



## **I don't believe DNA is a double helix. Does that make me a crank?**

As a student I was taught about the structure of DNA, how clearly the chemical structure reflected the function. I read the almost obligatory James Watson book "The Double Helix", I read the original papers; Watson and Crick had solved the structure of DNA. In fact they had not. The first time a deoxyribonucleotide structure was determined by X-ray crystallography was 25 years later. The Double Helix was a hypothesis, but it fitted the data, and the rest was history.

It was almost 30 years before I thought about it again. During a break in a BioUpdate course, my fellow tutor, Felix Franks, mentioned that DNA could not possibly be a double helix. He made me think, and he made me think that he was right. Watson and Crick had identified the problem with a double helix; it would take a lot of unwinding. As they summarised it "it is difficult....to see how these processes occur without everything getting tangled". But, biologists discovered enzymes which could cut and rejoin the DNA, Nature had taken care of the problem.

What Franks had realised was very simple. Isolated DNA has a *sharp* melting point, the temperature at which the two chains separate. This is inconsistent with a double helix, which takes too much unwinding. Cooling anneals the structure, which can then be melted again. Cycles of rapid strand separation lie at the heart of PCR, but there are no enzymes capable of nicking and annealing DNA in PCR mix. The rapid melting is even more puzzling in the case of circular bacterial "chromosomes" where unwinding would lead to interlinked chains. An alternative structure, which still "suggests a possible copying mechanism for the genetic material" does exist. The same base pairing, the same antiparallel strands, the same sugar phosphate backbone, in fact very similar to the double helix except that the DNA strands are side by side and need no unwinding. In this model regions of Watson and Crick right handed helices are broken by sections of left handed helices.

One molecular biologist remarked to us "I do remember the first side by side model I believe being presented at a Gordon conference in 1977 ...I also remember that the protagonist was shot down in flames at the time." Yet as a hypothesis it is as good as the Double Helix, it just does not assume that DNA is homogeneous throughout its length. I sometimes wonder if a double helix would be the most stable polymorph of DNA; and ask myself "Does it make sense to base life upon the most stable polymorph?"

The Double Helix is now so firmly entrenched in scientific lore, that it is heresy to challenge it. But that one small observation, the sharp melting point, does not go away. Yet to challenge the Double Helix seems to label the protagonist as a crank. Is this based on a critical assessment of the evidence? Or is it embarrassing to think that for almost 60 years we have ignored what does not fit? Watson and Crick did not ignore it!

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