

## Maximized LOD scores over genetic models

**Yun Joo Yoo PhD**

Biostatistician

Stony Brook University

### Abstract:

When the genetic model parameter values assumed in the calculation for LOD score analysis are incorrect, significant power loss can occur in detecting the linkage between marker and trait. Maximized LOD and HLOD scores have been suggested and used to avoid the risk of assuming wrong parameter values. In this study, the null distribution and power of maximized LOD and HLOD scores over a finite number of models (LOD2, LOD20, HLOD2, HLOD20) and over the entire range of parameter space (MLOD, MHLOD) are investigated.

The theoretical asymptotic null distributions are obtained using the asymptotic theory of likelihood ratio statistics with boundary restrictions and theory of order statistics. Also, empirical null distributions are obtained using simulated data and compared favorably with the theoretical distribution. The null distributions of the maximized LOD or HLOD statistics over 2 or 20 parameter values are a maximum of two chi-square distributions assuming these have independent and identical distributions. The null distributions of MLOD and MHLOD scores are mixture chi-square distribution with df 1~6. The critical values obtained from the derived null distributions corresponding to the Type I error of 0.0001 are 3.3, 3.6 and 4.9 for LOD2, LOD20 and MLOD and 3.4, 3.7 and 5.0 for HLOD2, HLOD20, and MHLOD respectively.

The power values of maximized LOD and HLOD scores have been computed using the simulated data for the various genetic models. When the true genetic model is one of the included model parameter values for the maximization over 2 or 20 values, less maximization yields more power. However, the true genetic model is not one of the included models for maximization over finite models, MLOD or MHLOD is more powerful.