Biomaterials for bone tissue Engineering Materials
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Structure of Bone /Tissue

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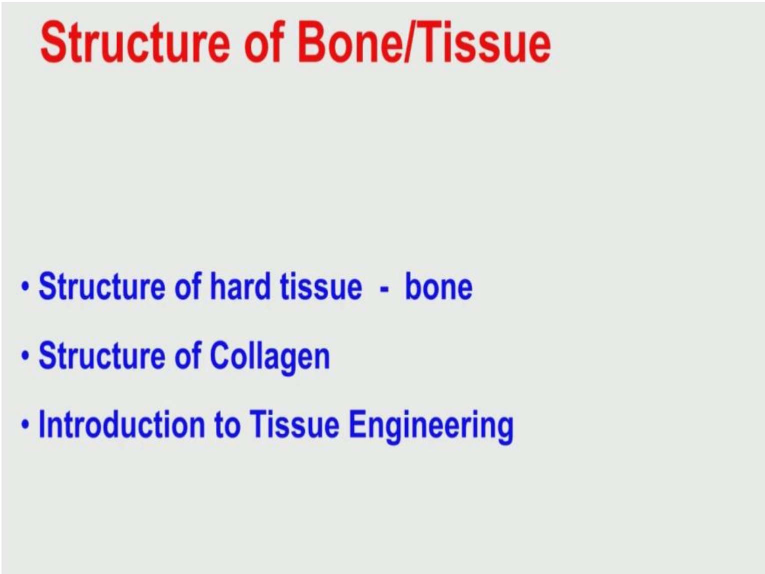

Welcome to this module on this of Bone Tissue so so far I have described the structure and properties of, so far I have discussed structure and properties of Cell, Bacteria, and Protein. So not only the structure but also certain characteristics which are of relevance to cell biology as well as Biomaterials Science that were discussed to greater extent for all this three (( )) (00:59) for all this three elements that is Cell, Bacteria, Protein.

Now, there are tissues in the in m tissues can be broadly classified into four categories, now, these four categories it can be it is summarized in one of the earlier slides

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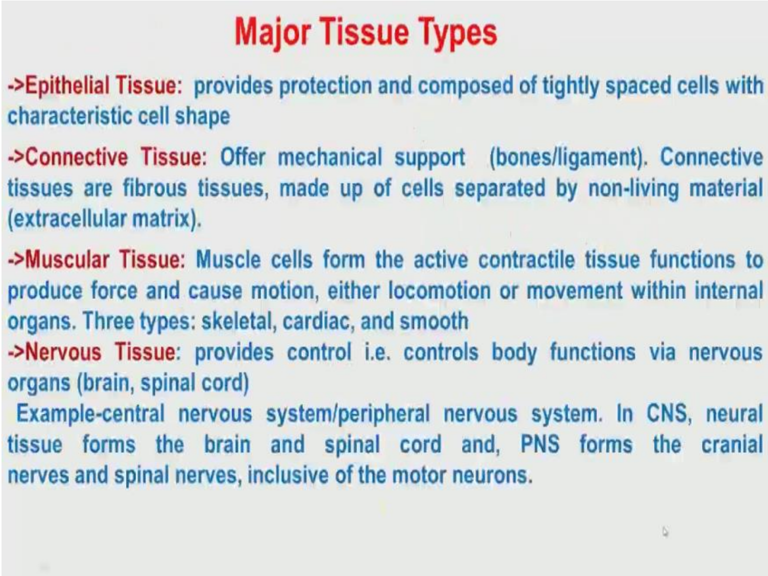

Which I would like to recall so there is is the four four broad (()) (01:35) four classes of tissue 1. Epithelial Tissue 2. Connective Tissue 3. Muscular Tissue 4. Nervous Tissue. So Epithelial Tissue provides protection and provides protection and composed of very tightly spaced cells with characteristic cell shape, so typically Epithelial Tissue cells they are extremely tightly spaced. Y

You remember in the contest of the cell signal in molecules or cell signal in processes, I have mentioned that how two tightly spaced cells that if you apply the fixed fast lock diffusion what is the total number of molecules that can be transported along these gap junctions and that example was valid for the tightly spaced cells like in Epithelial Tissue

Second one is the Connective Tissue that is that offer mechanical support and bone and ligament are the most popular example of this Connective Tissue. These Connective Tissues are made up of essentially Fibrous Tissue and here the cells are widely or physically widely separated from one another. However, they are dispersed all the different type of cells they are dispersed in extracellular matrix which has different composition, if you remember correctly the extracellular matrix is Collagen, elastin.

Now these two components Collagen, elastins are responsible to give the specific elastic stiffness property to extracellular matrix. So in different tissues, like whether it is Epithelial , Connective, Muscular, Nervous Tissue the extracellular matrix their composition may vary in terms of that biological micro molecules, in terms of their fibrous collagenous protein or different type of collagenous protein and elastin.

So, since their composition vary the constituents vary to some extent and that is why different extracellular matrix therefore the extracellular matrix in four different tissues they have different elastic stiffness property. And this extracellular matrix provides lot of structural support to the cells that this particular tissue contains. For example in the Connective Tissue you have fibroblast cells. One of the example I have given while discussing the cell migration and if your remember that in cell migration I said that typically fibroblast cells they kind of walk or they migrate with the speed of typically 20 to 30 micron per hour.

Also, in the Bone Tissue you have another type of cells that is called Osteoblast cells. Osteo means bone Osteoblast means bone forming cell or you have third type of cells Osteoclast cells that is bone (())(04:47) cells and also you have osteocytes which are like(())(04:51)blast cells. So this is this is all about the Connective Tissue.

The third classification is Muscular Tissue, essentially muscle cells. Now, examples of the muscle cells are the Myoblast cells, so this is one of the type of cells that abundant in the muscle tissue and this is that one of the one of the mm properties of the myoblast cells is that they are essentially they have the characteristic contractility property and therefore these these tissue essentially have a very active contractile nature and it also force and causes motion during locomotion and movement within internal organs.

There are three types of muscle tissues you have in your body. 1. Skeletal Muscle Tissue 2. Cardiac 3. Smooth Muscle Tissue. So, therefore in the development of any material for cardiac tissue or the the any biomaterials to show whether these particular materials can support the growth of the cardiac cells, Often people use for the cardiac cells like cardiac myocytes along with that they also use muscle tissue cells like myoblast cells.

Fourth one is the Nervous Tissue that provides control of all the activities that your body is supposed to perform and that is from the nervous organs and you have the brain, spinal cord most prominent example of the nervous tissue. In your body you have CNS what is called Central Nervous System and also you have is PNS that is Peripheral Nervous System. Central Nervous System is the neural tissue forms the brain and spinal cord and the Peripheral Nervous System essentially you have the nerves and some of the Cranial nerves and Spinal nerves at the end.

Many Times during an injury or during any operation some part of the Peripheral Nervous System is injured or cut, one can replace with certain biomaterials what they call nerve conduits. And these nerve conduits are the one of the clinically relevant solution.

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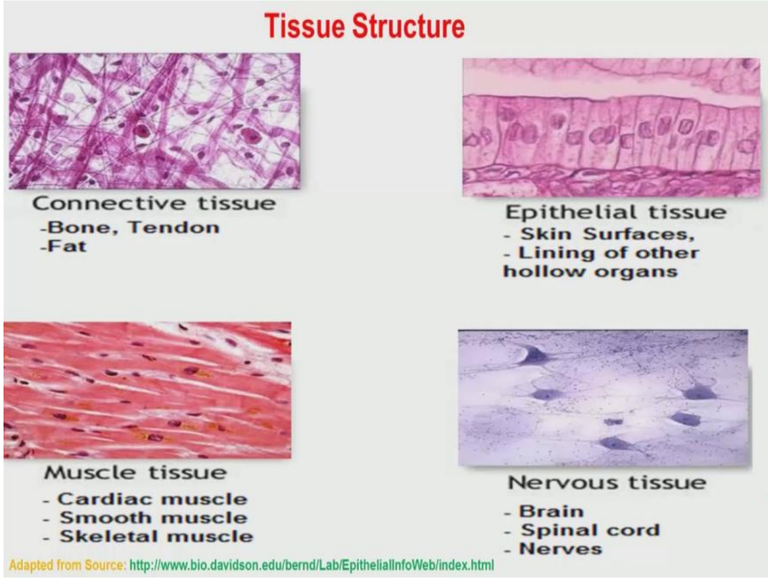

This is little bit about histology sections of this tissues. This is the Connective Tissue, you can see that the cells are well separated physically and they are like, you can see this fibrous nature, these are collagen fiber in the extracellular matrix examples are bone and tendon

Epithelial Tissue you can see in this histology section the cells are very closely spaced lined up one against another and this is the characteristic of the Epithelial Tissue. This is there in the skin surface as well as many lining of the several hollow organs.

Third is the Muscle Tissue; this three examples we have mentioned in the last slid e and you can very well see that the Muscle Tissue also has the very specific features and most of these features are kind of myotubes which is which forms as a result of fusion of the several Muscle cells which are lined up against one another and then they form these myotubes.

Fourth one is the Nervous Tissue; this is the histology section of the Nervous Tissue. A Nervous Tissue also has the very characteristic structure which is strikingly different from other three tissue structure. So this is very long elongated neural structure and then they are contained in brain, spinal cord and nerves.

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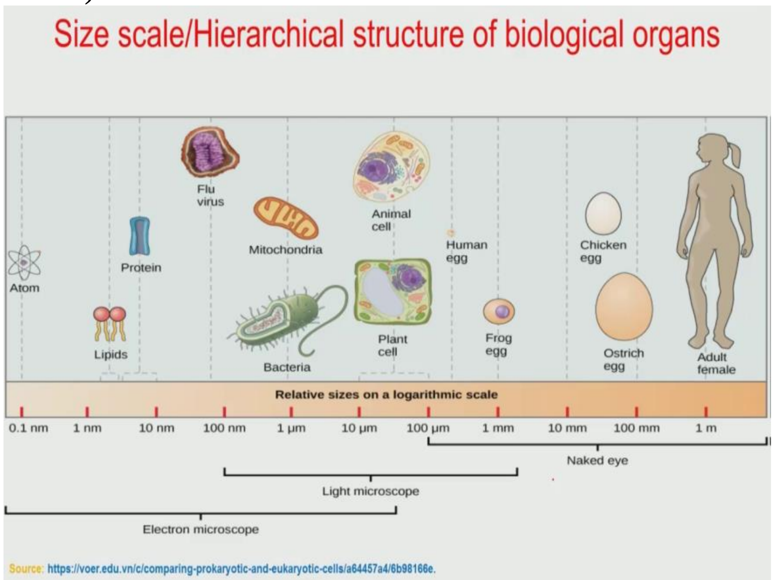

These structures this is fourth tissue structure; this is also one of the most important slide to get you familiarized with these numbers. For example you have ligands in a protein structure, these ligands typically has the length scale somewhere between 4 to 5 nano meters.

You have a protein structure which is like less than 10 nano meter, you have viruses, you have the bacteria like somewhere between 1 to 2 micron. Mitochondria that is the power house of the cells. This Mitochondria structure is somewhere 1 micron. You have plant cells and then you have animal cells. These plant and animal cells they somewhere vary between 20 to 30 micrometer.

You have human egg, you have frog egg and then you have chicken egg so these are like larger size and you have a human human and one of the human length of this somewhere between like meter and above. So, this is the large length scale that we deal in the biological systems and this biological system contains starting from ligands, proteins, cells, bacteria and so on.

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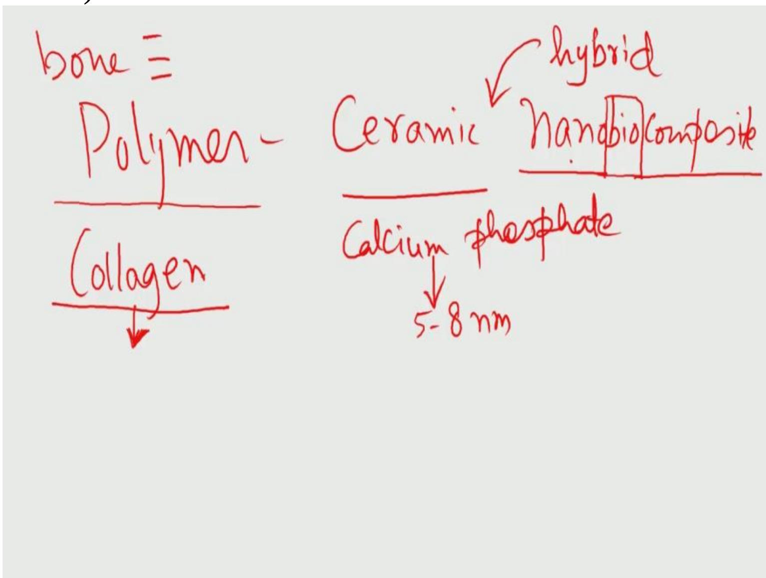

Now Let us focus our discussion more on the bone structure, so now that we have revisited the different tissue types and then how their structures are different. Let me focus the rest of the discussion on structure of this one of the hard tissue that is the bone. So, to start with, one has to know that natural bone is a classical example of a Polymer Ceramic based Bio Composite and where collagen is the example of the polymer that it contains and hydroxyapatite is the ceramic.

Now, therefore you will also discuss about the structure of collagen in the bone. So, as I said natural bone is Polymer Ceramic Nano bio composite. Why we say this bone as a Polymer Ceramic Nano bio composite because Polymer is represented by Collagen here, Ceramic is represented by Calcium phosphate. Why it is Nano because calcium phosphate has a size the length scale is 5 to 8 nanometer.

Collagen also at the structural level it is one of the protein molecule, it is protein then it has a triple helix structure, and this triple helix structure will describe you (( )) (12:28) This also has a almost like this also has Nano scale dimension. Why bio composite because it has a biological constituent natural biological constituent that is polymer Collagen, Nano because its constituents have a Nano scale size, and it also called hybrid composite.

Why hybrid composite because two different type of constituents that is one is the collagen and another is the hydroxyapatite contained in the bone structure

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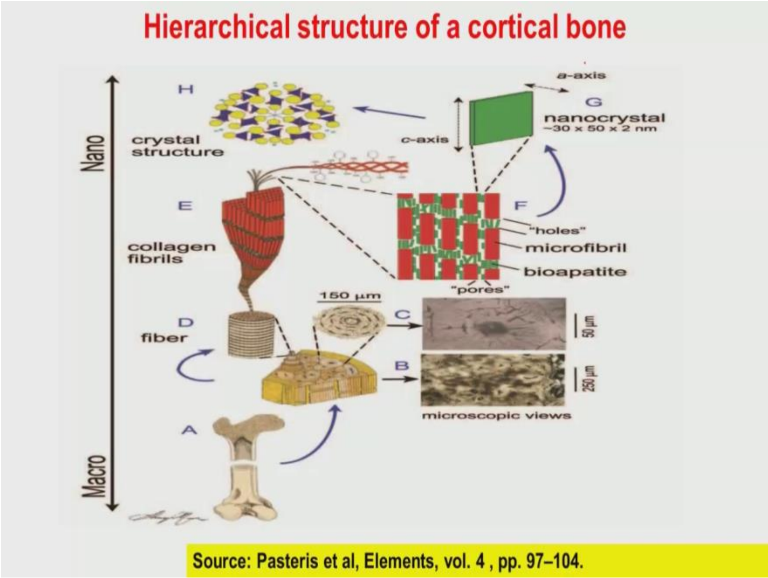

Okay. , So, these this is the hierarchical structure of the Cortical bone. You have the two types of structure in the bone one is cortical bone which is more mechanically stiffer and stronger structure and you have a Cancellous bone which is essentially very spongy type of structure. So, this (Fig A) is an example of a long bone structure you can see that it is a very irregular shape, now if you take a section from this long bone structure, then in the section you will see there are lot of canals here.

So, these canals are essentially Osteons, and these Osteons they have certain concentric circles. These length scale is somewhere between 00 to 50 nanometer. Now this, Now you can focus that how this individual canals they are built up. So this is our individual canals it is shown like a cylindrical shaped object. Now, this object if you focus more, then you will see that it individually they are built up on the collagen fibers.

These Collagen fibers they are the hydroxyapatite Nano platelets. They are like a dispersed in between the collagen fiber or in other words these collagen fibers in hydroxyapatite Nano platelets they are been sandwiched between different collagen bundles along the particular direction that is the C Axis. So It has a specific orientation of the hydroxyapatite Nano platelets. And this, hydroxyapatite Nano platelets not oriented or not dispersed in a random manner in the bone matrix. However, they are oriented or they are being sandwiched between these collagen fibers.

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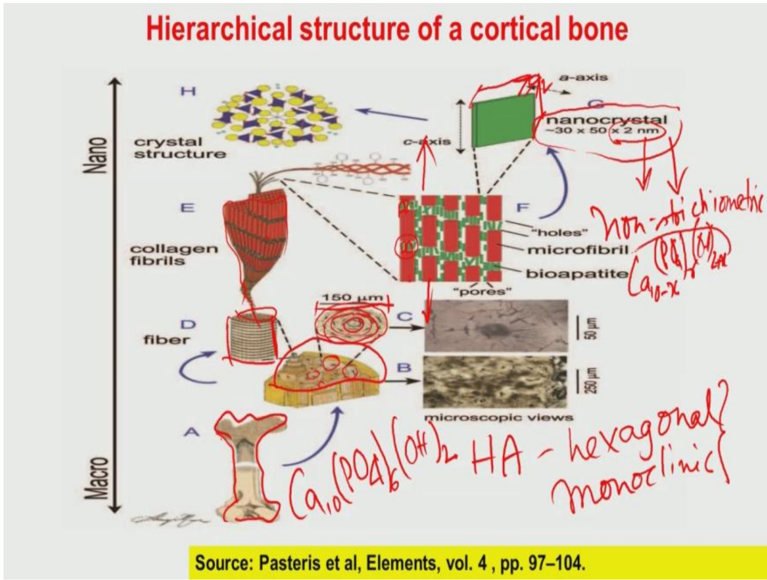

One thing that you must notice that this cortical bone though it is mechanically very stronger compared to collaa collag cancellous bone Nevertheless, it also have certain porosity. So it is not a extremely dense structure, but it is slightly porous structure, it is a hybrid structure because it contains both Collagen Polymer as well as the ceramic structure. Some more details are shown here like 30 to 50 nanometer I mean this size varies but many people mentioned in the book is that 5 to 8 nanometers is the size and 2 nanometer is the thickness that is in the other direction that is the platelet that third direction is 2 nanometer.

Okay, Now hydroxyapatite they also if you are from (()) (15:59) background hydroxyapatite they can exist in hexagonal structure, hydroxyapatite also exists in monoclinic structure. So these are the two possible structures of hydroxyapatite. Now, hydroxyapatite has a stoichiometric composition of Ca 10 PO 4whole6 whole OH whole 2 but this is a stoichiometric composition. But the bone contains largely non stoichiometric hydroxyapatite, so it is better to describe the inorganic composition of the bone is like some non stoichiometric structure essentially it has some Ca10 minus x and then PO 4whole 6 and then comes OH 2 or OH 2plus x or something. It is essentially non stoichiometric structure of hydroxyapatite

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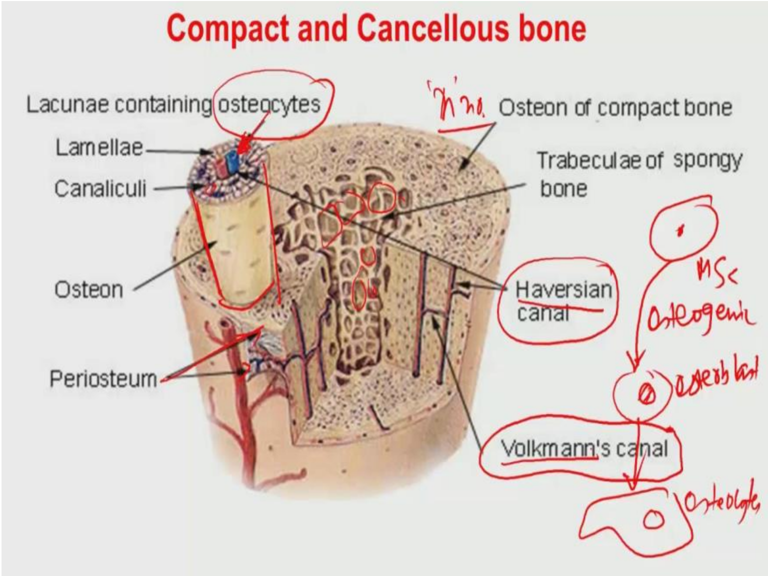

So, this is the structure that I was mentioning you in the last slide to some extent; this is much more very clear, more specific structure description. This is your Osteon and this Osteon is lifted up just for the illustration purpose, just to show that how it grows along the long axis of the bone and these Osteons you can see very closely if you see then it also count as Osteocytes. Your remember Osteocytes are the matured Osteoblast cells. So you have the stem cells, so if you have that Mesenchymal stem cells then it go in the Osteogenic lineage. And in the Osteogenic lineage it first forms pre Osteoblast then it forms Osteoblast. So once you have that Osteoblast after that the terminal member of this Osteo Osteo Osteogenic lineage is Osteocytes. So, this is the more matured bone cells which are contained in this in this Osteon

You also notice that there are some Canaliculi here and certain Lamellae. The Periosteum is also therein the bone structure, the Periosteum means the outer cover of the bone just like when you wear shirt and in shirt has certain collar or that in around your hand; so this bone also has a kind of outer cover which is called as Periosteum. And you have large number of Osteon, this is like ‘n’ number of Osteon are present in the bone structure. Internal structure of the bone if you see, this is more like a spongy structure; you see this is a large sponge.

So this kind of porous structure makes the bone essentially, internal structure of the bone or cancellous structure of the bone essentially weak mechanically. Outer structure of the bone although there are some porosity present as I mentioned in the last slide but also it is much much denser than the most spongy structure. And you also see there are Haversian Canals and Volkmann's Canals. Now, these canals many times are named after some of the scientists, who first discovered these canals. And these based upon based on that scientist name some of them are called Volkmann's Canal and Haversian Canal.

The general role of these canals is to transport oxygen, blood and food to the cells which contains and also takes and helps to the take this different waste products out from the cellular complexes.

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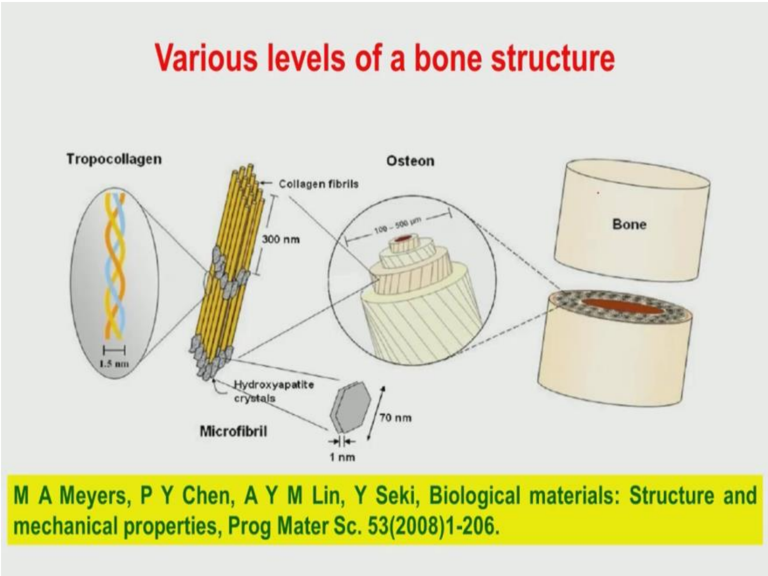

So, little bit on the numbers while describing the various levels of the bone structure. So, as I said in last two slides that you have a Collagen fiber. These Collagen fiber are very nicely oriented in the bone structure and the hydroxyapatite crystals also perfectly oriented along the C Axis of the bone. And this hydroxyapatite platelets crystals; if you look at them you can see 1 to 2 nanometer is their thickness of this platelets. And this Collagen fibrils along with the hydroxyapatite crystals this kind of aggregates they form the Osteon. And these Osteon are typically 100 to 500 nanometers. And this individual Osteon it is one of the major structural unit of the bone structure. So at the very micro scale the Osteons are the structural unit of this bone structure.

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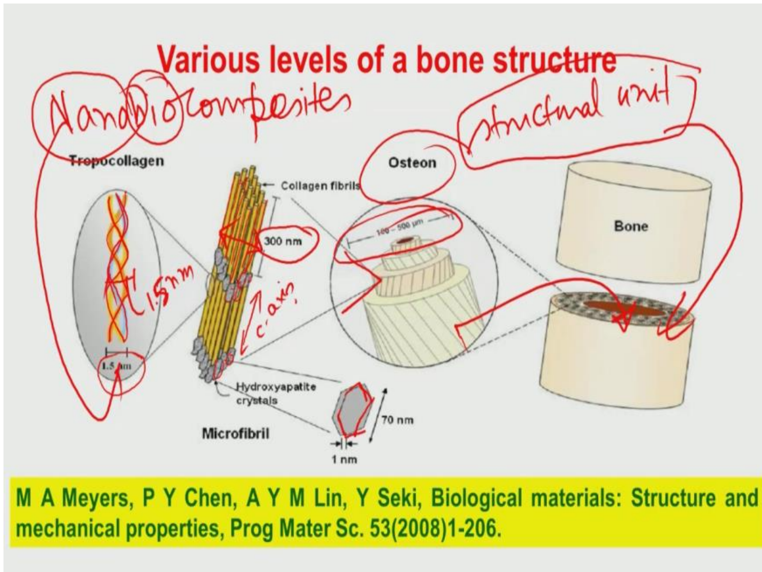

When I say that bone is a Nano bio composite; now I may like to emphasize once more that why it is called Nano bio composite; bio because it has Collagen; Nano because it has Nano scale Collagenous features, this is a very characteristic triple helix structure. You have earlier seen double helix structure of a DNA, similarly triple helix structure of a Collagen is also very famous in the cell biology. The other things that you notice, this is this dimension this width of the Collagen is of the order of 1.5 nanometer. This 1.5 nanometer individual Collagen Fibril, but when it makes this Collagen this this makes this bundle, then the length of this bundle is somewhere between 200 to 300 nanometer but the width of the bundle cannot exceed more than 100 nanometers. So, this individual bundle which called which along with that hydroxyapatite nano crystals make this bone structure to be called as Nano bio composite.

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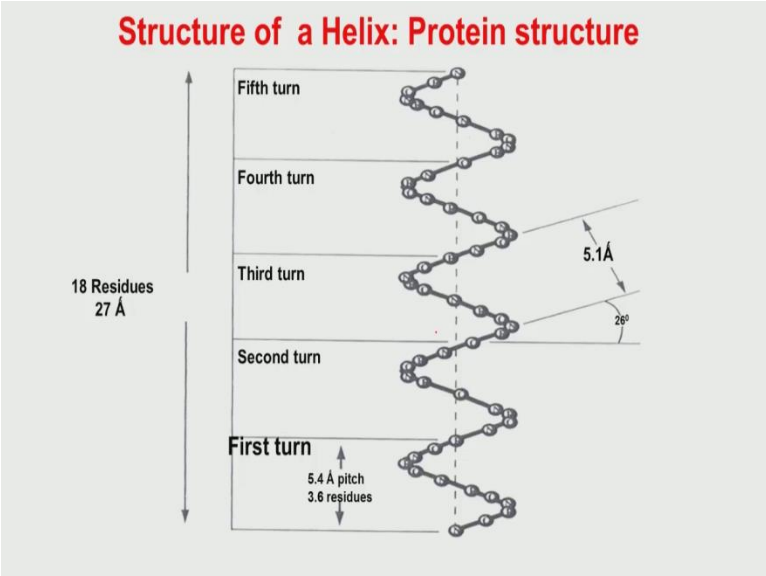

Okay, Now as I said that Collagen has a typical triple helix structure, now if you recall the typical protein structure it has a it has a very characteristic helical structure and this helix it has a five turns; this total length scale of this helical structure is somewhere 27 Armstrong, meaning that each turn has around 5.4 Armstrong. So this is extremely small, angle of this bending it is around less than 30 degree and therefore some simple geometry it is coming out to be roughly around to 5 Armstrong.

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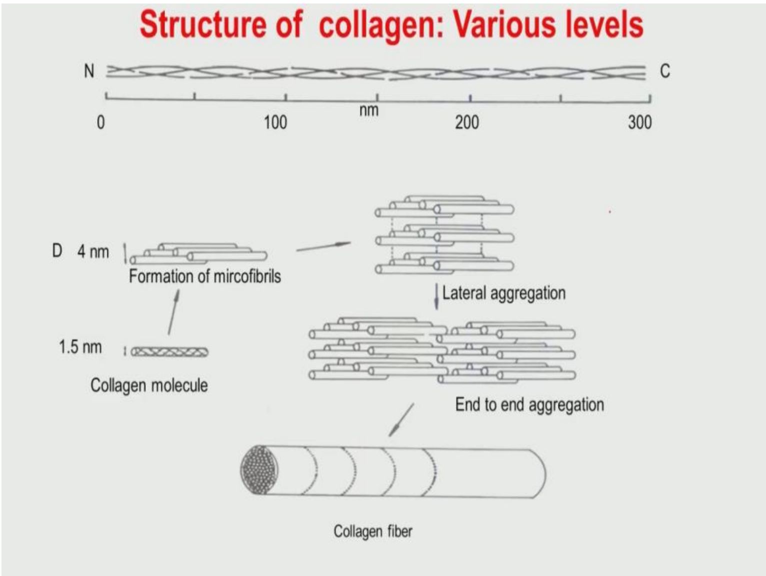

Now, when it comes to, in case of the Collagen what you notice here, so Collagen has a triple helix structure, so you have a N terminal here like a protein and you have a C terminal on the right hand side. So; this this structure then it goes upto this typical along this one direction it has a 300 nanometer length. That, initially that Collagen molecule which has a triple helix structure it has a width of 1.5 nanometer. At least 2, 3,5 micro Collagen molecules they comes together and they form what they call in cell biology is microfibrils. Microfibril has a dimension of diameter is around 4 nanometer.

Now this, these microfibrils can form 1 unit and several such units can bound to be can be bound to each other by weak hydrogen bonding. In the cell biology literature or book whenever you see dotted bonds it is always it always represent the weaker bonds, either hydrogen bonds or van der Waals type of bond. And then after this lateral aggregation there is also End to end aggregation is possible like this individual unit can become one unit here and similar another unit also can come here and then there will be then again some dotted bonds which are end to end bond. This entire structure then forms a large tube like structure and this you call as a Collagen fiber. These Collagen fibers are present in abundance in extracellular matrix as I said before. Along with Collagen fibers you have a elastin that is a second one. So both Collagen fibers and Elastin in view of their characteristic structure they provide certain mechanical support to this or structural support to the cells in the extracellular matrix.

So whenever you see that there is any fiber kind of a structure, normally they represent little bit robust structure compared to individual molecular level structure of the regular kind of a structure.

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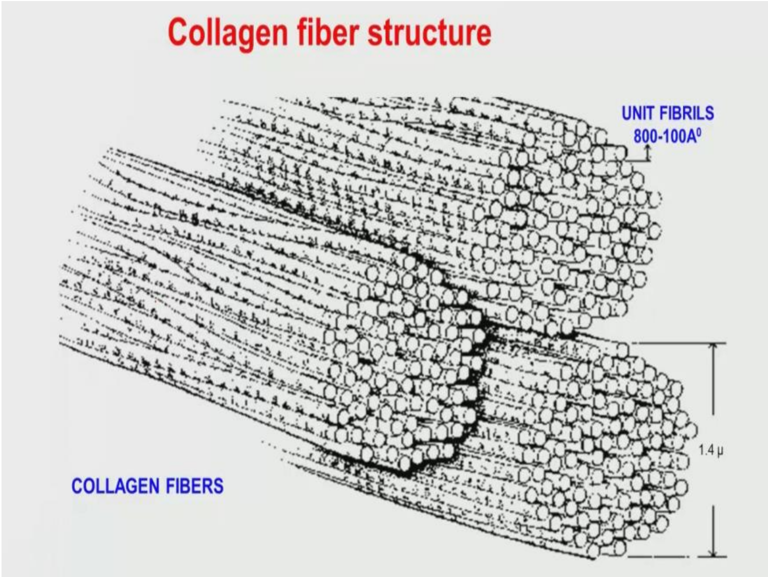

This is how these Collagen fibers they are actually contained in a bone structure. And these Unit fibrils they have a dimension 800 to 1000 Armstrong. And this is essentially this individual thing is like 1.4 Armstrong 1.4 micrometer.

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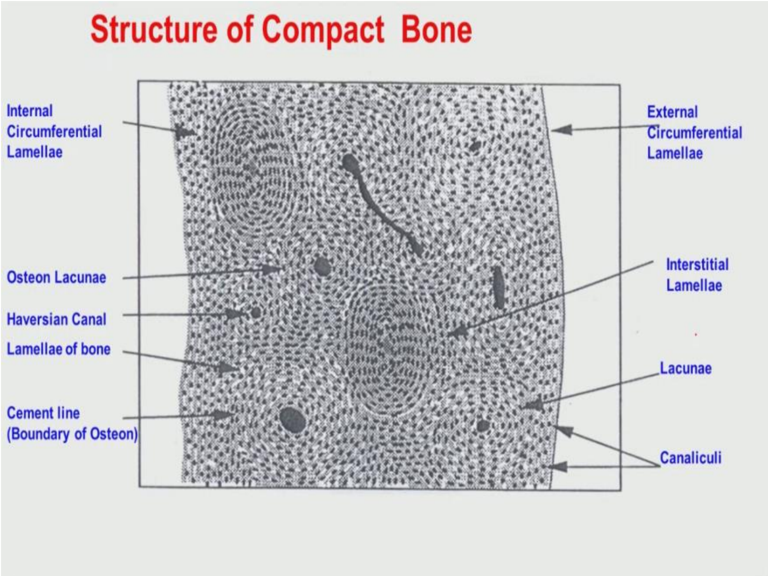

This is a 2 Dimensional section of a compact bone and again you can see this is a Osteon structure, this is two Osteons, they are not closely spaced but they are separated physically and there are several other structure elements which I have also mentioned in this earlier.

So this is all about the bone structure and then we will start with the bone composition and also the different types of natural bone in the next module.