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”De diffusie van een polymeer in een gel netwerk” (Engelse titel: ”Polymer diffusion in a gel network ”)

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Abstract

In this thesis, we model the diffusion of a tracer polymer inside of a gel network and simulate it, hoping to find a connection between the diffusion of the polymer and the strength of the gel network. This model is made by using the Rouse model for the gel network and the tracer polymer. The overdamped Langevin equation is then used to find a set of coupled stochastic differential equations for the motion of a single tracer bead and the Fourier modes of the gel particles. The single particle system is then analyzed using three different numerical methods: The Euler forward method, the Metropolis Monte Carlo method and the Gillespie algorithm. The Gillespie algorithm is then used to expand the single particle model to a model which again includes a tracer polymer instead of a single tracer bead. The simulations of the tracer polymer suggest that the motion of the tracer polymer is superdiffusive. This contradicts the theory and the measurements of the single tracer particle, which suggest that the simulation of the polymer should result in subdiffusion. This contradiction seems to be caused by an error in the implementation of the interaction between the different beads that make up the tracer polymer, as it creates a tendency for the polymer to move away from its original position. This possible error is hinted at by a simulation of the system with the tracer polymer where the gel is considered stationary. The simulation implies superdiffusion as well, which means that the superdiffusion is not caused by the gel network. In fact, the simulation with the frozen gel network is much further away from subdiffusion that the simulation with the gel network intact, which does seem to imply that the motion would be subdiffusive if the model was implemented correctly, but it is not conclusive.

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Chapter 1

Introduction

The human body is almost entirely made out of cells. Cells are quite complex, but they are also a very fundamental part of our understanding of the human body, as so much of our body is made up of cells. As modern medicine advances, understanding the smaller details of the human body becomes more important. One such detail is the structure of the cytoskeleton, which has many functions, including intracellular transport. The cytoskeleton is composed of many different substances, including actin filament, or F-Actin, networks. An F-Actin network is known as a gel network, a large group of polymers that are cross-linked at certain spots inside of a solvent. Gel networks have the remarkable property that simple particles do not diffuse as they would in water, for instance. Instead, the gel hinders the diffusion somewhat, resulting in subdiffusion. In this thesis, we will analyze the diffusion of a less simple particle, a polymer, in a gel network. In particular, we will look for ways in which the diffusion of a tracer polymer can tell us something about certain propertiesof the gelnetwork, such as the strength of the cross-links.

Chapter 2

Theory

2.1 The model

The situation that we will analyze is that of a tracer polymer in soft matter, specifically a gel. A tracer polymer is a polymer made up of simple tracer particles. These particles do not chemically interact with the environment and are only inserted into the system for the purpose of determining the physical effect its presence has on the environment. A gel, as described by Doi [1], is a mostly dried-up solution of colloids. Colloids are solid particles or fluid droplets that are quite small, but are still much bigger than single atoms, with a size typically between $1nm$ and $1\mu m$. The gel considered in this thesis is described by Doi [1] and consists of a polymer network inside of a solvent. A polymer network consists of a large group of chain-like polymers which are cross-linked to one another to form one big molecule. A gel is different from a regular polymer solution in that a gel has a regular shape, meaning that a gel will find an equilibrium state whenever it is left alone. Small deformations of the gel can be reversed. On the other hand, the polymer solution does not have it's own distinct shape as it consists of a group of chain-like polymers which get stuck on one another when it is poured, causing it to resist flow, but it does not have its own shape and if it is disturbed, it will not have a tendency to return to its original position.

In order to make the system of a tracer polymer diffusing inside of a gel more manageable to work with, the Rouse model for polymers is used. In the Rouse model, polymers are described as a long series of beads connected to their nearest neighbor by an ideal spring. This model is then extended to a gel network by proposing that the gel network consists of beads on a two-dimensional square mesh grid which are also connected to their nearest neighbors via springs. The size of the unit cell will fluctuate as a result of the interaction between the tracer and the gel, though not by much. The size of the tracer beads that make up the tracer polymer is proposed to be about half the size of the unit cell when the system is at rest, which is a size for which a single tracer bead displays subdiffusive behavior, as found by Wong et al. [2]. A sketch of the model can be found below.

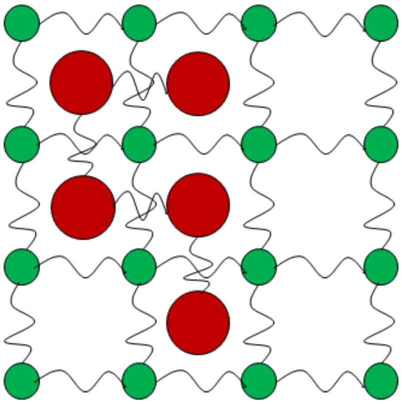


Figure 2.1: A sketch of the used model. The red circles represent the tracer polymer and the green circles represent the gel particles.

When looking at the way in which the interaction between the tracer particle and its surroundings is modeled it is important to note that, in this particular model, the gel mesh is taken to be very large, as this will allow us to ignore any interaction with the edge of the system. As a result, the gel consists of a very large number of beads. When keeping track of all these beads it becomes more convenient to describe their position using their Fourier modes or normal modes compared to just the x and y position of each individual particle. The connection between the one-dimensional position of a collection of particles and the Fourier modes of the system is described by the following formula:

$$x_n(t) = X_0(t) + \sum_{p\geq 1}^{N}(2X_p(t)\cos(\frac{\pi np}{N})) \tag{2.1}$$

where $x_n(t)$ is the x-coordinate of the nth particle in the chain at time t, $X_p(t)$ is the pth normal mode of the chain at time t and N is the total length of the chain. By using this representation one can describe the position of a large number of gel beads on the grid using fewer resources compared to using the x and y coordinate of every individual particle.

2.2 Mean Squared Displacement

Diffusion is a random process, so simply looking at the position of the polymer at different times would not yield a useful result, because if the experiment is performed again under the same conditions, the position will probably be different. Instead the quantity that should be looked at is some sort of average. However, the average of the position taken across multiple samples of the same experiment would not be interesting either, as diffusion of the system at rest is not biased towards one particular direction, so the average should be zero when taken across a large number of experiments. The quantity that is interesting to look at is the so called time-averaged mean square displacement, or MSD. The formula most commonly used to calculate the MSD looks as follows:

$$\langle \Delta r^2(\tau)\rangle = \frac{1}{N}\sum_{i=1}^{N}(x(i+\tau)-x(i))^2 + (y(i+\tau)-y(i))^2 \tag{2.2}$$

Where $\langle \Delta r^2(\tau) \rangle$ is the MSD of the particle in 2 dimensions, τ is the lag time, which signifies the difference in time between two of the measurements, N is the number of times a displacement with lag time τ takes place in the experiment and x and y are the x-coordinate and y-coordinate of the center of mass of the tracer polymer as a function of time. This definition is comparable to the definition used by Godec et al. [3], except equation 2.2 is discretized. When dissecting this formula we can see that for a particular value of τ, the timescale of the measurement is divided into sections that are not necessarily disjointed, which each have a length of τ. The change in position is then calculated for each of those smaller time windows and then the average is taken over all of them, creating a quantity that looks at the average distance the particle has moved over a certain period of time rather than just the average position of the particle at certain points in time.

For the MSD of a particle that preforms a random walk we have:

$$\langle \Delta r^2(\tau) \rangle = 2dD\tau \tag{2.3}$$

Where d is the number of dimensions in the system and D is the diffusion coefficient. A random walk is an example of regular diffusion. In the gel network, however, anomalous diffusion occurs when the tracer consists of only one bead. In particular, subdiffusion occurs. This type of diffusion is characterized by the following formula:

$$\langle \Delta r^2(\tau) \rangle = 2dD\tau^{\alpha}$$

If $0 < \alpha < 1$, the diffusion is said to be subdiffusive, while for $1 < \alpha < 2$, the diffusion is said to be superdiffusive. The value for α for a particular simulation can be found by plotting $\log\langle \Delta r^2(\tau) \rangle$ against $\log(\tau)$ and finding the slope of the linear fit of the poltted curve, as

$$\log\left(\langle \Delta r^2(\tau) \rangle\right) = \log\left(2dD\tau^{\alpha}\right) = \log(2dD) + \alpha \log(\tau) \tag{2.4}$$

Subdiffusion occurs whenever the environment that the diffusing particle is placed in works against the direction the particle ends up moving. This tendency to push back the particle is also present in a gel network. A gel network, as mentioned earlier, has its own distinct shape that it tends to return to whenever it is slightly disturbed. This is also the case whenever a particle inside of the gel network is diffusing. Due to the small coupling between the tracer bead and the gel beads, the gel is slightly deformed whenever the tracer bead moves away from its initial position at rest. The gel has a tendency to undo this deformation and as a result the tracer will feel a slight force back towards its initial position. As a result the displacements for higher values of τ are lower than for a regular diffusive particle, as the tracer has a slight tendency to linger around a its initial position, while a regular diffusive particle does not linger around one particular position.

2.3 Equations of motion

When looking at the different potentials that cause movement to take place, we will first take a look at a system where the tracer particle is a monomer and therefore consists of only one bead. The effect of using a tracer polymer with an arbitrary length will be considered later. For convenience we will also stick to a one-dimensional system for now, as the equations of motion are defined in the same way for the second dimension. The general equation of motion for the tracer particle and the gel beads are derived as follows from the Langevin equation, as descibed by Doi [1]:

$$F = m\frac{d^2x}{dt^2} + \gamma\frac{dx}{dt} + \xi(t) \tag{2.5}$$

Where F is the force on the particle, m is the mass of the particle, γ is the drag coefficient, x is the place coordinate of the particle and $\xi(t)$ represents the noise in the system. Given the fact that our system is primarily governed by Brownian motion, we can use the assumption commonly made in Brownian dynamics that m goes to zero. The force on the particle can be calculated by the general rule $F = -\frac{dU}{dx}$, where U is the potential acting on the particle. This leaves us with the so-called overdamped Langevin equation:

$$\gamma\frac{dx}{dt} = -\frac{dU}{dx} + \xi(t) \tag{2.6}$$

Where the noise has a mean of 0 and a variance of $\langle\xi(t_1), \xi(t_2)\rangle = 2\gamma k_B T\delta(t_1 - t_2)$, with k_B the Boltzmann constant, T the temperature. When looking at the equations of motion for the gel modes we can find that they look more or less the same:

$$\Gamma_p\frac{dX_p}{dt} = -\frac{dU}{dX_p} + \Xi_p(t) \tag{2.7}$$

Where, again, Γ_p is the drag coefficient and Ξ_p is the noise with zero mean and a variance of $\langle\Xi_p(t_1), \Xi_q(t_2)\rangle = 2\Gamma_p k_B T\delta(t_1 - t_2)\delta(p - q)$. We define a potential that is split up into three different parts, the potential $U_1(x)$ on the tracer particle caused by a unit cell of the mesh grid, the potential $U_2(X_p)$ caused by the perfect springs between the gel beads and the final potential $U_c(x, X_p)$ that dictates the coupling between the tracer and the gel. Combined, the total potential looks as follows:

$$U(x, X_p) = U_1(x) + U_2(X_p) + U_c(x, X_p) \tag{2.8}$$

with:

$$U_1(x) = \frac{1}{2}Ax^2 \tag{2.9}$$

$$U_2(X_p) = \frac{1}{2}\sum_p K_p X_p^2 \tag{2.10}$$

$$U_c(x, X_p) = (\sum_p s_p X_p)x \tag{2.11}$$

Where $K_p = k_0\left(\frac{p}{N}\right)^{1+2\nu}$ with k_0 the spring constant of the springs between the gel particles and $\nu = 0.588$ the Flory exponent. Similarly, $s_p = s_0\left(\frac{p}{N}\right)^{1+2\nu}$ with s_0 the coefficient that determines the strength of the coupling between the tracer and the gel. When looking at the shape of the potentials, we can see that the first two clearly form harmonic potentials. The third potential also resembles a harmonic potential, except it consists of a place coordinate multiplied by a different place coordinate multiplied by some sort of spring constant, instead of a place coordinate squared times a spring constant. Another important thing to note is that these potentials do not reflect the periodicity of the gel. To enforce the periodicity anyway, the potentials should depend on the sine or cosine of kx instead, where k is the wavenumber of the gel mesh at rest. When trying to enforce the periodicity we make use of the Taylor series. For the first potential, we use that:

$$\frac{1}{2}x^2 = 1 - 1 + \frac{(kx)^2}{k^2 2} \approx 1 - \cos(kx) \tag{2.12}$$

For the third potential, we use that:

$$x = \frac{kx}{k} \approx \sin(kx) \tag{2.13}$$

The potentials now become:

$$U_1(x) = \frac{1}{2}A(1 - \cos(kx)) \tag{2.14}$$

$$U_2(X_p) = \frac{1}{2}\sum_p K_p X_p^2 \tag{2.15}$$

$$U_c(x, X_p) = \sum_p s_p X_p \sin(kx) \tag{2.16}$$

Taking the sum of these potentials and substituting the result into the equation of motion leads to:

$$\gamma\frac{dx}{dt} = -\frac{dU}{dx} + \xi(t) = -\frac{Ak}{2}\sin(kx) - k\sum_p s_p X_p \cos(kx) + \xi(t) \tag{2.17}$$

$$\Gamma_p \frac{dX_p}{dt} = -\frac{dU}{dX_p} + \Xi_p(t) = -K_p X_p - s_p \sin(kx) + \Xi_p(t) \tag{2.18}$$

Next, the equations are transformed into their dimensionless forms, in order to reduce the amount of calculations needed for numerical simulations. We do so by first proposing the substitutions $x' = kx$, $X'_p = kX_p$ and $t' = \frac{t}{T_0}$, where T_0 is the reference time. In order to find the reference time these substitutions are filled in into the equations. The noise terms are also replaced by their respective second moments in order to find their new second moments:

$$\begin{aligned}
\gamma\frac{dx}{dt} &= -\frac{Ak}{2}\sin(kx) - k\sum_p s_p X_p \cos(kx) + \xi(t) \Leftrightarrow \\
\frac{\gamma}{kT_0}\frac{dx'}{dt'} &= -\frac{Ak}{2}\sin(x') - k\sum_p s_p \frac{X'_p}{k}\cos(x') + 2\gamma k_B T \delta(T_0(t'_1 - t'_2)) \Leftrightarrow \\
\frac{\gamma}{k^2 k_B T T_0}\frac{dx'}{dt'} &= -\frac{A}{k_B T 2}\sin(x') - \sum_p \frac{s_p}{k_B T k} X'_p \cos(x') + 2\frac{\gamma}{kT_0}\delta(t'_1 - t'_2)
\end{aligned}$$

It is desirable for the coefficient in front of the derivative to be equal to one, so $T_0 = \frac{\gamma}{k_B T k^2}$. This now leads to the equation

$$\frac{dx'}{dt'} = -\frac{a'}{2}\sin(x') - \sum_p s'_p X'_p \cos(x') + \xi'(t') \tag{2.19}$$

Where $x' = kx$,$t' = \frac{t}{T_0}$,$T_0 = \frac{\gamma}{k_B T k^2}$, $a' = \frac{A}{k_B T}$, $s'_p = \frac{s_p}{k_B T k}$, $X'_p = kX_p$ and $\xi'(t')$ is a new noise term with zero mean and variance of $\langle \xi'(t'_1), \xi(t'_2) \rangle = 2kk_B T \delta(t'_1 - t'_2)$

The same can now be done for the equations of the normal modes:

$$\begin{aligned}
\Gamma_p \frac{dX_p}{dt} &= -\frac{dU}{dX_p} + \Xi_p(t) = -K_p X_p - s_p \sin(kx) + \Xi_p(t) \Leftrightarrow \\
\frac{\Gamma_p k_B T k}{\gamma} \frac{dX'_p}{dt'} &= -\frac{K_p}{k} X'_p - s_p \sin(x') + 2\Gamma_p k_B T \delta(T_0(t'_1 - t'_2)) \Leftrightarrow \\
\frac{dX'_p}{dt'} &= -\frac{\gamma K_p}{\Gamma_p k_B T k^2} X'_p - \frac{\gamma s_p}{\Gamma_p k_B T k} \sin(x') + 2kk_B T \delta(t'_1 - t'_2) \Leftrightarrow \\
\frac{dX'_p}{dt'} &= -\gamma_r K'_p X'_p - \gamma_r s'_p \sin(x') + \Xi'_p(t')
\end{aligned}$$

Where $\gamma_r = \frac{\gamma}{\Gamma_p}$ and a $\Xi'_p(t')$ is a noise term with zero mean and a variance of: $\langle \Xi'_p(t'_1), \Xi'_q(t'_2) \rangle = 2kk_B T \delta(t'_1 - t'_2)\delta(p - q)$. This leaves us with the following equation of motion:

$$\frac{dx'}{dt'} = -\frac{a'}{2} \sin(x') - \sum_p s'_p X'_p \cos(x') + \xi'(t') \tag{2.20}$$

$$\frac{dX'_p}{dt'} = -\gamma_r K'_p X'_p - \gamma_r s'_p \sin(x') + \Xi'_p(t') \tag{2.21}$$

Chapter 3

Numerical method

To determine certain characteristics of the motion that takes place inside the system, the equations of motion are solved using numerical methods. Several different methods are considered, as the system might be too complex for some of the simpler methods. The considered methods are the Euler forward method, the Metropolis Monte Carlo method and the Gillespie algorithm. In order to get a better understanding of these methods the situation of a single tracer particle will again be analyzed first. Then, the pros and cons of each method are considered and the method which appears to be most suitable for modeling the motion of a tracer polymer is chosen.

3.1 Euler forward method

The Euler forward method uses the forward difference approximation of the derivative to solve a differential equation $\frac{dx}{dt} = f(x,t)$:

$$\frac{dx}{dt} \approx \frac{x(t+\Delta t) - x(t)}{\Delta t} \approx f(x,t) \Leftrightarrow x(t+\Delta t) = x(t) + f(x,t)\Delta t \tag{3.1}$$

This rather simple approximation, however, relies on the assumption that the function $f(x,t)$ remains more or less constant from t to $t + \Delta t$. Unfortunately, this assumption does not hold for the found equation of motion, as the noise term does not behave well when trying to make such an assumption. In particular, the function contains a very high number of discontinuities. In order to prevent the discontinuities from being an issue, a noise term W with mean 0 and a variance of σ is substituted by $\frac{\sigma}{\Delta t}N(0,1)$, as proposed by Volpe et al. [4].

While the Euler forward method is a fairly simple numerical method to implement, it has its drawbacks. The main problem is that when the time step used is too large, the algorithm becomes unstable. When this happens, the solution will oscillate very rapidly, which is incorrect. This is especially an issue due to the fact that it is quite a slow algorithm. For the calculations to be accurate, the time step must be small for the approximations to be accurate. When considering the fact that the simulation has to be repeated multiple times for the mean squared displacement to be accurate, the poor speed of the algorithm can be quite a hindrance. While it is possible to run very long simulations, it is far from desirable, and therefore an alternative must be found.

3.2 Metropolis Monte Carlo method

For the Metropolis Monte Carlo method, a random change in the configuration is proposed and is either accepted or rejected based on the change in total energy that is caused by the proposed change. If the total energy decreases, the proposed movement is accepted, as nature always strives to minimize the energy of any system. If the energy were to increase due to the proposed movement, the value of $e^{-\frac{\Delta E}{k_B T}}$ is calculated and is compared to a random variable r generated uniformly between 0 and 1. If r is bigger, the movement is rejected and if r is smaller the proposed movement is accepted. As noted previously when looking at the Euler forward method, the thermal energy is the factor that causes the random nature of the system. In this numerical method the randomness is implemented in the exponential used to determine whether or not a movement is accepted. If the temperature of the system is very high, the exponential will be close to 1 regardless of the proposed change in energy and the effect of the potentials in the system is lost. However, if the temperature of the system is very low the exponential will become very small as well and, as a result, the only proposed movements that will be accepted are ones that lower the energy and the system would find a local energy minimum and stay the same place indefinitely

Unfortunately, the Metropolis algorithm is not a very useful algorithm when trying to solve this particular problem. First of all, the algorithm does not consider the time it takes for a movement to take place, so it cannot be used to properly find the mean squared displacement of the tracer particle. Another issue that arises when trying to implement the algorithm is that the algorithm is mostly meant for finding an equilibrium state of the system. This is done by slowly decreasing the temperature of the system, which causes an energy minimum to be found. This is not an option when looking at the polymer in the gel, as that would not properly portray the movement in the system. Finally, due to the fact that the potential consists of mostly sines and cosines, the movement of the particle should consist of a lot of jumps between the different minimums. As a result, the temperature must be sufficiently high so that the particle only needs a few uphill movements with a high chance of getting accepted to escape a minimum. This, however, effectively weakens the effect of the potential on the particle, as mentioned earlier, which will again make the simulation less realistic.

3.3 Gillespie algorithm

A more suitable numerical method for this problem is the Gillespie algorithm. While the Monte Carlo method generates a random step and randomly accepts this based on the change in energy, the Gillespie method generates a number of predetermined steps and accepts one of them based on the change in energy. In particular, for every coordinate a step of a fixed length is taken in both the positive and negative direction. For each of these steps the rate of occurrence, κ_i, is calculated, which is essentially the speed of the particle during the stepping move. We then calculate $\kappa' = \sum_i \kappa_i$ and a random variable r uniformly distributed between 0 and 1 is generated. Finally the value j that corresponds to $\sum_{i=1}^{j} \frac{\kappa_i}{\kappa'} \leq r \leq \sum_{i=1}^{j+1} \frac{\kappa_i}{\kappa'}$ is found, the corresponding movement is executed and the algorithm is repeated.

As a simple illustration, consider a solution containing a large number of a certain molecule. If this molecule can be used in the chemical reactions A and B, a single Gillespie step calculate the probability of reaction A via $P(A) = \frac{\kappa_A}{\kappa_A+\kappa_B}$, with κ_A and κ_B the reaction rate of reaction A and B respectively. The algorithm then randomly picks a reaction according to the calculated probabilities. The algorithm then changes the solution as described by the found reaction and the whole process begins anew.

In order to find the appropriate value for κ_i, the equations of motion have to be analyzed. Before this is done, however, a choice for the different predetermined steps has to be made. For convenience, both the tracer particle and the Fourier modes of the gel will have an equal step size. In this thesis, two different step sizes will be considered, as different step sizes can have drastically different results. First a situation where the steps are the size of $\Delta x' = \frac{2\pi}{G}$ with $G \in \mathbb{N}$, and second a situation where the step sizes are equal to an entire period, so $\Delta x' = 2\pi$. When trying to calculate the value for κ_i these two different steps behave quite differently and will therefore be calculated separately.

First the values of κ_i for the smaller step size will be calculated. Before this can be done, however, a few assumptions have to be made about a particular movement. First of all, the randomness that occurs in the Gillespie algorithm is caused by the choice of the movement that will be occurring, rather than some sort of noise term in the equation. As such, the noise term will be ignored throughout the calculation of κ_i. Another important assumption is the assumption that during a single step of the algorithm, the particles that are not chosen to move around will remain stationary. This turns a group of coupled differential equations into a single differential equation, which makes finding a rate much more manageable. The rate for a certain movement is defined by the equation $\kappa_i = \frac{1}{t_e - t_0}$. Where t_0 is the starting time of the movement and t_e is the final time. Typically, t_0 is taken to be equal to 0, which leaves $\kappa_i = \frac{1}{t_e}$.

With these assumptions, the actual rates will be calculated. First, we will calculate the rate for the normal modes. Using the luxury that one of the coordinates is constant and the luxury that the noise is ignored, we can attempt to find a solution for the equations of motion to find a value for κ_i. For convenience we take $-\gamma_r K'_p = c_1$ and $-\gamma_r s'_p \sin(x') = c_2$:

$$\frac{dX'_p}{dt} \approx c_1 X'_p + c_2 \Leftrightarrow X'_p(t) = c_3 e^{c_1 t} + \frac{c_2}{c_1} \tag{3.2}$$

Substituting the initial condition $X_p(0) = X_p(t_0)$ yields the following t_e:

$$t_e = \frac{1}{c_1} \ln \left(\frac{X_p(t_e) - \frac{c_1}{c_2}}{X_p(t_0) + \frac{c_1}{c_2}} \right) \tag{3.3}$$

Finding κ_i for the tracer particle is quite a bit more challenging, due to the sine and cosine that in this case are not constant. To simplify the equation, the noise term is ignored. To deal with the $\sin(x')$ and $\cos(x')$, we recall that those were initially an x' and x'^2 term, so for small values of x' the Taylor series can again be used to make the equation more manageable. For convenience we take $-\frac{a'}{2} = c_1$ and $-\sum_p s'_p X'_p = c_2$

$$\frac{dx'}{dt} \approx c_1 x' + c_2 x'^2 \Leftrightarrow x'(t) = -\frac{c_1 e^{c_3 + c_1 t}}{c_2 e^{c_3 + c_1 t} - 1} \tag{3.4}$$

Substituting the initial condition $x'(0) = x'_0$ gives:

$$\begin{aligned} x'_0 = -\frac{c_1 e^{c_3}}{c_2 e^{c_3} - 1} &\Leftrightarrow e^{c_3}(c_2 x'_0 + c_1) = x'_0 \\ &\Leftrightarrow c_3 = \ln\left(\frac{x'_0}{c_2 x'_0 + c_1}\right) \end{aligned}$$

This expression yields the following t_e:

$$\begin{aligned} x'_e = -\frac{c_1 e^{c_3 + c_1 t_e}}{c_2 e^{c_3 + c_1 t_e} - 1} &\Leftrightarrow e^{c_3 + c_1 t_e}(c_2 x'_e + c_1) = x'_e \\ &\Leftrightarrow c_3 + c_1 t_e = \ln\left(\frac{x'_e}{c_2 x'_e + c_1}\right) \\ &\Leftrightarrow t_e = \frac{\ln\left(\frac{x'_e}{c_2 x'_e + c_1}\right) - c_3}{c_1} \end{aligned}$$

Next, the values for κ_i are calculated for the step size $\Delta x' = 2\pi$. For this, it is important to note that this situation no longer consists of a particle that goes up or down the slope of a harmonic potential. Instead, the type of movement that is considered is more comparable to that of a particle in a harmonic potential that goes from the equilibrium position to a higher energy level and then goes back down the slope back to it's equilibrium state. Or, in simpler terms, it roughly describes the motion of a simple oscillating spring. When calculating the time it takes for the spring to complete this motion, the relaxation time τ of the spring is used. This relaxation time is defined as $\tau = \frac{k}{\gamma}$, where k is equal to the spring constant and γ is the drag coefficient. When trying to apply this method to the problem of the diffusing polymer in the gel, the equations of motion are used, as they are derived from potentials that are harmonic in nature. This comes with the added benefit that the drag coefficients of those equations have already been incorporated into the constants. For the gel potentials, we find that:

$$\frac{dX'_p}{dt'} = -\gamma_r K'_p X'_p - \gamma_r s'_p \sin(x') + \Xi'_p(t') \approx (-\gamma_r K'_p - \gamma_r s'_p x')X'_p = -kX'_p \tag{3.5}$$

So for the Fourier modes, the relaxation time is equal to $(\gamma_r(K'_p + s'_p x'))$, which leads to the following value for κ_i:

$$\kappa_i = \frac{1}{2\tau} = \frac{1}{2\gamma_r(K'_p + s'_p x')} \tag{3.6}$$

Where the value for τ is multiplied by two as the motion performed is that of a particle going from equilibrium to an excited state, and then back to the equilibrium. For the tracer particle, we find that:

$$\frac{dx'}{dt'} = -\frac{a'}{2}\sin(x') - \sum_p s'_p X'_p cos(x') + \xi'(t') \approx (-\frac{a'}{2} - \sum_p s'_p X'_p)x' = -kx' \tag{3.7}$$

So for the tracer particle, the relaxation time is equal to $\frac{a'}{2} + \sum_p s'_p X'_p$, which leads to the following value for κ_i:

$$\kappa_i = \frac{1}{2\tau} = \frac{1}{2(\frac{a'}{2} + \sum_p s'_p X'_p)} \tag{3.8}$$

3.4 Extension of the model to a tracer polymer

Now that the situation of the single particle has been analyzed, the extension to a system with a tracer polymer instead of a single tracer bead can be made. This extension will only be used for the Gillespie algorithm, as it is the fastest algorithm out of the ones considered earlier. This property is important, as the interaction of the between the different beads in the polymer chain adds a significant amount of calculation time to every step of a numerical algorithm. When looking at the potentials, the values for the coordinates of the tracer particle is simply replaced by its center of mass, and the force of the tracer working on the gel modes is multiplied by the length of the polymer L. The only parts of the polymer that are able to move somewhat independently of the other beads are the beads on both ends of the polymer, so only the values of κ_i for those two beads are calculated. When considering the implementation of the bonding between two polymer beads, it is wise to analyze it separately for the two different step sizes. For the big step size, we propose a very rigid spring between the different beads that are connected, as the system would get too complicated if the beads in the middle of the chain are allowed to move as well. These rigid springs make it so that whenever one of the tail ends of the polymer gets to move, the rest will be dragged along with it. For two beads that are not connected, we propose a model of both a repulsive and attractive force. For the repulsive force, the simple condition that a bead cannot be in the same square as another bead suffices, as the size of the gel particles is in the same order of magnitude as the mesh grid. To simulate an attractive force, a force with the same magnitude as the gel mesh itself is added to the value of κ_i whenever the suggested movement goes away from the neighboring bead, so:

$$\kappa_i = \frac{1}{2(a' + \sum_p s'_p X'_p)} \tag{3.9}$$

whenever the suggested movement goes against the attractive force of the polymer bead.

When looking at the model for the smaller step size, there is a bit more freedom in terms of how the bonds between the polymer can be modeled. The attractive force is removed, as it might prove difficult to properly define the magnitude of such a force, as the simplicity of having two neighboring particles be at a set distance away from each other is no longer there. The repulsion between two particles is still considered to work in a similar fashion as the repulsion used for the big step. Whenever one of the beads at the end of the polymer comes within a certain number of steps to a different grid point that is already occupied by another tracer particle, a step towards that particle is considered to be impossible. The springs between two connected particles is still considered to be quite rigid, where the particles all get pulled along to the next well whenever one of the leading beads gets to a new well. While these assumptions are quite crude, they do prevent the algorithm from becoming too complex.

Chapter 4

Results

First, the system with a single tracer particle is simulated using all three numerical methods. For these simulations all parameters used are kept constant throughout all three simulations:

$$a = 5 \qquad k_B T = 1 \qquad k = 1 \qquad N = 5 \qquad k_0 = 1 \qquad s_0 = 1 \qquad \gamma_r = 1$$

All simualtions are averaged over 50 runs.

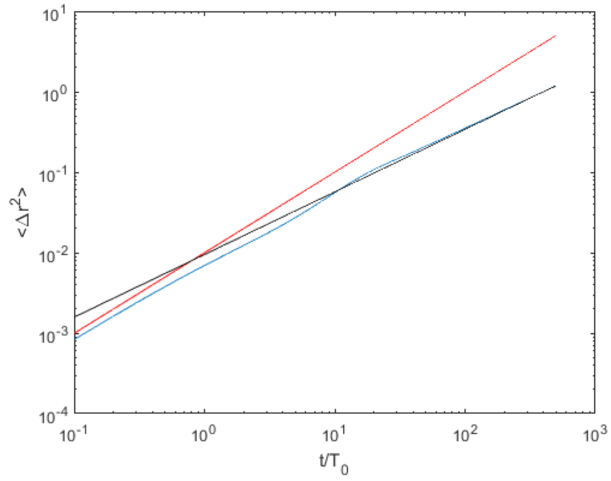


Figure 4.1: Plot of the average MSD of 50 single tracer particles, simulated using the Euler forward method. The blue line represents the found average MSD, the red line is a reference line with a slope of 1 and the black line is a linear fit of the blue line with a slope of 0.7924

Note that in Figure 4.1 the fitted line seems to have a lower slope than the plot of the average MSD, at least at first. However, due to the fact that the plot is made with a log scale, there are a lot more data points further along the timescale, so the fit is indeed accurate. The motion of the tracer is subdiffusive, as the slope of the fit is smaller than 1.

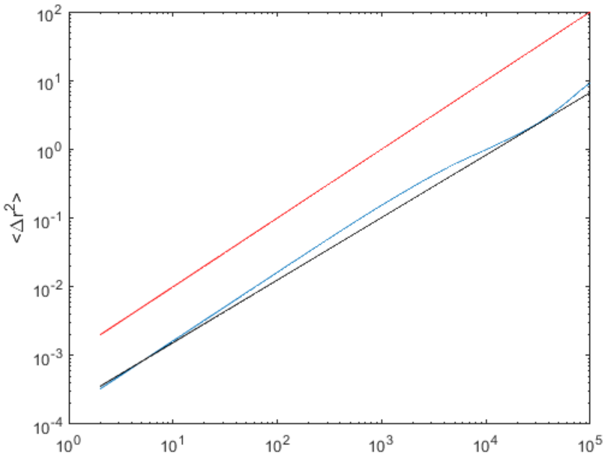


Figure 4.2: Plot of the average MSD of 50 single tracer particles, simulated using the Metropolis Monte Carlo method. The blue line represents the found average MSD, the red line is a reference line with a slope of 1 and the black line is a linear fit of the blue line with a slope of 0.9093. Note that the x-axis is not the timescale, as the Monte Carlo method does not make one. The x-axis represents the number og itterations of the algorithm instead.

Again, the slope of the linear fit is smaller than 1, so the motion of the tracer particle is subdiffusive.

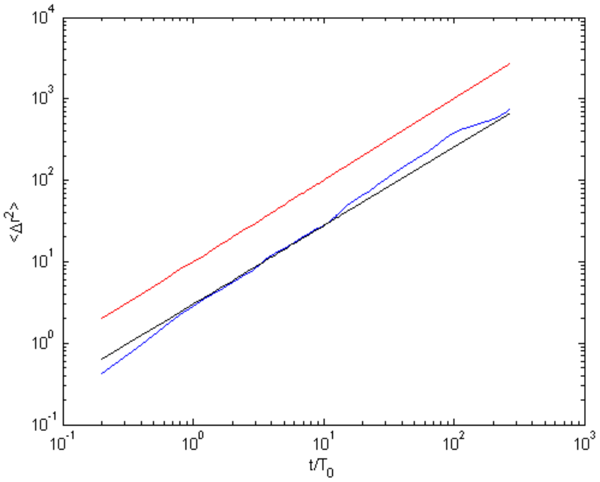


Figure 4.3: Plot of the average MSD of 50 single tracer particles, simulated using the Gillespie algorithm. The blue line represents the found average MSD, the red line is a reference line with a slope of 1 and the black line is a linear fit of the blue line with a slope of 0.9633

In this case the Gillespie algorithm with the smaller steps is used. The motion is still subdiffusive, but the slope is much closer to 1 for this method than for the other methods.

Next, the system with a tracer polymer of length 13 has been analyzed using the Gillespie algorithm. First with the bigger step size and then with the smaller step size. The code used for these calculations can be found in Appendix A and Appendix B, respectively. For these simulations, The following parameters are kept constant unless stated otherwise, as changing them will not tell us much about the system:

$$a = 5 \qquad k_BT = 1 \qquad k = 1 \qquad N = 5$$

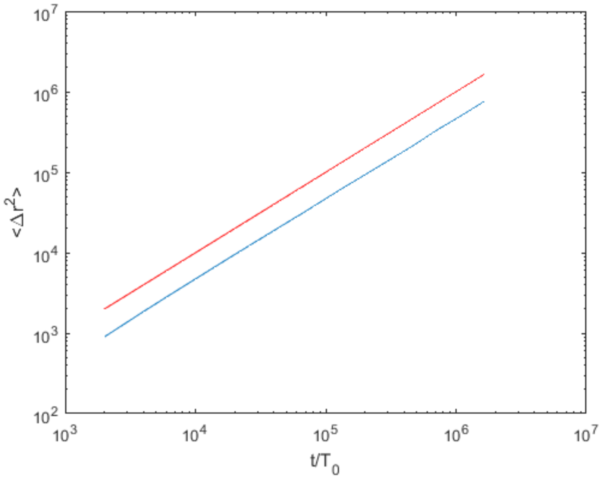


Figure 4.4: Plot of the average MSD of 5 tracer polymers with length 13 and $\gamma_r = 1, k_0 = 1, s_0 = 1$, simulated using the Gillespie algorithm using the bigger step sizes. The blue line represents the found average MSD, the red line is a reference line with a slope of 1

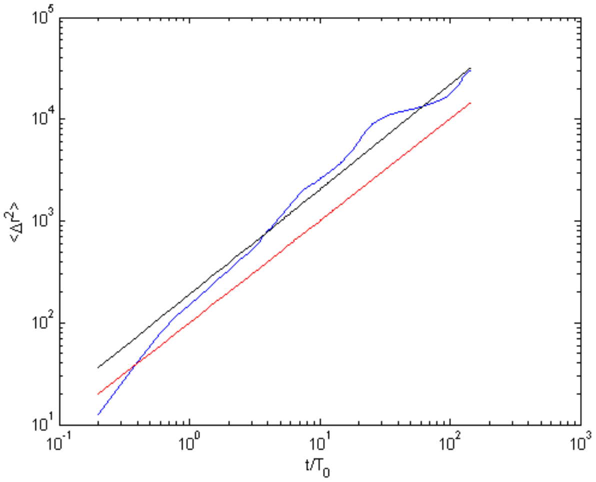


Figure 4.5: Plot of the average MSD of 50 tracer polymers with length 13 and $\gamma_r = 1, k_0 = 1, s_0 = 1$, simulated using the Gillespie algorithm using the smaller step sizes. The blue line represents the found average MSD, the red line is a reference line with a slope of 1 and the black line is a linear fit of the blue line

In Figure 4.4, we can see that the slope of the MSD is equal to 1, so regular diffusion takes place. In Figure 4.5, the linear fit of the MSD has a slope of $\alpha = 1.0290 \pm 0.017$. So the motion is superdiffusive. In order to find out more about why superdiffusion would take place, more simulations are done using the smaller step size. For these next simulations, a number of parameters are varied. First, we vary the strength of the springs between the gel particles.

Table 4.1: Found values of α for different values of k_0, where $\gamma_r = 1, s_0 = 1$

k_0	α
100	1.629 ± 0.023
10	1.397 ± 0.007
1	1.0290 ± 0.017
0.1	1.304 ± 0.006
0.01	1.627 ± 0.031

Then, we vary the strength of the coupling between the gel and the tracer.

Table 4.2: Found values of α for different values of s_0, where $\gamma_r = 1, k_0 = 1$

s_0	α
0.1	1.304 ± 0.006
1	1.0290 ± 0.017
10	1.397 ± 0.007

Then, we vary the drag of the system.

Table 4.3: Found values of α for different values of γ_r, where $s_0 = 1, k_0 = 1$

γ_r	α
0.1	1.652 ± 0.004
1	1.0290 ± 0.017
10	1.478 ± 0.01

To make sure that a low amount of data points is not the issue, a longer simulation is done.

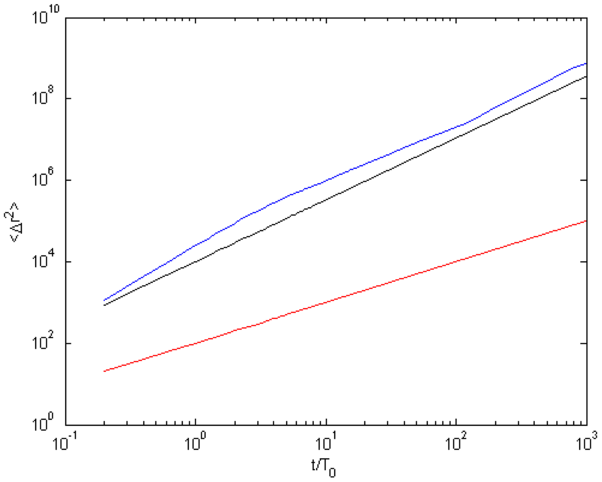
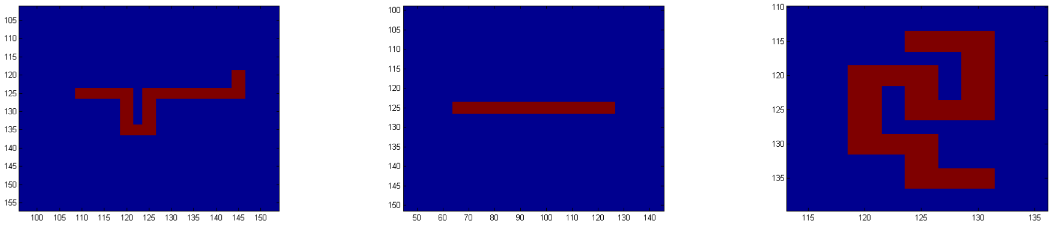


Figure 4.6: Plot of the average MSD of 50 tracer polymers with length 13 and $\gamma_r = 1, k_0 = 0.1, s_0 = 1$, in this case for 1000000 Gillespiesteps compared to the usual 100000. The blue line represents the found average MSD, the red line is a reference line with a slope of 1 and the black line is a fit of the blue line

Note that the slope of Figure 4.6 is smoother than that of other simulations using the same step size, so taking a longer measurement does indeed seem to help improve the accuracy of the measurement. Next, different starting configurations are tested in order to find out if they have a significant impact on the diffusion of the polymer.



(a)

(b)

(c)

Figure 4.7: Schemetic representations of the three different initial polymer configurations tested with the parameters $\gamma_r = 1, k_0 = 1, s_0 = 1$. (a) is the random initial condition used for all other simulations, (b) is a straight polymer and (c) is a very coiled up polymer.

These simulations resulted in the following values for α:

Table 4.4: Found values of α for the three different initial configurations, where $\gamma_r = 1, s_0 = 1, k_0 = 1$

configuration	α
(a)	1.0290 ± 0.017
(b)	1.096 ± 1.071
(c)	1.285 ± 0.005

Finally, the interaction with the environment is taken out in order to find out if the model is working as it should.

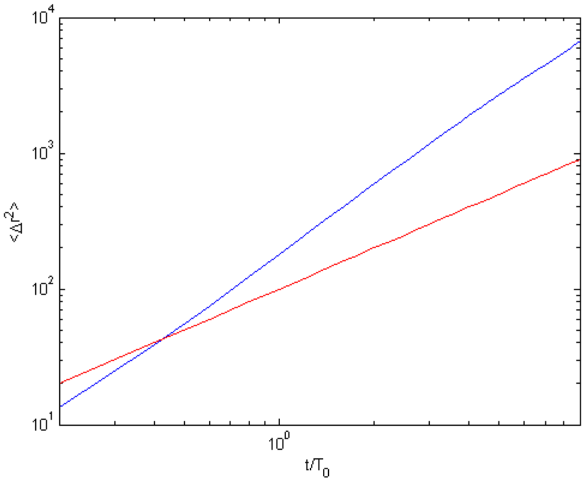


Figure 4.8: Plot of the average MSD of 50 tracer polymers with length 13 and $\gamma_r = 1, k_0 = 1, s_0 = 1$. In this case the gel is considered to be stationary. The blue line represents the found average MSD, the red line is a reference line with a slope of 1.

The MSD has a slope of $\alpha = 1.648 \pm 0.01$. This value implies superdiffusion by quite a bit.

Chapter 5

Discussion

First of all, the measurements for the single tracer particle seem to all correspond to the values that are expected. It does however seem as though the result found using the Gillespie algorithm is quite different from the results found using the other methods, as the slope is much closer to 1. This seems to imply that the coupling between the gel and the particle is not quite as strong for the Gillespie algorithm compared to the Euler forward method and the Metropolis Monte Carlo method, in spite of the fact that the parameter used to quantify this coupling is the same for all these simulations. The most likely reason for this difference is the step sizes used for Gillespie algorithm. By claiming that the movement takes place on a large grid, the tracer particle might get close to the edge of a well in only a few Gillespie steps. As a result, the gel might not have the opportunity to respond to this movement and as a result the effect of the gel on the tracer is lost. While we can still tell from the slope of the fit that there is some interaction left, it seems like some of it is still lost.

When looking at Figure 4.3 and comparing it to 4.1 and 4.2, It appears that it is not smooth as the other measurements. This can also be blamed on the random choice of steps during the Gillespie algorithm. Whenever a step for a gel particle is chosen, it affects the measurement more significantly than for the other two methods, as the step size for Gillespie tends to be bigger than the steps for the other two methods. Furthermore, the other two methods alternate between moving the tracer particle and moving the Fourier modes of the gel, so the randomness involved with modeling the interaction between the gel and the tracer particle gets evened out faster compared to the Gillespie algorithm. While this can of course be solved by taking the average over more measurements, it is worth pointing out, as it is important for the measurements to be accurate.

For the simulations with the Gillespie algorithm with the bigger steps, the motion appears to simply be diffusive. This implies that the environment does not affect the polymer. This is due to the step size of the algorithm. Normally, the gel beads vibrate a tiny bit, meaning that at the border between two unit cells on the grid, the gel beads behave like a gate. Whenever they are close together, the gate is closed and a tracer bead has a very hard time getting through and whenever they are far apart, the tracer can pass right through. The vibration of the gel particles is heavily influenced by the position of the tracer particle. In the simulations however, the steps of the tracer and the gel are so big that this subtle coupling is lost and as a result the tracer polymer can freely diffuse.

When looking at the different initial configurations, it appears that configuration 4.7c has a higher value for α. This seems to imply that the initial configuration does indeed matter. This is quite surprising, as the polymer should acquire a random shape relatively early on in the simulation. One possible explanation for this unexpected behavior is that the simulations do not run for long enough and as a result the tracer polymer does not completely lose the shape given by the initial condition. When looking at Figure 4.5, it appears that the motion, at least for this time frame, goes through different regimes where the slope is slightly higher or lower than the fitted average. This means that if the polymer of a simulation start off slower because of its initial condition, the simulation might end right before a slower regime. As a result, the fitted slope might be a bit higher.

When looking at the result for the tracer polymer without interaction from the environment, it becomes quite clear that something has gone wrong in the simulation. We expect the simulation to result in regular diffusion, but the actual result seems to be quite superdiffusive. This implies that something unrelated to the implementation of the gel network is causing problems. Unfortunately, this makes the simulations which very just one parameter as good as useless when it comes to describing the gel network, as it generates data for an incorrect system.

The most likely suspect of ruining the system is the implementation of the dynamics between the different parts of the tracer polymer. In the model for the interaction, the springs between the different beads that make up the tracer polymer are stiff. This choice was made in order to make the simulation simpler. If all the beads in the polymer have the freedom to move without moving the other beads, the number of κ_i's would increase by 4 for each bead in the polymer. This would increase the amount of computation time by a significant amount. By making these rough assumptions, however, the tracer polymer seems to slow itself down when it tries to go back to a spot it was in earlier. This is mostly due to the assumption that whenever on of the beads at the end of the polymer chain crosses a over to new well in the mesh, it will pull all other particles over to the well their neighbor was just in. This causes the second bead in the chain to prevent the leading bead from going back to its previous position, as two particles cannot occupy the same well at the same time. The only way for the leading bead to get back is if the bead on the other end of the chain jumps a to a new well too. This dynamic of blocking the moving beads makes it so that the tracer polymer has a tendency to diffuse away from the place it was just in, causing superdiffusion. The fact that the value for α is so much lower for Figure 4.5 does however seem to suggest that the gel network does something to slow down the diffusion of the polymer, but that does not necessarily mean that the tracer polymer shows subdiffusion when the model is improved, as it might just be counteracting the inaccuracies made by the poor implementation of the polymer.

5.1 Recommendations

When looking at the simulations, a few possible improvements come to mind. First of all, the modeling of the attractive and repulsive forces between different beads in the tracer polymer needs to be improved. An improvement that would not be difficult to implement would be to model proper springs at the two ends of the tracer polymer. By simply allowing the spring at the end to vary in length, we can model it such that the attraction used in the current model will apply whenever the spring is stretched as far as we allow it to and the repulsion used in the current model will apply whenever the spring is compressed as far as we allow it to. When making such an improvement, the tracer particles that are not on the ends of the polymer should be able to move along the smaller grid as well, because this way the springs at the ends of the polymer will not drastically change in size due to the other tracer beads suddenly making a big jump. With this new model, the tracer bead at the end of a polymer will no longer be forced to keep moving in the direction it just moved in whenever it crosses a well, as the spring between the two tracer particles will be able to contract a little before the repulsion becomes a factor. This should hopefully remove the superdiffusion of the system.

Another possible improvement of the system would be to give the tracer beads in the middle of the polymer the ability to move independently as well. This can be done by making removing the stiff springs in the middle of the polymer and replacing them by proper springs. This way we can allow the middle tracer particles to move by slightly increasing or decreasing the length of the springs connecting those particles to each other. This improvement, however, would increase the complexity of the system by quite a bit, as it would mean that for every bead in the polymer that are not on the ends of the polymer, 4 additional values for κ_i would have to be calculated. This would increase the computation time of the algorithm by quite a bit. So while letting the center beads move freely might make the model more realistic, it would also make the algorithm a lot slower.

Aside from these possible improvements it also seems that various parameters that determine the size of the algorithm can cause some issues. As found earlier by looking at the different configurations, it seems that the amount of iterations used for the algorithm can result in some problems. Specifically, the time it takes for the tracer polymer lose all its memory of the initial position appears to be so long that it has an impact on the found MSD. Another possible issue can be that the number of simulations done to find the average MSD might be too low as well. As mentioned earlier,Figure 4.3 appears to not be as smooth as Figure 4.1 and Figure 4.2. This is possibly due to the fact that because of the random way in which the Gillespie algorithm decides on the order in which each moving part of the system moves, two simulations made with identical parameters tend to vary quite a bit. This variation can be ironed out by simply taking the average over more samples. Finally, decreasing the size of the steps might help to further improve the accuracy of the system. As seen in Figure 4.4, taking steps that are very big results in a lack of coupling between the tracer polymer and the gel particles. This might still be the case for the smaller step sizes, so it might be advisable to take steps that are even smaller.

Chapter 6

Conclusion

The Gillespie algorithm with small step sizes seems to be the most useful numerical method when it comes to simulating the system. From the plots of the MSD we can conclude that the motion of a tracer polymer inside of a gel network is superdiffusive. This contradicts the expectation that the motion should be subdiffusive. This is most likely due to incorrect implementation of the model, specifically the interaction between the different tracer beads that make up the tracer polymer. This suspicion is supported by the fact that the plot of the MSD for the same simulation, but with a stationary gel network, shows super diffusion as well. The slope of the fit of the MSD is much higher for the simulation with the stationary gel network compared to the simulation with the moving gel network, which seems to imply that the gel network does indeed work against the diffusion of the tracer polymer. Due to the fact that the implementation of the model appears to be wrong, however, we cannot conclude that the gel network does indeed cause subdifusion if the model were implemented correctly.

Chapter 7

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7.1 References

[1] M. Doi, Soft Matter Physics, OUP Oxford, 2014, page 2,28,29,97.
[2] Y.Wong, M.L. Gradel, D.R. Reichmann, Eric R. Weeks, M.T. Valentine, A.R. Bausch, D.A. Weitz, Anomalous Diffusion Probes Microstructure Dynamics of Entangled F-Actin Networks, Physical Review Letters volume 92, number 17, 2004, page 2.
[3] A. Godec, M. Bauer, R. Metzler, Collective dynamics effect transient subdiffusion of inert tracers in flexible gel networks, New Journal of Physics 16, 2014, page 5.
[4] Giorgio Volpe, Giovanni Volpe, Simulation of a Brownian particle in an optical trap, American Journal of Physics, 81, 224 (2013), page 225