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¹G. M. Sessler and J. E. West, in *Annual Report Conference on Electrical Insulation and Dielectric Phenomena* (National Academy of Science, Washington, D. C., 1971), pp. 8-16; G. M. Sessler, *J. Appl. Phys.* **43**, 408 (1972).

²B. Gross, J. Dow, and S. V. Nablo, *J. Appl. Phys.* **44**, 2459 (1973).

³B. Gross, G. M. Sessler, and J. E. West, *J. Appl. Phys.* **45**, 2841 (1975).

⁴R. E. Collins, *Appl. Phys. Lett.* **26**, 675 (1975).

⁵R. E. Collins, to be published.

⁶P. Laurenceau, G. Dreyfus, and J. Lewiner, to be published.

⁷I. S. Sokolnikoff and R. M. Redheffer, *Mathematics of Physics and Modern Engineering* (McGraw-Hill, New York, 1958), p. 262.

⁸J. F. Fowler, *Proc. Roy. Soc. London, Ser. A* **236**, 464 (1956).

⁹G. M. Sessler, J. E. West, and D. A. Berkley, to be published.

¹⁰L. Pages, E. Bertel, H. Joffre, and L. Shlavenitis, *At. Data* **4**, 1 (1972).

¹¹T. J. Sonnonstine and M. M. Perlman, *Phys. Rev. B* **12**, 4434 (1975).

¹²P. C. Arnett and B. H. Yun, *Appl. Phys. Lett.* **26**, 94 (1975).

¹³H. Scher and E. W. Montroll, *Phys. Rev. B* **12**, 2455 (1975).

Soft Modes and the Structure of the DNA Double Helix*

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(Received 29 July 1976)

We show that a soft mode arises when the vibrational modes of double-helical DNA are perturbed by increasing the electrostatic or Van der Waals interactions between atoms. We believe this soft mode drives the *B* to *A* conformation change which is observed when DNA has water of hydration removed from it.

We have applied the method of vibrational mode softening to investigate conformation changes (i.e., changes in three-dimensional structure) in double-helical DNA. Conformation changes of these macromolecules are analogous to displacive phase changes in crystalline solids. We have calculated a mode softening which would drive the double helix from its *B* conformation to its *A* conformation. The mode is not softened by temperature change, but rather by changes in the macromolecular environment which mimics the conditions which cause the conformation change experimentally.

The DNA double helix can take on several conformations.¹ When dissolved in water or in gels at high humidity (much water of hydration) it is found in the *B* conformation. Upon drying the gel in an atmosphere of less than 92% relative humidity, it converts to the *A* conformation. RNA on the other hand is found only in *A*-type conformations. It has been suggested that DNA switches to *A* conformation locally when transcribing RNA *in vivo* and that this conformation change is an important switching mechanism in the biological function of nucleic acid.²

We have carried on extensive theoretical investigations of the lattice dynamics of DNA and RNA helices.³ These calculations were made using valence and Urey-Bradley force fields which were

obtained, by various authors, by refinement from the observed spectra of the constituent parts of nucleic acid. The calculations were done for artificial homopolymer DNA in which all the base units in a single helix were the same. Two such double-helical DNA compounds exist—poly(dA)·poly(dT) and poly(dG)·poly(dC)—where the bases are adenine, thymine, guanine, and cytosine, respectively. These homopolymer duplexes are available and a considerable amount of experimental ir and Raman analysis has been done for all the occurring conformations. A comparison of our theoretical lines with those observed shows quite good agreement for those regions of the spectrum where data exist.³ In our calculations for both poly(dG)·poly(dC) and poly(dA)·poly(dT) the lowest-lying optical mode is one in which the two single helices move up and down relative to each other along the double-helix axis. It is this mode which softens in our calculations.

The eigenvector of the mode that softens agrees very well with the description of the *B* to *A* conformation change. The *B* conformation has the bases of the helix perpendicular to the helix axes. In the *A* conformation, the bases are tilted from the perpendicular. The soft mode in which the two helices displace relative to each other along the axis does lead to such a tilting of the bases.

In doing our calculations for the soft mode, we

assumed that the simplest effect of removing water of hydration from the double helix was to reduce the effective dielectric constant for the electrostatic and van der Waals interactions between the atoms. This should occur since reducing the amount of water reduces its ability to shield or depolarize the regions of unbalanced charge in the double helix. We calculated the effect on the frequency of the low-lying modes of a perturbation which increased the electrostatic force between charged atoms. We have separately calculated the effect of enhanced van der Waals interactions on the frequency of these modes as well. Both effects associated with the removal of water caused the lowest-lying optical mode to soften. This change in polarizability caused by removal of water should occur whether the water has been removed by drying or for water displaced by less polar enzymes which interact with the DNA double helix.

The unbalanced charge q_i on atom i used in calculating the electrostatic perturbation came from a calculation of electron density by Renugopalakrishnan, Lakshminarayan, and Sasisekharan.⁴ The change in force constant between atoms i and j , Δk_{ij} , was then

$$\Delta k_{ij} = x q_i q_j / r_{ij}^3, \quad (1)$$

where x is the parameter that should increase as water is removed.

The behavior of the lowest-frequency modes was investigated with use of a near-degenerate-perturbation-theory scheme. The normal modes for both double-helical polymers had already been calculated with a set of fitted force constants.³ The electrostatic term was projected onto a manifold of "near-degenerate" eigenstates. This manifold consisted of the lowest ten eigenstates since it was only among these that any significant mixing occurred. Consequently, a 10×10 matrix was diagonalized for each value of x .

The electrostatic term consisted of atom-atom interactions between every pair of nonbonded atoms in the bases for the ten nearest bases. Interactions between two atoms in the same unit which are bonded to a common atom were excluded however, since these interactions are included in the unperturbed part of the potential energy. We were careful to include contributions made by the hydrogen atoms without increasing the dimension of the problem by rigidly fixing the hydrogen atoms to their atoms of attachment. This is consistent with the handling of the hydrogen atoms in the kinetic-energy term where the mass of the

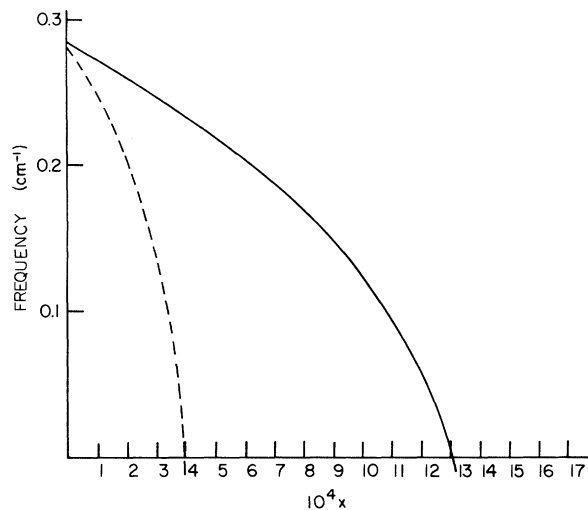


FIG. 1. Plot of the lowest optical-mode frequency in cm^{-1} as a function of electrostatic interaction parameter x . Solid line is for poly(dA)·poly(dT) and broken line is for poly(dG)·poly(dC). Frequency is imaginary below x axis.

hydrogen is added into its atom of attachment.³ The results of these calculations are shown in Fig. 1.

The relationship between x and the dielectric constant is $\epsilon_t^{-1} = \epsilon_s^{-1} + x$, where ϵ_t is the value of the dielectric constant at which the transition occurs and ϵ_s is the value of the dielectric constant for the fully hydrated stable helix. It is difficult to estimate what the effective dielectric constant ϵ_s should be in the interior of a hydrated helix. The value of ϵ in the absence of water should be $\epsilon \approx 4$. It is not known how much penetration of the water into the interior actually occurs. If the water were to raise the value of ϵ , to $\epsilon_s \approx 6$, then the transition would occur at $\epsilon_t = 5.98$ in the case of poly(dG)·poly(dC) and $\epsilon_t = 5.95$ for the case of poly(dA)·poly(dT).

The difference in the value of the effective dielectric constant at which the two compounds soften is also in agreement with experimental observations. X-ray analysis of the conformation change for the two homopolymer duplex shows that poly(dG)·poly(dC) readily undergoes the *B* to *A* conformation change upon drying but that poly(dA)·poly(dT) is much less likely to do so.⁵

The calculation for altered van der Waals forces was very similar to that for altered electrostatic forces. The van der Waals force constants between atoms were estimated from published phenomenological 6-12 potential models.⁶

The change in force constants due to reduction

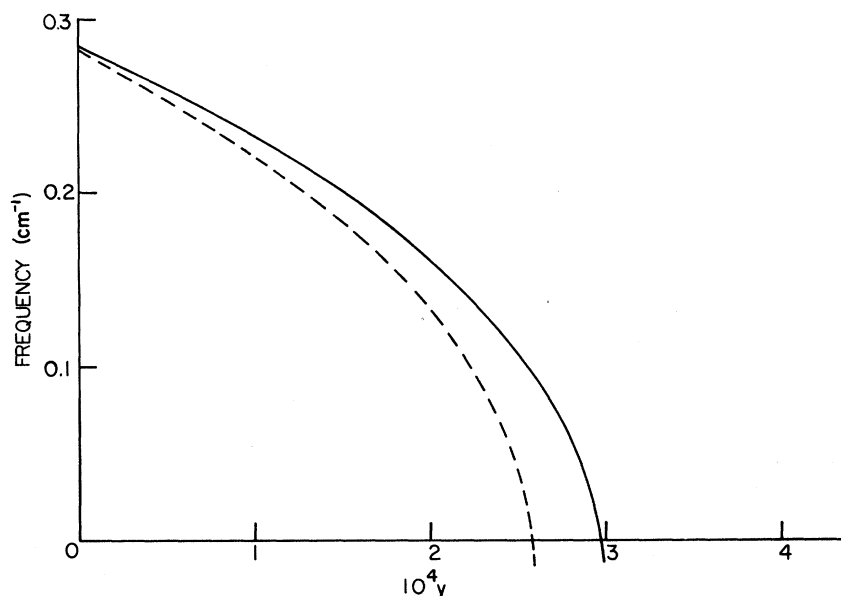


FIG. 2. Plot of lowest optical-mode frequency in cm^{-1} as a function of van der Waals interaction parameter y . Solid line is for poly(dA)·poly(dT) and broken line is for poly(dG)·poly(dC). Frequency is imaginary below the y axis.

of water was determined by multiplying the estimated force constants by a parameter y . The perturbed eigenvalues were determined in the same way as above. These results are plotted in Fig. 2. The change in interaction needed to bring about a mode-softened transition is also a fairly small percentage change in the interaction strength. Again poly(dG)·poly(dC) is seen to undergo the transition more readily.

The uncertainty of the appropriate dielectric constant, the uncertainty of the unbalanced charge distribution, the use of a rigid-ion approximation, and the uncertainty of the Van der Waals model will certainly alter details of our calculations. However, our experience with changing these parameters leads us to believe that the basic motion of the lowest-lying mode persists, and the perturbations which we have applied do soften it.

We believe that the above results indicate that the physics methods associated with the soft-mode approach can be very usefully applied to problems relating to basic biological mechanisms. It would also be of interest to determine if soft modes associated with biological processes could be experimentally observed. Such observations would lead to information on conformation changes of biomolecules which appear to be all important in biological function. Much infrared and Raman

work is being done on biopolymers. For the most part, this work is limited to frequencies above 200 cm^{-1} . The modes involved in biological dynamics are, however, expected to be at lower frequencies. It would be of great interest if low-frequency methods currently used in physics research could be successfully used on biomaterials. Some of the methods which may be of use are neutron scattering, inelastic electron tunneling, and microwave absorption.

We wish to thank Professor L. L. Van Zandt, Professor G. Ascarelli, and S. Arnott for many useful discussions.

*This work supported in part by National Science Foundation under Grant No. DMR74-14367 and Purdue Cancer Research Committee-American Cancer Society.

¹S. Arnott, *Prog. Biophys. Mol. Biol.* **21**, 265 (1970).

²S. Arnott *et al.*, *Nature (London)* **220**, 561 (1968).

³J. M. Eyster and E. W. Prohofsky, *Biopolymers* **13**, 2505, 2527 (1974); K. C. Lu and E. W. Prohofsky, to be published.

⁴V. Renugopalakrishnan, A. V. Lakshminarayanan, and V. Sasisekharan, *Biopolymers* **10**, 1159 (1971).

⁵S. Arnott and E. Selsing, *J. Mol. Biol.* **83**, 551 (1974).

⁶A. V. Lakshminarayanan and V. Sasisekharan, *Biopolymers* **8**, 475 (1969).