



THE UNIVERSITY OF
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Department of Statistics

DISSERTATION PROPOSAL

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A Bayesian Large-Scale Regression Model for Genome-Wide
Summary Data

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ABSTRACT

Statistical analysis of genome-wide data from large-scale studies has markedly increased our understanding of the role of genetic variation in complex human traits. Existing methods require data at the individual level, which are limitedly available due to privacy and technical issues. In contrast, summary statistics are often released into the public domain. It is hence of interest to dissect the effects of genetic variation on complex traits using summary data. To this end, we develop a novel Bayesian regression model for summary data, “Regression with Summary Statistics” (RSS). RSS has two major advantages over most summary-based methods. First, RSS has close connection to its full-data counterpart, because their likelihoods are parameterized by the same regression coefficients. Second, RSS provides a unified framework for multiple applications, including estimating heritability, detecting associations, inferring gene set enrichment, training trait prediction models and prioritizing causal variants. We apply RSS on the summary statistics of 1.06 million genetic variants from the largest study of adult human height. Results support a polygenic architecture hypothesis for height and reveal biological pathways involved in the development of the skeletal system, regulation of body size, and etiology of bone diseases.

Our future research goals are threefold. First, we will investigate the properties of RSS as a generic model and explore theoretical extensions. Second, we will expand the features of RSS to enable multiple-trait and functional genomic data analysis. Ultimately, we will release open-source software that implements RSS and use it to learn more about the biology of complex human traits from a wide range of published summary data.

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