Supplemental Material

Derivation of the Equation for Binding of EGF to a System Containing EGF Receptors and ErbB2

The model for EGF binding is shown in Figure 1B. For this model, $\bar{Y}$, the factional saturation of the EGF receptor, is given by the equation:

$$\bar{Y} = \frac{K_{11}[\mathrm{EGF}] + K_{21}L_{20}M_f[\mathrm{EGF}] + 2K_{22}K_{21}L_{20}M_f[\mathrm{EGF}]^2 + H_{21}J_{20}N_f[\mathrm{EGF}]}{1 + K_{11}[\mathrm{EGF}] + 2L_{20}M_f(1 + K_{21}[\mathrm{EGF}] + K_{22}K_{21}[\mathrm{EGF}]^2) + J_{20}N_f(1 + H_{21}[\mathrm{EGF}])} \quad \text{(Eq. 1)}$$

Here, the equilibrium association constants, L_{20} and J_{20} are as described in Figure 1, as are the binding constants, K_{11}, K_{21}, K_{22}, and H_{21}. M_f is the concentration of free EGF receptor monomers in the system. M_f can be calculated from the equation for the total concentration of EGF receptors in the system, M_T, which is:

$$M_T = M_f + K_{11}M_f[EGF] + 2L_{20}M_f^2 + 2K_{21}L_{20}M_f^2[EGF] + 2K_{22}K_{21}L_{20}M_f^2[EGF]^2 + J_{20}M_fN_f + H_{21}J_{20}M_fN_f[EGF] \quad \text{(Eq. 2)}$$

where N_f is the concentration of free ErbB2 monomers. N_f is an unknown variable but can be expressed in the same way as M_f, by defining N_f in terms of N_T, the total concentration of ErbB2.

$$N_T = N_f + J_{20}M_fN_f + H_{21}J_{20}M_fN_f[EGF]$$

By rearrangement,

$$N_f = \frac{N_T}{1 + J_{20}M_f + H_{21}J_{20}M_f[EGF]}$$

This expression for N_f can be substituted into equation (2) to yield:

$$\left[2L_{20}M_f^2\left(1 + K_{21}[EGF] + K_{22}K_{21}[EGF]^2\right) + M_f\left(1 + K_{11}[EGF]\right) - M_T\right]\left(H_{21}J_{20}M_f[EGF] + J_{20}M_f + 1\right) + J_{20}M_fN_T\left(1 + H_{21}[EGF]\right) = 0 \quad \text{(Eq. 3)}$$

This equation is cubic for M_f but can be solved analytically at each given value of M_T, N_T, and [EGF] using an approach adapted from Cardan's solution (1,2). Briefly, in the case where there is one real root and two imaginary roots, the one real root was chosen as the solution. In the case where there are three distinct real roots, only the positive solution that is also smaller than the total EGF receptor concentration is physically relevant and was therefore chosen as the solution. For a given set of parameters, K_{11}, K_{21}, K_{22}, L_{20}, J_{20} and H_{21}, the fitting program first solves Equation 3 analytically to compute M_f. Once M_f is calculated, the experimental data can be fit to equation (1) as described in Materials and Methods.

1. Nickalls, R. (1993) *The Mathematical Gazette* **77**, 354-359
2. Zwillinger, D. (ed) (2002) *CRC Standard Mathematical Tables and Formulae*, CRC Press, Boca Raton, FL