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#### X THE INVENTION OF THE 'WARPED ZIPPER' IN NEW ZEALAND

- (266) In the two preceding chapters, I have sought to show that both the New Zealanders and the Indians made rational and well grounded judgements when they decided independently, but for somewhat different reasons, to embark on the research which was to lead them to the SBS or 'warped zipper' model of the structure of DNA. But it is not only the motivation for the invention of this new scientific idea that is susceptible to logical analysis. In this chapter, and the next, I suggest that the process of inventing the SBS structure in New Zealand and India respectively, pace Popper, is also amenable to logical analysis [cf. Popper (1972), p.31].
- (267) As we have seen (chapters I and VIII), Clive Rowe's initial concern about replication in closed circular DNA, led Gordon Rodley and he to the conclusion that the problem lay in the topological dependence of the Watson-Crick double helix, necessitating as it apparently did rapid unwinding of the two exosketetal strands during their separation. Rodley and Rowe therefore decided that it was worth exploring the possibility of an alternative model of DNA. Rowe reports Rodley as having put it this way:

could we not propose an alternative mechanism [of separation] where the key point would be that both strands would be at all times topologically independent?

(268) They could. This chapter consists of reconstruction and analysis of the process of developing a model that permitted

such a mechanism. Popper maintains

If it is the stimulation and release of an inspiration which are to be reconstructed, then I should refuse to take it as the task of the logic of knowledge. Such processes are the concern of empirical psychology but hardly of logic [idem.]

For Popper, and for many other philosophers of science, there is a logical hiatus between the rejection of a previously accepted scientific theory and the appraisal of a candidate successor theory. But, reaching the edge of this gap, the principles which guided Rodley's way forward were not psychological, they were methodological.

(269) He first adopted a tactic subsumed in a canon often thought central to science: conservatism. Rodley says of this very early stage that he "was working on the idea... that any alternative model must look pretty similar to a double helix in order for it to fit the X-ray data as well as the double helix." In characterizing scientific method, Quine remarks:

Conservatism, a favouring of the inherited or invented conceptual scheme...is at once the counsel of laziness and a strategy of discovery [(1960), p.20, emphasis added].

The counsel of conservatism, according to Quine, "is in favouring minimum revision [idem.]." And that is what the New Zealanders sought: the minimum revision to the Watson-Crick double helix consistent with achieving topological independence. Moreover, as is evident from Rodley's remark quoted immediately above, both empirical data by which any alternative structure is to be judged and standard of that judgement were to remain those used in appraising the double helix.

(270) These decisions were based on the belief that Watson and Crick probably had come very close to the correct structure for DNA. Specifically, Rodley did not doubt the semi-conservative theory of replication, Watson-Crick base-pairing rules and structure, that DNA was two-stranded, or even (to begin with) that the strands were helical. And, as we have already noted, neither did he question the validity of diffraction data as evidence of DNA's structure, or of the Fourier method by which proposed models were compared to and refined against it. 58

early inquiries: the need for a sufficient change in the model of the structure of DNA as would permit topological independence and the requirement that whatever change was made be the minimum sufficient change. They operated in different ways. The first was positive, urging a change having a particular effect (though of no specific kind); the second is negative, constraining the degree of change and barring resort to changes in certain particular areas. Both considerations were grounded in reasoning they were not mere intuitions. Moreover, the intended function of these criteria was <a href="heuristic">heuristic</a>; namely, to direct development of new ideas, not to appraise existing ones. The particular areas in the second is negative, constraining the degree of change and barring resort to changes in certain particular areas. Both considerations were grounded in reasoning they were not mere intuitions. Moreover, the intended function of these criteria was <a href="heuristic">heuristic</a>; namely, to direct development of new ideas, not to appraise existing ones. In briefing himself on DNA, Rodley came across Wu's (1969) four-stranded



<sup>58</sup> Sasisekharan, as we saw in the previous chapter, did question these last two assumptions.

However, they were used to appraise the new ideas once they had been devised. Thus these criteria had a dual function, operating in both the context of invention and that of appraisal  $[\underline{q},\underline{v}]$ , (166), and n46].

model  $[\underline{q}.\underline{v}., (12)]$ . The mere existence of alternative models advanced by professionals in the field, and of the debate that they stirred, was important in convincing him of the possibility of an alternative to Watson and Crick's structure which, whilst topologically independent, was very similar in appearance  $[\underline{cf}., (20), (23)]$  and (25). So in this respect, too, Rodley's enterprise was grounded on the rational assessment of evidence.

Crick structure  $[q.\underline{v}., (18)]$ . They were reduced to the barest essentials of interest to him - two right-handed, anti-parallel helices made of coloured wire, string or wool. As such they exhibited the problem, the intertwining of the strands, in the simplest possible way. Base pairing, not being in question, was not represented; nor were the complications of bond angles, interatomic distances, and so on. In short, nothing was modelled but what, for Rodley, was the problematic feature of the double helix - the double helix itself. He then set about finding out how he could re-arrange two right-handed helices, searching for a juxtaposition where the two helices were not interlaced.

#### (273) Judson observes:

A model is a rehearsal for reality.... Building a model, a scientist can reduce an object, a system, or a theory to a manageable form. He can watch the behaviour of the model, tinker with it - then make predictions about how the plane will fly, how the economy will move, or how a protein chain is constructed [(1980b), p.112].

He emphasizes that "modeling, however serious, enshrines an element of play [ibid., p.114]." But it "has an essential aspect of seriousness - it's a way of grasping the way things are [idem]."

Rodley's models of DNA thus made an essentially spatial problem, which is very complex if treated mathematically, visual and palpable, manageable and manipulable. Watson and Crick, too, had stressed the importance of models and model-building to understanding structural hypotheses for DNA from the first  $[\underline{q}.\underline{v}., (66)]$ . In structural chemistry, and especially in structural biochemistry, the scale molecular model is omnipresent.

The advantages of modelling are, however, heavily offset if an attempt is made to represent every feature. Indeed, it may not be clear how to do so (a problem which is overcome by modelling the elements separately, and then attempting to unify them). Moreover, many details are irrelevant to the immediate puzzle, and their inclusion serves only to obscure it. Quine says of simplicity in general, that it "engenders good working conditions for the continued activity of the creative imagination; for, the simpler a theory, the more easily we can keep relevant considerations in mind [(1960), p.20]." For this reason, Judson holds that:

A model is a purposeful and often radical abstraction. It should contain only those elements...that are needed to solve the problem. The least necessary model is the best possible model for the purpose [(1980b), p. 116].

explore the topological potentialities of two helices. This automatically generated potential solutions to his problem. Each permutation of two helices was a candidate by the criteria he had settled in advance - for those criteria had defined what kind of manipulations he would try. Working through the topology of helices in association may seem algorithmic; and, in a way it

is - being essentially a spatial, manipulative analogue of the deduction of theorems from axioms. Each theorem is a possible structural hypothesis. Such a tool should not have its heuristic properties demeaned, for there was purpose in Rodley's play; and we should not need reminding that the theorems entailed by a set of axioms are by no means always obvious - Euclidean geometry is the standard example. In the same way, the topological properties of various arrangements of helices are by no means always obvious either - as we shall see.

- (276) All the same, Rodley did not work with his models only in an analogously deductive way. He varied his assumptions, and promptly arrived at a possible solution to his problem. This was achieved by introducing the idea of one of the helices being  $\frac{1}{1}$  handed. One right-handed and one left-handed helix together looked very like a double, right-handed structure. Moreover, lying  $\frac{1}{1}$  ying  $\frac{1}{1}$  (or, "on top of each other"), they were topologically independent  $\frac{1}{1}$  ying  $\frac{1}{1}$  This initial hypothesis had the merit of satisfying both Rodley's desiderata.
- (277) Rodley does not recall in detail how he arrived at the hypothesis of a left and a right-handed helix in association. He remembers playing with the two helices his schematic models, in the course of which the idea occurred to him. However, it is not difficult to construct a scenario of how he might have done so from two points he mentions. Rodley's modelling materials included a pliable plastic which was readily deformed, permitting rapid creation or modification of a helical forms. Moreover, Rodley observes that turning one right-handed helix upside down

in relation to another results in a relationship between the two essentially similar to an association of one right and one left-handed helix - something which can only be readily appreciated by doing it.

- So, Rodley might have arrived at his first alternative (278) to the Watson-Crick structure either by accidentally building a left-handed helix, or by incorrectly alligning two right-handed helices in relation to one another. Does the fact that, on this reconstruction, the crucial move is unintended invalidate the claim that there was logic in the invention of the hypothesis? I think not. These two possible scenarios I have painted certainly include an accidental element. But, if we ignor the reasoning which lead Rodley into the situation where such accidents might have occurred, we only obfuscate our understanding. There were, as we have seen, reasons why Rodley spent his winter evenings with bits of string, wire, wool and plastic; reasons why each model he made consisted of just two different coloured helices repeatedly re-arranged; reasons why Rodley pounced on a particular arrangement and ignored others. For these reasons (and, perhaps, some non-rational causes), certain kinds of accident were possible.
- (279) However, there is more to be said about left-handed helices as part of a hypothetical structure for DNA than that one can, in certain highly structured and rationally explicable circumstances, accidentally produce them. Left-handed helices are the single most common structural change to the Watson-Crick model that has been suggested. They pervade the entire history

of conformational work on DNA since unwinding was first raised as a difficulty for the double-helical model by Watson and Crick themselves [q.  $\underline{\mathbf{v}}$ ., (65)ff.]. They had then advanced a structure which consisted of equal lengths of alternating double left and double right-handed helical windings in succession [ $\underline{\mathbf{q}}$ . $\underline{\mathbf{v}}$ ., (68)]. Such a structure exhibits topological independence - though, again, this is not obvious without resort to a physical model.

- (280) Watson and Crick's (1953c), in which they make this suggestion, is an extra-ordinary document which prefigures most structural ideas for avoiding or minimizing unwinding that were subsequently advanced with the notable exception of the the SBS model. Delbruck and Stent (1956) reiterate it  $[q.\underline{v}., (50)]$  ff.]; but others were to independently conceive of left-handed helices and superhelices as a way to resolve the unwinding problem: Gamow (1955), Blatt (1955)  $[q.\underline{v}., (78)]$ , Pohl (1967)  $[q.\underline{v}., (23), (24) & (78), Mitsui et al. (1970) <math>[q.\underline{v}., (36)]$  and (37)], and Rowe himself who quite independently came up with Watson and Crick's original idea  $[q.\underline{v}., (9)]$ .
- (281) Watson and Crick rejected the possibility of alternating left and right-handed double helices because they were unable to build a stereo-chemically viable left-handed helix  $[\underline{q}.\underline{v}.$  (68)]. Fuller  $\underline{et}$   $\underline{al}.$  (1965) came to the same conclusion for A-DNA and, on different grounds, B-DNA  $[\underline{q}.\underline{v}.,$  (36)]. These counter arguments were constantly cited as the reason for abandoning left-handed models of DNA of one kind or another (cf., Delbruck and Stent  $[\underline{q}.\underline{v}.,$  (51)], Gorski  $[\underline{q}.\underline{v}.,$  (78)] and Rowe

 $[\underline{q}.\underline{v}., (9)]$ ). The idea kept re-surfacing only to be pushed under.

(282) One recurrence spawned Sasisekharan's interest in an alternative model of DNA  $[\underline{q}.\underline{v}., (35)]$  ff.]. And the issue was around again in the assessment of the result, with Crick  $\underline{et}$   $\underline{al}.$  (1979) confidently - though more moderately - re-asserting right-handedness against the left-handed half-helices of the SBS model  $[\underline{q}.\underline{v}., (100)]$ . No sooner had they done so, than Wang  $\underline{et}$   $\underline{al}.$  (1979) announced the 'discovery' of a left-handed, double-helical DNA, Z-DNA  $[\underline{q}.\underline{v}., (101)]$ . Arnott  $\underline{et}$   $\underline{al}.$  (1980), reporting observation of another left-handed structure, made the point that such conformations could help in understanding how strand separation takes place.

(283) Recurrence of independently conceived, left-handed structures for DNA, in many cases the same or very similar models, is significant because the constant re-invention is accompanied by a repetitious motivation; namely, constant concern throughout the history of work on the structure and function of DNA with the problems caused by the necessity for unwinding. But this does not explain why the results are so repetitive; why, time after time, left-handedness in general features in attempts to solve the problem of unwinding - let alone why particular incorporations of left-handedness (such as the Watson and Crick

of In fact, Watson and Crick were wrong. A stereochemically viable double, left-handed helical model of B-DNA can be built. Nevertheless Gorski and Rowe, among others, accepted Watson and Crick's argument <a href="mailto:ex">ex</a> cathedra, such is their stature.

idea) should recur. Indeed, the difficulty is compounded by the fact that re-investigations were usually not only prompted by the same problem, but also occurred in partial or complete ignorance of both earlier perceptions of the problem and of earlier (left-handed) solutions to it. They were, in short, often nearly or totally independent of each other.

- In one way, this is not surprising. Scientists work in a profoundly non-historical environment. Their training only touches on the high-watermarks of past research in the field, the great papers. Their practice takes them only to the papers published at the leading edge of the tide of research. Backruns of journals gather dust unconsulted, or are even consigned into archives out of sight. As a student one learns that the structure of DNA is a solved problem, and is referred to Watson and Crick's (1953a) as what Kuhn (1977a) calls an "exemplar" [see also Stokes (1982)]. As a post-graduate student learning to specialize in the structure and function of DNA, one learns that unwinding is, by and large, a solved problem having a few out-standing puzzles. 61
- (285) If it is unsurprising that so many scientists should have re-discovered the problem of unwinding, it is not plain why they should so commonly have advanced solutions to it that involved left-handed helices unless, as I suggest, the logic of

<sup>61</sup> A good example is Watson (1970) [see also chapter VIII], though any text, advanced or elementary, will suffice to illustrate the point.

the problem itself directs inquiry toward a left-handed solution. Schematically, the problem which presented itself to many scientists through the 50's, 60's and 70's was this: The Watson-Crick model of DNA, in conjunction with the semi-conservative theory of replication, apparently necessitates strand separation by unwinding. For a variety of compelling reasons, the semi-conservative theory of replication and strand separation should be retained. This locates the problem squarely - unwinding. Unwinding seems to be required by the topological properties of two helices which are anti-parallel, which have the same handedness, and which must be separated intact in fairly long sections. In order to eliminate unwinding one of these five characteristics must be changed.

At one time or another, each was nominated. There were (286)suggestions of more than two helices; for example, Wu (1969) proposed four [q.v. (12)]. Watson and Crick (1953c) and Cyriax and Gath (1978) tried totally non-helical exoskeletal strands [q.v., (68) and (69)]. Parallel or paranemic coiling was tried by Gamow (1955) and Linser (1955) [q.v. (70)]. Extreme fragmentation of the strands, the point where unwinding was not needed, was occasionally contemplated [q.v., (72)]. And, most popular of all, were left-handed helices. On any given occasion some of these possibilities would be rejected. Apart from other objections, employing more than two strands in the exoskeleton was never a popular move because it did not avoid unwinding. Totally non-helical conformations were never shown to fit the X-ray data competitively. Paranemic coiling, as Watson and Crick indicated early on, is not stereochemically viable. Total fragmentation created an enormous problem of co-ordination, control and accuracy. That left left-handedness.

- (287) With respect to coiling and handedness, there are but two alternatives to the Watson and Crick structure. If one does not use pleconemic coiling, there is but one option which is both helical and coiled: paranemic coiling. Though there are several different ways of combining left and right-handed helices, there are only two senses of hand, left and right. Moreover, accepting other Watson and Crick features such as plectonemic coiling eliminates many combinations of the two hands.
- (288) So, in attempting to resolve the problem of unwinding, the handedness of the exoskeletal helices arises as one of only a few possible changes to the Watson-Crick structure of DNA. And if attention is focussed on handedness, the bilateral symmetry of the phenomenon immediately suggests the incorporation of left-handed helices. Just as the topological possibilities of two right-handed helices can quickly be explored with simple physical models so, too, the various ways in which left-handed helices can be introduced into association with right-handed helices can be examined.
- (289) This schematization of the problem-situation of the scientist working on the unwinding problem reveals that frequent independent occurence of left-handed solutions may be explained as the outcome of a logical approach to a persisting difficulty. Rodley's left and right-handed helical structure obviously fits

the schema well; and so it provides a possible alternative explanation of origins of the model.

- (290) Toward the end of 1974, then, Rodley had reached an hypothesis which satisfied his intial criteria of permitting topological independence whilst closely resembling a double, right-handed helix. Nevertheless, the idea was far from mature. It had been invented, but it was not yet ready for appraisal by the scientific community. Rather, it now reached what Laudan (1977) calls "the stage of pursuit", and McLaughlin (1982a) terms "the enhancement stage of the context of appraisal [p.76, emphasis in the original]." A scientist, having invented an hypothesis or theory, tries "to decide whether it is worth adopting and putting to work, or whether it should be tossed back into the jungle of wild conjectures [ibid.,]."
- (291) Rodley's new model had initial plausibility in terms of the criteria which he had first set himself. But it had two hurdles to overcome before it could have sufficient plausibility to be seriously considered as a genuine alternative to the Watson-Crick structure. Firstly, the new conformation had to be shown to be stereochemically viable the bond angles and distances had to be within allowable limits. If that test were successfully overcome, the new model had to have its Fourier transforms calculated and compared against the fit of the Watson-Crick structure with the diffraction data from DNA.
- (292) Rodley used a venerable method of determining stereochemical viability. He tried to build a wire model of DNA, the

bond and angles and distances being represented by soldered pieces of wire  $[\underline{q}.\underline{v}., (19) - (21)]$ . Together with a student, Ross Scobie, he first built a Watson Crick double helix and then tried to fashion a model of his alternative structure. The radius of curvature of the two Watson-Crick right-handed helices is constant. Rodley and Scobie discovered, however, that in order to accomodate the Watson-Crick base pairing scheme which they were adopting in the alternative structure whilst maintaining correct bond angles and distances, the radius of curvature of the right and left helices had constantly to alter. This meant that the alternative structure no longer so closely resembled the Watson-Crick double helix as had the initial simple model which, by its very elemental simplicity, had obscured the difficulty. The differences between the gross appearance of the two structures, in Rodley and Scobie's judgement, were such as to suggest that the new model would not fit the X-ray data as well as the double, right-handed helix. They were sufficiently certain of this not to proceed to test their intuition by comparative Fourier analysis.

(293) Thus, what began as an attempt to enhance the plausibility of the alternative structural hypothesis, ended up greatly diminishing its prospects. So Rodley and Scobie were forced back into conjecture once more; returning to the task of developing an alternative hypothesis. They did this in much the same way as Rodley had done before - though now with the partially assembled full molecular model and not the simple schematic models. Rodley and Scobie pushed and pulled at the wire scale model, twisting the helices this way and that. Once again, they were engaged in

serious play. It was whilst they were doing this that it occurred to Rodley to try to construct the two sugarphosphate exoskeletal strands of alternating left and right-handed <u>half</u>-helices,  $[\underline{q},\underline{v},(21)]$ .

- that had never before been incorporated in a structure for DNA. The first was the use of discrete half helices. The second was the combination of half helices of opposite hand in a single strand, resulting in a structure which was not helical. This was the first non-helical structure for DNA since that advanced unenthusiatically by Watson and Crick in their (1953c) [q.v., (68)]; and it was the only non-helical structure to employ elements of helices of both possible hands.
- (295) Again, Rodley does not remember how he had devised the core idea of what he was to call the side-by-side model of DNA. He can only say that, just as had happened earlier, it occurred to him whilst he and, on this occasion, Scobie were pushing and pulling at the wire molecular model they had built to test the first proposal. Are we then to conclude that we have reached a limit to the explication of the rational elements to this invention? I think not.
- (296) Rodley was interviewed by the author several years after the event he was asked to recall; an event of a kind which he like any other scientist— is not encouraged to remember. Scientists are as susceptible to the prevailing dogma that there is no logic in invention as are the philosophers who devised it.

For a practicing scientist, nothing seems to hang on remembering how one arrived at an original idea. Yet it is hardly plausible to suppose that Rodley and Scobie played with their model thoughtlessly and without discussion of what they were doing.

- (297) In these circumstances, I do not propose to indulge in a 'rational reconstruction' passed off as history. Such 'history' with-the-truth-in-the-footnotes correctly annoyed many readers of Lakatos (1970). Nevertheless we may, I think, attempt to understand how Rodley and Scobie could have, and so might have arrived at the 'warped zipper' model without, however, pretending to claim that that is how they actually did it. This may be the original, and is certainly a legitimate sense of the term 'rational reconstruction'.
- can be achieved by examining either a three dimensional model of the double helix, such as Rodley had before him, or a two dimensional representation of it, such as may be found in Figure 11(a). Both provide visual cues to depth which, together with knowledge of what a helix looks like and the fact that one knows one is looking at a model of a helix, lead one to see it three-dimensionally as a helix. Attend to only one of the two right-handed helices represented in Figure 11(a). Try to ignore the other helix. Now try to ignore the visual cues to depth which help you interpret it as a helix, and see it, instead, as a two dimensional diagramme. Using the accompanying schematic representation of the SBS structure [Figure 11(b)] as a guide, and again attending only to one of the two strands, try to



re-interpret the helix as a 'zipper strand'. When one has a clear understanding of what the three-dimensional sine-curve of a single SBS strand looks like (think of a strand of wool unravelled from knitting) compared with a helix, and with practice, a model of either can be deliberately interpreted as one of the other by the process of <u>Gestalt</u> shift.

- a student is led to re-discover, to re-invent an idea most familiarly, a mathematical theorem and, secondly, they are the techniques by which inventions are made in the first place. This latter kind of heuristic, in turn, can be of two sorts: general principles of invention, or particular instanciations of such principles by means of which actual inventions were made. The heuristic by means of which an invention is devised may, of course, be used in order to re-invent it. Indeed, it might be well argued that re-inventing an idea by using a putative original heuristic establishes at least that it could have been the actual heuristic used in the original invention.
- (300) The experiment in perception which I have asked the reader to perform is not quite of that kind it utilizes know-ledge of both the double helical and the SBS schemata. Nevertheless, the <u>Gestalt</u> shift involved does permit us to see how the same perceptual data can be interpreted in two quite different ways. Moreover, it seems clear that one could experience the <u>Gestalt</u> without first seeing the 'warped zipper'. Having that model provides a prompt and directs the imagination, but does not appear to be necessary for the imaginative leap to

occur. Thus the role of imagination is obviously central. But so is the heuristic function of even a single, double-helical schematic model. For even alone it constrains and directs the creative imagination - and in no merely accidental way. As we have seen, Rodley had determined from the outset that whatever alternative to the double helix he devised, it must look very similar to the Watson-Crick model.

- (301) Having now the germ of another new idea, Rodley and Scobie turned again to the enhancement phase. Firstly, the wire model had to be properly made, and this required a decision as to the frequency with which the strands were to change handedness. The two men settled on what seemed the <u>simplest</u> arrangement each partial helix was to be a half-helix. Since they were consciously seeking to imitate the Watson-Crick model as closely as possible consistent with topological independence, they used the same pitch and diameter as the double helix for the half helices. This meant that the change of handedness occurred every five base pairs. The resulting structure seemed to be stereochemically viable, and so had passed its first plausibility test  $[\underline{q},\underline{v}, (25)]$ .
- (302) The next hurdle was 'fit' with the X-ray diffraction data. At first Rodley and Scobie tried out the technique of obtaining optical transforms of the model itself in order to

<sup>62</sup> Later refinement was to reveal some close contacts, and the limitations of wire models (as against Pauling-Corey spacefilling models) disguised others.

compare them with the crystallographic photographs. But Rodley was not familiar with this approach, and so not confident of its results  $[q.\underline{v}., (26)]$ . Rowe, however, interested the electrical engineer, R.H.T. Bates, in the project. Bates was familiar with the mathematics of Fourier transforms and, despite an initial skepticism, Bates and one of his students, R.M. Lewitt, undertook to calculate the theoretical (Fourier) transforms of the SBS model and compare their fit with the diffraction data to that of the Watson-Crick model. They quickly confirmed Rodley's hopes - the SBS structure produced the characteristic crosspattern exhibited by the B-DNA diffraction photographs and predicted by the Watson-Crick model. More precise calculations appeared the confirm that the 'fit' of the two structures was comparable  $[q.\underline{v}., (27)]$  and (28).

(303) The New Zealanders were jubilant - they believed that they had 'discovered' the structure of DNA.  $^{63}$  The SBS model now appeared to have passed through the enhancement phase successfully. The model had already been shown to a local crystallographer informally  $[\underline{q}.\underline{v}., (26)]$ , it now entered the context of appraisal proper as the New Zealanders began to prepare a paper for publication. The 'warped zipper' was, they judged, sufficiently plausible to face appraisal by the specialist scientific community [see (30)ff., and V].



The fact that the specialists on the structure of DNA were to disagree serves to illustrate, among other things, that the sensation of discovery ('Eureka!' - 'I have found it!') may be subjective, and not objective; a state of mind, not necessarily a state of affairs [q.v., (137)ff.].

- (304) In this chapter I have tried to show that the creative process which led to the invention of the 'warped zipper', examined closely, is penetrable and revealing. The New Zealand version of the SBS model was the outcome of conscious thought as well as of unconscious inspiration. Particular methodological assumptions and requirements were developed and deployed using specific techniques. Together they constrained, directed and facilitated creative thought, inspiration and even accident toward two successive alternative proposals. Similar standards constrained, directed and facilitated the appraisal of those proposals, favouring one and eliminating the other. As a result the advent of the SBS structure in New Zealand is significantly explicable by apppeal to reason as a cause.
- it consists only of a set of deductive and inductive relations leading to the 'warped zipper'. Certain accidental occurrences and psychological properties of perception have been adverted to. Nevertheless, and this is the key point, if only the non-cognitive features of the analysis I have presented are considered, then a great deal is left to be explained. To take but one example; at least two structures for DNA have been advanced which are totally non-helical [q.v., (68) and (69)]. Yet the New Zealanders never considered trying to devise such a structure. Is this to be 'explained' merely as a failure of the imagination? Again, I think not.
- (306) As we have seen, one guiding considerations was to make only the minimum necessary changes to the Watson-Crick

double helical model. To abandon helices totally is a radical departure. It is a departure that might have occurred to New Zealanders eventually - after all two other groups have apparently independently done so, and produced pretty similar alternatives. But, given their conscious methodological conservatism, Rodley and his colleagues began by making less extensive alterations. Similarly, the determination to keep closely to the Watson-Crick model explains why, when they did arrive at what was, strictly speaking, a non-helical structure, Rodley and his colleagues combined half-helices. Thus deliberate methodological conservatism, a rational principle, and not poor imagination, a psychological property, explains the Zealanders' failure to consider the possibility of a a purely non-helical structure.

(307) One of the most striking facts about the invention of the 'warped zipper' structure is that it occurred quite independently to that of another another group in India at roughly the same time. In itself, this begs for an explanation. The obvious kind of explanation for an inventionist to offer is that, at least in part, the phenomenon occurred because of the similarity of the logic in the situation of both groups. I turn now to an analysis of the invention of the SBS model of DNA in India by Sasisekharan and his co-workers.

- (308) As we have seen, the main motivation for the research leading to the development by Sasisekharan and his co-workers' of the SBS model for DNA lay in their perception that the standards by which the adequacy of the Watson-Crick structure had been appraised were insufficiently stringent (see chapters II and IX). Sasisekharan's desire to devise and implement a better methodology of assessment was prompted by his examination of a suggestion that one crystalline form of DNA, D-DNA, might be a left-handed double helix.
- (309) Not only did Sasisekharan conclude that current techniques of testing were not as systematic as they could be made, but also that artificially rigid assumptions concerning the bond angles of the constituent atoms of the DNA molecule may have been built into it. A possible, and equally artificial effect of this was to favour some particular structure against a number of different conformations [q.v., (40)].
- (310) Sasisekharan's disposition to try to fully exploit the potential of computer technology to improve the methodology of appraisal of structures for DNA has also been noted. He took advantage of the good computing facilities available to him when at Princeton to begin systematic investigation of the effects of the permissible bond angle flexibility on mononucleotides and dinucleotides. This preliminary work suggested that both double right and double left-handed helices were consistent

with the acceptable range of bonding angles  $[\underline{q}.\underline{v}., (40)]$  and (42). But this work was interrupted by Sasisekharan's move to Bangalore to take up the Chair of Molecular Biophysics at the Indian Institute of Science.

- (311) It was there that the main investigation began though only after a delay of two years arising from the difficulty of finding suitable and enthusiastic collaborators  $[q.\underline{v}., (42)]$  and (43). Once Pattabiraman and, later, Gupta joined the enterprise Sasisekharan was able to commence his programme in ernest. There were three basic propositions or 'boundary conditions' which the Indians shared with the New Zealanders and the specialist community: Watson-Crick base-pairing, "because there is no doubt that it is the chemical basis of genetics",  $^{64}$  stereochemical viability (i.e., no close contacts), and agreement with the crystallographic data  $[q.\underline{v}., (46)]$
- ekharan, as they had the New Zealanders, to the past successes of research in terms both of first order structural and second order methodological theory. Both groups focused their attention on the exoskeletal structure of DNA. Moreover, both began by working with a double-helical conception of it. Though they were not as much in the forefront of the Indians' concerns as they

<sup>04</sup> Ultimately, both the New Zealanders and the Indians were to question details of the Watson-Crick structure for base-pairing, but not the basic concept itself - for the reason that Sasisekharan gives here  $[\underline{q},\underline{v}]$ , (130).

were for the New Zealanders', Sasisekharan observed when I interviewed him that he and his colleagues

always bore in the back of our minds the various problems associated with the [Watson-Crick] double-helical model.... For example, the unwinding process.

- (313) Unlike the New Zealanders, Sasisekharan however, already had an alternative model whose merits he and his coworkers could consider - the <u>left</u>-handed (but otherwise Watson-Crick) structure advanced by Mitsui et al. (1970) which had sparked off the project. Nevertheless, Sasisekharan's approach did not involve direct and immediate comparison of the two models, as would normally have been done. Rather, as we saw in chapter IX, he had determined on a more systematic approach. In keeping with this, Sasisekharan set Pattabiraman the task of completing the bond angle flexibility work that he had begun in Madras, and continued at Princeton.
- (314) Pattabiraman confirmed that the bond angles of the sugar phosphate exoskeletal molecular structure of a mononucleotide could vary considerably whilst remaining stereochemically acceptable. Then Sasisekharan asked Pattabiraman to explore thoroughly all the possible stereochemically viable conformations of a polymer of DNA built of such a flexible monomer. Although there was the constraint that all such structures must conform to Watson-Crick base-pairing (the question of fit with the crystallographic data being deferred), this was a formidable task. As was noted at (47), nine or ten flexible parameters admitted of between 36 10 and 36 13 possible combinations!

- investigations entirely on a computer, solving at once for a polymer model. In principle, this would have yielded a complete catalogue of the polymer structures consistent with both the chemistry of the exoskeletal atoms and the core of bases, together with their structure. But the computing facilities at Bangalore were inferior to those at Princeton which had spawned this ambition. This meant that the job had to be broken into sub-sections to be worked on separately. Moreover, the hope of eliminating physical scale models in favour of computerized mathematical models had to be abandoned for the former were now needed to enable Pattabiraman to grasp the way in which work on the sub-sections related to the polymer as a whole.
- (316) These concessions to practical limitations were more than methodologically annoying. They complicated and clouded the work - leading Pattabirman to elicit only right-handed, helical structures. But, encouraged by Sasisekharan to persevere, he found that left-handed conformations, too, were consistent with the criteria  $[\underline{q}.\underline{v}., (48)]$ . Even so, at this stage they were dealing with a single-strand, left-handed structure which was stereochemically viable and fitted with the base-pairing conformation. It was necessary to find out, first, whether the same could be said of a double, left-handed model and, second, whether such a model was comparable to the right-handed Watsonfit with the X-ray diffraction Crick structure in its photographs.
- (317) Again Sasisekharan was as thorough as he could be. He

explored the position not merely for the B form of DNA (thought to be that present in vivo), but also for the D form that Mitsui et al. (1970) had considered, together with A-DNA and C-DNA. All of that took some time, but was eventually completed. A double-helical structure for DNA, whose handedness was opposite to that of Watson and Crick, but which was in all other respects essentially the same, appeared both stereochemically viable and as good a match with the crystallographic evidence (calculated by comparison of theoretical with the observed Fourier transforms) as was the older model [q.v., (49)].

- (318) If the Indians had proceeded no further their tactics would have been vindicated. As was discussed in the chapter X, left-handed models of DNA have been by far the most common and popular alternative to the Watson-Crick structure. Notwithstanding this, they have been as frequently rejected as they have been proposed. Though the precise details of the grounds for this rejection have varied, they have all turned upon a claim that it is not possible, a priori, to build a stereochemically viable, left-handed, double helical version of at least one of the various crystallographic forms of DNA (i.e., A-DNA, B-DNA, etc.) In the event, it was the a posteriori 'discovery' of the left-handed Z-DNA which finally brought this line of argument to an end and revitalized interest in the arguments of Mitsui et al. (1970) [q.v., (99)ff.].
- (319) Though their theoretical work on left-handed helical conformations was never published, the team led by Sasisekharan totally undermined the argument which had been used against



their existence by demonstrating that left-handed double-helical conformations were possible, indeed good alternatives to the Watson-Crick structure. And this had been done just exactly by improving (as far as was practicable) the techniques which had been used hitherto. But the improvements were, in essence, not to the refinement and testing of models of DNA's structure - there Sasisekharan proceeded fairly conventionally. Rather, it was in respect of the question of how such models where generated that Sasisekharan made his major contribution.

in the context of appraisal. As was shown earlier (chapter IX), Sasisekharan wanted to be sure that every possible structural hypothesis was exposed to the standard requirements of stereochemical viability, and consistency with the Watson-Crick basepairing, together with the crystallographic data on structure. Sasisekharan argued that only when assessed by those criteria could one be sure that whichever structural hypothesis seemed best by those criteria was truely the best of all possibilities. Therefore Sasisekharan needed some way of obtaining all the possible conformations within the constraints he accepted. In short, he needed and, in principle, developed a heuristic, a technique of invention which was required in the context of appraising models of DNA. 65

<sup>65</sup> However, whilst Sasisekharan did devise such a heuristic in principle, the limitation of computing facilities not fully adequate to the purpose meant that in practice he could not claim to have achieved his goal. As a result, the SBS model of DNA was not revealed by this technique alone.

- (321) The problem of unwinding now moved from the back to the fore-front of Sasisekharan's mind. A student brought to his attention Delbruck and Stent's (1957) discussion of the problems inherent in unwinding, and of one possible way of dealing with them alternating lengths of double right and double left-handed DNA  $[\underline{q},\underline{v}]$ , (50)ff.). 66 Delbruck and Stent had rejected this idea for the usual reason Watson and Crick's inability to construct stereochemically viable left-handed helices. But Sasisekharan knew that they and others [e.g., Fuller et al. (1965),  $\underline{q},\underline{v}$ , (36)] were wrong on this point: he knew that such structures could be built for all sub-variants of DNA.
- Thus Sasisekharan asked himself whether there might not be something to this idea after all  $[\underline{q}.\underline{v}., (52)]$ . Not only would it avoid "tangling the two chains", but it seemed to help with another difficulty. Despite decades of refinement there were still stereochemical difficulties confronting the Watson and Crick model of DNA. There were some problems in the detail of straight lengths; but these paled into insignificance beside those which arose when a model was built to simulate the superhelices and, especially, the convolutions which were exhibited  $\underline{in} \ \underline{vivo}$ . Here work had been, and still was plagued by close or short contacts between adjacent, unbonded atoms.
- (323) We have already seen that Sasisekharan was concerned

<sup>66</sup> If a length of right-handed double-helical DNA is succeeded by a double, left-handed section of exactly the same length, the resulting conformation is topologically independent. This is not intuitively obvious; but is easily demonstrated with a simple model  $[\underline{q},\underline{v}]$ , (275)ff.].

with the degree of inflexibility somewhat artificially imposed upon the Watson-Crick structure for DNA. But, even with the greater flexibility that he had discovered was stereochemically possible, Sasisekharan realised that a wholly double-helical conformation of DNA (right or left) is still rod-like in its rigidity  $[q.\underline{v}., (53)]$ . But, he reasoned, if one were to combine right and left-handed helices, this would not only resolve the unwinding problem, it would also, simultaneously, provide a solution to the inflexibility of the structure.

- feature arises. It derives from the necessarily non-helical joint between left-handed and right-handed helices. For it is the geometry of helices themselves which causes the rigidity in the structure. At the point where two helices of opposite hand abut, the topology cannot be a helix; and the shape which is described is far more tolerant of bending without introducing close contacts. (This join-shape is essentially that employed in the SBS model of DNA.) Since it is the non-helical joint between helical conformations of opposite hand that introduces flexibility, the more such joints occur the greater the flexibility of the resulting structure.
- (325) Thus the requirement of maximizing flexibility suggests maximizing non-helical joints between helical conformations of opposed hand. In addition, the need to have a conformation which minimized unwinding suggested that the helical conformations between the non-helical joints should be of equal length  $[\underline{q},\underline{v}]$ , fn 66]. Any departure from this arrangement re-introduces the

need for some unwinding. These two criteria are not conflicting and it was in following the first to its logical extreme that the Indians were led to the SBS structure for DNA.

- have a flexible model, you need both left and right [handed] helical sections [emphasis added, q.v., (54)]." Maximizing flexibility entailed progressively shortening the length of the equal, opposite-handed lengths until they are only one repeat (one helix, ten base pairs) long. Taking the process further eliminates all fully helical conformations, leaving only helical sections of opposite hand and equal length. Proceeding in this way one comes to the most regular (symmetrical) combination of helical segments of opposite hand two half helices of opposite hand. Because it is the most symmetrical, such an arrangement yields a joint-curve of greatest radius, closest the curvature of the half-helices themselves. This helps to provide a stereochemically acceptable joint.
- at the essence of the SBS structure. A new structural hypothesis had been born. And the point which arises out of the analytical account which I have given of the process, is that this new idea, soon to be dubbed the "warped zipper", was the outcome of, and is explicable in terms of the criteria which guided it. There is nothing surprising about the reasoning process that I have outlined. There are no miraculous inspirations. The SBS model did not occur suddenly, out of the blue. Rather, it was the result of systematic application of the criteria which

defined the Indians problem, constraining and directing their approach to it.

- The Indian invention of the SBS model probably would (328) not have occured had they not established that left-handed double helices are stereochemically viable. It was that which made Sasisekharan receptive when one of his students came across the reference to Delbruck and Stent's (1957) discussion of eliminating the unwinding problem by resort to left-handed helices. Quite possibly Sasisekharan would otherwise have accepted their rejection on stereochemical grounds (following Watson and Crick). The student's unearthing of this old paper may seem to have been an accidental occurrence pure and simple. But Sasisekharan, sensitive to the problem of unwinding, was at that time teaching a course on replication, his student's enquiries were motivated by his discussion of the problem posed by unwinding and, consequently, Sasisekharan immediately perceived the utility of the right and left handed model in resolving it.
- (329) But Sasisekharan's preoccupation with the question of stereochemical viability had, as we have seen, a multiple function: It motivated him to try and develop a model of DNA which had the flexibility to avoid the close contacts which plagued super-helical and convoluted Watson-Crick structures. It focussed his attention of the non-helical joint between two helices and towards maximizing such joints. Finally, the issue of sterochemical viability determined the half left, half right-handed helical mix.

- (330) But this alone does not suffice as an explanation of the Indian variant of the "warped zipper". For example, the Watson-Crick/Delbruck-Stent alternating left and right-handed double helical model could have caught their attention and led them to move into the 'enhancement' phase. To understand why this did not happen, why the process of invention was pursued further, it is necessary to take into account Sasisekharan's concern with maximizing structural flexibility.
- (331) Having arrived at a conformation which satisfied the various requirements demanded, the Indian group now entered the enhancement phase. Firstly, just as the New Zealanders had done, Sasisekharan and Pattabiraman built a wire model as a rough check on the new model's stereochemical viability. It passed this preliminary test, justifying application of the computer in conjunction with Pauling-Corey space-filling models (the latter perforce, because of the limited computing facility).
- (332) Gautam Gupta now joined Sasisekharan and Pattabiraman. Sasisekharan divided the task between the two post-graduates. Pattabiraman concentrated on exoskeletal conformation; Gupta, base pairing structure and its junction with the paired, sinecurving strands. Just as the boundary between the context of appraisal and that of enhancement is blurred, 67 so too is that

<sup>67</sup> For example, the judgement of one's collaborators clearly falls into the context of appraisal. But the Indians were to 'try out' their ideas first on their colleagues, and then at a seminar, before finally seeking to publish them [q.v., (60)].

between the context of invention and that of enhancement. Building a wire model of the SBS model thus served both as a preliminary test and required a more detailed fleshing out of the original concept. Still further testing and elaboration of the "warped zipper" idea was combined in the use of more sophisticated techniques. This was not mere detailing. Confirmation and disconfirmation occurred and, in the process, the Type II SBS model, was invented.

- an early conclusion of Pattabiraman's work. Although the bond angles that are sterochemically permissible between the atoms and atom-groups of DNA are not fixed, neither are all variants equally favoured. The "conformational energy" required to establish and maintain the various arrangements varies and, in general, that which requires the least such energy is preferred as "energetically favourable". Pattabirman investigated the comparative energetic favourability of left and right-handed helices and found that it depended on the particular base pairs around which they curved [q.v., (55)].
- (334) This raised the question of the base-pairing structure which had, hitherto, been adopted wholesale from Watson-Crick. This assumption, Sasisekharan decided, now needed investigation. In particular, he singled out for Gupta's attention the fixed but apparently arbitrary face-orientation of Watson-Crick base-pairing  $[\underline{q},\underline{v}]$ , (56). Some results of this new inquiry were very encouraging. Unmodified Watson-Crick base-pairing was shown to be compatible with both left and right-handed half-helices. And,

inverting the customary base-pairing arrangements was seen to be stereochemically acceptable - moreover energetically favourable at bend-regions (where the two half-helices met) compared with Watson-Crick orientations  $[\underline{q}.\underline{v}., (56)]$ . One result arising from the Indians' investigation of the base-exoskeleton interaction was quite surprising. Inverted base-pairing did not appear to be relevant to the energetic favourability of the left, compared with the right-handed half-helices. But the particular order of bases (which sequence of five A-T or G-C pairs occured) did seem important. Some sequences of base-pairs favoured a left-handed exoskeleton, whereas other orderings of the A-T, G-C pairs indicated a right-handed exoskeleton would be more energetically favourable.  $^{68}$  One result, however, was disconcerting. The SBS model with standard base-pairing (no inversion) at the bendregion exhibited worrying close contacts at just that point. However, when inverted base-pairing was employed, these were relieved.

(335) The energetic favourability and lack of close contacts of an SBS model with inverted base-pairing at the bend or joint region between the two opposite-handed half-helices meant that the Indians now had a second variant of their SBS model with this feature - a new invention emerging from the enhancement process. The original model, with the customary base-pairing

Thus Sasisekharan was not surprised when left-handed Z-DNA turned up, complete with an exoskeleton whose handedness and finer structure were determined by which bases were at its core [q.v., (101)ff.]. In the Watson-Crick model the pairs A-T or G-C are required but their sequence (the genetic code) is entirely unrestricted and structurally irrelevant.

arrangements (and close contacts), was dubbed Type I; and the new variant (evidently stereochemically satisfactory), Type II.

into the context of appraisal by presenting it at a seminar in the Indian Institute [q.v., (60) and fn 67]. Thorough by nature and cautious of his reputation [q.v., (59)], Sasisekharan discussed only the Type I structure. He was more worried about the possibility that the inverted base stacking of the Type II conformation was an unnatural artifact of the model-building process than he was by the close contacts of the Type I structure. Encouraged by the response - and under pressure to publish even before it - the Indians group began to prepare a paper [Sasisekharan and Pattabiraman (1976), q.v., (58) and (60)].

(337) Gupta's investigations had persuaded Sasisekharan that inverted base-pairing of the Type II model was a commonly reported phenomenon in molecules similar to DNA  $[\underline{q}.\underline{v}., (58)]$ , and his concern over the close contacts of the Type I model was alleviated by an appreciation the problem as a persistent one even for refinements of the Watson-Crick structure. Aware that he was lowering his standards somewhat in respect of this latter

These were the same close contacts which the New Zealanders discovered when they came to specify and refine their model of the SBS structure [q.v., (32) and fn 9]. Ultimately, they also led the New Zealanders to try to devise modifications to the Watson-Crick base structure in order to eliminate them. But the New Zealanders' approach was not that of the Type II Indian SBS model. Instead of inverting base-pairs, they staggered the base alignment out of plumb [q.v., (130)].

question, Sasisekharan nevertheless decided to exhibit Types I and II in this first paper. He came to regard this as having been a mistake. Refinement undertaken after the appearance of the first paper convinced Sasisekharan that the close contacts of the Type I model were irremediable. Thus, by the standard of stereochemical viability that Sasisekharan had set himself at the outset, it had to be abandoned. This was announced in a second paper [Sasisekharan, Pattabiraman, and Gupta (1978), q.v., (62) and (63)].

- into the context of appraisal, and out of our scope here. The invention of both variants of the "warped zipper" model in India is, as I have shown, a product of a conscious attempt to develop and apply thorough and explicit new methodological techniques which involved a conscious awareness of the possibility that comparable alternatives to the Watson-Crick double helix might exist. From the beginning, Sasisekharan and his collaborators had in mind equally explicit problems in the Watson-Crick structure for DNA as well as in its refinement and testing. These focussed and directed their work, and the kind of alternatives they sought and settled upon.
- (339) In all of this, of course, serendipity influenced the course of events for example the re-discovery of Delbruck and Stent's discussion of ways to resolve the unwinding problem, and the ironic manner in which Saisekharan first became interested in the method of appraising proposed structures for DNA. But the invention of the SBS model in India cannot be understood as a

chapter of fortunate accidents. Indeed, their significance itself derives from the <u>cognitive</u> context in which they occurred.

(340) A complete acount of the invention of the "warped zipper" would have to include a number of important sociological and psychological features which have been passed over in this analysis. Why, for example, did Sasisekharan have the problems he did in recruiting collaborators  $[\underline{q},\underline{v}, (42)ff]$ ? This and other interesting features of the process, together with aspects of the appraisal of the new model, I have considered elsewhere [Stokes (1982)]. They are not dealt with here, however, because they are not to the point. It may have been a quirk of Gupta's personality that led him to accept Sasisekharan's invitation to join and stay with his team. Pattabiraman certainly needed more careful management [q.v., (44) and (45)]. But the motivational psychology of these two men is irrelevant to the understanding of their conceptual contributions to the evolution of the Indian SBS structure. I am not concerned, here, with every aspect of why and how the "warped zipper" came into existence. Rather, I only seek to show the extent to which reason played a part and to exhibit the logical relations between stages of the work. In contrast, it is incumbent upon those who would maintain that there is no logic in invention, only a sociology and psychology of inspiration, to turn to those disciplines for their complete account. To the extent that this now seems an implausible ambition, I have made my point.

(341) It will have become obvious that the invention of the

SBS model in New Zealand and India has some crucial features in common - the most outstanding example is the role played by the unwinding problem. Equally clear are the differences between the two processes of innovation, though they both had essentially the same outcome. Both are the subject of the next chapter. There I examine the Indian and New Zealand inventions of the "warped Zipper" as an example of the phenomenon of multiple, independent and more or less simultaneous scientific 'discovery'.

XII REASON AND THE ZEITGEIST

(342)

The pages of the history of science record thousands of instances of similar discoveries having been made by scientists working independently of one another. Sometimes the discoveries are simultaneous or almost so; sometimes a scientist will make anew a discovery which, unknown to him, somebody else had made years before [Merton (1973b), p.371].

The invention of the SBS model of DNA in New Zealand and India is an instance of this phenomenon. The New Zealanders' 'warped zipper' structure is essentially identical with the Indians' Type I conformation, and the Type II Indian SBS model differs from it only in the use of inverted stacking at the bend region. Both groups worked in complete ignorance of one another. Though the New Zealanders have priority of first publication, both groups' models appeared in print in the same year, 1976.

(343) Multiple, independent and simultaneous scientific innovations have attracted attention since before the nineteenth century, <sup>70</sup> and their frequency has inspired several attempts at an explanation. <sup>71</sup> A striking feature of this response is that it has largely been made by sociologists, together with

<sup>70</sup> See Merton (1973a), pp.352ff.

<sup>71</sup> In the present century these may be dated from Ogburn and Thomas (1922). Interest among sociologists was stimulated by Merton (1973a) and (1973b), [originally published in 1961 and 1963 respectively]. For example, see Price (1963), Simonton (1978) and (1979), and Brannigan et al. (1981). But see also Kuhn (1977c) [originally published in 1959].

psychologists and historians of science. In particular, philosophers of science have shown little or no interest in multiple, simultaneous and independent scientific 'discoveries' - 'multiples' - as, for the sake of brevity, and following Merton (loc. cit.), I will call them.

- The reason for this lack of philosophical comment is straight-forward enough. Philosophers have, by and large, considered the phenomenon of 'discovery' outside their province [q.v., chapters VI and VII]. Since 'discovery' is regarded as being a subject fit only for inquiry by psychologists and sociologists so, too, are multiple 'discoveries'. Yet key features of the debate that has taken place ought to have attracted philosophical attention.
- (345) Merton (1973a) argued that the frequency of multiples is so high that

far from being odd or curious or remarkable, the pattern of independent multiple discoveries in science is in principle the <u>dominant</u> pattern rather than a subsidiary one. It is the singletons - discoveries made only once in the history of science - that are the residual cases, requiring special explanation. Put even more sharply, th[is] hypothesis states that all scientific discoveries are in principle multiples, including those that on the surface appear to be singletons. [p.356, emphasis added]

Merton went on to claim that his hypothesis was explained by the social determination of scientific advances; to suggest that they were inevitable "[o]nce the necessary cultural base has accumulated...[Simonton (1978), p.522]." Appraisal of Merton's views has dominated the subsequent sociological discussion.

Price (1963) accepted that the "evidence makes it very (346)plain that multiple discovery...occurs with remarkable frequency [pp.65-66]." But he was not so sure of Merton's "ripe apple" theory as an explanation. Rather Price cautiously argued there was support for the view that the number of successful and unsuccessful, single and multiple 'apple-pluckings' which occur is described by the Poisson distribution - which specifies these proportions for a random phenomenon. Simonton took up Price's argument, claiming that a "detailed inquiry reveals that the Poisson distribution can predict almost all the observed variation in the frequency distribution of multiples collected by Merton, and by Ogburn and Thomas [(1978), p.521]. Moreover, Simonton suggested, "the occurrence of independent discoveries and inventions probably cannot be taken as evidence for the inevitability of techno-scientific advance" since, if it is assumed that "any specific invention or discovery will usually have a low probability of appearing,...consequently...technoscientific progress must be largely indeterminate [idem., pp.530-531]."

(347) In the literature, there are three distinct kinds of explanation for multiples, which Simonton characterises as "zeitgeist [social determination], genius or chance [1979]." We have already encountered the first and third. According to the genius theory, which Simonton reports as having been popular among psychologists who investigated creativity during the 1950s and 1960s, "scientific discoveries and technological inventions are produced by great scientists and inventors who possess abilities, personalities and backgrounds that set them apart

from their colleagues [Simonton (1979), p. 1604]." Merton, as we have seen, favoured social determination as an explanation of multiples - though he thought it consistent with genius theory: "By conceiving the scientific genius sociologically, as one who in his own person represents the functional equivalent of a number and variety of often lesser talents...[(1973a), p.370]." Simonton's (1979) supports, but modifies his (1978) elaboration of Price's (1963) advocacy of chance. There he still argues that the "position that best meets all critical tests is the chance theory [(1979), p.1613]." But, though

on the whole, chance theory may be the best general explanation of the phenomenon...[we] must obviously acknowledge that the zeitgeist is probably a necessary if not a sufficient determinant [sic.] of discovery or invention. There can be no denying that some contributions are prerequisites to other contributions. [op.cit.].

And Simonton also admits scientific eminence, concluding finally

A small group of highly productive individuals are most likely to participate in multiples, including independent rediscoveries. These same geniuses, as it were, are also unusually intimate with the techno- scientific zeitgeist and are perhaps equally gifted with an inordinate amount of good luck [(1979), p.1615].

about the occurrence of multiples in science, and of how well that prediction accords with their actual frequency, would seem to be archetypally sociological in character and of no obvious interest to a philosopher. But whether chance, zeitgeist or genius explain multiples is pertinent nevertheless. For if chance and/or genius are the most plausible explanations, those who adhere to the dogma that the 'context of discovery' is beyond the pale of philosophy may do so in comfort. Their expectations of sociology and psychology will have been

fulfilled. No one will look for a logic of genius, or of chance.

(349) But, if 'discoveries' come when the time is ripe, and if they come in multiples when it is over-ripe; if it is the social determination in the zeitgeist of science that is looked to for an explanation of 'discoveries' and multiple 'discoveries', then philosophers should be much less content. At first glance, this is not obvious. Let us consider Simonton's characterization of the zeitgeist explanation:

According to this social deterministic view, the individual creator is largely irrelevant or epiphenomenal to the cultural progress represented by the inevitable accumulation of scientific knowledge and technical expertise. Rather, it is the sociocultural system as a whole, embodied in the spirit of the times, which is ultimately responsible for any given technoscientific advance [(1979), p.1603].

Though philosophers, nowdays, are not inclined to view science as an "inevitable accumulation", this looks harmless enough to philosophical dogma, a nice non-logical, non-rational explanation which would only annoy the inventionist.

(350) If events of a certain kind - say novel scientific ideas - regularly occur in pairs, triplets, quadruplicates, or more often still, we are inclined to suppose they might have a common cause. And it is against that possibility that Price and Simonton direct their argument from the Poisson distribution. Contrary to appearances, they suggest, multiples are a random occurrence. This tactic is used because the stratagem of those who seek to explain multiples in social deterministic terms (for example, Merton) is to argue from the <u>frequency</u> of multiples, to their <u>high probability</u>. The common cause is thus identified as

the common scientific cultural climate, the zeitgeist. That a sociologist of science like Merton should make this move, identify this common cause, is not surprising. Price and Simonton, dispute the frequency of multiples relative to singletons and their consequent probability. But, since they are sociologists of science, they do not object when Merton moves from a high relative frequency to the conclusion of determination by the zeitgeist. Sociologists, unlike philosophers, do not look for reasons-as-causes. But, since most philosophers are anti-inventionists, they would not in this case be tempted either. However, inventionists do see reasons-as-causes in the context of invention. They expect that there is reason in the zeitgeist. The common cause of multiple inventions such as the SBS model of DNA is a common reason for their invention.

(351) Multiples may lead us to suspect this. They do not, however, establish the claim. How might this be done? The three alternative kinds of explanation - genius, chance and social determination have been tested by examination of the frequency, probability and distribution of multiples treated as a class with certain sub-groups [e.g., Simonton (1979)]. This obviously suits the externalist sociological mode of explanation. All the same, an externalist approach manifestly cannot decide the question of whether the occurrence of simultaneous multiples is to be explained by similarities in the reasoning process associated with them - that is paradigmatically an internalist issue.

<sup>(352)</sup> Rather, what is called for is a close examination of

particular cases. Such an inspection of events leading to a simultaneous, multiple innovation offers the opportunity to decide the extent of the part played by reason and that played by other factors - such as those which the sociologists have identified as significant. Naturally, any given case study may well be atypical - whatever its conclusions. Whether any given episode of multiple invention is characteristic can only be established by comparative consideration of other cases. Nevertheless, a case study approach to multiples obviously can be decisive in particular instances, and has been used by others (for example, Kuhn (1977c) and Brannigan et al. (1981).

- (353) Before turning to consider the 'warped zipper' structure of DNA to see if it has anything instructive to tell us about multiples there is an objection that I want to deal with. It is this: We know that the SBS model of DNA was more or less simultaneously devised by two groups. But, by and large, the scientific community has rejected it [q.v., chapter V]. The 'warped zipper' is certainly a multiple invention. To be a multiple discovery, however, it must also be true [q.v. (138) (140)]. Though judgement against the SBS model by the specialist community does not show that it is false, it must be regarded as at least having established a prima facie case. What is the significance of this?
- (354) The terms 'invention' and 'discovery' are both used in the sociological literature on multiples  $[\underline{q},\underline{v}]$ , (346)]. There, however, the distinction drawn is that between scientific and technological innovation; between, for instance, the theory of

electricity and its practical applications. The epistemological status of multiple 'discoveries', and the functional utility of multiple 'inventions' is largely taken for granted. Indeed, Simonton remarks:

Histories seldom recount discoveries and inventions which no one ever made, and those null contributions which are recorded invariably have zero probabilities (for example, the <u>perpetuum mobile</u>, the squaring of the circle, the doubling of the square, the trisection of the angle, the proof of the parallel postulate, and the like) [(1978), p.523].

- (355) This is a very curious way to put things. Obviously the transcontextual character of 'discovery' does not permit the locution 'false discoveries' - it is self contradictory [q.v., (139)ff.]. The probability of false, especially analytically false discoveries, is plainly zero. But the probability of making false claims-of-discovery is not zero. It is, of course, widely accepted that many, even most (singleton) scientific hypotheses are hopelessly wrong, rejected immediately they emerge - certainly before they are published. The story is the same for patent applications. What proportion of novel ideas are false we do not know; but there is no doubt that the number is large. In these circumstances, one cannot plausibly claim a priori that the probability of multiple, false hypotheses is zero. Yet the question of of whether there exists a class of false simultaneous, multiple innovations is barely considered in discussions of the phenomenon.
- (356) The existence of such a class bears significantly on the plausibility of explanations for multiples. Chance theorists must calculate that random probability of false multiples

and compare it with the actual occurrence - just as they do for multiple discoveries. Genius theorists seem to require a greater number of multiple successes, and fewer multiple failures, among geni than among lesser talents. And explanation by social determination presumably requires "the spirit of the times" sometimes to deliver scientists two by two into epistemological error. An inventionist explanation would look for similar rationales among both multiple successes and multiple failures, expecting to find better heuristics in the former compared with the latter.

- this issue. Multiples, he says, "...confirm the truth of the discovery (though on occasion errors <u>have</u> been independently arrived at) [(1973b), p.376, emphasis in the original]." There is a hint here that Merton feels there is something about the <u>way</u> that multiples are arrived at which leads to truth otherwise why would their multiplicity confirm their truth? He never maintains this directly, though, perhaps because he is always at pains to distinguish sociological from philosophical inquiry, and to keep within his own domain.
- (358) One interesting multiple is the prediction of the existence of Neptune in the nineteenth century by the French astronomer Leverrier and an Englishman, Adams. Simonton suggests that it supports the social determinist view of the phenomenon:

Thus, if neither Adams nor Leverrier had predicted the existence of Neptune, someone else would certainly have done so [(1979), p.1603].

Yet there is more to the episode than this. Both Leverrier and Adams had sought to explain anomalies in the orbit of Uranus as

the result of perturbation by a trans-Uranic planet. And, fresh from his triumph, Leverrier turned his attention to what he thought might be similar difficulties in the behaviour of Mercury. He postulated an analogous cause - an intra-Mercurial planet which he called Vulcan.

- (359) As Hanson (1962) shows, Leverrier was not the first, nor was he the last to propose this kind of solution to the problem of the precession of Mercury's perihelion. But his success with Neptune meant that the Vulcan hypothesis was taken seriously. Vulcan was sought, and 'discovered', many times even by professional astronomers. Eventually, this was recognised for what it was, 'wishful seeing' though the intra-Mercurial hypothesis did not die until quite some time after Einstein proposed a very different solution to the problem.
- (360) Hanson's interest in all of this was that of an inventionist philosopher of science. He was concerned

not with the logical form of the argument which  $\underline{\text{tested}}$  the Neptune hypothesis, but with the historical development of the argument which  $\underline{\text{generated}}$  that hypothesis [(1962), p.365, emphasis in the original].

Moreover Leverrier, in Hanson's view, arrived at the Vulcan hypothesis "impelled by the very pattern of explanation which disclosed Neptune [ibid., p.368]." Thus:

The Vulcan hypothesis is false. But the way it is false holds lessons for historians. By noting what Leverrier did with Mercury, even when he did not succeed, we can understand better what he did with Neptune when he did succeed [ibid., p.374, emphasis in the original].

(361) Despite the problematic 'retroductive' terms in which Hanson couches his analysis  $[\underline{q}, \underline{v}, (182)]$ , it illustrates the way

in which an inventionist examination of true  $\underline{\text{and}}$  false multiples can effect zeitgeist interpretations such as that in the example given by Simonton [q.v., (358)]. Hanson demonstrates that one could as well say that if Leverrier had not predicted the existence of Vulcan, then someone else would certainly have done so (indeed they did) as make the same claim of the hypothesis of Neptune. Even leaving aside Hanson's claim that this results from a similarity in the reasoning process of those involved (or potentially involved), a zeitgeist approach can only explain the occurrence of these hypotheses as inventions - since one of them was not a discovery. We are reminded, too, that an argument in the context of invention cannot be asked to yield unambiguous epistemological judgements. As was argued in chapter VII, 'advancement arguments' are necessarily amplative; they must proceed beyond what is certain into what is possible. Thus the same argument may be expected to lead to both successes and failures. And, to the extent that the failures result only from the non-algorithmic character of such arguments, unsuccessful outcomes are not a good ground for ignoring them.

(362)

History with a happy end is always in danger of becoming a fairy tale; and this is especially true of one of its most precarious subspecialties, the history of science, where there never is an end [Chargaff (1976), p.289].

Yet historians of science must report scientific judgements, not make them. In this respect a nineteenth, and a twentieth century historian are no differently placed - though the story they tell of Newtonian Mechanics will differ considerably. Moreover, the treatment of apparent scientific successes by historians is

neither surprising nor objectionable <u>per se</u>. When Chargaff observes that the history of scientific "failures is only written if they pay for the treatment - and then not for publication [<u>loc</u>. <u>cit</u>.]", he is only half right. Historians of science <u>are</u> interested in failures, but usually only if they once seemed to be successes or helped achieve them.

Nevertheless, when 'the story so far' apparently has an (363)epistemologically happy ending, the treatment of scientific dissent against that view will inevitably be conditioned by the preponderant judgement of the scientific community. Thus, for example, to read the scientific and historical texts on the structure and replication of DNA leaves one with the overwhelming impression that the double helical model is confirmed by all the evidence.  $^{72}$  And unwinding is treated, by and large, as a solved problem with, at best, only a few details remaining to be worked out. There is almost universal acceptance that Watson and Crick had 'discovered' the structure of DNA. Of course, there is no attempt to falsify the record, to deliberately hide criticism of the double helix. But it is discussed only to a very limited extent because the aim is to show how an hypothesis, accepted as correct, came to be devised and adopted. Crick illustrates this when he says:

Looking back, I think we [he and Watson] deserve some credit for not being inhibited by the difficulty of unwinding...[(1974), p.141].

Yet chapters III and IV present quite a different picture; it is

<sup>72</sup> Hamilton (1968) among the scientists, and Jevons (1979) among the metascientists are exceptional in not declaring or implying that the question of the structure of DNA settled.

quite clear that a persistent minority, largely ignored by history, took a quite different view.

- Zealand and Indian inventors of the 'warped zipper' and, in different ways, it played a central role in their independent inventions of that model of DNA. The investigation of their invention prompted the investigation of the hidden history of critical work on the received view of DNA. Among other things, this study revealed a persistently recurrent heresy, left-handed DNA. And, in the course of the investigation, the left-handed, Z-DNA was 'discovered'. In this light, Crick's response to Z-DNA suddenly looks more than just lame; indeed simply ahistorical [q.v., (104)].
- (365) As Chargaff says, "in science...the final goal will invariably elude us, almost by definition [(1976), p.289]." This is a view of the 'discovery' of truth now widely accepted by philosophers. One consequence for the the investigation of multiples, is that we ought to pay attention to apparently failed multiples as well as to the celebrated multiple successes. Indeed, the occurrence of a multiple judged false by the scientific community should alert us, if we are inventionists, to the possibility that the appraisal of the scientific community may be incorrect. To accept this could be the case is merely a tentative, partial converse of Merton's view that a multiple 'discovery' confirms its truth [q.v., (358)].
- (366) Essentially the inventionist expectation of a multiple

such as the invention of the SBS model of DNA is this: A similar problem, similarly defined, constrained and pursued, will lead to a similar solution in different hands. Where there are differences in approach, they will tend to be expressed in differing results. That, it will be my contention, is precisely what we find when we examine the 'warped zipper' episode. But before attempting to establish this claim, I want to look briefly at the plausibility, for the SBS multiple, of the three alternative explanatory modes; social determination, genius and chance. My purpose, here, is to show that an inventionist explanation is called for by the inadequacy of these alternatives. However, in doing so, I am <u>not</u> claiming that they are totally inadequate or irrelevant. Rather, I will suggest that they are, severally and jointly, <u>insufficient</u>.

- According to this view, the occurrence of two independent versions of the 'warped zipper' hypothesis should be the result of a coalition of socio-cultural factors within the relevant scientific communities (molecular biochemistry/ biophysics and molecular genetics). But the evidence indicates quite an opposite conclusion. So far from the time being ripe for structural innovation in the understanding of DNA, part of the explanation for the suppression of the criticism of the Watson-Crick model alluded to above lies a coalition of social factors against change.
- (368) This emerges clearly in the difficulties which the New Zealanders had in publishing papers supporting their proposal

 $[\underline{q}.\underline{v}., (106) - (113)]$ , which led Rodley and Reanney to conclude that "it is very unlikely that current workers [will] consider the <u>possibility</u> of interpeting their results in terms of any model other than the double helix [(1977), pp.49-50, emphasis added]." Indeed, an Editor of <u>Acta Crystallographica</u> was moved to remark of his own referees: "I am certainly not very happy over the way these papers were treated or over the[ir] rejection  $[\underline{q}.\underline{v}., (111)]$ ." Resistence to innovation was not restricted to anonymous specialists, nor to the context of appraisal. We saw that Sasisekharan had to struggle to find collaborators who would treat his project seriously and, having found them, they in turn had to struggle against peer group pressure from among their fellow graduate students  $[\underline{q}.\underline{v}., (42) - (45)]$ .

(369) Kuhn, among many others, holds that resistence to innovation is a general feature scientific change. Yet as we have seen he also sees novel ideas as arising from a zeitgeist in 'crisis'. It is not obvious how both these claims can be true at once. Indeed, the resistence of the specialist community to the SBS model is most persuasively explained by the absence of a crisis of confidence in the double-helix. I have considered the social context out of which the SBS model arose, and its appropriate interpretation, in some detail elsewhere [Stokes (1982)]. It is not necessary to repeat that analysis here, for one feature of the 'warped zipper' multiple alone is enough to cripple any social determinist explanation. the Indians devised their version of the model within the zeitgeist of the specialist scientific community, and the New Zealanders invented theirs outside of it. Sasisekharan specialized in the structure of

biological macromolecules. The New Zealanders were not. Social determination can only explain the occurrence of a multiple if  $\underline{all}$  independent innovations are within a ripe zeitgeist. <sup>73</sup>

as due to the sheer creative prowess of its inventors is that the genius theory of multiples does not actually explain very much about them. It is all very well to establish that "the greatest men of science have been involved in a multiplicity of multiples [Merton (1973a), p.367]" as compared with lesser scientists, one wants to know why this is so. And, obviously, to attribute it to talent would be a circular argument. Moreover, not all multiple 'discoveries' are 'great' discoveries. It is hardly plausible to suggest that lessor 'discoveries' are the product of dimmer stars only. Are 'easier discoveries' to be explained by the lack of talent exhibited by their (multiple) 'discoverers'?.

(371) Of course no one would want to suggest that helpful new scientific hypotheses normally require little or no talent of any kind. But behind the appeal to genius as a total explanation

<sup>73</sup> Similarly, the SBS model cannot be explained as a multiple on the grounds that its inventers were <u>free</u> of the constraints of an ill-disposed cultural milieu. A case might be mounted for the New Zealanders, but not Sasisekharan, for he worked with the specialist community [See Stokes (1982), p.235.]. Of course the Indians were not at a major centre of research on DNA, nor was Sasisekharan a leading figure in the field. Both groups were on the fringe. But the furious controversy sparked by Donohue's criticism of the X-ray evidence supporting Watson-Crick base-pairing, and his development of an alternative base structure, undermines a fringe-centre explanation. Donohue had been, and was then, a leading figure in the field [q.v., (91)-(96)].

of multiples lies, perhaps, a view of creative scientific talent as inscrutable; to be pointed out and held in awed regard. 74 If so, we have located the reason why such explanations seem so inadequate. There is, however, an alternative, still incomplete, but entirely consistent with an inventionist perspective on the development of multiple novel hypotheses. It is to suggest great scientists are involved in more multiples than less remarkable talents because 'great minds think alike'. This completely changes the focus of our attention from an impenetrable given, genius in itself - or the comparative lack of it - to the thought processes whose outcome merits various degrees of admiration. So viewed, the genius theory of multiples can only be proven by the kind of inquiry here being undertaken. We can only attribute multiples to similar talent (a far less problematic expression) by showing that those who produced the multiples thought alike.

(372) The chance theory of multiples 'explains' multiples by suggesting, essentially, that there is nothing to explain. It is a claim about the causation of multiples which denies that there is any common cause to attribute. Multiples, according to this view, are independent in a very strong sense: their occurrence is utterly unrelated; unconnected to the zeitgeist in any relevant way, not the product of similar scientific talents, not the outcome of similar trains of reasoning - ever. The phenomenon is

<sup>74</sup> Indeed, one possible source of resistance to inventionism might be the feeling that explicating the logical elements of innovation somehow demeans the the inventor. But to appreciate genius is by no means the same as being able to emulate it - even post hoc.

a pseudo-problem. For the chance theorist, multiples and singletons are like paired head, tail and mixed tosses in a game of two-up - random events.

- model of DNA is thus grist to the chance theorist's mill against the social deteminist. In contradistinction, every like-thought, every similarity of reasoning employed by the Indians and New Zealanders is a counter-argument to that position. Of course, in establishing such conceptual connections one does not refute chance theorists decisively. However, with each increment, the position becomes more like the implausible parallelist solution to the mind-body question. Eventually, as the co-incidences mount up, they must amount to more than mere co-incidence.
- zipper' cannot be adequate; the 'genius' theory becomes an exploration of the sufficiency of the inventionist case, the success of which, in turn, undermines the chance account. It remains, then, to examine the inventionist case is the SBS model a multiple because two groups thought alike, their results differing only insofar as they thought somewhat differently?
- (375) This question can be addressed by considering first the ways in which the two 'warped zipper' proposals differ together from the Watson-Crick structure. The fundamental structural

<sup>75</sup> According to which there is an exact, completely causally unconnected parallel between every mental-state and a physical, brain-state.

difference lies in the use by both groups of alternating half left-handed helical, half right-handed helical segments, combined together to form a non-helical strand. As a direct consequence of this the structure exhibites topological independence; the two strands can be separated without the unwinding required by the double helix [but see (121) and n29].

- the New Zealand and Indian versions of the SBS structure is essentially the same. Both versions are non-helical because that avoids the unwinding problem. The SBS strand structure was devised by both the New Zealanders and the Indians in order to circumvent the need for unwinding, a goal which both groups had in common. We can therefore explain the principal common features of the outcome of the research in India and New Zealand in terms of a common criterion of success set before the 'warped zipper' was invented. Nor is it surprising that the two groups should have sought to solve the problem of unwinding it was a difficulty which many had recognised for many from 1953 onward.
- possible conformations for DNA which eliminate or reduce the need for unwinding, but which are not SBS models. For example, Watson and Crick (1953c) and Cyriax and Gath (1978) [the latter apparently independently of the former, q.v., (68) and (69)], proposed totally non-helical, topologically independent models of DNA which did not exhibit even the half-helices of the 'warped zipper'. Why did the SBS structure, and not this idea, occur to Sasisekharan, Rodley and their co-workers? A crucial

part of the answer to this question lies in other common features in their approaches which may be summed up as their common conservatism.

conditions - as I have called them - to their investigations: Watson-Crick base-pairing, sterochemical viability and conformity to the X-ray diffraction data [q.v., (269), (270), (312) and (313)]. Crick et al. (1979) recognized this, remarking: "The SBS model was ingenious because it incorporated the well-established features while altering the less certain ones [p.456, q.v., (123)]." Struther Arnott, perhaps the leading specialist on the structure of DNA and the man who dubbed the SBS model the 'warped zipper', makes the sense of this rationale clear:

The unwinding problem was certainly sufficient reason for the paradigm to be reviewed, but a new model must solve this problem and satisfy the other physical data at least as well as duplex models of the plectonemic type  $[\underline{q}.\underline{v}., (118).]$ 

consideration of totally non-helical structures a priori. Rather it directed attention first to the possibilities of helical arrangements of various kinds. It was the apparent adequacy of a partially helical conformation, the SBS model which blocked exploration of further, more radical conformations. Totally helical alternatives to the Watson-Crick model are plainly less radical than the 'warped zipper'. In keeping with their conservative approach, just such a model was the first resort of both the New Zealanders and the Indians - alternating double left and double right-handed regions. But both groups rejected this

conformation. The New Zealander, Rowe, bowed to the common wisdom of the specialist community that this frequently advanced solution was stereochemically unviable [q.v., (9)] and (281). The Indians however arrived at the opposite conclusion because of the major <u>difference</u> between their approach and that of the New Zealanders.

- (380) Whereas the New Zealanders began with, and narrowly focused on the problem of unwinding, the Indians began from Sasisekharan's methodological doubts; doubts which sprang from precisely the question of the viability of left-handed helical structures. And upshot of their initial inquiries was that such conformations were viable. It was then the double left-hand, double right-hand hypothesis and its potential as a solution to the unwinding problem came to the Indians attention. But, for the Indians, the merit of this hypothesis was mitigated against by considerations of structural inflexibility which it shared with the Watson-Crick model except at the point where the strands changed helical sense. And it was this that led them toward the SBS structure  $[\underline{q},\underline{v}, (322)ff.]$ .
- is easily explained in the Indian case by the fact that this question was constantly on their minds. Its use by the New Zealanders, however, leads us to a more profound understanding of the logic inherent in this particular zeigeist. I have argued at some length that resort to left-handedness is only to be expected given an analysis of the situation facing a scientist who wants to resolve the problem of unwinding whilst remaining

as close as possible to the verities  $[\underline{q},\underline{v}, (279) - (289)]$ . A major support for this claim is the ubiquitousness of the idea. Left-handedness is a very frequent multiple indeed - about as common as the concern over unwinding.

This redirects our attention to the relative position (382) of the inventors of the 'warped zipper' in the zeitgeist of polynucleotide conformation studies. I have already observed that in sociological terms the Indians were within the specialist tradition, and the New Zealanders outside of it. And, as I argued earlier, when our attention is directed to the hidden tradition of criticism of the established understanding of DNA quite a different, indeed the opposite picture emerges. The Indian and the New Zealand multiple fits very well into this obscured history of doubt and counter-proposal. The relation is symmetrical inasmuch each illuminates comprehension of the other - as, for example, in the history of left-handedness or of the problem of unwinding. Behind each recurrence of the former lies the latter. The detailed examination of the logic in the SBS episode shows why. Symmetrically, these recurrences help us see that the 'warped zipper' models are in a cognitive tradition. But it is a cognitive tradition embracing the whole scientific spectrum of invention and appraisal. The point of any given appraisal is to be understood fully only when we take into account the problem which the invention being appraised was devised to solve. Similarly, a characterization of the nature of any given invention must incorporate an appraisal of another invention and of its problems.

- Zealand 'warped zipper' models resemble one another in terms of the problem they both sought to address, and the similar constraints they placed on any adequate solution. But only the Type I Indian SBS structure is identical to the conformation arrived at by Rodley and his colleagues. The Indian Type II model employs inverted base-pairing at the bend region between the opposite handed half-helices, whereas the other two struct- ures utilize standard Watson-Crick base pairing. The reason why the Indians produced two variants of the 'warped zipper', only one of which is a complete duplication of the New Zealanders' results, lies again in the difference between the two groups' approaches.
- Whereas Rodley and his co-workers simply wanted to (384)solve the problem of unwinding, the Indians had methodological interests as an initial and first priority. The unwinding problem alone did not dictate which structures were of interest. Sasisekharan and his co-workers wanted to know the general limits on the conformation of DNA, and which structures were preferable. The concerns of the Indians were those of specialists. Even had the New Zealanders shared them they would have had difficulty undertaking them. The different interests and approach of the Indians lead to the investigation of the comparative energetic favourability of right and left-handed helices. They found that this depended on the particular base-pairs involved. This, in turn lead to questioning of Watson-Crick base-pairing, to the invention of inverted base stacking, and thence to the Type II structure  $[\underline{q},\underline{v}]$ , (334) and (335)]. The advantage of the Type II conformation was its lack of steric

compression as compared with the Type I structure. Once the New Zealanders accepted that their structure exhibited recalcitrant close contacts, they too re-examined base-pairing assumptions. However, they changed a different feature of Watson-Crick base pairing in order to ease the problem - staggering the bases out of plumb  $[\underline{q}.\underline{v}]$ . In 69 at (338). This produced yet another stereochemically viable variant of the 'warped zipper'.

Of the four kinds of SBS model devised by the New Zea-(385)landers and Indians, only two of are a true multiple invention. I have offered an inventionist explanation for all four - given the reasons why two were a multiple and why two were not. But the approach I have adopted here, does not deny the relevance in the scientific process of factors such as the social milieu. luck, skill and insight. Nor does it presume that these considerations will always be completely susceptible to logical analysis. There may well be cases where such analysis proves to be completely or comparatively unfruitful. However, the present chapter does make the claim that, considered as a multiple, the 'warped zipper' is better analysed in logical, than psychological and sociological terms. There was reason in the zeitgeist, and outside of it too. That, finally, is what the New Zealanders and Indians had in common. They thought alike.

## THE CONTINUUM OF INVENTION

- (386) I have established and elucidated the rational elements present in the invention of the SBS model of the structure of DNA. The context of that invention has thus been demonstrated both to call for and be susceptible of logical analysis contrary to the anti-inventionist dogma of Popper and others. The rational considerations which led, step by step, to the development of the 'warped zipper' have been elicited and explored. Moreover, analysis of the 'warped zipper' episode justifies further historical and philosophical investigation of the context of invention. It suggests that other studies are not only possible, but will also provide additional illumination on the philosophically neglected, yet central, creative facet of science.
- empirical basis necessary for a general characterization of the rational aspects of scientific invention. Though there is no reason to suppose that the invention of the 'warped zipper' was atypically rational, a single case study cannot reveal what is typical of invention in science. Nevertheless, in concluding, I want to try to locate the invention of the 'warped zipper' in relation to that of hypotheses such as Cairns' molecular swivel and the Watson-Crick structure itself. I hope to show that whilst the SBS model is not a routine creative event like the molecular swivel, neither is it unusual in quite the same way as the double-helix.

- (388) As was argued in Chapter VII, Kuhn is correct when he suggests that scientists are mostly occupied with the refinement, extension and use of established scientific theories ('normal science'). They are not particularly concerned to defend such theories, still less interested in falsifying them, and very uncommonly involved in developing radical alternatives to them ('extra-ordinary science'). This 'puzzle-solving' that normally engages scientists is quintessentially inventive. Lakatos (1970) made this clear when he described the process of defending and 'articulating' a 'scientific research programme' in terms that are redolent of invention, the 'positive heuristic' and the 'negative heuristic'.
- The development of replication theory since 1953 (389) illustrates this point very clearly. Watson and Crick remarked at the outset that their model "immediately suggests a possible copying mechanism for the genetic material [(1953a), p. 737, q. v., (65)]." The invention, refinement and use of this suggestion in the form of the semi-conservative theory of replication, was positive and creative in Lakatos's sense. Similarly, as the 'research programme' advanced, its 'hard core', the Watson-Crick model, was defended against the difficulties of explaining unwinding. Though 'negative', this process was also creative. For instance, it generated the molecular swivel hypothesis and its successor, the enzymatic theory. As a result, most specialists would have agreed with Crick when he remarked: "Looking back, I think that we deserve some credit for not being inhibited by the difficulty of unwinding... [(1974), p. 141,  $\underline{q}.\underline{v}.$ , (85)]."

(390) The positive and negative articulation of the research programme of molecular genetics prefigured in Watson and Crick's initial paper are 'normal' processes. Yet it is 'extra-ordinary' 'great' or 'revolutionary' science, like the invention of the double-helix, that has traditionally been taken as providing the model of good science. It is really only as a result of Kuhn's work that metascientists began to consider the possibility that routine science might be different in kind, rather than in degree, from such models. On this view, the ordinary requires separate treatment from the extra-ordinary and, being 'normal', even has primacy. Though I will argue that, finally, the distinction between the two is indeed one of degree, I want to begin with a basically Kuhnian perspective on invention in science. The following definitions of 'normal' and 'extra-ordinary' creativity are suggested by such a view:

(391) Scientific invention is 'normal', or routine, when it starts with a given theoretical base and seeks to refine it, extend it, apply it to practical problems, or eliminate anomalies threatening it - perhaps roughly in that order, with least emphasis being placed on the resolution of apparent 'counter-

However, in molecular genetics, the 'normal' science practiced since 1953 has so enlarged our understanding as to have attracted a good deal of attention - though invention of the double helical model is still treated as climacteric, seminal or pivotal [e.g., Olby (1974), Portugal and Cohen (1977), Judson (1980a)]. Because the invention of the double helical model has been quite properly celebrated as an extraordinarily inventive episode, there exists ample data for a reconstruction of its rationale. Indeed, Olby (1974) has done this very thoroughly - though not from an explicitly inventionist philosophical stance.

instances. The key feature of ordinary invention so understood, as of Kuhnian 'normal' science is that it begins from acceptance of a body of knowledge claims, and proceeds to ask a variety of questions about what might follow from that appraisal. How can these claims be made more precise? How can they be developed in detail, and to cover new areas? What utilitarian ends can they serve, and how can they serve them? How can apparently anomalous data be shown consistent with the knowledge-claims? The answers to these kinds of questions routinely fill the pages of the specialist journals. They are all questions which require inventions in order to be answered - whether they are theoretical, experimental or technological. However, they are not the result of questioning of existing theory, and so never constitute an alternative to it.

- extra-ordinary invention starts with the opposite epistemological judgement to 'normal science'. It begins from the decision that something is, or may be <u>incorrect</u> in previously accepted theory; in other words, something is <u>rejected</u>. This defines what is to be changed, and the question which then occupies those who engage in such unusual science is with what is it to be replaced? This type of question, too, demands theoretical, experimental and technological invention in order that it be answered. But, when successful, these inventions replace rather than amplify existing theory.
- (393) However, distinguishing 'normal' from 'extra-ordinary' science on the basis of acceptance and rejection will not do.

One problem that such an approach produces is that rather common scientific decisions, where what is rejected is only an earlier attempt at ordinary invention, must be considered as extraordinary. For example, Cairns' molecular swivel hypothesis is 'normal' in that it was an attempt to explain how  $\theta\text{--structures}$ are consistent with unwinding in co-valently closed, doublehelical DNA - an attempt to eliminate an anomaly. Questioning or rejecting his solution in favour of devising an alternative need not be a very radical move. One such alternative, the enzymatic theory, certainly is not. The two hypotheses share common presumptions about the structure of DNA and the need for unwinding, and both look like 'normal' means of dealing with anomalous data. Yet, because the latter rejects the former, we seem to be bound to call it extra-ordinary. Worse still, we are unable to distinguish a rejection of Cairns' hypothesis which led to an enzymatic theory from Clive Rowe's rejection of the same hypothesis, which was instrumental in the development of the New Zealand version of the SBS structure because it did not assume that DNA was double-helical, or that its strands must separate by unwinding.

(394) One way out of this dilemma is to use Lakatos' distinction between the 'hard core' of theory, not to be rejected under any circumstances, and a belt of 'auxiliary hypotheses' which can be adjusted to prevent rejection. So viewed, the double helix and unwinding are within the 'hard core' of molecular genetics, and various solutions to the problem of unwinding are dispensible 'auxiliary hypotheses' protecting it. It is not, then, that nothing is rejected in doing 'normal

science', as that nothing <u>fundamental</u> is questioned or rejected. So, although devising the enzymatic theory may involve questioning the molecular swivel hypothesis, the more basic structural assumptions and their consequences (the double helix and unwinding) are not. On the other hand, Rowe and Rodley <u>did</u> question them, with the much more radical consequences that could be anticipated as following from these more fundamental doubts.

- Though we can now distinguish the SBS model from the (395) molecular swivel and enzymatic solutions to the unwinding problem created by  $\theta\text{-structures}$ , it remains to locate it in relation to the double-helical hypothesis itself. Is it sufficient just to say that both are 'extra-ordinary' inventions? And what about various other candidates for the label - for example, Donohue's alternative base-pairing scheme [ $\underline{q}$ . $\underline{v}$ ., (91)], Wu's four-stranded helical model [ $\underline{q}$ . $\underline{v}$ ., (12)], and the commonplace left-handed proposals culminating in the 'discovery' of Z-DNA [q. $\underline{v}$ ., (101)]? These ideas are all based on questioning of one or more of the candidate elements of a 'hard core' of polynucleotide conformation studies and molecular genetics - Watson-Crick base-pairing, two-strandedness, right-handedness and, including the 'warped zipper' and Cyriax and Gath's proposal  $[\underline{q},\underline{v}]$ , (69), a helical structure. Are they all equally extra-ordinary?
- (396) Were we to construe Lakatos as claiming that the 'hard core' of a scientific research programme is <u>never</u> questioned, then polynucleotide conformation studies and molecular genetics do not have a 'hard core'. Every candidate element has been

questioned, and there have been hypotheses invented on a basis contrary to all of them. Even if we accept a more plausible and weaker claim - that doubts about the 'hard core' uncommon and their outcomes unpopular - Lakatos's concept of a 'hard core' does not enable us to distinguish between these extra-ordinary hypotheses. An item is either inside the 'hard core' or outside of it, an 'auxiliary hypothesis'. Any hypothesis or theory inconsistent with the 'hard core' is in another research programme. Yet a totally non-helical structure for DNA, such as Cyriax and Gath's, seems intutitively more radical than one that employs half-helices, like the SBS model. That, in turn seems more radical than a left-handed version of Watson and Crick's structure.

(397)These intuitions suggest that there may be degrees of non-routine, extra-ordinary science. This requires a criterion by which to measure the degrees. One standard would be how novel the new idea itself is, compared with what it purports to replace. Thus the SBS model structure seems to be a more novel way of resolving the same problem than the molecular swivel. But this is not quite the right way to put things. Novelty comes in degrees certainly, but degrees of originality. And both these two hypotheses are equally original, never having previously been advanced. They are not, though, equally radical. 'warped zipper' clearly rejects more of existing theory, and proposes a more fundamental change than does either the molecular swivel or the enzymatic theory. But how do we spell this out, measure how radical a rejection is, and how fundamental the alternative invented as a result?

Scientific theories are very rarely, and with great (398) difficulty, stated as formal systems with explicit deductive hierarchies linking axioms to theorems [see Suppe (1977)]. Scientific reasoning tends to be informal and crowded with enthymemes wherever claims are uncontroversial - though it will be more rigorous where they are contested. For all that predictions are often precise and calculated in detail, the argument becomes less complete the higher the level of theory to which it is being connected. Nevertheless, in principle, scientific theories can be treated as formal systems in order to exhibit the relationships between their components. However, in doing so, we need to be aware that such an ideal risks being artificial in practice as it becomes more detailed and complete. 77

or hypothesis may be ranked as more or less <u>fundamental</u>. For example, the molecular swivel is less fundamental a structural hypothesis than the Watson-Crick model, upon which it depends. The latter does not <u>imply</u> the former, so the relationship is not that between an axiom and a theorem. Yet Watson (1970) clearly had something of the kind in mind when he said that Cairn's hypothesis was <u>demanded</u> by the  $\theta$ -structures anomaly  $[q.\underline{v}., (196)]$ . The relation which does apply is <u>consistency</u>. And that is exactly what Cairns wanted - to make the  $\theta$ -structures consistent with a double-helical view of DNA. Indeed,

<sup>77</sup> I am indebted to F. John Clendinnen for helping me clarify this discussion.

the alternative, enzymatic theory shares has the same relation-ship, and for the same reason.

- theoretical elements enables us to identify more and less radical rejections of them, and resulting alternatives. A non-rountine invention must be involve rejection of some element of pre-existing theory. This is, however, only a necessary, and not a sufficient criterion. An invention is, as we have seen, 'normal' if it involves no rejection, rather an acceptance and extension of extant theory. But, even though an element of existing theory is rejected, if that element is sufficiently subordinate, we may still wish to consider the ensuing replacement routine. One attempt at resolving an anomaly without changing the theory it threatens may, for example, be rejected in order to develop another.
- away with the idea that routine invention is altogether different in kind from the development of extra-ordinary new ideas. Certainly, the refinement or elaboration of a theory is straight-forwardly 'normal', and radical invention involves rejecting and attempting to replace elements of a theory. But the question is not so much whether such new hypotheses are radical or routine, but how radical they are. How radical, even revolutionary an invention is, is a matter of degree, depending on how many and how fundamental are the rejected and replaced elements.

- This produces a schema whereby invention is viewed as (402) a continuum whose extremes are the mundane and the revolutionary. Since it admits of degrees, like baldness, this criterion potentially poses problems of demarcation. When is the rejection of an established hypothesis sufficiently fundamental for its replacement to count as extra-ordinary? When does a new idea change so little that it is really routine? This problem occurs at a specific point - the response to anomaly. It is there that the question of whether something is wrong with existing theory, what is wrong, and with what it should be replaced arises - most often, though not always, as a result of 'normal' research on the theory. The various responses to the  $\theta\text{-structures}$  anomaly illustrate this, ranging as we have seen from the 'normal' to the 'extra-ordinary'; from the molecular swivel and enzymatic theory to the SBS model [ $\underline{q}$ . $\underline{v}$ ., VIII]. In each case the inventors believed that they were changing as little of existing theory as necessary. What they disagreed about was how many changes were needed, and at how fundamental a level.
- (403) We can, however, distinguish the various proposed solutions to the  $\theta$ -structures anomaly in terms of how fundamental they were. The 'warped zipper' was clearly the most fundamental change suggested since it entailed changes to the strand structure to avoid unwinding two features of the established theory which no one else questioned, or sought to replace, in an attempt to resolve this anomaly. In chapter VIII, I argued that the reason for this lay in the attitudes the scientists involved took to the  $\theta$ -structures anomaly. There I distinguished between a mainstream and an avant garde,

placing the New Zealanders in the latter category, Cairns and the response he typified in the the former [see also chapter VI].

- 'normal' and 'extra-ordinary' science as a responses at the watershed of anomaly. The mainstream assessment of anomalies is conditioned by the 'normal' scientist's dominant pre-occupation with development and use of scientific theories. Avant garde scientists are principally concerned with appraisal. They focus their attentions on the question of whether a theory is adequate or inadequate to account for anomalous data. Mainstream and avant garde attitudes, too, admit of degrees; but they help us understand why some scientists are prepared to entertain the possibility that their most fundamental professional beliefs are incorrect whereas others seem to avoid seeing this even when, with hindsight, it seems plain.
- thesis of the structure of DNA to the New Zealand and Indian SBS models? The task that Watson and Crick set themselves was to devise a structure for a molecule for which no accepted structure existed. Still, they began by rejecting, before any structure was devised, the protein view of inheritance well enough accepted to be described as a 'proto-paradigm' [q.v., Stokes (1982), p. 211] in favour of a nucleic acid theory. The protein view of heredity had conditioned most, though not all research on the molecular basis of heredity to that time, and may have hindered appreciation of the significance of work

such that of Avery and Chargaff. It was, in short, pretty fundamental. But Watson and Crick still sought a conformation for DNA which would fit what was then thought to be known (as distinct from suspected) about inheritance and replication. Also accepted by them were the chemical composition of DNA (including Chargaff's rules of base proportion), the bonding physics of the constituents (stereochemistry), the crystallographic evidence, and Fourier techniques for comparing models with it [cf. Watson (1968), Olby (1974) and Judson (1980a).] Thus, despite seeking to innovate at a very basic level, Watson and Crick carried forward a great deal of past results.

(406) By comparison, the SBS invention was much less radical. In addition to accepting all that Watson and Crick had begun with, the Indians and New Zealanders accepted much of what they had achieved:- the semi-conservative theory of replication, a two chain structure caging, at first, an unchanged, and then little altered Watson-Crick base-pairing. The 'warped zipper' is not a double helix, but it does utilize half-helices. Rodley, Sasisekharan, and their groups rejected one element of Watson and Crick's model, its intertwining, because they could see no plausible way to avoid the problem of unwinding without doing so. The New Zealanders self-consciously changed as little as possible, given that decision. The Indians sought, within tight constraints shared with the specialist community, to find out how much room for alternatives there was. Both groups plainly aspired to, and produced a hypothesis involving less fundamental change in the existing understanding of DNA than had Watson and Crick.

- invention, ranging from 'normal' to 'extra-ordinary', measured by reference to what is accepted or rejected in existing theory, and how fundamental it is. This continuum of invention is intimately tied to the context of appraisal, each novel idea being motivated and guided by what is rejected and what is accepted from earlier findings. Within the whole range of hypotheses about DNA we have examined, there is a concern to conserve and build upon the past successes of research. However radical, none are innovations for innovation's sake. Rather, they differ over what the past successes of research are. This, in turn, is at least partly to be explained by different foci of interest.
- As we noted earlier, Quine's points to a "paradox" (408) whereby "a favouring of the inherited or invented conceptual scheme is at once the counsel of laziness and a strategy of discovery [(1960), p.20]." Kuhn (1977d) calls this "the essential tension" between "tradition and innovation in scientific research", rightly claiming that "only investigations firmly rooted in the contemporary scientific tradition are likely to break that tradition and give rise to a new one [p. 227]." Kuhn himself explains this in sociological terms. But, as I have shown [chapter VI], his approach is inadequate to the task. Scientific inventions which, when accepted, produce scientific changes great and small, can be susceptible to logical analysis because they do contain rational elements. It is not a psycho-social 'crisis' in the zeitgeist which links new scientific ideas with old successes and failures. Rather, it is reasoned thought.

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