

Transcription Network: Basic Concepts

2IF35 Formal Modelling in Cell Biology

Technische Universiteit Eindhoven

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4500 genes, 4000000 proteins

transcription 1 min/gene

translation 2 min/protein

10^4 ribosomes, mRNA lifetime 2–5 min



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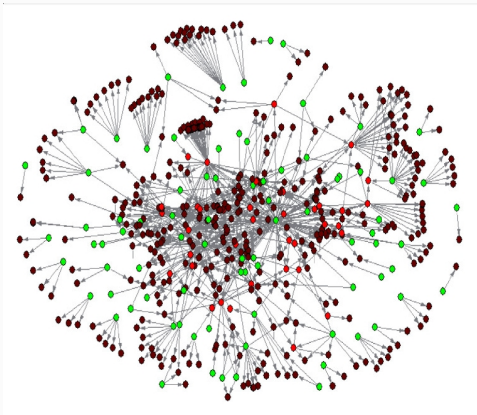
10^4 ribosomes, mRNA lifetime 2–5 min

regulation of protein levels by transcription networks

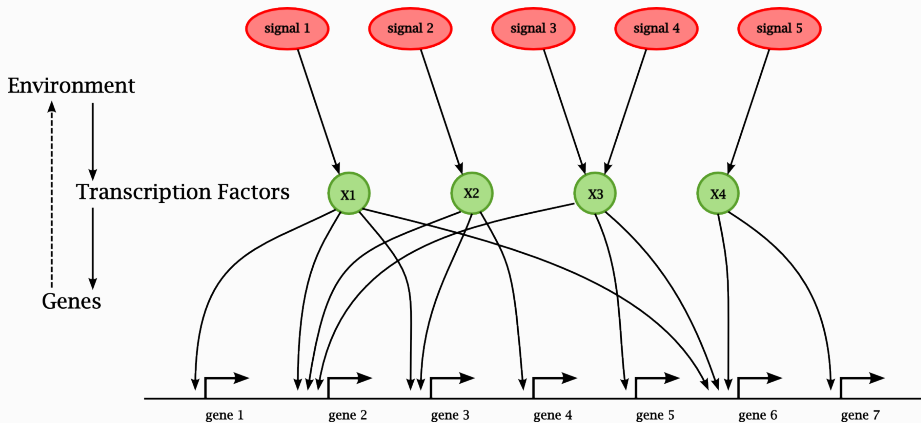
300 transcription factors to represent environment

inactive/active switching of protein in 1–100 μ sec

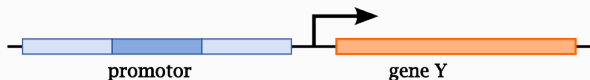
E. coli transcription network



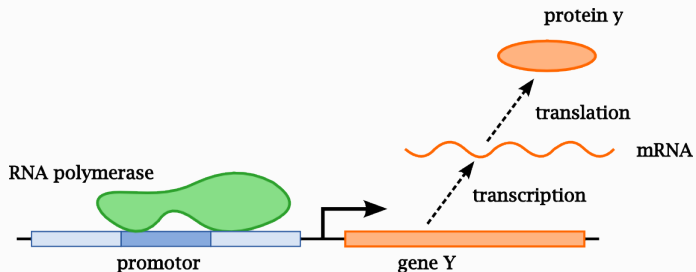
elements of transcription networks



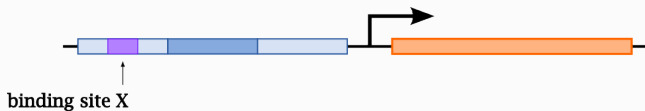
gene transcription regulation (base case)



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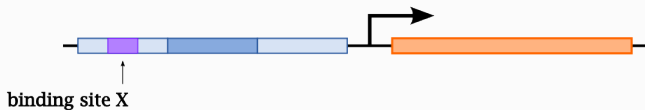


activated gene transcription regulation

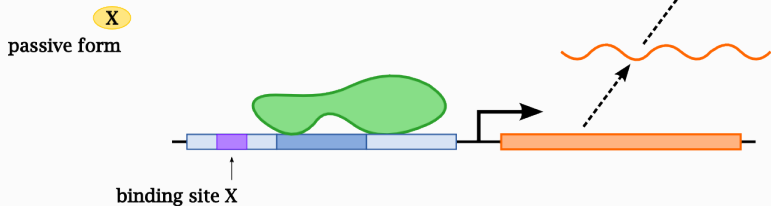


activated gene transcription regulation

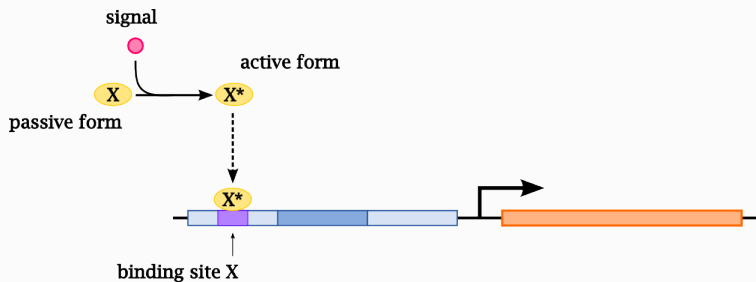
X
passive form



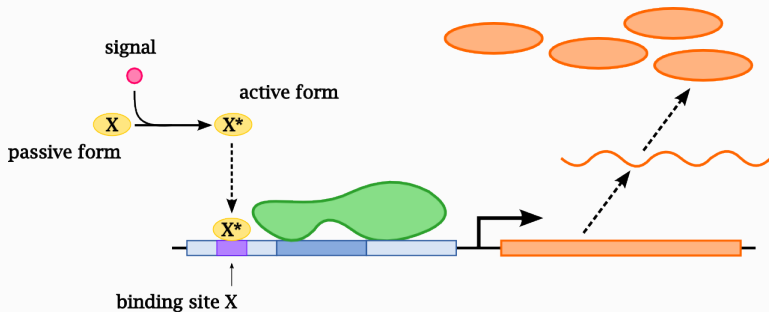
activated gene transcription regulation



activated gene transcription regulation

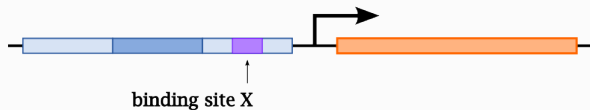


activated gene transcription regulation



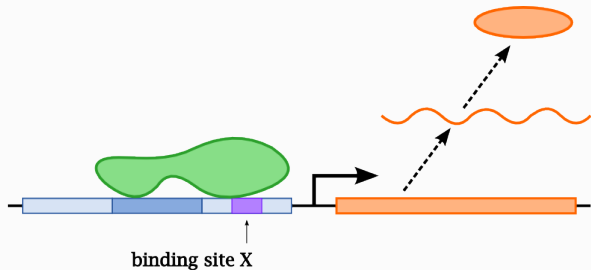
repressed gene transcription regulation

X
passive form

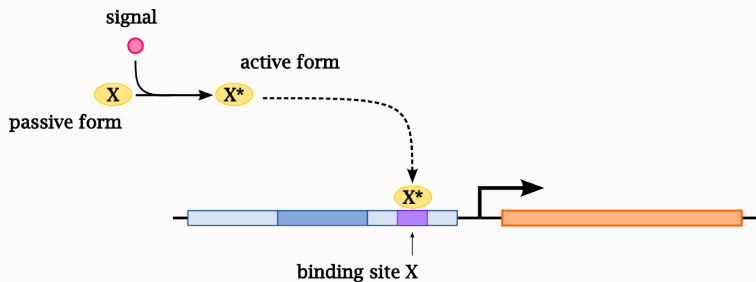


repressed gene transcription regulation

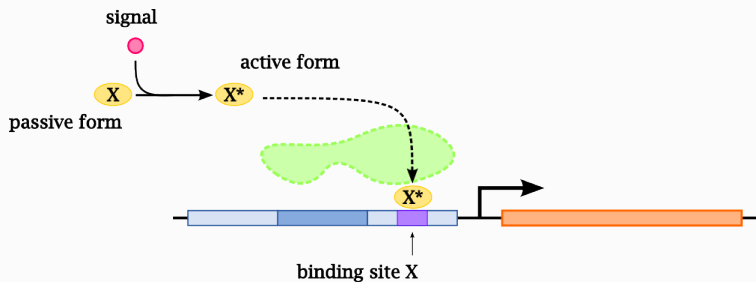
X
passive form



repressed gene transcription regulation



repressed gene transcription regulation



- 60% to 80% activators
- transcription factors mostly positive or mostly negative
- genes can both be activated and repressed

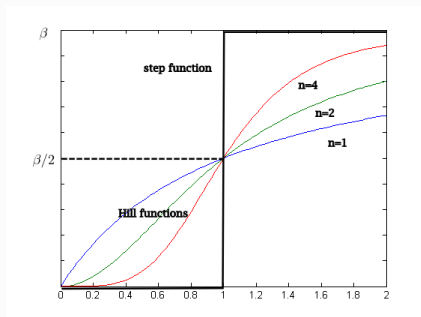
outgoing signs are correlated, incoming signs not

Hill input function for activator

rate of Y -production = $f(X^*)$

Hill input function for activator

rate of Y -production = $f(X^*)$



$$\text{Hill function for activator } f(X^*) = \frac{\beta \cdot (X^*)^n}{K^n + (X^*)^n}$$

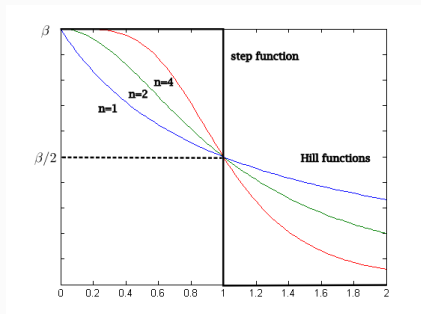
maximal expression level β , activation coefficient K , Hill coefficient n

Hill input function for repressor

rate of Y -production = $f(X^*)$

Hill input function for repressor

rate of Y-production = $f(X^*)$



$$\text{Hill function for repressor } f(X^*) = \frac{\beta \cdot K^n}{K^n + (X^*)^n}$$

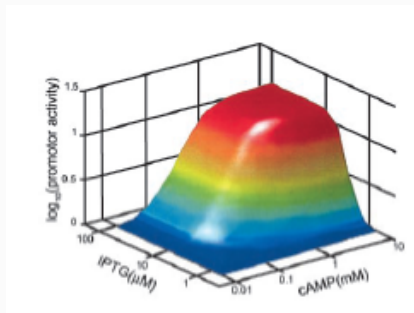
logical approximation

gene **OFF** : $f(X^*) = 0$ vs. gene **ON** : $f(X^*) = 1$

activated transcription $f(X^*) = \beta \cdot \theta(X^* > K)$

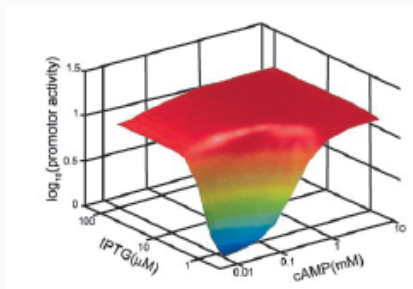
repressed transcription $f(X^*) = \beta \cdot \theta(X^* < K)$

threshold K , step-function θ : **if** *expr* **then** 1 **else** 0 **end**



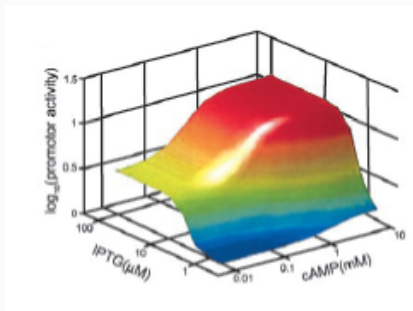
X AND Y

$$f(X^*, Y^*) = \beta \cdot \theta(X^* > K_X) \cdot \theta(Y^* > K_Y)$$



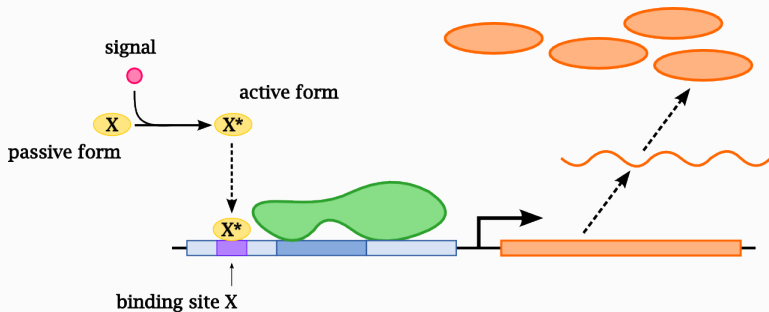
X OR Y

$$f(X^*, Y^*) = \beta \cdot \max\{\theta(X^* > K_X), \theta(Y^* > K_Y)\}$$



other $f(X^*, Y^*)$

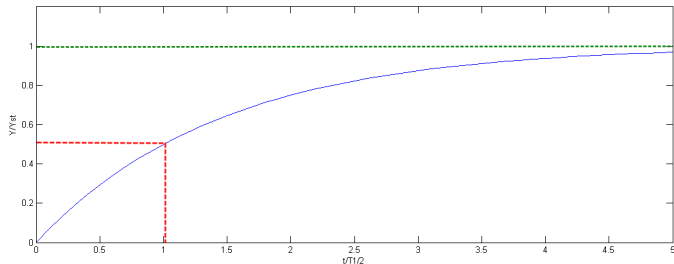
activated gene transcription regulation



“gene X activates gene Y ”

dynamics of simple gene regulation

dynamic equation $\frac{dY}{dt} = \beta - \alpha Y$

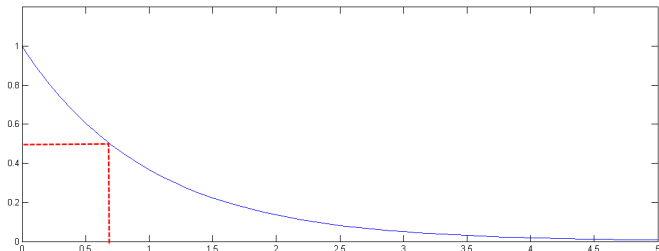


in case of activation $Y(t) = Y_{st} \cdot (1 - e^{-\alpha t})$

steady state $Y_{st} = \frac{\beta}{\alpha}$ response time $T_{\frac{1}{2}} = \frac{\log 2}{\alpha}$

dynamics of simple gene regulation (cont.)

dynamic equation $\frac{dY}{dt} = -\alpha Y$



on case of decay $Y(t) = Y_{st} \cdot e^{-\alpha t}$

steady state $Y_{st} = 0$ response time $T_{\frac{1}{2}} = \frac{\log 2}{\alpha}$