Role of Salt, Pressure, and Water Activity on Homogeneous Ice Nucleation

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ABSTRACT: Pure water can be substantially supercooled below the melting temperature without transforming into ice. The achievable supercooling can be enhanced by adding solutes or by applying hydrostatic pressure. Avoiding ice formation is of great importance in the cryopreservation of food or biological samples. In this Letter, we investigate the similarity between the effects of pressure and salt on ice formation using a combination of state-of-the-art simulation techniques. We find that both hinder ice formation by increasing the energetic cost of creating the ice–fluid interface. Moreover, we examine the widely accepted proposal that the
ice nucleation rate for different pressures and solute concentrations can be mapped through the activity of water [Koop, L.; Tsias, P. *Nature*, **2000**, *406*, 611]. We show that such a proposal is not consistent with the nucleation rates predicted in our simulations because it does not include all parameters affecting ice nucleation. Therefore, even though salt and pressure have a qualitatively similar effect on ice formation, they cannot be quantitatively mapped onto one another.
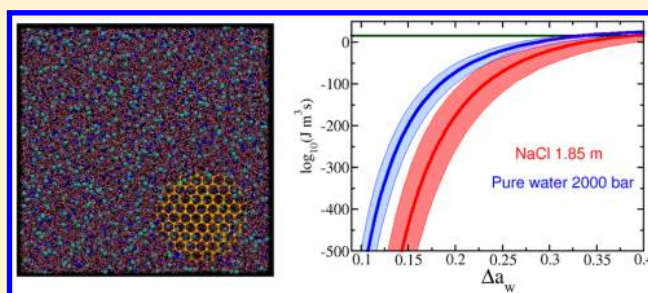
The formation of ice from supercooled water is the most important freezing transition on Earth. Despite its relevance and ubiquity, there are still many uncertainties about this phase transition. For instance, important issues such as the rate[1−3] and the mechanism[4,5] by which ice nucleates in supercooled water are still currently under debate.[6]

The urge to understand in detail water freezing comes from the fact that it has a central role in key industrial and environmental processes. For example, the content of ice in clouds has a strong impact on the Earth's albedo and, therefore, on climate change.[7] On the other hand, successful cryopreservation crucially depends on avoiding water freezing, which can be deleterious for the cells.[8]

A way to delay the formation of ice in cryopreservation protocols is to put the sample under hydrostatic pressure[9] to slow down ice nucleation.[10] Salt is also known to have a decelerating effect on ice nucleation.[11]

In a seminal work, Koop et al. compiled experimental data on the freezing of salty aqueous solutions at different concentrations and pressures. Quite remarkably, they were able to map the ice nucleation rate of all systems into a single curve that solely depends on the activity of water in solution.[12] This spectacular result, based on the parallelism between the effects of salt and pressure on ice nucleation, has had great acceptance in the scientific community studying water freezing.

The goal of the present work is to investigate the analogy between the effects of pressure and salt on water freezing by

means of computer simulations. By comparing the effects of salt and pressure, we are able to assess the validity of the proposal by Koop et al. To achieve this, we compare three systems: pure water at 1 bar, pure water at 2000 bar, and a 1.85 m NaCl aqueous solution at 1 bar. State-of-the art simulation techniques are required to compute the ice nucleation rate and the interfacial free energy for these systems. We use the Seeding[13−15] and the Mold Integration (MI)[16] methods for that purpose. These techniques enable us to gain understanding of the parameters that affect the ice nucleation rate.

We use the TIP4P/2005 water model[17] combined with the Joung Cheetham/SPC/E model for NaCl.[18,19] We perform molecular dynamics simulations at constant temperature and pressure with the GROMACS package.[20] We refer the reader to our previous work for further simulation details.[3,21]

The Seeding technique consists of simulating ice nuclei embedded in the supercooled fluid (either pure or salty water). We insert pure spherical ice Ih seeds as that shown in the graphical abstract. The embedded ice cluster configuration is equilibrated as described in ref 22. We make sure that the cluster interface is well equilibrated by looking at the ionic density profile.[23] Once we get an equilibrated configuration of an ice cluster embedded in the solution, we monitor the
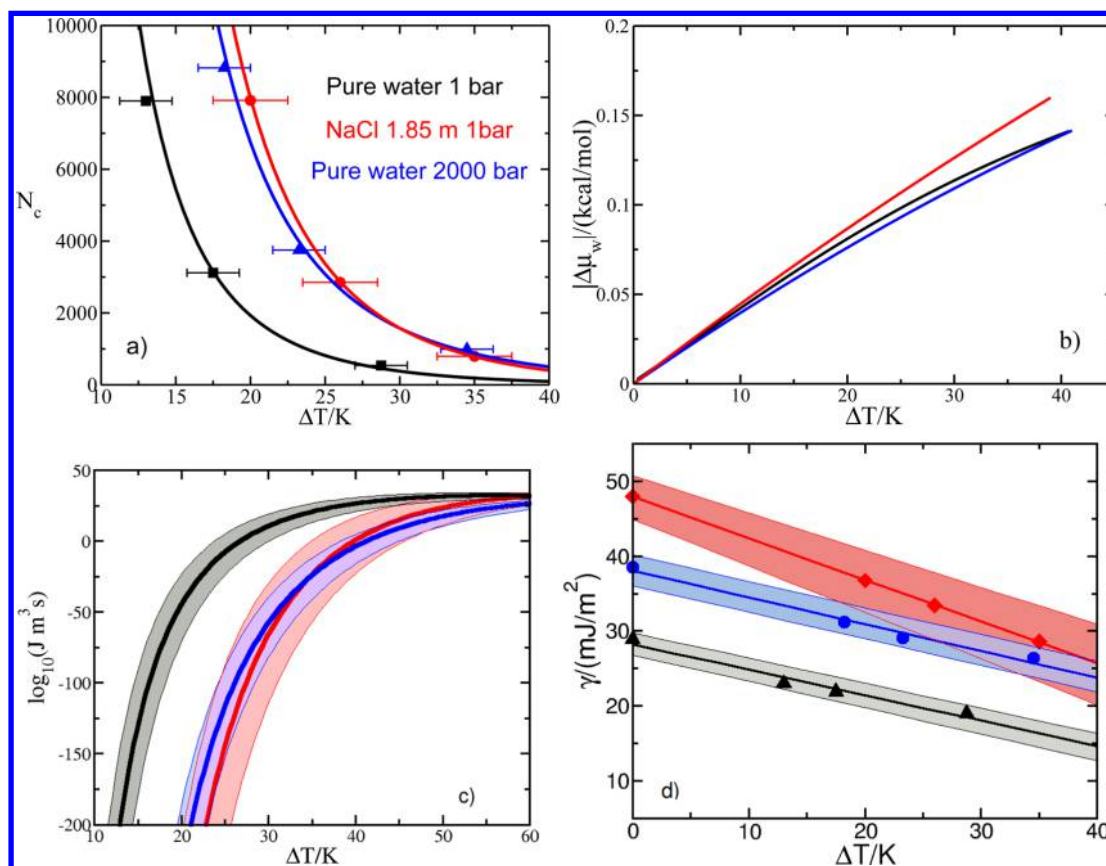
Figure 1. Plots for pure (black), salty (red), and compressed water (blue) as a function of the supercooling: (a) number of particles in the critical cluster; (b) water chemical potential difference between the liquid and the solid phases; (c) decimal logarithm of the nucleation rate; (d) ice−water interfacial free energy. Symbols in (d) for $\Delta T = 0$ and >0 correspond to our calculations of γ with MI and Seeding, respectively. Shaded regions in (c) and (d) indicate the error bar.

evolution of the nucleus at different temperatures. For temperatures higher than that at which the inserted cluster is critical, the cluster melts, and vice versa.

In this way, we obtain an estimate for the temperature at which the inserted cluster with N_c molecules is critical. We determine N_c using local bond order parameters,[24] as done in our previous work.[14,15,25] We use large system sizes to ensure that concentration changes are negligible as the cluster grows or melts in the brine solution.[23] In Figure 1a, we show N_c versus the supercooling, ΔT, which is the melting temperature, T_m, minus the temperature of interest (the model melting temperatures for pure ice in coexistence with pure water at 1 and 2000 bar[26] and with a 1.85 m NaCl aqueous solution at 1 bar[23] are 250, 227, and 240.5 K, respectively). Clearly, for a given ΔT, the number of molecules required to reach the critical size is larger in salty or compressed water than that in pure water at normal pressure. This is consistent with the experimental observation that salt and pressure hinder ice nucleation.[11]

To quantify the decelerating effect of salt and pressure on homogeneous ice nucleation, we compute the nucleation rate, J. In the Seeding method, simulations are used to obtain the parameters on which the J expression given by Classical Nucleation Theory (CNT)[27−29] depends[14,15,30]

$$J = \sqrt{\frac{-\Delta\mu_w}{6\pi k_B T N_c}} \rho_f f^+ \exp\left(\frac{N_c \Delta\mu_w}{2k_B T}\right) \qquad (1)$$

Such parameters are the fluid number density, ρ_f, the number of particles in the critical cluster N_c (Figure 1a), the chemical potential difference of water in ice and in the liquid, $\Delta\mu_w = \mu_w^i - \mu_w$ (Figure 1b), and the frequency with which particles attach to the critical cluster (the attachment rate, f^+). Further details on the calculation of these factors will be given in a forthcoming publication.[23] The nucleation rate as a function of the supercooling is plotted in Figure 1c for the three systems under comparison. For a given supercooling, pure water at normal pressure (in black) has the highest nucleation rate. In other words, the supercooling required to freeze water increases when adding salt (in red) or applying pressure (in blue), in agreement with the experimental trend.[10,11]

Because we have access to all variables required for the computation of J, we can rationalize which is the main factor behind the pressure/salt-induced deceleration of ice nucleation. The nucleation rate is given by $J = Ae^{-\Delta G_c/(k_B T)}$, where A is a kinetic prefactor and $\Delta G_c/(k_B T)$ is the Gibbs free energy barrier required to form a critical ice nucleus in the supercooled fluid. We have checked that A does not change by more than 1 or 2 orders of magnitude between different systems for a given supercooling, which is insignificant as compared to the large differences between the J curves in Figure 1c. The differences in J must be then ascribed to changes in $\Delta G_c/(k_B T)$. Within CNT, $\Delta G_c/(k_B T)$ is proportional to the third power of the ice−liquid interfacial free energy, γ, and inversely proportional to the second power of $|\Delta\mu_w|$. The latter does not significantly change from one system to another (see Figure 1b). Therefore,

the key to the decrease of J must be found in an increase of γ. This is in fact what we concluded in our recent study of ice nucleation under high pressure.[31] In Figure 1d, we represent γ versus the supercooling for the three studied systems (the points for the supercooled fluid have been obtained with the Seeding method, whereas those at coexistence, $\Delta T = 0$, were obtained with the MI method[16,21]). Indeed, the interfacial free energy increases when adding salt or applying pressure for a given supercooling. Therefore, both pressure and salt decelerate ice nucleation by increasing the ice–liquid interfacial free energy, which is one of the main conclusions of our work. This is a valuable simulation prediction given that there is no experimental consensus for the value of the ice–liquid interfacial free energy (not even for the case of pure water at 1 bar[32]).

The fact that pressure and salt hinder ice nucleation for the same reason is in principle consistent with the proposition that applying a certain pressure should have the same effect on ice nucleation as adding a given amount of salt.[12] Such a proposal is the basis of the so-called water-activity-based ice nucleation conjecture (WAB-INC).[12,33] The WAB-INC is based on an analysis of the freezing of salty water drops at different pressures and proposes that the nucleation rate depends only on the activity of water, a_w. This idea is extremely appealing because it enables one to obtain the nucleation rate for any solution at any pressure with a fit solely depending on a measurable thermodynamic parameter such as the activity. Although the WAB-INC apparently works,[12] it has never been carefully checked for three reasons: (i) a_w cannot be experimentally measured for deeply supercooled solutions due to the formation of ice (in fact, in many cases, it is assumed to be independent of temperature[33]); (ii) the general character of the theory has not been tested because the J range that can be measured is narrow (it is limited by the sample's volume and the cooling rate); (iii) the physical basis of the WAB-INC is unclear because many of the parameters that affect ice nucleation, like γ, N_c, or $\Delta\mu_w$ for $T < T_m$, cannot be measured experimentally. Our simulations do not have these shortcomings and enable us to test the validity of the WAB-INC in a wide range of nucleation rates.

To start with, we evaluate the temperature dependence of a_w in the brine solution at 1 bar and with salt concentration $c = 1.85$ m via

$$\mu_w(c, T, 1) = \mu_w(0, T, 1) + RT \ln[a_w(c, T, 1)] \quad (2)$$

In practice, the chemical potential difference with and without salt at 1 bar, $\mu_w(c,T,1) - \mu_w(0,T,1)$, is obtained as $\Delta\mu_w(0,T,1) - \Delta\mu_w(c,T,1)$, the difference between the black and the red curves in Figure 1b (the chemical potential of water in ice cancels out when both $\Delta\mu_w$'s are subtracted). In Figure 2, we plot $a_w(c,T,1)$ as a function of the supercooling (red curve). To our knowledge, this is the first time that the temperature dependence of water activity is reported up to such deep supercooling either in simulations or experiments (there are simulation works that report activities as a function of concentration at constant temperature[34]). As explained below, the cross with the orange curve (activity of water coexisting with ice) corresponds to the melting temperature, above which the water activity remains almost constant, in accordance with experimental observations for most simple ionic solutions.[33] By contrast, a_w sharply increases below the melting temperature.

The activity of pure water under pressure is in principle 1. However, in the framework of the WAB-INC, pure water under
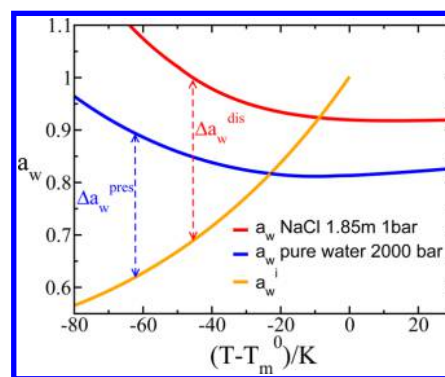

Figure 2. Water activity as a function of $T - T_m^0$, the difference between the temperature of interest and the melting temperature of pure water ($T_m^0 = 250$ K for the model). In red, we plot the activity of water in the studied 1.85 m solution, and in blue, we show the effective activity for pure water at 2000 bar as defined in the main text. In orange, we plot the activity of water coexisting with ice.

pressure p is effectively assigned the activity of a water solution at normal pressure having the same chemical potential difference with ice, $\Delta\mu_w$

$$\mu_w(0, T, p) - \mu_w^i(0, T, p) = \quad (3)$$

$$\mu_w(0, T, 1) + RT \ln a_w(c^{\text{eff}}, T, 1) - \mu_w^i(0, T, 1) \quad (4)$$

where c^{eff} is the effective concentration required to satisfy the equality above. Thus, we can compute $a_w(c^{\text{eff}},T,1)$ as exp-$[(\Delta\mu_w(0,T,1) - \Delta\mu_w(0,T,p))/(RT)]$ (the exponent is obtained by subtracting the black and the blue curves in Figure 1b). In Figure 2, we show $a_w(c^{\text{eff}},T,1)$ as a function of temperature (blue curve). Again, the activity sharply increases below the melting temperature of compressed water, given by the crossing with the orange curve. Therefore, according to our simulations, the assumption that a_w does not depend on temperature for most ionic solutions[12,33] cannot be safely made, especially at low temperatures where water behaves anomalously.[35,36]

As pointed out in ref 33, the validity of the WAB-INC does not rely on whether or not a_w depends on temperature.[12] What the WAB-INC really proposes is that $J(\Delta a_w)$ is a universal curve for any pressure or concentration. Δa_w is the difference, for a given temperature, between the activity of water in the solution (or in compressed water) and the activity of water at coexistence with ice, a_w^i. The latter can be obtained through

$$\mu_w^i(0, T, 1) = \mu_w(0, T, 1) + RT \ln[a_w^i(c, T, 1)] \quad (5)$$

The chemical potential difference $\mu_w^i(0,T,1) - \mu_w(0,T,1)$ is simply $\Delta\mu_w$ for pure water at 1 bar (black curve in Figure 1b). a_w^i is plotted in orange in Figure 2 (at the melting point, the orange and the red/blue curves cross because the activity of water becomes equal to a_w^i). Thus, to obtain Δa_w for the studied solution, we have to subtract, for a given temperature, the red and the orange curves in Figure 2, whereas for pure water under pressure, we compute the difference between the blue and the orange curves (see red and blue arrows in Figure 2, respectively). Knowing $\Delta a_w(T)$ and $J(T)$ (Figure 1c), we obtain $J(\Delta a_w)$. In Figure 3a, we plot $J(\Delta a_w)$ for compressed and salty water. Both curves are not the same for every Δa_w. Therefore, the WAB-INC proposal of a universal $J(\Delta a_w)$ curve is not consistent with our simulation predictions. However, the $J(\Delta a_w)$ curves lie close to each other beyond the rate value measured in typical experiments, $J \approx 10^{16}$ m^{-3} s^{-1}, given by the
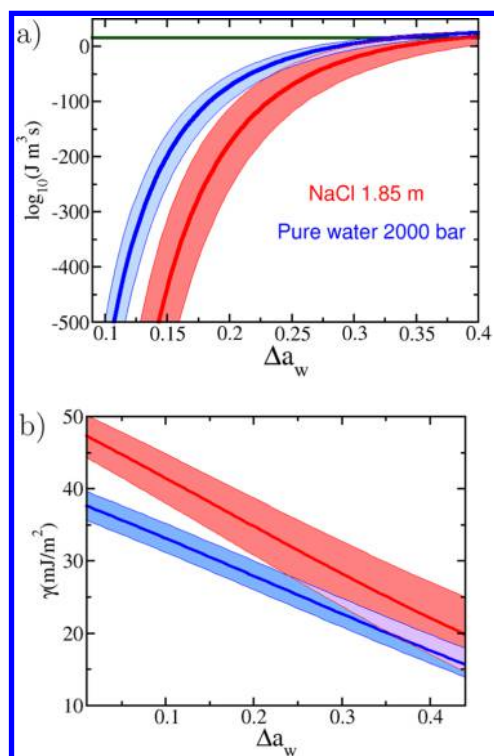
Figure 3. (a) Nucleation rate of salty (1.85 m NaCl) and compressed (2000 bar) water as a function of Δa_w. The horizontal green line corresponds to $J = 10^{16}$ m^{-3} s^{-1}. (b) Ice−fluid interfacial free energy as a function of Δa_w.

horizontal green line in Figure 3a. Thus, our results are compatible with the fact that the WAB-INC may seem to work when data of typical freezing experiments are analyzed.[12] Why would a theory that is not general seemingly work at high values of Δa_w?

On the one hand, it is perhaps worth noting that the WAB-INC is not as neat as it may appear. In the publication where the WAB-INC was proposed, variations of up to 15−20 K around the universal freezing curve can be clearly noticed.[12] In that temperature range, there may be many orders of magnitude difference in the nucleation rate. On the other hand, the WAB-INC may be a particular case of CNT in certain limits. Because in the WAB-INC framework the rate solely depends on the activity of the solvent (chemical potential), the WAB-INC will be compatible with CNT if, for a given Δa_w, all other parameters that affect ice nucleation are the same. We check if this is the case for the ice−fluid interfacial free energy, a parameter that we have shown to be central in understanding the effect of salt (this work) and pressure (ref 31) on homogeneous ice nucleation. Combining $\Delta a_w(T)$ and $\gamma(T)$ (Figure 1d), we obtain $\gamma(\Delta a_w)$, shown in Figure 3b. Clearly, γ is not the same for salty and compressed water at low Δa_w and becomes increasingly similar as Δa_w increases. When both Δa_w and γ are similar, the WAB-INC may seem to work, but this is just a particular case of CNT. That γ becomes similar between different systems at high Δa_w may be related to the nucleation of ice clusters in solute-depleted regions when the critical cluster size becomes small.[37] With our analysis, we conclude that CNT is a much more comprehensive theoretical framework than the WAB-INC to understand ice nucleation and that the WAB-INC may only seemingly work as a particular case of CNT at high nucleation rates. The fact that the

simulation approach employed in this work provides estimates of the nucleation rate in a much wider range than current experiments has clearly evidenced the deficiencies of the WAB-INC. We expect our work to inspire future attempts to derive phenomenological frameworks to describe ice nucleation that do not necessarily comply with the WAB-INC.[38]

Our conclusions are based on the results obtained with a water model. One may wonder if our observations can be safely applied to real water as well. We argue that if WAB-INC had a strong physical foundation it should be able to explain ice nucleation both in real water and in any family of realistic water models. Our model is quite realistic because it closely reproduces the behavior of real water for many thermodynamic and dynamic properties,[39] including anomalies[40] and, most importantly, homogeneous ice nucleation in pure[14,30] and salty water.[23] Moreover, in this work, we show that the model captures the experimentally observed deceleration of ice nucleation with pressure and salt[10,12] (Figure 1c), as well as the fact that the WAB-INC may seemingly work in the range of nucleation rates typically accessible to experiments (see Figure 3a). Furthermore, we do not need a perfect model for the NaCl ions to test the WAB-INC as the theory should in principle work for a wide variety of solutes. Therefore, even if the simulated solute does not behave exactly as real dissolved NaCl, it can be taken as any arbitrary solute for testing the WAB-INC. Be it as it may, we hope that our work will motivate future experiments to definitely confirm our prediction. As a matter of fact, there have been already experiments reporting inconsistencies with the WAB-INC.[41]

Our Seeding approach to ice nucleation relies on two assumptions: (i) the proposed structure of the critical cluster is the correct one and (ii) the formation free energy of such a cluster can be obtained via CNT. Our guess for the critical nucleus structure is that of a spherical pure ice Ih cluster. We use ice Ih because this structure, or stacking mixtures of ice Ic and Ih, has shown to be that of critical ice clusters at 1 bar.[4,14,25,31,42] We insert pure ice seeds disregarding the possibility that NaCl ions enter the ice lattice. This approximation is inspired by the experimental phase diagram, where the brine coexists with pure ice.[43] To make sure that this is a good approximation, we have performed a long (260 ns) direct coexistence simulation below the melting temperature and computed the fraction of ions incorporated into the grown ice lattice. Such a fraction was smaller than 0.2%, a value in agreement with previous simulation work[44,45] and sufficiently small to justify our approximation. We use spherical clusters, consistently with previous studies showing that the cluster's shape quickly equilibrates into a sphere,[25] with thermal fluctuations typical of a rough ice−fluid interface.[46,47] Assumption (ii), in turn, is expected to be satisfied for the large critical cluster sizes used in this work. Independent evidence of the validity of CNT to describe the free energy of crystal cluster formation can be found, for example, in ref 48. As long as conditions (i) and (ii) are satisfied, one can use seeding to obtain nucleation rates regardless of whether the pathway leading to the formation of the critical cluster is CNT-like (a one-by-one addition of particles to a growing crystal cluster) or a more sophisticated one like composition fluctuations followed by crystal cluster growth.[37,49−51] Thus, although Seeding does not provide any information on the way the critical cluster is formed, it can be used to obtain nucleation rates,[15] even in systems where the formation of the critical cluster has been reported to be two-step, like crystallization in hard spheres[52,53]

or in mw-water.[54] In any case, because we are dealing with the crystallization of the solvent and with large critical clusters whose size exceeds that of typical composition fluctuations, we do not expect the formation mechanism of the critical nucleus to be markedly two-step. It is also worth noting that Seeding has been successful in predicting crystal nucleation rates in the Lennard-Jones and the Tosi–Fumi NaCl systems[15] as well, which gives further confidence in the predictions made in this Letter. Moreover, in this work, we find consistent values between the γ obtained at coexistence with MI, a method that does not rely on CNT and that does not suffer from strong finite size effects,[16] and that obtained below the melting temperature with Seeding (see Figure 1d). This consistency test, and the considerations mentioned above, strongly support the validity of the approach followed in this work.

In summary, we compare the effects of pressure and salt on homogeneous ice nucleation. We find that both pressure and salt decelerate ice nucleation by increasing the ice–liquid interfacial free energy. Despite this qualitative similarity, it is not possible to quantitatively map ice nucleation rates of salty water onto those of compressed water through the activity of water. Our results question the validity of the so-called water-activity-based ice nucleation theory.[12]

Understanding and quantifying the effect of salt on homogeneous ice nucleation can be useful to develop climate change models.[7] On the other hand, improving cryopreservation protocols, aimed at vitrifying biological samples by averting ice nucleation and growth upon cooling, requires deep understanding of the effect of freezing-preventing factors like pressure, salt, or combinations of both.[8,9] Our work may also have implications in the experimental search of the putative liquid–liquid transition of water,[55−58] which in some cases uses pressure and solutes as strategies to approach the so-called no-man's land.[36,59,60]

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Notes

The authors declare no competing financial interest.

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