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A Kolmogorov-Smirnov-Type Test for Independence of Bivariate Failure Time Data Under Independent Censoring

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Abstract

We propose a Kolmogorov-Smirnov-type test for independence of paired failure times in the presence of independent censoring times. This independent censoring mechanism is often assumed in case-control studies. To do this end, we first introduce a process defined as the difference between the bivariate survival function estimator proposed by Wang and Wells (1997) and the product of the product-limit estimators (Kaplan and Meier (1958)) for the marginal survival functions. Then, we derive its asymptotic properties under the null hypothesis of independence. Finally, we assess the performance of the proposed test by simulations, and illustrate the proposed methodology with a dataset for remission times of 21 pairs of leukemia patients taken from Oakes (1982).

Keywords: Bivariate Survival Function; Independent Censoring; Independence Test; Kolmogorov-Smirnov Test; Product-Limit Estimator.

1. INTRODUCTION

In biomedical studies which deal with paired failure times, it may be useful to test whether they are independent or not because there exists natural or artificial pairing such that they may be correlated. Several approaches have been developed to test independence between failure times in bivariate failure time data. Oakes (1982) proposed a test based on an extension of Kendall's coefficient of concordance to censored data. Cuzick (1982) suggested a test based on the generalized ranks with calculations of the loss of efficiencies arising from the incorrect model specification in a particular class of models. Dabrowska (1986) studied linear rank statistics that generalize the Spearman rank correlation and the log-rank correlation in the presence of censoring. Pones (1986) and Pones and

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Turckheim (1991) proposed tests based on the difference between an estimator of joint cumulative hazard function and the product of the marginal cumulative hazard estimates. Shih and Louis (1996) proposed tests based on the covariance process of the martingale residuals for the marginal distributions.

In the next section we introduce a process defined as the difference between the bivariate survival function estimator proposed by Wang and Wells (1997) and the product of the product-limit estimators (Kaplan and Meier (1958)) for the marginal survival functions. We derive its asymptotic properties under the null hypothesis of independence and propose a Kolmogorov-Smirnov-type test for testing of independence of the bivariate failure time data under independent censoring mechanism. Finally, simulation studies are carried out to investigate the small sample performance of the proposed test, and we also illustrate the proposed test with a dataset for remission times of 21 pairs of leukemia patients taken from Oakes (1982).

2. A KOLMOGOROV-SMIRNOV-TYPE INDEPENDENCE TEST

Let $(X_i, Y_i)(i = 1, \ldots, n)$ be n independent and identically distributed pairs of failure times with continuous bivariate survival function $F(x, y) = P(X \geq x, Y \geq y)$ and let $(C_{1i}, C_{2i})(i = 1, \ldots, n)$ be an independent sample of n censoring times with survival function $G(x, y) = P(C_1 \geq x, C_2 \geq y)$. Let $F_j(\cdot)$ and $G_j(\cdot)(j = 1, 2)$ denote the marginal survival functions of X, Y, C_1, and C_2, respectively. Assume that (X_i, Y_i) are independent of (C_{1i}, C_{2i}) for all i, and also that C_1 and C_2 are independent. In case-control studies, it may be reasonable to assume that the patients in the case and control groups are subject to such an independent censoring mechanism. We observe $(\tilde{X}_i, \tilde{Y}_i, \delta_i^x, \delta_i^y)(i = 1, \ldots, n)$, where

$$\tilde{X}_i = X_i \wedge C_{1i},\ \tilde{Y}_i = Y_i \wedge C_{2i},\ \delta_i^x = I(X_i \leq C_{1i}),\ \delta_i^y = I(Y_i \leq C_{2i}).$$

Here and in the sequel, $I(\cdot)$ denotes the indicator function and $a \wedge b = \min(a, b)$. Let $H(x, y) = P(\tilde{X} \geq x, \tilde{Y} \geq y)$ be the bivariate survival function of $(\tilde{X}_i, \tilde{Y}_i)(i = 1, \ldots, n)$, and let $H_j(\cdot)(j = 1, 2)$ be the marginal survival functions of $\tilde{X}$ and $\tilde{Y}$, respectively.

Noting that $F(x, y)$ can be decomposed as

$$F(x, y) = \frac{H(x, y)}{G(x, y)}$$

from the assumption of independence between the paired failure times and the censoring times and $G(x,y) = G_1(x)G_2(y)$ under independent censoring, Wang and Wells (1997) proposed a bivariate survival function estimator of F given by

$$\hat{F}(x,y) = \frac{\hat{H}(x,y)}{\hat{G}_1(x)\hat{G}_2(y)}, \tag{2.1}$$

where $\hat{H}(x,y) = n^{-1}\sum_{i=1}^{n} I(\tilde{X}_i \geq x, \tilde{Y}_i \geq y)$, and $\hat{G}_j (j = 1,2)$ are the product-limit estimators for G_j based on $\{(\tilde{X}_i, 1-\delta_i^x), i = 1,\ldots,n\}$ and $\{(\tilde{Y}_i, 1-\delta_i^y), i = 1,\ldots,n\}$, respectively.

To make a test of independence between X and Y, we compare the bivariate estimator $\hat{F}$ in (2.1) of F with its estimator $\hat{F}_1\hat{F}_2$ under the hypothesis of independence, where $\hat{F}_j(j = 1,2)$ are the product limit estimators for F_j based on $\{(\tilde{X}_i, \delta_i^x), i = 1,\ldots,n\}$ and $\{(\tilde{Y}_i, \delta_i^y), i = 1,\ldots,n\}$, respectively.

Define a process Z at (x,y) on $[0,\tau_1] \times [0,\tau_2]$ as

$$Z(x,y) = n^{\frac{1}{2}}\{\hat{F}(x,y) - \hat{F}_1(x)\hat{F}_2(y)\},$$

where $(\tau_1,\tau_2) \in R^+ \times R^+$ satisfies $H(\tau_1,\tau_2) > 0$.

Theorem 2.1. *For $(x,y) \in [0,\tau_1] \times [0,\tau_2]$ such that $H(x,y) > 0$, the process $Z(x,y)$ converges weakly to a zero-mean Gaussian process $\tilde{Z}(x,y) = U(x,y) - F_2(y)U_1(x) - F_1(x)U_2(y)$, if X and Y are independent on the observed rectangle $[0,\tau_1] \times [0,\tau_2]$, otherwise $sup_{(x,y)\in[0,\tau_1]\times[0,\tau_2]}|Z(x,y)|$ tends to infinity, where $U(x,y)$, $U_1(x)$, and $U_2(y)$ are zero-mean Gaussian processes.*

Proof: We first write $Z(x,y)$ as

$$\begin{aligned} Z(x,y) &= n^{\frac{1}{2}}\{\hat{F}(x,y) - F(x,y)\} - n^{\frac{1}{2}}\{\hat{F}_1(x) - F_1(x)\}\{\hat{F}_2(y) - F_2(y)\} \\ &\quad - F_2(y)n^{\frac{1}{2}}\{\hat{F}_1(x) - F_1(x)\} - F_1(x)n^{\frac{1}{2}}\{\hat{F}_2(y) - F_2(y)\} \\ &\quad + n^{\frac{1}{2}}\{F(x,y) - F_1(x)F_2(y)\}. \end{aligned}$$

By the result of Theorem 4 in Wang and Wells (1997), the first term converges weakly to a zero-mean Gaussian process $U(x,y)$. Also, by the weak convergence of the product-limit estimator, the second term converges in probability to zero uniformly on $[0,\tau_1]\times[0,\tau_2]$, and the third and the fourth terms converge weakly to zero-mean Gaussian processes $F_2(y)U_1(x)$, $F_1(x)U_2(y)$, respectively. Moreover, $F(x,y) = F_1(x)F_2(y)$ if X is independent of Y. Thus, the last term converges to zero in probability uniformly on $[0,\tau_1] \times [0,\tau_2]$. If X and Y are not independent, $\sup_{(x,y)\in[0,\tau_1]\times[0,\tau_2]} n^{\frac{1}{2}}|F(x,y) - F_1(x)F_2(y)|$ tends to infinity as n goes to infinity, leading to $\sup_{(x,y)\in[0,\tau_1]\times[0,\tau_2]} n^{\frac{1}{2}}|Z(x,y)| = \infty$. □

Define the processes as follows:

$$A(x,y) = n^{\frac{1}{2}}\{\hat{H}(x,y) - H(x,y)\},$$
$$B_j(t) = n^{\frac{1}{2}}\{\hat{H}_j(t) - H_j(t)\} \quad (j=1,2),$$
$$C_j(t) = n^{\frac{1}{2}}\{\hat{F}_j(t) - F_j(t)\} \quad (j=1,2),$$

where $\hat{H}_j (j = 1, 2)$ are the empirical survival functions of $\tilde{X}$ and $\tilde{Y}$, respectively.

Theorem 2.2. *If X is independent of Y, for $(x, y) \in [0, \tau_1] \times [0, \tau_2]$ such that $H(x, y) > 0$, the variance of the process $\tilde{Z}(x, y)$ equals to*

$$\sigma^2(x,y) = \{F_1(x)F_2(y)\}^2 \left\{ \frac{1}{H(x,y)} - \frac{1}{H_1(x)} - \frac{1}{H_2(y)} + 2\frac{H(x,y)}{H_1(x)H_2(y)} - 1 \right\},$$

and $\sigma^2(x, y)$ can be consistently estimated by

$$\hat{\sigma}^2(x,y) = \{\hat{F}_1(x)\hat{F}_2(y)\}^2 \left\{ \frac{1}{\hat{H}(x,y)} - \frac{1}{\hat{H}_1(x)} - \frac{1}{\hat{H}_2(y)} + 2\frac{\hat{H}(x,y)}{\hat{H}_1(x)\hat{H}_2(y)} - 1 \right\}.$$

Proof: Let Avar$(\cdot)$ and Acov$(\cdot,\cdot)$ denote the asymptotic variance of $(\cdot)$ and the asymptotic covariance of $(\cdot,\cdot)$. By using the arguments of Wang and Wells (1997) and some elementary probability arguments, under the null hypothesis of independence of X and Y, it can be easily shown that

$$\text{Avar}\{C_j(t)\} = F_j^2(t) \int_0^t \frac{\Lambda_j(du)}{H_j(u)} \quad (j=1,2), \tag{2.2}$$

$$\text{Acov}\{B_j(t), C_j(t)\} = F_j(t)H_j(t) \int_0^t \frac{\Lambda_j(du)}{H_j(u)} \quad (j=1,2), \tag{2.3}$$

$$\text{Acov}\{A(x,y), C_1(x)\} = F_1(x)H(x,y) \int_0^x \frac{\Lambda_1(du)}{H_1(u)}, \tag{2.4}$$

$$\text{Acov}\{A(x,y), C_2(y)\} = F_2(y)H(x,y) \int_0^y \frac{\Lambda_2(du)}{H_2(u)}, \tag{2.5}$$

$$\text{Acov}\{B_1(x), C_2(y)\} = \text{Acov}\{B_2(y), C_1(x)\} = \text{Acov}\{C_1(x), C_2(y)\} = 0, \tag{2.6}$$

where $\Lambda_j(du) = -dF_j(u)/F_j(u) (j = 1, 2)$ are marginal hazard functions of X and Y, respectively. Specially, it is given in Appendix for details of (2.6). Using the results in (2.2)-(2.6) and the fact from Wang and Wells (1997) that $n^{\frac{1}{2}}\{\hat{F}(x,y) - F(x,y)\}$ is asymptotically equivalent to $F(x,y)\{H^{-1}(x,y)A(x,y) - H_1^{-1}(x)B_1(x) + F_1^{-1}(x)C_1(x) - H_2^{-1}(y)B_2(y) + F_2^{-1}(y)C_2(y)\}$, we get the following:

$$\operatorname{var}\{U_j(t)\} = F_j^2(t)\int_0^t \frac{\Lambda_j(du)}{H_j(u)} \quad (j=1,2), \tag{2.7}$$

$$\operatorname{cov}\{U_1(x), U_2(y)\} = 0, \tag{2.8}$$

$$\operatorname{cov}\{U(x,y), U_1(x)\} = F_1^2(x)F_2(y)\int_0^x \frac{\Lambda_1(du)}{H_1(u)}, \tag{2.9}$$

$$\operatorname{cov}\{U(x,y), U_2(y)\} = F_1(x)F_2^2(y)\int_0^y \frac{\Lambda_2(du)}{H_2(u)}. \tag{2.10}$$

Therefore, the variance $\sigma^2(x,y)$ of the process $\tilde{Z}(x,y)$ directly holds from the above results in (2.7)-(2.10) and the equation (3.11) of $\operatorname{var}\{U(x,y)\}$ in Theorem 4 of Wang and Wells (1997), which, from (2.6) under the null hypothesis of independence of X and Y, reduces to

$$\operatorname{var}\{U(x,y)\} = \{F_1(x)F_2(y)\}^2\left\{\frac{1}{H(x,y)} - \frac{1}{H_1(x)} - \frac{1}{H_2(y)} + 2\frac{H(x,y)}{H_1(x)H_2(y)} - 1 + \int_0^x \frac{\Lambda_1(du)}{H_1(u)} + \int_0^y \frac{\Lambda_2(du)}{H_2(u)}\right\}.$$

In addition, the consistency of the variance estimator $\hat{\sigma}^2(x,y)$ follows from the consistency of the empirical survival function estimators $\hat{H}$ and $\hat{H}_j(j=1,2)$. □

To test independence of paired failure time data under independent censoring, we propose a Kolmogorov-Smirnov-type test given by

$$S = \sup_{(x,y)\in[0,\tau_1]\times[0,\tau_2]} |Z(x,y)|.$$

It follows from Theorem 2.1 that the test S is consistent for any alternative such that $\sup_{(x,y)\in[0,\tau_1]\times[0,\tau_2]} |F(x,y) - F_1(x)F_2(y)| \neq 0$. As is evident from $\sigma^2(x,y)$, the process $Z(x,y)$ does not have an independent increment structure asymptotically. Therefore, it is difficult to evaluate analytically the limiting distribution of the test S. To overcome this difficulty, we introduce a bootstrap approach proposed by Beran (1986) to our problem.

Let $d(\alpha)$ be an upper $\alpha(0 < \alpha < 1)$-quantile of the distribution of S. The $d(\alpha)$ can be approximated by generating the bootstrap distribution of S. To do this we first obtain B bootstrap samples of size n each of which consists of $\{(Z_1^*, D_1^*), \ldots, (Z_n^*, D_n^*)\}$, where $Z_i^* = (X_i^*, Y_i^*)(i = 1, \ldots, n)$ has the distribution $\hat{F}_1 \otimes \hat{F}_2$ under the null hypothesis of independence, and each component of $D_i^* = (C_{1i}^*, C_{2i}^*)(i = 1, \ldots, n)$ has the distribution $\hat{G}_j(j = 1, 2)$, respectively. To be specific, let $\{\tilde{x}_{u_1}, u_1 = 1, \ldots, k_u(\leq n)\}$ be the ordered sequence of uncensored distinct time points among the observed values $\{\tilde{x}_i, i = 1, \ldots, n\}$, and $\{\tilde{y}_{u_2}, u_2 = 1, \ldots, l_u(\leq n)\}$ be that of uncensored distinct time points among the observed values $\{\tilde{y}_i, i = 1, \ldots, n\}$. Also, let $\{\tilde{x}_{c_1}, c_1 = 1, \ldots, k_c(\leq n)\}$ be the ordered sequence of censored distinct time points among $\{\tilde{x}_i, i = 1, \ldots, n\}$, and $\{\tilde{y}_{c_2}, c_2 = 1, \ldots, l_c(\leq n)\}$ be that of censored distinct time points among $\{\tilde{y}_i, i = 1, \ldots, n\}$. The Z_i^* are generated from the distribution with mass of size $[\{\hat{F}_1(\tilde{x}_{u_1}) - \hat{F}_1(\tilde{x}_{u_1}+)\} \times \{\hat{F}_2(\tilde{y}_{u_2}) - \hat{F}_2(\tilde{y}_{u_2}+)\}]$ at each point $(\tilde{x}_{u_1}, \tilde{y}_{u_2})(u_1 = 1, \ldots, k_u;\ u_2 = 1, \ldots, l_u)$ on the grid $\{(\tilde{x}_1, \tilde{y}_1), (\tilde{x}_1, \tilde{y}_2), \ldots, (\tilde{x}_{k_u}, \tilde{y}_{l_u})\}$. Similarly, the C_{1i}^* are generated from the distribution with mass $\{\hat{G}_1(\tilde{x}_{c_1}) - \hat{G}_1(\tilde{x}_{c_1}+)\}$ at each point $\tilde{x}_{c_1}(c_1 = 1, \ldots, k_c)$, and the C_{2i}^* from the distribution with mass $\{\hat{G}_2(\tilde{y}_{c_2}) - \hat{G}_2(\tilde{y}_{c_2}+)\}$ at each point $\tilde{y}_{c_2}(c_2 = 1, \ldots, l_c)$. Then, for each bootstrap sample, we compute the bootstrap value of the test statistic S, say S^*, based on $\{(\tilde{X}_1^*, \tilde{Y}_1^*, \delta_1^{x*}, \delta_1^{y*}), \ldots, (\tilde{X}_n^*, \tilde{Y}_n^*, \delta_n^{x*}, \delta_n^{y*})\}$, where $\tilde{X}_i^* = X_i^* \wedge C_{1i}^*, \tilde{Y}_i^* = Y_i^* \wedge C_{2i}^*, \delta_i^{x*} = I(X_i^* \leq C_{1i}^*)$, and $\delta_i^{y*} = I(Y_i^* \leq C_{2i}^*)$. Let $S_1^*, \ldots, S_B^*$ be the bootstrap values of S. The estimated value $\hat{d}(\alpha)$ of $d(\alpha)$ is given as the upper α-empirical quantile based on $S_1^*, \ldots, S_B^*$. Thus, we reject the null hypothesis of independence when the observed value of the test statistic S exceeds $\hat{d}(\alpha)$ at α significance level.

3. NUMERICAL STUDIES

A series of 1,000 simulations are carried out to investigate the small sample ($n = 30, 50$) performance of the proposed test S. In each run of each simulation 500 bootstrap samples of size n are generated from the distribution $\hat{F}_1 \otimes \hat{F}_2 \otimes \hat{G}_1 \otimes \hat{G}_2$ to approximate the value $d(\alpha)$ by $\hat{d}(\alpha)$, the upper α-empirical quantile based on 500 bootstrap values of S under the null hypothesis of independence. We generate the pairs of failure times with unit exponential marginal distributions. The pairs of failure times are generated from two independent exponential distributions with mean of 1 to study the size of the test S, and generated from the Clayton (1978) bivariate exponential model

$$F(x,y) = (e^{\frac{x}{\theta}} + e^{\frac{y}{\theta}} - 1)^{-\theta}$$

with $\theta = 0.25$ and generated from the Gumbel (1960) bivariate exponential model

$$F(x,y) = e^{-(x+y)}\{1 + \theta(1 - e^{-x})(1 - e^{-y})\}$$

with $\theta = 1$ using the algorithm discussed in Section 5 of Prentice and Cai (1992) to study the power of the test S. The Clayton model with $\theta = 0.25$ represents fairly strong positive dependence, while the Gumbel model with $\theta = 1$ represents fairly weak positive dependence. These values are subject to censorship by means of pairs of independent exponentially distributed censoring times with mean of c, where c is suitably chosen according to the desired censoring fraction. Hence each failure time has a $\frac{1}{10}$ marginal probability of being censored when c equals 9, a $\frac{1}{3}$ marginal probability when c equals 2, and a $\frac{1}{2}$ marginal probability when c equals 1.

Table 3.1 presents the simulation results for the empirical sizes and powers of the proposed test S under independent censoring. We note from the column of independent model (A) *that the sizes of the test* S are, *in general, controlled under* the light and heavy censorship, while the test S is conservative when the marginal censoring fraction is one-third, but this drawback is overcome as the sample size increases according to the results not reported here. When the assumed model is the Clayton model (B) with strong dependency, the test S is fairly powerful. This trend is remarkable as the sample size increase and as the censoring fraction is low. However, as expected, when the assumed model is the Gumbel model (C) with weak dependency, the test S is not as powerful as the Clayton model (B).

Table 3.1: Empirical Sizes of 1,000 Samples from Two Independent Exponential Distributions with Mean of 1, and Empirical Powers of 1,000 Samples, Respectively, from the Clayton Bivariate Exponential Distribution with $\theta = 0.25$ and from the Gumbel Bivariate Exponential Distribution with $\theta = 1$

		Model								
		(A) Independence			(B) Clayton			(C) Gumbel		
		% Censoring			% Censoring			% Censoring		
n	α	10	33	50	10	33	50	10	33	50
30	.05	.031	.025	.046	.960	.258	.149	.218	.072	.078
	.10	.080	.066	.105	.983	.497	.308	.359	.154	.183
50	.05	.045	.027	.060	1.00	.453	.169	.365	.079	.100
	.10	.114	.085	.115	1.00	.708	.329	.548	.184	.191

We illustrate the proposed test S with a dataset taken from Oakes (1982). The dataset, given in Table 3.2, consists of remission times in weeks for 21 pairs of leukemia patients treated with 6-mercaptopurine (6-MP) or placebo. The test statistic S equals 0.3983, and the $p-$value corresponding to the observed value, based on 10,000 bootstrap samples, is approximately 0.1340. This indicates no evidence against independence of remission times of leukemia patients between treatment and control groups.

Table 3.2: Remission Times for 21 Pairs of Leukemia Patients Treated with 6-MP or Placebo. The Sign + Indicates the Censored Observations

Pair	1	2	3	4	5	6	7	8	9	10	11
Placebo	1	22	3	12	8	17	2	11	8	12	2
6-MP	10	7	32+	23	22	6	16	34+	32+	25+	11+
Pair	12	13	14	15	16	17	18	19	20	21	
Placebo	5	4	15	8	23	5	11	4	1	8	
6-MP	20+	19+	6	17+	35+	6	13	9+	6+	10+	

APPENDIX

DERIVATION OF (2.6). To show $\text{Acov}\{C_1(x), C_2(y)\} = 0$, it suffices to show that the integrand of the equation $\text{Acov}\{C_1(x), C_2(y)\}$ in Appendix of Wang and Wells (1997),

$$H(s,t)\Lambda_{11}(ds,dt) - H(ds,t)\Lambda_2(dt) - H(s,dt)\Lambda_1(ds) + H(s,t)\Lambda_1(ds)\Lambda_2(dt) \quad (\text{A.1})$$

equals 0, where $\Lambda_{11}(ds,dt) = P\{X \in [s, s+ds), Y \in [t, t+dt) | X \geq s, Y \geq t\}$, $H(ds,t) = P\{\tilde{X} \in [s, s+ds), \tilde{Y} \geq t\}$, and $H(s,dt) = P\{\tilde{X} \geq s, \tilde{Y} \in [t, t+dt)\}$. At first, note that by the assumption of independence of (X, Y) and (C_1, C_2),

$$\begin{aligned} P\{X \in [s, s+ds), Y \geq t\} &= P\{X \in [s, s+ds), Y \geq t | C_1 \geq s, C_2 \geq t\} \\ &= \{P(C_1 \geq s, C_2 \geq t)\}^{-1} P\{X \in [s, s+ds), Y \geq t, C_1 \geq X, C_2 \geq t\} \\ &= \{P(C_1 \geq s, C_2 \geq t)\}^{-1} H(ds, t). \end{aligned}$$

Thus, under the null hypothesis of independence of X and Y,

$$\begin{aligned} H(ds,t) &= P\{X \in [s, s+ds) | X \geq s, Y \geq t) H(s,t) \\ &= P\{X \in [s, s+ds) | X \geq s\} H(s,t). \end{aligned}$$

So, $H(ds,t) = H(s,t)\Lambda_1(ds)$. Similarly, $H(s,dt) = H(s,t)\Lambda_2(dt)$. Also, under the null hypothesis of independence of X and Y, it can be easily shown to be $\Lambda_{11}(ds,dt) = \Lambda_1(ds)\Lambda_2(dt)$. Therefore, the (A.1) becomes zero. Furthermore, to show $\text{Acov}\{B_1(x), C_2(y)\} = 0$, it suffices to show that the integrand of the equation $\text{Acov}\{B_1(x), C_2(y)\}$ in Appendix of Wang and Wells (1997),

$$P\{\tilde{X} \geq s, \tilde{Y} \in [t, t+dt), \delta^y = 1\} - H(s,t)\Lambda_2(dt) \tag{A.2}$$

equals 0. Noting that by the assumption of (X,Y) and (C_1, C_2) and under the null hypothesis of independence of X and Y,

$$\begin{aligned} P\{\tilde{X} \geq s, \tilde{Y} \in [t, t+dt), \delta^y = 1\} &= P\{X \geq s, Y \in [t, t+dt), C_1 \geq s, C_2 \geq t\} \\ &= P\{Y \in [t, t+dt) | Y \geq t\} H(s,t), \end{aligned}$$

the (A.2) equals to be zero. Similarly, $\text{Acov}\{B_2(y), C_1(x)\} = 0$. □

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