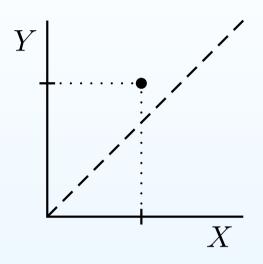
Computation of the MLE for bivariate interval censored data

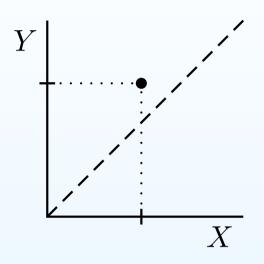
Marloes H. Maathuis

ETH Zürich, Seminar für Statistik maathuis@stat.math.ethz.ch http://stat.ethz.ch/~maathuis

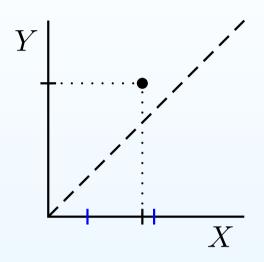
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 - \circ X: time of HIV infection
 - \circ Y: time of onset of AIDS



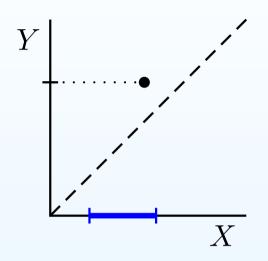
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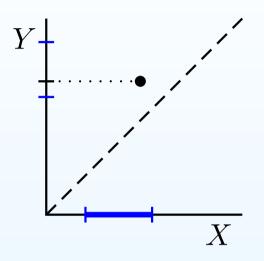
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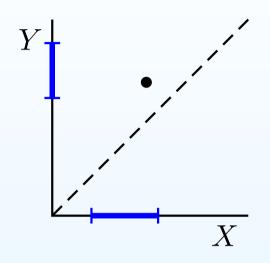
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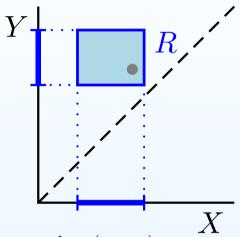
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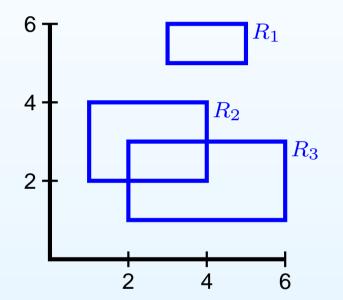
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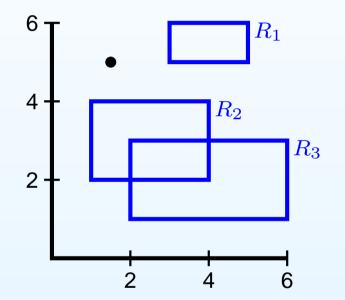


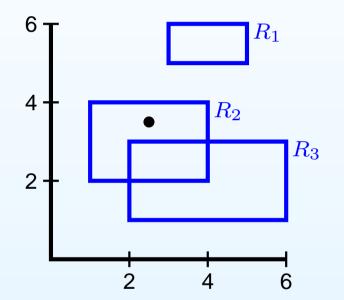
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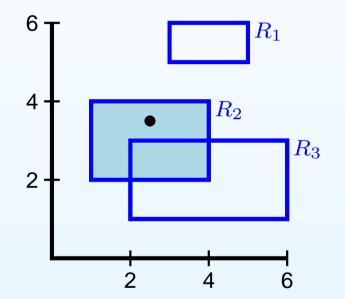


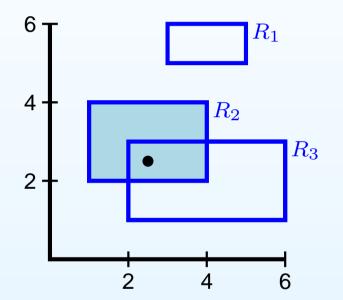
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 - \circ X: time of HIV infection
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- X and Y can be interval censored. Instead of a realization (x, y), we observe Xan observation rectangle R that is known to contain (x, y).
- Goal: based on n i.i.d observation rectangles R_1, \ldots, R_n we want to compute the MLE for the joint distribution function of (X, Y).

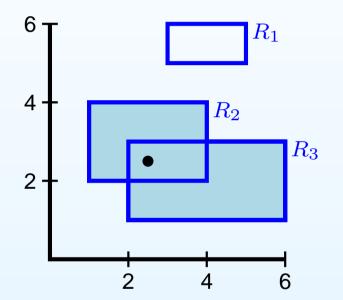


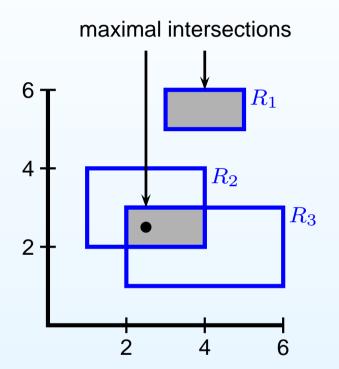


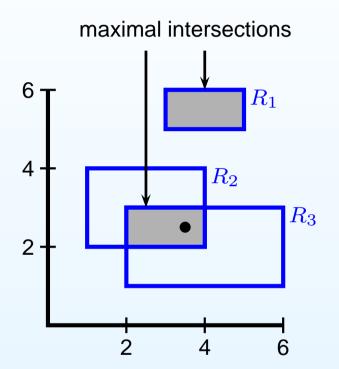






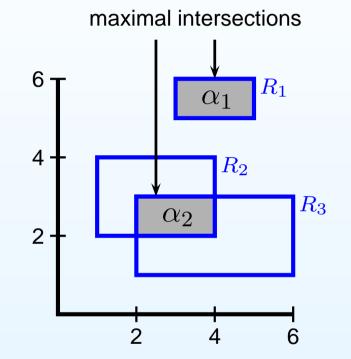




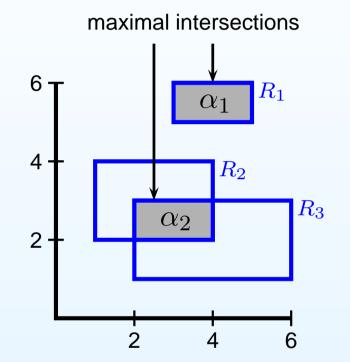


 $\max_{F \in \mathcal{F}} \sum_{i=1}^{n} \log(P_F(R_i))$

 $\max_{F \in \mathcal{F}} \sum_{i=1}^{n} \log(P_F(R_i))$ $= \max_{\alpha_1, \alpha_2} \log(\alpha_1) + 2\log(\alpha_2)$



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$$maximal intersections$$

$$\alpha_1 = \frac{1}{3}, \quad \alpha_2 = \frac{2}{3}$$

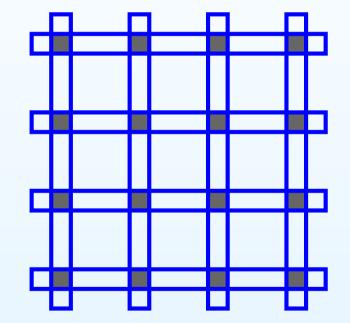
 R_1 α_1 R_2 R_3 α_2 2 6

Computation of the MLE:

- Reduction step: find maximal intersections
- Optimization step: solve optimization problem in α

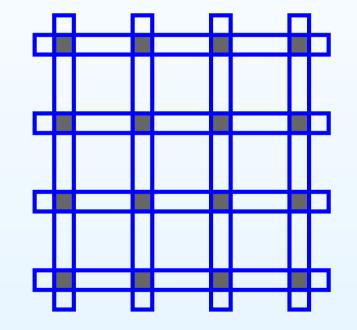
Difficulty in the computation of the MLE

- Number of maximal intersections can be very large:
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Difficulty in the computation of the MLE

- Number of maximal intersections can be very large:
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 \circ For *d*-variate censored data: $O(n^d)$

Outline

- Reduction step
- Optimization step
- R-package 'MLEcens'

Reduction step

Previous work:

- Betensky and Finkelstein (1999)
- Song (2001)
- Gentleman and Vandal (2001), time complexity $O(n^5)$
- Bogaerts and Lesaffre (2004), time complexity $O(n^3)$

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Related algorithm: finding the maximum number of rectangles having a non-empty intersection:

• Lee (1983), time complexity $O(n \log n)$

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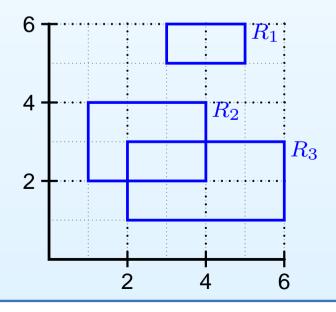
• Lee (1983), time complexity $O(n \log n)$

Our reduction algorithm, motivated by Lee (1983):

• Height Map Algorithm, time complexity $O(n^2)$

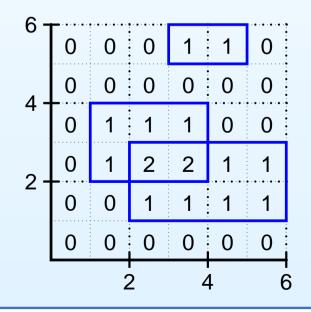
Height Map Algorithm

• Definition: $A_j \neq \emptyset$ is a maximal intersection if and only if $A_j = \bigcap_{i \in \beta_j} R_i$ for some set $\beta_j \subset \{1, \ldots, n\}$ and there is no strict superset $\beta_j^* \subset \{1, \ldots, n\}$ of β_j for which $\bigcap_{i \in \beta_j^*} R_i \neq \emptyset$.



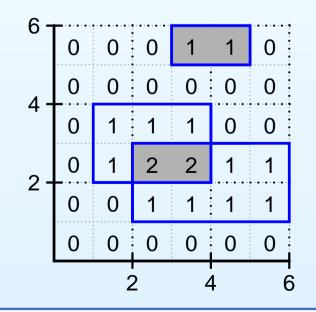
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- Basic idea of the Height Map Algorithm:
 - Define a height map of the observed sets:



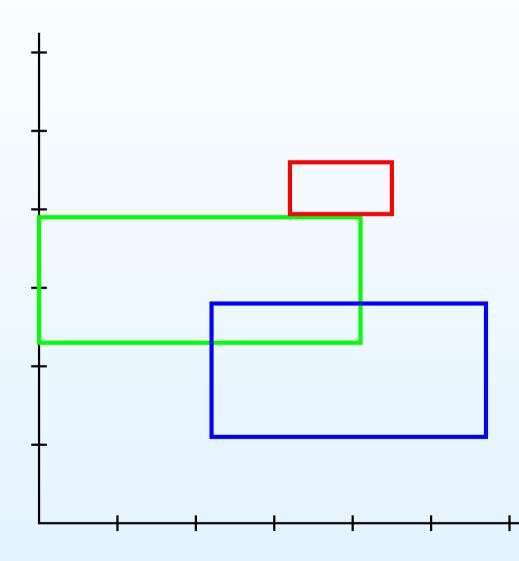
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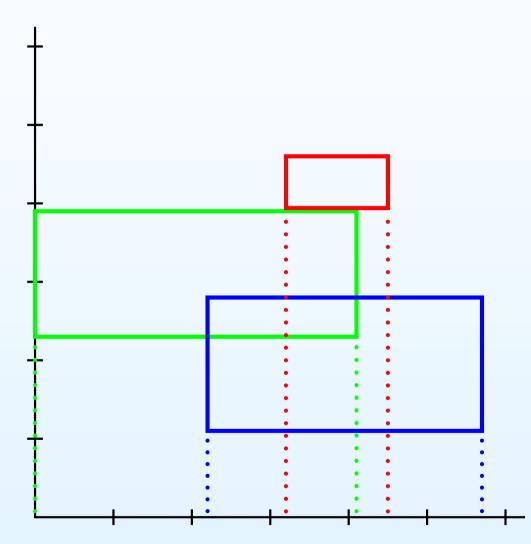
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- Basic idea of the Height Map Algorithm:
 - Define a height map of the observed sets:
 - The maximal intersections are exactly the local maximum regions of the height map

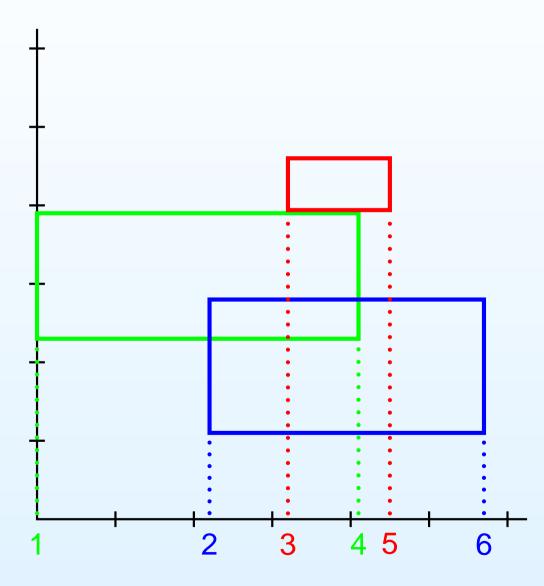


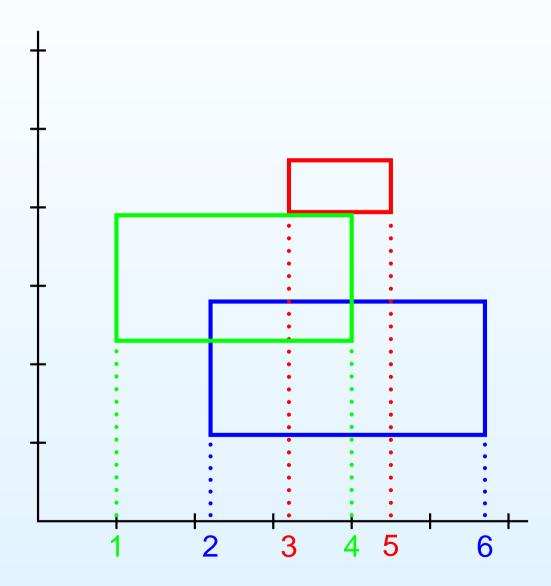
The algorithm

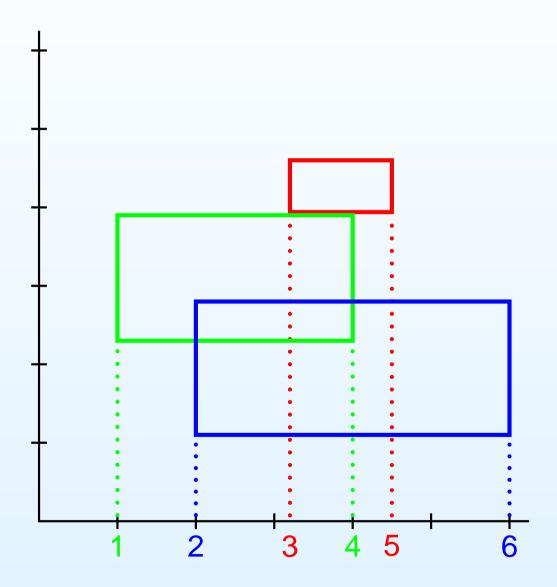
- Transform the observation rectangles into "canonical rectangles"
- Find local maximum regions of the height map of the canonical rectangles (by sweeping)
- Transform local maxima back to original coordinates

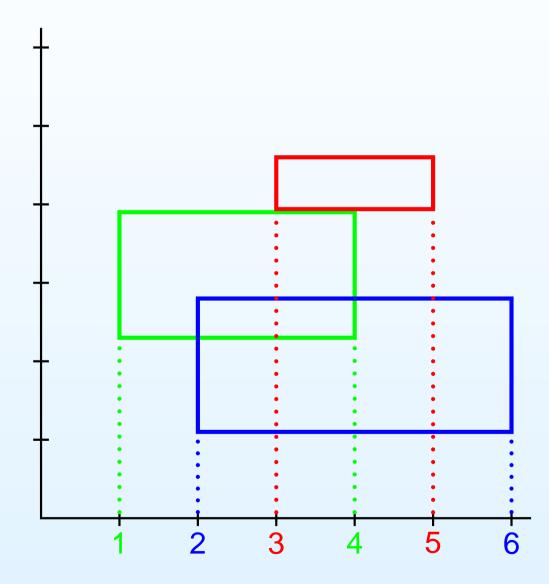




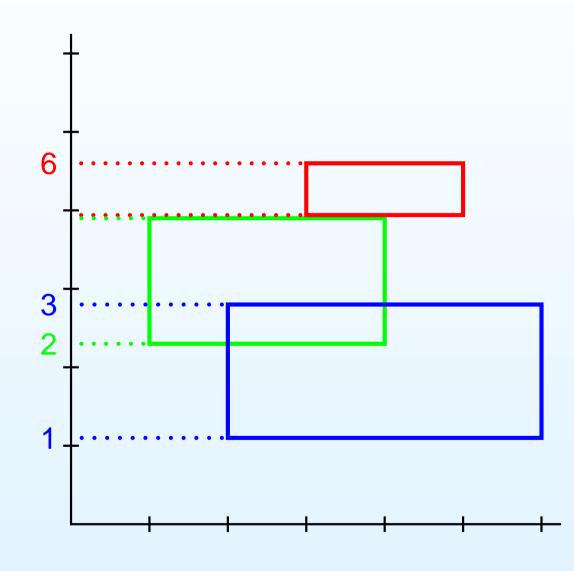




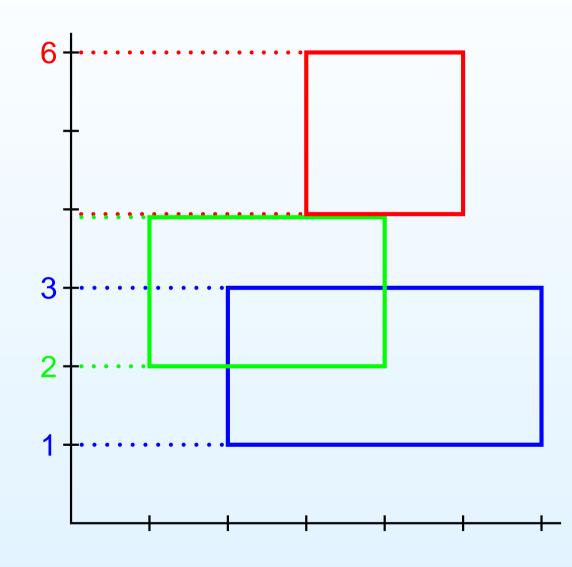




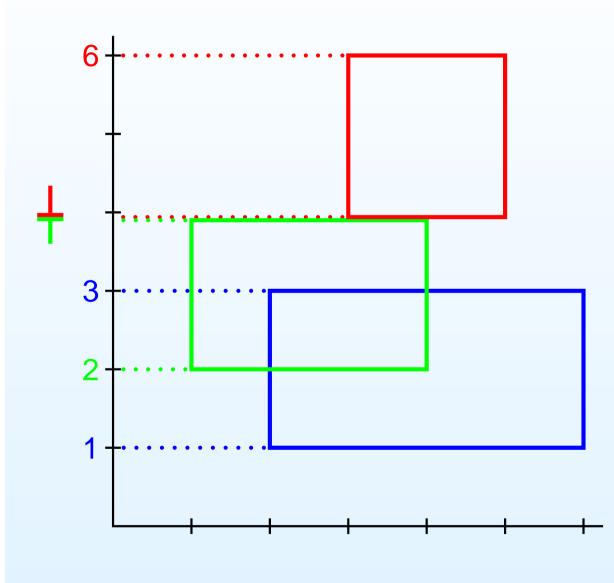
• Replace *x*-coordinates by their order statistics.



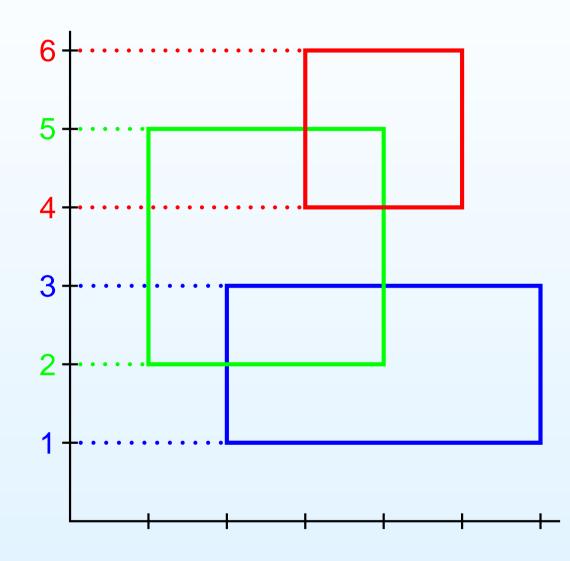
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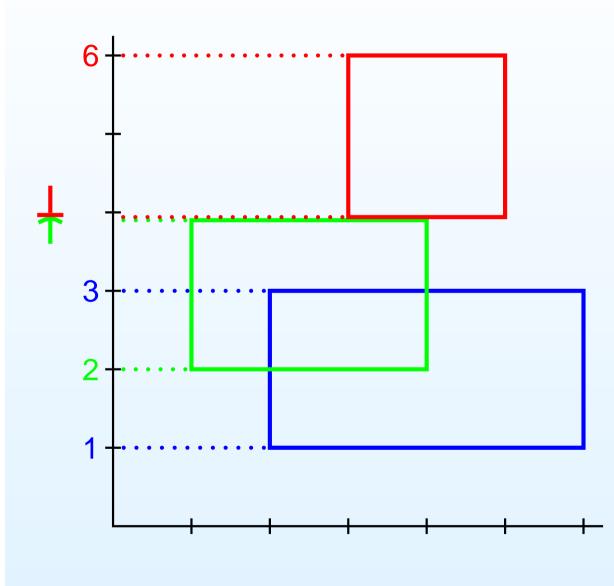
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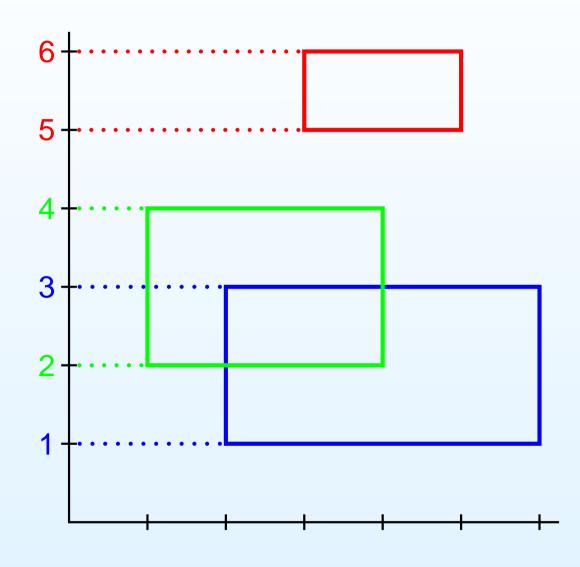
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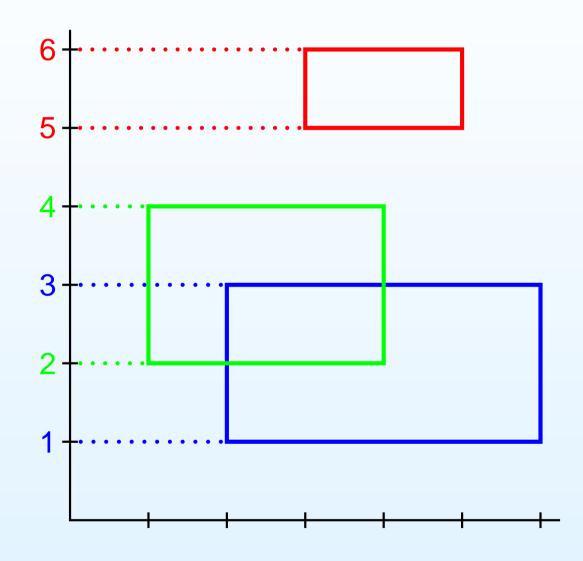
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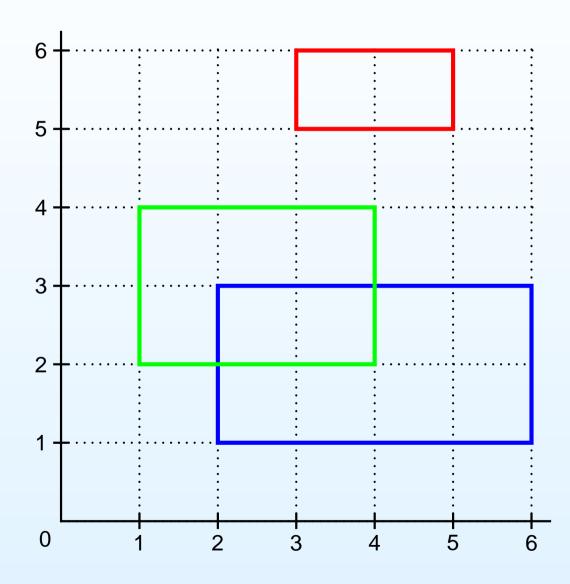
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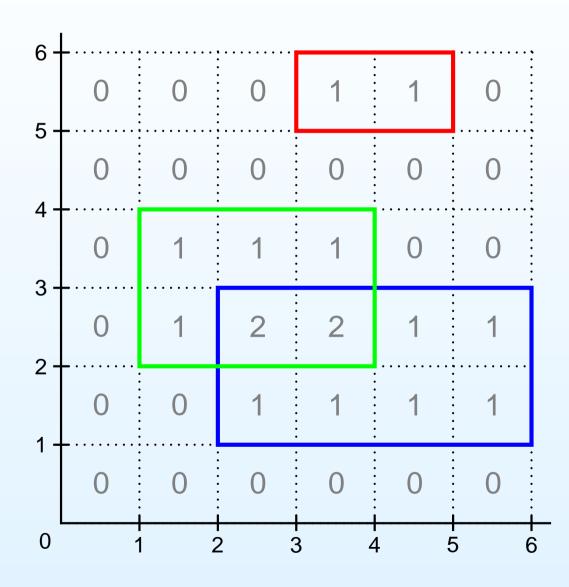


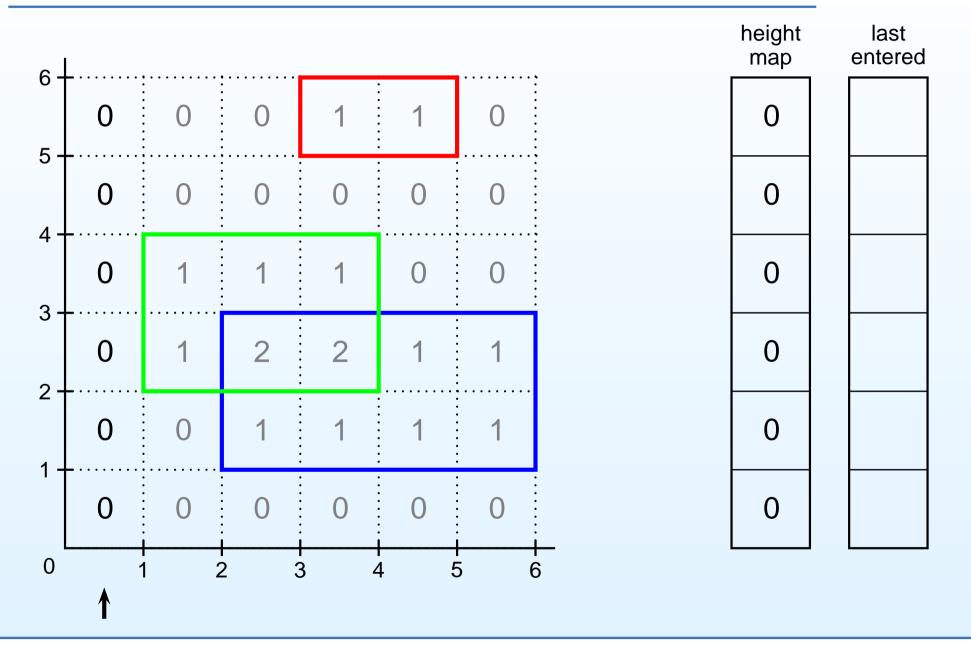
- Replace *x*-coordinates by their order statistics.
- Replace *y*-coordinates by their order statistics.
- All x-coodinates are different and take values in {1, 2, ..., 2n} (same for y-coordinates).
- Intersection structure of the original and canonical rectangles is identical.

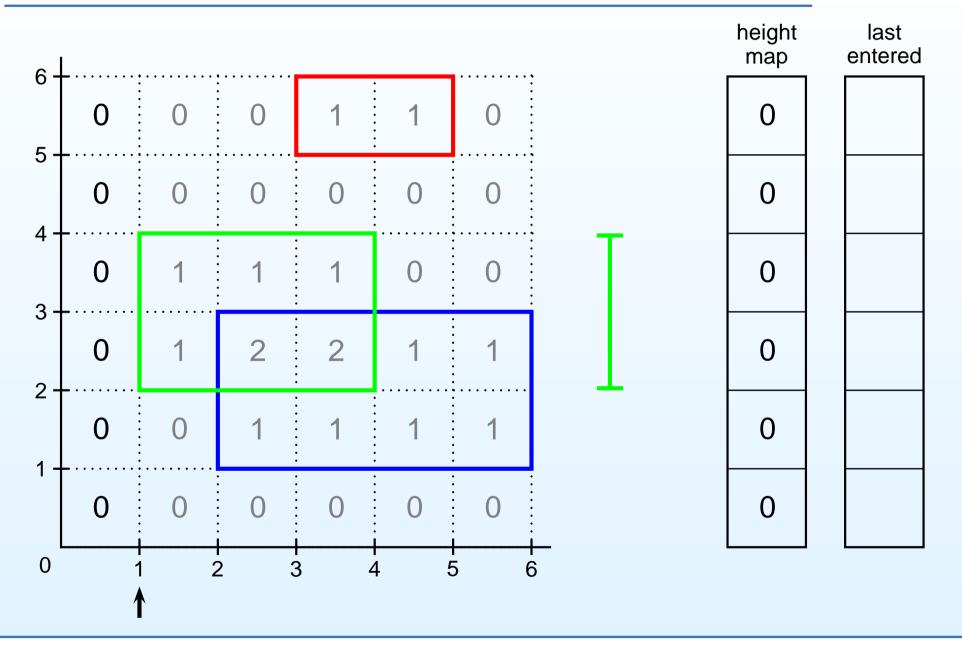
Why use canonical rectangles?

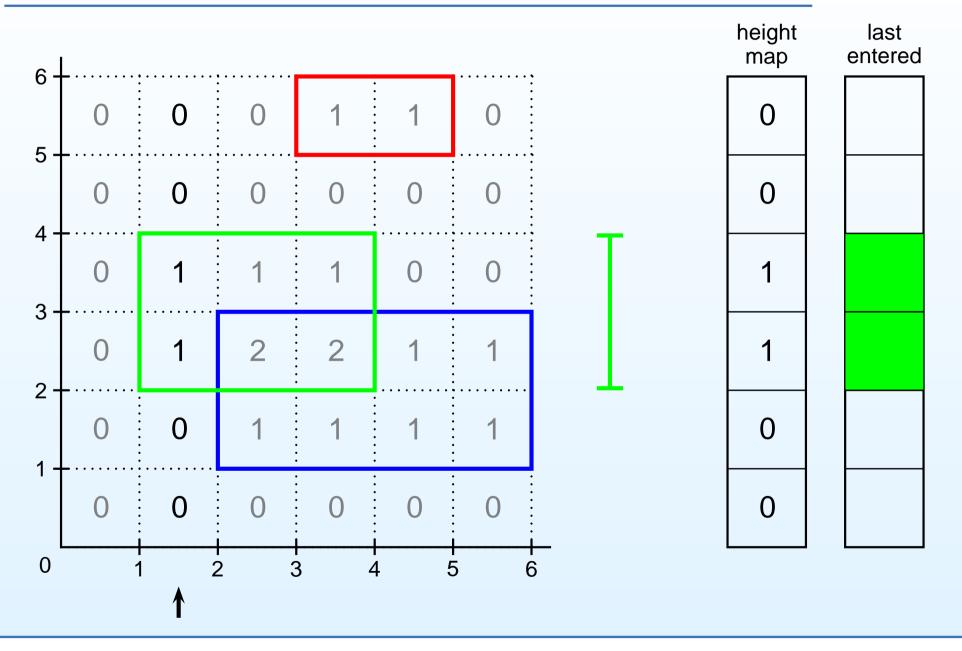
- We break possible ties early, so that we don't have to worry about this anymore
- It is easier and faster to work with integer coordinates

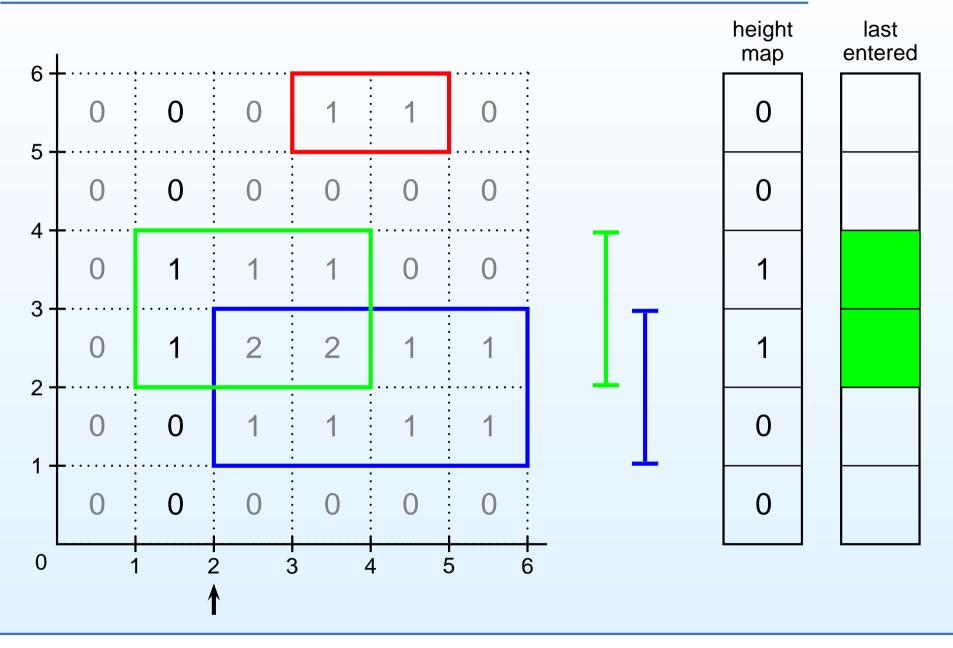


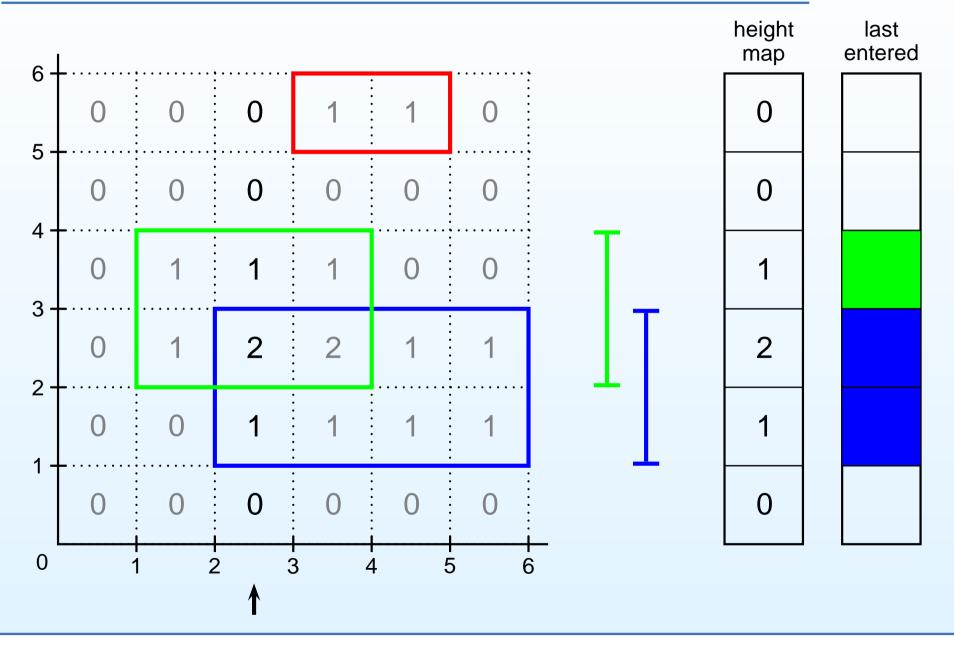


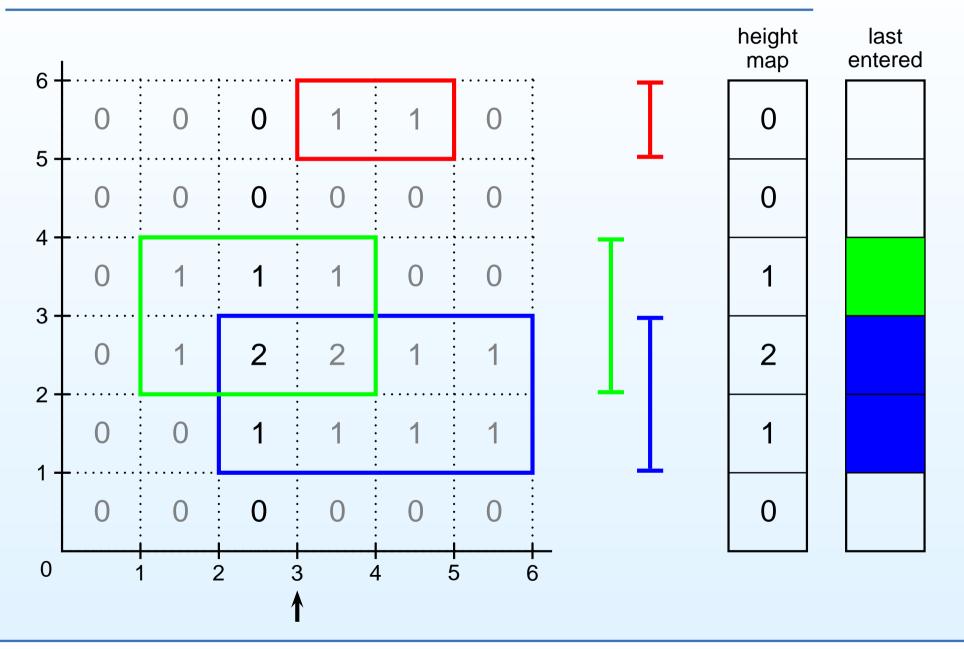


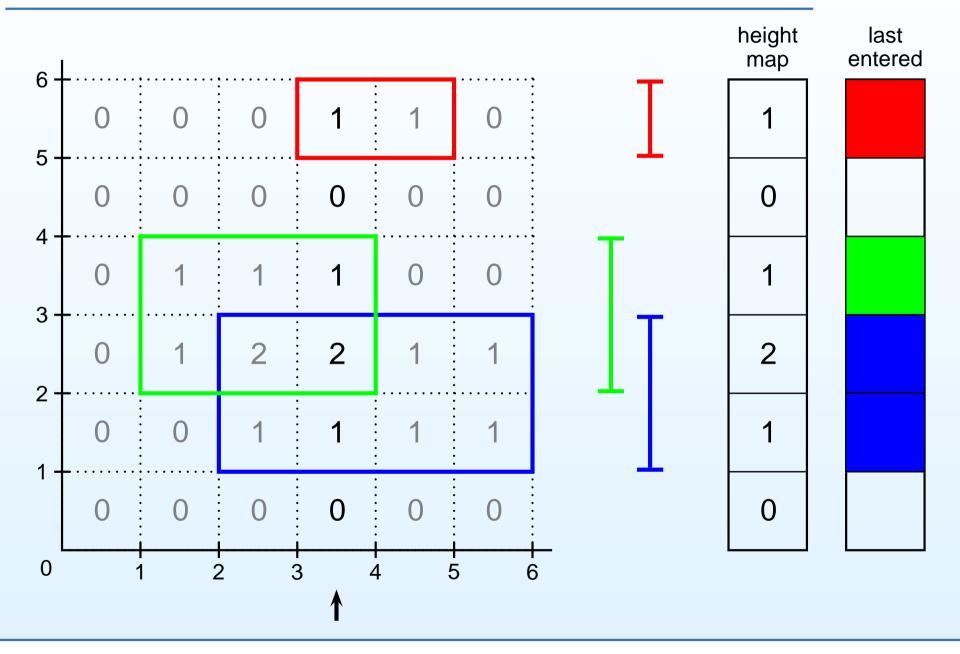


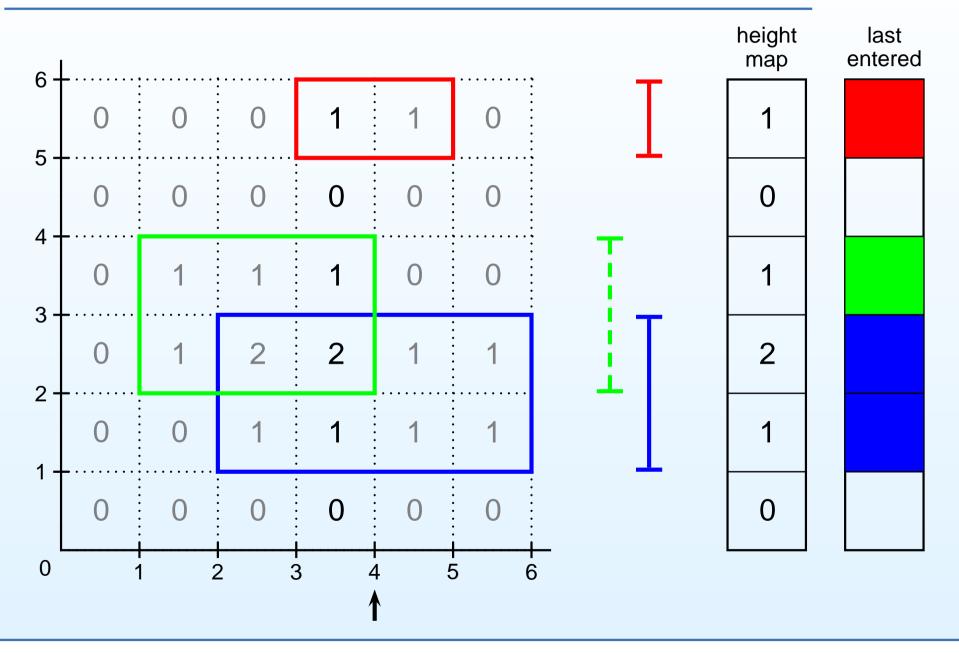


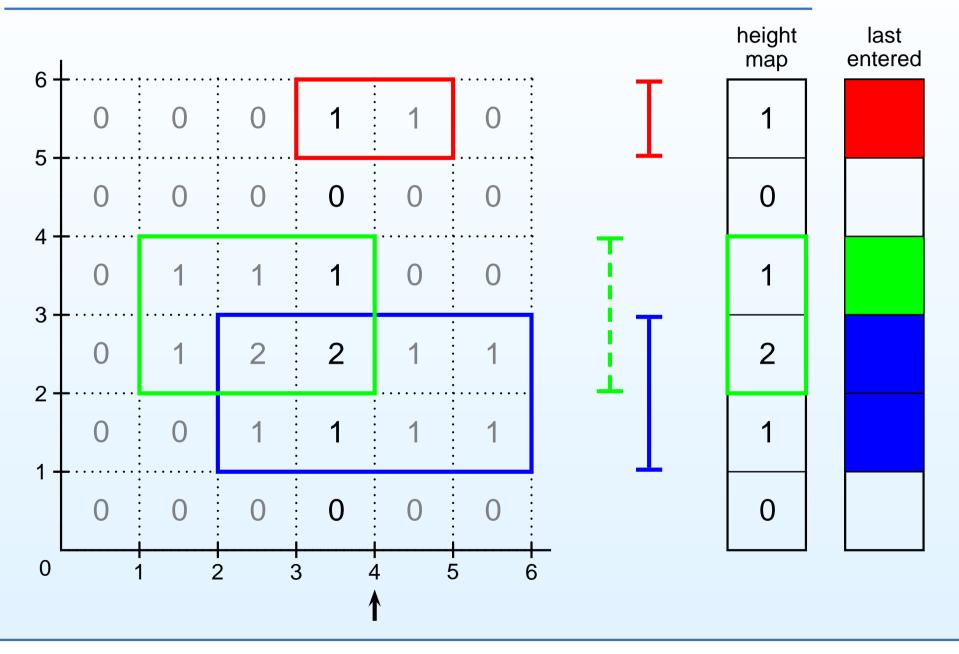


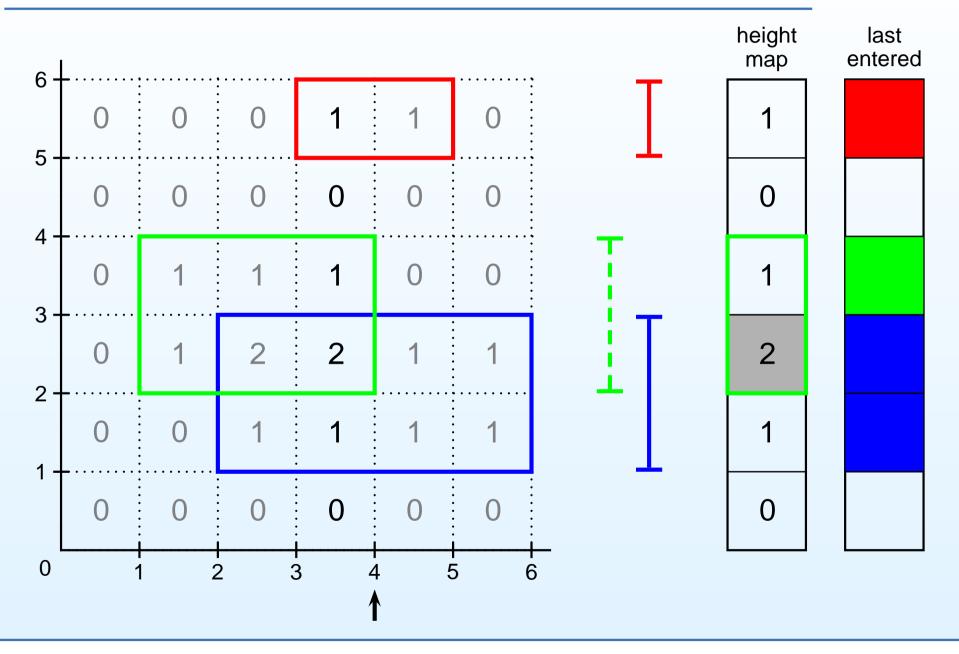


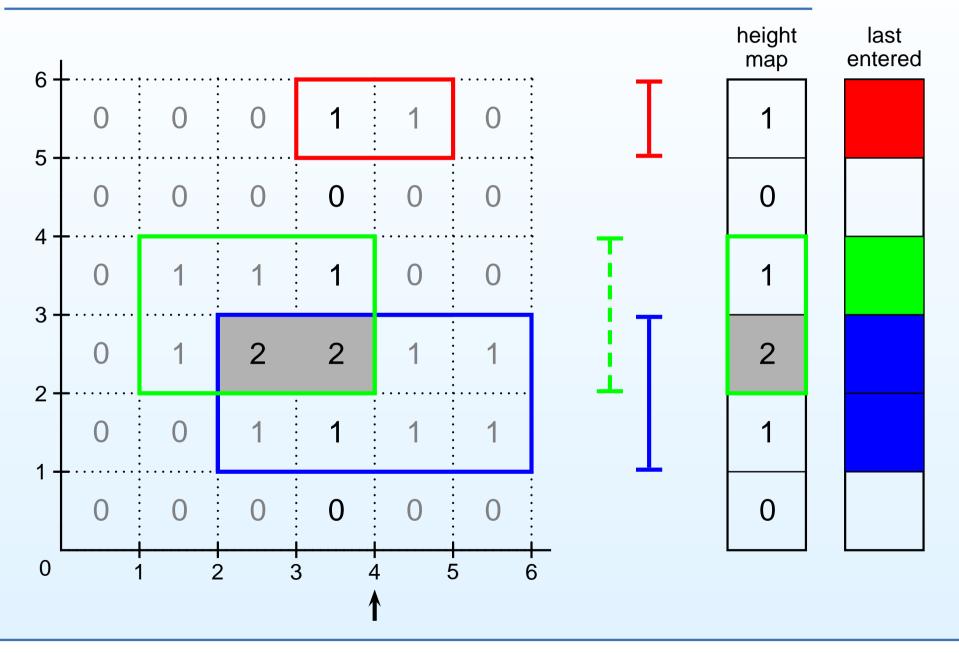


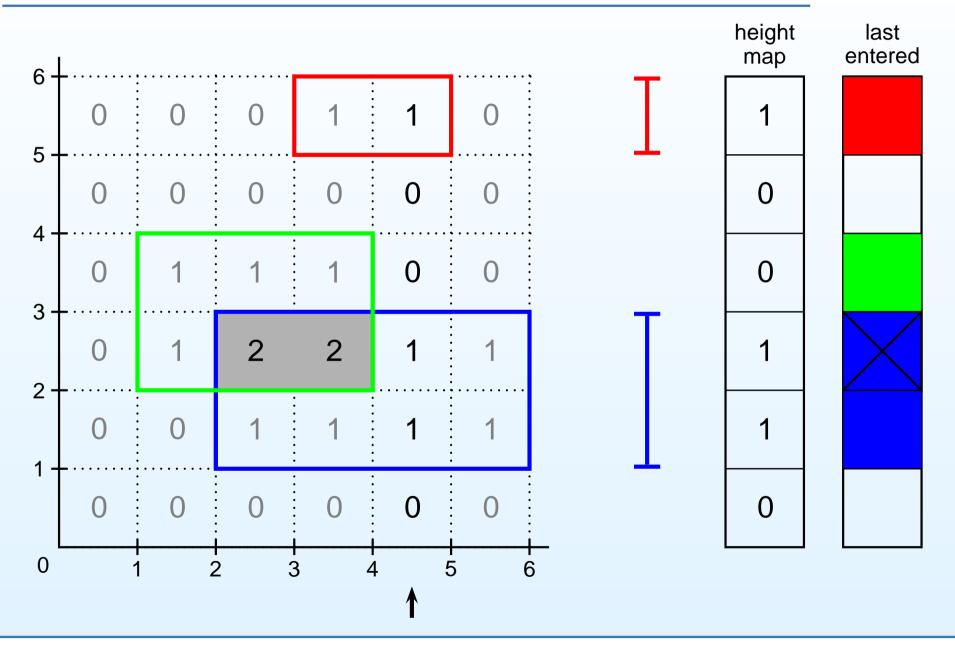


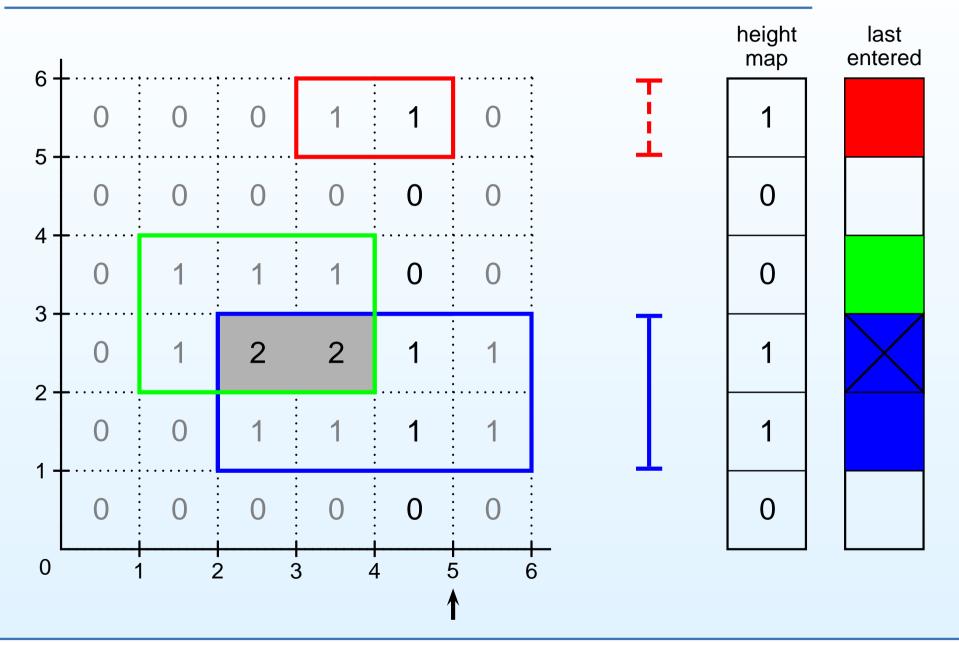


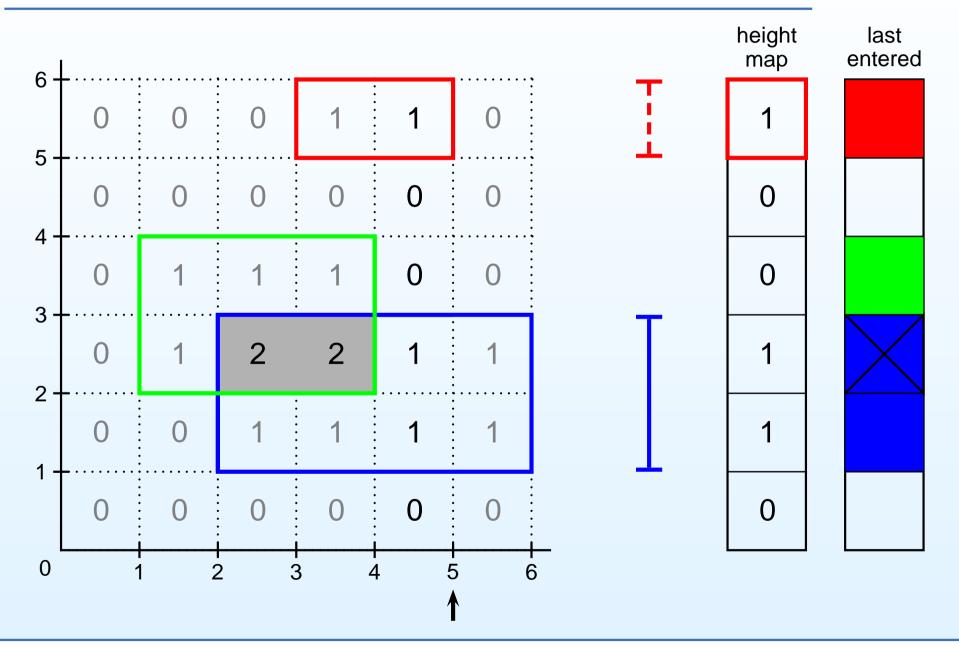


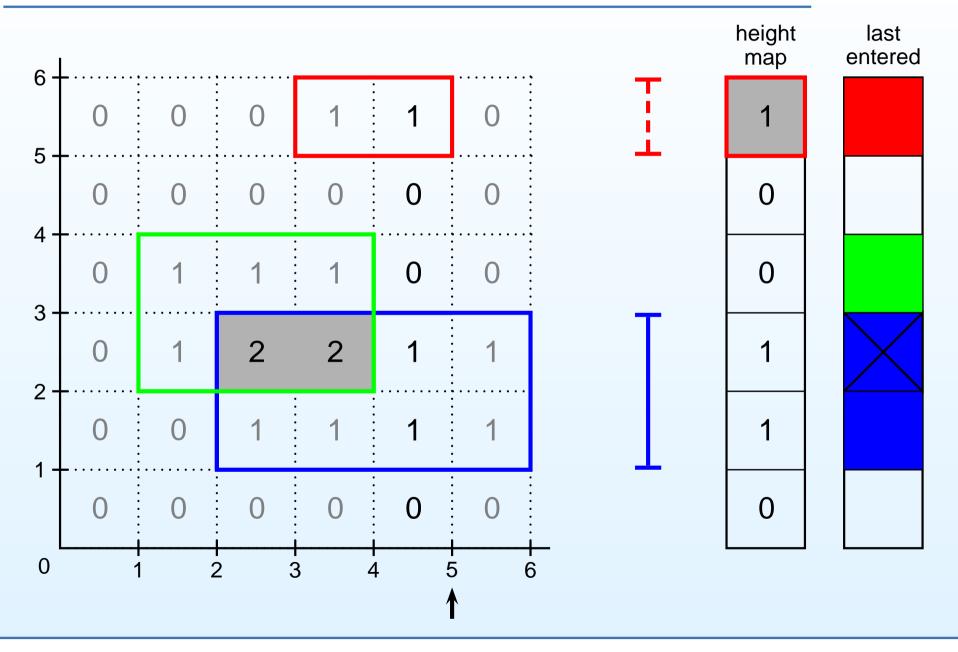


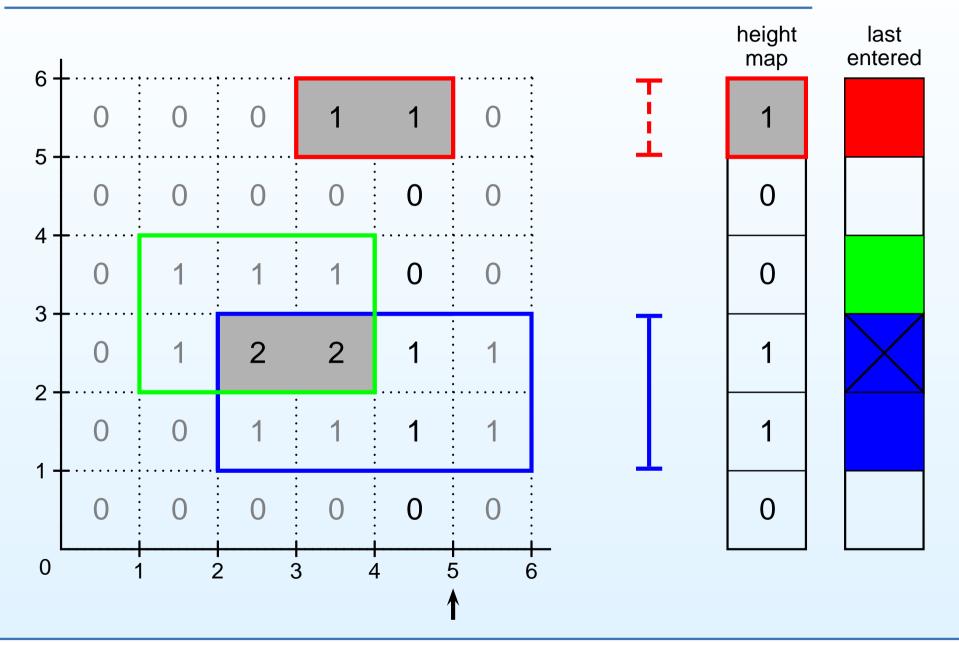


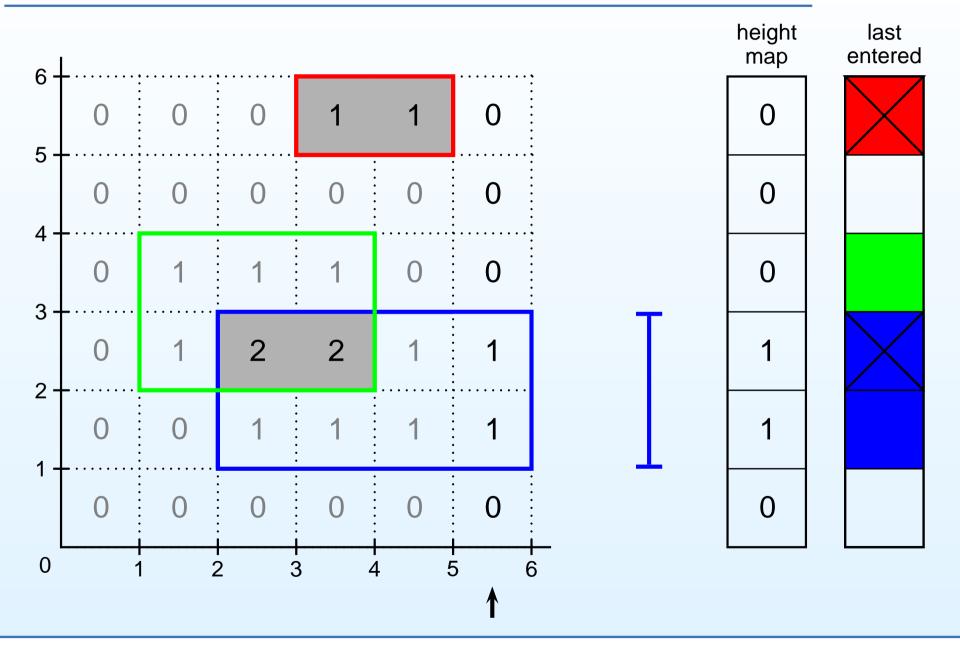


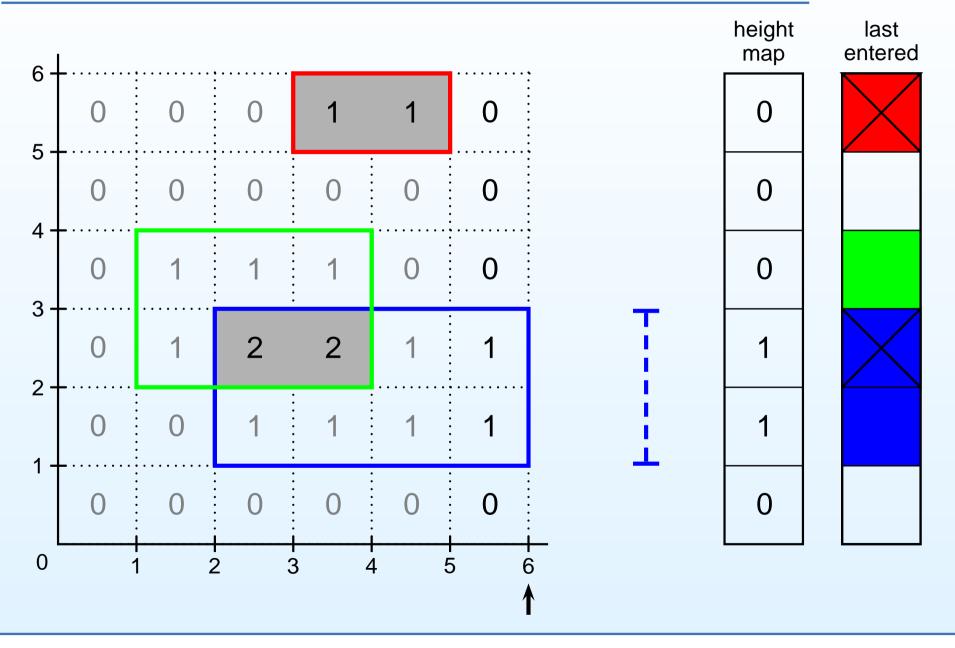


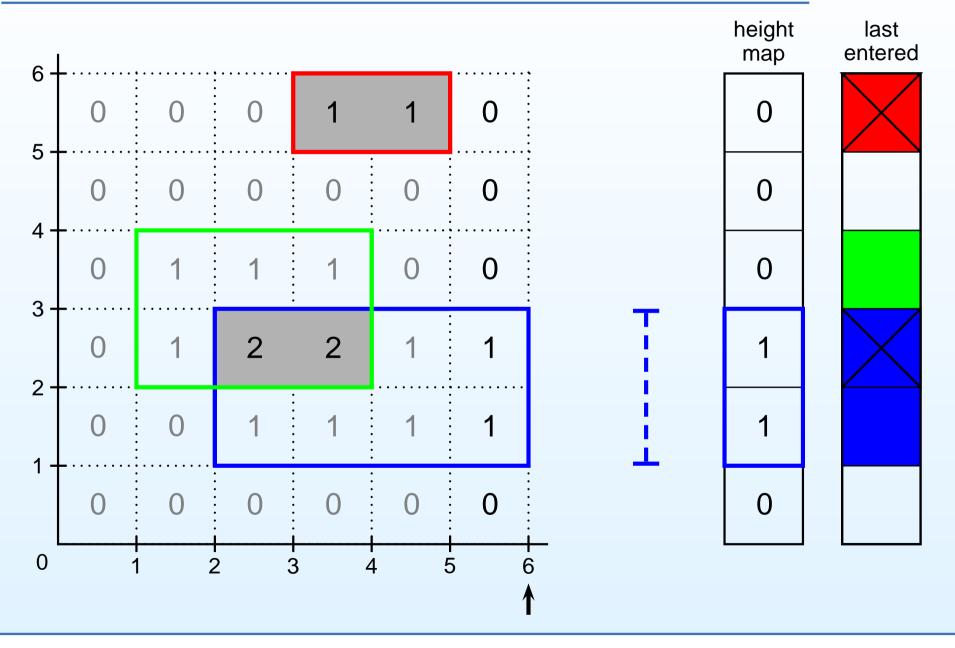


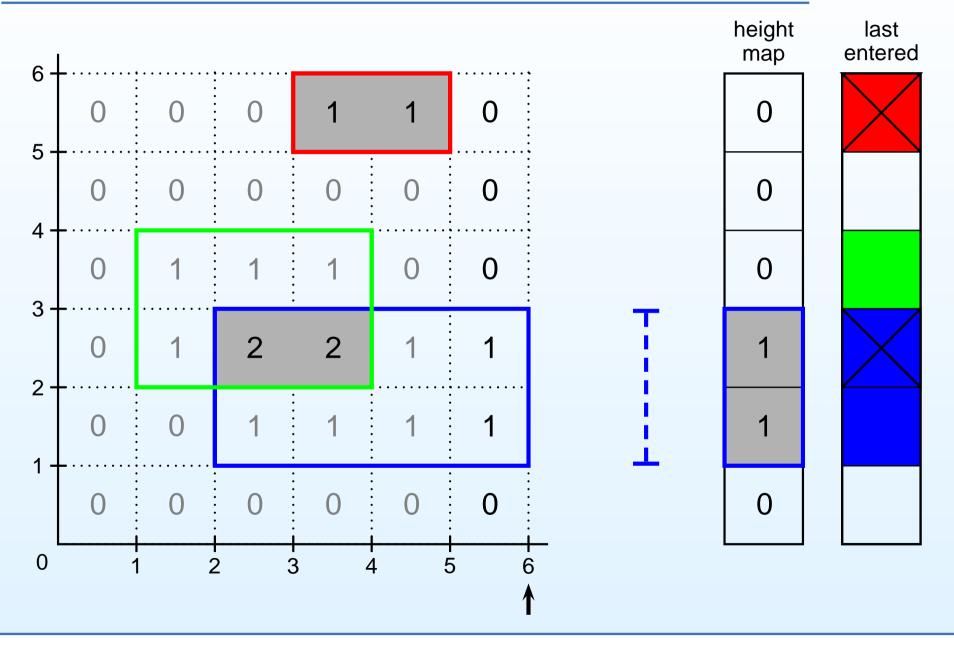


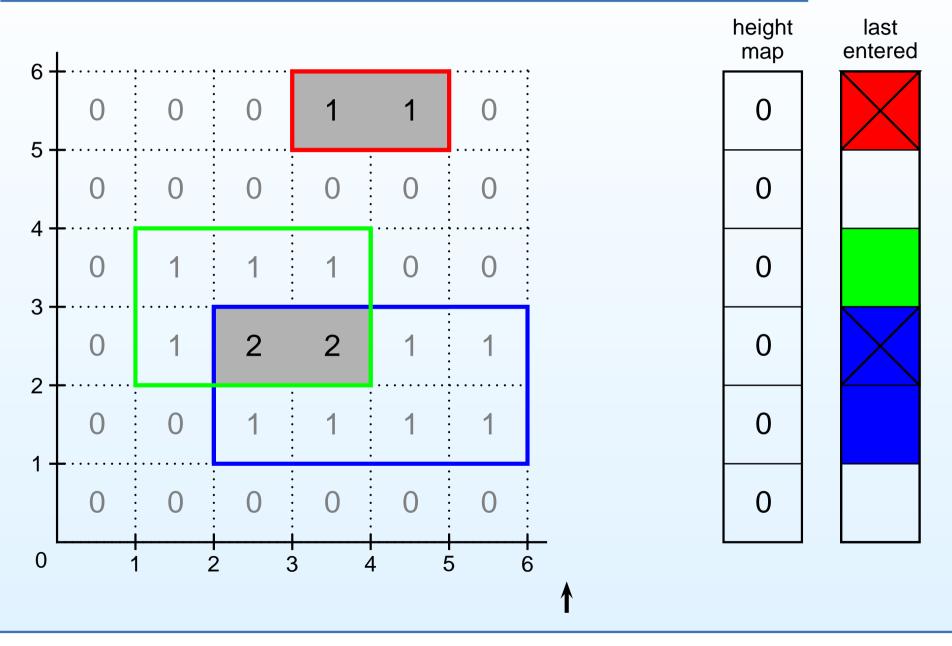












Time and space complexity of the algorithm

For bivariate interval censored data:

- time complexity: $O(n^2)$
- space complexity:
 - \circ computation: O(n)
 - \circ output: $O(n^2)$

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For *d*-dimensional interval censored data:

- time complexity: $O(n^d)$
- space complexity:
 - \circ computation: $O(n^{d-1})$
 - \circ output: $O(n^d)$

Simulation study

Bivariate current status data from a simple exponential model:

- Variables of interest: $X, Y \sim \text{Exp}(1)$
- Observation times: $U, V \sim \text{Exp}(1)$
- *X*, *Y*, *U*, *V* mutually independent
- 50 simulations for sample sizes

50 100 250 500 1,000 2,500 5,000 10,000

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Observation rectangles:

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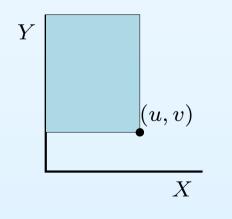
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$$Y$$
 (u, v) X

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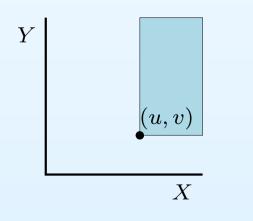
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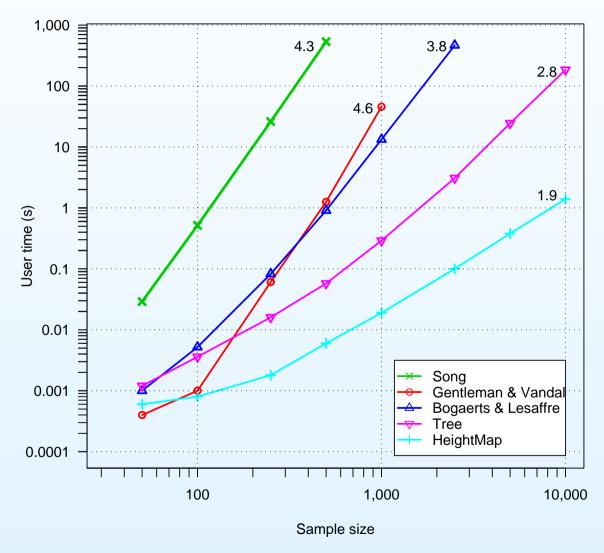


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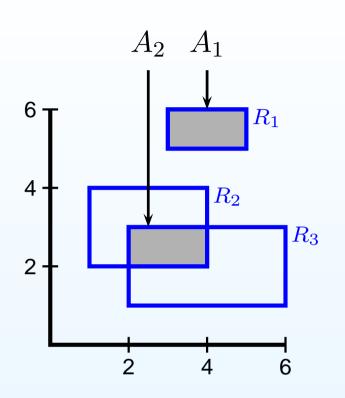
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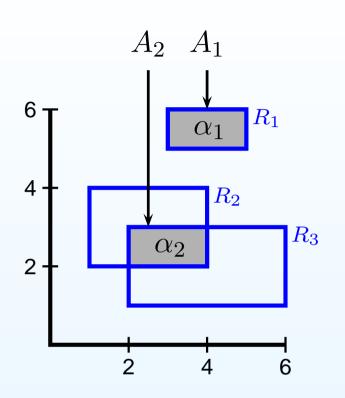


Comparison of five reduction algorithms

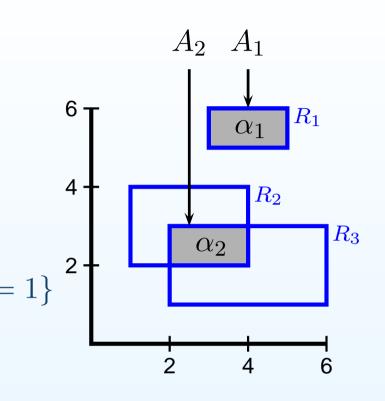
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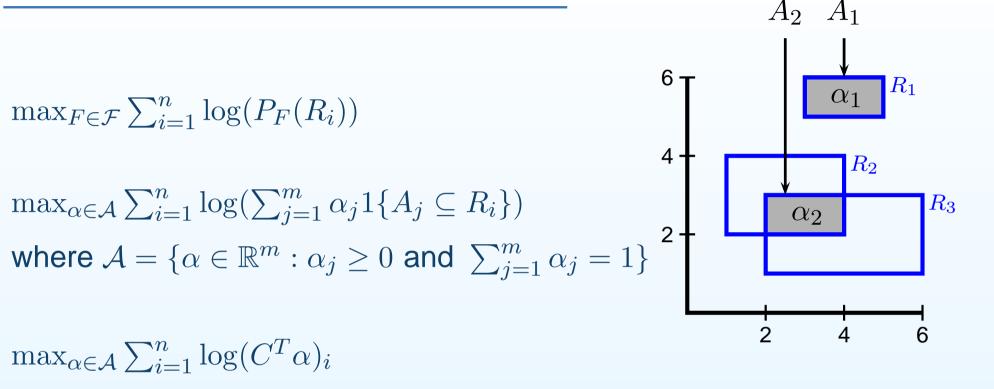


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$$\max_{F \in \mathcal{F}} \sum_{i=1}^{n} \log(P_F(R_i))$$
$$\max_{\alpha \in \mathcal{A}} \sum_{i=1}^{n} \log(\sum_{j=1}^{m} \alpha_j 1\{A_j \subseteq R_i\})$$
where $\mathcal{A} = \{\alpha \in \mathbb{R}^m : \alpha_j \ge 0 \text{ and } \sum_{i=1}^{m} \alpha_j = 0$





where *C* is the $m \times n$ clique matrix, $C_{ji} = 1\{A_j \subseteq R_i\}$

Computation of the MLE forbivariate interval censored data - p. 15/23

$$\max_{F \in \mathcal{F}} \sum_{i=1}^{n} \log(P_F(R_i))$$

$$\max_{\alpha \in \mathcal{A}} \sum_{i=1}^{n} \log(\sum_{j=1}^{m} \alpha_j 1\{A_j \subseteq R_i\})$$

where $\mathcal{A} = \{\alpha \in \mathbb{R}^m : \alpha_j \ge 0 \text{ and } \sum_{j=1}^{m} \alpha_j = 1\}$

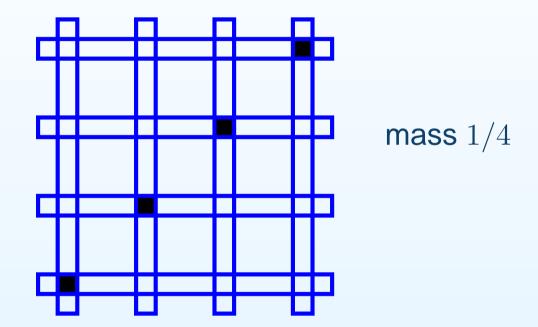
$$\max_{\alpha \in \mathcal{A}} \sum_{i=1}^{n} \log(C^T \alpha)_i$$

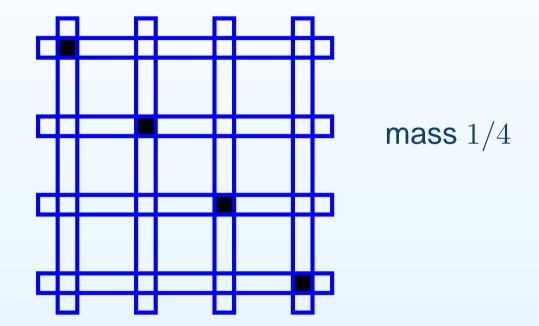
where *C* is the $m \times n$ clique matrix, $C_{ji} = 1\{A_j \subseteq R_i\}$

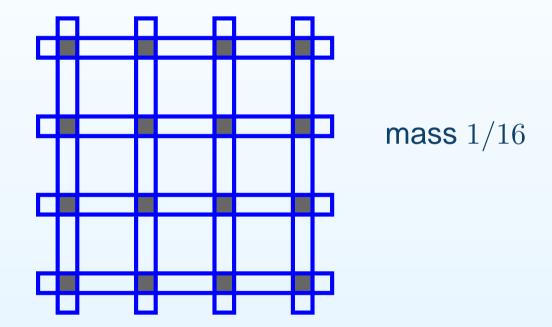
$$\min_{\alpha \in \mathcal{A}^*} \left[-\frac{1}{n} \sum_{i=1}^n \log(C^T \alpha)_i + \sum_{j=1}^m \alpha_j \right] = \min_{\alpha \in \mathcal{A}^*} \phi(\alpha)$$

where $\mathcal{A}^* = \{ \alpha \in \mathbb{R}^m : \alpha_j \ge 0 \}$

 $A_2 \quad A_1$







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• We compute $\hat{\alpha}$ with an iterative algorithm, and stop if (*) is satisfied within some tolerance ϵ , e.g. $\epsilon = 10^{-10}$

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• Let k = k + 1

R-packages for interval censored data

- Existing packages:
 - Icens (Gentleman and Vandal): several functions for univariate/bivariate interval censored data
 - bicreduc (Maathuis):
 height map algorithm for the reduction step
 - intcox (Henschel, Heiss and Mansmann)
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- New package MLEcens
 - Includes package bicreduc (which is no longer maintained)
 - Some overlap with Icens, but MLEcens has:
 - Very fast reduction step
 - Fast and stable optimization step
 - Various new plotting functions

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 - We finally chose to use the open source BLAS (Basic Linear Algebra Subprograms) and LAPACK (Linear Algebra PACKage) libraries that come with R

- Available functions:
 - Basic plot function: plotRects
 - Canonical rectangles: real2canon, canon2real
 - **Reduction step:** reduc, plotHM, plotCM
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- Demonstration...

Possible extensions of R-package

- 3d-plotting functions
- Specialized algorithms for univariate interval censored data
- Extension to 3-dimensional interval censored data

• • • • •

I am happy to modify the package. So please let me know if you are interested in any extensions, or if you have any other feedback/suggestions.

References

- Reduction step:
 - Maathuis (2005). "Reduction algorithm for the NPMLE for distribution function of bivariate interval censored data", JCGS 14 352–362.
- Optimization step:
 - Groeneboom, Jongbloed and Wellner (2007). "The support reduction algorithm for computing nonparametric function estimates in mixture models", *Submitted*.
 - Maathuis (2003). "Nonparametric maximum likelihood estimation for bivariate censored data", Master's Thesis, Delft University of Technology, The Netherlands.
- R-package:
 - Maathuis (2007), "R-package MLEcens", CRAN.

Thanks!

Presentation (including R-code), papers, and R-package are posted on my website:

http://stat.ethz.ch/~maathuis