Multifactorial methods integrating haplotype and epistasis effects for genomic estimation and prediction of quantitative traits

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Text S1. Quantitative Genetics Models and Genomic Epistasis Relationship Matrices

Quantitative genetics (QG) model with additive and dominance effects and values
The mixed model with single-SNP additive and dominance effects, haplotype additive effects and pairwise SNP epistasis effects described below is based on the quantitative genetics (QG) model resulting from the genetic partition of single-SNP genotypic values (Da et al., 2014; Wang and Da, 2014), haplotype genotypic values (Da, 2015), and pairwise genotypic values (Cockerham, 1954). An advantage of this QG model is the readily available quantitative genetics interpretations of SNP additive and dominance effects, values and variances; haplotype additive effects, values and variances; epistasis effects, values and variances; and the corresponding SNP, haplotype and epistasis heritability estimates.

This section describes the QG-model of SNP additive and dominance effects of two loci that will be used for defining the epistasis models. Assuming two SNPs with alleles \(A\) and \(a\) at SNP 1 and \(B\) and \(b\) at SNP 2, the two-locus model with SNP additive and dominance effects for the nine two-locus genotypic values can be expressed as:

\[
\mathbf{g} = \mathbf{1}_9 \mu + \mathbf{a}_1 + \mathbf{a}_2 + \mathbf{d}_1 + \mathbf{d}_2 = \mathbf{1}_9 \mu + \mathbf{w}_{a1} \alpha_{1o} + \mathbf{w}_{a2} \alpha_{2o} + \mathbf{w}_{\delta1} \delta_{1o} + \mathbf{w}_{\delta2} \delta_{2o} \quad (S1.1)
\]

where \(\mathbf{g} = 9 \times 1\) column vector of genotypic values; \(\mu = \) common mean; \(\alpha_{io} = \) additive effect of SNP \(i\) \((i = 1, 2)\); \(\mathbf{w}_{ai} = 9 \times 1\) model matrix of \(\alpha_{io}\); \(\delta_{io} = \) dominance effect of SNP \(i\) \((i = 1, 2)\); \(\mathbf{w}_{\delta1} = 9 \times 1\) model matrix of \(\delta_{io}\), \(\mathbf{a}_i = \mathbf{w}_{ai} \alpha_{io} = 9 \times 1\) column vector of additive values of SNP \(i\) \((i = 1, 2)\);
and $d_i = \mathbf{w}_{a1} \delta_{io} = 9 \times 1$ column vector of dominance values of SNP $i$ ($i = 1, 2$). The additive codings of the genotypes of the $i$th SNP in $\mathbf{w}_{ai}$ are $w_{ai}^{11} = 2q_i$, $w_{ai}^{12} = q_i - p_i$, $w_{ai}^{22} = -2p_i$, and the dominance codings in $\mathbf{w}_{ai}$ are $w_{ai}^{11} = -2q_i^2$, $w_{ai}^{12} = 2p_i q_i$, and $w_{ai}^{22} = -2p_i^2$ for $A_iA_i$, $A_iA_2$ and $A_2A_2$ genotypes of the $i$th SNP respectively, with $p_i = \text{allele frequency of } A_i$ and $q_i = \text{allele frequency of } A_2$ (Da et al., 2014). Equation (S1.1) is the foundation for pairwise epistasis effects as the interaction between $\alpha_{io}$ and $\alpha_{2o}$, $\alpha_{io}$ and $\delta_{2o}$, $\delta_{io}$ and $\alpha_{io}$, and $\delta_{io}$ and $\delta_{2o}$ under the assumption of linkage equilibrium (LE) that allows simplified genomic epistasis relationship matrices based on SNP additive and dominance relationship matrices without creating the epistasis model matrices. Subscript ‘o’ denotes a genetic effect form the original quantitative genetics model of Equation (S1.1) and later will be removed in the parameterized and equivalent model resulting from the use of genomic relationship matrices.

**Epistasis effects, model matrices and values**

The epistasis effects defined by Cockerham method can cover high-order epistasis effects. However, the biological significance of high-order epistasis is unknown. This study only considers second- and third-order epistasis. Based on the single-SNP model of two loci defined by Equation (S1.1) and the epistasis effects defined by Cockerham (Cockerham, 1954), the model matrices of pairwise epistasis effects for $n$ individuals are expressed as the Hadamard products between the model matrices of the additive and dominance effects:

$$
\mathbf{E}_{2} = \mathbf{w}_{a1} \# \mathbf{w}_{a2} (a\alpha)_{o} + \mathbf{w}_{a1} \# \mathbf{w}_{\delta i} (a\delta)_{o} + \mathbf{w}_{a2} \# \mathbf{w}_{\delta i} (\delta\alpha)_{o} + \mathbf{w}_{\delta i} \# \mathbf{w}_{a2} (\delta\delta)_{o}
$$

(S1.2)

where $(a\alpha)_{o} = \text{additive \times additive (A\times A) epistasis effect} = \text{allele \times allele interaction effect}$, $(a\delta)_{o} = \text{additive \times dominance (A\times D) epistasis effects} = \text{allele \times genotype interaction effect}$, $(\delta\alpha)_{o} = \text{dominance \times additive (D\times A) epistasis effect} = \text{genotype \times allele interaction effect}$, $(\delta\delta)_{o} = \text{dominance \times dominance (D\times D) epistasis effect}$, $\mathbf{w}_{a1} \# \mathbf{w}_{a2} = \text{coefficients of } (a\alpha)_{o}$, $\mathbf{w}_{a1} \# \mathbf{w}_{\delta i} = \text{coefficients of } (a\delta)_{o}$, $\mathbf{w}_{a2} \# \mathbf{w}_{\delta i} = \text{coefficients of } (\delta\alpha)_{o}$, and ‘#’ indicates the Hadamard product. For $m$ SNPs and $n$ individuals, the total epistasis values of the genome as the summation of all pairwise epistasis values defined by Equation (S1.2) are:

$$
\mathbf{E}_{2} = \sum_{i=1}^{m-1} \sum_{j=i+1}^{m} \mathbf{w}_{ai} \# \mathbf{w}_{aj} (a\alpha)_{o} + \sum_{i=1}^{m-1} \sum_{j=i+1}^{m} \mathbf{w}_{a1} \# \mathbf{w}_{\delta i} (a\delta)_{o} + \sum_{i=1}^{m-1} \sum_{j=i+1}^{m} \mathbf{w}_{a2} \# \mathbf{w}_{\delta i} (\delta\alpha)_{o} + \sum_{i=1}^{m-1} \sum_{j=i+1}^{m} \mathbf{w}_{\delta i} \# \mathbf{w}_{a2} (\delta\delta)_{o}
$$

(S1.3)

$$
\mathbf{E}_{2} = \mathbf{a}a + \mathbf{a}d + \mathbf{d}a + \mathbf{d}d = \mathbf{a}a + (\mathbf{a}d)^{2} + \mathbf{d}d
$$

where $(a\alpha)_{o} = (\begin{smallmatrix} m \\ 2 \end{smallmatrix}) \times 1$ column vector of A\times A epistasis effects (with $(\begin{smallmatrix} m \\ 2 \end{smallmatrix}) = \text{m(m-1)/2 = allele \times allele interaction effects}$, $\mathbf{W}_{\alpha\alpha} = n \times (\begin{smallmatrix} m \\ 2 \end{smallmatrix})$ model matrix of $(a\alpha)_{o}$, $(a\delta)_{o} = (\begin{smallmatrix} m \\ 2 \end{smallmatrix}) \times 1$ column vector of A\times D epistasis effects = allele \times genotype interaction effects, $\mathbf{W}_{\alpha\delta} = n \times (\begin{smallmatrix} m \\ 2 \end{smallmatrix})$ model matrix of $(a\delta)_{o}$, $(\delta\alpha)_{o} = (\begin{smallmatrix} m \\ 2 \end{smallmatrix}) \times 1$ column vector of D\times A epistasis effects = genotype \times allele interaction effects, $\mathbf{W}_{\delta\alpha} = n \times (\begin{smallmatrix} m \\ 2 \end{smallmatrix})$ model matrix of $(\delta\alpha)_{o}$, $(\delta\delta)_{o} = (\begin{smallmatrix} m \\ 2 \end{smallmatrix}) \times 1$ column vector of D\times D epistasis effects =
genotype × genotype interaction effects, \( W_{\delta\delta} = n \times (m) \) model matrix of \((\delta\delta)_o\), \( aa = W_{aa} (aa)_o = n \times 1 \) column vector of genomic A×A epistasis values, \( ad = W_{ao} (a\delta)_o = n \times 1 \) column vector of genomic A×D epistasis values, \( da = W_{\delta a} (\delta a)_o = n \times 1 \) column vector of genomic D×A epistasis values, \( dd = W_{\delta\delta} (\delta\delta)_o = n \times 1 \) column vector of genomic D×D epistasis values, \( (a\delta)^{(2)}_o = n \times 1 \) column vector of genomic A×D and D×A epistasis values, \( \delta\alpha^{(2)}_o = [(a\delta)_o ',(\delta a)_o '] = 2(m) \times 1 \) column vector of A×D and D×A epistasis effects, \( W_{aa}^{(2)} = (W_{aa'}, W_{aa}) = n \times [2(m)] \) model matrix of \((a\delta)^{(2)}_o\), and superscript ‘(2)’ indicates the vector or matrix involves two alternative expressions.

Third-order epistasis effects, model matrices and values

The third-order epistasis values and effects under the QG model are:

\[
E_3 = \sum_{i=1}^{m-2} \sum_{j=1}^{m-1} \sum_{k=1}^{m} \left( w_{ai} \# w_{aj} \# w_{ak} \right) (a\alpha\alpha)_o + \sum_{i=1}^{m-2} \sum_{j=1}^{m-1} \sum_{k=1}^{m} \left( w_{ai} \# w_{aj} \# w_{ak} \right) (a\delta\delta)_o + \sum_{i=1}^{m-2} \sum_{j=1}^{m-1} \sum_{k=1}^{m} \left( w_{ai} \# w_{aj} \# w_{ak} \right) (a\alpha\delta)_o + \sum_{i=1}^{m-2} \sum_{j=1}^{m-1} \sum_{k=1}^{m} \left( w_{ai} \# w_{aj} \# w_{ak} \right) (a\alpha\delta)_o
\]

where

\( (aaa)_o = (m) \times 1 \) column vector of A×A×A effects with \((m) = m(m-1)(m-2) / 6\),

\( (aa\delta)_o = (m) \times 1 \) column vector of A×A×D effects,

\( (a\delta a)_o = (m) \times 1 \) column vector of A×D×A effects,

\( (\delta a\alpha)_o = (m) \times 1 \) column vector of D×A×A effects,

\( (a\delta\delta)_o = (m) \times 1 \) column vector of A×D×D effects,

\( (\delta a\delta)_o = (m) \times 1 \) column vector of D×A×D effects,

\( (\delta\delta a)_o = (m) \times 1 \) column vector of D×A×D effects,

\( (\delta\delta\delta)_o = (m) \times 1 \) column vector of D×D×A effects,

\( (aa\delta)^{(3)}_o = [(aa\delta)_o ',(a\delta a)_o ',(\delta a\alpha)_o '] = 3(m) \times 1 \) column vector of A×A×D, A×D×A and D×A×A effects,

\( (a\delta\delta)^{(3)}_o = [(a\delta\delta)_o ',(a\delta a)_o ',(\delta a\alpha)_o '] = 3(m) \times 1 \) column vector of A×D×D, D×A×D and D×D×A effects,
$W_{aaa} = n \times \binom{m}{3}$ model matrix of $(aaa)_o$,

$W^{(3)}_{aabd} = (W_{aad}, W_{a\deltaa}, W_{\deltaaa}) = n \times [3\binom{m}{3}]$ model matrix of $(a\delta\delta)_o$,

$W^{(3)}_{a\delta\delta} = (W_{a\delta\delta}, W_{\delta\deltaa}, W_{\delta\deltaa}) = n \times [3\binom{m}{3}]$ model matrix of $(a\delta\delta)_o$,

$W_{\delta\delta\delta} = n \times \binom{m}{3}$ model matrix of $(\delta\delta\delta)_o$,

$aaa = W_{aaa}(aaa)_o = n \times 1$ column vector of $A \times A \times A$ epistasis values,

$aad = n \times 1$ column vector of $A \times A \times D$ epistasis values,

$ada = n \times 1$ column vector of $A \times D \times A$ epistasis values,

$dad = n \times 1$ column vector of $D \times A \times D$ epistasis values,

$daa = n \times 1$ column vector of $D \times A \times A$ epistasis values,

$add = n \times 1$ column vector of $D \times D \times A$ epistasis values,

$ddc = n \times 1$ column vector of $D \times D \times D$ epistasis values.

An important point of Equations (S1.3) and (S1.4) is that the epistasis model matrices are expressed as the Hadamard products between SNP additive and dominance model matrices. This result is the foundation for calculating genomic epistasis relationship matrices using SNP additive and dominance model matrices without creating the epistasis model matrices.

Quantitative genetics model with haplotype additive effects and values
The haplotype additive effects and values are derived by the multiallelic genetic partition of haplotype genotypic values and variances, and the relationship between the haplotype additive effects and values is:

$h_a = W_{ah} a_{oh}$ (S1.5)

where $a_h = n \times 1$ haplotype genomic additive values, $a_{oh} = n_{oh} \times 1$ column vector of haplotype additive effects ($n_{oh} =$ number of haplotype additive effects), and $W_{ah} = n \times n_{oh}$ model matrix of $a_{oh}$. The haplotype coding represented by $w_{ij,k}$ in $W_{ah}$ is: $w_{ij,k} = 2p_k$ for $i, j \neq k$ ($a_{ij}$ and $a_{oik}$ do not share allele $k$), $w_{ij,k} = -(1 - 2p_k)$ for $i \neq j$ but $i \neq k$ or $j \neq k$ ($a_{ij}$ and $a_{oik}$ share allele $k$, $i \neq j$), and $w_{ij,k} = -2(1 - p_k)$ for $i = j = k$, where $a_{ij}$ = additive value of haplotype genotype with the $i^{th}$ and $j^{th}$ haplotypes, and $a_{oik}$ = additive effect or the average effect of gene substitution as the difference between the allelic (haplotype) effects of the first and the $k^{th}$ haplotypes (Da, 2015).
Integrated QG model and multifactorial notations (Model-I)

This integrated model is advantageous over the separate SNP, haplotype, and epistasis models, because the predicted effects or values of each effect type is based on the phenotypic values after removing the predicted effects or values of the remaining effect types, whereas such predicted effects or values are unavailable from the separate models, as shown in the main text.

Combining the additive and dominance values (Da et al., 2014), haplotype additive values (Equation S1.5), and the epistasis values (Equations S1.3 and S1.4), The integrated QG model with SNP additive and dominance, haplotype additive and epistasis effects and values is:

\[
g = 1\mu + a + d + a_a + aa + ad(2) + dd + aaa + aad(3) + add(3) + ddd
\]

\[
= 1\mu + W_a a_o + W_{\delta} \delta_o + W_{aa} a_{ao} + W_{aa}(aa)_{o} + W_{a\delta}(a\delta)_{o} + W_{\delta\delta}(\delta\delta)_{o} \\
+ W_{aaa}(aa\delta)_{o} + W_{aad}(aad)_{o} + W_{add}(add)_{o} + W_{\delta\delta\delta}(\delta\delta\delta)_{o}
\]

\[\text{(S1.6)}\]

where \( a_o = m \times 1 \) column vector of additive effects, \( W_a = N \times m \) model matrix of \( a_o \) with \( 2q_i \), \( q_i - p_i \), \( -2p_i \) values for the \( i \)th column; \( \delta_o = m \times 1 \) column vector of dominance effects, \( W_{\delta} = N \times m \) model matrix of \( \delta_o \) with \( -2q_i^2 \), \( 2p_i q_i \), and \( -2p_i^2 \) values for the \( i \)th column, \( a = n \times 1 \) column vector of additive values, \( d = n \times 1 \) column vector of dominance values.

With the precise definitions of genetic effects, values and model matrices by Equations S1.3-S1.6, the integrated QG model of Equation S1.6 can be expressed succinctly using multifactorial notations as:

\[
g = \mu I + \sum_{i=1}^{10} W_i \tau_{io} = \mu I + \sum_{i=1}^{10} u_i
\]

\[\text{(S1.7)}\]

where \( \tau_{io} = \) genetic effects of the \( i \)th effect type from the original QG model, \( W_i = \) model matrix of \( \tau_{io} \), \( u_i = W_i \tau_{io} = \) genetic values of the \( i \)th effect type.

Intra- and inter-chromosome pairwise epistasis effects, model matrices and values

An epistasis GWAS in Holstein cattle showed that intra- and inter-chromosome epistasis effects affected different traits differently, e.g., daughter pregnancy rate was mostly affected by inter-chromosome epistasis effects whereas milk production traits were mostly affected by intra-chromosome epistasis effects (Prakapenka et al., 2021). Genomic heritability estimates of intra- and inter-chromosome heritabilities using methods in this article showed that intra-chromosome A×A heritability was 0.031, and inter-chromosome A×A heritability 0.178 for daughter pregnancy rate (Liang et al., 2022), consistent with the GWAS results of 21% intra-chromosome and 79% inter-chromosome A×A effects among the top 33,552 pairs of A×A effects. Therefore, dividing pairwise epistasis effects into intra- and inter-chromosome epistasis effects for genomic prediction and estimation provides a tool to help understand epistasis effects.

Pairwise epistasis values of Equation (S1.3) are partitioned into intra- and inter-chromosome pairwise epistasis values:
\[ E_2 = W_{aa}^{\text{int}ra} (aa) + W_{ao}^{\text{(2)int}ra} (a\delta) + W_{\delta\delta}^{\text{int}er} (\delta\delta) = aa + (ad)^{(2)} + dd \]
\[ = [W_{aa}^{\text{int}ra} (aa) + W_{aa}^{\text{int}er} (aa)] + [W_{ao}^{\text{(2)int}ra} (a\delta) + W_{ao}^{\text{(2)int}er} (a\delta)] + [W_{\delta\delta}^{\text{int}er} (\delta\delta) + W_{\delta\delta}^{\text{int}er} (\delta\delta)] \]
\[ = [(aa) + (aa)] + [(ad)^{(2)} + (ad)^{(2)}] + [(dd) + (dd)] \]

where superscript ‘intra’ represents intra-chromosome and ‘inter’ represents inter-chromosome, \((aa)^{\text{intra}} = W_{aa}^{\text{intra}} (aa)\) is a column vector of intra-chromosome A×A values, \((aa)^{\text{inter}} = W_{aa}^{\text{inter}} (aa)\) is a column vector of inter-chromosome A×A values, \((ad)^{(2)} \) is a column vector of inter-chromosome A×D and D×A values, \((dd)^{(2)} \) is a column vector of inter-chromosome D×D values, \((aa)_{\text{intra}} = c_1 \) is a column vector of intra-chromosome A×A effects, \((aa)_{\text{inter}} = c_2 \) is a column vector of inter-chromosome A×A effects, \((a\delta)_{\text{intra}} = 2c_1 \) is a column vector of intra-chromosome A×D and D×A effects, \((a\delta)_{\text{inter}} = 2c_2 \) is a column vector of inter-chromosome A×D and D×A effects, \((\delta\delta)_{\text{intra}} = c_1 \) is a column vector of intra-chromosome D×D effects, \((\delta\delta)_{\text{inter}} = c_2 \) is a column vector of inter-chromosome D×D effects, \(W_{aa}^{\text{intra}} = n \times c_1 \) is a model matrix of \((aa)_{\text{intra}}\), \(W_{aa}^{\text{inter}} = n \times c_2 \) is a model matrix of \((aa)_{\text{inter}}\), \(W_{ao}^{\text{(2)intra}} = n \times 2c_1 \) is a model matrix of \((a\delta)_{\text{intra}}\), \(W_{ao}^{\text{(2)inter}} = n \times 2c_2 \) is a model matrix of \((a\delta)_{\text{inter}}\), \(W_{\delta\delta}^{\text{intra}} = n \times c_1 \) is a model matrix of \((\delta\delta)_{\text{intra}}\), \(W_{\delta\delta}^{\text{inter}} = n \times c_2 \) is a model matrix of \((\delta\delta)_{\text{inter}}\).

**Integrated QG model with intra- and inter-chromosome epistasis effects and multifactorial notations (Model-II)**

Replacing the pairwise epistasis effects, values and model matrices in Equation S1.6 with the intra- and inter-chromosome epistasis effects, values and model matrices of Equation S1.8 the integrated QG model with intra- and inter-chromosome epistasis effects is:

\[
g = \mu I + a + d + a_n + [(aa)^{\text{intra}} + (aa)^{\text{inter}}] + [(ad)^{(2)}^{\text{intra}} + (ad)^{(2)}^{\text{inter}}] + [(dd)^{(2)} + (dd)^{(3)} + (dd)] \]
\[= W_{aa}^{\text{int}ra} (aa) + W_{ao}^{\text{(2)int}ra} (a\delta) + W_{\delta\delta}^{\text{(3)int}er} (\delta\delta) + W_{\delta\delta}^{\text{(3)int}er} (\delta\delta) \]

With the precise definitions of genetic effects, values and model matrices by Equations S1.6 and S1.8, the integrated QG model of Equation S1.9 can be expressed succinctly using multifactorial notations as:
\[ g = \mu I + \sum_{i=1}^{13} W_i \tau_{io} = \mu I + \sum_{i=1}^{13} u_i \]  
(S1.10)

where \( \tau_{io} \) = genetic effects of the \( i^{th} \) effect type from the original QG model, \( W_i \) = model matrix of \( \tau_{io} \), \( u_i = W_i \tau_{io} \) = genetic values of the \( i^{th} \) effect type.

**General multifactorial model that covers both Model-I and Model-II**

The multifactorial model of Equations S1.7 and S.19 can be summarized by one general multifactorial model as:

\[ g = \mu I + \sum_{i=1}^{f} W_i \tau_{io} = \mu I + \sum_{i=1}^{f} u_i \]  
(S1.11)

where \( \tau_{io} \) = genetic effects of the \( i^{th} \) effect type from the original QG model, \( W_i \) = model matrix of \( \tau_{io} \), \( u_i = W_i \tau_{io} \) = genetic values of the \( i^{th} \) effect type, and \( f \) = number effect types, with \( f = 10 \) for Model-I of Equations S1.6 and S1.7, and \( f = 13 \) for Model-II of Equations S1.9 and S1.10.

**Genomic epistasis relationship matrices using model matrices**

Based on the general multifactorial model of Equation S.11 that covers both Model-I and Model-II, the genomic relationship matrices are:

\[ S_i = (W_i W_i') / k_i \]  
(S1.12)

\[ k_i = tr(W_i W_i')/n \]  
(S1.13)

where \( S_i \) = genomic epistasis relationship matrix of the \( i^{th} \) effect type, and \( k_i \) = the average of the diagonal elements of \( W_i W_i' \), originally proposed for genomic additive relationship matrix (Hayes and Goddard, 2010).

This article uses the \( k_i \) value of Equation S1.13 because the heritability estimate of each effect type has the interpretation of being the average variance of the genetic values for the effect type over all individuals, as shown in the main text. The original genomic relationship matrix uses the coefficient of total additive variance of all SNPs as the \( k_i \) value (VanRaden, 2008). We referred to the VanRaden method as Definition-I and the Hayes-Goddard method Definition-II (Da et al., 2014; Wang and Da, 2014). Definition-I is the genomic version of the pedigree additive relationship because Definition-I maintains the properties of the pedigree relationships and would be conceptually appropriate as the ‘genomic version’ of pedigree relationships. However, Definition-II will be used in this study because Definition-II yields the interpretation that the variance component is the average of the genetic variances of all individuals for the \( i^{th} \) type of genetic effects, although Definition-I and Definition-II have the same prediction accuracy, as shown in the main text.

Equations S1.12 and S1.13 use the original model matrices. For epistasis effects, the model matrices are difficult or impossible to compute. Two methods are available for calculating Equations S1.12 and S1.13 without creating the epistasis model matrices.

**Genomic epistasis relationship matrices without creating epistasis model matrices**

The computing difficulty due to creating epistasis model matrices can be removed by computing the approximate genomic epistasis relationship matrices (AGERM) as the genomic version of Henderson’s Hadamard products between additive and dominance relationship matrices (Su et al.,
2012; Muñoz et al., 2014; Vitezica et al., 2017), or by the exact genomic epistasis relationship matrices (EGERM). AGERM contains intra-locus epistasis that should not exist (Martini et al., 2020) and EGERM removes intra-locus epistasis from AGERM based on products between SNP genomic additive and dominance relationship matrices (Jiang and Reif, 2020; Martini et al., 2020). Although EGERM is theoretically more appealing than AGERM for being exact, the difference between these two methods in prediction accuracy and heritability estimates was nonexistent for a Holstein dataset with 78,964 SNPs (Liang et al., 2022) and was negligible for a swine dataset with 52,842 SNPs in this article, but EGERM required 21 times as much computing time as required by AGERM for the Holstein dataset, and required about 9 times as much computing time as required by AGERM for the swine dataset in this article. The lack of difference between these two methods and the computing inefficiency of EGERM should favor AGERM for its mathematical simplicity and computing efficiency at least for datasets with 50,000 or more SNPs. In this article, we use general notations of genomic epistasis relationship matrices defined by Equation S1.12 that can be either AGERM or EGERM. The EPIHAP computing package (Liang et al., 2021, 2022) implements both AGERM or EGERM. The use of AGERM or EGERM implies the assumption of linkage equilibrium (LE). Both AGERM and EGERM have general formulations to cover any order of epistasis effects, but no evidence is available in livestock populations showing the epistasis beyond the third-order have contributions to the phenotypic variance and prediction accuracy. Therefore, this article limits to second- and third-order epistasis effects.

**Exact genomic epistasis relationship matrices (EGERM)**

For EGERM, we use the general formula of Jiang and Reif (Jiang and Reif, 2020). For the example of pairwise epistasis effects in Equation S1.6, the products of the epistasis model matrices for defining pairwise EGERM are calculated as:

\[
W_{aa}W_{aa}^{'} = \frac{1}{2}[(W_{a}W_{a}^{'}#(W_{a}W_{a}^{'})) - (W_{a}W_{a}^{'})(W_{a}W_{a}^{'})] \quad (S1.14)
\]

\[
W^{(2)}_{aa}W^{(2)}_{aa}^{'} = W_{aa}W_{aa}^{'} + W_{aa}W_{aa}^{'}
\]

\[
= \{(W_{a}W_{a}^{'}#(W_{a}W_{a}^{'})) - (W_{a}W_{a}^{'})(W_{a}W_{a}^{'})\}
\]

\[
+ \{(W_{a}W_{a}^{'}#(W_{a}W_{a}^{'})) - (W_{a}W_{a}^{'})(W_{a}W_{a}^{'})\} / 2
\]

\[
= \{(W_{a}W_{a}^{'}#(W_{a}W_{a}^{'})) - (W_{a}W_{a}^{'})(W_{a}W_{a}^{'})\}
\]

\[
W_{aa}W_{aa}^{'} = \frac{1}{2}[(W_{a}W_{a}^{'}#(W_{a}W_{a}^{'})) - (W_{a}W_{a}^{'})(W_{a}W_{a}^{'})] \quad (S1.16)
\]

In Equations S1.14-S1.16, SNP additive and dominance model matrices are used, and no epistasis model matrix needs to be created. In Equation 3.1.34, \(W_{a}W_{a}^{'} = W_{a}W_{a}^{'}\).

**Pairwise intra- and inter-chromosome EGERM**

Based on the products of the epistasis model matrices, the numerators of intra- and inter-chromosome pairwise EGERM are calculated as:

\[
W_{aa}^{int\text{ra}} (W_{aa}^{int\text{ra}})^{'} = \sum_{i=1}^{ch} (W_{ai}^{i}W_{ai}^{i})
\]

\[
= \frac{1}{2} \sum_{i=1}^{ch} [(W_{ai}^{i}W_{ai}^{i})#(W_{ai}^{i}W_{ai}^{i}) - (W_{ai}^{i}W_{ai}^{i})(W_{ai}^{i}W_{ai}^{i})]
\]

\[
W_{aa}^{int\text{er}} (W_{aa}^{int\text{er}})^{'} = W_{aa}^{'} - W_{aa}^{int\text{ra}} (W_{aa}^{int\text{ra}})^{'} \quad (S1.17)
\]

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where ch = number of chromosomes. The intra- and inter-chromosome pairwise EGERM are:

\[
W_{\text{int}Ra} (W_{\text{intra}}) = \sum_{i=1}^{\text{ch}} (W_{\text{intra}}^{ij} W_{\text{intra}}^{ij} + W_{\text{intra}}^{ij} W_{\text{intra}}^{ij})
\]

\[
W_{\text{inter}} (W_{\text{intra}}) = W_{\text{intra}}^{(2)} - W_{\text{intra}}^{(2) \text{intra}}[W_{\text{intra}}^{(2) \text{intra}}]
\]

\[
W_{\text{int}Ra} (W_{\text{intra}}) = \sum_{i=1}^{\text{ch}} (W_{\text{intra}}^{ij} W_{\text{intra}}^{ij})
\]

\[
W_{\text{inter}} (W_{\text{intra}}) = W_{\text{intra}}^{(2)} - W_{\text{intra}}^{(2) \text{intra}} (W_{\text{intra}}^{(2) \text{intra}})
\]

Approximate genomic epistasis relationship matrices (AGERM)
Let A = pedigree additive relationship matrix, and D = pedigree dominance relationship matrix. Then, Henderson defined each epistasis relationship matrix as a Hadamard product of A and D matrices (Henderson, 1985). For Model-I:

\[
S_4 = S_{4Ra} = W_{\text{intra}}^{(4)} / k_{\text{intra}}
\]

\[
S_5 = S_{5Ra} = W_{\text{inter}}^{(5)} / k_{\text{inter}}
\]

\[
S_6 = S_{6Ra} = W_{\text{intra}}^{(6)} / k_{\text{int}Ra}
\]

\[
S_7 = S_{7Ra} = W_{\text{inter}}^{(7)} / k_{\text{int}Ra}
\]

\[
S_8 = S_{8Ra} = W_{\text{intra}}^{(8)} / k_{\text{intra}}
\]

\[
S_9 = S_{9Ra} = W_{\text{inter}}^{(9)} / k_{\text{int}Ra}
\]

where

\[
k_{\text{intra}} = \text{tr}[W_{\text{intra}} (W_{\text{intra}})] / n
\]

\[
k_{\text{inter}} = \text{tr}[W_{\text{inter}} (W_{\text{inter}})] / n
\]

\[
k_{\text{int}Ra} = \text{tr}[W_{\text{intra}}^{(2) \text{intra}}] / n
\]

\[
k_{\text{intra}} = \text{tr}[W_{\text{intra}}^{(2) \text{intra}} (W_{\text{intra}}^{(2) \text{intra}})] / n
\]

\[
k_{\text{int}Ra} = \text{tr}[W_{\text{int}Ra} (W_{\text{int}Ra})] / n
\]

As shown by Equations S1.14-S1.22, the calculations of Equations S1.23-S1.34 are based on the model matrices of SNP additive and dominance effects and do not involve the epistasis model matrices.
Approximate genomic epistasis relationship matrices are the genomic version of Henderson’s epistasis relationship matrices with the pedigree A and D matrices replaced by the genomic additive and dominance relationship matrices (Su et al., 2012). Using notations in this article, genomic additive and dominance relationship matrices that are the genomic versions of pedigree additive and dominance relationship matrices are:

\[
A = S_1 = S_2 = W_a W_a' / (2\sum_{i=1}^{m} p_i q_i) = W_i W_i' / (2\sum_{i=1}^{m} p_i q_i)
\]  

(S1.42)

\[
D = S_2 = S_2 = W_\delta W_\delta' / (4\sum_{i=1}^{m} p_i^2 q_i^2) = W_2 W_2' / (4\sum_{i=1}^{m} p_i^2 q_i^2)
\]  

(S1.43)

Replacing the A and D in Equations S1.35-S1.41 with those of Equations S1.42 and S1.43 yields the AGERM.

**Pairwise intra- and inter-chromosome AGERM**

For Model-II, the numerators of the intra- and inter-chromosome AGERM can be derived from those of AGERM. In Equations S1.14-S1.16, the minus term is for removing intra-locus epistasis that is contained in AGERM but should exist. Therefore, removing the minus terms of Equations S1.14-S1.16 yields the numerators of AGERM, i.e.:

\[
W_{aa}W_{aa}' = \frac{1}{2}(W_a W_a')#(W_a W_a ')
\]  

(S1.44)

\[
W^{(2)}_{aa}W^{(2)}_{aa}' = W_{aa}W_{aa} + W_{aa}W_{aa} = (W_a W_a')#(W_\delta W_\delta ')
\]  

(S1.45)

\[
W_{\delta\delta}W_{\delta\delta}' = \frac{1}{2}(W_\delta W_\delta')#(W_\delta W_\delta ')
\]  

(S1.46)

noting that the left-hand-side of Equations S1.14-S1.16 and S1.23-S1.25 are the same, but the right-hand-side are different. Similarly, the numerators of the intra-chromosome epistasis relationships based on the additive and dominance model matrix of each chromosome, i.e.:

\[
W^{\text{int ra}}_{aa} (W^{\text{int ra}}_{aa})' = \sum_{i=1}^{ch} (W_{aa}^{i} W_{aa}^{i}) = \frac{1}{2} \sum_{i=1}^{ch} (W_a^{i} W_a^{i}) #(W_a^{i} W_a^{i})
\]  

(S1.47)

\[
W^{(2)}_{aa} [W^{(2)}_{aa}] = \sum_{i=1}^{ch} (W_{aa}^{i} W_{aa}^{i} + W_{aa}^{i} W_{aa}^{i}) = \sum_{i=1}^{ch} (W_a^{i} W_a^{i}) #(W_\delta^{i} W_\delta^{i})
\]  

(S1.48)

\[
W^{\text{int ra}}_{\delta\delta} (W^{\text{int ra}}_{\delta\delta})' = \sum_{i=1}^{ch} (W_\delta^{i} W_\delta^{i}) = \frac{1}{2} \sum_{i=1}^{ch} (W_\delta^{i} W_\delta^{i}) #(W_\delta^{i} W_\delta^{i})
\]  

(S1.49)

where ch = number of chromosomes. Then, the numerators of the inter-chromosome epistasis relationship matrices are calculated as the difference between the numerators of the A # A, A # D and D # D genomic relationships matrices and the numerators of the intra-chromosome relationship matrices, i.e.:

\[
W^{\text{inter}}_{aa} (W^{\text{inter}}_{aa})' = W_{aa}W_{aa}' - W^{\text{int ra}}_{aa} (W^{\text{int ra}}_{aa})'
\]  

(S1.50)

\[
W^{(2)}_{aa} [W^{(2)}_{aa}] = W^{(2)}_{aa} W^{(2)}_{aa} - W^{(2)}_{aa} W^{(2)}_{aa} [W^{(2)}_{aa}]
\]  

(S1.51)

\[
W^{\text{inter}}_{\delta\delta} (W^{\text{inter}}_{\delta\delta})' = W_{\delta\delta}W_{\delta\delta}' - W^{\text{int ra}}_{\delta\delta} (W^{\text{int ra}}_{\delta\delta})'
\]  

(S1.52)
Then, the pairwise intra- and inter-chromosome AGERM are:

\[ S_4 = S_4^{\text{intra}} = (W_{aa}^T W_{aa})^{\text{int}} / k_{aa}^{\text{int}} = \left[ \sum_{i=1}^{\text{ch}} (W_{ai}^T W_{ai}) \right] / k_{aa}^{\text{int}} \] (S1.53)

= intra-chromosome A×A AGERM

\[ S_5 = S_4^{\text{inter}} = W_{aa}^T W_{aa}^{\text{inter}} / k_{aa}^{\text{inter}} = \left[ \sum_{i=1}^{\text{ch}} (W_{ai}^T W_{ai}) \right] / k_{aa}^{\text{inter}} \] (S1.54)

= inter-chromosome A×A AGERM

\[ S_6 = S_6^{\text{intra}} = \left( W_{a\delta}^T W_{a\delta} \right) / k_{a\delta}^{\text{intra}} = \left[ \sum_{i=1}^{\text{ch}} (W_{ai}^T W_{ai}) \right] / k_{a\delta}^{\text{intra}} \] (S1.55)

= intra-chromosome A×D AGERM

\[ S_7 = S_7^{\text{inter}} = W_{a\delta}^T W_{a\delta}^{\text{inter}} / k_{a\delta}^{\text{inter}} = \left[ \sum_{i=1}^{\text{ch}} (W_{ai}^T W_{ai}) \right] / k_{a\delta}^{\text{inter}} \] (S1.56)

= inter-chromosome A×D AGERM

\[ S_8 = S_6^{\text{intra}} = W_{a\delta}^T W_{a\delta}^{\text{inter}} / k_{a\delta}^{\text{intra}} = \left[ \sum_{i=1}^{\text{ch}} (W_{ai}^T W_{ai}) \right] / k_{a\delta}^{\text{intra}} \] (S1.57)

= intra-chromosome D×D AGERM

\[ S_9 = S_6^{\text{inter}} = W_{a\delta}^T W_{a\delta}^{\text{inter}} / k_{a\delta}^{\text{inter}} = \left[ \sum_{i=1}^{\text{ch}} (W_{ai}^T W_{ai}) \right] / k_{a\delta}^{\text{inter}} \] (S1.58)

= inter-chromosome D×D AGERM

where

\[ k_{aa}^{\text{int}} = \text{tr} \left[ W_{aa} W_{aa}^T \right] / n = \text{tr} \left[ \sum_{i=1}^{\text{ch}} (W_{ai}^T W_{ai}) \right] / n \] (S1.59)

\[ k_{aa}^{\text{inter}} = \text{tr} \left[ W_{aa} W_{aa}^T \right] / n = \frac{1}{2} \text{tr} \left[ \sum_{i=1}^{\text{ch}} (W_{ai}^T W_{ai}) \right] / n \] (S1.60)

\[ k_{a\delta}^{\text{intra}} = \text{tr} \left[ \left( W_{a\delta}^T W_{a\delta} \right) \right] / n = \text{tr} \left[ \left( W_{a\delta}^T W_{a\delta} \right) \right] / n \] (S1.61)

\[ k_{a\delta}^{\text{inter}} = \text{tr} \left[ \left( W_{a\delta}^T W_{a\delta} \right) \right] / n = \text{tr} \left[ \left( W_{a\delta}^T W_{a\delta} \right) \right] / n \] (S1.62)

\[ k_{a\delta}^{\text{intra}} = \text{tr} \left[ \left( W_{a\delta}^T W_{a\delta} \right) \right] / n = \frac{1}{2} \text{tr} \left[ \sum_{i=1}^{\text{ch}} (W_{ai}^T W_{ai}) \right] / n \] (S1.63)

\[ k_{a\delta}^{\text{inter}} = \text{tr} \left[ \left( W_{a\delta}^T W_{a\delta} \right) \right] / n = \text{tr} \left[ \left( W_{a\delta}^T W_{a\delta} \right) \right] / n \] (S1.64)

Note that AGERM of Equations S1.53-S1.58 and EGERM of Equations S1.23-S1.28 have the same general expression defined by Equations S1.12-S1.13 but the right-hand-side of the EGERM and AGERM are different.

References
Cockerham, C. C. 1954. An extension of the concept of partitioning hereditary variance for analysis of covariances among relatives when epistasis is present. Genetics 39(6):859.
Da, Y. 2015. Multi-allelic haplotype model based on genetic partition for genomic prediction and variance component estimation using SNP markers. BMC Genetics 16(1):144.
Da, Y., C. Wang, S. Wang, and G. Hu. 2014. Mixed model methods for genomic prediction and variance component estimation of additive and dominance effects using SNP markers. PLoS One 9(1):e87666.
Hayes, B., and M. Goddard. 2010. Genome-wide association and genomic selection in animal breeding. Genome 53(11):876-883.
Henderson, C. 1985. Best linear unbiased prediction of nonadditive genetic merits in noninbred populations. Journal of Animal Science 60(1):111-117.
Jiang, Y., and J. C. Reif. 2020. Efficient algorithms for calculating epistatic genomic relationship matrices. Genetics 216(3):651-669.

Liang, Z., D. Prakapenka, and Y. Da. 2021. EPIHAP: a computing tool for genomic estimation and prediction using global epistasis effects and haplotype effects. Abstract P167, page 223 of ADSA2021 Abstracts, ADSA 2021 Virtual Annual Meeting. https://www.adsa.org/Portals/0/SiteContent/Docs/Meetings/2021ADSA/ADSA2021_Abstracts.pdf.

Liang, Z., D. Prakapenka, and Y. Da. 2022. Comparison of two methods of genomic epistasis relationship matrices using daughter pregnancy rate in U.S. Holstein cattle. Abstract 2466V, page 409 of ADSA2022 Abstracts. https://www.adsa.org/Portals/0/SiteContent/Docs/Meetings/2022ADSA/Abstracts_BOOK_2022.pdf?v=20220613.

Martini, J. W., F. H. Toledo, and J. Crossa. 2020. On the approximation of interaction effect models by Hadamard powers of the additive genomic relationship. Theoretical population biology 132:16-23.

Muñoz, P. R., M. F. Resende, S. A. Gezan, M. D. V. Resende, G. de los Campos, M. Kirst, D. Huber, and G. F. Peter. 2014. Unraveling additive from nonadditive effects using genomic relationship matrices. Genetics 198(4):1759-1768.

Prakapenka, D., Z. Liang, J. Jiang, L. Ma, and Y. Da. 2021. A Large-scale genome-wide association study of epistasis effects of production traits and daughter pregnancy rate in US Holstein cattle. Genes 12(7):1089.

Su, G., O. F. Christensen, T. Ostersen, M. Henryon, and M. S. Lund. 2012. Estimating additive and non-additive genetic variances and predicting genetic merits using genome-wide dense single nucleotide polymorphism markers. PloS One 7(9):e45293.

VanRaden, P. M. 2008. Efficient methods to compute genomic predictions. Journal of Dairy Science 91(11):4414-4423.

Vitezica, Z. G., A. Legarra, M. A. Toro, and L. Varona. 2017. Orthogonal estimates of variances for additive, dominance, and epistatic effects in populations. Genetics 206(3):1297-1307.

Wang, C., and Y. Da. 2014. Quantitative genetics model as the unifying model for defining genomic relationship and inbreeding coefficient. PLoS One 9(12):e114484.
Text S2. Numerical Demonstration

This is a summary of the results from DEMO.R program for numerical demonstration of the methods in this article. The small dataset is for the convenience of reading the numerical results. The haplotype data is adopted from the numerical example in Da (2015) and is not derived from the small SNP data set, which does not have any accuracy for imputing haplotypes. Detailed procedure to produce haplotype data from the SNP data is described in the GVHHAP computing pipeline (Prakapenka et al., 2020). The SNP and haplotype data are completely artificial for showing calculations only without any genetic or methodology implications.

Phenotypic values, SNP and haplotype genotypes, fixed effects

The dataset in this demo consists of 5 individuals with one missing phenotypic value for individual #5.

The column vector of the phenotypic values for the four individuals with phenotypic observations is:

\[ y = (1.753222, 1.617655, 1.713119, 1.738835)' \]

The fixed non-genetic effects are male and female, with individuals 1 and 2 having a sex code of ‘2’, and individuals 3 and 4 having a sex code of ‘1’. The \( X \) matrix for these fixed effects is:

\[
\begin{array}{ccc}
1 & 0 & 1 \\
2 & 0 & 1 \\
3 & 1 & 0 \\
4 & 1 & 0 \\
\end{array}
\]

Each individual has one phenotypic observation, so the \( Z \) matrix is an identity matrix.

Each individual has 6 SNP markers:

```
#6 MARKERS, 5 INDIVIDUALS
# LOC1:  0-0-1-0-1
# LOC2:  2-0-1-1-1
# LOC3:  0-0-1-0-1
# LOC4:  1-1-2-0-1
# LOC5:  0-2-0-1-1
# LOC6:  2-0-1-1-0
```

where ‘0’ indicate a homozygous genotype (AA), ‘2’ indicates the other homozygous genotype (aa), and ‘1’ indicates the heterozygous genotype (Aa) of the SNP.

The 5 individuals have one haplotype block that is treated as a ‘locus’ with four haplotypes that each was treated as an ‘allele’. The haplotype frequencies of the four haplotypes are 0.4, 0.3, 0.2 and 0.1 for haplotypes 1, 2 3 and 4 respectively.

Calculation of allele frequencies

Lines 42-75 in DEMO.R calculate the allele frequencies of the 6 SNPs from the SNP genotypes of the 5 individuals.
SNP additive and dominance codings

Lines 78-100 in DEMO.R calculate the additive coding for each SNP genotype, and lines 110-132 calculate the dominance coding for each SNP genotype using formulae described in the main text.

Model matrices of SNP additive and dominance effects

Lines 102-107 and line 144 in DEMO.R calculate the SNP additive model matrix, and lines 110-139 and line 145 calculate the SNP dominance model matrix.

\[ W_α(W_1): \]

|     | SNP1 | SNP2 | SNP3 | SNP4 | SNP5 | SNP6 |
|-----|------|------|------|------|------|------|
| ID1 | 0.4  | -1   | 0.4  | 0    | 0.8  | -1.2 |
| ID2 | 0.4  | 1    | 0.4  | 0    | -1.2 | 0.8  |
| ID3 | -0.6 | 0    | -0.6 | -1   | 0.8  | -0.2 |
| ID4 | 0.4  | 0    | 0.4  | 1    | -0.2 | -0.2 |
| ID5 | -0.6 | 0    | -0.6 | 0    | -0.2 | 0.8  |

\[ W_δ(W_2): \]

|     | SNP1 | SNP2 | SNP3 | SNP4 | SNP5 | SNP6 |
|-----|------|------|------|------|------|------|
| ID1 | -0.08| -0.5 | -0.08| 0.5  | -0.32| -0.72|
| ID2 | -0.08| -0.5 | -0.08| 0.5  | -0.72| -0.32|
| ID3 | 0.32 | 0.5  | 0.32 | -0.5 | -0.32| 0.48 |
| ID4 | -0.08| 0.5  | -0.08| -0.5 | 0.48 | 0.48 |
| ID5 | 0.32 | 0.5  | 0.32 | 0.5  | 0.48 | -0.32|

Haplotype additive codings

Lines 519-541 in DEMO.R calculate the haplotype additive coding for each genotype of two pairing haplotypes. The haplotype data is artificial for showing calculations only.

Model matrix of haplotype additive effects

Lines 546 in DEMO.R calculates the haplotype additive model matrix.

\[ W_{αh}(W_3): \]

|     | HAP1 | HAP2 | HAP3 |
|-----|------|------|------|
| ID1 | 0.6  | 0.4  | 0.2  |
| ID2 | -1.4 | 0.4  | 0.2  |
| ID3 | 0.6  | -1.6 | 0.2  |
| ID4 | 0.6  | 0.4  | -1.8 |
| ID5 | -0.4 | 0.4  | 0.2  |
Pairwise epistasis
Lines 152-501 in DEMO.R calculates the pairwise epistasis model matrices.

\[ W_{aa} (W_4 \text{ under Model-I}): \]

|        | SNP1_2 | SNP1_3 | SNP1_4 | SNP1_5 | SNP1_6 |
|--------|--------|--------|--------|--------|--------|
| ID1    | -0.4   | 0.16   | 0      | 0.32   | -0.48  |
| ID2    | 0.4    | 0.16   | 0      | -0.48  | 0.32   |
| ID3    | 0      | 0.36   | 0.6    | -0.48  | 0.12   |
| ID4    | 0      | 0.16   | 0.4    | -0.08  | -0.08  |
| ID5    | 0      | 0.36   | 0      | 0.12   | -0.48  |

|        | SNP2_3 | SNP2_4 | SNP2_5 | SNP2_6 | SNP3_4 |
|--------|--------|--------|--------|--------|--------|
| ID1    | -0.4   | 0      | -0.8   | 1.2    | 0      |
| ID2    | 0.4    | 0      | -1.2   | 0.8    | 0      |
| ID3    | 0      | 0      | 0      | 0      | 0.6    |
| ID4    | 0      | 0      | 0      | 0      | 0.4    |
| ID5    | 0      | 0      | 0      | 0      | 0      |

|        | SNP3_5 | SNP3_6 | SNP4_5 | SNP4_6 | SNP5_6 |
|--------|--------|--------|--------|--------|--------|
| ID1    | 0.32   | -0.48  | 0      | 0      | -0.96  |
| ID2    | -0.48  | 0.32   | 0      | 0      | -0.96  |
| ID3    | -0.48  | 0.12   | -0.8   | 0.2    | -0.16  |
| ID4    | -0.08  | -0.08  | -0.2   | -0.2   | 0.04   |
| ID5    | 0.12   | -0.48  | 0      | 0      | -0.16  |

\[ W_{ab} (\text{part of } W_5 \text{ under Model-I}): \]

|        | SNP1_2 | SNP1_3 | SNP1_4 | SNP1_5 | SNP1_6 |
|--------|--------|--------|--------|--------|--------|
| ID1    | -0.2   | -0.032 | 0.2    | -0.128 | -0.288 |
| ID2    | -0.2   | -0.032 | 0.2    | -0.288 | -0.128 |
| ID3    | -0.3   | -0.192 | 0.3    | 0.192  | -0.288 |
| ID4    | 0.2    | -0.032 | -0.2   | 0.192  | 0.192  |
| ID5    | -0.3   | -0.192 | -0.3   | -0.288 | 0.192  |

|        | SNP2_3 | SNP2_4 | SNP2_5 | SNP2_6 | SNP3_4 |
|--------|--------|--------|--------|--------|--------|
| ID1    | 0.08   | -0.5   | 0.32   | 0.72   | 0.2    |
| ID2    | -0.08  | 0.5    | -0.72  | -0.32  | 0.2    |
| ID3    | 0      | 0      | 0      | 0      | 0.3    |
| ID4    | 0      | 0      | 0      | 0      | -0.2   |
| ID5    | 0      | 0      | 0      | 0      | -0.3   |

|        | SNP3_5 | SNP3_6 | SNP4_5 | SNP4_6 | SNP5_6 |
|--------|--------|--------|--------|--------|--------|
| ID1    | -0.128 | -0.288 | 0      | 0      | -0.576 |
| ID2    | -0.288 | -0.128 | 0      | 0      | 0.384  |
| ID3    | 0.192  | -0.288 | 0.32   | -0.48  | 0.384  |

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\( \mathbf{W}_{ss} (\text{part of } \mathbf{W}_s \text{ under Model-I}): \)

|        | SNP1_2 | SNP1_3 | SNP1_4 | SNP1_5 | SNP1_6 |
|--------|--------|--------|--------|--------|--------|
| ID1    | 0.08   | -0.032 | 0      | -0.064 | 0.096  |
| ID2    | -0.08  | -0.032 | 0      | 0.096  | -0.064 |
| ID3    | 0      | -0.192 | -0.32  | 0.256  | -0.064 |
| ID4    | 0      | -0.032 | -0.08  | 0.016  | 0.016  |
| ID5    | 0      | -0.192 | 0      | -0.064 | 0.256  |

|        | SNP2_3 | SNP2_4 | SNP2_5 | SNP2_6 | SNP3_4 |
|--------|--------|--------|--------|--------|--------|
| ID1    | -0.2   | 0      | -0.4   | 0.6    | 0      |
| ID2    | -0.2   | 0      | 0.6    | -0.4   | 0      |
| ID3    | -0.3   | -0.5   | 0.4    | -0.1   | -0.32  |
| ID4    | 0.2    | 0.5    | -0.1   | -0.1   | -0.08  |
| ID5    | -0.3   | 0      | -0.1   | 0.4    | 0      |

|        | SNP3_5 | SNP3_6 | SNP4_5 | SNP4_6 | SNP5_6 |
|--------|--------|--------|--------|--------|--------|
| ID1    | -0.064 | 0.096  | 0.4    | -0.6   | 0.384  |
| ID2    | 0.096  | -0.064 | -0.6   | 0.4    | -0.576 |
| ID3    | 0.256  | -0.064 | -0.4   | 0.1    | 0.064  |
| ID4    | 0.016  | 0.016  | 0.1    | 0.1    | -0.096 |
| ID5    | -0.064 | 0.256  | -0.1   | 0.4    | 0.384  |

\( \mathbf{W}_{ss} (\mathbf{W}_s \text{ under Model-I}): \)

|        | SNP1_2 | SNP1_3 | SNP1_4 | SNP1_5 | SNP1_6 |
|--------|--------|--------|--------|--------|--------|
| ID1    | 0.04   | 0.0064 | -0.04  | 0.0256 | 0.0576 |
| ID2    | 0.04   | 0.0064 | -0.04  | 0.0576 | 0.0256 |
| ID3    | 0.16   | 0.1024 | -0.16  | -0.1024 | 0.1536 |
| ID4    | -0.04  | 0.0064 | 0.04   | -0.0384 | -0.0384 |
| ID5    | 0.16   | 0.1024 | 0.16   | 0.1536 | -0.1024 |

|        | SNP2_3 | SNP2_4 | SNP2_5 | SNP2_6 | SNP3_4 |
|--------|--------|--------|--------|--------|--------|
| ID1    | 0.04   | -0.25  | 0.16   | 0.36   | -0.04  |
| ID2    | 0.04   | -0.25  | 0.36   | 0.16   | -0.04  |
| ID3    | 0.16   | -0.25  | -0.16  | 0.24   | -0.16  |
| ID4    | -0.04  | -0.25  | 0.24   | 0.24   | 0.04   |
| ID5    | 0.16   | 0.25   | 0.24   | -0.16  | 0.16   |

|        | SNP3_5 | SNP3_6 | SNP4_5 | SNP4_6 | SNP5_6 |
|--------|--------|--------|--------|--------|--------|
| ID1    | 0.0256 | 0.0576 | -0.16  | -0.36  | 0.2304 |
| ID2    | 0.0576 | 0.0256 | -0.36  | -0.16  | 0.2304 |
| ID3    | -0.1024 | 0.1536 | 0.16   | -0.24  | -0.1536 |
| ID4    | -0.0384 | -0.0384 | -0.24  | -0.24  | 0.2304 |
Additive and dominance genomic relationship matrices

Lines 552-554 in DEMO.R calculate the additive genomic matrix, and lines 559-561 calculate the dominance genomic matrix.

\[
S_a(S_1): \\
\begin{array}{ccccc}
ID1 & ID2 & ID3 & ID4 & ID5 \\
ID1 & 1.4166667 & -1.0833333 & 0.1666667 & 0.1666667 & -0.6666667 \\
ID2 & -1.0833333 & 1.4166667 & -0.6666667 & 0.1666667 & 0.1666667 \\
ID3 & 0.1666667 & -0.6666667 & 1 & -0.66667 & 0.1666667 \\
ID4 & 0.1666667 & 0.1666667 & -0.6666667 & 0.583333 & -0.25 \\
ID5 & -0.6666667 & 0.1666667 & 0.1666667 & -0.25 & 0.5833333 \\
\end{array}
\]

\[
S_d(S_2): \\
\begin{array}{ccccc}
ID1 & ID2 & ID3 & ID4 & ID5 \\
ID1 & 1.0662152 & 0.9157261 & -0.74717833 & -0.92777 & 0.02407825 \\
ID2 & 0.91572611 & 1.0662152 & -0.44620015 & -0.92777 & -0.27689992 \\
ID3 & -0.74717833 & -0.4462002 & 0.97592175 & 0.494357 & -0.09631302 \\
ID4 & -0.92776524 & -0.9277652 & 0.49435666 & 0.915726 & 0.02407825 \\
ID5 & 0.02407825 & -0.2768999 & -0.09631302 & 0.024078 & 0.97592175 \\
\end{array}
\]

Haplotype additive genomic relationship matrix

Lines 593-595 in DEMO.R calculate the haplotype additive genomic relationship matrix.

\[
S_{ah}(S_3): \\
\begin{array}{ccccc}
ID1 & ID2 & ID3 & ID4 & ID5 \\
ID1 & 0.28571429 & -0.3265306 & -0.122449 & 0.081633 & -0.02040816 \\
ID2 & -0.32653061 & 1.1020408 & -0.7346939 & -0.53061 & 0.3877551 \\
ID3 & -0.12244989 & -0.7346939 & 1.5102041 & -0.32653 & -0.42857143 \\
ID4 & 0.08163265 & -0.5306122 & -0.3265306 & 1.918367 & -0.2244898 \\
ID5 & -0.02040816 & 0.3877551 & -0.4285714 & -0.22449 & 0.18367347 \\
\end{array}
\]
Pairwise epistasis genomic relationship matrices calculated from epistasis model matrices
Lines 566-588 in DEMO.R calculates the pairwise epistasis genomic relationship matrices using the epistasis model matrices.

\[ S_{aa} \text{ (} S_4 \text{ under Model-I):} \]

|    | ID1  | ID2  | ID3  | ID4  | ID5    |
|----|------|------|------|------|--------|
| ID1| 1.796561605 | 0.865329513 | -0.09455587 | 0.005731 | 0.33524355 |
| ID2| 0.865329513  | 1.796561605  | 0.33524355 | 0.005731 | -0.09455587 |
| ID3| -0.094555874 | 0.335243553 | 0.91547278 | 0.317335 | -0.03366762 |
| ID4| 0.005730659  | 0.005730659  | 0.31733524 | 0.202722 | 0.0487106  |
| ID5| 0.335243553  | -0.094555874 | -0.03366762 | 0.048711 | 0.28868195 |

\[ S_{a\delta} \text{ (} S_5 \text{ under Model-I):} \]

|    | ID1  | ID2  | ID3  | ID4  | ID5    |
|----|------|------|------|------|--------|
| ID1| 1.38554743 | -0.9142301 | -0.15525187 | -0.16796 | 0.07119021 |
| ID2| -0.9142301  | 1.38554743  | 0.46845702 | -0.16796 | -0.05593517 |
| ID3| -0.15525187 | 0.46845702  | 1.03873351 | -0.31634 | -0.08136024 |
| ID4| -0.1679644  | -0.1679644  | -0.31634356 | 0.542547 | -0.03051009 |
| ID5| 0.07119021  | -0.05593517 | -0.08136024 | -0.03051 | 0.64762434 |

\[ S_{\delta\delta} \text{ (} S_6 \text{ under Model-I):} \]

|    | ID1  | ID2  | ID3  | ID4  | ID5    |
|----|------|------|------|------|--------|
| ID1| 1.0454473  | 0.85066432 | 0.4449322 | 0.836686 | -0.24017 |
| ID2| 0.85066432 | 1.04544735 | 0.02619429 | 0.836686 | -0.2012741 |
| ID3| 0.4449322  | 0.02619429 | 1.02922049 | 0.086969 | -0.2168325 |
| ID4| 0.8366861  | 0.83668614 | 0.08696902 | 0.850664 | -0.24017 |
| ID5| -0.24017   | -0.20127414 | -0.21683247 | -0.24017 | 1.0292205 |

**GREML Estimation of the variance components under Model-I (EM-REML)**
Lines 613-651 in DEMO.R estimate variance components (excluding third-order variance components) using EM-REML for one iteration.

Variance_component_A    5.29E-04
Variance_component_D    1.04E-04
Variance_component_AA   1.68E-03
Variance_component_AD2  8.79E-04
Variance_component_DD   6.97E-05
Variance_component_AH   2.92E-04
Variance_component_E    1.48E-04
Heritability estimate for each effect type under Model-I

Lines 657-664 in DEMO.R estimate variance components (excluding third-order variance components) using EM-REML for one iteration.

Heritability_A 0.143042
Heritability_D 0.028118
Heritability-AA 0.453261
Heritability-AD2 0.23773
Heritability-DD 0.018861
Heritability_AH 0.079069
Heritability_G 0.96008

GBLUP and reliability

Lines 672-708 in DEMO.R calculate GBLUP and reliability (excluding third-order epistasis values).

|            | Gblup_A | Reliably_A | Gblup_D | Reliably_D |
|------------|---------|------------|---------|------------|
| ID1        | 0.0030404 | -0.007875  | 0.0098429 | 0.0012264 |
| ID2        | 0.0047594 | 0.0046453  | -0.000713 | 0.0069185 |
| ID3        | -0.000412 | 0.0012506  | 0.0134085 | -0.03868 |
| ID4        | -0.001009 | 0.0008768  | 0.0013323 | 0.002898 |
| ID5        | -0.024791 | 0.0226529  | 0.0400866 | 0.0171162 |

|            | Gblup-AA | Reliably-AA | Gblup-AD | Reliably-AD |
|------------|---------|------------|---------|------------|
| ID1        | -0.004475 | -3.92E-04  | -0.003651 | -0.001009 |
| ID2        | -0.003026 | 9.19E-03   | 0.002585  | -0.024791 |
| ID3        | 0.0440865 | 6.98E-02   | 0.0291752 | 0.0030404 |
| ID4        | -0.001553 | 4.74E-03   | 0.031094  | 0.0047594 |
| ID5        | 0.000632  | -9.70E-05  | 0.0009413 | -0.000412 |

|            | Gblup-DD | Reliably-DD |
|------------|---------|-------------|
| ID1        | 0.0008768 | 0.0013323 |
| ID2        | 0.0226529 | 0.0400866 |
| ID3        | -0.007875 | 0.0098429 |
| ID4        | 0.0046453 | -0.000713 |
| ID5        | 0.0012506 | 0.0134085 |

|            | Gblup-AH | Reliably-AH | Gblup_G | Reliably_G |
|------------|---------|------------|--------|------------|
| ID1        | 0.002898 | -0.001553  | 4.74E-03 | 0.031094 |
| ID2        | 0.0171162 | 0.000632   | -9.70E-05 | 0.0009413 |
| ID3        | 0.0012264 | -0.004475  | -3.92E-04 | -0.003651 |
| ID4        | 0.0069185 | -0.003026  | 9.19E-03  | 0.002585 |
| ID5        | -0.03868 | 0.0440865  | 6.98E-02  | 0.0291752 |
**Effect and heritability for each level of an effect type**

Lines 717-750 in DEMO.R calculate the effect and heritability of each level of an effect type (excluding third-order variance components).

| SNP   | mrk_eff_A   | mrk_eff_D      |
|-------|-------------|----------------|
| SNP1  | -8.14E-03   | 0.002033998    |
| SNP2  | 9.74E-04    | -0.006038177   |
| SNP3  | -2.13E-05   | -0.010138082   |
| SNP4  | 1.68E-03    | -0.001188418   |
| SNP5  | -2.03E-03   | -0.002473631   |
| SNP6  | 7.02E-04    | 0.000274859    |

| HAP   | mrk_eff_AH  |
|-------|-------------|
| HAP1  | 0.00518     |
| HAP2  | 0.001074    |
| HAP3  | -0.00107    |

| SNP   | mrk_eff_AA          | mrk_eff_AD       | mrk_eff_DA          | mrk_eff_DD          |
|-------|---------------------|------------------|---------------------|---------------------|
| SNP1  | -0.006141951        | 0.009212927      | 0.0149407           | 0.005354            |
| SNP1  | -0.002303232        | 0.004549962      | -0.022301           | -0.006885           |
| SNP1  | 0.00077178          | 0.010358489      | 0.0146719           | 0.0030952           |
| SNP1  | 0.001145562         | -0.000763708     | -0.004582           | -0.000863           |
| SNP1  | 0.023119953         | -0.001548663     | -0.010549           | 0.0050232           |
| SNP2  | 0.013940898         | -0.013649829     | 0.01388             | -0.003493           |
| SNP2  | -0.012133598        | 0.005018198      | -0.00523            | -0.005184           |
| SNP2  | 0.003456305         | 0.003456305      | 0.0023885           | -0.003583           |
| SNP2  | -0.02487345         | 0.00729717       | 0.0023885           | -0.012274           |
| SNP3  | 0.015425695         | 0.014643962      | -0.002176           | -0.012618           |
| SNP3  | 0.020501353         | -0.001227232     | 0.0081324           | -0.009043           |
| SNP3  | 0.02345172          | -0.006625493     | -0.007864           | -0.003981           |
| SNP4  | -0.002607671        | 0.001998911      | 0.0013763           | 0.0071227           |
| SNP4  | -0.011030802        | 0.005416921      | 0.0115912           | 0.0065652           |
| SNP5  | 0.002057625         | 0.001433362      | 0.0054789           | -0.011279           |

| SNP   | h2_A    | h2_D    |
|-------|---------|---------|
| SNP1  | 0.000536 | 3.91E-04 |
| SNP2  | 0.049876 | 1.43E-30 |
| SNP3  | 0.000536 | 3.91E-04 |
| SNP4  | 0.002142 | 1.43E-30 |
| SNP5  | 0.040075 | 1.82E-02 |
| SNP6  | 0.049876 | 9.11E-03 |

| HAP   | h2_AH   |
|-------|---------|
| HAP1  | 0.072813 |

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Pairwise epistasis genomic relationship matrices calculated from additive and dominance model matrices

Lines 761-780 in DEMO.R calculate the pairwise epistasis genomic relationship matrices using the SNP additive and dominance model matrices. The resulting epistasis model matrices are identical to those calculated from the epistasis model matrices.

Third-order epistasis effects, Lines 784-1245

Line 784-930 calculate the epistasis model matrices of the third-order epistasis effects.

Lines 951-980 calculate third-order epistasis genomic relationship matrices.

\( S_{aaa} (S_7): \)

| ID1       | ID2       | ID3       | ID4       | ID5       |
|-----------|-----------|-----------|-----------|-----------|
| ID1       | 2.02779616 | -0.09000662 | -0.02382528 | -0.01058901 | -0.14295169 |
| ID2       | -0.09000662 | 2.02779616 | -0.14295169 | -0.01058901 | -0.02382528 |
| ID3       | -0.02382528 | -0.14295169 | 0.77696889 | -0.11647915 | -0.02382528 |
| ID4       | -0.01058901 | -0.01058901 | -0.11647915 | 0.05724686 | -0.00397088 |
| ID5       | -0.14295169 | -0.02382528 | -0.02382528 | -0.00397088 | 0.11019193 |

\( S_{aad} (S_8): \)
| ID1 | ID2 | ID3 | ID4 | ID5 |
|-----|-----|-----|-----|-----|
| ID1 | 1.659640724 | 0.550220613 | 0.13641916 | -0.009827415 | -0.05075649 |
| ID2 | 0.550220613 | 1.659640724 | -0.32112132 | -0.009827415 | 0.06016241 |
| ID3 | 0.136419159 | -0.321121316 | 1.07177285 | 0.209244351 | -0.01644558 |
| ID4 | -0.009827415 | -0.009827415 | 0.209244351 | 0.226198768 | 0.01727377 |
| ID5 | -0.050756490 | 0.060162413 | -0.01644558 | 0.017273770 | 0.38274693 |

$S_{\alpha\alpha} (S_0)$:

| ID1 | ID2 | ID3 | ID4 | ID5 |
|-----|-----|-----|-----|-----|
| ID1 | 1.659640724 | 0.550220613 | 0.13641916 | -0.009827415 | -0.05075649 |
| ID2 | 0.550220613 | 1.659640724 | -0.32112132 | -0.009827415 | 0.06016241 |
| ID3 | 0.136419159 | -0.321121316 | 1.07177285 | 0.209244351 | -0.01644558 |
| ID4 | -0.009827415 | -0.009827415 | 0.209244351 | 0.226198768 | 0.01727377 |
| ID5 | -0.050756490 | 0.060162413 | -0.01644558 | 0.017273770 | 0.38274693 |

$S_{\delta\delta} (S_{10})$:

| ID1 | ID2 | ID3 | ID4 | ID5 |
|-----|-----|-----|-----|-----|
| ID1 | 0.913906125 | 0.7716022 | -0.07232653 | -0.685148497 | 0.003383527 |
| ID2 | 0.771602240 | 0.9139061 | 0.29408068 | -0.685148497 | 0.258695683 |
| ID3 | -0.072326535 | 0.2940807 | 1.20029276 | -0.204747972 | 0.103343980 |
| ID4 | -0.685148497 | -0.6851485 | -0.20474797 | 0.771602240 | 0.003383527 |
| ID5 | 0.003383527 | 0.2586957 | 0.10334398 | 0.003383527 | 1.200292755 |
Lines 1026-1078 calculate variance components and heritabilities using EM-REML for 1 iteration.

Variance_component_A  0.000206
Variance_component_D  0.000050
Variance_component_AA 0.000717
Variance_component_AD2 0.000366
Variance_component_DD  0.000027
Variance_component_AAA 0.000921
Variance_component_AAD3 0.000543
Variance_component_ADD3 0.000399
Variance_component_DDD  0.000088
Variance_component_AH  0.000124
Variance_component_E   0.000060

Heritability_A  0.05894
Heritability_D  0.01426
Heritability_AA 0.20477
Heritability_AD2 0.10451
Heritability_DD  0.00782
Heritability_AAA 0.26307
Heritability_AAD3 0.15512
Heritability_ADD3 0.11401
Heritability_DDD  0.02509
Heritability_AH  0.03531
Heritability_G   0.98289

Lines 1082-1134 calculate GBLUP and reliability.

|    | Gblup_A | Rel_A  | Gblup_D | Rel_D  | Gblup_AA | Rel_AA |
|----|---------|--------|---------|--------|----------|--------|
| ID1| -0.02246| -0.30616| 0.001853| 0.004462| 0.014082 | 0.054619|
| ID2| 0.023339 | -0.37694| -0.00102| 0.011056| -0.01367 | 0.052242|
| ID3| -0.00924 | -0.22103| -0.00264| 0.014952| -0.00551 | 0.038634|
| ID4| 0.001313 | -0.12264| -0.00053| 0.01067 | 0.000205 | 0.000507 |
| ID5| 0.00705  | -0.07668| 0.003098| 0.007093| 0.006435 | 0.070652 |

|    | Gblup_AD2 | Rel_AD2 | Gblup_DD | Rel_DD | Gblup_AAA | Rel_AAA |
|----|-----------|---------|----------|--------|-----------|---------|
|    | 0.076042  | 0.976758| 0.000476 | 2.43E-03| -0.01736  | -0.13975|
|    | -0.07353  | 0.895727| -0.00092 | 1.29E-02| 0.017504  | -0.14467|
|    | -0.01537  | 0.294887| 0.00169  | 2.27E-02| -0.00183  | -0.04823|
|    | -0.00332  | 0.228947| -0.00029 | 1.12E-02| 0.000167  | -0.02204|
|    | 0.004004  | 0.005834| -0.00012 | 3.46E-05| 0.000996  | -0.00896|

|    | Gblup_AAD3 | Rel_AAD3 | Gblup_ADD3 | Rel_ADD3 |
|----|------------|----------|------------|----------|

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Lines 1143-1169 calculate third-order epistasis genomic relationship matrices using additive and dominance model matrices. The results are the same as the direct calculations using the third-order epistasis model matrices.
**Heritability estimates from EPIHAP**

All results of DEMO.R are verified by the EIPHAP program (Liang et al., 2021), and DEMO.R and EPIHAP have identical results, which provide strong mutual validation for the correct implementation of the methods in this article. The following only the heritability estimates from EPIHAP without repeating all identical results.

Additive heritability: 5.893893e-02
Dominance heritability: 1.425995e-02
Additive x Additive heritability: 2.047676e-01
Additive x Dominance heritability: 1.045092e-01
Dominance x Dominance heritability: 7.814957e-03
Additive x Additive x Additive heritability: 2.630716e-01
Additive x Additive x Dominance heritability: 1.551156e-01
Additive x Dominance x Dominance heritability: 1.140088e-01
Dominance x Dominance x Dominance heritability: 2.509076e-02
Additive Haplotype heritability: 3.530722e-02
Total heritability: 9.828847e-01
R Program. DEMO.R for Numerical Demonstration

# Program name: DEMO.R
# Authors: Zuoxiang Liang, Dzianis Prakapenka, Yang Da. November 11, 2021.
# Purpose: numerical demonstration
# 1. Pairwise epistasis genomic relationship matrices
#   using epistasis model matrices
# 2. GREML estimation of variance components and heritability
# 3. GBLUP and reliability values
# 4. Effect and heritability estimates for all levels of all effect types
# 5. Pairwise epistasis genomic relationship matrices
#   using additive and dominance model matrices
# 6. GREML and GBLUP with third-order epistasis effects

# Genotype
# 6 markers, 5 individuals

# LOC1:  0-0-1-0-1
# LOC2:  2-0-1-1-1
# LOC3:  0-0-1-0-1
# LOC4:  1-1-2-0-1
# LOC5:  0-2-0-1-1
# LOC6:  2-0-1-1-0

# Phenotype
# 5 individuals

# ID   FIX   y
# ID1 2   1.753222323
# ID2 2   1.617654738
# ID3 1   1.71311938
# ID4 1   1.738835045
# ID5 -9999 -9999
# -9999 indicates missing value, and FIX means fixed effects

library(matrixcalc)
library(MASS)
library(pedigree)

ID<-c("ID1","ID2","ID3","ID4","ID5")
FIX<-c(2,2,1,1,1)
y<-c(1.7532222323,1.617654738,1.71311938,1.738835045,-9999)

# 1. Genomic relationship matrices of AA, AD and DD using epistasis model matrices

# CALCULATION OF ALLELE FREQUENCIES
# THE NEXT LINE IS LINE 42 REFERENCED BY TEXT S4
P1_II = 3/5
P1_IJ = 2/5
P1_JJ = 0/5
P1_I = P1_II +0.5*P1_IJ
P1_J = P1_JJ + 0.5*P1_IJ

P2_II = 1/5
P2_IJ = 3/5
P2_JJ = 1/5
P2_I = P2_II +0.5*P2_IJ
P2_J = P2_JJ + 0.5*P2_IJ

P3_II = 3/5
P3_IJ = 2/5
P3_JJ = 0/5
P3_I = P3_II +0.5*P3_IJ
P3_J = P3_JJ + 0.5*P3_IJ

P4_II = 1/5
P4_IJ = 3/5
P4_JJ = 1/5
P4_I = P4_II +0.5*P4_IJ
P4_J = P4_JJ + 0.5*P4_IJ

P5_II = 2/5
P5_{IJ} = \frac{2}{5}
\text{P5}_{JJ} = \frac{1}{5}
P5_{I} = P5_{II} + 0.5 \times P5_{IJ}
P5_{J} = P5_{JJ} + 0.5 \times P5_{IJ}

P6_{II} = \frac{2}{5}
P6_{IJ} = \frac{2}{5}
P6_{JJ} = \frac{1}{5}
P6_{I} = P6_{II} + 0.5 \times P6_{IJ}
P6_{J} = P6_{JJ} + 0.5 \times P6_{IJ}

#ADDITIVE SNP CODING
WA1_0 = 2 \times P1_{J}
WA1_1 = P1_{J} - P1_{I}
WA1_2 = -2 \times P1_{I}

WA2_0 = 2 \times P2_{J}
WA2_1 = P2_{J} - P2_{I}
WA2_2 = -2 \times P2_{I}

WA3_0 = 2 \times P3_{J}
WA3_1 = P3_{J} - P3_{I}
WA3_2 = -2 \times P3_{I}

WA4_0 = 2 \times P4_{J}
WA4_1 = P4_{J} - P4_{I}
WA4_2 = -2 \times P4_{I}

WA5_0 = 2 \times P5_{J}
WA5_1 = P5_{J} - P5_{I}
WA5_2 = -2 \times P5_{I}

WA6_0 = 2 \times P6_{J}
WA6_1 = P6_{J} - P6_{I}
WA6_2 = -2 \times P6_{I}
WA1 = rbind(WA1_0, WA1_0, WA1_1, WA1_0, WA1_1)
WA2 = rbind(WA2_2, WA2_0, WA2_1, WA2_1, WA2_1)
WA3 = rbind(WA3_0, WA3_0, WA3_1, WA3_0, WA3_1)
WA4 = rbind(WA4_1, WA4_1, WA4_2, WA4_0, WA4_1)
WA5 = rbind(WA5_0, WA5_2, WA5_0, WA5_1, WA5_1)
WA6 = rbind(WA6_2, WA6_0, WA6_1, WA6_1, WA6_0)

# DOMINANCE SNP CODING
WD1_0 = -2*P1_J**2
WD1_1 = 2*P1_I*P1_J
WD1_2 = -2*P1_I**2

WD2_0 = -2*P2_J**2
WD2_1 = 2*P2_I*P2_J
WD2_2 = -2*P2_I**2

WD3_0 = -2*P3_J**2
WD3_1 = 2*P3_I*P3_J
WD3_2 = -2*P3_I**2

WD4_0 = -2*P4_J**2
WD4_1 = 2*P4_I*P4_J
WD4_2 = -2*P4_I**2

WD5_0 = -2*P5_J**2
WD5_1 = 2*P5_I*P5_J
WD5_2 = -2*P5_I**2

WD6_0 = -2*P6_J**2
WD6_1 = 2*P6_I*P6_J
WD6_2 = -2*P6_I**2

WD1 = rbind(WD1_0, WD1_0, WD1_1, WD1_0, WD1_1)
WD2 = rbind(WD2_2, WD2_0, WD2_1, WD2_1, WD2_1)
WD3 = rbind(WD3_0, WD3_0, WD3_1, WD3_0, WD3_1)
WD4 = rbind(WD4_1, WD4_1, WD4_2, WD4_0, WD4_1)
WD5 = rbind(WD5_0, WD5_2, WD5_0, WD5_1, WD5_1)
WD6 = rbind(WD6_2, WD6_0, WD6_1, WD6_1, WD6_0)

rownames<-ID
SNPs_name<-c("SNP1","SNP2","SNP3","SNP4","SNP5","SNP6")
colnames<-SNPs_name

WA<-matrix(c(WA1, WA2, WA3, WA4, WA5, WA6), nrow=length(rownames), ncol=length(colnames), byrow=FALSE, dimnames=list(rownames, colnames))
WD<-matrix(c(WD1, WD2, WD3, WD4, WD5, WD6), nrow=length(rownames), ncol=length(colnames), byrow=FALSE, dimnames=list(rownames, colnames))

print("WA matrix")
print(WA)
print("WD matrix")
print(WD)

# PAIRWISE
WAA1_12=WA1_0*WA2_2
WAA1_13=WA1_0*WA3_0
WAA1_14=WA1_0*WA4_1
WAA1_15=WA1_0*WA5_0
WAA1_16=WA1_0*WA6_2
WAA1_23=WA2_2*WA3_0
WAA1_24=WA2_2*WA4_1
WAA1_25=WA2_2*WA5_0
WAA1_26=WA2_2*WA6_2
WAA1_34=WA3_0*WA4_1
WAA1_35=WA3_0*WA5_0
WAA1_36=WA3_0*WA6_2
WAA1_45=WA4_1*WA5_0
WAA1_46=WA4_1*WA6_2
WAA1_56=WA5_0*WA6_2
WAD1_12=WA1_0*WD2_2
WAD1_13 = WA1_0 * WD3_0
WAD1_14 = WA1_0 * WD4_1
WAD1_15 = WA1_0 * WD5_0
WAD1_16 = WA1_0 * WD6_2
WAD1_23 = WA2_2 * WD3_0
WAD1_24 = WA2_2 * WD4_1
WAD1_25 = WA2_2 * WD5_0
WAD1_26 = WA2_2 * WD6_2
WAD1_34 = WA3_0 * WD4_1
WAD1_35 = WA3_0 * WD5_0
WAD1_36 = WA3_0 * WD6_2
WAD1_45 = WA4_1 * WD5_0
WAD1_46 = WA4_1 * WD6_2
WAD1_56 = WA5_0 * WD6_2

WDA1_12 = WD1_0 * WA2_2
WDA1_13 = WD1_0 * WA3_0
WDA1_14 = WD1_0 * WA4_1
WDA1_15 = WD1_0 * WA5_0
WDA1_16 = WD1_0 * WA6_2
WDA1_23 = WD2_2 * WA3_0
WDA1_24 = WD2_2 * WA4_1
WDA1_25 = WD2_2 * WA5_0
WDA1_26 = WD2_2 * WA6_2
WDA1_34 = WD3_0 * WA4_1
WDA1_35 = WD3_0 * WA5_0
WDA1_36 = WD3_0 * WA6_2
WDA1_45 = WD4_1 * WA5_0
WDA1_46 = WD4_1 * WA6_2
WDA1_56 = WD5_0 * WA6_2

WDD1_12 = WD1_0 * WD2_2
WDD1_13 = WD1_0 * WD3_0
WDD1_14 = WD1_0 * WD4_1
WDD1_15 = WD1_0 * WD5_0
WDD1_16 = WD1_0 * WD6_2
WDD1_23 = WD2_2 * WD3_0
WDD1_24 = WD2_2 * WD4_1
WDD1_25 = WD2_2 * WD5_0
WDD1_26 = WD2_2 * WD6_2
WDD1_34 = WD3_0 * WD4_1
WDD1_35 = WD3_0 * WD5_0
WDD1_36 = WD3_0 * WD6_2
WDD1_45 = WD4_1 * WD5_0
WDD1_46 = WD4_1 * WD6_2
WDD1_56 = WD5_0 * WD6_2

WAA2_12 = WA1_0 * WA2_0
WAA2_13 = WA1_0 * WA3_0
WAA2_14 = WA1_0 * WA4_1
WAA2_15 = WA1_0 * WA5_2
WAA2_16 = WA1_0 * WA6_0
WAA2_23 = WA2_0 * WA3_0
WAA2_24 = WA2_0 * WA4_1
WAA2_25 = WA2_0 * WA5_2
WAA2_26 = WA2_0 * WA6_0
WAA2_34 = WA3_0 * WA4_1
WAA2_35 = WA3_0 * WA5_2
WAA2_36 = WA3_0 * WA6_0
WAA2_45 = WA4_1 * WA5_2
WAA2_46 = WA4_1 * WA6_0
WAA2_56 = WA5_2 * WA6_0

WAD2_12 = WA1_0 * WD2_0
WAD2_13 = WA1_0 * WD3_0
WAD2_14 = WA1_0 * WD4_1
WAD2_15 = WA1_0 * WD5_2
WAD2_16 = WA1_0 * WD6_0
WAD2_23 = WA2_0 * WD3_0
WAD2_24 = WA2_0 * WD4_1
| Equation | Description |
|----------|-------------|
| WAD2_25 | WA2_0 * WD5_2 |
| WAD2_26 | WA2_0 * WD6_0 |
| WAD2_34 | WA3_0 * WD4_1 |
| WAD2_35 | WA3_0 * WD5_2 |
| WAD2_36 | WA3_0 * WD6_0 |
| WAD2_45 | WA4_1 * WD5_2 |
| WAD2_46 | WA4_1 * WD6_0 |
| WAD2_56 | WA5_2 * WD6_0 |
| WDA2_12 | WD1_0 * WA2_0 |
| WDA2_13 | WD1_0 * WA3_0 |
| WDA2_14 | WD1_0 * WA4_1 |
| WDA2_15 | WD1_0 * WA5_2 |
| WDA2_16 | WD1_0 * WA6_0 |
| WDA2_23 | WD2_0 * WA3_0 |
| WDA2_24 | WD2_0 * WA4_1 |
| WDA2_25 | WD2_0 * WA5_2 |
| WDA2_26 | WD2_0 * WA6_0 |
| WDA2_34 | WD3_0 * WA4_1 |
| WDA2_35 | WD3_0 * WA5_2 |
| WDA2_36 | WD3_0 * WA6_0 |
| WDA2_45 | WD4_1 * WA5_2 |
| WDA2_46 | WD4_1 * WA6_0 |
| WDA2_56 | WD5_2 * WA6_0 |
| WDD2_12 | WD1_0 * WD2_0 |
| WDD2_13 | WD1_0 * WD3_0 |
| WDD2_14 | WD1_0 * WD4_1 |
| WDD2_15 | WD1_0 * WD5_2 |
| WDD2_16 | WD1_0 * WD6_0 |
| WDD2_23 | WD2_0 * WD3_0 |
| WDD2_24 | WD2_0 * WD4_1 |
| WDD2_25 | WD2_0 * WD5_2 |
| WDD2_26 | WD2_0 * WD6_0 |
| WDD2_34 | WD3_0 * WD4_1 |
WDD2_35 = WD3_0 * WD5_2
WDD2_36 = WD3_0 * WD6_0
WDD2_45 = WD4_1 * WD5_2
WDD2_46 = WD4_1 * WD6_0
WDD2_56 = WD5_2 * WD6_0

WAA3_12 = WA1_1 * WA2_1
WAA3_13 = WA1_1 * WA3_1
WAA3_14 = WA1_1 * WA4_2
WAA3_15 = WA1_1 * WA5_0
WAA3_16 = WA1_1 * WA6_1
WAA3_23 = WA2_1 * WA3_1
WAA3_24 = WA2_1 * WA4_2
WAA3_25 = WA2_1 * WA5_0
WAA3_26 = WA2_1 * WA6_1
WAA3_34 = WA3_1 * WA4_2
WAA3_35 = WA3_1 * WA5_0
WAA3_36 = WA3_1 * WA6_1
WAA3_45 = WA4_2 * WA5_0
WAA3_46 = WA4_2 * WA6_1
WAA3_56 = WA5_0 * WA6_1

WAD3_12 = WA1_1 * WD2_1
WAD3_13 = WA1_1 * WD3_1
WAD3_14 = WA1_1 * WD4_2
WAD3_15 = WA1_1 * WD5_0
WAD3_16 = WA1_1 * WD6_1
WAD3_23 = WA2_1 * WD3_1
WAD3_24 = WA2_1 * WD4_2
WAD3_25 = WA2_1 * WD5_0
WAD3_26 = WA2_1 * WD6_1
WAD3_34 = WA3_1 * WD4_2
WAD3_35 = WA3_1 * WD5_0
WAD3_36 = WA3_1 * WD6_1
WAD3_45 = WA4_2 * WD5_0
WAD3_46=WA4_2*WD6_1
WAD3_56=WA5_0*WD6_1

WDA3_12=WD1_1*WA2_1
WDA3_13=WD1_1*WA3_1
WDA3_14=WD1_1*WA4_2
WDA3_15=WD1_1*WA5_0
WDA3_16=WD1_1*WA6_1
WDA3_23=WD2_1*WA3_1
WDA3_24=WD2_1*WA4_2
WDA3_25=WD2_1*WA5_0
WDA3_26=WD2_1*WA6_1
WDA3_34=WD3_1*WA4_2
WDA3_35=WD3_1*WA5_0
WDA3_36=WD3_1*WA6_1
WDA3_45=WD4_2*WA5_0
WDA3_46=WD4_2*WA6_1
WDA3_56=WD5_0*WA6_1

WDD3_12=WD1_1*WD2_1
WDD3_13=WD1_1*WD3_1
WDD3_14=WD1_1*WD4_2
WDD3_15=WD1_1*WD5_0
WDD3_16=WD1_1*WD6_1
WDD3_23=WD2_1*WD3_1
WDD3_24=WD2_1*WD4_2
WDD3_25=WD2_1*WD5_0
WDD3_26=WD2_1*WD6_1
WDD3_34=WD3_1*WD4_2
WDD3_35=WD3_1*WD5_0
WDD3_36=WD3_1*WD6_1
WDD3_45=WD4_2*WD5_0
WDD3_46=WD4_2*WD6_1
WDD3_56=WD5_0*WD6_1
WDA4_15 = WD1_0 * WA5_1
WDA4_16 = WD1_0 * WA6_1
WDA4_23 = WD2_1 * WA3_0
WDA4_24 = WD2_1 * WA4_0
WDA4_25 = WD2_1 * WA5_1
WDA4_26 = WD2_1 * WA6_1
WDA4_34 = WD3_0 * WA4_0
WDA4_35 = WD3_0 * WA5_1
WDA4_36 = WD3_0 * WA6_1
WDA4_45 = WD4_0 * WA5_1
WDA4_46 = WD4_0 * WA6_1
WDA4_56 = WD5_1 * WA6_1

WDD4_12 = WD1_0 * WD2_1
WDD4_13 = WD1_0 * WD3_0
WDD4_14 = WD1_0 * WD4_0
WDD4_15 = WD1_0 * WD5_1
WDD4_16 = WD1_0 * WD6_1
WDD4_23 = WD2_1 * WD3_0
WDD4_24 = WD2_1 * WD4_0
WDD4_25 = WD2_1 * WD5_1
WDD4_26 = WD2_1 * WD6_1
WDD4_34 = WD3_0 * WD4_0
WDD4_35 = WD3_0 * WD5_1
WDD4_36 = WD3_0 * WD6_1
WDD4_45 = WD4_0 * WD5_1
WDD4_46 = WD4_0 * WD6_1
WDD4_56 = WD5_1 * WD6_1

WAA5_12 = WA1_1 * WA2_1
WAA5_13 = WA1_1 * WA3_1
WAA5_14 = WA1_1 * WA4_1
WAA5_15 = WA1_1 * WA5_1
WAA5_16 = WA1_1 * WA6_0
WAA5_23 = WA2_1 * WA3_1
WAA5_24 = WA2_1 * WA4_1
WAA5_25 = WA2_1 * WA5_1
WAA5_26 = WA2_1 * WA6_0
WAA5_34 = WA3_1 * WA4_1
WAA5_35 = WA3_1 * WA5_1
WAA5_36 = WA3_1 * WA6_0
WAA5_45 = WA4_1 * WA5_1
WAA5_46 = WA4_1 * WA6_0
WAA5_56 = WA5_1 * WA6_0

WAD5_12 = WA1_1 * WD2_1
WAD5_13 = WA1_1 * WD3_1
WAD5_14 = WA1_1 * WD4_1
WAD5_15 = WA1_1 * WD5_1
WAD5_16 = WA1_1 * WD6_0
WAD5_23 = WA2_1 * WD3_1
WAD5_24 = WA2_1 * WD4_1
WAD5_25 = WA2_1 * WD5_1
WAD5_26 = WA2_1 * WD6_0
WAD5_34 = WA3_1 * WD4_1
WAD5_35 = WA3_1 * WD5_1
WAD5_36 = WA3_1 * WD6_0
WAD5_45 = WA4_1 * WD5_1
WAD5_46 = WA4_1 * WD6_0
WAD5_56 = WA5_1 * WD6_0

WDA5_12 = WD1_1 * WA2_1
WDA5_13 = WD1_1 * WA3_1
WDA5_14 = WD1_1 * WA4_1
WDA5_15 = WD1_1 * WA5_1
WDA5_16 = WD1_1 * WA6_0
WDA5_23 = WD2_1 * WA3_1
WDA5_24 = WD2_1 * WA4_1
WDA5_25 = WD2_1 * WA5_1
WDA5_26 = WD2_1 * WA6_0
WDA5_34=WD3_1*WA4_1
WDA5_35=WD3_1*WA5_1
WDA5_36=WD3_1*WA6_0
WDA5_45=WD4_1*WA5_1
WDA5_46=WD4_1*WA6_0
WDA5_56=WD5_1*WA6_0
WDD5_12=WD1_1*WD2_1
WDD5_13=WD1_1*WD3_1
WDD5_14=WD1_1*WD4_1
WDD5_15=WD1_1*WD5_1
WDD5_16=WD1_1*WD6_0
WDD5_23=WD2_1*WD3_1
WDD5_24=WD2_1*WD4_1
WDD5_25=WD2_1*WD5_1
WDD5_26=WD2_1*WD6_0
WDD5_34=WD3_1*WD4_1
WDD5_35=WD3_1*WD5_1
WDD5_36=WD3_1*WD6_0
WDD5_45=WD4_1*WD5_1
WDD5_46=WD4_1*WD6_0
WDD5_56=WD5_1*WD6_0
WAA1=cbind(WAA1_12,WAA1_13,WAA1_14,WAA1_15,WAA1_16,WAA1_23,WAA1_24,WAA1_25,WAA1_26,WAA1_34,WAA1_35,WAA1_36,WAA1_45,WAA1_46,WAA1_56)
WAA2=cbind(WAA2_12,WAA2_13,WAA2_14,WAA2_15,WAA2_16,WAA2_23,WAA2_24,WAA2_25,WAA2_26,WAA2_34,WAA2_35,WAA2_36,WAA2_45,WAA2_46,WAA2_56)
WAA3=cbind(WAA3_12,WAA3_13,WAA3_14,WAA3_15,WAA3_16,WAA3_23,WAA3_24,WAA3_25,WAA3_26,WAA3_34,WAA3_35,WAA3_36,WAA3_45,WAA3_46,WAA3_56)
WAA4=cbind(WAA4_12,WAA4_13,WAA4_14,WAA4_15,WAA4_16,WAA4_23,WAA4_24,WAA4_25,WAA4_26,WAA4_34,WAA4_35,WAA4_36,WAA4_45,WAA4_46,WAA4_56)
WAA5=cbind(WAA5_12,WAA5_13,WAA5_14,WAA5_15,WAA5_16,WAA5_23,WAA5_24,WAA5_25,WAA5_26,WAA5_34,WAA5_35,WAA5_36,WAA5_45,WAA5_46,WAA5_56)
WAA=rbind(WAA1,WAA2,WAA3,WAA4,WAA5)
SNPs_pair<-c("SNP1_2","SNP1_3","SNP1_4","SNP1_5","SNP1_6","SNP2_3","SNP2_4","SNP2_5","SNP2_6","SNP3_4","SNP3_5","SNP3_6","SNP4_5","SNP4_6","SNP5_6")
colnames<-SNPs_pair
WAA<-matrix(WAA,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))

WAD1=cbind(WAD1_12,WAD1_13,WAD1_14,WAD1_15,WAD1_16,WAD1_23,WAD1_24,WAD1_25,WAD1_26,WAD1_34,WAD1_35,WAD1_36,WAD1_45,WAD1_46,WAD1_56)

WAD2=cbind(WAD2_12,WAD2_13,WAD2_14,WAD2_15,WAD2_16,WAD2_23,WAD2_24,WAD2_25,WAD2_26,WAD2_34,WAD2_35,WAD2_36,WAD2_45,WAD2_46,WAD2_56)

WAD3=cbind(WAD3_12,WAD3_13,WAD3_14,WAD3_15,WAD3_16,WAD3_23,WAD3_24,WAD3_25,WAD3_26,WAD3_34,WAD3_35,WAD3_36,WAD3_45,WAD3_46,WAD3_56)

WAD4=cbind(WAD4_12,WAD4_13,WAD4_14,WAD4_15,WAD4_16,WAD4_23,WAD4_24,WAD4_25,WAD4_26,WAD4_34,WAD4_35,WAD4_36,WAD4_45,WAD4_46,WAD4_56)

WAD5=cbind(WAD5_12,WAD5_13,WAD5_14,WAD5_15,WAD5_16,WAD5_23,WAD5_24,WAD5_25,WAD5_26,WAD5_34,WAD5_35,WAD5_36,WAD5_45,WAD5_46,WAD5_56)

WAD=rbind(WAD1,WAD2,WAD3,WAD4,WAD5)

WAD<-matrix(WAD,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))

WDA1=cbind(WDA1_12,WDA1_13,WDA1_14,WDA1_15,WDA1_16,WDA1_23,WDA1_24,WDA1_25,WDA1_26,WDA1_34,WDA1_35,WDA1_36,WDA1_45,WDA1_46,WDA1_56)

WDA2=cbind(WDA2_12,WDA2_13,WDA2_14,WDA2_15,WDA2_16,WDA2_23,WDA2_24,WDA2_25,WDA2_26,WDA2_34,WDA2_35,WDA2_36,WDA2_45,WDA2_46,WDA2_56)

WDA3=cbind(WDA3_12,WDA3_13,WDA3_14,WDA3_15,WDA3_16,WDA3_23,WDA3_24,WDA3_25,WDA3_26,WDA3_34,WDA3_35,WDA3_36,WDA3_45,WDA3_46,WDA3_56)

WDA4=cbind(WDA4_12,WDA4_13,WDA4_14,WDA4_15,WDA4_16,WDA4_23,WDA4_24,WDA4_25,WDA4_26,WDA4_34,WDA4_35,WDA4_36,WDA4_45,WDA4_46,WDA4_56)

WDA5=cbind(WDA5_12,WDA5_13,WDA5_14,WDA5_15,WDA5_16,WDA5_23,WDA5_24,WDA5_25,WDA5_26,WDA5_34,WDA5_35,WDA5_36,WDA5_45,WDA5_46,WDA5_56)

WDA=rbind(WDA1,WDA2,WDA3,WDA4,WDA5)

WDA<-matrix(WDA,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))

WDD1=cbind(WDD1_12,WDD1_13,WDD1_14,WDD1_15,WDD1_16,WDD1_23,WDD1_24,WDD1_25,WDD1_26,WDD1_34,WDD1_35,WDD1_36,WDD1_45,WDD1_46,WDD1_56)

WDD2=cbind(WDD2_12,WDD2_13,WDD2_14,WDD2_15,WDD2_16,WDD2_23,WDD2_24,WDD2_25,WDD2_26,WDD2_34,WDD2_35,WDD2_36,WDD2_45,WDD2_46,WDD2_56)

WDD3=cbind(WDD3_12,WDD3_13,WDD3_14,WDD3_15,WDD3_16,WDD3_23,WDD3_24,WDD3_25,WDD3_26,WDD3_34,WDD3_35,WDD3_36,WDD3_45,WDD3_46,WDD3_56)

WDD4=cbind(WDD4_12,WDD4_13,WDD4_14,WDD4_15,WDD4_16,WDD4_23,WDD4_24,WDD4_25,WDD4_26,WDD4_34,WDD4_35,WDD4_36,WDD4_45,WDD4_46,WDD4_56)

WDD5=cbind(WDD5_12,WDD5_13,WDD5_14,WDD5_15,WDD5_16,WDD5_23,WDD5_24,WDD5_25,WDD5_26,WDD5_34,WDD5_35,WDD5_36,WDD5_45,WDD5_46,WDD5_56)

WDD=rbind(WDD1,WDD2,WDD3,WDD4,WDD5)

WDD<-matrix(WDD,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
# Print WAA, WAD, WDA and WDD matrices
print("WAA")
print(WAA)
print("WAD")
print(WAD)
print("WDA")
print(WDA)
print("WDD")
print(WDD)

# Haplotype frequencies
P1=0.4
P2=0.3
P3=0.2
P4=0.1

# Haplotype additive coding
WAH11=2*P2
WAH12=2*P3
WAH13=2*P4
WAH1_1=cbind(WAH11,WAH12,WAH13)

WAH21=-2*(1-P2)
WAH22=2*P3
WAH23=2*P4
WAH2_2=cbind(WAH21,WAH22,WAH23)

WAH31=2*P2
WAH32=-2*(1-P3)
WAH33=2*P4
WAH3_3=cbind(WAH31,WAH32,WAH33)

WAH41=2*P2
WAH42=2*P3
WAH43=-2*(1-P4)
WAH4_4 = cbind(WAH41, WAH42, WAH43)

WAH51 = -(1-2*P2)
WAH52 = 2*P3
WAH53 = 2*P4
WAH1_2 = cbind(WAH51, WAH52, WAH53)
WAH = rbind(WAH1_1, WAH2_2, WAH3_3, WAH4_4, WAH1_2)

Haps_name <- c("HAP1", "HAP2", "HAP3")
colnames <- Haps_name

WAH <- matrix(WAH, nrow = length(rownames), ncol = length(colnames), byrow = FALSE, dimnames = list(rownames, colnames))
print("WAH matrix")
print(WAH)

# Making S matrices
colnames <- ID

WWA = WA%*%t(WA)
KA = mean(diag(WWA))
SA <- WWA/KA
SA <- matrix(SA, nrow = length(rownames), ncol = length(colnames), byrow = FALSE, dimnames = list(rownames, colnames))
print("SA matrix")
print(SA)

WWD = WD%*%t(WD)
KD = mean(diag(WWD))
SD <- WWD/KD
SD <- matrix(SD, nrow = length(rownames), ncol = length(colnames), byrow = FALSE, dimnames = list(rownames, colnames))
print("SD matrix")
print(SD)

WWAA = WAA%*%t(WAA)
KAA = mean(diag(WWAA))
SAA <- WWAA/KAA
SAA <- matrix(SAA,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
print("SAA matrix")
print(SAA)

WWAD = WAD %*% t(WAD)
KAD = mean(diag(WWAD))

WWDA = WDA %*% t(WDA)
KDA = mean(diag(WWDA))

WWAD2 = WWAD + WWDA
KAD2 = mean(diag(WWAD2))
SAD2 <- WWAD2 / KAD2
SAD2 <- matrix(SAD2,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
print("SAD2 matrix")
print(SAD2)

WWDD = WDD %*% t(WDD)
KDD = mean(diag(WWDD))
SDD <- WWDD / KDD
SDD <- matrix(SDD,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
print("SDD matrix")
print(SDD)

WAHWAHt = WHA %*% t(WHA)
KAH = mean(diag(WAHWAHt))
SAH = WAHWAHt / KAH
SAH <- matrix(SAH,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
print("SAH matrix")
print(SAH)
# 2. GREML estimation of variance components and heritability

```r
ID<-factor(ID)
FIX<-factor(FIX)
data<-data.frame(ID,y)
Z<-model.matrix(y ~ID-1)
Z<-Z[-5,]
Zt<-t(Z)
X<-model.matrix(y~FIX-1)
X<-X[-5,]
y<-y[-5]

# Iteration
ZAZ=Z%*%S%*%(Zt)
ZDZ=Z%*%S%*%D%*%(Zt)
ZAAZ=Z%*%S%*%A%*%A%*%(Zt)
ZAD2Z=Z%*%S%*%A%*%D%*%2%*%(Zt)
ZDDZ=Z%*%S%*%D%*%D%*%(Zt)
ZAHZ=Z%*%S%*%A%*%H%*%(Zt)

var_a=3
var_d=1
var_aa=6
var_ad2=4
var_dd=2
var_ah=3
var_e=1
zrows<-nrow(Z)

k<-1
for(i in 1:k){

  vge<-diag(var_e,zrows,zrows)
  V<-var_a*ZAZ+var_d*ZDZ+var_aa*ZAAZ+var_ad2*ZAD2Z+var_dd*ZDDZ+var_ah*ZAHZ+vge
  IV<-ginv(V)
  XIV<-t(X)%*%IV
  XIVX<-XIV%*%X
```
XIVY <- XIV * y
P <- IV - (t(XIV) %*%ginv(XIVX) %*% XIV)

# Get new var_a, var_d, var_aa, var_ad2, var_dd, var_ah, var_e

PZAZ = P %*% ZAZ
PZDZ = P %*% ZDZ
PZAAZ = P %*% ZAAZ
PZAD2Z = P %*% ZAD2Z
PZDDZ = P %*% ZDDZ
PZAHZ = P %*% ZAHZ

var_a = (t(y) %*% PZAZ %*% P %*% y * (var_a / sum(diag(PZAZ))))[1]
var_d = (t(y) %*% PZDZ %*% P %*% y * (var_d / sum(diag(PZDZ))))[1]
var_aa = (t(y) %*% PZAAZ %*% P %*% y * (var_aa / sum(diag(PZAAZ))))[1]
var_ad2 = (t(y) %*% PZAD2Z %*% P %*% y * (var_ad2 / sum(diag(PZAD2Z))))[1]
var_dd = (t(y) %*% PZDDZ %*% P %*% y * (var_dd / sum(diag(PZDDZ))))[1]
var_ah = (t(y) %*% PZAHZ %*% P %*% y * (var_ah / sum(diag(PZAHZ))))[1]
var_e = (t(y) %*% P %*% P %*% y * (var_e / sum(diag(P))))[1]

rownames <- c("Variance_component_A", "Variance_component_D", "Variance_component_AA", "Variance_component_AD2", "Variance_component_DD", "Variance_component_AH", "Variance_component_E")
colnames <- c("Value")

c <- matrix(c(var_a, var_d, var_aa, var_ad2, var_dd, var_ah, var_e), nrow=length(rownames), ncol=length(colnames), byrow=FALSE, dimnames=list(rownames, colnames))

print(c)

# Get Heritability

var_p <- var_a + var_d + var_aa + var_ad2 + var_dd + var_ah + var_e
Heritability_A <- var_a / var_p
Heritability_D <- var_d / var_p
Heritability_AA <- var_aa / var_p
Heritability_AD2 <- var_ad2 / var_p
Heritability_DD <- var_dd / var_p
Heritability_AH <- var_ah / var_p
Heritability_Gc <- Heritability_A + Heritability_D + Heritability_AA + Heritability_AD2 + Heritability_DD + Heritability_AH

rownames <- c("Heritability_A", "Heritability_D", "Heritability_AA", "Heritability_AD2", "Heritability_DD", "Heritability_AH", "Heritability_G")
colnames<-c("Value")

outhr2<-matrix(c(Heritability_A,Heritability_D,Heritability_AA,Heritability_AD2,Heritability_DD,Heritability_AH),nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))

print(outhr2)

# 3. GBLUP and reliability values

vge<-diag(var_e,zrows,zrows)
GA<-var_a*SA
GD<-var_d*SD
GAA<-var_aa*SAA
GAD2<-var_ad2*SAD2
GDD<-var_dd*SDD
GAH<-var_ah*SAH
ZGAZ=Z%*%GA%*%(Zt)
ZGDZ=Z%*%GD%*%(Zt)
ZGAAZ=Z%*%GAA%*%(Zt)
ZGAD2Z=Z%*%GAD2%*%(Zt)
ZGDDZ=Z%*%GDD%*%(Zt)
ZGAHZ=Z%*%GAH%*%(Zt)
V<-2*GAZ+2*GDZ+2*GAAZ+2*GAD2Z+2*GDDZ+2*GAHZ+vge
IV<-ginv(V)
XIV<-t(X)%*%IV
XIVX<-XIV%*%X
XIVY<-XIV%*%y
P<-IV-(t(XIV)%*%ginv(XIVX)%*%XIV)
PY<-P%*%y
ZPY<-Zt%*%PY
ZtPZ<-Zt%*%P%*%Z
Gblup_A<-GA%*%ZPY
Rel_A<-diag(GA%*%ZtPZ%*%GA)/diag(GA) #Reliability_A
Gblup_D<-GD%*%ZPY
Rel_D<-diag(GD%*%ZtPZ%*%GD)/diag(GD)
Gblup_AA<-GAA%*%ZPY
Rel_AA<-diag(GAA%*%ZtPZ%*%GAA)/diag(GAA)
Gblup_AD2 <- GAD2 %*% ZPY
Rel_AD2 <- diag(GAD2 %*% ZtPZ %*% GAD2) / diag(GAD2)
Gblup_DD <- GDD %*% ZPY
Rel_DD <- diag(GDD %*% ZtPZ %*% GDD) / diag(GDD)
Gblup_AH <- GAH %*% ZPY
Rel_AH <- diag(GAH %*% ZtPZ %*% GAH) / diag(GAH)
Gblup_G <- Gblup_A + Gblup_D + Gblup_AA + Gblup_AD2 + Gblup_DD + Gblup_AH
G <- GA + GD + GAA + GAD2 + GDD + GAH
Rel_G <- diag(G %*% ZtPZ %*% G) / diag(G)
rownames <- ID
colnames <- c("Gblup_A", "Rel_A", "Gblup_D", "Rel_D", "Gblup_AA", "Rel_AA", "Gblup_AD2", "Rel_AD2", "Gblup_DD", "Rel_DD", "Gblup_AH", "Rel_AH", "Gblup_G", "Rel_G")
outebv <- matrix(c(Gblup_A, Rel_A, Gblup_D, Rel_D, Gblup_AA, Rel_AA, Gblup_AD2, Rel_AD2, Gblup_DD, Rel_DD, Gblup_AH, Rel_AH, Gblup_G, Rel_G), nrow=length(rownames), ncol=length(colnames), byrow=FALSE, dimnames=list(rownames, colnames))
print(outebv)

# 4. Effect and heritability estimates for all levels of all effect types

# A and D effects
TA = t(WA) / sqrt(KA)
TD = t(WD) / sqrt(KD)
TAH = t(WAH) / sqrt(KAH)
rownames <- SNPs_name
colnames <- c("Effect_A", "Heritability_A", "Effect_D", "Heritability_D")
mrk_eff_A = var_a * TA %*% ZPY
Her_eff_A = (mrk_eff_A^2 / sum(mrk_eff_A^2)) * Heritability_A
mrk_eff_D = var_d * TD %*% ZPY
Her_eff_D = (mrk_eff_D^2 / sum(mrk_eff_D^2)) * Heritability_D
SNP_A_D <- matrix(c(mrk_eff_A, Her_eff_A, mrk_eff_D, Her_eff_D), nrow=length(rownames), ncol=length(colnames), byrow=FALSE, dimnames=list(rownames, colnames))
print(SNP_A_D)

# AH effect
rownames <- Haps_name
colnames<-c("Effect_AH","Heritability_AH")

mrk_eff_AH=var_ah*TAH*ZPY

Her_eff_AH=(mrk_eff_AH^2/sum(mrk_eff_AH^2))*Heritability_AH

SNP_eff_AH<-matrix(c(mrk_eff_AH,Her_eff_AH),nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))

print(SNP_eff_AH)

# AA,AD,DA and DD effects

TAA=t(WAA)/sqrt(KAA)
TAD=t(WAD)/sqrt(KAD)
TDA=t(WDA)/sqrt(KDA)
TDD=t(WDD)/sqrt(KDD)

mrk_eff_AA=var_aa*TAA*ZPY

Her_eff_AA=(mrk_eff_AA^2/sum(mrk_eff_AA^2))*Heritability_AA

mrk_eff_AD=var_ad2*TAD*ZPY

Her_eff_AD=(mrk_eff_AD^2/sum(mrk_eff_AD^2))*Heritability_AD2

mrk_eff_DA=var_ad2*TDA*ZPY

Her_eff_DA=(mrk_eff_DA^2/sum(mrk_eff_DA^2))*Heritability_AD2

mrk_eff_DD=var_dd*TDD*ZPY

Her_eff_DD=(mrk_eff_DD^2/sum(mrk_eff_DD^2))*Heritability_DD

Her_eff_epi<-cbind(mrk_eff_AA,Her_eff_AA,mrk_eff_AD,Her_eff_AD,mrk_eff_DA,Her_eff_DA,mrk_eff_DD,Her_eff_DD)

rownames<-SNPs_pair

colnames<-c("Effect_AA","Heritability_AA","Effect_AD","Heritability_AD","Effect_DA","Heritability_DA","Effect_DD","Heritability_DD")

SNP_epi_eff<-matrix(Her_eff_epi,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))

print(SNP_epi_eff)

# 5. Genomic relationship matrices of AxA, AxD and DxD using additive and dominance model matrices

# Method of Jiang and Reif, 2020

rownames<-ID

colnames<-ID
WWAA = 0.5 * ((WA * t(WA))^2 - (WA^2) * (t(WA^2)))
KAA = mean(diag(WWAA))
SAA = WWAA / KAA
SAA <- matrix(SAA, nrow=length(rownames), ncol=length(colnames), byrow=FALSE, dimnames=list(rownames, colnames))
print("SAA matrix")
print(SAA)

WWAD2 = (WA * t(WA)) * (WD * t(WD)) - (WA * WD) * t(WA * WD)
KAD2 = mean(diag(WWAD2))
SAD2 <- WWAD2 / KAD2
SAD2 <- matrix(SAD2, nrow=length(rownames), ncol=length(colnames), byrow=FALSE, dimnames=list(rownames, colnames))
print("SAD2 matrix")
print(SAD2)

WWDD = 0.5 * ((WD * t(WD))^2 - (WD^2) * (t(WD^2)))
KDD = mean(diag(WWDD))
SDD <- WWDD / KDD
SDD <- matrix(SDD, nrow=length(rownames), ncol=length(colnames), byrow=FALSE, dimnames=list(rownames, colnames))
print("SDD matrix")
print(SDD)

#*************
# Third order epistasis
# Genomic relationship matrices using SNP model matrices
# Method of Jiang and Reif, 2020.
genostat_update_epi <- function(M=NULL, mtype){
  colnames <- c("genotype_000", "genotype_001", "genotype_002", "genotype_010", "genotype_011", "genotype_012", "genotype_020", "genotype_021", "genotype_022", "genotype_100", "genotype_101", "genotype_102", "genotype_110", "genotype_111", "genotype_112", "genotype_120", "genotype_121", "genotype_122", "genotype_200", "genotype_201", "genotype_202", "genotype_210", "genotype_211", "genotype_212", "genotype_220", "genotype_221", "genotype_222")
  mrkn <- ncol(M)
  Mepi <- matrix(0, choose(mrkn, 3), 27)
  a <- 1
for(i in 1:mrkn){
    for(j in 2:mrkn){
        for(k in 3:mrkn){
            if((k>j)&&(j>i)){
                if(mtype=="AAA"){
                    first_s<-c(M[1,i],M[2,i],M[3,i])
                    second_s<-c(M[1,j],M[2,j],M[3,j])
                    third_s<-c(M[1,k],M[2,k],M[3,k])
                    rownames<-
                    c("WAAA_123","WAAA_124","WAAA_125","WAAA_126","WAAA_134","WAAA_135","WAAA_136","WAAA_145","WAAA_146","WAAA_156","WAAA_234","WAAA_235","WAAA_236","WAAA_245","WAAA_246","WAAA_256","WAAA_345","WAAA_346","WAAA_356","WAAA_456")
                } else if(mtype=="DDD"){
                    first_s<-c(M[4,i],M[5,i],M[6,i])
                    second_s<-c(M[4,j],M[5,j],M[6,j])
                    third_s<-c(M[4,k],M[5,k],M[6,k])
                    rownames<-
                    c("WDDD_123","WDDD_124","WDDD_125","WDDD_126","WDDD_134","WDDD_135","WDDD_136","WDDD_145","WDDD_146","WDDD_156","WDDD_234","WDDD_235","WDDD_236","WDDD_245","WDDD_246","WDDD_256","WDDD_345","WDDD_346","WDDD_356","WDDD_456")
                } else if(mtype=="AAD"){
                    first_s<-c(M[1,i],M[2,i],M[3,i])
                    second_s<-c(M[1,j],M[2,j],M[3,j])
                    third_s<-c(M[4,k],M[5,k],M[6,k])
                    rownames<-
                    c("WAAD_123","WAAD_124","WAAD_125","WAAD_126","WAAD_134","WAAD_135","WAAD_136","WAAD_145","WAAD_146","WAAD_156","WAAD_234","WAAD_235","WAAD_236","WAAD_245","WAAD_246","WAAD_256","WAAD_345","WAAD_346","WAAD_356","WAAD_456")
                } else if(mtype=="ADA"){
                    first_s<-c(M[1,i],M[2,i],M[3,i])
                    second_s<-c(M[4,j],M[5,j],M[6,j])
                    third_s<-c(M[1,k],M[2,k],M[3,k])
                    rownames<-
                    c("WADA_123","WADA_124","WADA_125","WADA_126","WADA_134","WADA_135","WADA_136","WADA_145","WADA_146","WADA_156","WADA_234","WADA_235","WADA_236","WADA_245","WADA_246","WADA_256","WADA_345","WADA_346","WADA_356","WADA_456")
                }
            }
        }
    }
}

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else if(mtype=='DAA'){
    first_s<-c(M[4,i],M[5,i],M[6,i])
    second_s<-c(M[1,j],M[2,j],M[3,j])
    third_s<-c(M[1,k],M[2,k],M[3,k])
    rownames<-c("WDAA_123","WDAA_124","WDAA_125","WDAA_126","WDAA_134","WDAA_135","WDAA_136","WDAA_145","WDAA_146","WDAA_156","WDAA_234","WDAA_235","WDAA_236","WDAA_245","WDAA_246","WDAA_256","WDAA_345","WDAA_346","WDAA_356","WDAA_456")
}
else if(mtype=='DDA'){
    first_s<-c(M[4,i],M[5,i],M[6,i])
    second_s<-c(M[4,j],M[5,j],M[6,j])
    third_s<-c(M[1,k],M[2,k],M[3,k])
    rownames<-c("WDDA_123","WDDA_124","WDDA_125","WDDA_126","WDDA_134","WDDA_135","WDDA_136","WDDA_145","WDDA_146","WDDA_156","WDDA_234","WDDA_235","WDDA_236","WDDA_245","WDDA_246","WDDA_256","WDDA_345","WDDA_346","WDDA_356","WDDA_456")
}
else if(mtype=='DAD'){
    first_s<-c(M[4,i],M[5,i],M[6,i])
    second_s<-c(M[1,j],M[2,j],M[3,j])
    third_s<-c(M[4,k],M[5,k],M[6,k])
    rownames<-c("WDAD_123","WDAD_124","WDAD_125","WDAD_126","WDAD_134","WDAD_135","WDAD_136","WDAD_145","WDAD_146","WDAD_156","WDAD_234","WDAD_235","WDAD_236","WDAD_245","WDAD_246","WDAD_256","WDAD_345","WDAD_346","WDAD_356","WDAD_456")
}
else if(mtype=='ADD'){
    first_s<-c(M[1,i],M[2,i],M[3,i])
    second_s<-c(M[4,j],M[5,j],M[6,j])
    third_s<-c(M[4,k],M[5,k],M[6,k])
    rownames<-c("WADD_123","WADD_124","WADD_125","WADD_126","WADD_134","WADD_135","WADD_136","WADD_145","WADD_146","WADD_156","WADD_234","WADD_235","WADD_236","WADD_245","WADD_246","WADD_256","WADD_345","WADD_346","WADD_356","WADD_456")
}

snp1<-rep(first_s,each=9)
snp2<-rep(second_s,each=3,time=3)
snp3<-rep(third_s,9)
one_comb<-snp1*snp2*snp3
Mepi[a,]<-one_comb
    a<-a+1
    Mepi<-matrix(Mepi,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
    return (Mepi)
}

geno_transform_epi<-function(G=NULL,Gepi=NULL){
    my_3_order_dic=array(0,dim=c(3,3,3))
    my_3_order_dic[1,1,1]=1
    my_3_order_dic[1,1,2]=2
    my_3_order_dic[1,1,3]=3
    my_3_order_dic[1,2,1]=4
    my_3_order_dic[1,2,2]=5
    my_3_order_dic[1,2,3]=6
    my_3_order_dic[1,3,1]=7
    my_3_order_dic[1,3,2]=8
    my_3_order_dic[1,3,3]=9
    my_3_order_dic[2,1,1]=10
    my_3_order_dic[2,1,2]=11
    my_3_order_dic[2,1,3]=12
    my_3_order_dic[2,2,1]=13
    my_3_order_dic[2,2,2]=14
    my_3_order_dic[2,2,3]=15
    my_3_order_dic[2,3,1]=16
    my_3_order_dic[2,3,2]=17
    my_3_order_dic[2,3,3]=18
    my_3_order_dic[3,1,1]=19
    my_3_order_dic[3,1,2]=20
    my_3_order_dic[3,1,3]=21
    my_3_order_dic[3,2,1]=22
    my_3_order_dic[3,2,2]=23
my_3_order_dic[3,2,3]=24
my_3_order_dic[3,3,1]=25
my_3_order_dic[3,3,2]=26
my_3_order_dic[3,3,3]=27

indv<-nrow(G)
mrnk<-ncol(G)
r=choose(mrnk,3)
rownames<-ID
colnames<-c("SNP_123","SNP_124","SNP_125","SNP_126","SNP_134","SNP_135","SNP_136","SNP_145","SNP_146","SNP_156","SNP_234","SNP_235","SNP_236","SNP_245","SNP_246","SNP_256","SNP_345","SNP_346","SNP_356","SNP_456")

W=matrix(0,indv,r)

for(m in 1:indv){
  a=1
  for(i in 1:mrnk){
    for(j in 2:mrnk){
      for(k in 3:mrnk){
        if((k>j) && (j>i)){
          indx1=G[m,i]+1
          indx2=G[m,j]+1
          indx3=G[m,k]+1
          W[m,a]<-
          Gepi[a,my_3_order_dic[indx1,indx2,indx3]]
        }
        a<-a+1
      }
    }
  }
}

W<-matrix(W,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))

return (W)
}

rownames<-SNPs_name
colnames<-ID
genotype_file <- matrix(c(0, 2, 0, 1, 0, 2, 0, 1, 0, 1, 1, 2, 0, 1, 0, 1, 0, 0, 1, 1, 0, 1, 1, 1, 1, 0), nrow=length(rownames), ncol=length(colnames), byrow=FALSE, dimnames=list(rownames, colnames))

geno <- t(genotype_file)

rownames <- c("Additive_0", "Additive_1", "Additive_2", "Dominance_0", "Dominance_1", "Dominance_2")
colnames <- SNPs_name


geno_stat <- matrix(c(WA1_0, WA2_0, WA3_0, WA4_0, WA5_0, WA6_0, WA1_1, WA2_1, WA3_1, WA4_1, WA5_1, WA6_1, WA1_2, WA2_2, WA3_2, WA4_2, WA5_2, WA6_2, WD1_0, WD2_0, WD3_0, WD4_0, WD5_0, WD6_0, WD1_1, WD2_1, WD3_1, WD4_1, WD5_1, WD6_1, WD1_2, WD2_2, WD3_2, WD4_2, WD5_2, WD6_2), nrow=length(rownames), ncol=length(colnames), byrow=TRUE, dimnames=list(rownames, colnames))

Mepi <- genostat_update_epi(geno_stat, "AAA")

WAAA <- geno_transform_epi(geno, Mepi)

Mepi <- genostat_update_epi(geno_stat, "AAD")

WAAD <- geno_transform_epi(geno, Mepi)

Mepi <- genostat_update_epi(geno_stat, "ADA")

WADA <- geno_transform_epi(geno, Mepi)

Mepi <- genostat_update_epi(geno_stat, "DAA")

WDAA <- geno_transform_epi(geno, Mepi)

Mepi <- genostat_update_epi(geno_stat, "ADD")

WADD <- geno_transform_epi(geno, Mepi)

Mepi <- genostat_update_epi(geno_stat, "DAD")

WDAD <- geno_transform_epi(geno, Mepi)

Mepi <- genostat_update_epi(geno_stat, "DDA")

WDDA <- geno_transform_epi(geno, Mepi)

Mepi <- genostat_update_epi(geno_stat, "DDD")

WDDD <- geno_transform_epi(geno, Mepi)

# Print WAAA, WAAD, WADA, WDAA, WADD, WDAD, WDDA, and WDDD matrices

print("WAAA")
print(WAAA)

print("WAAD")
print(WAAD)

print("WADA")
print(WADA)

print("WDAA")
print(WDAA)

print("WADD")
print(WADD)
print(WADD)
print("WDAD")
print(WDAD)
print("WDDA")
print(WDDA)
print("WDDD")
print(WDDD)
#
rownames<-ID
colnames<-ID
WWAAA=WAAA**t(WAAA)
KAAA=mean(diag(WWAAA))
SAAA<-WWAAA/KAAA
SAAA<-matrix(SAAA,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
print("SAAA matrix")
print(SAAA)
#
WWAAD=WAAD**t(WAAD)
WWADA=WADA**t(WADA)
WWDAA=WDAA**t(WDAA)
WWAAD3=WWAAD+WWADA+WWDAA
KAAD3=mean(diag(WWAAD3))
SAAD3<-WWAAD3/KAAD3
SAAD3<-matrix(SAAD3,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
print("SAAD3 matrix")
print(SAAD3)
#
WWADD=WADD**t(WADD)
WWDAD=WDAD**t(WDAD)
WWDDA=WDDA**t(WDDA)
WWADD3=WWADD+WWDAD+WWDDA
KADD3=mean(diag(WWADD3))
SADD3<-WWADD3/KADD3
SADD3<-matrix(SADD3,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
print("SADD3 matrix")
print(SADD3)
#
WWDDD=WDDD%*%t(WDDD)
KDDD=mean(diag(WWDDD))
SDDD<-WWDDD/KDDD
SDDD<-matrix(SDDD,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
print("SDDD matrix")
print(SDDD)
FIX<-c(2,2,1,1,1)
y<-c(1.753222323,1.617654738,1.71311938,1.738835045,-9999)
ID<-factor(ID)
FIX<-factor(FIX)
data<-data.frame(ID,y)
Z<-model.matrix(y ~ID-1)
Z<-Z[-5,]
Zt<-t(Z)
X<-model.matrix(y~FIX-1)
X<-X[-5,]
y<-y[-5]

#Iteration
ZAZ=Z%*%SAA%*%(Zt)
ZDZ=Z%*%SD%*%(Zt)
ZAAZ=Z%*%SAA%*%(Zt)
ZAD2Z=Z%*%SAD2%*%(Zt)
ZDDZ=Z%*%SDD%*%(Zt)
ZAAAZ=Z%*%SAAA%*%(Zt)
ZAAD3Z=Z%*%SAAD3%*%(Zt)
ZADD3Z=Z%*%SADD3%*%(Zt)
ZDDDZ=Z%*%SDDD%*%(Zt)
ZAHZ=Z%*%SAH%*%(Zt)
var_a=3
var_d=1
var_aa=6
var_ad2=4
var_dd=2
var_aaa=9
var_aad3=7
var_add3=5
var_ddd=3
var_ah=3
var_e=1
zrows<-nrow(Z)

#EM-REML
k<-1
for(i in (1:k)){
  vge<-diag(var_e,zrows,zrows)
  V<-var_a*ZAZ+var_d*ZDZ+var_aa*ZAAZ+var_ad2*ZAD2Z+var_dd*ZDDZ+var_aaa*ZAAAZ+var_aad3*ZAA
  D3Z+var_add3*ZADD3Z+var_ddd*ZDDDZ+var_ah*ZAHZ+vge
  IV<-ginv(V)
  XIV<-t(X)%*%IV
  XIVX<-XIV%*%X
  XIVY<-XIV%*%y
  P<-IV-(t(XIV)%*%ginv(XIVX)%*%XIV)
  # Get new var_a, var_d, var_aa, var_ad2, var_dd, var_ah, var_e
  P2AZ=P%*%ZAZ
  P2DZ=P%*%ZDZ
  P2AAZ=P%*%ZAAZ
  P2AD2Z=P%*%ZAD2Z
  P2DDZ=P%*%ZDDZ
  P2AAA2Z=P%*%ZAAAZ
  P2AAD3Z=P%*%ZAAD3Z
  P2ADD3Z=P%*%ZADD3Z
  P2DDDZ=P%*%ZDDDZ
PZAHZ=P%*%ZAHZ
var_a=(t(y)%*%PZAZ%*%P%*%y*(var_a/sum(diag(PZAZ))))[1]
var_d=(t(y)%*%PZDZ%*%P%*%y*(var_d/sum(diag(PZDZ))))[1]
var_aa=(t(y)%*%PZAAZ%*%P%*%y*(var_aa/sum(diag(PZAAZ))))[1]
var_ad2=(t(y)%*%PZAD2Z%*%P%*%y*(var_ad2/sum(diag(PZAD2Z))))[1]
var_dd=(t(y)%*%PZDDZ%*%P%*%y*(var_dd/sum(diag(PZDDZ))))[1]
var_aaa=(t(y)%*%PZAAAZ%*%P%*%y*(var_aaa/sum(diag(PZAAAZ))))[1]
var_aad3=(t(y)%*%PZAAD3Z%*%P%*%y*(var_aad3/sum(diag(PZAAD3Z))))[1]
var_add3=(t(y)%*%PZADD3Z%*%P%*%y*(var_add3/sum(diag(PZADD3Z))))[1]
var_ddd=(t(y)%*%PZDDDZ%*%P%*%y*(var_ddd/sum(diag(PZDDDZ))))[1]
var_ah=(t(y)%*%PZAHZ%*%P%*%y*(var_ah/sum(diag(PZAHZ))))[1]
var_e=(t(y)%*%P%*%P%*%y*(var_e/sum(diag(P))))[1]
}
rownames<-c("Variance_component_A","Variance_component_D","Variance_component_AA","Variance_component_AD2","Variance_component_DD","Variance_component_AAA","Variance_component_AAD3","Variance_component_ADD3","Variance_component_DDD","Variance_component_AH","Variance_component_E")
colnames<-c("Value")
outv3<-matrix(c(var_a,var_d,var_aa,var_ad2,var_dd,var_aaa,var_aad3,var_add3,var_ddd,var_ah,var_e),nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames,colnames))
print(outv3)
# Get Heritability
var_p<-var_a+var_d+var_aa+var_ad2+var_dd+var_aaa+var_aad3+var_add3+var_ddd+var_ah+var_e
Heritability_A<-var_a/var_p
Heritability_D<-var_d/var_p
Heritability_AA<-var_aa/var_p
Heritability_AD2<-var_ad2/var_p
Heritability_DD<-var_dd/var_p
Heritability_AAA<-var_aaa/var_p
Heritability_AAD3<-var_aad3/var_p
Heritability_ADD3<-var_add3/var_p
Heritability_DDD<-var_ddd/var_p
Heritability_AH<-var_ah/var_p
Heritability_G <-
Heritability_A + Heritability_D + Heritability_AA + Heritability_AD2 + Heritability_DD + Heritability_AAA + Heritability_AAD3 + Heritability_ADD3 + Heritability_DDD + Heritability_AH

rownames <-
c("Heritability_A", "Heritability_D", "Heritability_AA", "Heritability_AD2", "Heritability_DD", "Heritability_AAA", "Heritability_AAD3", "Heritability_ADD3", "Heritability_DDD", "Heritability_AH", "Heritability_G")

colnames <- c("Value")

outher <-
matrix(c(Heritability_A, Heritability_D, Heritability_AA, Heritability_AD2, Heritability_DD, Heritability_AAA, Heritability_AAD3, Heritability_ADD3, Heritability_DDD, Heritability_AH, Heritability_G), nrow = length(rownames), ncol = length(colnames), byrow = FALSE, dimnames = list(rownames, colnames))

print(outher)

# 3. GBLUP and reliability values

vge <- diag(var_e, zrows, zrows)
GA <- var_a * SA
GD <- var_d * SD
GAA <- var_aa * SAA
GAD2 <- var_ad2 * SAD2
GDD <- var_dd * SDD
GAAA <- var_aaa * SAAA
GAAD3 <- var_aad3 * SAAD3
GADD3 <- var_add3 * SADD3
GDDD <- var_ddd * SDDD
GAH <- var_ah * SAH
ZGAZ <- Z %*% GA %*% (Zt)
ZGDZ <- Z %*% GD %*% (Zt)
ZGAAZ <- Z %*% GAA %*% (Zt)
ZGAD2Z <- Z %*% GAD2 %*% (Zt)
ZGD2Z <- Z %*% GDD %*% (Zt)
ZGAAAZ <- Z %*% GAAA %*% (Zt)
ZGAAD3Z <- Z %*% GAAD3 %*% (Zt)
ZGADD3Z <- Z %*% GADD3 %*% (Zt)
ZGDADD3Z <- Z %*% GDDD %*% (Zt)
ZGAHZ <- Z %*% GAH %*% (Zt)
V <- ZGAZ + ZGDZ + ZGAAZ + ZGAD2Z + ZGD2Z + ZGAAAZ + ZGAAD3Z + ZGADD3Z + ZGDADD3Z + ZGAHZ + vge
IV<-ginv(V)
XIV<-t(X)%*%IV
XIVX<-XIV%*%X
XIVY<-XIV%*%y
P<-IV-(t(XIV)%*%ginv(XIVX)%*%XIV)
PY<-P%*%y
ZPY<-Zt%*%PY
ZtPZ<-Zt%*%P%*%Z
Gblup_A<-GA%*%ZPY
Rel_A<-diag(GA%*%ZtPZ%*%GA)/diag(GA) #Reliability_A
Gblup_D<-GD%*%ZPY
Rel_D<-diag(GD%*%ZtPZ%*%GD)/diag(GD)
Gblup_AA<-GAA%*%ZPY
Rel_AAA<-diag(GAAA%*%ZtPZ%*%GAAA)/diag(GAAA)
Rel_AA<-diag(GAAD3%*%ZtPZ%*%GAAD3)/diag(GAAD3)
Rel_AD2<-diag(GAD2%*%ZtPZ%*%GAD2)/diag(GAD2)
Rel_DD<-diag(GADD3%*%ZtPZ%*%GADD3)/diag(GADD3)
Gblup_DDD<-GDDD%*%ZPY
Rel_DDD<-diag(GDDD%*%ZtPZ%*%GDDD)/diag(GDDD)
Gblup_AH<-GAH%*%ZPY
Rel_AH<-diag(GAH%*%ZtPZ%*%GAH)/diag(GAH)
Gblup_G<-Gblup_A+Gblup_D+Gblup_AA+Gblup_AD2+Gblup_DD+Gblup_AAA+Gblup_AAD3+Gblup_ADD3+Gblup_DD+Gblup_AH
G<-GA+GD+GAA+GAD2+GDD+GAAA+GAAD3+GADD3+GDDD+GAH
Rel_G<-diag(G%*%ZtPZ%*%G)/diag(G)
rownames<-ID
colnames<-c("Gblup_A","Rel_A","Gblup_D","Rel_D","Gblup_AA","Rel_AA","Gblup_AD2","Rel_AD2","Gblup_DD")
outgblup<-matrix(c(Gblup_A,Rel_A,Gblup_D,Rel_D,Gblup_AA,Rel_AA,Gblup_AD2,Rel_AD2,Gblup_DD,Rel_DD,Gblup_AAA,Rel_AAA,Gblup_AAD3,Rel_AAD3,Gblup_ADD3,Rel_ADD3,Gblup_DDD,Rel_DDD,Gblup_AH,Rel_AH,Gblup_G,Rel_G),nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
print(outgblup)

# 6. Third order epistasis genomic relationship matrices using additive and dominance model matrices
# Method of Jiang and Reif, 2020

rownames<-ID
colnames<-ID
WWAAA=(1/6)*((WA%*%t(WA))^3)-(1/2)*(((WA^2)%*%(t(WA^2)))*(WA%*%t(WA)))+(1/3)*((WA^3)%*%(t(WA^3)))
KAAA=mean(diag(WWAAA))
SAAA<-WWAAA/KAAA
SAAA<-matrix(SAAA,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
print("SAAA matrix")
print(SAAA)

WWAAD3=0.5*(((WA%*%t(WA))^2)*(WD%*%t(WD))-((WA^2)%*%(t(WA^2)))*(WD%*%t(WD)))-((WA*WD)%*%(t(WA*WD)))*(WA%*%t(WA))+(WA*WA*WD)%*%(t(WA*WA*WD))
KAAD3=mean(diag(WWAAD3))
SAAD3<-WWAAD3/KAAD3
SAAD3<-matrix(SAAD3,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
print("SAAD3 matrix")
print(SAAD3)

WWADD3=0.5*(((WD%*%t(WD))^2)*(WA%*%t(WA))-((WD^2)%*%(t(WD^2)))*(WA%*%t(WA)))-((WA*WD)%*%(t(WA*WD)))*(WD%*%t(WD))+(WA*WD*WD)%*%(t(WA*WD*WD))
KADD3=mean(diag(WWADD3))
SADD3<-WWADD3/KADD3
SADD3<-matrix(SADD3,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
print("SADD3 matrix")
print(SADD3)

WWDDD=(1/6)*((WD%*%t(WD))^3) - 
(1/2)*(((WD^2)%*%(t(WD^2)))*(WD%*%t(WD)))+(1/3)*((WD^3)%*%(t(WD^3)))
KDDD=mean(diag(WWDDD))
SDDD<-WWDDD/KDDD
SDDD<-matrix(SDDD,nrow=length(rownames),ncol=length(colnames),byrow=FALSE,dimnames=list(rownames, colnames))
print("SDDD matrix")
print(SDDD)
| TABLE S1 | Notations of the quantitative genetics (QG) model, reparameterized and equivalent QG (RE-QG) model, and multifactorial (MF) model. |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Model-I**: pairwise epistasis effects without dividing into intra- and inter-chromosome effects |
| **Additive effects** | $\mathbf{a}_o$ | $\mathbf{u}_i$ | $\mathbf{a} = k_\alpha^{1/2} \mathbf{a}_o$ | $\mathbf{u}_i = T_\alpha \mathbf{a}$ |
| **Model matrix** | $W_\alpha$ | $W_\delta$ | $T_\alpha = W_\alpha / k_\alpha^{1/2}$ | $T_\delta = W_\delta / k_\delta^{1/2}$ |
| **Additive values** | $\mathbf{a} = W_\alpha \mathbf{a}_o$ | $\mathbf{u}_2$ | $\mathbf{a} = T_\alpha \mathbf{a}$ | $\mathbf{u}_2 = T_\delta \mathbf{a}$ |
| **Variance of additive effects** | $\sigma_{a \alpha}^2$ | $\sigma_{a \delta}^2$ | $\sigma_{a \alpha}^2 = k_\alpha \sigma_{a \alpha}^2$ | $\sigma_{a \delta}^2 = k_\delta \sigma_{a \delta}^2$ |
| **Variance of additive values** | $G^a_{\alpha} = \sigma_{a \alpha}^2 = \sigma_{a \alpha}^2 (W_\alpha W_\alpha)^{ii}$ | $G^a_{\delta} = \sigma_{a \delta}^2 = \sigma_{a \delta}^2 (W_\delta W_\delta)^{ii}$ | $G^a_{\alpha} = \sigma_{a \alpha}^2 = \sigma_{a \alpha}^2 (S_{\alpha})^{ii}$ | $G^a_{\delta} = \sigma_{a \delta}^2 = \sigma_{a \delta}^2 (S_{\delta})^{ii}$ |
| **k value** | $k_\alpha = \text{tr}(W_\alpha W_\alpha)^{\prime} / n$ | $S_{\alpha} = T_\alpha T_\alpha^{\prime}$ | $k_\delta = \text{tr}(W_\delta W_\delta)^{\prime} / n$ | $S_{\delta} = T_\delta T_\delta^{\prime}$ |
| **Genomic relationship matrix** | $G_\alpha = \sigma_{a \alpha}^2 W_\alpha W_\alpha^\prime$ | $G_\delta = \sigma_{a \delta}^2 W_\delta W_\delta^\prime$ | $G_\alpha = \sigma_{a \alpha}^2 S_{\alpha}$ | $G_\delta = \sigma_{a \delta}^2 S_{\delta}$ |
| **Dominance effects** | $\mathbf{d}_o$ | $\mathbf{u}_2$ | $\mathbf{d} = T_\delta \mathbf{a}$ | $\mathbf{u}_2 = T_\delta \mathbf{a}$ |
| **Model matrix** | $W_\delta$ | $W_\delta$ | $T_\delta = W_\delta / k_\delta^{1/2}$ | $T_\delta = W_\delta / k_\delta^{1/2}$ |
| **Dominance values** | $\mathbf{d} = W_\delta \mathbf{d}_o$ | $\mathbf{u}_2$ | $\mathbf{d} = T_\delta \mathbf{a}$ | $\mathbf{u}_2 = T_\delta \mathbf{a}$ |
| **Variance of dominance effects** | $\sigma_{a \delta}^2$ | $\sigma_{d \delta}^2$ | $\sigma_{d \delta}^2 = k_\delta \sigma_{d \delta}^2$ | $\sigma_{d \delta}^2 = k_\delta \sigma_{d \delta}^2$ |
| **Variance of dominance values** | $G^d_{\delta} = \sigma_{d \delta}^2 = \sigma_{d \delta}^2 (W_\delta W_\delta)^{ii}$ | $G^d_{\delta} = \sigma_{d \delta}^2 = \sigma_{d \delta}^2 (W_\delta W_\delta)^{ii}$ | $G^d_{\delta} = \sigma_{d \delta}^2 = \sigma_{d \delta}^2 (S_{\delta})^{ii}$ | $G^d_{\delta} = \sigma_{d \delta}^2 = \sigma_{d \delta}^2 (S_{\delta})^{ii}$ |
| **k value** | $k_\delta = \text{tr}(W_\delta W_\delta)^{\prime} / n$ | $S_{\delta} = T_\delta T_\delta^{\prime}$ | $k_\delta = \text{tr}(W_\delta W_\delta)^{\prime} / n$ | $S_{\delta} = T_\delta T_\delta^{\prime}$ |
| **Genomic relationship matrix** | $G_\delta = \sigma_{a \delta}^2 W_\delta W_\delta^\prime$ | $G_\delta = \sigma_{a \delta}^2 W_\delta W_\delta^\prime$ | $G_\delta = \sigma_{a \delta}^2 S_{\delta}$ | $G_\delta = \sigma_{a \delta}^2 S_{\delta}$ |
| **Haplotype additive effects** | $\mathbf{a}_{oh}$ | $\mathbf{a}_h = k_{ah}^{1/2} \mathbf{a}_{oh}$ | $\mathbf{a}_h = k_{ah}^{1/2} \mathbf{a}_{oh}$ | $\mathbf{a}_h = k_{ah}^{1/2} \mathbf{a}_{oh}$ |
| **k value** | $k_{ah} = \text{tr}(W_{ah} W_{ah}^\prime) / n_{ah}$ | $S_{ah} = T_{ah} T_{ah}^{\prime}$ | $k_{ah} = \text{tr}(W_{ah} W_{ah}^\prime) / n_{ah}$ | $S_{ah} = T_{ah} T_{ah}^{\prime}$ |
| **Genomic relationship matrix** | $G_{ah} = \sigma_{a \delta}^2 W_{ah} W_{ah}^\prime$ | $G_{ah} = \sigma_{a \delta}^2 W_{ah} W_{ah}^\prime$ | $G_{ah} = \sigma_{a \delta}^2 S_{\delta}$ | $G_{ah} = \sigma_{a \delta}^2 S_{\delta}$ |
| Model matrix | \( W_{ah} \) | \( W_3 \) | \( T_{ah} = W_{ah} / k_{ah}^{1/2} \) | \( T_3, n \times n_{ah} \) |
|--------------|--------------|--------------|-------------------|-------------------|
| Haplotype additive values | \( a_h = W_{ah} a_{ah} \) | \( u_3 \) | \( a_h = T_{ah} a_n \) | \( u_3, n \times 1 \) |
| Variance of haplotype additive effects | \( \sigma_{ah}^{2} \) | \( \sigma_{5o}^{2} \) | \( \sigma_{ah}^{2} = k_{ah} \sigma_{ho}^{2} \) | \( \sigma_3^{2} \) |
| Variance of haplotype additive values | \( G_{ah}^{ij} = \sigma_{ah}^{2} = \sigma_{ah}^{2} (W_{ah} W_{ah}^{-1})^{ij} \) | \( G_{3}^{ij} = \sigma_{3}^{2} (W_{3} W_{3}^{-1})^{ij} \) | \( G_{ah}^{ij} = \sigma_{ah}^{2} = \sigma_{ah}^{2} (S_{ah})^{ij} \) | \( k_{ah} = \text{tr}(W_{ah} W_{ah}^{-1}) / n \) |
| k value | | | \( k_3 \) | |
| Genomic relationship matrix | \( G_{ah} = \sigma_{ah}^{2} W_{ah} W_{ah}^{-1} \) | \( G_3 \) | \( S_{ah} = T_{ah} T_{ah}^{-1} \) | \( S_3, n \times n \) |
| G matrix | | | | |

**A×A effects**

| \( (\alpha \alpha)_{o} \) | \( \tau_{4o} \) | \( (\alpha \alpha) = k_{\alpha \alpha}^{1/2} (\alpha \alpha)_{o} \) | \( \tau_{4}, \binom{m}{2} \times 1 \) |
| \( W_{\alpha \alpha} \) | \( W_4 \) | \( T_{\alpha \alpha} = W_{\alpha \alpha} / k_{\alpha \alpha}^{1/2} \) | \( T_4, n \times \binom{m}{2} \) |
| \( a a = W_{\alpha \alpha} (\alpha \alpha)_{o} \) | \( u_4 \) | \( a a = T_{\alpha \alpha} (a a) \) | \( u_4, n \times 1 \) |
| Variance of A×A effects | \( \sigma_{o \alpha o}^{2} \) | \( \sigma_{4o}^{2} \) | \( \sigma_{o \alpha o}^{2} = k_{o \alpha o} \sigma_{0 o \alpha o}^{2} \) | \( \sigma_4^{2} \) |
| Variance of A×A values | \( G_{\alpha a}^{ij} = \sigma_{\alpha a j}^{2} = \sigma_{\alpha o a o}^{2} (W_{\alpha \alpha} W_{\alpha \alpha}^{-1})^{ij} \) | \( G_{4}^{ij} = \sigma_{4}^{2} (W_{4} W_{4}^{-1})^{ij} \) | \( G_{\alpha a}^{ij} = \sigma_{\alpha a j}^{2} = \sigma_{\alpha o a o}^{2} (S_{\alpha \alpha})^{ij} \) | \( k_{\alpha a} = \text{tr}(W_{\alpha \alpha} W_{\alpha \alpha}^{-1}) / n \) |
| k value | | | \( k_4 \) | |
| Genomic relationship matrix | \( G_{\alpha a} = \sigma_{\alpha a o}^{2} W_{\alpha \alpha} W_{\alpha \alpha}^{-1} \) | \( G_4 \) | \( S_{\alpha a} = T_{\alpha \alpha} T_{\alpha \alpha}^{-1} \) | \( S_4, n \times n \) |
| G matrix | | | | |

**A×D and D×A effects**

| \( (\alpha \delta)_{o}^{(2)} \) | \( \tau_{5o} \) | \( (\delta \alpha) = k_{\delta \alpha}^{1/2} (\alpha \delta)_{o}^{(2)} \) | \( \tau_{5}, 2 \binom{m}{2} \times 1 \) |
| \( W_{\alpha \delta}^{(2)} \) | \( W_5 \) | \( T_{\alpha \delta}^{(2)} = W_{\alpha \delta}^{(2)} / k_{\alpha \delta}^{1/2} \) | \( T_5, n \times 2 \binom{m}{2} \) |
| \( a d^{(2)} = W_{\alpha \delta}^{(2)} (\alpha \delta)_{o}^{(2)} \) | \( u_5 \) | \( a d^{(2)} = T_{\alpha \delta}^{(2)} (\alpha \delta)_{o}^{(2)} \) | \( u_5, n \times 1 \) |
| Variance of A×D and D×A effects | \( \sigma_{o \alpha o}^{2} \) | \( \sigma_{5o}^{2} \) | \( \sigma_{o \alpha o}^{2} = k_{o \alpha o} \sigma_{o \alpha o}^{2} \) | \( \sigma_5^{2} \) |
|                      | $\sigma^2_{\text{var}}$ | $k$ | $G_\text{matrix}$ | $G_\text{matrix}$ | $G_\text{matrix}$ |
|----------------------|------------------------|-----|-------------------|-------------------|-------------------|
| **Variance of $A \times D$ and $D \times A$ values** | $G_{ad}^i = \sigma^2_{ad} = \sigma^2_{a_0d_0} [W_{a0} W_{a0}]^i$ | $-\sigma^2_{ad}$ | $\sigma^2_{a0d0}$ | $\sigma^2_{a0d0}$ | $\sigma^2_{a0d0}$ |
| **k value** | $G_{ad}^i = \sigma^2_{ad} = \sigma^2_{a_0d_0} [W_{a0} W_{a0}]^i$ | $-\sigma^2_{ad}$ | $\sigma^2_{a0d0}$ | $\sigma^2_{a0d0}$ | $\sigma^2_{a0d0}$ |
| **Genomic relationship matrix** | $G_\text{ad} = \sigma^2_{a0d0} W_{a0} W_{a0}$ | $G_\text{ad} = \sigma^2_{a0d0} W_{a0} W_{a0}$ | $G_\text{ad} = \sigma^2_{a0d0} W_{a0} W_{a0}$ | $G_\text{ad} = \sigma^2_{a0d0} W_{a0} W_{a0}$ | $G_\text{ad} = \sigma^2_{a0d0} W_{a0} W_{a0}$ |
| **$D \times D$ effects** | | $\tau_{60}$ | $(\delta \delta)_o$ | $T_{65} = W_{65}/k_{65}^{1/2}$ | $u_6$, $n \times 1$ |
| **Model matrix** | | | $W_{65}$ | | $u_6$, $n \times 1$ |
| **$D \times D$ values** | | $d d = W_{65} (\delta \delta)_o$ | | | $u_6$, $n \times 1$ |
| **Variance of $D \times D$ effects** | | | $\sigma^2_{60}$ | | $u_6$, $n \times 1$ |
| **Variance of $D \times D$ values** | | | $G_{66}^i = \sigma^2_{60} [W_{66} W_{66}]^i$ | | $u_6$, $n \times 1$ |
| **k value** | | | $-\sigma^2_{60}$ | | $u_6$, $n \times 1$ |
| **Genomic relationship matrix** | $G_{66} = \sigma^2_{60} W_{66} W_{66}$ | $G_6$ | $G_{66} = \sigma^2_{60} W_{66} W_{66}$ | | |
| **$A \times A \times A$ effects** | | | $\tau_{70}$ | $(a a a) = k_{a0a0} (a a a)_o$ | $\tau_{70}$, $(\frac{m}{3}) \times 1$ |
| **Model matrix** | | | | | $\tau_{70}$, $(\frac{m}{3}) \times 1$ |
| **$A \times A \times A$ values** | | | $W_{a0a0}$ | | $\tau_{70}$, $(\frac{m}{3}) \times 1$ |
| **Variance of $A \times A \times A$ effects** | | | $\sigma^2_{a0a0}$ | | $\tau_{70}$, $(\frac{m}{3}) \times 1$ |
| **Variance of $A \times A \times A$ values** | | | $G_{aaa}^i = \sigma^2_{aaa} = \sigma^2_{a0a0} W_{a0a0} W_{a0a0}$ | $G_{aaa}^i = \sigma^2_{aaa} = \sigma^2_{a0a0} W_{a0a0} W_{a0a0}$ | $G_{aaa}^i = \sigma^2_{aaa} = \sigma^2_{a0a0} W_{a0a0} W_{a0a0}$ |
| **k value** | | | $-\sigma^2_{aaa}$ | | $\sigma^2_{a0a0}$ |
| **Genomic relationship matrix** | $G_{aaa} = \sigma^2_{a0a0} W_{a0a0} W_{a0a0}$ | $G_7$ | $G_{aaa} = \sigma^2_{a0a0} W_{a0a0} W_{a0a0}$ | | |
| **$A \times A \times D$ effects** | | | | | $\tau_{80}$, $(\frac{m}{3}) \times 1$ |
| **$A \times A \times D$ values** | | | $\tau_{80}$ | $(a a d) = k_{a0a0} (a a d)_o$ | $\tau_{80}$, $(\frac{m}{3}) \times 1$ |
| Model matrix | \( W^{(3)}_{\alpha\alpha\delta} \) | \( W_{8} \) | \( T^{(3)}_{\alpha\alpha\delta} = W^{(3)}_{\alpha\alpha\delta}/k_{\alpha\alpha\delta}^{1/2} \) | \( T_{8}, n \times 3^{(m)} \) |
|--------------|---------------------------------|---------|---------------------------------|------------------|
| \( aad^{(3)} = W^{(3)}_{\alpha\alpha\delta}(\alpha\alpha\delta)_{o} \) | \( \sigma^{2}_{\alpha\alpha\delta} \) | \( u_{8} \) | \( aad^{(3)} = T^{(3)}_{\alpha\alpha\delta}(\alpha\alpha\delta)_{o} \) | \( u_{8}, n \times 1 \) |
| \( \sigma^{2}_{\alpha\alpha\delta} \) | | | \( \sigma^{2}_{\alpha\alpha\delta} \) | \( \sigma_{8}^{2} \) |
| \( G_{8} = \sigma^{2}_{\alpha\alpha\delta} W^{(3)}_{\alpha\alpha\delta} W^{(3)}_{\alpha\alpha\delta} \) | \( G_{8} \) | | \( G_{8} = \sigma^{2}_{\alpha\alpha\delta}(S_{\alpha\alpha\delta})_{i}^{i} \) | \( G_{8}, n \times n \) |
| A×D×D effects | \( (\alpha\delta\delta)_{o}^{(3)} \) | \( \tau_{9} \) | \( (\alpha\delta\delta)_{o}^{(3)} = k_{\alpha\delta\delta}^{1/2}(\alpha\delta\delta)_{o}^{(3)} \) | \( \tau_{9}, 3^{(m)} \times 1 \) |
| Model matrix | \( W^{(3)}_{\alpha\delta\delta} \) | \( W_{9} \) | \( T^{(3)}_{\alpha\alpha\delta} = W^{(3)}_{\alpha\delta\delta}/k_{\alpha\delta\delta}^{1/2} \) | \( T_{9}, n \times 3^{(m)} \) |
| \( \sigma^{2}_{\alpha\delta\delta} \) | \( u_{9} \) | \( add^{(3)} = T^{(3)}_{\alpha\delta\delta}(\alpha\delta\delta)_{o}^{(3)} \) | \( u_{9}, n \times 1 \) | \( \sigma_{9}^{2} \) |
| \( G_{9} = \sigma^{2}_{\alpha\delta\delta} W^{(3)}_{\alpha\delta\delta} W^{(3)}_{\alpha\delta\delta} \) | \( G_{9} \) | | \( G_{9} = \sigma^{2}_{\alpha\delta\delta}(S_{\alpha\delta\delta})_{i}^{i} \) | \( G_{9}, n \times n \) |
| Genomic relationship matrix | \( G \) | \( S_{\alpha\alpha\delta} \) | \( S_{\alpha\alpha\delta} = T^{(3)}_{\alpha\alpha\delta}T^{(3)}_{\alpha\alpha\delta} \) | \( S_{\alpha\alpha\delta}, n \times n \) |
### D×D×D values

| Variance of D×D×D effects | $d_{oo} = W_{oo} (\delta\delta\delta)_{oo}$ | $u_{10}$ | $d_{oo} = T_{oo} (\delta\delta\delta)$ | $u_{10}$, n×1 |
|---------------------------|----------------------------------------|----------|-------------------------------------|----------------|
| Variance of D×D×D values | $\sigma^2_{oooo} \delta^2_{oo} \delta_{oo}^2 = \sigma^2_{oooo} \delta^2_{oo} \delta_{oo}^2$ | $\sigma^2_{1oo} \delta^2_{1oo} \delta_{1oo}^2 = \sigma^2_{1oo} \delta^2_{1oo} \delta_{1oo}^2$ | $G_{1oo} = \sigma^2_{1oo} \delta^2_{1oo} \delta_{1oo}^2$ | $G_{1oo}$, n×n |
| k value                   | --                                     | --       | G_{1oo} = \sigma^2_{1oo} S_{1oo}     | --                     |
| Genomic relationship     | --                                     | --       | G_{1oo} = \sigma^2_{1oo} S_{1oo}     | --                     |
| matrix                    | G matrix                               | G_{1oo}  | G_{1oo} = \sigma^2_{1oo} S_{1oo}     | G_{1oo}, n×n |

### Model-II: pairwise epistasis effects dividing into intra- and inter-chromosome effects

- Subscripts 1-3 of the MF model are the same for Model-I and Model-II
- Subscripts 4-9 of the MF Model-II are intra- and inter-chromosome terms
- Subscript J of the QG Model-II indicates intra-chromosome terms
- Subscript B of the QG Model-II indicates inter-chromosome terms
- Subscripts 7-10 of the MF Model-I for 3rd-order epistasis effects are changed to 10-13 for the MF Model-II

| Additive effects | $\alpha_o$ | $\alpha = k_{\alpha}^{1/2} \alpha_o$ | $\alpha_{10}$ | $\alpha = k_{\alpha}^{1/2} \alpha_o$ |
|------------------|------------|-----------------------------------|---------------|-----------------------------------|
| Model matrix     | $W_{\alpha}$ | $W_{1}$                           | $T_{\alpha} = W_{\alpha} / k_{\alpha}^{1/2}$ | $T_{1}$, n×m |
| Additive values  | $a = W_{\alpha} \alpha_o$ | $u_{1}$                           | $a = T_{\alpha} \alpha_o$ | $u_{1}$, n×1 |
| Variance of additive effects | $\sigma^2_{\alpha o o o}$ | $\sigma^2_{\alpha o o o} = k_{\alpha} \sigma^2_{\alpha o o o}$ | $\sigma^2_{\alpha o o o} = k_{\alpha} \sigma^2_{\alpha o o o}$ | $\sigma^2_{\alpha o o o}$ |
| Variance of additive values | $G_{\alpha}^{ij} = \sigma^2_{\alpha o o} (W_{\alpha} W_{\alpha})^{ij}$ | $G_{i o}^{ij} = \sigma^2_{1 o o} (W_{1} W_{1}^\prime)^{ij}$ | $G_{i o}^{ij} = \sigma^2_{1 o o} (S_{1})^{ij}$ | $G_{i o}^{ij} = \sigma^2_{1 o o} (S_{1})^{ij}$ |
| k value          | --         | --                                | $k_{\alpha} = tr(W_{\alpha} W_{\alpha}^\prime) / n$ | $k_{\alpha}$ |
| Genomic relationship matrix | G matrix | $G_{\alpha} = \sigma^2_{\alpha o} W_{\alpha} W_{\alpha}^\prime$ | $G_{i} = \sigma^2_{i} S_{i}$ | $G_{i}$, n×n |
| Dominance matrix  | $\delta_o$ | $\delta = k_{\delta}^{1/2} \delta_o$ | $\delta_o = T_{\delta} W_{\delta} / k_{\delta}^{1/2}$ | $\delta_o = T_{\delta} W_{\delta} / k_{\delta}^{1/2}$ |
| Dominance values | $d = W_{\delta} \delta_o$ | $u_{2}$                           | $d = T_{\delta} \delta$ | $u_{2}$, n×1 |
| Variance of dominance effects | \( \sigma^2_{\alpha_0} \) | \( \sigma^2_{\alpha_0} \) | \( \sigma^2_{\delta} = k_\delta \sigma^2_{\alpha_0} \) | \( \sigma^2_2 \) |
| Variance of dominance values | \( G_{ij}^{ij} = \sigma^2_{\delta} = \sigma^2_{\alpha_0} (W_\delta W_\delta')^{ij} \) | \( G_{ij}^{ij} = \sigma^2_{\alpha_0} (W_\alpha W_\alpha')^{ij} \) | \( G_{ij}^{ij} = \sigma^2_{\alpha_0} (S_\delta')^{ij} \) | \( G_{ij}^{ij} = \sigma^2_2 (S_2')^{ij} \) |
| k value | \( \sigma^2_{\alpha_0} \) | \( \sigma^2_{\alpha_0} \) | \( \sigma^2_{\delta} = k_\delta \sigma^2_{\alpha_0} \) | \( \sigma^2_2 \) |
| Genomic relationship matrix | \( G_d = \sigma^2_{\alpha_0} W_\delta W_\delta' \) | \( G_d = \sigma^2_{\alpha_0} W_\alpha W_\alpha' \) | \( G_d = \sigma^2_{\alpha_0} S_\delta \) | \( G_d = \sigma^2_{\alpha_0} S_\alpha \) |

| Haplotype additive effects | \( a_{oh} \) | \( \tau_{30} \) | \( a_h = k_{1/2} a_{oh} \) | \( \tau_3 \), \( n_{uh} \times 1 \) |
| Model matrix | \( W_{ah} \) | \( W'_3 \) | \( T'_{ah} = W_{ah} / k_{1/2} \) | \( T_3 \), \( n \times n_{ah} \) |
| Haplotype additive values | \( a_{h} = W_{ah} a_{oh} \) | \( u_j \) | \( a_h = T_{ah} a_{h} \) | \( u_j \), \( n \times 1 \) |
| Variance of haplotype additive effects | \( \sigma^2_{dho} \) | \( \sigma^2_{dho} \) | \( \sigma^2_{dho} = k_{ah} \sigma^2_{dro} \) | \( \sigma^2_3 \) |
| Variance of haplotype additive values | \( G_{ah}^{ij} = \sigma^2_{dho} (W_{ah} W_{ah}')^{ij} \) | \( G_{ah}^{ij} = \sigma^2_{dho} (W_{ah} W_{ah}')^{ij} \) | \( G_{ah}^{ij} = \sigma^2_{dho} (S_{ah}')^{ij} \) | \( G_{ah}^{ij} = \sigma^2_3 (S_3')^{ij} \) |
| k value | \( \sigma^2_{dho} \) | \( \sigma^2_{dho} \) | \( \sigma^2_{dho} = k_{ah} \sigma^2_{dro} \) | \( \sigma^2_3 \) |
| Genomic relationship matrix | \( G_d = \sigma^2_{dho} W_{ah} W_{ah}' \) | \( G_3 \) | \( G_d = \sigma^2_{dho} S_{ah} \) | \( G_3 \), \( n \times n \) |

| A×A effects | \( (aa)^{\text{intra}}_0 \) | \( \tau_{40} \) | \( (aa)^{\text{intra}}_0 = (k_{\text{intra}})^{1/2} (aa)^{\text{intra}}_0 \) | \( \tau_4 \), \( c_1 \times 1 \) |
| Model matrix | \( W_{\text{intra}} \) | \( W'_4 \) | \( T_{\text{intra}} = W_{\text{intra}} / (k_{\text{intra}})^{1/2} \) | \( T_4 \), \( n \times c_1 \) |
| A×A values | \( (aa)^{\text{intra}}_0 = W_{\text{intra}} (aa)^{\text{intra}}_0 \) | \( u_j \) | \( (aa)^{\text{intra}}_0 = T_{\text{intra}} (aa)^{\text{intra}}_0 \) | \( u_j \), \( n \times 1 \) |
| Variance of A×A effects | \( (\sigma^2_{\text{intra}})_0 \) | \( \sigma^2_{\alpha_0} \) | \( (\sigma^2_{\text{intra}})_0 = (k_{\text{intra}})^{1/2} (\sigma^2_{\text{intra}})_0 \) | \( \sigma^2_4 \) |
| Variance of A×A values | \( (G_{aa})^{ij} = (\sigma^2_{\text{intra}})^{\text{intra}} [W_{\text{intra}} (W_{\text{intra}}')]^{ij} \) | \( G_{ij}^{ij} = \sigma^2_4 (W_{\text{intra}} W_{\text{intra}}')^{ij} \) | \( (G_{aa})^{ij} = (\sigma^2_{\text{intra}})^{\text{intra}} (S_{\text{intra}}')^{ij} \) | \( (G_{aa})^{ij} = \sigma^2_4 (S_4')^{ij} \) |
| k value | \( \sigma^2_{\text{intra}} \) | \( \sigma^2_{\text{intra}} \) | \( \sigma^2_{\text{intra}} = k_{\text{intra}} \sigma^2_{\text{intra}} \) | \( k_4 \) |
| Genomic relationship matrix | \( G_{\alpha_0}^{ij} = (\sigma^2_{\text{intra}})^{\text{intra}} [W_{\text{intra}} (W_{\text{intra}}')]^{ij} \) | \( G_{\alpha_0}^{ij} = \sigma^2_4 (W_{\text{intra}} W_{\text{intra}}')^{ij} \) | \( G_{\alpha_0}^{ij} = \sigma^2_4 (S_{\text{intra}}')^{ij} \) | \( G_{\alpha_0}^{ij} = \sigma^2_4 (S_4')^{ij} \) |

\[ \sigma^2_2 \]
| A×D and D×A effects | (aδ)_{o}^{(2)\text{intra}} | \tau_{5o} | (aδ)_{o}^{(2)\text{intra}} | \tau_{5}, 2c_1 \times 1 |
|---------------------|-----------------------------|-----------------|-----------------------------|-------------------|
| Model matrix        | \mathbf{W}_{o\delta}^{(2)\text{intra}} | \mathbf{W}_{o\delta}^{(2)\text{intra}} | \mathbf{W}_{o\delta}^{(2)\text{intra}} | \mathbf{W}_{o\delta}^{(2)\text{intra}} |
| A×A and D×A values  | (aδ)_{o}^{(2)\text{intra}} | \mathbf{T}_{a\delta}^{(2)\text{intra}} | (aδ)_{o}^{(2)\text{intra}} | \mathbf{T}_{a\delta}^{(2)\text{intra}} |
| Variance of A×D and D×A effects | \sigma_{a\delta o}^{2} \mathbf{W}_{d\delta o}^{\text{intra}} | \sigma_{a\delta o}^{2} \mathbf{W}_{d\delta o}^{\text{intra}} | \sigma_{a\delta o}^{2} \mathbf{W}_{d\delta o}^{\text{intra}} | \sigma_{a\delta o}^{2} \mathbf{W}_{d\delta o}^{\text{intra}} |
| Variance of A×D and D×A values | \mathbf{G}_{a\delta d}^{(2)\text{intra}} | \mathbf{S}_{d\delta o}^{(2)\text{intra}} | \mathbf{G}_{a\delta d}^{(2)\text{intra}} | \mathbf{S}_{d\delta o}^{(2)\text{intra}} |
| k value             | \mathbf{k}_{d\delta}^{(2)\text{intra}} | \mathbf{k}_{d\delta}^{(2)\text{intra}} | \mathbf{k}_{d\delta}^{(2)\text{intra}} | \mathbf{k}_{d\delta}^{(2)\text{intra}} |
| Genomic relationship matrix | \mathbf{S}_{d\delta}^{(2)\text{intra}} | \mathbf{S}_{d\delta}^{(2)\text{intra}} | \mathbf{S}_{d\delta}^{(2)\text{intra}} | \mathbf{S}_{d\delta}^{(2)\text{intra}} |
| G matrix            | \mathbf{G}_{a\delta d}^{(2)\text{intra}} | \mathbf{G}_{a\delta d}^{(2)\text{intra}} | \mathbf{G}_{a\delta d}^{(2)\text{intra}} | \mathbf{G}_{a\delta d}^{(2)\text{intra}} |
| D×D effects         | (d\delta)_{o}^{(2)\text{intra}} | \tau_{6o} | (d\delta)_{o}^{(2)\text{intra}} | \tau_{6}, c_1 \times 1 |
| Model matrix        | \mathbf{W}_{\delta\delta}^{(2)\text{intra}} | \mathbf{W}_{\delta\delta}^{(2)\text{intra}} | \mathbf{W}_{\delta\delta}^{(2)\text{intra}} | \mathbf{W}_{\delta\delta}^{(2)\text{intra}} |
| D×D values          | (d\delta)_{o}^{(2)\text{intra}} | \mathbf{T}_{\delta\delta}^{(2)\text{intra}} | (d\delta)_{o}^{(2)\text{intra}} | \mathbf{T}_{\delta\delta}^{(2)\text{intra}} |
| Variance of D×D effects | \sigma_{d\delta o}^{2} \mathbf{W}_{d\delta o}^{\text{intra}} | \sigma_{d\delta o}^{2} \mathbf{W}_{d\delta o}^{\text{intra}} | \sigma_{d\delta o}^{2} \mathbf{W}_{d\delta o}^{\text{intra}} | \sigma_{d\delta o}^{2} \mathbf{W}_{d\delta o}^{\text{intra}} |
| Variance of D×D values | \mathbf{G}_{d\delta d}^{(2)\text{intra}} | \mathbf{S}_{d\delta o}^{(2)\text{intra}} | \mathbf{G}_{d\delta d}^{(2)\text{intra}} | \mathbf{S}_{d\delta o}^{(2)\text{intra}} |
| k value             | \mathbf{k}_{d\delta}^{(2)\text{intra}} | \mathbf{k}_{d\delta}^{(2)\text{intra}} | \mathbf{k}_{d\delta}^{(2)\text{intra}} | \mathbf{k}_{d\delta}^{(2)\text{intra}} |
| Genomic relationship matrix | \mathbf{S}_{d\delta}^{(2)\text{intra}} | \mathbf{S}_{d\delta}^{(2)\text{intra}} | \mathbf{S}_{d\delta}^{(2)\text{intra}} | \mathbf{S}_{d\delta}^{(2)\text{intra}} |
| G matrix            | \mathbf{G}_{d\delta d}^{(2)\text{intra}} | \mathbf{G}_{d\delta d}^{(2)\text{intra}} | \mathbf{G}_{d\delta d}^{(2)\text{intra}} | \mathbf{G}_{d\delta d}^{(2)\text{intra}} |
| Inter-chromosome pairwise epistasis | \mathbf{A}\times\mathbf{A} effects | \mathbf{A}\times\mathbf{A} effects | \mathbf{A}\times\mathbf{A} effects | \mathbf{A}\times\mathbf{A} effects |
| Model matrix        | \mathbf{W}_{\alpha\alpha}^{\text{inter}} | \mathbf{W}_{\alpha\alpha}^{\text{inter}} | \mathbf{W}_{\alpha\alpha}^{\text{inter}} | \mathbf{W}_{\alpha\alpha}^{\text{inter}} |
| A×A values          | \mathbf{W}_{\alpha\alpha}^{\text{inter}} | \mathbf{W}_{\alpha\alpha}^{\text{inter}} | \mathbf{W}_{\alpha\alpha}^{\text{inter}} | \mathbf{W}_{\alpha\alpha}^{\text{inter}} |

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| Section | Formula |
|---------|---------|
| **Variance of A×A effects** | \((\sigma_{\text{aa}}^2)_{\text{inter}} = \sigma_{\text{aa}}^2 \)  |
| **Variance of A×A values** | \(G_{\text{aa}}^{ij} = (\sigma_{\text{aa}}^2)_{\text{inter}} (W_{\text{aa}} (W_{\text{aa}}'))_{ij} \)  |
| **k value** |  |
| **Genomic relationship matrix** | \(G_{\text{aa}}^{j} = (\sigma_{\text{aa}}^2)_{\text{inter}} (W_{\text{aa}} (W_{\text{aa}}'))_{j} \)  |
| **G matrix** | \(G_{7}^{j} = (\sigma_{\text{aa}}^2)_{\text{inter}} (S_{\text{aa}} (S_{\text{aa}}'))_{j} \)  |
| **A×D and D×A effects** | \((\alpha\delta)^{2}_{\text{inter}} = (\alpha\delta)_{o} \)  |
| **Model matrix** | \(\tau_{80}^{o} \)  |
| **A×A and D×A values** | \((ad)^{2}_{\text{inter}} = W_{\text{aa}}^{2}_{\text{inter}} (ad)_{o} \)  |
| **Variance of A×D and D×A effects** | \(G_{8}^{j} = \sigma_{80}^{2} (W_{8} (W_{8})')_{j} \)  |
| **Variance of A×D and D×A values** | \(G_{8}^{j} = (\sigma_{\text{aa}}^2)_{\text{inter}}(W_{\text{aa}} (W_{\text{aa}}'))_{j} \)  |
| **k value** |  |
| **Genomic relationship matrix** | \(G_{8}^{j} = (\sigma_{\text{aa}}^2)_{\text{inter}}(W_{\text{aa}} (W_{\text{aa}}'))_{j} \)  |
| **G matrix** | \(G_{8}^{j} = (\sigma_{\text{aa}}^2)_{\text{inter}}(S_{\text{aa}} (S_{\text{aa}}'))_{j} \)  |
| **D×D effects** | \((\delta\delta)^{2}_{\text{inter}} = (\delta\delta)_{o} \)  |
| **Model matrix** | \(\tau_{90}^{o} \)  |
| **D×D values** | \((dd)^{2}_{\text{inter}} = W_{\text{dd}}^{2}_{\text{inter}} (dd)_{o} \)  |
| **Variance of D×D effects** | \(G_{9}^{j} = \sigma_{90}^{2} (W_{9} (W_{9})')_{j} \)  |
| **Variance of D×D values** | \(G_{9}^{j} = (\sigma_{\text{aa}}^2)_{\text{inter}}(W_{\text{aa}} (W_{\text{aa}}'))_{j} \)  |
| **k value** |  |
| **Genomic relationship matrix** | \(G_{9}^{j} = (\sigma_{\text{aa}}^2)_{\text{inter}}(S_{\text{aa}} (S_{\text{aa}}'))_{j} \)  |
| G matrix | G_{int} = (\sigma_{000}^2) W_{000} W_{000} | G_{\alpha} | G_{\alpha} = (\sigma_{000}^2) S_{000} | G_{\alpha}, n \times n |
| --- | --- | --- | --- | --- |
| A×A×A effects | (a a a) | \tau_{100} | (aaa) = k^{1/2}_{\alpha}(aaa)_{0} | \tau_{10}, (m_{3}) \times 1 |
| Model matrix | W_{a a a} | W_{10} | T_{\alpha a a} = W_{a a a} / k^{1/2}_{\alpha a a} | T_{10}, n \times (m_{3}) |
| A×A×A values | a a a = W_{a a a} (a a a) | u_{10} | a a = T_{a a a} (a a a) | u_{10}, n \times 1 |
| Variance of A×A×A effects | \sigma_{000}^2 | \sigma_{000}^2 | \sigma_{000}^2 = k_{\alpha a a} \sigma_{000}^2 | \sigma_{000}^2 |
| Variance of A×A×A values | C_{aa}^{i j} = \sigma_{a a a}^2 W_{a a a} W_{a a a} ' | G_{i j}^{i j} = \sigma_{100}^2 W_{10}^{(2)} W_{10}^{(2)} | G_{i j}^{i j} = \sigma_{100}^2 (S_{a a a})_{i j} | k_{10} = \text{tr}(W_{a a a} W_{a a a}) / n |
| k value | - | - | k_{10} | k_{10} |
| Genomic relationship matrix | G_{a a} = \sigma_{000}^2 W_{a a a} W_{a a a} ' | G_{10} | G_{a a} = \sigma_{000}^2 S_{a a a} | G_{10}, n \times n |
| A×A×D effects | (a a d)_{0}^{(3)} | \tau_{10} | (a a d)_{0}^{(3)} = k^{1/2}_{a a d} (a a d)_{0}^{(3)} | \tau_{10}, 3_{3}^{(m)} \times 1 |
| Model matrix | W_{a a d}^{(3)} | W_{11} | T_{a a d}^{(3)} = W_{a a d} / k^{1/2}_{a a d} | T_{11}, n \times [3_{3}^{(m)}] |
| A×A×D values | a a d^{(3)} = W_{a a d}^{(3)} (a a d)_{0}^{(3)} | u_{11} | a a d^{(3)} = T_{a a d}^{(3)} (a a d)_{0}^{(3)} | u_{11}, n \times 1 |
| Variance of A×A×D, A×D×A and D×A×A effects | \sigma_{a a d}^2 | \sigma_{110}^2 | \sigma_{a a d}^2 = \sigma_{a a d}^2 | \sigma_{a a d}^2 |
| Variance of A×A×D, A×D×A and D×A×A values | G_{a a d}^{i j} = \sigma_{a a d}^2 W_{a a d}^{(3)} W_{a a d}^{(3)} | G_{i i}^{i j} = \sigma_{110}^2 W_{11}^{(2)} W_{11}^{(2)} | G_{i i}^{i j} = \sigma_{110}^2 (S_{a a d})_{i j} | k_{11} = \text{tr}(W_{a a d} W_{a a d}) / n |
| k value | - | - | k_{11} | k_{11} |
| Genomic relationship matrix | G_{a a} = \sigma_{000}^2 S_{a a d} | G_{11} | G_{a a} = \sigma_{000}^2 S_{a a d} | G_{11}, n \times n |
| A×D×D effects | (a d d)_{0}^{(3)} | \tau_{12} | (a d d)_{0}^{(3)} = k^{1/2}_{a d d} (a d d)_{0}^{(3)} | \tau_{12}, 3_{3}^{(m)} \times 1 |
| Model matrix | W_{a d d}^{(3)} | W_{12} | T_{a d d}^{(3)} = W_{a d d} / k^{1/2}_{a d d} | T_{12}, n \times [3_{3}^{(m)}] |
| A×D×D values | $\text{add}^{(3)} = W_{\alpha\delta\delta}^{(3)} (a\delta\delta)_{o}$ | $u_{12}$ | $\text{add}^{(3)} = T_{\alpha\delta\delta}^{(3)} (a\delta\delta)_{o}$ | $u_{12}, n\times 1$ |
| D×D×D effects | $\sigma^2_{\alpha\delta\delta}$ | $\sigma^2_{120}$ | $\sigma^2_{220}$ | $\sigma^2_{12}$ |
| Model matrix | $G_{pp} = \sigma^2_{pp} [\hat{W}_{pp}^{(3)} \hat{W}_{pp}^{(3)}]'$ | $G_{12}$ | $G_{12} = \sigma^2_{12} (S_{12})_{jj}^2$ | $G_{12}, n\times n$ |
| D×D×D values | $\text{variance of A×D×D, D×A×D, and D×D×A effects}$ | $\text{k value}$ | $k_{12}$ | $S_{12}, n\times n$ |
| D×D×D values | $\text{Genomic relationship matrix}$ | $G_{pp}$ | $G_{13} = \sigma^2_{13} (S_{13})_{jj}^2$ | $G_{13}, n\times n$ |

### Table:

| A×D×D values | $\text{add}^{(3)} = W_{\alpha\delta\delta}^{(3)} (a\delta\delta)_{o}$ | $u_{12}$ | $\text{add}^{(3)} = T_{\alpha\delta\delta}^{(3)} (a\delta\delta)_{o}$ | $u_{12}, n\times 1$ |
| D×D×D effects | $\sigma^2_{\alpha\delta\delta}$ | $\sigma^2_{120}$ | $\sigma^2_{220}$ | $\sigma^2_{12}$ |
| Model matrix | $G_{pp} = \sigma^2_{pp} [\hat{W}_{pp}^{(3)} \hat{W}_{pp}^{(3)}]'$ | $G_{12}$ | $G_{12} = \sigma^2_{12} (S_{12})_{jj}^2$ | $G_{12}, n\times n$ |
| D×D×D values | $\text{variance of A×D×D, D×A×D, and D×D×A effects}$ | $\text{k value}$ | $k_{12}$ | $S_{12}, n\times n$ |
| D×D×D values | $\text{Genomic relationship matrix}$ | $G_{pp}$ | $G_{13} = \sigma^2_{13} (S_{13})_{jj}^2$ | $G_{13}, n\times n$ |