Brownian Dynamics Simulation of Colloidal Gels as Matrix for Controlled Release Application

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**Abstract.** The form of crystallization colloidal gels is important as matrix for controlled release application. In this work, we use the Brownian Dynamics simulation to study the formation of gels by varying the inverse Debye length. We choose a fixed volume fraction, \(\phi = 0.1\) and a fixed quenched temperature at room temperature, while the inverse Debye length, \(\kappa\), is varied. To ensures that the simulations cover the fluid-phase region down to the unstable phase region above the critical coagulation concentration, the inverse Debye length is varied between \(\kappa = 120\sigma^{-1}\) to \(250\sigma^{-1}\). It shows that at the inverse Debye length \(\kappa = 250\sigma^{-1}\) the gel forms by colloidal particles that can support the active ingredient by forming long range network.

**Keywords:** Computer Simulation, Brownian Dynamic, Colloidal, Gels, Inverse Debye Length

1. Introduction

One of the application of controlled release system is on the drug delivery. The development of this controlled drug delivery systems has greatly helped in improving patient compliance and drug effectiveness by reducing in the frequency of dosage administration and also give less side effects. The major goal of controlled release systems is to supply therapeutic levels of a drug agent at a physical site in the body for a prolonged period [1]. Thus the design and development of controlled release systems has become a key issue in current research. The controlled release system consists of the matrix and the active agent, the rate of drug release can be influenced by the drug concentration in the matrix. The potential of dependal-M loaded hydrogel matrix has been used in the rehydration therapy and the hydrogel with lesser cross linker amount has a higher drug loading capacity [2]. It has been reported that polymer nanoparticles are the responsive materials for drug delivery applications [3,4].

In this work, we study the aggregation of colloidal particles in an ionic solution by using Brownian Dynamic simulation. According to Dickinson, the Brownian Dynamics is a good approach in assessing the role of colloidal interaction during development of a particle gel network [5]. The colloidal gel is a
special type of aggregation process when a space-filling network or a percolating structure is formed that can be stable for a considerable time. In the gelation process, the colloidal particles form aggregates which grow rapidly in size until they fill the available space. Further restructuring is then only possible by connecting these aggregates and it results in a structure spanning the whole system, known as a gel. The formation of gels structures promotes stabilization of the components as it prevents a phase separation over the life of the products application. In principle, the controlled release of drug can be obtained by varying system design parameters. Therefore, we simplify the model by describing the colloidal particles as spherical. We are going to report the effect of inverse Debye length in the colloidal particle gels that possible to use as a matrix of controlled release application. We use the DLVO potential to describe the interaction between the colloidal particles in ionic solution. It is shown that the percolating network of long-lived inter particle bonds between identical particles is shown at inverse Debye length \( \kappa = 250\sigma^{-1} \) and \( \phi = 0.1 \).

2. Simulation Procedure
In this work, we use Brownian Dynamic simulation. The system is simulated in a three dimensional box of volume \( V \). The model consists of \( N \) spherical particles and the volume fraction, \( \phi \), of the system is,

\[
\phi = \frac{\pi N \sigma^3}{6V}
\]

where \( \sigma \) is the diameter of the colloidal particles. The periodic boundary conditions are applied in all directions to simulate a macroscopic system. In our simulation, we set the diameter of the particles, \( \sigma \), the viscosity, \( \eta \), and the energy, \( k_B T \), are set to unity.

\[
k_B T = 1 \\
\eta = 1 \\
\sigma = 1
\]

Time is in units of the Brownian relaxation time, \( \tau_R \). This is defined as the time for a particle to diffuse a distance on the order of one diameter in the absence of other forces and is given as,

\[
\tau_R = \frac{\eta \sigma^3}{k_B T}
\]

For a particle of one micron in diameter suspended in water (\( \eta = 0.001 \text{ Ns/m}^2 \)) at room temperature, the relaxation time is in the order of 0.24 s. The trajectories of the interacting particles were calculated using the position Langevin equation in finite time steps

\[
r_i(t + \Delta t) = r_i(t) + \frac{\Delta t}{m \xi} F^C_i(t) + \Delta r^B_i
\]

\( \Delta r^B_i \) is the displacement resulting from the Brownian force and is also taken to have a mean average of zero. It has the mean square value of \( 6k_B T \Delta t / 3\pi \eta \sigma \), where \( \Delta t \) is the time step used in the simulation. We set the time step for the simulation at \( 4.71 \times 10^{-6} \tau_R \). This corresponds to the mean square displacement of \( 10^{-6} \sigma^2 \).

The conservative force is calculated from the DLVO (Derjaguin and Landau, Verwey and Overbeek) interaction. The force exerted by particle \( j \) on particle \( i \) at a distance of \( r_{ij} \) is given by,

\[
F_i(r_{ij}) = -\frac{\partial U_{DLVO}(r_{ij})}{\partial r_i}
\]

\( U_{DLVO}(r_{ij}) = U_{el}(r_{ij}) + U_{vdw}(r_{ij}) \)
\[
U_{vdw}(r_{ij}) = -\frac{A_{H}}{12} \left[ \frac{\sigma^2}{r_{ij}^2 - \sigma^2} + \frac{\sigma^2}{r_{ij}^2} + 2\ln \left( \frac{r_{ij}^2 - \sigma^2}{\sigma^2} \right) \right] \tag{6}
\]

\[
U_{el}(r_{ij}) = \pi \varepsilon_{0} \varepsilon_{0} V_{0}^2 \sigma \ln \left( 1 + e^{-\kappa [r_{ij} - \sigma]} \right) \tag{7}
\]

In this study, we use the parameters suitable for colloidal particles (\(\sigma = 1 \text{ \mu m}, A_{H} = 0.1 \text{ eV}, \psi_{0} = 17.7 \text{ mV}\)) immersed in water (\(\eta = 8.854 \times 10^{-4} \text{ Pa.s}\)) at room temperature in the presence of a monovalent salt. The equation for the electrostatic repulsion is valid for large value of the inverse Debye length, \(\kappa\), we choose \(\kappa\) for 250. The surface potential is set to values that give sufficiently high maximum barrier as we are mainly interested in the study weak aggregation.

We use the step-strain method by applying a sudden shear displacement and measure the stress relaxation as the gel network is trying to release the stress. In a very small deformation, a colloidal suspension has a stress response which increases linearly with the strain amplitude. Under this condition, the changes of the stress, \(\sigma_{xy}\), as a function of time can be written as [6]

\[
\sigma_{xy}(t') = \int_{-\infty}^{t'} G(t' - t) \dot{\gamma}(t) dt \tag{8}
\]

\(G(t)\) is called the relaxation modulus of the suspension and \(\dot{\gamma}\) is the shear rate. We measure the mechanical strength by imposing a sudden strain of \(\dot{\gamma}\) at the first step between \(t' = -\Delta t\) and \(t' = 0\). The shear rate is then equal to \(\dot{\gamma}/\Delta t\) and the shear stress becomes,

\[
\sigma_{xy}(t') = \int_{t_{0} - \Delta t}^{t_{0}} G(t' - t) \left( \frac{\dot{\gamma}}{\Delta t} \right) dt \tag{9}
\]

We modify the equation by calculating the average value of the relaxation modulus between \(t_{0} - \Delta t\) and \(t_{0},\)

\[
\int_{t_{0} - \Delta t}^{t_{0}} G(t) dt = \Delta t G(t_{0} - \Delta t + c\Delta t)
\]

\[
= \Delta t G(t_{0} - (1 - c)\Delta t) \tag{10}
\]

where \(0 \leq c \leq 1\). It can then be written as,

\[
\sigma_{xy}(t') = \frac{\dot{\gamma}}{\Delta t} \Delta t G(t' - (t_{0} - (1 - c)\Delta t) )
\]

\[
\approx \gamma G(t') \tag{11}
\]

for \(t_{0} = 0\) and \(t' \gg \Delta t\).

In the simulation, the relaxation modulus is the unknown quantity and we compute the stress tensor by through the virial equation,

\[
\sigma_{\alpha\beta} = \rho k_{B} T - \frac{1}{V} \sum_{j=1}^{N-1} \sum_{j=1}^{N} r_{ij} r_{\alpha j} \frac{dU_{ij}}{dr_{ij}} \tag{12}
\]
where $V$ is the volume of the simulation box and $U_{ij}$ is the interaction potential between $i$ and $j$ and $r_{\alpha ij}$ is the $\alpha$-component of the inter particle vector. In the limit of $t$ approaching zero, the relaxation modulus give the high frequency limit of the storage modulus, $G_\infty$. The storage modulus at infinite frequency can also be calculated using the equation proposed by Zwanzig and Mountain [7],

$$G_\infty = \rho k_B T + \frac{2\pi \rho^2}{15} \int_{0}^{\infty} \frac{d}{dr} \left( r^4 \frac{dU_{ij}}{dr} \right)$$  \hspace{1cm} (13)

In the long time limit, the modulus will decay and reach some equilibrium value. In a fluid system, the stress is expected to decay immediately to zero, i.e. relax completely, after a short period of time. A complete relaxation may not occur within the length of the simulation in a system which exhibits a solid-like response.

3. Results and discussion

In this work, the interaction between particles and its aggregation were calculated based on Derjaguin-Landau-Verwey-Overbeak (DLVO) theory [8,9]. The DLVO theory showed that the primary minimum of colloidal particles interaction potential was raised from the mutual van der Waals attraction where it is not accessible at low electrolyte concentrations because of a large energy barrier [10]. When the electrolyte concentration is raised above the critical coagulation concentration, the barrier height drops down to zero, leading to colloidal flocculation and precipitation. In this model, we simulate with a fixed volume fraction $\phi = 0.1$ and the inverse Debye length is varied between $\kappa = 120\sigma^{-1}$ to $250\sigma^{-1}$. This simulation model shows that the behavior of the system is very sensitive to the ionic concentration. The concentration of the ions in the solution determines the strength of the repulsive electrostatic interaction, which can be calculated using the DLVO equation. A weaker repulsion result in the van der Waals attraction becomes more dominant and the effective interaction becoming more attractive as shown in Figure 1.

We plot the configurational energy per particle as a function of time in Figure 2. It shows that for systems with $\kappa$ less than $220\sigma^{-1}$, the equilibrium states are reached almost immediately on the simulation timescale with no aggregates detected. The systems are essentially still in the fluid phase after the quenches. This is confirmed in Figure 3, which show the configurations in the late stages, taken at time $471.24\tau_\kappa$. In Fig. 3(a), the configuration for $\kappa = 200\sigma^{-1}$ is above the unstable region. The configuration demonstrates that the suspension stays dispersed throughout the simulation.

![Figure 1](image-url)  
**Figure 1.** The profile of the DLVO, the attractive perturbation potentials as a function inter particles distance at $\kappa = 250\sigma^{-1}$. 
At $\kappa = 220\sigma^{-1}$, the plot of the interaction potential as a function of time displays an inflection point at intermediate times. Beyond this point, the interaction potential decreases rapidly with time until it levels out at larger times. This suggests a dramatic departure towards the formation of a more compact structure in the system for $\kappa > 220\sigma^{-1}$. The interaction potential then shows a slow decrease until the end of the simulation and because equilibrium has not been reached.

![Figure 2](image)

**Figure 2.** The average configurational energy as a function of time at different $\kappa$.

We also show that the transition relates to the onset of crystallization in the gel structure. In Figure 3, we observe the changes in the resulting gel structures as $\kappa$ is varied. As we increase $\kappa$ to $220\sigma^{-1}$, we start to see the formation of a gel in which the suspension forms a percolating network that fills the entire simulation box. At $\kappa > 220\sigma^{-1}$, the particles with low number densities have the short-range, hard-sphere-like interaction and the system jammed to form disordered. When $\kappa$ is smaller the inter-particle interactions are featured with long-range repulsion, the particles can spontaneously assemble into disorder structure. The gel formed at lower $\kappa$ is seen to have larger voids surrounding it, which suggests a denser gel is formed in this system (Figure 3b).
Figure 3. The pictures of the resulting structures taken at times 471.24 \( \tau_R \) and \( \phi = 0.1 \) for \( \kappa = (a) 200\sigma^{-1}, (b) 220\sigma^{-1}, (c) 230\sigma^{-1} \) and (d) 250\sigma^{-1}.

4. Conclusion
We have found that at the inverse Debye length \( \kappa = 250\sigma^{-1} \) the particles form percolating gel compare with others inverse Debye length. It shows that the structural evolution of colloidal gels from the long-range to the short-range orders. The colloidal particles form interconnecting network that is suitable to support active ingredients in controlled release applications.

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