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Applications of nanomaterials in medicine

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Recent advances in nanotechnology, particularly for diagnostic, therapeutic, and bone tissue engineering purposes, are discussed.

Nanomaterials—natural, incidental, or manufactured materials in which 50% or more of the particles that they contain have at least one external dimension in the 1–100nm size range—are used in medicine for many diagnostic and therapeutic applications (e.g., for several diseases that affect different organs). Furthermore, nanotechnology has applications in every engineering discipline, and engineers who specialize in nanotechnology contribute to important innovations in the fields of energy, defense, and civil engineering.[1,2] The mechanical properties of nanomaterials are of considerable interest because these characteristics determine the utility of the structures.[3]

Over the past 30 years, much research has been conducted on the use of nanomaterials for medical applications, and most of these studies have focused on the safety and toxicity of the nanomaterials to human cells and tissue function.[1] There is a lack of consensus, however, about the influences of particle size, morphology, and surface charge on the interactions between nanomaterials and tissues, about the uptake of nanomaterials by immune system cells, and concerning toxicity or safety risks. Indeed, there are several critical issues that need to be explored. For instance, how to translate inorganic nanoparticles from purely academic studies to industrial-scale processes that comply with commercial-quality systems, governmental standards, and regulatory contexts for human use. In particular, the size and shape, physicochemical properties, and surface and interfacial properties of inorganic nanoparticles in biological systems are important parameters to consider.[4] Moreover, compared with in vivo exposures, in vitro tests may provide only a partial indication of toxicity potential.

The aim of this work[5] is to give a brief overview of some of the recent nanotechnology advances in medicine and bone tissue engineering, and to explore some typical applications of these emerging technologies. For example, we present and discuss some experimental nanotechnology models for the treatment of diseases of the nervous system and the osteoarticular system in various populations (e.g., infants, adults, and elderly people). We also propose a theoretical model that can be used to predict the bending strength of a nanobeam. This model includes a fracture approach that accounts for imperfections on the beam surface and for crack growth.

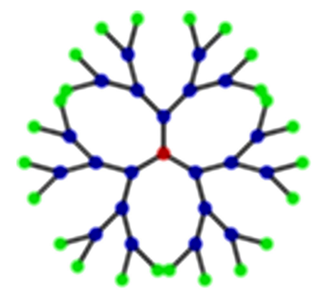

Figure 1. *A schematic representation of a dendrimer, i.e., a soft globular molecule that is 3–10nm in diameter. The structure contains a high density of tailorable surface functional groups (as represented by the different colors).*

An important field of nanomaterial application is alterations of the nervous system (i.e., developmental, psychiatric, traumatic, inflammatory, infectious, and degenerative disorders). In these scenarios, the nanoparticles may allow for the transport of therapeutic or imaging-contrast agents across the blood–brain barrier (BBB) into the nervous system. It may thus be possible to achieve targeted delivery of these agents to appropriate brain or spinal cord subregions.[6] In addition, much effort has recently been devoted to finding drugs that can circumvent the BBB and enter directly into the central nervous system (either on their own, or with the use of carriers).[7] The arsenal of nanoparticle-based technologies has been expanded even further with the design of multifunctional constructs that combine diagnostic and therapeutic functions within the same nanocarrier.[8] These ‘theranostic’ platforms enable a noninvasive assessment of the pharmacokinetics, tissue biodistribution, and accumulation of drugs at the target site, and some recently developed examples are being used for cancer treatment.[9] Dendrimers (see Figure 1)—soft globular molecules that are about 3–10nm in size, with a high density of tailorable surface functional groups—are also emerging as promising candidates for diagnostic platforms, and for targeted drug and gene delivery. For example, polyamidoamine dendrimers have been used to deliver an antioxidant and anti-inflammatory

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agent—*N*-acetyl cysteine (NAC)—to the brain, to help treat immune diseases.[10]

In another study,[11] it has been demonstrated (in an animal model) that intravenously administered dendrimer–NAC conjugates become localized at inflammation sites associated with cerebral palsy (CP) symptoms. CP is the most common cause of childhood disability, and prematurity is thought to be a leading risk factor in the development of the disorder. Administering such dendrimers to affected newborns may thus be one way to treat CP. In addition, it may also be possible to administer the dendrimer nanodevices to the amniotic fluid to help prevent perinatal brain injuries in high-risk patients.[12]

Tissue engineering is another field in which nanotechnologies may play a promising role. For example, it may be possible to use nanotechnologies for skeletal reconstructions (i.e., following bone fracture). This is of particular interest because of the increasingly aging population. Indeed, bone tissue is required to treat bone fractures and other bone defects, as well as for ring reconstructions and tissue transplants.[13] Other potential nanotechnology bone tissue engineering applications include treatments for trauma, congenital bone malformations, skeletal diseases, and tumor resections. In these applications, nanotechnologies can be used to form scaffolds, and to deliver drugs and growth factors to a lesion site. In this way, thanks to the high surface-to-volume ratio of nanoparticles, they can enhance new bone formation.

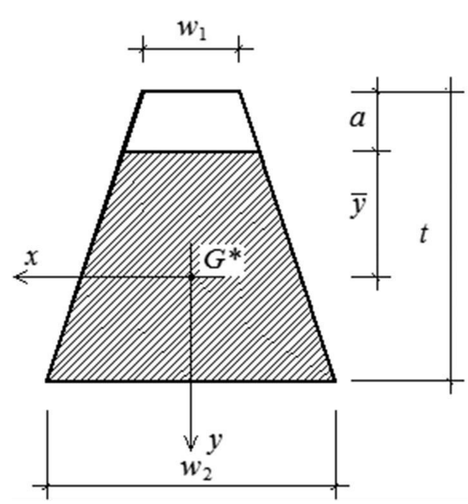

Figure 2. *Cross section (in the x-y plane) of a cracked trapezoidal silicon nanobeam, showing the parameters used in the theoretical model for predicting the bending strength of a cracked nanobeam. G*: Center of mass. a: Crack length.* $\bar{y}$*: Crack tip coordinate, y. t: Height of trapezoid.* w_1, w_2*: Width of the top and bottom of the trapezoid, respectively.*

Although scaffolds have good in vivo biological performance, their low fracture toughness has so far limited their applications in bone tissue engineering. To increase the strength and mechanical performance of the scaffold, it is current practice to add nanoparticles, whiskers, and coatings to the structures.[14] Surface roughness, however, is frequently observed on the surfaces of such nanobeams, and we have thus proposed a theoretical model to predict the bending strength of a cracked nanobeam.[15] In this model, we use a fracture approach that takes into account imperfections on the beam surface, as well as crack growth. Specifically, we use the scale invariant criterion to describe the failure of a cracked trapezoidal silicon nanobeam (see Figure 2) that is subjected to a bending moment. This criterion includes the so-called strain energy density factor, which is a function of the stress intensity factors. The critical crack length values obtained with this mathematical approach can be compared with atomic-force-microscopy measurements.

In summary, nanotechnology offers a wide range of potential benefits in medicine. Indeed, nanoparticles are being extensively studied for several applications and, in animal models, are showing promising results for many diagnostic and therapeutic purposes. Emerging fields of application are for the treatment of cardiovascular disease, for oral insulin administration, and for the diagnosis and therapy of cancer.[16–18] Further research is now needed to demonstrate the potential benefits of nanotechnology in humans (i.e., a major concern is the long-term safety of nanoparticles). In the next stage of our work, we will compare different characteristics (e.g., mechanical properties) of currently patented scaffolds.

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