Exercise 4

$$f(x) = y = \theta_1 + \frac{\theta_4 - \theta_1}{1 + \exp((x-\theta_2)\theta_3)}$$

a) Calculate slope of 4pLL model at concentration "θ_2".

$$\frac{d}{df} f(x) = \frac{(\theta_4 - \theta_1)\left(\exp((x-\theta_2)\theta_3)\right).(-\theta_3)}{[1 + \exp((x-\theta_2)\theta_3)]^2}$$

$$\left.\frac{d}{df} f(x)\right]_{x=\theta_2} = \frac{(\theta_4 - \theta_1)\left(\exp((\theta_2-\theta_2).\theta_3)\right).(-\theta_3)}{[1 + \exp((\theta_2-\theta_2)\theta_3)]^2}$$

$$= \boxed{-\frac{\theta_3}{4}(\theta_4 - \theta_1)}$$

b) Show that $\theta_3 > 0$, it holds $\lim_{x\to\infty} \theta_1 + \frac{\theta_4 - \theta_1}{1+\exp((x-\theta_2)\theta_3)} = \theta_1$

and that for $\theta_3 < 0$, it holds, $\lim_{x\to\infty} \theta_1 + \frac{\theta_4 - \theta_1}{1+\exp((x-\theta_2)\theta_3)} = \theta_4$

From lecture,

for $\theta_3 > 0$, $\lim_{x\to\infty} (x-\theta_2)\theta_3 = \infty$

holds s.t. $\lim_{x\to\infty} \theta_1 + \underbrace{\frac{\theta_4 - \theta_1}{\underbrace{1 + \exp(\underbrace{(x-\theta_2)\theta_3}_{x\to\infty \ \to\infty})}_{x\to\infty \ \to\infty}}}_{x\to\infty \ \to 0.} = \theta_1$

Hence

Similarly, for $\theta_3 < 0$, $\lim_{x\to\infty} (x-\theta_2)\theta_3 = -\infty$, s.t.

$$\lim_{x\to\infty} \theta_1 + \underbrace{\frac{\theta_4 - \theta_1}{\underbrace{1 + \underbrace{\exp((x-\theta_2)\theta_3)}_{x\to\infty \ \to 0}}_{=1}}} = \theta_4$$

Hence, $\theta_1 + \theta_4 - \theta_1 = \theta_4.$

c) Show the equivalence of (sigmoidal) Emax model as defined in lecture, Define the parameters of the model in terms of parameter $\theta_1, \theta_2, \theta_3, \theta_4$.

we know, 4plL model,

$$f_{4pll}(x) = \theta_1 + \frac{\theta_4 - \theta_1}{1 + \exp((x - \theta_2)\theta_3)}$$

Also, $$f_{sigmoidal}(x) = E_0 + \frac{x^n \cdot E_{max}}{x^n + ED50^n}. \quad \text{——— (I)}$$

where, n – Hill parameter (usually $n > 0$)

For ~~estimating~~ defining parameters of model, let's assume w.l.o.g. $\underline{\theta_4 > \theta_1}$.

Now, we assume case 1 :- $\theta_3 < 0$

case 2 :- $\theta_3 > 0$.

Case 1 :- $\theta_3 < 0$.

$$f_{4pll}(x) = \theta_1 + \frac{\theta_4 - \theta_1}{1 + \left(\frac{x}{\theta_2}\right)^{\theta_3}} \quad \text{——— (II)}$$

Now, we know, for $\theta_3 < 0$,

$E_0 = \theta_1$

$E_{max} = \theta_4 - \theta_1$

$n = -\theta_3 > 0$ [since $\theta_3 < 0$]

and, $ED50 = \theta_2$

Now, we plug into equation (I), we get,

$$f_{sigm}(x) = \theta_1 + (\theta_4 - \theta_1) \cdot \frac{x^{-\theta_3}}{x^{-\theta_3} + \theta_2^{-\theta_3}}$$

$$= \theta_1 + (\theta_4 - \theta_1) \cdot \frac{1}{1 + \left(\frac{x}{\theta_2}\right)^{\theta_3}}$$

[divide by x^{θ_3} both numerator and denominator].

$= $ (II) $= f_{4pll}(x)$.

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Analogously,

Case II: $\theta_3 > 0$.

$$E_0 = \theta_1$$
$$E_{max} = \theta_1 - \theta_4$$
$$n = \theta_3 > 0 \qquad [\text{since } \theta_3 > 0]$$
$$ED_{50} = \theta_2$$

plug these values in eq^n 1, again we get,

$$f_{sigm}(x) = \theta_4 + \frac{(\theta_1 - \theta_4)\, x^{\theta_3}}{x^{\theta_3} + \theta_2^{\theta_3}}.$$

Now, divide both Nr. & dr. by $\frac{1}{\theta_2^{\theta_3}}$,

$$= \theta_4 + (\theta_1 - \theta_4) \cdot \left[\frac{\left(\frac{x^{\theta_2}}{\theta_2^{\theta_3}}\right)}{1 + \frac{x^{\theta_3}}{\theta_2^{\theta_3}}} \right].$$

$$= \theta_4 + (\theta_1 - \theta_4)\left(1 - \frac{1}{\frac{x^{\theta_3}}{\theta_2^{\theta_3}} + 1}\right)$$

$$= \cancel{\theta_4} + \theta_1 - \cancel{\theta_4} + (\theta_4 - \theta_1) \frac{1}{\left(\frac{x^{\theta_3}}{\theta_2^{\theta_3}} + 1\right)}$$

$$= \theta_1 + \frac{(\theta_4 - \theta_1)}{1 + \left(\frac{x}{\theta_2}\right)^{\theta_3}} = f_{4pLL}(x) = \text{(ii)}.$$

X ——————————————————— X.