Genetics Exercises
M1 Genotype-Phenotype

For Monday 19 November 2018

1. Draw the steps of meiosis for a cell with 2 pairs of chromosomes (a pair of long blue chromosomes and a pair of short red chromosomes).
At which meiotic division do crossing-overs occur?

2. Draw a cross between two parents, each homozygote for different alleles at two loci, *a* and *b*. Which generation may present the first recombined alleles between the two loci?
What will be the possible genotypes of the second generation (F2) after a cross among F1s? Calculate the frequency of the different genotypes of F2 individuals:
2.1 if *a* and *b* are not linked, and
2.2 if they are located 1 cM apart on the same linkage group.

3. How many alleles of a given gene can be found in a haploid individual? in a diploid individual? in a population of diploid organisms after a chemical mutagenesis? in a natural population of diploid organisms?

4. Among the following sentences, which ones are correctly written? Correct when necessary.
a. The mutant *m* lies on chromosome XII.
b. The *distalless* gene is responsible for appendage formation.
c. The *m2* mutant does not complement *m1*.
d. The *hairy* mutation has an excess of bristles on the thorax.
e. The *dpy-20* gene is autosomal.
f. The *curly* gene is dominant.
g. Flies carrying the null allele of the *white* locus in the homozygous state have white eyes.
h. The *unc-53* mutant renders the worms incapable of movement.
i. The *lin-15(n765)* allele is recessive compared to wild type for its Multivulva phenotype.
j. The *b* gene is epistatic to the *a* gene.
h. The *m1* and *m2* mutants are allelic.
k. The cross of a mutation with a wild strain produces heterozygote progeny.
l. *Hox5* is a transcription factor.
m. All the SNPs present in coding regions affect the amino acid sequence of the corresponding protein.

5. Two snapdragons, one red and one white, are crossed. Their progeny is pink. What do you conclude? How many genes are involved in the color difference between the two parents?

6. One albino pigeon is caught in the Luxembourg garden and another in Central Park. The albino phenotype is caused by recessive alleles. What can you do to determine whether the same allele is responsible for the albino phenotype of both pigeons?
Unfortunately both are males. What can you propose instead?

For Tuesday 20 November 2018 (all the following exercices)

7. A mutant *Drosophila* strain has no eyes. An eye-less female is crossed with a male of a wild-type line and F1 flies all have eyes. The F1 males are then backcrossed to the eye-less mother. The F2 generation displays a total of 87 flies with no eyes and 92 flies with normal eyes. What can you conclude concerning the genetic locus associated with no eyes?

8. A line of *Drosophila* flies without eyes obtained after mutagenesis is crossed to a wild-type line showing a mean of 108 (+/- 5) ommatidia per eye. The F1 generation displays a mean of 35 (+/-18) ommatidia per eye. What can you conclude?
What can you expect in the F2 generation if a single locus is involved?

9. A strain of flies with no hairs on part of the anterior legs is isolated from the Orsay orchard. It is crossed to a wild strain that was isolated on the Place Monge market, which shows a stable mean of 10.8 (+/- 0.5) hairs. The F1 generation displays a mean of 3.5 (+/-1.8) hairs. What can you conclude?
What can you expect in the F2 generation?

10. A butterfly species exists in two forms, "normal" (N) and crenelated (C). Five butterfly pairs are mated:

	Parent phenotypes		F1	
cross	Males	Females	Males	Females
#1	N	N	100% N	100% N
#2	C	C	100% C	100% C
#3	C	N	50% N, 50% C	50% N, 50% C
#4	C	N	100% C	100% C
#5	N	C	100% C	100% N

Write the genotypes of the parents of each cross and the mode of inheritance and of phenotypic expression of the alleles. (NB: The chromosomal basis for sex determination is not the same in all organisms.)

11. In 1999 (Neff et al.), a large sequencing effort was done to better characterize the dog genome. 268 markers were assigned to 40 linkage groups.
Given that a dog caryotype contains 38 canine autosomes, how can you explain that 40 linkage groups were found?
Twenty-nine linkage groups had ordered markers. Three linkage groups could be assigned to specific canine autosomes, while 36 linkage groups remained anonymous. Five markers were located on the X chromosome, and no markers were Y-linked.
Explain the experiments and observations behind each sentence.

12. *C. elegans* hermaphrodites of genotype *unc-2(0)*, showing a Unc phenotype, are crossed to *mut-5(0)* males showing a Mut phenotype. The F1 generation shows a wild-type phenotype. After self-fertilization of F1 hermaphrodites, 20 F2 with an Unc phenotype are isolated, each on one plate. Following self-fertilization, these F2s produce only Unc progeny (non-Mut). Propose several explanations. How can you test them?

13. In a black, diploid, beetle species, loss-of-function mutant lines in four genes, *A*, *B*, *C*, *D,* as well as double and triple mutant combinations are available. They show the following phenotypes:

A: black	*A; D*: albino	*A; B; C*: yellow
B: brown	*C; D*: yellow	*A; B; D*: albino
C: yellow	*A; C*: yellow	*A; C; D*: albino
D: black	*B; C*: yellow	*B; C; D:* yellow
	A; B: brown	

Draw the genetic and biochemical pathways for pigment synthesis.
Which pigment accumulates in:
- animals of genotype *B; D?*
- in the F1 progeny of *A* and *D* animals?

14. The term « gene » can have several meanings (Table 1). Choose which definition(s) have been implicitly used in the following sentences:

a. Many of the **genes** not targeted by our library encode olfactory receptors that are unlikely to be cell-essential. (Blomen et al., Science 2015)
b. These Polycomb-repressed domains harbour **genes** encoding key developmental transcription factors, whose misexpression can have detrimental consequences in differentiated cells. (Boettiger et al., Nature 2016)
c. There has not yet been sufficient time for the corresponding resistance **genes** to spread into environmental reservoirs. (Versluis et al., Scientific Reports 2015)
d. Parkinson Disease is generally considered a multifactorial disorder that arises owing to a combination of **genes** and environmental factors.(Hou et al., Nature Reviews Neurology 2015)
e. ARID1B and ARID2 participate in widespread cooperation to repress hundreds of **genes**.(Raab et al., PLoS Genetics 2015)
f. Simulations reveal that hybrid populations rapidly and frequently become isolated from parental species by fixing combinations of **genes** that hinder successful reproduction with parental species. (Schumer et al., PLoS Genetics 2015)

Table 1. Definition of the Term “Gene” according to Several Biological Databases Consortia and Textbooks

A) Sequence Ontology Consortium (Pearson, 2006) A gene is a locatable region of genomic sequence, corresponding to a unit of inheritance, which is associated with regulatory regions, transcribed regions and/or other functional sequence regions.
B) Population Genetics Textbook (Hedrick, 2011) Gene: Unit of inheritance that is transmitted from parents to offspring.
C) Molecular Biology of the Cell (Alberts et al., 2008) Gene: Region of DNA that is transcribed as a single unit and carries information for a discrete hereditary characteristic, usually corresponding to a single protein or a single RNA.
D) Genes IX (Lewin, 2006, p. 845 and 852, Glossary) A gene is the segment of DNA specifying a polypeptide chain; it includes regions preceding and following the coding region (leader and trailer), as well as intervening sequences (introns) between individual coding segments (exons).
E) Quantitative Genetics (Falconer & Mackay, 1996, pp. 1–2) Suppose for simplicity that we were concerned with a certain autosomal locus, A, and that two different alleles at this locus, A1 and A2. [...] Each A1A1 individual contains two A1 genes.

15. What are the following numbers?
a. Number of telomeres in a cell in G1 phase if its karyotype is 2n=16
b. Number of telomeres in a cell in G2 phase if its karyotype is 2n=16
c. Size of the human genome in base pairs

d. Number of recombination event per chromosome
e. % identity between human and chimpanzee DNA
f. Number of genes in the human mitochondrial genome
g. Number of different amino acids in the genetic code table
h. Total number of possible codons
i. Average nucleotide difference between humans and chimpanzee DNA
j. Average number of de novo mutations in a person (germline-mutations) compared to his parents

16. Xeroderma pigmentosum is a rare disorder characterized by an extreme sensitivity to ultraviolet (UV) rays from sunlight, leading to severe sunburns after spending just a few minutes in the sun. It is estimated to affect about 1 in 1 million people in the United States and Europe. Inherited mutations in at least eight genes have been found to cause xeroderma pigmentosum.
You got tested by 23andme (error rate ~99.98%) and they found one of the mutations associated with xeroderma pigmentosum. What can you conclude?

17. Compare the two visions of the genes below. What do you think?
"Now they swarm in huge colonies, safe inside gigantic lumbering robots, sealed off from the outside world, communicating with it by tortuous indirect routes, manipulating it by remote control. They are in you and me; they created us, body and mind; and their preservation is the ultimate rationale for our existence." (Dawkins, 1976)
"Now they are trapped in huge colonies, locked inside highly intelligent beings, moulded by the outside world, communicating with it by complex processes, through which, blindly, as if by magic, function emerges. They are in you and me; we are the system that allows their code to be read; and their preservation is totally dependent on the joy we experience in reproducing ourselves. We are the ultimate rationale for their existence." (Noble, 1999)

18. You integrated a GFP transgene at random in a wild-type Drosophila genome and you would like to know on which chromosome it is, using recessive morphological markers for the four chromosomes (three autosomes and the X chromosome). Describe the crosses you do to map the transgene. Recombination occurs in Drosophila females but not in males.

19. In nature, we find a polymorphic population of *Drosophila*, including individuals with either black or yellow posterior abdomen. We catch 100 flies, observe their individual phenotype and genotype markers along the four chromosomes on these 100 individuals. Ten markers on chromosome II are found to be statistically linked to the phenotype. Explain what this means. What do you conclude? Fourty other markers on chromosome II are not statistically linked to the phenotype. How many markers would have been statistically associated with the phenotype shortly after the appearance of the *yellow* mutation: more or less than ten?

20. A plant produces many seeds. Their individual weight is measured. What will be the weight distribution in the next generation if you select the 10% of higher weight and plant them in the same conditions as their parent?
Give possible mechanistic explanations of the variation in weight among the seeds.

21. If you cross a small bean line with a large bean line, is it possible to obtain in the F1, F2, F3… generations a size outside the parental range and that at all previous generations?
Give a possible mechanistic explanation.

For Wednesday 21 November 2018 (the two following problem sets)