PERSPECTIVES

FUNDAMENTAL PHYSICS

Quantum probe of space-time curvature

An atom interferometer measures the quantum phase due to gravitational time dilation

By **Albert Roura**

In Einstein's theory of general relativity, gravity is a manifestation of space-time curvature. As predicted by general relativity and confirmed by numerous measurements, clocks moving at different velocities or located in different regions of a gravitational field tick at different rates (*1*), a phenomenon known as relativistic time dilation. Under appropriate conditions, time dilation can affect the oscillation phase of quantum waves and give rise to a measurable effect in interference experiments. On page 226 of this issue, Overstreet *et al*. (*2*) present an atom interferometry experiment in which this effect has been measured for gravitational time dilation. In addition to the importance of the results for fundamental physics, the methods used can lead to more accurate measurements of Newton's gravitational constant, which parametrizes the strength of the gravitational interaction and is by far the least accurately known of all fundamental constants (*3*).

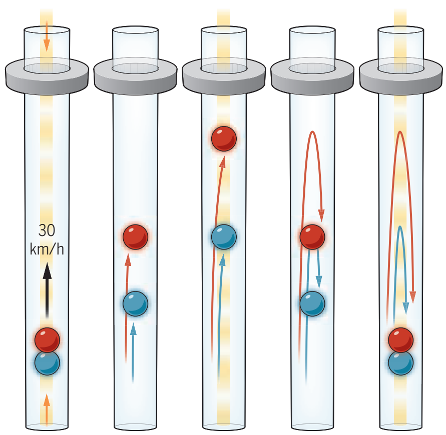
In quantum mechanics, microscopic particles can behave as waves, and each particle is characterized by a "wave packet." Forces modify a wave packet's propagation in the same way they would alter a particle's trajectory in classical mechanics. However, uniform changes to the potential energy can modify the oscillation phase of the wave packet without affecting its trajectory—a phenomenon with no classical counterpart. As early as the 1950s, Aharonov and Bohm (*4*) conceived an interferometry experiment with charged particles to observe this quantum effect. Since then, several versions of the experiment involving electromagnetic fields have been realized (*5*, *6*). By contrast, analogous measurements for the much weaker gravitational interaction had remained elusive and have only been possible thanks to extremely sensitive atom interferometers with arm separations of up to half a meter (*7*).

Atom interferometers rely on the wave nature of quantum particles and can serve as highly sensitive inertial sensors for both fundamental physics measurements and practical applications (*8*). In the atomic fountain setup used by Overstreet *et al*., the atoms are launched vertically at the bottom of a 10-m vacuum tube and follow a free-fall trajectory (see the figure). Short laser pulses are applied at different times and act as light gratings that split, redirect, and recombine the atomic wave packets. Each atom is thus in a quantum superposition simultaneously following two different trajectories, sometimes referred to as the upper and the lower arm. Differences between the phase changes experienced by the wave packets as they evolve along the two arms can be read out from the interference signal.

There are two kinds of contributions to these phase changes. One corresponds to the propagation of the wave packets and is proportional to the proper time along each arm, which is the time that an ideal clock following the same trajectory would measure and includes relativistic time-dilation effects. The other contribution is connected to the laser pulses. Every time a wave packet is diffracted by a laser pulse, it gets a momentum kick, but it also experiences a phase change that depends on its position with respect to the light-grating wavefronts.

Interferometry experiment in an atomic fountain

The atoms are launched vertically at the bottom of a 10-m vacuum tube and follow a free-fall trajectory. Laser pulses were applied at three different times to split, redirect, and recombine the atomic wave packets. The gravitational influence of the ring mass on the upper interferometer arm can be detected in the interference signal.



About a decade ago, researchers proposed a hypothetical experiment for realizing a gravitational analog of the Aharonov-Bohm experiment (*9*). In this proposal, atoms in the two arms spend a sufficiently long time at two specific points where the net gravitational force from a pair of massive spherical shells vanishes. Yet, the different value of the gravitational potential at these two points leads to a measurable phase difference. Within the framework of general relativity, this phase difference corresponds to the proper-time difference between the two interferometer arms due to gravitational time dilation. Such a hypothetical experiment, however, has not been realized yet because any imperfection in the optical lattice needed for suspending the atoms in Earth's gravity field would overwhelm the interference signal.

By comparison, standard atom interferometers such as the one used by Overstreet *et al.* are much less sensitive to imperfections of the laser fields, because each laser pulse is applied only for a short time and atoms are otherwise freely falling. The momentum kicks applied by vertical laser beams separate the two arms along the vertical direction. Therefore, the different gravitational time dilation experienced by atoms at different heights should lead to a proper-time difference between the upper and lower arm. Nevertheless, in a uniform gravitational field, this difference is exactly cancelled out by changes in kinetic energy caused by the gravitational acceleration, as can be understood by considering a freely falling reference frame (*10*). The interferometer outcome is thus entirely a consequence of the phase changes associated with the laser pulses, whose net contribution is proportional to the relative acceleration between the atoms and the light gratings.

By contrast, for sufficiently large arm separations, the effects of space-time curvature, which is linked to gravity gradients, lead to non-negligible deviations from a

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uniform gravitational field. Thanks to the large arm separation in the experiments performed by Overstreet *et al.*, the gravitational field of the massive ring at the top of the atomic fountain influenced the upper arm much more than the lower one, thus producing a measurable proper-time difference between the two. In principle, this difference could also be obtained by comparing two clocks following the same trajectories as the interferometer arms, but the difference would be far too small to be resolvable. Notably, interferometry experiments with atoms acting as quantum clocks can be sensitive to the substantially larger time dilation due to Earth's gravitational field by initializing the clock once the arms are spatially separated (*10*).

Measuring the effect of gravitational time dilation on matter-wave interference is a major step in the emerging field of gravitational quantum mechanics. Furthermore, the impressive sensitivity achieved in these experiments could be exploited in future measurements of Newton's gravitational constant (*3*), gravimetry applications (*11*), and tests of the universality of free fall (*12*, *13*). Yet, important challenges remain because gravity gradients also lead to the dependence of the interference signal on the initial position and velocity of the atomic wave packets. This unwanted sensitivity to initial conditions is a major source of systematic uncertainties for precision measurements in nonuniform gravitational fields. Fortunately, a very effective technique to overcome these difficulties has recently been proposed (*14*) and is already playing a key role in high-precision tests of the universality of free fall (*13*). The prospects for improved measurements of Newton's gravitational constant based on atom interferometry are therefore very promising (*15*). ■

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CELL BIOLOGY

Fetal bovine serum—a cell culture dilemma

Ethical and possible reproducibility issues arise when using fetal bovine serum in cell culture media

By **Jan van der Valk**

Fetal bovine serum [FBS, also known as fetal calf serum (FCS)] is a popular supplement to the basal medium used in cell and tissue culture. FBS is sourced from unborn calves at the slaughterhouse, raising ethical concerns about animal welfare. Recently, two different laboratories performed in vitro experiments that applied an identical experimental procedure and used cells and FBS from the same suppliers (*1*). The results they obtained were very different. Further analyses revealed that one cause for the difference in cell response was the supplementation of the cell culture medium with FBS, which had originated from different batches. Given the ubiquitous use of cell culture throughout research, it is important to ensure reproducibility as well as ethical sourcing of research products, such as the development of synthetic media.

To maintain and proliferate cells and tissues outside the body, an optimal environment with growth factors and nutrients is required. This is often a liquid medium. Since the first in vitro cell culture experiments that maintained frog nerve fibers in frog lymph fluid (*2*), there has been a search for the optimum medium composition. Over the years, both animal-derived media and artificial media were developed. Examples of artificial media are the Eagles medium and its improvements modified Eagles medium (MEM) and Dulbecco's MEM (DMEM), as well as Ham's F10, F11, and F12. Not all cells flourish in these artificial media. In 1958, it was discovered that cells can be maintained in active growth for longer periods of time in media containing FBS (*3*). Because it was also reported that several different human biopsies and primary cell cultures could successfully be proliferated in such supplemented media, this led to the widespread use of FBS that continues today.

FBS is naturally optimized for prenatal development of unborn calves, and it contains a wide range of nutrients and growth and adhesion factors in excess and has a low antibody content. Combined with its relatively inexpensive availability, FBS is historically the first choice for supplementing almost all eukaryotic cell culture media. Most cell types appear to respond well to FBS with regard to proliferation and viability. Unfortunately, two important observations from the first report of its use in cell culture have been largely overlooked: FBS can contain "toxic factors" that affect the quality of experiments, and the serum obtained in different seasons showed "appreciable variations of performance" [(*3*), p. 946].

That different batches of FBS, which are produced in different regions and during different times of the year, have different effects on cells is not surprising, given that it is a biological product with a largely unknown composition. This variance may become apparent in cell culture through effects on cell morphology, growth rate, and viability, as well as by altering responses in experimental settings (*1*). To avoid intralaboratory disparities in cell performance when a new batch of serum must be obtained, laborious batch-testing to check in-house quality criteria with the available cell lines in the lab are required. Although this solves in-house inconsistency, it does not address interlaboratory consistency, because different laboratories will not have access to the same batch of FBS. Interlaboratory reproducibility becomes crucial when in vitro methods are used in applied research, such as preclinical studies with human cells, or for regulatory safety testing of pharmaceuticals and chemicals. Because of these interlaboratory reproducibility issues, the Organisation for Economic Co-operation and Development (OECD) began to discourage the use of FBS in 2017, especially for human health risk assessments of chemicals (*4*).

Since 1989, the bovine spongiform encephalitis (BSE) crisis fueled efforts to replace bovine-derived material, particularly in clinical or pharmaceutical products. Because of the potential contamination with nonhuman pathogens, the risk of eliciting an unwanted immune response, and issues with product reproducibility, the US Food and Drug Administration (FDA) (*5*) and the European Medicines Agency (EMA) (*6*) discourage the use of FBS in cell and tissue culture for human clinical application.

There is a need to replace FBS supple-

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