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Spectroscopy Beyond the Single-Particle Limit

Gregory V. Hartland and Shun Shang Lo

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over time, it is still necessary to understand how individuals convey information on food location (*7*). They may do so passively, with birds first dispersing homogeneously and then joining other birds of the same species that have located a food patch (*8*). Alternatively, they may convey the information actively, similar to the way in which bees transfer information on food location in the hive by their dance (*5*). No study has so far been able to demonstrate this latter hypothesis, but some recent studies have suggested that the information may be passed not in the colony but through aggregations away from the colony that signal the direction of food resources (*9*).

To date, studies on seabird foraging have mostly remained descriptive, focusing on the patterns of distribution and their relation with the environment. Wakefield *et al.* go beyond this to not only show clear segregation patterns, but also examine the underlying processes through modeling. The next step will be to use empirical or experimental research to explore how these behaviors may have evolved through culture and social behaviors. These investigations will be facilitated by further technological developments that allow us to determine not only an animal's location but also its precise behavior, activity, energy expenditure, and prey capture. Studying interactions between individuals in the colony and at sea is also technically feasible but requires large numbers of individuals to be tracked (*10*). These future data on animal foraging and social interactions will open new perspectives in our understanding and ability to make more robust predictions on many aspects, such as colony dynamics and the future impact of climate change or of fisheries (*11*).

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PHYSICS

Spectroscopy Beyond the Single-Particle Limit

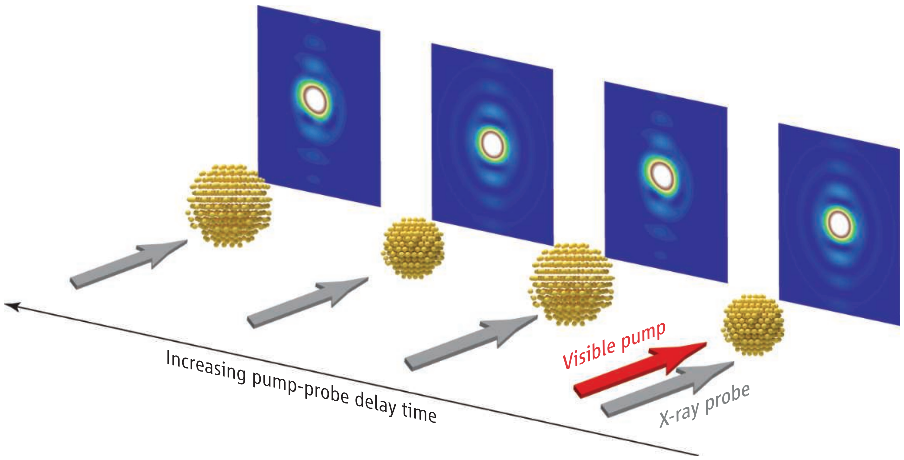
Ultrafast x-ray diffraction studies reveal the lattice vibrations of single gold nanoparticles.

Gregory V. Hartland and Shun Shang Lo

Scientists can now routinely detect and study single molecules and nanoparticles (*1*). However, direct observation of chemical processes and/or atomic motions in real time remains a challenge, primarily because ultrafast (subpicosecond) time resolution is needed. Optical techniques have recently been developed to study the dynamics of individual molecules or nanoparticles where two laser beams (a pump and a probe) are focused onto a single nano-object under a microscope (*2*, *3*). The spatial resolution of these measurements is limited by the diffraction of light, so that the movements of the individual atoms can only be inferred. On page 56 of this issue, Clark *et al.* (*4*) present a study of the lattice motions of individual gold nanoparticles recorded using ultrafast coherent x-ray pulses as a probe. These measurements yield three-dimensional images of the atomic displacements in the particles as a function of time, with a spatial resolution that is orders of magnitude better than what can be achieved with optical microscopes.

The usual way of studying single molecules or particles, by selecting isolated objects with a high-magnification microscope, is not currently possible for x-ray sources. To overcome this limitation, Clark *et al.* used a fundamentally different approach to single-particle spectroscopy. Particles with different orientations have spatially separated Bragg diffraction patterns at the image plane of the detector (*5*). By analyzing the position and phase of the diffraction patterns, the authors could reconstruct the time-dependent lattice distortions of selected particles. These data experimentally determine the form of the vibrational normal modes that are excited by the pump laser in the experiments, as well as their frequencies (see the figure).

This type of information is not accessible in conventional optical transient absorption measurements, where the assignment of the observed modes (that is, a picture of what the vibrational motion looks like) relies on comparing the measured oscillation periods to continuum mechanics calculations (*6*, *7*). For particles with simple shapes (spheres and wires), these calculations can



Particularly revealing. Time-resolved x-ray measurements by Clark *et al.* reveal the lattice motions of single nanoparticles with subnanometer spatial resolution.

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be done analytically, whereas for complex-shaped particles, numerical approaches are needed. However, in both cases, fairly precise knowledge of the size and shape of the nanoparticle is required in order to assign the vibrational modes.

The analysis of Clark *et al.* does not rely on a priori knowledge of the particle's size and shape: Both the size and shape and the form of the vibrational modes come directly from the experiments. The combination of single-particle sensitivity, atomic-scale information, and ultrafast time resolution represents a tour de force in nanoscience. In addition to providing detailed information about lattice motions, x-ray measurements can be used to study any crystalline material, and are sensitive to all the vibrational motions of the object, not just ones that are strongly coupled to optical transitions (*2*, *6*, *7*). These advantages are what we mean by spectroscopy beyond the single-molecule limit.

However, there are many challenges to overcome before this technique makes conventional transient absorption microscopy measurements performed with table-top visible and near-infrared laser sources obsolete. For example, in studies of the acoustic phonon modes of nanoparticles, an important question is the time scale for energy dissipation, in particular, the effect of liquids on the relaxation of the vibrational modes (*8*). These questions can be studied in conventional single-particle transient absorption measurements by using optically trapped particles (*9*), or by examining nanowires suspended over trenches (*10*). These types of experiments will be difficult to do with x-ray pulses, although it may be possible to interrogate particles in thin liquid cells by borrowing methods developed for transmission electron microscopy measurements (*11*).

The particles interrogated by Clark *et al.* were also fairly large—more than several hundred nanometers, which is considerably bigger than the detection limits in optical transient absorption experiments. Substantial improvements in sensitivity will be needed before particles with sizes on the order of 10 nm can be studied, which is the size range where new effects in the properties of nanoparticles start to emerge.

Advances in science often come from advances in measurement technology. The technique described by Clark *et al.* represents a fundamentally new way of studying the dynamics of single nanoparticles. The use of x-ray diffraction as a probe circumvents several of the limitations of current single-particle experiments. These measurements give direct information about atomic motions and should work for all crystalline nanomaterials. By contrast, optical transient absorption measurements can only be used to study samples that have resonances within the tuning range of the laser source. With the current time resolution available, time-resolved x-ray measurements are well suited to studying the acoustic modes of nanomaterials. The ability to image the form of the acoustic modes, as well as follow their evolution in time, can potentially provide information about how vibrational energy is redistributed in materials after ultrafast excitation. In particular, these measurements may allow researchers to watch energy transfer between internal modes of the nanoparticle, as well as between the particles and their surroundings.

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IMMUNOLOGY

Fueling Function Over Expansion in T Cells

Cellular metabolism plays an active role in regulating immune cell function.

Joseph P. Argus[1,2] **and Steven J. Bensinger**[1,2,3,4]

Vertebrates generate millions of unique T cell receptors during T cell development, ensuring that the immune system can recognize any number of potential pathogens. A compromise for this extraordinary molecular diversity is that the T cell population of a given individual contains only a handful of cells that can recognize any particular foreign invader. To solve this problem, T cells can undergo extraordinary proliferation in response to infection (*1*). Upon activation, they adopt specialized metabolic programs, such as aerobic glycolysis [the Warburg effect (*2*–*5*)], which has long been thought to meet the biosynthetic and bioenergetic requirements associated with rapid expansion (*2*). But a recent study by Chang *et al.* (*6*) raises questions about this model and suggests instead that aerobic glycolysis is necessary for T cell effector function rather than proliferation.

Rapidly proliferating cells must accumulate biomass at a rate that keeps up with cell division. To support rapid growth, cells have evolved common metabolic themes including heightened energy production, increased protein, nucleic acid, and lipid synthesis, and aerobic glycolysis (*3*). Glycolysis converts glucose into pyruvate through a series of biochemical reactions that produce adenosine triphosphate (ATP), an energy source for many cellular processes. Aerobic glycolysis involves heightened glycolytic flux and the conversion of pyruvate to lactate (fermentation) despite sufficient oxygen to support the mitochondrial breakdown of pyruvate to CO_2 (cellular respiration). Inhibiting aerobic glycolysis often severely attenuates cell survival and growth, whereas promoting glycolysis supports proliferation and renders cells resistant to many environmental and metabolic stressors (*3*). However, it is largely unclear how aerobic glycolysis and many of the accompanying metabolic programs

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