Current Research in Food Science 5 (2022) 1873–1881

Contents lists available at ScienceDirect

Current Research in Food Science

journal homepage: www.sciencedirect.com/journal/current-research-in-food-science

A review on application of molecular simulation technology in food molecules interaction

Yan Wang [a], Tianjiao Liu [a], Jinhui Xie [a], Meijia Cheng [a], Lirui Sun [a], Shuai Zhang [a], Jiaying Xin [a,b], Na Zhang [a,*]

[a] Key Laboratory for Food Science & Engineering, Harbin University of Commerce, Harbin, 150076, PR China
[b] State Key Laboratory for Oxo Synthesis & Selective Oxidation, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou, 730000, PR China

ARTICLE INFO

Keywords:
Advantages
Application in foods
Development trend
Molecular simulation

ABSTRACT

Molecular simulation is a new technology to analyze the interaction between molecules. This review mainly summarizes the application of molecular simulation technology in the food industry. This technology has been employed to assess structural changes of biomolecules, the interaction between components, and the mechanism of physical and chemical property alterations. These conclusions provide a deeper understanding of the molecular interaction mechanism in foods, break through the limitations of scientific experiments and avoid blind and time-consuming scientific research. In this paper, the advantages and development trends of molecular simulation technology in the food research field are described. This methodology can be used to contribute to further studies of the mechanism of molecular interactions in food, confirm experimental results and provide new ideas for research in the field of food sciences.

1. Introduction

In recent years, molecular simulation technology has been widely used in physics, chemistry and other fields, but it is a relatively new technology in the field of food sciences. With the development of computer simulation technology, it is possible to obtain copious amounts of important information that is difficult to obtain experimentally. Although it does not completely replace experiments, molecular simulation technology provides an important reference for scientific researchers, guides experiments, verifies some theoretical hypotheses, and reduces the blindness encountered in experiments (Al-Khafaji and Tok, 2020; Hata et al., 2019; Harris et al., 2020).

In the field of food sciences, molecular simulation technology has mainly been applied to proteins, lipids and carbohydrates. (Cao et al., 2020; Wang et al., 2021a; Russell et al., 2021; Miao et al., 2021; Zhang et al., 2022). These food components are often combined with other substances or processed under different conditions to improve their functional properties. In the exploration of protein processing, nuclear magnetic resonance imaging, X-ray crystallography and cryogenic scanning electron microscopy provided very important information of various conformations, but it was very difficult to provide dynamic information of molecular functional motion directly (Schlichting and Miao, 2012; Heel et al., 2000; Mcilwain et al., 2021). For the dynamic description of protein molecules, fluorescence resonance energy transfer (FRET) and stop flow spectroscopy can provide measurement data of biomolecular structures (Roy et al., 2008; Schuler and Eaton, 2007; Mckinney et al., 2006). These experiments provide considerable structural information about biomolecular systems. However, it is very difficult for these methods to provide high-resolution structural information for each conformation in the functional movement of biological macromolecules. Molecular simulation technology can provide the dynamics and structural information of biological macromolecules simultaneously (Culletta et al., 2020; Moradi et al., 2020; Azadeh et al., 2020). Carbohydrates are often combined with other substances or processed under different conditions to improve their functional properties (Kang et al., 2022; Cai et al., 2020). During these processes, the structure of the carbohydrate is altered. The structure of carbohydrates can also be modified when they are processed through high pressure and heating (Mapengo et al., 2022; Wang et al., 2021b). Molecular simulation technology has been used in the structural analysis of carbohydrates, such as starch. Molecular simulation technology could provide an opportunity to explore the description of molecular properties that cannot be achieved in experiments. In addition, on the basis of traditional experimental and theoretical methods, molecular simulation

* Corresponding author.
E-mail address: foodzhangna@163.com (N. Zhang).

https://doi.org/10.1016/j.crfs.2022.10.012
Received 7 July 2022; Received in revised form 7 October 2022; Accepted 9 October 2022
Available online 11 October 2022

technology could provide some supplementary information for scientific experimental research, which could help us to better understand the structure and function of food materials. Molecular dynamics (MD) simulation technology was first applied to carbohydrates in 1986 by introducing this well-developed technology to understand the relationship between carbohydrate structure and its function. This prompted a breakthrough in the study of the interaction mechanism between carbohydrates and other molecules. Due to the limitation of computer hardware, resources, performance and MD simulation software, the starch simulation could only use 6, 7 or 8 glucose units to represent single chain starch molecules. Related studies showed that the bond length of a virtual angle formed by O4–O4′- O1′ could describe the change in twist angle of glucose residues. Koehler et al. (Koehleret al., 1988) studied the configuration change of α-cyclodextrin in aqueous solution by MD simulation, but the simulation time was only tens of picoseconds. Subsequently, Momany et al. (Momany and Willett, 2002) measured the glass transition temperature under different hydration conditions using the AMB99C force field with 10 glucose units as a part of amylose, and the simulation results were consistent with the experimental results. Godet et al. (Godet et al., 1993) intuitively demonstrated the formation of a V-shaped construction between amylose and fatty acids using molecular docking simulation technology, X-ray diffraction, and differential scanning calorimetry (DSC). The following construction features were noted. Hydrophobic long chains of fatty acids were located in the spiral cavity by the traction of hydrophobic forces. The polar ends of fatty acids were located outside of their spiral cavity due to steric hindrance and electrostatic repulsion. The change in starch structure during gelatinization of fermented dough was studied using the MD simulation technique, and the melting process of amylose and amylopectin was dynamically analyzed (Nivelle et al., 2019). Lipids can be processed in many ways, including frying and emulsifying. These processing could enrich food nutrients, extend the storage period and enhance flavor. However, during processing, a series of chemical reactions, such as oxidation and saponification, occur in lipids (Chen et al., 2017). These reactions could change the molecular structure and properties of lipids. Therefore, it is crucial to explore the changes in lipids during processing from a molecular perspective (Tian et al., 2014). Some scientists have used spectral imaging technology combined with molecular dynamics to explore changes in lipid processing (Cavaliere et al., 2020; Zhang et al., 2020). Especially in recent years with the rapid development of computers, molecular simulation technology has been able to deal with the system, and the time scale has been significantly improved. The theoretical method based on molecular simulation technology has become an important means to study the functional movement of biological macromolecules.

In summary, molecular simulation technology is critical to explain the experimental mechanism, so it has been widely used in the field of food sciences. This review focused on the commonly used software of molecular simulation technology and summarized in detail the application of molecular simulation technology in the field of proteins, lipids, and carbohydrates. This review provides a comprehensive overview of the application of molecular simulation techniques in the food field. That will assist researchers in selecting appropriate simulation techniques in the future.

2. Molecular simulation technology

2.1. Molecular docking

The history of molecular docking receptor theory can be traced back to the 19th century. With the development of receptor theory, people have a deeper understanding of the interaction between physiological activities and biological molecules. Molecular docking focused on the principle of complementarity. In 1894, Emil Fischer et al. (Fischer, 1894) believed that enzymes and substances have specific shapes that could be complementary to each other and fixed. This notion served as the foundation for the lock-key model, which was later termed the rigid. In 1958, Koshland proposed that the initial interaction between substrate and enzyme would change the conformation of enzyme, thus enhancing the binding with substrate and creating a flexible model based on space and energy matching (Riziotis et al., 2022). The optimization of the model makes it easier to simulate the interaction between molecules. The rapid development of computers and computing science makes it possible to deal with large amounts of data. These two factors contributed to the emergence of molecular docking methods (Ding et al., 2022).

Molecular mechanics or quantum chemistry methods were used to calculate molecular recognition between small molecules in the early stage of molecular docking technology. Some molecular simulation packages also contained molecular docking modules. However, it was difficult to handle the docking process with macromolecules using early molecular docking technology due to the limitations of algorithms and computer processing power. Currently, some commercial or free molecular docking software has been developed that prompted the application of molecular docking. Therefore, early molecular docking technology has evolved into modern molecular docking technology. The software was suitable for use in rigid docking, semiflexible docking, flexible docking and other docking methods. Modern molecular docking technology has been mainly applied to explore the interaction patterns between small and large molecules, biomolecular recognition, molecular self-assembly, and supramolecular structures (Gray et al., 2003).

At present, many scholars had applied molecular docking software. Common software were shown in Table 1.

2.2. Molecular dynamics simulation

2.2.1. Overview of molecular dynamics simulation

As early as 1957, Alder (Alder and Wainwright, 1957) first used MD simulation to calculate the states of gas and liquid in the condensed state and set a precedent for applying MD simulation to study the macroscopic properties of substances. As a frontier technology combining mathematics, physics, chemistry and biology, MD simulation has been developed and perfected in recent decades. It has become one of the most widely used molecular simulation methods. In the last decade, with the progression of computer science and technology, computing power has improved by leaps and bounds, and MD simulation has begun to demonstrate its powerful ability in many fields. Particularly in the field

Table 1
Introduction of molecular docking simulation software.

MD software	Is it free?	Main application scope	Download URL
AutoDock	Yes	It is designed to predict how small molecules, such as substrates or drug candidates, bind to a receptor of known 3D structure.	https://autodock.scripps.edu/
LeDock	Yes	It is designed for fast and accurate flexible docking of small molecules into a protein.	http://www.lephar.com/software.htm
rDock	Yes	It can be used to dock small molecules against proteins and nucleic acids.	http://rdock.sourceforge.net/
UCSF DOCK	Yes	It can predict binding modes of small molecule-protein complexes, search databases of ligands for compounds that inhibit enzyme activity and search databases of ligands for compounds that bind a particular protein.	https://dock.compbio.ucsf.edu/
Glide	No	Glide reliably identifies the correct binding modes for a large set of test cases. It outperforms other docking programs in achieving lower RMS deviations from native cocrystallized structures.	https://www.schrodinger.com/products/glide

of biological macromolecules, MD simulation increasingly showed its advantages of fast speed and high agreement with experimental results (Baildya et al., 2022; Mukut et al., 2022; Anwar et al., 2020; Chamani et al., 2022). Mr. Martin Karplus, one of the pioneers of MD simulation, also won the Nobel Prize in chemistry in 2013. One of the most important characteristics of MD simulation is that it can observe the evolution of the system over time. With improvements in computers, MD simulation has reached the picosecond (Ps) time scale (Shaw et al., 2010; Raval et al., 2012).

2.2.2. Common software for MD simulation

Table 2 shows some commonly used MD simulation software. Some of the software is free, but the focus of each software is slightly different.

Among them, GROMACS is the most commonly used MD simulation software (Lange et al., 2010). GROMACS is MD simulation software developed by the Department of Biophysics and Chemistry of Groningen University in the Netherlands. First, the main purpose of GROMACS was to study the folding of biomolecules, such as lipids, nucleic acids and proteins, as well as the internal interactions of biomolecules (Hess et al., 2008). Later, GROMACS performed a large number of algorithm optimizations. GROMACS offered great advantages in simulating the Newtonian motion of systems with several hundred to several million particles, and its applicable research scope was also extended to liquid crystals, crystals, polymers, biological macromolecules and other fields. The simulation package of GROMACS mainly used the force field of GROMACS combined with MD, stochastic dynamics or the path integral method to simulate the motion of any molecule in the system and analyze the internal interaction and conformational changes of the system. In addition, GROMACS provides a visual trajectory program with a user-friendly interface, which is convenient for users to operate. GROMACS software also provides many plug-in tools for trajectory analysis, and users do not need to write any scripts and programs for conventional analysis. GROMACS can also be used on Windows, Unix, Linux and other operating systems. The most important point is that GROMACS software is free to download, and related application tutorials can be found on the website. The latest version of GROMACS can be freely downloaded at http://www.gromacs.org/.

Assisted Model Building with Energy Refinement (AMBER) is one of the most widely used MD simulation software programs in the world (Pearlman et al., 1995; Salomon et al., 2013; David et al., 2005). AMBER is not only a program but also a collection of programs useful for system preparation, dynamics simulation and trajectory analysis. AMBER is also the name of a series of force fields (Wang et al., 2004; Jayaram et al., 1998), including proteins, nucleic acids, sugars, lipids and many other biological macromolecules. AMBER is especially good at dealing with biological systems, and it is one of the most important software for biomolecular simulation.

Table 2
Introduction of MD simulation software.

MD software	Is it free?	Main application scope	Download URL
AMBER	No	It covers a variety of biomolecules, including small drug molecules, proteins and nucleic acids.	http://ambermd.org/
GROMACS	Yes	It is mainly suitable for the study of protein folding and protein–protein interactions.	http://www.gromacs.org/
LAMMPS	Yes	It is suitable for the simulation of macromolecular systems with hundreds of thousands to billions of particles.	http://lammps.sandia.gov/
OPEP	Yes	Models for protein folding; polymerization research; structure prediction of peptides and small proteins; and simulation of the role of fluid dynamics in protein relaxation and peptide aggregation.	http://www-lbt.ibpc.fr/
CHARMM	No	A widely recognized and applied molecular dynamics simulation program for biomolecular simulation, including energy minimization, molecular dynamics and Monte Carlo simulation.	http://www.charmm.org/

2.3. Quantum mechanics

Quantum mechanics (QM) can be used to describe the structure, motion and change of molecules, electrons, nuclei and other microscopic substances. Compared with other molecular simulations, quantum mechanics focuses more on electrons. It has been used to explore electronic structures, including the formation and breaking of chemical bonds. QM plays an extremely important role in explaining complex chemical systems. The techniques were mainly divided into ab initio algorithms, semiempirical methods and density functional theory calculations (Seritan et al., 2020; Gundelach et al., 2021). In the early days, quantum mechanics could only be used to study atoms or highly symmetrical systems. However, with the development of computer technology, it is currently easier to model density functional theory to study large molecules (Schmitz et al., 2020). QM could be applied to more realistic experimental systems, including molecular configurations and properties, chemical reaction mechanisms and biomolecular interactions. For the microsystem, the computational accuracy of QM reached or even exceeded the experimental accuracy. However, QM requires a large amount of calculation in complex systems. In contrast to quantum mechanics, molecular mechanics can be used to calculate larger, more complex systems. However, molecular mechanics technology cannot accurately describe the process of bond formation and rupture. Therefore, it is necessary to combine quantum mechanics and molecular mechanics. Professor Martin et al. jointly applied QM and molecular mechanics (MM) for chemical modeling through a process referred to as QM/MM (Zhang et al., 2019).

QM/MM divides the whole research system into local areas in the system (such as the need for precise calculation of the reaction area) treated with the method of quantum mechanics. The remaining part is treated by MM, which can reflect the change in electronic structure more accurately (Vennelakanti et al., 2021). QM/MM was used to deal with host-guest systems with more flexibility and larger conformational space (Caratzoulas and Vlachos, 2011). Among biomolecules, QM/MM is mostly used in the field of medicine but used less often in the field of food sciences. In the future, with the development of computer technology and the continuous determination of molecular structures, QM/MM is expected to be widely used in the food industry, and these studies will promote the development of food processing mechanisms and technology.

3. Application of molecular simulation in foods

3.1. Application of molecular simulation in carbohydrates

The structure and function of carbohydrates is an important component of food research. The solvation of carbohydrates determines the behavior of carbohydrates in water, significantly influencing the taste, viscosity, storage and gelatinization of food. The interaction of carbohydrates with proteins, lipids and other components determines the proliferation or decline of microorganisms in the human intestinal tract, which affects the balance of the microecosystem in the human body and human health. To better understand these behaviors of carbohydrates at the atomic scale, MD simulation is helpful to further explore its mechanism of action. Therefore, MD simulation is necessary for further study of food carbohydrates. In addition, the development of new force field or MD simulation programs on food carbohydrates represents another research field for food scientists.

Molecular simulation techniques were used to study cyclodextrin, artichoke pectin oligosaccharides and several microbial glycosidases

and mannose (Sabater et al., 2020; Parthasarathi et al., 2011; Gornas et al., 2009). The relationship between the host and object was explored by simulating the cyclodextrin-ferrocene complex and cyclodextrin-ferrocene acrylate complex. This analysis allowed for the design of effective "enzyme simulation" capabilities. The MD of the β-cyclodextrin inclusion complex formed with phenol, chlorogenic acid and caffeic acid in aqueous solution and the stability of the inclusion complex were determined. At the molecular level, the inclusion complex was mainly stabilized by van der Waals interactions, and hydrogen bonding improved the stability of the inclusion complex. These results provide a reference for the control of the release of bitter compounds in coffee by cyclodextrin. By studying the hydration of monosaccharide, the compatibility of basic carbohydrates with water could be further studied. To explore the hydration of glycosidic bonds, the conformation of glycosidic bonds should be analyzed first, which requires molecular simulation technology. The interaction mechanism between artichoke pectin oligosaccharides and several microbial glycosidases was also proposed by molecular simulation. The established structure-activity relationship was helpful for further experimental research. In addition, the structural basis and energetics of sugar-phospholipid interactions can be obtained using quantum mechanics. Different phospholipids (POPC and DOPC) and their interactions with mannose were studied. The results showed that the interactions of OH–O, CH–O and CH–P had important effects on the stability of intermolecular complexes. The interaction of mannose with phospholipids caused changes in charge distribution and conformation. In summary, molecular simulation could effectively explore the structural changes in small molecules. These findings should be verified with experimental results, and this information could further predict the location of structural changes.

At present, MD simulation has been used in carbohydrate research. Especially in recent years, MD simulations have been used to further explain the mechanism of starch binding and structural change. The influence of xanthan gum (XG) on the color stability of black rice anthocyanin (BRA) and its mechanism could be measured by FTIR and XRD as previously reported. However, the application of a molecular simulation technique could supplement the experimental results of XG action on BRA (Zhao et al., 2020). The results showed that the interaction between XG and BRA was mainly driven by hydrogen bonding and hydrophobic interactions, thus improving the stability of BRA (Zhao et al., 2021). Molecular simulation techniques could also describe the dynamics of amylose in lipid solutions at the molecular level. Amylose eventually folds into a V-shaped conformation driven by the interaction between the aliphatic lipid tails and the hydrophobic core of the polysaccharide (López et al., 2012). This study deepened the theoretical solution of the formation of amylose in the v-conformation. This information provided a theoretical basis for V-amylose to deliver hydrophobic nutrients. The stability of the amylopectin-linoleic acid complex in water was obtained by molecular simulation (Cheng et al., 2018). The following conclusions were reported. In the simulation process, linoleic acid and amylose molecules formed a spiral structure and existed stably in water. $^4C_1$ was the main ring conformation in the interaction between the glucose unit and linoleic acid in amylose. The complexation mechanism of amylose and linoleic acid was completely understood at the atomic level using MD technology. This information provided a new method for regulating starch regeneration and gelatinization and inhibiting the oxidation of unsaturated fatty acids.

The structure of the carbohydrate is altered upon binding with the ligand. Traditional experiments can only reveal the final structure of the complex and cannot describe the dynamic changes during its formation. There are two mechanisms by which starch binds with polyphenols. In one mechanism. the amylose structure changed, and a spiral structure formed by hydrogen bonding of starch under the action of external conditions (Lorentz et al., 2012). For example, phenols enter the helix cavity of starch through hydrophobicity and form a V-amylose complex (Chi et al., 2018). Another mechanism relies on hydrogen bonding and van der Waals forces to form the complex of starch and polyphenol (Gidley and Bociek, 1988; Kong et al., 2014). Determining how starch interacts with polyphenols is very difficult in practice. Concentrated chestnut rose juice was added to common wheat starch under microwave treatment (Zhu et al., 2021). The initial conformation for MD was obtained based on molecular docking. The docking conformation and nonbonding interaction between juice and starch were obtained by MD technology. This information promoted the progress of subsequent experiments.

Rice starch has a multiscale structure (Pérez and Bertoft, 2010; He et al., 2021), and different treatments alter the digestibility of starch to varying degrees. For example, rice starch can be treated using the moist heat method (Yang et al., 2019), or anthocyanins are combined with rice starch (Ratseewo et al., 2019). These treatments lead to structural changes in starch, thus altering the digestion characteristics of starch. However, understanding the relationship between the specific structure of starch and its digestibility remains unrealistic. Traditional research methods do not clearly elucidate how the structure of starch changes. Molecular simulation technology is the only way to solve this issue. The interaction between anthocyanins and amylose by molecular docking and the effect of anthocyanins on the physicochemical properties of rice starch have been reported. (Miao et al., 2021). The effects of anthocyanins on the digestibility of rice starch could be divided into two aspects: the combination of anthocyanins and rice starch and the combination of anthocyanins and α-amylase. As shown in Fig. 1, the conformation of amylose changed over time. The alteration of its conformation could prevent the hydrolysis of α-amylase to starch. In addition, anthocyanins occupied the active binding site of α-amylase. This resulted in competition with substrates and reduced starch digestibility. In particular, some amino acid residues form hydrogen bonds with anthocyanins, which could improve the stability of anthocyanins and α-amylase. These results explained the reduction mechanism of rice starch digestibility in the presence of anthocyanins at the molecular level. These results also confirmed that the presence of anthocyanins could cause structural changes in starch. In addition to anthocyanins, polyphenols can complex with starch (Kan et al., 2020).

Flavonoids, quercetin and rutin inhibit the digestion of starch and alter the structure of starch. The molecular docking technique revealed the binding sites of rutin and quercetin (Wang et al., 2021a). Part of the structure of rutin is similar to quercetin, but its exhibits reduced inhibition of enzymatic activity compared with quercetin. Specifically, rutin interacted with the enzyme mainly through C–H and O–H on the glycoside structure, causing a spatial site block that limited the inhibitory effect of quercetin. The glycosidic structure of rutin weakens the inhibitory effect on the free digestive enzymes but did not affect the anti-digestive effect of the starch-rutin complex. Molecular simulation technology, an emerging experimental approach in the food field, illustrates the interaction of anthocyanins with starch digestive enzymes. This information could help to further demonstrate the mechanism of altered starch digestibility (Miao et al., 2021). Molecular docking techniques were used to study the interactions between molecules, such as cyclodextrin and branched amylase as well as flavanols and α-amylase (Chao et al., 2021). These scientific results revealed that the ligands in the complex could not only combine with starch to alter its structure but could also inhibit the digestion of starch by binding to amylase. In conclusion, molecular simulation is an effective technology that can be used to clarify the interaction mechanism between carbohydrates and enzymes. This information also provides a new theoretical basis for screening active substances and structural modifications. In addition, it is helpful to understand the regulatory mechanism of enzyme activity to promote the application of active substances as functional food components. In addition, MD simulations have been used to gain an in-depth understanding of the incorporation of nanoparticles self-assembled from macromolecular components (amylose, protein and fatty acids) in food into soluble small molecules (1-naphthol), solving the problem of the limited application of small molecules with low solubility activity (Bhopatkar et al., 2015). MD technology is a powerful tool to describe

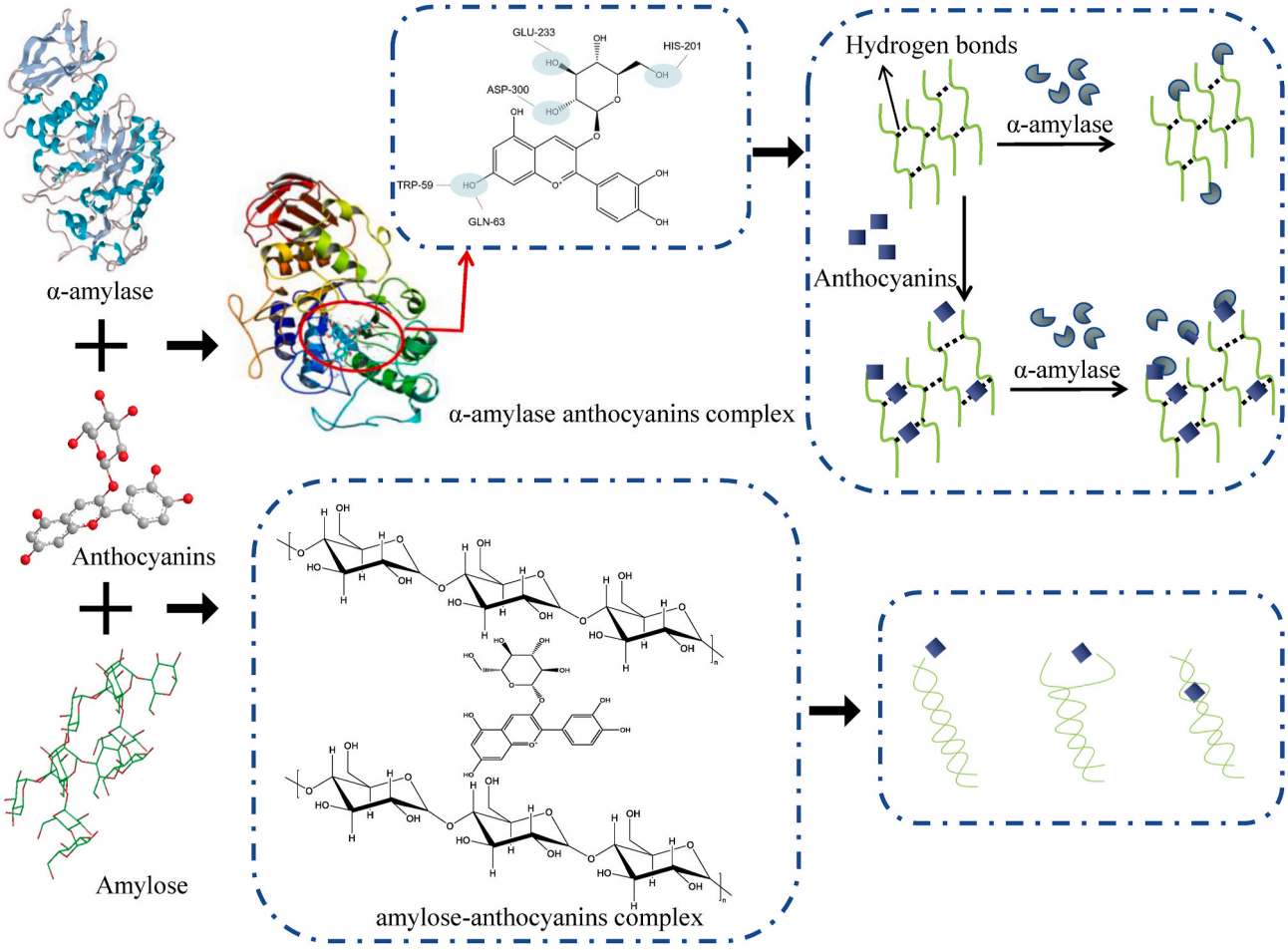

Fig. 1. Schematic illustration of the inhibitory digestion of amylase-anthocyanin complexes and α-amylase-anthocyanin complexes. Cyan circle, bonding site. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

the state of carbohydrates in solution and provides theoretical guidance for starch modification, recombination of carbohydrates with small molecules and the solubility of small molecule active substances.

3.2. Application of molecular simulation in proteins

Protein is also one of the main sources of energy in food. In addition, proteins provide essential amino acids for the human body. The main proteins in food included whey protein, casein, collagen, soy protein and wheat protein. Taking α-lactalbumin as an example, the structure of α-lactalbumin and how it is affected by medium conditions have been elucidated. The effect of Ca^{2+} on the thermal stability of α-lactalbumin and the conformational change of α-lactalbumin were confirmed by fluorescence spectrometry, circular dichroism spectrometry and calorimetry. However, MD was used to study the molecular characteristics of the α-La structure. The study findings revealed that Ca^{2+} binding sites in α-La of different structures gradually opened with increasing time. Ca^{2+} depletion triggered the complete loss of h2b and h3c helices and S1, S2 and S3 β-sheets and partial losses of H1, H2 and H3 α-helices. Specific depleted structures (APO-α-La) were observed near the ends of the time traces. The removal of Ca^{2+} from α-La affected Asp82, Asp84 and Asp87, causing electrostatic repulsion among these amino acids. Hydrophobic clusters were formed in Phe9, Phe31, Ile1, Va42, Ile55, Phe80 and Leu81. These conformational changes led to a decrease in interfacial tension and an increase in foaming ability (De Oliveira et al., 2021). Proteins can also form complexes with other molecules. The possibility and mechanism of binding could be explored by molecular docking and molecular dynamics simulation. For example, zein interacted with EGCG (Liu et al., 2021). The fluorescence quenching of zein by EGCG was mainly static. The formation of the zein EGCG complex was confirmed by scanning electron microscopy. In addition, molecular dynamics simulations showed that residues Y171, Q174, L176 and L205 could form zein pockets, to which EGCG binds. The interactions mainly involved electrostatic and van der Waals forces.

As shown in Fig. 2, the key residue formed binding pockets with L205, and the conformation of the protein also changed. According to RMSD analysis, the system reached equilibrium after 30 ns. Therefore, in RMSF analysis, the trajectory in the equilibrium state was selected. The results showed that the RMSD and RSMF values of Holo-Zein were lower than those of APO-Zein, and EGCG promoted the structural stability of zein. Similarly, the curcumin and myosin complex could be confirmed by UV–VIS spectra. However, the specific mechanism of action needs to be observed through molecular dynamics simulation. When curcumin was added, the structure near the binding pocket of myosin could be changed, but the folding of myosin remained unchanged (Zhang et al., 2020). Molecular dynamics simulations confirm that the stability of vanillic acid was dynamic in nature in the experiment assessing the combination of β-lactoglobulin and vanillic acid (Abdollahi et al., 2021). β-Lactoglobulin is a major food allergen. Enzymatic hydrolysis could reduce the antigenicity of β-lactoglobulin. The antigenicity of β-lactoglobulin significantly differed based on different cleavage sites. Protein docking bags could form between the residues Tyr20, Glu157 and His161 using molecular docking technology. According to the analysis of binding free energy, the energy of the AY-10 cleavage site of the Gln amino acid was the lowest, and enzymic hydrolysates with low antigenicity were obtained. AY-10 cleavage exhibited excellent antigenicity.

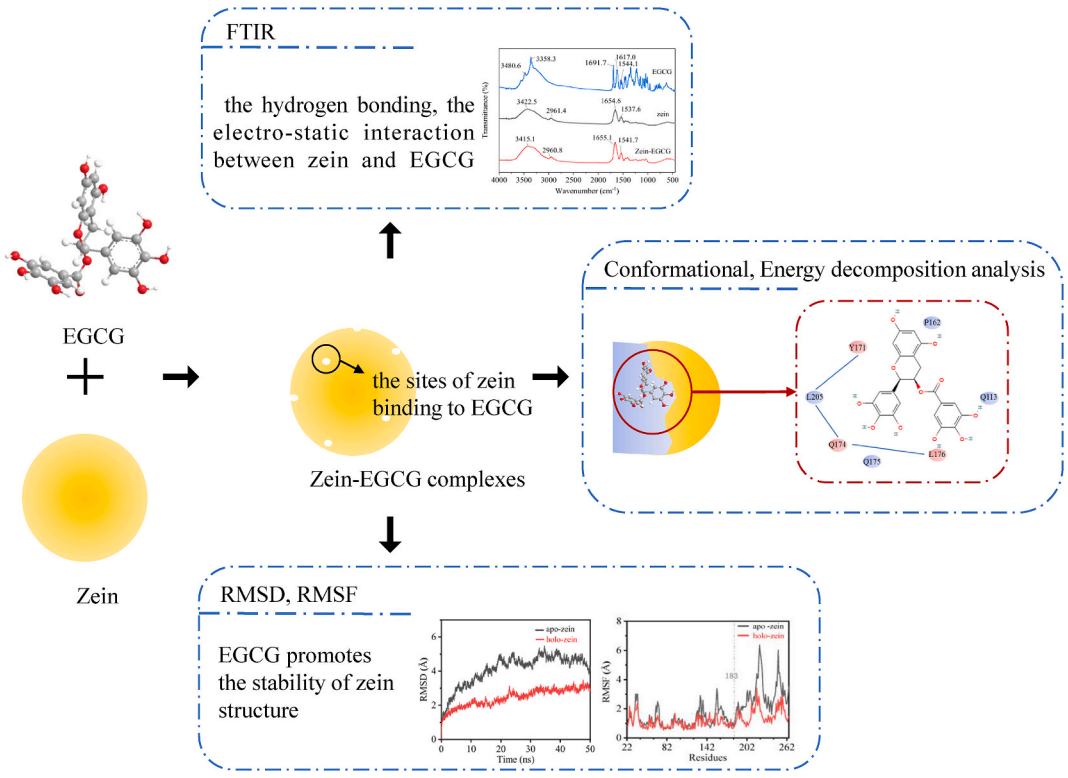

Fig. 2. Schematic diagram of the interaction mechanism between zein and EGCG.

This method is expected to be an effective method to reduce its antigenicity. The identification of epitopes has been considered of important practical value for guiding the development of hypoallergenic dairy products (Yu et al., 2021). Bambara bean protein also has broad application prospects in the food industry. The structural changes of Bambara bean protein isolate (BBPI) under pH and high-pressure treatment (HPP) were analyzed by fluorescence spectroscopy and MD (Martin et al., 2020). After BBPI modification, a fluorescence shift was observed, indicating that the structure of BBPI was extended. MD molecular analysis was used to dynamically observe the decrease in the hydrogen

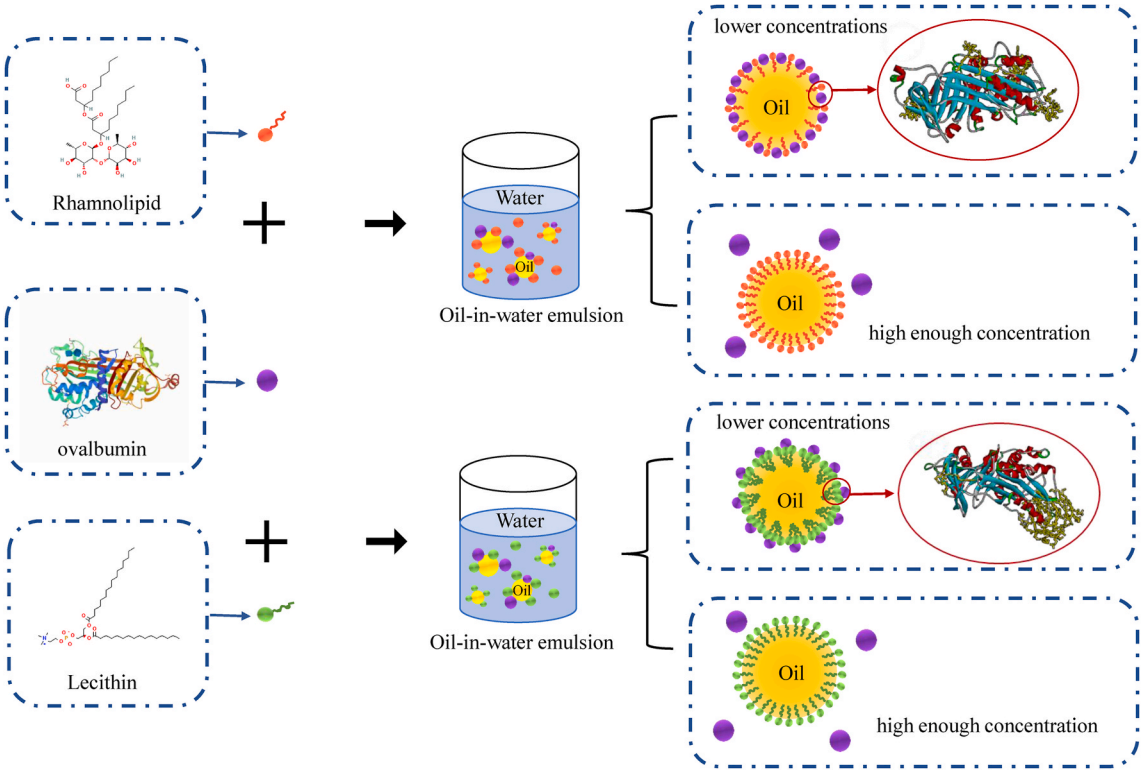

Fig. 3. Mechanism by which surfactant molecules bind to ovalbumin.

bond content of the protein in BBPI under HPP conditions, resulting in the exposure of Tyr and Trp residues, which further explained the mechanism of structural change. Similarly, exogenous substances can be added to improve the quality of some protein-rich products. MD simulation could be used to effectively observe the dynamic process of protein binding with exogenous substances, providing a supplement to the experimental conclusions (Jia et al., 2021).

3.3. Application of molecular simulation in lipids

The application of MD simulation in lipids is not as extensive as that in proteins. In this review, the application of MD simulation in emulsions is briefly described. The emulsion consists of two parts, the oil phase and water phase, and is widely used in the food industry. Although a series of experiments, such as microscopic characterization, could be used to explore the structural changes of the emulsion, it is not possible to observe the structural change process dynamically. Therefore, molecular dynamics simulation could further explain the mechanism of emulsion structural changes. The thermal stability of the egg white protein emulsion was affected by different concentrations of monoglyceride, lecithin and rhamnoid biosurfactants (Russell et al., 2021). The mechanisms of high concentrations of surfactant and lower concentrations of surfactant differ. Therefore, molecular docking and molecular dynamics simulation could be used to observe the binding of emulsifier to protein, further exploring the influencing mechanism. As shown in Fig. 3, the combination of surfactants with proteins could affect the stability of the emulsion. At lower concentrations, mixing interfaces were formed between surfactants and protein, leading to conformational changes in the protein. The mechanisms by which proteins interact with different types of surfactants differ. Rhamnolipids bind to ovalbumin by adsorption of a single surfactant molecule. However, monoglycerides were adsorbed to ovalbumin in micelle clusters. At high concentrations, proteins were completely replaced, leaving surfactants to stabilize the emulsion, which also affected its stability.

Dihydromyricetin could also be used to stabilize Pickering latex gels (Geng et al., 2021). Molecular dynamics simulation was used to characterize the microscopic behavior of two statins in emulsions. This method revealed that dihydromyricetin particles formed a relatively stable three-dimensional network structure by overlapping and separating oil droplets, thus stabilizing the gel structure of the emulsion. MD simulation of the self-assembly process of palmityl ester nanoemulsion also reflected the advantages of molecular dynamics simulation. This was a dynamic simulation process in which the palmityl ester nanoemulsion system continuously aggregates and depolymerizes to achieve the final stability (Abdul Rahman et al., 2009). In addition, MD simulation was used to investigate the structural properties of swollen micelles of oleyl oleate. The composition of oil and surfactant would affect the shape of swelling micelles in nanoemulsions. The addition of oleic oleate (OE) molecules changed the structure of the swelling micelles. When OE/S20 ranged from 10% to 50%, micellar shapes were generated and changed constantly. The structure can be an infinite cylinder, cube or slice. (Abdul Rahman et al., 2010). Molecular simulation technology was helpful for exploring the structure of lipids.

4. Conclusion and prospects

With the continuous progression of science and the rapid development of computer software and hardware, molecular simulation technology has gradually occupied an indispensable position in the field of food biomacromolecule research. Molecular simulation technology can effectively simulate the dynamic process of the structural changes in biological macromolecules and push the time scale to the picosecond level. Molecular simulation technology can be used to observe the binding between molecules and the changes in molecular bond length and bond angle from another angle. The simulation results were closer to the real experimental data, which prevented the research from being completed or realized in the laboratory. Although molecular simulation technology has developed rapidly, the internal structure of the organism system is more complex than imagined. Uncertain factors would change with time; thus, the simulation process of biological macromolecules is confined. This process requires the improvement of the computing software and hardware as much as possible to meet the needs of solving practical problems. Therefore, extensive research should be performed to enhance the practical significance, expand the scope of application and improve the value of guidance. Molecular simulation technology could be used to explore the mechanism of structural changes in biological macromolecules, which would further supplement the experimental results. Therefore, this review is expected to provide some help for follow-up studies.

CRediT authorship contribution statement

Yan Wang: Conceptualization, Literature Search, Writing-original draft, Writing-review and editing. **Tianjiao Liu:** Literature Search, Writing, and Editing. **Jinhui Xie and Meijia Cheng:** Literature Search. **Lirui Sun and Shuai Zhang:** Investigation. **Jiaying Xin and Na Zhang:** Supervision. All authors discussed the results and contributed to the final manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (32072258), the National Key Research and Development Program of China (2021YFD2100902-3), the financial support from the Major Science and technology Program of Heilongjiang (2021ZX12B07), the Natural Science Foundation of Heilongjiang (LH2021C051), Central financial support for the development of local colleges and Universities.

References

Abdollahi, K., Condict, L., Hung, A., Kasapis, S., 2021. Binding parameters and molecular dynamics of β-lactoglobulin-vanillic acid complexation as a function of pH-part A: acidic pH. Food Chem. 360, 130059 https://doi.org/10.1016/j.foodchem.2021.130655.

Abdul Rahman, M.B., Huan, Q.Y., Tejo, B.A., Basri, M., Salleh, A.B., Rahman, R.N.Z.A., 2009. Self-assembly formation of palm-based esters nano-emulsion: a molecular dynamics study. Chem. Phys. Lett. 480 (4–6), 220–224. https://doi.org/10.1016/j.cplett.2009.08.073.

Abdul Rahman, M.B., Latif, M.A.M., Basri, M., Salleh, A.B., Abdul Rahman, R.N.Z., 2010. Molecular dynamics simulation of oleyl oleate swollen micelles system. Mol. Simulat. 36 (5), 403–407. https://doi.org/10.1080/08927020903544535.

Alder, B., Wainwright, T., 1957. Phase transition for a hard sphere system. J. Chem. Phys. 27 (5), 1208–1209. https://doi.org/10.1063/1.1743957.

Al-Khafaji, K., Tok, T., 2020. Molecular dynamics simulation, free energy landscape and binding free energy computations in exploration the anti-invasive activity of amygdalin against metastasis. Comput. Methods Progr. Biomed. 195, 105660 https://doi.org/10.1016/j.cmpb.2020.105660.

Anwar, S., Kar, R.K., Haque, M.A., Dahiya, R., Gupta, P., Islam, A., Ahmad, F., Hassan, M. I., 2020. Effect of pH on the structure and function of pyruvate dehydrogenase kinase 3: combined spectroscopic and md simulation studies. Int. J. Biol. Macromol. 147, 768–777. https://doi.org/10.1016/j.ijbiomac.2020.01.218.

Azadeh, K., Ahmad, R., Amin, H., 2020. Investigation on penetration of saffron components through lipid bilayer bound to spike protein of SARS-CoV-2 using steered molecular dynamics simulation. Heliyon 6 (12), e05681. https://doi.org/10.1016/j.heliyon.2020.e05681, 2020.

Baildya, N., Ghosh, N.N., Chattopadhyay, A.P., Mandal, V., Majumdar, S., Ansary, D., Sarkar, M.M., 2022. Inhibitory effect of compounds extracted from Monochoria

hastata (L.) Solms on SARS-CoV-2 main protease: an insight from molecular docking and MD-simulation studies. J. Mol. Struct. 1257, 132644 https://doi.org/10.1016/j.molstruc.2022.132644.
Bhopatkar, D., Feng, T., Chen, F., Zhang, G., Carignano, M., Park, S.H., Zhuang, H., Campanella, O.H., Hamaker, B.R., 2015. Self-assembled nanoparticle of common food constituents that carries a sparingly soluble small molecule. J. Agric. Food Chem. 63 (17), 4312. https://doi.org/10.1021/acs.jafc.5b00037.
Cai, J., Chao, C., Niu, B., Copeland, L., Wang, S., 2020. New insight into the interactions among starch, lipid and protein in model systems with different starches. Food Hydrocolloids 112, 106323. https://doi.org/10.1016/j.foodhyd.2020.106323.
Cao, Q., Huang, Y., Zhu, Q., Song, M., Xiong, S., Manyande, A., Du, H., 2020. The mechanism of chlorogenic acid inhibits lipid oxidation: an investigation using multi-spectroscopic methods and molecular docking. Food Chem. 333 (15), 127528 https://doi.org/10.1016/j.foodchem.2020.127528.
Caratzoulas, S., Vlachos, D.G., 2011. Converting fructose to 5-hydroxymethylfurfural: a quantum mechanics/molecular mechanics study of the mechanism and energetics. Carbohydr. Res. 346 (5), 664–672. https://doi.org/10.1016/j.carres.2011.01.029.
Cavaliere, F., Lorenzetti, S., Cozzini, P., 2020. Molecular modelling methods in food safety: bisphenols as case study. Food Chem. Toxicol. 137, 111116 https://doi.org/10.1016/j.fct.2020.111116.
Chamani, R., Taleqani, M.H., Imanpour, A., Khatami, M., 2022. New insights into short peptides derived from the collagen NC1 α1, α2, and α3 (IV) domains: an experimental and MD simulations study. Biochim. Biophys. Acta, Proteins Proteomics 1870, 140769. https://doi.org/10.1016/j.bbapap.2022.140769.
Chao, J., Yu, C., Xin, Y., Li, W., Shao, J., Jing, H., Jiang, C., Wang, H., Ma, C., 2021. Three flavanols delay starch digestion by inhibiting α-amylase and binding with starch. Int. J. Biol. Macromol. 172, 503–514. https://doi.org/10.1016/j.ijbiomac.2021.01.070.
Chen, H., Wang, Y., Cao, P., Liu, Y., 2017. Effect of temperature on thermal oxidation of palmitic acid studied by combination of EPR spin trapping technique and SPME-GC–MS/MS. Food Chem. 234, 439–444. https://doi.org/10.1016/j.foodchem.2017.04.135.
Cheng, L., Feng, T., Zhang, B., Zhu, X., Hamaker, B., Zhang, H., Campanella, O., 2018. A molecular dynamics simulation study on the conformational stability of amylose-linoleic acid complex in water. Carbohydr. Polym. 196, 56–65. https://doi.org/10.1016/j.carbpol.2018.04.102.
Chi, C., Li, X., Feng, T., Zeng, X., Chen, L., Li, L., 2018. Improvement in nutritional attributes of rice starch with dodecyl gallate complexation: a molecular dynamic simulation and in vitro study. J. Agric. Food Chem. 66 (35), 9282–9290. https://doi.org/10.1021/acs.jafc.8b02121.
Culletta, G., Almerico, A., Tutone, M., 2020. Comparing molecular dynamics-derived pharmacophore models with docking: a study on cdk-2 inhibitors. Chem. Data Collect. 28, 100485 https://doi.org/10.1016/j.cdc.2020.100485.
De Oliveira, T.V., Polêto, M.D., Barbosa, S.V., Coimbra, J.S.D.R., De Oliveira, E.B., 2021. Impacts of Ca^{2+} cation and temperature on bovine α-lactalbumin secondary structures and foamability insights from computational molecular dynamics. Food Chem. 367, 130733 https://doi.org/10.1016/j.foodchem.2021.130733.
Ding, B.T., Yu, Y.D., Geng, S., Liu, B.G., Hao, Y.J., Liang, G.Z., 2022. Computational methods for the interaction between cyclodextrins and natural compounds: technology, benefits, limitations, and trends. J. Agric. Food Chem. 70 (8), 2466–2482. https://doi.org/10.1021/acs.jafc.1c07018.
Fischer, E., 1894. Einfluss der Configuration auf die Wirkung der Enzyme. Ber. Dtsch. Chem. Ges. 27 (3), 2985–2993. https://doi.org/10.1002/cber.18940270364.
Geng, S., Jiang, Z., Ma, H., Pu, P., Liu, B., Liang, G., 2021. Fabrication and characterization of novel edible pickering emulsion gels stabilized by dihydromyricetin. Food Chem. 343 (1), 128486 https://doi.org/10.1016/j.foodchem.2020.128486.
Gidley, M.J., Bociek, S.M., 1988. 13C CP/MAS NMR studies of amylose inclusion complexes, cyclodextrins, and the amorphous phase of starch granules: relationships between glycosidic linkage conformation and solid-state 13C chemical shifts. J. Am. Chem. Soc. 110 (12), 3820–3829. https://doi.org/10.1002/chin.198839296.
Godet, M., Tran, V., Delage, M., Buléon, A., 1993. Molecular modelling of the specific interactions involved in the amylose complexation by fatty acids. Int. J. Biol. Macromol. 15 (1), 11–16. https://doi.org/10.1016/S0141-8130(05)80082-0.
Gornas, P., Neunert, G., Baczynski, K., Polewski, K., 2009. Beta-cyclodextrin complexes with chlorogenic and caffeic acids from coffee brew: spectroscopic, thermodynamic and molecular modelling study. Food Chem. 114 (1), 190–196. https://doi.org/10.1016/j.foodchem.2008.09.048.
Gray, J., Moughon, S., Wang, C., Schueler-Furman, O., Kuhlman, B., Rohl, C., Baker, D., 2003. Protein–protein docking with simultaneous optimization of rigid-body displacement and side-chain conformations. J. Mol. Biol. 331 (1), 281–299. https://doi.org/10.1016/s0022-2836(03)00670-3.
Gundelach, L., Fox, T., Tautermann, C.S., Skylaris, C.K., 2021. Protein-ligand free energies of binding from full-protein dft calculations: convergence and choice of exchange-correlation functional. Phys. Chem. Chem. Phys. 23 (15), 9381–9393. https://doi.org/10.1039/D1CP00206F.
Harris, D., Muzzopappa, F., Glaser, F., Wilson, A., Adir, N., 2020. Structural dynamics in the c terminal domain homolog of orange carotenoid protein reveals residues critical for carotenoid uptake. Biochim. Biophys. Acta Bioenerg. 1861 (8), 148214 https://doi.org/10.1016/j.bbabio.2020.148214.
Hata, H., Nishiyama, M., Kitao, A., 2019. Molecular dynamics simulation of proteins under high pressure: structure, function and thermodynamics. Biochim. Biophys. Acta Gen. Subj. 1864 (2), 129395 https://doi.org/10.1016/j.bbagen.2019.07.004.
He, H., Bin, H., Xie, F., Chen, L., 2021. Different effects of pectin and κ-carrageenan on the multiscale structures and in vitro digestibility of extruded rice starch. Food Hydrocolloids 111, 106216. https://doi.org/10.1016/j.foodhyd.2020.106216.
Heel, M., Gowen, B., Matadeen, R., Orlova, E., Finn, R., Pape, T., Cohen, D., Strark, H., Schmidt, R., Schatz, M., 2000. Single-particle electron cryo-microscopy: towards atomic resolution. Q. Rev. Biophys. 33 (4), 307–369. https://doi.org/10.1017/s0033583500003644.
Hess, B., Kutzner, C., Spoel, D., Lindahl, E., 2008. Gromacs 4: algorithms for highly efficient, load-balanced, and scalable molecular simulation. J. Chem. Theor. Comput. 4 (3), 435–447. https://doi.org/10.1021/ct700301q.
Jayaram, B., Sprous, D., Beveridge, D., 1998. Solvation free energy of biomacromolecules: parameters for a modified generalized born model consistent with the amber force field. J. Phus. Chem. B 102 (47), 9571–9576. https://doi.org/10.1021/jp982007x.
Jia, Y., Kowalski, P., Lopez, I., 2021. Using yeast two-hybrid system and molecular dynamics simulation to detect venom protein-protein interactions. Chem. Res. Toxicol. 2, 93–98. https://doi.org/10.1016/j.crtox.2021.02.006.
Kan, L., Oliviero, T., Verkerk, R., Fogliano, V., Capuano, E., 2020. Interaction of bread and berry polyphenols affects starch digestibility and polyphenols bio-accessibility. J. Funct.Foods 68, 103924. https://doi.org/10.1016/j.jff.2020.103924.
Kang, X., Jia, S., Gao, W., Wang, B., Zhang, X., Tian, Y., Sun, Q., Mohammed, A., Cui, B., El-Aty, A., 2022. The formation of starch-lipid complexes by microwave heating. Food Chem. 382, 132319 https://doi.org/10.1016/j.foodchem.2022.132319.
Koehler, J., Saenger, W., Van, G., 1988. Conformational differences between a-cyclodextrin in aqueous solution and in crystalline form:A molecular dynamics study. J. Mol. Biol. 203 (1), 241–250. https://doi.org/10.1016/0022-2836(88)90105-2.
Kong, L., Lee, C., Kim, S.H., Ziegler, G.R., 2014. Characterization of starch polymorphic structures using vibrational sum frequency generation spectroscopy. J. Phys. Chem. B 118, 1775–1783. https://doi.org/10.1021/jp411130n.
Lange, O., Schäfer, L., Grubmüller, H., 2010. Flooding in GROMACS: accelerated barrier crossings in molecular dynamics. J. Comput. Chem. 27 (14), 1693–1702. https://doi.org/10.1002/jcc.20473.
Liu, C., Lv, N., Ren, G., Wu, R., Wang, B., Cao, Z., Xie, H., 2021. Explore the interaction mechanism between zein and EGCG using multi-spectroscopy and molecular dynamics simulation methods. Food Hydrocolloids 120, 106906. https://doi.org/10.1016/j.foodhyd.2021.106906.
López, C., De Vries, A., Marrink, S., 2012. Amylose folding under the influence of lipids. Carbohydr. Res. 364, 1–7. https://doi.org/10.1016/j.carres.2012.10.007.
Lorentz, C., Pencreac'h, G., Soultani-Vigneron, S., Rondeau-Mouro, C., de Carvalho, M., Pontoire, B., Ergan, F., Le Bail, P., 2012. Coupling lipophilization and amylose complexation to encapsulate chlorogenic acid. Carbohydr. Polym. 90, 152–158. https://doi.org/10.1016/j.carbpol.2012.05.008.
Mapengo, C.R., Ray, S.S., Naushad Emmambux, M., 2022. Granular morphology, molecular structure and thermal stability of infrared heat-moisture treated maize starch with added lipids. Food Chem. 382, 132342 https://doi.org/10.1016/j.foodchem.2022.132342.
Martin, A., Nicoleta, S., Leontina, G., Luliana, A., Daniela, B., 2020. Structural changes induced by high pressure processing in Bambara bean proteins at different pH. Lebensm. Wiss. Technol. 124, 109187 https://doi.org/10.1016/j.lwt.2020.109187.
Mcilwain, B., Erwin, A., Davis, A., Koff, B., Stockbridge, R., 2021. N-terminal transmembrane-helix epitope tag for x-ray crystallography and electron microscopy of small membrane proteins. J. Mol. Biol. 433 (16), 166909 https://doi.org/10.1016/j.jmb.2021.166909.
Mckinney, S., Joo, C., Ha, T., 2006. Analysis of single-molecule fret trajectories using hidden markov modeling. Biophys. J. 91 (5), 1941–1951. https://doi.org/10.1529/biophysj.106.082487.
Miao, L., Xu, Y., Jia, C., Zhang, B., Zhao, S., 2021. Structural changes of rice starch and activity inhibition of starch digestive enzymes by anthocyanins retarded starch digestibility. Carbohydr. Polym. 261 (1), 117841 https://doi.org/10.1016/j.carbpol.2021.117841.
Momany, F., Willett, J., 2002. Molecular dynamics calculations on amylose fragments. i. glass transition temperatures of maltodecaose at 1, 5, 10, and 15.8% hydration. Biopolymers 63 (2), 99–110. https://doi.org/10.1002/bip.10014.
Moradi, H., Azizpour, H., Bahmanyar, H., Mohammadi, M., Akbari, M., 2020. Prediction of methane diffusion coefficient in water using molecular dynamics simulation. Heliyon 6 (11), e05385. https://doi.org/10.1016/j.heliyon.2020.e05385.
Mukut, K.M., Roy, S., Goudeli, E., 2022. Molecular arrangement and fringe identification and analysis from molecular dynamics (MAFIA-MD): a tool for analyzing the molecular structures formed during reactive molecular dynamics simulation of hydrocarbons. Comput. Phys. Commun. 276, 108325 https://doi.org/10.1016/j.cpc.2022.108325.
Nivelle, M., Beghin, A., Bosmans, G., Delcour, J., 2019. Molecular dynamics of starch and water during bread making monitored with temperature-controlled time domain ^{1}h NMR. Food Res. Int. 119, 675–682. https://doi.org/10.1016/j.foodres.2018.10.045.
Parthasarathi, R., Tian, J., Gnanakaran, S., 2011. Quantum chemical study of carbohydrate–phospholipid interactions. J. Phys. Chem. A 115 (45), 12826–12840. https://doi.org/10.1021/jp204015j.
Pearlman, D., Case, D., Caldwell, J., Ross, W., Iii, T., Debolt, S., Ferguson, D., Seibel, G., Kollman, P., 1995. Amber, a package of computer programs for applying molecular mechanics, normal mode analysis, molecular dynamics and free energy calculations to simulate the structural and energetic properties of molecules. Comput. Phys. Commun. 91 (1–3), 1–41. https://doi.org/10.1016/0010-4655(95)00041-D.
Pérez, S., Bertoft, E., 2010. The molecular structures of starch components and their contribution to the architecture of starch granules: a comprehensive review. Stärke 62 (8), 389–420. https://doi.org/10.1002/star.201000013.
Ratseewo, J., Warren, F.J., Siriamornpun, S., 2019. The influence of starch structure and anthocyanin content on the digestibility of Thai pigmented rice. Food Chem. 298, 124949 https://doi.org/10.1016/j.foodchem.2019.06.016.

Raval, A., Piana, S., Eastwood, M., Dror, R., Shaw, D., 2012. Refinement of protein structure homology models via long, all-atom molecular dynamics simulations. Proteins 80 (8), 2071–2079. https://doi.org/10.1002/prot.24098.

Riziotis, I.G., Ribeiro, A.J.M., Borkakoti, N., Thornton, J.M., 2022. Conformational variation in enzyme catalysis: a structural study on catalytic residues. J. Mol. Biol. 434 (7), 167517 https://doi.org/10.1016/j.jmb.2022.167517.

Roy, R., Hohng, S., Ha, T., 2008. A practical guide to single-molecule fret. Nat. Methods 5 (6), 507–516. https://doi.org/10.1038/nmeth.1208.

Russell, C., Zompra, A., Spyroulias, G., Salek, K., Euston, S., 2021. The heat stability of rhamnolipid containing egg-protein stabilised oil-in-water emulsions. Food Hydrocolloids 116 (10), 106632. https://doi.org/10.1016/j.foodhyd.2021.106632.

Sabater, C., Blanco-Doval, A., Margolles, A., Corzo, N., Montilla, A., 2020. Artichoke pectic oligosaccharide characterisation and virtual screening of prebiotic properties using in silico colonic fermentation. Carbohydr. Polym. 255, 117367 https://doi.org/10.1016/j.carbpol.2020.117367.

Salomon, R., Case, D., Walker, R., 2013. An overview of the amber biomolecular simulation package. Wiley Interdiscip. Rev. Comput. Mol. Sci. 3 (2), 198–210. https://doi.org/10.1002/wcms.1121.

Schlichting, I., Miao, J., 2012. Emerging opportunities in structural biology with X-rayfree-electron lasers. Curr. Opin. Struct. Biol. 22 (5), 613–626. https://doi.org/10.1016/j.sbi.2012.07.015.

Schmitz, S., Seibert, J., Ostermeir, K., Hansen, A.G., Andreas, H., Grimme, S., 2020. Quantum chemical calculation of molecular and periodic peptide and protein structures. J. Phys. Chem. B 124 (18), 3636–3646. https://doi.org/10.1021/acs.jpcb.0c00549.

Schuler, B., Eaton, W., 2007. Protein folding studied by single-molecule FRET. Curr. Opin. Struct. Biol. 18 (1), 16–26. https://doi.org/10.1016/j.sbi.2007.12.003, 2008.

Seritan, S., Bannwarth, C., Fales, B.S., Hohenstein, E.G., Isborn, C.M., Kokkil-Schumacher, S.I.L., et al., 2020. Terachem: a graphical processing unit-accelerated electronic structure package for large-scale ab initio molecular dynamics. Wiley Interdiscip. Rev. Comput. Mol. Sci. 11 (2), e1494 https://doi.org/10.1002/wcms.1494.

Shaw, D.E., Maragakis, P., Lindorff-Larsen, K., Piana, S., Dror, R.O., Eastwood, M.P., Bank, J.A., Jumper, J.M., Salmon, J.K., Shan, Y., Wriggers, W., 2010. Atomic-level characterization of the structural dynamics of proteins. Science 330 (6002), 341–346. https://doi.org/10.1126/science.1187409.

Tian, H., Li, F., Qin, L., Yu, H., Ma, X., 2014. Discrimination of chicken seasonings and beef seasonings using electronic nose and sensory evaluation. J. Food Sci. 79 (11), S2346–S2353. https://doi.org/10.1111/1750-3841.12675.

Vennelakanti, V., Nazemi, A., Mehmood, R., Steeves, A.H., Kulik, H.J., 2021. Harder, better, faster, stronger: large-scale QM and QM/MM for predictive modeling in enzymes and proteins. Curr. Opin. Struct. Biol. 72, 9–17. https://doi.org/10.48550/arXiv.2105.12873.

Wang, L., Wang, L., Wang, T., Li, Z., Gao, Y., Cui, S.W., Qiu, J., 2021a. Comparison of quercetin and rutin inhibitory influence on Tartary buckwheat starch digestion in vitro and their differences in binding sites with the digestive enzyme. Food Chem. 367, 130762 https://doi.org/10.1016/j.foodchem.2021.130762.

Wang, L., Wang, M., Zhou, Y., Wu, Y., Ouyang, J., 2021b. Influence of ultrasound and microwave treatments on the structural and thermal properties of normal maize starch and potato starch: a comparative study. Food Chem. 377, 131990 https://doi.org/10.1016/j.foodchem.2021.131990.

Wang, J., Wolf, R., Caldwell, J., Kollman, P., Case, D., 2004. Development and testing of a general amber force field. J. Comput. Chem. 25 (9), 1157–1174. https://doi.org/10.1002/jcc.20035.

Yang, X., Chi, C., Liu, X., Zhang, Y., Wang, H., 2019. Understanding the structural and digestion changes of starch in heat-moisture treated polished rice grains with varying amylose content. Int. J. Biol. Macromol. 139, 785–792. https://doi.org/10.1016/j.ijbiomac.2019.08.051.

Yu, X.X., Liang, W.Y., Yin, J.Y., Zhou, Q., Zhang, Y.H., 2021. Combining experimental techniques with molecular dynamics to investigate the impact of different enzymatic hydrolysis of β-lactoglobulin on the antigenicity reduction. Food Chem. 350, 129139 https://doi.org/10.1016/j.foodchem.2021.129139.

Zhang, X., Lu, Y., Zhao, R., Wang, C., Wang, C., Zhang, T., 2022. Study on simultaneous binding of resveratrol and curcumin to β-lactoglobulin: multi spectroscopic, molecular docking and molecular dynamics simulation approaches. Food Hydrocolloids 124, 107331. https://doi.org/10.1016/j.foodhyd.2021.107331.

Zhang, Y., Aryee, A., Simpson, B.K., 2019. Current role of in silico approaches for food enzymes. Curr. Opin. Food Sci. 31, 63–70. https://doi.org/10.1016/j.cofs.2019.11.003.

Zhang, Y., Li, J., Yan, Y., 2020. Molecular dynamics study of the migration of bisphenol A from polycarbonate into food simulants. Chem. Phys. Lett. 741, 137125 https://doi.org/10.1016/j.cplett.2020.137125.

Zhao, L., Pan, F., Mehmood, A., Zhang, Y., Hao, S., Rehman, A.U., Wang, C., Wang, Y., 2020. Protective effect and mechanism of action of xanthan gum on the color stability of black rice anthocyanins in model beverage systems. Int. J. Biol. Macromol. 164, 3800–3807. https://doi.org/10.1016/j.ijbiomac.2020.09.027.

Zhao, L., Pan, F., Mehmood, A., Zhang, H., Wang, C., 2021. Improved color stability of anthocyanins in the presence of ascorbic acid with the combination of rosmarinic acid and xanthan gum. Food Chem. 351, 129317 https://doi.org/10.1016/j.foodchem.2021.129317.

Zhu, J., Zhang, B., Tan, C.P., Ding, L., Shao, M., Chen, C., Fu, X., Huang, Q., 2021. Effect of rosa roxburghii juice on starch digestibility: a focus on the binding of polyphenols to amylose and porcine pancreatic α-amylase by molecular modeling. Food Hydrocolloids 123, 106966. https://doi.org/10.1016/j.foodhyd.2021.106966.