hw4

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Chapter 7

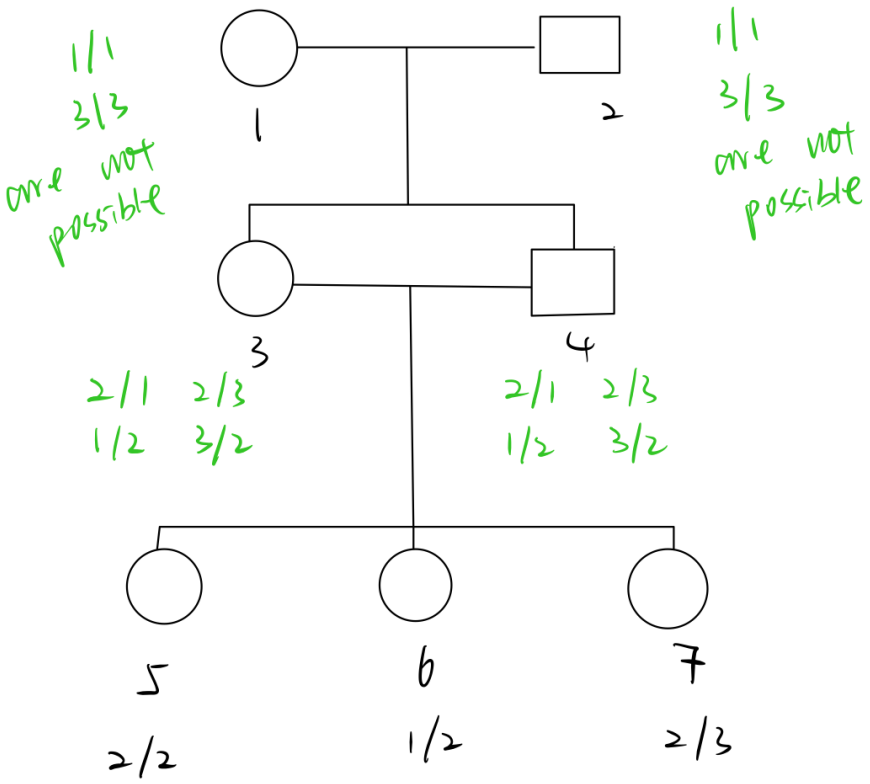
Question 1

$$\textit{We knew that } \theta = \frac{1}{2}(1 - e^{-2d})$$

$$\textit{Assume genetic distances between loci 1 and loci 2 is } d_{12}$$
$$\textit{between loci 2 and loci 3 is } d_{23}$$
$$\textit{between loci 1 and loci 3 is } d_{13}$$

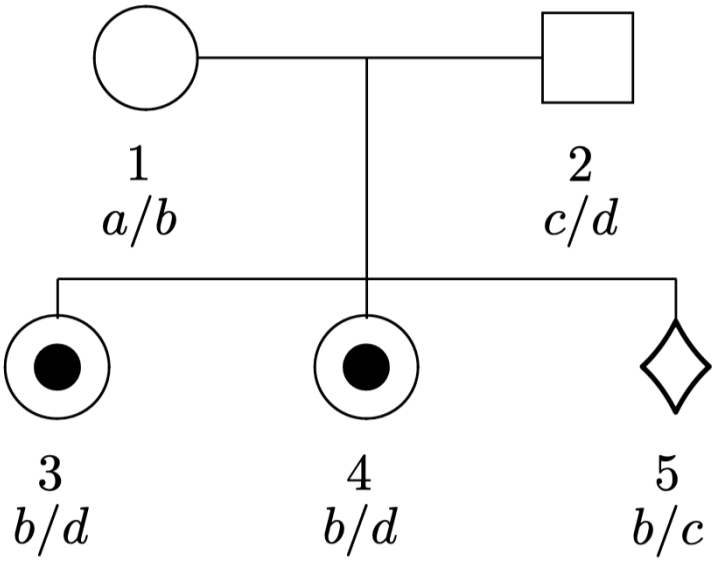
$$\begin{aligned}
1 - 2\theta_{13} &= 1 - 2 \cdot \frac{1}{2}(1 - e^{-2d_{13}}) \\
&= e^{-2d_{13}} \\
&= e^{-2d_{12} - 2d_{23}} \\
&= [1 - 2 \cdot \frac{1}{2}(1 - e^{-2d_{12}})][1 - 2 \cdot \frac{1}{2}(1 - e^{-2d_{23}})] \\
&= (1 - 2\theta_{12})(1 - 2\theta_{23}) \\
&= \Pi_{k=1}^{2}(1 - 2\theta_{k,\, k+1})
\end{aligned}$$

Qestion 2



- 2/1 x 2/3 and 2/3 x 2/1 are possible. The both parents (3, 4) must carry an 2 allele because of genotype 2/2 for the child 5 and, second, that one parent must carry an 1 allele and the other carry an 3 allele because of the presence of an 1 allele in the child 6 and an 3 allele in the child 7. Neither the genotype 1/1 of the child 6 nor the genotype 3/3 of the child 7 is compatible with either of these two parental mating types. Hence, step B of the algorithm applied to this family {3, 4 , 5, 6 ,7} produces the genotype sets shown in the figure above.
- Now, consisting of individuals 1, 2, and 3. If indivedual 1 is assigned the genotype 1/3, individual 2 can be assigned the genotype 2/2. The mating type 1/3 x 2/2 then produces the child genotype 1/2 as one of its zygotes. Step B applied to the family {1, 2, 3}, but 1/1, 3/3 are not possible for individuals 1 and 2, therefore yields the situation shown in above figure. Step C amounts to repetition of step B for each nuclear family. In both cases, no new genotypes are eliminated and the algorithm stops.
- The pedigree in figure contains a brother x sister mating between individuals 3 and 4. Since 3 and 4 have identical genotype sets after the first application of step B to the nuclear family 3, 4, 5, 6, and 7, inclusion of individual 4 in the second nuclear family can add no new information to the exclusion process involving 1, 2, and 3. However, the two children, 3 and 4, must have either of the symmetric mating types 1/2 x 3/2 or 3/2 x 1/2 in the context of their own family 3, 4, 5, 6, and 7. It follows that none of the two genotypes 1/1, 3/3 are possible for individuals 1 and 2 after the conclusion of the algorithm can form part of a compatible genotype for the whole pedigree. Thus, the algorithm is not always fully efficient in the presence of inbreeding loops.

Quesiton 7



- Assume a recessive autosomal disease gene e (with alleles E and e) is linked to markers a, b, c, and d, respectively.
- In order to produce affected kids numbers 3 and 5, both parents must be carriers of the Ee genotype. So there are different ways to combine the markers with the autosomal alleles E and e. For mom we can have (Ea/eb, ea/Eb), for dad we can have (Ec/ed, ec/Ed), etc.
- We already know that fetus 5 has the markers b/c, where b is 100% from mom and c is 100% from dad. This fetus must inherit recessive alleles from both parents in order to be affected. We end up with (be/ce).
- Because there are different ways to combine the markers with the autosomal alleles E and e for both parents. So first we assume (Ea/eb) and (Ec/ed) are the parental genotype, another ways are from recombination. See following table.

		Given phase i, probability that fetus 5 is	
	phase i	*eb*	*Eb*
1 *Ea/eb*	$(1-\theta)(1-\theta)$	$(1-\theta)(1-\theta)$	$\theta \cdot \theta$
2 *ea/Eb*	$\theta \cdot \theta$	$\theta \cdot \theta$	$(1-\theta)(1-\theta)$
.			
.			
.			
	phase i	*ec*	*Ec*
3 *Ec/ed*	$(1-\theta)(1-\theta)$	$\theta \cdot \theta$	$(1-\theta)(1-\theta)$
4 *ec/Ed*	$\theta \cdot \theta$	$(1-\theta)(1-\theta)$	$\theta \cdot \theta$
.			
.			
.			

$From\ above\ table:$

$$P(fetus\ 5\ is\ "genotype") = \sum_{i=1}^{i} P(fetus\ 5\ is\ "genotype"|\ phase\ i)P(phase\ i)$$

$$notice: \quad \sum_{i=1}^{i} P_i = 1$$

$Therefore\ the\ risk\ for\ fetus\ 5\ to\ be\ affect\ is:$

$$R = P(fetus\ 5\ is\ "ee"|\ observed\ phenotypes\ within\ the\ pedigree)$$

$$= \frac{P(ee, bc)}{P(EE, bc) + P(Ee, bc) + P(ee, bc)}$$

$$= \frac{(1-\theta)^5\theta + (1-\theta)^4\theta^2 + (1-\theta)^2\theta^4 + (1-\theta)\theta^5}{(1-\theta)^4 + 2(1-\theta)^2\theta^2 + \theta^4}$$

$$0 \leq R \leq 1$$