VIRTUAL REALITY FOR MATERIALS DESIGN

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Abstract

A materials design laboratory incorporating an interactive molecular docking simulator has been set-up at the Materials Directorate of Wright Laboratory at Wright-Patterson AFB, based on Project GROPE, directed by Dr. Fred Brooks, Department of Computer Science, University of North Carolina, Chapel Hill. The capability for molecular docking through applied virtual reality with tactile feedback to enable interactive molecular design for multiple molecular systems, allows a researcher to experience the interactions between two molecular systems. The force information obtained in calculating the energies in real time using the GROPE code is used interactively to feed a mechanical robot. The best positions for the docked structures can be found by manipulating the movable structure on the display unit more efficiently than by performing a systematic search. These then lead to good starting positions for further optimization. The simulator is implemented as four cooperating servers: an energy server, a display server, a force-reflective arm controller, and a user interface controller. This effort is part of the Materials Directorate's extensive utilization of scalable DoD High Performance Computing (HPC) capabilities for materials design. In this paper we overview our computational materials design studies and the virtual reality laboratory.

New Materials Design. The molecular design of novel nonlinear optical material systems, as well as their atomic-level processing control, are promising, yet challenging. Indeed, our research objectives consist of the development of methods to address limitations and advance the state-of-the-art in computational chemistry and materials science; design novel materials with controlled properties for laser hardening by the application of newly developed methods, algorithms and parallelized advanced computer software; and understand and elucidate structure-to-property relationships for the design and optimization of materials in devices.

In general, new materials with fast nonlinear optical (NLO) response over broad spectral band-widths, self-assembled nanostructures for optical switching, and advanced absorbing dyes, all of which are critical for laser eye and sensor protection, are being explored. The design of such novel materials is promising yet challenging. Material properties have to be carefully optimized, for example, to achieve large NLO coefficients, high conjugation, appropriate ground and excited state absorption, and specific transition energies, as well as exhibit defined structural motifs and folding patterns, especially when derivatized with chromophores. In particular, series of organometallics, photochromics,
fullerenes, as well as biologically-based systems and liquid crystals are being investigated. Indeed, the focus of our effort is to develop fundamental theoretical and computational approaches that enable us to derive crucial structure-to-property relationships for candidate materials and enhance the capability for 'real materials' design and atomic-scale control, all of which utilize extensively scalable High Performance Computing (HPC) and advanced scientific visualization techniques.

The development, validation, and application of global optimization techniques\(^1\) for determining energy minima of complex macromolecular systems is the first stage in the design of these materials, for example, by using adaptive simulated annealing\(^2,3\), genetic algorithms\(^4,5,6\), as well as a novel hierarchical approach for determining a global topology of large systems at a low resolution\(^7,8,9\). These studies are followed by modeling of intermolecular interactions in very large molecular ensembles, requiring the development and implementation of 3-D fast multipole methods to calculate long range electrostatic interactions within a parallel molecular dynamics (MD) code\(^10\), and utilizing parallel HPC capabilities\(^11\). Large scale MD simulations of liquid crystalline (LC) models\(^12,13,14\) emphasize the importance of modeling long range electrostatics, and provide insight into the bulk phase behavior of the LC, and good agreement with experiment. Also, an additional potential was developed for modeling the LC state, and applied to predict structure-property relationships in nematic LCs. For reliable estimations of the properties of optical limiters, for example, electronic structures, particularly transition energies and intensities, hyperpolarizabilities, and reaction energetics, a fundamental understanding of solvent effects


\(^11\) Lupo, J. A. and Pachter, R., J. Mol. Graphics, accepted for publication

\(^12\) Patnaik, S., Pachter, R., Bunning, T. J., Crane, R. L. and Adams, W. W., Liquid Crystals 16 911 (1994)


is essential, and large molecules have to modeled from first principles. Calculations of interactions with the effective-fragment potential method, where solvent molecules are placed around a solute to generate correctly the first solvation cell within an \textit{ab initio} framework, have provided crucial insight and good agreement with experiment for the peptide and NLO properties\textsuperscript{15,16}. Density Functional Theory (DFT) calculations predicted the most stable configurations for a series of fullerenes\textsuperscript{17,18}, and the properties of organometallic systems, for example, phthalocyanine-based materials and porphyrins with meso-acetylene substituents, which are promising for optical limiting. These fundamental advances provide the basic understanding and means for more effective and efficient design of materials, and guide the exploratory research and advanced development programs in the Hardened Materials Branch, Electromagnetic Materials Division, Materials Directorate, Wright Laboratory. Furthermore, the development of parallel codes, combined with a strong participation in the DoD High Performance Computing (HPC) initiative, are being undertaken. In addition, full participation in a tri-service DoD Software Initiative for Chemistry and Materials Science is being carried out, which include classical molecular dynamics, quantum chemistry, tight-binding molecular dynamics, and Car-Parrinello methods for solids.

\textbf{Virtual Reality Lab.} In order to complement these materials design efforts, particularly when studying intermolecular interactions and increase the efficiency of configurational search, a capability for molecular docking through applied Virtual Reality with tactile feedback is being developed. Indeed, scientific visualization aims to improve perception of data\textsuperscript{19}. In particular, these techniques address the problem of searching conformational space of molecular systems to find the position and orientation of one molecule with respect to the other, such that the interaction energy would be at a global energy minimum, without performing a full algorithmic search. The search of configuration space by systematic brute force of positioning one molecule with respect to another treated as a rigid body with rotatable bonds, has to deal with the following parameters: 3 degrees of freedom (\textit{dof}) in translation, 3\textit{dof} in rotation, where there are N \textit{dof} rotatable bonds in the one molecule and M \textit{dof} rotatable bonds in the second molecule. The time complexity of such a search will be $O$ (the time for 1-D search$^{M+N+6}$).

The first molecular docking facility to enable a decrease in this time complexity was set up in the Virtual Reality Lab headed by Dr. Fred Brooks in the Department of Computer Science at the University of North Carolina. This capability enables interactive molecular design for multiple molecular systems, and a good starting position for further optimization can be rapidly obtained. The force information which results from calculating the energies in real time is used interactively to feed a mechanical robot, so that the best position for the docked structure

\textsuperscript{16} Day, P. and Pachter, R., \textit{J. Chem. Phys.}, submitted
can be found by manipulating the movable structure on the screen in a more efficient way than by performing a systematic search.

This approach was well demonstrated in a set of experiments we performed at the Virtual Reality Lab in the Department of Computer Science, University of North Carolina, for studying the siloxane macromolecular system, where only a movable mesogen model with no rotatable bonds (ca. 100 atoms) could be studied. Their force feedback ARM used a MasPar MP-1 parallel computer operating with 4096 processors to calculate the intermolecular energy (using electrostatic and Lennard-Jones potentials of the CHARMm force-field) between this rigid structure and movable docking model. The resulting force information was used interactively to feed the ARM, so that a stable configuration for the molecular ensemble could be found. The structural model was further improved by an energy minimization.

Liquid crystalline systems consisting of siloxane rings with a variety of attached pendant mesogens are of increasing recent interest in novel materials design. Several studies have been reported on the optical and thermal behavior of these compounds. One such system, consisting of cyclic pentamethylsiloxane with combinations of cholesteryl - 4' - allyloxybenzoate \{C\} and biphenyl - 4' -allyloxybenzoate \{B\} mesogens LC \{BC\} was studied in detail in our Laboratory. The following experiments were performed at the Virtual Reality Lab (where 2/3\{C\} denotes two/three cholesteryl 4'-allyloxybenzoate side-chains at an axial position, and 3\{B\} denotes three biphenyl 4'-allyloxybenzoate mesogens at an equatorial position):

<table>
<thead>
<tr>
<th>Rigid Structure</th>
<th>Movable Structure</th>
</tr>
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<tbody>
<tr>
<td>2{C}</td>
<td>2{C}</td>
</tr>
<tr>
<td>2{C}</td>
<td>3{B}</td>
</tr>
<tr>
<td>3{B}</td>
<td>2{C}</td>
</tr>
<tr>
<td>3{B}</td>
<td>3{B}</td>
</tr>
<tr>
<td>2{C}+2{C} (translation in y:17Å)</td>
<td>3{B}</td>
</tr>
<tr>
<td>2{C}+2{C} (translation in y:12Å)</td>
<td>3{B}</td>
</tr>
<tr>
<td>2{C}+2{C} (translation in y:12Å)</td>
<td>2{C}</td>
</tr>
<tr>
<td>3{B}+3{B} (translation in y:12Å)</td>
<td>3{B}</td>
</tr>
<tr>
<td>3{B}+3{B} (translation in y:12Å)</td>
<td>2{C}</td>
</tr>
<tr>
<td>3{B}+3{B} (translation in y:12Å)</td>
<td>3{B}+3{B}</td>
</tr>
<tr>
<td>2{C}+2{C} (translation in y:12Å)</td>
<td>3{B}+3{B}</td>
</tr>
</tbody>
</table>

In each case a few starting positions were attempted. The results of these experiments indicate that the interdigitation of the \{B\} mesogens is qualitatively more favorable in all cases. On the other hand, attempts to dock the \{C\} system were not successful (these results were published, in part, in Ref. 20).

The current molecular docking simulator at the Materials Directorate (cf. Figure 1) is implemented as four cooperating servers: an energy server, a display server, a force-reflective arm controller, and a user interface controller. The controller also provides the central control for the entire system.

Interactive molecular design has three computationally intensive components: back-computation and control of a force-reflection system; high-resolution stereoscopic image generation; and computation of the atomic forces, energies, positions and momenta which describe the interaction of two molecules. The rates at which each of these elements can be completed establish constraints on the fidelity of the model. The constraints due to the force-

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reflection system are based on the response of the human haptic sense requirements for perceiving relatively continuous forces. The reflected forces for a slowly varying interaction must achieve at least 20 ups (updates per second) to be sensed as continuously varying. The required rates for rapidly varying forces are much higher. For instance, the perception of a solid surface, which can be represented as an extremely large magnitude step function of force, requires rates exceeding 1000 ups.

Figure 1: Set-up of molecular docking simulator

Force-reflection is provided by a Cybernet PERforce six degree of freedom manipulator. Translation and rotation relative to the three principle axes is allowed (4" travel; 0.0003" linear resolution; up to 25 lbs. of force; 90° yaw, pitch, 180° roll; 40” angular resolution; up to 30 oz-in of torque). Sensors provide position and orientation information, and motors provide translational forces along each axis and torques about each axis. The user holds on to a joy-stick-like grip with two buttons for motor control, and three for other types of user input. The manipulator is controlled by an Intel 80386 based computer, which is connected via Ethernet to the rest of the system. It is treated as a server which receives force and torque information from the user interface, and sends back position information. The manipulator is capable of supporting 300 ups.

The two forces involved in the simulation are the non bonded electrostatic and Lennard-Jones 6-12 van der Waals forces. Note that the energy of interaction for a molecular structure determination is well represented by the molecular mechanics approach, using the CHARMM21 functional form for the force-field, where for a configuration \( \mathbf{r} \) the potential energy is:

\[
E(\mathbf{r}) = \frac{1}{2} \sum_b K_b (b-b_0)^2 + \frac{1}{2} \sum_{\theta} K_\theta (\theta-\theta_0)^2 + \frac{1}{2} \sum_{\phi} K_\phi \left[ 1 + \cos(n\phi-\delta) \right] + \sum_r \left( \frac{A}{r^{12}} - \frac{C}{r^6} + q_i q_j / r \right)
\]

where \( b, \theta, \phi, \) and \( r \) denote bonds, bond angles, dihedral angles, and nonbonded intramolecular distances, respectively, with the force-field parameters \( K_b, K_\theta, K_\phi, A, C, D, \) and geometrical reference values \( b_0, \theta_0, n, \delta. \) and the partial atomic charges \( q \) are described elsewhere.

The electrostatic force does not represent a problem, except when the positions of two atoms are overlaid almost exactly. This is a highly unphysical condition for the molecular systems being simulated, and would not intentionally be sought out. However, the van der Waals forces represent the primary forces, and the \( (1/r^{12}) \) term presents a rapid onset condition. The full 300 ups would be required if the van der Waals surface itself was to be probed. At 20 ups, user-induced oscillations in the force-reflection device occur if atoms are pushed together too aggressively.

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The image displayed consists of a few text labels and the remaining elements are composed of line segments. The two molecules are presented as stick models, with the connecting segments representing bonds between atoms, and the color indicating the type of atom. Each atom is typically connected to 2 or 3 other atoms, so the number of segments drawn per atom is a linear function of the number of atoms displayed. Image generation is required at 60 fps (frames per second), allowing images to be split between right/left eye views at the 30 fps required for the sensation of continuous motion. Since the molecules are free to move, the system must be capable of displaying approximately \((300 \times \text{number of atoms})\) segments per second. The current display system is implemented as a server which receives position information from the user interfaces, and updates the image. It is based on a SGI 4D/420 VGX PowerSeries with two 40MHz R3000 CPU's installed. On an otherwise quiescent system, the user interface controller and the display server run on separate CPU's.

Finally, the molecular interactions between the two molecules must be calculated. The computations scale as the product of the number of atoms in each molecule, since all pair-wise interactions between the two molecules must be considered. The calculations are implemented as an energy server, which receives position information from the user interface and returns energy, force and torque data. The energy server is implemented on an Intel Paragon XP/E system configured with 27 nodes, each with 32MB of memory. Timing studies using the 620 atom model show a potential update rate in excess of 90 per second.

The force-reflection device and the energy server are connected to the user interface controller via UNIX sockets interconnected via Ethernet. Thus there is an inherent latency introduced by the network which limits the update rate to 20-25 per second. Given the scaling performance of the energy server, the system should be capable of supporting models totaling 6000 atoms with current levels of sensitivity.

A recent set of experiments was completed for a polypeptide of interest and a series of dyes to ascertain the best position for molecular docking. The structural models were then further improved by energy minimization. The results provide good information on the sites of attractive interaction.

In addition to current capabilities we described, a headmount display unit will be integrated in the near future, having 1280x1024 pixel resolution and 24-bit color per pixel from n-Vision, McLean, VA, as part of a Memorandum of Agreement (MOA) with Armstrong Laboratory. These growing capabilities of advanced visualization and computing offer many potential applications including, among others, drug and materials design, the study of surfaces and defects, flight simulation, and education at all levels.