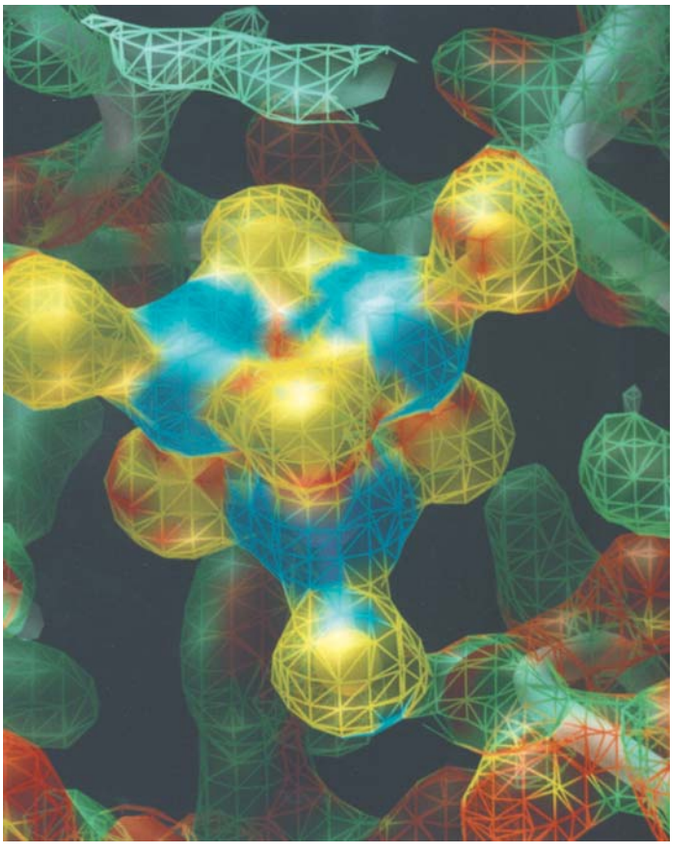

Fig. 17.2.3.7. Crystallographic electron-density isosurfaces, showing details of a protein iron–sulfur cluster. The surfaces are coloured by the gradient of the electron density, highlighting the iron and sulfur densities. Image by Michael Pique, The Scripps Research Institute.

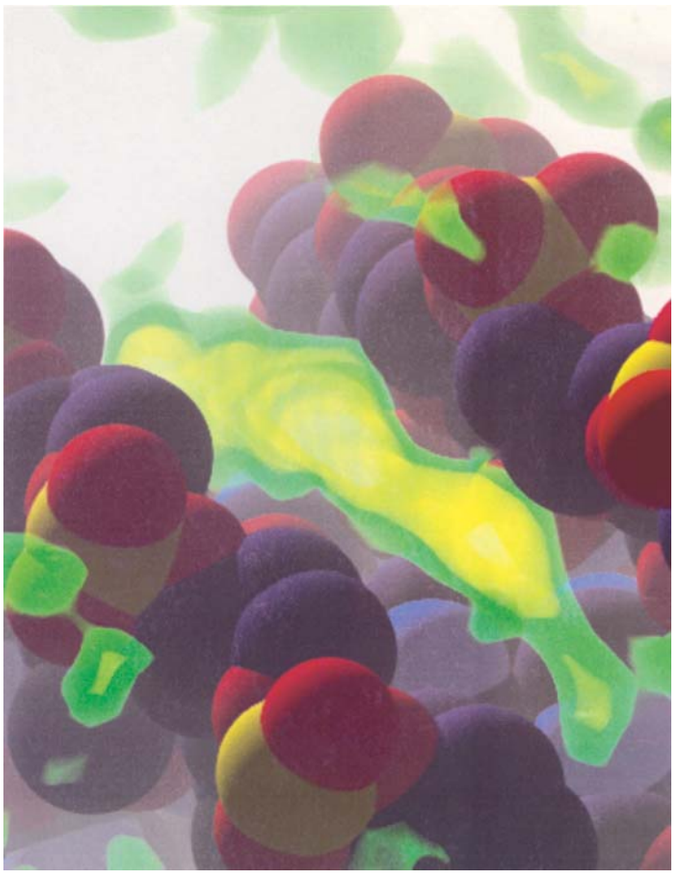

Fig. 17.2.3.8. A difference-electron-density map of a minor-groove drug binding in DNA. This image combines volumetric rendering of the electron density with a geometric model of the DNA molecule. Data courtesy of R. E. Dickerson, UCLA. Image by David Goodsell, The Scripps Research Institute.

can simulate the passage of light rays through the volume, projecting the resulting rays onto the image plane. Given an appropriate transfer function or look-up table, the image represents the distribution of all of the values within the volume, circumventing the need to select only certain values as required for isocontouring. Such techniques have been used extensively in medical tomography (Höhne *et al.*, 1989) and electron microscopy (Kremer *et al.*, 1996; Hessler *et al.*, 1996). Their use has also been explored in the rendering of volumetric properties of molecules (Goodsell *et al.*, 1989). The images that are obtained by direct volume rendering tend to appear cloud-like, with soft edges. While this may be a 'true' representation of the molecular characteristics, it is sometimes difficult to interpret visually. Techniques for imparting shading cues into these renderings by using gradient information in the volume has made this type of rendering more interpretable (Drebein *et al.*, 1988). Another potential drawback to these methods is the cost of the computations. Since these methods require computing the effect of every element of the volume, the amount of computation scales as the cube of the linear dimension. There have been several clever software and hardware approaches to overcoming this problem. One novel hardware approach is to use three-dimensional texture mapping. By stacking texture-mapped planes to represent the colour and opacity of the volume, and using the hardware depth-buffer capabilities to compose the final image in the viewing plane, one can manipulate and render reasonable-size volumes (128^3) at highly interactive rates. For molecular visualization, one would like to be able to represent both geometric and volumetric characteristics in the same rendering to visualize, for instance, model and data (Fig. 17.2.3.8). The three-dimensional texture-mapping approach enables this easily, since the planes upon which the volume data are mapped are in fact geometric. Other direct-volume rendering codes provide this capability as well.

17.2.3.3. *Information visualization*

While molecular-structure research deals directly with objects in three dimensions, it is at times advantageous to abstract this three-dimensional information into diagrams that show relationships that are not readily apparent by examination of a set of geometric models or volumes themselves. This type of representation is broadly termed 'information visualization'. In the arena of molecular structure, probably the best known and most widely used diagram of this type is the Ramachandran plot (Ramachandran & Sasisekharan, 1968), which maps the positions of each of a protein's amino-acid residues into the backbone torsion-angle space of φ and ψ. Such a diagram readily pinpoints the parts of the protein backbone that have unusual (and sometimes erroneous) configurations. It also nicely shows the clustering of residues into the standard secondary structural motifs and their variations. There have been several enhancements of the Ramachandran plot over the years, some of which superimpose computed energy contours or colour-code residues by characteristics such as sequence order.

Another visualization approach that has become very useful is the distance matrix plot, and its derivative, the difference distance matrix (Phillips, 1970). By constructing a matrix of distances between each amino-acid α-carbon and contouring or colouring the resulting values, one can readily see the patterns of α-helices and β-sheets within the structure. An advantage of this type of

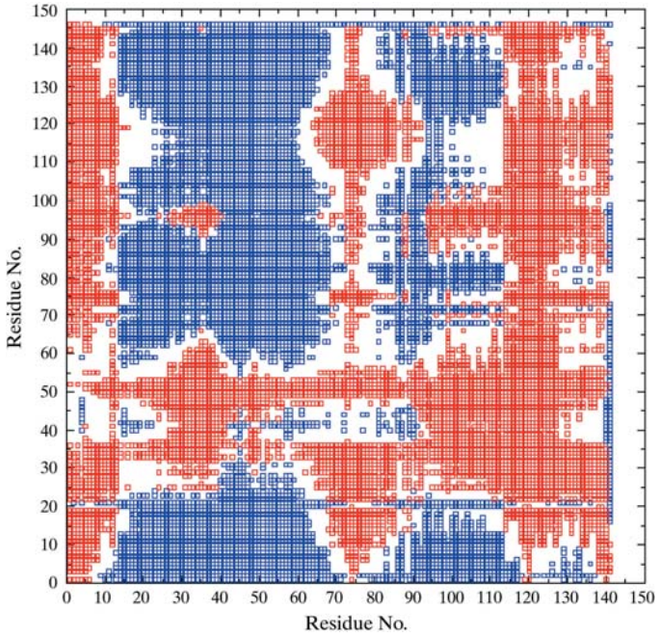

Fig. 17.2.3.9. A difference distance matrix plot of the α_1–β_2 interface of haemoglobin in the T to R transformation. The x-axis reperesents the α_1 subunit and the y-axis the β_2 subunit. Red points indicate residues that are closer following the transformation and blue points indicate residues that move farther apart. Plot by Raj Srinivasan, Johns Hopkins University.

visualization is that it is coordinate-frame independent. Thus two structures can be compared for features without first superposing their coordinates in the same frame. This approach also works well when comparing two different structures of the same molecule, where there may be some movement between the two. By computing the distance matrix for each structure, and then computing the difference between the two distance matrices, the resulting difference distance matrix will indicate those parts of the structure that stay in the same relative relationships and those that may move relative to each other (Fig. 17.2.3.9).

Animating trajectories of molecular structures and changes in volumetric properties over time is one way to look for trends and patterns in molecular dynamics and other time-course simulations. However, other modes of information visualization can assist analysis and communication of results, sometimes more effectively. Plotting an array of small images showing the time course of key properties can reveal patterns that may be difficult to see in a trajectory. For instance, using the program *MolMol* (Koradi *et al.*, 1996), the time course of the seven nucleic-acid backbone torsion angles during a dynamics simulation of an RNA polynucleotide can be plotted on a circular graph (starting from the centre and progressing outward) to uncover patterns of change and correlation between a large number of variables over time.

In addition to the enormous amount of information generated by computational simulations of molecular dynamics, dockings and other multi-structure, multi-modal techniques, the floodgates of molecular information have opened, gushing data from genomics and high-throughput structure determination. Thus, the need for novel visualization methods has become even more acute. Circle maps defining genomic structure at various levels of detail and annotation have become a common graphical form for organizing and communicating the positional and functional aspects of genome structure. Aligned nucleic acid or amino-acid sequences coded by conservation, chemical property, or any number of other functional relationships have become the *lingua franca* of gene hunters and gatherers. As the protein structure database continues its exponential growth, the opportunities for defining and refining structural family relationships abound. Developing methods for effectively visualizing the relationships that arise from all-by-all computational comparisons of the entire database is an important current challenge in molecular graphics.

17.2.4. Presentation graphics

Much of molecular graphics can be classified as working or 'throw-away' graphics. Typically this involves the interactive creation of graphical representations on screen or paper that are used in the course of research to build, modify and analyse molecular structures, their motions and interactions. Such graphics need only be intelligible to the researchers involved. On the other hand, a presentation or publication graphic must be able to stand on its own to convey information to a broader audience. Thus it requires additional thought and work in its creation. It is unfortunate that many scientists simply capture the working graphics on their computer screens for use in publications or other forms of communication. Both interpretability and intelligibility may suffer badly if a number of issues are not considered in the production of a presentation graphic: What is the medium of publication? What is the main point of the graphic? Who are the target audience? How will reproduction or the viewing environment affect the impact of the graphic? Even seemingly simple issues such as when and how to use colour can in reality be a complex mixture of aesthetics, psychology, technology and economics. While an in-depth discussion of these issues is beyond the scope of this chapter, it is worthwhile to look at two categories of publication graphics, illustration and animation, in this context.

17.2.4.1. *Illustration*

In print media, shaded colour images can present a number of difficulties. In addition to the issue of cost, colour shifting, reproducibility and loss of detail in the half-toning process may lead to less than the desired result. Simple line art is an effective way to bypass many of these complications. Since the advent of printing in the middle ages, artists and scientists have explored the problems of creating illustrations within the limitations of the printing process. Over time, artists have built a vocabulary of outlines, hatched shading and varied textures to simplify and clearly portray an object. While the creation of such illustrations was time consuming and required considerable artistic talent, they effectively portrayed the observational science of the day. The advent of computers and computer graphics removed any requirement for skilled hand draftsmanship in the production of molecular representations, but did not solve all of the problems of good illustration. As mentioned above, prior to the widespread use of interactive computer graphics, molecular structures were often published as outline drawings of ball-and-stick models using programs such as *ORTEP* or *PLUTO* (Motherwell & Clegg, 1978). More recently, programs such as *MOLSCRIPT* (Kraulis, 1991) have re-established the popularity of line-art illustration in the molecular realm. A good *ORTEP* drawing usually took a great deal of preparation time in order to get the best representation and viewpoint to display the structure effectively. As the visual repertoire of molecular structure has expanded to a wide variety of shapes including ribbons, tubes and solvent-based surfaces, the challenge of automating the general illustration process has grown. A number of techniques have been developed in the computer-graphics community to generate images in the style of technical or artistic illustrations (Fig. 17.2.4.1). These approaches use lighting, depth information and geometry to produce black-and-white drawings with shapes defined by silhouette lines and cross-hatched

references