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Application of molecular dynamics simulation in food carbohydrate research—a review

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ABSTRACT

Molecular dynamics (MD) simulation is an emerging technique in studying the interactions between macromolecules with small ligands in different media. In this review, the application of MD simulation in food carbohydrate research, including carbohydrate hydration, carbohydrate interaction with other components and carbohydrate inclusion complexation, will be discussed. The advantages and disadvantages of MD simulation in food carbohydrate research and trends will be proposed. The frequently used software to run the MD simulation and a standard protocol for MD simulation procedures have been discussed. This review offers a general idea about how to use MD simulation in food carbohydrate research, and what could be expected from such research. *Industrial relevance:* This review offers a general idea about how to use MD simulation in food carbohydrate research, and what could be expected from such research. This review might be useful for the flavor and nutraceuticals encapsulation, dietary carbohydrate and modified starch industries.

Contents

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1. Introduction

The molecular dynamics method was first introduced by Alder and Wainwright in the late 1950s (Alder & Wainwright, 1957, 1959) in studying the interactions of hard spheres. Many important insights regarding the behavior of simple liquids emerged from their studies. The next major advance of molecular dynamics was in 1964, when Rahman carried out the first simulation using a realistic potential for liquid argon (Rahman, 1964). The first molecular dynamics (MD) simulation of a real system was done by Rahman and Stillinger in simulation of liquid water in 1974 (Stillinger & Rahman, 1974), and the first protein simulations appeared in 1977 using bovine pancreatic trypsin inhibitor (BPTI) as the material (McCammon, Gelin, & Karplus, 1977).

Molecular dynamics (MD) simulation is one of the principal tools in the theoretical study of biological molecules that can calculate the time-dependent behavior of a molecular system. Molecular dynamics (MD) is a computer simulation in which atoms and molecules move under the influence of physical forces, such as gravity. In order to get a view of the motion of the atoms and molecules, they are allowed to interact for a period of time. By solving the Newton's numeric equations of motion for a system of interacting particles, the trajectories of atoms and molecules are able to drawn. During the calculation, molecular mechanics force fields between particles also need to be considered. The method was originally well-known within theoretical physics in the late 1950s but is applied nowadays mostly in physical chemistry, materials chemistry and biomolecules modeling (Papaport, 2004). MD simulations have provided detailed information on the fluctuations and conformational changes of macromolecules such as proteins and nucleic acids (Haile, 1992). These methods are now routinely used to investigate the structure, dynamics and thermodynamics of biological molecules and their complexes. They are also used in the determination of macromolecule structures from X-ray crystallography and NMR experiments (Rapaport, 2004).

Biological molecules exhibit a wide range of timescales over which specific processes occur. There are several examples listed in Table 1 (Karplus & McCammon, 2002). Molecular dynamics simulations are very good at the study of complex, dynamic processes such as protein stability, conformational changes, protein folding, molecular recognition (proteins, DNA, membranes and complexes) and ion transport in biological systems. In addition, it also provides the means for studies of drug design and chemical structure determination using X-ray and NMR (Warshel, 2002). Table 2 shows the development of the application of molecular dynamics simulation in history (van Gunsteren & Berendsen, 1990).

1.1. Definition of MD simulation and its function

The simplest definition of MD simulation is a computer simulation developed to study the motion of molecules over a period of time (Haile, 1992). In more detail, the MD simulation is a form of computer simulation where atoms and molecules are allowed to interact for a period of time under known laws of physics, such as quantum and classical mechanics theories. Because general molecular systems consist of a large number of particles, it is hard to investigate the properties of such complex systems technically. MD simulation circumvents this problem by using numerical methods, which combines laboratory experiments with theoretical study to be a virtual experiment (Rapaport, 2004).

In molecular mechanics, a force field refers to the functional form and parameter sets used to describe the potential energy of a system of particles (typically but not necessarily atoms). The parameter sets include mass, van der Waals radius, partial charges, equilibrium bond lengths, angles, dihedrals, force constants, etc.

MD explores the relationship between molecular structure, movement and function, which can generate information at the microscopic level, including atomic positions and velocities. The conversion of this microscopic information into macroscopic observables such as pressure, energy, heat capacities, etc., requires statistical mechanics. Statistical mechanics is fundamental to the study of the behavior of biological systems by MD simulation (Haile, 1992; Rapaport, 1999).

Computer simulation trajectories can be used to interpret experimentally measured data, e.g. the difference in stability between protein mutants, or to resolve seeming contradictions between NMR and X-ray data on the same protein. A second feature of computer simulation results is that they may provoke experiments. Simulation can only replace the practical experiments when its results are more accurate than the measured ones, which, for biomolecular systems, is rarely the case (van Gunsteren & Dolenc, 2008).

1.2. Programs of MD simulation used in food carbohydrate research

Table 3 lists some computer programs predominantly used for MD simulation. Some of them are offered free, but most of them should be paid for a license. These programs are often used by different researchers for different purposes.

The most frequently used software is GROMACS published by ScalaLife Competence Center, Sweden (Lange, Schäfer, & Grubmüller, 2006). It is primarily designed for the simulation of biochemical molecules like proteins, lipids and nucleic acids that have a lot of complicated bonded interactions. However, since GROMACS is extremely fast at calculating the nonbonded interactions (that usually dominate simulations); many groups are also using it for research on non-biological systems, e.g. grafted copolymers.

Table 1
Examples of specific processes occurring in biological molecules.

Local Motions (0.01 to 5 Å, 10^{-15} to 10^{-1} s)	Rigid Body Motions (1 to 10 Å, 10^{-9} to 1 s)	Large-scale Motions (>5 Å, 10^{-7} to 10^{4} s)
Atomic fluctuations	Helix motions	Helix coil transitions
Side-chain motions	Domain motions (hinge bending)	Dissociation/association
Loop motions	Subunit motions	Folding and unfolding

Table 2
History of computer simulations of molecular dynamics.

Year	System	Length of Simulation/s	Required CPU Time On Supercomputer/h
1957	Hard two-dimensional disks		
1964	Monatomic liquid	10^{-11}	0.05
1971	Molecular liquid	5×10^{-12}	1
1971	Molten salt	10^{-11}	1
1975	Simple small polymer	10^{-11}	1
1977	Protein in vacuo	2×10^{-11}	4
1982	Simple membrane	2×10^{-10}	4
1983	Protein in aqueous crystal	2×10^{-11}	30
1986	DNA in aqueous solution	10^{-10}	60
1989	Protein–DNA complex in solution	10^{-10}	300
	Large polymers	10^{-8}	10^{3}
	Reactions	10^{-4}	10^{7}
	Macromolecular interactions	10^{-3}	10^{8}
	Protein folding	10^{-1}	10^{9}