

Predicting Transport in Lyotropic Liquid Crystal Membranes with Molecular Dynamics Simulations – Outline

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March 7, 2017

1 Introduction

Nanostructured membrane materials have become increasingly popular for aqueous separations applications because they offer the ability to control membrane architecture at the atomic scale.

- Current state-of-the-art reverse osmosis membranes are dense and unstructured with tortuous and polydisperse pores which lead to inconsistent performance
- Tortuosity and polydispersity drive up energy requirements which strain developing regions and contribute strongly to CO₂ emissions
- Designing RO membranes to achieve targeted separations of specific solutes is nearly impossible due to the separation (hypothesized to be) controlled by fluctuating polymer voids
- RO has difficulty separating neutral organics because they tend to dissolve in polymer matrix
- Many current RO membranes degrade in typical chlorine filled municipal water supplies (debating this point because there aren't any studies of LLC membrane fouling resistance)
- With nanostructured materials, solute rejecting pores can be tuned uniformly – drives down energy requirements
- Targeted separations can be accomplished by tuning the molecular building blocks which form these materials
- Entirely different mechanisms govern the separation processes in various nano structured materials which can inspire novel separation techniques

Development of nanostructured materials has been limited by the ability to synthesize and scale various fundamentally sound technologies.

- Leading technologies and their limitations:
 - Graphene sheets -atomically thick which gives excellent permeability but defects during manufacturing severely impact
 - Carbon Nanotubes - MD studies are promising but synthetic techniques unable to achieve necessary alignment and pore monodispersity
 - Track-etch membranes
 - Molecular squares
 - Macrocyclic surfactants

Self assembling lyotropic liquid crystals (LLCs) share the characteristic ability of nanostructured membrane materials to create highly ordered structures with the benefits of low cost and synthetic techniques feasible for large scale production.

- LLCs are versatile and controllable with a large chemical design space available for membrane design
- Synthetic techniques are cheap and amenable to creating any monomer in this large design space
- LLCs forms lamellar, bicontinuous cubic and hexagonal phase based on solution composition
- Na-GA3C11 forms two types of self assembled LLCs - thermotropic (Colh) and lyotropic (HII)
- The thermotropic, Colh, is formed by the self assembly of neat monomer
- The lyotropic, HII phase is formed in the presence of small amounts of water
- Both assemble into cylinders with hydrophilic groups oriented inward towards the pore center and hydrophobic group facing outward. The only difference is the inclusion of water in the structure which leads to minor variations in the structure with potentially different filtration properties (although no filtration experiments have been done on Colh)
- Hydrophilic regions point towards pore centers
- Until recently, they could not be aligned - hindered progress
- Yale aligns them, then crosslinks them to lock in the structure - reference 2014 and 2016 papers

- LLC HII phase membranes offer potential for high permeability and selectivity which equals low energy consumption
- The Colh phase shares the same structural features with the HII phase with the exception of the presence of water. This paper will focus on the development of a model of the Colh phase since it is a simpler starting point and has just as much experimental data. The analysis used in this paper can be readily extended to the HII phase.

A molecular level understanding of LLC membrane structure will elucidate small molecule transport mechanisms, providing guidelines for design of monomers used to create separation-specific membranes.

- We do not yet understand how to reduce the effective pore size and/or tune the chemical environment in the HII nanopores for effect water desalination and small organic separations. Rejection studies show that this membrane can't do desalination
- We can create a molecular model that will give us the desired understanding
- Our focus is on Colh since it is a simpler system and has the same experimental data
- Colh phase studies currently limited mostly to one monomer
- Optimization efforts performed through trial and error
- Macroscopic models are the only source of predictive modeling and existing theories do not adequately describe transport at these length scales
- An atomistic understanding of the mechanism of solute transport can identify performance bottle necks and direct design of future monomers/membranes
 - Do ions have trouble getting through because of interactions with other things in the pores (e.g. ions, carbonyl groups, benzene rings)
 - related to ionic conduction
 - Does concentration of ions in the pore repel incoming ions?
 - Do neutral solutes get rejected based solely on size rejection, or do interactions within the pore lead to selective rejection
 - Is water structured inside the pores leading to transport barriers?

A clear picture of the microscopic structure of LLC membranes, gained by building a molecular model, will confirm or deny past drawn conclusions that have largely guided our understanding of separation mechanisms.

- The arrangement of sodium ions in the channels is thought to be confined to the pore walls. It is possible they are arranged more randomly

- This could change how one thinks about molecules diffusing through membrane
- Could also be a difference between lyotropic and thermotropic phases
- The Colh phase is described as having pores made of disks or layers stacked on top of one another, each containing a set number of monomers.
- A simple simulation study of a similar molecule (Head group is a sulfonate in the meta position) suggests that there are 4 monomers in each disk
- Calculations based on the volume of the liquid crystal suggest that there are seven monomers in each
- We can use fourier analysis to determine if there are distinct layers, and if so, how many monomers are situated in each layer.

We must show that the developed molecular model is consistent with physical observations so that we can trust conclusions drawn about structural features characteristic of the system.

- This paper will illustrate the careful development of a predictive molecular model and the steps taken to ensure it mimics the real system as best we can
- To understand how physically realistic the model is, validation by comparison to experiment is necessary
- We are primarily interested in reproducing the conclusions about structure which can be made from SAXS experiments, predicting ionic conductivity with a reasonable comparison to experiment, and reproducing experimental density measurements.
- We can simulate x ray diffraction patterns based on atomic coordinates
- We can predict ionic conductivity using two agreeing methods
- Density? - I will ask Mike to take more density measurements. It seems worthwhile

2 Methods

HII monomers were parameterized using the Generalized Amber Forcefield with the Antechamber package provided with AmberTools16. All molecular dynamics simulations were run using Gromacs version 5.1.2.

An ensemble of characteristic, low-energy vacuum monomer configurations were constructed by applying a simulated annealing process to a parameterized monomer.

- Structure cooled from 1000 to 50 K over 10 nanoseconds

- Result not global minimum but close enough for structure building
- Antechamber used for atomtyping with gaff forcefield
- Used Openeye Quacpac molcharge.py to assign charges
- Anneal again
- Multiple configurations saved from annealing trajectory to prove independence of starting config

The timescale for self assembly of monomers into the hexagonal phase is unknown and likely outside of a reasonable length for an atomistic simulation, calling for a more efficient way to build the system.

- Work done shows coarse grain model self assembly in 1000 ns , Citation: J. Phys. Chem. B 2013, 117, 4254-4262
- Attempts with Colh system not fruitful
 - Packed monomers into box
 - Simulated for 100 ns with no progress shown towards self assembly
- Wrote code to assemble monomers into Colh configuration close to what is expected
- Equilibration simulations allow structure to relax into expected configuration

Each pore is made of twenty stacked monomer layers, the smallest number of layers possible without sacrificing the expected aligned hexagonal morphology.

- Space between membrane layers in z direction - semi-isotropic sims fix z box dimension
- 5 layers create micellar structure
- Beyond 20 layers is unnecessary to get expected configuration
- layers spaced far enough apart to avoid large energy repulsions but close enough to prevent disks slipping between one another 5 angstroms works.
- How far into membrane do we have to go to avoid effects of the surface (this is a TODO)

FIGURE: initial configuration

caption: A representative initial configuration. Each pore is rotated about the z axis rotated to prevent overlaps between pores

Initial guesses for the remaining structural parameters were chosen based on experimental data and treated as variables during model development

- SAXS gives an idea of Pore-to-Pore distances
- TEM images and rejection studies give a pore size estimate
- To prevent unrealistic jumps during initial equilibration steps, the following equilibration scheme was adopted
 - Apply position restraints to monomer head groups during energy minimization
 - Leave position restraints for npt simulations to allow tails to intermingle (this also helps ensure independence of starting configuration)
 - Gradually reduce force constants (by square root every 50 ps) until they are completely off
 - Run long NPT simulations at 300 K and 1 bar (>200 ns) to fully equilibrate

Using an equilibrated structure, a crosslinking procedure was performed in order to better parallel synthetic procedures.

- Crosslinking maintains alignment of cylindrical mesophases - emphasize that replicating the mechanism/kinetics is not important
- head to tail addition dominates so I only implemented that
- racemic mixture - don't have to be too concerned about direction of attack
- Details of crosslinking algorithm (refer to appendix or supplemental info but give a brief overview here)

3 Results and Discussion

Appropriate selection of initial structural parameters including interlayer spacing, relative interlayer orientation, and pore spacing results in an equilibrated model that is experimentally consistent.

- Visual perspective
 FIGURE: shows top view and cross section (with pbcs on)
 caption:
 (a) The expected hexagonal membrane morphology is preserved upon equilibration
 (b) Straight cylindrical pore regions are present
- System dimensions and properties are consistent upon equilibration using multiple monomer configurations
- Pore to pore distance

- We know from SAXS data what the distance between pores should be
- We require long simulation times to reach an equilibrated structure with the correct dimensions
- Crosslinking locks in structure, maintaining pore distances even after long simulations

FIGURE - 2 panels

- (a) Measuring the distance between pores over time indicates equilibration when the distances stop changing
- (b) A crosslinked system run for 100 ns shows that the system maintains itself close to its initial position

- Simulated X-ray Diffraction

- We used the 3 dimensional fourier transformed electron density to generate simulated 1D and 2D diffraction patterns
- The 1D patterns are generated by spherical integration of the FT
- 2D patterns are generated by taking cross sections of the FT in the qx, qy and qz planes
- We matched experiments based on iterative improvement of our choice in initial structure and equilibration procedure

FIGURE - 4 panels

- (a) Experimental Small Angle X-ray Scattering data confirms a hexagonally packed morphology and tells us the average distance between pores
- (b) A simulated 1D x-ray diffraction pattern generated from atomic coordinates matches experimental measurements
- (c) Experimental Wide Angle X-ray Scattering patterns provide details of structure on a length scale less than 1 nm. The diffuse ring at $q = 1.4 \text{ \AA}^{-1}$ represents the average distance between carbons in packed alkyl chains. Meridional reflections at $q = \text{TBD } \text{\AA}^{-1}$ are caused by pi-stacking. The weak meridional reflections at $q = \text{TBD } \text{\AA}^{-1}$ are hypothesized to be a consequence of parallel-displaced stacking of benzene rings
- (d) Simulated X-ray diffraction pattern show the same dominant reflections which appear experimentally

- Pore Radius - a less reliable validation because we don't have an agreed upon way to measure this parameter experimentally
- Density - there are crude lab measurements which my model is in agreement with (no one has reported any values since it wasn't relevant to them)

Experiments to be run!

- Layered vs. offset configuration
 - All simulations involving 'offset' configurations (which seems to be the correct configuration) will have a 'layered' counterpart in order to highlight difference between the two configurations.
 - The comparison can be a figure in supplemental information
- Measures of stability / analysis (These methods will be applied to all simulations run)
 - Pore-to-pore distances
 - Tilt angle vs. time
 - Radial distribution functions
 - Simulated diffraction patterns
- Effect of temperature on stability of configurations
 - Three different temperature systems have been set up and simulated for 20 ns (All with 20 layers and no vapor gap): 260K, 280K and 300K
 - I have systems with no restraints on at all three temperatures
 - We can look at them with weak restraints in case the systems misbehave as time goes on. As of now, the tilt angles look to stabilize after 10 ns
 - If we get stable configurations with correct XRD patterns at lower temps but not higher, it may be a consequence of the forcefield
- Effect of restraints on stability
 - Run out simulations with weak restraints ($f = 0.1 \text{ kJ/mol*nm}^2$)
 - Higher restraints may cause the system to be too ordered, but it may be worth running in the case of long term movement
 - Run out simulations with no restraints (same simulation as 300K, no restraints from temperature stability sims)
 - Hopefully this will let us abandon restraints after equilibration
- Other simulations
 - Offset, no vapor gap, 20 layer : No tilt (i.e. use monomers that I have previously used). I want to see if the diagonal spots still show up. The concern here is that I wont be able to get the monomers close enough together without causing some unreconcilable energy minimization errors.
 - Offset, higher tilt. I'm working on a monomer that tilted more than the one I previously used. Can I make spots appear based purely on tilt? Also, what implications does this have for the pore spacing.

The monomers are arranged into disks containing 5 monomers in each layer.

- It has been suggested that there are 4 monomers in a each disk/layer, however, simulations have shown that this leads to unstable configurations with dimensions that are too small compared to experiment.
- Stable simulations with 6 and 7 monomers have been performed which give structural characteristics consistent with experiment
- Stable systems have also been simulated consisting of varying numbers of monomers per layer
- Calculating the number density of components in the z direction has shown defined groups

Figure

(a) The number density of benzene ring centers in the z direction shows regions with higher concentrations of the component

(b) A power spectrum of the data in (a) indicates that a new layer is defined every 4 angstroms implying that there are 5 monomers per layer.

- Even though there are defined regions of higher component density, there is still considerable variation in the position of the components (shown by the extra noise in the power spectrum)
- This suggests that the arrangement of monomers is more complicated than simple layers stacked on top of each other
- Density of components along Z axis
- There are not clear layers despite the defined layers in the starting configuration.

The arrangement of sodium counterions within the hydrophilic pore regions can be fit to a gaussian distribution.

- Past literature reports ions arranged in a circle about pore walls implying some kind of void space as a pore. Simulations under a variety of conditions suggest that ions prefer disorder within the pores.
- A size exclusion mechanism has been proposed in the past, however that might no be the only force at play
- Ions may play a role in transport, hindering flux of solute and solvent by slowing their diffusion
- The membrane may exhibit the permeability-selectivity tradeoff inherent to solution-diffusion type membranes.

FIGURE - plot from grant - sodium, benzene, tail densities in pores caption: The densities of sodium (blue), benzene (red), and alkyl tail carbons (cyan) surrounding the membrane pore centers indicate that each the pore region is a soup of the three components opposing the previously assumed hollow region.

The model gives reasonable estimates of ionic conductivity.

- There are a few ways to estimate ionic conductivity as seen in literature. We prefer a method which can extract an estimate based purely on an equilibrium trajectory
- We must also be sure that our analysis of results is consistent with the method use for experimental evaluation (i.e. AC impedance spectroscopy)
- We must also link our perfectly straight microscopic system to the not-so-straight macroscopic system
- Two methods used to for prediction
- Nernst Einstein Relation:
 - Widely used equation for estimating ionic conductivity
 - Estimates DC ionic conductivity – Frequency used during AC impedance slow enough to be approximated by dc at short enough timescales
 - Relates the diffusive motion of ions in the membrane to the membrane’s ionic conductivity
 - Concentration is concentration of ions in the whole membrane, not just channels
- Collective Diffusion:
 - Defines a collective coordinate, Q (charge), to quantify the amount of charge transfer through the system
 - In the limit of infinite time, the MSD of Q can be used to formulate a diffusion coefficient of Q that can be related to ionic conductivity
 - The model is valid for non-equilibrium and equilibrium simulations. Our analysis is based on the latter
 - A similar model has been derived and validate to predict water permeability using equilibrium simulations
 - The pore region is defined as the entire membrane system since lab IC measurements are done on bulk membrane rather than on individual pores. One would expect single channel IC to be much larger than the bulk membrane

TABLE: Calculated ionic conductivity using Nernst-Einsten and Collective Diffusion agree within error

The procedure used to create and validate our model can be used to evaluate other liquid crystalline assemblies. Using the design framework and analysis methods applied herein, we have the ability to reliably predict properties of new nanoporous membranes.

4 Conclusion

In this work, we have suggested a more detailed picture of the structure of a self assembled thermotropic liquid crystal membrane using an atomistic molecular model.

- The model’s physical properties are consistent with experimental measurements
- Channels are more disordered than previously thought and are filled with organic matter rather than hollow
- There are likely no defined layers
- Results presented for Colh phase monomer but methods are readily adapted to other LCs

5 Supplemental Information

Monomer configurations

- show all pore-to-pore equilibration plots used to prove independence of starting configuration
- 3D visualizations of different configurations tested
- 7 monomer per layer configurations and others if needed.

Crosslinking details

- Algorithm description. Link to full algorithm in git repository
- A figure showing the new crosslinks

Ionic conductivity

- MSD plots