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Deviation from Mendelian inheritance expectations for haplotypes

Assume we have this pedigree for 4 animals and their genotypes for 5 SNPs in 012 format:

Animal	Sire	Dam	SNP1	SNP2	SNP3	SNP4	SNP5
1	0	0	1	0	2	2	1
2	1	0	2	1	1	0	2
3	1	2	1	0	1	1	2
4	3	2	1	0	2	1	2

**Phasing**: Genotypes need to be phased. There are many software options to get genotypes phased. Genotypes 0, 1 or 2 will have 4 different phased values (AB is not the same as BA). Phased genotypes could be phased in different ways. One of them is:

0 (AA): 0

1 (AB): 3

1 (BA): 4

2 (BB): 2

Based on this coding, the phased for the example above would be:

Animal	SNP1	SNP2	SNP3	SNP4	SNP5
1	3	0	2	2	4
2	2	4	4	0	2
3	4	0	3	3	2
4	3	0	2	3	2

Haplotypes could be created for 2 or more SNPs. In this example we will use a 3-SNP window. Thus, for the first window (SNPs 1 to 3) we have:

Animal	SNP1	SNP2	SNP3
1	3	0	2
2	2	4	4
3	4	0	3
4	3	0	2

Now we need to create the first and the second haplotype for each animal. To distinguish the differences between these genotypes, we can assign each genotype a different numeric value:

0 11

2 2 2

3 12

4 21

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Animal 1	Haplotype 1	1	1	2
	Haplotype 2	2	1	2
A mim of 2	Haplotype 1	2	2	2
Animal 2	Haplotype 2	2	1	1
12	Haplotype 1	2	1	1
Animal 3	Haplotype 2 2 Haplotype 1 2 Haplotype 2 2 Haplotype 2 2 Haplotype 1 2 Haplotype 2 1 Haplotype 1 1	1	1	2
Animal 4	Haplotype 1	1	1	2
	Haplotype 2	2	1	2

Duplicated haplotypes give the same results! Thus, we need to get the unique haplotypes among all the generated haplotypes. In this example, unique haplotypes are 4:

- 1. 112
- 2. 212
- 3. 222
- 4. 211

Now, these haplotypes will be as if they are the genotypes! Yes, for example, the haplotype 112, the animals that carry two copies of the 112 will be AA, one copy will be AB and BB if the animal does not carry this haplotype. The following are all possible matings:

Parent 1		Parent 2	Offspring
AA	X	AA	AA
AA	X	AB	AA
AA	X	AB	AB
AA	X	BB	AB
AB	X	AA	AA
AB	X	AA	AB
AB	X	AB	AA
AB	X	AB	AB
AB	X	AB	BB
AB	X	BB	AB
AB	X	BB	BB
BB	X	AA	AB
BB	X	AB	AB
BB	X	AB	BB
BB	X	BB	BB

Since we have four unique haplotypes, then we need to use them to obtain all possible matings. Animals 1 and 2 (from the pedigree) had at least one parent missing, so they would not be involved in this calculation as the focus here is to use trios only. We start from animal 3. The parents for animal 3 are 1 and 2:

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Haplotype	Sire(1)		Dam(2)	Offspring
112	AB	X	BB	AB
212	AB	X	BB	BB
222	BB	X	AB	BB
211	BB	X	AB	BB

The same could be done for animal 4 (the parents are 3 and 2):

Haplotype	Haplotype Sire (3)		Dam(2)	Offspring
112	AB	X	BB	AB
212	BB	X	BB	AB
222	BB	X	AB	BB
211	AB	X	AB	BB

The same steps can be followed for other haplotype windows. The summary for all haplotypes is shown in the following table and the haplotypes from the first window are highlighted.

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chr	1	1	1	1	1	1	1	1	1	1	1	1
snpOrder	1	1	1	1	2	2	2	2	3	3	3	3
snpID	SNP1	SNP1	SNP1	SNP1	SNP2	SNP2	SNP2	SNP2	SNP3	SNP3	SNP3	SNP3
windowSize	3	3	3	3	3	3	3	3	3	3	3	3
startPosition	100	100	100	100	110	110	110	110	125	125	125	125
endPosition	125	125	125	125	200	200	200	200	230	230	230	230
AB_AA:AA	0	0	0	0	0	0	0	0	0	0	0	0
AB_AA:AB	0	0	0	0	0	0	0	0	0	0	0	0
AB_BB:AB	2	0	0	0	1	0	0	0	2	0	0	0
AB_BB:BB	0	1	0	0	0	0	0	0	0	1	0	0
AA_AB:AA	0	0	0	0	0	0	0	0	0	0	0	0
AA_AB:AB	0	0	0	0	0	0	0	0	0	0	0	0
BB_AB:AB	0	0	0	1	0	0	1	0	0	0	1	1
BB_AB:BB	0	0	2	0	0	2	0	0	0	0	1	0
AB_AB:AA	0	0	0	0	0	0	0	0	0	0	0	0
AB_AB:AB	0	0	0	0	0	0	0	0	0	0	0	0
AB_AB:BB	0	0	0	1	0	0	1	0	0	0	0	1
AA_AA:AA	0	0	0	0	0	0	0	0	0	0	0	0
AA_BB:AB	0	0	0	0	1	0	0	0	0	0	0	0
BB_AA:AB	0	0	0	0	0	0	0	0	0	0	0	0
BB_BB:BB	0	0	0	0	0	0	0	1	0	1	0	0
haplotype	112	212	222	211	122	221	111	121	222	221	212	112
haplotypeFreq	0.375	0.25	0.125	0.25	0.375	0.125	0.25	0.125	0.375	0.125	0.25	0.25
numSires	2	2	2	2	2	2	2	2	2	2	2	2
numDams	1	1	1	1	1	1	1	1	1	1	1	1
hSires	3	2	0	1	3	0	1	0	3	2	0	1
hDams	0	0	2	2	0	2	2	0	0	0	2	2
numProg	2	1	0	1	2	0	1	1	2	0	1	1