Pure Appl. Chem., Vol. 72, Nos. 1–2, pp. 3–9, 2000.

Colloidal quantum dots. From scaling laws to biological applications*

Paul Alivisatos

Departments of Chemistry and Materials Science, University of California, Berkeley and Materials Science Division, Lawrence Berkeley National Laboratory

Abstract: Over a twenty-year period, condensed matter physicists and physical chemists have elucidated a series of scaling laws which successfully describe the size dependence of solid state properties [1,2]. Often the experiments were performed under somewhat exotic conditions, for instance on mass-selected clusters isolated in molecular beams or on quantum dots grown by molecular beam epitaxy and interrogated at low temperatures and in high magnetic fields. As a result, we now have an understanding of how thermodynamic, optical, electrical, and magnetic properties evolve from the atomic to the solid state limit. This area of research is presently undergoing a remarkable transformation. The scaling laws, previously the direct subject of research, now provide a tool for the design of advanced new materials. In the case of colloidal quantum dots, or semiconductor nanocrystals, these new insights are poised to have impact in disciplines remote from solid state physics [3].

NANOCRYSTAL AS "SINGLE STRUCTURAL DOMAIN"

Industrial processing of semiconductor materials is our most advanced technology, an amazing but also very complicated affair. Because even a few defects or impurities can alter the performance of a device, great effort is extended to ensure precise control of atomic composition at every stage. While very expensive, this is necessary for materials that are comprised of large (order microns) component domains. Using some scaling laws from magnetism and phase transitions as a guide, we can quickly see that it is possible, and indeed perhaps preferable, to prepare extremely high-quality *nanometer*-size components in more simple ways.

One of the most famous size-dependent scaling laws concerns the variation of magnetic properties as a function of the size. Over fifty years ago, Neél provided a theory that successfully describes the size dependence of magnetization reversal [4]. In a small magnetic crystal the spins within each unit cell couple to each other, resulting in a single, giant magnetic moment (single magnetic domain). An external field can be used to align this magnetic moment. If this field is now reversed rapidly, it will take time for the magnetic moment of the crystal to realign. In the simple model of Neél, this time depends exponentially upon the volume of the small crystal. This can be understood if each unit cell of the crystal contributes equally to an energetic barrier (the crystalline anisotropy) that must be overcome thermally. The larger the crystal, the greater the barrier. Interestingly, recent studies of magnetization reversal in individual single domain magnets show that the Neél model provides a qualitatively correct picture, despite many simplifying assumptions [5] (chief among them neglect of the surface). Even more recent work suggests that in extremely small, molecular-size magnets, the magnetic moment changes in a discrete series of steps, corresponding to tunneling of the magnetization [6].

How can this scaling law for magnetization reversal teach us anything about processing of nanometer size materials? Consider what happens in ever-larger magnetic crystals. A sufficiently large

Pure Appl. Chem.* **72, 1–331 (2000). An issue of reviews and research papers based on lectures presented at the 1st IUPAC Workshop on Advanced Materials (WAM1), Hong Kong, July 1999, on the theme of nanostructured systems.

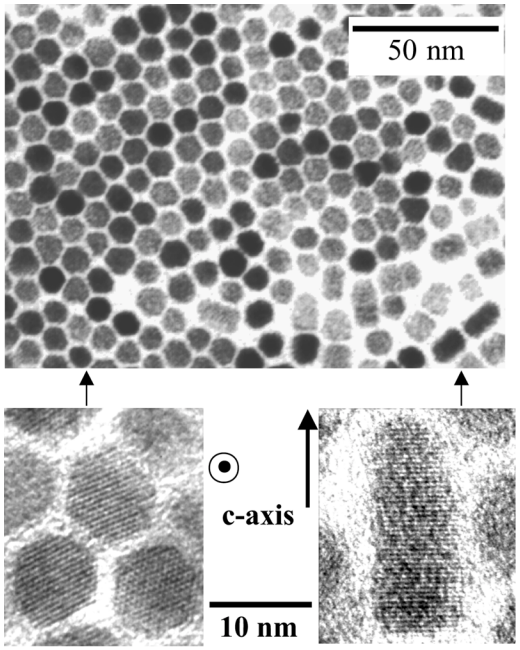

Fig. 1 Transmission electron micrograph of a field of CdSe nanocrystals. Each crystallite is faceted, and surrounded by one monolayer of surfactant. Surfactant-coated nanocrystals may be considered a class of macromolecule. By exchanging one surfactant for another, the colloidal dots can be dissolved in essentially any liquid. If the surface of the inorganic solid needs to be passivated, core-shell dots can be grown to manipulate the interior interface. Finally, the shapes of the nanocrystals can be adjusted from dots to rod.

crystal will contain a domain wall, a thermodynamic defect that dramatically lowers the barrier to magnetization reversal. This defect costs some energy, but will occur at finite temperature with a statistical probability, provided the number of atoms is large enough. Incidentally, the presence of these defects explains why we can use an external field to re-align the magnetic moment of a macroscopic magnet (otherwise the barrier would be too large).

Now consider the interior crystal structure of nanocrystals, prepared with the utmost care to ensure they are as perfect as possible. By analogy with the magnetic case, thermodynamically we expect all the unit cells in a nanocrystal to be in registry (single structural domain), with no "high energy" defects, such as grain boundaries. Only when the number of atoms in each crystal is very big (hundreds of thousands), will each crystal possess such a defect on average. What if the processing is not very careful, and impurities or defects are introduced into a growing nanocrystal? In any crystal, a non-equilibrium impurity or defect will eventually anneal out. One thing we know for sure is that the annealing time will be far shorter in nanocrystals than in an extended solid. As an added bonus, another scaling law teaches us that smaller crystals melt at lower temperatures than larger ones. The melting temperature scales as the surface to volume ratio in simple models, and the reductions can be quite dramatic, so the growth temperature need not be as high for nanocrystal synthesis as it is for extended solids [7,8].

All of these arguments suggest that it should be possible to prepare high-quality nanometer-size crystals in comparatively simple ways. In fact, this is now fully demonstrated. High-quality metal and semiconductor nanocrystals can be prepared routinely by simple and inexpensive wet chemistry colloidal techniques. If adequate care is taken in the growth process, large numbers of nearly identical, defect-free crystallites can be produced in a short period of time [9–11]. To complete the argument, we can even observe solid–solid phase transitions in these nanocrystals, at high pressure and temperature [12]. The time scale for an ensemble of nanocrystals to switch from one structure to another increases almost exponentially with volume, in a manner reminiscent of single domain magnetization reversal. Deviations from Neél-like behavior (barrier proportional to volume) are observed. This may arise because the nanocrystals undergo structural transformation by a sliding planes mechanism, and it is the

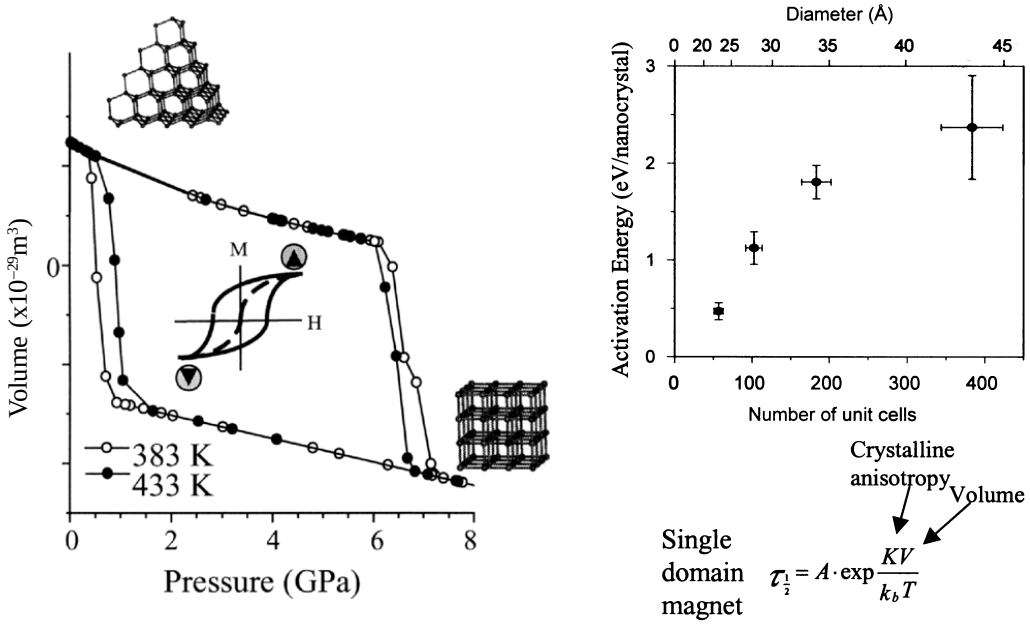

Fig. 2 There is a strong analogy between magnetization reversal in single domain magnets and structural phase transitions in nanocrystals. In both cases massive hysteresis is observed, because the highly perfect crystals contain no high energy defects. The barrier blocking the phase transition increases with size within the single domain regime. In larger crystals, defects substantially lower the barrier. These results help to explain why it is possible to make high-quality nanocrystals with modest processing methods.

area of a plane in the crystal that determines the size of the barrier, rather than the volume. Alternatively, nucleation may occur at the nanocrystal surface, rather than as a coherent deformation of the whole crystal. In either case, the enormous hysteresis in the nanocrystal solid–solid phase transitions confirms the expected absence of high-energy defects, which would act to reduce the barrier. Nanocrystals may thus be considered single structural domains, and are high-quality building blocks for a new generation of advanced materials [13].

QUANTUM DOTS AS LUMINESCENT BIOLOGICAL LABELS

In the case of semiconductor nanocrystals, one of the most famous scaling laws concerns the variation of the band gap as a function of the size. Higher energy photons are required to generate electron-hole pairs when they are confined to a smaller volume. This is familiar from optical studies of quantum wells in high magnetic fields, from MBE grown quantum dots, from clusters precipitated in glasses, and of course from studies of colloidal dots. Many effects contribute to the precise scaling of band gap versus size, including variations of the Coulomb and exchange interaction between electron and hole, band mixing, tunneling of electrons and holes through finite confinement barriers, and changes in the dielectric constant [14]. These effects have been investigated in detail, and come into play in determining the luminescence energy of a series of colloidal quantum dots of differing size. In practice, by variation of size and composition of colloidal quantum dots, the luminescence photon energy can be tuned in steps of 30 nm from the IR to the UV. Borrowing from the field of molecular beam epitaxy, colloidal chemists

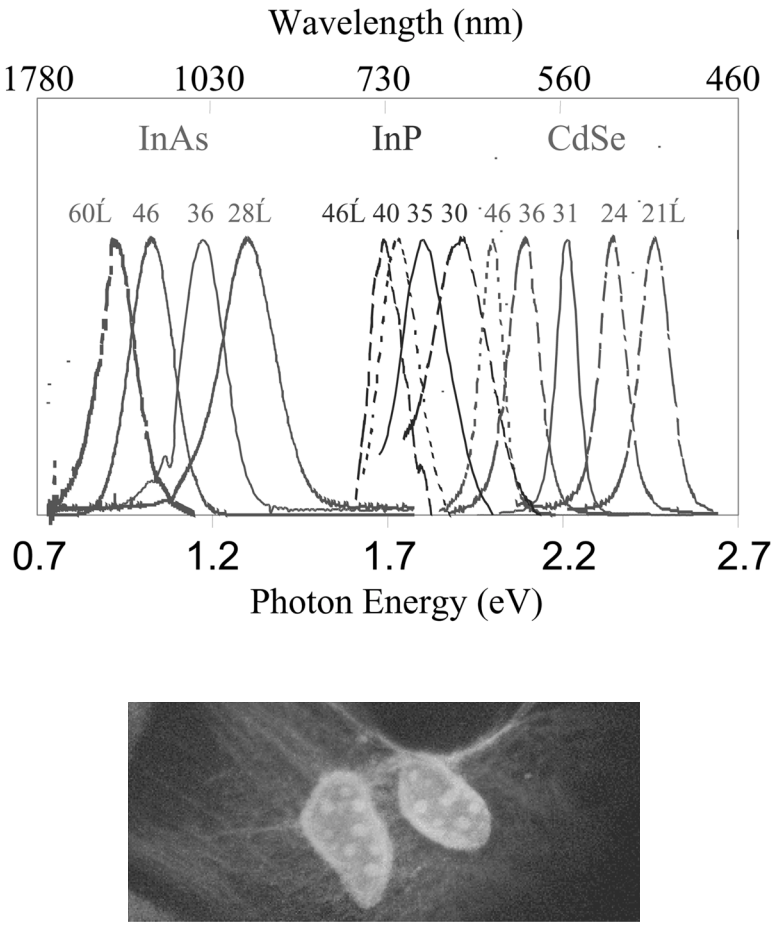

Fig. 3 Colloidal quantum dots as fluorescent biological labels. The luminescence energy of colloidal quantum dots depends strongly upon the size and composition. Unlike molecular bio-labels, the colloidal dots can all be excited with a single excitation source. An example of a two-color labeling experiment is shown here. The actin fibers of a mouse fibroblast cell have been labeled with larger size dots, while the cell nuclei are labeled with smaller, green emitting dots.

have learned to prepare core-shell quantum dots, with a small gap core and a large gap shell, substantially reducing the influence of surface trapping, and providing samples with reasonably high quantum yields.

Research into applications of colloidal quantum dots has largely focussed on opto-electronic devices. The dots can be dissolved in almost any liquid by manipulation of organic surfactant molecules bound to the exterior surface. Thus it has been possible to cheaply spin-coat colloidal dots into polymer-based LEDs and photovoltaics, and many similar applications have been envisioned. Recently we and others have come to realize that the advent of colloidal quantum dots opens the door to the use of the concepts of dimensional control in entirely new arenas, for instance in the biological arena. One of the most powerful tools available to the biologist is fluorescent labeling. A molecule that emits light can be attached to a specific bio-molecule, and then the fluorescence can be used to image the location of the molecule or to probe its environment. Quantum dots potentially offer significant advantages over conventional light-emitting biological probes [15,16].

A major need in biological analysis is the ability to detect multiple optical signals simultaneously. For instance, cell biologists sort populations of cells according to which combination of several antibodies will bind to them. Molecular biologists would like to screen for the presence of numerous DNA sequences simultaneously. Combinations of conventional fluorescent tags are not well suited to these tasks, since they are molecules with discrete energy levels, and each one must be excited at resonance. Semiconductor quantum dots emit light at a specific energy determined by size and composition; however, much as in a bulk semiconductor, as one tunes above the threshold for absorption, more and more channels for absorption of light open up, so that the excitation spectrum is essentially continuous. Thus, combinations of emitting colors can readily be excited with a single excitation source. The colloidal nanocrystal emission is more narrow and symmetric than that of the organic dyes, potentially allowing a larger number of probes within a detectable spectral region. The efficacy of using water-soluble core-shell colloidal quantum dots for two-color fluorescent biological labeling has been demonstrated, and many related applications are now actively under investigation. For instance, the quantum dots may prove to be more resistant to photo bleaching than conventional labels, and deep-red emitting dots may fill a region of the spectrum for which the available dyes are inadequate. The colloidal quantum dots will likely prove to be complementary to the organic dyes, which of course are extremely well established probes, with many distinct advantages, for instance much higher radiative rates for emission than the quantum dots.

DNA-DIRECTED ASSEMBLY OF NANOCRYSTALS

In the example above, we saw that quantum dots have the potential to serve as an important new tool in biological diagnostics. The nanocrystal-biology interface is a two-way street. Several years ago, Seeman recognized that DNA, with its amazing ability to encode information and to adopt designed conformations, has the potential to play an important role in the organization of new materials [17]. Inorganic nanocrystals are small compared to the features prepared by photolithography or even e-beam lithography, yet they are comprised of precisely the same materials as are used to make electrical circuits. Could there be a way to spatially organize colloidal nanocrystals into complex, non-periodic spatial arrangements using DNA? The study of DNA-nanocrystal complexes is emerging as an exciting new area of research.

DNA is a macromolecule that encodes information on a nanometer scale. Each base pair in DNA is weakly bound, so about twelve base pairs must associate to form a double strand that is stable at room temperature. An oligonucleotide of twelve base pairs is comparable in size to the diameter of a nanocrystal, and this is also a long enough sequence to encode very specific information, through the precise sequence of base pairs. It is possible to attach single strands of a particular DNA sequence to a given type of nanocrystal. Then, one can prepare a long "template strand." If the sequence of base pairs attached to the nanocrystal is complementary to a portion of the sequence on the template strand, then the formation of the DNA double strand will direct the nanocrystal into a position along the template strand [18]. In principle, many different types or sizes of nanocrystal, each with an oligonucleotide of a specific sequence attached, can be placed into relative spatial arrangements. An example of this type of patterning is demonstrated in Figure 4. Other schemes for DNA-nanocrystal composites are under active study, including the creation of reversible periodic arrays for biological detection, and the formation of Ag wires along pre-aligned DNA strands [19,20].

CONCLUSION

In the field of colloidal quantum dots, advances in physics and chemistry have occurred in parallel and with synergy. The scaling laws provide a basis for predicting the behavior of nanocrystal-based materials. Development of the concept of nanocrystal as macromolecule opens up a wide range of new situations

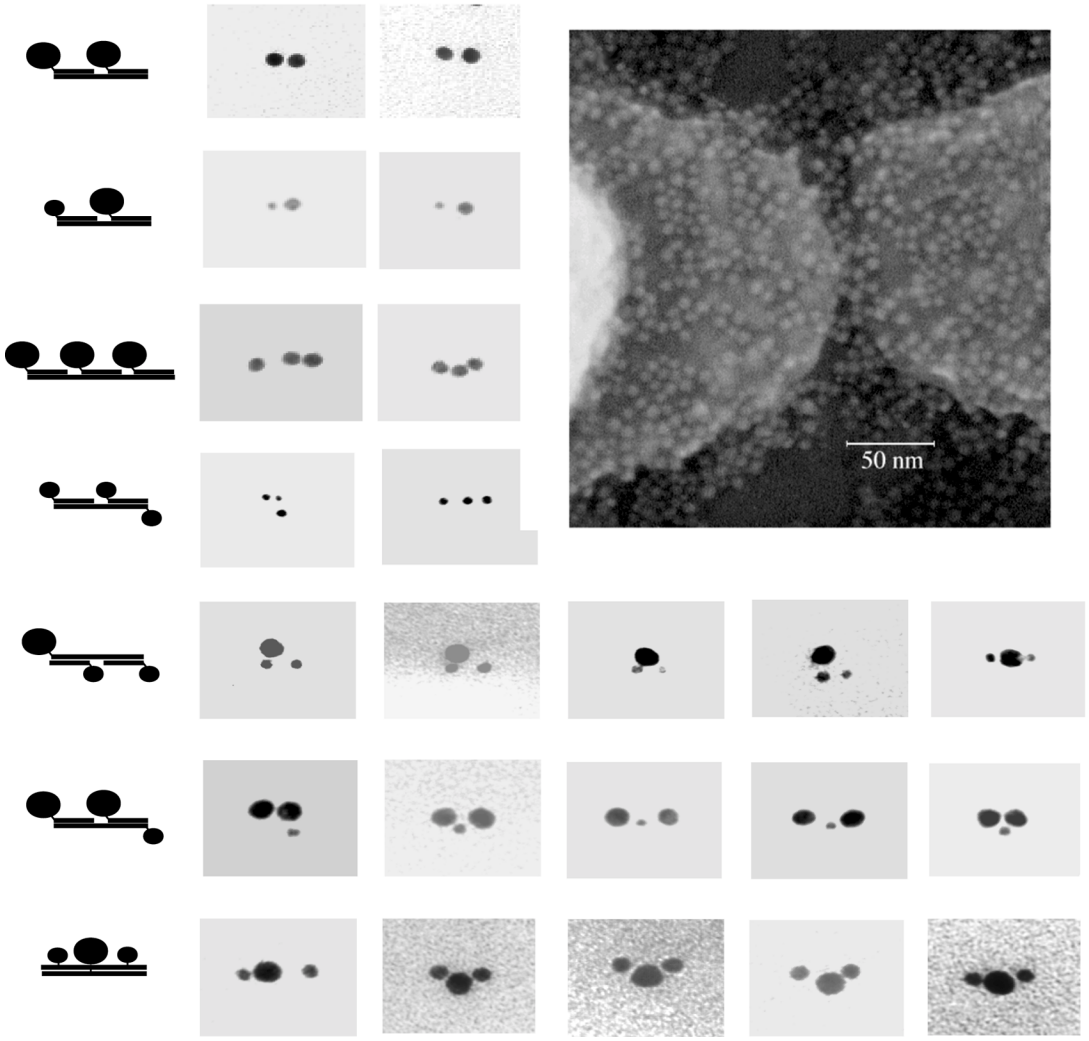

Fig. 4 DNA-directed spatial organization of Au nanocrystals. Inset: The disparity in length scale between lithographically patterned features and colloidal dots is apparent from a scanning electron micrograph image of dots embedded in the gap between two electrodes [21]. DNA has been used to pattern dimers and trimers of 5 and 10 nm Au nanocrystals. These have been deposited at low density on a substrate, and imaged by TEM.

in which the size-dependent scaling laws can find application. As is so often the case, this is leading to discoveries in areas not at first envisioned. Now a third partner is being drawn in, as new connections between artificial semiconductor quantum structures and the biological sciences are being forged. Many exciting developments are sure to follow.

REFERENCES

1. W. A. Deheer. *Rev. Mod. Phys.* **65**, 611 (1993).
2. M. A. Kastner. *Rev. Mod. Phys.* **64**, 849 (1992).

3. A. P. Alivisatos. *Science* **271**, 933 (1996).
4. C. Kittel. *J. Geophys. Res.-Solid Earth* **103**, 30533 (1998).
5. W. T. Coffey, D. S. F. Crothers, J. L. Dormann, et al. *Phys. Rev. Lett.* **80**, 5655 (1998).
6. L. Thomas, F. Lionti, R. Ballou, et al. *Nature* **383**, 145 (1996).
7. P. Buffat and J. P. Borel. *Phys. Rev. A* **13**, 2287 (1976).
8. M. Schmidt, R. Kusche, W. Kronmuller, et al. *Phys. Rev. Lett.* **79**, 99 (1997).
9. C. B. Murray, D. J. Norris, M. G. Bawendi. *J. Am. Chem. Soc.* **115**, 8706 (1993).
10. X. G. Peng, J. Wickham, A. P. Alivisatos. *J. Am. Chem. Soc.* **120**, 5343 (1998).
11. R. L. Whetten, J. T. Khoury, M. M. Alvarez, et al. *Adv. Mater.* **8**, 428+ (1996).
12. C. C. Chen, A. B. Herhold, C. S. Johnson, et al. *Science* **276**, 398 (1997).
13. C. P. Collier, T. Vossmeyer, J. R. Heath. *Annu. Rev. Phys. Chem.* **49**, 371 (1998).
14. U. Woggon, *Optical Properties of Semiconductor Quantum Dots*, Springer, Berlin, New York (1997).
15. W. C. W. Chan and S. M. Nie. *Science* **281**, 2016 (1998).
16. M. Bruchez, M. Moronne, P. Gin, et al. *Science* **281**, 2013 (1998).
17. N. C. Seeman, *Annu. Rev. Biophys. Biomol. Struct.* **27**, 225 (1998).
18. A. P. Alivisatos, K. P. Johnsson, X. G. Peng, et al. *Nature* **382**, 609 (1996).
19. C. A. Mirkin, R. L. Letsinger, R. C. Mucic, et al. *Nature* **382**, 607 (1996).
20. E. Braun, Y. Eichen, U. Sivan, et al. *Nature* **391**, 775 (1998).
21. D. L. Klein, R. Roth, A. K. L. Lim, et al. *Nature* **389**, 699 (1997).