8.1 Markov Processes

8.1.1 Finite State Markov Processes

Definition 8.1 Transition Matrix: What is $X_{t+1}$ given $X_t$?

$X_t = \{\text{Eat, Sleep, Active}\}, t = 1, 2, 3$

$$M = \begin{pmatrix}
0.5 & 0 & 0.5 \\
0.5 & 0 & 0.5 \\
0 & 0.5 & 0.5
\end{pmatrix}$$

Note: The rows sum to 1.

If we know $x_o = E$, $X_1 \sim M \begin{pmatrix} 1 \\ 0 \\ 0 \end{pmatrix}$. If we think that the state at time $t$ is $P_t = \begin{pmatrix} 0.1 & 0.9 \\ 0.8 & 0.2 \end{pmatrix}$, then we can push $P_t$ through $M$ to get the distribution over states at time $t + 1$.

$P_{t+1} = MP_t$

so for $x_o = E$, $X_2 \sim MX_1 = M^2 \begin{pmatrix} 1 \\ 0 \end{pmatrix}$.

The transition from time 1 to time 3, $X_3|X_1$, is $M^2$. (Composition property of the transition matrix)

As $t \to \infty$, $P_t \to$ top eigenvector of $M$, $P_\infty$ (stationary distribution).

$P_\infty M = P_\infty$, ie $\lambda = 1$

Exercise to check: A matrix whose rows sum to 1 will always have an eigenvector with $\lambda = 1$.

8.1.2 Finite State Continuous Time Markov Processes

Transition rates, eg $r_{e\to s}$, $r_{s\to e}$, are exponential random variables. Whichever event happens first is the path you choose.
8.1.3 Continuous Time, Continuous State Markov Processes

Definition 8.2 A transition kernel is a map from point $x$ in state space $\chi$ to distributions on state space.

$$
\gamma : x \mapsto \gamma(\cdot|x)
$$

The probability that $x$ transitions to somewhere in $A$ is $\gamma(A|x)$ for any set $A \subset \chi$.

A continuous time Markov process has a transition kernel for every pair of time points $t_1 < t_2$.

$\gamma_{t_2|t_1}(\cdot|x)$ is the probability distribution for the state at time $t_2$ given we start from state $x$ at time $t_1$.

$\gamma_{t_2|t_1}(dy|x)$ is the probability of transitioning into $dy$.

Denote the state at time $t$ by $X_t$. Then $\gamma_{t_2|t_1}(\cdot|x)$ is the law of $X_{t_2}|X_{t_1} = x$.

8.1.3.1 Compositional Property

$$(\gamma_{t_2|t_1} \circ \gamma_{t_3|t_2})(dz|x) = \int \gamma_{t_3|t_2}(dy|x) \gamma_{t_2|t_1}(dz|y)$$

$$= \gamma_{t_3|t_1}(dz|x) \quad \text{definition of Markov}$$

(8.1)
8.2 Developmental Stochastic Processes

\[ P \] describes the population of cells at time \( t \). \( \gamma_{t_2|t_1}(\cdot|x) \) describes the "transitions". We interpret \( \gamma_{t_2|t_1}(\cdot|x) \) as the distribution of descendants of \( x \).

\[ \gamma : x \xrightarrow{\text{at time } t_1} \gamma_{t_2|t_1}(\cdot|x) \xrightarrow{\text{descendants at time } t_2, \text{ probability measure on } \chi} \]

For any set \( A \subset \chi \), \( \gamma(A|x) \) is the probability that the cell \( x \) has a descendant in \( A \).

**Note:**

Consider a random cell \( X_{t_2} \) at time \( t_2 \). \( X_{t_2} \sim P_{t_2} \). Define \( A_{t_1} \) to be the unique ancestor of \( X_{t_2} \).

\[ A_{t_1} = \text{Ancest}(X_{t_2}) \]

\[ A_{t_1} \sim Q_{t_1} \neq P_{t_1} \]

We can define a joint distribution \( \gamma_{t_2,t_1} = (A_{t_1}, X_{t_2}) \). There is a nice relationship between \( \gamma_{t_2|t_1} \) and \( \gamma_{t_2,t_1} \).

Details next class.

8.2.1 Sampling from an Elemental Stochastic Process with a scRNA-seq Time Course

**Goal:** Learn about \( \gamma_{t_2|t_1} \). But measurements kill cells. So we can’t look at transitions in high dimensional \( \chi \).

**Steps:**

1. Prepare independent populations following the same process
2. Sample at different time points

At time \( t_1 \) get samples \( X_1, X_2, \ldots, X_{n_1} \sim P_{t_1} \)
At time \( t_2 \) get samples \( Y_1, Y_2, \ldots, Y_{n_2} \sim P_{t_2} \)
At time $t_T$ get samples $Z_1, Z_2, ..., Z_{nT} \sim P_{tT}$.

We can construct $\hat{P}_{t1} = \sum_{i=1}^{n} \delta_{x_i}$, but how do we construct $\gamma_{t2|t1}$?

**Methods to construct lineage trajectories:**

1. Computationally infer from samples $\hat{P}_{t1}, \hat{P}_{t2}, \hat{P}_{t3}, ...$

2. Lineage tracing at time $t_i$

   Gives information on lineage tree, but not state of the ancestors.

   Use CRISPR to create mutations in an unimportant part of DNA. It is still a bit of an open problem how to merge this data with scRNA-seq.

3. RNA velocity

   If we read enough of the RNA sequence, we can tell if it has been spliced or not. Splicing occurs with a given rate. The longer mRNA has been around, the more likely it has been spliced.