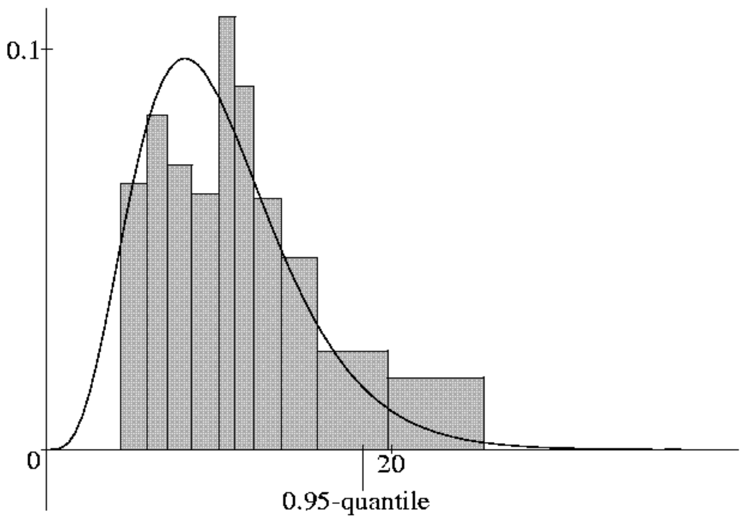
UNIVERSITÄT POTSDAM
Institut für Mathematik

Testing the Acceleration Function in Life Time Models

Hannelore Liero

Matthias Liero



Mathematische Statistik und Wahrscheinlichkeitstheorie

Universität Potsdam – Institut für Mathematik

Mathematische Statistik und Wahrscheinlichkeitstheorie

Testing the Acceleration Function in Life Time Models

Hannelore Liero

Institute of Mathematics, University of Potsdam
e-mail: liero@uni-potsdam.de

Matthias Liero

Humboldt-University of Berlin
e-mail: mliero@gmx.de

Preprint 2006/03

November 2006

Impressum

Herausgeber: Mathematische Statistik und Wahrscheinlichkeitstheorie
am Institut für Mathematik

Adresse: Universität Potsdam
PF 60 15 53
14415 Potsdam
Telefon: +49-331-977 1500
Fax: +49-331-977 1578
E-mail: neisse@math.uni-potsdam.de

ISSN 1613-3307

Testing the acceleration function in life time models

Hannelore Liero
Institute of Mathematics, University of Potsdam
e-mail: liero@uni-potsdam.de

Matthias Liero
Institute of Mathematics, Humboldt - University of Berlin
e-mail: mliero@gmx.de

Abstract

The accelerated life time model is considered. First, test procedures for testing the parameter of a parametric acceleration function is investigated; this is done under the assumption of parametric and nonparametric baseline distribution. Further, based on nonparametric estimators for regression functions tests are proposed for checking whether a parametric acceleration function is appropriate to model the influence of the covariates. Resampling procedures are discussed for the realization of these methods. Simulations complete the considerations.

Keywords and phrases: Accelerated life time model, parametric regression, nonparametric regression estimation, L_2-type test, resampling, simulation

AMS subject classification: Primary 62N03, 62G10

1 Introduction

Let T be a random life time which depends on some explanatory variable X; examples for X are the dose of a drug, temperature or stress. To describe the influence of the covariate X on the life time there are several proposals. A well-known model is the accelerated life time model (ALT), which is intensively studied in the book of V. Bagdonavičius and M. Nikulin (2001). In difference to the models studied by these authors we will assume throughout the paper that the covariate does not depend on time. We suppose that the covariate X reduce a basic life time, say T_0, by a factor $\psi(X)$ and write the life time T as

$$T = \frac{T_0}{\psi(X)}.$$

The conditional survival function of T given $X = x$ is defined by

$$S(t|x) = \mathsf{P}(T > t|X = x) = S_0(t\psi(x)),$$

where $S_0(\cdot) = \mathsf{P}(T_0 > \cdot)$ is the survival function of the baseline life time T_0. The distribution function is denoted by F_0. It is assumed that T is an absolute continuous random variable.

In the present paper we study the problem of testing the acceleration function ψ under different assumptions on the underlying model. Given independent copies (T_i, X_i), $i = 1, \dots, n$ of the pair (T, X) we will propose test statistics and consider their limit distributions under the hypotheses. Test procedures formulated on the basis of these limit statements are only *asymptotic* α-tests. Thus it seems to be useful to discuss some resampling methods for the realization of these tests in practice. We will complete these discussions by simulations. The program files (written in the R-language) for these simulations can be found on our web site http://www.mathematik.hu-berlin.de/ liero/.

---

2 The parametric ALT model

We start with the simplest model, namely the completely parametric model, where it is assumed that both the survival function S_0 and the acceleration function ψ belong to a known parametric class of functions. That is, there exist parameters $\nu \in \mathbb{R}^k$ and $\beta \in \mathbb{R}^d$ such that

$$S_0(t) = S_0(t;\nu) \qquad \text{and} \qquad \psi(x) = \psi(x;\beta),$$

where the functions $S_0(\cdot;\nu)$ and $\psi(\cdot;\beta)$ are known except the parameters ν and β. A hypothesis about the function ψ is then a hypothesis about the parameter β, and we consider the test problem

$$\mathcal{H} \,:\, \beta = \beta_0 \qquad \text{against} \qquad \mathcal{K} \,:\, \beta \neq \beta_0$$

for some $\beta_0 \in \mathbb{R}^d$.
The classical way for the construction of a test procedure is to estimate β by the maximum likelihood estimator (m.l.e.) and to use the likelihood ratio statistic (or a modification like the Rao score statistic or the Wald statistic) for checking $\mathcal{H}$. In V. Bagdonavičius and M. Nikulin (2001) this approach is carried out for several distributions, for $\psi(x;\beta) = \exp(-x^T\beta)$ and for censored data.
Another possibility is to take the logarithm of the life time $Y = \log T$. Then with

$$m(x;\vartheta) = \mu - \log\psi(x;\beta) \qquad \vartheta = (\mu,\beta)$$

we obtain the parametric regression model

$$Y_i = m(X_i;\vartheta) + \varepsilon_i \tag{1}$$

with

$$\mu = \mathsf{E}\log T_0 = \mu(\nu) \qquad \text{and} \qquad \mathsf{E}\varepsilon_i = 0.$$

Assuming $\psi(0;\beta) = 1$ the parameter β can be estimated by the least squares estimator (l.s.e.).
In the case that T_0 is distributed according to the log normal distribution the resulting regression model is the normal model. Then the maximum likelihood estimator and the least squares estimator coincide. Furthermore, assuming $\psi(x;\beta) = \exp(-x^T\beta)$ we have the linear regression, and for testing $\mathcal{H}$ we apply the F-test, which is exact in this case.
Now, suppose that $\log T$ is not normally distributed. Then it is well-known that under regularity conditions the m.l.e. for β is asymptotically normal, and an asymptotic α- test is provided by critical values derived from the corresponding limit distribution.
Let us propose another method, a resampling method, to determine critical values. We restrict our considerations here to maximum likelihood method; the regression approach is discussed in detail in the following section. For simplicity of presentation we consider the case $d = 1$.

1. On the basis of the (original) data (t_i, x_i), $i = 1,\ldots,n$ compute the maximum likelihood estimates for ν and β, say $\hat{\nu}$ and $\hat{\beta}$.

2. For $r = 1, \ldots, R$

   (a) generate
   $$t_i^* = \frac{t_{0i}^*}{\psi(x_i;\hat{\beta})} \qquad \text{where} \quad t_{0i}^* \sim F_0(\cdot;\hat{\nu})$$

   (b) Compute for each sample the m.l.e. $\hat{\beta}^{*(r)}$.

3. (a) *Naive approach* Take the quantiles of the empirical distribution of these $\hat{\beta}^{*(r)}$'s as critical values, i.e. let $\hat{\beta}^{*[1]}, \hat{\beta}^{*[2]}, \ldots, \hat{\beta}^{*[R]}$ be the ordered estimates, then reject the hypothesis $\mathcal{H}$ if
   $$\beta_0 < \hat{\beta}^{*[R\alpha/2]} \qquad \text{or} \qquad \beta_0 > \hat{\beta}^{*[R(1-\alpha/2)]}.$$
   (The number R is chosen such that $R\alpha/2$ is an integer.)

   (b) *Corrected normal approach* Estimate the bias and the variance of the estimator by
   $$b_R = \overline{\beta^*} - \hat{\beta}, \quad v_R = \frac{1}{R-1}\sum_{r=1}^{R}(\hat{\beta}^{*(r)} - \overline{\beta^*})^2,$$
   where $\overline{\beta^*} = \frac{1}{R}\sum_{r=1}^{R}\hat{\beta}^{*(r)}$ and accept the hypothesis $\mathcal{H}$ if β_0 belongs to the interval
   $$[\hat{\beta} - b_R - \sqrt{v_R}\,u_{1-\alpha/2}\,,\; \hat{\beta} - b_R + \sqrt{v_R}\,u_{1-\alpha/2}].$$
   Here $u_{1-\alpha/2}$ is the $1-\alpha/2$-quantile of the standard normal distribution.

   (c) *Basic bootstrap* As estimator for the quantiles of the distribution of $\hat{\beta} - \beta$ take $\hat{\beta}^{*[R\alpha/2]} - \hat{\beta}$ and $\hat{\beta}^{*[R(1-\alpha/2)]} - \hat{\beta}$, respectively. Thus, accept $\mathcal{H}$ if β_0 belongs to
   $$\left[\hat{\beta} - (\hat{\beta}^{*[R(1-\alpha/2)]} - \hat{\beta})\,,\; \hat{\beta} - (\hat{\beta}^{*[R\alpha/2]} - \hat{\beta})\right]$$

To demonstrate this proposal we have carried out the following **simulations:** As baseline distribution we have chosen the exponential distribution, the covariates are uniformly distributed and for computational simplicity the acceleration function has the form $\psi(x;\beta) = \exp(-x\beta)$.
We generated n realizations (t_i, x_i) of random variables (T_i, X_i): The X_i's are uniformly distributed over $[2,4]$, the T_i's have the survival function
$$S(t|x_i) = \exp(-t\psi(x_i;\beta_0)/\nu) \qquad \text{with} \quad \psi(x;\beta_0) = \exp(-x\beta_0)$$

for the parameters

$$n = 12, \quad \beta_0 = 2, \quad \nu = 2.$$

As values of the m.l.e. we obtained $\hat{\beta} = 1.82$ and $\hat{\nu} = 3.42$ The asymptotic confidence interval based on the asymptotic normality of the m.l.e. was:

$$[0.839\,,\,2.800]$$

With $R = 1000$ resamples constructed by the methods given above we obtained as confidence intervals ($\alpha = 0.05$) for β

Method	lower bound	upper bound
naive approach	0.550	2.973
corrected normal	0.681	2.979
basic bootstrap	0.666	3.089

Figure 1 shows a histogram of the $\hat{\beta}^{*(r)}$'s. In this case the true parameter $\beta_0 = 2$ is covered by all intervals, also by that based on the limit distribution. Moreover, this interval is shorter. We repeated this approach $M = 100$ times. The number of cases, where the true parameter is not covered, say w was counted. Here are the results:

Method	w
asymptotic distribution	8
naive approach	4
corrected normal	4
basic bootstrap	5

Thus, the price for the shortness of the interval based on the normal approximation is that the coverage probability is not preserved.

---

3 The ALT model with nonparametric baseline distribution

Consider the situation that the acceleration function ψ has still a known parametric form $\psi(\cdot;\beta)$, $\beta \in \mathbb{R}^d$ but the underlying distribution of the baseline life time is completely unknown. Thus we have an infinite dimensional nuisance parameter and the application of the maximum likelihood method is not possible. We use the regression approach to estimate and to test the

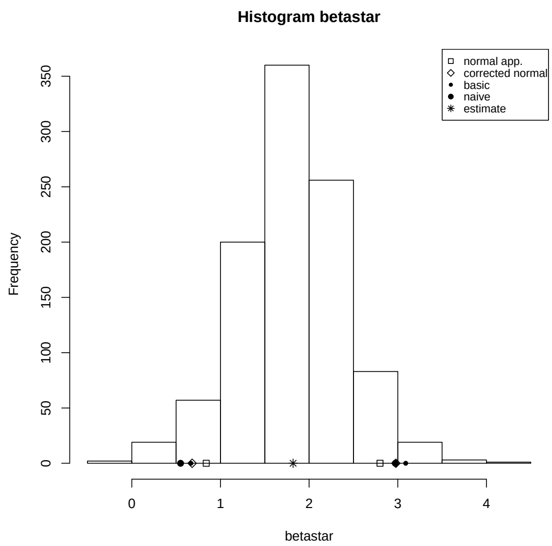


Figure 1: Histogram of the resampled beta's

parameter β. Using the asymptotic normality of the l.s.e. in the regression model often confidence intervals or tests for β are based on the quantiles of the normal ($d = 1$) or χ^2-distribution ($d > 1$). For large n the results will turn out satisfactory. But for small n this asymptotic approach is not justified. Here one can use resampling procedures for regression, see for example Davison and Hinkley (1997) or Efron and Tibshirani (1993).
For simplicity we consider the problem of testing a single component β_j. In our simulation study we compared the following two methods:

1. On the basis of the regression model (1) with the original data compute the l.s.e. $\hat{\mu}$ and $\hat{\beta}$ for μ and β, respectively. Derive the residuals e_i and let

$$r_i = \frac{e_i}{\sqrt{(1-h_i)}} = \frac{y_i - \hat{y}_i}{\sqrt{(1-h_i)}}$$

   be the modified residuals. Here the $\hat{y}_i$'s are the fitted values $m(x_i; \hat{\mu}, \hat{\beta})$, and the h_i's are the leverages.

   Let V be a variance estimator for the $\mathsf{Var}\hat{\beta}$.

2. For $r = 1, \ldots, R$
   1. (a) *Model- based resampling*
      For $i = 1, \ldots, n$
      i. set $x_i^* = x_i$
      ii. randomly sample ε_i^* from the centered modified residuals $r_1 - \overline{r}, \ldots, r_n - \overline{r}$
      iii. set $y_i^* = m(x_i^*; \hat{\mu}, \hat{\beta}) + \varepsilon_i^*$

      (b) *Resampling cases*
      i. sample $l_1^*, \ldots, l_n^*$ randomly with replacement from the index set $\{1, \ldots, n\}$
      ii. for $i = 1, \ldots, n$ set $x_i^* = x_{l_i^*}$ and $y_i^* = y_{l_i^*}$.
   2. Derive the l.s.e. $\hat{\beta}^{*(r)}$ and the variance estimator $V^{*(r)}$ based on the observations (y_i^*, x_i^*).
   3. Compute the standardized
   $$z_j^{*(r)} = \frac{\hat{\beta}_j^{*(r)} - \hat{\beta}_j}{\sqrt{V_{jj}^{*(r)}}}.$$
3. A confidence interval for the component β_j is given by
$$\left[\hat{\beta}_j - \sqrt{V_{jj}}\, z_j^{*[R(1-\alpha/2)]}, \hat{\beta}_j - \sqrt{V_{jj}}\, z_j^{*[R\alpha/2]}\right].$$

For our simulation study we took the same parameter constellation as before. As estimator for the variance we used
$$V = \frac{\sum e_i^2}{n \sum (x_i - \overline{x})^2}.$$

Again this approach was repeated M times. In the following table confidence intervals constructed by the methods above ($R = 1000,\ M = 1$) are given; in the last column you find the number of cases out of $M = 100$, where the true parameter is not covered.

Method	lower bound	upper bound	w
asymptotic normality	0.641	3.536	11
model- based resampling	0.389	3.808	9
resampling cases	0.752	4.00	7

4 The ALT model with parametric baseline distribution and nonparametric acceleration function

Now, consider an ALT model where it is not assumed that the acceleration function has a parametric form, but we wish to check whether a prespecified parametric function $\psi(\cdot;\beta)$ fits the influence of the covariates. In this section we assume that the baseline distribution is known, except a finite dimensional parameter ν. The test problem can be formulated in the following way:

$$\mathcal{H} : S \in \mathcal{A}_{\text{par}} \qquad \text{against} \qquad \mathcal{K} : S \in \mathcal{A}, \tag{2}$$

with

$$\mathcal{A}_{\text{par}} = \{S \mid S(t|x) = S_0(t\psi(x;\beta);\nu) \;\; \beta \in \mathbb{R}^d, \; \nu \in \mathbb{R}^k\}$$

and

$$\mathcal{A} = \{S \mid S(t|x) = S_0(t\psi(x);\nu) \;\; \psi \in \Psi, \; \nu \in \mathbb{R}^k\}$$

where Ψ is a nonparametric class of acceleration functions.
A possible solution for this test problem is to apply a goodness-of-fit test similar to the classical Kolmogorov test or the Cramér-von Mises test. The conditional survival function S can be estimated by a conditional empirical survival function $\hat{S}$, which is a special case of the so-called U-statistics considered by Stute (1991) and Liero (1999). Such a test would compare $\hat{S}$ with $S_0(\cdot\,\psi(\cdot;\hat{\beta});\hat{\nu})$. But this approach seems to be inadequate. Namely the alternative does not consist of "all conditional survival functions", but of functions defined by $\mathcal{A}$, and $\hat{S}$ is an estimator, which is "good for all conditional survival functions".
So we follow the regression approach: Instead of (2) we consider model (1) and the test problem

$$\mathcal{H} : m \in \mathcal{M} \qquad \text{against} \qquad \mathcal{K} : m \notin \mathcal{M},$$

where

$$\mathcal{M} = \{m \mid m(x) = m(x;\vartheta) = \mu - \log\psi(x;\beta), \; \beta \in \mathbb{R}^d, \mu \in \mathbb{R}\}.$$

Again, for simplicity we consider $d = 1$, and as test statistic we propose a L_2-type distance between a good estimator for all possible regression functions m, that is a nonparametric estimator, and a good approximation for the hypothetical $m \in \mathcal{M}$. The general form of a nonparametric estimator is the weighted average of the response variables

$$\hat{m}_n(x) = \sum_{i=1}^{n} W_{b_n i}(x, X_1, \ldots, X_n) Y_i$$

where $W_{b_n i}$ are weights depending on a smoothing parameter b_n. The hypothetical regression function can be estimated by $m(\cdot; \hat{\beta}, \hat{\mu})$, where $\hat{\beta}$ and $\hat{\mu}$ are estimators under the hypothesis. It is well-known that nonparametric estimators are biased, they are a result of smoothing. So it seems to be appropriate to compare $\hat{m}_n$ not with $m(\cdot; \hat{\beta}, \hat{\mu})$, but with the smoothed parametric estimator

$$\tilde{m}_n(x) = \sum_{i=1}^{n} W_{b_n i}(x, X_1, \ldots, X_n) m(X_i; \hat{\beta}, \hat{\mu}).$$

A suitable quantity to measure the distance between the functions $\hat{m}_n$ and $\tilde{m}_n$ is the L_2-distance

$$\begin{aligned} Q_n &= \int \Big(\hat{m}_n(x) - \tilde{m}_n(x) \Big)^2 a(x)\,\mathrm{d}x \\ &= \int \Big(\sum_{i=1}^{n} W_{b_n i}(x, X_1, \ldots, X_n)(Y_i - m(X_i; \hat{\beta}, \hat{\mu})) \Big)^2 a(x)\,\mathrm{d}x. \end{aligned}$$

Here a is a known weight function, which is introduced to control the region of integration. The limit distribution of (properly standardized) integrated squared distances is considered by several authors; we mention Collomb (1976), Liero (1992) and Härdle and Mammen (1993). Under appropriate conditions asymptotic normality can be proved.

For the presentation here let us consider kernel weights, that is m is estimated nonparametrically by

$$\hat{m}_n(x) = \frac{\sum_{i=1}^{n} K_{b_n}(x - X_i) Y_i}{\sum_{i=1}^{n} K_{b_n}(x - X_i)},$$

where $K : \mathbb{R} \to \mathbb{R}$ is the kernel function, $K_b(x) = K(x/b)/b$, and b_n is a sequence of smoothing parameters. To formulate the limit statement for Q_n let us shortly summarize the assumptions [1]:

1. Regularity conditions on kernel K and conditions on the limiting behavior of b_n.

[1] The detailed conditions can be found in Liero (1999).

2. Smoothness of the regression function m and the marginal density g of the X_i's.

3. Conditions ensuring the $\sqrt{n}$-consistency of the parameter estimators $\hat{\beta}$ and $\hat{\mu}$.

If these assumptions are satisfied we have under $\mathcal{H}$

$$nb_n^{1/2}\,(Q_n \;-\; e_n) \;\stackrel{\mathcal{D}}{\to} \mathrm{N}(0,\tau^2)$$

with

$$e_n = (nb_n)^{-1}\sigma^2 \int g^{-1}(x)\,a(x)\,\mathrm{d}x\,\kappa_1 \qquad \tau^2 = 2\sigma^4 \int g^{-2}(x)a^2(x)\,\mathrm{d}x\,\kappa_2$$

where

$$\kappa_1 \;=\; \int K^2(x)\,\mathrm{d}x \quad \text{and} \quad \kappa_2 = \int (K*K)^2(x)\,\mathrm{d}x$$

and

$$\sigma^2 \;=\; \sigma^2(\nu) \;=\; \mathsf{Var}(\log T_0).$$

On the basis of this limit theorem we can derive an asymptotic α-test: Reject the hypothesis $\mathcal{H}$ if

$$Q_n \geq (nb_n^{1/2})^{-1}\,\hat{\tau}_n\,z_\alpha \;+\; \hat{e}_n$$

where $\hat{e}_n$ and $\hat{\tau}_n$ are appropriate estimators of the unknown constants e_n and τ^2, and $z\alpha$ is the $(1-\alpha)$-quantile of the standard normal distribution. Note, that the unknown variance σ^2 depends only on the parameter ν of the underlying baseline distribution. A simple estimator is $\hat{\sigma}^2 \;=\; \sigma^2(\hat{\nu})$. The density g is assumed to be known or can be estimated by the kernel method.

To demonstrate this approach we have carried out the following **simulations**: First we simulated the behavior under $\mathcal{H}$. We generated $M = 100$ samples (t_i, x_i), $i = 1,\ldots,n$, with $t_i = t_{0i}\,\exp(x_i\beta)$, where the t_{0i}'s are values of exponentially distributed random variables with expectation ν (β and ν as before). The sample size was $n = 100$, since the application of nonparametric curve estimation always requires a large sample size. In each sample the m.l.e.'s $\hat{\beta}$ and $\hat{\nu}$ and the nonparametric kernel estimate were determined. To evaluate the nonparametric estimates we used the normal kernel and an adaptive procedure for choosing b_n. Based on these estimators Q_n was computed. As weight function a we took the indicator of the interval $[2.25, 3.75]$; so problems with the estimation at boundaries were avoided. Note, that in this case the variance σ^2 is known. It is $\sigma^2 = \frac{\pi^2}{6}$, independent of ν. Thus, in our simple simulation example it is not necessary to estimate e_n and τ. The result of the simulations was that $\mathcal{H}$ was rejected only once.

The error which occurs by approximating the distribution of the test statistic by the standard normal distribution depends not only on the sample size n but also on the smoothing parameter. Thus, it can happen, that this approximation is not good enough, even when n is large. So we considered the following resampling procedures:
Carry out the step 1 and step 2(a) described in Section 2. Then

3. based on the resampled (y_i^*, x_i), $y_i^* = \log(t_i^*)$ compute for $r = 1, \ldots, R$ the nonparametric estimates $\hat{m}_n^{*(r)}$ and the smoothed estimated hypothetical regression $\tilde{m}_n^{*(r)}$.
   (a) *Resampling* Q_n
   Evaluate the distances $Q_n^{*(1)}, Q_n^{*(2)}, \ldots, Q_n^{*(R)}$.
   (b) *Resampling* T_n
   Compute
   $$T_n^{*(r)} = n b_n^{(r)\,1/2} \left(Q_n^{*(r)} - \hat{e}_n^{*(r)}\right) / \hat{\tau}_n^{*(r)}.$$
4. From the ordered distances a critical value is given by $Q_n^{*[(1-\alpha)R]}$, and the hypothesis $\mathcal{H}$ is rejected if
   $$Q_n > Q_n^{*[(1-\alpha)R]}.$$
   Or, based on the $T_n^{*(r)}$'s we obtain: The hypothesis $\mathcal{H}$ is rejected if
   $$n b_n^{1/2} \left(Q_n - \hat{e}_n\right) / \hat{\tau}_n = T_n > T_n^{*[(1-\alpha)R]}.$$

Histograms of resampled $Q_n^{*(r)}$'s and $T_n^{*(r)}$'s for our chosen simulation parameters and $R = 1000$ are shown Figure 2. We repeated this resampling procedure also M-times. The numbers of rejections are given in the second column of the following table:

Method	Hypothesis true	Hypothesis wrong
normal distribution	1	22
resampling Q_n	5	40
resampling T_n	3	30

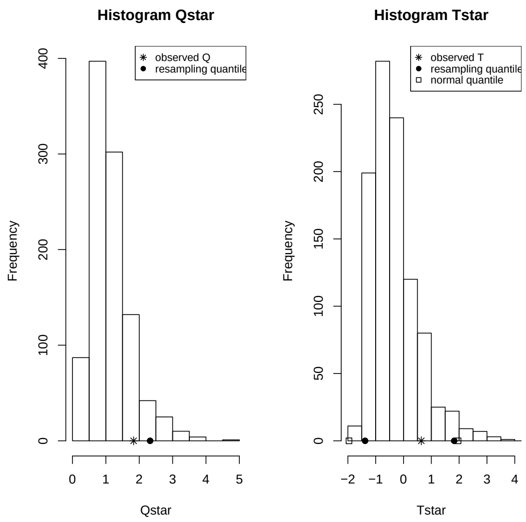


Figure 2: Resampling under $\mathcal{H}$, $R = 1000$

Furthermore, we repeated the whole approach to demonstrate the behavior under an alternative. That means, our original data (t_i, x_i) satisfy the model

$$t_i = t_{0i}\ \exp(x_i\beta\ +\ \sin(\pi * x_i/2)),$$

where the baseline times t_{0i} are as above. The numbers of rejections in this simulation are also given in table above.
Furthermore, Figure 3 shows the simulation results for one resampling procedure ($M = 1$). In the left figure you see the R resampled nonparametric estimates curve estimates (thin lines) and the $\hat{m}_n$ based on the original data (bold line). The right figure shows the same, but here the nonparametric estimates are resampled under the (wrong) hypothetical model, and the bold line is the nonparametric estimate based on the original data from the alternative model.
Note, that our simulations under the alternative are only for illustration. A further investigation of the power of these test procedures under alternatives is necessary.

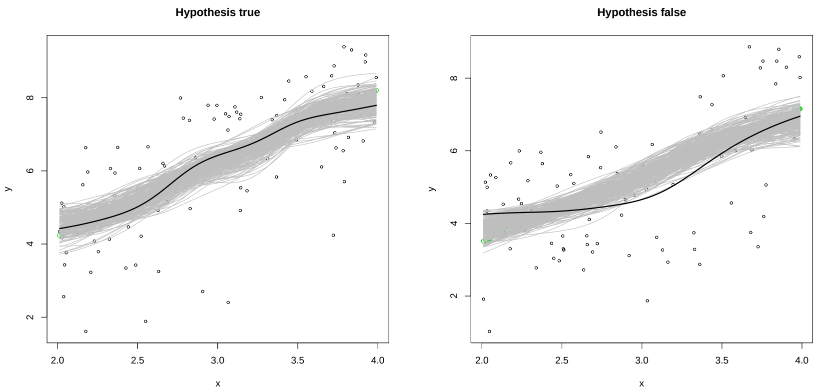


Figure 3: Resampled nonparametric regression estimates under the hypothesis and an alternative.

5 The nonparametric ALT model

Let us consider the same test problem as in the previous section, but in difference we do not suppose that the baseline distribution is parametric. Thus, the underlying model is a completely nonparametric one. The test problem has the form

$$\mathcal{H} \,:\, S \in \mathcal{C}_{\text{par}} \qquad \text{against} \qquad \mathcal{K} \,:\, S \in \mathcal{C},$$

with

$$\mathcal{C}_{\text{par}} = \{S \mid S(t|x) = S_0(t\psi(x;\beta)) \;\; \beta \in \mathbb{R}^d,\; S_0 \in \mathcal{S}\}$$

and

$$\mathcal{C} = \{S \,|\, S(t|x) = S_0(t\psi(x)) \;\; \psi \in \Psi,\; S_0 \in \mathcal{S}\},$$

where $\mathcal{S}$ is a nonparametric class of survival functions.
We will apply the same idea of testing. The only difference is, that the variance σ^2 in the standardizing terms e_n and τ^2 has to be estimated nonparametrically. Since the limit theorem gives the distribution under the hypothesis, σ^2 can be estimated by the usual variance estimator in the parametric regression model.
Furthermore, resampling methods for the determination of the empirical critical values must take into account the lack of knowledge of the underlying distribution in the hypothetical model. Thus we combine the methods described in Section 3 with those from the previous section:

1. The parameter $\vartheta = (\mu, \beta)$ is estimated by the least squares method.
2. (a) Based on the modified residuals r_i, construct R samples of pairs (y_i^*, x_i^*), $i = 1, \ldots, n$, by *model-based resampling.*
   (b) Generated R samples of pairs (y_i^*, x_i^*) by the method "*resampling cases*".
3. Use these data to construct the nonparametric estimates $\hat{m}_n^{*(r)}$ and the smoothed estimated regression $\tilde{m}_n^{*(r)}$.
4. Evaluate the distances $Q_n^{*(r)}$ and$T_n^{*(r)}$. Reject the hypothesis as described before on the basis of the ordered $Q_n^{*[r]}$ and $T_n^{*[r]}$.

Using these procedures we obtained the following numbers of rejections:

Method	Hypothesis true	Hypothesis wrong
normal distribution	2	7
model- based resampling Q_n	5	30
resampling cases Q_n	0	0
model- based resampling T_n	5	26
resampling cases T_n	6	0

The results concerning the "resampling cases" can be explained as follows: If $\mathcal{H}$ is true Q_n is small, the same holds for the resampled $Q_n^{*(r)}$'s. And under the alternative Q_n is large, and again, the same holds for the $Q_n^{*(r)}$'s. That is, with this resampling method we do not mimic the behavior under the hypothesis. Thus, this resampling method is not appropriate.
Moreover, let us compare these results with those obtained in the previous section. It turns out that the test in the completely nonparametric model distinguishes worse between hypothesis and alternative than in the model with parametric baseline distribution.
A histogram for a simulation under the alternative is given in Figure 4. Here we see that the values of the $Q_n^{*(r)}$'s are much larger for "resampling cases".

Final remark. The resampling methods presented here are only first intuitive ideas. The proposed methods were demonstrated by very simple examples, this was done to avoid computational difficulties. But, nevertheless, the results show, that resampling can be an useful tool for testing the acceleration function.

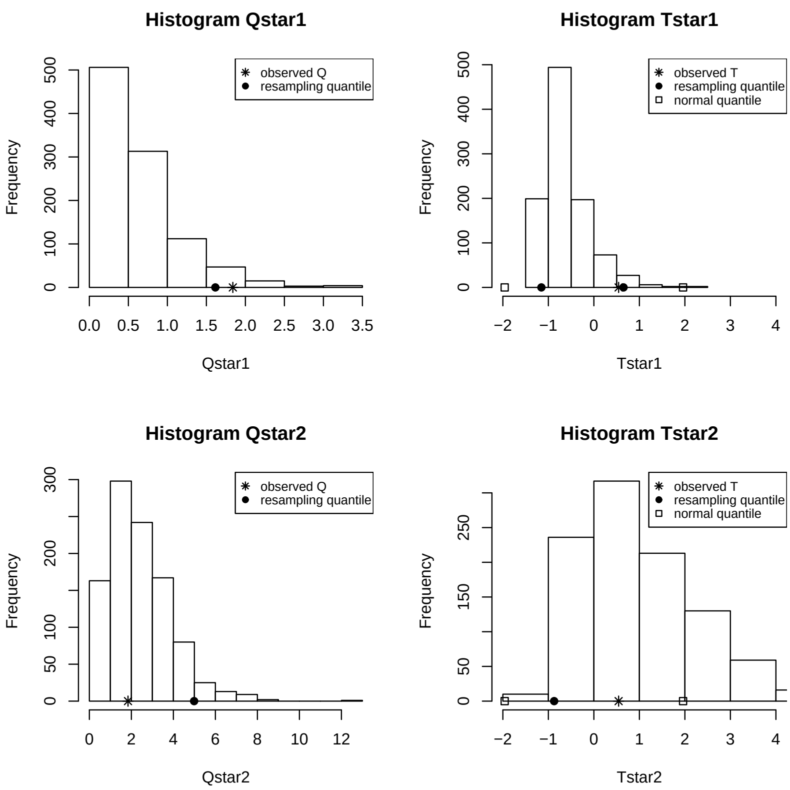


Figure 4: Histogram for simulations under the alternative. The histograms in the bottom show the results for "resampling cases".

References

1. Bagdonavičius, V. and Nikulin, M. (2001). *Accelerated Life Models*, Chapman & Hall, Boca Raton.

2. Collomb, G. (1976). Estimation non paramétrique, de la régression par la méthode du noyau, *Thèse, Université Paul Sabatier, Toulouse*,

3. Davison, A. C. and Hinkley, D. V. (1997). *Bootstrap Methods and their Application*, Cambridge University Press, Cambridge.

4. Efron, B. and Tibshirani, R. J. (1993). *An Introduction to the Bootstrap*, Chapman & Hall, Boca Raton.

5. Härdle, W. and Mammen, E. (1993). Comparing nonparametric versus parametric regression fits , *Annals of Statistics*, **21**, 1926–1947.

6. Liero, H. (1992). Asymptotic normality of a weighted integrated square error of kernel regression estimates with data-dependent bandwidth, *Journal Statistical Planning and Inference*, **30**, 307–325.

7. Liero (1999). Global Measures of Deviation of Nonparametric Curve Estimators. *Habilitationsschrift, Mathematisch- Naturwissenschaftliche Fakultät der Universität Potsdam*

8. Stute, W. (1991). Conditional U-statistics, *Annals of Probability*, **19**, 812–825.