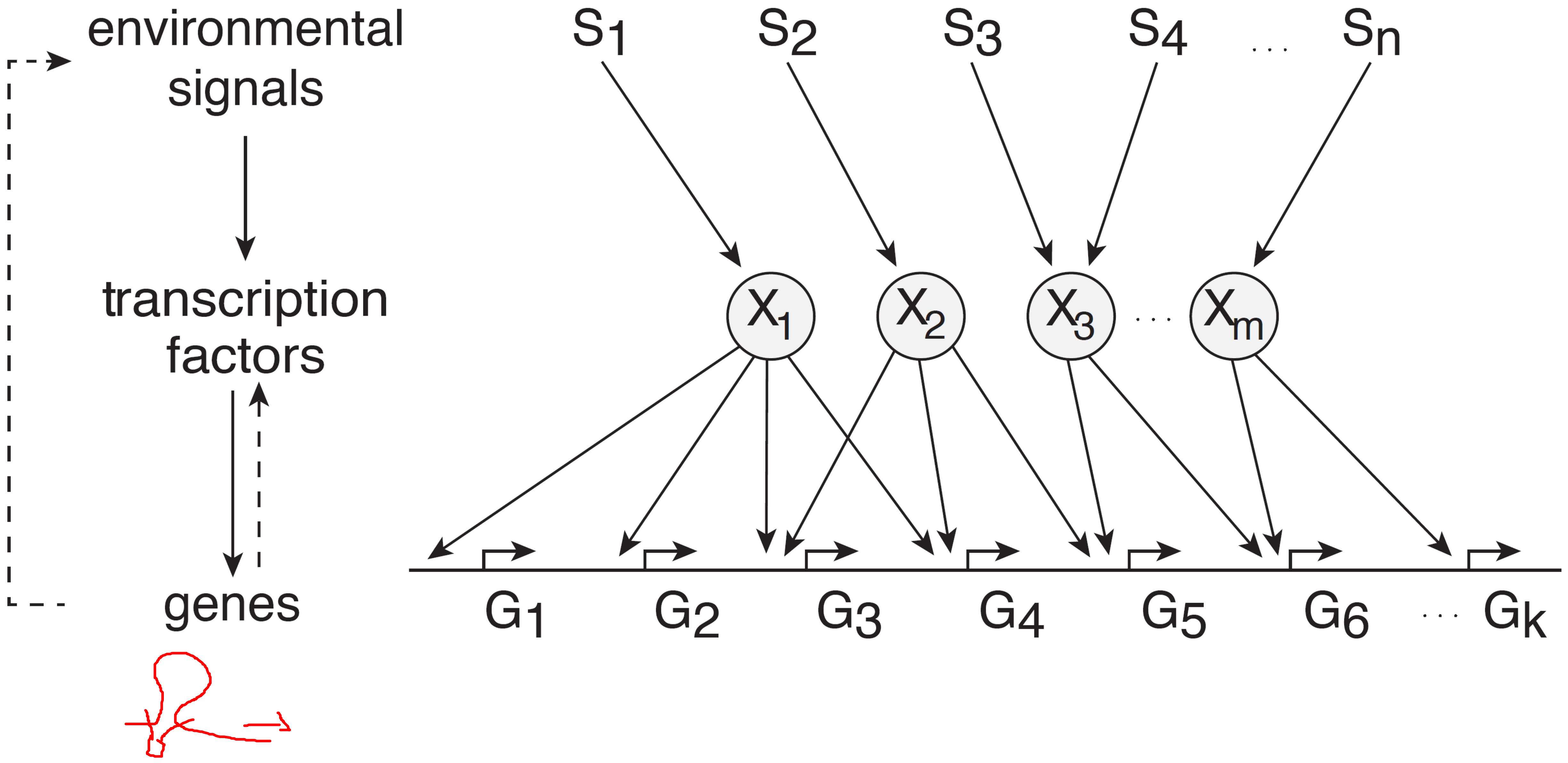
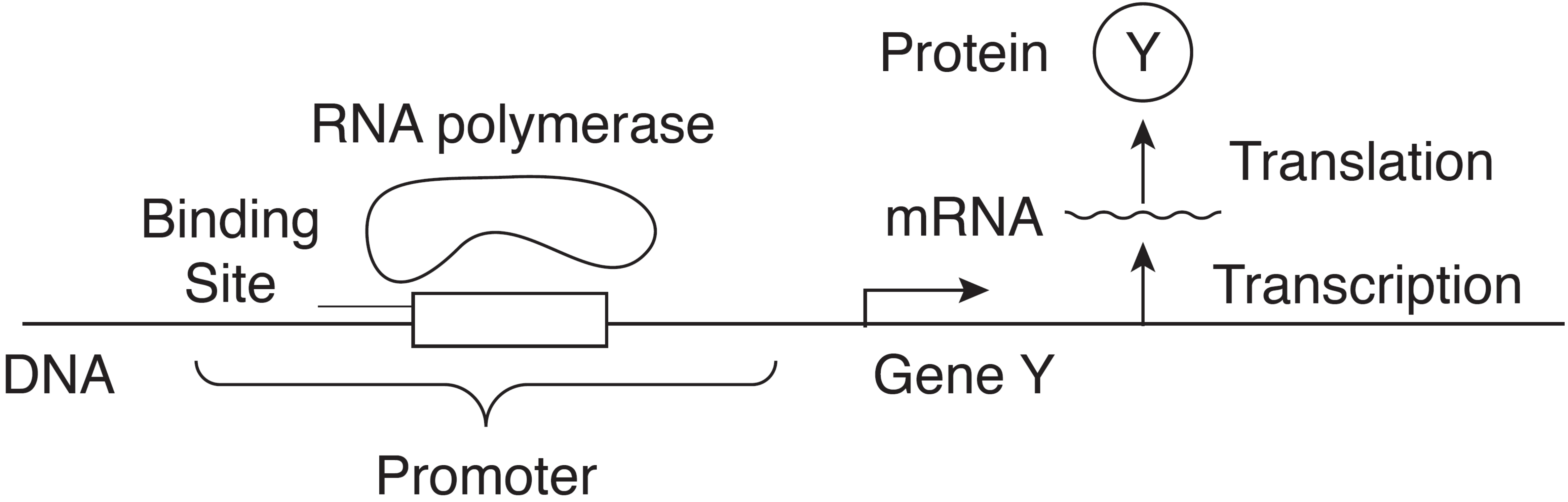
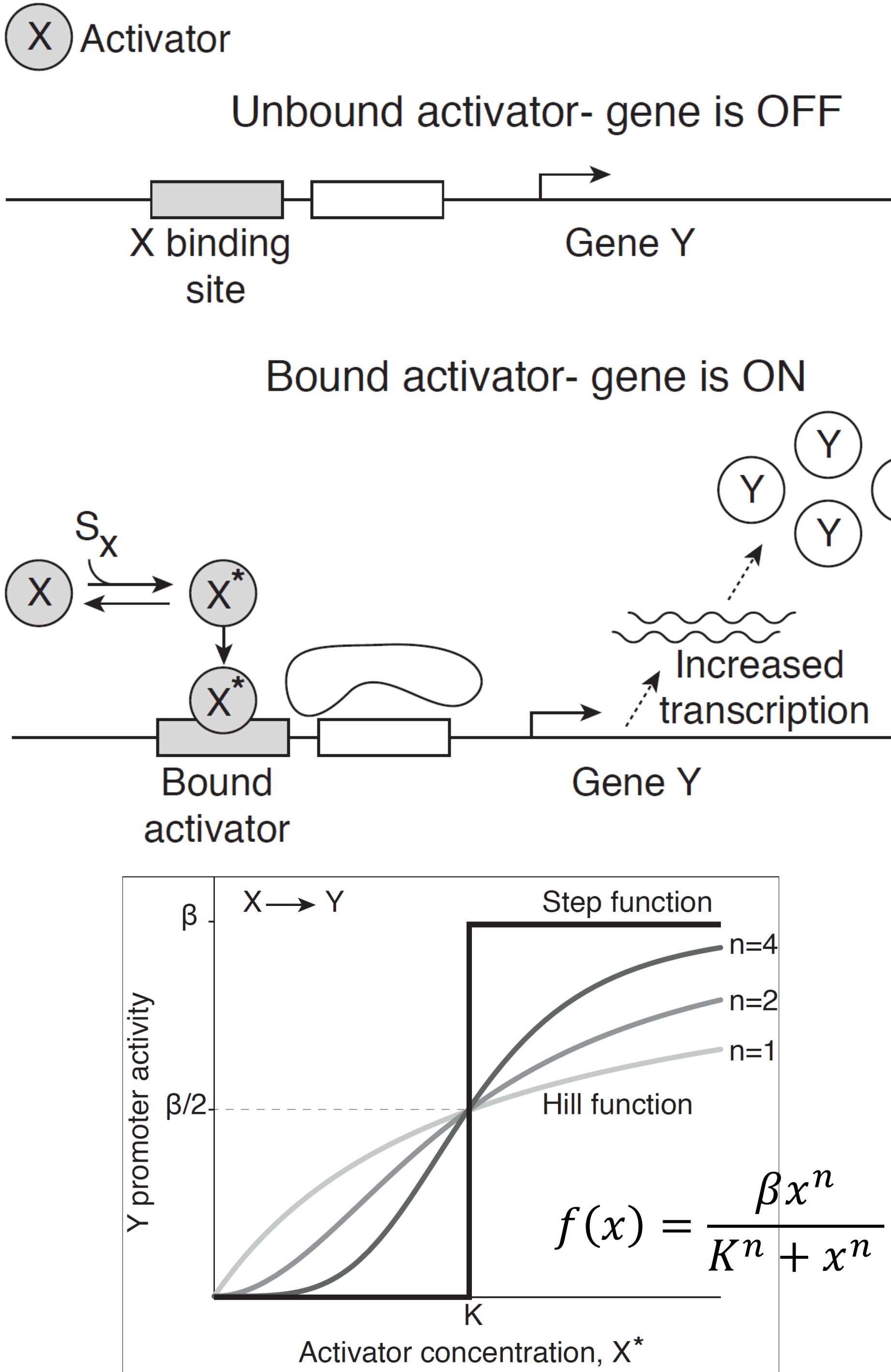
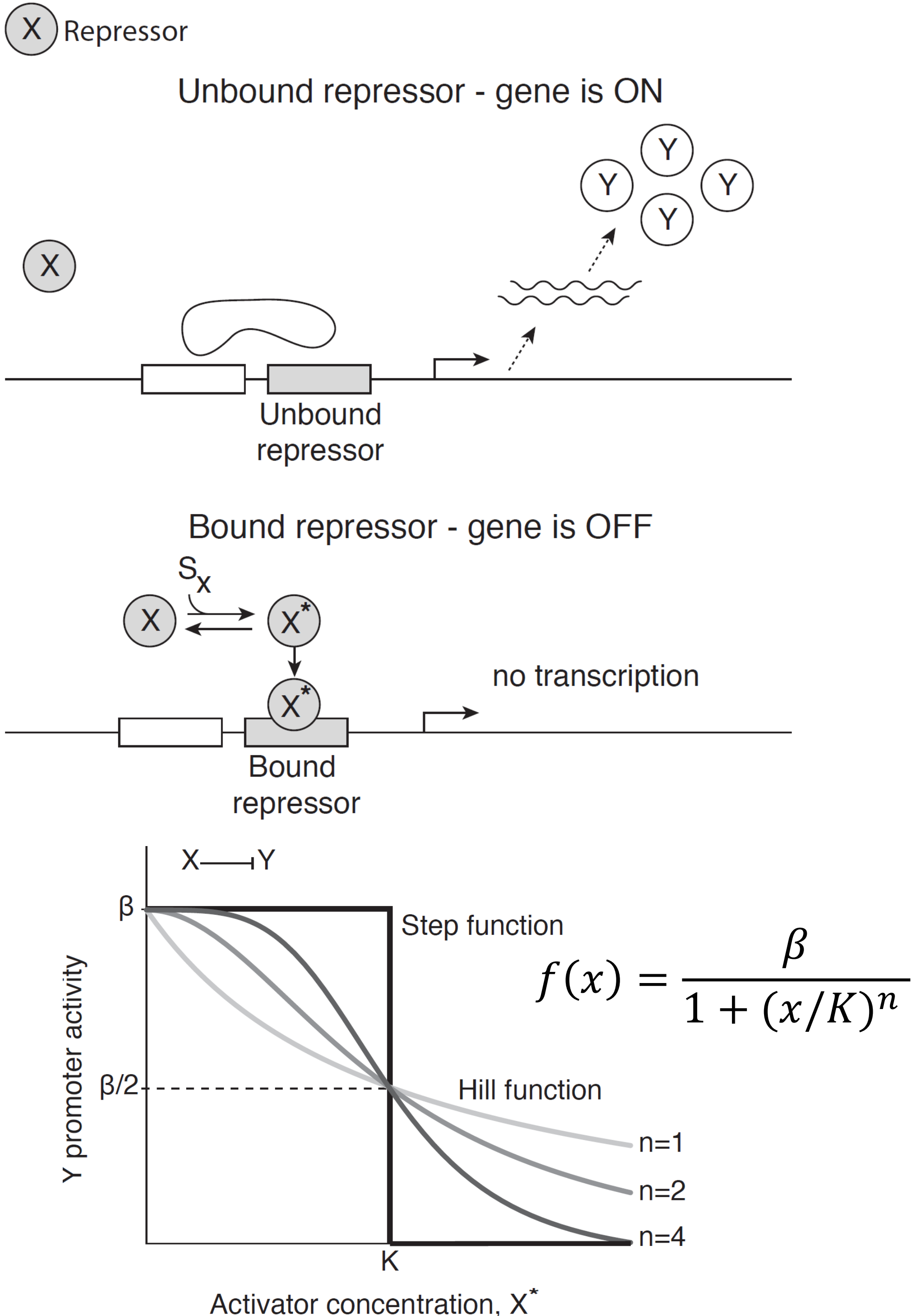
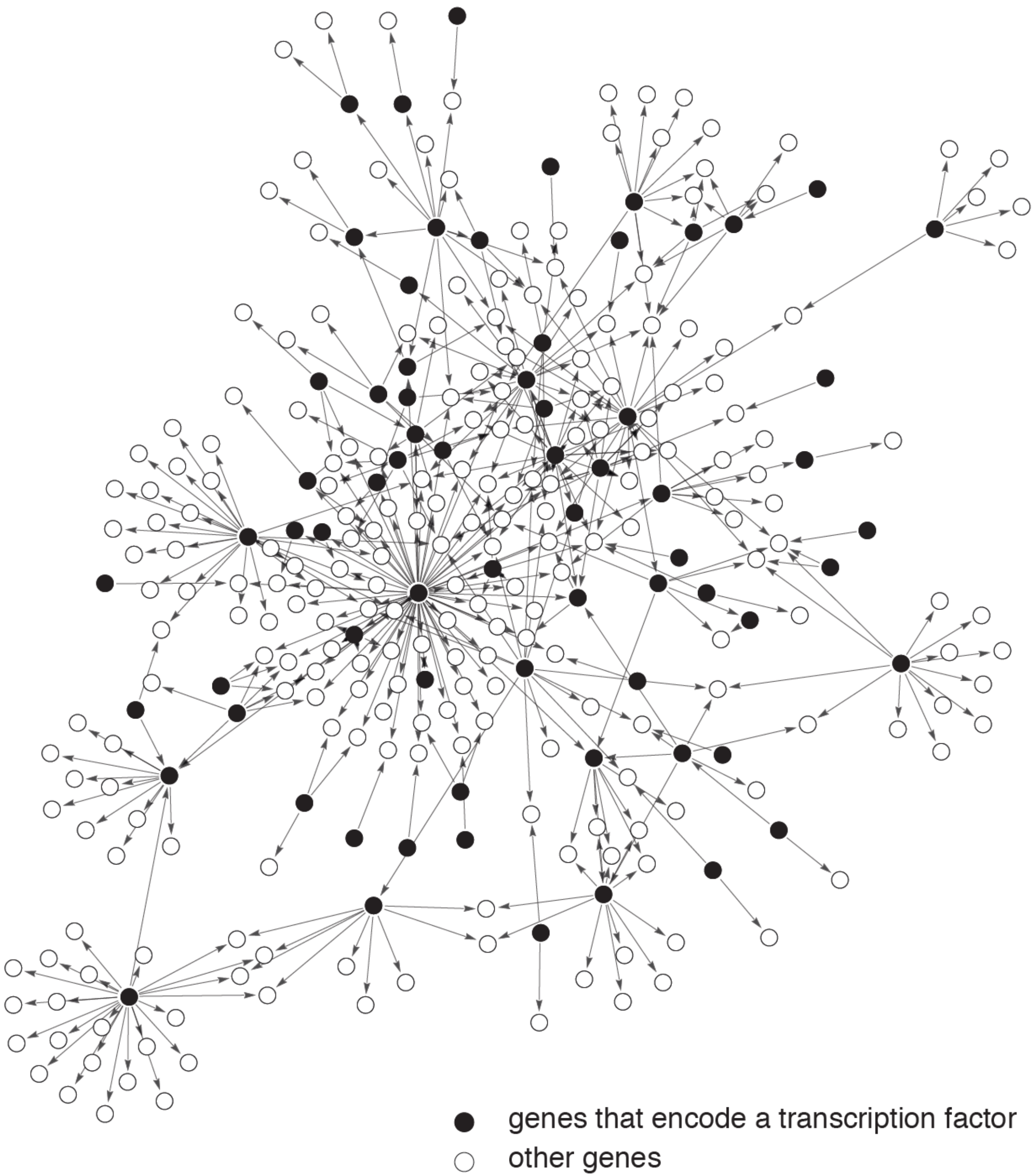
Motives in transcription networks: supressors, and why they are so useful


environmental signals
transcription factors
genes
S_1
S_2
S_3
S_4
...
S_n
X_1
X_2
X_3
...
X_m
G_1
G_2
G_3
G_4
G_5
G_6
...
G_k


Protein
Y
RNA polymerase
Translation
Binding
Site
mRNA
Transcription
DNA
Gene Y
Promoter

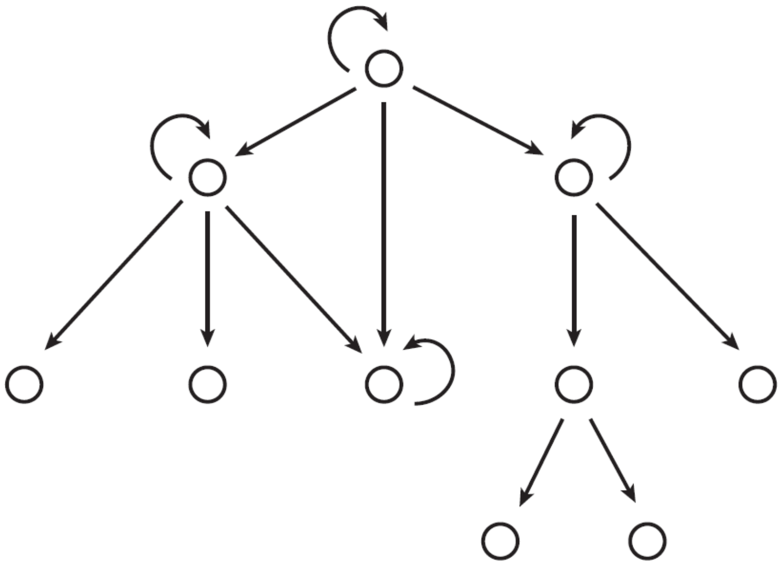

X Activator
Unbound activator- gene is OFF
X binding site
Gene Y
Bound activator- gene is ON
S_X
X
X*
Y
Increased transcription
Bound activator
Gene Y
X → Y
Step function
β
n=4
n=2
n=1
β/2
Hill function
Y promoter activity
$f(x) = \frac{\beta x^n}{K^n + x^n}$
K
Activator concentration, X*


X Repressor
Unbound repressor - gene is ON
Y
X
Unbound repressor
Bound repressor - gene is OFF
S_X
X*
no transcription
Bound repressor
X ⊣ Y
β
Step function
$f(x) = \frac{\beta}{1 + (x/K)^n}$
Y promoter activity
β/2
Hill function
n=1
n=2
n=4
K
Activator concentration, X*



genes that encode a transcription factor
other genes

‘Real’ network



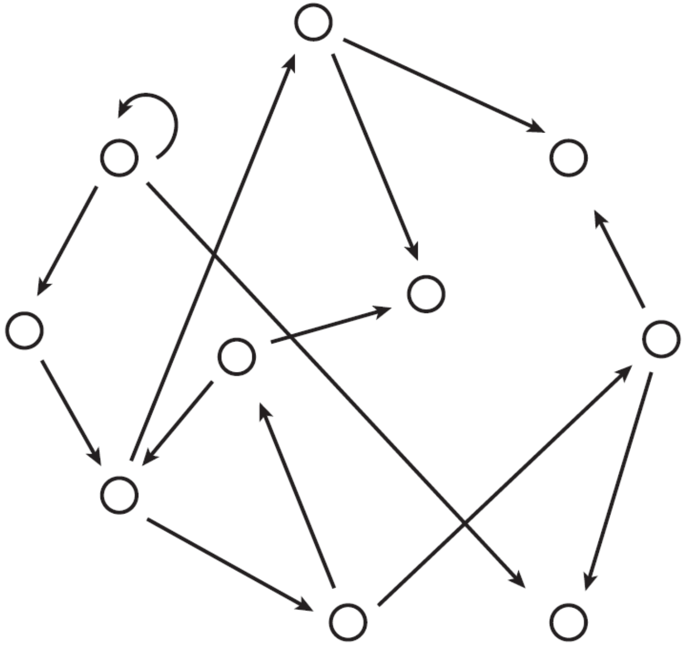
N=10 nodes

A=14 arrows

N_{self}=4 self arrows

Randomised network (Erdos - Renyi)

$N \cdot (N-1) + N$



N=10 nodes

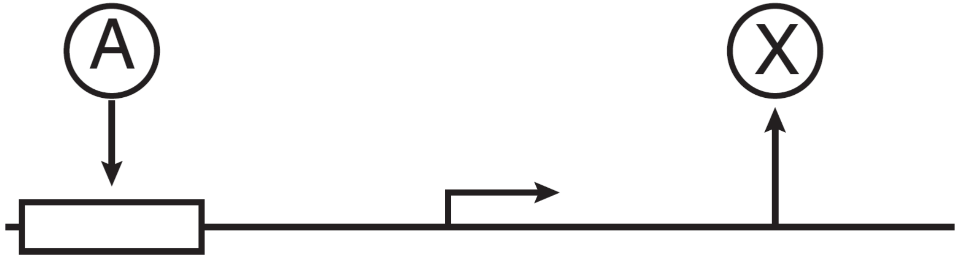
A=14 arrows

N_{self}=1 self arrow

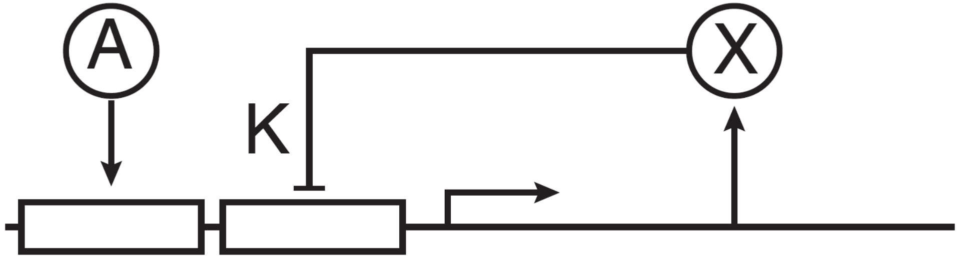
Possible arrangements: N^2

Looking at: Self-Edges, negative are found in 34 out of 40 occurrences in e.coli…. A chance?

Simple regulation



Negative autoregulation



$$p_{self} = \frac{1}{N} \quad (random\ network)$$

$$< N_{self} > \approx E\ p_{self} = E/N$$

$$\sigma \approx \sqrt{\frac{E}{N}}$$

In bacteria as shown we have
N = 424, E=519

Hence, we expect only 1 ± 1 self nodes -> not by chance, buy is a system.

Are negative autoregulation motives useful?

$$\frac{dX}{dt} = f(X) - \alpha X$$

$$f(x) = \frac{\beta}{1 + (x/K)^n}$$

$$f(X) = \beta\, \Theta(X < \mathrm{K})$$

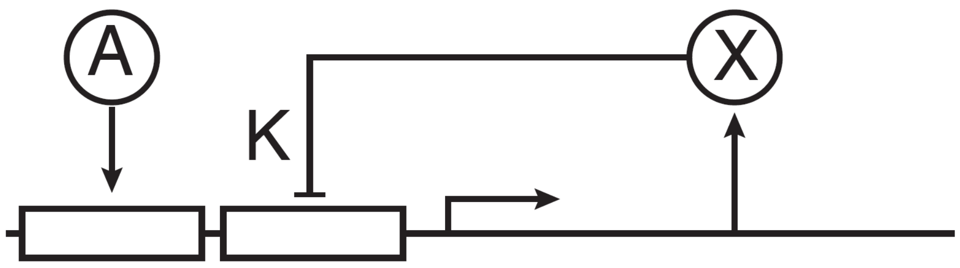
$$\frac{dX}{dt} = \beta - \alpha X$$

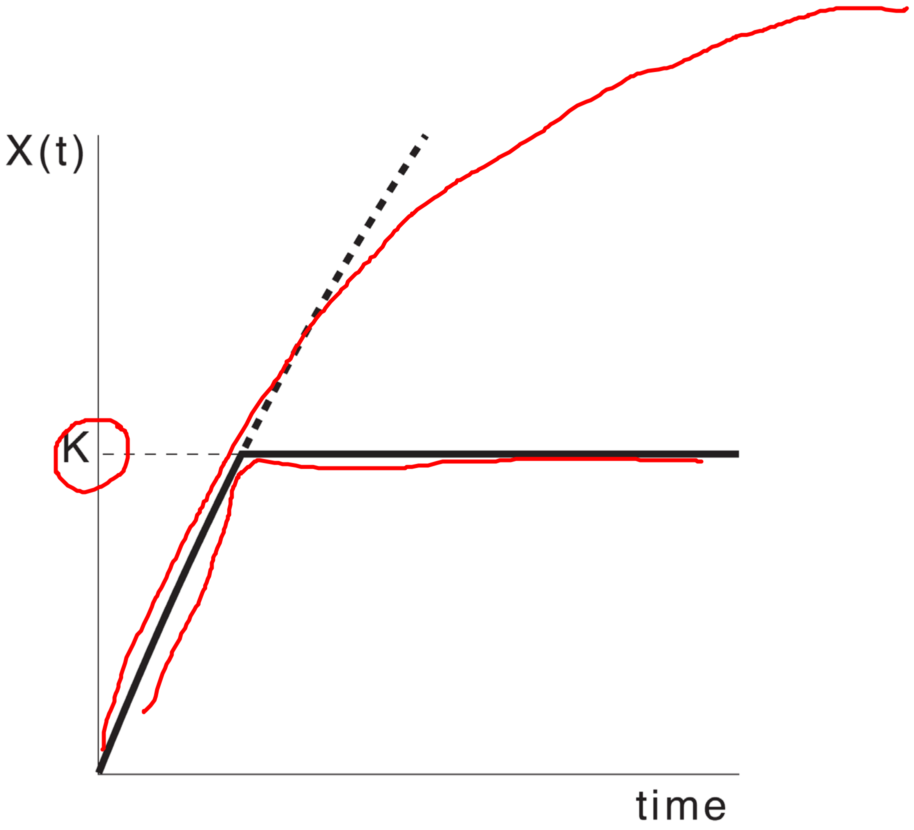
initially $X(t) \approx \beta t\ (linear\ regime, \alpha X\ small)$

Once at K $X_{st} = K$

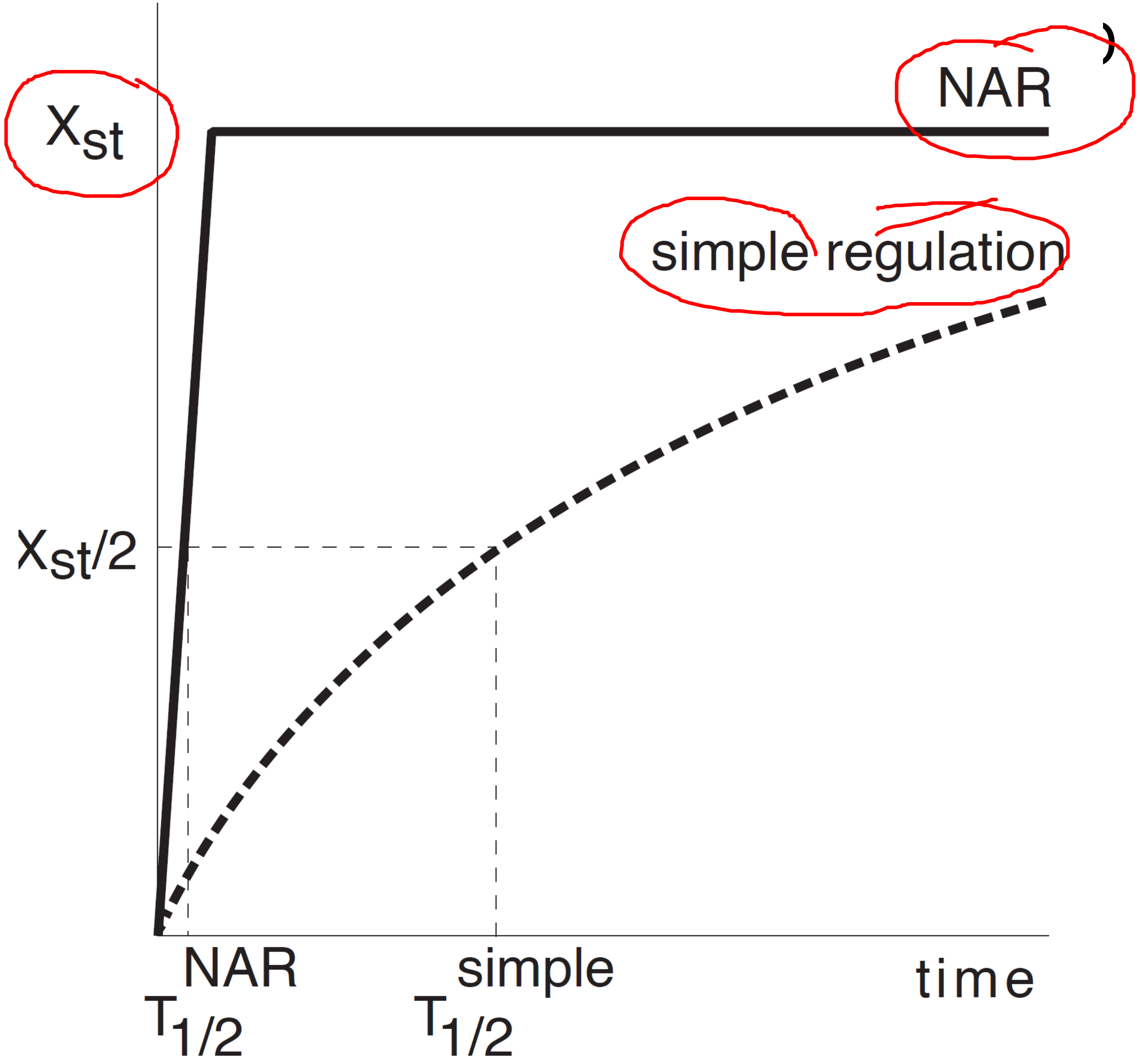
Allows rapid increase and then production stop at desired concentration

Negative autoregulation





When using a simple expression, the final
the production rate



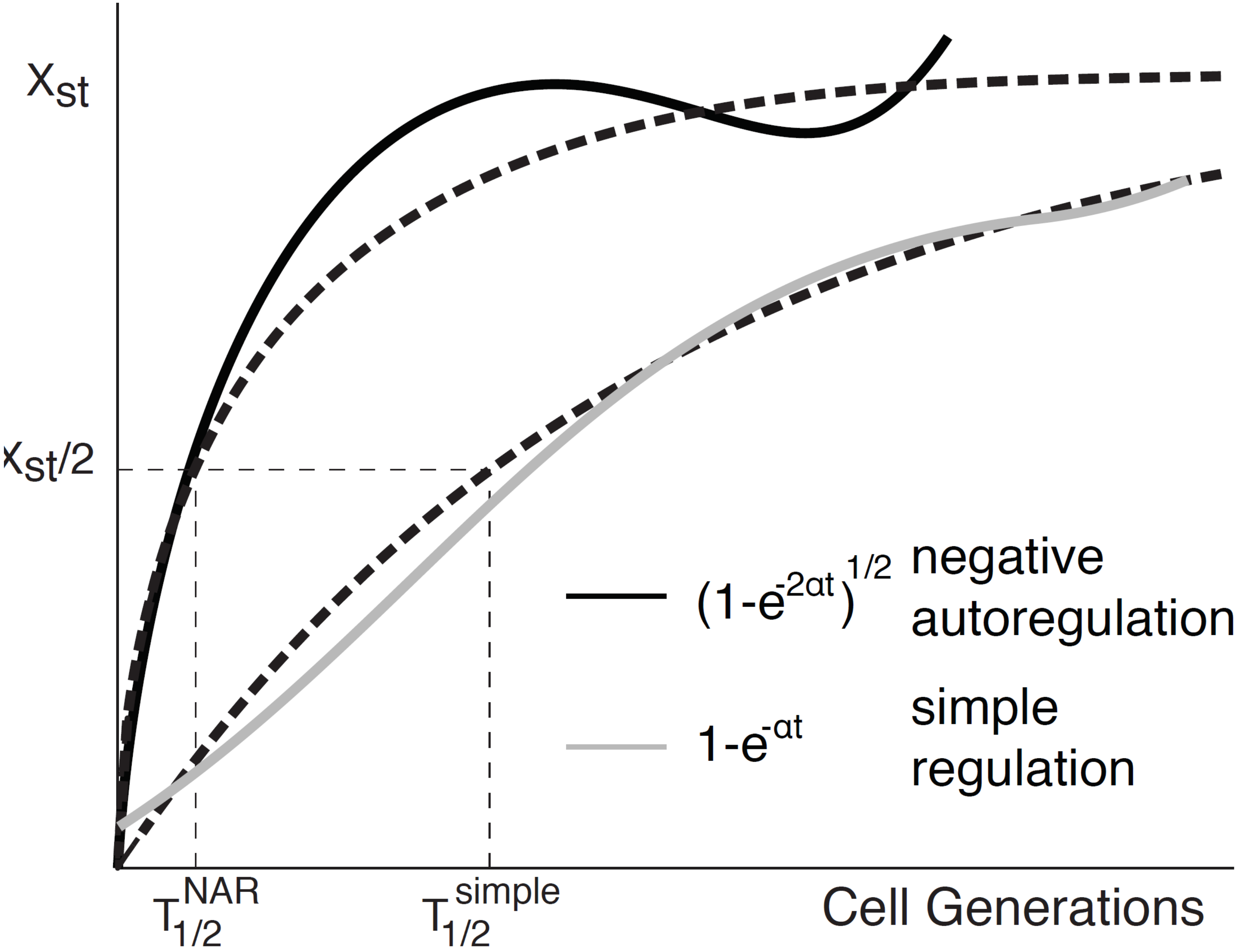
Recall solution to simple network:

$$\boxed{\frac{dX}{dt} = \beta - \alpha X}$$

$$\frac{dX}{dt} X(t) = \frac{\beta}{\alpha} - \frac{c_0}{\alpha} * \exp(-t\alpha)$$

Fast, means large alpha, but then to control the concentration also beta must be larger: -> huge waste!!!

Additionally, more robust against fluctuations in beta by overall conditions



X_{st}
$X_{st}/2$
$T_{1/2}^{NAR}$
$T_{1/2}^{simple}$
Cell Generations
$(1-e^{-2\alpha t})^{1/2}$
negative autoregulation
$1-e^{-\alpha t}$
simple regulation