

Solving for  $\beta$  to estimate the B-spline bases resolves to finding the score function  $\mathbf{S}(\beta)$  and Hessian matrix  $\mathbf{H}(\beta)$ , which are respectively the first derivative of the partial log-likelihood function with respect to  $\beta_j$  and the  $p \times p$  matrix of second derivatives of the log-likelihood function with respect to  $\beta_j, \beta_k$ .

$$\begin{aligned}\mathbf{S}(\beta) &= \frac{\partial}{\partial \beta_j} \phi(y, \delta | \mathbf{x}, \beta) \\ &= \delta B_j(y | \mathbf{x}) - \int_0^y B_j(u | \mathbf{x}) \exp(\alpha(u | \mathbf{x}, \beta)) du, \quad 1 \leq j \leq p, \quad y \geq 0, \quad \delta \in \{0, 1\} \\ \mathbf{H}(\beta) &= \frac{\partial^2}{\partial \beta_j \partial \beta_k} \phi(y, \delta | \mathbf{x}, \beta) \\ &= - \int_0^y B_j(u | \mathbf{x}) B_k(u | \mathbf{x}) \exp(\alpha(u | \mathbf{x}, \beta)) du, \quad 1 \leq j, \quad k \leq p, \quad y \geq 0, \quad \delta \in \{0, 1\}.\end{aligned}$$

This means the estimation procedure is not much different from most numerical solutions to statistical computations. In HARE, the Newton-Raphson method is used to estimate  $\hat{\beta}$ . The initial value for  $\hat{\beta}$  is  $\hat{\beta}^{(0)}$  and  $\hat{\beta}^{(m+1)} = \hat{\beta}^{(m)} - 2^{-\nu} [\mathbf{H}(\hat{\beta}^{(m)})]^{-1} \mathbf{S}(\hat{\beta}^{(m)})$  where  $\nu$  is a step-halving constant (Lange, 2010). The iterations stop when the difference between repeated log-likelihood calculations is  $< 10^{-6}$ . The primary goal for HARE, then, is to determine what basis functions should be used to estimate  $\alpha(t | \mathbf{x})$ .

Denote the space of all acceptable basis functions  $B_j$  for HARE as  $\mathcal{G}$ .  $B_j$  are linear, which minimizes numerical integrations over the knot sequence of  $\mathbf{t} := (t_1, t_2, \dots, t_k)$  (Kooperberg, Stone, & Truong, 1995a) and ensures  $L_2$  convergence in function estimation. (Stone, 1994; Kooperberg, Stone, & Truong, 1995b). Formally, the allowable spaces  $G \in \mathcal{G}$  in HARE are defined as follows:

- There is only one  $G \in \mathcal{G}$  with minimal dimension  $p_{min}$ ,
- Each  $G \in \mathcal{G}$  is a linear space having dimension  $p \geq p_{min}$ ,
- If  $G \in \mathcal{G}$  has dimension  $p > p_{min}$ , then there is at least one subspace  $G_0 \in \mathcal{G}$  of  $G$  with dimension  $p - 1$ ,
- If  $G_0 \in \mathcal{G}$  has dimension  $p$ , then there is at least one space  $G \in \mathcal{G}$  with dimension  $p + 1$  whose subspace is  $G_0$ .

These criteria state that HARE determines  $B_j$  and estimates its corresponding  $\beta_j$  in a stepwise fashion where tensor products of two basis spaces require each single factor space. Let  $k$  represent a knot along a knot sequence. Then HARE has basis functions of the form  $1, (t_k - t)_+, x_m, (x_{mk} - x_m)_+, x_m x_n, (t_k - t)_+ x_m, (t_k - t)_+ (x_{mk} - x_m)_+, x_m (x_{nk} - x_n)_+, (x_{mk} - x_m)_+ x_n$ , and  $(x_{mk} - x_m)_+ (x_{nk} - x_n)_+$ , where  $x_m, x_n$  are separate covariates,  $t_k$  is a knot in time,  $x_k$  is a knot in a covariate, and  $(\cdot)_+$  represents the positive part of the function. The tensor products  $x_m x_n, (t_k - t)_+ x_m, (t_k - t)_+ (x_{mk} - x_m)_+, x_m (x_{nk} - x_n)_+, (x_{mk} - x_m)_+ x_n$ , and  $(x_{mk} - x_m)_+ (x_{nk} - x_n)_+$  are allowable only if the factor basis functions are included. For example, if  $x_1, x_2$ , and  $(7 - t)_+$  are included in the estimate of  $\alpha(t|\mathbf{x})$ , but  $x_3$  is not, then  $x_1 x_2, x_1 (7 - t)_+$ , and  $x_2 (7 - t)_+$  are allowable, but  $x_3 (7 - t)_+$  is not.

HARE begins the partitioning procedure of determining  $G \in \mathcal{G}$  with the constant space  $G_{min} = 1$ . The process adds new spaces  $G \in \mathcal{G}$  where each  $(p - 1)$ -dimensional space  $G_0$  is replaced by a  $p$ -dimensional space  $G$  that includes  $G_0$  as a subspace. When determining the new  $G$  allowable space, candidate basis functions  $B_j$  include linear covariates, a new knot in time, a new knot in a covariate, and a tensor product of two existing basis functions from  $G_0$ .  $G$  is determined from finding the candidate basis function that maximizes the Rao statistic  $R = \mathbf{S}(\hat{\beta}_p^{(0)}) / \sqrt{\mathbf{I}^{-1}(\hat{\beta}^{(0)})_{pp}}$ , where  $\hat{\beta}^{(0)}$  is the maximum likelihood estimate of  $\beta$  corresponding to space  $G$ ,  $\beta_p$  is the coefficient for the basis function needed to go from  $G_0$  to  $G$ ,  $\mathbf{S}(\cdot)$  is the score function, and  $\mathbf{I}^{-1}(\cdot)$  is the observed Fisher information matrix. The addition of new  $G$  allowable spaces follows this algorithm:

- Calculate Rao statistic for all spaces obtained from  $G_0$  by adding a basis function  $B_{l0}(x_l) = x_l$  to  $G_0$
- Calculate Rao for all allowable spaces obtained from  $G_0$  by adding a basis function to  $G_0$  comprising a tensor product of two tensor functions in  $G_0$
- Calculate Rao statistic for a space obtained from  $G_0$  by adding a basis function constructed by adding a new knot in  $t$
- Calculate Rao statistic for a space obtained from  $G_0$  by adding a basis function constructed by adding a new knot in covariate  $m$
- Select space  $G$  that maximizes the absolute value of the Rao statistic.

After each space  $G$  is determined, the BIC (Schwarz, 1978) is stored for model selection procedures. Candidate basis functions are no longer added when either (a) the number of basis functions included is  $\min(6n^{1/5}, n/4, 50)$ , (b) the change in the maximized log-likelihood function is  $< \frac{1}{2}(P - p) - \frac{1}{2}$  where  $P$  is the number of basis functions and  $p$  is the dimensionality of  $G$ , or (c) the algorithm yields no possible new basis function.

Following the addition phase of  $G \in \mathcal{G}$  is the deletion phase, which carries out the candidate basis function algorithm above with two features changed: (i) the deletion phase goes from space  $G$  to space  $G_0$ , and (ii) Wald statistic  $\hat{\beta}_p/SE(\hat{\beta}_p)$  is used instead of the Rao statistic. This latter modification is needed because the Rao statistic is based on the maximum likelihood estimate in  $G_0$  whereas Wald is based on  $G$  space (Kooperberg, Stone, & Truong; 1995a). After each model has been estimated through the iterative addition and deletion phases of  $G$  construction, the model that minimizes BIC is the final estimate of the conditional log-hazard function  $\alpha(t|\mathbf{x}, \beta)$ .

## References

- Kooperberg, C., Stone, C. J., & Truong, Y. K. (1995a). Hazard regression. *Journal of the American Statistical Association*, 90(429), 78-94.
- Kooperberg, C., Stone, C. J., & Truong, Y. K. (1995b). The L2 rate of convergence for hazard regression. *Scandinavian Journal of Statistics*, 22(2), 143-157.
- Lange, K. *Numerical Analysis for Statisticians*. Springer, New York, USA, second edition, 2010.