Nanoparticle Motion

Ben Morris bm14144@my.bristol.ac.uk

Duncan Cassells dc14709@my.bristol.ac.uk

Rachel Spencer rs14550@my.bristol.ac.uk

Yiyoung Kim yk14297@my.bristol.ac.uk

Siyang Zhan sz14093@my.bristol.ac.uk

29/04/2016

Contents

Chapter 1

Abstract

Nanoparticles are increasingly being used for biomedical applications, hence, becoming a more relevant area for research. The overall aim of the project is to graphically model nanoparticle motion. Other goals of this project are to model the motion of diffusing nanoparticles in 2D and 3D with different shapes and concentrations, the fluid viscosity will also be taken into account. The diffusion coefficient and Stokes-Einstein Equation will be studied to understand diffusion theory. Random walk models based on Brownian motion, continuous plane and coordinate system will be generated using MATLAB. Results from the models will be validated with trajectories of diffusing fluorescent nanoparticles visualised under the microscope.

Chapter 2

Introduction

2.1 Nanoparticles

Nanoparticle research is currently an area of intense scientific research, due to a wide variety of potential applications in biomedical, optical, and electronic fields. Nanoparticles are particles between 1 and 100 nanometres in size and can show different properties compared to larger particles of the same material. Forces of attraction between surfaces can appear to be weak on a larger scale, but on a nanoscale they are strong. One reason for this is that nanoparticles have a large surface area to volume ratio. This provides a great driving force for diffusion, especially at high temperatures.

2.2 Nanoparticles in medicine

Some of the uses of nanoparticles in biology and medicine include:

- Creating fluorescent biological labels for important biological markers and molecules in research and diagnosis of diseases
- Drug delivery systems
- Gene delivery systems in gene therapy
- For biological detection of disease causing organisms and diagnosis
- Detection of proteins
- Destruction of tumours with drugs or heat

Nanoparticles are being used more in drug delivery systems the size and surface characteristics of nanoparticles can be easily manipulated. Also nanoparticles can be made to control and sustain release of the drugs during transportation as well as the location of the release. However, the random movement of these particles is difficult to predict and manipulate.

2.3 Objectives [4]

The purpose of this project is to construct a model of a diffusing nanoparticle in 2D and 3D with a diversity of shapes and concentrations.

It is difficult to perform experimental work with regard to imaging the movements of diffusing nanoparticles. However, the trajectories of diffusing fluorescent nanoparticles can be visualized and observed under the microscope, which also assists to generate results from the models. It can be seen that the particles move randomly by the process of diffusion. Setting up 2D and 3D models of nanoparticle motion would be a great aid for studying their diffusion.

Chapter 3

Research

3.1 Diffusion of particles

Diffusion is one of the fundamental processes by which particles can move through a medium. It is a consequence of the constant thermal motion of atoms, molecules, and particles, resulting in materials moving from areas of high to low concentration. Thus the end result of diffusion would be a constant concentration throughout the environment.

3.2 Mean Square Distance

To obtain the diffusion coefficient, the mean square displacement must be known first. Let t_1 be the time of each step and b the displacement, so the mean square displacement of N steps in time t will be $\mathrm{t} = \mathrm{N}t_1$. Therefore, the mean squared displacement can be calculated by equation (1) below.

$$\langle[\mathrm{r(t)} - \mathrm{r(0)}]^2\rangle = \mathrm{N}b^2 \qquad (1)^{[1]}$$

With a known diffusion coefficient D (typical units are cm^2/s), mean square displacement can also be represented in another way:

$$\langle x^2\rangle = q_i D t \qquad (2)$$

Where x is the mean distance from the starting point that a molecule will have diffused in time t and its square is the mean squared displacement. q_i is a numerical constant which depends on dimensionality: qi = 2, 4, or 6, for 1, 2, or 3 dimensional diffusion.[2]

3.3 Diffusion Coefficient [2]

As it shown in equation (1), mean square distance is proportional to the total time t. In general, the mean square displacement divided by 6 for the three dimensions, multiplied by the time gives, the diffusion coefficient. It is shown in the equation (3) below:

$$\mathrm{D} = \frac{\langle[\mathrm{r(t)} - \mathrm{r(0)}]^2\rangle}{6t} \qquad (3)$$

For random walking particles in 3D space, the formula changes into the following equation (4):

$$\mathrm{D} = \frac{\mathrm{N}b^2}{6Nt_1} = \frac{b^2}{6t_1} \qquad (4)$$

3.4 - Stoke-Einstein Equation

In order to drag a particle suspended in a viscous medium at a constant velocity, constant force must be applied to the particle. Stoke showed that the friction coefficient f, for a sphere of radius r in a solvent of viscosity η is given by equation (5):

$$f = 6\pi\eta\mathrm{r} \quad (5)^{[1]}$$

Einstein showed that the diffusion coefficient of the particle in a solution at temperature is related to the friction coefficient. There is also another way to find the diffusion coefficient:

$$\mathrm{D} = \frac{1}{f} K_B T \qquad (6)^{[1]}$$

Where K_B is the Boltzmann constant, T is absolute temperature.

The rate of diffusion is affected by 3 main parameters; temperature, size or mass of the particle and the viscosity of the environment, all of which are taken into account by the diffusion coefficient. Combining equations (5) and (6) gives the diffusion coefficient of a sphere shown in equation (7), i.e. Stokes-Einstein equation:

$$D = \frac{K_B T}{6\pi\eta \mathrm{r}} \qquad (7)^{[2]}$$

This equation shows that diffusion is proportional to temperature and inversely proportional to viscosity and size of particle. By assuming constant temperature and viscosity, the coefficient is constant. The diffusion is faster at a higher temperature, in a less viscous solvent, and for a smaller particle. The concept of the Stokes radius can also be extended to non-spherical suspensions and molecules. [2]

Chapter 4

Random walk models

4.1 Brownian motion

Brownian motion is a random motion of particles in liquid or gas. In general, particles moving in liquid are more active at high temperatures; this results from colliding with solvent molecules. In liquid or gas, solvent molecules are moving randomly so particles frequently collide with solvent molecules, and the velocities of the particles change. The random motion of the particles is known as diffusion and the diffusion motion is continuous, however, there is no net movement when all particles are evenly spread since particles diffuse from a place of high concentration to a place of low concentration. As particles move randomly, there is no way to know where particles will go. However, we can use a transition probability in given time and predict the motion. Brownian motion in one dimension is composed of a sequence of normally distributed random displacements. The distribution of these displacements is shown by the histogram in Figure 1 below.

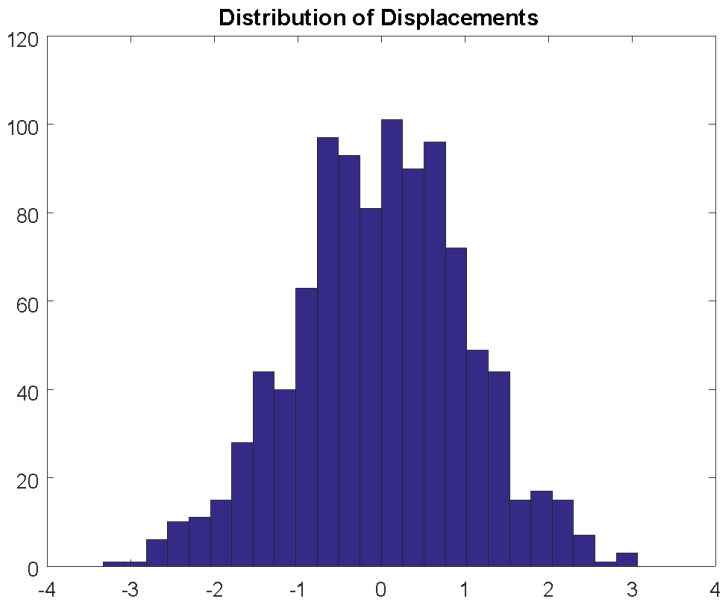

Figure 1: The normal distribution of displacements

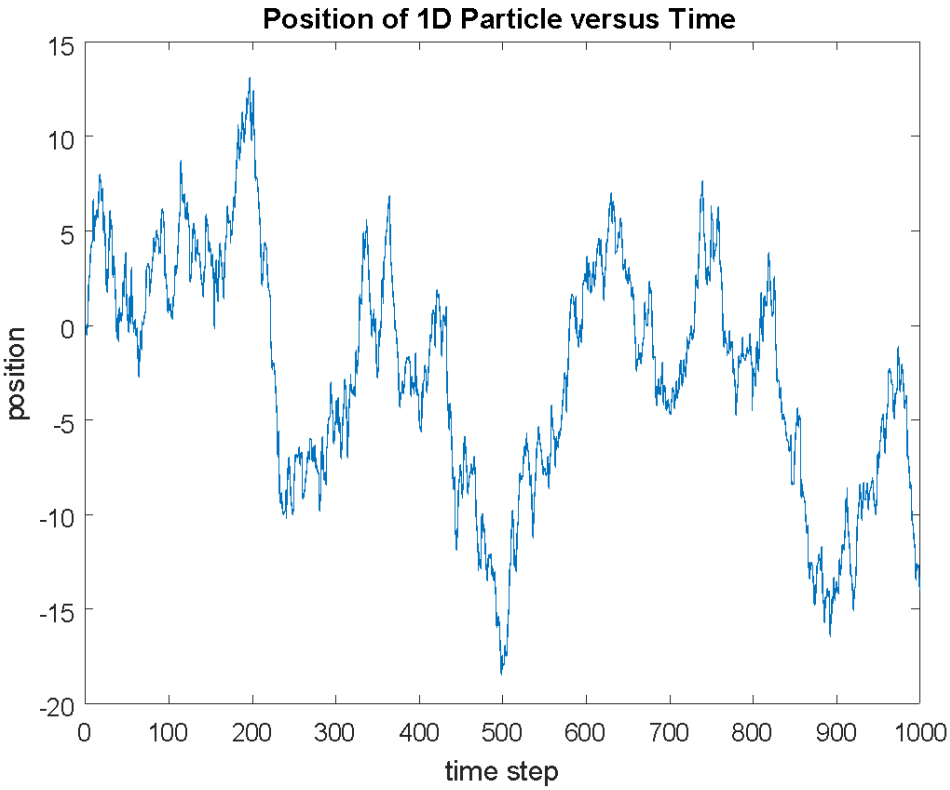

Figure 2: Brownian motion in 1D

Figure 2, shows the trajectory of one nanoparticle in 1D over 1000 time step intervals. When a particle is moving with discrete steps, each displacement is randomly set. The random displacement is according to the normal distribution which is shown in figure 1, so to see trajectory, the position is set by accumulating the sum of each distance. This principle can be extended into 2 dimensions.

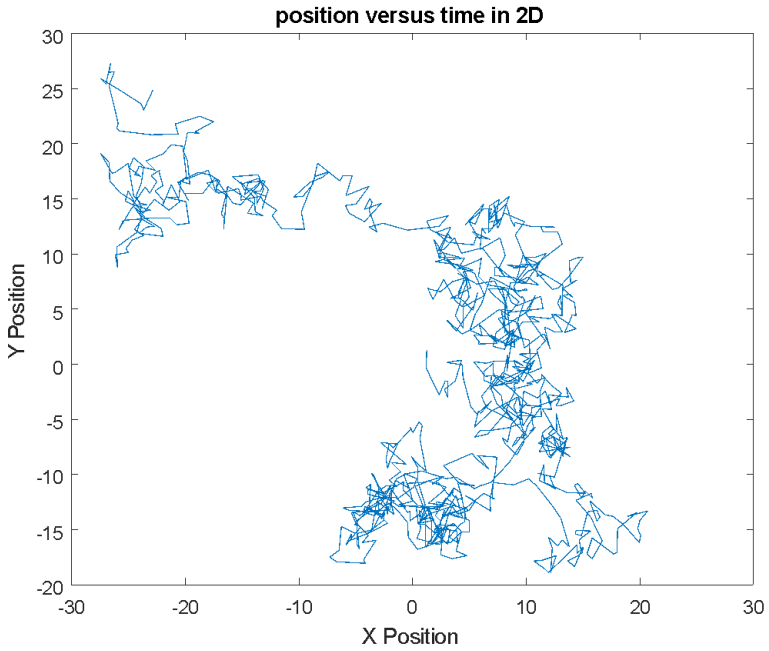

Figure 3: Brownian motion of a single nanoparticle in 2D

In two dimensions, both X and Y positions are based on a normally distributed distance for each step, and the position is calculated by accumulating the sum of each distance. The random walk has a mean of 0 since the net movement of diffusion is 0, but has proportionally increased variance in time.

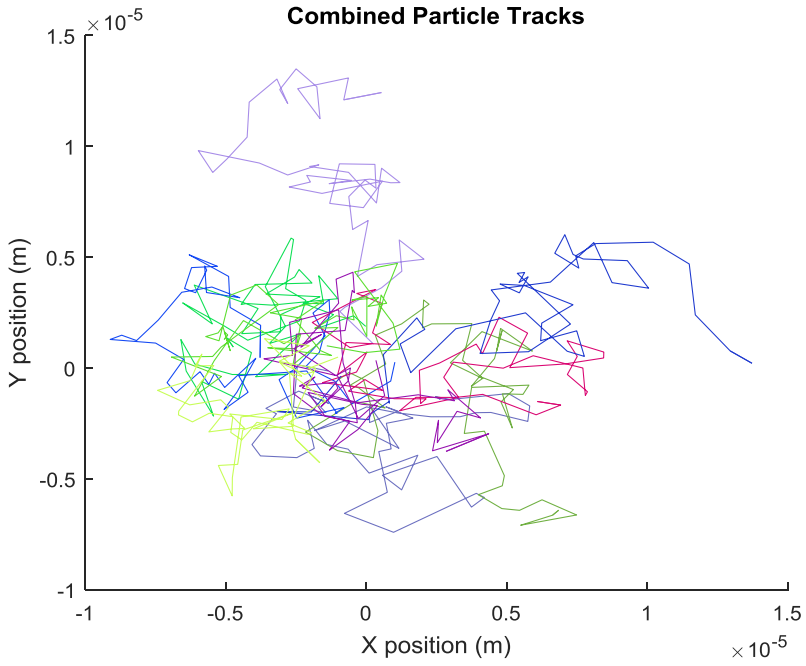

Figure 4: Brownian motion of 10 nanoparticles in 2D

Figure 4 shows that this principle can be applied to many particles. The random paths travelled by each particle over time is represented with a different coloured line.

The equation below, describes the theoretical displacement of a particle in 2 dimensions.

$$< x >= 4Dt$$

Where D is the diffusion coefficient and t is the time. The diffusion coefficient is described by equation 1. In this case, the diffusion coefficient considers the viscosity of tissue and average body temperature. The theoretical diffusion coefficient was calculated to be 4.5391×10^{-12} $cm^{-1}s^{-1}$. However the simulated diffusion coefficient was 4.6677×10^{-12} $cm^{-1}s^{-1}$, therefore a marginal error of 1.2862×10^{-13} $cm^{-1}s^{-1}$ implies that the simulation is fairly realistic and representative.

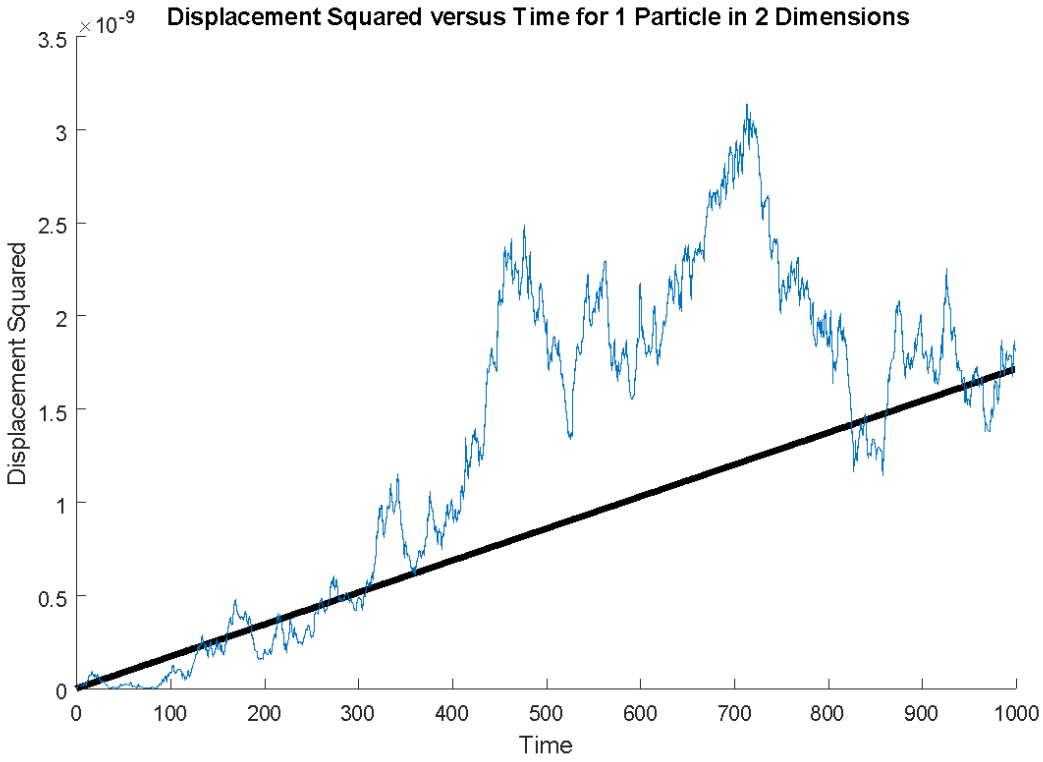

Figure 5: Displacement squared against time for one particle

Displacement should increase in proportion to the square root of time. The theoretical value of displacement squared is plotted with a black line on Figure 5. It can be seen that with a single particle, that there can be a large deviation from the theoretical displacement due to the random motion of the particle, however, the simulated displacement roughly matches the theoretical value, this shows that it does represent the general trend of the displacement of the particle.

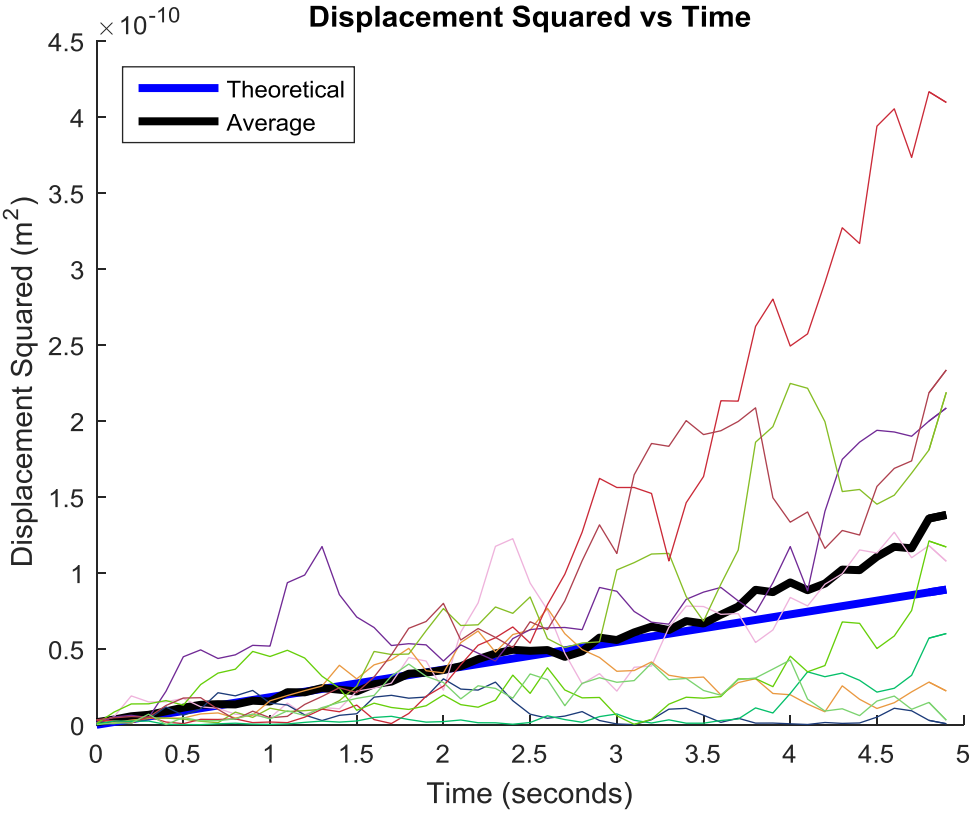

Figure 6: Displacement squared against time for many particles

With many particles it can be observed that the average squared displacement has a much smaller deviation from the theoretical displacement, represented by the black and blue lines on figure 6. Concluding that considering more particles, produces an average squared displacement that can be closely represented by the squared displacement equation.

4.2.1- Continuous plane model 2D

Assumptions

- The model assumes every nanoparticle has a radius of 5×10^{-9} M
- The viscosity of tissue is approximately 10 times the viscosity of water, so has a value of 1×10^{-2} in SI units (Pascal-seconds)
- Boltzman constant is equal to $1.38064852 \times 10^{-23}$
- Assuming absolute temperature of average human body is 310.15 K
- Mass of every particle is 1.01×10^{-17} Kg

Method

This model simulates a chosen number of nanoparticles trajectories on a continuous plane in 2D and 3D. The model will also calculate the diffusion coefficient, mean squared displacement and frequency of collisions. In both, 2D and 3D models, very particle is travelling with a velocity determined by equation (8) below.[5]

$$v_s = \sqrt{\frac{k_B T}{m}} \qquad (8)$$

Where,

K_B = Boltzman constant

T = Absolute temperature of body

m = Mass of particle

The initial positions for all particles is in both dimensions are set to the origin.

Results

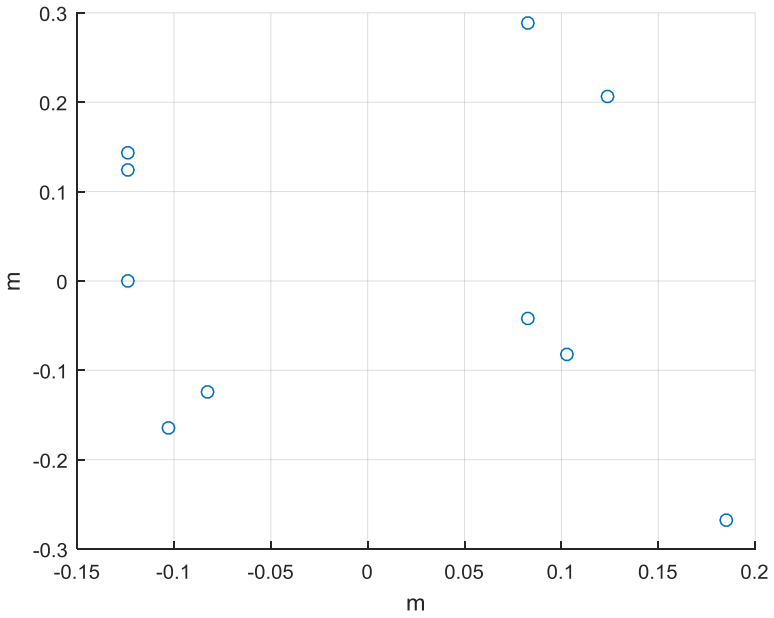

Figure 7: shows the 2D positions of 10 nanoparticles after 100 seconds

In 2D the diffusion coefficient was calculated to be 6.815×10^{-12} $cm^{-1}s^{-1}$, mean squared distance was $2.276 \times 10^{-9}M^{-1}s^{-1}$. However, the simulated mean squared distance was only 6.625×10^{-6} $M^{-1}s^{-1}$. This suggests the velocity equation used above has large errors, this could be due to the equation not considering the diffusion coefficient.

4.2.2- Continuous plane model 3D

The model is situated in a Cartesian coordinate system in a three-dimensional Euclidean space. In other words, a vector with three components represents each individual nanoparticle as an x, y and z coordinate. A large matrix is then used to store the coordinate information for n nanoparticles. At each time step each position is updated by the addition of normally distributed pseudorandom numbers with mean 0 and standard deviation 1. This process loops until t time steps have been completed.

Due to the approach of using large matrices to approximate the positions and movements of the nanoparticles, it was possible to run simulations with lots of particles in a relatively short period of time to get a better idea of general behaviour. For example, simulating with 10,000 nanoparticles for 10 seconds could be done in a relatively short period of time of 7.5 seconds. Using numerous

nanoparticles means that the data generated from the model is more likely to be representative of the model, and if the model is similar to a real life scenario then the data will give a good representation and prediction for actual diffusive behaviour.

The relationship$\langle(x - x_0)^2\rangle = q_i Dt$, where the mean squared displacement equals the product of the numerical constant of dimensionality, the diffusion coefficient and the time elapsed, describes diffusion with respect to time. Figures 8 to 10 verify this relationship as they show the mean squared displacement to be linearly proportional to time. In each figure, the blue dashed line shows $y = x$ and the red line plots the mean squared displacements for each time step $1 \leq t \leq 20$.

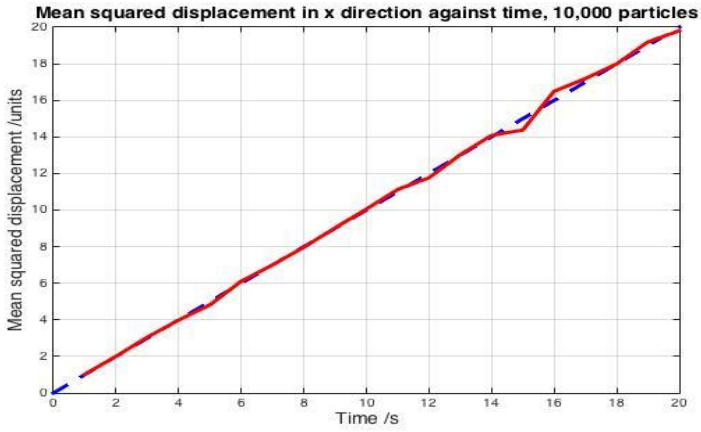

Figure 8: mean squared displacement in x against time, for 10,000 nanoparticles

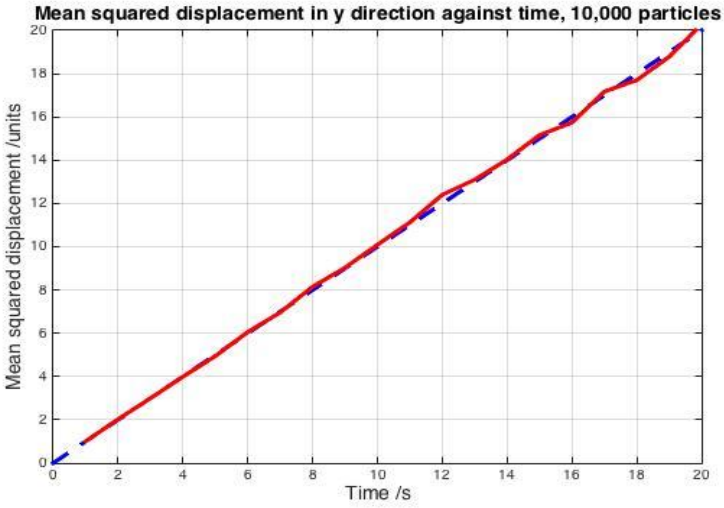

Figure 9: mean squared displacement in y against time, for 10,000 nanoparticles

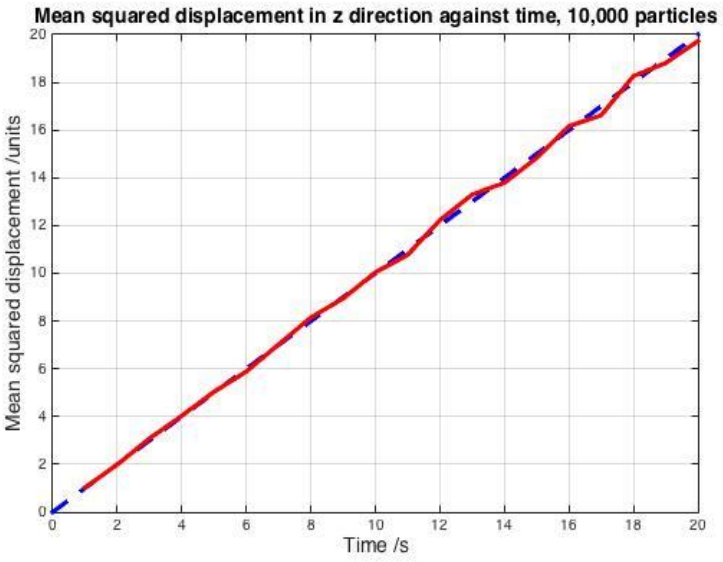

Figure 10: mean squared displacement in z against time, for 10,000 nanoparticles

The next stage of model development was to input collisions. Due to the random nature of the motion, collisions resulted in a new random displacement change for both particles. This method of modelling was chosen because of the random and chaotic nature of movement under Brownian motion, meaning that movement at one moment in time cannot be correlated to movement at any other time. Intentionally making all particles collide at the first time step and seeing what happened afterwards tested it. However, when the simulation was left to run freely collisions rarely occurred. The reason for this was down to tuning the parameters involved. In this experiment, the rate of diffusion is too fast compared to the particle size for collisions to regularly occur. This could be an improvement in the future to get a more realistic rate of collisions.

4.3- Coordinate system

Assumptions

- The model assumes that every nanoparticle can move up to 1 grid space in any direction per unit time
- Dimensions of every nanoparticles are restricted to one grid space
- Environmental effects such as temperature and viscosity are ignored
- Particles cannot exceed grid dimensions

Method

The model works by allowing particles to move within a specified grid space by the user. This model investigates the movement of molecules with and without collisions and different size particles. The model loops through a certain number of iterations, with the particles moving one unit in any direction in the coordinate space on each iteration. Once they have moved, their coordinates are recalculated and plotted on a scatter graph which is reprinted each time to show the movement of the particles. This is the same process for the diffusion aspect of this model where the particles start out already randomly distributed in the grid space. In order to investigate the effect of collisions, particles start off in a clump in one corner of the axis and move randomly into the rest of the coordinate space, initially not taking into account the element of the particles colliding into each

other so that the model could be developed at a simple level and understood before taking it further. Figures 11 and 12, show the initial and final positions of the nanoparticles without collisions.

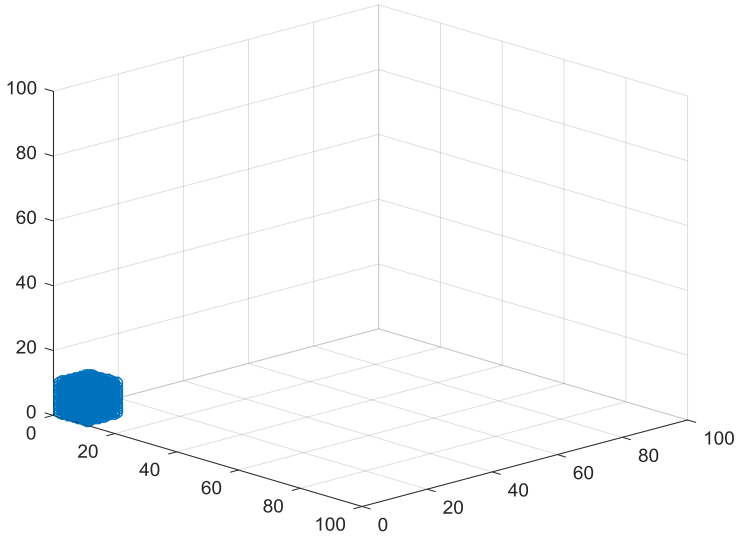

Figure 11: shows the initial position of nanoparticles

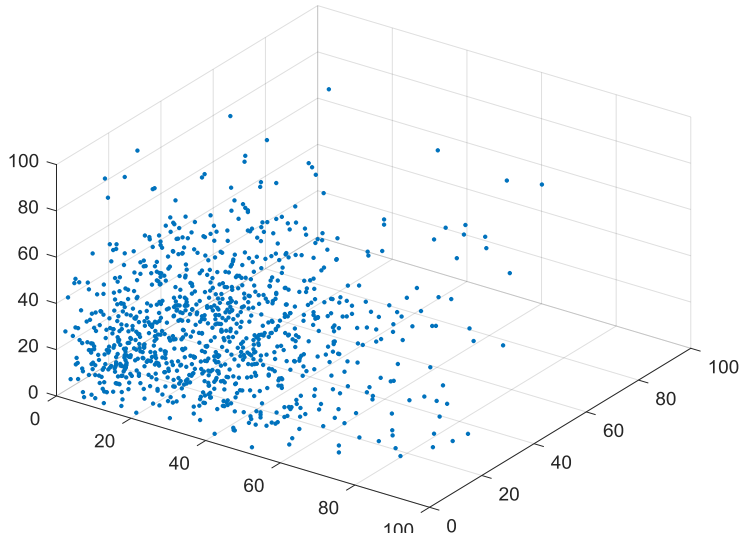

Figure 12: shows the final position of nanoparticles after 1500 iterations

The final positions of the nanoparticles show that there is still a high concentration in the corner they started in, however, if the model was allowed to run with more iterations, the particles would appear to be equally distributed, with all areas of the grid having roughly equal concentrations.

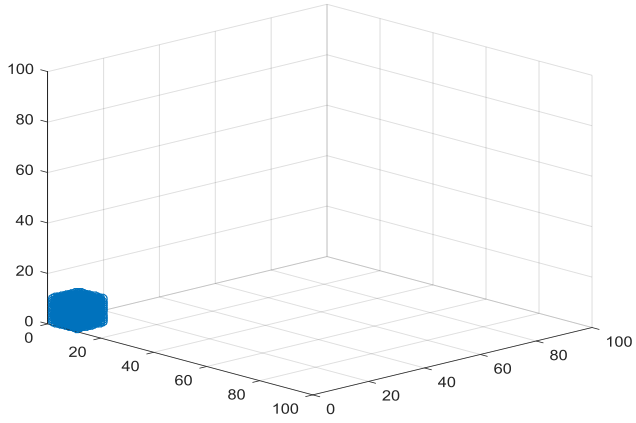

Figure 13: shows the initial position of nanoparticles

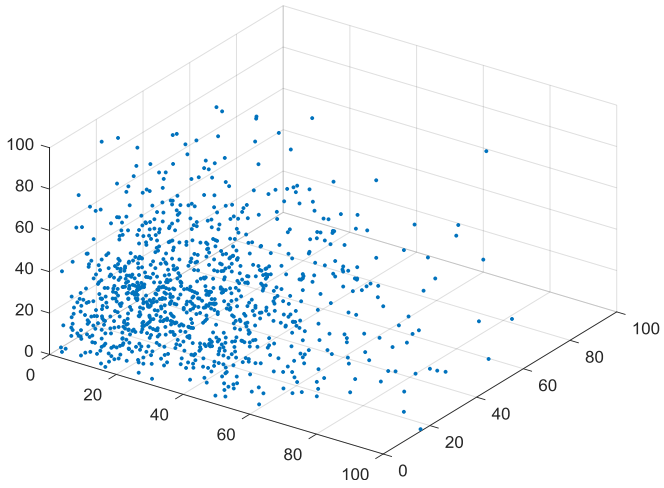

Figure 14: shows the initial position of nanoparticles

Figures 13 and 14, show the initial and final positions of the nanoparticles with collisions. The figures for collisions and without collisions look every similar, however, in the model where collisions are considered, particles move further. This can be seen in figures 15 and 16, which show the distribution of distances travelled by the particles.

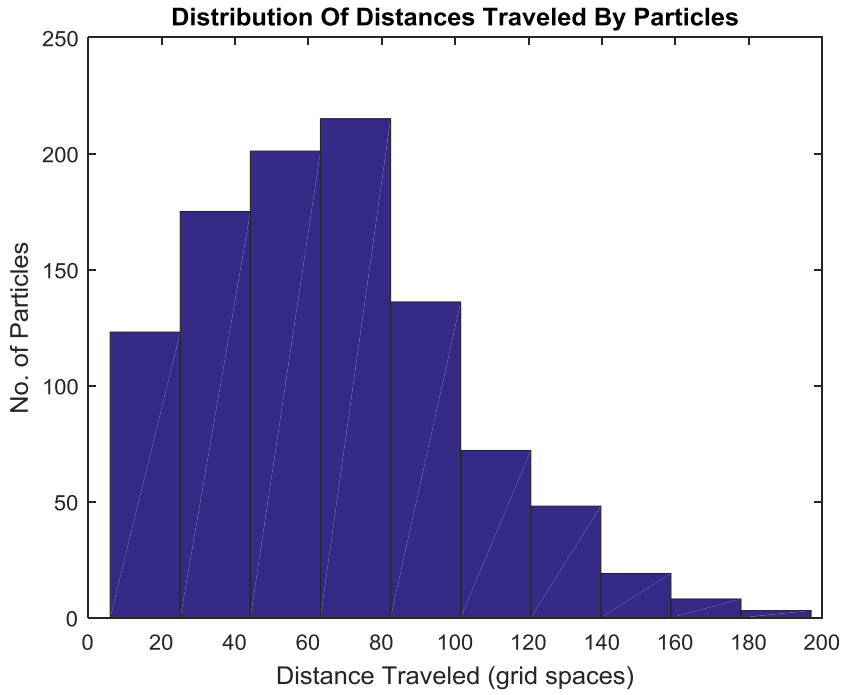

Figure 15: Distribution of distances travelled by particles without collisions

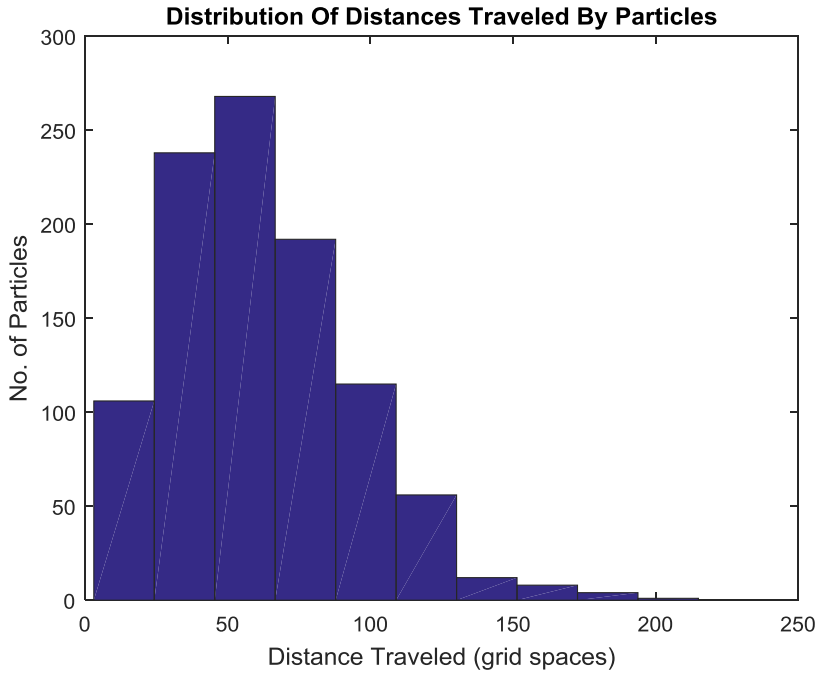

Figure 16: Distribution of distances travelled by particles with collisions

Comparing figures 15 and 16, it is clear that a higher proportion of nanoparticles move further. This is because if a particle collides with another they will move away from each other, increasing the likelihood of particles spreading out in less time.

The model can also simulate the motion of larger particles. In theory, larger particles move slower. This is because the diffusion coefficient is inversely proportional to the radius of a particle, or the cube root of the volume. So, if the mass of one spherical particle is 8 times greater than another, its diffusion coefficient is only 2 times smaller. Therefore, a smaller particle will diffuse faster than a larger one.

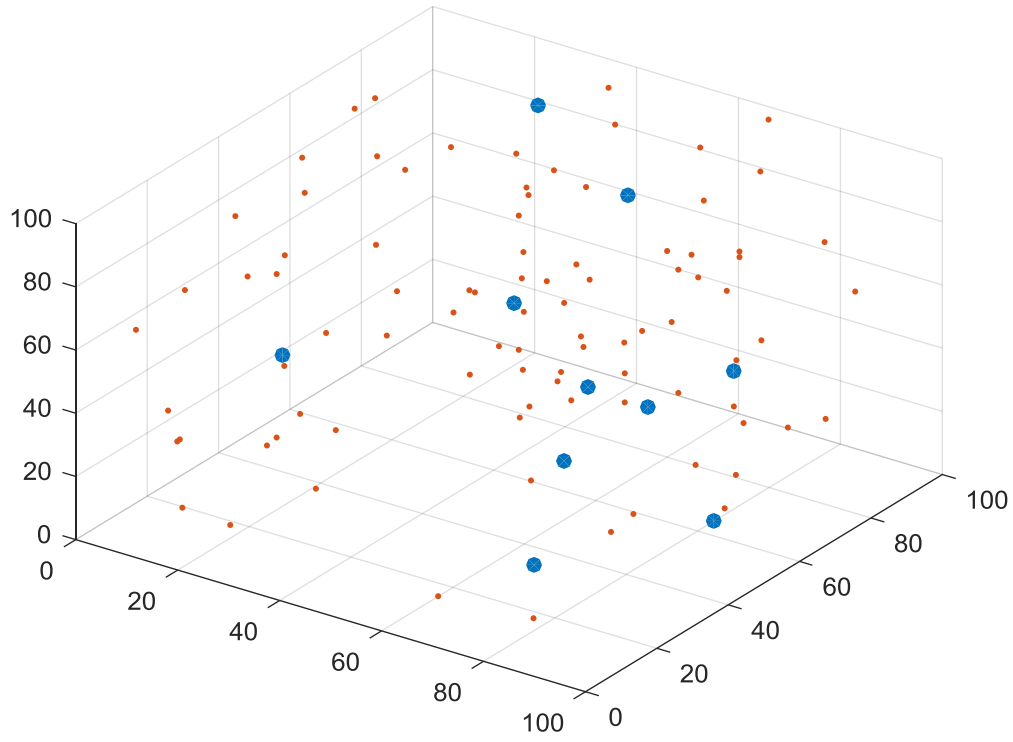

Figure 17: Final positions of 10 large nanoparticles and 90 smaller nanoparticles

This model allows the smaller particles to move twice as much as the larger particles therefore the larger particles are modelled to be 8 times greater than the smaller particles, however, large particles are still restricted to one grid space.

Chapter 5

Conclusions

There are multiple conclusions that have been made during this report. It can be concluded that 2D and 3D models behave similarly when concentration of nanoparticles is similar. However when modelled in 3D, nanoparticles appear to move further, especially when considering how collisions affect the motion of nanoparticles.

It can also be concluded that diffusion is proportional to temperature and inversely proportional to viscosity and the size of the particle. This conclusion has been drawn through research of the diffusion coefficient and Stokes-Einstein equation. The mean squared

displacement can be calculated using the diffusion coefficient and it has been shown that average squared displacement of many particles has a much smaller deviation from the theoretical squared displacement than a single particle.

Chapter 6

Further Study

Further work for this project would start with more investigation into the behaviour of the nanoparticles along a different sized channels that could represent the nanoparticles are travelling through blood vessels in the human body. A number of important factors would need to be taken into account such as inner body temperature, viscosity, collisions with other particles, hitting a vessel wall and either bouncing off or attaching then dispersing through the tissue. In addition to this, the width of the vessel would need to be considered as it plays an important part in the collisions between particles. The very narrow vessels in the human body mean that collisions are unavoidable and have to be taken into account in order for accurate behaviour to be modelled.

Another aspect of further work is including the drugs delivery system, where the model could take into account where the drugs need to be delivered and display which nanoparticles correctly delivered to the target area and which nanoparticles did not deliver. To begin with the movement would be random and then through developing the model, the more complex factors start to be taken into account; collisions, diffusion coefficient based on temperature and viscosity of the surroundings and effect of the coating of the drugs. Further experiments with this model could lead to decreasing the delivery time.

References

[1] Diffusion – useful equations: http://www.life.illinois.edu/crofts/bioph354/diffusion1.html

[2] I. Teraoka, Polymer Solutions: An Introduction to Physical Properties, Chapter 3 http: //www.eng.uc.edu/~beaucag/Classes/Properties/Polymer%20Textbook.pdf

[3] NanoDoc: http://nanodoc.org | Video: http://youtu.be/nETSs12tj7w

[4]Nanoparticle Diffusion: https://www.ole.bris.ac.uk/bbcswebdav/pid-2419368-dt-content-rid-6473749_2/courses/EMAT22220_2015/project1%281%29.pdf

[5] Tristan S. Ursell, The Diffusion Equation A Multi-dimensional Tutorial: http://www.rpgroup.caltech.edu/~natsirt/aph162/diffusion_old.pdf

[6] S. Hauert, S. Berman, R. Nagpal, S.N. Bhatia, A computational framework for identifying design guidelines to increase the penetration of targeted nanoparticles into tumours, Nano Today, Volume 8, Issue 6, pp. 566-576, 2013

[7] S. Hauert, S.N. Bhatia, Mechanisms of cooperation in cancer nanomedicine: towards systems nanotechnology, Trends in biotechnology 32 (9), 448-455