cation selectivity. But even sceptics will have to admit that, until another structure with such selectivity is found, the hypothesis about quadruplex formation conforms to the principle of Occam's razor.

Sundquist and Heaphy speculate that quadruplex formation may mediate RNA dimerization *in vivo* in HIV and other retroviruses, which would represent the first example of a defined biological function for nucleic acid quadruplexes. *In vitro*, RNA molecules form dimers very slowly, as do DNA quadruplexes, and *in vivo* a protein should facilitate the dimerization. The authors believe that the protein helps to form the quadruplex, functioning as a kind of RNA chaperone.

If Sundquist and Heaphy are correct that quadruplexes form a structural basis for the 'dangerous liaisons' *in vivo* between two HIV RNA molecules, new possibilities to find effective drugs or vaccines to combat AIDS can be contemplated[2,3]. For instance, one can imagine that drugs destabilizing or stabilizing quadruplexes would interfere with HIV infection. □

Maxim Frank-Kamenetskii is in the Institute of Molecular Genetics, Russian Academy of Sciences, Moscow 123182, Russia.

INTERMOLECULAR BONDS

The potential to surprise

William Klemperer

HYDROGEN bonding is generally regarded as the strongest and the most directional of the weak intermolecular interactions that cause molecules to form liquids and solids: because of it, water boils at a temperature 160 °C higher than does hydrogen sulphide. Hydrogen bonding is also a primary structure-determining force in biological molecules. Yet results reported on page 735 of this issue[1] show that we know less about this bonding than we should.

Rodham *et al.*[1] have determined the structure of the dimer composed of benzene and ammonia. They find that one proton on the ammonia is directed towards the benzene ring. This discovery is surprising because ammonia, in virtually all other complexes, acts as an exceptionally poor proton donor. In NH_3–C_6H_6, although only one proton points towards the benzene plane at any time, the structure is quite dynamic with the ammonia unit undergoing rotation so that all three protons are equivalent. Proton interchange is a general occurrence with complexes of water where monodentate hydrogen-bonded structures are very common.

Advances in spectroscopic techniques over the past two decades have made it possible for chemists to determine the structure of all sorts of molecular complexes. Complexes of virtually any pair of molecules are easily formed by adiabatic expansion, through a pinhole into a vacuum, of a dilute mixture of the pair in an inert gas, usually argon. The effective temperature of the molecular beam formed in such an expansion is below 10 K; thus even the weakest bonds are stable. Spectroscopic measurements of the complexes are made by a variety of techniques. Having the species at very low temperatures, with few quantum states populated, provides a welcome simplification of the spectra. This is especially useful as the weakness of intermolecular bonds means that large-amplitude, low-frequency motions can be a nightmare. In addition, a rich variety of quantum tunnelling motions occur in systems with either identical units or identical chemical bonds. For example, the water dimer, which is held together by a single hydrogen bond, exhibits interchange of proton donor and proton acceptor as well as interchange of bonded proton and free proton of a water unit[2]. The high resolution of pure rotational and far-infrared spectroscopy even allows nuclear hyperfine structure and electric dipole moments to be measured precisely, which is invaluable for learning the orientation of the molecular units with respect to one another[3].

A wealth of structures of gas-phase binary complexes is now available, allowing comparisons with first-principles structure calculations and semi-empirical models of intermolecular potentials. It is, of course, an aim of this research to develop an understanding of intermolecular potentials, which will often be applicable to condensed-phase systems as well. For example, rotational spectroscopy[4] seems to show that the monomer units in the benzene–benzene dimer are arranged in a T-shaped polar structure (not arranged parallel and offset, as some supposed), with a centre-to-centre separation of 4.96 Å. This is almost identical to the geometry of nearest neighbours in liquid and crystalline benzene.

The hydrogen bond is the archetypal stereospecific weak interaction found in complexes. The precise structural characterization of binary hydrogen-bonded complexes allows us to find out exactly how two units held together by a hydrogen bond orient themselves and how strong the bonds are. Experiments are revealing that hydrogen bonding seems to be subject to many subtle factors. Ammonia forms simple, hydrogen-bonded dimers with the hydrogen halides in the gas phase, but ionic $NH_4^+X^-$ in the crystalline solid phase (X^- being any halide ion). On the other hand, the ammonia homologue trimethylamine forms an ionic complex $(CH_3)_3NH^+I^-$ with hydrogen iodide, even in the gas phase[5]. Of course, in these cases, the ammonia acts as a proton acceptor. In the proton-donating compound studied by Rodham *et al.*[1], NH_3–C_6H_6, the hydrogen bond is very weak and relatively floppy, whereas in the trimethylamine–hydrogen-halide complex it is strong and rigid (there is a twentyfold difference in dissociation energy). Another factor now becoming accessible to study is the effect vibration can have on hydrogen bonding[6]. It will be interesting to study the initiation of proton transfer in vibrationally excited hydrogen-bonded complexes.

A further complication is that the linearity of hydrogen bonds appears to depend upon the asymmetry of the molecular unit. For example, the complex OC–HF has a linear equilibrium structure, whereas in OC–HOH, the hydrogen bond deviates by 12° from linear[7,8]. There is a growing body of evidence that the minimum-energy orientation of the molecules in a complex is a function of the distance of their separation. Indeed, where the orientation oscillates, one finds that there is also a fluctuation in bond length. Even the effects of the unavoidable zero-point vibrations can be accompanied by significant angular reorientation.

The curious, floppy complex studied by Rodham and colleagues touches on many of these issues. It also brings this archetypally chemical-physics field into the domain of biochemistry. As the authors themselves point out, the ammonia–benzene complex is representative of the amino–aromatic interactions that are particulary relevant to protein structure. □

William Klemperer is in the Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138, USA.

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