LECTURE #2

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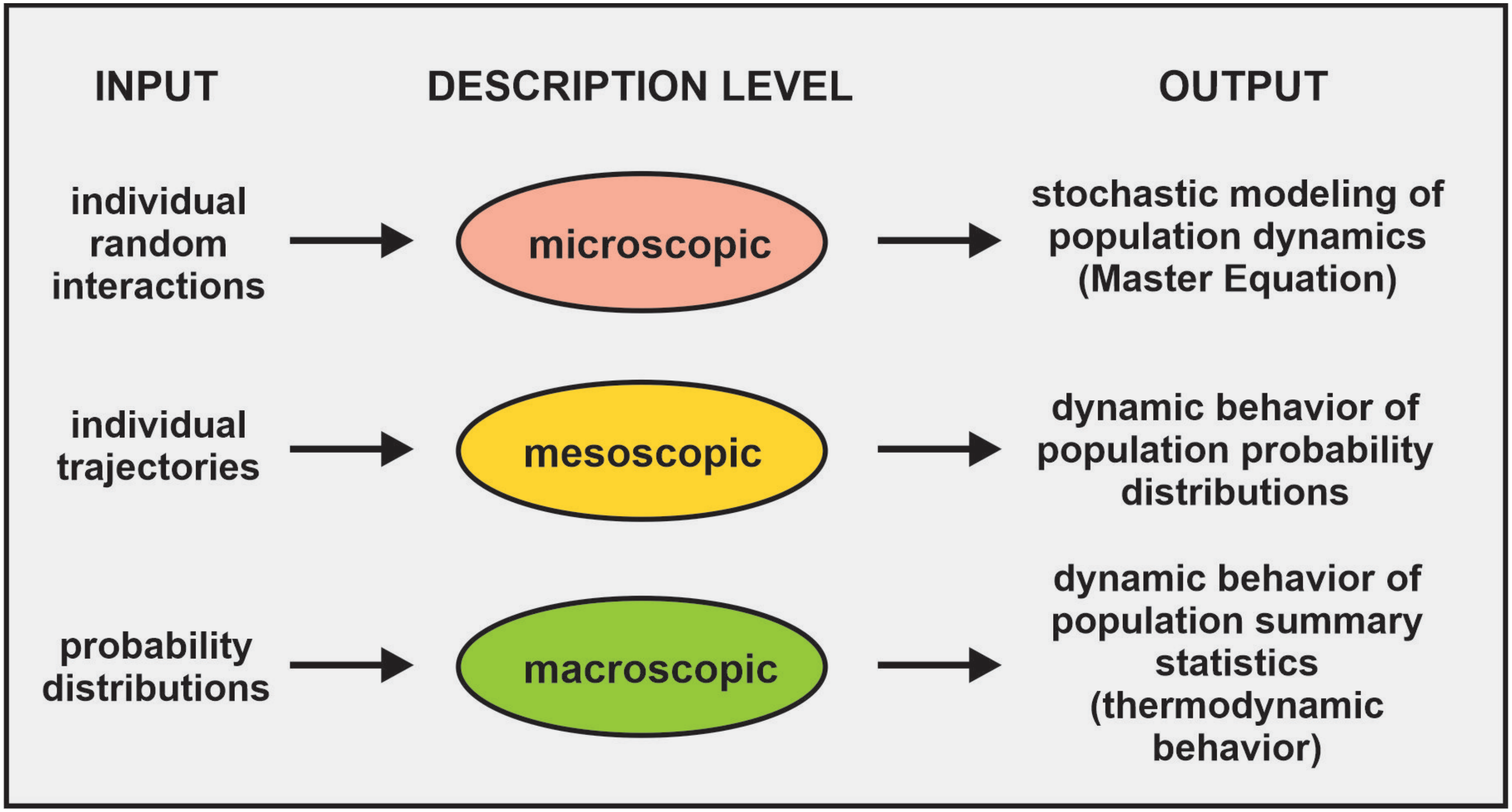
MICROSCOPIC DESCRIPTION

Description Levels of Complex Systems



Stochastic Modeling

- Each interacting component X_n in a complex network assumes a state $X_n(t)$ at each time $t \geq 0$.
- The $N \times 1$ state vector $\mathbf{X}(t)$ completely characterizes the system at time t.
- Here, $\mathbf{X}(t)$ evolves with time, but not deterministically.

Stochastic Modeling

- If we run multiple simulations of the same system from identical initial conditions, we cannot expect to obtain the same dynamics in each simulation.

- Therefore, $\mathbf{X}(t)$ is a multivariate stochastic process with realizations $\mathbf{x}(t)$.

- We are interested in calculating the probability

$$p_X(\mathbf{x};t) \triangleq \Pr[\mathbf{X}(t) = \mathbf{x} \mid \mathbf{X}(0) = \mathbf{x}_0], \quad t > 0$$

Markov Processes

- A Markov process (or continuous-time Markov Chain) is a particular case of a stochastic process that satisfies an important property.
- The dynamic evolution of a Markov process does not depend on all past values but only on the immediate past values:

$$\Pr[\mathbf{X}(t_q) = \mathbf{x}_q \mid \mathbf{X}(t_{q-1}) = \mathbf{x}_{q-1}, \mathbf{X}(t_{q-2}) = \mathbf{x}_{q-2}, \ldots, \mathbf{X}(t_1) = \mathbf{x}_1]$$

$$= \Pr[\mathbf{X}(t_q) = \mathbf{x}_q \mid \mathbf{X}(t_{q-1}) = \mathbf{x}_{q-1}]$$

$$t_q > t_{q-1} > \cdots > t_1$$

transition probability

https://en.wikipedia.org/wiki/Markov_chain

Markov Processes

- For a Markov process, we have:

$$\Pr[\mathbf{X}(t_1)=\mathbf{x}_1,\mathbf{X}(t_2)=\mathbf{x}_2,\ldots,\mathbf{X}(t_q)=\mathbf{x}_q]$$

$$=\underbrace{\Pr[\mathbf{X}(t_1)=\mathbf{x}_1]}_{\text{initial probability}}\prod_{i=1}^{q-1}\underbrace{\Pr[\mathbf{X}(t_{i+1})=\mathbf{x}_{i+1}\,|\,\mathbf{X}(t_i)=\mathbf{x}_i]}_{\text{transition probability}}$$

- Therefore, only the <u>initial</u> and <u>transition probabilities</u> are required for specifying the joint probabilities of a Markov process.

Markov Processes

- Chapman-Kolmogorov equation:

$$\Pr[\mathbf{X}(t_{q+1}) = \mathbf{x}_{q+1} \mid \mathbf{X}(t_{q-1}) = \mathbf{x}_{q-1}]$$
$$= \sum_{\mathbf{x}_q} \Pr[\mathbf{X}(t_{q+1}) = \mathbf{x}_{q+1} \mid \mathbf{X}(t_q) = \mathbf{x}_q] \Pr[\mathbf{X}(t_q) = \mathbf{x}_q \mid \mathbf{X}(t_{q-1}) = \mathbf{x}_{q-1}]$$

see supplement #1 for proof

- An alternative form of this identity is known as the master equation and is fundamental when modeling stochastic dynamics on complex networks.

Homogeneous Markov Processes

- We will focus on <u>homogeneous</u> Markov processes.

- This means that the transition probabilities depend only on the difference between time points:

$$\Pr[\mathbf{X}(t_q) = \mathbf{x}_q \mid \mathbf{X}(t_{q-1}) = \mathbf{x}_{q-1}] = \Pr[\mathbf{X}(t_q + \tau) = \mathbf{x}_q \mid \mathbf{X}(t_{q-1} + \tau) = \mathbf{x}_{q-1}]$$

for any constant τ.

The Master Equation

- Consider transitions in the <u>infinitesimally small</u> time-interval $[t, t+dt)$
- $T(\mathbf{x}_{q+1} \mid \mathbf{x}_q)dt$: probability that a transition from $\mathbf{x}_q$ to $\mathbf{x}_{q+1}$ takes place during $[t, t+dt)$.
- We set $T(\mathbf{x} \mid \mathbf{x}) = 0$.
- $a_0(\mathbf{x}_q)dt$: probability that a transition takes place during $[t, t+dt)$.
- $1 - a_0(\mathbf{x}_q)dt$: probability that no transition takes place during $[t, t+dt)$.
- Note that

$$a_0(\mathbf{x}_q) = \sum_{\mathbf{x}} T(\mathbf{x} \mid \mathbf{x}_q)$$

The Master Equation

- For small enough dt, note that:

$$\Pr[\mathbf{X}(t+dt) = \mathbf{x}_{q+1} \mid \mathbf{X}(t) = \mathbf{x}_q] \\ = [1 - a_0(\mathbf{x}_q)dt]\delta(\mathbf{x}_{q+1} - \mathbf{x}_q) + T(\mathbf{x}_{q+1} \mid \mathbf{x}_q)dt$$

Kronecker delta $\delta(x) = \begin{cases} 1, & \text{if } x = 0 \\ 0, & \text{if } x \neq 0 \end{cases}$

- This requires the assumption that <u>at most one</u> transition can take place during $[t, t+dt)$.

The Master Equation

- From
  - $\Pr[\mathbf{X}(t_{q+1}) = \mathbf{x}_{q+1} \mid \mathbf{X}(t_{q-1}) = \mathbf{x}_{q-1}]$
    $= \sum_{\mathbf{x}_q} \Pr[\mathbf{X}(t_{q+1}) = \mathbf{x}_{q+1} \mid \mathbf{X}(t_q) = \mathbf{x}_q] \Pr[\mathbf{X}(t_q) = \mathbf{x}_q \mid \mathbf{X}(t_{q-1}) = \mathbf{x}_{q-1}]$
  - $\Pr[\mathbf{X}(t+dt) = \mathbf{x}_{q+1} \mid \mathbf{X}(t) = \mathbf{x}_q] = [1 - a_0(\mathbf{x}_q)dt]\delta(\mathbf{x}_{q+1} - \mathbf{x}_q) + T(\mathbf{x}_{q+1} \mid \mathbf{x}_q)dt$
  - $a_0(\mathbf{x}_q) = \sum_{\mathbf{x}} T(\mathbf{x} \mid \mathbf{x}_q)$

  we can show that $(\text{set } t_{q-1} = 0, t_q = t, t_{q+1} = t + dt)$

$$\frac{\Pr[\mathbf{X}(t+dt) = \mathbf{x}_{q+1} \mid \mathbf{X}(0) = \mathbf{x}_{q-1}] - \Pr[\mathbf{X}(t) = \mathbf{x}_{q+1} \mid \mathbf{X}(0) = \mathbf{x}_{q-1}]}{dt}$$
$$= \sum_{\mathbf{x}_q} T(\mathbf{x}_{q+1} \mid \mathbf{x}_q) \Pr[\mathbf{X}(t) = \mathbf{x}_q \mid \mathbf{X}(0) = \mathbf{x}_{q-1}]$$
$$- \sum_{\mathbf{x}_q} T(\mathbf{x}_q \mid \mathbf{x}_{q+1}) \Pr[\mathbf{X}(t) = \mathbf{x}_{q+1} \mid \mathbf{X}(0) = \mathbf{x}_{q-1}]$$

see supplement #2 for details

The Master Equation

- By taking the limit as $dt \to 0$, we obtain

$$\frac{\partial \Pr[\mathbf{X}(t)=\mathbf{x}_{q+1} \mid \mathbf{X}(0)=\mathbf{x}_{q-1}]}{\partial t}$$
$$= \sum_{\mathbf{x}_q} \left\{ T(\mathbf{x}_{q+1} \mid \mathbf{x}_q) \Pr[\mathbf{X}(t)=\mathbf{x}_q \mid \mathbf{X}(0)=\mathbf{x}_{q-1}] - T(\mathbf{x}_q \mid \mathbf{x}_{q+1}) \Pr[\mathbf{X}(t)=\mathbf{x}_{q+1} \mid \mathbf{X}(0)=\mathbf{x}_{q-1}] \right\}$$

- This differential form of the Chapman-Kolmogorov equation is called the Master Equation (ME).
- For simplicity, we write the ME in the form:

$$\frac{\partial \Pr[\mathbf{X}(t)=\mathbf{x} \mid \mathbf{X}(0)=\mathbf{x}_0]}{\partial t}$$
$$= \sum_{\mathbf{x}'} \left\{ T(\mathbf{x} \mid \mathbf{x}') \Pr[\mathbf{X}(t)=\mathbf{x}' \mid \mathbf{X}(0)=\mathbf{x}_0] - T(\mathbf{x}' \mid \mathbf{x}) \Pr[\mathbf{X}(t)=\mathbf{x} \mid \mathbf{X}(0)=\mathbf{x}_0] \right\}$$

The Master Equation

- This leads to:

$$\frac{\partial p_X(\mathbf{x};t)}{\partial t} = \sum_{\mathbf{x}'} \left\{ T(\mathbf{x} \mid \mathbf{x}') p_X(\mathbf{x}';t) - T(\mathbf{x}' \mid \mathbf{x}) p_X(\mathbf{x};t) \right\}, \quad t > 0$$

  since we have defined $p_X(\mathbf{x};t) = \Pr[\mathbf{X}(t) = \mathbf{x} \mid \mathbf{X}(0) = \mathbf{x}_0], \quad t > 0.$

- The ME is initialized with $p_X(\mathbf{x};0) = \delta(\mathbf{x} - \mathbf{x}_0)$. Kronecker delta
- Note that $p_X(\mathbf{x};t)$ depends on the initial condition $\mathbf{x}_0$ in general.
- We do not show this dependence explicitly for notational simplification.

Master Equations for Complex Networks

- The state of a general complex network can only be updated based upon the firing of reactions.
- When a reaction fires, the state instantaneously updates according to the stoichiometry of the network.
- If the m-th reaction is the only one that fires within the time interval $[t, t+dt)$ and if $\mathbf{s}_m$ is the m-th column of the net stoichiometric matrix $\mathbf{S}$, then we would have:

$$\mathbf{x}(t+dt) = \mathbf{x}(t) + \mathbf{s}_m$$

Master Equations for Complex Networks

- If we assign a firing rule $\pi_m(\mathbf{x})$, characteristic to the m-th reaction, such that the probability that the reaction will fire during the time interval $[t, t+dt)$ when $\mathbf{X}(t) = \mathbf{x}$ is given by

$$T(\mathbf{x} + \mathbf{s}_m \mid \mathbf{x})dt = \pi_m(\mathbf{x})dt$$

then we can arrive at the following ME:

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

propensity function

- This is because

$$T(\mathbf{x}' \mid \mathbf{x}) = 0 \quad \text{for any} \quad \mathbf{x}' \neq \mathbf{x} + \mathbf{s}_m$$

Master Equations for Complex Networks

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

- From the ME, we have that:

$$p_X(\mathbf{x};t+dt) \simeq p_X(\mathbf{x};t) + \boxed{\sum_{m=1}^{M} \pi_m(\mathbf{x}-\mathbf{s}_m)dt\, p_X(\mathbf{x}-\mathbf{s}_m;t)} - \boxed{\sum_{m=1}^{M} \pi_m(\mathbf{x})dt\, p_X(\mathbf{x};t)}$$

probability that the system will switch to state $\mathbf{x}$ within the infinitesimal time interval $[t,t+dt)$.

probability that the system will switch state within the infinitesimal time interval $[t,t+dt)$, given that it is in state $\mathbf{x}$ at time t .

Degree of Advancement

- Let $Z_m(t)$ be the number of times that the *m*-th reaction occurs within the time interval $[0,t)$.
- This is known as the <u>degree of advancement</u> of the m-th reaction.
- The degree of advancement is random and $\{Z_m(t), t \geq 0\}$ is a <u>counting process</u>.
- By convention, $Z_m(0) = 0$.
- The state of a complex network can also be characterized by the degree of advancement vector $\mathbf{Z}(t)$.
- We refer to $\{\mathbf{Z}(t), t \geq 0\}$ as the <u>DA process</u>.

Degree of Advancement

- What is the best choice for the state of a complex network, the <u>population process</u> $\{\mathbf{X}(t), t \geq 0\}$ or the <u>DA process</u> $\{\mathbf{Z}(t), t \geq 0\}$?
- Note that

$$\mathbf{X}(t) = \mathbf{x}_0 + \mathbf{S}\mathbf{Z}(t), \quad t \geq 0$$

- Therefore,

$$\mathbf{Z}(t) \Rightarrow \mathbf{X}(t), \quad t \geq 0$$

- However,

$$\mathbf{X}(t) \not\Rightarrow \mathbf{Z}(t), \quad t \geq 0$$

  in general (unless $\mathbf{S}^T\mathbf{S}$ is invertible).

- This implies that the DA process is <u>more informative</u> than the population process!

Master Equations for Complex Networks

- If we denote

$$p_Z(\mathbf{z};t) = \Pr[\mathbf{Z}(t) = \mathbf{z} \mid \mathbf{Z}(0) = 0]$$

  then we have the following ME:

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

  m-th column of the $M \times M$ identity matrix

  where

$$a_m(\mathbf{z}) = \begin{cases} \pi_m(\mathbf{x}_0 + \mathbf{S}\mathbf{z}), & \text{if } \mathbf{z} \geq 0 \\ 0, & \text{otherwise} \end{cases}$$

- This equation is initialized with $p_Z(\mathbf{z};0) = \delta(\mathbf{z})$.

  Kronecker delta

Master Equations for Complex Networks

- If the previous equation is solved for $p_Z(\mathbf{z};t), t > 0$, then

$$p_X(\mathbf{x};t) = \sum_{\mathbf{z} \in \mathcal{B}(\mathbf{x})} p_Z(\mathbf{z};t)$$

where

$$\mathcal{B}(\mathbf{x}) = \{\mathbf{z} : \mathbf{x} = \mathbf{x}_0 + \mathbf{S}\mathbf{z}\}$$

Topological Structure and Propensity Functions

- The MEs

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

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

may give the impression that the probabilities $p_X(\mathbf{x};t)$ and $p_Z(\mathbf{z};t)$ do not depend on a detailed knowledge of the topological structure of the network.

- The first ME seems not to depend on the stoichiometric coefficients ν, ν', whereas, the second equation seems to depend only on the net stoichiometric coefficients $s = \nu' - \nu$.

Topological Structure and Propensity Functions

- It turns out that, for all reactions encountered in practice, the propensity function $\pi_m(\mathbf{x})$ does not depend on all elements of the state vector $\mathbf{x}$ but only on those elements associated with the adjacent reactant nodes, as specified by the stoichiometric matrix $\mathbf{V}$.
- Consequently, the topological structure of a reaction network directly affects its dynamics through this mathematical property of the propensity functions.