Department of Physics and Astronomy
Heidelberg University

Bachelor Thesis in Physics
submitted by

Gabriel Scherer

born in Mainz (Germany)

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About ...

This Bachelor Thesis has been carried out by Gabriel Scherer at the
Institute for theoretical Physics in Heidelberg
under the supervision of
Prof. Tristan Bereau

Abstract

Contents

1 Introduction

Coarse-grained (CG) molecular dynamic (MD) models are a very effective method to simulate large molecular systems. In contrast to all atom simulation which resolve individual atomistic trajectories, CG models represent atomic groups as interaction sites or beads.

The reduced complexity of the system offers substantial acceleration compared to the atomistic approach making it possible to simulate much larger systems which are unattainable in all atom simulations. The most popular method for CG molecular dynamics is the MARTINI model with the Lennard-Jones potential as the underlying force-field.

This thesis employs the MARTINI model as a baseline for a system but then applies a different force-field, namely **dissipative particle dynamics** (DPD). To test this approach the self-assembly of a lipid bilayer is monitored and afterwards the mechanical properties are determined, more specifically the bending modulus.

Lipid bilayers are a fundamental biological structure as they constitute the basis of almost all membranes in cells. The polar heads act as a barrier for any polar or charged particles and molecules thus making it a very effective structure and worth exploring with DPD. The chosen lipid 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) consists of a choline head group which is connected with the oleoyl and palmitoyl tails by a phosphate and glycerol group.

The simulations were carried out using the LAMMPS software which is a versatile molecular dynamics simulation package.

2 Methods

2.1 Coarse-grained simulations

Central to CG models is the representation of different groups of atoms as beads. MARTINI distinguishes between five basic bead types: water (W), polar (P), non-polar (N), apolar (C), charged (Q). The P and C beads are also assigned a number from 1 to 5 depending on the polarity, reaching from P1 being the least polar and P5 being the most polar whereas C1 is the most apolar and C5 the least apolar. The W bead is identical to the P4 bead. The Q and N beads can also have subtypes which quantify the hydrogen bond forming capabilities. There is 0 meaning no capabilities, d meaning some donor capabilities and a meaning some acceptor capabilities.

In the case of the POPC lipid this results in a charged Q0 choline head group, a Qa phosphate group and two Na glycerol groups which connect to the two tails. These consist of 4 C1 or 3 C1 and 1 C3, respectively. The resulting molecule is shown in Fig. 2.1.

The topology of the molecule is defined in the `martini_v_2.0_POPC.itp` file which can be downloaded from the MARTINI website. It serves as the baseline for the parametrization in the following sections. It lists the employed potential for the bonds and angles, including their equilibrium parameters in MARTINI units, as well as the bead types used in the representation.
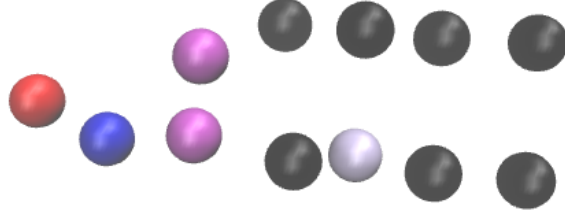
2.2 Dissipative particle dynamics

The equations of motion for a particle i influenced by all other particles j in a DPD force field is

$$m\frac{\mathrm{d}\mathbf{v}_i}{\mathrm{d}t} = \sum_{j\neq i}\mathbf{F}^C_{ij} + \mathbf{F}^D_{ij} + \mathbf{F}^R_{ij}\,,\tag{2.1}$$

containing three different parts, more specifically the conservative force $\mathbf{F}^C$, the dissipative force $\mathbf{F}^D$ and the random force $\mathbf{F}^R$.

The conservative force can be expressed as

Figure 2.1: Coarse-grained POPC molecule representation in LAMMPS. The Q0 choline head group is red, the Qa phosphate group is blue, the connecting Na glycerol groups is violet and the apolar tails are made up of the black C1 beads and the silver C3 bead.

$$\mathbf{F}_{ij}^C = \begin{cases} A_{ij}\left(1 - \frac{r_{ij}}{r_c}\right)\hat{\mathbf{r}}_{ij}, & r_{ij} \leq r_c \\ 0, & r_{ij} > r_c \end{cases}, \tag{2.2}$$

where r_c is a cutoff distance and A_{ij} is a particle pair specific repulsion parameter. Furthermore, $\mathbf{r}_{ij} = \mathbf{r}_i - \mathbf{r}_j$ defines the distance vector, with $r_{ij} = |\mathbf{r}_{ij}|$ being its magnitude and $\hat{\mathbf{r}}_{ij} = \mathbf{r}_{ij}/r_{ij}$ the corresponding unit vector .

Usually the cutoff distance is set to $r_c = 1$ when working with reduced units, which will be discussed in Sec. 2.5, making it redundant in the formula above. DPD distinguishes itself from MARTINI in not postulating a potential which results in a force field but it employs a force field without starting from a fundamental potential. To further illustrate this the Lennard-Jones potential

$$U^{LJ} = 4\epsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^6\right], \tag{2.3}$$

with its parameters σ and ϵ depending on the particles, which is commonly used in the MARTINI method is compared to the DPD force field in Fig. 2.2. The key difference between both approaches is that the DPD force and the corresponding potential do not diverge at $r = 0$ which means that overlapping particles are allowed making it a soft potential. Adding to this DPD is a purely repulsive force whereas Lennard-Jones has a clear attractive part and a minimum.

The dissipative and random force can best be described by using two weight functions w^D and w^R. Using the work of Espanol and Warren (**cite here**) one weight functions can be arbitrarily chosen but in turn fixes the other one. The usual choice is

$$w^D(r_{ij}) = \left[w^R(r_{ij})\right]^2 = \begin{cases} \left(1 - \frac{r_{ij}}{r_c}\right)^2, & r_{ij} \leq r_c \\ 0, & r_{ij} > r_c \end{cases}. \tag{2.4}$$
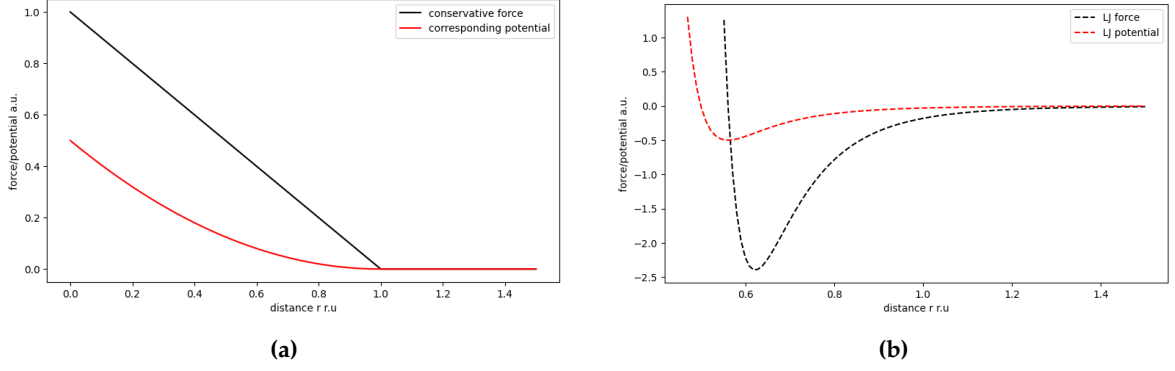
Figure 2.2: (a) The DPD force and its corresponding potential. (b) The Lennard-Jones potential used in the MARTINI method. Key difference is the DPD force and potential do not diverge at the pair distance $r_{ij} = 0$.

Both forces are controlled by strength coefficients, namely σ for the random force and γ for the drag force. The fluctuation dissipation theorem connects these two parameters with the thermal Energy $k_B T$ and yields

$$\sigma^2 = 2\gamma k_B T. \tag{2.5}$$

Defining $\mathbf{v}_{ij} = |\mathbf{v}_i - \mathbf{v}_j|$ as the relative velocity between two particles and α_{ij} as a random number with zero mean and unit variance results in a final expression for both forces

$$\mathbf{F}_{ij}^D = -\gamma w^D(r_{ij})(\hat{\mathbf{r}}_{ij} \cdot \mathbf{v}_{ij})\hat{\mathbf{r}}_{ij} \tag{2.6}$$

$$\mathbf{F}_{ij}^R = \sigma w^R(r_{ij})\alpha_{ij}\Delta t^{-1/2}\hat{\mathbf{r}}_{ij}. \tag{2.7}$$

Notably a factor of $\Delta t^{-1/2}$ appears in the random force. This follows the argument of Groot and Warren (**cite here**) as this corrects the time dependency of displacement to the known expression $\langle x^2 \rangle \propto t$.

To summarize to fully describe DPD interaction, the only parameters to determine are the repulsion parameters A_{ij} and the drag coefficient γ which in turn fixes the random force parameter σ. This step will be further discussed in Sec. 2.6.

2.3 Electrostatic Interaction

The DPD force in Sec. 2.2 does not differentiate between a charged or an uncharged bead, meaning some kind of coulomb interaction has to be added to the force field, or the repulsion have to be adapted correspondingly, to the force field. Crucially a simple coulomb potential is an unfitting choice because it would destroy the soft property of the potential at $r = 0$. To solve this a exponentially smeared charge distribution resulting in a Slater potential is employed . This is following the work of Wang and Hernandez (**cite here**) who also introduce

a factor β which controls the strength of the smearing effect. The charge distribution then reads

$$\rho(r) = \frac{q\beta^2}{\pi r} \exp(-2\beta r)\,. \tag{2.8}$$

Using earlier works from Gonzales-Melchor et al (**cite here**) this factor and its inverse λ which is used in the LAMMPS implementation of the potential was calculated as:

$$\beta = 0.844, \quad \lambda = 1/\beta = 1.185\,.$$

With this and a conversion constant C the coulomb interaction follows

$$\mathbf{F}_{ij}^E = \frac{Cq_i q_j}{4\pi r_{ij}} [1 - \exp(-2\beta r_{ij})(1 + 2\beta r_{ij}(1 + \beta r_{ij}))]\hat{\mathbf{r}}_{ij}\,. \tag{2.9}$$

2.4 Intramolecular Interactions

Sec. 2.2 and Sec. 2.3 define the interaction between non-bonded beads. Beyond that the beads are also bonded inside a molecule. Like described in Sec. 2.1 the corresponding information are found in the `martini_v_2.0_POPC.itp` file. For POPC there are only bond and angle interactions.

For the bond interaction the potential is a simple harmonic potential, which is implemented in LAMMPS as

$$E_{ij} = K^b (r_{ij} - r_{ij}^0)^2\,.\,, \tag{2.10}$$

where K_b is a spring constant in the unit of force that contains the usual factor of $1/2$ and r_{ij}^0 is the equilibrium bond distance of the bead pair. This works similarly for the angle using the potential

$$E_{ijk} = K^a [\cos(\theta_{ijk} - \cos(\theta_{ijk}^0))]^2\,, \tag{2.11}$$

with K_a being a constant in the unit of energy including the factor of $1/2$ and similarly to before θ_{ijk}^0 the equilibrium angle between the three beads. Though the choice is given by the MARTINI database it is interesting to ask why potential of choice is not simply harmonic for the angles. The simple answer is that the potential in Eq. (2.11) is much more computationally efficient because the calculation of a cosine does not include the $\arccos(\theta)$ function, which is costly and not robust.

2.5 DPD units

Molecular dynamics simulations often employ reduced units. Meaning there are reference parameters which are used to make every physical quantity dimensionless. For MARTINI these are usually the parameters of the Lennard-Jones potential ϵ and σ as in Eq. (2.3). But since DPD has a very different force and thus potential one needs different reference parameters. For the length parameter, the work of Wang and Hernandez (**cite here**) is followed who choose the length scale as the length of a cube containing three CG water beads. The number three is not arbitrarily chosen and follows the early work of Groot and Warren (**cite here**) who used the number density $\rho = 3$ beads per unit of volume. In MARTINI every water bead contains $N_w = 4$ molecules and the volume of one water molecule V_w can be calculated by using the molar mass $M = 18.02\text{g/mol}$, the density $\rho_w = 1\text{g/cm}^3$ and the avogadro constant $N_A = 6.022 \cdot 10^{23}\text{molecules/mol}$

$$V_w = \frac{M}{\rho_w N_A} = 2.99 \cdot 10^{-23}\text{cm}^3 = 29.9\text{Å}^3. \tag{2.12}$$

The DPD length follows directly

$$r_{\text{ref}} = \sqrt[3]{\rho \cdot N_w \cdot V_w} = 7.11\text{Å}, \tag{2.13}$$

which from now on can be used to convert every length into DPD units dividing it.

For an energy scale the chosen value is much simpler. The reference temperature was defined as $T_{\text{ref}} = 298.15\text{K}$ and used the thermal energy as a reference resulting in

$$\epsilon_{\text{ref}} = k_B T_{\text{ref}} = 4.12 \cdot 10^{-21}\text{J} = 25.7\text{meV}. \tag{2.14}$$

Similarly to the length scale this value can now be used to convert different energies into DPD units. Furthermore, the combination of scales allows conversion of every physical quantity.

2.6 Determination of DPD bonded parameters

As Sec. 2.1 suggests the equilibrium parameters are found in the `martini_v_2.0_POPC.itp` file

$$r_1^0 = 0.47\text{nm}, \qquad\qquad k_1^b = 1250\text{kJ/(mol\,nm}^2)$$
$$r_2^0 = 0.37\text{nm}, \qquad\qquad k_2^b = 1250\text{kJ/(mol\,nm}^2).$$

While the bond length can simply be divided by the reference length from Sec. 2.5, the spring constant has to be handled with more care. As described in Sec. 2.4 the MARTINI definition still has a factor $1/2$ in front of the harmonic potential which is absorbed in the LAMMPS implementation, see Eq. (2.10). This yields

$$\hat{K}_i^b = \frac{1}{2} k_i^b \frac{r_{\text{ref}}^2}{e_{\text{ref}} N_A} , \tag{2.15}$$

resulting in the following dimensionless values

$$\hat{r}_1^0 = 0.661 , \qquad\qquad \hat{K}_1^b = 127.5$$
$$\hat{r}_2^0 = 0.520 , \qquad\qquad \hat{K}_2^b = 127.5 .$$

This calculation for the angle parameters only differs in the units of the equilibrium parameters

$$\theta_1^0 = 180° , \qquad\qquad k_1^a = 25\text{kJ}/\text{mol}$$
$$\theta_2^0 = 120° , \qquad\qquad k_2^a = 25\text{kJ}/\text{mol}$$
$$\theta_3^0 = 120° , \qquad\qquad k_3^a = 45\text{kJ}/\text{mol} .$$

Similarly to before the factor of $1/2$ has to be included

$$\hat{K}_i^a = \frac{1}{2} \frac{k_i^a}{e_{\text{ref}} N_A} . \tag{2.16}$$

Substituting the values yields the angle parameters

$$\hat{\theta}_1^0 = 180° , \qquad\qquad \hat{k}_1^a = 5.04$$
$$\hat{\theta}_2^0 = 120° , \qquad\qquad \hat{k}_2^a = 5.04$$
$$\hat{\theta}_3^0 = 120° , \qquad\qquad \hat{k}_3^a = 9.08 .$$

2.7 Determination of DPD Charge

Introducing a length and energy sclaes also has an effect on the charge quantization. To adjust the charge the energy of a point charge in reals units with the corresponding energy in DPD units yielding

$$E = \frac{q^2}{4\pi\epsilon_0 r} \overset{!}{=} \hat{E}e_{\text{ref}} = \frac{\hat{q}^2}{\hat{r}}e_{\text{ref}} \tag{2.17}$$

$$\hat{q} = \frac{q}{\sqrt{4\pi\epsilon_0 r_{\text{ref}} e_{\text{ref}}}} = 8.86 \,. \tag{2.18}$$

Defining this charge means that a charge of one elemental charge in real units corresponds to a DPD charge of $\hat{q} = 8.86$.

2.8 Determination of DPD force parameters

The repulsion parameters A_{ij} for the DPD force are the core of the force field and determine the maximum repulsion at $r_{ij} = 0$. In addition to that the drag parameter γ has to be determined. The latter follows from the early work of Groot and Warren (**cite here**) who found at $\hat{T} = 1$ the optimal value for the random force parameter was $\hat{\sigma} = 3$. Employing the connection given by the fluctuation dissipation theorem yields a values of

$$\hat{\gamma} = 4.5 \,,$$

where $k_{\text{B}}T$ was set to unity. The γ value is a fix parameter in the DPD force field utilized by the LAMMPS package. Changing the desired temperature of the DPD force adjusts the σ parameter according to the fluctuation dissipation theorem.

The repulsion parameters used in the simulation were derived by Wang and Hernandez (**cite here**). The values are shown in Table 2.1. The derivation method is described below.

The baseline is the repulsion parameter between two water beads W-W, called a_{ww}. This is done by matching the inverse compressibility κ^{-1} from experimental data to the corresponding value of a_{ww}. Similarly to the MARTINI model where the σ parameter of W-W interaction is used for every other same bead interaction this value is also adapted for every same bead interaction here as well ,meaning $a_{AA} = a_{ww}$ for all beads. The measured value was

$$a_{ww} = 102.067 \,.$$

From there the interaction of two arbitrary beads can be expressed as

$$a_{AB} = a_{ww} + \Delta a_{AB} \,, \tag{2.19}$$

with Δa_{AB} being connected to the Flory-Huggins parameter

Bead pair	A_{ij}	Bead pair	A_{ij}
W - C1	130.616	Q0 - Q0	102.067
W - C3	121.734	Q0 - C1	121.099
W - Na	108.411	Q0 - C3	117.293
W - Q0	84.938	Q0 - Na	98.895
W - Qa	94.454	Na - Na	102.067
Qa - Qa	102.067	Na - C1	115.390
Qa - C1	130.616	Na - C3	115.390
Qa - C3	126.809	C3 - C3	102.067
Qa - Na	108.411	C3 - C1	102.067
Qa - Q0	98.895	C1 - C1	102.067

Table 2.1: DPD force repulsion parameter a_{ij} for every bead pair. The same bead interaction are the same as the water-water interaction which was derived by matching simulation data to experimental data. Other parameters were derived using the Flory-Huggins parameter and the interaction paramters of the MARTINI model.

$$\chi_{AB} = \lambda \Delta a_{AB}, \tag{2.20}$$

using a fitting parameter λ that has to be determined. Earlier works by Groot and Rabone (**cite here**) indicate that the Flory-Huggins parameter scales linear with the size of the beads which in this system is always $N_m = 4$ molecules per bead, meaning

$$\chi_{AB} = \bar{\chi}_{AB} N_m. \tag{2.21}$$

This results in a final formula for the interaction parameter

$$a_{AB} = a_{ww} + \bar{\chi}_{AB} N_m / \lambda. \tag{2.22}$$

To determine the λ fitting parameter a box seperately filled with two different beads A and B is simulated. After equilibration the volume fraction is measured. This method is repeated for different values of Δa_{AB}. For each simulation run the Flory-Huggins paremter is calculated with

$$\chi = \frac{\ln[(1 - \phi)/\phi]}{1 - 2\phi} \tag{2.23}$$

and plotted against the parameter Δa_{AB}. The slope of the resulting linear graph is the desired fitting parameter

$$\lambda = 0.28.$$

Wang and Hernandez (**cite here**) found a formula which uses a baseline interaction matrix ϵ_{AB} to calculate the size dependant Flory-Hugigns parameter.

$$\bar{\chi}_{AB} = \chi_{AB} = \frac{z}{k_{\mathrm{B}}T}\left[\epsilon_{AB} - \frac{1}{2}(\epsilon_{AA} + \epsilon_{BB})\right], \tag{2.24}$$

using z as the effective number of nearest neighbors.

The employed database is the MARTINI model. The calculated values can be substituted into Eq. (2.22) and result in the values shown in Table 2.1.