Modelling isotope labelling in atom transition networks

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Introduction & Motivation

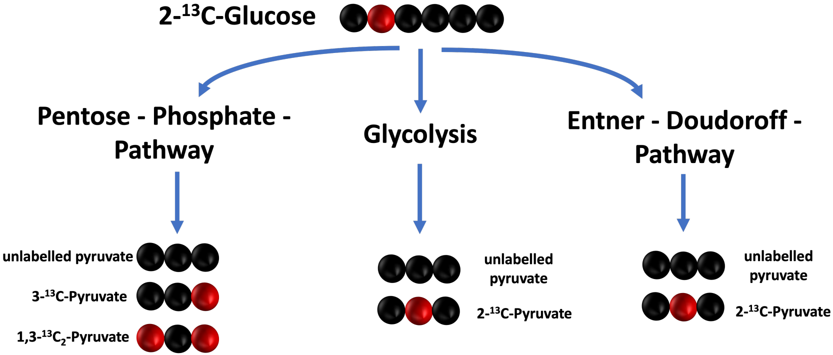


Figure: Metabolic development of 2-^{13}C-Glucose via different metabolic pathways.

Methodology

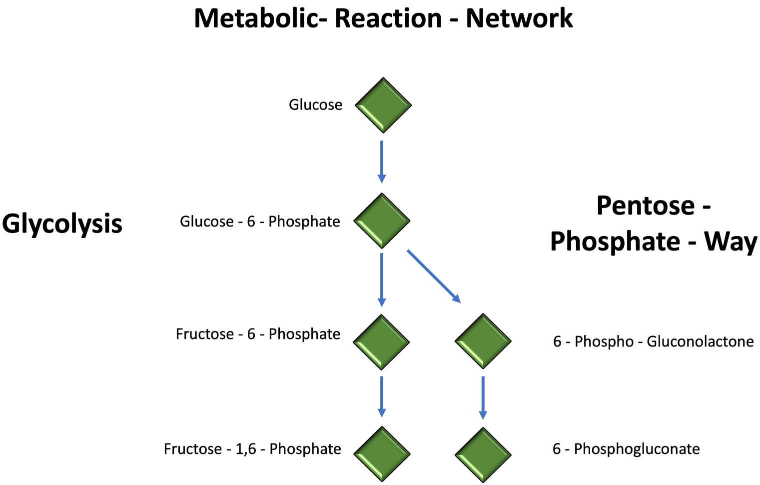


Figure: Schematic depiction of a part of a metabolic network.

Methodology

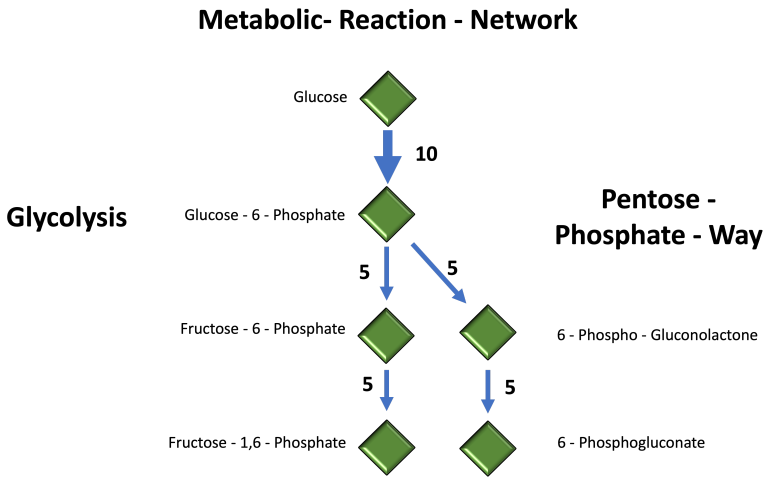


Figure: Schematic depiction of a part of a metabolic network with established flux.

Methodology

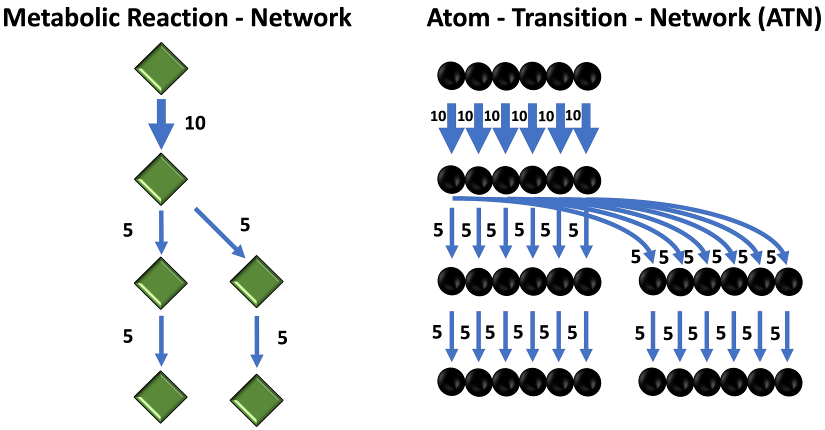


Figure: Schematic depiction of a part of a metabolic network and an atom-transition network with established flux.

Methodology

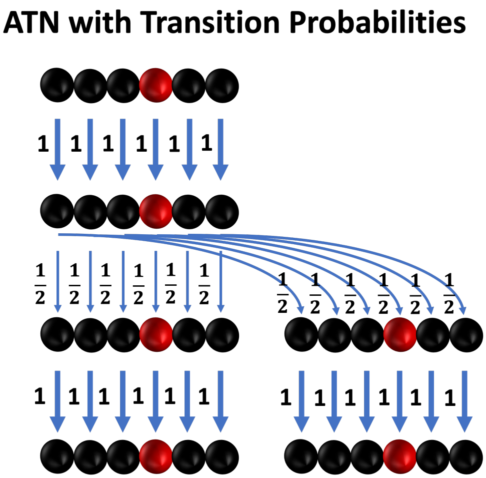
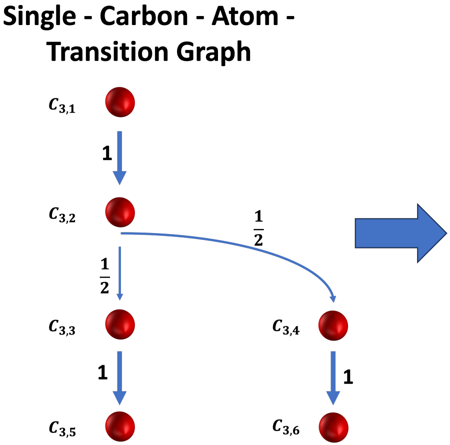


Figure: Schematic depiction of an ATN with transition probabilities.

Methodology



Transition - Matrix

$$P = \begin{bmatrix} 0 & 0 & \cdots & 0 \\ 1 & 0 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & 1 \end{bmatrix}$$

Figure: Schematic depiction of an atom-transition network with transition probabilities.

Definition (Markov Processes and Markov Chains[1])

Let $(\Omega, \mathfrak{A}, \mathbb{P})$ be a probability space and $(Y, \mathfrak{B})$ a measurable space. Let S be the state space with $\Omega = \prod_{i=0}^{n} \mathcal{S}$ and T an index set. A **stochastic process**

$$X : \Omega \times T \to Y, t \in T$$

is called Markov Process, if and only if:

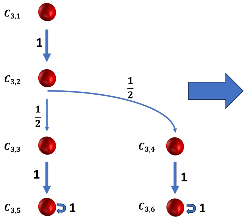
$$\begin{aligned} \mathbb{P}(X_{t_{n+1}} | X_{t_n} = x_n, \ldots, X_{t_0} = x_0) = \mathbb{P}(X_{t_{n+1}} = x_{n+1} | X_{t_n} = x_n), \\ t_i < t_{i+1}, \forall i \in \{1, \ldots, n\}, x_j \in S \end{aligned} \tag{1}$$

which is called the **Markov Property**.

[1] Introduction to stochastic processes, Gregroy F. Lawler, 2006

Markov Chain

Single - Carbon - Atom - Transition Graph



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$$P = \begin{bmatrix} 0 & 0 & \cdots & 0 \\ 1 & 0 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & 1 \end{bmatrix}$$

- $\mathcal{S}$: state space, $S = \{C_{3,1}, C_{3,2}, \ldots\}$

[2] Dynamics of Markov Chains for Undergraduates, Ursula Porod, 2021

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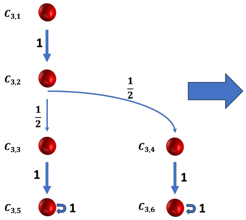

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- $\mathcal{S}$: state space, $S = \{C_{3,1}, C_{3,2}, \ldots\}$
- Transition probabilities: $P \in [0,1]^{|\mathcal{S}| \times |\mathcal{S}|}$

Definition (Stochastic Matrix[2])

$P \in [0,1]^{n \times n}$ is called a **row-stochastic matrix**, if: $\sum_{j=1}^{n} p_{ij} = 1, \forall i \in \{1, \ldots, n\}$.

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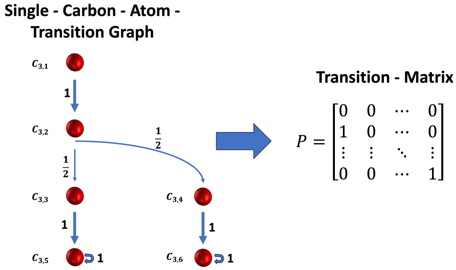

- $\mathcal{S}$: state space, $S = \{C_{3,1}, C_{3,2}, \ldots\}$
- Transition probabilities: $P \in [0,1]^{|\mathcal{S}|\times|\mathcal{S}|}$
- Markov Property:

$$\mathbb{P}(X_{t_{n+1}} | X_{t_n} = x_n, \ldots, X_{t_0} = x_0)$$
$$= \mathbb{P}(X_{t_{n+1}} = x_{n+1} | X_{t_n} = x_n), \qquad (2)$$
$$t_i < t_{i+1}, \forall i \in \{1, \ldots, n\}, x_j \in S$$

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Basic computation on Markov Chains

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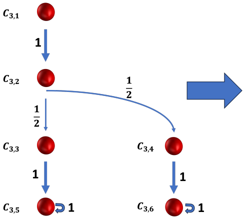

Transition - Matrix

$$P = \begin{bmatrix} 0 & 0 & \cdots & 0 \\ 1 & 0 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & 1 \end{bmatrix}$$

- $\pi^0 \in [0,1]^{1\times|\mathcal{S}|}$: probability distribution
- Probability of an event $\omega \in \Omega$:

$$\begin{aligned} \pi^1_i &= \sum_{i=1}^{j} \pi^0_j \cdot P_{i,j} \\ \pi^1 &= \pi^0 \cdot P \\ \pi^2 &= \pi^1 \cdot P = \pi^0 \cdot P^2 \\ &\vdots \\ \pi^k &= \pi^{k-1} \cdot P = \ldots = \pi^0 \cdot P^k \end{aligned} \tag{3}$$

Basic computation on Markov Chains

- Accumulation of labeled carbon atoms caused by constant influx of labeled material (π^0):

$$\pi^{\infty} = \pi^0 \cdot I + \pi^0 \cdot P + \pi^0 \cdot P^2 + \ldots = \sum_{k=0}^{\infty} \pi^0 \cdot P^k \qquad (4)$$

[3] Handbook of Linear Algebra, Second Edition, Leslie Hogben, 2013

Basic computation on Markov Chains

- Accumulation of labeled carbon atoms caused by constant influx of labeled material (π^0):

$$\pi^\infty = \pi^0 \cdot I + \pi^0 \cdot P + \pi^0 \cdot P^2 + \ldots = \sum_{k=0}^{\infty} \pi^0 \cdot P^k \tag{4}$$

- $\rho(P) \not< 1 \Rightarrow \lim_{n \to \infty} P^n \neq 0 \Rightarrow$ (4) is not convergent[3]

[3] Handbook of Linear Algebra, Second Edition, Leslie Hogben, 2013

Transient states and recurrent states

Definition (Transience and Recurrence[4])

Let $(X_n)_{n\in\mathbb{N}}$ be a Markov chain with state space $\mathcal{S}$, $x \in \mathcal{S}$ and

$$T^x = \min\{n \geq 1 : X_n = x\}$$

the first return time. A state x is called:

- recurrent if $\mathbb{P}(T^x < \infty | X_0 = x) = 1$.
- transient if $\mathbb{P}(T^x < \infty | X_0 = x) < 1$.

A Markov chain is recurrent (transient) if all of its states are recurrent (transient).

[4] Dynamics of Markov Chains for Undergraduates, Ursula Porod, 2021

Canonical decomposition of the state space

Proposition (Characterization of Recurrency[5])

Let $(X_n)_{n\geq 0}$ be a Markov chain with state space $\mathcal{S}$ and $x, y \in S$. If x is recurrent and $x \to y$, then y is also recurrent.

[5] Dynamics of Markov Chains for Undergraduates, Ursula Porod, 2021

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Let $(X_n)_{n\geq 0}$ be a Markov chain with state space $\mathcal{S}$ and $x, y \in S$. If x is recurrent and $x \to y$, then y is also recurrent.

- $S = \mathcal{R} \cup \mathcal{T}$

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- $S = \mathcal{R} \cup \mathcal{T}$
- $$P = \begin{array}{c} \\ \mathcal{R} \\ \mathcal{T} \end{array} \begin{array}{c} \begin{array}{cc} \mathcal{R} & \mathcal{T} \end{array} \\ \left(\begin{array}{c|c} \mathcal{P}' & 0 \\ \hline \mathcal{T} & \mathcal{Q} \end{array}\right) \end{array}$$

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- $\mathcal{Q}$ is substochastic and transient
- $\sum_{n=0}^{\infty} Q^n < \infty$

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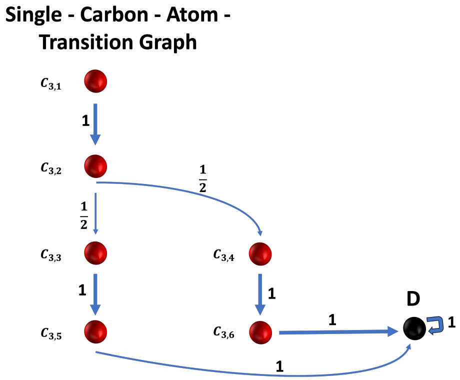
Canonical decomposition of the state space



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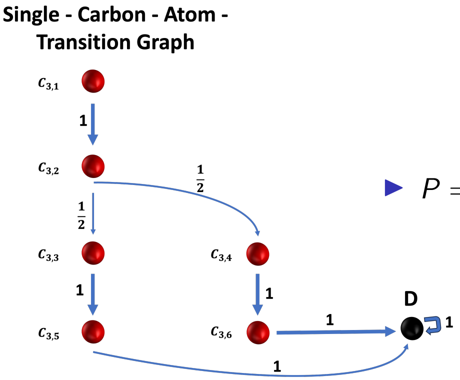

- $$P = \begin{array}{c} \\ \mathcal{T} \\ \mathcal{D} \end{array} \begin{array}{c} \begin{array}{cc} \mathcal{T} & \mathcal{D} \end{array} \\ \left(\begin{array}{c|c} \mathcal{Q} & \\ \hline 0 & 1 \end{array} \right) \end{array}$$

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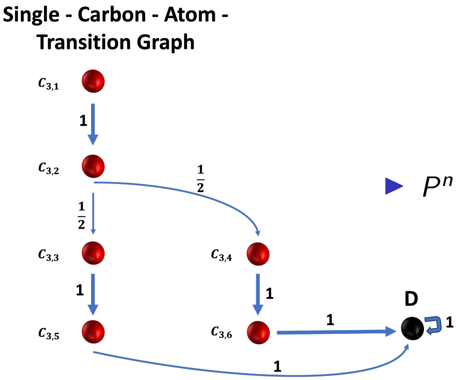


- $$P^n = \begin{array}{c|c|c} & \mathcal{T} & \mathcal{D} \\ \hline \mathcal{T} & \mathcal{Q}^n & \\ \hline \mathcal{D} & 0 & 1 \end{array}$$

Lemma (Fundamental Matrix[6])

Let $(X_n)_{n\geq 0}$ be a Markov chain with state space $\mathcal{S}$ and $\mathcal{Q}$ the substochastic matrix, representing all transient states as constructed above, then the matrix

$$V = \sum_{n=0}^{\infty} Q^n$$

is called the **fundamental matrix** of the Markov chain and is given by: $V = (I - Q)^{-1}$

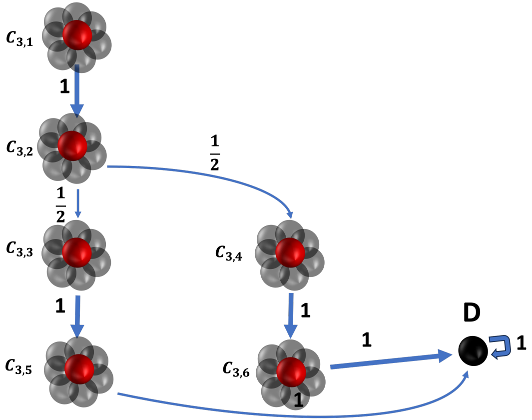
- Stable solution:

$$\pi^{\infty} = \pi^{0} \cdot \sum_{n=0}^{\infty} \mathcal{Q}^n = \pi^{0}(I - \mathcal{Q})^{-1}$$

[6] Dynamics of Markov Chains for Undergraduates, Ursula Porod, 2021

Reservoir Solution

Single - Carbon - Atom - Transition Graph



Reservoir Solution

- The quantity of labeled carbon atoms can be computed recursively via

$$
\begin{aligned}
n_i^{t+1} &= n_i^t - \text{Efflux} + \text{Influx} \\
&= n_i^t - n_i^t \cdot \frac{f_i}{r_i} + \sum_{j=1}^{m} n_j^t \cdot \frac{f_j}{r_j} \cdot q_{ji} + \pi_i^0
\end{aligned} \tag{5}
$$

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- With f_i and r_i being the outflux and reservoir of a compound, respectively, we define:

$$C = \begin{pmatrix} \frac{f_1}{r_1} & 0 & \dots & 0 \\ 0 & \frac{f_2}{r_2} & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \dots & \frac{f_m}{r_m} \end{pmatrix}$$

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- Yielding:

$$\begin{aligned} n^{t+1} &= n^t - n^t \cdot C + n^t \cdot C \cdot \mathcal{Q} + \pi^0 \\ &= n^t \cdot (I - C + C \cdot \mathcal{Q})) + \pi^0 \\ &= n^t \cdot (I + C \cdot (\mathcal{Q} - I)) + \pi^0 = n^t \cdot \mathcal{M} + \pi^0 \end{aligned} \tag{7}$$

Reservoir Solution

- By induction we obtain

$$
\begin{aligned}
n^{t+1} &= n^t \cdot \mathcal{M} + \pi^0 \\
&= (n^{t-1} \cdot \mathcal{M} + \pi^0) \cdot \mathcal{M} + \pi^0 \\
&= n^{t-1} \cdot \mathcal{M}^2 + \pi^0 \cdot (I + \mathcal{M}) \\
&\;\;\vdots \\
&= \pi^0 \cdot \mathcal{M}^{t+1} + \sum_{k=0}^{t} \pi^0 \cdot \mathcal{M}^k \\
&= \pi^0 \cdot \sum_{k=0}^{t+1} \mathcal{M}^k \overset{t \to \infty}{\longrightarrow} \;???
\end{aligned}
\tag{8}
$$

Reservoir Solution

Lemma

$\mathcal{M}$, as constructed above, is substochastic and transient. Moreover, the stable reservoir solution can be calculated directly, via:

$$\pi^\infty = \pi^0 \cdot \sum_{k=0}^{\infty} \mathcal{M}^k = \pi^0 (I - \mathcal{M})^{-1} = \pi^0 \cdot (I - \mathcal{Q})^{-1} \cdot C^{-1}$$

Proof: With $\mathcal{M} = I + C \cdot (\mathcal{Q} - I)$ it follows:

$$\begin{aligned}
\pi^0 \cdot (I - \mathcal{M})^{-1} \cdot C &= \pi^0 \cdot (I - (I + C \cdot (\mathcal{Q} - I))^{-1} \cdot C \\
&= \pi^0 \cdot (C \cdot (I - \mathcal{Q}))^{-1} \cdot C \\
&= \pi^0 \cdot (I - \mathcal{Q})^{-1} \cdot C^{-1} \cdot C \\
&= \pi^0 \cdot (I - \mathcal{Q})^{-1}
\end{aligned} \tag{9}$$

Summary

- Solutions at particular timepoints: $\pi^t = \pi^0 \cdot \sum_{k=n}^{t} \mathcal{Q}^n$

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Summary

- Solutions at particular timepoints: $\pi^t = \pi^0 \cdot \sum_{k=n}^{t} \mathcal{Q}^n$
- Stable solution (without reservoir): $\pi^\infty = \pi^0 \cdot (I - \mathcal{Q})^{-1}$
- Reservoir solutions at particular timepoints: $\pi^t = \pi^0 \cdot \sum_{k=n}^{t} \mathcal{M}^n$

Summary

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- Reservoir solutions at particular timepoints: $\pi^t = \pi^0 \cdot \sum_{k=n}^{t} \mathcal{M}^n$
- Stable reservoir solution: $\pi^\infty = \pi^0 \cdot (I - Q)^{-1} \cdot C^{-1}$

Outlook

- Stable and timepoint isotopomer solution
- ITN - Isotopomer Transition Graph
- Modelling atom solution with continuous Markov chains[1.0em]

Acknowledgement

- Peter F. Stadler
- Thomas Gatter
- Nora Beier

MATOMIC

UNIVERSITÄT LEIPZIG

Thank you.


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Algebras and σ-Algebras

Definition (Algebra and σ-Algebra)

Let $\Omega \neq \emptyset$ be non-empty set and $\mathfrak{P}(\Omega)$ the power set of Ω. A collection $\mathfrak{A} \subseteq \mathfrak{P}(\Omega)$ is called Algebra if the following properties hold:

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- $A \in \mathfrak{A} \Rightarrow \Omega \setminus A \in \mathfrak{A}$

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$\mathfrak{A}$ is called a σ-Algebra if additionally:

- $A_n \in \mathfrak{A}, n \in \mathbb{N} \Rightarrow \bigcup_{n=1}^{\infty} A_n \in \mathfrak{A}$

Measurable spaces and measures

Definition (Measurable space)

Let $\Omega \neq \emptyset, \mathfrak{P}(\Omega)$ the power-set on Ω and $\mathfrak{A} \subseteq \mathfrak{P}(\Omega)$ a σ-Algebra on Ω. Then the tuple $(\Omega, \mathfrak{A})$ is called a measurable space

Definition (Measure and probability measure)

Let $(\Omega, \mathfrak{A})$ be a measurable space. A function $\mu : \mathfrak{A} \to [0, \infty]$ and $\mathbb{P} : \mathfrak{A} \to [0, 1]$ is called a measure and a probability measure, respectively, if the following holds

- $\mu(\emptyset) = 0, \mathbb{P}(\emptyset) = 0$
- $\mu, \mathbb{P}$ are σ-additive, i. e. for $A_n \in \mathfrak{A}, A_i \cap A_j = \emptyset, \forall i \neq j$ the following holds:

$$\mu\left(\bigcup_{n=1}^{\infty} A_n\right) = \sum_{n=1}^{\infty} \mu(A_n) \text{ and } \mathbb{P}\left(\bigcup_{n=1}^{\infty} A_n\right) = \sum_{n=1}^{\infty} \mathbb{P}(A_n)$$

- $\mathbb{P}(\Omega) = 1$

$(\Omega, \mathfrak{A}, \mu)$ and $(\Omega, \mathfrak{A}, \mathbb{P})$ are called a measure space and probability space, respectively.

Measurability and random variables

Definition (Measurability)

Let $(X, \mathfrak{A}), (Y, \mathfrak{B})$ measurable spaces. A function $f : X \to Y$ is called $\mathfrak{A} - \mathfrak{B}$ measurable, if:

$$\{x \in X \mid f(x) \in B\} =: f^{-1}(B) \in \mathfrak{A}$$

Definition (Random variable)

Let $(\Omega, \mathfrak{A}, \mathbb{P})$ be a probability space and $(\Sigma, \mathfrak{B})$ a measurable space. A $\mathfrak{A} - \mathfrak{B}-$measurable function:

$$f : \Omega \to \Sigma$$

is called Σ-random variable on Ω or just random variable.

Stochastic Process and Markov Process

Definition (Stochastic process)

Let $(\Omega, \mathfrak{A}, \mathbb{P})$ be a probability space, $(Y, \mathfrak{B})$ a measurable space and T an index set. A stochastic process X is a collection of random variables: $X_t : \Omega \to Y, t \in T$, i. e. a map:

$$X : \Omega \times T \to Y, \omega \mapsto X(\omega)$$

Definition (Markov process)

Let $(\Omega, \mathfrak{A}, \mathbb{P})$ be a probability space and $(Y, \mathfrak{B})$ a measurable space. Let S be the state space with $\Omega = S^{n+1}$ and T an index set. A stochastic process $X : \Omega \times T \to Y, t \in T$ is called Markov Process, if and only if:

$$P(X_{t_{n+1}|X_{t_n}=x_n,\ldots,X_{t_0}=x_0}) = \mathbb{P}(X_{t_{n+1}=c_{n+1}|X_{t_n}=x_n}),$$

which is called the Markov Property.

Markov Chains

Lemma

Consider $S \neq \emptyset$ be a discrete (finite or countably infinite) set, named *state space*, with $\pi^0 \in [0,1]^{1\times|S|}$, being a probability distribution, meaning $\sum_{i=0}^{n} \pi^0(x_i) = 1$, and $\Omega = S^{n+1}$. Furthermore, let $\mathfrak{A} \subseteq \Omega$ be a σ - Algebra on Ω as well as:

$$p : S \times S \to [0,1] \text{ with } \sum_{x_j \in S} p(x_i, x_j) = 1, \forall x_i \in S.$$

Then the function:

$$\mathbb{P} : \mathfrak{A} \to [0,1], \mathbb{P}(A) = \begin{cases} 0 & \text{if } A = \emptyset \\ \sum_{\omega \in A} \pi^0(x_0) \cdot p(x_0, x_1) \cdot \ldots \cdot p(x_{n-1}, x_n) & \text{else} \end{cases}$$

is a probability measure on $\mathfrak{A}$, i. e. $(\Omega, \mathcal{P}(\Omega), \mathbb{P})$ is a probability space.

Proof of the Lemma

$\mathcal{P} : \Omega \to [0,1], \mathcal{P}(\omega) = \pi^0(x_o) \cdot (x_0, x_1) \cdot \ldots \cdot (x_{n-1}, x_n)$ yields:

$$\mathbb{P} : \mathfrak{A} \to [0,1], \mathbb{P}(A) = \begin{cases} 0 & \text{if } \omega = \emptyset \\ \sum_{\omega \in A} \mathcal{P}(\omega) & \text{else} \end{cases}$$

1. $\mathbb{P}(\emptyset) = 0$, nach Defintion

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1. $\mathbb{P}(\emptyset) = 0$, nach Defintion
2. σ-Additivität: Seien $A_n \in \mathfrak{A}, n \in \mathbb{N}$ beliebig, sodass $A_i \cap A_j = \emptyset, \forall i \neq j$. Dann gilt:

$$\mathbb{P}\left(\bigcup_{n=1}^{\infty} A_n\right) = \sum_{\omega \in \bigcup_{n=1}^{\infty} A_n} \mathcal{P}(\omega) \overset{A_i \cap A_j = \emptyset}{=} \sum_{n=1}^{\infty} \sum_{\omega \in A_n} \mathcal{P}(\omega) \overset{\text{Def. } \mathbb{P}}{=} \sum_{n=1}^{\infty} \mathbb{P}(A_n)$$

Proof of the Lemma

$\mathcal{P} : \Omega \to [0,1], \mathcal{P}(\omega) = \pi^0(x_o) \cdot (x_0, x_1) \cdot \ldots \cdot (x_{n-1}, x_n)$ yields:

3. $\mathbb{P}(\Omega) = 1$:

$$\mathbb{P} : \mathfrak{A} \to [0,1], \mathbb{P}(A) = \begin{cases} 0 & \text{if } \omega = \emptyset \\ \sum_{\omega \in A} \mathcal{P}(\omega) & \text{else} \end{cases}$$

$$\begin{aligned} \mathbb{P}(\Omega) &= \sum_{\omega \in \Omega} \mathcal{P}(\omega) = \sum_{\omega \in \Omega} \pi^0(x_0) \cdot p(x_0, x_1) \cdot \ldots \cdot p(x_{n-1}, x_n) \\ &= \sum_{x_{i_0} \in S} \pi^0(x^{i_0}) \sum_{x_{i_1} \in S} p(x^{i_0}, x^{i_1}) \ \ldots \sum_{x_{i_{n-1}} \in S} p(x^{i_{n-1}}, x^{i_n}) \\ &= \sum_{x_{i_0} \in S} \pi^0(x^{i_0}) \sum_{x_{i_1} \in S} p(x^{i_0}, x^{i_1}) \ \ldots \sum_{x_{i_{n-2}} \in S} p(x^{i_{n-2}}, x^{i_{n-1}}) \cdot 1 \\ &= \ldots = \sum_{x_{i_0} \in S} \pi^0(x^{i_0}) \cdot 1 = 1 \end{aligned} \tag{10}$$

Proposition

Proposition (Markov Property)

Let $(\Omega, \mathfrak{P}(\Omega), \mathbb{P})$ be the probability space as defined above and $(X_k)_{0 \leq k \leq n}$ the random vector whose components are the coordinate random variables as defined above. Then for all $0 \leq i \leq n-1$ and for all $x_0, x_1, ..., x_{i+1} \in S$:

$$\mathbb{P}(X_{i+1} | X_0 = x_0, \ldots, x_i = x_i) = \mathbb{P}(X_{i+1} = x_i) = p(x_i, x_{i+1})$$

Proof: By definition we have:

$$\begin{aligned} \mathbb{P}(X_{i+1} | X_0 = x_0, \ldots, x_i = x_i) &= \frac{\mathbb{P}(X_0 = x_0, \ldots, X_{i+1}) = x_{i+1}}{\mathbb{P}(X_0 = x_0, \ldots, X_i = x_i}) \\ &= \frac{\pi(x_0) \cdot p(x_0, x_1) \ldots p(x_{i-1}, x_i) \cdot p(x_i, x_{i+1})}{\pi(x_0) \cdot p(x_0, x_1) \ldots p(x_{i-1}, x_i)} = p(x_i, x_{i+1}) \end{aligned} \tag{11}$$

Additionally we let: $\omega' = \{x_i\} \times \omega = (\omega, x_i), \forall \omega \in \prod_{j=0}^{i-1} S$ and obtain:

$$\begin{aligned} \mathbb{P}(X_{i+1} = x_{i+1} | X_i = x_i) &= \frac{\mathbb{P}(X_i x_i, X_{i+1} = x_{i+1})}{\mathbb{P}(X_i = x_i)} \\ &= \frac{\sum_{\omega \in S^{i-1}} \mathcal{P}(\omega') \cdot p(x_i, x_{i+1})}{\mathbb{P}(X_i = x_i)} \\ &= \frac{\mathbb{P}(X_i = x_i) \cdot p(x_i, x_{i+1})}{\mathbb{P}(X_i = x_i)} = p(x_i, x_{i+1}) \end{aligned} \tag{12}$$

Homogenous Markov chains and stochastic matrices

Definition (Homogenous Markov Chain)

We call $(X_k)_{0 \leq k \leq n}$ constructed above a homogeneous Markov chain of length n with state space S, one-step transition probabilities $P_{xy}, x, y \in S$, and initial distribution π^0.

Definition (Stochastic Matrix)

A matrix $P \in [0,1]^{n \times n}$ is called a **row-stochastic matrix**, if:

$$\sum_{j=1}^{n} p_{ij} = 1, \forall i \in \{1, \dots, d\}$$

.

Irreducibility of Markov Chains

Definition (Irreducibility)

Let $(X_k)_{0\leq k\leq n}$ be a Markov chain with state space S and $x, y \in S$.

- x leads to y, denoted by $x \to y$, if there exists $n \geq 1$ such that $(P^n)_{xy} > 0$.
- x and y communicate with each other, denoted by $x \leftrightarrow y$, if and only if $x \to y$ and $y \Rightarrow x$.
- A Markov chain is irreducible, if for all $x, y \in S$, we have $x \to y$. Otherwise, we say the Markov chain is reducible.

Lemma (Communication is an equivalence relation)

The relation $\leftrightarrow$ as defined above, is an equivalence relation.

Proof:

- a and b follow directly from the definition.
- c : Let $x, y, z \in S$ with $x \leftrightarrow y$ and $y \leftrightarrow z$. Then there exists k, l, n, m with $(P)^l_(xy) > 0, (P)^k_(yz) > 0, (P)^m_(zy) > 0, (P)^l_(yx) > 0$

Lemma (Expected value for visits)

Let $(X_n)_{n\geq 0}$ be a Markov chain with state space $\mathcal{S}$ and $x, y \in \mathcal{S}$. Then for $k \geq 1$:

$$\mathbb{P}(V^y \geq k | X = x) = f_{xy} f_y y^{k-1}$$

Proof:

$$\begin{aligned}\mathbb{P}(V^y \geq k | X_0 = x) = & \ \mathbb{P}(V^y = 1 | X_0 = x) \cdot \mathbb{P}(V^y \geq (k-1) | X_0 = y) \\ & = \mathbb{P}(T^y < \infty | X_0 = x) \cdot \mathbb{P}(T^y < \infty | X_0 = y)^{k-1} \qquad (13) \\ & = f_{xy} \cdot f_{yy}^{k-1}\end{aligned}$$

Theorem

Let $(X_n)_{n\geq 0}$ be a Markov chain with state space $\mathcal{S}$.

a *If $y \in \mathcal{S}$ is recurrent, then*

$$\mathbb{P}(V^y = \infty | X_0 = y) = 1$$

and hence

$$E^y(V^y) = \infty$$

Furthermore, $\mathbb{P}(V^y = \infty | X_0 = x) = f_{xy} \forall x \in \mathcal{S}$.

b *If y is transient, then*

$$\mathbb{P}(V^y < \infty | X_0 = x) = 1$$

and

$$E_x(V^y) = \frac{f_{xy}}{1 - f_{yy}} < \infty$$

for all $x \in \mathcal{S}$.

Proof of the Theorem (continued)

By the previous lemma $\mathbb{P}(V^y \geq k | X_0 = x) = f_{xy} \cdot f_{yy}^{k-1}$. If y recurrent $f_{yy} = \mathbb{P}(T^x < \infty | X_0 = y) = 1$ by definition. Then:

$$\begin{aligned}
\mathbb{P}(V^y = \infty | X_0 = y) &= \lim_{k \to \infty} \mathbb{P}(V^y \geq k | X_0 = y) \\
&= \lim_{k \to \infty} f_{xy} \cdot f_{yy}^{k-1} \\
&= \lim_{k \to \infty} f_{xy} \cdot 1 \\
&= \lim_{k \to \infty} \mathbb{P}(Ty < \infty | X_0 = x) \\
&= \mathbb{P}(Ty < \infty | X_0 = x) = 1 \\
&\Rightarrow f_{xy} > 0 \Rightarrow \mathbb{E}(V^y) = \infty
\end{aligned} \tag{14}$$

Proof of the Theorem (continued)

If y is transient, so $f_{yy} = \mathbb{P}(Ty < \infty | X0 = x) < 1$. Then we obtain:

$$\begin{aligned}
\mathbb{P}(V^y = \infty | X_0 = y) &= \lim_{k\to\infty} \mathbb{P}(V^y \geq k | X_0 = y) \\
&= \lim_{k\to\infty} f_{xy} \cdot f_{yy}^{k-1} = 0 \\
&\Rightarrow \mathbb{P}(V^y < \infty | X_0 = x) = 1 - \mathbb{P}(V^y = \infty | X_0 = y) = 1 \\
\text{Furthermore} : E_x(V^y) &= \sum_{k=1}^{\infty} \mathbb{P}(V^y \geq k) = \sum_{k=1}^{\infty} f_{xy} \cdot f_{yy}^{k-1} \\
&= f_{xy} \cdot \sum_{k=0}^{\infty} f_{yy}^{k} = \frac{f_{xy}}{1 - f_{yy}} < \infty
\end{aligned} \tag{15}$$

Corollary

Corollary (Convergence of transient states)

Let $(X_n)_{n\geq 0}$ a Markov chain with state space $\mathcal{S}$. If $y \in \mathcal{S}$ is transient, it holds:

$$\lim_{n\to\infty} (P^n)_{xy} = 0, \forall x \in S$$

Proof: Let $\mathbb{1}_y(z) = \begin{cases} 1 & \text{if } y = z \\ 0 & \text{else} \end{cases}$. Since $V^Y = \sum_{n=1}^{\infty} \mathbb{1}_y(X_n)$ we obtain with the Monotone Convergence Theorem:

$$\begin{aligned} \mathbb{E}_x(V^y) = \mathbb{E}\left(\sum_{k=1}^{\infty} \mathbb{1}_y(X_n)\right) \overset{MCT}{=} \sum_{n=1}^{\infty} \mathbb{E}(\mathbb{1}_y(X_n)) = \sum_{n=1}^{\infty} \mathbb{P}(X = y | X_0 = x) \\ = \sum_{n=1}^{\infty} (P^n)_{xy} < \infty \Rightarrow \lim_{n\to\infty} (P^n)_{xy} = 0, \forall x \in \mathcal{S} \end{aligned} \tag{16}$$

Monotone Convergence Theorem

Theorem (Monotone Convergence Theorem)

Let $(X_n)_{n\geq 0}$ be a sequence of nonnegative random variables and X a (not necessarily finite) random variable with

$$\lim_{n\to\infty} X_n = X \qquad \text{almost surely}$$

If

$$0 \leq X_0 \leq X_1 \leq X_2 \leq \dots \qquad \text{almost surely}$$

then

$$\lim_{n\to\infty} \mathbb{E}(X_n) = \mathbb{E}(X)$$

Substochastic Matrices

Definition

A square matrix $P \in [0,1]^{n \times n}$ is called row substochastic, if:

$$\sum_{j=1}^{n} p_{ij} = 1, \forall i \in \{1, \ldots, n\}$$

and

$$\exists k \in \{1, \ldots, n\} : \sum_{j=1}^{n} p_{kj} < 1$$

Definition

Let $(X_n)_{n\geq 0}$ be a Markov chain with state space $\mathcal{S}$ and $\mathcal{Q}$ the substochastic matrix, representing all transient states as constructed above, then the matrix

$$V = \sum_{n=0}^{\infty} Q^n$$

is called the **fundamental matrix** of the Markov chain.

Lemma

Let $(X_n)_{n\geq 0}$ be a Markov chain with state space $\mathcal{S}$ and V the fundamental matrix of the Markov chain. Then:

$$V = (I - Q)^{-1}$$

Proof of the Lemma

Proof: $(I-Q)\cdot\sum_{k=0}^{n}Q^k=\sum_{k=0}^{n}Q^k-\sum_{k=0}^{n+1}Q^k=\sum_{k=0}^{n}Q^k(I-Q),\forall n\in\mathbb{N}$

Since, $\sum_{k=0}^{\infty}Q^k$ exists, we obtain:

$$
\begin{aligned}
(I-\mathcal{Q})\cdot V &= (I-\mathcal{Q})\cdot\lim_{n\to\infty}\sum_{k=0}^{n}\mathcal{Q}^k=\lim_{n\to\infty}(I-\mathcal{Q})\cdot\sum_{k=0}^{n}\mathcal{Q}^k\\
&=\lim_{n\to\infty}\left(\left(\sum_{k=0}^{n}\mathcal{Q}^k\right)\cdot(I-\mathcal{Q})\right)=\left(\lim_{n\to\infty}\sum_{k=0}^{n}\mathcal{Q}^k\right)\cdot(I-\mathcal{Q})\\
&=\left(\sum_{k=0}^{\infty}\mathcal{Q}^k\right)\cdot(I-\mathcal{Q})=V\cdot(I-\mathcal{Q})\\
&\Rightarrow V(I-\mathcal{Q})=(I-\mathcal{Q})\cdot V=I\Rightarrow V=(I-Q)^{-1}
\end{aligned}
\tag{17}
$$

Proposition

Let $(X_n)_{n\geq 0}$ be a Markov chain with state space $\mathcal{S}$ and $x, y \in \mathcal{S}$. If x is recurrent and $x \to y$, then

- y is also recurrent, and
- $y \to x$, and $f_{xy} = f_{yx} = 1$

Proof: Assume $x \neq y$. Since $x \to y$,there exists a $k \geq 1$ such that $(P^k)_{xy} > 0$. If we had $f_{yx} < 1$, then with probability $(1 - f_{yx}) > 0$, the Markov chain, once in state y, would never visit x at any future time. It follows that:

$$\mathbb{P}(T^x = \infty | X = x) = (1 - f_{xx}) \geq Pk(1 - f_{yx}) > 0$$

However, since x is recurrent, $f_{xx} = 1$, and so it must be that $f_{yx} = 1$. In particular, $y \to x$.

Proof continued

Since $y \to x$, there exists an $l \geq 1$ such that $P^l_{xy} > 0$. We have:

$$\mathbb{E}(V^y) = \sum_{n=1}^{\infty} (P^n)_{yy} \geq \sum_{m=1}^{\infty} (P^l)_{yx} \cdot (P^m)_{xx} \cdot (P^k)_{yx} = (P^l)_{yx} \cdot (P^k)_{yx} \cdot \sum_{m=1}^{\infty} (P^m)_{xx} = \infty$$

and thus:

$$\mathbb{E}_y(V^y) = \infty$$

which implies that y is recurrent by Proposition 1.8.3. Switching the roles of x and y in the argument, yields $f_{xy} = 1$. This completes the proof.

Methodology

- Model atom transitions as a discrete-time markov - chain (DTMC)

$$(X_n)_{n\in\mathbb{N}} = (X_1, X_2, \ldots)$$

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- Hence:

$$(T)_{ij} = Pr(X_{n+1} = i | X_n = j)$$

Methodology

- Model atom transitions as a discrete-time markov - chain (DTMC)

$$(X_n)_{n\in\mathbb{N}} = (X_1, X_2, \ldots)$$

- Hence:

$$(T)_{ij} = Pr(X_{n+1} = i | X_n = j)$$

- Use mathematical tool box provided by markov - chains

Classification of Markov Processes

Time space	State Space: Discrete	State Space: Continuous
Discrete	Discrete-Time Markov Chain (DTMC)	Discrete-time Markov Process (DTMP)
Continuous	Continuous-Time Markov Chain (CTMC)	Continuous-time Markov Process (CTMP)

Discrete-Time Markov Chain

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