

Optimum dilution rate for cell/product productivity -- /w Substrate Inhibition, Vary both D and  $s_f$ .

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Model parameters:

$$\mu_m := 0.7 \quad K := 0.02 \quad K_i := 0.1 \quad Y_x := 0.5 \quad Y_p := 0.15 \quad \alpha := 0.1 \quad \beta := 0.02$$

$$\mu(s) := \frac{\mu_m \cdot s}{K + s + K_i \cdot s^2}$$

Initial guesses:

$$x := 1 \quad s := 0 \quad p := 0$$

Given Steady-state equations:

$$dx/dt: \quad 0 = (\mu(s) - D) \cdot x$$

$$ds/dt: \quad 0 = D \cdot (s_f - s) - \frac{1}{Y_x} \cdot \mu(s) \cdot x - \frac{1}{Y_p} \cdot (\alpha \cdot \mu(s) \cdot x + \beta \cdot x)$$

$$dp/dt: \quad 0 = \alpha \cdot \mu(s) \cdot x + \beta \cdot x - D \cdot p$$

$$\text{ans}(D, s_f) := \text{Find}(x, s, p) \leftarrow \text{Allow both } D \text{ and } s_f \text{ to be optimized. An example: } \text{ans}(0.1, 1) = \begin{pmatrix} 0.249 \\ 0.003 \\ 0.075 \end{pmatrix}$$

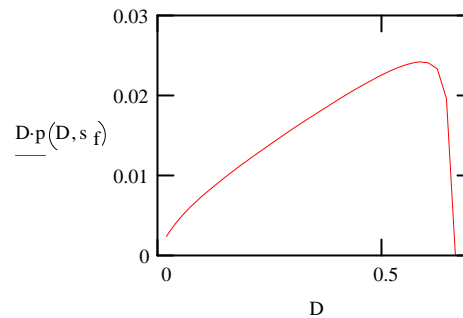
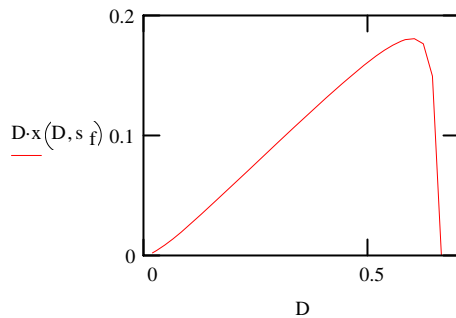
$$x(D, s_f) := \text{ans}(D, s_f)_0 \quad p(D, s_f) := \text{ans}(D, s_f)_2$$

$$\text{Max Profit}(D, s_f) := D \cdot p(D, s_f) - w_x \cdot D \cdot x(D, s_f) - w_s \cdot D \cdot s_f$$

$$w_x := 0.01 \quad w_s := 0.04$$

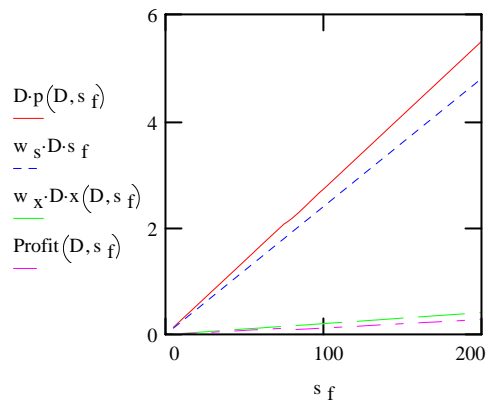
Dependence of D·p and D·x on D:  $D := 0.02, 0.04 \dots 0.699$

$$s_f := 1$$



Note that productivity is the highest near  $D = \mu_m$ , but drops off very quickly at  $D = \mu_m$ .

Dependence of  $D \cdot p$  and  $D \cdot x$  on  $s_f$ :  $D := 0.6$   $s_f := 5, 10 \dots 200$



Note that productivity  $D \cdot p$  increases linearly with  $s_f$ ; thus, Profit also increases quite linearly with  $s_f$ . This seems to be true for various models (with substrate inhibition). Solubility limits the maximum  $s_f$ .