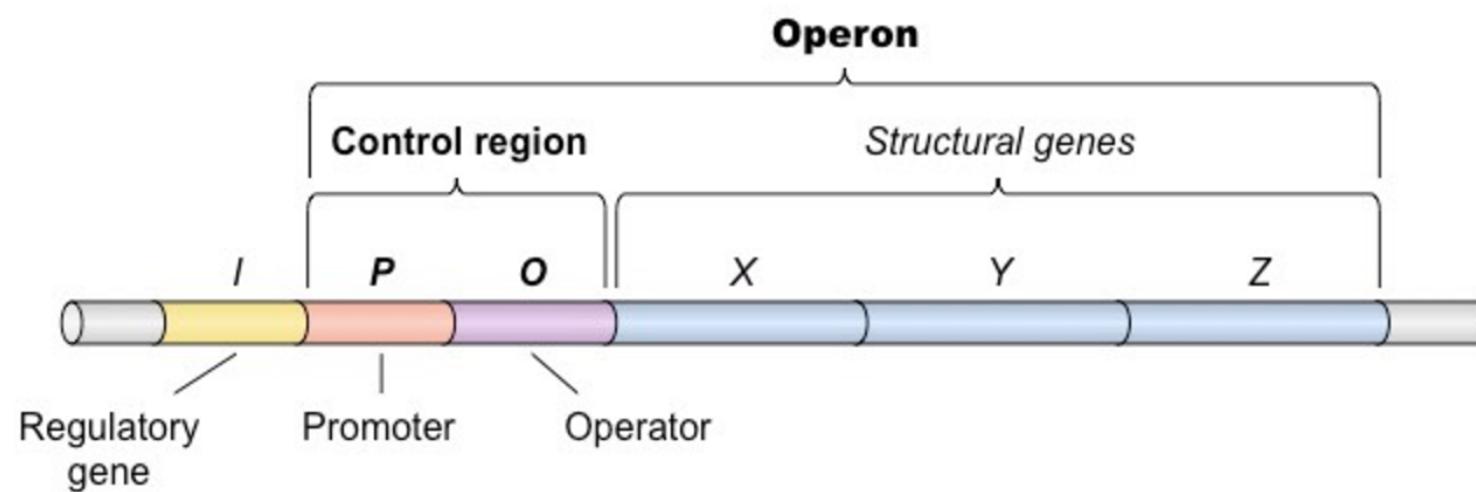
Not quite true (not just repression in general), but key ideas remain.

# GENETIC SWITCHES AND REGULATION

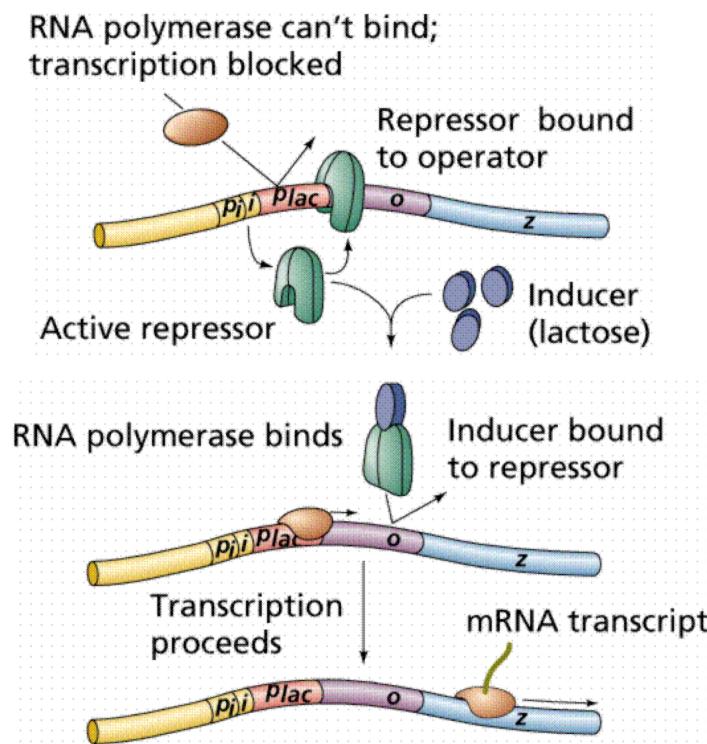
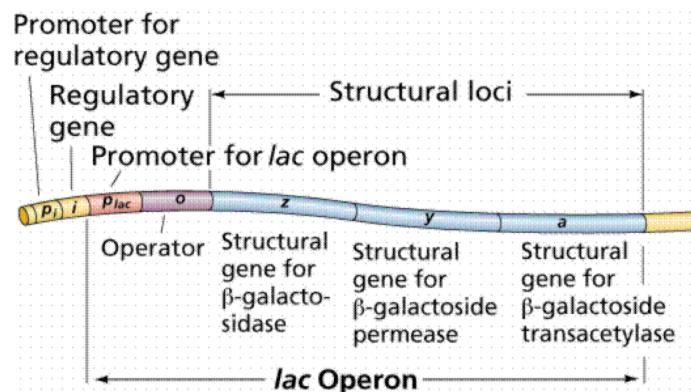


(Alberts et al. Molecular Biology of the Cell. 4th edition)

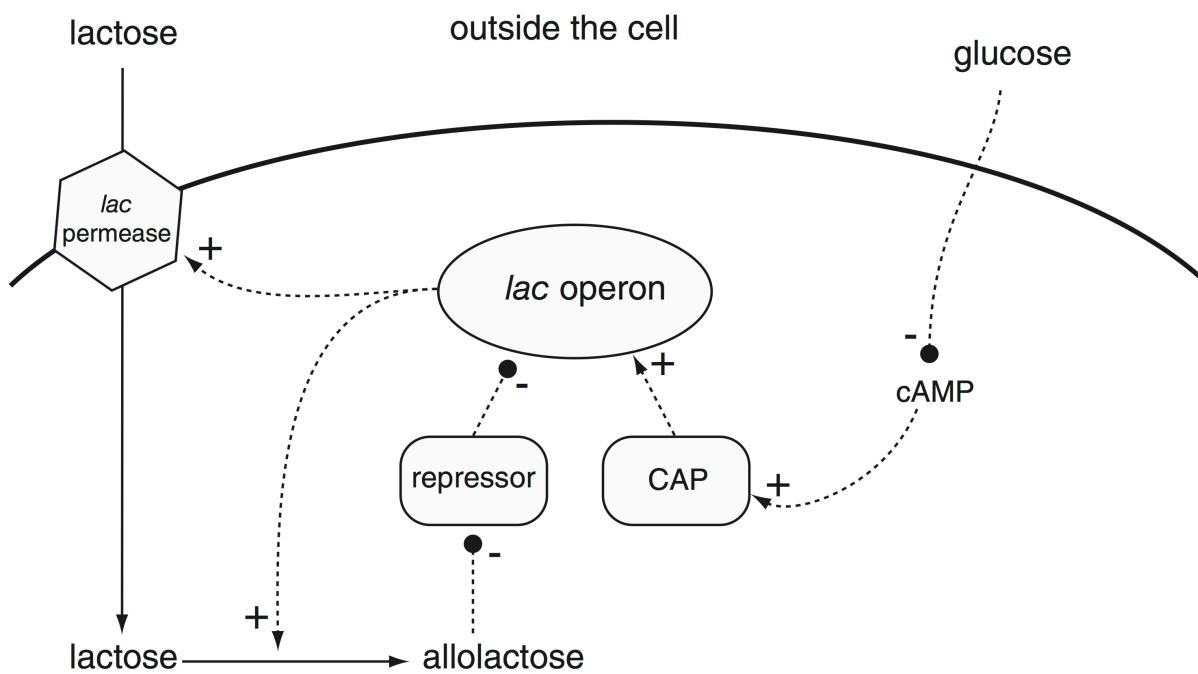
# OPERONS



# THE LAC OPERON

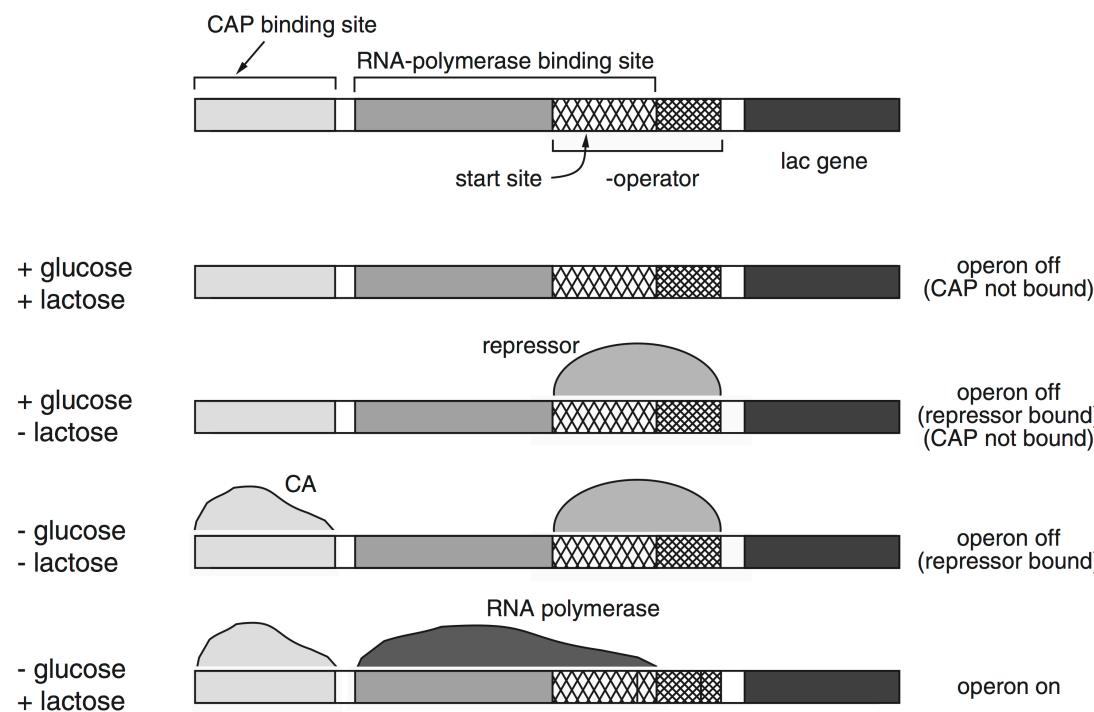


# LAC OPERON REGULATORY NETWORK



(Keener and Sneyd 2008)

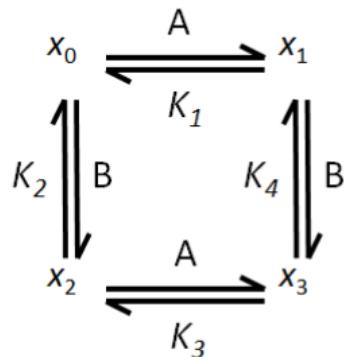
# LAC OPERON REGULATION SUMMARY



# UPSHOT? EXAMPLE QUESTION (2016)

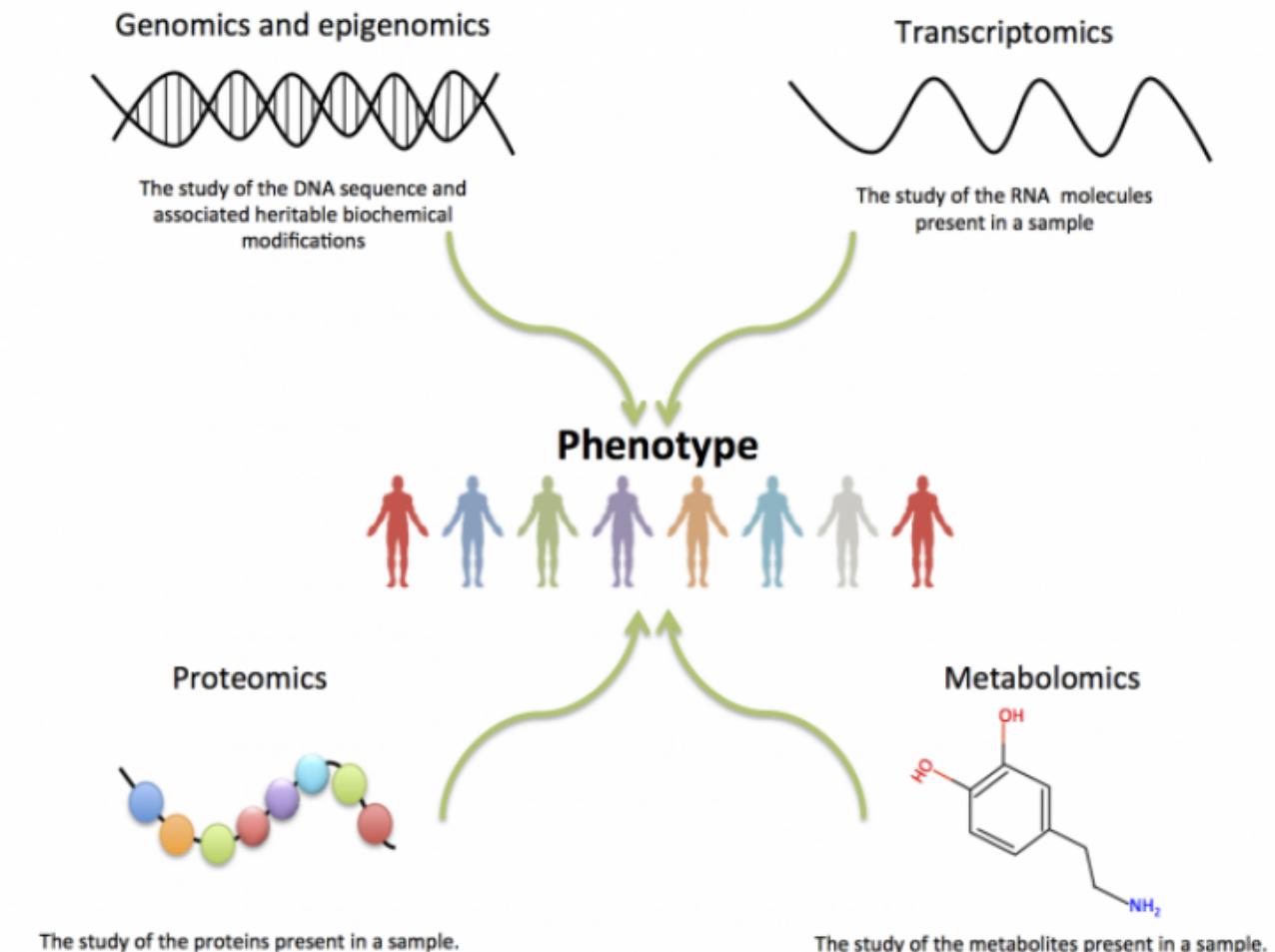
## Question 3

- (a) Consider a gene regulated by two transcription factors, A and B. The schematic representation of the four state model is:

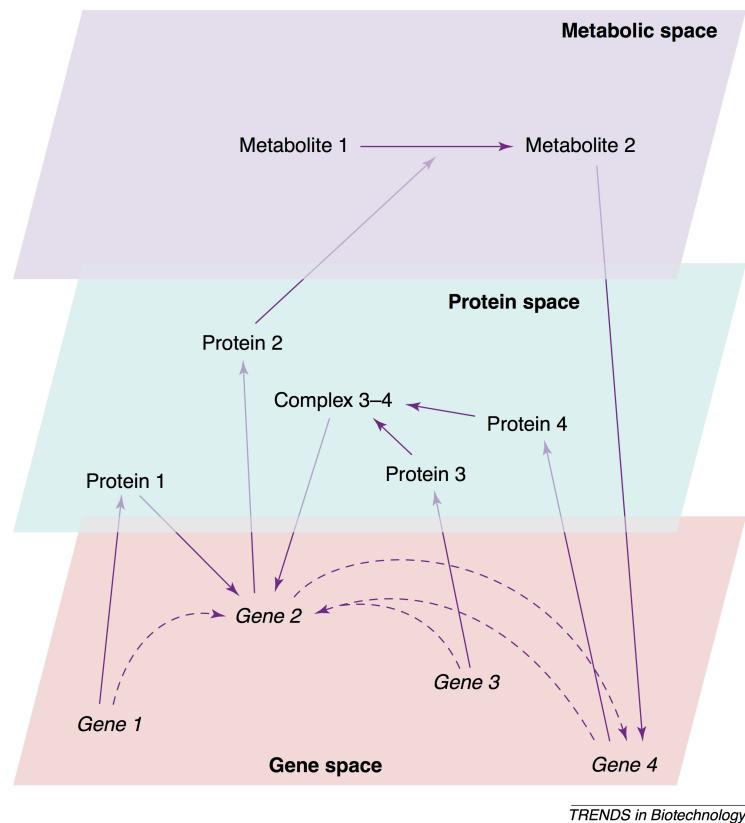


- (i) What do  $K_2$  and  $K_3$  represent in the sketch above? (2 marks)
- (ii) Suppose the above scheme is used to model the regulation of the *lac* operon in *E.coli* where A represents the enhancer (CRP-cAMP) and B represents the repressor. If *E. coli* is grown in a medium high in both glucose and lactose, how are the concentrations of A and B affected? Why? (4 marks)

# MUCH LARGER SYSTEMS - 'OMICs'



# GENE SPACE



See: Brazhnik et al. (2002) 'Gene networks - how to put the function in genomics' (on Canvas)

# TRANSCRIPTOMICS

- A subfield of *functional genomics*
  - Functional genomics: study of how genes and intergenic regions contribute to biological function
- The focus is on *gene expression*
  - In particular, via *measuring mRNA* (the transcripts)

See: Lowe et al. (2017) 'Transcriptomics technologies' (on Canvas)

# EXPRESSION ANALYSIS

- *Microarrays*
  - Mature technology
  - Relatively well-established data analysis methods
- *RNA-seq*
  - Newer technology, rapidly overtaking microarrays
  - Less standardisation of analysis methods
  - Much more computationally/storage intensive

But: *microarrays still relevant and useful*: we will consider  
these (easier and better understood)