

longitudinally oriented (for example, $n \rightarrow \pi^*$ transitions in helical polynucleotides), the spectrum is expected to be hyperchromic⁶, not hypochromic as predicted by Bolton and Weiss.

A more detailed description of this treatment, with applications to solvent effects on solute spectra, is being prepared for submission elsewhere.

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- ¹ Bolton, H. C., and Weiss, J. J., *Nature*, **195**, 666 (1962).
² Kauzmann, W., *Quantum Chemistry*, 579 (Academic Press, 1957).
³ Simpson, W. T., and Peterson, D. L., *J. Chem. Phys.*, **26**, 588 (1957).
⁴ Tinoco, jun., I., *J. Amer. Chem. Soc.*, **82**, 4785 (1960); **83**, 5047 (1961).
⁵ Tinoco, jun., I., *J. Chem. Phys.*, **33**, 1332 (1960); **34**, 1067 (1961).
⁶ Rhodes, W., *J. Amer. Chem. Soc.*, **83**, 3609 (1961).
⁷ Nesbet, R. K., *Mol. Phys.*, **5**, 63 (1962).
⁸ Ref. 2, 578.
⁹ Rich, A., and Tinoco, jun., I., *J. Amer. Chem. Soc.*, **82**, 6409 (1960).
¹⁰ DeVoe, H., and Tinoco, jun., I., *J. Mol. Biol.*, **4**, 518 (1962).

WE have read with interest the preceding communication but we have the impression that DeVoe has misunderstood to some extent both Nesbet's and our work. In the first part of his communication, DeVoe refers to the well-known classical equation for a pair of coupled oscillators with regard to a given direction of the electric field. However, in our treatment of the dimer, it is explicitly stated that our equation refers to isotropic oscillators and averaged over all directions of the electric field vector. We have, in fact, calculated the absorption coefficient for the frequency corresponding to the maximum absorption in the monomer. However, in the case under consideration, this also corresponds to the frequency of maximum absorption in the dimer. In fact, the absorption due to the longitudinal dipole oscillations in the dimer is shifted in frequency (without change of intensity or width) and that due to the transverse oscillations is shifted in the opposite sense, but the mean frequency for the isotropic case (one longitudinal plus two transverse polarizations) is not changed. In the hypothetical case of a very narrow band, this would appear as a splitting, or if the monomer band is already visibly split this would result in opposite displacements of the components. In the cases under consideration we were concerned with a situation corresponding to nucleic acid, where the absorption bands would be too broad (half-width $\sim 300 \text{ \AA}$) for this splitting to be observed. Thus the net effect here is a reduction of the absorption at the peak, which, however, should be compensated by some additional broadening elsewhere so as to preserve the total oscillator strength; there is therefore no violation of the sum rule.

In the nucleic acids there are four different monomer units, the light absorption of which varies quite significantly around 2600 \AA , each unit having two transitions polarized perpendicular to each other. It is clear, therefore, that any theory which is based on very few assumptions can only be regarded as a first approximation for such a complex structure.

The importance of the sum rule in these situations has been emphasized on a previous occasion¹, although in the later paper it was suggested that it might possibly not hold in this case. However, I am reassured now that it is valid and remains so even if the small retardation effects due to the finite distance between the monomer units are taken into account. In any event, neither our calculations nor Nesbet's treatment do, in fact, imply a violation of the sum rule for the oscillator strength. Nesbet² has given a quantum mechanical treatment for the hypochromic effect. This takes as its basis that in quantum mechanics the ground-state of the dimer contains an admixture of the state in which two units are

excited due to the interaction between the virtual dipole moments of the units, which is also responsible for the van der Waals force. This can be interpreted in such a way that as a result of this there exists a radiative transition from the ground state to the state in which three units are excited, corresponding to the frequency 3ν , if ν is the frequency of maximum absorption of the single unit. This frequency, 3ν , is likely to be outside the region normally accessible to spectroscopic observations (in the case of the nucleic acids it would be around 900 \AA) and it would, in general, be masked by absorption processes of a different kind situated in this region. This transition would use up some of the oscillator strength of the polymer, so that the fundamental absorption in the ultra-violet is reduced; there is, therefore, here again, no violation of the sum rule.

In the second part of his communication, DeVoe suggests a theory of hypochromism on the basis of our treatment but taking into account the non-absorbing oscillators present in the system. Such a treatment, although formally correct, raises doubts as to its significance both on theoretical and experimental grounds. DeVoe's statement that such an interaction is without change in position of the absorption band is not correct; in fact, the reduction in oscillator strength to compensate for that which would appear near the resonance frequency of the particular (non-absorbing) oscillator is always associated with a shift in frequency. Moreover, taking, for example, a transition at 2000 \AA , as has been suggested, there is no obvious reason why this should only be significant in the polymer and not in the monomer, as the monomer unit is itself a relatively very large and complex unit which absorbs quite strongly at 2000 \AA .

Therefore, it is not at all obvious, without making very special assumptions, why such a transition in the polymer should be more effective compared with a transition in the same spectral region within the same monomer unit. Moreover, as the interaction between oscillators decreases relatively rapidly with increasing distance, one should expect that an interaction within the same monomer would be more effective. This model would not therefore explain, without very special assumptions, the difference between the monomer and the polymer in any convincing way. DeVoe's treatment of this effect is purely qualitative, as indeed it has to be because the effect must depend on some definite assumptions regarding the number and frequencies of the non-absorbing oscillators which are taken into account, so that the whole treatment would be based on more or less arbitrarily chosen parameters.

Finally, it should be pointed out that in undenatured nucleic acid any hyperchromism at 2000 \AA , or for that matter at any other wave-length in the ultra-violet region, as required by this theory, is not supported by experimental evidence.

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- ¹ Weiss, J. J., *J. Chim. Phys.*, **58**, 924 (1961).
² Nesbet, R. K., *Mol. Phys.*, **5**, 63 (1962).

BIOCHEMISTRY

5-Chloro-2-cyclohexyl-1-oxo-6-sulphamoyl isoindoline : a New Diuretic

THE introduction of chlorothiazide (Table 1, I) in 1957 marked a major advance¹ in the search for improved non-mercurial diuretics. Its advent was followed by a succession of more potent derivatives². Clinically, however, apart from the size of dose, all these derivatives produced a similar therapeutic response³. One of the few disadvan-