Size, Shape and Functionality Dependence of Solute Transport Mechanisms in a Cross-linked H$_{\text{II}}$ Phase Lyotropic Liquid Crystal Membrane

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1 Introduction

We need highly selective membranes in order to perform efficient separations.

H$_{\text{II}}$ phase lyotropic liquid crystals have densely packed, uniform sized pores and have the potential to disrupt conventional membrane separation techniques by being selective based not only on size and charge, but on chemical functionality as well.

We can only learn so much from experiment. MD can give us mechanistic insights with atomistic resolution so that we can intelligently design new membranes for solute-specific separations.

In previous work, we determined the most likely structure of the hexagonal phase formed by the monomer Na-GA3C11.

- We developed techniques for equilibrating the hexagonal phase made by neat monomer as well as with varying amounts of water in the pores.

In this work, we have determined the transport mechanisms and macroscopic transport properties exhibited by a number of polar solutes with varying size, chemical functionality and hydrophilic character.

- Many of the separations we are interested in involve polar organic compounds.

We have compared our calculated diffusion coefficients with experimental measurements made using DOSY NMR.

2 Methods

2.1 Molecular Dynamics Simulations

System Setup

Stable H$_{\text{II}}$ phases, assembled with Na-GA3C11, can be formed using a broad range of water concentrations.

- In the literature, this system is typically synthesized with close to 10 wt % water [1, 2]

- However, Resel et al. noted that the system is likely fully hydrated with less than 7 wt % water. [3]

- We decided to test two different levels of water content: 5 and 10 wt %

We observed that water partitions into the tail region of our system and therefore built our initial configurations with water in both regions close to the expected equilibrium value.

- There is about 2:1 water in the pores versus in the tails for the 10 wt % system.

- The amount of water present in the tails may or may not be experimentally consistent but if we don't put it in, the results will not be thermodynamically consistent, which will give issues with measurements and calculations.

- See supporting info for water equilibration simulation data.

- We adjusted the pore radius in our systems so that the right amount of water fits in the pores without any vacuum using `gmx solvate`.

- We placed water molecules in the tail region one at a time in random locations with short energy minimizations between insertions.

We equilibrated an initial solvated configuration before adding solutes.

- We equilibrated the initial configuration using the 'wet' equilibration procedure described in our previous work [4].

- We cross-linked the equilibrated solvated configuration using the cross-linking procedure described in our previous work.

We added 6 solute molecules to each pore of the equilibrated cross-linked configuration.

- We equally spaced each solute in the pore

- 6 solutes per pore provided a balance of a useful amount of data for generating statistics and a low degree of interaction between solutes (reference to supporting information to show low degree of interaction)

- At each insertion point we placed a randomly oriented solute molecule then ran a short energy minimization.

- We allowed the solutes to equilibrate for 5 ns using berendsen pressure control

- We collected transport data using 1 μs simulations

Radial Distribution Functions

We measured the average radial distance of each solute of interest from the pore centers.

- We binned the radial distances and then normalized by the volume of the annulus defined by the bin edges.

- Although the pores are often described as straight, they have a small degree of tortuosity which disrupts the RDF calcuation

- We obtain the best RDF by constructing splines that run through the pore centers.

- We construct the splines by dividing the membrane into 20 slices in the z-direction. Within each slice, we calculate the location of the pore centers based on the average location of the aromatic rings that make up the monomer head groups.

- When calculating the RDF, the radial distance from the pore center is based on the distance between the solute center-of-mass and the (x, y) coordinates of appropriate point on the spline.

Coordination number

We quantified the coordination of solutes with surrounding molecules.

- For each frame, we counted the identities and number of coordinated molecules to a given solute based on a distance cut-off.

- We found that this approach is more useful than calculating the 3D spherical radial distribution function because it gives detailed frame-by-frame information rather than an average.

3 Results and Discussion

Governing Mechanisms

On the timescales simulated in our study, solutes exhibit subdiffusive transport behavior as evidenced by their sublinear MSD curves.

- As an example, the MSD curve for ethanol is plotted in Figure 1a.

All solutes exhibit hop diffusion, characteristic of a continuous time random walk.

- Figure 1b shows the z-coordinate versus time of 3 representative ethanol centers of mass.

- There are clear periods of entrapment separated by relatively large hops.

- The length of entrapment follows a power law distribution (Figure 1c) and the distribution of hop lengths can be described with a Gaussian distribution (Figure 1d).

- Power law distributed dwell times are responsible for the ageing phenomenon which causes the MSD curve to decrease with increasing measurement time as longer dwell times get sampled.

The direction of each hop is anti-correlated to the direction of the previous hop.

- Figure 1e shows the autocovariance function of ethanol step vectors.

- The negative autocovariance at low values of k indicates anti-correlation between steps.

- If solutes followed a pure CTRW mechanism, the autocovariance function would decay to zero immediately.

- Although the autocovariance function is relatively noise, due to the somewhat small number of hops observed over the course of each solute trajectory, there is the least uncertainty at k=1, the most insightful data point. This behavior is consistent across all solutes molecules.

- Therefore, we believe transport can be described as subordinated fractional Brownian motion where the leading process is a CTRW with hops that are dictated by the parent process, FBM.

- Future publications will focus on modeling the solute's transport characteristics with an sFBM model

We calculated the time-averaged MSD of each solute in the set over the course of 1 μs MD simulations.

- Because the MSDs are non-linear and because of the ageing phenomenon, we did not attempt to calculate a diffusion constant as one might for a Brownian particle with a linear MSD.

- Instead, the MSD values plotted in Figure 2 represent the average MSD of each solute after a 400 ns time lag.

The MSDs are not a monotonic function of solute molecular weight.

- We plotted the solute molecular weights alongside their MSDs in Figure 2.

- Transport is clearly affected by factors other than molecular weight.

- Tetrose, our third heaviest solute, has an MSD higher than more than half of all solutes studied.

- The three slowest solutes have lower molecular weights than 8 faster solutes.

The MSDs in Figure 2 are a strong function of two solute trapping mechanisms.

- Solutes that are hydrogen bond donors can be stabilized through hydrogen bonds with one of the five oxygen atoms attached to each monomer head group.

- In a separate interaction, solutes can become kinetically trapped between monomer head groups. These interactions likely lead to the observed anti-correlated hopping behavior.
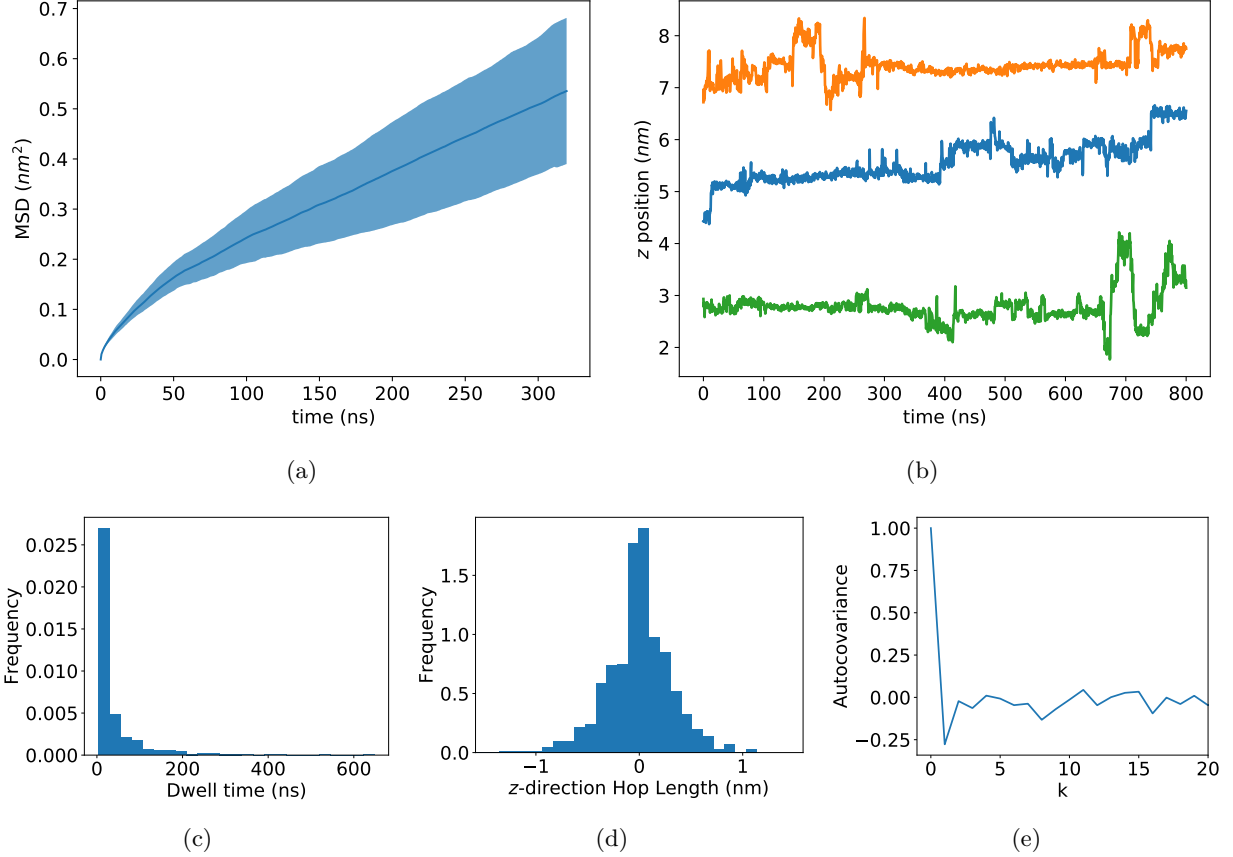
Figure 1: All solutes show subdiffusive transport behavior inside the membrane's nanopores, similar to that exhibited by ethanol. (a) The time-averaged MSD of ethanol is not linear which suggests transport is governed by an anomalous subdiffusion process. (b) The z-coordinate trace of 3 representative ethanol COMs shows clear periods of entrapment separated by hops. (c) The distribution of dwell times follows a power law. (d) The distribution of hop lengths appears Gaussian. (e) Hops are anti-correlated to their previous hop as indicated by the negative value of the autocovariance function at $k = 1$.
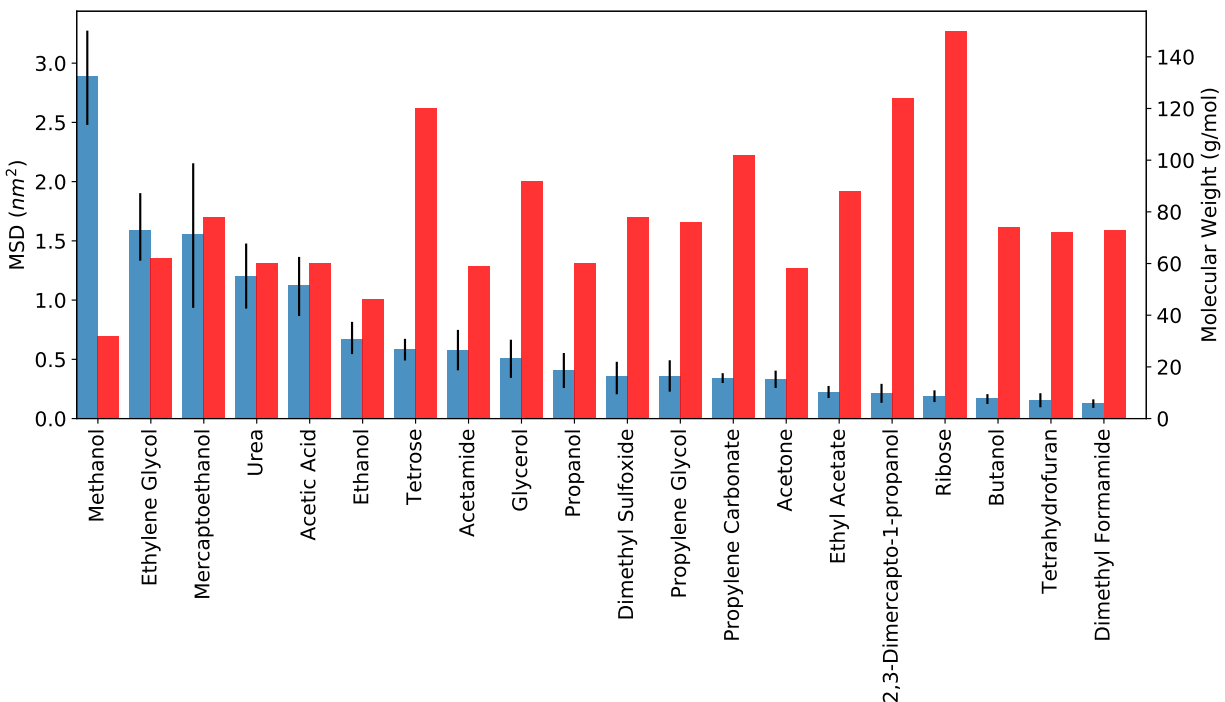
Figure 2

- Generally, both mechanisms affect each solute to varying degrees.

The degree to which solutes are influenced by each entrapment mechanism is a complex function of a solute's size, shape, and polarity.

- In general, solutes can move fastest in the pore center, where there is comparatively little resistance to diffusion.

- The 5 fastest solutes in our study have a low molecular weight and spend a significant amount of time in the pore center. They are only slowed by hydrogen bonds with monomer carboxylate groups.

- Bulky solutes with many hydrogen bond donating groups, like glycerol, spend most of their time in the pore center, but their large size combined with a higher solute-head group hydrogen bond frequency, makes their dynamics slow.

- Solutes with high hydrophobic character tend to partition into the head group region where entrapment occurs.

- We observe low MW solutes with lower-than-expected MSDs because they spend more time trapped between monomer head groups due to low water solubility.

- Small, planar molecules like acetone exhibit some of the slowest MSDs. Their flat geometry and small size makes it easy for them to get lodged deep between head groups.

- Overall solutes exhibit some degree of trapping, by one or a combination of the above mechanisms, with anticorrelated hops between each period of immobility due to obstructions.

We will revisit these observations in the the context of specific groups of molecules in the discussion that follows.

Transport of Water

Water molecules also exhibit hop diffusion.

The overwhelming number of water molecules reduces

Even in the center of the pore, where the density of water molecules is highest, individual water molecules exhibit hop diffusion as they create a tight hydrogen bond network.

- Water sticks to pore walls

- Dwell times are short

- Water tumbles across pore for a while until it sticks again.

- Water gets caught in h-bonds with other water molecules away from pore center.

In this confined environment, the diffusion constant is x times lower than expected bulk diffusion coefficient of tip3p water.

Transport of Simple Alcohols

The MSD of methanol, ethanol, propanol and butanol descends in order of their molecular weight, however, methanol travels faster than expected.

- The radial distribution as a function of distance from the pore center for each alcohol is plotted in Figure 3a.

- On average, the density of methanol in the pore center is only slightly less than the density near the head groups.

- All other alcohol molecules are concentrated in the head group region.

All simple alcohols participate in a similar number of hydrogen bonding interactions with the monomer head groups, but with varying preference towards hydrogen bonds with the monomer carboxylate oxygen atoms (See Figure 3b).

- If all 5 hydrogen bonding acceptor sites on the monomer head groups were equal, we would expect the ratio of the number of hydrogen bonds between solutes and the two carboxylate oxygen atoms to the number of hydrogen bonds between solutes and the three ether groups to be 2/3.

- There is a clear preference towards hydrogen bonding with the carboxylate oxygen atoms for all simple alcohols.

- This is largely due to the more highly crowded environment surrounding the ether oxygen atoms.

- Butanol shows the largest preference towards hydrogen bonds with carboxylate head groups.

- The radial distribution function of atoms located at opposite ends of butanol shows that, on average, oxygen atoms are situated 0.25 nm closer to the pore centers than the distal carbon atoms.

- This suggests that alcohols tend to orient themselves like the liquid crystal monomers, with hydrophilic components point towards the pore centers.

Transport of Diols, Triols and Sugars

Transport is both facilitated and hindered by additional solute hydroxyl groups.

- Extra hydroxyl groups cause solutes to favor the water-rich pore region where there is the least hindrance to movement.

- However, these extra hydroxyl groups facilitate a larger number of hydrogen bond interactions that work to hold solutes in place.
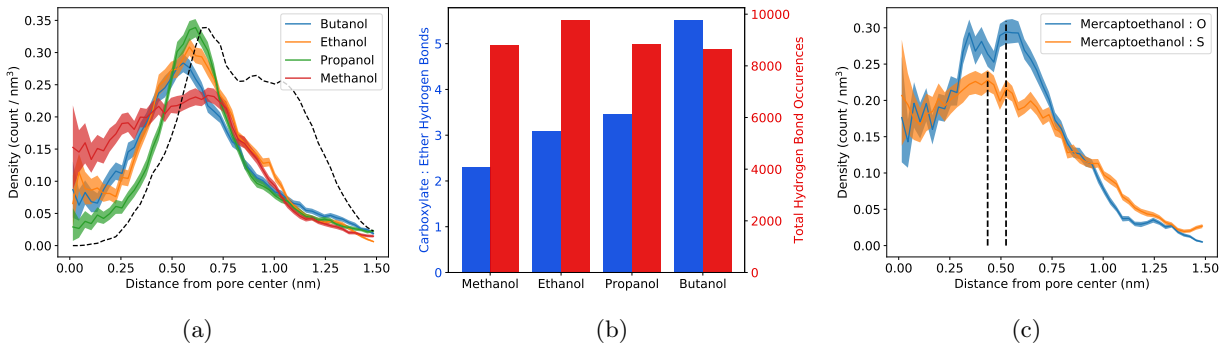
Figure 3: (a) The radial distribution functions of each simple alcohol shows a maximum close to the highest density of monomer head groups (dashed line, normalized for easier visual comparison). Methanol spends the largest proportion of time, relative to the other alcohols, near the pore center, which may help explain its fast dynamics. (b) Despite relatively little difference in the total number of hydrogen bond occurences, a given alcohol's preference towards hydrogen bonds with the carboxylate groups increases with molecule size. (c) The average location of butanol's oxygen atom is significantly closer to the pore center than its most distal carbon atom, suggesting that the molecule is oriented with hydrophobic tails pointing away from the pore center.

- At the same time, solute molecular weight increases, which inherently causes them to move more slowly.

- Ethylene glycol, the fastest solute in this grouping (and second fastest overall), obtains the best balance of both effects.

The number of hydrogen bonding interactions between solutes and head groups increases with the number of solute hydroxyl groups.

- These solutes frequently undergo simultaneous hydrogen bond interactions as shown in Figure 4.

- For example, both hydroxyl groups of ethylene glycol can undergo hydrogen bonds with different hydrogen bond acceptors at the same time.

- In some cases, all 4 hydroxyl groups of ribose are hydrogen bonded to monomer head groups simultaneously.

Between the two diols, ethylene glycol moves significantly faster than propylene glycol due to propylene glycol's affinty for the monomer head groups.

- The distribution of each solute's dwell time and hop length distributions shows that ethylene glycol has shorter dwell times and longer hop lengths, which combine to create a relatively fast MSD.

- Both diols have comparable densities close to the pore center, however propylene glycol's density has a large peak near the monomer head groups relative to ethylene glycol.

- Combined with an increase in molecular weight, the addition of a single methyl group increases the molecule's hydophobic character and causes propylene glycol to favor positions near monomer head groups.

- This causes propylene glycol to form more highly stablized hydrogen bonds with carboxylate groups, explaining the higher incidence of hydrogen bonds shown in Figure 4.

Solutes with three or more hydroxyl groups have the highest density at the pore center which contributes to overall faster than expected transport.

- These molecules are highly water soluble but relatively large

- They can easily hydrogen bond in multiple locations.

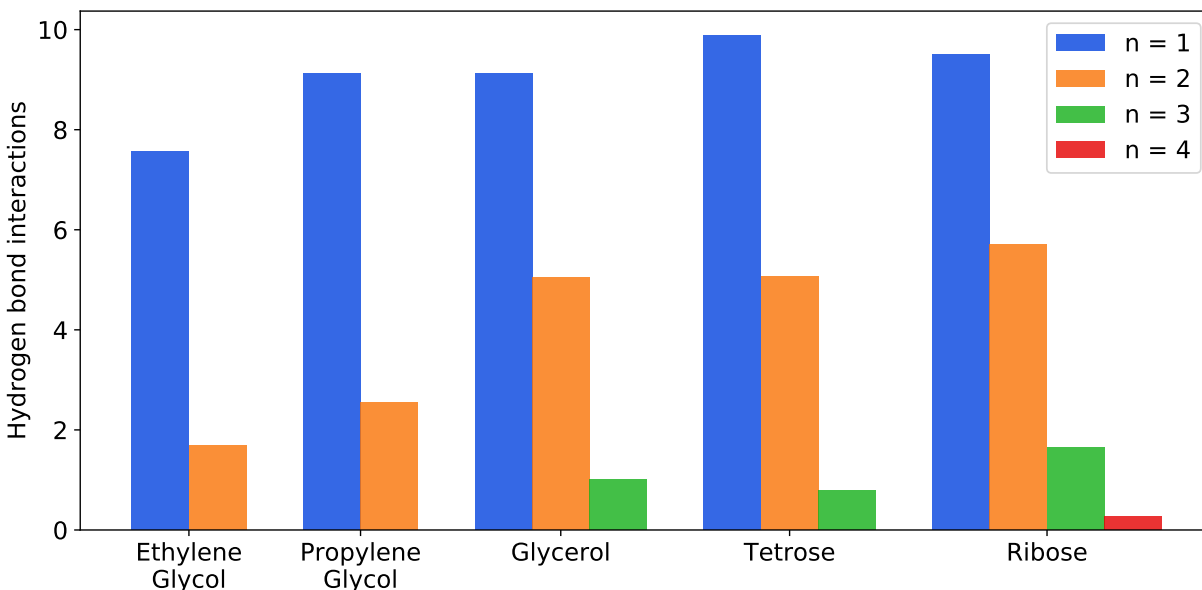- Their large size and high hydrogen bonding capability prevents them from have larger MSDs.

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Figure 4: The number of hydrogen bond interactions between solutes and monomers increases as solutes gain additional hydroxyl groups. Multiple hydroxyl groups within a solute often hydrogen bond in different locations simultaneously. Occasionally, all four hydroxyl groups of Ribose ($n = 4$) are involved in a hydrogen bond interaction at the same time.

Sulfur Analogs

We studied the transport properties of sulfur analogs of glycerol and ethylene glycol.

- We replaced all but one oxygen atom of each solute with sulfur atoms

- Sulfur is unable to hydrogen bond, however it is soluble in water

- Comparisons of their RDFs are shown in Figure 5.

Mercaptoethanol has a similar average RDF and MSD to ethylene glycol.

- There is a much larger uncertainty associated with mercaptoethanol's MSD

- Mercaptoethanol exhibits some of the largest single observed hops among all solutes.

- Less frequent hydrogen bonding and an affinity for the pore region may be responsible for these hops.

2,3-Dimercapto-1-propanol exhibits slower transport than glycerol because it spends more time near monomer head groups.

- Glycerol frequently hydrogen bonds with more than one head group at a time.

- It can also hydrogen bond with water molecule

- 2-3-Dimercapto-1-propanol preferentially hydrogen bonds with head groups so it stays close to pore walls.

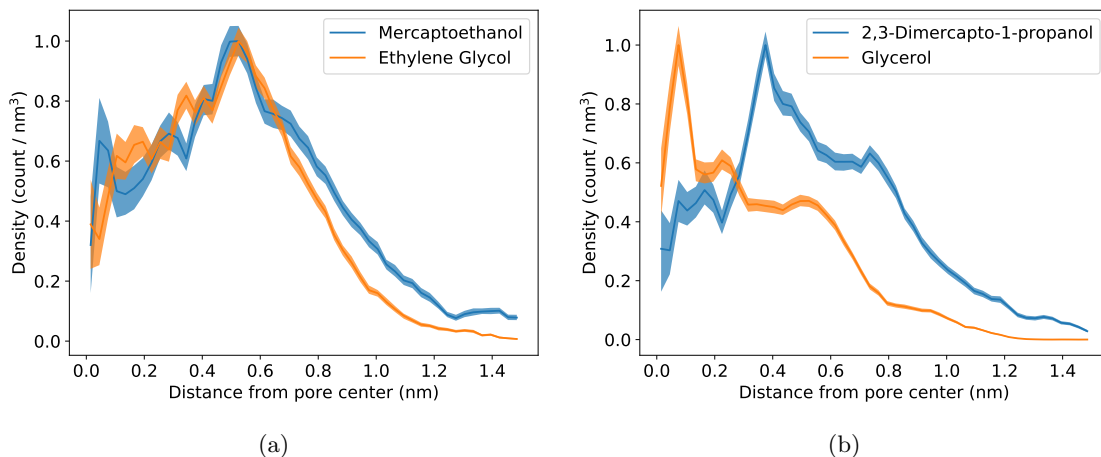Similar rdfs of ethylene glycol and dimercaptoethanol reinforces the lack of influence of hbonding

Figure 5

Transport of Ketone-like Solutes

The carbonyl group of Acetone is a hydrogen bond acceptor and therefore only form hydrogen bonds with water molecules in the pore.

The hydrophobic character of the two methyl groups on acetone causes the methyl groups to gravitate towards the outside of the pore, while the carbonyl group reaches towards the pore center in order to hydrogen bond with water molecules.

- Order parameter defined between vector along carbonyl and vector extending from acetone COM to pore center is non-zero.

Acetic acid, since we modeled it solely in its protonated state, has hydrogen bond donor and acceptor groups.

Transport of Ions

Sodium ions also exhibit hop diffusion because polarized water and carboxylate head groups both work to neutralize its charge.

- Ions get trapped in oxygen 'cages' composed of combinations of water molecules, carboxylate head groups and ether oxygens connecting the head groups to their tails.

- Interesting coordination number data

- Dwell time proportional to surrounding charge within coordination shell

Remarks

Overwhelming amount of water in 10 wt% system makes hydrogen bonding competitive between head groups and water.

3.1 Design Suggestions

Water content affects pore size. Experiments to understand this could be useful.

Separate polar molecules by creating monomers with more hydrophilic head group components. More incentive to dwell on walls.

Make ions move faster by placing charges in sterically inaccessible places.

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4   Conclusion

We have examined the transport characteristics of a series of small polar molecules in our model of the H_{II} phase formed by Na-GA3C11.

We calculated the macroscopic diffusion coefficients of each solute as approximated by a CTRW model and validated our estimates using experimental DOSY NMR measurements.

We have studied the influence of water content on the diffusion coefficients.

We showed that hydrogen bonding between solutes and Na-GA3C11 monomers plays a major role in mechanism by which molecules traverse the nanopores.

We can use this intuition in order to modify our monomers for a specific separation.

- Increase number of h-bond sites to increase selectivity towards water over polar molecules

- Also separate acetone (things with only h-bond accepting groups) in this way

Supporting Information

Detailed explanations and expansions upon the results and procedures mentioned in the main text are described in the Supporting Information. This information is available free of charge via the Internet at http://pubs.acs.org.

Acknowledgements

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