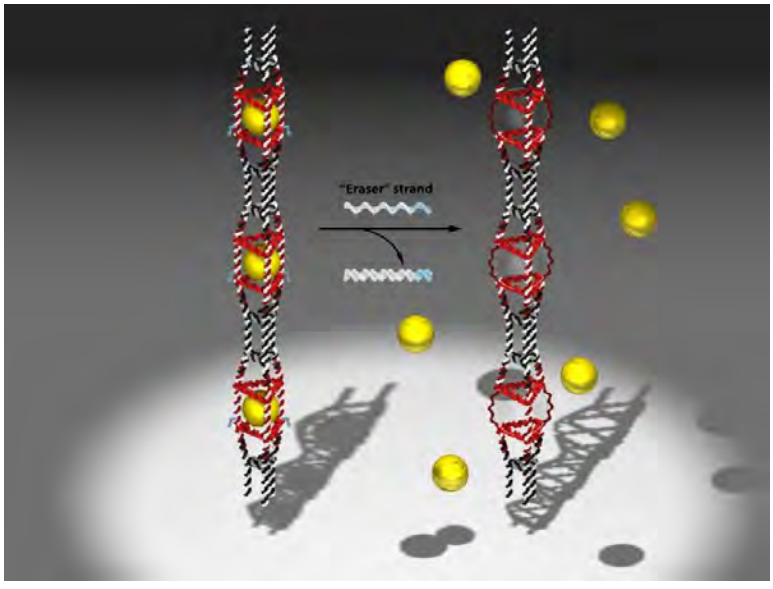
(1) Could you explain, in essence, what you did and why?

We have created the first examples of DNA nanotubes that encapsulate and load cargo on their inside, and then release it rapidly and completely, when a specific external DNA strand is added. One of the dreams of nanotechnology is to create a 'nanocapsule' that would deliver drugs using an external trigger, but would also deliver these drugs specifically to the site of a diseased cell. This contribution is a step in this direction. There are also a number of materials applications to this design, which I describe below.

(2) Could you describe the results?

1. We constructed DNA nanotubes that have two different capsules sizes down their length: one larger capsule (about 15 nm) and one smaller capsule (about 7 nm), that alternate down the length ; that is large-small-large-small etc.
2. By assembling these nanotubes in the presence of guests, we can encapsulate and trap these guests within the inside of the nanotubes. The guests in this case are gold nanoparticles. This creates 'peas in a pod' structures, with the encapsulated gold nanoparticles sitting neatly in a line and evenly spaced out within the nanotubes.
3. Moreover, this process is highly selective. Only 15 nm particles can be encapsulated within the 15 nm capsules of the nanotubes. Other sizes which are too big or too small do not get encapsulated. So in effect the nanotubes act like sieves, and select the correct sizes to encapsulate.
4. The nanotubes are 'closed up' by strands of DNA that are slightly longer than the nanotube strands. (Please see the picture below, and the movie in the following link **http://snurl.com/uw2q1**). When an 'eraser' DNA strand that is fully complementary to these 'closing strands' is added, the closing strands dissociate from the nanotubes, thus now the nanotubes are now in their open, single-stranded form. At this point, all the nanoparticles leave the inside of the nanotube.



Is this the first time that this approach has been taken for the uptake and release of cargoes?

Prior to our work, there were no examples of encapsulation and release of guests within DNA three-dimensional objects; specifically as well, ours is the first example of any guest encapsulation within DNA nanotubes.

Could this concept be realised in real applications? What are the obstacles to realising such a goal? In particular, the use in drug delivery.

For the anticipated applications of these nanotubes as drug delivery vehicles, we will have to overcome a number of challenges: namely,

1. the stability of these nanotubes to nucleases will need to be studied (we have no data on this yet, but there are methods to enhance this stability),
2. We need to carefully select non-immunogenic DNA sequences as building blocks for these nanotubes, and
3. We will most likely need to 'coat' these nanotubes with polyethylene glycol or other molecules that control their circulation and localization within organisms. As the nanotubes are currently negatively charged, they will have a hard time entering into cells, and they would need to deliver the cargo near a diseased cell, rather than inside the cell.

Future developments include making these nanotubes with neutral DNA analogues (such as peptide nucleic acids) to facilitate cell penetration.