Mixtures of partially observed continuous-time multi-state models

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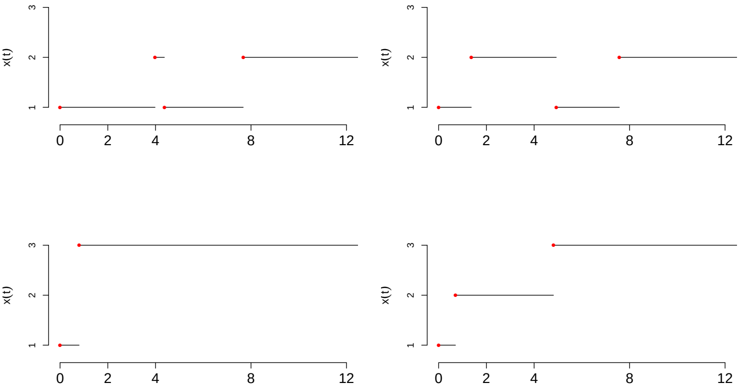
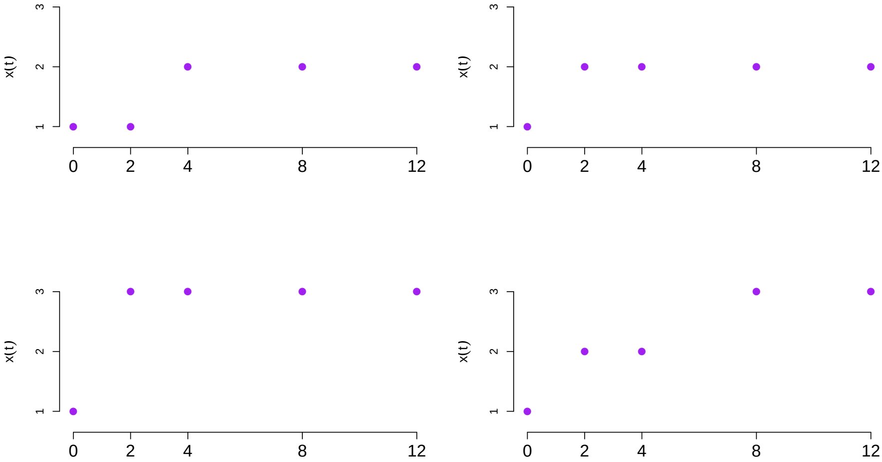
Multi-state models

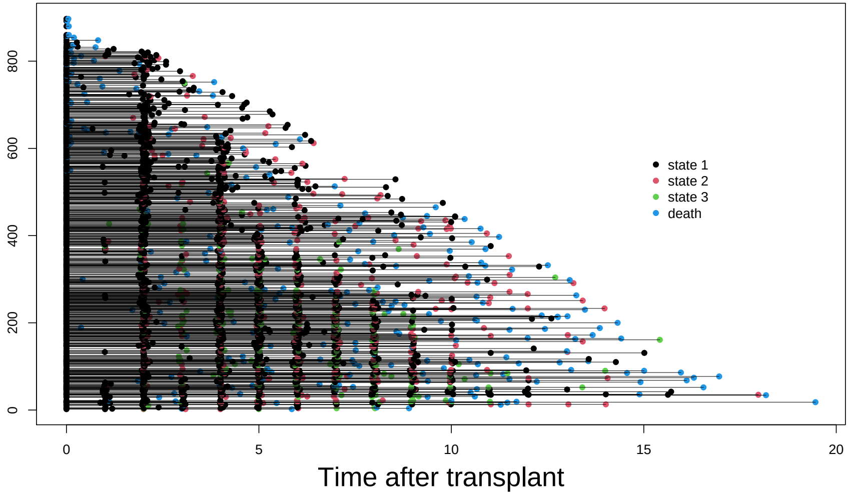
- Continuous time multi state models (CTMSM) are continuous processes $\{Y(t), t \geq 0\}$ with state space $\mathcal{S} = \{1, 2, \ldots, S\}$.



- Completely observed path



- **Partially observed paths.** Let $x_i = (x_{i\,0}, x_{i\,1}, \ldots, x_{i\,n_i})$ be the observed states at the times $0{=}t_{i\,0} < t_{i,1} < \cdots < t_{i,n_i}$ for the *i-th* unit.



0
200
400
600
800
0
5
10
15
20
Time after transplant
state 1
state 2
state 3
death

Classes of continuous time multi-state models

- Markov models

$$P\{Y(t+\delta t)=s|Y(t)=r,\mathcal{F}_t\} = \begin{cases} \gamma_{rs}\delta t + o(\delta t) & s \neq r \\ 1+\gamma_{rr}\delta t + o(\delta t) & s = r \end{cases}$$

- semi-Markov models

$$P\{Y(t+\delta t)=s|Y(t)=r,T^*=t-u\} = \begin{cases} q_{rs}(u)\delta t + o(\delta t) & s \neq r \\ 1-\sum_{l\neq r} q_{rl}(u)\delta t + o(\delta t) & s = r \end{cases}$$

- time-inhomogeneous Markov models

$$P\{Y(t+\delta t)=s|Y(t)=r,\mathcal{F}_t\} = \begin{cases} \gamma_{rs}(t)\delta t + o(\delta t) & s \neq r \\ 1+\gamma_{rr}(t)\delta t + o(\delta t) & s = r \end{cases}$$

MSM density

MSM over $[0.T]$ are characterized by the r.v. (Z, S)

- $Z = (Z_1, Z_2, \ldots, Z_M)$ provides the ordered jump times
- $S = (S_1, S_2, \ldots, S_M)$ provides the state sequences

Thus, $Y(t) \leftrightarrow (Z, S)$ and for Markov MSM

$$p_M(y) = p_M(z, s) = \left(\prod_{rs} p_{rs}^{n_{rs}}\right) \left(\prod_{r} \gamma_r^{n_r} e^{-\gamma_r d_r}\right)$$

- Analytical expression also for **completely observed** semi-Markov and inhomogeneous Markov models
- **Likelihood intractability** for partially observed paths

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BIOMETRIC PRACTICE

WILEY Biometrics

Approximate Bayesian inference for discretely observed continuous-time multi-state models

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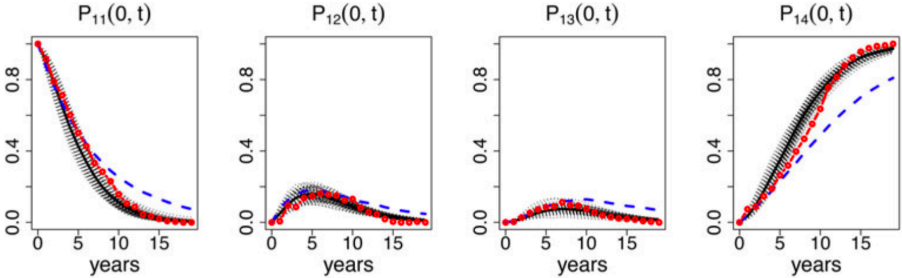

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RESEARCH ARTICLE

Statistics in Medicine WILEY

Bayesian inference for discretely observed continuous time multi-state models

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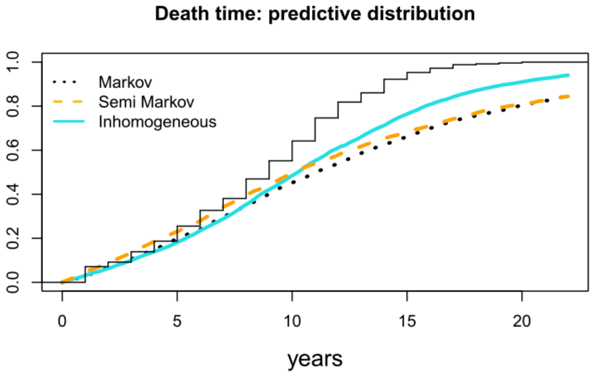
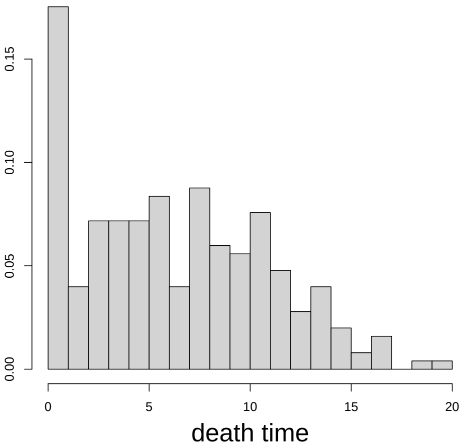
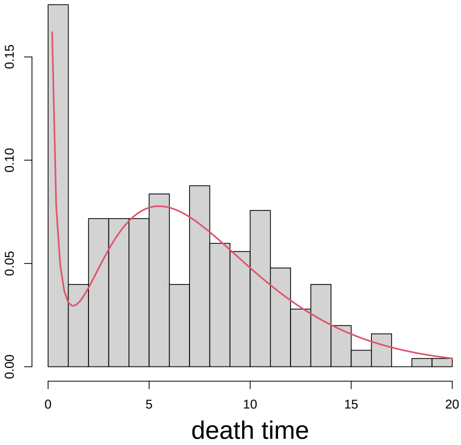


Mixture models

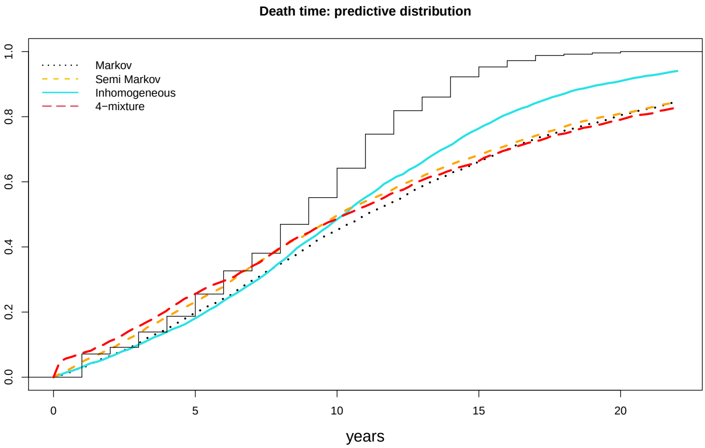


Mixture models



$$f(t) = p_1 f_{\theta_1}(t) + p_2 f_{\theta_2}(t)$$

- Mixtures of multi-state Markov models



Dirichlet Process Mixtures

- Let f_θ be a continuous probability density function, with $\theta \in \Theta$ and let G be a probability distribution on Θ. The density function of a mixture f_θ with respect to G is

$$f_G(y) = \int f_\theta(y) dG(\theta).$$

- With a Dirichlet Process prior on the mixing distribution G, we get a DP Mixture (DPM) model.
- Let $y_i = (z, s)_i$ for $i = 1, \ldots, n$ be MSM data on $[0, t_i]$. We take

$$y_i | \theta_i \overset{ind}{\sim} f_{\theta_i}$$

$$\theta_i | G \overset{iid}{\sim} G$$

$$G \sim DP(MG_0)$$

which is a DPM mixture of multi-state models .

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