Mathematical modelling of polymer capsules in solution

Introduction

Vesicles are bag-like structures composed of a bilayer of amphiphiles and an enclosed solvent (FIG). They are sometimes used to encapsulate and deliver drugs. Controlling the size of the vesicles is a potential way to control the dosage of the drug which it carries. They are roughly spherical but do not follow the underlying physics one would expect from similar spherical structures, e.g. a micelle. Recent experiments by Warren et al found that vesicles with a narrow size distribution can be formed in a solution of a single type of copolymer. Comparing this with the formation of vesicles with comparable size distributions suggested that a suspension of vesicles of a well-defined size is the equilibrium phase in this system. Interdigitation occurs where the respective hydrophobic parts of the inward and outward-facing amphiphiles are mixed together. In this project, it was found that including interdigitation improved on the original case as the results were closer to the experimental data.

Aim

The aim of this project was to investigate the effect of involving interdigitation in the calculations involving the free energy of a vesicle.

Methodology

The computational model used relied on mean field theory, meaning contributions to the free energy of the vesicle were used. It also means that fluctuations are not considered. The equations for the contributions of free energy from the micelle (not including bulk contributions) were adapted from the original paper and are as follows for diblock copolymers formed of N_A A monomers and N_B B monomers, with the Boltzmann constant k, and temperature T:

Elastic energy term for the inner leaflet

$$F_d^{in} = \frac{3}{2}kTp_1\left\{\frac{(R_1-R_0)^2}{N_Aa^2}+\frac{N_Aa^2}{(R_1-R_0)^2}+\frac{(R_2-R_1)^2}{N_Ba^2}+\frac{N_Ba^2}{(R_2-R_1)^2}-4\right\}$$

And outer leaflet

$$F_d^{out} = \frac{3}{2}kTp_2\left\{\frac{(R_2-R_1)^2}{N_Aa^2}+\frac{N_Aa^2}{(R_2-R_1)^2}+\frac{(R_3-R_2)^2}{N_Ba^2}+\frac{N_Ba^2}{(R_3-R_2)^2}-4\right\}$$

Where p_1 and p_2 are the number of copolymers in the inner and outer leaflets, respectively, and a is the segment length

The energy representing the entropy of mixing the solvent with the copolymer chains

$$F_m = \sum_{i=1}^{3}\frac{4\pi}{3}\frac{R_i^3-R_{i-1}^3}{a^3}kT\frac{1-\eta_i}{N_h}\ln(1-\eta_i)$$

Where η_i is the volume fraction of copolymer in the layer i.
The repulsive energy between the solvent and the hydrophobic blocks

$$F_{core} = \frac{4\pi}{3}\frac{(R_2^3-R_1^3)}{a^3}kT\eta_2(1-\eta_2)\chi$$

Where X is the Flory-Huggins parameter. This is what represents the strength of the repulsion between the solvent and the hydrophobic block.
And the free energy corresponding to the surfaces between hydrophobic and hydrophilic regions

$$F_{int} = \frac{4\pi}{3}R_1^2\frac{kT}{a^2}\sqrt{\frac{\chi}{6}}\eta_2+\frac{4\pi}{3}R_2^2\frac{kT}{a^2}\sqrt{\frac{\chi}{6}}\eta_2$$

From here, we could see whether the vesicles which form under certain conditions (values of NA, NB, CHI) have a preferred size. The outer radius was set to an initial value and the total free energy (the sum of equations 1:4) was minimised with respect to R_0, R_1, R_2, p_1, p_2 and φ_1 (where φ_1 is the fraction of monomers outside vesicles that belong to copolymers) by a direction set method. This was then repeated for many values of R_3 to find a minimum for the total free energy and a preferred radius for a vesicle in the set conditions.

References

N. J. Warren, O. O. Mykhaylyk, A. J. Ryan, M. Williams, T. Doussineau, P. Dugourd, R. Antoine, G. Portale, and S. P. Armes, J. Am. Chem. Soc. 137, 1929 (2014).

M. J. Greenall, Phys. Chem. Liq. **56**, 281 (2018)

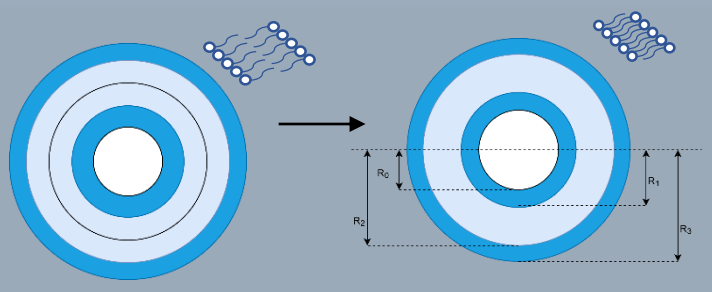

Fig. 1 – Geometry of a spherical vesicle showing interdigitation. Light blue areas represent the hydrophobic areas of a vesicle, while dark blue areas represent hydrophilic areas. Upon interdigitation, hydrophobic areas are mixed.

Results

We first looked at systems with relatively short copolymers and explored the effect of a different value for N_B when N_A was at a constant value of 100.

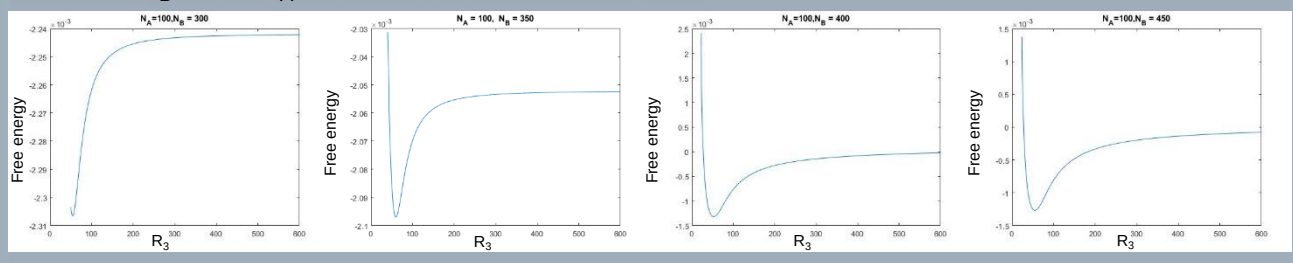

Fig. 2-Free energy against outer radius for an interdigitated vesicle with N_A =100, χ = 2, N_B =a)300, b)350, c)400, d)450

Fig.2 shows that, in the whole range of parameters explored, there were clear minimum values. These correspond to favoured sizes of vesicles for the different ratios of monomers.
We then explored systems with longer copolymers. We increased the value of N_A to 1000 and repeated at higher values of N_B.

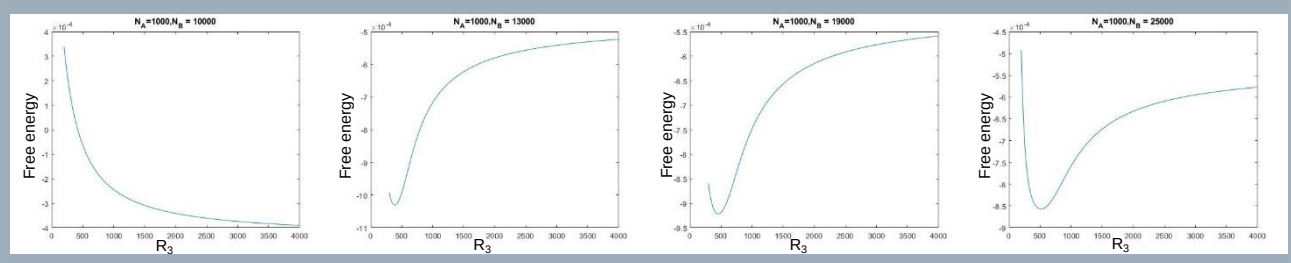

Fig. 3-Free energy against outer radius for an interdigitated vesicle with N_A =1000, χ = 2, N_B =a)10000, b)13000, c)19000, d)25000

Fig.3a shows no minimum, suggesting that the system may have a broad spectrum of formed vesicles, with the given parameters. The other plots show that, for some higher values of N_B , there are preferred sizes of vesicles.
Finally, we took a closer look at the different sizes of a vesicle across different values of N_B, both for short and long copolymers.

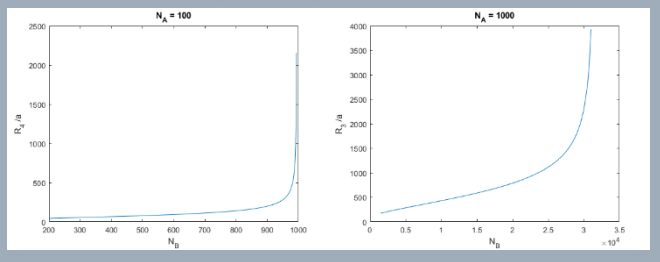

Fig. 4 – Outer radius of a vesicle against degree of polymerisation of hydrophobic block with N_A =a)100, b)1000

In both case, the radius increases slowly before diverging at a critical point, suggesting that the vesicles become unstable when approaching the critical point.

Conclusion

The graphs of Fig.1 and Fig.2 agree with the experimental data and support the idea that, for a range of degrees of polymerisation, vesicles have a favourable size.

In the interdigitated results (Fig.4), the vesicle grows slowly at first and the final divergence is rapid. This is closer to the experiments and an improvement on the original case, where the graph is much smoother.

Student: Henry Macpherson

Supervisor: Dr Martin Greenall