EVALUATION OF SELF-HEALING PERFORMANCE OF POLYACRYLAMIDE/POLYVINYL ALCOHOL HYDROGEL USING MOLECULAR DYNAMIC SIMULATION

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A project report submitted in partial fulfilment of the requirements for the award of Bachelor of Engineering (Honours) Chemical Engineering

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DECLARATION

I hereby declare that this project report is based on my original work except for citations and quotations which have been duly acknowledged. I also declare that it has not been previously and concurrently submitted for any other degree or award at UTAR or other institutions.

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APPROVAL FOR SUBMISSION

I certify that this project report entitled **"EVALUATION OF SELF-HEALING PERFORMANCE OF POLYACRYLAMIDE/POLYVINYL ALCOHOL HYDROGEL USING MOLECULAR DYNAMIC SIMULATION"** was prepared by **WONG MING ZHEN** has met the required standard for submission in partial fulfilment of the requirements for the award of Bachelor of Engineering (Honours) Chemical Engineering at Universiti Tunku Abdul Rahman.

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ABSTRACT

In this study, the self-healing property of polyacrylamide/polyvinyl alcohol (PAM/PVA) hydrogel was examined using the molecular dynamic simulation. The Material Studio software was utilised to study the effect of temperature and hydrogel water content on the self-healing capability of the hydrogel. In the simulation, the hydrogel models with different water content were created. To evaluate how temperature affects the hydrogel's self-healing capcity of the hydrogel, the hydrogel with 80% water content was run under different temperatures which are 273K, 298K, 323K, 348K and 398K. In order to study the effect of hydrogel water content on the self-healing property, the hydrogel water content were varied from 0%, 20%, 40%, 60% to 80%. The models with different hydrogel water content were run under room temperature which is 298K. All the models are examined in terms of diffusion coefficient which is determined using Mean Square Displacement (MSD) function, self-healing duration from the bilayer density and the molecular aggregation using Radial Distribution Function (RDF). After obtaining the diffusion coefficient of the hydrogel models with different water content at different temperatures, the activation energy and pre-exponential factor of the models are studied. The result shows that the self-healing performace of PAM/PVA hydrogel is enhaced by increasing the temperature and hydrogel water content.

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A	Pre-exponential factor, cm^2/s
D	Diffusion coefficient, $Å^2$ /ps
E_a	Activation energy, kJ/mole
T	Temperature, K
Å	angstrom
Cal	calories
J	joule
K	kelvin
MSD	Mean square displacement
PAM	Polyacrylamide
PVA	Polyvinyl alcohol
RDF	Radial distribution function

CHAPTER 1

INTRODUCTION

1.1 General Introduction

Hydrogels is a rubber-like gel. It is the polymeric matrix which has the ability to swell but not dissolve in water. Hydrogel also has the properties of high versatility, high tenability and self-healing ability. All these properties have led to numerous researches being conducted on hydrogel for its advancement and exploitation.

"Hydrogel" was introduced by Lee, Kwon and Park in 1894. The hydrogel is known as a colloidal gel made from inorganic salts. In 1960, the first hydrogel introduced in literature was the polyhydroxyethylmethacrylate (pHEMA) hydrogel which has the high affinity to water. The invention of hydrogel is aimed to be applied in permanent contact application with human tissues. Hydrogel is also known as the first substance which is developed and used in human body. There are three generation in development of hydrogel (Yahia, 2015).

In the first generation, the researches were carried out on the wide range of crosslinking for the synthesis of synthetic hydrogels. The studies also focused on the application of hydrogel in ophthalmic and drug delivery (Buwalda et al., 2014). The main goal of first generation hydrogel was to develop the material which has good mechanical properties, high swelling ability in water and also relatively simple rationale (Yahia, 2015).

In the 1970s, the second generation of hydrogel was introduced. In the second generation hydrogels development, the researches were shifted from the water-swollen macromolecular network and focused on the hydrogels which have the ability to counter the difference in environment factors such as pH, temperature and biomolecules concentration. This type of hydrogel is known as stimuli responsive hydrogel. This type of hydrogels can be applied for gel formation or drug release (Buwalda et al., 2014).

After the development of stimuli responsive hydrogel, the researches for third generation hydrogel were carried out in mid of 1990s. The main objective of third generation hydrogel researchers is to investigate and develop stereo

complexes hydrogel with other physical interaction rather than hydrophobic and ionic interaction (Yahia, 2015). The aim of developing hydrogel with different crosslinking is to enhance the characteristics of hydrogel such as the mechanical, thermal and degradation properties (Buwalda et al., 2014).

The incensement of knowledge in organic chemistry leads to the "smart hydrogel" with chemically cross-linked was being developed. This type of hydrogel has a wide spectrum of tuneable properties such as mechanical stability. With the tailorable properties, these hydrogels can be modified and applied in different fields (Yahia, 2015).

Hydrogel has been widely used in biomedical field. Hydrogel can be used in drug delivery where the drug is carried and transported to target tissue by the hydrogel. In tissue engineering, hydrogel can be used as the scaffold which protects the bioactive molecules during transportation, acts as the agent for vacant spaces filling and supports ideal tissue formation. The smart hydrogel which is sensitive to environmental factors can be used as the biosensor in human body.

1.2 Importance of the Study

In human body, the regeneration capacity is limited for most of our tissues. When humans experience serious damage caused by trauma or degenerative diseases, this may lead to irreversible disability or even death as we depend on tissues itself for self-regeneration. The organ transplantation is introduced to the patient who experiences serious tissue damages to recover the function of the damaged tissue. However, the organ transplantation is limited to organ recipient and donor. In order to overcome such situation, the new technology is introduced by tissue engineering to restore the damaged tissues using the scaffolds incorporated with the human's own tissue (Guan et al., 2017). Among most of the biomaterial, hydrogel is mostly used as the material for scaffolds. This is due to its high water absorbing and retaining properties, tuneable and injectable. The self-healing ability also helps to heal the minor injuries (Talebian et al., 2019).

According to Ferreira et al. (2018), even a large amount of literature on different hydrogel development is reported by the scientists, the number of hydrogel being used in clinical trials is still low. This is due to a large series of

studies that must be carried out before the hydrogels are applied. There are many efforts required to study hydrogel in different aspects such as the effect of microenvironment factors and the fabrication method of hydrogel. Other than that, several parameters of hydrogels are also required to be investigated such as degradation rates, inflammation and immunological response (Mantha et al., 2019).

This research is important to study the self-healing process carried out by hydrogel. The environment factor such as pH, temperature, and biomolecular concentration may affect the self-healing behaviour of hydrogel. The hydrogel water content also has significant effect onto the self-healing process of hydrogel. Thus, the temperature which is one of the environmental factors and the hydrogel water content are the main focus in this study. The indices used to indicate self-healing mechanism is carried out by the hydrogel also being identified in this study.

The self-healing process can be examined by physical experimentation and simulation. The physical experiment provides more accurate results on the study of hydrogel self-healing behaviour. The limitation of physical experiment is consuming a lot of time. Thus, the simulation method which is more time saving is chosen.

1.3 Problem Statement

For the hydrogel self-healing performance study available online are mostly conducted via physical experiment. The number of hydrogel self-healing performance study using molecular dynamic available is still very insufficient. At the same time, the hydrogel's self-healing process still cannot be fully understand through the physical experiment. However, the simulation methods able to evaluate the hydrogel self-healing process in term of hydrogel molecular structure. Thus, the evaluation of hydrogel self-healing performance using molecular dynamic is very important.

On the other hand, temperature is one of the microenvironment factors which will affect the properties and performance of the hydrogel. According to Guan et al. (2017), temperature is one of the microenvironment factors which affected the degradability of hydrogel. In a study carried out by Kabiri, Mirzadeh and Zohuriaan-Mehr (2008), the temperature of hydrogel plays an

important role in affecting the swelling capacity. The high temperatures will enhance the swelling capacity of hydrogel. Another research is carried to study the relationship between temperatures and the mechanical properties of hydrogels. Wang et al. (2020) reported that the storage modulus and loss modulus can be manipulated, by varying the hydrogel's environmental temperature. The changes in the storage modulus and loss modulus indicates the changes in the mechanical properties of hydrogel when the surrounding temperature is varied.

In addition, water content within the hydrogel also play an important role onto its properties and performance. The high water content helps to promote the biocompatibility of the hydrogel. This condition also provide a suitable environment for the growth of cells and to carry out the cellular activity (Tran, Mredha and Jeon, 2020). The high water content also enable the hydrogel to alter its shape and size easily by swelling (Shi et al., 2019). The water molecules within the hydrogel also has significant effect to the regeneration process carried out by the hydrogel.

Thus, the effect of temperatures and hydrogel water content on the self-healing performance of hydrogel are focused in this project.

1.4 Aim and Objectives

The self-healing process carried out by hydrogel may affect its application in different fields. Thus, this study forcuses on the self-healing performance of hydrogel. The objective of this study are:

1. To understand the self-healing mechanism of hydrogels.
2. To determine the indices as a measure of self-healing behaviour.
3. To examine the effect of temperature and water content of hydrogel on the self-healing property

1.5 Scope and Limitation of the Study

This research is mainly focused on the hydrogel's self-healing performance. The indices used to measure self-healing behaviour such as energy changes is identified. The environmental factor also will affect the self-healing behaviour of hydrogel. The temperature and water content level are selected as the factor used to study the effect on the self-healing behaviour of hydrogels.

There are some limitations in this study. The study is carried out using the Material Studio software simulation to replace the physical experiments. However, the amount of journals which study the self-healing behaviour of hydrogel is limited. The information can be obtained for the hydrogel study using Material Studio software is insufficient. Thus, the journal for seal-healing material of other material is used as the reference for this research.

1.6 Contribution of Study

Throughout this research, the self-healing performance can be studied more easily using the BIOVIA Material Studio software. The indices which can be used to determine the self-healing mechanism also can be identified in this study. The effect of temperature on the self-healing mechanism can also be concluded at the end of this study. The finding and knowledge obtained for this research could help for further study of other researches on hydrogel characterisation and application.

1.7 Outline of Study

In this study, the chapter 1 is the introduction which is about the general introduction, problem statement, importance, objective, scope and limitation and contribution of study. Chapter 2 is the literature review which includes the introduction to hydrogel, self-healing mechanism, classification, applications, production technology, parameter affect self-healing performance and the methods to assess the self-healing performance of hydrogel. Chapter 3 is the methodology and work plan which cover the introduction to BIOVIA Material Studio Software, procedure for molecular dynamics simulation and characterisation techniques used. Chapter 4 is the result and discussion part where the simulation results are analysed and discussed. Chapter 5 is the conclusion for this study.

CHAPTER 2

LITERATURE REVIEW

2.1 Hydrogel

Hydrogels is a rubber-like gel as shown in Figure 2.1. The hydrogel has the ability to undergo a self-healing process in order to recover back to original properties and structures once it experiences any damages (Li et al., 2017). It is known as a smart material which can adapt to different environment condition (Wei et al., 2013).

Figure 2.1: Hydrogels. (Wang, Gao and Yu, 2017)

Hydrogel is the material with three dimensional polymeric networks (Morteza Bahram, Mohseni and Moghtader, 2016). It can swell in water and retain large quantities of water. The water absorbability of hydrogels arises from the hydrophilic functional group found in the polymeric backbone. At the same time, the cross-links between network chains cause hydrogels to have the dissolution resistance (Ahmed, 2015). Hydrogels also have high porosity and soft rubbery consistency which is similar to living tissues. These characteristics increase the application of hydrogels in different aspects (Ullah et al., 2015). Hydrogels also have the biocompatible properties. This enables hydrogels to perform as an appropriate host response in specific applications (Nguyen, 2018)

2.2 Self-healing Mechanism of Hydrogel

Self-healing is the mechanism where the material has the ability to repair crack itself. The self-healing mechanism of materials can be illustrated through the following steps. Once the hydrogel experiences any damages, the mobile phase of the materials is triggered. For physically self-healing mechanisms, the damage is started to be filled up by the transportation of substances to the wound and mending reaction is carried out (Yuan and Wang, 2017). The reformation of non-covalent cleaved and dynamic covalent bonding is carried out in the chemically self-healing mechanism (Li, Tian and Wu, 2016).

The hydrogels with chemically self-healing mechanisms are produced using different chemistries and mechanisms. The three major categories of self-healing hydrogels are based on the chemistries and mechanisms which are dynamic covalent bonds, non-covalent interactions and multi-mechanism interactions as shown in Figure 2.2 (Liu and Hsu, 2018).

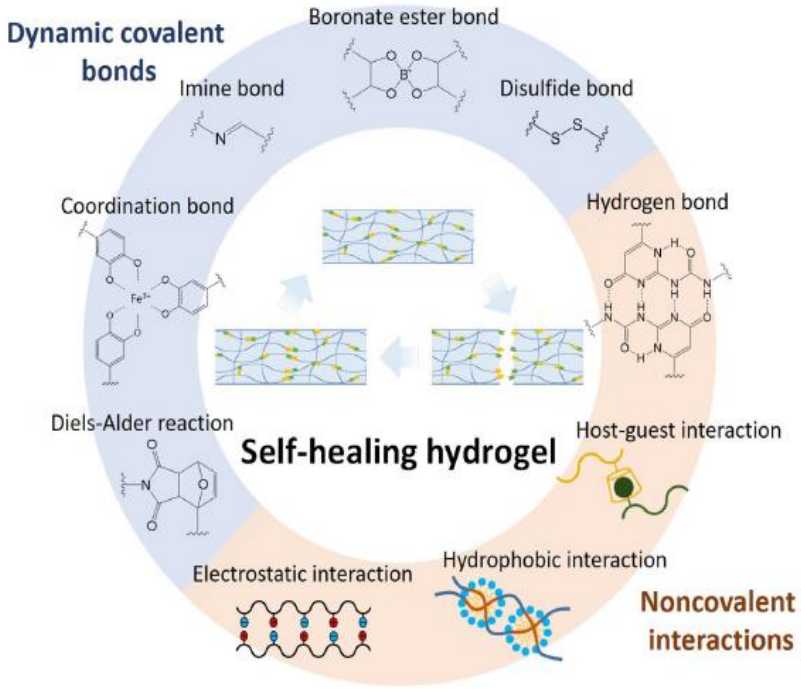

Figure 2.2: Chemistries and Mechanism for Different Self-healing Hydrogels. (Liu and Hsu, 2018)

2.2.1 Dynamic Covalent Bonding

Dynamic covalent bonding is the chemical bond which can be formed or broken in a mild condition. This type of bonding is reversible to become non-covalent physical bonds or become the permanent conventional covalent bonding which depends on the conditions (Taylor and in het Panhuis, 2016). Dynamic covalent bonds are stronger than non-covalent interactions. However, it consumes more time to achieve dynamic equilibrium. The type of dynamic covalent bonding used to synthesize hydrogels consist of the formation of imine bond, complexation of boronate ester bond, catechol-iron coordination, Diels-Alder reaction and disulphide exchange.

The imine is the molecule with carbon-nitrogen double bond. It can be formed through the nucleophilic attack to amine to aldehyde as well as ketone (Liu and Hsu, 2018). As the formation of the imine group involves the amine group, it turns the polymer with high amino into hydrogels by combination with another aldehyde polymer (Talebian et al., 2019).

The boronate ester bond is the product complication of boronic acid and dial. The stability of the bond is affected by the pH-value and concentration of glucose available (Liu and Hsu, 2018).

The reversible coordinate bond is one of the chemistries which can be used to produce the hydrogel with self-healing ability. The reaction takes place between the catechol and iron. The adjustment of environment pH condition can control the coordinated bond formed within the hydrogel. When the pH condition changes from acidic to basic, the self-healing hydrogel with high strength will be formed (Liu and Hsu, 2018).

The disulphide bond is formed through the thiol/disulphide exchange reactions where the thiol groups undergo oxidation. This dynamic covalent bond is sensitive to pH value of the environment and a proper oxidation agent is required. The hydrogel formed has the self-healing capacity which is not stable in physiological tissues. The main reason is the presence of reducing agents in human body (Talebian et al., 2019).

The last dynamic covalent chemistry is the thermally reversible Diels-Alder reaction. It is a reaction between conjugated diene and dienophile. This type of hydrogels has limitations in biomedical applications. This is due to the

Diels-Alder bond requiring a relative high reaction temperature. It also takes longer time to cleave and reform which contribute to the self-healing in the hydrogel (Liu and Hsu, 2018).

2.2.2 Non-covalent Interaction

The hydrogel can be formed using non-covalent interactions. The non-covalent bonding is one of the intermolecular forces which is dominant in supramolecular chemistry (Hu, 2013). The non-covalent interaction is the process where the molecular cluster is formed (Müller-Dethlefs and Hobza, 2000). These types of interactions are chemically less stable compared to covalent bonds.

Hydrogen bonding is one of the non-covalent interactions applied in production of hydrogel. It is the interaction between hydrogen atoms and electronegative atoms. Hydrogen bonding strength is depending on the negative charge acceptor atom. The association and dissociation rate of the bonding occur rapidly. This enables hydrogel production to have fast healing time (Liu and Hsu, 2018).

Hydrophobic interactions occur when the hydrophobes in aqueous medium. The hydrophobic interaction is stronger than hydrogen bond and can be controlled easily (Talebian et al., 2019). When producing the hydrogel via hydrophobic interactions, the surfactant micelles and amphiphilic polymers are used as the medium to link the hydrophilic and hydrophobic monomers (Liu and Hsu, 2018). The self-healing mechanism is depending on the dissociation and reassociation of micelles.

In host-guest interactions, cyclodextrin, a molecule with lipophilic inner cavity and a hydrophilic outer surface is attached onto the backbone of hydrogel. In this non-covalent interaction, one of the limitations is the low water-uptake will lead to a hydrophobic region formed in the hydrogel (Talebian et al., 2019).

Reversible electrostatic interactions are the interactions that take place in charged polymers and ions. The charged polymers are mixed to produce the hydrogels (Liu and Hsu, 2018).

2.2.3 Multi-mechanism Interaction

The current challenge is to produce hydrogels with high performance such as high recovery rate, high stability, better mechanical property and multi-responsive behaviour. Multi-mechanism interaction is the technique which applies different interactions such as the combination of dynamic covalent bond and non-covalent interaction. The main objective of this technique is to enhance the chemical and physical characteristics of the hydrogel produced (Liu and Hsu, 2018).

2.3 Classification of Hydrogel

Hydrogel can be classified based on the different physical and chemical properties. The classification of hydrogel can be divided into six major categories which is according to the source, composition of polymer network, configuration, crosslinking, physical appearance and electrical charge of polymer network (Garg, Garg and Vishwavidyalaya, 2016; Ahmed, 2015). The ordinary type of hydrogel classification is based on source. There are three types of hydrogels which are natural, synthetic and hybrid hydrogels.

2.3.1 Natural Hydrogels

Natural hydrogels are the hydrogels which compose of natural components (Gyles et al., 2017). Natural hydrogels has the properties of biocompatibility and biodegradability (Dhandayuthapani et al., 2011). This enables it to be widely used in stem cell culture. The natural hydrogels also have the ability to promote cellular functions and improvement of proliferation, viability and the development of different types of cell (Tibbitt and Anseth, 2009)These factors of natural hydrogels help to improve its usage. The natural hydrogels also can be produced using adhesion protein including fibronectin and laminin. This type of natural hydrogels can be used for essential cell function such as adhesion and migration (Toh and Loh, 2015). The natural resource used for hydrogels synthesis can be obtained through the extraction of seaweed, brown algae or via bacterial culture (Khansari et al., 2017). The common natural polymers used to produce hydrogel including collagen, gelatine, chitosan and dextran (Gull et al., 2019).

2.3.2 Synthetic Hydrogels

Synthetic hydrogels are produced using the man-made polymer (Gyles et al., 2017). The type of hydrogels are more inert as compared to hydrogels derived from natural sources (Khansari et al., 2017). The synthetic hydrogels provide more advantages over natural hydrogel. The properties of synthetic hydrogels can be modified during the production of polymer chains. Thus, the synthetic hydrogels produced normally have the more desired properties (Garnica-Palafox and Sánchez-Arévalo, 2016). The type of synthetic polymers used for the production of hydrogels are polyethylene glycol and polyacrylamide (Khansari et al., 2017).

2.3.3 Hybrid Hydrogels

Hybrid hydrogels are also known as the nanocomposite hydrogels. This hydrogel is the combination of two or more different molecules from naturals or synthetic materials (Khansari et al., 2017). The natural and synthetic hydrogels with different properties can be altered and combined to form nanocomposite polymers with specific properties. This combination helps to improve the physical, electrical, chemical and biological properties of the hydrogels (Wu, Yang and Kopeček, 2011; Messing and Schmidt, 2011).

2.3.4 Comparison of Different Type of Hydrogels

Each type of hydrogel has advantages and disadvantages. The natural hydrogel is highly biocompatibility and biodegradable. This cause natural hydrogels can act as the cell growth medium. However, the natural hydrogel has relatively poor mechanical strength. The production of hydrogels using natural polymers is often expensive. This is due to the production is in high batch-to-batch variations and has chances of chronic immunogenic responses to occur (Mehdi, 2016).

The synthetic hydrogels have a long shelf time. The properties of synthetic hydrogels are also easy to be modified (Garnica-Palafox and Sánchez-Arévalo, 2016). The water absorption capacity of synthetic hydrogels is higher compared to natural hydrogels. The disadvantages of this type of hydrogels is

lack of vivo biocompatibility and degradation at relatively slower rate compared to natural hydrogels (Khansari et al., 2017).

The hybrid hydrogels have highly modifiable physical, chemical and electrical properties as it is the combination of both synthetic and natural polymer chains (Wu, Yang and Kopeček, 2011). The mechanical strength of the hydrogel is also improved. Based on current studies, the long-term biocompatibility, nanotoxicity and mechanical strength of hybrid hydrogel is still inconclusive (Khansari et al., 2017).

2.4 Application of Hydrogel

The hydrogels are widely used in different fields. The specific structure and compatibility of hydrogels helps to enhance its usage in different fields. The flexibility of hydrogels, the materials used to produce hydrogels which is biocompatible and the chemical behaviour of hydrogels to different environments cause the wide application of hydrogels (Morteza Bahram, Mohseni and Moghtader, 2016). The application of hydrogels is this study is primarily focused on the biomedical field.

2.4.1 Drug Delivery

The drug delivery system (DDS) is the system where transportation of pharmaceutical compounds to the target region in order to achieve therapeutic effect (Tiwari et al., 2012). The hydrogels can be used as the carrier in DSS which helps to deliver the drugs to target tissue inside the human body. These hydrogels help to solve the problems of regular drug formulations. The porosity of hydrogel can be controlled by cross-linking degree within the hydrogel matrix and the affinity to aqueous condition during the swelling process of hydrogels. The high porosity in hydrogels cause the hydrogels to have high permeability to drugs. The drugs are carried and delivered easily using the hydrogels. The binding of the drug to the hydrogels matrix can be enhanced by the electrostatic interactions and covalent bonding within the hydrogels. The hydrogels have the ability to store, protect and release the drugs at the desired kinetics. The mechanism of drug release can be stimulated through different microenvironment factors such as pH, temperature, specific enzyme and physical stimuli (Morteza Bahram, Mohseni and Moghtader, 2016). Following

are some examples of usage of hydrogels in drug delivery. The drug can be delivered to the oral cavity via hydrogels for disease treatment such as stomatitis and oral cavity cancers. The hydrogels have the ability to store gelatine. The hydrogels deliver the gelatine to the target region and are used for wound protection from bacterial infection. The active component, Desonide which is used as anti-inflammatory may face the problem of scaling and dryness during transportation. However, this problem can be overcome when using hydrogels as the delivery agent due to its moisturising properties (Nguyen, 2018).

2.4.2 Tissue Engineering

In tissue engineering, a proper type of cell is needed to be found and culture in a suitable scaffold under certain conditions. Hydrogels become the appropriate type of scaffold material. This is due to hydrogels having a similar structure with the extracellular matrix of many tissues. They also have the ability to be processed under mild conditions. This allows the hydrogels to be processed to become scaffolds for different tissues. The applications of hydrogel in tissue engineering are to act as the agent for vacant spaces filling, acts as support for ideal tissue formation and bioactive molecules carrier (Morteza Bahram, Mohseni and Moghtader, 2016).

The vacant spaces filling agent include the scaffolds which provide bulking, prevent adhesives and bioadhesives. The natural hydrogels which compose of alginate, chitosan and collagen have the potential to be processed to become scaffolds as bulking agents. The hydrogels with chitosan and chitin can be used as biological adhesives in surgery. This type of hydrogels helps to seal the wounds which the leakage of air or body fluid may occur. The effectiveness of wound dressings can be improved by using this hydrogel. The scaffold derived from synthetic hydrogels commonly used as the anti-adhesive materials. This is due to the cells not having the adhesion receptors and the protein will not be absorbed by the cells (Morteza Bahram, Mohseni and Moghtader, 2016).

The hydrogels can provide signal and environment for cells to carry out tissue development. The hydrogel scaffolds can be used to trigger the tissue and produce a wide range of tissue. The technique is applied in producing different tissues such as cartilage, bone, cardiac and neurons (Talebian et al., 2019).

Hydrogel scaffolds also have the potential to act as the carrier for bioactive molecules to specific tissues or encapsulate secretory cells. The hydrogel scaffold for bioactive molecules carriers still does not imply a current situation. The problem facing without the scaffold is the degradation of the drug and the transportation of the drug to non-target tissue. This may lead to poisonous to other tissues. Thus, scaffold became the important carrier for bioactive molecules (Morteza Bahram, Mohseni and Moghtader, 2016).

2.4.3 Biosensor

A biosensor defined as a type of integrated receptor-transducer device. It can be used to analyse selective quantitative via the biological recognition element (Khan et al., 2016). The biological recognition element is the biology element such as antibodies, enzymes and tissues. The biological recognition element used for the biosensor should only be sensitive to the specific analyte and inert to other analyte (Liu et al., 2018).

The properties of hydrogels which are biocompatible, high water content and hydrophilic nature are alike with the void-filling component in extracellular matrix. Thus, the hydrogels can be used to provide a suitable environment for biosensing molecules and act as the protection to the biosensing element to prevent any interaction between biosensing molecules and other components. There are two types of biosensor which are the molecular interactions and living sensors (Morteza Bahram, Mohseni and Moghtader, 2016).

The molecular interactions type is the usage of stimuli-responsive hydrogel as the biosensor. One of the molecular interaction type biosensors is the glucose-responsive hydrogel. The glucose-responsive hydrogel is sensitive to the glucose level in the human body. Thus, it can be used to detect the glucose level in the human body. Once the glucose level increases, it can act as the automatically insulin depots to maintain the glucose at appropriate level. The release of insulin can be carried out through the swelling of hydrogel (Adams et al., 2006).

The living sensor is the combination of living cells or microorganisms with the hydrogel as the biosensor. Microorganism has the ability to detect different chemical substances and can be amenable for modification of genes.

These properties allow it to become an ideal biosensing element and applied in the living sensors (Buenger, Topuz and Groll, 2012). The Arxula adeninivorans is one of the biosensing microorganisms used in living sensors. It has the ability to determine the biodegradable pollutants concentration in wastewater (Renneberg et al., 2004).

2.5 Technology of Hydrogel Production

The hydrophilic monomers become an important monomers for the synthesis of hydrogels which has high water absorbability. The technique commonly used in the synthesis of hydrogels is copolymerisation/cross-linking free-radical polymerisations where the reaction occurred across the hydrophilic monomers and multifunctional cross-linking. The principles commonly used in natural and synthetic hydrogels are (Ahmed, 2015):

1. Using chemical reaction to link polymer chains
2. Generation of main-chain free radicals that able to recombine as cross-link junctions via ionizing radiation
3. Through physical interaction

2.5.1 Free Radical Generation

2.5.1.1 Free Radical Polymerisation

Free radical polymerisation is also known as addition polymerisation. It is the chain reaction where the monomer is added to the active-chain-end. After the monomer is added, the regeneration active side at the chain end takes place. (Selimis and Farsari, 2017). The polymers which are functionalized with radically polymerisable groups such as acrylates, amides and vinyl lactams are suitable to be used in this polymerisation method to form hydrogels. This polymerisation technique involves the principle of free-radical polymerisation where the initiation, propagation, chain transfer and termination mechanism will be carried out (Nguyen, 2018). The radical is created through a variety of visible, thermal, ultraviolet and redox initiators during the initiation step. In the propagation step, the monomers are being converted into active forms when reacted with the radicals. The termination is carried out by the long radical chain via the radical combination by developing polymeric matrices or chain transfer.

The polymerisation can be carried out in solution or neat (bulk). The solution polymerisation requires a solvent which typically is water. The bulk polymerisation is faster than liquid polymerisation and no additional solvent is required (Saini, 2017). Chitosan-based hydrogels is one of the hydrogels produced through free radical polymerisation (El-Sherbiny, Harding and Abdel-Bary, 2006).

2.5.1.2 Polymerisation by Irradiation

Ionizing-radiation technique is the polymerisation which was initiated using radiation (Platzer, 1967). This technique is used for the synthesis of hydrogels of unsaturated compounds. The radiation with high energy such as electron beams and gamma rays are employed as the initiator. The radicals are formed on the polymer chains when the irradiation of the polymer solution occurs. The recombination of macro-radicals with different chains takes place and the covalent bonding is formed. This method is used to produce hydrogels which are relatively pure and initiator free (Nguyen, 2018). The energy required for the irradiation of polymer solution consumes less energy to form the macroradicals. The other advantage of irradiation polymerisation is no additives or catalyst is required and the process is relatively easier to be controlled. This hydrogel production method is not suitable for the polymers which may disgrace during irradiation. Acrylic acid hydrogels is the hydrogel produced using irradiation polymerisation (Saini, 2017).

2.5.2 Chemical Cross-linking

Chemical cross-linking is the major and popular technique in hydrogel synthesis. During the production using chemical cross-linking, the bi-functional crosslinking agent into the dilute solution filled with hydrophilic polymer. The polymer must have the ability to react with the crosslinking agent. The chemical cross-linking of the hydrogels can be developed through addition and condensation polymerisation, radiation polymerisation and chain growth polymerisation. This method can be used to produce both natural and synthetic hydrophilic hydrogels. The albumin and gelatin-based hydrogels is produced by using dialdehyde or formaldehyde as the cross-linking agent (Saini,

2017). There are some benefits and limitations of using chemical cross-linking for hydrogel production. This synthesis method is relatively easy. The hydrogel being produced also has a wide range in network structure. However, the hydrogel produced may contain chemical residue and leads to the hydrogel become toxic (Singhal and Gupta, 2016).

2.5.3 Physical Cross-linking

The formation of hydrogels via the physical cross-linking is the most common and easiest way. There are several ways can be employed to produce the hydrogels with different physical cross-linking.

2.5.3.1 Ionic Interaction

The production of hydrogel using ionic interaction can be carried out at room temperature and physiological pH (Saini, 2017). The hydrogels can be synthesized when a divalent/trivalent ion with opposite charge is added into an ionic polymer. This causes the cross linking to take place to form polymers. In this interaction, the principle of gelling of the ion with opposite charged polyelectrolyte solution is employed. The hydrogel produced using metallic ions is stronger than others (Nguyen, 2018).

Alginate is produced using the ionic interaction. It is a polysaccharide with the ionic interaction between calcium ion and mannuronic and glucuronic acid. The crosslink of alginate hydrogel can be formed at ambient temperature and pH. Thus, it can be repeatedly used as an encapsulation matrix of living cells. The extraction of calcium ions using chelating agents makes the hydrogel become unstable and the protein is released for drug delivery (Saini, 2017). Figure 2.3 shows the illustration of ionic interaction between alginate with divalent metal ions.

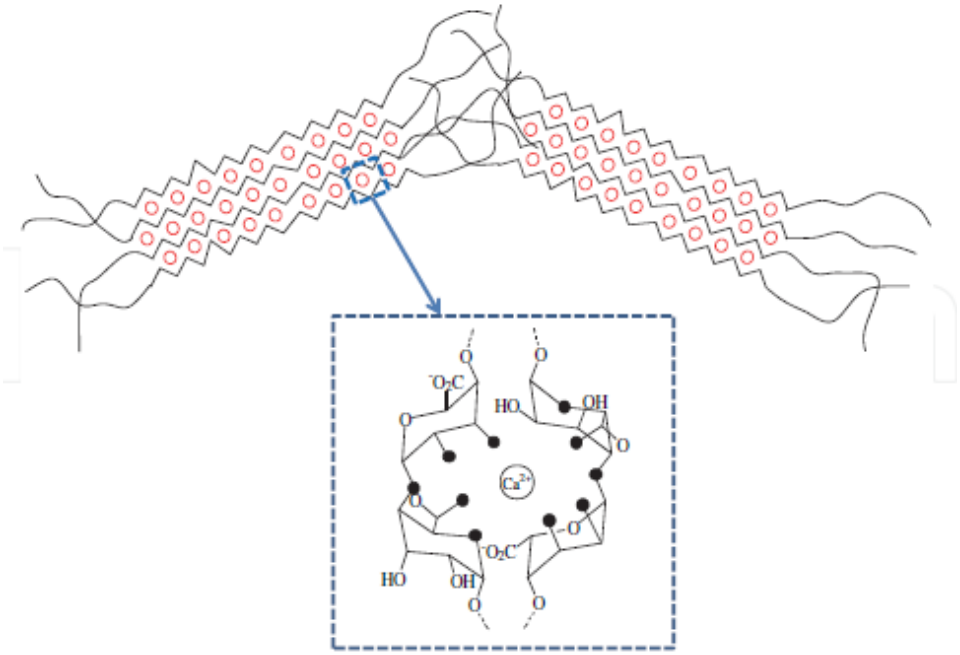

Figure 2.3: Illustration of Ionic Interaction Between Alginate (COO-) with Divalent Metal Ions (Ca2+) (Gulrez, Saphwan Al-Assaf and Phillips, 2011)

2.5.3.2 Crosslinking by Crystallisation

The crosslinking of crystallisation can be produced through the freezing-thawing process. Freezing-thawing is the process where the freezing, cooling at room temperature and heating process is carried out to samples (Microchemlab.com, 2018). The repeated freeze-thawing process caused the formation of micro crystals. PVA based hydrogels can be produced through the physical crosslinking of crystallisation. The PVA aqueous solution will become gel when stored at room temperature. However, the gel produced will have low mechanical strength. When PVA aqueous solution undergoes repeated freeze-thawing process, the physical crosslinking has formed. Thus, the gel produced will be strong and more elastic (Singhal and Gupta, 2016).

2.6 Parameters Affecting the Activity of Hydrogel

There are two types of self-healing hydrogels which are non-autonomic and autonomic self-healing hydrogels. The external sources such as heat, light and ultrasound are required to trigger the self-healing mechanism of non-autonomic self-healing hydrogels. The environment pH changes of the hydrogels also can trigger the self-healing mechanism to occur. For the autonomic self-healing hydrogel, the hydrogel will carry out the self-healing once it experiences any damage. There is no additional stimulation required to trigger the self-healing mechanism (Li, Tian and Wu, 2016). The self-healing mechanism carried out by hydrogel may be affected by the environmental stimuli. The stimuli may trigger self-healing mechanism of hydrogel as well as its application and its properties. This type of smart hydrogel is known as stimuli responsive hydrogel. There are two different types of stimuli which are physical and chemical stimuli. The physical stimuli included the light, temperature, pressure, electric fields and mechanical fields while the chemical stimuli which affected the performance of hydrogel included the environment pH, chemical agents, ionic factor and the interaction between the solvents and the polymer chains (Ullah et al., 2015)

2.6.1 pH

pH-responsive hydrogel is the hydrogel which is very sensitive to ambient environment pH changes. During the changes in environment pH, the hydrogel will experience swelling and shrinking behaviour. The mechanism which causes the swelling and shrinking of hydrogel is the deprotonation and protonation process of the functional pendant group causing redistribution of hydrogel charge density as shown in Figure 2.4 (Shi et al., 2019). Acidic hydrogels composed of anionic pendant groups while basic hydrogels composed of cationic pendant groups. When the environment acidity decreases, the surrounding pH exceeds the acid dissociation constant of hydrogel causing the loss of protons. The polyacidic hydrogels will experience swelling. The polybasic hydrogels will swell when the ambient environment becomes acidic (Sudhakar et al., 2015). The pH-responsive hydrogels are commonly used in the

drug delivery to target tissues. Polydiethylaminoethyl methacrylate is one of the pH-responsive types of hydrogel (Bossard et al., 2006).

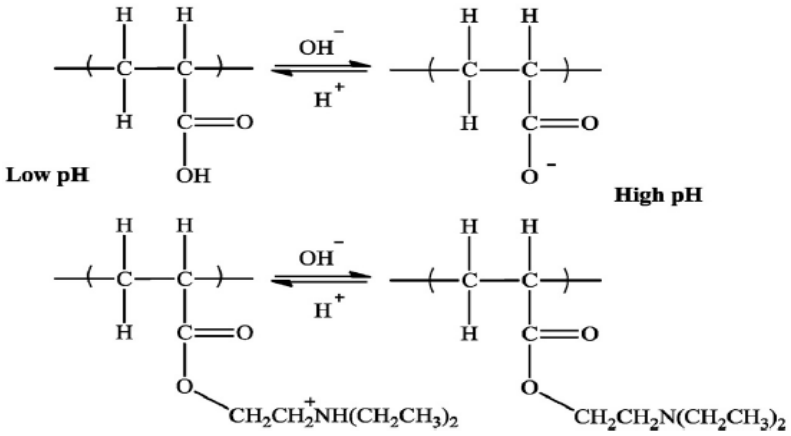

Figure 2.4: pH Dependent Ionisation of Polyelectrolyte (Polydiethylaminoethyl Methacrylate) (Ullah et al., 2015)

2.6.2 Temperature

Thermoresponsive hydrogel is the hydrogel whose behaviour is governed by the temperature changes (Sudhakar et al., 2015). The swelling mechanism of thermoresponsive hydrogel is due to the temperature-triggered solubility shift in aqueous solution. The critical solution temperature is the index used for the hydrogel volume-phase transition (Shi et al., 2019). There are two types of thermoresponsive hydrogel which are positive and negative temperature hydrogel.

The parameter introduced to positive temperature hydrogel is the upper critical solution temperature (UCST). The hydrogels will release the substances carried inside the matrix when the temperature drops below UCST. The hydrogels will swell when the temperature exceeds the USCT cause by the deformation of hydrogen bonding at the high temperature (Serra, Doménech and Peppas, 2006). Poly(acrylamide-co-butyl methacrylate-co-acrylic acid) type hydrogels is the example of positive temperature hydrogels (Chatterjee, Hui and Kan, 2018).

The low critical solution temperature (LCST) is the parameter used for the negative temperature hydrogels. The swelling of hydrogel occurs when the

temperature above the LCST while shirk when the temperature below LCST. The polyvinylpyrrolidone/poly(*N*-isopropylacrylamide) based negative temperature hydrogels apply for the drug delivery (Chatterjee, Hui and Kan, 2018).

2.6.3 Glucose level

The glucose-responsive hydrogel is sensitive to the glucose concentration of the human body. These types of hydrogels are produced using glucose oxidase, concanavalin A and boronic acid. These hydrogels are used for the diabetes treatment as it helps for self-regulation of glucose level by releasing insulin (Sudhakar et al., 2015). These hydrogels which contain immobilized glucose oxidase are very sensitive to pH. The gluconic acid and hydrogen peroxide will be produced when glucose is reacted with the glucose oxidase. The acid reduces the environment pH level and causes the swelling of hydrogels. Thus, the insulin within the hydrogels can be released to reduce the glucose level (Peppas, Slaughter and Kanzelberger, 2012). Figure 2.5 shows the mechanism where the glucose cause the swelling of the glucose-responsive hydrogel.

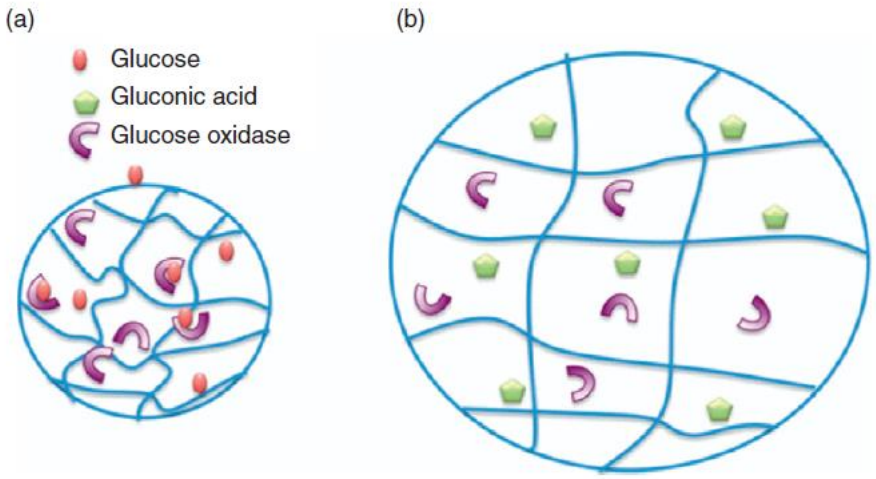

Figure 2.5: a) Glucose Diffuse into Hydrogel and React with Glucose Oxidase; b) Hydrogel Swell when the Gluconic Acid is Produced (Peppas, Slaughter and Kanzelberger, 2012)

2.7 Method to Assess Self-healing Performance

The self-healing behaviour of material can be studied through physical experiments and the molecular dynamic simulation.

2.7.1 Photography Monitoring of Self-healing Process

The self-healing performance can be observed under a photography method. The two different cut hydrogels are placed together for a long period and the result is observed (Li et al., 2017).

A self-healing process study on poly(vinyl alcohol) (PVA) hydrogel is carried out and the process is recorded using photographs method. The Figure 2.6 (a) shows the original hydrogels and one of the hydrogels contains red pigment for visualisation. Both hydrogels are cut and placed together. The hydrogels are placed together for 12 hour as shown in Figure 2.6 (c). After 12 hour of experiment, the result shows that the cut areas are still visible. However, both of the hydrogel pieces are combined together to become one particular hydrogel. This indicates that the self-healing mechanism is carried out by the hydrogels pieces. The hydrogel formed after 12 hours does not break after different mechanical forces such as bending and stretching are applied as shown in Figure 2.6 (d) & (e) (Zhang, Xia and Zhao, 2012).

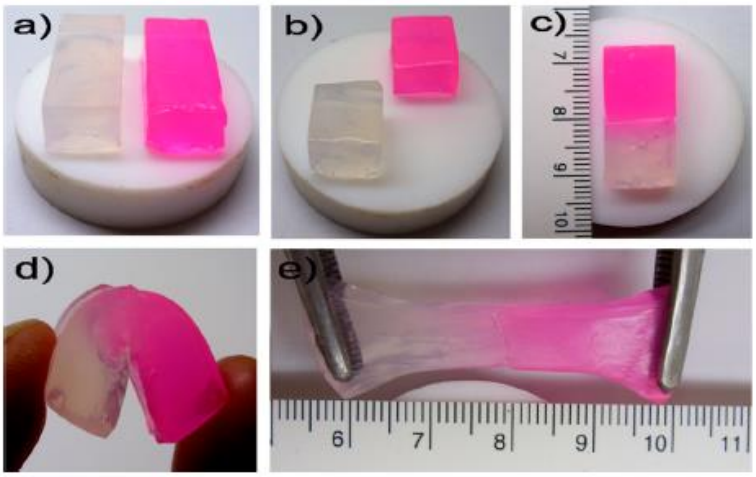

Figure 2.6: Photographs of Self-healing Mechanism Study of PVA Hydrogels: (a) Two Original Hydrogels; (b) Both Hydrogels Cut into Half; (c) Both Hydrogels Pieces Placed in Contact for 12 hours; (d) Bending of Hydrogel; (e) Stretching of Hydrogel (Zhang, Xia and Zhao, 2012)

Another similar study is carried out to the poly(acrylic acid) (PAA) hydrogels. In that particular experiment, two halves PAA hydrogels are placed in contact at room temperature for 6 hours. After 6 hours, there is no damage at the contact areas of both halves hydrogels. The hydrogel formed can withstand the stretching of approximately 200 % of the original length (Wei et al., 2013). Figure 2.7 shows the result of self-healing experiment on poly(acrylic acid) (PAA) hydrogels.

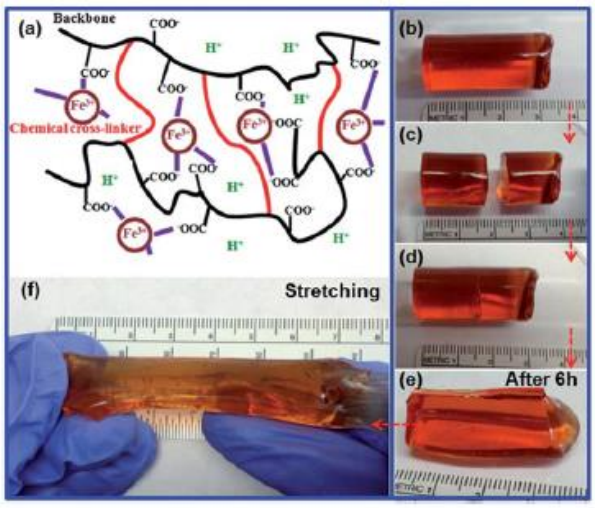

Figure 2.7: Photographs to Study of PAA Self-healing Hydrogels: (a) Illustration of Self-healing Hydrogel Structure; (b) Original PAA Hydrogel; (c) Hydrogel Being Cut into Halves; (d) Both Halves Placed in Contact for 6 Hours Bending of Hydrogel; (e) Reformation of Hydrogel after 6 Hours (f) Stretching of Hydrogel Formed (Wei et al., 2013)

The similar experiment is carried out and the microscope is used to study the self-healing mechanism of hydrogel. The chitosan/carboxymethyl chitosan/silver nanoparticles (CTS/CMCTS/AgNP) composite hydrogels are used in this experiment. The hydrogel is cut using a surgical blade. After the 30 s, the hydrogel pieces start to recombine to become one hydrogel. The gap between hydrogel pieces is observed using the microscope. The result shows that the gap between two hydrogel pieces gradually disappear within 5 minutes as shown in Figure 2.8 (Yang et al., 2020).

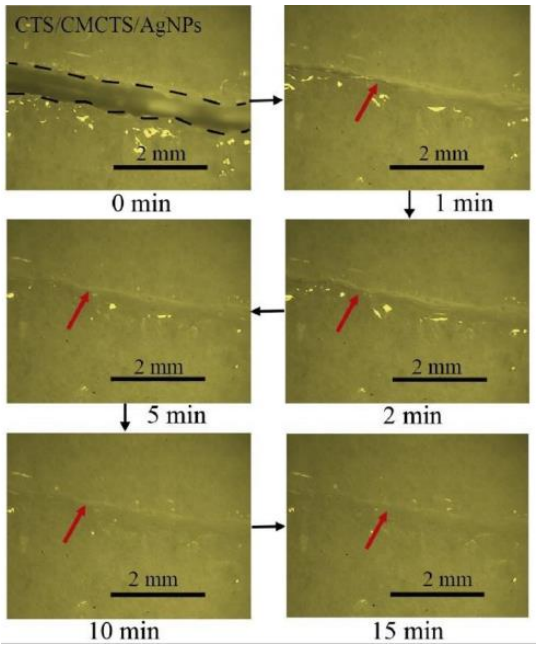

Figure 2.8: Microscopic Self-healing Result of Chitosan/Carboxymethyl Chitosan/Silver Nanoparticles (CTS/CMCTS/AgNP) Composite Hydrogel (Yang et al., 2020)

2.7.2 Rheology Testing

The seal-healing performance can be studied through the rheology test. The AR2000 rheometer and a plate which is 40mm attached to a transducer are employed for the study. The experiment is carried out at room temperature. A special care is carried out to the hydrogel sample to prevent the evaporation of water. The recovery properties of the hydrogel can be investigated through the step strain sweep measurement by varying the applied shear forces (Ding et al., 2015).

A study on self-performance of poly(acrylic acid) hydrogel is carried out by Wei et al. (2013). The experimental result is shown in Figure 2.9. In this study, the oscillatory strain amplitude (γ) is varied and the changes of storage modulus G' and loss modulus G'' are studied. The G' is larger than G'' when strain applied is 5 %. When the strain is increased to 400 %, the G' value drops drastically from 27k to 6k dyne per cm^2 which is very near to the G'' value. After the strain is decreased to 5 %, the G' and G'' value starts to recover to initial values.

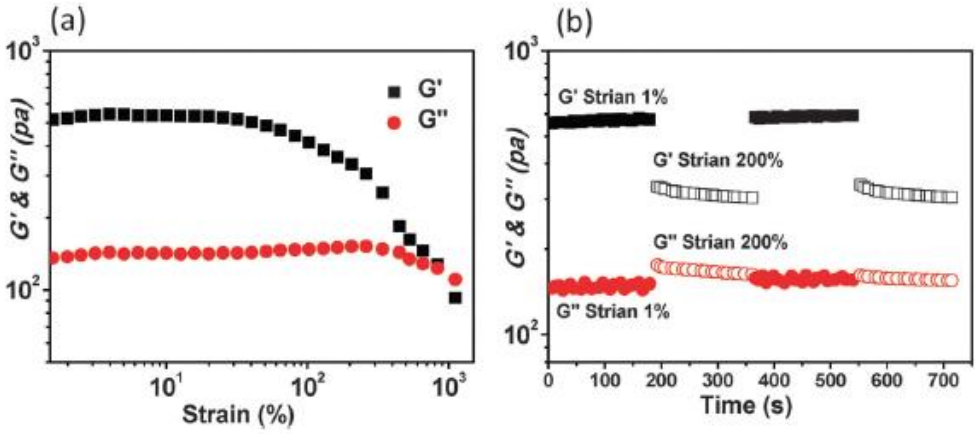

Figure 2.9: Storage Moduli, G' and Loss Moduli, G'' as A Function of Strain and against Time (Wei et al., 2013)

In another experiment, the rheology measurement is carried out to the polysaccharide hydrogels (Ding et al., 2015). The results show that the G' value decreases when the strain amplitude is increased to 100 %. The G' value started to return to its initial value when the strain was decreased to 1 % as shown in Figure 2.10.

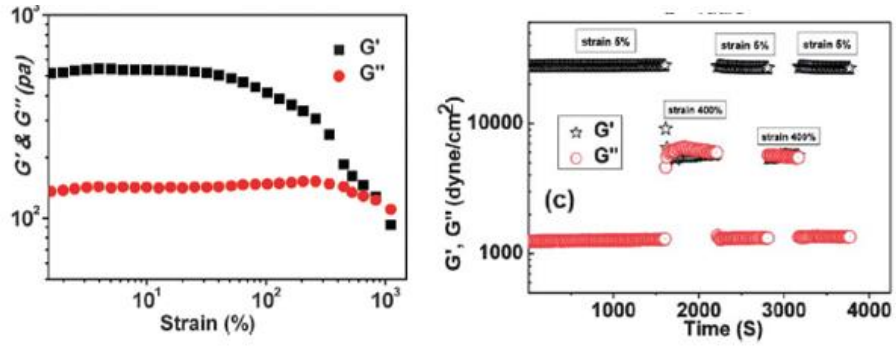

Figure 2.10: Storage Moduli, G' and Loss Moduli, G'' Values of Strain Sweep Test and against Time (Ding et al., 2015)

Based on both experiments above, when the strain amplitude increases to a critical level, the G' value starts to decline until to the level which is close to G'' value. This indicates the collapse of hydrogels. However, when the strain applied decreases, the G' value starts to increase and returns to initial value. This proves the self-healing process is carried out by the hydrogel.

2.7.3 Conductivity Testing

The self-healing mechanism performance also can be studied through conductivity testing. In the study, the self-healing performance of gelatine-tannic acid-silver network (Gel-TA-Ag NW) hydrogel is carried out using conductivity testing. During the experiment, the self-healing performance is studied using the green LED bulb as the indicator. When the hydrogels are connected to the circuit with 1.5V power supply, the LED bulb is being lighted as shown in Figure 2.11 a(i). The LED bulb becomes dim when the hydrogels is cut using the razor blade as shown in Figure 2.11 a(ii). When two divided parts are being contacted together, the LED bulb lights up again. The circuit is then connected to the circuit measurement system. Based on Figure 2.11 (b), there is no current flow when the hydrogels are cut into two pieces and the circuit current recovers when the hydrogels pieces are contacted together. Both hydrogel pieces are then in contact and left for a long period. The hydrogel formed is then connected back to the circuit. The LED bulb lights up when the hydrogel is connected to the circuit. This indicated that the self-healing process had been carried out by the hydrogel (Wang et al., 2020a).

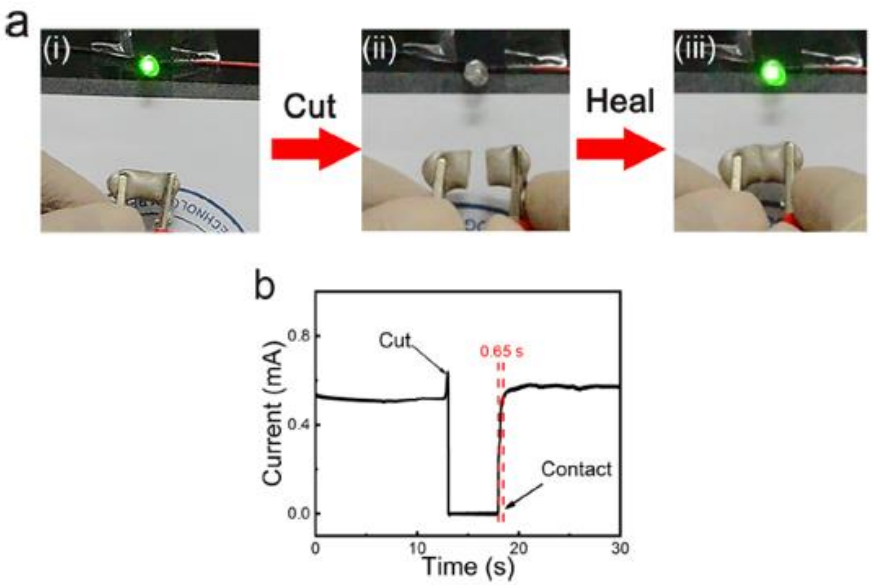

Figure 2.11: Conductivity Test: (a) LED Bulb Condition when Different Hydrogel is Connected to the Circuit: (i) Original; (ii) Cut Hydrogel; (iii) Hydrogel after Self-healing Process; (b) Real-time Current Graph (Wang et al., 2020a)

2.7.4 Simulation

The self-healing performance of materials can be studied through the molecular dynamic simulation by using different computation software. In this section, the BIOVIA Material Studio is employed for the dynamic simulation.

2.7.4.1 Self-healing Performance of chitosan/carboxymethyl chitosan/silver nanoparticles (CTS/CMCTS/AgNPs) hydrogel

In this study, the self-healing performance of chitosan/carboxymethyl chitosan/silver nanoparticles (CTS/CMCTS/AgNPs) hydrogel by modelling using Material Studio software. The CTS/CMCTS/AgNPs hydrogels is one of the polyelectrolyte complexation (PEC). The PEC hydrogel is formed using the natural anion and cation polyelectrolytes. The silver nanoparticles (AgNP) are added for the antibacterial properties. Thus, the silver nanoparticles do not involve the material studio modelling. The sodium alginate (SA) is added during the preparation of hydrogel to act as the anions supplement (Yang et al., 2020).

In the dynamic simulation, the negative charged CMCTS, SA and CMC are blended with positive charged CTS. The two-component system is employed to study the energy changes in different anion and cation systems as shown in Figure 2.12. Table 2.1 showed the changes in system energy before and after dynamic simulation (Yang et al., 2020).

Table 2.1: System Energy Change Before and After Dynamic Simulation (Yang et al., 2020)

	CTS/CMCTS		**CTS/SA**		**CTS/CMC**	
	Initial	**Final**	**Initial**	**Final**	**Initial**	**Final**
Total Energy (kcal/mol)	-21891	-22085	-24182	-22162	-25904	-24336
Potential Energy (kcal/mol)	-26296	-26537	-27748	-25691	-29840	-28263
Kinetic Energy (kcal/mol)	4405	4452	3566	3530	3936	3928
Total Enthalpy (kcal/mol)	-29320	-24284	-21567	-22039	-31770	-20238
Volume(A^3)	85755	85388	73499	73799	80512	79315

The result shows the increases of total energies to various systems for all two-component systems while the total energy CTS/CMCTS system decreases which indicates that the system will become stable after the dynamic movement of CTS/CMCTS. Based on changes of total system energy, the CTS/CMCTS are compatible and the interfaces are close to each other. Thus, the self-healing behaviour of this hydrogel is indicated to take place in the CTS/CMCTS system (Yang et al., 2020).

Based on the simulation result, the electrostatic interaction of the hydrogel between $–COO^-$ and NH_3^+ ions is reversible. Thus, it can recover after being destroyed and leads to self-healing behaviour in this hydrogel. As shown in the simulation, the CTS and CMCTS are similar and high compatibility between each other also contributes to the self-healing behaviour. In short, the electrostatic charge effect of PEC and strong hydrogen bonding formed contribute to the self-healing behaviour of the CTS/CMCTS/AgNPs hydrogel (Yang et al., 2020)

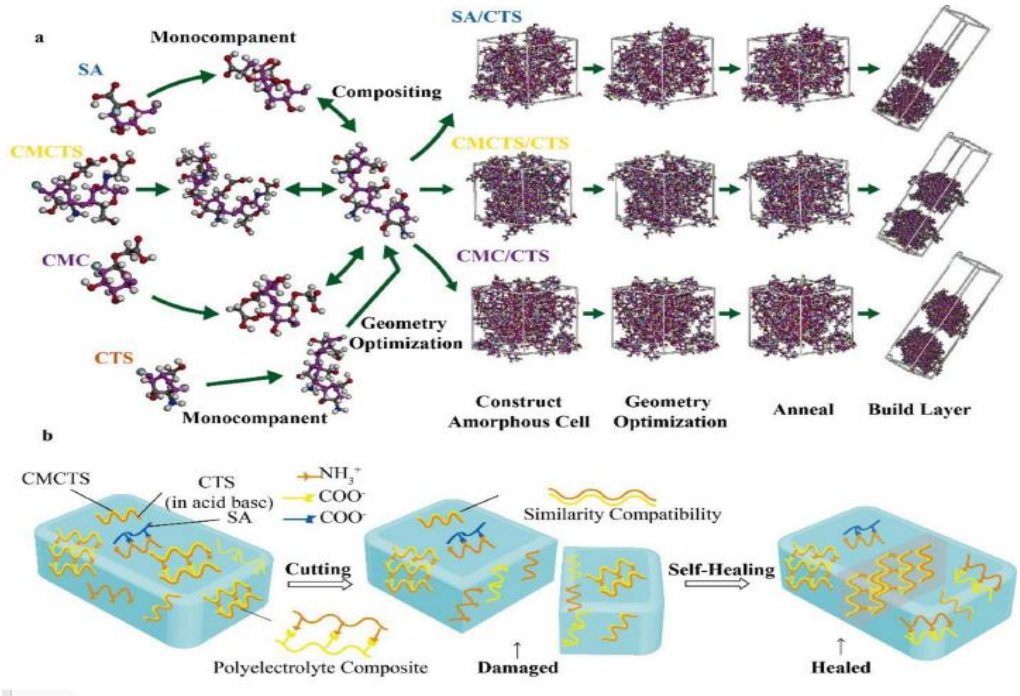

Figure 2.12: Molecular Dynamic Simulation Result and Plausible Mechanism of Hydrogel: (a) Molecular Simulation Process; (b) Self-healing Behaviour Based on Similarity and Compatibility (Yang et al., 2020)

2.7.4.2 Wetting time estimation of crumb rubber modified asphalt (CRMA)

In this research, the duration of self-healing mechanism being carried by the crumb rubber modified asphalt (CRMA) is estimated using the Material Studio simulation.

Wetting time is the duration carried out by the CRMA model to undergo the self-healing mechanism. In the Material Studio simulation, the wetting time can be estimated by using the simulation time required for the crack surface to be in contact. Thus, the model of CRMA with 10 Å crack is created as shown in Figure 2.13 (Hu et al., 2019).

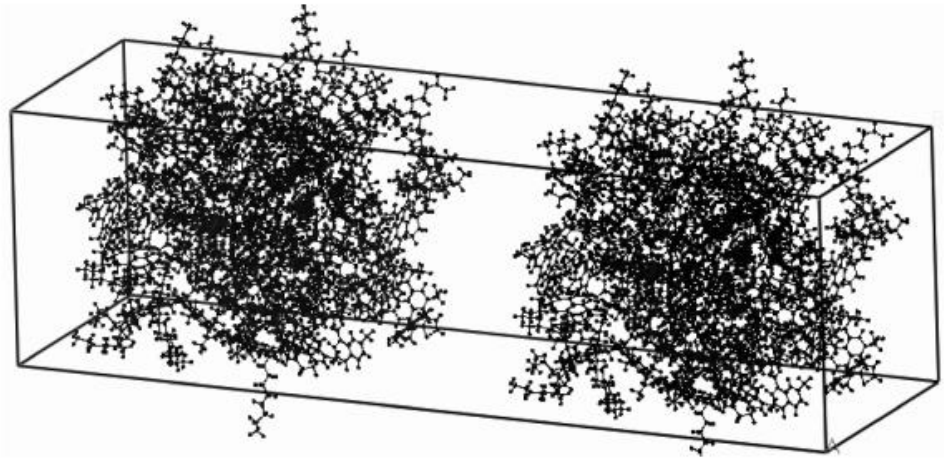

Figure 2.13: CRMA Models with 10 Å Crack. (Hu et al., 2019)

The wetting of asphalt surface can be observed by applying the Forcite dynamics module for 100 ps using NPT at 298 K and 1 atm to the crack model and the configuration changes of the model are observed. The configuration animation shows that the crack within the model is approaching each other. The volume of the model also decreases until the crack surfaces are in contact. The wetting time is the simulation time required for the model to achieve constant density (Hu et al., 2019).

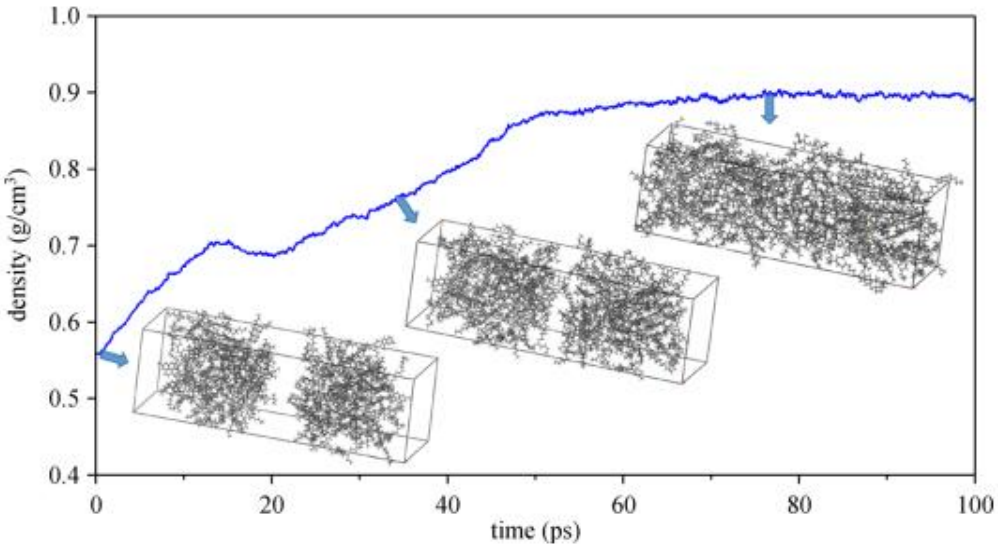

Figure 2.14: Density and Configuration of CRMA Model with Crack against Simulation Time. (Hu et al., 2019)

Based on Figure 2.14, the density of the model becomes constant when the simulation time is around 50-60 ps. Thus, it can be indicated that the duration of self-healing being carried out in CRMA is around 50-60 ps.

2.7.4.3 Self-healing Performance of Polyurethane Elastomer Study

In this study, the Material Studio simulation is employed to study the effect of the number of hydrogen bonding Polyurethane (PU) elastomers with the self-healing behaviour.

There are two different types of PU with different molecular composition and three different experiment temperatures are applied for the simulation. The sample A is the PU1 at 75 ˚C, sample B, C and D are PU2 at different experiment temperatures which are 25 ˚C, 50 ˚C and 75 ˚C. In the simulation, there are 9 different type of hydrogen bonds possibly formed in each PU as shown in Figure 2.15 (Chen et al., 2020).

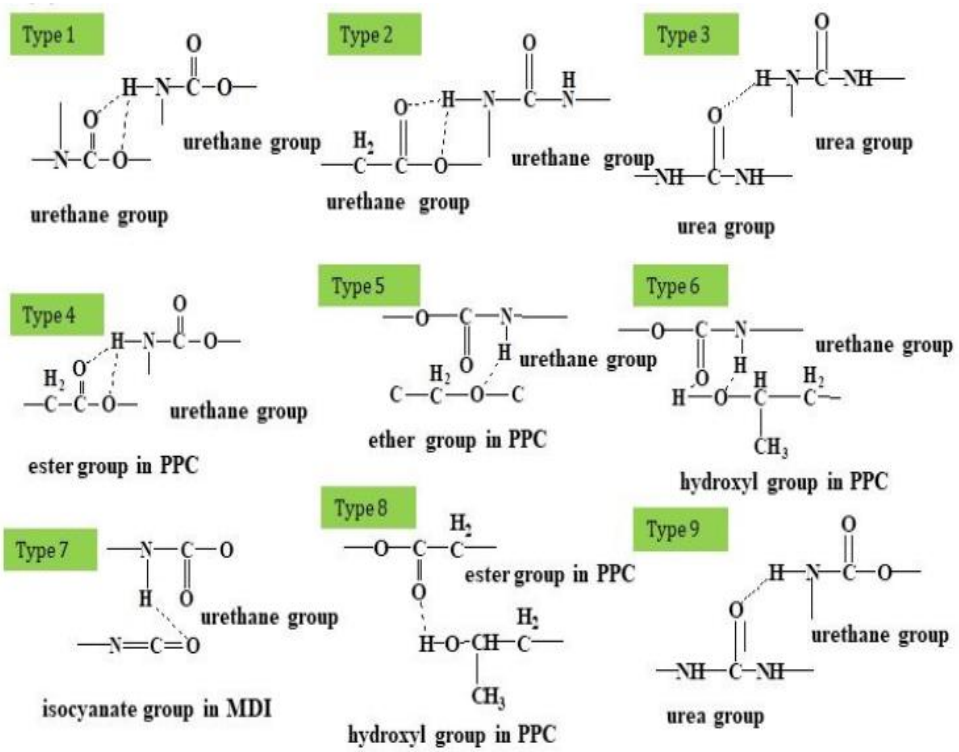

Figure 2.15: Type of Hydrogen Bonding in PU (Chen et al., 2020)

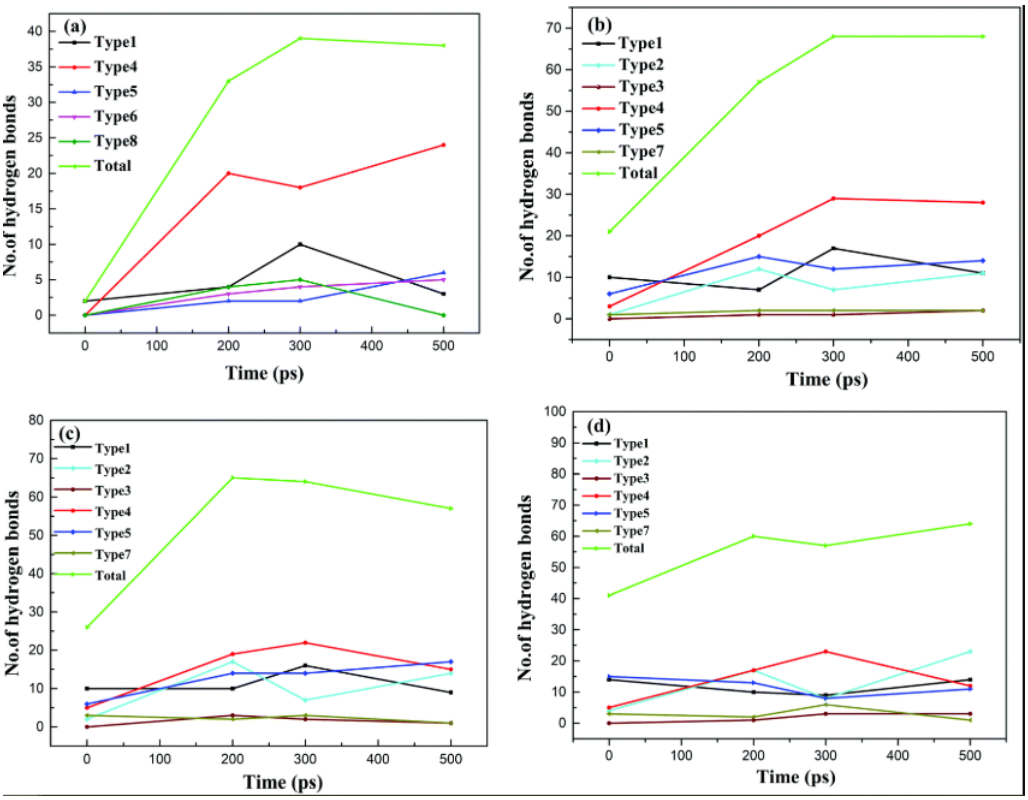

Figure 2.16: Number and Type of Hydrogen Bonding against Time in PU: (a) Sample 1 ; (b) Sample 2; (c) Sample 3; (d) Sample 4 (Chen et al., 2020)

The changes of each type hydrogen bonding number are recorded at the 5, 200, 300 and 500 ps. According to the result as shown in Figure 2.16, the quantity of hydrogen bonding Type 1, 4 and 5 are large and have the similar changes trend in all experiment samples. These three types of hydrogen bonding are the dominant type hydrogen bonding which contribute to the self-healing mechanism of PU. The number of these three type hydrogen bonding fluctuated during the experiment period. This is due to the dynamic exchange of hydrogen bonding. For sample 2, 3 and 4 which use the PU2 as the experiment sample, the quantity of type 2 hydrogen bond is also high. The result shows the number of type 2 hydrogen bonding. The number of type 2 hydrogen bonding in sample 2, 3 and 4 increase sharply and then stabilise. The trend is caused by the formation of type 2 hydrogen bonding during the self-healing process and may lead to crack heal which causes the number of type 2 hydrogen bonding stabilise (Chen et al., 2020).

The number of effective hydrogen bonding is also calculated. The effective hydrogen bonding is the hydrogen bonding which is present in the sample more than the simulation period (Chen et al., 2020).

Table 2.2: The Number of Effective Hydrogen Bonds in Different Samples (Chen et al., 2020)

	Sample 1 (PU1, 75˚C)	**Sample 2 (PU2, 25˚C)**	**Sample 3 (PU2, 50˚C)**	**Sample 4 (PU2, 75˚C)**
Type 1	5	24	27	31
Type 2				2
Type 4	18	26	22	17
Type 5		4	3	1
Type 6	4	1		
Type 8	3			

Based on the Table 2.2, the number of effective hydrogen bonding for type 1 and 4 are relatively higher compared to other types of hydrogen bonding. This indicates that hydrogen bonding type 1 and 4 provide the strength for PU after self-healing mechanism is carried out (Chen et al., 2020).

2.7.4.4 Self-healing Capability of Asphalt Binder

This research uses the molecular dynamic simulation to examine the self-healing capability of the asphalt binder. In the simulation the asphalt model is constructed and the system is conducted at 1 atm and different temperatures are applied. The Mean Square Displacement (MSD) is applied to the model to study the self-healing capability of asphalt binder (Sun et al., 2016).

The MSD is used to indicate the diffusion coefficient of the asphalt binder. Figure 2.17 shows that the MSD value of asphalt binder at different temperature against simulation time.

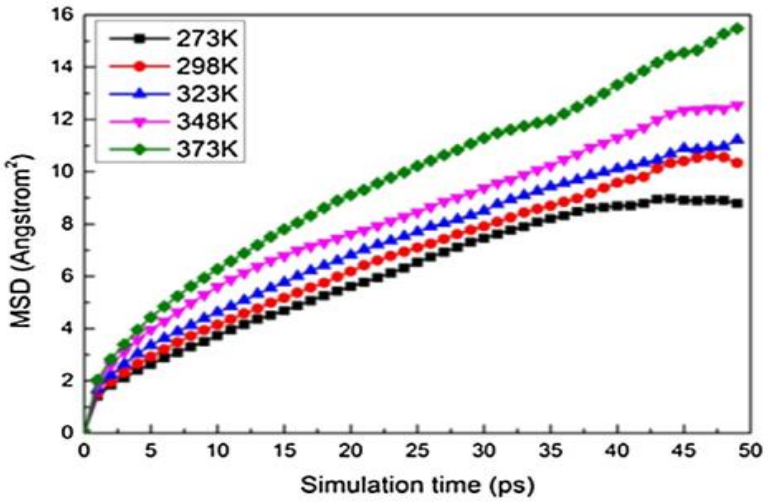

Figure 2.17: MSD Value of Asphalt Binder at Different Temperature against Simulation Time (Sun et al., 2016)

Table 2.3: Diffusion Coefficient of Asphalt Binders at Different Temperatures (Sun et al., 2016)

Temperature (K)	**273**	**298**	**323**	**348**	**373**
Diffusion Coefficient ($\mathbf{10^{-6}}\ \boldsymbol{cm^2/s}$)	2.835	3.147	3.218	3.500	4.298

Based on Table 2.3, the diffusion coefficient of asphalt binder increases with the temperature. This proves that the increase in temperature helps to facilitate the diffusion of asphalt binder and further promote the self-healing capability (Sun et al., 2016).

2.8 Summary

Hydrogels is a rubber-like gel which can carry out the self-healing mechanism to heal itself once it experiences any damages. The self-healing mechanism of hydrogel can be divided into two types which is the physically and chemically self-healing mechanism. The physically self-healing mechanism is the transportation of healing substances to the wound for recovery purposes while the chemically self-healing mechanism involves the reformation of bonding and molecular interaction. The hydrogel with self-healing mechanism can be produced using the principle of dynamic covalent bonding, non-covalent interaction and multi-mechanism interaction.

The most common classification of hydrogel can be done based on the source. The hydrogel can be classified into natural, synthetic and hybrid hydrogels. Natural hydrogel is the hydrogel which is produced from natural polymers such as gelatine while synthetic hydrogels are produced using man-made polymers. The hybrid hydrogels can be produced through the combination of natural and synthetic polymers.

Hydrogel are widely used in biomedical field. Hydrogel can be applied in the drug delivery system which helps to transport the drug to target tissues for treatment. It also can be used in tissue engineering. It can be used as the scaffold which protects the bioactive molecules during transportation, acts as the agent for vacant spaces filling and supports ideal tissue formation. Hydrogel also can be used as the biosensor which is very sensitive to the environment conditions and release of bioactive molecules once the critical condition is achieved.

There are five major production methods of hydrogel discussed in this research which are the free radical polymerisation, polymerisation by irradiation, chemical cross-linking, physical cross-linking of ion interaction and crystallisation. Free radical polymerisation is the chain reaction involving formation of radical, propagation and termination. The polymerisation by irradiation employed the high energy radiation for the polymerisation to be carried out. The chemical cross-linking involves the addition of a crosslinking agent to trigger the polymerisation to occur. The physical cross-linking of ionic interaction involves the principles of gelling of polyelectrolyte solution with a

multivalent ion of opposite charges. The synthesis of hydrogel through the crystallisation involves the repeated freezing-thawing process.

The self-healing performance of hydrogel can be studied through different experiments and simulation. The photography method, rheology testing and conductivity testing are the physical experiments which can be employed to observe and study the self-healing behaviour of hydrogels. For the simulation, the Material Studio is one of the suitable software which can be used to study various factors which affect the self-healing performance of hydrogel.

CHAPTER 3

METHODOLOGY AND WORK PLAN

3.1 Introduction

BIOVIA Material Studio is software with a complete modelling and simulation environment. It has the easy-to-use environment for modelling and evaluation of material performance. BIOVIA Material Studio provides a wide range of complete simulation capabilities from quantum, atomistic, mesoscale, statiscal, analytics and crystallisation tools (Sharma, Kumar and Chandra, 2019). It allows the researchers who focus on material science and chemistry to have better understanding on the relationship between molecular structure and material's atomicity. Material Studio is also useful for studying the molecular properties and behaviour of the material. This software can be employed in study on different material performance such as catalysts, polymers, alloys and pharmaceuticals (3ds.com, 2020).

There are several benefits of using the BIOVIA Material Studio software for material researchers. The researchers are able to use Material Studio software to replace physical experiments. This helps them to reduce experiment cost and time. The usage of Material Studio software also helps to accelerate the process to develop new material, modify material properties and performance. This helps to improve the research and develop efficiency at the same time. The researchers also can have better understanding on material properties, molecular structure and behaviour through the illustration via Material Studio software (Sharma, Kumar and Chandra, 2019). The Material Studio software also provide complement laboratory experimentation with powerful materials informatics (3ds.com, 2020).

3.2 Molecular Dynamic (MD) Simulation

Molecular Dynamic (MD) simulation is the powerful molecular modelling tool used recently for small molecules. Molecular modelling is the description of molecular interaction behaviour of physical systems. It is very important to connect the macroscopic and microscopic world which is supported with

statistical mechanics theory (Cuendet, 2008). The main objective of molecular dynamics is to simulate a model which demonstrates the actual changes in the molecule against the time once the energy is added to the sample molecule which is in the equilibrium state (Jakubowski, 2019).

The molecular dynamic has been cooperated with the ab initio electronic structure in simulation. This helps to produce the model with more realistic molecular interactions such as bond formation and bond breaking process (Kapral and Ciccotti, 2005). The al initio also helps to minimise the molecular structure of small molecules while the energy of large molecular structure molecules is minimized using the molecular mechanics which is based on Newton's Law. The summation of energy for overall atoms, molecular interaction and bonding between molecules is calculated using the force field created which provides all the parameters required for the calculation. In the calculation for energy minimisation, the atomic position in the molecule must be systematically and randomly moved. The energy of the simulation model is calculated repeatedly until the lowest energy is obtained and indicates that the molecule produced is stable. The energy minimisations is done in the condition of without solvent. CHARMM, AMBER and GROMOS are the common type of force field used. Other parameters such as atomic mass and bond length are normally obtained through the experiments and theoretical calculations (Jakubowski, 2019).

3.3 Simulation Details

In the molecular dynamic (MD) simulation, the polyacrylamide/polyvinyl (PAM/PVA) alcohol hydrogel is selected as the target hydrogel in this study.

3.3.1 Model Developing of PAM & PVA Polymer Chain

The Material Studio Visualizer module in Materials Studio is used for this MD simulation. Material Studio Visualizer module is the main modelling system of Material Studio. The module provides the complete tools which are essential for the construction of graphical models of molecules, crystalline materials and polymers. The analytic tools provided enable the models being viewed and analyse easily (University of Minnesota, 2020). The PAM polymer chain with

35 monomers and PVA chain with 40 monomers were formed. The carbon atoms at the end of the polymer chain were added with hydrogen to become saturated. The Smart Minimizer was also applied to the polymer chain form to obtain the stable configuration.

3.3.2 Model Developing of PAM/PVA Hydrogel

Once both the PAM and PVA were done, the Amorphous Cell was employed for the PAM/PVA hydrogel modelling. Amorphous Cell is the module which is mostly used for the construction and prediction of material property for the amorphous materials such as polymers (University of Minnesota, 2020). The number of polymer chains for the amorphous cell were set to 2 PAM and 2 PVA chain in order to minimise the model size. The COMPASS (Condensed-phased, Optimized Molecular Potential for Atomistic Simulation Studies) force field was employed for the simulation calculation. COMPASS is the general and all-atom force field atomic simulation. This force field was developed with the empirical parameterization technique and state-of-the-art ab initio (Sun, 1998). The model with different water content is constructed by using the information in Table 3.1.

Table 3.1: Parameters of PAM/PVA Hydrogel with Different Water Content

Water Content (%)	**0**	**20**	**40**	**60**	**80**
Number of Water Molecule	0	106	283	635	1695
Density (g/cc)	1.12	1.08	1.04	1.03	1.02

After the models were constructed, the models were then optimised using the Energy Minimize in order to keep the energy of the model steady and the molecular configuration of the model at stable condition (Wei et al., 2015a). After the optimisation of the model, the annealing process was carried out where the PAM/PVA hydrogel model was constructed using the NPT(number of particles, pressure and temperature) at 1 atm and 298 K and followed by NVT (number of particles, volume and temperature) at 298 K with the time step of 1 fs for 50 ps. The Newton equation of motion was solved by using the Andersen thermostat with the velocity Verlet integration. This is to produce the models to

reach the equilibrium state where the density, temperature and energy have achieve the stable condition as shown in Figure 3.1(Chen et al., 2020). The effect of temperature on the self-healing performance of hydrogels can be evaluated by varying the set temperature (Wei et al., 2015a). After the annealing process, the models were run using Forcite dynamic NVT module at different temperature to carry out the study of of temperature and hydrogel water content to the self-healing process.

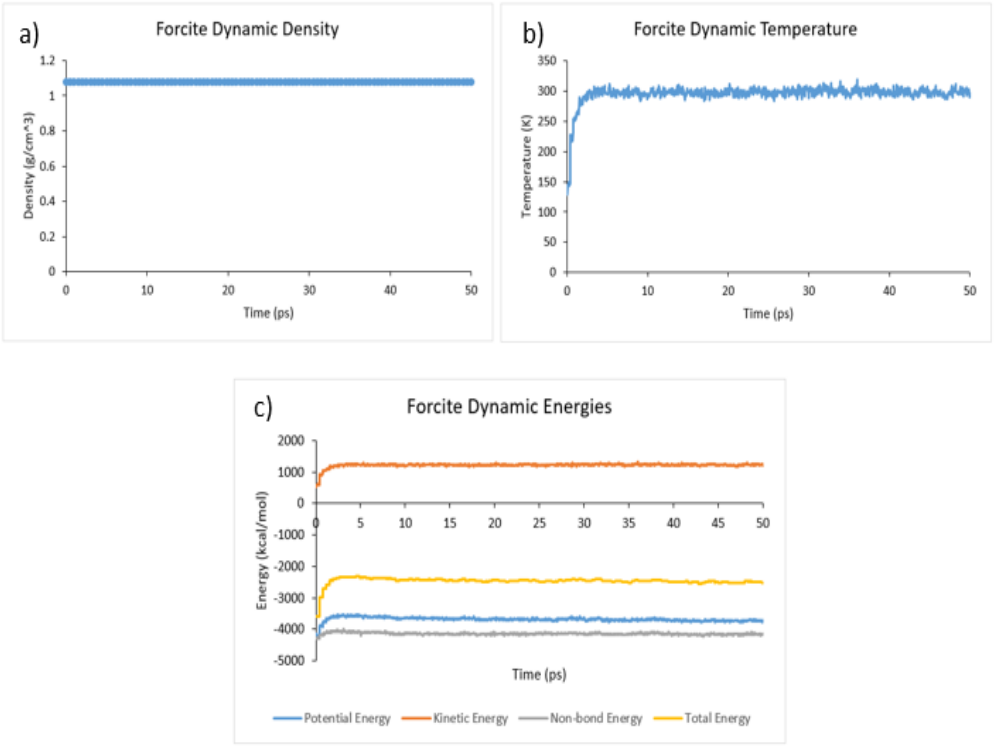

Figure 3.1: (a) Density Profile; (b) Temperature Profile; (c) Energy Profile as the Function of Time

3.4 Characterisation

3.4.1 Mean Square Displacement (MSD)

Mean Square Displacement (MSD) is the most prominent performance in molecular dynamic simulation. The usage of MSD is to calculate the dynamic characteristic of different molecules and atoms in the system. The MSD in the molecular dynamic simulation represents the motion of PVA molecules. The MSD can be used in order to study the healing capability of hydrogel. The temperature in the simulation can be varied to study the effect of temperature to

the healing capability of hydrogel. The MSD is increases with time and it is related to the diffusion coefficient, D. The slope of MSD against simulation time can be used to determine the diffusion coefficient of a particle which helps to indicate the self-healing capability of hydrogel. The diffusion coefficient can be simplified to:

$$D = \frac{a}{6} \tag{3.1}$$

Where a is the gradient of straight line fitted by MSD versus time (Sun et al., 2016).

3.4.2 Radial Distribution Function (RDF)

Qu et al. (2019) claimed that "The radial distribution function is the probability of finding a pair of atoms at a distance r apart relative to the probability for a completely uniform distribution." It can be used to determine the distance of the atoms apart from the polymer chain as shown in Figure 3.2. It also helps to study the molecular aggregation state of hydrogel (Qu et al., 2019).

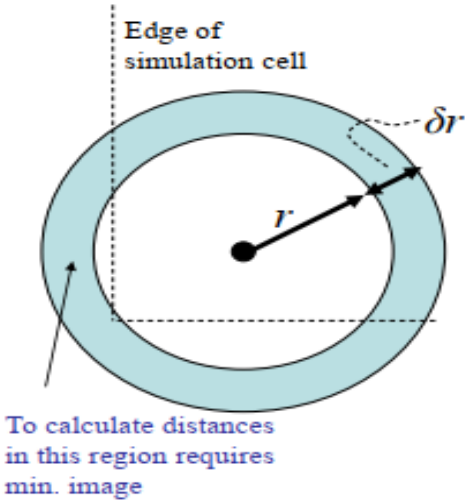

Figure 3.2: Illustration of Radial Distribution Function (RDF) (Willock, 2014)

CHAPTER 4

RESULT AND DISCUSSION

4.1 Diffusion Coefficient of Pure PAM, Pure PVA and PAM/PVA Hydrogel with 80% Water Content.

In this section, the diffusion coefficient of pure PAM, pure PVA and PAM/PVA hydrogel with 80 % water content is studied. The models were constructed and run using the Forcite NVT module at 298 K. Figure 4.1 shows the MSD values against simulation time obtained from the simulation. According to Figure 4.1, as the temperature increases, the MSD value of all of the models is also increased. After the graph is plotted, the diffusion coefficient of three models are calculated by using Equation 3.1 and the result is tabulated in Table 4.1.

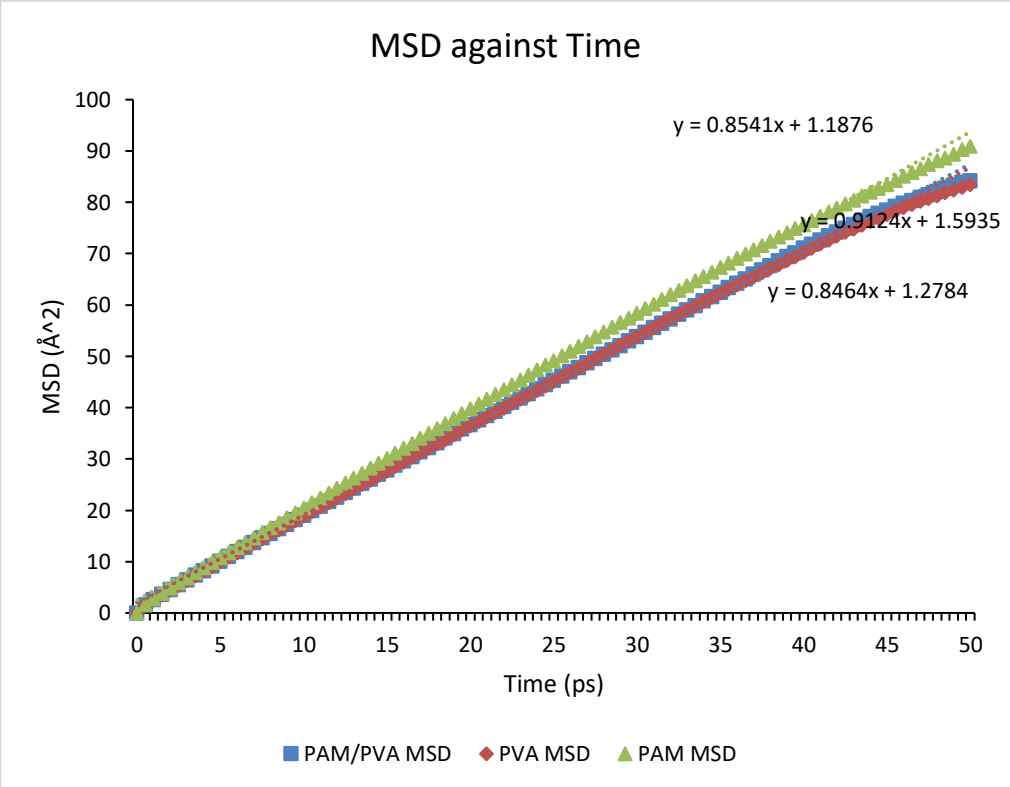

Figure 4.1: Graph of MSD against Time of Different Models.

Table 4.1: Diffusion Coefficient of Pure PAM, Pure PVA and PAM/PVA Hydrogel with 80% Water Content

Model	**PAM**	**PVA**	**PAM/PVA**
Diffusion Coefficient ($\mathbf{10^{-5}}\ \frac{cm^2}{s}$)	1.5207	1.4107	1.4235

Table 4.1 shows that the diffusion coefficient of pure PAM hydrogel model is highest, followed by PAM/PVA hydrogel model and lastly is the pure PVA hydrogel model. This shows that the pure PAM hydrogel model has the highest self-healing capability as the highest diffusion coefficient for transportation of molecules during self-healing process meanwhile the pure PVA has lowest self-healing capability. Although these three model has quite similar diffusion coefficient, however the PAM/PVA hydrogel is selected in this study due to its better overall performance. The PAM/PVA blends hydrogel has better thermal stability and stronger mechanical strength as compare to pure polymer hydrogel. This is due to the formation of hydrogel bonding between the PAM and PVA polymers (Patel and Sureshkumar, 2014). Thus, the PAM/PVA blends hydrogel is more commonly used in real-life as it has better characteristic and performance as compare to pure PAM and pure PVA hydrogel.

4.2 Effect of Temperature on Self-healing Behaviour of PAM/PVA Hydrogel

4.2.1 Diffusion Coefficient

The self-healing capability of hydrogel can be determined using the MSD value. In order to study the effect of temperature on MSD value of the PAM/PVA hydrogel, the 80 % water content PAM/PVA hydrogel was simulated using the Forcite module of Material Studio under the NVT at different temperatures. Figure 4.2 shows the MSD values against simulation time obtained from the simulation. The best fitted linear line of the MSD value is plotted and the equations of the fitted line are shown. Based on Figure 4.2, as the temperature increases, the MSD value of the model is also increased.

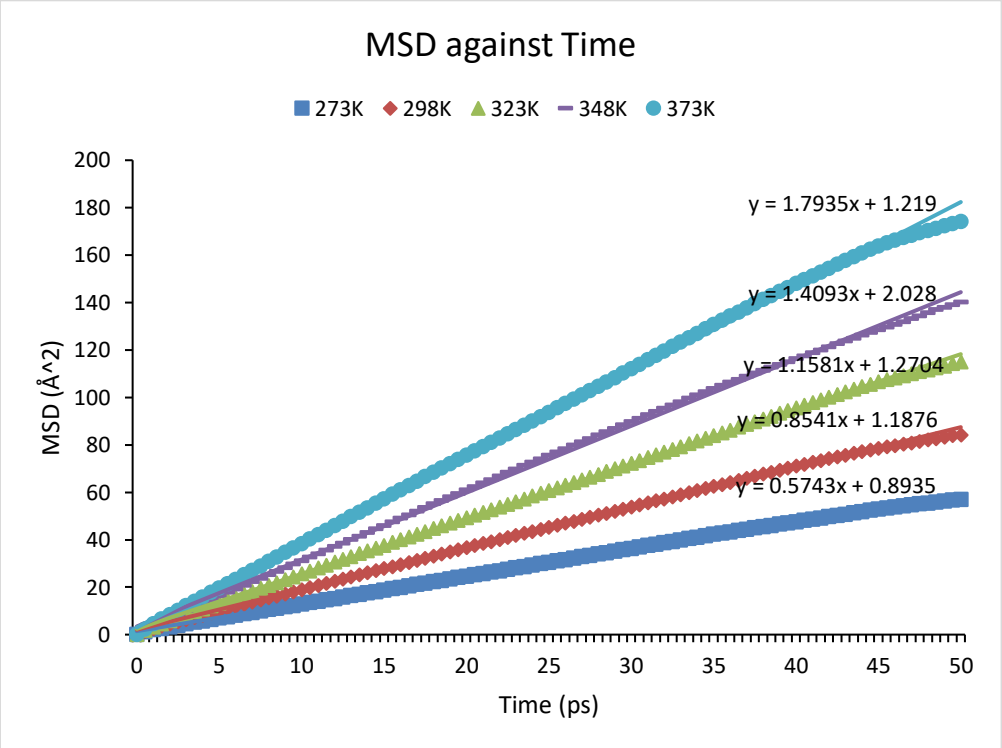

Figure 4.2: Graph of MSD against Time of PAM/PVA Hydrogel at Different Temperature.

The diffusion coefficient is then calculated using equation 3.1 and The diffusion coefficient of the models within the 80 % water content PAM/PVA hydrogel is tabulated in Table 4.2.

Table 4.2: Diffusion Coefficient within 80 % Water Content PAM/PVA Hydrogel Model at Different Temperature.

Temperature (K)		**273**	**298**	**323**	**348**	**373**
Diffusion Coefficient ($\mathbf{10^{-5}}\ \frac{\boldsymbol{cm^2}}{\boldsymbol{s}}$)		0.9572	1.4235	1.9302	2.3488	2.9892

Based on Table 4.2, as the temperature increases from 273 K to 373 K, the diffusion coefficient within 80 % water content PVA/PAM hydrogel also increases. According to Arrhenius Equation (Equation 4.1), the diffusion coefficient is temperature dependent factor (Bag, Yap and Wohland, 2014).

$$\mathrm{D} = Ae^{(\frac{-E_a}{RT})} \tag{4.1}$$

Where D is the diffusion coefficient, A is the pre-exponential factor, E_a is the activation energy, R is the universal gas constant and T is the temperature.

As the temperature increase, the diffusion coefficient will also increase. According to Wei et al. (2015), as the temperature increase, the energy needed to form or break down the interaction force between PAM/PVA hydrogel molecules decreases. The intermolecular forces within PAM/PVA hydrogel is also decreased as the temperature increases (Wei et al., 2015a). According to collision theory, as the temperature increases, the collision between the molecules will also increase and cause an increase in the effective collision of the molecule within the hydrogel. At the same time, high temperature cause the flexibility of hydrogel to increase and causes increases in the space for diffusion (Wang et al., 2017). Thus, the diffusion coefficient increases as the temperature increases. In the self-healing mechanism of the hydrogel, the "mobile phase" will be responsible for transporting the molecules or substances to the crack area to carry out the self-regeneration process (Yuan and Wang, 2017). The higher the diffusion coefficient, the higher the transportation rate of the molecules. Thus, the self-healing rate is higher at the high temperature.

4.2.2 Self-healing Time

The self-healing time can be determined by constructing the model with a crack interface and running under different temperatures. The bilayer was built using the 80 % water content PAM/PVA hydrogel model with a 10 Å vacuum crack in between as shown in Figure 4.3. The model is then run using Forcite module NPT at 1 atm and different temperatures for 50 ps. The self-healing time is defined as the time where the crack surface becomes in contact with each other. Figure 4.4 and 4.5 show the models at 3 ps and 50ps.

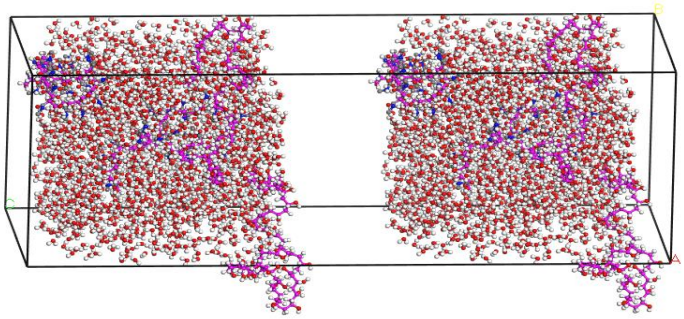

Figure 4.3: Molecular Models of 80 % Water Content PAM/PVA Hydrogel with 10 Å Crack at 0 ps

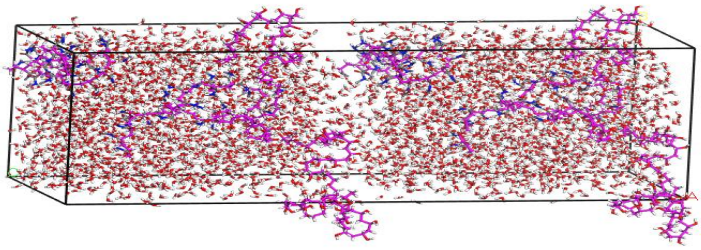

Figure 4.4: Molecular Models of 80 % Water Content PAM/PVA Hydrogel at 3 ps

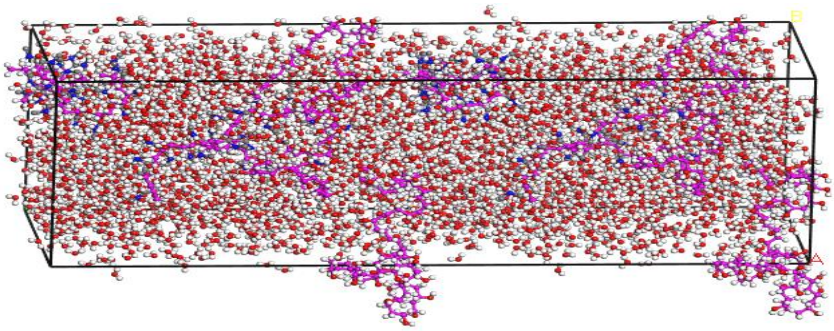

Figure 4.5: Molecular Models of 80 % Water Content PAM/PVA Hydrogel at 50 ps

In Material Studio, the self-healing time is determined using the density graph obtained after the models are run using Forcite NPT module. The time needed for the model to obtain constant density is known as self-healing time for the hydrogel as shown in Figure 4.6. The interception of red lines in Figure 4.6 represents the self-healing time for the hydrogel model.

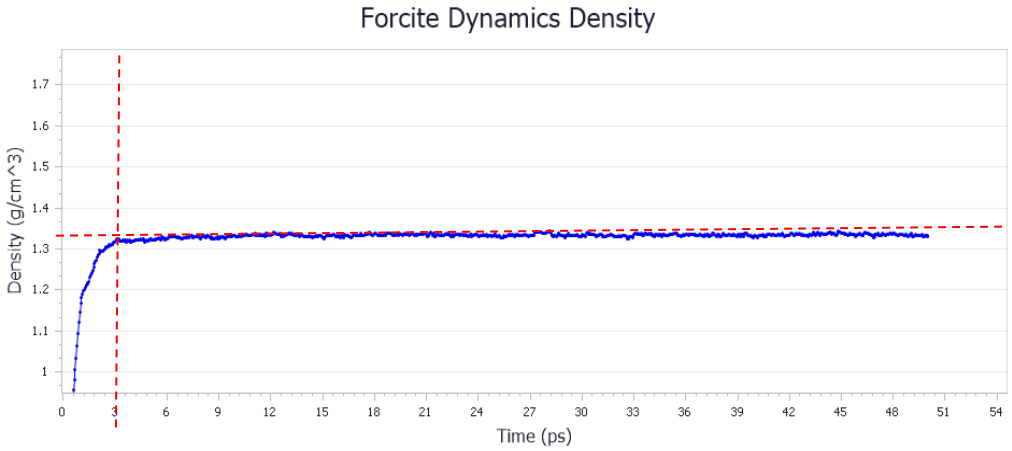

Figure 4.6: Forcite Dynamics Density Graph and Self-healing Time Determination

Table 4.3: Temperature against Self-healing Time of Hydrogel

Temperature (K)	**273**	**298**	**323**	**348**	**373**
Self-healing Time (ps)	3.45	3.18	2.70	2.54	2.33

The self-healing time for 80 % water content PAM/PVA hydrogel at different temperatures is tabulated in Table 4.3. According to the result, the higher the temperature, the shorter the self-healing time. This is due to the increase in temperature cause the diffusion coefficient of the molecules to increase and further increase the self-healing rate of the hydrogel. Thus, the self-healing time of the hydrogel decreases as the temperature increases. According to Chen et al. (2020), a similar method is applied to study the self-healing capability of polyurethane elastomer under different temperatures. The result shows that polyurethane with different characters has different self-healing capabilities at different temperatures. The polyurethane elastomer does not have self-healing capability at a lower temperature but the self-healing process is carried out at a higher temperature (Chen et al., 2020).

4.2.3 Molecular Aggregation

The radial distribution function, RDF can be used to study the molecular aggregation of PAM/PVA hydrogel molecules. In this case, RDF is used to study the distribution of PAM/PVA hydrogel at different radius from the referencing point. The PAM/PVA hydrogel with 80 % water content is used. The models are analysed after running using the Forcite NVT module at different temperatures. The RDF value for models at different temperatures is shown in Figure 4.7.

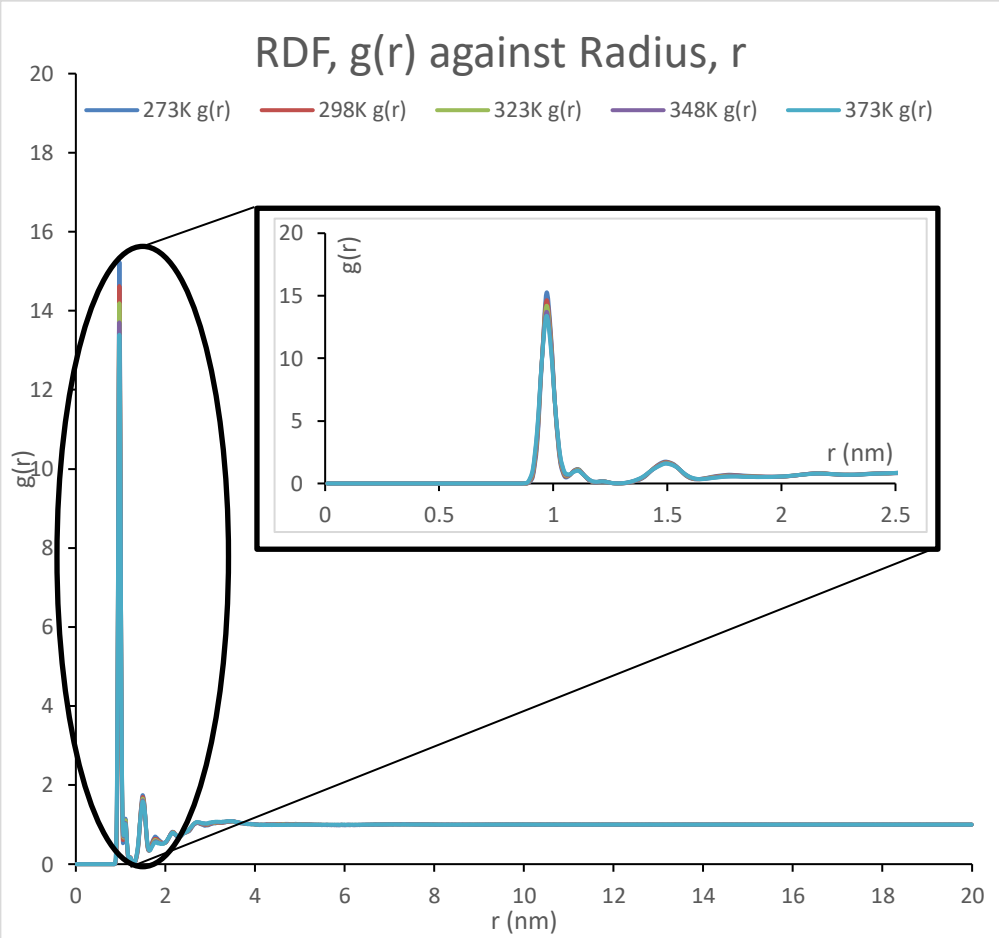

Figure 4.7: The Graph of Radial Distribution Function, RDF at Different Radius for 80 % Water Content PAM/PVA Hydrogel at Different Temperature.

The result showed that there are three peaks obtained at the radius less than 2 nm which are at 0.97 nm, 1.11 nm and 1.51 nm. For the radius exceeding

2 nm, the RDF values for the models at different temperatures fluctuate at the value around 1. In order to study the relationship between molecular aggregation of hydrogel and the self-healing behaviour, the graph of radial distribution function (RDF) value (maximum peak) against temperature at different molecular radius is plotted (Figure 4.8).

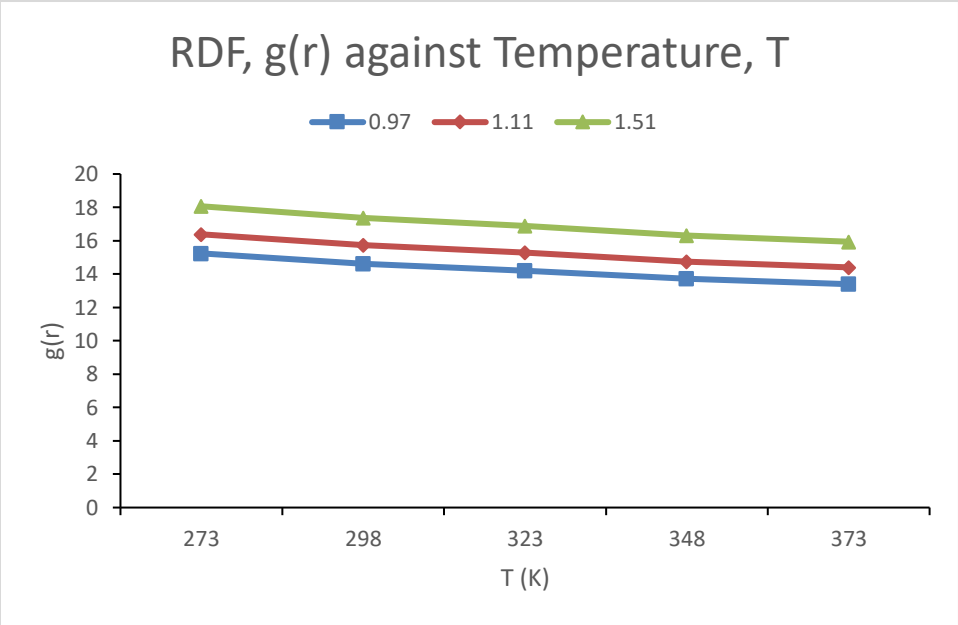

Figure 4.8: The Graph of Radial Distribution Function (RDF) Value (maximum peak) against Temperature at Different Molecular Radius.

According to the result, as the temperature increases, the RDF value is decreasing. This indicates that the hydrogel is less dense at a higher temperature. As the hydrogel is less dense, the hydrogel becomes less compact and the spacing in between the hydrogel is bigger. The bigger spacing between hydrogels easier the diffusion process be carried out within hydrogel. Higher temperature also provide higher energy to hydrogel to carry out the diffusion process. Thus, the diffusion coefficient of the hydrogel is higher and the self-healing rate is higher at high temperature conditions.

4.3 Effect of Water Content on Self-healing Behaviour of PAM/PVA Hydrogel

4.3.1 Diffusion Coefficient

In order to study the effect of water content on the self-healing capability of PAM/PVA hydrogel, the PAM/PVA hydrogel with 0 %, 20 %, 40 %, 60 %, and 80 % water content was run using the Forcite module under NVT at 298 K. Figure 4.9 shows the graph of MSD value against the time of PAM/PVA hydrogel with different water content. Based on Figure 4.9, as the hydrogel water content increases, the MSD value will also increase.

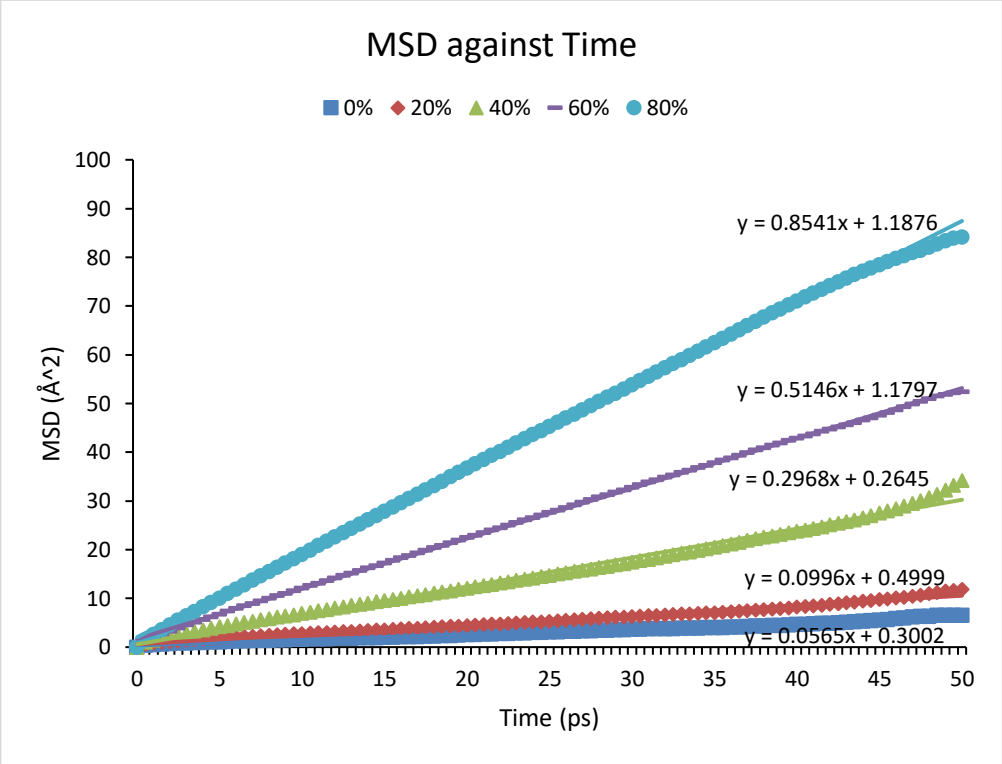

Figure 4.9: Graph of MSD against Time of PAM/PVA Hydrogel with Different Water Content.

Table 4.4: Diffusion Coefficient of PAM/PVA Hydrogel Model with Different Water Content.

Water Content (%)	**0**	**20**	**40**	**60**	**80**
Diffusion Coefficient $(\mathbf{10^{-5}}\ \boldsymbol{cm^2/s})$	0.0942	0.1660	0.4947	0.8577	1.4235

The diffusion coefficient of PAM/PVA with different water content is calculated and tabulated in Table 4.4. From the result obtained, as the water content increases, the diffusion coefficient in hydrogel also increases. As mentioned in the previous part, the transportation of molecules for the self-healing process is carried out by the "mobile phase" within the hydrogel. The transportation of the molecule can be enhanced by increasing the water molecule present in the hydrogel. Thus, the diffusion coefficient increases as the hydrogel water content increases. However, the water content of hydrogel has a less significant effect on the diffusion coefficient within the system with fewer water molecules. Once the water content of hydrogel reaches a certain level, the effect of hydrogel water content on the diffusion coefficient will become more obvious (Wei et al., 2015b).

4.3.2 Self-healing Time

In the study of the hydrogel water content to the self-healing time, the five PAM/PVA hydrogel models with 10 Å vacuum crack were constructed using hydrogels with different water content as shown in Figure 4.10 and the condition of hydrogel models at 3 ps is shown in Figure 4.11.

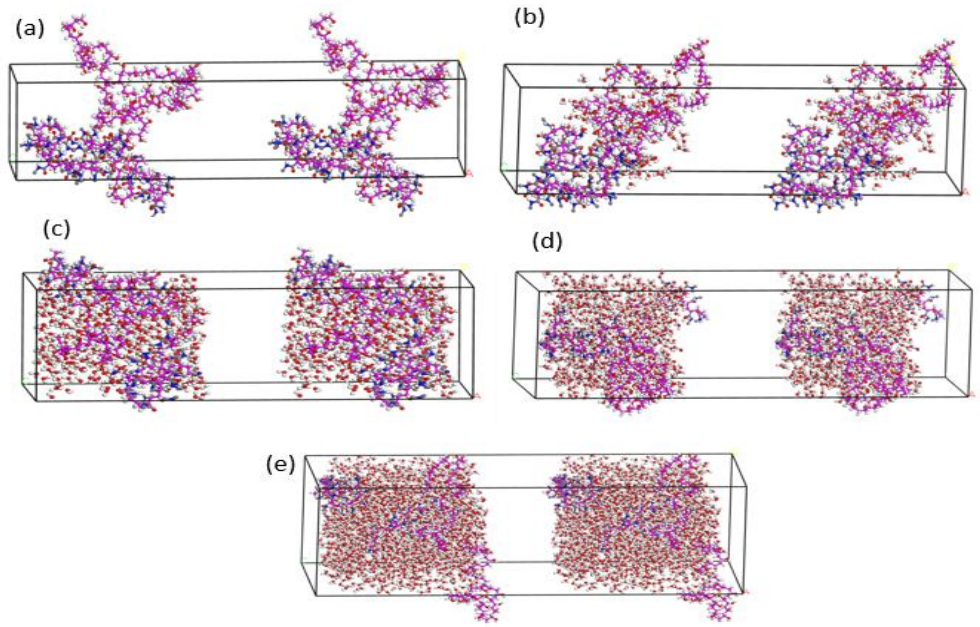

Figure 4.10: Different Water Content PAM/PVA Hydrogel Model at 0 ps. a) 0 %; b) 20 %; c) 40 %; d) 60 %; e) 80 %

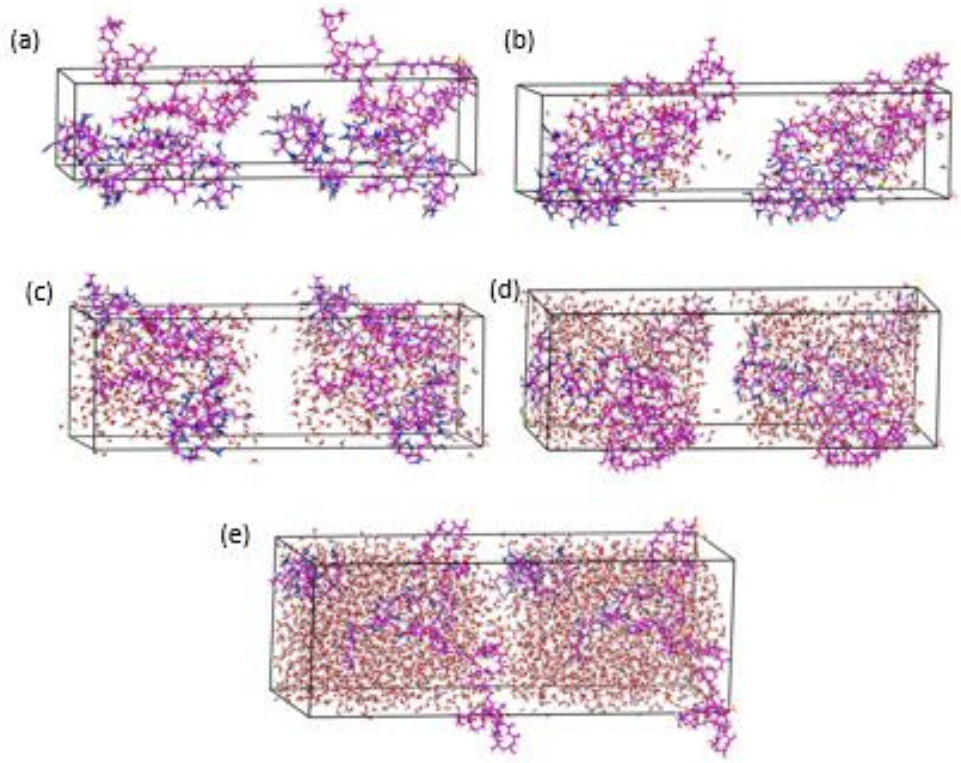

Figure 4.11: Different Water Content PAM/PVA Hydrogel Model at 3 ps. a) 0 %; b) 20 %; c) 40 %; d) 60 %; e) 80 %

After the models are constructed, the models are run using Forcite NPT module at 298 K and 1 atm for 50 ps. The time required for the models to obtain constant density is determined as the self-healing time for the models. After the self-healing process is carried out by the hydrogels, the crack disappears and the hydrogel layers contact with each other as shown in Figure 4.12. The time required for the models with different water content to obtain stable density is tabulated in Table 4.5.

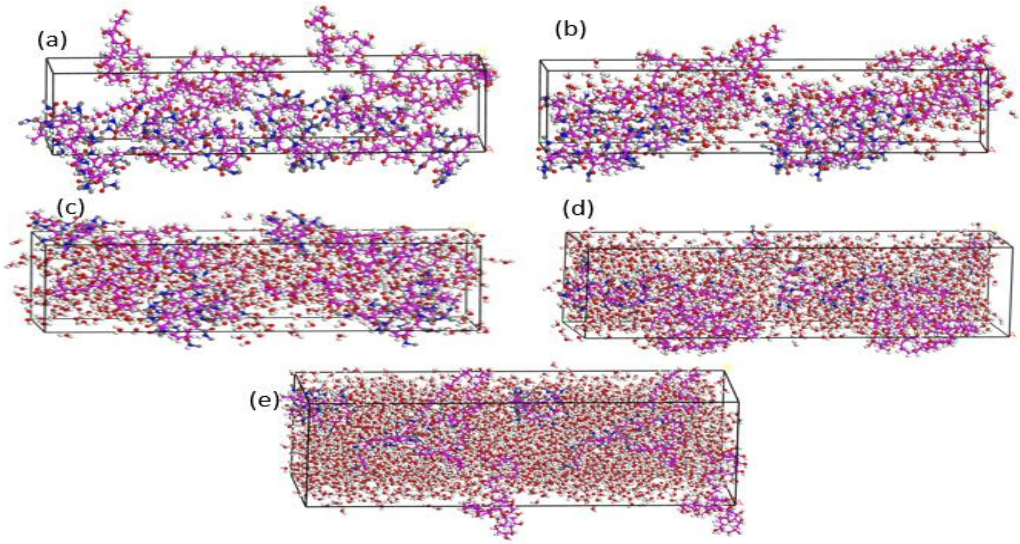

Figure 4.12: Different Water Content PAM/PVA Hydrogel Model after Self-healing Process. a) 0 %; b) 20 %; c) 40 %; d) 60 %; e) 80 %

Table 4.5: Self-healing Time for PAM/PVA Hydrogel Model with Different Water Content

Water Content (%)	**0**	**20**	**40**	**60**	**80**
Self-healing Time (ps)	8.22	5.94	5.19	3.45	3.18

According to the result shown in Table 4.5, as the water content of the hydrogel increases, the time required for the models to carry out the self-healing process is shorter. As mentioned in the previous session, the diffusion coefficient of the molecules can be enhanced by the hydrogel water content. At the same time, the higher the water content in the hydrogel, the more water molecules available to form hydrogen bonding during the self-healing process. This helps to speed up the self-healing process carried out by hydrogel.

4.3.3 Molecular Aggregation

In this section, the relationship between the molecular aggregation of hydrogel with different water content and the self-healing rate of the hydrogel is studied. In this study, the PAM/PVA hydrogels with different water content are run using Forcite NVT module at 298 K. The radius distribution function of the hydrogels with different models is analysed. Figure 4.13 shows the RDF values of the PAM/PVA hydrogel with different water content.

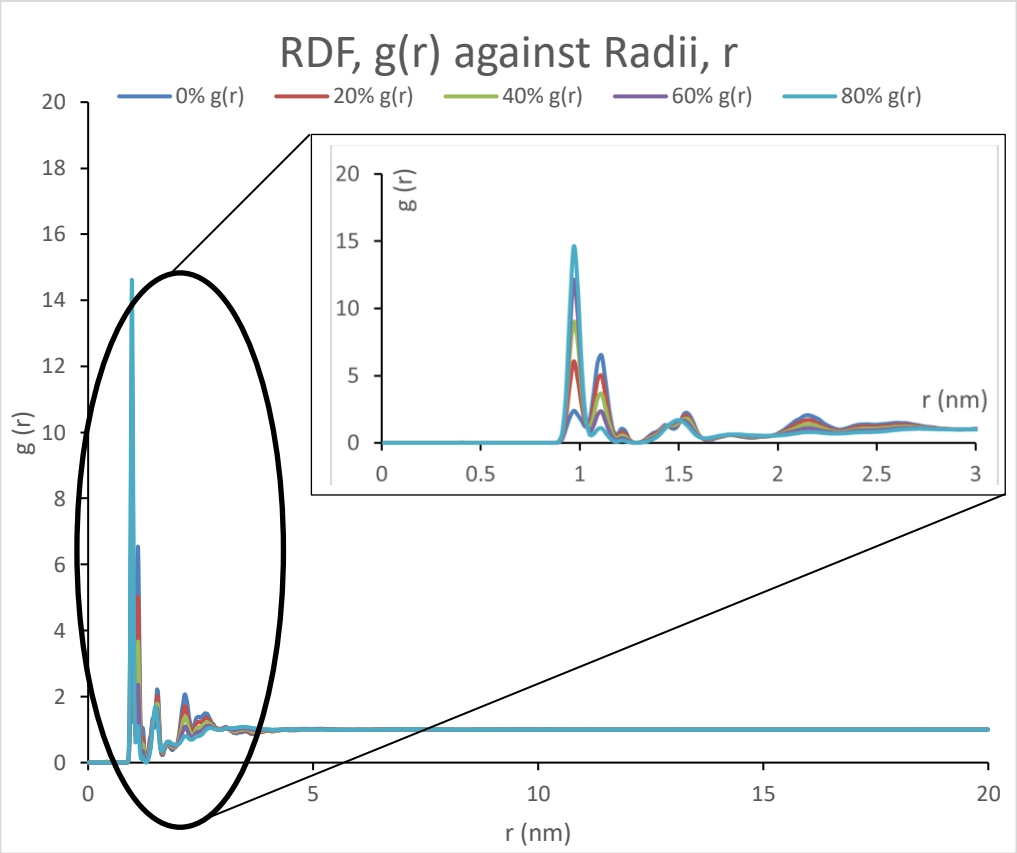

Figure 4.13: The Graph of Radial Distribution Function, RDF of PAM/PVA Hydrogel with Different Water Content at 298 K.

Figure 4.13 shows that five maximum peaks are obtained at a radius less than 3 nm. For the radius more than 3nm, the RDF value is fluctuated at around 1. However, some of the maximum points of the graph are obtained at different radii for the hydrogel with different water content. Thus, the PAM/PVA hydrogel with 0 % water content is used as the reference. In order to study the relationship between molecular aggregation and hydrogel diffusion coefficient, the graph of radial distribution function (RDF) value for the model at the molecular radius where the maximum values are obtained for 0 % water content PAM/PVA hydrogel against the diffusion coefficient of the hydrogel is plotted as shown in Figure 4.14.

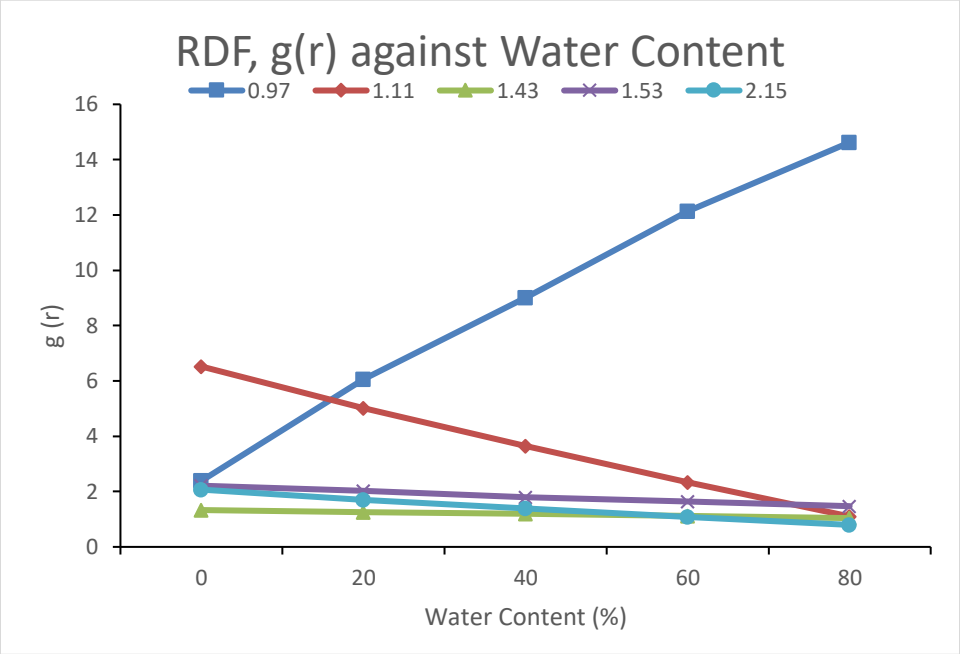

Figure 4.14: The Graph of Radial Distribution Function (RDF) Value at the Molecular Radius for the PAM/PVA Hydrogel where the Maximum Values are Obtained against the Hydrogel Water Content.

According to the result in Figure 4.14, for the radius of 0.97 nm, it shows that the higher the hydrogel water content, the higher the RDF value of the models. Meanwhile, for the radius of 1.11 nm, 1.43 nm, 1.53 nm and 2.15 nm, it gives the opposite trend with 0.97 nm where the higher the hydrogel water content, the lower the RDF value. Based on the overall result, as the water content increases, the ratio of water to PAM/PVA polymer increases causes the RDF value which indicates the distribution of PAM/PVA polymer decreases. More “mobile phase” available to carry the self-healing subtances to the damage area as the hydrogel water content increase . Thus, the diffusion process is easier to be carried out and has better self-healing performance. The molecular aggregation at 0.97 nm which gives the opposite trend may be due to some other factors such as the areas studied is too small which causes the result to become not significant.

4.3.4 Activation Energy and Pre-exponential Factor

In this study, the activation energy and pre-exponential factor of PAM/PVA hydrogel with different water content are determined. The activation energy and pre-exponential can be determined using Equation 4.1

There are some assumptions made in order to apply the Arrhenius equation to determine the activation energy and pre-exponential factor. The assumptions are the physical properties of the polymers are not affected by the water diffusion and the activation energy calculated is independent of temperature (Wang et al., 2020b).

In order to study the relationship between hydrogel water content and activation energy of the hydrogel, the PAM/PVA hydrogel with 0 %, 20 %, 40 %, 60 % and 80 % water content was run using Forcite NVT module at five different temperature which are 273 K, 298 K, 323 K, 348 K and 373 K in order to obtain the diffusion coefficient. After the diffusion coefficient of water molecule within hydrogel is obtained, the graph $\ln D$ against $\frac{1}{T}$ is plotted as shown in Figure 4.15. The activation energy and pre-exponential factor are obtained using the gradient and the y-intercept of the graph based on the Equation 4.2.

$$\ln D = \ln A - (\frac{E_a}{R})(\frac{1}{T}) \qquad (4.2)$$

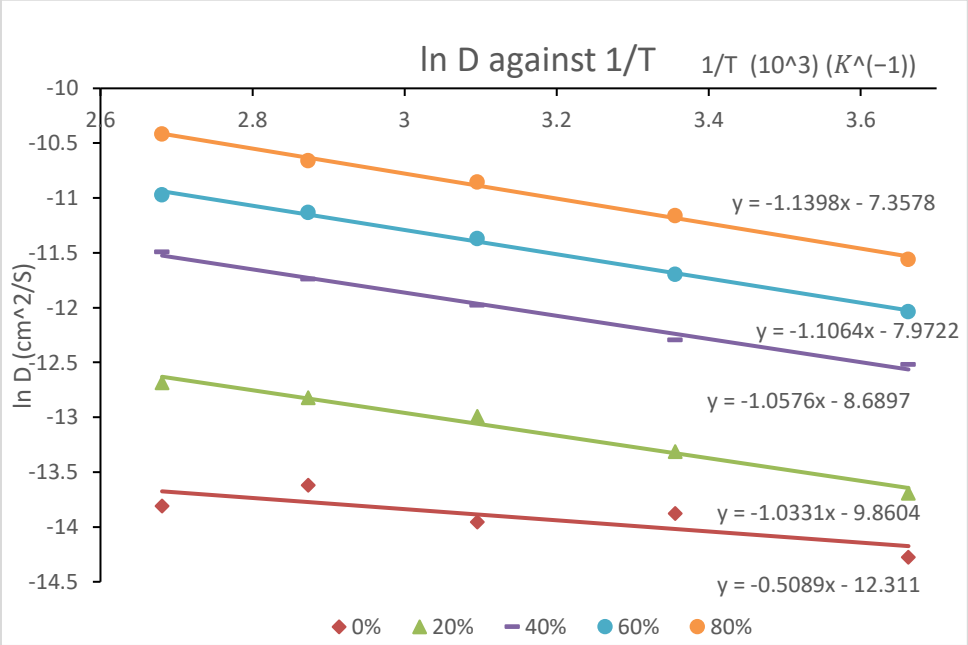

Figure 4.15: Graph of ln D against 1/T of Hydrogel with Different Water Content

Based on the equation shown in Figure 4.15, the pre-exponential factor is calculated by using exponential of y-intercept while the gradient of the graph multiply with the universal gas constant is the activation energy. The activation energy and the exponential factor for the hydrogel with different water content are tabulated in Table 4.6.

Table 4.6: Activation Energy and Pre-exponential Factor for Hydrogel with Different Water Content

Water Content (%)	**Activation Energy (kJ/mol)**	**Pre-exponential Factor ($10^{-5}\ cm^2/s$)**
0	4.2311	0.4502
20	8.5892	5.2201
40	8.7929	16.8311
60	9.1986	34.4919
80	9.4763	63.7600

According to Table 4.6, the result shows that the hydrogel water content is proportional to the activation energy and the pre-exponential factor of the PAM/PVA hydrogel. As the water content in the hydrogel increases, the

activation energy of the hydrogel also increases. According to Wei et al. (2015), the electrostatic forces within PAM/PVA hydrogel increases as the water content increases. This is due to the increase in water content leading to the hydrogen bonding formed within the hydrogel increases. The increase in hydrogen bonding causes the intermolecular forces in the hydrogel to become stronger. Thus, more energy is required for the formation and deformation of hydrogen bonding in order to carry out the self-healing process. The pre-exponential factor is defined as the number of collisions between molecules increases as the water content of hydrogel increases. This is due to the increase of water content causing the reduction of free volume fraction within the hydrogel (Chen et al., 2013). As the free volume decreases, the hydrogel becomes more compact. This causes the probability of collision between molecules within the hydrogel to increase. Thus, the pre-exponential factor increases as the hydrogel water content increases.

4.4 Summary

According to the result, the hydrogel works best at the highest temperature which is 373K. It has higher diffusion coefficient which enables the diffusion rate within the hydrogel to become higher. The hydrogel is also less dense at a higher temperature. This makes the hydrogel become less compact and has a bigger space for diffusion to be carried out. As the diffusion rate becomes higher, the time needed for the self-healing process is shorter. Thus, the self-healing capability for the hydrogel at high temperatures is higher.

The result also shows that the hydrogel with 80% water content has the best self-healing performance. The water content enhances the diffusion rate of the hydrogel. Thus, the diffusion rate for hydrogel with higher water content is higher. In addition, the hydrogel becomes less dense as the water content increases. This makes the hydrogel become less compact and the diffusion is easier to be carried out. As the diffusion rate of the self-healing molecules increases, the time required for the self-healing process becomes shorter. This causes the hydrogel with higher water content to have better self-healing capability.

CHAPTER 5

CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

In this research, the self-healing process of the hydrogel is studied and the self-healing performance of polyacrylamide/polyvinyl alcohol (PAM/PVA) hydrogel is evaluated. The self-healing properties of the hydrogel are successfully evaluated using the molecular dynamic method through the Material Studio software.

By using Material Studio software, the PAM/PVA hydrogel was constructed and the indices to study the self-healing behaviour of hydrogel was determined. According to the simulation, the diffusion coefficient is one of the useful parameters to evaluate the self-healing behaviour of hydrogel. The activation energy and the pre-exponential factor of the hydrogel models are the other parameters that can be used to study the self-healing property of hydrogel.

Lastly, the simulation shows that the temperature and water content have a significant effect on the self-healing performance of PAM/PVA hydrogel. At high temperatures, the hydrogel is less dense and the diffusion coefficient is high compared to the low temperature environment. As the diffusion coefficient of the hydrogel is higher, the diffusion rate of molecules also will be higher. Thus, the duration of the self-healing process is shorter. For hydrogel water content, the lower the hydrogel water content, the denser the hydrogel. The diffusion coefficient is lower and the diffusion rate of the molecule also will be lower causes the duration of the self-healing process is longer for the hydrogel with low water content. On the other hand, the pre-exponential which indicates the collision of molecules and the activation energy is low for the hydrogel with low water content. This demonstracted that a hydrogel with low water content forms less hydrogen bonds.

5.2 Recommendations for Future Work

In this study, the relationship between temperature and hydrogel water content with the self-healing property of hydrogel is studied. However, there many parameters are still required to be studied in order to apply this type of hydrogel for clinical use. The environment pH value which may cause the degradation of polymer cause the hydrogel to lose its shape and swelling capability. Besides that, the mechanical strength of the hydrogel is another concern for the application of hydrogel. The hydrogel with low mechanical strength only can be used in a limited area. The mechanical strength of the hydrogel can be affected by several factors such as the type of monomer used to synthesis the hydrogel and the molecular percentage of the polymer chain. This is due to the type of polymer chain used will vary the electrostatic forces between the molecules and further cause the difference in the hydrogel mechanical strength. Lastly, the hydrogel production technique applied to produce the hydrogel also will affect the physical and chemical properties of the hydrogel.

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APPENDICES

Sample Calculation for Diffusion Coefficient

From Figure 4.1,

The line equation for PAM/PVA hydrogel,

$$y = 0.9124x + 1.5935$$

From Equation 3.1,

Diffusion Coeffcient, $\mathrm{D} = \frac{a}{6}$

$$\mathrm{D} = \frac{0.9124}{6}$$

$$\mathrm{D} = 1.4235$$

Sampla Calculation for Activation Energy and Pre-exponential Factor

From Figure 4.15,

The line equation for 80 % water content PAM/PVA hydrogel,

$$y = -1.1398x - 7.3578$$

From Equation 4.2,

$$\ln D = \ln A - \left(\frac{E_a}{R}\right)\left(\frac{1}{T}\right)$$

For pre-exponential factor,

$$\ln A = -7.3578$$

$$A = e^{-7.3578}$$

$$= 63.79 \times 10^{-5}\ cm^2/s$$

For activation exnergy,

$$-\left(\frac{E_a}{R}\right) = -1.1398$$

$$E_a = 1.1398R$$

$$= 1.1398(8.314\ J/mol \cdot K)$$

$$= 9.4763\ kJ/mol$$