FCO. VAZQUEZ

THIS IS THE TITLE OF THE THESIS

Contents

1

Introduction

Scope of the Thesis   In this thesis, the general objective is to explore the relation between the topological features commonly seen in hydrogels with the properties of the polymer network, such as elasticity and yield stress. . . . we use molecular dynamic simulations . . . we focus on the cross-linking mechanisms.

From materials to hydrogels   Materials -> soft matter -> Polymeric Networks -> Gels -> Hydrogels. Bunch of atoms. Length scales. Rehology response to clasiffy the materiales. Phases of materials.

Curiosity/phenomenology   Paragraph that will tell the reader that hydrogels are cool. Talk about solid/liquid behaviour. Non newtonian materials.
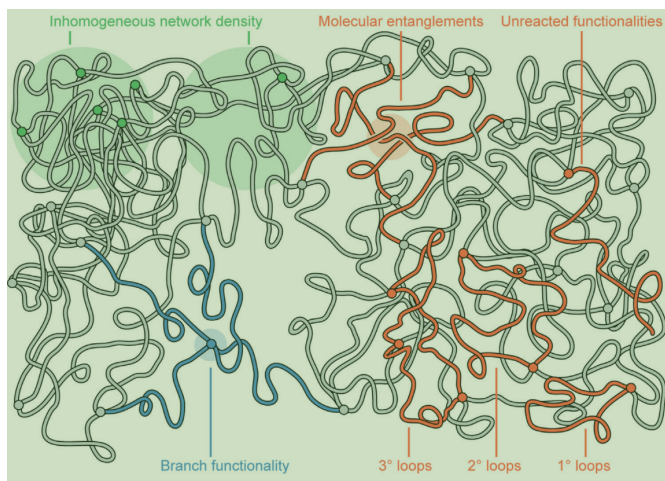
1.1   State of art: Hydrogels

Intro   In a broad perspective we can describe a hydrogel as a polymeric structure, where the chemical and topological structure of polymer networks are interconnected, influencing their overall characteristics. The chemical structure is defined by the chemical composition of the network components and tuning this structure effectively enables the incorporation of functions to polymer networks. In contrast, polymer network topology refers to the configuration of junctions and strands within a polymer network. Given that many properties of polymer networks (e.g., elasticity, porosity, and swellability) have topological origins, there is growing interest in understanding and controlling polymer network topology from a molecular perspective[Gu et al., 2020].

Length scales   Those properties can be explained in terms of topological features across different length scales, ranging from the molecular to the submicron scale. From 10–100 nm, polymer network topology is characterized by inhomogeneity in junction/strand density (Figure 1.1), which results from concentration fluctuations during network formation[1] [20]. From 1–10 nm, dangling/unreacted strands and/or junctions, entanglements, and loops of various

[1] Small-angle scattering techniques provide semi-quantitative information at this length scale (see below).[21,22]

orders[2] comprise the macromolecular features that dominate network structure[3] (Figure 1.1). From less than a nanometer, network features are primarily dictated by chemistry rather than topology; branch functionality, however, is a critical molecular-scale feature that dictates network topology (Figure 1.1). While branch functionality is difficult to characterize experimentally[4], it can typically be predicted based on the functionality of network precursors[Gu et al., 2020].

Delimit the scope   The numerical solutions allow us to explore the topology in the length scales of 5 to 100 nm ish. We are going to describe by the general properties and stuff to the specifics of a hydrogels. With this in mind let's introduce the idea of polymeric structures.

1.1.1   Polymeric Structures

Intro   From a structural standpoint, polymer networks are characterized by network "juctions" also known as "crosslinks", which consist of three or more groups departing from a core, interconnected by "strands". The precise functionality of these branches is referred to as "f". Strand configurations may include linear polymer chains, flexible short molecules, rigid struts/linkers, and other possible forms[Gu et al., 2020].

CrossLinking   The junctions and strands in polymer networks can be linked together via physical interactions (e.g., van der Waals interactions, hydrophobic interactions, Coulombic interactions, metalligand coordination) or covalent bonds[5]. Consequently, polymer networks are conventionally classified as either "physical" (supramolecular) or "chemical" (covalent) networks. It is important to acknowledge that this classification does not always accurately reflect material properties. Bond strengths and exchange rates are much more informative[6], because the properties of polymer networks exhibit significant

[2] Dangling chains, occur when a reactive group from the network precursors remains unreacted after network formation, meanwhile, the loops are cyclic structures defined by the number of strands and junctions in the cycle.

[3] Although they contain rich topological information, conventional scattering and spectroscopic methods fail to characterize these macromolecular features.[23]

[4] To characterize the topological features in Figure 1.1: Multilength stuff. Scale from amorphous regions of polymer networks, 10 to 100 nm shown in green, 1 to 10 nm theory/ simulation, swelling experiments, shown in red and <1 nm shown in blue. and mechanical tests are often used.

[5] A deep explation is in the theoretical framework.

[6] To illustrate, when sufficiently strong and static physical interactions are present, physical networks can exhibit behavior analogous to that of chemical networks. On the other hand, the incorporation of mechanisms for covalent bond exchange can result in chemical networks that demonstrate adaptable mechanical properties regulated by external stimuli.

variability, contingent on the composition of the junctions and strands, as well as the formation and utilization conditions.

From this point of view, virtually all polymer networks, irrespective of their colloquial designation, structural characteristics, and physical properties, can be categorically classified into one of four predominant classes: thermosets, thermoplastics, elastomers, and gels[Gu et al., 2020]. Given our research focus on polymer networks associated with gels, we will not delve extensively into the properties of other polymer networks. However, it should be noted that these networks share certain properties.

1.1.2 Basic Mechanical Properties

Intro ... are elasticity, swelling and viscoelasticity.

Elasticity The physical explanation of rubber elasticity comes from the reduction in conformational entropy that occurs as a strand in a network is stretched, this process is often modeled as the unwinding of flexible, random coils. Once the external stretching force is removed, an elastic entropic force restores the strands to their unstretched and higher entropy state. Therefore, it is concluded that network strands act as entropic molecular springs[Gu et al., 2020].

Swelling Polymer networks constructed from strong (e.g., covalent) bonds typically do not dissolve in solvents. Instead, such networks absorb solvent up to an equilibrium concentration and undergo a concomitant increase in volume. The equilibrium degree of swelling is dictated by a balance between the free energy of polymer-solvent mixing and the free energy cost of expanding the network, which is expressed by the Flory–Rehner equation[11,133][7]

[7] for isotropic swelling of an affine polymer network [Eq. (12)]:

$$\ln(1 - \phi_{\text{eq}}) + \phi_{\text{eq}} + \xi \phi_{eq}^2 = \eta_{eff} V_1 (\phi_{\text{eq}}/2 - \phi_{eq}^{1/3})$$

Viscoelasticity Polymeric materials exhibit both viscous and elastic characteristics upon deformation, meaning that their properties may vary with the time scale or frequency at which measurements are performed. To characterize this viscoelasticity with respect to tensile, compressive, or shear deformation, several types of experimental measurements are commonly applied, such as stress relaxation, creep, and oscillatory shear tests[Gu et al., 2020].

Delimit Now we are going to explore what is commonly refer as a hydrogel ... to connect the elasticity, swelling and viscoelasticity to the gels.

1.1.3 What is a hydrogel?

A hydrogel is commonly describe as a material composed by a network of polymers chains that exhibits the abilitiy to swell and retain a significant fraction of water within its structure, but will not dissolve in water[Ahmed, 2015, Ahmed et al., 2025, Priya et al., 2024, Bustamante-Torres et al., 2021].[8]

[8] the main difference with the microgels, is the size. Hydrogel is bulk, and microgelgel is particle.

The water absorption capacity, network stability of hydrogels, and the conformation of the network with polymer chains are attributable to crosslinking mechanisms[Priya et al., 2024, Ahmed, 2015]. Meanwhile, the polymer chains are predominantly composed with hydrophilic functional groups and can be modified to suit a variety of applications[Ahmed, 2015, Priya et al., 2024, Bustamante-Torres et al., 2021].

Hydrogels come in many flavors, with diverse capabilities and limitations, but in general these systems can all be described as cross-linked macromolecular networks that retain a significant amount of water. As much as 99% of the weight of a hydrogel can be water, which makes these materials quite friendly to water-enriched biological environments such as the human body[Correa et al., 2021].

While the analysis of the impact of functional groups is important, the present project prioritizes the examination of mechanisms that are more pertinent to the mechanical response. The crosslinking mechanisms[9], in particular, are of particular interest, as they are responsible for resisting dissolution. This suggests that crosslinking mechanisms enable the network to undergo modification by external stimuli.

[9] The hydrogels are prepared using different methods like chemical cross-linking of monomers, physical cross linking using temperature or pH changes, and blending of natural or synthetic polymers.

The subsequent sections will present the essential information to facilitate a comprehensive understanding of the crosslinking mechanisms, their relationship to the mechanical response, the reported mechanical response of hydrogels, and the correlation between rheology experiments and stress curves.

Here, we define dynamic hydrogels as any hydrated polymer network cross linked via reversible chemistries, which can include both covalent and noncovalent chemistries. Early reports of the unique rheology of dynamic networks emerged in the late 1980s with polysaccharide based networks covalently cross linked through boric esters, which identified intriguing self healing capabilities.71 73 However, it was only in the early 2000s that noncovalent chemistries began to be leveraged to make shear thinning supramolecular hydrogels based on cyclodextrins,74 engineered peptides,75 and the physical interactions resulting from biopolymer blends.76 Although they can be prepared through diverse chemistries, dynamic hydrogels share unique rheological properties that are directly related to their translational potential as injectable systems[Correa et al., 2021].

Overview and general problems   In earlier technologies, harsh mechanisms for macromolecular cross-linking (e.g., toxic agents, radiation, etc.)24 28 meant that gelation needed to occur prior to introducing gels to biological systems. Unsurprisingly, this limited the bioengineering applications of hydrogels to superficial environments such as the surface of the eye, an open wound, or an exposed surgical bed. Subsequent work developed safer cross-linking mechanisms, which began a trend toward triggering gelation in situ after injection, providing a minimally invasive way of administering hydrogels to practically any organ or tissue.29,30 The most biocompatible iterations of these injectable

in situ gelling platforms use specific cues from the body to trigger gelation: physiological temperature,31 pH,32 or ionic strength.33 Unlike earlier hydrogels that relied on covalent cross links, some of these hydrogels have self healing properties and possess mechanical properties akin to native tissue, capable of countering natural forces and stresses of a body in motion[Correa et al., 2021].

For example, significant advancements have been made to transform simple PEG based hydrogels into responsive systems based on Boolean logic gating decisions (e.g., YES, AND, OR operations) by incorporating functional peptides and proteins into the hydrogel network.45,49,50[Correa et al., 2021] Programmable biotechnologies are already leading to smart injectable materials with the potential to degrade or release drugs based on either endogenous or exogenous triggers.51,52[Correa et al., 2021] As these capabilities continue to mature, multifunctional and programmable hydrogels may provide the technological foundation for platforms that can engage more effectively with the complex, multistage biological events that govern processes such as tissue regeneration and immunity.

Enviromental applications   3-5 examples.

Medical applications   3-5 examples.

Soft robots applications   3-5 examples.

Smart materials   3-5 examples.

Applications/Market size of the applications sectors   An overview of applications. If the previous paragraph does not convince the reader, well my last hope is that money does.

Besides, because of such a wide variety of response triggers, hydrogels can serve as sensors or actuators or can be utilized in controlled drug delivery systems, biosensors, tissue engineering scaffolds, and others [20], because of their biomimetic properties and multi functionalities [21][Bustamante-Torres et al., 2021].

In particular, biomedical applications are very popular and include cell culture [5], wound dressing and healing [2,6], drug delivery [2,7,8], tissue engineering scaffolds [9], bone repair [10], and cartilage regeneration [11][Picchioni and Muljana, 2018].

The explosion of hydrogel technologies has made significant contributions in biomedical applications that impact the dayto-day lives of millions of people. For example, hydrogels contributions to modern life in the form of soft contact lenses, creating a new class of optically tunable soft materials and establishing what is today a multibillion dollar industry.2 Early studies also revealed the usefulness of engineered hydrogels for delivering diverse drugs,3 5

establishing a field for local controlled release of bioactive compounds.6 10 In the 1970s, surgeons recognized the utility of hydrogels for reconstructive surgeries,11,12 and by the 1990s, hydrogels were becoming a foundational technology for tissue regeneration.13 16 The history of hydrogel materials is well reviewed,17 19[10] and the consistent theme has been that hydrogels continue to find new and exciting applications as the underlying technology improves. Emerging applications for hydrogels today include device coatings,20 environmental engineering,21 soft robotics,22 and adoptive cell therapy.23 [Correa et al., 2021]

[10] Checar estas referencias

1.2 About computer simulations

2
Theoretical framework

2.1 Soft Colloids

What is a colloid?   A colloid is a many-body system composed of tiny[1] par-
ticles, typically named colloids, dispersed in a continuum medium called sol-
vent. This model is used to represent physical phenomena such as equilibrium[2]
and non-equilibrium phase states[3], as well as to construct effective interaction
potentials in many-body systems and to explore the mechanical response of
materials. Also serves as an introductory guido to the physics of dispersions,
emulsions, pastes, paints, polymers, gels, and liquid crystals, granular media
and living cells and tissues[Castaneda-Priego, 2021, Yunker et al., 2014].

Why colloids are used   The main features of the colloidal model are that they
are relatively slow, typical around 1 μs to 1 s, allowing to observe the dynamics
in real time. The interaction between the particles are of the order of the ther-
mal energy. They can be studied on a single-particle level by means of different
complementary techniques[Castaneda-Priego, 2021, Yunker et al., 2014]. This
features allow to use mathematical tool such as brownian motion or molecular
dynamics to analyze the systems with computer simulations and mathematical
analysis, also to be easily observed and tracked via optical microscopy.

What is soft colloid   Now that we have a general understanding of the concept
of colloids, we will explore the concept of soft colloids. There are a variety of
explanations to softenss: particle elasticity, diversity of particle interactions,
and particle volume fraction. The particle elasticity represents the ratio of the
elastic free energy ΔF with the thermal energy kT[4] In contrast, the softness
explain by particle interactions is characterized by the form of the repulsive
pair potential between two particles. Finally, the particle volume fraction con-
tributes to the ability of the particles to deform or compress, in contrast to hard
spheres[5][Vlassopoulos and Cloitre, 2014].

[4]

$$\varepsilon = \frac{\Delta F}{kT}. \qquad (2.1)$$

2.2 *Mechanical response*

Hooks Law For many isotropic solid materials, the mechanical behavior is traditionally characterized by a constitutive stress-strain relation. Initially, the relation is linear until a limit is reached, at which point the material either fractures or begins to plastically deform. In cases where deformation and strains are small, the response can be estimated using a three-dimensional tensor. This tensor is commonly referred to as Hooke's law[6]. This establishes a connection between the stress tensor (σ), the shear modulus (G) of the material, the applied strain (E), and the Lame first parameter (λ) of the material[Bonyadi et al., 2020].

Rheological properties of concentrated dispersions strongly depend on the microstructure, which not only depends on the interaction potential but also on the size distribution of the particles[Senff and Richtering, 1999].

[6]
$$\sigma_{ij} = 2GE_{ij} + \lambda \delta_{ij} E_{kk}$$

Hydrogels response Hydrogels generally exhibit high and non-linear strains prior to failure.[7]. In their fully swollen and hydrated state, hydrogels are capable of withstanding significant compressive and tensile strains without incurring plastic deformation. Two distinctive properties of hydrogels appear to govern their response to strain: The water content influence the elastic response in the linear-elastic regime, typically for strains less than 40%. Meanwhile, the crosslink density and network characteristics of a material determine its fracture toughness.Several models have been utilized in an effort to recapitulate the complex responses observed in these materials[8]. Each model has its limitations, as most were not developed to handle a hydration-dependent, multi-network material. However, experimental and computational validation has identified specific solutions and applicable strain ranges for hydrogels[Bonyadi et al., 2020].

[7] a characteristic that is also typical of hyper-elastic elastomers

[8] These include the Mooney-Rivlin model, the Neo-Hookean model, and the Ogden model.

Hydrogels response Experiments Contact mechanics measurements[9] performed in the linear-elastic range suggest that bulk hydrogel response to compressive loads is dependent upon the osmotic pressure of the hydrogel and is consistent with Hertzian predictions over several timescales [18, 19]. Additional measurements showed that this was geometry dependent, suitable for solid (or thick) samples that lack sharp edges [20, 21]. For example, by changing a solid hydrogel indenting probe to a thin-walled design the mechanical response (contact area to force) became nearly linear, and by indenting a hydrogel with a conic punch locally exceeded the osmotic pressure of the gel allowing fluid flow. While strains are traditionally high at failure for hydrogels [6, 7, 22–24] stresses are typically very low (on the order of kilopascals)[10][Bonyadi et al., 2020].

[9] critical to evaluating the tribological performance of a hydrogel

[10] this remains one of the major hurdles in more robust applications of hydrogels in medicine [1]

2.3   Hydrogels

2.3.1   Gels

Gel point   For any polymer network formation, a critical point exists at which the reaction phase transitions from liquid to solid. This point is referred to as the gel point. Although gelation is not the focus of the research, the "gel point" is a crucial concept that demonstrates how certain characteristics can be shared. At this point, many properties of the polymer networks change abruptly, and the properties that are more useful for applications can be reached beyond the gel point. Consequently, numerous theoretical models[11] have been developed to predict the gel point for various network formation processes, including mean-field theory, critical percolation theory, and the kinetic gelation model[Gu et al., 2020].

[11] The classical approches to predict the relationship between gelation and the extent of reaction in step-growth polymerzation are the Carothers model and Flory-Stockmayer[Gu et al., 2020].

Gels   Once the polymer network exceeds its gelation point, gels can be described as polymer networks that form through crosslinks or supramolecular bonds. These gels can become swollen in liquid media, such as water or organic solvents. The network structure guarantees that the liquid is retained within the material. Gels generally display Young's moduli within the range of 103–104 Pa, yet they often exhibit the capacity for significant deformation. Examples of gels include gelatin, fibrin, and polyacrylamide hydrogel[Gu et al., 2020].

Microgels   Microgel particles consist of crosslinked macromolecules of colloidal size that swell in the solvent. The particle interaction potential strongly depends on the crosslinking density, and microgels exhibit a behavior ranging from that of polymer solutions to that of hard spheres. At intermediate degree of crosslinking and swelling the microgels start to resemble the behavior of multiarm star polymers or block copolymer micelles[Senff and Richtering, 1999].

Hydrogels   In the swollen state of the gel, most of the water is in a "free" state and can freeze at the usual freezing point. However, some water molecules which are associated with the polymeric chains of the gel network cannot freeze at the usual freezing point. This water is called "bound water"[Lele et al., 1997].

Water is bound to the polymer chains through hydrogen-bonding associations and through physical (hydrophobic) interactions[12][Lele et al., 1997].

Hydrogels are tunable soft and aqueous gels[Bonyadi et al., 2020].

[12] The total bound water content (BWC) can be calculated from the ratio of total number of polymer-water contacts in the gel to the number of polymer-water contacts per molecule of bound water.

Argument   Why we can use a simulation protocol for microgels to modeled hydrogels?

2.3.2 Cross-linking mechanisms

Intro to cross linking A crosslinker is a molecule that functions as a bridge between polymer chains, thereby facilitating the formation of an interconnected network. As previously suggested, it is pertinent to understand the mechanisms of crosslinking in order to gain insight into the correlation between these mechanisms and mechanical properties, such as elasticity, viscosity, solubility, glass transition temperature, strength, toughness, and melting point stiffness, swelling capacity, viscosity, and so forth[Priya et al., 2024]. The elements under consideration form stable bonds, which are comonly categorized into two main types: covalent (permanent) and physical (reversible)[Bustamante-Torres et al., 2021]. However, recent mechanisms, such as mechanical crosslinker mechanics, have been demostrated to form bridges due to the topology of the constituents of the hydrogel.
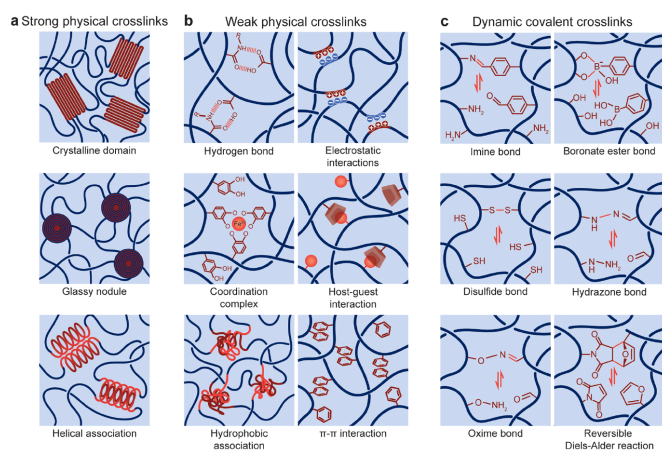

Figure 2.1: Image with the three different crosslinker mechanisms

Difference between physical and chemical bonds Although the concept of bonding is central to comprehending chemical structures and reactions. The criteria employed to characterize a chemical bond, its physical origin, and its nature remain subjects of debate[Kumar et al., 2021]. Consequently, establishing a precise distinction between "covalent" and "non-covalent" bonds remains challenging. Therefore, the description of crosslinker mechanisms is limited to the principal interactions reported in articles and the synthesis process, rather than focusing on the classification of interactions as "covalent" or "non-covalent", but rather as "reversible" or "irrevarsible". Also in the recent work [Picchioni and Muljana, 2018] it is shown a "covalent" reversible network. Nonetheless, a general consensus exists that non-covalent bonds are, as a rule, recognized as being weaker than covalent bonds and it is widely accepted that a distinguishing characteristic between covalent and noncovalent bonds is the energy of interaction and equilibrium bond distance[Kumar et al., 2021, Novikov, 2023].
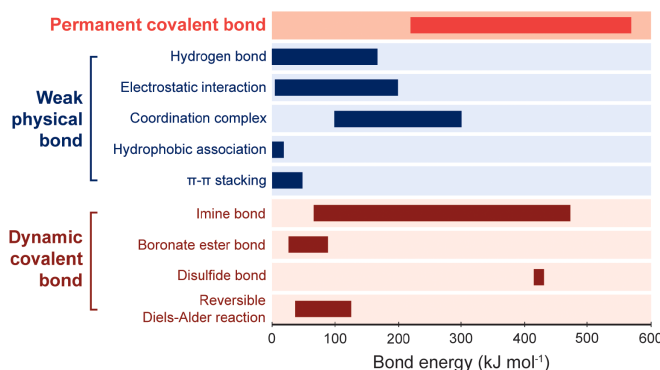
Figure 2.2: Bond energies of various types of permanent covalent crosslinks, weak physical cross-links, and dynamic covalent crosslinks.

Irreversible Cross-linking   In irreverisble cross-linked hydrogels, polymer chains are synthesized by chain growth polymerization, graft copolymerization, addition and condensation polymerization, ezymatic method, reactive functions groups and gamma and electron beam polymerization[Maitra and Shukla, /26/2014, Bustamante-Torres et al., 2021]. This types of crosslinking mechanisms exhibit a high degree of strength and stability, leading to a structural arrangement of interconnected polymer chains that is more robust and resistant to alterations in environmental conditions, such as temperature and pH[Maitra and Shukla, /26/2014].

Reversible Cross-linking   In reversible cross-linked hydrogels, polymer chains are held together by molecular entanglements or physicochemical interactions, including van der Waals forces, hydrogen bonds, hydrophobic interactions, charge condensation, crystallite formation, and supramolecular chemistry[Bustamante-Torres et al., 2021, Maitra and Shukla, /26/2014]. Some of the syhtesis methods for reverisble crosslinkin mechanisms are ionic interaction, crystallization, stereocomplex formation, hydrophobized polysaccharides, protein interaction, amphilic copolymers and hydrogen bond[Maitra and Shukla, /26/2014, Bustamante-Torres et al., 2021]. Furthermore, molecular reversibility can be actually achieved in two different ways: either by making use of equilibrium reactions (e.g., the Diels-Alder one) or through dynamic exchange reactions (e.g., reaction of an excess amino groups with epoxide ones)[Picchioni and Muljana, 2018].

Mecanical bonds   As previously mentioned, a novel class of polymer architecture has recently emerged within the field of polymer science kwnon as mechanically interlocked polymers (MIPs). These polymers are distinguished by the presence of a mechanical bond, that is, a constraint of two (or more) molecular components in space without the formation of covalent bonds[Hart et al., 2021]. While these types of hydrogels exhibit substantial conformational flexibility while preserving a persistent spatial correlation between their components, their synthesis remains challenging.

2.3.3 Mechanical properties

[Covalent and non covalent cross linking] More recently, shear-thinning hydrogels were developed that are formed through dynamic and reversible cross-linking.34 For example, physical hydrogels use noncovalent interactions (e.g., supramolecular chemistries) between soluble building blocks in order to self-assemble into a dynamic, reversibly cross-linked network.35,36 Likewise, reversible covalent cross-linking strategies can yield dynamic networks with similar properties.37,38 These "dynamic hydrogels" assembled through reversible cross-links afford the unique property of being injectable even after having formed a gel, due to their shear-thinning and selfhealing behaviors. Current research on dynamic hydrogels has revealed novel and useful capabilities that have opened new frontiers for this technology. For example, they can stabilize delicate protein and cellular cargoes to combat pharmaceutical cold-chain limitations,39 they can adhere strongly to tissues to form protective barriers and bandages,40 and they can be delivered through spray applications to coat complex biological geometries.41[Correa et al., 2021]

[Like a transition but I don't know] While dynamic hydrogels are opening up new translational possibilities, significant progress is also being made to introduce unprecedented levels of functionality into biomaterials. This includes features such as nanoscale patterning of bioactive molecules,42,43 programmable drug release,44,45 and stimuli-responsive behaviors.46,47[Correa et al., 2021]

As a consequence, much of the research in this space is trending toward increasingly interdisciplinary projects that recruit the expertise of nanotechnologists, chemists, protein engineers, and synthetic biologists to develop sophisticated multifunctional hydrogels[Correa et al., 2021].

dynamic hydrogels, which can seamlessly transition back and forth from solid like to liquid like during injection thanks to their shear thinning and self healing capabilities. These materials, which are gelled within the syringe before injection, additionally have the ability to stabilize drugs over broad temperature ranges and maintain homogeneously mixed cell solutions.68 70[Correa et al., 2021]

General mechanical properties of the croslsinking Eventhough, physical crosslinking mechanisms are weaker than chemical ones, there numerous interactions contribute to complex behaviors. Meanwhile chemical crosslinking mechanisms are easier to control than physical crosslinking mechanisms because their preparation is independent of pH[Bustamante-Torres et al., 2021] and they are very brittle due to structural inhomogeneity and lack of energy dissipation[Xu et al., 2018].

Reversible crosslinking The aforementioned interactions enable hydrogels to undergo structural changes without the rupture of any covalent bonds. Con-

sequently, these materials exhibit enhance responsiveness to external stimuli, such as temperature, pH, or ionic strength. Additionally, hydrogels demonstrate high water sensitivity and thermal reversibility[Bustamante-Torres et al., 2021, Priya et al., 2024]. These materials are known to exhibit distinctive properties, including "self-healing" behavior, where the gel can reform after being broken. The lifespan of these hydrogels is brief, ranging from a few days to a maximum of a month, when maintained within physiological media.

Ir-reversible croslsinkg   Consequently, chemically cross-linked hydrogels generally exhibit greater mechanical strength and long-term stability. Furthermore, it generally contains regions of the high cross-linking density and low degree of swelling (clusters), dispersed in the regions of the low cross-linking density and high swelling index due to the hydrophobic aggregation of the cross-linking agent[Bustamante-Torres et al., 2021]..

Network-mechanical response relation   Introduce the idea of how by understanding the network we can manipulate/control the mechanical response.

The research of hydrophilic polymers has been complex because the physical properties of solubility or swellability depend on different factors, such as the type of polymer, molecular weight, the ratio of polar groups, and degree of cross-linking[Bustamante-Torres et al., 2021]. High molecular weight and a high degree of cross-linking will reduce the hydrophilicity of the molecule [18,19][Bustamante-Torres et al., 2021].

2.4   Molecular Dynamics

2.4.1   Langevin dynamics

From a general point of view there are two types of methods to make a quatitative description of systems: one focused on simulating dynamics at the microscale, and the other dedicated to deriving or establishing evolutionary equations at the macroscale[Wang et al., 2025]. Since the assumption is made that the mechanical response of a hydrogel is predominantly derived from its internal structure[13] we choose to simulate the dynamics at the microscale. Additionally, by treating the hyrogel as a colloid, permits applying molecular dynamics to model its response under shear deformation. Finally, there are two commonly used mathematical frameworks to model the molecular dynamics, the continuous time random walk (CTRW) model and the Langevin equation[Wang et al., 2025], in this work we decided[14] to use the langevin dynamics mathematical framework.

This is because, the solid phase of the colloid has a large mass and will change their momenta after many collisions with the solvent molecules and the picture which emerges is that of the heavy particles forming a system with a much longer time scale than the solvent molecules[Thijssen, 2007] and

[13] Poner citas que desmuestrén que no es hipótesis, si no que se sabe

[14] Supongo que eventualmente justificaré la desición.

Langevin theory takes advantage of this difference in time scale to eliminate the details of the degrees of freedom of the solvent particles and represent their effect by stochastic and dissipative forces allowing longer simulations that would be impossible if the solvent were explicitly included[Pastor, 1994]. However, the representation of the solvent by a stochastic and dissipative force, introduce the problem of characterize two very different timescales, one associated with the slow relaxation of the initial velocity of the brownian particle and another linked to the frequent collisions that the brownian particle suffers with particles of the bath[Hansen and McDonald, 2006][15]. Therefore, two terms are used to create a mathematical representation of the solvent: a frictional force proportional to the velocity of the particle and a fluctuating force. Hence,

$$m\frac{\mathrm{d}\vec{v}(t)}{\mathrm{d}t} = \vec{F}(t) - m\gamma\vec{v}(t) + \vec{R}(t). \qquad (2.2)$$

The friction constant γ[16] parametrises the effect of solvent damping and activation and is commonly referred to as the collision frequency in the simulation literature, even though formally a Langevin description implies that the solute suffers an infinite number of collisions with infinitesimally small momentum transfer. Also, the fact that the second term is not a function of the position of any of the particles involves the neglect of hydrodynamic interaction or spatial correlation in the friction kernel spatial correlation in the friction kernel[Pastor, 1994]. On the other hand, $\vec{R}(t)$[17] is a "random force" subject to the following conditions

$$\left\langle \vec{R}(t) \right\rangle = 0$$
$$\left\langle \vec{R}(t)\vec{R}(t') \right\rangle = 2k_B T\gamma\delta(t-t')$$

The no time correlation is equivalent to assuming that the viscoelastic relaxation of the solvent is very rapid with respect to solute motions[18].

In comparing the results of Langevin dynamics with those of other stochastic methods [28-31], the relevant variable is the velocity relaxation time, τ_v which equals γ^{-1}[Pastor, 1994] The Langevin equation improves conformational sampling over standard molecular dynamics[Paquet and Viktor, 2015].

- Hablar acerca de que la fuerza aleatoria puede tener distribución gaussiana, pero no necesariamente.

- hablar de la ecuación de Green-Kubo:

$$\eta = \frac{V}{k_B T} \int_0^\infty \left\langle \sigma_{xy}(t)\sigma_{xy}(0) \right\rangle \mathrm{d}t$$

- No se que tanto hablar de la idea de correlación y su aplicación en estos temas.

[15] Para traer a colación la sensibilidad de la respuesta mecánica al parámetro de damp.

[16] Cuidado con las unidades. Hacer análisis dimensional, porque por la condición de correlación en R, γ ocupa tener unidades de masa entre tiempo, pero en la ecuación, solo ocupa unidades de $1/s$.

[17] No me acuerdo en donde está que se puede asumir que tiene distribución gaussiana.

[18] Grote land Hynes [26] have investigated this assumption for motions involving barrier crossing and have found that while it is seriously in error for passage over sharp barriers (such as 12 recombination); it is quite adequate for conformational transitions such as might be found in polymer motions.[Pastor, 1994]

2.4.2   Velocity Verlet

L Verlet. Computer" experiments" on classical fluids. I. Thermodynamical properties of Lennard-Jones molecules. Physical Review, 159(1):98103, 1967.

J. M. Haile. Molecular Dynamics Simulation: Elementary Methods. John Wiley & Sons, Inc., New York, NY, USA, 1st edition, 1992.

Richard L. Burden and J. Douglas Faires. Numerical Analysis. Brooks Cole, 8 edition, 12 2008.

Molecular Dynamics, Method For, and Microscale Heat Transfer. Molecular Dynamics Method. Bioinformatics, 2(Md):189–226, 2000.

Shichi Nose. A molecular dynamics method for simulations in the canonical ensemble. Molecular Physics, 52(2):255–268, 1984.

M Tuckerman, B J Berne, and G J Martyna. Reversible multiple time scale molecular dynamics. The Journal of Chemical Physics, 97(3):1990, 1992.

2.4.3   How to compute stres sin molecular dynamics

Motivation: Molecular stress is equivalent to continuum stress . . . This derivation can be found in the apendix of[Admal and Tadmor, 2010][19].[20] Consider a system of N interacting particles with each particle position given by

$$\vec{r}_\alpha = \vec{r} + \vec{s}_\alpha, \tag{2.3}$$

where $\vec{r}$ is the position of the center of mass of the system and $\vec{s}_\alpha$ is the position of each point relative to the center of mass. Hence, we can express the momentum of each particle as

$$\vec{p}_\alpha = m_\alpha\left(\dot{\vec{r}} + \dot{\vec{s}}_\alpha\right) = m_\alpha\left(\dot{\vec{r}} + \vec{v}_\alpha^{\mathrm{rel}}\right). \tag{2.4}$$

Before starting the procedure, lets take into account that the center of mass of the system is given by

$$\vec{r} = \frac{\sum_\alpha m_\alpha \vec{s}_\alpha}{\sum_\alpha m_\alpha}, \tag{2.5}$$

and by replacing (2.3) in (2.4) we get the following relations, which will be used later,

$$\sum_\alpha m_\alpha \vec{r}_\alpha = \vec{0}, \quad \sum_\alpha m_\alpha \vec{v}_\alpha^{\mathrm{rel}} = \vec{0}. \tag{2.6}$$

Now we can start by computing the time derivative of tensorial product $\vec{r}_\alpha \otimes \vec{p}_\alpha$[21],

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(\vec{r}_\alpha \otimes \vec{p}_\alpha\right) = \underbrace{\vec{v}_\alpha^{\mathrm{rel}} \otimes \vec{p}_\alpha}_{\text{Kinetic term}} + \underbrace{\vec{r}_\alpha \otimes \vec{f}_\alpha}_{\text{Virial term}}, \tag{2.7}$$

which is known as the *dynamical tensor virial theorem* and it is simply an alternative form to express the balance of linear momentum. This theorem becomes useful after making the assumption that there existis a time scale τ, which is short relative to macroscopic processes but long relative to the characteristic time of the particles in the system, over which the particles remain

[19] Describe more if what is done in this article

[20] (Eventualmente pondré esto en párrafo) Notation: σ Tensor, $\vec{\sigma}$ vector, $\sigma_{i,j}$ tensor, $\overline{\sigma}$ time average,

[21] It is interesting to note that the tensorial product $\vec{r}_\alpha \otimes \vec{p}_\alpha$ has units of action and by tacking the time derivative we are dealing with terms that has units of energy.

close to their original positions with bounded positions and velocities. Taking advantage of this property we can compute the time average of (2.7),

$$\frac{1}{\tau}\left.(\vec{r}_\alpha \otimes \vec{p}_\alpha)\right|_0^\tau = \overline{\vec{v}_\alpha^{\text{rel}} \otimes \vec{p}_\alpha} + \overline{\vec{r}_\alpha \otimes \vec{f}_\alpha}. \tag{2.8}$$

Assuming that $\vec{r}_\alpha \otimes \vec{p}_\alpha$ is bounded, and the time scales between microscopic and continuum processes are large enough, the term on the left-hand side can be as small as desired by tacking τ sufficiently large and by summing over all particles we achieve the *tensor virial theorem*:

$$\overline{\mathbf{W}} = -2\overline{\mathbf{T}}, \tag{2.9}$$

where

$$\overline{\mathbf{W}} = \sum_\alpha \overline{\vec{r}_\alpha \otimes \vec{f}_\alpha} \tag{2.10}$$

is the time-average virial tensor and

$$\overline{\mathbf{T}} = \frac{1}{2}\sum_\alpha \overline{\vec{v}_\alpha^{\text{rel}} \otimes \vec{p}_\alpha} \tag{2.11}$$

is the time-average kinetic tensor. This expression for the tensor virial theorem applies equally to continuum systems that are not in macroscopic equilibrium as well as those that are at rest.

The assumption of the difference between the time scales allow us to simplify the relation by replacing (2.4) in (2.11), so that,

$$\overline{\mathbf{T}} = \frac{1}{2}\sum_\alpha m_\alpha \overline{\vec{v}_\alpha^{\text{rel}} \otimes \vec{v}_\alpha^{\text{rel}}} + \frac{1}{2}\left[\overline{\sum_\alpha m_\alpha \vec{v}_\alpha^{\text{rel}}}\right] \otimes \dot{\vec{r}}, \tag{2.12}$$

which is not the simplification we expected, however, by the relations from (2.6), equation (2.12) simplifies to[22]

$$\overline{\mathbf{T}} = \frac{1}{2}\sum_\alpha m_\alpha \overline{\vec{v}_\alpha^{\text{rel}} \otimes \vec{v}_\alpha^{\text{rel}}}. \tag{2.13}$$

On the other hand, instead of reducing the expression, we start to create the conection with the Cauchy stress tensor by distributing (2.10) into an internal and external contributions,

$$\overline{\mathbf{W}} = \underbrace{\sum_\alpha \overline{\vec{r}_\alpha \otimes \vec{f}_\alpha^{\text{int}}}}_{\overline{\mathbf{W}}_{\text{int}}} + \underbrace{\sum_\alpha \overline{\vec{r}_\alpha \otimes \vec{f}_\alpha^{\text{ext}}}}_{\overline{\mathbf{W}}_{\text{ext}}}. \tag{2.14}$$

The time-average internal virial tensor takes into account the interaction between particle α with the other particles in the system, meanwhile, the time-average external virial tensor considers the interaction with atoms outside the system, via a traction vector $\vec{t}$ and external fields acting on the system represented by $\rho\vec{b}$, where ρ is the mass density of it and $\vec{b}$ is the body force per unit mass applied by the external field. Therefore we can express the following,

$$\sum_\alpha \overline{\vec{r}_\alpha \otimes \vec{f}_\alpha^{\text{ext}}} := \int_{\delta\Omega} \vec{\xi} \otimes \vec{t}\,dA + \int_\Omega \vec{\xi} \otimes \rho\vec{b}\,dV. \tag{2.15}$$

[22] No estoy muy seguro si incluir una discusión acerca del término cinético en la expresión del virial. Posiblemente un párrafo. . . posiblemente lo ponga en la interpretación del teorema. También, no se si ir metiendo interpretación durante la derivación o no, pero bueno.

Where $\vec{\xi}$ is a position vector within the domain Ω occupied by the system of particles with a continuous closed surface $\delta\Omega$. Assuming that Ω is large enough to express the external forces acting on it in the form of the continuum traction vector $\vec{t}$.

With this we can substitute the traction vector with $\vec{t} = \sigma\vec{n}$, where σ represent the Cauchy stress tensor and applying the divergence theorem in (2.15), we have

$$\overline{\mathbf{W}}_{\text{ext}} = \int_\Omega \left[\vec{\xi} \otimes \rho\vec{b} + \text{div}_{\vec{\xi}}\left(\vec{\xi} \otimes \sigma \right) \right] dV = \int_\Omega \left[\sigma^{\text{T}} + \vec{\xi} \otimes \left(\text{div}_{\vec{\xi}}\sigma + \rho\vec{b} \right) \right] dV \tag{2.16}$$

Since we assume that we are under equilibrium conditions, the term $\text{div}_{\vec{\xi}}\sigma + \rho\vec{b}$ is zero (2.16) it simplifies to

$$\overline{\mathbf{W}}_{\text{ext}} = V\sigma^{\text{T}}. \tag{2.17}$$

By tacking into account that we integrate over the domain Ω we can say that we compute the spatial average of the Cauchy stress tensor,

$$\sigma_{\text{av}} = \frac{1}{V} \int_\Omega \sigma dV, \tag{2.18}$$

in which V is the volume of the domain Ω. Replacing (2.17) into (2.14), the tensor virial theorem (2.9) can be expressed as,

$$\sum_\alpha \overline{\vec{r}_\alpha \otimes \vec{f}_\alpha^{\text{int}}} + V\sigma_{\text{av}}^{\text{T}} = -\sum_\alpha m_\alpha \overline{\vec{v}_\alpha^{\text{rel}} \otimes \vec{v}_\alpha^{\text{rel}}}. \tag{2.19}$$

Finally, solving for the Cauchy Stress tensor we get,

$$\sigma_{\text{av}} = -\frac{1}{V} \left[\sum_\alpha \overline{\vec{f}_\alpha^{\text{int}} \otimes \vec{r}_\alpha} + \sum_\alpha m_\alpha \overline{\vec{v}_\alpha^{\text{rel}} \otimes \vec{v}_\alpha^{\text{rel}}} \right], \tag{2.20}$$

an expression that describe the macroscopic stress tensor in terms of microscopic variables[23].

To end the section it is important to show that (2.20) is symmetric. Therefore, we rewrite the internal force as the sum of forces between the particles,

$$\vec{f}_\alpha^{\text{int}} = \sum_{\substack{\beta \\ \beta \neq \alpha}} \vec{f}_{\alpha\beta}, \tag{2.21}$$

and substituting (2.21) into (2.20), we have

$$\sigma_{\text{av}} = -\frac{1}{V} \left[\sum_{\substack{\alpha,\beta \\ \beta \neq \alpha}} \overline{\vec{f}_{\alpha\beta} \otimes \vec{r}_\alpha} + \sum_\alpha m_\alpha \overline{\vec{v}_\alpha^{\text{rel}} \otimes \vec{v}_\alpha^{\text{rel}}} \right]. \tag{2.22}$$

Due to the property $\vec{f}_{\alpha\beta} = -\vec{f}_{\beta\alpha}$ we obtain the following identity

$$\sum_{\substack{\alpha,\beta \\ \beta \neq \alpha}} \vec{f}_{\alpha\beta} \otimes \vec{r}_\alpha = \frac{1}{2} \sum_{\substack{\alpha,\beta \\ \beta \neq \alpha}} \left(\vec{f}_{\alpha\beta} \otimes \vec{r}_\alpha + \vec{f}_{\beta\alpha} \otimes \vec{r}_\beta \right) = \frac{1}{2} \sum_{\substack{\alpha,\beta \\ \beta \neq \alpha}} \vec{f}_{\alpha\beta} \otimes \left(\vec{r}_\alpha - \vec{r}_\beta \right). \tag{2.23}$$

[23] It is important to acknowledge that several mathematical subtleties were not taken into consideration, however all the mathematical formality is adressed by Nikhil Chandra Admal and E. B. Tadmor in [Admal and Tadmor, 2010]

Therefore, by replacing the identity of (2.23) into (2.22), we have

$$\sigma_{\text{av}} = -\frac{1}{V}\left[\frac{1}{2}\sum_{\alpha,\beta_{\beta\neq\alpha}}\overline{\vec{f}_{\alpha\beta}\otimes(\vec{r}_\alpha-\vec{r}_\beta)}+\sum_\alpha m_\alpha\overline{\vec{v}_\alpha^{\text{rel}}\otimes\vec{v}_\alpha^{\text{rel}}}\right], \qquad (2.24)$$

expressed with indexical notation and using the eistein summation convention,

$$\sigma_{ij}^{\text{av}} = -\frac{1}{V}\left[\frac{1}{2}\sum_{\alpha,\beta_{\beta\neq\alpha}}\overline{f_i^{\alpha\beta}r_j^\alpha+f_i^{\beta\alpha}r_j^\beta}+\sum_\alpha m_\alpha\overline{v_i^{\alpha\,\text{rel}}v_j^{\alpha\text{rel}}}\right], \qquad (2.25)$$

which is the same expression implemented in LAMMPS[Thompson et al., 2022a].[24]

[24] No se si poner la referencia a la pagina de documentacionhttps://docs.lammps.org/compute_stress_atom.html

3

Numerical Experiments

3.1 Simulation tools

Description of what is in this chapter   Becuase yes

3.1.1 LAMMPS

Talk about LAMMPS   LAMMPS is a computational engine for modeling interacting particles at any length scale, so long as the interactions are primarily short-range, and particles densities are moderately bounded[Thompson et al., 2022b]. LAMMPS implemented MD algorithms to enable parallelism across CPUs via MPI, and some versions of these algorithms for GPUs.

For test simulations we used the mpi paralelization scheme, meanwhile the final results where computed with the serial version, since we had access to a cluster.

A LAMMPS input script (text file) is simply a series of lines each beginning with a command name followed by one or more whitespace separated arguments. Programming-like commands are included which define variables, perform conditional tests, execute loops, or invoke shell commands, eg to launch a program external to LAMMPS. The input script is parsed and executed one line at a time which means a single script can be used to run a simulation in stages, altering one or more parameters between the stages, or to run a series of independent simulations where the entire system is reinitialized multiple times.

- Pair styles - Atom styles - Fix styles - Computes styles - units definitions

Make a resume of   partitioning, communication, neighbr lists

Since we had access to the lavis cluster we...

Talk about the Fix styles   Fix styles implement operations performed during a dynamics timestep or an energy minimization iteration[Thompson et al., 2022b]. The initial_integrate() and final_integrate() methods of fix styles can

be used to implement portions of the velocity-Verlet algorithm for various ensembles at the appropriate points in the timestep.

Units Lennar Jones units. distance $= \sigma$. time = reduce LJ τ. mass = ratio to unitless 1.0. temperature = reduced LJ temp. pressure = reduced LJ pressure energy $= \varepsilon$. velocity $= \sigma/\tau$. force = reduce LJ force (σ/τ^2). https://docs.lammps.org/99/units.html

3.2 Simulation methodology

Overview of the simulation workflow.

The simulation methodology is based on the work presented in[Gnan et al., 2017] and[Sorichetti et al., 2023], with the objective of create a representative polymer structure of a microgel and characterize the mechanical response under shear deformation. This methodology creates the structure by using a mixture of two types of patchy particles. The patchy particles are spheres of identical size and mass decorated by patches to represent interaction sites. One type represent a *Crosslinker* and is define by 1 central particle with 4 patches placed at the vertices of a circumscribed tetrahedron. The other one represent a *Monomer* define by 1 central particle and 2 patches placed at the poles.

The interaction between the central particles is modeled with a Weeks-Chandler-Andersen repulsive potential,

$$U_{WCA}(r_{i,j}) = \begin{cases} 4\varepsilon_{i,j}\left[\left(\frac{\sigma}{r_{i,j}}\right)^{12} - \left(\frac{\sigma}{r_{i,j}}\right)^{6}\right] + \varepsilon_{i,j}, & r_{i,j} \in [0, 2^{1/6}\sigma], \\ 0, & r_{i,j} > 2^{1/6}\sigma \end{cases} , \quad (3.1)$$

where $r_{i,j}$ is the distance between the center of the central particles, σ is the diameter of the particles and $\varepsilon_{i,j}$ is the energy of the interacton. The patch-patch interaction is modeled with an attractive potential,

$$U_{\text{patchy}}(r_{\mu\upsilon}) = \begin{cases} 2\varepsilon_{\mu\upsilon}\left(\frac{\sigma_p^4}{2r_{\mu\upsilon}^4} - 1\right)\exp\left[\frac{\sigma_p}{(r_{\mu\upsilon}-r_c)} + 2\right], & r_{\mu\upsilon} \in [0, r_c], \\ 0, & r_{\mu,\upsilon} > r_c, \quad (3.2) \end{cases}$$

where $r_{\mu\upsilon}$ is the distance between two patches, σ_p is the diameter of the patches, r_c is the cut distance of interaction set to $1.5\sigma_p$ and $\varepsilon_{\mu,\upsilon}$ is the interaction energy between the patches. Moreover, the interaction between patches is complemented by a three-body repulsive potential, defined in terms of (3.2), that provides an efficient bond-swapping mechanism making possible to easily equilibrate the system at extremely low temperatures, while at the same time, reataining the single-bond-per-patch condition[Sciortino, 2017],

$$U_{\text{swap}}(r_{l,m}, r_{l,n}) = w \sum_{l,m,n} \varepsilon_{m,n} U_3(r_{l,m}) U_3(r_{l,n}), \quad r_{l,n} \in [0, r_c], \quad (3.3)$$

where

$$U_3(r) = \begin{cases} 1 & r \in [0, r_{\min}], \\ -U_{\text{patchy}}(r)/\varepsilon_{m,n}, & r \in [r_{\min}, r_c] \end{cases} . \quad (3.4)$$

The sum in (3.3) runs over all triples of bonded patches (patch l bonded both with m and n). $r_{l,m}$ and $r_{l,n}$ are the distances between the reference patch and the other two patches. The parameter $\varepsilon_{m,n}$ is the energy of repulsion and w is used to tuned the swapping ($w = 1$) and non-swapping bonds ($w \gg 1$). The cut off distance r_c is the same as in the potential of interaction between patches, meanwhile the minimum distance $r_{\min}$ is the distance at the minimum of (3.2), *i.e.* $\varepsilon_{m,n} \equiv \left| U_{\text{patchy}}(r_{\min}) \right|$. Finally, the energy of interaction between crosslinker patches ($\varepsilon_{\mu^i,\mu^i}$) are set to 0 to allow only crosslinker-monomer and monomer-monomer bonding (figure 3.2).
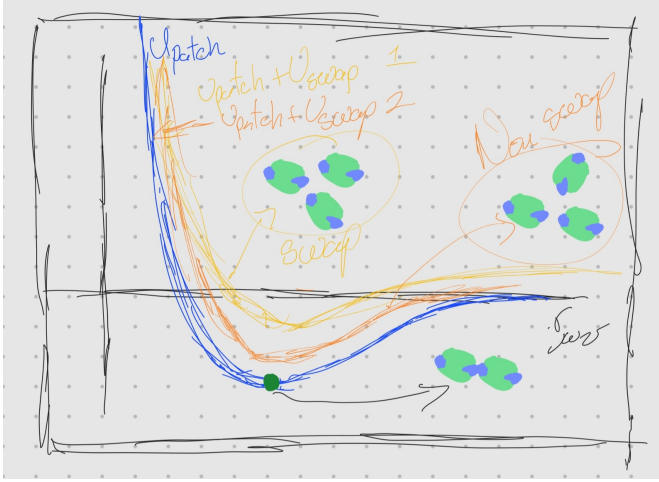

Figure 3.1: La idea de la figura es poner el pontecial de interacción entre paches y ver el efecto del pontecial de 3 cuerpos cuando $w = 1$ y cuando $w \gg 1$.
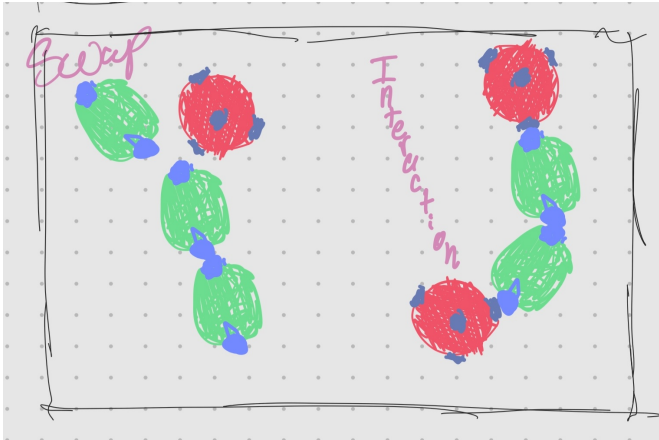

Figure 3.2: La idea de esta es mostrar las posibles configuraciones (monomero-monomero, monomero-crosslinker y un poco de pontecial de 3 cuerpos)

3.2.1   Assembly protocol

We perform molecular dynamics (MD) simulations at fixed temperature $T = kBT/\varepsilon = 0.05$, where kB is the Boltzmann constant. Thanks to such a low temperature, the system tends to maximize the number of bonds. In addition, owing to the bondswapping mechanism, the system is able to continuously

restructure itself, until the large majority of possible bonds are formed. It is important to said that the main difference between the articles cited and the implementation in this htesis are the absence of FENE bonds and the swelling potential.

3.2.2   Shear protocol

Parameters discussion   because yes, why shear rate and that stuff and discussion obout the damp

Figures   about the deformation?

3.3   Results

3.3.1   Network analysis

After   the shear

Before   the shear

3.3.2   Mechanical response

Varying shear rates and stuff

4
Conclusion

- What we achieve

- Future work

4.1   Discussion

About the mechanical response.   If it works or not and so on.

About the network characterization.   What it work or order arameters and so on.

4.2   Future work

About different crosslinking mechanisms.   To use FENE in some crosslinkers and yes.

About parameters   Shear rate, temperature, damp

5

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