The chemical formula of DNA is ~~well~~ now well established. It ~~consists~~ is a long fibrous molecule containing purine and pyrimidine nucleotide bases linked together ~~by~~ ~~with~~ 3-5 phospho-di ester linkages at ~~the 3 and~~ 5 ~~positions~~. The back bone of the molecule thus consists of a regular alternation of sugar and phosphate groups as shown in Figure 1. Four different types of nucleotide bases are possible, and as far as is known the sequence of bases is irregular. Two of the possible bases, adenine and guanine - are purines, and the other two - thymine and cytosine - are pyrimidines.

~~Our structure~~ ~~Previous consideration of the structure of DNA~~ Since the chemical formula of DNA consisted of one very long polynucleotide chain, it was generally assumed 4, 6 that its stereochemical structure would also consist of one chain. ~~Crystallographic evidence~~ crystallographic and density considerations however make ~~it most likely that~~ suggested that the ~~crystallographic~~ stereochemical structure must consist of more than one chain. ~~We that~~ We ~~have then have proposed formulated~~ a ~~structure consisting~~ of Our structure therefore consists of not one but two polynucleotide chains both coiled round a common fibre axis, as is shown diagrammatically in Figure 2. The two chains are held together by hydrogen bonds between the bases.

there was only one chain in
It has ~~been commonly~~ often been assumed that since ~~the chemical formula~~
there would only be one in the
the chemical formula ~~there would~~ There would ~~[illegible]~~ This ~~would also be true for the~~
However the
~~logs~~ ~~had only one chain~~ ~~the~~ ~~the sine~~ ~~The x-ray evidence and the density~~ than the density,
structural unit.
4,5 suggests
taken with the X-ray evidence, ~~indicates~~ very strongly that ~~the structural~~
there ~~must be more~~
chain. ~~polynucleotide chain~~ ~~than one~~
~~unit, consists of more than one chain.~~
are probably two.

PP/CR1/H/1/12/7

We should emphasize that while the sequence of bases is indeterminable, the necessity for specific pairing demands a complementary relationship between the sequence of bases on the opposite chains. ~~That~~, If the sequence on one chain is given then the sequence on the other is automatically determined. The ~~one chain is, as it were, the complement of the other~~. Our model, consists, in effect of a pair of chains, either of which can be regarded as the complement of each other. This feature appears to us most important as can be seen by rephrasing the previous sentence to read. Our model consists of a pair of *templates*, either of which we can be regarded as the negative of ~~it~~ each other. Thus if a single chain ~~could~~ acts as a template (or mould) for the formation of its complement, the mechanism of DNA self duplication would in principle be ~~solved~~ understood.

The idea that a single chain could act as a template for the formation of its complement seems reasonable. ~~Our~~ model suggests that this could be done most simply if the single chain (on the ~~[illegible]~~ relevant portion of it takes up the helical configuration of our structure.

Under our the above scheme, ~~of autoreproduction~~ the sequence of the pairs of bases will ~~have been~~ be duplicated exactly. ~~That is as i Due the necessity for specific pairing~~. If, however, a bases occurs in one of the less likely tautomeric forms, at the moment when the complementary chain is formed, a mistake in the copying process will result. For example adenine will normally pair with thymine, but if there is a tautomeric shift of one of its hydrogen atoms it can pair with cytosine. The next time ~~pairing~~ duplication occurs. The adenine would pair with thymine, but the cytosine with guanine. As we do not know the exact energy difference between the tautomeric forms we cannot as yet predict with what frequency mistakes might occur. If the energy difference were ~~was~~ about 20 Kcal, then a mistake would occur once in 109 ~~10 8~~ duplication of one pair of bases, and if we assume that there are 1000 pairs of bases in ~~the~~ a gene this have a frequency comparable to ~~the~~ natural ~~of~~ of spontaneous mutations.

We fel.

of our structure. ~~we imagine~~. Under this hypothesis we would imagine that ~~say~~ at this stage in the life of cell free nucleotides (strictly polynucleotide precursors) become available and join up by hydrogen bonds to one of the bases on the ~~old~~ already formed chain. We would postulate that the polymerization of the ~~new~~ nucleotides to form a new chain is only possible if the resulting chain can form the proposed structure. That is to satisfy the requirement of specific pairing. This is plausible ...

Naturally for this process to ~~work~~ be important, at some stage in the cell division, the two complementary strands must separate from themselves, that is, they must untwine themselves. As the ~~number of~~ ~~turn~~ one turn of our helix occurs every 34 A, a very large number ~~number~~ of untwistings must occur (in fact ~~a~~ 1500 turns for ~~every~~ per molecular weight of 10^6). The postulation of such a large amount of uncoiling, however, does not seem to us an unsurmountable objection to our proposed scheme of autoreproduction, ~~and~~ especially in view of the extensive coiling and uncoiling of chromosomes which occurs during mitosis. While this microscope coiling is on a scale many fold larger than our microscopic coiling, it does not seem unlikely that this coiling ~~could~~ ~~can be~~ is based on a such process on the molecular level.

It is of interest to consider what would happen if a base ~~should. happen to~~ ~~the~~ occurred in ~~one~~ one of its less ~~to~~ likely tautomeric forms at the moment when the complementary chain is being formed. ~~For example~~ While adenine, for example, will normally pair with thymine, if there is a tautomeric shift of one of its hydrogen atoms it can pair with cytosine. The next ~~the~~ time pairing occurs, the adenine (having resumed its more usual tautomeric form) will pair with thymine, but the cytosine will pair with guanine, and thus a mistake will have occurred in the copying process. It seems possible that this ~~might~~ may be the ~~cause~~ explanation of ~~the~~ spontaneous mutation, ~~rate~~. ~~As~~ ~~If~~ The difference in energy of between tautomers under physiological conditions is not known, but making ~~a~~ plausible biological assumptions a difference of about 10 kilocalories would be necessary to obtain the right order of magnitude for the observed rate. ~~of spontaneous mutation~~.

It is ~~not~~ also ~~to~~ possible that one chain of a pair, ~~perhaps~~ under the strain of twisting, ~~might~~ occasionally breaks. The polynucleotide chain remaining intact could then relax the accumulated twist by rotation about single bonds ~~and~~ following this, the broken ends, being still in close proximity, might rejoin. ~~At present~~ ~~[illegible]~~. Such a process obviously bears

~~it is not possible to judge~~ ~~but the fact that they are still~~
~~the plausibility of this suggestion is uncertain~~

it ~~bears close~~ a resemblance
~~note that it is formally equivalent~~ to ~~the theory~~ Darlington's theory of
and may in fact prove a clue to this phenomenon.
crossing over, ~~and may in fact provide a clue for this phenomena.~~
If this ~~process~~ occurs, ~~however,~~ ~~the broken ends must rejoin always rejoin, a~~

~~process~~

Legends to Figures

1. The chemical formula of ~~DNA shown schematically~~ a single chain of DNA.

2. This figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

3. The chemical formula of a pair of DNA chains. The hydrogen bonding is ~~[illegible]~~ symbolized by dotted lines.

~~4~~

~~5~~