MERS (Middle East respiratory syndrome) coronavirus first emerged in 2012 and causes severe acute respiratory illness.

4000 genomic traits (such as amino acid bias or codon pair bias) were deployed in training, optimization, and validation algorithms. This markedly improved the predictions of vector type (to 91% accuracy) and host type (to 72% accuracy). Although the genomic traits themselves show strong phylogenetic signals, this result suggests that they also contain information not (or not easily) captured by analyses based on relatedness alone.

The algorithms can be used to predict unknown natural reservoirs or vectors. For example, they predict that Bas-Congo tibrovirus is transmitted by midges from an artiodactyl (even-toed ungulates) reservoir and that two species of ebolavirus—Bundibugyo and Taï Forest—have primate reservoirs. These assignations should be regarded as hypotheses to be tested empirically. Some predictions may be helpful in confirming or challenging current understanding. For example, they predict that Crimean-Congo hemorrhagic fever virus is not vector-borne, although it is thought to be transmitted by ticks.

Babayan *et al.* propose that their methodology could also be used for rapid assessment of emerging viruses of which we have no prior knowledge [a scenario that the World Health Organization calls "Disease X" (*7*)]. In the early stages of a public health emergency, knowledge of reservoir host and/or vector species could be vital for effective outbreak management. In this situation, the stakes are higher and greater caution is appropriate. It is helpful that the in silico predictions are assigned a confidence level and that the next best possibilities are identified: 95% confidence in a particular vector type is more useful than 60% confidence in a choice of three different host types. However, even if the reservoir host and/or vector are predicted with high confidence, the taxonomic resolution is currently insufficient; we need to identify species rather than broadly defined "types" such as sandflies or rodents. Even then, empirical confirmation would still be necessary.

Could confidence and resolution of the predictions be improved in the future? Methodological advances may help; Babayan *et al.* found variation in the performance of different machine-learning algorithms. However, the key requirement is for more and better-quality data, and here there is much still to do. It is likely that we currently know of only a small fraction of RNA viruses of mammals and birds (*8*). Finding and sequencing this hidden diversity of viruses would be an enormous undertaking (*9*), but the advent of metagenomics (techniques for sequencing all the genetic material in a sample) makes it considerably more feasible (*10*).

A collection of virus sequences from animal reservoirs would be especially valuable if it could be used to predict whether a virus is capable of infecting humans, even before any human cases are detected (*11*). Babayan *et al.* did not look for predictors of human infectivity, and it is not clear whether their approach would predict preadaptation to a potential new host as well as it predicts adaptation to an established reservoir host.

More focused approaches may be needed. For example, a key determinant of host range is cell receptor usage; host switching has been linked to a virus gaining cell entry via a phylogenetically conserved host receptor (*12*). Cell receptor usage also determines tissue tropism, and this is associated in turn with both pathogenicity and transmissibility, two traits that are highly relevant to the level of threat to human health. Predicting cell receptor usage directly from virus genome sequences is beyond our current capabilities, but undeniably the genome does contain the information. As our knowledge of viral cell receptors improves and the number and diversity of virus genome sequences accumulates, machine-learning approaches applied to protein-protein interactions (*13*) may provide a way forward.

Currently, our ability to predict human infectivity among RNA viruses is limited to (mostly weak) ecological correlates (*14*), and the value of massive investment in virus discovery and sequencing programs is hotly debated (*9*, *15*). This debate is timely, however, given that databases are growing fast and analytical methods are evolving rapidly. The study of Babayan *et al.* is a valuable step forward and hopefully presages further advances in our ability to extract information of public health value directly from virus genome sequences. ■

REFERENCES

1. S. S. Morse *et al.*, *Lancet* **380**, 1956 (2012).
2. M. E. J. Woolhouse, L. Brierley, *Sci. Data* **5**, 180017 (2018).
3. S. A. Babayan *et al.*, *Science* **362**, 577 (2018).
4. J. S. M. Peiris *et al.*, *Lancet* **361**, 1319 (2003).
5. B. Hoffman *et al.*, *N. Engl. J. Med.* **373**, 154 (2015).
6. M. E. J. Woolhouse *et al.*, *Sci. Transl. Med.* **7**, 307rv5 (2015).
7. World Health Organization, *A Research and Development Blueprint for Action to Prevent Epidemics* (2018); www.who.int/blueprint/en/.
8. J. L. Geoghegan, E. C. Holmes, *R. Soc. Open Biol.* **7**, 170189 (2017).
9. D. Carroll *et al.*, *Science* **359**, 872 (2018).
10. P. Simmonds *et al.*, *Nat. Rev. Microbiol.* **15**, 161 (2014).
11. G. T. Keusch *et al.*, *Sustaining Global Surveillance and Response to Emerging Zoonotic Diseases* (National Academies Press, 2009).
12. M. E. J. Woolhouse, J. L. Ashworth, *Biochemist* **39**, 8 (2017).
13. B. Kim *et al.*, *J. Bioinf. Comp. Biol.* **15**, 1650024 (2017).
14. K. J. Olival *et al.*, *Nature* **546**, 646 (2017).
15. E. C. Holmes *et al.*, *Nature* **558**, 180 (2018).

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PHYSICS

Disorder at the border

The photoinduced phase transition in vanadium oxide involves ultrafast loss of coherence

By **Andrea Cavalleri**[1,2]

How does an ensemble of closely packed atoms rearrange when a solid undergoes a morphological change? Do the atoms follow a common, synchronized path, or do they move independently into their new positions? These elusively simple questions underpin many key problems in modern condensed-matter physics and also affect fields as far removed as soft-matter research and biological sciences. On page 572 of this issue, Wall *et al.* (*1*) use the Linac Coherent Light Source x-ray free-electron laser (*2*) to provide decisive new information on the nature of a structural phase transition. They study the time evolution of the monoclinic phase of crystalline vanadium dioxide (VO_2) after it is destabilized with light (*3*–*5*). Previous studies have assumed that this photoinduced structural transition proceeds coherently, that is, as a concerted structural rearrangement in which all atoms move at once (*6*, *7*). Wall *et al.* turn this notion on its head and find a prompt increase in disorder immediately after photoexcitation, long before the material heats.

"...immediately after photoexcitation, different dimers become uncorrelated at short distances..."

To understand the nature of the problem, it is helpful to recall the idea of crystal symmetry, which physicists define as a collection of mathematical operations that leave a unit cell unchanged. For example, a cubic crystal is invariant against all rotations

[1]*Department of Physics, University of Oxford, Oxford, UK.* [2]*Max Planck Institute for the Structure and Dynamics of Matter, Hamburg, Germany. Email: andrea.cavalleri@mpsd.mpg.de*

at right angles, because a cube is indistinguishable if looked at from the top, from the bottom, or from any one of its sides. Similarly, the cube is also invariant against reflections about a number of planes, for example, those that bisect the edges. However, if a phase transition takes place that distorts the unit cell—for example, one of the edges becomes longer—the material loses a subset of these symmetry elements.

A phase transition is in fact about acquiring or losing elements of symmetry, but how does this proceed microscopically? Instead of the geometric parameters of a unit cell, let us consider, for graphic simplicity, a magnetic material in which spin moments point either up or down at neighboring sites. The classical theory of phase transitions is based on a so-called mean-field approach. It is assumed that fluctuations of local order occur uniformly over long length scales. It follows that the order must be finite everywhere below the transition temperature T_c and zero everywhere above it. In this view, x-ray diffraction from an antiferromagnet would show a diffraction peak for all temperatures below T_c and no peak for all temperatures above it (see the figure, top). This type of transition is termed "displacive."

However, let us relax the constraint on the correlation length of the order and consider instead a situation in which the moments at each site do not necessarily disappear when crossing T_c, but rather become uncorrelated near the transition. That is, the size and angle of a moment at one site do not influence the size and angles of spins only a short distance away. Also in this limit, which is that of an "order-disorder" transition, the diffraction peak disappears when the transition temperature is crossed (see the figure, bottom). Hence, one cannot tell apart a displacive and an order-disorder transition by looking at the Bragg scattering alone. However, in the displacive case, the diffraction peak disappears because the individual spins are not there to scatter the light, whereas in the order-disorder case, it disappears because of a lack of constructive interference at the Bragg angle. In the order-disorder case, the x-rays are still scattered by the nonzero local moments, but in a more incoherent manner to other diffraction angles.

In the VO_2 structural transition discussed by Wall *et al.*, the increase in symmetry between the low- and high-temperature phases involves the disappearance of V^{4+} dimers, which in the low-temperature phase are arranged in chains with alternate elongated and contracted bonds. Such an antiferrodistortive transition can be thought of in the same terms as the magnetic case of the figure if the spin direction and size are substituted with the contracted or elongated bonds of different amplitudes. The authors differentiated the two possibilities of a displacive and of an order-disorder transition by measuring not only the dynamical changes in the Bragg peaks after photoexcitation, but also those x-ray photons scattered in the weak "halo" between peaks. As the cations acquired the high-temperature symmetry, a large increase in the diffuse scattering was also detected, indicating an ultrafast order-disorder transition.

The reason why this disordering happens so fast is that immediately after photoexcitation, different dimers become uncorrelated at short distances and start to move independently. This loss of correlation is a defining feature of the high-temperature state of VO_2, in which the frequency of the molecular vibration is independent of the wavelength at short length scales. A wavelength-independent frequency in a chain of atoms implies that if a single bond is "plucked" at one site in the crystal, no sound wave is launched, but the vibration remains localized. Thus, photoexcited low-temperature VO_2 acquires the essence of the high-temperature phase, that is, nonpropagating short-wavelength sound waves, even before the atoms have had time to rearrange completely. A photoinduced structural transition is then not only about atomic positions, but also about their oscillation frequencies and correlation lengths.

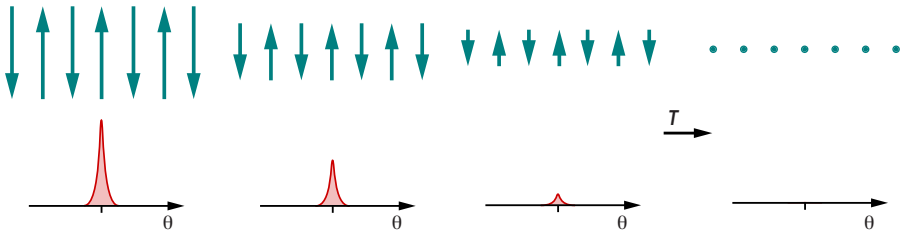
The most important implication of these measurements is that the much-publicized molecular movie, the idea that atomic positions as a function of time provide a complete picture of the microscopic physics, becomes a slippery concept of limited validity. The experiments reported here show the crucial importance of diffuse and inelastic x-ray scattering in dynamical experiments. No transition can be understood without a complete measurement of elastic and inelastic components of the scattered signal. More generally, the work of Wall *et al.* shows that x-ray free-electron lasers are opening up far more avenues of research than what was envisaged when these light sources were being planned, forcing us to reevaluate many old notions taken for granted up until now. ■

Symmetry changes can be in lockstep at all sites, or incoherent

Two ways in which a phase transition can proceed are illustrated for an antiferromagnetic spin system and its diffraction pattern (measured as angle θ) as a function of temperature *T*.

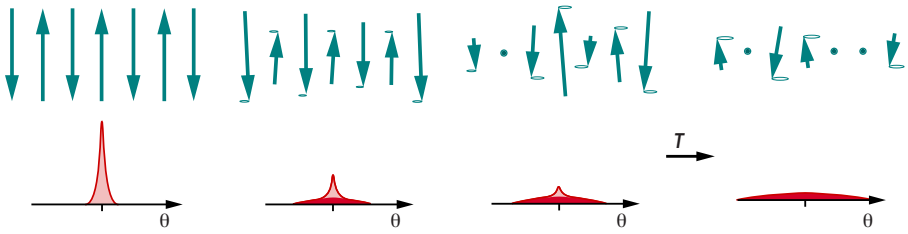
Displacive transitions

The ordering of spins uniformly decreases at each site with increasing temperature in a cooperative fashion, and diffraction peaks simply decrease in intensity.



Order-disorder transitions

The decrease in spin order occurs independently at each site. Diffraction peaks decrease in amplitude with temperature, but x-rays are also reflected incoherently into a diffuse background.



REFERENCES

1. S. Wall *et al.*, *Science* **362**, 572 (2018).
2. P. Emma *et al.*, *Nat. Photon.* **4**, 641 (2010).
3. A. Cavalleri *et al.*, *Phys. Rev. Lett.* **87**, 237401 (2001).
4. V. R. Morrison *et al.*, *Science* **346**, 445 (2014).
5. P. Baum *et al.*, *Science* **318**, 788 (2007).
6. A. Cavalleri *et al.*, *Phys. Rev. B* **70**, 161102 (2004).
7. C. Kübler *et al.*, *Phys. Rev. Lett.* **99**, 116401 (2007).

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