Solving differential equations

A system of differential equations:

$$\left.\begin{array}{l} \dot{x}_1 = f(x_1, \dots x_n; t) \\ \vdots \qquad\qquad \vdots \\ \dot{x}_n = f(x_1, \dots x_n; t) \end{array}\right] \quad \dot{x} = f(x,t) \quad x \in \mathbb{R}^n, \; f \in \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}^n$$

$$\dot{x}_i = dx_i / dt$$

Example 1: mRNA degradation

$$\frac{d[m]}{dt} = -\gamma_m [m] \;, [m](t=0) = m_0 \quad \text{(linear homogeneous ODE)}$$

Separation of variables and integration

$$\int \frac{d[m']}{[m']} = -\gamma_m \int dt'$$

$$\ln([m](t)) = -\gamma_m t + K$$

Exponentiate:

$$[m](t) = e^K e^{-\gamma_m t} = K' e^{-\gamma_m t} \qquad K' := e^K$$

Initial condition: $[m](0) = K \overset{!}{=} m_0$

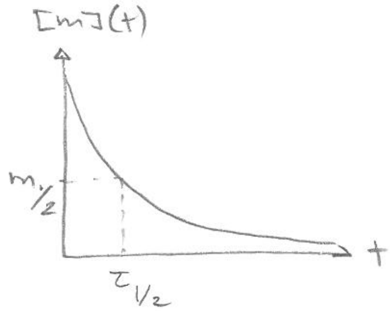
$$\Rightarrow \underline{[m](t) = m_0 e^{-\gamma_m t}}$$

mRNA half life:

$$[m](t_{1/2}) = m_0/2 = m_0 e^{-\gamma_m t_{1/2}} \quad \Rightarrow \quad \underline{t_{1/2} = \ln(2)/\gamma_m}$$

Bacteria: $t_{1/2} \sim$ minutes

human cells: $t_{1/2} \sim$ hrs

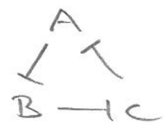


$t = 0: [m](0) = m_0$

$t = t_{1/2} = [m](t_{1/2}) = m_0/2$

$t \to \infty: m(t) = 0$

why does it matter for synthetic biology?
Control half-life to engineer system dynamics
Repressilator example:



Example 2: mRNA production and degradation

$\dot{[m]} = -\gamma_m [m] + \alpha_m$ (linear <u>inhomogeneous</u> ODE)
$[m](0) = m_0$

(i) Solve hom. eq. $\dot{[m]} = -\gamma [m] \Rightarrow [m]_H(t) = m_0 e^{-\gamma_m t}$

(ii) Ansatz: $[m]_I(t) = K(t) e^{-\gamma_m t}$ (variation of the constant)

Substitute into equation:

$$\dot{K}(t) e^{-\gamma_m t} - \cancel{\gamma_m K(t) e^{-\gamma_m t}} = - \cancel{\gamma_m K(t) e^{-\gamma_m t}} + \alpha_m$$

$$\dot{K}(t) = \alpha_m e^{\gamma_m t}$$

$$K(t) = \frac{\alpha_m}{\gamma_m} e^{\gamma_m t} + K'$$

<u>Theorem</u>: The solution to the inhom. eq. is the sum of the solution to the hom. eq. with inital condition $[m](t) = m_0$ and any solution to the inhom. eq.

$$[m](t) = [m]_H(t) + [m]_I(t) = m_0 e^{-\gamma_m t} + \left(\frac{\alpha_m}{\gamma_m} e^{\gamma_m t} + K'\right) e^{-\gamma_m t}$$

$[m](0) = m_0 \Rightarrow K' = -\alpha_m/\gamma_m$

Skipped in class

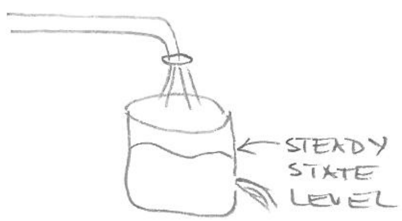
$$[m](t) = m_0 e^{-\gamma_m t} + \underbrace{\frac{\alpha_m}{\gamma_m}\left(1 - e^{-\gamma_m t}\right)} = [m]_H(t) + [m]_I(t)$$

solution to hom. eq.

particular solution to inhom. eq

$t \to \infty : [m(t)] = \alpha_m / \gamma_m$

Important concept: <u>steady-state approximation</u>



Not equilibrium!
When the water is switched off, the bucket empties out.

$$\frac{d}{dt}[m](t) = \alpha_m - \gamma_m [m](t) \stackrel{!}{=} 0$$ Production and degradation are balanced!

$$\Rightarrow \underline{[m]_{ss} = \alpha_m / \gamma_m}$$

Include protein production/degradation

$$\frac{d}{dt}[P](t) = \alpha_p [m] - \gamma_p [P] \stackrel{!}{=} 0 \quad (\text{Use } [m]_{ss})$$

$$\Rightarrow [P] = \frac{\alpha_p}{\gamma_p}[m] = \underline{\frac{\alpha_p \alpha_m}{\gamma_p \gamma_m}}$$

Example: Hybridization

$$\frac{d[S]}{dt} = -k[S][\bar{S}] \qquad (S+\bar{S} \xrightarrow{k} S\bar{S})$$

(i) $[S](0) = [\bar{S}'](0) = S_0 \Rightarrow [S](t) = [\bar{S}](t)$

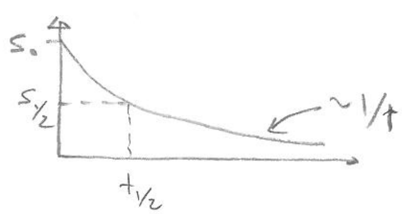
$$\frac{d[S]}{dt} = -k[S]^2$$ (separate variables, then integrate

$$\int \frac{d[S']}{[S]^2} = -k\int dt'$$

$$-\frac{1}{[S](t)} = -kt + K \Rightarrow [S](t) = \frac{1}{kt - K}$$

$t = 0 \Rightarrow K = -1/S_0$

$$\Rightarrow [S](t) = \frac{S_0}{1 + kS_0 t}, \quad t_{1/2} = 1/kS_0$$



(ii) $[\bar{S}](0) = \bar{S}_0$, $[S](0) = S_0$, $\bar{S}_0 > S_0$

Conservation law:

$S_0 = [S] + [S\bar{S}]$, $\bar{S}_0 = [\bar{S}] + [S\bar{S}] \Rightarrow S_0 - [S] = \bar{S}_0 - [\bar{S}]$

$$\frac{d[S]}{dt} = -k[S][\bar{S}] = -k[S]\big(\underbrace{\bar{S}_0 - S_0}_{\Delta} + [S]\big)$$

$\Delta := \bar{S}_0 - S$

$$\int_{S_0}^{[S]} \frac{d[S']}{[S'](\Delta+[S'])} = \frac{1}{\Delta}\int_{S_0}^{[S]} d[S']\left(\frac{1}{[S']} - \frac{1}{\Delta+[S']}\right) =$$

$$= \frac{1}{\Delta} \ln\left(\frac{[S]}{S_0}\right) - \ln\left(\frac{\Delta+[S]}{\Delta+S_0}\right) = -kt$$

$$\ln\left(\frac{[S]}{S_0}\cdot\frac{\bar{S}_0}{\Delta+[S]}\right) = -k\Delta t$$

$$\frac{[S]}{S_0}\cdot\frac{\bar{S}_0}{\Delta+[S]} = e^{-k\Delta t}$$

$$[S]\left(1-\frac{S_0}{\bar{S}_0}e^{-k\Delta t}\right) = S_0\left(1-\frac{S_0}{\bar{S}_0}\right)e^{-k\Delta t}$$

$$[S] = \frac{S_0(1-S_0/\bar{S}_0)\,e^{-k\Delta t}}{1-S_0/\bar{S}_0\,e^{-k\Delta t}}$$

$t=0$: $[S](t=0) = \dfrac{S_0(1-S_0/\bar{S}_0)}{1-S_0/\bar{S}_0} = S_0$ ✓

$t\to\infty$: $[S]=0$ ✓