|  |  |  |
| --- | --- | --- |
|  | Design matrix for fixed and random effects | Covariance matrix *G* |
| Model (A) |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameters |  |  |  |  |
|  | intercept | gene 1 | gene 2 | gene 3 |
| SNP A | 1 | 1 | 0 | 0 |
| SNP B | 1 | 1 | 1 | 0 |
| SNP C | 1 | 0 | 1 | 1 |

 |   |
| Model (B) |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameters |  |  |  |  |
|  | intercept | gene 1 | gene 2 | gene 3 |
| SNP A | 1 | 1 | 0 | 0 |
| SNP B | 1 | 1 | 1 | 0 |
| SNP C | 1 | 0 | 1 | 1 |

 | distance between physical locations of gene *i* and gene *i’* |

**Supplementary Fig. 1** The proposed Generalized Linear Mixed Models, with design matrix and covariance matrix for a hypothetical gene set with three genes and three SNPs: SNP A is on gene 1, SNP B is on genes 1 and 2, SNP C is on genes 2 and 3. For both models, the outcome variable for the mixed models is the chi-square statistic for Cochran-Armitage trend test for single SNP.