# Controlled Discovery and Localization of Astronomical Point Sources via Bayesian Linear Programming (BLiP) 

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## Coauthor



Asher Spector (First-year PhD student at Stanford Statistics)

## Outline

- Motivation
- Problem statement
- Methodological contribution: Bayesian Linear Programming (BLiP)
- Simulations
- Application to genetic fine-mapping
- Application to astronomical point-source detection


## Astronomical point source detection



Figure: Cartoon of partial point source data

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Test
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Solution: adaptively selected regions

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Existing work: no formalization of what "power" means, so cannot optimize it

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- If want to precisely know the number of sources in each $G$ :
- Pair each $G$ with a $J \subset \mathbb{N}$ representing possible numbers of sources in $G$
- Set $w(G, J)=1 /|J|$ (we call this the "separation-based" weight function)


## Optimizing resolution-adjusted power

Sum weights of true rejections to get Power():

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\operatorname{Power}\left(G_{1}, \ldots, G_{R}\right)=\sum_{r=1}^{R} I_{G_{r}} w\left(G_{r}\right)
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Then the power of a Bayesian method that discovers $G_{1}, \ldots, G_{R}$ is
$\mathbb{E}\left[\operatorname{Power}\left(G_{1}, \ldots, G_{R}\right) \mid\right.$ Data $]=\mathbb{E}\left[\sum_{r=1}^{R} I_{G_{r}} w\left(G_{r}\right) \mid\right.$ Data $]=\sum_{G \subseteq \mathcal{L}} p_{G} w(G) x_{G}$,

- $x_{G} \in\{0,1\}$ is indicator that $G$ is one of the method's discoveries
- $p_{G}=\mathbb{E}\left[I_{G} \mid\right.$ Data $]$ is posterior inclusion probability (PIP)


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Mixed-integer linear program (MILP) non-convex; fast solvers for small problems

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Empirically, Very few $x_{G}^{\star} \notin\{0,1\}$, and $\left\{x_{G}^{\star}\right\}$ very nearly MILP-optimal

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An exact upper-bound for the suboptimality of $\left\{x_{G}^{\star \star}\right\}$ is

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Figure: Expected power (objective function) of $\left\{x_{G}^{\star \star}\right\}$ (BLiP) vs. $\left\{x_{G}^{\star}\right\}$ (Upper bound). Optimization dimension $\geq 50,000$.

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Can also solve problem as if $|\mathcal{G}|$ were much bigger via adaptive pruning

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Just needs posterior inclusion probabilities $p_{G}$ as input

- From any Bayesian algorithm for computing/approximating the posterior,
- E.g., MCMC (average over posterior samples whether $G$ contains a signal)
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Type
$\rightarrow$ Model only
$\rightarrow$ Total
Method
$\rightarrow$ (Model+BLiP)
$\rightarrow$ (niter $=5000$ )
$\rightarrow$ (niter (MCMC)
$\rightarrow$ SuSiE (variational)
$\rightarrow$

Figure: $p$ denotes dimension of linear model being fit, with $n=p / 2$

## Comparison with alternatives

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Figure: Linear model w/ autocorrelated $X$, sparsity $s$, sample size $n$, and dimension $p$

## Other error rates

BLiP idea works for other error rates: local FDR, PFER, FWER


Measurement

- BLiP
$-\ldots$ Upper bound
Method
- FDR
- Local
${ }^{-}$FDR
$\rightarrow$ PFER

Figure: BLiP's solution indistinguishable from upper-bound for optimal solution

## Change point detection

BLiP applies out of the box to change point detection


Harder example


Figure: Green bands denote LSS+BLiP's outputted regions; left is example SuSiE fails on due to variational approximation

## Point-source detection

$100 \times 100$ pixel sub-image of Messier 2 star cluster from Sloan Digital Sky Survey

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StarNet + BLiP (q=0.25)


StarNet (MAP)


Figure: $20 \times 20$ pixel sub-image; green dots $=$ ground truth, red regions $=$ false discoveries, blue regions $=$ true discoveries

## Point-source detection (contd)

## Inverse Radius Weight Fn.



## Point-source detection (contd)

## Inverse Radius Weight Fn.



Separation-based Weight Fn.


## Fine-mapping

UK Biobank data: $n \approx 337,000, p \approx 19,000,000$; BLiP takes $\leq 1 \mathrm{~min}$ per trait

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Cumulative Frequency of Discovered Group Sizes




## Conclusion

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Thank you!
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## References

Katsevich, E., Sabatti, C., and Bogomolov, M. (2021). Filtering the rejection set while preserving false discovery rate control. Journal of the American Statistical Association, 0(0):1-12.
Lee, Y., Luca, F., Pique-Regi, R., and Wen, X. (2018). Bayesian multi-snp genetic association analysis: Control of fdr and use of summary statistics. bioRxiv.
Liu, R., McAuliffe, J. D., and Regier, J. (2021). Variational inference for deblending crowded starfields.
Wang, G., Sarkar, A., Carbonetto, P., and Stephens, M. (2020). A simple new approach to variable selection in regression, with application to genetic fine mapping. Journal of the Royal Statistical Society: Series B (Statistical Methodology), 82(5):1273-1300.
Yekutieli, D. (2008). Hierarchical false discovery rate-controlling methodology. Journal of the American Statistical Association, 103(481):309-316.

