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<https://doi.org/10.1038/s42005-020-0303-9>

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Freezing water at constant volume and under confinement

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Water expands upon freezing. What happens when water is cooled below 0 °C in an undeformable, constant-volume container? This is a fundamental question in materials thermodynamics, and is also relevant in biological, geological, and technological applications in which ice forms under nano-, meso-, or macroscale confinement. Here, we analyze the phase-equilibria and kinetic behaviors of water and ice-1h in an isochoric (constant-volume) system. By making use of the Helmholtz potential $F(\text{temperature, volume})$, in contrast to the Gibbs potential $G(\text{temperature, pressure})$, we demonstrate significant changes in phase behavior when the specific volume of the container is constrained below that of ice-1h. We construct a T - V (temperature–volume) phase diagram for water and ice that features a broad two-phase equilibrium region, and we further derive an isochoric nucleation theory that reveals the existence of a critical confinement volume, on the order of microns, below which ice-1h is kinetically prohibited from forming.

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Water is essential to nearly all biological, climatological, and industrial functions on planet Earth. Of enduring scientific interest are the various phase transitions undergone by water, both within the liquid state and between its numerous condensed phases^{1–6}. One phase transformation of emerging importance is the freezing of water in an undeformable, constant-volume container. This transformation has been identified in the bioengineering community as a compelling potential route to the ice-free cryopreservation of organs and tissues^{7–10}, is being investigated for low-temperature thermal phase-change energy storage¹¹, and may aid in describing fundamental atmospheric and climatological processes¹². Recent molecular dynamics simulations and physical observations have suggested that confinement of water in various meso- and nanoscale constrained-volume contexts can limit ice formation^{12–20}, and recent experimental work has also demonstrated that macroscopic confinement in isochoric (constant-volume) systems also restricts ice growth²¹ and alters kinetic behavior^{11,22}. Given this recent interest, a robust, multi-scale theoretical treatment of the thermodynamics and kinetics of freezing water in isochoric (constant-volume) systems is needed.

The phase transitions of water are generally described using natural variables of temperature T and pressure P , which correspond to the Gibbs thermodynamic potential $G(T, P)$. Consider the freezing of pure water in an undeformable container (i.e., at constant volume). Water expands upon freezing to ice-1h, and should the container have a lower specific volume than that of ice-1h, the contents of the system will never be able to freeze entirely, resulting in a two-phase water-ice equilibrium. The standard T – P phase diagram for pure water includes only single-phase regions, so this anticipated two-phase equilibrium of water and ice under isochoric conditions cannot be quantified in a straightforward fashion from the traditional water phase diagram. By retaining pressure as a natural variable, one is forced to analyze this two-phase equilibrium as occurring between two distinct entities—the ice and the water—and one must solve for mechanical equilibrium by balancing the bulk moduli of the solid and liquid phases against the hydrostatic pressure that emerges as the ice forms and expands²¹. While the equilibrium states of the system can indeed be predicted using this approach, the mathematical formulation proves awkward, and must be continuously re-solved as temperature and pressure are altered.

While the Gibbs potential is appropriate under most physical contexts, it is only one of many possible Legendre transforms of the internal energy, $U(S, V)$, which has natural variables of entropy S and volume V . Should a situation arise in which the Gibbs free energy ceases to be convenient, it should be replaced in favor of a better-suited potential. For the case of freezing under isochoric conditions, a more elegant thermodynamic approach is to exchange pressure as a natural variable in favor of volume, thereby leveraging the Helmholtz thermodynamic potential for this analysis. In this description, the thermodynamic boundary conditions are reframed around the containing vessel, describing the entire two-phase water-ice system at once.

Herein, we use the Helmholtz free energy to derive the equilibrium phase behaviors of water held in a constant-volume system at subzero temperatures. Our derivation yields the T – V phase diagram for water and ice, featuring a prominent two-phase equilibrium region, analogous to those found in binary eutectic phase diagrams. We also derive a classical nucleation theory for ice under isochoric conditions, which reveals fundamental differences between the kinetics of freezing under constant volume versus constant pressure. In isochoric systems, we reveal the existence of a critical absolute volume threshold (on the order of microns), under which nucleation of ice becomes kinetically prohibited. Our analyses here provide a classical

foundation from which to analyze the thermodynamics and kinetics of freezing in isochoric systems, establishing context to interpret the phenomenology of water and ice under these important boundary conditions.

Results

T – V phase diagram based on the Helmholtz free energy. Phase diagrams are constructed by a projection of the lowest free-energy phases onto axes of the natural thermodynamic variables. The choice of natural variables governs the geometry of the free-energy surfaces, and thereby the phase-coexistence behavior in the resulting phase diagram.

In order for a homogeneous single-phase substance to be stable, its internal energy surface, U , must be positive definite; $\partial^2 U / \partial X^2 > 0$, where X are the extensive thermodynamic variables $X = S$ (entropy), V (volume), N (particle number), and so on. When it is not convenient to use an extensive natural variable, a new thermodynamic potential can be constructed with intensive natural variables, $Y = T$ (temperature), P (pressure), μ (chemical potential), and so on, by a Legendre transformation of the extensive variable with respect to its intensive conjugate, $U - (\partial U / \partial X)X = U - YX$ ²³. Following a Legendre transformation, the curvature of the free-energy surface becomes concave down in the corresponding intensive thermodynamic variable(s)²⁴, or otherwise retains the convex curvature of U in the extensive variable(s)²⁵.

The Gibbs potential has intensive natural variables of temperature and pressure, and thus Gibbs free-energy surfaces are concave down in both T and P . Projection of the lowest Gibbs free-energy phase onto the temperature and pressure axes recovers the standard T – P phase diagram, as shown for H_2O in Fig. 1a, constructed using thermodynamic data from the International Association for the Properties of Water and Steam (IAPWS)^{26,27}. For a single-component system like H_2O , phase coexistence is governed by the intersection of these concave-down free-energy surfaces, resulting in a one-dimensional (1D) phase-coexistence line in the T – P plane.

In an isochoric system however, the natural variables should be temperature and volume, rather than pressure, which corresponds to the Helmholtz thermodynamic potential, F . We can construct $F(T, V)$ for water and ice-1h by a Legendre transform of Gibbs free-energy data as:

$$F(T, V) = G(T, P(V)) - PV. \quad (1)$$

Because V is extensive and T is intensive, F is convex in volume ($\partial^2 F / \partial V^2 > 0$), and concave down in temperature.

The convexity of the Helmholtz free energy as a function of volume fundamentally changes the nature of phase coexistence in the T – V space. The lowest free-energy envelope now includes tangent lines between the convex $F_{\text{water}}(V)$ and $F_{\text{ice}}(V)$ curves, which signify a two-dimensional two-phase equilibrium region, as opposed to a 1D phase-coexistence line. Gibbs called these tangent lines “Lines of Dissipated Energy,”²⁸ along which a single-phase homogeneous substance can reduce its free energy by forming a heterogeneous mixture of two phases. These tangent lines are analogous to those used in the convex hull construction of binary eutectic phase diagrams, which are constructed from the Gibbs free energy, $G(T, x)$ ²⁹. The convex hull construction can be applied to both $G(x)$ and $F(V)$ because both composition (x) and volume (V) are extensive variables, and thus their free-energy surfaces are convex.

By projecting the lowest-energy convex hull formed by the F_{water} and F_{ice} surfaces in Fig. 1b, we construct the T – V phase diagram for water, shown in Fig. 1c. To the best of our knowledge, this phase diagram has not been reported previously

Fig. 1 Free-energy surfaces of water and ice-1h under different thermodynamic boundary conditions. **a** Gibbs free-energy surfaces of water and ice-1h in a system with natural variables temperature and pressure. The projection of the lowest free-energy phase onto the temperature–pressure plane gives the standard T - P (temperature–pressure) phase diagram for water. **b** Helmholtz free-energy surfaces of water and ice-1h in a system with natural variables temperature and specific volume. Common tangents between the phases define the range over which a two-phase mixture in equilibrium will produce the lowest system free energy. The slope of the common tangent, $\partial F/\partial V$, gives the equilibrium pressure of the system. **c** T - V (temperature–volume) phase diagram for water and ice-1h. **d** Phase fraction of ice-1h as a function of temperature at various system-specific volumes in an isochoric system.

in the literature. The T - V phase diagram of water features a two-phase equilibrium region, where the equilibrium phase fraction can be solved using the Lever rule, in the same manner employed for T - x binary eutectic phase diagrams²⁹. For the reader's reference, the phase fraction as a function of temperature and system-specific volume is shown in Fig. 1d.

At a given temperature, the slope of these tangent lines, $(\partial F/\partial V)_T$, provides the pressure that the two-phase mixture exerts onto the constant-volume container. We mark these pressure isoclines on the T - V phase diagram in Fig. 1c. Note that in the equilibrium two-phase region, the tangent lines connect the water and ice-1h free-energy curves, implying that water and ice experience the same pressure, which is indeed a requirement for mechanical equilibrium.

Physical motivations for an isochoric nucleation theory. The equilibrium T - V phase diagram produced in Fig. 1c is dependent on the specific volume (v), as the phase-coexistence regions

define thermodynamic equilibrium regardless of the amount of material present. We next show that the kinetics of nucleation in isochoric systems are additionally dependent on the absolute volume (V) of the system container, and we leverage both dependencies to derive an isochoric theory of ice nucleation.

Consider the process of isochoric freezing, in which a closed, fixed-volume container filled with pure water is brought below 0°C to a metastable supercooled state (Fig. 2a). Before ice nucleates, the supercooled water will experience some pressure P_1 , which is given by the slope of the tangent line $\partial F_{\text{water}}/\partial v$ at the specific volume of the container, as marked on Fig. 2b. When ice-1h nucleates, the nascent nucleus will exert further pressure on the water and the container, and because the total system volume cannot change, the container will exert equal and opposite pressure back on both the water and the ice nucleus (Fig. 2c). This reduces the specific volume of ice and water, and increases their specific free energy according to the $F(v)$ curves shown in Fig. 2b. We name the energy required for this pressurization of the system and densification of the initial liquid

Fig. 2 Conceptual formulation of the nucleation process in an isochoric system. **a** The initial state of the system, in which the contents are entirely liquid. In this state, the absolute volume V and specific volume v of the system will equal that of the water phase by definition, as no ice is present. **b** Parallel tangent construction. For an emergent ice nucleus of absolute volume V_{ice} in a system of absolute volume V_{system} , the specific volume and free energy of each phase can be found by identifying the points on each curve that will satisfy conservation of system mass, absolute volume, and specific volume, while producing tangent lines $(\partial F/\partial v)$ that are parallel to one another, indicating continuity of pressure P throughout the system. At equilibrium, the tangent lines of the two phases will become colinear and the system will experience the equilibrium pressure $P_{\text{equilibrium}}$. **c** A second state of the system, in which the finite mass and volume of the system are now split between water and ice phases possessing different absolute volumes ($V_{\text{ice}}, V_{\text{water}}$) and specific volumes ($v_{\text{ice}}, v_{\text{water}}$). The pressure within the system increases to $P_2 > P_1$ due to the expansion of the ice nucleus. **d** Statement of the conservation relations governing the system.

phase the “isochoric growth penalty,” which can be interpreted as an energetic penalty that the solid phase must pay in order to grow within a system of constrained absolute and specific volume.

Intuitively, the magnitude of this penalty must vary with the absolute volume of the system; growth of a single ice nucleus confined in an ocean will cause no appreciable effect, but growth of the same nucleus in a nanoscale container may compress the remaining water significantly.

The pressure within the system is therefore a function of the relative phase fraction of ice that has grown. Because water and ice remain in constant mechanical equilibrium, the pressure experienced by both phases will be equal. Recalling that the pressure within a given phase at a given specific volume is described by the slope of the line tangent to its $F(v)$ curve at that volume, this physical constraint can be illustrated by a “parallel tangent construction” as shown in Fig. 2b, whereby the specific volumes and energies of each phase for a given phase fraction of ice are identified by the points on the $F(v)$ curves for water and ice that yield parallel tangents between the phases.

The use of this parallel tangent construction to track continuity of pressure between phases is analogous to the tangent construction originally used by Gibbs to describe continuity of chemical potential between phases in binary systems at constant temperature and pressure³⁰. During the growth of ice in an isochoric system (and the accompanying densification of both phases), the tangent lines will remain parallel while gradually increasing in slope until the two lines merge and form the

common tangent, which marks the two-phase equilibrium state shown in Fig. 1 and provides the equilibrium pressure $P_{\text{equilibrium}}$.

Mathematical formulation of the system. In the preceding section, it was established that in an isochoric system, the specific free energies of water and ice do not remain constant during the process of nucleation and growth, instead shifting dynamically along their respective $F(v)|_T$ curves according to the parallel tangent construction. In order to mathematically describe this behavior, an expression relating the specific volumes (and thus free energies) of the phases as a function of ice nucleus growth is needed.

Given a closed isochoric system, mass and volume must be conserved

$$m_{\text{system}} = m_{\text{ice}} + m_{\text{water}}, \quad (2)$$

$$V_{\text{system}} = V_{\text{ice}} + V_{\text{water}}, \quad (3)$$

which further implies conservation of specific volume. However, we note that the conservation of specific volume does not take the form $v_{\text{system}} = v_{\text{ice}} + v_{\text{water}}$ as might be expected, because the system-specific volume is not itself an inherently conserved quantity; it is instead conserved as a simple mathematical consequence of the conservation of the system mass and volume,

and is thus as:

$$v_{\text{system}} = \frac{V_{\text{system}}}{m_{\text{system}}} = \frac{V_{\text{ice}} + V_{\text{water}}}{m_{\text{ice}} + m_{\text{water}}}. \quad (4)$$

The requirement of equal pressure throughout the system provides the final constraint. Leveraging the parallel tangent logic, the pressures of ice and water during the non-equilibrium nucleation process can be tracked along the F - v curves by their derivatives:

$$-\left(\frac{dF_{\text{water}}}{dv}\right)|_{v_{\text{water}}} = -\left(\frac{dF_{\text{ice}}}{dv}\right)|_{v_{\text{ice}}}. \quad (5)$$

In the Supplementary Note 1, we use these four constraints to determine the specific volumes of each phase as a function of nucleus volume ($v_{\text{water}}(V_{\text{ice}})$, $v_{\text{water}}(V_{\text{ice}})$) along the reaction coordinate of the nucleation process. These specific volumes thereby give the specific free energy for both water and ice, $F_{\text{water}}(v_{\text{water}}(V_{\text{ice}}))$, $F_{\text{ice}}(v_{\text{ice}}(V_{\text{ice}}))$ as a function of the ice nucleus volume, enabling derivation of the nucleation barrier.

Derivation of an isochoric nucleation barrier. We consider now two states that the isochoric system may occupy (Fig. 2a, c), subject to the established physical constraints (Fig. 2d). For clarity, we will describe the total free energy of the system with the variable $\emptyset$, and the specific Helmholtz free energies of each phase as F_{water} and F_{ice} . The subscripts 1 and 2 will be used to denote the values of parameters in States 1 and 2.

In State 1, the entire system is in the liquid phase, and its free energy is thus given by:

$$\emptyset_1 = F_{\text{water}_1} m_{\text{system}}, \quad (6)$$

in which $F_{\text{water}_1} = F_{\text{water}}(v_{\text{water}_1} = v_{\text{system}})$. In State 2, an ice-1h nucleus of absolute volume V_{ice} has formed, dividing the system into two phases with specific volumes $v_{\text{water}}(V_{\text{ice}})$ and $v_{\text{ice}}(V_{\text{ice}})$. Defining the ice phase fraction of the system as

$$f = \frac{m_{\text{ice}}}{m_{\text{system}}} = \frac{V_{\text{ice}} v_{\text{system}}}{v_{\text{ice}} V_{\text{system}}} \quad (7)$$

and incorporating a standard interfacial free-energy term γ , which scales with the surface area of the ice nucleus A_{ice} , the total free energy of State 2 is given by:

$$\emptyset_2 = \emptyset_1 + \Delta\emptyset = [F_{\text{water}_2} \times (1 - f) + F_{\text{ice}_2} \times f] m_{\text{system}} + \gamma A_{\text{ice}}, \quad (8)$$

in which $F_{\text{water}_2} = F_{\text{water}}(v_{\text{water}_2} = v_{\text{water}}(V_{\text{ice}}))$ and $F_{\text{ice}_2} = F_{\text{ice}}(v_{\text{ice}_2} = v_{\text{ice}}(V_{\text{ice}}))$. Rearranging these equations and grouping specific free-energy terms by phase, the free-energy change $\Delta\emptyset$ upon formation of a nucleus is given by:

$$\Delta\emptyset = \emptyset_2 - \emptyset_1 = [(F_{\text{water}_2} - F_{\text{water}_1}) + (F_{\text{ice}_2} - F_{\text{water}_2})f] m_{\text{system}} + \gamma A_{\text{ice}}. \quad (9)$$

The two energy difference terms in Eq. (9) have distinct and meaningful physical significance. $(F_{\text{water}_2} - F_{\text{water}_1})$ describes the “isochoric growth penalty,” or the energy required to pressurize the system and densify the water phase, which the emergent ice nucleus must provide in order to grow. This term will always be positive. $(F_{\text{ice}_2} - F_{\text{water}_2})$, which will always be negative, gives the bulk free-energy difference between the phases at their present specific volumes, which is weighted by the phase fraction f in order to capture the two-phase nature of the equilibrium system.

The free-energy change accompanying the formation of an ice nucleus in an isochoric system can thus be reduced to the

following:

$$\Delta\emptyset = [\Delta F_{\text{isochoric growth}} + \Delta F_{\text{bulk}} f] m_{\text{system}} + \gamma A_{\text{ice}}. \quad (10)$$

The interfacial and bulk free-energy terms in Eq. (10) are roughly analogous to those found in classical nucleation theory; the former will scale with the surface area of the nucleus in the positive direction, the latter with its volume or mass in the negative. However, it is crucial to note that within the Gibbs formulation, the bulk free-energy difference between water and ice is considered constant—whereas in an isochoric system, it varies as a function of the ice phase fraction, decreasing in magnitude as the ice grows in a reflection of the fact that the ultimate thermodynamic destination of the system is a state of two-phase water-ice equilibrium, not complete freezing.

The isochoric growth penalty term is unique to systems of constrained volume, and will be shown next to fundamentally alter the nucleation behavior.

Kinetic effects of isochoric confinement. In Fig. 3a, we plot the total free-energy change $\Delta\emptyset$ alongside the three separate energy contributions; the interfacial energy, the bulk energy, and the isochoric growth penalty. Our calculations for Fig. 3a describe a single ice-1h nucleus of spherical geometry in a system of absolute volume $V_s \sim 2 \times 10^{-22} \text{ m}^3$ at a temperature of -4.15°C , with an assumed interfacial free-energy relation³¹ of $\gamma = (28.0 + 0.25T) \text{ mJ m}^{-2}$ (additional parameters available in Supplementary Note 2). Figure 3b features additional $\Delta\emptyset$ curves for the same temperature, but varying absolute system volumes V_s . These plots reveal a fundamental difference between ice formation at constant volume and ice formation at constant pressure: in the classical Gibbs formulation, the $\Delta G(\text{radius})$ curve features one critical point, while in an isochoric system there are two critical points.

Classically, the critical point of the free-energy curve is a maximum and defines the nucleation barrier, or the energetic barrier after which continued ice growth will lower the free energy of the system indefinitely until the entirety has changed phase. In the isochoric case however, ice growth is not indefinite—it must cease upon reaching the equilibrium phase fraction, in accordance with the T - V phase diagram (Fig. 1c, d). This limitation is captured kinetically by the isochoric growth term, and thus the $\Delta\emptyset$ curves can possess two critical points: the first a maximum at which the bulk driving force for phase transition overcomes the penalty of forming a new phase interface, and the second a minimum at which the isochoric growth energy overcomes the bulk driving force.

Importantly, because the isochoric growth term is a function of the absolute system volume (scaling as $V_{\text{ice}}/V_{\text{sys}}$), its contribution vanishes at the infinite volume limit, consistent with intuition. In this case, which we label the Gibbs limit in Fig. 3b, the $\Delta\emptyset$ free-energy curve will be identical to that found using the classical Gibbs formulation, featuring only an initial maximum.

Conversely, as the system volume decreases the relative contribution of the isochoric growth term increases, both introducing the second critical point (corresponding to the phase fraction limitation) and increasing the critical radius of the nucleation barrier. This increase is captured in Fig. 3c, given as a function of absolute system volume for various sub-freezing temperatures. Note that at temperatures close to the freezing point, the effect of the volume constraint on isochoric nucleation can be significant even under relatively large system volumes—on the order of microns.

Our derivation further reveals the existence of a discrete absolute system volume, which we term the critical confinement volume, below which the second critical point will reach an energy equal to the first, erasing the inflection point between

Fig. 3 Nucleation kinetics in isochoric systems. **a** Total free-energy change $\Delta\Phi$ accompanying the formation of a spherical ice-1h nucleus as a function of radius. The interfacial, isochoric growth, and bulk free-energy components contributing to the total are plotted independently. **b** $\Delta\Phi$ curves for varying absolute system volumes. The Gibbs limit gives the system behavior at the limit of infinite system volume, and the Helmholtz limit at the critical system volume at which the free-energy curve begins to increase monotonically. **c** Critical radius as a function of system volume for various temperatures, with critical system volumes marked. **d** Phase diagram mapping the critical system volume as a function of temperature. In the kinetically dominated regime, all $\Delta\Phi$ curves will be monotonically increasing, and thus no kinetic pathway to nucleation will exist.

them and yielding a nucleus free-energy curve that increases monotonically with radius. A representative free-energy curve at this absolute volume threshold is labeled as the Helmholtz limit in Fig. 3b. These critical confinement volumes are also marked on the critical radius curves in Fig. 3c, indicating the system volume at which the critical radius for nucleation would become infinite. These critical system volumes are then plotted independently against temperature in Fig. 3d, resulting in a “kinetic phase diagram” for freezing water under confined volumes. Our kinetic phase diagram reveals a unique implication for systems of constant volume: there exists a volumetric regime in which nucleation of ice-1h from the supercooled liquid state is kinetically impossible.

Notably, the existence of ice within this regime is not thermodynamically prohibited—comparing Fig. 3c with Fig. 1d

it can be seen that these critical ice nucleus volumes are orders of magnitude smaller than the equilibrium phase fraction limit. These results indicate that ice could theoretically exist at these system volumes (e.g., if an ice crystal was artificially seeded in the system and the volume was then constrained), but that supercooled water simply has no kinetic pathway to freezing in a sufficiently confined isochoric system.

Discussion

Many recent studies, based principally on molecular dynamics simulations or experimental observations, have suggested that confinement of water at small volumes limits ice formation^{12–19}. This effect has been variously described as a depression of the equilibrium melting point, a purely probabilistic effect, a result of complex hydrogen or polar interactions, and so on, and has been

reported nigh exclusively in systems with geometric constraints on the order of single nanometers^{12,13,15,18}. Our results corroborate these previous findings of confinement-based freeze inhibition, but also suggest that this behavior has more fundamental origins, and can in fact occur at characteristic length scales up to hundreds of nanometers (Fig. 3c, d). By making an appropriate choice of thermodynamic boundary conditions, in this case constant volume vs. constant pressure, we are able to infer this effect directly from high-level thermodynamic and kinetic analysis, without resorting to atomistic arguments. Furthermore, because volume itself is incorporated as a natural variable within our model, its applicability is not limited to a single system scale, and can instead be applied continuously from the nanoscale to the macroscale.

Other recent works have leveraged similarly unconventional thermodynamic boundary conditions to reveal previously inaccessible thermodynamic and kinetic information³², using free-energy expressions that can include forms of thermodynamic work beyond temperature and pressure—including surface work (size, adsorption)^{33,34}, elastic work (epitaxy, stress-strain)^{35,36}, electromagnetic work (electrical polarization, magnetic polarization)^{37,38}, chemical work (such as compositional variation, precursor activity)^{39,40}, and more. These findings as a whole suggest that the Gibbs free energy alone is unable to capture the wide range of thermodynamic equilibria and kinetic behaviors encountered in materials systems in the diverse modern technological environment.

The kinetic analysis provided herein only describes the formation of the first ice-1h nucleus in an infinitely rigid container (e.g., a container of truly constant volume), and is subject to further simplifying assumptions, including the assumptions of spherical nuclei and that the first nucleus to form from supercooled water will be hexagonal and not cubic in structure⁴¹. A standard form of the temperature-dependent interfacial free energy is also assumed³¹, although this relation may, in fact, vary in as-of-yet undetermined ways under the described isochoric conditions. Despite these simplifying assumptions, the conceptual insights revealed herein provide the foundations for a wide range of further study, and outline the limiting energetic behaviors of ice nuclei in isochoric systems. We anticipate that in systems that deviate from the conditions and assumptions described herein, ice nucleation kinetics will lie somewhere between the identified Gibbs and Helmholtz limits. For example, systems of nanoscale volume found in biological matter may experience a reduced isochoric growth penalty due to the finite rigidity of the container, but the excess energy required to grow in a constrained volume is still a physically pertinent feature. Conversely, within the thick-walled metallic containers employed in cryopreservation, the assumption of infinite rigidity is likely acceptable, but the macroscopic volumes are too large to appreciate the effect of a single ice nucleus. The continuity of pressure within the system remains however, forcing every growing nucleus to interact with every other via pressure, and thus some macroscopic effect on the kinetics may still be observed. This may have useful implications, such as enhanced or high-stability supercooling due to heightened nucleation barriers, and ensemble-level analysis built from the single-nucleus isochoric nucleation theory should be studied in the future.

We further anticipate that additional analytical study of water under alternative thermodynamic boundary conditions (e.g., constant electric field, polarization density, etc.) may yield further profound results currently inaccessible under the constant-pressure Gibbs formulation. It should also be noted that the isochoric nucleation analysis developed herein is not exclusive to the water/ice-1h transition, but can also be applied to any other

confined system in which a phase transformation results in a higher molar volume, such as in elemental gallium.

Finally, the ability to hold liquid water and ice in equilibrium at controlled and predictable phase fractions tens of degrees below the atmospheric freezing point presents a transformative prospect in the decade-long effort to cryopreserve biological matter (including full organs for transplantation) with neither the threat of uncontrolled ice formation nor the requirement of toxic freeze-combatting chemical agents. Early experimental validation of this notion has been realized recently by groups employing high-strength metallic containers as constant-volume vessels^{8–10}, and we anticipate that the thermodynamically complete outline of the water/ice-1h equilibrium phase space will accelerate experimental progress in this field.

Data availability

All data available from the corresponding authors upon reasonable request.

Received: 13 September 2019; Accepted: 30 January 2020;

Published online: 21 February 2020

References

- Tulk, C. A., Molaison, J. J., Makhluף, A. R., Manning, C. E. & Klug, D. D. Absence of amorphous forms when ice is compressed at low temperature. *Nature*. <https://doi.org/10.1038/s41586-019-1204-5> (2019).
- Fitzner, M., Sosso, G. C., Cox, S. J. & Michaelides, A. Ice is born in low-mobility regions of supercooled liquid water. *Proc. Natl Acad. Sci. USA*. <https://doi.org/10.1073/pnas.1817135116> (2019).
- Stern, J. N., Seidl-Nigisch, M. & Loerting, T. Evidence for high-density liquid water between 0.1 and 0.3 GPa near 150 K. *Proc. Natl Acad. Sci. USA*. <https://doi.org/10.1073/pnas.1819832116> (2019).
- Zhu, W. et al. Room temperature electrofreezing of water yields a missing dense ice phase in the phase diagram. *Nat. Commun.* <https://doi.org/10.1038/s41467-019-09950-z> (2019).
- Kim, Y.-J., Lee, Y.-H., Lee, S., Nada, H. & Lee, G. W. Shock growth of ice crystal near equilibrium melting pressure under dynamic compression. *Proc. Natl Acad. Sci. USA* <https://doi.org/10.1073/pnas.1818122116> (2019).
- Cheng, B., Engel, E. A., Behler, J., Dellago, C. & Ceriotti, M. Ab initio thermodynamics of liquid and solid water. *Proc. Natl Acad. Sci. USA*. <https://doi.org/10.1073/pnas.1815117116> (2019).
- Taylor, M. J., Weegman, B. P., Baicu, S. C. & Giwa, S. E. New approaches to cryopreservation of cells, tissues, and organs. *Transfus. Med. Hemother.* <https://doi.org/10.1159/000499453> (2019).
- Powell-Palm, M. J., Zhang, Y., Aruda, J. & Rubinsky, B. Isochoric conditions enable high subfreezing temperature pancreatic islet preservation without osmotic cryoprotective agents. *Cryobiology*. <https://doi.org/10.1016/j.cryobiol.2019.01.003> (2019).
- Wan, L. et al. Preservation of rat hearts in subfreezing temperature isochoric conditions to -8°C and 78 MPa. *Biochem. Biophys. Res. Commun.* <https://doi.org/10.1016/j.bbrc.2018.01.140> (2018).
- Mikus, H. et al. The nematode *Caenorhabditis elegans* survives subfreezing temperatures in an isochoric system. *Biochem. Biophys. Res. Commun.* **477**, 401–405 (2016).
- Powell-Palm, M. J. & Rubinsky, B. A shift from the isobaric to the isochoric thermodynamic state can reduce energy consumption and augment temperature stability in frozen food storage. *J. Food Eng.* <https://doi.org/10.1016/j.jfoodeng.2019.02.001> (2019).
- David, R. O. et al. Pore condensation and freezing is responsible for ice formation below water saturation for porous particles. *Proc. Natl Acad. Sci. USA*. <https://doi.org/10.1073/pnas.1813647116> (2019).
- Salvati Manni, L. et al. Soft biomimetic nanoconfinement promotes amorphous water over ice. *Nat. Nanotechnol.* <https://doi.org/10.1038/s41565-019-0415-0> (2019).
- Levinger, N. E. Water in confinement. *Science* (80-). <https://doi.org/10.1126/science.1079322> (2002).
- Mashl, R. J., Joseph, S., Aluru, N. R. & Jakobsson, E. Anomalous immobilized water: a new water phase induced by confinement in nanotubes. *Nano Lett.* <https://doi.org/10.1021/nl0340226> (2003).
- Rasaiah, J. C., Garde, S. & Hummer, G. Water in nonpolar confinement: from nanotubes to proteins and beyond. *Annu. Rev. Phys. Chem.* <https://doi.org/10.1146/annurev.physchem.59.032607.093815> (2007).

17. Alba-Simionesco, C. et al. Effects of confinement on freezing and melting. *J. Phys. Condens. Matter*. <https://doi.org/10.1088/0953-8984/18/6/R01> (2006).
18. Schmidt, R., Walther Hansen, E., Stacker, M., Akporiaye, D. & Henrik Ellestad, O. Pore size determination of MCM-41 mesoporous materials by means of NMR spectroscopy, N₂ adsorption: a preliminary study. *J. Am. Chem. Soc.* <https://doi.org/10.1021/ja00119a021> (1995).
19. Zuber, B. & Marchand, J. Predicting the volume instability of hydrated cement systems upon freezing using poro-mechanics and local phase equilibria. *Mater. Struct. Constr.* <https://doi.org/10.1617/14165> (2004).
20. De Luca, S. et al. Effects of confinement on the dielectric response of water extends up to mesoscale dimensions. *Langmuir*. <https://doi.org/10.1021/acs.langmuir.6b00791> (2016).
21. Rubinsky, B., Perez, P. A. & Carlson, M. E. The thermodynamic principles of isochoric cryopreservation. *Cryobiology*. <https://doi.org/10.1016/j.cryobiol.2004.12.002> (2005).
22. Zhang, Y. et al. Isochoric vitrification: an experimental study to establish proof of concept. *Cryobiology*. <https://doi.org/10.1016/j.cryobiol.2018.06.005> (2018).
23. Alberty, R. A. Use of Legendre transforms in chemical thermodynamics. *Pure Appl. Chem.* <https://doi.org/10.1351/pac200173081349> (2001).
24. Zia, R. K. P., Redish, E. F. & McKay, S. R. Making sense of the Legendre transform. *Am. J. Phys.* <https://doi.org/10.1119/1.3119512> (2009).
25. Callen, H. B. Thermodynamics and an introduction to thermostatistics 2nd edn. *Am. J. Phys.* **66**, 164 (1998).
26. International Association for the Properties of Water and Steam. *Guideline on Thermodynamic Properties of Supercooled Water* (IAPWS, 2015). <http://www.iapws.org/relguide/IAPWS95-2018.pdf>.
27. International Association for the Properties of Water and Steam. *Revised Release on the Equation of State 2006 for H₂O Ice Ih* (IAPWS, 2009). <http://www.iapws.org/relguide/Ice-Rev2009.pdf>.
28. Gibbs, J. W. On the equilibrium of heterogeneous substances. *Am. J. Sci.* **96**, 441–458 (1878).
29. Gordon, P. *Principles of Phase Diagrams in Materials Systems* (McGraw-Hill Inc., New York, 1968).
30. Clouet, E. in *ASM Handbook Vol. 22A, Fundamentals of Modeling for Metals Processing* (eds Furrer, D. U. & Semiatin, S. L.) 203–219 (ASM International, Materials Park, 2009).
31. Pruppacher, H. R. & Klett, J. D. *Microphysics of Clouds and Precipitation* (Kluwer Academic Publishers, Dordrecht, 1997).
32. Sun, W. et al. The thermodynamic scale of inorganic crystalline metastability. *Sci. Adv.* <https://doi.org/10.1126/sciadv.1600225> (2016).
33. Navrotsky, A. Nanoscale effects on thermodynamics and phase equilibria in oxide systems. *ChemPhysChem*. <https://doi.org/10.1002/cphc.201100129> (2011).
34. Sun, W., Kitchaev, D. A., Kramer, D. & Ceder, G. Non-equilibrium crystallization pathways of manganese oxides in aqueous solution. *Nat. Commun.* <https://doi.org/10.1038/s41467-019-08494-6> (2019).
35. Shi, T. et al. Shear-assisted formation of cation-disordered rocksalt NaMO₂ (M = Fe or Mn). *Chem. Mater.* <https://doi.org/10.1021/acs.chemmater.8b03490> (2018).
36. Ding, H. et al. Computational approach for epitaxial polymorph stabilization through substrate selection. *ACS Appl. Mater. Interfaces*. <https://doi.org/10.1021/acsami.6b01630> (2016).
37. Potticary, J. et al. An unforeseen polymorph of coronene by the application of magnetic fields during crystal growth. *Nat. Commun.* <https://doi.org/10.1038/ncomms11555> (2016).
38. Aber, J. E., Arnold, S., Garetz, B. A. & Myerson, A. S. Strong dc electric field applied to supersaturated aqueous glycine solution induces nucleation of the polymorph. *Phys. Rev. Lett.* <https://doi.org/10.1103/PhysRevLett.94.145503> (2005).
39. Kitchaev, D. A., Dacek, S. T., Sun, W. & Ceder, G. Thermodynamics of phase selection in MnO₂ framework structures through alkali intercalation and hydration. *J. Am. Chem. Soc.* <https://doi.org/10.1021/jacs.6b11301> (2017).
40. Sun, W. et al. Thermodynamic routes to novel metastable nitrogen-rich nitrides. *Chem. Mater.* <https://doi.org/10.1021/acs.chemmater.7b02399> (2017).
41. Hudait, A., Qiu, S., Lupi, L. & Molinero, V. Free energy contributions and structural characterization of stacking disordered ices. *Phys. Chem. Chem. Phys.* <https://doi.org/10.1039/c6cp00915h> (2016).

Acknowledgements

W.S. acknowledge funding provided by the US Department of Energy, Office of Science, Basic Energy Sciences, under contract no. UGA-0-41029-16/ER392000 as a part of the DOE Energy Frontier Research Center “Center for Next Generation of Materials Design: Incorporating Metastability.” M.J.P.-P. acknowledges funding provided by the USDA National Institute of Food and Agriculture, AFRI project proposal #2017-05031, Award #2018-67017-27826 “Preservation of food by isochoric (constant-volume) freezing”.

Author contributions

M.J.P.-P., B.R., and W.S. conceived the premise. M.J.P.-P. and W.S. developed the derivations. M.J.P.-P. performed the calculations. M.J.P.-P. and W.S. wrote the manuscript. B.R. revised the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary information is available for this paper at <https://doi.org/10.1038/s42005-020-0303-9>.

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