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Review

The Mössbauer and magnetic properties of ferritin cores

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ABSTRACT

Background: Mössbauer and magnetization measurements, singly or in combination, extract detailed information on the microscopic or internal magnetism of iron-based materials and their macroscopic or bulk magnetization. The combination of the two techniques affords a powerful investigatory probe into spin relaxation processes of nanosize magnetic systems. The ferritin core constitutes a paradigm of such nanomagnetic system where Mössbauer and magnetization studies have been broadly combined in order to elucidate its composition, the initial steps of iron nucleation and biomineralization, particle growth and core-size distribution. In vivo produced and in vitro reconstituted wild-type and variant ferritins have been extensively studied in order to elucidate structure/function correlations and ferritin's role in iron overloading or neurodegenerative disorders.
Scope of Review: Studies on the initial stages of iron biomineralization, biomimetic synthetic analogues and ferrous ion retention within the ferritin core are presented. The dynamical magnetic properties of ferritin by Mössbauer and magnetization measurements are critically reviewed. The focus is on experiments that reveal the internal magnetic structure of the ferritin core. Novel magnetic measurements on individual ferritin molecules via AFM and nanoSQUID investigations are also mentioned.
Major Conclusions: A complex two-phase spin system is revealed due to finite-size effects and non-compensated spins at the surface of the anti-ferromagnetic ferritin core. Below the blocking temperature surface spins participate in relaxation processes much faster than those associated with collective magnetic excitations of interior spins.
General Significance: The studies reviewed contribute uniquely to the elucidation of the spin-structure and spin-dynamics of anti-ferromagnetic nanolattices and their possible applications to nano/bio-technology.

1. Background

The magnetic properties of particles of nanometric dimensions have attracted the attention of investigators ever since the 1930s, when it was realized that these nanoparticles constitute single-magnetic-domains. Among these ferritin, containing a magnetic core of ~7 nm diameter protected against aggregation by protein coat, has enjoyed unique consideration and intensive investigation. In the era of interdisciplinary science of the 21st century and the extraordinary developments in nanotechnology we are witnessing daily, the study of the magnetic properties of the ferritin core is uniquely contributing to advances in a broad range of scientific disciplines. Beyond furthering our understanding of the physiological function of ferritin [1–4] and its role in iron overloading and neurodegenerative disorders [5–14], it affords a unique platform for scientific inquiry into the process of biomineralization [15–19], the spin-structure and spin-dynamics of antiferromagnetic nano-lattices [20], superparamagnetic relaxation [21–23], nanoparticle functionalization for biotechnological applications [24], the production of well defined nanoparticle arrays for applications in nano-electronics [25,26] and the fabrication of advanced electrodes and electrochemical sensors [27–29], to name a few.

Magnetization studies of ferritin span several decades with the earliest studies reported in the 1940's [30], while a steady stream of publications continues to appear in the scientific literature today [31–43]. Unraveling the magnetic properties of the ferritin core presents a special challenge to investigators, due to the fact that the iron biomineral phase of the core is available to us only in nanometric dimensions. Thus, fundamental magnetic properties, such as its Néel temperature, T_N, the critical temperature at which the magnetic moments of the ferric ions in the core become antiferromagnetically ordered, are still in dispute [44] with estimates ranging from 200 K [45] to 240 K [46] to 460 K [32] and 500 K [47]. These estimates of T_N rely on theoretical modeling and experimental data extrapolation. This is due to the fact that superparamagnetism sets in at a temperature far below

Abbreviations: HoSF, horse spleen ferritin; HuHF, human H-Chain ferritin; δ, isomer shift; ΔE_Q, quadrupole splitting; AC, alternating current; DC, direct current; ZFC, zero-field-cooled; FC, field-cooled; AFM, atomic force microscopy; SQUID, superconducting quantum interference device; THF, tetrahydrofuran; MRI, magnetic resonance imaging

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the estimated Néel temperature, prohibiting its determination by usual methods. Uncertainties of the homogeneity of the iron oxy hydroxide phase of the core and its degree of crystallinity [48–50], the presence of various amounts of phosphate in wild-type ferritins, coupled with strong manifestations of finite-size effects in the intrinsic magnetic order of the core [51], further complicate the picture.

Mössbauer spectroscopic studies on ferritin appeared soon after the discovery of the Mössbauer effect and the establishment of Mössbauer spectroscopy as a versatile spectroscopic tool for investigations on the electronic and magnetic structure of iron containing materials, in the 1960s [52]. Mössbauer and magnetic studies were initially pursued separately, but increasingly investigators have combined the two techniques to carry out simultaneous Mössbauer and magnetic measurements on the same sample. The combination of the two techniques affords a powerful investigatory probe into the dynamic magnetic properties of magnetic nanoparticles, such as spin relaxation and collective magnetic excitations. Mössbauer spectroscopy captures the internal magnetism of the core, without, necessarily, the need to apply an external magnetic field. It detects the local magnetic moments at the iron sites via the magnetic hyperfine interactions of the ^{57}Fe nucleus with its surrounding electrons [53]. In contrast, magnetization measurements deduce the total magnetic moment of the iron core, via its interaction with an externally applied magnetic field [54]. Furthermore, the characteristic measuring times of the two techniques differ by about 10 orders of magnitude, affording examination of dynamic magnetic properties in two very different time domains, of the order of 10^{-8} s for Mössbauer spectroscopy and 10 s to 100 s for direct current (DC) magnetization measurements. Alternating current (AC) susceptibility measurements at various frequencies provide additional time windows between these two extremes [40]. Mössbauer investigations employing externally applied magnetic fields [55] can also be utilized, which further empowers Mössbauer spectroscopy into probing for the presence of spin frustration, canting and surface spin effects, all common in small magnetically ordered systems.

2. Scope of review

In this article we review important contributions to the literature on the Mössbauer and magnetization properties of the iron ferritin core and their impact in (a) elucidating the processes involved in core formation and (b) determining the magnetic properties of the fully developed core. Emphasis is placed on studies of mammalian wild-type, recombinant and reconstituted iron cores, rather than those derived from bacterial ferritins [56,57]. In section 3, we review Mössbauer-based studies of iron nucleation and hydrolytic polymerization processes active in the initial stages of the ferric-ion-biomineral formation and synthetic analog models of polynuclear ferric-ion clusters that mimic iron nucleation in the ferritins. Mössbauer spectroscopic studies of ferrous ion complexation to apoferritin and evidence of Fe(II)-ion retention within the iron mineral core is also presented. In section 4, studies in which the ferritin core is modeled as a single-phase magnetically ordered particle with uniaxial magnetic anisotropy, allowing determination of parameters that govern superparamagnetic relaxation processes, are reviewed. In section 5, studies that account for finite-size, surface and spin non-compensation effects are presented, while in section 6, some future directions in ferritin Mössbauer investigations are pointed out and in the development of ferritin-like, novel biopharmaceuticals. Finally, we conclude in section 7 with a brief discussion of recent advances in ferritin core magnetization studies on single ferritin molecules employing nano-squid and atomic force microscopy.

3. Iron nucleation and polymerization in ferritin and synthetic analog clusters

The biomineral iron hydroxide core of ferritin is encapsulated within a spherical protein shell of 24 amino acid chains. Protein shells from animal tissues contain two different types of amino acid chains denoted by Heavy and Light or H and L subunits, which have about 55% identity in amino acid sequence. The ratio of H:L varies; ferritins found in heart and brain tissue contain about 65% H subunits and those in liver and spleen have up to 90% L subunits. The H subunits contain dinuclear ferroxidase centers where Fe(II) becomes oxidized to Fe(III) prior to moving into the protein cavity for deposition as ferrihydrite [1]. Recombinant H-chain human ferritin (HuHF) has been extensively used in investigations aiming at elucidating the role of the ferroxidase center in iron biomineralization. Natural and reconstituted horse spleen ferritins (HoSF) at various iron loading levels have been used in studies of the magnetic properties of ferritin and their dependence on core size.

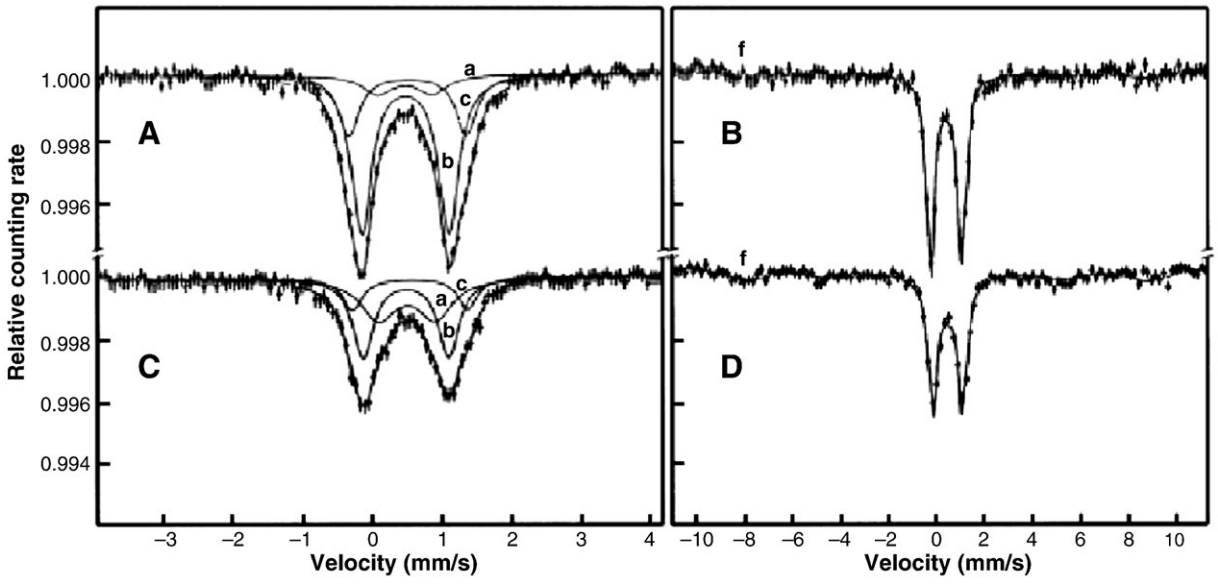

Fig. 1. Initial iron-apoferritin complexation and iron cluster nucleation in HuHF. Mössbauer spectra collected at 90 K with 10 ^{57}Fe atoms/apoferritin molecule loaded at pH 6.5. Identification of simulated subspectra: (a) Fe(III) clusters, (b, c) Fe(III) dimers, (f) Fe(III) monomer. Spectra (A) and (B) were obtained on rapid-freeze-quenched samples 0.5 min after addition of ferrous ion, spectra (C) and (D) after 10 min of reaction. Spectra (B) and (D) were recorded on an expanded velocity scale (reproduced with permission from Bauminger et al. [59]).