Analytic expressions titration curves for multisite binding

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Abstract

1 Statistical mechanics

This note outlines the grand canonical partition and analytic expressions for the average number of molecules in a system. These expressions are used to validate the free energies calculated with the grand canonical integration (GCI) equation derived in the JACS manuscript.

The grand canonical partition function, denoted $Z_G = Z_G(\mu, V, T)$, is a weighted sum over the partition function of the canonical partition function, denoted $Z = Z(N, V, T)$:

$$Z_G(\mu, V, T) = \sum_{N=0}^{\infty} \exp(N\mu\beta)\, Z(N, V, T) \tag{1}$$

$$= \sum_{N=0}^{\infty} \exp(N\mu\beta - F(N)\beta), \tag{2}$$

where $F(N, V, T)\beta = -\ln\big(Z(N, V, T)\big)$ has been inserted in the second line, and all unnamed terms have their standard thermodynamic meaning. Constant V and T will be assumed throughout, so their dependence will be henceforth remain implicit.

We are interested in how the average number of particles $\langle N \rangle$ varies with the applied chemical potential, this is integrated over in the GCI equation to give the ideal gas insertion free energies.

From statistical mechanics,

$$\begin{aligned}\langle N \rangle(\mu) &= -kT \frac{\partial \ln(Z_G(\mu))}{\partial \mu} \\ &= \frac{\sum_{N=0}^{\infty} N \exp(N\mu\beta - F(N)\beta)}{\sum_{N=0}^{\infty} \exp(N\mu\beta - F(N)\beta)},\end{aligned} \tag{3}$$

which is nothing more than the ensemble average of N at a fixed μ.

The idea is to relate the above expression for $\langle N \rangle(\mu)$ to the GCI equation:

$$\beta \Delta F_{\text{trans}}(\langle N_i \rangle \to \langle N_f \rangle) = \langle N_f \rangle B_f - \langle N_i \rangle B_i + \ln\left(\frac{\langle N_i \rangle!}{\langle N_f \rangle!}\right) - \int_{B_i}^{B_f} \langle N(B) \rangle dB, \tag{4}$$

where $\Delta F_{\text{ex}}(\langle N_i \rangle \to \langle N_f \rangle)$ is the change in the excess free energy to change the average number of particles from $\langle N_i \rangle$ to $\langle N_f \rangle$, and B is the Adams value. It's related to μ via

$$B = \mu\beta + \ln \frac{V}{\Lambda^3}. \tag{5}$$

As the analytic expression for $\langle N \rangle(\mu)$ (equation 3) depends of the free energies $F(N)$, these can be compared to the free energies calculated by GCI (equation 4), which integrates over $\langle N \rangle(B)$.

So that $\langle N \rangle(\mu)$ (equation 3) can be related to the GCI equation (equation 4), we need to express it terms of B. First, we expand free energy into its excess and ideal parts:

$$F(N) = F_{\mathrm{ex}}(N) + F_{\mathrm{ideal}}(N), \tag{6}$$

where

$$F_{\mathrm{ideal}}(N)\beta = -\ln\left[\frac{1}{N!}\left(\frac{V}{\Lambda^3}\right)^3\right], \tag{7}$$

so that the terms in the exponents of equation 3 expand to

$$\begin{aligned} N\mu\beta - F(N)\beta &= -N\mu\beta - F_{\mathrm{ex}}(N)\beta - F_{\mathrm{ideal}}(N)\beta \\ &= N(\mu\beta + \mu\beta + \ln\frac{V}{\Lambda^3}) - F_{\mathrm{ex}}(N)\beta - \ln(N!) \\ &= NB - F_{\mathrm{ex}}(N)\beta - \ln(N!) \end{aligned}$$

This allows us to rewrite equation 3 as

$$\langle N \rangle(B) = \frac{\sum_{N=0}^{\infty} N \exp(NB - F_{\mathrm{ex}}(N)\beta - \ln(N!))}{\sum_{N=0}^{\infty} \exp(NB - F_{\mathrm{ex}}(N)\beta - \ln(N!))}, \tag{8}$$

2 Multisite binding

In this section, expressions for $\langle N \rangle(B)$ (equation 8) will be explicitly written for systems that have capacities for up to three particles. All free energies will be defined in reference to $F(0)$, so that we set $F(0) = 0$.

2.1 Single site

A single site system has a capacity for only one particle, and adding any more particles is massively unfavourable. We represent this by setting all $F(N) = +\infty$ for all $N > 1$. Putting this information into equation 8 gives us

$$\begin{aligned} \langle N \rangle(B) &= \frac{\exp(B - F_{\mathrm{ex}}(1)\beta)}{1 + \exp(B - F_{\mathrm{ex}}(1)\beta)} \\ &= \frac{1}{1 + \exp(F_{\mathrm{ex}}(1)\beta - B)}, \end{aligned}$$

which is the same as the logistic equation in the JACS manuscript. There, it was explicitly proven that $F_{\mathrm{ex}}(1)$ is equal to the free energy as calculated using GCI.

2.2 Two sites

In case, $F(N) = +\infty$ for all $N > 2$, giving us

$$\langle N \rangle(B) = \frac{\exp(B - F_{\mathrm{ex}}(1)\beta) + 2\exp(2B - F_{\mathrm{ex}}(2)\beta - \ln(2))}{1 + \exp(B - F_{\mathrm{ex}}(1)\beta) + \exp(2B - F_{\mathrm{ex}}(2)\beta - \ln(2))}$$

2.3 Three sites

Here, $F(N) = +\infty$ for all $N > 3$, giving us

$$\langle N\rangle(B) = \frac{\exp(B - F_{\mathrm{ex}}(1)\beta) + 2\exp(2B - F_{\mathrm{ex}}(2)\beta - \ln(2)) + 3\exp(3B - F_{\mathrm{ex}}(3)\beta - \ln(6))}{1 + \exp(B - F_{\mathrm{ex}}(1)\beta) + \exp(2B - F_{\mathrm{ex}}(2)\beta - \ln(2)) + \exp(3B - F_{\mathrm{ex}}(3)\beta - \ln(6))}$$

And so on for more sites.

2.4 Notebook

The Jupyter notebook accompanying this write-up numerically verifies the free energies calculated with GCI compared to the free energies contained in the expressions for $\langle N\rangle(B)$. The numerical agreement is excellent, and indicates that the GCI equation is correct.