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Supporting Material

Membrane mediated interactions measured using membrane domains

Stefan Semrau, Timon Idema, Thomas Schmidt, and Cornelis Storm

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1 Materials and methods

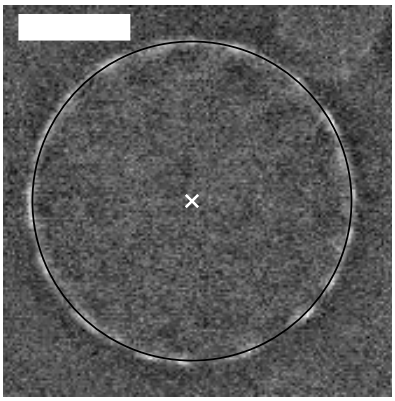

Figure 1: L_d phase of a phase separated vesicle with fitted circle (black) superimposed. The cross marks the position of the center. Scalebar: 20 μm.

2 Monte Carlo simulation of domain size distributions

For short enough times, when the system is still far from complete phase separation, the evolution of domain sizes can be modeled by a master equation (1):

$$\dot{N}_n = \frac{1}{2}\sum_{m=1}^{n-1} k_{m,n-m} N_m N_{n-m} - \sum_{m=1}^{\infty} k_{n,m} N_n N_m \tag{1}$$

where N_n is the number of domains with area n, $k_{n,m}$ the fusion rate for domains of area n and m and the dot refers to the time derivative. Since N_n can assume continuous values, the master equation approach breaks down for domain numbers on the order of 1.

In agreement with our experimental observations we do not allow for scission events, i.e. the fission of a domain into two smaller domains. Due to the high line tension such events never occur in our experiments.

If the fusion rate is assumed to be independent of domain area ($k_{n,m} = k$) the continuous master equation

$$\frac{\partial}{\partial t} N(x,t) = k\left(\frac{1}{2}\int_0^x dy\; N(y,t)N(x-y,t) - \int_0^\infty dy\; N(x,t)N(y,t)\right) \tag{2}$$

can be solved exactly. The ansatz $N(x,t) = a(t)\exp(-b(t)x)$ results in a system of ordinary differential equations for the functions a and b:

$$\left\{\begin{array}{l} \dot{a}(t) = -\frac{k}{2}a(t) \\ \dot{b}(t) = -k\frac{a^2(t)}{b(t)} \end{array}\right. \Rightarrow \left\{\begin{array}{l} a(t) = \left(k_0 + \frac{k}{2}t\right)^{-2} \\ b(t) = \left(k_0 + \frac{k}{2}t\right)^{-1} \end{array}\right. \tag{3}$$

With the initial condition of $1/\varepsilon$ equally sized domains of area ε and $\varepsilon \to 0$ the solution is:

$$N(x,t) = \frac{1}{\left(\frac{k}{2}t\right)^2} e^{-\frac{1}{\frac{k}{2}t}x} \tag{4}$$

While the total domain area is constant

$$\int_0^\infty dx\ xN(x,t) = 1, \tag{5}$$

the total number of domains decays over time

$$\int_0^\infty dx\ N(x,t) = \frac{1}{\frac{k}{2}t}, \tag{6}$$

and consequently the average domain size increases

$$\frac{\int_0^\infty dx\ xN(x,t)}{\int_0^\infty dx\ N(x,t)} = \frac{k}{2}t. \tag{7}$$

Obviously, the master equation approach is only valid for $t \ll \frac{2}{k}$.

The solution of the continuous master equation is an approximate solution of the discrete master equation if the distribution is binned with binsize ε

$$N_n(t) \approx \varepsilon \frac{1}{\left(\frac{k}{2}t\right)^2} e^{-\frac{1}{\frac{k}{2}t}n} \tag{8}$$

Figure 2a shows a comparison of the exact solution Eq. 8 of the continuous master equation to Monte Carlo simulations results for the corresponding discrete master equation. The good agreement proves the validity of our Monte Carlo scheme.

As shown in the main text, interaction between domains leads to the occurrence of a local maximum in the domain size distributions and an exponentially decaying tail. Here we want to substantiate the claim that, to get this qualitative result, it is sufficient to have a probability for domain merger which is monotonically decreasing with domain size. In the main text we use the probability $p_{n,m}^{\text{merge}} = c/(n*m)$ for the merger of two domains of sizes n and m respectively. Here we supplement the results presented there by a simulation in which we use $p_{n,m}^{\text{merge}} = c/\sqrt{n*m}$. The resulting size distributions, shown in Figure 2b, are qualitatively identical to the ones obtained in the main text.

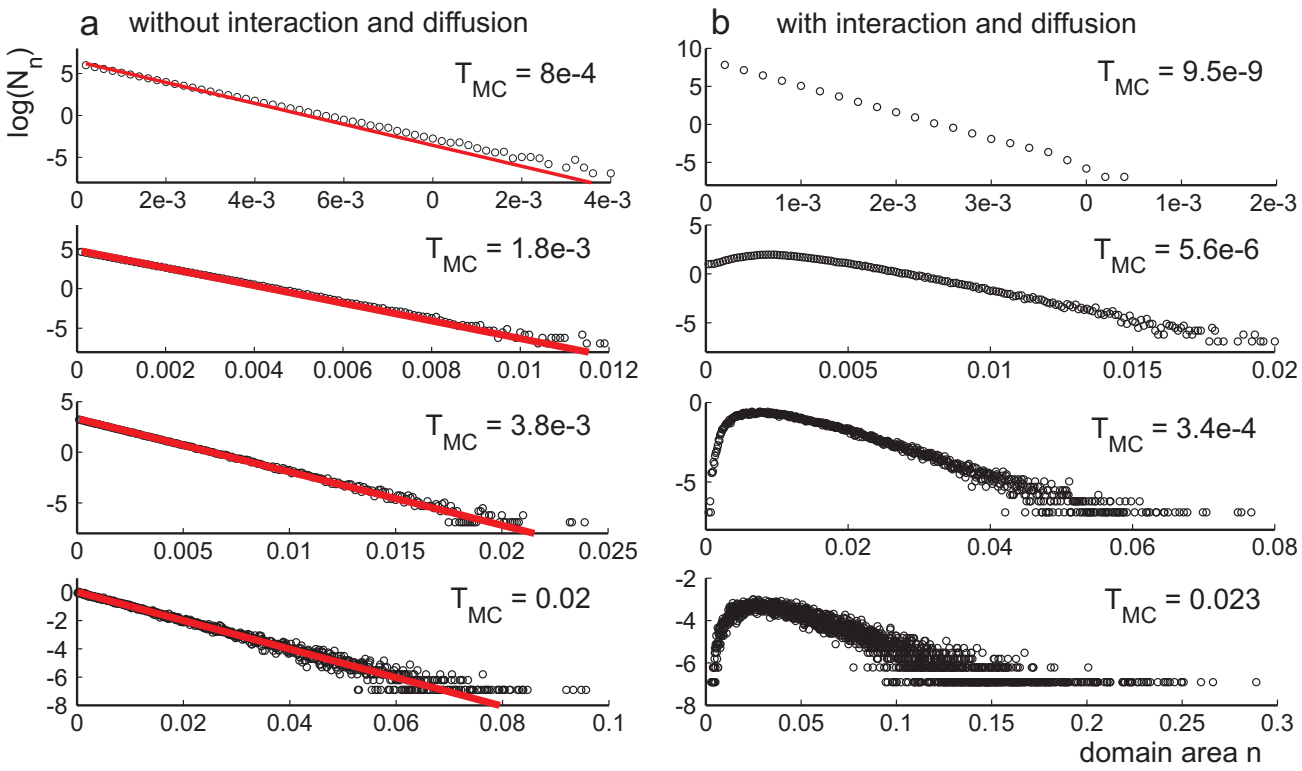

Figure 2: Domain size distributions determined using Monte Carlo simulations. (a) Domain size distribution for 4 different Monte Carlo times averaged over 1000 simulation runs (open circles) with theoretically expected distribution (red line) for fusion rate $k = 1$. Initial condition: 10^4 domains of area $\varepsilon = 10^{-4}$. (b) Domain size distribution for 4 different Monte Carlo times averaged over 1000 simulation runs (open circles) including diffusion and interaction of domains. Here $p_{n,m}^{\text{merge}} = 10^{-3}/\sqrt{n * m}$. Initial condition: 10^4 domains of area $\varepsilon = 10^{-4}$.

3 Domain budding

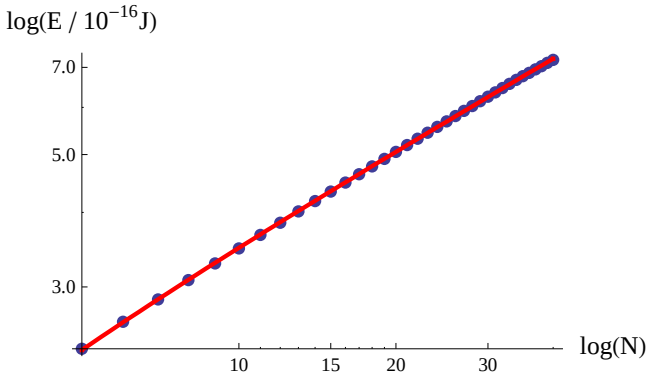

Figure 3: Minimum of the energy (Eq. 14 in the main text) for a given number of domains. Since the line tension contribution is the largest, decreasing the number of domains (and hence shortening the total domain boundary) lowers the energy, in correspondence with the result that the fully phase-separated vesicle is the ground state. From the logarithmic plot shown here we find that the total energy as a function of the number of domains behaves as a power law with exponent 0.53.

4 Measuring the interactions

The diffusion coefficient depends only very weakly on the domain size r. With micrometer sized, liquid ordered domains in a liquid disordered background (with a sufficiently small membrane viscosity) one would expect the diffusion coefficient to follow (2):

$$D(r) = \frac{k_\mathrm{B}T}{16\eta}\frac{1}{r} \tag{9}$$

where $\eta \approx 10^{-3}$ Ns/m^2 is the bulk viscosity of water (see dashed line in Fig. 4). This relation holds if the friction between the domain and the surrounding water is big compared to the friction between domain and surrounding membrane. Therefore the 2D membrane viscosity η' does not play a role and does not appear in Eq. 9. The fact that the measured diffusion coefficients are significantly smaller than predicted by Eq. 9 shows that either the membrane friction is much higher than expected or the interaction between the domains has some influence on the diffusion coefficient.

In order to determine the 2D membrane viscosity η' we employ the Hughes-Pailthorpe-White (3) model for the radius-dependent diffusion constant $D(r)$ which is valid for arbitrary domain size r, water viscosity η and membrane viscosity η'. Instead of the exact form of this model we use an approximation due to Petrov and Schwille (4). By fitting this approximation to the data (thick solid line in Fig. 4) we find the 2D membrane viscosity to be $\eta' = 4.8 \times 10^{-8}$ Ns/m. This value is comparable to the values found in (2) where the diffusion of unbudded, liquid disordered domains in a liquid ordered background is measured.

5 Movie

Movie S1: repelling domains, 55 × 51 μm, sped up 5 times. The L_d phase is stained and appears light, the L_o domains are dark.

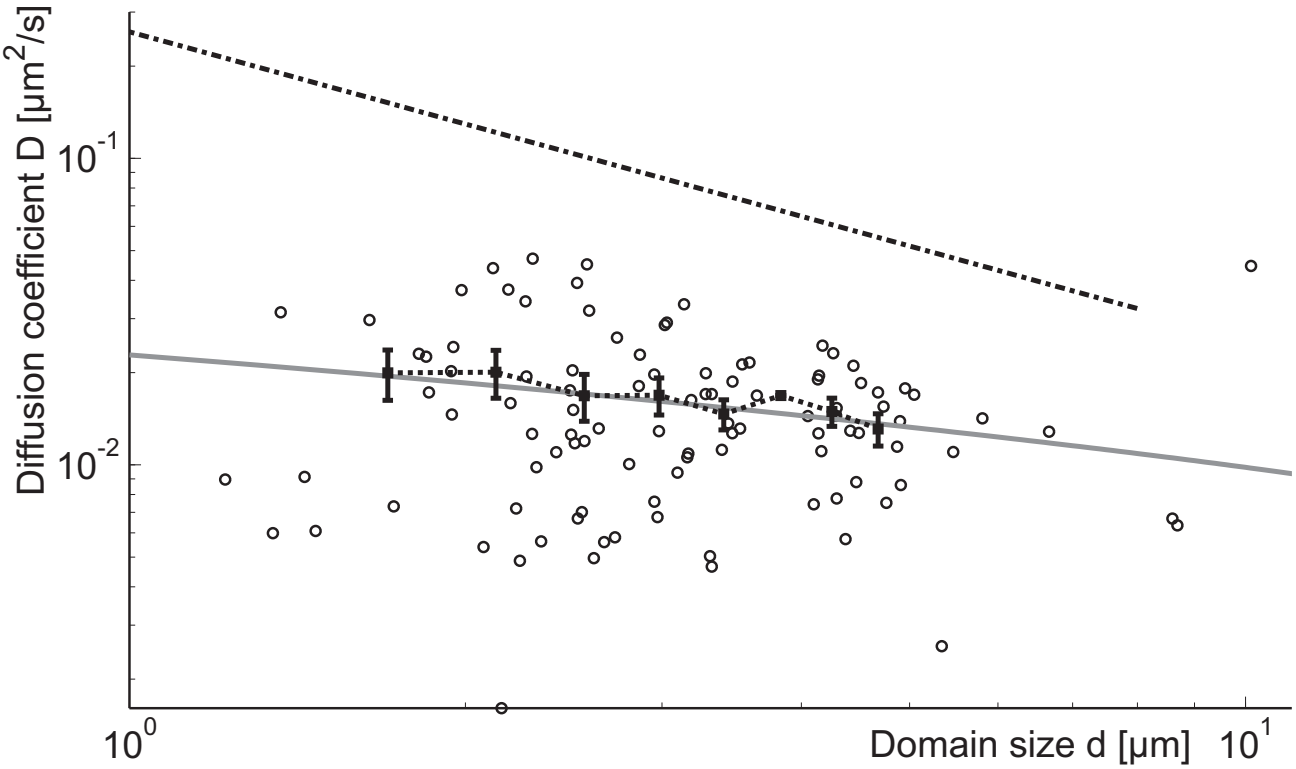

Figure 4: Diffusion coefficient versus domain radius (circles) for 103 trajectories. The squares represent binned data. For comparison, the dashed-dotted line gives the behavior of $D(r)$ according to Eq. 9 if the viscosity of water is dominant. The gray solid line shows a fit to the model described in (4) which gives $\eta' = 4.8 \times 10^{-8}$ Ns/m for the 2D membrane viscosity. Reported error bars are standard errors of the mean.

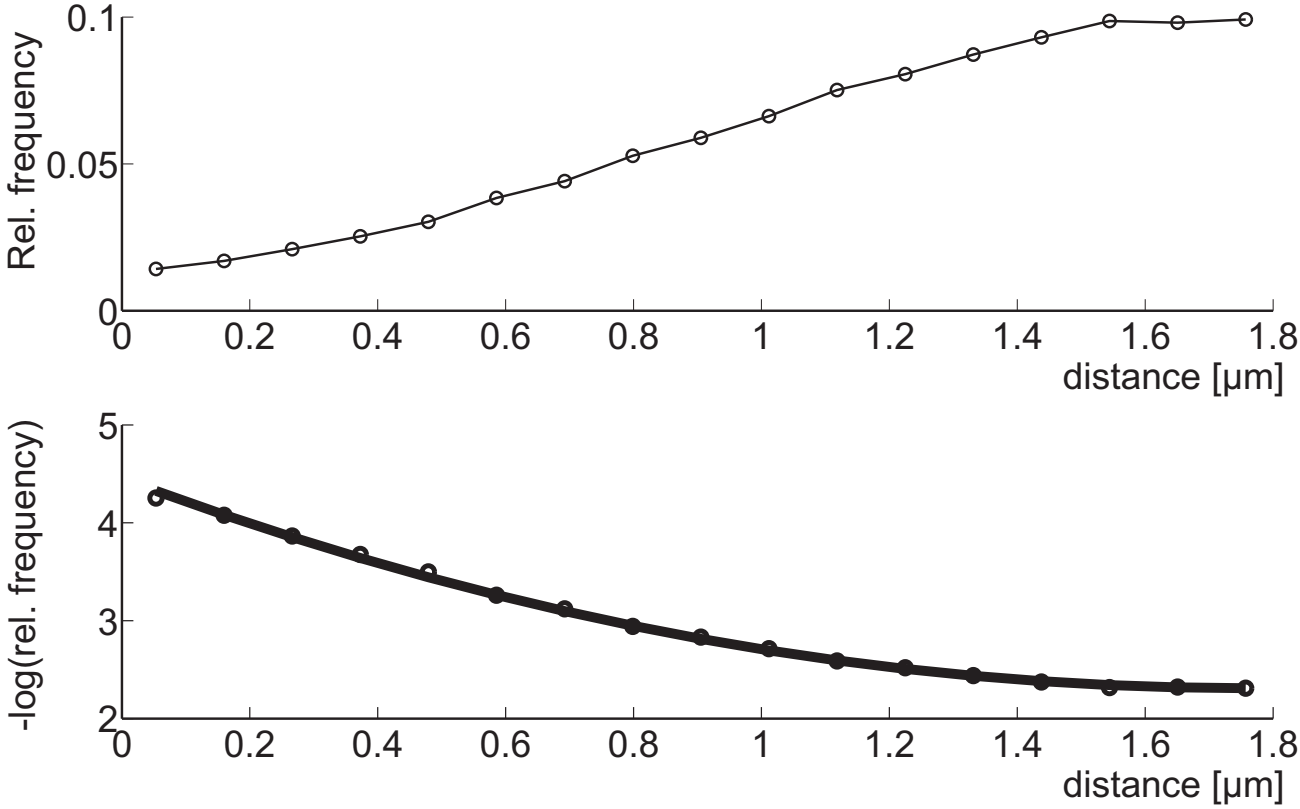

Figure 5: Spring constant determined by domain distance statistics. Upper plot: relative frequency of edge-edge distances; lower plot: -log(rel. frequency) with fit to harmonic potential (solid line).

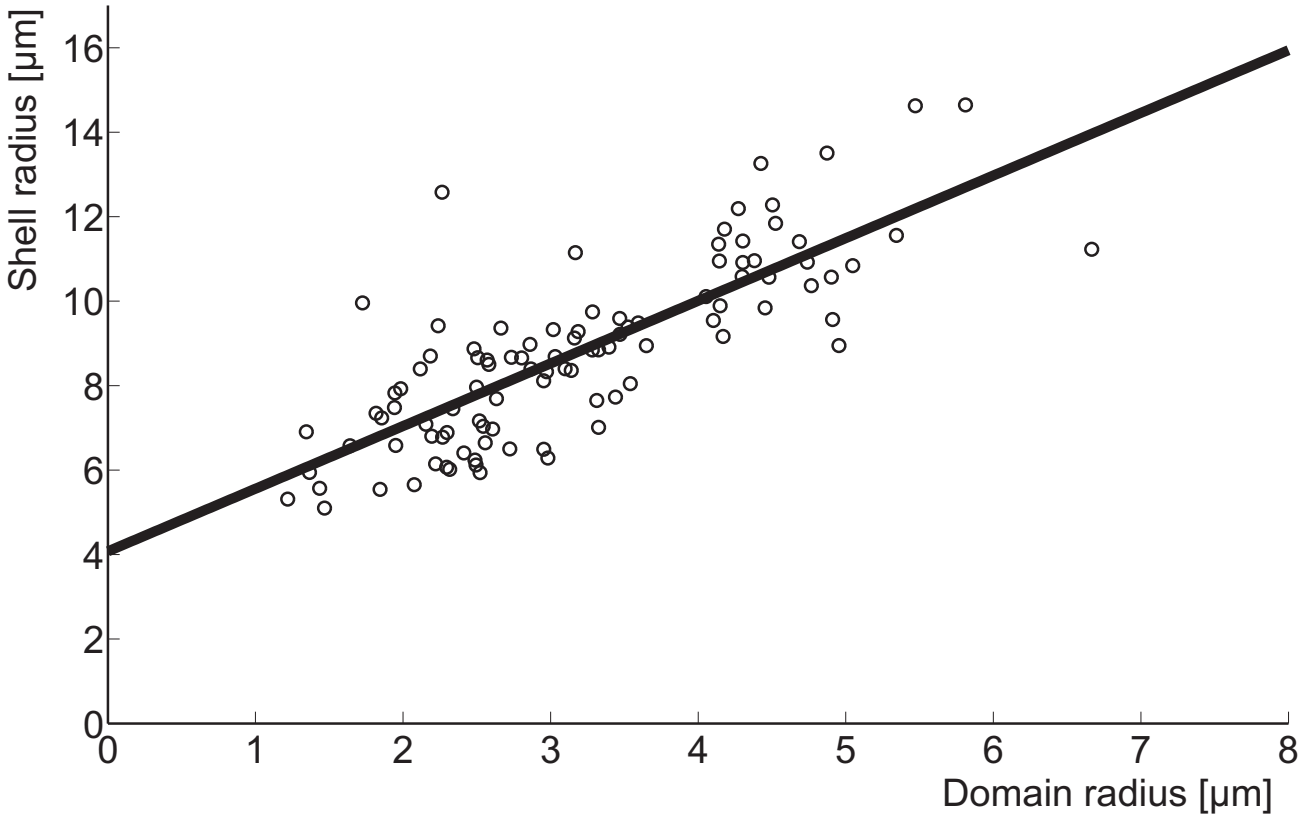

Figure 6: Shell radius versus central domain radius, the solid line corresponds to a linear fit with slope 1.5 and offset 4.1 μm.

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