Supplementary Material

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A novel equation for cooperativity of the allosteric state function

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Derivation of the equation for the Hill coefficient of the state function. By analogy with $\bar{Y}$, the Hill coefficient for $\bar{R}$, here represented by n'_H, can be defined as:

$$n'_{\mathrm{H}} = \frac{d\,log\left(\frac{\bar{R}}{1-\bar{R}}\right)}{d\,log\,\alpha} = \frac{\alpha}{\bar{R}\,(1-\bar{R})}\left(\frac{d\,\bar{R}}{d\,\alpha}\right) \qquad \text{(S1)}$$

where $\bar{R}$ is defined by the Monod-Wyman-Changeux equation for an oligomer with n subunits:[1]

$$\bar{R} = \frac{(1+\alpha)^n}{(1+\alpha)^n + L(1+c\alpha)^n} \qquad \text{(S2)}$$

In order to replace the terms in the denominator on the right side of equation (S1), the term $1-\bar{R}$ is recast as:

$$1-\bar{R} = \frac{(1+\alpha)^n + L(1+c\alpha)^n - (1+\alpha)^n}{(1+\alpha)^n + L(1+c\alpha)^n} = \frac{L(1+c\alpha)^n}{(1+\alpha)^n + L(1+c\alpha)^n} \qquad \text{(S3)}$$

Combining terms in equations (S2) and (S3) for $\bar{R}\,(1-\bar{R})$ gives:

$$\bar{R}\,(1-\bar{R}) = \frac{(1+\alpha)^n\,L(1+c\alpha)^n}{[(1+\alpha)^n + L(1+c\alpha)^n]^2} \qquad \text{(S4)}$$

For the term $\frac{d\,\bar{R}}{d\,\alpha}$, use is made of the equation previously reported:[2]

$$\frac{d\,\bar{R}}{d\,\alpha} = \frac{nL\left(\frac{1+c\alpha}{1+\alpha}\right)^{n-1}(1-c)}{\left[1+L\left(\frac{1+c\alpha}{1+\alpha}\right)^n\right]^2(1+\alpha)^2} \qquad \text{(S5)}$$

Incorporating the terms in equations (S4) and (S5) into equation (S1) yields the following equation for n'_{H}:

$$n'_H = \frac{\alpha[(1+\alpha)^n + L(1+c\alpha)^n]^2}{(1+\alpha)^n\,L(1+c\alpha)^n}\,\frac{nL\left(\frac{1+c\alpha}{1+\alpha}\right)^{n-1}(1-c)}{\left[1+L\left(\frac{1+c\alpha}{1+\alpha}\right)^n\right]^2(1+\alpha)^2} \qquad \text{(S6)}$$

Equation (S6) can be rearranged to a form that facilitates cancellation of terms:

$$n'_{\mathrm{H}} = \frac{n(1-c)L(1+c\alpha)^{n-1}}{L(1+c\alpha)^{n}} \frac{\alpha[(1+\alpha)^{n} + L(1+c\alpha)^{n}]^{2}}{[(1+\alpha)^{n}+L(1+c\alpha)^{n}]^{2}} \frac{(1+\alpha)^{n}\,(1+\alpha)^{n}}{(1+\alpha)^{n-1}(1+\alpha)^{2}(1+\alpha)^{n}} \quad \text{(S7)}$$

Upon cancellation of identical terms in the numerator and the denominator, the simple equation (4) in the main text for the Hill coefficient of $\bar{R}$ is obtained:

$$n'_{\mathrm{H}} = \frac{n(1-c)}{(1+c\alpha)} \frac{\alpha}{(1+\alpha)} \quad \text{(S8)}$$

Reference:

1. Monod, J., Wyman, J. & Changeux, J.-P. (1965). On the nature of allosteric transitions: A plausible model. *J. Mol. Biol.* **12**, 88-118.
2. Edelstein, S. J., Stefan, M. I. & Le Novere, N. (2010). Ligand depletion in vivo modulates the dynamic range and cooperativity of signal transduction. *PLoS One* **5**, e8449.