



THE UNIVERSITY OF
CHICAGO

Department of Statistics

DISSERTATION PROPOSAL

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Bayesian Variable Selection Using Summary Statistics with
Application to Fine-Mapping

MONDAY, December 02, 2019, at 12:30 PM
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ABSTRACT

Fine-mapping methods are useful to pinpoint causal variants contributing to complex traits using summary data from genome-wide association studies. The most successful fine-mapping approaches frame the problem as a variable selection problem and use Bayesian variable selection methods, which quantify uncertainty in the causal genetic variables by taking into account patterns of Linkage Disequilibrium (LD). However, current Bayesian variable selection methods either rely on computationally intensive procedures to make posterior inferences (e.g., exhaustive enumeration, stochastic search), or require individual-level genotype and phenotype data. We develop a computationally efficient method ‘Sum of Single Effect Regression’ with summary statistics (SuSiE-RSS). The model structure yields independent credible sets, each designed to capture one effect, making the results easy to interpret and ideal for guiding follow-up studies. In numerical experiments we show that misspecification of the LD panel can lead to unreliable inferences, and we describe an approach for correcting inconsistencies to improve performance. We apply our method to fine-map associations for several phenotypes in the UK Biobank data with about 500,000 individuals. Lastly, we generalize our method to multi-phenotype fine-mapping. Joint analysis of multiple related traits can increase power and our method can distinguish the pleiotropy from LD induced effects.