An Introduction to Evolutionary Biology

Prof. Sutirth Dey

Biology Department, Population Biology Lab

Indian Institute of Science Education and Research (IISER) Pune

Week 12 Lecture 51

Applications of Evolution: Part 2

Hi. So, in our last discussion, we started looking at how evolution and evolutionary principles are important in our contemporary lives. And we discussed how antibiotic resistance and its evolution are a A huge, huge thing in the context of public health currently and in the very near future. Today, we are going to discuss another aspect of how evolution affects our health. And this is in the context of this fascinating sub-discipline known as evolutionary medicine. Now, what is it? So, evolutionary medicine, or Darwinian medicine as it is also called, is Trying to apply the concepts of evolutionary biology to understand diseases, particularly human diseases and it asks why it is and how it is that our evolutionary history makes us vulnerable to various illnesses. Now, why is this important? Remember when we were talking about, you know, various aspects of evolution in the first week? We distinguished between proximate causes and ultimate causes. So, typically, medicine, particularly Western medicine, is about proximate causes of diseases. What causes it? Which deficiency, which germ, which physiological issue, and so on? On the other hand, evolutionary medicine says that, look, diseases can also have some ultimate causes.

Evolutionary reasons, and that is what they are trying to figure out. Now, although there have been some writings prior to it, in general, it is thought that the field begins with a 1996 book. by the famous physicians called Randolph Nesse and G. C. Williams. If you remember G. C. Williams, we met his work when we were talking about the evolution of

aging, right? So, the book was called "Why We Get Sick: The New Science of Darwinian Medicine," a very nicely written book. Now, if you look at evolutionary medicine, there are a few core concepts. So, there was a 2008 study that mentioned 14 core concepts.

Now, it turns out that most of these core concepts we have already discussed, you know, in this course. So, I am going to talk about only two that we have not really covered, you know, in our last 11 weeks of discussion. So, these two; the first one is related to the concept of defense mechanisms. So, what it suggests is that many symptoms which we consider to be bad are not really, you know, bad things. They are actually defenses that have evolved over millennia, and they have very nice positive fitness effects.

They help us fight illnesses; they help us fight certain kinds of injuries. The other major concept is that of evolutionary mismatch, which says that we human beings We have actually evolved for most of our evolutionary history as hunter-gatherers. And therefore, all our genes, our proteins, and our various biochemical pathways are optimized for that kind of lifestyle. However, today we are in a world that has a very different lifestyle, Then that ends up placing a very different kind of environmental pressure to which we are not evolutionarily adapted. And it is this mismatch between how we have evolved and the environment we are finding ourselves in now.

That is what is leading to a number of major health problems. So, we are going to look at a bunch of examples to see what is meant by these two concepts in evolutionary medicine. But one thing you have to keep in mind here is that it is a relatively recent discipline. Only 30-40 years old, and therefore many of the examples that I am going to show you are all works in progress. So, there are good reasons in many cases for us to believe that you know those things are working the way I am telling you.

But in some cases, the jury is still out, and that is why I am going to specifically tell you, you know, where we know. That this works and what the cases are where there are still, you know, experiments to be done and more concepts to be cleared. So, the first example is in the context of morning sickness. All of you know that morning sickness is

something that affects about 70-80% of all pregnant women to some extent or another. What happens during morning sickness? Essentially, you have a lot of nausea; there is vomiting, and there is a major aversion to certain kinds of food.

So, these are the main symptoms of this condition. Now, obviously, you know it is a major cause of discomfort, and therefore, The question arises as to why you know this particular condition is present. Is it because something goes wrong in the physiology, and that is what people thought for a very long time? Although, to be frank, even today we do not know the precise underlying causes of morning sickness. But people have been trying to, you know, cure this with different kinds of drugs, sometimes with very, very bad results. But all this changed when, in 1988, this lady called Margie Profet came up with this hypothesis saying that morning sickness is actually an adaptation to protect the growing fetus is not at all an illness. So, it has an evolutionary reason. Now, why exactly did she say that? So one of the reasons she said that is that symptoms of morning sickness are particularly strong during the first trimester. And this is the period when the fetus is most vulnerable to toxins. Now, where are toxins coming from? Now it turns out that the plants have evolved all kinds of chemicals to fight off herbivores, both insects and larger animals.

Now, most of the time, when it comes to crop plants, we human beings do not even notice that there is a toxin. Simply because the adult body of a human being is typically capable of neutralizing or taking care of most of those toxins. We have evolved like that. However, when the baby is evolving or developing, particularly during the first three months, The baby is still not expressing all the adult genes correctly. As a result, the baby is a lot more vulnerable to those plant toxins compared to the adult.

And it is not only about plants; even if you look at other things, like, you know, fish or meat, Sometimes they end up containing other pathogens that may not be good for the baby. Therefore, the whole idea is that nausea and aversion to food are primarily related to those items. Food items that can carry these kinds of pathogens or toxins. Now this sounds like a slightly far-fetched idea, but it is actually not. So you know, I strongly

recommend that you look at this second paper, Flaxman and Sherman (2000), where They have actually looked at the various aspects of this morning sickness as an evolutionary adaptation hypothesis.

And they have talked about, you know, among other things, what the various vegetables and food items are. Towards which aversion occurs and what kind of toxins they can contain. Now this explains nausea; what about vomiting? So the whole idea is that we have to eat right; the mothers have to eat. Because the energy expenditure of carrying a baby is pretty high. So there are some toxins that are still going in.

So the whole idea is that vomiting helps to expel any of those harmful substances that are still coming in through the food. Now what reason do we have to believe that this works? There are many lines of evidence, as I told you; look at the Flexman-Sherman paper. But the main thing, the main reason for which We believe that this works because if you look at what happens to women who have morning sickness, it turns out that their The probability of having miscarriages is much lower compared to those women who did not have, you know, morning sickness. So, this is one reason why the view right now is that we do not really fight morning sickness; it is an evolutionary adaptation. So, let it be; it is actually going to be more helpful for the mother.

A similar thing can be said about something that we really hate, which is fever. Now, whenever we have a fever, the first thing that we typically do is We take some paracetamol, ibuprofen, or any of the many other antipyretics. Now, perhaps you would not be so willing to take an antipyretic if you knew that this particular symptom of An increase in body temperature due to a microbial infection; humans are not the only organisms to have it. Turns out that several vertebrates and non-vertebrate species tend to show this thing, which suggests that this is a very old thing, a very old physiological response, and it is something that is quite widespread. Which essentially means that it is something that can potentially have evolutionary benefits.

And in this particular case, people have actually worked out that. An increase in body

temperature actually helps the body fight various infections. In what way does it do that? Many, many ways. I am giving you this paper for people who are interested and want to get into it in some detail. At a very rough level, what happens is that A, that increased temperature. That can end up, you know, taking the body temperature outside the optimal temperature range for some microbes. More importantly, that increased temperature. It ends up recruiting the immune cells and making it easier for the immune cells to fight the infections. Now, in spite of that, very interestingly, doctors many times prefer to reduce the fever using antibiotics. Now, why exactly is that happening? What are the various changes that happen at the molecular level? Because of this, an increase in temperature can help in fighting infections.

I am not going to deal with that here, but I will recommend that you check out this video. It is not a long video, it is very nicely done, and the information in this video is part of this course. So, you definitely need to look at it. So, this is another example where what we think is bad is actually part of our evolved defense system. Now, we will go to the other hypothesis, which is related to evolutionary mismatch.

One of the major examples of a potential evolutionary mismatch is myopia. It is a very, very common thing; I mean, you can see it when I have it. And this is a situation where the light that is coming from a distance, instead of being focused on the retina, It actually ends up getting focused in front of the retina, which is why the image that we see. From a distance, you know, that image is blurred. And this primarily happens because there is elongation of the eyeball.

Now, very interestingly, if you look at hunter-gatherers or people who practice subsistence agriculture, you might wonder, what is subsistence agriculture? So, you know, there are lots of people who grow only that amount of food that is sufficient for themselves. They do not sell their agricultural products. So, that is what is known as subsistence agriculture. So, if you look at such people, the rate of myopia among them is actually less than 3 percent. Yet, if you look at the global population, in 2000, 1,406 million people had myopia, which is about 23% of the world's population.

And if you try to project it forward, by 2050, the estimate is that about 50% of the world's population, About 4,758 million people will have myopia. Myopia nowadays has become so common that most of the time we do not even notice someone you know wearing glasses. In fact, in many cases, it has become a fashion statement; it is that common, right? But the question is: how and why? Among hunter-gatherers, just a few thousand years ago, the rate was so low. If you look at modern humans, the rate is very high. So, something has changed; what has changed? So, the most common theory for why you have so much myopia is what is called the near-work hypothesis.

What does it mean? It means that, let us say, you focus on a book or you focus on a computer screen for a very, very long time. That ends up increasing the pressure inside the eye, and that increasing pressure is what elongates the eyeball. And as I showed you, when the eyeball gets elongated, that is when the light does not focus on the retina. It focuses in front of the retina, and you see blurry images. Now, this was the hypothesis that had been thought to be correct for a very long time.

And yet, if you look at the empirical evidence for it, it is equivocal. There are some studies that suggest that this might be the case. There are many studies which actually find no correlation between a lot of near work and myopia. So, what exactly is going on? So, it turns out there is a much more recent hypothesis that says this normal eye elongation, So the normal level of elongation and normal magnitude require a mix of complex visual stimuli. It is not about knowing the strain that you put on your eyes by reading on the screen.

It is about what the various kinds of stimuli that your eye are receiving. Now, people whose eyes lack all this complex visual stimuli have eyeballs that do not elongate properly. In fact, it ends up elongating a bit more, and they are the people who end up developing myopia. Now, one of the things that we know has happened is that, in modern times, Particularly in cities, the kind of visual stimulus that we get is actually very, very limited. And particularly, you know, if you are, let us say, spending most of your time in a

high-rise building, Indoors, looking at a computer or a book, you are not really being exposed to, let us say, greenery.

You are not really being exposed to, you know, changes in stimulus; very importantly, you are not being exposed to the bright sunlight. So, bright sunlight turns out to be one of the biggest things, you know, over here. So, all these modern environments in which we find ourselves, Most of them are actually leading to this kind of situation, because of which the incidence of myopia is going up. Now, it turns out that there is quite a bit of support from studies on other animals. There is quite a bit of support even from human studies, but not everything has yet been worked out.

So, if you want to look at the support from the human studies that Lingham et al. reviewed in 2020, That is what talks about that support, but still, I do not think this is something that is, you know, totally accepted. People are still working on it to show that, yes, this is undoubtedly the cause. We will go to the next example of evolutionary mismatch, which is related to the fact that over the last few decades, The incidences of autoimmune diseases and allergy-related diseases have greatly increased all over the world. It has again, you know, it has not yet become an epidemic at the level of myopia, but it is almost at the level of an epidemic.

And there is a hypothesis here that a significant increase in the use of antibiotics. And sorry, this is not a hypothesis; this is actually an observation that there has also been a significant increase. The use of antibiotics and our overall exposure to microbes has generally reduced quite a bit. This is also true of those microbes with which we have co-evolved, you know, over our evolutionary history. So, there is this hypothesis called the hygiene hypothesis, which suggests that If you are exposed to certain microbes during your childhood while you are growing up, Then this actually ends up educating your immune system.

It ends up telling your immune system, Hey, look, these microbes are okay; these are good. These are something that we need to be able to tolerate. Also, this creates a kind of

memory thing. And because of all that, later in life, the risk of allergy and autoimmune disorders actually goes down drastically. So, this hypothesis was first proposed by a person named David Strachan in 1989.

And today, this is again a somewhat controversial hypothesis. There are many studies that claim to support it. Unfortunately, there are many studies that say it does not really work. So, this is something on which people are really working. We need to keep our minds and eyes open to see which way the science is going.

The third major example that I am going to talk about is diabetes. Now, diabetes is one of those ancient diseases; it has been mentioned by the ancient Egyptians around 1650 BC. Even ancient Indian texts from the 5th and 6th centuries BC talk about it, and the Chinese talk about it too. Pretty much all old civilizations that have a history of traditional medicine talk about it. Now it was never a very common disease, and yet particularly in the last 40 years or so, the disease incidence has gone up drastically.

So in 1980, we had an estimated 108 million individuals with diabetes, not today. In 2014, the number climbed up to about 422. If you think about it, that is about 3.5 times, or more close to a 4 times increase in a span of just 34 years, right? That is, you know, 1.5 human generations, roughly speaking. In 2025, that is today, 589 million adults, or 1 in 9 adults, are living with diabetes. The prediction is that by 2050, this number will rise to 853 million. 1 million, remember, is 10 lakhs. I mean, these are mind-boggling numbers—absolutely mind-boggling numbers—and therefore, The whole question is whether you know that if you think about 1980 levels, where it is 108 million, to 2050, where it is 853 million. So, in a span of about 70 years, we expect it to increase by about 8 times.

That is mind-boggling. Obviously, something is happening. What is happening? Now one of the hypotheses that has been put forward to explain this evolutionary hypothesis. It is what is known as the thrifty gene hypothesis proposed by James V. Neel in 1962. What does it say? So it says that our ancestors never really had a constant supply of food. So

they had situations where, you know, suppose someday they had a big hunt.

So they would be getting a lot of meat, and then there would be periods when they would get nothing, and they would simply starve. So there will be cycles of so-called feast or feigning. Now, because of this, we evolved genes that favored, you know, becoming very good. In terms of extracting as much nutrition as possible when food is available and storing it in the body, particularly as fat. Such that when there was a famine, you knew you could have some stored nutrients that you could use.

Now, unfortunately, the situation today is not like that. Today we have a constant supply of food, and most often, this food is very, very high in calories. Therefore we now these thrifty genes which are extremely good at you know extracting the nutrition and storing it, Now it has actually turned into a bane. Now it is essentially storing all that nutrient and releasing it when we actually do not need it to do so. And that is what has led to both obesity and type 2 diabetes, which are known to be very strongly related to one another. So this hypothesis, prima facie, you know, makes a lot of sense, but what evidence do we have for or against it? Turns out that, again, it is a mixed bag.

So there are studies in which people claim that they have identified the thrifty genes in certain populations. I am giving you one example, but there are other studies that have not been able to find any consistent evidence. So it is again a mixed bag, and overall the situation is that We do not have sufficient evidence to either conclusively accept or reject it. Now there is something you know: one has gone forward with the same overall understanding about an evolutionary cause of diabetes. And that is something which is known well; it does not really have a name, but we can call it the doves and diplomats hypothesis.

So, this is associated with a famous evolutionary biologist from India called Professor Milind Watve. He was my colleague at IISER Pune until 2019. So, what Milind proposed is that again when we evolved as hunter-gatherers, But a hunting-gathering lifestyle carries a lot of risk, particularly the risk of injury to the skin. Now, he proposed, and he

actually, you know, has an enormous amount of data to validate his proposition that humans have evolved. several biochemical pathways that are optimized for a situation in which you have a high risk of getting these kinds of injuries.

Now it turns out that one of the things that has happened in our modern lifestyle, even in low-income countries, is known. For low-income sections of society, the risk of physical injury has actually gone down drastically. Now, because of that, the suggestion is that all these biochemical pathways that have evolved for that kind of, you know, A risky lifestyle, nowadays, in the absence of that risk, has turned these biochemical pathways against us. And that is what is leading to all this diabetes, obesity, and so on. Now it is a very interesting hypothesis that the book I am showing you over there contains an enormous amount of information about why they think that this is, you know, the way in which it has happened. But the reason I am showing you this particular hypothesis is that this has actually led to something practical and tangible. What is that? So, in this particular context, note that the whole idea is that initially we had, you know, a risk of injury. Or we led a more aggressive lifestyle, which is why you know the doves part. And now we are living the lifestyle of a diplomat, which is a more sedentary, risk-free kind of thing.

So, if that is the case, this automatically suggests that one potential way of controlling diabetes is to simulate those kinds of, you know, injuries or at least the risks of injury. So, taking this into account, Professor Watve actually tied up with a local Pune hospital. There is a hospital here, a very famous hospital called Deenanath Mangeshkar Hospital. So, they came up with what is known as the BILD exercise clinic where BILD stands for Behavioral Intervention for Life Cycle Disorders. So, what they do is exercise, but these are not your regular gym kind of exercises. These are exercises where, for example, you can see over here that they are punching bags, right? Here is Professor Milind Watve. So, here you can see him balancing himself on an inflatable rubber ball. Which actually is surprisingly difficult, particularly when you are slightly older, because it is very easy to fall. So, it turns out that these are the kinds of exercises that actually have some, you know, potential for injury.

There is some potential in knowing those biochemical pathways that have evolved to fire in a slightly different way. Professor Watve's claim is that this is what will control diabetes in a way much more effective than the current drugs. Now, is that really the case? I do not know. I have been chatting with Professor Watve for quite some time.

They are still collecting the data. I think they were trying to get a medical trial done; I do not know where it went, but, Essentially, this is a very interesting, you know, potential, at least, of treating diabetes in a very different way. So, this was about evolutionary medicine, which is primarily about our health. Turns out that there is a full sub-discipline called evolutionary psychology. which tries to do in terms of mental health what evolutionary medicine does in terms of physical health. So, this is a subject that studies contemporary human behaviors and mental processes.

As products of evolution operating on our ancestors. And essentially, it is a selectionist way of thinking, and people have used that to explain many phenomena. So, for example, you know, humans have a moral code; many of us do, at least, and the evolutionary psychology explanation. For that is why humans have evolved a moral code, because it allows us to reduce conflict and thereby live in a group. Similarly, you know many humans help each other. So, evolutionary psychology tries to explain this in terms of reciprocal altruism and kin selection, right? You know the concepts that we talked about.

And it essentially says that we are altruistic either towards our kin, because that increases our inclusive fitness, or we are Altruistic under those situations wherein you know that if we help somebody, then we expect that they will help us back tomorrow. Similarly, you know about mental health and depression. So, evolutionary psychologists would say that depression can be good for us under certain situations. One of the situations that has been proposed is that when we evolved, anything that led us away from the group was a problem. And therefore, just like we have evolved pain to tell us that something has gone wrong in the body, we have, you know, evolved melancholy or some kind of mental pain that allows us to notice situations where we have gone away from the group. So, in this

way of thinking, the depression that we face nowadays is because of our highly, you know, sorry, not neutral. You know nuclear families have become the norm, which is causing us to lose connection with our fellow human beings. And because of that, our evolved, you know, mental pain circuit has now started firing all the time, because of which we feel depressed. So, these are all somewhat controversial theories, and there are many reasons for these controversies.

And although evolutionary psychology is a fairly established field, there are multiple textbooks on the topic. In spite of that, there are many people who tend to be, you know, strong critics of this theory. Major criticisms include the assumption that everything is in the genes. But when it comes to behavior, we know that the context, the social context, and the environmental context play. a much bigger role in shaping our behavior than, let us say, shaping some kind of physiological mechanism.

So, many people have argued that evolutionary psychology suggests all things are just determined by genes. The context does not matter, which many people argue is not at all correct, and I would somewhat agree along that axis. Another major point is that evolutionary psychology assumes that everything is an adaptation. Not everything needs to be an adaptation, many things might be just, you know, collateral responses. And therefore, many people are uneasy with this way of trying to explain everything as an effect of selection. They argue many times that you know the hypothesis that people in evolutionary psychology are coming up with. They are essentially unfalsifiable because all of them assume that something was very good for our hunter-gatherer ancestors. There is no way we can prove this.

We cannot go back in time to our hunter-gatherer ancestors and see whether. That particular behavior was indeed something that was providing a, you know, fitness advantage at that point in time. So, it is essentially a lot of just-so stories. So, overall, evolutionary psychology is something that evokes an emotional response. But as I said, there is a critical mass of people who are trying to, you know, make this area more scientifically rigorous. I am sure that at some point we are going to get more information

and more data when more experiments are done.

So, whatever we did up to this point was the application of evolution in the context of biology. Now, of course, that is where you know I focused, because this course was an introduction to evolutionary biology. But I would like to end this by telling you about how the principles of evolution can and are actually applied far beyond biology. So, we have this concept called universal Darwinism. Which suggests that any system that exhibits variation, selection, and heredity will undergo a process of evolution. If you think about it closely, that makes sense, and in this particular context, variation is in terms of random changes, or you know which are analogous to biological mutations that occur within a population of what is here called replicators. So, this could be, say, a new idea; it could be a new meme. It could be a new design for a robot, or for any machine, or anything. So, this is how variation comes into play. Then there has to be some kind of fitness differential, which means that certain variations should have A greater likelihood of survivorship, a greater likelihood of being chosen, or a greater likelihood of being copied, and so on.

So, for example, you know that in the context of business, a strategy that leads to higher profit or In the context of memes, a meme that has greater appeal compared to another meme, and so on. And finally, there has to be something analogous to heredity, which in this case is typically called retention. which is that the successful variants are the ones which have a higher quote unquote fitness They are preserved, and they are passed on to the next iteration or next generation of replicators. For example, suppose you have a meme and people are forwarding that meme on WhatsApp to different people. So, each time a forward is happening, one extra copy of the meme is being generated and it is reaching out to somebody else.

So, that is the way you will have the information going forward. So, this concept is applied across many, many, many disciplines. Frankly speaking, the examples are too large. It has been applied in linguistics, art, music, epistemology, economics, ethics, and cultural selection; even the list is very, very long. And in each one of these cases, there is

a, you know, proper sub-discipline within those disciplines.

They are trying to apply these principles. We do not really have time to get into all of that. What we will do is look at just two. One is in the context of computer science, so-called evolutionary computation. and the other is in the context of chemistry, the so-called directed evolution. So let us first look at evolutionary computation. What is it? So it is essentially a set of computational methods that solves complex problems using evolutionary principles.

Now there are many, many paradigms. One of the paradigms is known as a genetic algorithm. This is the one that has been used most often, and this works as follows, you know. Pretty much the same three steps that I told you about in evolutionary Darwinism and universal Darwinism. So, it creates a random population of solutions. So, here, population is not a biological population; here, population simply means a collection, a collection of some kinds of entities.

So, it creates a random population of solutions and then evaluates their performance. this is analogous to fitness and then it breeds or propagates the best solutions to create a new improved generation. So, this is how you get selection and heredity, and then these three steps. These keep happening in a loop until the desired goal is reached. So, let me give you one example of this that should make the concept a little clearer.

So, suppose you have a target. In this particular case, it is a photo of Darwin, and you need to reach that target starting from some starting point. How will you reach that? So, in the context of evolutionary computation or genetic algorithms, the first step that will be done will be to Get hold of a large number of populations; get hold of a large number of individuals, each one of whom has Different, you know, are basically just pixel values, each one of them composed of some random pixels. So, here each pixel has a value; you know a pixel is the dot in a picture cell, the dot that is used to compose this image. So, each pixel has a grayscale value that goes from 0 to 255.

So, one side is black, the other side is white, and everything in between is contained within those values. Now, what you have is a population of many such pictures. Where each pixel has been initialized from random grayscale values from this link, 0 to 255. So, you have all these values. Now, what you do is evaluate the fitness of each picture.

How do you evaluate the fitness of each picture? So, what you do is suppose you take this pixel over here. This is your pixel in the target, and then you take this corresponding pixel over here in this one. Now, what you do is, let us say, the value of this pixel, you know, this one, is, say, 10. Let us say the value you have started from, a random thing, over here is, say, 15. So, you do (10 - 15) and then you square this. So, this gives you $5^2 = 25$. Then, you take the second pixel over here and subtract that value from the second pixel over here, say, Say (23-13) and square that up. So, that is $10^2 = 100$, correct? So, you keep doing this for every single pixel in this particular picture. So, when you do that, you are going to get some sum over here, right? And that sum is essentially the sum of the squared differences from the target in the grayscale value for each pixel. So, that sum that you are getting here is a measure of fitness. Now, in this particular case, it actually goes in the other direction because, The closer the pixel value is to this, the lower this sum will be, and the higher the fitness will be.

So, a lower sum is equal to higher fitness. Correct? So, the basic point is that by doing this for this picture, you will obtain a fitness value. So, call it fitness value one. Similarly, you will get one for here, fitness 2 of 2, 3, and so on and so forth, correct? So, you have each picture, and you have figured out how different it is from the target.

In the process, you have figured out the fitness values. Now, yeah, the lower the sum, the fitter the picture. Now, what are the steps in evolution? So, you have evaluated the fitness as I told you. Then what you do is rank all the individual pictures in descending order of their fitness. So, let us assume that my, you know, say, 20th picture is the fittest one and has the lowest sum.

So, this rank is equal to one. So, let us assume the next one, say, picture number 35, has

rank 2 and so on and so forth. So, you rank each of them in descending order of their fitness. Now, in this particular example, what we are doing is mixing some pixel color from the next higher individual. So, let us say that this is my highest rank. So, randomly I will take some pixels in this picture and replace them with the pixel values of the next one.

So, that is what is meant by going from 2 to 1. Similarly, let us say I have rank 3; I will take some pixel values from this randomly. And I will replace the pixel values over here with pixel values from here, correct? And I do this for every single picture. Now, what happens? I have had a mutation; I have had changes. And now, these three steps, I will keep doing them in a loop. Now, because I have done this mutation, Now, whichever was the fittest picture earlier may not necessarily remain the fittest picture.

So, now again I will do the re-ranking, and then I will keep on doing this. And with each iteration, I will simply take the picture that has the highest fitness. which means the picture that summed over all pixel values is closest to my target. That is the process. Can you see how this is analogous to evolution? You, this particular step is creating mutation, and this ranking is essentially analogous to selection.

Now, what happens if you do all of that? Let us see. So, here is my target picture, and each frame that you are seeing is the fittest picture. And it is now being replaced by the fittest picture in the next iteration, and so on, to see where it goes. Can you see this? Starting from a totally random population of values, see how this converges towards the target. Now, what is the main difference between normal evolution, biological evolution, and this one? In this particular case, a target has been given, and because a target has been given, Therefore, you are evaluating fitness in terms of the difference from that target.

So, this is directed evolution in some sense, as opposed to the random nature of biological evolution. That is where the main difference arises. So, now obviously the big question is, you know, fine, this looks like a nice game, but can this be of any use? And it

turns out that this is actually of major use, and I will just show you one example, which is in the context of antennas. Now, what is an antenna? So, an antenna is an electronic device that converts alternating electric current into radio waves or vice versa. So, people who are my age will remember that when we had televisions at home, There used to be this antenna, or the aerial as we used to call it, on the roof, and every now and then.

We had to go up on the roof and turn that antenna to improve the signal reception. Now, it turns out that although we have moved to satellite television and, you know, set-top boxes and so on and so forth, Turns out that one area that still depends on antennas is actually the space missions. Because when you are going to space, you need to have continuous communication with, you know, Earth. And for that, you need to have antennas of various shapes depending on what kind of radio frequency is being used. And what is the way in which that radio frequency is going to reach you? So, the people who have probably done more research on this than anybody else are NASA.

And since the early 2000s, NASA has actually been using a genetic algorithm of the kind that I showed you. To design these antennae particularly for unusual use cases. And one of their most famous designs, the first one that went to space, was in a 2006 NASA mission. called Space Technology 5, or ST5, and this is the antenna that they set. So, this antenna was totally developed using a genetic algorithm, and you can see the very peculiar shape of the antenna over here.

Now, they also tried to do it manually. But it turned out that this was the design that gave far better results compared to, you know, what was coming out manually. So, this is just one example; definitely not the only example. Many more such antennae have been designed and used subsequently by NASA. So, this brings us to our second example, a very important example nowadays, which is known as directed evolution primarily in the areas of chemistry or protein engineering. So, what is it? It is a protein engineering method. Which steers proteins or nucleic acids towards a user-defined goal using a selection-based process. What do I mean by all of that? So, I will just give you one example. So, suppose there is a protein, and you want to improve the properties of that

protein. What will you do? So, what is done here is that you extract the gene for that protein and create some mutations randomly.

So, you have a library of genes, and then you put all those genes into a vector like E. coli. So, here you have, you know, E. coli expressing the gene library. Then you let the E. coli grow, and then you essentially do an assay to see how your protein is working and once you have done that assay, you have a rank saying this E. coli strain is doing the best, this is 2nd, this is 3rd, 4th, etc. So, what you do is reject the lowest performing ones and take the one that is doing the best. Or you know a few, let us say a top 4 or 5 of those, then from these isolate the genes and then use things like Either you know error-prone PCR, using transposons, or using chemical mutagenesis, in which case. Some of these cases, you have to do right here; then you create the library for the next iteration. Keep doing this again and again until you reach your desired level of enhancement in functioning.

Now, the best thing about this is that when you compare it with how normal protein designing is done. So, for normal improvement of protein and protein engineering, what you do is take the structure of the protein. And using your knowledge of bioinformatics, you try to predict what will happen if I change this residue from, say, a valine to a leucine. If an isoleucine is replaced with a proline, something like that, then the structure of the protein will change like this and If the structure of the protein changes like this, then this is the way in which the function will change; it will either improve or not. So, here in the traditional method, you know, using side-directed mutagenesis, you need to have an excellent understanding of what the structure of the protein is and how changing one residue to another will lead to an improvement. Now that we have all the computational methods, it is not at all easy. What this method does is say that you need no such knowledge. You just keep doing it randomly and hope that evolution will take care of it at some point.

And it turns out that it is actually an extremely effective method. Evolution is indeed very useful in designing proteins with good function. So much so that in 2018, the Nobel Committee recognized this and awarded the, you know, Nobel Prize in Chemistry. To

Frances Arnold, George Smith, and Gregory Winter for their work in directed evolution. What is more important to note here is that not only is this a method that is very interesting, This has actually led to several commercial products that are currently on the market. This method of directed evolution, many people hope, will be one of our major ways by which we will be able to create new drugs.

So, if antibiotics and other things are involved. So, if you remember from our last discussion, we saw that we have not been able to discover a new antibiotic…I will take that back. We have been discovering new antibiotics. But at an extremely low rate, most of those antibiotics are actually not making it to the market. So, the whole idea is that directed evolution will be one way in which we will be able to make such drugs at scale and much faster. So, this was about the application of evolution. This is where the course ends, but in reality, you know that although the course ends, The journey of evolutionary biology obviously continues.

So, this is the website that is associated with this course. I strongly recommend that you visit this website. You are going to get quite a few extra things over here. So, for example, for every video, you will find a summary. All the links that I mention in the videos, we are going to put up over there. We are also going to put up many extra resources for you to explore on your own.

We still have not done that, but hopefully we will do it over the coming months. And, more importantly, you know, I mean, this was a basic course, right? For everything I was able to discuss with you, there were so many other things we could not discuss. So I intend, hopefully, if I get time, to create many other interesting videos about different aspects of evolution. And if all goes well over the next few months, or next several months, actually, I want to create those videos and put them on the website. So, you know, you will find a lot of food for thought over there, as well. So that's about it. Thank you very much for being part of the course. See you whenever we next see you. Bye.