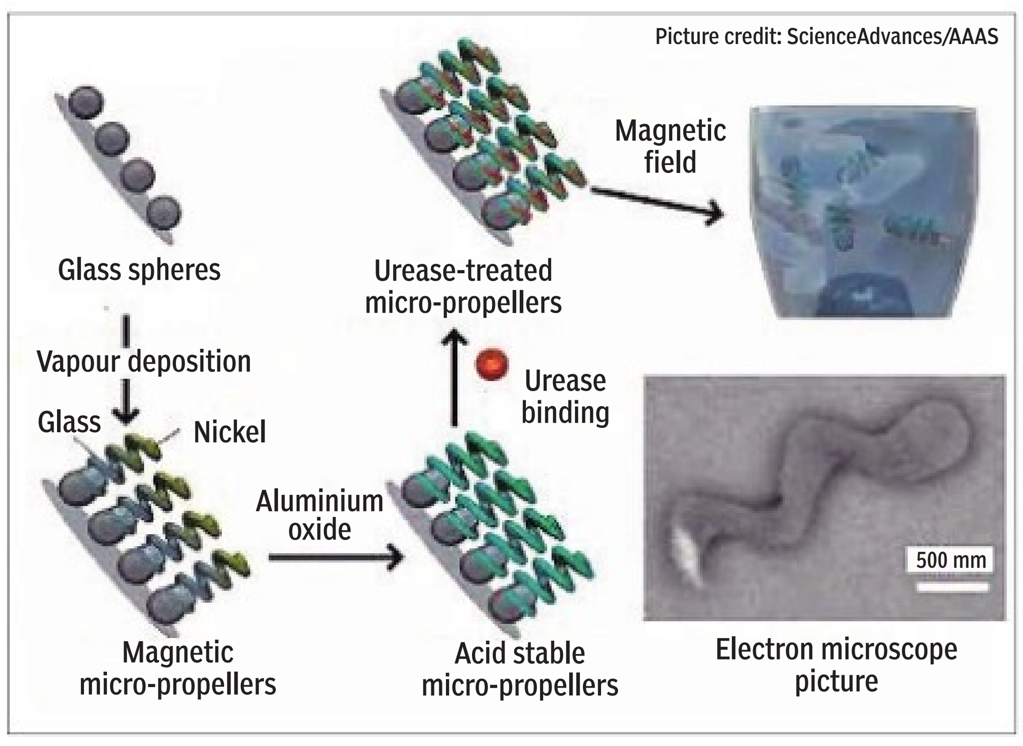
Slipping friends through the barrier

THE BODY"S DEFENCES TO KEEP INVADERS OUT ALSO BLOCK MEDICINES FROM MAKING AN ENTRY, WRITES **S ANANTHANARAYANAN**

A most convenient way of taking medicine is by swallowing a pill, but the body has created barriers to prevent pathogens, like bacteria that could come in along with food, from entering the bloodstream. These same barriers could also prevent useful drugs that are taken orally from reaching the place where they are needed. Oral medication thus needs to have special arrangements to ensure absorption.

Debora Walker, Benjamin T Käsdorf, Hyeon-Ho Jeong, Oliver Lieleg and Peer Fischer at the Max Planck Institute for Intelligent Systems at Stuttgart, the University of Stuttgart and the Institute for Medical Engineering at the Technical University at Munich, report a step in this direction in the journal *Science Advances*. They have piggybacked, they report, on a stratagem used by an adapted bacterium to design a drug carrier that can drill its way through the mucus armour of the stomach wall.

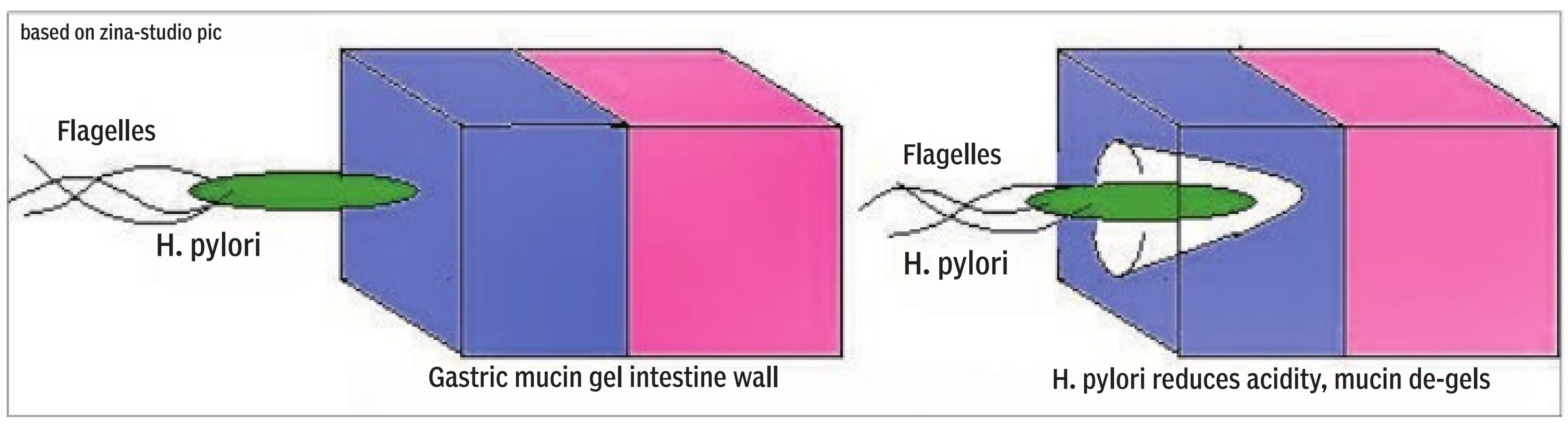


One of the main defences of the body is the layer of mucus, a viscous fluid that covers some tissue, either internal or which is exposed to the exterior, like the nostrils, eyelids, the airways in the lungs, the stomach and intestines, the genitals or the anus. The function is both to moisten and prevent the loss of moisture through exposed tissue as well as to prevent access by dirt, toxins or micro-organisms. The primary component of mucus is the protein, *mucin*, whose molecules form an interconnected network that serves to prevent larger particles from passing through, but does not come in the way of nutrients in the food being absorbed by the intestines. But this barrier, compounded by the acidic environment in the stomach, is also an impediment in the oral administration of therapeutic agents, which are often large molecules or encapsulated to be effective and have large particle size.

One way to get around this difficulty is with the use of chemical agents that break up the mucin network and clear the way. But this method cannot be followed to any great extent as it would compromise the protective role of mucus. Many pathogens have devised ways to get around the barrier, the Stuttgart/Munich paper says, including interaction with the mucus surface, affecting the production of mucin and then of liquefying the mucus. The only way available to drug carriers, so far, the paper says, has been to coat the carriers with agents that affect the mucus-surface interaction, if not to use enzymes whose effect of degrading the mucus layer is not reversible. A particular bacterium, *Heliobacter pylori*, which has flagelles, or whip-like organs for propulsion, however, uses a variation in the form of an enzyme called *urease* that directly affects only the level of acidity of the medium but manages to get through the mucus barrier anyway.

In the highly acid environment of the stomach, *H. pylori* secretes a large quantity of *urease* that has a first effect of neutralising the acidity. How it works is that *urease* acts on urea, which is a waste product that is present in circulation. Urea arises in the liver out of digestion of protein and reduction of levels of ammonia and gets taken out for excreting by the action of the kidneys. But at the spot where H. pylori has secreted *urease*, the enzyme works as a catalyst to convert urea back to ammonia. The rising ammonia level is alkaline and this reduces the local level of acidity, which is good for the bacterium. But the fall in acidity is not so good for the mucin membrane, which undergoes changes that make it less viscous. The *H. pylori* then has free passage and its flagelles propel the bacterium through the mucus to the intestine wall, where it does its work of promoting peptic ulcers and gastritis. The paper says that the bacterium is able to move through mucus so long as there is urea and the medium is not acidic. But even moving flagelles cannot help if there is acidity and there is no urea and the movement resumes when urea is added.

Once the bacterium has gone through and there is no more *urease*, acidity is restored and the mucin network thickens again to close the door to other large particles. This "altruism", of letting the fence get mended once its purpose is served, may be the secret of *H. pylori's* success, as the body may have evolved differently if the damage had been long lived.



Imitating *H. pylori*

The Stuttgart/Munich group has created an artificial drug delivery microstructure with a magnetic propulsion arrangement and a *urease* dispenser to make use of the *H. pylori* method of breaching the mucus layer. Magnetic propulsion, where a screw-like piece of magnetic material is subjected to a rotating magnetic field, has been found to work in low viscosity fluids in a number of studies, the paper says. The micro-helices, or screw-shaped propellers were fashioned by a process of "vapour deposition" and made of glass, with nickel as the magnetic material deposited towards the end of the fabrication. The surface was then coated with alumina, aluminum oxide, to protect the nickel from acid. The nickel material was magnetised in a sense transverse to the axis of the screw so that a rotating magnetic field set the screw turning, which would move it forward.

Just before the micro-propellers were magnetised, a charge of *urease* was deposited on their surface using agents that would bind to the surface and then hold on to the *urease*. Testing with glass beads of the same dimensions and treated in the same way showed that they effectively acted on urea to reduce acidity below the level needed for mucin to remain gelled and viscous.

In practice, however, it was found that even *urease*-treated rotating micro-propellers were not able to actually get moving when placed in mucus. This appeared to be because mucin adheres to the propeller surface, which gets entangled with the web of mucin molecules. After trying different agents to reduce this adhesion, it was found that bile salts, which are present in any case in the intestines, were effective. Trials then showed that micro-propellers could effectively go through a layer of mucus that was largely like the conditions found in the stomach and intestines, except for the need to adjust some parameters.

The study would prove useful both for artificial devices like remotely steerable "robot-type" devices and even to help non-propelled drug or particle delivery across the mucus barrier in the gastro-intestinal tract, the paper says.

THE WRITER CAN BE CONTACTED AT
response@simplescience.in

LIFE'S BUILDING BLOCKS

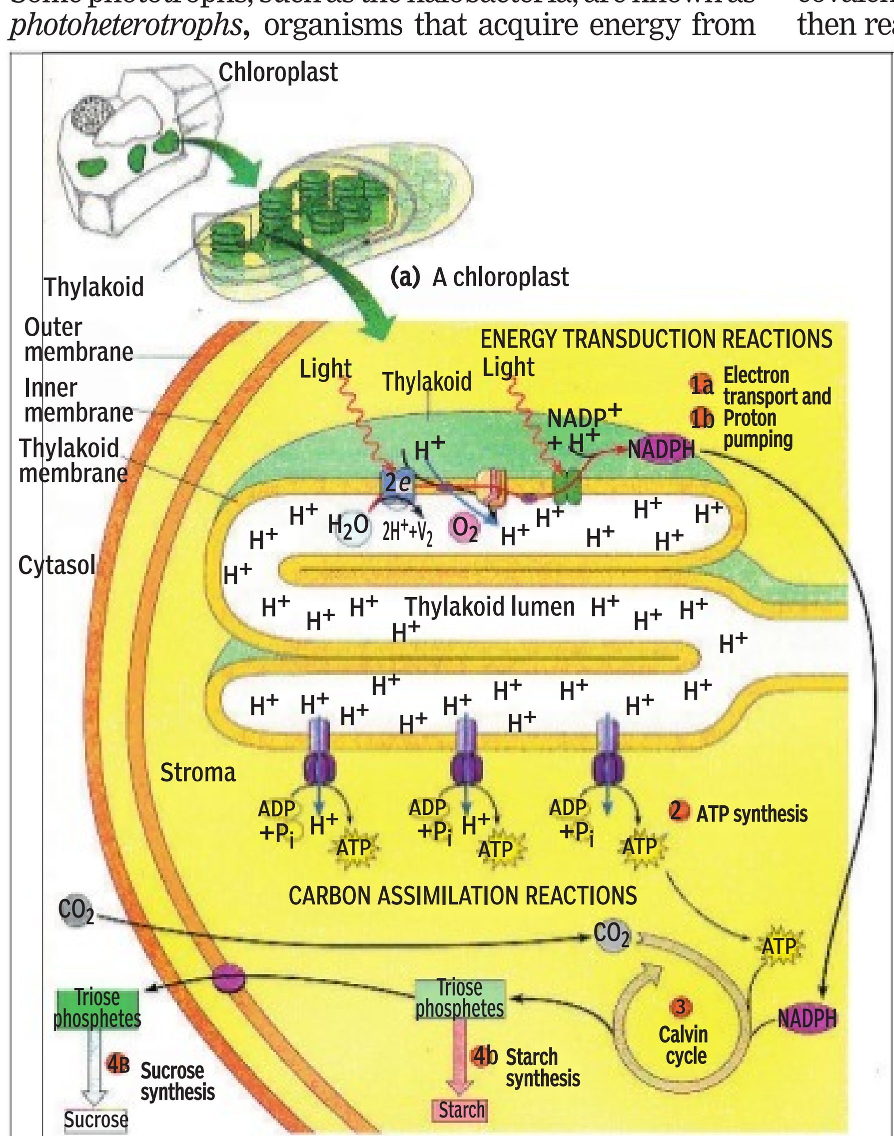
TAPAN KUMAR MAITRA
PROVIDES AN OVERVIEW OF PHOTOSYNTHESIS

How photosynthetic organisms replenish chemical energy and organic carbon drained from the biosphere by chemotrophs is explained by their use of solar energy to drive the reduction of CO_2 (the most oxidised form of carbon) to produce carbohydrates, fats, and proteins — the reduced forms of carbon upon which all chemotrophs depend.

The use of solar energy to produce these reduced building blocks of life is aptly named *photosynthesis* — the conversion of light energy to chemical energy — and its subsequent use in synthesising organic molecules. Nearly all life on earth is sustained by the cascade of energy that arrives as sunlight. *Phototrophs* are organisms that convert solar energy to chemical energy in the form of ATP. Some phototrophs, such as the halobacteria, are known as *photoheterotrophs*, organisms that acquire energy from sunlight but depend on organic sources of reduced carbon. Most other phototrophs — including plants, algae and most photosynthetic bacteria — are known as *photoautotrophs*, organisms that use solar energy to drive the biosynthesis of energy-rich organic molecules from simple inorganic starting materials: carbon dioxide and water. Many photoautotrophs, appropriately called *oxygenic phototrophs*, release molecular oxygen as a byproduct of photosynthesis.

Thus, phototrophs not only replenish reduced carbon in the biosphere but also provide molecular oxygen in the atmosphere, completing the cyclic flow of energy. Two general aspects of photosynthesis involve how photoautotrophs capture solar energy and convert it to chemical energy, and how this energy is used to transform energy-poor carbon dioxide and water into energy-rich organic molecules, such as carbohydrates, fats, and proteins.

Photosynthesis involves two major biochemical processes: energy transduction and carbon assimilation During *energy transduction reactions,* light energy is captured by chlorophyll molecules and converted to chemical energy in the form of ATP and the reduced coenzyme NADPH. ATP and NADPH generated by the energy transduction reactions subsequently provide energy and reducing power for the *carbon assimilation reactions,* commonly known as the *Calvin cycle,* during which fully oxidised carbon atoms from carbon dioxide are *fixed* (reduced and covalently attached) to organic acceptor molecules and then rearranged to form carbohydrates and other organic compounds required for building a living cell.



An Overview of Photosynthesis. (a) A diagram of a chloroplast, the site of photosynthesis in eukaryotes. (b) The sites and processes of photosynthesis in the chloroplast. Photosynthesis can be divided into two major processes: energy transduction and carbon assimilation. The energy transduction reactions include (1a) electron transport, (1b) proton pumping, and (2) ATP synthesis, whereas the carbon assimilation reactions include (3) the Calvin cycle and the biosynthesis of (4a) sucrose and (4b) starch.

Light energy is captured by members of a family of green pigment molecules called *chlorophylls,* which play a key role in every photoautotroph's energy transduction pathway. These are present in green leaves as well as the cells of algae and photosynthetic bacteria. Light absorption by a chlorophyll molecule excites one of its electrons, which is then ejected from the molecule and flows energetically downhill through an Electron Transport System. As in mitochondria, this flow of electrons is coupled to unidirectional proton pumping, which stores energy in an electrochemical proton gradient that drives an ATP synthase. In photosynthetic organisms, ATP synthesis driven by energy derived from the sun is called *photophosphorylation.*

To incorporate fully oxidised carbon atoms from carbon dioxide into organic molecules, photoautotrophs need not only ATP but also NADPH, the reduced form of $NADP^+$. In *oxygenic phototrophs* — plants, algae, and cyanobacteria — light energy absorbed by chlorophyll and other pigment molecules drives the movement of electrons from water, which has a very positive reduction potential, to *ferredoxin,* which has a very negative reduction potential.

From ferredoxin, electrons then travel exergonically to $NADP^+$, thereby generating NAD PH. In *anoxygenic phototrophs* — green and purple bacteria compounds with less positive reduction potentials than that of water, such as sulfide (SH–), thiosulfate ($S_2O_3{}^{2}$–), or succinate — serve as electron donors. In both oxygenic and anoxygenic phototrophs, the light-dependent generation of NADPH is called *photoreduction*.

The most important pathways for our consideration are the biosynthesis of sucrose and starch. Sucrose conveys energy and reduced carbon from photosynthetic cells to non-photosynthetic cells and is, therefore, the major transport carbohydrate in most plant species. Starch, or glycogen in photosynthetic bacteria, on the other hand accumulates when photosynthetic carbon assimilation exceeds the energy and carbon demands of a photoautotroph and is, therefore, the major storage carbohydrate.

THE WRITER IS ASSOCIATE PROFESSOR, HEAD, DEPARTMENT OF BOTANY, ANANDA MOHAN COLLEGE, KOLKATA, AND ALSO FELLOW, BOTANICAL SOCIETY OF BENGAL, AND CAN BE CONTACTED AT
tapanmaitra59@yahoo.co.in

No carbon footprint

JESS STAUFENBERG REPORTS ON A DANISH ISLAND THAT IS SET TO RUN COMPLETELY OFF GREEN ENERGY 20 YEARS AHEAD OF THE REST OF THE COUNTRY

It's been hailed as the community with no carbon footprint that could be the inspiration to solving the world's energy crisis. And now a tiny island off mainland Denmark can continue with its quest to become 100 per cent free of fossil fuels following a dispute over funding with the before the same target must be reached by the rest of the country.

Soren Hermansen, director of the Samsø Energy Academy, said the renewed funding was a sign that the island was "onto something… It's certainly a relief. It's fantastic, that we can continue.

This picture taken on 2 May 2007 shows wind-powered turbines that cover 100 per cent of the electrical needs of the 4,200 residents on the Danish island of Samso. Solar panels cover heating for islanders.

Danish government.

In 1997, Samso (population 3,600) won a government-sponsored contest to create a model community for renewable energy, sourcing all its electricity from a combination of wind, solar and geothermal energy. Yet proposed budget cuts to green funding by the Danish government this year threatened to stop the islanders' plans to make their community run completely fossil-fuel free.

And in October, the Danish government dropped Samsø from its list of grant receipts — despite the island hosting between 5,000-6.000 international guests who came for "green energy inspiration".

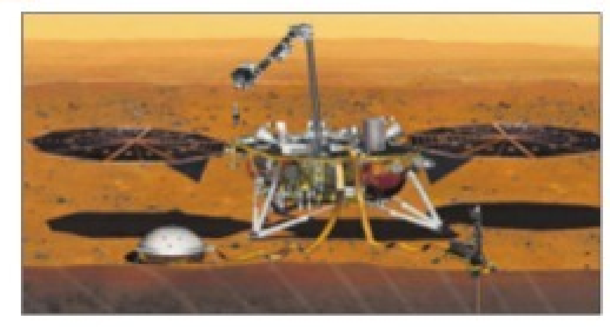
Now, however, the government has made a U-turn on the policy, according to *The Local*, pledging 7.5 million kroner to the cause of being a "fossil-free island" by 2030. This would make Samsø fossil-fuel free at least 20 years We have perspective that goes above and beyond our current means, and are thinking several years ahead," he told *The Local*. "It's also a sign that we're onto something — there was broad support for the pledge."

Yet in other areas of green energy policy, Denmark has been accused of losing its crown as a world leader. Climate minister Lars Christian Lilleholt said in August that a 37 per cent reduction in carbon emission levels, rather than 40 per cent, would be sufficient. And his government recently announced that it would phase out tax breaks on electric cars.

For the record, green energy group Climate Action Network gave the Danish government the mocking "Fossil of the Year" award at the Paris conference talks.

THE INDEPENDENT

PLUS POINTS



Mars mission off

The National Aeronautics and Space Administration has suspended a mission to Mars scheduled for March 2016 because of the *Rover* lander springing a leak. The InSight Mission on the Red Planet was called off after technical staff failed to repair a leak in one of its prime instruments.

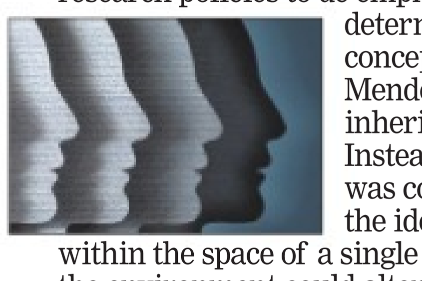
John Grunsfeld, associate administrator for Nasa's Science Mission Directorate in Washington, said, "We push the boundaries of space technology with our missions to enable science, but space exploration is unforgiving, and the bottom line is that we're not ready to launch in the 2016 window. A decision on a path forward will be made in the coming months, but one thing is clear: Nasa remains fully committed to the scientific discovery and exploration of Mars."

The affected instrument, which measures seismic activity, needs to maintain a vacuum seal around its three main sensors in order to survive Mars's harsh atmosphere.

DOUG BOLTON/THE INDEPENDENT

Ghosts in the genome

In one of the 20th century's most disastrous collisions of political ideology and science, Russian botanist Trofim Lysenko steered the USSR's agricultural research policies to de-emphasise the deterministic concepts of Mendelian inheritance. Instead, Lysenko was committed to the idea that, within the space of a single generation, the environment could alter the phenotype of future generations, an idea that is now often (imprecisely) referred to as "Lamarckian" inheritance. In Lysenko's view, Mendelian inheritance, along with Darwinian evolution, emphasises competition, whereas he believed that biology was based on cooperation, and that hard work in one generation should rapidly lead to the betterment of the species.



Lysenko was among the most infamous purveyors of the idea that the environment experienced by an organism could influence the phenotype in future generations, and he was rightly denounced as a charlatan because he falsified results in pursuit of his goal. However, the scientific community has discovered over the past few decades that the idea that acquired characters can be inherited may not be completely off the mark. It turns out that epigenetic marks, information not encoded in the genome's sequence, do respond to environmental conditions within an organism's lifetime, and recent evidence suggests that such information may be inherited.

Researchers are now beginning to understand the mechanisms of epigenetic inheritance and to generate evidence for the idea that the experiences of an ancestral population can influence future generations.

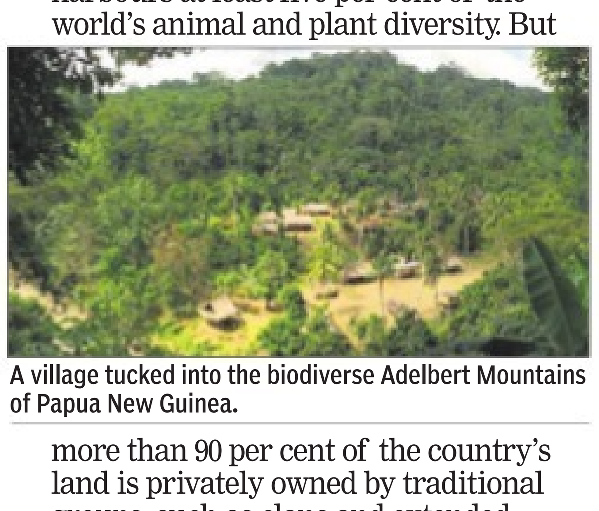
OLIVER J RANDO/THE SCIENTIST

Rainforest chorus

In the rainforests of Papua New Guinea, sound is everywhere. Birds of paradise sing amid the canopy, mammals rustle along the forest floor, and frogs call to each other from their perches. Over everything, the insects' incessant buzzing creates a noise that fills any remaining gaps.

This natural orchestra is what Eddie Game and his team are there to capture. By continuously recording sounds across a wide range of frequencies, Game — a researcher with The Nature Conservancy — gathers information about the different soundscapes in the extraordinarily biodiverse Adelbert Mountains.

Papua New Guinea lies on the eastern half of New Guinea, an island that harbours at least five per cent of the world's animal and plant diversity. But more than 90 per cent of the country's land is privately owned by traditional groups, such as clans and extended families, under a system called customary land tenure. A single community might own several thousand hectares. The Nature Conservancy began helping villagers in Papua New Guinea manage their land 15 years ago. Communities carefully zoned gardens and hunting grounds, setting other areas aside for conservation. The borders were religiously monitored by local rangers. "I've never worked anywhere where the connection to nature is stronger than it is in Melanesia," says Game.



A village tucked into the biodiverse Adelbert Mountains of Papua New Guinea.