



Quantum dots wide absorption pattern, photo stability and greater quantum yields provides a gate way to power full applications in nano medicine and nano biotechnology

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Received 23 January 2017; Accepted 27 February 2017
Available online 17.03.2017 with doi: 10.5455/medscience.2017.06.8601

Abstract

Quantum dots have specific optical and electronic properties which makes their wide application in the field of nano bio technology. The emitted photon energy in a quantum dot increases with a decrease in the dot size. Since quantum dots are tunable hence by injecting quantum dot based probes multi color imaging of tumor cells, cancer cells and lymph nodes can be accomplished which is very advantageous in the medical field. Various researches have been done and much is going on where quantum dots works as an efficient drug carrier system during analysis or treatment in targeted drug delivery. Quantum dots can be applied to cell for drug screening and analysis. Linking with antibodies as biological labels makes them appropriate for various applications in cellular and molecular imaging.

Keywords: Colloidal synthesis, fluorescence multiplexing, ligand exchange, molecule tracking, peptides, quantum dots

Introduction

Utilization of quantum dots in medical field had increased a lot since the past years. With a function of size and shape their optoelectronic properties changes. Depending upon the composition of quantum dots the specific colors vary [1]. The major way to prepare quantum dots is by colloidal synthesis in which at high temperature the nano crystals is generated after the monomer formation [2]. High temperature and concentration of monomers are the major factors in determining optimal conditions for the nano crystal growth for the annealing and arrangement of atoms during the synthesis. The growth process of nano crystals can be focusing and defocusing [3]. When the monomer concentrations are high the critical size will be small resulting growth of all particles. The particles which are smaller will grow faster than those particles which are large. They can be suspended in solution for the application in printing and coating [4]. Many studies have been conducted earlier on the applications of quantum dots in human welfare. The main objective of this research is the maximum utilization of quantum dots in various medical research, diagnostics and treatments.

Quantum dots have wide applications in cellular and molecular imaging because they can be linked with

peptides, antibodies, molecules as biological labels [5, 18]. It can be used to measure the motility of cells and for labeling the live cells which remain stable during the culture. Multicolor labeling of cells makes visualizing various structures simultaneous and elucidating intracellular processes. Because of the broad absorption and photo bleach resistance quantum dots are an excellent fluorescent probes for long term multicolor cell labeling. The energy level of a large quantum dot is high and more closely spaced making it to absorb the photons which have lower energy. Figure 1 shows the band gap of a quantum dot. Quantum dots exhibits unique optical properties due to their material band gap energy and quantum well phenomena. When an electron is excited by a photon striking the quantum dot it cannot escape from the quantum dot. A hole created by an excited electron behaves in the same way. The excited electron exists in the conduction band as one of the n energy states and hole exists in the valence band as one of the n energy states. Quantum dots have wide absorption pattern, photo stability and greater quantum yields [6]. For improving the fluorescence quantum yield, quantum dots can be prepared by the shells of a band gap semiconductor material which are larger. But the major problem is the decreased access of electron-hole to non radiative surface recombination pathways and decreased auger recombination. This makes it the best for the application of fluorescence multiplexing, molecule tracking and high throughput screening. As there is a decrease in the dot size there will an increase in the emitted photon energy. Phase separation is used for forming large area of mono layers of quantum dots [7, 19].

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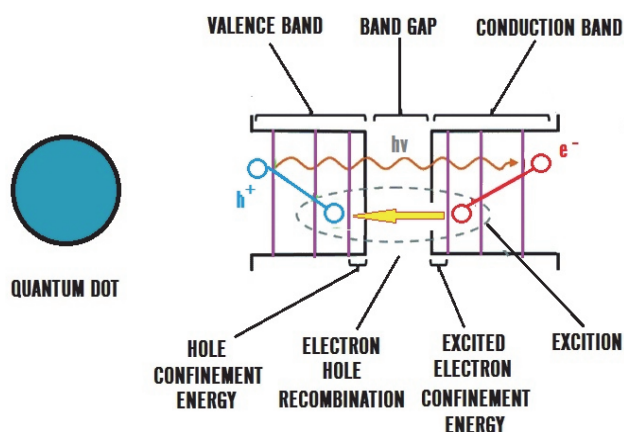


Figure 1. Quantum Dot

Scope of Approach

Quantum dots are very effective for the labeling of endosomes and due to the narrow emission spectra it can be used for efficient tracking of membrane receptors along with regulatory proteins. Because of increased photo stability, broad excitation and narrow emission spectra they are the best for use as donor fluorophores. Quantum dots protein conjugates which act as catalysts or actuators have a major role in biomedical research, disease diagnostics and treatments. The major problem is the nonspecific adsorption, but it can be lowered by creating improvements in quantum dots. Targeted development in these applications will create a new era in the medical field.

Augmented Design Critiques

The typical quantum dots are made of binary compounds like lead sulfide, cadmium selenide, or indium phosphide. It can also be made from ternary compounds such as cadmium selenide sulfide [8]. But cadmium based quantum dots are unsuitable for consumer applications due to the use of heavy metals and toxicity [9]. Cadmium selenide quantum dots are extremely toxic during cell culture under ultra violet irradiation since they dissolve during photolysis and releases high toxic cadmium ions. If ultra violet irradiation is absent and quantum dots have a stable polymer coating they can be non toxic. The toxicity is because of the semiconductor materials that constitute the quantum dots core and due to the formation of free radical and reactive species during the excitation. These heavy metals enter the blood and brain barrier and accumulate, while promoting toxic effects to the kidneys and liver.

By adopting colloidal synthesis large batches of quantum dots can be synthesized which makes it the best for commercial applications. Silicon and germanium quantum dots can be synthesized using non thermal plasma where the shape, size and composition of quantum dots can be controlled. The synthesized Quantum dots will be in the form of powder, for which modification of surface is carried out. It leads to the dispersion of quantum dots in

organic solvents. Under some conditions a self assembled quantum dots nucleate spontaneously [10]. Individual quantum dots can be made from 2 dimensional hole or electron gases available in doped quantum wells. By controlling the size, shape, and strength of the potential the energy spectrum of a quantum dot can be engineered.

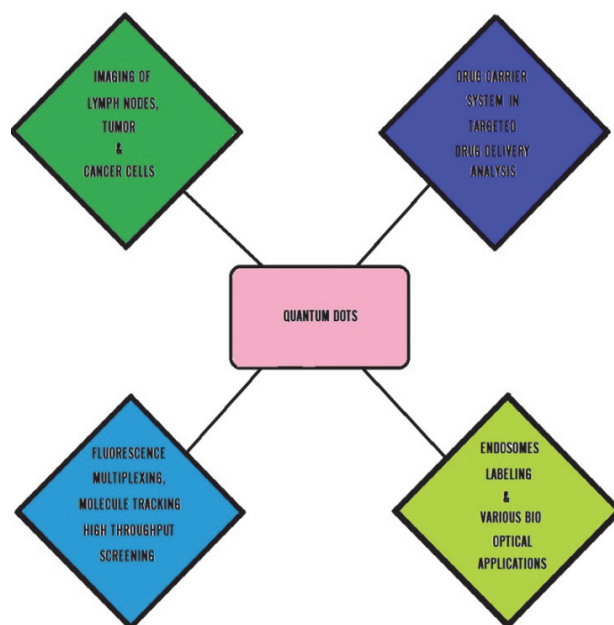


Figure 2. Quantum Dots Vivid Applications

Water stabilized quantum dots shows an improved colloidal stability and solubility [11]. The resultant bio imaging will have a great detailing and brightness which can be used to check trafficking events in live cells. The core shell quantum dots can be manipulated to generate water stabilized quantum dots which have good aqueous solubility and colloidal stability. Water soluble quantum dots are used as tracers inside living cells in biological research. It is injected into the tissue and excited using short wavelength light which causes the fluorescing dots to be seen at their peak frequency. By ligand exchange the hydrophobic capping surface ligands can be replaced by hydrophilic bi functional ligands. The photo stability of quantum dots allows the collection of many images which can be reconstructed into a high-resolution image. Quantum dots do well in tracking membrane receptor. Figure 2 shows vivid applications of quantum dots. For the fabrication of silicon quantum dots complementary metal oxide semiconductor technology can be employed. The electrons and holes bind with each other in a semiconductor to form an exciton. This exciton recombines and the energy is emitted as light. The energy depends upon the size of quantum dot's, which makes the emission to be tuned by changing the quantum dot size during its synthesis. The endocytic uptake accommodate large quantum dots ligand conjugates and carrying a large probe must not tamper the regulation of endocytic trafficking of ligand receptor complexes [12,20].

The main problem of using quantum dots as tracking molecules in live cells is their adsorption, which leads to the up taking of ligand and receptor cell. They gets bind to by electrostatic interactions to various intracellular membrane and proteins which leads to cellular staining. It prevents the ligands from interacting with cellular receptors reducing their ability. They bind nonspecifically to various cellular proteins which lead to decreased signal to noise ratios [13,23].

The ligand targeted quantum dots which induce multiple binding of receptor and cross linking have an increased uptake of cells. The high level of ligand density causes an increased cyto toxicity in selective cells which is helpful for effective cancer treatment. Multi valency can affect the behavior of quantum dots ligands disrupting the motility, trafficking and signaling of membrane receptors. It makes a significant reduction in the SBT signal and keeps the needed spectral overlap for fluorescence resonance energy transfer [14,21]. Fluorescence resonance energy transfer is the non radiative energy transfer in close proximity from a donor fluorophore to an acceptor fluorophore. Energy will be transferred to an acceptor fluorophore when a donor fluorophore is excited by an external energy source. The significant spectral overlap between the donor and the acceptor absorption spectra allows the energy transfer. When selecting a quantum dot dye or fluorophore donor-acceptor pair the distance where the energy transfer efficiency becomes 50% must be considered. Quantum dots ligand conjugation should avoid multi valency and potential cross link of receptor proteins when tracking membrane receptors. A tumor cell which is fast developing lacks effective lymphatic drainage system and has more permeable membranes comparing to healthy cells. It causes small nano particles leakage and accumulation into the cell. Quantum dots in the distant red region minimize the auto fluorescence and boost the tissue penetration depth. Quantum dot immune fluorescence allows the determination of the cellular localization of expressed protein.

Silicon quantum dots have lower toxicity for use as fluorescent probes in biological applications along with photo bleaching resistance. Ligand exchange and polymer coating are effective for the common problem of aqueous solubility of quantum dots. But Silicon quantum dots have poor solubility and unstable photoluminescence in aqueous solutions [15,22]. Mono disperse quantum dots in non polar organic solvents can be produced by organo metallic mode. Synthesizing quantum dots by this yields high quantum and the size distribution. Quantum dots synthesis in aqueous solution is eco friendly and costs low. It can be directly used without ligand exchange procedure in biological researches. Quantum dots with good water solubility have a wide application in biological imaging. Quantum dots of various colors can be excited form a single light source and they glows much longer [16].

Strategical Analysis

Quantum dots being very tiny particles in the order of a nanometer are composed of a hundred to a thousand atoms. The quantum dots small size makes them to be penetrated in the body for various bio medical applications [17]. With a discrete quantized energy spectrum quantum dot consists of a finite number of conduction band electrons, valence band holes, or a finite number of elementary electric charges. Like the dyes used as biosensors a quantum dots does not show rapid degradation. Quantum dots can be used as the inorganic fluorophore for the detection of tumors using fluorescence spectroscopy. Individual quantum dots delivered by cell squeezing are detectable in the cell cytosol. The dots which are larger have more closely spaced energy levels which provides them a longer lifetime. Quantum dots which are big have a great spectrum-shift towards red. Quantum dots fluorescence spectrum is shown in Figure 3. Because of the high extinction coefficient, quantum dots are best suited for various optical applications. Energy levels in a quantum dot are dependent on the size of the structure. Density matrix can be employed to study the absorption spectra of small quantum dots under the confinement regime, where the findings can be obtained for a single quantum dot and inhomogeneous quantum dots with Gaussian distribution of dot sizes. Due to the bi excitonic contribution, a negative change occurs in the absorption coefficient in the shorter wavelength part of the spectrum. The wavelength at which crossover change in absorption coefficient occurs will depend upon the size and the excitation intensity.

A new type of multifunctional quantum dots therapeutic use can be made from the conjugation of quantum dots with photo sensitizers and targeting agents. Bio molecules can be attached to the surface of quantum dots to generate complex bio conjugates which merge the biological function and specificity [5,18]. The advanced development in surface coating of quantum dots and bio conjugation makes them the most appropriate probes for live cell applications. A significant advancement has been made with the eukaryotic applications of quantum dot conjugates. Human aldose reductase high expression levels can be achieved using the eukaryotic cell model. Initially quantum dots are synthesized in non polar solvents; being hydrophobic its surface needs to be applied with amphiphilic coatings for biological applications. The surface coatings not only retain the photo physical and size of quantum dots but also provide extra reactive group for conjugation of bio molecular recognition molecules. The photo physical properties of quantum dots get influenced by the peptide adhesive domain. By varying the binding sequence through molecular evolution quantum dots with increased stability, high emission rate and reduced blinking can be generated. Quantum dots enable the Imaging and sensing of various infectious diseases in diagnostic applications.

Membrane receptors are intuitive targets for quantum dots imaging since they do not need intracellular delivery through the impermeable plasma membrane. Many biological processes occur in the cytosolic space. Three dimensional tracking capability developments of quantum dots will provide important macromolecular processes information like trafficking and translocation [18]. Quantum dots with different types of coating have different interactions between its surface and bio molecule. Quantum dots can be used as a tool for the visualization of nucleic acid array detection and homogenous mutation assays. In homogenous mutation assays the target and the probe are labeled with different quantum dots which are detected by the presence of both in a small focal volume by their coincidence. Quantum dots can enable the detection of cancer biomarkers in cancer tissues and blood assays during the forecasting, diagnosis and treatment.

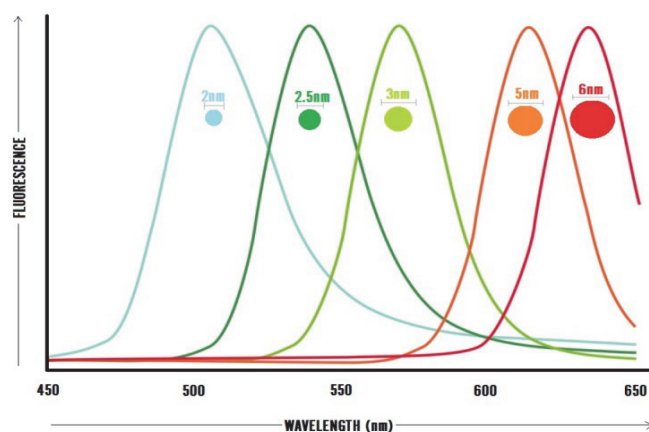


Figure 3. Quantum Dots Fluorescence Spectrum

Apart from live cell fluorescence imaging and vitro protein assays, quantum dots protein assemblies have wide biological applications [13]. The most durable attachment of a bio molecule to a quantum dot is by covalent coupling. But this causes aggregation of nano particle which requires purification steps causing the loss and depression of the overall yield of the functional construct. The affinities between bio molecule domains and various substrates will be exploited by the alternative conjugation strategy. The diagnosis of sentinel lymph node contributes to an operative strategy in surgery of cancer [21]. During the metastasis of lymph node, cancer cells reach the sentinel lymph node first through the lymph flow. The use of quantum dots enables the cancer cells to be detected with high sensitivity and increase the detection rate of cancer metastasis.

The encapsulated and ligand exchange quantum dots have good dispersion in water and reduced nonspecific binding. The shape and size of quantum dots plays an important role in endocytosis. The overall shape and size of the quantum dots ligand complexes must be considered for cell uptake purposes. Near infra red region is best suited for imaging through tissues because of the increasing wavelength the

light scattering diminishes. The auto fluorescence of living tissue reaches to minimum at this range making the fluorescent signal to be detected at nano molar quantities and sufficient depths for imaging. Quantum dots will further advance the ability of receptor imaging technology with three dimensional resolutions.

Conclusion

The special properties of quantum dots enable them for a wide range of uses in the medical and clinical field. It has a great impact in the treatment and analysis of tumor and cancer cells. During drug screening and analysis it can be used to work as an efficient drug carrier system. By tuning the quantum dot the color can be changed which makes it unique. Quantum dots with wavelength from 700 nm to 900 nm will have a maximum depth of penetration in tissue. Bio molecules and proteins conjugation to inorganic nano particles plays a tremendous role in the development and application of nano medicine which enables the optimal design of bio molecule nano particle hybrids. Thus the major development in this field will change the method of disease treatment to an easier way with high output result.

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