UN MODELO DE SUPERVIVENCIA BIVARIANTE GENERADO POR UN FRAILTY ESTABLE POSITIVA Y COVARIABLES BAJO HIPOTESIS DE VIDA ACELERADA

Esteban Navarrete Alvarez
Julia García Leal
Jorge Ollero Hinojosa

Departamento de Estadística e Investigación Operativa
Universidad de Granada.
Facultad de Ciencias, Campus de Fuentenueva, s/n. 18071 Granada, España.
E-mail: Estebang@goliat.ugr.es

RESUMEN

Consideramos un modelo de supervivencia bivariante basado en la presencia de una covariable aleatoria no observada, frailty, que induce dependencia entre los tiempos de fallo y actúa bajo hipótesis de riesgo proporcional. Consideramos una distribución estable positiva para el frailty y distribuciones marginales Weibull e introducimos covariables explicativas que actúan bajo hipótesis de vida acelerada. La estimación de los parámetros se realiza considerando la posibilidad de censuras.

PALABRAS CLAVE: Supervivencia bivariante; Frailty; Riesgo proporcional; Vida acelerada; Estable positiva; Asociación; Covariables; Weibull; Estimación.

1. Introducción

La construcción de modelos para tiempos de supervivencia bivariante ha sido enfocada de diferentes formas dependiendo, entre otras cuestiones, del tipo de datos a examinar. Un tipo de estos datos se refiere a pares de tiempos de supervivencia correspondientes a individuos relacionados, por ejemplo, con cierto parentesco, datos "familiares" en un sentido amplio. Cierta asociación o dependencia está inducida entre los miembros de los pares de individuos, a través de una común covariable aleatoria que no es observada. Dicha covariable, denominada frailty, se supone que actúa multiplicativamente en las funciones de riesgo marginales. Hougaard (1986a,b) y Oakes (1989) han estudiado modelos bajo estas hipótesis. Hougaard (1986a) examinó un modelo con un frailty con distribución estable positiva y marginales Weibull y propuso la introducción de covariables explicativas bajo hipótesis de riesgo proporcional.

En el apartado 2, nosotros proponemos un modelo mixto, donde consideramos un frailty bajo hipótesis de riesgo proporcional y covariables explicativas bajo hipótesis de vida acelerada. En el apartado 3 consideramos el problema de la estimación de los parámetros en un modelo particular con marginales con distribución Weibull.

2. El modelo mixto

Procedemos a construir un modelo, denominado modelo misto, en el cual las covariables explicativas actúan bajo hipótesis de vida acelerada [$h_i(t_i, \psi_i(x_i)) = \exp(\beta_i x_i)\, h_i(t_i \exp(\beta_i x_i))$] mientras que el frailty actúa multiplicativamente en las funciones de riesgo marginales, esto es, un modelo de riesgo proporcional [$\tilde{h}_i(t_i, z) = z h_i(t_i)$]. Es decir, partimos de la siguiente hipótesis (asumimos que E(Z)=1):

$$h_i(t_i, z, \psi_i(x_i)) = z.\exp(\beta_i x_i)\, h_i(t_i.\exp(\beta_i x_i)), \quad i=1,2.$$

$$\exp(\beta_i x_i) = \exp\Big(\sum_{k=1}^{k_i} \beta_{ik} x_{ik}\Big) = \exp(\beta_{i1} x_{i1} + \ldots + \beta_{ik_i} x_{ik_i}), \quad i:1,2$$

donde la covariable x_{ik}, (k:1,...,k_i) en el término j (j:1,...,n) tomará el valor x_{ikj}. La función de supervivencia marginal condicionada es

$$S_i(t_i, \psi_i(x_i), z) = \exp[-z.\Lambda_i(t_i \exp(\beta_i x_i))].$$

La función de supervivencia condicionada conjunta es

$$S(t_1, t_2 / z, \psi_1(x_1), \psi_2(x_2)) =$$

$$=\exp[-z(\Lambda_1(t_1\exp(\beta_1x_1))+\Lambda_2(t_2\exp(\beta_2x_2)))].$$

Realizando la mixtura de distribuciones, la función de supervivencia conjunta es

$$S(t_1,t_2)=\int\exp[-z(\Lambda_1(t_1\exp(\beta_1x_1))+\Lambda_2(t_2\exp(\beta_2x_2)))]\,dF(z).$$

Si Z sigue una distribución estable positiva y la marginales tienen distribuciones Weibull con los parámetros iguales, la función de supervivencia conjunta es

$$S(t_1,t_2)=\exp[-\epsilon^{\alpha}(t_1^{\gamma}\exp(\gamma\beta_1x_1)+t_2^{\gamma}\exp(\gamma\beta_2x_2))^{\alpha}].$$

Las funciones de supervivencia marginales son

$$S_i(t_i)=\exp[-\epsilon^{\alpha}t_i^{\gamma\alpha}\exp(\alpha\gamma\beta_ix_i)]$$

e incluyendoun factor escala quedaría

$$S_i(t_i)=\exp[-t_i^{\alpha\gamma}\exp(\alpha\gamma\beta_ix_i)].$$

3. Estimación

Si tenemos la muestra $(t_{1i},t_{2i}),\ i:1,\ldots,n$ y un dato expresado por el vector (t_1,t_2), establecemos cuatro situaciones diferentes (consideraremos censuras a la derecha en lo que sigue):

Grupo 1	si t_1 y t_2 no son censurados.
Grupo 2	si t_1 no es censurado pero t_2 sí lo es.
Grupo 3	si t_1 es censurado pero t_2 no lo es.
Grupo 4	si t_1 y t_2 son censurados.

Usaremos los siguientes indicadores de censura (j:1,2,3,4):

$$I(j)=\begin{cases}1 & \text{si } (t_1,t_2) \text{ está en el grupo j}\\ 0 & \text{si } (t_1,t_2) \text{ no está en el grupo j}\end{cases}$$

La función de supervivencia del modelo con un frailty con distribución estable positiva, marginales Weibull y covariables es

$$S(t_1,t_2)=\exp[-(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha}].$$

α, el parámetro de asociación, proviene de la distribución del frailty. $\alpha=1$ corresponde al caso de variables independientes. Los otros parámetros corresponden a la distribución Weibull, siendo β_j un vector de parámetros asociado con el vector de covariables x_j (j:1,2). La expresión de la función de las covariables es

$$\exp(\beta_jx_j)=\exp(\sum_{k=1}^{k_j}\beta_{jk}x_{jk})=\exp(\beta_{j1}x_{j1}+\ldots+\beta_{jk_j}x_{jk_j}) \quad , \quad j:1,2$$

donde la covariable x_{jk}, (k:1,...,k_j) en el término i (i:1,...,n) tomará el valor x_{jki}. Los parámetros a estimar son

$$\epsilon \ , \ \gamma \ , \ \alpha \ , \ \beta_1=(\beta_{11},\ldots,\beta_{1k_1}) \ , \ \beta_2=(\beta_{21},\ldots,\beta_{2k_2})$$

es decir, hay $1+1+1+k_1+k_2$ parame ros a es imar.

Los parámetros son estimados por el método de máxima verosimilitud. Cada tipo de dato aporta una cantidad diferente a la función de verosimilitud. Un dato no censurado (grupo 1) aporta a la función de verosimilitud la cantidad

$$g1=\frac{\partial^2S(t_1,t_2)}{\partial t_1\partial t_2}$$

es decir, el correspondiente valor de la función de densidad. Un dato del grupo 2 aporta la cantidad

$$g2=\frac{-\partial S(t_1,t_2)}{\partial t_1}.$$

Un dato del grupo 3 aporta la cantidad

$$g3=\frac{-\partial S(t_1,t_2)}{\partial t_2}$$

y un dato del grupo 4 aporta el correspondiente valor de la función de supervivencia, es decir, la cantidad $g4=S(t_1,t_2)$.

La función de verosimilitud para una muestra de tamaño n será

$$L=\prod_{I=1}^{n}\left[\left(\frac{\partial^2 S(t_{1i},t_{2i})}{\partial t_{1i}\partial t_{2i}}\right)^{I(1)}\cdot\left(\frac{-\partial S(t_{1i},t_{2i})}{\partial t_{1i}}\right)^{I(2)}\cdot\right.$$
$$\left.\cdot\left(\frac{-\partial S(t_{1i},t_{2i})}{\partial t_{2i}}\right)^{I(3)}\cdot\left(S(t_{1i},t_{2i})\right)^{I(4)}\right].$$

En estas condiciones, el logaritmo de la función de verosimilitud es

$$lgL(\alpha,\gamma,\epsilon,\beta)=\sum_{I=1}^{n}lg[(g1)^{I(1)}\cdot(g2)^{I(2)}\cdot(g3)^{I(3)}\cdot(g4)^{I(4)}]=$$
$$=\sum_{I=1}^{n}[I(1)lg(g1)+I(2)lg(g2)+I(3)lg(g3)+I(4)lg(g4)]=$$
$$=I(1)\sum_{I=1}^{n}lg(g1)+I(2)\sum_{I=1}^{n}lg(g2)+I(3)\sum_{I=1}^{n}lg(g3)+I(4)\sum_{I=1}^{n}lg(g4).$$

La derivada respecto t_1 es

$$\frac{\partial S(t_1,t_2)}{\partial t_1}=-\alpha\epsilon\gamma t_1^{\gamma-1}\exp(\gamma\beta_1x_1)[\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma}]^{\alpha-1}\cdot$$
$$\cdot\exp[-(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha}],$$

La derivada respecto t_2 es

$$\frac{\partial S(t_1,t_2)}{\partial t_2}=-\alpha\epsilon\gamma t_2^{\gamma-1}\exp(\gamma\beta_2x_2)[\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma}]^{\alpha-1}\cdot$$
$$\cdot\exp[-(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha}]$$

y

$$\frac{\partial^2 S(t_1,t_2)}{\partial t_1\partial t_2}-\alpha\epsilon^2\gamma^2t_1^{\gamma-1}t_2^{\gamma-1}\exp(\gamma\beta_1x_1)\exp(\gamma\beta_2x_2)\cdot$$
$$\cdot\exp[-(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha}]\cdot$$
$$\cdot[\alpha(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{2\alpha-2}-$$
$$-(\alpha-1)(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha-2}]$$

y

$$\frac{-\partial S(t_1,t_2)}{\partial t_j}>0 \ , \quad j:1,2$$

$$\frac{\partial^2 S(t_1,t_2)}{\partial t_1 \partial t_2}>0$$

puesto que

$$\alpha(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{2\alpha-2}-$$

$$-(\alpha-1)(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha-2}\geq 0 .$$

La función de verosimilitud es

$$lgL(\alpha,\gamma,\epsilon,\beta)=$$

$$=I(1)\sum_{i=1}^{n}[lg\alpha+2lg\epsilon+2lg\gamma+(\gamma-1)lg(t_1t_2)+(\gamma\beta_1x_1+\gamma\beta_2x_2)-$$

$$-(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha}+$$

$$+lg(\alpha(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{2\alpha-2}-$$

$$-(\alpha-1)(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha-2})]+$$

$$+I(2)\sum_{i=1}^{n}[lg\alpha+lg\epsilon+lg\gamma+(\gamma-1)lgt_1+\gamma\beta_1x_1+$$

$$+(\alpha-1)lg(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})-$$

$$-(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha}]+$$

$$+I(3)\sum_{i=1}^{n}[lg\alpha+lg\epsilon+lg\gamma+(\gamma-1)lgt_2+\gamma\beta_2x_2+$$

$$+(\alpha-1)lg(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})-$$

$$-(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha}]-$$

$$-I(4)\sum_{i=1}^{n}(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha}=$$

$$=I(1)[nlg\alpha+2nlg\epsilon+2nlg\gamma+(\gamma-1)\sum lg(t_1t_2)+\sum(\gamma\beta_1x_1+\gamma\beta_2x_2)-$$

$$-\sum(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha}+$$

$$+\sum lg(\alpha(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{2\alpha-2}-$$

$$-(\alpha-1)(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha-2})]+$$

$$+I(2)[nlg\alpha+nlg\epsilon+nlg\gamma+(\gamma-1)\sum lgt_1+\sum\gamma\beta_1x_1+$$

$$+(\alpha-1)\sum lg(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})-$$

$$\sum(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha}]+$$

$$+I(3)[nlg\alpha+nlg\epsilon+nlg\gamma+(\gamma-1)\sum lgt_2+\sum\gamma\beta_2x_2+$$

$$+(\alpha-1)\sum lg(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})-$$

$$-\sum(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha}]-$$

$$-I(4)\sum(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha}.$$

La derivada respecto α es

$$\frac{\partial lgL(\alpha,\gamma,\epsilon,\beta)}{\partial\alpha}=$$

$$=I(1)\Big[\frac{n}{\alpha}-\sum[(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha}.$$

$$.lg(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})]+$$

$$+\sum\{(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{2\alpha-2}+$$

$$+\alpha(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{2\alpha-2}lg(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})-$$

$$-(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha-2}-$$

$$-(\alpha-1)(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha-2}.$$

$$.lg(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})\}\ /\ \{\alpha+$$

$$+(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{2\alpha-2}-$$

$$-(\alpha-1)(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha-2}\}\Big]+$$

$$+I(2)\Big[\frac{n}{\alpha}+\sum lg(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})-$$

$$-\sum(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha}lg(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})\Big]+$$

$$+I(3)\left[\frac{n}{\alpha}+\sum lg(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})-\right.$$

$$\left.-\sum(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha}lg(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})\right]+$$

$$I(4)\sum(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha}lg(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})$$

La derivada respecto γ es

$$\frac{\partial lgL(\alpha,\gamma,\epsilon,\beta)}{\partial\gamma}=$$

$$=I(1)\left[\frac{2n}{\gamma}+\sum lgt_1t_2+\sum(\beta_1x_1+\beta_2x_2)-\sum\alpha(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha-1}\right.$$

$$\cdot(\epsilon\exp(\gamma\beta_1x_1)(\beta_1x_1)t_1^{\gamma}(1+lgt_1)+\epsilon\exp(\gamma\beta_2x_2)(\beta_2x_2)t_2^{\gamma}(1+lgt_2))+$$

$$+\sum\{\alpha(2\alpha-2)(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{2\alpha-3}\cdot$$

$$\cdot(\epsilon\exp(\gamma\beta_1x_1)(\beta_1x_1)t_1^{\gamma}(1+lgt_1)+\epsilon\exp(\gamma\beta_2x_2)(\beta_2x_2)t_2^{\gamma}(1+lgt_2))-$$

$$-(\alpha-1)(\alpha-2)(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha-3}\cdot$$

$$\cdot(\epsilon\exp(\gamma\beta_1x_1)(\beta_1x_1)t_1^{\gamma}(1+lgt_1)+\epsilon\exp(\gamma\beta_2x_2)(\beta_2x_2)t_2^{\gamma}(1+lgt_2))\}/\{\alpha\cdot$$

$$\cdot(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{2\alpha-2}-$$

$$\left.(\alpha-1)(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha-2}\}\right]+$$

$$+I(2)\left[\frac{n}{\gamma}+\sum lgt_1+\sum\beta_1x_1+\right.$$

$$+(\alpha-1)\sum\frac{(\epsilon\exp(\gamma\beta_1x_1)(\beta_1x_1)t_1^{\gamma}(1+lgt_1)+\epsilon\exp(\gamma\beta_2x_2)(\beta_2x_2)t_2^{\gamma}(1+lgt_2))}{(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})}-$$

$$-\sum\alpha(\epsilon\exp(\gamma\beta_1x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2x_2)t_2^{\gamma})^{\alpha-1}\cdot$$

$$\left.\cdot(\epsilon\exp(\gamma\beta_1x_1)(\beta_1x_1)t_1^{\gamma}(1+lgt_1)+\epsilon\exp(\gamma\beta_2x_2)(\beta_2x_2)t_2^{\gamma}(1+lgt_2))\right]+$$

$$+I(3)\Big[\frac{n}{\gamma}+\sum lgt_2+\sum \beta_2 x_2+$$

$$+(\alpha-1)\sum \frac{(\epsilon\exp(\gamma\beta_1 x_1)(\beta_1 x_1)t_1^{\gamma}(1+lgt_1)+\epsilon\exp(\gamma\beta_2 x_2)(\beta_2 x_2)t_2^{\gamma}(1+lgt_2))}{(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})}.$$

$$-\sum \alpha(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha-1}\cdot$$

$$\cdot(\epsilon\exp(\gamma\beta_1 x_1)(\beta_1 x_1)t_1^{\gamma}(1+lgt_1)+\epsilon\exp(\gamma\beta_2 x_2)(\beta_2 x_2)t_2^{\gamma}(1+lgt_2))\Big]+$$

$$-I(4)\sum \alpha(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha-1}\cdot$$

$$\cdot(\epsilon\exp(\gamma\beta_1 x_1)(\beta_1 x_1)t_1^{\gamma}(1+lgt_1)+\epsilon\exp(\gamma\beta_2 x_2)(\beta_2 x_2)t_2^{\gamma}(1+lgt_2)).$$

Si

$$a=\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma}$$
$$b=\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\exp(\gamma\beta_2 x_2)t_2^{\gamma}$$

entonces

$$\frac{\partial lgL(\alpha,\gamma,\epsilon,\beta)}{\partial\epsilon}=$$

$$=I(1)[\frac{2n}{\epsilon}-\sum \alpha a^{\alpha-1}b+\sum \frac{\alpha(2\alpha-2)a^{2\alpha-3}b-(\alpha-1)(\alpha-2)a^{\alpha-3}b}{\alpha a^{2\alpha-2}-(\alpha-1)a^{\alpha-2}}]+$$

$$+I(2)[\frac{n}{\epsilon}+(\alpha-1)\sum \frac{b}{a}-\sum \alpha a^{\alpha-1}b]+$$

$$+I(3)[\frac{n}{\epsilon}+(\alpha-1)\sum \frac{b}{a}-\sum \alpha a^{\alpha-1}b]-$$

$$-I(4)\sum \alpha a^{\alpha-1}b.$$

La derivada respecto β es

$$\frac{\partial lgL(\alpha,\gamma,\epsilon,\beta)}{\partial\beta_{1k}}=$$

$$=I(1)\Big[\sum \gamma x_{1k}-\sum \alpha(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha-1}\epsilon t_1^{\gamma}\exp(\gamma\beta_1 x_1)\gamma x_{1k}+$$

$$+\sum\{\alpha(2\alpha-2)(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{2\alpha-3}\epsilon t_1^{\gamma}\exp(\gamma\beta_1 x_1)\gamma x_{1k}-$$

$$-(\alpha-1)(\alpha-2)(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha-3}\epsilon t_1^{\gamma}\exp(\gamma\beta_1 x_1)\gamma x_{1k}\}\;/\;\{\alpha\cdot$$

$$\cdot(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{2\alpha-2}-(\alpha-1)\cdot$$

$$\cdot(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha-2}\}\Big]+$$

$$+I(2)\Big[\sum\gamma x_{1k}+(\alpha-1)\sum\frac{\epsilon t_1^{\gamma}\exp(\gamma\beta_1 x_1)\gamma x_{1k}}{(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})}-$$

$$-\sum\alpha(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha-1}\epsilon t_1^{\gamma}\exp(\gamma\beta_1 x_1)\gamma x_{1k}\Big]+$$

$$+I(3)\Big[(\alpha-1)\sum\frac{\epsilon t_1^{\gamma}\exp(\gamma\beta_1 x_1)\gamma x_{1k}}{\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma}}-$$

$$-\sum\alpha(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha-1}(\epsilon t_1^{\gamma}\exp(\gamma\beta_1 x_1)\gamma x_{1k})\Big]-$$

$$-I(4)\sum\alpha(\epsilon\exp(\gamma\beta_1 x_1)t_1^{\gamma}+\epsilon\exp(\gamma\beta_2 x_2)t_2^{\gamma})^{\alpha-1}\epsilon t_1^{\gamma}\exp(\gamma\beta_1 x_1)\gamma x_{1k}$$

con

$$k:1,\ldots,k_1$$

y

$$\frac{\partial lgL(\alpha,\gamma,\beta)}{\partial\beta_{2k}}\qquad k:1,\ldots,k_2.$$

Las soluciones del sistema de ecuaciones

$$\left.\begin{array}{l}\frac{\partial lgL(\alpha,\gamma,\epsilon,\beta)}{\partial\alpha}=0\\ \frac{\partial lgL(\alpha,\gamma,\epsilon,\beta)}{\partial\gamma}=0\\ \frac{\partial lgL(\alpha,\gamma,\epsilon,\beta)}{\partial\epsilon}=0\\ \frac{\partial lgL(\alpha,\gamma,\epsilon,\beta)}{\partial\beta_{jk}}=0\end{array}\right\}$$

son los estimadores de máxima verosimilitud $\hat{\alpha},\hat{\gamma},\hat{\epsilon},\hat{\beta}_k$. La obtención de estos estimadores ha de hacerse utilizando métodos numéricos, por ejemplo, el método de Newton Raphson.

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