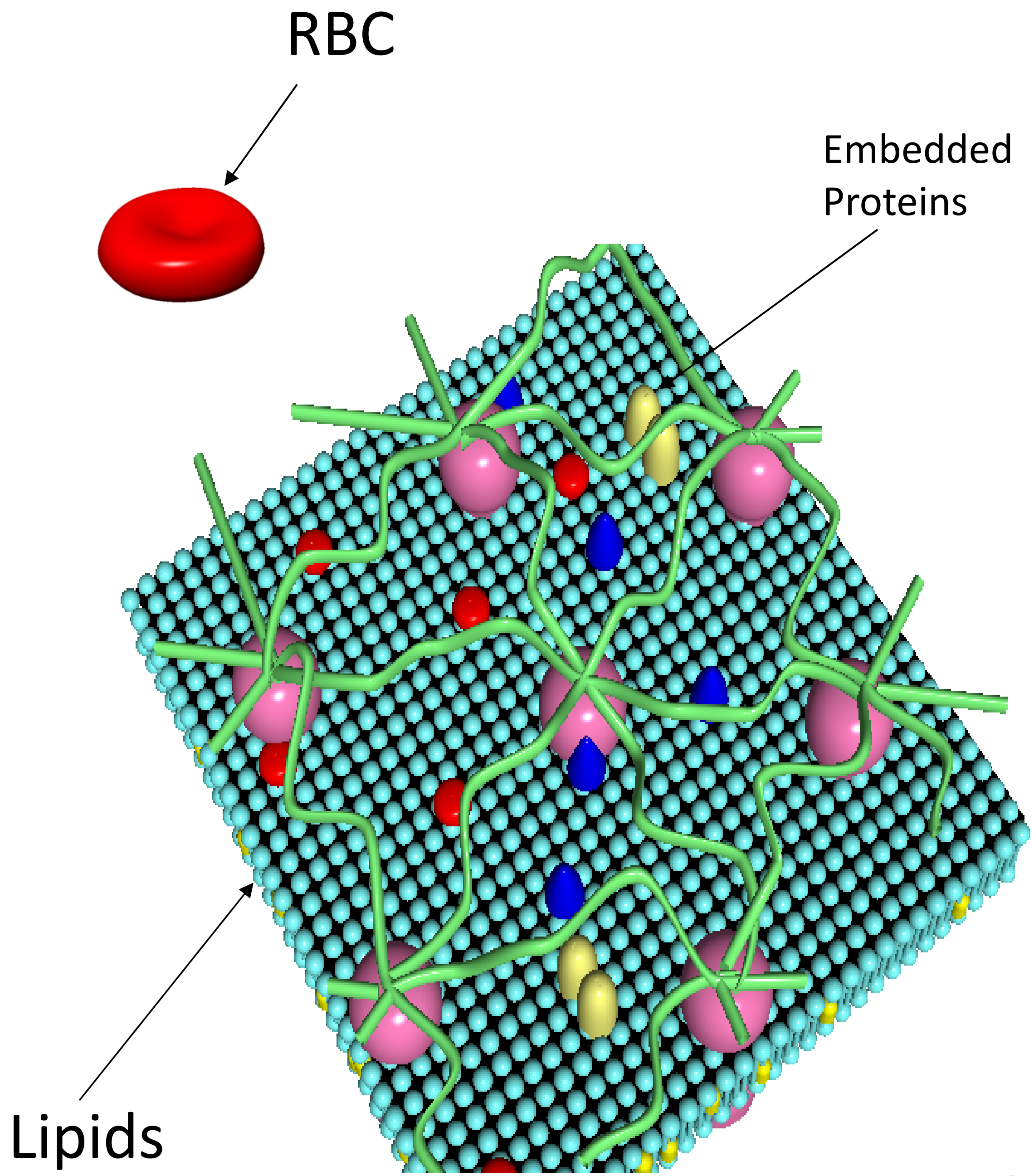
Computational Study of Protein Diffusion in a Membrane

By Kate Schneider

Advisor Dr. Ken Ritchie

Cell Membrane

- •Red blood cell membrane.
- •Membrane protects the cell.
- •Lipids have two parts
  - •Head which is hydrophilic
  - •Tail which is hydrophobic
- •Not solid structure
- •Moves in an undulating fashion.

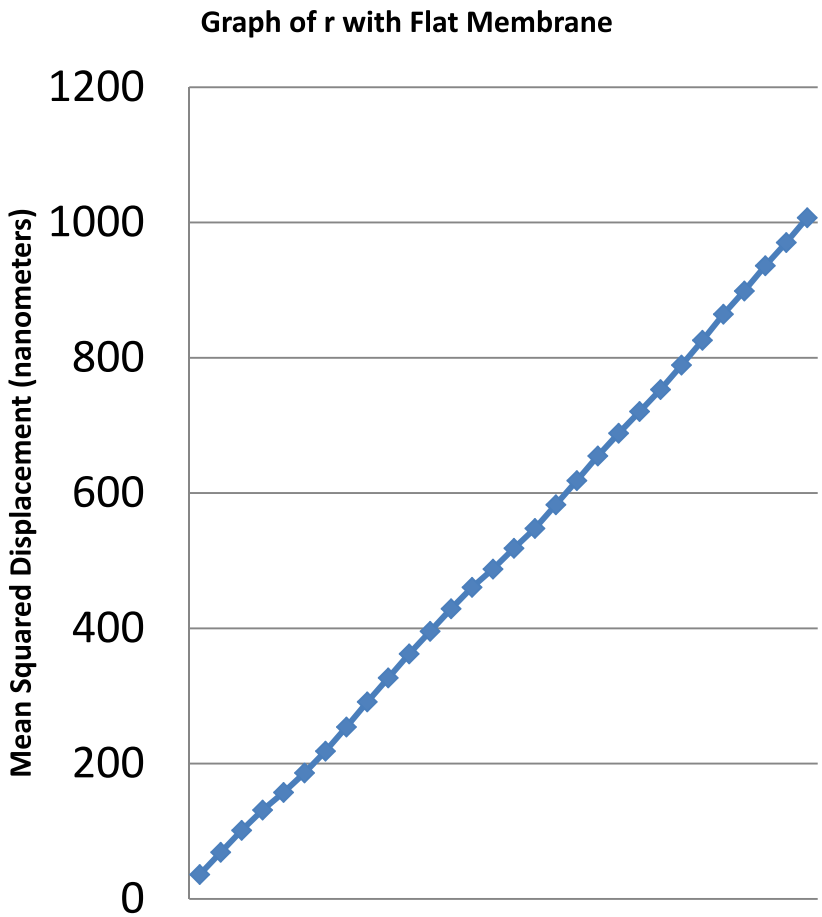


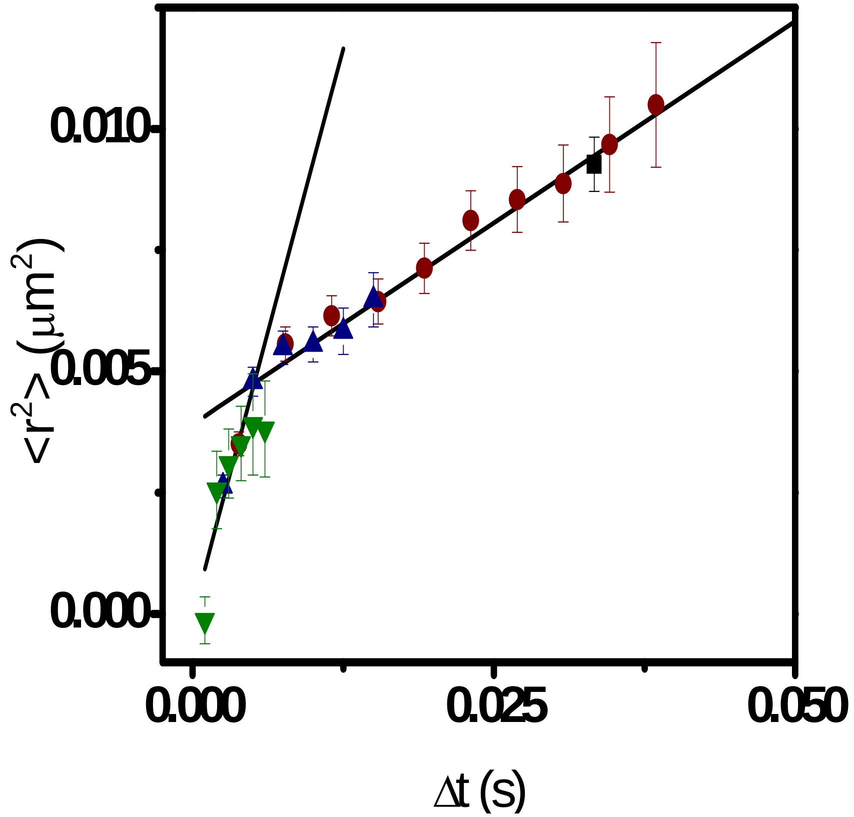
Current Assumption

- When protein diffusion is imaged over a range of length (time) scales, cell-type dependent structure is seen in the membrane at specific lengths.

- Could this be caused by the undulation of the membrane?

Predicted and Experimental Results



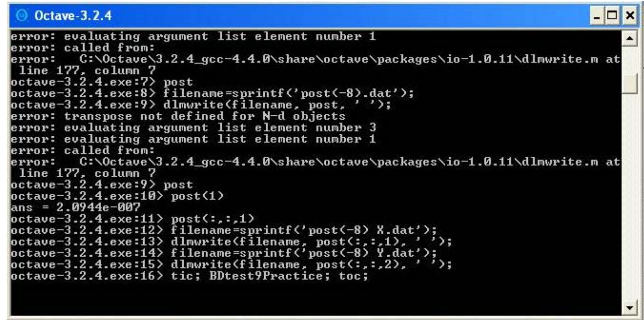


Project

- Previous experiments were analyzed assuming a flat membrane.

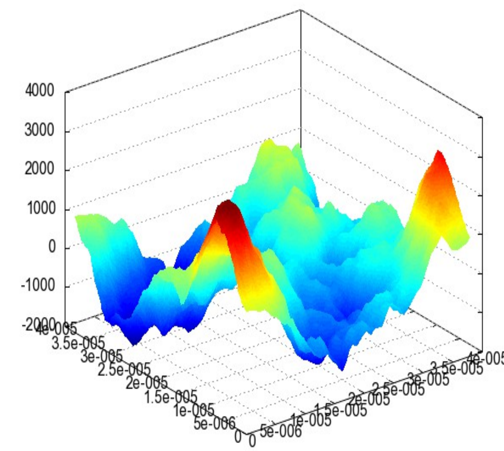
- Main Goal
  - Determine the effects of membrane undulation on future experiments.
  - We wish to determine if we need to include undulations in our analysis.

Project Description



•Use Brownian Motion to fluctuate a membrane in k-space.

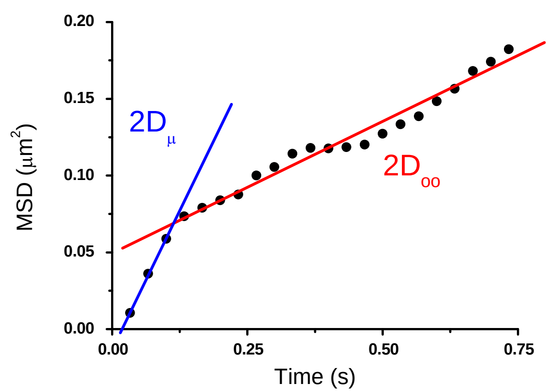
•Produce a Monte Carlo style random walk on the surface.



•Display the random walk on a two dimensional plane.

•Determine the MSD of the projected walk.

•Analyze the data and determine if we need to take the undulation into account.

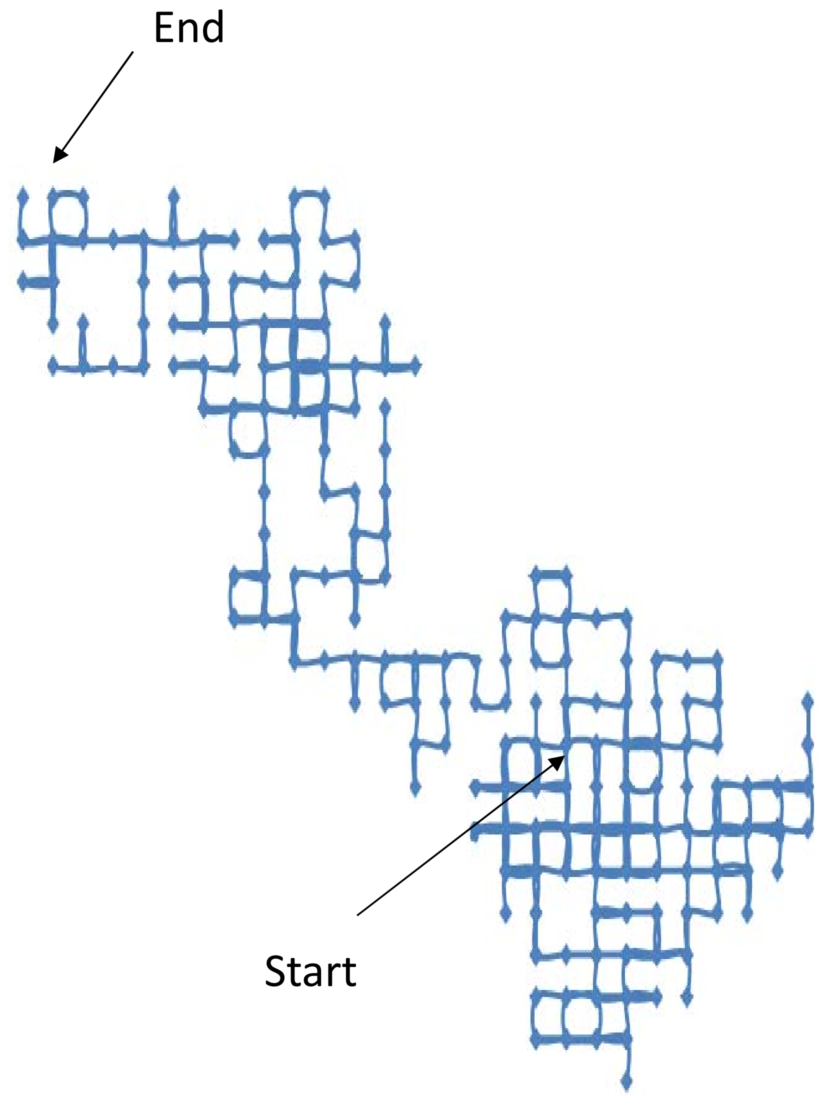


Monte Carlo Simulation

•Like flipping a coin.

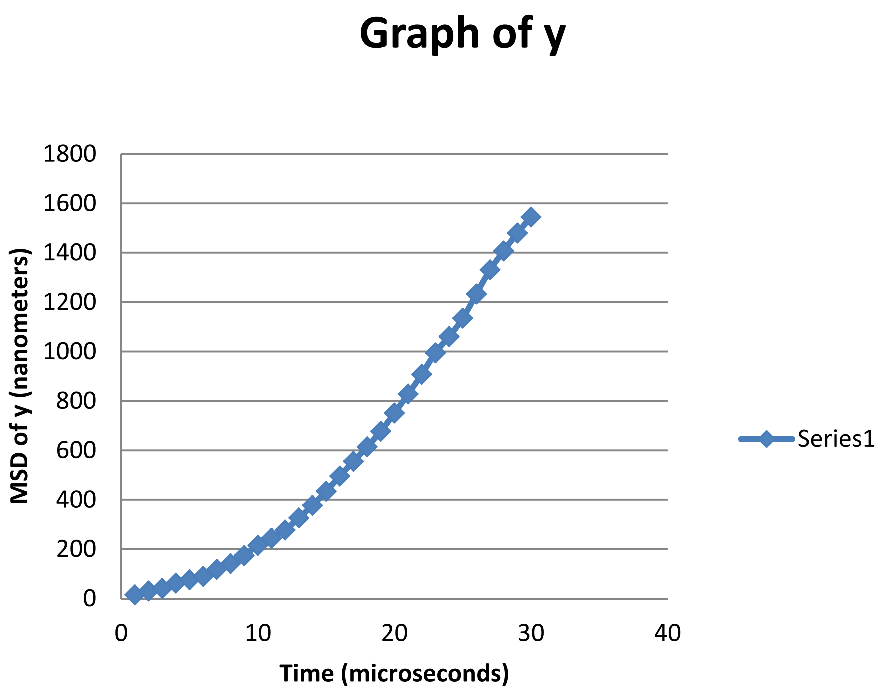
•We flip a coin and decide which direction to go.

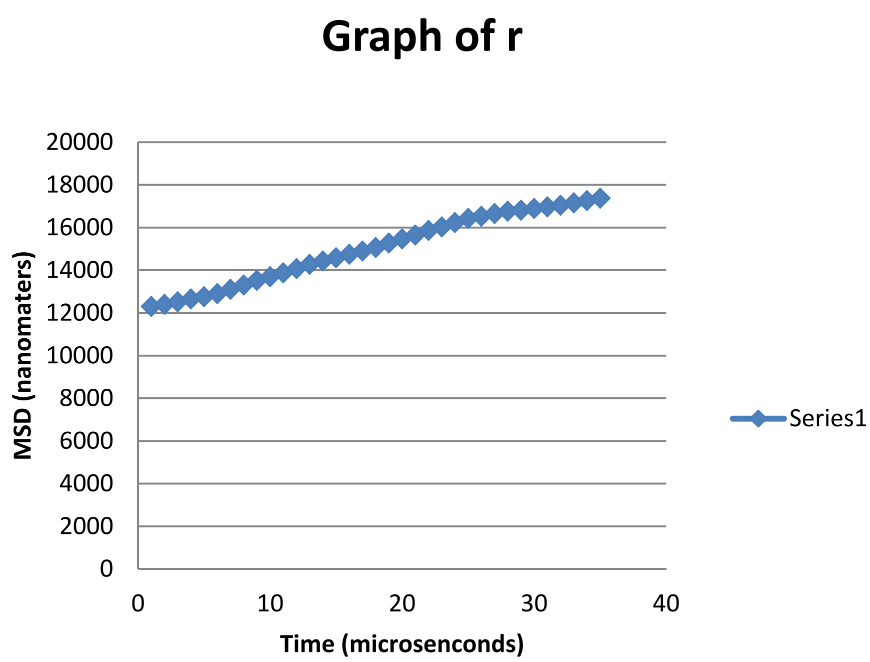
•We use it for simulating the walk of a protein.



Monte Carlo on Visual Studio

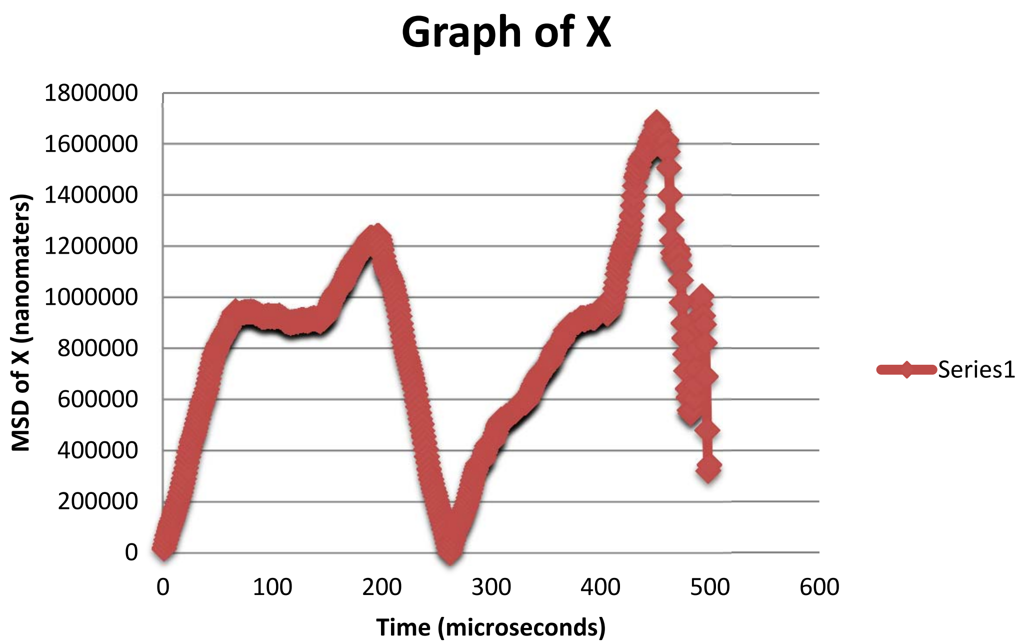
- Free range random walk.
- About 35 steps taken.
- Good data for a small number of steps.

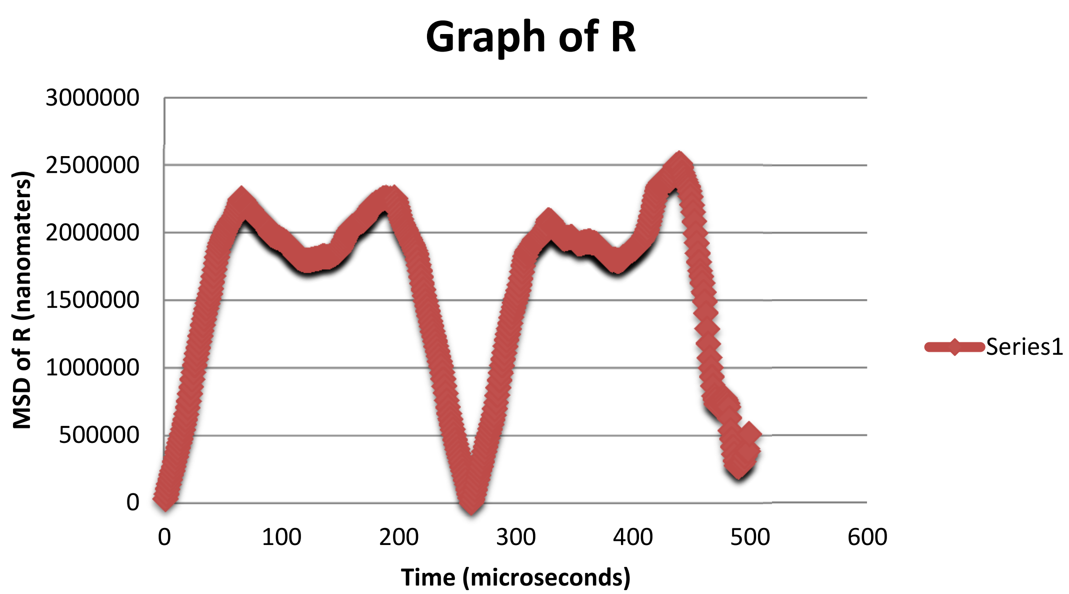




5,000 Steps in Visual Studio

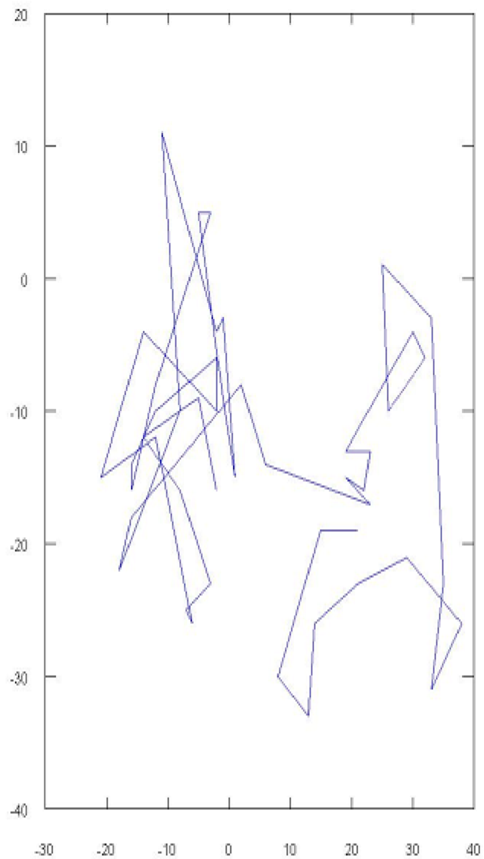
- Next move was to add more steps.
- Graphs deviated from expected results.
- Data did not change much from run to run.
- First believed to be the random generator.
- Changed program to Octave.

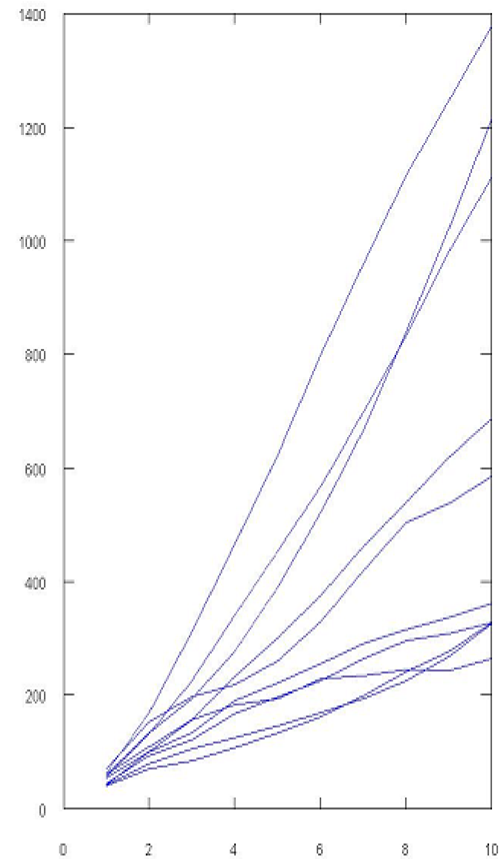




Octave Free Range Random Walk

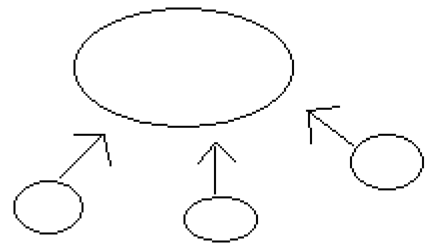
- This run had fifty steps with 100 sub-steps (equal to 5,000 steps).
  - -10 different particles were run at the same time.
- Graph on the left shows random walk for one of the particles.
- Graph on the right shows the MSD for each particle.



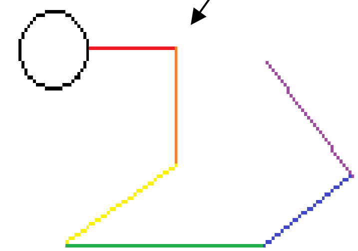


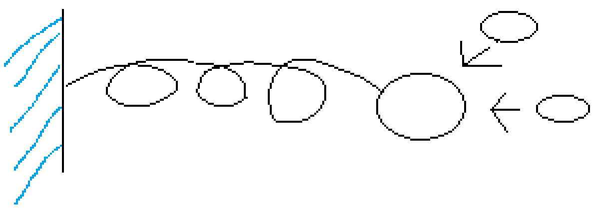
Brownian Motion –

The random movement of particles when hit by other particles in some fluid.



Random Walk



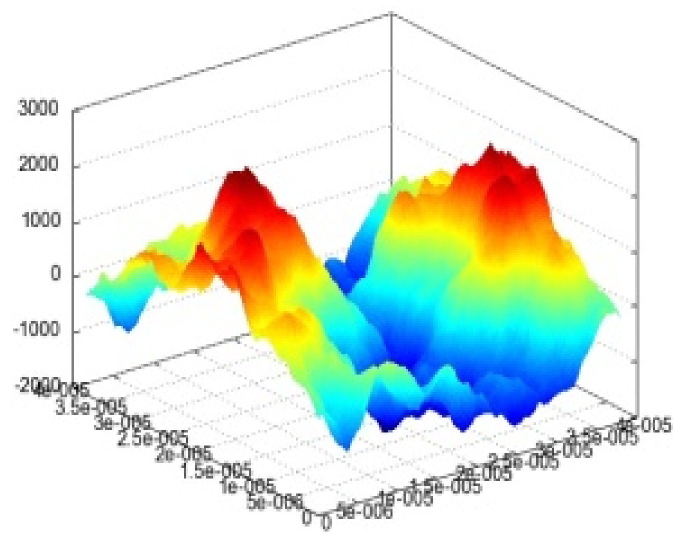


Particle on a Spring

If you place the particle on a spring and analyze it in 1 dimensions it can only go in and out when hit by another particle.

This particle attached to a spring is the basic concept behind creating the fluctuating membrane surface like the one pictured.

Fluctuating Surface



Brownian Motion for a Membrane

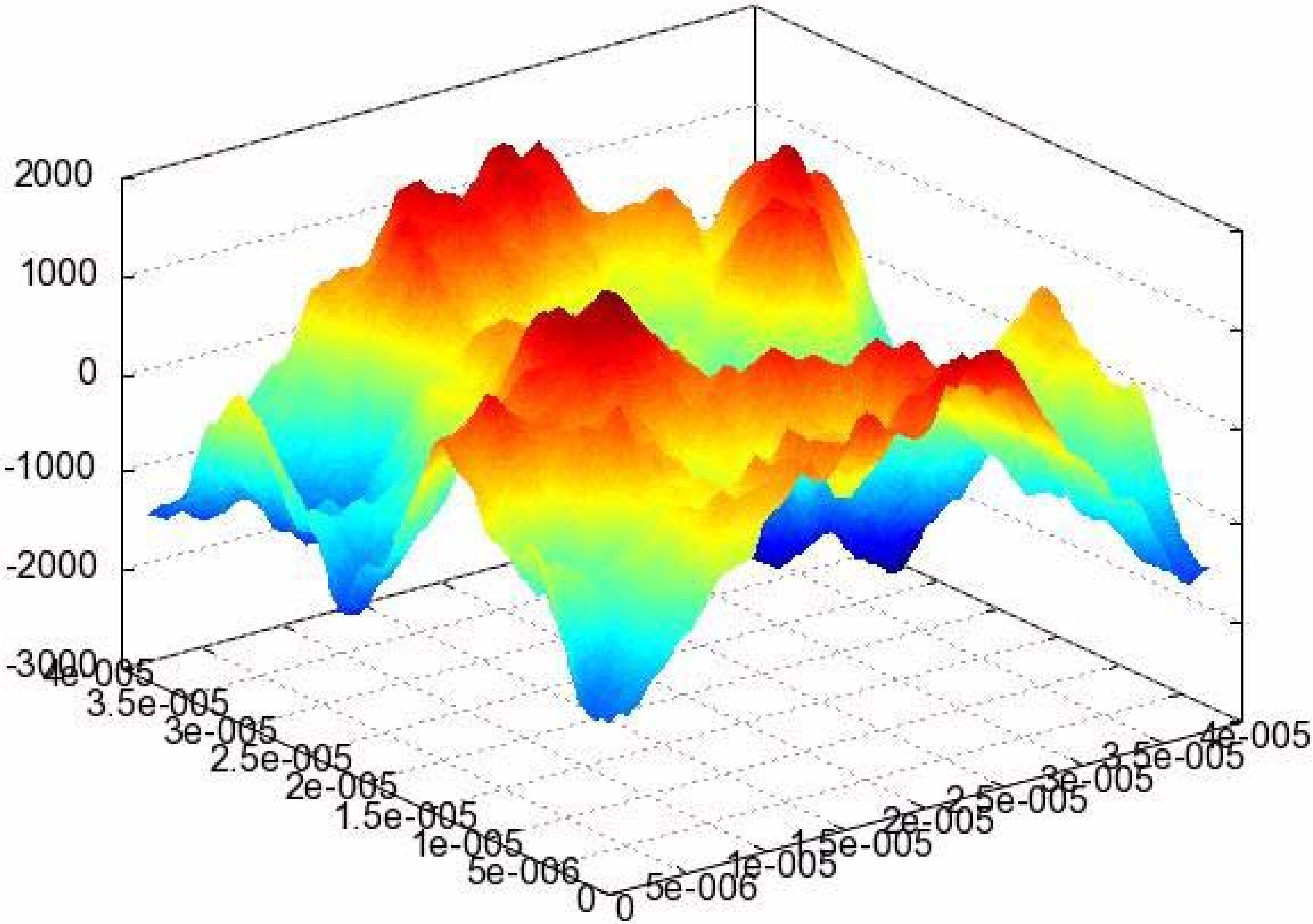
- For a normal spring $E \sim \frac{1}{2} k x^2$

- With a bending surface we want an energy in the spring form $E \sim \frac{1}{2} k_b c^2$

  - Curvature of a line $C = \frac{d^2 F}{dx^2}$

- For a two-dimensional surface $E \sim \frac{1}{2} k_b (\nabla^2 f(x, y))^2$

- Change to k-space $E_K = \frac{1}{2} k q^4 f_K^2$ The equation for our fluctuation.


2000
1000
0
-1000
-2000
-3000
4e-005
3.5e-005
3e-005
2.5e-005
2e-005
1.5e-005
1e-005
5e-006
0
0
5e-006
1e-005
1.5e-005
2e-005
2.5e-005
3e-005
3.5e-005
4e-005

Completed Code

- In the beginning we pick a random membrane that has correct energies.
- That membrane is then project forward in time so that it can produce the fluctuations.
  - Each mode has its own persistent time.
- Then we create a real space membrane by doing the inverse transform of the membrane.
- We then take the first and second derivative of the real space membrane.
  - Gives us the slope and curvature.
- Then a random step is taken on the surface using the first and second of the surface topology to determine the size of the step that we will be taking.
- Then the MSD is figured for both X and Y.

Simulations Run

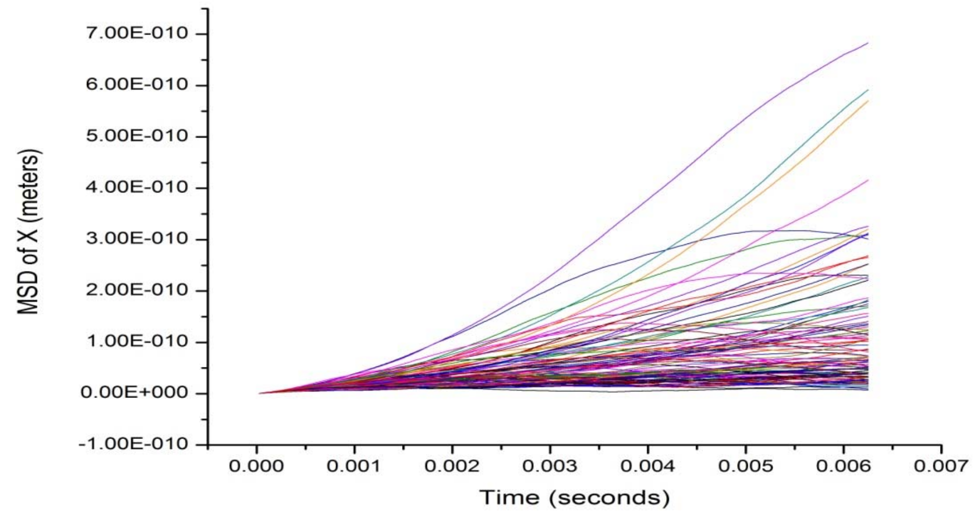
D $(\frac{cm^2}{s})$	N	L(cm)	Time
$1 * 10^{-12}$	32	.375	59 mins
$1 * 10^{-11}$	128	.375	1 hr 6 mins
$1 * 10^{-10}$	128	1	1 hr 7 mins
$1 * 10^{-9}$	128	3	1 hr 7 mins
$1 * 10^{-8}$	512	3	4 hrs

- Each simulation was run with 100 particles walking simultaneously.
- 500 steps taken for each particle with 25 sub-steps to equal 1 microsecond.
- The MSD was figured for each particle.

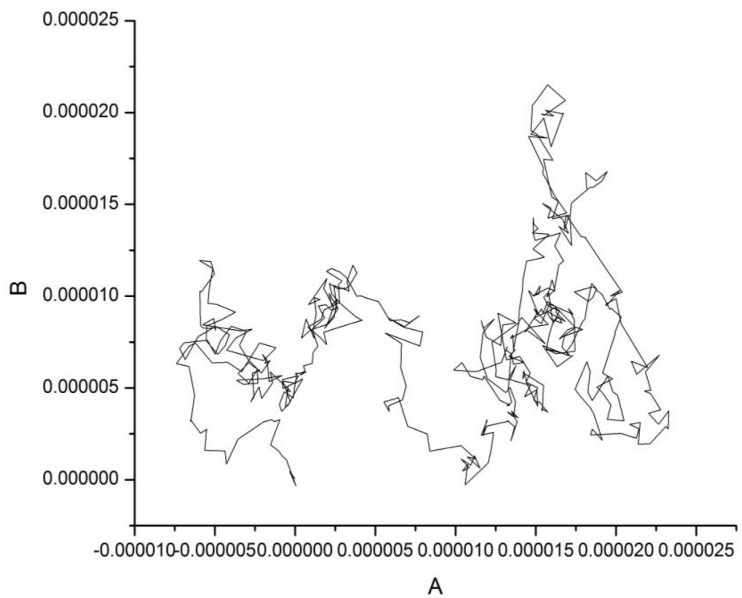
Results

$$D = 1 * 10^{-8}$$

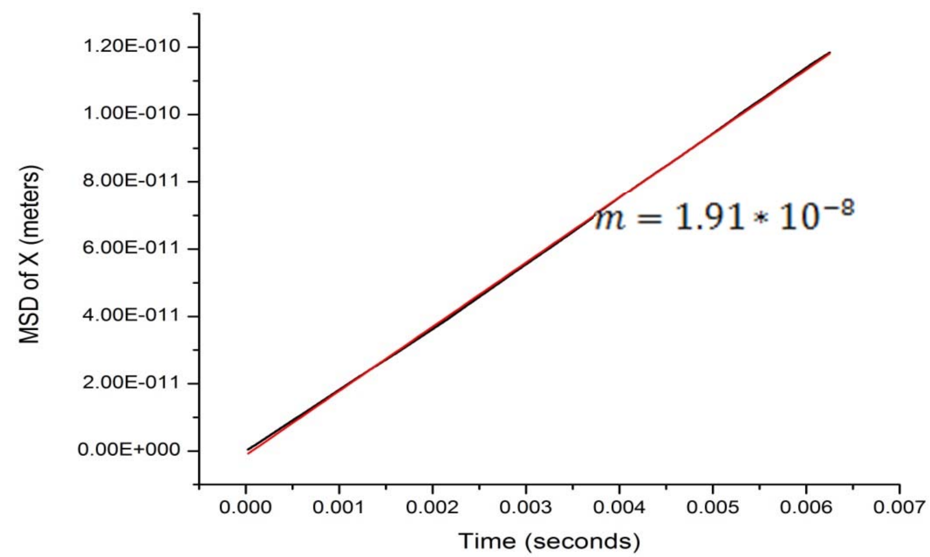
Percentage of original diffusion coefficient
found in the average:
X = 85%



MSD of X for all 100 Particles

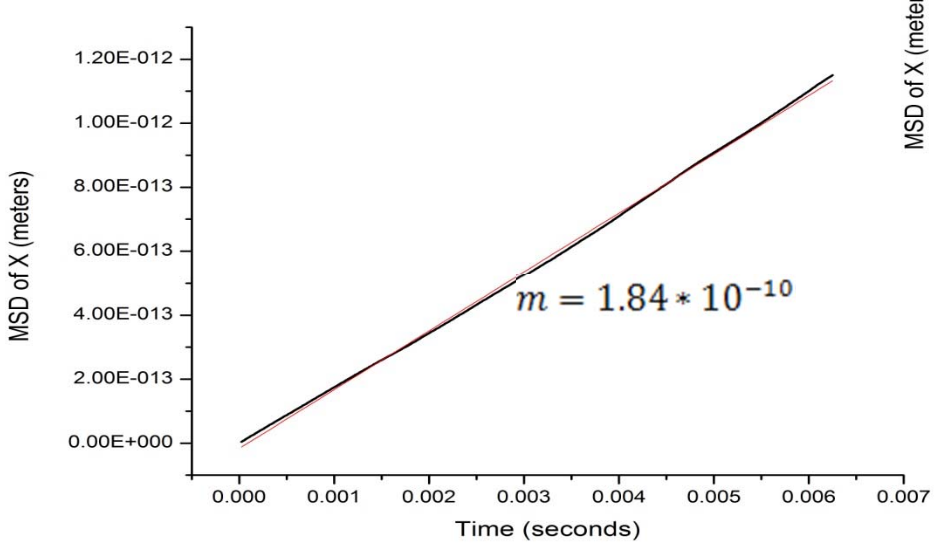


Random walk



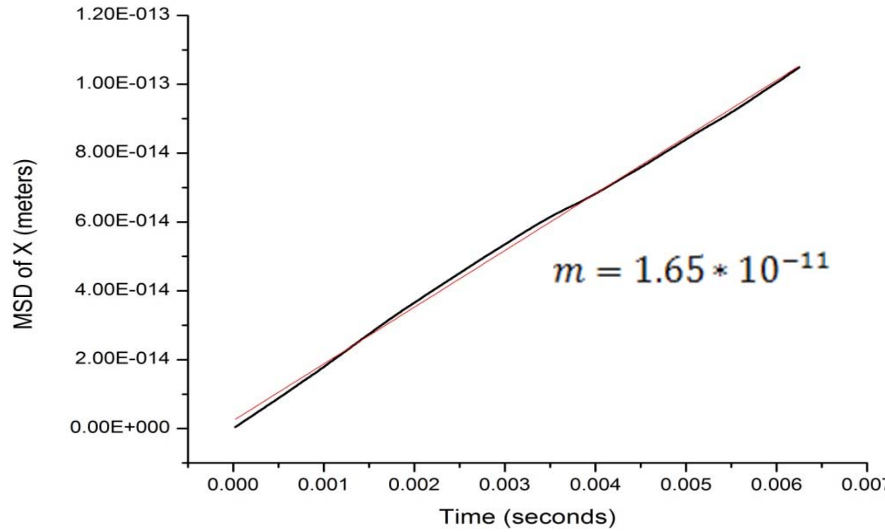
Average MSD for X

Results part 2



$1 * 10^{-10}$

Average MSD for X



$1 * 10^{-11}$

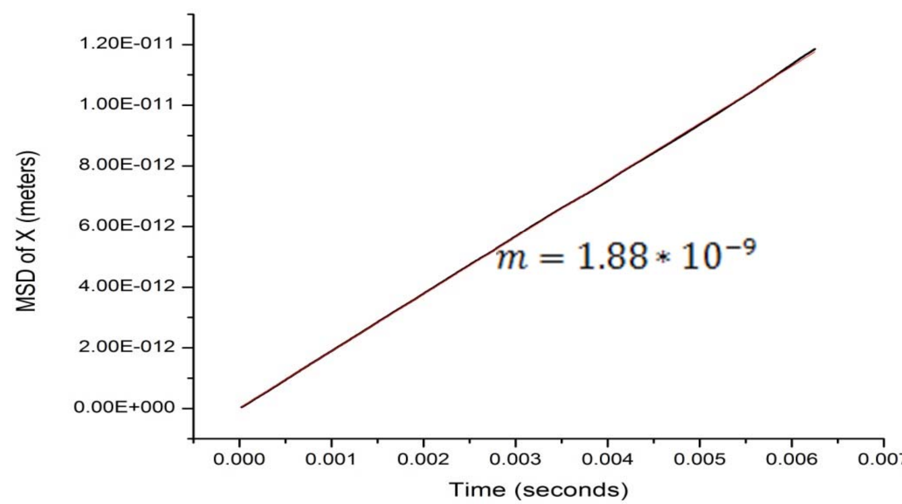
Average MSD for X

Percentage of original diffusion coefficient found in the average of X:

$1 * 10^{-11}$ ➡ 85%

$1 * 10^{-10}$ ➡ 84%

$1 * 10^{-9}$ ➡ 94%

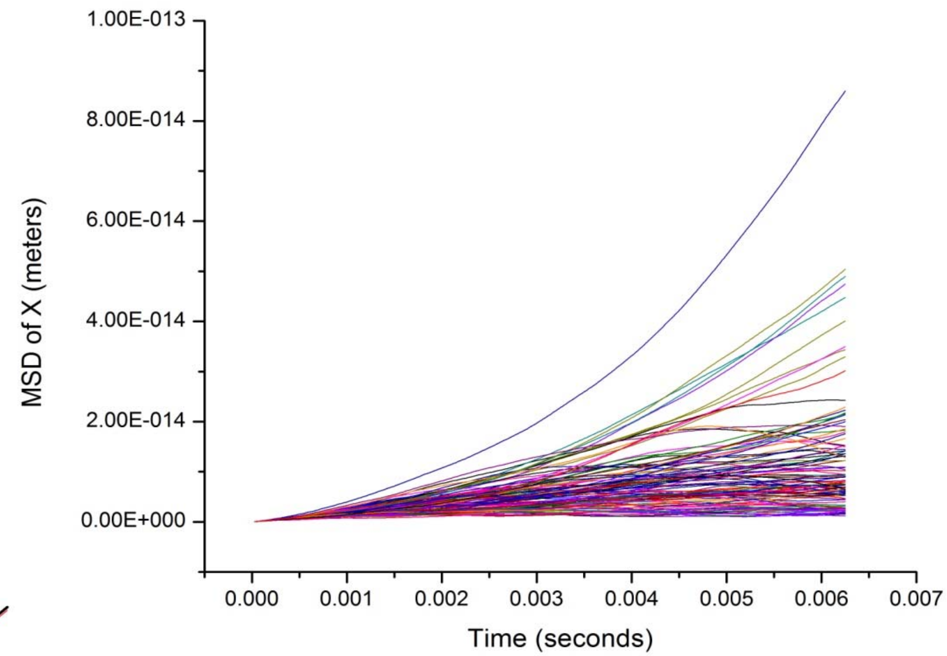


$1 * 10^{-9}$

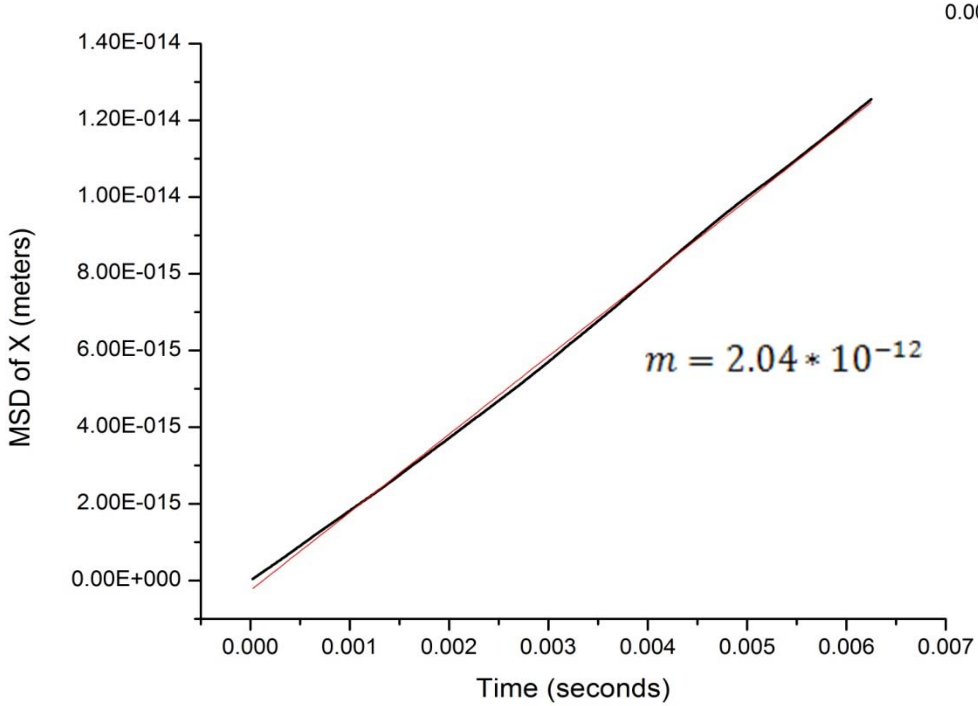
Average MSD for X

Results

$$D = 1 * 10^{-12}$$



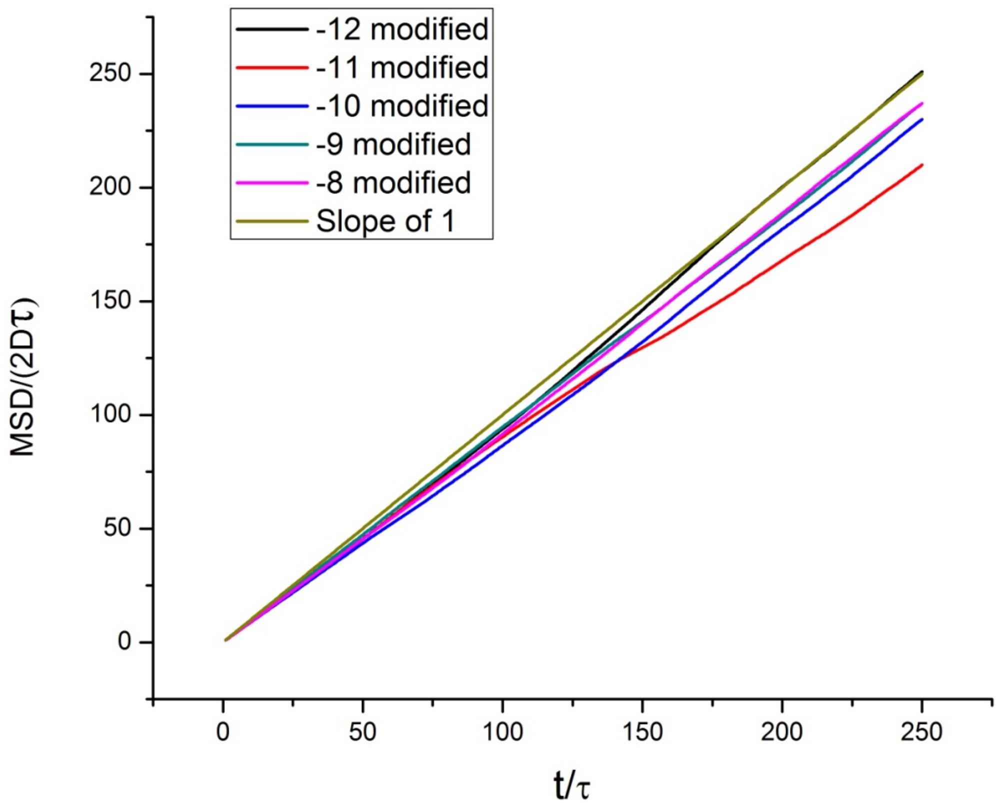
MSD of X for all 100 Particles



Average MSD for X

Percentage of original diffusion coefficient in the two averages:
X = 102%

Comparison of all Simulations



Scaled Version

- Shows the slight difference between each simulation produced and the original diffusion coefficient.

- Only a 10% difference or less.
  - Very good results and close to what we hoped to see.

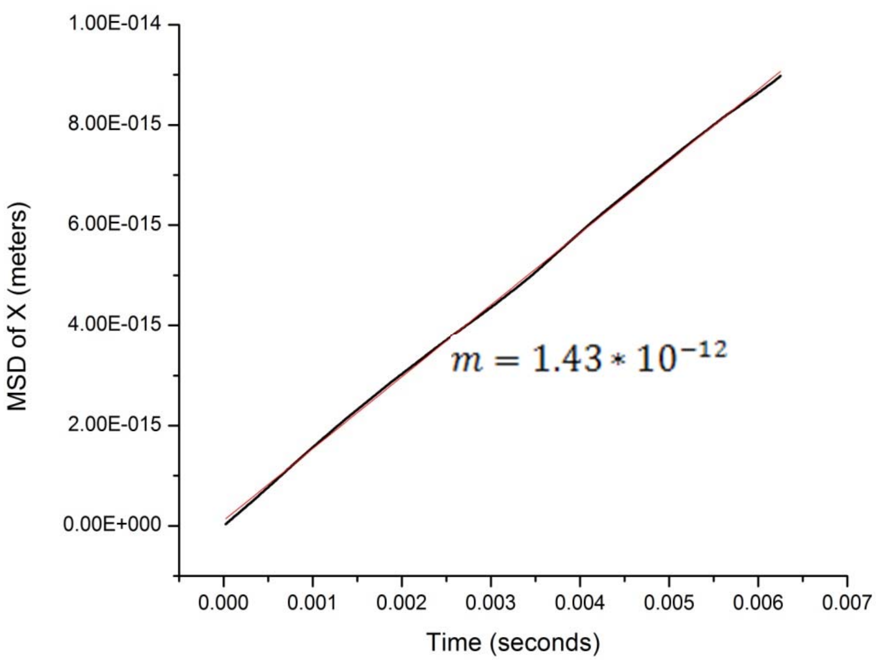
- D is the true diffusion coefficient.

- τ = 25 microseconds

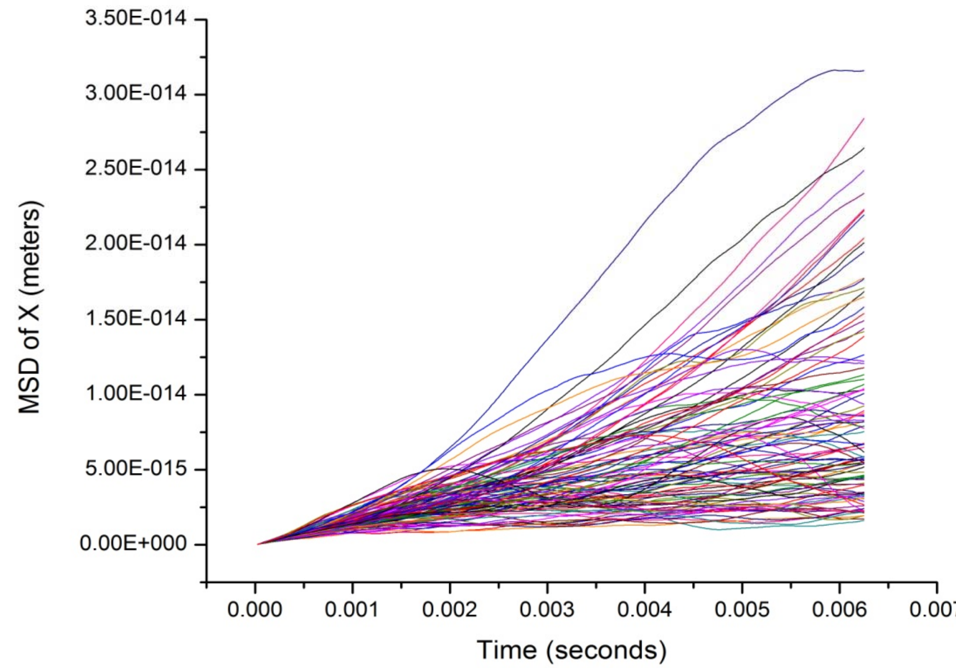
Stationary Results $D = 1 * 10^{-12}$

- Membrane did not fluctuate during the random walk.

D $(\frac{cm^2}{s})$	N	L(cm)
$1 * 10^{-12}$	1024	.375

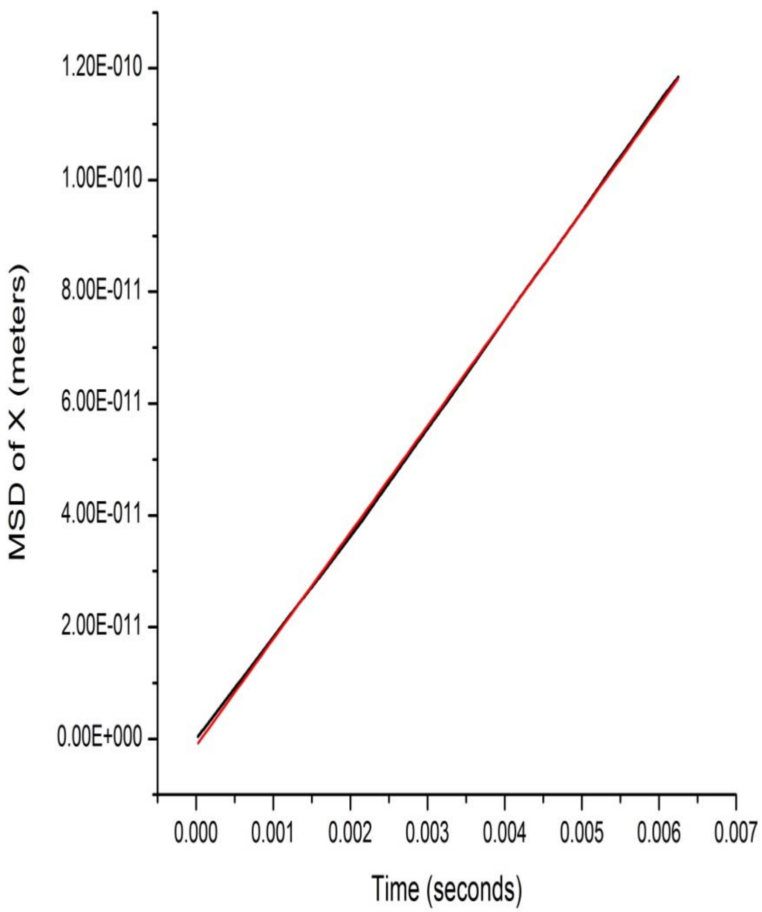


Average MSD for X

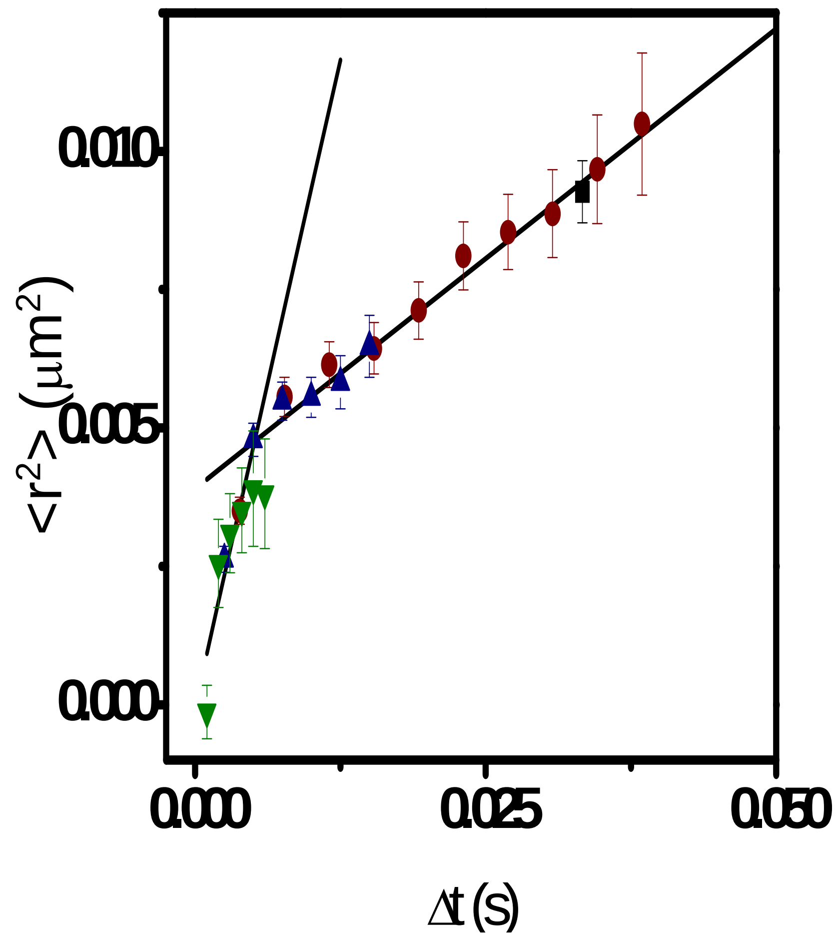


MSD of X for all 100 Particles

Percentage of original diffusion coefficient found in the average:
X = 70%



$$D = 1 * 10^{-8}$$



Previous Experimental Graph

Our Conclusion

- The results show that the undulation of the membrane does not cause an effect on the time scales.

- No compartmentalization with fluctuations.

- Diffusion coefficient is about 90% of what we expected it to be (90% of the values that were put into the simulation).

Questions?