

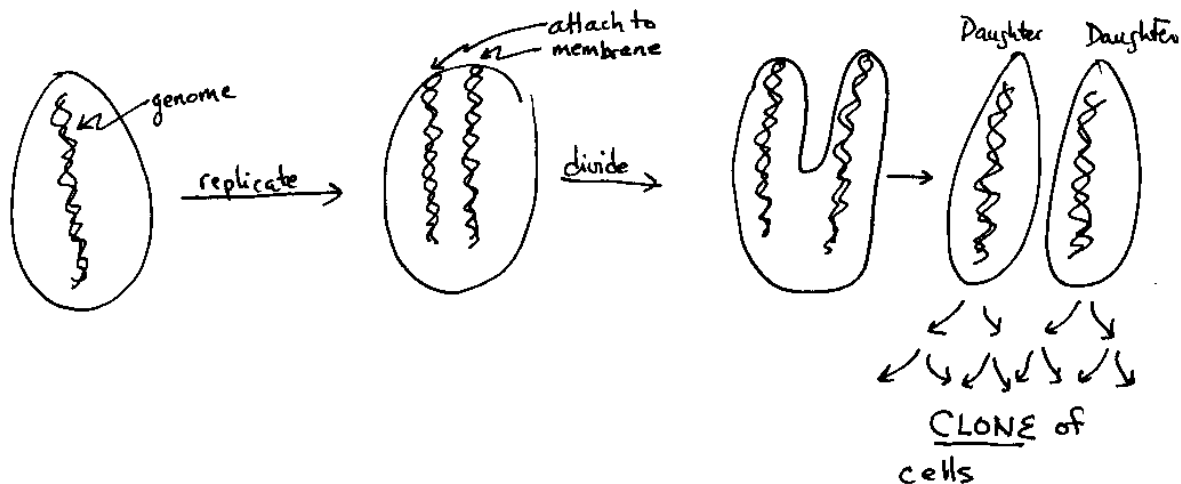
Epic of Evolution: Life, the Earth and the Cosmos (BEP 210A)  
April 19, 2000 - Lecture by Ursula Goodenough

Today I'm going to talk about sex and on Friday I'm going to talk about sexuality, both in an evolutionary context. The sex part is by definition less interesting than the sexuality because the sexuality has to do with behavior and all of the ways that sexual behavior influences the course of evolution, and that we will get to, but I can't leave you in a course about biological evolution without going through sex and what that entails. I promise there'll be no Mendel, no peas, no ratios, none of that stuff that probably bored you senseless, but the ideas that undergird all of that thinking are essential to understand the evolution of life.

Let me also take a moment while we're assembling to say that one of the lectures that I promised you on the syllabus was going to be a lecture on hominid evolution. I had great ambitions for reading about hominid evolution and synthesizing it for you in a lecture. This semester got incredibly more busy than I was able to anticipate, and when I started to read I realized that the topic is so huge and so complex that I was going to need to allocate a lot more time than I had to allot. So students in BEP 210 next year will hopefully get a lecture from me on hominid evolution, but you guys in fact have -- and they will too -- a much more robust option, which is to take Dr. Smith's human evolution course that's offered in the anthro department. It's another A course and I know a number of you have already taken it and have raved about it. If you haven't taken it, and if any of the things that we're telling you about in this course have caught your fancy, you should definitely sign up for that one because I understand it's terrific.

Okay, so to get into sex we can first review what it is that we already know about this whole business of the replication and the transmission of genomes. So we'll start with a bacterium, but this could also be our original guy in the soup, our original cell that we made at the beginning of the course. We said that this individual has a genome, where the genome is all the instructions needed to make that organism -- all the genes plus all the promoter regions that have to do with regulating when those genes are expressed.

One of our definitions of life is that these instructions need to be replicated, and since in almost all modern organisms the instructions are encoded in DNA, we talked about how DNA can be copied. Once you have two copies of these instructions, the final task is to transmit one complete copy to each daughter cell. What bacteria do, and the simplest way to think about how this goal might be achieved, is to attach each copy of the genome to special membrane attachment sites that form at the time that the cell is big enough that it wants to divide. And then there's an ingrowth in between those two attachment sites to generate the two daughter cells, each of which has one genome.



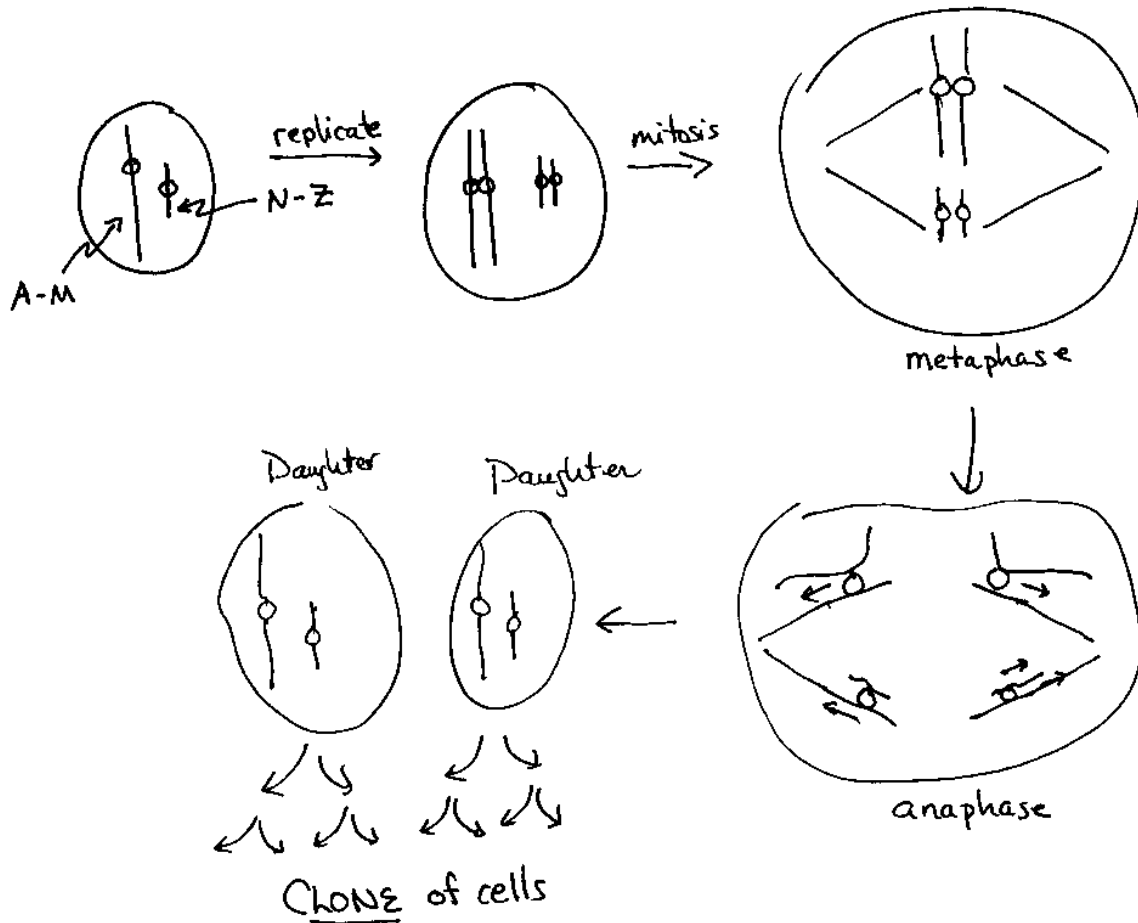
Each of these daughter cells does the same thing and each of these does the same thing, and so as you let this process run you start from one bacterium to a whole boatload of bacteria, with all of them having the same instructions, give or take the occurrence of a mutation here or there. All the descendants from this first bacterium are called a clone. They are genetically identical to one another.

Probably even the first eukaryotes, and certainly all the eukaryotes that are on the planet today, have an important variation on this theme and that is that the genome is divided up into several pieces called chromosomes. A good analogy for that is the encyclopedia analogy. So if you say an encyclopedia contains all the information that it takes to make human culture, then you could have the Britannica let's say be in one book that you move around with a wheelbarrow, or you can take that information and divide it into a number of volumes, which is how encyclopedias are usually packaged. And in fact, that is probably the evolutionary pressure that gave us these chromosomes, which is that as organisms evolved, gene duplications kept occurring, more instructions got generated, until genomes just became too big to fit in one DNA molecule. So they got divided up into volumes.

Every species has a distinctive number of chromosomes: to consider the species we're most interested in, the human genome is divided up among 23 chromosomes. That's obviously going to be too hard for my blackboard art, so I'm going to draw a eukaryotic green alga that is a single-celled organism like a lot of the ones that we saw in our movie. I'm going to say that this alga's genome is divided up into two chromosomes -- the simplest case we can think of. One of them is bigger and one of them is smaller and this bigger one let's say has all the A-M information and the smaller one has all the N-Z information.

The trick about this arrangement is that now you have to get copies of A-Z information to the offspring -- that is, each daughter cell needs to inherit a large chromosome and a small chromosome in order to have a complete set of instructions. This is where mitosis comes in. If you remember what I said about mitosis on Monday (4/17), I said that the kinetochores contain the motor protein called dynein, and that when the cell divides what it's going to do is line up its

chromosomes (here are the two) in the center of the cell at the so-called metaphase plate, and polymerize spindle microtubules, and then the paired kinetochores are going to split and one will walk to the left and the other to the right -- the anaphase separation that we saw so beautifully in the videos. As a consequence, each daughter cell is going to get a large chromosome and a small chromosome.



So it's the same thinking for the bacterium and the single-celled alga except this spindle business and the kinetochore business has been set up to make sure that each daughter cell gets a complete copy of the genome, a complete set of instructions -- in order to do that you have to make sure you get one of each kind of chromosome. Each of these daughter cells, just as with our bacterium, can go on and do mitosis again, copying and separating again, the result being a clone of genetically identical individuals (save the occasional mutation).

Okay, so all modern eukaryotes and presumably therefore the original eukaryote (common ancestor) replicate and divide their cells by mitosis using very, very conserved mechanisms for doing that. If you remember our basic 3-kingdom lineage of the bacteria and the archaea and the eukaryotes, and then we had up here the Cambrian explosion (this is a handout

that's in your pack somewhere), we had a bunch of lineages coming off the eukaryotic pathway before the Cambrian explosion. The modern representatives of these lineages all divide by mitosis, but these eukaryotes -- and presumably therefore their ancestors -- are not sexual, meaning that the only way they know how to move their genomes through time is by mitosis. In contrast, all of the modern representatives of the lineages that derive from the Cambrian explosion are all sexual, suggesting that the invention of sex had something to do with the Cambrian explosion -- we'll fool around with that idea on Friday.

But before we fool around with the idea we have to understand what it means to be sexual. (Let me begin with an aside. Bacteria occasionally exchange some DNA with one another, and this is sometimes called bacterial sex, but it doesn't have anything to do with sex as I'm going to describe it here, so as far as I'm concerned it's not really sex). Okay, so a sexual species has the following 3 characteristics:

1. There are always two sexes. There are differences between the kinds of organisms in that particular group such that some are considered male and some female. One of the many interesting questions is why aren't there many sexes? Why is it that you don't have lots of choices? But you don't.

2. In all sexual species we see alternations between haploid and diploid organisms.

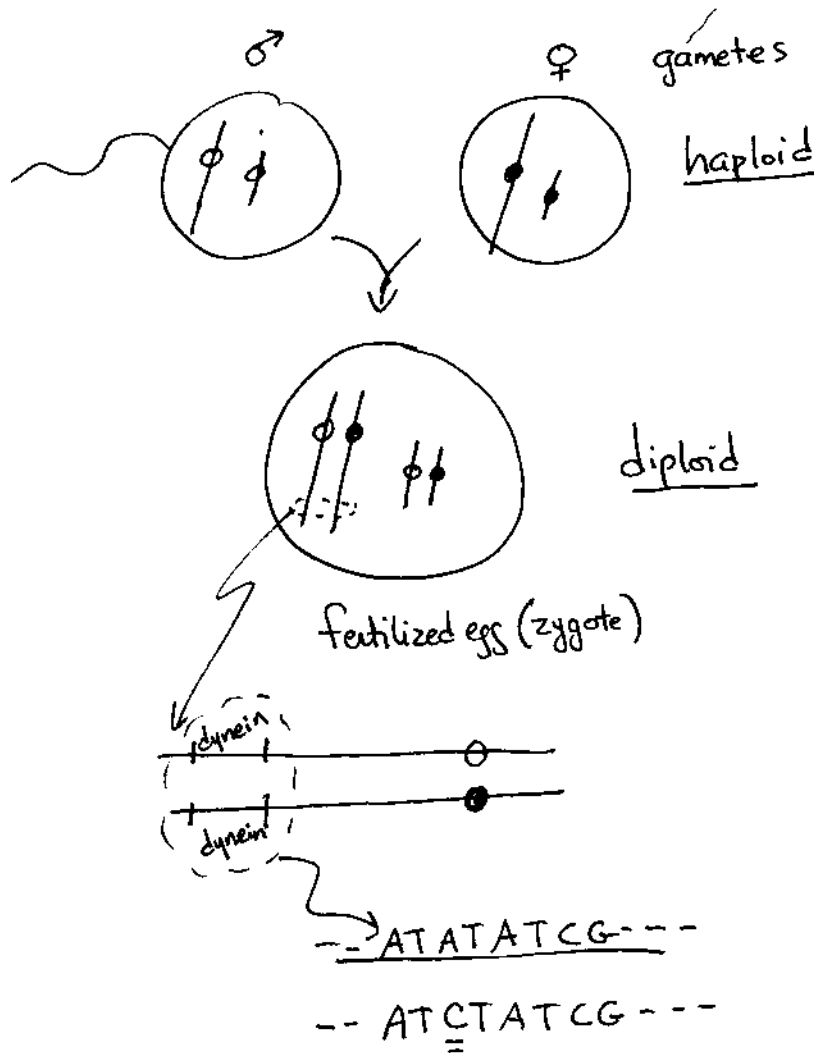
3. Haploid cells arise by meiosis (which is different from mitosis) and diploid cells arise by fertilization.

In the rest of the lecture I will discuss what is meant by #2 and #3. In the course of this, I will be pointing out the evolutionary advantages of sex because, as we've stressed many times, if a trait persists through evolution the way sex has, this signals that the trait is somehow adaptive, somehow gives organisms an advantage -- otherwise it would be lost. I will list up 3 advantages: first, the advantages of diploidy; second, the advantages of recombination; and third, and most important to us -- the real place that I'm going here -- is that sex allows you to get multicellularity, which we of course think is a terrific idea.

Okay, diploidy, and diploidy versus haploidy. I'm going to start with the same single-celled alga, the one that had two chromosomes, only now I'm going to say that in fact this alga is sexual. It divides by mitosis, but it can also do a second thing. It can also serve as a gamete if it's starved. Throughout evolution, in most life cycles (mammals being an exception), creatures "go sexual" when times are bad. When times are good they make clones that expand out into the niche. But when there's a brake on productivity -- for example, when they're starved for nitrogen so they can't make protein anymore -- then these same cells "go sexual," meaning that they switch on genes that allow them to be gametes.

A gamete, as we've considered before, is a cell that can fertilize. Because our alga is sexual, it comes in two sexes, male and female, so I'll draw two gametes and I'll put a sperm tail on one of them so you know who's who. The male and the female gamete have two chromosomes apiece (a big one and a little one, one with A-M instructions and one with N-Z instructions); to track them I've drawn the kinetochores as open circles in the boy and closed

circles in the girl. The gametes have receptors on their surfaces that recognize and bind to each other, and the net result (and we saw some beautiful examples of this in the videos) is that the sperm and the egg fuse together to form a fertilized egg. The net result, then, is that the fertilized egg, or zygote, is going to contain the chromosomes of both gametes: it's going to have a white and a black long one and it's going to have a white and a black short one. So now what we have is two sets of encyclopedias (white and black) and the name for a cell that two complete sets of the genome, this is called a diploid. In contrast, cells or gametes that only have one set of genetic instructions are called haploid.



So now we can ask what do you get by being diploid? Why would you want to bother doing that? And to think about that let's just look at a little region of this big chromosome so

we're now going to zoom in on this part, which carries a gene that codes for dynein. Because these two chromosomes are the same ones (the A-M chromosomes), we're going to expect that a dynein gene is going to be the same place in both chromosomes. But if we go ahead and actually zoom in even more and look at the sequence of these two dynein genes, we might find that they're absolutely identical but we also might find -- considering that one of these chromosomes comes from a male alga that swims around and another from a female alga that swims around -- we might find that they're different -- in the drawing above there's a single nucleotide difference between these two genes. Both of these genes code for dynein. We're just looking at variance. They're not identical but it's the same idea. When two genes that occupy equivalent positions on a chromosome are the same but not identical, they are called alleles. So we're looking at two alleles of the dynein gene. Allele comes from a Greek word that as near as I can tell is only used here [Mike Wysession points out that it's also used in "parallel," meaning two lines that are equivalent but not exactly alike.] It means a version of the other. To continue with our encyclopedia analogy, we could say that you go into a bookstore and you see there are two sets of Britannicas there and they're different printings, and you go to page 1, Aardvark, in one printing and then you read Aardvark in the second printing and the second printing they messed up a little bit. Both are clearly Aardvark entries but one is a little different from the other. They are alleles of one another.

So now we can think about why being diploid might be advantageous to an organism. One possibility is that one of these alleles, let's say the one that has an A in this position, may actually be nonfunctional or code for a dynein that works poorly, moves slowly, can't bind to microtubules very well. In which case having this second dynein gene sort of covers your butt, right? It gets you a good copy of the dynein gene, so having two copies of each gene is a good idea just like having two copies of an encyclopedia is a good idea -- in case you can't read the first one you go to the second one. So we can say that diploidy gets you a "rescuing" function. You've probably heard that it's not a good idea to inbreed, to marry your cousins, and that's in fact because you and your cousins are likely to have the same alleles. If you have a crummy copy of a gene, your cousin might very likely have the same crummy copy of that gene coming through the family, and so you get two crummy copies of the gene and your kids might not be so healthy.

There's a second way of thinking about the advantage of diploidy, which is that maybe both of the alleles encode functional proteins but they function best in different contexts. This allele of the dynein gene, the protein that it encodes may be a really good dynein in terms of binding to microtubules. This one might be really good in terms of being fast. And if you have both of them present in the cell you're actually more adaptive, you're more flexible. You've got more ideas going. So it's good to be various, and in fact there's a popular understanding of this as well, the so-called hybrid vigor. You try in fact to out-cross your plants or your horses so that they will carry allele-pairs at many gene loci, meaning that they have more options, more different kinds of reasonably good protein.

Now in the case of sexual single-celled organisms like our alga, this fertilized egg has one fate: it differentiates into a spore. A spore is like a seed. It elaborates a protective coat around itself, it can over-winter, it can lie dormant for many years and then germinate. So diploids in the case of single-celled organisms tend to become spores whereas, as we'll see in a

few minutes, the multicelled diploid has a very different fate. But it's in this spore that we can examine our next important feature of sex, which we can generically call meiotic recombination.

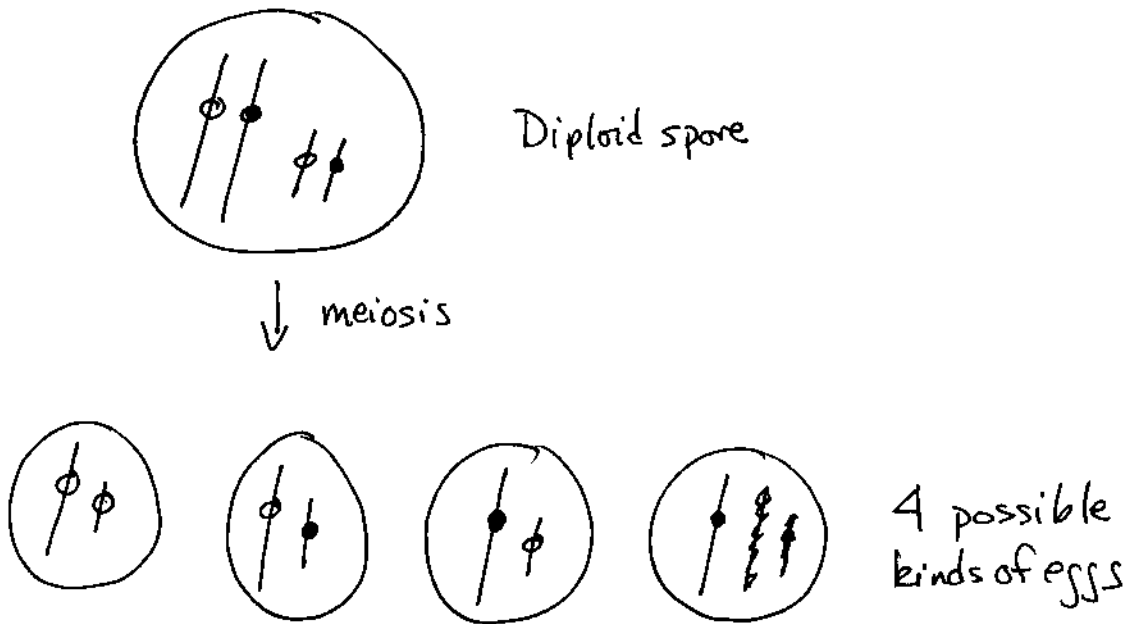
The basic proposition is as follows. Just as we created a diploid by fusing haploid gametes together, and in this case made a spore, we have to get our haploid cells back again so that we can keep doing this. The diploid --> haploid route occurs via a process called meiosis so in the case of our alga this diploid spore undergoes a meiotic process to get us haploid cells just as fertilization gets us going the other way to get diploid cells. I'm not going to go through what happens in meiosis because it's not important -- I mean it is important but it's not important for our story. What we need to talk about are the two rules that govern meiosis and not worry about how this happens.

Meiosis generates haploid cells from a diploid cell. In some cases, as with our alga, the haploid cells are able to undergo mitosis and generate large clones. In other cases, as with us, the haploid cells can only function as gametes.

The first rule of meiosis is that each egg has to carry a complete genome: for the alga, it has to have an A-M chromosome and an N-Z chromosome. A gamete is going to be useless if it doesn't have all of the genome in it. If a single chromosome is missing, and hence lots of instructions are missing, that gamete is going to be junk.

The second rule of meiosis is that it doesn't matter whether a given chromosome derives from the male or the female parent.

So here's our spore and we're going to have it do meiosis and it's going to obey these rules. These rules dictate that there are four possibilities, drawn below, for the kinds of gametes that this kind of spore can make. One kind of egg can have a white big one and a white little one. The second type can have a white big one and a black small one from the mother. The third possibility would be a black large one from the mother and a white small one from the father. And the fourth possibility is that both of them are from the mother. That is, meiosis generates new combinations of chromosomes, and this then is recombination. Those of you who have taken biology courses know that there's an additional way to mix things up even more, called crossing over. I will remind you that that can also happen, but those of you whose minds are not polluted by crossing over don't need to begin now.



So let me repeat this using a human example, although we can't draw it because there are too many chromosomes to draw. All the cells in your body are diploid, so therefore all the cells in your body have two times the core chromosome number of 23, that is, all the cells in your body have 46 chromosomes. You can now say, with what you understand about fertilization, that 23 of these chromosomes are going to come from Mom and 23 from Dad (23 from the sperm that made you and 23 from the egg that made you at fertilization). For a human male, all of the cells in his testis that are going to give rise to sperm, all the cells that are poised to undergo meiosis, are also going to have 46 chromosomes. (Every day every male in this room makes many millions of sperm, which means millions of meiosis are going on as we speak.) So if we now just start looking at sperm that might be present in a given testis, and we look at sperm A, we can quickly realize that chromosome #1 in that sperm might be from Mom, chromosome #2 from Dad, #3 from Dad, #4 from Dad, #5 from Mom, etc., the only rule being that you have one of each kind, a complete set of encyclopedia volumes. Sperm B is going to have a different combination -- chromosome 1 from Dad, 2 from Dad, 3 from Mom, etc. All you have to do is get a complete set.

Let's now say that sperm A is going to fertilize egg Q. The same thing has been going on in the ovary of the female, so in egg Q, chromosome 1 is going to be let's say from her Mom, chromosome 2 from her Dad, etc. Because her Mom and her Dad were let's say from Akron, Ohio and his Mom and his Dad were from Africa (Benin), there's going to be lots of different alleles on the two sets of chromosomes (46 in all) that wind up in the fertilized egg (zygote). Therefore, to start this human being off, you start with a recombinant set of chromosomes that's completely different from the set that's in the mother and the set that's in the father. One way to express this is to say that when two people have a kid, they each contribute half of their genome to that kid and they wind up with a stranger.

So now we can take this to the whole human population and not just these two individuals, and we can think about what it is that recombination does, which is that if you look at the 5 billion people that there are on the planet, that means that there are 5 billion reproductive individuals and therefore lots and lots of copies of chromosome 1 in the human population, lots of copies of chromosome 2, each one of which having a particular string of alleles. If we look at chromosome 1 and gene #1 on that chromosome, the Aardvark entry, and say that this gene #1 codes for the acetylcholine receptor (the receptor on muscle that makes it twitch), then if we could look at all the chromosome 1's in the human population, 75 percent of them have allele A, a particular sequence, and 15 percent have allele B. And then you'd go all the way down to very, very rare alleles -- .001% might have allele G. That is, there are lots of different ideas for making, in this case, the acetylcholine receptor in what's called the human gene pool. The same will be true for gene#2 on chromosome 1, and indeed for each of the estimated 100,000 genes in the human genome, not to mention all the promoter elements. Because there's recombination, a sexual species basically "struts its stuff" at every generation. You put all of the chromosomes out there, reshuffle them with all of the other chromosomes in every mating, and get whole new sets of configurations. Each individual has a complete set of A-Z information, but each one of them is distinctive.

And now we can finally bring evolution in here, and remember that what evolution is about is variation and natural selection. What we've done here is we've greatly upped the ante in variation. We have a lot more variance out there than if you just do this clone business, and so there's lots more to select from. And so having all of these different ideas is a great idea in terms of how natural selection works.

We now come to the final result of sexuality, which is that sex is what makes multicellularity possible. For a multicellular lineage like ours, you start with a fertilized egg (zygote), but instead of that cell having only one possibility, which is to become a spore and then divide by meiosis, the zygote can instead undergo mitosis. Moreover, as we've said in an earlier lecture, the daughter cells from the mitoses stay together to form an embryo and then a multicellular organism. So all of the cells in your body you can think of as being a clone, a clone of the fertilized egg that you started out with. Each of them is switching on and off different kinds of genes but all of the cells in your body have the same 46 chromosomes. Importantly, though, as this embryo is developing, one lineage of cells has its own idea. In this lineage, certain genes get switched on such that these cells and their daughters constitute what's called the germ line. These cells migrate to the gonads -- either the developing ovary or the developing testes -- and these cells are uniquely capable of undergoing meiosis to give rise to sperm or eggs, to become haploid, to do what we've just done.

So the human, and all sexual multicellular creatures, is a mosaic in the sense that most of our cells are what's called somatic and a few are germ line. So what does this get you? Well, what it does is best understood by thinking about the two basic jobs that are involved in being alive. The first job is to negotiate the environment, get resources, food, all the other stuff that you need to grow and replicate. And the second is to transmit the instructions for how to be that organism to the next generation. If you can do those two things, you're alive. So let's think about that in terms of the various kinds of creatures that have evolved. In bacteria both of those

jobs are entrusted to the same cell. It's the same cell that has to go about and get food and grow and replicate the DNA and also transmit the instructions. For our sexual single-celled alga, and there are all sorts of variations on this theme, the haploid cell is supposed to negotiate the environment and it's also supposed to transmit the genome to its clones by mitosis, and it's also supposed to serve as a gamete and transmit the genome to the next generation via the meiotic spore. The spore, in turn, is also supposed to negotiate the environment (e.g. over-winter), and it's also supposed to generate the haploid gametes. So even though we have two different kinds of cells in this case, each one of them is set up to do both functions, both to negotiate the environment and to transmit instructions to the next generation. Whereas for the multicellular sexual organisms you've in fact accomplished a division of labor. Negotiating the environment is the job of the soma and transmitting the genome to the next generation is the job of the germ line.

So now we are finally at a very interesting place. Now we can look at the kinds of life cycles that these three different strategies have generated. For both for bacteria and for single-celled sexual organisms, there is no death programmed into their life cycle. Of course you can kill a bacterium. You can boil it, you can step on it, whatever you need to do. It's not like they're immortal in that sense. But there's no part of the life cycle where the cell is supposed to die. And this is because, of course, every cell type in these life cycles is necessary for both negotiating the environment and for transmitting the instructions to the next generation. So you can't kill any of them off, they're all necessary. Whereas in the multicellular strategy, death is part of every life cycle. The somatic cells have only one job to do and that's to negotiate the environment, so natural selection, in focusing on the somatic cells, is focusing only on how it is that they go about negotiating the environment. As a consequence, somatic cells are splendid substrates for evolution. The only thing that's important is what they do. So there's selection for their ability to get food, to fight predators, to find a mate, to nurture the offspring. All sorts of traits, all sorts of behaviors start to emerge in these multicellular creatures with a soma just because this soma is in the end dispensable. The germ line takes care of the "immortality" part, the transmission of the instructions.

We saw this playing out when we were talking about the evolution of the brain. What we stressed was that brain cells are programmed to die. A lot of them are completely irrelevant. And now the punch line. Which is that not only are individual cells in the soma programmed to die or to differentiate into cell types that could never exist on their own; in addition, the whole soma is programmed to die. One of the products of somatic evolution, of course, is our sentient brains. Our sentient brains are uniquely capable, as far as we know, of experiencing fear and anxiety and sorrow at the prospect of our death. But it is because death is programmed into our life cycle that it's possible to have brains. So that's your thought for today.