Computational investigations of the formation mechanism of bone-like minerals from phospholipids

Kunioshi N[1*], Cheng Y[1], Hara ES[2].
*: nilson@waseda.jp
1 Waseda University, Japan
2 Okayama University, Japan

We have previously found that nanofragments from cell membranes, which contain phospholipids as the main structural unit, can induce *in vitro*, the formation of bone-like minerals in one day, while conventional methods using live cells require two or three weeks [1, 2]. Phospholipids are biomolecules that are relatively large compared to inorganic molecules; they have two main moieties linked to the central phosphate group: a hydrophilic head and a long hydrophobic (lipidic carbon chain) tail. Examples of bone-like minerals obtained as the result of mineralization are amorphous calcium phosphate (ACP) and hydroxyapatite, which is composed of calcium ions, oxygen, hydrogen, and phosphorous atoms only. The mechanism of mineralization of phospholipids involves therefore aspects that are still obscure. In this research, with the purpose of elucidating important steps in the mineralization process of phospholipids, we analyze chemical reactions that occur in an aqueous solution containing calcium ions and phospholipids only.

We first assume that hydrolysis is an important step in the process, because the phosphate group in phospholipids should react with calcium ions to form ACP, and eventually be released from the hydrophilic and hydrophobic chains, so that it becomes free to form hydroxyapatite. The analysis of hydrolysis reactions is conducted using Gaussian 16. The optimized structures of reactants, transition state, and products of each step are obtained at the B3LYP/6-31g(d,p) level of theory. This level of approximation has been shown accurate enough for analyzing chemical reactions in the growth mechanism of silicon surfaces [3–5]. The activation energies are evaluated more accurately at the APFD/6-311+G(2d,p) level of theory. The reaction dynamics is analyzed in detail for identifying the chemical reactions that may occur more easily.

References

[1] Hara S, Okada M, Nagaoka N, Hattori T, Nakano T, Matsumoto T. Bioinspired mineralization using chondrocyte membrane nanofragments. *ACS Biomater Sci Eng* 2018;4(2):617-625.
[2] Hara S, Okada M, Kuboki T, Nakano T, Matsumoto T. Rapid bioinspired mineralization using cell membrane nanofragments and alkaline milieu. *J Mater Chem B*. 2018;6:6153-6161.
[3] Kunioshi N, Anzai K, Ushijima H, Fuwa A. Effects of cluster size on calculation of activation energies of silicon surface reactions with H_2 and HCl. *J Cryst Growth* 2015;418: 115-119.
[4] Anzai K, Kunioshi N, Fuwa A. Analysis of the dynamics of reactions of $SiCl_2$ at Si(100) surfaces. *App Surf Sci*. 2017;392:410-417.
[5] Kunioshi N, Hagino S, Fuwa A, Yamaguchi K. Novel pathways for elimination of chlorine atoms from growing Si(100) surfaces in CVD reactors. *App Surf Sci*. 2018;441:773-779.