Summary Lecture 3

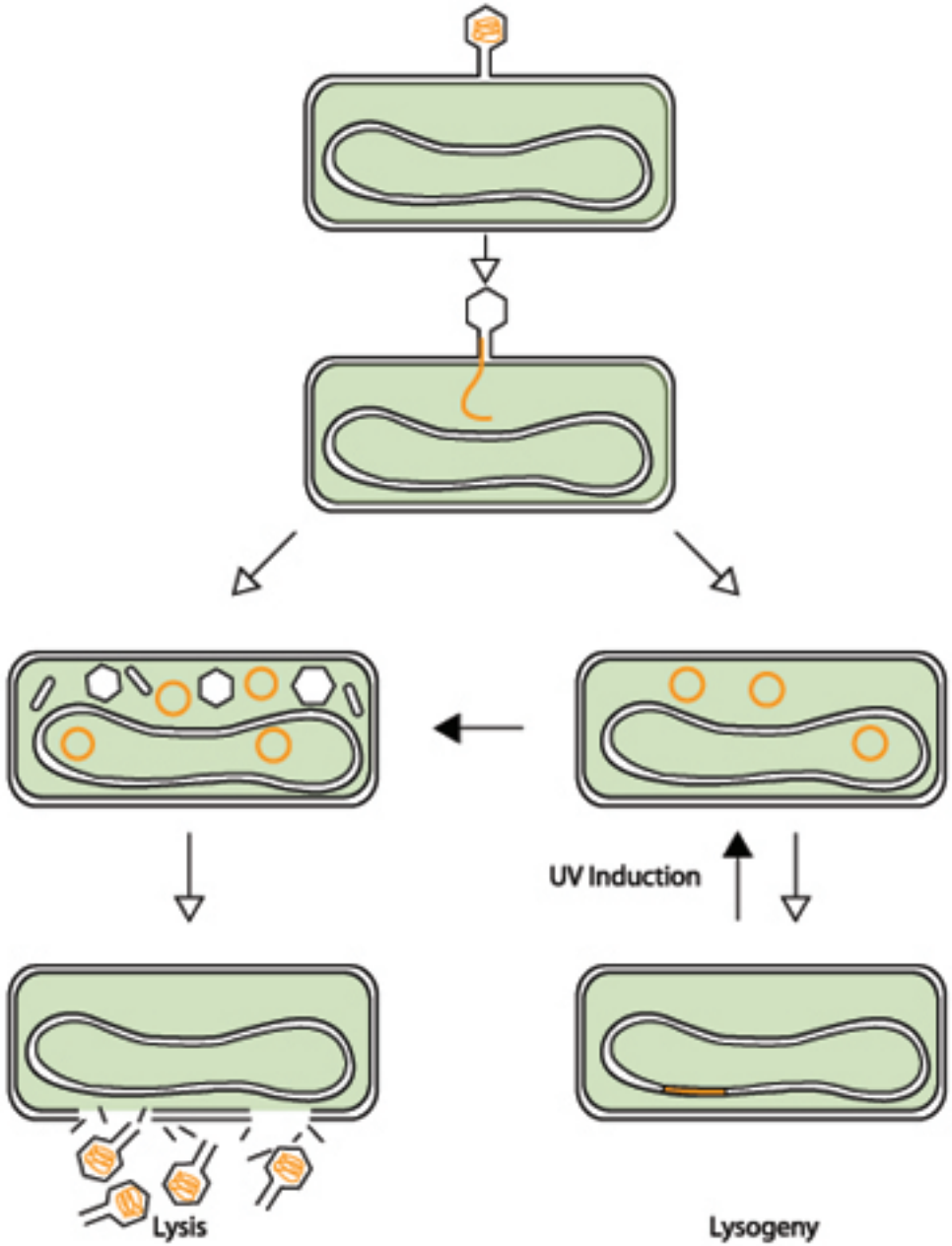
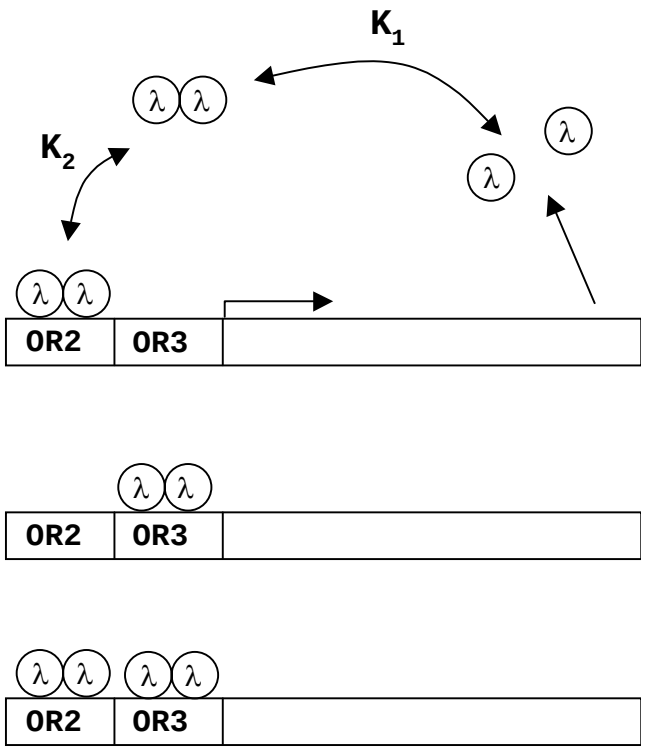


Image by MIT OCW.

L4: Cooperativity & introduction λ phage model

λ phage model (Hasty et al.) as example for applying mass action law.



most important step in modeling !!

$$2X \underset{}{\overset{K_1}{\longleftrightarrow}} X_2$$

$$D + X_2 \overset{K_2}{\longleftrightarrow} DX_2$$

$$D + X_2 \overset{K_3}{\longleftrightarrow} DX_2^*$$

$$DX_2 + X_2 \overset{K_4}{\longleftrightarrow} DX_2DX_2$$

} fast

$$DX_2 + P \xrightarrow{k_t} DX_2 + P + nX$$

$$X \xrightarrow{k_d} A$$

} slow

most important step in modeling !!

biology → **math**

$$2X \xleftrightarrow{K_1} X_2$$

$$D + X_2 \xleftrightarrow{K_2} DX_2$$

$$D + X_2 \xleftrightarrow{K_3} DX_2^*$$

$$DX_2 + X_2 \xleftrightarrow{K_4} DX_2DX_2$$

$$DX_2 + P \xrightarrow{k_t} DX_2 + P + nX$$

$$X \xrightarrow{k_d} A$$

mass action

$$\frac{dx}{dt} = \frac{\alpha x^2}{1 + (1+\sigma_1)x^2 + \sigma_2 x^4} - \gamma x + 1$$

$$\sigma_1 = \frac{K_3}{K_2}$$

$$\sigma_2 = \frac{K_4}{K_2}$$

relative binding constants

$$\alpha = \frac{n k_t p_0 d_T}{r}$$

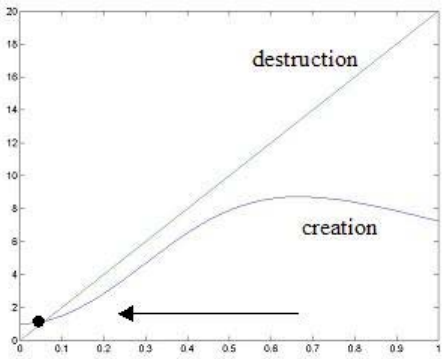
~ synthesis/basal rate

$$\gamma = \frac{k_d}{r\sqrt{K_1 K_2}}$$

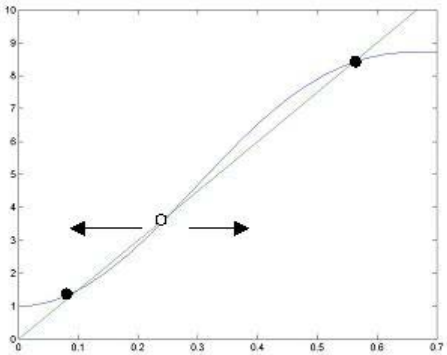
~ degradation/basal rate

choose elegant (dimensionless, relative) variables !

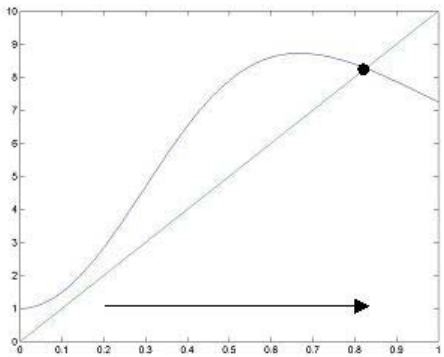
graphical stability analysis



high destruction rate:
one stable low state



medium destruction rate:
two stable states,
one metastable state



low destruction rate:
one stable high state

f(x), g(x)

x

How to experimentally verify these ideas ?

Synthetic Biology

Build your own designed network ‘from scratch’
and test your model

Examples for synthetic genetic switches:

Isaacs *et al.* Prediction and measurement of an autoregulatory genetic module. PNAS **100**, 7714 (2003)

Gardner *et al.* Construction of a genetic toggle switch in Escherichia coli. Nature **403**, 399 (2000)

First a short intro on ‘Genetic Engineering’

Toolbox of the genetic engineer:

1. Restriction enzymes

2. Plasmids

3. PCR (Polymerase Chain Reaction)

4. Fluorescent proteins