analyses. The authors found that existing algorithms for the analysis of data from single-cell RNA sequencing routinely discard information about immature, unspliced mRNA. By completely reworking their computational pipelines to salvage these data, they could recover information about both spliced and unspliced forms of each transcript, and therefore predict RNA velocity.

As is often the case, much effort and technical ingenuity were required for La Manno *et al.* to translate their initial idea into a robust set of working algorithms. Among the challenges that they had to overcome was the fact that measuring gene expression in single cells can be noisy. This is because most of the mRNA molecules in each cell are lost in the attempt to sequence them, leaving researchers with only a patchy picture of gene expression. Another challenge was determining how to infer the baseline ratio of spliced to unspliced transcripts for each gene when it is undergoing stable transcription. The authors needed to apply cutting-edge approaches in statistics and machine learning to solve these problems.

La Manno and co-workers beautifully demonstrate the usefulness of their approach using both published and newly collected data sets. For instance, they showed that RNA velocity could accurately detect the increases and decreases in gene expression that cells in the embryo are known to undergo as they differentiate from a cell type called a neural crest cell into chromaffin cells of the adrenal glands. The authors also used RNA velocity to investigate gene-expression dynamics in the developing hippocampus of the mouse brain, during intestinal stem-cell differentiation and more. This array of examples suggests that the method will have wide value. Among the group's most important achievements was the analysis of human embryonic tissue, in which other forms of dynamic measurement would be very difficult, or even impossible, to carry out because of the technical and ethical issues that are associated with studying living human embryos.

Developing an analysis of RNA velocity for single cells is a major breakthrough. But, of course, it has limitations. By its nature, RNA velocity cannot actually track a given cell over time, it is limited to the study of mRNA, and it does not provide information about the spatial organization of cells. These limitations could be restrictive when exploring phenomena in stem-cell biology, embryonic development or the onset of disease, which are likely to depend on the lineage and arrangement of cells, and which can be driven by mechanisms other than transcription, including protein phosphorylation. The method gives only a probabilistic description of cell dynamics, which is pieced together from instantaneous velocities. As a result of these limitations, there is little doubt that the spatio-temporal expression dynamics of genes will continue to be studied using complementary methods such as live imaging.

Nonetheless, the ability to infer true, instantaneous RNA velocities in single cells is a leap forward for studies of gene-expression dynamics on the whole-genome scale. Indeed, the authors' approach has already been applied by other researchers[6]. In the immediate future, I can foresee RNA velocity easily becoming an essential tool for single-cell analysts. ■

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This article was published online on 8 August 2018.

CONDENSED-MATTER PHYSICS

Electric and magnetic domains inverted

Certain materials contain both electric dipoles and magnetic moments. An experiment demonstrates that these properties can be coupled in previously unrecognized ways, leading to advanced functionality. **See Letter p.466**

JOHN T. HERON & JULIA A. MUNDY

The ability to use an electric or magnetic field to manipulate the orientation of electric dipoles or magnetic moments associated with atoms, ions or molecules in a material provides a vast array of functions. In rare materials called magnetoelectric multiferroics, the dipoles are intimately coupled to the moments, and a single field can control both[1]. After the field is applied, however, the dipoles and moments typically all have the same orientation, and the original pattern that they formed is lost. On page 466, Leo *et al.*[2] show that, in two particular materials, a magnetic field can flip each of the dipoles or moments while preserving the structure of the original pattern. The work illustrates how the complex coupling in these materials could be used to uncover other, previously unobserved electric and magnetic effects.

When most materials are placed in an electric field, their positive and negative charges shift by a tiny amount (less than 0.1 nanometres, which is about the radius of an atom). This microscopic movement leads to a macroscopic, measurable response: an electric polarization. In ferroelectric materials, however, clusters of ions assemble in a way that results in electric dipoles and a macroscopic polarization, even in the absence of an electric field.

Ferroelectrics are typically composed of domains — mesoscopic regions, often 100 nm to several micrometres in size, in which dipoles are aligned. Applying a strong electric field to a ferroelectric material causes all of the dipoles

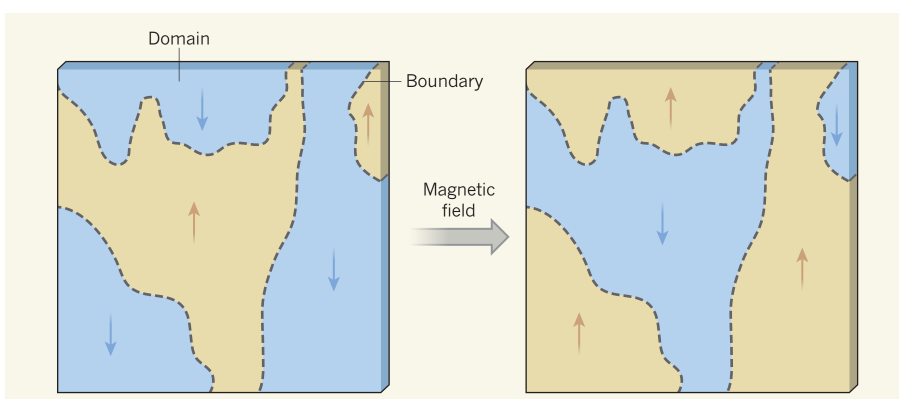

Figure 1 | Domain inversion. Certain materials are composed of regions of aligned electric dipoles or magnetic moments, known as domains. The arrows indicate the direction of the dipoles or moments in each domain. Leo *et al.*[2] show that, in two fundamentally different materials, a uniform magnetic field can reverse these directions, without changing the boundaries between the domains — rather than causing all the dipoles or moments to point in the same direction.

to point in a single direction, erasing both the original domain pattern and any engineered functions of the domain structure or of the boundaries between domains[3].

There is a magnetic analogue to this phenomenon. A ferromagnetic material contains concerted arrangements of electron magnetic moments, which are located on specific sites of the material's atomic lattice. These moments generate a macroscopic magnetization that can be controlled using a magnetic field. Most ferromagnetic materials are also composed of mesoscopic domains.

Despite the apparent macroscopic similarities between ferroelectricity and ferromagnetism, materials that exhibit both phenomena, known as multiferroics, are exceedingly rare[4]. Magnetoelectric materials — those in which electric and magnetic properties are coupled, but that do not necessarily possess ferroelectric or ferromagnetic order — are also uncommon. Most exotic are magnetoelectric multiferroics, in which ferroelectricity and ferromagnetism are intrinsically coupled. This coupling holds great potential for next-generation devices, such as data-storage units that run on ultra-low power, highly sensitive magnetic-field detectors[5] and energy-efficient nanoscale motors[6]. Much of the research focus on magnetoelectric multiferroics so far has centred on the control of magnetism using electric fields of ever-decreasing strength[7].

Identifying multiferroics is a great challenge. In the current work, however, Leo and colleagues recognize that once such a material is identified, the complex parameters that give rise to this state of matter can be combined or manipulated in completely distinct ways. They illustrate this new way of thinking about multifunctional materials by considering the intertwined electric and magnetic properties of two such materials, imaging the domain structure while applying an external magnetic field.

The authors observed domains in the materials using a technique called optical second-harmonic generation. In this approach, two photons interact with a material to produce a single photon that has twice the frequency of the incident photons. The technique is sensitive to the spatial and magnetic (point-group) symmetry of the material's lattice, making it a powerful probe of structural, electronic and magnetic order. Of particular relevance to the authors' work is that second-harmonic generation is sensitive to magnetism even when the magnitude of the magnetic moments in the material is 1,000 times smaller than that of the moments in a typical ferromagnet[1,8] — a sensitivity that can be matched by few complementary techniques.

Leo *et al.* studied ferromagnetic domains in one of the materials as a perpendicular magnetic field was swept across the material, and ferroelectric domains in the other material during application of a parallel magnetic field. They found that when the field was gradually changed from one direction to the opposite direction, the boundaries between the domains moved. But, remarkably, when this process was complete, the polarization or magnetization of each domain was reversed and the original domain pattern was recovered (Fig. 1).

Such an effect is similar to switching the black and white squares of a chessboard, without changing the boundaries between the squares. It is in sharp contrast to what is usually observed when a uniform field is applied to a material: an alignment of all the electric dipoles or magnetic moments, or in the chess analogy, a conversion of all the squares to a single colour.

The authors explain the inversion effect as being due to the coupling of three order parameters — variables that describe the alignment of dipoles or moments in a material. The first parameter represents the observed domain distribution. The second parameter, which is unaffected by the applied magnetic field, imprints the original domain pattern onto the first parameter. Finally, the third parameter, which is directly controlled by the field, causes the observed domain distribution to be inverted.

Leo and colleagues' results suggest that the coupling of multiple order parameters is generic, but it remains to be seen how frequently it manifests in other materials. Perhaps more importantly, however, the study shows how multiple order parameters in certain materials can be exploited. Although magnetoelectric multiferroics have garnered much interest because of their strongly coupled magnetization and ferroelectric polarization, future work might find ways to combine the many order parameters in these materials to derive new functions. Precisely what other relationships might be lurking between these parameters is uncertain. Nevertheless, the authors' demonstration of domain-pattern inversion resulting from the coupling of three order parameters is a big step forward in our understanding of complex coupling in multiferroic materials. ■

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MICROBIOLOGY

Checkpoint for gut microbes after birth

The route to the establishment of a beneficial microbial community in the gut after birth is not fully understood. It now emerges that a gut-cell protein in newborn mice shapes the long-term composition of this community. **See Letter p.489**

ANDREW J. MACPHERSON & STEPHANIE C. GANAL-VONARBURG

Although people think of divorce, bereavement and job loss as major life events, perhaps no change in a person's life is quite as dramatic as the moment of their birth. As a baby exits the birth canal, the newborn infant loses placental support, and the respiratory system and gut must start to function. Moreover, both beneficial and pathogenic microorganisms will be encountered, and will compete to colonize the baby's body. Writing in *Nature*, Fulde *et al.*[1] report that the intestinal receptor protein TLR5 is involved in actively shaping the long-term composition of the gut microbial community, termed the microbiota, in newborn mice.

The bacterial colonization of the gut normally starts in the birth canal[2]. Then, successive waves of increases and decreases in microbial species occur during a period of microbiotal change, which lasts approximately 18 months in humans[3]. Nutritional conditions and immune-system development in early life both affect gut colonization, with far-reaching consequences for later growth and health. Tragically, more than 15 million children around the globe under the age of 5 years suffer from malnutrition and severe wasting (go.nature.com/2n3rxob). This is caused by a combination of insufficient calorie intake and a type of immune dysfunction that is linked to abnormal bacterial colonization in the gut, called environmental enteropathy. The correct functioning of immune cells called B cells and T cells is partly determined by exposure during their early development to non-pathogenic microbes, which can therefore have long-term consequences for the composition of microbial