1. **Introduction about Ising Model**

1.1. **Physical Background.** The Ising Model is concerned with the physics of phase transitions. In this project, we try to model the domain formation of lipids by Ising model. Our starting point is lattices, which for us will be a finite set of regularly spaced points of a space of dimension $d = 1, d = 2,$ or $d = 3$. Generally, each lattice site in a $d$-dimensional lattice has $2^d$ nearest neighbors. The way we deal with the boundary is called a **wrap-around** model. An independent variable $\sigma_i$ is attached to each lattice site $i = 1, 2, \ldots, N$. The total energy of our system is as follows:

$$H = -E \sum_{<i,j>} \sigma_i \sigma_j - J \sum_i \sigma_i$$

in our simulation.

At low temperatures, there is not much random motion, and configurations lined up with external field ($J$ term) is favored and vice versa. At the critical temperature, spontaneous magnetization or phase transformation will occur (refer to fig1 or [2]). One important factor of Ising Model is the partition function. However, it is almost impossible to compute every probability of all the configurations.

In our model, since we only care about the domain formations, i.e. how lattice sites swap, we can draw the flip with probability from Boltzmann distribution. We have
not tested any simulation of phase transformation yet, which require to compute another physical quantity called free energy:

\[ F = F(\beta, E, J) = \lim_{N \to \infty} \frac{1}{N} \log Z(\beta, E, J, N) \]

([2]) If our model succeeds, F should be continuous function in 1-d case, and discontinuous (spontaneous magnetization) at the critical temperature.

1.2. Keller results. The main results in Keller’s paper – When domains are present in asymmetric membranes, each leaflet contains regions of three distinct lipid compositions, implying strong inter-leaflet interactions. Currently, we are able to simulate both symmetric and asymmetric bi-layers (just make the initial matrix identical or not), to the domain induction or suppression. In reality, compositions in one leaflet are affected by compositions in the apposed leaflet. However, our code doesn’t implement this feature. By the way, it’s meaningful to compare mono-layers with bi-layers.

When domains are present in asymmetric membranes, each leaflet contains regions of three distinct lipid compositions, implying strong inter-leaflet interactions.

1.3. Description of structure and its limitations (grid). As mentioned above, we use the wrap-up structure of lattices \( J = 0 \) here, i.e. no external field. \( \sigma_i \) is designated to up and down, or 1 and -1. 3 values, \( \alpha, \beta \) and \( \gamma \) serve as the contribution coefficients of our pair-units. If they are both 1, we multiply \( \alpha, \beta \) of -1 and \( \gamma \) if they do not parallel. Notice: since each time we just swap one pair of lattices, so we will just compute the energy of that specified unit.
2. Ising model

Energy comes from the nearest neighbor and the external field.

Energy is:

\[ H = - \sum_{(i,j)} \delta_{ij} \sigma_i \sigma_j - J \sum_i \sigma_i \]

Here

\[ \delta_{ij} = \begin{cases} 
\alpha, & \sigma_i = \sigma_j & \sigma_i > 0 \\
\beta, & \sigma_i = \sigma_j & \sigma_i < 0 \\
\gamma, & \sigma_i \neq \sigma_j \\
c, & c = r.max(\alpha, \beta) 
\end{cases} \]

\[ J = 0, \text{ no external field} \]

2.1. 1D Model.

2.1.1. Numerical Implementation.

(1) State 1: \( \begin{bmatrix} A \parallel B \parallel A \parallel B \end{bmatrix} \)
(2) State 2: \( \begin{bmatrix} A \parallel A \parallel B \parallel B \end{bmatrix} \)
(3) \( H_1 = \sum_{(i,j)} \sigma_i \sigma_j = -(1 - 1 - 1 - 1) = 4 \)
(4) \( H_2 = \sum_{(i,j)} \sigma_i \sigma_j = -(1 - 1 + 1 - 1) = 0 \)
(5) If \( H_2 < H_1: \)
   - Accept State 2
(6) Else:
   - \( p^* = e^{-\phi \Delta H} \)
   - \( p = \text{Unif}(0, 1) \)
   - If \( p < p^* \rightarrow \text{Accept State 2} \)
   - Else \( \rightarrow \text{Reject State 2} \)
2.1.2. Boltzmann Parameter, $\phi$. 
2.1.3. High $\phi \rightarrow$ Low $T \rightarrow$ Less Random $\rightarrow$ More Domains.
2.1.4. *Low φ → High T → More Random → Less Domains.*

![Bar charts showing domain formation in Lipid A and B](image)

2.1.5. *Quantifying Domain Formation.*

![Histograms showing averaged number of domains](image)
2.2. 1.5D Model.

State 1
\[ \ldots \parallel B \parallel A \parallel A \parallel B \parallel B \parallel A \ldots \]

State 2
\[ \ldots \parallel B \parallel A \parallel A \parallel B \parallel B \parallel A \ldots \]

\[ \ldots \parallel A \parallel A \parallel B \parallel B \parallel B \parallel A \ldots \]

\[ \ldots \parallel A \parallel A \parallel A \parallel B \parallel B \parallel A \ldots \]

2.2.1. Low inter-leaflet coupling, \( c \approx 0 \).

2.2.2. High inter-leaflet coupling, \( c \approx 1 \).
2.2.3. **Energy Decreasing with time.**

![Energy vs. Time Graph](image)

2.3. **3D Model.**

Top Layer

```
... : : : : ... 
... B A B B ... 
... B A B A ... 
... B A A B ... 
... : : : : ... 
```

Bottom Layer

```
... : : : : ... 
... A B A B ... 
... B B A A ... 
... A A A B ... 
... : : : : ... 
```

2.3.1. **Numerical Implementation.** using matlab to get the graphs:
2.3.2. Domain formation quantification.

3. Continuum Model

- An alternate approach using a continuum formulation was examined.
- Newtonian attraction/repulsion force analysis.

3.1. Model Formulation. We use an alternate approach to examine a continuum formulation. And Newtonian attraction/repulsion force analysis is also used.

The model is derived by writing $F = ma$ for each particle in the system.
The force felt by a particle is:

\[ F = \sum F_{\text{longrange attract/repel}} + \sum F_{\text{shortrange}} \]

The distance between particle 1, and particle 2 is:

\[ d_{12} = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2} \]

The attract force between particle I and particle 2 is:

\[ F_{12} = -\frac{k_1 \sigma_i \sigma_j}{d_{12}^2} \]

The attract force on particle i:

\[ F_i = -\sum_{i \neq j} \frac{\sigma_i \sigma_j k_1(\sigma_i, \sigma_j)}{d_{ij}^2} \]

The repel force on particle i:

\[ F_i = \sum_{i \neq j} \frac{\sigma_i \sigma_j k_2(\sigma_i, \sigma_j)}{d_{ij}^n} \]

Thus, the total combined forces upon particle j gives

\[ F_i = -\sum_{i \neq j} \frac{\sigma_i \sigma_j k_1(\sigma_i, \sigma_j)}{d_{ij}^2} + \sum_{i \neq j} \frac{\sigma_i \sigma_j k_2(\sigma_i, \sigma_j)}{d_{ij}^n} \]

For small \( d_{ij} \), \( k_2(\sigma_i, \sigma_j) = \begin{cases} 0 & \sigma_i \neq \sigma_j \\ k_2 & \text{etc} \end{cases} \)

Using Newton Method, we can get:

\[ m \ddot{x}_i + b \dot{x}_i = -\sum_{i \neq j} \frac{\sigma_i \sigma_j k_1(\sigma_i, \sigma_j)}{d_{ij}^2} + \sum_{i \neq j} \frac{\sigma_i \sigma_j k_2(\sigma_i, \sigma_j)}{d_{ij}^n} \]

Here \( b \dot{x}_i \) is the drag force.

\[ m \ddot{x}_i + b \dot{x}_i = -\sum_{i \neq j} \frac{\sigma_i \sigma_j k_1(\sigma_i, \sigma_j)}{d_{ij}^2} + \sum_{i \neq j} \frac{\sigma_i \sigma_j k_2(\sigma_i, \sigma_j)}{d_{ij}^n} \]

Here

\[ \sigma_i = \begin{cases} +1 & \text{on } A \\ -1 & \text{on } B \end{cases} \]

\[ k_1(\sigma_i, \sigma_j) = \begin{cases} c_1 & \sigma_i = \sigma_j \\ c_2 & \sigma_i \neq \sigma_j \end{cases} \]

\[ k_2(\sigma_i, \sigma_j) = \begin{cases} 0 & \sigma_i \neq \sigma_j \\ k_2 & \text{etc} \end{cases} \]
3.2. Non-dimensionalization. Non-dimensionalize the variables:

Let \( \tilde{t} = \frac{t}{T} \), \( \tilde{x} = \frac{x}{L} \) and \( \tilde{y} = \frac{y}{L} \)

So then \( \frac{d}{dt} = \frac{1}{T} \frac{d}{d\tilde{t}} \), \( \frac{dx}{dt} = \frac{1}{L} \frac{d}{d\tilde{x}} \) and \( \frac{d^2}{dt^2} = \frac{1}{T^2} \frac{d^2}{d\tilde{t}^2} \)

The dimension of \( k_1 \) is: \( [k_1] = \frac{mL}{T^2} \)

The dimension of \( k_2 \) is: \( [k_2] = \frac{m^{1+\alpha}}{T^\alpha} \)

so we can get \( b \tilde{x} = b \frac{d\tilde{x}}{dt} = \frac{bL}{T} \frac{d\tilde{x}}{d\tilde{t}} = \frac{bL}{T} \tilde{x} \) and \( \tilde{d}_{ij} = \frac{d_{ij}}{L} \)

\[
\frac{mL}{k_1 T^2} \ddot{x} + \frac{bL}{T} \dot{x} = \frac{1}{L^2} \sum_{i \neq j} \sigma_i \sigma_j \left( \frac{k_1 (\sigma_i, \sigma_j)}{L^2 \tilde{d}_{ij}^2} + \frac{k_2 (\sigma_i, \sigma_j)}{L^{\alpha-2} \tilde{d}_{ij}^\alpha} \right)
\]

Then

\[
\frac{mL}{k_1 T^2} \ddot{x} + \frac{bL^3}{k_1 T} \dot{x} = \frac{1}{L^2 k_1} \sum_{i \neq j} \sigma_i \sigma_j \left( \frac{1}{\tilde{d}_{ij}^2} + \frac{k_2}{k_1} \frac{1}{L^{\alpha-2} \tilde{d}_{ij}^\alpha} \right)
\]

so then we could get

\[
\begin{cases}
  bL^3 = k_1 T \\
  \frac{k_2}{k_1} \frac{1}{L^{\alpha-2}} = 1
\end{cases}
\]

then

\[
T = \frac{b}{k_1} \left( \frac{k_2}{k_1} \right)^{\frac{\alpha}{\alpha-2}}
\]

\[
L = \left( \frac{k_2}{k_1} \right)^{\frac{1}{\alpha-2}}
\]

since \( \frac{mL^3}{k_1 T^2} = \frac{mk_0}{b \left( \frac{k_2}{k_1} \right)^{\frac{3}{\alpha-2}}} \ll 1 \), then we can get

\[
m << \frac{b}{k_1} \left( \frac{k_2}{k_1} \right)^{\frac{3}{\alpha-2}}
\]

then

\[
\dot{x} = \sum_{i \neq j} \sigma_i \sigma_j \left( \frac{1}{\tilde{d}_{ij}^2 + \tilde{d}_{ij}^\alpha} \right) \cos \theta_{ij}
\]

\[
\dot{y} = \sum_{i \neq j} \sigma_i \sigma_j \left( \frac{1}{\tilde{d}_{ij}^2 + \tilde{d}_{ij}^\alpha} \right) \sin \theta_{ij}
\]

here

\[
\begin{cases}
  \cos \theta_{ij} = \frac{|x_i - x_j|}{d_{ij}} \\
  \sin \theta_{ij} = \frac{|y_i - y_j|}{d_{ij}}
\end{cases}
\]
3.3. **Results of Continuum Model.**

- The model formulation is consistent with the expected behavior of lipids in the leaflets.
- Takes into account the attraction between similar lipids, repulsion between dissimilar lipids, and “drag” through the cell membrane.
- The numerical implementation proved to be too complicated for math camp of this duration.

4. **Conclusions**

- Domain formation!
- Trend in $\phi$ Boltzmann parameter corresponding to critical temperature observed.
- A/B interactions difficult to observe for equal distribution of both types.

**References**


