Interactive computer graphics for bio-stereochemical modelling

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Abstract. Several computer graphics programs for bio-stereochemical modelling are discussed for display and manipulation of molecules. The RPMI system which is currently running on the Univac 70 computer, is easily adaptable to any computer, with or without sophisticated graphics hardware. Hence, we emphasize the avail-ability of an easy to handle and inexpensive means for building, manipulating, and displaying molecules. The RPMI system also includes an automated, noninteractive program for fast construction of specified molecular structures. The NASA system is running on an Evans and Sutherland display system which has sophisticated hardware and which is capable of continuously rotating the molecule with constant adjustment of perspective and intensity. Details are given for the important geometrical mani-pulations such as translations, rotations, and juxtapositions, and several procedures for building of molecules are described. A method is described for exploration of the fitting of peptides around DNA by means of isogeometric helices.

Several illustrations are presented for the applications of the programs to the study of interactions of proteins with DNA.

1. Introduction

The programs described in this paper were developed in our laboratories in connection with a study of the interaction of proteins with DNA and RNA. The feasibility of such a study has significantly increased with the recent progress in the general theoretical and experimental study of conformations of molecules in solution on one hand, and with the progress in the study of the interaction of polypeptides with poly-nucleotides on the other hand.

The existence of stereospecific complexes between nucleic acids and proteins is well established (Huberman 1973; Sobell 1973; Delange and Smith, 1972).

The theoretical approach to the question of steric complementarity and energetics of polynucleotide-polypeptide complexes may be based on the known stereochemistry of nucleic acids and proteins and on interaction energy calculations. Physical model building is a very valuable tool but this technique suffers from the excess amount of time required for construction of the models. The most versatile approach is through computational methods which allow rapid construction and transformation of mole-cules, as well as visual display of the model. A polynucleotide of a selected base

sequence and a peptide with selected amino-acid residues can be manipulated under visual observation into positions which would allow them to interact optimally, avoiding at the same time steric conflict between the two structures. This combined man-machine capability can eliminate an enormous amount of unnecessary calculations. Once the computer model building and visualization has established the stereochemically compatible configurations, the strength of the interactions can be calculated and energy minimization procedures may be applied. Thus the model building, displaying, and manipulating programs also provide stored coordinates which may be used as a starting point in energy calculations.

The number of currently existing programs is quite extensive, and we will outline only a few of the most widely known: ORTEP (Johnson 1970), CHEMGRAF (Levinthal 1966; Katz and Levinthal 1972), and CRYSNET (Collins and co-workers 1975). See Feldman (1976) for a review of these and other computerized molecular modelling systems. The CHEMGRAF and CRYSNET programs have graphics and display capabilities as well as a model-building feature and are particularly powerful in crystallographic applications. Recently, Barry and co-workers (1975) developed an interactive display system. Our programs resemble the latter program in their interactive display character. We have laid emphasis on easy building and manipulation of any molecular structure. Computer graphics has already been applied by Stellman (1974) in the solution of the chain deformation problem which had been treated mathematically by Gō and Scheraga (1970).

This study, which has involved the use of a variety of computers, is a collaborative project between the group at Roswell Park Memorial Institute (RPMI), Buffalo, New York, and NASA-Ames, California.

The system at NASA-Ames, is based on a sophisticated displaying and manipulating terminal, the Evans-Sutherland. A movie on its application is probably an impressive and lively demonstration of its power. However, most of the users may find more interest in the application of the RPMI system, which is easily adaptable to any computer with or without sophisticated graphics hardware. Hence, we emphasize the availability of an easy-to-handle and inexpensive means for building, displaying, and manipulating molecules. Some of our sub-routines might be found useful by readers in supplementing already existing building or displaying programs. Correspondingly, we will discuss the RPMI program in greater detail. In addition, we will outline a more efficient fitting of peptide around DNA by means of isogeometric helices.

2. Basic geometrical manipulations

The basic transformations are translations and rotations. Each atom is represented by a three-dimensional vector which contains its x, y, and z coordinates with respect to a given set of coordinates fixed in space. Let us denote a general vector by **F**. The operation of *Translation* by a vector **T** gives a transformed vector **G** given by

$$G = F + T. \qquad (1)$$

Assume that we have a fixed molecular fragment (a) and we want to move another molecular fragment (b) in such a way that a particular atom in (b), given by **F**, will

coincide with a particular atom in (a), given by **G**,   Hence, in the notation of eq. 1, the vector of translation **T** is given by

$$\mathbf{T} = \mathbf{G} - \mathbf{F} \tag{2}$$

and a general atom in (b), given by **R** will transform into **S**,

$$\mathbf{S} = \mathbf{R} + \mathbf{T} = \mathbf{R} + (\mathbf{G} - \mathbf{F}). \tag{3}$$

This is the initial step in the *Juxtaposition* operation, which will be explained later.
Rotations.

In a general rotation, we want a molecular fragment (b) to rotate about a given axis, which may be one of the bonds in (b) or in another fragment (a).   We will follow a treatment similar to that given by Goldstein (1959) where a positive angle specifies counter-clockwise rotation.   A rotation axis is defined by any given two points located on it.   According to this convention, a positive angle of rotation is defined by a clockwise rotation of the molecular fragment about the axis, when looking down the axis from the first to the second point.   Thus, the order in which these points are specified determines the sense of the rotation.   Let us first consider the case where the first point is the origin.   The matrix representation of an operator which transforms the position vectors of the atoms by rotating about a coordinate axis is known.   For example, a rotation of θ about the x axis will transform a vector **F** into

$$\mathbf{G} = A_x \mathbf{F} \tag{4}$$

where A_x is given by

$$A_x = \begin{pmatrix} 1 & 0 & 0 \\ 0 & \cos\theta & -\sin\theta \\ 0 & +\sin\theta & \cos\theta \end{pmatrix} \tag{5}$$

The matrices for rotations around the other axes are given by cyclic permutations of the indices.   Note that a clockwise rotation of a vector yields the same transformed coordinates as a counter-clockwise rotation of the coordinate axes.   Now let us assume that the compound is in a particular coordinate system, which will be denoted as the " body " system.   The two systems have the same origin.   A point which is specified by the vector **F** in the fixed system, will be specified by the vector **F′** in the body system.   These vectors are related by

$$\mathbf{F} = B\,\mathbf{F'} \tag{6}$$

where B is a matrix of transformation of the body system to the fixed one.   Assume that we want to rotate around a particular axis which will be arbitrarily denoted as the x axis of the body system.   In the body system, the vector **F′** will transform to **G′**.

$$\mathbf{G'} = A_x \mathbf{F'} \tag{7}$$

where the matrix A_x is given by eq. (5).   We want to obtain the matrix of transformation A such that

$$G = A \ F. \tag{8}$$

The matrix B will also give the relation between G' and G according to

$$G = BG' = BA_x F'. \tag{9}$$

By rearranging eq. (6) in the form

$$F' = B^{-1} F \tag{10}$$

we have from eqs (9) and (10) the final relation

$$G = BA_x B^{-1} F \tag{11}$$

or

$$A = BA_x B^{-1}. \tag{12}$$

The matrix A_x is given by eq. (5) and the matrix B is given by a matrix of the scalar products

$$B = \begin{pmatrix} (i \cdot i') & (i \cdot j') & (i \cdot k') \\ (j \cdot i') & \dots & \dots \\ (k \cdot i') & \dots & (k \cdot k') \end{pmatrix} \tag{13}$$

where i', j', k' are the unit vectors along the x, y and z axes of the body system.   For instance, in a rotation about a particular bond of length d, which is defined by the coordinates of the atoms C and D, the i' is given by

$$i' = \frac{1}{d} \begin{pmatrix} X_D - X_c \\ Y_D - Y_c \\ Z_D - Z_c \end{pmatrix} \tag{14}$$

The expression for the matrix B in eq. (13) follows directly from the fact that the same vector r can be given in the fixed coordinate system by

$X i + Y j + Z k$, and in the body system by $X' i' + \dots + z' k'$, where

$$\left. \begin{aligned} i' &= (i' \cdot i)i + (i' \cdot j)j + (i' \cdot k)k \\ &\vdots \\ k' &= (k' \cdot i)i + (k' \cdot j)j + (k' \cdot k)k \end{aligned} \right\} \tag{15}$$

A general rotation about an axis which does not pass through the origin and given by two points P and Q is performed by first translating the vectors to an origin at the initial point of the axis, P, then applying the transformation as given by eq. (12), and

finally translating the vectors back. The vector **F** is transformed to a vector **G** by

$$G = A(F-P)+P, \tag{16}$$

where **A** is given by eq. (12).

In addition to a general rotation as described above, the program can generate a rotation around an axis perpendicular to a plane defined by three points or around one of the axes of the fixed frame. In each case the first stage consists of the determination of two points which define the axis of rotation.

Juxtaposition

The *juxtaposition* subroutine displaces and rotates one molecular fragment relative to another which remains fixed. The input parameters include the specification of three atoms in each of the structures. The result of the operation is a coincidence of two atoms, collinearity of two bonds (with the same sense), and coplanarity of the two triads of points. When the corresponding distances and angles between the points are the same in both triads, the result of the operation is a complete coincidence of the coordinates of the respective atoms. The *juxtaposition* operation is the starting point in any fitting of molecular structures. As will be explained later, it is also the basis for quickly building a large molecule from its constituent units.

The sequence of operations in this subroutine consists of three steps. First, the molecular fragment to be juxtaposed is translated such that one of its atoms coincides with point **A** in the fixed fragment, according to eq. (3). Then a vector which is now fixed at point **A** and defined by the points A_1 ($A_1 = A$) and B_1 in the moving fragment, is aligned with a vector given by the points **A** and **B** in the fixed fragment. This step requires a rotation about an axis perpendicular to the plane spun by the vectors **AB·**($=B-A$) and AB_1. If these vectors are not initially aligned, then this alignment may require one or two rotations.

The third stage consists of one or two rotations about the vector **AB** until the plane spun by the points A_1, B_1, C_1 coincides with that given by **A**, **B**, and **C**.

3. The RPMI system

The RPMI system for molecular modelling contains options for building and display of molecules, as well as allowing interactive manipulation by such routines as rotation, translation, and juxtaposition.

The models can be built either by providing cartesian coordinates or internal coordinates (i.e. bond lengths, bond angles, and dihedral angles; according to the conventions of IUPAC). In addition, both types of coordinates can also be output. The main elements of these programs have been presented in Nir *et al* (1977 a, b). Recently, a composite version has been prepared, (Haydock 1977) which combines and extends these available options. In particular, polymers, helices, and complex macromolecules can now be quickly built and manipulated.

The program is employed interactively. The present version of the program is running on the UNIVAC 70 computer and is operated from a Tektronix display terminal, which is supported by a hard copy unit. An adaptation to other computers

would only require a modification of the plotting subroutines and a different enumeration of tape or disk units. The hard copy unit enables the user to trace and record all the steps performed. The program provides perspective, and stereoscopic views, which are given both for standard observer locations relative to the object and for locations determined and varied by the user. The size of the picture can be varied.

One of the main advantages of this program is that the user does not have to memorize the procedure since the various steps become self-explanatory by messages on the screen. For example, when the user is asked by a message to make a decision or to input information to control the construction or manipulation of a molecule, there is often the option to ask for a more detailed explanation of the available options by typing HELP.

An outline of the options available to the user can be seen in the flow chart (figure 1).

3.1. *Building options*

Atomic coordinates can be input from files, or they can be added directly from the terminal. Input files contain the coordinates of each group of atoms from which the desired macromolecules can be built.

The coordinates may be either cartesian or internal. In the first case, the input files contain the name of each group and, for each atom, the user specifies a name (or atomic identification), the x, y, z, coordinates and the connections.

The connections will specify the bonds drawn between the atoms, and are specified by listing the numerical indices (which are given by the sequential ordering of the atoms) of the atoms to which this particular atom is connected. If internal coordinates are input, the format of each atom is: the ATOMIC ID., the bond length, the bond angle, the dihedral angle, the connections (same as above), and the numerical indices of the three atoms with respect to which the bond length, bond angle, and dihedral angle were specified, respectively. When the atoms are initially input in terms of their internal coordinates a sequential conversion to cartesian coordinates occurs. Atoms can be added to or deleted from a molecule at any time in the execution of the program.

3.2. *Construction of polymers from pre-existing units*

The only requirement is that each subunit from which the polymer will be constructed should contain three 'dummy' atoms, onto which three atoms of the subsequent group will be juxtaposed, thus positioning each adjoining group in the chain. This building subroutine also contains the option for adding sidegroups to the backbone of a polymer, and is particularly well suited for the construction of a peptide.

The input information is: the total number of groups desired, the name of each group and the number of times each group occurs consecutively, and a flag to specify whether or not the subroutine should connect the first and last atoms of sequential groups. The end result is that the desired groups will be added to the working array in the specified order. The connections between atoms will be adjusted to reflect the new sequential order. The 'dummy' atoms are deleted during the process of building.

Thus, according to this building procedure, a peptide of any secondary structure can be constructed either: 1. from amino acid units with different appropriate backbone conformations; 2. by first building the backbone from several backbone
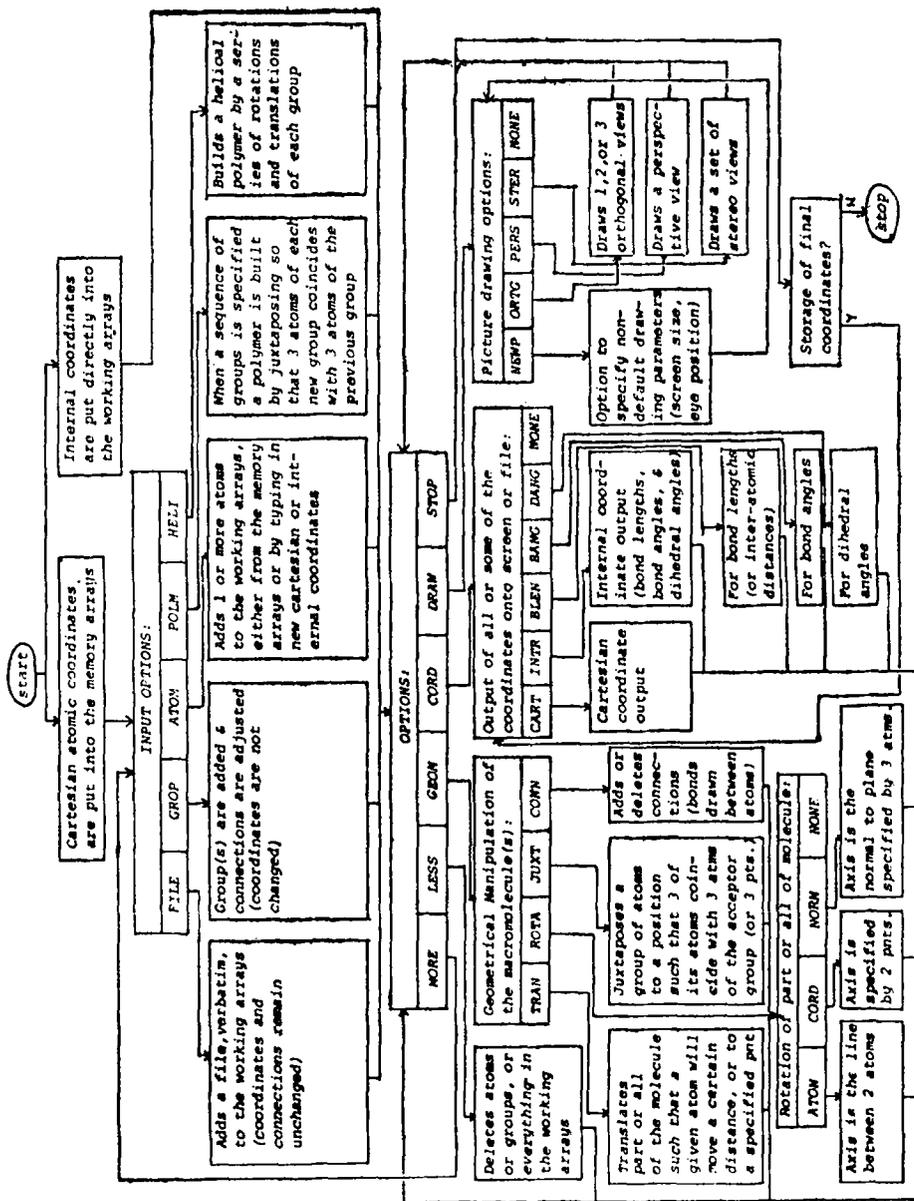
start

Cartesian atomic coordinates are put into the memory arrays

Internal coordinates are put directly into the working arrays

INPUT OPTIONS:

FILE   GROP   ATOM   POLM   HELI

Adds a file, verbatim, to the working arrays (coordinates and connections remain unchanged)

Group(s) are added & connections are adjusted (coordinates are not changed)

Adds 1 or more atoms to the working arrays, either from the memory arrays or by typing in new cartesian or internal coordinates

When a sequence of groups is specified a polymer is built by juxtaposing so that 3 atoms of each new group coincides with 3 atoms of the previous group

Builds a helical polymer by a series of rotations and translations of each group

OPTIONS:

MORE   LESS   GEOM   CORD   ORAW   STOP

Deletes atoms or groups, or everything in the working arrays

Geometrical manipulation of the macromolecule(s):

TRAN   ROTA   JUXT   CONN

Translates part or all of the molecule such that a given atom will move a certain distance, or to a specified pnt

Juxtaposes a group of atoms to a position such that the 3 of its atoms coincide with 3 atms of the acceptor group (or 3 pts.)

Adds or deletes connections (bonds drawn between atoms)

Rotation of part or all of molecule:

ATOM   CORD   NORM   NONE

Axis is the line between 2 atoms

Axis is specified by 2 pnts.

Axis is the normal to plane specified by 3 atms

Output of all or some of the coordinates onto screen or file:

CART   INTR   BLEN   BANG   DANG   NONE

Cartesian coordinate output

Internal coordinate output (bond lengths, bond angles, & dihedral angles)

For bond lengths (or inter-atomic distances)

For bond angles

For dihedral angles

Picture drawing options:

NEWP   ORTG   PERS   STER   NONE

Option to specify non-default drawing parameters (screen size, eye position)

Draws 1,2,or 3 orthogonal views

Draws a perspective view

Draws a set of stereo views

Storage of final coordinates?

N   stop

Y

Figure 1.   Flow chart describing the use of the molecular model building program which is described in the text.

groups with different conformations, and then adding sidechains; or 3. by building an extended β-chain backbone from one backbone group, then using the geometrical options available to rotate and adjust its dihedral angles, and then add the sidechains. See figure 2 for an example.

3.3. *Building of helices*

This subroutine will build a helix according to specified helical parameters (i.e. step height and turn angle) when the user inputs the names of the desired groups which are on file in the memory arrays of the program. It does this by performing a series of translations and rotations of each group by a multiple of the step height and turn angle, respectively. The intramolecular geometry of each input group is not changed, so they should be input with a geometry which will conform to the desired helix. The z-axis is the helix axis, and the positions of all the of input groups should correspond to the first position in the desired helix. The helix can be either right or left handed, and can be built in either the positive or negative z direction, depending on the signs of the turn angle and step height.

Although this subroutine can be used to construct any type of helical macromolecule, it is particularly well suited to build either a single or double stranded nucleic acid helix. In this case, the user provides groups containing the coordinates of the atoms in each of the bases, as well as a backbone (sugar and phosphate) group. They should be positioned in space such that the z-axis is the helix axis, the x-axis is the dyad axis, and each of the bases is in position to be bound to the sugar. Then, by typing in the sequence of bases in the order of their desired positions, a double helix will automatically be constructed. As each base is found in the memory arrays it is added to the working arrays, together with a backbone group. Alternate backbone-base units are rotated 180° about the dyad axis, and each unit is translated in the z direction by the proper multiple of the step height and rotated about the helix axis by the same multiple of the turn angle. The same procedure can be used to build a helical polypeptide.

Several options serve to make this subroutine more general, for the construction of other types of helices. For example, if the user specifies that there is no backbone group, each unit will consist of only one group. This option could be used to construct
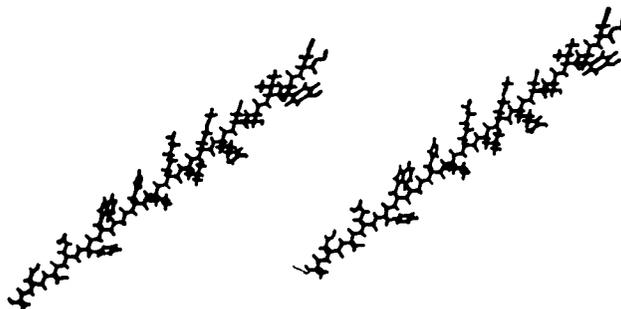
Figure 2. A stereo view of a peptide chain in the fully extended β-conformation. This was built by naming the amino acid sequence, from groups containing the coordinates of each of the residues. The peptide is ALA-ASP-CYS-GLU-PHE-TRP-GLY-HIS-ILE-LYS-LEU-MET-ARG-SER-THR-VAL-TYR-CYSH.

base pairs arranged in a helix without the backbone, or it could be used in cases where the building block units already contain the entire group which is desired (e.g. both a base and a backbone, or both a backbone and a sidechain).

Another option open to the user is the freedom to leave a position without a base, but with a backbone group. Also, an entire helix could be built consisting solely of a backbone.

It is also possible to automatically construct a single stranded helix merely by directing every other position to be blank. Also single positions in the helix can be left blank if desired.

These options are illustrated in figures 3 and 4.

It may be worthwhile to mention that the user has also the option to check whether the distance between any two atoms is too close, say, closer than the sum of their van der Waals' radii. This option helps to avoid structures which may visually appear to be acceptable.

Figures 5 and 6 illustrate a fitting of DNA with tri-tyrosine. These figures show a plausible model for the specific recognition by this peptide of the base sequence

$$\begin{array}{l} \uparrow T{-}A \,| \\ | \, T{-}A \downarrow \end{array} .$$
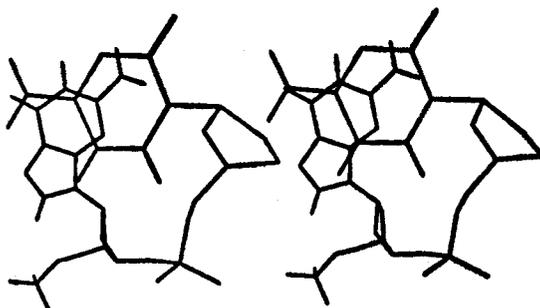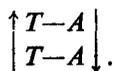
Figure 3. A stereo view of a dinucleotide containing the bases guanine and cytosine. This demonstrates the ability to automatically construct a single-stranded helix.
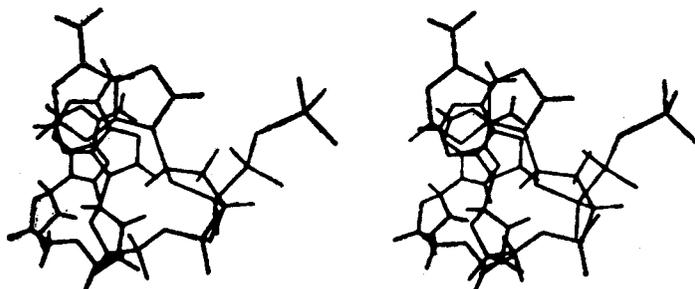
Figure 4. In order to obtain this structure, the program was used to add hydrogen atoms to the backbone by specifying the desired bond lengths, bond angles, and dihedral angles. The helix building subroutine was then employed to construct this model, which is pA-A-A.
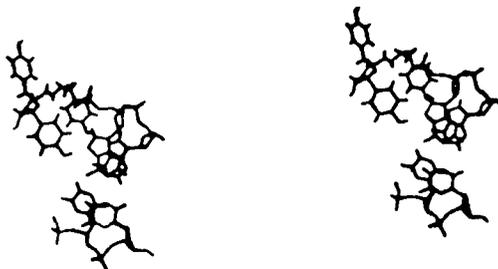
Figure 5. A stereo view of tri-tyrosine hydrogen bonded to $\uparrow \begin{array}{c} T-A \\ T-A \end{array} \downarrow$
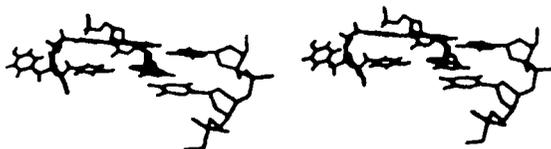
Figure 6. A side view of the same recognition complex as figure 5.

4. Search for isogeometric helices

In order to explore the steric fitting of peptides around DNA, we developed a proce-
dure which allows us to select polypeptide helices whose helical parameters fall within
specified ranges.   Following known theoretical methods, (e.g. Sugeta and Miyazawa,
1967) we have implemented a program which calculates helical parameters from the
internal coordinates of any repeat unit.   The helical parameters are: distance from
the axis for the nearest backbone atom (minimum radius), angle of rotation, and
step height.   The output includes other parameters which can be derived from the
above, such as the number of repeat units per full turn, as well as cartesian or cylindric-
al coordinates for all backbone atoms.

The dihedral angles are then varied systematically within the program, and contour
plots of helical parmeters can be obtained.   From these contour plots, one can
choose ranges of dihedral angles which might warrant a more refined search.

A dipeptide is the smallest repeat unit which can conform to a helical symmetry
similar to that of DNA, while adhering to the steric requirements and allowed ranges
of angles (Ramachandran and Sasisekharan 1968).   For this reason, we have
chosen a dipeptide backbone and have tried to establish which ranges of its four
dihedral angles, ψ_1, ϕ_1, ψ_2 and ϕ_2 will allow the resulting helix to wrap itself around the
major or minor grooves of DNA, at least for some distance.   For the simplest case,
we will consider values of these angles which are close to those of a β-chain conforma-
tion.   We note that Chothia (1975) has shown that helical structures of proteins with
a β-pleated backbone can be formed.

Thus, we first choose a region of allowed ψ and ϕ angles from the Ramachandran
plots; within this region, we then vary ψ and ϕ systematically by 10 degree intervals
for both peptides, and trace contour plots for each of the three crucial parameters
(i.e. minimum radius, units per turn, distance per turn).   We select desired ranges for
each parameter and finally choose the intersection of all allowed regions (figures 7–10).

If the helical parameters need to be chosen in more restricted ranges, the search may proceed in the same manner within the selected regions by varying the dihedral angles in smaller intervals. Of course, the object is to focus in on the interesting regions while keeping the expenditure of computer time at a minimum. It is interesting to notice that even a rather coarse search by jumps of 10 degrees in the dihderal angles yields interesting geometries, as shown for instance, by helices No. 1, 2, 3, and 4 in table 1. In figure 11 we provide a top view of the abovementioned helices. The stereo pictures, Figures 12–15 illustrate how their geometry compares with the standard dimensions of a DNA double helix: distance per turn at 34Å, 10 units per turn and diameter of 20Å (Kornberg 1974).

The program and the procedure are readily adaptable to any kind of helical polymer.
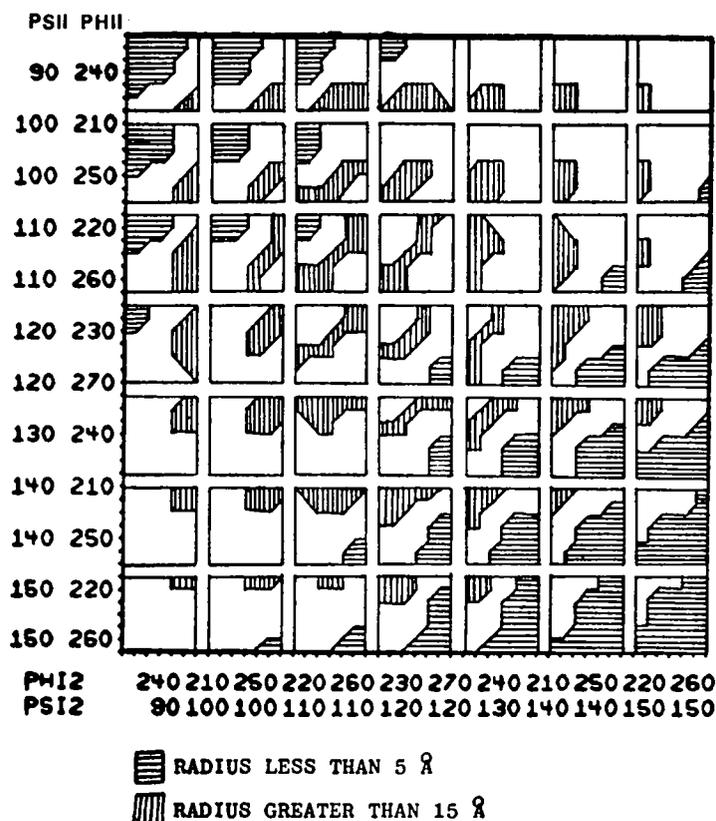
Figure 7. Plot for the minimum radius. The allowed region is chosen between 5 and 15Å. For both axes ϕ_1 and ϕ_2 vary between 210° and 270°, while ϕ_1 and ϕ_2 vary between 90° and 150°. ϕ_1 and ϕ_2 are incremented by 10° in each new square. For instance, the axis values for (ϕ_1, ϕ_1) and (ϕ_2, ϕ_2) in the upper-most left square would be 90°–210°, 90°–220°, 90°–230°, 90°–230°, 90°–240°, 90°–250°, 90°–260°, 90°–270°. The same subdivision is also used in figures 8 and 9.

Table 1. Parameters of the 4 helices chosen from figure 10. Included are the dihedral angles of the dipeptide units (in degrees).

	Helix 1	Helix 2	Helix 3	Helix 4
Minimum Radius (Å)	6·66	9·18	9·07	9·72
Units/ Turn	8·49	10·57	10·90	10·64
Dist/ Turn	33·54	33·03	38·06	32·74
Step Height	3·96	3·13	3·50	3·08
Turn Angle (degree)	42·41	34·09	33·05	33·85
ϕ_1	140	140	130	150
ϕ_1	260	250	260	240
ϕ_2	110	100	110	110
ϕ_2	230	240	230	230
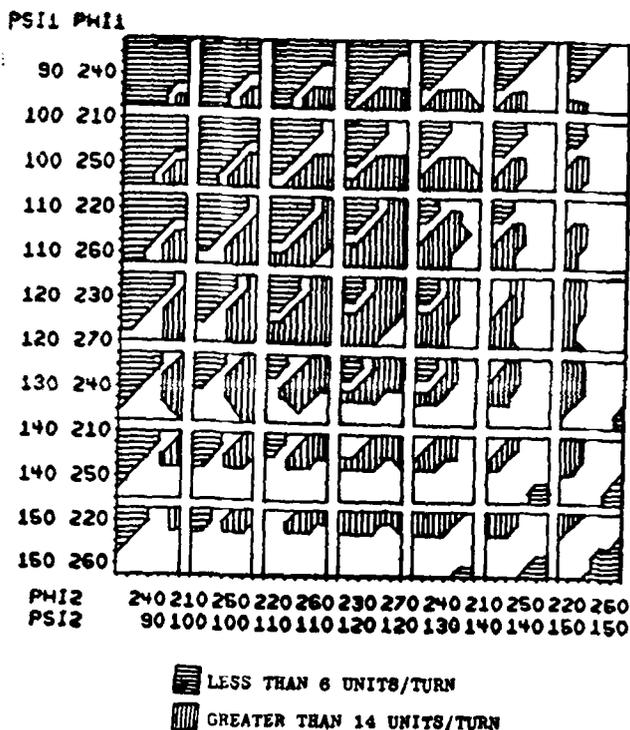
Figure 8. Plot for number of units per turn. The allowed region is chosen between 6 and 14 units.
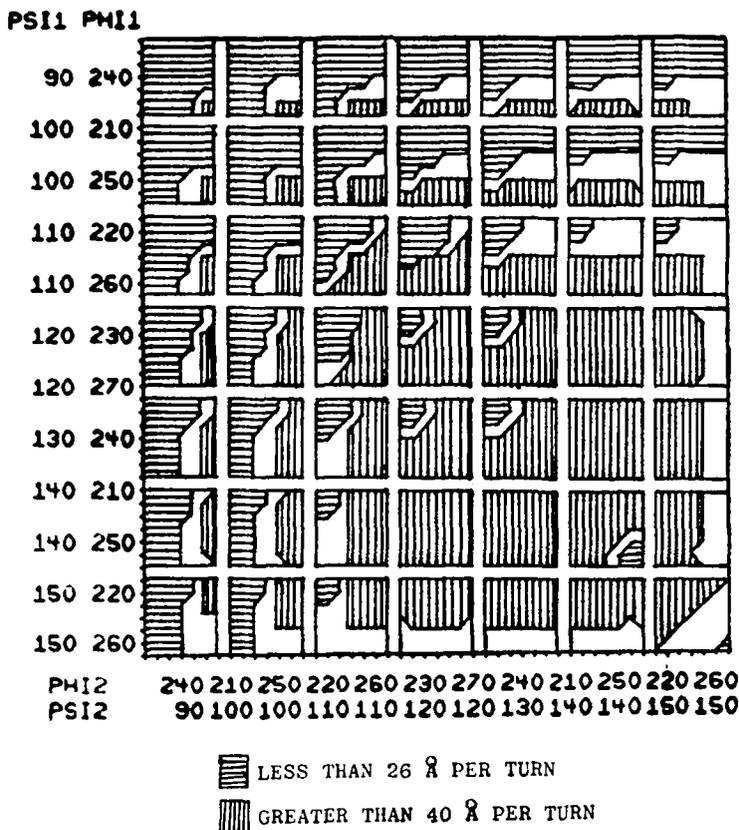
Figure 9. Plot for distance per turn. The allowed region is chosen between 26 and 40Å.

5. The AIMS system

The molecular modelling system in use at Ames, called the Ames Interactive Modelling System (AIMS), consists of 4 functionally identifiable components. The first is a molecule construction system which operates interactively with an IBM 360 computer used in a time-sharing mode (TSS). This system allows the assembly of instructions for building a molecular model. The operator enters the coordinates of the atoms of a molecule or of the subunit of a molecule, and indicates which atoms are to be connected with bonds. Alternatively, the structure can be built by specifying bond lengths and bond angles. Once the structure has been completed, it can be stored in a library. This second component can contain instructions for all of the building blocks necessary for the construction of the molecule; for example, all of the side chain residues of the amino acids, plus a backbone residue, would permit the construction of a protein of any amino acid composition. The secondary conformation of the protein, or part of it, can be achieved by including backbones of the form of an alpha helix, or a beta ribbon, or an anti-parallel pleated sheet. The information from the library can be assembled in the molecule building program (*Molecule*), or it can be accessed directly from the display device.

EXCLUDED REGION
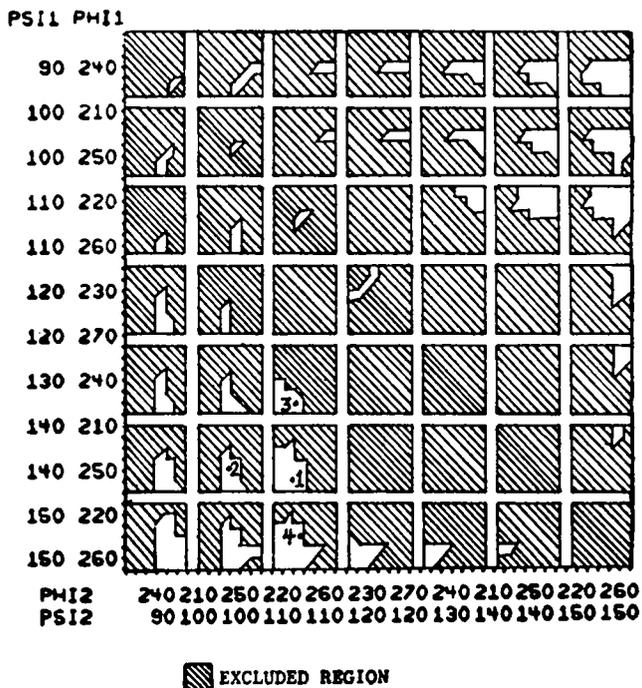
Figure 10. Result of the intersection of the allowed regions for all chosen parameters. Only the unshaded areas are allowed. Points 1, 2, 3 and 4 taken as examples yield the helices shown in table 1.

The display system is an Evans and Sutherland Picture System, consisting of a high resolution cathode ray tube (CRT) plus a dedicated computer which can rapidly manipulate the coordinate matrices to produce a dynamic image. This third component is directed in its operations by instructions sent to it from a DEC PDP 11-45 computer. The CRT can display data sets describing large molecules or building blocks, and the system can assemble molecules by concatenating data sets which can then be treated as single units. Single data sets can be treated separately so that individual bonds can be made on the axis of rotation. This permits conformational alteration at will. The interactive controls allowing image manipulation consist of a magnetic tablet, a keyboard, and a switching system. With these controls, data can be identified and specific operations performed on it.

Since the display must be in two dimensions on the surface of the cathode ray tube, several cues of the three-dimensional nature of the molecules are included. One cue is that of perspective which places points in the background closer together than they would be in the foreground. Another cue is that the intensity of background points is less than that of foreground points. A final cue to three-dimensionality is that the molecule can be rotated on any plane with continuous adjustment of perspective and intensity. These aspects of the display are controlled by programmed hardware which is part of the display terminal. Movement on the cathode ray tube can be controlled either by keyboard or by a magnetic tablet.

Once the molecule has been assembled, displayed, and manipulated, it is necessary to determine whether the new conformation violates the principle that van der Waals
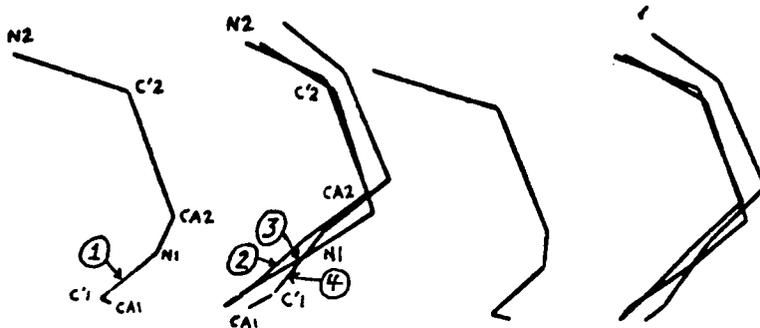
Figure 11.   This is a stereo picture of a top view comparing the dipeptide units of the 4 helices in table 1.
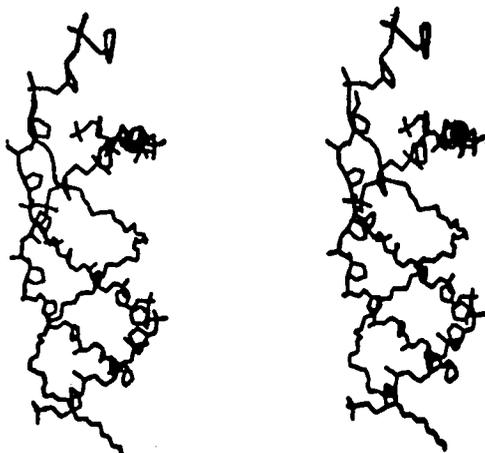
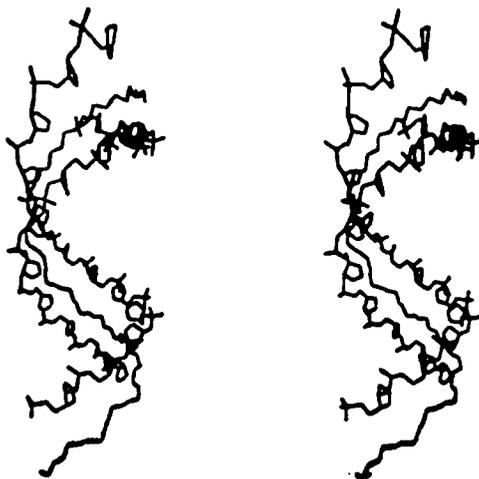**Figure 12(a).**   Helix 1 in the major groove of DNA.

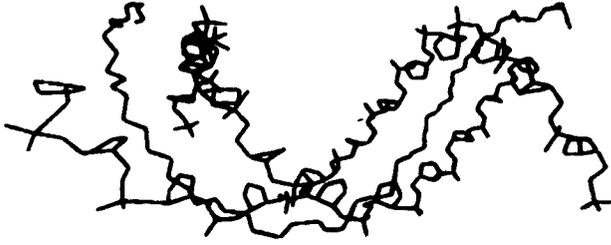**Figure 12(b).**   Helix 1 in the minor groove of DNA.
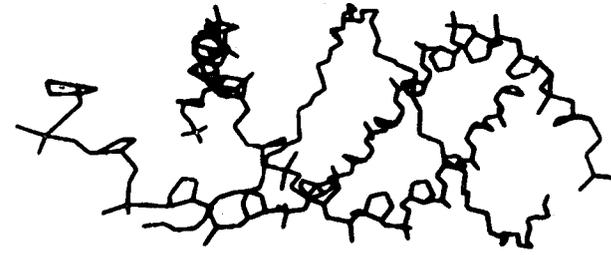
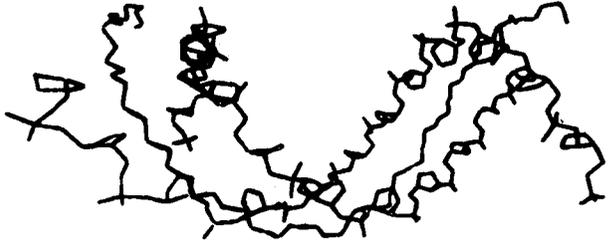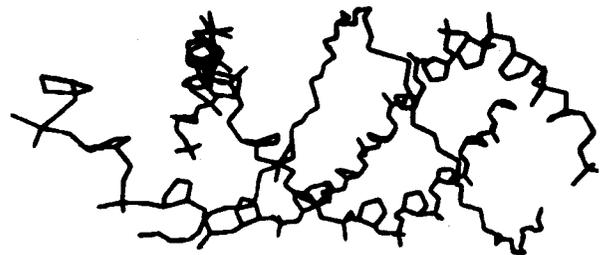Figure 13(b).   Helix 2 in the minor groove.

Figure 13(a).   Helix 2 in the major groove.
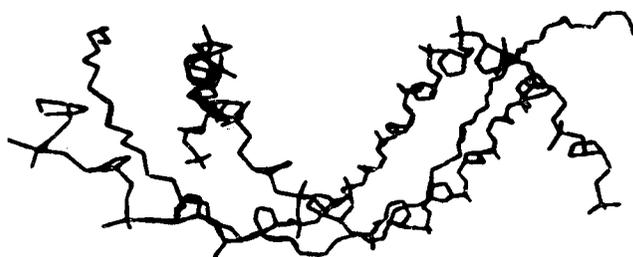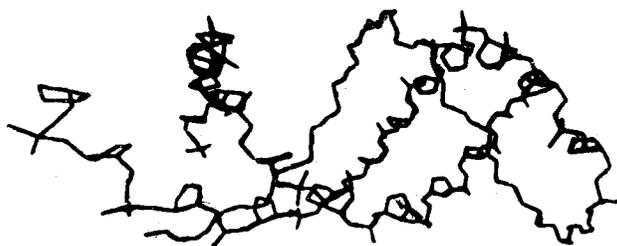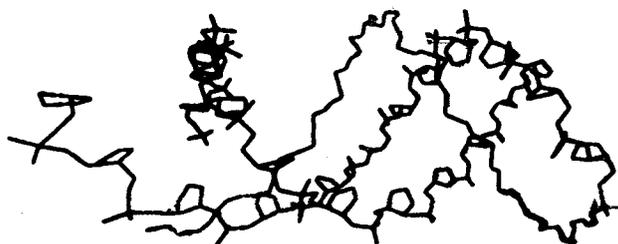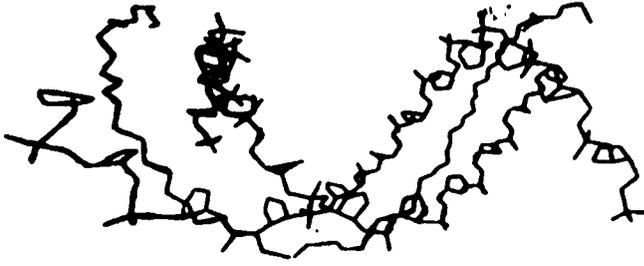
Figure 14(b). Helix 3 in the minor groove.

Figure 14(a). Helix 3 in the major groove.

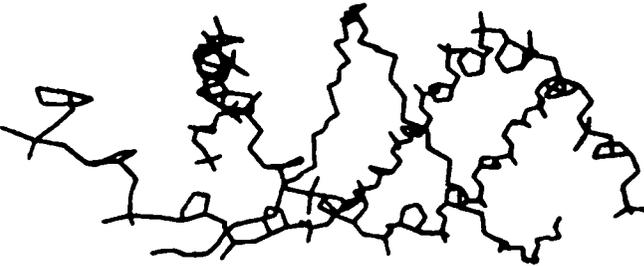Figure 15(b).   Helix 4 in the minor groove.
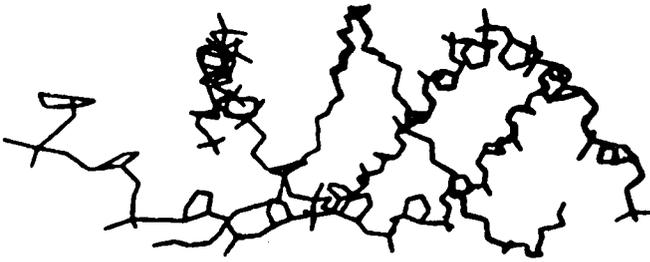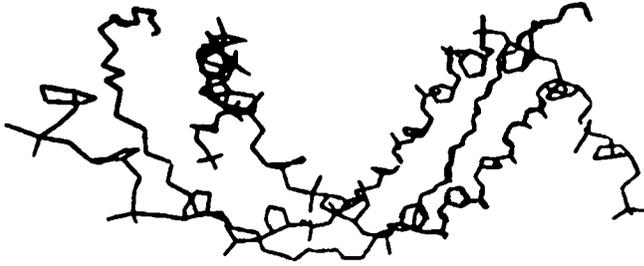
Figure 15(a).   Helix 4 in the major groove.

radii must not overlap.   Such violations can be identified by taking the new coordinates, calculating interatomic distances and comparing the results with accepted values for the sum of the van der Waals radii.   The fourth component of the system performs these functions, and in addition can retrieve parameters, such as charge distribution, and other chemical information necessary for estimations of interaction energies.   These values are stored in the library and must be located and associated with the correct set of data.   Illustrations of some of the modelling which has been undertaken with this system can be found in Coeckelenbergh *et al* (1977) and MacElory *et al* (1977).

Acknowledgements

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