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.

While RO anad NF have seen many advances in the past few decades, they are far from perfect separation technologies

- 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)
- nanofiltration was introduced as an intermediate between RO and ultrafiltration
- Larger and well-defined pores drive down energy requirements while still affording separation of solutes as small as ions, to some degree
- Like RO membranes, NF membranes have a pore size distribution which limits their ability to perform precise separations

Nanostructured membranes can bypass many of the performance issues which plague traditional NF and RO membranes.

- 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
  - Zeolites - sub-nm pores with good MD results but interstitial defects created during manufacturing kill selectivity

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
  - What does the microscopic pore structure look like?
  - 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
  - Is rejection of ions due to donnan exclusion?
  - 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, restricting low energy pathways for solutes to follow?
- How can microscopic pore structure guide membrane design
- 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 provide evidence to support or call into question 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 rings exhibit an even stronger pi-stacking attraction
  - 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

- 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 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 comparied simulated X-ray diffraction patterns to experiment in order to match major features present in the 2D patterns
- We can predict ionic conductivity using two agreeing methods – Collective diffusion and nernst einstein
- We examined crosslinking mechanism and understand its influence on membrane structure

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.

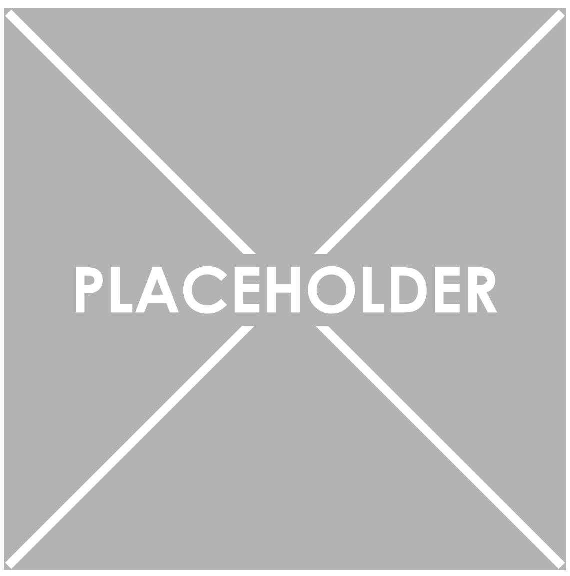
- Structure cooled from 1000 to 50 K over 10 nanoseconds
- Result not global minimum but close enough for structure building
- Antechamber used for atomtyping with gaff forcefield
- Used Openeye Quacpac molcharge.py to assign charges
- The am1bccsym method provided with Quacpac performs a conformational search and applies charges symmetrically based on the lowest energy subset of possible conformations
- Anneal again
- Multiple configurations saved from annealing trajectory to prove independence of starting config. A representative structure is given in Figure 1b
- Manual modifications to the structure were made to create specific geometries for X-ray 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.

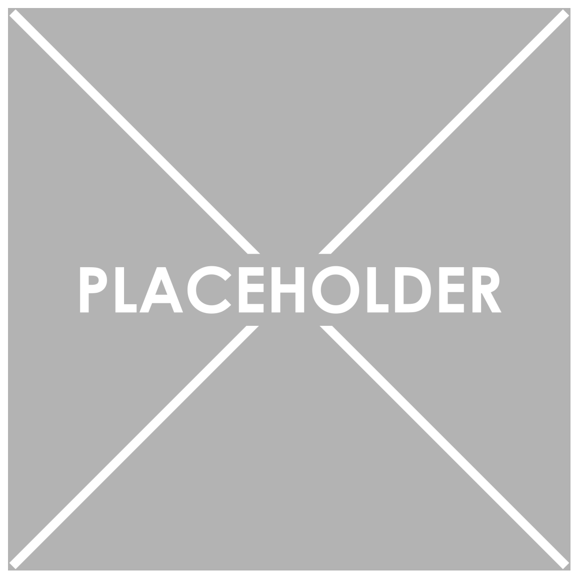
- Work done shows coarse grain model self assembly in 1000 ns , Citation: J. Phys. Chem. B 2013, 117, 4254-4262
- Attempts with Colh system not fruitful
  - Packed monomers into box with Packmol
  - Simulated for 100 ns with no progress shown towards self assembly
- Wrote code to assemble monomers into 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. 5)

- 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
- Decided on 20 layers using a system which held a vacuum gap above and below the membrane
- Too few layers leads to micelle-like formations



(a)



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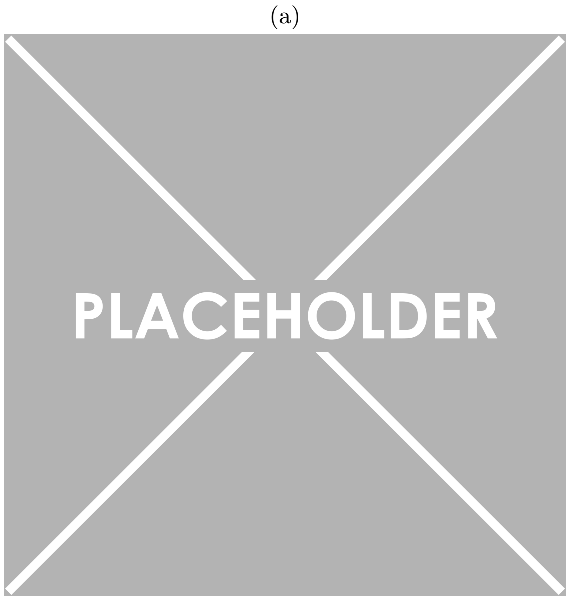

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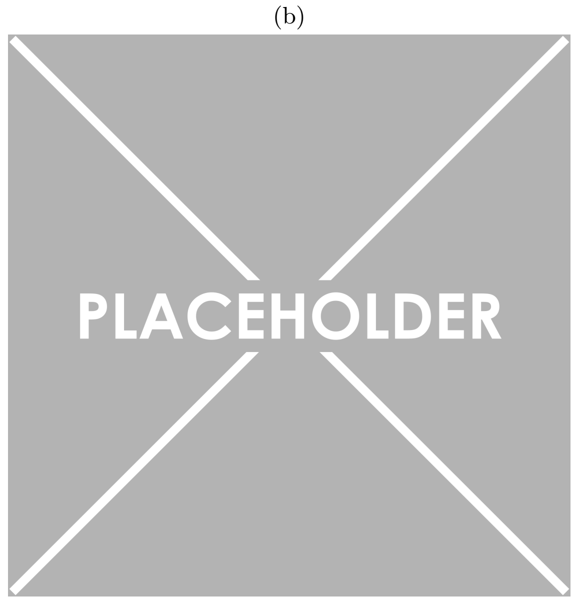


(d)

Figure 1: (a) The chemical structure of NAGA3C11 (b) The chemical structure visualized atomistically enhances intuition about system behavior (c) Wedge-shaped monomers assemble into layers (d) An atomistic view of a layer suggests geometric constraints based on monomer structure

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 Å(see figure 4) 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 Åapart which is not consistent with WAXS.
- 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 intermingle (this also helps ensure independence of starting monomer 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
- 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

The Nernst Einstein relation and the Collective Diffusion model were both applied to the system in order to estimate 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 (reference to computational electrophysiology)
- We must also be sure that our analysis of results is consistent with the method used 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

3 Results and Discussion

In order to construct an initial configuration which gives reliable trends, we need to understand the composition of layers, how far apart to stack the layers, and how to orient them with respect to each other.

To understand the composition of the monomer layers, we ran simulations created with 4 - 8 monomers per layer

- All configurations were stable for at least a short time
- We showed that we can rule out systems consisting of 4, 7, and 8 monomers based purely on membrane dimensions (Table 1)

The initial distance between layers is a key determining factor of the equilibrium configuration.

- In the real system, layers are stacked 3.7 Åapart based on WAXS data.
- 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 3a)
- This will be called phase A for simplicity
- Simulations of systems built with layers stacked 5 Åapart results in a pore structure characterized by high radial disorder.
  - This will be called phase B (Fig 3b)
  - The arrangement of sodium ions (which are closely bound to carbonyl head groups) can be well-approximated by a gaussian distribution
  - Like phase A, phase B can form at 280K. The only difference in simulations leading to this state, is the initial interlayer spacing
  - 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 3)
    * 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

We varied the relative interlayer orientation between sandwiched and parallel-displaced based on our knowledge of the stability of these two pi-stacking modes.

- Simulated Xray diffraction patterns generated from initial configurations of each pi-stacking mode, shows a clear relation between the parallel displaced configuration and major features present in the XRD patterns
- Diagonal spots in the alkane chain region are only generated for structures created in the parallel displaced configuration
- However, both configurations are stable for 100's of nanoseconds
- Xray diffraction of the sandwiched configuration after equilibration shows the spots. This indicates that there is a shift towards the offset configuration.

The stability of crystalline phases is strongly dependent on temperature, requiring evaluation of our force field's ability to represent the temperature at which we are simulating.

- All of the above simulations were ran at 280K and 300K
- Phase A is very stable at 280K
- when bumped to 300K it is also stable, however with a larger degree of disorder
- We see a clear transition to Phase B for any starting configuration when the temperature is raised above 310K (2)

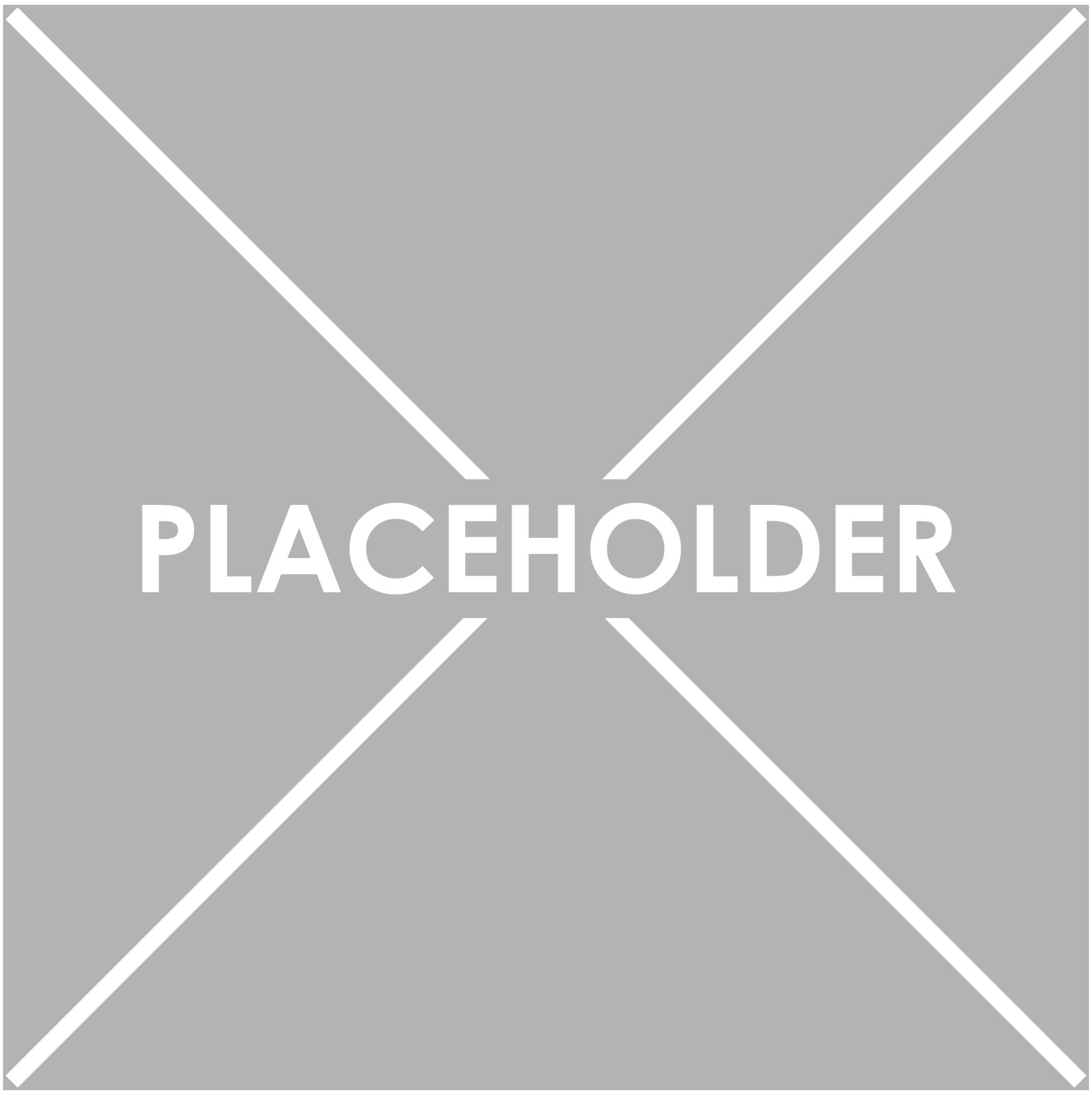
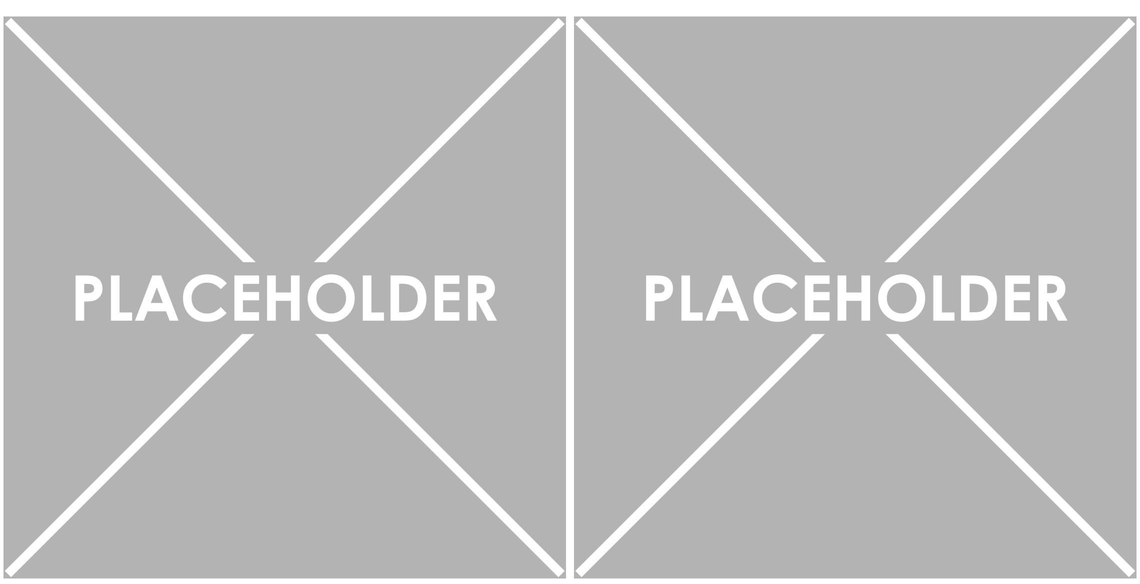


Figure 2: As temperature is increased, Phase A transitions to Phase B, as indicated by the shown order parameter. An order parameter of 1 indicates perfect ordering, while 0 indicates disorder

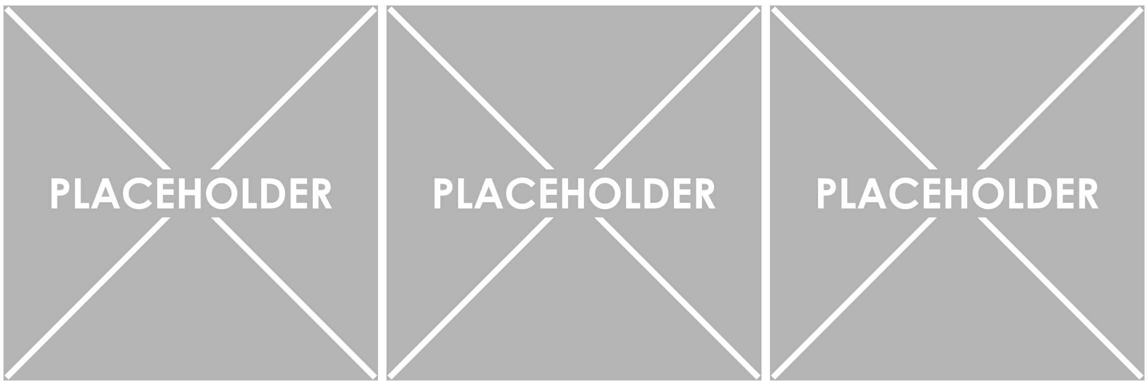
table	here

Table 1: A system built with 5 monomers per layer in a parallel displaced configuration results in a structure closest to experimental data



(a) (b)

Figure 3: There are clear differences in pore structure between systems built with layers stacked (a) 3.7 Åapart and (b) 5.0 Åapart



(a) (b) (c)

Figure 4: Phase A (a) provides a good match to experiment (b). Phase B (c) is missing reflections present in the experimental pattern

Nernst Einstein	Collective Diffusion

Table 2: Calculated ionic conductivity using Nernst-Einsten and Collective Diffusion agree within error. Both methods give calculated values of ionic conductivity which are higher than experimental values

- Simulating the system at room temperature should be sufficient to see both phases

A summary of all experiments and relevant structural parameters are presented in table 1

Full comparison of experimental 2D WAXS with simulated X-ray diffraction patterns produced from MD trajectories shows the most consistency with the parallel-displaced configuration made up of 5 monomers per layer.

- 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
  - 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.
  - Interestingly, the spots, which are usually associated with alkyl chain tilt, still appear with an average tilt angle of 0 degrees
- Phase B
  - Stacking refelctions present indicating separation of ≈ 5 Å
  - No spots at all which is consistent with the disorder shown by the rings in the pore
- Both phases show a ring in the simulated 2D WAXS patterns at q ≈ 1.4 Å^{-1} which is typical of packed alkane chains
- Both phases exhibit axial reflections. Even though the rings are not ordered in phase B, they are still partitioned into layers which gives rise to an axial refelction at the same distance where we expect alkane chain packing to be present

The model gives reasonable estimates of ionic conductivity for both phases.

- See comparison of methods in Table 2
- The methods agree reasonably well within error
- In the future, we will probably only use Nernst Einstein because it requires less simulation to get good statistics.
- Our calculated values are higher than experimental values, as expected.
- The real system, although mostly aligned and straight, still has a distribution of azimuthal angles, lowering the effective ionic conductivity of the bulk membrane.
- The ordering from isotropic to mostly aligned mesophases showed an 85x increase in ionic conductivity. We would expect more gains in a perfect system.
- The ordered phase has a higher calculated ionic conductivity than the disordered phase.

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 structures of new nanoporous membranes.

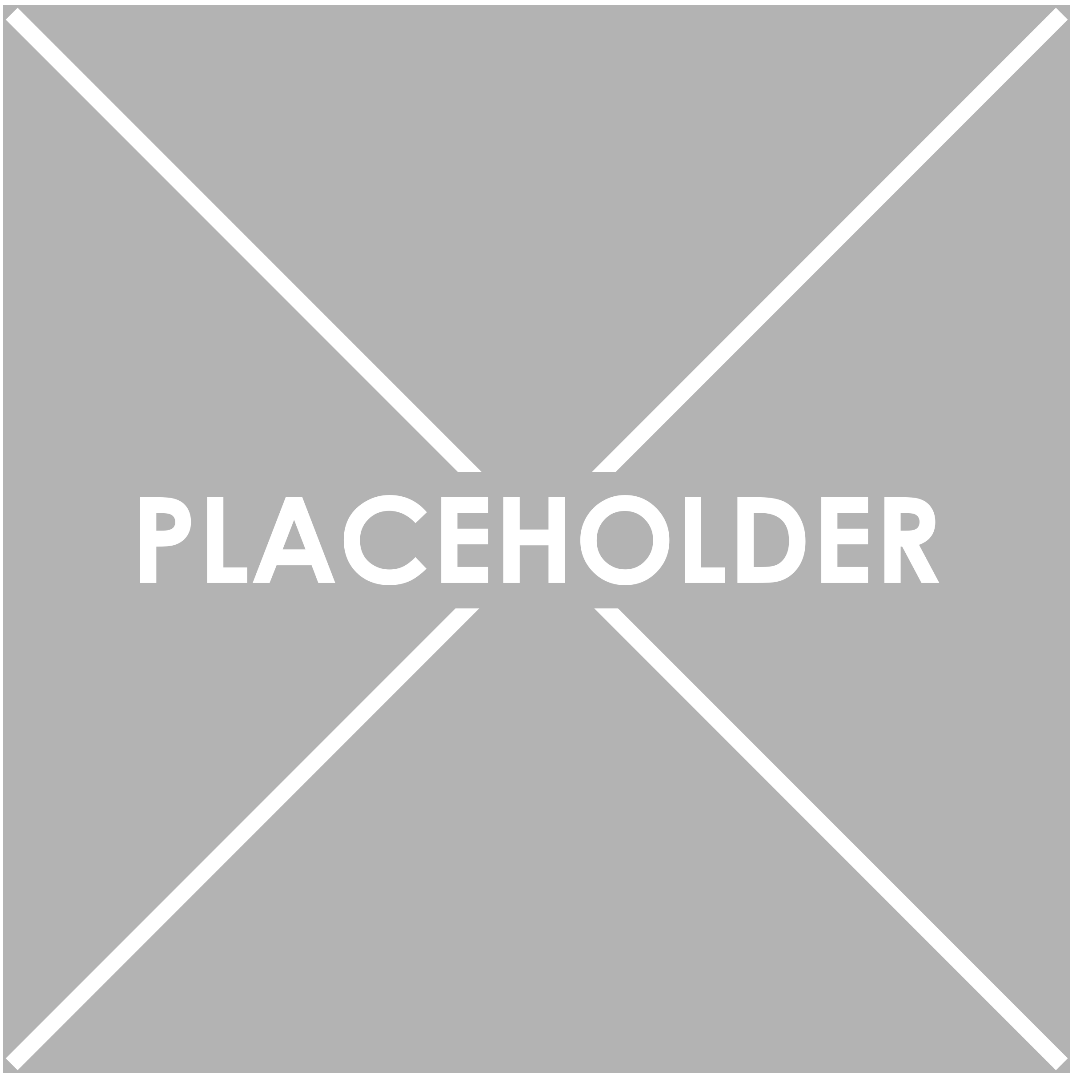


Figure 5: Monomers are placed in an initial configuration close to the expected equilibrium configuration and allowed to relax

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
- We have discovered the existence of two metastable configurations that persist at room temperature
- This methodology has been developed for a specific case but can be readily adapted to other LLCs

5 Supplemental Information

Monomer configurations

- Pore-to-pore equilibration plots
- Plots of other things that level off indicating equilibration
- 3D visualizations of different configurations tested
- Sodium ion distribution in disordered phase

Crosslinking details

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

Ionic conductivity

- MSD plots