Continuous Time Markov Chains. Applications in Bioinformatics

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Outline

- Definitions
- Steady-state distribution
- Examples
- Alternative presentation of CTMC: *embedded DTMC* of a CTMC
- Applications in Bioinformatics

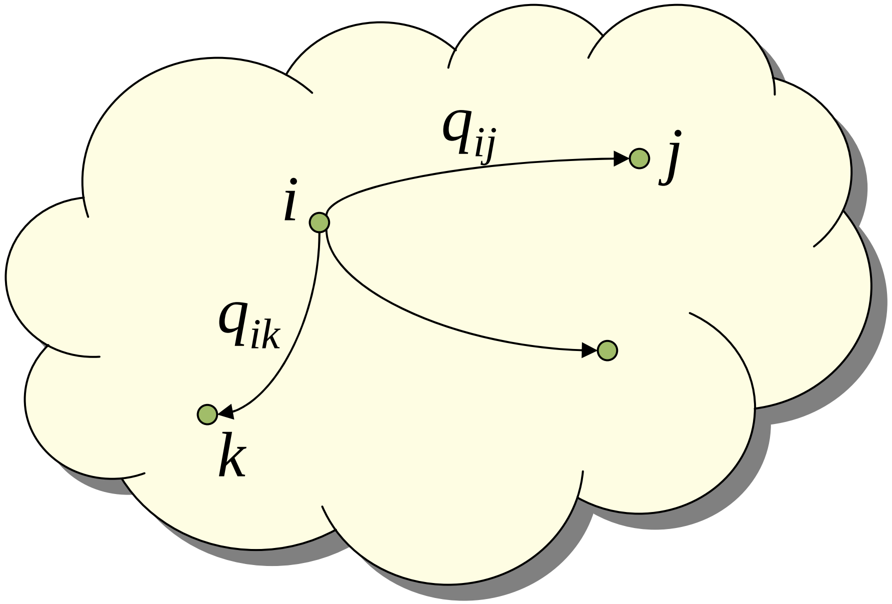
Definitions

- Remember DTMC
  - p_{ij} is the transition probability from i to j over one time slot
  - The time spent in a state is geometrically distributed
    - Result of the Markov (memoryless) property
  - When there is a jump from state i, it goes to state j with probability

$$\frac{p_{ij}}{\sum_{k \neq i} p_{ik}}$$

Definitions

- Continuous time version



  - q_{ij} is the **transition rate** from state *i* to state *j*

Definitions

- Formally:
  - A CTMC is a stochastic process $\{X(t) \mid t \geq 0, t \in IR\}$ s.t. for all $t_0, \ldots, t_{n-1}, t_n, t \in IR$, $0 \leq t_0 < \ldots < t_{n-1} < t_n < t$, for all $n \in IN$

$$P(X(t)=x \mid X(t_n)=x_n, X(t_{n-1})=x_{n-1}, \ldots, X(t_0)=x_0)=$$
$$=P(X(t)=x \mid X(t_n)=x_n)$$

  - Alternative (equivalent) definition:
    $\{X(t) \mid t \geq 0, t \in IR\}$ s.t. for all $t,s \geq 0$

$$P(X(t+s)=x \mid X(t)=x_t, X(u), 0 \leq u \leq t)=$$
$$=P(X(t+s)=x \mid X(t)=x_t)$$

Definitions

- Homogeneity
  - We are considering discrete state (sample) space, then we denote

$$p_{ij}(t,s) = P(X(t+s)=j \mid X(t)=i), \text{ for } s > 0.$$

  - A CTMC is called (time-)homogeneous if

$$p_{ij}(t,s) = p_{ij}(s) \quad \text{for all } t \geq 0$$

Definitions

- Time spent in a state (*sojourn time*):
  - Markov property and time homogeneity imply that if at time *t* the process is in state *j*, the time remaining in state *j* is independent of the time already spent in state *j* : memoryless property.

    Let *S* be the random variable "time spent in state *j*".

$$
\begin{aligned}
P(S > t+s \mid S > t) &= P(X_{t+u} = j, 0 \leq u \leq s \mid X_u = j, 0 \leq u \leq t) \\
&\quad \text{where S} = \text{time spent in state } j \\
&\quad \text{state } j \text{ entered at time } 0 \\
&= P(X_{t+u} = j, 0 \leq u \leq s \mid X_t = j) \text{ by MP} \\
&= P(X_u = j, 0 \leq u \leq s \mid X_0 = j) \text{ by T.H.} \\
&= P(S > s)
\end{aligned}
$$

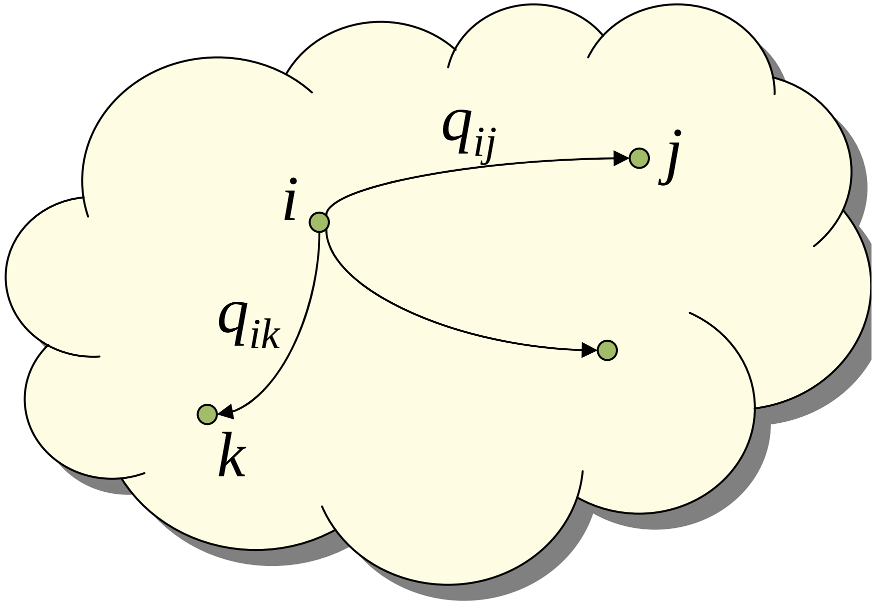
$\Rightarrow$ time spent in state *j* is exponentially distributed.

$\boxed{\text{Sojourn times of a CTMC are exponentially distributed.}}$

Definitions

- Transition rates:
  - In time-homogeneous CTMC, $p_{ij}(s)$ is the probability of jumping from i to j during an interval time of duration s.
  - Therefore, we define the instantaneous transition rate from state i to state j as:

$$q_{ij} = \lim_{\Delta t \to 0} \frac{p_{ij}(\Delta t)}{\Delta t}$$



  - And the exit rate from state i as $-q_{ii}$

$$q_{ii} = -\sum_{j \neq i} q_{ij} = \lim_{\Delta t \to 0} \frac{p_{ii}(\Delta t) - 1}{\Delta t}$$

  - $Q = [q_{ij}]$ is called **infinitesimal generator matrix** (or transition rate matrix or Q *matrix*)

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Steady-state distribution

- Kolmogorov differential equation:

  Denote the distribution at instant t: $\pi_i(t) = P(X(t)=i)$

  And denote in matrix form: $P(t) = [p_{ij}(t)]$

  Then $\pi(t) = \pi(u)P(t-u)$, for $u < t$
  (we omit vector transposition to simplify notation)

  Substituting $u = t - \Delta t$ and substracting $\pi(t-\Delta t)$:

  $\pi(t) - \pi(t-\Delta t) = \pi(t-\Delta t)\,[P(\Delta t) - I]$, with I the identity matrix

  Dividing by Δt and taking the limit $\dfrac{d}{dt}\pi(t) = \pi(t)\lim_{\Delta t \to 0}\dfrac{P(\Delta t) - I}{\Delta t}$

  Then, by definition of $Q = [q_{ij}]$, we obtain the
  Kolmogorov differential equation

$$\frac{d}{dt}\pi(t) = \pi(t)\,Q$$

Steady-state distribution

- Since also $\pi(t)e = 1$, with $e = (1,1,\ldots,1)$

  If the following limit exists

  $$\lim_{t\to\infty} \pi(t)$$

  then taking the limit of Kolmogorov differential equation we get the equations for the steady-state probabilities:

$$\boxed{\begin{aligned} \pi Q &= 0 \\ \pi e &= 1 \end{aligned}}$$

(*balance* equations)

(*normalizing* equation)

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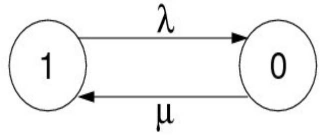
Examples

- Example 1: A 2-state CTMC
  - Consider a simple two-state CTMC



  - The corresponding Q matrix is given by

$$Q = \begin{bmatrix} -\mu & \mu \\ \lambda & -\lambda \end{bmatrix}$$

  - The Kolmogorov differential equation yields:

$$\frac{d}{dt}\pi_0(t) = -\mu\pi_0(t) + \lambda\pi_1(t)$$

$$\frac{d}{dt}\pi_1(t) = \mu\pi_0(t) - \lambda\pi_1(t)$$

$$\pi_0(t) + \pi_1(t) = 1$$

  - Given that $\pi_1(0) = 1$, we get the transient solution:

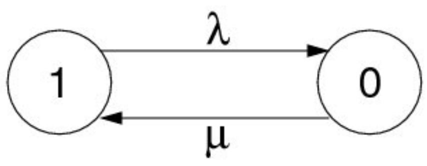
$$\pi_1(t) = \frac{\mu}{\lambda+\mu} + \frac{\lambda}{\lambda+\mu} e^{-(\lambda+\mu)t}$$

$$\pi_0(t) = \frac{\lambda}{\lambda+\mu} - \frac{\lambda}{\lambda+\mu} e^{-(\lambda+\mu)t}$$

Examples

– And the steady-state solution comes from $\pi Q = 0$; $\pi e = 1$:

$$\lambda \pi_1 - \mu \pi_0 = 0$$
$$\mu \pi_0 - \lambda \pi_1 = 0$$
$$\pi_0 + \pi_1 = 1$$



balance eq.

– We get:

$$\pi_0 = \frac{\lambda}{\lambda+\mu}; \qquad \pi_1 = \frac{\mu}{\lambda+\mu}$$

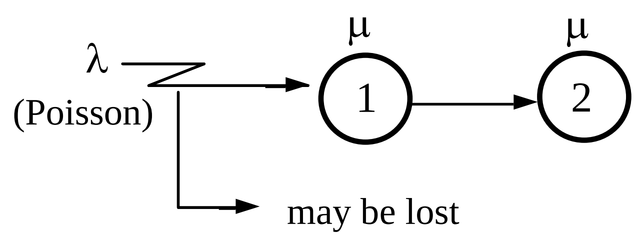
- Which can also be obtained by taking the limits as t → ∞ of the equations for $\pi_1(t)$ and $\pi_0(t)$.

$$\pi_1 = \lim_{t\to\infty} \pi_1(t) = \lim_{t\to\infty} \frac{\mu}{\lambda+\mu} + \frac{\lambda}{\lambda+\mu} e^{-(\lambda+\mu)t} = \frac{\mu}{\lambda+\mu}$$

$$\pi_0 = \lim_{t\to\infty} \pi_0(t) = \lim_{t\to\infty} \frac{\lambda}{\lambda+\mu} - \frac{\lambda}{\lambda+\mu} e^{-(\lambda+\mu)t} = \frac{\lambda}{\lambda+\mu}$$

Examples

- Example 2:
  A simple open system with loss



  - Works enter to the system with exponentially distributed (parameter λ) interarrival time (Poisson process)
  - The service time in both processing stations is exponentially distributed with rate μ
  - If a work ends in station 1 when station 2 is busy, station 1 is blocked
  - If station 1 is busy or blocked when a work arrives, arriving work is lost
  - Questions:
    - proportion of lost works?
    - mean number of working stations?
    - mean number of works in the system?

Examples

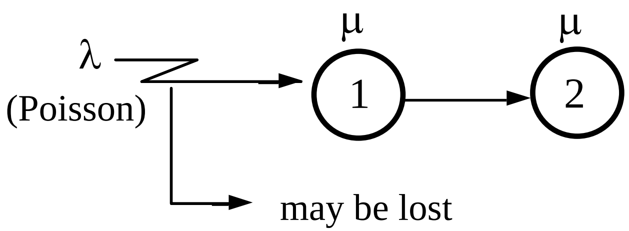
– The set of states of the system:

S={(0,0), (1,0), (0,1), (1,1), (b,1)}

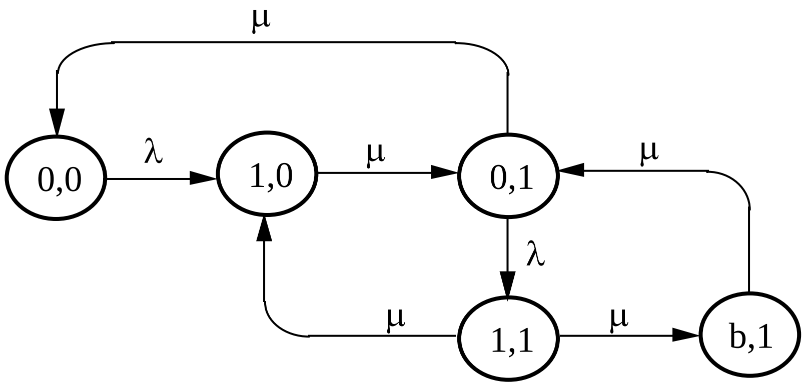
0 → empty station

1 → working station

b → blocked station



State transition diagram:



Infinitesimal generator matrix:

$$Q = \begin{array}{c} 00 \\ 10 \\ 01 \\ 11 \\ b1 \end{array} \begin{bmatrix} -\lambda & \lambda & 0 & 0 & 0 \\ 0 & -\mu & \mu & 0 & 0 \\ \mu & 0 & -(\lambda+\mu) & \lambda & 0 \\ 0 & \mu & 0 & -2\mu & \mu \\ 0 & 0 & \mu & 0 & -\mu \end{bmatrix}$$

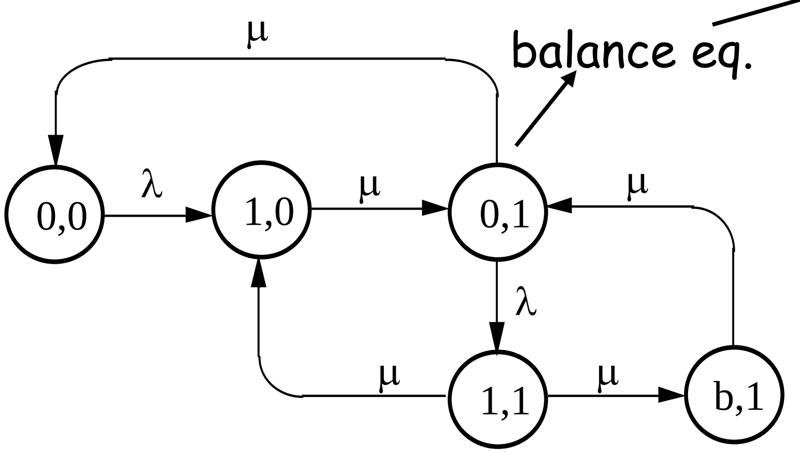
Examples

– Steady-state solution:

$$\left.\begin{aligned}\pi Q &= 0\\ \pi e &= 1\end{aligned}\right\} \longrightarrow \left|\begin{aligned}&\lambda\pi_{00} = \mu\pi_{01}\\ &\lambda\pi_{00} + \mu\pi_{11} = \mu\pi_{10}\\ &\mu\pi_{10} + \mu\pi_{b1} = (\lambda+\mu)\pi_{01}\\ &\lambda\pi_{01} = 2\mu\pi_{11}\\ &\mu\pi_{11} = \mu\pi_{b1}\end{aligned}\right.$$

$$\pi_{00} + \pi_{10} + \pi_{01} + \pi_{11} + \pi_{b1} = 1$$

balance eq.



$$\Rightarrow \pi = \left(\frac{2}{\Delta}, \frac{2\rho+\rho^2}{\Delta}, \frac{2\rho}{\Delta}, \frac{\rho^2}{\Delta}, \frac{\rho^2}{\Delta}\right) \quad \text{where } \rho = \frac{\lambda}{\mu} \quad \text{and} \quad \Delta = 3\rho^2 + 4\rho + 2$$

Examples

- Proportion of lost works?
  - Is the probability of the event "when a new work arrives, the first station is non-empty", i.e.:

$$\pi_{10}+\pi_{11}+\pi_{b1}=\frac{3\rho^2+2\rho}{3\rho^2+4\rho+2}$$

- Mean number of working stations?
  - In state (0,0) there is no working station and in state (1,1) there are two; in the rest of states there is only one, thus

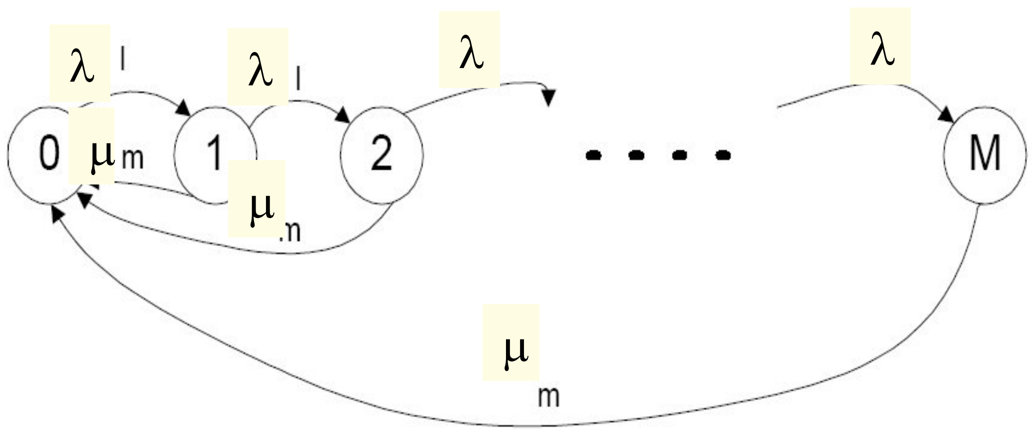
$$B=\pi_{01}+\pi_{10}+\pi_{b1}+2\pi_{11}=\frac{4\rho^2+4\rho}{3\rho^2+4\rho+2}$$

- Mean number of works in the system?
  - In state (0,0) there is no one; in states (1,1) and (b,1) there are two and in the rest there is only one, thus

$$L=\pi_{01}+\pi_{10}+2\pi_{b1}+2\pi_{11}=\frac{5\rho^2+4\rho}{3\rho^2+4\rho+2}$$

Examples

- Example 3: I/O buffer with limited capacity
  - Records arrive according to a Poisson process (rate λ)
  - Buffer capacity: M records
  - Buffer cleared at times spaced by intervals which are exponentially distributed (parameter μ) and independent of arrivals



Examples

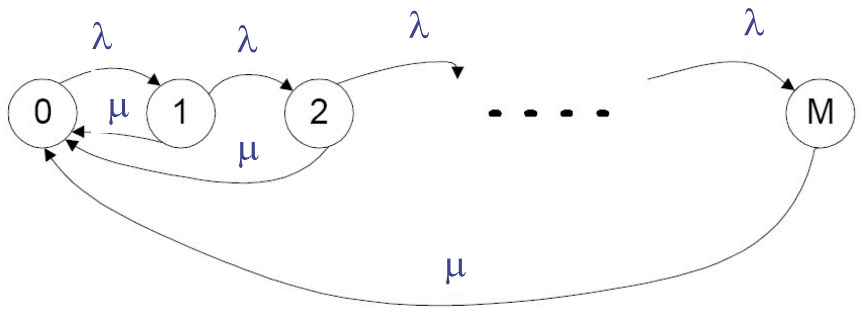
– Steady-state solution:

$$\lambda\pi_0 = \mu(\pi_1 + \cdots + \pi_M)$$

$$(\lambda+\mu)\pi_i = \lambda\pi_{i-1},\ 1 \le i \le M-1$$

$$\mu\pi_M = \lambda\pi_{M-1}$$

$$\pi_0 + \cdots + \pi_M = 1$$



$$\Rightarrow$$

$$\pi_i = \left(\frac{\lambda}{\lambda+\mu}\right)^i \frac{\mu}{\lambda+\mu},\ 0 \le i \le M-1$$

$$\pi_M = \left(\frac{\lambda}{\lambda+\mu}\right)^M$$

Thus, for example, the mean number of records in the buffer in steady-state:

$$B = M\alpha^M + \sum_{i=0}^{M-1} i\alpha^i \frac{\mu}{\lambda+\mu}, \quad \text{where } \alpha = \frac{\lambda}{\lambda+\mu}$$

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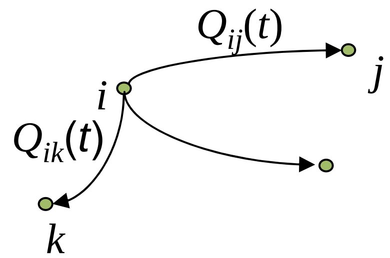
Semi-Markov processes

- Also called Markov renewal processes
  - Generalization of CTMC with arbitrary distributed sojourn times
  - As in the case of CTMC, they can be used for obtaining both steady-state distribution and transient distribution

Semi-Markov processes

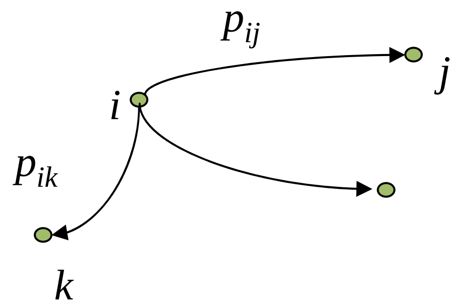
- (Time homogeneous) Semi-Markov process:

Distribution, from *i* to *j* in time *t*:



$$
\begin{aligned}
Q_{ij}(t) &= Pr(X_{n+1}=j, T_{n+1}-T_n \le t | X_n = i) \\
&= p_{ij} H_{ij}(t)
\end{aligned}
$$

Transition probability from *i* to *j*:



$$p_{ij} = \lim_{t\to\infty} Q_{ij}(t) = Pr(X_{n+1} = j | X_n = i)$$

Sojourn time distribution in state *i* when the next state is *j*:

$$H_{ij}(t) = Pr(T_{n+1} - T_n \le t | X_{n+1} = j, X_n = i)$$

Transition prob. matrix of the embedded Discrete Time Markov Chain: $P = [p_{ij}]$

Sojourn time distribution in state *i* regardless of the next state:

$$D_i(t) = Pr(T_{n+1} - T_n \le t | X_n = i) = \sum_{j=1}^{m} Q_{ij}(t)$$

Semi-Markov processes

- Steady-state analysis
  - Build transition probability matrix, *P*, and mean residence (sojourn) time vector, $\overline{D}$.
  - From them, compute steady-state distribution:

$$\tilde{\pi} = [\tilde{\pi}_1, ..., \tilde{\pi}_m] \qquad \tilde{\pi} = \tilde{\pi}P, \ \sum_{i=1}^{m} \tilde{\pi}_i = 1$$

Steady-state of embedded DTMC

$$\bar{D} = [\bar{d}_i]$$

Mean residence time vector

$$\pi = [\pi_i] \qquad \pi_i = \frac{\bar{d}_i \tilde{\pi}_i}{\sum_{j=1}^{m} \bar{d}_j \tilde{\pi}_j}$$

Steady-state distribution of semi-Markov process

Embedded DTMC of a CTMC

- CTMC can be seen as a particular case of semi-Markov process when sojourn time distributions are exponential
- In other words, if we consider a DTMC with null diagonal elements and we add exponentially distributed soujourn times in the states, we get a CTMC.

this is called the
Embedded DTMC
of the CTMC

CTMC = DTMC *(where to move)* +
+ exponential holding times *(when to move)*

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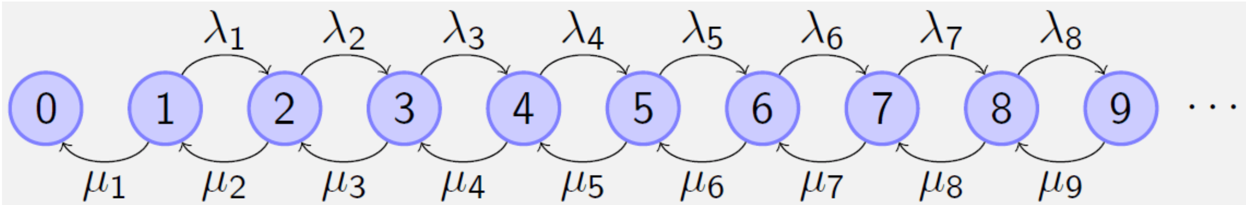
Simple population size model

- We model the size of the population (n = 0,1,2…)



λ_n is the birth rate in a population of size n; μ_n is the death rate
0 is an absorbing state

A case of relevance to population dynamics is the choice:

$\lambda_n = n\lambda$ and $\mu_n = n\mu$, for constants λ and μ.

We can ask:

What is the extinction probability starting from state k?
(i.e., probability of being absorbed into state 0 (ever))

If extinction is certain, what is the mean time to extinction?

Extinction probability

- Let u_k be the probab. of absorption at 0, starting from state k.
- Then, since the first step away from k is either to k+1, with probability $\lambda_k / (\lambda_k + \mu_k)$ or to $k-1$, with probability $\mu_k / (\lambda_k + \mu_k)$,

$$u_k = \frac{\lambda_k}{\lambda_k + \mu_k} u_{k+1} + \frac{\mu_k}{\lambda_k + \mu_k} u_{k-1}, \qquad k \geq 1$$

  and $u_0 = 1$.
- Let $\rho_0 = 1$ and $\rho_j = (\mu_j / \lambda_j)\, \rho_{j-1}$ for $j \geq 1$.
  - If $\Sigma_j\, \rho_j = \infty$ then $u_k = 1$ for all k (extinction is certain).
  - If $\Sigma_j\, \rho_j$ is finite then

$$u_n = \left(1 + \sum_{i=1}^{\infty} \rho_i\right)^{-1} \sum_{i=n}^{\infty} \rho_i.$$

Mean time to extinction

- Let w_k be the mean time to absorption at 0, starting from state k. By first-step analysis

$$w_k = \frac{\lambda_k}{\lambda_k + \mu_k} w_{k+1} + \frac{\mu_k}{\lambda_k + \mu_k} w_{k-1} + \frac{1}{\lambda_k + \mu_k}, \qquad k \geq 1$$

and $w_0 = 0$.

  - If $\displaystyle\sum_{i=1}^{\infty} \frac{1}{\lambda_i \rho_i} = \infty$ then the mean time to absorption is infinite.
  - If $\displaystyle\sum_{i=1}^{\infty} \frac{1}{\lambda_i \rho_i}$ is finite then

$$w_n = \sum_{i=1}^{\infty} \frac{1}{\lambda_i \rho_i} + \sum_{k=1}^{n-1} \rho_k \sum_{j=k+1}^{\infty} \frac{1}{\lambda_j \rho_j}.$$

Many other applications…

- As embedded analytical model for more abstract modelling paradigms:
  - birth-death processes and population dynamics
  - queueing processes and queueing networks
  - stochastic Petri nets
  - stochastic process algebras…