Bioengineering: An Interface with Biology and Medicine
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Lecture - 01
Why Biology for Engineers: Part-I

Welcome to the MOOC NPTEL course on bioengineering an interface with biology and medicine. Hi I am Sanjeeva Srivastava, an associate professor in Department of Biosciences and Bioengineering at IIT Bombay. Let us first talk about why this course? Integration of biology and medicine with engineering can broaden the scope to address major societal problems.

So in this course we will mainly focus on few biological concepts and their practical applications. This course will also try to bridge the gap between biologists and engineers which may offer diverse career opportunities and employment opportunities in the areas of bioengineering and biomedical sciences. At IIT Bombay, we teach engineering first year undergrads a basic course in biology.

Few of my lectures are also from this BB101 course. This course for a MOOC; however, will not cover details of bioengineering principles.

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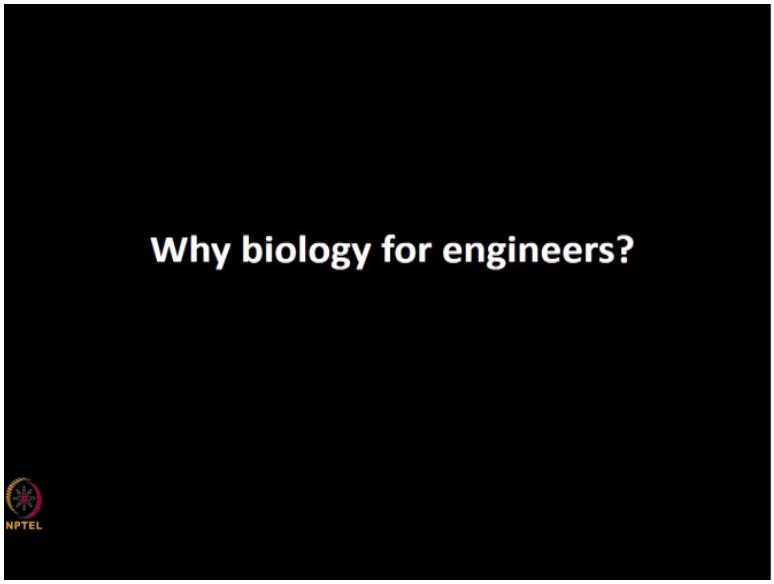

Let us first talk about why biology for engineers?

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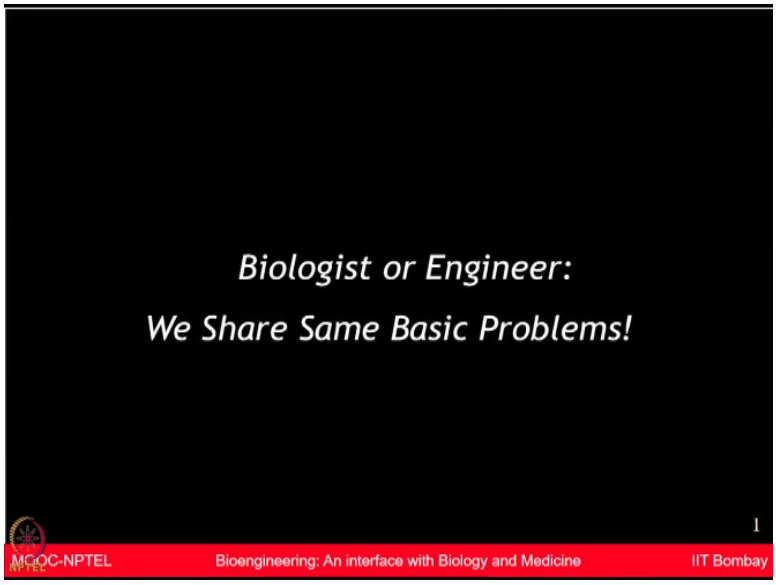

So whether it is biologist or engineer we share same basic problems. Second year students can you tell me which are the major global problems which required all of our attention, of course there is no boundary for engineers or biologists when it comes to the global problems. So you have rightly mentioned there are many possible reasons, many global problems which requires our attention whether we are biologists or engineers. Let us try to discuss some of these problems one by one.

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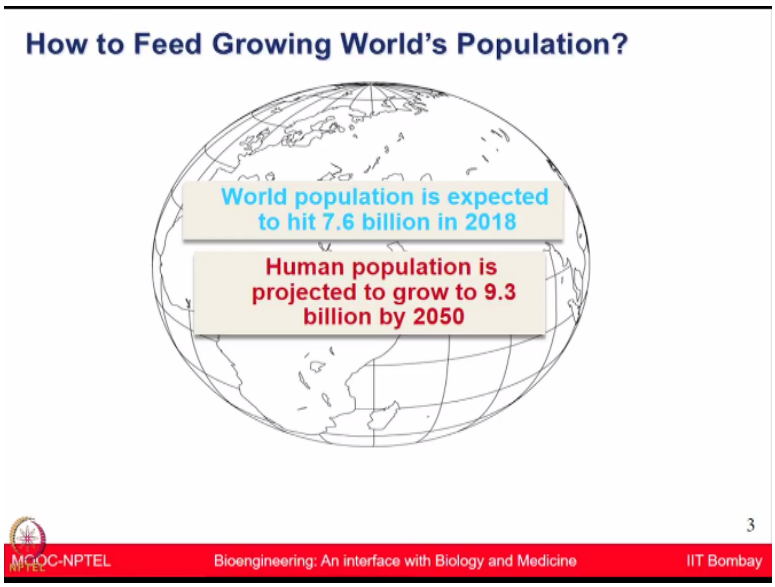

First of all how to feed the growing world's population? Let us think about the way population explosion is happening. World population is expected to hit almost 7.6 billion in 2018. The human population another hand is projected to grow 9.3 billion by 2050. So how are we going to feed the growing world population when most of the arable land, the land where food crops already being grown is under cultivation.

Let us also think about another hand, the environmental impact on the food production, the different type of stress conditions such as salinity, drought, cold, different stress conditions affect plant productivity worldwide.

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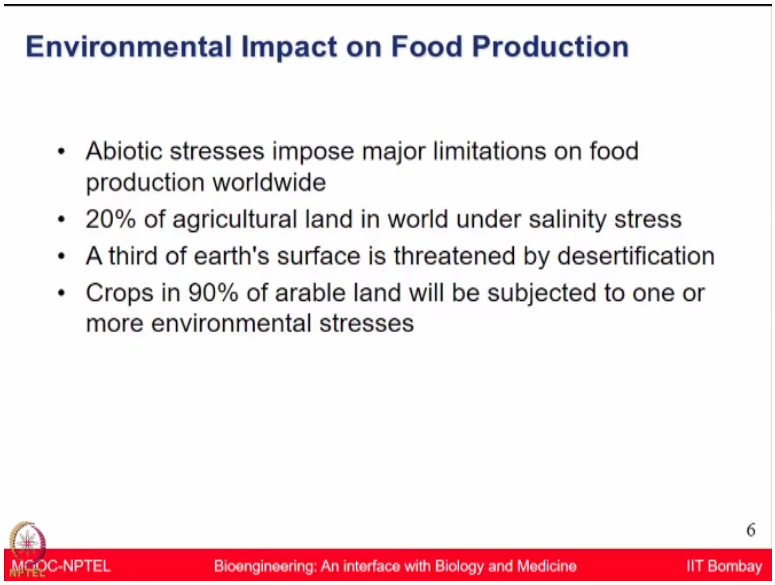

Almost 20% of world's agricultural land is under salinity stress. Third of the earth's surface is threatened by desertification. The crops in 90% of arable land is expected to encounter one or the other type of environmental stress condition. So question is how are we going to feed the growing world population?

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Let us look at some of these images from various news clips. The impact of environmental calamities on food production.

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After these cyclones and different natural catastrophes especially you know you are in Mumbai you have seen recently the cyclone Ockhi in December.

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A very untimely rain, very untimely cyclone devastated lot of you know the crop area and the fields which were used for the cultivation. These are the images shown for sure that you know after 1967 they saw the highest rainfall received in the month of December. Just one of these untimely rains, untimely cyclone could actually ruin the efforts of the farmers for you know which they have put in for months and years' time.

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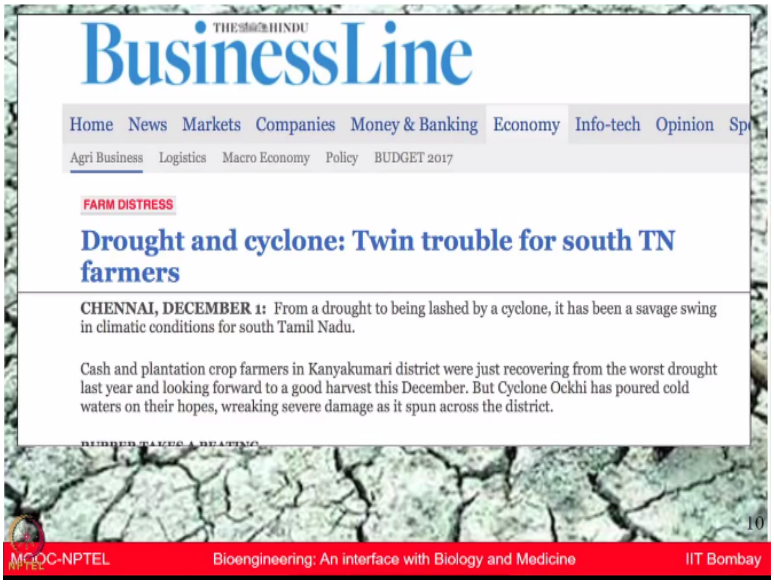

Again I am showing you a few news clips. Drought and cyclone, the twin trouble for South Tamil Nadu farmers.

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Around 900 farmers suicide in drought-hit Marathwada this year. Imagine the farmers worked so hard and after a hard work of full year this kind of untimely natural catastrophes could actually destroy their entire effort and now these kind of barren land can be seen. So in which way genetic engineering and biotechnology can offer some help to increase the plant productivity and the overall food production.

So one of the easier way of moving forward is the genetic engineering approach where DNA cloning can be utilized for this process. So what is DNA cloning? DNA cloning is a process

in which we can produce multiple identical copies of a defined DNA segment oftenly bacteria such as a E. coli are commonly used for DNA cloning purpose.

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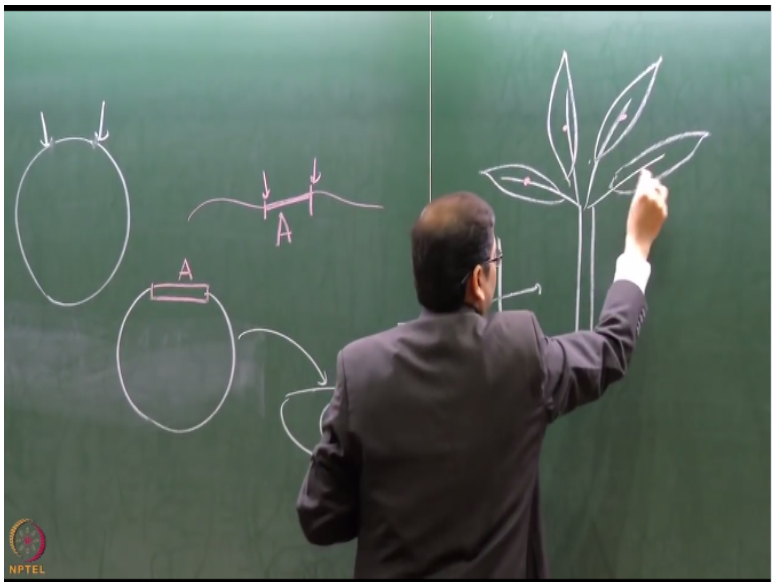

The bacteria contains plasmids which is a small circular extra chromosomal DNA molecule which replicates separately.

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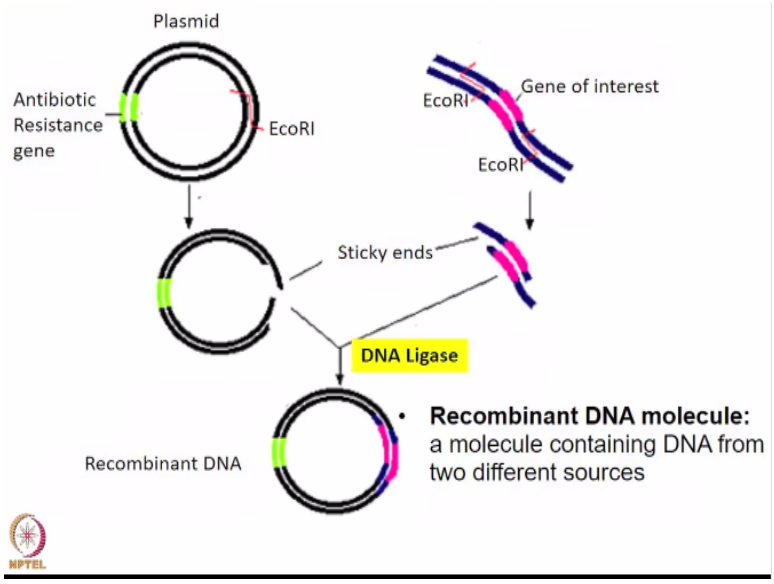

So let us see this is you know for DNA cloning we are taking a plasmid which is known as a vector and then gene of interest which you want to make multiple copies. Let us say you identified a gene of interest which may increase the food productivity. So now this gene of interest known as insert you want to introduce in this plasmid to make multiple copies. To do that you can use restriction enzymes to cut the plasmid and DNA of interest from the same enzyme.

And now you want to move the gene of interest into the plasmid, so you will use some enzymes like DNA ligases which could now produce a recombinant DNA molecule. These plasmids are then introduced back in the bacteria by the process of transformation which makes multiple copies of DNA which now you are growing inside a bacteria multiple generations are producing multiple copies of these plasmids.

And therefore your gene of interest is also being produced. Now this could again be introduced back into a plant to make a transgenic plant which may express the foreign gene of your interest. So now let us look at the process here. How genetic engineering and biotechnology can offer to introduce the genes of interest into a new system.

For example, on the left side shown is the circular plasmid in which we have antibiotic resistance gene. Let us say you know for example you can have ampicillin resistance gene or chloramphenicol, tetracycline etc and then you have restriction sites where the restriction enzymes are going to work. In this case, one of the enzyme which is EcoR1 is shown with the red.

On the right side we have the DNA segment where a gene of interest you want to clone further and again there are you know restriction sites at EcoR1 is present which can be used for the restriction digestion. So you can use now the restriction enzyme to cut both the plasmid and the gene of interest and then they have to get stitched together in the presence of an enzyme which is known as DNA ligases.

Now DNA ligase is going to make the recombinant DNA molecule. A molecule which contains both DNA and the plasmid from two different sources and now this recombinant DNA molecule could be used for different applications. So the same concept although we are going to talk in much more detail later when I come to the gene cloning and come to the plant biotechnology aspects.

But in this slide I have illustrated couple of examples from the textbook which shows that you know genetic engineering has many applications.

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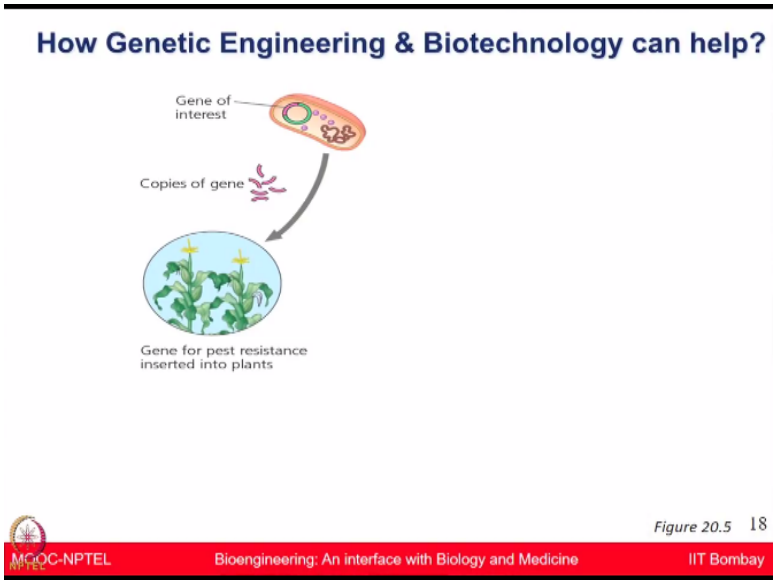

It could be used to make transgenic crops which may incorporate useful traits for example herbicide or pest resistance or it could be salinity tolerance which can you know provide a plant more ability to survive in the abiotic stress conditions or example is a Golden rice which contains genes for synthesis of vitamin A. So we will have more detail of these in the you know detailed lectures.

But I just want to illustrate that you know biotechnology and genetic engineering has come forward to at least you know try to make an attempt to provide solutions for these global problems where you want to increase the food productivity on the very limited arable land.

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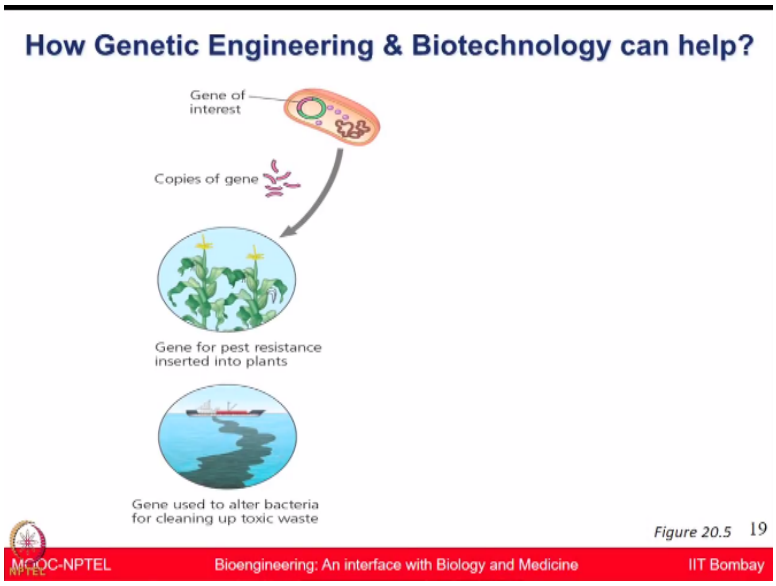

Another example could be genetic engineering microbes. They could be produced which is crucial to clean up highly toxic mining wastes.

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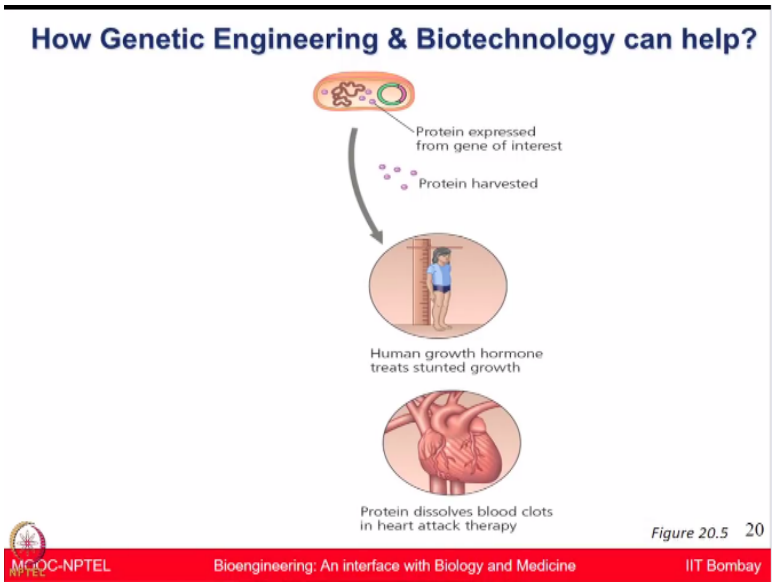

Even proteins for medical uses such as insulin, different type of growth factors, growth hormones they can be produced in the large quantity by using different type of genetic engineering technologies. So in some way, the first major problem which is to increase the food production, to increase the vitamins and nutrients supplements I think genetic engineering may provide some solutions to those problems.

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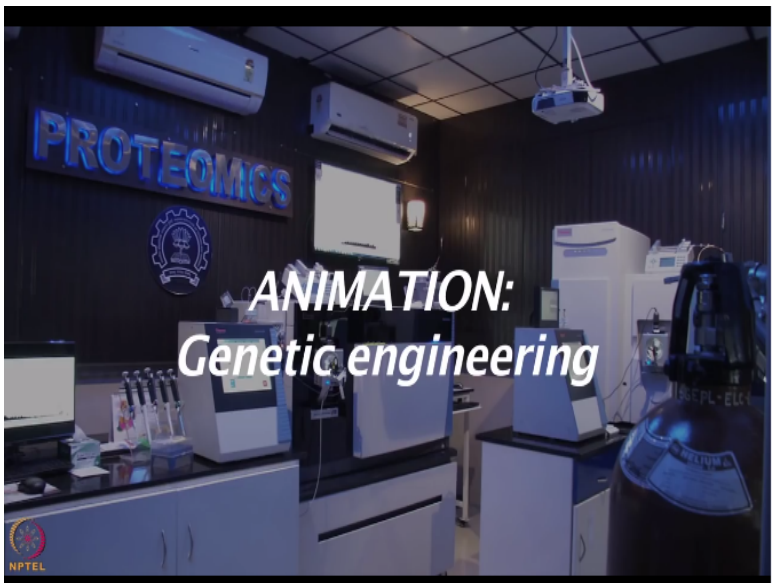

Let me explain you this in more detail in the following animation.

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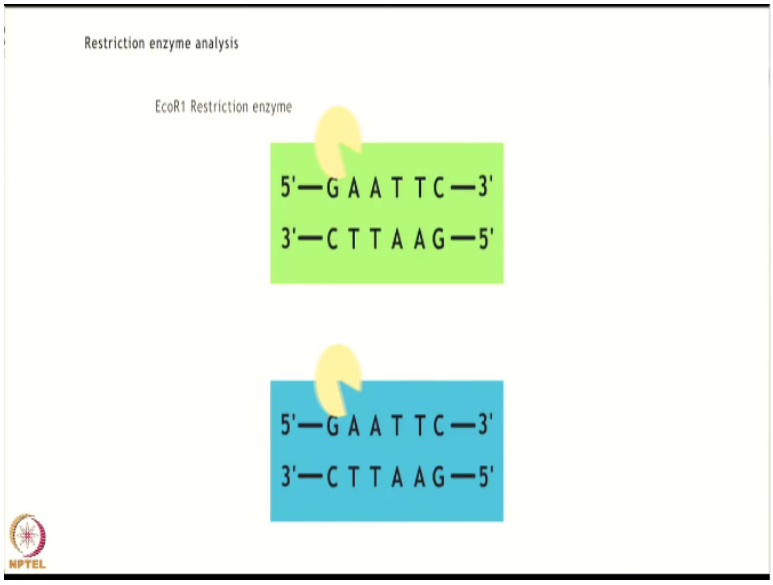

Restriction endonucleases cleave double-stranded DNA at specific recognition sequences which can be used for isolating genes and cloning new DNA molecules.

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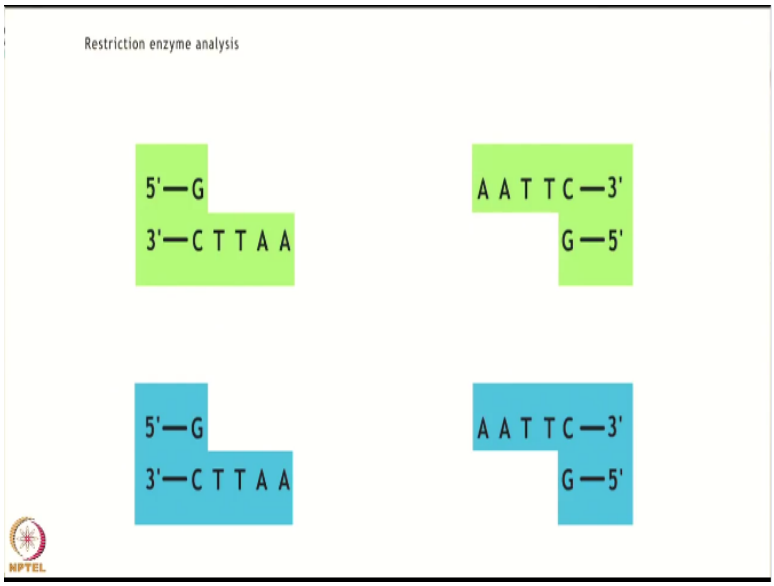

These enzymes are typically found in prokaryotes where they function as a defense mechanism against foreign DNA. Recognitions sites are typically 4 to 8 base pairs long and are very often palindromic.

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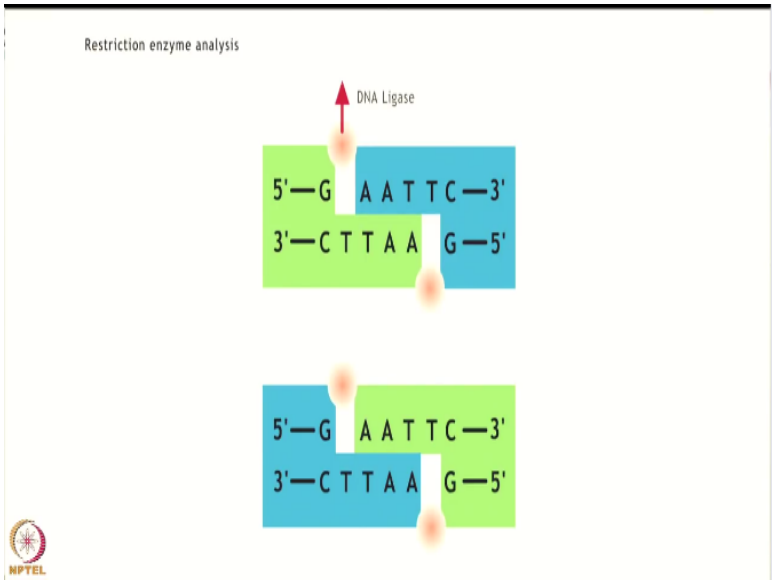

That is, they read the same in both directions. Cleavage at a phosphodiester bond can produce either blunt ends or cohesive ends to DNA molecules that have been cleaved by the same restriction enzyme can be ligated using DNA ligase to produce a recombinant molecule. The fragments may also be separated using electrophoresis techniques.

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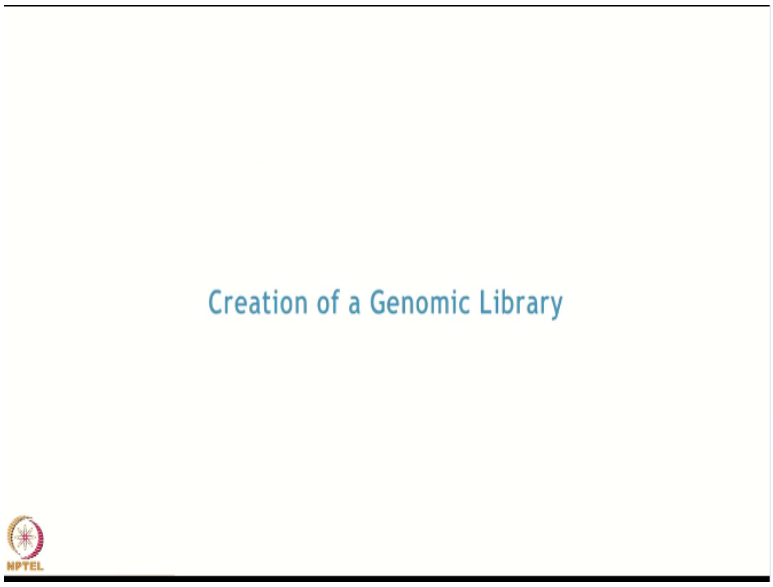

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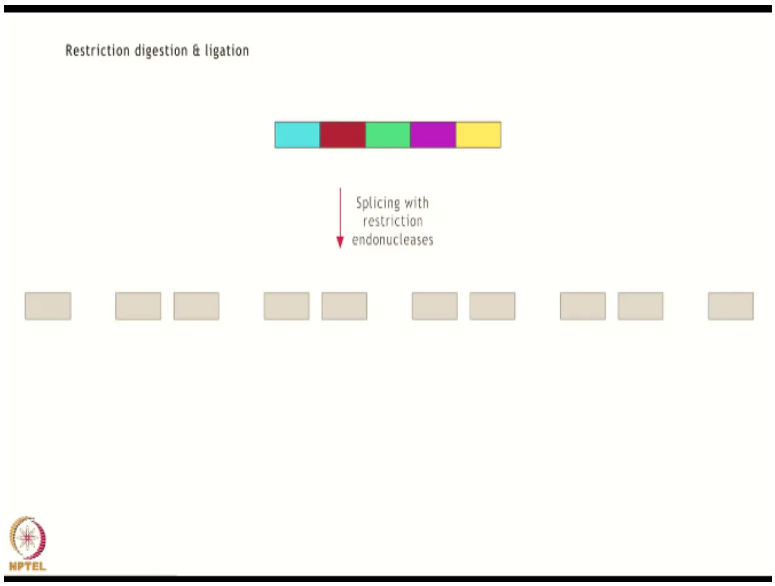

Genomic DNA and DNA of the vector molecule are cleaved with the same restriction enzyme. So as to generate complementary and sequences.

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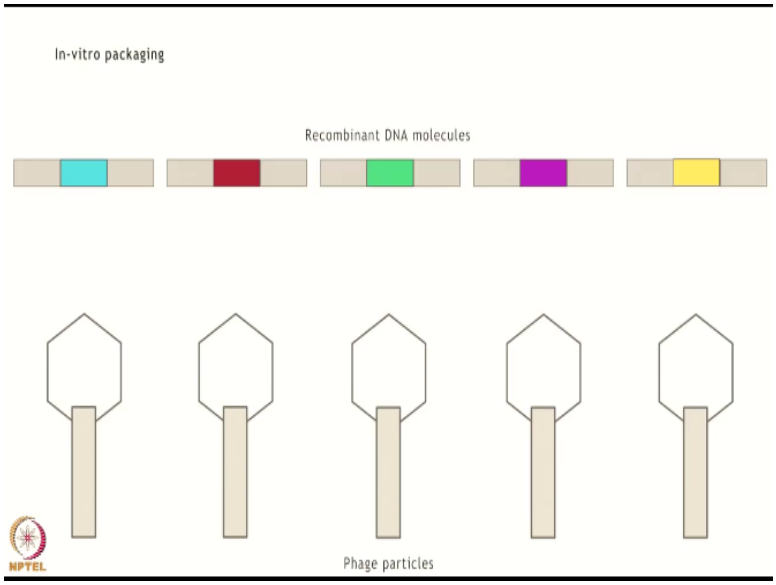

These are then ligated by means of the enzyme DNA ligase to generate recombinant DNA molecules. These recombinant molecules can be packaged in-vitro into a suitable phage particles which serve as useful vectors to carry the foreign DNA molecules.

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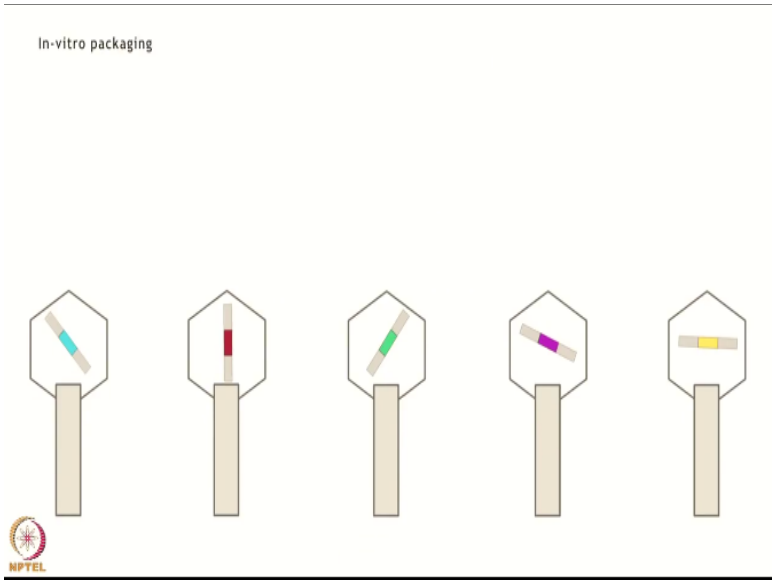

Lambda and M13 are 2 of the most commonly used phage particles for this purpose. DNA inserts up to 10 kilo bases can be inserted into these phage particles.

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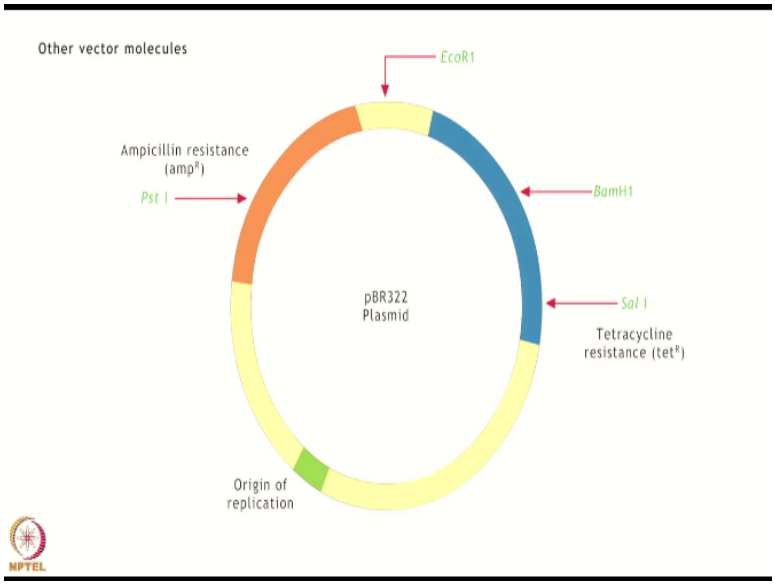

There are other vector molecules that can take up DNA fragments from genomic DNA, plasmids possessed sites for various restriction enzymes as well as antibiotic resistance sites which help for screening purposes. Certain plasmids like pBR322 can only take up smaller DNA inserts up to nearly 10 KB.

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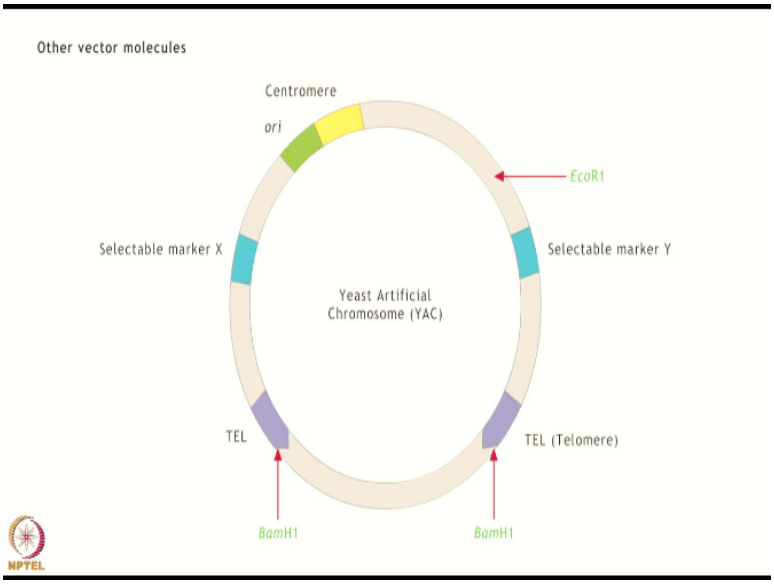

While larger plasmids known as bacterial artificial chromosomes can take up larger inserts up to 300 KB. The yeast artificial chromosome is a eukaryotic vector that can take up large DNA inserts and consists of restriction sites centromere and two telomeric sites.

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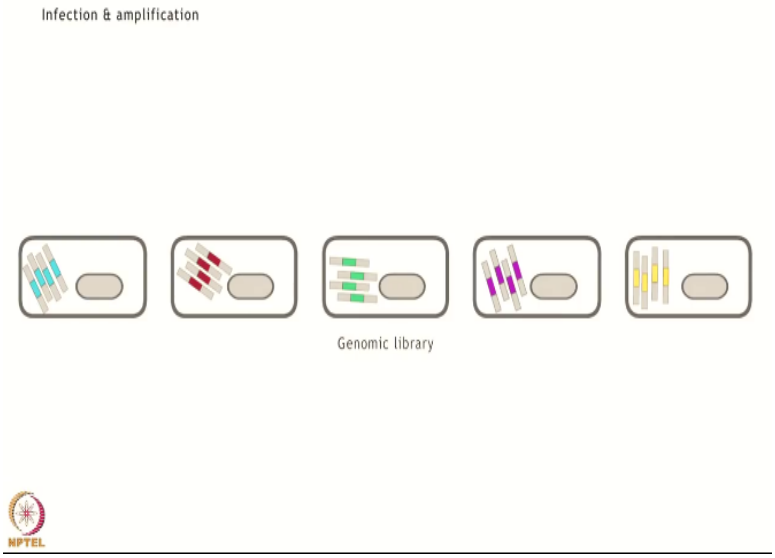

The phage molecules carrying the recombinant DNA with genomic inserts are used to infect E. coli cells. These molecules then get amplified with each round of replication of the E. coli cell. This collection of bacterial cells harboring the various genomic DNA fragments is known as a genomic library.

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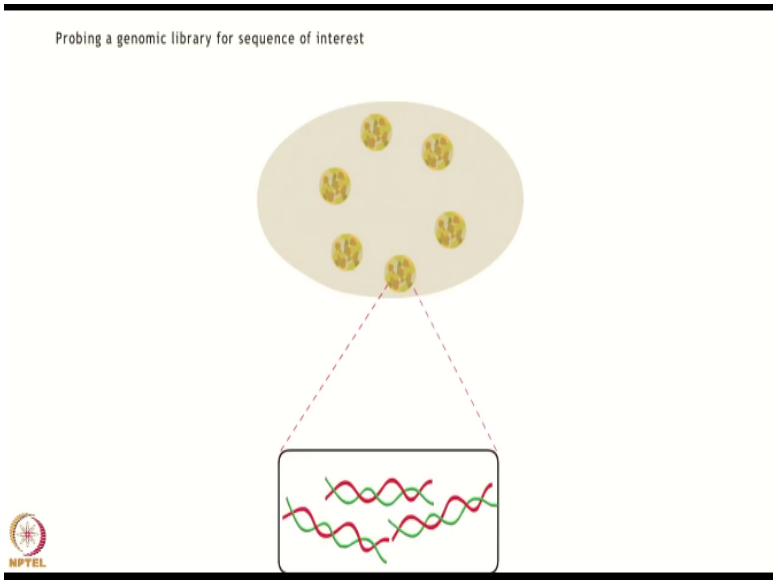

Once the library has been created, it is essential to have techniques to retrieve a sequence of interest. The transformed cells are selected and plated on agar after which the plate is plotted on to a nitrocellulose paper.

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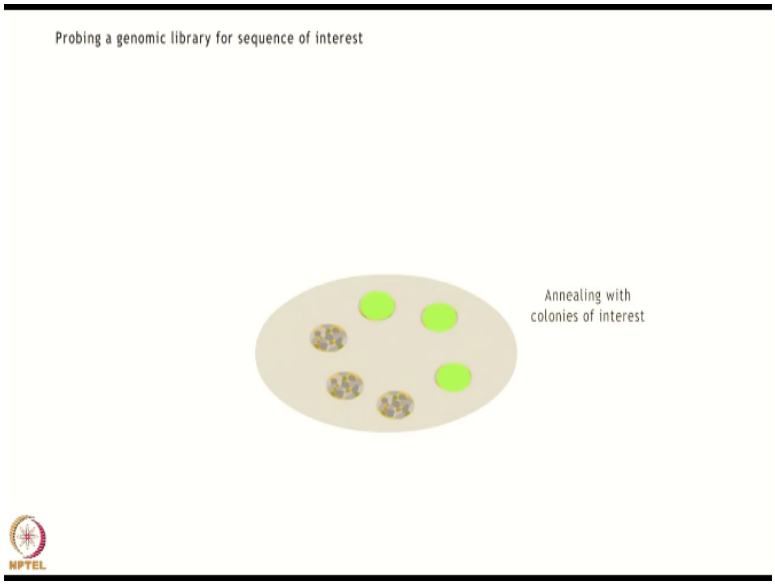

This is then treated with alkali bringing about disruption of the cells and the denaturation of the dsDNA. The denatured DNA is then probed for the sequence of interest by a radiolabeled molecule having a complimentary sequence.

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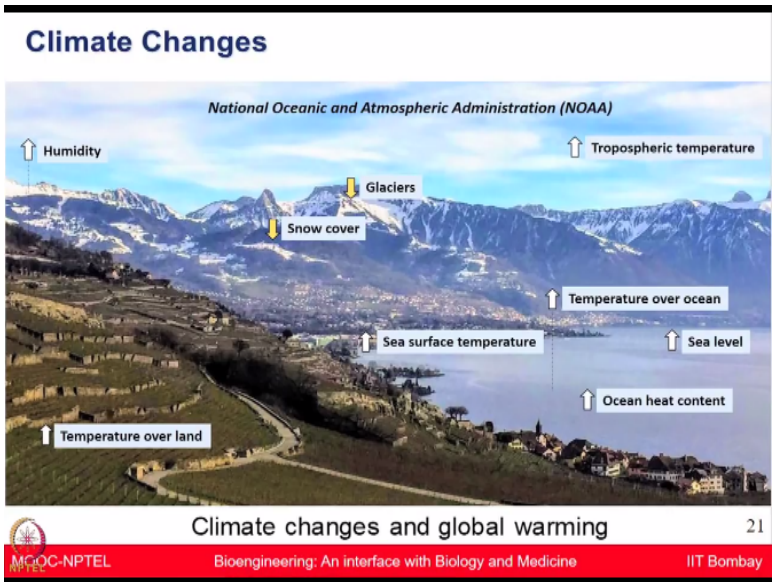

Let us move on to another major issue which is the climate change and global warming as shown in this particular beautiful image here that entire environment, entire climate is getting changed and lot of global issues which we can start seeing now for example you can see untimely rain sometime you know very high temperature.

And if you can follow on this image for the global warming the humidity is increasing, the temperature over land is increasing, then tropospheric temperature is also increasing, temperature over ocean is increasing, ocean heat contents are increasing and then as a result lot of you know things are getting melted like the glaciers, snow cover, those are getting melted and therefore the sea levels are getting high, getting rise further.

So these are overall climate changes and global problem which are going to affect us tremendously and again we have to think together how biologists and engineers especially the bioengineers could actually try to bridge this gap and address these global problems. Next problem let us think about how to treat deadly diseases.

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I have shown you couple of examples here. Some of the disease which is still you know post lot of challenge in front of us, in front of scientist for example tuberculosis, AIDS and cancer. These are still major problems which are affecting the entire population, entire humanity equally in the whole world.

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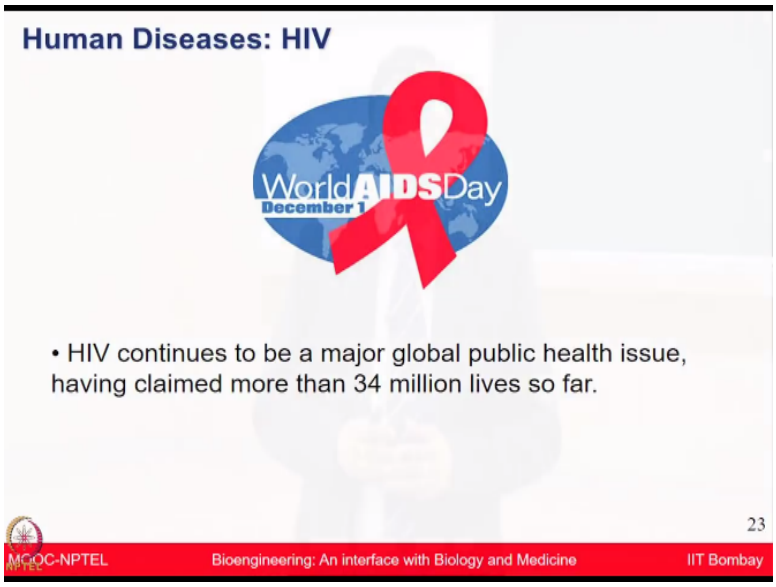

For example, HIV, human immunodeficiency viruses, it continues to be a major global public health issue having claimed more than 34 million lives so far. Millions of people have died from the HIV related causes globally. We have made some progress but still we have not solved this problem completely.

On other hand, tuberculosis which is the second most deadly disease due to a single infectious agent Mycobacterium tuberculosis is causing almost 95% of death in low and

middle-income countries because of the tuberculosis and more recently there are rise of the drug-resistant tuberculosis screens which are creating more and more challenges in front of us, how to control these deadly diseases.

And of course it comes the most challenging problem in front of us which is cancer. It is a global problem; whole population whole world is getting affected because of cancer but let us look at what is situation in India right now.

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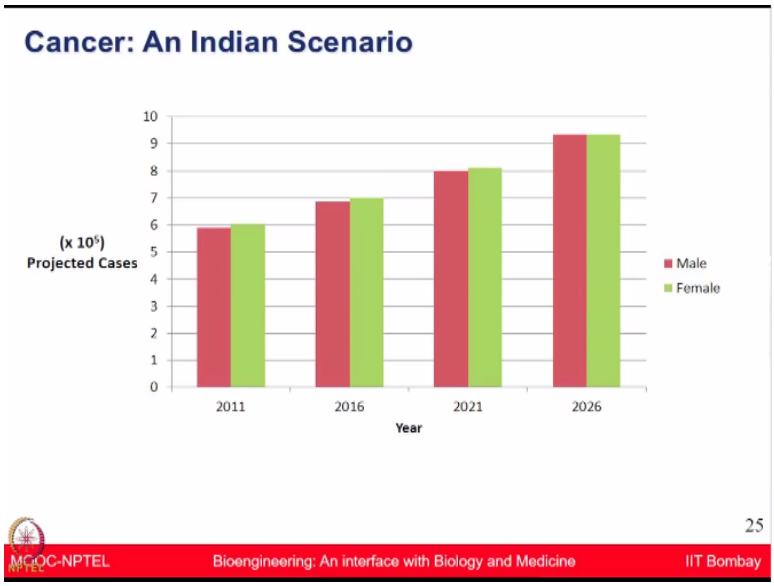

If you look at this graph from 2011 to 2026, the projected cases on the y-axis shown to you is keeping going to keep rising both in male and female population equally.

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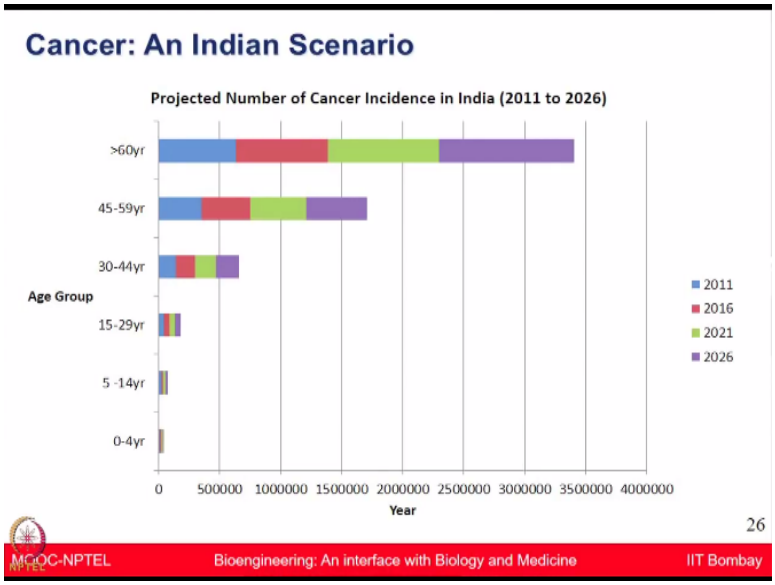

Let us look then this graph now, the projected number of cancer incidences in India in various type of age groups for example if you look at even age group of 15 to 29 the very young age group or 30 to 44 years and as you know the we are getting aged and old 45 to 59 years and more than 60 years, the cancer is going to be on rise in all of these population in all of these age groups and that is going to really affect all of us in some other way.

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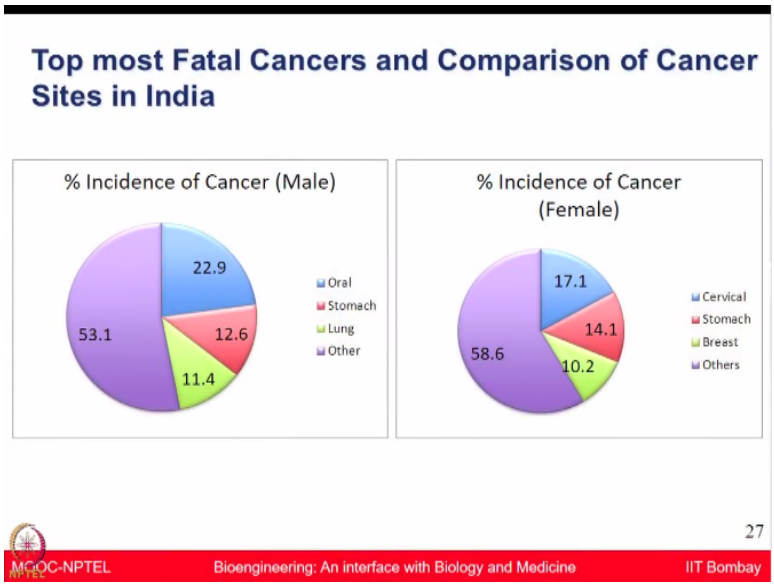

What are the top most fatal cancers and different you know comparison of the cancer sites in India? First let us look at the male data which is % of incidence of cancer in male. On rise in India we have essentially oral cancer, stomach cancer, lung cancer and of course all other cancers are you know constituting almost 53% or so. In female population, we have high incidence of cervical cancer, stomach cancer, breast cancer and other cancers are almost 58%.

What is interesting that you know one would observe that there is geographical prevalence of cancers in India.

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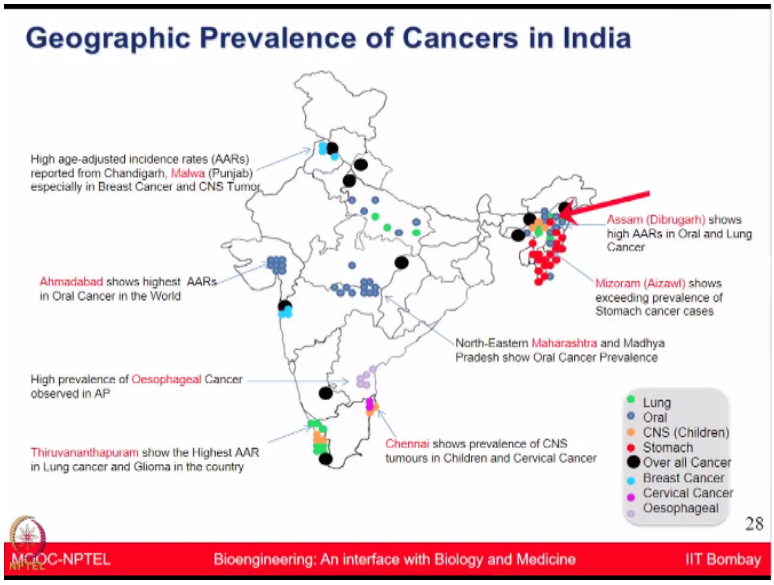

For example, especially you know in specific states in India are showing you know higher prevalence of certain tumor type which is you know if you look at the Punjab population especially the Malabar region, there is you know lot of cases of cancer on the rise and more specifically on the breast cancer and CNS tumors people can see on rise. Ahmedabad, they show high cancer incidence rate in the overall cancer.

Now if you come to Andhra Pradesh there is a high prevalence of oesophageal cancer observed in Andhra Pradesh. Thiruvananthapuram, it shows very high incidence for the lung cancer and glioma and now you come to Chennai, it shows high prevalence of CNS tumors in children and cervical cancer. The North-Eastern Maharashtra and Madhya Pradesh they have high incidence for the oral cancer.

Mizoram or the Aizawl of Northeast shows very high prevalence of stomach cancers. Assam or Dibrugarh shows high incidence raised in oral and lung cancer. So what when you observe here that you know there are specific regions which shows you know somehow very high incidence rate for a specific type of tumor and you know you can see some of the news clip here.

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For example, Malwa zone of Punjab sitting on cancer volcano, a survey in Times of India showed that. Stomach cancer incidence are set to rise; experts are concerned about it.

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Aizawl has highest incidence of stomach cancer after Japan.

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Oral cancer doubles in Ahmedabad in two decades.

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Is Kerala cancer's own country?

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Stats reveal oesophageal cancer common among Northeast women. So I am sure after giving you these scary examples of HIV, tuberculosis and cancer now let us think about other major aspects which we all want to see for the essential requirements of life. So what do we need for you know a good quality of life? We want clean air right, the clean air which is pollution free and to do that a lot of microorganism testing happens.

Just imagine recently you know we had a match in Delhi between cricket match you are all fan of the cricket match between India and Sri Lanka and on the field there was so much smog on one of these days because of pollution in Delhi that you know the Sri Lankan players opted out not to play that day and that actually you know showed that in which way you know different main metro cities have started encountering a high level of pollution.

We all need clean and adequate water. Because of drought conditions, because of low water rains water levels are getting low and many times when we are spraying the chemicals and fertilizers in the field, those also getting leached out in the water level. So water is getting polluted because of them. So we have to clean these before we provide people the clean and adequate water for drinking.

Let us think about food and nutritional security. It is not only food which is required, we also need the nutritional supplements and I think the latest you know initiated some government is that at least can we also look into the nutritional requirements for country and how to supplement that along with the basic food requirements. Those things are very crucial for us

and those are going to post challenges of how to increase both food as well as the nutritional supplements for the entire population.

Now let us think about the next major issue which is energy. Energy has been always the major challenge. All of these gadgets you know in this room for the what we are using, all of your devices, everything requires energy for its operation. Energy resources are very limited and I am sure you have you know you are aware that lot of you know the wars; lot of global issues happens because people want to occupy the limited energy resources.

And they want to use that and want to have more monopolies on them and therefore the price for the petrol and you know diesel, all of these energy resources are always on rise. We always have that fear that you know how are we going to replenish and going to maintain the energy requirements. So we have to start exploring some alternate resources of energy.

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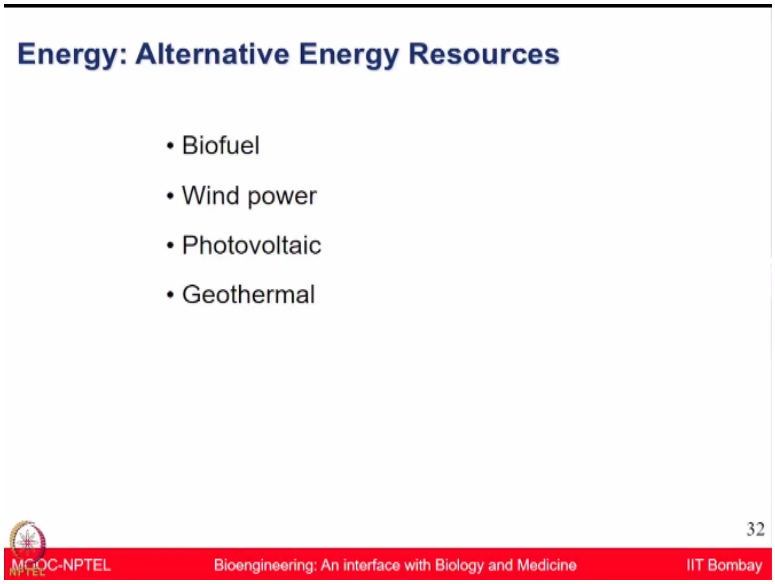

For example, with the biofuel, wind power, photovoltaic system or geothermal power could be used as the alternate energy resources which could be utilized to meet the global energy requirements. Again biotechnology how it can help?

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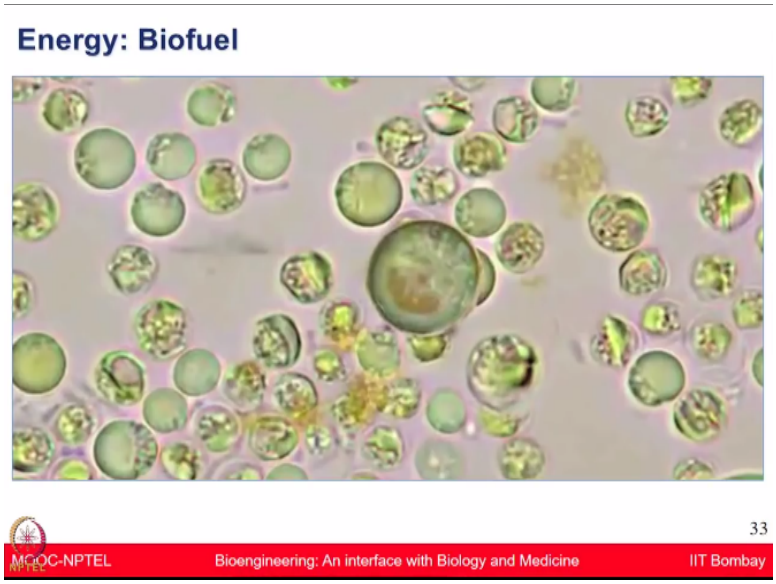

People have started exploring different strains of cyanobacteria and algae and looking at these microalgae which could produce these lipids which can give us the biofuel.

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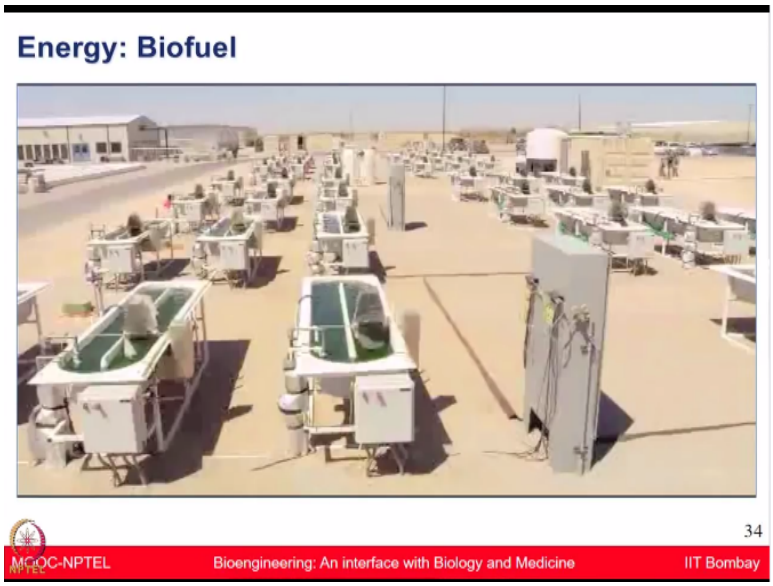

That can be very clean and you know a very efficient way of producing biofuels. Although, you know to produce at that mass level to produce that level which could provide sufficient energy requirements for large population is challenging and but the lot of research is actually happening how to harness the powers of these microalgae a kind of bacteria to utilize different alternate clean biofuel for the entire population.

So in general we have been discussing about different issues which are affecting the health and humanity and there is no boundary between engineers and doctors and biologists and the basic scientist. Everybody is going to affect equally from these problems whether we talk

about pollution, natural disasters, population explosion, climate changes, global warming whereas public health issues, deforestation, natural resource depletion, biodiversity loss, increase of the drug resistance in the bacteria, waste disposal system, deforestation etc.

So all of these are the major issues which are in front of us which again brings the question why this course and why we need to discuss all of these points.

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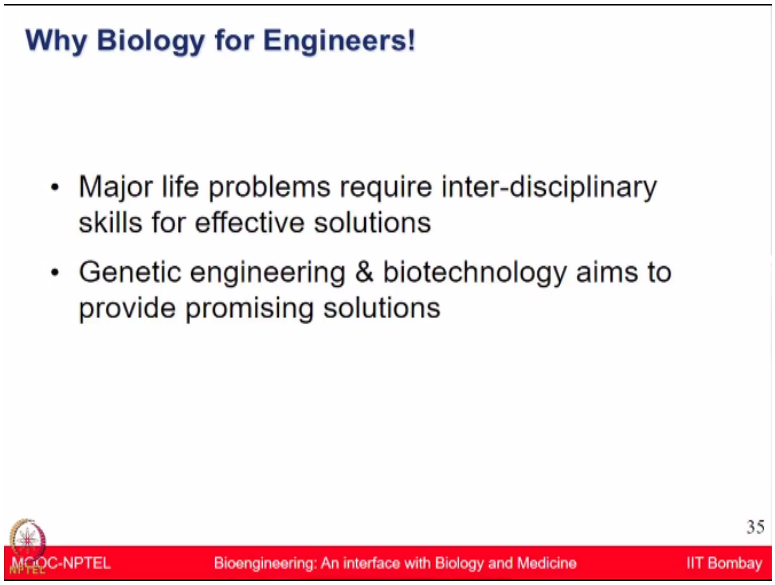

So major life problems, they require inter-disciplinary skills for effective solutions of these major problems. Genetic engineering and biotechnology aims to provide some of these promising solutions. Additionally, now we see there lot of healthcare devices are coming to the play where people want to use lot of apps and medical devices and biosensors simultaneously for the healthcare management.

And those again requires lot of understanding of health and the biological system and the engineering devices and how to make these kind of smart devices for healthcare solutions. So let us stop here. I am sure you know you are now aware that there are many issues which we have to tackle which we have to understand together. I am going to continue some of the other important points which are linked to this course in the continuing lecture in the next class. Thank you.

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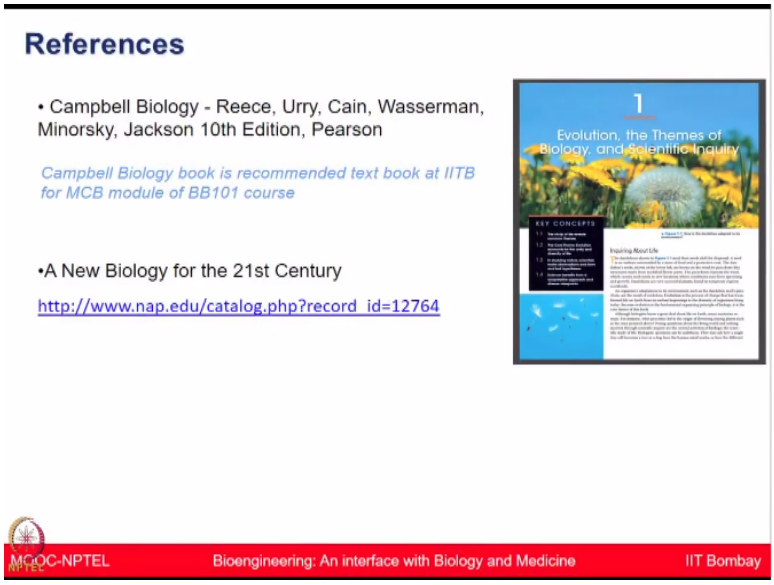

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