

## Crosslinked Poly(vinyl Alcohol) Hydrogels as Swollen Elastic Networks

NIKOLAOS A. PEPPAS\* and EDWARD W. MERRILL, *Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts, 02139*

### Synopsis

Transparent crosslinked PVA hydrogels were prepared by electron beam irradiation of aqueous solutions under nitrogen. These weak hydrogels, upon swelling at 30 °C in water, showed low elastic moduli (up to 50 psi), low ultimate tensile strength (up to 4 psi), and low extensibility to break (not higher than 85%). Values of the molecular weight between crosslinks  $M_c$  were calculated from swelling and from tensile experiments. In fact, two values of  $M_c$  were calculated for each swelling experiment, (a) allowing for observed variation in the polymer-solvent interaction parameter  $\chi_1$  with concentration, and (b) fixing  $\chi_1 = 0.494$  according to literature data. The correlation of the  $M_c$  obtained from tensile data with the  $M_c$  obtained from swelling data, by (a) or (b), was approximately linear and gave the same per cent agreement.

### INTRODUCTION

For the past 15 years, a number of investigators have devoted their time and experience in developing various complex biomaterials for diverse applications. A wide variety of polymeric materials have been studied in reference to their ability to prevent blood coagulation when blood comes in contact with them, without the continuous administration of heparin solution, as is the practice these days.

Evidence available in the literature<sup>1</sup> shows that when a network is in its rubbery or solvated state, it is less thrombogenic than when it is in a semicrystalline state, because the molecular units at the blood interface are in a "liquid state" of lower attractive force fields than the crystalline cells. It was under this theory that a series of hydrogels of poly(vinyl alcohol) (PVA) have been recently developed by Merrill et al.<sup>2,3</sup> Pure homogeneous PVA hydrogels have been recently prepared by electron beam irradiation of aqueous PVA solutions under various conditions. Upon irradiation, the solutions became crosslinked and formed transparent hydrogels.<sup>4-6</sup> Characterization of the physical properties of these hydrogels and especially of their swelling characteristics and the crosslinking density has been reported in a previous publication by Bray and Merrill,<sup>4</sup> along with some data on their mechanical properties.

\* Present address: School of Chemical Engineering, Purdue University, West Lafayette, Indiana 47907.

It was the subject of this study to characterize the crosslinking of the networks using the results of the tensile experiments, in comparison with swelling experiments, and in addition to evaluate the ultimate stress-strain properties.

### Crosslinked PVA Networks Formed Via Irradiation

When aqueous solutions of poly(vinyl alcohol), PVA, are irradiated by electron beams or  $\gamma$ -rays, crosslinking occurs and the solution is transformed to a transparent homogeneous hydrogel containing an amount of water which depends on the concentration of the initially irradiated solution.<sup>7-9</sup> This is not the case with the irradiation of solid PVA films below their glass transition temperature, where, because of the absence of mobility of the free radicals formed by irradiation, there is impairment of coupling of radical pairs.<sup>10,11</sup>

Crosslinked polymeric networks are conveniently characterized by the crosslinking density  $\rho$  which is inversely related to the average molecular weight per crosslinking unit  $M_c$ , according to eq. (1), where  $\bar{v}$  is the specific volume of the polymer:

$$\rho = 1/\bar{v}M_c \quad (1)$$

Bray and Merrill<sup>4</sup> recently published data on the effect of the dose delivered by electron beam irradiation, of the temperature of irradiation, and of the initial concentration of PVA solutions on  $M_c$ . They reported (within the range of 3–15 megarads of irradiation, 5–30% PVA concentrations, and 0–85°C) that increase of the dose delivered, decrease of the temperature, and decrease of the PVA concentration favored the formation of higher crosslinking density  $\rho$ .

### Study of Hydrogel Networks

In hydrogel networks, the knowledge of the crosslinking density is of importance because of its effect on the mechanical properties of these materials and their behavior upon practical applications.

In the original equilibrium swelling theory of Flory,<sup>12</sup> an initially nonsolvated, crosslinked network is swollen by the absorption of solvent until the increase of elastic energy of the chains forming the network balances the decrease in the free energy consequent to mixing of polymer segments with solvent molecules. This led to the well-known expression

$$\frac{1}{M_c} = \frac{2}{M_n} - \frac{\frac{\bar{v}}{V_1} [\ln (1 - v_{2,s}) + v_{2,s} + \chi_1 v_{2,s}^2]}{\left[ v_{2,s}^{1/3} - \frac{v_{2,s}}{2} \right]} \quad (2)$$

where  $v_{2,s}$  is the final swollen equilibrium polymer volume fraction,  $V_1$  is the molar volume of solvent = 18 cm<sup>3</sup>/mole,  $\bar{v}$  is the specific volume of bulk polymer in the amorphous state = 0.788 cm<sup>3</sup>/g,  $M_n$  is the number-average molecular weight of the primary chains = 88,880, and  $\chi_1$  is the Flory polymer-solvent interaction parameter.

The above expression was modified by Flory<sup>13</sup> for the case of a swollen network where the crosslinks were introduced into the polymer which was already in the

solution state and which has a volume fraction  $v_{2,r}$  after the crosslinking process but prior to the equilibration with more pure solvent. Similar analysis was reported by Bray and Merrill.<sup>4</sup> In this case, the swelling equation is found to be

$$\frac{1}{M_c} = \frac{2}{M_n} - \frac{\bar{v}}{V_1} \frac{[\ln(1 - v_{2,s}) + v_{2,s} + \chi_1 v_{2,s}^2]}{v_{2,r} \left[ \left( \frac{v_{2,s}}{v_{2,r}} \right)^{1/3} - \frac{1}{2} \left( \frac{v_{2,s}}{v_{2,r}} \right) \right]} \quad (3)$$

In the companion experiment of determining force–elongation relations suggested by the theory of rubber elasticity, Flory et al.<sup>14</sup> showed that when an initially unswollen crosslinked elastomer is first swollen so that the volume fraction of polymer decreases to  $v_2$  (the remainder being solvent), the tensile stress  $\tau$  expressed as force per unit area of the *swollen, unstretched* sample, is related to the extension ratio  $\alpha$  by the equation

$$\frac{\tau}{[\alpha - (1/\alpha^2)]} = \frac{RT}{\bar{v}M_c} \left( 1 - \frac{2M_c}{M_n} \right) v_2^{1/3} \quad (4)$$

For the case in which the polymer is initially in solution at a mass concentration  $C_{2,r}$  g/cm<sup>3</sup>, Flory et al.<sup>14</sup> showed that the appropriate version of eq. (4) led to the result

$$\frac{\tau}{\alpha - (1/\alpha^2)} = RT \frac{C_{2,r}}{M_c} \left( 1 - \frac{2M_c}{M_n} \right) Q^{-1/3} \quad (5)$$

wherein  $Q$  is the volume swelling ratio of the polymer after thermodynamic equilibrium with its solvent. Thus,

$$Q = v_{2,r}/v_{2,s} \quad (6)$$

where  $v_{2,s}$  and  $v_{2,r}$  have the meanings defined for eq. (3). This equation was used by Silliman<sup>15</sup> for evaluation of  $M_c$  of chemically crosslinked PVA networks from simple tensile experiments.

In this study, values of  $M_c$  of radiation-crosslinked PVA hydrogels<sup>16</sup> were calculated by eqs. (3) and (5).

## EXPERIMENTAL

The poly(vinyl alcohol) (PVA) used in this study was Elvanol 73-125 G grade of du Pont with  $\bar{M}_n = 88,880$  as calculated by gel permeation chromatography. It was hereafter assumed that  $\bar{M}_n$  did not decrease significantly under irradiation. This PVA contains less than 0.7% acetyl groups, 1% head-to-head units, and less than 0.1% carbonyl groups.

Weighed portions of PVA were placed in small 50-mm-diameter Pyrex culture dishes and degassed, and distilled water was added under nitrogen until the desired PVA concentration of 10% was reached. The samples were put in an oven at 90°C for 6 hr to dissolve the PVA, and they were subsequently treated by a freezing–thawing process (freezing –20°C for 60 min, thawing in room temperature 23 ± 1°C for 6 hr) to avoid gas bubble formation upon irradiation.<sup>17</sup>

A Van de Graaff accelerator of the high-voltage laboratory at M.I.T., delivering

3 MeV electrons at a dose rate of  $(90\text{--}150) \times 10^3$  rads/sec, was used for irradiation at  $0^\circ\text{C}$  (ice-water bath) with total doses of 3–15 megarads. None of the irradiated samples was thicker than 2.5 mm, to ensure uniform dosage throughout the volume of the sample.

In evaluating eqs. (3) and (5), the reference volume fraction  $v_{2,r}$  was taken as the volume fraction of polymer in the gel after irradiation at  $0^\circ\text{C}$  and after taking into account any possible shrinkage of the gel due to syneresis. In contradistinction, the final swollen volume fraction refers to the irradiated gel after being transferred to and equilibrated under distilled water at  $30^\circ\text{C}$ .

For the tensile experiments, samples prepared in 150-mm-diameter culture dishes were used. They were cut with the standard 0.25-in.-neck ASTM die and tested on a table model Instron tester at a strain rate of 1 in./min while immersed in a water bath at  $30^\circ\text{C}$ . The thickness of the samples was 0.050 cm. Young's modulus, ultimate tensile strength, and elongation at break were calculated.

## RESULTS AND DISCUSSION

### Evaluation of $M_c$ from Swelling Experiments

Selected electron beam radiation-crosslinked and at  $30^\circ\text{C}$  swollen PVA hydrogels were studied. Table I includes the conditions of irradiation and the number-average molecular weight between crosslinks  $M_c$  as calculated from swelling experiments using eq. (3) with  $\chi_1 = 0.494$  as reported by Sakurada et al.<sup>18</sup> The same table includes the initial values of  $v_{2,r}$  immediately after irradiation. Although these values should be constant at  $v_{2,r} = \bar{v}C_c = 0.0788$  (for runs 1–6 where  $C_c = 0.1$ ) and  $v_{2,r} = 0.1182$  (for run 7 where  $C_c = 0.15$ ), there is a considerable variation with the dose of irradiation. This variation is to be expected due to a syneresis phenomenon which is profound at these high doses (5–15 Mrads) and dose rates (0.15 Mrads/sec) as reported earlier.<sup>7,10</sup>

The values of  $M_c$  calculated from these data vary between 12377 and 1778. If we allow for variation of values of  $\chi_1$  with concentration<sup>16,18</sup> as elsewhere reported,<sup>19</sup> a second set of values of  $M_c$  are found, also shown in Table I.

Comparison of these two sets of values of  $M_c$  show that a small change of the  $\chi_1$  factor can change the  $M_c$  from 5% to 30%. The initial modulus characterizing the rigidity of the hydrogels is plotted versus the crosslinking density  $\rho$  (Fig. 1) and gives a linear relationship with higher values of  $E_1$  for lower  $M_c$ . This can be explained because upon crosslinking the stress is redistributed to a larger number of points of reinforcement.

Table I also includes the variation of the ultimate tensile strength and the elongation at break as a function of the crosslinking density. One notes that these values are in all cases so low as to preclude use of these materials in biomedical applications<sup>20</sup> without some kind of reinforcement.<sup>21</sup>

### Evaluation of $M_c$ from Tensile Measurements

Using experimental data of the tensile tests of PVA hydrogels and eq. (5) developed for crosslinked hydrogels with the crosslinks introduced in the solution state,  $M_c$  could be evaluated. The swelling ratio increases with decreasing crosslinking density, whereas the polymer volume fraction decreases at the same

TABLE I  
Swelling Characteristics and Mechanical Properties of PVA Hydrogels as a Function of Radiation Dose

| Data set number | Radiation dose, megarads | $\nu_{2,r}$ | $\nu_{2,s}$ | $Q$   | $M_c$ eq. (5), $\chi_1 = 0.494$ | $M_c$ eq. (5), variable $\chi_1$ | $M_c$ tensile | Initial modulus $E_i^a$ , psi <sup>b</sup> | Ultimate tensile strength, psi | Elongation at break, % |
|-----------------|--------------------------|-------------|-------------|-------|---------------------------------|----------------------------------|---------------|--|--------------------------------|------------------------|
| 1               | 3                        | 0.079       | 0.066       | 1.197 | 12,377                          | 9,542 ( $\chi = 0.482$ )         | 9,867         | 4.6  | 2.6                            | 84.1                   |
| 2               | 5                        | 0.098       | 0.084       | 1.167 | 4,175                           | 3,334 ( $\chi = 0.484$ )         | 3,305         | 11.8                                       | 4.0                            | 40.8                   |
| 3               | 8                        | 0.119       | 0.106       | 1.123 | 2,648                           | 2,349 ( $\chi = 0.488$ )         | 2,362         | 20.8                                       | 2.3                            | 11.7                   |
| 4               | 10                       | 0.141       | 0.125       | 1.128 | 1,960                           | 1,795 ( $\chi = 0.489$ )         | 1,862         | 31.7                                       | 3.8                            | 13.6                   |
| 5               | 15                       | 0.143       | 0.128       | 1.117 | 1,853                           | 1,788 ( $\chi = 0.492$ )         | 1,228         | 49.4                                       | 4.0                            | 9.3                    |
| 6               | 10                       | 0.164       | 0.114       | 1.439 | 3,038                           | 2,715 ( $\chi = 0.488$ )         | 3,166         | 19.3                                       | 2.4                            | 13.8                   |
| 7               | 10                       | 0.141       | 0.129       | 1.093 | 1,778                           | 1,606 ( $\chi = 0.488$ )         | 1,938         | 30.7                                       | 4.3                            | 15.5                   |

<sup>a</sup> In all samples, initial concentration  $C_c = 0.10$  and temp. =  $0^\circ\text{C}$ , except run 6, temp. =  $30^\circ\text{C}$ , and run 7,  $C_c = 0.15$ .

<sup>b</sup>  $E_i = 3[\tau/(\alpha - 1/\alpha^2)]$ .

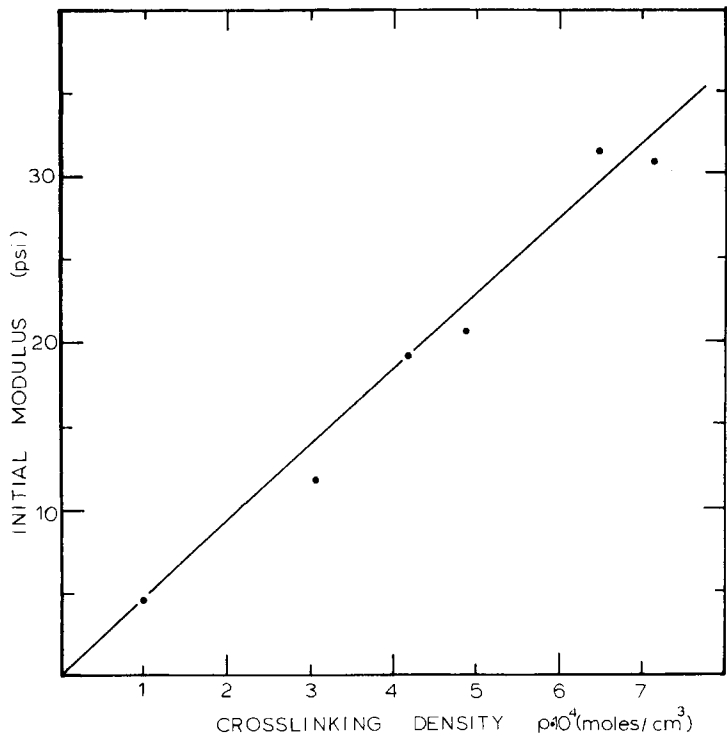


Fig. 1. Initial modulus of swollen PVA networks as a function of crosslinking density  $\rho$  (moles/cm<sup>3</sup>), calculated at constant  $\chi_1 = 0.494$ .

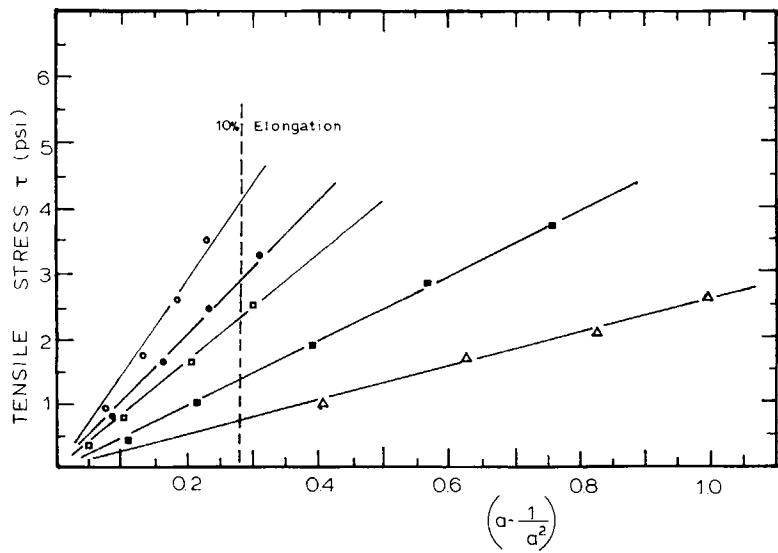


Fig. 2. Dependence of tensile stress of PVA hydrogels on extension factor  $\alpha - 1/\alpha^2$  for various  $M_c$ . Irradiation of 10% aqueous PVA solutions at 0°C.

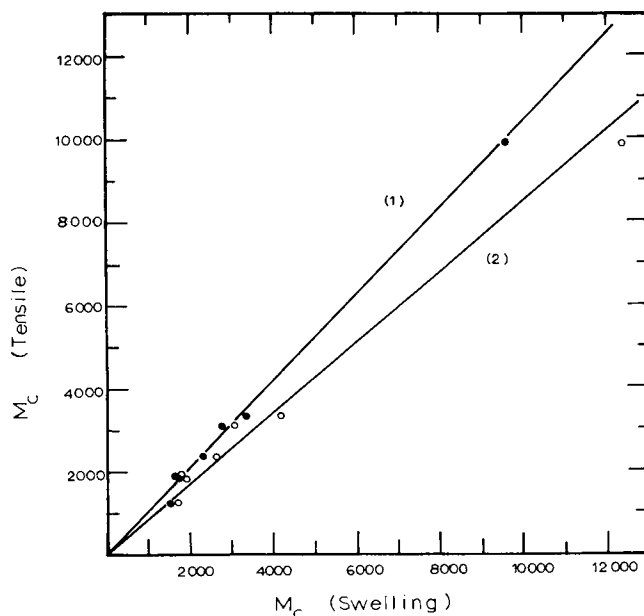


Fig. 3. Comparison of  $M_c$  calculated via tensile tests to  $M_c$  calculated via swelling experiments (in two different ways, using values of  $\chi_1$  from refs. 19 and 18, respectively, lines 1 and 2).

time. This is to be expected since less crosslinked materials are thermodynamically expanded more freely than highly crosslinked ones.

The tensile stress is directly proportional to the extension group  $\alpha - (1/\alpha^2)$ ; and from this relation,  $M_c$  can be calculated by eq. (5), this linear relationship holding for values up to  $\alpha = 3$ . In the case of swollen PVA hydrogels, the elongation at break is much lower, so that it should be expected that the above relation holds for the whole range of the test. Figure 2 shows data of the tensile stress  $\tau$  (in psi) as a function of the above-defined extension factor. The experimental points for five tested samples (irradiation of 10% PVA solution at 0°C with different total doses) fit on straight lines, in agreement with theory.

It has been stated in the literature<sup>12</sup> that the thermodynamic swelling experiments give generally more reliable results of  $M_c$  than the tensile experiments, because in the latter case entanglements and other defects of the chains affect the mechanical properties, the stress, and ultimately the calculated values of  $M_c$ .

Our calculations of  $M_c$  from tensile experiments compared to the two values of  $M_c$  determined from swelling experiments yield the plot of Figure 3. Line 1 refers to  $M_c$  calculated with  $\chi_1$  varying with concentration, and line 2 refers to  $M_c$  calculated with  $\chi_1 = 0.494$ . The respective slopes of the two lines bracket the expected slope of unity, providing little basis for decision on the importance of variability of  $\chi_1$ .

## CONCLUSIONS

Because of the other complications present in the synthesis of the networks, e.g., possible microcrystallization of the solution prior to irradiation, main chain

scission to an unknown degree, and crosslinks other than tetrafunctional, we believe that the concordance of tensile and swelling data is reasonable. Therefore, this contribution is an addition to the already existing theory of the structure and swelling behavior of swollen networks of Flory.<sup>16</sup>

These data provide additional evidence for the applicability of Flory's original analysis, i.e., eqs. (2) and (4), to solvent swollen polymers, through eqs. (3) and (5), including those networks produced from polymer *solutions*, as described herein.

The authors express thanks for the support of this work under U.S. Public Health Grant No. NIH-5-P01-HL14322 and are grateful to E. I. du Pont de Nemours for supplying the materials used in this work.

### References

1. B. D. Halpern, H. Cheng, S. Kuo, and H. Greenberg, *Art. Heart Progr. Conf.*, June 1969, Chap. 9, p. 87.
2. E. W. Merrill, E. W. Salzman, P. S. L. Wong, T. P. Ashford, A. H. Brown, and W. G. Austen, *J. Appl. Physiol.*, **29**, 723 (1970).
3. E. W. Merrill, E. W. Salzman, P. S. L. Wong, and J. L. Silliman, *Polym. Prepr.*, **13**, 511 (1973).
4. J. C. Bray and E. W. Merrill, *J. Appl. Polym. Sci.*, **17**, 3779 (1973).
5. J. C. Bray and E. W. Merrill, *J. Biomed. Mat. Res.*, **7**, 431 (1973).
6. N. A. Peppas and E. W. Merrill, *J. Polym. Sci., Polym. Chem.*, **14**, 441 (1976).
7. A. Danno, *J. Phys. Soc. Japan*, **13**, 722 (1958).
8. I. Sakurada and Y. Ikada, *Bull. Inst. Chem. Res., Kyoto Univ.*, **41**, 123 (1963).
9. I. Sakurada and Y. Ikada, *Bull. Inst. Chem. Res., Kyoto Univ.*, **42**, 22 (1964).
10. A. Danno, *J. Phys. Soc. Japan*, **13**, 609 (1958).
11. I. Sakurada, A. Nakajima, and H. Aoki, *Mem. Fac. Eng., Kyoto Univ.*, **21**, 84 (1959).
12. P. J. Flory, *Principles of Polymer Chemistry*, Cornell University Press, Ithaca, 1959.
13. P. J. Flory, *J. Chem. Phys.*, **18**, 108 (1950).
14. P. J. Flory, N. Rabjohn, and M. C. Shaffer, *J. Polym. Sci.*, **4**, 225, 435 (1949).
15. J. E. Silliman, Sc.D. Thesis, M.I.T., Chem. Eng. Dept., 1972.
16. P. J. Flory, personal communication, 1973.
17. N. A. Peppas and E. W. Merrill, *J. Appl. Polym. Sci.*, **20**, 1457 (1976).
18. I. Sakurada, A. Nakajima, and H. Fujiwara, *J. Polym. Sci.*, **35**, 497 (1959).
19. N. A. Peppas and E. W. Merrill, *J. Polym. Sci. Polym. Chem. Ed.*, **14**, 459 (1976).
20. T. Akutsu and A. Kantrowitz, *J. Biomed. Mat. Res.*, **1**, 33 (1967).
21. N. A. Peppas and E. W. Merrill, *J. Biomed. Mat. Res.*, **11**, 423 (1977).

Received November 7, 1975

Revised May 3, 1976