

Institute of Mathematical Statistics

LECTURE NOTES — MONOGRAPH SERIES

INFERENCE ON RANDOM COEFFICIENT MODELS FOR HAPLOTYPE EFFECTS IN DYNAMIC MUTATIONS USING MCMC.

Richard M. Huggins¹, Guoqi Qian¹ & Danuta Z. Loesch²¹Department of Statistical Sciences, La Trobe University, Bundoora, 3083,
Australia.²School of Psychological Science, La Trobe University, Bundoora, 3083,
Australia.

Abstract

Modern genetic research involves complex stochastic processes and difficult inference problems and research in this area is necessarily a collaboration with geneticists and biologists. The major difficulty is in defining stochastic processes which are biologically meaningful yet amenable to analysis. To illustrate this we examine a class of random effects models for dynamic mutations. Dynamic mutations characterize several inherited disorders in humans. In these disorders a mutated segment of the gene typically increases in size as it is transmitted from generation to generation until the gene fails. Biological interest is in the effect of various genetic markers on the rate of expansion of the mutated segment and to what extent these markers describe alternate pathways. We concentrate on the widely studied fragile X disorder as there are data sets available for statistical analysis. We use hierarchical Bayes models fitted via MCMC methods to examine some data and hence determine a class of random coefficients, branching, time series models which have applications in genetical research.

1 Introduction

The realistic modelling of the stochastic processes occurring in biology quickly leads to analytically intractable models. However, these models may be of enormous practical importance. Here we examine a model for the recently discovered phenomenon of dynamic mutations, that lead to a number of genetic disorders. In these disorders rather than an on-off allele being transmitted from a parent to their offspring the mutation itself changes upon transmission. The mutation arises through expansion at a region of the gene, i.e. the insertion of extra genetic material in the form of trinucleotide