Appendix B

Equilibrium lateral distribution of membrane constituents

The equilibrium lateral distribution of the membrane constituents in a particular layer for a given membrane shape in the sequence, is obtained by minimization of the free energy of the respective layer (Eq.(1)):

$$\frac{F_{\mathrm{j}}}{kT} = \int_A \left\{ \sum_{i=1}^{2} \left(m_{i,j} \frac{f_{i,j}}{kT} + m_{i,j} \ln m_{i,j} \right) + \frac{w z_2}{2} m_{2,j}^2 \right\} m_0 \, \mathrm{d}A\,, \qquad j = \text{in, out} \tag{B.1}$$

The average relative densities

$$\bar{m}_{i,j} = \frac{1}{A} \int_A m_{i,j} \mathrm{d}A\,, \qquad j = \text{in, out} \tag{B.2}$$

for each of the species are allowed to be different in the two membrane layers.

We construct a Lagrangian for each of the monolayers

$$L_j = \sum_{i=1}^{2} \left(m_{i,j} \frac{f_{i,j}}{kT} + m_{i,j} \ln m_{i,j} + \lambda_{i,j} (m_{i,j} - \bar{m}_{i,j}) \right) + \frac{w z_2}{2} m_{2,j}^2\,, j = \text{in, out,} \tag{B.3}$$

where $\lambda_{i,j}$ (j = in, out) are the Lagrange multipliers. Inserting into the Lagrangian the relations $m_{1,j} = 1 - m_{2,j}$ and $\bar{m}_{1,j} = 1 - \bar{m}_{2,j}$ (j = in, out), we can eliminate one Lagrange multiplier in each layer by defining $\lambda_j = \lambda_{2,j} - \lambda_{1,j}$, ($j$ = in, out). Using the Euler-Lagrange equations $\partial L_j / \partial m_{2,j} = 0$ (j = in, out) and Eq.(B3), we can derive the relative area densities $m_{2,j}$ in both monolayers (j = in, out). For small direct interactions ($|w| < 1$), the relative area densities $m_{2,j}$ (j = in, out) can be expressed analytically (up to the first relevant term in w):

$$m_{2,j} = m_{2,j}^{(0)} \left(1 - w z_2 m_{2,j}^{(0)} (1 - m_{2,j}^{(0)}) \right), \qquad j = \text{in, out,} \tag{B.4}$$

where $m_{2,j}^{(0)}$ is defined as:

$$m_{2,j}^{(0)} = \frac{\overline{m}_{2,j}}{\overline{m}_{2,j} + \overline{m}_{1,j}\,\mathrm{e}^{\lambda_j - (f_1 - f_2)/kT}} \tag{B.5}$$

and λ_j is calculated from the condition that the average of $m_{2,j}$ over the whole membrane is equal to $\overline{m}_{2,j}$.

The orientational effects are contained in the single-constituent energies $f_{i,j}$.