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CALCULATED YIELDS OF AMMONIA IN THE RADIOLYSIS OF DEOXYGENATED SOLUTIONS OF GLYCYLGLYCINE

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DISCLAIMER

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ABSTRACT

This paper presents detailed Monte Carlo simulations of physical and chemical interactions occurring within electron tracks in deoxygenated solutions of glycylglycine. Hydrated electrons produced within these tracks react with the solute to produce ammonia and a peptide secondary free radical. Calculated yields of ammonia are presented for a range of solute concentrations and electron energies. Excellent agreement is found between calculated and measured yields of ammonia in solutions irradiated by 250-kVp X-rays and ^{60}Co gamma rays.

INTRODUCTION

Researchers at the Oak Ridge National Laboratory have developed a Monte Carlo computer model which simulates the transport of charged particles and their secondary electrons through liquid water[1-3]. This code, OREC, calculates the spatial coordinates of each H_2O^+, H_2O^*, and e^-_{sub} produced within electron, proton, or alpha-particle tracks. Through a collaborative effort with radiation chemists at Lawrence Berkeley Laboratory, a second Monte Carlo code, RADLYS, was developed which simulates the conversion of these intermediate species into free radical species. The simulations continue with the diffusion and chemical reaction of track species up to one microsecond. Previous

studies have been limited to pure water irradiation[4-6]. One study was made of irradiated oxygenated water[7] and one of irradiated pure water containing a simplistic model of the DNA double helix[8]. The present study is a first attempt at using these codes to model indirect radiation damage to a more realistic biomolecular system.

The molecule chosen for study is glycylglycine, a dimer of the amino acid glycine. The radiation chemistry of glycylglycine, $NH_3^+CH_2CONHCH_2COO^-$, in aqueous solution begins with the following three reactions:

$$H + NH_3^+CH_2CONHCH_2COO^- \longrightarrow H_2 + NH_3^+CH_2CONHCHCOO^- \quad (1)$$

$$OH + NH_3^+CH_2CONHCH_2COO^- \longrightarrow H_2O + NH_3^+CH_2CONHCHCOO^- \quad (2)$$
(H-abstraction radical)

$$e_{aq}^- + NH_3^+CH_2CONHCH_2COO^- \xrightarrow{H^+} NH_4^+ + CH_2CONHCH_2COO^- \quad (3)$$
(deamination radical)

In keeping with the terminology of Garrison *et al.*[9], the ammonium ion generated in reaction (3) is referred to as free ammonia. The two secondary peptide radicals react with one another or with the solute to form various precursor species. With the addition of strong acid to the

sample after irradiation, these precursors yield products such as diaminosuccinic acid, aspartic acid, succinic acid, glyoxylic acid, and additional ammonia.

This paper presents microsecond yields of free ammonia calculated for a range of electron energies and solute concentrations. At each concentration, these yields are weighted by the spectrum of electron energies produced during irradiation by 250-kVp X-rays. These weighted yields of free ammonia are then compared to measured yields.

CALCULATIONS FOR MONOENERGETIC ELECTRONS

Figure 1 presents calculated, time-dependent yields of hydrated electrons within 50-keV electron tracks in solutions of glycylglycine at various concentrations. The top curve gives the calculated yield of e^-_{aq} in pure water and thus represents the maximal supply of hydrated electrons available to react with the solute at any given time. The yield of e^-_{aq} in 0.025 M glycylglycine equals that within pure water up until $\sim 3 \times 10^{-9}$ s. This suggests that glycylglycine at 0.025 M is ineffective in competing with intratrack reactions for the supply of hydrated electrons until the track species have diffused outward for $\sim 3 \times 10^{-9}$ s. After that time, track species become increasingly separated such that solute scavenging becomes more likely than intratrack reaction. Solute scavenging continues until all hydrated electrons are consumed by one microsecond. At a concentration of 1.2 M, solute scavenging within the track becomes important at an earlier time, $\sim 6 \times$

10^{-11} s, and no hydrated electrons remain after ~10^{-8} s. Since the pure water yield of e^-_{aq} is greater at earlier times, and since e^-_{aq} scavenging occurs at earlier times with increasing solute concentration, the total yield of free ammonia is expected to be greater in systems of higher glycylglycine concentration.

The yield of free ammonia within 50-keV electron tracks as a function of time and solute concentration is presented in Fig. 2. As predicted, increases in solute concentration result in a greater and earlier production of free ammonia within the track.

Similar calculations are made over a range of electron energies. Figure 3 shows calculated microsecond yields of free ammonia at various solute concentrations for electron energies between 1 keV and 140 keV. At each solute concentration, the yield of free ammonia decreases with decreasing electron energy and this is attributed to changes in mean LET. At lower electron energies, the track's average LET increases and thus there is a greater intratrack consumption of hydrated electrons; consequently, there are fewer hydrated electrons available to undergo reaction (3).

CALCULATIONS FOR IRRADIATION BY 250-KVP X-RAYS

So as to provide experimental support for these calculations, measured yields of free ammonia are obtained for solutions of glycylglycine irradiated by 250-kVp X-rays[10]. An estimate of the spectrum of electron energies produced within irradiated samples is

shown in Fig. 4. The spectrum gives the fraction of total energy contributed by photon-produced electrons of energy E per energy interval. This spectrum was calculated by the Monte Carlo code PHOEL-2[11,12] using an incident photon spectrum estimated by Kramers distribution. Contributions by photoelectrons and Compton electrons is also shown.

By weighting each curve in Fig. 3 by the total electron spectrum in Fig. 4, calculated yields of free ammonia under X irradiation are obtained for comparison with measured yields, as shown in Fig. 5. The solid curves indicate the 95% confidence limits of the calculations and represent the magnitude of statistical fluctuations observed between individual simulated electron tracks. Excellent agreement between calculated and measured yields is shown over the concentration range 0.05 M to 1.2 M glycylglycine.

The curves shown in Fig. 3 can also be weighted by an electron spectrum corresponding to ^{60}Co gamma irradiations. Calculated yields of free ammonia under ^{60}Co irradiation are 2.98 ± 0.09 at 0.05 M and 3.78 ± 0.09 at 1.0 M glycylglycine. Garrison *et al.* reports measured free ammonia yields of 2.8 ± 0.3 at 0.05 M and 3.8 ± 0.4 at 1.0 M glycylglycine[9]. Again, measured and calculated yields are in excellent agreement.

The calculated yield of free ammonia exceeds the measured value at 0.025 M glycylglycine for X irradiation. This may be attributed to solute depletion at earlier times within electrons tracks at low solute

concentration. In the simulation model, reactions (1), (2), and (3) are treated by pseudo-first-order kinetics in which each H, OH, and e^-_{aq} is given an exponential probability of reacting with the solute over each simulated time interval. In this manner, solute molecules are not modeled explicitly and local depletion of the solute is assumed negligible. If such depletion does occur, the calculations would overestimate the number of reactions between hydrated electrons and the solute, thus overestimating the yield of free ammonia.

CONCLUSIONS

These results suggest that Monte Carlo computer simulations represent a unique and feasible method of understanding indirect radiation damage at the molecular level. The following items support this assertion. First, the simulations predict yields of free ammonia consistent with experiment over the concentration range 0.05 M to 1.2 M glycylglycine. Second, the simulations are able to mechanistically explain several phenomena. For example, the dependence of free ammonia yields on both electron energy and solute concentration is readily understood in terms of track diffusion, track LET, and the competition between intratrack and solute consumption of hydrated electrons. Third, the simulations suggest values for quantities that, in most instances, would be difficult to obtain experimentally. For example, the model readily provides product yields as a function of time during the interval 10^{-12} s to 10^{-6} s within charged-particle tracks. This time

interval is important in cellular systems since free radical scavengers exist in high concentration. Indirect damage in these systems is thus highly localized and is complete well within this time interval.

Future work will focus on simulating alpha-particle irradiation of glycylglycine solutions. Comparison of calculated and measured yields of several radiolysis products for both photon and alpha-particle irradiations would provide further tests of the Monte Carlo simulations. It is hoped that this combined calculational and experimental approach can be extended to investigate mechanisms of radiation damage to DNA and DNA subunits.

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FIGURE TITLES

Fig. 1. Yield of hydrated electrons calculated for 50-keV electrons in deoxygenated glycylglycine solution as a function of time and solute concentration.

Fig. 2. Yield of free ammonia calculated for 50-keV electrons in deoxygenated glycylglycine solution as a function of time and solute concentration.

Fig. 3. Calculated yield of free ammonia in deoxygenated glycylglycine solution as a function of electron initial energy and solute concentration.

Fig. 4. Electron energy distribution within solutions irradiated by 250-kVp X-rays. Total curve is normalized to unit area and gives the fraction of total energy deposition by photon-produced electrons of initial energy E per energy interval.

Fig. 5. Yield of free ammonia in deoxygenated solution. Solid curves indicate the limits of the 95% confidence interval for calculated yields of free ammonia. Points indicate measured mean yields from Reference 10. Error bars on the points give the 95% confidence interval as determined from replicate analyses.

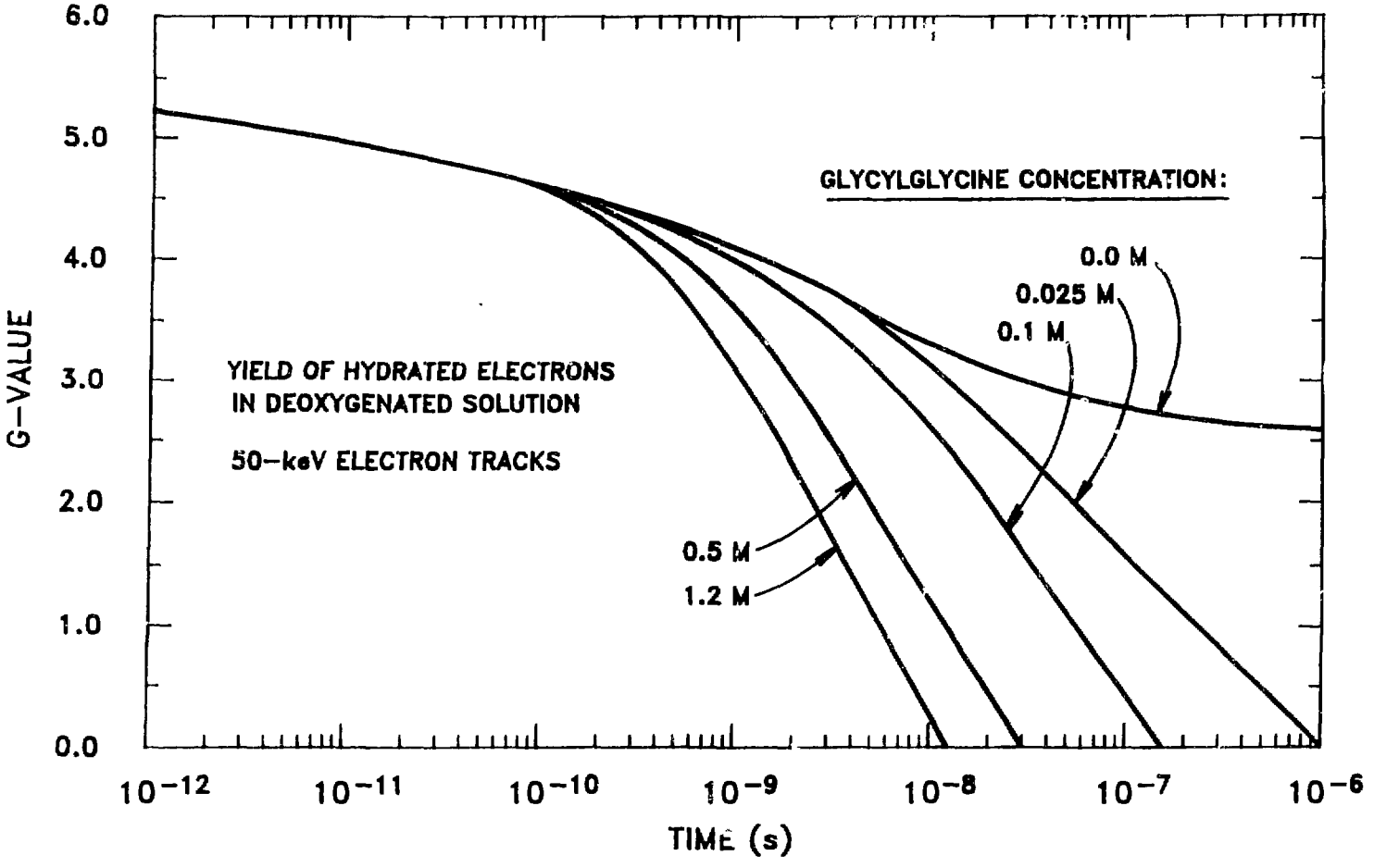
6.0
5.0
4.0
3.0
2.0
1.0
0.0
G-VALUE
GLYCYLGLYCINE CONCENTRATION:
0.0 M
0.025 M
0.1 M
0.5 M
1.2 M
YIELD OF HYDRATED ELECTRONS
IN DEOXYGENATED SOLUTION
50-keV ELECTRON TRACKS
10^{-12}
10^{-11}
10^{-10}
10^{-9}
10^{-8}
10^{-7}
10^{-6}
TIME (s)

Figure 1

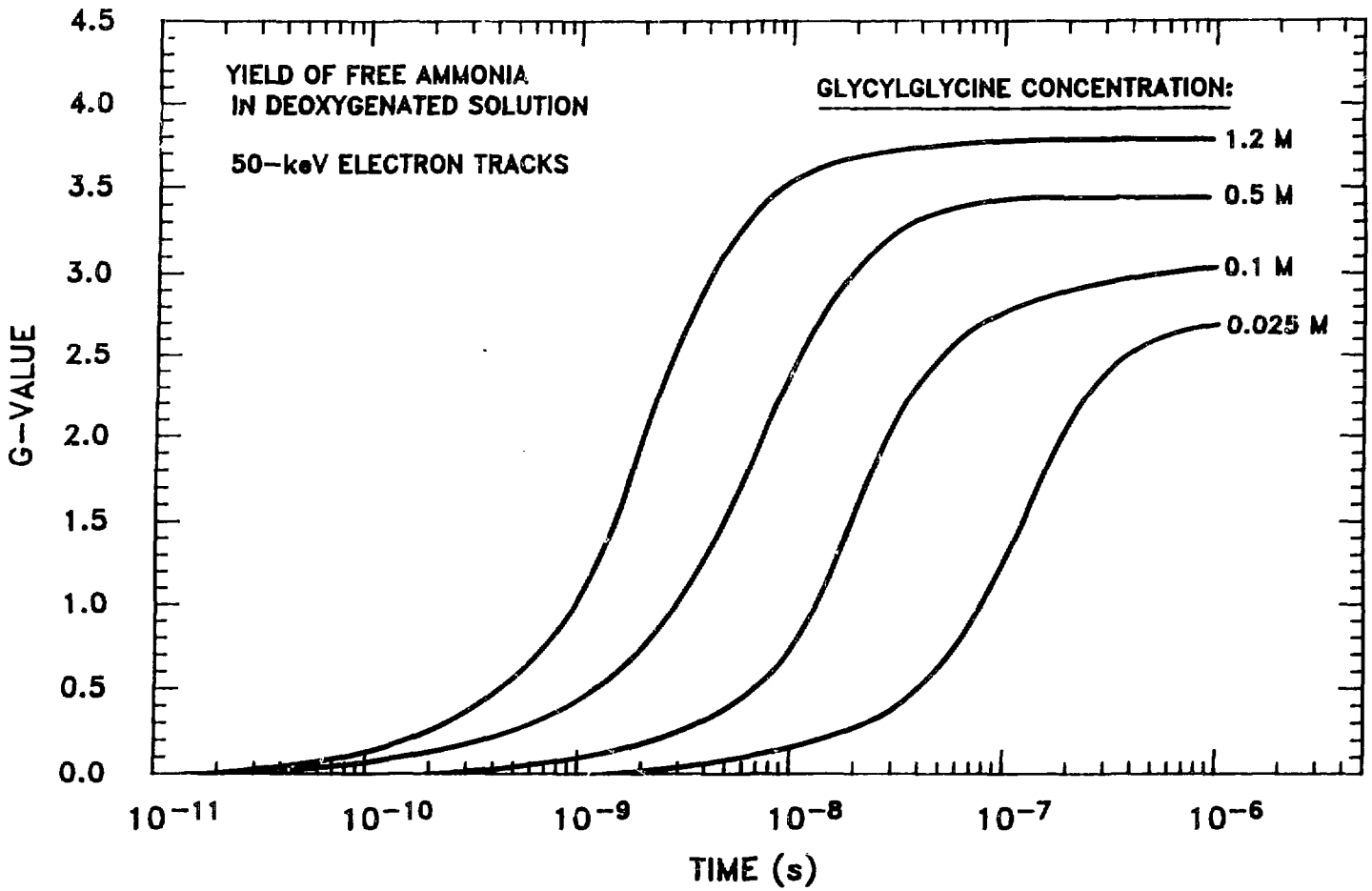
YIELD OF FREE AMMONIA
IN DEOXYGENATED SOLUTION
50-keV ELECTRON TRACKS
GLYCYLGLYCINE CONCENTRATION:
1.2 M
0.5 M
0.1 M
0.025 M
G-VALUE
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
10^{-11}
10^{-10}
10^{-9}
10^{-8}
10^{-7}
10^{-6}
TIME (s)

Figure 2

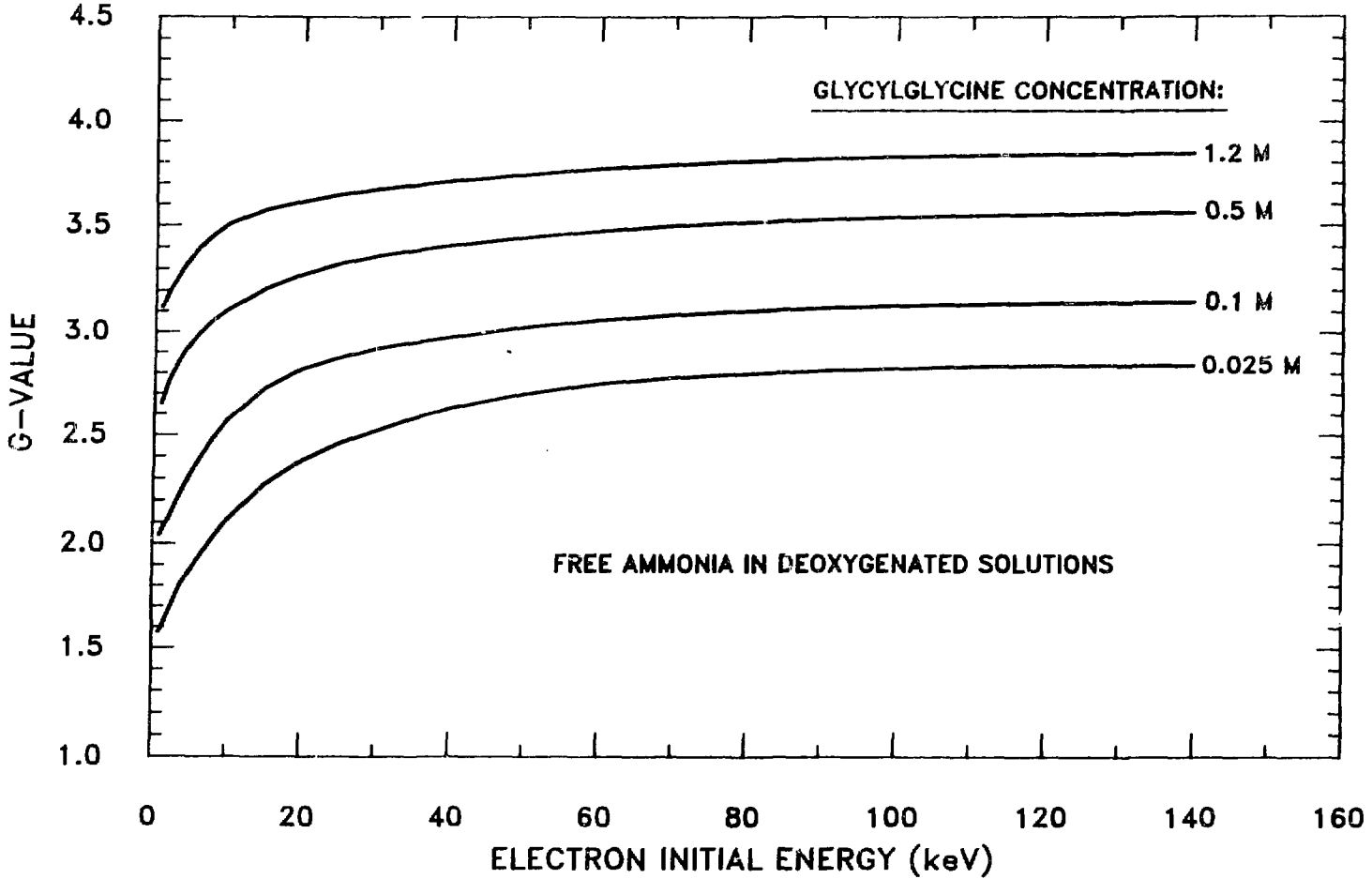
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
G-VALUE
GLYCYLGLYCINE CONCENTRATION:
1.2 M
0.5 M
0.1 M
0.025 M
FREE AMMONIA IN DEOXYGENATED SOLUTIONS
0
20
40
60
80
100
120
140
160
ELECTRON INITIAL ENERGY (keV)

Figure 3

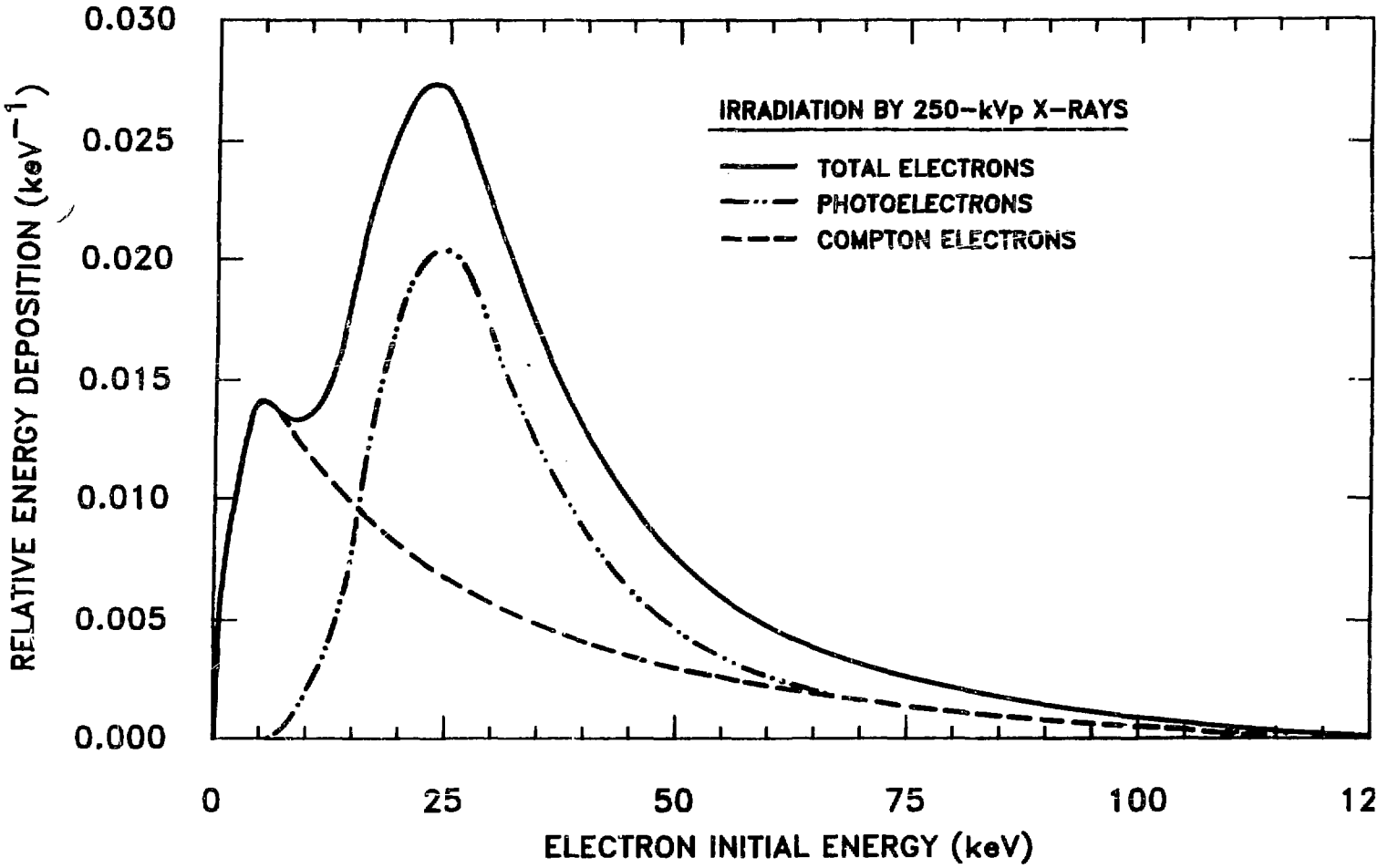
IRRADIATION BY 250-kVp X-RAYS
TOTAL ELECTRONS
PHOTOELECTRONS
COMPTON ELECTRONS
RELATIVE ENERGY DEPOSITION (keV^{-1})
0.030
0.025
0.020
0.015
0.010
0.005
0.000
0
25
50
75
100
12
ELECTRON INITIAL ENERGY (keV)

Figure 4

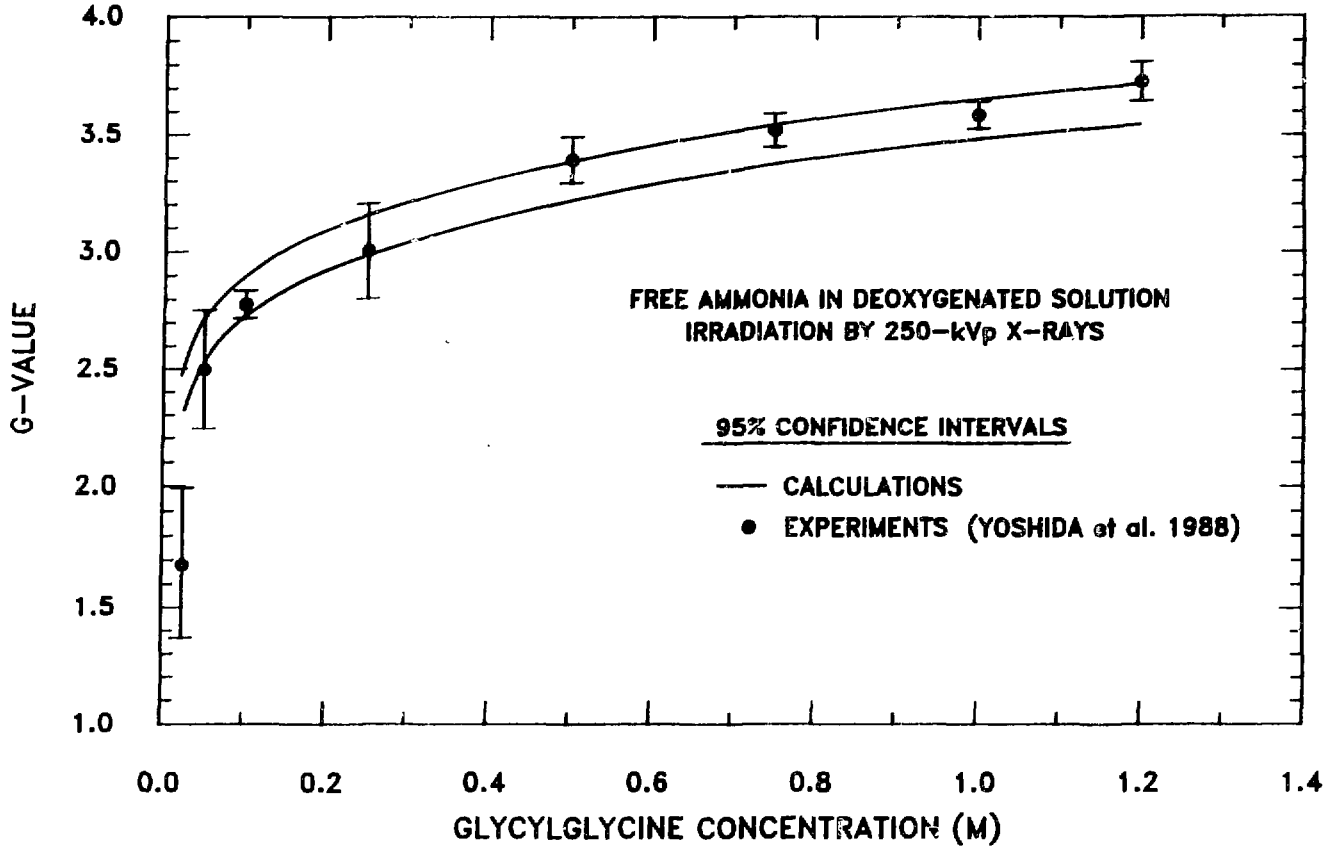
4.0
3.5
3.0
2.5
2.0
1.5
1.0
G-VALUE
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
GLYCYLGLYCINE CONCENTRATION (M)
FREE AMMONIA IN DEOXYGENATED SOLUTION
IRRADIATION BY 250-kVp X-RAYS
95% CONFIDENCE INTERVALS
CALCULATIONS
EXPERIMENTS (YOSHIDA et al. 1988)

Figure 5