The concept that water in living cells may exist in a physical state different from that of normal liquid water\(^1\) stimulated considerable interest in the nuclear magnetic resonance (NMR) relaxation times of water protons in living cells.\(^6\) \(^\text{\textmd{\ldots}}\) The low \(T_1\) and \(T_2\), as well as the high ratio of \(T_1/T_2\) observed in living cells, led some scientists to the belief that the NMR data lent direct support to the association-induction hypothesis, according to which all or nearly all cell water exists in a state of polarized multilayers (PMW).

Subsequent investigations, however, led many to a different conclusion. It was argued that the short \(T_1, T_2\) and high \(T_1/T_2\) ratio reflect only the properties of a minor-phase water in rapid exchange with bulk-phase water, which is simply normal liquid water.\(^9\) \(^\text{\textmd{\ldots}}\)

It is gratifying to note that these efforts aimed primarily at solving a basic science problem have already led to the recognition of one fundamental attribute of cancer\(^11\) and the development of a potentially powerful tool for clinical medicine, the FONAR.\(^12\) In both, Damadian played a major and critical role.

A major difficulty in using NMR relaxation time studies to determine whether or not the bulk-phase water exists in the PMW state lay in the lack of recognized criteria by means of which NMR proton relaxation times could be used to differentiate normal water and PMW. This lack of known distinguishing NMR traits of PMW in turn reflected the fact that at the time the PMW model was proposed there was no readily available specimen of water firmly established as existing in the polarized multilayer state. Without an inanimate model, the assumption that the major phase cell water is entirely normal liquid water became the more appealing, whereas in truth the "cover-up" effect of a minor phase rapidly relaxing water is so powerful that the bulk-phase water may very well have relaxation times quite different from those of normal liquid water and still remain camouflaged.

Over the last few years, however, this laboratory has succeeded in developing a simple but efficient method of diagnosing PMW. By use of that method, the existence of PMW has been established as well as the conditions that convert normal liquid water into PMW. Specifically, the method consists of exposing water to a matrix of fairly closely placed chains containing oxygen atoms, the distances between the nearest neighboring oxygen atoms being roughly equal to twice the diameter of a water molecule.\(^13\) \(^\text{\textmd{\ldots}}\) The number of layers of water that can be effectively polarized between chains is estimated as falling below 10 molecules between a pair of polarizing chains.

Among the water-affecting polymers studied as matrices, the most intriguing is poly (ethylene oxide) (PEO) (\(-\text{CH}_2\text{-O-CH}_2\)\(^n\)), because of its extreme simplicity; this polymer has no side chains whatsoever. Other effective polymers are polyvinylmethyl ether (PVME), polyvinyl-pyrrolidine (PVP), and gelatin.

We have now carried out a series of studies of the NMR proton relaxation times of water in highly purified polymer-water systems.
Reserving the detailed data for a full presentation elsewhere, we report here the following basic findings:

1. Both $T_1$ and $T_2$ of the polymer-oriented water are considerably shorter than those of normal liquid water, becoming shorter with increase of polymer concentrations.

2. The ratio $T_1/T_2$, on the other hand, is close to unity (1.0 to 1.4) in all concentrations of PEO, PVME, and PVP solutions; it resembles the $T_1/T_2$ ratio of normal liquid water at near neutral pH.

3. Gelatin solution like that of native bovine serum albumin, shows a much higher $T_1/T_2$ ratio at high polymer concentrations. Taken as a whole, the data can be interpreted as follows: water in the dynamic state of polarized multilayers does indeed suffer additional dispersion of wet lysozyme powder. The dielectric rotational correlation time ($\tau_{rd}$) is equal to 2.5 $\tau_c$.\(^\text{16-18}\) The corresponding $\tau_{rd}$ should be 2.5 $\times$ $10^{-11}$ sec. It is interesting to compare this value with the additional dispersion of wet lysozyme powder with a $\tau_{rd}$ of 2 $\times$ $10^{-11}$ sec that Harvey and Hoekstra\(^\text{19}\) observed when the water content increased beyond 0.35 g/g protein. This water content corresponds roughly to the limit of polar group hydration.\(^\text{20}\) Therefore the additional hydration referred to might be largely due to polarization by the polypeptide NHCO groups and thus would be polarized in a manner similar to polarization of the PEO-water system.\(^\text{13,14,20}\)

The $T_1/T_2$ ratios were found to be quite different in the two proteins studied. Here a minor phase of more rapidly relaxing water in rapid exchange with the major phase water can explain the different behavior of both native bovine serum albumin solution, whose water is essentially normal as judged by its solvency for Na', sucrose, and glycine, and of gelatin "gel" where water has reduced solvency for these probe molecules.\(^\text{13}\)

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