Titanium Foams Fabricated for Bone-Tissue Engineering Applications

Titanium and its alloys are widely used as biological implants because of their superior biocompatibility, corrosion resistance, and lower modulus. However, the elastic moduli of these materials are still high when compared to those of human bone, particularly cancellous (porous) bone. Metallic foams are an option since the porous structure can more closely resemble that of bone. The optimum pore structure for these foams has been determined to be ~200–500 μm for permeation, attachment, and growth of osteoblasts. Producing metallic foams with pore sizes in this range using methods such as investment casting has proven difficult. Now, C.E. Wen and coworkers from the National Institute of Advanced Industrial Science and Technology, Japan, have fabricated titanium foams by using a powder metallurgical process incorporating space-holder particles to form a porous structure. They reported their work in the October issue of the *Journal of Materials Research*.

Pure titanium powder (purity ≥99.9%) was used along with ammonium hydrogen carbonate powder as the space-holder material. The size of the ammonium hydrogen carbonate powder was selected to be 200–500 μm, with the size of the titanium powder selected to be <45 μm. The two were mixed, compacted using a pressure of 100 MPa, and then heat-treated and sintered to burn out the ammonium hydrogen carbonate. This resulted in the formation of titanium foams with relative densities ranging from 0.20 to 0.65. Scanning electron microscopy (SEM) revealed a bimodal porous structure with macropores in the 200–500-μm range and micropores in the several micron-size range.

Compression tests showed that the mechanical properties of the titanium foams with relative densities of 0.20–0.30 (Young's modulus 2.90–3.40 GPa; compressive strength 25–53 MPa) were close to those of cancellous bone. The femoral head, for example, has a Young's modulus of 2.9 GPa and a compressive strength of 68 MPa. The compressive properties of the foams with relative densities of 0.50–0.65 were similar to those of cortical (surface) bone. The results indicate that the mechanical properties of the titanium foam can be tailored by selecting the appropriate density.

Biocompatibility of the foams was tested by using an alkaline treatment on the samples first to yield a bioactive titania layer on exposed surfaces. The samples were then immersed in simulated body fluid that has ion concentrations similar to those of human plasma for *in vitro* assessment. SEM observations after six days of immersion indicated that a bonelike apatite layer formed throughout the foam at the cell edge surfaces of the pores. This indicated excellent permeability of the open-cell structure of the foam thereby endowing bioactivity throughout the foam.

The researchers said that their titanium foams appear to be promising biological implant materials for human bone-tissue engineering by virtue of their excellent biomechanical properties and bioactivity.

GOPAL RAO

Covalent Nanoassemblies of Carbon Nanotubes and DNA Oligo-Nucleotides Synthesized

The ability of single stranded (ss) DNA to selectively bind to a complementary strand combined with its ready availability make it an ideal material for "bottom up" nanoassembly construction. The stability of such assemblies is enhanced when the individual components are joined by covalent bonds. Recently, professor Robert Hamers, graduate student Sarah Baker, and co-workers in the Department of Chemistry at the University of Wisconsin—Madison, have demonstrated a covalent adduct of ssDNA and single-walled carbon nanotubes (SWNTs). The researchers observed that the covalent interactions were stable even at temperatures that would normally remove noncovalently bound DNA, and that covalent linking of DNA to the nanotubes also increased the solubility of the adduct in aqueous buffer solution. More importantly, the ssDNA-SWNT adducts could be very selectively and reversibly hybridized to other ssDNA molecules in solution, showing good biochemical accessibility. According to Hamers, "[T]hese nanostructures have a number of potential uses, such as nano building blocks in complex nanostructures, or in highly sensitive, reversible biosensors."

As reported in *Nano Letters* (Web release October 5, 2002), the first step in the synthesis of the covalent adduct was to functionalize the surface of the nanotubes with carboxylic acid groups. The acid groups were then converted to amide functionalities which were treated with the cross-linker succinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate (SMCC) to produce maleimide functionalized nanotubes. In the last step, the maleimide groups were covalently attached to ssDNA. The assemblies were detected by labeling the ssDNA with a fluorescein dye group and measuring its photoluminescence (PL), or by linking unlabeled ssDNA to the tubes and then hybridizing the ssDNA-SWNT adducts with dye labeled DNA. In either case, the observed PL comes only from dye labeled DNA that is either directly bonded to the nanotubes or is hybridized to the ssDNA-SWNT adducts, not from the solution itself.

Hybridization experiments using complementary ssDNA and 4-base mismatched ssDNA showed that the covalently bound DNA maintains its specificity of binding, and that the DNA hybridization remains reversible. The specificity of hybridization proves that the DNA strand is available for hybridization, and is not intercalated inside or wrapped around the outside of the nanotube. This result demonstrates that despite being strongly bound to a SWNT, the DNA retains all the chemical properties of a free molecule. Thus, the covalent attachment would still allow the utilization of the ssDNA-SWNT adduct in very selective binding assays or the construction of complex nanostructures, and would result in improved stability of such systems.

GREG KHITROV

Large, Crack-Free Photonic Films Developed

Periodic dielectric superstructures are attracting interest, particularly for the formation of photonic bandgaps. However, application is limited because of the difficulty of preparing large, monocrystalline photonic structures with low defect density. Researchers from the Department of Chemistry at the University of Mainz have demonstrated a method for the preparation of large, crack-free photonic films. As reported in the October issue of *Chemistry of Materials*, B. Griesebock, M. Egen, and R. Zentel have developed a method to crystallize poly(methyl methacrylate) (PMMA) colloids on molten metals (Ga or Hg) as liquid substrates, which resulted in crack-free, nearly monocrystalline (low defect density) photonic-crystal films of millimeter size.

The researchers performed the crystallization by spreading several drops of a colloidal suspension onto the surface of the liquid substrate, then drying the film for 24 h at room temperature. The absence of cracks was checked by optical and scanning electron microscopy. With this method, the researchers prepared crack-free crystals of ~1 cm^2 area on liquid gallium and liquid mercury substrates. Polymer colloids prepared from poly(ethyl methacrylate), poly *tert*-butyl methacrylate, or fluorinated methacrylates also produced the same results.

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Transferring the film from the liquid substrate to a solid substrate has proven difficult. The researchers tried two techniques. For the investigation of the upper side of the film, a microscope slide can be slid into the liquid just under the monocrystalline film to lift it slowly. With this method, the film broke, but crystal fragments of more than 2 mm^2 area were preserved. To investigate the underside of a crystal, tape affixed to a sample holder was drawn down until it gently touched the monocrystalline film. Then the film was lifted from the liquid. With this method, 7-mm-diameter crystals could be separated without breaking.

The researchers concluded that this is a potentially useful approach for producing large photonic single crystals, which are the prerequisite for the preparation of resonators or, more generally, for wave guiding in photonic structures.

ANDREI A. ELISEEV

Predetermined Chiroptical Properties Expressed on Rosette Nanotubes

Chirotechnology is an emerging field with the potential for application in the design of sensors, chiral cholesteric phases, catalysts, and materials with electromagnetic, optoelectronic, information-storage, display-system, nonlinear optical, and novel chiral light-emitting applications. Induction of nonrandom symmetry breaking in supramolecular systems by external means, such as chiral vortex forces, electron transfer, and photoswitches, have the advantages of predictability and reproducibility. As a step toward a better understanding of nature's approach to generating supramolecular structures with predefined stereochemistry and architecture, researchers at the H.C. Brown Chemistry Laboratory, Purdue University, have extended the functionality of self-assembled helical rosette nanotubes by imparting on them adjustable chiroptical properties.

As reported in the August 24 issue of the *Journal of the American Chemical Society*, a team of Purdue University researchers led by H. Fenniri induced supramolecular chirality in rosette nanotubes (see figure) using two methods: by inducting symmetry breaking in a preexisting racemic mixture of M- and P-helical rosette nanotubes; and by employing a chiral promoter on a prochiral molecular module to trigger the hierarchical self-assembly of chiroptical rosette nanotubes. Both methods employ promoters that transfer their molecular chirality to the supramolecular ensemble as well as stabilize the nanotube assembly.

Rosette nanotubes are a class of organic nanostructures whose aqueous self-assembly is entropically driven. The single building block in these assemblies is a bicyclic molecule—compound **1**—with a hydrogen-bond donor–donor–acceptor array on one side, an acceptor–acceptor–donor array on the other, and a crown ether substituent (see figure). Rosettes, which consist of a six-membered macrocycle held together by 18 hydrogen bonds, stack to form a nantobube with a central pore and peripheral channels formed by the crown ethers. As expected by Fenniri and co-workers, induced circular dichroism (ICD) resulted from the binding of a chiral amino acid (either L- or D-alanine) to the prochiral crown ether. Transmission electron microscope (TEM) and small-angle x-ray scattering (SAXS) studies of concentrated rosette nanotubes in the absence of any amino-acid promoter confirmed a tube diameter of about 4 nm. Dynamic light scattering (DLS) showed that the average hydrodynamic radius of the nanotubes is 32.5 nm, which indicates that the nanotubes are composed of about 140 rosettes, on average, if 4.5 Å between stacks is assumed. DLS and TEM were used to confirm nanotube formation in the presence of L-alanine. The researchers believe that their investigations demonstrate not only self-assembly in the presence of L-alanine but that the assembly is expressing collectively the promoter's molecular chirality at the nanotube level.

The research team classified 20 promoters as inducing a strong, a medium, or no circular dichroism (CD) signal. All active promoters with the same chirality were found to induce the same helicity. For L-alanine analogues, primary ammonium or carboxylate functions were deemed essential for supramolecular chirality induction. The inductive effect was shown to be both promoter-specific and highly sensitive to minor structural variations. The researchers believe that the inability of a promoter to induce chirality is due to nanotube destabilization, weak interactions, or an achiral structure. Nanotubes were found to disassemble at low concentration [**1**(0.04 mM)] in the absence of any promoter. Monitoring of the CD as **1**(0.04 mM) was titrated with L-alanine showed that the transition from racemic to helical rosette nanotubes occurs in the range of 4–30 equivalents of L-alanine. Therefore, almost all of the binding sites must be promoter-occupied for a complete transition—an all-or-none response that the researchers said is at variance with a classical "sergeant-and-soldiers" mechanism whereby a few chiral species determine the overall chirality.

The researchers demonstrated several promoter phenomena: enantiospecificity, in which all of the L amino acids were found to induce the exact opposite CD response as their D-isomers; reversibility, in which heating caused the ICD to decrease sharply but cooling restored it to 70% within minutes and to 100% within 24 h; and dominant/recessive behavior, in which the addition of a large excess of D-alanine to **1** preequilibrated with L-alanine resulted in an ICD identical to **1** preequilibrated with D-alanine. Analysis of the P↔M equilibrium suggests to the researchers that the promoters "within their sterically matching nanotubes must interact cooperatively not only to stabilize but also to feed their nanotube host with additional rosette stacks and **1**-promoter complexes." The researchers propose these interactions are electrostatic bonds between the carboxylate and ammonium groups.

The researchers found two pathways

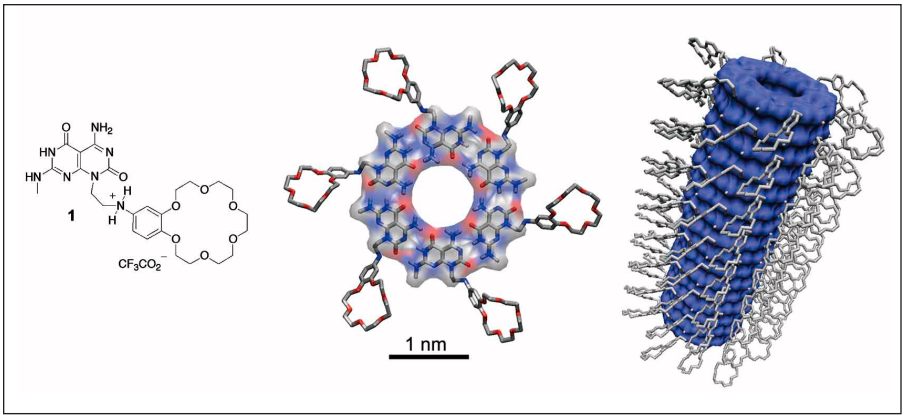

*Figure. Compound **1** (left) self-assembles to form a rosette assembly (middle), which then self-organizes into a rosette nanotube (right).*

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