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How to calculate deviation from Mendelian inheritance expectations based on haplotypes:

Assume we have this pedigree for 4 animals:

Animal	Sire	Dam
1	0	0
2	1	0
3	1	2
4	3	2

And their genotypes for 5 SNPs in format 012 are:

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

Phasing: There are many software options to get the genotypes phased. The genotypes 0, 1 or 2 will have 4 different phased values (AB is not the same as BA)

0 (AA): 0 1 (AB): 3 1 (BA): 4 2 (BB): 2

Assume our data phasing gave these results:

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

To create haplotypes, we need to decide the number of SNPs per window. In this example will use a 3-SNP window:

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First window (SNPs 1 to 3):

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

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

0	1 1
2	22
3	12
4	2 1

Animal 1	Haplotype 1	1	1	2
	Haplotype 2	2	1	2
Animal 2	Haplotype 1	2	2	2
Ammai 2	Haplotype 2	2	1	1
A mim o 1 2	Haplotype 1	2	1	1
Animal 3	Haplotype 2	1	1	2
Animal 4	Haplotype 1	1	1	2
Allilliai 4	Haplotype 2	2	1	2

Now, we need to get the unique haplotypes among all these generated haplotypes. So, we need to remove all duplicated haplotypes (In this example, highlighted are the unique):

112

212

<mark>222</mark>

211

211

112112

212

Now, these haplotypes will be as if they are the genotypes. For example, the haplotype 112:

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.

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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. We start from animal 3. The parents for animal 3 are 1 and 2:

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	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 haplotypes windows. The summary for the haplotypes in the first window is shown in the next table:

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AB_AA:AA	AB_AA:AB	AB_BB:AB	AB_BB:BB	AA_AB:AA	AA_AB:AB	BB_AB:AB	BB_AB:BB	AB_AB:AA	AB_AB:AB	AB_AB:BB	AA_AA:AA	AA_BB:AB	BB_AA:AB	BB_BB:BB	Haplotype	HaplotypeFreq
0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	112	0.375
0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	211	0.25
0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	212	0.25
0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	222	0.125