Course Outline from 2020

Please note that the order of delivery and detailed content of the course may change.

- **The course lasts four years.**
- **Year 1 is a foundation year leading to preliminary examination which must be passed but does not contribute to your final examination marks.**
- **Years 2 and 3 lead to Part I of your final examinations worth 60% of your degree.**
- **Year 4 leads to Part II of your final examination worth 40% of your degree.**

Below is an outline of the topics to be studied in each year and the method of assessment for each topic.

Prelims (Year 1) has five courses:

- Cellular Biochemistry
- Molecular Biochemistry
- Mechanistic Biochemistry
- Physical Biochemistry
- Quantitative Biochemistry

The course has approximately 168 lectures and 18 classes/workshops supported by 1 day of practical work each week for 20 weeks and approximately 18-20 tutorials (1 per week) plus revision sessions.

Assessment will be by a combination of short answer questions or problems and some longer problem questions or essays, as appropriate to the topic.

Cellular Biochemistry	21%
Molecular Biochemistry	21%
Mechanistic Biochemistry	21%
Physical Biochemistry	21%
Quantitative Biochemistry	16%

Outline syllabus for Year 1 leading to Preliminary examinations. Teaching will be a combination of lectures, practical, classes, workshops supported by tutorials.

- **PHYSICAL BIOCHEMISTRY**

Thermodynamics I

Basic principles:

1. Introduction to thermodynamics. Basic definitions. 1st Law (conservation of energy) and enthalpy.
2. Change requires work energy. 2nd Law and entropy. Free energy as a measure of work energy. Changes in free energy, spontaneous change and equilibrium. Application to single component systems and phase equilibria.
3. Chemical potential as a measure of work energy for individual chemical species. Equilibrium constants. Mass action ratio.
4. Variation of K with temperature. Measuring thermodynamic quantities. Coupled reactions, application to biochemical pathways.

Solution thermodynamics:

5. Ideal solutions, non-ideal solutions, activities.
6. Behaviour of ionic solutions and the qualitative molecular model to explain this. Quantitative model of ionic solutions, Debye-Hückel Theory.

Kinetics I – Chemical Kinetics

1. **Rates and rate constants:** Thermodynamics versus kinetics. Rates of reaction and their measurement. Factors affecting reaction rates. Rate constants, reaction orders and rate laws. Elementary reactions and reaction mechanisms. Usefulness of rate laws.
2. **Handling rate laws:** Integrating rate laws. Zeroth, first and second order reactions. Determination of reaction orders, including the isolation and initial rate methods. Analysis of consecutive reactions and reversible reactions.
3. **Theories of reaction rates:** Temperature dependence of reaction rates. The Arrhenius equation. Collision theory of reaction rates. Comparison of predicted and measured rate constants. Need for a theory that focuses on the formation and breakdown of the transition state in the reaction profile.
4. **Transition state theory:** Kinetic scheme for transition state theory. Derivation of the Eyring equation. Reinterpretation of the Arrhenius equation parameters. Reactions between ions. Kinetic isotope effects. Trends in reactivity.

Atomic and molecular structure I

Classical and Quantum Mechanics:

1. **Introduction**. Building blocks of matter, fundamental particles. Forces between particles. Electrostatics, Coulomb's Law.
2. **Classical mechanics**. Particles and waves. Bond energy. Electrostatics and dielectric constant. Newton's Laws. Molecular modelling. Effects of electric fields, electrophoresis.
3. **Breakdown of classical mechanics**. Wave-particle duality of matter and wavefunctions. De Broglie's relationship. Heisenberg's Uncertainty Principle. Zero-point energy.
4. **Boundary conditions and quantisation of energy**. Particle in a box. Quantum numbers. Schrödinger's equation. Energy levels in molecules. Boltzmann and Maxwell-Boltzmann distribution.
5. **Atomic orbitals and quantum numbers**. Orbital energies. Aufbau principle.

Molecular Bonding:

6. **Introduction**, types of bonding, electrons in molecules. Crystal field theory.
7. **Molecular orbital theory**. Simple diatomics.
8. **More complex examples of molecular orbital theory**.

Kinetics II

1. **Rate enhancement by enzymes:** Catalysis and $\Delta G‡$. Factors contributing to rate enhancement by enzymes. Enzyme catalysis of single substrate reactions. Derivation of the Michaelis-Menten equation by the equilibrium method and the steady state method. Determination of V_{max} from kinetic data. Lineweaver-Burk, Hanes and Eadie-Hofstee plots. Cornish-Bowden direct linear transformation.
2. **Steady state kinetics:** Interpretation of V_{max} and K_m. The specificity constant k_{cat}/K_m. Diffusion control and kinetic perfection. Limitations of the Michaelis-Menten equation. Reactions involving two substrates. Effect of pH on enzyme-catalysed reactions.
3. **Regulation of enzyme activity – 1:** Effect of temperature on enzyme-catalysed reactions. Strategies for regulation – reversible and irreversible changes in conformation and covalent structure. Kinetic scheme for reversible inhibition. Competitive inhibition, uncompetitive inhibition and non-competitive inhibition.

4. **Regulation of enzyme activity – 2:** Determination of dissociation constants for inhibitor binding. Catalysis by enzymes with multiple substrate binding sites. Positive cooperativity and the analysis of sigmoidal rate curves. Concerted model for oligomeric enzymes. Explanation of the sigmoidal curve in terms of R and T states. Sequential model for oligomeric enzymes. Regulation of allosteric enzymes. Regulation by reversible phosphorylation.

EM radiation I

1. **How do microscopes work?**
2. **How do you detect molecules inside cells?**

Thermodynamics II

Equilibria

1. **Water**: Ionic dissociation of water and definition of pH. Definition of acids and bases by their effect on water (Arrhenius equation). Strong/weak acids and bases and introduction of amino acids as zwitterions. The concept of pKa for functional groups and effect of the environment on pKa values for specific groups. Neutralisation of acids and bases by mono and poly-protic acids. The Henderson-Hasselbalch equation and its application. Definition of Buffers and calculation of buffer pH. Variation in buffering power. Measuring pH using indicators.
2. **Ligand binding:** Scenarios for ligand binding to macromolecules. Dissociation constant. Number of ligands bound per molecule and fractional saturation. The concept of affinity and the relationship to on and off rates. Scatchard plot. Multiple ligands and multiple binding sites. Cooperativity. Oxygen binding to hemoglobin. The Hill plot. Thermodynamics of cooperativity. Multivalent ligand binding.

Electrochemistry and membrane potentials:

3. **Principles of electrochemistry and electrochemical cells**: The concepts of oxidation and reduction. Ionization energy and electronegativity. Multiple oxidation states of transition metals. Half-cells. Electrochemical cells. Measurement of EMF. Thermodynamics of reversible cells. The relationship between DG and E. Conventions for writing half cells and constructing cells from half-cells. Types of common half-cell. EMF of a cell. The standard hydrogen electrode. The Nernst equation for cells and half cells.
4. **Practice of electrochemistry in the laboratory and outside world**: Significance of the values of redox potentials - oxidizing agents and reducing agents. Application of the Nernst equation. Redox potentiometry and its analysis. Concentration cells. Effect of temperature on cell EMF. Calculation of thermodynamic quantities from electrochemical data. pH electrodes. Biological electron transfer. Coupled electron transport in the mitochondrial respiratory chain and in photosynthesis. Blood glucose sensing. The Clark oxygen electrode.
5. **Membrane potentials**: Charges in electric fields. Membranes as capacitors and capacitance. How membrane potentials arise. Ion distribution at equilibrium and the Nernst equation for membranes. The Goldman equation for multiple ions. Why a very small difference in ion concentration can lead to a large membrane potential. Ion electrochemical gradients (ion not at equilibrium). The proton gradient. Electrochemical gradients as energy stores and active transport. Oxidative phosphorylation. Protonmotive force. Nerve cells - Action potentials.

Atomic and molecular structure II

1. **Do we understand how proteins fold? Attractive forces (electrostatics):** Briefly examine the protein folding problem. What force do two electrically charged particles experience? What are the differences between the Coulombic force, the electrostatic potential energy, the electric field and the electrostatic potential? How do we treat situations where the charges are surrounded by other atoms (a solvent)? Look at some simple example from proteins.

2. **More attractive forces. Repulsive forces. Torsion angles and the Ramachandran plot:** Describe the properties of an electrical dipole. Understand how the differences in polarisabilities of atoms leads to polar molecules and how non-polar molecules may induce dipoles in one another leading to the London dispersion interaction. Examine the origins of why molecules don't collapse and combine with the London dispersion interaction to form the Lennard-Jones 6-12 potential. How do the repulsive forces limit the conformational space of polypeptides? What conformations can polysaccharides and nucleic acids adopt?
3. **Hydrogen bonds and water:** Elicit the importance of hydrogen bonding in biology. What is a hydrogen bond and how can it be described? What effect does the solvent have on the formation of hydrogen bonds? What are the implications for the structures of biological macromolecules in water? What are the different kinds of secondary structure found in proteins. How do hydrogen bonds affect the structure of DNA.
4. **The hydrophobic effect:** What is hydrophobicity? What is the experimental evidence for the formation of hydrogen bond networks by water? What is the temperature dependence of the hydrophobic effect for neopentane and what is the physical (i.e. molecular) description that accounts for this temperature dependence? Can we correlate the hydrophobic effect with any molecular properties? What are the consequences for the folding of biological macromolecules, especially proteins?
5. **Cooperativity of intramolecular non-covalent interactions:** Check understanding of the hydrophobic effect. Examine the thermodynamics of how a protein folds. Determine what drives the formation of the folded, native structure. Show how cooperativity works. Investigate the consequences for protein folding.
6. **Protein folding and misfolding:** Restate how proteins fold. Examine the thermodynamics of how a protein folds. Determine what factors affect the stability of the folded, native structure. Resolve the Levinthal Paradox. Investigate the role misfolded proteins play in disease

EM radiation II

1. **Radioactivity** α, β, γ, and X-ray emission. Examples of decaying nucleotides. Derivation and use of radioactive decay law. Decay constant, lifetime, half-life and specific activity. Detection of radiation: Geiger-Muller counters and scintillation counters. Dating using (a) beta decay of Rubidium 87, (b) beta decay of Carbon 14, and (c) accelerator mass spectroscopy to find the Carbon 14/Carbon 12 ratio directly.
2. **Radiation and radiation damage** Units of radioactivity, average doses, sources of background doses, permitted doses. Effects of radiation doses on rodents, humans, cells and DNA. Energy loss of radiation in matter, photoelectric effect, Compton effect, pair production. Mechanism of free radical formation by incident radiation. Repair of damage. Nuclear fission. Chenobyl disaster: cause of accident and mechanisms of damage to humans. Radio isotopes used frequently in biochemistry.

These 37 Lectures will be supported by 6 classes/workshops

- **MECHANISTIC BIOCHEMISTRY**

Introduction to Organic Biochemistry

Basic principles

1. **Introduction:** What does a biological molecule look like in 3D (peptides, nucleic acids, lipids and sugars).

Orbitals and Bonding

2. **Orbitals and bonding:** Types of orbital

3. **Orbitals and bonding:** VSEPR. Hybridisation.
4. **Orbitals and bonding:** MO diagrams. Frontier molecular orbitals and reactivity.
5. **Orbitals and bonding**: Resonance. Conjugation. Aromaticity,

Conformational Analysis

6. **Conformational analysis**: Shapes: conformation, configuration. Sterics and hyperconjugation. Eclipsed versus staggered. Syn, anti, gauche, synclinal
7. **Conformational analysis:** Degrees of freedom. Conventions. Torsional strain. Chair and boat. Axial and equatorial. Newman projections.

Lectures, Acids and Bases

8. **Acids and Bases:** How do identify acids and bases. Isolectric point. Trends from polarizability,resonance and hybridization.
9. **Acids and Bases:** Influence of environment. Inductive effects. Ranking relative acidity.

Lectures, Substitution and elimination reactions in a biochemical context

10. Substitution
11. Elimination

<u>Chemistry of enzymatic reactions</u>

Underlying chemistry

1. **Reactivity:** What makes a group likely to react as an acid, base, nucleophile or electrophile?
2. **Facilitating reactions:** Given active site structure or residues, how might the enzyme facilitate the reaction?
3. **Cofactors**: are they necessary? Why?
4. **Assessing mechanism:** What features would make a mechanism unreasonable? What experiments could be done to substantiate or disprove your mechanistic proposal?

Chemistry of reactions

1. **Introduction to enzyme mechanism and analysis:** Nature of active sites. Enzyme families. Principles of biological catalysis. Monitoring enzyme reactions. Irreversible inhibitors.
2. **Serine protease mechanism:** Chymotrypsin mechanism and catalytic triad. Analysis by affinity labels. Analysis by crystallography. Oxyanion hole. Site-directed mutagenesis to test mechanism.
3. **Serine protease regulation**: Chymotrypsin compared to blood clotting enzymes. Zymogens and activation
   Specificity pockets. Specificity constant. tPA as a serine protease therapy.
4. **Lipases:** Problems with insoluble substrates. Recurrence of the catalytic triad - convergent evolution. Lipase assays. Application of lipase inhibition.
5. **Dehydrogenases:** NAD+ and NADPH as cofactors for catalysis. Mechanism of lactate dehydrogenase
   Isoenzymes and their use in diagnosis. Cofactor regeneration features would make a mechanism unreasonable? What experiments could be done to substantiate or disprove your mechanistic proposal?
6. **Ribozymes:** Discovery of the first ribozymes. Mechanism of type I intron and convergent evolution. Limitations of ribozymes compared to protein catalysts. Insight from ribozymes into RNA world hypothesis.

<u>Protein structure and chemistry</u>

1. **Amino acids and peptide bonds:** Amino acid chemistry and stereochemistry. Proteins as polymers. Peptide bond properties and geometry. Non-covalent forces (van der Waals,

Hydrogen bonds, electrostatics. Mostly nonpolar amino acids (Ala, Val, Leu, Ile, Phe, Tyr, Trp, Met).

2. **Polypeptide structure and regular secondary structure:** Dihedral angles. Ramachandran plot. Sidechain conformations. Helical conformations. β-strand. Turns. The special case of proline. Side chain conformations. Acidic amino acids (Asp, Glu). Basic amino acids (Lys, Arg, His*).
3. **Motifs of protein structure:** Motifs and topology. Protein domains and tertiary structure. Visual representations of proteins. Hydrophobic packing. Quaternary structure / oligomerisation. Polar uncharged amino acids (Asn, Gln, Ser, Thr). Cysteine/Cystine.
4. **Protein folding:** The Anfinsen experiments. Kinetics of protein folding. Methods for studying protein folding. Relationship between protein sequence, structure, and function. Protein structure prediction. Protein mutagenesis and engineering. Protein motion.

Medicinal chemistry of enzymes

1. **Assessing reactivity within the pocket:** Role of environment, stability of intermediates etc.
2. **Application to pharmaceutical design:** How basic mechanism is important for drug design.

Biological Chemistry of the elements

1. **Biological elements and molecules - an introduction:** Large and small molecules - size range of molecules in biochemistry. Formation of macromolecules by condensation reactions. Roles of other elements
2. **Phosphorous Chemistry:** Multiple dissociation reactions. Stability of the phosphate ion. Condensation reactions: phosphate esters and anhydrides. 'High energy bonds' and free energy of hydrolysis. Phosphate ions as a PTM.
3. **Sulphur Chemistry:** Nucleophilic and acid-base properties: thiol proteases. Esters and Thioesters: acyl co-enzyme A. Oxidation-reduction chemistry of sulphur. Cysteine and cystine
4. **Iron:** iron in haem proteins, iron-sulphur proteins and oxo-bridge proteins.
5. **Calcium:** Ca as a signalling ion. Extracellular and intracellular roles of Ca^{2+}. Analysis of how low intracellular concentrations of Ca^{2+} can signal against the background of a higher concentration of Mg^{2+}.
6. **Magnesium & Zinc:** Relationship of the properties of these ions to their biological functions. ATP, zinc fingers.

Carbohydrates in biochemistry

1. **The Abiotic Origins of Biomolecules, including Carbohydrates:** Where do carbohydrates come from? Their role in biology.
2. **Structure and Stereochemistry of Carbohydrates:** Glycosidic linkages, nomenclature.
3. **Chemistry of Simple Carbohydrates:** Mutarotation, Reactions at the anomeric position.

These 36 lectures would be supported by 4-6 tutorials and 2 workshops

- **MOLECULAR BIOCHEMISTRY**

DNA is the code of life

1. DNA is the genetic material
2. The chemistry of DNA
3. DNA replication

4. DNA makes RNA
5. Distinctive features of eukaryotic transcription and transcript processing
6. The genetic code
7. Making a protein
8. Mutations I small scale changes, their consequences and their repair
9. Mutations II large scale mutations and their consequences
10. Eukaryotic genome organisation and evolution

The molecular biology toolbox

1. Basic methods in molecular biology I (DNA enzymes, basic cloning, hybridisation technology)
2. Basic methods in molecular biology II (DNA libraries, PCR, dideoxy sequencing, protein expression strategies)
3. Basic methods in molecular biology III (NGS: illumina and nanopore, databases, applications)
4. Protein methods I - extraction and purification strategies
5. Protein methods II - protein detection and analysis
6. Immunochemical methods (Antibodies, IP, western, immunocytochemistry, ELISA, applications)

Making the most of your genome

Gene regulation
1. Transcriptional control of gene expression
2. Chromatin structure influences gene expression
3. Co-transcriptional control of gene expression
4. Control of gene expression in the cytoplasm

Generating diversity from the genome

1. Basic principles of development
2. Basic principles of immunology

From genotype to phenotype

1. Genetic analysis in bacteria
2. Genetic analysis in eukaryotes
3. Transgenesis and the manipulation of genomes
4. Transmission genetics I – Mendel's first law and exceptions
5. Transmissions genetics II – Mendel's second law and exceptions
6. Transmission genetics III – linkage and recombination
7. Transmission genetics IV – genetic interactions
8. Extrachromosomal genetics

Proteins

1. Introduction to post-translational modifications
2. Introduction to protein localisation – understanding the GPS
3. Introduction to protein turnover
4. Methods for studying protein sequence and structure
5. From structure to function - Myoglobin
6. Haemoglobin: structure and cooperativity
7. Haemoglobin: allostery and polymorphism

37 lectures to be supported by tutorials and practicals

- **CELLULAR BIOCHEMISTRY**

Cells as the basic unit of life

1. Basic introduction to cells and their analysis
2. Cell compartmentalisation and organelles
3. Cellular trafficking
4. Cell organisation and movement I: eukaryotes
5. Cell organisation and movement II: prokaryotes
6. The chromosome
7. Cell division I Mechanics of cell division
8. Cell division II Biochemistry of cell division
9. Cell differentiation and stem cells
10. Specialised cell types
11. Integrating cells into tissues

Cell Signalling, Sensing and Multicellularity

1. Sensing and signalling in bacteria
2. Introduction to multicellularity and communication
3. Introduction to the 7 classic signal transduction pathways
4. Biochemistry of signal transduction I: RTKs signalling through Ras MapK
5. Biochemistry of signal transduction II: STATs/steroid receptors and PI3K lipid signalling
6. Biochemistry of signal transduction III: eg Wnts cleavage, Notch

Biological Membranes

1. Introduction to biological membranes
2. Models, detergents and methods
3. "Passive" transport through membranes
4. Properties of membranes
5. Active transport and receptors

Cell Metabolism

1. Total dependence on glucose and the dangers of oxygen
2. Making the most of glucose as a fuel: glycolysis and TCA cycle
3. The chemistry of glycolysis and the TCA cycle
4. Electron transport chain and oxidative phosphorylation
5. Energy storage as body fat
6. A surprising preference for fatty acids as a fuel
7. Providing the brain with access to body fat
8. Turning nearly everything into glucose
9. Amino acid and lipid metabolism
10. Nitrogen disposal
11. How triacylglycerols function in an aqueous environment
12. Cholesterol: an essential cellular nutrient
13. Features of starch synthesis and sugar metabolism
14. Introduction to Photosynthesis
15. Chemistry of photosynthesis in lower and higher organisms

16. Plant metabolism versus mammalian metabolism

38 lectures to be supported by tutorials and practicals

- **<u>QUANTITATIVE BIOCHEMISTRY</u>**

Principles and Applications of Mathematics:

1. Graphs and graphical representation, **Units**, **Significant Figures, Dimensions**
Why Biochemists need some tools of Mathematics. Graphs, axes, intercepts, gradients, labelling. Equation of a straight line. Polynomial functions and graphs of them. Curve sketching, asymtotes.

2. Logarithms and indices. Examples
Manipulation of indices. Logarithms to different bases. Laws of logs, changing the base of a logarithm. Use of logs to test whether or not data can be fitted by a power law.

3. Introducing differentiation
Gradients of curves. First differential. Second differential: Turning and inflexion points: second derivative +ve for minimum, -ve for maximum, zero for inflexion.

4. Differentiation II: Trig functions and the Product Rule
Introduction to trigonometric functions and differentiating them. Polar coordinates. Derivation of Linear Approximation: f(b) = f(a) + h f'(a) where h = b-a. Derivation and application of product rule.

5. Differentiation III: The Chain and Quotient Rules, The exponential function
Chain and Quotient Rules for differentiating functions. The number e as the value at which the gradient of y = ax at (0,1) is 1. Derivation of differential of e^x. Examples of applying product and chain rules to exponential functions.

6. Differentiation IV
Differentiating functions of e^x. Expansion of e^x by the Binomial Theorem.
Functions of more than one variable: partial differentiation. Gas Law, Laplace's equation.
7. Introducing integration.
Areas under curves. Summing areas. Idea of integration. Simple examples. Integral of 1/x. Substitution method and changing the variable to do harder integrals (e.g. y= (2 x +3)^4. Indefinite integrals. Importance of constant of integration. Integral of 1/x.

8. Integration II: by parts
Integration by parts and examples, including exponential and trigonometric functions. Maxwell-Boltzmann distribution.

9. **Integration III: by partial fractions**
Using method of partial fractions to simplify integrals Recap of properties of e^x and ln x.

10. Integration IV: Examples and recap
More examples of integration by substitution, by parts and by partial fractions. Recap on integration methods. The Osmotic Pressure formula.
11. Elementary differential equations and their solution I
Basic separable differential equations. Zeroth order processes.

12. Elementary differential equations II

Solving differential governing first order biochemical processes. Examples: bacterial growth and radioactive decay (first order).

13. Elementary differential equations III
More examples of solving various differential equations for zeroth and first order processes. Newton's Law of Cooling.

14. Reaction Rates
Integrated Rate Laws, Reaction rate laws: solving differential governing for second order biochemical processes, A + B - >products (second order).

15. Basic Scalar and Vector algebra, basic matrix algebra
Basic scalar and vector algebra. Basic introduction to matrices. Units revisited.

16. Various small topics useful for data handling
Partial Differentiation revisited. The display, processing and manipulation of various types of data, for use later in the Biochemistry course.

Principles and Applications of Statistics:

1. Statistics and the Scientific Method; Probability and Distributions
How statistics relates to the biosciences. Basic axioms of probability, distributions, properties of distributions. Bayes's theorem. Measures of central tendency -- i.e. the mean, median and mode *of a distribution* -- and measures of dispersion -- i.e. variance and centiles *of a distribution*.

2. Sampling and the *t*-test
Random sampling and frequentist statistics. Sampling distributions and estimators (i.e. the *sample* mean and variance, and their distinction from that of the underlying *distribution*). Bias. The *t*-distribution, its relation to the sampling distribution of the mean. Confidence limits. The "SEM" as the standard error on the [sample] mean. Factors and boxplots. The use of the *t*-test comparing a sample mean to (1) a quantity known exactly; (2) another sample assumed to come from a distribution with either (i) equal and (ii) unequal variance. Paired tests.

3. The perils of the *t*-test

Type I and Type II errors. Statistical power. Correction for multiple comparisons, Bonferroni's method. The central limit theorem. The need for non-parametric tests. The Wilcoxon rank sum test. The (qualitative) concept of robustness. Effect size, Cohen's *d*, and power calculations.

4. Dealing with Data: Likelihood, Regression and Correlation

Likelihood as a concept. Maximum likelihood estimation. A proof that the sample mean is the maximum likelihood estimator for the population mean. Extending PDFs to more than one dimension; correlation and covariance. Pearson's rho and its estimator, r. The problem with simple correlation statistics. Spearman's rank and non-parametric correlation estimates. An introduction to regression. Linear regression and least squares. R^2 and goodness of fit.

32 interactive sessions including lectures and classes

<u>PART I</u> (Years 2 and 3)

Part I of the M.Biochem. will be taught in 40 4-day blocks over five terms of the two academic years, plus one final term of revision and preparation for examinations (Part I) which are held at the end of the third year. Each of the 40 blocks will be part of five main threads/themes that are not even in weight/content

1. Tool Boxes for Biochemistry (TB)
2. Information Transfer (IT)
3. Molecular Processes in the Cell (MP)
4. Cellular Chemistry (CC)
5. The Cell in Time and Space (TS)

Teaching methods will include practicals, interactive classes, seminars, discussion workshops, computer-based laboratories and lectures and these methods will be supported by weekly tutorials

Assessments

Years 2 and 3: 15% via termly summative assessment (TSA) – computer based – 4 x 2 hours

Year 3: 45% via examination over 7 papers – 15 hours

1. DH: Data Handling – 3 hours 15 min (15 mins reading time)
2. RP: Critical Reading and Analysis of Research Papers – 2 hours
3. IT: Information Transfer in Biological Systems: 2 hours
4. MP: Molecular Processes in the Cell: 2 hours
5. CC: Cellular Chemistry: 2 hours
6. TS: The Cell in Time and Space: 2 hours
7. GP: General Paper – 2 hours

Total 60% (equivalent to 600 marks out of a total of 1000 for FHS)

In addition, the students will have to maintain a suitable level of attainment in all non-lecture-based sessions including practical classes.

Example course outline for Part I

2nd Year

MT
Week 1. (TB1) How do I isolate and characterize a gene?
Week 2. (TB1/2)
Week 3. (TB2) How do I make and use a protein?
Week 4. (MP1) How does cell signaling work?
Week 5. (CC1) How do cells do chemistry?
Week 6. (IT1) How is DNA packages in the cell?
Week 7. (IT2) How are genes expressed I ?
Week 8. (MP2) How do chemicals move across membranes?

HT

Week 1. (CC2) How do cells make energy?
Week 2. (TS1) What are the principles of development I?
Week 3. (TB3) How do I understand protein interactions?
Week 4. (TB4) How do I get a structure?
Week 5. (CC3) How do plants capture sunlight?
Week 6. (IT3) How do cells divide?
Week 7. (IT4) How is DNA copied and maintained?
Week 8. (TB5) How do I visualize events in a cell?

TT
Week 1. (TB6) How do I predict protein structure?
Week 2. (MP3) How are macromolecules moved around cells?
Week 3. (CC4) How do plants perform metabolism?
Week 4. (MP4) How do neurons convey information?
Week 5. (TS2) When, how and why do cells kill themselves?
Week 6. (TS3) What are the principles of the immune response?
Week 7. (CC5) How do prokaryotes contribute to health, disease and environment?
Week 8. Synoptic block 1

3rd Year

MT
Week 1. (TB7) How do I understand genes and genomes?
Week 2. (TB8) How do I analyse genomes?
Week 3. (MP5) How are proteins processed?
Week 4. (CC6) How do humans regulate metabolism?
Week 5. (TS4) How do viruses work?
Week 6. (IT5) How do cells copy and maintain chromosomes?
Week 7. (MP6) How do cells maintain their shape?
Week 8. (IT6) How are genes expressed II?

HT
Week 1. (TS5) What are the principles of development II?
Week 2. (IT7) How is chromatin accessed?
Week 3. (TS6) How do organisms regenerate and maintain themselves?
Week 4. (TS7) How is a nervous system put together?
Week 5. (MP7) How does the environment influence cell movement?
Week 6. (IT8) How do cellular events influence gene expression?
Week 7. (CC7) How can biotechnology solve grand challenges?
Week 8. Synoptic block 2

TT
Revision sessions (generally 20 sessions) and preparation for Part I examinations.

The order and content of the blocks are subject to change.

Proposed Syllabus

Tool Boxes (TB).

TB1. How do I isolate and characterize a gene? [Note: 6-day block]
Extracting DNA, cutting it up etc. moving it around, basic libraries.
Visualization : Gels, labels, fluorophores, FISH etc.

Putting DNA into things: Transformations, transfections, transgenics.
DNA sequencing – Sanger, ABI and then NGS
Primers/inverse PCR sequencing and PCR, real time PCR/RTPCR
Data handling/workshop on primer design.
Practicals (over 2 weeks- can incorporate some of current genetics practical)
Practical ideas: cloning, engineering a Tag. PCR up a gene, insert into vector with tag (His or GFP), transform E. coli ready to express protein. 2nd week could be existing 2nd year protein purification practical. Elements of current prac (MH) could also be rolled into this. This might take 8 afternoons – hence the 6-day block to run back to back with TB2, also a 6-day block.

TB2. How do I make and use protein? [Note: 6-day block]

How to express a protein
Western blots, SDS, Native PAGE, coomassie, antibody, ECL detection.
Looking at proteins in cells and in vitro
Detecting PPIs: Co-IP, Y2H
Data handling (pre-existing data handling in genetics prac)

TB3. How do I understand protein interactions?

Protein purification
SPR/AUC/dialysis
Data handling

TB4. How do I get a structure?

crystallography/NMR/cryo EM
Protein-protein or protein lipid interactions (complexes and membrane proteins)
Mass spec and Proteomics

TB5. How do I visualize events in the cell?

Microscopy
Spectroscopy
FACS
ImageJ
Single molecule stuff
Could include Raspberry Pi based microscope design

TB6. How do I visualize, model and predict protein structure?

The PDB and molecular graphics
Protein bioinformatics
Structure Prediction and Graphics

TB7. How do I understand genes and genomes?

Linkage and Mapping (inc QTLs and GWAS)
Genome editing -CRISPR/RNAi. siRNA
Genetic networks
Evolution of genes and genomes
Incorporate current genetics practical (eg RNAi, epistasis, could include a mapping prac)

TB8. How do I analyse genome sequence?

Bioinformatic and statistical analysis
How to decode genomes (ChIP, RNA-seq)

Practicals – (eg SNPs to match to a chromosome) – in comp lab

Information Transfer in Biological Systems (IT)

IT1. How is DNA packaged in the cell?
Chromatin/chromosome structure/packaging etc
How does this introduce constraints?

IT2. How are genes expressed I?
Focus on events around initiation
There is a gene expression lac operon practical.
Data handling/maths/stats

IT3. How do cells divide?
Cell division
8 lectures plus some data handling, some practical work eg yeast cc mutants
Mathematical Cell Biology/Practical

IT4. How is DNA copied and maintained?
DNA –replication/repair/recombination/mutation
Computational analysis

IT5. How do cells copy and maintain chromosomes?
Genome Biology
Higher order structures – related to cell cycle, chromosome segregation

IT6. How are genes expressed II?
Focus on events co/post transcription

IT7. How is chromatin accessed?
Chromatin remodeling etc, when and how are chromatin constraints overcome

IT8. How do cellular events influence gene expression?
Links between metabolism and gene expression/chromatin

Molecular Processes in Cell (MP)

MP1. How does cell signaling work?
Molecular principles of cellular signalling
7 pathways to cover. Why certain pathways for certain things etc
eg. Notch is good for binary decisions, Wnt is good for longer range polarity

MP2. How do chemicals move across membranes?
Membrane Transport and Signalling
Graphics practical to be retained.

MP3. How are macromolecules moved around cells?
Trafficking
Ensure right balance between proks and euks
Workshop based around imaging

MP4. How do neurons convey and sense information?
Molecular Neurobiology

Channels
Muscle contraction
Synaptic transmission

MP5. How are proteins processed?
Protein processing
glycobiology, PTMS, ubiquitin

MP6. How do cells maintain their shape and interaction with the ECM?
Cytoskeleton, microtubule dynamics
Cell junctions
ECM

Cellular Chemistry (CC)

CC1. How do cells do chemistry?
Enzymes
Practical
Assay design practical has lots of enzymes and introduces basic techniques that will be required for TB

CC2. How do cells make energy?
Energy Conversion
Mitochondria, proton pumps, ATP synthesis

CC3. How do plants capture sunlight?
Photosynthesis

CC4. How do plants perform metabolism?
Metabolic principles for plants – metabolic flux
Can incorporate current practical

CC5. How do prokaryotes contribute to health, disease & environment?
Specialized metabolic strategies and pathogenesis
Microbiome
Extreme environments – thermophiles, halophiles etc.

CC6. How do humans regulate metabolism?
What is the condition of the cell from metabolism (link to neurobiology)
Metabolism in health and disease: obesity, diabetes etc..

CC7. How can biotechnology solve grand challenges?
Disease and Biotechnology
Biosecurity/biofuels

Cell in Time and Space (TS)

TS1. What are the principles of development I?
Focus on principles of development and examples from invertebrates

TS2. When, how and why do cells kill themselves?
Apoptosis and development
Apoptosis and cancer
Importance of apoptosis in immune system

TS3. What are the principles of the immune response?

Innate immunity
Adaptive immunity

TS4. How do viruses work?

Including a broad range of viruses: DNA tumour virus (plus links to cell cycle and cancer), retroviruses etc

TS5. What are the principles of development II?

Focus on vertebrate systems

TS6. How do organisms regenerate and maintain themselves?

Ageing, senescence
Regeneration and stem cells
Autophagy

TS7. How is a nervous system put together?

Developmental neurobiology, axon guidance

Synoptic Block (SB) 1 (TT week 8 2nd year)

Reprise of second year

Synoptic Block (SB) 2 (HT (week 8 3rd year)

Synoptic topics for example Structure-based drug design/ advanced structural biology

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PART II (YEAR 4)

Students would undertake a whole year (23 weeks) of research (starting mid-September in "week -2" (as at present) and continuing to the end of 3rd week of TT) plus two weeks for writing the project report (total 25 weeks). Students will be embedded in research groups in Oxford and, where appropriate, outside Oxford.

Assessment would comprise this project, along with broader research skills displayed in their written work - the project dissertation and a review article (extended essay) along the lines of a "*Current Opinions*" style review.

The advanced skills training will be provided on Friday afternoons of weeks -2, -1 and 0 MT (when they will attend the D.Phil. symposium) (e.g. advanced statistics, how to read a paper, the scientific method, presentation skills, scientific writing).

Values of the assessments in the overall FHS: The 4th year will count for 400 marks out of the 1000 for the whole FHS. This will be:

Current Opinions style review	150 marks
Project dissertation and viva	250 marks
	TOTAL 400