* Secondary structure – only about 80% of proteins are folded in regular ways – the rest are unstructured
* Fibrous proteins – special proteins that cannot be degraded by trpsins and chemotrypsin – cardilage and muscle tissues
* Globular proteins – spell up into specific shape – biological functions – tertiary structure – the biological function is connected with shapes
* Dynamic of globular protein structure – certain flexibility to bind things
* Prediction – amino acid sequence – use computer to predict 2nd and 3rd structures
* Local folding is secondary
* Naturally occurring secondary structure – right handed alpha helix, beta sheet, 310 helix – backbone held by hydrogen bond – thousand bonds in DNA – H bond on its own is weak
* Alpha sheet - Yellow lines are H bond – side chains stick out – backbone like a circle (wheel etc) – using 3D viewer can rotate proteins
* Beta - Secondary structure – backbone like a plain – sidechains going above and below plain – hydrophobic may be on a face
* Only 2 types of rotation are permitted – planarity enforces that the backbone between one and another C-alpha are all in one plane – forces proteins to only adopt certain changes
* Steric interaction determines how proteins are folded – only certain foldings are allowed
* Alpha helix – closes packing of backbone and atoms – most common in protein structures
* Simple poly-L-alanine – only certain angles are permitted - +180 and -180 are converts
* Ramachandran plot – Ramachandran is the scientist name who figures out those angles
* Fibrous proteins – a lot of glycines, alanine, serine, cystine – collagen has a lot of proline – everything else very low
* Specific structural proteins – keratin, fibroin, collagen – very peculiar – not providing lots of arginine and aromatic compounds – cannot be chewed down by trypsin – unlike normal proteins – only have few proteins – which predetermine what structures they form
* Keratin forms alpha helix – coils region – form long fibres and twist around each other – twisting provides strength
* Silk – softness and flexibility but extremely strong – beta sheet – strength is attributed to the layers that can sit on top of each other and difficult to break apart
* Collagen – connective tissues – a lot of proline – hydroxyl proline and hydroxyl lysine – can assemble as multi-stranded helices – vitamin C is important for proline hydroxylation – vitamin C deficiency causes scurvy
* Collagen – 3 strands bind together – form strong pattern – lots of diseases are caused by mutagen to collagen sequences during protein making
* Alpha helix - Hydrogen bonding between first and fifth residues – second to sixth – i+4 – first carbonyl group bonded to fifth NH – oxygen has negative dipole – H has positive dipole – create vertical ladder – build up H bonding pattern – end of helix has free NH that is slightly positive charge – other end has free CO which is slightly negative
* Proline doesn’t have H on N because side chain comes back to bind N – proline not happy with alpha-helix – occur before or at the end of proline
* Beta-sheet – H bond between the strand – antiparallel – almost 180 degrees in H bond – most stable
* Parallel sheet – crooked H bond – H bond not 180 maybe 160 – 170 – not as stable
* The chains have to be connected – the loop – can be U bend or go back and form parallel beta sheet – if they turn around called turns
* Turns can be stabilised by H bond – glycine loves to be in turns – cuz no side chains – no steric
* Loops provide stability
* Chou table – may appear in exam
* 2nd structure compacting themselves form 3D
* Globular proteins form 3D – found globules in proteins – call them globular proteins
* There can be mixtures of helices and strands – cartoon can show spirals and strands – 2nd structure hidden from view but does exist
* Stands are like arrows – arrows can tell parallel or antiparallel
* 6.15a – mostly antiparallels – but also have 1 parallel
* Stick models show atoms – H bond between CO and NH – H bond dotted lines – couldn’t see H cause too tiny
* Surface models – can be coloured in different ways to tell us what aa at the surface – atom colouring not so helpful – positive (blue) and negative (red) more helpful
* MSEP – calculated view
* Experimentally – proteins are salts
* Electron microscope of collagen – big ones use this one – more reliable
* X-ray diffraction – better zoom
* NMR for soluble proteins – show that proteins can flex – get multiple structures from NMR
* Protein Data Bank – all protein structures – only one unlike sequences
* X-ray diffraction – X-ray getting reflected by nuclei – can get pattern of proteins – patterns are then analysed – using computers now – originally by hands and maths – computer program looks for blop of density and fit side chains into them – sometimes don’t see side chains but imagine that it is there
* Crystal diffraction – collect images at different resolution 4 armstrongs more detailed than 16
* Most crystallography collected at 2 armstrongs – coming out at 1.3-1.4 – but still can’t figure out density of H – H is too small – which is why we don’t show H in crystal structures
* NMR – shows proton shifts so can see hydrogen bond location – have to be small and soluble proteins – spectrum that shows proton shifts – water (solvent) has a single shift
* Without the folded shape, proteins cannot have proper structures – different architecture – may contain many domains – one protein can have 2 or 3 folds
* Typical domain has 200 aa
* Domain retains its own function
* At least 40 enzymes that bind the same co-factor – structure passes on to different enzyme
* Classification of protein structure based on helices and sheets
* Turns are short, regularly structured regions that connect 2nd structures
* Parallel beta – call alpha + beta
* Few 2nd structures – call disorder proteins – regular proteins – expressed and translate – have function but don’t have shapes
* Common features – hydrophilic exterior and hydrophobic interior
* H bond in the backbone is the main stabilising structure
* Beta sheets twisted and wrapped into barrel
* Polypeptide chain can turn corners – beta or gamma turns
* When look at sequence, hydrophobic residues are green, hydrophilics are pink, not sure in black – does not make sense in writing sequences but make sense when fold into 3D
* Hydrophobicity is the main driving force to form 3D structure
* Nonpolar residues prefer hydrophobic interior
* Charged polar residues contact with aqueous
* Uncharged prefer surface but when buried, can form H bond
* Thermodynamics of how proteins fold – just know that there is a driving force
* H bonds are typically noncovalent interaction
* Disulphides are covalent interaction
* Disulphide bonds are main contributors in small proteins
* We see that different proteins adopted different shapes and methodology to stabilise themselves
* Zinc finger binds DNA – have zinc ion that hold the protein in shape – start transcription
* Heme group makes myoglobin compact and red
* Proteins need to be maintained at particular temperature, pH, detergents, etc
* Denaturation is when proteins lose their shapes – lose functions too
* pH maintains shape and charged – H bond
* Detergents can invert the proteins – stabilise the hydrophobic side chains – ruin the shapes
* Guanidium ion – at the end of arginine – is also an independent ion – and urea – N compounds can cause proteins to unravel – called chaotropic agents
* Ribonuclease A – Add urea – break disulphide bond – become cystine – proteins just swim around – can also oxidise the denatured ribonuclease A with BME
* The funnel – thermodynamic folding – the lowest energy part is the native state at the bottom – along the rim is the denatured proteins – some structures lead down into the hole – some lead to local cavity – so large proteins can misfold – protease comes to cut them out
* Chaperonins hold large proteins – let them fold and unfold properly
* Misfoldings lead to diseases
* Slide 45 – dimer of molecules called transthyretin – one yellow – one magneta – show assembly that there is a centre of symmetry shown by black dots – two molecules appear to be twisted around each other – sometimes have hydrogen bond – 2-fold dimer
* Cartoon – no side chains shown
* Tetrameric enayme phosphor… - 4 subunits – one centre of symmetry – ending in –ase meaning enzyme