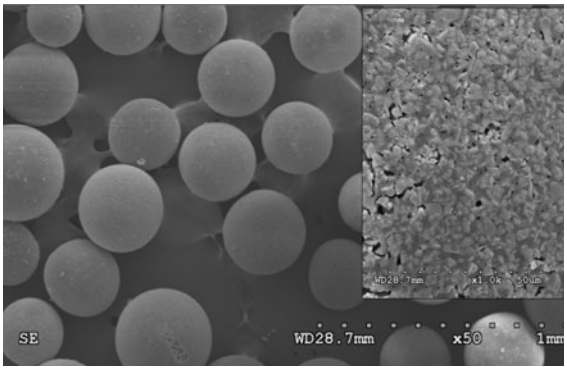
Bio Focus

Drug-eluting calcium phosphate microparticles developed as self-setting 3D scaffold for bone tissue regeneration

Regeneration of defects in the bone tissue due to disease or trauma continues to be a major challenge in orthopedics and dentistry. Autologous transplants that are commonly used in the clinic suffer from limited availability of harvestable tissue in addition to significant patient discomfort. Engineered tissues offer a promising alternative to transplants and there is a growing need to develop three-dimensional (3D) scaffolds for tissue regeneration.

Owing to their excellent osteoconductive properties, calcium phosphate-based materials have emerged as promising candidates for bone tissue regeneration. Typically, these materials require processing at a high temperature (hundreds of degree Celsius) for mechanical integrity which renders them unsuitable for encapsulation of bioactive molecules like drugs and growth factors to enhance the therapeutic effects. In a recent study, researchers from Dankook University in South Korea have prepared ceramic microparticles for sustained delivery of biomolecules at room temperature in an aqueous environment that afford easy encapsulation of drugs and proteins.

Self-setting calcium phosphate cements (CPCs) are being widely studied as potential injectable biomaterials to fill bone defects of any shape. Reporting in the February issue of the *Journal of the American Ceramic Society* (DOI: 10.1111/j.1551-2916.2010.04314.x; p. 351), J.-H. Park, H.-W. Kim, and their colleagues introduce a technique to fabricate self-hardening microspheres with sizes of hundreds of micrometers for use as 3D bone tissue matrix prepared by emulsification of α-tricalcium phosphate (α-TCP)-based CPC mixed with collagen. CPC-collagen composites constitute the two major components of the calcified bone matrix. Biomolecules can be easily incorporated into these microparticles by adding them to the collagen liquid phase during emulsification.



Scanning electron micrograph of calcium phosphate cements-collagen composite microparticle morphology and surface microstructure (inset) prepared by aqueous emulsification at room temperature.

Release kinetics of encapsulated bovine serum albumin indicated a two-step sustained release well-suited for controlled delivery of encapsulated drugs or growth factors to enhance cell function in these scaffolds. Furthermore, the surface of the α-TCP microspheres was covered by nanocrystals of bone mineral-like hydroxyapatite phase when the particles incubated in simulated body fluid. Results from *in vitro* cell studies indicated that osteoblasts adhere, spread, and proliferate on these microsphere substrates. Thus, these protein-releasing CPC-collagen microspheres hold promise as a 3D scaffold for bone tissue regeneration.

Kaushik Chatterjee

Programmable, autonomous molecular robot fabricated and fueled with DNA

Machines constructed from DNA can be made to walk along self-assembled DNA tracks. The simplest devices are controlled by sequential addition of DNA signals (molecules of single-stranded DNA, or oligonucleotides). Signal strands interact by hybridizing with complementary single-stranded DNA to form a double-helical duplex; they can also displace a strand from an existing duplex. For example, a signal strand can hybridize to bind a foot of the walker to its track. A complementary signal strand can then reverse this reaction by displacing the "binding" strand, forming a double-stranded waste product and freeing the foot to step forward. Such strand-exchange reactions can be accelerated by several orders of magnitude by the provision of "toeholds"—short sections of exposed single-stranded DNA that can initiate hybridization to the invading strand. Strategies for sequestering and activating toeholds, for example in an autonomous reaction cycle where toehold strands are progressively revealed, have progressed to the point where an external operator is no longer required to control the reaction sequence of the walker. Autonomous bipeds that walk on a reusable track have been designed by coordinating the reactions of DNA fuels with the two feet so that the front foot remains bound to the track while the back foot is lifted. Researchers from the same group that demonstrated the biped, R. Muscat, J. Bath, and A. Turberfield of the University of Oxford, recently demonstrated a DNA motor whose sequence of movements can be programmed by instructions embedded in its DNA fuel molecules. Unlike typical bipedal walking devices, this new motor is normally bound to a single anchorage, operates autonomously, and can be programmed to choose between branches on the track.

As reported in the January 28th online edition of *Nano Letters* (DOI: 10.1021/nl1037165), Turberfield and co-researchers produced a track consisting of addressable anchorages tethered to a double-stranded DNA backbone.

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The single-stranded cargo can bind to any anchorage. Parts of the anchorage and cargo that remain single-stranded are held together to form a structure the researchers refer to as a "split-toehold," which not only signals the cargo's presence but identifies the current anchorage by displaying its address (a specific sequence of nucleotides). Cargo transfer is mediated by a DNA fuel molecule that provides both energy and a routing instruction; it carries address domains that mediate transfer of the cargo between two specific anchorages.

The researchers used a simple two-anchorage track to demonstrate the coupling of fuel hairpins to control cargo movement by sequential activation of split toeholds. A three-anchorage track was then used to demonstrate the control of directional transport by information stored in the fuel hairpins. Furthermore, a T-junction track with four anchorages and branch points was used to demonstrate that the DNA motor could navigate complex paths. The researchers said, "We have made a further step in the development of molecular robotics by showing that the behavior of an autonomous motor on a branched track can be programmed by a rewritable external program encoded in DNA."

Steven Trohalaki

Nano Focus

Thermodynamics predict enhanced vacancies formation in nanoparticles compared to the bulk

When an atom is lacking in a crystalline lattice, the thermal, electronic, and mechanical properties of the material change. In nanomaterials, these properties are not always easily measurable and theoretical studies can help researchers understand and predict modifications of the structure and properties of materials at the nanoscale. G. Guisbiers of the Catholic University of Louvain recently studied vacancies formation in nanoparticles with the help of classical thermodynamics.

Thermodynamics is a top-down approach that avoids many-body calculations. It is known to be relevant when the thermal fluctuations, proportional to the inverse square root of the number of particles in the system, are small. Thus, issues concerning nanoparticles with diameters down to 4 nm can be addressed by thermodynamics, as reported in the February 17th issue of the *Journal of Physical Chemistry* (DOI: 10.1021/jp108041q; p. 2616).

Guisbiers uses a universal equation linking the bulk property of a material and the size and shape of the particle to deduce the corresponding property in nanoparticles for a number of metals and semiconductors. Results show that vacancies form more easily in nanosized materials than in the bulk. In energetic considerations, this can be related intuitively to the augmentation of the surface-to-volume ratio, since vacancies can be thought of as internal surfaces.

"Even if the vacancy concentration of a nanoparticle increases compared to its bulk vacancy concentration, this model can also explain why nanomaterials appear to be perfect. It is due to the limited number of atoms in a particle," said Guisbiers.

The predicted increase in concentration of vacancies matches several experimental results. It leads to bond length contraction. This induces that nanomaterials are harder and possess higher yield strengths than bulk materials, a phenomenon known as the Hall–Petch effect. The higher concentration of vacancies also lowers phonon frequencies, an effect that is observed experimentally. It results in lower electronic and thermal conductivities due to enhanced electron and phonon scattering.

Guisbiers said that this study could help in the understanding of the formation of nanopores, widely used in nanotechnology applications.

Elsa Couderc

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