MODELADO CON EDEs EN BIOLOGÍA

Formulación, Análisis y Simulación Numérica.

First day: modeling with SDEs in biology

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UQ

ODE + noise = Better Model

UQ

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Population growth

$$\frac{dN}{dt} = a(t)N(t) \qquad N_0 = N(0) = cte.$$

UQ

$ODE + noise = Better\ Model$

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$$a(t) = r(t) + \text{"}noise\text{"}$$

UQ

$$ODE + noise = Better\ Model$$

mm 40 60 80 100 120

Electric Circuits

$$L \cdot Q''(t) + R \cdot Q'(t) + \frac{1}{C} \cdot Q(t) = F(t)$$

$$Q(0) = Q_0$$

$$Q'(0) = I_0$$

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UQ

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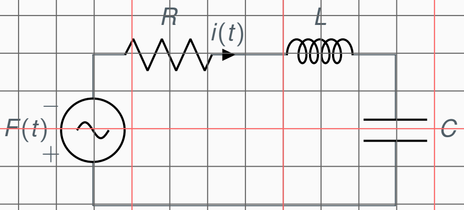

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UQ

$$ODE + noise = Better\ Model$$

Electric Circuits

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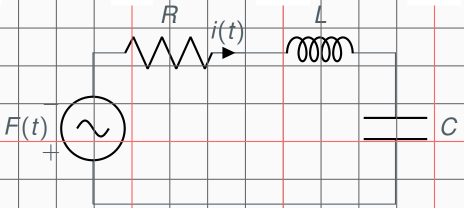

$$F(t) = G(t) + "noise"$$

To fix ideas

Example

$$dN(t) = aN(t)dt$$

Example

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Perturb in $[t, t + dt)$

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Perturb in $[t, t+dt)$

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Get a SDE

$$dN(t) = aN(t)dt + \sigma N(t)dB(t)$$

Example

$$dN(t) = aN(t)dt$$

Perturb in $[t, t + dt)$

$$adt \rightsquigarrow adt + \sigma dB(t)$$

Get a SDE

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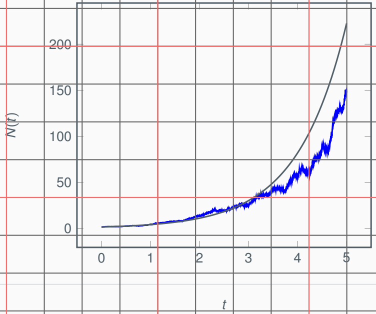

Some Important applications

- Finance
- Physics
- Chemistry
- Biology
- Epidemiology

Henston

$$dS_t = \mu S_t dt + \sqrt{V_t} S_t \left(\sqrt{1 - \rho^2} dW_t^{(1)} + \rho dW^{(2)} \right)$$

$$dV_t = \kappa(\lambda - V_t)dt + \theta \sqrt{V_t} dW_t^{(2)}$$

Hutzenthaler, M. and Jentzen, A. (2015).
Numerical approximations of stochastic differential equations with non-globally lipschitz continuous coefficients.
Memoirs of the American Mathematical Society, 236(1112).

Some Important applications

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Langevin

$$dX_t = -(\nabla U)(X_t)dt + \sqrt{2\varepsilon}dW_t$$

Hutzenthaler, M. and Jentzen, A. (2015).
Numerical approximations of stochastic differential equations with non-globally lipschitz continuous coefficients.
Memoirs of the American Mathematical Society, 236(1112).

Some Important applications

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Brusselator

$$dX_t = \left[\delta - (\alpha+1)X_t + Y_t X_t^2\right] dt + g_1(X_t) dW_t^{(1)}$$
$$dY_t = \left[\alpha X_t + Y_t X_t^2\right] dt + g_2(X_t) dW_t^{(2)}$$

Hutzenthaler, M. and Jentzen, A. (2015).
Numerical approximations of stochastic differential equations with non-globally lipschitz continuous coefficients.
Memoirs of the American Mathematical Society, 236(1112).

Some Important applications

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Lotka Volterra

$$
\begin{aligned}
dX_t &= (\lambda X_t - kX_t Y_t)dt + \sigma X_t dW_t \\
dY_t &= (kX_t Y_t - mY_t)dt
\end{aligned}
$$

Hutzenthaler, M. and Jentzen, A. (2015).
Numerical approximations of stochastic differential equations with non-globally lipschitz continuous coefficients.
Memoirs of the American Mathematical Society, 236(1112).

Some Important applications

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SIR

$$
\begin{aligned}
dS_t &= (-\alpha S_t I_t - \delta S_t + \delta)dt - \beta S_t I_t dW_t \\
dI_t &= (\alpha S_t I_t - (\gamma + \delta) I_t)dt + \beta S_t I_t dW_t \\
dR_t &= (\gamma I_t - \delta R_t)dt
\end{aligned}
$$

mm 120

Main objective

To present two of the common approaches in stochastic modeling with SDEs.

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Allen's approach

$$DTMC \to CTMC \to SDE$$

Stochastic perturbation

$$dN(t)/dt = aN(t)$$

$$adt \rightsquigarrow adt + \sigma dB(t)$$

$$dN(t) = aN(t)dt + \sigma N(t)dB(t)$$

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Table of contents

Environmental effects

- Extinction
- Outbreaks

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Why noise?

Environmental effects

- Extinction
- Outbreaks

Environmental Brownian noise suppresses explosions.

Mao, X., Marion, G., and Renshaw, E. (2002). **Environmental brownian noise suppresses explosions in population dynamics.** *Stochastic Processes and their Applications*, 97(1):95–110.

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Why noise?

Environmental effects

- Extinction
- Outbreaks

Noise color induces extinction

Ripa, J. and Lundberg, P. (1996).
Noise Colour and the Risk of Population Extinctions.
Proceedings of the Royal Society B: Biological Sciences, 263(1377):1751–1753.

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Why noise?

Environmental effects

- Extinction
- Outbreaks

$\mathscr{R}_0$: Endemic g.a.e. $\to$ periodic oscillations

Allen, L. and van den Driessche, P. (2013).
Relations between deterministic and stochastic thresholds for disease extinction in continuous- and discrete-time infectious disease models.
Mathematical Biosciences, 243(1):99–108.

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mm 40 60 80 100 120

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In Biology

- **DTMC, CTMC**
- Stochastic perturbation of parameters
- Mean reverting processes

DTMC + CTMC + ME → *SDE*

Allen, L. J. (2017).
A primer on stochastic epidemic models: Formulation, numerical simulation, and analysis.
Infectious Disease Modelling, 2(2):128–142.

Alternativas

mm 40 60 80 100 120

In Biology

- DTMC, CTMC
- **Stochastic perturbation of parameters**
- Mean reverting processes

$\varphi dt \rightsquigarrow \varphi dt + \sigma dB_t$

Gray, A., Greenhalgh, D., Hu, L., Mao, X., and Pan, J. (2011).
A Stochastic Differential Equation SIS Epidemic Model.
SIAM Journal on Applied Mathematics, 71(3):876–902.

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In Biology

- DTMC, CTMC
- **Stochastic perturbation of parameters**
- Mean reverting processes

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$\varphi dt \rightsquigarrow \varphi dt + F(x) dB_t$

Schurz, H. and Tosun, K. (2015).
Stochastic Asymptotic Stability of SIR Model with Variable Diffusion Rates.
Journal of Dynamics and Differential Equations, 27(1):69–82.

mm 40 60 80 100 120

In Biology

- DTMC, CTMC
- Stochastic perturbation of parameters
- Mean reverting processes

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$$d\varphi_t = (\varphi_e - \varphi_t)dt + \sigma_\varphi dBt$$

Allen, E. (2016).
Environmental variability and mean-reverting processes.
Discrete and Continuous Dynamical Systems - Series B, 21(7):2073–2089.

Formulation of SDE: *DTMC* $\to$ *CTMC* + *ME* $\to$ *SDE*

To fix ideas we recall the deterministic philosophy to formulate ODEs

- We study a process in a small interval of time Δt
- Describe the resulting information in Δt
- Letting $\Delta t \to 0$ gives a ODE

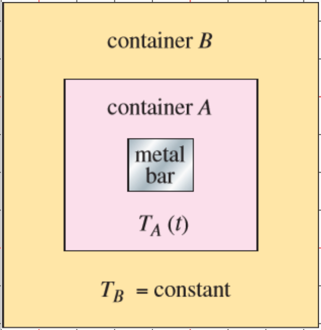
Newton's Cooling Law

$$T_A(t+\Delta t) - T_A(t) = \alpha(T_B - T_A(t))\Delta t$$

$$\frac{T_A(t+\Delta t) - T_A(t)}{\Delta t} = \alpha(T_B - T_A(t))$$

Letting $\Delta t \to 0$

$$\frac{dT_A(t)}{dt} = \alpha(T_B - T_A(t))$$



A stochastic analogy.

i) Formulate a discrete stochastic model for the dynamical system under study, which describe changes in a small time interval Δt

ii) Compute the expected value and covariance for the change in a small time Δ

iii) Letting $\Delta t \rightarrow 0$, the above information leads to the a CTMC

iv) Thus, we infer the SDE from the similarities in the forward backward Kolmogorov equation between the discrete and Continuous Markov Chain

Example: Formulation of a stochastic SIS model

Consider the deterministic SI model:

$$\frac{dS}{dt} = -\frac{\beta}{N} SI + (b+\gamma) I$$
$$\frac{dI}{dt} = \frac{\beta}{N} SI - (b+\gamma) I$$
$$N = S(t) + I(t)$$

Where N is constant and $S(t) = N - I(t)$.

$$\mathscr{R}_0 = \frac{\beta}{b+\gamma}$$

$$\mathscr{R}_0 \leq 1$$
$$\Rightarrow \lim_{t \to \infty} (S(t), N(t)) = (N, 0)$$

$$\mathscr{R}_0 > 1$$
$$\Rightarrow \lim_{t \to \infty} (S(t), N(t)) = (N, 0)$$

Consider the process $\{\mathscr{I}_t\}_{t=0}^{\infty}$ with time discrete and space of states $\{0,1,\cdots,N\}$.

$$p_{ji}(\Delta t) := \begin{cases} \frac{\beta i(N-i)}{N}\Delta t, & j = i+1 \\ (b+\gamma)i\Delta t, & j = i-1 \\ 1 - \left[\frac{\beta i(N-i)}{N} + (b+\gamma)i\right]\Delta t, & j = i, \\ 0 & \text{otherwise} \end{cases}$$

(H-1) $\{\mathscr{I}_t\}_{t=0}^{\infty}$ define

$$p_i(t) := \mathbb{P}[\mathscr{I}(t) = i]$$

$$i = 0,1,2\ldots,$$

$$t = 0, \Delta t, 2\Delta t, \cdots,$$

where Δt is sufficient small s.t.

$$\max_{i\in\{1,\ldots,N\}} \{[b(i)+d(i)]\Delta t\} \leq 1$$

(H-2) Markov property

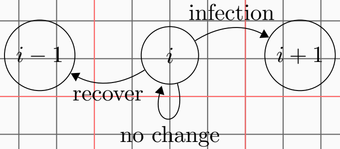
$$\mathbb{P}\left[I_{t+\Delta t} | I_0, I_{\Delta t}, \cdots, I_t\right] = \mathbb{P}\left[I_{t+\Delta t} | I_t\right]$$

(H-3) The unique transitions with positive probability

$$p_{ji}(t+\Delta t) = \mathbb{P}\left[I_{t+\Delta t} = j | I_t = i\right]$$

are

$$i \to i+1, \; i \to i-1, \; i \to i$$



Example: Formulation of a stochastic SIS model

Letting

$$b(i) := \frac{\beta i(N-i)}{N}\Delta t$$

$$d(i) := (b+\gamma) i \Delta t$$

FKE

$$\begin{aligned} p_i(t+\Delta t) &= p_{i-1}(t) b(i-1)\Delta t \\ &+ p_{i+1}(t) d(i+1)\Delta t \\ &+ p_i(t)(1-[b(i)+d(i)]\Delta t) \end{aligned}$$

Thus $P(\Delta t) =$

$$\begin{pmatrix} 1 & d(1)\Delta t & 0 & \cdots & 0 & 0 \\ 0 & 1-(b+d)(1)\Delta t & d(2)\Delta t & \cdots & 0 & 0 \\ 0 & b(1)\Delta t & 1-(b+d)(2)\Delta t & \cdots & 0 & 0 \\ 0 & 0 & b(2)\Delta t & \cdots & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & d(N-1)\Delta t & 0 \\ 0 & 0 & 0 & \cdots & 1-(b+d)(N-1)\Delta t & d(N)\Delta t \\ 0 & 0 & 0 & \cdots & d(N-1)\Delta t & 1-d(N)\Delta t \end{pmatrix}$$

$$p(t+\Delta t) = P(\Delta t) p(t) = P^{n+1}(\Delta t) p(0), \qquad t = n\Delta t$$

Expected Value of the SIS-DTMC

$$
\begin{aligned}
\mathbb{E}(I_{t+\Delta t}) &= \sum_{i=0}^{N} i p_i(t+\Delta t) \\
&= \sum_{i=0}^{N} i p_{i-1}(t) b(i-1)\Delta t + \sum_{i=0}^{N-1} i p_{i+1}(t) d(i+1)\Delta t \\
&+ \sum_{i=0}^{N} i p_i(t)\Delta t - \sum_{i=0}^{N} i p_i(t) b(i)\Delta t - \sum_{i=0}^{N} i p_i(t) d(i)\Delta t
\end{aligned}
$$

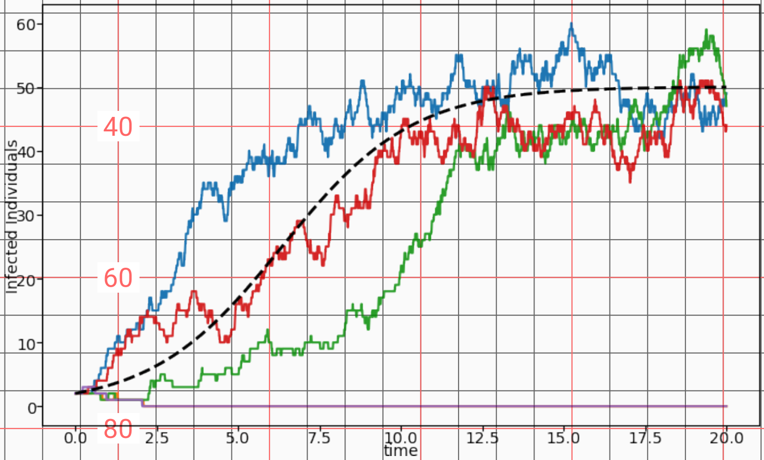
$$
\begin{aligned}
\mathbb{E}(I_{t+\Delta t}) = \mathbb{E}(I_t) &+ \sum_{i=1}^{N} p_{i-1}(t) \frac{\beta(i-1)(N-[i-1])}{N}\Delta t \\
&- \sum_{i=0}^{N-1} p_{i+1}(t)(b+\gamma)(i+1)\Delta t \\
&= \mathbb{E}(I_t) + [\beta-(b+\gamma)]\Delta t \mathbb{E}(I_t) - \frac{\beta}{N}\Delta t \underbrace{\mathbb{E}(I_t^2)}_{\geq \mathbb{E}^2(I_t)}
\end{aligned}
$$

$$\frac{\mathbb{E}(I_{t+\Delta t}) - \mathbb{E}(I_t)}{\Delta t} \leq [\beta - (b+\gamma)]\mathbb{E}(I_t) - \frac{\beta}{N}\mathbb{E}^2(I_t)$$

$$\begin{aligned} \frac{d\mathbb{E}(I_t)}{dt} &\leq [\beta - (b+\gamma)]\mathbb{E}(I_t) - \frac{\beta}{N}\mathbb{E}^2(I_t) \\ &= \frac{\beta}{N}[N - \mathbb{E}(I_t)]\mathbb{E}(I_t) - (b+\gamma)\mathbb{E}(I_t) \end{aligned}$$

$$\boxed{\frac{d\mathbb{E}(I_t)}{dt} \leq \frac{\beta}{N}\mathbb{E}(S_t)\mathbb{E}(I_t) - (b+\gamma)\mathbb{E}(I_t)}$$

$N = 100$, $\Delta t = 0.01$, $\beta = 1$,
$b = 0.25$ $\gamma = 0.25$



$\mathscr{R}_0 = 2$,
$\bar{I} = 50$

$$\boxed{\begin{aligned} &FKE : \frac{dp}{dt} = Qp \\ &p(t) = (p_0(t), \dots, p_N(t)) \end{aligned}}$$

$$Q = \begin{pmatrix} 0 & d(1) & 0 & \dots & 0 \\ 0 & -[b(1)+d(1)] & d(2) & \dots & 0 \\ 0 & b(1) & -[b(2)+d(2)] & \dots & 0 \\ 0 & 0 & b(2) & \dots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & \dots & d(N) \\ 0 & 0 & 0 & \dots & -d(N) \end{pmatrix}$$

Results that

$$\lim_{t \to \infty} p(t) = (1, 0, \dots, 0)^{\top}$$

and

$$Q = \lim_{\Delta t \to 0} \frac{P(\Delta t) - I}{\Delta t}$$

Let

$$\{I_t\}_{t>0},$$
$$p_i(t) = \mathbb{P}[I_t = i].$$

Thus, the Markov porperty becomes in

$$\mathbb{P}\left[I_{t_{n+1}} \middle| I_{t_0}, \cdots, I_{t_n}\right] = \mathbb{P}\left[I_{t_{n+1}} \middle| I_{t_n}\right]$$
$$\text{for all } t_0 < t_1 < \cdots < t_n$$

$$p_{ji}(\Delta t) := \begin{cases} \frac{\beta i(N-i)}{N}\Delta t + o(\Delta t), & j = i+1 \\ (b+\gamma)i\Delta t + o(\Delta t), & j = i-1 \\ 1 - \left[\frac{\beta i(N-i)}{N} + (b+\gamma)i\right]\Delta t + o(\Delta t), & j = i \\ o(\Delta t) & \text{otherwise} \end{cases}$$

$$\lim_{t\to\infty} \frac{o(\Delta t)}{\Delta t} = 0$$

Using the notation for birth and death processes, we have

$$p_{ij}(\Delta t) := \begin{cases} b(i)\Delta t + o(\Delta t), & j = i+1 \\ d(i)\Delta t + o(\Delta t), & j = i-1 \\ 1 - [b(i) + d(i)]\,\Delta t + o(\Delta t), & j = i \\ 0 & \text{otherwise} \end{cases}$$

Assuming $\mathbb{P}[I_0 = i_0] = 1$, then

$$\begin{aligned} p_i(t+\Delta t) =& p_{i-1}(t) b(i-1)\Delta t \\ &+ p_{i+1}(t) d(i+1)\Delta t \\ &+ p_i(t)[1 - (b(i) + d(i))]\Delta t + o(\Delta t) \\ i =& 1, 2, \dots, N \end{aligned}$$

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