



21st European Conference on Fracture, ECF21, 20-24 June 2016, Catania, Italy

Cortical Bone as a Biomimetic Model for the Design of New Composites

Flavia Libonati*, Laura Vergani

Department of Mechanical Engineering, Politecnico di Milano, Milano, Italy

Abstract

Composite materials are widely used to build structures for their great mechanical performance combined with a low weight. However, the relatively low toughness of some composite materials is often a limitation as it can cause sudden failure. At present, there is a need for new lightweight materials with a good combination of strength and toughness, to be used for a variety of structural applications. Strength and toughness are the key requirements for structural materials. However, they are often mutually exclusive. Examples of effective design solutions can be found in natural materials, showing an optimal strength-toughness balance. Such materials can be a good source of inspiration for the design of new smart materials, by following a biomimetic approach. Among natural materials, bone tissue is an intriguing one. Bone combines few meagre constituents, hydroxyapatite and collagen, as building blocks to build up a complex hierarchical structure, reaching remarkable mechanical properties and a large amplification in toughness not observed in synthetic counterparts. For this reason, bone can be considered as a biomimetic model material that many researchers have recently tried to mimic adopting different techniques. In this study, we take inspiration from bone to design and manufacture new FRC (fiber-reinforced composite) materials inspired by the microstructure of cortical bone, with the aim of mimicking some toughening mechanisms and improving the toughness of conventional composites. We focus on the microstructural level, since the fundamental toughening mechanisms occur at the microscale, and we mimic the main features involved in the fracture process in our new design. The choice of the key features to be mimicked in the biomimetic material design process is guided by a previous experimental campaign performed on bovine cortical bone. Here we describe the design of a new bio-inspired material and an experimental campaign to assess the mechanical performance and the failure modes. The results of the tests allow us to confirm the promising mechanical characteristics of such material, compared to our previous design solutions and to similar classic structural composites (e.g. laminates). Moreover, the failure modes show many similarities with some of the toughening mechanisms occurring in cortical bone, confirming the key role, played by the mimicked bone-inspired microstructural features, in determining and enhancing the fracture toughness of the composites.

Copyright © 2016 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Peer-review under responsibility of the Scientific Committee of ECF21.

* Corresponding author. Tel.: +30-02-2399-8667; fax: +39-02-2399-8263.
E-mail address: flavia.libonati@polimi.it

© 2016 The Authors. Published by Elsevier B.V.
Peer-review under responsibility of the Scientific Committee of ECF21.

Keywords: Biomimetics; Cortical bone; Toughening mechanisms; Composites; FRC.

1. Introduction

The increasing demand for lightweight structural materials with superior mechanical properties is driving the research towards new composites tailored to meet strict requirements. Nowadays composite materials are widely used to build structures for their great mechanical performance combined with a low weight. However, the relatively low toughness of some composites is often a limitation as it can cause sudden failure. At present, there is a need for new lightweight materials, with a good combination of stiffness, strength and toughness, yet flexibility, to be used for a variety of structural applications. Since structural materials are generally used for applications where catastrophic failure occur, such as for aircraft jet engines, gas pipelines, pressure vessels, and also for critical medical implants like cardiovascular stents, fracture toughness plays a crucial role among mechanical characteristics. For this reason, current research is focusing on how to increase fracture toughness of structural materials, without affecting the strength and stiffness (Argon and Cohen, 2003; Wetzel et al., 2006). Examples of effective design solutions can be found in natural materials, showing an optimal balance of stiffness, strength and toughness balance, amongst other beneficial characteristics, such as self-healing and remodeling capabilities (Barthelat and Rabiei, 2011; Bhushan, 2009; Espinosa et al., 2009; Fratzl and Weinkamer, 2007; G, 2005; Ji and Gao, 2010; Meyers et al., 2008; Nair et al., 2014). Such materials can be a good source of inspiration for the design of new smart materials, by following a biomimetic approach (Barthelat, 2007, 2010; Espinosa et al., 2009; Fratzl, 2007; Libonati et al., 2014a; Liu and Jiang, 2011; Luz and Mano, 2010; P, 2007).

Among natural composites, the biomineralized ones, such as bones, teeth and sea shells take advantage of rigid nanoscale mineral platelets to reinforce a soft polymeric organic matrix (Barthelat, 2007; Currey, 2005; Ji and Gao, 2004, 2010; Nair et al., 2014; Olszta et al., 2007). The mineral platelets and the protein matrix are the basic building blocks of many biominerals (Fratzl et al., 2004). They are universally present in many biological structural materials, present in the environment with a wide variety of structures. Indeed, a peculiarity of Nature is to make use of few meagre base materials and arrange them into different hierarchical structures to reach a wide diversity, characteristic of biological materials (Ackbarow and Buehler, 2008). These building blocks, which constitute the pillars of diversity, are brittle mineral platelets (e.g. aragonite, calcium phosphate) and weak proteins (e.g. collagen). By properly combining them, nature achieves a large amplification of mechanical properties, not observable in synthetic counterparts. Hence, although natural materials are generally inferior to engineering ones in terms of absolute properties, their key feature of property amplification makes them proper biomimetic models for the design of de novo advanced materials and structures.

Among natural materials, bone tissue represents an interesting case. Bone combines few meagre constituents, hydroxyapatite and collagen, as building blocks to build up a complex hierarchical structure, reaching remarkable mechanical properties and a large amplification in toughness not observed in synthetic equivalents. For this reason, we choose bone as a biomimetic model for the design of new FRCs. Our design are intended to mimic the characteristic structural features of the microstructure of cortical bone, with the purpose of implementing the key bone microscale toughening mechanisms and achieving an increase in toughness. Through deep study and testing of natural materials, we learnt how superior material properties in nature and biology can be mimicked in bioinspired materials for applications in new technology. Indeed, previous studies have been carried out on bovine bone to investigate the structure-property relationship at multiple length scale and to understand the role of the building blocks and that of different hierarchies on the overall mechanical properties (Libonati et al., 2014a; Libonati et al., 2013, 2014b; Libonati and Vergani, 2016; Vergani et al., 2014). In (Libonati et al., 2014a) we demonstrated how to successfully mimic some of the microscale toughening mechanisms characteristic of the bone Haversian structure in a de novo biomimetic FRC. However, this design was not providing an improvement in toughness compared to classic laminates, besides showing a strong anisotropic behavior, with some limitations in the transversal direction.

In the following, we present a new material, which represent a design improvement, with the aim of achieving an increase in toughness with respect to the previous design and to classic laminates. The new material is intended to provide an alternative to classic composite design, ensuring an increase in toughness and a remarkable strength-toughness tradeoff.

2. Materials and Methods

2.1. Design

The design is inspired by the microstructure of cortical bone. Bone is generally considered as a composite made of two basic building blocks: the hydroxyapatite in the form of mineral nano-platelets and fibrils of collagen, which is the main component of the organic matrix. These basic components are arranged into diverse structures at different length scales, leading to a complex hierarchical organization made of seven levels, each one characterized by specific size and pattern (Reznikov et al., 2014; Rho et al., 1998; Weiner and Wagner, 1998). The mechanical behavior and fracture of bone is largely governed by these sophisticated architectures, by the failure mechanisms activated at each level and by the interaction between consecutive levels (Espinosa et al., 2009; Gautieri et al., 2011). As it is difficult to implement the whole hierarchical structures, we decided to mimic the microstructural level, which is the one giving the major contribution to the overall toughness. In particular, we borrow inspiration from the Haversian structure of cortical bone, resulting from the remodeling process. The Haversian structure also is a composite, characterized by a repeating cylindrical unit, called osteon, embedded into an interstitial matrix. Both the osteons and the matrix are made of lamellae, which can be assimilated to composite layers made of organic fibers and reinforcing platelets.

Here, we provide a simplified representation, where we mimic the osteons as tubes made of CF and filled up with glass fibers, embedded into a glass/epoxy matrix. Fig. 1 shows the biomimetic process, from the microscopic observation of the Haversian structure of bovine cortical bone (Fig. 1a) to the new design of the biomimetic material (Fig. 1b) and the final obtained structure ((Fig. 1c). The osteon-like structure was chosen for the simple geometry and for the role played in enhancing the toughness, by deflecting and twisting the crack. Conventional structural materials, widely used in the field of composites, such as fiberglass, carbon fibers and epoxy matrix, were chosen for the new structural material. Some simplifications were introduced in the initial design to make it feasible, with respect to the available manufacturing process.

For the osteon-like features we adopted CF tubes made of CF_{Twill 2x2} [$\pm 45^\circ$] and filled up with UD-GF rowing. To mimic the interstitial lamellae we used UD-GF-NCF [90°] 220 g/m². Then we used two layers of GF_{Twill 2x2}, placed at the top and bottom of the final plate, to mimic the bone outer circumferential system.

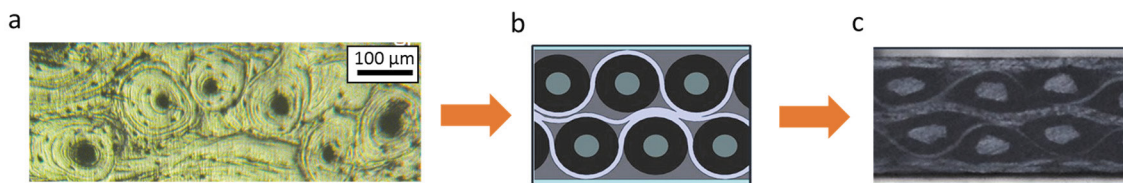


Fig. 1. (a) Haversian structure from bovine femur (Image from optical microscope); (b) Design of bio-inspired structure; (c) Cross section of the manufactured bio-inspired structure.

This new design represents an improved version of the first one, presented in (Libonati et al., 2014a). Indeed, the outcome of the experimental study carried out on the previous design and those from numerical and experimental studies carried out on the bone tissue (Libonati and Vergani, 2016; Vergani et al., 2014) were useful to improve the initial biomimetic design. By observing the Haversian structure of bone and the mechanical behavior of the first

proposed solution, we realized that the weak point of the bone-like composite is the mechanical response in transversal direction. Therefore, to improve the transversal behavior we needed to enhance the osteon-osteon interactions, for instance by creating a multi-layer osteon structure, allowing simultaneous inter-osteon interactions in different directions. A solution was given by the addition of a weave composite fabric, alternatively placed under and over each osteon (UD-GF-NCF [90°] 220 g/m²). Moreover, to further improve the composite toughness, by amplifying the crack-deflection mechanism, we decided to use smaller CF-tubes (i.e. diameter of 2.5 mm), placed into two rows and organized into a staggered configuration. The new design maintained the average osteon volume ratio that is also found in cortical bone, about 60 % (Abdel-Wahab et al., 2012).

For the manufacturing process, we used a VARTM (i.e. vacuum assisted resin transfer molding) technique. To reduce the manufacturing time and increase the geometrical precision, we developed a tool, allowing us to directly weave the tubes in the mold by means of nails. This tool allowed us to considerably reduce the ‘lamination’ time, from 6 h to 20 min. Furthermore, we bought CF tubes already filled up with UD-GF, recurring the probability of manual induced defects, and allowing for a further reduction in the ‘lamination’ time.

To allow a direct comparison in terms of mechanical performance, we also designed a classic laminate, by using the same type and amount of base materials used for the biomimetic composite. The fiber volume fraction was equal to 50 % for all the materials and with an equal contribution of CF and GF (50% CF and 50% GF). The laminate designed for comparative aims had the following stacking sequence:

- (GF_{Twill} [0°-90°] ; CF_{Twill} [±45°] ; UD-GF [0] ; CF_{Twill} [±45] ; UD-GF [90])_s.

2.2. Mechanical Testing

We performed fracture toughness tests and tensile tests on the new bioinspired design and on a similar laminate.

We cut all the samples by Waterjet technology, allowing for a proper finishing, and reducing the probability of manufacture-induced defects.

For the tensile tests, we followed the American standard D3039/D3039M-08 (ASTM, 2008). The geometry (rectangular) and the size of the samples (250-20-5 mm, for the longitudinal samples and 175-25-5 mm, for the transversal ones) were chosen according to the standard D3039/D3039M-08 (ASTM, 2008). However, some dimensions, such as the thickness and width, were modified compared to those recommended by the standard. For instance, the thickness was fixed by that of the manufactured plates and, consequently, by the diameter of the tubes; the width, instead, was increased to 20 mm for the longitudinal samples so as to include in each specimen a more statistically relevant quantity of tubes. As suggested by the standard (ASTM, 2008), the specimens were endowed with adhesively bonded tabs at both ends, avoiding stress concentration and misalignment due to the grip pressure (equal to 15 MPa), and ensuring a uniform stress distribution and a correct load transfer through the grips. Tabs were bonded adopting an Araldite epoxy adhesive glue (DP490). Both transversal and longitudinal tensile tests were performed in displacement control mode with a cross-head speed of 2 mm/min, using a universal tensile testing machine MTS Alliance RT-100, equipped with a Load cell of 150 kN. Force data were acquired through the load cell, whereas the deflection data through a deflectometer (MTS model 632-06H-30). Data acquisition frequency was set to 5 Hz.

Translaminar fracture toughness tests were carried out according to the standard ASTM E1922-04 (ASTM, 2010), which describes a method for the determination of translaminar fracture toughness, K_{TL} , for laminated and pultruded polymer matrix composite materials, using test results from monotonically loaded notched specimens. This method involves eccentrically single edge notch tension specimens, ESE(T), in mode I loading. In addition, this type of test can serve as a method to investigate how the fracture propagates in the bioinspired composite and in the comparative laminate, allowing a final comparison. The dimensions and geometry were chosen according to the standard (100-25-5 mm, with a crack length extending over half of the specimen width). The thickness is not constrained in the standard and it was set to 5 mm. This type of test can quantitatively establish the effects of fiber and matrix variables and stacking sequence of the laminate on the translaminar fracture resistance of composite laminates. A displacement gage was used to measure the displacement at the notch mouth during loading. The gage was attached to the specimen edges using adhesively bonded knife-edges. Tests were performed at room temperature, in displacement control mode with a cross-head speed of 1 mm/min, by using a universal tensile testing machine MTS Alliance RF-150, endowed with a load cell of 150 kN. Data acquisition frequency was set to 20 Hz.

3. Results

The new VARTM technique allowed us to speed up the process and to improve its repeatability (reducing the manual-induced errors) and to halve the final cost of the material (from about 60 to about 30 €/plate).

The new material showed a progressive failure behavior, with large dissipation of energy before rupture. Comparing the results with the previous design presented in (Libonati et al., 2014a), it was possible to notice that the new design, object of the present study, preserved high longitudinal properties, with a significant increase in the transversal properties (about 4-5 in terms of strength, whereas the stiffness is comparable for the old and new design), as shown in Table 1.

Table 1. Results from tensile tests and fracture toughness t_c carried out on the bio-inspired composites: ‘Old design’ refers to the first design solution presented in (Libonati et al., 2014a), whereas ‘New design’ refers to the biomimetic design solution presented in this paper.

Type of test	Direction	Material	Strength (MPa)	Stiffness (GPa)	K_{II} (MPa \sqrt{m})
Tensile	Longitudinal	New design	732 ± 57	56.3 ± 2.0	-
Tensile	Longitudinal	Old design	797 ± 53	46.5 ± 5.0	-
Tensile	Transversal	New design	126 ± 9	15.0 ± 0.2	-
Tensile	Transversal	Old design	28 ± 3	14.6 ± 1.0	-
Fracture toughness	Longitudinal	New design	-	-	47.88 ± 3.10
Fracture toughness	Longitudinal	Old design	-	-	26.9 ± 2.9

Indeed, it was possible to note that the introduction of transversal layers in the osteon-like material design provided a mutual interaction between adjacent osteons, leading to a significant increase in the transversal properties of the laminate (in terms of strength and stiffness), as shown in Fig. 2, and reducing the gap with the transversal properties of the comparative laminate.

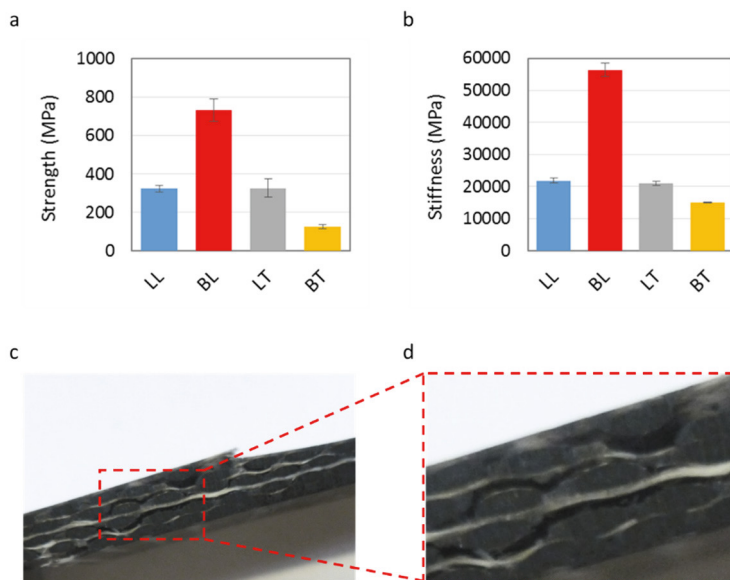


Fig. 2. Bar plots summarizing the results from tensile testing for all the materials: Bioinspired design tested in longitudinal direction (BL) and transversal direction (BT), and Laminate tested in longitudinal (LL) and transversal (LT) directions. (a) Bar plot showing the results in terms of Strength; (b) Bar plot showing the results in terms of Stiffness; (c) Figure showing the failure mode of the Bioinspired design after tensile testing in transversal direction; (d) Figure showing the zoom on the failure mode, highlighting the crack deflection around the osteon-like tubes.

The presence of transversal layers in the new osteon-like design had a positive effect on the fracture properties as well. Indeed, the presence of more osteons promoted additional crack deflection, leading to a significant increase in the translamellar fracture toughness with respect to both the comparative material (see Fig. 3) and the previous design (see Table 1).

Owing to the osteon-like features, the new biomimetic design is still markedly anisotropic. For this reason, it could be particularly suitable for applications with critical loads oriented along a preferential direction. The new design showed a good combination of mechanical properties under tensile loading and remarkable fracture properties.

The outcome from this preliminary experimental campaign showed a noticeable improvement of the mechanical performance of the new biomimetic design, compared to the previous one. Also, this series of experimental tests allowed us to highlight strengths and shortcomings of the new biomimetic material, compared to a classic composite with a laminate internal structure.

The difference between the two materials are mainly due to the internal organization. It is interesting to note that in longitudinal direction the osteon structure did not fail in purely brittle mode, in spite of its strongly anisotropy and brittle constituents. In fact, in all the tests, the new biomimetic material showed a progressive damage, involving each osteon, before final failure occurred, making it suitable for structural applications, where catastrophic failure is a plausible scenario, such as in gas pipelines, nuclear containment vessels.

It was interesting to observe how failure of each structural element (i.e. osteon) occurred separately from each other, and in sequence, progressively increasing the energy required for failure. Moreover, we could observe failure mechanisms similar to those occurring in bone at microscale, such as crack deflection. Fig. 3b shows a picture taken during a fracture toughness test carried out on the new bio-inspired design and showing the failure mode. In the magnification, provided in Fig. 3c it is possible to see how the crack propagated: here the crack propagation process seems to be affected by the internal biomimetic structure, resulting in a nonlinear path owing to osteon-induced deflections.

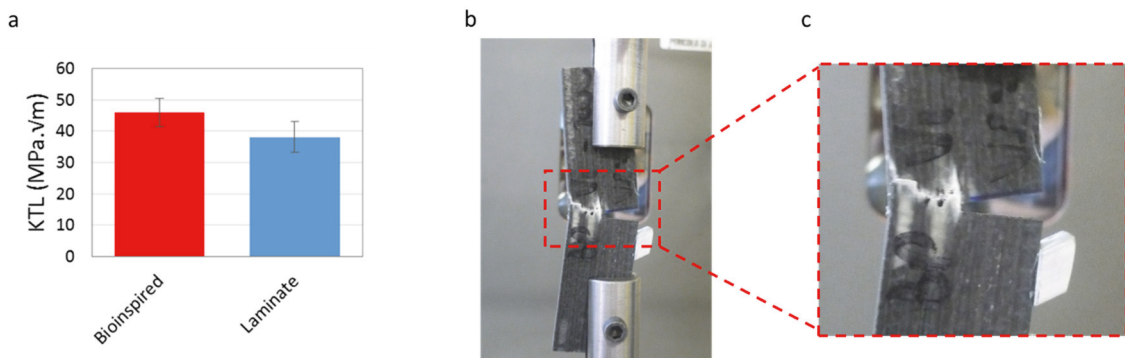


Fig. 3. (a) Bar plot showing Fracture toughness (K_{TL}) of the new bio-inspired design and the classic laminate used for comparison. The new design (Osteonic laminate) shows Fracture toughness than that of the classic laminate; (b) Picture taken during a fracture toughness test carried out on the bio-inspired design and showing the failure mode; (c) Zoom of the figure shown in panel b, showing the area of fracture: the crack path is jagged, being affected by the internal biomimetic structure. In particular, the presence of osteons causes many deflections leading to a nonlinear path.

The results from the experimental campaign were promising and the new design was able to reach a remarkable ‘property amplification’, offering an optimal stiffness-toughness tradeoff. In particular, the new design showed better performance than the previous one and than the new laminated adopted for comparison. Moreover, it was interesting to note that the new design has higher mechanical properties if compared to similar CF/epoxy and GF/epoxy laminates, whose properties were taken from CES EduPack database (Granta Design Limited, 2015). These results are summarized in the Ashby plot, provided in Fig.4.

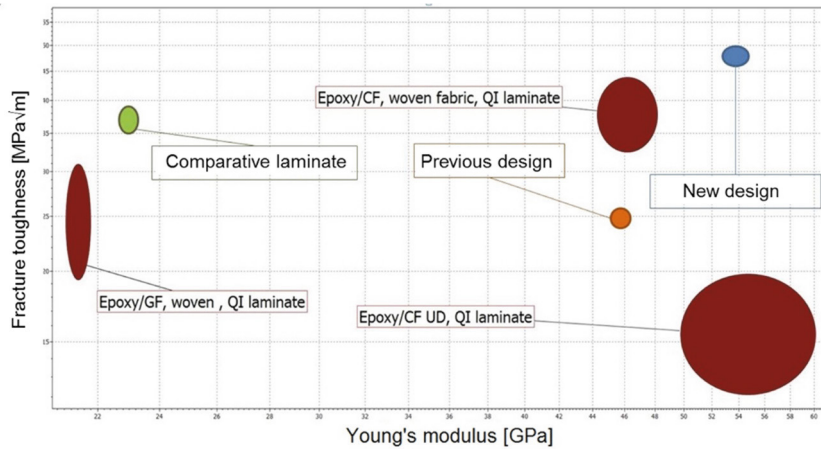


Fig. 4. Ashby plot showing Fracture toughness vs. Young modulus of our Bio-inspired designs (previous design presented in (Libonati et al., 2014a) and the new one) and classic laminates. The new design (Osteonic laminate) shows higher mechanical properties than similar CF/epoxy and GF/epoxy laminates, whose properties are taken from CES EduPack database (Granta Design Limited, 2015).

4. Concluding Remarks

In this study we described how, by using Nature's inspiration of structural architectures, advanced composite materials can be developed, with strength and toughness properties superior to those of their individual constituents and to those of classic composites (e.g. laminates) made of similar constituents. Inspired by the Haversian structure, characteristic microstructural organization of cortical bone, we developed a new FRC material aimed at mimicking main bone microscale toughening mechanisms, to achieve an increase in toughness with respect to classic composite laminates. To reach this goal we implemented the key features of the bone tissue, involved in the fracture process, in our new synthetic design. The proposed design is intended to be an improvement of a previous one, presented in (Libonati et al., 2014a).

The new biomimetic design presented here was able to successfully reproduce the fundamental mechanism of crack deflection, characteristic of bone tissue at microscale and responsible of the major contribution to toughness increase. Moreover, the new design was able to improve the weaknesses of the previous design, showing higher mechanical properties under tensile loading, hence reducing the anisotropy, and considerably increasing the fracture toughness. Further testing, under different loading conditions, are needed to confirm the validity of this design.

As future perspective, we aim to implement even hierarchical organization, bridging multiple features, characteristic of different length- and time-scales, to push the limit towards the materials of the future.

Acknowledgements

The authors would like to acknowledge Prof. Ziegmann and Dilmurat Abliz from Clausthal University of Technology and the master student Francesco Ielmini, for materials manufacturing, and the technician Lorenzo Giudici for helping in mechanical testing.

References

- Abdel-Wahab, A. A., A. R. Maligno, V. V. Silberschmidt, 2012, Micro-scale modelling of bovine cortical bone fracture: Analysis of crack propagation and microstructure using X-FEM: *Computational Materials Science*, 52, 128-135.
- Ackbarow, T., M. J. Buehler, 2008, Hierarchical Coexistence of Universality and Diversity Controls Robustness and Multi-Functionality in Protein Materials: *Journal of Computational and Theoretical Nanoscience*, 5, 1193-1204.
- Argon, A. S., R. E. Cohen, 2003, Toughenability of polymers: *Polymer*, 44, 6013-6032.
- ASTM, 2008, D3039/D3039M-08. Standard Test Method for Tensile Properties of Polymer Matrix Composite Materials.
- ASTM, 2010, E1922-04. Standard Test Method for Translaminar Fracture Toughness of Laminated and Pultruded Polymer Matrix Composite Materials.
- Barthelat, F., 2007, Biomimetics for next generation materials: *Philosophical Transactions of the Royal Society of London A: Mathematical, Physical and Engineering Sciences*, 365, 2907-2919.
- Barthelat, F., 2010, Nacre from mollusk shells: a model for high-performance structural materials: *Bioinspiration & Biomimetics*, 5, 035001.
- Barthelat, F., R. Rabiei, 2011, Toughness amplification in natural composites: *Journal of the Mechanics and Physics of Solids*, 59, 829-840.
- Bhushan, B., 2009, Biomimetics: lessons from nature-an overview: *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences*, 367, 1445-1486.
- Currey, J. D., 2005, Materials science: hierarchies in biomineral structures: *Science*, 309, 253.
- Espinosa, H. D., J. E. Rim, F. Barthelat, and M. J. Buehler, 2009, Merger of structure and material in nacre and bone - Perspectives on de novo biomimetic materials: *Progress in Materials Science*, 54, 1059-1100.
- Fratzl, P., 2007, Biomimetic materials research: What can we really learn from nature's structural materials?: *Journal of the Royal Society Interface*, 4, 637.
- Fratzl, P., H. S. Gupta, E. P. Paschalis, P. Roschger, 2004, Structure and mechanical quality of the collagen-mineral nano-composite in bone: *Journal of Materials Chemistry*, 14, 2115-2123.
- Fratzl, P., R. Weinkamer, 2007, Nature's hierarchical materials: *Progress in Material Science*, 52, 1263.
- G, M., 2005, Rigid biological systems as models for synthetic composites: *Science*, 310, 1144.
- Gautieri, A., S. Vesentini, A. Redaelli, M. J. Buehler, 2011, Hierarchical Structure and Nanomechanics of Collagen Microfibrils from the Atomistic Scale Up: *Nano Letters*, 11, 757-766.
- Ji, B., H. Gao, 2004, Mechanical properties of nanostructure of biological materials: *Journal of the Mechanics and Physics of Solids*, 52, 1963-1990.
- Ji, B., H. Gao, 2010, Mechanical Principles of Biological Nanocomposites: *Annual Review of Materials Research*, 40, 77-100.
- Libonati, F., C. Colombo, L. Vergani, 2014a, Design and characterization of a biomimetic composite inspired to human bone: *Fatigue & Fracture of Engineering Materials & Structures*, 37, 772-781.
- Libonati, F., A. K. Nair, L. Vergani, M. J. Buehler, 2013, Fracture mechanics of hydroxyapatite single crystals under geometric confinement: *Journal of the mechanical behavior of biomedical materials*, 20, 184-191.
- Libonati, F., A. K. Nair, L. Vergani, M. J. Buehler, 2014b, Mechanics of collagen-hydroxyapatite model nanocomposites: *Mechanics Research Communications*, 58, 17-23.
- Libonati, F., L. Vergani, 2016, Understanding the structure-property relationship in cortical bone to design a biomimetic composite: *Composite Structures*, 139, 188-198.
- Liu, K., L. Jiang, 2011, Bio-inspired design of multiscale structures for function integration: *Nano Today*, 6, 155-175.
- Luz, G. M., J. F. Mano, 2010, Mineralized structures in nature: Examples and inspirations for the design of new composite materials and biomaterials: *Composites Science and Technology*, 70, 1777-1788.
- Meyers, M. A., Y. Chen, A. Y. M. Lin, Y. Seki, 2008, Biological materials: Structure and mechanical properties: *Progress in Materials Science*, 53, 1-206.
- Nair, A. K., F. Libonati, Z. Qin, L. Dimas, M. J. Buehler, 2014, Mechanical and interface properties of biominerals: Atomistic to coarse-grained modeling, *in* E. DiMasi, L. B. Gower, eds., *Biomineralization Handbook: Characterization of biomineral and biomimetic materials*, CRC Press, 337-351.
- Olszta, M. J., X. Cheng, S. S. Jee, R. Kumar, Y.-Y. Kim, M. J. Kaufman, E. P. Douglas, L. B. Gower, 2007, Bone structure and formation: a new perspective: *Materials Science and Engineering: R: Reports*, 58, 77-116.
- P, F., 2007, Biomimetic materials research: What can we really learn from nature's structural materials?: *J. R. Soc. Interface*, 4, 637.
- Reznikov, N., R. Shahar, S. Weiner, 2014, Bone hierarchical structure in three dimensions: *Acta Biomaterialia*, 10, 3815-3826.
- Rho, J.-Y., L. Kuhn-Spearing, P. Zioupos, 1998, Mechanical properties and the hierarchical structure of bone: *Medical Engineering & Physics*, 20, 92-102.
- Vergani, L., C. Colombo, F. Libonati, 2014, Crack Propagation in Cortical Bone: A Numerical Study: *Procedia Materials Science*, 3, 1524-1529.
- Weiner, S., H. D. Wagner, 1998, The material bone: structure mechanical function relations: *Annual Review of Materials Science*, 28, 271-298.
- Wetzel, B., P. Rosso, F. Hauptert, K. Friedrich, 2006, Epoxy nanocomposites – fracture and toughening mechanisms: *Engineering Fracture Mechanics*, 73, 2375-2398.