Structural Biology
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Lecture – 41
History of Molecular Visualizations of Biological Macromolecules

Hi everyone, welcome again to the course of structural biology. For the last few modules, we have discussed the core of the course, the structural biology techniques. Now, we are out of that; in this module, we will talk about visualization. So, to start visualization, very interestingly, I will take you to the first slide, which was used to start the course.

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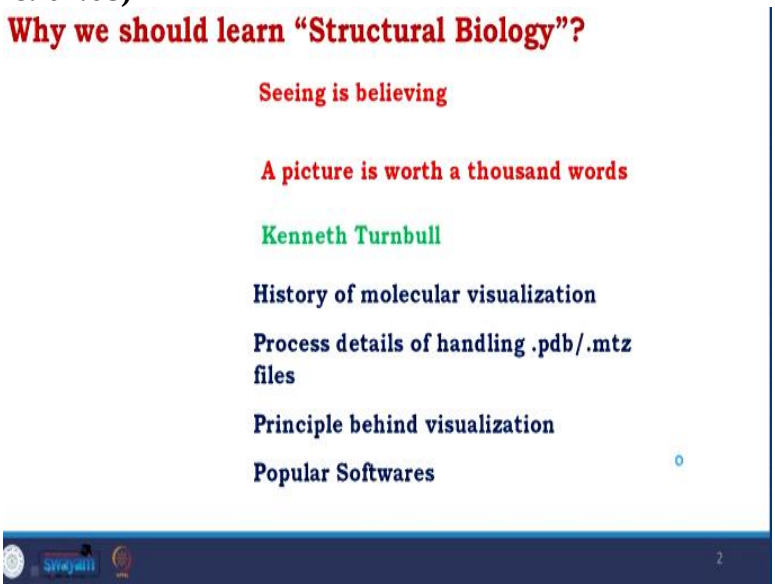

Why should we learn structural biology? And one of the reasons I started with seeing is believing. I also quoted Kenneth Turnbull, who said a picture is worth 1000 words. Today, I am going to talk about a module which is about visualization. But interestingly, when I started, I talked about picture visualization. Now, it is not limited to visualizing the picture; through the course, I have shown a lot of movies.

So, first of all, the techniques have improved a lot, the computational power improved and. So, today I will talk about visualization, but the whole module includes the history of molecular visualization because it is very interesting for you to know about how actually the visualizing happened from where it started from where people started the idea of making it under computation, what they did before computation all would be under the history of molecular visualization then process details of handling pdb and mtz files.

In the last modules, we discussed the structure, which is deposited under pdb and mtz; what was the electron density you will get? So, for an X-ray crystallographic structure for cryoelectron microscopy, you will need an electron density map we will talk about them. Then we will talk about the principle behind visualization what are the type of analysis we do, and what they are having an impact on the application. And then, we will discuss popular softwares like COOT, and PyMOL; why COOT and PyMOL? I will describe that also. So, let us welcome the history of molecular visualization of biological macromolecules.

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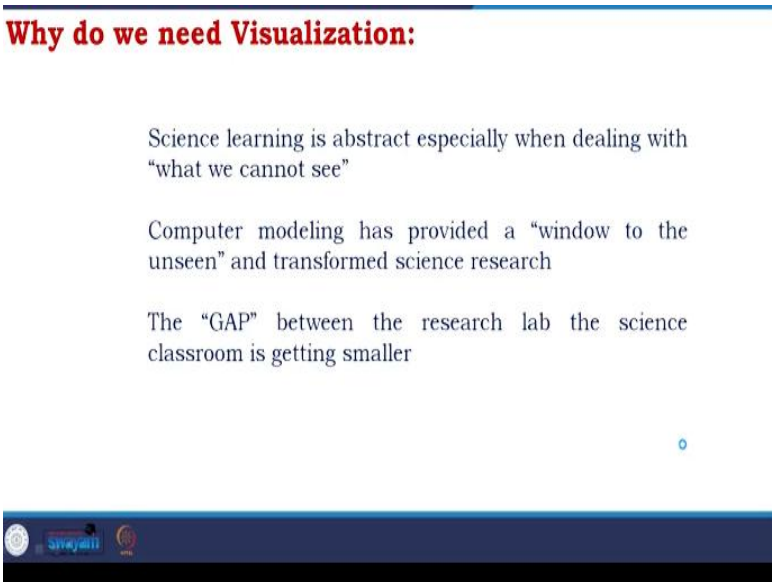

So, as I talk, why do we need visualization? Since learning is abstract, especially when dealing with what we cannot see, we have discussed the power of an eye. So, what is not coming under the power of an eye, we need some instrumentation starting from a simple lens, going to compound microscope, electron microscope getting more powerful resolution, other spectroscopic signals which will give us information all those comes under this.

If we could see that, we could merge them in microscopy; if we cannot see them, we take the information and build up the models. Computer modeling has provided a window to unseen and transformed science research. So, before a lot of things, people have to imagine themselves. But now, with the advent of high-resolution microscopy, spectroscopy, and computation, we can see the unseen. The gap between the research lab and the science classroom is getting smaller.

So, one thing was what the scientists were doing, what they saw, can the students could see them it was not possible, sometimes it was very expensive, the setups of the instruments. So, how the journey happened is the topic of today.

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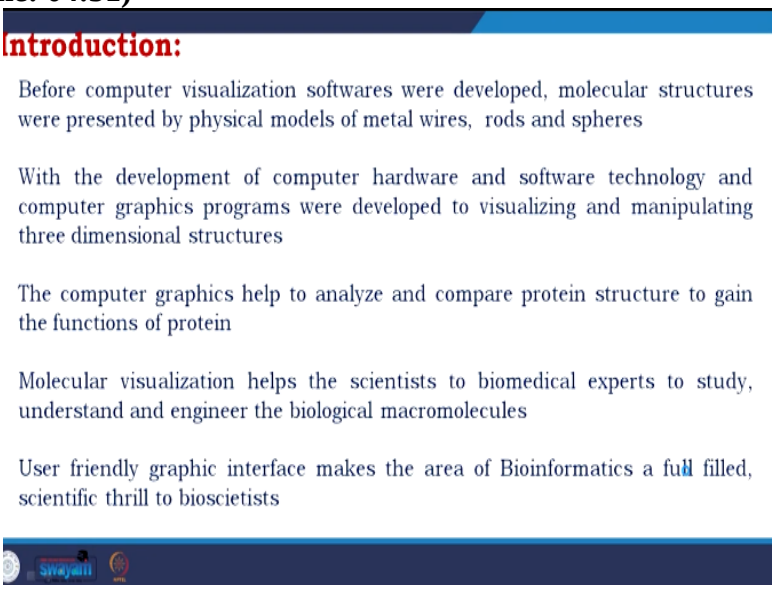

Before computational visualization or computer visualization, softwares were developed for molecular structures are present and physical models of metal wires, rods, and spheres. So, people see the signals, and from there, they want to develop a real-life model. With the development of computer hardware and software technology, computer graphics programs were developed to visualize and manipulate 3-dimensional structures.

The computer graphics helped analyze and compare protein structures to gain protein functions. It is applicable to all biological macromolecules, but as I always say, protein is a functional molecule. So, a lot of interests are always there in focus to the protein. Molecular visualization helps scientists and biomedical experts study, understand, and engineer biological macromolecules.

So, as I told in the previous modules, structural information is vital, but being able to look at it in high resolution is always helping our imagination power to be used at a higher level, and from understanding the system understanding a protein, DNA and all to engineer them comes from that concept, when we see them, when we compare between them when we compare between as we say when we imagine the comparison was difficult.

But when you are comparing, initially we are comparing between, let us say an apple with a pineapple and then we are comparing between an apple and an orange. And now we are getting the opportunity to compare apples and apples. That is where we are fortunate we could see them, we could compare them in front of us, and from there understand the real system. Because we have now a very good understanding of the real system we are going to engineer them.

A brief that I will talk about in the protein engineering part of the course, the user-friendly graphic interface makes the area of bioinformatics a fulfilled scientific thrill to bioscientists.

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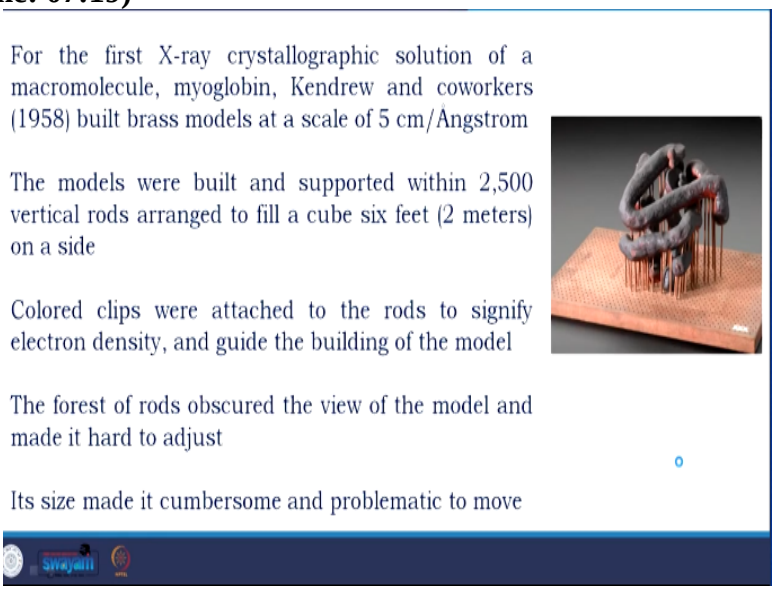

For the first X-ray crystallographic solution of a macromolecule we all know myoglobin Kendrew and co-workers built the brass model at a scale of 5 centimeters per angstrom this is the brass model. The models were built and supported within 2500 vertical rods arranged to fill a cube 6 feet which means 2 meters on a side. The colored clips were attached to the rods to signify electron density and guide the building of the model.

The forest of rods obscured the view of the model and made it hard to adjust, it is much more difficult when than what we do nowadays a computer model. Its size made it cumbersome and problematic to move, so it stayed in one place. Because it is heavy, you cannot take it in the class. So, as I start with a difference between where the work is going on and where the model is established, from where the students are coming, there was a gap.

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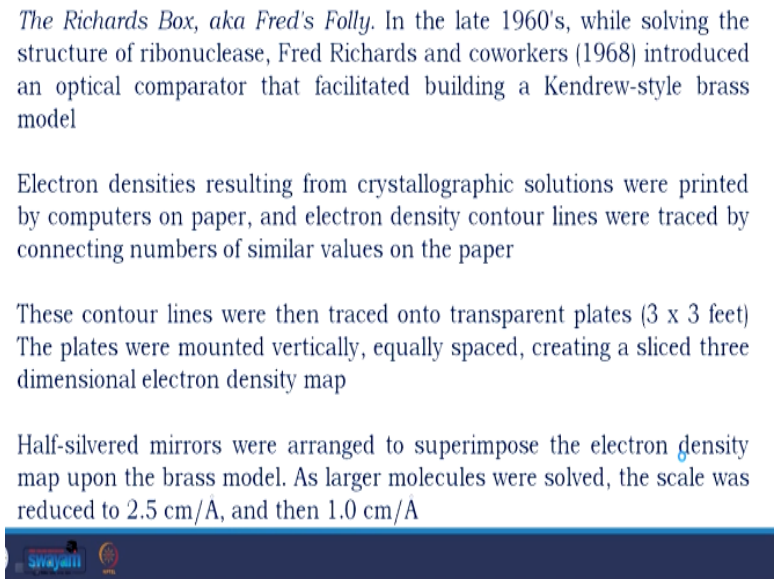

The Richards Box aka Fred's Folly. In the late 1960's; while solving the structure of ribonucleotides, Fred Richards and co-workers introduced an optical comparator that facilitate building a Kendrew-style brass model. Electron densities resulting from crystallographic solutions are printed by computer on paper, this is the first time when computers are coming to be involved and from there actually, the idea of computer graphics is developed.

And electron density contour lines were pressed by connecting numbers of similar values on the paper. These contour lines were then placed onto transparent plates 3 into 3 feet the plates were mounted vertically equally spaced, creating a slice of 3-dimensional electron density maps. Half-slivered mirrors were arranged to superimpose the electron density map upon the brass model. As larger molecules were solved, the scale was reduced to 2.5 centimeters per angstrom and then 1 centimeter per angstrom. So, there is an even journey to make finer structures.

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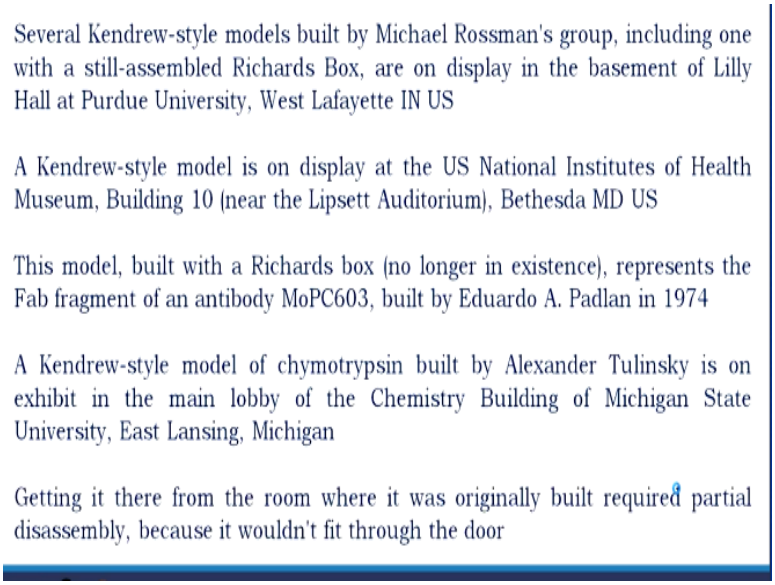

Several Kendrew-style models built by Michael Rossman's group including one which is still assembled by Richards Box are on display in the basement of Lily Hall at Purdue University, West Lafayette in the US So, you all know about Michael Rossman, Michael Rossman has developed molecule replacement contributing greatly to the advancement of crystallography. So, in his group, they have developed a lot of models and they like some of them are still there.

A Kendrew-style model is on display at the US National Institute of Health Museum, Bethesda, US This model built with the Richards Box, represents the Fab fragment of an antibody built by Eduardo A. Padlan in 1974. A Kendrew-style model of chymotrypsin built by Alexander Tulinsky is on exhibit in the main lobby of the chemistry building of Michigan State University in Lansing Michigan. Getting it there from the room where it was originally built required partial disassembly because it would not fit through the door.

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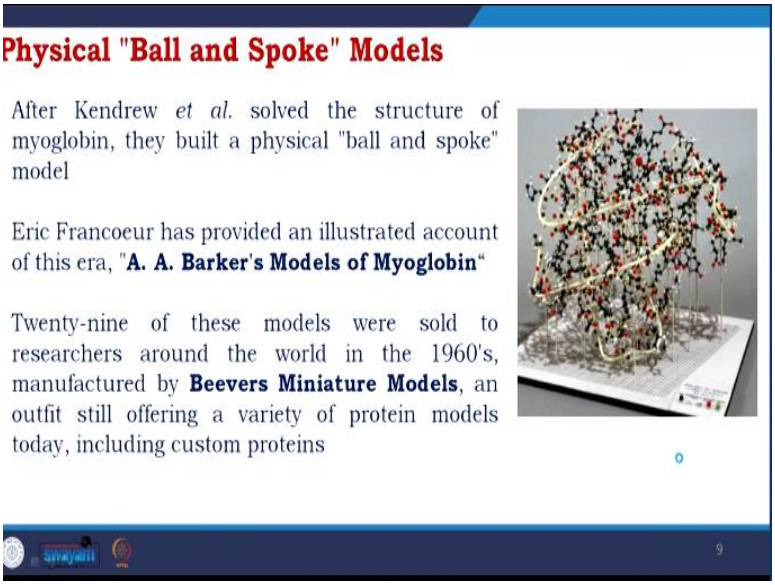

From all those initial level models come the physical ball and spoke model where the Mac Crow arrangement of the Halle city atomic level representation is introduced. After Kendrew et al solved the structure of myoglobin, they built his physical ball and spoke model. Eric Francoeur has provided an illustrated account of this era which is A.A. Barker's model of myoglobin.

As you could see 29 of these models were sold to researchers around the world in the 1960's manufactures by Beevers Miniature Models and Outfit still offers a variety of protein models today, including custom proteins. So, the company is still there, but at that time making them contributed to science because scientists were looking at that and designing further experiments so it was very important. Now, it is not so important, because thanks to the improvement of computational modeling, but still for educational purposes, to make people interested in protein, related structure, and related work, these models are indispensable.

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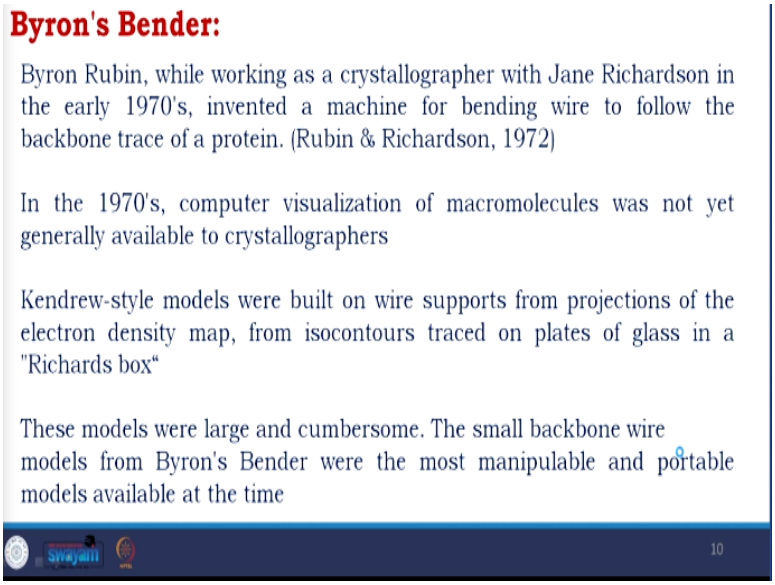

Byron's Bender, Byron Rubin, while working as a crystallographer with Jen Richardson, in the early 1970's invented a machine of bending to follow the backbone trace of the protein. In 1970's computer visualization of macromolecules was not yet generally available to crystallographers. Kendrew-style models are built on where supports from projections of the electron density map from isocontours traced on plates of blast in a Richards box.

These models were large and cumbersome the small backbone wire models from Byron's Bender were the most manipulable and portable models available at the time. So, as I told you when I was talking about the previous models, the previous models are made up of metal and also they were very heavy, very difficult to carry and all Byron's Bender makes a revolution in comparison to that.

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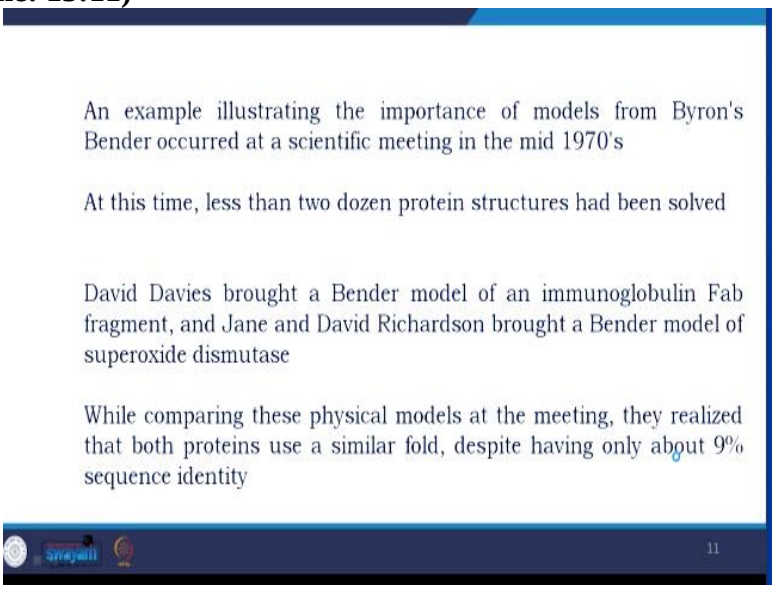

An example illustrating the importance of the model from Byron's Bender occurred at a scientific meeting in the mid-1970s. At this time, less than 2 dozen protein structures had been solved, as we have already looked at while our journey in structural biology, David Davies brought a bender model of an immunoglobulin Fab fragment, and Jane and David Richardson brought a bender model of superoxide dismutase.

While comparing these physical models at the meeting, they realized that both proteins use a similar fold, despite having only about 9% sequence identity. So, at that time, as I told you the computational analysis, computational alignment, sequence alignment, structure alignment, and structure comparison were not available. So, David Davies's group, they have solved the immunoglobulin structure, and David Richardson's group, they have solved the superoxide dismutase.

But when both the structures are given to them, Byron's Bender they have developed the models, you look at the physical model and you realize them these 2 models are very similar. So, the folds are similar, though the sequence is very dissimilar, and only 9% sequence identity is available. So, this is not only helping you to learn, this is helping you to understand science. This is one of the major break-through where understanding the sequence to fold there is always thought about the correlation between sequences.

If there is a high identity, there is a chance of having a similar fold but it could be otherwise also, a similar fold could be found without having sequence identity. Byron's Bender has helped scientists looking at that, physically get a view and understand.

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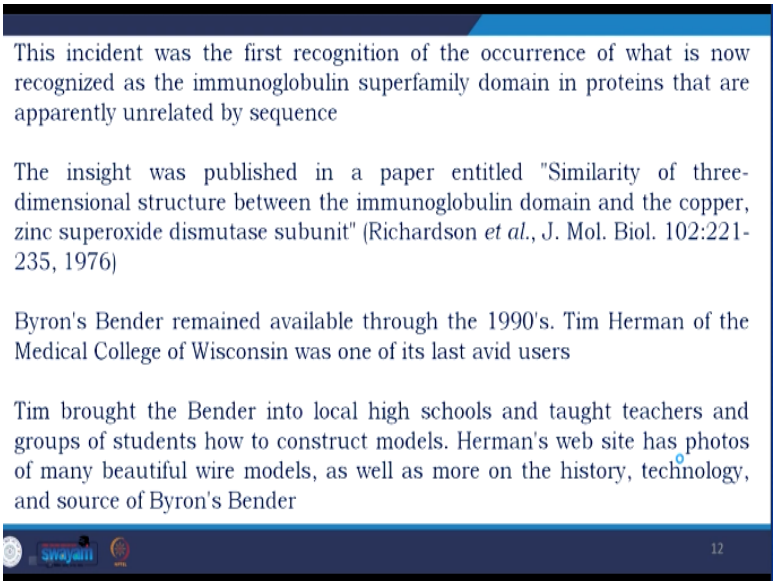

This incident was the first recognition of the occurrence of what is now recognized as the immunoglobulin superfamily domain in proteins that are apparently unrelated by sequence. The insight was published in a paper and titled Similarity of 3-dimensional structures between the immunoglobulin domain and the copper, zinc superoxide dismutase subunit. Byron's Bender remained available through the 1990's Tim Herman of the Medical College of Wisconsin was one of the last avid users of the models.

Tim brought the bender into the local high schools and taught teachers and groups of students how to construct models. Herman's website has photos of many beautiful wire models as well as many more of the history technology and source of Byron's Benders. So, if you are interested go to Herman's website and take a look.

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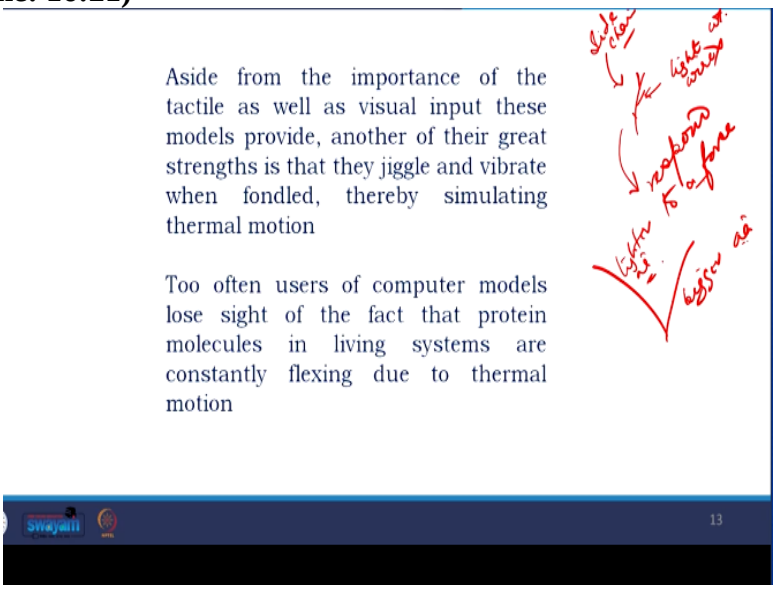

Aside from the importance of the tactile as well as visual input these models provide, another of their great strengths is that they jiggle and vibrate when fondled, they are by simulated thermal motion show I just tried to help you understand that. So, those are light wires light means light with wire. So, depending on how the side chains are they respond to force. So, suppose this is one branch and that is another if this is having bigger amino acids, this is having lighter or smaller amino acids.

They would like to jiggle and vibrate differently giving an idea about the thermal motion. Too often, users of computer models lose sight of the fact that protein molecules in living systems are constantly flexing due to thermal motion, but these models help you understand them physically.

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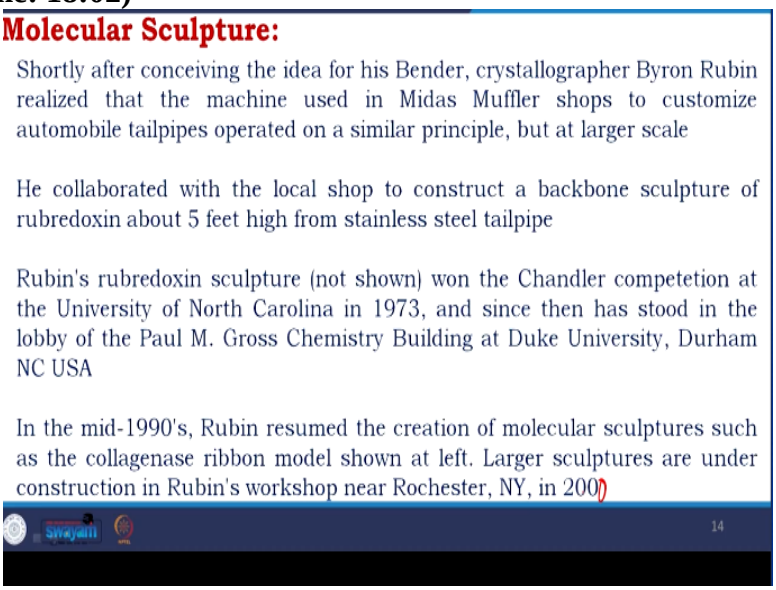

Now coming to molecular sculpture shortly after convincing the idea from his Bender crystallographer Byron Rubin realized that the machine used in the Midas Muffler shops to customize automobile tailpipes operated on a similar principle, but at a larger scale. He collaborated with the local shop to construct a backbone sculpture of rubredoxin about 5 feet high from stainless steel tailpipe.

So, this was used for other purposes automobile tailpipes and Byron Rubin try to, use them in developing model and develop the model of rubredoxin. Rubin's rubredoxin sculpture won the Chandler competition at the University of North Carolina in 1973. And since then, has stood in the lobby of the Paul M. Gross Chemistry Building at Duke University, Durham NC USA.

In the mid -1990's, Rubin resumed the creation of molecular sculptures, such as the collagenase ribbon model. So, larger sculptures are under construction in Rubin's workshop near Rochester New York in 2000.

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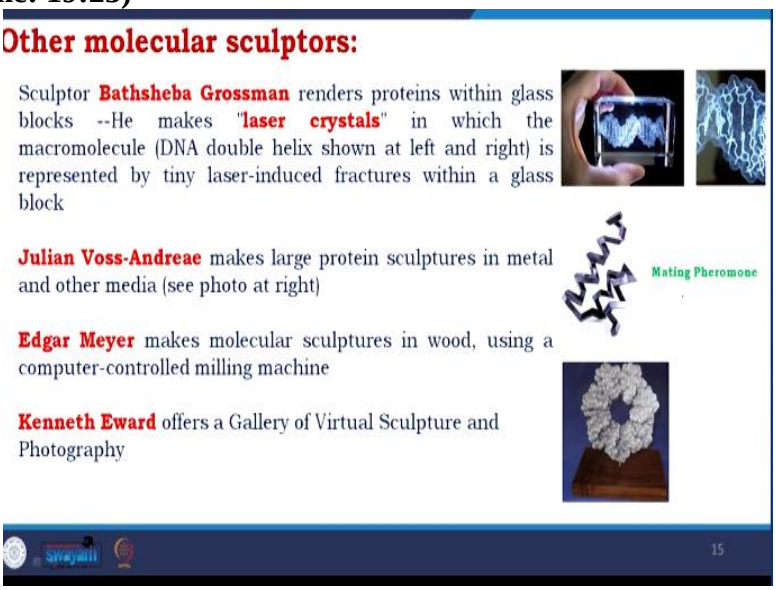

Other molecular sculptures, and sculptures made by Bathsheba Grossman render protein within glass blocks, he makes laser crystals in which the macromolecule DNA double helix as you see here, it is represented by tiny laser-induced fractures within a glass block. If you search Bathsheba Grossman you will see a lot of such laser models. They are still working with a lot of people a lot of crystallographer's electron microscopy they used to gift their students or people they want by making those models now.

Julian Voss-Andreae makes large protein sculptures in metal and other media. So, this is a model of mating pheromones. Edgar Meyer makes molecular sculptures in wood using a computer-controlled milling machine, so this is the model made by Edgar Mayer. Kenneth, you would offer a gallery of virtual sculpture and photography, but somehow they are not available nowadays but they contribute that time significantly.

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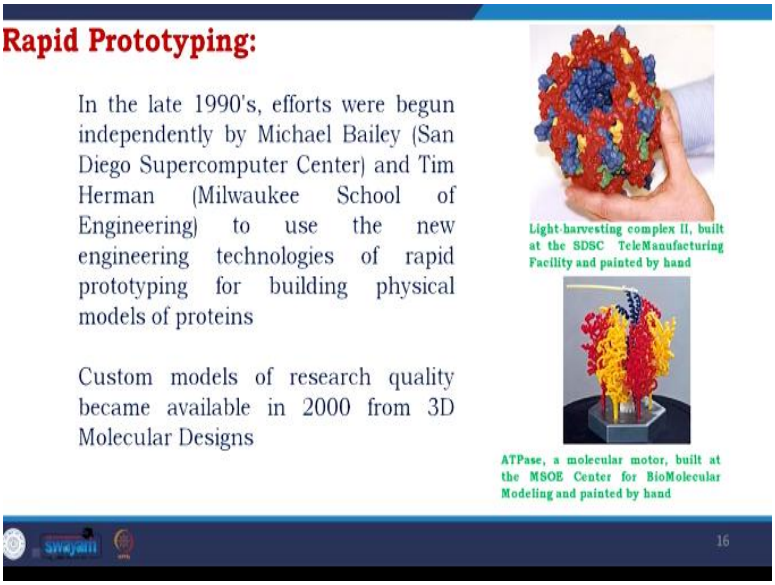

Rapid prototyping in the late 1990s, efforts were begun independently by Michael Bailey, San Diego Supercomputer Center, and Tim Herman Milwaukee School of Engineering to use the new engineering technologies for rapid prototyping for building physical models of proteins. Custom models of research quality became available in 2000 from 3D molecular designs.

So, this is one they produced which is light-harvesting complex II built at the SDSC tele manufacturing facility and painted by hand according to the actual content. This is ATPase, a molecular motor built at the MSOE of biomolecular modeling and again painted by hand.

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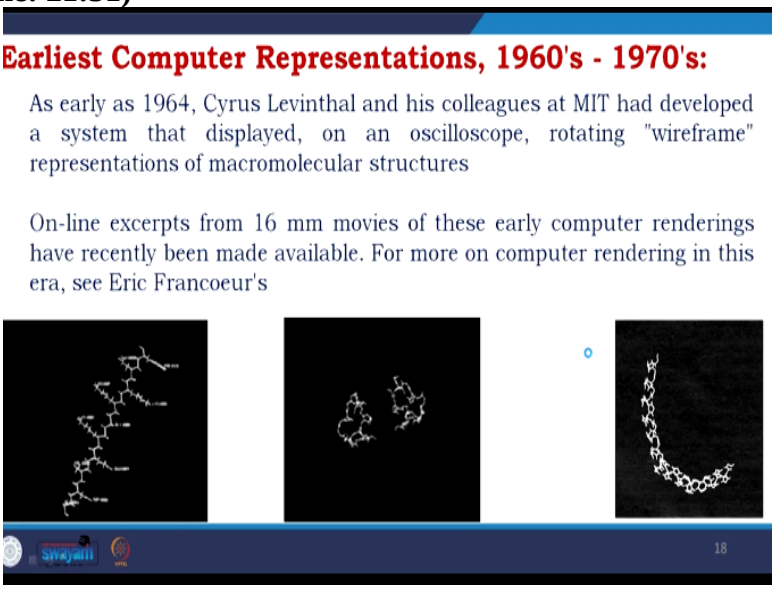

Coming to computer representations, so, what we are looking at, are early representations that are later brought together and made into movies. So, as early as 1964, Cyrus Levinthal and his colleagues at MIT developed a system that displayed on an oscilloscope rotating

wireframe representation of macromolecule structures. Online excerpts from 16-millimeter movies of these early computer renderings have recently been made available.

As I told for more on computer rendering you could see Eric Francoeur's gallery you could get many of them, but So, these are examples of how the initial attempt to make structural visualizations and structural graphics was done.

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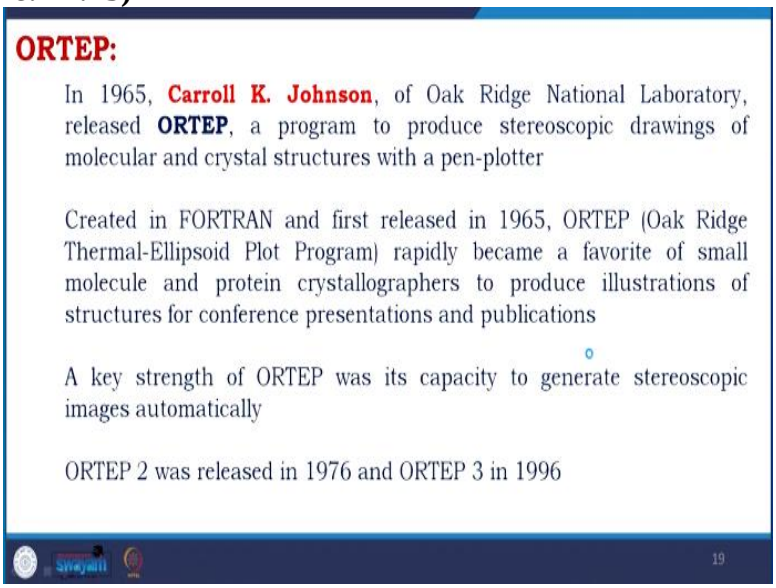

Then come ORTEP in 1965, Carroll K. Johnston of Oak Ridge National Laboratory released ORTEP, a program to produce stereoscopic drawings of molecule and crystal structures with a pen plotter. So, it is a pen plotter which you know, you could use for plotting graphs and all but this was very effective coming into creation in FORTRAN and first release in 1965, ORTEP Oak Ridge Thermal Ellipsoid Plot Program rapidly became a favorite of small molecule and protein crystallographers to produce an illustration of structures for conference presentation and publications.

A key strength of ORTEP was its capacity to generate stereoscopic images automatically. So as I told this to specificity, the Keitel environment is a really interesting thing for protein. So, because ORTEP automatically generates stereoscopic images, it got instant popularity, ORTEP 2 was released in 1976 and 3 was released in 1996.

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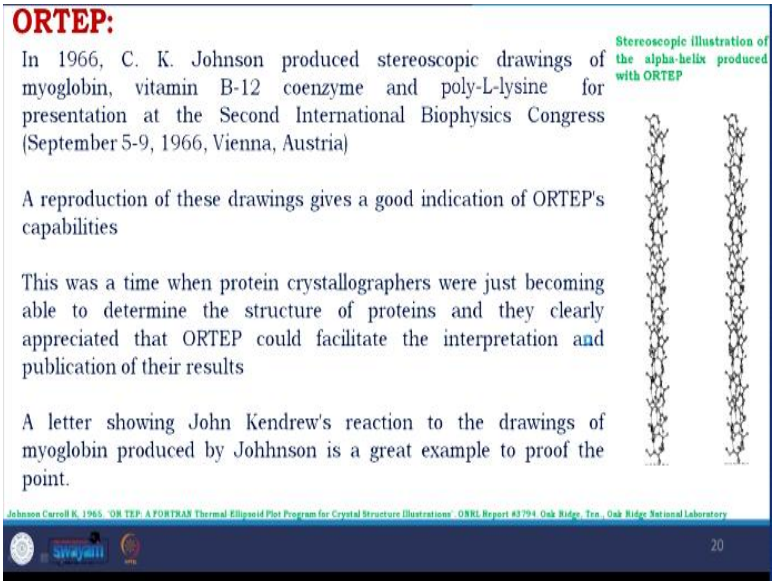

In 1966, C.K. Johnson produced the stereoscopic drawing of myoglobin, vitamin B-12 coenzyme, and poly-L-lysine for presentation at the second international biophysics Congress in Vienna, Austria. A reproduction of So, drawings gives a good indication of ORTEP's capabilities. This was the time when protein crystallographers were just becoming able to determine the structure of proteins and they clearly appreciated that ORTEP could facilitate the interpretation and publication of their results.

So, this is the stereoscopic illustration of the alpha helix produced with ORTEP one of the very good examples of how the crystallographic community of that time was excited comes from a letter showing John Kendrew's reaction to the drawings of the myoglobin produced by Johnson.

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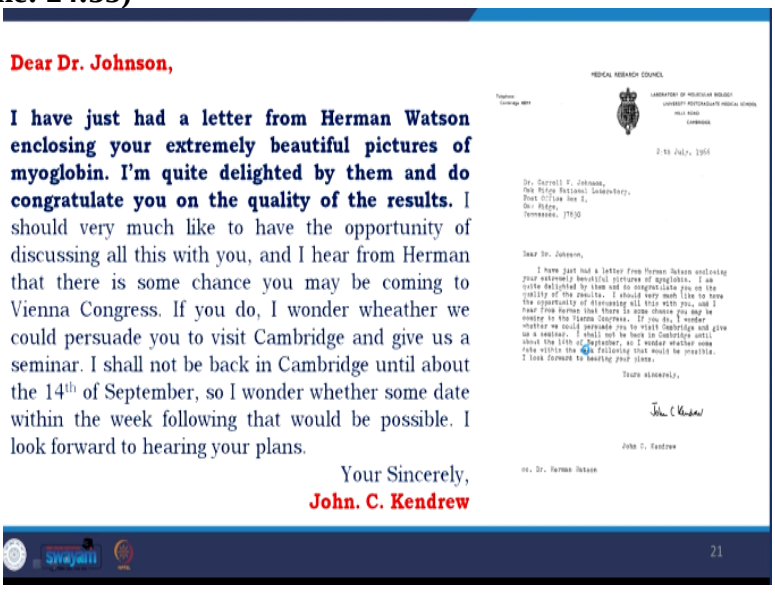

So, this is the letter I am not going into details the 2 lines indicate dear Dr. Johnson, I have just had a letter from Herman Watson en closing, your extremely beautiful pictures of myoglobin. I am quite delighted by them and do congratulate you on the quality of the results. So that will help to understand a letter from Kendrew, that time Nobel laureate how excited he was and this is the original letter coming from Kendrew

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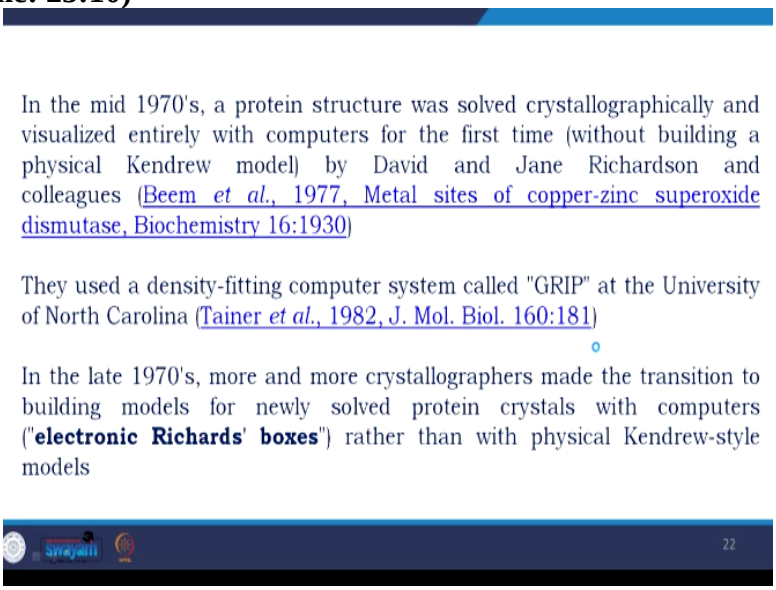

In the mid-1970s, a protein structure of salt crystallographically and visualized entirely with computers for the first time without building a physical Kendrew model by David and Jane Richardson and colleagues, I have given that paper so that if you are interested, you could go to the paper and go to the details of the work. They used a density-fitting computer system called GRIP at the University of North Carolina. In the late 1970s, more and more crystallographers made the transition to building models for newly solved protein crystals with computers, the electronic Richards boxes rather than the physical Kendrew style model.

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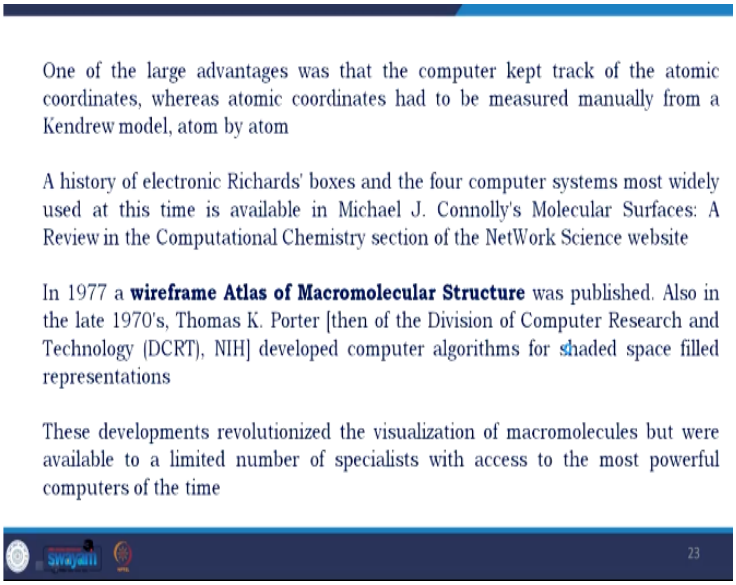

One of the large advantages was that the computer kept track of the atomic coordinates whereas atomic coordinates had to be measured manually from a Kendrew model atom by atom you have to actually physically measure and then develop or construct a physical model. But for a computer, if you could construct if you could know the conversion from the atomic information to the model, the computer could do that by itself. So that is a major advantage.

A history of electronic Richard's boxes and the 4 computer systems most widely used at this time is available in Michael J. Connolly's molecular surfaces. A review in the computational chemistry section of the network's website is an informative and revolutionary review because Connolly has worked on the molecular surface, if you see all the current visualization programs and the servers they all use that principle.

In 1977, a wireframe Atlas of Macromolecular Structure was published also in the late 1970s, Thomas K. Porter then of the Division of Computer Research and Technology DCRT NIH, USA developed computer algorithms for shaded space-filled representations. These developments revolutionized the visualization of macromolecules, but were available to a limited number of specialists with access to the most powerful computers at the time. So, they are specific for a specialized set of computers which are very expensive so, even the common scientist cannot get access to them.

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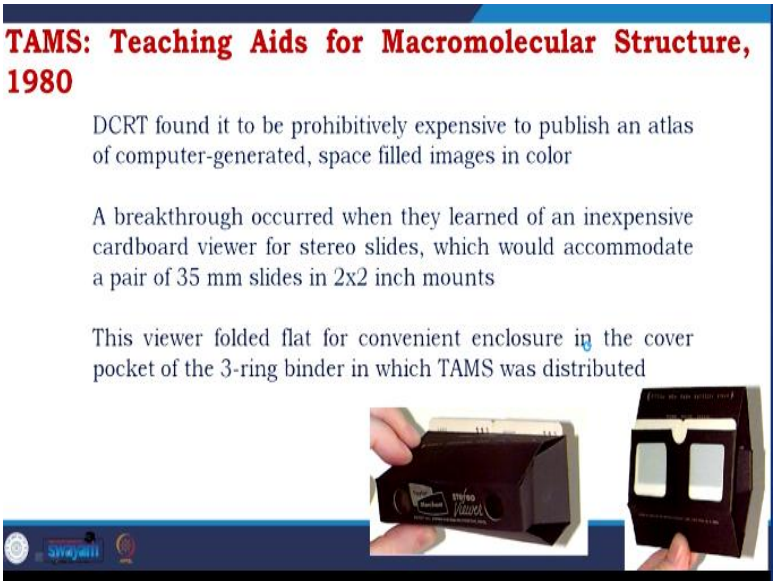

And then comes, TAMS which is called Teaching Aids for Macromolecular Structure. That is one of the initial components of DCRT. DCRT found it to be prohibitively expensive to publish an atlas of computer-generated specific images in color. A breakthrough occurred when they learned of an inexpensive cardboard viewer for stereo slides you could see here in stereo slides and you could get the stereo-specific view which could accommodate a pair of 35-millimeter slides 2 into 2 inches mounts.

This viewer folded flat for convenient enclosure in the cover pocket of the 3-ring binder in which TAMS was distributed. So, even when you get the publication to get the journal you get the viewer in the package so you could see the protein you could get the stereo-specific view.

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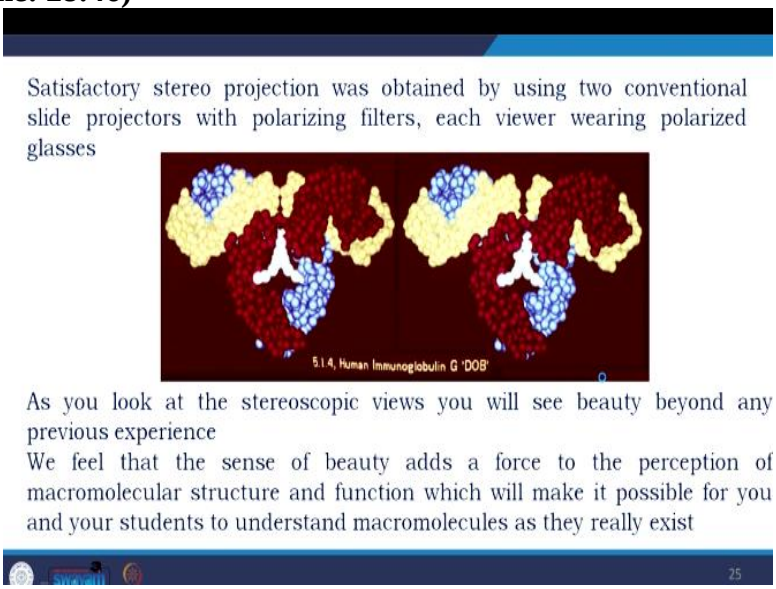

The satisfactory stereo projection was obtained by using 2 conventional slide projectors with polarizing filters, each viewer wearing polarized glasses. This is how it could look the human immunoglobulin G. As you could look at the stereo-specific or stereoscopic views, you will see the beauty beyond any previous experience so that was the evolution. We feel that the sense of beauty adds a force to the perception of macromolecular structure and function which will make it possible for you and your students of them to understand macromolecules as they exist.

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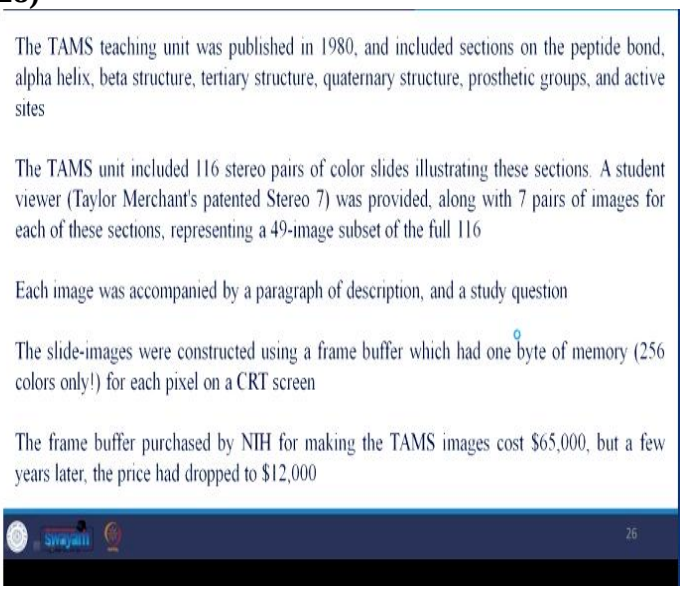

The TAMS teaching unit was published in 1980 and included sections on the peptide bond alpha helix beta structure, tertiary structure, quaternary structure, prosthetic group, and active sites. The TAMS unit included 116 stereo pairs of color slides illustrating So, sections is student viewer Taylor Merchant's patented stereo 7 was provided along with 7 pairs of images for each of So, sections, representing a 49-image subset of the full 116 stereo pairs.

Each image was accompanied by a paragraph of description and a study question. The slide images were constructed using a frame buffer which had 1 byte of memory and 256 colors only for each pixel on a CRT screen. The frame buffer purchased by NIH for making the TAMS images cost dollar 65,000 but a few years later, with more refining more improvement, it comes only to 12,000 which is on that time respecting was a really good price down.

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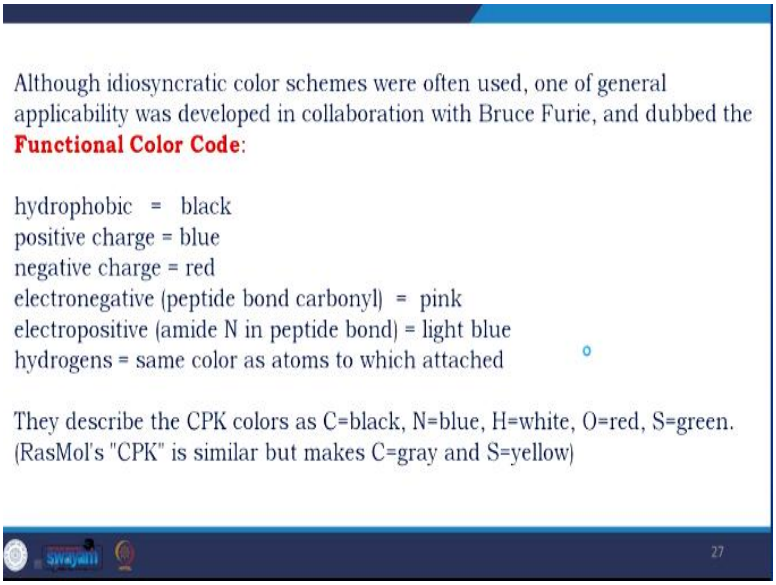

Although idiosyncratic color schemes are often used one of general applicability was developed in collaboration with Bruce Furie and dubbed the functional color code. The hydrophobic could we present it in black color, the positive charge in blue color, the negative charge in red color, electronegative in peptide bond carbonyl pink color, electropositive with light blue color, hydrogens same color attempt to which it is attached. They describe the CPK color as C black, N blue, H white, O red, and S green, and that was maintained still we maintained those functional codes.

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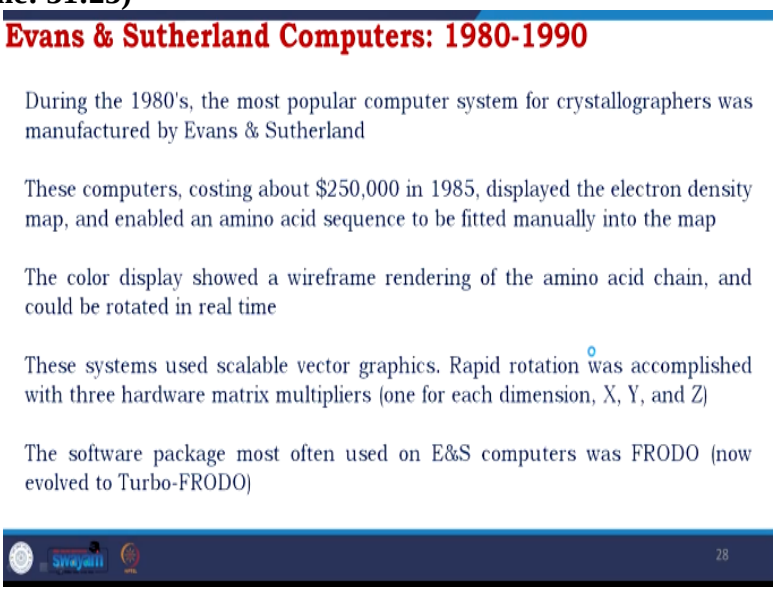

And then come Evans and Sutherland Computers during the 1980's the most popular computer system for crystallographers was manufactured by Evans and Sutherland. These computers costing about 250,000 dollars in 1985 displayed the electron density map and enabled an amino acid sequence to be fitted manually into the map. Again, that is a revolution

in how we could model a protein structure. The color display showed a wireframe rendering of the amino acid chain which could be rotated in real-time.

These systems use scalable vector graphics rapid rotation was accomplished with 3 hardware matrix multipliers, one for each direction X, Y, and Z. The software package often used on E and S computers was FRODO. I will talk about FRODO and its advancement when I talk about the details of Robert Crook's soft tracker COOT.

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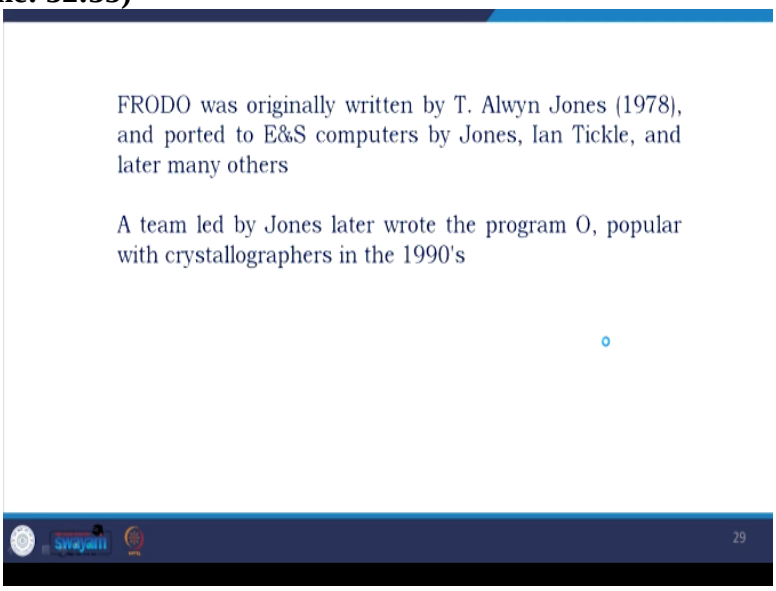

So FRODO now evolved as Turbo Frodo. FRODO was originally written by T. Alwyn Jones in 1978 and ported to E and S computers by Jones Ian Tickle and letter later by many others. A team led by Jones Letter later wrote the program O popularized crystallographers in the 1990s.

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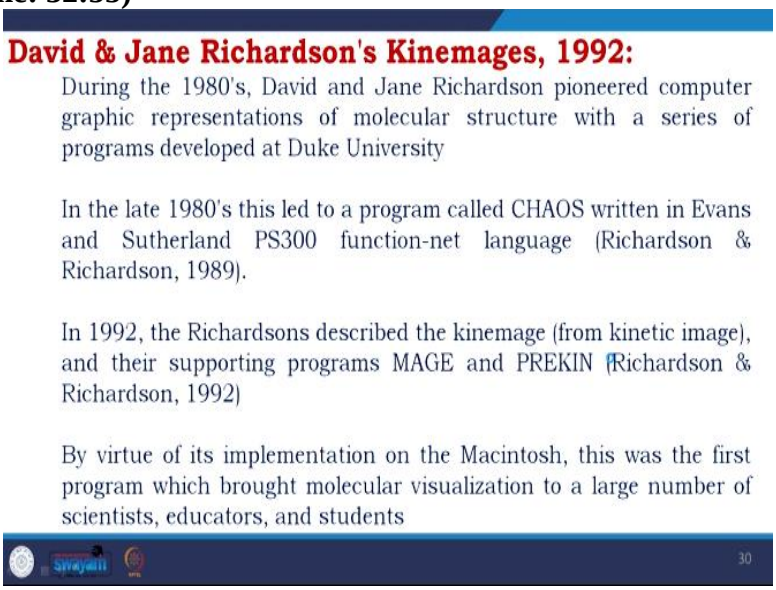

Coming to David and Jen Richardson's, whom we talked about earlier Kinemages, during the 1980s, David and Jen Richardson pioneered computer graphic representation of molecular structure with a series of programs developed at Duke University. In the late 1980s this led to a program called CHAOS there was written in Events and Sutherlands PS300 function net language. In 1992, Richardson described the Kinemage from kinetic images and the supporting program MAGE and PREKIN.

With its implementation on the Macintosh, this was the first program that brought molecular visualization to a large number of scientists, educators, and students the first time it comes to common scientists.

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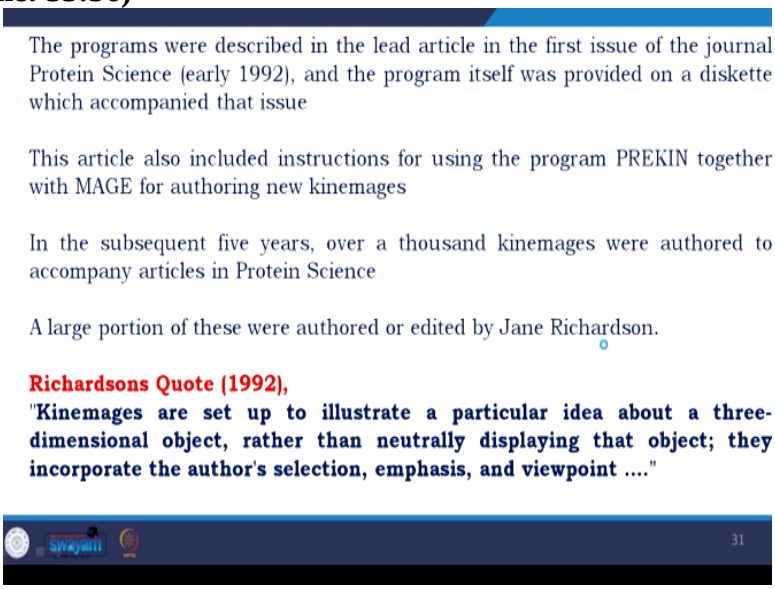

The programs are described in the lead article in the first issue of the journal protein science, early 1992 and the program itself was provided on a diskette which accompanied that issue. This article also included instructions of using the program PREKIN together with MAGE for authoring new Kinemages. In the subsequent 5 years, over 1000 Kinemages are authored to accompany articles in protein science. A large portion of this was authored or edited by Jane Richardson.

In his language Kinemages are set up to illustrate a particular idea about a 3-dimensional object, rather than neutrally displaying that object. They incorporate the author's selection impasses and viewpoint. So, this is kind of evolution I would say because when you think about that and when you think about students' structural biology, we get a structure and we

correlate the structure with function which is the major challenge where we are working as I talked about, we have sequence we have structure and we have function.

When you have to correlate between structure and function, you cannot only generate a total structure, you might emphasize a particular loop, you might talk about one particular active site, one particular amino acid, one particularly interesting part alpha leagues, beta seeds anything or interaction between like and an enzyme between protein DNA, protein RNA, protein-small molecule any salt you want to focus. So, that focus was provided for the first time by the Kinemages.

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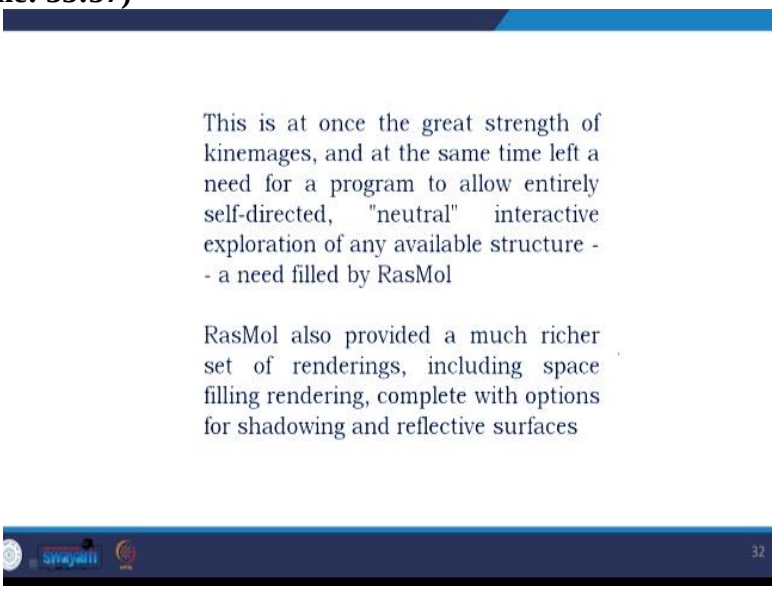

This is at once the great strength of Kinemages and at the same time left a need for a program to allow entirely self-directed, neutral, interactive exploration of any available structure. So, it is good, but it opens up our eyes that over the possibilities is going. So, scientists want to do more and that is where the RasMol was filled. RasMol was a really good handy tool for all of us who have learned around 1997 to 2002, 3,5.

RasMol also provided a much richer set of renderings, including space-filling rendering complete with options for shadowing and reflective surfaces. So that time making a figure and correlated to the function, this was the best home.

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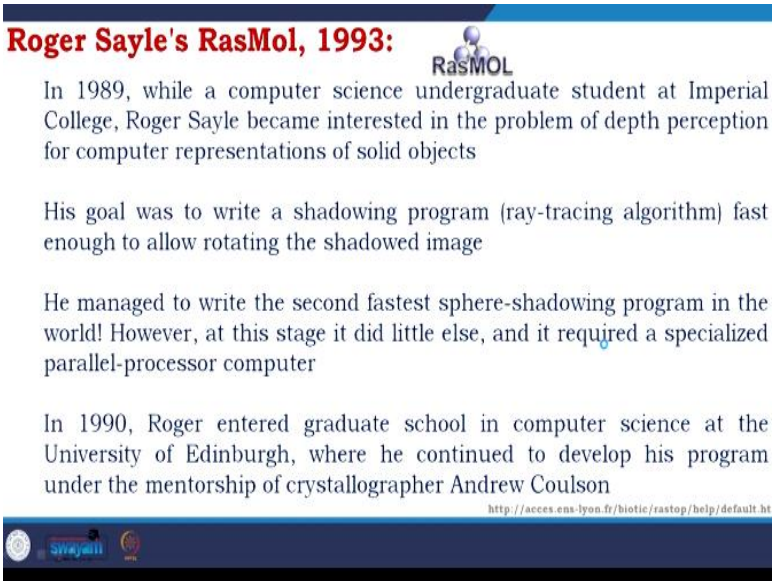

So, talking about RasMol in 1989, while a computer science undergraduate student at Imperial College, London, Roger-Sayle became interested in the problem of depth perception for computer representations of solid objects. His goal was to write a shadowing program a ray tracing algorithm fast enough to allow rotating the shadowed image. He managed to write the second-fastest sphere soldering program in the world. However, at this stage, it did little else and it required a specialized parallel processor computer.

In 1990, Roger entered graduate school in Computer Science at the University of Edinburgh, where he continued to develop his program under the mentorship of crystallographer Andrew Coulson.

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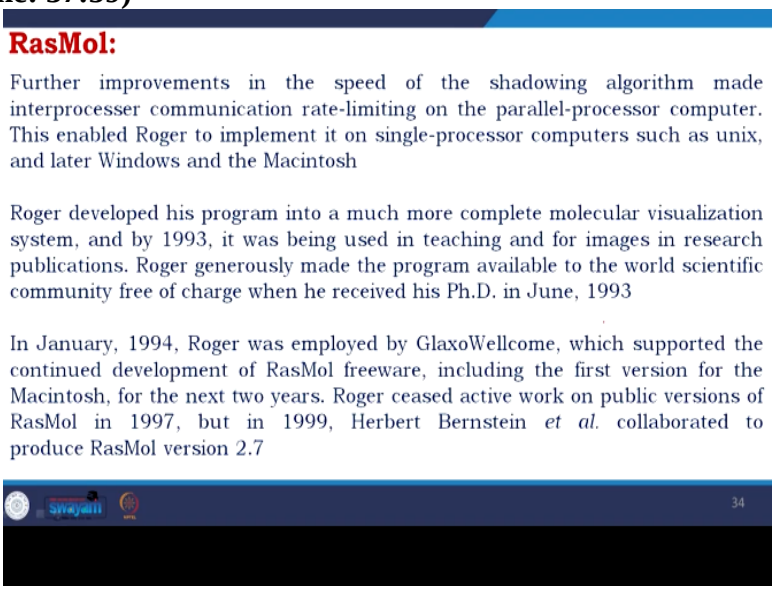

Further improvements in the speed of the shadowing algorithm made inter-processor communication rate-limiting on the parallel processor computer. This enabled Roger to

implement it on single-processor computers such as Unix and later Windows and Macintosh. Roger developed his program and was a much more complete molecular visualizing system by 1993. It was being used in teaching and for images in research publications.

Roger generously made the program available to the world scientific community free of charge when he received his Ph.D in June 1993. It is a huge contribution I would say, you know, I still remember I was in my Masters in the department of biophysics and molecular biology at Calcutta University, and Professor Rahul Banerjee from Saha Insitute of nuclear physics India used to come and that was my first lab when I see the molecules with the platform, RasMol like me.

There are a lot of that times students, who were inspired, and motivated and today they are making their career in the field of structural biology thanks to RasMol. In January 1994, Roger was employed by Glaxo Wellcome which supported the continued development of RasMol freeware, including the first version for the Macintosh for the next 2 years. Roger ceased active work on public versions of the RasMol in 1997. But in 1999, Herbert Bernstein collaborated to produce RasMol version 2.7.

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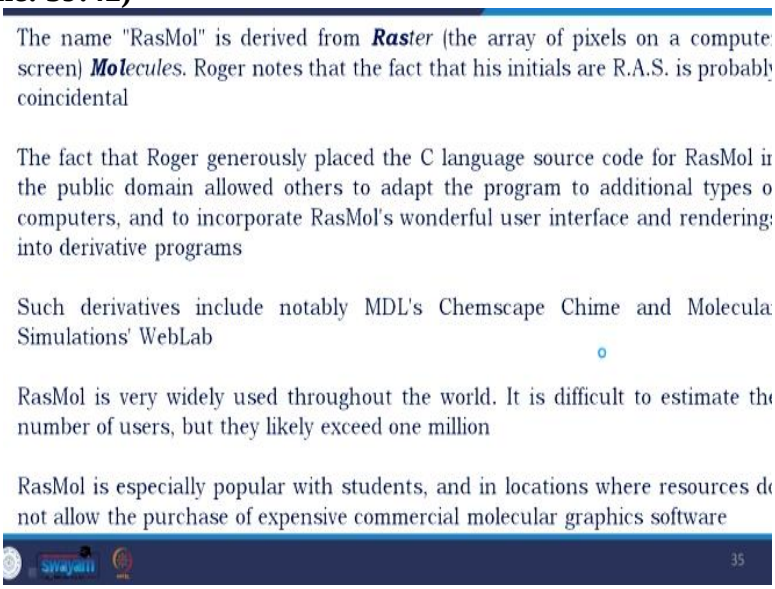

Why RasMol? The name RasMol is derived from Raster the array of pixels on a computer screen Molecules. So, Raster Molecules RasMol and Roger specifically mentioned that his initial which is RAS is probably coincidental. The fact that Roger generously placed the C language source code for RasMol in the public domain allowed others to adopt the program

to additional types of computers enter the corporate RasMol wonderful user interface and render it into derivative programs.

Such derivatives include notably M.D.L.s, Chemscape, Chime, and Molecular Simulations WebLab. RasMol is very widely used throughout the world it is difficult to estimate the number of users but it is likely to exceed 1 million at least. RasMol is especially popular with students and in locations where resources do not allow the purchase of expensive commercial molecular graphic software. As I have already mentioned, my personal experience like me, a lot of people have a similar experience.

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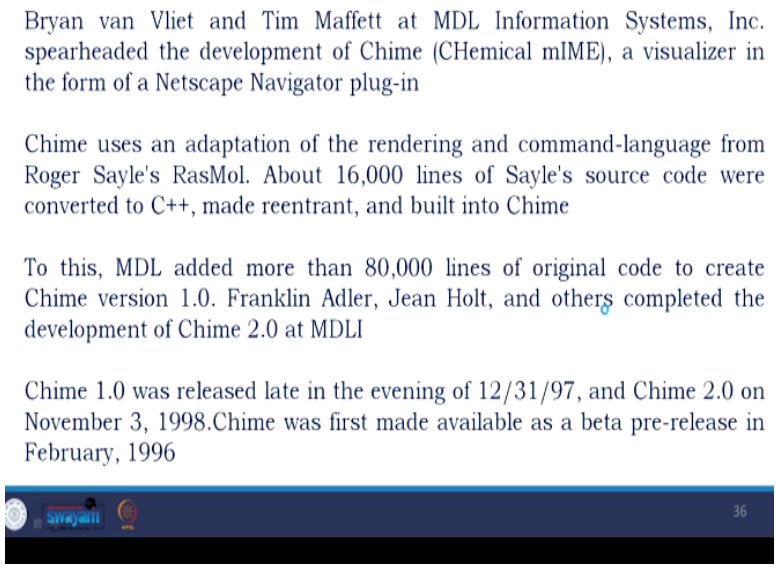

Bryan van Vliet and Tim Maffet at MDL information system in Corporation spearheaded the development of Chime CHemical mIME, a visualizer in the form of the Netscape Navigator plugin. Chime uses an adaptation for the rendering and command language from Roger Sayle’s RasMol. About 16,000 lines of Sayle’s source code were converted to C++ made reentrant and built into Chime. To this, MDL added more than 80,000 lines of original code to create crime version 1.0 Franklin Adler, Jean Holt and others completed the development of Chime 2.0.

Chime 1.0 was released late in the evening of 12/31/97 and Chime 2.0 on November 3, 1998. Chime was first made available as a beta pre-release in February 1996.

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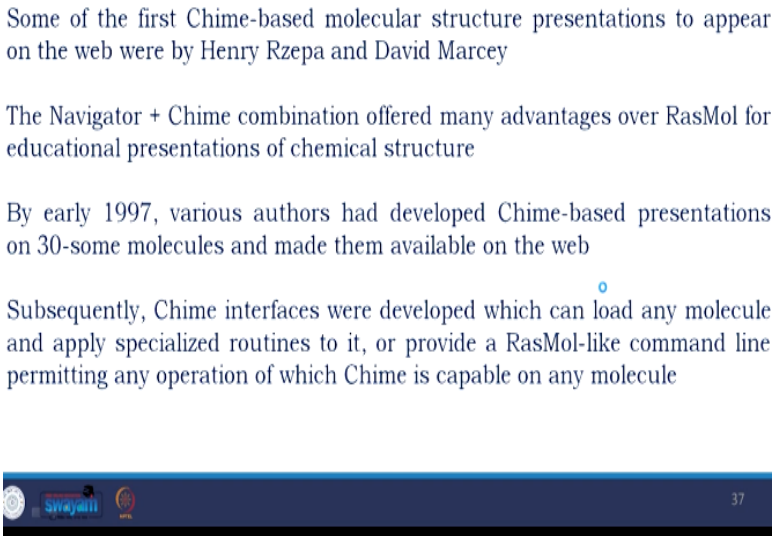

Some of the first Chime-based molecular structure presentations to appear on the web were by Henry Rzepa and David Marcey. The navigator plus Chime combination offered many advantages over RasMol for the educational presentation of chemical structure. By early 1997 various authors had developed Chime-based presentations on 30 molecules and made them available on the web. Subsequently, Chime interfaces were developed which can load any molecule and apply specialized routines to it or provide a RasMol-like command line permitting any operation of which Chime is capable on any molecule.

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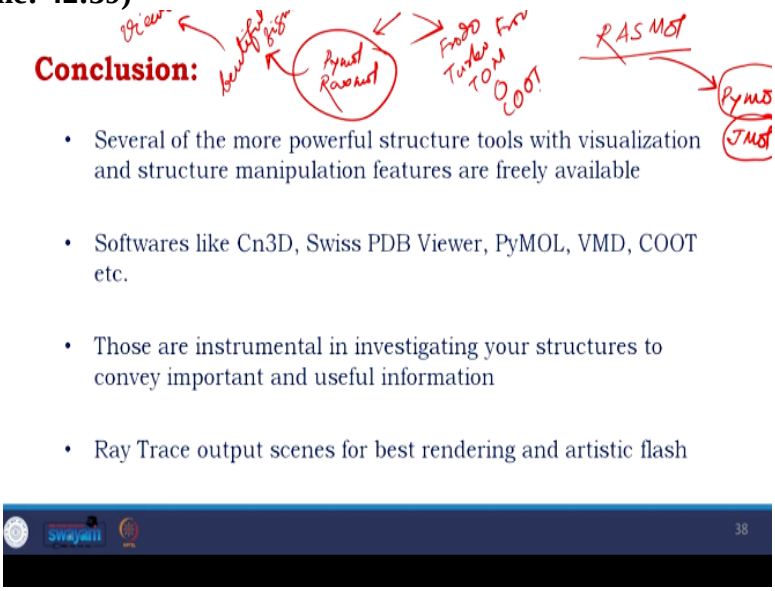

So, coming to conclusion of the history, several of the more powerful structured tools with visualization and structure manipulation features are freely available now. Software's like Cn3D, Swiss PDB Viewer, PyMOL, V.M.D., COOT etcetera coming as Roger starts with a rather small we get a series of MOL like PyMOL to be like conscious most important JMOL

to be named MOL viewer MOL MOL a lot of there was an explosion of different in your techniques.

But if you compare between those techniques, they have 2 definite category one category where PyMOL, RasMol and all of their molecular viewers, they are producing beautiful pictures, beautiful figures so, we call them molecular viewer. And there are another set where it comes like FRODO, Turbo FRODO, Tom O COOT here actually you could work on so, we call them builder. So, one is viewer type up another is builder type up.

And, as I told, I am going to talk about the popular software's one I picked up PyMOL which is again a molecular few are written in Python language and COOT, COOT which is named on a small bird is a builder program and in this current time, it is the most popular molecular builder program. So, those all those software's are instrumental in investigating your structures to convey important and useful information for understanding and designing better experiments.

Ray Trace output is again a revolution the Ray Trace output since for based rendering and artistic flash have given much better quality to the current publication quality structures.

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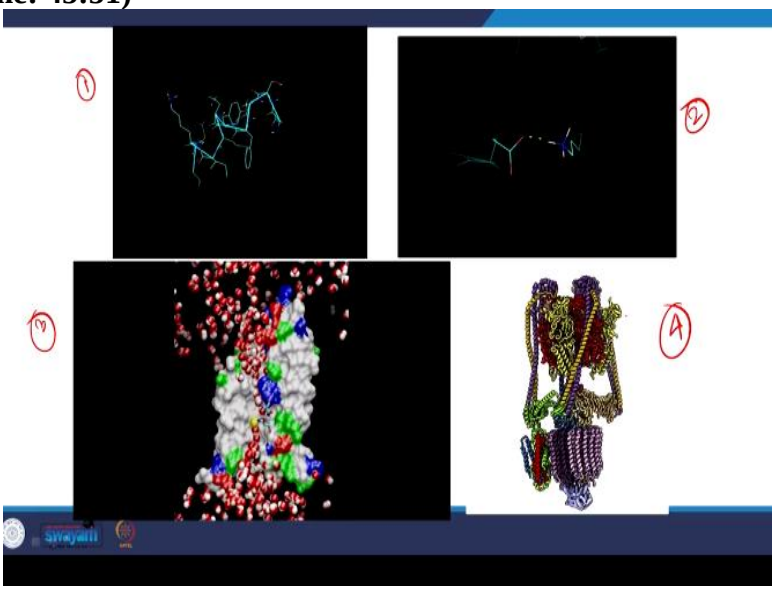

So, if you look at the movie 1 and movie 2, this is a representation of how you could normally work in PyMOL or how you could work and develop high resolution movies. As I told the current journey is not only restricted to the high quality high resolution static figures,

but we are developing movies which is giving us more insight. So, here is one which is a movie of aquaporin, you see that how the channel is taking part in the flow of water.

And this one the show this if I consider So, 3 aquaporin the fourth one is ATpase which is solved by electron microscopy taking one lakh 0.1 million micrographs and then develop this 3D structure which could move and which shows you the bending the flexibility and all the functional aspects of the structure. So, we have gone through a huge journey starting from the metal mid models, going through better models shiftng from there to the Byron Bender.

And there are many other sculptures which contributed in between we shifted it to computer at last and then developing better computer model and current moment. We have very, very high quality movies very, very high quality static pictures which are helping us to understand science in a next level. Not only to as I told you, not only to understand or know about a system, but also designing protein designing, protein engineering is something which is going through its golden era. And a huge thanks to the molecular visualization with that I thank all of you for listening. Thank you very much.