Model Diagnostics for Censored Regression via Randomized Survival Probabilities

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Outline

Section 1

Introduction

Introduction

- Residuals in normal regression are used to assess a model's goodness-of-fit (GOF) and discover directions for improving the model. However, there is a lack of residuals with a characterized reference distribution for censored regression.
- In this paper, we propose to diagnose censored regression with a new residual called normalized randomized survival probabilities (NRSP).
- Our simulation studies show that, although the GOF tests with NRSP residuals are not as powerful as a traditional GOF test method, a non-linear test based on NRSP residuals has significantly higher power in detecting non-linearity.
- The applications to a real dataset show that the NRSP residual diagnostics successfully captures a subtle non-linear relationship in the dataset, which is not detected by the graphical diagnostics with CS residuals and existing GOF tests.

Section 2

Review of Existing Model Diagnostics Methods for Censored Regression

Cox-Snell Residuals in Absence of Censored Observations

- Suppose the survival function of T_i^* based on a postulated model is defined as $S_i(t_i^*) = P(T_i^* > t_i^*)$, where the subscript i indicates that the probability depends covariate x_i for the ith individual.
- The survival probabilities $S_i(T_i^*)$ are uniformly distributed when $S_i(\cdot)$ is the survival function of the true model for T_i^*.
- The widely used Cox-Snell (CS) residual is defined as $r_i^c(T_i^*) = -\log(S_i(T_i^*))$, where $-\log(\cdot)$ is the inverse survival function of $\exp(1)$. Therefore, CS residuals are exponentially distributed under the true model.
- One can also define normally-distributed residuals: $r_i^n(T_i^*) = \Phi^{-1}(S_i(T_i^*))$, which we call by **normalized SPs**. Then we can apply a variety of residual diagnostic methods for normal regression to diagnose $S_i(\cdot)$.

Cox-Snell Residuals in Presence of Censored Observations

- When T_i^* is right-censored, we only observe (T_i, d_i), where $T_i = \min(T_i^*, C_i), d_i = I(T_i^* < C_i)$.
- The **unmodified survival probability (USP)**, $S_i(T_i)$, is larger than $S_i(T_i^*)$ since $T_i < T_i^*$. The distribution of $S_i(T_i)$ is no longer uniformly distributed under the true model.
- The **unmodified CS residuals**, $r_i^c(T_i) = -\log(S_i(T_i))$ is a censored observation from exp(1) under the true model.
- The **normalized unmodified SPs (NUSP)**, $r_i^n(T_i)$ is a censored observation from N(0,1) under the true model.
- The most widely used diagnostic tool is to apply KM methods to $\{(r_i^c(T_i), d_i) | i = 1, \ldots, n\}$ to get an estimate of the CHF of CS residuals. Under the true model, the CHF of CS residuals is expected to be close to the 45° straight line.
- Many GOF test methods are proposed to check the distributions of censored observations. The function `gofTestCensored` in R package EnvStats provides an SF test for multiply censored data.

Modifying Residuals for Censored Observations

- Checking the distribution of residuals is only the first-line model diagnostics. The GOF test results typically cannot reveal the nature of model mis-specification, especially that related to x_i, such as non-linearity, lack of independence, non-constant variances.
- A commonly used method is to shrink the USPs of the censored failure times:

$$S_i'(T_i, d_i, \eta) = \begin{cases} S_i(T_i), & \text{if } T_i \text{ is uncensored, i.e., } d_i = 1, \\ \eta\, S_i(T_i), & \text{if } T_i \text{ is censored, i.e., } d_i = 0, \end{cases} \tag{1}$$

  where $\eta \in (0, 1)$.
- Different choices of η exist based on different arguments, eg, $1/2, 1/e$. However, their distributions under the true model are very complicated due to censoring.

Section 3

Normalized Randomized Survival Probabilities

Definition of Randomized Survival Probabilities

- The randomized survival probability (**RSP**) for T_i is defined as:

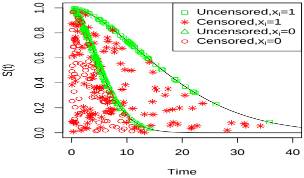
$$S_i^R(T_i, d_i, U_i) = \begin{cases} S_i(T_i), & \text{if } T_i \text{ is uncensored, i.e., } d_i = 1, \\ U_i\, S_i(T_i), & \text{if } T_i \text{ is censored, i.e., } d_i = 0, \end{cases} \tag{2}$$

  where U_i is a uniform random number on $(0, 1)$.
- We will show that the randomized SP is uniformly distributed on $(0, 1)$ given x_i under the true model. Therefore, we can transform them into residuals with any desired distribution. We prefer to transforming them with the normal quantile:

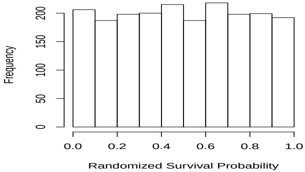
$$r_i^{\text{NRSP}}(T_i, d_i, U_i) = \Phi^{-1}(S_i^R(T_i, d_i, U_i)). \tag{3}$$

- We call the residuals in (3) by normalized randomized SP (**NRSP**) residuals.

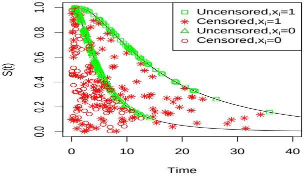
Illustration the Definition and Uniformity of RSP



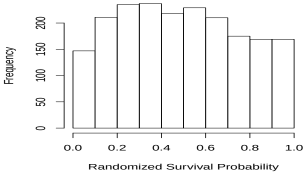
(a) **RSPs, True Model**



(b) **Hist of RSPs, True Model**



(c) **RSPs, Wrong Model**



(d) **Hist of RSPs, Wrong Model**

Figure 1: Illustration of the uniformity of RSPs.

A Upper-bound for Replicated NRSP-based Test p-values

- Suppose $p_1, \ldots, p_J$ are J replicated NRSP test p-values for a fitted model.
- A formula for bounding tail probabilities of order statistics of correlated samples gives the following inequality for the rth order statistics $p_{(r)}$:

$$P(p_{(r)} < t) \le \min\left(1, t\frac{J}{r}\right). \tag{4}$$

- Based on (4), a p-value upper bound for observed (simulated) rth statistics $p_{(r)}^{\text{obs}}$ is given by $\min\left(1, p_{(r)}^{\text{obs}}\frac{J}{r}\right)$.
- To avoid the selection of r, we report the minimal upper bound for $r = 1, \ldots, J$, denoted by $p_{\min}$:

$$p_{\min} = \min_{r=1,\ldots,J} \min\left(1, p_{(r)}^{\text{obs}}\frac{J}{r}\right). \tag{5}$$

When a model has a small $p_{\min}$, it is highly suspected that the model can be improved for better fitting the dataset.

Section 4

A Simulation Study

Data Generation

- The response variable is simulated from a Weibull AFT regression model with a non-linear link function: $\log(T_i^*) = 2 + 5\sin(2x_i) + \epsilon_i$. The covariate x_i was generated uniformly on $(0, 3\pi/2)$. The shape parameter of the Weibull distribution was set as 1.8. The censoring times C_i were generated from $\exp(\theta)$ with θ varied for obtaining different censoring rates.
- We considered fitting a Weibull AFT model assuming $\log(T_i^*) = \beta_0 + \beta_1 x_i + \epsilon_i$ as a wrong model, and fitting a Weibull AFT model assuming $\log(T_i^*) = \beta_0 + \beta_1 \sin(2x_i) + \epsilon_i$ as the true model.

Graphical Model Checking

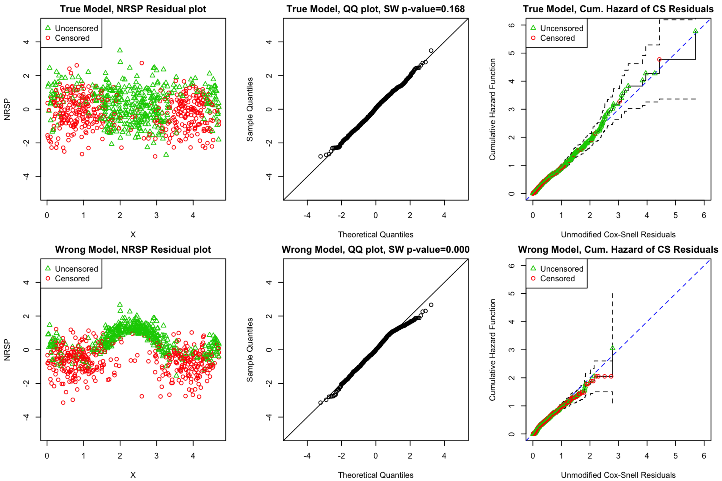


Figure 2: Performance of the NRSP residuals as a graphical tool for detecting non-linear effect in covariate. The dataset has a sample size n = 800 and a censoring rate $c \approx 50\%$.

Comparison of GOF Tests

Table 1: Comparison of the percentages of model rejections of various statistical tests. A model is rejected when the test p-value is smaller than 0.05.

		Under the true model							Under the wrong model						
n	$100c$	NRSP-SW	NRSP-SF	NUSP-CSF	NRSP-AOV	NRSP-KS	NMSP-SW	Dev-SW	NRSP-SW	NRSP-SF	NUSP-CSF	**NRSP-AOV**	NRSP-KS	NMSP-SW	Dev-SW
100	0	4.90	4.65	4.65	3.00	0.00	4.90	4.80	62.30	43.85	43.85	**100.00**	0.40	62.30	63.85
200	0	3.75	4.60	4.60	3.75	0.00	3.75	3.75	95.00	89.85	89.85	**100.00**	5.90	95.00	95.75
400	0	4.50	4.15	4.15	3.60	0.00	4.50	4.20	99.95	99.95	99.95	**100.00**	45.80	99.95	99.95
800	0	4.45	4.50	4.50	3.05	0.05	4.45	5.10	100.00	100.00	100.00	**100.00**	98.40	100.00	100.00
100	20	4.90	5.10	4.80	3.50	0.10	30.35	12.40	50.55	34.60	50.70	**100.00**	0.20	78.15	80.00
200	20	5.45	5.15	5.35	4.35	0.00	55.20	20.25	88.05	80.05	91.55	**100.00**	2.00	98.85	98.85
400	20	5.00	5.25	4.45	3.30	0.05	88.00	37.90	99.75	99.60	99.90	**100.00**	25.20	100.00	100.00
800	20	5.35	5.60	5.00	2.60	0.20	99.60	68.80	100.00	100.00	100.00	**100.00**	89.25	100.00	100.00
100	50	4.45	4.95	3.25	3.75	0.35	99.95	94.25	40.35	26.55	56.95	**100.00**	0.30	99.80	99.80
200	50	5.70	6.30	2.65	3.40	0.55	100.00	99.75	82.35	72.05	92.80	**100.00**	0.60	100.00	100.00
400	50	5.45	5.15	1.60	3.20	0.85	100.00	100.00	99.50	99.05	99.85	**100.00**	7.95	100.00	100.00
800	50	4.55	4.10	1.35	3.60	0.65	100.00	100.00	100.00	100.00	100.00	**100.00**	55.75	100.00	100.00
100	80	4.46	4.67	1.73	2.64	1.98	100.00	100.00	8.52	5.33	21.36	**92.03**	1.12	100.00	100.00
200	80	4.28	4.58	1.83	3.16	2.04	100.00	100.00	24.49	14.77	47.00	**99.90**	2.49	100.00	100.00
400	80	5.07	5.23	0.72	4.20	3.02	100.00	100.00	59.92	46.44	83.24	**100.00**	2.20	100.00	100.00
800	80	4.90	5.01	0.46	3.41	2.17	100.00	100.00	93.86	89.73	98.61	**100.00**	4.44	100.00	100.00

Section 5

A Real Data Example

A Breast Cancer Recurrent-free Dataset

- Source:
  Schumacher M, Bastert G, Bojar H, et al. Randomized 2 x 2 Trial Evaluating Hormonal Treatment and the Duration of Chemotherapy in Node-Positive Breast Cancer Patients. German Breast Cancer Study Group.. Journal of Clinical Oncology 1994; 12(10): 2086-2093. doi: 10.1200/JCO.1994.12.10.2086
- The sample size is 686. The censoring rate is 56.5%.
- The response variable of interest is the recurrence-free time, which is the time from entry to the study until a recurrence of cancer or death.
- We consider the following covariates: the tamoxifen treatment indicator, patient age, menopausal status, size and grade of the tumour, number of positive lymph nodes, progesterone and estrogen receptor status.

Graphical Checking and NRSP-based GOF Tests

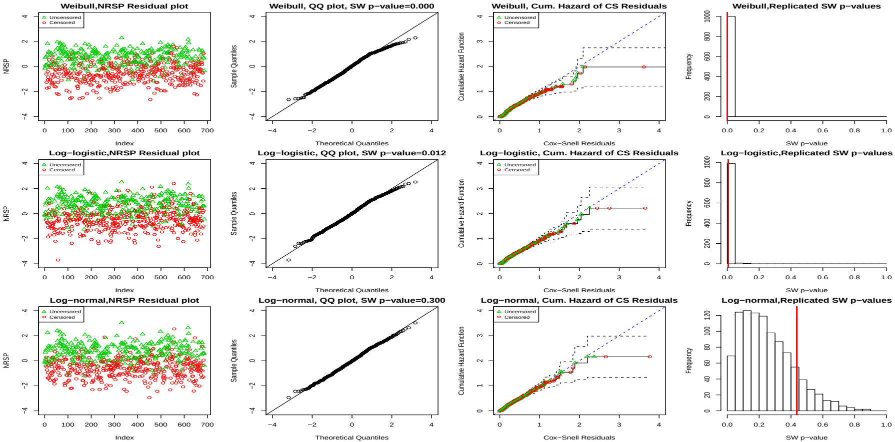


Figure 3: NRSP residuals of the Weibull, log-logistic, and log-normal AFT models fitted to the breast cancer patients dataset. The last column presents the histograms of 1000 replicated NRSP-SW p-values of each model. The vertical red lines indicate $p_{\min}$ calculated with the 1000 replicated NRSP p-values.

Table 2: Model diagnostic test p-values or $p_{\min}$ for NRSP tests and AIC values of different models for the breast cancer data. The numbers in brackets for NRSP tests are the percentages of replicated NRSP test p-values being ≤ 0.05.

Model	Weibull	log-logistic	log-normal	log-normal with log(nodes)
AIC	5181	5153	5139	5121
NUSP-CSF p-values	1.69e-5	1.94e-3	0.133	0.172
NRSP-SW $p_{\min}$	2.43e-05 (100.00)	6.01e-03 (99.00)	4.36e-01 (6.90)	5.29e-01 (5.70)
NRSP-SF $p_{\min}$	9.50e-05 (100.00)	1.52e-02 (97.00)	4.85e-01 (5.80)	6.37e-01 (3.50)
NRSP-AOV $p_{\min}$	1.97e-02 (60.40)	7.21e-02 (46.00)	**5.22e-02 (52.40)**	9.99e-01 (0.50)

Graphical Checking of Non-Linearity

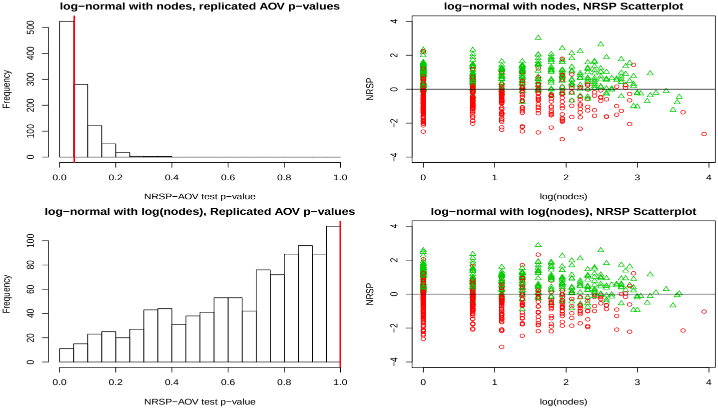


Figure 4: NRSP non-linearity residual diagnosis for the breast cancer data. The red vertical lines in the histograms of replicated NRSP-AOV p-values show the $p_{\min}$ values.

Conclusion and Future Work

- This paper has proposed using randomized survival probabilities (RSPs) to conduct model diagnostics for censored regression. NRSP residuals are approximately distributed with $N(0,1)$ under the true model. With this unified reference distribution for NRSP residuals, we can conduct a wide variety of residual diagnostics for censored regression.
- Our simulation studies show that a non-linearity test with NRSP residuals has significantly higher power in detecting non-linearity than existing GOF tests. The real data analysis shows that the NRSP residual diagnostics successfully captures a subtle non-linear relationship in the dataset.
- We expect that many other specific model mis-specification tests that target a particular model discrepancy have higher powers than GOF tests. For example, statistical tests for checking proportional hazard assumption in Cox regression seem to be demanded very often.

References

- These slides are extracted from this paper: Li, L., Wu, T., Feng, C., 2021. Model Diagnostics for Censored Regression via Randomized Survival Probabilities. Statistics in Medicine 40, 14821497. https://doi.org/10.1002/sim.8852
- A link to the published version is available from my website: `https://math.usask.ca/~longhai/`.
- R functions for computing NRSP residuals for `survreg` and `coxph` objects are also available on my website.