1. A standard lab strain of mice has the following arrangement of genes on its first chromosome (where capital and small letters represent different alleles of the same locus):

A–B–C–centromere–D–E–F–G (type 1)

a–b–c–centromere–d–e–f–g (type 2)

(a) (2 pts) If we have an animal which is heterozygous for the two chromosomes shown, and a crossover takes place between the E and F loci, what will the two recombinant daughter chromosomes look like? Be sure to show whether each locus has the capital or small allele, and where the centromeres are.

A–B–C–centromere–D–E–f–g
a–b–c–centromere–d–e–f–g

(b) 3 pts An inversion occurs which reverses the D-E-F part of the chromosome, so that the arrangement is now A-B-C-cen-F-E-D-G (call this type 3). If we have an animal which is heterozygous for type 1 and type 3, and a crossover takes place between the E and F loci, what will the two recombinant daughter chromosomes look like? You will need a looping diagram to predict the results, which are:

A–B–C–centromere–D–E–F–centromere–C–B–A
G–D–E–F–G

plus two healthy chromosomes, one of type 1 and one of type 3. Many students showed the two chromosomes lying flat along each other, but they don’t pair that way; they will loop around to keep homologous DNA together.

(c) (3 pts) What does this predict about the fertility of the animal in part (b)? Will it be higher, lower, or the same as in part (a)? It will probably be lower. Whenever a recombination occurs within the inversion, half of the meiotic products are hopelessly broken (no centromere or two centromeres) and those gametes will probably be inviable. Fertility could be normal if there is no recombination, or if the organism has some way to sort out the defective gametes and avoid using them (and is not limited by number of gametes produced). We can’t predict that fertility will be halved, because the bad effects happen only when there is a recombination, so it depends on the length of the inversion and the rate of recombination.

(d) (3 pts) Which is worse for an animal, a big inversion or a small one? Why? This was a more subtle question than I realized and I gave credit for several different answers.

Inversions cause trouble when there is recombination, and the bigger the inversion, the more likely is a recombination within it, so in this sense bigger is worse.

However, inversions which contain the centromere are a bit better than ones which don’t (at least they don’t lead to chromosomes with too many or too few centromeres), so you could argue that a big inversion containing the centromere may do better than a smaller one not containing the centromere.

Finally, when a recombination does occur, the amount of DNA duplicated or deleted depends more on the position of the inversion than on its length, so it’s hard to tell which will be most survivable.

2. Humans have one chromosome less than other great apes, because two chromosomes have become fused together. The centromere of one chromosome was lost in the fusion, but assume for this problem that no genes were lost.

(a) (3 pts) What difficulties would a heterozygote for the old (24 chromosomes) and new (23 chromosomes) arrangements encounter? Correctly segregating its chromosomes in meiosis. There is no recombination issue here, but segregation may lead to unbalanced gametes with too many or too few copies of some genes.

I did not give full credit for answers that talked about the problem of the new chromosome having two centromeres, or about damage to genes happening during the fusion, because I specifically ruled those out in the problem statement.

(b) What problem would the new chromosome face in becoming established in the population? It may be useful to know that most human chromosomes contain genes which are severely harmful if present in zero or three copies.
The chromosome rearrangement is probably underdominant—heterozygotes will have segregation problems which reduce their fertility. So when it first arises the new chromosome will have a very high chance of being lost due to selection (as well as the usual high chance of being lost due to drift).

(c) (3 pts) Suggest a situation which could have helped the new chromosome become established. The most likely possibilities are small population size, so that it could overcome the initial underdominance problem by rapid drift; heavy inbreeding, so that homozygotes would be quickly produced; and presence of a selectively favorable allele on the new fused chromosome, so that selection in its favor would help counteract selection against it. In non-primates, a period of self-fertilization or cloning could also help, but primates have never been observed to do this.

The fusion might be a recurrent mutation, so that it has many chances to establish itself.
Finally, the species could develop some mechanism to segregate the chromosomes correctly in the heterozygote. This would remove the underdominance and allow the new chromosome a much better chance. Such mechanisms are known to exist in some species; the muntjaks with two Y and one X chromosomes can segregate them reliably, and triploid toads manage it with their whole genome.