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# Preparation of functionalized and gold-coated cobalt nanocrystals for biomedical applications

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## Abstract

We present the synthesis, structural and magnetic characterization of cobalt-based nanocrystals with controlled size (5–25 nm;  $\pm 1$  nm) and tailored morphologies (spheres, discs with specific aspect ratio of  $5 \times 20$  nm and core-shell structures). The reproducible synthesis route for Au-coated, high moment, cobalt nanocrystals presented here opens up possibilities for a number of biomedical applications and surface functionalities.

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Magnetic nanoparticles (NPs) have potential applications in many biological and medical applications such as drug delivery, hyperthermia treatment, magnetic resonance contrast enhancement and cell separation. Even though biocompatible iron oxide NPs is currently the material of choice, there is significant interest in developing alternative high moment cobalt (and related alloys) for specific biomedical applications. While the majority of magnetic NPs prepared at present for biomedical applications are bead-like or spheres, other anisotropic shapes with larger dipole moment

per unit volume have been considered for cell manipulation [1]. Irrespective of their shape, the challenge here is to prepare uniform, un-agglomerated particles with controlled size, shape and narrow size distribution. However, since metallic cobalt NPs are highly sensitive to oxidation and are toxic for biological application, it would be highly desirable to coat them with an inert shell for biocompatibility and stability. Further, if the shell could provide additional functionality, such as sensitivity to optical probes and other biomolecules, it would be highly desirable for a number of applications. Gold coating of the magnetic nanocrystals would be a natural choice to accomplish both of these goals.

We have recently developed a synthesis route involving the rapid decomposition of organometallic

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precursors in a surfactant environment to prepare cobalt nanocrystals with tailored size and shape [2,3]. The magnetic NPs are characterized by a wide range of techniques: morphology is examined by transmission electron microscopy (TEM), crystallography is studied by X-ray diffraction (XRD) and magnetic properties in powder form are measured by vibrating sample magnetometer (VSM) and superconducting quantum interference device (SQUID). Two different shapes of particles are prepared: spherical cobalt nanocrystals in a size range 5–25 nm with narrow size distribution and anisotropic cobalt nanodiscs with specific aspect ratios (Fig. 1A, C). The spherical cobalt particles are  $\epsilon$ -Co, a metastable cubic form, isomorphous with  $\beta$ -Mn struc-

ture [4], and the nanodiscs are the common HCP structure.

In our synthesis method, surfactants control both the size and shape of the nanocrystals. The size is mainly controlled by adjusting the ratio of surfactant to precursor and type of surfactants. The shape is determined by a judicious choice of surfactants that adhere selectively to certain crystallographic planes promoting anisotropic particle shapes. Selection of appropriate surfactants for shape control is accomplished by growing epitaxial cobalt thin films along different crystallographic directions and monitoring the reactivity of a specific surfactant in synthesis condition as a function of crystallographic orientation of the films by X-ray photoelectron spectroscopy

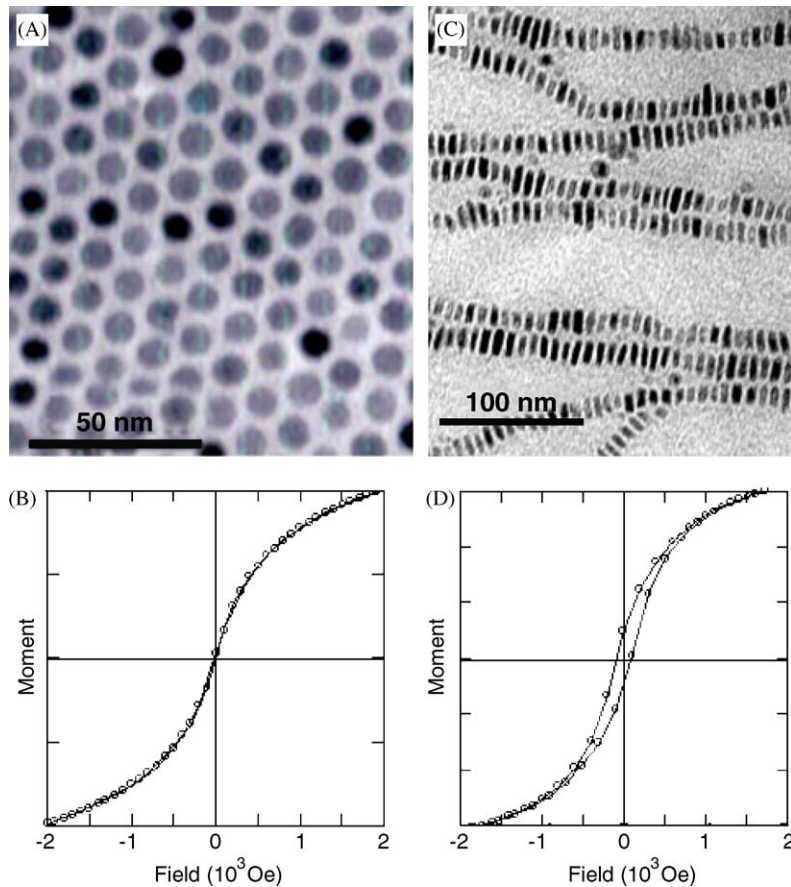


Fig. 1. (A) TEM image of 10 nm cobalt NPs (B) VSM hysteresis loop which shows superparamagnetic behavior (C) TEM image of  $5 \times 20$  nm cobalt nanodiscs (D) VSM hysteresis loop which shows ferromagnetic behavior.

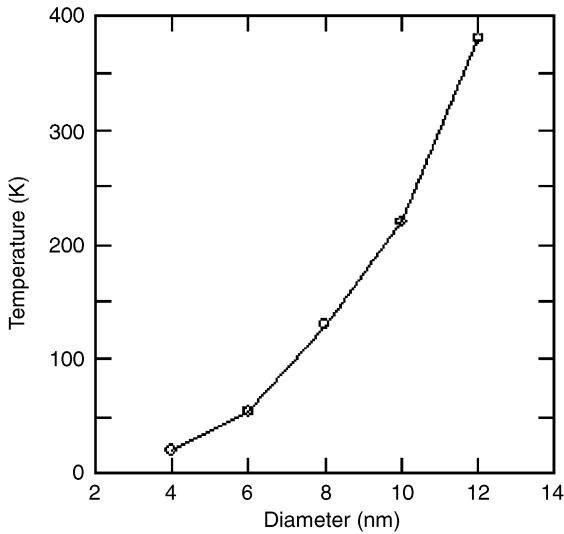


Fig. 2. Blocking temperature increase with of particle size from SQUID ZFC measurements

(Y. Bao, K.M. Krishnan, unpublished results). Detailed magnetometry at room temperature confirms the smaller particles to be superparamagnetic while the larger spheres and the discs are ferromagnetic (Fig. 1B, D). For cobalt nanocrystals at room temperature, using a SQUID magnetometer with a time constant of 100 s, the transition from superparamagnetic to ferromagnetic behavior occurs at a diameter  $\sim 10$  nm. Since the magnetic transition from superparamagnetic to ferromagnetic state is a function of particle size, it can be precisely controlled by the synthesis chemistry. Zero field cooled (ZFC) magnetic measurements shows the blocking temperature increases as a function of particle size (Fig. 2).

Polymer-coated iron oxide has been traditionally used as a marker for genetic screening devices [4], but their relatively small magnetic moment for a given size, strongly affects their efficacy. Micron-sized particles are required to generate an adequate moment, but this impedes the biomolecular reorganization and interaction. Alternatively, cobalt can serve as a good candidate for biosensor applications because of their high magnetic moment (Table 1). The forces generated on magnetic NPs  $F_m = (m \cdot \nabla)B$  [5] are sufficiently large to make them an attractive candidate for various applica-

Table 1

Saturation magnetization ( $M_s$ ) of iron oxide and cobalt nanoparticles

Nanoparticles	$M_s$		
	Bulk value (emug/g)	Literature value (emug/g)	Measured value (emug/g)
Maghemite	80	45–75	—
Magnetite	91	30–78	—
Cobalt	161	105–180	100

tions. For example, the magnetic force can be used for cell separation, detection and drug delivery. The magnitude of the force is directly proportional to the magnetic moment of the particles and for cobalt NPs it can be more than three times higher than the same size magnetite NPs based on the bulk magnetization values. Even though cobalt nanocrystals produce high magnetic moment their biological applications are limited by their poor biocompatibility and resistance to oxidation.

To achieve biocompatibility and stability, as well as to satisfy the needs for high moment NPs in biological applications, we are synthesizing core-shell structures of both gold-coated cobalt (Co@Au) and cobalt-coated gold (Au@Co) NPs. Growing a gold shell on iron NPs has been reported by different groups [6–8]. However, in addition to reproducibility, the growth processes do not lend themselves to the production of sufficient quantities of uniformly coated core-shell particles. Gold NPs have been routinely synthesized by a two-phase approach originally proposed by Brust [9]. Growing a gold shell on cobalt seeds in this environment is difficult because these seed particles are not soluble in water and an environment rich in oxygen and water will accelerate the formation of cobalt hydroxide. Moreover, in this method, the use of a strong reducing agent (borohydride) makes the reduction reaction happen too rapid to form a uniform shell. It is also possible that instead of forming a shell, individual Au NPs are formed. To form a uniform gold shell, it is critical to synthesize particles in a non-polar solvent under a mild reducing condition. We accomplish this by dissolving the gold compound

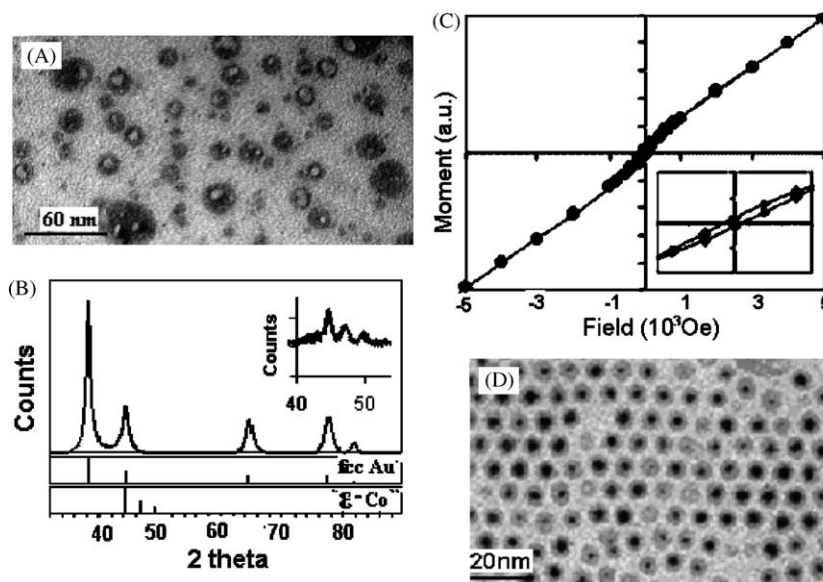


Fig. 3. (A) TEM image of Co@Au NPs (B) the XRD  $\theta-2\theta$  scan shows fcc gold structure,  $\epsilon$ -Co XRD spectrum is shown in the inset. (C) Hysteresis loop of Co@Au NPs measured at room temperature. The open loop in the inset shows ferromagnetic behavior (D) TEM image of Au@Co NPs

in toluene under alkaline conditions in argon atmosphere. This is critical to make the cobalt seeds soluble and form a uniform solution. Hydrazine, a mild reducing agent at room temperature is then added to the solution to grow a gold shell on the cobalt seed surface in the non-polar solvent. Preliminary TEM analysis (Fig. 3A) of the nanocrystals synthesized by this method show that it is possible to form a core-shell structure. The XRD pattern (Fig. 3B) only shows peaks corresponding to the FCC metallic gold structure and the cobalt peaks are not clearly resolved, probably, due to strong absorption of Cu- $K_{\alpha}$  radiation by Co and peak broadening. However, the particles are ferromagnetic and show open hysteresis loops (Fig. 3C), indicating the presence of cobalt. Even though cobalt seeds 6–7 nm in diameter are used, Co@Au samples show ferromagnetic behavior at room temperature. This is attributed to the aggregation of cobalt particles, which is also seen in the TEM image. Aggregation can be reduced by sonicating cobalt seeds before adding them to the gold solution. This core-shell system may find a number of biological applications because of the strong magnetic signal

and the well-studied gold chemistry that leads to a wide range of surface modification strategies.

We are simultaneously synthesizing the reverse core-shell structure, in which the gold core is surrounded by a cobalt shell, to investigate the stability of immiscible metallic binary (such as Au-Co) alloys where competing surface and bulk thermodynamic/kinetic factors may lead to unexpected results. For this structure, the gold seeds are synthesized by a modified Brust method using amine as surfactants instead of thiol. The gold seeds are precipitated with methanol and then re-dispersed in dichlorobenzene. This solution is heated up to 140 °C, and a solution of cobalt carbonyl is injected to grow the cobalt shell. The temperature is critical during this step. It should be high enough to decompose the precursor, but low enough to avoid isolated nucleation of cobalt clusters. A TEM micrograph of this system appears in Fig. 3D.

The ability to synthesize cobalt nanocrystals with narrow size distributions and controlled shapes may have strong impact on the development of magnetic sensors and other medical diagnostic devices. Specifically, the synthesis of gold-coated cobalt nanocrystals may display

multiple functionalities (optical and magnetic). In addition, combined with the well-established gold–thiol surface chemistry [10,11], these cobalt–gold core-shell nanocrystals can be functionalized with proteins, DNA and/or other bio-molecules, thereby opening up possibilities in bio-labeling, magnetic separation and optical sensing.

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