Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/jmbbm


Research Paper

# Molecular dynamics simulation of mechanical behavior of osteopontin-hydroxyapatite interfaces

*Zheng Bo Lai, Mingchao Wang, Cheng Yan*, Adekunle Oloyede*

*School of Chemistry, Physics and Mechanical Engineering, Science and Engineering Faculty, Queensland University of Technology, 2 George Street, GPO Box 2434, Brisbane, QLD 4001, Australia*

ARTICLE INFO

*Article history:*
Received 5 February 2014
Received in revised form
3 April 2014
Accepted 5 April 2014
Available online 13 April 2014

*Keywords:*
Osteopontin
Hydroxyapatite
Mechanical property
Interface
Molecular dynamics

ABSTRACT

Bone is characterized with an optimized combination of high stiffness and toughness. The understanding of bone nanomechanics is critical to the development of new artificial biological materials with unique properties. In this work, the mechanical characteristics of the interfaces between osteopontin (OPN, a noncollagenous protein in extrafibrillar protein matrix) and hydroxyapatite (HA, a mineral nanoplatelet in mineralized collagen fibrils) were investigated using molecular dynamics method. We found that the interfacial mechanical behavior is governed by the electrostatic attraction between acidic amino acid residues in OPN and calcium in HA. Higher energy dissipation is associated with the OPN peptides with a higher number of acidic amino acid residues. When loading in the interface direction, new bonds between some acidic residues and HA surface are formed, resulting in a stick–slip type motion of OPN peptide on the HA surface and high interfacial energy dissipation. The formation of new bonds during loading is considered to be a key mechanism responsible for high fracture resistance observed in bone and other biological materials.

© 2014 Elsevier Ltd. All rights reserved.

## 1. Introduction

While the basic building blocks of bone are hydroxyapatite (HA) platelets and protein molecules, this biological material possesses exceptional mechanical properties, i.e., combined high stiffness and toughness, attracting considerable attention (Dunlop and Fratzl, 2010; Wegst and Ashby, 2004). Bone is featured by a complicated microstructure, with at least seven hierarchical levels (Launey et al., 2010). In bone microstructure, extrafibrillar protein matrix can be found between mineralized collagen fibrils (MCF) and osteopontin (OPN) is found in this extrafibrillar protein matrix (Launey et al., 2010; McKee and Nanci, 1995, 1996; Nanci, 1999). MCF consists of HA nanoplatelets with a thickness of 1.5–4.5 nm (Fratzl et al., 1991, 1992, 2004; Launey et al., 2010). In previous studies, separation of MCFs was observed at bone fracture surface (Fantner et al., 2005; Hassenkam et al., 2004; Thurner et al., 2007). OPN is non-collagenous protein and acts as an adhesive (natural glue) in bone (Fantner et al., 2005; McKee and Nanci, 1995, 1996; Nanci, 1999). OPN is highly flexible and consists of many acidic amino acid (AA) residues (Azzopardi et al., 2010; Fisher et al., 2001). For instances, in human OPN, about 25% of the AA residues are acidic, and about 19% of the AA residues are expected to be added with negatively charged groups (e.g. phosphate group) during posttranslational modification (Blom et al., 1999; Zappone et al., 2008).

*Corresponding author. Tel.: +6 1731386630.
*E-mail address:* c2.yan@qut.edu.au (C. Yan).

http://dx.doi.org/10.1016/j.jmbbm.2014.04.002
1751-6161/© 2014 Elsevier Ltd. All rights reserved.

Based on atomic force microscopy (AFM) tests on a layer of protein deposited on mica (Adams et al., 2008; Fantner et al., 2007; Zappone et al., 2008), force–displacement curves with few noticeable force peaks were observed and a mechanism called sacrificial bonds and hidden lengths was proposed. Sacrificial bonds shield parts of molecule from being stretched. These protected molecules are referred as hidden lengths. Continuously breaking of the sacrificial bonds leads to the stretching of the hidden lengths and high energy dissipation. This was considered to be the reason responsible for the excellent fracture resistance of bone. Certainly, other mechanisms were also proposed, as detailed by Launey et al. (2010).

The adsorption of OPN peptide on HA surface was investigated using atomic-scale simulation (Addison et al., 2010; Azzopardi et al., 2010). It was found that the flexibility of peptide is critical for the adsorption of OPN peptide on HA surface (Azzopardi et al., 2010). However, the desorption process of OPN peptide from HA surface has not been understood. In fact, OPN may detach from HA surface when bone is subjected to daily loading. Due to the tiny sizes of MCF and OPN, a large interfacial area is expected. Therefore, a better understanding of the interfacial behavior between OPN and HA surface is critical to explain the mechanical behavior of bone and other biological materials. In addition, it is necessary to investigate the effects of loading conditions on the deformation and failure mechanisms.

In this study, the mechanical behavior of OPN and HA interface was investigated using molecular dynamics (MD) simulation, which has been proven to be a powerful tool for investigating biological materials at smaller material length scales (Azzopardi et al., 2010; Buehler et al., 2008; Chen et al., 2007; Gautieri et al., 2012; Grohe et al., 2007; Ji, 2010). The attention was focused on the interaction between OPN and HA under different loading modes. Four types of 18-residue OPN peptide with different numbers of acidic AA residue and net charge were investigated.

## 2. Materials and methods

### 2.1. Computational model

A hexagonal-type HA ($Ca_{10}[PO_4]_6[OH]_2$) substrate was modeled, as shown in Fig. 1. The initial atomic coordination of HA is based on previous experimental work (space group $P6_3/m$ and unit cell parameters of $a=b=9.423$ Å, $c=6.883$ Å, $\alpha=\beta=90^\circ$, $\gamma=120^\circ$) (Wilson et al., 1999). It is worth mentioning that the mineral thickness in this computational model (~2 nm) is close to that of the HA platelet found in bone (1.5–4.5 nm) (Fratzl et al., 1991, 1992, 2004; Launey et al., 2010). A {100} crystal face was created near the hydroxyl (OH) columns, as this is the main crystal face in biological minerals (Corno et al., 2011; Sato et al., 2002).

Four different types of OPN peptide were considered and each OPN peptide has 18 AA residues (Table 1). The atomic structures are obtained from Addison et al. (2010). OPN A is an OPN peptide (AA 198–215) with a neutral net charge. It has an acidic AA residue (aspartate (D)) and a basic AA residue (lysine (K)). OPN B is an OPN peptide (AA 115–132) with 8 acidic AA residues (aspartate (D) and glutamate (E)) and a net charge of −8. Each of these acidic AA residues has a negatively charged carboxyl (–$COO^-$) side chain. OPN C and OPN D are two different phosphorylated forms of OPN B. OPN C has three negatively charged phosphoserines (pS) and a net charge of −14, while OPN D has five negatively charged phosphoserines and a higher net charge of −18. Each phosphoserine (pS) has a negatively charged phosphate (–$PO_3^{2-}$) side chain.

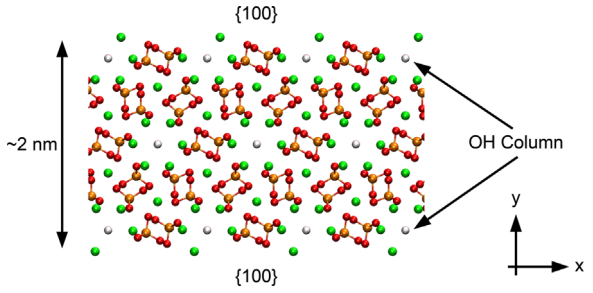


**Fig. 1 – HA substrate used in this study. {100} surfaces are modeled near the hydroxyl (OH) columns (Ca—green; P—orange; O—red; H—white). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)**

The OPN peptide was placed approximately 1 nm on top of {100} crystal face of HA atomic structure. Both OPN and HA substrate were placed within a simulation box with periodic boundary condition (PBC). The OPN peptide and HA substrate did not cross the box edges. Big simulation boxes were used to prevent any significant interaction of OPN peptide and HA substrate with their periodic images. Box size of $9.4\times30.0\times18.1\ nm^3$ was used for the pulling simulation in HA thickness direction (y-direction), while box size of $9.4\times8.0\times35.0\ nm^3$ was used for pulling simulation in HA interface direction (z-direction). The empty space of simulation box was filled with single point charge (SPC) water molecules (Berendsen et al., 1981). Then, some calcium and chloride ions were added carefully to ensure the whole system has a neutral net charge.

### 2.2. Force field

GROMOS force field (van Gunsteren et al., 1996) was used for OPN peptide. The Hauptmann apatite model (Hauptmann et al., 2003) was adopted for HA and Lennard–Jones potential converted from Born–Mayer–Huggins (BMH) potential was used (Pan et al., 2007). Lennard–Jones parameters for the interaction between OPN peptide and HA were calculated based on Lorentz–Berthelot mixing rule (Hirschfelder et al., 1954), i.e.

$$V_{LJ}(r_{ij})=4\varepsilon_{ij}\left(\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12}-\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right) \quad (1)$$

$$\sigma_{ij}=\frac{\sigma_i+\sigma_j}{2} \quad (2)$$

$$\varepsilon_{ij}=\sqrt{\varepsilon_i\varepsilon_j} \quad (3)$$

Download English Version:

https://daneshyari.com/en/article/7208849

Download Persian Version:

https://daneshyari.com/article/7208849

Daneshyari.com