(1)

Dear Delbrück,

It was very kind of you to send me a copy of your paper, which I ~~was~~ have read with great interest. ~~It is~~ The idea of making systematic breaks had ~~so~~ not occurred to either Tim or myself. ~~and it is [illegible]~~ ~~idea of breaks~~ I have built a schematic model of sine but what I should prefer to do would be to make a proper model of the region near the growing points. This ~~would~~ might show for example ~~[illegible]~~ ~~[illegible] the transphosphorilation [illegible]~~ how plausible the transphosphorilation (nucleotide) process would appear from the stearic point of view. However I have no suitable models here, and I shall have to wait till I return to Cambridge.

As I understand it the scheme of a regular break even 5th link implies that the new pair of chains (near the growing point) lie side-by-side in a definite relationship, otherwise how would the chains know "when to break. However

this is not implausible because after all they do this in the crystalline form of the extrastated fibre. Whether they do so in the paracrystalline form is less certain.

I dear think I should be committed to your scheme unless models show that it might occur as a natural consequence of the spacial arrangements. I admit that irregular breaks are indeed, but I am not convinced that elegance is an essential feature of this part of the process.

or of course if of some really concrete evidence comes up to support it.

The scheme Jim & I favoured has never been fully described in print, and in fact Jim cut down the drafts description in our Cold Spring Harbour paper. It might be worth while therefore setting it out in more detail.

Our scheme, like yours, is postulating that the polynucleotide chains are never really single. That is, we imagine duplication to start as soon as unwinding, and indeed that the former provides the motive power for the latter. The growing point region is regarded as a well defined structure with one pair of chains ~~on one~~ at the top, and two pairs of

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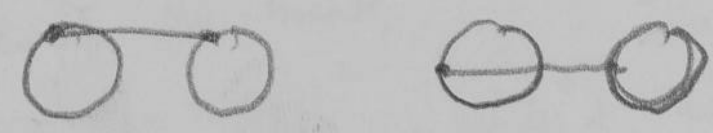
chains at the bottom, ~~at~~ the intermediate region ~~as~~ consisting of the minimum number of ~~one two or~~ three nucleotides.

The first point one would notice is that the ~~[illegible]~~ two-chain structure is probably rather a stiff one. Therefore two such paired chains ~~would~~ could only wind round each other very slowly, and would tend to lie parallel to one another. Therefore for growth to occur the twin pairs must twist relative to the single pair, and indeed the act of growth would tend to generate a couple. The energy of course would come from the fact that twice as many hydrogen bonds were being formed as were being broken. It is also easy to see that mechanically there would be a zipper action, since the two original chains will be further apart ~~in the~~ after growth than before, since they are normally closer together than the diameter of the twin structure. Strictly their average distance after growth would be greater, but if the process is orderly the ~~average~~ distance may be constant, just as the connecting rod on two locomotive wheel has a constant length i.e.



Thus we have a source of energy, a zipper (or lever) action ~~and~~

to separate the two chains, and a couple to produce untwisting.

What, therefore, will resist untwisting? I made a very rough calculation at Cambridge on the viscous resistance, but for short lengths this seemed to small to produce any effect. For very great lengths however it might be sufficient. Suppose therefore that we regard the far end of the original chromosome as fixed. Twisting will then produce a ravelling effect, which will gradually build up a resistance to further twisting. At this point we imagine a break to occur in one of the chains. Since ~~for~~ rotation about single bonds is relatively free this would allow all the accumulated ravelling to ~~wit~~ relax, and the structure would twist rapidly about the remaining single chain until most of the stored-up twist had been relieved. The two broken ends ~~are~~ being still in a very favourable position for rejoining, and ~~we~~ ~~ing~~ since there must in any case be a "joining up" mechanism in the cell for constructing the new chains, we imagined that this same mechanism repaired the break.

In addition to this idea we felt it very probable that the DNA is folded into some sort of superstructure, ~~this~~ on a

larger scale. This ~~was~~ would ~~mean~~ mean that ~~the~~ as ~~the~~ growth proceeded the original structure was unwarily, but most important, the two new chains would, after a short stretch side by side, fold up into the superstructure. This would make it even more difficult for them to get coiled round one another, assuming the superstructure to be rather stiff and compact.

~~The one~~ A new idea that has come up since last summer is that perhaps the breaks dont get repaired, ~~but are already~~ and always exist in the intact struct. There is now considerable evidence that the extracted DNA has breaks in its backbones, and I think the matter is likely to be established beyond doubt within a year. However ~~it~~ these breaks may have been produced during the extraction process, and ~~the~~ evidence for preexisting breaks in the ~~intact~~ ~~of~~ DNA inside the cell may be difficult to obtain. A further extension of this would be to consider breaks as part of the specificity ~~to~~ of the structure. However we know nothing complementary to a break, so it would not be easy to get breaks to replicate, though again a model might suggest a way. Possibly the alternative ~~p~~ pairing of guanine + cytosine (using the ~~other~~ third hydrogen bonding position) might ~~provide~~ ~~a~~ do the trick, ~~if breaks~~ assuming breaks always

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