BYU22V01: From Molecules to Cells II (International)

Semester 1, 5 credits

Prerequisite: First year college biology.

Module coordinator: Prof Emma Creagh, ecreagh@tcd.ie Phone: 01 8962539

Notes: this module is a 'lectures only' version of the 10 credit module BYU22201. BYU22V01 contains all of the lectures but none of the laboratory work contained in BYU22201.

Contact Hours: 34 hours lectures

Module Personnel: E. Creagh, K. Mok, A. Khan, J. Hayes, D. Nolan, M. Hankir, M. Ramaswami, S. Martin, M. Campbell, K. Roberts

Learning Aims:
This module aims to give students a detailed understanding of cellular structure, composition and function. The molecular composition of organelles, the processes carried out in each organelle, and how these processes are integrated in cellular function are presented in detail. Students are also introduced to enzyme kinetics; cellular metabolism; DNA structure and replication, transcription and translation; the regulation of gene expression; Mendelian inheritance and genetic disease. This module also introduces students to virology – how viruses replicate, mutate, enter cells and take over cellular processes during infection.

Module content:
Programme of lectures, four lectures a week, Monday at 13:00, Wednesday at 17:00, Friday at 9:00 and 12:00

Lecture Topic	Lecturer
Introduction to Module BYU22201 "From Molecules to Cells"	E. Creagh
Cell structure & intracellular transport	E. Creagh
Cell cytoskeleton I	E. Creagh
Cell cytoskeleton II	E. Creagh
Proteins & amino acids	K. Mok
Protein folding and purification	K. Mok
Oxygen binding proteins	K. Mok
Enzymes, catalysis and assays	A. Khan
Enzyme kinetics, inhibition & regulation	A. Khan
Lipids - fatty acids & phospholipids	J. Hayes
Lipids – beta-oxidation & fatty acid synthesis	J. Hayes
Glycolysis and Gluconeogenesis	M. Hankir
The TCA Cycle	M. Hankir
Glycogen Metabolism	M. Hankir
Powering Life: energy transduction & life	D. Nolan

Bioenergetics 1: oxidative phosphorylation	D. Nolan
Bioenergetics 2: the universality of chemiosmosis	D. Nolan
Harvesting the light: photosynthesis	D. Nolan
Summary & integration of metabolism	D. Nolan
DNA – structure, replication, repair, recombination I	M. Ramaswami
DNA – structure, replication, repair, recombination II	M. Ramaswami
DNA – structure, replication, repair, recombination III	M. Ramaswami
Transcription – RNA types, mRNA processing	M. Ramaswami
Regulation of gene expression: general principles	S. Martin
Gene expression in prokaryotes and eukaryotes	S. Martin
Chromatin and epigenetic effects on gene expression	S. Martin
Alternative splicing and protein translation	S. Martin
Mendelian inheritance	M. Campbell
Mapping Mendelian traits	M. Campbell
Quantitative traits and heritability	M. Campbell
Genetics of common diseases	M. Campbell
Virology (1)	K. Roberts
Virology (2)	K. Roberts

Lecture Content:

- Revision of Cell structure (Podcast), Membrane structure & Intracellular protein transport mechanisms. (Elements Flipped classroom)
- Cellular cytoskeleton I (Actin filaments, myosin motor protein) (combination of flipped classroom & traditional lectures material) - Principles of cellular movement & the process of muscle contraction.
- Cellular cytoskeleton II – Importance of Microtubules & Intermediate filaments for cellular function (combination of flipped classroom & traditional lectures material). Specialised microtubules involved in the motility of cilia/flagella will be discussed.
- What are proteins? The 20 amino acids and their structures and properties, acid-base equilibria, the isoelectric point. (Combined flipped classroom and traditional lectures) The polypeptide chain and general properties of proteins. The hierarchy of protein structure (primary / secondary / tertiary / quaternary structures).
- Protein folding and protein misfolding diseases / neurodegenerative diseases. Protein purification and protein characterization techniques.
- Oxygen-binding proteins as an example of protein-ligand binding. Comparison of myoglobin and haemoglobin. Cooperativity. Bis-phosphoglycerate's role in oxygen affinity. Sickle cell anaemia.
- Catalysis and the enzyme substrate relationship; Activation energy and the transition state. Michaelis-Menten kinetics; The active site- physicochemical properties; Enzyme assays.
- Principles of enzyme catalysis; Mechanisms of catalysis with examples; Reversible Inhibition; Allosteric regulation; Enzyme inhibitors as drugs Michaelis-Menten kinetics, limiting velocity, rate/enzyme correlation. Reversible inhibition and allosteric regulation.

- Lipids-Fatty Acids and phospholipids. What are lipids? Chemical and functional properties of diverse lipids such as steroid hormones, fat soluble vitamins and ketone bodies. Fatty acids, phospholipids and membranes.
- Lipids- β-oxidation and fatty acid synthesis. Energy production through the mobilisation of fatty acids from triacylglycerols and their oxidation in mitochondria. Energy storage through the synthesis of fatty acids and storage of triacylglycerols in adipocytes.
- Catabolism and anabolism. Sources of sugars in our diet. Glycolysis, its control and regulation. Catabolism of fructose and galactose. Fermentation.
- The necessity for gluconeogenesis. Its control and regulation. Substrate sources. Reciprocal control of gluconeogenesis and glycolysis in liver.
- Pyruvate dehydrogenase and control of regulation of oxidative catabolism of substrates via the tricarboxylic acid (TCA) cycle. The TCA cycle as a source of biogenic amines. The TCA cycle as a source of anabolic substrates. Anapleurotic reactions.
- What is glycogen? Breakdown of glycogen/glycogenolysis in liver and skeletal muscle. Its control and regulation. Flight or fight! The effect of starvation. Glycogen biosynthesis.
- Powering Life: Energy transduction & life. Introduction to basics: energy transduction in biological systems: concept of displacement from equilibrium, chemical potential, electrochemical potential and redox potentials. ATP and energy coupling: key concepts: Is ATP a high energy compound?
- Bioenergetics 1: Oxidative Phosphorylation. The machinery of oxidative phosphorylation: The electron transport chain and the universal turbine of life: the F_1F_0-ATPase.
- Bioenergetics 2: The Chemiosmotic view of Life and the universality of the concept.
- Harvesting the light: Photosynthesis. The light reactions of photosynthesis: photophosphorylation, the Z scheme, PSI & II and C_1C_0-ATPase. A comparison of oxidative and photo phosphorylation.
- Summary & Integration of Metabolism
- DNA – Structure, Replication, Repair, Recombination I. Discovery of DNA as the genetic material; structure, properties and conformation(s) of DNA; mechanism for DNA replication in prokaryotes and eukaryotes: DNA polymerases and the replisome.
- DNA - Structure, Replication, Repair, Recombination II. The role of telomeres in DNA replication in eukaryotes. Spontaneous and induced mutations; mutagens and the effects of mutations.
- DNA - Structure, Replication, Repair, Recombination III. DNA repair mechanisms; non-homologous end joining and homologous recombination.
- Transcription - RNA types and processing I. Discovery of RNA; properties and classes of RNAs; types of RNA polymerases; transcription in prokaryotes: initiation, elongation and termination.
- Transcription - RNA types and processing II. Types of RNA polymerases; transcription in eukaryotes: initiation, elongation and termination.
- Regulation of gene expression. The general principles of the regulation of gene expression in prokaryotes and eukaryotes.
- Gene expression in prokaryotes and eukaryotes. Mechanisms of the regulation of gene expression in prokaryotes and eukaryotes: promoters. Sigma factors, transcription factors, enhancers, silencers, insulators
- Chromatin and epigenetic effects on gene expression. Introduction to epigenetics; structure and composition of chromatin; histone and DNA modifications and their effects on chromatin and gene expression.
- Alternative splicing – protein translation. Mechanisms of alternative splicing. Initiation, elongation and termination of translation
- Mendelian Inheritance. Mendel's laws (revision of BYU11101) and molecular basis of inheritance patterns; pedigree analysis; gene interactions: dominance, co-dominance, incomplete dominance, recessivity, penetrance, expressivity, and epistasis.
- Mapping Mendelian traits: This lecture outlines the historical methods that were used to identify mutations in genes associated with Mendelian diseases. It highlights the methodology and underlying analysis with a focus on linkage and recombination.

- Quantitative traits and heritability: somatic mutations and heritability and how they pertain to human disease. The lecture uses examples of conditions such as breast cancer to describe the identification of genes that ascribe relative risk scores to disease.
- Genetics of common diseases: This lecture focuses on giving a wide range of examples of human disease that show Mendelian and non-mendelian modes of inheritance. It aims to give the student a broad understanding of the complexities of these diseases and the underlying genetic causes.
- Virology I: genetic diversity of viruses. The diversity of viral genomes and particle structures will be explored in this lecture. Introduction to viral replication - how different viruses enter cells and an example of viral strategies for producing mRNA.
- Virology II: Replication continued– we will explore how replication and assembly of new virions is dependent on location within the cell and also the cellular processes a virus needs to utilise during replication. In this lecture we will touch on viruses causing emerging infections and how their replication cycles have changed to adapt to new hosts/cell types.

Learning Outcomes:

- On completion of this module students should be able to demonstrate an understanding of fundamental concepts in the following cellular structures and processes: the structure and function of cells and organelles; structures and functions of nucleic acids, proteins, carbohydrates and lipids; the fundamental concepts and regulation of metabolism; the composition, structure, synthesis and function of DNA and RNA; regulation of gene expression in prokaryotes and eukaryotes; chromatin structure and epigenetic regulation of gene expression; the principles of genetic inheritance; genetic diseases and fundamental concepts in virology.

Recommended Reading List:

The topics and concepts presented in this module will be found in many general textbooks on cell biology, biochemistry and genetics. The following are recommended for your guidance:

Essential Cell Biology. Alberts, Hopkin, Johnson, David Morgan, Raff, Roberts, Walter. (4th / 5th Editions). W. W. Norton & Company.
Biochemistry. Berg, Tymoczko, Gatto, Stryer (8th edition). Macmillan International.
Introduction to Genetic Analysis. Griffiths, Wessler, Carroll, Doebley (11th edition). W.H. Freeman and Co.

Assessment Details:
(A) **End of semester written examination: 85% of module mark**
The examination paper is divided into two sections, equally weighted.

- **Section 1: Essay** One essay from a choice of three**.**
- **Section 2** Ten short answer questions from across the module.

(B) **Course Work:**

- Two in-course MCQ tests of lecture material, 7.5% each.

To pass the module a student must obtain an overall module mark of 40%

Contact:
The Biology Teaching Centre
Executive Officer: Daniel McCormick btcadmin@tcd.ie, Phone: 01 896 1117

BYU22V02: From Cells to Organisms (International)

Semester 2, 5 credits

Prerequisite: First Year Biology

Module coordinator: Prof Colm Cunningham**,** colm.cunningham@tcd.ie, Phone: 01 8963964

Notes: this module is a 'lectures only' version of the 10 credit module BYU22202. BYU22V02 contains all of the lectures but none of the laboratory work contained in BYU22202.

Contact Hours: 37 hours lectures

Learning Aims:
This module aims to bring the student from the functioning of prokaryotic unicellular organisms right up to the integrated functioning of perceiving, thinking, and acting multicellular organisms. The module will give the students an appreciation of the highly specialised and dynamic communication between cells and tissues that brings about the functioning organism.

Module content:
A programme of lectures, four lectures a week, Monday at 9:00, Tuesday at 9:00 and 13:00, Wednesday at 17:00

Lecture Topics
Introduction
The bacterial world: diversity & unique extracellular structures
Energy, transport and scavenging in bacteria
Motility and chemotaxis in bacteria
Cell: Cell communication & bacterial development
Introduction to the bacterial cell envelope I
Introduction to the bacterial cell envelope II
Cell: Cell communication; autocrine, juxtacrine, paracrine & endocrine signalling
Cargo packaging for export
Calcium-dependent exocytosis for signal release (Neurotransmission I)
Signalling via ligand-gated ion channels (Neurotransmission II)
Intracellular signal-transduction: conserved mechanisms for responding to extracellular signals
Signalling through G-protein coupled receptors
Signalling through receptor tyrosine kinases and MAP kinases

Conservation of signalling pathways between organisms
Organising a body plan in multicellular organisms
Cell signaling/cell communication in the context of development
Elaboration of positional information/progressive specification/cell lineage analysis
How a cell responds to positional information
Evolution/Development –body plan changes through evolution
Organogenesis
Nervous control of physiological function
Pharmacology of autonomic nervous system

There will be two in-course assessments of Lecture material (multiple choice format).
The first will be immediately after reading week, the second in the last week of semester.

Lecture Content:

Unicellular to multicellular life

- Examples of signalling molecules released by bacteria and their effects on individual cells and populations
- Quorum sensing as a method of communication between bacteria within a population
- Regulatory and physiological adaptations to stress in bacteria
- ATP synthesis and the generation of proton motive force in bacteria
- Nutrient uptake mechanisms and transporters in bacteria
- Motility and chemotaxis in bacteria
- Extracellular structures such as fimbriae, capsules and S-layers and their role in adaptation to the environment
- Mechanisms employed by bacteria to attach to and interact with eukaryotic cells

Cell-cell communication & Signal Transduction

- The basic mechanisms of cell-cell communication including juxtacrine, autocrine, paracrine & endocrine signaling. From gap junctions and plasmodesmata (metabolic or electrical coupling), to contact-dependent signaling, neurotransmitter release at short range to hormone release at long range
- Packaging of cargo for export: protein synthesis and export via the trans-golgi network and the secretory pathway versus vesicular transporter-mediated packaging of synaptic vesicles (with provision of online resources)
- Neurotransmission as a specialized form of calcium-dependent exocytosis. Resting membrane potential and depolarization, the action potential, voltage-dependent calcium channels (with provision of online resources).
- Signalling via ligand-gated ion channels: neurotransmitter binding and gating of ion channels. Acetylcholine and end plate potentials at the neuromuscular junction. Glutamate and GABA receptors, excitation and inhibition.
- Highly conserved components of intracellular signal-transduction pathways-G proteins used as on/off molecular switches; protein kinases/phosphatases employed in virtually all signalling pathways; second messengers carry and amplify signals from many receptors. Concept of crosstalk between signalling pathways. Signal termination.

- General elements of G protein coupled receptor systems. GPCRs that activate or inhibit adenylyl cyclase. GPCRs that activate phospholipase C. Mechanisms that downregulate signalling from GPCRs. Integrating responses of cells to environmental influences.
- Receptor tyrosine kinases (e.g. EGF). Activation of ras and MAPK pathways. The role of protein binding domains in the specific interactions between signalling molecules. Pathways that involve signal-induced protein cleavage (e.g. Notch/Delta signalling).
- Signalling networks that respond to changes in nutrient and energy status of cell (e.g. SnRK1 and TOR kinases in plants). Signalling pathway conservation between organisms. Defects in signalling pathways leading to disease with emphasis on cancer.

Development

- **Organising a body plan in multicellular organisms:** The concepts of multicellular life and how an organized body plan, composed of different cell types and tissues, is established. Examples of relatively simple (hydra) organisms to the most complex (examples of drosophila, mouse, human and others) will be used. Fundamental similarities and differences in the organisation of animals and plants will be covered. Molecular and biophysical mechanisms governing cellular behaviour will be discussed.
- **Cell signalling/cell communication in the context of development**. Cell communication is fundamental to building an organized body plan. The main developmental signalling pathways (Wnt, BMP, Hedgehog, FGF, YAP/hippo etc) will be introduced with examples of how they guide development. Pathway conservation and elaboration through evolution related to developmental complexity will be examined.
- **Elaboration of positional information over time.** Exploration of key concepts, moving from the "French flag model" to more sophisticated ways of thinking. The concept of gradients and graded influence across tissues. Progressive specification and how information builds over developmental time. Cell lineage analysis and tracing a cell through time. Stem cells and how stem cell niches are established during development
- **How a cell responds to positional information**. Transcriptional and post-transcriptional regulation leading to cellular differentiation. The integration of different types of information at the cellular level determining how a cell responds. The importance of the cellular context and epigenetics. Hox genes and how they relate to positional information – the concept of a positional code. Mutations that change the body plan.
- **Evolution & Development**: How body plans can change through evolution. The concept of "the Toolkit" for building an organism and "tinkering with the toolkit" – genetic changes that can lead to major body plan shifts such as loss of limbs or acquisition of specialised structures such as a turtle shell.
- **Organogenesis**: Development of organ and organ systems; e.g. heart, kidney, lung etc. building on the concepts and mechanisms involved in building complex structures, current knowledge on how specific organs are established will be presented and explained.

Human physiology

- Nervous control of physiological function: sensory and autonomic nerves. CVS as model system.
- Muscle function and its nervous control. Disorders of skeletal muscle, cardiac hypertrophy (physiological via exercise & pregnancy; pathophysiological via hypertension)
- Neuropharmacology, with specific emphasis on pharmacology of the autonomic nervous system; effect of toxins on neuromuscular junction
- Endocrine regulation of physiological function, highlighting endocrine disorders.
- Fundamentals of cardiovascular and respiratory physiology and their interaction (homeostatic responses to altitude, exercise)
- Fundamentals of cardiovascular and renal physiology and their interaction (regulation of blood pressure and volume, acid-base balance)

- Pathophysiology and treatment of hypertension (pharmacology of ANS, role of exercise in prevention and treatment)
- Digestion and metabolism, metabolic syndrome, the gut-brain axis.
- Immune regulation of physiological function (innate vs adaptive, role of inflammation in infection and cancer. Regulation of tissue homeostasis and role in obesity, diabetes and brain injury/neurodegenerative disease.
- Pathophysiology of diseases of the nervous system (MS, AD, PD, encompassing nervous, endocrine and immune regulation of physiology).

Neuroscience and Behaviour

- Sensation and perception. Students will gain an understanding of how the brain makes sense of sensory input. They will be aware of and able to explain fundamental discoveries (e.g. Hubel & Wiesel). They will be able to describe neuronal circuitry that enables us to distinguish between sensory input from the external world and that which is internally generated (sensory cancellation and efference copy mechanisms).
- Pain, nociception, and interoception. Students will attain and understanding of the internal awareness of the animal body to states such as pain.
- Motor coordination and control. Students will learn how the complexity of an animal's movement is constrained by the underlying neural circuitry. Simple behaviours in simpler animals and their underlying neural control (e.g. CPGs) through to complex voluntary action and manipulative tasks.
- Emotion and motivation. Students will develop an understanding of how we empirically study animal behaviours that can be attributed to motivational drives and emotional states and will attain knowledge of how environment experience and genetic background can alter these behaviours.
- Learning and memory. Students will be able to describe the basic learning theory models in the context of Pavlovian and operant conditioning, and basic invertebrate and vertebrate experimental models of learning-induced brain plasticity and memory storage.
- Understanding brain function through pathology/disease. Students will gain an understanding of how clinical studies of humans with brain damage and disease, when combined with careful behavioural and psychiatric analysis, and give us new insights into brain function at a systems level. An introduction to the use of animal disease models and a few highlights of how animal models have been used to develop an understanding of disease processes.

Learning Outcomes:

On successful completion of this module students will be able to:

- Describe the regulatory and physiological adaptations that bacteria undergo to acquire nutrients, respond to stress, and describe the structure, function and importance of bacterial extracellular structures and their roles in modulating cell-cell interactions. Utilise phenotypic tests and microscopy to characterise bacteria in the laboratory (Practical).
- Demonstrate an understanding of the role of signalling in bacterial communication in forming communities and the mechanisms used by bacteria to interact with eukaryotic cells.
- Describe the multiple ways in which cells communicate with each other over short and long distances.
- Demonstrate an understanding of how biological signals are prepared for export, are temporally and spatially controlled, are sent, received, transduced and amplified in the cellular context (signal transduction), and provide examples as to how this is achieved in cells.
- Utilise online tools and databases to explore fundamental concepts relating to neurotransmission and to answer specific questions related to embryonic development including an appreciation of the power of using shared data in research (Practical's).

- Articulate the concepts of how biological complexity is established as the body plan of multicellular organisms emerge and integrate these concepts in the context of how body plans have evolved.
- Describe the contribution of the nervous, endocrine and immune systems to regulation of whole-body physiological homeostasis in humans and detail cell, tissue and organ integration in the cardiovascular, respiratory, immune, renal and digestive systems.
- Describe how alterations in physiological variables as a result of exercise, changes in barometric pressure or pathophysiological processes impact on homeostasis in different organ systems
- Measure and understand fundamental cardiovascular and respiratory variables in human subjects (Practical).
- Articulate how the brain achieves basic functions for the animal using examples from invertebrate & vertebrate neurobiology.
- Provide explanatory accounts of movement and motor control; sensation and interoception; emotion and memory, and how brain injury in human patients can inform us about brain function
- Describe, integratively, how the fundamental physiology of neural circuits can be used to explain behavioural function in both vertebrates and invertebrates.

Recommended Reading List:

The topics and concepts presented in this module can be found in selected chapters of the following textbooks:

- Biology, A global Approach. Campbell *et al.* 12TH Edition. Pearson.
- Prescott's Microbiology 10th edition. McGraw Hill.
- Biochemistry. Berg, Tymoczko, Gatto, Stryer 8th edition. Macmillan International.
- Molecular Cell Biology. Lodish *et al*.., 8th edition. Macmillan International.
- Principles of Development. Wolpert, Tickle, Martinez-Arias. 5th Edition Oxford University Press.
- Developmental Biology. Gilbert, Barresi, 11th Edition. Sinauer, Oxford University Press
- Human Physiology from Cells to Systems. Sherwood. 9th Edition. Cengage Learning.
- Principles of Neurobiology. Liqun Luo. 1st edition. Garland Science.

Assessment Details:
Marks are allocated across two components, course work (two multiple choice tests of lecture material, 15% of module mark) and end-of-module examination (85% of module mark).

Contact:
The Biology Teaching Centre
Executive Officer: Daniel McCormick btcadmin@tcd.ie, Phone: 01 896 1117