Bayesian variable selection method for modeling dose-response microarray data under simple order restrictions

Martin Otava¹, Ziv Shkedy¹, Dan Lin², Willem Talloen³ and Adetayo Kasim⁴

¹ Interuniversity Institute for Biostatistics and Statistical Bioinformatics (I-BioStat), Center for Statistics, Universiteit Hasselt, Campus Diepenbeek, Belgium
² Zoetis, Zaventem, Belgium
³ Janssen, Pharmaceutical companies of Johnson & Johnson, Beerse, Belgium
⁴ Wolfson Research Institute for Health and Wellbeing, Durham University, UK

Bayesian modeling of dose-response microarray data offers the possibility to jointly establish the dose-response relationships between gene expression and increasing doses of therapeutic compound, and to determine the nature of the relationships wherever it exist. We focus on an order restricted one-way ANOVA model which can be used in order to test the null hypothesis of no dose effect against an ordered alternative. Within the framework of dose-response modeling, model uncertainty can be addressed using model averaging techniques. In this setting, uncertainty is related to the number of all possible models that can be fitted to the data and should be taken into account for both inference and estimation. We propose an order restricted Bayesian variable selection (BVS) model that addresses model uncertainty and can be used for both inference and estimation. Moreover, correction for multiplicity adjustment for Bayesian modeling of dose-response microarray data can be based on the direct posterior probability of the null model. The posterior probabilities are obtained by translating the inequality constraints for monotone relationship into BVS problem. The extensive simulation studies were conducted to monitor actual performance of BVS for both gene-by-gene case as well for case of multiplicity adjustment and false discovery rate control. Results show that BVS can compete with available frequentist methods in terms of power.

Reference List