### Biochemical Processes

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### Genetic and Signaling Networks
- Control metabolic processes

**Multilevel system**
Level 1 regulators control the activity/concentration of enzymes
Level 2 regulators control the activity/concentration of level 1 regulators, … etc.
DNA transcription

RNA polymerase (RNAP) and gene

A, C, U, G

mRNA

Ribosome

Nuclease

Protease

Shea & Ackers mechanism

- R = RNA polymerase, P = DNA promoter, A = protein
  
  \[ R + P \rightleftharpoons RP_c \rightarrow RP_o \rightarrow R + P + A \]

- \( RP_c \), the closed complex, is in equilibrium with R and P with equilibrium constant \( K \)

- The rate of production of a protein, \( v \), is proportional to \( K \)

- \( K \) is a function of concentrations of regulatory proteins \( B, C, \ldots \):

  \[
  \frac{dA}{dt} = K(B, C, \ldots)v - \gamma A
  \]

  where \( \gamma \) is the natural degradation rate of the protein A

Basic regulatory mechanisms

Activation: increases \( K \), and hence \( v \)

\[
\frac{\partial K}{\partial B} > 0
\]

Repression: decreases \( K \), and hence \( v \)

\[
\frac{\partial K}{\partial B} < 0
\]
Additional regulatory mechanisms

- control of DNA accessibility – chromatin remodeling
- control of mRNA accessibility and lifetime – miRNA, siRNA, degradation
- control of protein lifetime – ubiquitination

Examples of regulatory networks

Switches

- systems with multiple equilibrium states
- logical control, computation, signal integration, memory

Controls

- systems with nonlinear input-output relation
- continuous adjustment: feedback and feed-forward loops

Oscillators

- systems with limit cycles
- periodic transitions between states: synchronization, carry signal

Amplitude filters

- amplify signals of intermediate strength: autoregulation

Noise filters or amplifiers

- regulation using noisy components

Fundamental question – Can every network be decomposed into elements?
Mathematical description

Many alternative models available.

*Variables:* DNA, mRNA, protein, cofactor abundances  
  – continuous/discrete,  
  – spatially homogeneous/inhomogeneous

*Influences:*  
  – relational/dynamical

*Dynamics:*  
  – continuous in time/discrete in time  
  – deterministic/stochastic/delayed

**Cons**

- Multitude of levels of description available – difficult to gauge the correct amount of detail needed
- Lack of information about the parameters of the system
- Lack of experimental data for quantitative comparison of models and data
- Qualitative evaluation of models is subjective

**Pros**

- Amount of data is growing exponentially
- Time resolved in situ measurements possible
- Opportunity to do interesting and applicable mathematics