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Stochastic models for the chemostat

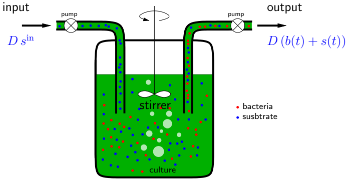
Fabien Campillo, Marc Joannides, Irène Larramendy-Valverde

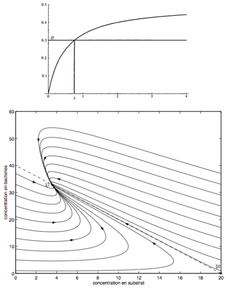
classical ODE model

- continuous culture with single species/single substrate

$$\begin{aligned} \text{biomass} \quad \dot b &= [\mu(s) - D]\, b \\ \text{subtrate} \quad \dot s &= -k\,\mu(s)\, b + D\,[s^{\text{in}} - s] \end{aligned} \qquad \text{(ODE)}$$

$x = (b, s)$; $D > 0$ dilution rate ; $s^{\text{in}} > 0$ inflow substrate concentration ; $k > 0$ stoichiometric coefficient ; $\mu(s)$ specific growth rate function (Monod)



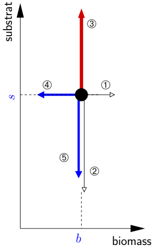


aim

- sources of randomness
  - demographic
  - environmental
  - measurement

→ a model that accounts for the demographic randomness

pure jump process $X_t = (B_t, S_t)$



- five types of jump :

biology	① biomass $\nearrow$	of $\nu_1(x)$	at rate $\lambda_1(x)$
	② substrate $\searrow$	of $\nu_2(x)$	at rate $\lambda_2(x)$
inflow	③ substrate $\nearrow$	of $\nu_3(x)$	at rate $\lambda_3(x)$
outflow	④ biomass $\searrow$	of $\nu_4(x)$	at rate $\lambda_4(x)$
	⑤ substrate $\searrow$	of $\nu_5(x)$	at rate $\lambda_5(x)$

- starting from $X_t = x = (b, s)$:

$$X_{t+\Delta t} = x + \underbrace{\Delta X_t^1 + \Delta X_t^2 + \Delta X_t^3 + \Delta X_t^4 + \Delta X_t^5}_{\text{cumulated jumps of type ① ② ③ ④ ⑤}}$$

pure jump process $X_t = (B_t, S_t)$ II

- for ① & ②
  - on the one hand the stochastic mass action law gives :

$$\mathbb{E}[\Delta X_t^1 | X_t = x] \simeq \begin{pmatrix} \mu(s)\, b\, \Delta t \\ 0 \end{pmatrix} \quad \mathbb{E}[\Delta X_t^2 | X_t = x] \simeq \begin{pmatrix} 0 \\ -k\, \mu(s)\, b\, \Delta t \end{pmatrix}$$

  - on the other hand the number jumps of type ①, ② are approximatively Poisson, $\mathcal{P}(\lambda_1(x)\,\Delta t)$ and $\mathcal{P}(\lambda_2(x)\,\Delta t)$, so

$$\mathbb{E}[\Delta X_t^1 | X_t = x] \simeq \lambda_1(x)\,\nu_1(x)\,\Delta t \quad \mathbb{E}[\Delta X_t^2 | X_t = x] \simeq \lambda_2(x)\,\nu_2(x)\,\Delta t$$

  - so that

$$\lambda_1(x)\,\nu_1(x) = \begin{pmatrix} \mu(s)\, b \\ 0 \end{pmatrix} \qquad \lambda_2(x)\,\nu_2(x) = \begin{pmatrix} 0 \\ -k\, \mu(s)\, b \end{pmatrix}$$

pure jump process $X_t = (B_t, S_t)$ III

- introduce scale parameters K_1 and K_2 and choose :

$$\lambda_1(x) \stackrel{\text{def}}{=} K_1\,\mu(s)\,b \qquad \nu_1 \stackrel{\text{def}}{=} \begin{pmatrix} \frac{1}{K_1} \\ 0 \end{pmatrix}$$

$$\lambda_2(x) \stackrel{\text{def}}{=} K_2\,k\,\mu(s)\,b \qquad \nu_2 \stackrel{\text{def}}{=} -\begin{pmatrix} 0 \\ \frac{1}{K_2} \end{pmatrix}$$

(this choice is not unique) K_i acts on the variance of the increments $\rightarrow$ tuning parameters

- the approach leads to

	① biomass increase	② substrate decrease	③ substrate inflow	④ biomass outflow	⑤ substrate outflow
	biology		inflow	outflow	
rate $\lambda_i(x)$	$K_1\,\mu(s)\,b$	$K_2\,k\,\mu(s)\,b$	$K_3\,D\,s^{\text{in}}$	$K_4\,D\,b$	$K_5\,D\,s$
jump $\nu_i(x)$	$\begin{pmatrix} \frac{1}{K_1} \\ 0 \end{pmatrix}$	$-\begin{pmatrix} 0 \\ \frac{1}{K_2} \end{pmatrix}$	$\begin{pmatrix} 0 \\ \frac{1}{K_3} \end{pmatrix}$	$-\begin{pmatrix} \frac{1}{K_4} \\ 0 \end{pmatrix}$	$-\begin{pmatrix} 0 \\ \frac{1}{K_5} \end{pmatrix}$

pure jump process $X_t = (B_t, S_t)$ IV

- Poisson process representation :

$$X_t = X_0 + \sum_{i=1}^{5} \int_{(0,t]\times[0,\infty)} \nu_i(X_{u^-})\, 1_{\{v\leq\lambda_i(X_{u^-})\}}\, N^i(\mathrm{d}u\times\mathrm{d}v)$$

  N^i independent random Poisson measures with intensity measure $\mathrm{d}u\times\mathrm{d}v$

  or, after martingale decomposition :

$$\mathrm{d}B_t = \big(\mu(S_t) - D\big)\, B_t\,\mathrm{d}t + \frac{\mathrm{d}\bar m_t^1}{\sqrt{K_1}} + \frac{\mathrm{d}\bar m_t^4}{\sqrt{K_4}}$$

$$\mathrm{d}S_t = \big(-k\,\mu(S_t)\,B_t + D\,(s^{\mathrm{in}} - S_t)\big)\,\mathrm{d}t + \frac{\mathrm{d}\bar m_t^2}{\sqrt{K_2}} + \frac{\mathrm{d}\bar m_t^3}{\sqrt{K_3}} + \frac{\mathrm{d}\bar m_t^5}{\sqrt{K_5}}$$

  $\bar m_t^i$ are independent square integrable martingales with zero mean and the $\langle m^i\rangle_t$ are known

- can be exactly simulated (Gillespie method) : asynchronous, valid for small population size

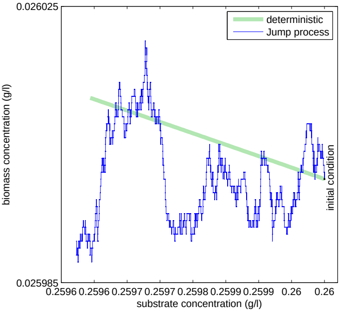
Poisson approximation $\tilde{X}_{t_n} = (\tilde{B}_{t_n}, \tilde{S}_{t_n})$

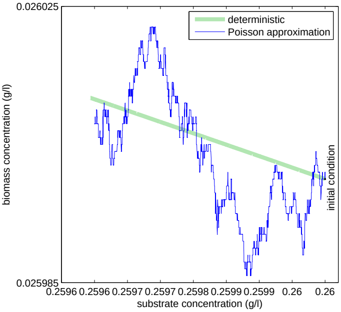
- fixe time step : $t_n = n\,\Delta t$
- froze $\lambda_i(X_t)$ and $\nu_i(X_t)$ to $\lambda_i(X_{t_n})$ and $\nu_i(X_{t_n})$ on $[t_n, t_{n+1})$, so that in $X_{t+\Delta t} = x + \Delta X_t^1 + \Delta X_t^2 + \Delta X_t^3 + \Delta X_t^4 + \Delta X_t^2$ we have $\Delta X_t^i \sim \nu_i(x)\,\mathrm{Poisson}(\Delta t\,\lambda_i(x))$, we get

$$\tilde{X}_{t_{n+1}} = \tilde{X}_{t_n} + \sum_{i=1}^{5} \nu_i(\tilde{X}_{t_n})\,\mathcal{P}_n^i(\Delta t\,\lambda_i(\tilde{X}_{t_n})) \qquad \text{(Poisson)}$$

  - $\mathcal{P}_n^i(\rho)$ independent Poisson variables with intensities ρ
  - boundary conditions
- τ-leaping
- the time step can be adapted

from pure jump to Poisson approximation





pure jump process
1,237,928 events

Poisson approximation
3456 time steps

diffusion approximation $\tilde{\xi}_{t_n} = (\tilde{\beta}_{t_n}, \tilde{\sigma}_{t_n})$

- for $\Delta t\, \lambda_i(x)$ large : $\mathcal{P}_n^i(\Delta t\, \lambda_i(x)) \simeq \mathcal{N}(\Delta t\, \lambda_i(x), \Delta t\, \lambda_i(x))$
- diffusion approximation

$$\tilde{\xi}_{t_{n+1}} = x + \sum_{i=1}^{5} \nu_i(x)\, \mathcal{N}_n^i$$

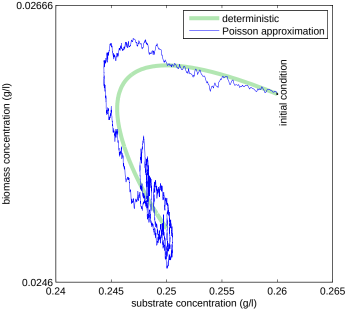
  - independent $\mathcal{N}_n^i \sim \mathcal{N}\big(\lambda_i(x)\, \Delta t\,,\, \lambda_i(x)\, \Delta t\big)$
  - same instantaneous mean and covariance
- given $\tilde{\beta}_{t_n} = b$ and $\tilde{\sigma}_{t_n} = s$:

$$\tilde{\beta}_{t_{n+1}} = b + \big[\mu(s) - D\big]\, b\, \Delta t + \sqrt{\Delta t\, \tfrac{\mu(s)\, b}{K_1} + \Delta t\, \tfrac{D\, b}{K_4}}\; w_n^{\mathrm{b}}$$

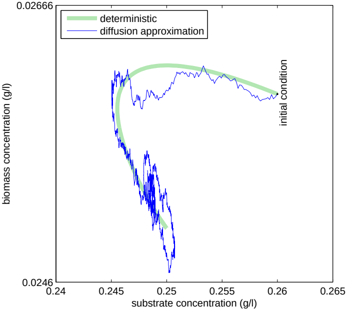
$$\tilde{\sigma}_{t_{n+1}} = s + \big[- k\, \mu(s)\, b + D\, s^{\mathrm{in}} - D\, s\big]\, \Delta t + \sqrt{\Delta t\, \tfrac{k\, \mu(s)\, b}{K_2} + \Delta t\, \tfrac{D\, s^{\mathrm{in}}}{K_3} + \Delta t\, \tfrac{D\, s}{K_5}}\; w_n^{\mathrm{s}}$$

  - w_n^{b}, w_n^{s} i.i.d. $\mathcal{N}(0,1)$
  - boundary conditions (absorbing in b, reflecting in s)
  - Euler-Maruyama approximation of an SDE

Poisson to diffusion



Poisson approximation
3004 time steps



diffusion approximation
2000 time steps

SDE

- diffusion approximation $\xi_t = (\beta_t, \sigma_t)$

$$\mathrm{d}\beta_t = \big[\mu(\sigma_t) - D\big]\,\beta_t\,\mathrm{d}t + \sqrt{\tfrac{\mu(\sigma_t)\,\beta_t}{K_1} + \tfrac{D\,\beta_t}{K_4}}\,\mathrm{d}W_t^{\mathrm{b}}$$

$$\mathrm{d}\sigma_t = \big[-k\,\mu(\sigma_t)\,\beta_t + D\,(s^{\mathrm{in}} - \sigma_t)\big]\,\mathrm{d}t + \sqrt{\tfrac{k\,\mu(\sigma_t)\,\beta_t}{K_2} + \tfrac{D\,s^{\mathrm{in}}}{K_3} + \tfrac{D\,\sigma_t}{K_5}}\,\mathrm{d}W_t^{\mathrm{s}}$$

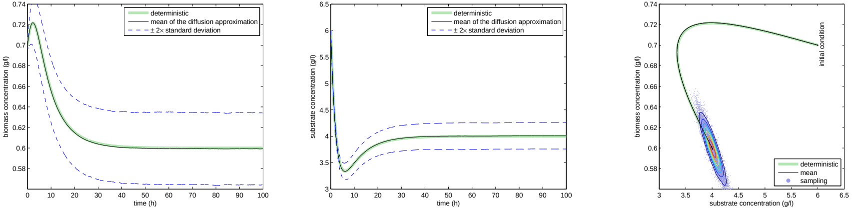
  - W^{b}, W^{s} independent standard Wiener processes
  - behavior near the axes

asymptotic analysis

- (jump) & (SDE) $\to$ (ODE) as all $K_i \to \infty$

$$\mathbb{P}\Big(\sup_{0\leq t\leq T} \big\{ \|X_t^K - x(t)\| + \|\xi_t^K - x(t)\| \big\} \geq \delta \Big) \xrightarrow[K_i\to\infty]{\text{all}} 0$$

asymptotic behavior



- surprisingly $\mathbb{E}\xi_t \simeq x(t)$
- quasi-stationary distribution
  - support of limit distribution $\subset \{(b,s); b=0\}$ (washout)

    $\mathbb{P}(B_t = 0) > 0$ for all t

    $B_t \to 0$ a.s. as $t \to \infty$
  - $\exists$ quasi-stationary distribution
  - different time scales

logistic I

click here

logistic II

click here

logistic III

click here

conclusion

- advantages of the ODE model + more realistic model of extinction
- coupled with measurement models $\rightarrow$ statistical models (likelihood function)

F. Campillo, M. Joannides, I. Larramendy-Valverde. Stochastic modeling of the chemostat, *Ecological Modelling*, 222(15) :2676-2689, 2011.