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THE METHOD OF LIMITS AND ITS APPLICATION TO THE ANALYSIS OF COUNT DATA IN GENOME-WIDE ASSOCIATION STUDIES

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Abstract: We propose a new method of statistical inference, called the method of limits (MoL), which may be viewed as an extension of the method of moments. This method is motivated by the need to analyze count data for genome wide association studies (GWAS), where the existing methods are hindered in statistical inference due to computational challenges. We establish consistency and asymptotic normality of the MoL estimator of heritability from GWAS data, which is seen as an advantage over the existing PQLseq method. Furthermore, we derived a consistent estimator of the proportion of causal SNPs. MoL also showed an advantage of both statistical and computational efficiency measured by average statistical efficiency (ASE) in our simulation studies compared to PQLseq. We also illustrate the usefulness of MoL through its application to the UK Biobank data to infer the heritability of weekly champagne consumption and weekly red wine consumption using the count data.

Key words and phrases: Asymptotic distribution, Big GWAS data, computation, consistency, MoL, proportion of causal SNPs, relative average statistical efficiency.

1. Introduction

The method of moments (MoM) is a classical statistical method known to produce consistent estimators of model parameters. Although the method is known to be less efficient compared to the maximum likelihood (ML), MoM often has a computational advantage over the ML (Jiang and Nguyen, 2021). The latter is an attractive feature, especially in the modern era of Big Data. In fact, in large samples, the difference between ML and MoM estimators may be ignorable from a practical standpoint.

Despite its popularity, difficulties are encountered in executing the MoM idea. To see this, note that an MoM equation can often be expressed as

$$S = \mathrm{E}_\theta(S), \tag{1.1}$$

where S is a vector of statistics, and $\mathrm{E}_\theta(S)$ is the vector of expected values, or moments, of S under the parameter vector θ. Sometimes, the expression of

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