

Information in a Two-Stage Adaptive Optimal Design

Adam Lane
Cincinnati Children's Hospital Medical Center
aclpp9@mail.missouri.edu

In *adaptive optimal designs*, each stage uses a locally optimal design evaluated at the maximum likelihood estimates derived using cumulative data from all prior stages. This dependency on prior stages affects Fisher's information, the asymptotic variance of the of maximum likelihood estimates. Fisher's information is motivated for use in adaptive designs with small samples by deriving the Cramèr-Rao lower bound for such experiments. Then the usefulness of Fisher's information is shown from both a design and analysis perspective. From a design perspective, the locally optimal stage one sample size is defined in terms of Fisher's information and a procedure to approximate it is suggested. From an analysis perspective, Fisher's information is compared to a commonly used information measure derived by ignoring the stage dependencies and to the observed information. To make the analysis explicit, a two stage design with fixed first stage is examined in the context of a general nonlinear regression model.