Supporting Information.

Quadratic. A model of the reaction between analyte (G) and recognition moiety (H), which has one set of binding sites, is as follows:

$$H + G \rightleftharpoons HG \qquad \text{Eq.1}$$

The binding constants for this process can be expressed as a ratio of product over substrates:

$$K_{HG}=\frac{[HG]}{[H][G]} \qquad \text{Eq.2}$$

The absorbance in this process is define by Beer's Law (Eq. 3), where $_{HG}$ and $_{H}$ are molar absorptivity of host-guest complex and host respectively, b is path length of light through the sample and [HG] and [H] are the concentrations of host:guest complex and host respectively.

$$A=\varepsilon_{HG}b[HG]+\varepsilon_{H}b[H] \qquad \text{Eq.3}$$

The mass balances for this process are

$$[H]_T = [HG] + [H] \qquad \text{Eq.4}$$

$$[G]_T = [HG] + [G] \qquad \text{Eq.5}$$

It is desired that binding isotherms for every process which is based on this assumption are drawn we need to know how to calculate the host:guest [HG] and guest [G] concentration. First, we have to multiply both sides of Eq.2 by [H][G] to give:

$$K_{HG}[H][G] = [HG] \qquad \text{Eq.6}$$

Solving both Eq.4 for [H], and Eq.5 for [G] and substituting into Eq.6 gives the following expression, Eq.7.

$$K_{HG}([H]_T-[HG])([G]_T-[G]) = [HG] \qquad \text{Eq.7}$$

Expanding the terms to the left of the equation, yields Eq.8.

$$K_{HG}[H]_T[G]_T-K_{HG}[HG][H]_T-K_{HG}[HG][G]_T+K_{HG}[HG]^2 = [HG] \qquad \text{Eq.8}$$

Setting the equation equal to zero and combining the linear terms now provides the quadratic function below:

$$K_{HG}[HG]^2-[HG](K_{HG}[H]_T+K_{HG}[G]_T+1)+K_{HG}[H]_T[G]_T=0. \qquad \text{Eq.9}$$

Solving the quadratic equation gives two possible values for [HG]:

$$[HG]_1=[+(K_{HG}[H]_T+K_{HG}[G]_T+1)+\sqrt{[-(K_{HG}[H]_T+K_{HG}[G]_T+1)^2-4K_{HG}{}^2[H]_T[G]_T]}]/2K_{HG}$$

$$[HG]_2=[+(K_{HG}[H]_T+K_{HG}[G]_T+1)-\sqrt{[-(K_{HG}[H]_T+K_{HG}[G]_T+1)^2-4K_{HG}{}^2[H]_T[G]_T]}]/2K_{HG}.$$

Substituing these values into equation 4 enables us to calculate the host concentration. Based on these calculations ([HG] and [H]) we are able to simulate the binding isotherm plot for the host-guest binding process.

Cubic. A model of the indicator displacement reaction is as follows:

$$HI + G \rightleftharpoons HG + I \qquad \text{Eq.10}$$

The binding constant for the indicator displacement assay can be expressed as the ratio of the concentrations of products over the concentration of substrates (Eq.11)

$$K = \frac{[HG][I]}{[HI][G]} \qquad \text{Eq.11}$$

The total concentrations of each species give us our mass balance equations for each process (Eq.12, Eq.13, Eq.14).

$$[H]_T = [H] + [HG] + [HI] \qquad \text{Eq.12}$$

$$[G]_T = [HG] + [G] \qquad \text{Eq.13}$$

$$[I]_T = [HI] + [I] \qquad \text{Eq.14}$$

The following two equilibria occur during this process:

$$H + I \rightleftharpoons HI \qquad \text{Eq.15}$$

$$H + G \rightleftharpoons HG \qquad \text{Eq.16}$$

The binding constant for process in Eq.16 can be expressed as ratio of the products over reactants thus affording the binding constant K_{HG} as depicted in Eq.2.

$$K_{HG} = \frac{[HG]}{[H][G]} \qquad \text{Eq.2}$$

The absorbance in an indicator displacement assay is again defined by Beer's Law (Eq.17) where ε_{HI} and ε_I are the molar absorptivities of the host:indicator complex and the free indicator respectively, b is the path length of light through the sample, and [HI] and [I] are the concentrations of the host:indicator complex and the free indicator respectively.

$$A = \varepsilon_{HI} b[HI] + \varepsilon_I b[I] \qquad \text{Eq.17}$$

Solving equations 13 and 14 for [G] and [I] respectively and incorporating the solutions into Eq.11 gives Eq.18.

$$K = \frac{[HG]([I]_T - [HI])}{[HI]([G]_T - [HG])} \qquad \text{Eq.18}$$

Solving Eq.18 for [HI] provides Eq. 19.

$$[HI]=\frac{[HG][I]_T}{[HG](1-K)+K[G]_T} \qquad \text{Eq.19}$$

Solving equation 12 and 13 for [H] and [G] respectively and substituting into Eq.2 gives Eq.20.

$$K_{HG}=\frac{[HG]}{([H]_T-[HG]-[HI])([G]_T-[HG])} \qquad \text{Eq.20}$$

Multiplying each side of Eq.20 by $([H]_T-[HG]-[HI])([G]_T-[HG])$ and substituting Eq.19 in for the term [HI], provides Eq.21.

$$K_{HG}\left([H]_T-([HG]-\frac{[HG][I]_T}{[HG](1-K)+K[G]_T}\right)\left([G]_T-[HG]\right)=[HG] \qquad \text{Eq.21}$$

Now Eq.21 must be solved for [HG]. The left side of the equation is multiplied by a common denominator for all fractions that gives Eq.22

$$K_{HG}\left(\frac{[H]_T([HG](1-K)+K[G]_T)-[HG]([HG](1-K)+K[G]_T)-[HG][I]_T}{[HG](1-K)+K[G]_T}\right)\left([G]_T-[HG]\right)=[HG] \qquad \text{Eq.22}$$

Multiplying each side of the equation by $[HG](1-K)+K[G]_T$, yields Eq.23

$$K_{HG}([H]_T[HG](1-K)+K[H]_T[G]_T-[HG]^2(1-K)-K[HG][G]_T-[HG][I]_T)([G]_T-[HG]) =$$
$$[HG]([HG](1-K)+K[G]_T) \qquad \text{Eq.23}$$

Expending the terms to the left of the equal sign gives Eq.24.

$$K_{HG}[H]_T[HG][G]_T(1-K)+K_{HG}K[H]_T[G]_T^2-K_{HG}[G]_T[HG]^2(1-K)-K_{HG}K[HG][G]_T^2-$$
$$K_{HG}[HG][I]_T[G]_T-K_{HG}[H]_T[HG]^2(1-K)-K_{HG}K[H]_T[G]_T[HG]+K_{HG}[HG]^3(1-K)+$$
KHGK[HG]2[G]T+KHG[HG]2[I]T
$$= [HG]^2(1-K)+K[HG][G]_T \qquad \text{Eq.24}$$

Setting the equation equal to zero and combining line terms now provides the cubic in Eq.25

$$K_{HG}(1-K)[HG]^3+$$
$$(K_{HG}K[G]_T+K_{HG}[I]_T-(1-K)-K_{HG}[G]_T(1-K)-K_{HG}[H]_T(1-K))[HG]^2+$$
$$(K_{HG}[H]_T[G]_T(1-K)-K_{HG}K[G]_T^2+K_{HG}[I]_T[G]_T-K_{HG}K[H]_T[G]_T-K[G]_T)[HG]+$$
$$K_{HG}K\,[H]_T[G]_T^2 = 0 \qquad \text{Eq.25}$$

Then, we solve the cubic equation by the method of Viète.

$$[HG]_1 = Temp*\cos(\Phi/3) - S/3T$$

$$[HG]_2 = -Temp*\cos((\Phi+\pi)/3) - S/3T$$

$$[HG]_3 = -Temp*\cos((\Phi-\pi)/3) - S/3T$$

if

$$\left(\frac{Q^2}{4} + \frac{P^3}{27}\right) < 0$$

where

$$T = K_{HG}(1-K)$$

$$S = (K_{HG}K[G]_T + K_{HG}[I]_T - (1-K) - K_{HG}[G]_T(1-K) - K_{HG}[H]_T(1-K))$$

$$F = (K_{HG}[H]_T[G]_T(1-K) - K_{HG}K[G]_T^2 + K_{HG}[I]_T[G]_T - K_{HG}K[H]_T[G]_T - K[G]_T)$$

$$N = K_{HG}K\,[H]_T[G]_T^2$$

$$P = \frac{\left(3\left(\frac{F}{T}\right) - \left(\frac{S}{T}\right)^2\right)}{3}$$

$$Q = \frac{\left(2\left(\frac{S}{T}\right)^3 - 9\left(\frac{S*F}{T^2}\right) + \frac{27N}{T}\right)}{27}$$

$$\Phi = \operatorname{Arccos}\left[\frac{-0.5\,Q}{\sqrt{(P^3/27)}}\right]$$

$$Temp = 2\sqrt{\frac{P}{3}}$$