Steering them away from targets

A TENDENCY OF MOSQUITOES TO PREFER INFECTED HUMANS AFFECTS HOW FAST MALARIA SPREADS IN A COMMUNITY, WRITES **S ANANTHANARAYANAN**

This unexpected bias of mosquitoes, which has been recently discovered, is one of the factors that have been considered in developing a mathematical formula of how an outbreak of malaria may progress.

Xiunan Wang and Xiao-Qiang Zhao, of the department of mathematics and statistics, Memorial University of Newfoundland, St John's, Canada, publish in the journal of the *Society for Industrial and Applied Mathematics*. their study of malaria transmission dynamics or the factors that influence how the numbers of infected persons rise or fall and how mosquitoes flourish or flounder.

"Mathematical models provide powerful tools for explaining and predicting malaria transmission trends, and also for quantifying the effectiveness of different intervention and eradication strategies in malaria-endemic regions," the authors say in the paper. As the data of instances of infection is often inadequate, statistical methods need to be employed both to devise and

A female anopheles mosquito

evaluate strategies for the prevention and then, management of malaria. In this context, it is useful to have an understanding of how the malaria pathogen behaves and adapts in different conditions.

Whether instances of malaria in a community would persist depends how soon mosquitoes may pick up the pathogen from infected persons, how soon they are ready to infect others and then also on how fast mosquitoes breed and on how likely they are to bite infected persons, to acquire the pathogen and then to bite susceptible persons.

The model that Wang and Zhao have created takes into account three factors that affect the infection cycle — first is the climate, which affects the breeding of mosquitoes. Second is the time it takes for the malaria parasite, once it has entered the mosquito's body, to develop into the form for the mosquito to be able to infect a person. And third is the recently discovered feature that the mosquito, in taking a blood meal, appears to select infected persons in place of going for all persons with equal likelihood. The climate factor, and particularly the temperature, is found to be important, as the breeding time for mosquitoes reduces from 65 days to 7.3 days if the ambient temperature rises from 12 ^{o}C to 31 ^{o}C, the paper says. The second limiting factor is the time it takes for the malaria parasite to develop within the mosquito and migrate to the salivary glands, from which it can enter the bloodstream of a person or animal that the mosquito feeds upon. This time, a delay, after the mosquito picks up the infection, is called the extrinsic incubation period and can range from 10 to 30 days. As the lifetime of a mosquito can be from three to 100 days, some of the mosquitoes may not live long enough to be infective, while those that live longer than the incubation period would be infective for the rest of their days.

The third factor, called vector-bias, or the selective behaviour of the mosquito, which is the agent that carries the infective material, has been observed and studied by a number of researchers since the 1980s. Experiments showed that mosquitoes preferred malaria-infected hosts at the stages of attraction and penetration, of probing and location of blood, and again during the taking of blood. This was the case with experimental mice and hens infected with malaria and the attraction for infected targets was there even when the mosquitoes were prevented from performing the actual bite.

A more recent study, in 2005, was with three groups of children in western Kenya, where one group was uninfected; the second group was infected with the non-infective stage of falciparum malaria and the third group with the active phase of the infection. The third group was found to attract twice as many mosquito bites as the first two groups. A follow-up trial was then conducted after the children were cleared of the infection by treatment, and it was found that mosquitoes now showed no preference, including for the group that had earlier harboured the active infection.

This bias of mosquitoes towards malaria-infected hosts appears to be some effect that the malaria parasite has evolved to have upon hosts, to act as a signal to attract mosquitoes. This would be an adaptation by which the parasite promotes its own transmission to new hosts and hence its perpetuation. Here, it should be mentioned that it is the female mosquito, which needs protein for her reproductive role, feeds on blood meals from people and animals. The male mosquito, in contrast, is content with nectar from plants. While the female mosquito needs to get blood, there are features in the blood of infected individuals that make this the preferred nutrition for the female mosquito.

It has been found that the feeding time is shortened by a whole minute when mosquitoes fed on malaria infected mice, there are also theoretical bases to hold that the mechanics of blood extraction by mosquitoes would favour blood with a lower red blood corpuscle content — a feature of malaria-infected blood.

Wang and Zhao hence factored the preference of mosquitoes to go for malaria-infected over malaria-susceptible targets into the mathematical model. The model analyses the fraction of the population that is infected, and is hence a source for mosquitoes, and then the susceptible fraction, which is the field for infected mosquitoes to successfully infect; the lifetime of mosquitoes; the time it takes for the parasite to get active; the breeding time of mosquitoes, and then the probability of mosquitoes going for infected or non-infected targets. The model then arrives at an expression that would indicate whether the infection would rise in the community or decline.

One can see that with a rise in the number of infected targets, the number of mosquitoes that are capable of infecting targets would increase but this would also limit the number of those susceptible for new infections. There would also be the reduction of the number of all targets, both by natural attrition as well as a result of the disease. At what level the addition to the numbers infected would stop rising, or start falling, or fluctuate, would depend on the preference that the mosquitoes show for infected hosts. The net result of the study was then the development of a measure, which is called the reproduction ratio, whose value, either less or greater than one, indicates whether the disease would die out or stabilise at a positive, periodic state.

The significant things learnt from the analysis are the importance of the ambient temperature and the extrinsic incubation period. While the dependence on temperature points to another danger that would increase with global warming, the dependence on the incubation period is an invitation to scientists to develop drugs that infected persons could take and thereby affect the internal processes of mosquitoes that feed on them — a case of the human hosts becoming the vectors for administering the drug to the mosquito.

The growth of the infection is also seen to depend on the ratio of the preference of mosquitoes to bite infected persons over susceptible persons. If the medium by which this condition is communicated to mosquitoes were discovered, scientists could design ways to steer mosquitoes away from susceptible targets and hence the disease itself towards extinction.

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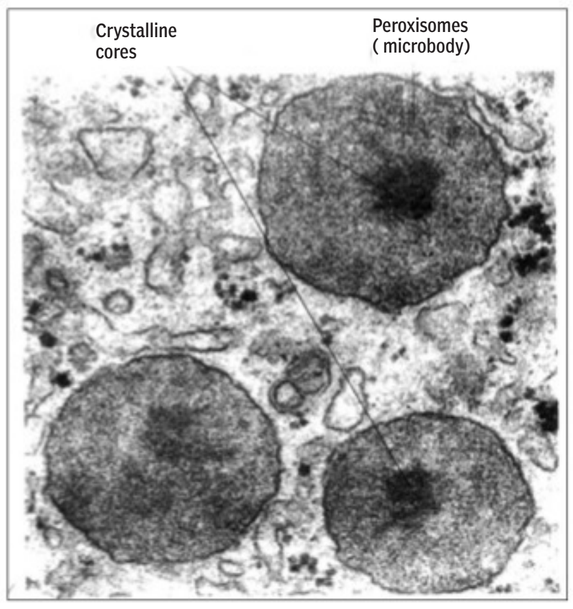
ESSENTIAL ORGANELLE

TAPAN KUMAR MAITRA EXPLAINS THE FUNCTION OF PEROXISOMES

Peroxisomes, like the Golgi complex and lysosomes, are bound by single membranes. This organelle is found in all eukaryotic cells but is especially prominent in mammalian kidney and liver cells, in algae and photo-synthetic cells of plants, and in germinating seedlings of plant species that store fat in their seeds. Peroxisomes are somewhat smaller than mitochondria, though there is considerable variation in size, depending on the tissue in which they are found.

Regardless of location or size, the defining characteristic of a peroxisome is the presence of catalase — an enzyme essential for the degradation of hydrogen peroxide (H_20_2). Hydrogen peroxide is a potentially toxic compound that is formed by a variety of oxidative reactions catalysed by oxidases. Both catalase and the oxidases are confined to peroxisomes. Thus, the generation and degra-dation of H_20_2 occur within the same organelle, thereby protecting other parts of the cell from exposure to this harmful compound. Before discussing the functions of peroxisomes further, let us look at how peroxisomes were discovered and how they are distinguished from other organelles when viewed by electron microscopy.



This electron micrograph shows several peroxisomes (microbodies) in the cytoplasm of a rat liver cell. A crystalline core is readily visible in each microbody. In animal microbodies, the cores are almost always crystalline urate oxidase.

Christian de Duve and his colleagues discovered not only lysosomes but also peroxisomes. During the course of their early studies on lysosomes, the researchers encountered at least one enzyme, urate oxidase, which appeared to be associated with lysosomal fractions but was not an acid hydrolase. By using a gradient of sucrose concentration, the researchers found that the urate oxi-dase from rat liver was recovered in a region of the gradient having a slightly higher density than that of other organelles, such as lysosomes and mitochondria.

Once separation of this new organelle was achieved, additional enzymes were identified in the fractions containing urate oxidase, including catalase and D-amino acid oxidase. Catalase degrades H_20_2 and like urate oxidase, D-amino acid oxidase generates H_20_2. Because of its apparent involvement in hydrogen peroxide metabolism, the new organelle became known as a peroxisome.

Once peroxisomes had been identified and isolated biochemically, the existence of organelles with the expected properties was confirmed by electron microscopy- first in isolated peroxisomal fractions from density gradients and then in intact cells. Peroxisomes turned out to be the functional equivalents of organelles that had been seen earlier in electron micrographs of both animal and plant cells. Because their function was not known at the time, these organelles were simply called microbodies. In both plant and animal cells, a microbody is usually about 0.2-2.0/lm in diameter, is surrounded by a single membrane, and generally has a finely granular matrix (interior of the organelle).

Animal peroxisomes often contain a distinct crystalline core, which usually consists of a crystalline form of urate oxidase. Crystalline cores are also often present in the peroxisomes of plant leaves but these usually consist of catalase instead. When such cores are present, it is easy to identify microbodies as peroxisomes, since urate oxidase and catalase are two of the enzymes by which peroxisomes are defined. In the absence of a crystalline core, however, it is not always easy to spot peroxisomes ultrastructurally. A useful technique in such cases is a cyto-chemical test for catalase called the diaminobenzidine reaction. This assay depends on the ability of catalase to oxidise DAB to a polymeric form that causes deposition of electron-dense osmium atoms when the tissue is treated with osmium tetroxide (O_s0_4). The resulting electron-dense deposits can be readily seen in cells from stained tissue. In animal peroxisomes, the entire internal space often stains intensely with DAB, indicating that catalase exists as a soluble enzyme uniformly distributed throughout the matrix of the organelle. In plant leaf cells, DAB treatment preferentially stains the crystalline cores of the peroxisomes, thereby definitively identifying the cores as crystalline catalase.

Because catalase is the single enzyme present in all peroxisomes and does not routinely occur in any other organelle, the DAB reaction is a very reliable and highly specific means of identifying organelles unambiguously as peroxisomes.

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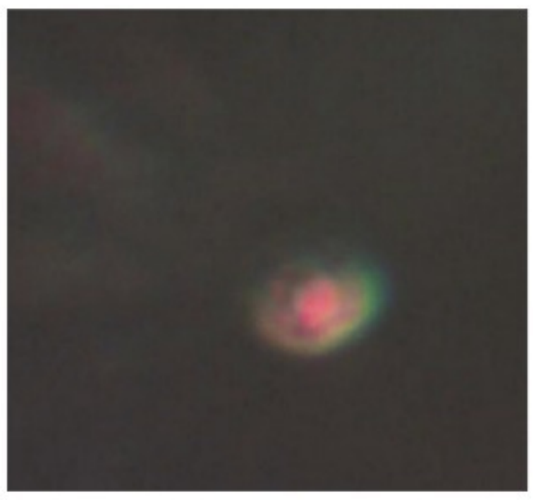
May not be what it seems

EXPERTS HAVE SAID THAT TWO HARVARD UNIVERSITY PHYSICISTS MIGHT HAVE MADE A MISTAKE IN CLAIMING TO HAVE TURNED HYDROGEN INTO A METAL. **ANDREW GRIFFIN** REPORTS



The scientists who claim to have crushed hydrogen into a metal might have made one important mistake, according to experts.

Two physicists claimed that they had finally succeeded in a feat that scientists have been attempting for almost a hundred years — crushing hydrogen and turning it into metal through an "alchemical" process. Such a discovery would potentially revolutionise technology and space travel, and has been hailed as one of the biggest breakthroughs in history.

But experts have cast doubts on the claims of the two scientists, Ranga Dias and Isaac Silvera, both physicists at Harvard University. They might have mistaken something else for the important metal, a number of other scientists have said.

The Harvard researchers first posted their work to *arXiv*, a website that collects scientific studies before they are published through peer-reviewed journals, in October. At that point it attracted huge amounts of criticism from other scientists who argued that it was based on a mistake. But the paper was published recently in the journal *Science* all the same, heralding a succession of headlines that claimed that humanity had made a huge breakthrough that could shed light on some of the central questions of the universe. The news was covered in a range of newspapers and websites, including *The Independent*.

But five different experts have told *Nature*'s news reporters that they don't believe the claim and that it could be based on an error. One scientist told the news organisation that the paper isn't "convincing at all".

To do the research, the scientists crushed tiny bits of hydrogen beneath diamond anvils, exerting more pressure on it than is found at the centre of the Earth. Small steps forward have been made through the work but researchers have yet not been able to show off the shiny metal that would be expected to be seen.

That is what the two Harvard scientists claimed to have done. But they cannot yet show off the piece of metal because it is still stuck between the jaws of the anvil — and they say that removing it might cause it to disappear entirely.

The researchers believe, however, that the reflective and shiny material they can see crushed in the anvil is metallic hydrogen. One of the scientists, Silvera, said that when looking through a microscope at the sample it looked to be shiny and so "you can only believe (it) is a metal".

But other researchers have said that they don't necessarily believe that it is a metal. The shininess may be something else entirely — like aluminium oxide, which is known to coat the diamonds that sit in the anvil and may become shiny under high pressure.

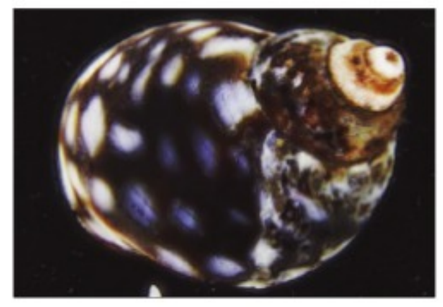
Scientists have also cast doubts on the amount of pressure that the paper claims to have pushed onto the hydrogen. The researchers didn't take detailed enough measurements throughout the process and so it's hard to see whether they were pushing as hard as they claimed onto the hydrogen. Even before the paper was criticised, other researchers have criticised the lab's approach and methods, arguing that it could lead to false positives.

Scientists have also questioned why the team published their results before they have taken the material out of the anvil, and will get to work on doing other experiments.

But the researchers claimed in press materials that they had done so in order to publicise their "breakthrough event", and that further experiments would shed more light.

THE INDEPENDENT

PLUS POINTS



Forced into exile

Tropical fish and other marine species have been discovered hundreds of miles further north in waters from California to the Indian Ocean and the Atlantic, according to a new study.

Researchers examined reports of "first sightings" of new species from around the world as part of efforts to monitor how marine creatures react to rising ocean temperatures. A shift towards both poles is expected as a result, but some species have made remarkable journeys.

A Monrovia doctorfish was discovered in European Atlantic waters — just off the coast of Portugal — for the first time in 2013. It was more than 1,600km (about 1,000 miles) north of tropical waters. And blue-spotted cornetfish have been found even further north in temperate waters, having spread through the sub-tropical region. A species of sea snail from the peri-winkle family, called *Echinolittorina punctate*, which historically lived in the southern Mediterranean Sea, is now to be found off the south coast of France.

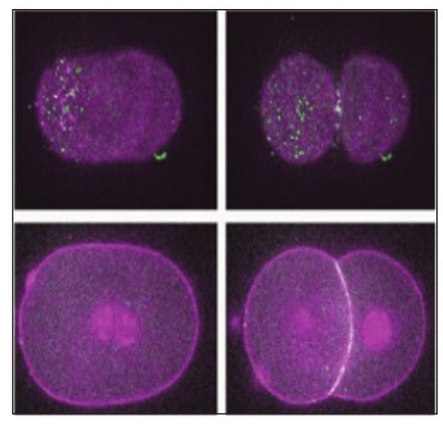
Writing in the journal *Global Change Biology*, the researchers from the UK and Australia said, "Shifts in species ranges are a global phenomenon, well known to occur in response to a changing climate.

"New species arriving in an area may become pest species, modify ecosystem structure, or represent challenges or opportunities for fisheries and recreation. Early detection of range shifts and prompt implementation of any appropriate management strategies is therefore crucial." They said most of the first sightings appeared to be tropical and sub-tropical species moving to higher latitudes "as would be expected in climate warming".

"Our results indicate that first sightings are likely related to longer-term climatic processes, and therefore have potential use to indicate likely climate-driven range shifts" the researchers said.

Most of the sightings were clustered in four parts of the world — the California Current, the Mediterranean, the Atlantic coast of South America, and Indian coastal waters. However the researchers said that "mobile species like fish" would probably be better able to cope with the warming waters than land animals as they can swim to a different part of the sea. "For things that are not mobile, like coral reefs, it's a real problem," professor Michael Burrows, of the University of the Highlands and Islands, UK, said.

IAN JOHNSTON/THE INDEPENDENT



Single embryo cell

Scientists from the Mechanobiology Institute at the National University of Singapore have discovered that clusters of cadherin — a type of cell protein known for forming junctions between cells — also play a role in stabilising the cell cortex, a region under the cell membrane.

The microscope images show a single embryo cell (right) and two cells after cell division (far right). The top set of images gives a surface view of the cells. Here, the green dots are the "non-junctional" and non-adhesive cadherin clusters on the surface of the cells.

The bottom set of images shows a cross-sectional view of the cells — where a belt of cadherin (white-green line) can be seen forming a junction between the two daughter cells.

With this new discovery, scientists around the world will have to re-evaluate their understanding of cadherin. They must now consider its role in stabilising the cell cortex along with its classical function in maintaining junctions between cells.

This fresh perspective may unlock new avenues of investigation regarding the role of cadherin in health and disease, the scientists said. The study was published in the scientific journal *Current Biology*.

THE STRAITS TIMES/ANN