Inference with Recurrent Event Data

by

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Basic Data Accrual

- A reliability or engineering unit, or a biomedical subject.

- A recurrent event (such as stoppages of nuclear power plants, warranty claims for products, bouts with migraine headaches, recurrence of a tumor) is monitored for this unit over a random observation period $[0, \tau]$.

- $\tau$ has distribution $G(\cdot)$.

- $T_1, T_2, \ldots$ are the inter-occurrence times of the event, which are assumed to be IID from a distribution $F(\cdot)$.

- $S_1, S_2, \ldots$ are the calendar times of event occurrences, so $S_k = \sum_{j=1}^{k} S_j$.

- $K = \max\{k : S_k \leq \tau\}$ = # of observed event occurrences in $[0, \tau]$.

- Observable Vector: $D = (K, T_1, T_2, \ldots, T_K, \tau - S_K)$

- Example: $\tau = 18$ and $T_1 = 5, T_2 = 2, T_3 = 6, T_4 = 1, T_5 = 5$. Thus, $S_1 = 5, S_2 = 7, S_3 = 13, S_4 = 14, \tau - S_4 = 4$ and $K = 4$. 

![Calendar Time Graph](calendar_time_graph.png)
“Points to Ponder”

- $K$ is informative about $F$.

- $T_{K+1}$ is right-censored by $\tau - S_K$.

- Censoring mechanism is informative and dependent.

- Inter-occurrence time that gets censored tends to be larger (selection bias).

**Problems Considered**

- Suppose $n$ units/subjects are available, with the $i$th unit observed over the period $[0, \tau_i]$.

- $\tau_1, \tau_2, \ldots, \tau_n$ are IID from $G$.

- $T_{i1}, T_{i2}, \ldots$ are IID $F$, $i = 1, 2, \ldots, n$.

- $S_{i1}, S_{i2}, \ldots$ are the calendar times of event occurrences.

- $K_i = \max\{k : S_{ik} \leq \tau_i\}$.
- Observables:

<table>
<thead>
<tr>
<th>Unit #</th>
<th>Vector of Observables</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$D_1 = (K_1, T_{11}, T_{12}, \ldots, T_{1K_1}, \tau_1 - S_{1K_1})$</td>
</tr>
<tr>
<td>2</td>
<td>$D_2 = (K_2, T_{21}, T_{22}, \ldots, T_{2K_1}, \tau_2 - S_{2K_2})$</td>
</tr>
<tr>
<td>\vdots</td>
<td>\vdots</td>
</tr>
<tr>
<td>$n$</td>
<td>$D_n = (K_n, T_{n1}, T_{n2}, \ldots, T_{nK_n}, \tau_n - S_{nK_n})$</td>
</tr>
</tbody>
</table>

- Given this data, how to estimate nonparametrically the event interoccurrence distribution $F$?

- Properties of the estimator?

- Comparison with existing estimator, for example with the Wang and Chang (JASA, 1999) estimator?

- Given this data, how do we perform goodness-of-fit tests?
Existing Approaches

- Consider the first, possibly right-censored, observation and use PLE.
- Ignore the right-censored last observation and use EDF.
- Wang and Chang (1999, JASA) proposed a PLE-type estimator.
- Aalen and Husebye’s (1991) variance component model
  \[ g(T_{ij}) = \mu + U_i + E_{ij}, \]
  and an intensity-based model incorporating a frailty component.
- Gill (80): very general paper dealing with a Markov renewal process.
- Vardi (82): an algorithm for the MLE when \( T_{ij} \)’s are arithmetic and the process starts at its stationary distribution.
- Sellke (88): nonparametric estimator for a single renewal process observed for a long time.
- Soon and Woodroofe (97): extended Vardi’s results.
Theoretical Developments

**Relevant Processes**

- Hazard rate function: \( \lambda(\cdot) = f(\cdot)/F(\cdot) \).

- Cumulative hazard function: \( \Lambda(\cdot) = \int_0^\Lambda \lambda(w)dw \).

- **Calendar-time** processes

  \[
  N_i^\dagger(s) = \sum_{j=1}^{\infty} I\{S_{ij} \leq s; S_{ij} \leq \tau_i\} = \# \text{ of events in } [0, s] \text{ for subj } i; \\
  Y_i^\dagger(s) = I\{\tau_i \geq s\} = \text{at-risk indicator for subj } i; \\
  \mathcal{F}_s^\dagger = \text{event history up to calendar-time } s.
  \]

- \( A_i^\dagger(s) = \int_0^s Y_i^\dagger(v)\lambda \left(v - S_{iN_i^\dagger(v-)}\right)dv, \quad i = 1, \ldots, n, \)

- \( M^\dagger(s) = (M_1^\dagger(s), \ldots, M_n^\dagger(s)) \) with \( M_i^\dagger(s) = N_i^\dagger(s) - A_i^\dagger(s) \) is a vector of square-integrable martingales with predictable covariance processes

  \[
  \langle M_i^\dagger, M_{i'}^\dagger \rangle(s) = \begin{cases} 
  A_i(s) & \text{if } i = i' \\
  0 & \text{if } i \neq i'
  \end{cases}
  \]

- **Calendar-Duration Space** Processes: Define

  \[
  Z_i(s, t) = I\{s - S_{iN_i^\dagger(s-)} \leq t\}.
  \]

  Indicates whether \( i \)th subject at calendar time \( s \) has been event-free for up to time \( t \) since last event occurrence.

- \( Z_i(\cdot, t) \) is a bounded predictable process, nonincreasing in

  \[
  s \in [S_{iN_i^\dagger(s-)}, S_{iN_i^\dagger(s-)+1}),
  \]

  for fixed \( t \), and nondecreasing in \( t \) for fixed \( s \).
Figure 1: Picture of data \((K, T_1, T_2, T_3, T_4, \tau - S_4) = (4, 5, 2, 6, 1, 4)\). Inner horizontal lines: \(t = 1.75, 4.5\). Inner vertical lines: \(s = 4.5, 15\).

- From graph:

\[
Z_1(4.5, 1.75) = 0 \quad \text{and} \quad Z_1(4.5, 4.5) = 1;
\]

\[
Z_1(15, 1.75) = 1 \quad \text{and} \quad Z_1(15, 4.5) = 1.
\]

- Define the processes:

\[
\text{\(N_i(s, t) = \int_0^s Z_i(v, t)N_i^\dagger(dv)\)}
\]

\[
\text{\(A_i(s, t) = \int_0^s Z_i(v, t)A_i^\dagger(dv)\)}
\]

\[
\text{\(M_i(s, t) = \int_0^s Z_i(v, t)M_i^\dagger(dv) = N_i(s, t) - A_i(s, t)\)}
\]

\[
\text{\(Y_i(s, t) = \sum_{j=1}^{N_i^\dagger(s-)} I\{T_{ij} \geq t\} + I\{(s \land \tau_i) - S_{iN_i^\dagger(s-)} \geq t\}\)}
\]

- \(N_i(s, t)\): \# of events in \([0, s]\) with gap times at most \(t\).

- \(Y_i(s, t)\): \# of events in \([0, s]\) with gap times at least \(t\).  

• For data in Figure 1:

\[ N_1(4.5, 1.75) = 0 \quad \text{and} \quad Y_1(4.5, 1.75) = 1; \]
\[ N_1(4.5, 4.5) = 0 \quad \text{and} \quad Y_1(4.5, 4.5) = 1; \]
\[ N_1(15, 1.75) = 1 \quad \text{and} \quad Y_1(15, 1.75) = 3; \]
\[ N_1(15, 4.5) = 2 \quad \text{and} \quad Y_1(15, 4.5) = 2. \]

• Aggregated processes:

\[ N(s, t) = \sum_{i=1}^{n} N_i(s, t); \]
\[ A(s, t) = \sum_{i=1}^{n} A_i(s, t); \]
\[ M(s, t) = \sum_{i=1}^{n} M_i(s, t). \]
**Intermediate Results**

- **Change-of-Integration Formulas**

  - Identity #1:
    \[
    A(s, t) = \sum_{i=1}^{n} \int_{0}^{s} Z_i(v, t) A_i^t(dv) = \int_{0}^{t} Y(s, w)\lambda(w)dw
    \]

  - Identity #2: For a predictable process \( H_i(s, t) \),
    \[
    \int_{0}^{s} H_i(s, v - S_{iN_i(v-1)}) M_i(dv, t) = \int_{0}^{t} H_i(s, w) M_i(s, dw)
    \]

- **Important Properties:**

  - Property #1: For fixed \( t \), \( M(\cdot, t) \) is a square-integrable martingale with predictable quadratic variation process
    \[
    \langle M(\cdot, t), M(\cdot, t) \rangle(s) = \int_{0}^{t} Y(s, w)\lambda(w)dw.
    \]

  - Property #2: With
    \[
    G_s(w) = \begin{cases} 
    G(w) & \text{if } w < s \\
    1 & \text{if } w \geq s
    \end{cases},
    \]
    \[
    E\{Y_1(s, t)\} = y(s, t) \equiv \bar{F}(t) \left\{ \bar{G}_s(t-) + \int_{[t, \infty)} R(w - t)dG_s(w) \right\},
    \]
    where
    \[
    R(t) = \sum_{j=1}^{\infty} F^{\ast j}(t) = \text{renewal function of } F;
    \]
    \[
    F^{\ast j} = j\text{th convolution.}
    \]
A Weak Convergence Theorem

Fix \( s \in (0, \infty) \) and suppose for \( t, t_1, t_2 \in [0, t^*] \) where \( t^* \in (0, \infty) \):

(a) \( \{H_i(v, w) : 0 \leq v \leq s, 0 \leq w \leq t^*\} \) are left-continuous in \((v, w)\); and there is a deterministic function \( h(v, w) \) on \([0, s] \times [0, t^*] \), continuous in \((v, w)\) and bounded, with

\[
\max_{1 \leq i \leq n} \sup_{0 \leq w \leq t^*} |H_i(s, w) - h(s, w)| \xrightarrow{pr} 0;
\]

(b) For all \( s \in (0, \infty) \), \( \inf_{w \in [0, t^*]} y(s, w) > 0 \);

(c) Matrix functions

\[
V^{(n)}(s, t) = \frac{1}{n} \sum_{i=1}^{n} \int_{0}^{t} H_i(s, w) \otimes^2 Y_i(s, w) \lambda(w)dw;
\]

\[
\Sigma(s, t) = \int_{0}^{t} h(s, w) \otimes^2 y(s, w) \lambda(w)dw,
\]

satisfies for each \( t_1, t_2 \in (0, t^*) \) with \( t_1 < t_2 \),

\[
0 < \det\{\Sigma(s, t_2) - \Sigma(s, t_1)\} < \infty \quad \text{and} \quad \|V^{(n)}(s, t) - \Sigma(s, t)\| \xrightarrow{pr} 0.
\]

Then, the integral transforms,

\[
\left\{ W^{(n)}(s, t) = \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \int_{0}^{t} H_i^{(n)}(s, w) dM_i^{(n)}(s, dw) : t \in [0, t^*] \right\}
\]

converges weakly to a zero-mean Gaussian process \( \{W^{(\infty)}(s, t) : t \in [0, t^*]\} \) with covariance matrix function

\[
\text{Cov} \{W^{(\infty)}(s, t_1), W^{(\infty)}(s, t_2)\} = \begin{bmatrix}
\Sigma(s, t_1) & \Sigma(s, t_1) \\
\Sigma(s, t_1) & \Sigma(s, t_2)
\end{bmatrix}, \quad \text{for} \quad t_1 \leq t_2.
\]
Nonparametric Estimation of $\Lambda$ and $F$

**Estimating $\Lambda$**

- For fixed $t$,
  \[
  \left\{ M(v,t) = N(v,t) - \int_0^t Y(v,w) \, d\Lambda(w) : \ 0 \leq v \leq s \right\}
  \]
  is a square-integrable martingale.

- Let $J(v,w) = I\{Y(v,w) > 0\}$.

- Then
  \[
  \int_0^t \frac{J(s,w)}{Y(s,w)} M(s,dw) = \int_0^t \frac{J(s,w)}{Y(s,w)} N(s,dw) - \int_0^t J(s,w) \, d\Lambda(w).
  \]

- By change-of-integration identity,
  \[
  \int_0^t \frac{J(s,w)}{Y(s,w)} M(s,dw) = \sum_{i=1}^n \int_0^s \frac{J(s,v - S_i N_i(v-))}{Y(s,v - S_i N_i(v-))} M_i(dv,t).
  \]

- By stochastic integration theory,
  \[
  \left\{ \sum_{i=1}^n \int_0^s \frac{J(s,v - S_i N_i(v-))}{Y(s,v - S_i N_i(v-))} M_i(dv,t) : 0 \leq s < \infty \right\}
  \]
  is a square-integrable zero-mean martingale.

- Consequently,
  \[
  \mathbb{E} \left\{ \int_0^t \frac{J(s,w)}{Y(s,w)} N(s,dw) \right\} = \mathbb{E} \left\{ \int_0^t J(s,w) \, d\Lambda(w) \right\}.
  \]

- Method-of-moments estimator of $\Lambda(t)$:
  \[
  \hat{\Lambda}(s,t) = \int_0^t \frac{J(s,w)}{Y(s,w)} N(s,dw) = \int_0^t \frac{N(s,dw)}{Y(s,w)}, \quad 0 \leq t < \infty.
  \]
Estimating $\tilde{F}$

- Product-integral representation of $\tilde{F}(t)$: $\tilde{F}(t) = \prod_{w \leq t} [1 - \Lambda(dw)].$

- Substitution principle: Generalized PLE of $\tilde{F}(t)$ is
  
  $$\hat{F}(s, t) = \prod_{w \leq t} [1 - \hat{\Lambda}(s, dw)] = \prod_{w \leq t} \left[1 - \frac{N(s, \Delta w)}{Y(s, w)} \right].$$

- Case where $s \to \infty$ and under fixed (Type I) censoring considered by Gill (1980, 1981).

Asymptotic Properties

- **Generalized NAE:** If $s \in (0, \infty)$ and $t^* \in (0, \infty)$ such that $y(s, t^*) > 0$ and if $\Lambda(t^*) < \infty$, then

  $$\{V(s, t) = \sqrt{n}[\hat{\Lambda}(s, t) - \Lambda(t)] : t \in [0, t^*]\} \Rightarrow \{V^{\infty}(s, t) : t \in [0, t^*]\},$$

  a zero-mean Gaussian process with covariance function

  $$\text{Cov}\{V^{\infty}(s, t_1), V^{\infty}(s, t_2)\} = d[s, \min(t_1, t_2)]$$

  $$d(s, t) = \int_0^t \frac{\Lambda(dw)}{y(s, w)},$$

  $$y(s, t) \equiv \tilde{F}(t) \left\{ \hat{G}_s(t) - \int_{[t, \infty)} R(w - t) d\hat{G}_s(w) \right\}.$$  

- **Generalized PLE:** Under same conditions,

  $$\{W(s, t) = \sqrt{n}[\hat{F}(s, t) - \tilde{F}(t)] : t \in [0, t^*]\} \Rightarrow \{W^{\infty}(s, t) : t \in [0, t^*]\},$$

  a zero-mean Gaussian process with covariance function

  $$\text{Cov}[W^{\infty}(s, t_1), W^{\infty}(s, t_2)] = \tilde{F}(t_1)\tilde{F}(t_2)d[s, \min(t_1, t_2)].$$
“A Sense of Closure”

Complete Data

- $T_1, T_2, \ldots, T_n$ IID positive with continuous SF $\bar{F}(t) = P\{T > t\}$.

- EDF of $\bar{F}$:
  \[
  \hat{F}(t) = \frac{1}{n} \sum_{i=1}^{n} I\{T_i > t\}.
  \]

- Asymptotics:
  \[
  \sqrt{n} \left[ \hat{\bar{F}} - \bar{F} \right] \Rightarrow W_1
  \]

  $W_1$ a zero-mean Gaussian process with variance function
  \[
  v_1(t) = \frac{\bar{F}(t) \cdot F(t)}{\bar{F}^2(t)} = \frac{\bar{F}(t)}{\bar{F}(t)} \int_0^t \frac{d\Lambda(w)}{F(w)}.
  \]

Right-Censored Data

- Setting:
  
  Failure Times: $T_1, T_2, \ldots, T_n$ IID $\bar{F}(t) = P\{T > t\}$
  
  Censoring Times: $C_1, C_2, \ldots, C_n$ IID $\bar{G}(t) = P\{C > t\}$

- Right-Censored Data:
  
  $(Z_1, \delta_1), (Z_2, \delta_2), \ldots, (Z_n, \delta_n)$

  \[
  Z_i = \min\{T_i, C_i\} \quad \text{and} \quad \delta_i = I\{T_i \leq C_i\}.
  \]

- PLE of $\bar{F}$:
  \[
  \hat{F}(t) = \prod_{\{i: Z(i) \leq t\}} \left[ 1 - \frac{1}{n(i)} \right]^{\delta(i)}
  \]
$Z(1) < Z(2) < \ldots < Z(n)$ the ordered values of the $Z_i$'s, and $\delta(i)$'s are the associated $\delta_i$'s; and

\[ n(i) = \sum_{j=1}^{n} I\{Z_j \geq Z(i)\} = \# \text{ at risk at } Z(i). \]

- **Asymptotics:**
  \[
  \sqrt{n} \left[ \frac{\hat{F} - F}{\sqrt{n}} \right] \Rightarrow W_2
  \]

  $W_2$ a zero-mean Gaussian process with variance function

  \[
  v_2(t) = \bar{F}(t)^2 \int_0^t \frac{d\Lambda(w)}{\bar{F}(w)\bar{G}(w)}. \]

- $v_2(t)$ reduces to $v_1(t)$ when $\bar{G}(w) = 1$.

**Recurrent Data Setting**

- **Generalized PLE of $\bar{F}$ (no tied values):**
  \[
  \hat{F}(t) = \prod_{i=1}^{n} \left( \prod_{j} \left\{ \begin{array}{l}
  T_{ij} \leq t \\
  S_{ij} \leq \tau_i 
  \end{array} \right. \right) \left[ 1 - \frac{1}{Y(T_{ij})} \right]
  \]

  where

  \[
  Y(t) = \sum_{i=1}^{n} \left\{ \sum_{j=1}^{K_i} I\{T_{ij} \geq t\} + I\{\tau_i - S_{ik} \geq t\} \right\}.
  \]

- **Asymptotics:**
  \[
  \sqrt{n} \left[ \frac{\hat{F} - F}{\sqrt{n}} \right] \Rightarrow W_3,
  \]

  a zero-mean Gaussian process with variance function

  \[
  v_3(t) = \bar{F}(t)^2 \int_0^t \frac{d\Lambda(w)}{\bar{F}(w)\bar{G}(w)} \left\{ 1 + \frac{1}{\bar{G}(w)} \int_0^\infty R(u-w) \mathrm{d}G(u) \right\}.
  \]
\[ R(t) = \sum_{j=1}^{\infty} F^*(t) = \text{renewal function of } F; \]

\[ F^* = j\text{th convolution of } F, j = 1, 2, \ldots. \]

- Effect in variance of sum-quota accrual scheme:

\[ \left\{ 1 + \frac{1}{G(w)} \int_{w}^{\infty} R(u-w)dG(u) \right\}^{-1}. \]

- **An Approximation:** For large \( t \), \( R(t) \approx \frac{t}{\mu_F} \) where \( \mu_F \) is the mean of \( F \). So,

\[ v_3(t) = \bar{F}(t)^2 \int_0^t \frac{d\Lambda(w)}{F(w)G(w)} \{1 + (\mu_F)^{-1}\mu_G(w)\}, \]

with

\[ \mu_G(w) = \mathbb{E}\{\tau - w|\tau \geq w\} \]

\[ = \text{MRL of } \tau \text{ given } \tau \geq w. \]
A Concrete Example

• Assume: \( F = \text{EXP}(\theta), G = \text{EXP}(\eta) \).

• Then: \( v_3(t) = \left( \frac{\eta}{\theta + \eta} \right) v_2(t) \).

• Therefore, if \( \frac{1}{\theta} \ll \frac{1}{\eta} \), a considerable gain in efficiency accrues by using all the data compared to just using the first, possibly right-censored, observation.

• Furthermore,

\[
d(s, t) = I\{t \leq s\} \times \theta \int_0^t \frac{\exp\{(\theta + \eta)w\}}{1 + \frac{\theta}{\eta} [1 - \exp\{-\eta(s-w)\} - \eta(s-w) \exp\{-\eta(s-w)\}]} \, dw.
\]

• If \( s \to \infty \):

\[
d(\infty, t) = \frac{\theta \eta}{(\theta + \eta)^2} \{\exp\{\theta + \eta\}t\} - 1 \}.
\]

• Thus:

\[
\text{Avar} \left( \sqrt{n} \hat{F}(\infty, t) \right) = \frac{\theta \eta}{(\theta + \eta)^2} \times \exp\{-\theta + \eta\}t [1 - \exp\{-\theta + \eta\}t].
\]

• How adequate are these asymptotic results for moderate sample sizes?

• Results of simulation under the exponential model follow.
<table>
<thead>
<tr>
<th>$t$ ((\hat{F}(t)))</th>
<th>Simulated Property of the Sampling Distribution</th>
<th>Sample Size ((n))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>Mean</td>
<td>.0163</td>
<td>.0053</td>
</tr>
<tr>
<td>Std. Error</td>
<td>.2340 ((.2250))</td>
<td>.2361 ((.2250))</td>
</tr>
<tr>
<td>(Theoretical)</td>
<td></td>
<td>.2274 ((.2250))</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histogram</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>.0329</td>
<td>.0138</td>
</tr>
<tr>
<td>Std. Error</td>
<td>.2818 ((.2681))</td>
<td>.2723 ((.2681))</td>
</tr>
<tr>
<td>(Theoretical)</td>
<td>.2697 ((.2681))</td>
<td></td>
</tr>
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<tr>
<td>Histogram</td>
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</tr>
<tr>
<td>Mean</td>
<td>.0330</td>
<td>.0158</td>
</tr>
<tr>
<td>Std. Error</td>
<td>.2790 ((.2442))</td>
<td>.2549 ((.2442))</td>
</tr>
<tr>
<td>(Theoretical)</td>
<td>.2469 ((.2442))</td>
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<tr>
<td>Mean</td>
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<td>.0123</td>
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<tr>
<td>Std. Error</td>
<td>.2007 ((.1578))</td>
<td>.1738 ((.1578))</td>
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<tr>
<td>(Theoretical)</td>
<td>.1668 ((.1578))</td>
<td></td>
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</tr>
<tr>
<td>Histogram</td>
<td></td>
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</tr>
</tbody>
</table>

Table 1: Simulated properties of $\sqrt{n}[\hat{F}(\infty, t) - \hat{F}(t)]$ under exponential model with $\theta = 3$ and $\eta = 1$. 
Comparison with Wang and Chang Estimator

- Wang and Chang Estimator (JASA, 1999) of $\hat{F}$:

\[
K^*_i = \begin{cases} 
1 & \text{if } K_i = 0 \\
K_i & \text{if } K_i > 0
\end{cases}
\]

\[
d^*(t) = \sum_{i=1}^{n} \left\{ \frac{I\{K_i > 0\}}{K^*_i} \sum_{j=1}^{K_i} I\{T_{ij} = t\} \right\}
\]

\[
R^*(t) = \sum_{i=1}^{n} \frac{1}{K^*_i} \left[ \sum_{j=1}^{K_i} I\{T_{ij} \geq t\} + I\{\tau_i - S_{iK_i} \geq t\} I\{K_i = 0\} \right]
\]

\[
\hat{S}(t) = \prod_{i=1}^{n} \prod_{j: T_{ij} \leq t} \left[ 1 - \frac{d^*(T_{ij})}{R^*(T_{ij})} \right]
\]

- Estimator developed for a model with correlated data; so comparison a bit unfair to their estimator.

- Simulated comparison of $\hat{S}(t)$ and $\hat{F}(\infty, t)$ for the exponential model.

- Simulated biases and root-mean-square errors (RMSE) obtained for several time points.

- Results of the simulation presented in Figure 2.
<table>
<thead>
<tr>
<th>((n, \theta, \eta))</th>
<th>Simulated Biases</th>
<th>Simulated RMSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>((10, 3, 1))</td>
<td><img src="image1" alt="Simulated Biases" /></td>
<td><img src="image2" alt="Simulated RMSE" /></td>
</tr>
<tr>
<td>((10, 3, 3))</td>
<td><img src="image3" alt="Simulated Biases" /></td>
<td><img src="image4" alt="Simulated RMSE" /></td>
</tr>
<tr>
<td>((30, 3, 1))</td>
<td><img src="image5" alt="Simulated Biases" /></td>
<td><img src="image6" alt="Simulated RMSE" /></td>
</tr>
</tbody>
</table>

Figure 2: Simulated biases and root-mean-squared errors of the estimator \(\hat{F}(\infty, t)\) (SOLID) and the WC estimator.
Application to a Real Data


- Consecutive migrating motor complex (MMC) periods for 19 healthy subjects (15 men and 4 women).

<table>
<thead>
<tr>
<th>Unit #</th>
<th># of Complete Obs.</th>
<th>Complete Observed Periods</th>
<th>Censored Obs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i)</td>
<td>(#)</td>
<td>((T_{ij}) ’s)</td>
<td>((\tau_i - S_{ik_i}))</td>
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<tr>
<td>1</td>
<td>8</td>
<td>112 145 39 52 21 34 33 51</td>
<td>54</td>
</tr>
<tr>
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<td>2</td>
<td>206 147</td>
<td>30</td>
</tr>
<tr>
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<td>3</td>
<td>284 59 186</td>
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</tr>
<tr>
<td>4</td>
<td>3</td>
<td>94 98 84</td>
<td>87</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>67</td>
<td>131</td>
</tr>
<tr>
<td>6</td>
<td>9</td>
<td>124 34 87 75 43 38 58 142 75</td>
<td>23</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>116 71 83 68 125</td>
<td>111</td>
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<tr>
<td>8</td>
<td>4</td>
<td>111 59 47 95</td>
<td>110</td>
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<td>98 161 154 55</td>
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<tr>
<td>19</td>
<td>5</td>
<td>147 134 78 66 100</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 2: Gastroenterology data set from Aalen and Husebye (1991) consisting of the migrating motor complex (MMC) periods (in minutes) for 19 individuals.

- Estimate of the mean MMC period is: 104 minutes (s.e. = 5.87 minutes); while from Aalen and Husebye’s variance component model, they obtained the mean estimate of 106.8 minutes (s.e. = 6.9 minutes).
Figure 3: Graph of the estimate of the MMC period survival function together with its asymptotic 95% pointwise confidence interval.

Figure 4: Graphs of the generalized PLE (solid line) and the Wang and Chang PLE (dashed line) for the MMC Data.
Related Problems

- **Goodness-of-Fit Problem**: $F = F_0$? (the simple case), or $F \in \{F(\cdot; \theta) : \theta \in \Theta\}$? (the composite case). The idea introduced in Peña (1998) and Agustín and Peña (2000) for hazard-based smooth goodness-of-fit tests apply to this situation. Still being worked out!

- Frailty or random mixing component in the model.

- Model validation and generalized residuals?

- Testing that the renewal assumption is valid.