**Text transcript of handout 2 summary.**

Hi there. In the second handout, we really want to zoom in a little bit on proteins, a biomolecule that we had mentioned in the first handout as being key, and one that we're going to really focus on a little bit now. We commenced this discussion around the versatility of these macromolecules or these biomolecules in the cell. We saw how they have so many different types of roles and how those roles are ultimately dependent on their structure, so their structure:function relationship I guess is coming through again and how that is also dependent on its composition, as in how the protein is built and what it's made-up of, what components are there, and then how this folds into a functional shape that gives it a structure relevant to (and needed for) its function.

We discussed the idea of the building blocks of proteins, and we zoomed in a little bit on amino acids, so these structural entities that have an amino acid group and a carboxylic acid group, that's where their name came from, amino acids, and we looked at the structure of a common amino acid observing what's attached to the central carbon and we often refer to that central carbon as an alpha carbon. We saw that when four different groups are attached to an alpha carbon that we have chiral molecules being possible, so we talked a little bit about chirality and how we can have enantiomers or stereoisomers of molecules being formed. So in regard to amino acids, we talked a little bit about plane polarised light being shone at,or through, an amino acid, and how it can be deflected left, so levo and becomes an L amino acid, or it could be deflected to the right, dextro or D amino acid and when we looked at the structures we saw that the amino group is often a good indicator if it's in L or D form based on its position so the amino group is normally on the left for the L form and on the right for the D form. So that just gives you a nice indicator as to differentiating between the structures (our own proteins are composed of amino acids in the L form; while D amino acids exist in bacterial cell walls and some peptide antibiotics) so we spent a bit of time talking about those enantiomers and stereoisomers and different forms of the molecules that are technically mirror images of each other but they're not superimposable on top of each other. We looked at a few structures as examples and we discussed thalidomide as well here. With regards to the structures, I asked you through exercises to be able to draw the L form and the D form of an amino acid so we specified the amino acid alanine which had a methyl group as its functional group and that was an exercise we did in class, so drawing the L and the D form. We then, once we had a grasp on the structures, we started looking at amino acids and realising that there were twenty general amino acids or standard amino acids. There are a few variations on this that we can get but generally there are 20 standard amino acids. In order to communicate with other scientists on a protein level we have to know the names of those 20 standard amino acids and we have to know there are three letter code and their one letter code. We saw how Glycine was GLY or G and we saw Alanine was ALA and A, but then things get a little bit more, I suppose, tricky because we have other amino acids which don't kind of follow the obvious, how would you say, nomenclature naming system so phenylalanine is one example with Phe and it's one letter code is the F, because P was already taken by Proline so it's important that you're very aware of that three letter and one letter codes. We went back to the structures of amino acids and we said well how do they look and how do they appear in our cells, and we looked at the pH of our cells being approximately 7.2 meaning that the amino acids will exist in a zwitterionic form as opposed to a non-ionic form, so you'll see exercises that we completed comparing the non-ionic to the zwitterionic forms of the amino acids and we sketched out those structures. We looked at those 20 standard amino acids again and we said well scientists love to organise things and they often like to put things in different classifications or different groups, so we saw the 20 standard amino acids are actually split across five classes: nonpolar, polar, positively charged, negatively charged and then aromantic if there's a ring structure. So we glanced around those five classes and we looked at charges, we looked at the presence of say tryptophan which had a double ring structure, we looked at a unique feature of cysteine because it had a sulfhydryl group attached, and so there was quite a lot of kind of features in that table that we would have gone around the different amino acids. I think it's important that you're aware of some of those features and how they're going to actually play a role in I guess in functionality or in their kind of structural entities that they bring to proteins when they're there. So a good example of that would be glycine, and when we think of glycine, it has the smallest functional group, in a hydrogen atom, that would mean that a small amino acid might be very useful in an area of a protein where we require rotation or twists or turns, because it's so small, it will help that bendability and that flexibility to be present because there can be a lot of rotation because it's so small. Then when we look at other amino acids, they can be very big and bulky and that might hinder or prevent the rotation or flexibility. So as I said when we scope around the different amino acids, we did note that there was a Sulfhydryl group in Cysteine, now we also see this in methionine too, but the thing with cysteine’s is that it's located at the terminus of the functional group. So you might look at those structures and see how the sulfhydryl entity is located at the end of the functional group in Cysteine when compared to methionine. That led us to talk about how cysteines actually play a really big role in how proteins are kept in their shape, and that's from the formation of a disulfide bond or a disulfide bridge, you see them referred to. So we talked about insulin and we looked at those disulfide connections between the chains of insulin, but also within one of the chains as well. We discussed this characteristic and feature with regards to antibodies too, so it really helps proteins hold their shape in a particular way and breaking the sulfide bonds is very difficult. In the lab, we use a chemical called beta-mercaptoethanol to break disulfide bonds, whereas we saw earlier with hydrogen bonds in DNA that we could separate them with some heat in the lab.

So once we started thinking about these amino acids, we said well they have to be stuck together, so we looked at small peptides, and even hormones, that we saw as being quite short. We looked at how we have these amino acids are stuck together, and how we read them from the amino end to the carboxy end, so this is like reading left to right or reading DNA from five prime to three prime. We read the proteins from the amino to the carboxy end and we had examples of that, but our main focus was the peptide bond being a very rigid and planar structure with 40% double bond characteristics, and we saw in the diagrams that the rotation around the bonds actually comes from around the alpha carbon of the amino acid. So the diagrams we looked at were really about looking at the peptide bond like a sheet of glass, a planar structure that is very flat and rigid, as opposed to around the carbon, the alpha carbon, of the amino acid where we could get some rotation, more so in the case of amino acids like glycine where the functional group is very small. We discussed a little bit more about cis and trans in regard to where the functional groups are located across proteins, and then we kind of went back and thought well, we have all these different amino acids and building blocks but what encodes the final shape? The last few slides were really focusing on a particular amino acid order and identity, so particular sequences of amino acids can form a particular shape. Other sequences of amino acids, even if it's the same amino acids but just in a different order, can't form that shape as in the same one as the first example. So the order and the identity, i.e. which amino acid is in which position is vital for us for folding to the right shaped protein. And where are all the instructions that tell us how to do this? Well that all came from our genes and our DNA. In the 1.5% of our genome that codes for proteins, that tells us what amino acid to put in what position to build the right functional (shaped) protein.

So we concluded the handout is the way we'll start the next one. We reviewed the idea of primary structure, secondary structure, tertiary and quaternary. And these are the four levels of how proteins fold to ultimately become functional, and we'll be zooming in a lot more detail into those four levels or layers in the subsequent handout.

Hope this helps!