throughout this study is only 27 Hz, but this can be attributed to our use of an iron-cored electromagnet to apply the rotating field. If these devices were mounted on a high-frequency stripline, operating speed would ultimately be limited by the domain wall propagation time through a single gate. For domain wall mobility, \( \mu = 30 \text{ ms}^{-1} \text{ Oe}^{-1} \) (23), and current experimental conditions, we calculate an operating frequency of \( >200 \text{ MHz} \) for devices with a 1-\( \mu \)m radius of curvature. This operating frequency will increase as the size of the gate is further reduced. We estimate the switching energy of the magnetic NOT gates presented here to be 35 eV per transition (24) (1400\( kT \), where \( k \) is Boltzmann’s constant and \( T \) is room temperature), indicating very great stability of data against thermal loss.

A particularly interesting feature of these NOT gates is that they can perform real logic operations on real data without the use of any semiconductor material. This makes scaling to the nanoscale very simple: first, because of the much higher carrier density in metals than in semiconductors; and second, because of the lack of multilayer heterostructures requiring precise alignment. Domain wall widths should not limit this miniaturization because we expect their value to decrease with track widths, tending to the exchange length (5 nm for Permalloy) as track widths approach the film thickness. However, it is currently unclear whether miniaturization will cause appreciable domain wall pinning at defects.

Three further logic elements are required in addition to the NOT gate and shift register described here in order to make a fully universal logic architecture. These are a two-input logic gate that performs an AND, OR, or XOR function; a fan-out structure that converts one domain wall into two walls; and a structure that allows magnetic tracks to cross over each other. An advantage of the rotating clock field is that domain walls move in orthogonal directions at different times. Consequently, it may be possible to cross two tracks in the same plane without interference of the magnetic signals. Domain wall replication should be possible by simply splitting a magnetic track into two branches. The extra energy needed to create the second domain wall comes from the work done by the applied magnetic field against the domain wall pinning force at the junction. The opposite structure, in which two tracks feed into one, may be used to achieve the two-input logic function, using the wire-OR method from microelectronics. In this case, some magnetic biasing will also be required, analogous to the pull-up resistor in the wire-OR scheme.

For a fully functioning nanomagnetic logic system, it will also be necessary to interface conventional electronic signals. Data can be written into the magnetic structures by a current-carrying stripline; and data can be read out by incorporating spin tunnel junctions or spin valves into magnetic tracks or, alternatively, by measuring domain wall resistance.

**References and Notes**

18. The magnetization transitions shown in Fig. 2C indicate that domain walls require a parallel magnetic field of just 3 Oe to propagate in continuous wire sections, which is when the orthogonal component of the rotating field is close to its maximum value.
21. In the previous case of one NOT gate in a feedback loop, no pulsed-field initialization was required owing to the simpler topology involved.
24. Switching energy was calculated with the area of the magnetization hysteresis loop and suitable bulk constants.
25. This work was supported by Eastgate Investments Ltd.

R E P O R T S

Ferroelectric Bi\(_{3.25}\)La\(_{0.75}\)Ti\(_3\)O\(_{12}\) Films of Uniform a-Axis Orientation on Silicon Substrates

Ho Nyung Lee, Dietrich Hesse, Nikolai Zakharov, Ulrich Gösele

The use of bismuth-layered perovskite films for planar-type nonvolatile ferroelectric random-access memories requires films with spontaneous polarization normal to the plane of growth. Epitaxially twinned a-axis-oriented La-substituted Bi\(_3\)Ti\(_5\)O\(_{12}\) (BLT) thin films whose spontaneous polarization is entirely along the film normal were grown by pulsed laser deposition on yttria-stabilized zirconia-buffered Si(100) substrates using SrRuO\(_3\) as bottom electrodes. Even though the \( \langle 110 \rangle \) orientation competes with the \( \langle 100 \rangle \) orientation, epitaxial films with almost pure \( \langle 100 \rangle \) orientation were grown using very thin, strained SrRuO\(_3\) electrode layers and kinetic growth conditions, including high growth rates and high oxygen background pressures to facilitate oxygen incorporation into the growing film. Films with the a-axis orientation and having their polarization entirely along the direction normal to the film plane can achieve a remanent polarization of 32 microcoulombs per square centimeter.

Ferroelectric bismuth-layered perovskite films are being studied for use as nonvolatile digital memories. Polycrystalline films, such as SrBi\(_2\)Ta\(_2\)O\(_6\) (SBT) (1) and La-substituted Bi\(_{3}\)Ti\(_5\)O\(_{12}\), including Bi\(_{3.25}\)La\(_{0.75}\)Ti\(_3\)O\(_{12}\) (BLT) (2), are of great interest in part because of their high fatigue endurance. However, randomly oriented polycrystalline films have certain limitations, and they may have unacceptable cell-to-cell variations when the lateral size of the ferroelectric cells is below 100 nm, as is required for gigabit memories (3).

Conceptually, epitaxially grown films should overcome this nonuniformity problem, and numerous attempts have been made to grow thin films by pulsed laser deposition (PLD) (4–8) as well as other methods (9–12). Because of their highly anisotropic structure [Bi\(_3\)Ti\(_5\)O\(_{12}\) is pseudo-orthorhombic with \( a = 0.545 \text{ nm} \), \( b = 0.541 \text{ nm} \), and \( c = 3.283 \text{ nm} \)], epitaxial thin films of these materials can easily be grown with the \( \langle 001 \rangle \) axis perpendicular to the film plane (i.e., in the so-called c-axis orientation). However, c-axis-oriented films have a negligible polarization component along the film normal, because the vector of the (major) spontaneous polarization in these layered perovskite materials is along the a axis (13, 14). Recent efforts have concentrated on the growth of epitaxial films with non-c-axis orientations.
and more or less equiaxed ones (Fig. 1). The long grains correspond to the (118)-oriented part of the film, whereas the equiaxed grains represent the (100)-oriented part (7, 8, 16). The needle-like (118)-oriented BLT grains occur with four different azimuthal orientations, corresponding to the four possible azimuthal orientations of the SrRuO 3 grains in (110)-oriented SrRuO 3 layers on (100)-oriented YSZ buffer layers (Fig. 1D) (15, 16, 19). As a consequence, azimuthal difference angles of 19.5° occur between the needle-like (118)-oriented BLT grains growing on top of the SrRuO 3 grains.

The optimum substrate temperature for the (100)-oriented growth of BLT was found by depositing BLT films at different temperatures onto YSZ(100) single-crystal substrates covered with (110)-oriented SrRuO 3 layers and determining the volume fraction \( \alpha_{(100)} \) as was low as 4% at \( T = 650°C \) (Fig. 1A) and reached its maximum of 46% at \( T = 765°C \) (20) under the same deposition conditions of \( J = 2.3 \, \text{J/cm}^2, f = 5 \, \text{Hz}, \) and \( P = 40 \, \text{Pa} \). A further increase of \( \alpha_{(100)} \) was possible by reducing the thickness of the (110)-oriented SrRuO 3 electrode layer down to 10 nm, which resulted in an additional increase of \( \alpha_{(100)} \) from 46% to 78%. This drastic effect is most probably due to the thin SrRuO 3 layer being strained as a result of the influence of the lattice mismatch (~6.3%) between SrRuO 3 (\( a = 3.93 \, \text{nm} \)) and YSZ (\( a = 5.14 \, \text{nm} \)) along the direction SrRuO 3 [111] || YSZ[001]. This strain results in an increased SrRuO 3 lattice parameter, which reduces the BLT-SrRuO 3 lattice misfit of nominally +4.6% along the direction BLT[001] || SrRuO 3[001], thus providing better nucleation conditions for (100)-oriented BLT grains relative to (118)-oriented grains. The same effect was observed for BLT films grown on the YSZ-buffered SrTiO 3 substrates. A further increase of \( \alpha_{(100)} \) was achieved by a systematic variation of the other deposition conditions. Finally, a value of \( \alpha_{(100)} = 99% \) was attained at \( T = 765°C, J = 3.4 \, \text{J/cm}^2, f = 7 \, \text{Hz}, \) and \( P = 100 \, \text{Pa} \) (Fig. 1C). Deviations from these conditions resulted in intermediate values of \( \alpha_{(100)} \) as shown in Fig. 1B, where optimum conditions were used but for \( J = 1.7 \, \text{J/cm}^2 \) and \( P = 40 \, \text{Pa} \), resulting in \( \alpha_{(100)} = 48% \).

The high oxygen pressure necessary to grow a axis-oriented BLT films can most likely be explained in terms of effects related to an improved oxygen incorporation into the growing film as a result of increased collisions between vapor and ambient oxygen gas (21, 22). If an enhanced oxidation of bismuth is one such effect, the bismuth desorption from the a axis-oriented BLT films may be reduced as a result. The a axis-oriented BLT films have the Bi 2 O 2 layers perpendicular to the film plane, so that the desorption of bismuth could be rather easy at the relatively high substrate temperature used. In addition, the high laser repetition rate will favor suppression of desorption events by a more frequent supply of ablated species. Moreover, the high film growth rate resulting from the high laser repetition rate probably favors the (100) orientation by a kinetic growth mechanism, as is the case for (110)-oriented TiS 2 films (23) and (100)-oriented YBa 2 Cu 3 O 7–δ films (24–26), both of which involve a layered crystal struc-

**Fig. 1.** (A to C) AFM topography images (5 \( \mu \text{m} \) by 5 \( \mu \text{m} \)) of BLT films grown under different conditions: (A) on SrRuO 3[110]-YSZ(100) at \( T = 650°C, t = 50 \, \text{nm}, J = 2.3 \, \text{J/cm}^2, f = 5 \, \text{Hz}, \) and \( P = 40 \, \text{Pa} \); (B) on SrRuO 3[110]-YSZ(100)-Si(100) at \( T = 765°C, t = 10 \, \text{nm}, J = 1.7 \, \text{J/cm}^2, f = 5 \, \text{Hz}, \) and \( P = 40 \, \text{Pa} \); and (C) on SrRuO 3[110]-YSZ(100)-Si(100) at \( T = 765°C, t = 10 \, \text{nm}, J = 3.4 \, \text{J/cm}^2, f = 7 \, \text{Hz}, \) and \( P = 100 \, \text{Pa} \). In (C), the height scale ranges from 0 to 200 nm; the height scale for (A) and (B) is shown at the lower right. (D) Schematic of the diagonal-type rectangle-on-cube epitaxy of SrRuO 3[110] on YSZ(100) with four variants of SrRuO 3 on YSZ, showing the origin of the +20° azimuthal rotation.
ture. Indeed, (100)-oriented films showed a considerably larger film thickness than an almost (118)-oriented film for the same number of laser pulses. This effect is probably due to a higher growth rate along the $a$ axis and/or a reduction of desorption.

The crystallographic orientation, epitaxial relationship, and microstructure of $a$ axis–oriented BLT films with different values of $\alpha_{(100)}$ were analyzed by XRD scans and transmission electron microscopy (TEM) in plan view and cross section. An XRD $0$-$2\theta$ scan (Fig. 2A) and a pole figure of the BLT 117 reflection (Fig. 2B) were recorded from the sample shown in Fig. 1C ($\alpha_{(100)} = 99\%$). The BLT 200/020 and the YSZ 200 and 400 peaks are clearly seen. SrRuO$_3$ peaks are not visible because the layer thickness is very low (10 nm). The full width at half-maximum (FWHM) of the 200/020 peak in an $\omega$ scan was $0.8^\circ$, demonstrating the good crystallinity. Detailed XRD investigations showed that the BLT film has lattice constants $a = 0.542$ nm, $b = 0.541$ nm, and $c = 3.271$ nm. Several pole figures and $\phi$ scans were recorded. Figure 2B is a pole figure using the 117 reflection of the BLT film shown in Figs. 2A and 1C. There are four sets of peaks at $\psi \approx 57^\circ$, confirming the (100) orientation of the film, because the angle between the (100) plane and the diffracting (117) plane is $56.9^\circ$. Each set of peaks, however, consists of two subsets (of two peaks each) with an offset $\Delta \phi \approx 20^\circ$ as marked in Fig. 2B, showing that four different azimuthal domains are occurring within the same $a$ axis–oriented BLT film as a result of the four azimuthal domains within the underlying SrRuO$_3$ electrode layer (Fig. 1D). This mix of four azimuthal domains (or twins) obviously gives rise to the grainy structure of the films (compare to Fig. 1C)—a fact that otherwise would be difficult to understand in a uniformly (100)-oriented film. The corresponding epitaxy relationship is BLT(100) $\parallel$ SrRuO$_3$(110) $\parallel$ YSZ(100) $\parallel$ Si(100); BLT[001] $\parallel$ SrRuO$_3$[001], where SrRuO$_3$(111) $\parallel$ YSZ(011) $\parallel$ Si(011) including four azimuthal domains ($15, 16$).

TEM investigations confirmed the $a$-axis orientation, as shown in Fig. 3. Both plan-view and cross-sectional TEM images of a BLT film with $\alpha_{(100)} = 90\%$ clearly show the (002) lattice fringes. As plan-view TEM images (Fig. 3, A and B) show, the $c$ axis of the $a$ axis–oriented grains indeed lies in the film plane. As a result of the four azimuthal orientations discussed above, the electron diffraction pattern (Fig. 3A, inset) consists of four rows of BLT (002) reflections that include azimuthal difference angles of $\sim 20^\circ$ when considered pairwise. Cross-section TEM images of the entire BLT-SrRuO$_3$-YSZ-Si heterostructure (Fig. 3C) and high-resolution TEM investigations of cross-section samples (Fig. 3D) confirm the (100) orientation of the film. In the (100)-oriented BLT grain marked “$M$” in Fig. 3C, the (002) BLT fringes extending vertically (at an angle of $90^\circ$ with respect to the film plane) can clearly be recognized. The inset shows the corresponding diffraction pattern. The small grain marked “$N$” is a (118)-oriented grain in which, upon close inspection, the (002) fringes can be seen at an angle of about $45^\circ$ with respect to the film plane. In the rest of the visualized film area in Fig. 3C, no fringes can be seen, because the
other domains (twins) have different azimuthal orientations. Figure 3D shows a high-resolution structure image of a thin area of grain “M,” showing a good correspondence to the inserted structure model.

It is now possible to implement control strategies that yield new modes of spatiotemporal activity (11), suggesting a means for enhancing catalytic efficiencies, and focused laser light has been used to direct wave propagation in this system by thermally altering local catalytic activity (2). Pattern formation (3) and spiral waves (6, 7) in the Belousov-Zhabotinsky (BZ) reaction (8) have also been controlled by using feedback techniques, which point to the possibility of regulating spatiotemporal dynamics in excitable biological tissues. A recent advance in this direction is the control of seizure-like events in hippocampal brain slices with adaptive electric fields (9). The ability to manipulate spatiotemporal behavior provides both a means of generating desired dynamical patterns and the tools for probing underlying mechanisms.

Here, we describe the implementation of control methods that yield particle-like waves that propagate in, effectively, user-defined patterns. Unstable waves in the photosensitive BZ reaction (10) are stabilized by global feedback that affects the overall excitability of the medium (11), and the motion of these waves can be calculated using the relation that the high growth temperature most probably does not comply with memory device fabrication, it can probably be reduced by using other oxidants instead of O2, including nitrous oxide (N2O) or nitrogen dioxide (NO2) (29, 30).

20. Although this high growth temperature most probably does not comply with memory device fabrication, it can probably be reduced by using other oxidants instead of O2, including nitrous oxide (N2O) or nitrogen dioxide (NO2) (29, 30).

28. Materials and methods are available as supplementary material on Science Online.
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Orienting Ferroelectric Films

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As silicon technology continues to dominate the microelectronics market, researchers around the world are looking at new ways to combine silicon with other materials in new devices. One of the key goals is the integration of functional materials, such as ferroelectric oxides, with silicon technology to produce commercially viable high-density, nonvolatile memories and other technologies (1).

First and foremost, this integration requires the ability to grow highly ordered thin ferroelectric films on silicon and other semiconductor surfaces. But crystallographic order is not enough: To maximize performance, the films also need to be oriented in particular ways, and the interface between film and substrate must be controlled. On page 2006 of this issue, Lee et al. (2) show how optimal control of crystallographic orientation can be achieved for a class of layered ferroelectrics that have been particularly challenging to grow.

Some ferroelectrics have the perovskite structure (see the upper figure, A); others have perovskite-related structures. The spontaneous polarization of layered perovskite-related ferroelectrics is generally quite small along the c axis but much larger along the a axis. Piezoelectric properties are similarly dependent on direction. This is why researchers are trying to control the crystallographic orientation of films of these materials.

Two important examples are the superconductor YBa2Cu3O7-δ and the ferroelectric Bi4Ti3O12. In the former, three cubic perovskite units are stacked to create a layered structure. In contrast, in Bi4Ti3O12 pyramidal Bi2O2 layers alternate with structurally distinct tripled-perovskite layers (see the upper figure, B). This difference between the two materials is crucial when it comes to controlling their orientation.

In the case of ferroelectric perovskites, high-quality epitaxial films can be grown on silicon through the use of structural templates and chemical buffer layers between the silicon substrate and the ferroelectric film (3–6). The key to controlling their orientation is that the perovskite structure has comparatively little structural anisotropy (it is essentially cubic at the growth temperature) and that the crystallographic orientation and crystalline perfection are therefore controlled by the “template” surface.

When the template surface is a cubic perovskite (or has a similar crystal chemistry in terms of oxygen coordination), epitaxial growth is facilitated. Conductive perovskite layers such as (La,Sr)CoO3 or SrRuO3 can be used to provide a bottom electrode that is also a suitable epitaxial template for growth of the overlying perovskite ferroelectric. The resulting optimally oriented epitaxial layer has improved piezoelectric properties (see the lower figure).

Can analogous “template” approaches be used to grow single-crystalline films of perovskite-related ferroelectrics with controlled crystallographic orientations? In the case of the layered superconductor YBa2Cu3O7-δ, this has been shown to be possible (7, 8) by taking advantage of the tripled perovskite crystal structure of YBa2Cu3O7-δ. Growth at elevated temperatures leads to an epitaxial film oriented with its long (c) axis standing up (perpendicular to the plane of the substrate). By simply reducing the growth temperature by about 100°C, the long axis can be made to lie down (an a axis–oriented film) on the same cubic perovskite surface.

In the case of layered bismuth-based perovskite-related ferroelectrics such as Bi4Ti3O12, however, orientation control through purely thermal means has proven elusive. The difficulty arises from the additional complexity of the crystal structure. The Bi2O2 layers and crystallographic glide planes in these ferroelectrics destroy the in-plane lattice match between the long axis (the c axis) of the ferroelectric and a perovskite substrate.

One tripled-perovskite-layer segment of Bi4Ti3O12 can be well lattice-matched with the perovskite substrate, but the next tripled-perovskite layer will be offset from the substrate, destroying the lattice match for Bi4Ti3O12 growth with its long axis lying down (see the upper figure, B).

Thus, while it is quite easy to grow films of Bi4Ti3O12 in which the long axis stands up (c axis–oriented films) (4, 9), growing a-axis- or b axis–oriented films of layered bismuth-based perovskite-related ferroelectrics has been more difficult. This is especially true when growth on a bottom electrode is required for ferroelectric capacitor-type applications.

The pioneering work of Wu and colleagues (10, 11) demonstrated the epitaxial growth of high-quality a axis– and b axis–oriented Bi4Ti3O12 films on (110) MgO and (110) MgAl2O4 substrates, but not on silicon. Because the films were grown without bottom electrodes, they had to be peeled off from the insulating substrates to make electrical measurements (10).

In the 30 years since then, some progress has been made in tilting the c axis of layered bismuth-based perovskite-related ferroelectrics and growing them on a conductive bottom electrode. Such a geometry is favored for ferroelectric capacitor applications, including memories, which require a bottom electrode for vertical measurements. For example, when the c axis was tilted by ~57° through epitaxial growth on a (111)-oriented conductive perovskite buffer layer, an increase in spontaneous polarization was observed (12). This approach was recently extended to silicon substrates (13). A tilt of 57°, however, is not the full 90° tilt desired for the optimization of...
Microbial Forensics—
“Cross-Examining Pathogens”
Craig A. Cummings and David A. Relman

Microbial pathogens cause disease as a result of their intrinsic adaptive strategy for replication and survival within a host. In a problematic modern world, however, microbial-related disease may also be the consequence of a forced interaction between microbe and host or manipulation of the microbe’s genome by malevolent persons. In the case of both naturally occurring “emerging” infectious diseases, and disease induced by human intent (bioterrorism), it is important to establish “attribution.” When explored in either a scientific or legal courtroom, the source of a pathogen, and its origins and relatedness to other strains and species, reveal mechanisms by which virulence arises and the host-microbial equilibrium becomes disrupted. In the arena of emerging microbial diseases, these critical issues are addressed with increasing frequency using molecular microbial signatures. The study of emerging infectious diseases and new pathogens (1), and the criminal justice system have evolved in a similar fashion: Both have shifted away from reliance on biological phenotypes of the suspected perpetrator, such as fingerprints, and toward more reliable and quantifiable molecular markers, such as polymorphisms (variations) in the DNA sequence.

Comparative genome sequencing, in particular, offers a powerful approach for analyzing genetic variation and relatedness within and between species, and for resolving differences between two strains that superficially look identical. However, the speed of the evolutionary clock (that is, the rate of accumulation of genetic variations) for some microbial species, such as Bacillus anthracis, the causative organism of anthrax, is quite slow. For these organisms, the ability to discriminate between strains has been limited by the paucity of known genetic polymorphisms.

Read and co-workers from The Institute for Genomic Research (TIGR) now report on page 2028 of this issue the comprehensive identification of genetic polymorphisms in two related strains of B. anthracis by comparative full-genome sequencing (2). They compared the Porton isolate of the Ames strain with an isolate from the index case in Florida of the October 2001 mail anthrax attacks (2, 3). Importantly, they introduce a statistical model that distinguishes between true genetic polymorphisms and random sequencing errors. Furthermore, the discriminating power of these polymorphism markers is demonstrated by the typing of closely related B. anthracis strains. Their impressive demonstration of polymorphism detection and analysis, especially in such a genetically homogeneous bacterium, is an important contribution to the molecular typing field. Their work establishes a methodology for the comprehensive identification of sequence polymorphisms and their deployment as typing markers.

Microbial forensics, as we define it, is the detection of reliably measured molecular variations between related microbial strains and their use to infer the origin, relationships, or transmission route of a particular isolate. These variations or markers include genome sequence polymorphisms, which can be detected by direct sequencing or by hybridization-based methods; genomewide patterns of gene expression, which can be easily measured with DNA microarrays; and differences in protein or small-molecule patterns, which can be detected by spectroscopic or other methods. These same techniques can be used to study population structure, species evolution, and acquisition of virulence (4, 5).

The application of molecular markers in forensic studies has led to some high-profile discoveries. For example, the alleged transmission of HIV from a Florida dentist to several patients was supported by sequencing of amplified viral fragments from the dentist and the infected patients (6). Recently, using multiple-locus variable number tandem repeat (VNTR) analysis, the Aum Shinrikyo B. anthracis bioterrorism strain was identified as the veterinary vaccine strain, Sterne 34F2 (7). Although TIGR’s interest in B. anthracis genomics predates October 2001, the choice of the Florida strain for analysis was influenced by the ensuing public health and criminal investigations. Both criminal investigation of bioterrorism attacks and studies of naturally occurring disease outbreaks will continue to be important applications of this technology. In fact, in some cases, it is difficult at the outset to distinguish mother nature from man as the perpetrator. The investigation of the West Nile virus outbreak in the northeastern United States in 1999 eventually revealed a single strain from birds and humans in New York with greatest similarity to a strain originally isolated from a dead goose in Israel, leading to the conclusion that the outbreak was of natural origin (8, 9). Cultivation of an organism may not be necessary for genotyping: Random or targeted genome amplification from picogram quantities of DNA (10) may facilitate microbial forensic analysis of micromanipulated single cells, and direct analysis of clinical specimens.

How can we improve upon the use of polymorphic sequence markers to distinguish and establish relationships between strains reliably and unambiguously? Comparison of two strains will identify only a