* What is metabolism?
  + A process by which your body converts what you eat and drink into energy
* Metabolism – induces changes that allow us to convert foods to energy and building blocks for molecules, and elimination of nitrogenous wastes
* Nowadays, metabolism means all the chemical reactions in an organisms – now the old metabolism is called intermediary or intermediate metabolism
* We are focusing on intermediate metabolism
* We need resources or energy to power metabolism so need signalling to tell they system that everything is ready for process – we need enzymes that are proteins – and where we get proteins from – aa
* Metabolism involves catabolism which is breaking down and anabolism which is building up molecules
  + Break down food and dead cells
  + Build up fresh things as required based on signalling
* Enzymes function as teams – called biochemical pathways
* Metabolic strategies provide way to assist the enzymes by keeping the team together – enzyme clustering
* Everything under control of thermodynamic
* All enzymes in the pathway need to be regulated – functioned as required to deliver the product on time – powered by energy
* Energy is in chemical bond – look at molecules that store energy in high energy bond – mostly phosphate molecules
* No waste, no accumulation – the moment the molecules are made – they are turnover
* Organsims evolve to use different sources of energy and reducing power
  + Need reducing agent
  + Need carbon – cannot use coal directly – can use organic compound
* Earliest form of life called chemoautotroph – oxidise inorganic compound for reducing power and use carbon dioxide from air
* Bule-green algae clled photoautotroph – use sunlight directly and water as reducing agent – use carbon from air
* Humans are heterotroph – require organic compound as source of ATP – depend on organic compound to provide us reducing agent – need pre-built organic carbon
* Overview of metabolism
  + Synthesis and degradation of small molecules to provide us carbon, reducing agent, and energy
  + Energy metabolism – to generate and store energy
  + Other central pathways that account for mass transfer and energy in the cell
* Catabolic or degradation – take nutrients and cell components (that we don’t need) and break them down – salvage – make energy or small molecule – then funnel through biosynthesis pathway to generate complex molecules – ATP – NADPH gets oxidised to NADP+ - the biosynthesis is anabolism
* Anabolism – makes the molecules that our cells, tissues, organs require at that moment – depending on the signal received
* Metabolic pathways consist of a series of reaction – the energy and substances from some reactions are used in the other until we get the final products that we are interested – most cases only the end products are important – the sequence is only needed for the end product
* Some pathways are 10 to 12 steps long and need a lot of enzymes – will tell what to remember – catabolism takes figure (b) slide 12 – the energy and small molecules are resembled into the metabolites we need and go back as the figure shows – very organism-specific – also specific to the circumstances – food availability, pathogen, etc.
* Metabolomics – metabolites varying in physical and chemical properties are targeted and scanned…refer to slide
* Investigating metabolism – will use non-invasive methods and look for all mutants that contribute to changing metabolism of the organism – in heamap – reds are the ones going up – greens going down – black normal – look who are overexpressed and degraded
* Traditional method of tracing pathway is to make mutants – if mutants accumulate then the next enzyme has been mutated – eg. if C accumulates, enzyme III has mutated – the mutation has to be in the critical part of the proteins for example active site to put the end of the substrate – can see step of the pathway it is at
* Controlling these mechanisms and pathway – through multiple pathways
  + Membranes – how to get materials in when there are plenty of materials for us – how to turn them over immediately
  + The cell has a limited volume and the solvent capacity is small – need to act very quickly to make the product
* Enzyme clustering – the product of the first enzyme is the substrate of the next one – can’t let them diffuse – make sure intermediates don’t disappear
* Membrane provides location where proteins can be integrated or peripheral – membrane holds them down together
* Unlinked enzymes - The intermediates are located close to each other – not clinging to each other but in the same area
* Multienzyme complex – multi subunit complex – quaternary arrangement of protein subunit – organise most pathways b keeping enzyme close to each other
* Membrane bound multienzyme complex – all enzymes involved are stuck in membranes – can be peripheral or integral – pass intermediates to each other
* Sometimes biosynthetic and degradative pathways can be in different compartment – this reduces energy and material waste – don’t make aa and break them down immediately – by separating preventing “futile cycling” – making up and breaking down in the same location – wasting material and energy
* All these pathways are interconnected – some materials can be diverted from one pathway to another if needed
  + Oxidising – burning
* Thermodynamic – delta G – small reactions added up to make big reactions
* Catabolic and anabolic are slightly different as they need to follow delta G – if they are mirror of each other, only one is favoured so cannot go in both direction
* A pathway has to be exergonic -> Delta G has to be negative
* Use separate enzymes so that we don’t make and break things at the same time
* When we have a lot of ATP – can make fatty acids – make acetyl-CoA and release ATP – synthesise of fatty acids in cytosol – break down of fats in mitochondria – avoid futile cycle
* Critical component of reaction is the amount of substrate – called metabolic flux – how much flowing through the pathway
* Enzyme regulation in the pathway is very critical – have long series of passing the ball – 3 ways
  + Simple linear – eventual product D is the inhibitor of the first step A to B – feedback control
  + Sometimes an intermediate can branch off to make a different product – can be a product or another series – Branch point products controlled by the regulation branch point – common in aa
  + Also possible that eventual enzyme stops the beginning – isozyme which catalyses the first step
* Question – B enzyme is accumulating – which enzyme is mutating?
* 6 different types of enzymes – cells get tired of controlling – majority under cell concentration control – based on absolute temperature and delta G
  + The only way cell controls is when it needs sth – when delta G negative – cells control
  + If it is slow – delta G is 0 – cells can’t be bothered – homeostasis
  + If have sudden requirement for energy, fats, etc…- hormones come into play – hormones are triggered immediately and push cells to provide what is needed under the circumstance – control, regulate, and fight or flight situation
* Energy currency of the cell – ATP – adenosine triphosphate – adenosine is adenine nucleotide base attached to sugar ring -1 phosphate called AMP – 2 called ADP – 3 called ATP – mono, di, tri – normally forms ATP when the bond is cut – rarely can cut both make AMP – difficult to take P from AMP – ADP is easily converted to ATP – very rarely see adenosine – ADP can give off phosphate to form AMP
* Those bonds are called high enery phosphate bond – family of hight enery chemical bond – store energy in the form of valence bond
* ADP hydrolyses to ATP
* The more the negative the delta G – the higher the charge – the more energy – high-energy phosphate compounds and low energy – high energy is ready to give up energy to the lower energy
* Thermodynamically impossible reaction needs ATP to happen
* Charge on cell is calculated by the total amount of ATP (ATP + ADP + AMP) – at about energy charge of 9 can maintain catabolic and anabolic at the same rate