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# MODELADO CON EDEs EN BIOLOGÍA

Formulación, Análisis y Simulación Numérica.

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**First day: modeling with SDEs in biology**

Saúl Díaz Infante Velasco

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CONACYT-UNIVERSIDAD de SONORA, Cimat, Guanajuato Gto

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UQ

*ODE + noise = Better Model*

UQ

*ODE + noise = Better Model*

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Population growth

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

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UQ

*ODE + noise = Better Model*

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Population growth

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

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

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UQ

*ODE + noise = Better Model*

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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

*ODE + noise = Better Model*

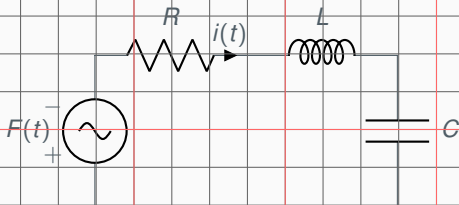
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Electric Circuits

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

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UQ

ODE + noise = Better Model

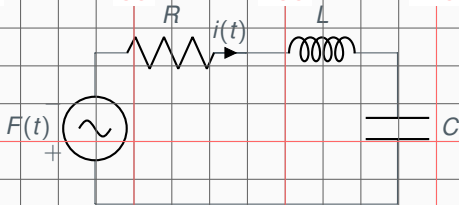
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Electric Circuits

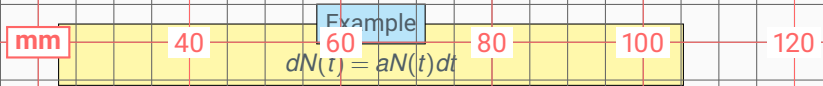
$$L \cdot Q''(t) + R \cdot Q'(t) + \frac{1}{C} \cdot Q(t) = F(t)$$

$$Q(0) = Q_0$$

$$Q'(0) = I_0$$

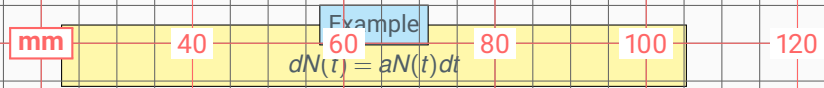


$$F(t) = G(t) + \text{"noise"}$$





# To fix ideas



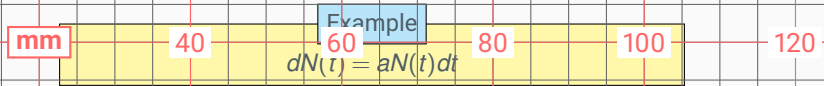
Perturb in  $[t, t + dt)$

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# To fix ideas



Perturb in  $[t, t + dt)$

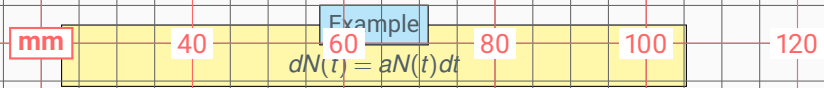
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$$adt \rightsquigarrow adt + \sigma dB(t)$$

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# To fix ideas



Perturb in  $[t, t + dt)$

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

Get a SDE

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

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# To fix ideas

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

Perturb in  $[t, t + dt)$

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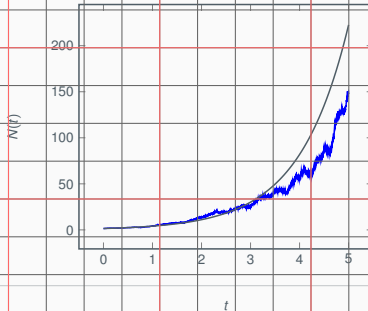
$$adt \rightsquigarrow adt + \sigma dB(t)$$

Get a SDE

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

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# Some Important applications

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Henston

- Finance

- Physics
- Chemistry

- Biology
- Epidemiology

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

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

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Hutzenthaler, M. and Jentzen, A. (2015).

**Numerical approximations of stochastic differential equations with non-globally lipschitz continuous coefficients.**

*Mem. of the American Mathematical Society*, 236(1112).

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# Some Important applications

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Langevin

- Finance

- **Physics**

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- Chemistry

- Biology

- Epidemiology

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

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Hutzenthaler, M. and Jentzen, A. (2015).

**Numerical approximations of stochastic differential equations with non-globally lipschitz continuous coefficients.**

*Annals of the American Mathematical Society*, 236(1112).

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# Some Important applications

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Brusselator

- Finance
- Physics
- Chemistry

- Biology
- Epidemiology

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

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

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Hutzenthaler, M. and Jentzen, A. (2015).

**Numerical approximations of stochastic differential equations with non-globally lipschitz continuous coefficients.**

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# Some Important applications

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Lotka Volterra

- Finance
- Physics
- Chemistry
- **Biology**

• Epidemiology

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

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Hutzenthaler, M. and Jentzen, A. (2015).

**Numerical approximations of stochastic differential equations with non-globally lipschitz continuous coefficients.**

*Annals of the American Mathematical Society*, 236(1112).

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# Some Important applications

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SIR

- Finance
- Physics
- Chemistry
- Biology
- Epidemiology

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

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## Main objective

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

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## Allen's approach

$DTMC \rightarrow CTMC \rightarrow SDE$

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## Stochastic perturbation

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

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

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

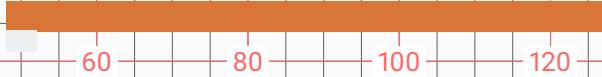
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# Why noise?

## 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

$\mathcal{R}_0$ : Endemic g.a.e.  $\rightarrow$  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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## In Biology

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

**DTMC + CTMC + ME  $\rightarrow$  SDE**



Allen, L. J. (2017).

**A primer on stochastic epidemic models: Formulation, numerical simulation, and analysis.**

*Infectious Disease Modelling*, 2(2):128–142.

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## 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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# Alternativas

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## In Biology

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

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



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.

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## In Biology

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

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



Allen, E. (2016).

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

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# Formulation of SDE: $DTMC \rightarrow CTMC + ME \rightarrow SDE$

To fix ideas we recall the deterministic philosophy to formulate ODEs

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

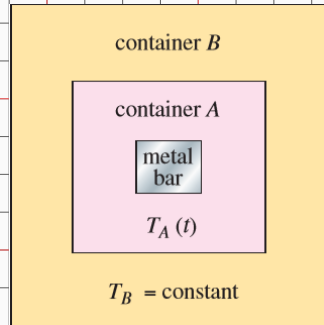
## Newton's Cooling Law

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

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

Letting  $\Delta t \rightarrow 0$

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



A stochastic analogy.

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- i) Formulate a discrete stochastic model for the dynamical system under study, which describe changes in a small time interval  $\Delta t$
- ii) Compute the expected value and covariance for the change in a small time  $\Delta$
- 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

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# 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  $S(t) = N - I(t)$ .

$$\begin{aligned} R_0 &= \frac{\beta}{b + \gamma} \\ R_0 &\leq 1 \\ &\Rightarrow \lim_{t \rightarrow \infty} (S(t), I(t)) = (N, 0) \\ R_0 &> 1 \\ &\Rightarrow \lim_{t \rightarrow \infty} (S(t), I(t)) = (N, 0) \end{aligned}$$

# Example: Formulation of a stochastic SIS model

Consider the process  $\{\mathcal{I}_t\}_{t=0}^{\infty}$  with time discrete and space of states

$\{0, 1, \dots, N\}$

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

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

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

where  $\Delta t$  is sufficient small s.t.

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

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

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

(H-2) Markov property

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

(H-3) The unique transitions with positive probability

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

are

$$i \rightarrow i+1, i \rightarrow i-1, i \rightarrow i$$



# 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

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

Thus  $P(\Delta t) =$

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

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



# Expected Value of the SIS-DTMC

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

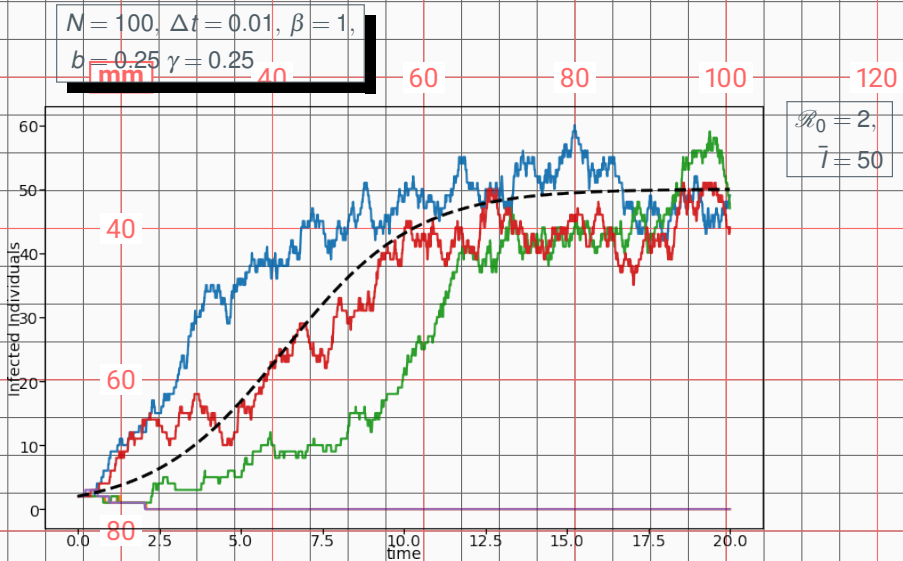
# Expected Value of the SIS-DTMC

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

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

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

# Example: Formulation of a stochastic SIS model



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$$\text{FKE: } \frac{dp}{dt} = Qp$$

$$p(t) = (p_1(t), \dots, p_N(t))$$

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

Result: 60 at

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

and

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

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# Formulating a SIS-CTMC

Let

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$$\{I_t\}_{t \geq 0},$$

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

Thus, the Markov property becomes in

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$$\mathbb{P}[I_{t_{n+1}} | I_{t_0}, \dots, I_{t_n}] = \mathbb{P}[I_{t_{n+1}} | I_{t_n}]$$

for all  $t_0 < t_1 < \dots < t_n$

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

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

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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