Web-based Appendix 1

Asymptotic Equivalence of $W_{loc}(x_1, x_2|b)$ and $\hat{W}_{loc}(x_1, x_2|b)$, given the observed data, for the Cumulative Geographic Martingale Residual

We will begin by first showing the asymptotic equivalence of $W_{loc}(x_1, x_2|b)$ and another process $\tilde{W}_{loc}(x_1, x_2|b)$, assuming the Cox's proportional hazards model (Equation 3 in Paper),

$$\lambda(t|\mathbf{X_i}) = \lambda_0(t)\exp[\boldsymbol{\beta}\mathbf{X_i}].$$

Consider the following one-term Taylor series expansion of $W_{loc}(x_1, x_2|b)$ (Equation 6 in Paper) at $\boldsymbol{\beta}$,

$$\begin{aligned}
W_{loc}(x_1, x_2|b) &= \frac{1}{\sqrt{n}} \sum_{i=1}^{n} I_i(x_1, x_2, b)\hat{M}_i(\tau) \\
&\approx \frac{1}{\sqrt{n}} \sum_{i=1}^{n} I_i(x_1, x_2, b)\left[N_i(\tau) - \int_0^{\tau} \frac{V_i(u)\exp(\beta\mathbf{X}_i)}{\sum_{l=1}^{n} V_l(u)\exp(\beta\mathbf{X}_l)}\right] d\bar{N}(u) \\
&\quad - \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \int_0^{\tau} \left[\frac{I_i(x_1,x_2,b)V_i(u)\exp(\beta\mathbf{X}_i)}{S^0(\beta,u)}\left[\mathbf{X}_i - \bar{\mathbf{X}}(\boldsymbol{\beta}, u)\right]\right] d\bar{N}(u) \\
&\quad \times (\hat{\boldsymbol{\beta}} - \boldsymbol{\beta}) \\
&= \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \int_0^{\tau} \left[I_i(x_1, x_2, b) - g(\boldsymbol{\beta}, u, x_1, x_2, b)\right] dM_i(u) \\
&\quad - \frac{1}{n} \sum_{i=1}^{n} \int_0^{\tau} \left[I_i(x_1, x_2, b)V_i(u)\exp(\boldsymbol{\beta}\mathbf{X}_i)\left[\mathbf{X}_i - \bar{\mathbf{X}}(\boldsymbol{\beta}, u)\right]\right] d\hat{\Lambda}(u) \\
&\quad \times \sqrt{n}(\hat{\boldsymbol{\beta}} - \boldsymbol{\beta})
\end{aligned}$$

where $\bar{N}(t) = \sum_{i=1}^{n} N_i(t)$, $I_i(x_1, x_2, b) = I[x_1 - b < s_i \le x_1 + b, x_2 - b < r_i \le x_2 + b]$, $g(\boldsymbol{\beta}, t, x_1, x_2, b)$ defined as equation 8 in paper, and τ is the pre-specified length of the study period. Then, by performing a Taylor series expansion of $U(\hat{\boldsymbol{\beta}})$ (Equation 4 in paper) around $\boldsymbol{\beta}$ yields that $\sqrt{n}(\hat{\boldsymbol{\beta}} - \boldsymbol{\beta})$ is asymptotically equivalent to $\sqrt{n}\mathbf{I}^{-1}(\boldsymbol{\beta})U(\boldsymbol{\beta})$, where $\mathbf{I}(\boldsymbol{\beta}) = -\partial U(\boldsymbol{\beta})/\partial\boldsymbol{\beta}$. By further invoking the property that $\hat{\Lambda}(u)$ converges almost surely to

$\Lambda(u)$, the process $W_{loc}(x_1, x_2|b)$ is asymptotically equivalent to the process $\tilde{W}_{loc}(x_1, x_2|b)$,

$$\begin{aligned}\tilde{W}_{loc}(x_1, x_2|b) &= \tfrac{1}{\sqrt{n}} \sum_{i=1}^{n} \int_0^{\tau} [I_i(x_1, x_2, b) - \tilde{g}(\boldsymbol{\beta}, u, x_1, x_2, b)]\, dM_i(u) \\ &- \sum_{i=1}^{n} \int_0^{\tau} \left[I_i(x_1, x_2, b) V_i(u) \exp(\boldsymbol{\beta}\mathbf{X}_i) \left[\mathbf{X}_i - \tilde{\mathbf{X}}(\boldsymbol{\beta}, u) \right] \right] d\Lambda(u) \qquad (1) \\ &\times \tfrac{1}{\sqrt{n}} \mathbf{I}^{-1}(\boldsymbol{\beta}) \sum_{i=1}^{n} \int_0^{\tau} \left[\mathbf{X}_i - \tilde{\mathbf{X}}(\boldsymbol{\beta}, u) \right] dM_i(u).\end{aligned}$$

where $\tilde{X}(\boldsymbol{\beta}, t)$ is the limit of $\bar{X}(\boldsymbol{\beta}, t)$ and $\tilde{g}(\boldsymbol{\beta}, t, x_1, x_2, b)$ is the limit of $g(\boldsymbol{\beta}, t, x_1, x_2, b)$.

Now that it has been shown that $W_{loc}(x_1, x_2|b)$ is asymptotically equivalent to $\tilde{W}_{loc}(x_1, x_2|b)$ it is sufficient to show that $\tilde{W}_{loc}(x_1, x_2|b)$ and $\hat{W}_{loc}(x_1, x_2|b)$ are asymptotically equivalent. We will first prove the tightness of $\tilde{W}_{loc}(x_1, x_2|b)$. The first term in (1) is tight since $[I_i(x_1, x_2, b) - \tilde{g}(\boldsymbol{\beta}, t, x_1, x_2, b)]$ is bounded (Lemma 1 from **?**). By the law of large numbers,

$$\mathbf{I}^{-1}(\boldsymbol{\beta}) \sum_{i=1}^{n} \int_0^{\tau} \left[I_i(x_1, x_2, b) V_i(u) \exp(\boldsymbol{\beta}\mathbf{X}_i) \left[\mathbf{X}_i - \tilde{\mathbf{X}}(\boldsymbol{\beta}, u) \right] \right] d\Lambda(u)$$

converges to some non-random function and since $\left[\mathbf{X}_i - \tilde{\mathbf{X}}(\boldsymbol{\beta}, u) \right]$ is a deterministic function, implies $\frac{1}{\sqrt{n}} \sum_{i=1}^{n} \int_0^{\tau} \left[\mathbf{X}_i - \tilde{\mathbf{X}}(\boldsymbol{\beta}, u) \right] dM_i(u)$ converges in distribution implying tightness. Therefore, the entire stochastic process, $\tilde{W}_{loc}(x_1, x_2|b)$, is tight.

For fixed t and (x_1, x_2), $\tilde{W}_{loc}(x_1, x_2|b)$ is essentially the sum of n independent and identically distributed zero-mean random vectors. By the multivariate central limit theorem, the finite-dimensional distributions of $\tilde{W}_{loc}(x_1, x_2|b)$ are asymptotically zero-mean normal, implying the same for $W_{loc}(x_1, x_2|b)$. This fact, together with the tightness of $W_{loc}(x_1, x_2|b)$, implies that $W_{loc}(x_1, x_2|b)$ converges weakly to a zero-mean Gaussian process with covariance function, $E\left(\frac{1}{n}\tilde{W}_{loc}(x_{1a}, x_{2a}|b)\tilde{W}_{loc}(x_{1b}, x_{2b}|b)\right)$ equals

$$E\left(\int_0^\tau h_k(\boldsymbol{\beta}, x_{1a}, x_{2a}, u)h_k(\boldsymbol{\beta}, x_{1b}, x_{2b}, u)V_k(u)\exp(\boldsymbol{\beta}\mathbf{X}_k)d\Lambda(u)\right), \tag{2}$$

where

$$\begin{aligned} h_k(\boldsymbol{\beta}, x_1, x_2, u) \quad = \quad & [I_i(x_1, x_2, b) - \tilde{g}(\boldsymbol{\beta}, t, x_1, x_2, b)] \\ - \quad & \left[I_i(x_1, x_2, b)V_i(u)\exp(\boldsymbol{\beta}\mathbf{X}_i)\left[\mathbf{X}_i - \tilde{\mathbf{X}}(\boldsymbol{\beta}, u)\right]\right] d\Lambda(u) \\ \times \quad & \mathbf{I}^{-1}(\boldsymbol{\beta})\sum_{i=1}^{n}\int_0^t \left[\mathbf{X}_i - \tilde{\mathbf{X}}(\boldsymbol{\beta}, u)\right]. \end{aligned}$$

Next we will establish the weak distribution of $\hat{W}_{loc}(x_1, x_2|b)$. Conditional on the data $(T_i, \delta_i, \mathbf{X}_i, s_i, r_i)(i = 1, \ldots, n)$, the only random components in $\hat{W}_{loc}(x_1, x_2|b)$ are the independent mean 0 variance 1 variables $(G_1, \ldots, G_n)$. Thus it follows from the multivariate central limit theorem that, conditional on the data, the finite-dimensional distributions of $\hat{W}_{loc}(x_1, x_2|b)$ are asymptotically zero-mean normal. Since $\hat{W}_{loc}(x_1, x_2|b)$ consists of monotone functions in (x_1, x_2), which are manageable, the functional central limit theorem implies that $\hat{W}_{loc}(x_1, x_2|b)$ is tight. By the strong consistency of $\hat{\boldsymbol{\beta}}$ and $\hat{\Lambda}_0(.)$ (**?**) and **?**)),

$$E\left(\hat{W}_{loc}(x_1, x_2|b) - \hat{W}^*_{loc}(x_1, x_2|b)^2\right) \to 0$$

almost surely, conditional on the data, $((T_i, \delta_i, \mathbf{X}_i, s_i, r_i))$, where

$$\hat{W}^*_{loc}(x_1, x_2|b) = \frac{1}{\sqrt{n}}\sum_{i=1}^{n}\int_0^\tau h_i(\boldsymbol{\beta}, x_1, x_2, u)dN_i(u)G_i.$$

Therefore, conditional on $(T_i, \delta_i, \mathbf{X}_i, s_i, r_i)$, the asymptotic covariance function for $\hat{W}_{loc}(x_1, x_2|b)$ is

$$\frac{1}{n}\sum_{i=1}^{n}\int_0^\tau h_i(\boldsymbol{\beta}, x_{1a}, x_{2a}, u)h_i(\boldsymbol{\beta}, x_{1b}, x_{2b}, u)dN_i(u),$$

which converges almost surely to (2) by the law of large numbers since $V_i(u)\exp(\boldsymbol{\beta}\mathbf{X}_i)\lambda_0(u)$ is the intensity function of $N_i(u)$.

References

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