Cytotoxicity of boron nitride nanotubes

The superior mechanical properties of nanotubes make them promising materials for commercial and biomedical uses. Preliminary work is performed in the investigation of boron nitride nanotube structures and their compatibility with living cells. New insights are gained into the toxicity and stability of boron nitride nanotubes and cell membranes using a computational molecular dynamics approach.

Nanomaterials represent a relatively new field of materials science, and there is ever-increasing interest in their applications over a broad range of fields [2]. The interest is justified due to the superior mechanical properties of nanostructured materials [7]. The 1991 discovery of carbon nanotubes [1] prompted great interest in the structural and mechanical properties of similar tube-like structures. Nanotubes are the strongest one-dimensional fibers that have ever been discovered with strengths two orders of magnitude greater than steel [10]. Materials science researchers are continually proposing new and exciting applications for nanotube-reinforced materials [3, 4, 6, 9], but the biological safety of such materials is important if they are to be used commercially. Furthermore, interest in biomedical applications of nanotubes is increasing, prompting an investigation into the biocompatibility of nanotubes [8].

Carbon nanotubes are known to be biologically destructive, severely damaging the lipid bilayer of cells [8]. Boron nitride nanotubes, on the other hand, are generally considered to be nontoxic [8], suggesting their use in biomedical applications. Overall, the destructive nature of nanotubes (cytotoxicity) is not well understood [8] and investigation is necessary if nanotubes are ever to be used widely.

Researchers from La Trobe University, Melbourne and the Victorian Life Sciences Computation Centre in Carlton, Australia recently performed an investigation into the interaction mechanisms between cellular lipid bilayers and boron nitride nanotubes. They used a computational molecular dynamics approach to analyze the stability of boron nitride nanotubes in lipid bilayers and to investigate the process through which the nanotubes enter the lipid bilayer. Their goal was to understand the reduced toxicity of boron nitride nanotubes compared to that of carbon nanotubes. Dr. Michael Thomas of La Trobe

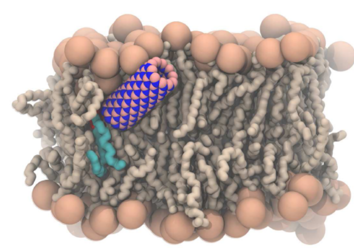

Figure 1: Boron nitride nanotube embedded in a lipid bilayer.

University explains that there has not been much research into the toxicity of boron nitride nanotubes, and that their investigation was a first step to characterize the interactions of boron nitride nanotubes with living cells.

As nanotubes enter the lipid bilayer, they can act like straws, providing a channel for water transport into and out of the bilayer [8]. They began their investigation by embedding a boron nitride nanotube in the lipid bilayer membrane, perpendicular to the membrane surface. They found that the nanotubes are stable in this configuration, oscillating only slightly from their initial positions. This configuration created a channel across the membrane which could facilitate the transfer of molecules into and out of the cell. Such behaviour would be potentially advantageous for drug transport, allowing a pathway for the administration of drugs directly into cells. They found that the ability to transport molecules was dependent on the size of the nanotube. Large lipid molecules blocked the opening of small diameter nanotubes completely, preventing water transport through the nanotube. Larger nanotubes allowed some water to pass through the membrane, however, lipid molecules were seen to enter the interior of the nanotube and interact with the walls of the tube, partially clogging the channel and slowing down the transport rate of material into the cell.

Additionally, they performed an exploratory investigation into the mechanism by which nanotubes insert themselves into the membrane. Using molecular dynamics, they placed nanotubes above the lipid bilayer surface and ran simulations to gain insight into the interaction between the membrane surface and the nanotube. In all cases, the nanotubes approached the surface of the membrane and reoriented so that they were roughly parallel to the bilayer surface before entering. Even if the nanotubes began perpendicular to the surface, they would not cross the membrane until they had rotated to be parallel to the surface. Dr. Thomas explained that once parallel, an interaction would be established between a single lipid head and a nitrogen atom in the nanotube. The lipid would then pull the nanotube into the interlayer area at roughly a 45 degree angle. Once inside the inter-membrane layer, Dr. Thomas says that the nanotubes experienced an energy barrier and would thus remain there for the remainder of the simulation.

This suggests a potential vehicle for drug delivery to cells: a drug molecule which would generally be rejected by the cell membrane could be embedded in the nanotube which might then be guided into the membrane. This method of drug delivery is better suited for boron nitride nanotubes than it is for carbon nanotubes, as minimal degradation of the membrane was seen as a result of boron nitride nanotube interactions. Dr. Thomas confirms that boron nitride nanotubes seem to be less cytotoxic than carbon nanotubes, though he doesn't completely rule out the possibility of boron nitride nanotubes possessing cytotoxic properties. He suggests that if future work were to indicate the presence of cytotoxic behaviour, this behaviour might be leveraged to create antibacterial substances or even anti-cancer therapies (which have previously been investigated [5] for carbon nanotubes).

"[This research] is very exploratory at the moment", notes Dr. Thomas. The group is continuing to pursue this research and wants to gather more quantitative information about the energetic properties of the insertion mechanism. “We’re developing some new techniques...[to] look at the aggregation of boron nitride nanotubes...in the membrane”, said Dr. Thomas, “there’s a big demand for these sorts of studies on these nanotubes as they haven’t been done before”.

With the potential for vast commercial applications, nanotubes could soon be found in many commercial products, making their biological safety of utmost importance. Dr. Thomas’ group is making significant initial progress in a necessary area of material science.

–Kyle Mills

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