Short Problems:

1. We breed flies for increased heat tolerance. To quantify this, we put the flies in a "prostratometer" and slowly heat them until they can no longer cling to the sides of the bottle: call this the drop-off temperature T.

   (a) (1 pt) We start with flies with mean T=38 degrees. We select a subgroup with mean T=42 degrees to breed. The offspring of this subgroup have T=41 degrees. What is the heritability of T in this population under these circumstances? (Assume that T is appropriately measured in degrees; in practice this is probably the wrong scale.) *$R = h^2S$ where R is 3 degrees and S is 4 degrees, so $h^2 = 0.75$.*

   (b) (2 pts) After 100 generations, we have flies with T=45, but improvement has stopped. Give two possible hypotheses for the failure of continued selection to produce a continued response. *Genetic variation may be exhausted, or may be reduced to non-additive types such as overdominant loci. Natural selection may be opposing artificial selection. Alleles may be stuck in unhelpful linkage relationships. Drift may have led to fixing some unhelpful traits.*

   (c) (2 pts) Suggest an experiment which could distinguish between your hypotheses, and explain what you would expect if each were true. *Relaxing or reversing selection can show if there is still genetic variation. Relaxing selection can test for opposing natural selection (a sharp reversal of the trait indicates natural selection). Starting multiple replicate lines can show whether 45 degrees is a hard physiological limit or just an accident due to available variants. Once you have multiple lines, you can try crossing them together to see if they have fixed the same variants.*

   (d) (2 pts) For each of your hypotheses, what, if anything, would you recommend we try to restore response to selection and allow a higher T to be reached? *If genetic variability, or specifically additive genetic variability, has run out, adding some new flies may get selection restarted by introducing new variants. A mutagen might do the same. If natural selection is opposing artificial selection, we could try coddling the flies to keep them alive–diet? water? vitamins?–but it would be guesswork. It wasn't mentioned in answers, but we could also try to reduce environmental variance to maximize the use of whatever genetic variance we have left, for example by making sure all tested flies are the same age and raised under exactly the same conditions.*

2. (2 pts) Consider a locus with complete dominance (the heterozygote is identical in phenotype to the dominant homozygote, while the recessive homozygote is different). Does such a locus contribute anything to V_A or is its whole contribution in V_D? Explain or give an example. *It will contribute to both; the relative amount depends on allele frequency. For example if the dominant allele is quite rare, possessing one gives a clear prediction of higher trait value. If the dominant allele is very common, knowing that an individual has one gives almost no predictive power. One student showed this by drawing a trait histogram and then overlaying a linear relationship.*

3. In Japan, heritability of male height is high, as in most human populations: tall fathers have tall sons on average.

   (a) (2 pts) When Japanese people settled in the US, there was a period where this heritability was much lower, even among families with no non-Japanese ancestry. Propose an explanation. *The variation in environment increased greatly; where you spent the first few years of life was more predictive of height than genetics. Height can be affected by early environment and this increase in V_E decreases h^2. This effect is very clear in my Japanese-American relatives, where the US-born males are several inches taller than the Japanese-born ones, probably due to diet.*

   (b) (2 pts) In general, would adding a proportion of intermarriage with Europeans be likely to increase or decrease the heritability of this trait? (If this question cannot be answered, explain why.) *This is difficult to answer without more information. On the genetic side, adding European genetic material is likely to increase the number of available variants affecting height and thus increase heritability, though there could be trouble with things like alleles that have one effect in a European background and a different effect in a Japanese one. But a bigger problem is that it is hard to predict the environment of Japanese-American children–more or less diverse? If the admixed population has wildly different diets from household to household, that could add a lot of V_E and reduce heritability. (The biggest determinant of your height could be which of your parents does the cooking....) Furthermore, if there is a correlation between how many European genes you inherit and how European your diet is, that will cause V_{GE} and inflate heritability (so it would seem to go up, but the cause would not be purely inheritance).*
   I did not give full credit to answers that ignored the genetic differences between Japanese and Europeans.

4. (3 pts) The "Wilson Effect" is the observation that the heritability of IQ is low in children and increases until around age 18-20, after which it stabilises. (IQ here is defined as "the thing that IQ tests measure.") In other words, if we

use your age-20 IQ to predict your child's age-20 IQ we will be more accurate than if we use your age-8 IQ to predict your child's age-8 IQ. Suggest an explanation for this. *Several good suggestions were made. IQ tests in children may be more affected by environmental factors than in adults, either because the trait just behaves that way, or because it's hard to write good IQ tests for young children. Differences in developmental rate or other factors (like age of starting school) may have a temporary effect on IQ which smooths out later. It was also suggested that child environment varies more than adult environment, which would reduce heritability. One thing I'd do right away if studying this would be to estimate the consistency between multiple tests on the same person in adults and children. If testing a child twice produces wildly variable results, that would explain the lower heritability very simply.*

Long Problem:

Consider an overdominant locus with the following fitnesses:

Genotype	Fitness
AA	0.9
Aa	1.0
aa	0.7

I gave these fitnesses and never used them–sorry!

When the heterozygote is more fit than either homozygote, a (sufficiently large) random-mating population will move to the overdominant equilibrium for any starting value of pA except 0 or 1. A totally inbreeding population (f=1) has no equilibrium, because heterozygote advantage is useless when there are no heterozygotes. What about partial inbreeding?

Write a small program which calculates the change in allele frequencies each generation, for 1000 generations or so, as a function of starting pA, wAA, waa, and f. (If you do not wish to program, this can be done analytically by solving for zeros of the formula for change in allele frequency; I think the program is much easier....)

Consider the case of $wAA = 0.8$, $wAa = 1.0$, $waa = 0.9$.

1. (3 pts) Please attach the program to your homework or show your analytical calculation. *See end of homework key.*
2. (2 pts) What is the theoretical equilibrium without inbreeding? (Test to see if your program actually finds it!) *pA = $t/(s+t)$ = -0.1/(-0.1-0.2) = 0.3333. Always check programs against a known case if one is available.*
3. (3 pts) We'll consider a pA value to be an equilibrium if the population reaches it whether starting above or below it. Are there values of f where there is an equilibrium, but at a different point than before? *When I run this, I see a steadily lower and lower pA at equilibrium for increasing f up to around $f = 0.5$. With higher f I get very low values which are probably equivalent to zero.*
4. Are there values of f (other than 1) where there appears to be no equilibrium (the frequency goes very close to 0 or 1)? *Values of f greater than 0.5 appear to have no equilibrium.*
5. In words, how do you understand these results? *This locus has heterozygote advantage and without inbreeding will maintain the worse allele at fairly high frequency because it is good in heterozygotes. The more inbreeding, the fewer heterozygotes and the weaker this effect becomes, so the equilibrium frequency of the bad allele decreases. Eventually the harm to the common homozygotes outweighs the advantage of the rare heterozygotes and the equilibrium is lost. I had trouble reasoning this out from first principles, so found writing the program quite educational.*

   A word of warning: Some students attached significance to the breakpoint at around $f = 0.5$, but it is specific to the these fitnesses, as you'll see if you change them. If the fitness of the worse allele is lowered, the equilibrium vanishes with much lower values of f. For example, if the worse allele is lethal, no value of f greater than around 0.1 seems to have an equilibrium.

Advice for those whose programs or calculations missed the right answer: Try to find edge cases you can check, and make sure the results make sense in those cases. For example, surely if $f = 1$ there cannot be an overdominant equilibrium as there are NO heterozygotes; if your program/calculation disagrees I would not bet on the program....

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# program inbreeding.py

fitnesses = [0.8,1.0,0.9]

for f in [0.0,0.1,0.2,0.3,0.4,0.5,0.6,0.7,0.8,0.9,1.0]:
  pA = 0.33
  pa = 1.0-pA
  for i in xrange(100000):
    hw = [pA*pA*(1.0-f)+pA*f, 2.0*pA*pa*(1.0-f), pa*pa*(1.0-f)+pa*f]

    newfreq = [hw[0]*fitnesses[0],hw[1]*fitnesses[1],hw[2]*fitnesses[2]]
    total = sum(newfreq)
    newfreq = [x/total for x in newfreq]

    pA = newfreq[0]+0.5*newfreq[1]
    pa = 1.0-pA
  print f, pA
```

Output:

```
0.0 0.333333333333
0.1 0.296296296296
0.2 0.25
0.3 0.190476190476
0.4 0.111111111111
0.5 6.00180463877e-05
0.6 3.26083326255e-322
0.7 1.38338380836e-322
0.8 7.41098468762e-323
0.9 6.42285339594e-323
1.0 3.45845952089e-323
```