Molecularly Informed Mesoscopic Modeling of Biological Lipid Membranes: A Phase-Field Based Multiscale Approach

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Summary

Molecular dynamics of even coarse-grained molecules only allows to simulate systems on the microscopic scale, due to the number of degrees of freedom accounted for in this description. A polymer model such as the Ohta-Kawasaki model however allows to capture the key microscopic and mesoscopic features of lipid systems over a wide range of length scales by an effective phase-field description.

We present a possible procedure of parametrization of the Ohta-Kawasaki model by molecular data of a pure DPPC lipid system. We also present the steady state predictions of patterns and specific features resulting from the intra- and interaggregate interactions similarly observed in vivo and in silico, for the preliminary parametrization which approximates DPPC and two more examples of relatively opposing lipid properties.

The latter examplifies the richness emerging from this procedure of parametrization, as well as its natural extension. By further three-dimensional simulations an additional classification will be introduced: separating topologies which are dissimilar in 3D but whose projections in 2D are similar. Also is a modification of the phase-field model necessary to satisfy limited lipid flip-flop rates.

Phase-Field Model

Definition of the fields: A system consists of a mixture of A-B diblock co-polymers and homopolymers C. With the assumption of incompressibility one finds the following two order parameters

$\eta \propto (\rho_A + \rho_B)$ **mesoscale field** - segregation of copolymers and homopolymers

$\Phi \propto (\rho_A - \rho_B)$ **microscale field** - spatial block arrangement of copolymers

monomer number densities

The model free energy: The *Ohta-Kawasaki model*[1] features short- and long-range contributions to its free energy: $F[\eta, \Phi] = F_\mathrm{S}[\eta, \Phi] + F_\mathrm{L}[\eta, \Phi]$
The short-range is of Ginzburg-Landau type

$$F_\mathrm{S}[\eta, \Phi] = \int \mathrm{d}\mathbf{r} \left(\frac{c_1}{2}(\nabla\eta)^2 + \frac{c_2}{2}(\nabla\Phi)^2 + W(\eta, \Phi) \right)$$

interfacial contributions — local interaction potential

with $$W(\eta, \Phi) = \frac{d_1}{4}(\eta^2 - 1)^2 + \frac{d_2}{4}(\Phi^2 - 1)^2 + b_1\eta\Phi - \frac{b_2}{2}\eta\Phi^2 - \frac{b_3}{2}\eta^2\phi + \frac{b_4}{2}\eta^2\Phi^2$$

potential wells — local coupling

The long-range connectivity is captured by

$$F_\mathrm{L}[\eta, \Phi] = \iint \mathrm{d}\mathbf{r}\mathrm{d}\mathbf{r}' G(\mathbf{r}, \mathbf{r}') \frac{\alpha}{2} \delta\Phi(\mathbf{r}) \delta\Phi(\mathbf{r}') \quad \text{with} \quad \delta\Phi(\mathbf{r}) = \Phi(\mathbf{r}) - \overline{\Phi}$$

Green's function — spatial average: A-B monomers ratio

Note: Further long-range contributions have been omitted.

Model parameters: The following table summarizes all presented parameters and the values these can take.

p_i	c_1 [J/m]	c_2 [J/m]	d_1 [J/m^3]	d_2 [J/m^3]	b_1 [J/m^3]	b_2 [J/m^3]	b_3 [J/m^3]	b_4 [J/m^3]	α [J/m^5]
Ohta et al.[1]	>0	>0	>0	>0	$\mathbb{R}$	>0	$\mathbb{R}$	>0	>0

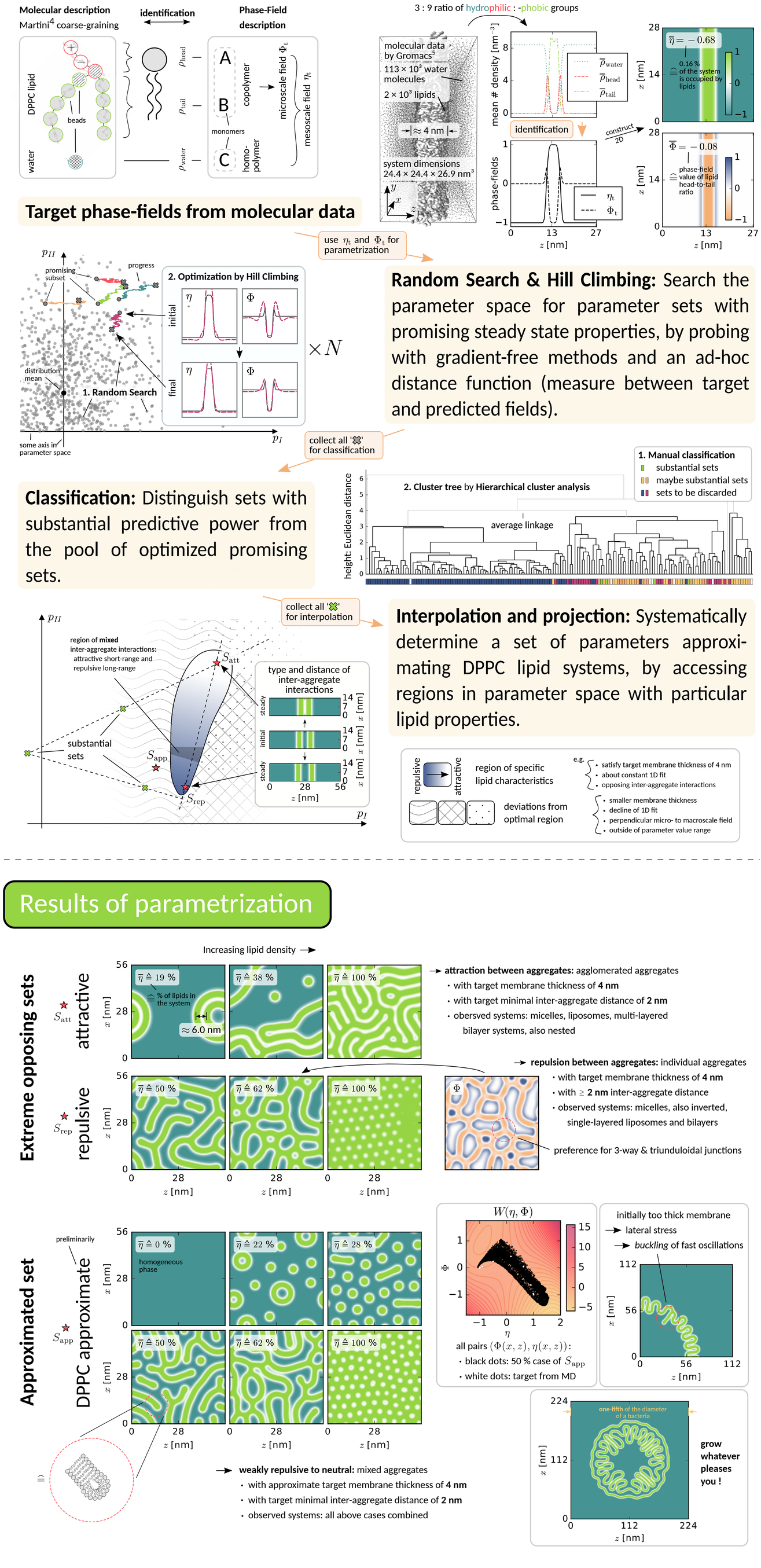
Evolution equations: A system of coupled non-linear PDEs in the fields follows from the *Cahn-Hilliard equation*[2] and is numerically solved with FiPy[3].

References

This work is based on Pascal S. Rogalla, Masters Thesis (2022)

[1] Ohta and Kawasaki, Macromolecules 19, 2621-2632 (1986).
[2] Cahn and Hilliard, The Journal of Chemical Physics 28, 258-267 (1958).
[3] Guyer et al., Computing in Science and Engineering, 11:6-15 (2009).
[4] Marrink et al., Chemical Society Reviews, 42:6801 (2013).
[5] Van Der Spoel et al., Journal of Computational Chemistry, 26:1701-1718 (2005).

Procedure of Parametrization



Results of parametrization