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INTERMOLECULAR POTENTIAL FUNCTIONS FROM SPECTROSCOPIC PROPERTIES OF WEAKLY BOUND COMPLEXES

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Third Progress Report

July 1, 1991 to June 30, 1992

John S. Muenter
Department of Chemistry
University of Rochester
Rochester, N.Y. 14627

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ABSTRACT

This report describes accomplishments over the past year in research supported by DOE Grant DE-FG02-87ER60514. Three projects, completed in the 7/1/'91 to 6/30/'92 time period, are briefly presented. The general goal of this work is to consolidate the information obtained from high resolution spectroscopy of weakly bound cluster molecules through a theoretical model of intermolecular potential energy surfaces. The ability to construct analytic intermolecular potential functions that accurately predict the energy of interaction between small molecules will have a major impact on many areas of chemistry, biochemistry, and biology. Ongoing work in this area is briefly described.

PROGRESS REPORT

The work done under DOE grant DE-FG02-87ER60514 is contained in the annual report, which is included here.

This project has occupied, and will continue to occupy, approximately 15% of the principal investigator's efforts.

PROPOSED TECHNICAL SCOPE

The purpose of the proposed work is to study weakly bound molecular complexes to better understand intermolecular interactions. Intermolecular potential functions play major roles in every aspect of chemistry, including both atmospheric and biological systems. Techniques involving infrared laser and microwave excitation and absorption of molecular beams will be developed. Theoretical models to analyze experimental data in terms of potential functions will be created.

FINANCIAL STATEMENT

The funds in the present budget for DE-FG02-87ER60514 will be expended by 11/30/1992.

STATEMENT OF OTHER GOVERNMENT AGENCY SUPPORT

This research is related to work funded by NSF grant CHE-9121534. The level of DOE funding is not sufficient to support a separate program that addresses both experimental and theoretical aspects of molecular spectroscopy of weakly bound systems. However, the equipment and personnel support requested here are entirely independent from the NSF grant.

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INTRODUCTION

This report covers the twelve months since the Second Progress Report (COO-87ER60514-5) was written for the present three year term of DE-FG02-87ER60514. This report will emphasize experimental spectroscopic results and the capabilities of a useful intermolecular potential function model.

PREVIOUS RESULTS

The past year has been devoted to the completion of experimental projects, refining and applying our intermolecular potential function theory, and writing papers. Three experimental projects have been finished. Intermolecular potential functions have been calculated for three new classes of complexes and, as a part of this work, our potential function model has be substantially modified and improved. Three publications have appeared during the past twelve months and a fourth paper has been submitted; two reprints and a preprint have been included with this progress report.

The three experimental projects completed are: infrared spectroscopy of argon–acetylene, Ar–HCCH; radio frequency and microwave spectroscopy of deuterated acetylene dimer, $(DCCD)_2$; and dipole moment measurements on rare gas–carbonyl sulfide, Rg–OCS, complexes. The Ar–HCCH work, which has been published (Journal of Molecular Spectroscopy, **153**, 486, 1992), analyzes data for three separate vibrational states obtained with our pulsed molecular beam--color center laser spectrometer. We obtained both structural and dynamic properties for each state. We also derived angular potential functions based on a fixed radial distance and internal rotation of the HCCH monomer within the complex. This model, which has been quite successful for other rare gas–linear molecule complexes, was only moderately successful for Ar–HCCH. The interest in Ar–HCCH intermolecular potential functions can be gauged by the fact that extensive dynamical calculations on a new potential surface, based on our data, are already in press: A. E. Thornley and J. M. Hutson, Chemical Physics Letters, **196**, XXX, 1992.

The second completed project has involved an extensive theoretical collaboration with Laurent Coudert, Universite Pierre et Marie Curie et CNRS, Paris. Molecular beam electric resonance spectroscopy data from Rochester consist of rovibrational transitions in $(DCCD)_2$ that contain rotational, tunneling, and deuterium hyperfine information. Because the complicated internal rotation tunneling mechanism can interchange the four identical deuterium atoms, we used sophisticated symmetry arguments to construct appropriate wave functions for the data analysis. This theoretical framework will be an important benchmark for the analysis of electronic properties in other complexes exhibiting large amplitude internal motions. The rotational constants, tunneling frequency, and angular expectation values from this paper will be important constraints on future dynamical calculations on acetylene dimer. This substantial effort, described in a 50 page preprint, has been submitted to the Journal of Chemical Physics.

The third completed project has also been a collaboration, this time with Robert Kuczkowski from the University of Michigan. This work addresses the question of how to best separate induction and dynamic effects on the electric dipole moments of weakly bound species. Since induction forces contribute to intermolecular interactions, this work nicely fits into our overall program. In this specific project, Stark effect measurements on Rg–OCS complexes have been made, both in Rochester and Ann Arbor. We analyzed

these data with a model based on harmonic internal motions and induction terms determined by electric fields from *ab initio* calculations. The results provide semi-quantitative insight into electronic properties of molecular complexes, but cannot give quantitative results. We are also taking an alternative approach to this problem by working on a distributed polarizability model for the dipole moment of the CO_2-CO complex, which has been studied in Rochester. The first draft of Rg–OCS paper has been written and the CO_2-CO calculations are in progress.

New intermolecular potential function calculations have been carried out on hydrogen halide dimers, $(HX)_2$, on carbon dioxide–hydrogen halides, CO_2-HX, and on carbonyl sulfide dimer, $(OCS)_2$. This work has led to significant improvements in our original potential function model. Perhaps the most important aspect of these improvements is that the model is now capable of describing the strong hydrogen bond found in hydrogen fluoride dimer without any special manipulations. This will be very significant in applications to biological molecules, where the strength and directional properties of hydrogen bonds are extremely important. The $(OCS)_2$ calculations point to the existence of a second stable isomeric form of this complex. Using predictions from the theoretical potential energy surface, we have tentatively assigned newly observed microwave transitions to this second form of $(OCS)_2$. Potential function calculations will be discussed in more detail below in the accompanying renewal proposal. We are currently in the beginning stages of writing three manuscripts on intermolecular potential functions for: trimers containing CO_2 and HCCH, hydrogen halide dimers, and CO_2-HX complexes.

Of the four publications that have appeared or been submitted, two have already been mentioned. Our infrared study of the nitrous oxide–acetylene complex has also appeared; Journal of Chemical Physics, **95**, 1537, 1991. This work discusses the acquisition and analysis of the pulsed molecular beam infrared absorption spectrum of $N_2O-HCCH$ and compares the similarities and differences exhibited by complexes containing N_2O and CO_2. This paper includes an $N_2O-HCCH$ potential function that is directly compared with our earlier (J. Chem. Phys. **94**, 2781 1991) results for CO_2-HCCH.

The final publication is a book chapter describing the molecular beam electric resonance technique: Electric and Magnetic Resonance Spectroscopy, J. S. Muenter, *Atomic and Molecular Beam Methods*, G. Scoles, ed., Vol. II, Chap. 2, 15-57 (Oxford University Press, London 1992). While this publication does not directly present new research results, this form of information dissemination is important in all areas of science.

A number of projects are currently in progress. This work, and new developments will be discussed in detail in the enclosed renewal proposal.

INTERMOLECULAR POTENTIAL FUNCTIONS

AND

HIGH RESOLUTION MOLECULAR SPECTROSCOPY

OF

WEAKLY BOUND MOLECULAR COMPLEXES

A research proposal submitted to:

Office of Health and Environmental Research

United States Department of Energy

John S. Muenter

Department of Chemistry
University of Rochester
Rochester, N.Y. 14627

INTRODUCTION

While it is certainly true that intermolecular potential functions control virtually every aspect of the molecular sciences, the quest to take advantage of this fact has been long and arduous. However, science has progressed to a point where many kinds of potential energy surfaces are routinely used in addressing a variety of practical problems:

- Molecular dynamics simulations of gas phase chemical reactions important to combustion, acid rain, stability of stratospheric ozone, and possible global climate change
- Molecular mechanics calculations to determine stabilities of pharmacologically important molecules
- Refinement of structures of biological macromolecules obtained from X-ray diffraction and 2D NMR experiments
- The study of secondary and tertiary structure in DNA
- Molecular recognition and enzyme catalysis
- The study of protein dynamics and protein folding

These topics represent just a few current research problems that require potential energy surfaces. The broad range of applications imposes a diverse set of requirements on the quality and complexity of the potential energy functions employed. However, since there are relatively few potential surfaces available and it has often been necessary to use only the simplest functions for computational reasons, it is difficult to relate current results to the quality of the potential function employed. With continual advances in computer power and the availability of new sources of potential function information, it is becoming increasingly important to test the efficacy of currently used potential function models. Only in this way will more useful descriptions of intermolecular interactions come into use.

One of the new sources of potential function information is high resolution molecular spectroscopy of weakly bound molecular complexes. Over the past dozen years, a relatively large number of molecular complexes held together by either hydrogen bonds or van der Waals forces have been studied.[1] These investigations produce geometric and dynamic properties of the complex, but do not generate any direct potential function data. This proposal will briefly discuss the general relationships between spectroscopic data and intermolecular potential functions, and then concentrate on a specific potential function model developed at Rochester. We will first present the evolution and current capabilities of this model and then describe plans for future developments and applications. Finally, this type of potential function model will be discussed in terms of the capabilities and needs of molecular dynamics and molecular mechanics simulations.

WEAKLY BOUND MOLECULAR COMPLEXES AND POTENTIAL ENERGY SURFACES

Different types of experiments are sensitive to different portions of the intermolecular potential energy surface, or PES.[2] With rare exception,[3] traditional sources of potential function information are sensitive only to the radial, or isotropic, portion of the PES. For example, transport properties, molecular beam elastic

scattering, and spectral line broadening all sample orientationally averaged molecular interactions and are insensitive to the angular, or anisotropic, portion of the PES. In contrast, the geometries of weakly bound bimolecular complexes exhibit strong dependences on both the position of the radial minimum and anisotropic interactions, but are relatively insensitive to overall well depths. There is no one source of experimental data that can describe all aspects of an intermolecular potential function. In addition, it is still virtually impossible to begin with experimental data, from all sources, and directly invert this data to obtain the desired potential function.

This situation raises the obvious question of "What have we learned about intermolecular interactions from the numerous spectroscopic studies of complexes?" A glib answer is that we have obtained a great deal of information, but certainly not all that we need. Spectroscopic data has been very successful at describing intermolecular interactions at two extreme limits. From qualitative and intuitive points of view, familiarity with the van der Waals molecule literature provides enormous insight into intermolecular interactions. For example, it is relatively easy to classify specific binding energies as "strong", "medium", or "weak"; or to categorize anisotropies as "rigid", "floppy", or "free to rotate". At the other extreme, exquisitely detailed potential functions have been constructed for a small but growing number of complexes.[4] Atom−diatom systems like Ar−HCl fit into this category, but this technology is currently limited to systems no larger than Ar−H_2O.[5] Unfortunately, the broad middle range of PES descriptions is much less well developed. What is needed are PES models that can generate quantitative or semi-quantitative results for interactions that have not yet been studied. In other words, we need models with useful predicting power.

The traditional approach to constructing a PES, the one that works very well for Ar−HCl, is to select a particular parametric functional form to describe the PES. Then the parameters in the chosen model are fitted to experimental data. It is not uncommon to have 20 or 30 freely adjustable parameters in such a function. Not only does this procedure have an enormous number of variables, but it also focuses on a specific interaction. The best PES of this kind for Ar−HCl contains no useful information on HCl dimer. So, while this procedure is well suited to the most accurate description of a specific PES, the extremely large number of possible bimolecular complexes makes this approach inappropriate for more general descriptions of intermolecular interactions. Only two choices exist for potential function models having broad applicability. Either it is necessary to resort to first principles (*ab initio*) calculations or the approach must be based on properties of the isolated monomer molecules. Both approaches are valid and complementary to one another. *ab initio* quantum chemical calculations are capable of generating excellent PES's for small systems,[6] but these calculations must be carried out at a very high level because of severe correlation and basis set superposition effects. (The basic origin of the dispersion interaction is electron correlation, which is ignored at the Hartree-Fock level.) This is a field for specialists. In addition, it will not be possible to extend the *ab initio* approach to large molecular systems in the foreseeable future. For these reasons, we have chosen to focus on using the properties of individual molecules as input to a general potential function model.

The challenge for any general description of intermolecular interactions is to include sufficient complexity to reflect the many observed properties of molecular complexes and, at the same time, contain few enough adjustable parameters for the model to have useful predicting powers. The most widely used monomer based description of intermolecular potential energy focuses on the electrostatic interaction between molecular charge distributions.[7,8,9,10] The strong angular dependence of electrostatic terms has correctly predicted the relative orientation of monomers within many bimolecular complexes.[11] In most of this work, the separation

of the individual molecules has been fixed at experimental values. The electrostatic interaction is then calculated either from a distributed multipole description of the monomer charge distributions[7,8,12] or from monomer electrostatic properties calculated in the monomer center of mass coordinate system.[9,10] In either case, the electrostatic properties of the monomer molecules are based on *ab initio* wave functions. Models using only electrostatic interactions are far from complete, and are fundamentally incapable of describing the radial portion of the PES. To avoid imposing arbitrary separation constraints on an intermolecular interaction, it is essential to include dispersion and repulsion terms.

A POTENTIAL FUNCTION MODEL

In our initial potential function model,[13] we have included repulsion, dispersion and electrostatic interactions. Thus we write the total energy of interaction between molecule m and molecule n, U(*nm*), as:

$$U(nm) = U^{mn}_{rep} + U^{mn}_{disp} + U^{mn}_{elec} .$$

We expressed the repulsion and dispersion energies, $U^{mn}_{rep} + U^{mn}_{disp}$, as a sum of atom-atom Lennard-Jones (12−6) terms, primarily because only two parameters are required for each atom pair in this formalism. The two Lennard-Jones parameters for the i^{th} atom of molecule m interacting with the j^{th} atom of molecule n are $C^{mn}_{12}(ij)$ and $C^{mn}_{6}(ij)$, and

$$U^{mn}_{rep} + U^{mn}_{disp} = \sum_{ij}[C^{mn}_{12}(ij)/R^{12}_{ij} - C^{mn}_{6}(ij)/R^{6}_{ij}] .$$

To eliminate the large number of C_{12} and C_6 parameters, we first describe the $C^{mn}_6(ij)$ in terms of known long range dispersion constants. These C_6 coefficients, usually obtained from dielectric constant data, are known for a large number of molecules.[14] To obtain the required $C^{mn}_6(ij)$, we distribute the long range C_6 among the individual atoms of the monomer using a Drude[15] approximation that weights the dispersion according to the number of electrons in each atom. Next we write the $C^{mn}_{12}(ij)$ in terms of $C^{mn}_6(ij)$ and the Lennard-Jones sigma parameter, σ^{mn}_{ij}, which is the distance where the energy for the *ij* atom pair crosses zero. This transformation is affected because σ^{mn}_{ij} represents the sum of the van der Waals radii for atoms *i* and *j*. With this in mind,

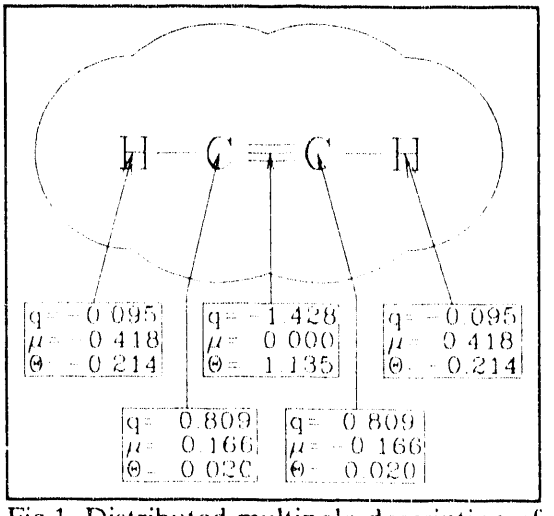

Fig.1. Distributed multipole description of the HCCH charge distribution.

$$\sigma^{mn}_{ij} = R^{m}_{i} + R^{n}_{j} \simeq S_m R_i + S_n R_j .$$

The R^m_i are the desired, but unknown, atomic radii that are approximated in the second half of the equation as the product of a conventional van der Waals radius, R_i, times a scaling factor, S_m, for each molecule in question. Using literature values[16] for R_i gives the repulsion energy in terms of a single parameter for each monomer. We adjust this parameter to make the calculated monomer-monomer separation in the symmetric dimer agree with the observed value. Once determined in this way, S_m is left fixed for all other interacting partner molecules. Finally, the electrostatic energy is calculated using the distributed multipole description of the molecular charge distributions. Fig. 1 shows how point charges, q, point dipoles, μ, and point

quadrupoles, Θ, are distributed through the acetylene molecule to reproduce its charge distribution.[7] This efficient scheme of charge representation has been published for many molecules.[7,8,12]

The above procedure describes a plausible PES model, but there is no guarantee that it will work. To establish the usefulness of the model, we have undertaken an aggressive program of testing, modification, and more testing. The first tests[13] were on acetylene dimer, $(HCCH)_2$, carbon dioxide dimer, $(CO_2)_2$, and acetylene–carbon dioxide, $HCCH-CO_2$. These complexes were chosen for two reasons. First, they are experimentally well studied and much of this work has been done in our labs.[17] Second, $(HCCH)_2$ exhibits a different geometry than $(CO_2)_2$, even though these two complexes would appear to have many similarities. Electrostatic models[7] predict identical structures for $(HCCH)_2$ and $(CO_2)_2$

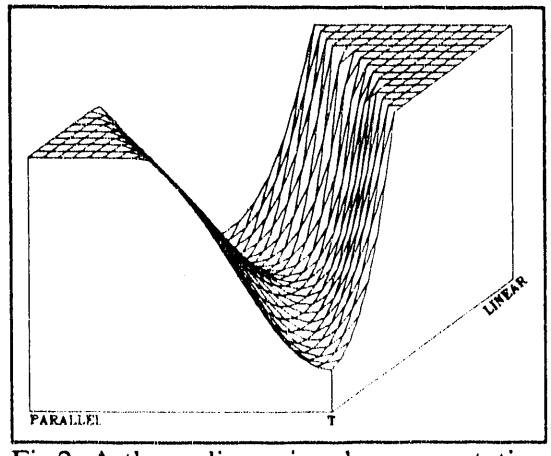

Fig.2. A three dimensional representation of the $(HCCH)_2$ angular potential.

It should be clear that the initial tests were successful, otherwise this proposal would be addressing different material. Acetylene dimer has a T shaped equilibrium geometry, but has a very low barrier to inversion that is accomplished by a "geared" internal rotation of the two monomers. This large amplitude motion is experimentally characterized by tunneling splittings[17(b)] and nuclear hyperfine structure.[18] Fig. 2 shows our calculated angular potential for $(HCCH)_2$, clearly displaying the proper equilibrium geometry and the necessary low inversion barrier. In contrast, Fig. 3 shows the angular potential for $(CO_2)_2$ from the same perspective. The very different properties of these two complexes are obvious. Both the $(HCCH)_2$ and $(CO_2)_2$ PES's agree very well with experimental data, indicating that our model and a single adjustable parameter describe these two complexes quite well. Thus we have a new source for rather accurate numerical potential functions and, perhaps of greater significance, the physical basis of the model provides substantial insight into why specific cluster geometries are favored. The contrast between $(HCCH)_2$ and $(CO_2)_2$ results from a non-obvious interplay between repulsion, dispersion, and electrostatic forces. In addition, the electrostatic interactions in $(HCCH)_2$ suggest the presence of a weak hydrogen bond.[13]

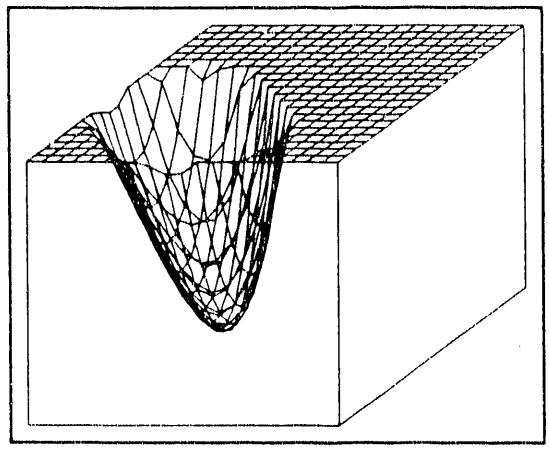
Fig.3. The angular potential for $(CO_2)_2$ shown from the same perspective as used in Fig.2.

The $HCCH-CO_2$ complex must be described without any adjustable parameters, and it was encouraging to see excellent results in this case also.[13] The trimers containing HCCH and CO_2 can also be described with no adjustable parameters, and the four possible complexes of this type have been investi-

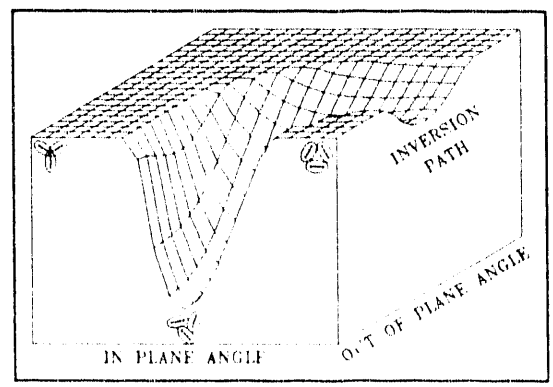

Fig.4. The angular potential for $(HCCH)_3$ showing an out-of-plane inversion path.

gated.[19] The calculated properties of $(HCCH)_3$ and $(CO_2)_3$ are in excellent agreement with experimental results.[20,21] We have also identified an interesting inversion path that involves out-of-plane vibrations for these two planar complexes. This is shown in Fig. 4 for $(HCCH)_3$. There are no experimental observations for either $(HCCH)_2-CO_2$ or $(CO_2)_2-HCCH$. Our potential surfaces suggest that these species will be very floppy molecules that will not exhibit a well-defined geometry. The spectral complexity and dilution of state populations caused by low frequency, large amplitude motions would explain the absence of experimental data.

At this stage we thought all was solved, and that any problem could be successfully attacked. We specifically wanted to look at a puzzling case, where the physical insight from the calculated PES would be particularly useful. One of the more surprising experimental observations in recent years was that the CO_2-HBr complex was observed[22] to be strongly bent, while the CO_2-HF and CO_2-HCl complexes were linear.[23,24] The first step in approaching the carbon dioxide–hydrogen halide problem was to study the hydrogen halide dimers, to obtain values for the S_{HF}, S_{HCl}, and S_{HBr} scaling parameters. This was an important project in its own right, since $(HF)_2$ and $(HCl)_2$ are two of the best studied bimolecular complexes and very high quality *ab initio* PES's exist for these species.[6,25] The angular portion of the hydrogen halide dimer potentials also presents a challenge to our model because the hydrogen halides are nearly spherically symmetric, with little extended geometric structure. Finally, HF dimer exhibits a strong hydrogen bond, comparable to that between water molecules, and our model contains no mechanism to specifically address hydrogen bonding. Will the model, as published,[13] correctly describe HF dimer?

In a word, no. All three HX dimers collapsed to a closely packed C_{2h} structure, such as H F F H, instead of having the well-known open configuration with a nearly linear hydrogen bond. Clearly, it was time to consider modifying the PES model. This process is in its initial stages, and the following description should be considered as a progress report rather than a final result. Two significant changes have been implemented. First, the R^{-12} repulsion has been replaced with an exponential term, $\exp[\alpha(1-R_{ij}/\sigma_{ij})]$. A 12–6, rather than an exponential–6, based model was employed in our initial formulation because 12–6 interactions contain two variables, while exponential–6 interactions require three parameters per atom pair. This problem has been avoided initially by fixing $\alpha \equiv 12$, which is an often assumed value for this parameter. Second, the distribution of the dispersion interaction within each monomer was altered to reflect the presence of electrons in covalent bonds. The long range dispersion coefficient was originally distributed to each atom on the basis of atomic number. Now, one electron is placed in the center of each covalent bond by taking a half electron from each adjacent atom. Double and triple bonds have two and three electrons at their center in the dispersion calculations.

These alterations had very little effect on the PES's for the already studied CO_2 and HCCH containing compounds. This presumably occurs because the linear configuration of several heavy atoms makes the overall

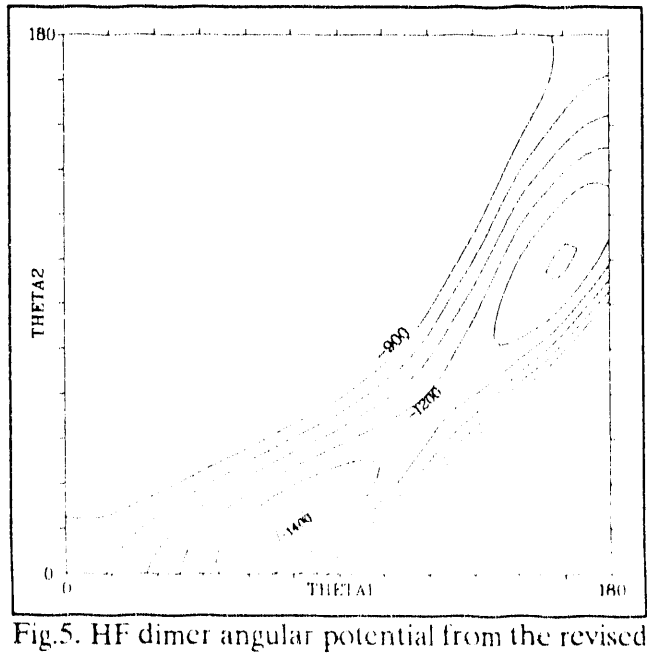

Fig.5. HF dimer angular potential from the revised PES model.

PES less sensitive to specific details of dispersion and repulsion. For the hydrogen halides, however, there is just a single heavy atom and the modified model produced very different results. Figure 5 shows the angular potential for HF dimer, displaying the necessary near linear hydrogen bonds and low barrier between equivalent structures. This low barrier is responsible for the hydrogen donor-acceptor interchange tunneling that is observed experimentally.[26] The potential shown in Fig. 5 is in good agreement with the best theoretical $(HF)_2$ results,[25] exhibiting just a slightly lower dissociation energy and barrier height. In particular, the model properly accounts for the strength of the HF dimer hydrogen bond; the calculated 1400 cm^{-1} dissociation energy is equivalent to 4.0 kcal/mole, well within the range of canonical strong hydrogen bonding. The HCl dimer results, shown in Fig. 6, are equally good. In particular, the lower binding energy, smaller barrier to inversion, and the more perpendicular geometry (note that the axes in Figs. 5 and 6 have different ranges) are in excellent agreement with theoretical[6] and experimental[27] results. There is no published information on HBr dimer. The monomer separation was taken from unpublished results[28] on HBr-DBr, and our angular PES is similar to the $(HCl)_2$ result shown in Fig. 6.

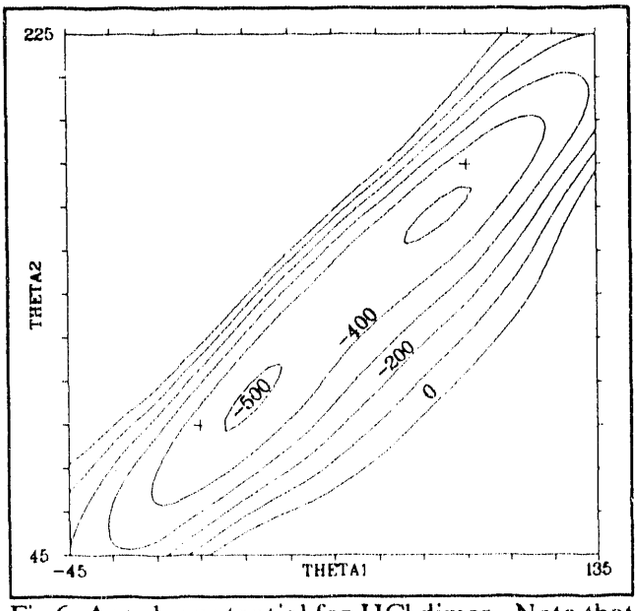

Fig.6. Angular potential for HCl dimer. Note that the axes are defined differently than those of Fig. 5. The crosses show the positions for an L shaped dimer.

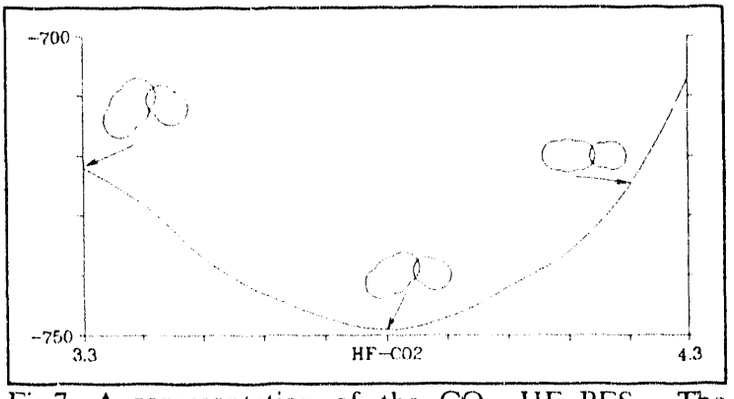

Fig.7. A representation of the CO_2–HF PES. The horizontal axis in the monomer separation, in Å; the vertical axis, in cm^{-1}, is the binding energy. The pictographs indicate how the bond angle varies.

We could now examine the carbon dioxide–hydrogen halide complexes. CO_2–HF has been extensively studied in both the microwave and IR portions of the spectrum.[22,23,29] This complex has been perplexing for several reasons. The original study[23(a)] found a linear complex with a relatively weak, but very short bond. The 2.5 micron IR study[23(b)] found the excited state to be bent. A very recent theoretical study,[29(c)] which generates a multi-parameter PES by fitting extensive spectroscopic data, explains these observations using a potential having extremely large stretch-bend interactions. Nesbitt describes the bending potential as being a hinge which, when it bends, brings the monomer centers of mass closer together. Our potential, which has no adjustable parameters, is in complete agreement with Nesbitt's results;[29(c)] moreover it provides an intuitive picture of this complex interaction. Figure 7 shows a two dimensional representation of our CO_2–HF PES in which the minimum binding energy is plotted as a function of the monomer separation. To show how the bond angle changes with separation, small pictographs are included in the figure. This potential can be used to describe Nesbitt's hinge, in simple terms, as follows: The pivot point of the hinge is supplied by the repulsive interaction; electrostatic forces try to keep the hinge open at its linear configuration, while dispersion forces want to bend

the hinge. In the CO_2–HF ground state, the electrostatic forces slightly dominate the dispersion forces and the bond is essentially linear. However, the large bending amplitude means that the bond length obtained from rotational constants appears to be exceptionally short. When the HF monomer is vibrationally excited, the repulsive wall moves out, reducing the electrostatic interaction. But on bending, the monomers move closer together, enhancing dispersion. The result is a bent excited state.

For CO_2–HCl, the potential is extraordinarily flat bottomed, as shown in Fig. 8. (Note that the horizontal axes in Figs. 7 and 8 are 1.0 and 1.4 Å respectively.) This results from increased dispersion, from the chlorine atoms, as the monomers bend and move closer to each other. This trend continues with CO_2–HBr, which is observed to be strongly bent in its ground state. The calculated potential for CO_2–HBr, shown in Fig. 9, follows this trend but is not sufficiently bent to agree with experiment. This problem is solved if the long range C_6 dispersion constant is increased by just 20%. This situation suggests that this potential function model is also capable of improving our knowledge about van der Waals radii and dispersion interactions in cases where there is good molecular spectroscopy. However, for the CO_2–HX complexes, our model is most useful in providing physical insight into why conflicting and unexpected observations have been made for these species. While these results have obvious structural implications, they also affect kinetics and dynamics experiments,[30] which were the prime motivations for studying CO_2–HBr.

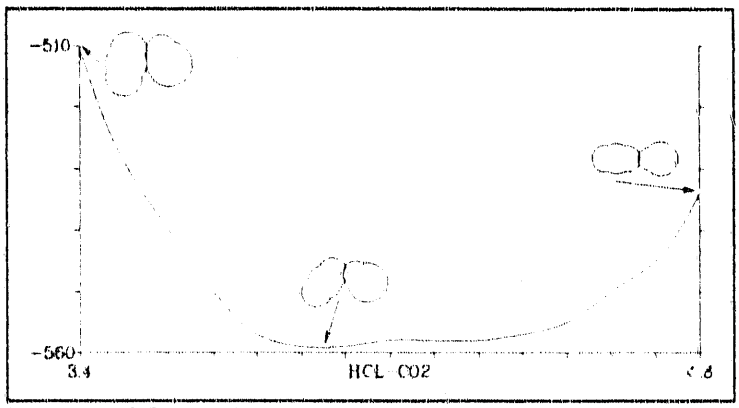

Fig.8. A CO_2–HCl potential shown in the same manner as Fig. 7, except that the horizontal axis is 1.4Å.

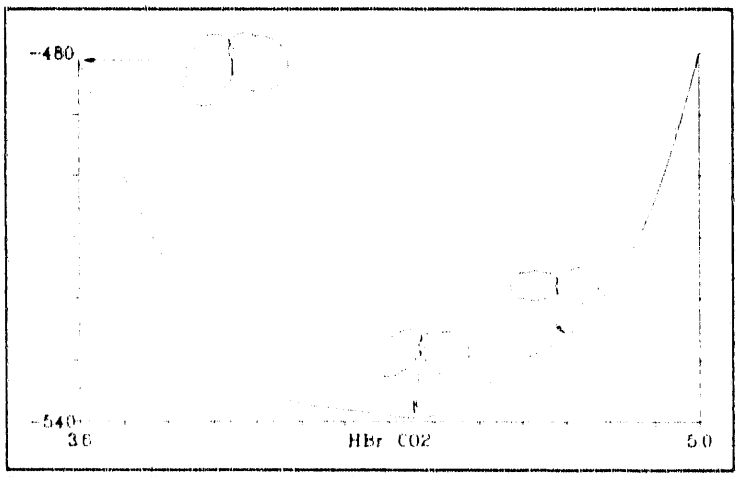

Fig.9. A CO_2–HBr potential shown in the same manner as Fig. 7, except that the horizontal axis is 1.4 Å.

While all of this potential function work is still in its early stages, we have currently calculated extensive potential functions for fifteen different molecular complexes containing seven different monomer molecules. Just seven parameters, one for each monomer, have been adjusted in this work. In most cases where experimental results are available, theory and experiment have shown excellent agreement. This initial work has been very encouraging, particularly in the way the HF dimer strong hydrogen bond has been properly described. But there are many questions remaining to be addressed and many applications waiting to be investigated. We will discuss some of the current questions, logical extensions, and new applications in the following sections.

FUTURE DEVELOPMENTS

Potential Function Model Extensions

The first questions that require attention are those raised by changing the repulsion and dispersion terms. Replacing the 12–6 atom-atom interaction with an exponential–6 form, and including bond centered dispersion interactions, produced important changes in the resulting PES's. These changes were introduced very recently, during the preparation of a paper presented at the 1992 Ohio State Molecular Spectroscopy Symposium,[31] and we have yet to properly evaluate the individual effects of the two alterations. The relative importance of the choice of α in the $\exp[\alpha(1-R_{ij}/\sigma_{ij})]$ repulsion term and the manner in which dispersion is distributed within the monomer molecules must be systematically investigated. We have some preliminary evidence that bond centered dispersion is more important than the exact form of the repulsive wall. However, the desired universality of the potential function model means that we have to examine many systems before drawing general conclusions.

After we sort out these questions, we still should investigate several fundamental aspects of the model. At present, the dispersion interactions are not damped and meaningless results can be generated if two atoms are forced too close to one another. This has not been a problem with manual searches for PES minima, since extraneous results can easily be rejected. However, undamped dispersion may be a serious problem for automated configuration searching. Several different methods to introduce damping exist in the literature.[32,33] In some cases,[14] data also exist for C_8 and higher order long range dispersion. Proper ways to incorporate this information should be investigated. In addition, long range dispersion data exist for many specific interacting pairs of molecules.[14] Using these data could produce better results than the geometric mean approach currently employed. The limitations of spherically symmetric atom-atom interactions can also be addressed by introducing an anisotropic scaling of the van der Waals radii. For example, the S_m scaling factor could incorporate a P_2 Legendre polynomial term. These, and other possible modifications need to be investigated in a systematic fashion that is consistent with the original premise; to develop relatively simple but useful PES models. If some of these variations are successfully introduced, it may become desirable to develop a family of models of increasing complexity. Which model would be used in any specific application would then depend on individual requirements, and on the availability of appropriate input data.

We also must continue to development the computer codes used to generate PES's from input data. The present code can only handle linear monomers, and one obvious extension is to incorporate code for nonlinear components. Adding the additional geometry for nonlinear substituents will be straightforward, if tedious. We will also have to modify the electrostatic energy subroutines to accommodate off diagonal elements of the point quadrupole moments. When monomers no longer have cylindrical symmetry, these off diagonal elements must be included in the distributed multipole descriptions of the charge distributions.[7] These improvements have a high priority because of the importance modelling interactions found in biochemical systems. We need to study complexes containing a variety of chemical functionalities, such as: water, methanol, formaldehyde, formic acid, ammonia, hydroxyl amine, formamide, *etc.*

A major extension of the PES model will be the inclusion of induction effects. We have already initiated this effort, but much remains to be accomplished. The analysis of virtually every aspect of molecular clusters begins with the basic assumption that the monomer properties are not altered by the formation of the complex. While this is generally considered to be a good approximation, it ignores the effects of the electric

fields produced by molecule 1 on the charge distribution of molecular 2 and *vice versa*. The electric field produced by each molecule polarizes its binding partner, which adds a term to the overall energy of interaction. The induced moments generated by this polarization interact with both the permanent moments and the induced moments of the binding partner. The sum of all of these interactions makes up the induction energy. The magnitude and directional properties of induction terms are difficult to calculate and are not well characterized. Most of the difficulty arises because conventional molecular polarizabilities should not be used for calculating these induced moments. Enormous electric field gradients cause this problem. A typical situation is shown in Fig. 10 for the carbon dioxide–carbon monoxide complex, CO_2–CO. Figure 10 displays constant electric field contours generated by the CO_2 molecule over the region occupied the CO, which is shown as an outline. The constant field contour closest to CO_2 in Fig. 10 is for 10^8 v/cm, while the contour partially shown in the upper corners of the figure is for 10^6 v/cm. The field strength varies from $>10^8$ v/cm to $\approx 10^6$ v/cm over the length of the CO molecule. The field variation in the direction transverse to the CO axis is just as severe. Two contours in Fig. 10 include arrows to show the field direction. The contour with arrows closer to CO_2 is for 3×10^7 v/cm and the field direction reverses over the dimension of the carbon atom. These field gradients exceed 10^{15} v/cm^2.

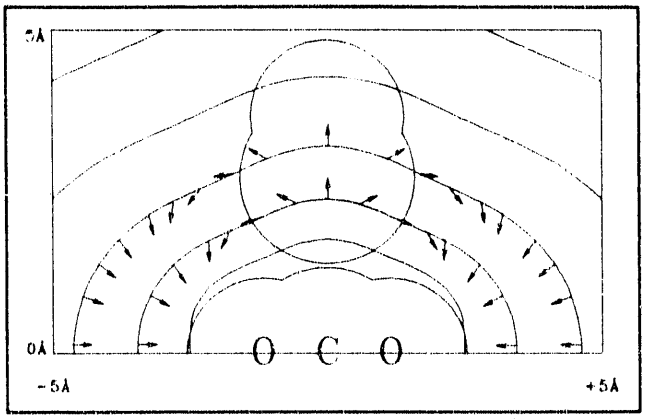

Fig.10. The electric fields generated by CO_2 in the vicinity of CO in the CO_2–CO complex. The contours with direction vectors are for 3×10^7 and 1×10^7 v/cm.

Stone[34] has developed a theoretical formalism to handle this complicated situation. He uses *ab initio* methods to calculate several orders of polarizability, which are distributed over different centers in the molecule. These distributed polarizabilities have been published for a significant number of molecules. We have initiated calculations of the induced moment of CO_2–CO, to compare with our experimental measurement of this moment.[35] These calculations have been held up by numerous typographical errors in some of Stone's papers,[34,36] but recent communications with Stone have hopefully cleared up all of these difficulties. Experimentally, we have also addressed induction effects through electric dipole moment measurements of complexes made up from nonpolar constituents. We have studied a number of examples,[37] observing dipole moments ranging from 0.03 to 0.3 Debye. Stone and coworkers have already calculated some of these moments with relatively good results.[38] As our calculations proceed, the effects of induction on energies will be evaluated. If necessary, induction will be incorporated into the PES model.

Potential Energy Calculation Procedures

Even with a perfect potential function model, problems with calculational procedures still exist. The model provides the means to calculate intermolecular energies for specified relative configurations of the two monomer molecules. It is up to the model user to choose molecular configurations and map out the PES over the geometric space of interest. Since six geometric parameters are required to specify the relative orientation of two general molecules, the process of searching for the PES minimum can be complicated. The majority of the calculations done to date have been limited to just three degrees of freedom. Complexes containing two linear molecules require only four spatial parameters, and the majority of this work has

considered planar configurations, which eliminates one more variable. In this relatively simple situation, we have used manual grid search methods to identify PES minima. Even here, however, we have fallen into local minima by using an overly coarse grid. As we attack more complicated systems, we will need more automated and effective searching procedures. We plan to implement a modified gradient search, using a Marquardt parameter,[39] to achieve efficient convergence from arbitrary starting points. Since weakly bound complexes with multiple minima are intrinsically interesting, care will always be required when investigating a new PES.

APPLICATIONS

Applications of this PES model fall into three different time frames: immediate, near term, and long term. Immediate applications include those already in progress, and ones that can be implemented with a minimum of new developments. Near term applications fall in a three to five year schedule, and will take advantage of the developments discussed above. Long term applications are, of course, more speculative, but near term work will be directed toward specific long term goals. Many of these long term goals relate to molecular mechanics and dynamics calculations on biological molecules. Each of these three areas will be discussed in more detail below.

Immediate Projects

Projects in progress that are nearly complete include PES calculations on trimolecular acetylene and carbon dioxide containing complexes, hydrogen halide dimers, hydrogen halide−carbon dioxide species, carbon dioxide−carbon monoxide, carbon monoxide dimer, and carbonyl sulfide dimer. The trimeric species containing HCCH and CO_2 were briefly discussed on page 11 and an angular potential for $(HCCH)_3$ is shown in Fig. 4. These calculations have to be reviewed considering recent modifications to the model, but few changes are anticipated. The hydrogen halide dimer calculations require a systematic investigation of the effects of altering the α coefficient in the exponential repulsion. In addition, the relative importance of exponential repulsion vs. bond centered dispersion must be investigated. The results of any further changes to the model used for the HX dimers will affect the HX−CO_2 calculations and these functions will be reviewed. In addition we need to pay more attention to how the stretch-bend interaction affects the dynamics of these molecules. Dipole moment calculations for CO_2−CO will test our ability to calculate induction effects. The carbon monoxide dimer project is in response to infrared experiments on this molecule. IR spectra of $(CO)_2$ exist from diode laser spectra of free jet expansions[40] and from Fourier transform measurements on a static gas cell,[41] but it has been impossible to analyze these data. The problem presumably results from large amplitude internal motions, and a potential function calculation may expedite the data analysis. Figure 11 shows a preliminary angular potential that exhibits two minima. Both are T

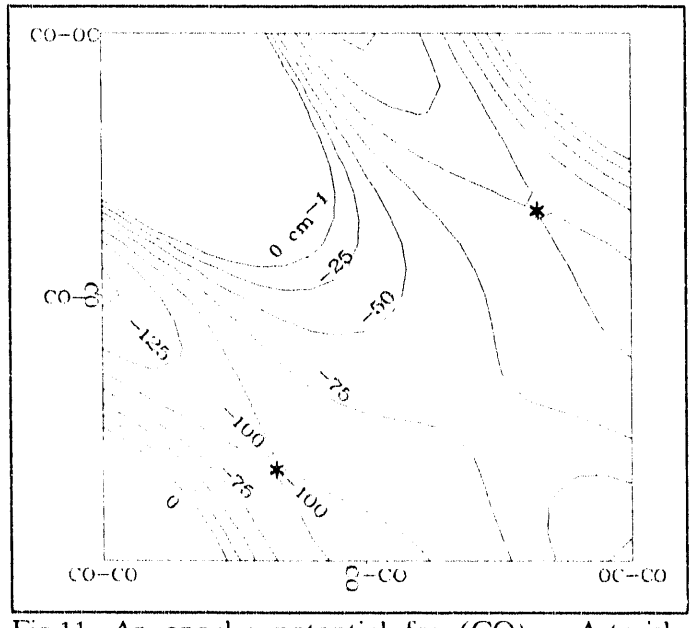

Fig.11. An angular potential for $(CO)_2$. Asterisks mark a low barrier between the carbon bonded and oxygen bonded form.

shaped, one carbon bonded (labelled at the bottom center of the figure) and one oxygen bonded (labelled at the left-center of the figure). Asterisks mark a very low barrier between these two minima, indicating almost free internal rotation in $(CO)_2$.

The two minima shown in Fig. 11 are not stable, *i.e.* there will be rapid interconversion between isomers, and only one dynamically averaged form will be observed in experiments. We see a much different situation in carbonyl sulfide dimer, $(OCS)_2$. An angular potential for $(OCS)_2$ is displayed in Fig. 12. The horizontal axis shows a 0-180° rotation for one OCS monomer and the vertical axis indicates a 0-360° rotation for the second OCS monomer. Four separate minima are seen. In the top half of the figure, the deep minimum corresponds to the two monomers being antiparallel to one another. This is the nonpolar, C_{2h}, geometry that we have studied by molecular beam infrared spectroscopy.[42] The shallower subsidiary minimum in the top half of the figure cannot be experimentally observed because any molecules initially in this well will freeze out into the deep minimum during the beam expansion. The two minima in the lower half of the figure are symmetric, identical configurations of a polar isomer of $(OCS)_2$. The two $+1000$ cm^{-1}, repulsive contours indicate that the polar and nonpolar isomers cannot interconvert in the nozzle expansion. We believe we have recently observed microwave transitions in this isomer, using pulsed molecular beam Fourier transform microwave spectroscopy.[43] This experimental work would not have been initiated if we had not had the predictions from the potential function calculations. Without the PES model, we would have missed an excellent opportunity to study isomerization in weakly bound cluster molecules.

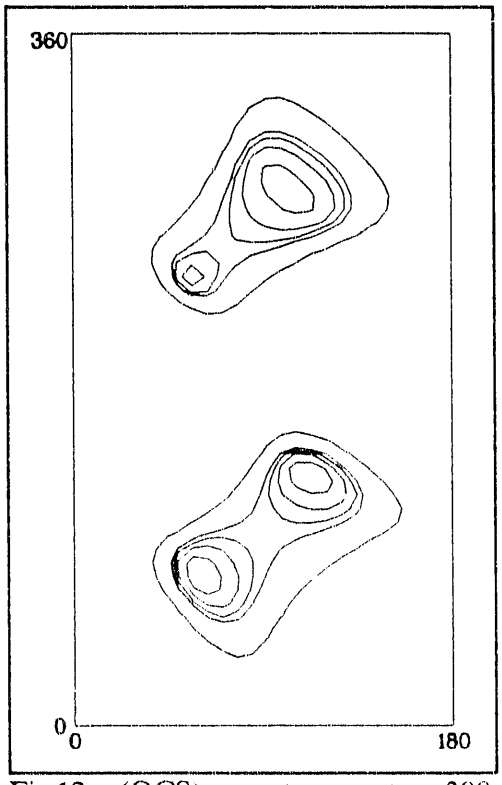

Fig.12. $(OCS)_2$ contours at -300, -200, -100, 0, and 1000 cm^{-1}.

Near Term Projects

Work planned for the near term will serve as a bridge between current research and long term efforts directed toward a better understanding of the structures, properties, and dynamics of biological molecules. Some of the computational developments required for this transition have been discussed above. As new tools become available, more complicated systems will be studied and additional model refinements will be pursued. The near term work will evolve from systems similar to those currently being studied, to more complicated and more biologically significant species.

A few linear-linear complexes still need to be studied, to test and improve the PES model. Since the $HBr-CO_2$ results suggest that the HBr C_6 dispersion coefficient is too small, we will investigate HBr bound to N_2,[44] CO,[45] and N_2O.[46] If these surfaces confirm the need for a larger HBr C_6, the ability of these calculations to generate new molecular properties will be confirmed. We will also look at HCN containing complexes, with interest in effects associated with its large electric dipole moment. The HF–HCN species[47] will be particularly interesting since it exhibits a strong hydrogen bond.

Our first PES calculation involving a nonlinear molecule will contain that most important of small, nonlinear species--water. Following the pioneering work on hydrogen fluoride dimer,[26] water dimer was the second weakly bound complex ever studied[48]. An accurate representation of its linear hydrogen bond is essential for the success of this approach to intermolecular potential functions. Following water dimer, a large number of water complexes are available for calculations.[1] Water also exhibits strong hydrogen bonding in H_2O--HF[49] and H_2O--HCN.[50] Properties of H_2O complexed with $HCCH$,[51] C_2H_4,[52] and CH_4[53] will be investigated to better understand hydrophobic interactions. Water interactions with carbonyl and amino groups are particularly important to the solvation properties of amino acids. To this end, H_2O complexes with CO,[54] CO_2,[55] H_2CO,[56] NH_3,[57] and NH_2CHO[58] will be studied. Water–sulfur dioxide[59] will also be studied, for atmospheric rather than biological reasons. The photo-oxidation of SO_2 to SO_3, leading to an important constituent of acid rain, is poorly understood and could involve transitory cluster formation.

Potential functions for ammonia bound to a variety of molecules will be calculated to model amino group interactions. Besides H_2O, mentioned above, NH_3,[60] CO_2,[61] CO,[62] and methanol[63] will be paired with ammonia for PES calculations. Finally, benzene dimer[64] and C_6H_5OH[65] dimer will be examined. These last two surfaces will improve our understanding of aromatic ring interactions, base stacking, and intercalation. As indicated in the quoted references, the majority of complexes targeted in this section have already been studied. In most cases, there are also literature values for DMA charge distributions and long rang C_6 coefficients. In the few situations where some information required to calculate a PES is missing, we will work with experts in the appropriate area. In particular, we have established good working relationships with David Buckingham (Cambridge), Patrick Fowler (Exeter), and Bill Meath (Western Ontario).

Long Term Projects

While it would be inappropriate to guess at specific projects to be done well into the future, it is essential to keep in mind long term needs that PES models should address. This section will serve both as a justification for the potential function development work presented above, and as a target toward which all work of this kind can aim. One important goal will be to take the parameters from the PES's discussed in the Intermediate Term Project section, and make them available for input to large molecule potential function models. The challenge here is to learn the most effective way to incorporate repulsion, dispersion, induction, and distributed multipole electrostatic terms into potential functions suitable for macromolecules. In this way, parametric descriptions of potential function components for different chemical functional groups can be achieved. Given a suitable library of such functional group descriptions, the PES for any large molecular species would be built up from component parts.

One of the most important applications of intermolecular potential function models is in molecular mechanics and molecular dynamics calculations. In particular, these computational methods are now routinely applied to the refinement of structures for biological molecules. Both X-ray crystallographic and 2D NMR structure determinations rely heavily on comparing results from calculated structures with observed data. Many review articles and books have been devoted to discussions relating molecular mechanics and dynamics to biological problems. A few examples follow. A concise description of molecular dynamics applied to biological issues is given in a *Nature* Review Article.[66] A much more detailed view of the application of molecular dynamics to proteins makes up the entirety of volume 61 of *Advances in Chemical Physics*.[67] The 1991 *Annual Review of Physical Chemistry* contains a detailed discussion of high resolution protein structures obtained from multi-dimensional NMR experiments.[68] Intermolecular potential functions play a central role

in all of this work, and a variety of comments on the specific functional forms used in molecular dynamics programs will be given below.

Molecular mechanics and dynamics applications to biological systems are routinely carried out with one of a small number of computer programs. Three of the best known and most widely used are AMBER,[69] CHARMM,[70] and ECEPP.[71] These programs share many similarities, but differ substantially in the details of their parameterization and execution. These three packages show significant differences in the specific approaches used to realize bonded and nonbonded potentials. The ECEPP potential function is the least general, assuming both rigid bond lengths and bond angles. AMBER and CHARMM permit harmonic distortion of bond lengths and angles. The CHARMM potential function is more general than AMBER's; *e.g.*, CHARMM includes angular energy dependence in its hydrogen bond description while AMBER and ECEPP contain only radially dependent hydrogen bonds. CHARMM also permits relatively easy user modification of its potential function. Even where the three programs use similar functional forms for specific energy terms, different numerical values for parameters are used. It is difficult to separate the effects of different sets of parameters from the effects of different algebraic forms used in the various potential function expressions. The application of these programs also requires important user choices. For example, hydrogen atoms can be specifically included or merged into adjacent heavy atoms in an "extended atom" or "united atom" approach. Similarly, water molecules involved in solvation can be included or their effects can be described with a distance dependent dielectric constant. The many choices available make direct comparisons between different computational procedures difficult to evaluate.

It is universally recognized that the nonbonded portion of potential functions is the most difficult to derive.[69,70] This is precisely where the properties of weakly bound molecular complexes have their greatest impact, and all the potential function information presented in this proposal is specifically describing nonbonded interactions. The macromolecule programs use nonbonded potentials that include Lennard-Jones terms and simple Coulomb energies associated with charges assigned to various atoms. This formalism cannot adequately describe hydrogen bonding, and extra terms are included for specific atom pairs that are thought to be hydrogen bonded. These terms typically contain a separate R^{-12} repulsion and a new, short range R^{-10} attractive term. Each atom pair involved in a hydrogen bond must be identified before the simulation is begun, so there is no opportunity for the dynamics calculation to sample weak or unanticipated hydrogen bonds. The strong angular dependence of hydrogen bond energies is ignored in most calculations of this type. It is important to note that the potential function models used in all computer simulation packages are incapable of producing the equilibrium geometries of the majority of the bimolecular complexes that have been spectroscopically studied. Not only is it impossible for these programs to correctly predict a T shaped geometry for $(HCCH)_2$ and a parallel configuration for $(CO_2)_2$, but they will also dramatically miss the structure of water dimer. The simplicity of the assumed nonbonded and hydrogen bonded potentials means that water dimer would be predicted to have a cyclic, $_H{}^O{}_H{}^H{}_O{}^H$, geometry rather than exhibiting the well-known linear hydrogen bond.[48] (The importance of our model predicting the correct structure for $(HF)_2$, and the need to study water dimer cannot be overestimated.)

While the simplicity of the potential functions used to calculate structures of macromolecules are inappropriate for small systems, it has been tacitly assumed that errors will cancel in larger calculations. Not only is there no proof for this cancellation, there is some evidence that errors can actually reinforce one another. A mixture of constructive and destructive interference in potential function errors can introduce serious problems. For example, these calculations must sample many configurations that exhibit local energy

minima. The statistical weight that each conformation contributes to the overall dynamic structure of a protein can be profoundly affected by the propagation of errors in each minima. Unfortunately, there have been very few direct comparisons between the results produced by different computer programs, each using its own potential function. However, Scheraga and coworkers have recently compared the results of AMBER, CHARMM, and ECEPP on two different prototypical biological complexes.[72,73] This extremely thorough work, occupying 60 pages in the Journal of Biomolecular Structure and Dynamics, reaches numerous conclusions that support the tenets of this proposal.

In their study[72] of the tandemly repeated peptide $(Asn\text{-}Ala\text{-}Asn\text{-}Pro)_9$, Scheraga *et al.* first chose eight initial starting configurations with which to begin optimization. Each of the three dynamics packages was applied to each of the eight initial configurations, to find the optimum, lowest energy structure. The resulting conformations of the 36 residues in each of these 24 optimizations were then compared in a least squares sense. The main conclusions from this effort were: (1) "energy minimization starting from the same conformation, but using any two different potentials, could lead to final conformations whose resemblance to each other varied from acceptable to highly unsatisfactory"; (2) "the ordering of the final energy-minimized conformations, and the energy differences between them, were quite different for all three potentials"; and (3) comparisons between AMBER and CHARMM, CHARMM and ECEPP, and AMBER and ECEPP did not indicate better agreement between any of the packages. The final conclusion of this paper was; "It is concluded that energy minimization starting from a large enough sample of initial conformations might on occasion lead to essentially the same conformational prediction whichever potential is used; however, if the sample of starting points is small, predictions based on the three potentials will usually diverge."[72]

The second of this two paper series by Scheraga and coworkers used AMBER, CHARMM, and ECEPP to calculate ϕ-ψ maps for N-acetyl alanine N′-methyl amide. These results were then contrasted with experimental information available for this system. It was these comparisons that indicated reinforcement of computational errors. The dominant message from this paper is: "It is concluded that none of these potentials leads to predictions that are completely compatible with all experimental results."[73] This paper concludes with a section titled *Design of an Improved Potential.* The authors do not make any specific recommendations, but they do lay down several appropriate procedures to follow. For example, Scheraga quotes a review article by Price:[74] "If a model potential is found inadequate for a simulation study, it will often be more effective to alter the form of the model potential according to the charge distribution, than to tinker with the parameters within an inadequate functional form." Scheraga gives a brief, interesting history of how the various potentials in current use came into being. A quotation from this historical description sums up his opinion well; "The process of simplification that led to the mathematical form for the interatomic potential in CHARMM, AMBER, ECEPP, and other potentials used in theoretical studies of peptides was justifiable 20 years ago, but with the advent of modern high speed computers it is no longer necessary or desirable to sacrifice accuracy for the sake of computational expedience. . . . We suggest that the time has come to reformulate the potential energy to be used in the simulations of peptides and proteins. In reaching a new formulation, simplification of the potential for the sake of computational speed alone should be avoided."[73] He goes on to say that "atom-atom potentials involving distributed multipoles invariably leads to a better fit to experiment".

In judging the validity of these remarks by Scheraga, it is worth noting that he has not been particularly self serving. One of the three computer programs and potential functions being criticized, ECEPP, comes directly from Scheraga's own laboratory.[71]

CONCLUSIONS

The potential function model outlined in this proposal is currently capable of giving quantitative descriptions of small molecular complexes containing linear molecules. Straightforward developments will extend this work to cluster molecules made up of nonlinear molecules. Additional refinements, such as the inclusion of induction terms, will make the model more accurate. This enhanced version of the program will be applied to a variety of bimolecular complexes containing water and ammonia, to achieve better understanding of biologically significant interactions. In addition, water–hydrocarbon and aromatic–aromatic interactions will be calculated to investigate hydrophobic and stacking interactions. The potential surfaces resulting from these calculations will define the effectiveness of the specific combination of repulsion, dispersion, induction, and distributed multipole electrostatic terms we have used to construct our model. The final step in moving this approach to large molecules will investigate the transferability of the small molecule parameters to large systems.

The need for better potential functions in simulation programs used to model biological systems is clearly established.[73] Fortunately, continuing growth of computer power means more complete functions can be built into the standard simulation programs. We still do not know the most effective form for these new potential functions, and a broad range of research is needed to insure that intelligent choices are made. Work outlined in this proposal addresses many of the questions that must be answered in order to advance the computational aspects of molecular biology. I strongly believe that the Radiological and Chemical Physics research program has to support this kind of effort to fulfill its role of supplying basic understanding at the interface between chemical physics and biology.

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