Ann. Inst. Statist. Math.
Vol. 46, No. 3, 487–495 (1994)

BOOTSTRAPPING A BAYES ESTIMATOR OF A SURVIVAL FUNCTION WITH CENSORED DATA

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(Received February 8, 1993; revised December 27, 1993)

Abstract. The large-sample frequentist property of a frequentist bootstrap for a posterior mean with respect to a Dirichlet prior of the survival function for a randomly censored data is given. The weak convergence of a bootstrap version of the Susarla-Van Ryzin estimator is established on the whole real line. An illustration of the technique and some Monte Carlo studies are also given.

Key words and phrases: Bayesian bootstrap, survival function, square-integrable martingales.

1. Introduction and the main result

Recently Lo (1993) introduced a Bayesian analogue of Efron's (1981) bootstrap method for censored data (CDB), called the Bayesian bootstrap for censored data (CDBB), and developed a (first-order) large-sample theory. Lo's CDBB is defined by replacing the 1's in the Kaplan-Meier (KM) estimator (cf. (1.2) below) by standard i.i.d. exponential random variables; and is a natural extension of Rubin's (1981) Bayesian bootstrap for complete data. (See also Lo (1987, 1988) and Weng (1989).) Both Rubin's Bayesian bootstrap and Lo's CDBB are based on simulation where Efron's CDB is based on resampling. Akritas (1986) showed that, for almost all sample sequences, Efron's CDB estimator for the underlying survival function, when suitably normalized, converges weakly to a Brownian bridge. Lo (1993) established a similar result for the CDBB, thus implying that the CDB and the CDBB are (first-order) asymptotically equivalent, and both are consistent bootstrap methods in approximating the sampling distribution of the KM estimator (Breslow and Crowley (1974) and Gill (1983)). Reid (1981) discussed another resampling method for censored data; Akritas (1986) showed that Reid's method and Efron's CDB are not asymptotically equivalent.

In this note, following Efron (1981), we propose a resampling method for censored data by resampling from the posterior mean of the survival function, a Dirichlet process prior derived by Susarla and Van Ryzin (1976). We shall call the proposed resampling as the *frequentist bootstrapping of the Bayes estimator for censored data* (CDFBBE).

Let $X_1, \ldots, X_n$ be survival times which are censored on the right by n follow-up times, $Y_1, \ldots, Y_n$. Assume that X_i's are i.i.d. with survival function (s.f.) F, and that Y_i's are i.i.d. with s.f. G. Let the support of F and G lie in $R^+ = (0, \infty)$. Define,

$$Z_i = X_i \wedge Y_i, \quad \delta_i = 1[X_i \le Y_i]; \qquad i = 1, \ldots, n, \tag{1.1}$$

where $a \wedge b = \min(a, b)$ and $1[\mathrm{A}]$ is the indicator of the event A. Define, the s.f. of Z_i's by $H \equiv FG$ with $\tau_H = \sup\{t : H(t) > 0\}$. The Z_i's represent a censored or uncensored observation according as δ_i is 0 or 1.

Following Lo (1993), let $t_{(1)} < \cdots < t_{(k)}$ be the distinct ordered values for times to death (uncensored data). For $j = 1, \ldots, k$, let $D(j) = \{i : Z_i = t(j), \delta_i = 1\}$ and $R(j) = \{i : Z_i \ge t(j)\}$. Then, the KM estimator of F is defined by

$$\hat{F}(t) = \prod_{j:t(j) \le t} \left(1 - \left\{ \sum_{q \in D(j)} 1 \Big/ \sum_{q \in R(j)} 1 \right\} \right). \tag{1.2}$$

Efron's CDB is the KM estimator of F based on a (bootstrap) sample taken with replacement from (Z_i, δ_i), $i = 1, \ldots, n$, where as Reid's bootstrap estimator of F is the empirical distribution function of an i.i.d. sample from (1.2). Lo's (1993) CDBB is given by

$$\tilde{F}(t) = \prod_{j:t(j) \le t} \left\{ 1 - \left\{ \sum_{q \in D(j)} T_q \Big/ \sum_{q \in R(j)} T_q \right\} \right) \tag{1.3}$$

where $T_1, \ldots, T_n$ are i.i.d. standard exponential random variables. (Note the change in notations in (1.3) from Lo (1993).)

Let $(1 - F)$ be a Dirichlet process on R^+ with parameter α (Ferguson (1973) and Ferguson *et al.* (1992)). Suppose that $(Y_1, \ldots, Y_n)$ is independent of $(F, X_1, \ldots, X_n)$. Susarla and Van Ryzin's (1976) nonparametric Bayes estimator of F is given by

$$\hat{F}_\alpha(t) = B_n(t) W_n(t), \qquad t > 0, \tag{1.4}$$

where

$$B_n(t) = (\alpha(t, \infty) + n\mathbb{H}_n(t))/(\alpha(\mathbb{R}^+) + n),$$
$$W_n(t) = \prod_{j=1}^{n} \left\{ \frac{\alpha[Z_j, \infty) + n\mathbb{H}_n(Z_j) + 1}{\alpha[Z_j, \infty) + n\mathbb{H}_n(Z_j)} \right\}^{1[\delta_j = 0, Z_j \le t]},$$

and $\mathbb{H}_n$ is the empirical s.f. of the Z's given by $n\mathbb{H}_n(t) = \sum_{i=1}^{n} 1[Z_i > t]$.

Let an estimator of the censoring s.f. be given by $\hat{G}_\alpha$, where

$$B_n \equiv \hat{F}_\alpha \hat{G}_\alpha. \tag{1.5}$$

The $\hat{G}_\alpha$ should be viewed only as a Bayes-like approximation to a maximum likelihood estimator of G. This estimator is not a NPB estimator of G as B_n is not a NPB estimator of H. (Indeed, B_n is a NPB estimator of H is a true fact only if *a priori* H is Dirichlet with parameter α.)

Following Efron (1981), the proposed CDFBBE is defined as follows: let $X_1^*, \ldots, X_m^*$ be i.i.d. with distribution function $(1 - \hat{F}_\alpha)$ and let $Y_1^*, \ldots, Y_m^*$ be i.i.d. with distribution function $(1 - \hat{G}_\alpha)$, and define

$$Z_i^* = X_i^* \wedge Y_i^* \quad \text{and} \quad \delta_i^* = 1[X_i^* \leq Y_i^*], \qquad i = 1, \ldots, m. \tag{1.6}$$

Define, $\hat{F}_\alpha^*$, $\hat{G}_\alpha^*$, B_m^*, W_m^* and $\mathbb{H}_m^*$ as using (1.4) and (1.5) except now evaluate the functions at the bootstrap sample (1.6) rather than the original data (1.1). Also, define $T_m^* = \max_{1 \leq i \leq m} Z_i^*$.

Note that, as pointed out by a referee, the CDFBBE allows user input of prior information through the choice of the Dirichlet parameter α. Let $Q^{-1} = 1/Q$, not the function inverse, and let $\bar{Q} = 1 - Q$. Let $D[0, \tau_H]$ be the space of cadlag (right continuous with left limits) functions with the Skorohod metric. Define the process,

$$\mathcal{X}_m^*(t) = \sqrt{m}\{\hat{F}_\alpha^*(t) - \hat{F}_\alpha(t)\}\hat{F}_\alpha^{-1}(t). \tag{1.7}$$

The main result is given below.

THEOREM 1.1. *Let R and G be continuous s.f. on $\mathbb{R}^+$. Then given the data (1.1), the process $\mathcal{X}_m^*(t)$ in (1.7) converges weakly to $\mathcal{X}(t)$ on $D[0, \tau_H]$, as n and m tend to infinity, for almost all sample sequences $(Z_1, \delta_1), \ldots, (Z_n, \delta_n)$, where $\mathcal{X}(t)$ is a mean zero Gaussian process with covariance function*

$$C(s,t) = \int_0^{s \wedge t} H^{-1} F^{-1} d\bar{F}.$$

Note that this result is the large-sample property of the CDFBBE on the entire space $D[0, \tau_H]$. Thus, if $\alpha \equiv 0$, Theorem 1.1 is an extension of Akritas' result to $D[0, \tau_H]$ rather than to the subset $D[0, \tau_H)$. The extension of Gill's (1983) classical results on the weak convergence of the normalized Kaplan-Meier process on $D[0, \tau_H]$ has been studied by Ying (1989).

The proof of Theorem 1.1 is given in the Appendix. In Section 2, we use this theorem to construct confidence bands for the survival function.

2. Confidence band for the survival curve

In this section we show how the weak convergence theorem of the previous section may be applied to obtain simultaneous CDFBBE confidence bands for the survival curve. The bands that we construct are asymptotically correct and do not require tables for construction. Similar bands for Efron's CDB were constructed by Akritas (1986). We will compare our CDFBBE bands to those of Akritas' CDB bands and illustrate that the CDFBBE bands have similar coverage but narrower width.

To construct the confidence bands we first need to make some remarks about the limiting Gaussian process in Theorem 1.1. The results of this theorem may be reformulated to say that the process $\mathcal{Z}_m(t) = \sqrt{m}\{\hat{F}^*_\alpha(t) - \hat{F}_\alpha(t)\}$ convergence weakly to $\mathcal{B}^0(K(t))F(t)/K(t)$ as m and $n \to \infty$, conditionally almost surely, where $\mathcal{B}^0$ is a Brownian Bridge,

$$K(t) = \left[1 + \left(\int_0^t H^{-1}(s)d\Lambda^F(s)\right)^{-1}\right]^{-1},$$

and Λ^F is the cumulative hazard function of F. Define K_n to be the empirical estimator of K, obtained by substituting in K the empirical analogs of H and Λ. Note that the bootstrapped process $\mathcal{Z}_m$ and the non-bootstrapped process $\sqrt{n}\{\hat{F}_\alpha(t) - F(t)\}$ converge to the same limiting Gaussian process. Therefore, if one would compute a constant $C_m(\hat{F}_\alpha)$ from the bootstrap distribution that is such that

$$P\left\{m^{1/2} \sup_{0\le t\le \tau_H} \left|(\hat{F}^*_\alpha(t) - \hat{F}_\alpha(t))\left(\frac{K_n(t)}{\hat{F}_\alpha(t)}\right)\right| < C_m(\hat{F}_\alpha)\middle|(Z_i, \delta_i), i = 1, \dots, n\right\}$$
$$= 1 - \alpha',$$

one would have the desired coverage probability $(1-\alpha')$. Note that if one computed a constant $C_n(F)$ as above, however, from the non-bootstrap distribution, $C_m(\hat{F}_\alpha)$ and $C_n(F)$ would be asymptotically equal as m and $n \to \infty$. These results may be proved by applying the continuous mapping theorem (cf. Billingsley (1968), Section 1.5). Using the bootstrap critical value one may construct the confidence band

$$\hat{F}_\alpha(t) - \frac{C_m(\hat{F}_\alpha)}{\sqrt{n}}\left(\frac{\hat{F}_\alpha(t)}{K_n(t)}\right)$$
$$\le F(t) \le \hat{F}_\alpha(t) + \frac{C_m(\hat{F}_\alpha)}{\sqrt{n}}\left(\frac{\hat{F}_\alpha(t)}{K_n(t)}\right)$$

as a $100(1-\alpha')\%$ confidence band for the unknown survival function. From Theorem 1.1 it follows that to construct a $100(1-\alpha')\%$ CDFBBE confidence band one must compute

$$\sqrt{m} \sup_{0\le t\le \tau_H} (\hat{F}^*_\alpha(t) - \hat{F}_\alpha(t))$$

for each of the B bootstrap samples, then approximate $C_m(\hat{F}_\alpha)$ by the $100(1-\alpha')\%$ percentile of the frequency distribution of these numbers.

Now we present the Monte Carlo studies. Following Akritas (1986), in the first study the survival times are generated from the unit exponential distribution with distribution $F(x) = 1-e^{-x}$, $x > 0$, and the censoring times from the uniform $(0, b)$

Table 1. Achieved confidence levels with 1,000 simulations using random samples of size $n = 30$ from unit exponential and uniform censoring distributions.

α'	20% Censoring	40% Censoring
.01	.009	.019
.05	.053	.062
.10	.094	.089
.20	.194	.177

Table 2. Simulated data with exponential survivals and uniform censoring. A comparison of the lengths of the CDB, the CDBB and CDFBBE are given.

	20% Censoring			40% Censoring		
x	LCDB	LCDBB	LCDFBBE	LCDB	LCDBB	LCDFBBE
.10	.2943	.2941	.2911	.2721	.2793	.2839
.25	.2943	.2913	.2718	.2721	.2797	.2992
.50	.3109	.3001	.2669	.3555	.3249	.3044
.75	.3099	.2992	.2752	.3555	.3249	.3094
1.00	.3094	.2992	.2639	.3555	.3252	.3091
1.25	.3094	.2989	.2642	.3642	.3252	.3162
1.50	.3327	.3164	.2701	.3442	.3441	.3201
1.75	.3327	.3241	.2745	.3793	.3676	.3349
2.00	.3672	.3367	.2837	.3793	.3553	.3416
2.25	.3672	.3375	.2842	.3793	.3653	.3502
2.50	.3551	.3241	.2938	.4014	.3894	.3567

distribution with 20% and 40% censoring ($b = 4.9651$ and 2.2316, respectively). We generated 1,000 simulations using random samples of size $n = 30$. The achieved confidence levels using the above CDFBBE confidence band are given in Table 1. We chose the parameter of Dirichlet process α to be given by $\alpha(x) = e^{-x}$, $x > 0$. (In this study we have not considered the effect of varying F and α. This is an interesting problem for future research.)

In the second study we compared the lengths of Akritas' CDB and Lo's CDBB bands with the corresponding lengths of our CDFBBE bands. Once again we generated survival times from the unit exponential distribution and the censoring times from the uniform $(0, b)$ distribution with 20% and 40% censoring. We took $n = m = 30$, and $B = 200$. The parameter α was taken to be $\alpha(x) = e^{-x}$, $x > 0$. The bands were constructed to have 90% coverage. The results are given in Table 2 wherein LCDB, LCDBB and LCDFBBE represent the lengths for the CDB, the CDBB and the CDFBBE bands, respectively.

The results of the simulations are quite clear. The achieved confidence levels are quite close to the nominal levels. This is also true in the CDB simulation of Akritas ((1986), Table 2). As for the lengths of the CDB, the CDBB and the CDFBBE bands, it appears that the CDFBBE bands are in general narrower than the CDB bands which in turn are narrower than the CDBB bands. As a referee pointed out a narrower band is not always better. In fact, one could use a point mass distribution at the Kaplan-Meier estimator as a basis for bootstrapping, resulting in a band with zero width. The not yet available second-order results for censored data bootstraps will have the final word. It is also noted that the CDF-BBE and the CDBB bands are smoother than the CDB bands. This should not be surprising since the KM estimator is a step function, where as NPB estimator is not. Both the KM and the NPB estimators are discontinuous at the uncensored observations (provided $\alpha(\cdot)$ is continuous). However, the NPB estimator is a smooth estimator resulting in the continuity at censored observations (provided $\alpha(\cdot)$ does not have any point masses). Thus, while the KM estimator have horizontal parts the NPB estimator is strictly decreasing. Therefore, it follows that the CDFBBE and the CDBB bands will be narrower and smoother than the CDB bands.

Acknowledgements

The authors would like to thank the referees for their helpful comments and suggestions.

Appendix

The proof of Theorem 1.1 is based on Akritas' martingale arguments, and the following lemmas.

LEMMA A.1. *Under the conditions of Theorem* 1.1, $\mathcal{X}_m^*$ *has the same asymptotic behavior as the process*

$$\begin{aligned}(\text{A.1})\quad \mathcal{Y}_m &= \sqrt{m}B_m^{-1}\{B_m^* - B_n\} + \sqrt{m}\left[\int_0^{\cdot} \mathbb{H}_m^{*-1} d\bar{\mathbb{H}}_m^{*(0)} - \int_0^{\cdot} \mathbb{H}_n^{-1} d\bar{\mathbb{H}}_n^{(0)}\right] \\ &= \mathcal{Y}_{1m} + \mathcal{Y}_{2m}, \qquad \textit{say},\end{aligned}$$

where $n\bar{\mathbb{H}}_n^{(0)}(t) = \sum_{i=1}^n 1[Z_i \le t, \delta_i = 0]$ *and* $m\bar{\mathbb{H}}_m^{*(0)}(t) = \sum_{i=1}^m 1[Z_i^* \le t, \delta_i^* = 0]$.

PROOF. Apply an argument similar to the one used by Susarla and Van Ryzin (1978) in Lemma 4.1 and Corollary 4.1. □

LEMMA A.2. *The process* $\mathcal{Y}_{1m}$ *in* (A.1) *has the same asymptotic behavior as*

$$\mathcal{Y}_{1m}^* = -\sqrt{m}\{\Lambda_m^{H^*} - \Lambda_n^H\},$$

where $\Lambda_n^H(t) = \int_0^t \mathbb{H}_n^{-1}(s) d\bar{\mathbb{H}}_n(s)$ *and* $\Lambda_m^{H^*}(t) = \int_0^t \mathbb{H}_m^{*-1}(s) d\bar{\mathbb{H}}_m^*(s)$.

PROOF. Note that $\|B_n - \mathbb{H}_n\|_0^{\tau_H} = O_p(n^{-1})$ and $\|B_m^* - \mathbb{H}_m^*\|_0^{\tau_H} = O_p(m^{-1})$, so that

$$\|\mathcal{Y}_{1m} - \sqrt{m}\mathbb{H}_n^{-1}\{\mathbb{H}_m^* - \mathbb{H}_n\}\|_0^{\tau_H} = O_p(m^{-1}). \tag{A.2}$$

Also, if $\Lambda^H(t) = \int_0^t H^{-1}(s)d\bar{H}(s)$ is the cumulative hazard function of $\bar{H}$, we have

$$-\sqrt{n}H^{-1}\{\mathbb{H}_n - H\} = \sqrt{n}\int_0^{\cdot} \mathbb{H}_n H^{-1} d[\Lambda_n^H - \Lambda^H].$$

Therefore, the Glivenko-Cantelli and the Lebesgue Dominated Convergence theorems imply that

$$\sqrt{n}\|H^{-1}\{\mathbb{H}_n - H\} + \{\Lambda_n^H - \Lambda^H\}\|_0^{\tau_H} \xrightarrow{P} 0 \quad \text{as} \quad n \to \infty.$$

A similar argument for the bootstrap versions of these processes implies that

$$\sqrt{m}\|\mathbb{H}_n^{-1}\{\mathbb{H}_m^* - \mathbb{H}_n\} + \{\Lambda_m^{H^*} - \Lambda_n^{H^*}\}\|_0^{\tau_H} \xrightarrow{P} 0 \quad \text{as} \quad m \to \infty \quad \text{and} \quad n \to \infty. \tag{A.3}$$

Finally, by applying the triangle inequality to (A.2) and (A.3) the results follows. □

PROOF OF THEOREM 1.1. Define the true and empirical cumulative hazard rate of $\bar{G}$ as

$$\Lambda^G(t) = \int_0^t G^{-1}(s-)d\bar{G}(s) \quad \text{and} \quad \Lambda_n^G(t) = \int_0^t \mathbb{H}_n^{-1}(s-)d\bar{\mathbb{H}}_n^{(0)}(s).$$

Let $\Lambda_m^{G^*}$ be the bootstrap analog. Clearly, $\mathcal{Y}_{2m}$ in (A.1) is equal to $\sqrt{m}\{\Lambda_m^{G^*}(t) - \Lambda_n^G(t)\}$. Therefore, Lemma A.2 implies that

$$\|\mathcal{X}_m^*(t) - \sqrt{m}\{\Lambda_m^{G^*}(t) - \Lambda_n^G(t)\} - \sqrt{m}\{\Lambda_m^{H^*}(t) - \Lambda_n^H(t)\}\|_0^{\tau_H} \xrightarrow{P} 0 \quad \text{as} \quad m \to \infty \quad \text{and} \quad n \to \infty.$$

The relation $H = FG$ implies that $\Lambda^H = \Lambda^F + \Lambda^G$, and hence

$$\|\mathcal{X}_m^*(t) - \mathcal{Z}_m^*(t)\|_0^{\tau_H} \xrightarrow{P} 0 \quad \text{as} \quad m \to \infty \quad \text{and} \quad n \to \infty,$$

where $\mathcal{Z}_m^*(t) = \sqrt{m}\{\Lambda_m^{F^*}(t) - \Lambda_n^F(t)\}$,

$$\Lambda_n^F(t) = \int_0^t \mathbb{H}_n^{-1}(s-)d\bar{\mathbb{H}}_n^{(1)}(s), \qquad n\bar{\mathbb{H}}_n^{(1)}(t) = \sum_{i=1}^n 1[Z_i \le t, \delta_i = 1]$$

and $\Lambda_m^{F^*}$ is the bootstrap analog of Λ_n^F.

Following Akritas (1986), define the square-integrable martingale

$$M_m^*(t) = \sqrt{m}\left[\mathbb{H}_m^{(1)*}(t) - \int_0^t \mathbb{H}_m^*(s-)d\Lambda_n^F(s)\right].$$

Then, it may be shown that the process $\mathcal{Z}_m^*$ may be expressed as the stochastic integral (cf. Gill (1980), p. 37)

$$\mathcal{Z}_m^*(t) = \int_0^t J_m^*(s)(\mathbb{H}_m^*(s-))^{-1}dM_m^*(s),$$

where $J_m^*(s) = 1[0 \le s \le T_m^*]$. Applying the results of Jacod (1975), the bracket function of M_m^* is given by

$$\langle M_m^*\rangle(t) = \int_0^t \mathbb{H}_m^*(s-)(1-\Delta\Lambda_n^F(s))d\Lambda_n^F(s),$$

where for a right-continuous function A, $\Delta A(t) \equiv A(t) - A(t-)$. Hence the bracket function of the stochastic integral $\mathcal{Z}_m^*$ is given by Lipster and Shiryayev ((1978), pp. 268–276)

$$\langle \mathcal{Z}_m^*\rangle(t) = \int_0^t J_m^*(s)(\mathbb{H}_m^*(s-))^{-1}(1-\Delta\Lambda_n^F(s))d\Lambda_n^F(s).$$

Since $J_m^*(s) \xrightarrow{P} 1$ on $[0, \tau_H]$, we have

$$\langle \mathcal{Z}_m^*\rangle(t) \xrightarrow{P} \int_0^t H^{-1}(s)d\Lambda^H(s) = \int_0^t H^{-1}(s)F^{-1}(s)d\bar{F}(s)$$

uniformly on $[0, \tau_H]$. Hence, following the approach of Akritas (1986), an application of Rebolledo's (1980) central limit theorem yields that $\mathcal{Z}_m^*(t)$ converges weakly to the Gaussian process $\mathcal{X}(t)$ on $D[0, \tau_H]$. Note that $\mathcal{Z}_m^*$ is a stopped process, and what we have proved is that $\mathcal{X}_m^*(t \wedge T_m^*)$ converges weakly to $\mathcal{X}$ on $D[0, \tau_H]$.

We now show that the process $\mathcal{X}_m^*$, not a stopped version, converges weakly on $D[0, \tau_H]$. First, note that for large m, $\|\hat{F}_\alpha^{-1}(t-)\|_0^{\tau_H} < \infty$ by applying the definition of τ_H. Next define, $p_\epsilon = \inf\{t : \sqrt{m}\{\hat{F}_\alpha(t) - \hat{F}_\alpha(\tau_H)\} = \epsilon\}$. An easy calculation shows that

$$\begin{aligned} P(\sqrt{m}\{\hat{F}_\alpha(T_m^*) - \hat{F}_\alpha(\tau_H)\} > \epsilon) &\le P(T_m^* \le p_\epsilon) = (1 - B_n(p_\epsilon))^m \\ &\le (1 - [\hat{F}_\alpha(p_\epsilon) - \hat{F}_\alpha(\tau_H)]\hat{G}_\alpha(p_\epsilon))^m \\ &= (1 - \epsilon\hat{G}_\alpha(p_\epsilon)/\sqrt{m})^m \xrightarrow{P} 0 \quad \text{as} \quad m \to \infty. \end{aligned}$$

Therefore, $\|\mathcal{X}_m^*(t \wedge T_m^*) - \mathcal{X}_m^*(t)\|_0^{\tau_H} \le \sqrt{m}\|\hat{F}_\alpha^{-1}(t-)\|_0^{\tau_H}\|\hat{F}_\alpha(T_m^*) - \hat{F}_\alpha(\tau_H)\|_0^{\tau_H} \xrightarrow{P} 0$ as $m \to \infty$, and the desired results on the entire space $D[0, \tau_H]$. This type of argument first appeared in Ying (1989).

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