

Dynamic simulation of microbial growth -- Incomplete mixing model by adding a second compartment
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Operating conditions:

$s_f := 10$... Feed substrate concentration

$D := 0.55$... Dilution rate

Constitutive relations:

$\mu_m := 0.5$... maximum specific growth rate

$K := 1$... Michaelis-Menten constant

$Y := 0.5$... yield coefficient

$\mu(s) := \frac{\mu_m \cdot s}{K + s}$... Monod specific growth rate

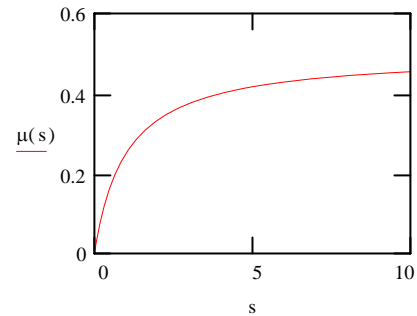
$s := 0, 0.1 \dots s_f$

Complete Mixing

Dynamic Equations:

$\frac{dx}{dt}(x, s) := (\mu(s) - D) \cdot x$ $x_0 := 1$... biomass

$\frac{ds}{dt}(x, s) := D \cdot (s_f - s) - \frac{\mu(s) \cdot x}{Y}$ $s_0 := s_f$... substrate



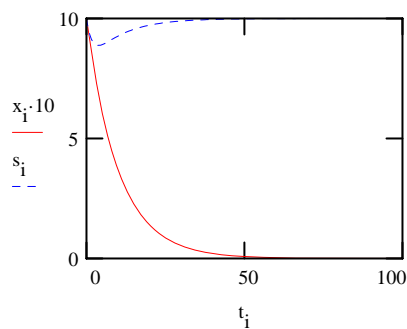
Combine individual functions into a vector function.

$$\text{ydot}(t, y) := \begin{pmatrix} \frac{dx}{dt}(y_0, y_1) \\ \frac{ds}{dt}(y_0, y_1) \end{pmatrix} \quad \text{I.C.: } y_{\text{initial}} := \begin{pmatrix} x_0 \\ s_0 \end{pmatrix}$$

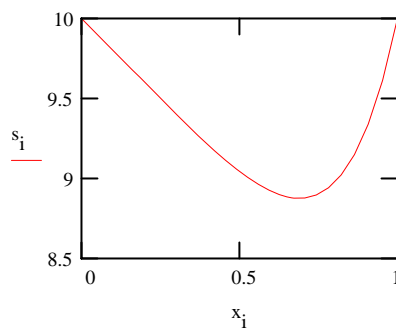
Integrate both ODEs from $t_0 := 0$ to $t_f := 100$ in $n_{\text{step}} := 200$

$\text{yout} := \text{rkfixed}(y_{\text{initial}}, t_0, t_f, n_{\text{step}}, \text{ydot})$ $t := \text{yout}^{\langle 0 \rangle}$ $x := \text{yout}^{\langle 1 \rangle}$ $s := \text{yout}^{\langle 2 \rangle}$ $i := 0 \dots \text{last}(t)$

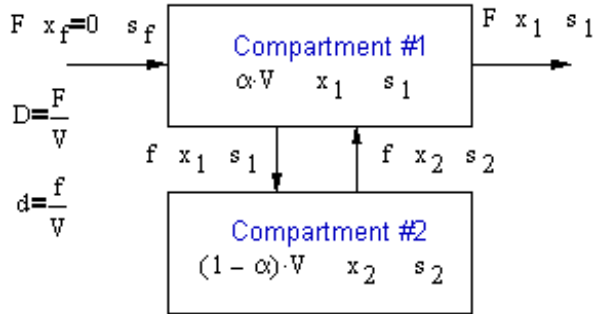
Plot of state variables



Phase diagram



Incomplete Mixing



$\alpha := 0.8$... fractional size of the 1st compartment

$d := 0.2 \cdot D$... exchange "dilution" rate of between two compartments

Dynamic equations:

$$dx_1dt(x_1, s_1, x_2, s_2) := \left(\mu(s_1) - \frac{D}{\alpha} - \frac{d}{\alpha} \right) \cdot x_1 + \frac{d}{\alpha} \cdot x_2 \quad \dots \text{Biomass in compartment 1}$$

$$ds_1dt(x_1, s_1, x_2, s_2) := \frac{D}{\alpha} \cdot (s_f - s_1) - \frac{\mu(s_1) \cdot x_1}{Y} - \frac{d}{\alpha} \cdot s_1 + \frac{d}{\alpha} \cdot s_2 \quad \dots \text{Substrate in compartment 1}$$

$$dx_2dt(x_1, s_1, x_2, s_2) := \left(\mu(s_2) - \frac{d}{1-\alpha} \right) \cdot x_2 + \frac{d}{1-\alpha} \cdot x_1 \quad \dots \text{Biomass in compartment 2}$$

$$ds_2dt(x_1, s_1, x_2, s_2) := \frac{d}{1-\alpha} \cdot (s_1 - s_2) - \frac{\mu(s_2) \cdot x_2}{Y} \quad \dots \text{Substrate in compartment 2}$$

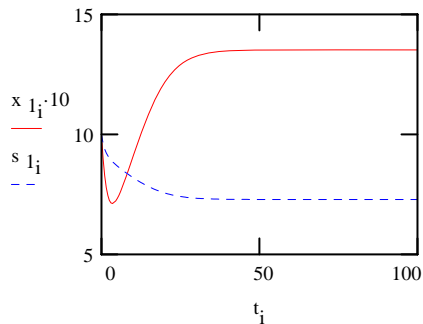
$$ydot(t, y) := \begin{bmatrix} dx_1dt(y_0, y_1, y_2, y_3) \\ ds_1dt(y_0, y_1, y_2, y_3) \\ dx_2dt(y_0, y_1, y_2, y_3) \\ ds_2dt(y_0, y_1, y_2, y_3) \end{bmatrix} \quad \text{I.C.: } y_{\text{initial}} := \begin{bmatrix} x_0 \\ s_0 \\ x_0 \\ s_0 \end{bmatrix}$$

Integrate all 4 ODEs

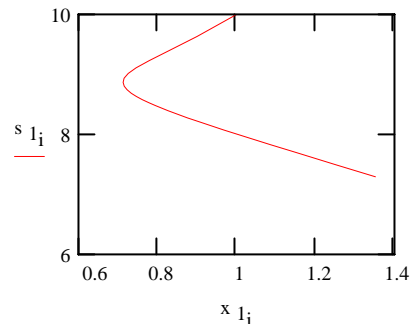
$yout := rkfixed(y_{\text{initial}}, t_0, t_f, nstep, ydot)$

$t := yout^{<0>} \quad x_1 := yout^{<1>} \quad s_1 := yout^{<2>} \quad x_2 := yout^{<3>} \quad s_2 := yout^{<4>} \quad i := 0 \dots \text{last}(t)$

Plot of state variables



Phase diagram



Incomplete mixing moderates the bioreactor dynamics by adding an extra dynamic layer and allows the bioreactor to be operated at a higher dilution rate before cell washout occurs.

Note: Setting the dynamic equations $d/dt=0$ failed to converge to an analytical steady-state solution.