Incorporating Historical Data when Determining Sample Size Requirements for Aquatic Toxicity Experiments

Jing Zhang[1]; Yunzhi Kong[2]; A. John Bailer[1]; Zheng Zhu[3]; Byran Smucker[1]>

[1] Department of Statistics, Miami University, Oxford, OH 45056
[2] Georgetown University, Washington D.C, 20057
[3] Boehringer Ingelheim, 900 Ridgebury Rd, Ridgefield, CT 06877

Abstract:
To assess the toxicity of a chemical, aquatic toxicity experiments are designed and conducted to observe responses of interest (e.g. survival, reproduction) from organisms exposed to various concentration levels of the testing chemical. The adverse effects of the chemical on the responses are then evaluated and quantified as a function of the concentration levels. The resulting potency estimates, such as the relative inhibition concentrations (RIp) associated with a specified level of inhibition to the control responses, are used in decision-making and risk management. While an aquatic toxicity test often utilizes outcomes from a single experiment, laboratories commonly have a history of conducting such experiments using the same organism species and following the same experimental protocols. Also labs may study chemicals from the same chemical class or may operate using the mode of action in terms of toxicity. Sample size determination (SSD) is a crucial aspect of the design of aquatic toxicity tests: it is desirable to use as few organisms as possible, yet retain the same quality or precision of potency estimation. When the same underlying concentration-response relationship generates the “historical” and “current” experiments, a Bayesian approach incorporates the historical experimental outcomes through priors, hence increasing the amount of information used for potency estimation without increasing the sample size of the ”current” experiment. Therefore, informative priors using historical data can reduce the number of organisms used in toxicity tests without sacrificing the precision of potency estimates. In the present study, we propose a simulation-based Bayesian approach to explore the possibility of reducing the sample size when the prior input uses historical data at varying levels in the analysis of toxicity test results: (a) historical experimental outcomes in all concentration groups are used; (b) only historical control data are used; or (c) no historical data are used. The proposed approach is illustrated with analysis of the experiment outcomes when three different biological endpoints are of interest: survival (dichotomous response), fecundity (counts), and biomass/growth (continuous response). To determine the sample size, two inferential performance criteria based on the posterior samples of RIp’s are used: the average posterior variance criterion (APVC) and the average length criterion (ALC).

Keywords:
Bayesian, Historical Experimental Information, Power Priors, Potency Estimation, Sample Size Determination