BIOMATERIALS

Research in the Department of Biomaterials

Peter Fratzl 13.09.1958
1980: Diploma (Ingénieur Diplômé de l'Ecole Polytechnique, Paris)
1983: PhD, Physics (University of Vienna)
Thesis: Investigation of an Al-Zn-Mg alloy using diffuse neutron scattering
1981-1985: Research Scientist (Austrian Academy of Sciences, Vienna; Laboratoire Leon Brillouin, Saclay, France); Visiting Research Fellow (Hahn Meitner Institute, Berlin; New York University)
1986-1998: Assistant and Associate Professor (Institute for Materials Physics of the University of Vienna, Austria)
1988 and 1989: Visiting Professor (Rutgers University, New Jersey, USA)
1991: Habilitation, Solid State Physics (University of Vienna)
Thesis: Precipitation in alloys - small-angle x-ray scattering and computer simulation
Since 1993: Research Associate (Ludwig Boltzmann Institute of Osteology, Vienna).
1993-1994: Visiting Research Fellow (Heriot-Watt University, Edinburgh)
1997: Visiting Professor, (Physics Department of the University of Munich)
1998-2003: Chair of Metal Physics (University Leoben, Austria)
Director (Erich Schmid Institute for Materials Science of the Austrian Academy of Sciences)
Since 2003: Director, Department of Biomaterials (Max Planck Institute of Colloid and Interfaces, Golm)

The Department of Biomaterials, founded 2003, will focus on interdisciplinary research on biological and biomimetic materials. The emphasis is on understanding how the mechanical or other physical properties are governed by structure and composition. Research on natural materials (such as bone or wood) has potential applications in many fields. First, design concepts for new materials may be improved by learning from nature. Second, the understanding of basic mechanisms by which the structure of bone or connective tissue is optimized opens the way for studying diseases and thus for contributing to diagnosis and development of treatment strategies. A third option is to use structures grown by nature and transform them by physical or chemical treatment into technically relevant materials (biotemplating). Given the complexity of natural materials, new approaches for structural characterization are needed. Some of these will be further developed in the department, in particular for studying hierarchical structures. Part of these activities have already been started at the Erich Schmid Institute of Materials Science (Austrian Academy of Science, Leoben, Austria) by the small group of scientists moving from Austria to Potsdam in 2003/2004 in order to form the initial nucleus of the Department of Biomaterials.

Hierarchical Structure of Natural Materials

The development of metals and alloys with increasing strength has been a constant trigger for the technical development of our societies. Interestingly, nature does not use metals as structural materials at all. Practically all biological materials are based on polymers and polymer-mineral composites.

The required mechanical performance is obtained by an intelligent structure which is hierarchical and optimized at all levels **[3]**. **Figure 1** shows the hierarchical structure of spruce wood as an example. Annual rings with a thickness of a few millimeters are visible in the light-microscopic image of a cross-section **(Fig. 1a)**. The structure at this level reveals a cellular material made of parallel tube-shaped cells, having a somewhat thicker cell-wall in latewood (LW) than in earlywood (EW). The cell wall itself is a fiber composite made of cellulose microfibrils embedded in a matrix of hemicelluloses and lignin. The cellulose microfibrils are helically wound around the axis of the wood cell with a diameter in the order of 20 micrometer **(Fig. 1b)**. The cellulose fibrils, finally, contain cellulose nanocrystals **(Fig. 1c)**. Studying the hierarchical structure of natural materials, such as wood **[4]**, bone **[12]**, tooth **[14]**, collagen **[11]** is one of the research goals, aimed at linking the hierarchical structure to mechanical requirements of the tissue and, hence, extract some of the principles used by nature for mechanical optimization.

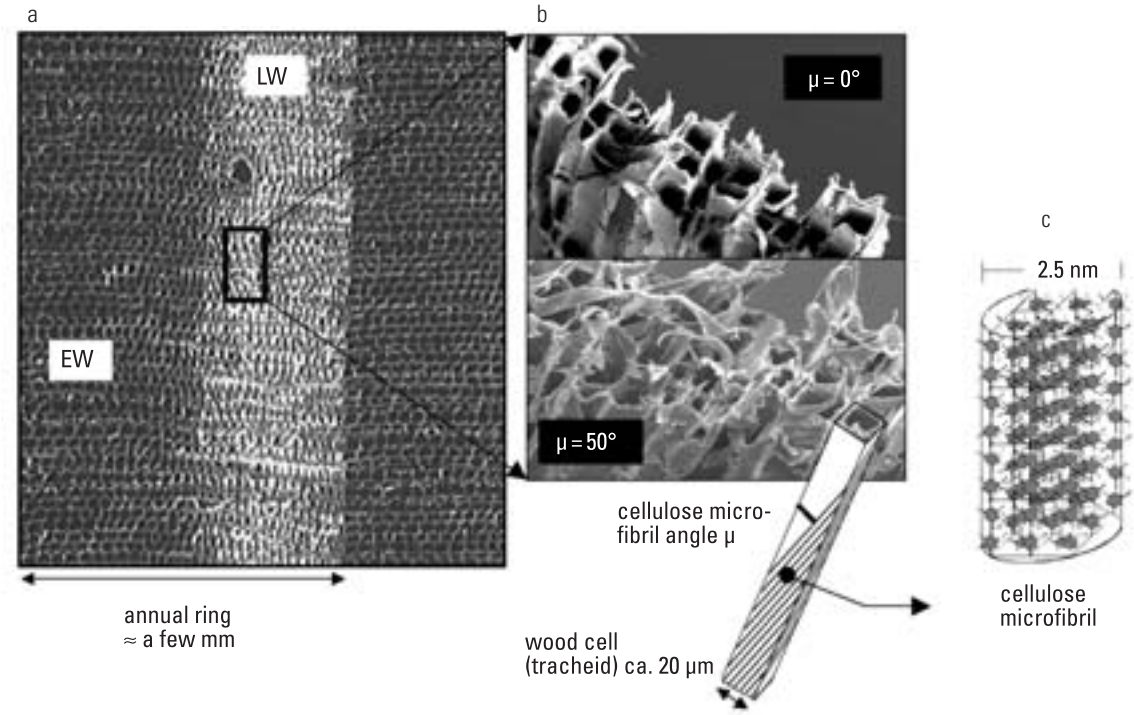

Fig. 1: Hierarchical structure of wood. (a) Cross-section through the stem. Each annual ring is composed of earlywood (EW) and latewood (LW). (b) Fracture surfaces showing individual wood cells. The cell wall material is a composite of cellulose fibrils in a matrix of hemicelluloses and lignin. μ is the spiral angle of the fibrils in the main cell wall layer. (c) Schematic representation of the crystalline structure of a typical cellulose fibril.

Biomimetic Materials

Some of the principles used by nature for mechanical optimization under the constraints imposed by the natural environment are tested for implementation in technical systems and materials. One of the methods used to explore these possibilities is rapid prototyping where extremely porous structures with designed geometry can be constructed out of virtually any material **[13]**. Porous scaffolds designed in hydroxyapatite (the bone mineral) with a strut thickness of a few hundred micrometers **(Fig. 2)** are currently tested in cell culture as a possible route for synthesizing bone replacement material. Research on biomimetic materials also includes the study of artificial collagen-mineral composites and metal nanoparticles synthesized in association with bacterial cell membranes.

Biotemplating

A further approach towards the design of new materials based on natural models is biotemplating. This process consists of transforming the biological materials (e.g. wood) directly into technical structures by physical or chemical processing. The aim is to preserve as much as possible of the original hierarchical structure, copying it into a different material. Ongoing activities include studies on the carbonization of wood and the transformation into porous carbon-based ceramics. Indeed, it has been shown by different groups in recent years, that wood tissue can be transformed into cellular ceramics via a two step procedure: i) pyrolytic decomposition of wood, resulting in a porous carbon template, and ii) direct reaction to form carbide-ceramics, or infiltration of non reactive species for further processing to yield oxide-ceramics. The formation and the structure of the carbon template plays a key role in this context, since preferred orientation and nano-porosity of the template may be controlled by the hierarchical structure of the original tissue and by the details of the conversion process. Current activities include studies on the chemical and structural development of wood during pyrolysis and on the microstructure and mechanical properties of the resulting carbon templates.

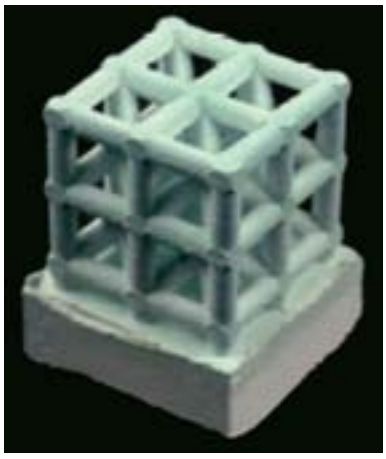

Fig. 2: Simple architecture made out of hydroxyapatite by rapid prototyping of the mould and subsequent gel casting (in collaboration with the Vienna University of Technology [13]). The strut thickness is close to the one of bone trabeculae (several hundred micrometers, see Fig. 3).

Mechanical Adaptation of Biomaterials

It is well-known that biological materials constantly adapt to (even changing) mechanical needs. This is achieved by a strain-sensing mechanism, which in most biological systems is not fully elucidated. In the case of bone, for instance, some specialized cells (osteocytes) are thought to act as strain sensors and to be at the centre of a feed-back loop, called bone remodeling cycle, where damaged bone is removed and replaced by new material. This process is crucial for the tissue's capability of mechanical adaptation and self-repair. Some basic principles are currently studied by computer simulation. The mechanical optimization of natural composites, such as the mineralized collagen fibril, are studied by theoretical modeling **[8]** and by investigating experimentally the detailed response (both mechanical and biological) of the biological system to mechanical loads. Other examples of current interest are the deformation mechanism of tendons **[11]**, of single wood fibers **[1]** or the structure development in systems with a defined load pattern, such as tree branches **[2]**.

Tendons contain helically wound collagen molecules with a length of 300 nm and a thickness of about 1.5 nm. These molecules are assembled into fibrils which consist of staggered periodic arrays of these molecules. The fibrils are further assembled into fibres and finally into tendons. Structural changes during deformation of native tendons can be monitored "in-situ" by diffraction of synchrotron radiation while the tendon is being stretched. The x-ray diffraction yields the helix pitch of the molecules as well as the staggering period of the fibrils. Monitoring the changes in these parameters during stretching permits to measure the elongation of the molecules as well as the fibrils. It turns out that the molecules are extending less than the fibrils which are extending much less than the tendon as a whole. This means that not only the structure but also the deformation is hierarchical. This is possible because the various elements in the hierarchy can shear with respect to each other **[11]**.

A similar approach is pursued for the analysis of the deformation of wood. In order to get a better understanding of how the elements in the hierarchy are optimized individually and contribute to the overall mechanical behavior of the tissue, methods have been developed to extract single native wood fibres without maceration or any other chemical treatment **[1]**. Such fibres have a thickness around 20 microns and can be individually analyzed by synchrotron radiation during deformation. Tree branches are particularly interesting to study mechanical adaptation since they have to grow horizontally and will experience predominantly tensile stresses on the upper side and compressive stresses on the lower side **[2]**.

References:

[1] Burgert, I, Keckes, J., Frühmann, K., Fratzl, P., Tschegg, S. E.: A comparison of two techniques for wood fibre isolation – evaluation by tensile tests on single fibres with different microfibril angle. Plant Biol. 4, 9-12 (2002).

[2] Färber, J., Lichtenegger, H. C., Reiterer, A., Stanzl-Tschegg, S., Fratzl, P.: Cellulose microfibril angles in a spruce branch and mechanical implications. J. Mater. Sci. 36, 5087-5092 (2001).

[3] Fratzl, P.: Von Knochen, Holz und Zähnen. Physik J. 1, 49-55 (2002).

[4] Fratzl, P.: Cellulose and collagen: from fibres to tissues. Curr. Opin. Coll. Interf. Sci., in press (2003a).

[5] Fratzl, P.: Small-angle scattering in materials science – a short review of applications in alloys, ceramics and composite materials. J. Appl. Cryst. 36, 397-404 (2003b).

[6] Fratzl, P., Klaushofer, K.: Röntgenkleinwinkelstreuung in der Osteologie. J. Mineralstoffwechsel 2, 12-19 (2001).

[7] Grabner, B., Landis, W. J., Roschger, P., Rinnerthaler, S., Peterlik, H., Klaushofer, K., Fratzl, P.: Age- and genotype dependence of bone material properties in the osteogenesis imperfecta murine model (OIM). Bone 29, 453-457 (2001).

[8] Jäger, I., Fratzl, P.: Mineralized collagen fibrils – a mechanical model with a staggered arrangement of mineral particles. Biophys. J. 79, 1737-1746 (2000).

[9] Misof, B. M. Roschger, P., Cosman, F., Kurland, E. S., Tesch, W., Meßmer, P., Demster, D. W., Nieves, J., Shane, E., Fratzl, P., Klaushofer, K., Bilezikian, J., Lindsay, R.: Effects of intermittent parathyroid hormone administration on bone mineralization density in iliac crest biopsies from patients with osteoporosis: a paired study before and after treatment. J. Clin. Endocrin. Metab. 88, 1150-1159 (2003).

[10] Paris, O., Zizak, I., Lichtenegger, H., Roschger, P., Klaushofer, K., Fratzl, P.: Analysis of the hierarchical structure of biological tissues by scanning x-ray scattering using a micro-beam. Cell. Mol. Biol. 46, 993-1004 (2000).

Bone Research and Medical Applications

The hierarchical structure of bone is schematically shown in **Fig. 3**. The interior of a human vertebra, for instance, is a cellular solid with struts of about 0.2 mm thickness. These struts are made of bone material which is a collagen matrix with lamellar organization and reinforced by calcium-phosphate nano-particles. Diseases may affect the bone structure at any of these levels and physical characterization helps elucidating how these diseases develop and how they contribute to fracture incidence, for example. Recent examples of studies with medical background relate to brittle bone disease **[7]**, to hypophosphatasia **[15]**, and to osteoporosis treatment with parathyroide hormone **[9]**.

These studies have been carried out in close collaboration with the Ludwig Boltzmann Institute of Osteology in Vienna, Austria. In the first example, the aim was to elucidate the origin of the bone fragility in brittle bone disease, a rare congenital disease characterized primarily by a collagen defect. A combination of methods, including electron microscopy, x-ray scattering and mechanical testing has been employed to show that a weaker collagen matrix joined to over-mineralization might be at the origin of the fragility. Osteoporosis, on the other hand, is a widespread disease associated with low bone mass and increased fracture incidence. Osteoporosis treatments aim at increasing or stabilizing the bone mass. One of the important questions in this context is whether the various treatment strategies also affect the bone material quality. We have been addressing this question for different (potential) treatments including fluoride, bisphoshphonates and, most recently, parathyroide hormone **[9]**.

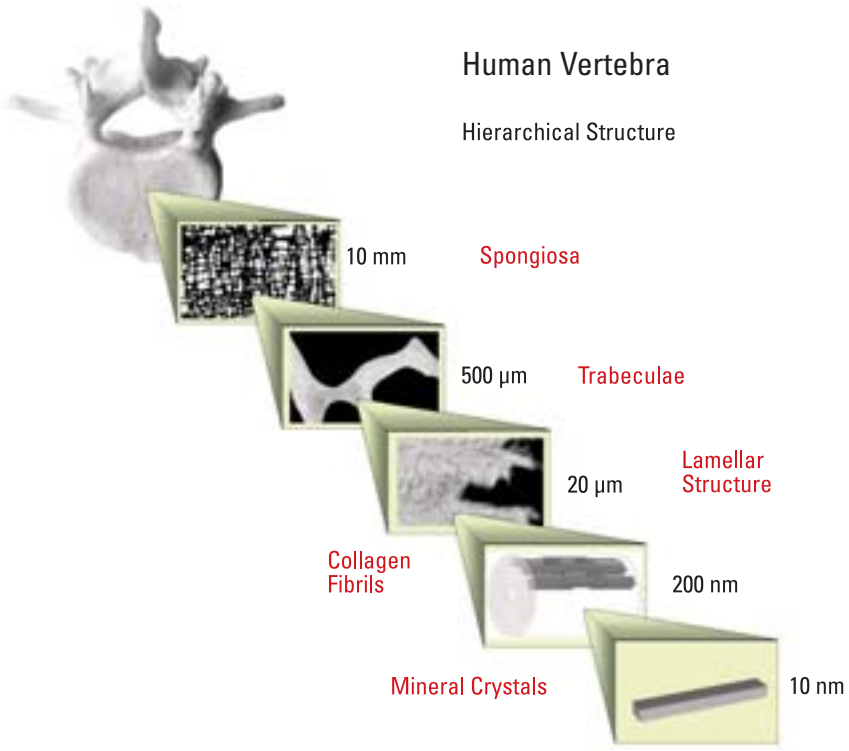

Fig. 3: Hierarchical structure of bone. The interior of a human vertebra is a spongy bone structure (spongiosa) with individual struts (trabaculae) having a thickness of about 0.2 mm. The bone material is a composite made of collagen fibrils reinforced with calcium phosphate nanoparticles. This fibre composite is assembled into a lamellar plywood-like structure. The mechanical properties depend on the detailed structure at each level of hierarchy. Similarly, diseases may affect any of these levels.

New Methods for Materials Analysis

Most of the structural research mentioned previously requires state-of-the-art experimental equipment, but some needs the development of new approaches. Scanning methods based of the diffraction of synchrotron radiation **[10]**, as well as the technique of small-angle x-ray scattering (SAXS) are continuously developed to improve the characterization of hierarchical biomaterials **[5]**. **Fig. 4** shows the principles of scanning-SAXS, used to characterize bone on two hierarchical levels simultaneously. This approach can be used, e.g. to assess the effects of osteoporosis treatment on the quality of bone material **[6]**. Further technical improvement is expected from a dedicated scanning set-up which is planned to be installed at the synchrotron BESSY in Berlin.

Prof. Peter Fratzl
Director of the Department of Biomaterials
peter.fratzl@mpikg-golm.mpg.de

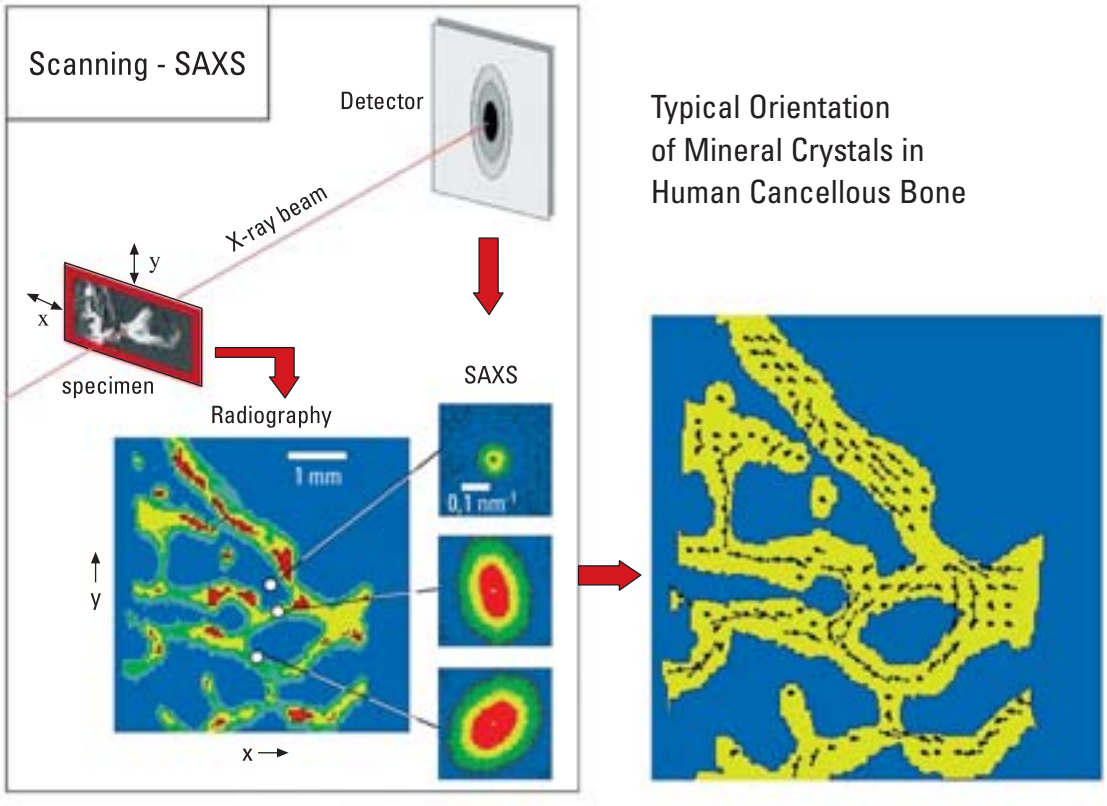

Fig. 4: The method of scanning small-angle x-ray scattering (scanning-SAXS) allows structure characterization at two hierarchical levels simultaneously. A narrow x-ray beam is scanned across the sample. This allows a resolution given by the size of the x-ray beam (typically in the order of micrometers). At each position, the evaluation of the SAXS-signal gives structural information at the nanometer level. The example shows the local orientation of plate-like mineral particles (represented by bars in the rightmost image) in a bone section.

[11] Puxkandl, R., Zizak, I., Paris, O., Keckes, J., Tesch, W., Bernstorff, S., Purslow, P., Fratzl, P.: Viscoelastic properties of collagen – synchrotron radiation investigation and structural model. Phil. Trans. Roy. Soc. London B 357, 191-197 (2002).

[12] Roschger, P., Grabner, B. M., Rinnerthaler, S., Tesch, W., Kneissel, M., Berzlanovich, A., Klaushofer, K., Fratzl, P.: Structural development of the mineralized tissue in the human L4 vertebral body. J. Struct. Biol. 136, 126-136 (2001).

[13] Stampfl, J., Wöß, A., Fratzl, P., Seidler, S.: Rapid Prototyping of ceramic and polymeric cellular materials. IFMBE Proceedings 2002 3, EMBEC'02 (eds: H.Hutten and P. Krösl), Vienna, Dec. 2002, pp 172-173.

[14] Tesch, W., Eidelman, N., Roschger, P., Goldenberg, F., Klaushofer, K., Fratzl, P.: Graded microstructure and mechanical properties of human dentin. Calcif. Tissue Int. 69, 147-157 (2001).

[15] Tesch, W., VandenBos, T., Roschger, P., Fratzl-Zelman, N., Klaushofer, K., Beertsen, W., Fratzl, P.: Orientation of Mineral Crystallites and Mineral Density during Skeletal Development in Mice Deficient in Tissue Non-specific Alkaline Phosphatase. J. Bone Miner. Res. 18, 117-125 (2003).