13 things that do not make sense

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1 The placebo effect

Don't try this at home. Several times a day, for several days, you induce pain in someone. You control the pain with morphine until the final day of the experiment, when you replace the morphine with saline solution. Guess what? The saline takes the pain away.

This is the placebo effect: somehow, sometimes, a whole lot of nothing can be very powerful. Except it's not quite nothing. When Fabrizio Benedetti of the University of Turin in Italy carried out the above experiment, he added a final twist by adding naloxone, a drug that blocks the effects of morphine, to the saline. The shocking result? The pain-relieving power of saline solution disappeared.

So what is going on? Doctors have known about the placebo effect for decades, and the naloxone result seems to show that the placebo effect is somehow biochemical. But apart from that, we simply don't know.

Benedetti has since shown that a saline placebo can also reduce tremors and muscle stiffness in people with Parkinson's disease (*Nature Neuroscience*, vol 7, p 587). He and his team measured the activity of neurons in the patients' brains as they administered the saline. They found that individual neurons in the subthalamic nucleus (a common target for surgical attempts to relieve Parkinson's symptoms) began to fire less often when the saline was given, and with fewer "bursts" of firing - another feature associated with Parkinson's. The neuron activity decreased at the same time as the symptoms improved: the saline was definitely doing something.

We have a lot to learn about what is happening here, Benedetti says, but one thing is clear: the mind can affect the body's biochemistry. "The relationship between expectation and therapeutic outcome is a wonderful model to understand mind-body interaction," he says. Researchers now need to identify when and where placebo works. There may be diseases in which it has no effect. There may be a common mechanism in different illnesses. As yet, we just don't know.

2 The horizon problem

OUR universe appears to be unfathomably uniform. Look across space from one edge of the visible universe to the other, and you'll see that the microwave background radiation filling the cosmos is at the same temperature everywhere. That may not seem surprising until you consider that the two edges are nearly 28 billion light years apart and our universe is only 14 billion years old.

Nothing can travel faster than the speed of light, so there is no way heat radiation could have travelled between the two horizons to even out the hot and cold spots created in the big bang and leave the thermal equilibrium we see now.

This "horizon problem" is a big headache for cosmologists, so big that they have come up with some pretty wild solutions. "Inflation", for example.

You can solve the horizon problem by having the universe expand ultra-fast for a time, just after the big bang, blowing up by a factor of 10^{50} in 10^{-33} seconds. But is that just wishful thinking? "Inflation would be an explanation if it occurred," says University of Cambridge astronomer Martin Rees. The trouble is that no one knows what could have made that happen.

So, in effect, inflation solves one mystery only to invoke another. A variation in the speed of light could also solve the horizon problem - but this too is impotent in the face of the question "why?" In scientific terms, the uniform temperature of the background radiation remains an anomaly.

3 Ultra-energetic cosmic rays

FOR more than a decade, physicists in Japan have been seeing cosmic rays that should not exist. Cosmic rays are particles - mostly protons but sometimes heavy atomic nuclei - that travel through the universe at close to the speed of light. Some cosmic rays detected on Earth are produced in violent events such as supernovae, but we still don't know the origins of the highest-energy particles, which are the most energetic particles ever seen in nature. But that's not the real mystery.

As cosmic-ray particles travel through space, they lose energy in collisions with the low-energy photons that pervade the universe, such as those of the cosmic microwave background radiation. Einstein's special theory of relativity dictates that any cosmic rays reaching Earth from a source outside our galaxy will have suffered so many energy-shedding collisions that their maximum possible energy is 5×10^{19} electronvolts. This is known as the Greisen-Zatsepin-Kuzmin limit.

Over the past decade, however, the University of Tokyo's Akeno Giant Air Shower Array - 111 particle detectors spread out over 100 square kilometres - has detected several cosmic rays above the GZK limit. In theory, they can only have come from within our galaxy, avoiding an energy-sapping journey across the cosmos. However, astronomers can find no source for these cosmic rays in our galaxy. So what is going on?

One possibility is that there is something wrong with the Akeno results. Another is that Einstein was wrong. His special theory of relativity says that space is the same in all directions, but what if particles found it easier to move in certain directions? Then the cosmic rays could retain more of their energy, allowing them to beat the GZK limit.

Physicists at the Pierre Auger experiment in Mendoza, Argentina, are now working on this problem. Using 1600 detectors spread over 3000 square kilometres, Auger should be able to determine the energies of incoming cosmic rays and shed more light on the Akeno results.

Alan Watson, an astronomer at the University of Leeds, UK, and spokesman for the Pierre Auger project, is already convinced there is something worth following up here. "I have no doubts that events above 10^{20} electronvolts exist. There are sufficient examples to convince me," he says. The question now is, what are they? How many of these particles are coming in, and what direction are they coming from? Until we get that information, there's no telling how exotic the true explanation could be.

4 Belfast homeopathy results

MADELEINE Ennis, a pharmacologist at Queen's University, Belfast, was the scourge of homeopathy. She railed against its claims that a chemical remedy could be diluted to the point where a sample was unlikely to contain a single molecule of anything but water, and yet still have a healing effect. Until, that is, she set out to prove once and for all that homeopathy was bunkum.

In her most recent paper, Ennis describes how her team looked at the effects of ultra-dilute solutions of histamine on human white blood cells involved in inflammation. These "basophils" release histamine when the cells are under attack. Once released, the histamine stops them releasing any more. The study, replicated in four different labs, found that homeopathic solutions - so dilute that they probably didn't contain a single histamine molecule - worked just like histamine. Ennis might not be happy with the homeopaths' claims, but she admits that an effect cannot be ruled out.

So how could it happen? Homeopaths prepare their remedies by dissolving things like charcoal, deadly nightshade or spider venom in ethanol, and then diluting this "mother tincture" in water again and again. No matter what the level of dilution, homeopaths claim, the original remedy leaves some kind of imprint on the water molecules. Thus, however dilute the solution becomes, it is still imbued with the properties of the remedy.

You can understand why Ennis remains sceptical. And it remains true that no homeopathic remedy has ever been shown to work in a large randomised placebo-controlled clinical trial. But the Belfast study (*Inflammation Research*, vol 53, p 181) suggests that something is going on. "We are," Ennis says in her paper, "unable to explain our findings and are reporting them to encourage others to investigate this phenomenon." If the results turn out to be real, she says, the implications are profound: we may have to rewrite physics and chemistry.

5 Dark matter

TAKE our best understanding of gravity, apply it to the way galaxies spin, and you'll quickly see the problem: the galaxies should be falling apart. Galactic matter orbits around a central point because its mutual gravitational attraction creates centripetal forces. But there is not enough mass in the galaxies to produce the observed spin.

Vera Rubin, an astronomer working at the Carnegie Institution's department of terrestrial magnetism in Washington DC, spotted this anomaly in the late 1970s. The best response from physicists was to suggest there is more stuff out there than we can see. The trouble was, nobody could explain what this "dark matter" was.

And they still can't. Although researchers have made many suggestions about what kind of particles might make up dark matter, there is no consensus. It's an embarrassing hole in our understanding. Astronomical observations suggest that dark matter must make up about 90 per cent of the mass in the universe, yet we are astonishingly ignorant what that 90 per cent is.

Maybe we can't work out what dark matter is because it doesn't actually exist. That's certainly the way Rubin would like it to turn out. "If I could have my pick, I would like to learn that Newton's laws must be modified in order to correctly describe gravitational interactions at large distances," she says. "That's more appealing than a universe filled with a new kind of sub-nuclear particle."

6 Viking's methane

JULY 20, 1976. Gilbert Levin is on the edge of his seat. Millions of kilometres away on Mars, the Viking landers have scooped up some soil and mixed it with carbon-14-labelled nutrients. The mission's scientists have all agreed that if Levin's instruments on board the landers detect emissions of carbon-14-containing methane from the soil, then there must be life on Mars.

Viking reports a positive result. Something is ingesting the nutrients, metabolising them, and then belching out gas laced with carbon-14.

So why no party?

Because another instrument, designed to identify organic molecules considered essential signs of life, found nothing. Almost all the mission scientists erred on the side of caution and declared Viking's discovery a false positive. But was it?

The arguments continue to rage, but results from NASA's latest rovers show that the surface of Mars was almost certainly wet in the past and therefore hospitable to life. And there is plenty more evidence where that came from, Levin says. "Every mission to Mars has produced evidence supporting my conclusion. None has contradicted it."

Levin stands by his claim, and he is no longer alone. Joe Miller, a cell biologist at the University of Southern California in Los Angeles, has re-analysed the data and he thinks that the emissions show evidence of a circadian cycle. That is highly suggestive of life.

Levin is petitioning ESA and NASA to fly a modified version of his mission to look for "chiral" molecules. These come in left or right-handed versions: they are mirror images of each other. While biological processes tend to produce molecules that favour one chirality over the other, non-living processes create left and right-handed versions in equal numbers. If a future mission to Mars were to find that Martian "metabolism" also prefers one chiral form of a molecule to the other, that would be the best indication yet of life on Mars.

7 Tetraneutrons

FOUR years ago, a particle accelerator in France detected six particles that should not exist. They are called tetraneutrons: four neutrons that are bound together in a way that defies the laws of physics.

Francisco Miguel Marquès and colleagues at the Ganil accelerator in Caen are now gearing up to do it again. If they succeed, these clusters may oblige us to rethink the forces that hold atomic nuclei together.

The team fired beryllium nuclei at a small carbon target and analysed the debris that shot into surrounding particle detectors. They expected to see evidence for four separate neutrons hitting their detectors. Instead the Ganil team found just one flash of light in one detector. And the energy of this flash suggested that four neutrons were arriving together at the detector. Of course, their finding could have been an accident: four neutrons might just have arrived in the same place at the same time by coincidence. But that's ridiculously improbable.

Not as improbable as tetraneutrons, some might say, because in the standard model of particle physics tetraneutrons simply can't exist. According to the Pauli exclusion principle, not even two protons or neutrons in the same system can have identical quantum properties. In fact, the strong nuclear force that would hold them together is tuned in such a way that it can't even hold two lone neutrons together, let alone four. Marquès and his team were so bemused by their result that they buried the data in a research paper that was ostensibly about the possibility of finding tetraneutrons in the future (*Physical Review C*, vol 65, p 44006).

And there are still more compelling reasons to doubt the existence of tetraneutrons. If you tweak the laws of physics to allow four neutrons to bind together, all kinds of chaos ensues (*Journal of Physics* G, vol 29, L9). It would mean that the mix of elements formed after the big bang was inconsistent with what we now observe and, even worse, the elements formed would have quickly become far too heavy for the cosmos to cope. "Maybe the universe would have collapsed before it had any chance to expand," says Natalia Timofeyuk, a theorist at the University of Surrey in Guildford, UK.

There are, however, a couple of holes in this reasoning. Established theory does allow the tetraneutron to exist - though only as a ridiculously short-lived particle. "This could be a reason for four neutrons hitting the Ganil detectors simultaneously," Timofeyuk says. And there is other evidence that supports the idea of matter composed of multiple neutrons: neutron stars. These bodies, which contain an enormous number of bound neutrons, suggest that as yet unexplained forces come into play when neutrons gather en masse.

8 The Pioneer anomaly

THIS is a tale of two spacecraft. Pioneer 10 was launched in 1972; Pioneer 11 a year later. By now both craft should be drifting off into deep space with no one watching. However, their trajectories have proved far too fascinating to ignore.

That's because something has been pulling - or pushing - on them, causing them to speed up. The resulting acceleration is tiny, less than a nanometre per second per second. That's equivalent to just one ten-billionth of the gravity at Earth's surface, but it is enough to have shifted Pioneer 10 some 400,000 kilometres off track. NASA lost touch with Pioneer 11 in 1995, but up to that point it was experiencing exactly the same deviation as its sister probe. So what is causing it?

Nobody knows. Some possible explanations have already been ruled out, including software errors, the solar wind or a fuel leak. If the cause is some gravitational effect, it is not one we know anything about. In fact, physicists are so completely at a loss that some have resorted to linking this mystery with other inexplicable phenomena.

Bruce Bassett of the University of Portsmouth, UK, has suggested that the Pioneer conundrum might have something to do with variations in alpha, the fine structure constant (see "Not so constant constants", page 37). Others have talked about it as arising from dark matter - but since we don't know what dark matter is, that doesn't help much either. "This is all so maddeningly intriguing," says Michael Martin Nieto of the Los Alamos National Laboratory. "We only have proposals, none of which has been demonstrated."

Nieto has called for a new analysis of the early trajectory data from the craft, which he says might yield fresh clues. But to get to the bottom of the problem what scientists really need is a mission designed specifically to test unusual gravitational effects in the outer reaches of the solar system. Such a probe would cost between $300 million and $500 million and could piggyback on a future mission to the outer reaches of the solar system (www.arxiv.org/gr-qc/0411077).

"An explanation will be found eventually," Nieto says. "Of course I hope it is due to new physics - how stupendous that would be. But once a physicist starts working on the basis of hope he is heading for a fall." Disappointing as it may seem, Nieto thinks the explanation for the Pioneer anomaly will eventually be found in some mundane effect, such as an unnoticed source of heat on board the craft.

9 Dark energy

IT IS one of the most famous, and most embarrassing, problems in physics. In 1998, astronomers discovered that the universe is expanding at ever faster speeds. It's an effect still searching for a cause - until then, everyone thought the universe's expansion was slowing down after the big bang. "Theorists are still floundering around, looking for a sensible explanation," says cosmologist Katherine Freese of the University of Michigan, Ann Arbor. "We're all hoping that upcoming observations of supernovae, of clusters of galaxies and so on will give us more clues."

One suggestion is that some property of empty space is responsible - cosmologists call it dark energy. But all attempts to pin it down have fallen woefully short. It's also possible that Einstein's theory of general relativity may need to be tweaked when applied to the very largest scales of the universe. "The field is still wide open," Freese says.

10 The Kuiper cliff

IF YOU travel out to the far edge of the solar system, into the frigid wastes beyond Pluto, you'll see something strange. Suddenly, after passing through the Kuiper belt, a region of space teeming with icy rocks, there's nothing.

Astronomers call this boundary the Kuiper cliff, because the density of space rocks drops off so steeply. What caused it? The only answer seems to be a 10th planet. We're not talking about Quaoar or Sedna: this is a massive object, as big as Earth or Mars, that has swept the area clean of debris.

The evidence for the existence of "Planet X" is compelling, says Alan Stern, an astronomer at the Southwest Research Institute in Boulder, Colorado. But although calculations show that such a body could account for the Kuiper cliff (*Icarus*, vol 160, p 32), no one has ever seen this fabled 10th planet.

There's a good reason for that. The Kuiper belt is just too far away for us to get a decent view. We need to get out there and have a look before we can say anything about the region. And that won't be possible for another decade, at least. NASA's New Horizons probe, which will head out to Pluto and the Kuiper belt, is scheduled for launch in January 2006. It won't reach Pluto until 2015, so if you are looking for an explanation of the vast, empty gulf of the Kuiper cliff, watch this space.

11 The Wow signal

IT WAS 37 seconds long and came from outer space. On 15 August 1977 it caused astronomer Jerry Ehman, then of Ohio State University in Columbus, to scrawl "Wow!" on the printout from Big Ear, Ohio State's radio telescope in Delaware. And 28 years later no one knows what created the signal. "I am still waiting for a definitive explanation that makes sense," Ehman says.

Coming from the direction of Sagittarius, the pulse of radiation was confined to a narrow range of radio frequencies around 1420 megahertz. This frequency is in a part of the radio spectrum in which all transmissions are prohibited by international agreement. Natural sources of radiation, such as the thermal emissions from planets, usually cover a much broader sweep of frequencies. So what caused it?

The nearest star in that direction is 220 light years away. If that is where is came from, it would have had to be a pretty powerful astronomical event - or an advanced alien civilisation using an astonishingly large and powerful transmitter.

The fact that hundreds of sweeps over the same patch of sky have found nothing like the Wow signal doesn't mean it's not aliens. When you consider the fact that the Big Ear telescope covers only one-millionth of the sky at any time, and an alien transmitter would also likely beam out over the same fraction of sky, the chances of spotting the signal again are remote, to say the least.

Others think there must be a mundane explanation. Dan Wertheimer, chief scientist for the SETI@home project, says the Wow signal was almost certainly pollution: radio-frequency interference from Earth-based transmissions. "We've seen many signals like this, and these sorts of signals have always turned out to be interference," he says. The debate continues.

12 Not-so-constant constants

IN 1997 astronomer John Webb and his team at the University of New South Wales in Sydney analysed the light reaching Earth from distant quasars. On its 12-billion-year journey, the light had passed through interstellar clouds of metals such as iron, nickel and chromium, and the researchers found these atoms had absorbed some of the photons of quasar light - but not the ones they were expecting.

If the observations are correct, the only vaguely reasonable explanation is that a constant of physics called the fine structure constant, or alpha, had a different value at the time the light passed through the clouds.

But that's heresy. Alpha is an extremely important constant that determines how light interacts with matter - and it shouldn't be able to change. Its value depends on, among other things, the charge on the electron, the speed of light and Planck's constant. Could one of these really have changed?

No one in physics wanted to believe the measurements. Webb and his team have been trying for years to find an error in their results. But so far they have failed.

Webb's are not the only results that suggest something is missing from our understanding of alpha. A recent analysis of the only known natural nuclear reactor, which was active nearly 2 billion years ago at what is now Oklo in Gabon, also suggests something about light's interaction with matter has changed.

The ratio of certain radioactive isotopes produced within such a reactor depends on alpha, and so looking at the fission products left behind in the ground at Oklo provides a way to work out the value of the constant at the time of their formation. Using this method, Steve Lamoreaux and his colleagues at the Los Alamos National Laboratory in New Mexico suggest that alpha may have decreased by more than 4 per cent since Oklo started up (*Physical Review D*, vol 69, p 121701).

There are gainsayers who still dispute any change in alpha. Patrick Petitjean, an astronomer at the Institute of Astrophysics in Paris, led a team that analysed quasar light picked up by the Very Large Telescope (VLT) in Chile and found no evidence that alpha has changed. But Webb, who is now looking at the VLT measurements, says that they require a more complex analysis than Petitjean's team has carried out. Webb's group is working on that now, and may be in a position to declare the anomaly resolved - or not - later this year.

"It's difficult to say how long it's going to take," says team member Michael Murphy of the University of Cambridge. "The more we look at these new data, the more difficulties we see." But whatever the answer, the work will still be valuable. An analysis of the way light passes through distant molecular clouds will reveal more about how the elements were produced early in the universe's history.

13 Cold fusion

AFTER 16 years, it's back. In fact, cold fusion never really went away. Over a 10-year period from 1989, US navy labs ran more than 200 experiments to investigate whether nuclear reactions generating more energy than they consume - supposedly only possible inside stars - can occur at room temperature. Numerous researchers have since pronounced themselves believers.

With controllable cold fusion, many of the world's energy problems would melt away: no wonder the US Department of Energy is interested. In December, after a lengthy review of the evidence, it said it was open to receiving proposals for new cold fusion experiments.

That's quite a turnaround. The DoE's first report on the subject, published 15 years ago, concluded that the original cold fusion results, produced by Martin Fleischmann and Stanley Pons of the University of Utah and unveiled at a press conference in 1989, were impossible to reproduce, and thus probably false.

The basic claim of cold fusion is that dunking palladium electrodes into heavy water - in which oxygen is combined with the hydrogen isotope deuterium - can release a large amount of energy. Placing a voltage across the electrodes supposedly allows deuterium nuclei to move into palladium's molecular lattice, enabling them to overcome their natural repulsion and fuse together, releasing a blast of energy. The snag is that fusion at room temperature is deemed impossible by every accepted scientific theory.

That doesn't matter, according to David Nagel, an engineer at George Washington University in Washington DC. Superconductors took 40 years to explain, he points out, so there's no reason to dismiss cold fusion. "The experimental case is bulletproof," he says. "You can't make it go away."

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