The Fascinating World of Polymer Clathrate Hydrates: An Overview

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Abstract

Polymer crystal hydrates (PCHs) are crystalline solids that form between a polymer and water. To date, only four distinct PCHs have been discovered – one of polyoxa- cyclobutane (POCB) and water, and three different polymorphs of polyethyleneimine (PEI) and water. These PCHs were first reported decades ago andhave fascinating structures and peculiar properties that make them potentially useful for a wide range of applications including refrigeration, proton conduction membranes, and desalination. This perspective revisits what is known about these compounds, categorizes their sim- ilarities and differences with other known compounds, and offers a perspective into future efforts to discover new PCHs to address technological needs for society.

The Fascinating World of Polymer Clathrate Hydrates: An Overview

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Abstract

Polymer crystal hydrates (PCHs) are crystalline solids that form between a polymer and water. To date, only four distinct PCHs have been discovered – one of polyoxacyclobutane (POCB) and water, and three different polymorphs of polyethyleneimine (PEI) and water. These PCHs were first reported decades ago andhave fascinating structures and peculiar properties that make them potentially useful for a wide range of applications including refrigeration, proton conduction membranes, and desalination. This perspective revisits what is known about these compounds, categorizes their similarities and differences with other known compounds, and offers a perspective into future efforts to discover new PCHs to address technological needs for society.

Introduction

In 1967, Tadokoro and coworkers reported that a crystal hydrate formed when high molecular weight polyoxacyclobutane (POCB) and water were combined,[1] while several crystal hydrates were reported between polyethyleneimine (PEI) and water in the early 1980s.[2,3] Apart from a relatively small number of studies,[4–9] polymer crystalline hydrates have received little attention in subsequent decades. We propose that these compounds be classified as "polymer crystal hydrates" (PCHs), which exhibit some similarities and some differences from traditional gas clathrate hydrates. This perspective aims to rekindle interest in PCHs that possess fascinating properties that would be potentially useful in a variety of applications.

We will first distinguish PCHs from other highly studied materials such as gas clathrate hydrates, polymer clathrates, and hydrogels. Gas clathrate hydrates consist of ice-like cages formed from water molecules that encapsulate guest molecules such as methane. These structures are naturally found in low temperature permafrost environments (e.g. temperatures below 2°C) and high pressure marine environments (at 500 to 2000 meters underwater).[10] Interest in their potential applications in refrigeration,[11] desalination,[12] and as organic solvents for pharmaceuticals[13] has made them the subject of extensive research for several decades.[14–16] Gas clathrate hydrates are classified as Type-I, Type-II, or Type-H clathrates depending on their water-cage structures.[17,18]

Polymers can also form clathrate structures with solvents besides water. For example, the δ-form of syndiotactic polystyrene (s-PS) forms a crystalline lattice that contains spaces in which a second, guest species can occupy.[19] This type of polymer clathrate has been found to form between s-PS and toluene or iodine.[20] Poly(ethylene oxide) (PEO) can also form a clathrate in the presence of urea.[21,22] In this case, urea forms a crystalline complex whereby linear PEO molecules occupy channels in the urea adduct. These complexes can have two modifications: a) a trigonal crystal structure and b) a hexagonal crystal structure formed upon melting and re-crystallization.[23] Numerous examples of such polymer-solvent molecular compounds have been reported.[24]

Lastly, hydrogels, like PCHs, are formed from a polymer and water. However, a distinguishing characteristic is that hydrogels are networks formed between one or more hydrophilic polymers and water. They are often categorized as either a) chemical hydrogels (permanent hydrogels) or b) physical hydrogels (reversible hydrogels). In chemical hydrogels, the crosslinking between polymers occurs through covalent bonds, resulting in strong, permanent junctions within the network. On the other hand, physical hydrogels crosslink via non-covalent interactions such as hydrogen bonding, hydrophobic interactions, crystallization of the polymer, and chain entanglement.[25] These polymer networks can be amorphous, semi-crystalline, crystalline, or hydrocolloid aggregates. Regardless of their structure, hydrogels can absorb solvating water molecules that reside in the amorphous regions of the network, and this uptake is not restricted to a well-defined ratio. Under equilibrium swelling conditions, the mass fraction of water may far exceed that of the polymer.[26] Depending on the components of the hydrogel, the absorbed solvent can be released into the environment via changes in factors such as temperature[27] and pH.[28]

All four of these systems: PCHs, gas hydrates, polymer clathrates, and hydrogels share the characteristic that they combine a polymeric species and a small-molecule species. But PCHs are distinct from these other substances. They are a subset of polymer-solvent molecular compounds where the solvent is water. Unlike gas hydrates, the water is not in the form of a cage structure that accommodates a guest. Also, the water fraction is usually much lower in a gas hydrate. Furthermore, unlike hydrogels, the structures of PCHs involve water molecules co-crystallizing with the polymer chains. While the nano-confined water community may find PCHs intriguing, this perspective focuses on the unique properties and structures of PCHs themselves.[29,30]

POCB

POCB as a Polymer

POCB was first discovered in 1958 by Bunn and Holmes[31] and later characterized in 1967 by Tadokoro. The POCB homopolymer has the lowest melting point, the lowest heat of fusion, and the most compact chain dimensions amongst all the polyalkylene oxides having a repeat unit of $[(CH_2)_n{-}O]$.[1] Its monomer unit is shown in Figure 1.

Tadokoro et al. first discovered that POCB exhibits three crystal modifications with

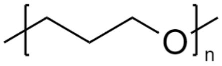

Figure 1: Chemical structure of a linear POCB monomer unit

distinct characteristics.[32] These modifications are achieved through various thermochemical treatments (see Figure 2). In 1981, a fourth modification of POCB was discovered.[33]

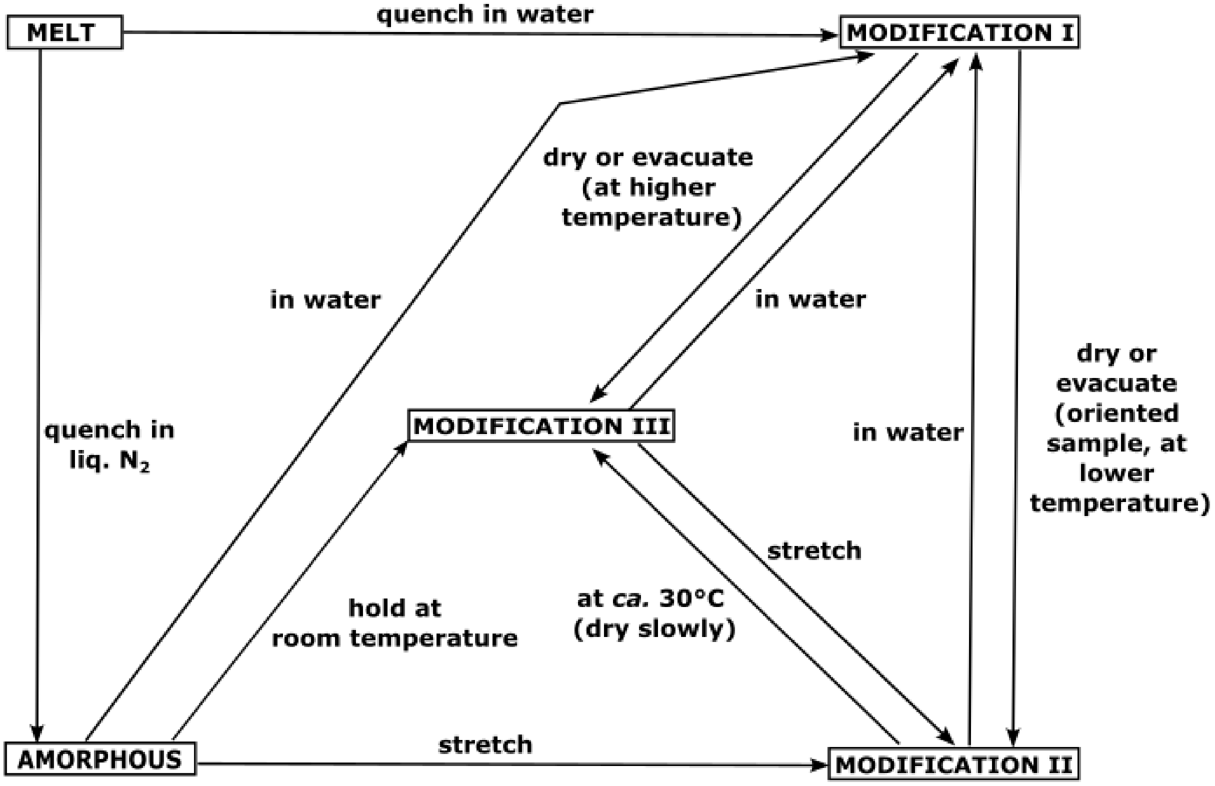

Figure 2: Methods of treatment of the polymer to form the three different modifications of POCB. Adapted from Tadokoro, H. Structure of crystalline polyethers. Journal of Polymer Science: Macromolecular Reviews 1967, 1, 119–172, eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1002/pol.1967.230010105.

Modification I exhibits a planar zigzag conformation over a fiber identity period of 4.80 Å. Each unit cell modification contains four monomers and four water molecules and forms a PCH structure. The crystal structure of Modification I is depicted in Figure 3 A and will be further discussed in the following subsection.

Apart from Modification I, none of the remaining crystal structures are hydrates; they

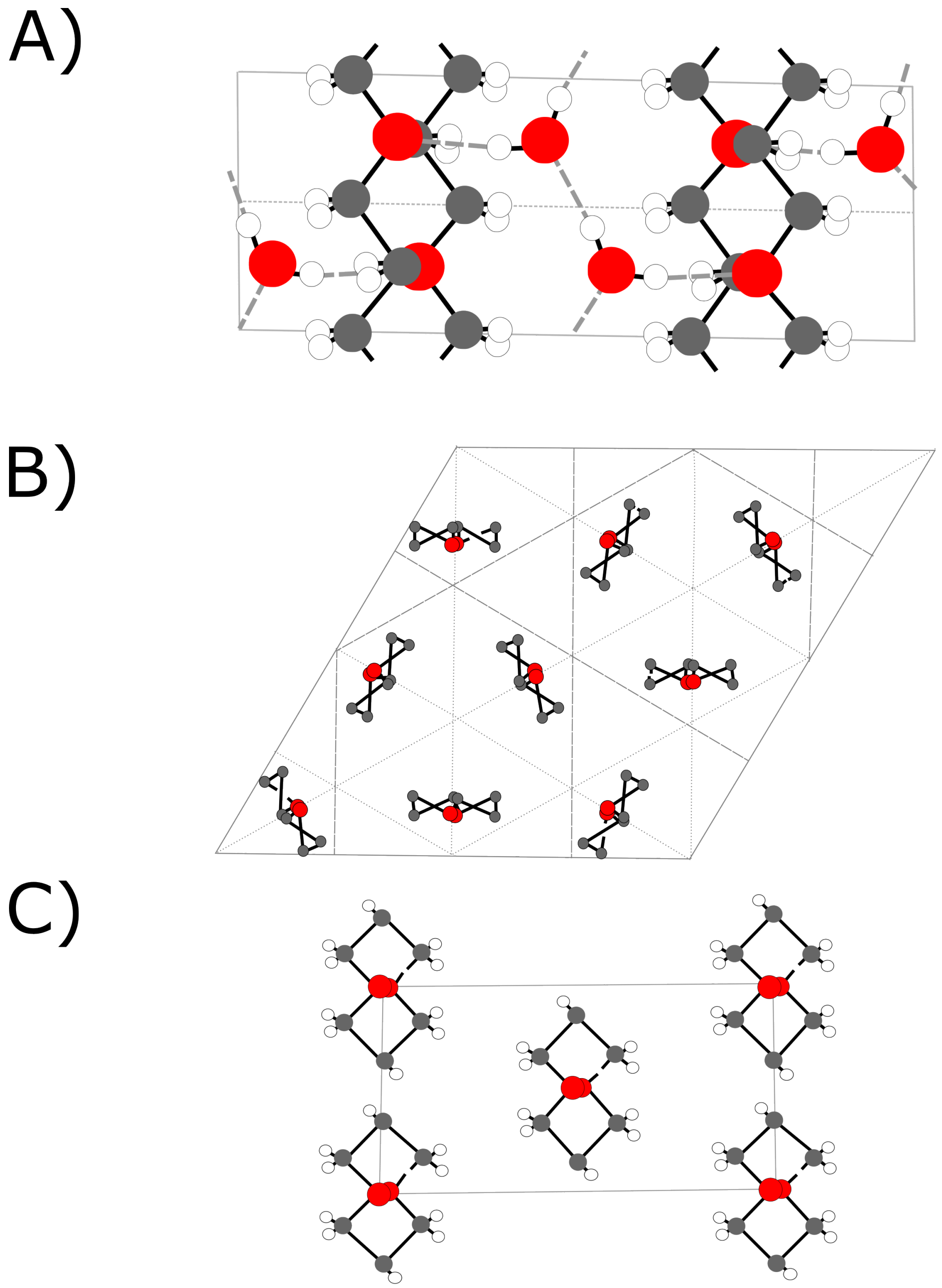

Figure 3: A) Crystal structure of Modification I of the POCB-water hydrate, B) Crystal structure of Modification II of the POCB crystal, C) Crystal structure of Modification III of the POCB crystal.[32]

are crystals of pure POCB. In contrast to Modification I, Modification II features a trigonal lattice with a space group of $\mathrm{R_3c{-}C_{3v}}^{6}$, a unit cell of a=14.13 Å and c=8.41 Å, and a fiber identity period of 8.41 Å. It consists of nine molecular chains that adopt a more helical conformation, with some chains forming a screw to the right and others to the left.[32] Figure

3 B shows the crystal structure of Modification II.

Modification III features an orthorhombic unit cell with dimensions of a=9.23 Å, b=4.82 Å, and c=7.21 Å. It adopts a helical conformation, and four monomers are present within the cell. This modification is the most stable of the four under dry conditions due to the strong dipole moments of the COC groups, which are arranged anti-parallel to each other. The $C_{2221}{-}D_2{}^5$ space group permits two unit cell orientations, one of which is displayed in Figure 3 C. The second orientation features the same molecular axis, but the helical axis is rotated by $\sim 90°$ from the first orientation, making it unclear which unit cell is more chemically accurate.[32]

Modification IV features a planar zigzag conformation similar to Modification I. However, Modification IV could only be synthesized in the presence of a large amount of Modification III.[33] Additionally, Modification IV is a disordered structure, with methyl groups and oxygen atoms randomly substituted for each other.

POCB as a PCH

As mentioned earlier, Modification I is a POCB hydrate. The melting point is 37−41°C, depending on the molecular weight.[34] For low molecular weight, the POCB hydrate melts at a temperature that is higher than that of either the polyer and water. Its structure was analyzed using infrared adsorption spectroscopy and x-ray diffraction measurements with Ni-filtered Cu Kα radiation.[35] The x-ray diffraction results revealed that the distances between oxygen atoms (water-water: 2.68 Å, water-polymer: 2.70 Å) were shorter than twice the van der Waals radius of an oxygen atom (2.80 Å), indicating hydrogen bonding between water molecules and POCB chains. The infrared analysis showed a dichroism in the OH stretching at 3480-3200, and HOH bending vibrations at around 1660cm^{-1}, similar to other species with hydrogen-bonded water molecules, such as ice VII and oxalic acid dihydrate. Additionally, the presence of translational or vibrational modes of water was detected, indicating that the water was bound in a crystal.[35]

Water molecules play a crucial role by forming a hydrogen bonding network that involves both the water molecules and POCB chains in a zigzag conformation.[32] In the absence of water, the zigzag conformation is unfavorable, and instead, modifications II and III both form helices.

The hydrate of POCB was subjected to isothermal dissociation pressure measurements at temperatures ranging from −25°C to 20°C. The results confirmed that the water molecules were present in the crystal in the same molar ratio as the monomer. Additionally, the dissociation heat was determined to be $3.25 \cdot 10^{3} \frac{\mathrm{J}}{\mathrm{mol}}$.[36]

The process of crystallization was found to be slow at room temperature and low water content, as reported in Banerjee et al.[7] As with most crystallization processes, crystallization slowed as the melting temperature was approached. Further, crystallization was also slowed as the POCB:water ratio of the crystallizing mixture increased far above the 1:1 molar ratio needed for the hydrate. At high water content and/or high molecular weight, POCB is immiscible with water, indicating that it is intrinsically hydrophobic. Accordingly, crystallization occurs from a two-phase LLE state, and it is significantly influenced by mixing conditions.[9] Incidentally, while co-crystallization of water is already unusual, it is especially remarkable considering that POCB is a hydrophobic polymer. This appears to be the only example of a polymer co-crystallizing with a small molecule with which it is immiscible.

Polyethyleneimine (PEI)

PEI as a Polymer

PEI has a long history of industrial use, dating back to 1938, when it was primarily used for water-repellent finishing of paper and textiles, manufacturing reactive dyes, and enhancing the dyeability of said materials.[37] PEI is a highly branched polymer that exhibits an increase in branching as the temperature and concentration of the acid catalyst increase. The branched form of PEI is synthesized via the ring-opening polymerization of the aziridine monomer.[38] In contrast, linear PEI is obtained through the ring-opening of polymerization of N-substituted aziridine,[39,40] and ring-opening polmerization of 2-phenyl-2-oxazoline,[41] and 2-ethyl-2-oxazoline are followed by hydrolysis.[42] The linear PEI crystals have a melting point of approximately 60°C and can achieve a maximum molecular weight of 10^5g/mol[41,43] with a monomer unit, as shown in Figure 4.

Figure 4: Chemical structure of a linear PEI monomer unit

The PEI crystal consists of double-stranded helical polymer chains. Each chain is a 5/1 helix with an identity period of 0.958nm. Two chains form a double strand with a relative rotation of 180° about the helical axis. The closest inter-chain atomic distances in the double strand are 0.396 and 0.417nm for C–C pairs and 0.310 and 0.316nm for N–N pairs.[44] These are comparable to twice the van der Waals radius, and thus the double strand is considered to be very tight. This crystallization is strongly correlated with hydrogen bonding between NH groups on each chain. All of the NH hydrogen atoms are able to participate in hydrogen bonding, making PEI an example of a double-stranded helical polymer that is stabilized by interchain hydrogen bonds[44] as seen in Figure 5a. These strands are packed into a large *Fddd* unit cell. In the structure, a right-handed strand is surrounded by two right-handed strands and four left-handed strands, and vice-versa as seen in Figure 5b.[44]

PEI as PCHs

Compared to POCB, PEI and its hydrates have a much larger body of work exploring their chemistry and possible applications.[45–59] It would be outside the scope of this article to discuss all of these studies, but we have collected many of them here for further reading.

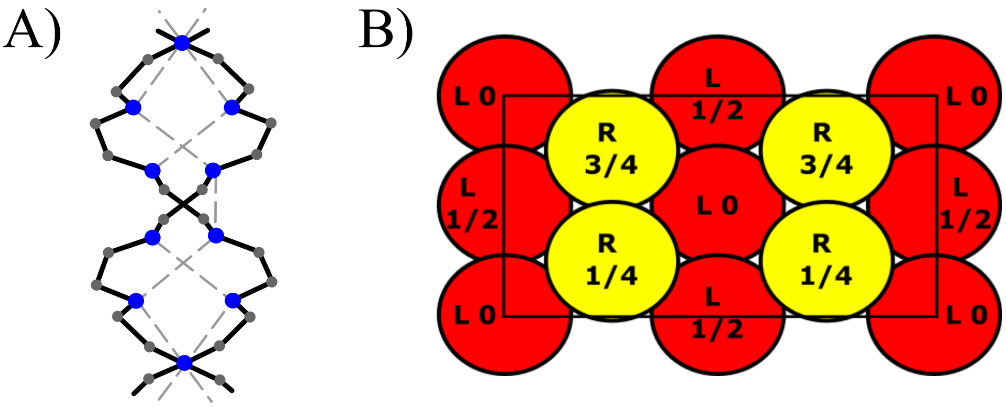

Figure 5: A) Double stranded helical chain of PEI. Broken lines indicate N−H· · · N hydrogen bonds, B) Packing of double strands viewed along the chain axis. R and L indicate right/left handed strands, and numbers indicate the fractional height of strands.

Hemihydrate

PEI, like POCB, forms a crystalline hydrate in the presence of water molecules. However, in contrast to POCB, PEI can form three different hydrates, depending on the molar ratio of water to PEI. The first of these hydrates is the hemihydrate, which contains PEI and water in a 1:0.5 molar ratio, with a unit cell with dimensions of a=1.089 nm, b=0.952 nm, c=0.731 nm, β=127.6 °, and a density of $1.14\frac{\mathrm{g}}{\mathrm{cm}^3}$.[3]

The chains in the hemihydrate are planar zigzag and parallel to the *bc* plane, while the water molecules are on a two-fold rotation axis parallel to the b axis. The water molecules are tetrahedrally coordinated by their oxygen atoms and the nitrogen atoms of the PEI. There are two types of hydrogen bonds in the hydrate, N−H· · · O and N· · · H−O. The first type has a bond length of 0.287 nm, while the second has a bond length of 0.305 nm. Unlike all other hydrate forms discussed in this article, the water molecules do not form hydrogen bonds with other water molecules. The full crystal structure of the hemihydrate is shown in Figure 6a.[3]

Sesquihydrate

The second hydrate formed by PEI is the sesquihydrate, which has a molar ratio of PEI monomer to water of 2:3. Similar to the hemihydrate, the PEI chains adopt a planar zigzag

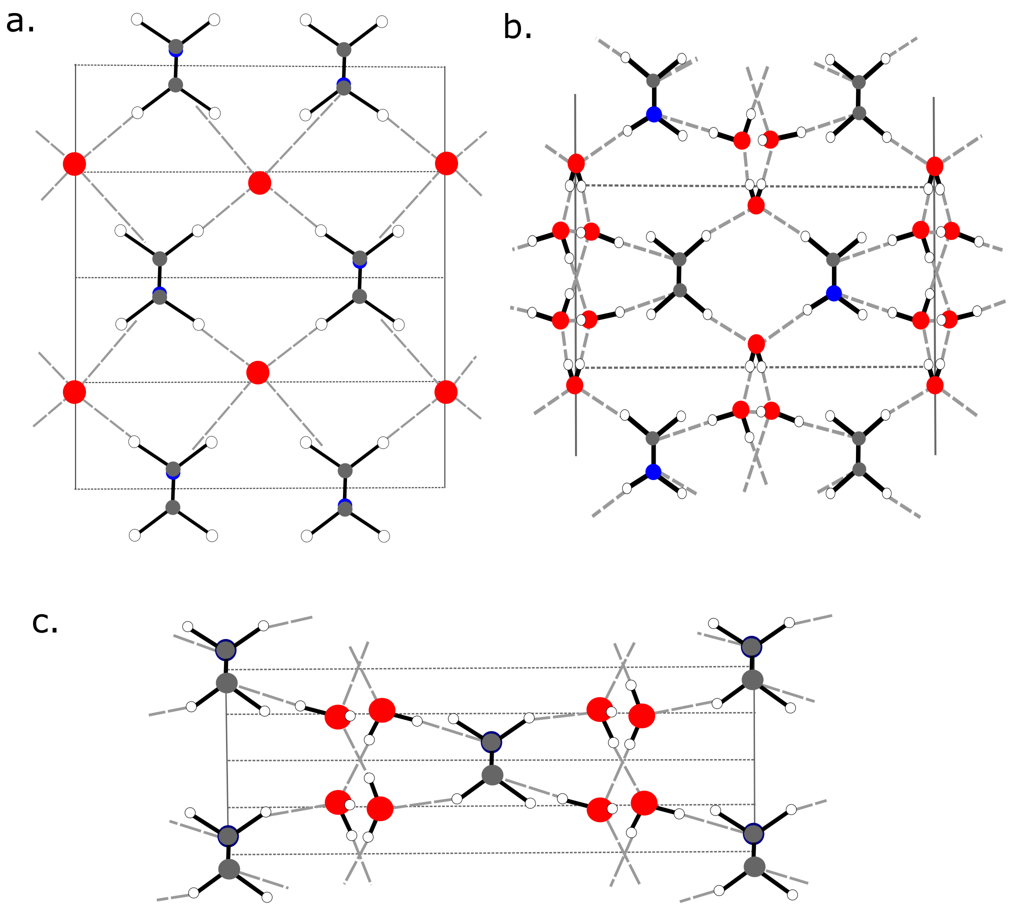

Figure 6: Crystal structures of the a) the PEI hemihydrate; b) PEI sesquihydrate; and c) PEI dihydrate. Broken lines indicate hydrogen bonds, but hydrogen atoms of NH groups and of water molecules are omitted.[3]

conformation and are parallel to the *bc* plane (Figure 6b). In this case, however, the eight monomer units of PEI are accompanied by twelve water molecules, which form a more complex network in the crystal. The monoclinic unit cell for this structure is a=11.55 Å, b=9.93 Å, c=7.36 Å, and β=104.5 °, with a space group of C2/c, as shown in Figure 6b.

In the water network, each water molecule's oxygen atom is bonded to four hydrogen atoms, two of which are covalent bonds, and two are hydrogen bonds from other water molecules, or NH groups. The water molecules form staggered pentagonal rings, which are similar to water cages found in clathrate and semiclathrate hydrates. The key difference between the water structure in the PEI hydrate and gas clathrates is that the five oxygen atoms are coplanar or nearly coplanar, as shown in Figure 7. In this structure, all possible hydrogen bonds that are able to participate do participate.[2]

Dihydrate

The final hydrate structure is the dihydrate, which has a molar ratio of PEI monomer to water of 1:2. Similar to the previous hydrates, the PEI chains adopt a planar zigzag conformation. However, only four monomer units of PEI are present, along with eight water molecules. The monoclinic unit cell of this structure is shown in Figure 6c, with dimensions a=13.26 Å, b=4.61 Å, c=7.36 Å, and β=101.0 °, and a space group of C2/c.

Like in the previous hydrates, each water molecule's oxygen atom is bonded to four hydrogen atoms, forming a water network that is very similar to ice I_h. The water network consists of hexagonal stacks of water molecules alternating with polymer chains arranged in parallel to the *bc* plane, as depicted in Figure 7. This water network only experiences slight distortion compared to I_h, which is expected given the different environment in which the water molecules are located.[2]

Thermodynamic Properties

The thermal behaviors of PEI and its hydrates in a water vapor atmosphere were also investigated in order to develop a phase diagram. Dried PEI polymer (anhydrate) was found to melt at about 60 °C during heating. Once a small amount of water was introduced, the anhydrate began to transition to a mixture of the hemihydrate and sesquihydrate at approximately 40 °C. The hemihydrate transitioned fully into the sesquihydrate at 60 °C, which melted at 80 °C. For a system with substantially more water forming a dihydrate, the system transferred to a sesquihydrate at about 65 °C, with the dihydrate melting at about 110 °C.[60] Differing initial water content did seem to affect the melting points of each hydrate slightly, creating a range of melting points over a phase diagram, which can be seen in Figure 8.

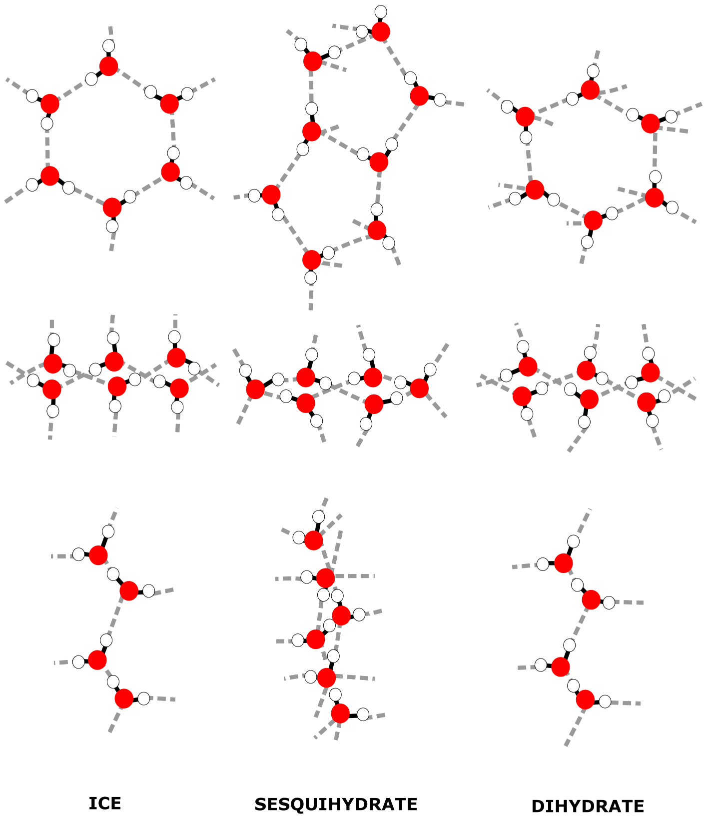

Figure 7: Water networks of ice Ih, the sesquihydrate, and the dihydrate.[2]

Computational Paths for Investigations of PCHs

Many computational algorithms presently exist for further study of these materials. Developing chemical descriptors by explicitly investigating intramolecular chemical bond energies via methods such as BEBOP[61] or non-chemical bonding intermolecular interactions via energy decomposition analysis (EDA) methods such as local energy decomposition (LED)[62,63] or symmetry adapted perturbation theory (SAPT)[64] methods would likely be an essential start to better understand the underlying atomic scale interactions that govern these materials. Theoretically, uncovering the specific chemical and physical interactions for why these compounds form may be transferable to develop new and presently undiscovered PCHs.

Efficient computational methods for high-throughput screening have already been developed for polymers[65–67] and hydrates[68–70] but to our knowledge they have not yet been used for polymer hydrates or PCHs. This screening has helped develop different design

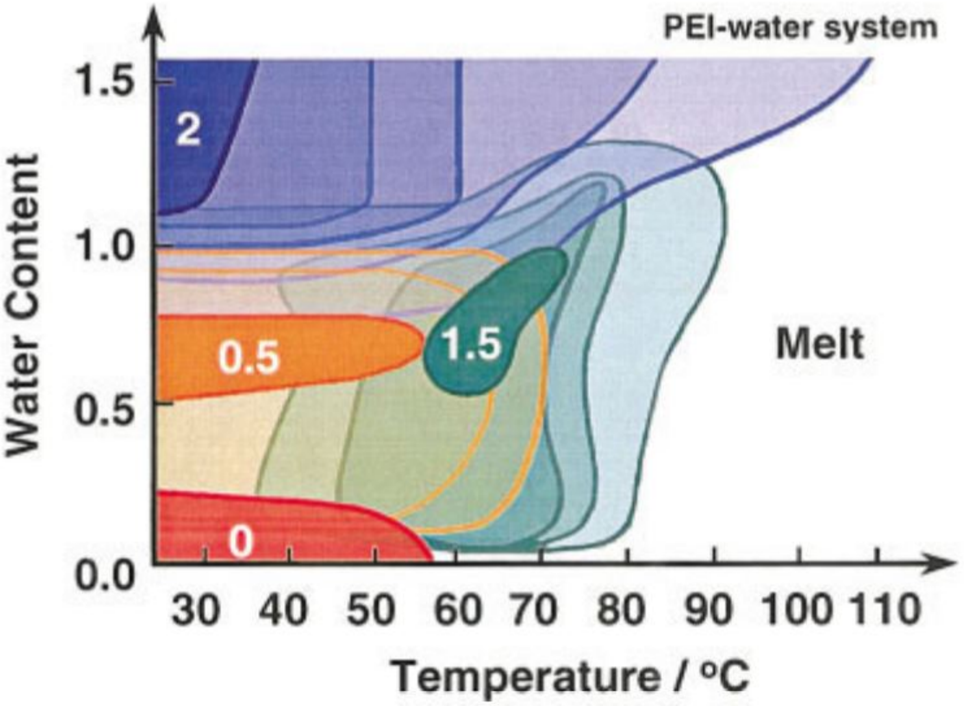

Figure 8: A phase diagram of PEI hydrates as a function of water content and temperature, where the water content is indicated by the relative intensity of the infrared water band reduced by an internal standard band.[60] Reprinted with permission from Hashida, T.; Tashiro, K.; Inaki, Y. Structural investigation of water-induced phase transitions of poly(ethylene imine). III. The thermal behavior of hydrates and the construction of a phase diagram. Journal of Polymer Science Part B: Polymer Physics 2003, 41, 2937–2948, eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1002/polb.10611.

principles based on the desired application of the screened material. For example, polymers designed specifically for interaction with the cyanobacterial toxin microcystin-LR is discussed in detail by Chianella *et al.* In the article, the authors discuss the design process, which included screening 20 commonly used monomers to test interactions with a molecular model of the toxin, and were scored according to binding.[71] Similar processes may be used for the screening of PCHs, including testing common polymers for possible interactions with water complexes.

Further methods for exploring the dynamics of configurations that dictate nucleation events include WESTPA,[72] a computational approach to efficiently sample large simulation data sets for rare events. The study of nucleation is an active field of study,[73] and it plays a fundamental role of the formation of traditional clathrate hydrates.[74,75] Therefore, computational efforts that to date have focused on exploring nucleation[76] could be extended into PCHs to bring useful insights into how and why nanoconfined water structures are formed. For example, microsecond simulations of the formation of PCHs, similar to that done by Walsh *et al.* for methane hydrates[77] might be useful to elucidate design principles for environmental conditions that enable PCH crystals growth.

Future Applications

While the formation of PCH from PEI or POCB has been known for decades, no practical applications have yet been brought forth to exploit this remarkable behavior. We conclude by listing some potential applications.

First, atomic scale structural analysis reveals that at least some of the PCH structures have water molecules in the form anisotropic water structures (e.g. 1-dimensional water chains in the POCB hydrate), and one might envision that such chains may enable high proton transport rates. Indeed, it was proposed that the 1-D chains of water molecules in the POCB hydrate align in such a way that it allows for trapping and shuttling of charge under applied gate bias by proton migration.[5] However, for such hydrates to function as a proton exchange membrane, these chains would require more macroscopic alignment than are grown naturally during crystallite formation.

A second opportunity with PCH formation is based on the observed liquid-to-solid transition. For instance, POCB of relatively low molecular weight is miscible with water, and simply cooling it changes it into a waxy solid. Similarly, there have been numerous studies on the gelation of PEI-water mixtures induced by simply cooling the initially-liquid mixture to below 80°C. As expected from a phase change, these changes are fully reversible. Moreover, POCB can form hydrates by absorbing water directly from humid air.[7] This offers the potential for smart materials to be used, for example, as humidity sensors, or materials that stiffen in response to humidity but soften upon drying. Furthermore, like most polymer crystallization, PEI or POCB hydrates crystallize via lamellar growth processes, resulting in spherulitic or dendritic morphologies. Such structures have been used for templating the deposition of inorganic materials, e.g. silica.[51,78–83]

A final aspect peculiar to POCB (but not PEI) is that it is an intrinsically hydrophobic polymer. Upon melting the hydrate, demixing occurs into a POCB-rich and water-rich state. It is possible that this behavior may be exploited for thermal desalination, i.e. by binding water at low temperature (while rejecting salt), and then recovering the water by melting the hydrate to induce demixing of water and POCB. Similar desalination approaches have been considered using gas hydrates[84,85] or other small molecules,[86,87] but POCB has the advantage of forming hydrates at atmospheric pressure and room temperature and then further releasing the water upon modest heating. If desalination approaches based on POCB hydrates are successful, this would constitute a large scale and potentially high impact application for PCHs.

As a last example of a large scale potential application, we postulate that PCHs may be used to stabilize gas hydrates. Large amounts of methane trapped in clathrate hydrates has sparked many studies, and some researchers suggest studying the possible impact of these clathrates on global climate change. For instance, in 2017 Ruppel *et al.*[88] suggested that if 0.1% of the estimated methane was released due to the clathrates melting, it would raise the amount of methane in the atmosphere by up to 60 %, a catastrophic amount according to MacDonald,[89] Bohannon,[90] and Whiteman.[91] To prevent this, some have suggested reinforcing methane sediments by injecting them with chemical promoters to prevent the hydrates from melting as temperatures increase.[92,93] We postulate that due to the similarities between clathrates and PCHs, PCHs may have a similar damping effect on the melting temperature of these large clusters of clathrates, whilst also being benign since they cannot evaporate, they are nontoxic, and they have no global warming potential.

In sum, PCHs are fascinating materials and present a promising avenue for future research in materials science. Computational modeling and screening, as well as exploration through methods previously discussed, can help advance understanding of the underlying chemistry of these materials and develop design principles for future use. While PCHs share some similarities with clathrates, their formation under ambient conditions and potential for numerous practical applications, such as proton transport, thermally-driven water desalination, and methane hydrate stabilization make them an exciting field of study. Additionally, while clathrates have been the focus of substantial research, their expense and technical limitations have limited their actual applications to date, and PCHs may provide an alternative route for similar applications with the added benefit of hydrates capable of forming under far less extreme conditions.

Data Availability and Reproducibility Statement

This is a perspective article that contains no new data.

Author Contributions

Dominick Filonowich: Conceptualization (shared); writing – original draft (lead); writing – review and editing (shared). **Sachin Velankar:** Writing – review and editing (shared). **John A. Keith:** Conceptualization (shared); writing – review and editing (shared).

References

(1) Tadokoro, H.; Takahashi, Y.; Chatani, Y.; Kakida, H. Structural studies of polyethers, [(CH2)mO]n. V. Polyoxacyclobutane. *Die Makromolekulare Chemie* **1967**, *109*, 96–111.

(2) Chatani, Y.; Tadokoro, H.; Saegusa, T.; Ikeda, H. Structural studies of poly(ethylenimine). 1. Structures of two hydrates of poly(ethylenimine): sesquihydrate and dihydrate. *Macromolecules* **1981**, *14*, 315–321.

(3) Chatani, Y.; Kobatake, T.; Tadokoro, H. Structural studies of poly(ethylenimine). 3. Structural characterization of anhydrous and hydrous states and crystal structure of the hemihydrate. *Macromolecules* **1983**, *16*, 199–204.

(4) Watanabe, M.; Ikezawa, R.; Sanui, K.; Ogata, N. Protonic conduction in poly(ethylenimine) hydrates. *Macromolecules* **1987**, *20*, 968–973.

(5) Chido, M. T.; Koronaios, P.; Saravanan, K.; Adams, A. P.; Geib, S. J.; Zhu, Q.; Sunkara, H. B.; Velankar, S. S.; Enick, R. M.; Keith, J. A.; Star, A. Oligomer Hydrate Crystallization Improves Carbon Nanotube Memory. *Chem. Mater.* **2018**, *30*, 3813–3818.

(6) Kobayashi, M.; Sato, H. Structure Analysis for Hydrate Models of Ethyleneimine Oligomer by Quantum Chemical Calculation. *Pharmacology & Pharmacy* **2010**, *01*, 60.

(7) Banerjee, J.; Koronaios, P.; Morganstein, B.; Geib, S. J.; Enick, R. M.; Keith, J. A.; Beckman, E. J.; Velankar, S. S. Liquids That Freeze When Mixed: Cocrystallization and Liquid–Liquid Equilibrium in Polyoxacyclobutane–Water Mixtures. *Macromolecules* **2018**, *51*, 3176–3183.

(8) Barker, E. F.; Banerjee, S.; Meyer, T. Y.; Velankar, S. Liquids that Freeze when Mixed: Homogeneous Cocrystallization Kinetics of Polyoxacyclobutane–Water Hydrate. *ACS Appl. Polym. Mater.* **2022**, *4*, 703–713.

(9) Banerjee, S.; Gresh-Sill, M.; Barker, E. F.; Meyer, T. Y.; Velankar, S. S. Polymer co-crystallization from LLE: Crystallization kinetics of POCB hydrate from two-phase mixtures of POCB and water. *Polymer* **2023**, 126087.

(10) Boswell, R.; Collett, T. S. Current perspectives on gas hydrate resources. *Energy Environ. Sci.* **2011**, *4*, 1206–1215.

(11) Bi, Y.; Guo, T.; Zhu, T.; Zhang, L.; Chen, L. Influences of additives on the gas hydrate cool storage process in a new gas hydrate cool storage system. *Energy Conversion and Management* **2006**, *47*, 2974–2982.

(12) Kang, K. C.; Linga, P.; Park, K.-n.; Choi, S.-J.; Lee, J. D. Seawater desalination by gas hydrate process and removal characteristics of dissolved ions (Na+, K+, Mg2+, Ca2+, B3+, Cl, SO42). *Desalination* **2014**, *353*, 84–90.

(13) Ogienko, A. G.; Myz, S. A.; Nefedov, A. A.; Ogienko, A. A.; Adamova, T. P.; Voronkova, O. M.; Amosova, S. V.; Trofimov, B. A.; Boldyrev, V. V.; Boldyreva, E. V. Clathrate Hydrates of Organic Solvents as Auxiliary Intermediates in Pharmaceutical Research and Development: Improving Dissolution Behaviour of a New Anti-Tuberculosis Drug, Perchlozon. *Pharmaceutics* **2022**, *14*, 495.

(14) English, N. J.; MacElroy, J. M. D. Perspectives on molecular simulation of clathrate hydrates: Progress, prospects and challenges. *Chemical Engineering Science* **2015**, *121*, 133–156.

(15) Ratcliffe, C. I. The Development of Clathrate Hydrate Science. *Energy Fuels* **2022**, *36*, 10412–10429.

(16) Khurana, M.; Yin, Z.; Linga, P. A Review of Clathrate Hydrate Nucleation. *ACS Sustainable Chem. Eng.* **2017**, *5*, 11176–11203.

(17) Buffett, B. A. Clathrate Hydrates. *Annual Review of Earth and Planetary Sciences* **2000**, *28*, 477–507.

(18) Das, S.; Tadepalli, K. M.; Roy, S.; Kumar, R. A review of clathrate hydrate nucleation, growth and decomposition studied using molecular dynamics simulation. *Journal of Molecular Liquids* **2022**, *348*, 118025.

(19) De Rosa, C.; Rizzo, P.; de Ballesteros, O.; Petraccone, V.; Guerra, G. Crystal structure of the clathrate form of syndiotactic polystyrene containing 1,2-dichloroethane. *Polymer* **1999**, *40*, 2103–2110.

(20) Chatani, Y.; Shimane, Y.; Inagaki, T.; Ijitsu, T.; Yukinari, T.; Shikuma, H. Structural study on syndiotactic polystyrene: 2. Crystal structure of molecular compound with toluene. *Polymer* **1993**, *34*, 1620–1624.

(21) Tadokoro, H.; Yoshihara, T.; Chatani, Y.; Murahashi, S. A preliminary report of structural studies on polyethylene oxide-urea complex. *Journal of Polymer Science Part B: Polymer Letters* **1964**, *2*, 363–368.

(22) Tadokoro, H.; Chatani, Y.; Yoshihara, T.; Tahara, S.; Murahashi, S. Structural studies on polyethers, [-(CH2)m-O-]n. II. Molecular structure of polyethylene oxide. *Die Makromolekulare Chemie* **1964**, *73*, 109–127.

(23) Ye, H.-M.; Peng, M.; Xu, J.; Guo, B.-H.; Chen, Q.; Yun, T.-L.; Ma, H. Conformation transition and molecular mobility of isolated poly(ethylene oxide) chains confined in urea nanochannels. *Polymer* **2007**, *48*, 7364–7373.

(24) Guerra, G.; Daniel, C.; Rizzo, P.; Tarallo, O. Advanced materials based on polymer cocrystalline forms. *Journal of Polymer Science Part B: Polymer Physics* **2012**, *50*, 305–322.

(25) Ahmed, E. M. Hydrogel: Preparation, characterization, and applications: A review. *Journal of Advanced Research* **2015**, *6*, 105–121.

(26) Bahram, M.; Mohseni, N.; Moghtader, M.; Bahram, M.; Mohseni, N.; Moghtader, M. *An Introduction to Hydrogels and Some Recent Applications*; IntechOpen, 2016.

(27) Qiu, Y.; Park, K. Environment-sensitive hydrogels for drug delivery. *Adv Drug Deliv Rev* **2001**, *53*, 321–339.

(28) Richter, A.; Paschew, G.; Klatt, S.; Lienig, J.; Arndt, K.-F.; Adler, H.-J. P. Review on Hydrogel-based pH Sensors and Microsensors. *Sensors (Basel)* **2008**, *8*, 561–581.

(29) Foroutan, M.; Fatemi, S. M.; Esmaeilian, F. A review of the structure and dynamics of nanoconfined water and ionic liquids via molecular dynamics simulation. *Eur. Phys. J. E* **2017**, *40*, 19.

(30) Leoni, F.; Calero, C.; Franzese, G. Nanoconfined Fluids: Uniqueness of Water Compared to Other Liquids. *ACS Nano* **2021**, *15*, 19864–19876.

(31) Bunn, C. W.; Holmes, D. R. Chain configurations in crystals of simple linear polymers. *Discuss. Faraday Soc.* **1958**, *25*, 95–103.

(32) Tadokoro, H. Structure of crystalline polyethers. *Journal of Polymer Science: Macromolecular Reviews* **1967**, *1*, 119–172.

(33) Takahashi, Y.; Osaki, Y.; Tadokoro, H. Planar zigzag modification of polyoxacyclobutane (modification IV) and its disordered structure1. *Journal of Polymer Science: Polymer Physics Edition* **1981**, *19*, 1153–1155.

(34) Banerjee, S.; Velankar, S. S. Manuscript in preparation. **2023**,

(35) Kakida, H.; Tadokorolb, H. Structural Studies of Polyethers [-(CH,)mO-jH. VIII. **1970**, *3*, 10.

(36) YosmnA, S.; Sakiyama, M.; Seki, S. Thermodynamic Studies of Solid Polyethers. I. Poly(Oxacyclobutane), [-(CH2) 30-]n and Its Hydrate. **1970**, *1*, 9.

(37) Zhuk, D. S.; Gembitskii, P. A.; Kargin, V. A. Advances in the Chemistry of Polyethyleneimine Polyaziridine. *Russ. Chem. Rev.* **1965**, *34*, 515–527.

(38) Zhang, W.; Chen, D.; Wang, X.; Xie, X. Insight into the synthesis of branched polyethylenimines from 2-haloethylamine via a one-pot two-stage process. *Polymer* **2022**, *255*, 125113.

(39) Stewart, I. C.; Lee, C. C.; Bergman, R. G.; Toste, F. D. Living Ring-Opening Polymerization of N-Sulfonylaziridines: Synthesis of High Molecular Weight Linear Polyamines. *J. Am. Chem. Soc.* **2005**, *127*, 17616–17617.

(40) Tauhardt, L.; Kempe, K.; Knop, K.; Altuntaş, E.; Jäger, M.; Schubert, S.; Fischer, D.; Schubert, U. S. Linear Polyethyleneimine: Optimized Synthesis and Characterization – On the Way to "Pharmagrade" Batches. *Macromolecular Chemistry and Physics* **2011**, *212*, 1918–1924.

(41) Tanaka, R.; Ueoka, I.; Takaki, Y.; Kataoka, K.; Saito, S. High molecular weight linear polyethylenimine and poly(N-methylethylenimine). *Macromolecules* **1983**, *16*, 849–853.

(42) Brissault, B.; Kichler, A.; Guis, C.; Leborgne, C.; Danos, O.; Cheradame, H. Synthesis of Linear Polyethylenimine Derivatives for DNA Transfection. *Bioconjugate Chem.* **2003**, *14*, 581–587.

(43) Gembitskii, P. A.; Chmarin, A. I.; Kleshcheva, N. A.; Zhuk, D. S. The polymerization of ethylenimine to give linear polyethylenimine. *Polymer Science U.S.S.R.* **1978**, *20*, 1695–1702.

(44) Chatani, Y.; Kobatake, T.; Tadokoro, H.; Tanaka, R. Structural studies of poly(ethylenimine). 2. Double-stranded helical chains in the anhydrate. *Macromolecules* **1982**, *15*, 170–176.

(45) Hashida, T.; Tashiro, K.; Inaki, Y. Crystallization of poly(ethylene imine) amorphous sample in water vapor atmosphere. *Polymer* **2003**, *44*, 1721–1724.

(46) Hashida, T.; Tashiro, K.; Ito, K.; Takata, M.; Sasaki, S.; Masunaga, H. Correlation of Structure Changes in the Water-Induced Phase Transitions of Poly(ethylenimine) Viewed from Molecular, Crystal, and Higher-Order Levels As Studied by Simultaneous WAXD/SAXS/Raman Measurements. *Macromolecules* **2010**, *43*, 402–408.

(47) Hashida, T.; Tashiro, K. Structural Study on Water-induced Phase Transitions of Poly(ethylene imine) as Viewed from the Simultaneous Measurements of Wide-Angle X-ray Diffractions and DSC Thermograms. *Macromolecular Symposia* **2006**, *242*, 262–267.

(48) Hashida, T.; Tashiro, K. Structural investigation on water-induced phase transitions of poly(ethylene imine), Part IV: Changes of intra- and intermolecular hydrogen bonds in the hydration processes as revealed by time-resolved Raman spectral measurements. *Polymer* **2007**, *48*, 7614–7622.

(49) Kakuda, H.; Okada, T.; Hasegawa, T. Temperature-Induced Molecular Structural Changes of Linear Poly(ethylene imine) in Water Studied by Mid-Infrared and Near-Infrared Spectroscopies. *J. Phys. Chem. B* **2009**, *113*, 13910–13916.

(50) Lott, G. A.; King, M. D.; Hill, M. W.; Scatena, L. F. Effects of Relative Humidity on the Surface and Bulk Structures of Linear Polyethylenimine Thin Films. *J. Phys. Chem. C* **2014**, *118*, 17686–17698.

(51) Yuan, J.-J.; Jin, R.-H. Fibrous Crystalline Hydrogels Formed from Polymers Possessing A Linear Poly(ethyleneimine) Backbone. *Langmuir* **2005**, *21*, 3136–3145.

(52) Buijs, W. Molecular Modeling Study to the Relation between Structure of LPEI, Including Water-Induced Phase Transitions and CO2 Capturing Reactions. *Ind. Eng. Chem. Res.* **2021**, *60*, 11309–11316.

(53) Soradech, S.; Williams, A. C.; Khutoryanskiy, V. V. Physically Cross-Linked Cryogels of Linear Polyethyleneimine: Influence of Cooling Temperature and Solvent Composition. *Macromolecules* **2022**, *55*, 9537–9546.

(54) Douyère, G.; Leclercq, L.; Nardello-Rataj, V. From polyethyleneimine hydrogels to Pickering-like smart "On/Off" emulgels switched by pH and temperature. *Journal of Colloid and Interface Science* **2022**, *628*, 807–819.

(55) Lambermont-Thijs, H. M. L.; van der Woerdt, F. S.; Baumgaertel, A.; Bonami, L.; Du Prez, F. E.; Schubert, U. S.; Hoogenboom, R. Linear Poly(ethylene imine)s by Acidic Hydrolysis of Poly(2-oxazoline)s: Kinetic Screening, Thermal Properties, and Temperature-Induced Solubility Transitions. *Macromolecules* **2010**, *43*, 927–933.

(56) Chatani, Y.; Irie, T. Crystal structure of poly(ethylenimine)-hydrogen chloride complex. *Polymer* **1988**, *29*, 2126–2129.

(57) Chatani, Y.; Yakura, Y.; Ishioka, T. Crystal structure of poly(ethylenimine)-acetic acid complex. *Polymer* **1990**, *31*, 208–211.

(58) Herlem, G.; Lakard, B. *Ab* initio study of the electronic and structural properties of the crystalline polyethyleneimine polymer. *The Journal of Chemical Physics* **2004**, *120*, 9376–9382.

(59) Herlem, G.; Gharbi, T.; Sedrine, N. B. Analyzing ab initio infrared spectra and electronic properties of polyethylenimine water complexes in the solid state. *Journal of Molecular Structure: THEOCHEM* **2010**, *945*, 27–32.

(60) Hashida, T.; Tashiro, K.; Inaki, Y. Structural investigation of water-induced phase transitions of poly(ethylene imine). III. The thermal behavior of hydrates and the construction of a phase diagram. *Journal of Polymer Science Part B: Polymer Physics* **2003**, *41*, 2937–2948.

(61) Zulueta, B.; Tulyani, S. V.; Westmoreland, P. R.; Frisch, M. J.; Petersson, E. J.; Petersson, G. A.; Keith, J. A. A Bond-Energy/Bond-Order and Populations Relationship. *J. Chem. Theory Comput.* **2022**, *18*, 4774–4794.

(62) Altun, A.; Neese, F.; Bistoni, G. Local energy decomposition analysis of hydrogen-bonded dimers within a domain-based pair natural orbital coupled cluster study. *Beilstein J. Org. Chem.* **2018**, *14*, 919–929.

(63) Altun, A.; Saitow, M.; Neese, F.; Bistoni, G. Local Energy Decomposition of Open-Shell Molecular Systems in the Domain-Based Local Pair Natural Orbital Coupled Cluster Framework. *J. Chem. Theory Comput.* **2019**, *15*, 1616–1632.

(64) Stasyuk, O. A.; Sedlak, R.; Guerra, C. F.; Hobza, P. Comparison of the DFT-SAPT and Canonical EDA Schemes for the Energy Decomposition of Various Types of Noncovalent Interactions. *J. Chem. Theory Comput.* **2018**, *14*, 3440–3450.

(65) Lu, X.; Wu, Y.; Wu, X.; Cao, Z.; Wei, X.; Cai, W. High-throughput computational screening of porous polymer networks for natural gas sweetening based on a neural network. *AIChE Journal* **2022**, *68*, e17433.

(66) Pilania, G.; Weis, E.; Walker, E. M.; Gilbertson, R. D.; Muenchausen, R. E.; Simakov, E. I. Computational screening of organic polymer dielectrics for novel accelerator technologies. *Sci Rep* **2018**, *8*, 9258.

(67) Kanal, I. Y.; Owens, S. G.; Bechtel, J. S.; Hutchison, G. R. Efficient Computational Screening of Organic Polymer Photovoltaics. *J. Phys. Chem. Lett.* **2013**, *4*, 1613–1623.

(68) Oluwunmi, P. A.; Finney, A. R.; Rodger, P. M. Molecular dynamics screening for new kinetic inhibitors of methane hydrate. *Can. J. Chem.* **2015**, *93*, 1043–1049.

(69) J. Frankcombe, T.; Kroes, G.-J. A new method for screening potential sII and sH hydrogen clathrate hydrate promoters with model potentials. *Physical Chemistry Chemical Physics* **2011**, *13*, 13410–13420.

(70) Kiyabu, S.; Lowe, J. S.; Ahmed, A.; Siegel, D. J. Computational Screening of Hydration Reactions for Thermal Energy Storage: New Materials and Design Rules. *Chem. Mater.* **2018**, *30*, 2006–2017.

(71) Chianella, I.; Lotierzo, M.; Piletsky, S. A.; Tothill, I. E.; Chen, B.; Karim, K.; Turner, A.

P. F. Rational Design of a Polymer Specific for Microcystin-LR Using a Computational Approach. *Anal. Chem.* **2002**, *74*, 1288–1293.

(72) Russo, J. D. et al. WESTPA 2.0: High-Performance Upgrades for Weighted Ensemble Simulations and Analysis of Longer-Timescale Applications. *J. Chem. Theory Comput.* **2022**, *18*, 638–649.

(73) Peters, B. Crystal nucleation: Rare made common and captured by Raman. *Proceedings of the National Academy of Sciences* **2022**, *119*, e2204971119.

(74) Agarwal, V.; Peters, B. *Advances in Chemical Physics: Volume 155*; John Wiley & Sons, Ltd, 2014; pp 97–160.

(75) Factorovich, M. H.; Naullage, P. M.; Molinero, V. Can clathrates heterogeneously nucleate ice? *J. Chem. Phys.* **2019**, *151*, 114707.

(76) Peters, B. Common Features of Extraordinary Rate Theories. *J. Phys. Chem. B* **2015**, *119*, 6349–6356.

(77) Walsh, M. R.; Koh, C. A.; Sloan, E. D.; Sum, A. K.; Wu, D. T. Microsecond Simulations of Spontaneous Methane Hydrate Nucleation and Growth. *Science* **2009**, *326*, 1095–1098, Publisher: American Association for the Advancement of Science.

(78) Jin, R.-H.; Yuan, J.-J. Synthesis of poly(ethyleneimine)s–silica hybrid particles with complex shapes and hierarchical structures. *Chem. Commun.* **2005**, 1399–1401.

(79) Matsukizono, H.; Jin, R.-H. Controlled Formation of Polyamine Crystalline Layers on Glass Surfaces and Successive Fabrication of Hierarchically Structured Silica Thin Films. *Langmuir* **2011**, *27*, 6338–6348.

(80) Matsukizono, H.; Zhu, P.-X.; Fukazawa, N.; Jin, R.-H. Turbine-like structured silica transcribed simply by pre-structured crystallites of linear poly(ethyleneimine) bounded with metal ions. *CrystEngComm* **2009**, *11*, 2695–2700.

(81) Yao, D.-D.; Jin, R.-H. Synthesis of comb-like poly(ethyleneimine)s and their application in biomimetic silicification. *Polym. Chem.* **2015**, *6*, 2255–2263.

(82) Noda, D.; Arai, Y.; Souma, D.; Nagashima, H.; Jin, R.-H. Poly(N-cyanoethylethyleneimine): a new nanoscale template for biomimetic silicification. *Chem. Commun.* **2014**, *50*, 10793–10796.

(83) Soma, D.; Jin, R.-H. Free-standing disk mold crystalline polyethyleneimine gels: physical properties and chemical function in mineralization. *Colloid Polym Sci* **2017**, *295*, 1585–1594.

(84) Khan, M. N.; Peters, C. J.; Koh, C. A. Desalination using gas hydrates: The role of crystal nucleation, growth and separation. *Desalination* **2019**, *468*, 114049.

(85) Montazeri, S. M.; Kolliopoulos, G. Hydrate based desalination for sustainable water treatment: A review. *Desalination* **2022**, *537*, 115855.

(86) Werber, J. R.; Osuji, C. O.; Elimelech, M. Materials for next-generation desalination and water purification membranes. *Nat Rev Mater* **2016**, *1*, 1–15, Number: 5 Publisher: Nature Publishing Group.

(87) Ayyar, A. S.-R.; Aregawi, D. T.; Petersen, A. R.; Pedersen, J. M. I.; Kragh, R. R.; Desoky, M. M. H.; Sundberg, J.; Vinum, L.; Lee, J.-W. Carbon Dioxide-Mediated Desalination. *J. Am. Chem. Soc.* **2023**, *145*, 3499–3506.

(88) Ruppel, C. D.; Kessler, J. D. The interaction of climate change and methane hydrates. *Reviews of Geophysics* **2017**, *55*, 126–168.

(89) MacDonald, G. J. Role of methane clathrates in past and future climates. *Climatic Change* **1990**, *16*, 247–281.

(90) Bohannon, J. Weighing the Climate Risks of an Untapped Fossil Fuel. *Science* **2008**, *319*, 1753–1753.

(91) Whiteman, G.; Hope, C.; Wadhams, P. Vast costs of Arctic change. *Nature* **2013**, *499*, 401–403.

(92) Seo, Y.-T.; Lee, H.; Yoon, J.-H. Hydrate Phase Equilibria of the Carbon Dioxide, Methane, and Water System. *J. Chem. Eng. Data* **2001**, *46*, 381–384.

(93) Holder, G. D.; Cugini, A. V.; Warzinski, R. P. Modeling Clathrate Hydrate Formation during Carbon Dioxide Injection into the Ocean. *Environ. Sci. Technol.* **1995**, *29*, 276–278.