Magneto-division of Vesicle: Theory and Possible Experiments

Yao-Gen Shu* and Zhong-Can Ou-Yang
CAS Key Laboratory of Theoretical Physics, Institute of Theoretical Physics, Chinese Academy of Sciences, Beijing 100190, China

Keywords: Nanoreactor, Division, Deformation Theory, Diamagnetic Amphiphilic Block-copolymers, Magnetic Manipulation.

Abstract: Our theory has revealed the possibility that the vesicle, which is self-assembled by the diamagnetic amphiphilic block-copolymers, can be manipulated into division by external magnetic field. For the case of the constraint of constant surface area, the passive division can successively take place for 10 times in the situation of $\Delta p = -15$ mV; and only 4.5% solution that is contained by the original vesicle with a radius of 4 μm can been retained by 512 vesicles that each contains about 2.31×10^7 nm^3. Thus, if the water channels are embedded in the membrane of vesicle, this method can not only concentrate the solution, but also produce a large number of nanoreactors, which is beneficial to yield an ensemble conclusion of chemical reaction in a very short times. Another case of the constraint of constant volume can also be easy realized by enough supply of the diamagnetic amphiphilic block-copolymers in the progress of division. The latter case is also important for reaction statistics because the original solution can be in equal volume divided into hundreds nanoreactors. This nanoreactor can be used to mimic the reaction of some organelles in vitro. We hope experimenters will try them in future experiments.

1 INTRODUCTION

In recent years, chemists and biologist have worked to understand how fundamental chemical principles change when systems are confined to spaces with nanoscale dimensions or sub-microliter volumes. Nanoreactors offer a means of creating unique nanoscale chemical environments partitioned from the surrounding bulk space to explore chemistry in a variety of different types of nanoreactors such as nanopores and nanoholes, hollow nanoparticles and porous architectures, and tubular nanostructures, as well as those that are native to biological structures, such as protein pores, channels and organelles. Such systems enable the number of molecules under study to be controlled in ways not possible with bulk systems. The different behaves of the same molecules between nanoreactors and bulk systems are possible to be revealed. Thus, nanoreactors can be exploited to gain new fundamental understanding of a chemical system or process or to develop an analytical tool based upon this insight(Petrosko et al., 2016). However, the lack of material with large spontaneous curvature has been blocking the development of nanoreactors.

The diamagnetic amphiphilic block-copolymers plays more and more important role in self-assembly of vesicle due to its highly anisotropic magnetic susceptibility. It has been used to assemble an infolded bowl-shaped vesicle(van Rhee et al., 2014; Hickey et al., 2011), which is called a stomatocyte, so that the mouth of the polymeric self-assembly can be reversibly opened and closed by varying an external homogeneous magnetic field. Thus, the artificial mouth functions as a magneto-valve, and the whole artificial stomatocyte has a great potential for the application of targeted release of drug.

The spontaneous curvature model of the equilibrium shapes and deformations of lipid bilayer vesicles(Helfrich, 1973), which was proposed by Helfrich for more than four decades, has been engaged by us to reveal the mechanism of reversible opening and closing of mouth and give out the relation between the size of mouth and the external magnetic field(Deng et al., 2018). In this paper, we try to propose the model of magneto-division of vesicle which is assembled by the diamagnetic amphiphilic block-copolymers with a highly anisotropic magnetic susceptibility. We hope this model will inspire experimenter to realize it and meet the needs of nanoreactors.

Shu, Y. and Ou-Yang, Z.
Magneto-division of Vesicle: Theory and Possible Experiments.
DOI: 10.5220/0007347001490153
In *Proceedings of the 12th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2019)*, pages 149-153
ISBN: 978-989-758-353-7

2 THE DEFORMATION THEORY OF A SPHERICAL VESICLE

Here, we consider an infinitesimal deformation of a spherical vesicle of radius $\mathbf{r}$ in a spatially uniform magnetic field intensity $\mathcal{H}$ ($= B/\mu$, where B is magnetic induction and μ is magnetic permeability.) by minimizing the sum of bending energy (curvature elastic energy: $F_c = \frac{1}{2}k_c \oint (c_1 + c_2 - c_0)^2 \mathrm{d}A$) and the free energies contributed by osmotic pressure ($\Delta p \int \mathrm{d}V$), the tension of membrane ($\lambda \oint \mathrm{d}A$) and the interaction between the magnetic field and the constituent molecules ($F_B = -\frac{1}{2}\Delta\chi t\mu \oint (\mathcal{H}\cdot\mathbf{n})^2 \mathrm{d}A$), that is(Iwamoto and Ou-Yang, 2013; Ou-Yang and Helfrich, 1987; Chandrasekhar, 1992),

$$\begin{aligned} F &= \frac{\kappa_c}{2}\oint (2H+c_0)^2\,\mathrm{d}A + \Delta p\int \mathrm{d}V + \lambda\oint \mathrm{d}A \\ &\quad -\frac{1}{2}\Delta\chi t\mu\oint (\mathcal{H}\cdot\mathbf{n})^2\,\mathrm{d}A, \end{aligned} \tag{1}$$

where κ_c is the bend modulus, c_1 and c_2 are the principal curvatures, while $H = -(c_1+c_2)/2$ is the mean curvature, c_0 is the spontaneous curvature, $\Delta p \equiv p_{\text{out}} - p_{\text{in}}$ is the difference pressure of the transmembrane, λ is the Lagrange multiplier of the membrane tension to ensure a constant area, t is the thickness of membrane, $\mathbf{n}$ is the outward unit normal and $\Delta\chi \equiv \chi_{\parallel} - \chi_{\perp}$, in which χ is the diamagnetic susceptibility, while $\chi_{\parallel}$ and $\chi_{\perp}$ are diamagnetic susceptibility parallel and perpendicular to $\mathbf{n}$ respectively.

To obtain a description of the deformation of a sphere of radius $\mathbf{r}$, we have to solve the variational equation:

$$\delta F = \delta F_1 + \delta F_B = 0, \tag{2}$$

where $F_1 \equiv F_c + \Delta p\int \mathrm{d}V + \lambda\oint \mathrm{d}A$. The equilibrium vesicle surface is specified by the position vector $\mathbf{r}(u,v)$ where u and v are surface parameters. We assume that the radius of sphere is $\mathbf{r_0}$ at $\mathcal{H} = 0$ and will be slightly distorted into

$$\mathbf{r} \equiv \mathbf{r}_0 + \psi(u,v)\mathbf{n} \tag{3}$$

due to any $\mathcal{H}$ perturbation, where $\psi(u,v)$ is a smooth infinitesimal function.

At first, we only consider the case of $\mathcal{H} = 0$, then,

$$\begin{aligned} \delta^{(1)}F_1 &= \frac{\kappa_c}{2}\oint \Big[(2H+c_0)^2\delta^{(1)}(\mathrm{d}A) \\ &\quad +4(2H+c_0)\delta^{(1)}H\mathrm{d}A\Big] \\ &\quad +\Delta p\int \delta^{(1)}(\mathrm{d}V) + \lambda\oint \delta^{(1)}\mathrm{d}A \\ &= \oint \big[\Delta p - \kappa_c(2H+c_0)(2H^2 - c_0H - 2K) \\ &\quad +2\kappa_c\nabla^2 H - 2\lambda H\big]\psi\sqrt{g}\mathrm{d}u\mathrm{d}v \\ &= 0, \end{aligned}$$

which leads to(Ou-Yang and Helfrich, 1987):

$$\begin{aligned} &\Delta p - \kappa_c(2H+c_0)(2H^2 - c_0H - 2K) \\ &\qquad +2\kappa_c\nabla^2 H - 2\lambda H = 0, \end{aligned} \tag{4}$$

where $K \equiv c_1c_2$ is a Gaussian curvature, the Laplace-Beltrami operator ∇^2 is defined as $\nabla^2 \equiv (1/\sqrt{g})\partial_i(g^{ij}\sqrt{g}\partial_j)$ $(i,j = u,v)$, in which $g_{ij} \equiv \partial_i\mathbf{r}\cdot\partial_j\mathbf{r}$, $g^{ij} \equiv (g_{ij})^{-1}$ and $g \equiv \det(g_{ij})$ are the coefficients of the first fundamental form of the surface.

For a convex surface, such as the outside spherical vesicle as shown in Fig.2 a, the curvature $H = -1/r$. Its radius r_0 (at $\mathcal{H} = 0$) then can be determined by(Ou-Yang and Helfrich, 1987)

$$\Delta p r_0^3 + 2\lambda r_0^2 - \kappa_c r_0 c_0(2 - c_0 r_0) = 0. \tag{5}$$

If $\mathcal{H} \neq 0$ ($\mathcal{H}$ is along with $\mathbf{z}$ in a spherical coordinate system), Eq.(2) will become

$$\delta F = \delta^{(1)*}F_1 + \delta^{(1)}F_B = 0$$

where $\delta^{(1)*}F_1$ is different from $\delta^{(1)}F_1$ by considering $\lambda \to \lambda + \delta\lambda$ due to $\mathcal{H} \neq 0$. Then,

$$\begin{aligned} \delta^{(1)*}F_1 &= \oint [\kappa_c(2\delta H)(2H_0^2 - c_0H_0 - 2K_0) \\ &\quad + \kappa_c(2H_0 + c_0)(4H\delta H - c_0\delta H - 2\delta K) \\ &\quad + 2\kappa_c(\delta\nabla^2)H_0 + 2\kappa_c\nabla_0^2\delta H\lambda H \\ &\quad -2\delta\lambda H_0 - 2\lambda\delta H]\psi\mathrm{d}A \\ &= \oint \Bigg\{\frac{2}{r_0}\delta\lambda + \sum\frac{\kappa_c}{r_0^4}\Bigg[4c_0r_0 - \frac{2\lambda r_0^2}{\kappa_c} - c_0^2r_0^2 \\ &\quad - 2l(l+1)\Bigg]\Bigg[1 - \frac{l(l+1)}{2}\Bigg]a_l\mathrm{Y}_l\Bigg\}\psi\mathrm{d}A, \end{aligned} \tag{6}$$

where $H_0 = -1/r_0$ and $H = -1/r$(Ou-Yang et al., 1999).

On the other hand,

$$\begin{aligned} \delta^{(1)}F_B &= -\frac{1}{2}\Delta\chi t\mu\Big[\oint (\mathbf{n}\cdot\mathcal{H})^2\delta^{(1)}(\mathrm{d}A) \\ &\quad +2\oint (\mathbf{n}\cdot\mathcal{H})\mathcal{H}\cdot\delta^{(1)}\mathbf{n}\mathrm{d}A\Big] \\ &= \Delta\chi t\mu\oint \left[(\mathcal{H}\cdot\mathbf{n})^2 H\psi + (\mathcal{H}\cdot\mathbf{n})\mathcal{H}\cdot\nabla\psi\right]\mathrm{d}A \\ &= \Delta\chi t\mu\oint \left\{H(\mathcal{H}\cdot\mathbf{n})^2 + \nabla\cdot[\mathcal{H}(\mathcal{H}\cdot\mathbf{n})]\right\}\psi\mathrm{d}A \\ &= \oint \left[\frac{t\Delta\chi}{\mu}\left(\frac{B^2\cos^2\theta}{r_0} - \frac{B^2\sin^2\theta}{r_0}\right)\right]\psi\mathrm{d}A \\ &\equiv -\oint (g_0\mathrm{Y}_0 + g_2\mathrm{Y}_2)\psi\mathrm{d}A, \end{aligned} \tag{7}$$

where $g_0 = t\Delta\chi B^2\sqrt{4\pi}/(3r_0\mu)$, $g_2 = 4g_0/\sqrt{5}$. In the derivation of Eq.(7), we have engaged the formulas:

$$\begin{aligned} \oint (\mathcal{H}\cdot\mathbf{n})\mathcal{H}\cdot\nabla\psi\mathrm{d}A &= \oint \{\nabla\cdot[\psi(\mathcal{H}\cdot\mathbf{n})\mathcal{H}] \\ &\quad - \psi\nabla\cdot[\mathcal{H}(\mathcal{H}\cdot\mathbf{n})]\}\,\mathrm{d}A, \\ \oint \nabla\cdot[\psi(\mathcal{H}\cdot\mathbf{n})\mathcal{H}]\mathrm{d}A &= \oint \left[-2(\mathcal{H}\cdot\mathbf{n})^2 H\psi\right]\mathrm{d}A, \end{aligned}$$

$\delta dA = -2H\psi dA$ and $\delta \mathbf{n} = -\nabla\psi = -g^{ij}\mathbf{r}_i\partial_j\psi$ ($\mathbf{r}_i = \partial_i\mathbf{r}$)(Weatherburn, 1927; Ou-Yang et al., 1999).

In a spherical coordinate system, $u = \theta$, $v = \phi$, $\mathbf{r}_0 = r_0(\cos\phi\sin\theta, \sin\phi\sin\theta, \cos\theta)$ and $\mathbf{n} = \mathbf{r}_0/r_0$. Thus, the weak deformation of the radius at (θ,ϕ) is $r = r_0 + \psi(\theta,\phi)$ with

$$\begin{aligned}\psi(\theta,\phi) &= \sum_{l,m} a_{l,m} Y_{l,m}(\theta,\phi) \\ &= \sum_{l=0}^{\infty} a_l Y_l \end{aligned} \quad (8)$$

where Y_l is a spherical harmonic function.

Now, we consider the constraint of the constant surface area of the vesicle during deformation,

$$\begin{aligned}\delta A &= \oint -2H\psi r_0^2 \sin\theta d\theta d\phi \\ &= \oint -2r_0\psi(a_0 Y_0 + a_2 Y_2)\sin\theta d\theta d\phi \\ &= 4\sqrt{\pi} r_0 a_0 \\ &= 0, \end{aligned} \quad (9)$$

which leads to $a_0 = 0$. Combining Eqs.(6), (7) with (9), we get:

$$\begin{aligned}\delta\lambda &= \frac{t\Delta\chi B^2}{6\mu}, \\ a_2 &= \sqrt{\frac{4\pi}{5}} \frac{-\frac{4}{3}t\Delta\chi B^2 r_0^3}{2\kappa_c\mu\left(\frac{2\lambda}{\kappa_c}r_0^2 + c_0^2 r_0^2 - 4c_0 r_0 + 12\right)}. \end{aligned}$$

Then,

$$\begin{aligned}\psi &= \sum_{l=0}^{\infty} a_l Y_l \\ &= a_2 Y_2 \\ &= -\frac{\frac{4}{3}t\Delta\chi B^2 r_0^3 P_2(\cos\theta)}{2\kappa_c\mu\left(\frac{2\lambda}{\kappa_c}r_0^2 + c_0^2 r_0^2 - 4c_0 r_0 + 12\right)}, \end{aligned} \quad (10)$$

where P_2 is a Legendre function.

The deformation equation of a spherical vesicle determined by Eq.(2) in the case of $\mathcal{H} \neq 0$ can be described by

$$\begin{aligned}r_B(\theta) &= r_0\left[1 - \frac{\frac{2t\Delta\chi}{3\kappa_c\mu}B^2 r_0^2 P_2(\cos\theta)}{\frac{2\lambda}{\kappa_c}r_0^2 + c_0^2 r_0^2 - 4c_0 r_0 + 12}\right] \\ &\equiv r_0\left[1 + \frac{qB^2 r_0^2(3\cos^2\theta - 1)}{\xi r_0^2 - 4c_0 r_0 + 12}\right] \end{aligned} \quad (11)$$

where $q \equiv -t\Delta\chi/(3\kappa_c\mu)$, $\xi \equiv 2\lambda/\kappa_c + c_0^2$.

3 RESULTS

Eq.(11) implies that the "division" of the vesicle occurs most likely at $\theta = \pi/2$. The magnitude of the manipulated magnetic field has to satisfy:

$$B_d^2 = \frac{1}{q}\left(\xi - \frac{4c_0}{r_0} + \frac{12}{r_0^2}\right). \quad (12)$$

Combining with Eq.(5), we get the magnitude of the external magnetic field for the first "division"

$$B_{d,1}^2 = \frac{1}{q}\left[\frac{12}{r_{0,1}^2} - \frac{2c_0}{r_{0,1}} - \frac{\Delta p}{\kappa_c} r_{0,1}\right], \quad (13)$$

so that for the i^{th} passive division

$$B_{d,i}^2 = \frac{1}{q}\left[\frac{12}{r_{0,i}^2} - \frac{2c_0}{r_{0,i}} - \frac{\Delta p}{\kappa_c} r_{0,i}\right], \quad (14)$$

$$r_{0,i} = \frac{r_{0,1}}{2^{(i-1)/2}}, \quad (15)$$

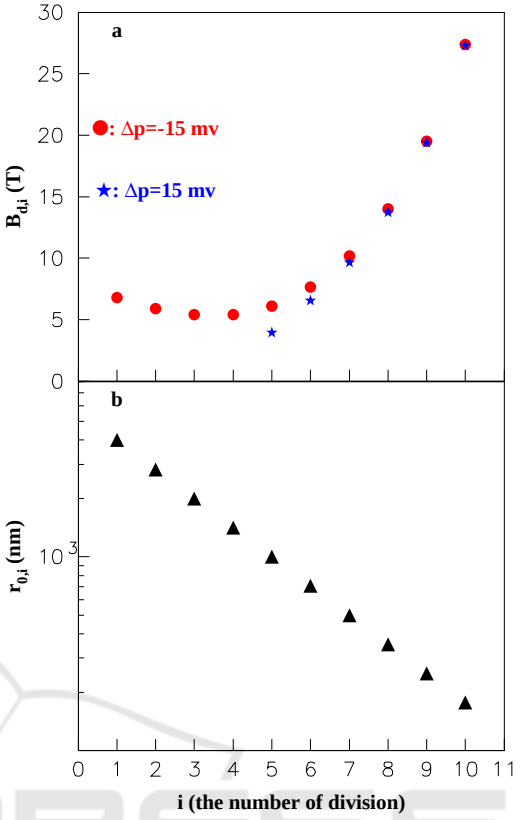

Figure 1: **a.** The relation between the magnitude of the manipulated magnetic field and i^{th} division according to Eq.(14), where red dot indicates the situation of $\Delta p = -15$ mV, while blue star does the one of $\Delta p = 15$ mV. There is a minimum manipulated magnetic field near $r = 2000$ nm for the situation of $\Delta p = -15$ mV. **b.** The radius varies for each division according to Eq.(15). $c_0 = -10^{-3}$ nm^{-1} with $r_{0,1} = 4\times10^3$ nm, $t = 26$ nm(van Rhee et al., 2014), $\kappa_c = 2.6\times10^{-21}$ J(Manyuhina et al., 2007), $\Delta\chi \approx -2.0\times10^{-7}$(van Rhee et al., 2014; Sutter and Flygare, 1969), and $\mu_{water} \approx 1.26\times10^{-6}$ N·A^{-2}.

because of the constraint of constant surface area. The results of Eqs.(14) and (15) have been indicated in Fig.1 **a** and **b** respectively. For the situation of $\Delta p = -15$ mV, $B_{\mathrm{d},i}$ rises no longer monotonically with decreasing of radius of the vesicle. It may be related with the combination of parameters such as c_0, r_0, Δp, κ_c, t, $\Delta\chi$ and λ. Thus, there is a optimal combination of magnetic manipulated division near $r_0 \approx 2000$ nm, at which $B_{\mathrm{d},i}$ achieves minimum value.

The deformation of vesical due to magnetic manipulation before i^{th} division can be described as:

$$r_{\mathrm{B},i}(\theta) = r_{0,i}\left[1 + \left(\frac{B}{B_{\mathrm{d},i}}\right)^2 (3\cos^2\theta - 1)\right]. \quad (16)$$

Fig.2 shows three different states during deformation due to the varying of the manipulated magnetic field. **a** and **d** (blue line) correspond the state of $B = 0$, then, the vesicle is spherical. **c** corresponds the critical state of division at B_{di}, the vesicle displays a pair of pearls which stick each other. **b** is the middle state between $B = 0$ and $B = B_{\mathrm{di}}$, and looks like a dumb-bell. The sum of the surface area in the progress of each division is constant, however, the volume of solution that is contained by the vesicles will lost $\frac{4}{3}\pi r_i^3(1 - 1/\sqrt{2})$ for each division.

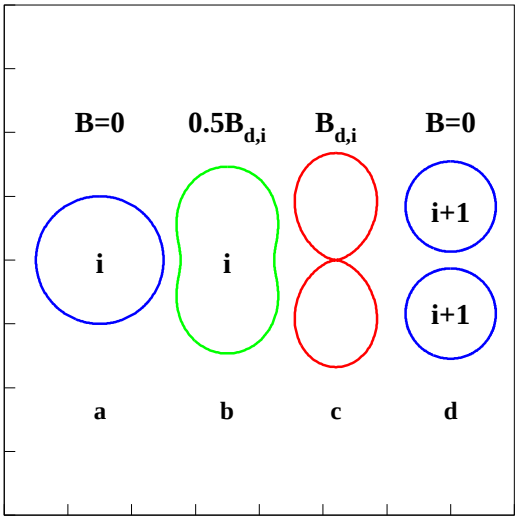

Figure 2: Schematic division of vesicle. The polymersome is assembled from diamagnetic amphiphilic block-copolymers with a highly anisotropic magnetic susceptibility ($\chi < 0$). Its deformation can be manipulated by varying a external homogeneous magnetic field (B) according to Eq.(16). **a:** A spherical vesicle with a radius of r_i at i^{th} division. **b:** The middle state of the deformation ($0 < B < B_{\mathrm{d},i}$). **c:** The passive division takes place at $B_{\mathrm{d},i}$ (see fig.1 a). **d:** Two spherical vesicles with a radius of $r_{i+1} = r_i/\sqrt{2}$ have been produced. The sum of the surface area is constant through the whole progress. However, the volume of solution that is contained by the vesicles will lost $\frac{4}{3}\pi r_i^3(1 - 1/\sqrt{2})$ for each division.

4 CONCLUSIONS AND DISCUSSION

Nanoreactor has a great potential for the application of medical, such as targeted transporting of drug via blood capillary, and digital PCR etc.. However, the manufacture of nanovesicles with uniform volume is still a challenge due to the lack of material with large spontaneous curvature. Our model has revealed the possibility that the vesicle, which is self-assembled by the diamagnetic amphiphilic block-copolymers, can be manipulated into division by external magnetic field. The passive division can successively take place for 10 times in the situation of $\Delta p = -15$ mV. The vesicle with radius of 4000 nm (about 2.68×10^{-7} μL solution contained) will be divided into 512 vesicles with radius of 177 nm (about 2.31×10^{-11} μL solution contained). Because of the constraint of constant surface area, the total volume of solution that is contained by the original vesicle will lost about 2.56×10^{-7} μL, that is, only 1.2×10^{-8} μL solution (about 4.5%) has been retained by 512 vesicles that each contains about 2.31×10^7 nm^3. Thus, if the water channels are embedded in the membrane of vesicle, this method can not only concentrate the solution, but also produce a large number of nanoreactors, which is beneficial to yield an ensemble conclusion in a short times. This nanoreactor can be used to mimic the reaction of some organelles in vitro.

We must point that Eq.(11) is precise just for the situation of small deformation such as $B < 0.5B_{\mathrm{d},i}$, so that the quantitatively prediction of Eq.(14) is no longer precise. However, the possibility of passive division does exist as long as the manipulated magnetic field is high enough. Here, we have just discussed the case of the constraint of constant surface area. Another case of the constraint of constant volume should be worth trying, in which experimenter can easily realize it by enough supply of the diamagnetic amphiphilic block-copolymers in the progress of division. The latter case is also important for the reaction statistics because the original solution can be in equal volume divided into hundreds nanoreactors. We hope experimenters will try them in future experiments.

ACKNOWLEDGEMENTS

The authors thank the financial support by the Key Research Program of Frontier Sciences of CAS (No. Y7Y1472Y61), the National Natural Science Foundation of China (No. 11574329, 11774358, 11747601, 11675017), the Joint NSFC-ISF Research Program(No. 51561145002), the CAS Biophysics Interdisciplinary Innovation Team Project (No. 2060299), CAS Strategic Priority Research Program (No. XDA17010504) and the Fundamental Research Funds for the Central Universities (No. 2017EYT24).

REFERENCES

Chandrasekhar, S. (1992). *Liquid Crystals*. Cambridge University, Cambridge.

Deng, Y.-X., Liu, Y., Shu, Y.-G., and Ou-Yang, Z.-C. (2018). Deformation theory of polymersome magneto-valves. *EPL*, 123:68002.

Helfrich, W. (1973). Elastic properties of lipid bilayers: theory and possible experiments. *Z. Naturforsch*, C28:693.

Hickey, R. J., Haynes, A. S., Kikkawa, J. M., and Park, S.-J. (2011). Controlling the self-assembly structure of magnetic nanoparticles and amphiphilic block-copolymers: From micelles to vesicles. *J. Am. Chem. Soc.*, 133:1517.

Iwamoto, M. and Ou-Yang, Z.-C. (2013). Anharmonic magnetic deformation of spherical vesicle: Field-induced tension and swelling effects. *Chem. Phys. Lett.*, 590:183.

Manyuhina, O., Shklyarevskiy, I. O., Jonkheijm, P., Christianen, P. C. M., Fasolino, A., Katsnelson, M. I., Schenning, A. P. H. J., Meijer, E., Henze, O., Kilbinger, A. F. M., Feast, W. J., and Maan, J. C. (2007). Anharmonic magnetic deformation of self-assembled molecular nanocapsules. *Phys. Rev. Lett.*, 98:146101.

Ou-Yang, Z.-C. and Helfrich, W. (1987). Instability and deformation of a spherical vesicle by pressure. *Phys. Rev. Lett.*, 59:2486.

Ou-Yang, Z.-C., Liu, J.-X., and Xie, Y.-Z. (1999). *Geometric Methods in the Elastic Theory of Membranes in Liquid Crystal Phases*. World Scientific, Singapore.

Petrosko, S. H., Johnson, R., White, H., and Mirkin, C. A. (2016). Nanoreactors: Small spaces, big implications in chemistry. *J. Am. Chem. Soc.*, 138:7743.

Sutter, D. H. and Flygare, W. J. (1969). Molecular g values, magnetic susceptibility anisotropies, second moment of the charge distribution, and molecular quadrupole moments in furan and thiophene. *J. Am. Chem. Soc.*, 91:4063.

van Rhee, P. G., Rikken, R. S. M., Abdelmohsen, L. K. E. A., Maan, J. C., Nolte, R. J. M., van Hest, J. C. M., Christianen, P. C. M., and Wilson, D. A. (2014). Instability and deformation of a spherical vesicle by pressure. *Nat. Commun.*, 5:5010.

Weatherburn, C. E. (1927). *Differential Geometry of Three Dimensions*. Cambridge Univ. Press, Cambridge.