



SALK INSTITUTE
FOR BIOLOGICAL STUDIES

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May 13, 2003

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Dear Mark,

By now you have got my letter confirming what Peter told you. About the C2 symmetry. Jim's account is only partly correct. It is possible that Rosalind reported the C2 (=face-centered monoclinic) in the seminar that Rosalind gave in King's in October 1951 that Jim attended, but even if she did it made no impression on Jim. The MRC report (the committee was set up to make the various relevant MRC units aware of each other's work) that we saw early in 1953 gave the C2 symmetry and also the exact dimensions, of the unit cell of the A form. Taken together with the fact that the diameter of the long thin DNA was about 20Å, the symmetry strongly suggested to me (but not to Rosalind) that the two chains in the structure were anti-parallel, with (pseudo) dyad axes perpendicular to the helical axis. (The dyad relates the position of the bases but not their composition. That is, at this resolution the different base pairs all look much alike.)

Now we know, from Rosalind's data, that the repeat of the B form was about 34 Å, with 3.4 Å between the base pairs (as Astbury had earlier suggested). So there must be about 10 base pairs per repeat. This has the following consequences. If the chains were parallel, with a dyad parallel to the dyad axis then the structure repeats after half a turn, so the screw axis has a vertical repeat of 34 Å, with a rotation of 18° (= 180°/10). On the other hand if the chains are anti-parallel, with the dyad perpendicular to the helical axis, then the structure repeats after a full turn, so the screw rotation is 36° (=360°/10).

Jim did not believe that the symmetry implied anti-parallel chains, so he repeatedly tried to build with a screw of 18°. This is impossible, as there is not room to fit in all the atoms. He asked me to try. I built a backbone with a 36° screw, and showed it to Jim. In spite of this Jim persisted in conceiving models with parallel chains and like-with-like pairing.

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He showed his parallel-chain model to Jerry Donahue, who told him some of his bases were in the wrong tautomeric forms, and said they should all be keto, not enol. It was immediately obvious that we should look at the details of the base-pairing. Jim became impatient, and made cardboard models of the bases in their correct keto form. On the morning of Saturday 28th February he was pushing the bases around and accidentally found that an AT pair matched a GC pair. He was not using Chargoff's rules (which he mistrusted). When I came in I pointed out (what Jim had not noticed) was that his base-pairs implied a dyad axis in the planes of the bases, perpendicular to the helical axis, and that this said that the two chains were anti-parallel. From my point of view the base pairs confirmed the anti-parallel chains deduced from the C2 symmetry, but Jim's view was different. He thought the C2 symmetry confirmed the anti-symmetry deduced from the base pairs (which he himself had not noticed).

So it is not true that the C2 symmetry was not used in constructing the model, but as Jim did not like (probably because he did not understand the argument) the C2 argument, he came to prefer the difficulty of building the backbone with parallel chains (i.e. with an 18° screw) although he had previously ignored this argument. I hope this is all clear!

It would not have been appropriate to acknowledge the C2 symmetry in the paper of 25 April, as this was a short Nature paper with few references. The acknowledgement of the paper was altered to confirm to Maurice's wishes. However, on looking back, we should have thanked Jerry Donahue for putting us right about the tautomeric forms.

We subsequently published a fuller account of our structure in a Royal Society paper. In recent years I assumed we had acknowledged the influence of the C2 symmetry in this paper, but there is no mention of it. Jim tells me that he wrote the paper, as I was busy trying to finish my thesis, but I must have read it before publication. Though this omission is understandable, it is now clear that in that paper we should have acknowledged the influence of the C2 symmetry on our (or at least, my) thinking.

In short, Jim failed to grasp the implication of the C2 symmetry (and did not trust Chargaff's rules) so his account does not agree with mine.

If you have further questions please do not hesitate to write.

Best wishes.

Francis