Biocomposites

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A Molecular Rationale of Shock Absorption and Self-Healing in a Biomimetic Apatite–Collagen Composite under Mechanical Load**

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While teeth and bone are well known for their hardness, an equally important property is the toughness of biominerals. The latter characteristic is a rare one among crystalline matter, including apatite which—in its pure form—is hard yet too brittle to serve endoskeleton requirements. By forming composites of apatite and collagen, nature has developed outstanding combinations of hardness and toughness. Dentine and bone comprise some 20 wt % of organics and may hence be interpreted as calcified tissue, which provides peculiar toughness through complex hierarchical structures.[1,2] On the other hand, the steel-like characteristics of enamel, which contains only 1–2 wt % protein (amelogenins and enamelins), is much less understood.

At the micrometer scale enamel is composed of apatite–protein composite prisms that are aligned along the *c* axis.[3] The resilience of enamel is attributed to a variety of mechanisms acting on different length scales. By sliding of prisms with respect to each other, enamel may sustain micrometer indentation without catastrophic failure. The slipping of prisms is supported by interprismatic sheets of proteins, which are believed to break and re-form bonds during creep and back-creep, respectively.[4–6] However, even at a smaller length scale, the individual enamel prisms were found to sustain mechanical load through steel-like characteristics.[7] While hardness is obviously associated with the 98–99 wt % of apatite, the mechanism of toughness, that is, withstanding millions of loading/unloading cycles, is much less clear.

To explore the interplay of apatite and proteins at the atomic level, it is imperative to reduce the complexity of living matter. This applies to both theory and experiment, and indeed here we shall focus on biomimetic apatite–collagen composites, the synthesis of which was elaborated by Kniep and Simon.[8] This biomimetic composite exhibits important similarities to enamel prisms (hierarchical structure, 2 wt % protein content) and should hence offer qualitative understanding of the more complex biomineral. Moreover, the interplay of experimental characterization and atomistic simulation provided a very detailed picture of the biomimetic composite,[9,10] and recently led to the creation of a nanometer-sized simulation model mimicking an apatite–collagen composite at the atomic level.[11]

For the present study, this model was further extended to encompass a hexagonal pattern of collagen molecules (approximated by $(\text{Hyp-Pro-Gly})_n$, see also references [9,10]) embedded into $20 \times 20 \times 10$ unit cells of apatite.[12] Periodic boundary conditions are applied to mimic a bulk material. Using a time step of 1 fs, molecular dynamics (MD) simulations are employed to explore the material under mechanical load. The latter is induced by gradually scaling the simulation cell along the *c* axis (the direction along which mechanical load is primarily applied to enamel during biting). To avoid volume compression, the system is allowed to expand along the perpendicular direction. A constant-temperature algorithm is used to maintain 300 K throughout the MD simulations, including the mechanical loading runs. Because of the limited timescales accessible to MD simulations of complex model systems, the strain rate $\Delta\dot{z}$ has to be chosen rather large compared to that of indentation experiments using AFM tips. To diminish putative errors from too fast compression along the *c* axis, a series of strain rates was explored and the maximum stress before material failure (σ_{yield}) was identified as a function of the applied strain rate. From this, compression rates of $\Delta\dot{z} < 12\,\text{ms}^{-1}$ were found to yield consistent results. Unless specified differently, the simulations described herein are based on a strain rate of $3\,\text{ms}^{-1}$.[13]

The simulation model is illustrated in Figure 1 (left). It mimics a nanometer-sized patch of an apatite–collagen composite, which in nature is arranged as hexagonal prisms with dimensions of several micrometers. By gradually compressing the model along the *c* axis, mechanical load is applied and the restoring force is monitored as a function of the

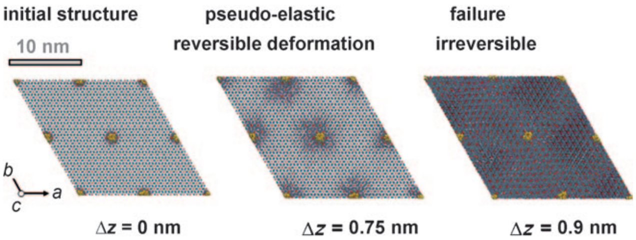

Figure 1. Snapshots of the composite model (comprising 212 340 atoms) during compression along the *c* axis. Before eventual failure, inelastic deformation is initiated near the collagen molecules (highlighted in yellow), which are suggested to act as nucleation seeds for local "melting" of ionic ordering. Using this mechanism, the material may stand a limited degree of inelastic deformation without losing overall structural integrity (failure). Because of the specific and local nature of the sacrifice of ionic ordering, the deformation of the composite is pseudo-elastic, and it may undergo self-healing after release of the mechanical load.

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compression Δz (Figure 2). After about 0.5 nm of indentation, the model exhibits nonelastic deformation characteristics. Within the range $0.5 < \Delta z < 0.8$ nm the force opposing compression is observed as roughly constant, which indicates a plastic deformation mechanism. Indeed, inhomogeneous atomic displacements are identified as i) disordering of the orientation of the phosphate/hydroxide ions and ii) shifting ions, which were initially aligned along the *c* axis into zigzag-type arrangements.

Strikingly, the inelastic deformation characteristics were always found to be initiated near the collagen molecules (Figure 1). Hence the collagen triple helices locally destabilize crystalline order and may be suggested as nucleation seeds for the "melting" of ionic ordering. At the beginning of inelastic deformation, this mechanism is locally confined to nearest-neighbor interactions of collagen and the apatite ions. At later stages of material compression, ionic disorder propagates into the bulk apatite regions. This gradual sacrifice of crystalline ordering allows the material to withstand a limited degree of inelastic deformation without losing overall structural integrity (failure).

These findings were confirmed from a small series of independent compression runs using strain rates of $\Delta\dot{z} = 1.5$, 3, and 6 ms^{-1} by identifying the maximum stress before failure as $\sigma_{\text{yield}} = 4.12$, 4.25, and 4.42 GPa, respectively. A linear fit is used to extrapolate the yield stress to vanishing strain rate as $\sigma_{\text{yield}}(\Delta\dot{z} = 0) = 4.04$ GPa. Similarly, the hardness of pure hydroxyapatite (calculated for the analogous $20 \times 20 \times 10$ unit cell model without collagen) was assessed as 8.96 GPa. Despite the closeness to the experimentally observed hardness of 8.1 and 4.2 GPa for hydroxyapatite and enamel, respectively,[5] we point out the strong simplifications intrinsic to the nanometer-sized simulation models. While quantitative agreement to biogenic enamel is beyond the scope of our simulations, we nevertheless expect our mechanistic findings to hold at least from a qualitative point of view.

Because of the specific and local nature of the sacrifice of ionic ordering, there is an important similarity of our composite model with earlier observations of bone deformation. AFM experiments revealed that collagen fibrils may gradually sacrifice bonds during the mechanical loading of bone.[1] A similar mechanism, protein unfolding and refolding, was recently suggested to account for creep and back-creep phenomena in enamel.[4–6] Inspired by such experimental evidence, we took snapshots of the deformed composite simulation model and performed relaxation runs in the absence of mechanical load.

By applying ambient conditions within constant-temperature, constant-pressure MD simulations, relaxation of the composite models was explored as a function of the preceding compression Δz. Unsurprisingly, deformation beyond the failure limit (indicated by the sharp drop in the repulsive force, see also Figure 2) was found to be irreversible. A much more striking observation is related to relaxation from plastic deformation through the sacrificial ordering mechanism outlined above ($z = 0.75$ nm, see also Figure 1). Such ionic disordering was found to be reversible. Thus, the material may undergo a self-healing process and eventually recovers to the initial state after sufficient relaxation.

Monitoring of the dimensions and the energy per unit cell (Figure 3) as functions of time revealed two relaxation modes: a) elastic response (shape change of the overall model system) and b) self-healing of the partially disordered regions (local reorganization of crystalline motifs). Thus, a double exponential fit is used to deduce the respective relaxation time constants (Figure 3). The elastic response occurs on a picosecond timescale and represents the fastest mode. However, only a fraction of the mechanical energy is released in this manner. About 13 kJ mol^{-1} is retained from immediate (elastic) relaxation and released at a much slower pace during self-healing, which is observed on a nanosecond timescale.

Snapshots of the relaxation process are illustrated in Figure 4. Upon comparing the structure after relaxation by 1.5 and 150 ps, we can clearly discriminate shape change (elastic response) and ionic reorganization (self-healing), respectively. During the latter process, the orientation of the

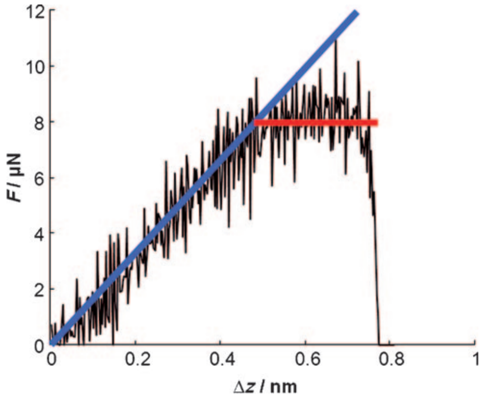


Figure 2. Resisting force *F* as a function of composite compression along the *c* axis. The blue line corresponds to a linear response, that is, elastic deformation, while the red line indicates inelastic deformation. Unlike brittle apatite, the composite exhibits a plastic deformation regime before eventually undergoing fracture.

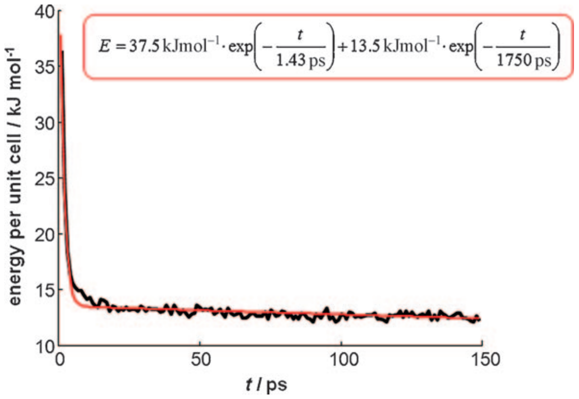


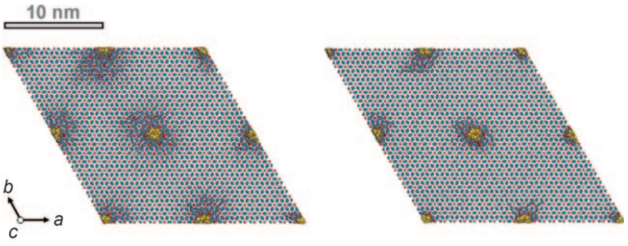
Figure 3. Energy release as a function of relaxation time *t* as observed from MD simulations and a double exponential fit (red curve). About 13 kJ mol^{-1} of mechanical energy (taken per apatite unit cell) is retained from immediate (elastic) relaxation, which occurs within a few picoseconds. Thereafter, the composite recovers from pseudo-elastic deformation on a nanosecond timescale. This allows the composite to temporarily absorb shock energy, the release of which occurs on a timescale that is decoupled from the elastic response.

hydroxide/phosphate ions as well as the alignment of the ions along the *c* axis of apatite is gradually restored. Strikingly, the collagen molecules experience only minor structural changes during the deformation and healing process. The sampling of collagen–ion distance distribution profiles reported in reference [11] was repeated for the configurations shown in Figures 1 and 4, and revealed only minor changes and practically constant coordination numbers. Thus, unlike bone and dentine, which sacrifice collagen–collagen bonds, enamel-like composites of low protein content must sacrifice ionic ordering (ion–ion bonds) instead. The latter type of bond is much stronger and is thus expected to account for the fast timescale of the healing process observed for our simulation model.

Up to the failure limit, plastic deformation is hence pseudo-elastic. During self-healing, the associated heat of "recrystallization" is dissipated to thermal degrees of freedom, that is, practically without volume/shape changes that would give rise to mechanical work. In other words, a full cycle of mechanical load, pseudo-elastic deformation, and self-healing during relaxation represents a molecular mechanism of transforming shock energy into heat.

Thus, the mechanisms of deformation and relaxation in the composite model comprise two aspects. During mechanical load, collagen locally destabilizes crystalline order and induces the local disordering of apatite ions. The latter process occurs in a controlled manner, by limited orientation disordering and zigzag arrangements. The controlled nature of this partial disordering may be related to the interface with crystalline apatite. Thus, apatite motifs are gradually degenerated with the degree of disordering being a function of the distance to the collagen molecules. This reserves regions of intact apatite crystals that are of key relevance for the self-healing process. During this "recrystallization", the restoring of crystalline motifs is triggered by back-propagation of the interface between distorted and intact regions in the apatite crystals.

In principle, molecules other than collagen could also promote or better localize plasticity, whilst healing always nucleates from the intact regions of the apatite crystal. However, a peculiar feature of collagen–apatite composites is the hierarchical structure that originates from the design of apatite motifs by ion association to collagen.[8–11] We expect the well-defined structure illustrated in Figure 1 (left) to play a key role in dividing sacrificial and intact regions in the composite.



t = 1.5 ps   *t* = 150 ps

Figure 4. Snapshots of the composite model during long-term relaxation runs after mechanical loading beyond the elastic limit ($z = 0.75$ nm, see also Figure 1). While fast relaxation is achieved by elastic deformation within a few picoseconds, on the nanosecond timescale the gradual reduction of potential energy is caused by ionic reorganization. Thus, the self-healing of the material occurs by "recrystallization" of the partially disordered structure. The released energy is dissipated to thermal rather than mechanical energy, and hence accounts for the reversible conversion of shock energy into heat.

In conclusion, our simulations reveal a molecular mechanism accounting for the steel-like characteristics of biomimetic apatite–collagen composites under mechanical load. The observed mechanism of locally sacrificing crystalline order and self-healing during relaxation provides a molecular rationale for shock-energy dissipation on the nanometer scale. While this refers to the shock response within individual composite prisms, at larger length scales nature makes use of further mechanisms for dissipating shock energy.[5,14] Indeed, we believe the hierarchical structure of enamel implies a cascade of different deformation/restoration mechanisms that act at different scales in both length and time to provide optimal resilience. The confirmation of this concept—and the elaboration of means to manipulate the material properties by biomolecule modification—requires increasingly complex composite models and poses an exciting challenge to future simulation studies.

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