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COURSE NOTES 44

APPLICATIONS OF COMPUTER GRAPHICS TO MOLECULAR MODELING

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Computer Graphics in Molecular Modeling
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Computer Graphics in Molecular Modeling

Course Abstract

Computer graphics has been used in chemistry since the beginning of computer graphics. Some of the very first computer graphics systems were used by chemists to display simple line drawings of their three dimensional molecular structures and dot surfaces surrounding them. The ability to visualize large and complex molecular structures as well as the ability to compute properties of molecules and their interactions has given rise to a new field of chemistry known as computer assisted molecular design (CAMD). While CAMD is sometimes compared to CAD/CAM, its purpose is not to design a shape before it is made into reality, but rather to understand the nature of the intricate interactions between molecules which is responsible for much of the usefulness of chemistry in our society. For example, the ability of a drug molecule to act upon its receptor in the body is directly and indirectly due to the three dimensional complementarity in shape of the drug and its receptor. Many molecular properties, such as electronic properties are indirectly dependent upon the 3-D shape of the molecule. Computer graphics and computational chemistry has become so useful that several commercial modeling systems are currently available and are being used in chemical and pharmaceutical companies throughout the world as well as in university and other research organizations.

In this course we will show how computer graphics is being used today in protein modeling, nuclear magnetic resonance (NMR) and in the display of black and white molecular illustrations. In protein modeling, the protein itself is a complex three dimensional association of atoms. We will explain ways in which proteins are graphically displayed and manipulated. We will also show how techniques of molecular modeling are used to construct models of drug receptor interactions. Electronic properties of proteins are studied to understand how they interact with each other and with smaller molecules. The electronic properties can be computed and displayed either on a molecular surface or in the space around the molecule. Techniques for displaying three dimensional contours of electronic properties are used for this. In NMR, multidimensional data is collected in order to deduce the three dimensional structure of a molecule. In the last several years, this approach has been used to determine the solutions structure of molecules as large as proteins. Graphical methods for interpreting the multidimensional data will be presented.

An important issue in computer graphics is how to present our work in more traditional media such as books, films and video, so that an audience without a graphics workstation can see the results of our efforts. We will discuss how best to select what you want to show, how to plan and produce animations. Future directions incorporating video with computer graphics as supplements to paper publications. We will also discuss a relatively new stereo viewing medium, the phscologram, and show results for two molecular systems.

Glen Eugene Kellogg, Ph.D.

Glen Kellogg has a B.S. degree from the University of New Mexico (1980, Chemistry) and a Ph.D. degree from the University of Arizona (1985, Chemistry). His graduate research (director: Dennis Lichtenberger) focused on experimental and theoretical investigations of electronic structure in organo-transition metal species. He took a postdoctoral at Northwestern University where he studied conductive polymers/molecular metals. Since 1989 Dr. Kellogg has been at Virginia Commonwealth University, where he is now Instructor, researching new methods and applications of molecular modeling in drug design and in understanding of biological function. In collaboration with Donald Abraham (VCU) the HINT computer model for studying hydrophobic interactions in biological systems is currently being developed. In addition, Dr. Kellogg has been one of the primary instructors for the molecular modeling courses at VCU since their inception in 1989.

Charles Hutchins, Ph.D.

Charles W. Hutchins is a Research Investigator with the Pharmaceutical Products Division of Abbott Laboratories. Dr. Hutchins obtained his Ph.D. in Organic Chemistry from The University of Illinois at Urbana-Champaign and completed post-doctoral studies at The University of California in Berkeley, California. Dr. Hutchins moved to Sterling-Winthrop Research Institute in Renesselaer, New York and worked as a medicinal chemist on a variety of therapeutic areas. It was here he realized that computer-assisted drug design could be an important factor in the drug industry. In 1987 Dr. Hutchins joined the Computer-Assisted Drug Design group at Abbott, working primarily with peptide and protein based projects.

Edward Thaddeus Olejniczak, Ph.D.

Ed Olejniczak is a researcher at Abbott Laboratories in the area of nuclear magnetic resonance (NMR). His interest is in the application of NMR to the study of molecular structure and dynamics of biological molecules. He received a Ph.D. in Physical Chemistry from Harvard University in 1982 and a B.S. in Chemistry from the University of Wisconsin in Madison in 1976. He had a postdoctoral fellowship in the Fransis Bitter National Magnet Laboratory at M.I.T from 1982 to 1984. In 1984, he joined Abbott Laboratories where he has carried out research on systems of pharmaceutical interest and written a "computerized lightbox" computer graphics program to help in the analysis of multi-dimensional NMR data.

Arthur Olson, Ph.D.

Arthur J. Olson currently holds the Anderson Research Chair in the Department of Molecular Biology at the Research Institute of Scripps Clinic, where he is also Director of the Molecular Graphics Laboratory. Dr. Olson's research centers around the development and application of computational and computer graphic methodology to the study of biological macromolecules. His focus is on protein-protein interaction in such systems as virus particles and immune complexes.

Dr. Olson received his Ph.D. degree in Physical Chemistry from the University of California at Berkeley for work on computational methodology in x-ray crystallography. He was then awarded a postdoctoral fellowship to work at Harvard University where he participated in mapping the first atomic resolution structure of a spherical virus particle. He then moved back to Berkeley where he was a Staff Scientist at Lawrence Berkeley Laboratory and Assistant Director of the NSF sponsored National Resource For Computation in Chemistry. He moved to La Jolla, California in 1981 taking up his present position at the Research Institute of Scripps Clinic.

Dr Olson has made a number of independent films on virus architecture, antibody structure, and enzyme structure and function as well as contributing some sequences of molecular animation to commercial endeavors, including one that is currently installed at Walt Disney's Epcott Center in Florida.

TJ O'Donnell, Ph.D.

TJ O'Donnell is a computational chemist and computer graphics specialist. He has devised and applied techniques for visualization of a wide range of chemical data. In 1980, he received a Ph.D. in physical chemistry from the University of Illinois in Chicago. As a postdoctoral fellow at the National Resource for Computation in Chemistry, he created the program GRAMPS, used by researchers throughout the world. As a researcher at Abbott Laboratories, he designed a molecular modelling system, with its graphics capabilities based on GRAMPS. In 1987, he formed a consulting company, specializing in computational chemistry and scientific visualization. He has published research articles on applied and theoretical computational chemistry and has created several films and videotapes. He is a member of the American Chemical Society/COMP division, American Association for the Advancement of Science and ACM/SIGGRAPH. He is currently serving as committee member to the Molecular Graphics Society.

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Presentation Schedule

TJ O'Donnell	Introduction, Brief History of Computer Graphics in Chemistry	15 minutes
Glen Kellogg	Computation and Display of Molecular Properties	40 minutes
Charles Hutchins	Use of Computer Graphics in Modeling Protein Interactions Interactions	40 minutes
.....	BREAK	15 minutes
Ed Olejniczak	Visualization and Analysis of Multi-dimensional NMR	40 minutes
Art Olson	Presentation Molecular Graphics	40 minutes
TJ O'Donnell	Phscolograms, Summary	15 minutes