

**Dynamic Simulation  
of a  
Presynaptic Nerve Terminal  
with a  
Tethered Particle System Model**

Rhys Goldstein and Gabriel Wainer  
Department of Systems and Computer Engineering  
Carleton University

and

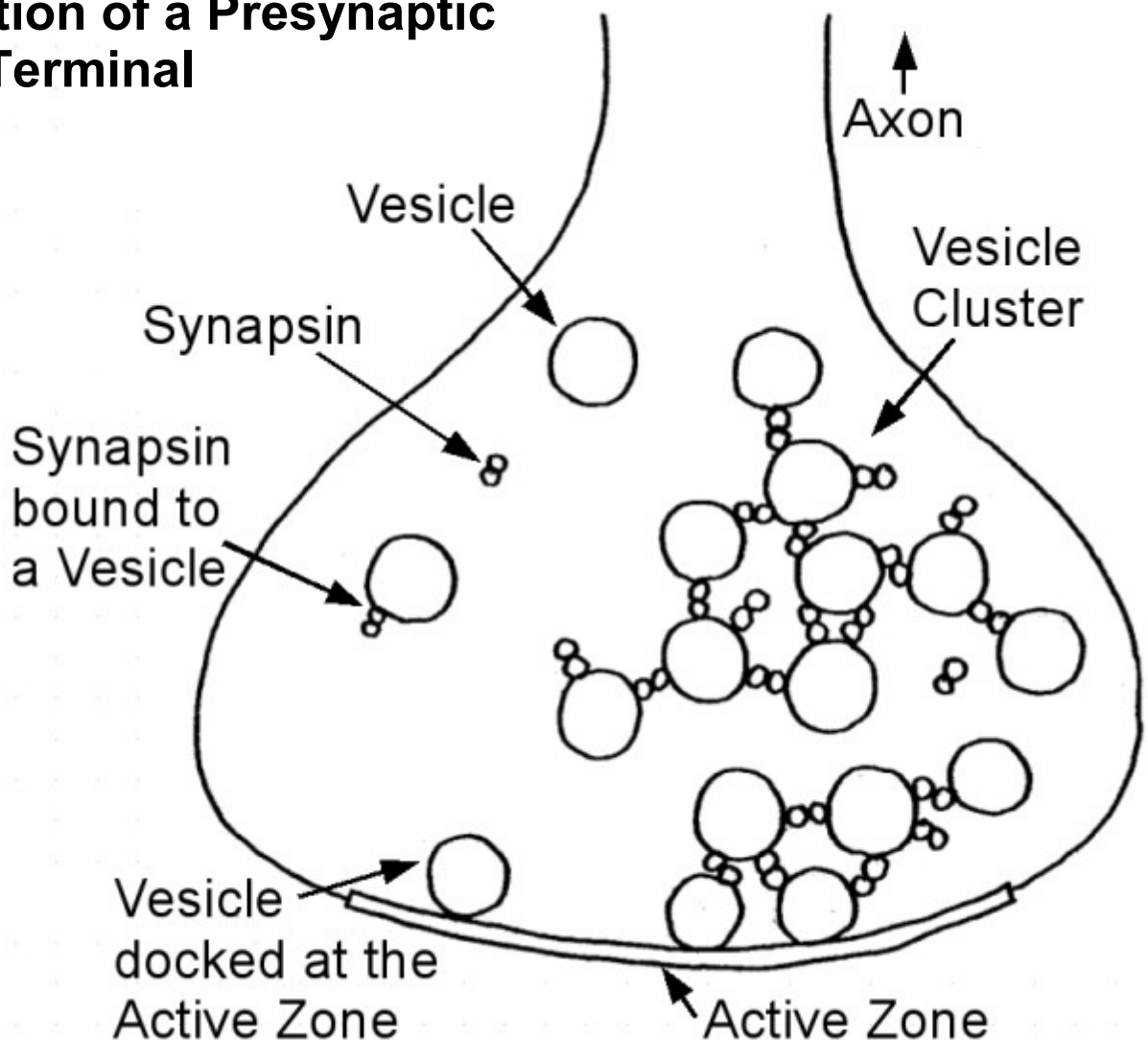
James J. Cheetham  
Department of Biology  
Carleton University

# Objective

Presynaptic nerve terminals contain clusters of neurotransmitter-containing synaptic vesicles, which are tethered to one another by protein named synapsin. The formation and disruption of vesicle clusters is important in the regulation of neurotransmitter release.

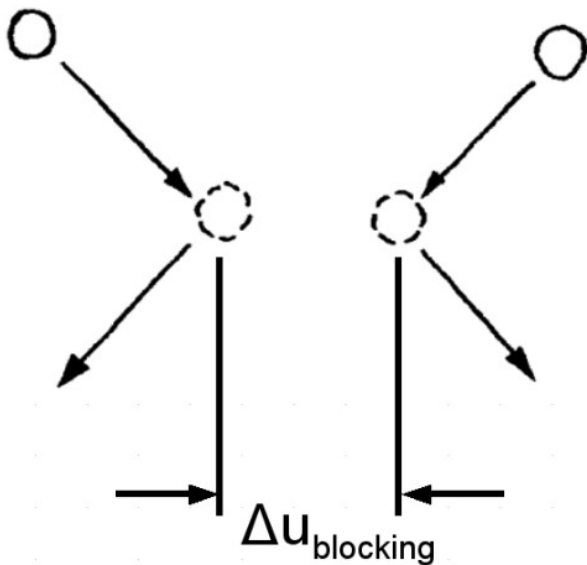
The objective of this project is to design realistic 3D models of a presynaptic nerve terminal, and simulate the effects of signaling pathways on synaptic vesicle dynamics.

## Illustration of a Presynaptic Nerve Terminal



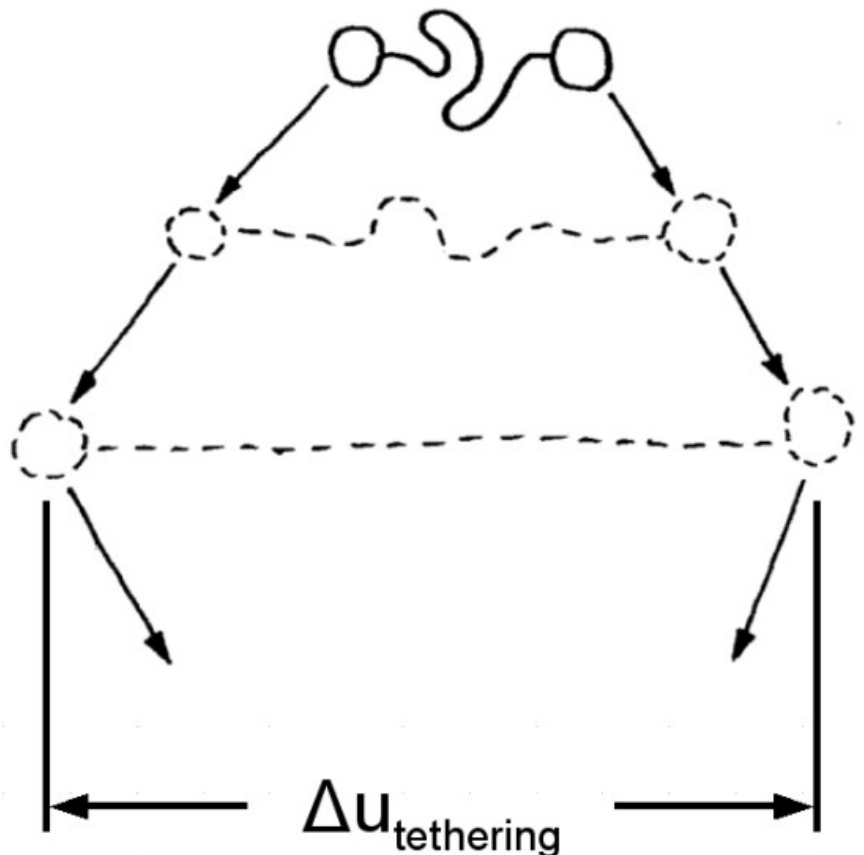
# Tethered Particle System

A Tethered Particle System (TPS) is a new type of model designed for the dynamic simulation of deformable structures. TPS models consist of particles that undergo two types of collisions: **blocking collisions** and **tethering collisions**.



A **blocking collision** is what normally comes to mind when one hears the term “collision.” As shown on the left, two approaching particles undergo a blocking collision upon reaching some inner limiting distance defined by the variable  $\Delta u_{\text{blocking}}$ . As a result of the collision, the particles rebound outwards.

A **tethering collision** is what differentiates a TPS from other particle collision models. As shown on the right, a tethering collision may occur if two separating particles reach an outer limiting distance  $\Delta u_{\text{tethering}}$ . As a result of the collision, the two particles retract inwards.



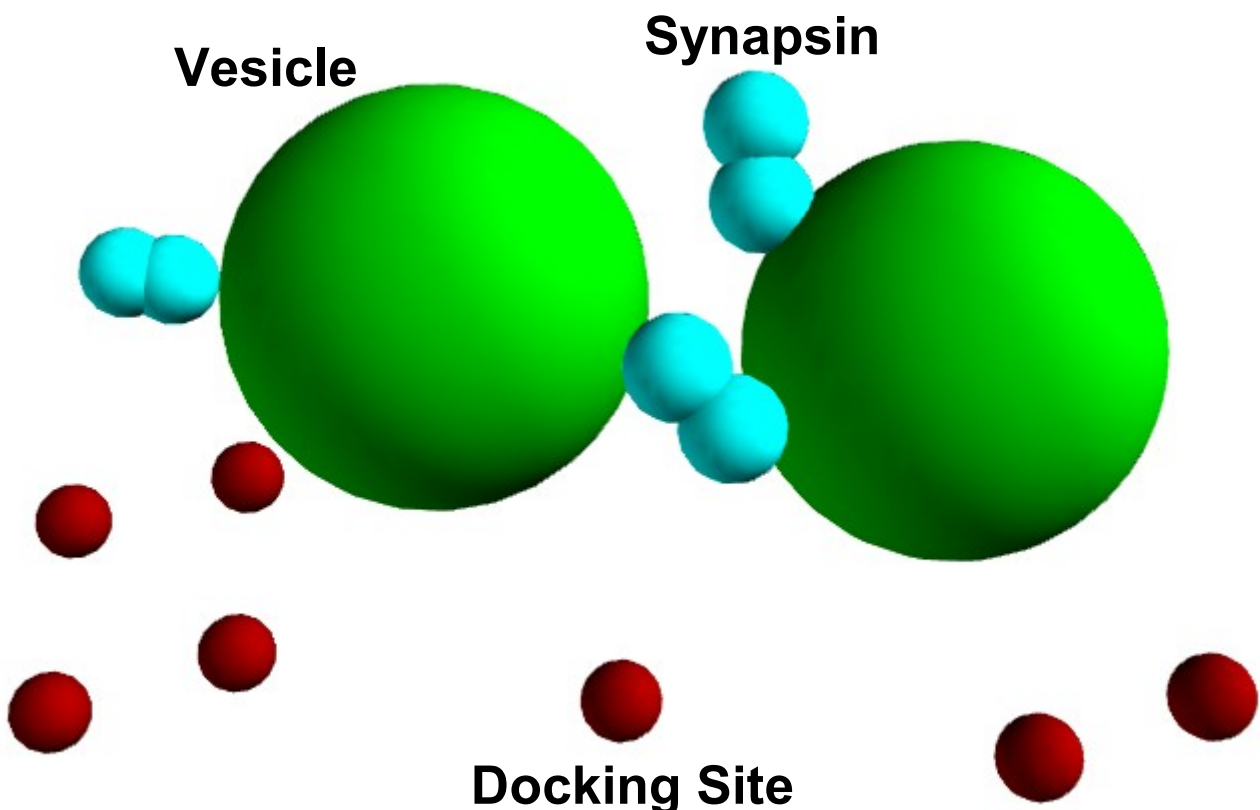
# Vesicle Clusters

In this project, the TPS is used to model a presynaptic nerve terminal.

**Synapsins**, being dimers, are modeled as pairs of particles. Blocking collisions prevent the two synapsin particles from passing directly through one another, whereas tethering collisions prevent the particles from separating completely.

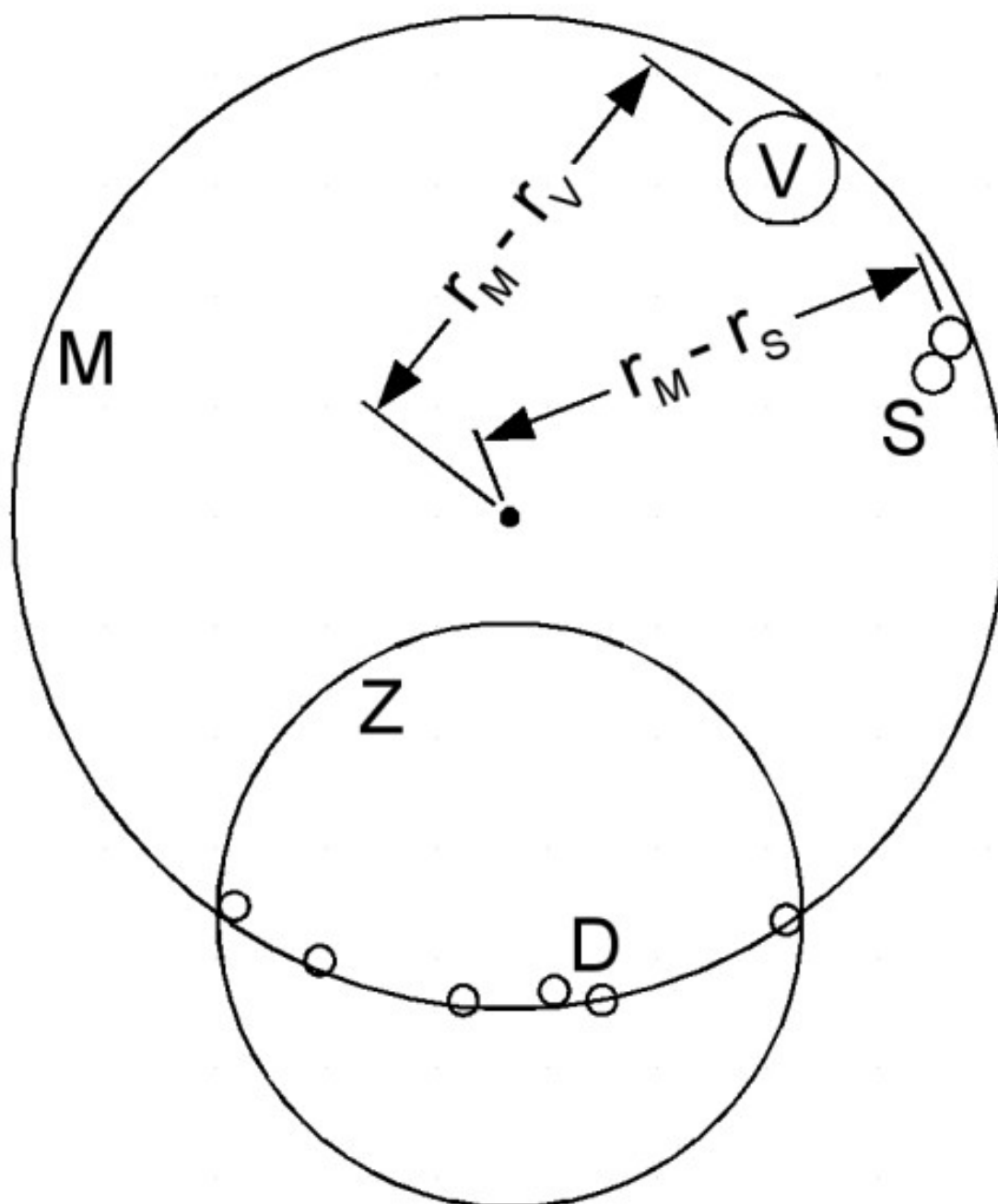
**Vesicles** are modeled as much larger particles. If a vesicle particle comes into contact with a synapsin particle, there is a probability that the two become tethered. This leads to the formation of vesicle clusters.

Vesicles also become tethered to particles representing **docking sites**. These docking sites are found on the region of the membrane known as the active zone.



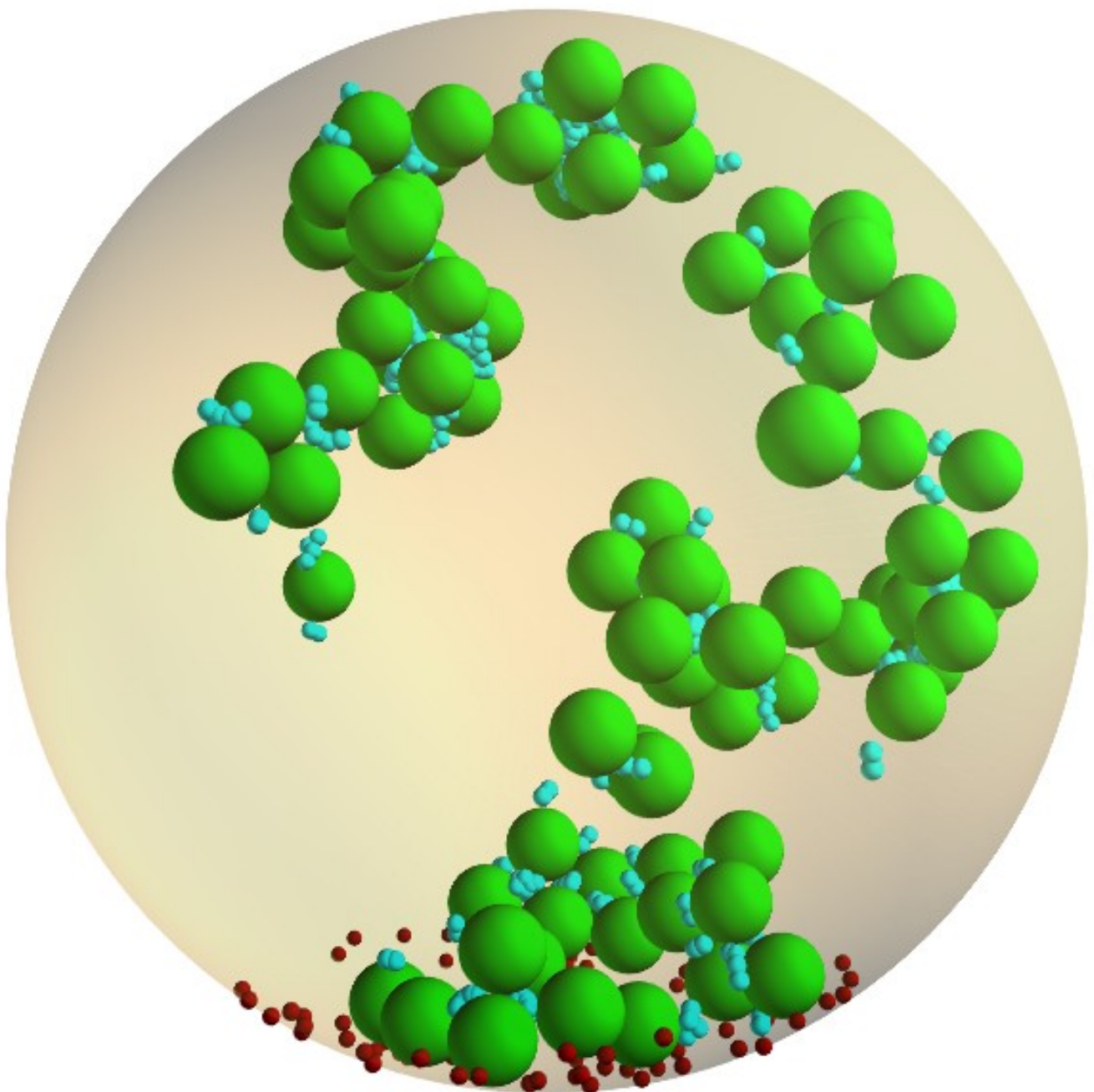
# Rigid Spherical Membrane

A rigid spherical membrane is modeled with two stationary particles identified by **M** and **Z**. All vesicles (**V**), synapsins (**S**), and docking sites (**D**) are tethered to the **M** particle in the diagram below, which prevents their escape. Docking sites (**D**) undergo blocking collisions with the **M** particle, which constrains them to the membrane. Docking sites also undergo tethering collisions with the **Z** particle, which constrains them to the active zone.



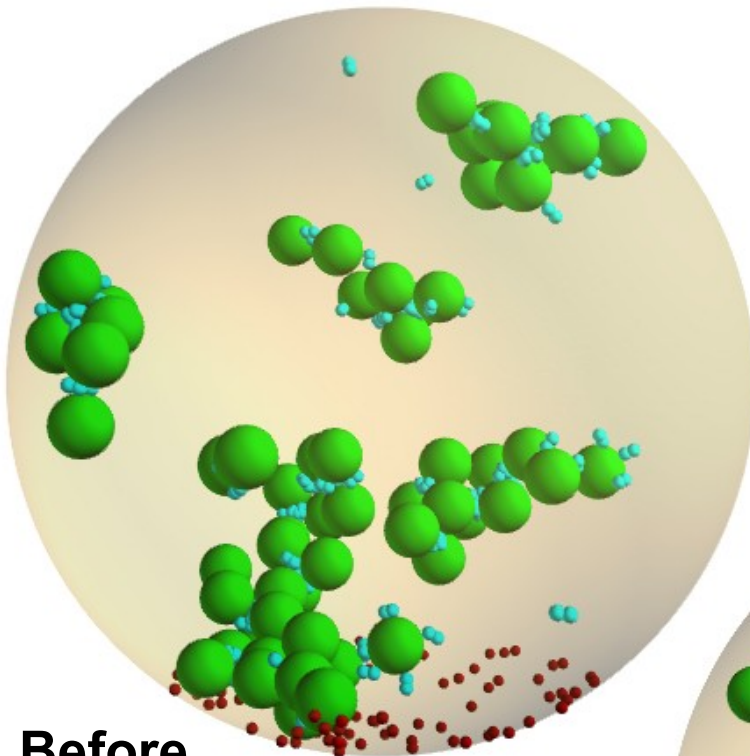
# Presynaptic Nerve Terminal (Rigid Spherical Membrane)

Below is a snapshot of a simulation with vesicle clusters contained by a rigid sphere representing the membrane of a presynaptic nerve terminal. The vesicles on the bottom are docked at the active zone.

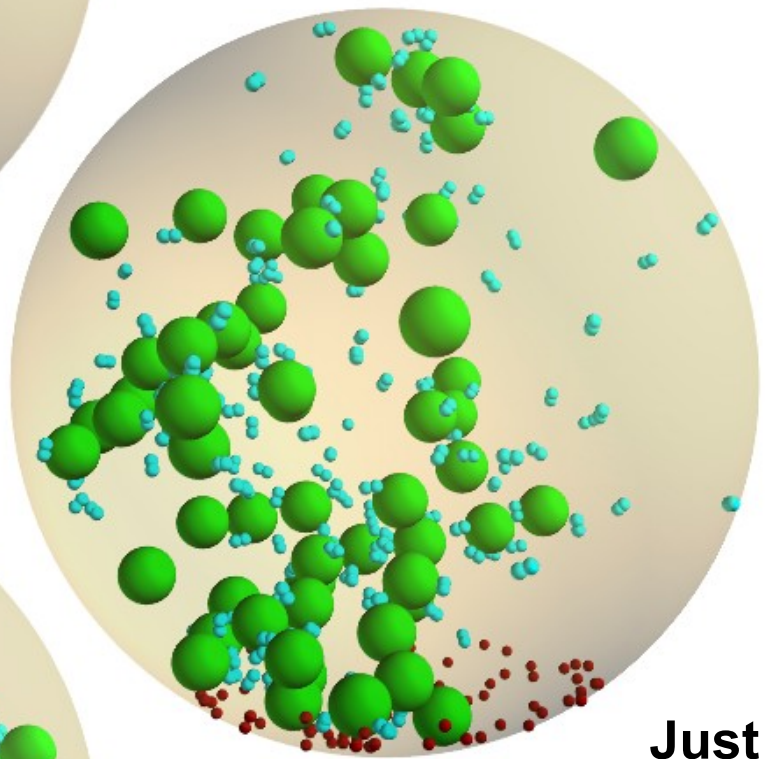


# Action Potentials

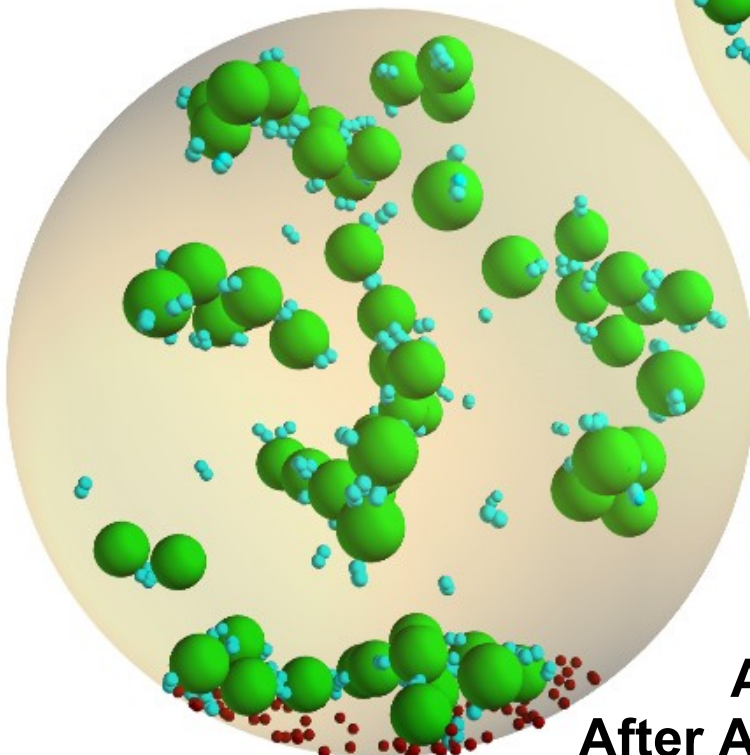
An arriving action potential triggers chemical reactions that cause synapsins to decrease their affinity for vesicles. This disrupts the vesicle clusters. The clusters reform after the action potential subsides.



**Before  
Action Potential**



**Just  
After Action Potential**



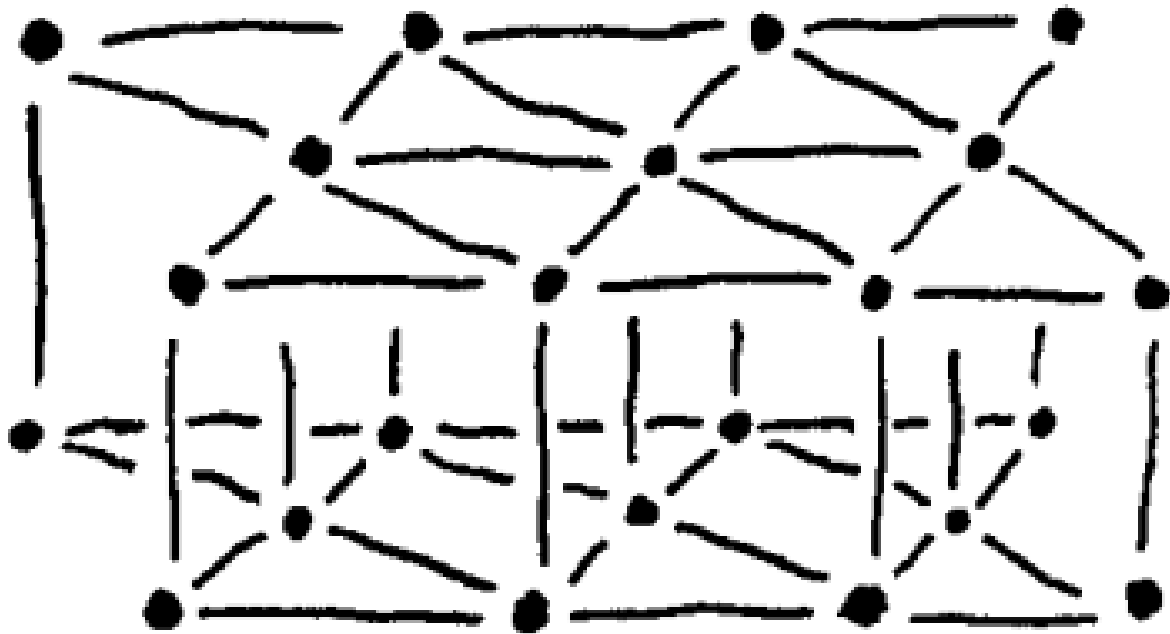
**A Longer Time  
After Action Potential**

# Deformable Membranes

A TPS can be used to model deformable membranes.

In a TPS model of a deformable membrane, individual particles do not represent individual real-world objects. Instead, it is a group of particles that collectively represent the real-world membrane.

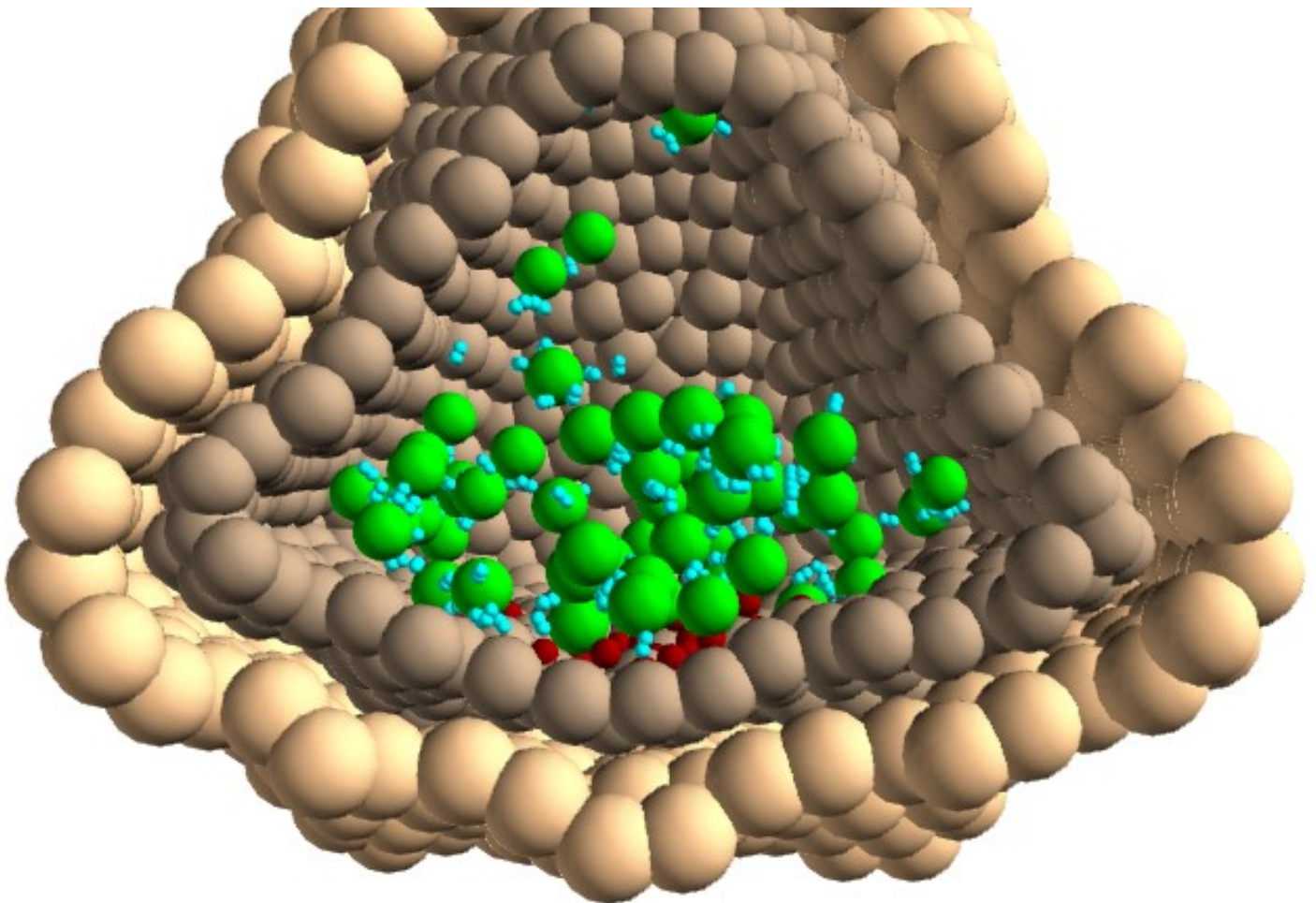
The dots in the illustration below indicate the positions of particles used to model a membrane. The lines between them show the pairs of particles that are tethered together. This tethering pattern keeps the membrane intact, but still allows it to move and deform.



It is important for a TPS model of a deformable membrane to have at least two parallel surfaces, like the one above. Otherwise unrealistically sharp folds appear as the membrane deforms.

# Presynaptic Nerve Terminal (Deformable Membrane)

Below is a snapshot of a simulation with vesicle clusters contained by a deformable membrane in the approximate shape of a presynaptic nerve terminal. A thinner membrane would be more realistic than the one shown, but the model would then require a greater number of particles and the simulation would require more time or computational power.



More information can be found at

[www.sce.carleton.ca/~rhy5](http://www.sce.carleton.ca/~rhy5)