Metrology

Optical clocks offer stable timing in a portable box

Bonnie L. S. Marlow & Jonathan Hirschauer

A highly precise timekeeping instrument has been adapted for the real world. The compact and robust device is smaller than its commercial counterparts and performs comparably in the laboratory and aboard a naval ship. **See p.736**

Precise timing is crucial for safe and efficient sea travel. Many ships are equipped with atomic clocks – devices that facilitate navigation, communication and scientific discovery in oceanographic and geological research. High-performance atomic clocks on ships can improve the reliability and accuracy of timekeeping, but many are bulky and impractical. On page 736, Roslund *et al.*[1] report the development and seaborne testing of iodine-based atomic clocks with performance comparable to that of the best commercial atomic clocks[2] – but in a much smaller package. This work demonstrates that iodine clocks can provide high-accuracy timekeeping across various applications owing to their size and insensitivity to environmental variations.

Small timekeeping errors can lead to substantial problems for many applications that depend on precise timing. For example, radio navigation systems, such as GPS, work by comparing the time it takes radio-frequency signals to propagate from different satellites to a particular location on Earth. Given that time errors of just one-millionth of a second can cause position errors of hundreds of metres, GPS satellites use atomic clocks to keep time to within 100 billionths of a second (see go.nature.com/4auws7b) relative to coordinated universal time (UTC). This, in turn, enables positioning accurate to within 30 metres.

Atomic clocks track time by sending an electromagnetic field through a group of atoms and measuring the frequency at which the atoms oscillate between two energy states. The stability of an atomic clock depends on the energy difference between these two states, and thus clocks that use higher-frequency electromagnetic fields to drive larger energy transitions are more stable than those that operate at lower frequencies. Commercially available atomic clocks drive atoms with microwave frequencies, but in the past 25 years there have been substantial advances in developing another type of clock that operates at much higher optical frequencies.

This technology was inaccessible until the development of a device known as the optical frequency comb[3], which allowed scientists finally to translate the optical-frequency 'ticks' of atoms to the microwave frequencies used in electronics. Since then, optical atomic clocks have enabled substantially better stability than the best microwave atomic clocks[4]. Their high performance has motivated international committees to consider changing the definition of the second from one based on a microwave-frequency transition in caesium atoms to one based on an optical-frequency transition in atoms of one or more types (see go.nature.com/3qkrjqt).

Despite these advances, optical atomic clocks have so far been confined to laboratories, owing to their size and sensitivity to their surroundings. Roslund *et al.* overcame these problems by making use of laser technology from the telecommunications industry along with custom-built optical and electronic components. The authors developed three compact and robust iodine optical clock prototypes that can achieve performance levels comparable to hydrogen masers, which are microwave analogues of lasers and form the basis of some of the most stable commercial clocks. They showed that the performance of their optical-clock prototypes could be maintained both in laboratory settings and in harsh maritime environments.

Before testing at sea, Roslund and colleagues set out to benchmark the performance of two of their optical clocks at the US National Institute of Standards and Technology (NIST) in Boulder, Colorado. The researchers compared the performance of two of their optical clocks with that of a hydrogen maser, as well as to that of an ensemble of atomic clocks, located at NIST, which contributes to UTC (see go.nature.com/3q1ncfb).

Over 34 days, Roslund *et al.* monitored the frequency output of the prototype clocks to measure whether they ticked faster or slower than those at NIST. They determined that their optical clocks were more stable than a hydrogen maser over short measurement intervals (less than 1,000 seconds). Over

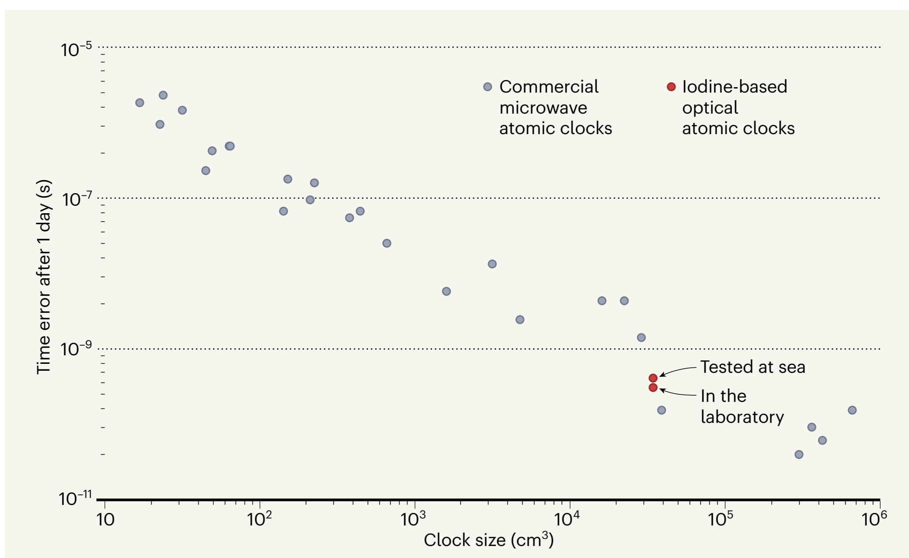

Figure 1 | A trade-off between portability and performance. Atomic clocks keep time by measuring the frequency with which atoms oscillate between energy states in response to an electromagnetic field. Commercial atomic clocks operate at microwave frequencies and vary in size and performance. Atomic clocks running at higher (optical) frequencies are more stable, but are generally confined to laboratories owing to their size and sensitivity to environmental variations. Roslund *et al.*[1] developed portable iodine-based optical atomic clocks that acquire time errors of less than 400 picoseconds (where 1 ps is 10^{-12} s) after operating for 24 hours on a naval ship at sea. The clocks' size and performance are particularly impressive when compared with commercial microwave atomic clocks operating in laboratories, for which comparable sea-based data are not available. The time errors for the microwave atomic clocks are estimated here by assuming no environmental variations, so the authors' feat is an important step towards stable timing for real-world applications. (Adapted from Fig. 6 in ref. 2.)

From the archive

Reflections on the discovery of the double helix, and Charles Darwin investigates a curious case of primrose punishment.

50 years ago

We celebrate in this issue the twenty-first anniversary of the appearance of ... *A Structure for Deoxyribose Nucleic Acid* in *Nature* ... [F]ew would carp at the ... announcement being given pride of place as a starting point of something absolutely new ... with Medawar ... calling it "the greatest achievement of science in the twentieth century".

From *Nature* 26 April 1974

150 years ago

I have observed every spring in my shrubberies and in the neighbouring woods, that a large number of the flowers of the primrose are cut off, and lie strewn on the ground close round the plants ... I once saw some greenfinches flying away from some primroses, I suspect that this is the enemy ... One of my sons ... suggested that the object was to get the nectar of the flowers; and I have no doubt that this is the right explanation ... [N]o animal that I can think of, except a bird, could make two almost parallel clean cuts, transversely across the calyx of a flower. The part which is cut off contains within ... the nectar. I have never heard of any bird in Europe feeding on nectar; though there are many that do so in the tropical parts of the New and Old Worlds, and which are believed to aid in the cross-fertilisation of the species. In such cases both the bird and the plant would profit. But with the primrose it is an unmitigated evil, and might well lead to its extermination; for ... flowers ... destroyed ... cannot produce a single seed. My object in this communication to NATURE is to ask your correspondents in England and abroad to observe whether the primroses there suffer ... If the habit of cutting off the flowers should prove, as seems probable, to be general, we must look at it as inherited or instinctive ... If, on the other hand, the evil is confined to this part of Kent, it will be a curious case of a new habit or instinct arising in this primrose-decked land. CH. DARWIN

From *Nature* 23 April 1874

long timescales, the authors' clocks were only narrowly outperformed in terms of the rate of change of the ticks — a metric known as frequency drift. This means that, after many hours of operation, the relatively small iodine optical clocks would be expected to acquire time errors at levels comparable to those of much larger hydrogen masers.

Roslund and colleagues then took the same two optical clocks, together with a third, smaller, optical clock, to Hawaii, where they tested all three continuously for 20 days aboard a naval ship. Despite experiencing substantial accelerations and vibrations as the ship moved over the ocean waves, the two optical clocks that had been tested at NIST maintained performance comparable with that observed in the laboratory. The frequency drift of the third clock was similar to those of the larger two, but it did not quite reach the same levels of stability. Notably, the two larger optical clocks maintained extremely low time errors (less than 400 picoseconds, where 1 ps is 10^{-12} s) over a 24-hour period (Fig. 1). Thus, even if the ship had lost access to external timing sources for an entire day, it could have used either optical clock to keep time to within 400 trillionths of a second per day.

> **"Optical atomic clocks have so far been confined to laboratories, owing to their size and sensitivity."**

The work reported by Roslund and colleagues represents a crucial step towards optical atomic clocks transitioning from the laboratory to the real world, where they could support maritime, airborne and space-based systems. To facilitate this transition, it will be important to conduct more testing under a wide range of varying environmental and physical conditions and to enable mass production of the necessary lasers and optical frequency combs. With the high performance and small sizes reported by the authors, optical atomic clocks could support precision timekeeping across many platforms, alleviating reliance on external timing sources such as GPS. Future portable optical atomic clocks could even enable innovative ways of studying fundamental physics and metrology, including tests of general relativity and geodesy[4].

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Drug discovery

Targeting RNA in efforts to treat Timothy syndrome

Silvia Velasco

A therapeutic strategy that alters gene expression in a rare and severe neurodevelopmental condition has been tested in stem-cell-based models of the disease, and has been shown to correct genetic and cellular defects. **See p.818**

Scientists understand more about the genetic causes of human diseases than ever before, but there are still many neurological conditions that do not have effective therapies. One barrier is the lack of adequate model systems that can be used to understand disease mechanisms and test therapeutics. *In vitro* models of the human brain hold a great potential to overcome this. Using stem cells, it is now possible to generate complex 3D neural tissues. These structures, known as brain organoids, can be made from a type of cell called induced pluripotent stem cells, which are reprogrammed from an individual's blood or skin cells and have the potential to become any cell type in the body. On page 818, Chen *et al.*[1] describe their use of brain organoids made from patient-derived stem cells to identify a potential therapeutic strategy for the treatment of a severe developmental condition called Timothy syndrome.

This rare genetic disorder is caused by a single-nucleotide alteration (variant) in the *CACNA1C* gene, which encodes the calcium