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**Abstract**

# 1 Notation

$R$: transcription factor (TF)
$O$: free operator
Suppose that the operator has 2 binding sites.
$RO$: 1 TF bound to the operator
$R_2O$: 2 TFs bound to the operator
$O_T$: total number of free and occupied operators
$R_T$: total number of free and bound TFs
$M$: mRNA

# 2 Cooperative TF binding

Assume that the operator has two binding sites and TFs bind to them cooperatively.
Assume that $R_T \gg O_T$ (much more TFs than operators) and $R \approx R_T$ (most TFs are free).

$$\mathrm{R} + \mathrm{O} \underset{k^1_-}{\overset{k^1_+}{\rightleftharpoons}} \mathrm{RO} \tag{1}$$

$$\mathrm{R} + \mathrm{RO} \underset{k^2_-}{\overset{k^2_+}{\rightleftharpoons}} \mathrm{R_2O} \tag{2}$$

Detailed balance:

$$R \cdot O \cdot k^1_+ = RO \cdot k^1_- \tag{3}$$

$$R \cdot RO \cdot k^2_+ = R_2O \cdot k^2_- \tag{4}$$

Total number of operators:

$$O_T = O + RO + R_2O \tag{5}$$

Using Eqs. (3) and (2),

$$O_T = O + R \cdot O \cdot \frac{k_+^1}{k_-^1} + R \cdot RO \cdot \frac{k_+^2}{k_-^2} \tag{6}$$

$$= O + R \cdot O \cdot \frac{k_+^1}{k_-^1} + R \cdot R \cdot O \cdot \frac{k_+^2}{k_-^2} \tag{7}$$

$$= O(1 + bR + cR^2) \tag{8}$$

Transcription:

$$\mathrm{O} \xrightarrow{k_m} \mathrm{M} + \mathrm{O} \tag{9}$$

$$\mathrm{M} \xrightarrow{k_d} \emptyset \tag{10}$$

Equations of kinetics for transcription:

$$\frac{dM}{dt} = k_m O - k_d M \tag{11}$$

$$= k_m \frac{O_T}{1 + bR + cR^2} - k_d M \tag{12}$$

$$= k_m O_T h(R) - k_d M \tag{13}$$

Transfer function:

$$h(R) = \frac{1}{1 + bR + cR^2} \tag{14}$$

When TF binding is strongly cooperative, then $c \gg b$ and

$$h(R) = \frac{1}{1 + cR^2} \tag{15}$$

# 3 Noncooperative TF binding

Assume that the operator has 2 identical binding sites and TFs bind to them noncooperatively.

$$\mathrm{R} + \mathrm{O} \underset{k_-}{\overset{2k_+}{\rightleftharpoons}} \mathrm{RO} \tag{16}$$

$$\mathrm{R} + \mathrm{RO} \underset{2k_-}{\overset{k_+}{\rightleftharpoons}} \mathrm{R_2O} \tag{17}$$

In (3), the association rate is 2 times less than in (3) because there is only 1 free binding site left on the operator. Dissociation rates are calculated analogously.

Substituting $k_+^1 = 2k_+$, $k_+^2 = k_+$, $k_-^1 = k_-$, and $k_-^2 = 2k_-$ into the Eq. 6, we get the transfer function:

$$h(R) = \frac{1}{(1 + cR)^2} \tag{18}$$