Amgen Biotech Experience

Scientific Discovery for the Classroom

United Kingdom

Review of the Molecular Biology and Biotechnology content of the new GCE AS and A level Biology exam specifications and how they complement the UK Amgen Biotech Experience (ABE) programme

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Objectives

From September 2015, the GCE AS and A level Biology requirements for teaching and learning, set out by the Department for Education, are changing. Exam structure, assessment of practical work, necessary acquisition of skills and subject content knowledge requirements have been revised. To ensure that the ABE programme in the UK remains relevant within schools and colleges, this document aims:

- to examine the Molecular Biology and Biotechnology content in the new GCE AS and A-level specifications for teaching from September 2015.
- to determine how the ABE programme in the UK complements the subject content knowledge and practical work requirements in this field.

GCE AS and A level Biology requirements

A summary of the areas of required subject knowledge and practical skills from the '*GCE AS and A level subject content for biology, chemistry, physics and psychology*' document issued by the Department for Education in April 2014[A], is shown in Table 1. In addition to information on the aims of the qualifications and skills intended to be taught, this document specifies 60% of the knowledge and understanding content for GCE AS and A level Biology qualifications. Exam boards can adapt the remaining 40% of knowledge and understanding required to best suit their qualification.

One major change is the inclusion of 'core' or 'required' practical activities. Relevant examples of these are included in Table 1 alongside the prescribed subject knowledge and understanding.

Another change will be the introduction of exam questions requiring longer answers, intended to improve the teaching and learning of links between the different topic areas.

As in the original document AS level requirements are in normal lettering and A level requirements are shown in bold font.

GCE AS and A level Biology requirements
12. Includes; • The living world can be studied at population, organism, cell and molecular levels. There are fundamental similarities as well as differences between plants, animals and microorganisms. 13. Biodiversity, includes; • the variety of life, both past and present, is extensive, but the biochemical basis of life is similar for all living things • biodiversity can be measured, for example within a habitat or at the genetic level 16. Biological molecules, includes; • in living organisms nucleic acids (DNA and RNA), carbohydrates, proteins, lipids, inorganic ions and water all have important roles and functions related to their properties • the sequence of bases in the DNA molecule determines the structure of proteins, including enzymes **18. Control systems, includes;** • **the genome is regulated by a number of factors** **19. Genetics and evolution** • **sequencing projects have read the genomes of organisms ranging from microbes and plants to humans. This allows the sequences of the proteins that derive from the genetic code to be predicted** • **gene technologies allow study and alteration of gene function in order to better understand organism function and to design new industrial and medical processes** 'Appendix 5c – Use of apparatus and techniques – biology', includes practical work requirements to; • use laboratory glassware apparatus for a variety of experimental techniques to include serial dilutions • use qualitative reagents to identify biological molecules • separate biological compounds using thin layer/paper chromatography or electrophoresis • use microbiological aseptic techniques, including the use of agar plates and broth

Table 1. Areas of required subject knowledge and practical skills relating to Molecular Biology and Biotechnology, taken from the '*GCE AS and A level subject content for biology, chemistry, physics and psychology*' document issued by the Department for Education[A].

Approach

The knowledge and understanding required about Molecular Biology and Biotechnology in the new GCE AS and A levels from September 2015, will be identified in the exam specifications from the three main GCE AS and A level Biology exam boards in the UK: AQA, Edexcel and OCR. AQA published their AS and A level Biology exam specification, on the 16th September 2014[B]. Edexcel offer two different specifications. Biology A (Salters-Nuffield) adopts a more practical approach[C], and Biology B a more topic-based framework[D]. OCR also offer two alternative exam specifications. Biology A adopts a topic-based framework[E], and Biology B (Advancing Biology) offers learners a 'context-based approach'[F].

When analysing the content of the new exam specifications, 8 categories will be used. The categories (shown below) were chosen from the information in Table 1 and previous experience of the exam specifications, and will be used to examine in more details the precise specification requirements relating to Molecular Biology and Biotechnology. Although inheritance, the processes of mitosis and meiosis and the genetic basis of evolution also relate to genetic material, they are not included in this analysis, as they cover subject material less relevant to the Biotechnology theme of the ABE programme.

1. DNA structure
2. DNA replication
3. DNA mutation
4. Protein synthesis (DNA transcription and translation)
5. Gene regulation (transcription factors, operons, epigenetics)
6. Practical techniques, including: agarose gel electrophoresis, DNA sequencing, PCR, DNA profiling, bacterial growth/culture
7. Genome analysis, including; genome sequencing, DNA profiling, further applications
8. Recombinant DNA technologies including; restriction enzymes, ligation, plasmid vectors, transformation, biotechnology/GMO examples

Exam specification summary

In this section data from the exam specification analyses, shown in Appendices 1-5, is used to provide specific information about: when subject content relevant to the ABE programme is taught and what requirement there is for molecular biology practical work. The following section then examines the overlap between the ABE programme knowledge content and that in the exam specifications.

When is subject content relevant to the ABE programme taught?

The 8 categories of subject content previously identified as being relevant to the ABE programme (in the Approach section), were analysed for whether they were taught at AS or A level in the 5 exam specifications from the UK's three main exam boards. Results are shown in Table 2 below.

Content	Exam specifications				
	AQA	Edexcel A	Edexcel B	OCR A	OCR B
Structure of DNA, RNA and protein	AS	AS	AS	AS	AS
DNA replication	AS	AS	AS	AS	AS
DNA mutation	AS/A	AS	AS/A	A	AS/A
Protein synthesis	AS	AS	AS	AS	AS
Gene regulation	A	AS/A	A	A	A
Practical techniques	A	A	AS/A	A	AS/A
Genome analysis	AS/A	AS/A	A	A	AS/A
Recombinant DNA technologies	A	A	A	A	A

Table 2. The timing for teaching and learning of subject content knowledge specified in different exam board's specifications. Blue is AS. Green is both AS and A level. Yellow is A level.

All 5 exam specifications examined address: the structure of DNA, RNA and protein; DNA replication, and; protein synthesis, exclusively at AS level. The topic of mutation is sometimes taught alongside structural information, and sometimes with genetic variation, replication, protein synthesis, or specific (usually health-related) examples. As a consequence the timing at which subject knowledge about mutation is introduced varies. Nevertheless, students should have covered subject content knowledge in these first 4 areas prior to progressing on to subject content knowledge about gene regulation, molecular biology practical techniques, genomes and recombinant DNA technologies.

The 2 categories that best fit with the ABE programme – practical techniques and recombinant DNA technologies - are taught primarily at A level, that is to students in year 13. So, as with the previous exam specifications, use of the ABE programme is likely to fit best with the teaching of A level content to Year 13 students.

What requirement is there for molecular biology practical work?

It is immediately apparent from the size of the appendices that a considerable amount of the exam specifications relates to the 8 molecular biology categories used. However, the requirement for practical work to accompany these topics remains low, probably at least in part due to the large financial costs and training requirements that would be required to enable all teachers to provide these opportunities for their students.

In the '*GCE AS and A level subject content for biology, chemistry, physics and psychology*' document, Appendix 5c – Use of apparatus and techniques – biology guidance (shown in Table 1), there is a requirement for a practical activity to 'separate biological compounds using thin layer/paper chromatography **or electrophoresis**' (my emphasis). The majority of the exam specifications have opted to adopt thin layer chromatography as their specialist technique (possibly because it requires less expensive, specialist equipment).

In contrast the Edexcel Biology A (Salters-Nuffield) specification requires students to '**Use gel electrophoresis to separate DNA fragments of different length**', as **core practical 14** (my emphasis again), contained in unit 6: Immunity, infection and forensics. The other 4 specifications examined do highlight when electrophoresis could be performed (as part of: AQA, 3.8.4.3 Genetic fingerprinting; Edexcel Biology B, 3.1 classification or 7.1 Using gene sequencing; OCR Biology A, 6.1.3 Manipulating genomes, and; OCR Biology B (Advancing Biology) 5.1.3 Gene technologies). Both OCR exam specifications require practical investigations into the purification of DNA by precipitation.

The Edexcel Biology B has the greatest amount of practical work with microbes of any of the specifications examined (section 6.1 Microbial techniques), requiring streak plating of bacteria and growth of bacteria in liquid culture (core practicals 13 and 12, respectively).

For the majority of students, this means that the chance to undertake molecular biology work at this stage of their education will remain limited unless (i) they study the Edexcel Biology A (Salters-Nuffield) course, or (ii) they have an enthusiastic and skilled teacher with access to the necessary equipment and consumables.

Alignment with activities offered by the ABE programme

The ABE programme is primarily designed to train and support teachers and technicians, as they enable students to experience practical biotechnology in the classroom. Practical opportunities are provided for students to undertake a series of molecular biology procedures used in the 'real world', using laboratory standard equipment. Whilst completing a series of specialised molecular biology techniques used in the production of protein therapeutics, the ABE programme aims:

- to increase student motivation
- to provide links to 'real world' science
- to strengthen knowledge and understanding of subject content
- to increase practical skills with specialist equipment and techniques
- to improve data interpretation skills
- to help students to consider their experimental work analytically to explain their results

In the UK it is vital that the ABE programme is linked to the Ofqual-accredited, exam specifications, as teaching time for GCE AS and A level Biology is limited and subject material related to exam content is more likely to be used by teachers. To determine how the ABE programme in the UK complements the subject content knowledge and practical work requirements in this field, subject content directly linked to specialist practical skills offered by the ABE programme was listed and compared to the subject knowledge content of the exam board specifications. The results are given on the next page, in Table 3.

In addition to the subject knowledge content that links directly to the ABE programme, the sequence of practical activities will require students to make links between: DNA structure, particularly the hydrogen bonding between bases; protein synthesis; the universality of the genetic code; DNA replication; DNA mutation as a part of directed evolution; transcriptional control of gene expression; the nature of restriction enzyme recognition sequences; the importance of promoters, start and stop codons; the use of reverse transcriptase in production of recombinant DNA; production of personalised medicine (protein therapeutics) using genome sequences as a basis; modes of antibiotic action; safe handling of micro-organisms, and; ethical and social issues surrounding the use of GMOs. All of these occur in the exam specifications analysed.

ABE programme content	Exam specifications				
	AQA	Edexcel A	Edexcel B	OCR A	OCR B
Micropipetting and volumetrics					
Vectors – plasmids					
Restriction enzymes					
Ligases					
Production of recombinant DNA					
Agarose gel electrophoresis		✦			
Bacterial transformation					
Selection marker genes					
Extraction of genomic DNA				✦	✦
Polymerase Chain Reaction (PCR)					
DNA profiling					
Production of protein therapeutics leading to personalised medicine					

Table 3. Linking the molecular biology content of the ABE programme to that required in the exam specifications. Green means this content is included. Red means that it is not. ✦ denotes that students are required to experience this practical technique.

A reverse analysis, linking the ABE programme to the Molecular Biology and Biotechnology content of the GCE AS and A level Biology exam specifications offered by the 3 main exam boards in the UK, was also undertaken. The results from this are shown in Table 4, on the next page. As longer exam questions, linking different areas of the exam modules or units are introduced, the ABE provides an excellent framework giving students the opportunity to make connections and metacognitive links between different areas of Molecular Biology.

Additional learning benefits from participation in the ABE programme have not been quantitated. However, it is known that student antipathy can be encountered In the area of Biotechnology[G], possibly due to the lack of links to 'the real world' or practical opportunities. Here in the UK, as in the US programme, we have found that getting 'hands on' with laboratory standard equipment and performing 'the sorts of stuff you see on the TV', has benefits in terms of student motivation[H], which is likely to impact on students' desire and willingness to learn. Certainly it provides participants with desirable Molecular Biology skills and experience of analysing experimental work to explain results for the scientific workplace. It can also offer insights into a range of career options.

Content	ABE programme provides
Structure of DNA, RNA and protein	Link to topic Context and relevance
DNA replication	Link to topic Context and relevance
DNA mutation	Link to topic Context and relevance
Protein synthesis	Link to topic Context and relevance Simulation/modelling exercise Practical work
Gene regulation	Link to topic Context and relevance Practical work
Practical techniques	Link to topic Context and relevance Simulation/modelling exercise Practical work
Genome analysis	Link to topic Context and relevance Practical work
Recombinant DNA technologies	Link to topic Context and relevance Simulation/modelling exercise Practical work

Table 4. Links between UK exam specification subject knowledge content and the ABE programme.

Conclusions

For the first time one of the 3 main exam boards in the UK has made gel electrophoresis a ‘core’ or ‘required’ practical activity for A level Biology students. The ABE programme is well-positioned to support this requirement. For the other exam specifications the practical activities offered by the ABE programme align well with the required subject knowledge content on Molecular Biology and Biotechnology. In fact they present a relevant and popular framework that provides students with opportunities to make metacognitive links between different areas of the exam specifications, a beneficial activity in composing responses to the longer answer questions being introduced in exams.

References

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Appendix 1. Exam specification analysis: AQA.

The exam board AQA published it's AS and A level Biology specification[B], for teaching from September 2015 onwards, on the 16th September 2014. Content in the topic areas is given below. As in Table 1, A-level material is given in bold font.

Topic area	AQA specification
Structure of DNA, RNA and proteins	3.1.4.1 General properties of proteins • Amino acids are the monomers from which proteins are made. The general structure of an amino acid, where NH_2 represents an amine group, COOH represents a carboxyl group and R represents a carbon-containing side chain. • The twenty amino acids that are common in all organisms differ only in their side group. • A condensation reaction between two amino acids forms a peptide bond. • Dipeptides are formed by the condensation of two amino acids. • Polypeptides are formed by the condensation of many amino acids. • A functional protein may contain one or more polypeptides. • The role of hydrogen bonds, ionic bonds and disulfide bridges in the structure of proteins. • Proteins have a variety of functions within all living organisms. The relationship between primary, secondary, tertiary and quaternary structure, and protein function. • The biuret test for proteins. • Students should be able to relate the structure of proteins to properties of proteins named throughout the specification. 3.1.5.1 Structure of DNA and RNA • Deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) are important information-carrying molecules. In all living cells, DNA holds genetic information and RNA transfers genetic information from DNA to the ribosomes. • Ribosomes are formed from RNA and proteins. • Both DNA and RNA are polymers of nucleotides. Each nucleotide is formed from a pentose, a nitrogen-containing organic base and a phosphate group: • The components of a DNA nucleotide are deoxyribose, a phosphate group and one of the organic bases adenine, cytosine, guanine or thymine. • The components of an RNA nucleotide are ribose, a phosphate group and one of the organic bases adenine, cytosine, guanine or uracil. • A condensation reaction between two nucleotides forms a phosphodiester bond. • A DNA molecule is a double helix with two polynucleotide chains held together by hydrogen bonds between specific complementary base pairs. • An RNA molecule is a relatively short polynucleotide chain.

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Topic area	AQA specification
	• Students should be able to appreciate that the relative simplicity of DNA led many scientists to doubt that it carried the genetic code. 3.4.1 DNA, genes and chromosomes • In prokaryotic cells, DNA molecules are short, circular and not associated with proteins. • In the nucleus of eukaryotic cells, DNA molecules are very long, linear and associated with proteins, called histones. Together a DNA molecule and its associated proteins form a chromosome. • The mitochondria and chloroplasts of eukaryotic cells also contain DNA which, like the DNA of prokaryotes, is short, circular and not associated with protein. A gene is a base sequence of DNA that codes for: the amino acid sequence of a polypeptide; a functional RNA (including ribosomal RNA and tRNAs). • A gene occupies a fixed position, called a locus, on a particular DNA molecule. • A sequence of three DNA bases, called a triplet, codes for a specific amino acid. • The genetic code is universal, non-overlapping and degenerate. • In eukaryotes, much of the nuclear DNA does not code for polypeptides. There are, for example, non-coding multiple repeats of base sequences between genes. Even within a gene only some sequences, called exons, code for amino acid sequences. Within the gene, these exons are separated by one or more non-coding sequences, called introns.
DNA replication	3.1.5.2 DNA replication • The semi-conservative replication of DNA ensures genetic continuity between generations of cells. • The process of semi-conservative replication of DNA in terms of: unwinding of the double helix; breakage of hydrogen bonds between complementary bases in the polynucleotide strands; the role of DNA helicase in unwinding DNA and breaking its hydrogen bonds; attraction of new DNA nucleotides to exposed bases on template strands and base pairing; the role of DNA polymerase in the condensation reaction that joins adjacent nucleotides. • Students should be able to evaluate the work of scientists in validating the Watson–Crick model of DNA replication. 3.2.2 All cells arise from other cells • Eukaryotic cells that do retain the ability to divide show a cell cycle. • DNA replication occurs during the interphase of the cell cycle. • Mitosis is the part of the cell cycle in which a eukaryotic cell divides to produce two daughter cells, each with the identical copies of DNA produced by the parent cell during DNA replication. • Binary fission in prokaryotic cells involves: replication of the circular DNA and of plasmids; division of the cytoplasm to produce two daughter cells, each with a single copy of the circular DNA and a variable number of copies of plasmids.
DNA mutation	3.4.3 Genetic diversity can arise as a result of mutation or during meiosis

Topic area	AQA specification
	• Gene mutations involve a change in the base sequence of chromosomes. They can arise spontaneously during DNA replication and include base deletion and base substitution. Due to the degenerate nature of the genetic code, not all base substitutions cause a change in the sequence of encoded amino acids. Mutagenic agents can increase the rate of gene mutation. 3.**8.1 Alteration of the sequence of bases in DNA can alter the structure of proteins** • **Gene mutations might arise during DNA replication. They include addition, deletion, substitution, inversion, duplication and translocation of bases.** • **Gene mutations occur spontaneously. The mutation rate is increased by mutagenic agents. Mutations can result in a different amino acid sequence in the encoded polypeptide.** • **Some gene mutations change only one triplet code. Due to the degenerate nature of the genetic code, not all such mutations result in a change to the encoded amino acid.** • **Some gene mutations change the nature of all base triplets downstream from the mutation, ie result in a frame shift.** • **Students should be able to relate the nature of a gene mutation to its effect on the encoded polypeptide.**
Protein synthesis	3.4.2 DNA and protein synthesis • The concept of the genome as the complete set of genes in a cell and of the proteome as the full range of proteins that a cell is able to produce. • The structure of molecules of messenger RNA (mRNA) and of transfer RNA (tRNA). • Transcription as the production of mRNA from DNA. The role of RNA polymerase in joining mRNA nucleotides. • In prokaryotes, transcription results directly in the production of mRNA from DNA. • In eukaryotes, transcription results in the production of pre-mRNA; this is then spliced to form mRNA. • Translation as the production of polypeptides from the sequence of codons carried by mRNA. The roles of ribosomes, tRNA and ATP. • Students should be able to: relate the base sequence of nucleic acids to the amino acid; sequence of polypeptides, when provided with suitable data about the genetic code; interpret data from experimental work investigating the role of nucleic acids. • Students will not be required to recall in written papers specific codons and the amino acids for which they code.
Gene regulation	**3.8.2.2 Regulation of transcription and translation** • **In eukaryotes, transcription of target genes can be stimulated or inhibited when specific transcriptional factors move from the cytoplasm into the nucleus. The role of the steroid hormone, oestrogen, in initiating transcription.** • **Epigenetic control of gene expression in eukaryotes.**

Topic area	AQA specification
	• **Epigenetics involves heritable changes in gene function, without changes to the base sequence of DNA. These changes are caused by changes in the environment that inhibit transcription by: increased methylation of the DNA or decreased acetylation of associated histones.** • **The relevance of epigenetics on the development and treatment of disease, especially cancer.** • **In eukaryotes and some prokaryotes, translation of the mRNA produced from target genes can be inhibited by RNA interference (RNAi).** • **Students should be able to: interpret data provided from investigations into gene expression; evaluate appropriate data for the relative influences of genetic and environmental factors on phenotype.** **3.8.2.3 Gene expression and cancer** • **The main characteristics of benign and malignant tumours.** • **The role of the following in the development of tumours: tumour suppressor genes and oncogenes; abnormal methylation of tumour suppressor genes and oncogenes; increased oestrogen concentrations in the development of some breast cancers.** • **Students should be able to: evaluate evidence showing correlations between genetic and environmental factors and various forms of cancer; interpret information relating to the way in which an understanding of the roles of oncogenes and tumour suppressor genes could be used in the prevention, treatment and cure of cancer.**
Practical techniques	**3.8.4.2 Differences in DNA between individuals of the same species can be exploited for identification and diagnosis of heritable conditions** • **The use of labelled DNA probes and DNA hybridisation to locate specific alleles of genes.** • **The use of labelled DNA probes that can be used to screen patients for heritable conditions, drug responses or health risks.** • **The use of this information in genetic counselling and personalised medicine.** • **Students should be able to evaluate information relating to screening individuals for genetically determined conditions and drug responses.** **3.8.4.3 Genetic fingerprinting** • **An organism's genome contains many variable number tandem repeats (VNTRs). The probability of two individuals having the same VNTRs is very low.** • **The technique of genetic fingerprinting in analysing DNA fragments that have been cloned by PCR, and its use in determining genetic relationships and in determining the genetic variability within a population.** • **The use of genetic fingerprinting in the fields of forensic science, medical diagnosis, animal and plant breeding.** • **Students should be able to: explain the biological principles that underpin genetic fingerprinting techniques;**

Topic area	AQA specification
	interpret data showing the results of gel electrophoresis to separate DNA fragments; explain why scientists might use genetic fingerprinting in the fields of forensic science, medical diagnosis, animal and plant breeding.
Genome analysis	3.4.7 Investigating diversity • Genetic diversity within, or between species, can be made by comparing: the frequency of measurable or observable characteristics; the base sequence of DNA; the base sequence of mRNA; the amino acid sequence of the proteins encoded by DNA and mRNA. • Students should be able to: interpret data relating to similarities and differences in the base sequences of DNA and in the amino acid sequences of proteins to suggest relationships between different organisms within a species and between species; appreciate that gene technology has caused a change in the methods of investigating genetic diversity; inferring DNA differences from measurable or observable characteristics has been replaced by direct investigation of DNA sequences. • Knowledge of gene technologies will not be tested. **3.8.3 Using genome projects** • **Sequencing projects have read the genomes of a wide range of organisms, including humans.** • **Determining the genome of simpler organisms allows the sequences of the proteins that derive from the genetic code (the proteome) of the organism to be determined. This may have many applications, including the identification of potential antigens for use in vaccine production.** • **In more complex organisms, the presence of non-coding DNA and of regulatory genes means that knowledge of the genome cannot easily be translated into the proteome.** • **Sequencing methods are continuously updated and have become automated.**
Recombinant DNA technologies	**3.6.4.2 Control of blood glucose concentration** • **The causes of types I and II diabetes and their control by insulin and/or manipulation of the diet.** **3.8.4.1 Recombinant DNA technology** • **Recombinant DNA technology involves the transfer of fragments of DNA from one organism, or species, to another. Since the genetic code is universal, as are transcription and translation mechanisms, the transferred DNA can be translated within cells of the recipient (transgenic) organism.** • **Fragments of DNA can be produced by several methods, including: conversion of mRNA to complementary DNA (cDNA), using reverse transcriptase; using restriction enzymes to cut a fragment containing the desired gene from DNA; creating the gene in a 'gene machine'.** • **Fragments of DNA can be amplified by *in vitro* and *in vivo* techniques.** • **The principles of the polymerase chain reaction (PCR) as an *in vitro* method to amplify DNA fragments.**

Topic area	AQA specification
	• **The culture of transformed host cells as an *in vivo* method to amplify DNA fragments.** • **The addition of promoter and terminator regions to the fragments of DNA.** • **The use of restriction endonucleases and ligases to insert fragments of DNA into vectors. Transformation of host cells using these vectors.** • **The use of marker genes to detect genetically modified (GM) cells or organisms. (Students will not be required to recall specific marker genes in a written paper.)** • **Students should be able to: interpret information relating to the use of recombinant DNA technology; evaluate the ethical, financial and social issues associated with the use and ownership of recombinant DNA technology in agriculture, in industry and in medicine; balance the humanitarian aspects of recombinant DNA technology with the opposition from environmentalists and antiglobalisation activists; relate recombinant DNA technology to gene therapy.**

Appendix 2. Exam specification analysis: Edexcel Biology A (Salters-Nuffield).

The exam board Edexcel published it's AS and A level Biology A (Salters-Nuffield) specification[C], for teaching from September 2015 onwards, in 2014. Content in the topic areas is given below. As in Table 1, A-level material is given in bold font.

Topic area	Edexcel Biology A (Salters-Nuffield) specification
Structure of DNA, RNA and proteins	2.5 and 2.9 from Genes and Health • Know the basic structure of mononucleotides (deoxyribose or ribose linked to a phosphate and a base, including thymine, uracil, cytosine, adenine or guanine) and the structures of DNA and RNA (polynucleotides composed of mononucleotides linked through condensation reactions). • Know how complementary base pairing and the hydrogen bonding between two complementary strands are involved in the formation of the DNA double helix. • Know the basic structure of an amino acid (structures of specific amino acids are not required). • Understand the formation of polypeptides and proteins (amino acid monomers linked by peptide bonds in condensation reactions). • Understand the significance of a protein's primary structure in determining its three-dimensional structure and properties (globular and fibrous proteins and the types of bonds involved in its three-dimensional structure). • Know the molecular structure of a globular protein and a fibrous protein and understand how their structures relate to their functions (including haemoglobin and collagen).
DNA replication	2.11 from Genes and Health • Understand the process of DNA replication, including the role of DNA polymerase. • Understand how Meselson and Stahl's classic experiment provided new data that supported the accepted theory of replication of DNA and refuted competing theories.
Protein synthesis	2.6, 2.7 and 2.8 from Genes and Health • Understand the process of protein synthesis (transcription) including the role of RNA polymerase, translation, messenger RNA, transfer RNA, ribosomes and the role of start and stop codons. • Understand the roles of the DNA template (antisense) strand in transcription, codons on messenger RNA and anticodons on transfer RNA. • Understand the nature of the genetic code (triplet code, non-overlapping and degenerate). • Know that a gene is a sequence of bases on a DNA molecule that codes for a sequence of amino acids in a polypeptide chain.

Topic area	Edexcel Biology A (Salters-Nuffield) specification
Gene regulation	3.12, 3.14 and 3.15 from Voice of the genome • Understand how cells become specialised through differential gene expression, producing active mRNA leading to synthesis of proteins, which in turn control cell processes or determine cell structure in animals and plants, including the lac operon. • Understand how phenotype is the result of an interaction between genotype and the environment. • Know how epigenetic changes, including DNA methylation and histone modification, can modify the activation of certain genes. • Understand how epigenetic changes can be passed on following cell division. • Understand how some phenotypes are affected by multiple alleles for the same gene at many loci (polygenic inheritance) as well as the environment and how this can give rise to phenotypes that show continuous variation. **6.10 from Immunity, infection and forensics** • **Understand how one gene can give rise to more than one protein through posttranscriptional changes to messenger RNA (mRNA).** **7.16 from Run for your life** • **Understand how genes can be switched on and off by DNA transcription factors including hormones.**
Practical techniques	**6.3, 6.4 and CORE PRCATICAL 14 from Immunity, infection and forensics** • **Know how DNA profiling is used for identification and determining genetic relationships between organisms (plants and animals).** • **Know how DNA can be amplified using the polymerase chain reaction (PCR).** • **CORE PRACTICAL 14: Use gel electrophoresis to separate DNA fragments of different length.**
Genome analysis	2.15 and 2.16 from Genes and Health • Understand the uses of genetic screening, including the identification of carriers, pre-implantation genetic diagnosis (PGD) and prenatal testing, including amniocentesis and chorionic villus sampling. • Understand the implications of prenatal genetic screening. • Be able to identify and discuss the social and ethical issues related to genetic screening from a range of ethical viewpoints. **8.16 from Grey matter** • **Understand how the outcomes of genome sequencing projects are being used in the development of personalised medicine and the social, moral and ethical issues this raises.**

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Topic area	Edexcel Biology A (Salters-Nuffield) specification
Recombinant DNA technologies	**8.17 and 8.18 from Grey matter** • **Know how drugs can be produced using genetically modified organisms (plants, animals and microorganisms).** • **Understand the risks and benefits associated with the use of genetically modified organisms.**

Appendix 3. Exam specification analysis: Edexcel Biology B.

The exam board Edexcel published it's AS and A level Biology B specification[D], for teaching from September 2015 onwards, in 2014. Content in the topic areas is given below. As in Table 1 A-level material is given in bold font.

Topic area	Edexcel Biology B specification
Structure of DNA, RNA and proteins	1.3 Proteins • Know the structure of an amino acid (structures of specific amino acids are not required). • Understand the formation of polypeptides and proteins (as amino acid monomers linked by peptide bonds in condensation reactions). • Understand the role of ionic, hydrogen and disulphide bonding in the structure of proteins. • Understand the significance of the primary, secondary, tertiary and quaternary structure of a protein in determining the properties of fibrous and globular proteins, including collagen and haemoglobin. • Understand how the structure of collagen and haemoglobin are related to their function. 1.4 DNA and protein synthesis • Know the structure of DNA, including the structure of the nucleotides (purines and pyrimidines), base pairing, the two sugar-phosphate backbones, phosphodiester bonds and hydrogen bonds. • Know the structure of mRNA including nucleotides, the sugar phosphate backbone and the role of hydrogen bonds. • Know the structure of tRNA, including nucleotides, the role of hydrogen bonds and the anticodon.
DNA replication	1.4 DNA and protein synthesis • Understand how DNA is replicated semi-conservatively, including the role of DNA helicase, polymerase and ligase. • Understand the processes of transcription in the nucleus and translation at the ribosome, including the role of sense and anti-sense DNA, mRNA, tRNA and the ribosomes. • Understand the nature of the genetic code, including triplets coding for amino acids, start and stop codons, degenerate and non-overlapping nature, and that not all the genome codes for proteins.
DNA mutation	1.4 DNA and protein synthesis • Understand the term gene mutation as illustrated by base deletions, insertions and substitutions. • Understand the effect of point mutations on amino acid sequences, as illustrated by sickle cell anaemia in humans. 2.3 Eukaryotic cell cycle and division • Understand that meiosis results in genetic variation through recombination of alleles, including independent assortment and crossing over. • Understand what chromosome mutations are, as illustrated by translocations.

Topic area	Edexcel Biology B specification
	• Understand how non-disjunction can lead to polysomy, including Down's syndrome, and monosomy, including Turner's syndrome. **8.1 Origins of genetic variation** • **Understand that mutations are the source of new variations and that the processes of random assortment and crossing over during meiosis give rise to new combinations of alleles in gametes.** • **Understand how random fertilisation during sexual reproduction brings about genetic variation.**
Protein synthesis	1.4 DNA and protein synthesis • Know that a gene is a sequence of bases on a DNA molecule coding for a sequence of amino acids in a polypeptide chain.
Gene regulation	**7.2 Factors affecting gene expression** • **Know that transcription factors are proteins that bind to DNA.** • **Understand the role of transcription factors in regulating gene expression.** • **Understand how post–transcription modification of mRNA in eukaryotic cells (RNA splicing) can result in different products from a single gene.** • **Understand that gene expression can be changed by epigenetic modification, including non-coding RNA, histone modification and DNA methylation.** • **Know that epigenetic modification is important in ensuring cell differentiation.**
Practical techniques	3.1 Classification • Understand how gel electrophoresis can be used to distinguish between species and determine evolutionary relationships. • Know that DNA sequencing and bioinformatics can be used to distinguish between species and determine evolutionary relationships. **6.1 Microbial techniques** • **Understand the basic aseptic techniques used in culturing organisms.** • **Understand the principles and techniques involved in culturing microorganisms.** • **Understand the use of different media (broth cultures, agar and selective media).** • **Understand the different methods of measuring the growth of a bacterial culture as illustrated by cell counts, dilution plating, mass and optical methods (turbidity).** • **Understand the different phases of a bacterial growth curve (lag phase, log phase, stationary phase and death phase) and calculate exponential growth rate constants.**

Topic area	Edexcel Biology B specification
	• **CORE PRACTICAL 12: Investigate the rate of growth of bacteria in liquid culture taking into account the safe and ethical use of organisms.** • **CORE PRACTICAL 13: Isolate individual species from a mixed culture of bacteria using streak plating taking into account the safe and ethical use of organisms.** **6.3 Action of antibiotics** • **Understand the action of bactericidal and bacteriostatic antibiotics, as illustrated by penicillin and tetracycline.** **7.1 Using gene sequencing** • **Understand how PCR can be used to amplify DNA samples, and how these samples can be used: to predict the amino acid sequence of proteins and possible links to genetically determined conditions, using gene sequencing; in forensic science, to identify criminals and to test paternity, using DNA profiling.**
Genome analysis	**7.1 Using gene sequencing** • **Understand what is meant by the term genome.**
Recombinant DNA technologies	**7.4 Gene technology** • **Understand how recombinant DNA can be produced, including the role of restriction endonucleases and DNA ligase.** • **Understand how recombinant DNA can be inserted into other cells, and the use of various vectors such as viruses and gene guns.** • **Understand how antibiotic resistance marker genes and replica plating are used to identify recombinant cells.** • **Understand how 'knockout' mice can be used as a valuable animal model to investigate gene function.** • **Understand the process of genetic modification of soya beans and how it has been used to improve production, including altering the balance of fatty acids to prevent oxidation of soya products.** • **Understand why the widespread use of genetic modification of major commercial crops and other transgenic processes have caused public debate of their advantages and disadvantages.**

Appendix 4. Exam specification analysis: OCR Biology A.

The exam board OCR published it's AS and A level Biology A specification[E], for teaching from September 2015 onwards, in 2014. Content in the topic areas is given below. As in Table 1, A-level material is given in bold font.

Topic area	OCR Biology A specification
Structure of DNA, RNA and proteins	2.1.2 Biological molecules • the general structure of an amino acid • the synthesis and breakdown of dipeptides and polypeptides, by the formation and breakage of peptide bonds • the levels of protein structure • the structure and function of globular proteins including a conjugated protein • the properties and functions of fibrous proteins 2.1.3 Nucleotides and nucleic acids • the structure of a nucleotide as the monomer from which nucleic acids are made • the synthesis and breakdown of polynucleotides by the formation and breakage of phosphodiester bonds • the structure of ADP and ATP as phosphorylated nucleotides • the structure of DNA (deoxyribonucleic acid) • practical investigations into the purification of DNA by precipitation
DNA replication	2.1.3 Nucleotides and nucleic acids • semi-conservative DNA replication • the nature of the genetic code
DNA mutation	**6.1.1 Cellular control** • **types of gene mutations and their possible effects on protein production and function**
Protein synthesis	2.1.3 Nucleotides and nucleic acids • transcription and translation of genes resulting in the synthesis of polypeptides.
Gene regulation	**6.1.1 Cellular control** • **the regulatory mechanisms that control gene expression at the transcriptional level, post-transcriptional level and post-translational level (To include control at the, transcriptional level: *lac* operon, and transcription factors in eukaryotes. post-transcriptional level: the editing of primary mRNA and the removal of introns to produce mature**

Topic area	OCR Biology A specification
	mRNA. post-translational level: the activation of proteins by cyclic AMP.) • the genetic control of the development of body plans in different organisms (Homeobox gene sequences in plants, animals and fungi are similar and highly conserved AND the role of Hox genes in controlling body plan development)
Practical techniques	**6.1.3 Manipulating genomes** • the principles of the polymerase chain reaction (PCR) and its application in DNA analysis • the principles and uses of electrophoresis for separating nucleic acid fragments or proteins • Opportunity for practical use of electrophoresis.
Genome analysis	**6.1.3 Manipulating genomes** • the principles of DNA sequencing and the development of new DNA sequencing techniques • how gene sequencing has allowed for genome-wide comparisons between individuals and between species • how gene sequencing has allowed for the sequences of amino acids in polypeptides to be predicted • how gene sequencing has allowed for the development of synthetic biology • the principles of DNA profiling and its uses (To include forensics and analysis of disease risk)
Recombinant DNA technologies	**5.1.4 Hormonal communication** • the differences between Type 1 and Type 2 diabetes mellitus • the potential treatments for diabetes mellitus (To include the use of insulin produced by genetically modified bacteria and the potential use of stem cells to treat diabetes mellitus.) **6.1.3 Manipulating genomes** • the principles of genetic engineering (To include the isolation of genes from one organism and the placing of these genes into another organism using suitable vectors.) • the techniques used in genetic engineering (To include the use of restriction enzymes, plasmids and DNA ligase to form recombinant DNA with the desired gene and electroporation.) • the ethical issues (both positive and negative) relating to the genetic manipulation of animals (including humans), plants and microorganisms (To include insect resistance in genetically modified soya, genetically modified pathogens for research and 'pharming' i.e. genetically modified animals to produce pharmaceuticals AND issues relating to patenting and technology transfer e.g. making genetically modified seed available to poor farmers.) **6.2.1 Cloning and biotechnology** • The use of microorganisms in biotechnological processes (To include reasons why microorganisms are used e.g.

Topic area	OCR Biology A specification
	economic considerations, short life cycle, growth requirements AND processes including brewing, baking, cheese making, yoghurt production, penicillin production, insulin production and bioremediation.) • **how to culture microorganisms effectively, using aseptic techniques (An opportunity for serial dilutions and culturing on agar plates.)** • **the importance of manipulating the growing conditions in batch and continuous fermentation in order to maximise the yield of product required** • **the standard growth curve of a microorganism in a closed culture** • **practical investigations into the factors affecting the growth of microorganisms (An opportunity for serial dilutions and the use of broth.)**

Appendix 5. Exam specification analysis: OCR Biology B (Advancing Biology).

The exam board OCR published it's AS and A level Biology B (Advancing Biology) specification[F], for teaching from September 2015 onwards, in 2014. Content in the topic areas is given below. As in Table 1, A-level material is given in bold font.

Topic area	OCR Biology B (Advancing Biology) specification
Structure of DNA, RNA and proteins	2.1.3 Proteins and enzymes • the basic structure of an amino acid and the formation of peptide bonds • the use of chromatography in the separation and identification of amino acids • the molecular structure of globular proteins as illustrated by the structure of enzymes and haemoglobin 2.1.4 Nucleic acids • the structure of a nucleotide as the monomer from which nucleic acids are made • the structure of adenosine di-phosphate (ADP) and adenosine tri-phosphate (ATP) as phosphorylated nucleotides • the structure of the DNA molecule, including a review of the evidence for complementary base pairing (Chargaff's rules) • practical investigation into the purification of DNA by precipitation • the structure of RNA (ribonucleic acid) and how it differs from that of DNA
DNA replication	2.1.4 Nucleic acids • semi-conservative DNA replication • the nature of the genetic code
DNA mutation	3.3.1 The cellular basis of cancer and treatment • how mutations to proto-oncogenes can lead to cancer (To include Ras and Myc proto-oncogenes.) • how mutations to tumour suppressor genes can lead to cancer (To include the p53 gene.) • the evaluation of epidemiological evidence linking potential risk factors with particular forms of cancer (To include smoking and lung cancer, diet and bowel cancer, BRCA1 gene mutations and breast cancer.) **5.1.1 Patterns of inheritance** • **gene mutations (To include cystic fibrosis, sickle cell anaemia, phenylketonuria (PKU) and Huntington's disease.)** • **chromosome mutations in humans (To include non-disjunction and translocations in the context of Turner's syndrome, Klinefelter's syndrome and Down's syndrome.)** **5.1.2 Population genetics and epigenetics** • **the link between the changes in the amino acid sequence to the change in structure and properties of proteins**

Topic area	OCR Biology B (Advancing Biology) specification
	(e.g. haemoglobin)
Protein synthesis	2.1.4 Nucleic acids • transcription and translation of genes resulting in the synthesis of polypeptides.
Gene regulation	**5.1.2 Population genetics and epigenetics** • **epigenetics in terms of the effect of environment on gene expression. (To include theories of the role of DNA methylation and histones in gene expression AND a review of some human epigenetic studies (such as the Norrbotten studies, studies on the effect of the Dutch Hunger Winter and twin studies) and possible implications from these studies.)** **5.1.3 Gene technologies** • **post transcriptional editing of mRNA (To include the production of mature mRNA in human cells, the nature of introns and exons and the potential to produce many different mature RNA molecules from a single gene (details of splicing mechanisms not required).)**
Practical techniques	3.2.3 Controlling communicable diseases • the use of antibiotics in the treatment of communicable disease (To include an outline of the modes of action of antibiotics e.g. inhibition of bacterial protein, DNA and cell wall synthesis **AND** the cellular differences between prokaryotic and eukaryotic cells that allow antibiotics to act on bacterial but not human cells.) **5.1.3 Gene technologies** • **the principles and uses of the Polymerase Chain Reaction (PCR). (To include the use of PCR in amplifying DNA, the role of primers and Taq polymerase in PCR AND the use of log scales to show the relationship between cycles of heating and cooling and increases in copy number.)** • **the principles and uses of agarose gel electrophoresis** • **Possible practical activity from Practical Activity group 6: Chromatography OR electrophoresis. Separation of biological compounds using thin layer / paper chromatography or electrophoresis**
Genome analysis	3.1.3 The development of species: evolution and classification • the types of evidence used in biological classification and consideration of how theories change as new evidence is found • Evidence for hominid classification to include observable features (e.g. fossils) and molecular evidence (e.g. DNA). • the use of DNA barcoding in biological classification, examples of the genes used and consideration of the reasons for the choice of these genes (To include the use of mitochondrial genes (e.g. cytochrome c oxidase 1) in animals, and chloroplast genes in plants (no details of electrophoresis are required).)

Topic area	OCR Biology B (Advancing Biology) specification
	5.1.1 Patterns of inheritance • **the role of the genetic counsellor and the ethical issues involved in advising families where a genetic disease has been identified. (To include pedigree analysis to predict the probability of genetic disease AND the use of genetic testing.)** **5.1.3 Gene technologies** • **the nature and use of haplotypes, SNPs (single nucleotide polymorphisms) and VNTRs (variable number tandem repeats) in human genome studies. (To include forensics, disease pre-disposition, ethnic migration, paternity testing, selection for clinical trials.)**
Recombinant DNA technologies	**5.1.3 Gene technologies** • **the use of genetic modification of bacterial cells to produce some human proteins. (To include the role of reverse transciptase, restriction enzymes, DNA ligase and plasmid vectors AND the palindromic nature of recognition sequences for restriction enzymes AND the need for reporter genes on plasmids such as those for antibiotic resistance AND example of human protein to include insulin.)** • **the use of genetic engineering in eukaryotic cells. (To include an outline of the use of genetic engineering to develop knockout mice as models for studying mammalian diseases (no details of genetic crossing to obtain homozygous individuals are required) AND an outline of the use of genetic engineering to produce human proteins in animals and genetically modified crops.)** • **the principles of RNA interference. (To include in outline only the action of siRNA and miRNA and the potential of RNA interference in disease treatment.)** **5.3.2 The hormonal control of blood glucose and the management of diabetes** • **the treatment and management of Type 1 and Type 2 diabetes**