

# Promotion of Homogeneous Ice Nucleation by Soluble Molecules

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## Supporting Information

**ABSTRACT:** Atmospheric aerosols nucleate ice in clouds, strongly impacting precipitation and climate. The prevailing consensus is that ice nucleation is promoted heterogeneously by the surface of ice nucleating particles in the aerosols. However, recent experiments indicate that water-soluble molecules, such as polysaccharides of pollen and poly(vinyl alcohol) (PVA), increase the ice freezing temperature. This poses the question of how do flexible soluble molecules promote the formation of water crystals, as they do not expose a well-defined surface to ice. Here we use molecular simulations to demonstrate that PVA promotes ice nucleation through a homogeneous mechanism: PVA increases the nucleation rate by destabilizing water in the solution. This work demonstrates a novel paradigm for understanding ice nucleation by soluble molecules and provides a new handle to design additives that promote crystallization.

Crystallization of water plays a decisive role in various fields that range from biology in subzero environments<sup>1</sup> and cryopreservation<sup>2</sup> to cloud science.<sup>3,4</sup> Ultrapure water droplets can be cooled to a temperature as low as 227 K,<sup>5</sup> where ice crystallization occurs via homogeneous nucleation, assisted only by thermal fluctuations. On the other hand, ice crystallization in nature often occurs at higher temperatures, facilitated by so-called ice nucleating agents.<sup>6,7</sup> Although it has long been assumed that ice nucleating agents must be insoluble substances, recent work indicates that water-soluble molecules can efficiently promote the nucleation of ice.<sup>8</sup>

Insoluble ice nucleating agents, such as dust, minerals, soot, and even organic monolayers, provide sufficiently large surfaces to stabilize the critical ice nuclei and promote heterogeneous ice nucleation.<sup>9–12</sup> Similarly, it has been proposed that soluble ice nucleating agents, such as proteins and pollen, promote ice nucleation through a heterogeneous mechanism.<sup>8</sup> Ice nucleation by poly(vinyl alcohol) (PVA) and a soluble polysaccharide for pollen is particularly intriguing because these molecules are expected to be highly flexible, and it has been shown that the flexibility of ice nucleating surfaces has a strong deleterious impact on ice nucleation.<sup>9</sup> Heterogeneous nucleation by flexible macromolecules would require their spontaneous arrangement to offer an ice-stabilizing surface, which would be penalized by a large loss of conformational entropy. Moreover, soluble molecules typically decrease the activity of water through a colligative effect, with a concomitant depression of the ice nucleation temperatures.<sup>13,14</sup> These issues raise the question of

what is the mechanism by which soluble flexible molecules assist in the nucleation of ice.

PVA is the only fully flexible soluble ice-nucleating agent for which the molecular structure is known.<sup>15–17</sup> PVA increases the experimental ice crystallization temperature by up to 4 K,<sup>15</sup> while birch pollen polysaccharides increase it by 15–22 K.<sup>8,18–20</sup> It has been conjectured that the distinct ice nucleating ability of these polymers can be explained by the different dimensionality of the template they offer to stabilize ice: PVA is conjectured to serve as a 1-D template for ice nucleation, whereas the polysaccharides are proposed to act as 2-D templates.<sup>8,15</sup> However, a 1-D template could only stabilize a mostly 1-D ice embryo, which would have an unfavorable area to volume ratio. Interestingly, both PVA and polysaccharides of pollen exhibit both inhibition and promotion effects on ice crystallization.<sup>15–19,21,22</sup>

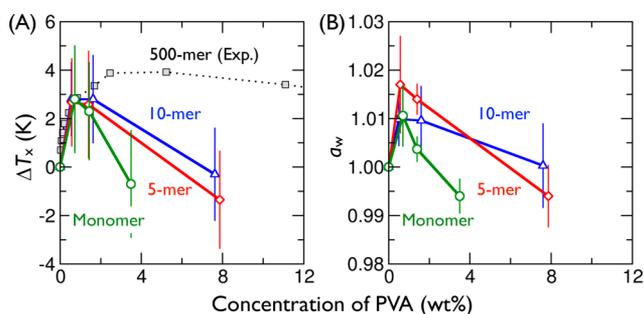
Here we use molecular simulations with computationally efficient and accurate coarse-grained models<sup>23,24</sup> to elucidate the molecular mechanism by which PVA nucleates ice. We first show that the simulations reproduce the experimental increase in ice nucleation temperatures by dilute PVA solutions, and then proceed to demonstrate that PVA does not heterogeneously nucleate ice, but it rather increases the homogeneous nucleation temperature through an increase in the water activity of the solution. To the best of our knowledge, this is the first demonstration that additives can increase the *homogeneous* nucleation temperature of ice.

First, we compute the effect of PVA monomer (2-propanol), 5-mer and 10-mer on the ice nucleation temperature, which we report as the freezing efficiency with respect to the homogeneous freezing temperature of pure water,  $\Delta T_x = T_x^{\text{solution}} - T_x^{\text{water}}$ , as a function of the weight percent (wt%) of PVA in the solution (Figure 1a). We find that all PVA oligomers promote ice crystallization in dilute solutions. The rise in  $\Delta T_x$  for the oligomers in the simulations is independent of the molecular weight and matches the raise for the larger, 40- to 2200-mer PVA polymers in the experiments.<sup>15</sup> The maximum increase in freezing efficiency for the oligomers in our study,  $\Delta T_x = 2.8 \pm 2$  K, is comparable to the 4 K found for the larger polymers in the experiment.<sup>15</sup> As in the latter,<sup>15</sup> the freezing efficiency decays at higher concentrations for all PVA oligomers. We find that the decrease in  $\Delta T_x$  is sharper with decreasing chain length. These results demonstrate that the simulations accurately reproduce the magnitude and non-

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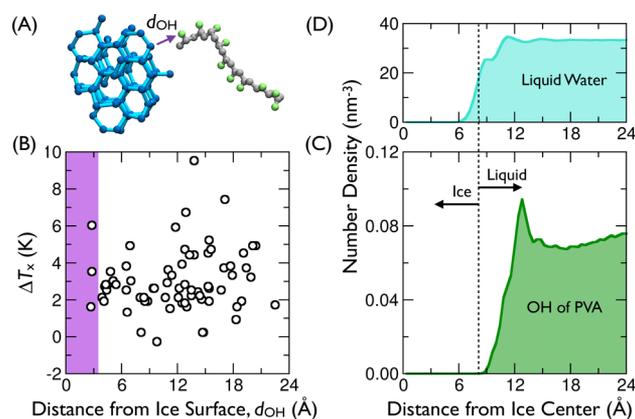
**Figure 1.** Freezing efficiency and water activity of PVA solutions. PVA monomer, 5- and 10-mer have a very similar effect on the ice crystallization efficiency  $\Delta T_x$  (panel A) and water activity  $a_w$ , measured at 275 K (panel B). The black dash line in panel A shows the experimental results for polydisperse PVA with molecular weight 17 600–26 400 g mol<sup>-1</sup>, corresponding to 500-mer in average.<sup>15</sup> Panel B shows that the decline of  $a_w$  at higher PVA concentrations becomes slower with increasing chain length, a colligative effect. The activity coefficients of water in the solutions are larger than 1 for the explored concentration range (Supporting Information, Figure S4).

monotonous concentration dependence of the ice crystallization temperature upon addition of PVA.

If ice nucleation by PVA were due to a heterogeneous mechanism, then PVA should be attached to the incipient crystalline embryo. Experimental and computational studies indicate that PVA strongly binds to the prismatic plane of ice, where it attaches in a linear, 1-D configuration.<sup>21,24</sup> The critical nuclei are stacking disordered<sup>25</sup> and small (about 100 molecules<sup>26</sup>); hence, they do not have well-developed prismatic faces. Indeed, 95.7% of ice nucleation events in the 0.55 wt% 10-mer solution occur without absorption of PVA to the ice crystallites. Moreover, we find no correlation between the freezing efficiency and the closest distance between PVA and the ice embryo (Figure 2a,b). We conclude that the increase in the ice freezing temperature of dilute PVA solutions cannot be attributed to heterogeneous nucleation.

This poses the question of how does PVA promote homogeneous ice nucleation. According to classical nucleation theory (CNT),<sup>27</sup> the nucleation rate is  $J = A \exp(-\Delta G^*/k_B T)$ , where  $A$  is the kinetic prefactor,  $\Delta G^*$  is the free energy barrier for nucleation,  $k_B$  is the Boltzmann factor, and  $T$  is the temperature. The kinetic prefactor  $A$  is only weakly dependent on  $T$ ; therefore, the increase in nucleation temperature  $\Delta T_x$  must be due to a decrease in the nucleation barrier  $\Delta G^*$ .

The homogeneous nucleation barrier  $\Delta G^*$  is controlled by the ice–liquid surface tension  $\gamma$ , the density of ice  $\rho_s$  and the difference in chemical potential between liquid and ice,  $\Delta\mu = \mu_{\text{liquid}} - \mu_{\text{ice}}$ :  $\Delta G^* = 16\pi\gamma^3/(3\rho_s^2\Delta\mu^2)$ . Additives that preferentially bind to the ice–liquid interface would decrease  $\gamma$ , thus decreasing the homogeneous nucleation barrier.<sup>28–31</sup> However, we find that PVA does not show preferential adsorption to the critical crystallites in the non-equilibrium nucleation trajectories (Figure 2b), nor in equilibrium simulations in which a hexagonal ice embryo is constrained to prevent its growth (Figure 2c,d). The distribution of PVA 10-mer around the ice nucleus is the same in equilibrium and non-equilibrium simulations (Supporting Information, Figure S1). This indicates that the weak adsorption of the polymer to the ice embryo is not due to dynamical effects or stacking disorder, but to the small size of the critical crystallites, which do not offer sufficient sites for adsorption of PVA to the



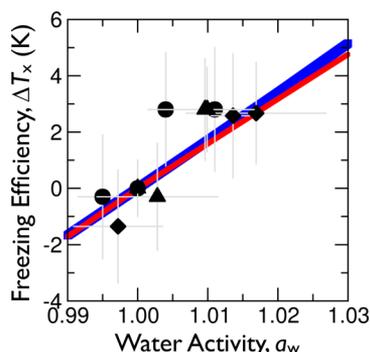
**Figure 2.** Ice nucleation in the presence of PVA proceeds through a homogeneous mechanism. Panel A shows snapshots of an ice embryo consisting of 81 water molecules and a PVA 10-mer. The purple arrow indicates the shortest distance ( $d_{\text{OH}}$ ) from the ice embryo to the hydroxyl group (OH) of PVA. Panel B shows the freezing efficiency  $\Delta T_x$  is uncorrelated to  $d_{\text{OH}}$  (obtained from 70 independent freezing trajectories, when the nucleus is of critical size, with  $\sim 105$  water molecules). We consider PVA to be absorbed to the ice embryo if its closest OH is within the first solvation shell of the water molecules in the crystal,  $d_{\text{OH}} < 3.5$  Å (purple region in B). Panels C and D show equilibrium distributions of the OH of PVA and liquid water, respectively, around the constrained ice embryo consisting of 99 molecules at 275 K, plotted against the distance from center of mass of the ice embryo. The black dashed line indicates the Gibbs dividing surface between ice and water, where the surface excess of liquid water is zero (Supporting Information, part G).

prismatic plane. The change in ice–liquid surface tension due to the presence of PVA,  $\Delta\gamma$  (Supporting Information, part G) is positive and very small, approximately 0.04 mJ m<sup>-2</sup>. This would result in a small, unfavorable, +0.5% change in the free energy barrier, with minute impact on the freezing temperature. We conclude that the promotion of homogeneous nucleation by PVA is not due to a decrease in the cost of the ice–liquid interface.

The analysis above suggests that PVA increases the freezing temperature of ice through an increase in the water activity  $a_w$  of the PVA solutions. The water activity is a measure of the difference in chemical potential of pure water,  $\mu_{\text{liquid}}^0$  and water in the solution,  $\mu_{\text{liquid}} = \mu_{\text{liquid}}^0 + RT \ln(a_w)$ . We compute  $a_w$  of PVA solutions through grand canonical molecular dynamics simulations (Supporting Information, part H),<sup>32,33</sup> which has been validated for the calculation of vapor pressures of bulk water,<sup>33</sup> nanodroplets,<sup>34</sup> capillary condensation in nanopores,<sup>35</sup> and the activity coefficients of electrolytes.<sup>32,36</sup> Figure 1b shows that the concentration dependence of the water activity of PVA solutions mirrors the one of  $\Delta T_x$ :  $a_w$  first increases upon addition of up to about 0.6 wt% PVA, driven by repulsive non-ideal interactions with the hydrophobic moieties of PVA (Supporting Information, part I), and then decreases mostly driven by entropic, colligative effects. The increase in  $a_w$  is up to 1.1–1.7%, which corresponds to a decrease of the nucleation barrier  $\Delta G^*$  from 3 to 4.6%. We conclude that small concentrations of PVA promote the homogeneous nucleation of ice through destabilization of the liquid phase.

Koop et al. demonstrated that the homogeneous nucleation temperature of ice in solutions is a function of the water activity, and independent of the nature of the solute.<sup>13</sup> This was validated by studies of ice nucleation in solutions of salts, organic molecules and polymers, all of which evinced a decrease

in freezing temperature correlated to a decrease in water activity.<sup>13,37,38</sup> Likewise,  $\Delta T_x(a_w)$  was previously parametrized from simulations with the mW water model and a salt.<sup>14</sup> In all previous cases, the addition of solutes was found to decrease  $a_w$  and depress ice nucleation. Here, we show that the increase in freezing temperature of PVA solutions follows the same relation  $\Delta T_x(a_w)$  derived from the salt solutions, extrapolated to  $a_w > 1$  (Figure 3). The transferability of  $\Delta T_x(a_w)$  across solutes



**Figure 3.** Ice freezing efficiency increases with the water activity of the solution. Symbols represent the simulation results for PVA solutions of monomer (circles), 5-mer (diamonds), and 10-mer (triangles). The solid lines correspond to the extrapolations of the empirical equations for  $\Delta T_x(a_w)$  obtained for  $a_w < 1$  from experiments of water solutions<sup>13</sup> (red line) and simulations of mW solutions<sup>14</sup> (blue line). Supporting Information, Figure S6, extends the empirical relations derived from experiments and simulations to higher water activity.

implies that these do not affect the ice–liquid surface tension of the ice embryo, consistent with our analysis for PVA. There is remarkable agreement between the  $\Delta T_x(a_w)$  predictions using the parametrization based on experiments<sup>13</sup> and simulations with mW<sup>14</sup> (Figure 3 and Supporting Information, Figure S6). This indicates that simulations with mW can accurately predict the effect of water activity on the freezing efficiency of solutions.

The present study demonstrates, for the first time, that ice nucleation can be promoted homogeneously through an increase of water activity, i.e., by further destabilizing the metastable liquid phase. Dilute solutions of other molecules that present hydrophobic and hydrophilic groups could, as PVA, also increase the rate of homogeneous ice nucleation. However, this effect alone might be insufficient to explain the high ice freezing efficiency measured for pollen:<sup>18,19</sup> Supporting Information, Figure S6, indicates that  $a_w = 1.12$  would be required for  $\Delta T_x = 15$  K. Solutions with such strongly non-ideal repulsive interactions may rather phase-segregate. A reduction of the ice–liquid surface tension would be required to achieve the ice nucleation potency of pollen.

We demonstrate that the prevailing paradigm for explaining promotion of ice nucleation should be expanded to include enhancement of nucleation rates through homogeneous mechanisms. Recent theoretical<sup>29,30</sup> and computational<sup>30,31,39</sup> studies of crystallization conclude that additives that reduce the surface tension of the crystal nucleus must promote homogeneous nucleation. The present study proves that additives can also promote homogeneous crystallization by destabilizing the liquid phase. This mode of action, here explored for the nucleation of ice, could also be relevant for the nucleation of clathrate hydrates of hydrophobic guests, which may also destabilize liquid water. More generally, the design of

additives that destabilize the mother phase can provide a new handle for the enhancement of nucleation rates through a homogeneous mechanism.

## ■ ASSOCIATED CONTENT

### 📄 Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.7b09549.

Models and methods, water activity coefficients, discussion of effect of hydrophobicity, and prediction of the effect of water activity on the homogeneous freezing temperature using empirical relations and classical nucleation theory (PDF)

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### Notes

The authors declare no competing financial interest.

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