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NewScientist

6 November 2004

WELCOME TO ATTOWORLD

Where a second lasts the age of the universe

Attack of the zombie computers

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Welcome to attoworld

The dial on your kitchen scales spins when a virus lands. The clock on the wall has gone berserk, ticking every billionth of a billionth of a second. Your camera flashes so fast that it captures single molecules in freeze-frame. Prepare to enter attoworld, the ultra-small realm so foreign that no one quite knows what's going on. **Hazel Muir** zooms in

WHEN experts in weights and measures from 35 nations got together at a palace near Paris in October 1964, they had some pressing problems to thrash out. There was the perennial debate about how to define a litre. But they were also keen to find words to describe some of the tiniest lengths and timescales in nature. A billionth of a billionth of a metre, for instance, or a billionth of a billionth of a second – wouldn't it be convenient to give them simpler names?

The vote was an almost unanimous yes, and the committee officially adopted the prefix "atto", meaning 10^{-18}, into the metric system of units. Now they had concise words – attometres, attoseconds and so on – to describe spaces and times so small they were beyond reach. After all, no clock was sensitive enough to notice an attosecond. If you slowed down time so that an attosecond lasted for a second, a second would last for 30 billion years — more than twice the age of the universe.

But what seemed impossible to measure then does not seem so difficult now. Today's scientists are inventing gadgets that can measure attoscale quantities, such as the mass of a virus, which is just a few attograms. They can sense attonewton forces so feeble they couldn't lift a protein molecule. And they are designing attosecond stopwatches and attolitre test tubes. Here are some of the new inventions finding their vocation in the head-swimmingly small attoworld.

TIM GRAVESTOCK

Atto kitchen scales

A grain of sand typically weighs about a thousandth of a gram. You would have trouble enough weighing that on your kitchen scales, but imagine trying to weigh a millionth of a billionth of a grain of sand. Harold Craighead of Cornell University and his colleagues don't find it daunting at all.

For the past few years, Craighead's team has been developing tiny cantilevers to detect masses as small as 6 attograms. Each cantilever is shaped like a mini diving board, about 4 micrometres long and just 0.5 micrometres wide – a few thousandths of the width of a human hair. The team applies electric fields or zaps it with lasers to make it vibrate, and then monitors the vibration frequency by watching the way the cantilever reflects laser light. Adding a tiny mass to the cantilever changes the vibration frequency slightly, allowing Craighead's team to calculate its weight.

By coating the cantilever with antibodies that bind to specific bacteria or viruses, the researchers can get a chosen pathogen to stick to the device so they can read out its weight. In 2001, they reported measuring the mass of a single *E. coli* bacterium – 665 femtograms (665,000 attograms). And this year they announced that they had successfully weighed a film of a few hundred molecules attached to a gold dot on a cantilever, a mass of only about 6 attograms (*Journal of Applied Physics*, vol 95, p 3694). They have also shown that their cantilevers can sense the weight of some viruses, which typically weigh about 10 attograms.

However, Craighead's team isn't interested in what viruses and bacteria weigh. What they really want to do is tell how many bacteria or viruses have taken the antibody "bait" on the cantilever. Their goal is to produce arrays of millions of cantilevers bristling with a whole library of different antibodies ready to grab even a single bacterium or virus. On the spot, the array could detect a specific bacterial or viral infection that might otherwise take days or even months to diagnose.

Today's HIV tests, for instance, require a build-up of antibodies in the bloodstream, and this can take three months from the time of infection. A test that identified a single virus from the bloodstream would diagnose the disease much quicker. "For any public health threat, it would be desirable to have a quick and definitive diagnosis," says Craighead. "If you show up at a doctor's office with a cough and a fever, you'd like to know pretty soon whether it's an exotic virus or a cold."

There are still hurdles, not least how to deal with messy samples from the real world. "We're not quite at the 'lump of goo' stage yet. We're taking highly engineered samples and ▶

we know precisely what's there," Craighead says. "Using real biological fluids from animals will take some time, but the path is clear to making a useful device in a few years' time."

Atto flash gun

Flash units on modern cameras are impressive enough – for high-speed photography, some flash on for just a hundred-thousandth of a second. But to Ferenc Krausz of the University of Munich and the Max Planck Institute for Quantum Optics in Garching, Germany, that's an eternity. His team has created single laser flashes that last just 250 attoseconds. In that brief instant, light doesn't even travel far enough to cross a bacterium.

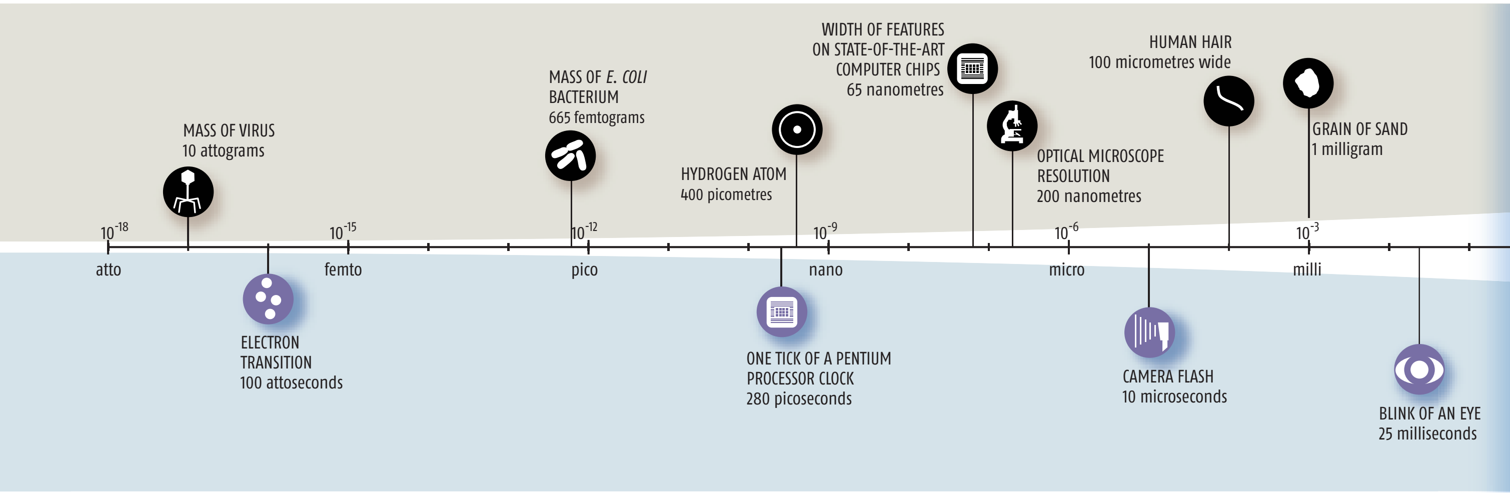
The route to producing such fast laser pulses was mapped out in 1993 by Paul Corkum of the National Research Council of Canada in Ottawa. He predicted that it should be possible to create attosecond pulses using longer, femtosecond pulses developed in the early 1980s. Corkum proposed shining a femtosecond laser pulse onto atoms to liberate their electrons. Light is an electromagnetic wave and with the right fine-tuning, the oscillating electric field of the femtosecond laser pulse could rip the electrons away at high speed, then smash them back onto the atoms as the field reversed. The energy would be released as a train of super-short bursts of X-rays or ultraviolet radiation.

Many labs gave it a go, and many probably succeeded. And by 1997, a team led by Krausz at Vienna University of Technology in Austria had found a way to isolate single ultraviolet flashes lasting just 650 attoseconds. However, that's something they only know in retrospect, because it took them another four years to prove it. To confirm the duration of their laser pulses, they needed to invent yet another attoscale gadget – the most accurate stopwatch on Earth.

TIM GRAVESTOCK

FROM THE INFINITESIMAL TO THE IMMENSE

The attoworld is as far removed from our own experiences as the size and age of the universe



Atto stopwatch

Krausz's super-short laser flashes might sound like a solution looking for a problem. What's the use of an invisible energy burst so short that it can't stretch the length of a microbe? It turns out that such a burst is the ideal tool for homing in on electrons as they zing around atoms, leaping from one atomic energy level to another in about 100 attoseconds.

"It's the same as taking a snapshot of a Formula One car passing by – to freeze the image, you have to use a short exposure time," says Krausz. "In the microworld, we need a pulse with a very short duration."

Krausz's team has probed the motions of electrons by generating a fleeting, extreme ultraviolet pulse using a femtosecond red laser pulse as described above. They fired a super-short UV pulse at a cloud of krypton atoms, knocking electrons out. As each electron emerged, its speed was either boosted or braked by the electric field of the red laser light, depending on the phase of the light at that instant. So by measuring the kinetic energy of each electron and knowing the period of the red light pulse, Krausz's team could calculate the precise moment the electron was emitted. In effect, the red light pulse acted as a stopwatch that clocked the timing of each electron.

In 2001, Krausz's team reported measuring the length of the burst of electrons from krypton – 650 attoseconds long, confirming the brevity of the UV pulse that had ejected them. Since then, the researchers have shortened the pulses to 250 attoseconds and used their stopwatch to look at what happens in a krypton atom after an electron has been kicked out from an inner orbital. An outer electron will then jump down to fill its place, releasing energy, often in the form of a second electron.

Using the laser technique, Krausz's team has measured the time it takes for those second electrons to emerge, and confirmed it takes about 8 femtoseconds. And earlier this year, he reported that fine-tuning allows electronic processes to be frozen in frames just 100 attoseconds apart (*Nature*, vol 427, p 817).

Krausz admits his technique is in its infancy and has not yet told us anything we didn't already know. But it could eventually be used to see in detail how electronic transitions take place, and for designing future electronic devices, which many hope will shrink to the size of molecules. It could even help chemists spy on chemical bonds. "We might be able to see the annihilation of electron bonds for the first time," says Krausz. "I think there might be a few surprises there."

More generally, Krausz thinks the work could help in the quest for compact, bright X-ray lasers. Today's bright beams of X-rays rely on particle accelerators housed in buildings the size of football stadiums. If the sources were small and cheap, they could be used in hospitals to target medical X-rays at specific parts of the body, reducing unnecessary radiation exposure.

Krausz thinks his work will also find applications no one has dreamed of yet. "Think of Röntgen doing his famous experiments with X-rays. He had no idea what they'd be any use for years later," he says. "Our work has a few applications we can foresee, but probably the majority can't be foreseen at all."

Atto force gauge

Imagine a force so puny that it can barely lift a single protein molecule. Earlier this year, scientists reported measuring just that – a magnetic tug of a mere 2 attonewtons from a single electron. That's minuscule. If the force of 1 attonewton were scaled up to the weight of a feather, the feather would weigh as much as the Hoover Dam.

The feat is a milestone for a technique called magnetic resonance force microscopy

> "A second in attoland lasts longer than the age of the universe"

(MRFM), which Dan Rugar and his team at IBM's Almaden Research Center in San Jose, California, have been pioneering for the past decade. Rugar's team detects tiny forces using an ultra-sensitive silicon cantilever just 100 nanometres thick, whose natural vibration frequency is 5500 times a second. Attached to its tip is a minuscule magnet.

Electrons behave like bar magnets thanks to their quantum mechanical property of spin. And just as two bar magnets can attract or repel one another, the spin of an electron can exert a force on a magnet. What Rugar's team measures is the magnetic force between the cantilever magnet and a single electron.

The team applies a high-frequency magnetic field that continually flips the spin of an electron inside a silica wafer underneath the cantilever. As the electron's spin flips, it alternately attracts and repels the vibrating cantilever, which slightly alters the vibration frequency of the cantilever. It is possible to detect this subtle change using a laser beam, and that's how the team measured the 2-attonewton magnetic force between the electron and the tip (*Nature*, vol 430, p 329).

The team aims to improve the sensitivity of the MRFM technique further so it can detect single protons and other nuclei, such as carbon-13, which have much weaker magnetic signals than electrons. That would allow MRFM to peer into large molecules and create three-dimensional pictures of the atoms inside.

"That's the dream we're pursuing – to develop a microscope that can take a 3D ▶

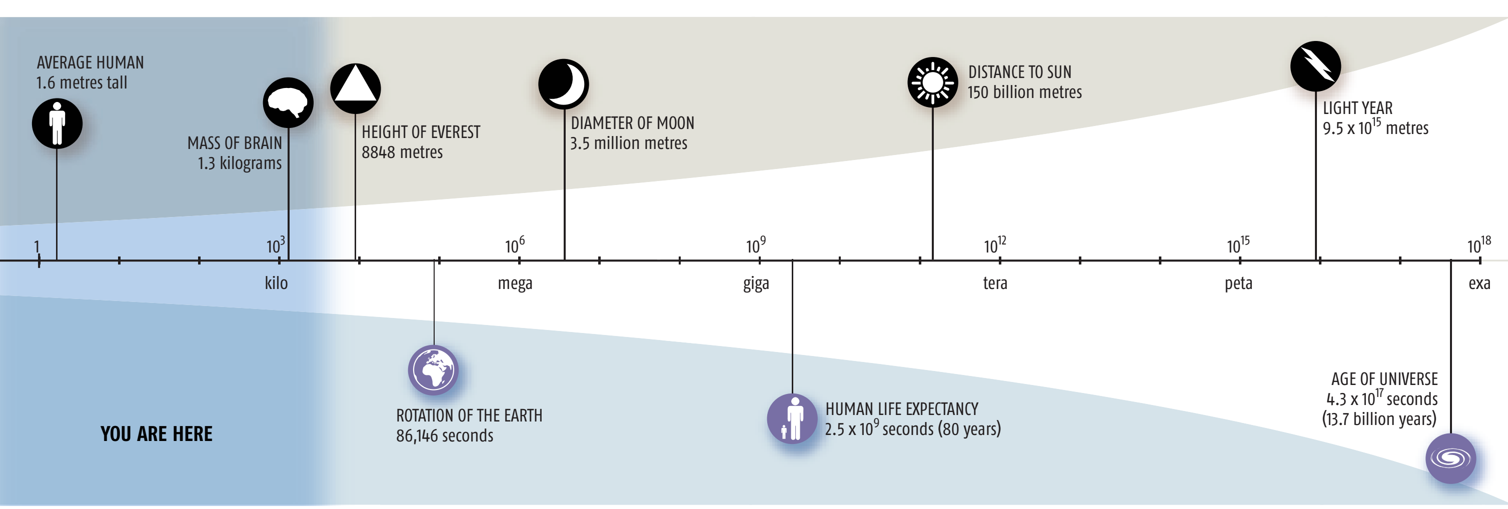


image of atoms within molecules," says Rugar. "It simply is not possible with any kind of microscope right now." He adds that there are still plenty hurdles to overcome. But if this tool becomes a reality, it could make a big difference to the ever-shrinking world of electronics, helping scientists to produce and study components such as transistors at the nanoscale.

It could have an even more revolutionary impact on biology and medicine. The biological activity of a large protein molecule, and the way it interacts with drugs, is determined largely by its intricately folded shape. But it is currently impossible to measure this shape directly. Scientists have to rely on either computer simulations or X-ray crystallography, for which proteins have to be turned into crystal form. And some proteins are either difficult or impossible to crystallise.

But Rugar is confident that one day MRFM could probe the structure of non-crystallised proteins and even create atom-scale descriptions of living cells, which is no mean feat. The number of atoms in a single human cell is about 100 million million, far more than the number of stars in our galaxy.

> "A feather would weigh as much as the Hoover Dam in attoland"

Atto test tubes

Since the late 1980s, chemistry has been following in the footsteps of electronics by going miniature. Just as computers have shrunk from leviathans that took up whole rooms to hand-held electronic notebooks, chemists have developed lab-on-a-chip devices for similar reasons: to do traditional bench-top chemistry faster and more cheaply.

Tools from the microelectronics industry have allowed chemists to develop microfluidic devices, typically made of silicon, plastic or glass, that are etched with channels just a few nanometres wide. These miniature pipes can be linked to valves, pumps and reservoirs to separate different chemicals and mix them with reagents.

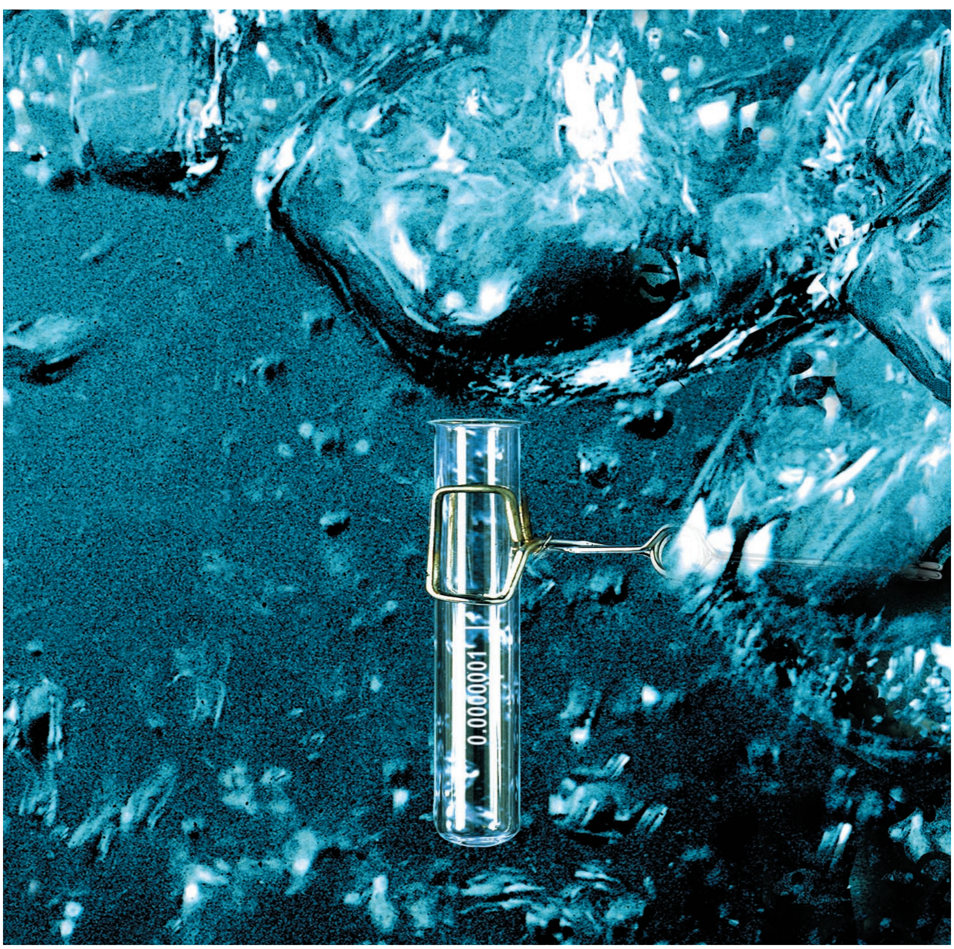
Combining thousands of these devices on a single chip a few centimetres wide allows hundreds of different chemical tests to take place simultaneously (*New Scientist*, 25 January 2003, p 38). This miniaturised, automated chemistry promises novel applications such as kits that allow police to do on-the-spot forensic tests at a crime scene.

Already these devices are entering the attoscale. For instance, Paul Bohn and his colleagues at the University of Illinois in Urbana-Champaign have designed molecular gates that can corral a few attolitres of fluid through a nanoscopic maze with amazing precision. The gates are membranes containing pores about 10 to 200 nanometres wide. By controlling the pore size and applying electric fields across the gates, Bohn's team can select the molecules they wish to isolate from an attolitre sample of fluid, and move them from one channel to another at will.

The team has proved that its devices can separate chemicals, perform reactions and isolate the reaction products. And soon the researchers hope to demonstrate a key application: detecting trace amounts of deadly poisons, such as botulinum toxin.

Today the test for botulism involves taking blood from a patient, injecting it into a mouse and then waiting to see if the mouse becomes paralysed or dies. It is not ideal for the mouse or the patient. By the time the mouse has succumbed, several days may have elapsed and the patient's condition may have worsened dramatically. "Sometime in the next year, I hope we'll demonstrate that we can identify a toxin molecule much faster than can be done with a mouse," says Bohn.

The team's technique could also revolutionise cell biology by allowing analysis of samples that are currently too small to handle. At the moment, biochemists do not understand the details of reactions that happen in certain tiny pockets within cells, such as the vesicles that store, transport and digest cellular products and waste. Typically, a vesicle might store just 1000 molecules of a key compound – that's just 0.002 attomoles. Bohn says molecular gates will make experiments with such small samples possible: "This is going to be a big area of opportunity."



TIM GRAVESTOCK

Beyond attoland

When even the attoworld becomes passé, scientists will set their sights on tinier goals. Already they're dreaming of zeptophysics, where nuclear reactions flutter on timescales of about 10^{-21} seconds. And don't forget the yoctoworld, a thousandth the size of the zeptoworld. It is a realm familiar only to subatomic particles: a proton weighs about 1.7 yoctograms and the heaviest known fundamental particle in nature, the mighty top quark, probably lives and dies in just 0.4 yoctoseconds.

Beyond yocto, there are no official prefixes to describe yet smaller worlds. But experts still meet near Paris every few years to consolidate our international units, and as the goalposts squeeze together in time and space, they will probably not be lost for words for long. ●