Perq interactive molecular modelling system

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A molecular modelling system for a single-user workstation operating under a Unix-type operating system (the ICL-Perq) is described. The system is capable of rotating and translating one or two molecules separately or together in real-time in 3D. Structures may be modified or superimposed and dot-surfaces calculated and plotted. Fragments may be rotated around selected bonds and molecular mechanics calculations performed. The system is menu-driven, and is designed so that the experimental chemist, with little or no computing knowledge, finds it easy to use.

Keywords: molecular modelling system, Unix operating system, molecules, rotation, translation, superimposition, real time

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Many workers see a major avenue in molecular graphics being the use of single user workstations in a Unix environment[1]. Such a system, the Perq interactive molecular modelling system (Pimms) written for the Perq workstation with the PNX operating system is described here. The program is available at nominal cost.†

Pimms is capable of rotating and translating one or two molecules separately or together, in real-time in 3D, and has facilities for:

- the calculation and editing of geometry;
- structure modification;
- the superimposition of two molecular structures;
- molecular mechanics calculations;
- the generation of dot surfaces and calculation of surface areas; and
- the rotation of selected molecular fragments around specified bonds.

Pimms is menu-driven with no complicated command strings to learn or remember; commands and their parameters are entered by pointing at the required command in a self-explanatory command-menu using a cursor controlled by a mouse moving on a bit-pad.

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PROGRAM PIMMS

The basic information required by any molecular display program is a list of atomic coordinates, and a definition of atom type for each atom in the list. After reading the structure input data, Pimms determines the atom–atom connectivity by a simple distance search algorithm using a table of standard bond lengths, which specifies the maximum bonded length between any two atoms. The input data is then scaled to screen coordinates, the initial command-menu is set up, and Pimms displays the input structure as a simple stick diagram.

Having displayed the initial structure, Pimms waits for the puck-button to be depressed, reads the cursor position in screen coordinates, and determines which menu option has been selected by searching a list of coordinates which mark the extremities of each command area. Pimms then calls the appropriate routine: the structure is redrawn if necessary, and the program then awaits the subsequent button press.

Pimms currently consists of 11 500 lines of FORTRAN and C source code.

PIMMS ENVIRONMENT

Pimms runs within the Window Management System[2] (WMS) of PNX. The Window Manager provides an ideal environment for running Pimms: not only is it an excellent interface to the graphics facilities of the Perq, but it allows the user to create new windows and hence new processes without exiting Pimms, and thus to use other programs, such as the PNX text-editor, Spy, during a Pimms session.

Pimms uses four windows within WMS: the control window from which Pimms is initiated, the command-menu window, the display window, and the file-input window. The latter usually lies out of view behind the three main windows. Pimms makes use of one puck-button only for all command input. In contrast, Spy, which also works under a menu-driven interface, uses all four puck-buttons: the role of each button changes according to the command being executed within Spy. Pimms uses one puck-button only in order to avoid any confusion with buttons having different roles for different Pimms commands. Each Pimms window may be moved around the screen, changed in size, or relegated to a position behind any other window.

FILE-INPUT

File-input to Pimms is menu-driven. The user does not need to remember a file-name, or where the file resides

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in the file system. Pimms permits file input from six different input directories, all subdirectories of the main directory, and imposes a limit of 70 files in each directory. When a new file is created in one of the input directories, the user must update the file containing the directory listing by typing 'update'.

At the start of a Pimms session the file-input window is created at the top right of the display; this window initially contains only the names of the six input directories, but once a directory name has been selected, a listing of input files from that directory will appear ready for selection.

FILE-TYPES

Pimms recognises several different file-types, and determines the structure and format of the input file from the extension to the file-name.

Valid extensions are:

.coo Orthogonal coordinate data file

Title				(A35)
At.no.	X	Y	Z	(I2,2X,3(F9.5,2X))

.qoo Orthogonal coordinate data file plus atomic charges

Title				(A35)
At.no.	X	Y	Z	(I2,2X,4(F9.5,2X))

.cip Fractional coordinate data file
This contains cell parameters and coordinates with respect to the unit cell, as obtained from the Crystal Structure Search Retrieval (CSSR) component of the Chemical Databank System[3]

Title				(A35)
A	B	C		(3(2X,F9.5))
Alpha	Beta	Gamma		(3(2X,F9.5))
Natoms				(I3)
At.no.	X	Y	Z	(I2,2X,3(F9.5,2X))

.pdb Protein Data Bank file
This is a modified format file from the Brookhaven Protein Databank[4]

Title						(A35)
At.no.	Resname	Resno	X	Y	Z	(I2,3X,A3,2X, I4,4X,3F8.3)

.zmt Z matrix file — Free Format
In this file atom positions are defined with reference to bond lengths, bond angles and torsion angles.

Any necessary calculations on the input data are now performed, i.e. generating coordinates from a Z matrix, or calculating orthogonal coordinates from fractional coordinates.

INITIAL MENU SETUP

After a structure has been input Pimms opens the display and menu windows; the initial command-menu is output and the structure drawn in the display window.

As there are many commands to be displayed, Pimms uses a side-menu system with three levels of command-menus. (See Figures 1–3.) The highlighted number next to the 'MENU ACTIVE' label shows the menu that is currently active. The user may activate any menu by selecting the relevant number.

The switching between menu levels illustrates an important feature of Pimms, that the label to the current command is always highlighted. In addition to the side-menu system, many commands have further submenus: these appear only in the display window.

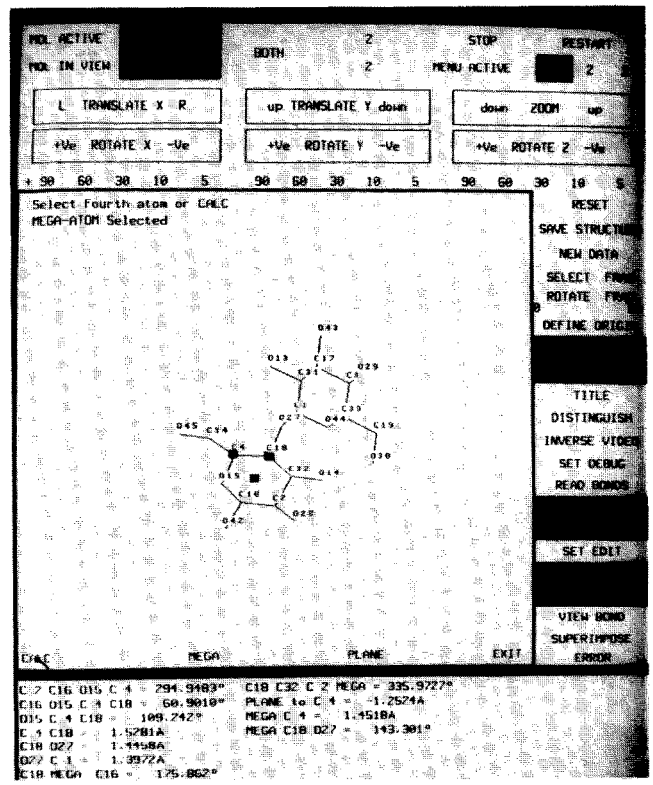

Figure 1. Initial menu setup of Pimms. A plane and a mega-atom have been defined, and the 'GEOMETRY CALCULATION' facility is now in use. The results of the previous calculations are displayed in the lower Pimms window. The 'CALC' label is about to be selected in order to calculate the angle between atoms C4, C18 and the mega-atom in the cellobiose structure

TOP-MENU COMMANDS

The area above the display window contains commands to 'ROTATE' and 'TRANSLATE' the structure in the display window.

At the start of a Pimms session, the labels '1' to the right of 'MOL ACTIVE' and 'MOL IN VIEW' are highlighted, showing that the input structure is in view in the display window, and is active to any rotations or translations that may be performed. The input of a second molecule causes these highlights to switch to the 'BOTH' labels, showing that both molecules are in view and both are active. The user may switch off the activity or display of either structure. It is possible to have both molecules in view, but only one active. The highlights show the status of activity/display at all times.

The activity/display flags are of particular importance to the 'ROTATE' and 'TRANSLATE' commands. On selection, the command label is highlighted, and movement of the structure begins. When one molecule is active, rotations and zooms (Z-translation) use the centre of gravity of the molecule as the origin of rotation. With two molecules active, rotations and zooms use the screen centre as the origin.

The 'ROTATE' and 'TRANSLATE' commands are different from other Pimms commands in that once the command is selected there is no need to hold down the puck-button in order to maintain motion. The speed of rotation or translation depends upon the cursor position in the highlighted area: rotation is slow at the centre of the box but increases in speed as the cursor is moved

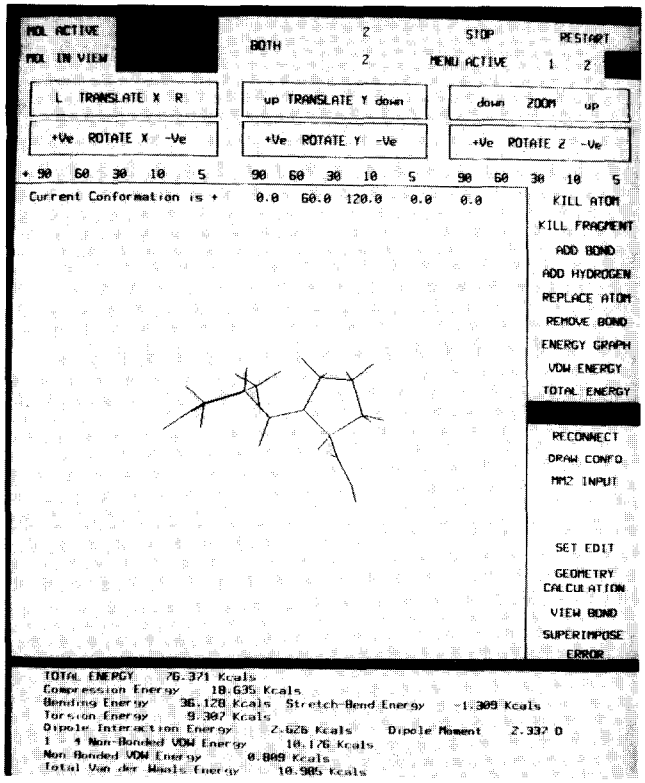

Figure 2. Pimms display during an energy 'SCAN' of captopril, performed around the three bonds drawn in double-strike mode, in 30° increments. The conformation displayed is specified by the summed rotation increments for each bond; in this case a Total Energy Scan has been requested. Pimms displays the total energy, summed from the separate MM2 terms, for each conformation

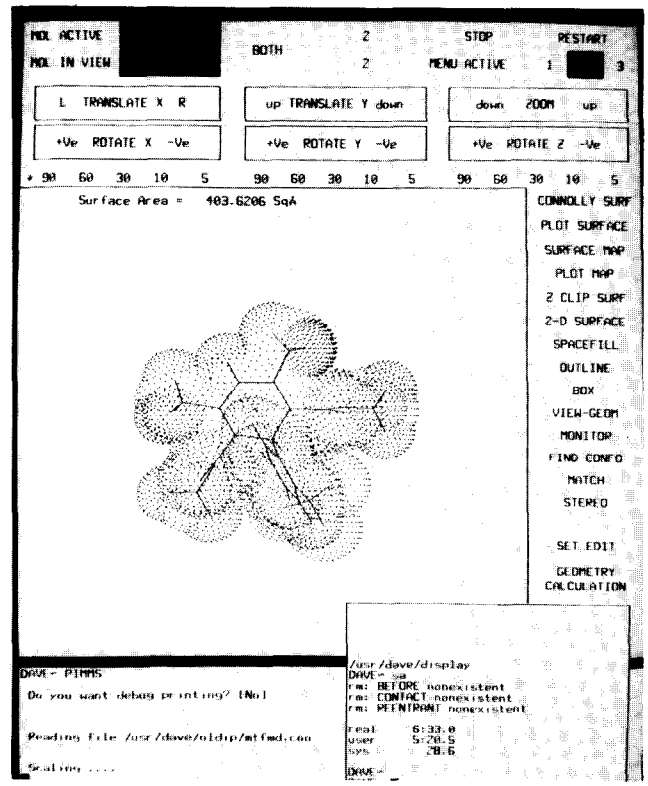

Figure 3. Connolly program input file 'consurin' has been created, and the user has opened a new window and run the Connolly program with the 'sa' command. The dot surface displayed using the 'PLOT SURFACE' command is shown

to the right or the left. Rotation and translation both change direction as the cursor passes through the centre of the box. Removing the cursor from the highlighted area stops motion, and the highlight disappears.

Selecting one of the '90', '60', '30', '10', or '5' commands rotates the molecule by the specified angle in degrees, around the axis denoted by the position of the command label. The direction of rotation may be toggled between '+' (clockwise) and '−' by selection of the current sign.

Selecting 'STOP' terminates Pimms and erases all windows, except the control window.

FORMS OF DISPLAY

The stick model is the default display-type, but Pimms allows other forms of structure display; some of these simply represent the molecule once in the new form, returning to a stick display at the start of the subsequent operation. Other command labels work to switch on or off a particular type of display, as follows:

- Selecting the 'INVERSE VIDEO' command inverts the current display colour. The label is highlighted if the display is black.
- The 'LABELS' command turns on atom labelling and numbering for the active molecule(s). The labelling routine uses a special character font, which can display the symbol of a chlorine atom as one character for example. The atom numbering depends upon the position of the atom in the input file and may change if the structure is modified. The command label should be reselected to turn off labelling.
- The 'NO HYDROGENS' command is used to remove temporarily all hydrogen atoms, bonds to hydrogen atoms and hydrogen atom labels from view, thus simplifying the display. No hydrogen atoms are present when the label is highlighted. Pimms adds back the hydrogen atoms in the correct position when this command is reselected.
- The 'BOX' command switches on a simple depth perception system. A box is drawn over each atom: the box size depends on the Z coordinate of the atom, while the 'heaviness' is determined by atom type.
- Selecting the 'SUPERIMPOSE' command prevents display window clearing between each structure drawing operation. This is useful when visualizing different conformations of the same molecule, especially when a selected bond is undergoing rotation. Reselecting the command reinitiates display window clearing.

Other forms of display include:

- In order to discriminate between two displayed structures, the 'DISTINGUISH' command draws the active molecule in double-strike mode. If both molecules are active, molecule 1 is drawn in this mode.
- The 'STEREO' command displays a stereo view of the active structure by generating a side-by-side view, and rotating the right-hand image by 6° around the vertical axis.

The following forms of display make use of the default van der Waals radii in the data file 'bonds.dat'.

- 'SPACEFILL' draws the active molecule in spacefill form. If the 'SET EDIT' label is highlighted, the atoms are shaded according to type.
- Selecting 'OUTLINE' generates a van der Waals outline around the active molecule(s).
- Selecting '2-D SURFACE' produces a 2D shadow of the active molecule's surface. The shading lines for molecule 1 are drawn perpendicularly to those for molecule 2, so surface overlaps are easily visible.

UTILITY COMMANDS

General purpose commands not concerned with energy calculation, structure modification and surface generation include:

1) *SET DEBUG.* When the DEBUG flag is set, and the label highlighted, Pimms writes the atomic coordinates after each rotation/translation operation, and the MM2 atom types before an energy calculation, to the control window. Reselecting 'SET DEBUG' switches off DEBUG printing.

2) *RESET.* This command resets the active molecule(s) to the position(s) and scale at the start of the Pimms session. The initial connectivity is regenerated, and the effects of any structure modifications are removed.

3) *RESTART.* Pimms clears the display window, and prompts for the selection of a new input file from the file-input window, which Pimms pops to the foreground of the display. This is a quick alternative to stopping and restarting Pimms.

4) *NEW DATA.* This command is used to input a new structure into Pimms. If two molecules are already present, Pimms prompts the user to select the molecule to be overwritten, from a submenu in the display window, before popping the file-input window to the foreground.

5) *SAVE STRUCTURE.* The user may write the current coordinate(s) or *Z* matrice(s) of the active molecule(s) to a disc file. Output file format is identical to Pimms input file format. When the command is selected, a submenu appears in the display window. The selection of 'COORDS' or '*Z* MATRIX' writes the file 'coords1' or 'zmatrix1'. Subsequent uses of 'SAVE STRUCTURE' writes the file 'coords2' or 'zmatrix2', and so on. Selecting 'QUIT' returns control to the main menu.

6) *READ BONDS.* This command reinputs the data file 'bonds.dat', and rereads the input directory file listing. For instance, if the user wishes to alter the van der Waals (VDW) radius of a particular atom type, then a new window must be created, and 'bonds.dat' modified before the command is selected; 'bonds.dat' contains the following parameters, together with comment lines explaining the meaning of each parameter:

- Bond length table used in connectivity calculation
- VDW radii
- scale factor for VDW radii
- probe sphere radii for surface generation
- surface point densities for surface generation
- angle increments for bond rotation in 'SCAN' and 'FIND CONFO'
- number of steps in bond rotation
- shading values for 'BOX' display
- shading values for 'SPACEFILL' display

7) *TITLE.* This simple utility outputs the title of the active molecule(s) at the top of the display window.

8) *DEFINE ORIGIN.* Pimms prompts the user to choose one atom in the displayed structure to act as the origin for all subsequent rotations. If an origin is not required, selecting the 'EXIT' command in the display window returns control to the main menu. The command label is highlighted if an atom is acting as an origin of rotation.

9) *VIEW BOND.* Pimms prompts the user to select two atoms from the structure in the display; the molecule is rotated around atom 1 generating a view with the atom 1–atom 2 'bond' lying along the *Z*-axis; the atoms need not be bonded.

10) *DEF MEGA-ATOM.* This facility allows the user to specify a dummy atom, for use in geometry calculations, which may be the middle of a bond, or the centre of a ring, as designated by the mean coordinates of all chosen atoms. Pimms prompts the user to choose the atoms: selecting 'EXIT' returns control to the main menu. If atoms have been selected then a mega-atom is defined and the command label is highlighted. Subsequent uses of 'DEF MEGA-ATOM' either define a new mega-atom, or clear the definition if the user selects 'EXIT' when prompted to select the first atom.

11) *DEF PLANE.* The user is prompted to select three atoms to define a plane; if 'EXIT' is specified before three atoms are selected, no plane is defined. The command label is highlighted if a plane is defined.

12) *GEOMETRY CALCULATION.* This is a utility which allows the user to calculate and modify interatomic distances, angles and torsion angles. Pimms prompts the user to select an atom, and presents a submenu of commands. This menu consists of the commands 'CALC' and 'EXIT'; in addition the command labels 'MEGA' and 'PLANE' are present if a mega-atom and a plane are defined. The calculation performed depends on the number of atoms specified before 'CALC' is selected. Each selected atom is highlighted and labelled, and the user may 'EXIT' to the main menu at any stage, in which case the main-menu highlight is switched off. The choice of 'CALC' after the selection of one atom outputs the current coordinates of this atom: if two, three, or four atoms are selected, then the subsequent selection of 'CALC' calculates the interatomic distance, angle and torsion angle respectively. Output is directed to the display window, and in addition, the results of all calculations are tabulated in the control window. After each calculation, Pimms prompts the user to select the next atom or command: the choice of 'CALC' with no atoms selected results in the 'ERROR' box flashing in the main menu. Pimms presents the user with comprehensive error messages if, for instance, the same atom is selected twice in succession. The mega-atom may be used as any normal atom in the above geometry calculations. Pimms also permits the user to calculate plane–atom distances if a plane is defined.

If the 'SET EDIT' label is highlighted, the user may enter a new value for each bond length, angle or torsion angle specified for calculation. The structure remains unmodified if a value of 0 is entered in response to the prompt, or if the connectivity of the selected atoms is inconsistent with geometry modification, e.g. Pimms does not allow the user to edit a distance if the atoms are not bonded. Pimms allows the user to modify bond lengths, angles and torsion angles in chain and ring structures. If a bond length in a ring is specified for modification, the second atom selected is moved along the

vector specified by the bond: all other ring atoms remain stationary. The user is informed if a ring parameter is chosen for modification.

13) *SELECT FRAG.* This command is used to select one moiety of a structure for rotation around a specified bond. Pimms prompts the user to select two atoms, the first at the stationary end, and the other at the rotating end of the bond. The user is informed if the selected atoms are not bonded, or if the fragment contains no atoms. The bond specifying the selected fragment is drawn in double-strike mode. The user may select to 'EXIT' to the main menu if no fragment is required. If a fragment is selected for rotation, the command label is highlighted.

14) *ROTATE FRAG.* This is used to rotate a fragment around the bond selected in 'SELECT FRAG': the rotating bond is drawn in double-strike mode. The total angle of rotation is output to the control window. The angle of each rotation depends upon the cursor position in the 'ROTATE FRAG' command label, the angle increasing from 0° to 60° from left to right. This facility may be used in conjunction with 'SUPERIMPOSE'.

15) *VIEW-GEOM/MONITOR.* VIEW-GEOM is used to specify a set of atomic distances, angles and torsion angles to be monitored during bond rotation with 'ROTATE FRAG'.

The user is prompted to select up to five sets of two, three and four atoms specifying distances, angles and torsion angle parameters respectively. If, for instance, three distances have been chosen the user may go on to select atom 1 of the first angle parameter by selecting 'ANG' in the display window. The selection of 'TOR' prompts the user to select torsion parameters; the user may then go on to choose to monitor the van der Waals energy during bond rotation by selecting 'YES' in the submenu. Control then returns to the main menu.

'MONITOR' is a simple switch: while highlighted, the selected parameters are monitored during bond rotation.

16) *FIND CONFO.* This enables the user to scan around up to five bonds, searching for conformations with distance and torsion angle parameters within user-specified limits.

The user is prompted to select, from a choice of three in a submenu, the angle increment for rotation about all bonds: these default values are set in 'bonds.dat'. The user is then prompted to select the first of the bonds around which to scan. An 'EXIT' at this stage returns control to the main menu, while an 'EXIT' after bond selection cyclically prompts the user to select sets of two atoms specifying a distance to be checked, and the maximum and minimum search limits for this distance. Selecting 'TOR' prompts the user to select the first set of four atoms specifying a torsion parameter, followed by maximum and minimum search limits for this parameter. Up to ten distance and ten torsion parameters may be chosen. The selection of 'FIND' after torsion parameter selection commences the search.

Each conformation is drawn and the rotation angles specifying the conformation are output to the display window. Pimms informs the user if the parameter limits are satisfied for a particular conformation: this output is also directed to the file 'Findconfo'. There is also a running count of the number of conformations which satisfy all parameter limits; the bond rotation angles, and the values of all parameters for such a conformation are written to the file 'Satisfied'.

Control is returned to the main menu at the end of the search; the user may examine a 'Satisfied' file and draw any conformation using the 'DRAW CONFO' command.

17) *DRAW CONFO.* If the user has set up a number of bonds around which Pimms has scanned in searching for a conformation using 'Find confo', this facility may be used to view a particular conformation, as specified by angles of rotation about the designated bonds from the starting conformation.

'DRAW CONFO' expects as input a number of angle values determined by the number of selected bonds. After one conformation has been drawn, the user is prompted to enter angle values specifying another conformation. On exiting this facility, the displayed structure is the last conformation drawn.

18) *MATCH.* Two molecular structures may be matched; the user is prompted to select the atoms to be matched alternately from each molecule. The match is performed by selecting the 'FIT' submenu command. This command is replaced by 'EXIT' when the number of selected atoms in the first molecule differs from the number in the second; the selection of 'EXIT' returns control to the main menu.

The fitting procedure positions the molecule from which the first atom was selected onto the second molecule; the r.m.s. deviation for the fit of the selected atoms is output. This value is defined as the root of the mean of the squares of the distances of the fitted atoms in molecule 2, from those to which they are fitted in molecule 1. For a perfect fit, this value is zero.

Pimms makes use of the procedure of Mackay[5], in which quaternions are used to represent the rotation needed to overlay the two structures. A quaternion is a set of four numbers representing a rotation in space. It is an alternative to the rotation matrix, carrying the same information in a form which is easier to handle.

The positional relationship between two structures is a combination of a rotation and a translation, although the translation may be excluded by referring both structures to their centres of gravity. In order to match the structures, it is necessary to find a rotation taking one structure to the other.

Given two unit vectors $\mathbf{r}$ and $\mathbf{r}'$, the rotation relating one to the other may be described by drawing an axis of rotation about which $\mathbf{r}$ may be rotated to $\mathbf{r}'$. This rotation may be represented by a quaternion, consisting of l, m, and n, the direction cosines which specify the orientation of the axis of rotation, and θ, the angle about which $\mathbf{r}'$ must be rotated to $\mathbf{r}$. Using quaternion algebra, it is possible to obtain the direction cosines and θ, from any pair of unit vectors. The matching procedure calculates the unit vector of each matched atom to the centre of gravity of its structure, and then finds the quaternion defining the rotation of each unit vector to the corresponding unit vector in the structure to be matched. Since the rotations for each pair of matched vectors may be different, a least squares approximation is used to find the best rotation to match the structures.

Pimms uses a FORTRAN translation of the BASIC program of Mackay. In the original version, the lengths of the vectors, before they are normalized to unit length to obtain the quaternion, are retained as weights for

the least squares procedure. Pimms uses a weighting scheme in which each atom is fitted with equal weight. The original version of the program could only handle structures containing equal numbers of atoms: Pimms permits the user to fit two structures, matching selected atoms. The atoms not selected for matching are not used in the calculation of the quaternion for each pair of unit vectors, or in the least squares procedure, but are rotated with the selected atoms when the structures are matched.

STRUCTURE MODIFICATION

These commands constitute a system which allows the user to modify molecular structures interactively.
1) *SET EDIT.* When selected and highlighted the 'EDIT' flag is set. It has several functions:

- When performing a 'GEOMETRY CALCULATION' the user is prompted to enter a new value for the calculated geometrical parameter.
- When using 'REPLACE ATOM' to alter atom type, all bonds to the replaced atom are set to a default length equivalent to 85% of the maximum bonded length specified in the data file 'bonds.dat'.

2) *KILL ATOM.* This facility removes selected atoms from a structure. The user is continually prompted to choose an atom for deletion, until an 'EXIT' returns control to the main menu. Atom numbering may be altered using this facility.
3) *KILL FRAGMENT.* This is used to remove all atoms in a selected fragment from the displayed structure. As in 'SELECT FRAG', the user is prompted to select two atoms to define the fragment. The fragment defined by this bond is then removed and control returned to the main menu.
4) *REMOVE BOND.* Pimms prompts the user to select two atoms which specify the bond to be removed, and informs the user if the bond does not exist. This facility may be used, for instance, to open up a ring.
5) *ADD BOND.* This facility adds a bond between two selected atoms. The user is informed if either atom has insufficient connectivities to form a new bond, if the atoms are already bonded, or if the atoms are not within bonding distance. The maximum limit for bonding is equal to the value for that bond in the bond length table in 'bonds.dat'.
6) *ADD HYDROGEN.* This feature is the basis of the molecular construction system in Pimms. The user may add different hydrogen atom types to a skeletal structure. If the 'NO HYDROGENS' switch is set a warning message is output.

Pimms initially prompts the user to select the hydrogen atom type to add from the sub menu, and highlights the selected type. The user is then prompted to select atoms to which the hydrogen atom(s) of the chosen type are to be added. The reselection of the sub menu highlights the new label, and resets the hydrogen atom type. The user may 'EXIT' to the main menu at any stage. Pimms informs the user if an impossible operation is attempted, e.g. the addition of one hydrogen atom to another; if the connectivity conditions are fulfilled the new structure is displayed.
7) *REPLACE ATOM.* The user is initially prompted to select the new atom type from the sub menu. The selected atom type is highlighted and any selected atoms assume this type unless a new atom type is specified. Pimms checks that the new atom type for a selected atom is consistent with the current connectivity, e.g. it does not permit a hydrogen atom to replace a tetrahedral carbon atom. The user may 'EXIT' to the main-menu at any stage. If the 'SET EDIT' label is highlighted, all bond lengths to the replaced atom are set to 85% of the bond length in the 'bonds.dat' table.

This facility is most often used in conjunction with the 'ADD HYDROGEN' command, e.g. to replace an added hydrogen atom with a carbon atom in order to commence the construction of a new fragment.
8) *RECONNECT.* If 'ADD BOND' or 'REMOVE BOND' have been used, this command regenerates the original connectivity for each active molecule. It differs from 'RESET' in retaining newly added atoms, and in not resetting the scale factor.

ENERGY CALCULATIONS

Pimms enables the user to calculate the steric energy of a structure using the MM2 molecular mechanics procedure[6]. The user may calculate the energy of a single conformation, rotate about selected bonds calculating the energy for each conformation, and optimize the geometry of the displayed structure. In each case, the user is not required to generate the complicated MM2 input, so it is possible to reap the full benefits of MM2 calculations with minimal effort.

Pimms starts by calculating the MM2 atom type for each atom. Pimms differentiates between sp^2 and sp^3 carbons on the basis of connectivity, i.e. it makes the assumption that an sp^2 carbon is connected to only three. Pimms also differentiates between type 6 (alcohol and ether), and type 7 (carbonyl) oxygens on the basis of connectivity; and between type 21 (alcohol) and type 24 (carboxyl) hydrogens by determining the connectivity of the carbon atom to which the hydroxyl group is bound. The MM2 procedure of treating carbonyl oxygens as spheres, as far as van der Waals calculations are concerned, is not satisfactory for alcohols and ethers. Pimms adds two lone-pairs (MM2 atom type 20) to type 6 oxygen atoms, at the two unoccupied corners of a tetrahedron, at 1.0 Å from the oxygen atom. Pimms also adds one lone-pair to amine type nitrogens, as required by MM2; Pimms differentiates between amine and amide nitrogen atoms, as amide nitrogens along with sulphur, halogens and nitriles are parameterized not to use lone-pairs. The user is informed if, and where, lone-pairs are added.

Pimms then generates a list of attached atoms (those atoms connected to only one other atom) according to the MM2 formalism, and calculates lists of connected atoms, i.e. those connected to two or more other atoms, purely by connectivity. This procedure is only used if Pimms is generating an MM2 input file in order that a structure may be optimized: if a single-point calculation is requested from the main menu, Pimms bypasses these calculations, and passes its connectivity lists, and the calculated MM2 atom types, directly to the MM2 routines internal to Pimms. These routines calculate whether any two atoms are bonded, or 1,3−, 1,4− or 1,5−nonbonded; compute the number of bond angles and torsional angles in the structure; and assign con-

stants to each bond, bond angle and torsional angle, prior to calculating the energy.

In this way, Pimms creates a standard MM2 input file in order to run structure optimization calculations, but allows the user to calculate the steric energy of a structure without calculating the MM2 attached and connected atom lists, and without generating an MM2 input file.

Other front-end programs to MM2 have been described[12,13]. These offer similar functionality to the energy calculation moiety of Pimms, but they run on micros and require MM2 input data to be transferred to a mainframe in order to run MM2. Pimms takes full advantage of the computational and graphics capabilities of a workstation: input-file generation, computation and graphical display all take place on the same computer. This is a boon to usability.

The force-field internal to MM2 is quite often insufficient: it may be either incomplete, or may need to be modified. During the data set up, Pimms reads in extra parameters from three files which are provided. These are echoed as input. The user is notified if extra parameters are required; additional parameters may be entered into the above files from more complete lists in master files.

1) *MM2 INPUT*. This allows the user to create a standard MM2 input file in a menu-driven manner, in order to optimize the geometry of the displayed structure. Pimms generates an MM2 input file, and then prompts the user to open a new window using WMS and run the stand alone MM2 program. This gives the user flexibility when running MM2: the user may wish to run MM2 during a Pimms session, or create a batch of input files to run overnight. MM2 prompts the user for a filename to which to write the coordinates of the optimized structure in Pimms format.

When the command is selected, Pimms calculates atom types, attached and connected atom lists, and adds lone-pairs if and where necessary. The user is then prompted to select keywords from a list of submenus, which specify the amount of printout, options for charge–dipole interaction calculations, and whether the heat of formation is to be calculated. Pimms then prompts the user to select any atoms whose motion is to be restricted during the optimization; the user is prompted to select the restricted atom, and then to specify whether or not this atom is to have motion in the x, y, or z planes. When the user selects 'EXIT' Pimms writes the input file 'mm2in'.

This input file generation does not handle any replaced atom functions, as Pimms allows the user to modify a structure interactively, or symmetry functions which are standard to MM2. This level of sophistication permits the novice user to optimize the geometry of a structure with little effort, but also provides the basis of an input file which the more expert user may wish to modify.

2) *TOTAL ENERGY*. This command calculates van der Waals, stretch–bend, bend, torsion and compression energies for one conformation of the active molecule. Charge interaction energy is calculated if atomic charges have been read in, otherwise dipole interaction energy is calculated, and a dipole moment is determined.

3) *VDW ENERGY*. This performs a single-point van der Waals energy calculation on the displayed structure. In addition, it is possible to monitor van der Waals energy during bond rotation using 'VIEW-GEOM'/'MONITOR' and 'ROTATE FRAG'.

4) *SCAN*. The user may scan around up to five selected bonds calculating either the van der Waals, or total steric energy for each conformation; the result of each energy calculation is output to the control window, and to the file 'SCAN'.

The user is prompted to select the type of scan, either 'TOTAL' or 'VDW', or to 'QUIT', from a submenu, and is then prompted to enter a value specifying a maximum energy limit for output to the 'SCAN' file. Conformations of high energy may thus be excluded from the output.

As in 'FIND CONFO', the user is prompted to select an angle increment for rotation around each bond, and is then prompted to select the bonds around which to scan. After the selection of the final bond, the selection of the 'SCAN' command commences the scan.

Each rotating bond is drawn in double-strike mode. An energy value is output for each conformation. The output to the 'SCAN' file consists of an angle value for each bond, thus specifying the conformation using the starting conformation as the origin, and an energy for each conformation. It is possible to view any of the scanned conformations using 'DRAW CONFO'.

5) *ENERGY GRAPH*. If a 'SCAN' has been performed, it is possible to plot a graph of energy against angle, for the first scanned bond only. No additional user input is required.

SURFACES AND SURFACE MAPPING

The 'SPACEFILL' and 'OUTLINE' displays in Pimms are very simple ways of representing the surface of a molecule. There are many more sophisticated algorithms available[7,8]. In keeping with the use of standard methods, Pimms makes use of the program developed by Connolly,[9–11] which is probably the most widely applied. Pimms allows the user to display dot surfaces, calculate surface areas, and to generate union surfaces for two structures. Exclusion surfaces, i.e. those portions of the surface of one molecule external to the surface of another may also be displayed.

1) *CONNOLLY SURF*. Pimms creates a Connolly program input file, 'consurin', prompting the user to select values for input parameters to the program. The surface is generated for the active molecule; if two molecules are active a union surface is calculated, in which case the two separate structures are treated as one.

The user is prompted to specify whether the surface is to be generated for the whole structure or a molecular fragment. The selection of 'QUIT' exits the file generation, returning control to the main menu, while the selection of 'YES' prompts the user to choose two atoms to define a fragment; in this case the surface generated is for the atoms in this fragment only.

Pimms now prompts the user to choose values for 'Probe Sphere Radius' and 'Surface Point Density' from the submenu; these are standard input parameters to Connolly's program. The default values for these parameters are set in the file 'bonds.dat' and may be altered using the 'READ BONDS' command.

If a probe sphere radius of 0.0 is selected, a simple van der Waals surface is generated, otherwise a solvent

accessible surface is calculated. The greater the value for the surface point density, the longer the surface calculation takes; more accurate values for the surface area are obtained if higher surface point densities are used.

The user is then prompted to select any atoms which are to be excluded from the surface calculation; the selection of 'NONE' bypasses this option. Pimms now writes the input file, and saves the coordinates of the molecule(s) in the file 'surf.coo'. To run the surface generation program a new window must be created, and 'sa' typed.

2) *PLOT SURFACE.* This facility plots the surface generated with 'CONNOLLY SURF'. The active molecule(s) are redrawn from the coordinates in 'surf.coo', and Pimms opens the file 'CONTACT', (and 'REENTRANT' if a solvent accessible surface has been generated). These files contain the coordinates of the surface points.

When the dot surface has been plotted, a value for the surface area is output, and control is returned to the main menu. Once plotted, the dot surface remains in view until the structure is redrawn. The dot surface itself appears more realistic if the display window is in 'INVERSE VIDEO'.

3) *Z CLIP SURF.* The user may set clip limits for surface plotting, so that regions of the dot surface at the front and rear of a molecule may be excluded from the display. The surface must be replotted in order to view the clipped surface.

When selected, a black ribbon appears at the right of the display window. This represents the current z range of the dot surface. The user is prompted to select maximum (furthest from the user), and minimum clip limits from within the black area: once both have been selected, the ribbon represents the z range within which surface dots are plotted. The top of the display window represents the area of the molecule furthest from the user. The selection of an area outside the black ribbon in response to a prompt bypasses the setting of that clip limit.

4) *SURFACE MAP.* Input files for the Connolly program are created for the two molecules currently being displayed; the surface map is formed by generating a normal van der Waals surface for each molecule, and then coding each surface point according to whether or not it lies within the surface of the other molecule. The user is prompted to select a value for 'Surface Point Density' as in 'CONNOLLY SURF'. In order to generate the surfaces for each molecule, it is necessary to create a new window and type 'samap' to run the Connolly program for each structure.

5) *PLOT MAP.* This utility plots surfaces and surface maps generated by 'SURFACE MAP' . Pimms codes the surface points and generates two files 'CSURF1' and 'CSURF2' which contain the coordinates of the surface points, together with a code defining the position of the surface point with respect to the surface of the other molecule. Pimms prompts the user to select the surface type required from a menu in the display window. The user may define a window which limits the plotting of surface points in the x-y plane, by selecting '1' from the menu when prompted, and then specifying the diagonal corners of this window. This facility may be used to plot the excluded surface of one molecule in a certain region of the structure only. The selection of any other number plots the requested surface map with no clip limits, and outputs a surface area value for the displayed surface. Pimms plots surface points as lines, three pixels in size, vertically for molecule 1 and horizontally for molecule 2.

CONCLUSIONS

Pimms is an integrated molecular modelling program, allowing the user to view and modify a molecule, calculate the energy and optimize the geometry of a structure, generate dot surfaces and calculate surface areas, and match two structures together. Pimms works almost entirely using a menu-driven interface; there are no complicated command strings to learn, and Pimms displays the status of the current command at all times by the use of command label highlights.

The Window Manager allows the user to leave Pimms temporarily and edit a file, for example. The benefits of having such a system in a dedicated package are demonstrated by the MM2 front-end programs that offer similar functionality to the energy calculation moiety of Pimms, but have MM2 running on a separate computer. The monochrome nature of the display is a drawback, although it is possible to provide the chemist with a set of display-types where colour is not an absolute requirement.

The system has been used by a wide range of chemists who have found the documentation sufficient to use the system without personal instruction.

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