

GENERAL PHYSICS



## I. MOLECULE MICROSCOPY

### Academic and Research Staff

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Our research objectives remain much as stated in RLE Progress Report No. 120. We repeat the introduction:

Measuring the variations in space and time of fluxes of neutral molecules from a sample can give information not otherwise obtainable concerning, for instance, biological systems. We call the group of techniques used molecule microscopy (MM) and we believe that when fully developed it will have the same kind of revolutionary impact on biology that electron microscopy and x-ray diffraction have had.

Why biology rather than, say, material science? Because in biology there are structures of interest – inhomogeneities – of various sizes, from microns to angstroms, and neutral molecules are a natural (if not very agile) conveyor of information about surfaces, binding properties, permeability, metabolism, and enzymatic processes. In materials science, angstrom resolution, which we do not yet have, is needed to reveal features of interest, and the refractory nature of the material (often made up of atoms with medium to high Z) permits the use of more energetic probes.

### 1. SCANNING DESORPTION MOLECULE MICROSCOPE

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John G. King

In connection with the development of the scanning desorption molecule microscope (SDMM) (Fig. I-2, p. 2, RLE PR No. 120, January 1978), Mr. Jeffrey G. Yorker has undertaken the development of suitable localized heaters. In order to supply the heat necessary for local desorption of molecules from our samples, we have been developing an array of microheaters called the thermal-desorption array (TDA). This device circumvents many of the problems encountered previously when electron beams were explored as a means of exciting desorption, such as insufficient intensity, the back-scattering of electrons into the detector, and especially, sample damage by radiation. Furthermore, future microminiaturization of these devices will be feasible as the microelectronics industry advances. The TDA is an  $n \times n$  array of diodes each of which can

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be addressed by a pair of the  $2n$  wires along the edges of the array. Diodes are needed rather than simple resistive elements so that current can be restricted to flow through only one junction. Calculations to determine the size of the region of power dissipation show that the thermal and electrical requirements are compatible.

The prototype TDA is being constructed in the M. I. T. Microelectronics Laboratory using standard integrated-circuit techniques. The prototype consists of an  $8 \times 8$  array of diodes diffused into a silicon wafer substrate and addressed by aluminum leads running along the tops of the devices and heavily doped p-type stripes into the wafer below the devices. Two completed prototypes show promising electrical characteristics; the heating characteristics have yet to be tested.

## 2. SCANNING MICROPIPETTE MOLECULE MICROSCOPE

Health Sciences Fund

John G. King

In the development of the scanning micropipette molecule microscope (SMMM) (Fig. I-3, *ibid.*), Dr. Joseph A. Jarrell has established, with test patterns, the ability of the SMMM to detect differences in the concentration of helium dissolved in water. The instrument was subsequently used to examine *in vitro*-dissolved helium fluxes through toad and frog urinary bladder and Necturus gall bladder. No differences that could be attributed to junctional pathways were observed. Significant differences were measured in the flux through capillaries and muscle fiber. Therefore the macroscopic permeability of dissolved helium through toad bladder (corrected for boundary layers) was measured in a separate experiment as being  $1 \times 10^{-2}$  cm/sec. This is nearly the same as the diffusive conductance of an equivalent thickness of unstirred water, implying that this tissue presents few barriers to helium diffusion. This is consistent with the lack of differences in microscopic helium permeability through junctional pathways.

Recently the apparatus has been modified to detect fluxes of water labelled with stable isotopes, in particular, deuterium. Results and calculations to date indicate that a resolution of about  $10^{-4}$  cm and time response of 10-20 sec may be attainable.

## 3. CELL SURFACE STUDIES

Health Sciences Fund (Grant 78-03)

John G. King

These studies were undertaken, and techniques of growing cells on the sample ribbon were developed. The departure of Dr. Dusan G. Lysy interrupted this project, and we are currently modifying the apparatus to increase the rate at which data can be

obtained and the flexibility with which it can be recorded and analyzed.

#### 4. MOLECULE FLUXES IN TISSUE

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John G. King

We have continued the study of molecule fluxes in tissue, a collaborative project with Dr. Alvin Essig of the Department of Physiology at Boston University Medical Center. Dr. Stanley J. Rosenthal has built the molecule flux apparatus which makes possible the simultaneous measurement of  $\text{CO}_2$  production and  $\text{O}_2$  uptake by surviving epithelia mounted in Ussing chambers. This instrument has a time resolution on the order of one minute, which is very rapid for this type of work. Results have revealed changes in the ratio of  $\text{CO}_2$  produced to active Na transport rates in toad urinary bladder, previously not seen. Further development should make possible the measurement of early transient metabolic phenomena in these tissues. Dr. Ying-Tung Lau has made related measurements of the basal rate of metabolism in transporting epithelia. A second molecular flux apparatus is being constructed to study the relative  $\text{H}_2\text{O}$  permeabilities of cells and tight junctions in "loose epithelia" with a spatial resolution of a few microns.

