Setting

Suppose that subjects are followed across time, and may experience multiple occurrences of the target event (e.g. myocardial infarction) before experiencing a single terminal event (e.g. censoring or death).

Anderson Gill (AG)

2.1 Model

The AG model assumes that the numbers of events occurring in non-overlapping increments are independent. All events share a common baseline hazard function $\lambda_0(t)$. The intensity process of the kth event in the ith subject is:

$$Y_i(t)\lambda_0(t)\exp\big\{X_i(t)\beta\big\},$$

where $Y_i(t)$ is the at-risk indicator, $X_i(t)$ is the covariate process, and β is the common log hazard ratio. The at-risk $Y_i(t)$ indicator remains 1 until a terminal event is experienced. The partial likelihood is:

$$L(\beta) = \prod_{j=1}^{J} \frac{\exp(X_j\beta)}{\sum_{l\in\mathcal{R}(\tau_j)}\exp(X_l\beta)},$$

where $\tau_1 < \cdots < \tau_J$ are the distinct ordered event times, and $\mathcal{R}(\tau_j)$ is the risk set at time τ_j, composed of those subjects who have not experienced a terminal event.

2.2 Implementation

Suppose that a subject experiences 2 events at times t_1 and t_2, then is censored at time t_3. The data are arranged in counting process format $\{[0, t_1], (t_1, t_2], (t_2, t_3]\}$, and all events belong to a single stratum:

idx	start	stop	status	stratum
i	0	t_1	1	1
i	t_2	t_2	1	1
i	t_2	t_3	0	1

Using the `survival` package in `R`, the proportional hazards model is fit using the syntax:

```
coxph(Surv(start, stop, status) ~ cluster(idx), data)
```

The term `cluster(idx)` identifies groups of observations that belong to the same subject. When a cluster term is specified, a robust standard error is estimated.

Prentice Williams Peterson

3.1 Model

The PWP model stratifies by the number of events a subject has experienced during the follow-up period. Each occurrence k of the recurrent event receives its own baseline hazard $\lambda_{0k}(t)$, and the association of the covariate process $X_i(t)$ with the intensity may vary across occurrences, hence β_k is indexed the event number. The intensity process for the kth event in the ith subject is:

$$Y_{ik}(t)\lambda_{0k}(t)\exp\left\{X_i(t)\beta_k\right\}.$$

The at-risk indicator $Y_{ik}(t)$ is zero until event $(k-1)$ occurs, then becomes one until the first of event k or censoring. The partial likelihood is:

$$L(\beta_1,\cdots,\beta_K)=\prod_{k=1}^{K}\prod_{j=1}^{J_k}\frac{\exp(X_{jk}\beta_k)}{\sum_{l\in\mathcal{R}(\tau_{jk})}\exp(X_{lk}\beta_k)}, \tag{3.1.1}$$

where $\tau_{1k}<\cdots<\tau_{J_kk}$ are the distinct ordered event k occurrence times, and $\mathcal{R}(\tau_{jk})$ is the risk set for the kth event at time τ_{jk}. In particular, $\mathcal{R}(\tau_{jk})$ is composed of those subjects who have experienced $(k-1)$ events, and have neither experienced a kth recurrent even nor a terminal event before time τ_{jk}.

3.2 Implementation

Suppose that a subject experiences 2 events at times t_1 and t_2, then is censored at time t_3. The data are again arranged in counting process format. However, in contrast to the AG model, each event belongs to a new stratum:

idx	start	stop	status	stratum
i	0	t_1	1	1
i	t_2	t_2	1	2
i	t_2	t_3	0	3

The proportional hazards model is fit using the syntax:

```
coxph(Surv(start, stop, status) ∼ cluster(idx) + strata(stratum), data)
```

The term `strata(stratum)` indicates to stratify the partial likelihood by the even occurrence number.

Wei Lin Weissfeld

4.1   Model

The WLW model stratifies by the maximum number of events a subject may experience during follow-up. Like the PWP model, the intensity process for the kth event in the ith subject takes the form:

$$Y_{ik}(t)\lambda_{0k}\exp\big\{X_i(t)\beta_k\big\}.$$

Consequently, the partial likelihood has the form of (3.1.1). The difference from PWP arises in the definition of the risk set. For WLW, a subject remains at risk for every recurrent event as long as they are under follow-up. That is, any subject who has not experienced a terminal event belongs to $\mathcal{R}(\tau_{jk})$. In this way, the dependence structure among recurrent events is left unspecified.

4.2   Implementation

Suppose that a subject may experience up to $K = 4$ events during follow-up. Events are observed at times t_1 and t_2. The subject is censored at time t_3. The data are arranged in time-to first event format, with each event belonging to a separate stratum. Note that a stratum is created for the 4th event, even though the subject was censored at t_3:

idx	start	stop	status	stratum
i	0	t_1	1	1
i	0	t_2	1	2
i	0	t_3	0	3
i	0	t_3	0	4

The proportional hazards model is fit using the syntax:

```
coxph(Surv(stop, status) ~ cluster(idx) + strata(stratum), data)
```