RESEARCH *in Brief*

COLLOID AND INTERFACE RESEARCH

The Bones of the Matter

Teeth, bones, tendons, ligaments and cartilage are all made of the same basic biological building material: collagen. The string-like molecules of this protein are themselves soft and elastic, but they can store mineral particles to form a tremendously solid, bone-hard composite. The mechanical properties of bone are also based mainly on a special hierarchical structure. Scientists at the Max Planck Institute of Colloids and Interfaces in Potsdam are looking into this functional architecture together with partners in Vienna, Trieste and Grenoble. To this end, they are removing mineralized leg tendons from turkeys – and using synchrotron beams to illuminate this "one-dimensional model bone" (PHYSICAL REVIEW LETTERS, October 8 and November 26, 2004).

One could say that material scientists have much to chew on in bone research. It has been known for over a century that bones adapt their structure to optimally cope with locally differing mechanical loads. But our understanding of how nature – with only two basic materials – manages such adaptable constructions is as yet rudimentary.

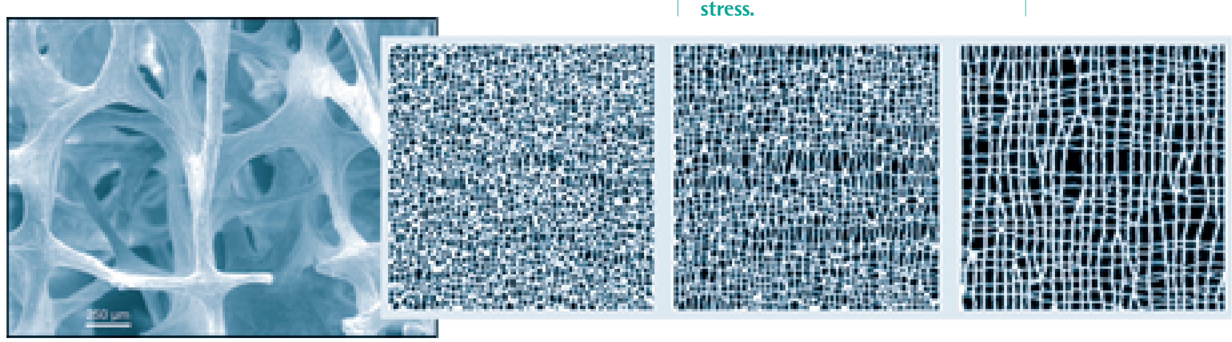
To penetrate here more deeply, making use of all the resources of modern structure research, is the goal of the Biomaterial Department at the Max Planck Institute of Colloids and Interfaces in Potsdam. Department head Peter Fratzl and his team are cooperating closely with medical personnel at the Ludwig Boltzmann Institute for Osteology in Vienna and material scientists at the synchrotron ELETTRA in Trieste, as well as the University of Grenoble.

Technically speaking, the material that bone is made of is a nano-composite: a compound made up of two molecular components. One component, collagen, comprises three protein chains wound around each other, forming a strand 300 nanometers (millionths of a millimeter) long and 1.5 nanometers thick. These soft and pliable molecule strands line up in parallel to form fibrils – and incorporated between these fibrils is the second component, mineral calcium phosphate in the form of tiny, circa 2- to 4-nanometer-thick crystalline platelets. Depending on the degree of mineralization, the flexible collagen scaffolding is mechanically reinforced and, moreover, hardened.

In addition, the mineralized collagen fibrils line up in parallel into strong bundles or layers, the so-called lamellae, which usually measure several micrometers in thickness. These lamellae, in turn, form trabeculae – tiny crossbeams and struts several tenths of a millimeter thick – which finally form a sponge-like, three-dimensional support and load-bearing scaffold (the *spongiosa*) inside the bone.

The purpose of this hierarchical structure is to distribute the forces applied to the bone as constantly as possible – without local overloading – from coarser to increasingly finer structures. Ultimately, the mineralized collagen strands must hold out: they take up the force as tensile stress and counteract it through elastic elongation.

The Potsdam researchers were recently able to follow in detail how bone achieves such great feats. For this purpose, the large leg tendons from turkeys served as "one-dimensional" model bones, as the collagen fibers are partially mineralized and resemble those in bone. At the same time, they are perfectly parallel to the tendons' pulling direction and arranged quasi in one dimension – similar to crystals and therefore regular enough for X-ray diffraction analysis. And Fratzl and his colleagues made use of just this: at the synchrotron ELETTRA in Trieste they exposed turkey leg tendons to the very short wavelength beams of this "X-ray lamp" and could then follow how collagen strands behave under increasing stretching.



The electron microscope reveals the porous spongiosa of a bone (left). The three pictures on the right show how a simulated bone in the computer forms the same sponge-like structure under stress.

PHOTOS: MPI OF COLLOIDS AND INTERFACES

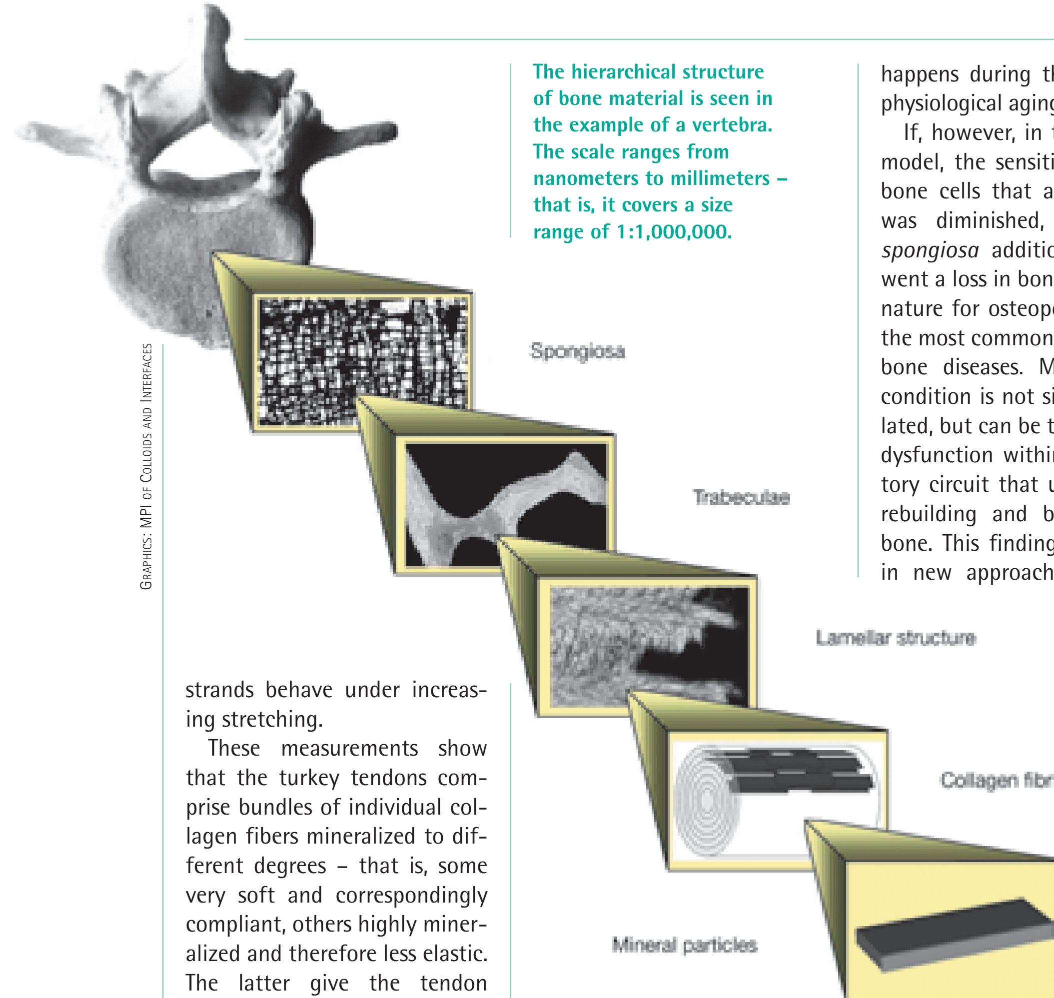
These measurements show that the turkey tendons comprise bundles of individual collagen fibers mineralized to different degrees – that is, some very soft and correspondingly compliant, others highly mineralized and therefore less elastic. The latter give the tendon strength with low stretching, but break with very large strains and contract back to a non-load-bearing state. Then the entire load is transferred to the softer, very compliant fibers, which ensure that the structural integrity of the tendon is maintained and prevent it from tearing completely. Such an over-stretched tendon then seems to be soft and elastic under renewed loading, even with little stretching, as the highly mineralized fibers no longer participate.

Further topics for the Potsdam scientists include how bones, as a biological material, grow into their function, and how their optimal structure is maintained over an entire lifetime and also adapts to each changing demand. These questions address rebuilding and breakdown processes within bones that must take place in a directed and controlled manner. It is certain that special cells within the bone function as mechanical sensors and trigger a regulatory circuit that controls the breakdown of old or damaged bone material and replacement with new material.

Based on these ideas, a computer model was developed that tracks bone remodeling in a simulated human vertebra under vertical load. Even if it begins with the unrealistic assumption of a vertebra completely filled with bone, the model always ends up generating the natural structure: a foam-like *spongiosa* enclosed in a comparatively thin layer of solid bone. Interestingly enough, over time, all such simulations delivered a constant value for the bone mass – whereas the remodeling within the *spongiosa* always led to increasingly coarser structures, and thus to fewer, but also thicker trabeculae. And this is precisely what happens during the process of physiological aging of bones.

If, however, in the computer model, the sensitivity of those bone cells that act as sensors was diminished, the coarser *spongiosa* additionally underwent a loss in bone mass: a signature for osteoporosis, one of the most common degenerative bone diseases. Moreover, this condition is not simply age-related, but can be traced back to dysfunction within the regulatory circuit that underpins the rebuilding and breakdown of bone. This finding could result in new approaches to osteoporosis therapy. But the Potsdam researchers also hope to deal with other diseases associated with reduced quantity or quality of bone mass, using their wide-ranging material technology equipment. This includes finding out next at what level within the structural hierarchy of the bone the relevant defect lies in order to discover the exact causes and, ultimately, a targeted therapy.

And even if they do not always succeed, the know-how of the material researchers is helpful: the better they understand the architecture and mechanics of bone material on every level, the closer to nature this natural material can be artificially reproduced. Biomimetic materials could then be made that would be comparable to natural bone and serve as a replacement for it in the form of implants.



The hierarchical structure of bone material is seen in the example of a vertebra. The scale ranges from nanometers to millimeters – that is, it covers a size range of 1:1,000,000.

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@ Further information from:
PROF. DR. PETER FRATZL
Max Planck Institute of Colloids and Interfaces, Potsdam
Tel.: +49 331 567-9401
Fax: +49 331 567-9402
e-mail: fratzl@mpikg.mpg.de