

Nonparametric computation of survival functions in the presence of interval censoring

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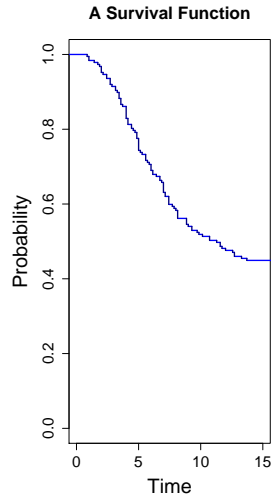
Research Aims

- Create a robust algorithm for solving the NPMLE problem
- One that is fastest in all circumstances

Adaptive Constrained Newton Method (ACNM)

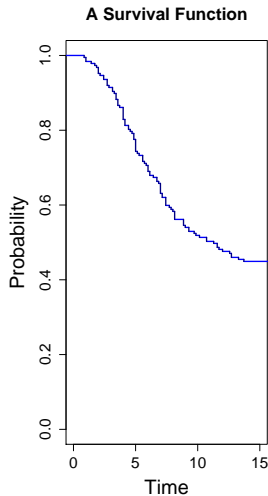
Survival Analysis

- Time to event data



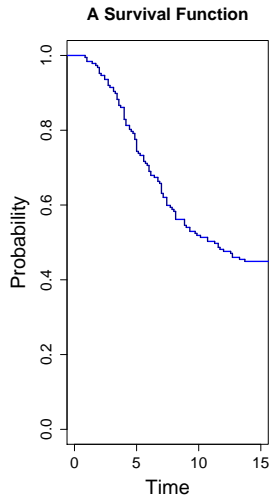
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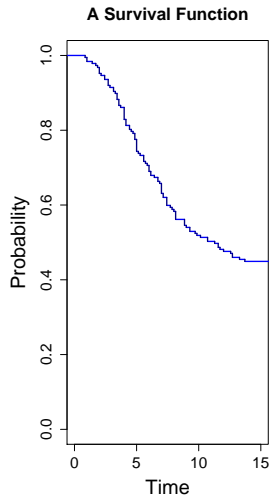
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- Example: Time to healing



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- Example: end of study or “lost to followup”

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- Call these intervals O_i for $i = 1, \dots, n$

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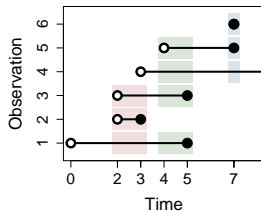
Why Nonparametric?

- Let the data speak for itself
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- Maximise the likelihood
- Explore the data before choosing a parametric model

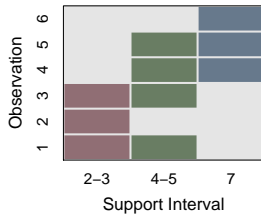
The NPMLE Survival Function with Interval Censored Data

- Partition the positive real line

Example Censor Intervals



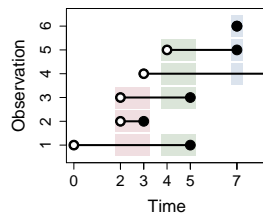
Clique Matrix



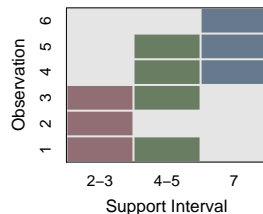
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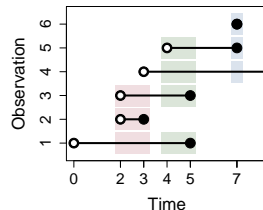
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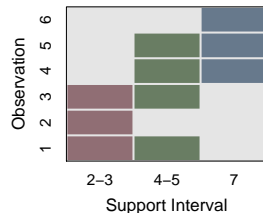
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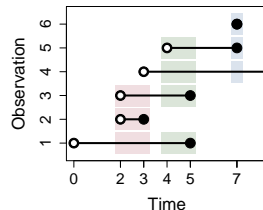
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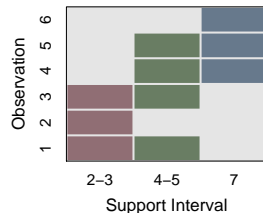
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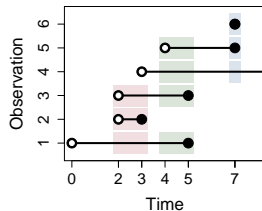
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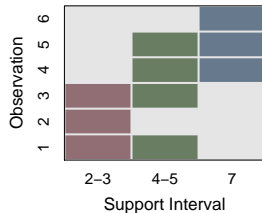
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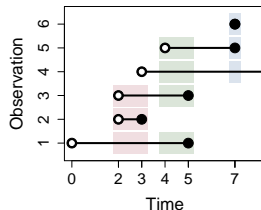
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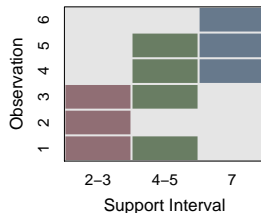
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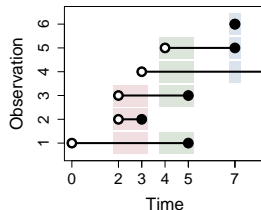
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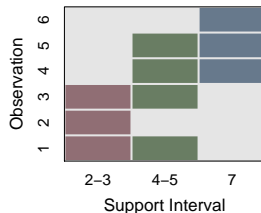
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- NPMLE assigns probability mass to each support interval

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- Subject to: $\hat{\mathbf{p}} \geq \mathbf{0}$ and $\hat{\mathbf{p}}^T \mathbf{1} = 1$

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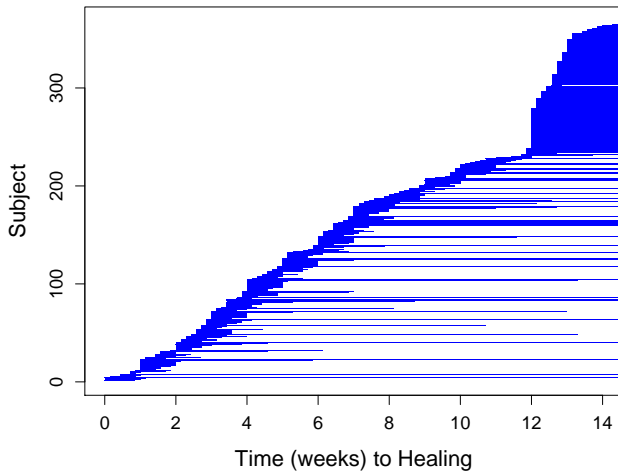
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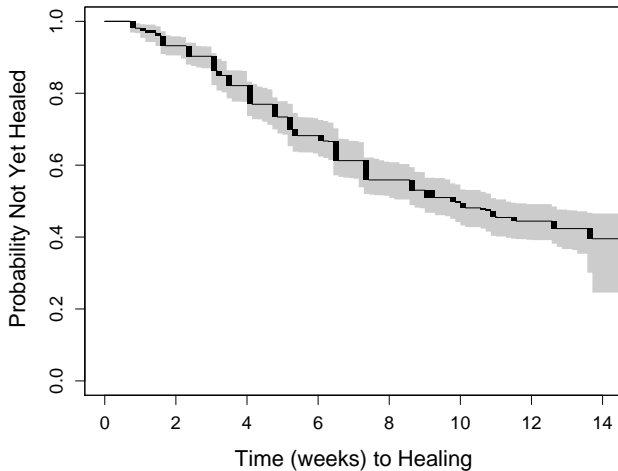
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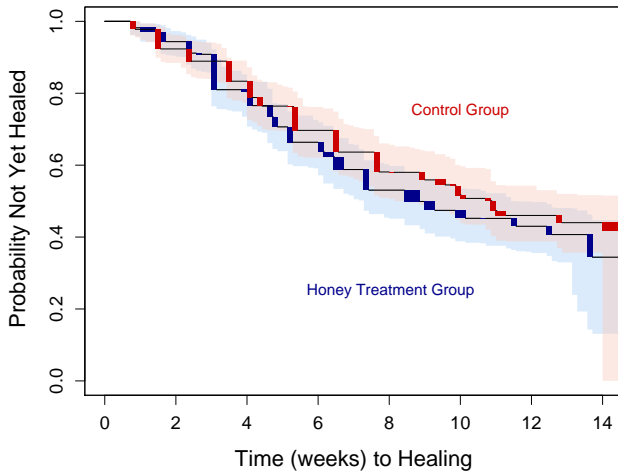
Censor Intervals for each Participant



NPMLE Survival Function with 95% Bootstrap ranges



NPMLE Survival Functions with 95% Bootstrap ranges



Existing Algorithms for finding the NPMLE

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 - Constrained Newton Method
 - Dimension-reduced approach to improve any algorithm

Times to compute the NPMLE survival function for 100 Bootstrap samples of the HALT data using:

- EMICM, PGM and VEM from the lcms package
- Methods SBN(DR) and EMICM(DR) from Wang (2008)
- The new ACNM algorithm (and CNM)

	Time (s)
EMICM	113.03
PGM	791.00
VEM	610.42
SBN(DR)	14.34
EMICM(DR)	26.93
ACNM	9.41

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- Best choice depends on size of dataset and proportion of exact observations

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- Can be slow in cases with many exact observations

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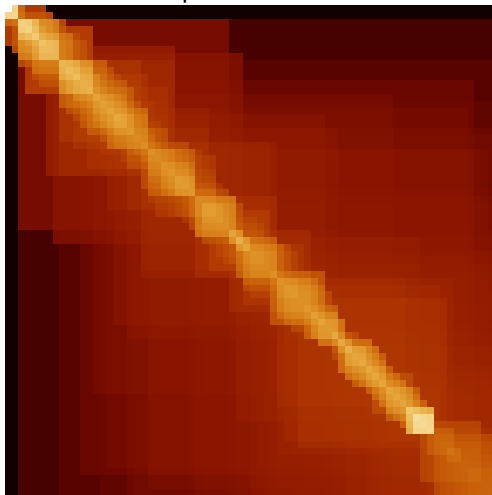
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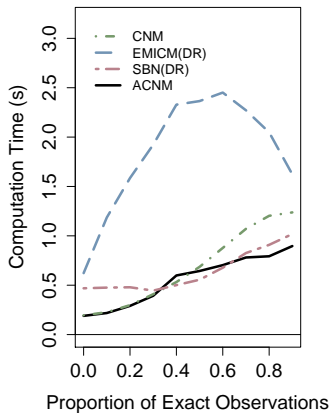
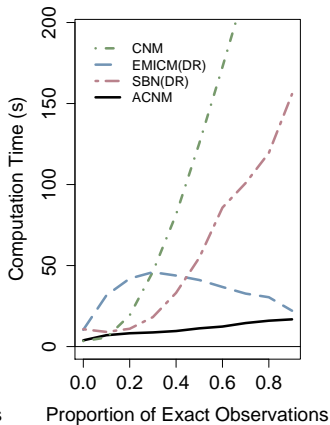
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- Globally reallocates probability among blocks, calling itself recursively
- Guaranteed convergence to the solution

Heatmap of HALT Hessian



Mean times, for $n=400$ and $n=1600$ 

Conclusions

- Where Interval Censoring is present in survival data, it can be allowed for in the analysis.
- The NPMLE Survival Function combined with Bootstrap methods can create an informative picture of survival progression in such cases.
- The ACNM algorithm provides a fast and robust solution to this problem.

Thanks to:

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