Numerical Methods for Genetic Analysis of Complex Traits

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Abstract

This presentation is dedicated to the survey of the work which was done during my PhD study. The focus of my research is numerical algorithms for the efficient solution of QTL analysis problem in genetics. Firstly, we consider QTL mapping problems where a standard least-squares model is used for computing the model fit. We develop optimization methods for the local problems in a hybrid global-local optimization scheme for determining the optimal set of QTL locations. Here, the local problems have constant constraints and may be non-convex and/or flat in or more directions. We propose an enhanced Quasi-Newton method, where non-convex objective functions are handled by a specific approach for the Hessian computation. Also, we implement several schemes for constrained optimization and adopt them to the QTL optimization problems. We show that it is possible to use the new schemes to solve problems with up to 6 QTL efficiently and accurately, and that the work is reduced with up to two orders magnitude compared to using only global optimization. Secondly, we study numerical methods for QTL mapping where variance component estimation and a REML model is used. This results in a non-linear optimization problem for computing the model fit in each set of QTL locations. Here, we compare different optimization schemes and adopt them for the specifics of the problem. The results show that our version of the Active Set method is efficient and robust, which is not the case for methods used earlier. We also study the matrix operations performed inside the optimization loop, and develop more efficient algorithms for the REML computations. We develop a scheme for reducing the number of objective function evaluations, and we accelerate

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the computations of the gradient of the log-likelihood by the efficient scheme for computing the inverse of the variance-covariance matrix.