Dear Crick,

May I congratulate you on your Nobel prize. I hope you will live to enjoy it, though the present news looks as if you might not. If you do, I hope you will consider the following points: DNA is orientated in the sense that ATGG differs from GGTA. But inversions are very common, at any rate in some species. Clearly an inversion either end of which passed through a region concerned with the specification of a protein would wreck that particular synthesis. What is more, it is far from clear how it would join up.

It seems to me that we must consider the following alternatives:

1. A segment of a chromosome can only rejoin as an inversion if the breaks occur in certain regions which do not consist of normal DNA.

2. A strand of DNA, after breakage, can join up in reverse order. If a break occurs in a gene, the gene is disrupted and generally inactivated. This is not rare, but on the whole unusual. It follows that most of the DNA in a Drosophila chromosome is genetically inactive.

3. (most probable). There is another possibility of which I have not thought.

The question which I want to ask you is this. Do you think a reversal of order followed by joining (so that the sugar molecules from some point on were, so to speak, upside down) would disrupt the spiral? If not, is there any way of detecting it by X-ray analysis? Presumably in an oriented preparation you have equal numbers of spirals in what may be called + and - directions. Given this, could you detect breaks?

So far as I know, no inversions have been found in bacteria or phage. This would be expected if most of the DNA was informative. But inversions may be peculiarities of a few groups. I have not followed the literature for the last five years.

Don't trouble to answer in a hurry. Clearly if one could find the number of inversions in a chromosome by physical methods this would be interesting, and might at least be of evolutionary significance.

Contd...
This is a pleasant place. But equipment arrives very slowly. Fortunately a biologist can do a very great deal without equipment.

I am thinking about spirals because my colleague Davis has found the following facts about coconut palms:

1. Left and right foliar spirals are almost equally frequent.

2. The character is not inherited.

3. Lefts produce, on an average, about 20% more nuts per year than rights (highly significant) and have a bigger leaf area (moderately significant). Presumably sugars fit a little better into one sort of spiral than another. "morphology"

Here we are busy studying gene frequencies (particularly colour-blindness) and building by wasps. One female of Polistes olivaceus, which builds paper nests of hexagonal cells, began as follows:—

<table>
<thead>
<tr>
<th>13</th>
<th>12</th>
<th>11</th>
<th>15</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>7</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

You will see that the first 10 cells were built according to the rule: "Left before right, below before above, touch 3 rather than 2 pre-existing cells, preserve symmetry if possible". After number 10 she found it a bit too difficult! The question remains whether such regularity characterises a particular female, a species, or even a family. This species is not very common, and J.D. Jayakar (quite a good mathematician) and my wife are putting in about 10 hours a day on mud nest builders, who also display considerable regularities when treated statistically. I don't think they are up your street, but if Davis' work interests you, I will ask him to send you reprints as they come out.

Yours sincerely,

Dr. F.H.C. Crick, F.R.S.
M.R.C. Laboratory for Molecular Biology,
Hills Road,
Cambridge,
United Kingdom.

J.B.S. Haldane
(J.B.S. Haldane) F.R.S.