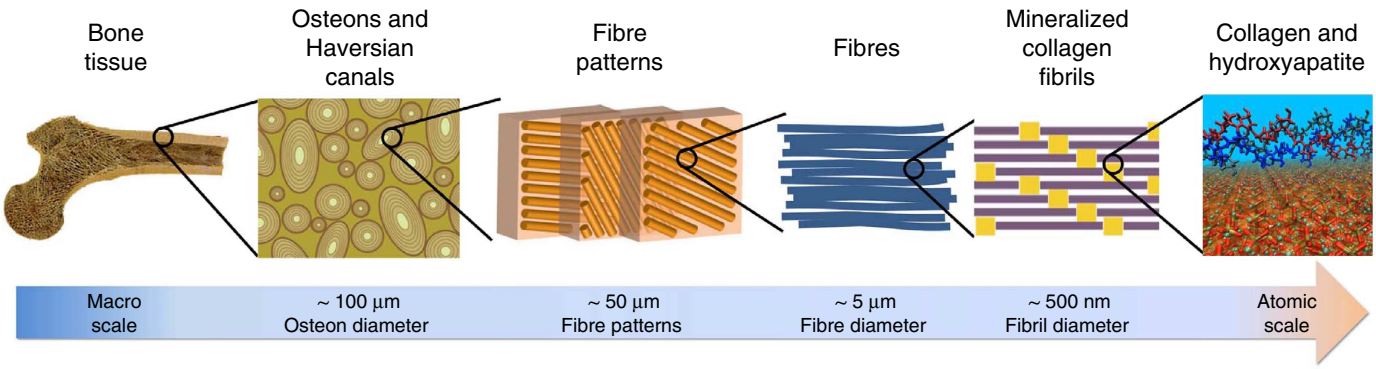
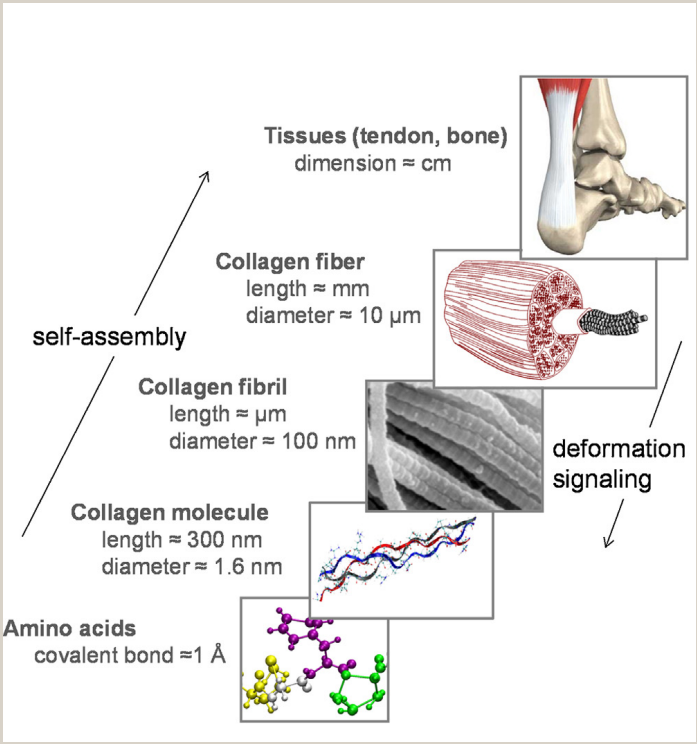
Decoding the atomic structure of bone: molecular insights into brittle bone disease



Abstract

Collagen constitutes one third of the human proteome, providing mechanical stability, elasticity and strength to organisms. Normal type I collagen is a heterotrimer and consists of two alpha-1 chains and one alpha-2 chain. A mouse model of the genetic brittle bone disease, osteogenesis imperfect (oim), is characterized by a replacement of the alpha-2 chain by a alpha-1 chain, resulting in a homotrimer collagen molecule. Experimental studies of oim mice tendon and bone have shown reduced mechanical strength compared to normal mice. How the molecular mutation affects the packing of collagen molecules at the microfibril level and the relationship between the molecular content and the decrease in strength is, however, still not clear. In this study, we use molecular simulations to study the structural and mechanical differences between the heterotrimer and homotrimer collagen microfibrils. The collagen microfibril models are generated based on the in situ structure of full length collagen type I molecule with the actual amino acid sequence of real mouse collagen. Through a detailed structural analyses, our results suggest that the oim microfibril is less dense compared to the normal microfibril as a result of local kink formations which explains the reduction of modulus of the oim microfibril. Our studies provide fundamental insight of the effect of the loss of alpha-2 chain at the molecular level and help understanding the molecular origin of the bone brittle disease at much larger length-scales.



Prof. Shu-Wei Chang

Department of Civil Engineering

National Taiwan University

Seminar & mPAM Lecture series

Place: 工科系大樓地下一樓越生講堂

Day: 21 March 2019

Time: 14:10-15:30

Bio-sketch

Dr. Shu-Wei Chang received his B.S. and M.S. degrees from National Taiwan University and his Ph.D. degree from Massachusetts Institute of Technology under the supervision of Prof. Markus J. Buehler. He is now an Assistant Professor in the Department of Civil Engineering at National Taiwan University (NTU), Taiwan. Prior to joining NTU, Dr. Chang had worked as a postdoctoral researcher at Massachusetts Institute of Technology. His research interests are associated with the employment of atomistic and multiscale computational modeling to understand the mechanics of materials, including biomaterials and synthetic materials at the nano- and micro- scales, with an aim to integrate nanoscale approaches to engineering problems.

Education

- Ph.D., Civil and Environmental Engineering, Massachusetts Institute of Technology, MA, USA, 2014
- M.S., Civil Engineering, National Taiwan University, Taipei, Taiwan, 2008
- B.S., Civil Engineering, Mathematics, National Taiwan University, Taipei, Taiwan, 2006

Honors and awards

- 2011 NSF Fellowship for Cancer Nanotechnology Summer Institute
- 2010 Presidential Graduate Fellowship, MIT
- 2007 Scholarship of Schoolfellow Association, NTU
- 2007 Scholarship of Sinotech Engineering Consultants Inc
- 2004 Scholarship of Schoolfellow Association, NTU
- 2002 Award of Outstanding Student, NTU

Research interests

- Computational Mechanics
- Computational Materials
- Biomechanics; Collagen; Mechanobiology
- Atomic Scale Modeling
- Multi-scale/Multi-physics Modeling

Related publications

- T. Li, S. W. Chang, N. Rodriguez-Florez, M. J. Buehler, S. J. Shefelbine, M. Dao, K. Zeng, Studies of chain substitution caused sub-fibril level differences in stiffness and ultrastructure of wildtype and oim/oim collagen fibers using multifrequency-AFM and molecular modeling. Biomaterials, Vol. 107, pp. 15-22, 2016
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- S.W. Chang, M.J. Buehler, 2014, Molecular biomechanics of collagen molecules. Materials Today, Vol. 17, pp. 70-76
- A. Nair , A. Gautieri, S.W. Chang, M.J. Buehler, Molecular mechanics of mineralized collagen fibrils in bone. Nature Communication. 4, 1724 doi:10.1038/ncomms2720, 2013. (MIT's homepage spotlight, April, 2013)
- S.W. Chang, B. Flynn, J. Ruberti, M.J. Buehler, "Molecular mechanism of force induced stabilization of collagen against enzymatic breakdown," Biomaterials, Vol. 33(15), pp. 3852-3859, 2012
- S.W. Chang, S.J. Shefelbine, M.J. Buehler, "Structural and mechanical differences between collagen homo- and heterotrimers: General insight and relevance for brittle bone disease," Biophysical Journal, Vol. 102(3), pp. 640-648, 2012