

BIO MODULE 6: GENETIC CHANGE

SYLLABUS SUMMARY

HOW DOES MUTATION INTRODUCE NEW ALLELES IN A POPULATION?

INQUIRY QUESTION



SYLLABUS POINT

- Explain how a range of mutagens operate;
 - Electromagnetic radiation sources
 - Chemicals
 - Naturally occurring mutagens

MUTAGENS

- Mutagens are environmental agents that modify the DNA sequence.
- DNA undergoes structural changes in base pairing as a result of **mutagenesis**. Resulting in mutations
 - Many mutagens are **carcinogenic** (cancer causing) as some mutations occur in genes that can regulate the cell cycle and thus play an important role in promoting or suppressing cell division.
 - Some carcinogenic mutagens can lead to increased cell division with no differentiation which results in masses of cells called tumours, responsible for cancer.
 - Main genes where mutations cause cancer: proto-oncogenes and tumour suppressor genes.

CHEMICAL MUTAGENS

- Mutagenic chemicals cause mutations in cells when exposed at high frequencies and for prolonged periods of time.
- These are usually structurally similar to bases in DNA and are often incorporated into DNA during replication -> mispairing results in production of non-functional protein, impairing cellular processes – Interfering with the cell cycle
 - Ingested chemicals -> alcohol, tobacco, chemicals in charred and fatty foods, food additives/preservatives (nitrates)
 - Environmental irritants/poisons -> organic solvents (benzene), asbestos, cleaning products, pesticides

NATURALLY OCCURING MUTAGENS

- Are present at normal levels in natural environment and the likelihood of such mutations increase with exposure and frequency
- Biological mutagens may trigger cancers from causing DNA damage and reducing the efficiency of DNA repair systems (releasing free radicals - oxygen species that cause oxidative stress)
 - **Non-biological** -> metals such as mercury, cadmium
 - **Biological**
 - Microbes -> viruses (hepatitis B, HIV), bacteria
 - Transposons -> sections of DNA that spontaneously fragment and relocate within the genome and can disrupt DNA sequencing and functioning when inserted into chromosomal DNA
 - End products of metabolism in fungi, animal or plant cells

PHYSICAL MUTAGENS

- Ionising radiation has enough energy to break chemical bonds in DNA and free electrons from atoms or molecules due to shorter wavelengths and higher energy frequencies
 - Electromagnetic radiation
 - UV radiation
 - Produces pyrimidine dimers where two adjacent T or C bases attach and prevent normal DNA replication
 - Direct impact – Removing an electron
 - Indirect impact – Formation of free radicals (H_2O and radiation)

SYLLABUS POINT

- Compare the causes, processes and effects of different types of mutation:
 - Point mutation
 - Chromosomal mutation

WHAT IS A MUTATION

WHAT IS A MUTATION?

Molecular level	A mutation is the change in the genetic material of a cell where the sequence of nucleotides in DNA is altered
Cellular level	Type of cell affected by mutation determines the extent of its influence (somatic or germline)
Individual	Mutations in certain genes can be translated into physical, behavioural, physiological or biochemical changes, affecting an organism's entire phenotype
Population	Mutations that are the direct source of new alleles – introduces variation. Natural selection can act upon these differences so that undesirable mutations are removed and desirable mutations remain

	POINT MUTATION: affects only a single gene (single gene mutation)	CHROMOSOMAL MUTATION: move blocks of genes to different parts of a chromosome or to another entirely
Causes	Can arise as a result of spontaneous or induced-mutagenic factors	Large-scale alterations to the structure of one or more chromosomes
Processes	<p>Single nucleotide variation</p> <p>Frameshift mutations</p> <p>Point mutation that involves the insertion or deletion of a single nucleotide</p>	<p>Deletion: section of DNA removed – reduction in number of genes</p> <p>Insertion: section of DNA is duplicated and inserted. Effects on phenotype is dependent on size of the duplicate, location on chromosome and number of repeats.</p> <p>Inversion: a piece of chromosome is removed, inverted and re-inserted so that the sequence is in reverse order</p> <p>Translocation: when a section of chromosome joins with another non-homologous chromosome leading to gene</p>

	POINT MUTATION	CHROMOSOMAL MUTATION
Effects on DNA	<p>Most result in a base line substitution – this may result in a different amino acid being inserted into a polypeptide during synthesis if the triplet does not code for the same acid as the original codon</p> <p>FM – the insertion or deletion of a base may shift the entire ‘reading frame’ of RNA if not a multiple of 3 (as codons are triplets), leading a non-functional protein</p>	<p>Overall structure of chromosome is changed or number of chromosomes in a cell is altered</p> <p>Change in chromosome number: Aneuploidy occurs when an organism has an abnormal amount of chromosomes - change in ploidy (down syndrome)</p>
Effects on phenotype	<p>Nonsense mutations: changes in amino acid to stop codon, cutting protein short</p> <p>Missense mutation: amino acid change (sickle cell anaemia)</p> <p>Silent mutations: when altered base codon triplet codes for the same amino acid, leading to no phenotypic change</p>	<p>Dependent on whether the mutation induced is neutral/silent, or potentially fatal (missense, nonsense)</p>

SYLLABUS POINT

- Distinguish between somatic mutations and germ-line mutations and their effect on an organism

SOMATIC AND GERMLINE MUTATIONS

SOMATIC MUTATIONS

- Occurs in somatic cells and arises as a result of spontaneous mutations not being corrected in G2 phase during DNA replication prior to mitosis
 - Can be passed onto daughter cells via mitosis
 - Usually caused by environmental factors (mutagens)

GERMLINE MUTATIONS

- Occurs in germline cells in the gonads with gametes produced
 - Cause can be internal or external

EFFECTS OF SOMATIC AND GERMLINE MUTATIONS

SOMATIC MUTATIONS

- **Localised effect** - development of a tumour in one part of an organism, but will NOT be inherited by offspring
- The earlier a mutation occurs, the greater the effect will be on an organism's phenotype as successive divisions of the cells by mitosis will induce spread of mutation with growth.
- As affected cell divides, a specific area of tissue with the mutation may develop, but the mutation will not alter composition of other cells, i.e. cancer.

~~GERMLINE~~ MUTATIONS

- Mutations in the genetic composition of a gamete WILL be passed down to an offspring which inherits the information.
- the mutation is replicated in every cell of the embryo as it divides and grows via mitosis, therefore affecting all cells in the child, i.e. sickle cell anaemia, cystic fibrosis, colour blindness.

SYLLABUS POINT

- Asses the significance of ‘coding’ and ‘noncoding’ DNA segments in the process of mutation

	Coding DNA - Exons	Non-coding DNA - Introns
Definition	DNA that codes for proteins	Does not code for proteins
Mutation in regions of DNA	<ul style="list-style-type: none"> - Directly affects the sequence and type of amino acids in a protein and therefore its function, which may lead to a phenotypic change - Eukaryotes – may affect gene splicing (excision of introns – non-coding nucleotides) 	<p>Gene Expression</p> <p>Despite there being no protein end-product, non-coding DNA contain regulatory sequences that promote 'switch on' or 'switch off' genes and code for products other than proteins such as rRNA and nuclear RNA, which have important functions in the process of gene expression.</p> <ul style="list-style-type: none"> - Small nuclear RNA determines which introns are spliced out of DNA - rRNA is the machinery that regulates translation of DNA
Asses its significance in process of mutation	<p>Mutations of genes in coding DNA become serious when proteins involved in DNA repair are affected. These enzymes are responsible for correcting errors in the sequence of bases, and if affected, will increase the chance and rate of mutations arising from errors in replication.</p> <p>Mutations in tumour suppressor genes can lead to cancer.</p>	<p>Embryotic development</p> <p>Research shows that such mutations in germline cells are link to developmental and congenital abnormalities (birth defects)</p> <p>Disease susceptibility</p> <p>Some mutations in regulatory DNA (enhancer, promoter, silencer) are associated with higher predisposition to non-infectious and infectious disease</p> <ul style="list-style-type: none"> - obesity, heart disease - non infectious <p>However, can hold evolutionary advantages:</p>

SYLLABUS POINT

- Investigate the causes of genetic variation relating to the process of fertilisation, meiosis and mutation

Genetic variability is crucial in populations as a minimal variation may create a static and unchanging population susceptible to extinction in the future by natural selection.

FERTILISATION	Recombination of genetic material <ul style="list-style-type: none">- Independent assortment as a result of genes occurring on separate chromosomes introduce new combinations of parental genes that increases variability- Further variation is induced when two random gametes fuse.
MEIOSIS	Variation during meiosis and fertilisation may arise as a result of mutation <ul style="list-style-type: none">- Replication errors - often a result in point mutations- Chromosomal errors - often result in chromosomal mutations<ul style="list-style-type: none">- Errors in crossing over can introduce chromosomal aberrations- Nondisjunction - chromosomes does not split into sister chromatids during nuclear division
MUTATION	Chromosomal changes can be brought about as a result of exposure to mutagens. Female gametes may remain in meiosis I for a long time, thus exposure to mutagens at any stage during reproductive life may be detrimental.

Increasing alleles

- A greater number of alleles for a particular trait introduces a new combination of genes in gametes produced by individuals

SYLLABUS POINT

- Evaluate the effect of mutation, gene flow and genetic drift on the gene pool of populations

EFFECT OF MUTATION ON THE GENE POOL OF POPULATIONS

- Formation of new alleles due to errors in DNA that arise during gametogenesis (meiosis)
- Very few mutated alleles are advantageous and selected to increase in frequency. This is because if an environment is stable and an abnormal phenotype is introduced into the population, it is highly likely that the mutation will not benefit the organism.
- **Deleterious mutations** are usually acted upon by natural selection and removed from the population.
- **Natural selection** is often considered ‘evolutionary back-up’ as they can provide variations that have no immediate effect but may provide a selective advantage into the future if sudden changes to the environment were to ensure.

EFFECT OF GENE FLOW ON THE GENE POOL OF A POPULATION

- Gene flow - change in allele frequency due to mixing of new alleles or loss of original alleles.
- Involves existing individuals leaving and new ones entering the population by *emigration* and *immigration*.
- This does not necessarily have to be of the same species.

EFFECT OF GENETIC DRIFT ON THE GENE POOL OF A POPULATION

- Genetic drift - change in allele frequency due to random chance which may not necessarily be beneficial to surviving alleles.
- The remaining individuals in a population may not be an accurate representation of the allele and genotype frequencies of the original
 - Bottleneck effect -> natural disasters
 - Founder Effect -> individuals become geographically isolated from original population

HOW DO GENETIC TECHNIQUES AFFECT EARTH'S BIODIVERSITY?

INQUIRY QUESTION

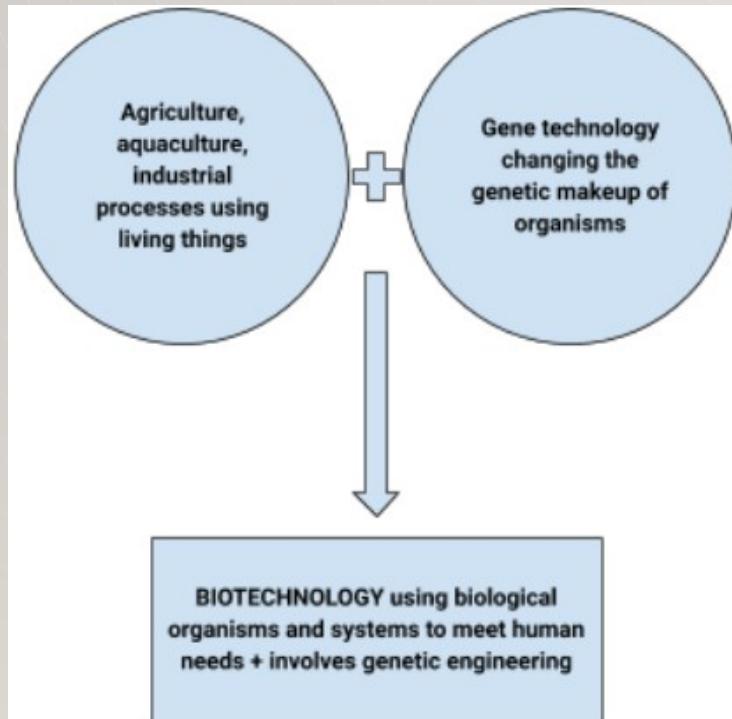


SYLLABUS POINT

- Investigate the uses and applications of biotechnology (past, present and future)

(next 4 syllabus points under this topic)

BIOTECHNOLOGY



- Biotechnology – manipulation of living systems and biological processes to develop tools and products that individuals can harness for human benefit. Involves the use of genetic techniques/engineering (methods, tools, skills) to study genetic phenomena and apply refined knowledge of biological processes to make efficient use of technologies.
- Biodiversity – the variety and variability within and between species and ecosystems
- Gene technology – manipulation of DNA where the end of products are precisely obtained
- Bioethics – ethical and moral implications of new biological discoveries and biomedical advances, particularly in genetic engineering and drug research. Study of the moral dimension of decision making in the treatment, improvement, prolongation and termination of biological systems.

SYLLABUS POINT

- Analyse the social implications and ethical uses of biotechnology, including plant and animal examples

SOCIAL IMPLICATIONS OF BIOTECHNOLOGY – POSITIVE

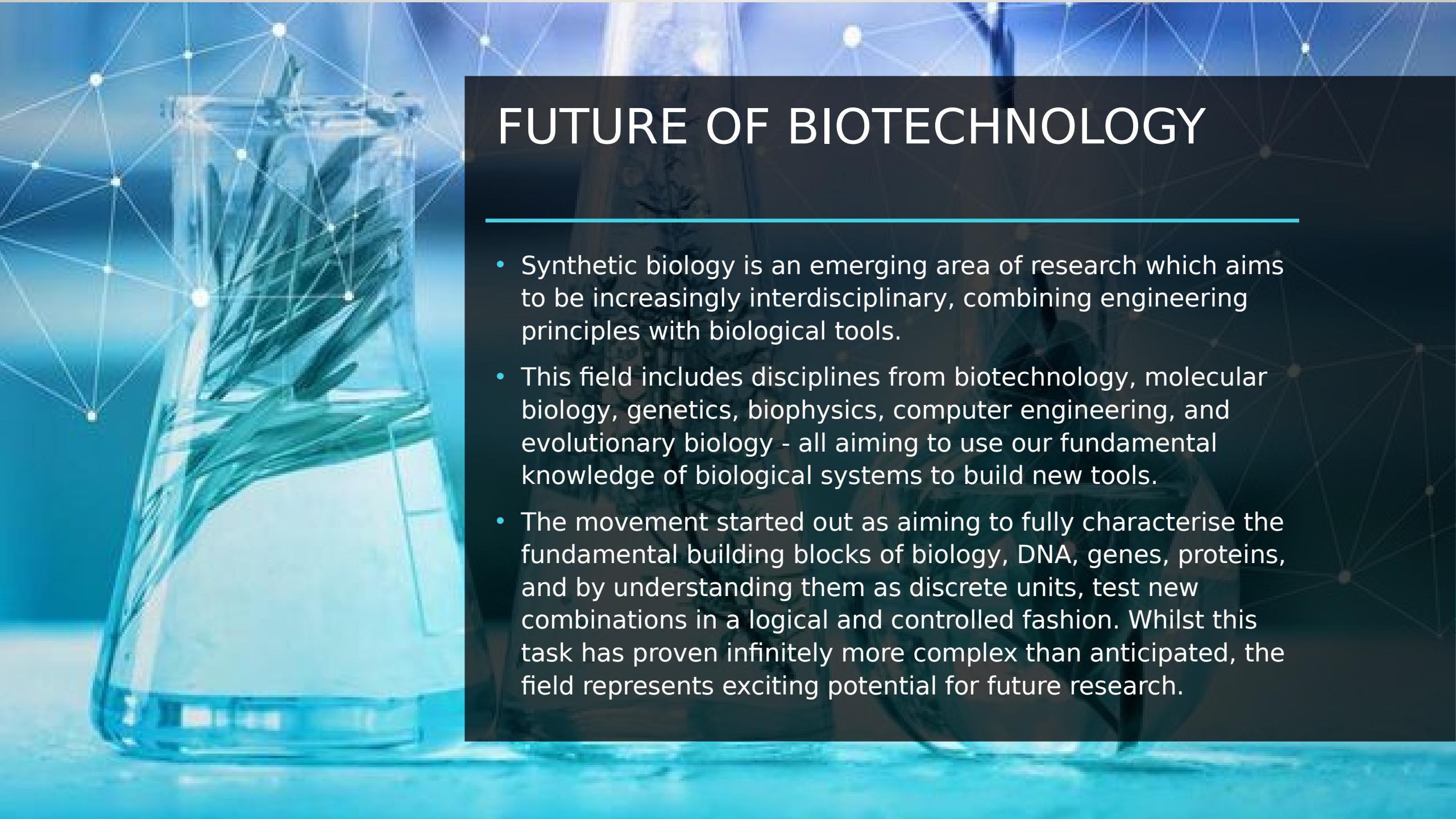
- Meets the growing needs of society
- Is decreasing poverty and hunger
- Working to improve health and wellbeing
- Providing access to clean water
- Produces clean energy
- Creating sustainable cities
- Genetic diversity – new arrangements of genes, increasing diversity of traits

SOCIAL IMPLICATIONS OF BIOTECHNOLOGY – NEGATIVE

- Potential for new information on humans to be exploited
- Intellectual property; can you claim rights to a gene?
 - In Australia, genetic information is not patentable, but there may be an issue in the future
- Monopolies: large and powerful companies can dominate the biotech market
 - This can see an increase in prices, biotech becomes less accessible to poorer countries
- Consumer rights: right to know if your product has been GM
- Regulations: legislations need to be put in place so the government can ensure safe control of biotechnology.
 - This may see backlash from biohackers
- Biohacking: is a do-it-yourself citizen science merging body modifications with technology
 - The motivation of biohackers includes cybernetic exploration, personal data acquisition, and advocating privacy rights and open-source medicine

SYLLABUS POINT

- Researching future directions of the use of biotechnology



FUTURE OF BIOTECHNOLOGY

- Synthetic biology is an emerging area of research which aims to be increasingly interdisciplinary, combining engineering principles with biological tools.
- This field includes disciplines from biotechnology, molecular biology, genetics, biophysics, computer engineering, and evolutionary biology - all aiming to use our fundamental knowledge of biological systems to build new tools.
- The movement started out as aiming to fully characterise the fundamental building blocks of biology, DNA, genes, proteins, and by understanding them as discrete units, test new combinations in a logical and controlled fashion. Whilst this task has proven infinitely more complex than anticipated, the field represents exciting potential for future research.

FUTURE OF BIOTECHNOLOGY

- Progress in synthetic biology has been helped by the establishment of international research competitions, such as iGEM (International genetically engineered machines) and BIOMED.
- These competitions capitalise upon the vast creative energy of researchers at the University level, and directed them towards developing technologies and techniques to address world issues.
- Future biotechnology opportunities in the medicinal area include a breakthrough in drugs that will lead to a world without cancer, or AIDS or Alzheimer's.
- Industrial biotech is helping to fight global warming as an alternative and safer form of global energy instead of diminishing and volatile fossil fuels.



SYLLABUS POINT

- Evaluating the potential benefits for society of research using genetic technologies

BENEFITS OF BIOTECHNOLOGY: MEDICAL FIELD

- Pharmaceuticals:
 - Vaccines - Using understanding of how human immune system response to invasion by foreign materials such as viruses, we can develop molecules to strengthen this response preemptively
 - Antibiotics - Developments have allowed scientists to specifically identify important systems for bacterial cell growth and repair. We are now able to synthetically design molecules (drugs) which specifically target certain proteins in bacteria, inhibiting their function.
- Stem cell treatments - Development of therapeutic cloning has allowed scientists to harness stem cells to create skin graft and treat certain cancers and autoimmune diseases.

BENEFITS OF BIOTECHNOLOGY: ENVIRONMENTAL FIELD

- Bioremediation – With our increased understanding of microorganisms and their abilities and roles in different ecosystems, scientists have developed techniques to clean up pollution. Bacteria able to metabolise pollutants may be augmented or introduced to polluted site. Significantly, bacteria have recently been engineered with the capability to degrade plastics.
- Agriculture – Techniques of transgenesis have been used to produce genetically modified crops, improving the plants ability to survive and increasing the nutritional value and crop yield. A higher crop yield is essential with the globes increasing population.

BENEFITS OF BIOTECHNOLOGY: INDUSTRIAL

- Biodegradable plastics – Creation of biopolymers derived from plant and bacterial systems have helped to address issues of pollution, as well as improve living systems due to their increased biocompatibility
- Energy sources
 - Biofuels – Technologies have been developed to extract fuel from biomass rather than petroleum, and to investigate potential for organisms such as bacteria to produce fuels in order to meet increasing demand
 - Photosynthesis – Scientists have been investigating the potential of exploiting the natural process of photosynthesis, which turns light energy into chemical energy, for the production of energy (using photosynthetic bacteria like a biological solar cell)

SYLLABUS POINT

- Evaluating the changes to Earth's biodiversity due to genetic techniques

CHANGES TO EARTH'S BIODIVERSITY DUE TO GENETIC TECHNIQUES

- Biotechnology has the potential to make irreversible changes to entire species, but the effect it has - positive or negative - is based on what people do with the technology. Humans have been using tools to influence biology and genetics for centuries (selective breeding) and we have created new species by influencing the emergence of traits which we have found desirable. However, with the rise of genetic technologies, we have the potential to implement changes at a more rapid rate.

CHANGES TO EARTH'S BIODIVERSITY DUE TO GENETIC TECHNIQUES

- **Creation of monocultures** – as the benefits of particular traits on an organism are observed, it is important that we do not rely so heavily on these favourable genes so as to wipe competitive alleles from species gene pools (Irish potato famine). The use of heritage breeds of crops and livestock are being promoted for the preservation of genetic variation in agriculture. (Berkshire pigs and heirloom tomatoes)
- **Horizontal gene transfer** – refers to the potential benefit transgenic organisms would have if released into the wild, posing competition to other naturally occurring alleles; ultimately leading to a biodiversity reduction
- Although we also have the potential to increase biodiversity, recombinant technologies allow us to transplant genes across species - introducing completely new traits, expanding the biodiversity

CHANGES TO THE EARTH'S BIODIVERSITY DUE TO GENETIC TECHNIQUE

- Biotechnology can also cause the loss of characteristics of wild species, i.e. domestic pigs do not have hair like wild boars have - wild boars have a wide genetic diversity while domestic pigs have been bred to be very similar (to produce the best meat).
- A loss of biodiversity can also occur due to non-target effects of GM plants on beneficial organisms (bees, moths, beetles). GM crops have also been known to affect soil ecosystems (nitrogen and carbon levels, decomposition rates ect.).

DOES ARTIFICIAL MANIPULATION OF DNA HAVE THE POTENTIAL TO CHANGE POPULATIONS FOREVER?

INQUIRY QUESTION



SYLLABUS POINT

- Investigate the use and advantage of current genetic technologies that include genetic change

Technology	Process	Advantages	Disadvantage
Selective breeding	Process whereby humans are able to control which males and females are bred and produce offspring with desirable traits. Both parent individuals are different varieties of the same species so that the resultant offspring is fertile.	<ul style="list-style-type: none"> - Hybrid vigour - healthier offspring with enhanced characteristics from parents - Allows farmers to improve the quality and longevity of livestock and reap the benefits of products derived from these animals 	<ul style="list-style-type: none"> - Hybridisation can potentially mix undesirable genes with desirable traits, producing harmful or unprecedented phenotypes - Time-consuming and costly - no guarantee for success of mating, requires transportation of whole animals, risk of injury while mating
IVF	Egg is fertilised outside of the female and in a petri dish. Resulting zygotes are cultured until they have progressed to an early stage of development. The cultured embryo is inserted using a catheter into the uterus of the biological mother.	<ul style="list-style-type: none"> - Favoured when there is decreased fertility in one or both parents - Can increase biodiversity in the short-term by introducing new alleles - Allows for genetic screening of embryos to avoid disease and birth defects 	<ul style="list-style-type: none"> - Reduction in genetic diversity if large numbers of viable embryos are produced from a small selection of parents - Can potentially introduce infertility into a population - Favourable traits may outcompete competitive alleles and eliminate or reduce the frequency of important genes (disease resistance)

Technology	Processes	Advantages	Disadvantages
Gene therapy	<p>The correction of genetic disorders by introducing normal functioning genes into cells</p> <ul style="list-style-type: none"> - Gene augmentation therapy – inserted genes are linked to cell function - Gene inhibition therapy – insertion of a ‘blocking’ gene to render another dysfunctional - Somatic/germline gene therapy – editing cells that have descended from the ameliorated cell/gamete 	<p>Allows for the treatment of diseases such as cystic fibrosis</p> <ul style="list-style-type: none"> - Drives research to treat other diseases e.g. Alzheimer’s disease - Can make lasting changes to an individual’s health, rather than mitigating symptoms 	<ul style="list-style-type: none"> - The way it is being delivered poses risks to the patient’s immune response - Viruses as vectors can cause organ failure and interfere with immunity - Reversion of virus once it is introduced into the body - If the new gene is wrongly inserted, it can cause harmful mutations in DNA - Expensive – possibly not covered by insurance
ELISA (Enzyme-Linked Immunosorbent Assay)	ELISA is an analytical bio-chem tool used to detect the presence of antigens/antibodies in a liquid sample	<ul style="list-style-type: none"> - Allows for the diagnosis of disease - Useful in forensic epidemiology studies 	<ul style="list-style-type: none"> - Micro-titre plates used in ELISA cannot be reused as the antibodies that bind