plasmid DNA, knot and unknot single stranded DNA, link and unlink rings of duplex DNA. However, its role *in vivo* is poorly understood. Sternglanz *et al.*[3] searched for mutations in the structural gene for DNA topoisomerase I by screening a bank of temperature-sensitive strains of *Escherichia coli*. The enzyme was assayed at the non-permissive temperature by using agarose gels to monitor the conversion of supercoiled phage PM2 DNA to its relaxed form. From 800 isolates, two, designated *top10* and *top250*, were found to have low topoisomerase activity. Mapping of the *top* gene showed that it and the temperature-sensitive mutation were unrelated and that *top* lies closely linked to the well characterized *cysB* gene at 28 min on the linkage map.

The proximity of *top* to *cysB* prompted a search for *top* deletions among strains known to be deleted in *cysB*. Four isolates with no detectable topoisomerase I activity were found, showing *top10* and *top250* mutants produce polypeptides with residual activity. The existence of *top* deletions indicates that DNA topoisomerase I trol of regulatory systems other than cAMP/CRP are affected.

Thus a gene for one of the many DNA topoisomerases has been identified and the role of DNA topoisomerase I *in vivo* has been indicated. At present this role is still somewhat hazy, but appears to be one of maintaining the superhelicity of the chromosome at the required level. The existence of *top* deletions will allow the genes for other topoisomerases to be identified and so help explain why deletions in these genes is non-lethal.

References

1 Abdel-Monem, M. and Hoffmann-Berling, H. (1980) *Trends Biochem. Sci.* 5, 128–130
2 Cozzarelli, N. R. (1980) *Cell* 22, 327–328
3 Sternlanz, R., Di Nardo, S., Voelkel, K. A., Nishimura, Y., Hirota, Y., Becherer, L., Zumstein, L. and Wang, J. C. (1981) *Proc. Natl Acad. Sci. U.S.A.* 78, 2747–2751
4 Shapiro, J. A. (1979) *Proc. Natl Acad. Sci. U.S.A.* 76, 1933–1937

MARTIN D. WATSON

Department of Botany, University of Durham, Durham DH1 3LE, U.K.

Are liposomes good models for biomembranes?

The celebrated model of the structure of biological membranes elaborated by Singer and Nicolson[1] and popularized in the phrase 'fluid mosaic' has served us well over the past decade. Studies on the rotation and translational diffusion of fluorescently- or radioactively-labelled membrane proteins has demonstrated that, indeed, in many cases the notion of peripheral and integral membrane proteins bobbing around in a sea of phospholipids is a good approximation to reality (see e.g. Ref. 2). In the case of the inner mitochondrial membrane, there is evidence that diffusion of proteinaceous electron transport complexes in the fluid phospholipids may be responsible for controlling the rate of electron transport under uncoupled conditions, since this rate correlates nicely with the inverse of the mean free path of randomly-colliding electron transport complexes in semi-synthetic membranes of different lipid:protein ratios[3].

Now, however, Singer and Michael Conrad have reported a series of experiments which may require us to revise our views on lipid-protein interactions and biological membrane structure[4]. The basis for such a provocative statement is an experimental protocol of such simplicity, and data of such a startling character, that no other conclusion seems warranted. They determined the degree of binding of amphipathic molecules: (a) to unilamellar vesicles containing only phospholipids (liposomes); and (b) to biological membranes such as erythrocyte ghosts or sarcoplasmic reticulum vesicles. The cationic amphipaths chlorpromazine and methochlorpromazine were studied in greatest detail, but similar results were obtained with the anionic dinitrophenol and the neutral molecule 1-decanol.

Solutions of the radiolabelled drugs were mixed with suspensions of liposomes. Bound and free drug molecules were separated by a filtration method, called hygroscopic desorption, and a partition coefficient for drug solubility in the membranes was calculated from the amount of drug bound and the volume fraction of the membranes. Both chlorpromazine and methochlorpromazine gave partition coefficients of 1490, consistent with the widely-held view that these compounds are rather hydrophobic. No surprises so far. But when the experiment was repeated with biological membranes such as erythrocyte ghosts, the partition coefficient came out to be about 0.1. Obviously, the presence of proteins and/or glycoproteins so modifies the structure of the phospholipids that the amphipathic molecules no longer dissolve in the membranes. The authors refer to this as an 'internal pressure' in the phospholipids.

However, this result contrasts with an earlier result of Seeman and colleagues[5], who performed a similar type of experiment but found that the partition coefficient for chlorpromazine into erythrocyte ghosts was rather high. The difference in experimental protocol was that Seeman used a more traditional centrifugal procedure for separating bound and free drug molecules. To try and resolve the discrepancy, Conrad and Singer repeated this type of experiment using the centrifugal procedure, and confirmed the anomaly; the centrifugal method gives high apparent partition coefficients whatever the nature of the membranous material studied. However, whereas the binding of chlorpromazine and methochlorpromazine are additive when judged by the hygroscopic desorption method, they are synergistic when observed by the centrifugal method. Conrad and Singer conclude that apparent partition coefficients determined with the centrifugal method correlate with the formation of micelles by the amphipaths, and thus do not give a useful indication of the true partition coefficients.

To what extent the principle that

emerges from this analysis (i.e. that liposomes are not necessarily good models for biomembranes) can be extrapolated throughout biology is presently unclear. Certainly the apparent lack of fluidity of the erythrocyte membrane appears to be dominated by the presence of the 'matrix' proteins between the cytoplasm and the bilayer[6], a factor not believed to be present in most other membrane systems. Conrad and Singer's paper ends with the sentence 'Phenomena may be observed in phospholipid vesicle systems that do not have their counterparts in real membranes because of the large "internal pressure" in the membranes.' In this regard one might consider the well-established principle that weak acid uncouplers of oxidative phosphorylation can catalyse the rapid electrogenic transfer of protons across phospholipid bilayer membranes (e.g. Ref. 7): despite this the evidence for a mitochondrial 'uncoupler-binding protein' seems unimpeachable[8]. One wonders how frequently phenomena in pure phospholipid membranes do not in fact 'have their counterparts in real membranes'. Whatever the outcome of the lively debate that seems certain to follow from Conrad and Singer's experiments, we may be certain that the idea of the liposome as a good biomembrane model may have lost some of its credibility.

References

1 Singer, S. J. and Nicolson, G. L. (1972) *Science* 175, 720–731

2 Cherry, R. J. (1979) *Biochim. Biophys. Acta* 559, 289–327

3 Hackenbrock, C. R. (1981) *Trends Biochem Sci.* 6, 151–154

4 Conrad, M. J. and Singer, S. J. (1981) *Biochemistry* 20, 808–818

5 Seeman, P. (1972) *Pharmacol. Rev.* 24, 583–655

6 Koppel, D. E., Sheetz, M. P. and Schindler, M. (1981) *Proc. Natl. Acad. Sci. U.S.A.* 78, 3576–3580

7 Cohen, P. S., Eisenberg, M. and McLaughlin, S. (1977) *J. Membr. Biol.* 37, 361–396

8 Hanstein, W. (1976) *Biochim. Biophys. Acta* 456, 129–148

DOUGLAS B. KELL

Department of Botany and Microbiology, The University College of Wales, Penglais, Aberystwyth, Dyfed SY23 3DA U.K.

The end of the scientific paper-chase?

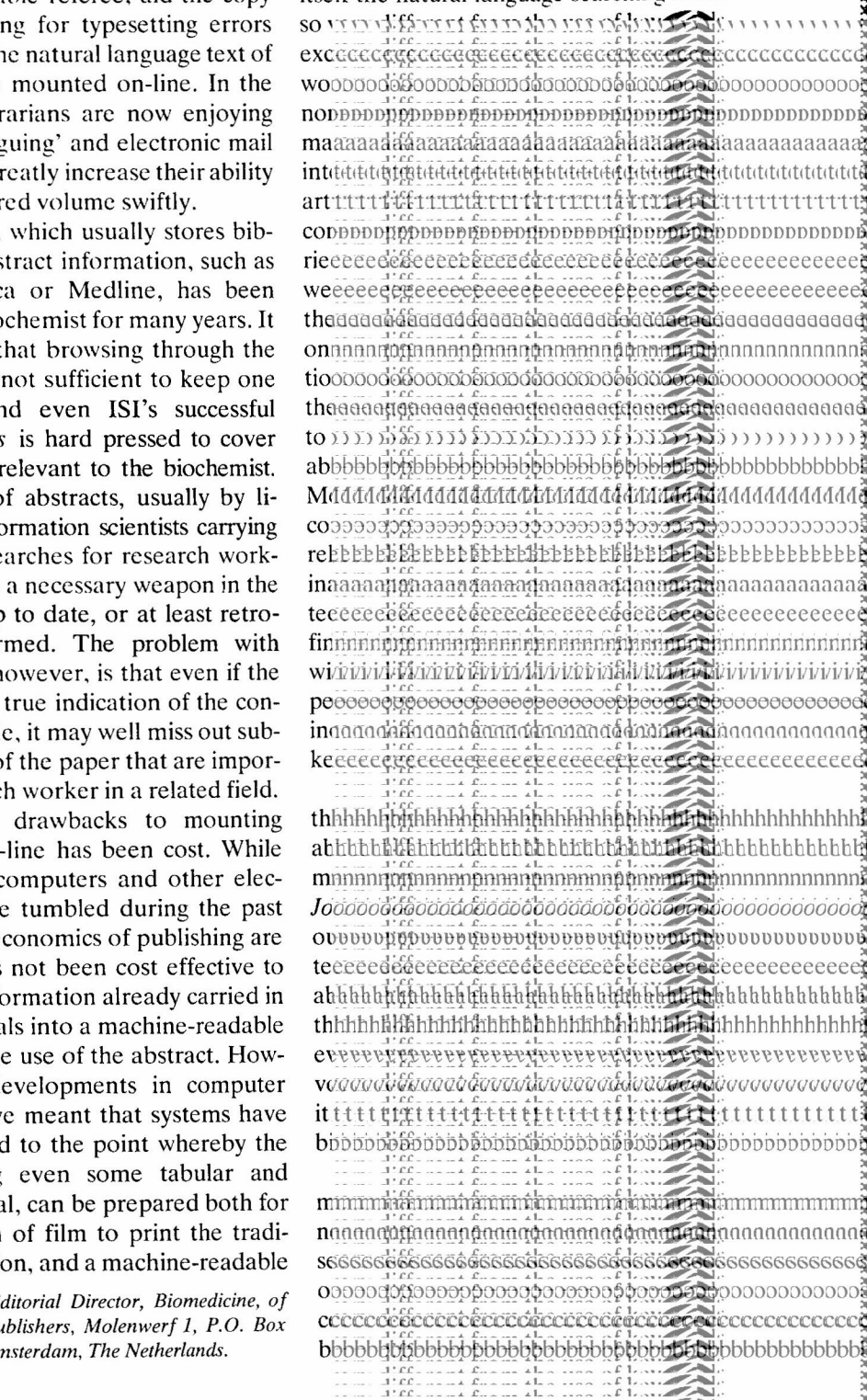
Jack Franklin

Electronic publishing – the use of computers and networks for transferring information – has arrived. For many years the information industry has been hearing of imminent moves which could make traditional forms of information transfer redundant, but most scientists are surprised to see how far this revolution has actually gone. Systems are now in operation which allow editors to use a computer to choose a suitable referee, aid the copy editor in checking for typesetting errors and even allow the natural language text of the article to be mounted on-line. In the book world, librarians are now enjoying 'common cataloguing' and electronic mail systems, which greatly increase their ability to locate a required volume swiftly.

The database, which usually stores bibliographic or abstract information, such as Excerpta Medica or Medline, has been known to the biochemist for many years. It is a fact of life that browsing through the journals is now not sufficient to keep one up to date, and even ISI's successful *Current Contents* is hard pressed to cover all the journals relevant to the biochemist. Thus, the use of abstracts, usually by librarians and information scientists carrying out literature searches for research workers, has become a necessary weapon in the fight to keep up to date, or at least retrospectively informed. The problem with these systems, however, is that even if the abstract gives a true indication of the content of the article, it may well miss out subsidiary aspects of the paper that are important to a research worker in a related field.

One of the drawbacks to mounting information on-line has been cost. While the prices for computers and other electronic aids have tumbled during the past few years, the economics of publishing are such that it has not been cost effective to repunch the information already carried in scientific journals into a machine-readable form. Hence the use of the abstract. However, recent developments in computer typesetting have meant that systems have been developed to the point whereby the text, including even some tabular and graphic material, can be prepared both for the production of film to print the traditional publication, and a machine-readable tape which can then be indexed and mounted on a database.

The American Chemical Society, in conjunction with Bibliographic Retrieval Services, now have the journal *Biochemistry* available on-line in natural language form; the illustrations, formulae and the majority of the tabular material are omitted. Thus the text can be searched using natural language terms. In itself the natural language searching is not so



Jack Franklin is Editorial Director, Biomedicine, of Elsevier Science Publishers, Molenwerf 1, P.O. Box 24000, 1000CK Amsterdam, The Netherlands.