Altered by human activity

EMISSIONS FROM FOSSIL FUELS ARE FOUND TO BE PUMPING OLDER CARBON INTO THE ATMOSPHERE, WRITES **S ANANTHANARAYANAN**

The carbon content of the atmosphere has a tiny part that is radioactive. As processes that add radioactive carbon to the atmosphere are in balance with the rate of its depletion by radioactivity, the percentage of carbon that is radioactive stays constant. During the last century, and more so lately, industry has added huge quantities of carbon from coal and petroleum, which are fossil fuels, to the atmosphere. This carbon is of great antiquity and almost all its radioactive material has decayed, therefore the proportions of normal and radioactive carbon in the atmosphere are being altered by human activity.

Heather D Graven at Imperial College, London, in a paper in the journal *Proceedings of the National Academy of Sciences* describes a study of how the composition, apart from sheer quantity, of atmospheric carbon is changing, and its implications.

The processes by which radioactive carbon enters and leaves the atmosphere make sure that the net quantity, under normal circumstances, stays constant. Creation of radioactive carbon comes about by the action of cosmic rays and the effects on nitrogen atoms in the upper atmosphere. The nitrogen atom has a nucleus with 14 particles, seven positively charged protons and seven neutrons, and is denoted as ^{14}N. As a result of cosmic ray action, one of the protons is exchanged for a neutron, leaving a nucleus with only six protons, which makes it a nucleus of carbon, and eight neutrons. The normal carbon nucleus has six protons and only six neutrons, with a total of 12 particles.

Although there are now two more neutrons, this does not change chemical properties, and the nucleus is still one of carbon, although with mass 14, in place of 12. But the extra load of neutrons creates instability and this form of carbon, denoted as ^{14}C, ultimately decays, going right back to ^{14}N, where it came from. The average time that ^{14}C takes to decay is 8,251 years, which works out to saying that the number of ^{14}C atoms, which are there in billions, in a sample would drop to half that number in 5,730 years. When a sufficient number of radioactive atoms accumulates, as a result of the production by the action of cosmic rays, the number that decay becomes equal to the number that are produced at any time. As the earth has been around for millions of years, there is now a balance in the number produced in the upper atmosphere and the number that decay, and the total number is almost constant.

Carbon dating

The tissue of living things contains a great deal of carbon, and this carbon content, which is regularly cycled through the atmosphere by respiration and nutrition, also has the same ratio of ^{14}C and normal C as the atmosphere. But when the animal dies, the exchange of carbon with the environment stops and the ^{14}C content only decays, without addition of fresh ^{14}C. The level of radioactivity in an organism that has died would, hence, gradually drop to half in 5,730 years and so on.

This declining rate of radioactivity in non-living organic matter has, thus, become a handy way to estimate how long it has been since a once living thing has died. If the level of radioactivity is one fourth of that of the atmosphere, for instance, we can say that it died 11,460 years ago, or 22,920 years ago if it is one eighth, and so on. This is the method now perfected for dating archaeological remains, specimens of art, making use of the carbon in bones, fossils, canvas or papyrus, or even vegetable dyes used for cave drawings, etc.

But the basis of the method, it will be noticed, is the presumption that the object, at the time when its material was living, had the same level of ^{14}C content as the atmosphere today. As the level of ^{14}C in the atmosphere is taken as having been constant for a long time, the presumption is generally valid and so has been the method of dating by radioactive carbon. This presumption, however, has started breaking down since the last century or so, when human action has started disrupting the environment.

The first large variations in the level of 14C in the atmosphere arose when nations began mid-air nuclear testing in the 1950s and 1960s.

Heather D Graven

The method of carbon dating itself was discovered only in 1949 and has since made a great difference to our view of antiquity. Radiocarbon dating has been verified and possible variations have been calibrated with the help of other standards, like known historical periods, changes of the thickness of layers in the bark of ancient trees during known climate extremes. Extensive studies have provided a "correction" chart with the help of which estimates made by direct carbon dating can be adjusted to take into account variations in the level of radioactive content of the atmosphere at different times, etc, and the method has been generally reliable.

Climate change

The first large variations in the level of ^{14}C in the atmosphere arose when nations began mid-air nuclear testing in the 1950s and 1960s. When largescale nuclear explosions are detonated in the air, as opposed to underground or in the sea, there is a huge generation of ^{14}C and also a spike in its levels in the atmosphere. Earth's carbon content is actually largely in its vegetative cover and very largely in the oceans. But in the years immediately after the epoch of mid-air testing, the newly created ^{14}C had not reached these carbon reservoirs and was concentrated in the atmosphere. The percentage, hence, almost doubled at the time, although it has greatly dropped since, as carbon spreads into the surface and then the deep sea.

The much larger effect on ^{14}C content, however, is the consequence, over the last century and very much in recent decades, of the carbon emission from the use of fossil fuels. Coal and petroleum represent vegetable matter of millions of years ago and the carbon they contain started off with the traces of ^{14}C that were present in the atmosphere, and, hence, in plants and trees at that time. But once buried and compressed, on the way to turning into coal or oil, they stopped communicating with the atmosphere and, hence, replenishing their content of ^{14}C, which has been decaying since millions of years. We can readily imagine that the radioactive carbon that remains after such a long time is negligible.

When coal or mineral oil is burnt in power plants, the CO_2 released hence contains very little radioactive carbon, and since the last century these depleted emissions have been reducing the relative ^{14}C content of the atmosphere. The research that Dr Graven has carried out is to make use of available records and extrapolations, with the help of the Intergovernmental Panel on Climate Change, estimates of CO_2 emission during the rest of the century, to study how projected emissions during climate change would affect the percentage of ^{14}C in the atmosphere.

The simulations carried out by her indicate a serious reduction in ^{14}C content, with depletion equal to an ageing by 1,000 years, compared to pre-industrial levels, by 2050, and by 2,000 years by 2100, if the present rate of emission of carbon from fossil fuels continues. This is to say that a specimen that belongs to 2100 would show the ^{14}C content of a specimen of 100 AD. Such distortion of the basis for carbon dating would affect a number of applications of the technique, with samples of recent origin simply not permitting dating, as they would display very low ^{14}C levels. The technique has been used for detecting forgeries, where the recent origin of a fake being passed off as an ancient original is revealed, for instance. This would no longer be available as the recent material of the fake would also show low ^{14}C levels, as it were older, Dr Graven says.

Another area that would be affected is the use of radiocarbon measurement for the purpose of estimating the volume of fossil-based carbon emissions in urban areas. The present comparison of global ^{14}C levels with the level in the urban area gives a fair measure. But with falling global levels, much more precise measurements would be necessary to attain equally reliable results, says Dr Graven.

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Interconnected processes

Ordinary carbon itself, like all other elements, did not arise on earth but in exploding stars, which gave rise to the cloud that led to the solar system. It is the radioactive 14C that is generated every instant on earth and, fortunately, not so fast that it builds up to make life impossible because of radioactivity. The active reservoirs of carbon, apart from fossil fuels, are the atmosphere, the surface ocean and the deep ocean. The atmosphere holds only 1.9 per cent of this and the ocean surface another 2.4 per cent, while the deep ocean has more than 90 per cent.

Radioactive carbon that arises in the atmosphere combines with oxygen as carbon dioxide and takes some years to mix with the surface ocean. The carbon in the deep sea is over 1,000 years old and this also mixes with the surface to some extent. The carbon content of fish in shallow waters is, thus, a little depleted in 14C and much more so deeper down. The most depleted reservoirs, of course, are coal and oil deposits that are millions of years old. But even if their release into the atmosphere were to wreck the value of carbon dating for archaeology, detecting forgeries or even estimating emissions in cities, etc, the loss would be negligible compared to other effects of global warming, sea level rise, crop disruption… But the drop in levels of radioactive carbon is an instance of how subtle and widespread – and not even connected with the climate – the effects of marginal warming and CO_2 rise are. And the study helps determine how inter-related the processes of earth are.

PLUS POINTS

Looking for aliens

Yuri Milner

Yuri Milner, a Russian entrepreneur who funds a range of science prizes, has launched a $100 million project called Breakthrough Listen, the biggest and most expensive search for alien life ever, backed by famous scientists including Stephen Hawking and Frank Drake. He will also launch another project called Breakthrough Message, which will work together to create a message that can be sent to aliens. The best messages will share a reward of $1 million.

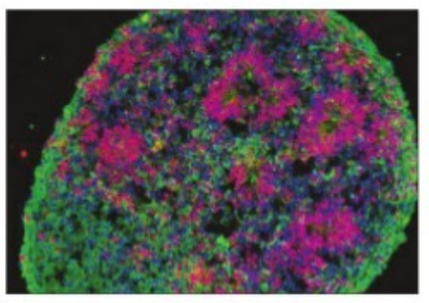
The project will now give those scientists looking for life elsewhere in the universe better access than ever to telescopes and computing power. Hawking said it differentiated itself from previous initiatives because of its increased resources — including extra time with telescopes and more data processing capabilities. He also warned against getting in touch with any extraterrestrial life that is found. Confrontations between more and less advanced civilisations have often gone wrong, and aliens could be billions of years ahead of us and so see us as no more valuable than we see bacteria. Other members of the group of high-profile scientists backing the mission said they didn't want to send a message for fear of upsetting people who worry that aliens might become enraged by our doing so. Using funds to send messages would also be a waste of limited funds, said Frank Drake.

But Ann Druyan, who is leading the work on Breakthrough Message, said the work to decide what to say to aliens was valuable even if it didn't actually get sent.

ANDREW GRIFFIN/THE INDEPENDENT

Idiopathic autism

An examination of tiny, brain-like organoids generated from the skin cells of patients with Autism Spectrum Disorder suggests that the condition may be associated with an



Human brain oganoid.

overproduction of inhibitory neurons, among other things. The study, published on 16 July in *Cell*, reveals that although the patients' symptoms arose spontaneously, their brain cells behaved similarly *in vitro*.

"These are patients with idiopathic autism that do not share any genetic causes, and yet the authors find phenotypes shared between their cells. That's impressive," said neuroscientist and stem cell biologist Alysson Muotri of the University of California, San Diego, who was not involved in the study. "If someone had asked me, I would have said, 'You won't find anything in common, it's probably going to be a mixed bag.' But no… there seems to be key things that are dysregulated in all of them."

RUTH WILLIAMS/THE SCIENTIST

Dengue treatment

Scientists in Singapore say they have found a potent antibody to fight the second of four types of viruses that cause dengue fever, bringing possible treatments closer. In a study published in Science earlier this month, researchers from the Duke-NUS Graduate Medical School in Singapore show which sites on the virus stimulate the immune system to

develop effective antibodies in mice. "These sites, when incorporated into a vaccine, will likely stimulate a protective response in recipients, making this antibody a candidate to develop treatments for humans," said Shee-Mei Lok, a lead researcher in the study.

In a statement to reporters, Lok said the new antibody could be used in a "cocktail treatment" combining four antibodies — one against each type. She added that her lab had already found antibodies that neutralised Types 1 and 3 of the virus, and were working to find an antibody against Type 4.

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SIGNALS OF IMPORT

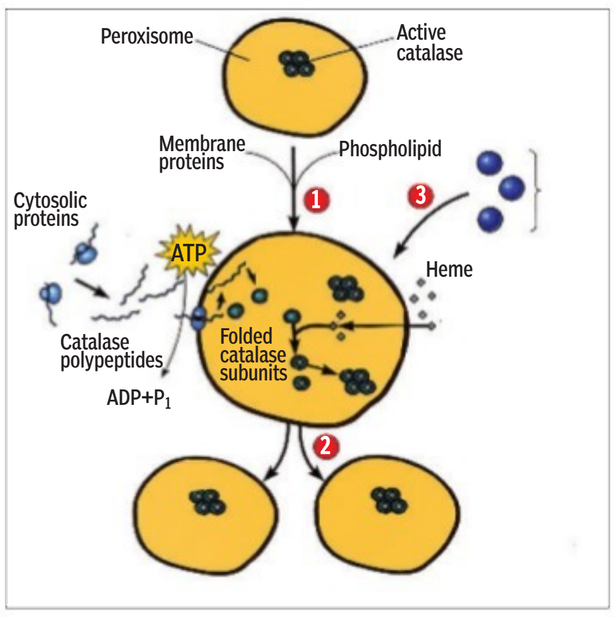
PEROXISOME BIOGENESIS OCCURS BY DIVISION OF PRE-EXISTING PEROXISOMES, SAYS **TAPAN KUMAR MAITRA**

Like other organelles, peroxisomes increase in number as cells grow and divide and this proliferation is called biogenesis. The proteins required for this process are known as peroxins. In the case of endosomes and lysosomes, biogenesis occurs by fusion of vesicles budding from the Golgi complex.

Peroxisomes were once thought to form from vesicles in a manner similar to endosome formation. Later, most investigators believed that their biogenesis occurred solely from the division of pre-existing peroxisomes, a mode similar to that of mitochondria and chloroplasts. Recent evidence suggests that new peroxisomes can be formed by either of these two methods, or perhaps by a combination of the two. Either way, their biogenesis raises two important questions.

First, where do the lipids that make up the newly synthesised peroxisomal membrane come from? The answer is that a portion of the lipids are synthesised by peroxisomal enzymes and the rest, especially phosphatidylcholine and phosphatidylethanolamine, are probably acquired from the ER. Most of these lipids are believed to be conveyed to the peroxisome by the phospholipid exchange proteins mentioned earlier. However, there is some evidence that these exchange proteins may not always be efficient enough to account for the rapid incorporation of new lipids and that some direct transfer from ER-derived vesicles may be involved.

Second, where are the new enzymes and other proteins that are present in the peroxisomal membrane and matrix synthesised? Proteins destined for peroxisomes are synthesised not on ER-associated ribosomes but on free cytosolic ribosomes. Thus, the new proteins' full-length polypeptides are incorporated into pre-existing peroxisomes post-translationally. This passage of polypeptides across the peroxisomal membrane is an ATP-dependent process mediated by specific membrane peroxins, although the precise role of ATP is unclear.



New peroxisomes typically arise by the division of existing peroxisomes rather than by fusion of vesicles from the Golgi complex. (1) Lipids, membrane proteins, and matrix enzymes are added to existing peroxisomes from cytosolic sources. The enzyme shown here is catalase, a tetrameric protein. The polypeptides are synthesised on cytosolic ribosomes and are threaded through the membrane posttranslationally. Heme, a co-factor, enters the peroxisomal lumen via a separate pathway. The polypeptides are then folded and assembled to form the active tetrameric protein. (2) After lipids and protein are added, new peroxisomes are formed by the division of the existing organelle. (3) Some researchers believe that peroxisomes can obtain proteins or form *de novo* from protoperoxisomal vesicles derived from the ER.

The protein depicted in the figure is catalase, a tetrameric entity with a heme group bound to each sub-unit. The sub-units are synthesised individually on cytosolic ribosomes imported into the peroxisome, refolded, and assembled, along with heme, into the active tetrameric enzyme. Peroxisomes have also been shown to be able to import not only single, unfolded polypeptides but also larger, folded polypeptides and even native oligomeric proteins.

Recent work suggests that some peroxins are synthesised in the cytosol but then travel to the ER before being incorporated into peroxisomes. Evidence for this route includes the presence on certain peroxins of N-linked oligosaccharides typical of ER-synthesised proteins. Additionally, treatment of yeast cells with the toxin brefeldin A, which prevents formation of ER-derived vesicles, causes accumulation of the peroxin Pex3p in the ER. Similarly, in plant cells, ascorbate peroxidase appears to be routed to a sub-domain of the ER after its synthesis in the cytosol but before its incorporation into the peroxisome.

This proposed sub-domain of the ER, presumably involved in sorting cytosolic proteins destined for the peroxisome, has been termed the peroxisomal ER (pER), although its very existence is currently still controversial. Likewise, the existence of the protoperoxisome, an ER-derived vesicle considered by some researchers to be capable of developing *de novo* into a peroxisome, is currently the subject of much debate.

For post-translational import to work, each protein destined for a specific organelle must have some sort of signal that directs, or targets, the protein to the correct organelle. Such a signal functions by recognising specific receptors or other features on the surface of the appropriate membrane. The signal in each case is a sequence of amino acids, which differ in sequence, length, and location for proteins targeted to different organelles. The signal that targets at least some peroxisomal proteins to their destination consists of just three amino acids and is found at or near the carboxyl terminus of the molecule. For example, the most common sequence is serine-lysine-leucine (SKL), though a limited number of other amino acids are possible at each of the three locations.

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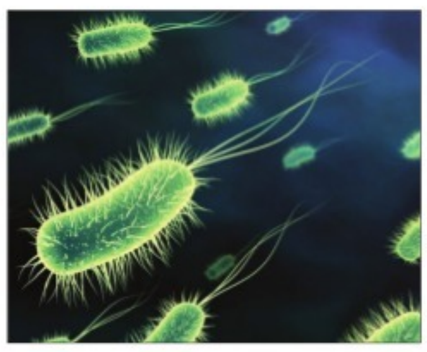
Potentially game-changing

BIPLOB BHATTACHARYA REPORTS ON A NOVEL TECHNIQUE TO FIGHT ANTIMICROBIAL RESISTANCE

Antibiotics — a class of antibacterials discovered in the early 20th century — play a vital role in controlling bacterial diseases. But though they seem simple enough, failure to understand these drugs can involve the risk of antibiotic resistance, especially in developing countries where more than 50 per cent of antibiotics worldwide are purchased privately without a prescription and result in inappropriate use.

The Centre for Disease Control and Prevention explains antibiotic/antimicrobial resistance as the ability of microbes to resist the effects of drugs — that is, the germs are not killed and their growth, not stopped.



Antibiotics, when not taken in the proper dosage, or for as long as prescribed, involve the risk of the infection not being adequately treated. The resultant surviving bacteria will slowly gain resistance to the antibiotic, leading to persistent or recurrent infections. Hence, both overuse and misuse of antibiotics can contribute to resistance.

Some common ways drug-resistant infections can be prevented include immunisation, safe food preparation, hand washing and using antibiotics as directed and only when necessary. It has been declared a crisis by the World Health Organisation, the Centres for Disease Control and Prevention, the Institute of Medicine, the Infectious Diseases Society of America and virtually all other relevant organisations.

Antibiotic resistance varies from person to person, some being at a higher risk than others but no one can completely avoid the threat of resistance development. Infections with resistant organisms are difficult to treat, requiring costly and sometimes toxic alternatives.

N-thiolated ß-lactams is a novel discovery, where a new family of bioactive agents has antibacterial, antifungal, and anticancer properties. Unlike penicillin, which inhibits cell wall cross-linking proteins and affords a broad spectrum of bactericidal activity, these N-thiolated lactams are bacteriostatic in nature and act by FabH-mediated inhibition of bacterial fatty acid synthesis. It can be administered through dual-action drugs — also known as "hybrids" or "combination drugs" that consist of a compound that is a combination of two drugs with different pharmacological actions at a similar efficacious dose. They have the ability to deliver two drugs simultaneously, with each one having an effect on a different or same target. In most cases, the active site of the drugs, also known as "pharmacophores", have different modes of action, which make it less resistant. The strategy herein is to decrease the threat by making a multi-action antibiotic pro-drug, in which two covalently bonded compounds can eventually kill its target.

This technique can not only increase the drug efficacy owing to inhibition of two targets at once but also the resistance to one or both antibiotics can be overcome. All the dual-acting N-thiolated lactams were tested against the Eskape pathogens, which are a collection of six deadly superbugs. Few compounds have displayed such promising bioactivity against the *S aureus* pathogen.

Therefore, among various new paradigms of antibiotic drug discovery N-thiolated ß-lactams have proved to be a novel class of compounds with immense potential.

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