Dielectric Constant and Density of Water as a Function of Pressure at Constant Temperature

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In order to simulate the effects of hydrostatic pressure on protein folding/unfolding it is necessary to accurately describe the behavior of the dielectric constant and the density of the solvent (water), in the range of pressures (between 0.1 MPa and 2.0 GPa) and temperatures (below 75 ˚C) required for pressure-induced unfolding. A simple equation of the form $X = X(T, P_i) + a_0 \ln (a_i + P)/(a_i + P_i)$ [were X is the property, P_i (in MPa) is the reference pressure and a_i are coefficients adjusted to fit experimental values] is proposed to describe both properties as function of pressure, at constant temperatures. The equation reproduces available data for dielectric constant and density of water to an accuracy of 0.1%. Because of its simplicity and accuracy, the proposed equation is useful for simulation studies and for any other problem where the knowledge of those properties as a function of pressure is needed.

1 Introduction

A relatively small number of studies on the measurement of the dielectric constant of water as a function of temperature (T) and pressure (P) have been reported in the literature[1]. Most of the experimental data available is for a relatively large range of temperatures (up to 670K) at relatively low pressures (under 200MPa). There are few measurements available for pressures between 200MPa and 500MPa. The accuracy of most of the high temperature data is better than 1%, while in the lower temperature limit (below 70°C) the accuracy of most of the data is around 0.1%.

As a consequence of this lack of data, attempts to estimate the properties of aqueous species at high temperature and/or high pressure rely on estimated or extrapolated values of the dielectric constant of water. High temperature and pressure conditions are important for engineering processes and geothermal studies. For this reason, several equations have been proposed for different ranges of temperature and pressure[1-5]. Almost all of them are entirely empirical. Although those equations may yield unphysical results if extrapolated too far outside the range of the experimental data, many of them were formulated to give some confidence about the extrapolated values.

Most of those equations are based on the Kirkwood equation, in which the parameter g (the Kirkwood correlation factor) can be expressed as a function of experimental variables, like density and temperature, and adjusted to fit experimental data[1,2,4]. An example of this approach has been recently reported[2] in the derivation of an equation for the dielectric constant of water at temperatures from 238 K to 873 K and at pressures up to 1200 MPa. Those authors used an empirical 12-parameter form for the g-factor as a function of the independent variables, temperature and density. Their formula correlates well a selected set of data from a collection of experimental data assembled by the authors. Another approach[3] uses a hard sphere model for the water molecule and a modified Ornstein-Zernike equation, where the parameters are fit to the experimental data for water. One of the simplest but effective description of the dielectric constant dependence on the pressure and temperature, proposed by Bradley and Pitzer[5], uses an equation suggested by Tait in 1880 for volumetric data. Bradley's equation was expressed in terms of the static dielectric constant of water (EPS) and its parameters were adjusted to reproduce experimental data. The resulting equation is valid in the range 0-70°C between 0.1-2000MPa, and 70-350°C between 0.1-5000MPa.

A number of molecular dynamics simulations of the static dielectric constant of water has also been published. There are simulations at low pressure and temperatures below 373K [6], over a wide range of density and temperature values along the liquid-vapor coexistence curve[7], and under high pressure and temperature conditions[8]. The SPC/E

potential for water molecule[9] was used in two of those simulations[6,7].

The simulations carried by Wasserman *et al.*[7] covered temperatures ranging from 324K to 1278K and densities from 0.257 g/cm^3 to 1.1108g/cm^3. Their simulations are in good agreement within the pressure-temperature range of the experimental data used. They showed that the SPC/E model tends to underestimate the values of the dielectric constant for densities greater than 1.0g/cm^3. The SPC/E potential used by those authors was parameterized to yield correct values of pressure and energy for a density of 0.998g/cm^3 at 300K and was not adjusted to experimental values of the dielectric constant.

In the last years a considerable number of papers appeared in the literature addressing the important problem of proteins' folding/unfolding mechanism, using molecular dynamics simulations[10-19]. Different proteins have been studied under very distinct conditions of temperature and pressure[20-25]. Since even the simplest proteins already have a large number of atoms, most simulations are carried out using a continuum dielectric medium (implicit solvent representation) to take the solvent molecules into account. Among the several different conditions that have been employed in computer simulations, the use of hydrostatic pressure at relatively low temperatures seems to be very promising at revealing the details of folding/unfolding mechanism. We have recently analyzed the effects of pressure on the conformation of Myoglobin[26,27] and showed that most of the experimental behavior of this system is well reproduced by the simulations.

However, very high pressures are usually required in order to conduct this type of study. Therefore, in order to simulate the effects of hydrostatic pressure on protein folding/unfolding it is necessary to accurately describe the properties of the solvent (water) under the simulation conditions. Two of these properties whose value depends on temperature and pressure are the static dielectric constant of water (EPS) and the density (DENS).

The conditions for the study of pressure effects on unfolding are temperatures below 75°C and pressures up to 20kbar (2000MPa). Under these conditions, the water remains in the liquid state, and most proteins are thermally stable at that temperature.

All the previous attempts at deriving equations describing the behavior of EPS and DENS with T and P, tried to cover relatively large ranges of temperature and pressure, and in order to do so, a large number of parameters are used. Bradley's[5] is the only one among the equations available in the literature to cover the range of T and P needed in the pressure simulation studies. Although much simpler than the others, this equation is not accurate enough in the specific range of T and P (especially for low T) of interest for biological applications, as will be shown.

It would be ideal to have an equation analytically simple as Bradley's and accurate enough for the biologically relevant ranges of T and P. However, Bradley's equation does not reproduce accurately enough the more recent experi-

mental data for relatively low temperatures, most probably because of the fact that they attempted to cover a large range of T and P. Since the pressure simulation studies require the knowledge of EPS and DENS in a large range of P but at a limited set of temperatures, we adopted the following strategy: starting from an equation as simple as Bradley's, we tried to adjust its parameters as to reproduce as accurate as possible the available data for EPS and DENS at selected values of T, appropriated for the simulation studies. While it may be argued that such a procedure generates equations of limited applicability, this is not really the case because the fitting procedure is very simple and can be performed for any other desired temperature. Besides, by selecting the temperature of interest we gain in accuracy. Therefore, although we exemplify its usage for the temperatures proper to our protein simulations, the equation is quite general and can be used in any simulation study where the knowledge of the water EPS and DENS as a function of P at different values of T is needed.

2 Dielectric Constant

The equation suggested by Bradley and Pitzer[5] for the region above saturation pressure and temperatures below 350°C was

$$EPS = EPS_{1000} + C\ln((B+P)/(B+1000)), \quad (1)$$

where P is the pressure in bars, EPS is the dielectric constant, and EPS_{1000} was chosen arbitrarily as a reference value (EPS at 1000 bar). EPS_{1000}, C and B are temperature dependent parameters described by the equations (T in Kelvin):

$$\begin{aligned}
EPS_{1000} &= U_1 \exp[U_2 T + U_3 T^2] \\
C &= U_4 + U_5/(U_6 + T) \\
B &= U_7 + U_8/T + U_9 T,
\end{aligned}$$

with

$$\begin{aligned}
U_1 &= 3.4279E(02) & U_6 &= -1.8289E(02) \\
U_2 &= -5.0866E(-03) & U_7 &= -8.0325E(03) \\
U_3 &= 9.4690E(-07) & U_8 &= 4.21452E(06) \\
U_4 &= -2.0525 & U_9 &= 2.1417 \\
U_5 &= 3.1159E(03) & & (2)
\end{aligned}$$

The parameters showed in equation (2) were optimized using a wide range of experimental data, including high temperature data. Although the experimental data below 70°C collected by the authors, had been fitted to better than 0.1%, the same agreement is not observed in the low temperature/high pressure range, when we use more recent data. This comparison is shown in Fig. 1. The original Bradley's

equation does not reproduce adequately the data available from the *International Association for the Properties of Water and Steam*[28] used in Figure 1 for P above 400MPa, particularly at and above 323K.
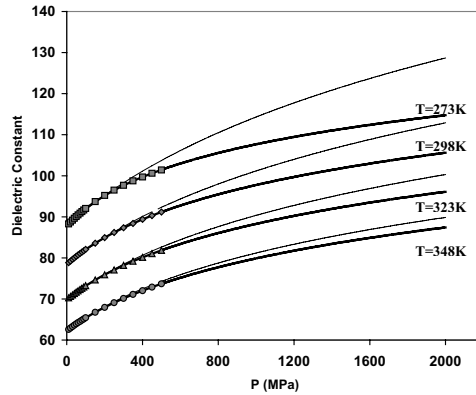

Figure 1. Dielectric constant of water as a function of pressure at constant temperatures (273K, 298K, 323K and 348K). (a) Bradley's [5] equation (fine lines); (b) proposed equation (thick lines) adjusted to (c) values extracted from the *International Association for the Properties of Water and Steam* [28] (symbols).

To circumvent this problem we optimized an equation with the same general form as the Bradley equation, for a restricted set of protein folding/unfolding suitable temperatures (273K, 298K, 323K, 348K). Therefore, an equation of the form

$$EPS = EPS(T, 10) + a_0 \ln((a_1 + P)/(a_1 + 10)) \quad (3)$$

was used to fit the data available from the *International Association for the Properties of Water and Steam*[28]. The fitting was performed using the program Xmgr v2.10 [29]. In the above equation EPS(T,10) is the dielectric constant of water at temperature T and at 10 MPa, $\{a_i\}$ are parameters optimized for each chosen temperature, and P is the pressure in units of MPa. The dependence of a_i with temperature was not estimated. The set of EPS values available for each temperature is in the range of 10 to 500MPa. The resulting equation fits the data to better than 0.1%. The extrapolated values for the dielectric constant at 1 atm are 87.78, at 273K, and 69.91, at 323K (experimental values are, respectively, 87.90 and 69.88). The optimized parameters are shown in the Table I. Fig. 2 shows the fitted results.

Table I. Dielectric constant of water as a function of pressure at constant temperature. Optimized parameters for equation 3.

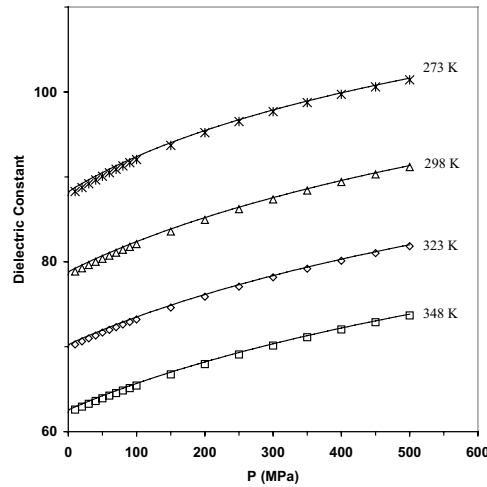| T(K)	273	298	323	348
EPS(T,10)	88.28	78.85	70.27	62.59
a_0	11.9240	14.1113	14.3899	13.9450
a_1	232.5026	341.5902	386.4825	393.2031

Figure 2. Dielectric constant of water as a function of pressure at constant temperature. The figure shows the proposed equation (solid) adjusted to fit data from the *International Association for the Properties of Water and Steam* [28] (symbols).

3 Density

The water density as a function of pressure, at constant temperature, can be described by the same equation used before, if we optimize its coefficients for the experimental data available for density [30,31]. The optimized equation, showed bellow, fits the experimental data to 0.1%. The optimized parameters are listed in the Table II. Fig. 3 compares the optimized equation to the experimental data[31].

$$DENS = DENS(T, 0.1) + a_0 \ln((a_1 + P)/(a_1 + 0.1)) \quad (4)$$

Table II. Optimized parameters for reproducing the experimental data [31] for the density of water at 298K.

T(K)	298
DENS(T,0.1)	0.997
a_0	0.214
a_1	476.693

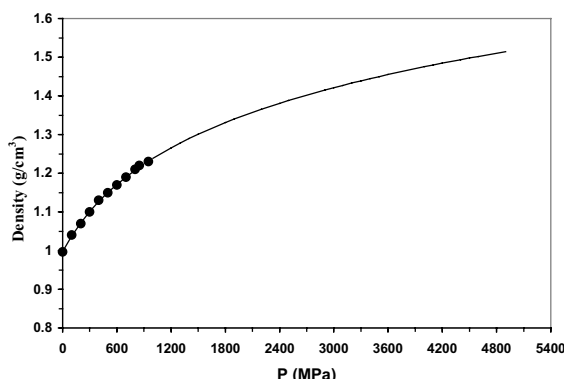Figure 3. Density of water as a function of pressure at 298K. The figure shows equation 4 (solid line) adjusted to experimental values [31] (●).

4 Conclusions

The dielectric constant and the density of water as a function of pressure, at constant temperature, are well described by an equation of the form

$$X = X(T, P_i) + a_0 \ln((a_1 + P)/(a_1 + P_i)) \qquad (5)$$

where X is the property, P_i (in MPa) is the reference pressure and the coefficients a_i are adjusted to fit experimental values. The equation reproduces the experimental data for both dielectric constant and density to an accuracy of 0.1%, for a large range of pressure values at a given temperature. This feature makes equation (5) particularly useful for simulation studies or for any other problem where the knowledge of these properties as a function of pressure is needed.

Acknowledgments

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