1 Cell biology

1.1 Introduction to cells

Testing the cell theory

- three atypical examples are striated muscle, giant algae, aseptate fungal hyphae
- striated muscle tissue is formed by division of pre-existing muscle fibre cells; they are much larger than most animal cells; instead of one nucleus they have many
- fungi consist of narrow thread-like structures called hyphae; in some fungi hyphae are divided by cross walls (septa); aseptate fungi have no septa and each hypha is an uninterrupted tube-like structure with many nuclei
- many algae are unicellular; giant algae grow to a much larger size but are still one cell (10cm)

Functions of life in unicellular organisms

- paramecium to investigate functions of life
- nucleus that divides for reproduction (asexual)
- food vacuoles containing consumed organisms which are gradually digested (provide energy)
- cell membrane controls chemicals entering and leaving; waste products simply diffuse out
- contractile vacuoles fill up with water, expel it through membrane: keeping same water content
- enzymes in cytoplasm catalyze metabolic reactions
- beating of cilia moves the paramecium through water

Therapeutic uses of stem cells

- few current uses of stem cells to cure diseases
- Stargardt's disease: genetic disease causing photoreceptive cells in retina degenerate, vision becomes progressively worse; researchers developed method for making embryonic stem cells develop into retina cells; cells are injected into eyes, they attach to retina and vision improved
- Leukemia: type of cancer; production of large numbers of white blood cells; they are produced in the bone marrow; stem cells are killed by chemotherapy put the patient needs them; fluid is removed from bone marrow, stem cells extracted from fluid, stored by freezing, chemotherapy drugs are given to patient, bone marrow loses ability to produce white blood cells, stem cells are returned to patient which re-establish themselves, produce white blood cells

Sources of stem cells and the ethics of using them

- stem cells from deliberately created embryos: unlimited growth potential, differentiate into any type in body, higher risk of becoming tumour, less chance of genetic damage, likely to be genetically different form patient, removal of cells kills the embryo
- blood from umbilical cord with stem cells: easily obtained, commercial collection available, fully compatible with patient, limited capacity to differentiate, limited quantities, cord is discarded
- adult stem cells from bone marrow: difficult to obtain, less growth potential, less chance of tumour formation, limited differentiation capacity, fully compatible with patient, removal of stem cells does not kill the adult
- most ethical objections are with embryonic stem cells as it kills the embryo: question of when human life begins; though in vitro fertilization (IVF) is purposefully made, the egg cells must be obtained for money (vulnerable groups can be exploited)
- potential to allow methods of treatment of diseases as argument in favor

1.2 Ultrastructure of cells

Exocrine gland cells of the pancreas

- gland cells secrete substances through plasma membrane
- two types of gland cells in pancreas: endocrine (secrete hormones into bloodstream), exocrine (secrete digestive enzymes into duct that carries them into small intestine)
- enzymes are proteins so exocrine gland cells have organelles needed to synthesize proteins in large quantities

Palisade mesophyll cells

- cell type carrying out most of photosynthesis in leaf is palisade cells

- shape of cells is roughly cylindrical

1.3 Membrane structure

The role of cholesterol in membranes

- hydrophobic hydrocarbon tails usually behave as liquids but hydrophilic phosphate heads act as solids; overall membrane is fluid as components are free to move
- fluidity of animal cell membranes needs to be carefully controlled
- cholesterol restricts regular packing of hydrocarbon tails of phospholipids so prevents them crystallizing and behaving as solid
- cholesterol restricts molecular motion and therefore fluidity of membrane
- reduces permeability to hydrophilic substances such as sodium ions and hydrogen ions
- helps membranes to curve into concave shape which helps in formation of vesicles

1.4 Membrane transport

Active transport of sodium and potassium in axons

- axon is part of neuron (nerve cell) and consists of tubular membrane
- function of axons is to convey messages rapidly form one part of body to another in an electrical form (nerve impulse)
- nerve impulse involves rapid movements of sodium, then potassium ions across axon membrane: occur by facilitated diffusion due to concentration gradients built up by active transport (sodium-potassium pump protein)
- pump follows cycle resulting in three sodium ions being pumped out and two potassium in; interior of pump is open to inside of axon and three sodium ions enter, ATP transfers phosphate form itself to pump causing pump to change and close interior, interior opens to outside of axon and three sodium ions are released, two potassium ions form outside enter, binding of potassium cause release of phosphate group and pump changes shape again and opens inwards, potassium ions are released and sodium ions can enter again
- with each cycle the pump uses one ATP

Facilitated diffusion of potassium in axons

- rapid movements occur by facilitated diffusion across sodium and potassium channels
- potassium channels as special example of facilitated diffusion: each channel consists of four protein subunits with narrow pore allowing potassium to pass, dissolved potassium becomes bonded to shell of water molecules making it too big to pass, to pass the bonds are broken and bonds temporarily form between water and series of amino acids at narrowest point of protein, after potassium ion passes it is associated with shell again
- specificity of pump: other positively charged ions are either too large to fit or too small to form bonds with amino acids at narrowest point
- potassium channels in axons are voltage gated: if axon has relatively more positive charges outside than inside channel is closed
- at one stage in nerve impulse there are relatively more positively charges inside: channels open and potassium passes through
- channel rapidly closes again with extra globular subunit/protein attached by flexible chain of amino acids; ball remains in place until potassium channel returns to original closed state

Preventing osmosis in excised tissues and organs

- animal cells can be damaged by osmosis
- solution with higher osmolarity is hypertonic; water leaves cells by osmosis so cytoplasms shrinks in volume, plasma membrane does not change so indentations (crenellations) appear
- solution with lower osmolarity is hypotonic; cells take in water by osmosis and swell up, cells may burst leaving ruptured plasma membranes (red cell ghosts)
- solution with same osmolarity is isotonic; water molecules leave and enter at same rate so cell remains healthy; important for any human tissue and organs to be bathed in isotonic solution
- normal saline: isotonic sodium chloride solution is usually used with osmolarity at 300mOsm
- normal saline can be introduced safely to patient’s blood system, used to rinse wounds, used as basis for eye drops, frozen to ‚slush‘ for packing donor organs

1.5 Origin of cells

Spontaneous generation and Pasteur's experiments

- Louis Pasteur made nutrient broth by boiling water containing yeast and sugar
- shows that if broth is kept in sealed flask it remains unchanged
- famous experiment with swan-necked flasks bent into variety of shapes: boiled broth in some flasks and unboiled as control: organisms soon appear in unboiled flasks while others remain clean; broth in flasks was in contact with air which was needed for spontaneous generation: organisms only appear after necks are snapped off
- Pasteur concludes that no organisms appear spontaneously

1.6 Cell division

Smoking and cancer

- correlation: relationship between two variable factors; positive correlation (when one increases the other does as well), negative correlation (when one increases the other decreases)
- there is a positive correlation between cigarette smoking and death rate due to cancer
- smokers are several times more likely to die from all cancers than non-smokers
- important to distinguish between correlation and cause; correlation does not prove a cause; in this case causal links are well established
- 20 of chemical substances cause tumours in experiments and at least 40 are carcinogenic

2 Molecular biology

2.1 Molecules to metabolism

Synthesis of urea

- urea is a nitrogen-containing compound and component of urine: it is a means of excreting nitrogen form amino acids
- cycle of reactions catalyzed by enzymes produce it in the liver
- urea can be synthesized artificially, chemical reactions are different but product is same

2.2 Water

Comparing water and methane

- methane is a waste product of anaerobic respiration
- water molecules are polar and can form hydrogen bonds whereas methane molecules are nonpolar and do not form hydrogen bonds: physical properties are different
- water has a higher specific heat capacity, higher latent heat of vaporization, higher melting point, higher boiling point; methane is liquid over range of 22 °C, water is liquid over 100 °C

Cooling the body with sweat

- sweat is secreted by glands in skin: heat needed for evaporation of water in sweat is taken form tissues of skin, reducing their temperature: blood is cooled
- sweat secretion is controlled by hypothalamus of brain: has receptors monitoring blood temperature and receives sensory inputs form temperature receptors on skin
- if body is under target temperature no sweat is produced
- when adrenalin is secreted, sweat is produced because intense activity is anticipated
- transpiration is evaporative loss of water from plant leaves

Transport in blood plasma

- blood transports variety of substances with several methods to avoid problems
- sodium chloride: ionic compound that is freely soluble in water, dissolves into sodium ions (Na^+) and chloride ions (Cl^-)
- amino acids: have negative and positive charges, solubility depends on R-group, some are hydrophilic while others are hydrophobic but all are soluble enough
- glucose: freely soluble in water and carried dissolved in blood plasma
- oxygen: nonpolar molecule, diffuses in water due to small size but water is saturated at low concentrations, amount that blood plasma can transport is too small to provide for aerobic respiration, problem solved with hemoglobin in red blood cells
- fats molecules: entirely nonpolar, insoluble in water, carried in lipoprotein complex (groups of molecules with single layer of phospholipid on outside and fats inside: heads face outwards and tails face inwards; proteins in phospholipid monolayer, hence lipoprotein)
- cholesterol: hydrophobic apart from small region at one end, transported with fats in lipoprotein complexes, hydrophilic region facing outwards with phospholipid heads

2.3 Carbohydrates and lipids

Polysaccharides

- starch, glycogen, cellulose are made by linking different glucose types
- glucose can have -OH group on carbon atom 1 pointing down (α-glucose) or up (β-glucose)
- cellulose is made by linking β-glucose molecules: condensation reactions link carbon atom 1 to carbon atom 4: glucose subunits in chain are oriented alternately up and downwards: cellulose is a straight chain, unbranched; can form bundles with hydrogen bonds forming cellulose microfibrils: great tensile strength in plant cell walls
- starch is made by linking α-glucose molecules: condensation reaction links carbon atom 1 to carbon atom 4: glucose molecules are orientated in same way: starch molecule is curved: two forms of starch are amylose and amylopectin
- amylose is unbranched and forms helix; amylopectin is branched and has globular shape

- starch is only made by plant cells: both types are hydrophilic but too large to be soluble in water: useful in cells where large amounts of glucose need to be stored: if stored as glucose too much water would enter by osmosis, so starch is means of storing energy
- glycogen is similar to amylopectin but has more branching: more compact; many by animals and fungi: acts as sore of energy in form of glucose
- starch and glycogen have no fixed size and number of glucose molecules

Energy storage

- lipids and carbohydrates as energy storage in humans; lipids for long-term storage: stored in specialized groups of cells (adipose tissue) located immediately beneath skin
- amount of energy released in cell respiration per gram of lipids is double amount released form gram of carbohydrates; lipids even form pure droplets in cells without associated water while glycogen is associated with water: lipids are six times more efficient in amount of energy stored per gram of body mass
- lipids are poor conductors of heat: used as insulators
- fat is liquid at body temperature: can act as shock absorber
- glycogen used for short-term storage as it can be broken down to glucose rapidly and transported easily in blood (fats cannot be mobilized as easily)
- glucose can be used in aerobic and anaerobic cell respiration while fats only in aerobic

Health risks of fats

- main concern of fat affecting coronary heart disease (CHD): coronary arteries become partially blocked by fatty deposits leading to clot formation and heart attacks
- positive correlation between saturated fatty acid intake and rates of CHD: correlation is not cause; could be low amount of dietary fibre casting CHD
- some populations do not fit correlation (Maasai in Kenya): high consumption of saturated fats but CHD is unknown
- genetic factors and other aspects form diet can explain CHD rates
- positive correlation between amounts of trans-fat consumed and rates of CHD: fatty deposits found in diseased arteries with high amount of trans-fats: more evidence for causal links

Analysis of data on health risks of lipids

- evaluation: assessment of implications and limitations
- visual display: how large is average difference? how widely spread is data? size of error bars? results of statistical tests?
- assessing methods: sample size? sample evenly distributed in sex, age, health? measurement?

2.4 Proteins

Denaturation of proteins

- three-dimensional conformation of proteins stabilized by bonds/interactions between R groups
- denaturation: broken bonds result in change of conformation
- denatured protein does not return to former structure: denaturation is permanent; soluble proteins often become insoluble (hydrophobic R groups in centre getting exposed)
- heat causes vibrations within molecule and can break intermolecular bonds: denaturation; proteins vary in heat tolerance (Thermus aquaticus works best at 80°C)
- pH extremes change charges on R groups breaking ionic bonds or causing new ones: denature

Examples of proteins

- rubisco (ribulose bisphosphate carboxylase): active city catalyses reaction fixing carbon dioxide from atmosphere; present in high concentrations in leaves
- insulin: hormone signaling absorption of glucose, reducing blood sugar; binds reversibly to receptor in cell membrane; secreted by beta-cells in pancreas; transported by blood
- immunoglobulin: antibodies, bind to antigens on pathogens; binding sites are hyper-variable; basis of specific immunity to disease
- rhodopsin: pigments absorbing light; membrane protein of rod cells of retina; when retinal molecule absorbs single photon of light it changes shape: small amounts detected
- collagen: rope-like proteins made of three polypeptides wound together; immense strength
- spider silk: polypeptides form parallel arrays; is extensible and resistant to breaking

2.5 Enzymes

Lactose-free milk

- lactose (glucose + galactose) is naturally present in milk and converted by enzyme lactase
- companies culture yeast and extract lactase from it to sell
- lactose-intolerant people cannot drink a lot of milk unless lactose-reduced
- galactose and glucose are sweeter than lactose so less sugar needs to be added
- lactose tends to crystallize during production of ice cream: glucose and galactose are more soluble and remain dissolved giving smoother texture of ice cream
- bacteria ferment glucose and galactose faster so production is faster

2.6 Structure of DNA and RNA

Crick and Watson's models of DNA

- testing possible structures by model-making
- first: triple helix with bases on outside and magnesium holding stands together with ionic bonds to phosphate groups: helical structure fitted X-ray diffraction pattern from Rosalind F.
- Rosalind Franklin points out that there would not be enough magnesium available and model does not take into account of Chargaff's finding that amount of adenine equals thymine and cytosine equals guanine
- investigation of base pairs show that both have equal length so would fit between two outer sugar-phosphate backbones
- flash of insight for making parts fit together they had to run in opposite directions: antiparallel
- new structure immediately suggested mechanism for copying DNA and leads to realization that genetic code must consist of triplets of bases

2.7 DNA replication, transcription and translation

PCR - the polymerase chain reaction

- technique used to make many copies of a selected DNA sequence
- small quantity is needed and cycle of steps repeatedly doubles the quantity
- two strands in DNA hold by hydrogen bonds which are weak but in high numbers hold the DNA successfully together; if DNA is heated enough they eventually break and strands separate
- if DNA is cooled again the strands pair up again: re-annealing
- PCR machine separates DNA strands by heating to 95 °C for 15 seconds, then cools to 54 °C for 25 seconds: large excess of short sections of single-stranded DNA (primers) is present: primers bind rapidly to target sequence and prevent re-annealing of parent strands
- next stage is synthesis of double-stranded DNA using primers as templates, done with Taq DNA polymerase (from bacterium Thermus aquaticus)
- Taq polymerase has optimum at 72 °C so mixture is heated for 80 seconds
- after that the cycle is repeated, amplifying number by more than billion in 30 cycles (<1h)

Production of human insulin in bacteria

- diabetes due to destruction of cells secreting insulin in pancreas
- porcine (pig) and bovine (cattle) insulin was used to treat diabetes but allergies might develop
- 1982: human insulin is commercially available: produced using genetically modified E. coli bacteria; later using yeast cells and safflower plants
- each species was genetically modified by transferring gene for making insulin to it
- important that all organisms use same genetic code as humans, making transfer possible

2.8 Cell respiration

Yeast and its uses

- yeast: unicellular fungus, lives where sugar is available, respires aerobically and anaerobically
- yeast is added to bread to create bubbles of gas to give it lighter texture; dough is kept warm to encourage yeast to respire; oxygen soon used up so it respires anaerobically
- ethanol is also produced by anaerobic cell respiration but evaporates during baking
- bioethanol: ethanol produced by living organisms, used as renewable energy source; produced form sugar cane and corn using yeast: converts sugars into ethanol in large fermenters; starch and cellulose must be broken down into sugars, achieved by enzymes

Anaerobic respiration in humans

- lungs and blood system supply oxygen to most organs rapidly enough for aerobic respiration
- sometimes we resort to anaerobic cell respiration in muscles because it can supply ATP very rapidly for short period of time: used when we need to maximize power of muscle contraction
- today mostly used during training or sport
- anaerobic cell respiration involves production of lactate; there is a limit to concentration that body tolerates: reason for short timescale over which power of muscle contractions can be maximized (we can only sprint up to 400 meters)
- after anaerobic respiration, lactate has to be broken down involving use of oxygen
- oxygen debt: demand for oxygen that builds up during period of anaerobic respiration

3 Genetics

3.1 Genes

Comparing numbers of genes

- we see ourselves as more complex in structure, physiology and behavior so we might expect to have more genes

Sickle cell anemia

- commonest genetic disease: due to mutation of gene coding for alpha-globin polypeptide in hemoglobin (Hb); healthy is Hb^A
- new allele Hb^S forms after base substitution mutation converts sixth codon of gene from GAG to GTG; when transcribed it produces mRNA GUG instead of GAG, changing sixth amino acid in polypeptide from glutamic acid (Glu) to valine (Val)
- change causes hemoglobin molecules stick together in tissues with low oxygen concentration: bundles are rigid enough to distort red blood cells into sickle shape
- sickle cells cause damage to tissue by becoming trapped in blood capillaries
- when they return to lungs they change shape again: over time this damages hemoglobin and plasma membrane reducing lifespan of red blood cell to 4 days
- body cannot replace red blood cells at rapid enough rate: anemia develops
- two copies of allele cause severe anemia; one copy causes mild anemia

3.2 Chromosomes

Measuring the length of DNA molecules

- John Cairns produced images from E. coli: cells grown in culture medium with tritiated thymidine, producing radioactively labelled DNA as it was used during DNA replication; cell walls were digested and cells were gently burst to release DNA onto dialysis membrane; thin film of photogenic emulsion was applied to surface and left in darkness for two months; atoms of tritium decayed and emitted high energy electrons reacting with film; film was developed and examined with microscope; point where a tritium atom decayed, position of DNA was indicated
- images produced by Cairns show chromosome of E. coli is a single circular DNA molecule with length of 1’100 µm, which is remarkably long given that length of cell is only 2 µm
- autoradiography was later used by researchers to produce images of eukaryotic chromosomes
- in contrast to prokaryotic chromosome, fruit fly chromosome was linear rather than circular

Comparing the genome sizes

- genomes of living organisms vary by huge amount
- genome size of eukaryotes depends on size and number of chromosomes; correlated with complexity of organism but not directly proportional: proportion of DNA acting as functional genes is variable and amount of gene duplication varies
- prokaryotes have a smaller genome size

Comparing chromosome numbers

- some eukaryotes have few large chromosomes and other have many small ones
- all eukaryotes have at least two different types of chromosome, so diploid chromosome number is at least four

Karyotypes and Down syndrome

- karyogram: image of chromosomes of organism, in homologous pairs of decreasing length
- karyotype: property of organism, number and type of chromosomes an organism has
- used to deduce whether individual is male (XY) or female (XX)
- used to diagnose Down syndrome and other chromosomal abnormalities; three copies of chromosome 21 in karyogram indicate Down syndrome (trisomy 21)

3.3 Meiosis

Obtaining cells from a fetus

- amniocentesis: passing needle through mother's abdomen wall using ultrasound to guide needle; needle used to withdraw sample of amniotic fluid containing fetal cells
- chronic villus sampling: sampling tool entered through vagina used to obtain cells from chorion (one of membranes from which placenta develops); can be done earlier in pregnancy
- risk of miscarriage: amniocentesis has 1% and chronic villus sampling has 2%

Non-disjunction and Down syndrome

- meiosis is sometimes subject to errors: homologous chromosomes fail to separate (non-disjunction): results in gamete with either extra chromosome or deficient in one: if gamete is fertilized it results in individual with either 45 or 47 chromosomes
- abnormal number of chromosomes often leads to person with syndrome
- Down syndrome (trisomy 21): non-disjunction leading to individual with three chromosomes 21
- most other trisomies in humans are so serious that offspring does not survive
- Klinefelter's syndrome: non-disjunction causing sex chromosomes XXY
- Turner's syndrome: non-disjunction causing only one X chromosome

3.4 Inheritance

ABO blood groups

- example of co-dominance
- before blood transfusions, the patient's blood group must be known to prevent complications due to coagulation of red blood cells
- genotypes I^AI^A and I^BI^B give blood groups A and B respectively while none of them is dominant the genotype I^AI^B gives a new blood group AB
- third allele *i* is recessive so I^Ai and I^Bi give blood groups A and B respectively
- genotype *ii* gives blood group O
- all three alleles cake the production of a glycoprotein in membrane of red blood cells
- I^A alters the glycoprotein by adding acetyl-galactosamine; people without this allele who come in contact with this blood will produce anti-A antibodies
- I^B alters the glycoprotein by adding galactose; people without this allele coming in contact with this blood will produce anti-B antibodies
- genotype I^AI^B alters the glycoprotein by adding both, so no antibodies are produced
- allele *i* does not modify the basic glycoprotein

Cystic fibrosis and Huntington's disease

- cystic fibrosis is the commonest genetic disease in parts of Europe
- due to recessive allele of the CFTR gene (chrom. 7); product of that gene is a chloride ion channel involved in secretion of sweat, mucus, digestive juices
- recessive allele causes sweat to contain excessive amounts of sodium chloride while digestive juices and mucus have insufficient sodium chloride: not enough water moves by osmosis into secretions: sticky mucus builds top in lungs causing infections and pancreatic duct is blocked
- Huntington's disease is due to dominant allele on HTT gene (chrom. 4): gene product is a protein called huntingtin
- dominant allele HTT causes degenerative changes in brain: changes in behavior, thinking and emotions become severe
- person eventually needs full nursing and succumbs to heart failure, pneumonia, or some other infectious disease
- late onset (age 30-50): already has children: can be tested

Red-green color blindness and hemophilia

- sex linkage mostly due to genes located on X chromosome
- red-green color blindness is caused by recessive allele of gene for one of the photoreceptor proteins: these detect specific wavelength ranges of visible light
- males only have one X chromosome: if that chromosome has it, the son has it as well
- daughter must get it from red-green color blind father and recessive from mother

- hemophilia is life threatening genetic disease; most cases are due to inability to make Factor VIII which is involved in blood clotting
- treatment is infusion of Factor VIII purified from blood of donors
- gene for Factor VIII is on X chromosome and is recessive

Consequences of nuclear bombing and accidents at nuclear power stations

- common feature of Hiroshima, Nagasaki, Three Mile Islands, Chernobyl is that radioactive isotopes were released into environment and people were exposed to them
- apart from cancer, other main predicted effects are mutations, leading to stillbirths, malformation or death
- affected children are monitored: no evidence has been found of mutations caused by radiation
- many animals and plants suffered after accident; but there is no clearly demonstrated increase in solid cancers or leukemia due to radiation in the most affected populations

3.5 Genetic modification

Paternity and forensic investigations

- DNA profiling is used in forensic investigations: blood stains, hair or semen
- in each example, DNA is taken from crime scene and compared to suspect or victim
- DNA profiling is used in paternity investigations
- DNA profiles of mother, child, father are needed; if bands in child does not occur in mother nor father, there must be a different father

Techniques for gene transfer to bacteria

- transfer of genes is referred to as genetic engineering
- gene transfer to bacteria usually involves plasmids, restriction enzymes and DNA ligase
- restriction enzymes (endonucleases) are enzymes that cut DNA molecules at specific base sequences; some endonucleases cut the DNA at different points, leaving single-stranded sections (sticky ends) which can be used to link pieces of DNA together
- DNA ligase joins DNA molecules: used to seal the nicks at the sticky ends to create the full sugar-phosphate backbone
- gene has to be transferred: easier to obtain mRNA than actual DNA: reverse transcriptase is an enzyme that makes DNA copies from RNA molecules called cDNA

Risks and benefits of GM crops

- potential benefits and risks can be grouped into environmental, health and agricultural parts
- environmental benefits: pest-resistant, reduces need plow and spray crops, shelf-life improved
- health benefits: nutritional value, crops lacking allergens, produce edible vaccines
- agricultural benefits: resistant to drought, herbicide resistance, resistant to diseases
- health risks: proteins produced could be toxic or cause allergic reactions, antibiotic resistance could spread to bacteria, genes could mutate
- environmental risks: non-target organisms can be affected, genes for herbicide resistance could transfer to wild plants, biodiversity can be reduced
- agricultural risks: unwanted plants with resistance difficult to control, produce resistance to toxin and a new wave of pests, strains adapted to local conditions cannot be developed

Methods used to produce Dolly

- somatic-cell transfer was used; has three stages
- somatic cell is a normal body cell with a diploid nucleus
- adult cells are taken from the udder of a sheep and grown in laboratory, in a medium with low concentrations of nutrients: genes in cell get inactive and lose pattern of differentiation
- unfertilized eggs are taken from ovaries of a different sheep, their nuclei are removed; cultured cells are placed to each egg cell and a small electric pulse causes them to fuse
- embryos are injected into a surrogate mother; one of 29 successfully developed: Dolly

4 Ecology

4.3 Carbon cycling

Carbon fluxes

- estimates based on ecosystems or mesocosms are done to show how much carbon is transferred from one pool to another in the carbon cycle
- global carbon fluxes are in gigatonnes ($1x10^{15}$grams)

Trends in atmospheric carbon dioxide

- data from atmospheric stations is freely available: long-term trends and annual fluctuations

4.4 Climate change

Opposition to the climate change science

- many claims that humans are not causing climate change
- many factors influence global temperature: volcanic activity and cycles in oceanic currents
- global warming continues but with varying increases each year
- not all sources in the internet are trustworthy

Coral reefs and carbon dioxide

- carbon dioxide emissions have effects on the ocean: dissolve into the ocean
- rising concentrations of atmospheric carbon dioxide cause ocean acidification
- marine animals that deposit calcium carbonate in there skeletons need to absorb carbonate ions from seawater
- dissolved carbon dioxide lowers the carbonate ion concentration: carbon dioxide reacts with water to form carbonic acid (H_2CO_3) which dissociates into hydrogen and hydrogen carbonate (HCO_3^-); hydrogen ions react with carbonate ions (CO_3^{2-}), reducing their concentration
- if carbonate ion concentrations drops, it is more difficult for corals to absorb them and existing skeletons tend to dissolve

5 Evolution and biodiversity

5.1 Evidence for evolution

Pentadactyl limbs

- pattern of bones or a modification of it is present in all amphibians, reptiles, birds, mammals
- differences are seen in relative lengths and thickness of the bones

Industrial melanism

- dark varieties of typically light-colored insects are called melanistic
- example of peppered moth: natural selection as the melanistic variety became commoner in polluted industrial areas where it is better camouflaged
- in unpolluted areas tree branches are covered in pale-colored lichens; sulphur dioxide pollution kills lichens and soot from coal burning blackens tree branches
- there might be other factors influencing the survival

5.2 Natural selection

Galápagos finches

- sizes and shapes of finches vary as does their diet
- Peter and Rosemary Grant have shown that beak characters and diet are closely related and when one changes so does the other
- *G. fortis* on island Daphne Major: drought causes shortage of small seeds so *G. fortis* feeds on larger harder seeds which only birds with larger beaks can open; severe El Niño event casques heavy rain and only small soft seeds are present so *G. fortis* has longer narrower beaks
- though mostly controlled by genes, environment can have effects too
- variation due to genes is called heritability

Antibiotic resistance

- antibiotic resistance is due to genes in bacteria: can be inherited
- evolution of multiple antibiotic resistance has occurred in just a few decades
- very widespread use of antibiotics for treating diseases and in animal feeds
- bacteria reproduce very rapidly (one generation in less than an hour)
- populations are huge: chance for antibiotic resistance due to mutation
- bacteria can pass on genes via plasmids so one species can give it to another

5.3 Classification of biodiversity

Plants

see p. 266 for full table

- all plants are classified in one kingdom
- four main phyla: Bryophyta (mosses, liverworts, hornworts), Filicinophyta (ferns), Coniferophyta (conifers), Angiospermophyta (flowering plants)

Animal phyla

- Porifera, Cnidaria, Platyhelminthes, Mollusca, Annelida, Arthropoda

see p. 267 for full table

Vertebrates

- most species of chordate belong to one of five major classes: bony ray-finned fish, amphibians, reptiles, birds, mammals
- all are vertebrates because they have backbones composed of vertebrae

see p. 268 for full table

5.4 Cladistics

Primate cladograms

- closest relatives of humans are chimpanzees and bonobos
- numbers on cladograms show estimates of population sizes and dates when splits occurred
- based on a molecular clock
- primates are an order of mammals that have adaptations for climbing trees

Classification of the figworts family

- more than 400 families of angiosperm
- figwort family was based on morphology and continuously enlarged with new species
- taxonomists investigated the evolutionary origins and compared base sequences: found that species in figwort family were not a true called and five clades had been incorrect combined
- major reclassification and less than half was retained in the family

6 Human physiology

6.1 Digestion and absorption

Starch digestion in the small intestine

- starch digestion illustrates catalysis, enzyme specificity, membrane permeability
- starch is a macromolecule composed of many α-glucose monomers
- cannot pass through membranes and must be digested in the small intestine for absorption
- reactions in digestion of starch are exothermic but happen at very slow rates without a catalyst
- amylase begins the digestion of amylose and amylopectin; most occurs in the small intestine catalyzed by pancreatic amylase
- any 1,4 bond can be broken down by amylase, so amylose is broken down into maltose and maltotriose; 1,6 cannot be broken down by amylase
- fragments remaining of amylopectin are called dextrins
- digestion of starch is completed by three enzymes in membranes of microvilli: maltase, glucosidase, dextrinase digest maltose, maltotriose, dextrins to glucose
- glucose is absorbed into villus epithelium cells by co-transport with sodium ions, then moves by facilitated diffusion into fluid in interstitial spaces in the villus
- close capillaries in epithelium ensure that glucose only has to travel short distance
- capillary walls consist of a single layer of thin cells with pores between adjacent cells
- blood carrying glucose and other products of digestion flows through villus capillaries to venules in sub-mucosa of wall of small intestine; blood in venules is carried via hepatic portal vein to the liver
- excess glucose can be absorbed by liver cells and converted to glycogen for storage

Modeling the small intestine

- to make a model of the small intestine, a dialysis tube is taken; suitable mixture is taken and knotted at both ends
- can be used to model the need for digestion or membrane permeability

6.2 The blood system

William Harvey and the circulation of blood

- William Harvey is usually credited with the discovery of the circulation of blood
- toured Europe to show experiments and this makes it generally accepted
- demonstrates that flow is unidirectional with valves that prevent backflow, rate of flow would not allow blood to be digested and so must be recycled and return to the heart, heart pumps blood in arteries and it returns in veins, predicts presence of fine vessels linking arteries to veins
- blood capillaries are too small to be seen and the microscope was only invented after his death

Atherosclerosis

- development of fatty tissue (atheroma) in the artery wall adjacent to the endothelium
- low density lipoproteins (LDL) containing fat and cholesterol accumulate which attracts phagocytes: these engulf them by endocytosis and grow very large
- artery wall bulges into the lumen, narrowing it and impeding blood flow
- in older people it can get advanced, goes unnoticed and blocks a major vessel and the tissues it supplies become comprised
- coronary occlusion is narrowing of arteries that supply blood containing oxygen and nutrients to the heart muscle; lack of oxygen (anoxia) causes pain and impairs ability to contract: heart beats faster to maintain blood circulation
- factors increasing risk: LDL, chronic high blood glucose concentrations, chronic high blood pressure (smoking), consumption of trans fats, infection of artery wall

The cardiac cycle

- pressure changes in atrium, ventricle and aorta happen in following steps
- atria contract: rapid but small pressure increase, pumps blood from atria to ventricles through open atrioventricular valves; semilunar valves are closed so blood pressure in arteries drops

- ventricles contract with rapid pressure build up causing atrioventricular valves to be closed; semilunar valves remain closed
- pressure in ventricles rises above pressure in arteries and semilunar valves open and blood is pumped from ventricles to arteries; pressure in atria slowly rises
- semilunar valves close as pressure in ventricles drops below arterial pressure; atrioventricular valves remain closed
- pressure in ventricles drops below pressure un atria and atrioventricular valves open; blood from veins drains into atria and from there to ventricles causing slow pressure increase

6.3 Defense against infectious disease

Coronary thrombosis

- blood clots form in coronary arteries in patients with coronary heart disease
- these arteries branch off from aorta close to semilunar valve; supply oxygen and nutrients to cardiac muscle fibers for cell respiration
- medical name for blood clot: thrombus
- coronary thrombosis: formation of blood clots in the coronary arteries
- if coronary arteries are blocked, part of heart is deprived of oxygen and nutrients: unable to produce sufficient ATP: contractions become irregular and uncoordinated
- heart starts making quivering movements called fibrillation
- atherosclerosis causes occlusion in the coronary arteries; where atheroma develops endothelium of arteries become roughened and artery wall is hardened by deposition of calcium salts; patches rupture causing lesion; all of these increase risk of coronary thrombosis
- risks: smoking, high blood cholesterol concentration, high blood pressure, diabetes, obesity

Human immunodeficiency virus

- production of antibodies by immune system is complex and includes different lymphocytes
- HIV destroys helper T-cells: consequence is progressive loss to produce antibodies
- in early stages immune system makes HIV-antibodies; if these are found a person is said to be HIV-positive
- HIV is a retrovirus: has genes made of RNA and uses reverse transcriptase to make DNA copies of its genes once in a host cell
- antibody production eventually becomes ineffective
- accumulation of diseases or conditions existing together are called a syndrome
- when the syndrome of conditions is present: acquired immune deficiency syndrome (AIDS)
- AIDS is spread by HIV infection; virus only survives outside of a body for a short time
- infection normally occurs if there is blood to blood contact; sexual intercourse, transfusion of blood, sharing of hypodermic needles

Testing penicillin

- Howard Florey and Ernst Chain investigate use of chemical substances to control bacterial infections; most promising is penicillin
- develop method for growing the fungus in conditions that stimulate it to secrete penicillin and also methods for producing reasonably pure samples
- penicillin kills bacteria on agar plates; test whether it can control bacteria in humans
- first test it on mice: works; for humans they need larger quantities
- test it on policeman: works but supplies run out and he dies
- proved highly effective against previously incurable infections

6.4 Gas exchange

Antagonistic muscle action in ventilation

- ventilation involves two pairs of opposite movements that change the volume
- inspiration: diaphragm moves down and flattens, ribcage moves up and out
- expiration: diaphragm moves up into a dome, ribcage moves down and in
- antagonistic muscles are needed to cause these movements
- movement of diaphragm: diaphragm itself and abdomen wall muscles
- movement of ribcage: external (inhalation) and internal (exhalation) intercostal muscles

Causes of lung cancer

- smoking causes 87% of cases; tobacco smoke contains mutagenic chemicals
- passive smoking causes 3% of cases
- air pollution causes 5% of cases; mostly vehicle exhausts and burning of organic matter
- on construction sites, solids in dust form can cause lung cancer
- in many cases it is discovered at a late stage; mortality rates are high; consequences are severe
- if a patient is cured, he will continue to have pain, breathing difficulties

Emphysema

- healthy lung tissue: bronchioles lead to group of smaller thin-walled alveoli
- emphysema: alveoli are replaced with larger air sacs with a thicker wall: total surface area for gas exchange is considerably lower; lung is also less elastic so ventilation is more difficult
- phagocytes normally prevent infections by engulfing bacteria and produce elastase (protein-digesting enzyme) to kill them
- enzyme inhibitor called alpha 1-antitrypsin (A1AT) usually prevents elastase to digest lung tissue; in smokers the number of phagocytes increases and produce more elastase
- emphysema is a chronic disease and damage is irreversible; causes low oxygen saturation

6.5 Neurons and synapses

Neonicotinoids

- synthetic compound similar to nicotine; bind to the acetylcholine receptor in cholinergic synapses in the central nervous system
- acetylcholinesterase does not break down neonicotinoids, so binding is irreversible: acetylcholine is unable to bind and synaptic transmission isn prevented
- consequence in insects is paralysis and death: effective insecticides
- not highly toxic to humans: much greater proportion of synapses in mammals and they bind much less strongly to acetylcholine receptors
- mainly used on crops; concerns about beneficial insects (honeybees)

6.6 Hormones, homeostasis and reproduction

Diabetes

- condition where a person has consistently elevated blood glucose levels; presence of glucose in urine; elevated glucose damages tissues, particularly their proteins; impairs water reabsorption from kidney resulting in large urine volume and dehydration
- two main types: type I diabetes and type II diabetes
- type I: early onset, inability to produce sufficient quantities of insulin; autoimmune disease: immune system destroys beta cells in islets of Langerhans
- type II: late onset, inability to process or respond to insulin due to deficiency of insulin receptors or glucose transporters on target cells; risk factors are sugary, fatty diets
- treatment of type I: testing blood for glucose regularly and injecting insulin if it is high or likely to become high (before meals); timing is important as insulin molecules do not last long
- treatment of type II: adjustment of diet; eat multiple times in small amounts rather than a couple of large meals; avoid foods with high sugar content; only eat starch if it is digested slowly

Leptin and obesity

- attempts to treat obesity in humans by injecting leptin (as in mice experiments)
- volunteers were taken, some with leptin and some with placebo; double blind procedure was used, so neither patients nor doctors knew who had which treatment
- leptin injections caused skin irritation and swelling
- results varied with loss and gain of weight; body mass lost was usually gained rapidly after that
- humans have high blood leptin concentrations but target cells in hypothalamus may have become resistant and do not respond: appetite is therefore not inhibited
- leptin is a short-lived protein and has to be injected several times a day
- leptin was shown to affect development and functioning of reproductive systems

Jet lag and melatonin

- symptoms are difficulty to remain awake during day and difficulty sleeping during night

- the suprachiasmatic nuclei (SCN in hypothalamus) and pineal gland are continuing to set a circadian rhythm to suit timing of the day and night at pint of departure
- jet lag only last for a few days until ganglion cells in retina adjust the SCN to new rhythm
- melatonin is used to prevent jet lag; taken when sleep should begin
- most trials are effective and reduce jet lag

In vitro fertilization

- natural method of fertilization is in vivo (in the body)
- fertilization can occur outside of the body in controlled laboratory conditions (in vitro)
- used to overcome fertility problems of either male or female parent
- first stage is down-regulation: woman takes a drug that stops pituitary gland to secrete FSH or LH: secretion of estrogen and progesterone stops: suspends normal menstrual cycle
- intramuscular injections of FSH and LH are given to stimulate follicle development; higher FSH concentrations are given so more follicles develop (super-ovulation)
- then follicles are stimulated to mature by injecting HCG and a micropipette is passed through uterus wall to wash eggs out of follicles
- each egg cells is mixed with 50’000 to 100’000 sperm in sterile conditions in a shallow dish
- if fertilization is successful, one or more embryos are placed into the uterus
- extra progesterone is given to maintain the uterus lining
- following pregnancy is no different than that by natural conception

William Harvey and sexual reproduction

- known for discovery of blood circulation; also pioneered into sexual reproduction
- Harvey tests Aristotle’s “seed and soil” (male produces seed, develops into egg and is then mixed with menstrual blood and develops into fetus in mother) using deer which are seasonal breeders and are only sexually active in autumn
- slaughters and dissects female deer during mating season; expects to find eggs in uterus immediately after mating but only finds signs of anything developing only after multiple months
- Harvey’s conclusion that fetus does not result from events during coitus is also wrong