

**Title: MULTI-STATE MODELS WITH MULTIPLE TIMESCALES: A BAYESIAN APPROACH**

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**Abstract:**

In the context of fitting a multi-state model to biomedical data, one often has to make what seems like an impossible tradeoff: model the time since the state transition (the gap-time), or model the time since enrollment in the study (the survival-time)? While there are cases where hazard varies more clearly according to the gap time, such as when considering transitions between states such as (1) disease-free, (2) with disease, and (3) fatality, there are counter-examples where the hazard depends more clearly on survival time, such as when considering states such as (1) on-treatment, (2) post-adverse-event, and (3) fatality.

Here, we describe a multi-state model implemented in Stan[1] that resolves this tradeoff by supporting multiple time scales, such that the log baseline event rate(log-hazard) at any follow-up time  $t$  reflects the sum of contributions from each time-scale[2].

We present this model in the context of a motivating example using simulated data: estimating the incidence of various disease progression and/or adverse events along with the risk of subsequent fatality. We discuss the similarities and differences between the multiple-time-scale approach vs a more standard semi-Markov Multi-State Model[3], and compare the cumulative estimated patient- and population-level event risk by approach since this is of primary interest for clinical decision making.

References

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