

CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA

DIVISION OF BIOLOGY
KERCKHOFF LABORATORIES OF BIOLOGY

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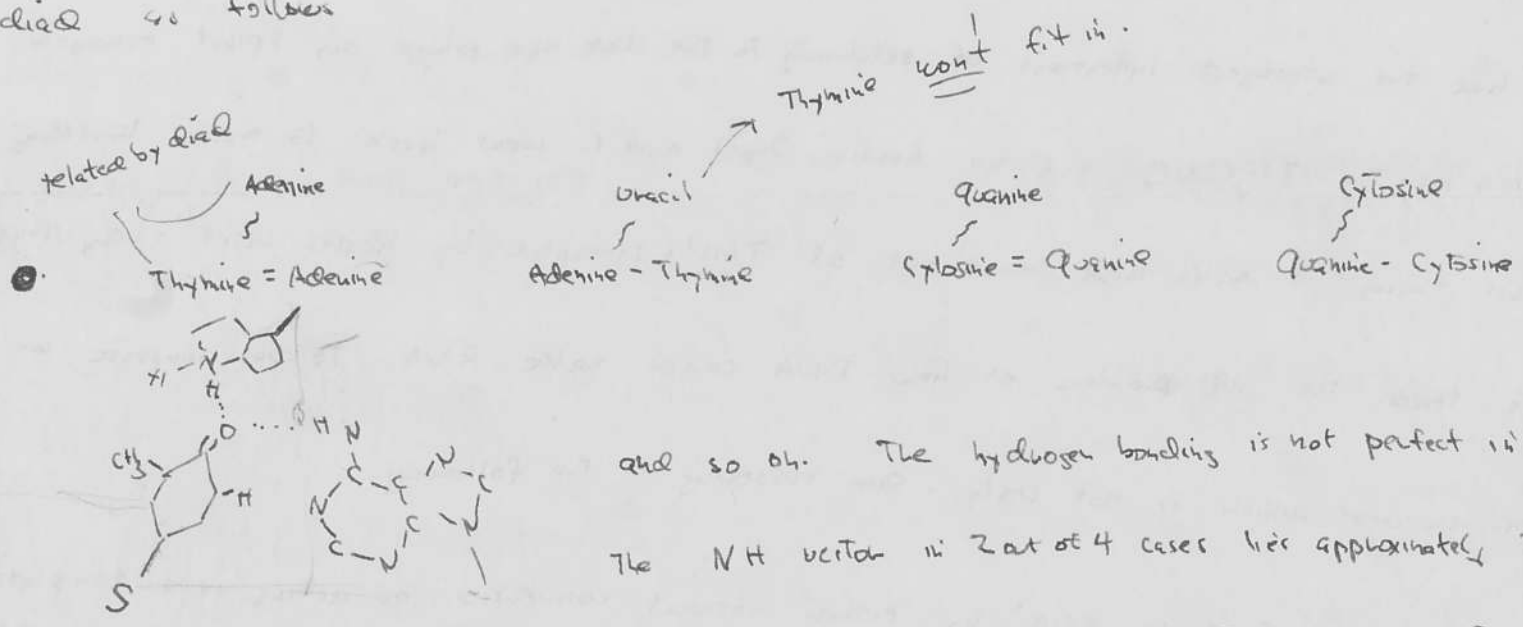
Dear Francis

I have meant to reply sooner but have been rather preoccupied with work. Though I had the strongest intentions of returning to the lab one phase, my spirit remained with RNA and the TIECLUB and so Leslie Ogel and I went back to model building. After first trying to make more sense out of TMV (prompted by Rosie's visit - very amiable!!) we tried the old problem of how DNA could make RNA. To our surprise we have an answer which is not ugly. Our reasoning is the following.

DNA could make RNA by either chemical confusion or acting as a template. The former is ruled out by isotope experiments and so we have to decide whether the two strand or one strand stage of DNA is active. If a one strand stage operates it likely does it by a DNA like base pairing mechanism. The answer in this case is trivial, even if it proved possible to stick a RNA strand in a two stranded structure. Of this I'm sceptical. Moreover I don't like the idea of the two strands having to separate since we have no reason to believe it would be stable. Still now I can't see an easy answer of why ribonucleotides & deoxy nucleotides wouldn't occasionally get mixed up and thus cause mistakes in the replication process.

We therefore consider it likely that the two stranded helix is the functional beast. For an attractive force only by hydrogen bonds need be considered since

under walls forces could not distinguish Adenine from Guanine with the required accuracy. likewise Uracil from Cytosine. Two types can be formed $NH \cdots O$ and $NH \cdots N$. The latter is too weak if used only $\approx 3-4$ kcal and so the $NH \cdots O$ bond must be employed. The requirement is that the 4 base pairs yield 4 specific holes in such a way that a regular backbone (is) of RNA can be formed. We have found only one arrangement which works. It employs a II diad as follows

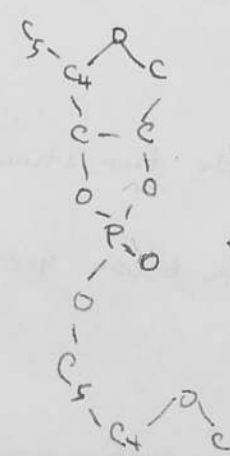


and so on. The hydrogen bonding is not perfect in that the NH vector in 2 of 4 cases lies approximately 20° from the $CN \cdots O$ angle of 120° . However Pauling

and the other chemists are not bothered. The bond is still strong enough to be useful. In this way we define exactly the backbone arrangement of the thick RNA chain. Its diameter is $\approx 15 \text{ \AA}$. At first site this seems nasty especially as the glycosidic angle does not point to wave the center. In fact I don't think it can be built even by cheating with its radius. The main difficulty is the OH groups of the sugar. This problem can be resolved ~~by~~ ^{by} eliminating it to form the cyclic anhydride. When this is

done, a very very pretty helix results in which everything fits nicely. It of course will be ~~need~~ a device to remove the we postulate its anhydride

PP/CRI/D/2/45



helix results in which everything fits unstable but this shouldn't bother us as we RNA once formed, from the DNA. That is to decompose to yield normal RNA

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The scheme is completely hypothetical but yet at the same time structurally possible. I don't have the coordinates yet for the 3rd chain but I know that this will not be an obstacle as there are no bad contacts at all.

It is likely that we shall write up the structure immediately and submit it to the Proceedings of the National Academy. Of course it may be wrong but at least it's a try to find a template in DNA and until a better one comes along, it's useful to consider. As soon as we get a MS, I'll send it to you for comments. The writing should take about 2 weeks.

I was in Cooper's Hole during "Edna" - rather fun - Sgt Gyolgy's cottage was blown to pieces during "Carol" and "Edna" blew the pierce still further away.

besides is Odile, John, Max, etc

Jim

P.S. The first RNA TIE has been woven. More on order
↳ The SMOG IS HELL