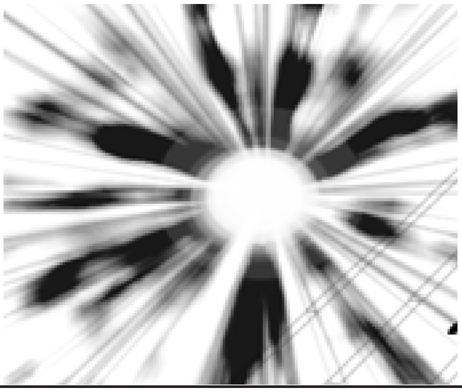


> *"These tiny nanocrystals indeed have the power to revolutionize the study of cell biology, the treatment of cancer, computing, and laser technology."*

Quantum Dots
Time to Shine

By Amrita Goyal

Would you believe that there is a single technology that will eventually help detect cancerous cells before they metastasize, build faster computers, better lasers, and image live cells in Technicolor? You should. This promising new technology is the quantum dot—a semiconductor crystal just a few atoms wide, with some of the most fantastic optical properties known to modern-day physics.

To understand the quantum dot, we must venture beyond the world of the microscopic, and into the world of nano—smaller than cells, smaller than viruses, smaller than proteins, down to the level of individual atoms. A quantum dot is a nanoscale semiconductor crystal, only a few atoms across. These synthetic molecules are manufactured in the lab, and are generally made from combinations of various types of semiconductor metals, most commonly a cadmium selenide (CdSe) core surrounded by a zinc sulfide (ZnS) shell (1).

The most important characteristic of quantum dots is their ability to fluoresce brightly at a frequency determined solely by their size (2). This unique feature is a result of the electronic structure of the quantum dot (3). When hit with light, smaller quantum dots fluoresce at shorter wavelengths, such as blue, while larger dots fluoresce at longer wavelengths, such as red (2). This property gives quantum dots the potential to revolutionize not only biology and medicine, but also computing and laser technologies.

By varying the size of the dots during production, scientists have been able to create a dizzying array of colors of dots—from red, to yellow, to green, to blue, to violet, and dozens of colors in between (2). Despite being made of cadmium and other elements that are generally toxic to living cells, it is possible to make the dots biocompatible through a variety of modifications to their surfaces (4). Quantum dots are thus being heralded as the future of cellular and biological imaging and could eventually replace traditional fluorescent molecules or fluorophores, such as rhodamine and green fluorescent protein (GFP) (1). The same fluorescent capabilities are also the means which may allow quantum dots to revolutionize computing and lasers.

Quantum Dots and Cellular Imaging

A primary method scientists use to learn about the structure and function of cells is by tracking the production and movement of proteins within the cell, and by observing cellular activity on a molecular level. Scientists typically do this by tagging a desired protein with a fluorescent marker, such as GFP or rhodamine. They can then view the cell under a microscope, observe the desired protein, and thus learn more about the function of the protein or cellular component. However, there are significant drawbacks to the fluorophores traditionally used to tag proteins and other cellular objects (1).

While there are a number of reliable fluorophores, usually it is only feasible to view two or three of them at a time. Often times, the excitation spectra of the fluorescent markers interfere with one another and prevent simultaneous viewing of all the markers within a single cell. It is possible to view each fluorescent tag individually and then superimpose the images of the cell, or simply to image the different tagged molecules within similar cells, but these methods yield a very choppy and incomplete picture of cellular activity (1). It would of course be preferable to be able to view half a dozen or more types of molecules simultaneously within the same cell. Quantum dots' fluorescent properties afford scientists this possibility.

Quantum dots each fluoresce at a unique wavelength based on their size, yet can all be excited by the same wavelength of light. However, their fluorescent spectrums are also narrow enough that they do not interfere with one another, thus making simultaneous viewing of several different colored dots possible (1). In comparison to dyes and other fluorophores, quantum dots are up to 20 times brighter and 100 times more resistant to fading (5). The dots have therefore proven to be vastly superior fluorescently to traditional fluorophores.

The next issues with which scientists must contend are how to specify which cellular component or molecule the quantum dots bind to, and how to overcome the hydrophobicity of the quantum dots.

One method of dealing with these problems is direct modification of the surface of the dots. Scientists have been able to attach hydrophilic molecules directly to the surface of the dot, and then covalently attach proteins to the dot surface that make the dots bind specifically to other cellular proteins and molecules (5). Another method by which scientists have attempted to resolve these issues is by simply encapsulating the dots in a phospholipid micelle. This method additionally appears to overcome the problem of cadmium and most other transition elements being toxic to living cells (6).

Recent work from scientists at Rockefeller University has demonstrated not only the viability of these encapsulated quantum dots for use in cellular imaging, but also suggested an additional use for the dots: lineage tracing experiments in embryogenesis. When scientists injected high concentrations of quantum dots into a single cell of a Xenopus (frog) embryo, they were able to trace the daughter cells of that single cell all the way through the tadpole stage. When a single cell of the embryo was injected at the two-cell stage, half of the cells in the grown tadpole were fluorescent; when injected later in embryogenesis, fluorescence was limited only to the daughter cells of the injected cell (6). Previously, it was impossible to track cell lineages in such a manner, as dyes and other fluorophores fade too quickly and are not equally distributed during division (2). This is a wonderfully promising application of quantum dots.

Targeting Cancer with Quantum Dots

Cancer is one of the leading causes of death in the United States today; it is estimated that cancer will claim more than half a million lives in the US alone in 2005 (7). Although there are a number of treatment options once cancer has been detected, such as chemotherapy, radiation therapy, and surgical removal of the cancer, the success of any of these treatments is based on the elimination of all cancerous cells from the body.

Although the logic behind cancer treatments is evident, treatment is often complicated by spreading of the cancer to other tissues in the body, or metastasis. Being able to image the spread of cancerous cells would be a great boon to both physicians and cancer patients, as it would enable doctors to more precisely focus their treatment plan. Quantum dots are well suited to this task.

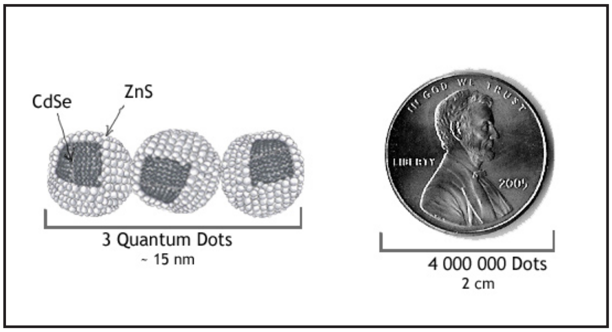


Figure 1. Quantum dots are miniscule compared to other objects.

credit: Eva Yung, HSR Contributor

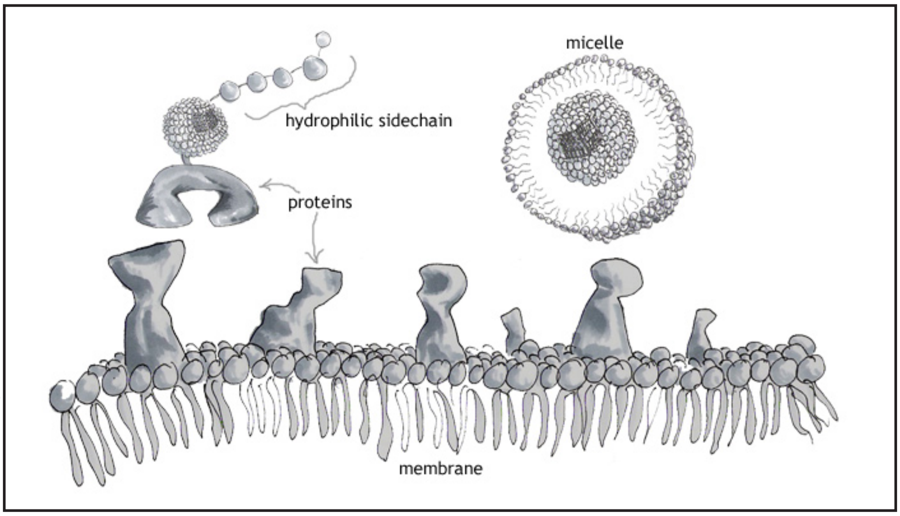
Scientists have been able to bioconjugate the quantum dots so that they bind specifically to a desired protein, cell surface receptor, or molecule. Hence, many scientists have begun investigating the possibility of using quantum dots to fluorescently tag cancerous cells in the body (8).

Cancer metastasizes by means of the circulatory and lymphatic system, starting at one location and traveling to another tissue of the body. A group of scientists from MIT, Harvard, and Beth Israel Deaconess Hospital were able to conjugate near-infrared light emitting quantum dots to molecules that would allow them to bind to cancerous cells in the lymphatic system. These dots were then used to mark cancerous lymph nodes. The fluorescence of the dots that localized in the cancerous lymph nodes was so intense that it was possible to see the nodes clearly through at least a centimeter of tissue (8).

Traditional methods of sentinel lymph node mapping involve use of a dye or radioactive tracer, followed by considerable amount of dissection to extract the sentinel node. When the quantum dots were used, surgeons were able to remove the nodes with minimal trauma to the tissues surrounding the node (9). This dramatic increase in the ability to detect the location and spread of cancers through the use of quantum dots could revolutionize cancer treatment and eventually save thousands of lives.

Imaging of cancerous tissue is not the only application of quantum dots to medicine. Scientists hypothesize that, by using quantum dots, it will be possible to develop cancer drug therapies that are targeted to only cancerous cells. The quantum dots could be conjugated to both a molecule selective for the cancer cell and a chemotherapy drug molecule; the dot would then be engineered only to release the drug when first bound to a cancer cell and then subseqently excited with the appropriate wavelength of light. Thus, quantum dots not only have the potential to improve cancer detection, but also reduce the side effects of chemotherapy by minimizing the number of healthy cells affected by the chemotheray drugs (2).

There are, however, several critical



credit: Eva Yung, HSR Contributor

Figure 2. Quantum dots' fluorescence can be used by attaching a protein and hydrophilic molecule or by encapsulating the dots in a phospholipid micelle.

questions that remain to be answered about the use of quantum dots in cancer treatment. Of primary importance are if the body would be able to eliminate the excess quantum dots, and how the dots' toxicity will affect their ability to be used in humans. The answers to these questions will prove critical to the future success or failure of the use of quantum dots in cancer screening and detection (10).

Building a Better Laser

Quantum dots not only have critical applications to biology and medicine, but also have the potential to revolutionize laser technology.

A laser is essentially a beam of directional, coherent, monochromatic light produced by stimulated emission. Lasers are used in a myriad of technologies, from CD and DVD players, to laser pointers, spectrometry equipment, to drilling, cutting, welding machinery, telecommunications technology, to holography technologies (11).

Although current lasers are very effective, the optical properties of quantum dots provide them many distinct advantages in the field of laser technology. A quantum dot laser is a laser that has a dense array of equal sized quantum dots in the laser's active region; the quantum dots emit the light of the laser beam.

The dots' superior quantum yield means that they would make for much more efficient and compact lasers. Since quantum dots' emissions color is based on size of the dot, the color of a quantum dot laser would be easily tunable. Such a laser would also be stable over a much wider range of temperatures, which would allow for use of lasers in conditions that would previously have been prohibitive (12).

A Leap into Quantum Computing

Computer technology has been advancing by leaps and bounds for the last three decades. Computers have advanced from room-sized monstrosities with the capability to do only simple arithmetic to featherweight laptops with enormous computing power. However, there are limitations to the size and speed that traditional computers will be able to achieve, and those boundaries are rapidly approaching. The next step in computing is not so much a step as a leap—a leap into the realm of quantum computing.

In traditional computing, bits are used to store information, either in the form of a "1" or a "0." These 1's and 0's are controlled by Boolean logic gates. In quantum computing, the unit of information is the quantum bit, or qubit, controlled by quantum gates. This qubit can exist in either the state of 1, 0, or blend of these two states. The quantum computer has exponentially faster processing ability because of the possible superposition of states. A quantum computer would also be able to perform many operations in parallel, while using only one processing unit (13).

But how do quantum dots play into this system of quantum computing? It is possible to couple, or bind two quantum dots together. These double quantum dots are then able to act as a qubit (13). Thus, quantum dots may be the means by which the possibility of quantum computing is able to become a reality.

Quantum dots are nothing more than miniscule semiconductor crystals. However, size is no indication of importance or power. These tiny nanocrystals indeed have the power to revolutionize the study of cell biology, the treatment of cancer, computing, and laser technology. Who would have though it possible for there to be so much potential in such a small package?

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