Introduction.

The details of applying the mixed effect model used in {PMID: 18385116}.

Matrix/vectors that will be used in this model:

, where represents the value for strain .

represent the design matrix for the haplotypes in the candidate block. In this example, suppose the haplotypes are , and .

since each strain has only one value.

: the kinship matrix, which will be estimated from the whole-genome SNP data

(so can be ignored and simply set to )

Here, , and are identical to all blocks, while is different for different blocks.

Function 0 (only calculated once)

Input (= if )

Decompose , where is orthonormal:

Function 1: from , , and , estimate , ,

Step 1: set . Decompose (= when ):

Where .

NOTE: Let , where is clearly independent of . Next, consider

Here, it is proved that we can find such that it is independent of as well, and the procedure to find is embedded in the proof.

Fixed an arbitrary decomposition of : . Here, and . We also have and . Note that if another matrix is orthonormal, then . Suppose that is decomposed to . Therefore, we have:

Therefore, with the choice of , the decomposition of is now independent of .

NOTE: for (or more generally, non-singular), the kinship matrix is assumed to be invertible, and has rank . So has the same rank as , which has rank .

Step 2: calculate .

Since is and is , is , i.e.:

Step 3: set the initial value of to each of

Step 4: for each , solve equation (9) use Newton-Raphson method:

Then, call Function 2 (the Newton-Raphson Method)

With final estimate , calculate the log-likelihood:

Since and are constant w.r.t. , only need to calculate:

Step 5:

Compare the log-likelihood function for each , find the with largest log-likelihood. Finally,

Function 2: New-Raphson method

Input . Using the function to calculate and , we have:

For

NOTE: we specify , so if , set and stop. if , set and stop. If , stop and return NULL.

Function 3 (hypothesis testing)

Le

I.e. . Here, is and full rank. Calculate:

Calculate p value as

Function 4: calculate the kinship matrix

Initialize diff\_count = .

For each SNP:

{

For each strain pair :

If allele at this SNP for strain and are both unambiguous and not equal to each other:

diff\_count[]++;

diff\_count[]++;

}

NOTE: because