Figures and figure supplements

The role of scaffold reshaping and disassembly in dynamin driven membrane fission

Martina Pannuzzo et al
Figure 1. Ingredients of the model. (a) CG lipids comprising three beads assemble into membranes via tail bead attractions and head bead repulsions. (b) the dynamin helix is built as a stack of disks with 19 CG beads each; it contains an adhesive membrane-binding strip (red) that represents the PH domains and that can rotate by an angle $\phi$ away from the inward-pointing direction. (c) a CG filament constricts the neck of a CG vesicle consisting of ~10,000 CG lipids.

DOI: https://doi.org/10.7554/eLife.39441.003
Figure 2. Dynamin shape changes and membrane response. (a) Top and (b) Side-view of dynamin dimers assembled into an unconstricted helical filament. (c) CG representation of a constricted filament. (d) Constricted and elongated filament. (e) Constricted and rotated filament. (f) Radius of gyration $R_g$ of the membrane neck (see Materials and methods section) as a function of filament radius $R$ under four protocols: constriction only (blue) constriction+rotation (cyan), constriction+rotation+elongation (dark cyan), constriction+elongation (dark blue). (g) An unconstricted filament resting on a membrane of matching radius (left) creates a Darboux-torque once the (red) adhesion strip is rotated (right), inducing the membrane to asymmetrically bulge; the two arrows indicate the torque couple. (h) Cross-sectional view of a 1- and 1.5-turn helical scaffold at $R = 10.5 \sigma$ and a 3.5-turn scaffold at $R = 10\sigma$. The filament was constricted and rotated, only the adhesion strip is shown. Hemifission seeds are small pores, visible as breaks in bilayer continuity (arrows). (i) Cross-cut illustration of membrane shape changes triggered by a simultaneous filament constriction, rotation, and gradual disassembly (Video 5), leading to hemifission. (j) Continuation of the previous sequence from hemifission to complete fission.

DOI: https://doi.org/10.7554/eLife.39441.004
Figure 2—figure supplement 1. Results of repeated simulation trajectories for the four different constriction protocols presented in Figure 2f. The black dots are the same data as shown in the main article, the red and blue dots stem from two additional runs. In the two cases of constriction and rotation (a) and constriction+rotation+elongation (b), the trajectories show a more spread out distribution compared to constriction only (c). The constriction+elongation (d) case shows a similar spread as the constriction only case.
constriction + rotation, all three trajectories transition into the hemifission state at exactly the same constriction step, while the cases constriction + elongation and constriction + rotation + elongation exhibit some scatter. We attribute this to the larger freedom that the enclosed membrane has in a helical scaffold that features an ever-widening groove due to the elongation component of the shape transformation. Figure 2—source data 1. The data from panel 2 f, as well as the repeated runs shown in Figure 2—figure supplement 1, are given as text-files containing $R_p$ as a function of $R$ for all four constriction scenarios.

DOI: https://doi.org/10.7554/eLife.39441.005
Box 1—Figure 1. Illustration of a tangential membrane torque.
DOI: https://doi.org/10.7554/eLife.39441.016
Figure 3. Time evolution of $R_g$. The neck’s gyration radius is shown in the end stages of a pure constriction protocol. The time series starts when the scaffold radius is $R = R_c = 10.5\sigma$, which leads to $R_g/\sigma = 4.187 \pm 0.02$ (as measured over the subsequent $600\tau$, with an error determined via blocking (Flyvbjerg and Petersen, 1989)). After that, a further constriction of the filament to $R = 10\sigma$ reduces the neck’s gyration radius to $R_g/\sigma = 3.890 \pm 0.04$ but does not trigger hemifission (which corresponds to the much smaller value $R_g \approx 2\sigma$—see Figure 2f). Turning off the adhesion between scaffold and membrane only reduces the gyration radius by a very minor amount, $R_g/\sigma = 3.841 \pm 0.035$, a change that is not statistically significant ($p = 0.36$). Once we additionally let the scaffold disassemble into (non-adhesive) dimers (see also Video 4), the neck very rapidly doubles its radius within about $200\tau$, after which the definition of its location becomes ambiguous.

DOI: https://doi.org/10.7554/eLife.39441.018
Figure 4. Hemifission via a transient pore. This time sequence of simulation snapshots shows slices through the membrane neck with a width of $2\sigma$, placed symmetric around the center of mass of the scaffold (not shown for clarity). The continuity of the tail region (yellow; blue are the head groups) is emphasized by using VMD’s ‘QuickSurf’ rendering on all tail beads (Humphrey et al., 1996), which creates an isosurface extracted from a volumetric Gaussian density map. In panel (a), chosen to be time-point $0\tau$ in this sequence, the tail region is still continuous and encloses an inner lumen with a diameter of about 1 nm. In panel (b) a small pore opens (red arrow) that connects the inner lumen to the exterior region of the vesicle. As it widens through panels (c) and (d), the pore rim above and below the imaged plane fuses to the inner leaflet of the lumen, which finally leaves in panel (e) a cylindrical hemifission micelle connecting two closed vesicles. See also Video 2.

DOI: https://doi.org/10.7554/eLife.39441.024
Figure 5. Definition of helicoidal coordinate system. The black vertical $z$-axis is surrounded by a cylinder, around which a helical dynamin tube winds. Its green center line with radius $R$ and pitch $2\pi p$ is given by (Equation 1). On this space curve we define the (right-handed) Darboux-frame $\{T, N, L\}$, consisting of a tangent vector $T$ (black), normal vector $N$ (blue) and co-normal vector $L$ (red), which are given by (Equation 2). In the $N$-$L$-plane we can then define the circular cross-section of the filament and place rings of CG beads at the correct distance from the green filament axis. The direction along $N$ points towards the enclosed cylinder, but it is easy to rotate it by an angle $\phi$ around the $T$ axis. This is how one may rotate the beads representing the PH domain (red) off the underlying substrate.

DOI: https://doi.org/10.7554/eLife.39441.025
Figure 6. Changes of filament geometry. Time sequence followed when driving the dynamin filament through changes in its radius $R$, pitch $2\pi p$, and rotation angle $\varphi$. As detailed in the results section, we conduct sets of simulations in which various combinations of these observables are adjusted, while others stay at their original value. For instance, in a constriction+elongation simulation the radius is successively decreased from 18 $\sigma$ to 9 $\sigma$, while the pitch is simultaneously tuned up from 11.5 $\sigma$ to 20 $\sigma$ in a way documented by the blue and black curves, respectively, while the rotation angle remains at $\varphi = 0$.

DOI: https://doi.org/10.7554/eLife.39441.026