diminished ability of some variants (45.6 ICR 4.68, 45.6.3.2 ICR 11.19, and 45.6.2.4 ICR 9) to secrete immunoglobulin heavy chains may confer a selective disadvantage on these cells, thereby allowing us to detect secondary variants in these populations. In contrast, primary variants synthesising heavy chains of molecular weight 40,000 and 55,000 seem quite stable. In the latter case, the heavy chains are assembled well into H_2L_2 (as shown in Fig. 1, panels *a*2 and *b*2) and are subsequently secreted from the cell[3,4]. Consequently, both primary and secondary variants of these stable types are especially valuable since they secrete myeloma protein into the sera of mice bearing tumours induced by subcutaneous or intraperitoneal injection of the variant cells. Thus, structural studies of the variant heavy chains are facilitated.

Many observations suggest that all our variants are the result of mutation: the variants are generally stable and are increased in number after mutagenesis, and the heavy chains they synthesise differ structurally from the parent. In addition, the variants we have seen, whether primary or secondary in origin, seem to fall qualitatively into the four groups shown in Table 1. These groups are defined by size of the heavy chain, assembly characteristics, and serological characteristics even though the members of each group differ somewhat by peptide mapping and, in some cases, by rate of assembly. Perhaps the quantal characteristics of the sizes of variant heavy chains produced will reflect the presence of certain genetic hot spots which are sites of rapid mutation.

On the other hand, the primary variants arise at a remarkably high incidence. For example, treatment of the parental population with 1 μg ml^{-1} of ICR-191 yields unstained clones at an incidence of 2%. One-third of these clones are synthesising altered heavy immunoglobulin chains. These incidences are extraordinary when compared to measurements in bacteria and other mammalian cell culture systems. This observation, together with the spontaneous generation of secondary variants from certain primary variants, makes us question whether the original lesion is within the structural gene dictating the parental heavy chain. It is possible, for example, that exposure to certain mutagenic agents will render a cell generally hypermutable because of an interaction with a regulatory element. It is interesting, therefore, that so far variants synthesising heavy chains of molecular weight 50,000 or 75,000, that is, those which have subsequently yielded secondary variants, have been selected only after treatment with ICR-191. The two stable types, those which synthesise short heavy chains of molecular weight 40,000 and those which synthesise γ2a heavy chains of molecular weight 55,000 have appeared after treatment with either ICR-191 or with Melphalan[3,4,7], a phenylalanine mustard used in clinical treatment of human myeloma. Whether particular primary variants may have an essential instability is a question we are actively exploring.

We hope that the combination of cellular studies with the careful structural analysis of variant heavy chains will help us to analyse the genetic and molecular nature of the variations observed in these cells.

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Annihilation of positrons in D and L isomers of various amino acids

GARAY *et al.*[1] have reported on experiments on positron annihilation in D and L isomers of various amino acids. I show here that one of the two interpretations which they put forward to explain their results is in error, and also discuss other possible experiments which may enable clarification of the rather unusual results they have reported.

In the experiment referred to (paraphrasing the authors' description) 'crystalline samples of D and L amino acids were packed around a 0.8-μCi Na^{22} (positron) source to a thickness of 6–7 mm, and it (source plus amino acid) was placed between two scintillation counters of NE111 plastic scintillator coupled to 56-AVP photomultipliers'. The positrons either annihilate directly, probability $>80\%$ and lifetime $\tau \sim 0.2$ ns, or form singlet or triplet positronium (Ps), with lifetimes $\tau_s \simeq 0.1$ ns and $\tau_t \sim 1$ ns (τ_t is reduced from its free space value of 138 ns by electron pickoff). Using standard fast coincidence techniques the authors find the intensity of the long-lived (presumably triplet) Ps components in D and L isomers of a series of 5 amino acids to satisfy the relation $I_L/I_D = 0.67$ (7), 0.72 (6), 0.82 (5), 0.83 (6), 0.94 (6). The numbers in parentheses are experimental errors and the results of 0.67 and 0.82 come from samples of tryptophan produced by different laboratories. The authors conclude from this data that "... D isomers of amino acids favour triplet states in the case of forward polarised β^- particles. It seems likely from this evidence that β decay was the cause of an initial asymmetry in the racemic mixtures present on the primordial Earth".

The authors interpret these results in terms of a possible correlation between the electron velocity and the electron spin within the sample, $\langle v_\alpha \sigma_\beta \rangle = K\delta_{\alpha\beta}$ where K has opposite sign for L and D and $\langle\ \rangle$ refers to an ensemble average. They also assume that the probability of Ps formation depends on the relative velocity of electron and positron. If then the positrons have a non-zero helicity h ($h = \langle \sigma(e^+) \cdot \mathbf{V}(e^+) \rangle$ where $\sigma(e^+)$ is the e^+ spin vector, $\mathbf{V}(e^+)$ the e^+ velocity direction, and $\langle\ \rangle$ refers to an ensemble average over the e^+ beam) the probability of triplet against singlet Ps formation will vary in switching from L to D. Thus one would expect that the intensity of the short and long components in the time spectrum should depend on the isomer under consideration. Note that in this interpretation it is the helicity, not the polarisation $\mathbf{P} = \langle \sigma(e^+) \rangle$ of the beam, on which I_L/I_D depends. As an instructive example to illustrate this point consider the limiting (and completely artificial) cases in which Ps formation occurs only for $\mathbf{V}(e^-)$ parallel to $\mathbf{V}(e^+)$ and for $K = +1$ for L and -1 for D. If we now note that the spinor direct products $\uparrow\ \downarrow$ or $\downarrow\ \uparrow$ ($\uparrow$, $\downarrow$; $\uparrow$, $\downarrow$ refer to e^-, e^+ spins) give half triplet and half singlet decays one may easily show that the situation $P = 0$ for $h = +1 - 1$ yields $I_L/I_D = 2$ or 0.5 while $h = 0$ yields $I_L/I_D = 1$ for any P.

We now remark that whatever the correlation between Ps formation and relative velocity and whatever the actual (presumably small) value of K is, $h \simeq 0$ at e^+ kinetic energies (~ 5 eV–15 eV) characteristic of Ps formation. This can be demonstrated by noting that experimental[2] and theoretical[3,4] studies have shown that if a beam of electrons (or presumably positrons) impinges on a surface with energy E_0 (10^4 eV $< E_0 <$ 10^6 eV) the beam will have a completely diffuse nature (velocities

completely random) by the time it has penetrated a distance where the mean energy of its constituent particles is still >3,000 eV. This may be most readily arrived at by applying formulas (4) and (5) of Archard[4] for the case $Z \sim 3$–10 (the result is insensitive to Z). Since at energies $\leqslant m_0c^2$ (=0.5 MeV) σ does not follow V (see ref. 5) it follows that $h \simeq 0$. Note that the energy range 10^4–10^6 eV brackets the energy of almost all e^+ emitted by ^{22}Na. In addition, though it is not relevant to the problem, we point out that the geometry of the experiment gives $P \simeq 0$ as well.

We conclude that the effect seen by Garay *et al.* is in all likelihood not a result of positron polarisation or helicity. If real it may be a result, as Garay *et al.* recognise, of the inhibition of Ps formation and/or greater triplet quenching in L as opposed to D, possibly because of an undetected chemical impurity. It may also be caused by some slight difference between the solid state structure of the L and D crystals. If so, a new simple, non-destructive and highly sensitive method of detecting such impurities is now available. Experiments to determine the dependence (or lack thereof) of I_L/I_D and the overall Ps formation rate on P and possibly on h are now being started. To try to investigate the dependence of I_L/I_D on h we may use the low energy positron beam available in our laboratory, if the polarisation of the beam is sufficiently high.

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Conformations of double-helical nucleic acids

A KNOWLEDGE of possible conformational states of double-helical nucleic acids is fundamental to an understanding of how they work[1,2]. Models for a series of conformations have been made on the basis of X-ray data[3–5]. Investigations of nucleic acids in solution point to the existence of a continuum of forms but do not make possible the quantitative determination of the conformational parameters. Here, theoretical investigation of the intramolecular interaction energy as a function of conformational parameters and a search for minimal energy regions in the space of these parameters become essential.

Two families of nucleic acid conformations are known, the A and B families, which differ by the mutual position of the base pairs, the conformational angles in the ribose–phosphate backbone and the conformation of the ribose ring. This last is a major factor determining whether a double-helical structure belongs to the A or B family of conformations. The C_3'-endo conformation in the A family and the C_2'-endo or C_3'-exo conformation in the B family are assumed[4]. Data on the conformation of the ribose ring cannot be obtained from the diffraction patterns of nucleic acid fibres. The ribose conformation is taken from X-ray data for the nucleic acid components. The ribose ring in double-stranded helical nucleic acids is, however, in different surroundings from that in monomer crystals. It may be rearranged in the course of transitions between both the families and the different forms of a family. In this connection, the intramolecular interaction energy of double-helical nucleic acids was considered in our work (unlike the recent works[6,7]) with an account of conformational possibilities of a ribose ring.

We calculated the intramolecular interaction energy for the regular double-helical polynucleotide containing rigid Watson–Crick pairs as a function of eight conformational variables. Four of them determine the mutual position of the base pairs (D is the distance from the pair centre to the helical axis, d the pair–pair distance along the helix axis, θ the tilt angle of the base pairs to the plane perpendicular to the helix axis, τ the rotation angle of one pair with respect to another around the helix axis), four others ($OC_1'C_2'$ and $C_1'C_2'C_3'$ bond angles and dihedral angles τ_1 and τ_2) determine the conformation of a ribose ring. The bond angles of a ribose ring were considered as variables in contrast with other bond angles. The bond lengths were fixed. The eight variables with the above-mentioned

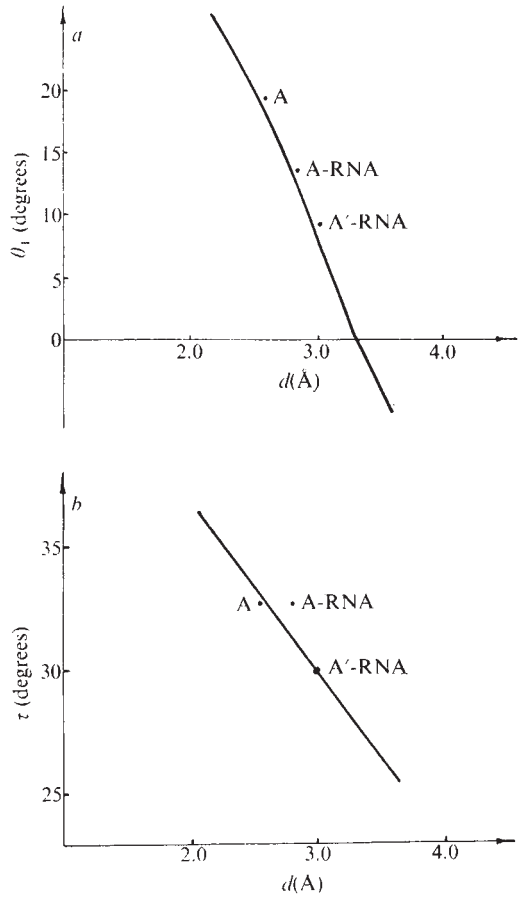

Fig. 2 Projections of the B-family bottom position for the poly(dA).poly(dU): *a*, on the (D, θ); and *b*, on the (D, τ) planes. The known forms are marked.

constraints completely determine the conformation of a regular polynucleotide.

Dihedral angles of sugar–phosphate backbone were determined by means of a procedure which resembles one of Go and Scheraga's[8]. The van der Waals' interactions were calculated by the atom–atom potential function method[9]. The Lennard–Jones potentials were used; the validity of parameters was verified by calculations on nitrogen base crystals. The heats of sublimation and lattice constants of a number of aromatic compound crystals were reproduced (V.I.P., unpublished). The tension energy of the bond angles in the ribose ring was assumed to be proportional to the square of the deviation of these angles from the tetrahedral ones. Previously[10] we studied the interaction energy between the base pairs as a function of parameters determining their mutual position in a double helix. We detected a limited region in the space of these parameters