Young's modulus determination of the collagen molecule via steered molecular dynamics simulations

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Abstract

Articular cartilage is a special kind of connective tissue and unique zonal architecture. In the different layers of cartilage, the functions of collagen fiber cannot be ignored. The mechanical properties of the cartilage directly related to its microstructure, and depended on the function of collagen fibers to some extent. The purpose of this paper is to use GROMACS 2016 and steered molecular dynamics (SMD) simulation method to directly measure the Young's modulus of collagen molecule. And under the condition of stretching rate of v=0.01nm/ps, we obtained the Young's modulus of collagen molecule is 6.1 ± 0.3 GPa.

Keywords: Articular cartilage, Collagen molecule, GROMACS 2016, Steered Molecular Dynamics

Introduction

The primary role of articular cartilage is to provide a low friction joint surface that resists wear, and distributing stresses in a demanding joint environment [1]. Articular cartilage is a special kind of connective tissue and have the unique zonal architecture (Figure 1).

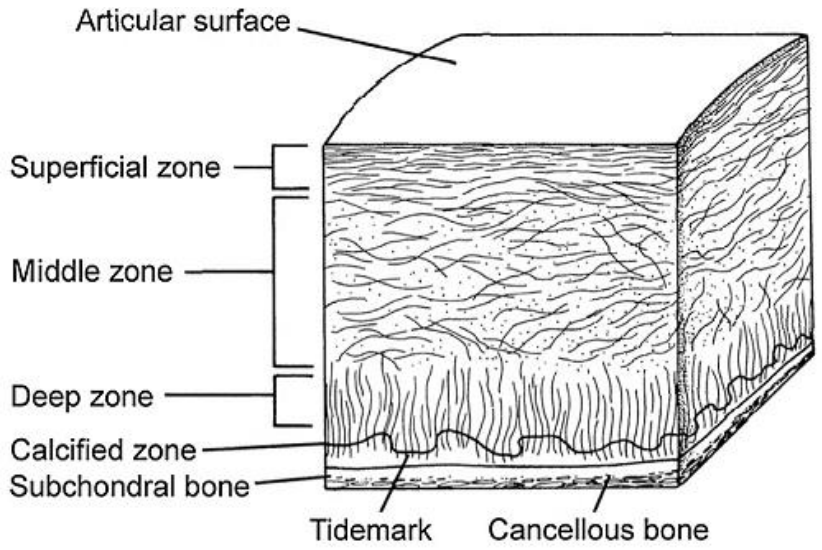

Figure 1. Schematic of the architecture of collagen fibers of human adult articular cartilage (Republished with permission from J. Am. Acad. Orthop. Surg. 2(4):193, 1994.)

The articular cartilage function is dependent on the molecular composition of the extracellular matrix—the interactions between interstitial fluid, the proteoglycan and Type II collagen [2]. Articular cartilage is composed of chondrocytes and extracellular matrix (ECM). Collagen is the most primary component of the extracellular matrix, which is approximately 60%-70% of dry weight of adult articular cartilage. Type II collagen, in articular cartilage, is the principal constituents of collagen.

The functions of collagen fiber cannot be ignored, in the different layers of cartilage [3]. The superficial zone provides a smooth, gliding surface with minimal friction [4], and the collagen fibers, which constrains the tensile stress, are arranged parallel to the joint surface. In middle zone, collagen fibers are mutually crosswise arranged, which plays a primary role in resisting the shear stress and compression stress. In deep zone, collagen fibers are perpendicular to the articular surface, which contributes to resisting the compression stress.

The mechanical properties of the cartilage directly related to its microstructure, and depend on the function of collagen fibers to some extent. In order to research the mechanical properties of the collagen molecule, Harley [5] and co-workers measured collagen Young's modulus to be 9.0 GPa, in 1977; Cusack [6] and Miller estimated 5.1GPa, in 1979; Sasaki [7] and Odajima obtained 2.9 GPa, in 1996; Sun [8] and co-workers reported the Young's modulus between 0.35 and 12.2 GPa, in 2002. Although the mechanical properties of collagen molecules can be determined by the experimental techniques, the results are largely dependent on the biological samples, and the nanoscale phenomena cannot be observed during the experiment. In order to overcome these disadvantages, molecular dynamics method is used to research the collagen molecules. Using molecular dynamics method, Lorenzo [9] and Caffarena obtained the Young's modulus of 4.8 GPa, in 2005; Buehler [10] assessed the Young's modulus ranging from 6.99 to 18.82 GPa, in 2006; Alfonso [11] assessed 4.6 GPa, in 2008; Andrzej [12] obtained 7.4 GPa, in 2015.

Due to the continuous improvement of the simulation software and the parameters of the biomolecular force field, the simulation results of the mechanical properties of collagen may be different. The purpose of this paper is to use GROMACS 2016 to directly research the mechanical properties of collagen molecule when submitted to the virtual traction along its principal axis with steered molecular dynamics (SMD) simulation method. The Young's modulus of collagen molecule was obtained, and compared with previous results.

Method

In order to study the mechanical properties of the collagen molecule, the SMD method is used to carry out the stretching along the principal axis. Due to the length of type II collagen molecules is too long (~300nm), it is time-consuming that use this structure to carry out full-atomistic simulation. Therefore, the collagen-like peptide: $(Pro\text{-}Hyp\text{-}Gly)_4$-Glu-Lys-Gly-$(Pro\text{-}Hyp\text{-}Gly)_5$, which widely used as a model for collagen, substituted for type II collagen.

The GROMACS 2016 simulation package is used to perform the SMD simulation, which GROMOS96 54a7 Force Field [13] and the extended single point charge (SPC/E) [14] water

model for solvent were considered. For the solvation, a 24nm×3.2nm×3.2nm cubic box containing 6719 water molecules, 20 $Na^+$and 20 Cl^- ions are implemented (Figure 2). This solution is equivalent to the normal saline.

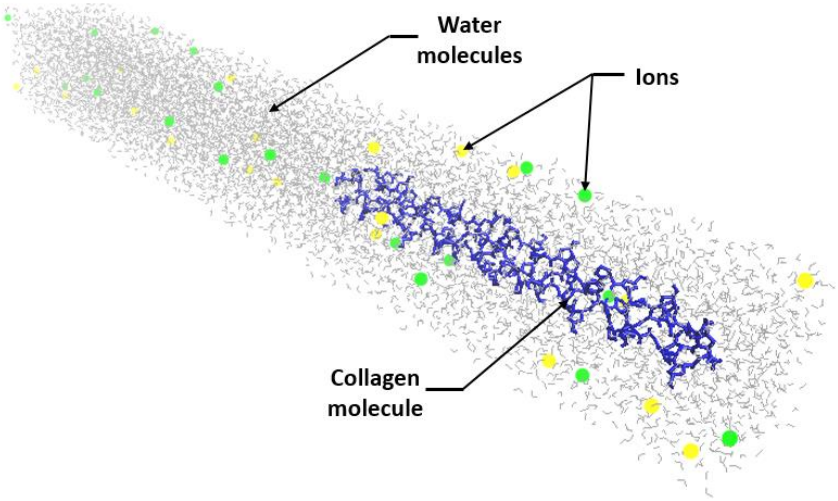

Figure 2. Schematic representation of the model

Since the simulation is to be carried out under isothermal and isobaric conditions, the system must be carried out the equilibrium simulation firstly. In the equilibrium process, Figure 3 indicates the fluctuant curve of the system temperature, and Figure 4 indicates the fluctuant curve of the system density. The system temperature is approximately equal to 300 K; the system density approximately approach to 1022 kg/m^3, equaling to the density of normal saline (1033 kg/m^3) basically. It is express that the system reaches equilibrium.

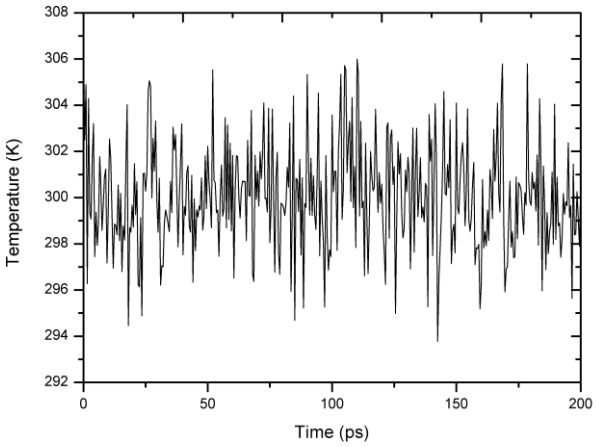

Figure 3. The fluctuant curve of the system temperature

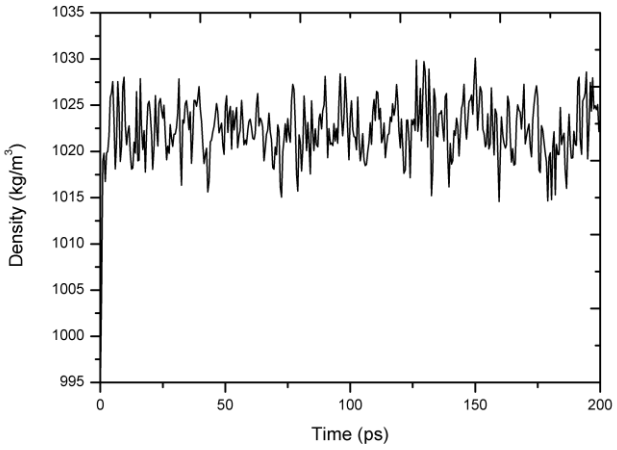

Figure 4. The fluctuant curve of the system density

To beginning the SMD simulations, the pull-group of this molecular is linked to a spring with an elastic constant k_{spring} =3800kJ/mol/nm^2, which is moved at a velocity of $\mathrm{v} = 0.01\mathrm{nm/pN}$ along the molecular axis. The values of velocity and the constant elastic are chosen based on previous works [10]-[11]. The fix-group is kept fixed with a strong position restraint (Figure 5).

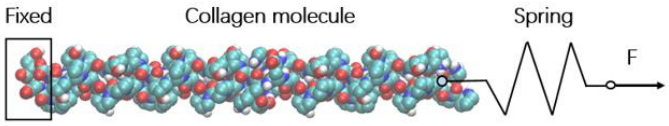

Figure 5. Schematic representation of the whole system of molecule plus virtual spring

The force applied by the virtual spring is

$$\mathrm{F(t)} = k_{spring}(x_{spring}(t) - x_{pill}(t))$$

Where x_{spring} represent the position of spring and x_{pill} represent the position of the pull-group.

On the assumption that the collagen molecule represents an elastic response when performed to stretching along the principal axis. Therefore, the whole system, molecule and spring, will respond as two springs connected in series of elastic constant k_{system}, given by the function:

$$\frac{1}{k_{system}} = \frac{1}{k_{collagen}} + \frac{1}{k_{spring}}$$

The value of k_{system} is calculated from the slot of $\mathrm{F(t)}$ versus ΔL_{system}.

We determined the structure of molecular is a cylindrical shape, and estimated a molecular radius and length, which we used to calculate the Young's modulus:

$$\mathrm{Y} = \frac{\sigma}{\varepsilon} = \frac{F/A}{\Delta L/L_0} = \frac{F}{\Delta L} \times \frac{L_0}{A} = k_{collagen} \times \frac{L_0}{A}$$

Where L_0 is the initial length of the molecule and A is the area of cross-section.

Results

We calculate the Young's modulus of the collagen molecule in terms of the elastic constant with SMD simulation method. As an example of the molecular response to the linear traction, Figure 6 indicates the Force, putting on the center of mass of the pull-group, versus collagen molecular elongation ΔL, and Table 1 shows the main features of collagen molecule. The Young's modulus of the collagen molecule is 6.1 ± 0.3 GPa.

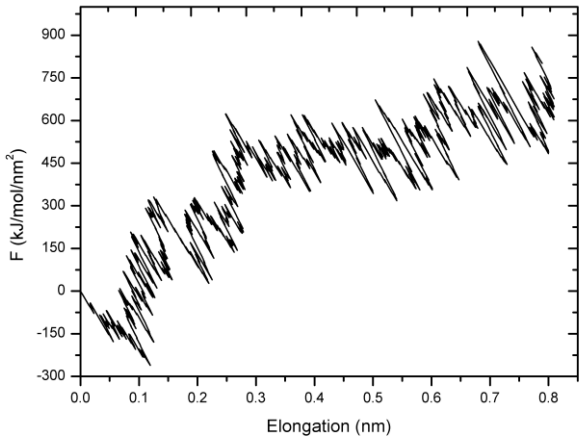

Figure 6. The force versus collagen molecular elongation ΔL

Table 1. The main features of collagen molecule

	(Pro-Hyp-Gly)$_4$-Glu-Lys-Gly-(Pro-Hyp-Gly)$_5$
$k_{collagen}$	1552 ± 59.2 pN/nm
L_0	84 Å
A	214.34 Å^2
Y	6.1 ± 0.3 GPa

Conclusions

In the present study, we build the aqueous environment of normal saline. Using GROMACS 2016 and SMD simulation method, we analyzed the Young's modulus of the collagen molecule in terms of the elastic constant. Using this model, we assessed the value of Young's modulus about 6.1 ± 0.3 GPa. The simulation results of the author are slightly larger than the simulation data of Lorenzo and Alfonso, and are slightly smaller than Buehler and Andrzej. Two reasons could be cause the difference of the result. For one thing, the reason is that the continuous improvement of the simulation software and the parameters of the biomolecular force field. For another thing, we use a kind of stretch ratio without considering other situations, in simulation process. This could be make our result less comprehensive. Further studies should focus on these situations. And we believe that these study will be published in our subsequent articles.

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