A Template-Free Synthesis of the One-Dimensional Nanostructure of Multiferroic BiFeO₃

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One-dimensional (1D) single-crystalline nanostructures of BiFeO₃ (BFO) and Bi₂Fe₄O₉ were for the first time successfully synthesized by a template-free route via soft chemistry with the precursor in a thin-film form. The phases, morphologies, and crystalline structures of 1D nanostructures of BFO and Bi₂Fe₄O₉ were characterized by means of X-ray diffraction, scanning electron microscopy, and transmission electron microscopy, respectively. It was found that the atmosphere plays a crucial role in determining not only the morphologies but also the phase formation of 1D nanostructures of BFO and Bi₂Fe₄O₉. The plausible development mechanism of 1D nanostructures of BFO and Bi₂Fe₄O₉ was suggested.

I. Introduction

ONE-DIMENSIONAL (1D) nanostructures like wires, rods, belts, and tubes have attracted extensive attention due to their unique properties in mesoscopic physics and applications for nanoscale devices. Making 1D nanostructures into practical uses and lowering the cost have been the recent focus of efforts. The chemical route may provide an intriguing strategy for fabricating 1D nanostructures in terms of materials diversity, cost, and the potential high-volume production.

Recently, multiferroic materials have attracted much attention because of their potential applications for new types of electronic devices, combining ferroelectric and ferromagnetic properties. The synthesis of multiferroic nanostructures with a controllable size and shape is crucial in new-device applications. BiFeO₃ (BFO) is one of the well-known multiferroic compounds, exhibiting a coexistence of ferroelectric and antiferromagnetic orders with a high Curie temperature (TC) of B₈30°C and antiferromagnetic Ne’el temperature TN₉370°C. Although processing techniques related to the preparation of films and ceramics have been well established, it is still a challenge to synthesize pure BFO nanostructures, especially the 1D nanostructures.
Unlike the easy formation of 1D nanostructures of the binary oxides, it is difficult to form that of the ternary oxides due to the involvement of the excessive reaction formation energy. Template was usually employed to assist the development of 1D nanostructures of BFO, wherein the anodized aluminum oxide template is found to be the best candidate for the synthesis of oxide nanowires. Moreover, the 1D nanostructures of BFO synthesized by the template method were usually polycrystalline. In this investigation, we highlight that a template-free route via soft chemistry with the precursor in a thin-film form can fabricate 1D BFO with single-crystalline nanostructures.

II. Experimental Procedure

High-purity chemicals of Bi$_2$O$_3$ and Fe(NO$_3$)$_3$·9H$_2$O were dissolved in diluted HNO$_3$, and then tartaric acid in 1:1 molar ratio with respect to metal nitrates was added to the parent solution. The solution was heated under stirring on a hot plate with temperature kept at 95°C for 2 h. The stoichiometric BFO solution of B2 mol/L concentration was spin coated on Au-coated Si (100) substrate at 3000 rpm for 30 s, and dried at 200°C for 2 min. In the previous work, it was evidenced that the low oxygen partial pressure would promote the development of 1D nanostructure in the citric process. Moreover, it also was reported that low oxygen partial pressure could avoid the development of the impurity phase of Bi$_2$Fe$_4$O$_9$ and produce single-phase BFO. Thus, in this investigation, the prepared nanofilms were subsequently heated at 600°C for 30 min in two ways: First, evacuating the air from furnace tube and then sealing it (assuring that the pressure keeps fixed in gauge for a reasonable time) and second, evacuating the air from furnace tube and then maintaining it in a steady-state flowing gas of N$_2$, designated as S1 and S2, respectively. X-ray diffractometer (Rigaku-D/Max-RC, Tokyo, Japan) with CuKa radiation was used to identify the phases, and the lattice parameters were calculated referring to the X-ray diffraction (XRD) spectra. The morphologies of the nanostructures were examined by using a scanning electron microscope (SEM) (Hitachi S4100 field emission, FE-SEM; Tokyo, Japan) and a transmission electron microscope (TEM) (FEI-TEM, Philips Technai F20 G2, Eindhoven, Holland).

III. Results and Discussion

The XRD spectra of samples S1 and S2 are shown in Fig. 1. The major phase was identified as BFO with a rhombohedral-perovskite structure of space group R3c, a=55.556 Å, and c=513.803 Å, in good agreement with the literature data. The impurity phase of Bi$_2$Fe$_4$O$_9$ was also detected in the XRD spectra of both samples, which can be
leached by dilute nitric acid. The development of the impurity phases in BFO has been detailed in recent reports. The observation of Bi$_2$Fe$_4$O$_9$ in S1 and S2 is speculated to be related to high Bi loss due to large exposed surface area of films or the effect of Si. (Although the substrate was coated with Au, it may not be good enough to prevent the films from reaction.) Furthermore, while some unidentified phases were present in sample S1, they were absent in S2, indicating that the atmosphere also has a significant influence on forming the single phase of BFO.

Figure 2 presents SEM images of 1D nanostructures of BFO for samples S1 (Fig. 2(a)) and S2 (Fig. 2(b)). As observed, it is interesting to point out that the morphologies and dimensions of these two 1D nanostructures of S1 and S2 are quite different, indicating that the oxygen partial pressure plays a key role in determining the morphologies of the nanowires or nanorods. The nanowires of S1 has an almost identical diameter of B50 nm and length of 1.5–5 μm, and its morphology is bamboo-like with several ligaments connected whereas S2 has longer nanorods of 200–400 nm in diameter and 10–20 μm in length with smooth surfaces. It should be noted that while some individual nanowires or nanorods were scattered on the substrate, most of them grow outwards from a heavily aggregated matrix.

In order to further analyze the crystalline 1D nanostructures, high-resolution TEM was employed to characterize both samples, shown in Figs. 3 and 4. The detailed morphology of sample S1 was shown in Fig. 3(a), where the heavily aggregated matrix is also present but less than S2, and 1D nanostructures grow outwards from the matrix. The structure of a typical individual 1D nanowire was further analyzed by a selected-area electron diffraction (SAED) pattern at a zone axis of [100] shown in Fig. 3(b). The sharp diffraction spots not only indicate a single-crystalline structure but also were identified as an orthorhombic structure of Bi$_2$Fe$_4$O$_9$, with a space group of Pbam and lattice parameters of a57.94 Å, b58.44 Å, and c56.01 Å in good agreement with other report. This was further confirmed by high-resolution TEM lattice image shown in Fig. 3(c), where plane spacings of 0.605 and 0.44 nm corresponding to {001} and {020} planes, respectively, were determined.

While Bi$_2$Fe$_4$O$_9$ was observed in S2, its nanorods were confirmed as BFO, which can be attributed to the lower oxygen pressure suggested by other reports. Thus, the oxygen partial pressure plays a key role in not only the formation of phases but also the determination of the morphologies of single-crystalline 1D nanostructures. Moreover, the related mechanisms of the carbon-assisted synthesis of inorganic nanowires gave a reasonable interpretation for the development of Bi$_2$O$_3$ nanowires synthesized by a citrate process. Therefore, the development of anisotropic 1D BFO can be explained as follows. There are three key elements for the development of the 1D BFO to be successful:
first, homogeneous mixing at an atomic level lowering the formation temperature of BFO nuclei, second, nanofilm hindering the development of bulk powders, and third, lower oxygen partial pressure retaining residue carbon for assisting in forming vapors of suboxides of Bi and Fe. It should be pointed out that Bi metal may develop, which would become liquids at lower temperatures <300°C.15 This can explain the observed heavily aggregated matrixes. On reaching the formation temperature of BFO at 600°C, the nuclei of BFO would develop, and vapors of suboxides of Bi and Fe would deposit on those nuclei and react to form the 1D nanostructures. Basically, the vapor–solid mechanism proposed in the carbon-assisted method can rationalize the formation of 1D nanostructures of BFO and Bi2Fe4O9 in this investigation. The possible reactions are proposed as follows, where two suboxides, BiOx and FeOy via the reactions of carbothermal reduction, are taken into account:

\[
2\text{BiO}_x(v) + 4\text{FeO}_y(v) + \frac{9 - 2x - 4y}{2}\text{O}_2(g) \rightarrow \text{Bi}_2\text{Fe}_4\text{O}_9(s) \quad (1)
\]

and

\[
\text{BiO}_x(v) + \text{FeO}_y(v) + \frac{3 - x - y}{2}\text{O}_2(g) \rightarrow \text{BiFeO}_3(s) \quad (2)
\]

where s, g, and v represent solid, gas, and vapor, respectively. Reactions (1) and (2) depend on the oxygen partial pressure.

IV. Conclusions

We highlight that for the first time, 1D nanostructures of BFO and Bi2Fe4O9 can be synthesized by a template-free novel route via soft chemistry with the precursor in a thin-film form, which provides possible mass-production and low-cost process. The oxygen partial pressure plays a key role in not only the formation of phases but also the determination of the morphologies of single-crystalline 1D BFO and Bi2Fe4O9. For S1 sample, nanowires of Bi2Fe4O9 with bamboo-like morphology and larger dimension with a diameter of 50 nm and length of 1.5–5 μm can be obtained. By contrast, nanorods of BFO were achieved under lower oxygen partial pressure for S2 sample, possessing smooth surface with dimension of 200–400 nm in diameter and 10–20 μm in length. The development of 1D nanostructures of BFO and Bi2Fe4O9 is suggested via the vapor–solid mechanism.
Reviewing the Hegemonic Governance: Power Downfall and Authority Eroding

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International Relations generally defines the hegemony as an international order within which one state constitute her dominance with power supremacy. This idea excludes the possibility of peaceful hegemonic transformation by empathizing the importance of military supremacy and coercive ruling.

This paper argues that the hegemonic ruling is a kind of domination, which refers to the hegemonic status in the international system as well as the obedience of subordinated state to the hegemonic leadership. The construction of hegemonic leadership, no matter it is built through the relative supremacy of coercive or institutional capabilities, echoes the authority that are vital to the status of international hegemony. Therefore this paper argues that the transformation of hegemonic power has correlated with the relative power supremacy, the obedience of subordinated states as well as the legitimacy of hegemonic ruling.
A Dose-Ranging Study of the Efficacy and Tolerability of Entecavir in Lamivudine-Refractory Chronic Hepatitis B Patients

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1. Introduction

Chronic hepatitis B infection affects more than 350 million people worldwide and lead to high morbidity and mortality due to the development of chronic liver disease, cirrhosis and HCC. In Taiwan, the prevalence of CHB is 15%~20% with about 3 million chronic HBV carriers. The high prevalence of CHB somehow arise intensive clinical trials of new drugs and therapies in Taiwan.

Two groups of CHB treatment have been practiced by physicians currently: interferons and nucleotide/nucleoside analogues (NAs). Although interferons lead to high HBeAg seroconversion rates, it is poorly tolerated and expensive. Lamivudine (LMV) is the first NA introduced and present high short-term efficacy. However, drug resistance develops after continuous treatment of LMV. It is principally associated with amino acid substitutions in the conserved tyrosine–methionine–aspartate–aspartate (YMDD) motif. LMV resistance occurs with the rebound in viral load, elevation of alanine aminotransferase (ALT) and increases the risk of liver diseases. The strategy toward LMV-resistant patients had been a dilemma. Long-term LMV therapy increased the occurring rate of resistance, but discontinuation of the therapy was associated with a significant increase in viral replication and flare of ALT levels. Thus, LMV therapy was often continued in LMV-refractory patients because viral loads may remain lower than pretreatment levels.

Entecavir (ETV) is a potent and highly selective inhibitor of HBV, and it has been reported to produce less drug resistance among several NAs introduced after LMV. The activity of ETV was initially addressed by animal models of viral hepatitis, and subsequently in NA naïve patients with CHB infection. Two phase II clinical trials showed the superior efficacy of ETV than LMV. In this multicenter and multinational clinical study, we aimed to assess the efficacy and safety of ETV versus continued LMV in patients with CHB who had documented LMV-associated mutations.

2. Results

We conducted a randomized and double-blind phaseII study. It is a dose-ranging trial comparing 3 doses of ETV monotherapy with continued LMV in adult LMV-refractory CHB patients. Patients enrolled in this study received 1.0, 0.5, and 0.1 mg ETV or 100 mg LMV daily for up to 76 weeks. Investigation of virologic and biochemical responses showed that the efficacy of ETV appeared with dose- and time-dependent manner (Fig.1, 2).
Virologic response was determined by bDNA assay after 24 weeks of study treatment (week-24), and a significant greater proportion of patients in the ETV 1.0 mg (79%) and 0.5 mg (51%) groups achieved low HBV DNA level (<0.7 MEq/ml by bDNA assay) compared with the LMV group (13%). At week-48, significant greater proportion of ETV 1.0 mg (26%) and ETV 0.5 mg (26%) groups achieved low HBV DNA by PCR assay (<400 copies/mL) compared with LMV group (4%), but no significant virologic response was observed in ETV 0.1 mg group. Normalization of ALT levels indicating biochemical response was detected significantly more in all ETV groups than LMV groups by 48 weeks (Fig. 2). Serologic response was also observed by determination of serum HBeAg and HBeAg antibody at week 48. However, among patients identified as HBeAg positive at baseline, no more than 11% of the patients in any treatment group lost HBeAg or achieve seroconversion. There were no significant differences in this parameter among all treatment groups.

A complete response (undetectable HBV DNA levels by bDNA assay, normal ALT levels, and HBeAg negative) was achieved by significantly greater proportions of patients in the ETV 1.0 mg (29%) and 0.5 mg (19%) groups than in the LMV 100 mg (4%) group. Rare viral rebounds and drug resistances were observed in ETV 1.0 mg group through 48 weeks; the treatment was also well tolerated with safety profile similar to that of LMV. Based on
these results, ETV treatment with dose of 1.0 mg was select to be used in subsequent phase III study. The efficacy of ETV and the impact of drug resistance over longer period would be investigated in the larger phase III study.

In conclusion, ETV treatment for up to 79 weeks had reduced viral load, normalized serum ALT levels in majority of patients who had previously failed to respond to LMV therapy. Of the three doses used in this trial, ETV 1.0 mg daily showed the most profound and consistent antiviral activity with good tolerability. Therefore, ETV therapy (with dose of 1.0 mg) was then considered as one appropriate therapy for LMV-refractory CHB infection.
Inhibition of CD36-dependent phagocytosis by prostaglandin E2 increases incidence of endometriosis

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Endometriosis, defined as the presence of endometria-like tissues outside of uterine cavity, is a highly prevalent, complex disease that causes chronic pelvic pain, dysmenorrhea, dyspareunia, and infertility. Endometriosis affects more than 10% of women of reproductive age; however, the etiology of endometriosis is still poorly defined. We hypothesized that the inability of immune system to effectively remove retrograded tissues is an important factor to allow the implantation and growth of retrograded tissues. During endometriosis development, immune cells are recruited to the peritoneal cavity due to inflammation. Among these immune cells, macrophages are the dominant cell type in the peritoneal cavity; they are involved in phagocytosis, especially in cleaning retrograded endometrial debris. However, due to some as yet unknown mechanism, macrophages may fail to phagocytose the retrograded tissues and thus allow the implantation and proliferation of endometriotic lesions.

The phagocytic function of macrophages is mediated via at least two lines of mechanisms. The first line of mechanism is the secretion and activation of matrix metalloproteinases (MMPs) to break down the extracellular matrix of foreign entities. The second line of phagocytic activity involves the expression of scavenger receptors on the macrophages to enhance the uptake and degradation of cell debris. Our previous study demonstrated that MMP-9 is downregulated in peritoneal macrophages isolated from patients with endometriosis (1). In these two papers, we discovered that the scavenger receptor, CD36, is markedly reduced in macrophages of patients with endometriosis and the loss of CD36 is associated with immune dysfunction and endometriosis development.

CD36 belongs to the scavenger receptor family that participates in the phagocytosis of apoptotic cells by macrophages. In peritoneal macrophages derived from endometriosis patients, the level of CD36 is reduced, which results in the loss of proper phagocytic ability. Normal macrophages (with high CD36 levels and great phagocytic ability) can be converted to endometriotic-like macrophages by simply inhibiting CD36 expression or blocking the function of CD36. In contrast, the ectopic expression of CD36 is sufficient to restore the phagocytic ability of endometriotic macrophages.

We further discovered that loss of CD36 expression in macrophage is due to the action of prostaglandin E2 (PGE2). PGE2 is a versatile eicosanoids that regulates numerous biological processes. In the peritoneal fluid of women with endometriosis, concentration of PGE2 is elevated due to overexpression of cyclooxygenase (COX) in ectopic endometriotic tissue and peritoneal macrophage (2, 3). The elevated concentration of PGE2 inhibits the expression of CD36, which results in reduced phagocytic ability. We use a mouse model to prove that PGE2 is the primary factor that causes immune dysfunction and the development of endometriosis. Mice that received intra-peritoneal injections of small pieces of endometrial tissues from donor mice developed endometriotic lesion-like cysts. In the
transplanted mice, the concentration of PGE2 in the peritoneal fluid was greater than that in sham control mice. The injection of PGE2 into the peritonea of recipients increased the number and size of cysts while treatment with COX inhibitors inhibited the development of cysts. As expected, peritoneal macrophages isolated from PGE2-treated mice express less CD36 protein and have reduced phagocytic ability while those from COX inhibitor-treated mice have increased CD36 expression and phagocytic ability.

Putting together our previous and current findings, it is clear that PGE2-controlled CD36 expression plays an indispensable role in controlling phagocytic ability of macrophage and the development and severity of endometriosis. In lights of our current results, restoring or enhancing the phagocytic capability of macrophages by targeting the signaling pathway of PGE2 may represent a new direction of thinking in developing novel strategies against endometriosis.

![Figure](image.png)

**Figure:** Schematic model illustrates inhibition of CD36 and MMP-9 by PGE2 results in formation of endometriosis.

**References**

