Evidence of a liquid–liquid phase transition in H₂O and D₂O from path-integral molecular dynamics simulations

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We perform path-integral molecular dynamics (PIMD), ring-polymer MD (RPMD), and classical MD simulations of H₂O and D₂O using the q-TIP4P/F water model over a wide range of temperatures and pressures. The density ρ(T), isothermal compressibility κ(T), and self-diffusion coefficients D(T) of H₂O and D₂O are in excellent agreement with available experimental data; the isobaric heat capacity C_p(T) obtained from PIMD and MD simulations agree qualitatively well with the experiments. Some of these thermodynamic properties exhibit anomalous maxima upon isobaric cooling, consistent with recent experiments and with the possibility that H₂O and D₂O exhibit a liquid-liquid critical point (LLCP) at low temperatures and positive pressures. The data from PIMD/MD for H₂O and D₂O can be fitted remarkably well using the Two-State-Equation-of-State (TSEOS). Using the TSEOS, we estimate that the LLCP for q-TIP4P/F H₂O, from PIMD simulations, is located at P_c = 167 ± 9 MPa, T_c = 159 ± 6 K, and ρ_c = 1.02 ± 0.01 g/cm³. Isotope substitution effects are important; the LLCP location in q-TIP4P/F D₂O is estimated to be P_c = 217 ± 4 MPa, T_c = 177 ± 2 K, and ρ_c = 1.13 ± 0.01 g/cm³. Interestingly, for the water model studied, differences in the LLCP location from PIMD and MD simulations suggest that nuclear quantum effects (i.e., atoms delocalization) play an important role in the thermodynamics of water around the LLCP (from the MD simulations of q-TIP4P/F water, P_c = 203 ± 4 MPa, T_c = 175 ± 2 K, and ρ_c = 1.03 ± 0.01 g/cm³). Overall, our results strongly support the LLPT scenario to explain water anomalous behavior, independently of the fundamental differences between classical MD and PIMD techniques. The reported values of T_c for D₂O and, particularly, H₂O suggest that improved water models are needed for the study of supercooled water.

Water is an anomalous liquid with thermodynamic and dynamical properties that behave unexpectedly upon cooling and/or pressurization; see, e.g., Ref.¹. For example, experiments performed in the 1970’s by Angell et al.²–⁴ show that water isobaric heat capacity C_p(T) and isothermal compressibility κ(T) exhibit an apparent divergency at T ≈ 228 K and P = 0.1 MPa. More recent experiments that extend Angell’s studies to lower temperatures identify a maxima in C_p(T) and κ(T) at T ≈ 228 K (P = 0.1 MPa)⁵–⁷. Although many theoretical approaches have been proposed to explain water anomalous behavior, the so-called liquid–liquid phase transition (LLPT) scenario⁷–¹⁰ is currently the explanation best-supported by experiments⁵–¹³, computer simulations⁷–²⁴, and theory¹⁴–²³. In the LLPT scenario, water at low temperatures exists in two distinct liquid states, low-density and high-density liquid (LDL and HDL). In the P–T plane, LDL and HDL are separated by a first-order LLPT line that ends at a liquid–liquid critical point (LLCP) at higher temperatures. Importantly, the LLPT hypothesis explains naturally the maxima in κ(T) and C_p(T) observed recently upon cooling water at P = 0.1 MPa⁵–²⁰. It also explains, naturally, the complex behavior of water in the glass state²⁵–³⁴ which, arguably, is not clearly explained by other approaches, such as the singularity free scenario³⁵.

Available experimental data suggest that the LLCP in water is located at about P_c = 50–100 MPa and T_c ≈ 220 K¹². Unfortunately, due to water rapid crystallization at these conditions, the existence of the LLCP in water has not been confirmed in experiments. Strong evidence for the existence of a LLPT in water is available.

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from recent sub-microsecond experiments at \( T \approx 205 \) K; additional evidence of the LLPT in water is available from experiments performed at \( T \approx 130–140 \) K, in the so-called ultraviolusc liquid state of water. Many computer simulations validate the LLPT hypothesis. Specifically, a LLCP has been identified in classical computer simulations using popular models, such as ST2, TIP4P/2005, and TIP4P/ice. A recent classical MD simulation using a water model developed from density functional theory combined with machine learning techniques also suggests that water exhibits a LLCP in the supercooled regime. Not surprisingly, the location of the LLCP in computer simulations varies with the water model considered. For example, in the case of the ST2 water model, the LLCP temperature is overestimated \( (T_c = 237 \) K, \( P_c = 167 \) MPa, \( \rho_c = 0.99 \) g/cm\(^3\)) \(^{41}\); while in the TIP4P/2005 and TIP4P/ice water models it is underestimated \( (T_c = 172 \) K, \( P_c = 186 \) MPa, and \( \rho_c = 1.03 \) g/cm\(^3\) for TIP4P/2005; \( T_c = 188 \) K, \( P_c = 175 \) MPa, \( \rho_c = 1.01 \) g/cm\(^3\) for TIP4P/Ice\(^{48}\). In all these cases, the LLCP pressure is overestimated by approximately 100 MPa. The computer simulation studies that find a LLCP in the glass transition temperature \( T_g \) has been shown to be able to reproduce remarkably well the properties of liquid water at classical MD simulations. The q-TIP4P/F water model was optimized for path integral computer simulations and molecules in a cubic box with periodic boundary conditions. \( H \) \( N \) which is consistent with recent computer simulations. Interestingly, while experiments in glassy water have estimated differences in the location of the LLCP in water occur even at standard temperatures and pressures. For example, the temperature of maximum density \( T_{\rho_{max}} \) of the LLCP in computer simulations vary with the water model considered. For example, in the case of the ST2 \( \) \( O \) and D\( _2 \)\( O \) \( \Delta T_{\rho_{max}} \approx 10 \) K, \( \Delta P_{\rho_{max}} \approx 50 \) MPa \(^{51,54}\), the issue of isotope effects on the location of the LLCP has not been explored in computational and theoretical studies.

In this work we perform extensive path-integral, ring-polymer, and classical molecular dynamics (PIMD, RPMD, MD) simulations of light and heavy water using the q-TIP4P/F model and explore the corresponding phase diagram and thermodynamic properties. The aim of this work is to determine the NQE (due to atoms delocalization) on the location of the LLCP, LLPT, and supercritical anomalous lines (such as \( \kappa_T \) in q-TIP4P/F water \( (H_2O) \)). The second goal of this work is to study isotope substitution effects in water, i.e., whether PIMD simulations of \( H_2O \) and \( D_2O \) can reproduce the subtle differences in the phase diagram and anomalous properties of \( H_2O \) and \( D_2O \) observed in experiments. In a previous study, we performed PIMD simulations of q-TIP4P/F water \( (P = 0.1 \) MPa) and showed that this model reproduces some signatures of the LLPT scenario, specifically, a maximum in \( \kappa_T \) \( (T) \) was found in \( H_2O \) and \( D_2O \) \( \approx 300–250 \) K \( (P = 0.1) \) MPa. Here, we extend our previous study to a wide range of temperatures and pressures in order to explore the possible existence of a LLCP in \( H_2O \) and \( D_2O \). By combining the PIMD/MD results and the two-state equation of state (TSEOS) \(^{14,23}\), we are able to identify a LLCP in both \( H_2O \) and \( D_2O \). The TSEOS is based on the assumption that liquid water is a mixture of two interchangeable (liquid) states. The TSEOS has been shown to fit remarkably well the computer simulations results obtained from classical MD simulations of ST2 and TIP4P/2005 water as well as a water model based on DFT and machine learning techniques \(^{14,19,21,23}\); it has also been applied to the case of real water \(^{61,54}\). While at low temperatures the TSEOS predicts that water separates into LD\( L \) and HD\( L \), at high temperatures \( (T > 270 \) K), it predicts a rather homogeneous liquid (HDL) which is consistent with recent computer simulations \(^{25,25}\).

Our paper is organized as follows. In “Simulation method”, we present the computer simulation details. In “Results”, we discuss the results from our PIMD/RPMD and classical MD simulations of \( H_2O \) using the q-TIP4P/F water model. The phase diagram of \( D_2O \) is briefly discussed and compared with the phase diagram of \( H_2O \). A summary and discussions are included in “Summary and discussion”.

**Simulation method**

Our results are based on PIMD/RPMD and classical MD simulations of a system composed of \( N = 512 \) water molecules in a cubic box with periodic boundary conditions. \( H_2O \) and \( D_2O \) molecules are represented using the non-rigid q-TIP4P/F model \(^{34}\). This model is based on the TIP4P/2005 model for water \(^{55}\), commonly used in classical MD simulations. The q-TIP4P/F water model was optimized for path integral computer simulations and has been shown to be able to reproduce remarkably well the properties of liquid water at \( P = 0.1 \) MPa \(^{46,54}\). Here, we perform PIMD and MD simulations at constant \( N, P, \) and \( T \) over a wide range of temperatures and pressures, \( 180 \leq T \leq 375 \) K and \( -250 \leq P \leq 500 \) MPa; see Supplementary Fig. S1 of the Supplementary Information (SI). The temperature of the system is maintained constant using a stochastic (local) path integral Langevin equation (PILE) thermostat \(^{68}\) while the pressure of the system is controlled by using a Monte Carlo Barostat (additional computational details can be found in Ref. \(^{56}\)). In the PIMD simulations, the time step \( dt \) is set to 0.25 fs and the number of beads per ring-polymer/atom was set to \( n_b = 32 \); in Ref. \(^{56}\), it is shown that this value of \( n_b \) is large enough to obtain well-converged dynamical, thermodynamic, and structural properties of q-TIP4P/F water \( (P = 0.1 \) MPa and \( T \geq 210 \) K). In order to ensure that the conclusions in Ref. \(^{56}\) applied to the pressures we considered in this work, we have also performed additional PIMD simulations using \( n_b = 72 \) beads per ring-polymer (see SI). Consistent with Ref. \(^{56}\), we found that most of the thermodynamic and dynamical properties converged with \( n_b = 32 \), with the enthalpy being the only expected exception. Short-range (Lennard–Jones pair potential) interactions are calculated using a cutoff \( r_c = 1.0 \) nm and long range electrostatic interactions are computed using the Particle Mesh Ewald (PME) method with the same cutoff \( r_c \). In the classical MD simulations, we employ a time step \( dt \) of 0.50 fs and set \( n_b = 1 \). All PIMD and classical MD simulations are performed using the OpenMM software package (version 7.4.0) \(^{57}\). The OpenMM software package is also used to perform the RPMD simulations which are used for the calculation of the diffusion coefficients of \( H_2O \) and \( D_2O \). Details on the calculation of the diffusion coefficients can be found in Ref. \(^{46}\). We note that in the OpenMM software package, the RPMD application sets the mass of the ring-polymer beads to the physical mass of the corresponding atom. When used
The values of $P_c$, $T_c$, and density $\rho_c$ of the LLCP of q-TIP4P/F $H_2O$. Values of $P_c$, $T_c$, and $\rho_c$ are obtained by using the TSEOS in combination with data from classical MD and PIMD simulations at $180 \leq T \leq 325$ K. Numbers in parenthesis are standard deviations.

|                  | PIMD     | Classical MD |
|------------------|----------|--------------|
| $P_c$ (MPa)      | 167 (9)  | 203 (4)      |
| $T_c$ (K)        | 159 (6)  | 175 (1)      |
| $\rho_c$ (g/cm$^3$) | 1.02 (0.01) | 1.03 (0.01) |

Table 1. Estimated pressure $P_c$, temperature $T_c$, and density $\rho_c$ of the LLCP of q-TIP4P/F $H_2O$. Values of $P_c$, $T_c$, and $\rho_c$ are obtained by using the TSEOS in combination with data from classical MD and PIMD simulations at $180 \leq T \leq 325$ K. Numbers in parenthesis are standard deviations.

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temperatures. The Helmholtz free energy of the system is 

$$F(N, V, T) = E - TS$$

and hence, a concavity in \(PE\) can lead to a concavity in \(F(V)\) (at constant \(N\) and \(T\)) at very low temperatures. A concavity in \(F(V)\) implies that the system exhibits a first-order (liquid–liquid) phase transitions, again, consistent with the presence of LLCP/LLPT at low temperatures.

**Thermodynamic response functions: \(\kappa_T\) and \(C_p\).** We obtain the isothermal compressibility of q-TIP4P/F water by calculating the density fluctuations of the system,

$$\kappa_T(T) = \frac{(V^2) - \langle V^2 \rangle}{k_B T \langle V \rangle},$$  \hspace{1cm} (1)

where \(\langle \ldots \rangle\) indicates average over time and \(k_B\) is the Boltzmann’s constant. Fig. 3a,b show the \(\kappa_T(T)\) for \(\text{H}_2\text{O}\) obtained from PIMD simulations (solid circles) together with available experimental data (open symbols) at low and high pressures, respectively. At \(P \geq 200\) MPa (Fig. 3b), the experimental and PIMD simulation values of \(\kappa_T(T)\) practically overlap; a similar agreement is found at \(P = 100\) MPa (Fig. 3a). However, at \(P = 0.1\) MPa, where more experimental data is available, the experimental \(\kappa_T(T)\) increases more rapidly upon cooling than found in PIMD simulations. Hence, relative to real water, the density fluctuation in q-TIP4P/F water are underestimated at \(P = 0.1\) MPa and in the supercooled regime. We note that the values of \(\kappa_T(T)\) obtained from classical MD simulations.

**Figure 1.** Density of q-TIP4P/F water as function of temperature along selected isobars. (a) Comparison of \(\rho(T)\) from classical MD (open circles) and PIMD simulations (solid circles). Pressures are (bottom to top) \(P = -100, 0.1, 100, 200, 300, 400, 500\) MPa. (b) Density of q-TIP4P/F water from PIMD simulations (solid circles) and experiments (open symbols; squares, left-triangles, up-triangles, right-triangles, and diamonds are, respectively, from Refs. 12,16,39-41). Pressures are (bottom to top) \(P = -100, -50, 0.1, 100, 200, 300, 400\) MPa. Deviations between experiments and simulations are noticeable only at high pressures, \(P > 200\) MPa, and low temperatures, \(T < 240\) K. (c) Fit of the q-TIP4P/F water densities shown in (a) using the TSEOS (solid lines). (d) Fit of the q-TIP4P/F water densities shown in (b) using the TSEOS (solid lines). Pressures in (c) and (d) are (bottom to top) \(P = -100, -50, 0.1, 50, 100, 150, 200, 250, 300, 350\) MPa. The liquid–liquid binodal line and LLCP predicted from the TSEOS are denoted by the black dashed line and red star.
and PIMD simulations overlap (within error bars) at \( T \geq 190 \) K and hence, they were omitted in Fig. 3a,b; the \( \kappa_T(T) \) obtained from MD simulations is shown in Fig. S2 of the SI.

An important result from Fig. 3a is the presence of maxima in \( \kappa_T(T) \) at \( P = 0.1 \) and 100 MPa. This is an anomalous property that was originally predicted by the LLPT hypothesis scenario and later confirmed by experiments\(^5,17\). The experimental data from Ref.\(^5\) is included in Fig. 3a; the experimental \( \kappa_T \)-maximum occurs at \( T = 228 \) K (\( P = 0.1 \) MPa; open right triangles) and it is very sharp. While the \( \kappa_T \)-maximum in PIMD simulations occurs at a similar temperature (\( T = 230 \) K), this maximum is much smaller and wider relative to the experiments. Within the LLCP hypothesis scenario, the \( \kappa_T \)-maximum is expected to increase as one approaches the LLCP and it should diverge at the LLCP. This is fully consistent with the PIMD simulations results shown in Fig. 3a. Specifically, as the pressure increases from \( P = 0.1 \) MPa to \( P = 100 \) MPa, the \( \kappa_T \)-maximum shifts to lower temperatures and increases in height. The same behavior of \( \kappa_T \) is found in classical MD simulations of water models that exhibit a LLCP\(^14,15,21,64\).

We also calculate \( \kappa_T(T) \) using the TSEOS. The TSEOS provides an expression for the Gibbs free energy of the system from which the isothermal compressibility can easily be obtained,

\[
\kappa_T(T) = -\left(\frac{\partial^2 G}{\partial P^2}\right)_T \left(\frac{\partial G}{\partial P}\right)_T
\]

A comparison of the values of \( \kappa_T(T) \) obtained from the TSEOS and our MD/PIMD simulations are presented in Fig. 3c,d. The predictions from the TSEOS agree rather well with the MD simulation results [inset of Fig. 3d]. In the case of PIMD simulations [inset of Fig. 3c], the TSEOS provides compressibility values that are in good

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**Figure 2.** Pressure of q-TIP4P/F water as a function of volume along selected isotherms. Circles are results from (a) classical MD and (b) PIMD simulation. The solid lines are the results from the TSEOS. Isotherms correspond to (top to bottom) \( T = 300, 260, 240, 220, 200 \) K and are shifted by \( \delta P = 100, 0, -100, -300, -500 \) MPa, respectively. An inflection point in \( P(V) \) seems to develop at \( T < 200 \) K consistent with the existence of a LLPT in q-TIP4P/F water at lower temperatures. (c) Potential energy for selected isotherms at (bottom to top) \( T = 200, 220, 240, 260, 300, 350, 375 \) K. Solid symbols are from PIMD simulations; lines are guides to the eye.
agreement with the simulation results at high temperatures. However, at lower temperatures, the TSEOS predicts slightly larger maxima in $\kappa_T(T)$ that are shifted to lower temperatures relative to the simulations. This suggests that, the location of the LLCP in q-TIP4P/F water from PIMD may be located at slightly lower $T_c$ and/or higher $P_c$ relative to the corresponding estimated values resulting from the TSEOS.

Next, we discuss the isobaric heat capacity, $C_P(T)$.

In our previous work (at $P = 0.1$ MPa)$^{46}$, the enthalpy was calculated directly from MD and PIMD simulations at selected temperatures and then, the values of $H(T)$ were fitted using a fourth-order polynomial. The resulting analytic expression for $H(T)$ was then used in Eq. (3) to calculate $C_P(T)$. The use of a fourth-order polynomial in the fitting procedure is rather arbitrary. It captures the qualitative increase of $C_P(T)$ upon cooling at low pressures but it may play a relevant role in identifying a $C_P$-maximum, which is known to occur in experiments$^{10}$. Accordingly, in this work, we take advantage of the TSEOS and use it to calculate $H(T)$ at selected pressures; after all, the TSEOS reproduces very well the behavior (and maxima) of $\rho(T)$ (see Fig. 1) and $\kappa_T(T)$ (see Fig. 3). Specifically, for a given pressure, we use the polynomial expression of $G(T)$ given by the TSEOS and obtain an analytical expression for $H(T)$ using the Gibbs–Helmholtz equation,

$$C_P(T) = \left(\frac{\partial H(T)}{\partial T}\right)_{N,P}.$$
The obtained $H(T)$ is then used in Eq. (3) to calculate $C_P(T)$. Figure 4a,b show the $H(T)$ of q-TIP4P/F water obtained from (i) the TSEOS (solid lines) and (ii) classical MD and PIMD simulations (empty/solid circles). Lines are the corresponding $H(T)$ obtained from the TSEOS. In both cases, the TSEOS predictions are in excellent agreement with the MD/PIMD simulation results.

Figure 4. Enthalpy $H(T)$ of q-TIP4P/F water as a function of temperature for selected pressures. Results are from (a) PIMD simulations (solid circles) and (b) classical MD simulations (empty circles). Lines are the corresponding $H(T)$ obtained from the TSEOS. In both cases, the TSEOS predictions are in excellent agreement with the MD/PIMD simulation results.

Figure 5. (a) Heat capacity $C_P(T)$ of q-TIP4P/F water for $P = -100, 0.1, 100, 200, 300$, and $400$ MPa. $C_P(T)$ was calculated by using Eq. (3) and the $H(T)$ expression obtained from the TSEOS and PIMD simulations (solid lines). Experimental data are indicated by empty triangles (left-triangles from Refs. 4,69; right-triangles from Refs. 59). (b) Same as (a) for the case of classical MD simulations. The experimental data from Pathak et al. 10 (green up-triangles) show a maximum at $T \approx 228$ K.

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\[ H(T) = -T^2 \left( \frac{\partial (G/T)}{\partial T} \right)_p \]  

The obtained $H(T)$ is then used in Eq. (3) to calculate $C_P(T)$. Figure 4a,b show the $H(T)$ of q-TIP4P/F water obtained from (i) the TSEOS (solid lines) and (ii) classical MD and PIMD simulations (empty/solid circles). The TSEOS predictions are in excellent agreement with our simulations throughout the entire temperature and pressure range considered in this work.

Figure 5a,b show, respectively, the $C_P(T)$ of q-TIP4P/F water from PIMD and classical MD simulations at selected pressures, above and below the estimated LLCP pressure; open symbols are experimental values. The $C_P(T)$ from classical MD and PIMD simulations are qualitatively similar. Specifically, at the temperature studied, $C_P(T)$ exhibits a maximum at approximately $P \leq 200$ MPa. This $C_P$-maximum increases and shifts to lower temperatures as the pressure increases towards the LLCP pressure. At $P > 200$ MPa $> P_c$, $C_P(T)$ is a monotonic decreasing function of $T$. Note that classical MD simulations predict much larger values of $C_P(T)$ than found in PIMD simulations (which is known to occur when NQE are omitted).

Differences between the experimental data and MD/PIMD simulations are noticeable. For example, as shown in Fig. 5a, at $P \geq 100$ MPa, PIMD simulations predict that $C_P(T)$ decreases upon heating while experiments show the opposite behavior. In particular, at $P = 0.1$ MPa, the $C_P(T)$ of q-TIP4P/F water is in semiquantitative
agreement with experiments down to \( T \approx 240 \) K. The maximum in \( \text{CP}(T) \), at \( P = 0.1 \) MPa, occurs at 228 K and 216 K in experiments and q-TIP4P/F water, respectively. However, the maxima of \( \text{CP}(T) \) in q-TIP4P/F water is much smaller and wider than found in the experiments of Pathak et al.\(^{10} \). This is consistent with the estimated location of the LLCP in experiments and in our simulations. The LLCP in real water is estimated to be located at \( P_C \approx 50 \)–100 MPa and \( T_C \approx 220 \) K, while in q-TIP4P/F water we find \( T_c = 159 \) K and \( P_c = 167 \) MPa. Accordingly, at \( P = 0.1 \) MPa, experiments are much closer to the corresponding LLCP than in the case of q-TIP4P/F water\(^6 \). Our results for \( \text{CP}(T) \) also imply that PIMD and MD simulations of q-TIP4P/F water cannot reproduce the entropy fluctuations observed in real water at low temperatures and pressures.

**Diffusion coefficient.** We also calculate the self-diffusion coefficient of q-TIP4P/F water \( D(T) \) as function of temperature at selected pressures. To obtain \( D(T) \), we employ the same methodology used in Ref.\(^{46} \). Briefly, using the RPMD simulation technique, we first calculate the mean-square displacement (MSD) of the oxygen atoms/ring-polymer centroids. \( D(T) \) is then evaluated from the slope of the MSD at long times, in the so-called diffusive regime. Figure 6a shows the \( D(T) \) of q-TIP4P/F water obtained from RPMD (solid circles) and classical MD simulations (empty circles); empty triangles correspond to experimental data (left-triangles and right-triangles from Refs.\(^70,71 \), respectively). An anomalous diffusivity maximum exist in q-TIP4P/F water at approximately \( T < 300 \) K.
Not surprising, as shown in the inset of Fig. 6a, the inclusion of NQE increases water diffusivities, particularly
MD simulations are in slightly better agreement with experiments compared to the RPMD simulation results.

\[ D(T) = D_0 \exp \left( -\frac{E_A}{k_B T} \right). \]  

where \( D_0, E_A \) are constants; \( k_B \) is the Boltzmann constant. At low temperatures, the behavior of \( D(T) \) depends on the pressure. Specifically, at high pressures, \( P \gg 200 \text{ MPa} \), in the HDL domain, \( D(T) \) is non-Arrhenius and its behavior is well described by Mode Coupling Theory (MCT), i.e.,

\[ D(T) = D_0 (T - T_{MCT})^\gamma, \]  

where \( D_0, \gamma, \) and the MCT temperature \( T_{MCT} \) are constants. At low pressures (\(< 200 \text{ MPa}\)), \( D(T) \) also obeys MCT but only down to approximately \( T = 200 - 220 \text{ K} \). Upon further cooling, \( D(T) \) seems to exhibit a crossover from non-Arrhenius (\( T > 200 - 220 \text{ K} \)) to Arrhenius (\( T < 200 \text{ K} \)) behavior. An Arrhenius regime at low temperatures can be identified in Fig. 6a for the case \( P = -100 \text{ MPa} \); the cases of \( P = 100, 0.1 \text{ MPa} \) are less evident due to the limited available data at \( T < 200 \text{ K} \).

The values of \( D \) from the MD/PIMD simulations are compared with the corresponding experimental values in Fig. 6b,c along different isotherms. At high temperatures, approximately \( T > 300 \text{ K} \) (Fig. 6c), the values of \( D(P) \) from classical MD and PIMD simulations practically overlap with the available experimental data at all pressures studied. Instead, at \( T < 300 \text{ K} \) (Fig. 6b), our simulation results predict values of \( D(P) \) that deviate by up to a factor of 4 from the corresponding experimental data, depending on pressure. Interestingly, overall, classical MD simulations are in slightly better agreement with experiments compared to the RPMD simulation results. Not surprising, as shown in the inset of Fig. 6a, the inclusion of NQE increases water diffusivities, particularly upon cooling within the supercooled regime.

One of the main points of Fig. 6b is the presence of an anomalous maximum in the diffusion coefficient of q-TIP4P/F water. Such a \( D \)-maximum is consistent with experiments and implies that there is a range of temperatures at which \( D \) increases (anomalously) with increasing \( P \).

**Phase diagram.** Figure 7a,b show, respectively, the phase diagram of q-TIP4P/F water obtained from PIMD and classical MD simulations. These phase diagrams include the LLCP, coexistence line, \( \kappa_T \)-maxima, and Widom line calculated from the TSEOS. Also included are the lines of \( \rho \)-maxima, \( D \)-maxima, \( \kappa_T \)-maxima, and \( \kappa_T \)-minima obtained from our MD/PIMD simulations. We also show the maxima/minima of these properties reported in experiments, where available. The liquid-vapor boundary lines shown in Fig. 7a,b correspond to the conditions at which spontaneous cavitation occurs during our computer simulation.

The phase diagrams of q-TIP4P/F water resulting from the classical MD and PIMD simulations are qualitatively similar. As found previously in ST242 and TIP4P/2005 water,

- the \( \kappa_T \)-maxima and \( \kappa_T \)-minima obtained from the TSEOS originate at the LLCP and deviate from each other at higher temperatures. The \( \kappa_T \)-maxima line (blue up-triangles) connects smoothly with the \( \kappa_T \)-minima line (blue down-triangles). In addition, as shown in Ref.\(^\text{35}\), the point in Figs. 7 and 8 where the \( \rho \)-maxima line has infinite slope is located on the \( \kappa_T \)-extrema line, at which \( \Delta(T/\beta \gamma) \rho = 0 \). The \( \rho \)-maxima line has a nose shape. In particular, our simulations suggest that, at low pressures, the \( \rho \)-maxima line is re-entrant and deviates from the liquid-vapor boundary line [see, in particular,
MD simulations. For example, the one may conclude that the reported location of the LLCP based on the TSEOS is robust in the case of classical Refs.7,72, where computer simulations performed using the ST2 and TIP4P water model found that the spinodal behavior is not supported by MD/PIMD simulations of q-TIP4P/F water. Hence, our results are consistent with MCT temperatures extracted from Fig. 6a. The experimental MCT temperature at \( T_c = 230 \text{ K} \), \( P_c = 50 \text{ MPa} \)\(^{49,50}\).

Regarding the \( D_{\text{max}} \)-maxima line, both MD and RPMD simulations overestimate the corresponding pressures relative to the experiments, with the RPMD simulations performing slightly better. We also include in Fig. 7a,b the MCT temperatures extracted from Fig. 6a. The experimental MCT temperature at \( P = 0.1 \text{ MPa} \) is \( T_{\text{MCT}} = 221 \text{ K} \) and hence, this temperature is underestimated in both MD and RPMD simulations.

Overall, the results from classical MD simulations in Fig. 7b are consistent with the TSEOS. Accordingly, one may conclude that the reported location of the LLCP based on the TSEOS is robust in the case of classical MD simulations. For example, the \( \kappa T \)-maxima from MD simulations and from the TSEOS (blue triangles and blue solid lines) overlap; similarly, the corresponding \( C_p \)-maxima lines (red triangles and red solid lines) also overlap. In addition, we find that the \( T_{\text{MCT}}(P) \) line shows a sudden change in slope at the intersection with the Widom line. This is consistent with the view that the Widom line separates the LDL-like liquid at low pressures from the HDL-like liquid at high pressures. The sharp crossover in \( T_{\text{MCT}}(P) \) is reminiscent of the glass transition temperature of water as a function of pressure which shows a sudden change as the system evolves from LDL (low pressure) to HDL (high pressure)\(^{31,74,75}\).

In the case of PIMD simulations (Fig. 7a), the \( \kappa T \)-maxima line obtained from the TSEOS (blue solid line) is located at slightly lower pressure relative to the PIMD simulation results (blue up-triangles). Similarly, the Widom line predicted by the TSEOS is located at a pressure slightly lower than the pressure at which the slope of \( T_{\text{MCT}}(P) \) suddenly changes. Hence, in the case of PIMD simulations for water, the reported location of the LLCP may shift slightly if additional data points at \( T < 180 \text{ K} \) are considered in the TSEOS calculation. Additional PIMD simulations are also needed to improve the determination of the \( \kappa T \)-maxima line at low temperatures.

The similarities in the phase diagrams of Fig. 7a,b imply that, at least for the q-TIP4P/F water model, the LLPT hypothesis scenario remains a solid, viable explanation of water anomalous behavior even if NQE (i.e., atoms delocalization) are included. This is important since (i) the LLCP scenario has been tested only in classical MD simulations and, mostly, rigid water models, and (ii) the location of the LLCP is extremely sensitive to small variations in the water model considered (e.g., small changes in the partial charges of the H and O atoms can easily shift the location of the LLCP to \( (P, T) \) conditions that are physically inaccessible to the liquid state; see, e.g., Refs. 76,77). Overall, including NQE shifts the location of the LLCP, LLPT line, and maxima/minima lines towards lower temperatures (see also Ref. 74,75).

So far, our discussion has been centered on \( \mathrm{H}_2\mathrm{O} \). The same analysis presented here for \( \mathrm{H}_2\mathrm{O} \) was done for the case of \( \mathrm{D}_2\mathrm{O} \) by performing PIMD simulations using the q-TIP4P/F model. The analogous to Figs. 1, 2, 3, 4, 5 and 6 are included in Figs. S4–S8 of the SI. Here, we only discuss the phase diagram of q-TIP4P/F \( \mathrm{D}_2\mathrm{O} \); see Fig. 8. The phase diagram of \( \mathrm{D}_2\mathrm{O} \) is qualitatively similar to the phase diagram of \( \mathrm{H}_2\mathrm{O} \). The LLCP in q-TIP4P/F \( \mathrm{D}_2\mathrm{O} \) is located at \( (\rho_c = 1.13 \text{ g/cm}^3, P_c = 176 \text{ MPa}, T_c = 177 \text{ K}) \). Relative to q-TIP4P/F \( \mathrm{H}_2\mathrm{O} \), the LLCP in \( \mathrm{D}_2\mathrm{O} \) is shifted by \( (\Delta \rho_c \approx 0.11 \text{ g/cm}^3, \Delta P_c \approx 9 \text{ MPa}, \Delta T_c \approx 18 \text{ K}) \). Accordingly, our results indicate that isotope substitution in water can play an important role in the phase behavior of low-temperature and supercooled water. These values of \( \Delta T_c \) and \( \Delta P_c \) are consistent with the locations of the LLCP in \( \mathrm{H}_2\mathrm{O} \) and \( \mathrm{D}_2\mathrm{O} \) estimated by Mishima and Stanley from decompression-induced experiments of ice IV\(^{49,50} \) where \( (\Delta P_c \approx 50 \text{ MPa}, \Delta T_c \approx 10 \text{ K}) \).
Summary and discussion

We performed classical MD, PIMD, and RPMD simulations of H$_2$O using the q-TIP4P/F model over a wide range of temperatures and pressures. At supercritical temperatures, most properties studied are practically insensitive to whether one employs classical MD and PIMD simulations ($-100 \leq P \leq 500$ MPa). Specifically, the $\rho(T)$ and $\kappa(T)$ obtained from classical MD or PIMD simulations overlap (within error bars) down to $T \approx 225$ K and $T \approx 200$ K, respectively (Fig. 1 and Fig. S2 of the SI). In the case of $C_p(T)$, the quantitative values vary for classical MD and PIMD results, but this is expected to occur due to NQE\(^a\). Nonetheless, the qualitative behavior of $D(T)$ is not affected whether one employs classical MD or RPMD simulations down to $T \approx 260$ K (Fig. 6a). Relative to the classical MD simulations, including NQE (RPMD simulations) increases the values of $D(T)$ at $T < 260$ K (inset of Fig. 6a). In both cases, the $D(T)$ from computer simulations are in good agreement with experiments where data is available (Fig. 6bc).

Deviations between MD and PIMD simulations become noticeable at approximately $P = 100–200$ MPa and $T < 225$ K. Our results strongly indicate that at these thermodynamic conditions, q-TIP4P/F water exhibits a LLCP. Using a two-state equation of state, we estimate that the LLCP is located at $(\rho_c = 1.03$ g/cm$^3$, $P_c = 203$ MPa, $T_c = 175$ K) when NQE are not included (classical MD); including NQE (PIMD simulations) shifts the location of the LLCP to $(\rho_c = 1.02$ g/cm$^3$, $P_c = 167$ MPa, $T_c = 159$ K); see Fig. 1c,d. Consistent with the existence of a LLCP, our study shows the presence of loci of maxima in $C_p$ and $\kappa_T$ in the P–T phase diagram of q-TIP4P/F water. These anomalous maxima lines, together with the loci of maxima in $D$ and $\rho$ are included in Fig. 7. We stress that the location of the LLCPs reported in this work are estimations provided by the TSEOS. Our estimation of the LLCP for H$_2$O is based on PIMD simulations using $n_b = 32$ beads per ring-polymer. While PIMD simulations with $n_b > 32$ are computationally expensive, additional PIMD simulations employing $n_b > 32$ beads per ring-polymer are desirable at low temperatures in order to obtain a more precise estimation of the LLCP location in H$_2$O (q-TIP4P/F water). While our results conclusively show that the LLCP in H$_2$O shifts to lower $T$ when NQE are included, obtaining the exact values of $(\rho_c, T_c, P_c)$ may require additional data at $T < 180$ K (particularly for the case of PIMD simulations of H$_2$O where $T_c$ is low).

Overall, our results for H$_2$O (e.g., Fig. 7) are consistent with previous classical computer simulations of water using the (rigid) ST2\(^{42}\) and TIP4P/2005\(^{15}\) water models. It follows that the present study validates the LLPT hypothesis for water to the case where NQE are included. We note, however, that the LLCP in q-TIP4P/F water, as well as in ST2, TIP4P/2005, and TIP4P/Ice water, is located at pressures and temperatures that are off compared to the experimental predictions\(^{6,46}\). This provides a thermodynamic explanation of why these water models are unable to reproduce the sharp increase in $C_p(T)$ and $\kappa_T(T)$ observed in experiments at $P = 0.1$ MPa\(^{5,10}\). Specifically, these water models predict that $P_c > 150$ MPa, while $P_c \approx 50 - 100$ MPa estimated from experiments\(^1,50\). Accordingly, computer simulations show a mild increase in $\kappa_T$ and $C_p$, relative to experiments, upon isobaric cooling at $P = 0.1$ MPa. We note that the $C_p(T)$ and $\kappa_T(T)$ quantify the fluctuations in entropy and volume, respectively. Hence, from a microscopic point of view, the weak increase of $\kappa_T$ and $C_p$ upon isobaric cooling at $P = 0.1$ MPa is due to the inability of current water models (ST2, TIP4P/2005, TIP4P/Ice, etc) to reproduce the anomalously large fluctuations (in entropy and volume) of real water in the supercooled regime. At least for the q-TIP4P/F model studied, the inclusion of NQE (quantum fluctuations due to atoms delocalization) is not sufficient to reproduce the anomalously large fluctuations (in entropy and volume) of real water at low temperatures. Accordingly, additional sources of fluctuations may be missed in rigid (e.g., TIP4P/2005, ST2) as well as flexible water models, such as q-TIP4P/F model.

We also performed extensive PIMD simulations of heavy water using the q-TIP4P/F model. The results are summarized in the phase diagram of Fig. 8 (see also the SI). The PIMD simulations confirm that isotope substitution has minor effects on the properties of water. While the phase diagram of D$_2$O is qualitatively identical to the phase diagram of H$_2$O, the location of the corresponding LLCP differ. Specifically, calculations based on the TSEOS, applied to PIMD data at $T \geq 190$ K, predict that in the case of D$_2$O, $(\rho_c = 1.13$ g/cm$^3$, $P_c = 176$ MPa, $T_c = 177$ K) which represents a non-negligible shift relative to H$_2$O ($\Delta \rho_c = 0.11$ g/cm$^3$, $\Delta P_c \approx 9$ MPa, $\Delta T_c \approx 18$ K). This is important since computer simulations of water-like models show that the introduction of NQE can indeed shift considerably the location of the LLCP\(^{47,48}\). In particular, the differences in the relative values of $(\rho_c, P_c, T_c)$ between q-TIP4P/F H$_2$O and D$_2$O are somewhat consistent with the predictions from experiments in glassy water ($\Delta \rho_c = 50$ MPa, $\Delta T_c = 10$ K\(^{49,50}\)) and with the relative location of the $\kappa_T$–maximum at 1 bar\(^{10}\). The present study shows that many questions previously addressed in computational studies of supercooled water at low temperatures, using classical water models, are accessible via PIMD simulations. For example, it would be interesting to explore the relationship between dynamics and structure of water at low temperatures and how the Stokes–Einstein and Stokes–Einstein–Debye relationships are affected by isotope substitution\(^{52,85}\).

Data availability

All study data are included in the article and/or SI.

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Competing interests
The authors declare no competing interests.
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