1 Smooth accelerated failure time models

1.1 Time-constant acceleration factors

Let survival to time t for covariates x be modelled as an accelerated failure time model using

$$S(t|x) = S_0(t\exp(-\eta(x;\beta)))$$

where η is a linear predictor. Moreover, let the baseline survival function be modelled as

$$S_0(t) = \exp(-\exp(\eta_0(\log(t);\beta_0)))$$

where η_0 is a linear predictor. Then the combined regression model is

$$S(t|x) = \exp(-\exp(\eta_0(\log(t) - \eta(x;\beta);\beta_0)))$$

We can calculate the hazard, such that

$$\begin{aligned}
h(t|x) &= \frac{\partial}{\partial t}\left(-\log(S(t|x))\right) \\
&= \exp(\eta_0(\log(t) - \eta(x;\beta);\beta_0))\eta_0'(\log(t) - \eta(x;\beta);\beta_0)/t
\end{aligned}$$

1.2 Time-dependent acceleration factors

We can model survival as an accelerated failure time model with time-dependent effects as

$$S(t|x) = S_0\left(\int_0^t \exp(-\eta_1(x,u;\beta))\mathrm{d}u\right) = S_0\left(t\exp(-\eta(x,t;\beta))\right)$$

for a time-specific linear predictor η_1 and where η now models for cumulative time-dependent effects. By differentiation with respect to time t, we have that

$$\begin{aligned}
\exp(-\eta_1(x,t;\beta)) &= \frac{\partial}{\partial t} t\exp(-\eta(x,t;\beta)) \\
&= \exp(-\eta(x,t;\beta))\left(1 - t\frac{\partial}{\partial t}\eta(x,t;\beta)\right)
\end{aligned}$$

so that $\eta_1(x,t;\beta) = \eta(x,t;\beta) - \log\left(1 - t\frac{\partial}{\partial t}\eta(x,t;\beta)\right)$. This shows that we can recover the time-specific acceleration factors from η.

The combined regression model is then

$$S(t|x) = \exp(-\exp(\eta_0(\log(t) - \eta(x,t;\beta);\beta_0)))$$

The hazard is then

$$\begin{aligned}
h(t|x) &= \frac{\partial}{\partial t} - \log(S(t|x)) \\
&= \exp(\eta_0(\log(t) - \eta(x,t;\beta);\beta_0))\,\eta_0'(\log(t) - \eta(x,t;\beta);\beta_0)\times \\
&\quad \left(1/t - \frac{\partial}{\partial t}\eta(x,t;\beta)\right)
\end{aligned}$$

1.3 R implementation

The linear predictor η_0 is modelled using natural splines. The linear predictor η can be modelled freely provided the linear predictor is a smooth function of time.

Initial values for the time-constant log acceleration factors were calculated from a Weibull regression. The time-varying log acceleration factors were assumed to be zero. Cox regression and the Breslow estimator was used to calculate baseline survival; parameters for the baseline were estimated using linear regression with natural splines fitted to the log-times at the event times.

We included quadratic penalties to ensure that $\eta_0'(\log(t) - \eta(x, t; \beta); \beta_0)$ and $1/t - \frac{\partial}{\partial t}\eta(x, t; \beta)$ were positive. For speed, the model has been implemented in C++, with optimisation using the Nelder-Mead algorithm.