Cheat Sheet for Push-Pull Models

I. NOISE MODEL

We assume the antibody and associated theoretical GFP measurements for the phosphorylated substrate each follow log-normal distributions. We define the means and variances as

$$\mathbf{E}[\log([\text{anti}])] = \mu_{\text{anti}} \qquad \text{Var}[\log([\text{GFP}])] = \sigma_{\text{anti}} \tag{1}$$
$$\mathbf{E}[\log([\text{GFP}])] = \mu_{\text{GFP}} \qquad \text{Var}[\log([\text{GFP}])] = \sigma_{\text{GFP}} \tag{2}$$

so that the distributions are then given by

$$P(\log([\text{anti}])) = \frac{1}{\sqrt{2\pi\sigma_{\text{anti}}^2}} \exp\left(-\frac{(\log([\text{anti}]) - \mu_{\text{anti}})^2}{2\sigma_{\text{anti}}^2}\right) \tag{3}$$
$$P(\log([\text{GFP}])) = \frac{1}{\sqrt{2\pi\sigma_{\text{GFP}}^2}} \exp\left(-\frac{(\log([\text{GFP}]) - \mu_{\text{GFP}})^2}{2\sigma_{\text{GFP}}^2}\right) \tag{4}$$

We define the Pearson correlations coefficient between the two measurements,

$$\rho = \frac{\text{Cov}[\log([\text{GFP}]), \log([\text{anti}])]}{\sigma_{\text{GFP}}\sigma_{\text{anti}}}, \tag{5}$$

The noise model for the phosphorylated substrate takes then takes the form of a conditional probability,

$$P(\log([\text{anti}])|\log([\text{GFP}])) = \frac{1}{\sqrt{\Sigma^2}} \exp\left(-\frac{[\log([\text{anti}]) - A\log([\text{GFP}]) - B]^2}{2\Sigma^2}\right) \tag{6}$$

Fit Parameters: Above we used the the following definitions for the unknown noise parameters

- Conditional antibody variance: $\Sigma^2 = \sigma_{\text{anti}}^2(1-\rho)$
- GFP to antibody unit conversion ratio: $A = \rho\frac{\sigma_{\text{anti}}}{\sigma_{\text{GFP}}}$
- GFP to antobody unit constant offset: $B = \mu_{\text{anti}} - \rho\frac{\sigma_{\text{anti}}}{\sigma_{\text{GFP}}}\mu_{\text{GFP}}$

II. PUSH MODEL

Fit Parameters: α_{WS}, v_{WS}^p, v_{bg}^p
Concentrations:

- Total writer: $[W_T] = [W] + [WS^u] + [WS^p]$
- Total substrate: $[S_T] = [S_T^u] + [S_T^p]$
- Total unphosporylated substrate: $[S_T^u] = [S^u] + [WS^u]$
- Total phosporylated substrate: $[S_T^p] = [S^p] + [WS^p]$
- Total unbound substrate: $[S_f] = [S^p] + [S^u]$

Binding Energies:

- Writer + substrate: $\Delta\epsilon_{WS}$

Reaction Rates:

- Phosphorylation of substrate by writer: k_{WS}^p
- Background phosphorylation of substrate (independent of binding state): k_{bg}^p

- Background dephosphorylation of substrate (independent of binding state): k^u_{bg}

Fit Parameters

- Phosphorylation velocity: $v^p_{WS} = k^p_{WS}/k^u_{bg}$
- Background phosphorylation velocity $v^p_{bg} = k^p_{WS}/k^u_{bg}$
- Writer binding affinity: $\alpha_{WS} = [WS]_0 e^{\beta \Delta \epsilon_{WS}}$

where $[WS]_0$ is a reference concentration typically defined as the concentration at half saturation.

Model Equations The model then satisfies the following quadratic equation for the free substrate

$$0 = \left(\frac{[S_f]}{\alpha_{WS}}\right)^2 + \left(1 + \frac{[W_T] - [S_T]}{\alpha_{WS}}\right)\frac{[S_f]}{\alpha_{WS}} - \frac{[S_T]}{\alpha_{WS}} \tag{7}$$

After solving for $[S_f]$, the fraction of free writer is

$$\frac{[W]}{[W_T]} = \frac{1}{1 + \frac{[S_f]}{\alpha_{WS}}} \tag{8}$$

which can then be used to calculate the amount of phosphorylated substrate

$$\frac{[S^p_T]}{[S_T]} = \frac{v^p_{WS} p(WS^u|W) + v^p_S}{v^p_{WS} p(WS^u|W) + v^p_S + 1} \tag{9}$$

where

$$p(WS^u|W) = \frac{\frac{[W]}{\alpha_{WS}}}{1 + \frac{[W]}{\alpha_{WS}}}. \tag{10}$$

III. PUSH-PULL MODEL