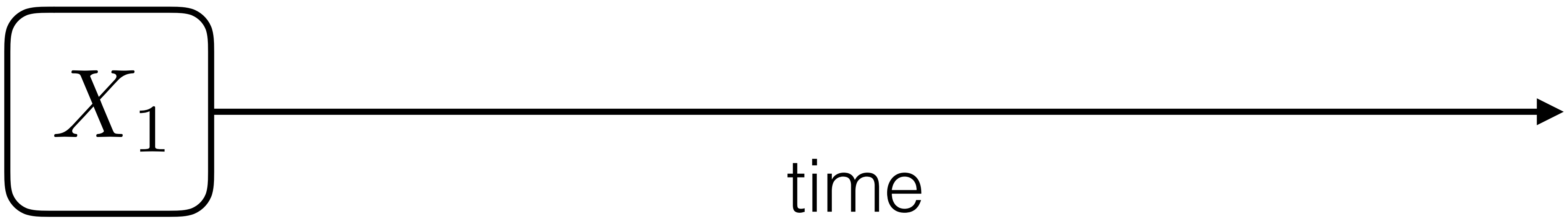
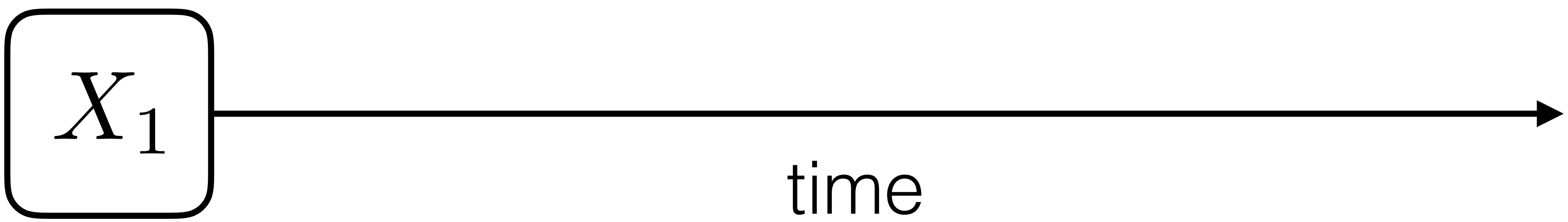
Continuous-Time Markov Chains



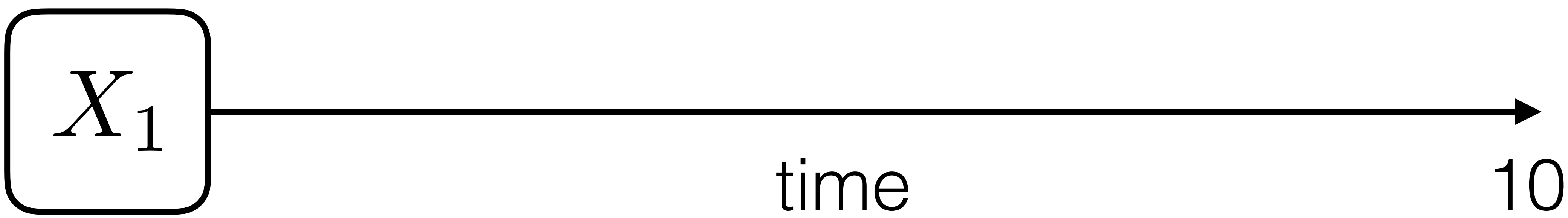
For a continuous-time Markov chain, time does not proceed in iterations. Rather, it is a continuous variable and state changes can occur at any point. Think of a discrete-time chain where the time between iterations is very short (too short to discern) and we go through many of them.

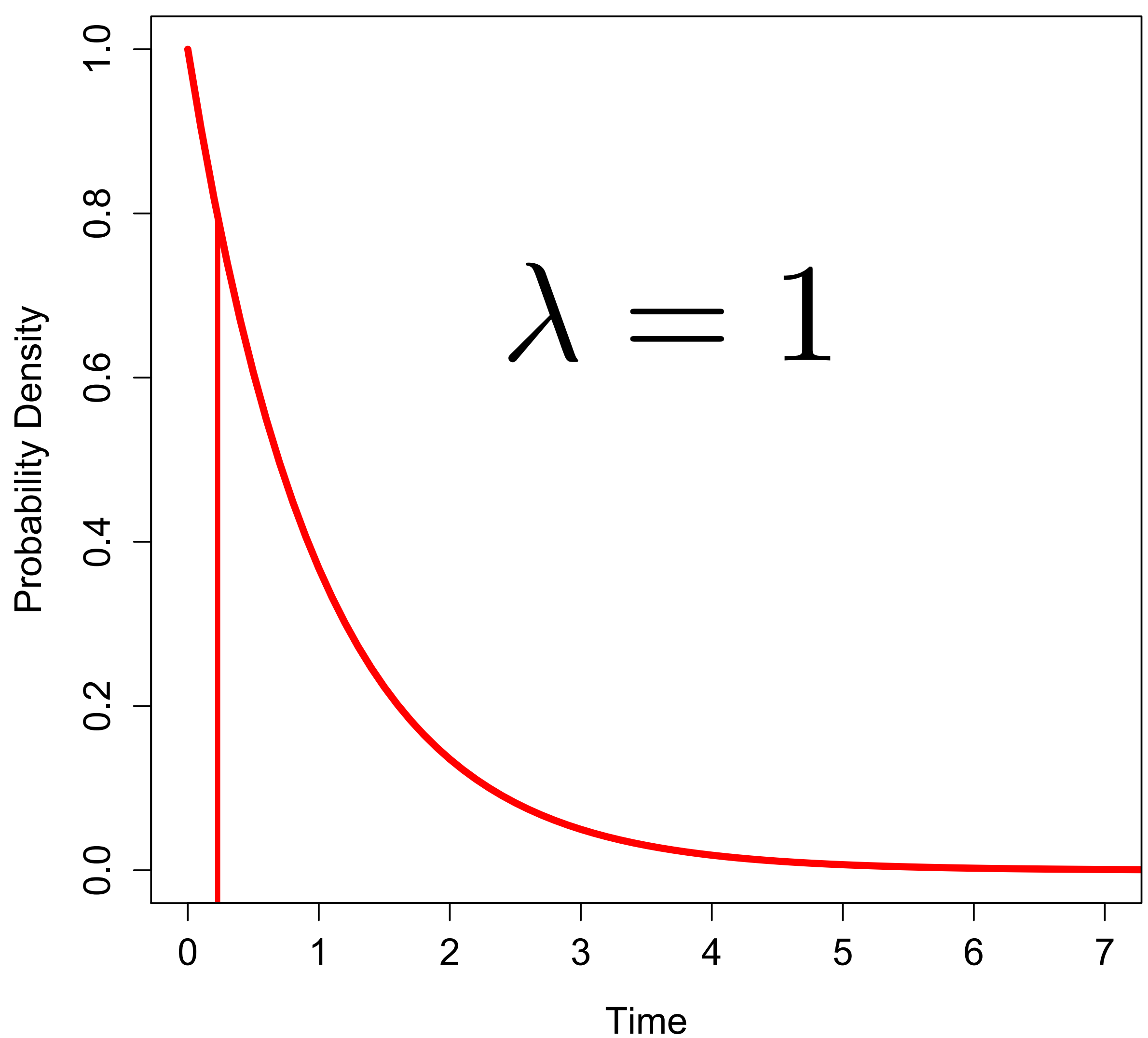
Continuous Time Markov Chains



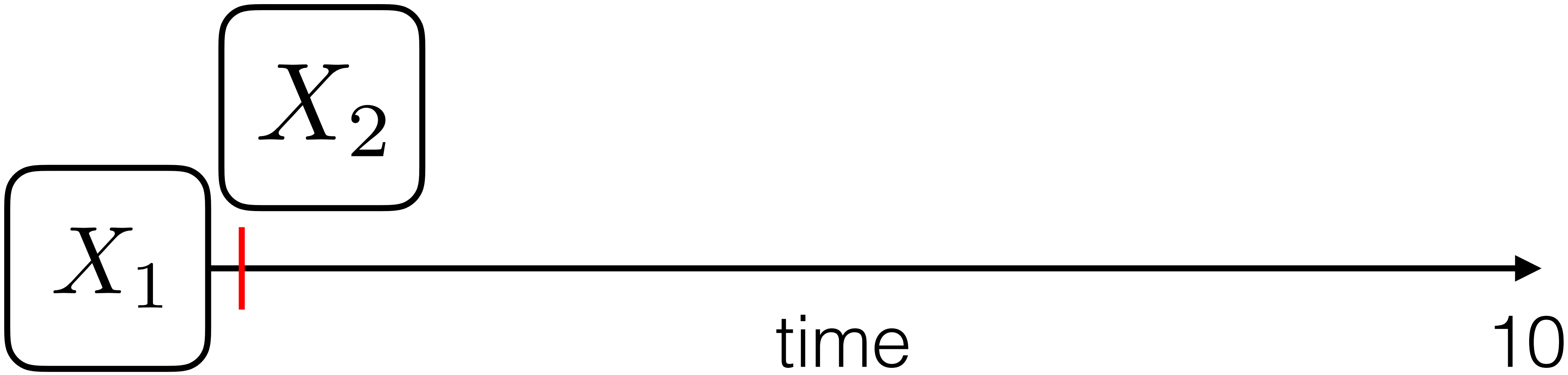
The waiting times between events (state changes) in a continuous-time Markov chain are exponentially distributed. The rate parameter (λ) determines how frequently those events occur.

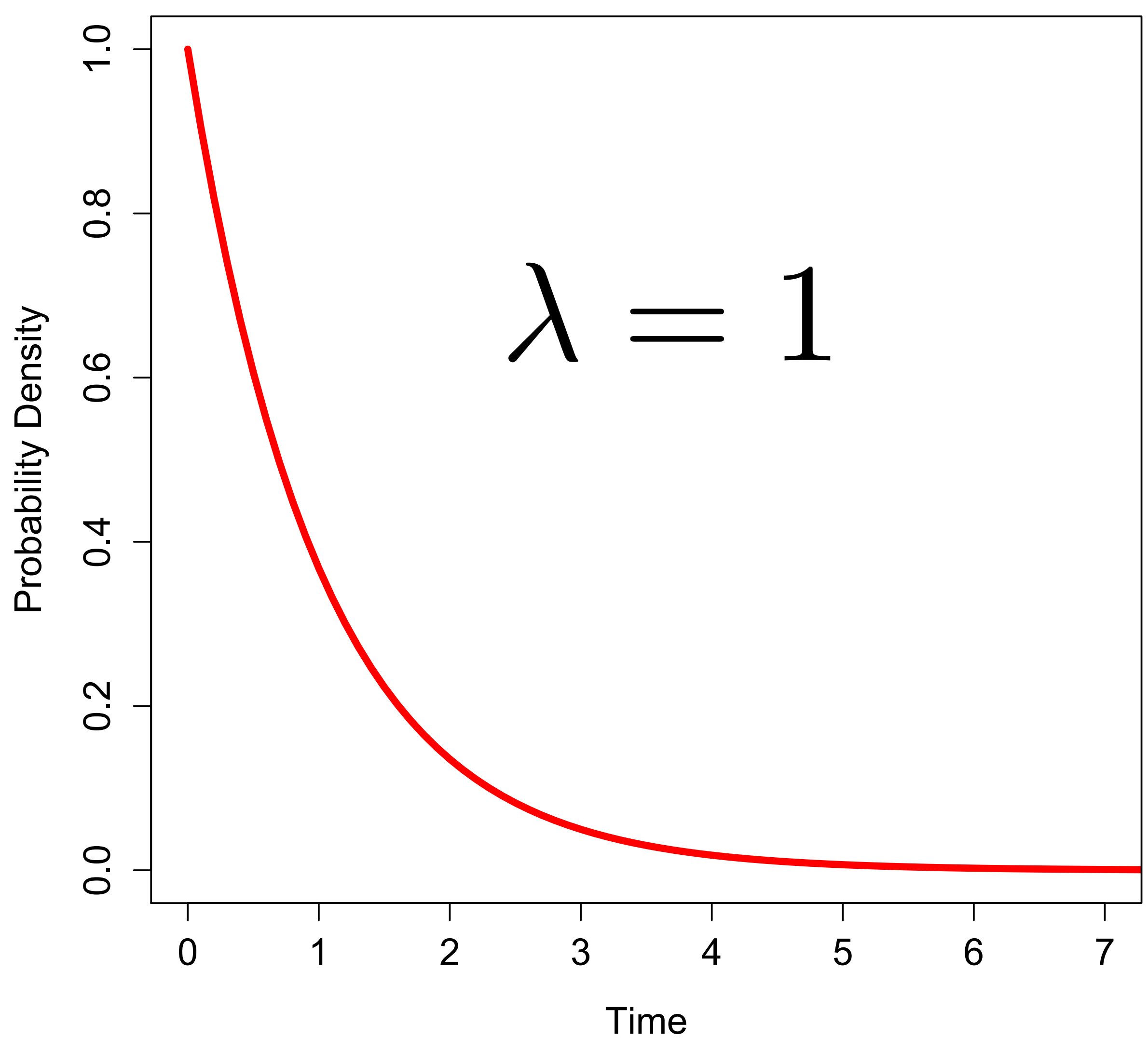
Continuous Time Markov Chains





Continuous Time Markov Chains





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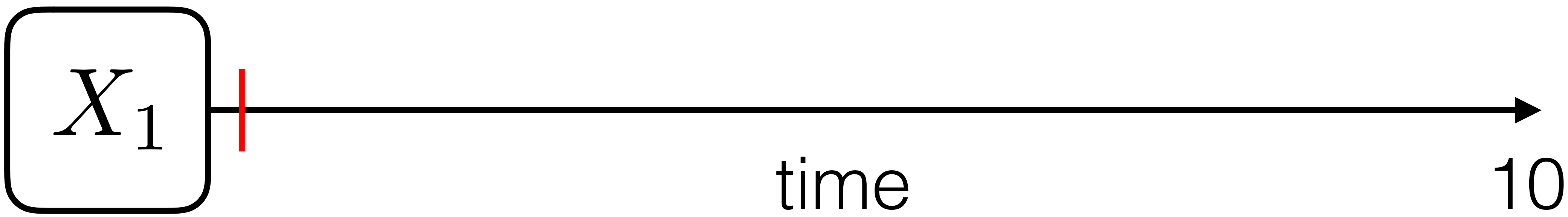

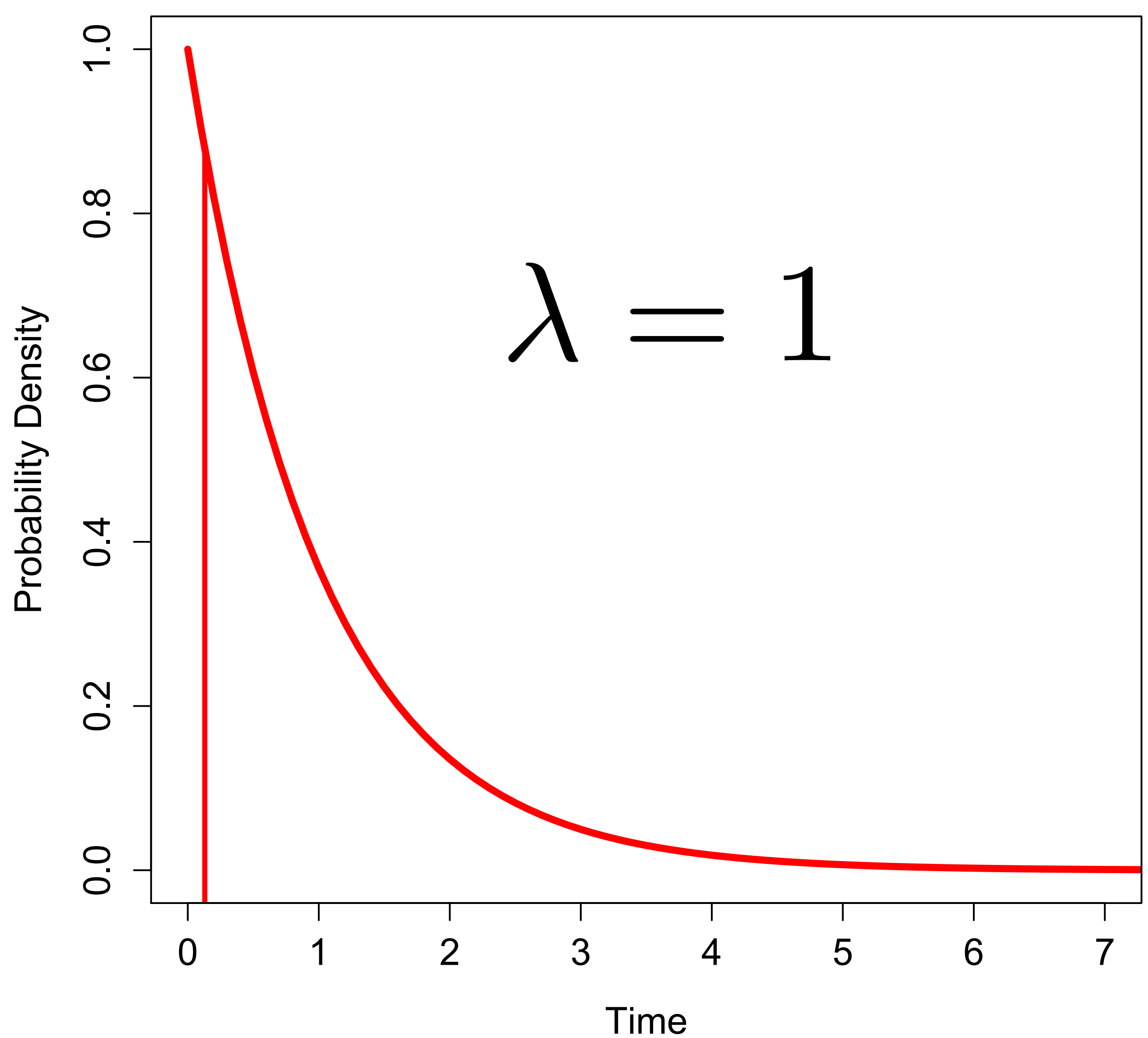

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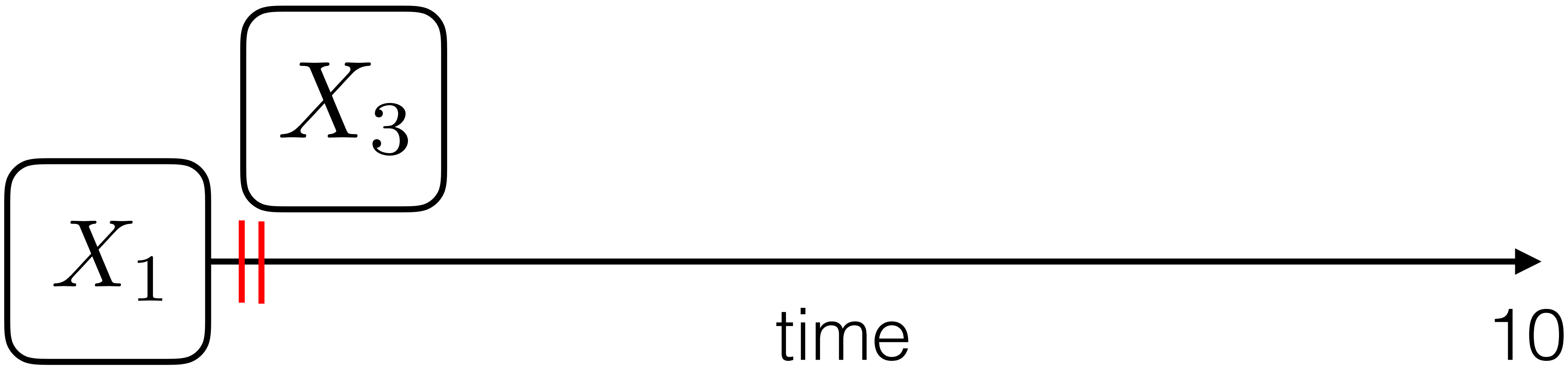

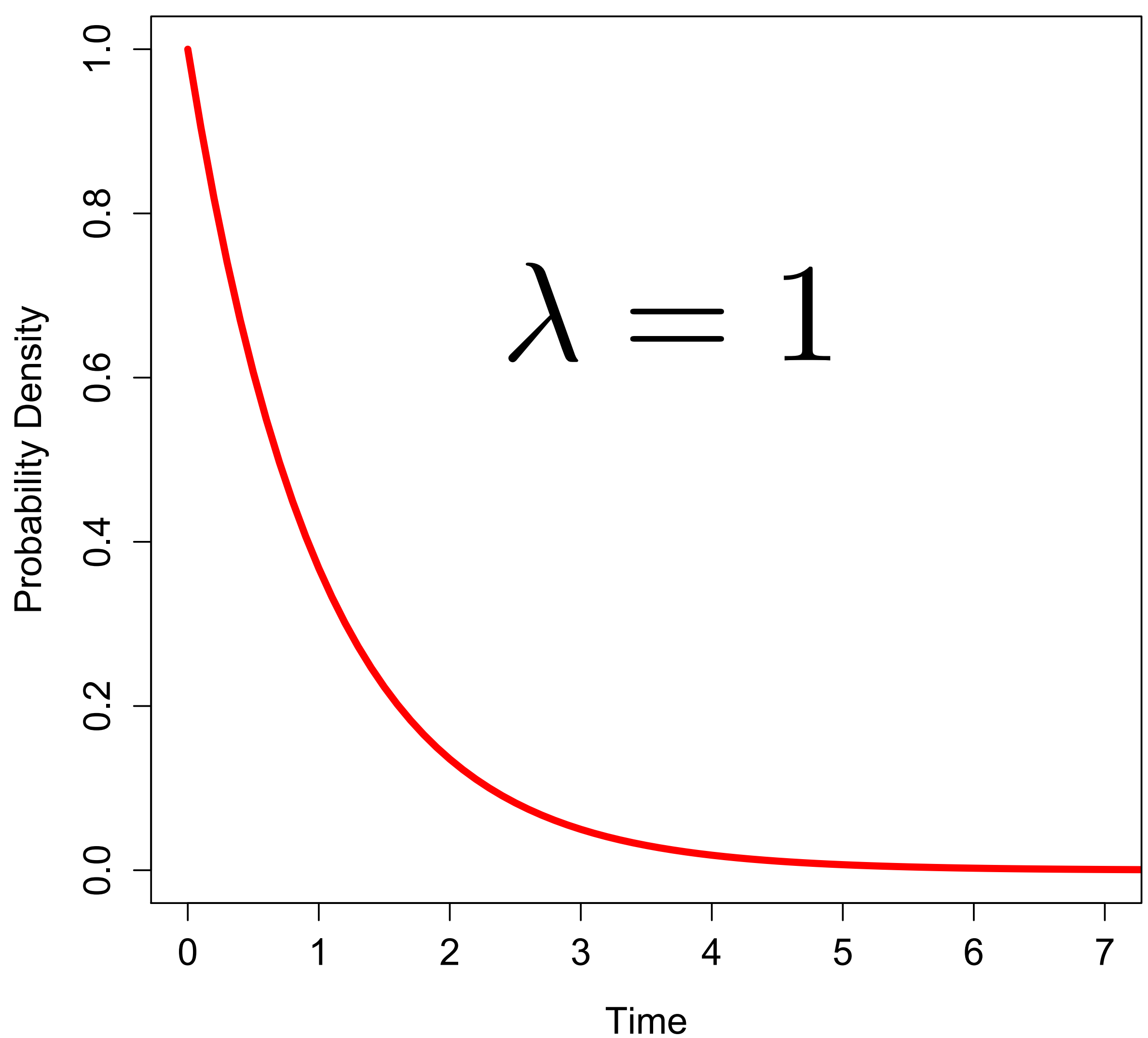

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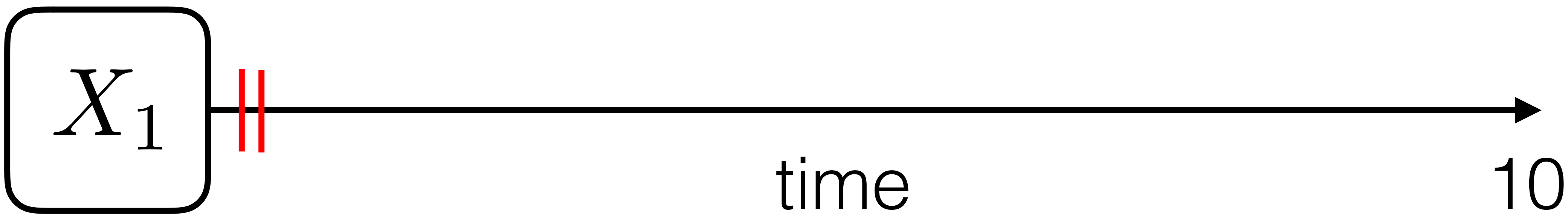

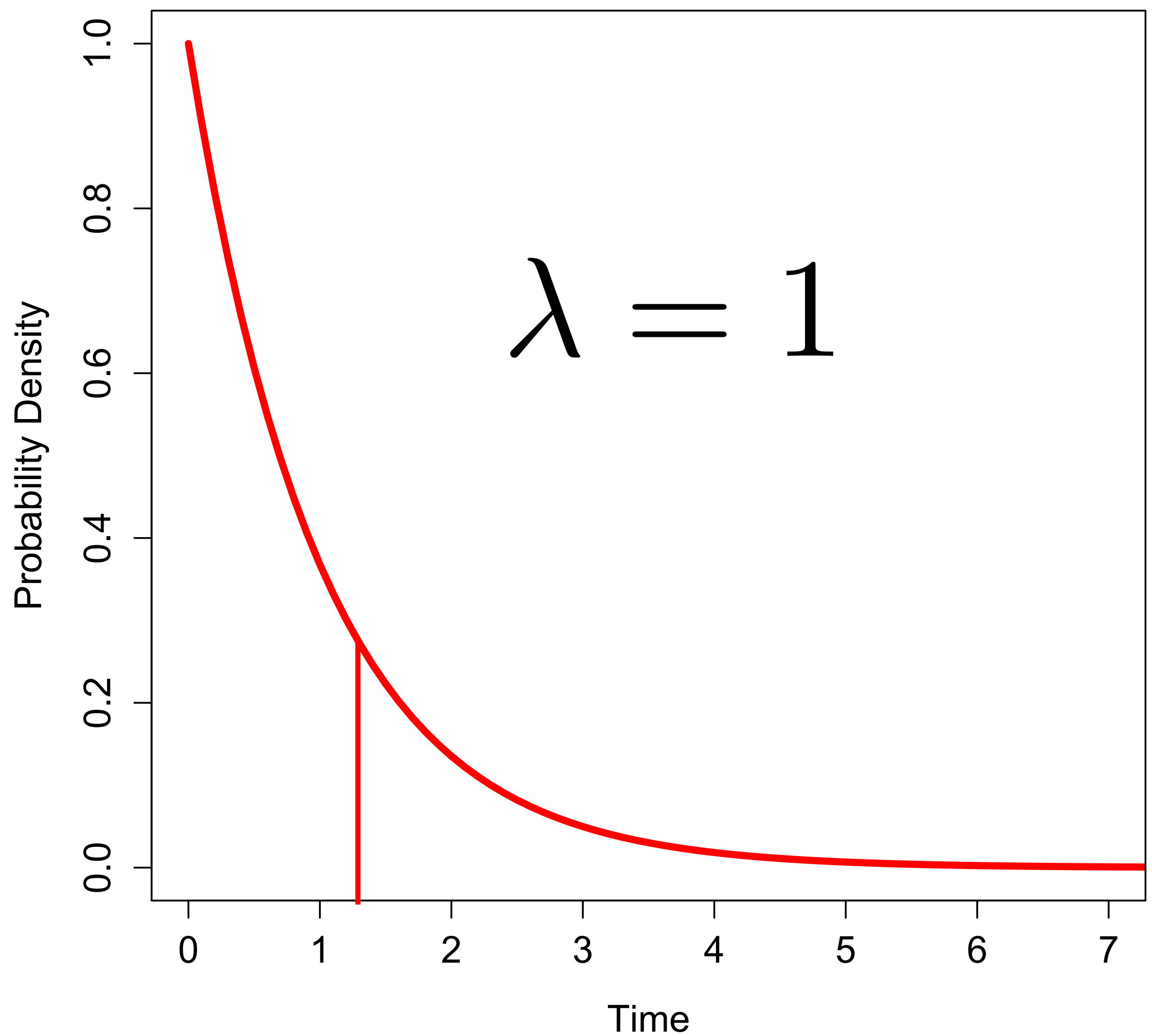

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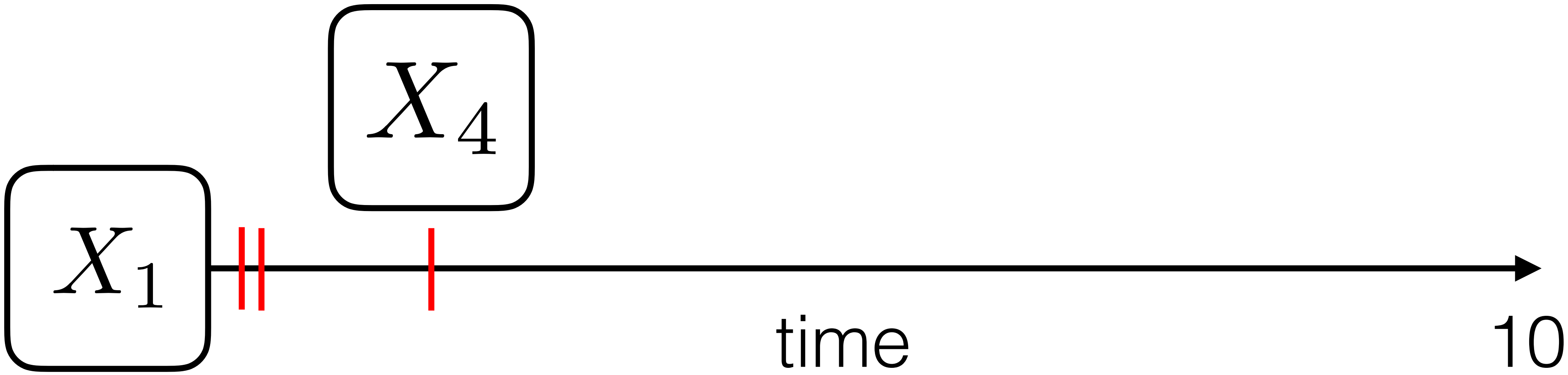

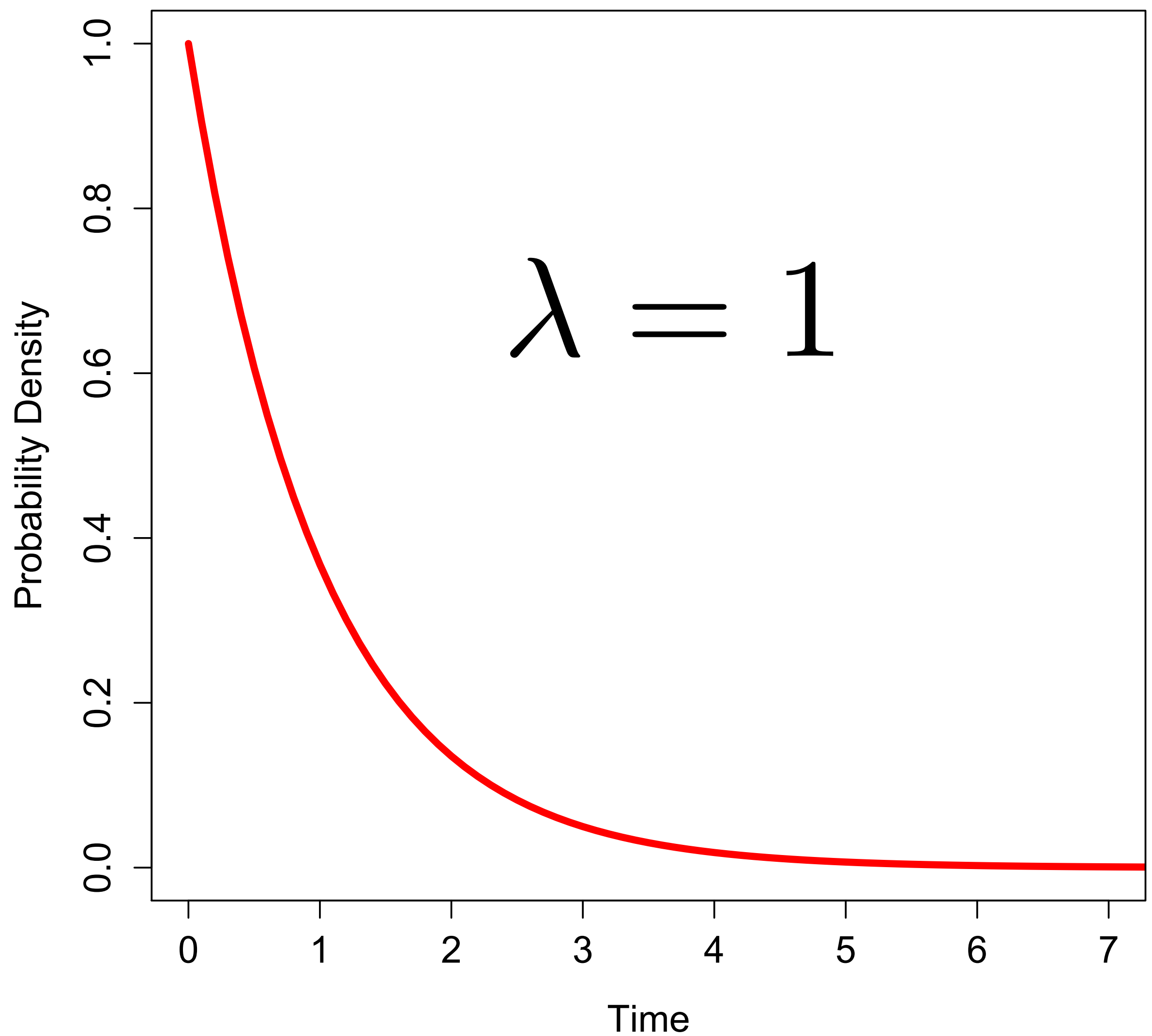

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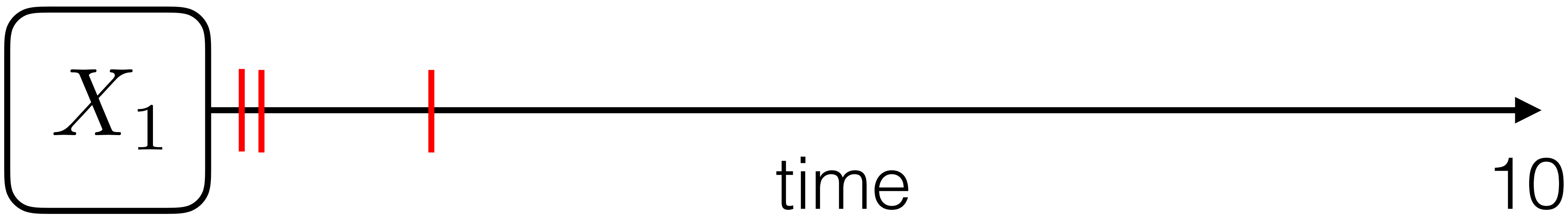

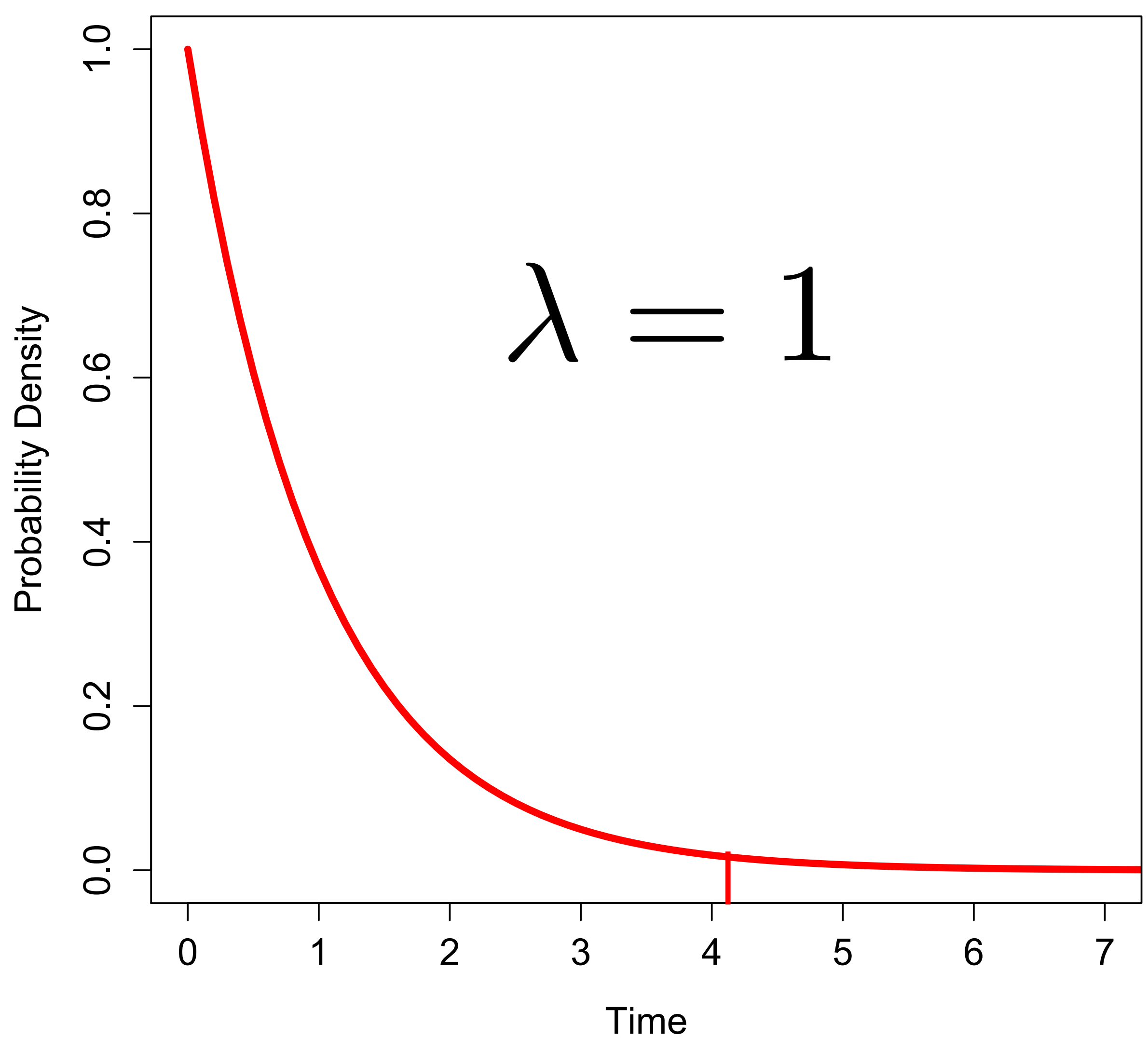

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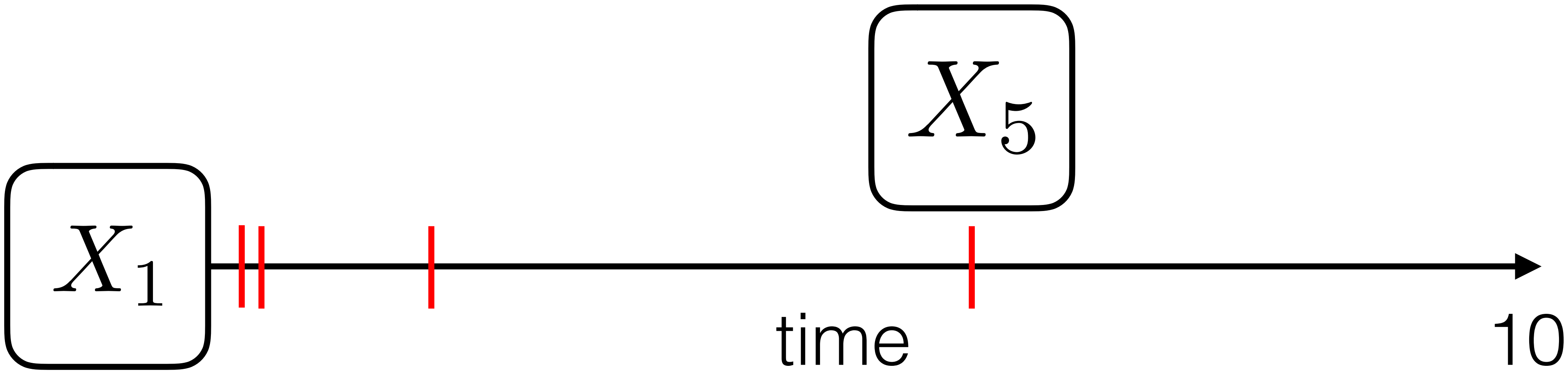

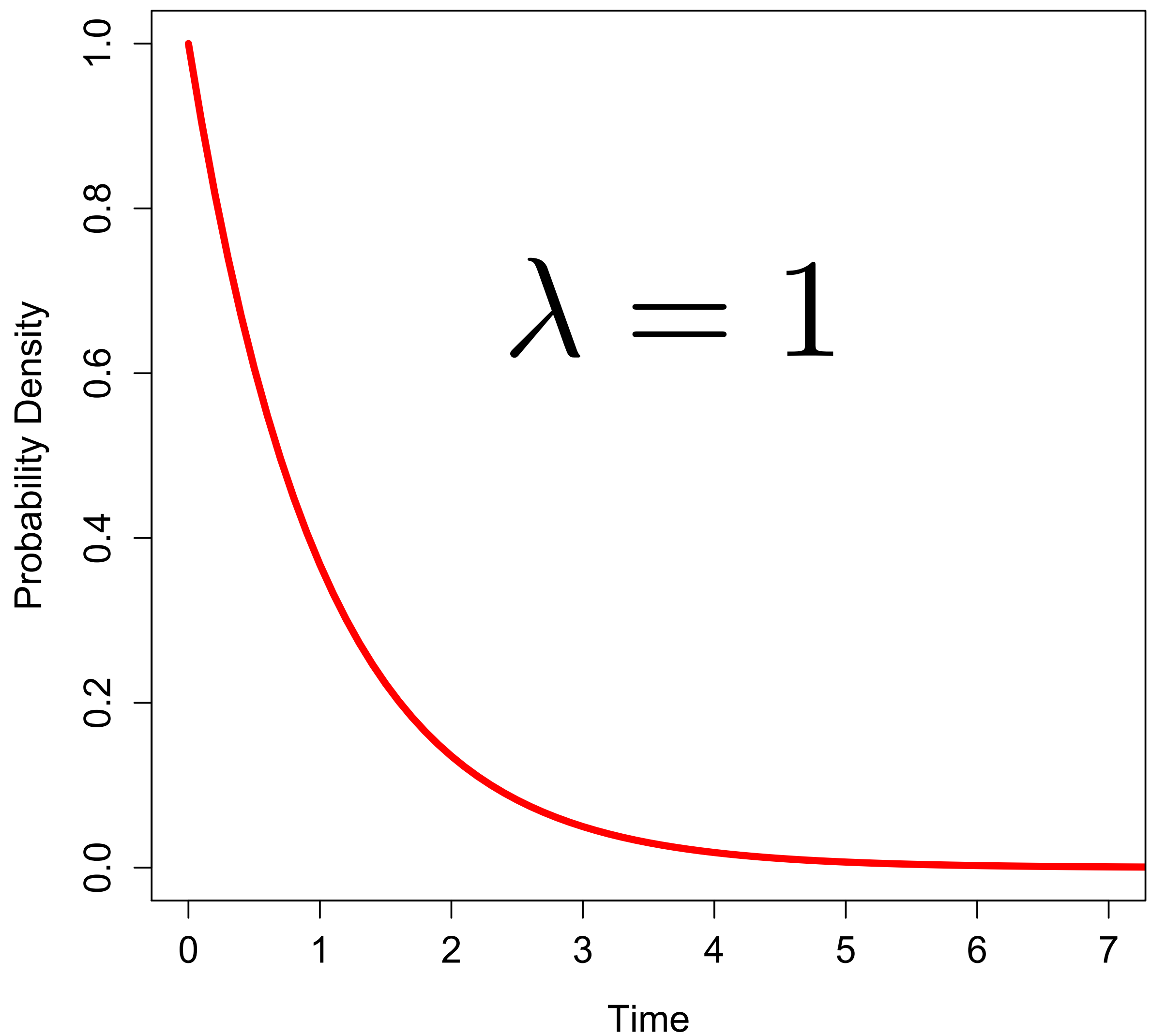

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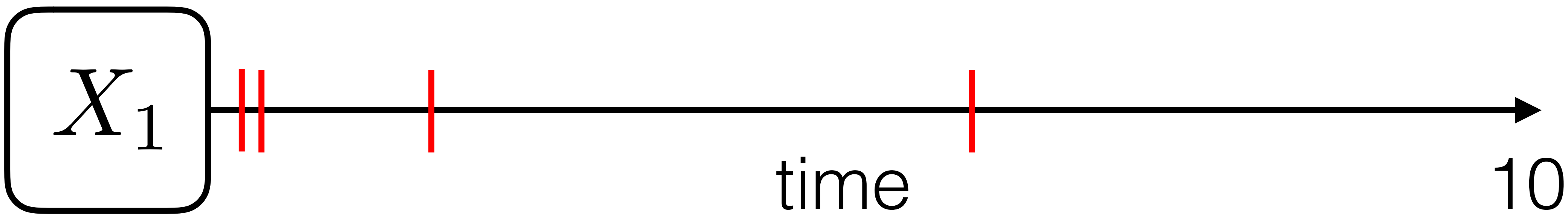

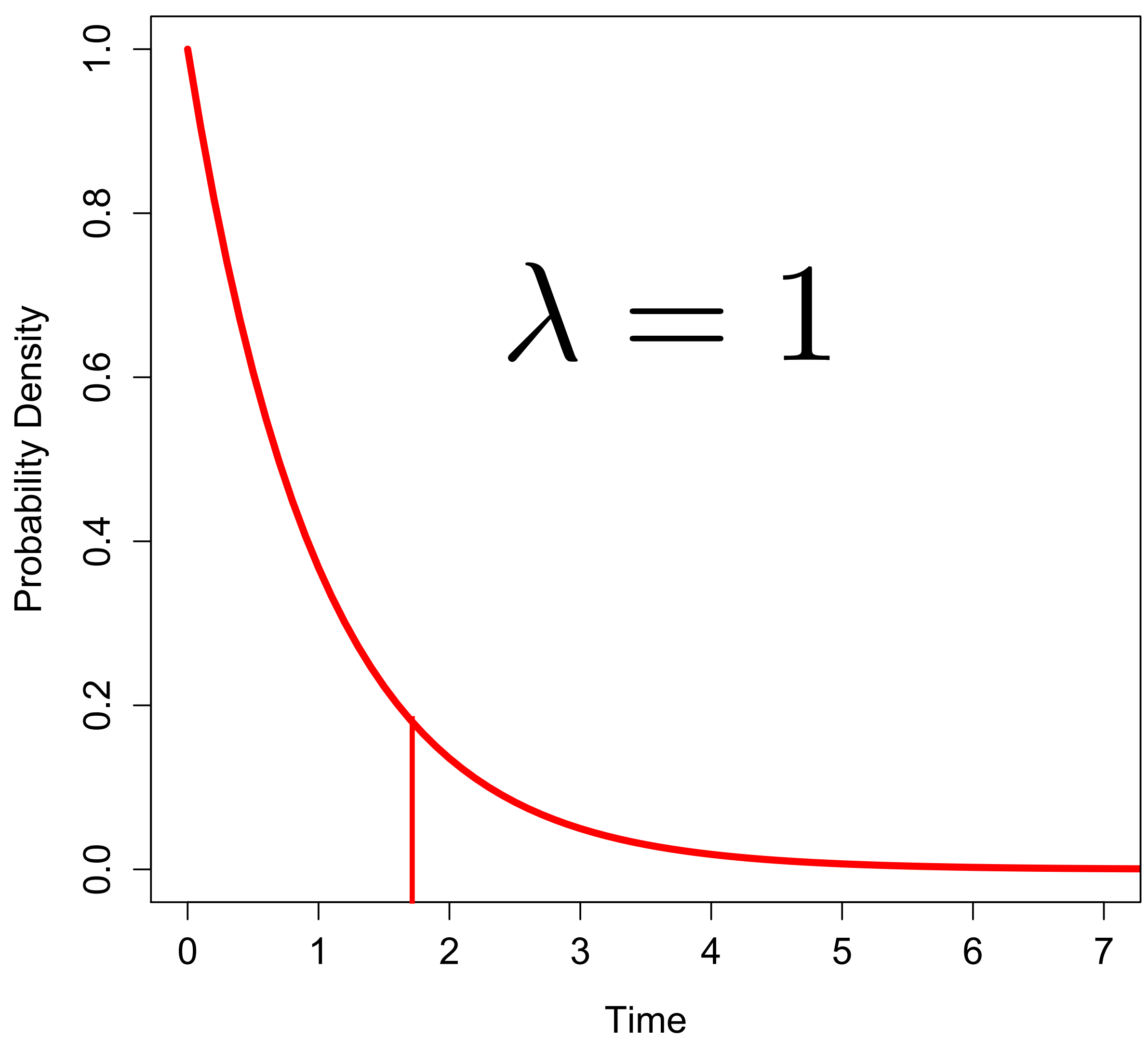

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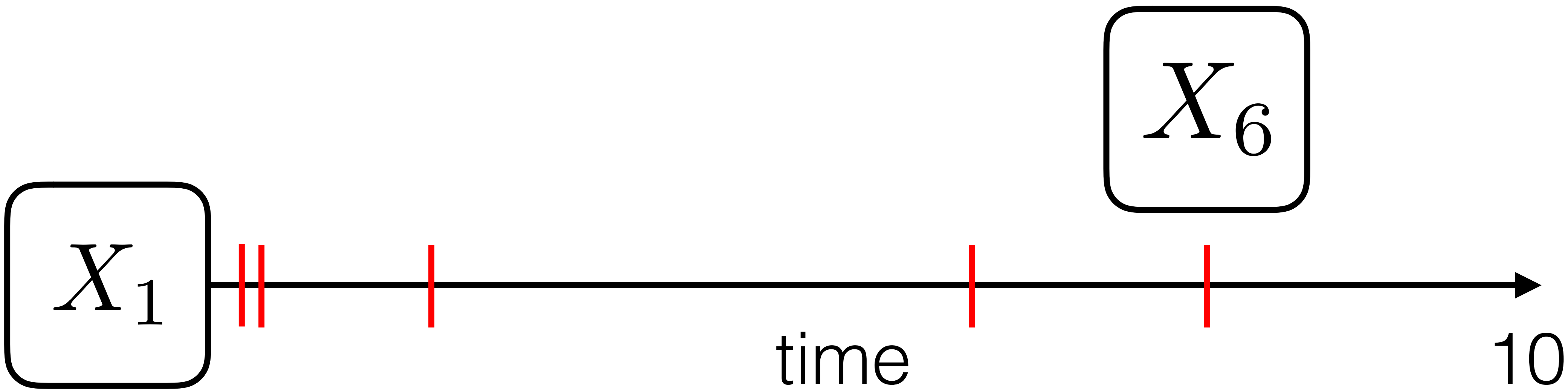

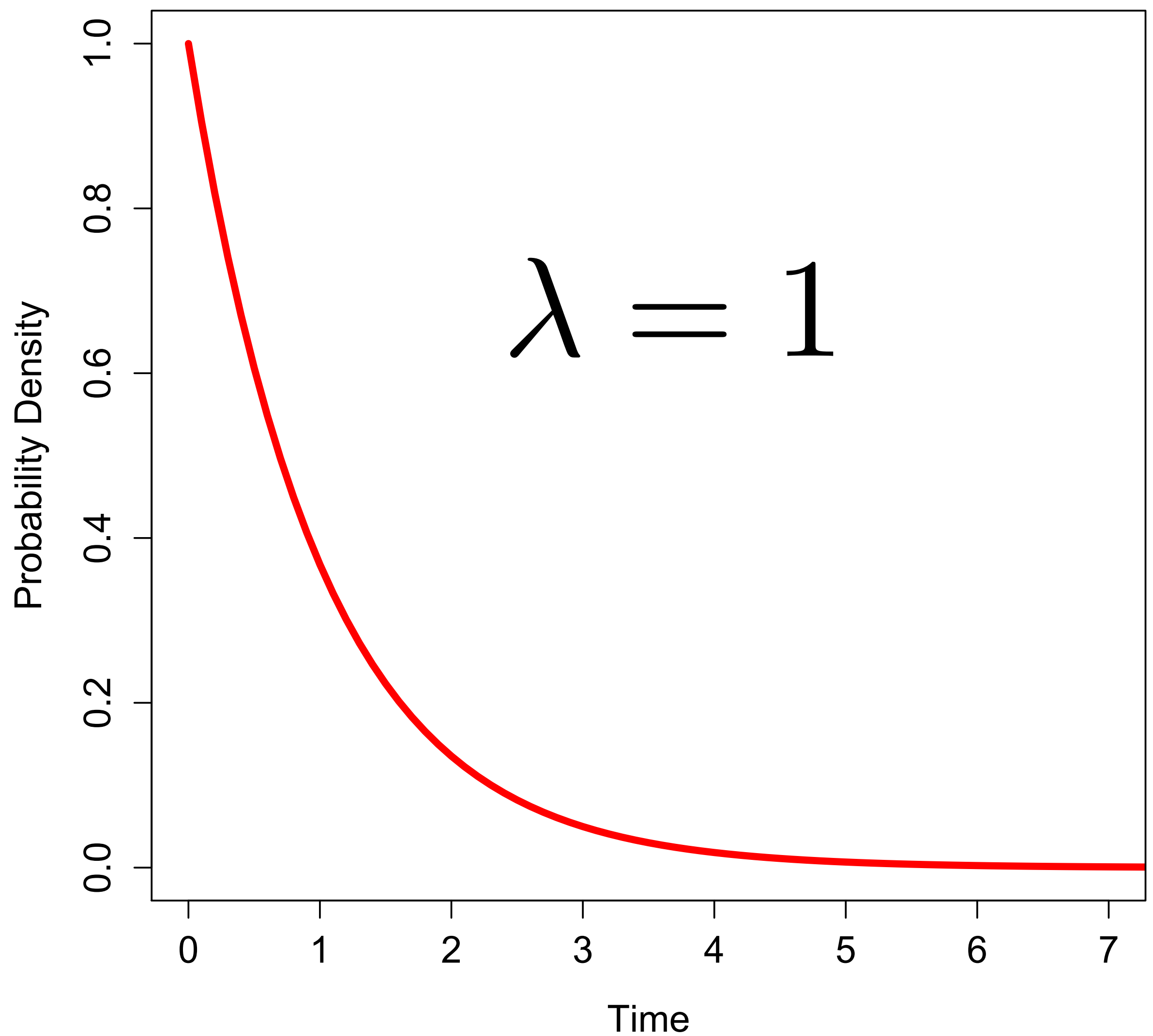

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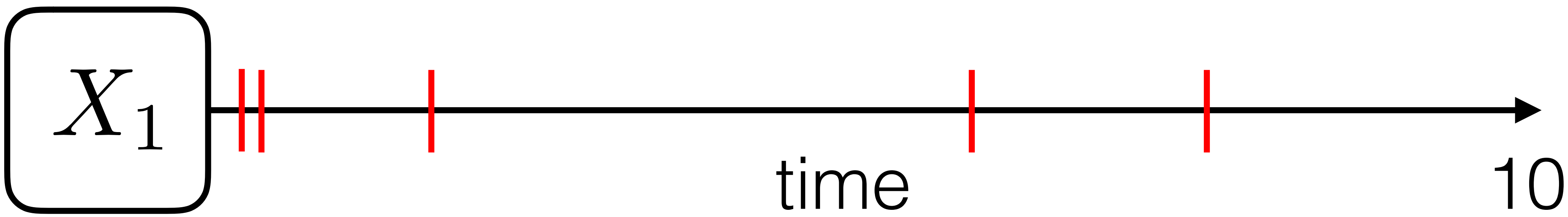

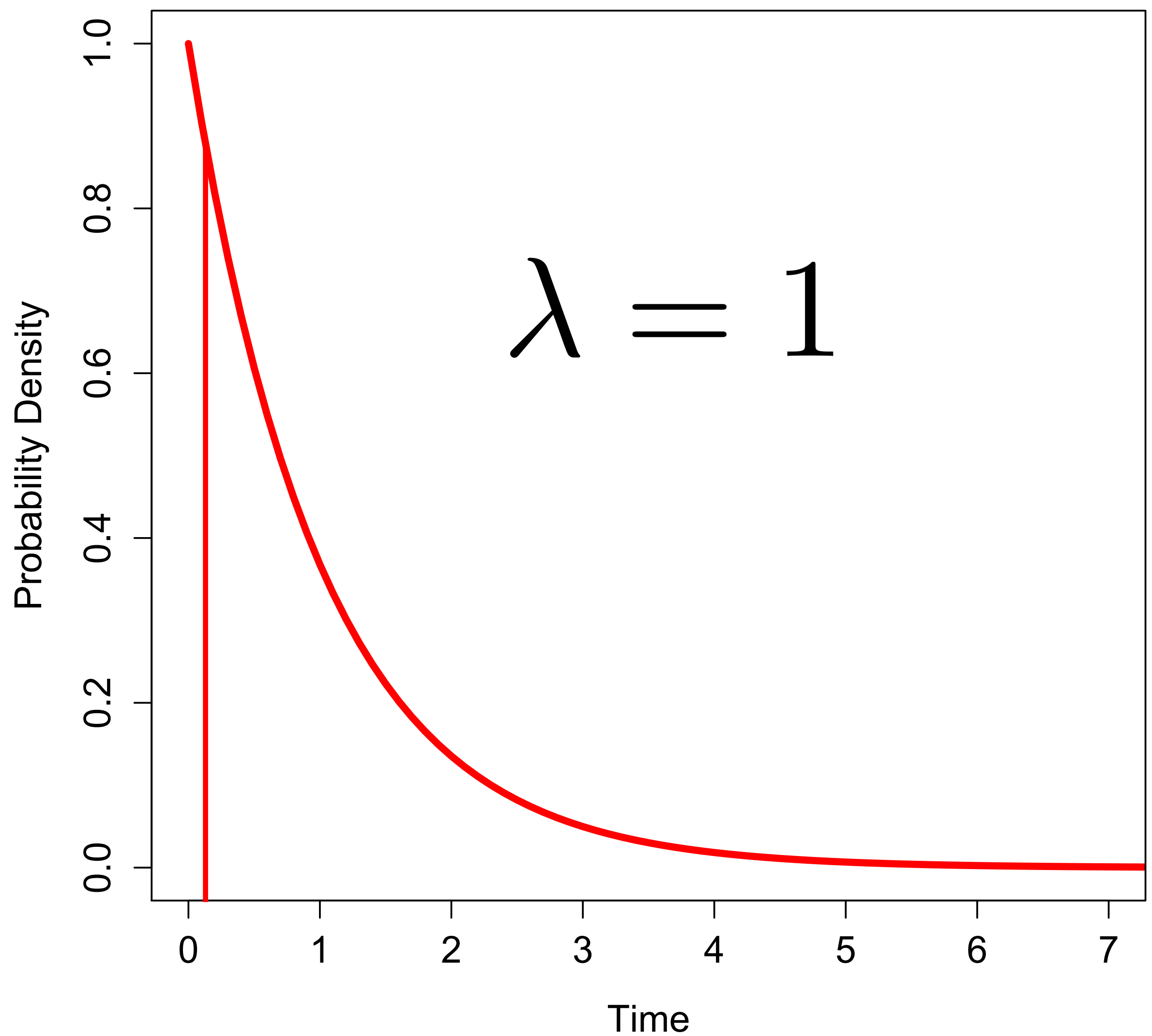

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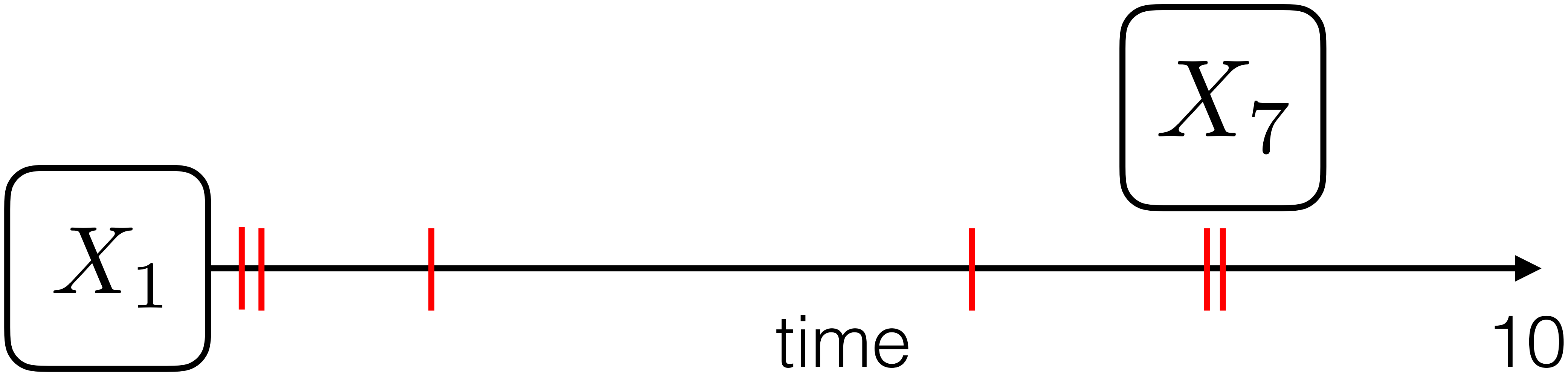

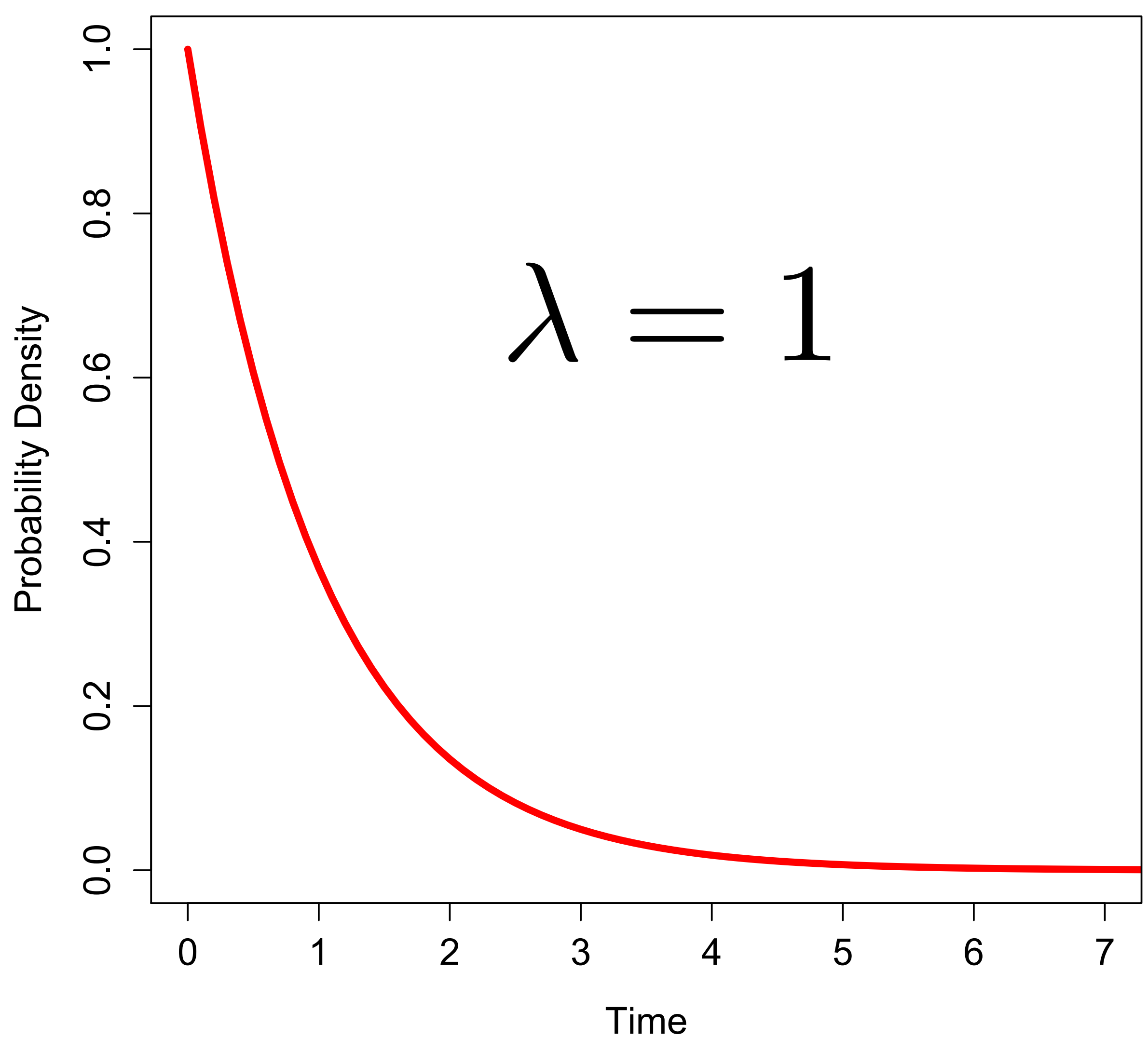

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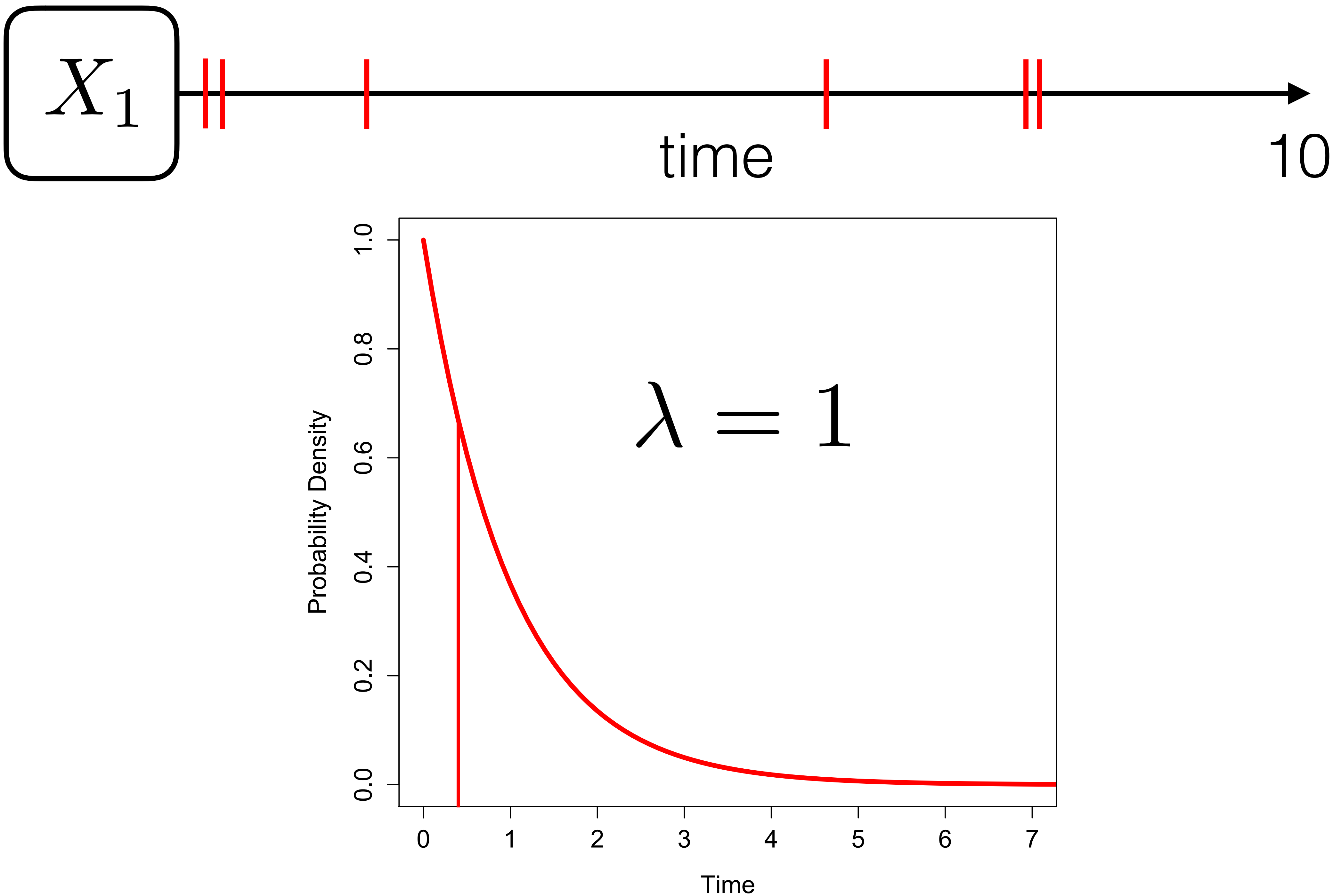

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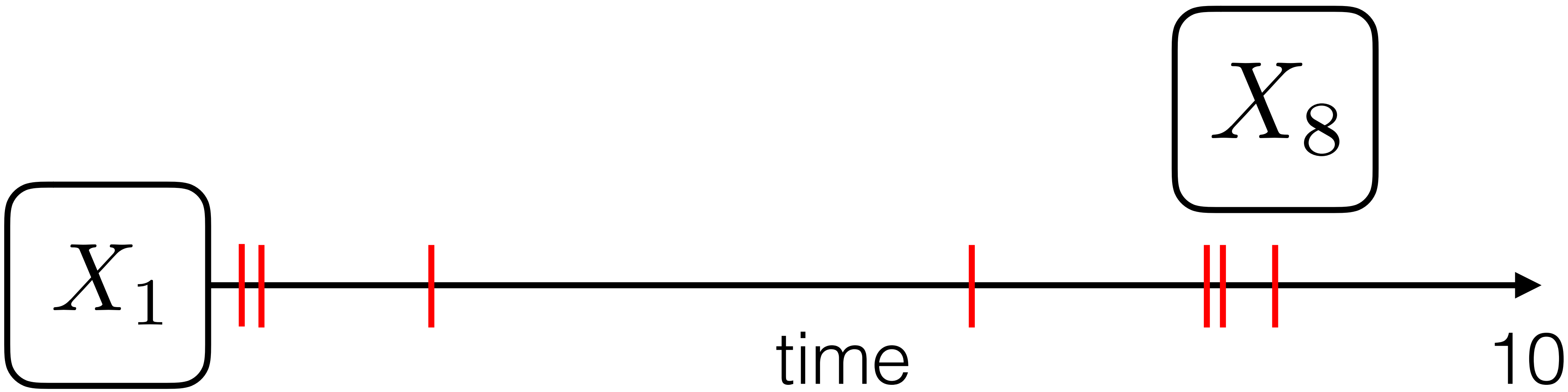

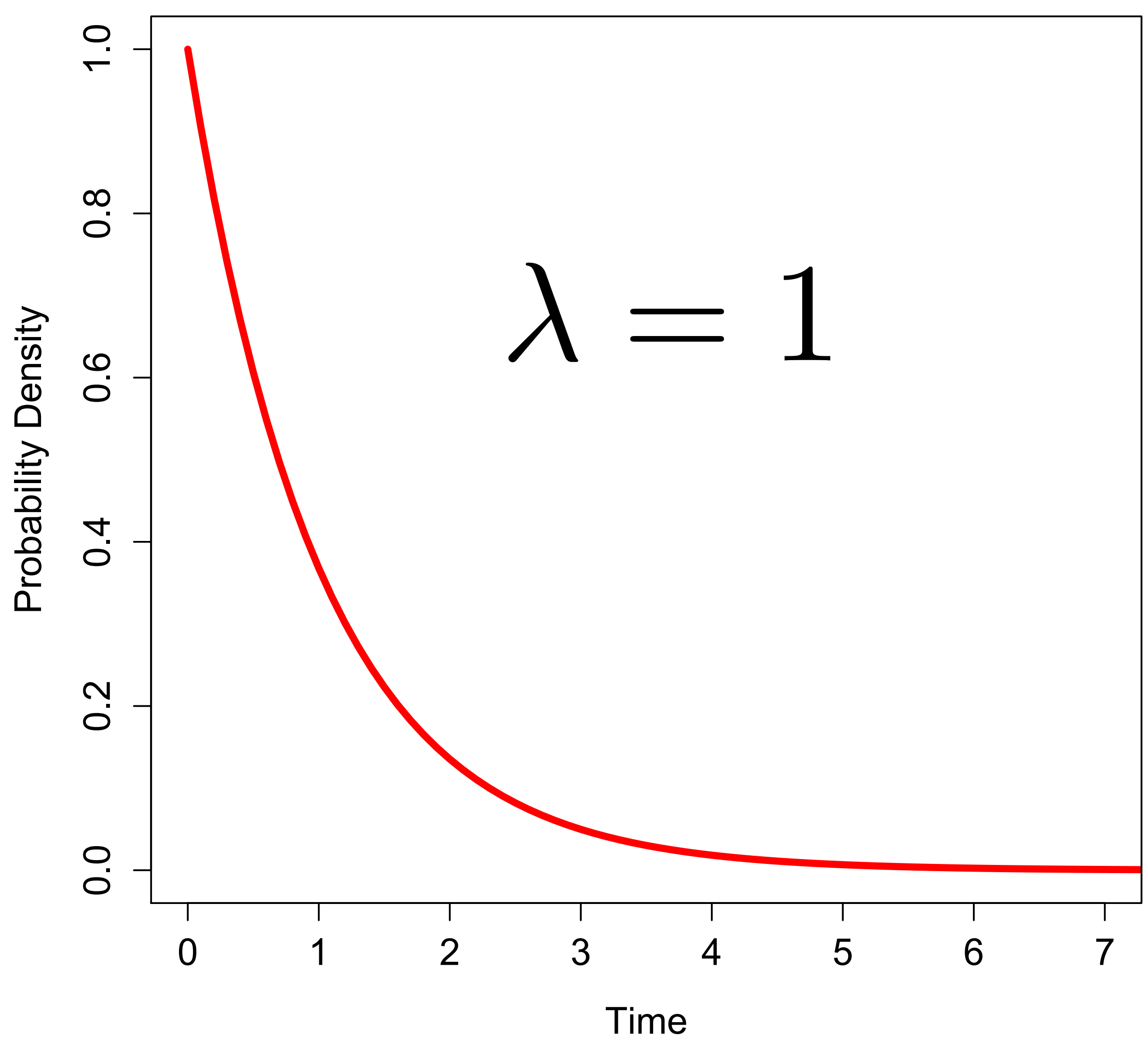

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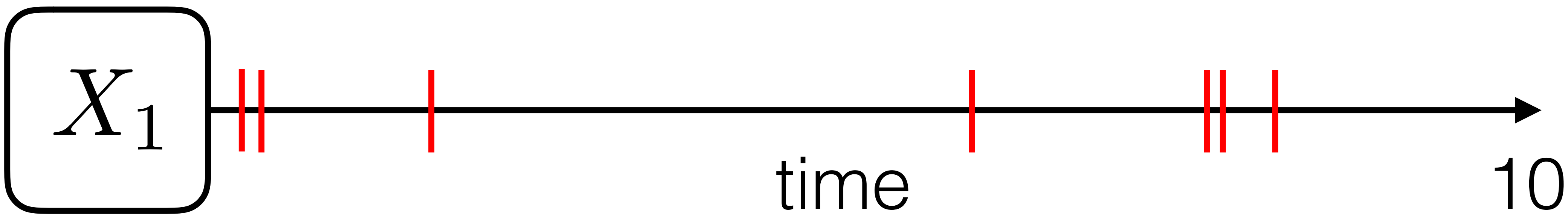

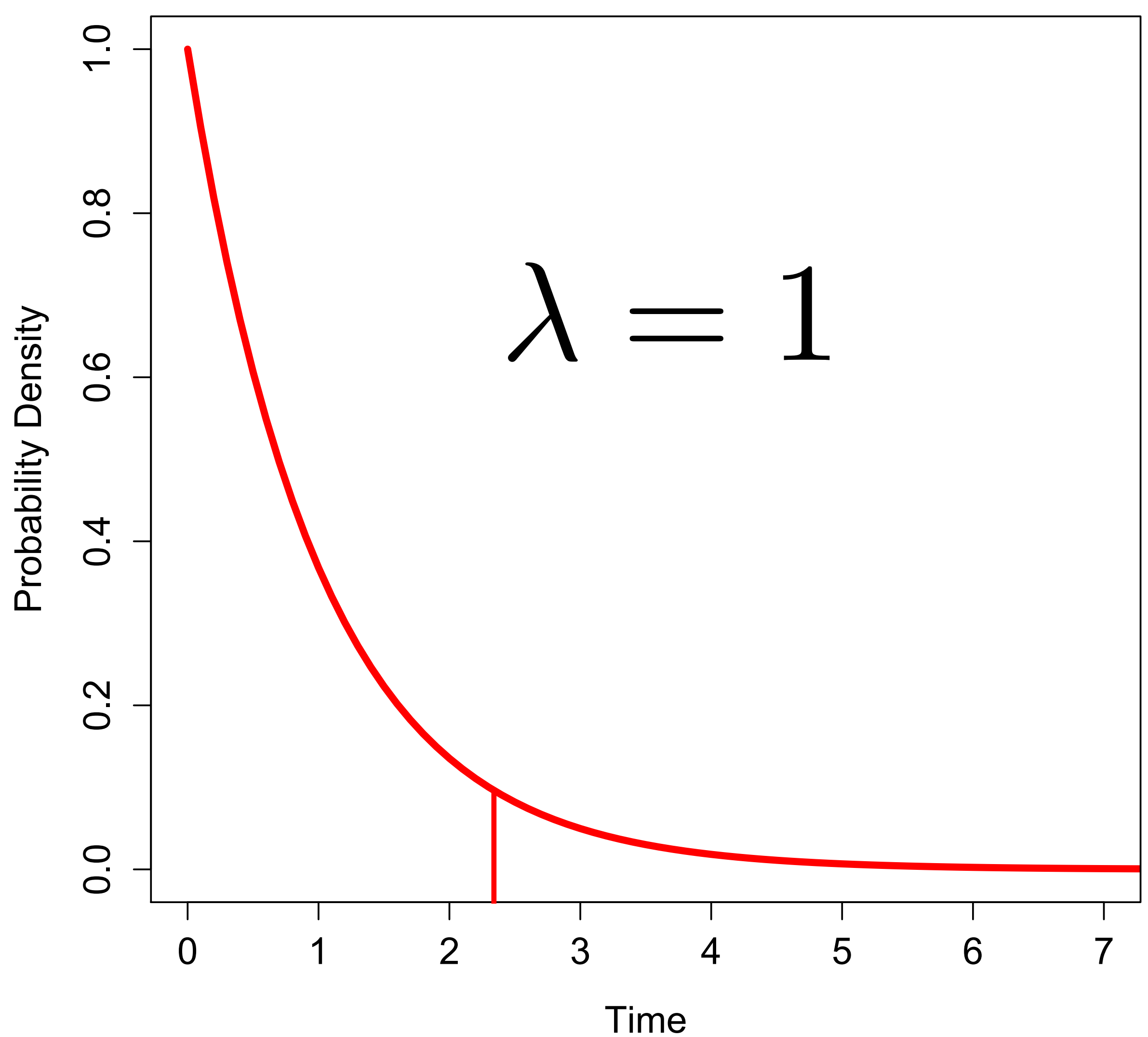

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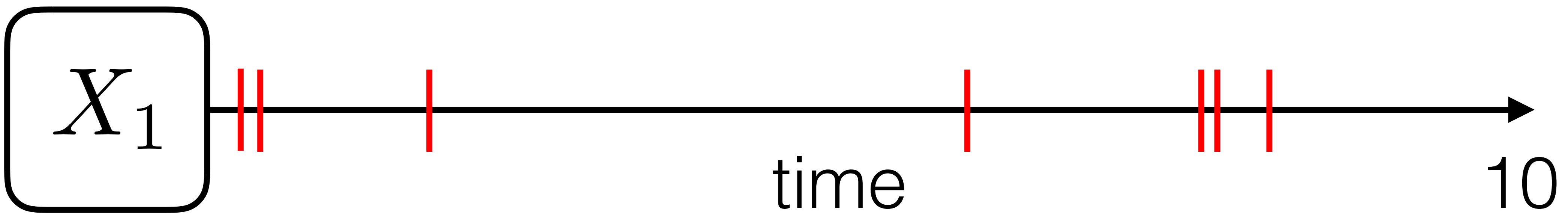

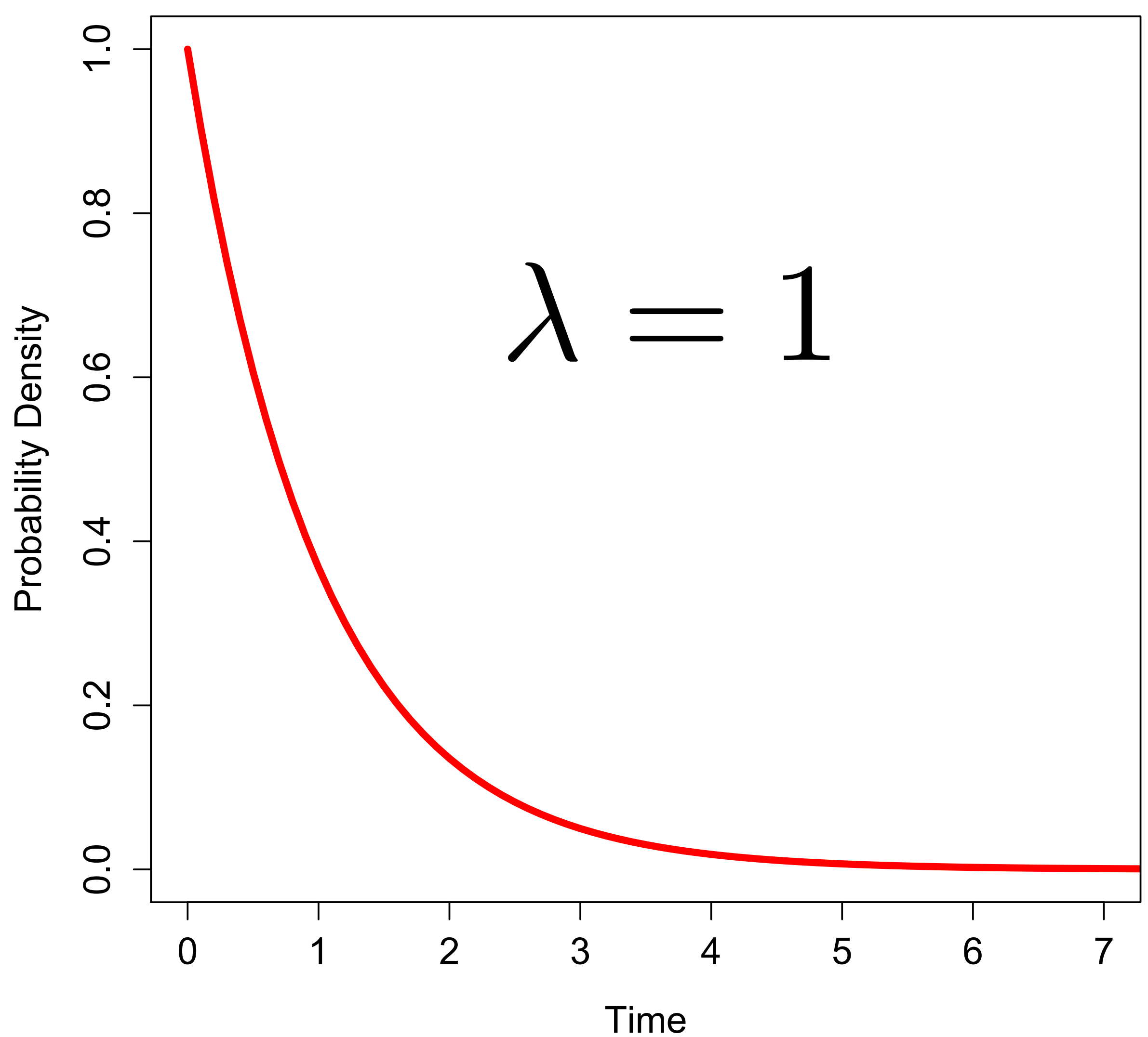

CTMC Transition Matrix

$$
\begin{array}{c c}
 & \begin{array}{cccc} A & C & G & T \end{array} \\
\begin{array}{c} A \\ C \\ G \\ T \end{array} &
\begin{pmatrix}
-1 & 1/3 & 1/3 & 1/3 \\
1/3 & -1 & 1/3 & 1/3 \\
1/3 & 1/3 & -1 & 1/3 \\
1/3 & 1/3 & 1/3 & -1
\end{pmatrix}
\end{array}
$$

Jukes and Cantor (1969)

CTMC Transition Matrix

$$
\begin{array}{c c}
 & \begin{array}{cccc} A & C & G & T \end{array} \\
\begin{array}{c} A \\ C \\ G \\ T \end{array} &
\begin{pmatrix}
\boxed{-1} & 1/3 & 1/3 & 1/3 \\
1/3 & -1 & 1/3 & 1/3 \\
1/3 & 1/3 & -1 & 1/3 \\
1/3 & 1/3 & 1/3 & -1
\end{pmatrix}
\end{array}
$$

Jukes and Cantor (1969)

CTMC Transition Matrix

Exponential Rate for State A

$$
\begin{array}{c} \\ A \\ C \\ G \\ T \end{array}
\begin{array}{c}
\begin{array}{cccc} A & C & G & T \end{array} \\
\begin{pmatrix}
\boxed{-1} & 1/3 & 1/3 & 1/3 \\
1/3 & -1 & 1/3 & 1/3 \\
1/3 & 1/3 & -1 & 1/3 \\
1/3 & 1/3 & 1/3 & -1
\end{pmatrix}
\end{array}
$$

Jukes and Cantor (1969)

CTMC Transition Matrix

Relative Probabilities of Transition

$$
\begin{array}{c c}
 & \begin{array}{cccc} A & C & G & T \end{array} \\
\begin{array}{c} A \\ C \\ G \\ T \end{array} &
\begin{pmatrix}
-1 & \boxed{1/3 \quad 1/3 \quad 1/3} \\
1/3 & -1 & 1/3 & 1/3 \\
1/3 & 1/3 & -1 & 1/3 \\
1/3 & 1/3 & 1/3 & -1
\end{pmatrix}
\end{array}
$$

Jukes and Cantor (1969)

CTMC Transition Matrix

$$
\begin{array}{c c}
 & \begin{array}{cccc} A & C & G & T \end{array} \\
\begin{array}{c} A \\ C \\ G \\ T \end{array} &
\begin{pmatrix}
 & \pi_C r_{AC} & \pi_G r_{AG} & \pi_T r_{AT} \\
\pi_A r_{AC} & & \pi_G r_{CG} & \pi_T r_{CT} \\
\pi_A r_{AG} & \pi_C r_{CG} & & \pi_T r_{GT} \\
\pi_A r_{AT} & \pi_C r_{CT} & \pi_G r_{GT} &
\end{pmatrix}
\end{array}
$$

General Time Reversible (GTR; Tavaré 1986)

CTMC Transition Matrix

$$\pi = (\pi_A, \pi_C, \pi_G, \pi_T) \qquad R = \begin{array}{cc} & \begin{array}{cccc} A & C & G & T \end{array} \\ \begin{array}{c} A \\ C \\ G \\ T \end{array} & \begin{pmatrix} & r_{AC} & r_{AG} & r_{AT} \\ & & r_{CG} & r_{CT} \\ & & & r_{GT} \\ & & & \end{pmatrix} \end{array}$$

$$Q = \begin{array}{cc} & \begin{array}{cccc} A & C & G & T \end{array} \\ \begin{array}{c} A \\ C \\ G \\ T \end{array} & \begin{pmatrix} & \pi_C r_{AC} & \pi_G r_{AG} & \pi_T r_{AT} \\ \pi_A r_{AC} & & \pi_G r_{CG} & \pi_T r_{CT} \\ \pi_A r_{AG} & \pi_C r_{CG} & & \pi_T r_{GT} \\ \pi_A r_{AT} & \pi_C r_{CT} & \pi_G r_{GT} & \end{pmatrix} \end{array}$$

General Time Reversible (GTR; Tavaré 1986)

Reversibility

$$\pi_i q_{ij} = \pi_j q_{ji}, \text{ for all } i \neq j$$

$$Q = \begin{array}{c c} & \begin{array}{cccc} A & C & G & T \end{array} \\ \begin{array}{c} A \\ C \\ G \\ T \end{array} & \begin{pmatrix} & \pi_C r_{AC} & \pi_G r_{AG} & \pi_T r_{AT} \\ \pi_A r_{AC} & & \pi_G r_{CG} & \pi_T r_{CT} \\ \pi_A r_{AG} & \pi_C r_{CG} & & \pi_T r_{GT} \\ \pi_A r_{AT} & \pi_C r_{CT} & \pi_G r_{GT} & \end{pmatrix} \end{array}$$

$$\text{if } i = \text{A and } j = \text{C},$$

$$\pi_A q_{AC} = \pi_C q_{CA}$$

$$\pi_A \pi_C r_{AC} = \pi_C \pi_A r_{AC}$$

Branch-Length Scaling

$$\begin{array}{c c} & \begin{array}{cccc} A & C & G & T \end{array} \\ \begin{array}{c} A \\ C \\ G \\ T \end{array} & \begin{pmatrix} & \pi_C r_{AC} & \pi_G r_{AG} & \pi_T r_{AT} \\ \pi_A r_{AC} & & \pi_G r_{CG} & \pi_T r_{CT} \\ \pi_A r_{AG} & \pi_C r_{CG} & & \pi_T r_{GT} \\ \pi_A r_{AT} & \pi_C r_{CT} & \pi_G r_{GT} & \end{pmatrix} \end{array}$$

Branch lengths typically denote expected number of substitutions. For this to be true, the weighted mean across all changes must be 1.