genetics, e.g. some of the yeast papers where both approaches are combined and used to their full potential, and only one purely genetical paper (Birky *et al.*). The articles in the book indicate that an extremely stimulating and unexpected result can be derived by just looking at the structure of genomes, and almost marks the high point of this approach. Perhaps a new Cold Spring Harbor book in a few years' time will not be organized taxonomically but around central problems like: Do mitochondrial introns transpose? Is there more than one mechanism of intron excision? What are the URFs doing? How do sequences move between the nuclear and the mitochondrial (and the chloroplast) genomes? How are proteins imported into the mitochondria and put in their right place? How is stoichiometry between nuclearly coded and mitochondrially coded components maintained? What is the mechanism of recombination in organelle genomes?

The attentive reader might find pointers to all these problems in the present book.

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Structures of DNA. Cold Spring Harbor Symposia on Quantitative Biology. Volume 47. Cold Spring Harbor Laboratory, Fulfillment Department, P.O. Box 100, Cold Spring Harbor, New York 11724. April 1983. $140 ($168 outside U.S.). ISBN 0 87969 046 1.

This extra-special Cold Spring Harbor Symposium, which appears in print in the thirtieth anniversary year of the discovery of the double helix, deals both with structure and with all aspects of DNA function that can be directly related to structure. Some idea of its scope and balance will be conveyed by the titles of its fourteen sections: handedness (19 papers), conformation (12), chemical modification (10), chemical synthesis (4), interactions with proteins (10), nucleosomes (9), methylation (9), replication (10), gyrases and topoisomerases (5), recombination and mutation (7), transcription and its control (15), gene organization (11), repetition and pseudogenes (7), and chromosomal replication origins, centromeres and telomeres (5). Almost everybody who is anybody in the DNA field is represented among the authors; this makes for a certain degree of repetition but not, I think, an excessive amount. The quality of the work presented is high, as one would expect in this company, and the standard of illustration is excellent. Indeed, some of the computer graphics showing DNA conformations are things of beauty.

My main criticism of the individual contributions (and it is more a criticism of editorial policy) is that, although they are not very different in complexity and density of content from the average research paper in, say, *Cell*, almost none of them has a summary. This makes needless difficulty for that great majority of readers who will not have time to read every one of the 1223 large double-column pages.

From a symposium of this quality it is not easy to pick out high spots for special discussion but two of its aspects may be especially noteworthy as signs of the times. Firstly, it is evident that the fascination with comparative structure and the urge to describe as fully and accurately as possible, often regarded as characteristics of an earlier generation, are still alive and well among the molecular biologists. Some of the fruits of the happy conjunction of rapid DNA sequencing and computerized information storage and retrieval are here on display, albeit in schematic form. The complete sequences of the bacteriophage lambda and T7 and the adenovirus-2 genomes stand as most impressive monuments, but information from selected regions of eukaryotic chromosomes –

for example, the MHC gene cluster of the mouse and centromeres and telomeres of yeast chromosomes – are no less interesting.

The second and perhaps most exciting trend is towards studies of DNA conformation in relation to gene expression. As Alex Rich explains in a lucid introductory paper, results described in the first sections of the Symposium provide us with the elements of an elegant theory of transcriptional regulation. The key concept is that of conservation of linking number – that is, of the number of turns that one strand of the duplex takes around the other. In a DNA domain of fixed or at least constrained linking number, unwinding in one region must be balanced by winding-up in another. Under- or overwinding in the primary duplex results in (or, conversely, will be promoted by) an increase or decrease in the degree of negative (i.e. left-handed) supercoiling. Native DNA has negative supercoils and there is much evidence from prokaryotes (stemming from mutational effects on topoisomerase and gyrase enzymes), and some from eukaryotes, that a degree of negative supercoiling is necessary for transcription into RNA. Presumably this is because negative supercoiling promotes the localized strand separation that allows access to RNA polymerase. Right-handed turns can be taken out of the primary duplex in at least two ways: by the looping-out of cruciform structure in regions containing closely juxtaposed inverted repeats, and by the formation of left-handed duplex (Z-DNA) in regions rich in alternating G and C residues. The stabilization of such structures has the effect of cancelling negative supercoils and, conversely, their destabilization will increase negative supercoiling. It is known that methylation stabilizes Z-DNA and, in principle, specific protein binding could stabilize or destabilize either kind of structure. Thus we can picture DNA regions capable of such conformational switches as *cis*-acting regulators of transcription, and their effects could be transmitted by torsional stress for long distances – perhaps across several genes. *Trans*-acting transcriptional controls, acting either positively or negatively, could be exercised by genes coding for sequence- and conformation-specific DNA-binding proteins.

It must be admitted, however, that the many studies of transcription recorded in this Symposium provide little hard information to fit into this theory. Relatively long-range *cis*-acting regulatory segments have, indeed, been defined in a number of eukaryotic systems; the SV40 72-base 'enhancer' segment and the yeast *his3* and mating-type controls are among the examples described here. But it is not yet understood how these work, and studies of regulatory DNA-binding proteins in eukaryotes are only just beginning. Eukaryotic chromatin is a difficult system to simulate *in vitro*. There is also the complicating factor of the nucleosomes which pin much of the supercoiling of chromosomal DNA, and must play an important role, as yet unclear, in transcriptional regulation.

In the course of his very judicious summarizing paper Aaron Klug remarks that he has 'little doubt that the [DNA] molecule will gyre and gimble in the wabe, and presumably there are proteins that help constitute the wabe'. That sounds plausible enough. It may be added that, as this Symposium shows, there are plenty of uffishly thoughtful people standing ready to slay or, better, capture the jabberwock as it comes whiffling through the chromatin.

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