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Computational Biophysics of the Lipidome

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Abstract

Lipids are an essential building block for human life. The amphipathic properties of these molecules enable them to form the cell membranes that act as a barrier between a cell's interior and exterior. By forming membranes, lipids are directly involved in various cell processes and in the regulation of membrane transport. In this work, we explored the effects of membrane asymmetry on red blood cells and on two types of placental cells. Membranes were analyzed using molecular dynamics simulations after utilizing existing experimental data. Changes in cholesterol partitioning and in membrane properties such as density and area per lipid revealed a clear impact of asymmetry on membrane dynamics. The results of this work provide new insight into membrane asymmetry and provide a framework for future studies to be completed.

Computational Biophysics of the Lipidome

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Introduction

Lipidomics

Lipids are one of four essential macromolecules found in nature. An essential building of every human cell, lipids are involved in various cell signaling processes[1]. They can also act as substrates for the post-translational modification of proteins or form glycolipids with carbohydrates[1,2]. Composed of a polar head and hydrophobic tail, a subclass of lipids known as phospholipids can inherently self-assemble into two distinct layers, known as a lipid bilayer[3]. This bilayer is present in cell membranes of all cells. The hydrophobic fatty acid tails of lipids are sequestered in the nonpolar interior of the bilayer, while the polar head groups are organized on the exterior of the bilayer[3]. The lipid bilayer provides a functional barrier between cell and environment where, along with proteins, lipids help mediate transport across the membranes[5]. The composition of the membrane will vary across different cell types to cater to their different environments and functions. It is also understood that the two leaflets of the lipid bilayer, the exoplasmic leaflet (EL) and cytoplasmic leaflet (CL), are asymmetric in composition. However, a detailed description of this asymmetry, and the consequences that result, remain an elusive goal in the study of lipids[6].

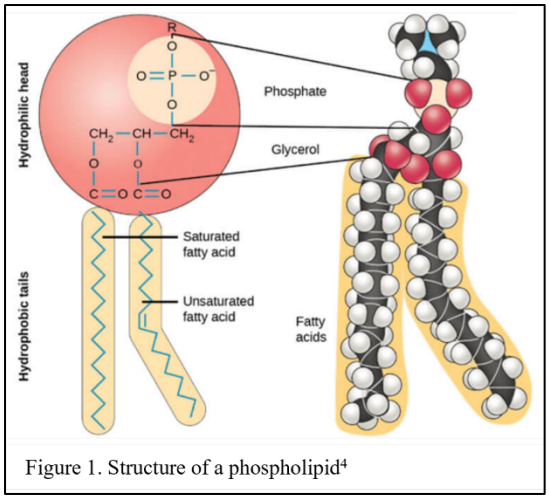


Figure 1. Structure of a phospholipid[4]

The lipidome describes the comprehensive profile of lipids within a cell[2]. The lipid profile of a plasma membrane varies among different organisms, organs, tissues, and cells. Tens of thousands of lipids have been identified at different concentrations across cell types[1]. Lipids are typically organized into families according to head group, then divided into subtypes based

on the acyl tail length and saturation. Each double bond in the fatty acid tail represents a degree of unsaturation. The diversity of lipids found in cells, and the presence and absence of various lipid subtypes in different cells, suggests that different lipids are responsible for different cellular functions. Furthermore, factors such as diet, disease, and age can influence the lipidome and change the composition of our cell membranes resulting downstream effects on cellular signaling and transport[5]. A multitude of major diseases including diabetes, Alzheimer's disease, cancer, cystic fibrosis, and dementia have been linked with alterations to the lipidome[2,5,7].

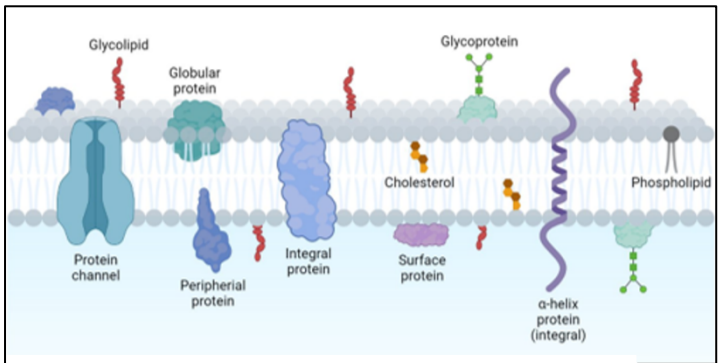


Figure 2. Cross-sectional example of a plasma membrane[4].

One goal of lipidomics is to determine how lipid diversity is responsible for various biological processes[1,5]. A thorough understanding of the lipid-lipid and lipid-protein interactions is needed as it is these interactions that yield many significant downstream effects[2]. Advancements in studying the biophysical and mechanical properties relevant to lipids can improve the understanding of lipid interactions and of lipid roles in facilitating membrane transport[1]. To accomplish this goal, comprehensive lipidomic profiles of cell membranes are needed. This would include the overall membrane composition of different cells as well as a description of lipid asymmetry and the lipid clusters that form laterally within the leaflets[2].

Placental Trophoblast Cells

The role of lipids in regulating the cell membrane is vital to the survival and proper functioning of all cells. This regulation is perhaps more important in the placenta than anywhere else. Regulating transport between the mother and fetus, the placenta provides the fetus with the

nutrients necessary for survival, while preventing entry of harmful substrates. It must also respond to the changing needs of the fetus throughout pregnancy, and as such, its composition and function is dynamic throughout pregnancy[8]. Within the placenta exist various cell types. Trophoblast cells are responsible for nutrient and waste transport as they are in direct contact with maternal blood[9]. The dynamic composition of trophoblast cells indicates that factors such as dietary intake, environmental toxins, and pharmaceutical agents can affect the fetus differently at different points of gestation. Although the effects of pharmaceutical agents on the developing fetus are not well understood, over 90% of women take at least 1 medication during pregnancy[8]. To address this concern, the CDC has emphasized the need for more data to better inform treatments during pregnancy[8].

In a recent study, the overall composition of the lipid membrane of placental trophoblast cells at different time points of gestation was reported[8]. This study provided a description of the lipid membrane of placental trophoblast cells during the first trimester and third trimester of pregnancy. However, the experimental methods used were unable to describe the asymmetric distribution of these lipids between the two leaflets. Understanding this asymmetry is necessary to complete our understanding of the membrane's biophysical properties and the lipid interactions that occur.

Red Blood Cells

Red blood cells (RBCs) are the most abundant cell type in human blood[10]. During the maturation process, RBCs lose all their organelles to allow the accumulation of as much hemoglobin as possible[10]. A fundamental part of all basic physiological dynamics, RBCs travel the body interacting with a wide variety of cell types to transport oxygen and carbon dioxide[10]. The cell's structure is also optimized to withstand the shear stress involved with navigating blood vessels[11].

This is accomplished through the linking of the cell's membrane to the cytoskeleton through two protein complexes creating a rigid yet flexible structure[11]. The multitude of interactions as well as the shear stress experienced by the RBC highlight the significance of the cell's membrane in regulating both facilitating transport and maintaining structure. Furthermore, various diseases such as HS, are associated with dysregulated lipid metabolism in the RBC membrane that interferes with the linkage of membrane to cytoskeleton[11]. While limitations in available methodologies introduce difficulty in investigating membranes of different cell types with organelles present, the lack of membrane bound organelles in the RBC makes studying this cell both easier and more preferable[6].

One recent report was able to describe the lipidome of the RBC membrane in detail[6]. Not only were they able to describe the lipid composition of the membrane in its entirety, but they were also able to define the asymmetric distribution of lipids across the two leaflets. While other studies have confirmed the presence of membrane asymmetry in different cell types, none have described it to the level of detail described in this study[6]. Utilizing this asymmetric data can not only better our understanding of the fundamental interactions that occur between the RBC membrane and cytoskeleton, but can also provide a starting point for studying plasma membranes of any cell type.

MD Simulations

Computational modeling utilizes mathematical and physics-based algorithms to study complex systems. It enables researchers to study systems of interest at high resolutions with increased efficiency compared to many experimental methods. The wide range of computational tools provide researchers the ability to manipulate systems to more accurately fine tune experiments to meet desired goals[12].

Molecular Dynamics (MD) simulations are a method for computationally studying biological systems and their molecular interactions at the atomic level[13]. The method employs the use of newton's laws of motion to investigate the motion of atoms and molecules and predict their trajectories over a given timeframe through an iterative process. A box shaped environment is constructed for systems and each atom is assigned specific coordinates in the x, y, and z-axes. Atoms move in response to the forces applied on them and continue to influence other atoms within the system. As atoms in the system move throughout the simulation, the changing interactive forces are continuously calculated and used to calculate the net force acting upon each atom. The predetermined masses of each atom and the changing velocity create new coordinates for atoms as the simulation progresses and forces act upon the atoms. MD systems have a limited volume that is determined by the box size of the system. By applying periodic boundary conditions, and infinite replication of the box in all three dimensions creates an unrestricted border that allows atoms to pass through the box walls[13].

Different models of simulations utilize different levels of resolutions. Depending on a researcher's system or goals, employing the use of different resolutions can ensure the desired information and level of detail are attained at the most efficient means possible. Atomistic systems describe each atom independently, providing the highest level of detail and accuracy. These systems are, however, computationally expensive as a simulation of a system on the nanosecond time scale can take up to weeks or months to complete. Coarse-grained (CG) systems can be conducted up to the millisecond timescale and work by grouping atoms together into "coarse-grained" beads[13]. By grouping small numbers of atoms together, this method become more computationally affordable and is still able to preserve a level of chemical detail needed for the system.

Experimental Overview

Despite their essential functions and wide diversity, lipids have not been as well studied as proteins[1]. In comparison to protein studies, there are a lack of reliable techniques to visualize lipids and manipulate their levels globally and locally[1]. Quantitative compositional analyses have been limited to specific lipid families and rarely include glycolipids or cholesterols[2]. Studies are typically carried out experimentally utilizing mass spectroscopy[14]. While experiments utilizing MS can aid in identifying membrane compositions, more information is needed on the mechanical and physical properties of lipid membranes as well as the lipid interactions that occur. Moreover, studying cells like those within the placenta, is difficult to conduct experimentally due to moral and ethical obstacles[8].

Computational simulations can help address this dilemma and bridge the gap between lipid composition and function to improve our understanding of the biophysical properties of the lipid membrane[5]. MD simulations can provide theoretical and computational insights at high resolutions that would otherwise be inaccessible or unfeasible experimentally. These simulations can enable the study of lipids and membranes at high levels of detail that would otherwise be unattainable through experimental methods. In this work, coarse-grained (CG) simulations were employed to study three distinct lipid membranes. To investigate the effects of lipid asymmetry on the biophysical properties of the plasma membrane, we developed cell membrane reflecting differing compositions of three cell types. Cell membranes of the red blood cell, placental 1st trimester trophoblast cell, and placental 3rd trimester trophoblast cell were constructed based on membrane compositional data from recent experimental studies[6,8]. Our coarse-grained MD simulations revealed differences in leaflet fluidity among the three membranes, resulting from

differences in lipid compositions, cholesterol partitioning, membrane dynamics, and lipid-lipid interactions.

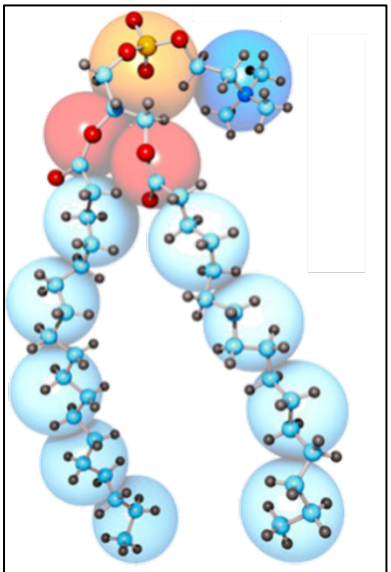


Figure 3. Coarse-grained representation of a lipid in the MARTINI model[17]

Methods

The Martini force field was utilized in the simulations of the lipid membranes[15]. The Martini model is based on a four-to-one mapping scheme, where and average of four non-hydrogen atoms and their associated hydrogen atoms are represented by single CG bead or interaction center. Each bead is classified as one of four categories; polar, nonpolar, apolar, and charged, and further classified into subtypes under each category. The Martini model was initially developed for lipid systems but has been extended for proteins carbohydrates and other molecules[16]. The Martini model was used to map lipids in our membrane as well as polarizable water molecules used in the systems.

The GROMACS 2019.4 package was used for all MD simulations[18]. The minimization was followed by equilibration in the isothermal-isochoric (*NVT*) conditions for 50 ns. This was followed by an isothermal-isobaric (*NPT)* equilibration for 100 ns. The temperature was maintained at 310.15 K and pressure was maintained at 1 bar. Periodic boundary conditions were applied in all three dimensions. The simulations were then performed in triplicates, each for 5 µs.

Table 1. Asymmetric ratios of lipid families.

Lipid Family Name	Two Letter Name	EL	CL
Phosphatidylcholine	PC	65%	35%
Sphingomyelin	SM	97%	3%
Phosphatidylserine	PS	4%	96%
Phosphatidylinositol	PI	50%	50%
Phosphatidylinositol - Phosphate	PIP	0%	100%
Phosphatidylethanolamine	PE	0%	100%
Phosphatidylethanolamine - Plasmalogen	PEP	20%	80%

Three lipid membranes, each patches 30×30 nm^2 in size, were constructed in the CG resolution using the *insane.py* script[19]. The membranes were each placed in a 30×30×15 nm^3 simulation box and solvated with standard Martini water (9:1 of W:WF) and 150 mM NaCl[16]. The overall membrane compositions for each of the three membranes were acquired from experimental studies and were subject to asymmetric partitioning according to data available on lipid head group asymmetry in the red blood cell[6,8]. Multiple subtypes of lipid families were present in the membranes and a detailed description of the membrane composition can be found in Table A1 and Figures A1-A3. This asymmetric partitioning of lipids in the three membranes was assigned according to lipid headgroup asymmetry[6] (Table 1). The two membrane leaflets, exoplasmic (EL) and cytoplasmic (CL), consisted of distinct lipid compositions with an equal total number of lipids in each leaflet (Table 2).

Table 2. Lipid compositions for each membrane

	RBC		P1T		P3T	
Lipid Family	EL	CL	EL	CL	EL	CL
PC	534	315	1063	478	862	386
PE	0	289	0	677	0	505
PEP	54	236	0	0	0	0
PI	0	52	112	100	197	180
PS	26	289	16	250	22	422
SM	593	26	322	8	425	13
CHOL	810	810	380	380	380	380
Total	2017	2017	1893	1893	1886	1886

Although cholesterol was reported to be present in the experimental studies of these membranes, a detailed description of the cholesterol distribution was unavailable from these studies. Previous studies of placental trophoblast cell suggest the cholesterol concentration to be roughly 20% of the lipid composition in the membrane, while red blood cell studies suggest it to be 40% [2, 20]. As such, these proportions were used for their respective membranes and cholesterol

was distributed evenly across the two leaflets for all three membranes at the start of each simulation.

Results and Discussion

The asymmetric lipid profiles for the three membranes analyzed for this work include the red blood cell (RBC), placenta 1st trimester trophoblast cell (P1T), and placenta 3rd trimester trophoblast cell (P3T). Analyses were conducted following the 5 μs simulations, and data was confirmed through triplicate runs of each membrane.

Much of the biophysical properties of the membrane, such as density, thickness, or lipid order, are believed to be heavily influenced by the presence and distribution of cholesterol within the membrane[21]. In most mammalian cells, cholesterol is the most abundant lipid in the plasma membrane[22]. While the asymmetric distribution of phospholipids is well established for the two leaflets of the plasma membrane, there remain contradictions in the literature regarding cholesterol distribution between leaflets in the bilayer[21, 23]. Due to its small size relative to phospholipids, cholesterol can flip readily between leaflets and can also reside in the midplane of a bilayer[22]. This dynamic presence in the membrane enables cholesterol to adjust its relative leaflet concentration as needed to respond to various stimuli. Analyzing this dynamic behavior of cholesterol is experimentally challenging due to limitations in existing methodology[1]. MD simulations, however, can track cholesterol flipping on the sub microsecond timescale. Some studies have indicated that cholesterol has a preference for the EL due to its interactions with saturated tails of SM and PC[21]. Contrarily, others claim that the abundance of PE in CL provides the leaflet a negative curvature that is favored by cholesterol[21]. Other reports indicate a symmetric distribution of cholesterol between leaflets[21].

An analysis of cholesterol distribution was done for each of the three membranes. Although cholesterol was evenly distributed between the two leaflets of each membrane at the start of the simulations (Table 2), cholesterol molecules were given the freedom to flip transversely between the leaflets over time. Cholesterol flipping began in pre-equilibrium NVT and NPT stages and persisted throughout the 5 μs simulations.

Of the three membranes, the RBC had the greatest proportion of cholesterol in the membrane, as it made up 40% of its total composition, compared to only 20% of the total composition of each of the placental membranes. Table 2 shows that composition of the EL in all three membranes is dominated primarily by the PC and SM lipid families. Meanwhile, the composition of the CL of all three membranes has a more balanced distribution of lipids.

As a result of its high cholesterol concentration, the RBC membrane had the greatest number cholesterol flipping events in our simulations. Cholesterol flipping events were measured every 0.1 μs and were defined as a change in a cholesterol's location within the membrane between two consecutive measurements. The rate of flipping remained relatively constant throughout each of the simulations. On average, the total number of flips per 0.1 μs timestep was ~456 flips, ~212 flips, and ~205 flips for the RBC, P1T, and P3T membranes, respectively (Figure 4a). Normalizing for cholesterol concentrations, the average number of flips per 0.1 μs for RBC would be ~228 flips. Although the RBC had the most flipping events, the rate of flipping per cholesterol was nearly identical to that of the two placental membranes, indicating the difference in composition among the three membranes did not affect cholesterol flipping.

An equilibrium cholesterol concentration is reached in each of the membranes within 0.5 μs. Cholesterol location was assigned to a location based on proximity of the -OH head group of cholesterol to the phospholipid head groups in one of the two leaflets. The cutoff distance was 11

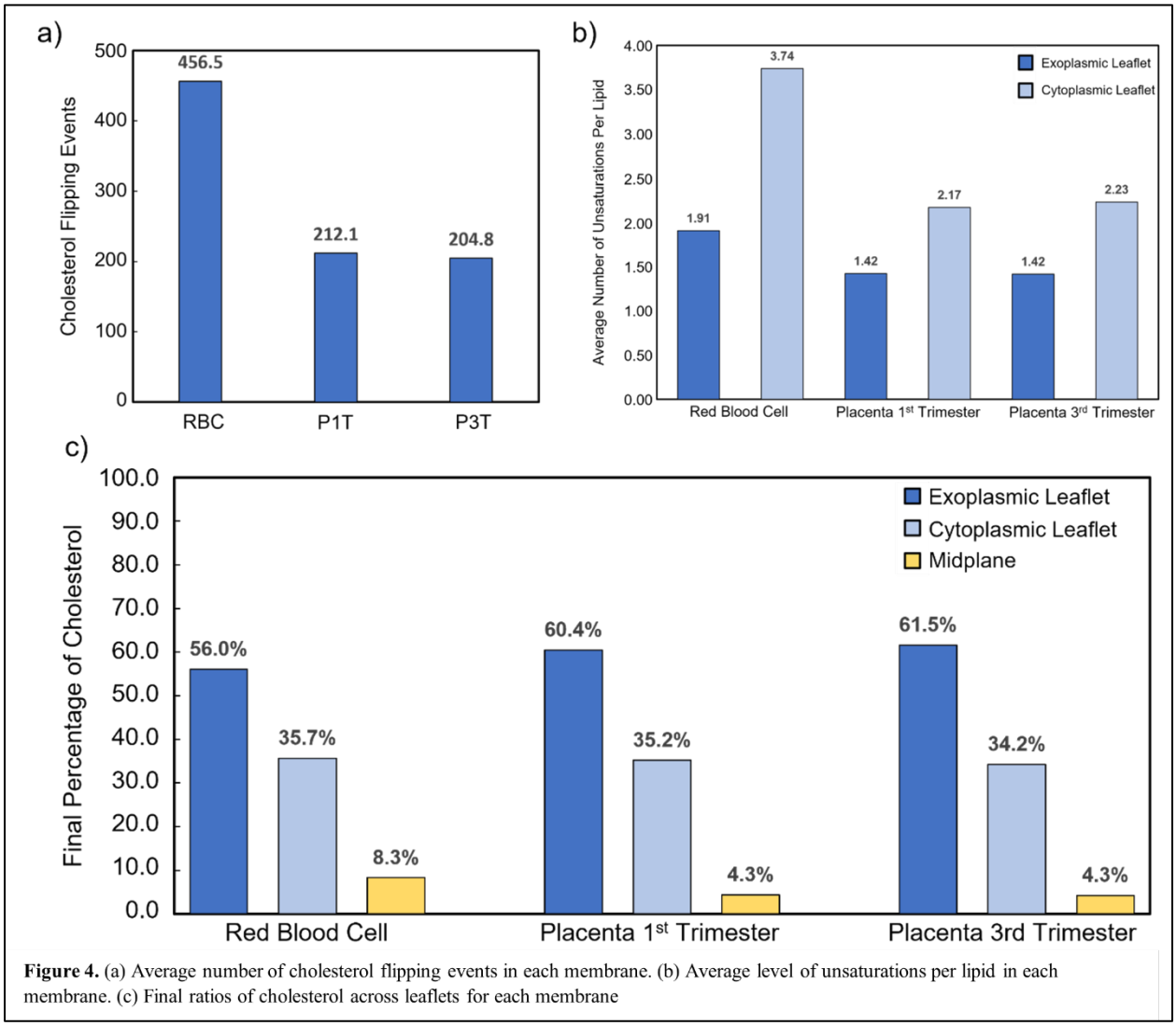


Figure 4. (a) Average number of cholesterol flipping events in each membrane. (b) Average level of unsaturations per lipid in each membrane. (c) Final ratios of cholesterol across leaflets for each membrane

angstroms from the phospholipid heads of each leaflet and any cholesterol that was outside the cutoff was assigned to the midplane of the bilayer. Because the membranes are not uniform in thickness, in certain regions of the membranes the bilayer was thin enough where a single cholesterol head group could be within 11 angstroms of both leaflets simultaneously. In these cases, cholesterol was assigned to the leaflet it was closer to. Figure 4c relates the final ratios of cholesterol across leaflets within each of the membranes.

For all three membranes, cholesterol reaches equilibrium concentration in the membrane within 0.5 μs. Our simulations reveal that for all three membranes, cholesterol favors the EL (Figure 4c). This may be due to a variety of factors. The partitioning of lipids according to head

group asymmetry resulted in the asymmetric distribution of acyl chain unsaturation, with a clear disparity across the two leaflets of all three membranes where the CL had more unsaturation on average that did the EL as seen in Figure 4b. The high saturation levels of the EL may be what is driving cholesterol towards it, as the acyl chains with less double bonds or "kinks" create more space for cholesterol to fit in between the phospholipid tails. Furthermore, the concentration of SM and PC lipids is biased towards the EL of all three membranes. These results are in agreement with previous studies that have suggested that strong interactions between cholesterol and the saturated tails of SM and PC drive cholesterol towards the EL[10].

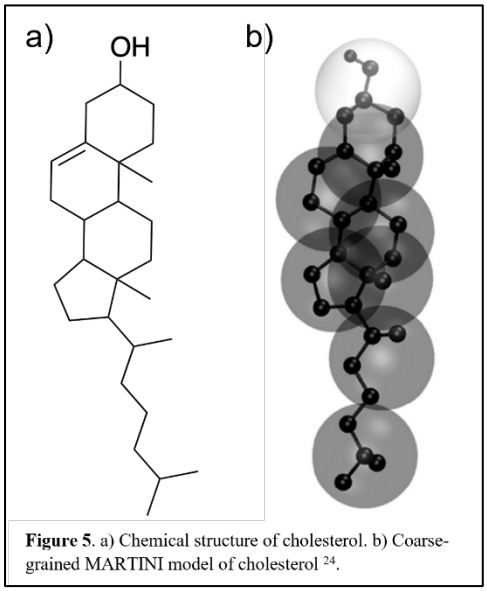


Figure 5. a) Chemical structure of cholesterol. b) Coarse-grained MARTINI model of cholesterol [24].

Of the three membranes, the RBC had the most unsaturation in both the EL and the CL (Figure 4b). The EL lipids of the RBC had an average of 1.91 unsaturations/lipid as compared to 1.42 unsaturations/lipid in both placental membranes. Similarly, the CL has 3.74 unsaturations/lipid in the RBC compared to 2.17 and 2.23 unsaturations/lipid in the two placental membranes. The abundance of cholesterol in the RBC in comparison to other cells is likely a mechanism to support membrane integrity. Being a cell that must withstand more sheer stress from its environment than most other cells, the RBC must have a rigid structure that can withstand such force. Specifically, the abundance of cholesterol in its EL could act as a mechanism to further withstand shear stress exhibited from the environment and more tightly regulate transport of external molecules into the cell.

The RBC also had the highest percentage of cholesterol in the midplane with ~9%, as opposed to ~4% in each of the placental membranes (Figure 4c). Some studies have shown that cholesterol has a greater preference for the midplane in the case of polyunsaturated bilayers, where there is a great deal of phospholipids that contain multiple unsaturations in their acyl chains[22]. This would agree with the results shown here, indicating that the high levels of unsaturation in the RBC will "push" more cholesterol molecules toward the midplane of the bilayer.

The asymmetric lipid distribution also yields differing area per lipid (APL) values between leaflets. In all three membranes the CL has a greater APL than the EL, likely resulting from differences in saturation levels (Figure 6). It is expected that since the CL has higher levels of unsaturation, its lipids would take up a greater area than the more saturated lipids of the EL. Moreover, membranes rich in saturated lipids are expected to be tightly packed and highly ordered whereas high levels of unsaturation are expected to yield less ordered and more loosely packed membranes[6]. The lipid order was assessed by calculating the order parameters (Scd) of hydrophobic tails for all lipids in each of the three membranes[25]. When comparing lipid families that are present in both the EL and CL, the EL lipids are on average more ordered than the CL lipids for every one of these families. This trend holds true for all three membranes.

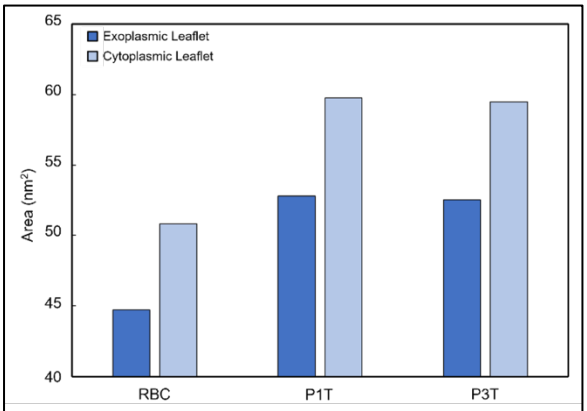


Figure 6. Area per lipid comparison of leaflets in each membrane

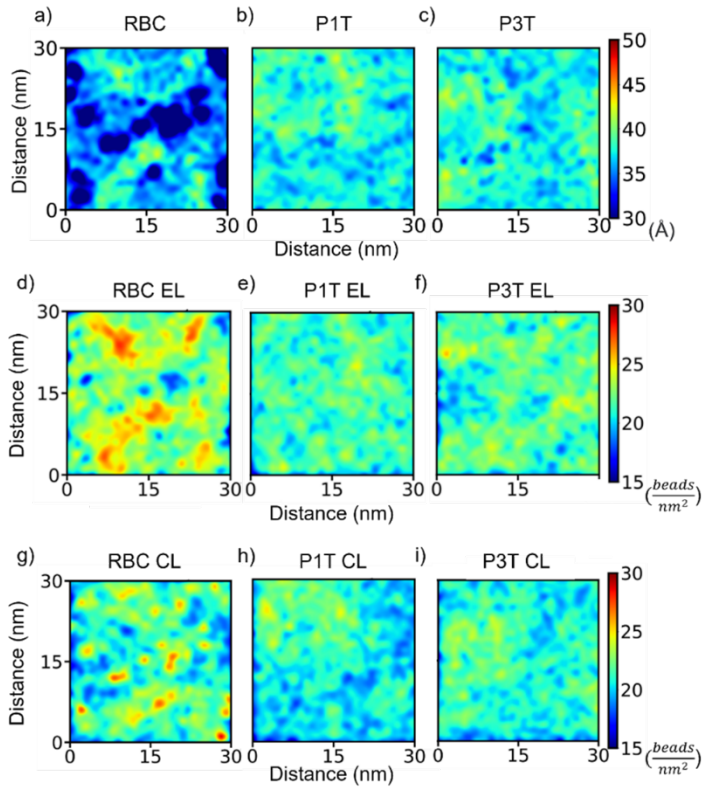


Figure 7. Thickness profiles of the (a) RBC, (b) P1T, and (c) P3T; the thickness color scale ranges from 30 Å (blue) to 50 Å (red). Density profiles of the (d) RBC EL, (e) P1T EL, (f) P3T EL, (g) RBC CL, (h) P1T CL, (i) P3T CL; the color scale ranges from 15 beads nm^{-3} (blue) to 30 beads nm^{-3} (red).

Being tightly packed systems, the three membranes all expand as they reach a state of equilibrium during the 5 μs simulations. The final box size of each system was larger than the initial box for each membrane (Table 3). The P1T and P3T membranes expanded more in the x and y planes than did the RBC membrane. Density profiles in all three membranes revealed the EL to be denser than the CL (Figure 7d-i). The favored partitioning of cholesterol towards the EL results in a greater total number of lipids in the EL by the end of the simulation and results in a more dense leaflet. In comparing the three membranes to one another, the RBC had the highest density in both the EL and CL in agreement with the result of this membrane expanding less than the other two in the x and y planes.

Table 3. Initial and final system box size for each of the three membranes

	Red Blood Cell	Placenta 1st Trimester	Placenta 3rd Trimester
Initial Membrane Size	30 x 30 x 15	30 x 30 x 15	30 x 30 x 15
Final Membrane Size	31.4 x 31.4 x 17.2	32.5 x 32.5 x 16.6	32.4 x 32.4 x 16.6

Membrane thickness plots also revealed the RBC to be the thinnest of the three membranes (Figure 7a-c). In comparison to the more saturated placental membranes, the high

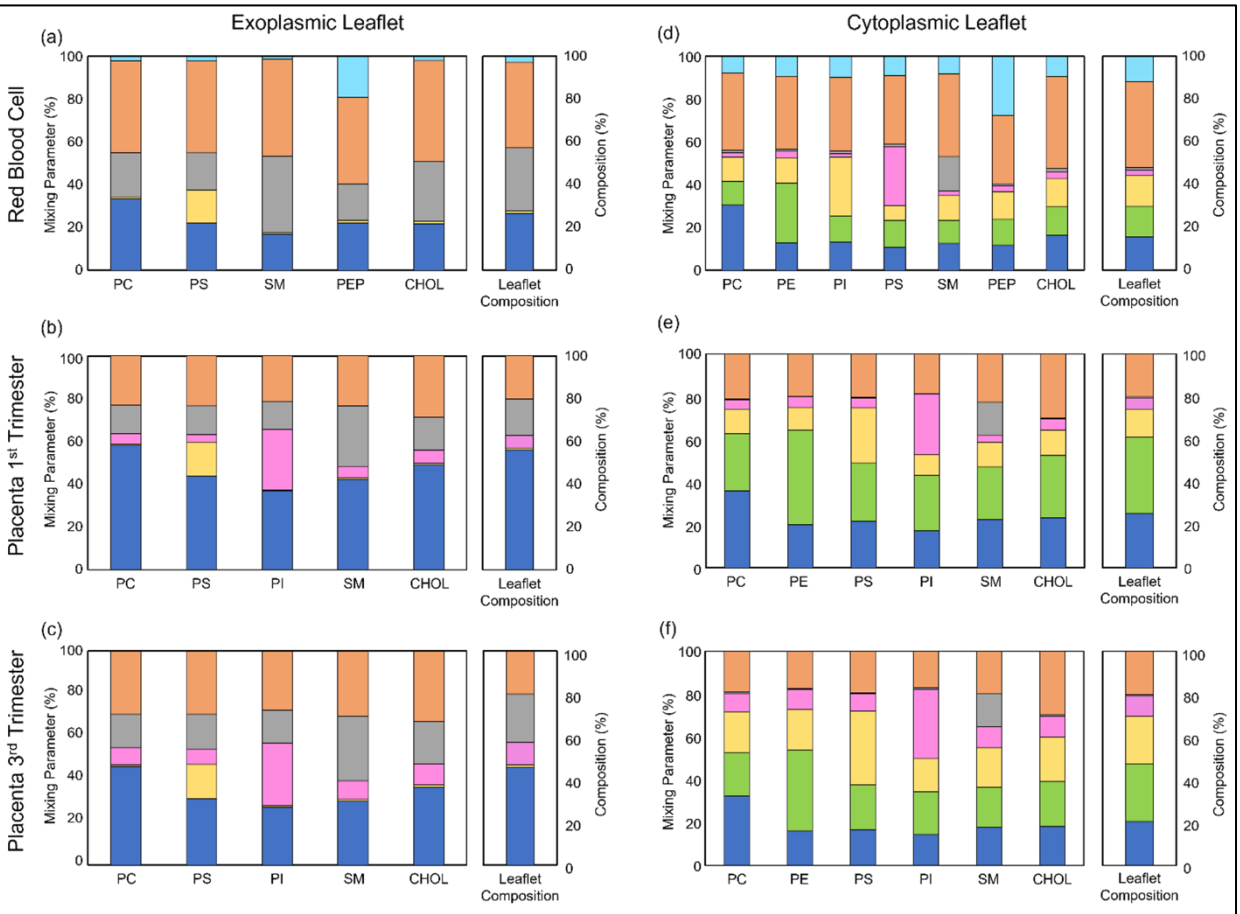


Figure 8. Lipid mixing profiles of lipids with other families in the (a) RBC EL, (b) P1T EL, (c) P3T EL, (d) RBC CL, (e) P1T CL, and (f) P3T CL. The lipid families include PC (dark blue), PE (green), PS (yellow), and PI (pink), SM (gray), cholesterol (orange), and PEP (light blue). The name of each reference lipid is on the x-axis, and the mixing parameter is shown in percentage on the y-axis. A profile of each leaflet's composition is represented to the right of each graph for comparison.

levels of unsaturation in the RBC create more kinks in acyl chains that create less upright and rigid tails and result in a thinner membrane.

A lipid mixing profile of each leaflet in the membranes was conducted to analyze the interactions between different lipid families (Figure 8). The interactions of lipids with other lipid families (co-localization) as well as within the same family (self-association) were determined by calculating lipid mixing parameters. Lipid mixing parameters provide a comparison of each lipid's affinity to establish interactions with other lipid types. Lipids showed a tendency to have higher self-association than colocalization with other lipids. Aside from this, mixing interactions closely followed trends in compositional data; lipids with a higher concentration in the leaflet

showed higher mixing with other lipid families, and lipids with low concentrations showed less mixing.

Conclusions

In this study, we investigated the asymmetrical membrane compositions of the RBC, P1T and P3T membranes using experimentally determined compositions of each membrane. Lipid-lipid interactions are primarily driven by relative leaflet concentrations and have a clear preference of lipid self-association. The differences in lipid membrane compositions between the three membranes in this work did not have a noticeable effect on the flipping dynamics of cholesterol. The clear preference of cholesterol towards the EL is likely a result of the similar asymmetric distribution of lipids. The EL is more saturated than the CL in all three membranes, where PC and SM are the prominent lipid families drawing cholesterol toward the leaflet. The increased in EL cholesterol results in an increase in leaflet density. On the other hand, the higher levels of unsaturation in the CL results in a less dense leaflet with greater APL.

High unsaturation levels of lipids in the RBC are the likely cause of the increased proportion of cholesterol within the RBC membrane's midplane, as well as the membrane being the thinnest amongst the three. Placental membranes showed greater membrane expansion in the x and y planes. This expansion along with the fact that the placental membranes were more highly saturated than the RBC, resulted in these placental membranes being less dense than the RBC making them less dense than the RBC.

The asymmetry of lipid distribution has a clear impact on membrane properties, but more work needs to be done. Experimental studies describing lipid membrane compositions are the bottleneck in the field of lipidomics, and new methodologies are needed. The presence of asymmetry across all cell types presents opportunities for research in all human cells, and also on

bacterial cells. Understanding the relationships of lipids in the membrane could reveal the roles of lipids in various cell processes and in controlling membrane transport.

Appendix

Table A1. List of names of lipid subtypes, their corresponding tails, and the lipid family they belong to according to head group

Four Letter Name	Corresponding Tails	Lipid Family by Head Group
LPPC	14:0-16:0	Phosphatidylcholine
DPPC	16:0-16:0	Phosphatidylcholine
POPC	18:0-18:1	Phosphatidylcholine
DOPC	18:1-18:1	Phosphatidylcholine
PIPC	16:0-18:2	Phosphatidylcholine
PAPC	16:0-20:4	Phosphatidylcholine
PQPC	16:0-20:3	Phosphatidylcholine
DPSM	18:1-18:0	Sphingomyelin
PNSM	18:1-24:1	Sphingomyelin
PLSM	18:1-24:0	Sphingomyelin
POPS	16:0-18:1	Phosphatidylserine
PGPS	16:0-20:1	Phosphatidylserine
PEPS	18:0-20:2	Phosphatidylserine
PAPS	16:0-20:4	Phosphatidylserine
POPE	18:0-18:1	Phosphatidylethanolamine
PUPE	16:0-22:6	Phosphatidylethanolamine
PEPE	18:1-20:4	Phosphatidylethanolamine
DOPE	18:1-18:1	Phosphatidylethanolamine
PIPE	16:0-18:2	Phosphatidylethanolamine
PAPE	16:0-20:4	Phosphatidylethanolamine
DIPE	18:2-18:2	Phosphatidylethanolamine
PEp1	18:1-20:4	Phosphatidylethanolamine - Plasmalogen
PEp2	18:2-20:4	Phosphatidylethanolamine - Plasmalogen
POPI	16:0-18:1	Phosphatidylinositol
DOPI	18:1-18:1	Phosphatidylinositol
PIPI	16:0-18:2	Phosphatidylinositol
PQPI	16:0-20:3	Phosphatidylinositol
PAPI	16:0-20:4	Phosphatidylinositol
PIP2	18:1-20:4	Phosphatidylinositol - Phosphate

Figure A1. Compositional distribution of RBC membrane across leaflets. Lipids separated by family, phosphatidylcholine (PC, cyan), sphingomyelin (SM, dark cyan), phosphatidylserine (PS, red), phosphatidylethanolamine (PE, blue), phosphatidylethanolamine plasmalogen (PEP, yellow), and phosphatidylinositol (PI, orange).

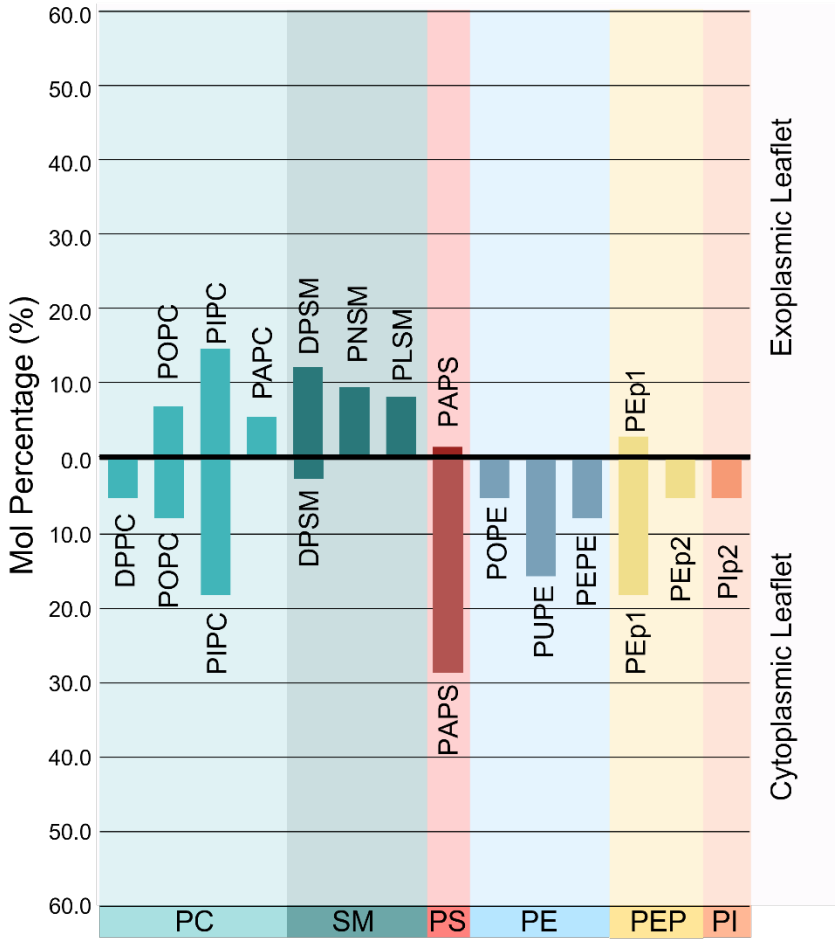
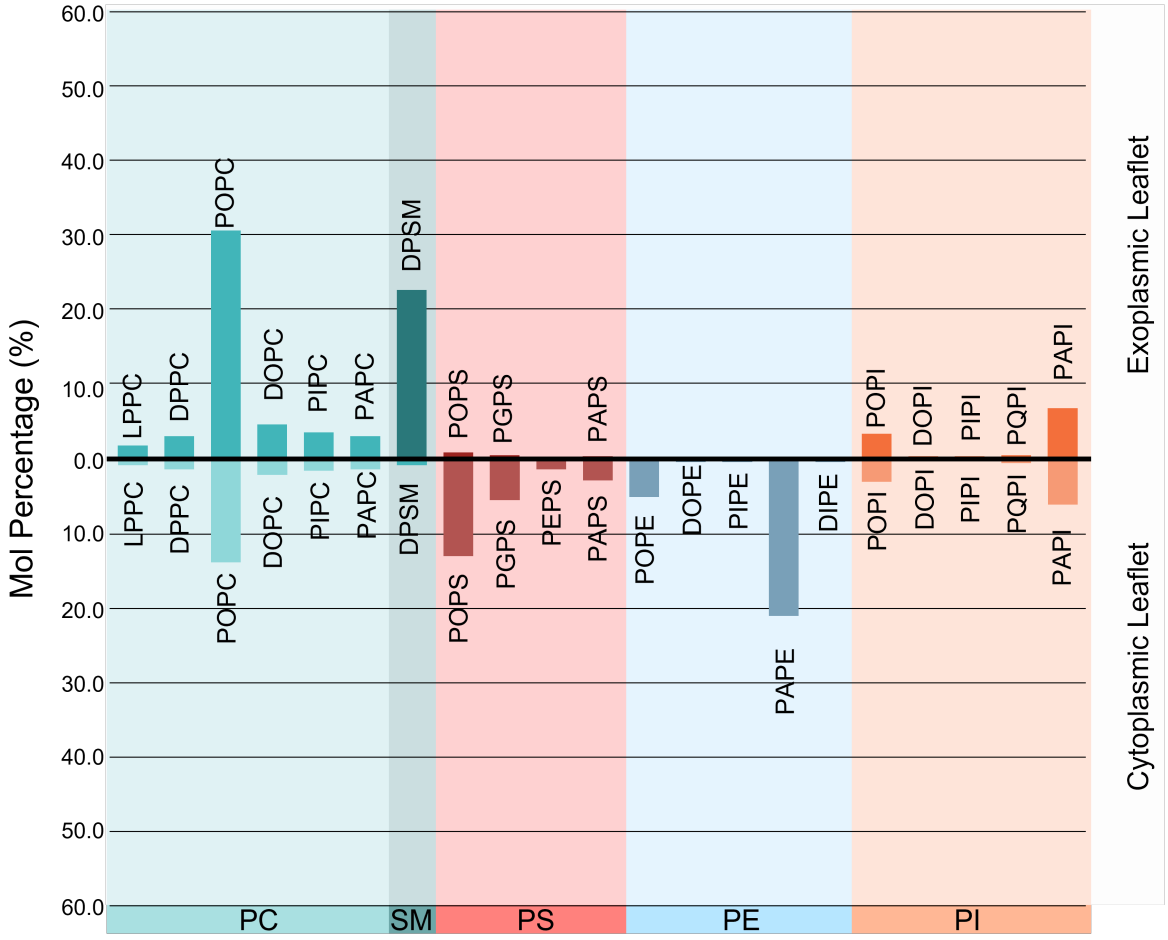


Figure A2. Compositional distribution of placental 1st trimester trophoblast membrane across leaflets. Lipids separated by family, phosphatidylcholine (PC, cyan), sphingomyelin (SM, dark cyan), phosphatidylserine (PS, red), phosphatidylethanolamine (PE, blue), and phosphatidylinositol (PI, orange).

Figure A3. Compositional distribution of placental 3rd trimester trophoblast membrane across leaflets. Lipids separated by family, phosphatidylcholine (PC, cyan), sphingomyelin (SM, dark cyan), phosphatidylserine (PS, red), phosphatidylethanolamine (PE, blue), and phosphatidylinositol (PI, orange).



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Vita

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Education

Syracuse University, College of Engineering and Computer Science

Chemical Engineering, Master of Science, May 2023

Le Moyne College

Chemistry, Bachelor of Science, December 2020

Presentations

Syracuse University, Graduate Research Day. April 2022.

Syracuse University, Stevenson Biomaterials Lecture Series. October 2021.

Work Experience

Research Assistant, Syracuse University January 21 – May 23

- Facilitated molecular dynamics simulations to study biological systems of lipids, proteins, and DNA structures
- Developed new Python and MATLAB scripts for improving existing systems and executing analyses
- Employed use of Excel and PowerPoint for data collection, analysis, and presentation

Teaching Assistant, Syracuse University January 21 – May 23

- Courses: Mass and Energy Balances, Experimental Methods in Chemical Engineering and Bioengineering, Biomaterials and Medical Devices, Senior Bioengineering Laboratory
- Taught concepts of reactor design, process flow diagrams, and statistical analysis
- Instructed students in projects involving: Python, JavaScript, App Development using React, CAD, and Arduino

Honors and Awards

Syracuse University Outstanding TA Award 2021

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