An Introduction to Evolutionary Biology

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Week 5 Lecture 28

Non-random mating and inbreeding

Hi, so before we move forward with today's discussion, I need to give you a quick disclaimer, which is that Typically, once you know one looks at the topic of genetic drift, it is followed by Moto Kimura's neutral theory. However, in the context of the present course, I am moving the neutral theory to week 10, when we are going to. Discuss how genomes evolve, primarily because you know this week there are already many other things. which need to be covered in some amount of detail. Generally, I have seen that you know this entirely. The neutral theory makes a lot more sense when you study it in the context of genome evolution.

So, that is one quick departure we are making from the announced syllabus. So, in the last discussion, we talked about genetic drift, and we said that there are other evolutionary forces. The one that we need to look at now and the one that we are going to look at during today's discussion is mating. So, if you remember, one of the conditions of Hardy-Weinberg equilibrium is that mating needs to be random.

Now what do we mean by that? Random mating, also known as panmixia, by definition is When any individual of one sex has an equal probability of mating with any individual of the other sex. So obviously, this allows us to do those nice, you know, Punnett squares and leads to going from. Allele frequency in the parent generation is related to the genotypic frequency in the next generation. However, as we all know, in real life, much of the time, mating is not really random; therefore, non-random mating is Simply any

departure from the above condition results in two major ways in which mating can be non-random. One is what is known as assortative mating, where individuals with similar phenotypes mate preferentially with each other with a greater probability, and the other is what is known as disassortative mating. Where individuals with dissimilar phenotypes tend to mate with each other with a greater probability. So, we will consider each one of them in turn and see what they end up doing for the evolution of the population. So, if you look at assortative mating, there are many examples. So, for example, one of the most well-known things among humans is that in many societies, particularly, In western societies, it has been shown that people tend to have assortative mating for height.

In other words, tall males typically tend to mate with tall females and vice versa. However, the point to be noted is that many times assortative mating can happen even if there is no direct mating preference. So, that is one example that I would like to give you here. So, this is an example of an insect called Enchenopa, not a plant, sorry. This is a kind of tree hopper, and these guys feed and develop on multiple plants.

Now it turns out that those that feed on similar plants or the same plant tend to mate with each other much more frequently. So, one can obviously say that this is assortative mating, for you know feeding on the same plant. But if you look at it a little more closely, as Wood and Keese did in 1990, They figured out that that is not exactly what is happening. So, it turns out that the chemistry of these plants differs slightly, and that determines What is the rate at which the insects that are feeding on them are going to develop? Now, when the insects, the males and the females, are feeding on the same plant. They tend to develop at a similar rate, and therefore they become sexually mature at the same time.

Now it turns out that in this particular species, the females are sexually receptive for a very small amount of time. So obviously the only male mates they know are the males that are available to them during that small duration. Essentially co-developed with them at roughly a similar rate, and those happen to be the ones that are on the same plant. So Wood and Keese showed this very nicely by providing the females. with sexually mature

males that were actually developed on different hosts.

So they artificially provided these males and ended up showing that this entire preference for mating, you know, with males from the same plants that completely disappear when there is availability of other kinds of males. So, this is just an example to show that not all assortative mating is necessarily due to mating preference. Similar findings have been shown in Drosophila. So, for example, if you have Drosophila that are coming out of crowded cultures, there is assortative mating. So, you know the development time of Drosophila becomes longer when you have larval crowding and all the flies.

Those who come out early tend to mate with each other; all the flies that come out late tend to mate with each other. But this is not really because you know there is any major preference; it is just that when The females are sexually mature; the only males that they find are, you know, males. who are of the early mating type or males who are of the late mating type, depending on when the females have come out. So, this is a reasonably well-known thing that not all assortative mating is due to mating preferences alone. So, what exactly does assortative mating lead to? In order to understand, we will do a quick example, and in this case, we will take an extreme case of what is known as complete assortative mating.

So, let us assume that we have a one-locus, two-allele scenario, and let us assume that our two alleles are A1 and A2. So, we have three genotypes: A1A1, A1A2, and A2A2. Let us also assume that these three genotypes have three different phenotypes such that the phenotypes are visible and distinguishable by the genotypes. And let us assume that the A1A1 phenotype only mates with the A1A1 phenotype. A1A2 phenotype mates with itself, and A2A2 similarly mates with the A2A2 phenotype.

So, in some sense, this is like selfing, except that in selfing, the individual mates with itself. In this particular case, the individual is mating with individuals of its own genotype; that is all. Now suppose we have a scenario like this: what is going to happen? You are going to get three kinds of individuals in the next generation again: A1A1,

A1A2, A2A2. However, the way they are produced will be slightly different. So, all the A1A1 individuals with a probability of 1 will produce A1A1 offspring.

Similarly, all the A2A2 individuals with a probability of 1 will produce A2A2 offspring. What will happen to the heterozygotes? A1A2 heterozygotes, when they are mating with each other, will produce all three genotypes: A1A1, A1A2, and A2A2. And assuming all other Hardy-Weinberg laws and conditions to be operative, These will be produced in proportions 1/4 A1A1, 1/2 A1A2, and 1/4 A2A2. So, if that is the case, look at what is happening to the A1A2 genotype or phenotype, whatever. What is happening is that they are producing offspring, of which one-fourth are of the A1A1 phenotype, one-fourth are of the A2A2 phenotype, and only half are the corresponding phenotype, which is A1A2. So, in other words, the A1A1 and the A2A2 are only producing babies of their own type, but A1A2 is producing only 50% of babies. Which are of its own type, the remaining 50% are going to be added to the A1A1 and the A2A2 phenotype. So, what happens if this continues across generations? I mean you do not even need to do any math, you realize that if Each generation, 50 percent of the offspring are lost to the other phenotypes. After some time, all the A1A2 genotypes in the population will cease to be.

And the population will now consist only of A1A1 individuals and A2A2 individuals, right? So, just to show you what is happening, if you look at the next generation, the P', So let us assume that P, Q, and R are the three genotypic frequencies for A1A1, A1A2, and A2A2. So, obviously, since you know one-fourth are coming over here, P' will become P + (1/4)Q; similarly, R' prime will become R + (1/4)Q, so the (1/4) is coming from here, and this Q' is going to become equal to (1/2)Q. As I said, in the long run, Q has to become equal to 0, but what will happen in the next generation? So, in the next generation, suppose we are trying to track the allele frequency, p; what will p be? Remember small p = P + (1/2)Q. Therefore, allele frequency p' in the next generation is going to be p' = P' + (1/2)Q'. Now, we have already given the expression for, you know, P' and Q'.

So, you simply add those up. So, P + (1/4)Q, this is capital P prime, and this (1/2) *

(1/2)Q, this is capital Q prime. p' = P + (1/4)Q + (1/2)(1/2)Q. So, this is (1/4)Q; add the two up and it becomes (1/2)Q. So, this becomes equal to capital P + (1/2)Q.

But as we already know, P + (1/2)Q = p, which is the allele frequency of allele A1, right? In other words, in the next generation, the allele frequency is not really changing in the population. All that is happening is that the genotypic frequencies end up changing. I mean, this you can also see intuitively, right? Because there is no selection happening. No allele is getting lost, no allele is getting created; all that is happening is that. The alleles are getting repartitioned among the genotypes in a particular way.

Therefore, the allele frequency does not really change; what changes are the genotypic frequencies. And you know that is what I am trying to show you and tell you over here because the allele frequency is not changing. Therefore, if you are defining evolution as a change in allele frequency, there is no evolution happening at the level of that locus. However, if you are defining evolution as a change in phenotypic frequencies, then you can clearly see that When you start with three different phenotypes, the proportions of those phenotypes change. And after some time, you are left with only two phenotypes, right? And not only are you left with two phenotypes, but you are also left with the corresponding homozygotes, right? It is the heterozygote which disappears and it is only the homozygotes that will survive in a condition like this.

So, this increase in homozygosity is the main point that we need to take from this. So, here I am showing you in the context of strict selfing. However, if you have assortative mating of any kind, this is typically what ends up happening. The homozygosity, the proportion of homozygotes in the population, keeps on increasing. And the heterozygosity, the proportion of heterozygotes in the population, keeps on going down.

Now, what is the net result of that? Now, suppose you have a population in which you have, let us say, many rare recessive alleles. Now, most of the diseased alleles that we have are actually of the recessive type; not all, but many. Now, when they are at low frequency, remember that those alleles are going to be found in the heterozygotes.

Therefore, they are not going to be seen by selection because they are not being expressed. However, when the homozygosity of the population increases, many of these rare alleles are now going to get expressed simply because they are now coming in as homozygotes in the genotypic sense.

And when that happens, all these rare alleles, the diseases caused by them, Their frequency starts going up in the population, and as a result, the overall fitness of the population starts suffering. So, just to give you one example from humans: So, there is this thing known as early onset deafness in humans, which basically means that from a very young age, people go deaf. Now, this can happen due to multiple reasons. In many cases, you know they are related to diseases and accidents. However, in about 68 percent of the cases, this is purely genetic, and people have looked into it.

This is not caused by a single gene; there are about 115 genes and mitochondrial DNA variants. Most of them are autosomal, recessive, and very rare, except for one. Which one? So, there is this gene called GJB2 that codes for a gap junction protein called connexin 26. Now, it turns out that if you have a particular mutation called the 35delG mutation, which is basically a 35 base pair mutation at this locus, Then, in the homozygous form, this can lead to early-onset deafness. Now, it turns out that the frequency of this particular allele in the population in the US and Europe is about 0.01, which is 10^(-2). So, if that is the case, what is my expected frequency of the homozygotes? This frequency is, you know, 10^(-2). So, the expected frequency assuming Hardy-Weinberg is going to be the square of that, right? In other words, the expected frequency under Hardy-Weinberg should be (10^(-2))*(10^(-2))=10^(-4), which is about 1 in 10,000. However, if you actually look at what the frequency is, you find that it is. About 3 to 5 times greater than that, which means it is about 3 to 5 in 10,000. So, what exactly is happening? Why is this? I mean, this is statistically significant, so why is it statistically significantly larger by about, you know, 3 to 5 times? So, it turns out that very often, since this is an early onset of deafness, kids who have this disease end up going into Special schools for people with hearing impairments allow them to meet others who also have the same problem.

Now, because they are learning together, many times you know, obviously, they learn. Sign languages and other means through which they are able to communicate with each other. And of course, they are able to communicate with each other a lot better than with people who do not know. The sign language or with people who, let us say, have learned it but are not very proficient at it. Therefore, it is known that there is a very high degree of assortative mating among people who are deaf, you know, in the US, the number is about 80 percent, more than 92 percent in Europe, and Once you factor that into your models, you realize that the observed frequency matches the expected frequency very well. So, essentially, the reason that this particular homozygous recessive allele is in high frequency The genotype is in high frequency in the population simply because of assortative mating. So, there are a few general insights about assortative mating that we should keep in mind. One, as I said, increases the frequency of homozygotes at the expense of the heterozygotes. More importantly, if you have assortative mating, then the population can become split.

It can become divided into multiple subsets due to genetic differentiation. So, this is something to which we will come back again when we do our speciation topic somewhere in the future. At that point, we will talk about this again, but right now, just keep a note somewhere about assortative mating. Because it can lead to genetic differentiation and substructuring within a population, It is a very potent force for microevolution, particularly speciation and the formation of new species. So, of course, that was about assortative mating.

Now, the other kind of non-random mating, as I said, is disassortative mating. where individuals with dissimilar phenotypes mate. So, this is a little less common than assortative mating. However, there are a few, you know, very well-known examples. One of the well-known examples is this famous Wedekind et al. experiment from 1995. So, what Wedekind et al. did was recruit a bunch of college students, males, and then requested that they wear the same t-shirt for about 2 days. And then, I mean, they took all kinds of precautions; they were to make sure that there was no other odor that came into

the t-shirt. And after 2 days, they took those t-shirts, put them in plastic bags, and then recruited a bunch of females. and told them to smell those t-shirts and rate the scent in terms of attractiveness and nothing else. And on the sides, what they also did was look at the kind of MHC gene.

Now, you must have heard about the MHC gene, the major histocompatibility gene. So, these are genes that are very important for the immune function of humans. Therefore, this is a highly variable kind of gene. So, when they did the profiling of both males and females, and They tried to correlate the MHC profile of the females with what kind of males they are choosing, you know. or what kind of males they are saying they find attractive based on the smell alone.

They found that females typically tended to choose males who had different MHC profiles. Compared to those who had the same MHC profile. In other words, if the male and not the male chose those, sorry, the female chose those males. who had the opposite MHC profile compared to those who had the same MHC profile as the female concerned. So, this is a very well-known experiment, and similar studies have been repeated with mice; again, similar results have been shown.

The same thing has been done with fowl, you know, jungle fowl. There, they inverted it. There, they asked what kind of females the males end up choosing, and very interestingly, Turns out that there was no major, you know, choice in terms of mating, per se. But there was a difference in terms of how much the males were investing in their sperm output. So, it turns out that when the females you know had a different MHC profile, The males tended to have a greater sperm investment compared to when the females had the same MHC profile as the males did.

So, this is one very nice example of how the MHC major histocompatibility complex genes. They end up affecting our perception of how desirable or attractive individuals of the opposite sex are. Now, I will not get into the models and everything, but generally, this assortative mating leads to An excess of heterozygotes with respect to the

corresponding Hardy-Weinberg predictions. And as a result of that, you know exactly the opposite of assortative. It ends up maintaining polymorphism in the population, and therefore it prevents the population from subdividing.

So, those were about two, you know, departures from random mating. There is one more thing that is very, very important in this context, which is inbreeding. Now, what is inbreeding? Inbreeding is mating between individuals that are genetically closely related. Now please appreciate one thing here. When we define random mating as all individuals of one sex having an equal probability of mating with individuals of the other sex, that also refers to, you know, close relatives and everybody else in the population. So, even under random mating you expect some amount of inbreeding to be happening. Here, when we are talking about inbreeding, we are essentially talking about when you know. That is happening in a much bigger way: mating between genetically close relatives. And it turns out that, like assortative mating, this also ends up increasing homozygosity.

Now, as I said, anything that increases homozygosity is going to increase the The probability of recessive deleterious alleles coming together, which in turn can have negative consequences at the population level. Now this has actually led to a term known as inbreeding depression. which is the reduced survival and fertility of the offspring of individuals who are related to each other. Now you can see a pattern over here, right? Genetic drift leads to homozygosity. Assortative mating leads to homozygosity; inbreeding also leads to homozygosity.

Therefore, although the term inbreeding depression is typically well-named in the context of inbreeding, It is essentially talking about increased homozygosity, which is common to multiple evolutionary forces. That is why sometimes instead of saying "inbreeding," This entire thing about homozygosity leading to a reduction in fitness is actually called inbreeding-like effects. That is a better way of saying it, but sometimes they simply use the term "inbreeding depression." but inbreeding depression does not necessarily have to come only from inbreeding, It can be coming from, as I said, genetic drift or assortative mating. So, what exactly can inbreeding depression lead to? As I said, bad things—how

bad? Let me give you two or three examples.

So, when it comes to inbreeding, the textbook example is this unfortunate gentleman: King Charles II of Spain. So, King Charles II belonged to the famous Habsburg family of Austria, and it is one of the most powerful royal families in Europe. So, it ruled the Holy Roman Empire for about 350 years, and this family produced kings for dozens of countries and empires. So, it was a huge family with lots of branches. But one of the things that they did very consciously was that they heavily intermarried, you know, within the family.

So, first cousins and second cousins, lots of marriage happened primarily for political reasons, you know, to make alliances. To make sure that King A does not, you know, launch an expedition against King B and so on. However, this massive amount of inbreeding led to very major physiological problems in the Habsburg family. And probably the biggest example of that is this gentleman, King Charles II. So, as it says he lived from 1661 to 1700, he became king at the age of 4.

However, right from childhood, it was clear that the kid was suffering. So, he had this you know you can see his jaw right, can you see how it is protruding below like this? That is the famous Habsburg jaw. So, this is a condition where the jaw grows elongated, and because of this, it is extremely painful; he could not chew. He had a very long tongue, because of which he could not speak properly. He had speech issues, and you know people around him could not understand.

But more importantly, he had very severe cognitive issues. He could not speak; sorry, he could not walk until the age of 8, and even then he just could not learn. And this guy was like the emperor of Spain and one of the most powerful people in the whole world. So, he, because he had cognitive issues, was not even educated, and most importantly, in this particular context, He was also infertile; he could not produce a baby, and because of that. The entire Habsburg dynasty in Spain ends with, you know, this particular person.

Basically, there was a massive war after he died. Because he did not have any successors, the Habsburg line in Spain essentially ends with this person. Now, this particular case shows what inbreeding can do. Particularly, what it did in the Habsburg family is a fascinating case with lots of well-studied information. So I will guide you towards these two videos, you know, excellently done videos. Although they are talking a lot about history, they are also talking a bit about genetics.

So have a look at it, and as usual, you know the contents of these videos are for fun. They have nothing to do with the exams, but that should not prevent you from looking at the videos anyway. Now, in an ideal world I should have been able to tell you that it is a disease, you know inbreeding is a disease of the royals alone Normal people are not affected by it, but unfortunately, that is not correct. So, it turns out that this thing about marrying relatives is actually present in many parts of the world.

And wherever it is, there it typically leads to lots of problems. So, here I am showing you some data from a paper by Bittles et al. in 1994. So, what they did was they went to 38 human populations from all over the world And for each population, they looked at some marriages that have happened due to, you know, mating between first cousins. And they also looked at those marriages that have happened because of, you know, mating between unrelated couples. Basically, the male and the female are not related to each other, and for both sets, they try to figure out.

What is the average percentage of mortality among the babies arising from those marriages? So, here what you have is the mortality of children of unrelated parents on the x-axis. and the percentage mortality of children of first cousins on the y-axis. And if you look at this red line, it assumes that the two mortalities are the same. And basically what you see is that in all the cases, the mortality percent of the first cousin, Kids coming out of first cousin marriages is much, much greater than I mean, this is one little exception. But otherwise, it is mostly much, much greater compared to the mortality that is coming out of, you know, children coming out of unrelated parents is a very stark example of what inbreeding depression can do. And this is just one generation of stuff we are talking

about here. This is not even multi-generational stuff. In one generation, this is what it can do. To give you an example in wild animals, this is the famous Soy sheep, which is extremely well studied.

In this particular case, we are talking about a breed of sheep on the island of Hirta near Scotland. So, this is a population that was established in 1932 with about 107 individuals. So, not a very small founding population, not very large either, somewhere in the middle. And this population size fluctuates between about 500 and 2000 sheep; it is an island, right? So, it depends on all kinds of environmental conditions. And because of this fluctuation, it has undergone a lot of drift, and that drift, as I told you, is showing up as inbreeding depression.

So what Coltman et al. did was take a large number of these sheep, and for each one of them, they did a lot of sequencing. To figure out what the fraction of heterozygosity is within the individuals of the sheep you know in that population. So, this is heterozygosity measured at the individual level, and then they grouped it into four equally spaced groups. So, if you are into statistics, basically the four quartiles, and that is what I am calling here, you know low, low, medium, medium, high, and high; those are the heterozygosity levels. And for each one of them in each of these groups, they tried to see. What is the survival probability, and that survival probability is what is being plotted here? So, as you can see, as you increase the heterozygosity levels, the predicted survival probability increases almost linearly. I mean that line is the regression line; you can see that it is very close to linear. Now, what survival probability is this? This is the survival probability of the lamps during the winter. So winter is bad in Scotland, right? So they are trying to see what the probability is that the lamp will survive.

And how does that probability change with heterozygosity? As I said, it increases linearly. Now, why does it happen? What exactly is heterozygosity doing here? So the reason I have chosen this example is that here they actually figured out what is happening. So it turns out that the individuals who have greater heterozygosity. They have greater tolerance towards gut parasites, specifically nematode worms.

Now that is what is leading to greater survivorship with greater heterozygosity. Now, if this is indeed correct, then what do you expect? You expect that this is happening because of the nematodes. So if you remove the nematodes, this pattern will disappear, right? That is exactly what they ended up seeing. So what they did was treat a group of these individuals with antihelminthic drugs. So antihelminthic drugs will eliminate all the worms, and the moment that happens These survivorship differences based on heterozygosity completely disappear. So this is what tells you that, in this particular case, the heterozygosity is operating through the presence of the nematodes.

So, a quick recap and quick retrospection: we have, up to this point, studied four or five different evolutionary forces. So we looked at selection, and we know that selection ends up reducing the variation in a population. In terms of its strength, it can be a very strong force. I mean, depending on, you know, the selection differential, depending on how much variation is there, etcetera.

But in the correct conditions, it can be a very strong force. We looked at mutation; we said that it is one of the major ways in which the variation in a population increases. But we also saw that it is, in general, a very weak force. It does not change the composition of the population extremely fast, particularly when it is, you know, The population is small; when it has to interact with drift, it becomes an even weaker force. Then we looked at drift itself and saw that drift in general reduces variation because there is loss or fixation of an allele.

It also reduces heterozygosity and anything that reduces heterozygosity. As we saw, it can reduce the overall fitness, and because of the reduction in fitness, selection will become important. And therefore, through an indirect effect, it can again lead to a reduction in variation. And as we saw, you know it can be strong in very small populations. But otherwise, generally, it is weaker than selection in large to moderately large populations; it is a weaker force. Then we looked at assortative mating in today's discussion, and we saw that it reduces fitness through Reduced heterozygosity, and again, as I said, anything

that reduces fitness will typically end up having a negative effect on how much variation there is, and sometimes assortative mating can be a strong evolutionary force, as I told you. And finally, we looked at inbreeding, which again reduces fitness through Reduced heterozygosity and therefore can reduce variation. And again, as I told you, inbreeding, in many cases, particularly when population sizes are small, can be a real big issue. So, what is this table telling us? This table is telling us that most evolutionary forces, barring mutation, They will typically lead to a loss of variation either directly or indirectly, the latter through the fitness effect, as I talked about. Now, if this is the case, then the only force that is opposing it is creating new variation, which, as we saw, is a weak force.

Everything else is a pretty strong force either by itself or under the correct conditions. So, if that is the case, then taking 0.1 and 0.2 together, most variation should have disappeared by now. We know that mutation rates are typically not very high; we also know, as I said, that it is a weak force. So, all the opposing forces are strong, all the creating forces are weak, so most variation should have disappeared by now.

But is that the situation? Remember our first discussion where we talked about the alien? One of the things that our alien saw was That no, no, no, there is a lot of variation; that is what kind of, you know, makes life so interesting to study. So, if that is the case, where exactly is this variation coming from? There has to be some evolutionary force. Which is allowing the populations to regain variation, to retain variation, at least to some extent. It cannot be one little mutation acting against all these other forces put together.

What is that evolutionary force? That is what we are going to look at in our next discussion. See you, bye.