Materials Science

Monodisperse Magnetic Single-Crystal Ferrite Microspheres**

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It has been thought that many novel properties and potential applications would emerge from monodisperse materials with small dimensions. Therefore, the synthesis of monodisperse nanoparticles has been intensively pursued for their technological and fundamental scientific importance.[1–7] The synthesis of nanostructured magnetic materials has become a particularly important area of research and is attracting a growing interest because of the potential applications such materials have in ferrofluids, advanced magnetic materials, catalysts, colored pigments, high-density magnetic recording media, and medical diagnostics.[8–13] Spinel ferrites (MFe_2O_4; M = Fe, Mn, Zn, or Co) are among the most important magnetic materials and have been widely used in electronic devices, information storage, magnetic resonance imaging (MRI), and drug-delivery technology.[8,9,14] Magnetite (Fe_3O_4) has recently been considered an ideal candidate for biological applications, both as a tag for sensing and imaging, and as an activity agent for antitumor therapy.[15–17] For high performance in function-specific biological applications, magnetic particles must be spherical and have smooth surfaces, narrow size distributions, large surface areas (for maximal protein or enzyme binding), high magnetic saturation (σ_s) to provide maximum signal, and good dispersion in liquid media.[6,18,19]

After Sugimoto and Matijević reported the preparation of magnetite particles with a narrow size distribution in the early 1980s,[20] monodisperse ferrite has been fabricated by various chemistry-based synthetic methods, including coprecipitation, the reverse micelle method, microwave plasma synthesis, sol-gel techniques, freeze drying, ultrasound irradiation, hydrothermal methods, laser pyrolysis techniques, and thermal decomposition of organometallic and coordination compounds.[1,9,14,18,20–27] However, most of these approaches were focused on the synthesis of ferrite particles limited to diameters below 30 nm. There are no reports on the synthesis of well-crystallized ferrite nanoparticles with sizes similar to protein molecules. The development of a facile and economic synthetic strategy for the synthesis of hydrophilic, biocompatible magnetite nanoparticles would benefit their technical use in biomedical fields, especially for applications in vivo. Herein we report a general approach for the fabrication of monodisperse, hydrophilic, and single-crystalline ferrite microspheres by a solvothermal reduction method. To the best of our knowledge, this is the first report on the synthesis of single-crystalline magnetic microspheres. The ferrite spheres had monodisperse diameters that were tunable in the range of 200–800 nm. This work resulted in an important method for obtaining various monodisperse, magnetic, and single-crystalline microspheres, and provided an opportunity to further apply these promising materials.

Typical syntheses of Fe_3O_4 and ferrite microspheres were carried out in a solvothermal system by modified reduction reactions between $FeCl_3$ and ethylene glycol. We confirmed the production of Fe_3O_4 by conducting controlled oxidation reactions in which α- and γ-Fe_2O_3 were produced (Supporting Information).[1b,28–29] The crystalline structures of MFe_2O_4 were characterized by XRD. As shown in Figure 1, the patterns can be easily indexed to Fe_3O_4 (JCPDS 75-1609), $MnFe_2O_4$ (JCPDS 74-2403), $ZnFe_2O_4$ (JCPDS 22-1012), and $CoFe_2O_4$ (JCPDS 22-1068). The Fe_3O_4 sample was determined by X-ray photoelectron spectroscopy (Supporting Information).

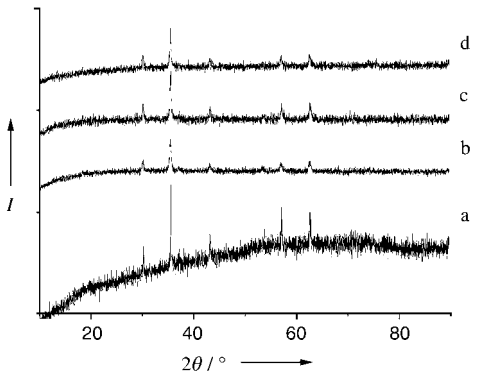

Figure 1. XRD patterns of Fe_3O_4, trace a; $MnFe_2O_4$, trace b; $ZnFe_2O_4$, trace c; and $CoFe_2O_4$, trace d.

The size and shape of the products were examined by TEM and scanning electron microscopy (SEM). Figure 2 shows representative images of the spinel ferrite compounds, which are spherical and have very narrow diameter distributions. The standard deviation for Fe_3O_4 particle diameters is ≈5%, excluding agglomerate particles (for diameter-distribution histograms of the MFe_2O_4 microspheres, see Supporting Information). Furthermore, the shape and size of the α-Fe_2O_3 and γ-Fe_2O_3 products remained unchanged from those of the Fe_3O_4 precursor. In a typical solvothermal process, the

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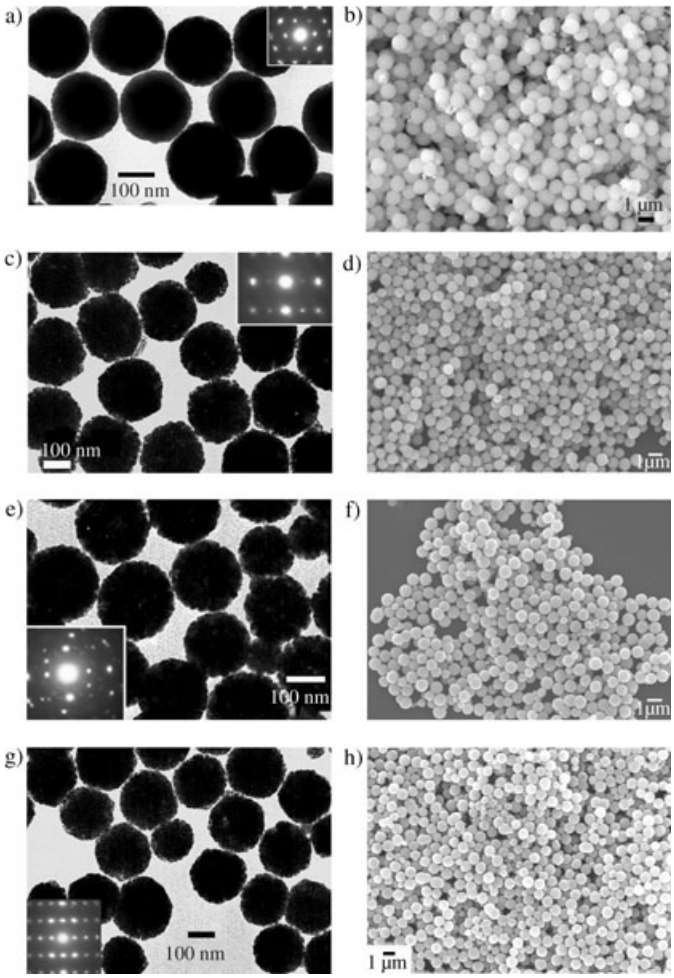

Figure 2. Representative TEM images (a, c, e, and g) and SEM images (b, d, f, and h) of microspheres of Fe_3O_4, (a and b); $MnFe_2O_4$, (c and d); $ZnFe_2O_4$, (e and f); and $CoFe_2O_4$, (g and h). Microsphere diameter is ≈800 nm in the SEM images, and ≈200 nm in the TEM images, in which the insets show the corresponding electron diffraction patterns.

diameters of the MFe_2O_4 ferrite microspheres were influenced by reaction time and the concentration of starting material. With precursor concentration (0.13 M) and temperature (200 °C) held constant, microsphere diameters were observed to be ≈200 nm at a reaction time of 8 h (Figures 2a, c, e, and g), ≈400 nm at 48 h, and ≈800 nm at 72 h (Figures 2b, d, f, and h). Likewise, microsphere diameters increased with an increase in precursor concentration. However, the complex nature of the growth process makes it difficult to obtain a straightforward correlation between particle diameter and changes in reaction time or precursor concentration. Electron-diffraction patterns taken from individual MFe_2O_4 microspheres revealed the single-crystalline nature of these samples. Energy-dispersive X-ray analysis (EDAX) was also measured to determine the chemical composition of the ferrite samples. Results from EDAX spectra from individual ferrite microspheres showed that samples contain only Fe and O for Fe_3O_4; Mn, Fe, and O for $MnFe_2O_4$; Zn, Fe, and O for $ZnFe_2O_4$; and Co, Fe, and O for $CoFe_2O_4$ (Supporting Information). The atomic ratio Fe/O for Fe_3O_4 was 3:4, and an analogous M/Fe/O ratio of ≈1:2:4 was observed for each of the other MFe_2O_4 products (M = Mn, Zn, Co), in agreement with the expected stoichiometry in each case.

High-resolution TEM (HRTEM) analysis provided more detailed structural information on the microspheres. A representative TEM image of the Fe_3O_4 microspheres is shown in Figure 3a, in which the HRTEM image (boxed area) further supports the single-crystalline nature of the particles (Supporting Information). The interlayer distance was calculated to be ≈0.48 nm, which agrees well with the separation between the (101) lattice planes.

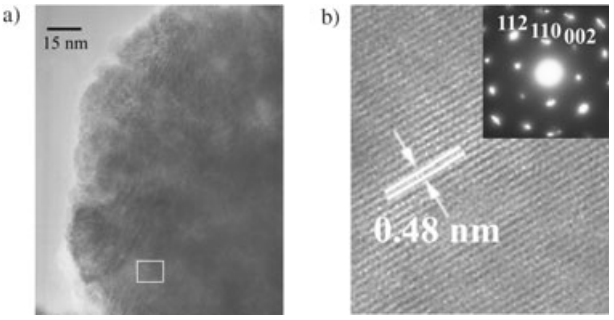

Figure 3. a) Representative TEM image of a Fe_3O_4 microsphere (diameter ≈200 nm); b) HRTEM image of the boxed region of part (a) and the electron-diffraction pattern of the individual Fe_3O_4 microsphere (inset).

Both the literature[6,7] and our own experimental evidence have led us to believe that ethylene glycol plays an important role in ferrite formation. Ethylene glycol is a strong reducing agent with a relatively high boiling point,[7] and has been widely used in the polyol process to provide monodisperse fine metal or metal oxide nanoparticles. However, magnetic spinel ferrite particles have a strong tendency to agglomerate during their formation in the liquid-phase process. To obtain monodisperse Fe_3O_4 particles, we designed a modified synthetic route in which three added features were found to be critical. First, NaAc was added for electrostatic stabilization to prevent particle agglomeration. Such benefits of NaAc were found in similar syntheses with Ru, Pt, and Rh particles.[30,31] In our system, NaAc was even more important, as its addition seems to assist in the ethylene glycol mediated reduction of $FeCl_3$ to Fe_3O_4. Control experiments showed that Fe^{3+} could not be reduced by ethylene glycol alone under the same reaction conditions. Second, polyethylene glycol was added as a surfactant and as an additional preventative measure against particle agglomeration. The third feature is the increased reaction temperature of 200 °C, which is necessary for the production of Fe_3O_4.

The magnetic properties of the ferrite microspheres were investigated with a vibrating sample magnetometer. Figure 4 shows the magnetization curves measured at 300 K for MFe_2O_4 microspheres with diameters of ≈200 nm. The magnetic saturation values are 81.9 emu g^{-1} for Fe_3O_4,

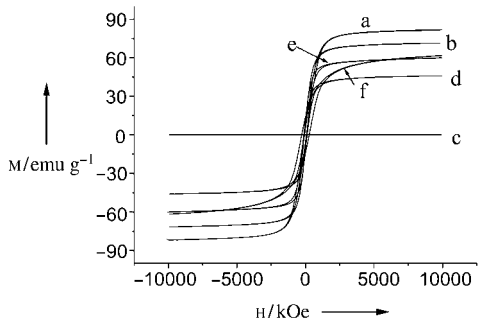

Figure 4. Room-temperature magnetization curves of ferrite microspheres (diameter ≈200 nm): Fe_3O_4, trace a; γ-Fe_2O_3, trace b; α-Fe_2O_3, trace c; $MnFe_2O_4$, trace d; $ZnFe_2O_4$, trace e; and $CoFe_2O_4$, trace f.

53.2 emu g^{-1} for $MnFe_2O_4$, 60.0 emu g^{-1} for $ZnFe_2O_4$, and 61.6 emu g^{-1} for $CoFe_2O_4$. More detailed investigations of the magnetic properties of these products are still in progress. The product of Fe_3O_4 oxidation in HNO_3 gave a σ_s value of 72 emu g^{-1} (Figure 4), which is close to the value of 74 emu g^{-1} determined from the analysis of commercial γ-Fe_2O_3 powder (Aldrich, 48-1-066-5), supporting the formation of γ-Fe_2O_3 under these conditions. After the Fe_3O_4 sample was oxidized in air at 400 °C for 3 h, the σ_s value of the product was negligible (Figure 4), which indicates that under these conditions Fe_3O_4 is transformed into α-Fe_2O_3.

To examine the colloid stability of ferrite samples, magnetic ferrite microspheres (20 mg) were dispersed in doubly distilled water (80 mL) by sonication. The magnetic particles remained in suspension for more than 1 day, which demonstrates that they can be well-dispersed in aqueous solution. Therefore, with the appropriate surface modifications, these microspheres may be suitable for clinical diagnosis and in the transport of drugs, proteins, viruses, or bacteria. The synthetic strategy developed in this study offers several important advantageous features for the technical application of microparticles. First, the ferrite spheres are magnetic, which means that they can be manipulated by an external magnetic field. Second, our strategy allows the direct production of highly crystalline, monodisperse, and hydrophilic spheres. Third, microsphere size is controllable, with diameters ranging from 200 to 800 nm. Finally, the raw materials are inexpensive and the yields are relatively high (92 %), which makes this process amenable to large-scale reactions for industrial needs.

In summary, the solvothermal reduction method has been used to successfully produce a series of ferrite MFe_2O_4 (M = Fe, Mn, Co, Zn) microspheres. This approach provides a one-step, simple, general, and inexpensive method for the preparation of monodisperse magnetic microspheres with a tunable diameter range of ≈200–800 nm. We believe that these hydrophilic and biocompatible microspheres will have important applications not only in advanced magnetic materials and ferrofluid technology, but also in biomedical fields such as biomolecular separations, targeted drug delivery, cancer diagnosis and treatment, as well as magnetic resonance imaging.

Experimental Section

Fe_3O_4 microsphere synthesis:[32] $FeCl_3 \cdot 6H_2O$ (1.35 g, 5 mmol) was dissolved in ethylene glycol (40 mL) to form a clear solution, followed by the addition of NaAc (3.6 g) and polyethylene glycol (1.0 g). The mixture was stirred vigorously for 30 min and then sealed in a teflon-lined stainless-steel autoclave (50 mL capacity). The autoclave was heated to and maintained at 200 °C for 8–72 h, and allowed to cool to room temperature. The black products were washed several times with ethanol and dried at 60 °C for 6 h.

The above process can be can be extended to the synthesis of MFe_2O_4 (M = Co, Mn, Zn) microspheres by coprecipitation of M^{II} and Fe^{III} chlorides ($M^{2+}/Fe^{3+} = 0.5$).[32] For example, a mixture of $MnCl_2 \cdot 4H_2O$ (0.50 g, 2.5 mmol) and $FeCl_3 \cdot 6H_2O$ (1.35 g, 5 mmol) under the same reaction conditions as used for the synthesis of Fe_3O_4 microspheres, produced microspheres of $MnFe_2O_4$.

All samples were characterized on a Bruker D8 Advance powder X-ray diffractometer with $Cu_{K\alpha}$ radiation ($\lambda = 1.5418$ Å). The TEM and HRTEM images were generated with a Hitachi H-800 transmission electron microscope and with a JEOL JEM-2010F high-resolution transmission electron microscope. SEM images were taken with a NORAN LDO 1530 apparatus. Magnetic studies were carried out on a Quantum Design SQUID magnetometer.

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[1] a) S. Sun, C. B. Murray, D. Weller, L. Folks, A. Moser, *Science* **2000**, *287*, 1989 – 1992; b) S. H. Sun, H. Zeng, D. B. Robinson, *J. Am. Chem. Soc.* **2004**, *126*, 273 – 279; c) S. Sun, H. Zeng, *J. Am. Chem. Soc.* **2002**, *124*, 8204 – 8205; d) K. E. Elkins, T. S. Vedantam, J. P. Liu, H. Zeng, H. S. H. Sun, Y. Ding, Z. L. Wang, *Nano Lett.* **2003**, *3*, 1647 – 1649.

[2] R. Jin, Y. Cao, C. A. Mirkin, K. L. Kelly, G. C. Schatz, J. G. Zheng, *Science* **2001**, *294*, 1901 – 1904.

[3] a) S. U. Son, Y. Jang, J. Park, H. B. Na, H. M. Park, H. J. Yun, J. Lee, T. Hyeon, *J. Am. Chem. Soc.* **2004**, *126*, 5226 – 5227; b) S. U. Son, Y. Jang, K. Y. Yoon, E. Kang, T. Hyeon, *Nano Lett.* **2004**, *4*, 1147 – 1151; c) S. W. Kim, J. Park, Y. Jang, Y. Chung, S. Hwang, T. Hyeon, Y. W. Kim, *Nano Lett.* **2003**, *3*, 1289 – 1291; d) J. Joo, T. Yu, Y. W. Kim, H. M. Park, F. X. Wu, J. Z. Zhang, T. Hyeon, *J. Am. Chem. Soc.* **2003**, *125*, 6553 – 6557.

[4] a) F. Caruso, R. A. Caruso, H. Mohwald, *Science* **1998**, *282*, 1111 – 1114; b) F. Caruso, *Adv. Mater.* **2001**, *13*, 11 – 22; c) F. Caruso, *Chem. Eur. J.* **2000**, *6*, 413 – 419.

[5] a) X. G. Peng, *Adv. Mater.* **2003**, *15*, 459 – 463; b) Z. A. Peng, X. G. Peng, *J. Am. Chem. Soc.* **2001**, *123*, 1389 – 1395.

[6] a) Y. Sun, Y. Xia, *Science* **2002**, *298*, 2176 – 2179; b) Y. Lu, Y. Yin, B. T. Mayers, Y. Xia, *Nano Lett.* **2002**, *2*, 183 – 186; c) Y. L. Wang, Y. N. Xia, *Nano Lett.* **2004**, *4*, 2047 – 2050.

[7] a) Q. Peng, Y. J. Dong, Y. D. Li, *Angew. Chem.* **2003**, *115*, 3135 – 3138; *Angew. Chem. Int. Ed.* **2003**, *42*, 3027 – 3030; b) Q. Peng, S. Xu, Z. B. Zhuang, X. Wang, Y. D. Li, *Small* **2004**, *1*, 216 – 221; c) X. M. Sun, Y. D. Li, *Angew. Chem.* **2004**, *116*, 3915 – 3919; *Angew. Chem. Int. Ed.* **2004**, *43*, 3827 – 3831; d) X. M. Sun, Y. D. Li, *Angew. Chem.* **2004**, *116*, 607 – 611; *Angew. Chem. Int. Ed.* **2004**, *43*, 597 – 601; e) J. W. Wang, X. Wang, Q. Peng, Y. D. Li, *Inorg. Chem.* **2004**, *43*, 7552 – 7556; f) Y. Zhang, Y. D. Li, *J. Phys. Chem. B* **2004**, *108*, 17805 – 17811.

[8] F. Caruso, M. Spasova, A. Susha, M. Giersig, R. A. Caruso, *Chem. Mater.* **2001**, *13*, 109 – 116.

[9] a) T. Hyeon, *Chem. Commun.* **2003**, *8*, 927 – 934; b) T. Hyeon, Y. Chung, J. Park, S. S. Lee, Y. W. Kim, B. H. Park, *J. Phys. Chem. B*

2002, *106*, 6831 – 6833; c) T. Hyeon, S. S. Lee, J. Park, Y. Chung, H. B. Na, *J. Am. Chem. Soc.* **2001**, *123*, 12798 – 12801.
[10] Y. Xiong, X. Xie, S. Chen, Z. Li, *Chem. Eur. J.* **2003**, *9*, 4991 – 4996.
[11] K. Woo, H. J. Lee, J. Ahn, Y. S. Park, *Adv. Mater.* **2003**, *15*, 1761 – 1764.
[12] a) X. Teng, H. Yang, *J. Mater. Chem.* **2004**, *14*, 774 – 779; b) Y. Wang, J. Wong, X. Teng, X. Lin, H. Yang, *Nano. Lett.* **2003**, *3*, 1554 – 1559; c) Y. Wang, X. Teng, J. Wang, H. Yang, *Nano. Lett.* **2003**, *3*, 789 – 793.
[13] A. Yu, M. Mizuno, Y. Sasaki, H. Kondo, *Appl. Phys. Lett.* **2002**, *81*, 3768 – 3771.
[14] a) S. Yu, M. Yoshimura, *Adv. Funct. Mater.* **2002**, *12*, 9 – 15; b) S. Yu, M. Yoshimura, *Chem. Mater.* **2000**, *12*, 3805 – 3810.
[15] a) J. M. Perez, T. O'Loughlin, F. J. Simeone, R. Weissleder, L. Josephson, *J. Am. Chem. Soc.* **2002**, *124*, 2856 – 2857; b) J. M. Perez, F. J. Simeone, A. Tsourkas, L. Josephson, R. Weissleder, *Nano Letter.* **2004**, *4*, 119 – 122; c) J. M. Perez, L. Josephson, T. O'Loughlin, D. Hogemann, R. Weissleder, *Nat. Biotechnol.* **2002**, *20*, 816 – 820.
[16] A. Y. Louie, M. M. Huber, E. T. Ahrens, U. Rothbacher, R. Moats, R. E. Jacobs, S. E. Fraser, T. J. Meade, *Nat. Biotechnol.* **2000**, *18*, 321 – 325.
[17] U. Häfeli, W. Schütt, J. Teller, M. Zborowski, *Scientific and Clinical Application of Magnetic Carriers*, Plenum, New York, **1997**.
[18] S. H. Gee, Y. K. Hong, D. W. Erickson, M. H. Park, *J. Appl. Phys.* **2003**, *93*, 7560 – 7562.
[19] K. Woo, J. Hong, S. Choi, H. Lee, J. Ahn, C. S. Kim, S. W. Lee, *Chem. Mater.* **2004**, *16*, 2814 – 2818.
[20] a) T. Sugimoto, E. Matijević, *J. Colloid Interface Sci.* **1980**, *74*, 227 – 243; b) E. Matijević, *Acc. Chem. Res.* **1981**, *14*, 22 – 29; c) T. Sugimoto, *Monodispersed Particles*, Elsevier, New York, **2001**.
[21] J. Jolivert, C. Chanéac, E. Tronc, *Chem. Commun.* **2004**, 481 – 487.
[22] F. Li, J. Liu, D. G. Evans, X. Duan, *Chem. Mater.* **2004**, *16*, 1597 – 1602.
[23] X. Chen, Z. Deng, L. Li, Y. Li, *Chin. J. Inorg. Chem.* **2002**, *18*, 460 – 464.
[24] L. A. Harris, J. D. Goff, A. Y. Carmichael, J. S. Riffle, J. J. Harburn, T. G. S. Pierre, M. Saunders, *Chem. Mater.* **2003**, *15*, 1367 – 1377.
[25] Z. H. Zhou, J. Wang, X. Liu, H. S. O. Chan, *J. Mater. Chem.* **2001**, *11*, 1704 – 1709.
[26] Y. Sahoo, M. Cheon, S. Wang, H. Luo, E. P. Furlani, P. N. Prasad, *J. Phys. Chem. B* **2004**, *108*, 3380 – 3383.
[27] Q. Song, Z. J. Zhang, *J. Am. Chem. Soc.* **2004**, *126*, 6164 – 6168.
[28] J. L. Lyon, D. A. Fleming, M. B. Stone, P. Schiffer, M. E. Williams, *Nano Lett.* **2004**, *4*, 719 – 723.
[29] R. M. Comell, U. Schwertmann, *The Iron Oxides: Structure, Properties, Reactions, Occurrences and Uses*, VCH, New York, **1996**.
[30] a) G. Viau, P. Toneguzzo, A. Pierrard, O. Acher, F. Fiévet-Vincent, F. Fiévet, *Scr. Mater.* **2001**, *44*, 2263 – 2267; b) G. Viau, R. Brayner, L. Poul, N. Chakroune, E. Lacaze, F. Fiévet-Vincent, F. Fiévet, *Chem. Mater.* **2003**, *15*, 486 – 494.
[31] K. R. Brown, D. G. Walter, M. J. Natan, *Chem. Mater.* **2000**, *12*, 306 – 313.
[32] Y. D. Li, H. Deng, Chinese Patent 200410009788.9, **2004**.

