A Berry Sweet Development: Microscopy of the Future

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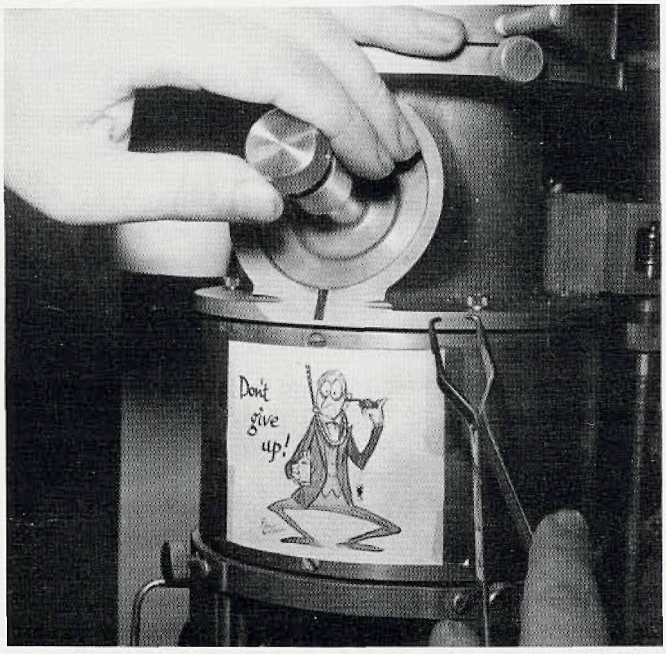
One of the most pervasive problems in microscopy is that of making sure that what one is observing represents reality. The complex specimen preparation steps which have to be followed to obtain images of biological samples all produce artifacts, at least in the sense that they modify the sample. The investigator has to somehow show that these changes in the sample reveal true microscopic features, rather than structures which do not exist in the living. This, of course, is why polarized light microscopy, phase and interference microscopy and their derived approaches, all of which reveal detail in live untreated specimen, are so important, in spite of the limited resolution which can be achieved.

When electron microscopy was in its infancy there were, and justifiably so, even more severe fears about the reality of what could be seen. Even visionary people like Gabor had their doubts and the first steps in biological microscopy were taken with the realization that if the sample was burned to a crisp, perhaps examination of its cinders would still give valuable information[1]. It was very important in the early days to have independent confirmation of the structures and this was to some extent achieved by comparison of the data obtained by X-ray diffraction experiments with that revealed by electron microscopy. Thus the work of pioneer biophysicists on nerve myelin and other "quasi" crystalline systems was of great importance. The myelin sheath of nerve was a regular array of membranes which could be studied "alive" by X-ray and also after processing for electron microscopy . . .

At the MSA meeting in Cincinnati last month it became obvious even to this jaded microscopist that another approach to the study of live samples was likely to become increasingly important. The technique in question is nuclear magnetic resonance (NMR) imaging (see Wehrli[2] for review), also called MRI so as not to raise fears associated with anything atomic. It is already a very powerful tool in the hands of the physician because insofar as one can presently ascertain it is "non invasive" and also gives good contrast in soft tissues. It is often used in imaging brain and other body structures. Even today it can be applied to the study of some dynamic events such as blood flow. As a result magnetic resonance angiography is a reality. Spectroscopic imaging, a very promising approach, allowing metabolic studies in vivo, is also being used for medical and other purposes. An example of the increasing pervasiveness of MRI can be found in its application to the study of water, lipid and carbohydrate distribution in the berries of Suitana, Chardonnay, Riesling and Shiraz grapes[3], a berry sweet application indeed! NMR is also fast becoming a very important tool, complementing X-ray techniques, for the study of molecules in solution.



The results presented at the meeting showed that NMR is also about to invade, nay has already done so, the field of microscopy! J. Slides of the University of Washington in Seattle discussed new methods for the detection of magnetic resonance, derived in part on approaches to magnetic force microscopy. They measure the small oscillatory magnetic force (10^{-14}N) acting on a paramagnetic sample (a smidgen < 30 ng of diphenylpicrylhydrazide) which has been excited into magnetic resonance in an inhomogeneous magnetic field. The force is detected by optical sensing the vibration of a cantilever on which the sample is mounted[4]. While a spatial resolution of only 19 micron was demonstrated, it became clear that the prospects for the future are much greater than that. The audience at the Presidential Symposium where this data was presented was left breathless by the prospect of this elegant approach. Another presentation by R. Jacobs and S. Fraser from Caltech addressed the biological applications of microscopic MRI, showing scans of a mouse embryo in utero. This group has already shown several years ago that NMR microscopy could be used to image and follow individual cells in developing Xenopus embryo[5]. Many problems have to be overcome if spatial resolution is to read in the submicron range, which theory says is possible. It appears however that ground is being covered rapidly and that MRI might well become one of the exciting new microscopies of the 21st Century. ■

References:

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