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Domains on a Sphere: Neutron Scattering, Models, and Mathematical Formalism

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Introduction

Analytical and semi-analytical approaches to scattering processes from lipid domains on spherical vesicles can provide direct relations between numerical and/or analytical models for interpreting small angle neutron or X-ray scattering from such systems. The vesicle lipid bilayer and the types of domains that can be analyzed using the methods mentioned here is shown in Figure 1.

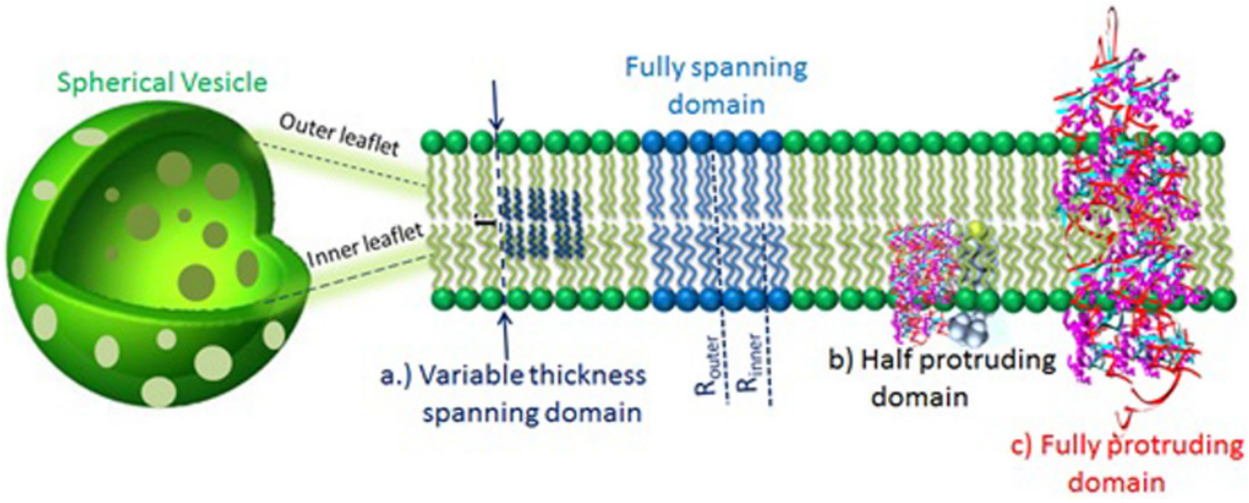

Figure. 1. (Anghel et al 2018) A cross section of a spherical vesicle populated with domains and inclusions. The vesicle's lipid bilayer (i.e., thickness) is made of two lipid leaflets, or monolayers (inner and outer). The lipid bilayer may also contain inclusions such as proteins and cholesterol-rich domains

Analysis and prediction of domain pair correlations from scattering experiments is simplified when using the numerical and analytical approaches described herein, thus greatly reducing the need for access to

powerful computational facilities. In other words, when analytical models for phase separated systems are made available, data analysis is expedited over a wide range of parameters.

The paper is divided in two parts:

(i) The first part describes a set of general formulas applicable to any hollow sphere populated by a finite number of domains of any shape. Consequently, both intra-domain correlations and center-to-center correlations are represented by arrays. The inputs for this approach can be either numerical results from molecular dynamics (MD) models, or results from other, but simpler analytical models.

(ii) The second part outlines results from analytical models of domains. This part deals specifically with circular domains, as both intra-domain and center-to-center correlations are represented by scalars, and not by arrays. Both intra- and inter- domain correlations are discussed.

From Model Description to Scattering Theory Results

Analytical and numerical models are capable of producing a density function $\rho(\boldsymbol{r})$ (in the case of neutrons this is the scattering length density, SLD), which is taken as input by the scattering calculation presented here. The details for computing the integrated cross-section from the SLD are summarized below.

The starting point is the calculation of the form factor $F(\boldsymbol{q})$, which is used to compute the integrated cross-section, $I(q)$ (S. C. Harrison, 1969):

$$I(q) = \frac{1}{4\pi}\int F(\boldsymbol{q})F^*(\boldsymbol{q})d\hat{q}\,. \qquad (1)$$

The form factor is given by:

$$F(\boldsymbol{q}) = -\int \rho(\boldsymbol{r})e^{-i\boldsymbol{q}\cdot\boldsymbol{r}}d^3\boldsymbol{r}\,. \qquad (2)$$

The density function is the sum of the contributions from the vesicle wall, $\mu(\boldsymbol{r})$, and the domains $\omega(\boldsymbol{r})$, and is written as:

$$\rho(\boldsymbol{r}) = \mu(\boldsymbol{r}) + \omega(\boldsymbol{r})\ , \qquad (3)$$

where $\omega(\boldsymbol{r})$ includes deviations from the vesicle wall density function (i.e., in the absence of domains $\omega(\boldsymbol{r})$=0).

$F(\boldsymbol{q})$ is then expressed as a spherical harmonic expansion (Newton 2002) written as follows:

$$F(\boldsymbol{q}) = -\int [\mu(r) + \omega(\boldsymbol{r})]e^{-i\boldsymbol{q}\cdot\boldsymbol{r}}d^3\boldsymbol{r} = -4\pi \left(Y_0^0(\hat{q})\int_0^\infty \mu(r)r^2 j_0(qr)dr \int Y_0^{0\,*}(\hat{r})d\hat{r} + \sum_{l,m}(-i)^l Y_l^m(\hat{q})\int_0^\infty r^2 j_l(qr)w_l^m(r)dr\right), \qquad (4)$$

where $Y_l^m(\hat{u})$ is a spherical harmonic depending on the unit vector, $\hat{q}$ is a unit vector in the direction of $\boldsymbol{q}$, $\hat{r}$ is a unit vector in the direction of $\boldsymbol{r}$, and j_l is a spherical Bessel function of the first kind. Taking

advantage of the linearity of the Born approximation, one can express the total contribution of the domains as:

$$\omega(\boldsymbol{r}) = \sum_{J} \omega_J(\boldsymbol{r}) \,,$$

where $\omega_J(\boldsymbol{r})$ correspond to the domains on the surface. It should be pointed out that the domains can be of different shape.

Rotations in spherical harmonics allows for the use of Wigner functions, as the relative positions of the domains can be described through rotation transformations (Edmonds 1957). For example, the position of a domain on a spherical surface can be defined by the Euler angles (see general angles in Figure 1 A) α_J,β_J,γ_J (Figure 1 B) that determine its position relative to the sphere's north pole: $\alpha_J$determines the longitude of the domain J center on the sphere, β_J determines the latitude of the domain center J on the sphere, and γ_J determines the rotation of the domain J around its fixed center compared to its position at the north pole, as shown in Figure 1.

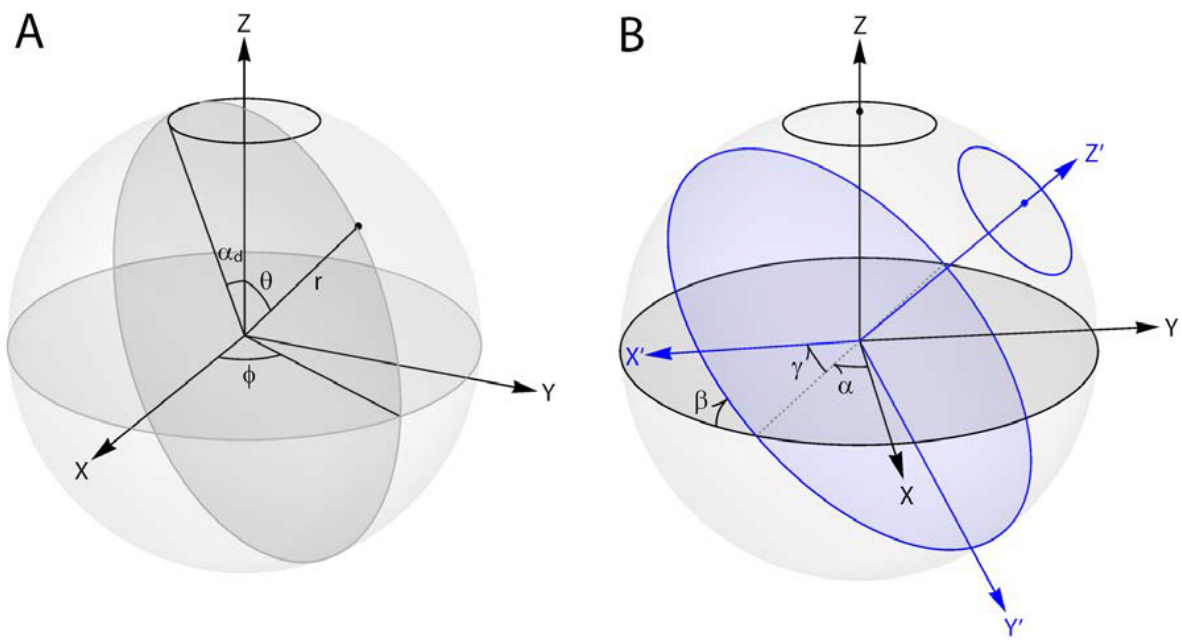

Figure 2. (Heberle et al. 2015) Coordinate systems used to define the form factor for a laterally heterogeneous vesicle wall of domains.

If the domains are distributed in a non-random fashion, such as their centers at the vortices of a Platonic solid (e.g., black patches on a soccer ball, Figure 3).

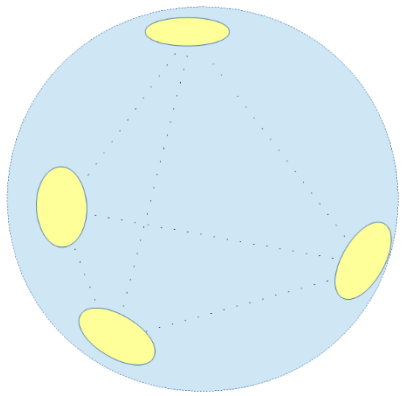

Figure. 3. A sketch of 4 domains placed at the vertices of a regular tetrahedron (shown by dotted lines).

For regularly distributed domains, the integrated cross-section is given by (Heberle et al. 2015) and written as follows:

$$I(\boldsymbol{q}) = (4\pi)^2|M_0(q)|^2 + 2(4\pi)^{3/2}M_0(q) \sum_J \tilde{W}_0(\alpha_{d,J},q) + 4\pi \sum_{J,K}\sum_{l=0}^{\infty} \tilde{\boldsymbol{W}}^*_{l,J}(\alpha_{d,J}) D_l^*(\alpha_J,\beta_J,\gamma_J) D_l(\alpha_K,\beta_K,\gamma_K)\, \tilde{\boldsymbol{W}}_{l,K}(\alpha_{d,K}), \quad (5)$$

where $M_0(q)$ is the contribution resulting from integrating $\mu(\boldsymbol{r})e^{-i\boldsymbol{q}\cdot\boldsymbol{r}}$, $\tilde{W}_0(\alpha_{d,J},q)$ is the $l=0$ contribution from integrating $\omega(\boldsymbol{r})e^{-i\boldsymbol{q}\cdot\boldsymbol{r}}$ for the Jth domain, $D_l(\alpha_K,\beta_K,\gamma_K)$ is the Wigner function for the Kth domain, and the intra-domain correlation is represented by the array:

$$\tilde{W}^{\prime m}_{l,J}(\alpha_{d,J},q) = \int_0^{\infty} r^2 j_l(qr) w_l^m(r)\, dr. \quad (6)$$

For randomly distributed domains, the integrated cross-section is given by (Anghel et al. 2018):

$$I(\boldsymbol{q}) = (4\pi)^2|M_0(q)|^2 + 2(4\pi)^{3/2}M_0(q) \sum_J \tilde{W}_0(\alpha_{d,J},q) + 4\pi \sum_{J,K}\sum_{l=0}^{\infty} \left\langle \tilde{\boldsymbol{W}}^*_{l,J}(\alpha_{d,J}), \boldsymbol{C}_{l,\,JK}(\alpha_{d,J},\alpha_{d,K}) \tilde{\boldsymbol{W}}_{l,K}(\alpha_{d,K}) \right\rangle, \quad (7)$$

where $M_0(q)$ is the form factor of the original vesicle wall $\tilde{\boldsymbol{W}}^*_{l,J}(\alpha_{d,J})$, and $2l+1$ is the component array for the l th harmonic of a domain, $\boldsymbol{C}_{l,\,JK}(\alpha_{d,J},\alpha_{d,K}) = \overline{D_l^*(\alpha_J,\beta_J,\gamma_J) D_l(\alpha_K,\beta_K,\gamma_K)}$ is the center-to-center correlation of the average of Wigner functions given by an ($2l+1$ X $2l+1$) array for domain center correlations, and $\langle .,. \rangle$ denotes a scalar product. The coefficients in Eq. 7 can be computed either from MD numerical data of the vesicle wall and domains, or from an analytical model. Any other approach

that produces the intradomain correlation and center-to-center correlations can also provide inputs for these formulae.

Eq. 5 may be used when the domains are ordered on the surface, such as on the vertices of a regular polyhedron, while Eq. 7 should be used when the domains are randomly distributed on the vesicle surface and are described by a probability distribution function, similar to that of a gas or liquid.

Analytical Form Factors

In the case of circular domains interacting as hard bodies, both intra-domain correlations and correlations between domain centers can be computed by simpler methods, either analytical for the domain correlation function or by discretization for domain center correlation functions. Analyses dealing with domain area and the number of domains are also easier to perform. Moreover, the simpler calculations allow for the easier adjustment of parameters, so that the calculated results approximate those obtained by experiment.

All analytical cases discussed thus far deal with circular domains and are relatively easy to calculate because both spherical and Wigner functions for circular domains reduce to Legendre polynomials P_l $(\cos\theta_{JK})$ written as follows:

$$I(q) = 4\pi\left[2\sqrt{\pi}M_0(q) + \sum_J \tilde{W}_{0,J}(\alpha_{d,J};q)\right]^2 + 4\pi\sum_J\sum_{l=1}^{\infty}\left|\tilde{W}_{l,J}(\alpha_{d,J};q)\right|^2 + 4\pi \sum_{J\neq K}\sum_{l=1}^{\infty}\tilde{W}^0_{l,J}(\alpha_{d,J};q)\tilde{W}^0_{l,K}(\alpha_{d,K};q)P_l(\cos\theta_{JK}), \quad (8)$$

where J and K identify domains, θ_{JK} is the angle between vectors pointing from the origin to domain centers J and K, and $\tilde{W}^0_{l,J}(\alpha_d;q)$ and $\tilde{W}^0_{l,K}(\alpha_d;q)$ (both real) are given by Eq. 6. The average of P_l $(\cos\theta_{JK})$ is then a simple scalar instead of a matrix.

Intradomain Factors

Intra-domain factors can be computed for a variety of circular domains, such as domains of variable thickness, half protruding domains, fully protruding domains, annular domains(channels), etc. In all these cases, $\omega(\boldsymbol{r})$ is taken as the difference between the density of the domain and that of its neighboring medium for a given height in the wall or outside of it (i.e., within the wall the difference is between the domain and wall at a given height; above the wall the difference is between the density of the domain and the outside of the vesicle, similar to the case of protruding inside the vesicle; for domains with a hole, the difference is between the hole contents and the density of the vesicle wall at a given height).

Center to Center Correlation

The center-to-center correlation problem does not seem to have an obvious analytical solution. However, an approximate solution can be developed assuming that the domains behave like hard particles. In this case, an equation similar to the Percus Yevick can be assumed, where its numerical solution approximates the distribution of hard domains. If data on inter-domain interactions becomes available, other liquid theory equations may be used to describe domains on spherical vesicles.

The centers of domains can be either correlated, where domains on the vesicle wall move together, or uncorrelated, where domains in the wall's two layers move independently of each other. The scattering from the correlated and uncorrelated domains can be estimated.

The center-to-center correlation is simplest (a step function) for the case of only two domains on the vesicle wall. In the case of three domains, an analytical formula is derived based on spherical trigonometry.

Assuming the domains are hard objects, an analog to the Percus-Yevick (PY) equation was developed as an approximation to the exact two domain probability distribution and is given by:

$$g_N(\cos\theta) - 1 - c_N(\cos\theta) - \rho \int c_N(\cos\theta')\left(g_N\left(\overrightarrow{\Omega'} \cdot \vec{\Omega}\right) - 1\right)\sin\theta' d\theta' d\varphi' + \frac{1}{N} = 0. \quad (9)$$

PY conditions for the functions g_N, the analog on the sphere of the radial distribution function and c_N, the direct correlation function on the sphere are given as:

$$g(\cos\theta) = 0, \cos\theta < \cos 2\alpha_d \ (10)$$

$$c(\cos\theta) = 0, \cos\theta > \cos 2\alpha_d, \ (11)$$

where θ is the azimuthal angle on the surface and α_d is the "radial" domain opening angle.

This equation was tested against Monte Carlo results and found to be accurate. The algorithm used to solve it was found to work well for domains covering up to 30% of the vesicle surface.

Summary and Conclusions

We have developed numerical and analytical approaches for computing scattering from domains on spherical vesicle walls. The main features of the methods described are:

- (i) There are no real restrictions as to which model can be used for describing the scattering data of domains on a vesicle, i.e., the input model may either be numerical or analytical.
- (ii) Analytical approaches have two main advantages:
    - Provided with numerical data, they allow for fast computation of the scattering cross-sections.
    - Allow for a more detailed analysis of experimental data.
- (iii) The number of series terms used in the method depends on the scattering data resolution.

- (iv) Models for circular rigid domains were introduced. They include exact solutions for 2 and 3 domains and an analog of the PY equation for multiple domains.
- (v) The described numerical and analytical approaches can be further generalized to describe more complicated experimental systems.

References

This presentation summarizes the following work:

- "Models for randomly distributed scopic domains on spherical vesicles" by V. N. P. Anghel, D. Bolmatov, J. Katsaras, Phys. Rev. E 97, 062405 (2018), https://journals.aps.org/pre/abstract/10.1103/PhysRevE.97.062405

- "Scattering from phase-separated vesicles. I. An analytical form factor for multiple static domains" by F.A. Heberle, V.N.P. Anghel, & J. Katsaras, (2015). J. Appl. Cryst. 48, doi:10.1107/S160057671501362X.

- "Scattering from Laterally Heterogeneous Vesicles II: The Vesicle Form Factor", by V. N. P. Anghel, N. Kuˇcerka, N., J. Pencer, & J. Katsaras, (2007). J. Appl. Cryst. 40, 513–525.

The theoretical bases of this work are given in:

- "Structure of Tomato Bushy Stunt Virus, I The Spherically Averaged Electron Density" by S. C. Harrison, (1969). J. Mol. Biol. 42, 457–483, (1969).

- R. G. Newton, Scattering Theory of Waves and Particles. New York: Dover (2002).

- A. R. Edmonds, Angular Momentum in Quantum Mechanics (Princeton University Press, Princeton, NJ,1957).

The Ornstein Zernike approach for a finite system is adapted to a spherical surface from the case of a finite number of domains in Euclidean space given in:

- "The Ornstein-Zernike Equation in the Canonical Ensemble" by J. A. White, S. Velasco, Europhys. Lett. 54 (2001) 475-481.