LECTURE #4

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SOLVING THE MASTER EQUATION – PART 1

Problem

- Given the master equations (MEs)

$$\frac{\partial p_Z(\mathbf{z};t)}{\partial t} = \sum_{m=1}^{M} \left\{ a_m(\mathbf{z}-\mathbf{e}_m) p_Z(\mathbf{z}-\mathbf{e}_m;t) - a_m(\mathbf{z}) p_Z(\mathbf{z};t) \right\}, \quad t>0$$

$$\frac{\partial p_X(\mathbf{x};t)}{\partial t} = \sum_{m=1}^{M} \left\{ \pi_m(\mathbf{x}-\mathbf{s}_m) p_X(\mathbf{x}-\mathbf{s}_m;t) - \pi_m(\mathbf{x}) p_X(\mathbf{x};t) \right\}, \quad t>0$$

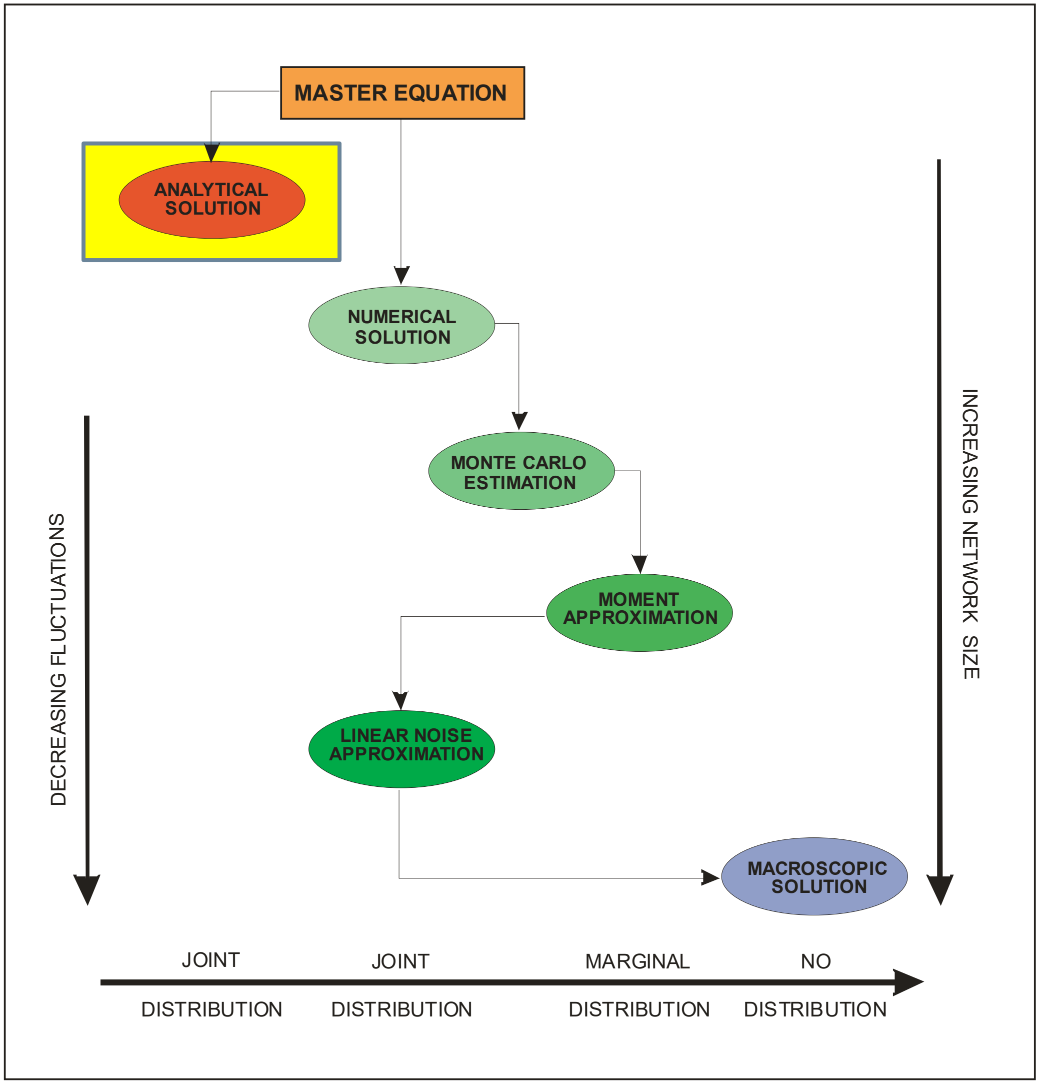
  we want to calculate the probabilities $p_X(\mathbf{x};t)$ and $p_Z(\mathbf{z};t)$, for every $t>0$.

- This is a <u>difficult</u> task in general !!

Important Theoretical Result

- Markovian reaction networks with mass action propensities have been theoretically shown to perform Turing universal computations with an error that becomes zero only at the thermodynamic limit (at which no randomness is present).
- This amazing result turns out to be one of the most profound weaknesses of Markovian reaction networks: there will be no single analytical or even computational method capable of calculating the exact solution of the underlying master equation in complete generality away from the thermodynamic limit using finite resources.
- This is a consequence of the fact that any problem that is not computable by the universal machine is considered not to be computable by any machine.
- Consequently, developing accurate and computationally feasible techniques for studying the dynamic behavior of large nonlinear Markovian reaction networks is still the most important and challenging problem.

Available Methods



Analytical Solution

- Possible only in some simple cases.
- An analytical solution can also be derived in the case of a linear reaction network (a network with linear propensity functions).
- The probability distribution $p_X(\mathbf{x};t)$ of the population process in a linear reaction network can be expressed as the convolution of multinomial and Poisson distributions with time-dependent parameters that evolve according to well-defined systems of first-order linear differential equations.

Analytical Solution

- **<u>Example (birth and death process – closed system)</u>**
  - Consider the following <u>linear</u> reaction network:

$$X_1 \rightarrow X_2 \quad \text{(birth reaction)}$$
$$X_2 \rightarrow X_1 \quad \text{(death reaction)}$$

$$\mathbf{S} = \begin{bmatrix} -1 & 1 \\ 1 & -1 \end{bmatrix}$$

  - The (mass-action) propensity functions are given by:

Kronecker delta

$$\pi_1(x_1, x_2) = \kappa_1 x_1 \delta(N - x_1 - x_2)$$
$$\pi_2(x_1, x_2) = \kappa_2 x_2 \delta(N - x_1 - x_2)$$

Kronecker delta

  - <u>Mass conservation</u> equation: $x_1 + x_2 = N$ (system is <u>closed</u>).

Analytical Solution

- **<u>Example (birth and death process – closed system)</u>**
  - The network is governed by the following <u>population</u> ME:

$$\frac{\partial p_X(x_1,x_2;t)}{\partial t} = [\kappa_1(x_1+1)\,p_X(x_1+1,x_2-1;t) + \kappa_2(x_2+1)\,p_X(x_1-1,x_2+1;t) - (\kappa_1 x_1 + \kappa_2 x_2)\,p_X(x_1,x_2;t)]\,\delta(N - x_1 - x_2)$$

Kronecker delta

  - A solution can be found in certain circumstances by transforming the ME using the [probability generating function](https://en.wikipedia.org/wiki/Probability-generating_function) and by solving the resulting equation.

https://en.wikipedia.org/wiki/Probability-generating_function

Analytical Solution

- **Example (birth and death process – closed system)**
  - If $X_1(0) = 0$ and $X_2(0) = N$, then the solution is given by:

$$p_x(x_1, x_2; t) = \binom{N}{x_1} [p(t)]^{x_1} [1 - p(t)]^{x_2} \delta(N - x_1 - x_2)$$

Kronecker delta

$$p(t) = \frac{\kappa_2}{\kappa_1 + \kappa_2} [1 - e^{-(\kappa_1 + \kappa_2)t}]$$

binomial distribution

Analytical Solution

- **<u>Example (birth and death process – closed system)</u>**
  - If $X_1(0) = N$ and $X_2(0) = 0$, then the solution is given by:

$$p_x(x_1, x_2; t) = \binom{N}{x_1} [q(t)]^{x_1} [1 - q(t)]^{x_2} \delta(N - x_1 - x_2)$$

Kronecker delta

$$q(t) = \frac{\kappa_2 + \kappa_1 e^{-(\kappa_1 + \kappa_2)t}}{\kappa_1 + \kappa_2}$$

binomial distribution

Analytical Solution

- **Example (birth and death process – closed system)**
  - If none of the previous initial conditions is true, then the solution cannot be found analytically.
  - However, it can be shown that

$$\lim_{t\to\infty} p_x(x_1, x_2; t) = \binom{N}{x_1} \bar{p}^{x_1} (1-\bar{p})^{x_2} \delta(N - x_1 - x_2)$$

Kronecker delta

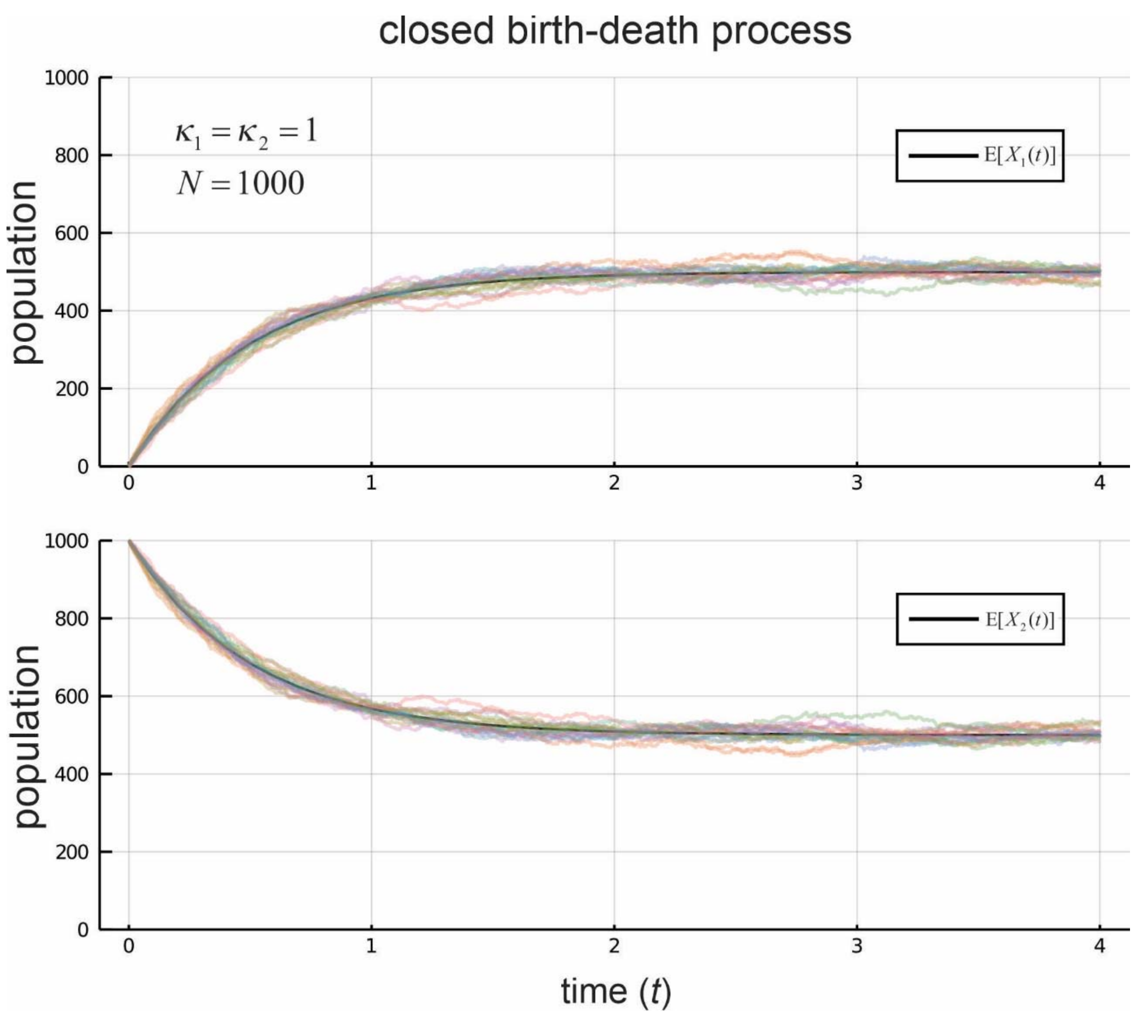
$$\bar{p} = \lim_{t\to\infty} p(t) = \lim_{t\to\infty} q(t) = \frac{\kappa_2}{\kappa_1 + \kappa_2}$$

binomial distribution

regardless of the initial condition.

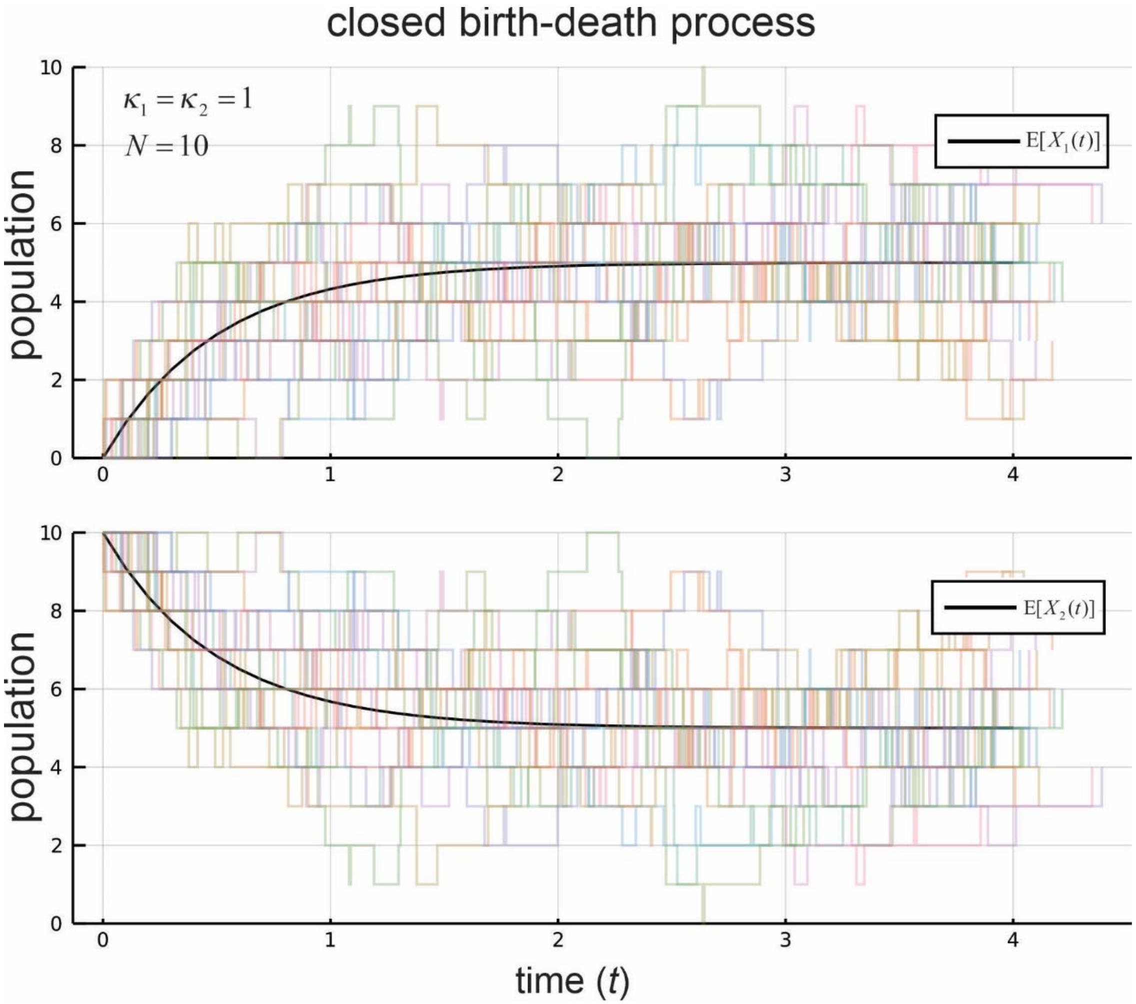
  - It is easier to derive the solution of the ME at steady-state !!

Analytical Solution



Large *N* is associated with low stochasticity.

Analytical Solution



Small *N* is associated with high stochasticity!

Analytical Solution

- **<u>Example (birth and death process – open system)</u>**
  - Consider now the following linear reaction network:

$$\begin{aligned} \varnothing &\rightarrow X \quad \text{(birth reaction)} \\ X &\rightarrow \varnothing \quad \text{(death reaction)} \end{aligned}$$

$$\mathbf{S} = \begin{bmatrix} 1 & -1 \end{bmatrix}$$

  - The (mass-action) propensity functions are given by:

$$\begin{aligned} \pi_1(x) &= \kappa_1 \\ \pi_2(x) &= \kappa_2 x \end{aligned}$$

  - It is assumed here that reactants enter the system from its surroundings, and that there is an unlimited number of such reactants.

Analytical Solution

- **<u>Example (birth and death process – open system)</u>**
  - The network is governed by the following <u>population</u> ME:

$$\frac{\partial p_X(x;t)}{\partial t} = [\kappa_1 p_X(x-1;t) + \kappa_2 (x+1) p_X(x+1;t) - (\kappa_1 + \kappa_2 x) p_X(x;t)$$

Analytical Solution

- **Example (birth and death process – open system)**
  - If $X(0) = 0$, then the solution is given by:

$$p_x(x;t) = e^{-\lambda(t)} \frac{[\lambda(t)]^x}{x!}$$

$$\lambda(t) = \frac{\kappa_1}{\kappa_2}(1 - e^{-\kappa_2 t})$$

Poisson distribution

Analytical Solution

- **<u>Example (birth and death process – open system)</u>**
  - If $X(0) \neq 0$, then the solution <u>cannot be found</u> analytically.
  - However, it can be shown that

$$\lim_{t\to\infty} p_x(x;t) = e^{-\bar{\lambda}} \frac{\bar{\lambda}^x}{x!}$$

$$\bar{\lambda} = \lim_{t\to\infty} \lambda(t) = \frac{\kappa_1}{\kappa_2}$$

Poisson distribution

<u>regardless</u> of the initial condition.

Analytical Solution