Dynamic simulation of microbial growth (Linearized stability analysis based on eigenvalues.)
Instructor: Nam Sun Wang

Constitutive relations:

$$\mu(s) := \frac{0.3 \cdot s}{50 + s}$$ ... Monod specific growth rate

$$Y(s) := 0.004 + 0.001 \cdot s$$ ... yield coefficient

Dynamic Equations:

$$dxdt\left(x, s, D, s_f\right) := (\mu(s) - D) \cdot x$$

$$dsdt\left(x, s, D, s_f\right) := D \cdot \left(s_f - s\right) - \frac{\mu(s)}{Y(s)} \cdot x$$

Steady-states: (calculated by setting d/dt=0 with initial guesses: $x := 1$ $s := 0$

Note that with an initial guess of x=0, computer gives the washout steady-state, which leads to one positive and one negative eigenvalues. Thus, the washout steady-state is unstable. With an initial guess of x=1, computer gives the non-washout steady-state. If the non-washout steady-state is also unstable, we have a limit cycle.

Given $dxdt\left(x, s, D, s_f\right) = 0$

$dsdt\left(x, s, D, s_f\right) = 0$

$$ss\left(D, s_f\right) := Find(x, s)$$

The 0th answer is the biomass steady-state: $x_{ss}\left(D, s_f\right) := ss\left(D, s_f\right)_0$

The 1st answer is the substrate steady-state: $s_{ss}\left(D, s_f\right) := ss\left(D, s_f\right)_1$

An example: $ss(0.1, 200) = \begin{pmatrix} 5.075 \\ 25 \end{pmatrix}$

Form the Jacobian matrix such that dX/dt=AX, where X is the deviation variable. (Evaluate d/dx and d/ds with **|Symbolic|Differentiate on Variable|** on dynamic equation.)

$$A\left(x, s, D, s_f\right) := \begin{bmatrix} \mu(s) - D & \frac{d}{ds}\mu(s) \cdot x \\ \frac{-\mu(s)}{Y(s)} & -D - \frac{\frac{d}{ds}\mu(s)}{Y(s)} \cdot x + \frac{\mu(s)}{Y(s)^2} \cdot x \cdot \frac{d}{ds}Y(s) \end{bmatrix}$$

Find the eigenvalue of matrix A, evaluated at steady-state points

$$eigenvals\left[\begin{bmatrix} \mu(s) - D & \frac{d}{ds}\mu(s) \cdot x \\ \frac{-\mu(s)}{Y(s)} & -D - \frac{\frac{d}{ds}\mu(s)}{Y(s)} \cdot x + \frac{\mu(s)}{Y(s)^2} \cdot x \cdot \frac{d}{ds}Y(s) \end{bmatrix}\right]$$

Evaluate the above expression symbolically gives the following long expressions for eigenvalues:

$$\left[\begin{matrix} \frac{1}{\left(2\cdot Y(s)^2\right)}\cdot\left[\mu(s)\cdot Y(s)^2 - 2\cdot D\cdot Y(s)^2 - \frac{d}{ds}\mu(s)\cdot x\cdot Y(s) + \mu(s)\cdot x\cdot\frac{d}{ds}Y(s) + \sqrt{\mu(s)^2\cdot Y(s)^4 - 2\cdot\mu(s)\cdot Y(s)^3\cdot\frac{d}{ds}\mu(s)\cdot x - 2\cdot\mu(s)^2\cdot}\right. \\ \frac{1}{\left(2\cdot Y(s)^2\right)}\cdot\left[\mu(s)\cdot Y(s)^2 - 2\cdot D\cdot Y(s)^2 - \frac{d}{ds}\mu(s)\cdot x\cdot Y(s) + \mu(s)\cdot x\cdot\frac{d}{ds}Y(s) - \sqrt{\mu(s)^2\cdot Y(s)^4 - 2\cdot\mu(s)\cdot Y(s)^3\cdot\frac{d}{ds}\mu(s)\cdot x - 2\cdot\mu(s)^2\cdot}\right. \end{matrix}\right.$$

Steady-state stability changes from unstable to stable when the real part (i.e., the part preceeding the square root sign) crosses 0. ==> stable(D,sf)=0.

$$\text{stable}\left(x, s, D, s_f\right) := \mu(s)\cdot Y(s)^2 - 2\cdot D\cdot Y(s)^2 - \frac{d}{ds}\mu(s)\cdot x\cdot Y(s) + \mu(s)\cdot x\cdot\frac{d}{ds}Y(s)$$

$D := 0.1$ $\quad s_f := 20$

$\text{stable\_D}\left(s_f\right) := \text{root}\left(\text{stable}\left(x_{ss}\left(D, s_f\right), s_{ss}\left(D, s_f\right), D, s_f\right), D\right)$ $\quad \text{stable\_D}(50) = 0.054$

$\text{stable\_sf}(D) := \text{root}\left(\text{stable}\left(x_{ss}\left(D, s_f\right), s_{ss}\left(D, s_f\right), D, s_f\right), s_f\right)$ $\quad \text{stable\_sf}(0.1) = 2.315$

Approach to steady-state changes from exponential to oscillatory when the imaginary part (i.e., the part within the square root sign) crosses 0. ==> oscillation(D,sf)=0

$$\text{oscillation}\left(x, s, D, s_f\right) := \mu(s)^2\cdot Y(s)^4 - 2\cdot\mu(s)\cdot Y(s)^3\cdot\frac{d}{ds}\mu(s)\cdot x - 2\cdot\mu(s)^2\cdot Y(s)^2\cdot x\cdot\frac{d}{ds}Y(s)\ \ldots$$
$$+\left(\frac{d}{ds}\mu(s)\right)^2\cdot x^2\cdot Y(s)^2 - 2\cdot\frac{d}{ds}\mu(s)\cdot x^2\cdot Y(s)\cdot\mu(s)\cdot\frac{d}{ds}Y(s) + \mu(s)^2\cdot x^2\cdot\left(\frac{d}{ds}Y(s)\right)^2$$

$\text{oscillation\_D}\left(s_f\right) := \text{root}\left(\text{oscillation}\left(x_{ss}\left(D, s_f\right), s_{ss}\left(D, s_f\right), D, s_f\right), D\right)$ $\quad \text{oscillation\_D}(200) = 0.075$

$\text{oscillation\_sf}(D) := \text{root}\left(\text{oscillation}\left(x_{ss}\left(D, s_f\right), s_{ss}\left(D, s_f\right), D, s_f\right), s_f\right)$ $\quad \text{oscillation\_sf}(0.1) = 15.808$

An alternate approach: Eigenvalue:

$$\lambda\left(D, s_f\right) := \text{eigenvals}\left(A\left(x_{ss}\left(D, s_f\right), s_{ss}\left(D, s_f\right), D, s_f\right)\right)$$

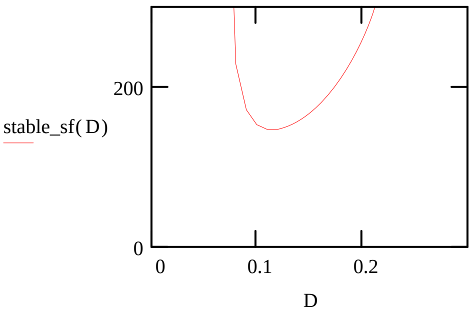
An example: $\lambda(0.1, 200) = \begin{pmatrix} 0.01839 + 0.21524i \\ 0.01839 - 0.21524i \end{pmatrix}$

Possitive real part shows that the non-washout steady-state is unstable, and the imaginary part shows spiral.

$s_f := 200$ ... initial guess

$\text{stable\_sf}(D) := \text{root}\left(\text{Re}\left(\lambda\left(D, s_f\right)_0\right), s_f\right)$ $\quad \text{stable\_sf}(0.1) = 152.941$

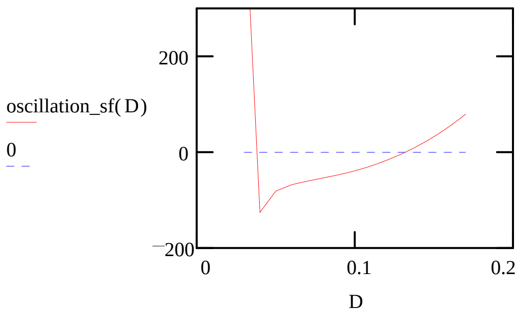
$D := 0.07, 0.08 .. 0.22$



$s_f := 100$

$\text{oscillation\_sf}(D) := \text{root}\left(\text{Im}\left(\lambda\left(D, s_f\right)_0\right), s_f\right)$ $\text{oscillation\_sf}(0.1) = -38.454$

$D := 0.03, 0.04 .. 0.17$



Dynamic simulation with initial conditions $x_0 := 0.5$ $s_0 := 30$

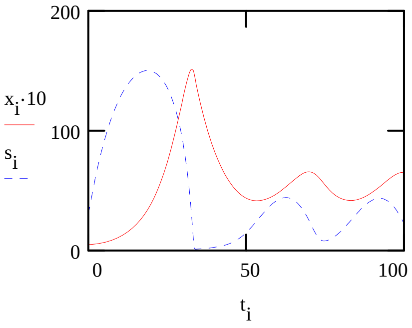
and operating conditions $D := 0.1$ $s_f := 200$

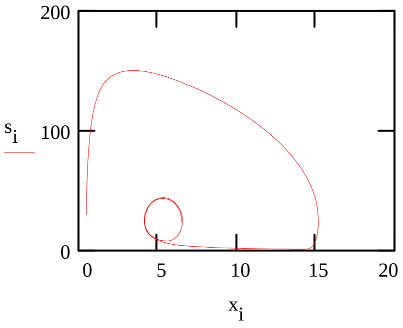
$\text{ydot}(t, y) := \begin{pmatrix} \text{dxdt}\left(y_0, y_1, D, s_f\right) \\ \text{dsdt}\left(y_0, y_1, D, s_f\right) \end{pmatrix}$ $y_{\text{initial}} := \begin{pmatrix} x_0 \\ s_0 \end{pmatrix}$ ... biomass ... substrate

Solve both sets of ODEs (integrate from $t_0 := 0$ to $t_f := 100$ in $\text{nstep} := 1000$

$\text{yout} := \text{rkfixed}\left(y_{\text{initial}}, t_0, t_f, \text{nstep}, \text{ydot}\right)$ $t := \text{yout}^{\langle 0 \rangle}$ $x := \text{yout}^{\langle 1 \rangle}$ $s := \text{yout}^{\langle 2 \rangle}$

Plots of state variables $i := 0 .. \text{last}(t)$ Phase diagram





$$\overline{Y(s)^2\cdot x\cdot\frac{d}{ds}Y(s)+\left(\frac{d}{ds}\mu(s)\right)^2\cdot x^2\cdot Y(s)^2-2\cdot\frac{d}{ds}\mu(s)\cdot x^2\cdot Y(s)\cdot\mu(s)\cdot\frac{d}{ds}Y(s)+\mu(s)^2\cdot x^2\cdot\left(\frac{d}{ds}Y(s)\right)^2}\Bigg]$$

$$\overline{Y(s)^2\cdot x\cdot\frac{d}{ds}Y(s)+\left(\frac{d}{ds}\mu(s)\right)^2\cdot x^2\cdot Y(s)^2-2\cdot\frac{d}{ds}\mu(s)\cdot x^2\cdot Y(s)\cdot\mu(s)\cdot\frac{d}{ds}Y(s)+\mu(s)^2\cdot x^2\cdot\left(\frac{d}{ds}Y(s)\right)^2}\Bigg]\Bigg]$$