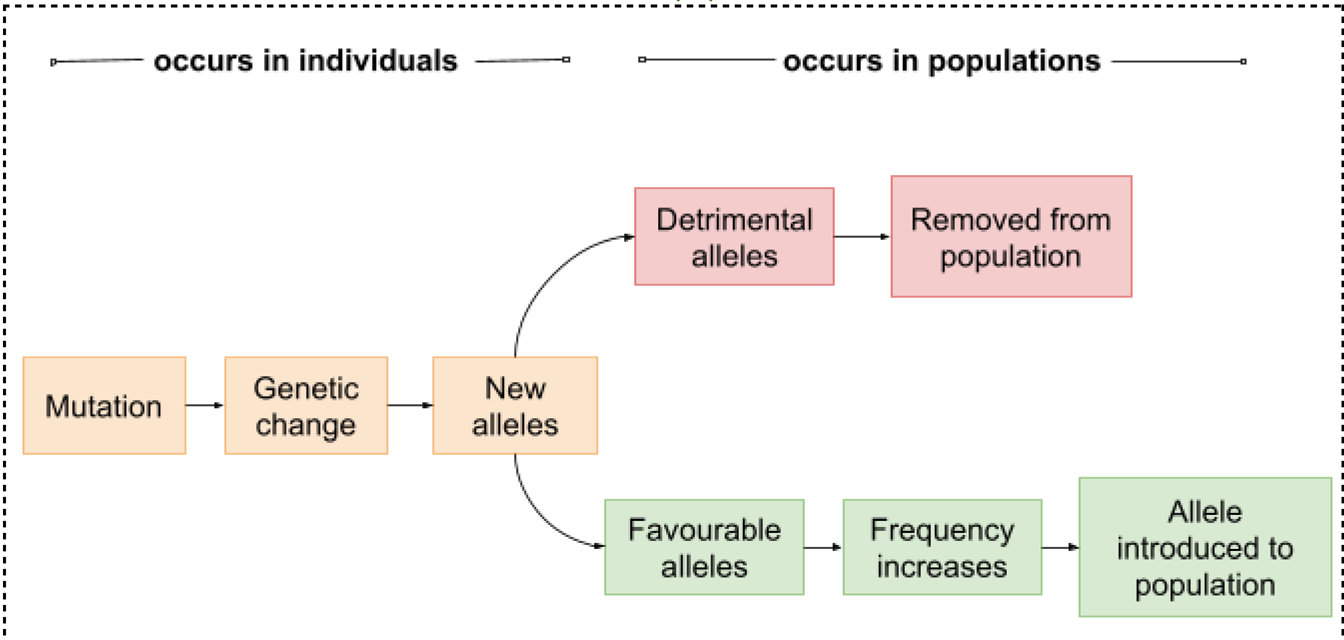
Module 6: Genetic Change

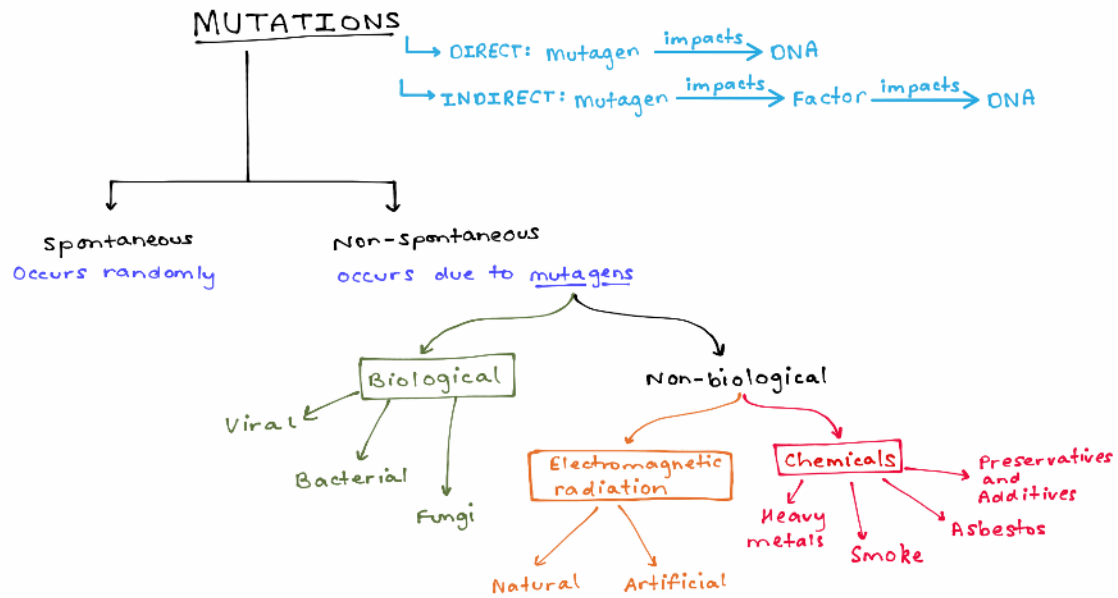
6.1: Mutation

How does mutation introduce new alleles into a population?



[6.1.1] Mutations and Mutagens

MUTAGENS: Agents which alter DNA and cause mutations.



Mutations occur in the synthesis (S) phase of the cell cycle.

ELECTROMAGNETIC RADIATION

Physical

Radiation : Any transfer of energy

Ionising radiation : Enough energy to damage molecules

Eg. X-rays
gamma rays

Direct impact

ionises DNA

- Breaks sugar-phosphate backbone
- Separates complimentary base pairs by breaking hydrogen bonds
- Covalent bonds form between adjacent pairs

Mutation

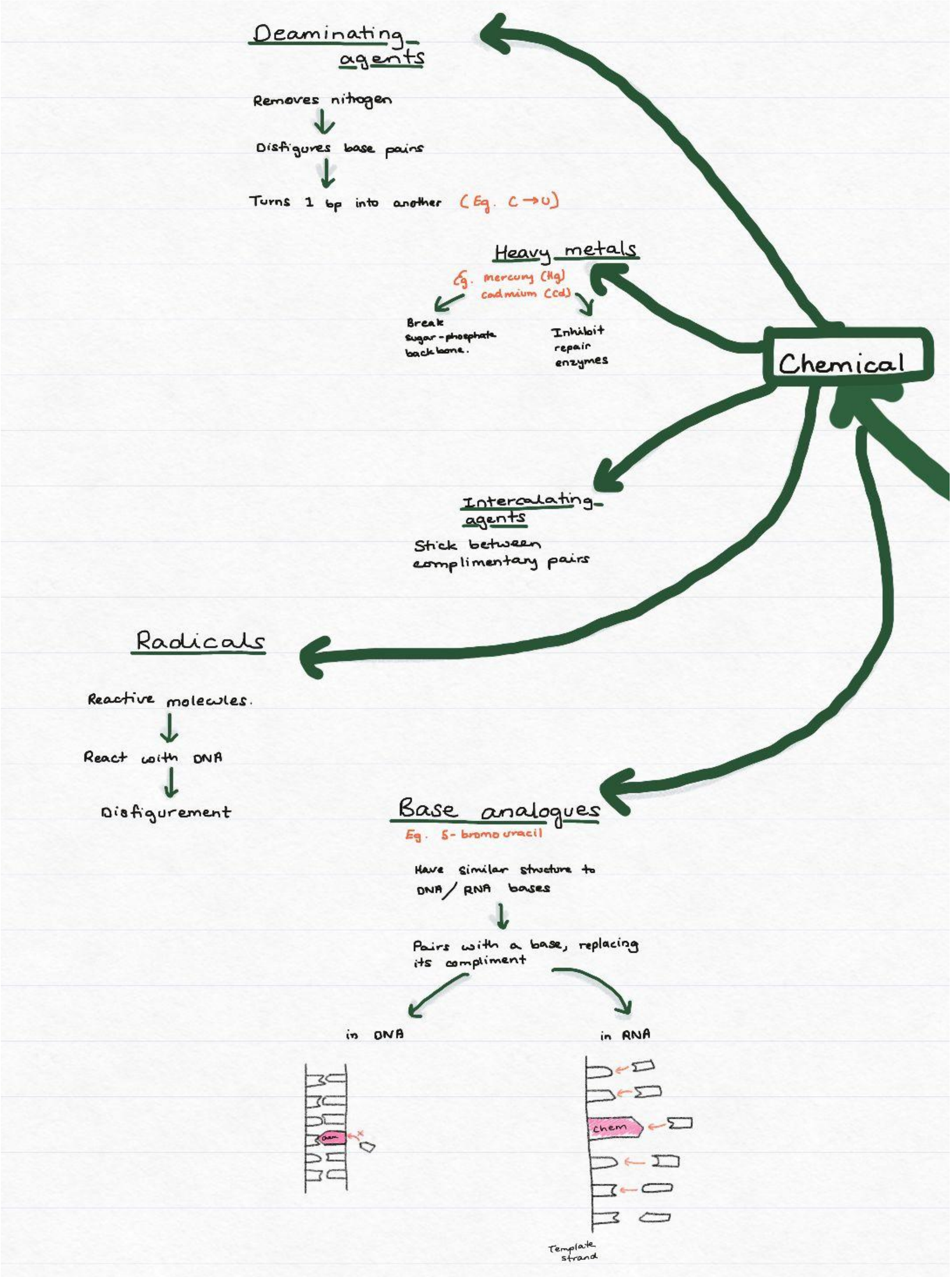
Indirect Impact

Removes electron from molecule

Creates a radical
→ charged
→ free
→ REACTIVE

- Produces toxic compounds
- Reacts with DNA

CHEMICAL MUTAGENS



If these mutagens can cause cancer, they are **carcinogenic**.

BIOLOGICAL MUTAGENS

Viruses

Infect the host cell and injects nucleic material.

↓

Uses host cell's replication mechanism to replicate itself

↓

Mutations occur during replication

↓

Virus-induced mutations

Eg. HIV virus causes AIDS.

HBV virus causes hepatitis-B.

Bacteria & Fungi

Release mycotoxins

↓

Trigger cell death

↓

Mitosis forced to replace

↓

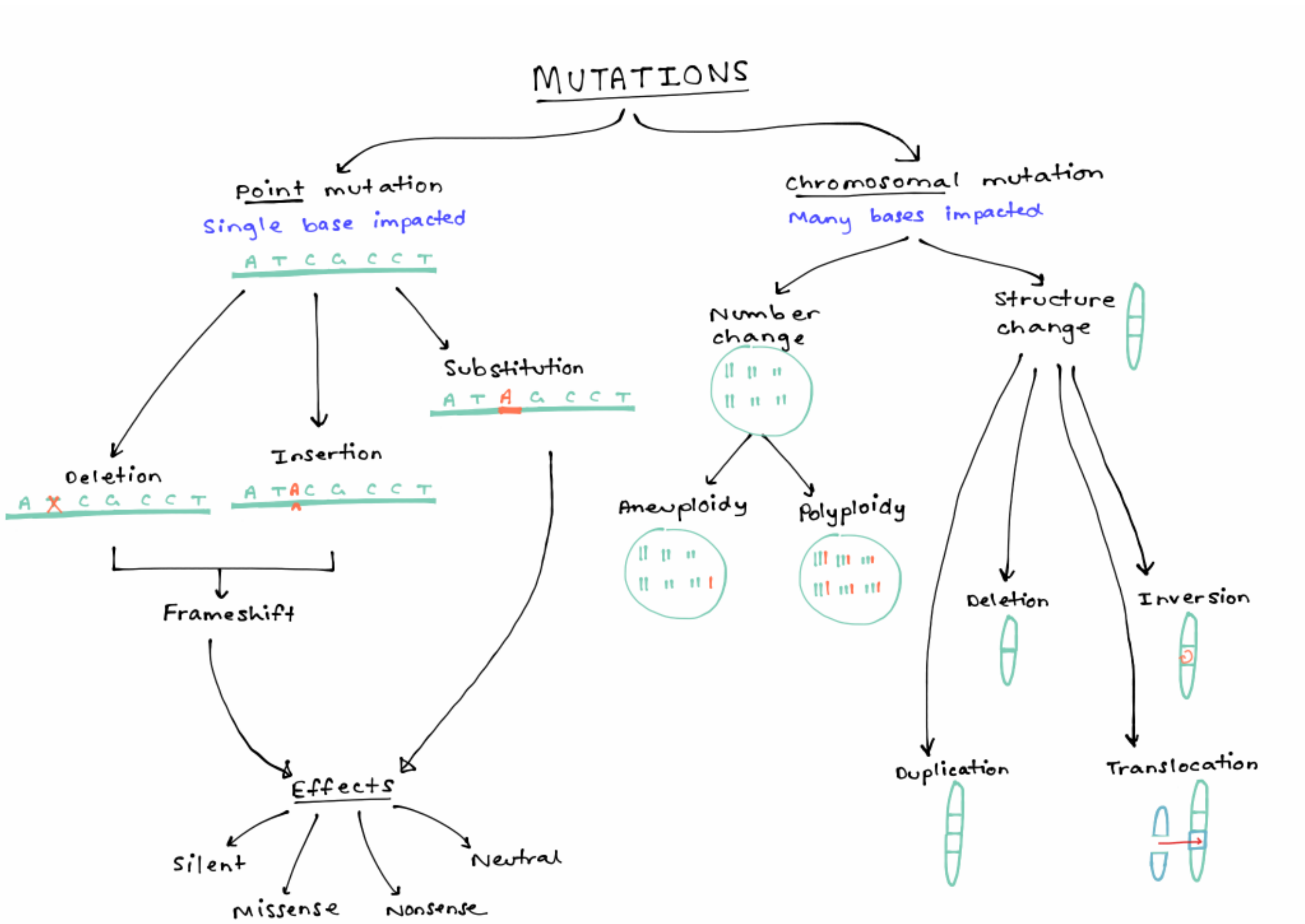
Increases opportunity for mutation

Eg. Helicobacter-pylori (bacteria) causes stomach inflammation/ cancer.

Aspergillus flavus (fungi) produces carcinogenic toxin which causes liver cancer.

[6.1.2] Types of mutations

OVERVIEW



gene → genotype → protein → trait

mutation → Altered gene → Altered genotype → **If not silent** → Altered protein → Altered trait

POINT MUTATIONS

Impact a single nucleotide, which may affect the expression of a specific gene.

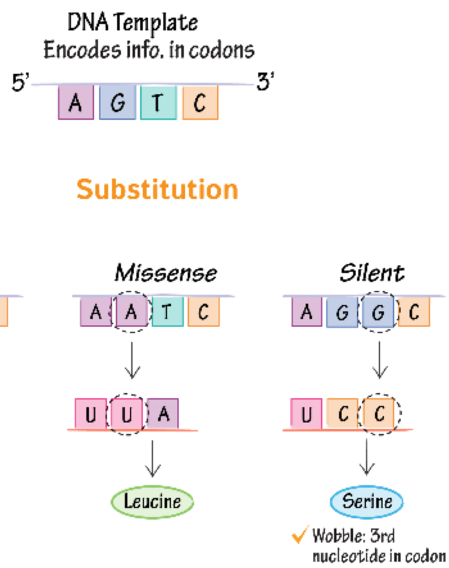
Types

- Deletion: Base pair removed
- Insertion: Base pair added
    - Start or middle = Frameshift
    - End = NOT frameshift

- Substitution: Base pair replaced

Effects

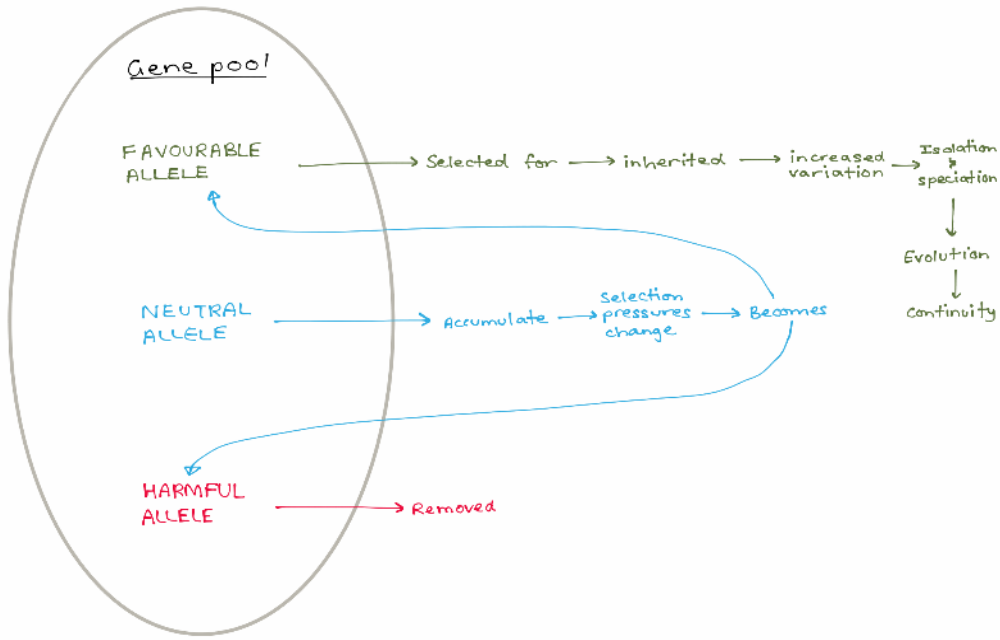
- Nonsense: Premature stop codon forms, shortening the chain
- Missense: One amino acid altered due to different codon
- Silent: No change, as the codons code for the same amino acid



A neutral mutation is any that does not significantly impact the final protein structure. (All silent are neutral, some neutral may also be missense).

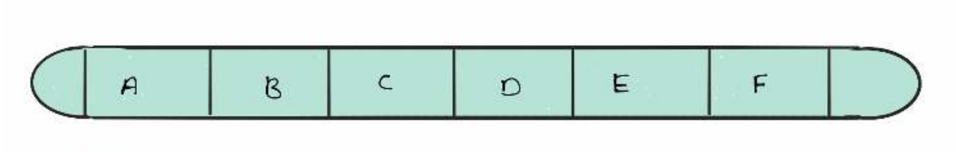
Population genetics

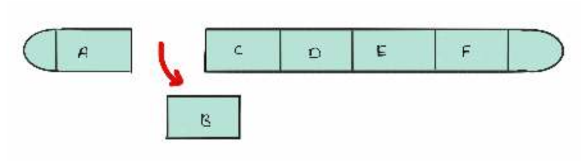
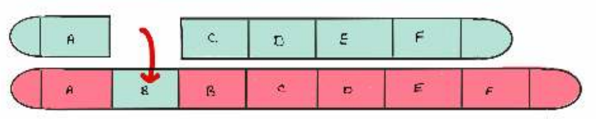
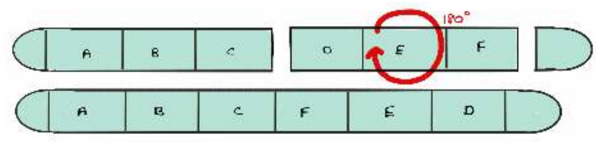
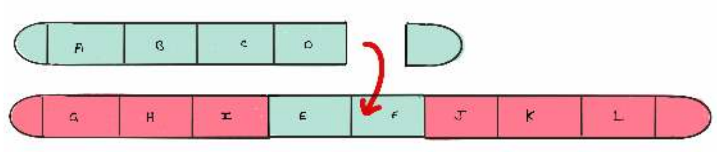
Mutations produce new alleles



CHROMOSOMAL MUTATIONS

Structural mutations



Deletion Segment of a chromosome is removed.	
Duplication Identical segment of chromosome 1 breaks off and attaches to chromosome 2, so that chromosome 2 has double the genetic information.	
Inversion A segment of a chromosome is rotated 180° and rejoined.	
Translocation (insertion) In homologous chromosomes, a segment of chromosome 1 breaks off and attaches to chromosome 2. Chromosomes no longer homologous.	

Deletion, duplication and translocation mutations can be **frameshift** if they are not on the end of a chromosome.

NUMBER MUTATIONS

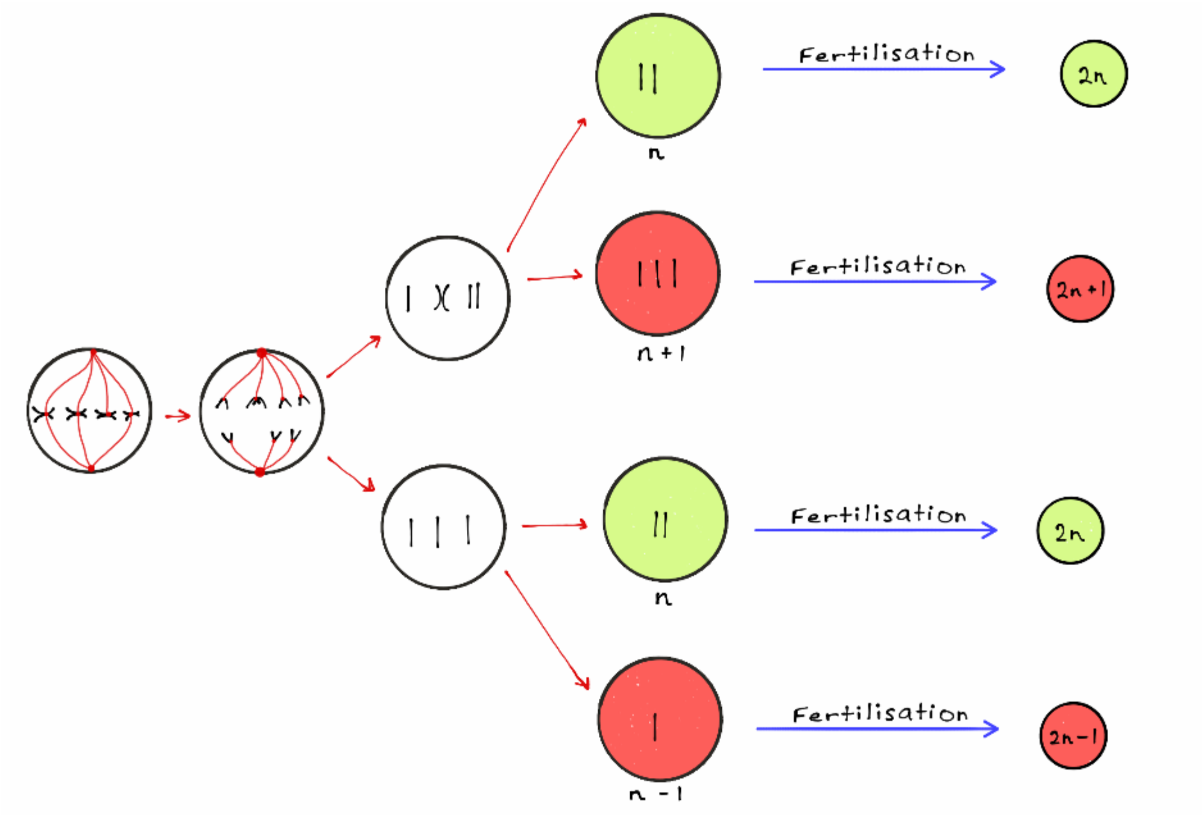
Aneuploidy
A pair of homologous gametes fail to split in metaphase II (nondisjunction)

↓

Creates:
- 2 gamete with *n* chromosomes
- 1 gamete with *n+1*
- 1 gamete with *n-1*

↓

When fertilised, this creates a zygote with one extra/ less chromosome in the genome
- Trisomy: 1 extra chromosome
- Monosomy: 1 less chromosome



Number Mutation (in humans)	Condition
Extra chromosome 21	Down’s syndrome
Extra X chromosome in females (XXX)	Triple-X syndrome
Extra X chromosome in males (XXY)	Klinefelter’s syndrome

Polyploidy

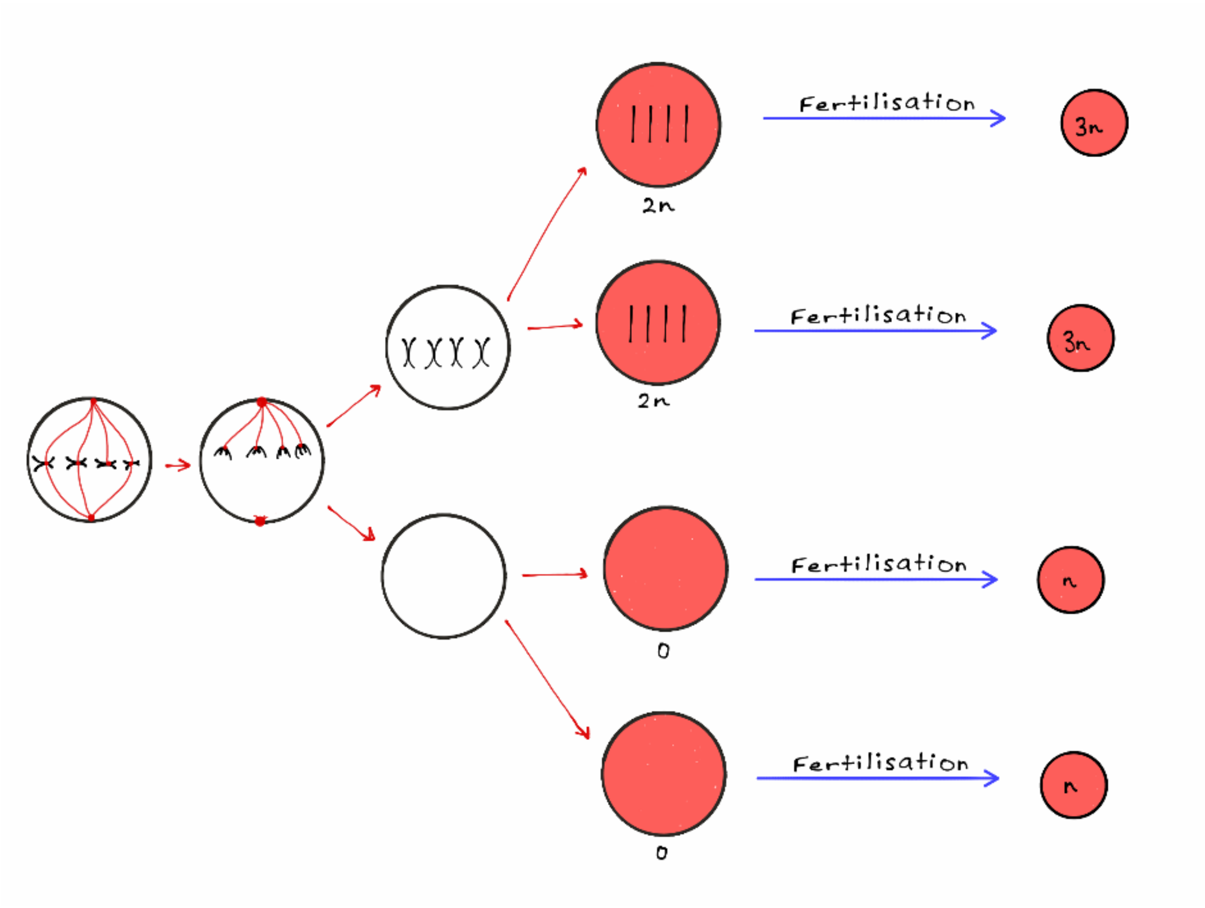
Reduction division fails to occur during anaphase I in meiosis.

↓

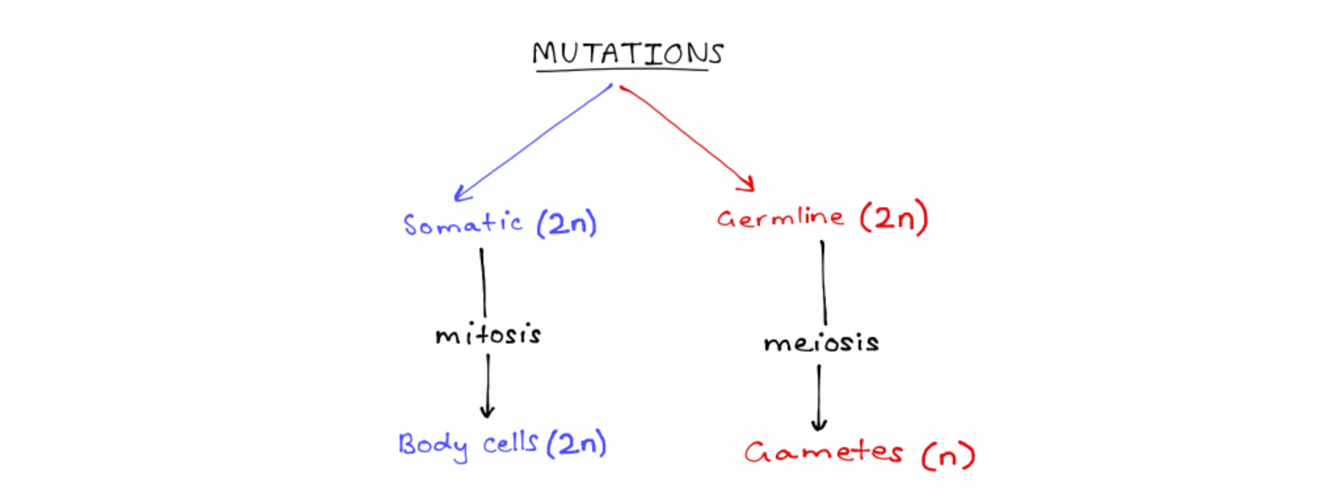
Creates a gamete with a full genome

↓

When this fertilises, creates a zygote with an extra chromosome per set



[6.1.3] Location of mutations



Since both cell types have the **same genome**, the **same mutations** can occur.

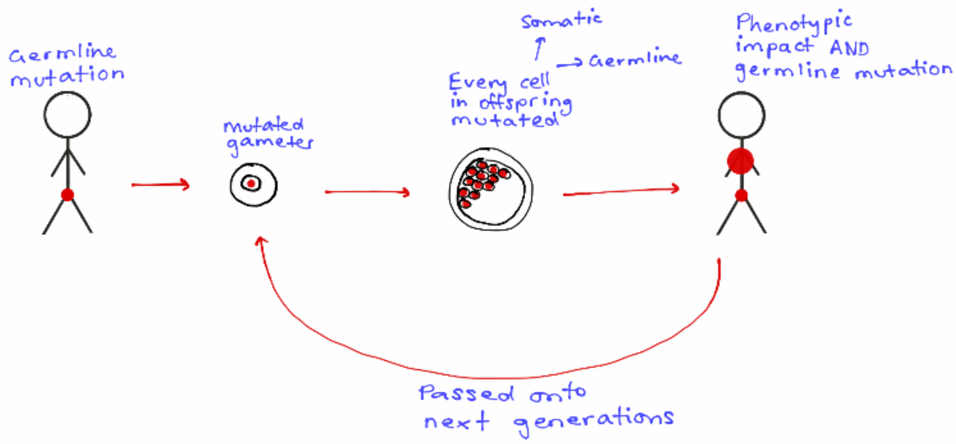
Mutation in somatic cell	→	Expressed in individual	→	No inheritance	→	Removed from gene pool after death
Mutation in germline cell	→	Not expressed in individual	→	Inheritance in every cell of the offspring (somatic AND germline)	→	Remains in gene pool unless offspring dies before reproductive maturity

Eg. BRCA gene mutations in women.

Mutations to the BRCA gene increase susceptibility of breast cancer.
Breast cancer predisposition will only be expressed if this mutation occurs in breast cells.

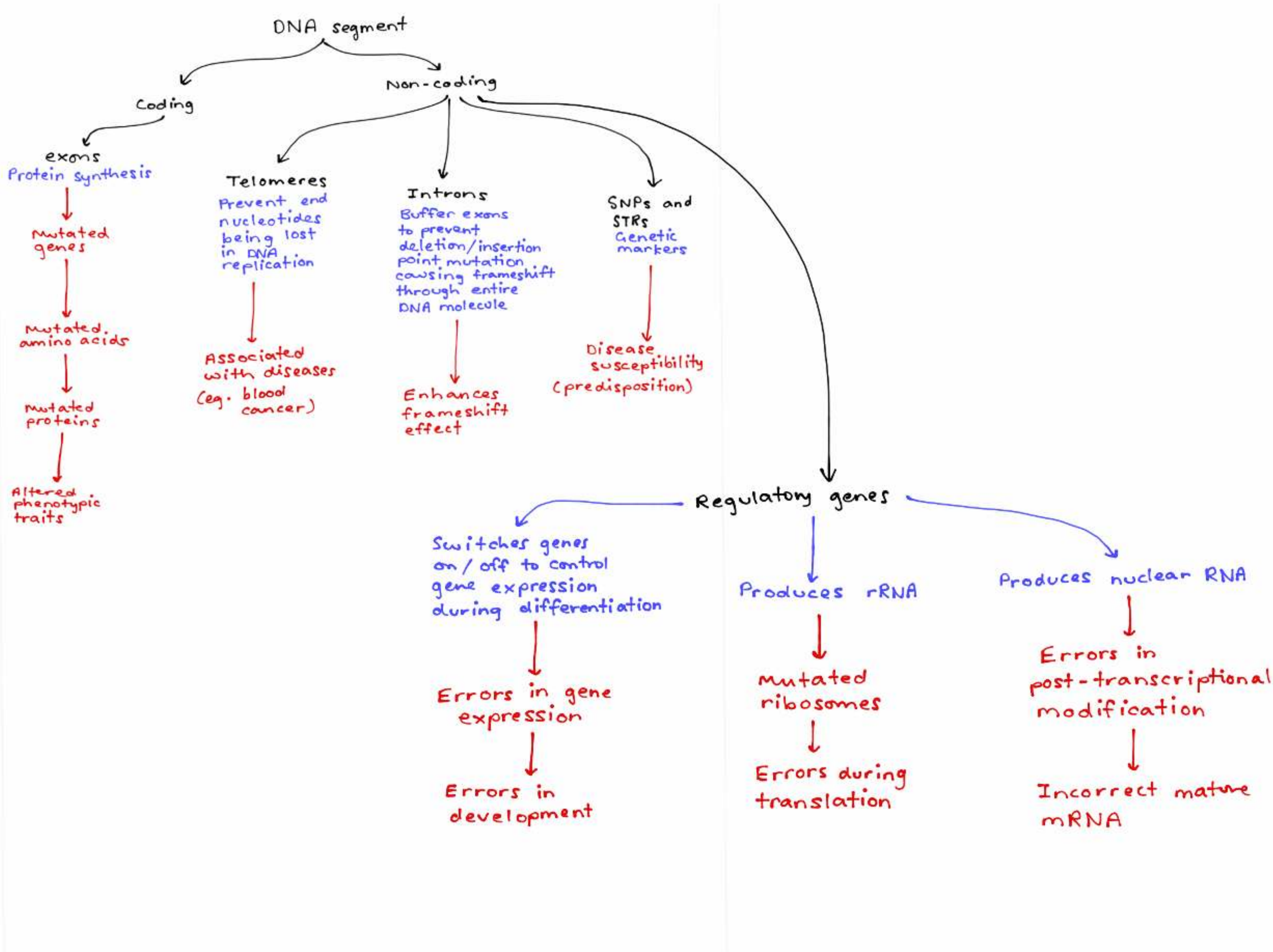
$\frac{1}{600}$ *women carry the BRCA mutation in their germline cells, which can be passed on to every cell of their offspring (germline AND somatic).*

Thus, the offspring is susceptible to breast cancer, AND can pass the mutation onto the next generation.



[6.1.4] Regions of mutated DNA

Mutations in coding (exons) and non-coding (introns) sequences of DNA are **equally significant**.



[6.1.5] Causes of genetic variation

Meiosis → Crossing over (Prophase I)

Meiosis → Independent assortment & Random segregation (Metaphase I) → Allele recombination

Random fertilisation → Allele recombination

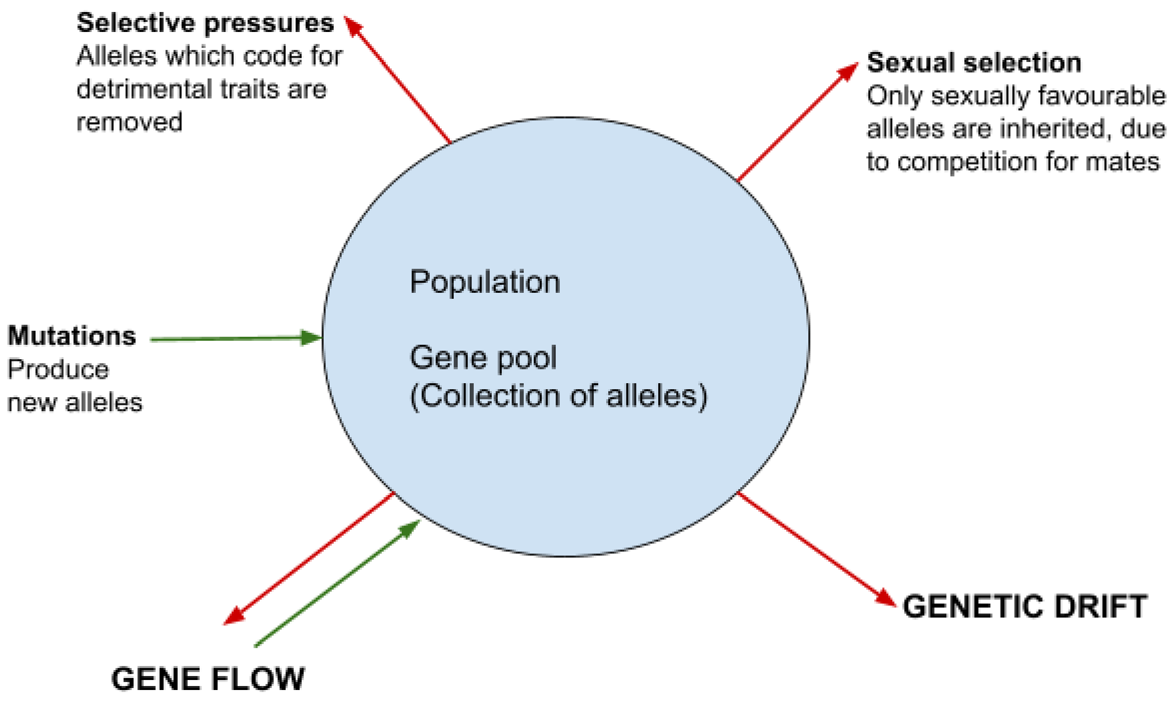
Allele recombination, Random fertilisation, Mutations: GENETIC VARIATION

Mutations → New alleles

New alleles → Detrimental allele → Removed from population

New alleles → Favourable allele → Natural selection → (growth) → Reproductive maturity → Inheritance → Reproductive isolation → Speciation → Biodiversity → Evolution

[6.1.6] Impact on the gene pool



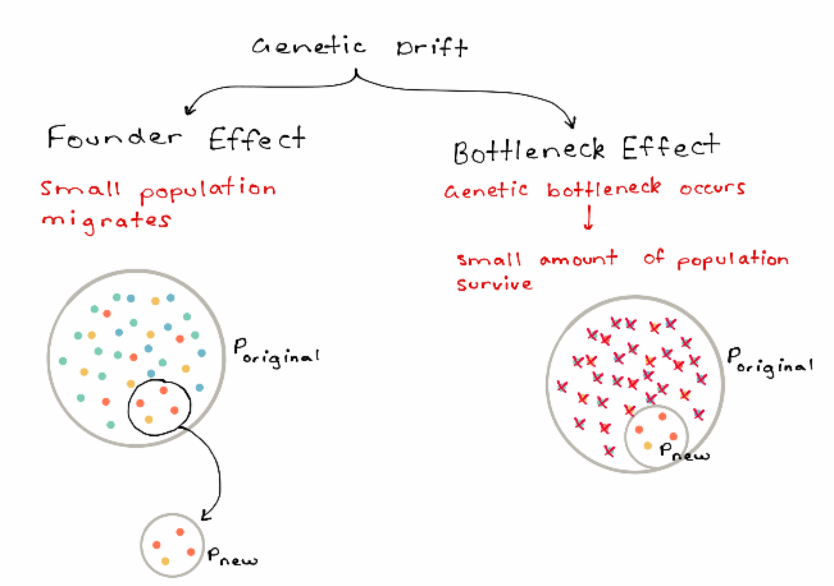
GENE FLOW

Alleles are moved between populations when species enter (immigrate) or leave (emigrate).

This changes the allele frequencies of both populations, reducing differences between populations and lowering the likelihood of speciation.

GENETIC DRIFT

Occurs when only a small number of individuals in a population remain. The gene pool is reduced and may not resemble the original one.



6.2: Biotechnology

How do genetic techniques affect Earth's biodiversity?

Population → Genetic variation → Selection pressure

↓

Biotechnology

↓

Artificial selection

↓

Hybrid vigour

Short-term

↓

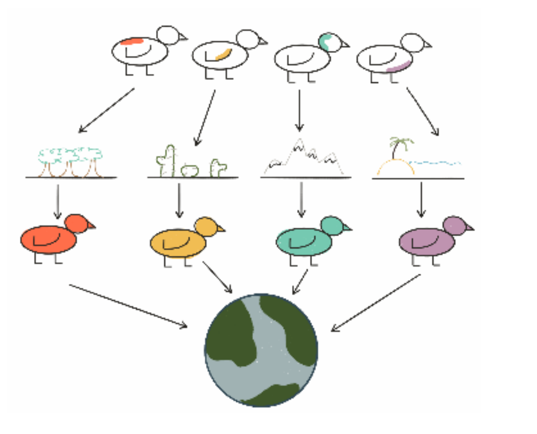
New genotypes
↓
More variation

Long-term

↓

Same alleles crossed
OR
Organism cloned
↓
Variation decreases
↓
Threatens continuity of species

LEVELS OF BIODIVERSITY

Genetic diversity Variation in the genotype of each member of a species	
Ecosystem diversity Variation in the ecosystems a species moves into	
Species diversity Variation of species in ecosystem due to speciation	
Biodiversity Variation of all living organisms	

Biodiversity begins with genetic diversity, which is reduced in the long term by biotechnology.

BIOTECHNOLOGY

The manipulation of living organisms or biological processes for human benefit.

Ancient biotechnology	Done by trial-and-error, without knowledge of biochemical processes. *Eg. Adding yeast to cause bread dough to rise*
Classical biotechnology	Done with knowledge of biochemical processes, but NOT knowledge of DNA. *Eg. Antibiotic penicillin* *Selective breeding of plants and animals* *Yeast fermentation to produce alcohol*
Present biotechnology	Done with knowledge of biochemical processes AND DNA. *Eg. Genetic technology (gene manipulation)*

PAST BIOTECHNOLOGY

Ancient (before 1800s)

Application	Description
Artificial selection	Organisms with favourable traits were crossbred to produce offspring with **hybrid vigour**.
Farming	Capturing and breeding animals increased populations of animals and plants in captivity, increasing biodiversity.
Aquaculture	Capturing eels and using them as food sources. Reduced the population, decreasing biodiversity.
Bread-making	Yeast accidentally found in the bread mixture fermented the sugar and released CO_2 , causing the bread to rise.
Cheese and yoghurt	Bacteria in the milk acted on lactose sugar, producing curd. When this was dehydrated, it produced cheese or yoghurt.
Medicine	Parts of plants (by trial and error) were used to treat disease. *Eg. Turmeric for inflammation*.

Classical (1800s-1900s)

Application	Description
Fermentation	Fermentation was proven to be caused by yeast. Yeast produces an enzyme which ferments sugar in fruits, forming alcohol and CO_2
Medicine	Penicillin antibiotic produced from the *penicillium notatum* fungus

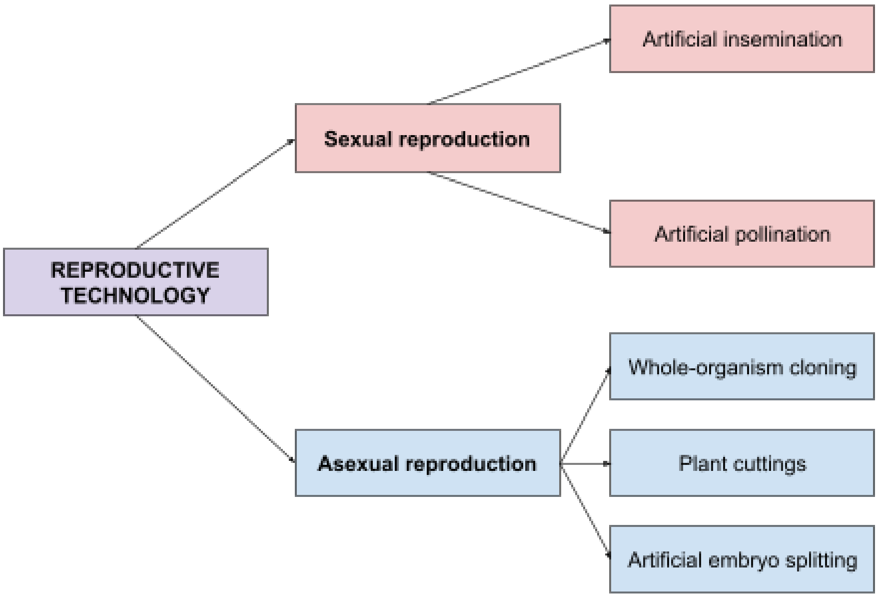
6.3: Genetic Technologies

Does artificial manipulation of DNA have the potential to change populations forever?

Reproductive technology: Increases the rate of reproduction by increasing frequency of selective breeding.

Genetic technology: Manipulation of genes for desired traits to be expressed for many fields.

REPRODUCTIVE TECHNOLOGIES (PRESENT BIOTECHNOLOGY)



Reproductive technologies are based on selective breeding. They increase the efficiency of producing offspring.

Issues with traditional selective breeding:

<table>
<tr><td>➔ If the male is in a different location, the whole organism has to be transported
◆ Affects survival of the animal
◆ High cost

➔ The rate of reproduction is slow, as one male can only fertilise one female at a time

➔ Animals may be injured in mating process</td><td>Can be fixed with reproductive tech.</td></tr>
<tr><td>➔ Cross-breeding can lead to the expression of unexpected, undesirable traits</td><td>Can’t be fixed.</td></tr>
</table>

Artificial insemination

Semen is collected from a male with desirable traits

↓

Stored and transported

↓

At location, it is thawed and placed into an insemination gun

↓

Gun is placed in the cervix of **many** female (with desirable traits), and the sperm is shot in

↓

Many females can be fertilised from the semen

Artificial pollination

Pollen (containing sperm) is harvested from the stamen of a plant with desirable traits

↓

Transferred onto the stigma of **many** flowers on:

- The same plant (self-pollination) or the same flower itself
- A different plant (cross-pollination)

↓

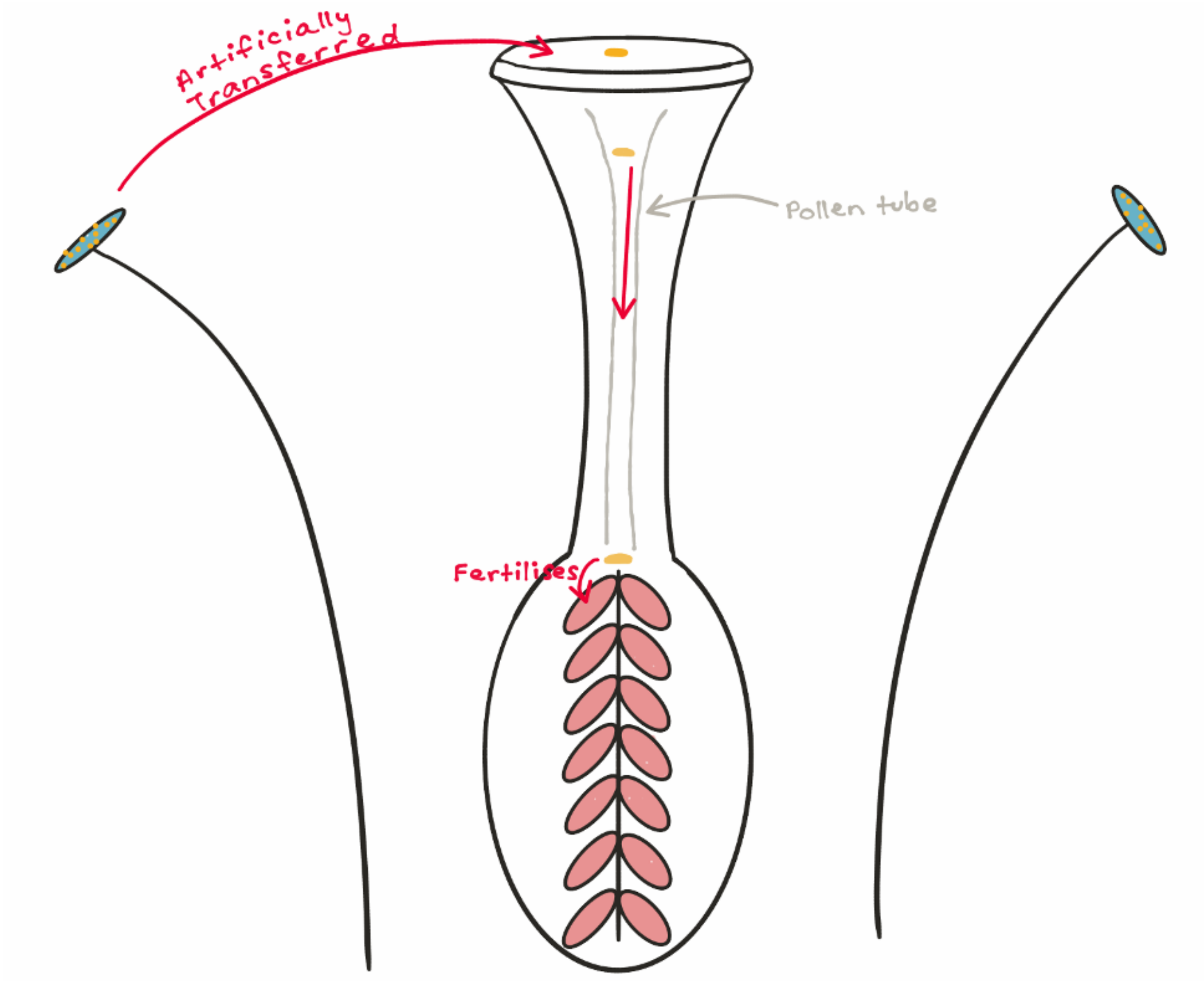
Pollen grows a pollen tube and moves down the style

↓

Enters the ovary

↓

Fertilises the ovules



Invitro fertilisation

Sperm and eggs collected from man and woman

↓

Fertilised externally in lab

↓

Zygote forms

↓

Develops into blastocyst externally

↓

Blastocyst implanted into woman's uterus
(Biological or surrogate mother)

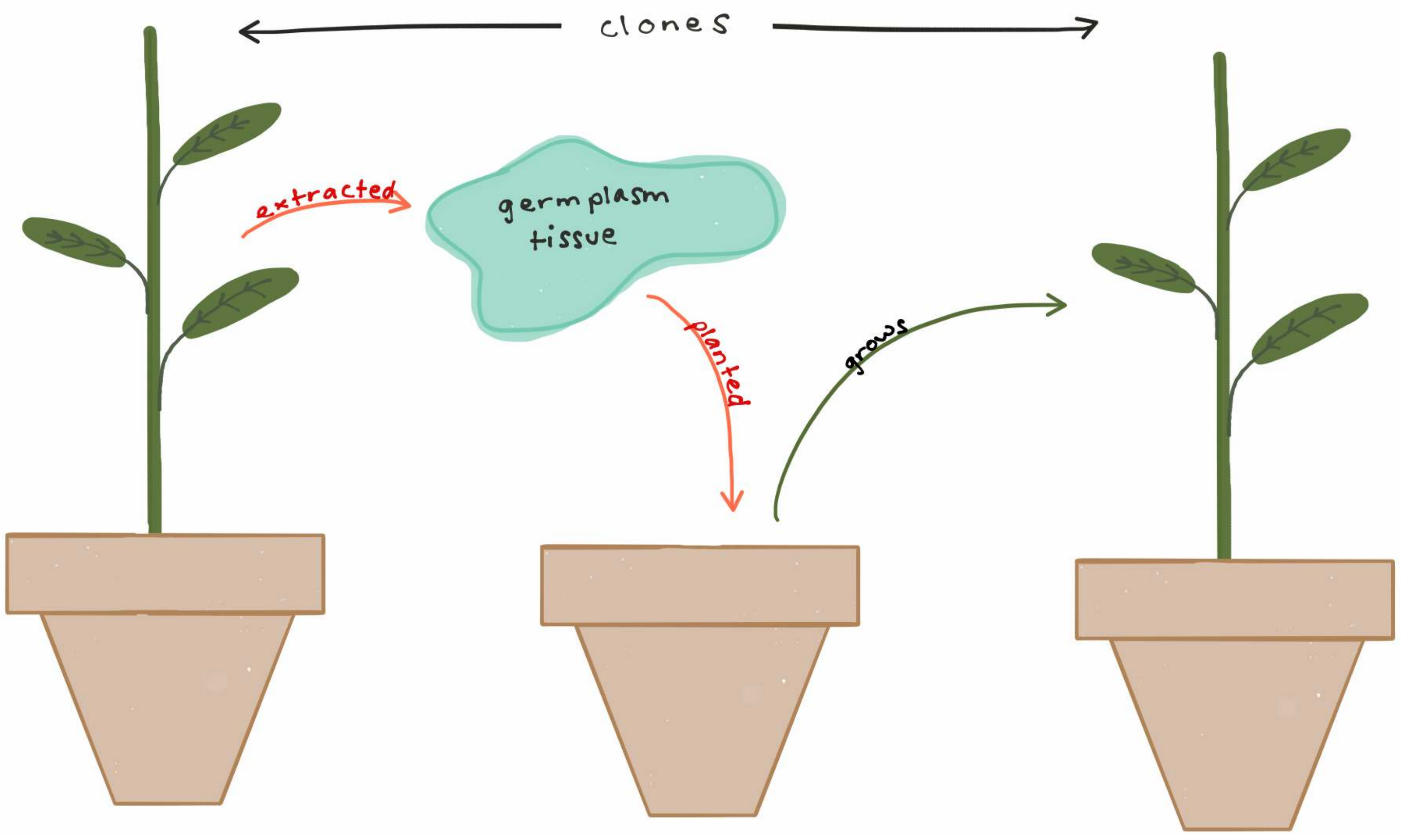
↓

Child develops internally

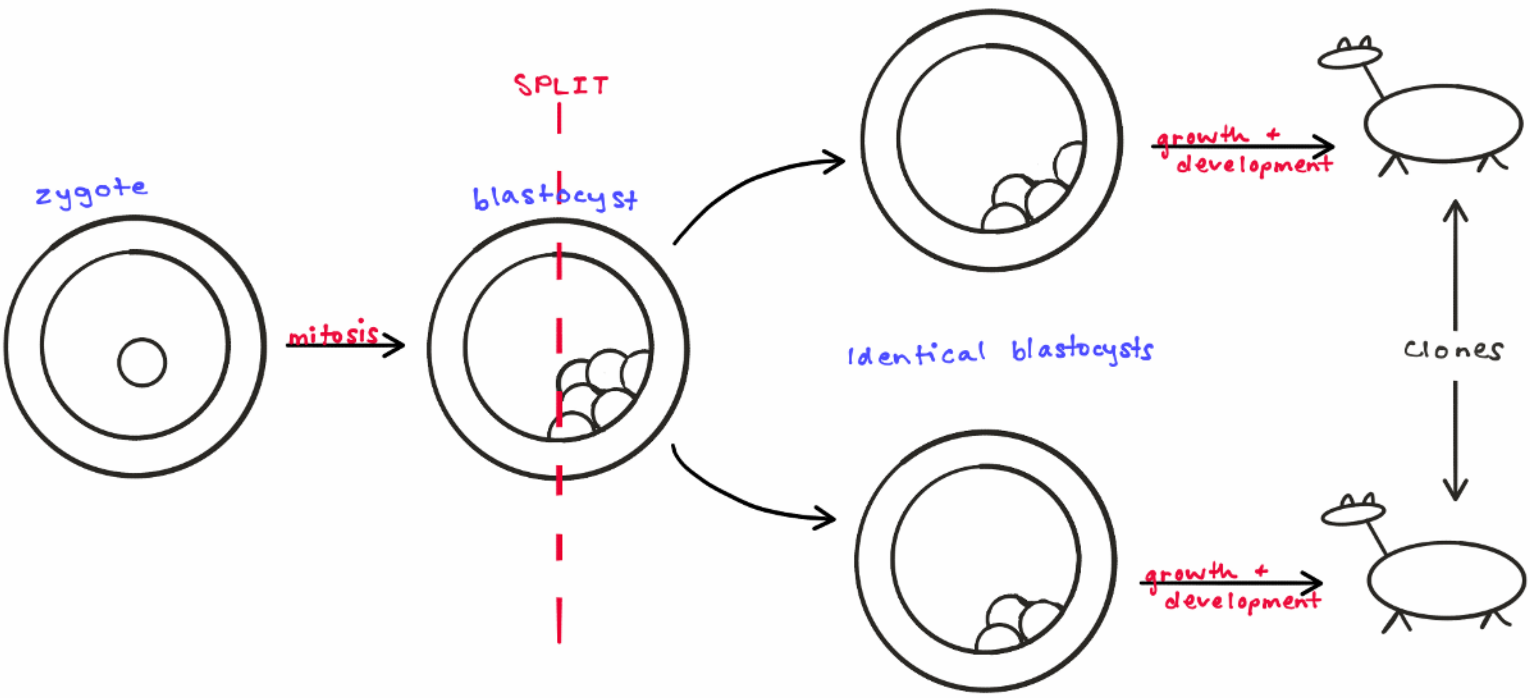
WHOLE ORGANISM CLONING

Clones are organisms which are genetically identical to each other.

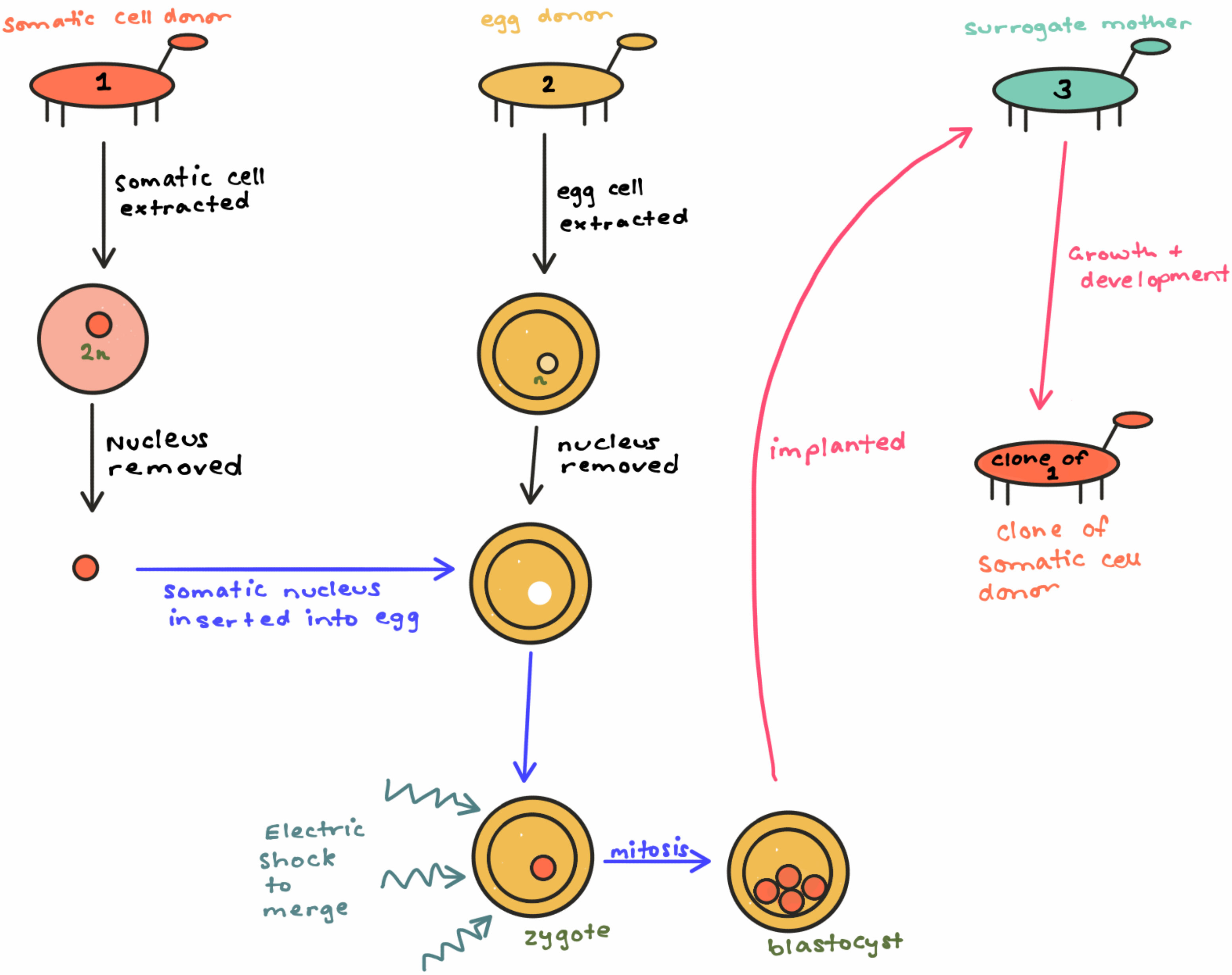
Plant cuttings (plants)



Artificial embryo splitting (animals)

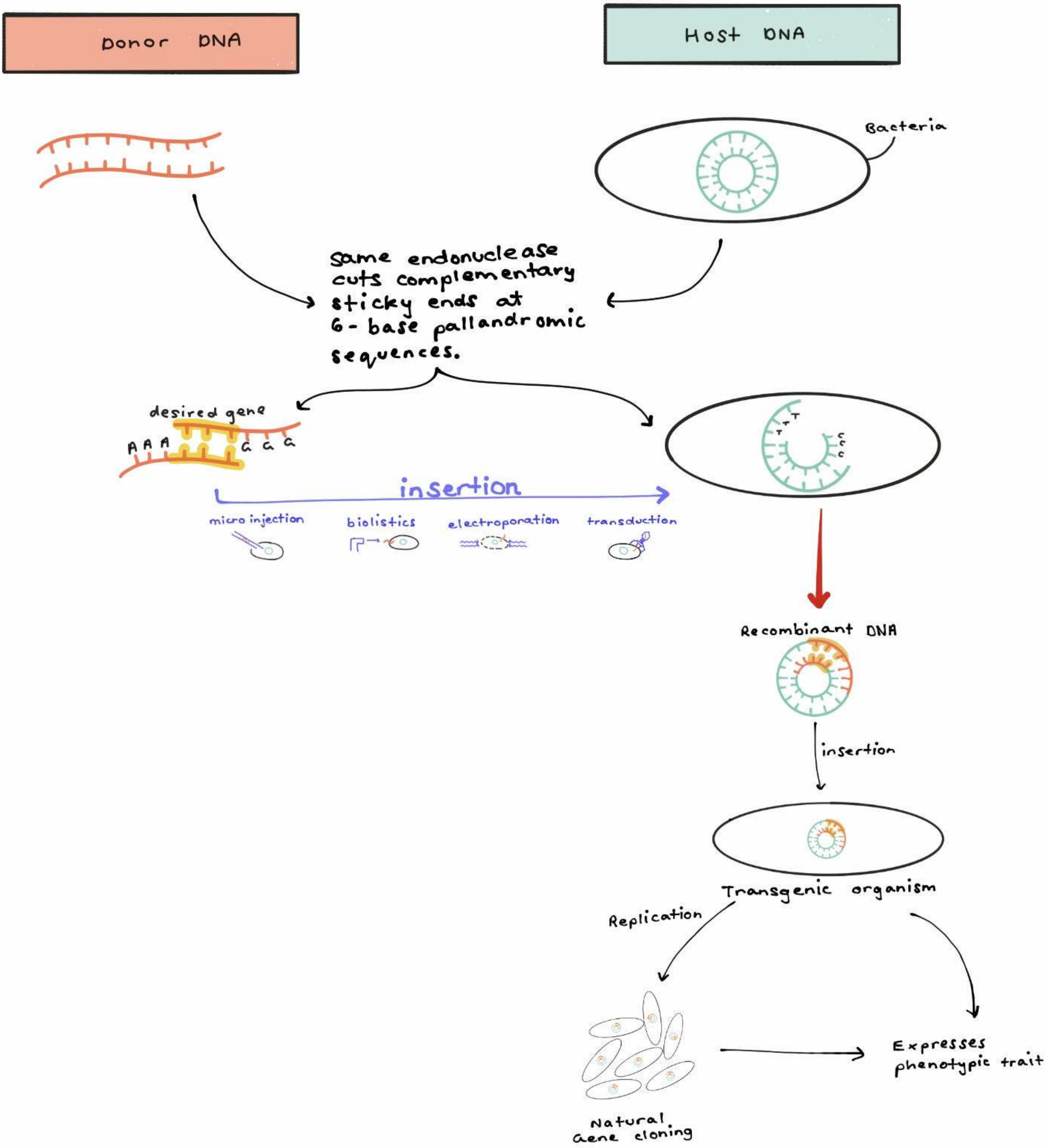


Somatic cell nuclear transfer (animals)



GENETIC TECHNOLOGIES

Recombinant DNA and transgenic organisms

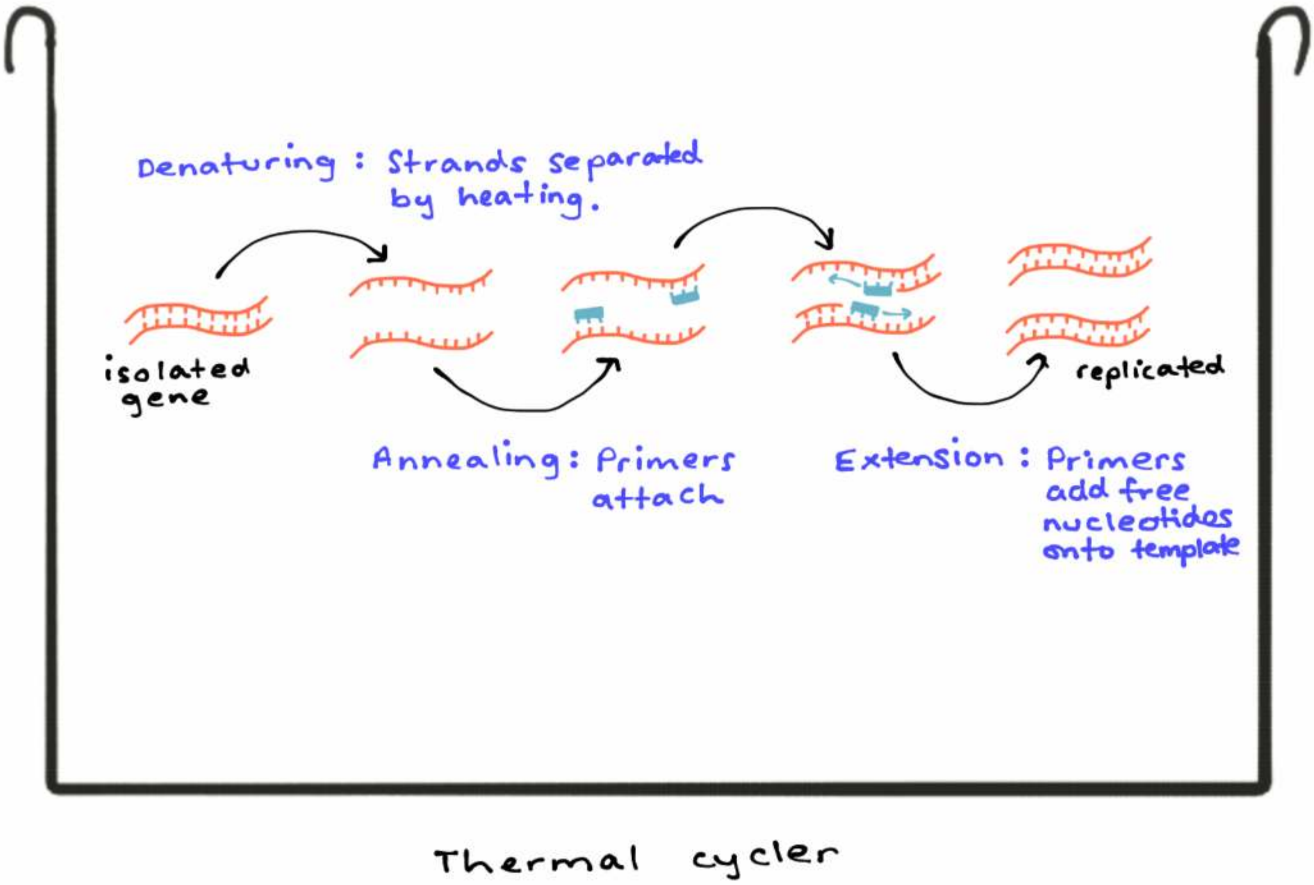


Uses:

- **Insulin bacteria**
  Human gene for insulin is inserted into bacterial DNA. The bacteria produces insulin for treatment of diabetes.

- **Bt-cotton**
  Gene from pest-resistant Bacillus thuringiensis bacteria is inserted into a cotton plant. Allows the plant to produce a protein which makes it pest-resistant.

Artificial gene cloning
Done through polymerase chain reaction.



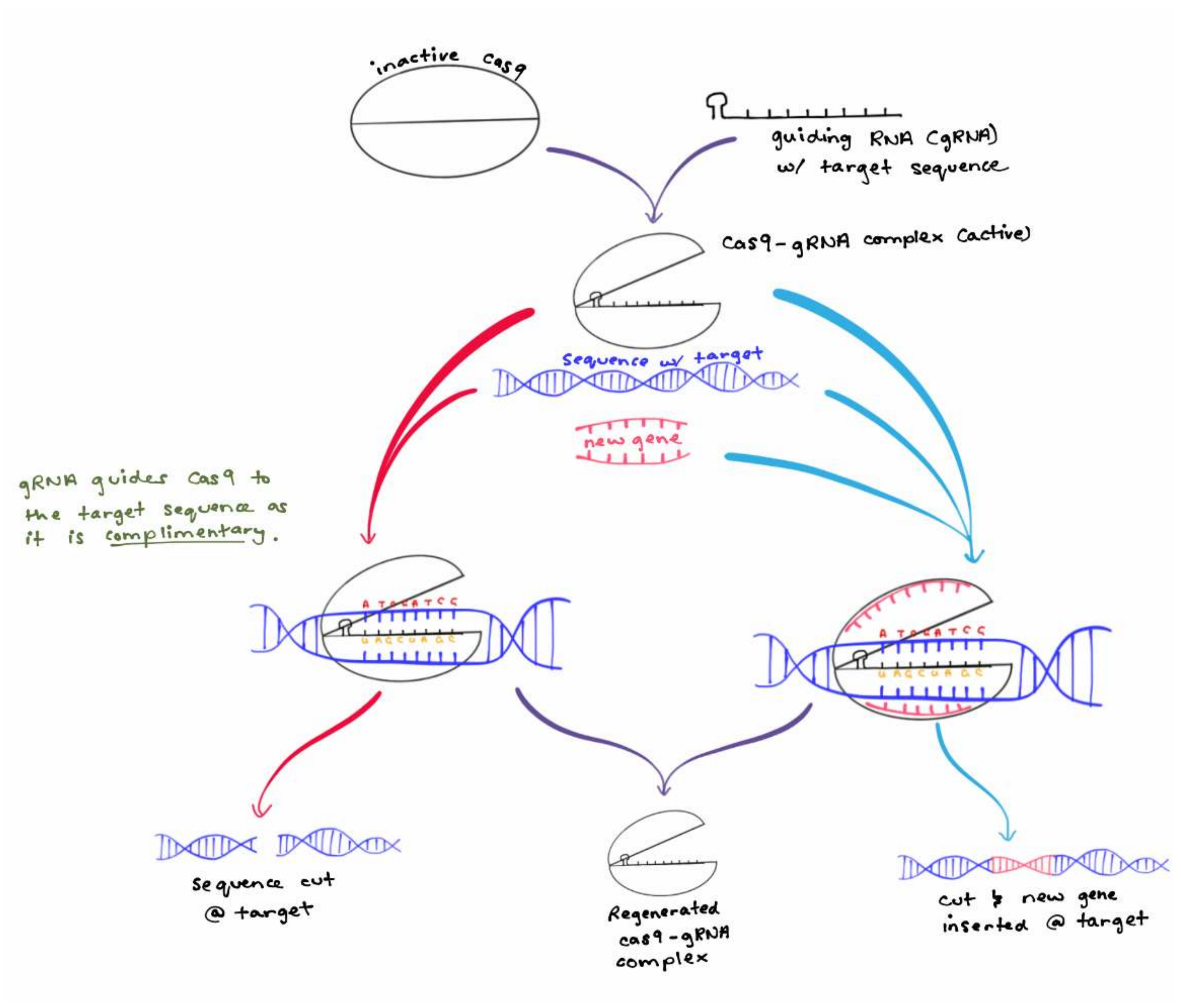
Input	Output
- Isolated gene - Primers - Free nucleotides - DNA polymerase enzyme - Ligase enzyme - Buffer solution	- Many copies of isolated gene

Comparing cloning

	Gene cloning	Whole-organism cloning
Aim	Create copy of one gene/ its products.	Recreate a genetically identical copy of an organism.
Products	Many cloned genes or products	Whole genome & all genotypes are cloned
Numbers cloned	Many	Few
Time period	Short	Long
Method	- Recombinant DNA - PCR	- SCNT
	Efficient	Inefficient

FUTURE DIRECTION

Synthetic biotechnology	Production of a cell with a synthetic genome. This cell may be able to communicate with normal cells to switch genes on/off. *Eg. Switching off cancerous cells*
Biofabrication	Stem cells can be used to 3D print tissue and organs. - Reduces death rate of people waiting for organ transplants - Reduces likelihood of rejecting transplanted organ, as it has the same surface proteins
CRISPR/ Cas9	Cuts a gene with higher precision than restriction endonuclease as it does not *only* have to cut at 6-base palindromic sequences.



[6.3.5] Uses of genetic technology

INDUSTRY

- Genetically modified microorganisms used for cleaning
    - Bacteria breaks down oil spills
    - Enzymes using in washing powders
- Environmentally friendly
    - Biofertilisers
    - Biopesticides
    - Biofuels
- Synthetic biology
    - Production of an artificial genome

AGRICULTURE

- Artificial insemination, pollination, selective breeding
    - Increases likelihood of inheritance of a favorable trait
- Genetically modified organisms
    - Hybrid vigour

CONSERVATION

- Preservation of genome to recreate extinct organisms
- Storage of plant germplasm for regermination
- Artificial insemination/pollination
    - Increases reproductive rate if endangered animals
    - Can increase biodiversity if many parents are used
- Preserved gametes or stem cells

MEDICINE

- Transgenic species produce deficient chemicals
    - T.bacteria produce insulin for diabetes
    - T.sheep produce blood-clotting factor for hemophilia
- Gene therapy
    - Replacing a faulty gene with a functioning gene to prevent/treat genetic disorders
    - Done through the method for transgenic species
- Biomaterial for transplants
    - Artificial heart valves
    - Artificial cartilage
- Biofabrication
    - Using 3D printing to produce biomaterial
- Altering surface proteins for transplant organisms
- Antibiotics, antibodies, antivirals

ETHICAL USES OF BIOTECHNOLOGY

Issue	**Benefit**	**Harm**
Environmental	- Production of environmentally friendly products - Conservation management - Monitoring & regulation of pollution - By increasing the yield, overexploitation of species is reduced	- Long-term decline in biodiversity - Alters the path of evolution by altering the gene pool though artificial selection

Economical	- Higher yields lead to economic return
	- Profit contributes to further research to advance biotechnology
		- High cost of biotechnology makes products unaffordable
		- Creates economic inequality between groups
		    - Commercial and small-scale farmers
		    - Developed and developing countries

Health & safety	- Higher yields can solve world hunger - Reduction of pollution - Disease treatment	- Long-term health risks not tested - Nutritional values altered - While one increases, the other may decrease - Allergies to one product may move to another if a gene is transferred - Bioterrorism: GMOs used to cause harm
Regulation	- Laws and legislations need to be introduced to monitor and regulate the production of GMOs	- Traditional farmers will be outcompeted - Labelling issues mean that not all GMO information will reach a consumer
Rights	- Legislations required to protect the rights of people and GMOs	- Vegetarians/ vegans may consume a GMO with an animal gene - Questionable ethics of tampering with a genome - Religious issues - Is it right to produce a ‘superhuman’ race using CRISPR?

INFLUENCE OF BIOTECHNOLOGY

Social

Benefits	Harms
- Improved forensics - Improved paternity testing - Treatment of genetic disease	- Creation of a ‘superhuman’ generation through CRISPR

Economical

Benefits	Harms
- Increases yield and quality of food - Profit	- Reduction of biodiversity - Traditional farmers go out of business - Unaffordability of GMOs for poorer people/ countries - One biotech company can monopolise the market with patent rights on a technology

Cultural

Benefits	Harms

- Can establish lineage, which helps with Indigenous land rights	- Religious objections against:
	    - Tampering with genome
	    - Human acts of creation
	    - Humanising organisms
	- Violation of human and animal rights
	- Issues with vegetarianism if an animal gene is transferred