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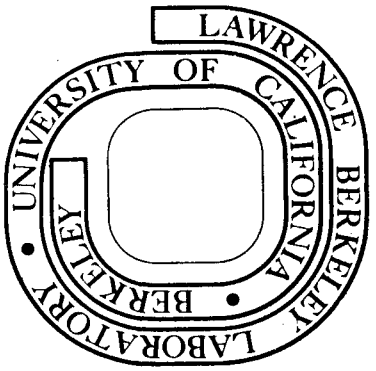

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METHODOLOGY IN THE RADIOLYSIS OF BIOCHEMICAL COMPOUNDS WITH CYCLOTRON BEAMS AT LOW FLUX DENSITIES*

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SUMMARY: A modification of the standard beam-optics of the LBL 88-Inch Cyclotron now makes it practicable to use cyclotron radiations in the detailed study of the effects of linear energy transfer (LET) in the radiation chemistry of organic compounds in the solid state. Dosages and dose-rates are comparable to those employed in conventional γ-ray studies. The modification involves passing the focused beam through a pair of "beam-sweeping" electromagnets so that a circular target area up to 10 cm in diameter can be uniformly irradiated with beams in the nanoamp range. Yield data are given for the radiolysis of the Fricke dosimeter with beams of H^{+}, H^{+2}, Be^{+4}, C^{+6} and Ne^{+10} at ~10 MeV per nucleon. Preliminary data on the effects of LET in the radiolysis of solid glycine are reported.

Most of our knowledge of the chemical actions of ionizing radiations on biochemical compounds has been derived from studies involving fast electrons produced either directly by an accelerator or secondarily through the absorption of X or γ radiation. In recent years, the increasing interest in the effects of high-energy heavy-ion beams on biological systems[1,2] has emphasized the need for expanding our knowledge of the effects of linear energy transfer (LET) in the radiation chemistry of biochemical compounds both in the solid state and in aqueous solution.

We have undertaken such a study using the 88 inch cyclotron at the Lawrence Berkeley Laboratory as the radiation source. This is a sector focused machine capable of producing fully-stripped ions up to argon at maximum energies of $\frac{Z^2}{A}$ x 140 MeV where Z is the charge of the accelerated ion and A is the mass of the particle in proton units[3].

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Heretofore, the use of cyclotron beams in the radiation-chemical study of organic solids has been limited by the fact that the amount of irradiated material obtained from a single exposure with conventional beam optics and target geometries is generally not more than a few tens of milligrams. For example, C^{+6} ions at an energy of ~10 MeV per nucleon have a range of ~.05 cm in a bio-organic material such as glycine. If the diameter of the focused beam is in the order of 0.5 - 1 cm then the irradiated mass would correspond to 10-40 mg. While this amount of irradiated material is adequate for certain types of measurement (e.g. esr spectroscopy), any extensive chemical determination of product yields is impracticable.

Another limiting factor in the cyclotron irradiation of organic solids under conventional target conditions is that the dose-rates are inherently much higher than those encountered in the γ-ray literature. For example, with a beam of C^{+6} ions at an energy of 10 MeV per nucleon and at a beam current as low as 1 nanoamp over a 0.5 cm diameter target area, the dose-rate corresponds to 9.2×10^{20} eV/gm-min. This is roughly 600 times the maximum dose-rate delivered by a ^{60}Co γ-ray source of $\sim 10^4$ curies.

These problems, of course, have been less limiting in the radiation-chemical study of aqueous solutions and other liquids of low viscosity since vigorous mechanical mixing can be employed to average the energy of the absorbed beam over a large sample volume.[4-6]

In adapting the LBL 88 inch cyclotron to the radiation-chemical study of biochemical systems we use a pair of "beam-sweeping" magnets so that a circular target area 6 cm * in diameter can be uniformly irradiated with beams in

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* With a 6 cm aperture we use a 19 μm aluminum foil "window" to contain the cyclotron vacuum. Larger areas can be irradiated with the present equipment but the "window" thickness must be increased to withstand the pressure differential.

the nanoamp range. The "sweep" magnets are energized with approximately square-wave alternating currents of different frequencies. Usually the frequencies are in the 100 ± 20 Hz range with a difference between them of 10 Hz so that the beam covers the target every o.1 sec. The beam current is measured in the vacuum pipe with a secondary-emission monitor which consists of two aluminum foils 6.4 μm in thickness of a separation of 12.7 mm. The upstream foil is maintained at 70 volts negative while the down stream one is connected to a capacitor box and a feed-back type electrometer. The monitor is calibrated against a Faraday cup which is located in a magnetic field of 500 gauss. It is also connected to a calibrated capacitor box and electrometer.

In the irradiation of solids, the sample material is compressed into the circular cell (Lucite) under hydraulic pressure (7000 lb/sq.in.) in an argon atmosphere. A mylar foil (2.5 μm) is then affixed with a retaining ring and the two gas ports are sealed-off before removing the cell from the inert atmosphere. Cells for the irradiation of liquids are of a similar design with minor modifications to permit aeration and stirring of the solution during irradiation. In the irradiation, the target cell replaces the Faraday cup and dose to the sample is measured with the calibrated emission-monitor. Appropriate corrections are made for energy loss in the foils and air gap.[7]

As a further check on dosimetry we measured Fe^{+3} production in the Fricke chemical dosimeter (.01 M Fe^{+2} in o.8 N H_2SO_4, 0_2-saturated) for several different beams. Typical data for a C^{+6} beam at an energy of ~10 MeV/nucleon are shown in Fig. 1. With a 1 nanoamp beam uniformly distributed over the 6 cm diameter target the dose-rate to the irradiated volume corresponds to ~5 x 10^{18} ev/gm-min. As is evident from Fig. 1, no mechanical stirring is required at the low flux densities provided by the "beam-sweep" technique. In Table 1 we summarized $G(Fe^{+3})$ values * obtained with several different ion beams at

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* The G value represents the number of product species formed per 100 ev absorbed energy.

8.5-10 MeV/nucleon. Numbers in parenthesis are literature values obtained at high flux densities with mechanical stirring.

We are presently using this low-flux facility in the study of LET effects in the radiolysis of the simpler α-amino acids and their peptide derivatives. Preliminary data on the radiolysis of solid glycine by H^+ and C^{+6} at 10 MeV/nucleon are given in Table 2. Results previously obtained with γ-rays are included for purposes of comparison. Although it is not our intent here to present a detailed consideration of LET effects in the radiolysis of solid glycine, we would note, however, that with γ-rays the major products ammonia, acetic acid and glyoxylic acid have been shown to arise as a consequence of charge separation[8] i.e.

$$NH_3^+CH_2COO^- \rightsquigarrow NH_3^+\dot{C}HCOO^- + H^+ + e^- \quad (1)$$

$$e^- + NH_3^+CH_2COO^- \longrightarrow NH_3 + \dot{C}H_2COO^- \quad (2)$$

followed by

$$NH_3^+\dot{C}HCOO^- + CH_2COO^- \longrightarrow NH_2^+=CHCOO^- + CH_3COO^- \quad (3)$$

$$NH_2^+=CHCOO^- + H_2O \longrightarrow NH_3 + CHOCOOH \quad (4)$$

where steps 3,4 occur on dissolution of the irradiated sample in O_2-free water. With γ-rays, essentially all of the electrons escape the postive charge and are removed via the reductive deamination reaction 2. This also appears to be the case with 10 MeV protons which also have a relatively low LET. However with the C^{+6} beam we observe a pronounced decrease in the yield of products derived from the charge-separation reacts 1,2. A high LET radiation such as C^{+6} at 10 MeV/nucleon produces a track which is comprised of a core of high ionization density surrounded by a sheath of lower ionization density which is formed by the secondary electrons ejected from the core.[9,10] Since it is in the regions of low ionization density that reactions 1-4 can occur, it would appear then that approximately one-half the ion-pairs produced on absorption of a 120 MeV C^{+6} ion in solid glycine are produced in the sheath region.

Ion-recombination in the core leads to other products among them being methylamine the yield of which increases regularly with LET. A detailed discussion of LET effects in the radiolysis of solid glycine in terms of the recent developments in track theory[10] will be forthcoming.

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TABLE I. FERRIC ION YIELDS IN THE HEAVY-PARTICLE IRRADIATION OF THE FRICKE DOSIMETER [a]

Radiation	Energy (MeV)	$G(Fe^{+3})$
He^{+2}	34	8.3
	34	8.1
	34	(8.3)[b]
Be^{+4}	91	6.5
C^{+6}	102	5.2
	102	(5.0)[c]
Ne^{+10}	206	4.8

[a] $\sim$0.1N Fe^{+2} in 0.8N H_2SO_4, O_2-saturated.
[b] Ref. 11.
[c] Ref. 12.

TABLE II. LET EFFECTS IN THE RADIOLYSIS OF SOLID GLYCINE

Radiation	LET (eV/A°)[a]	Products (G)		
		NH_3	CH_3COOH	CHOCOOH
^{60}Co-γ	~ 0.1	4.8	2.3	2.0
10 MeV H^+	~ 1	4.4	2.3	1.9
120 MeV C^{+6}	~ 24	3.5	1.1	0.95

[a]Average value as given by energy/range.

FIGURE LEGEND

Fig. 1. Ferric ion production in the Fricke dosimeter as a function of dose for 102 MeV C^{+6} ions.

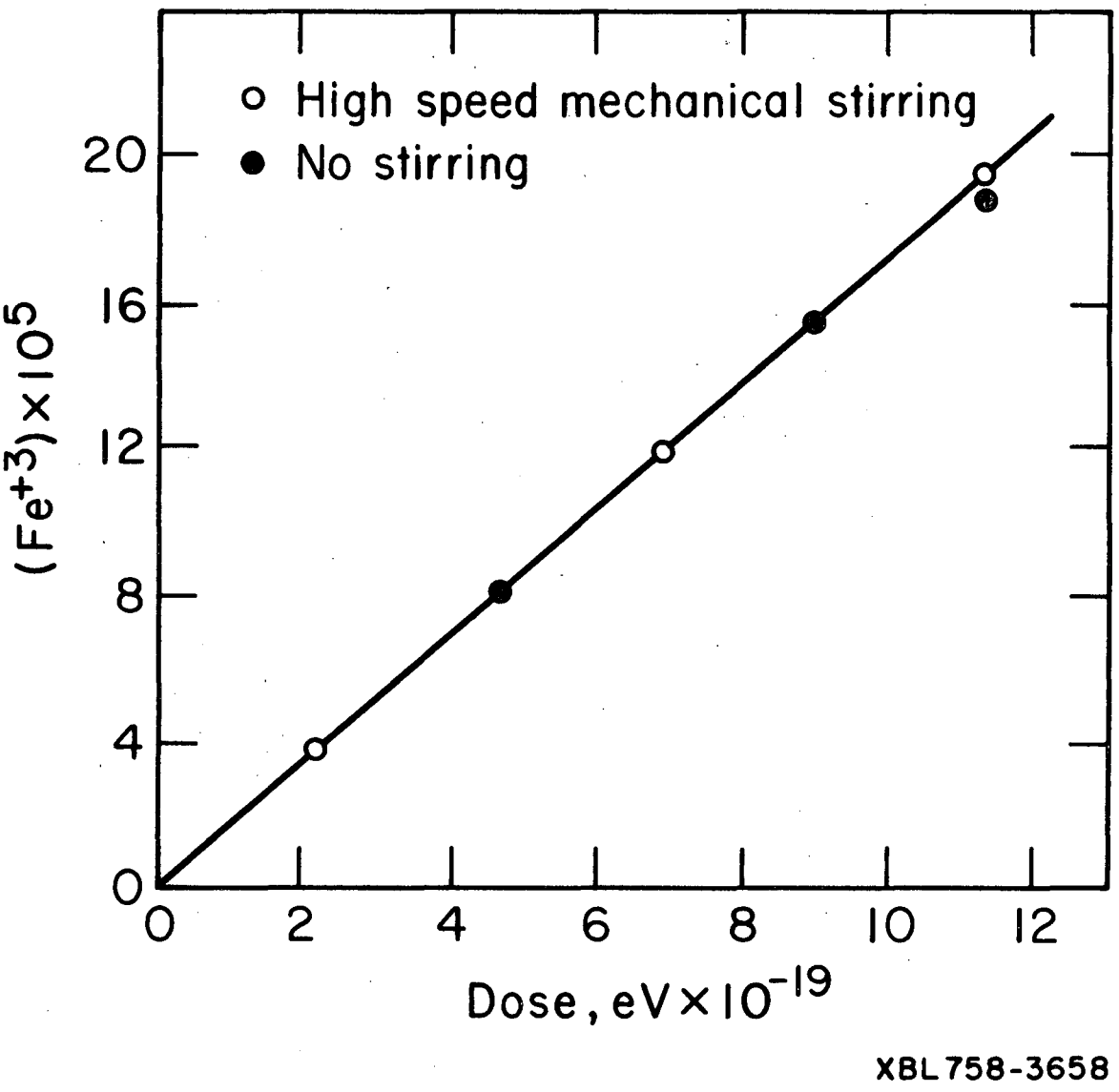

Fig. 1

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