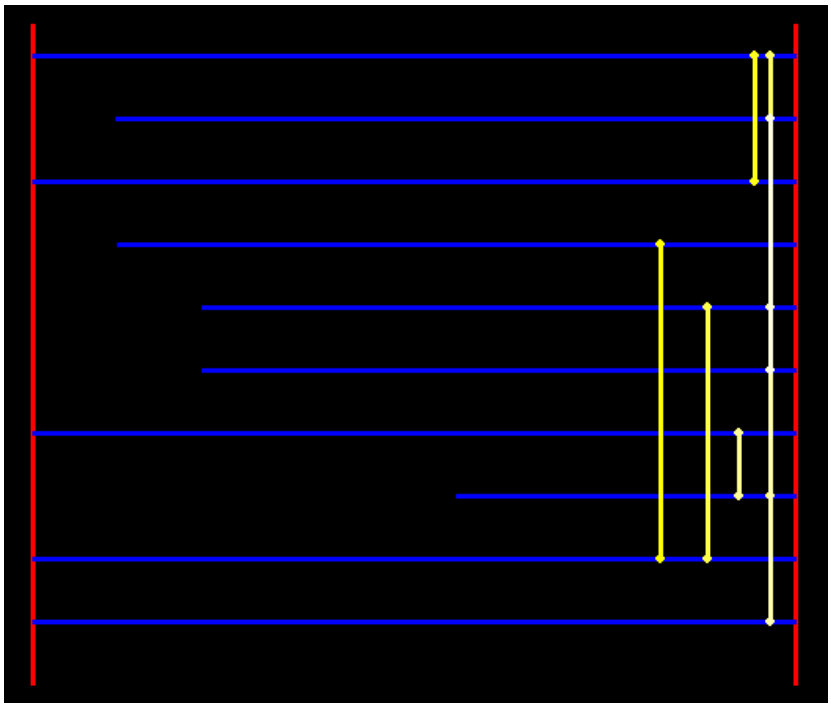

Figure 1: A snapshot from the simulation running. The blue lines are actin filaments. The red line on the left is the outer membrane of the cell. The red line on the right represents the tether at the tip of the invagination. The yellow lines represent bundling proteins, each of which is bound to two filaments.

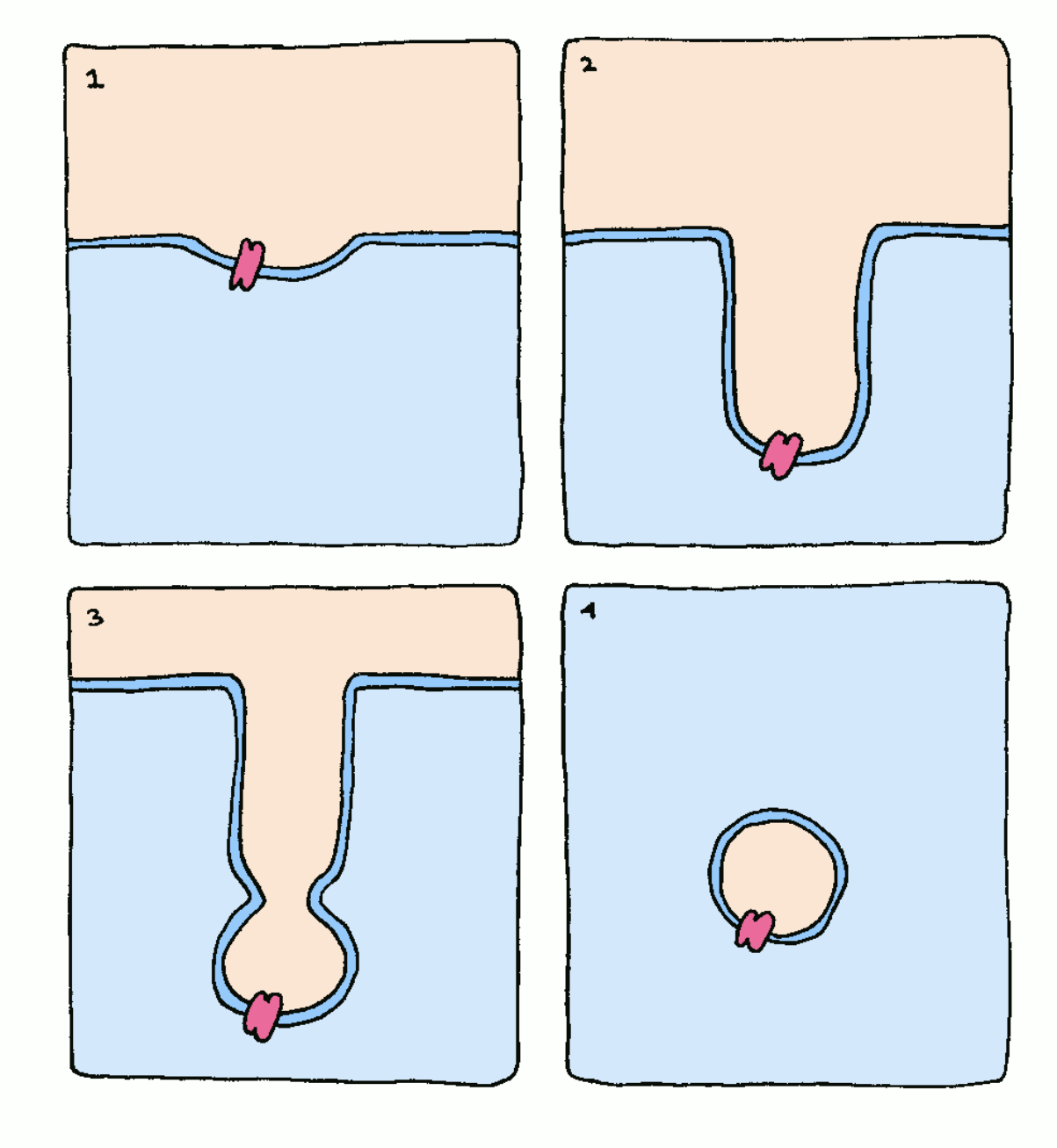

Figure 2: Endocytosis

1) A pit is created in the plasma membrane containing cargo (e.g. a membrane protein for recycling).
2) The pit elongates to form a tubule with a round bud at the end, containing the cargo.
3) The bud pinches off from the tubule to form a free vesicle.
4) The cargo is delivered to the endo-lysosomal membrane system for processing.

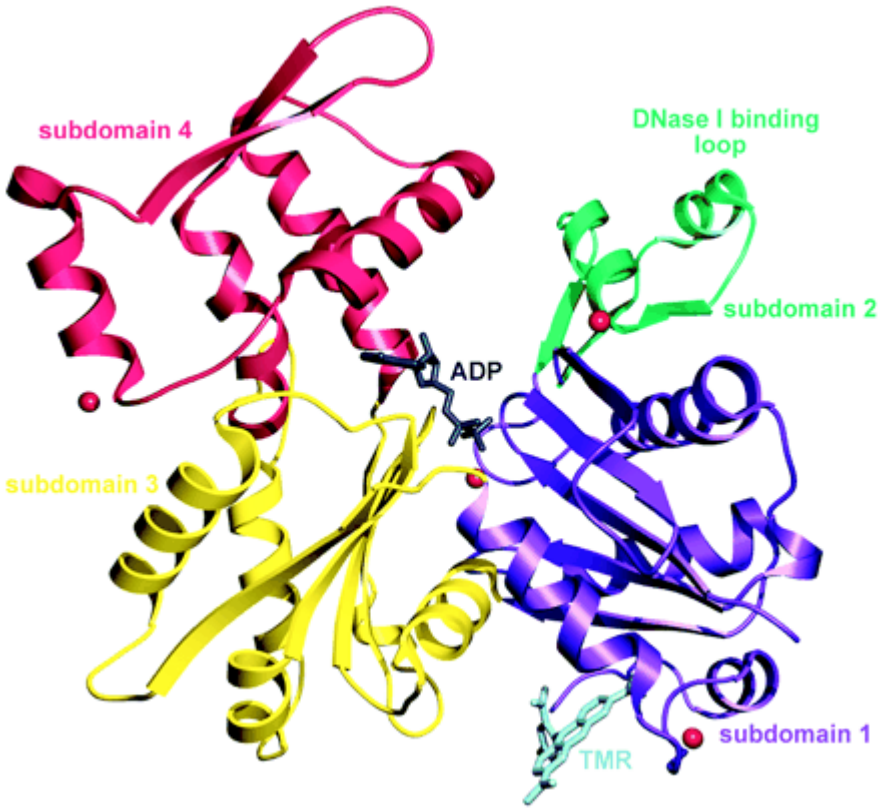

Figure 3: Uncomplexed actin in the ADP-bound state
From Otterbein *et al*, 2001.

A single actin monomer with a molecule of ADP bound in the nucleotide binding cleft. Subdomains 1 (purple) and 2 (green) form the smaller domain, which is found on the outside of filaments when actin polymerises. The larger domain consists of subdomains 3 (yellow) and 4 (pink).

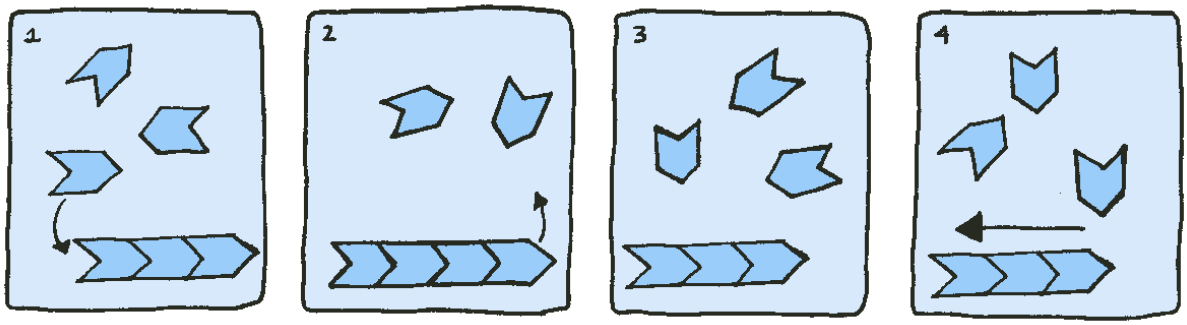

Figure 4: Treadmilling

1) There is a pool of G-actin and an F-actin filament
2) G-actin monomers bind to the barbed end of the filament more readily than to the pointed end
3) Monomers dissociate from the pointed end
4) The filament has moved through the cytoplasm, but each monomer inside the filament has remained stationary.

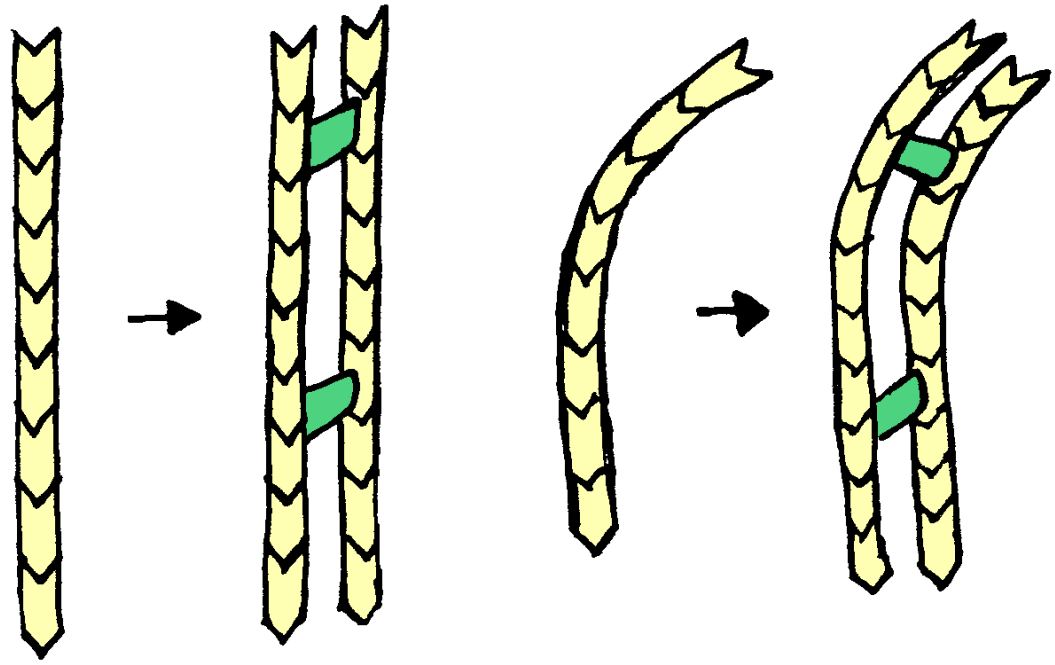

Figure 5: Bundling proteins

Bunding proteins (such as fimbrin) attach two parallel actin filaments to each other. These bundles of filaments take more energy to bend than a single filament, since they have a larger cross-section.

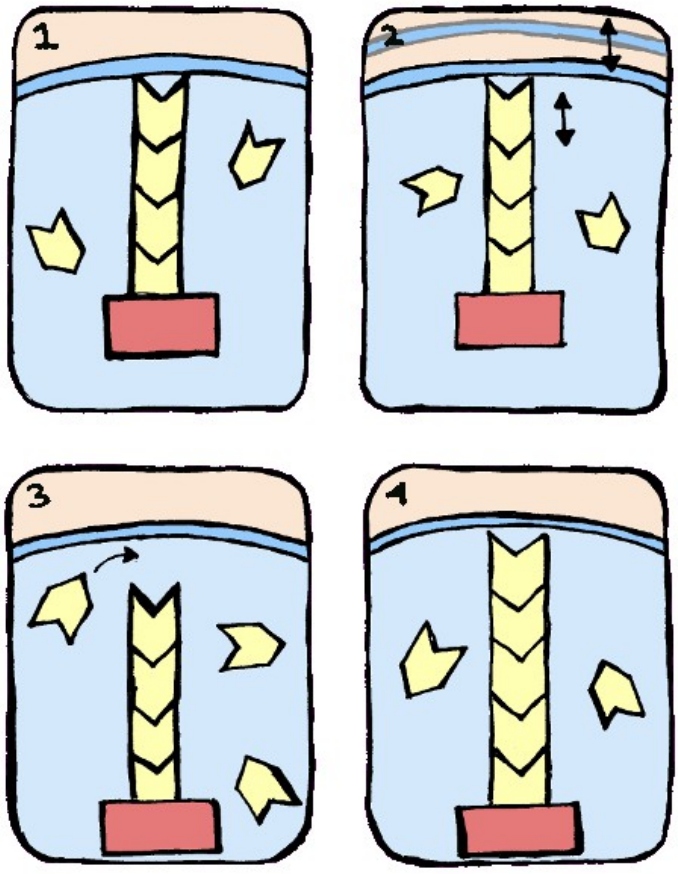

Figure 6: Brownian Ratchet Mechanism

1. A filament grows until its barbed end is touching the cell membrane. No monomers can diffuse in, so the filament can't grow any longer. The filament is tethere at its pointed end to an object (red), which is now a set distance away from the membrane.

2. The cell membrane and the filament are both moving constantly due to the thermal motion of water molecules (also known as Brownian motion).

3. Occasionally, there will be enough space between the membrane and the filament that a monomer can diffuse in and attach to the end of the filament.

4. The filament has grown in length. The red object is now further away from the membrane. Since on-rate for polymerisation is significantly higher than the off-rate, it is unlikely that the filament will shrink. This gives the process directionality, hence the name “ratchet”.

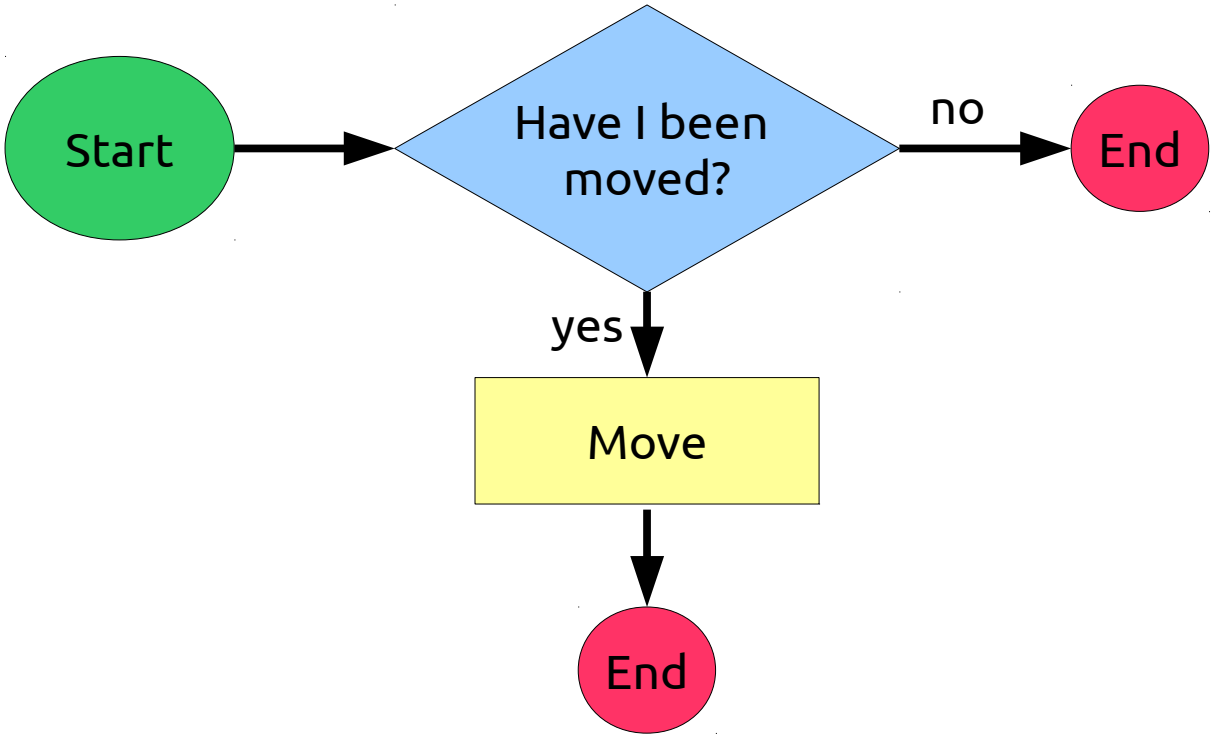

Figure 7: Membrane agent

When the invagination has been lengthened, the membrane agent recieves information from the filament agents and changes its position.

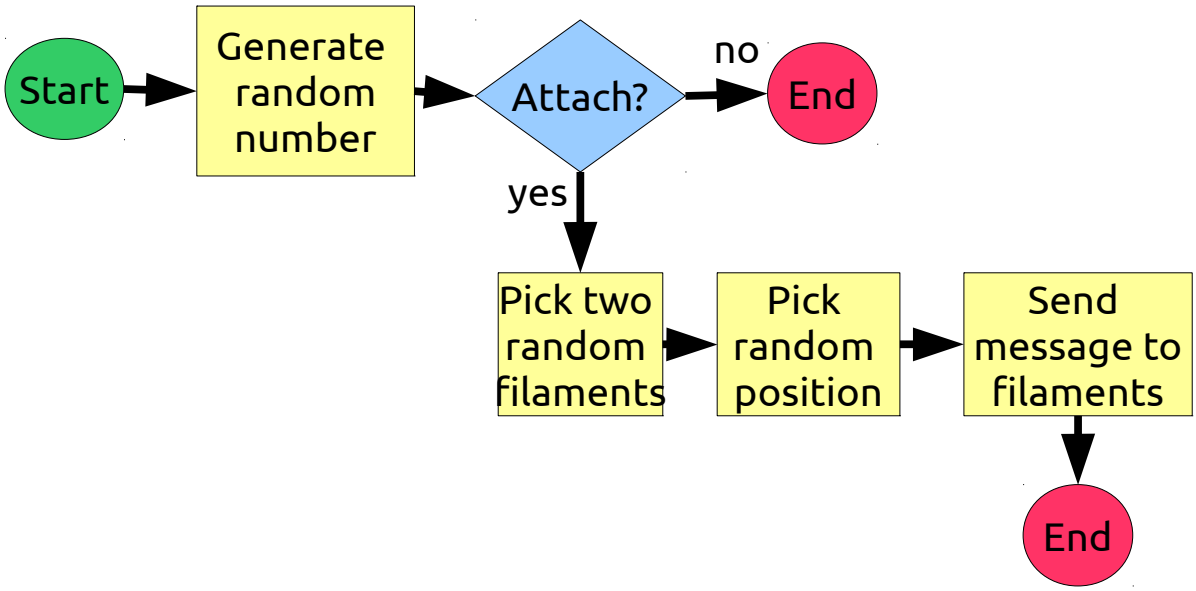

Figure 8: Bundling protein agent

First, a random number is generated. If the random number is over the threshold probability for attaching, it will use two further random numbers to pick two filaments and a position. In this simulation, the probability of a bundling protein attaching is the same for each filament and each position along the filaments.

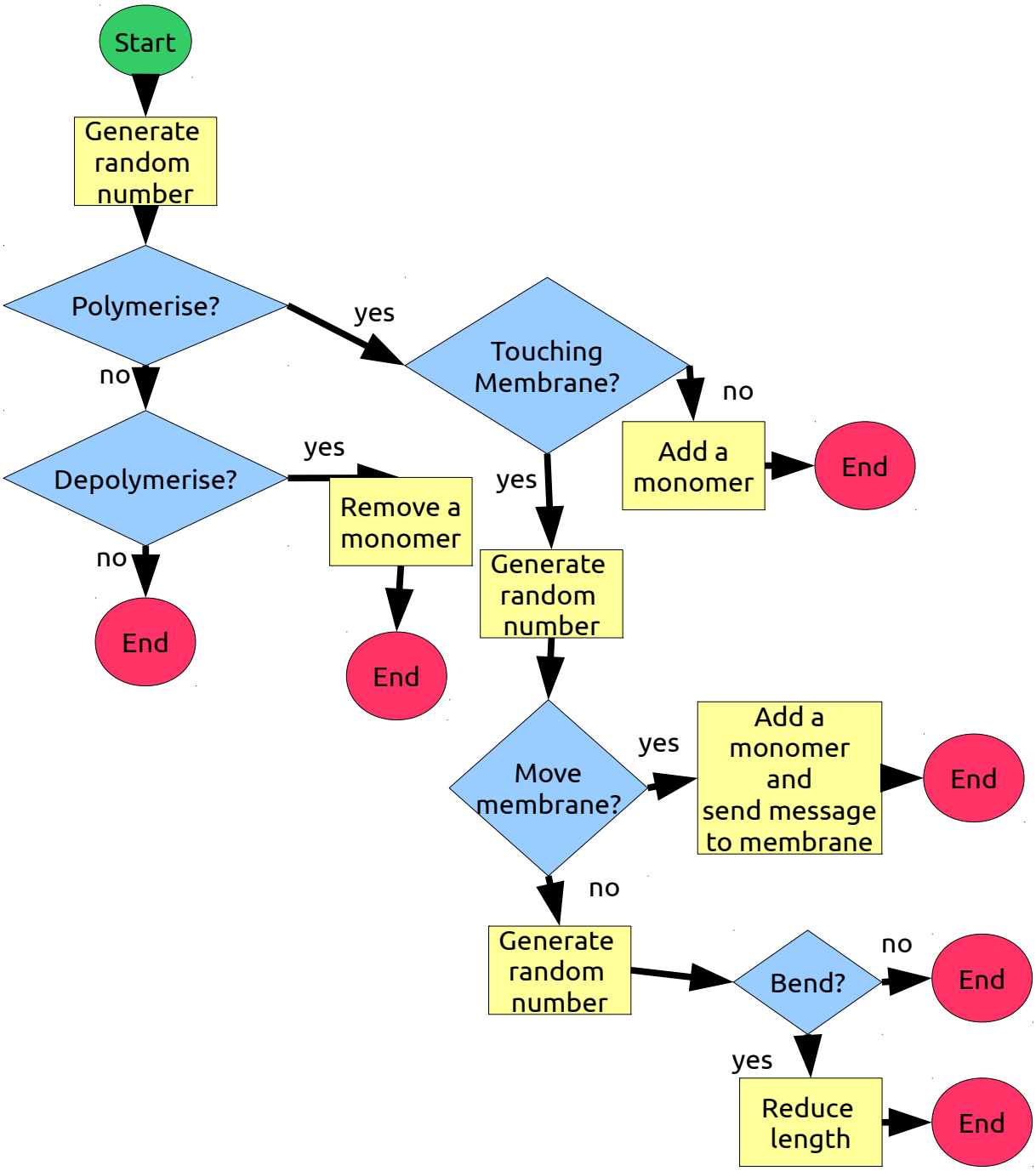

Figure 9: Filament agent flow chart

First, the filament agents decide whether to polymerise or depolymerise, based on a random number. In order to polymerise, the filament must first check that it is not touching the outer membrane. If the filament is touching the membrane, the filament decides whether or not to polymerise, and push the tip of the invagination further inside the cell, sending a message to the membrane agent to change position. If the filament does not move the membrane, a further random number is generated to decide whether or not the filament should bend.

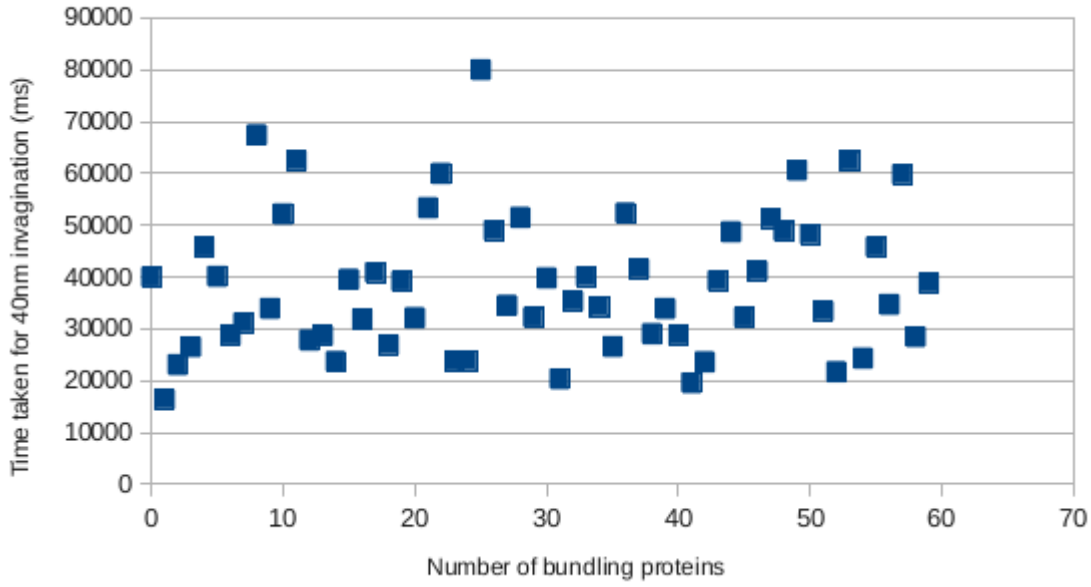

Figure 10: Graph showing mean of 20 runs of the simulation with each of the number of bundling proteins shown on the X-axis. The Y-axis shows the time that the simulated membrane invagination took to reach 40nm. This simulation used a curvature of $0.001nm^{-1}$.

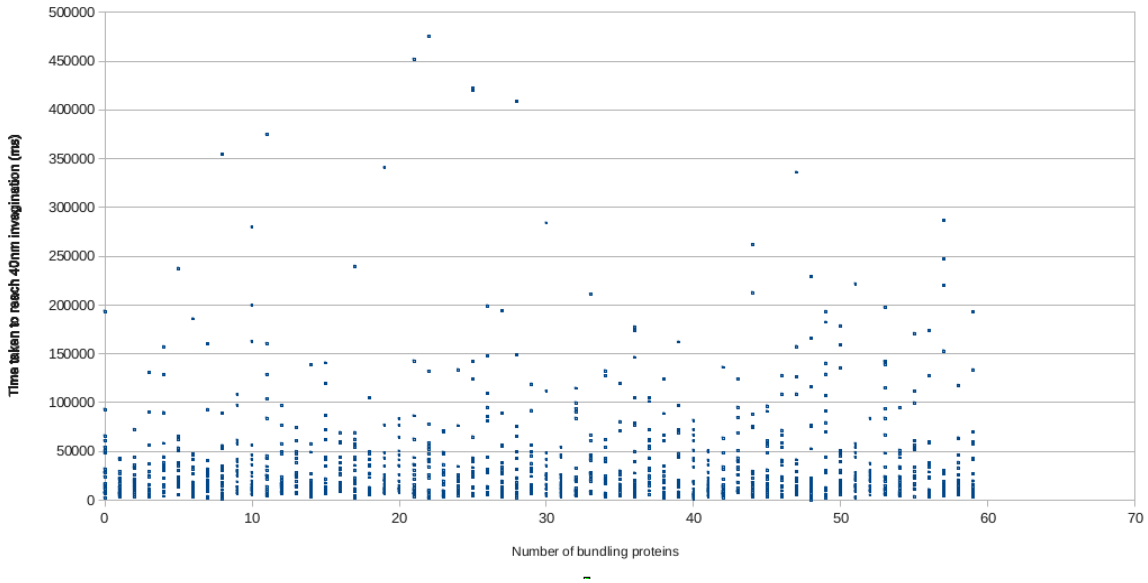

Figure 11: Graph showing each run of the simulation, using each of the number of bundling proteins shown on the X-axis. The Y-axis shows the time that the simulated membrane invagination took to reach 40nm. This simulation used a curvature of $0.001nm^{-1}$.

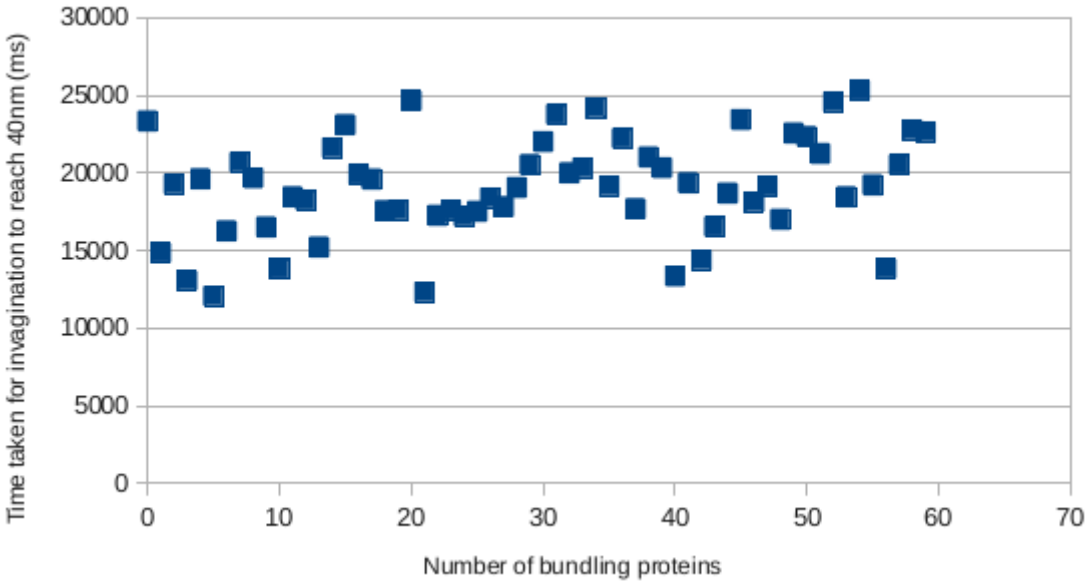

Figure 12: Graph showing mean of 20 runs of the simulation with each of the number of bundling proteins shown on the X-axis. The Y-axis shows the time that the simulated membrane invagination took to reach 40nm. This simulation used a curvature of $0.01nm^{-1}$.

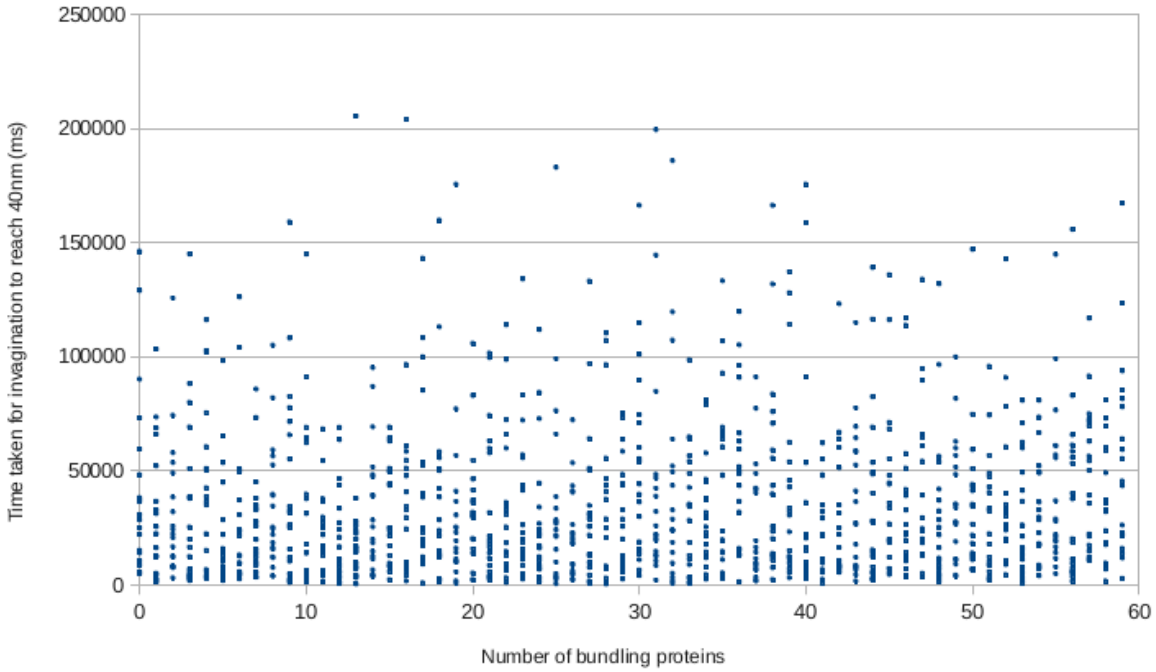

Figure 13: Graph showing each run of the simulation with each of the number of bundling proteins shown on the X-axis. The Y-axis shows the time that the simulated membrane invagination took to reach 40nm. This simulation used a curvature of $0.01nm^{-1}$.