

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

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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 allowing design of solute-specific separation membranes.

- 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 nanostructured 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 selectivity
 - 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 phases based on solution composition
- Na-GA3C11 has been described in literature as forming two types of self assembled phases - 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 groups 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. They say that they are scalable techniques

- 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 to reduce the chemical space 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 effective water desalination and small organic separations. Rejection studies show that this membrane can not do desalination yet
- Colh phase studies currently limited to one monomer
- Optimization efforts performed through trial and error over the past 20 years
- Macroscopic models are the only source of predictive modeling and existing theories do not adequately describe transport at these length scales
 - 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?
 - What does the microscopic pore structure look like and how can we relate that to monomer design and transport?
- An atomistic understanding of the mechanism of solute transport can identify performance bottle necks and direct design of future monomers/membranes
- We can use molecular dynamics simulations to enhance our understanding

A clear picture of the nanoscopic 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.
 - How do the monomer head groups pack together? Do the benzene rings prefer to be stacked on top of each other or in another pi-stacking mode.
 - Gas phase ab initio studies of benzene dimers have shown a clear energetic advantage for a parallel displaced or T-shaped conformation versus a stacked conformation.
 - Substituted benzene preferred stacking mode? Learning more about this
 - 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 layer
 - Does the equilibrated structure exist in distinct layers? Fourier analysis can help answer this question
- It is possible there is more than one metastable states associated with this LLC system
 - Which phase is consistent with experiment?
 - Can both phases be created experimentally?
 - How will each state affect transport?

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 have been made from XRD experiments and ionic conductivity measurements.
- We have written an algorithm to simulate the crosslinking mechanism and understand its influence on membrane structure

- We can simulate x ray diffraction patterns based on atomic coordinates in order to compare major features present in the 2D patterns
- We can predict ionic conductivity using two agreeing methods – Collective diffusion and nernst einstein

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 and Gromacs version 2016.

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
- Manual modifications to the structure were made to create specific geometries for xray diffraction experiments

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 with periodic continuity in all directions, avoiding any edge effects and creating an infinite length pore ideal for studying transport (Fig. 1)

- A thinner system is better to reduce the computational cost and allow us to look at longer timescales
- Number of layers chosen to give sufficient resolution when simulating XRD patterns

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

- XRD gives Pore-to-Pore distances of 4.1 nm and indicates possible pi-stacking at 3.7 Angstroms (see figure blah blah later on - comparison of experimental vs. simulated)
- Pi-stacking exists in multiple stable configurations: sandwiched, T-shaped and parallel-displaced
- T-shaped and parallel-displaced are nearly isoenergetic and more stable than the sandwiched configuration.
- T-shaped configuration is most stable when benzene centers are 5 Å apart which is not consistent with WAXS. <http://www.jbc.org/content/273/25/15458.full>
- System made with stacked and parallel-displaced benzene rings to see what is favored and matches XRD
- TEM images and rejection studies give a pore size estimate

An equilibration scheme with position restraints placed on benzene rings prevents unrealistic jumps during early equilibration steps.

- Equilibration scheme:
 - Apply position restraints to monomer head groups during energy minimization
 - Leave position restraints on for nvt simulations to allow tails to inter-mingle (this also helps ensure independence of starting configuration)
 - Gradually reduce force constants from 1000000 (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

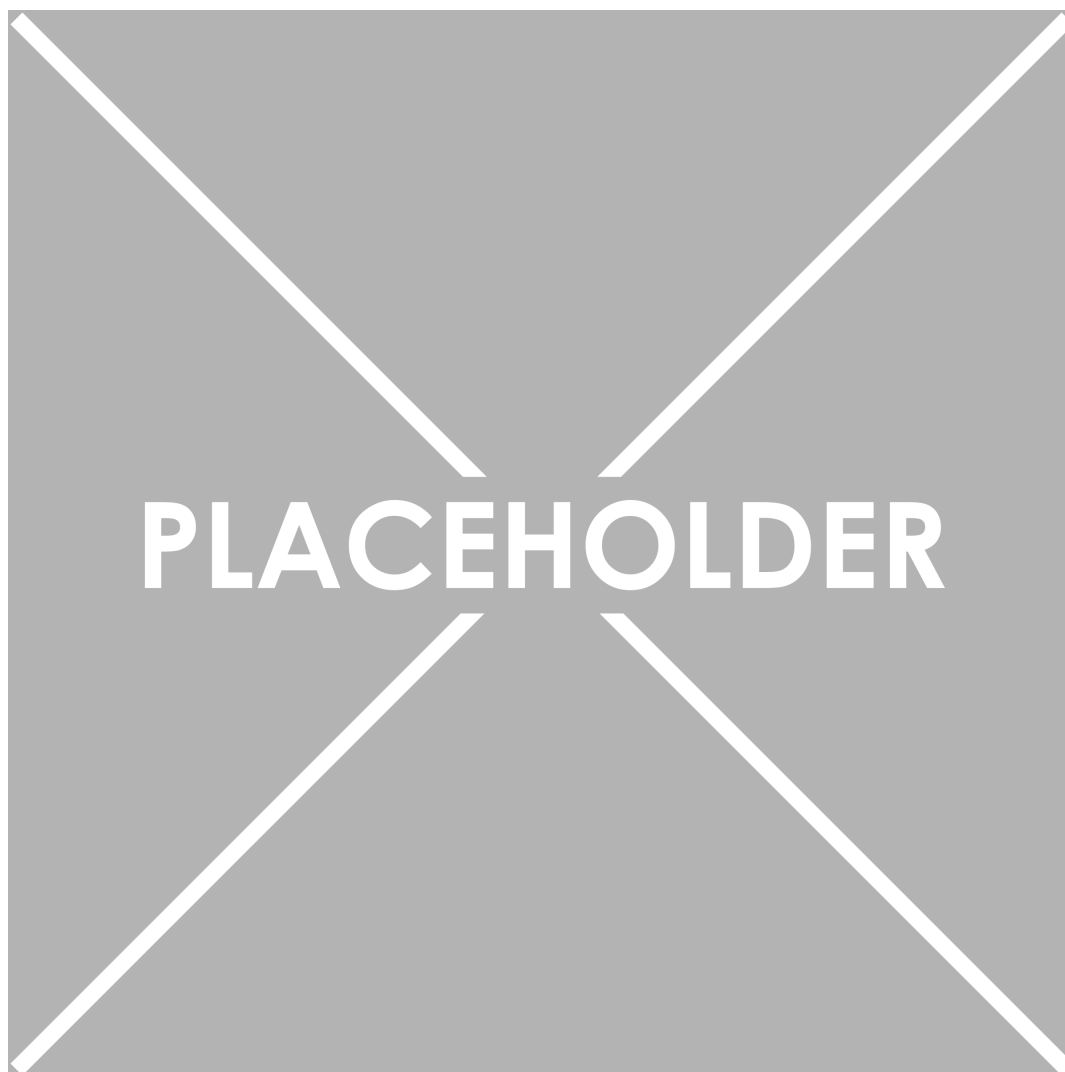


Figure 1: Monomers are placed in an initial configuration close to the expected equilibrium configuration and allowed to relax

- 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)

Simulated X-ray diffraction patterns were generated based on atomic coordinates to give a deeper understanding of the pore structure and spacing.

- 3 dimensional fourier transformed electron density generates 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

3 Results and Discussion

Varying number of monomers in each stacked layer between 4 and 8, as well as the benzene stacking configuration between sandwiched and parallel displaced, results in more than one stable structures.

- We did a systematic study of the properties resulting from each starting configuration
- In the real system, layers are stacked 3.7 Å apart based on WAXS data. Pore spacing should be $\approx 4.1\text{nm}$
- We showed that we can rule out systems consisting of 4, 7, and 8 monomers based purely on membrane dimensions ??
- A characteristic of all systems simulated in this way, is a defined, cylindrical and open pore structure. Benzene rings arrange in a helical conformation after equil. Membrane about 8 nm thick (Fig 2a)
- This will be called phase A for simplicity
- Sandwiched and parallel-displaced configurations are both stable for 100's of nanoseconds and give reasonable xray diffraction patterns.
- hypothesis: Parallel displaced is more stable and allows the benzene rings to stack closer together

Simulations of systems built with layers stacked 5 Å apart results in a pore structure characterized by high radial disorder.

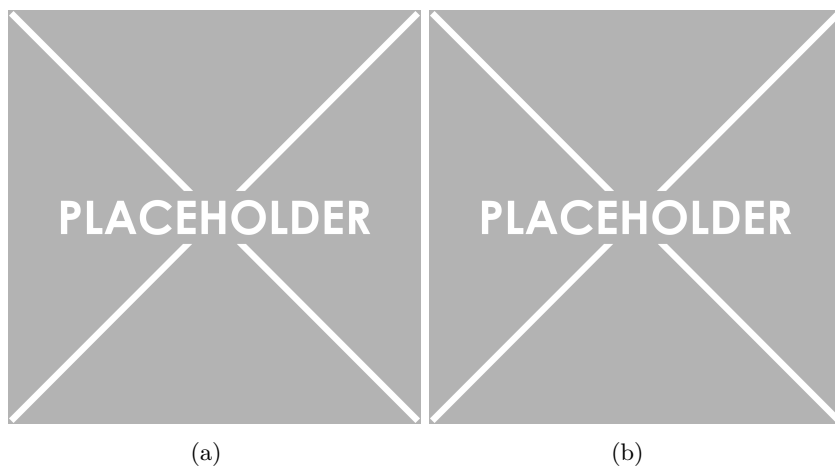


Figure 2: Different pore structure are clear between systems built with benzene rings stacked (a) 3.7 Å apart and (b) 5.0 Å apart

- This will be called phase B (2b)
- Like phase A, phase B can form at 280K. The only difference in simulations leading to this state, is the starting configuration
- The phase is also present when phase A is heated close to its isotropic transition point
- There are distinct differences in the membrane and pore structures between each state (Fig 2)
 - Phase B has a closed pore, while phase A is open. This will impact transport mechanisms
 - Phase B membranes are thicker
 - Consequently, the pore spacing is smaller
- We have at least two metastable states

Comparison of experimental 2D WAXS with simulated X-ray diffraction patterns produced from MD trajectories shows the most consistency with the parallel-displaced configuration

- Phase A
 - Purely stacked configuration is missing reflections at 2, 4, 8 and 10 0'clock, but they are there in the parallel displaced conformation
 - There is evidence that the stacked configuration will shift towards an offset configuration over time. WAXS spots show up after short simulations, in which case there is visible movement away from a perfectly stacked, towards a parallel displaced conformation

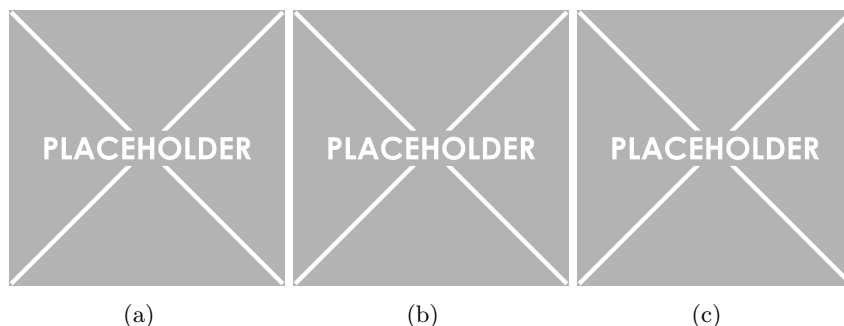


Figure 3: Phase A (a) provides a good match to experiment (b). Phase B (c) is missing reflections present in the experimental pattern

- Pi-stacking reflections are present in all cases but at spacings higher than shown experimentally. This is not surprising since GAFF will not properly treat pi-stacking.

- Phase B

- Stacking reflections present indicating separation of $\approx 5\text{\AA}$
- No spots at all which is consistent with the disorder shown by the rings in the pore

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 not 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 herin, 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