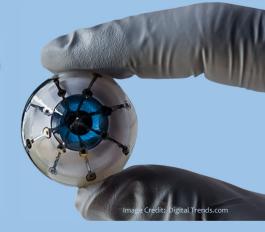
# Is Bionics the Future of Medicine?



Stem cells and tailored medications are all the hype in the therapeutic world, but recent advances in another area could overcome side effects of current practices. Bionics applies biological methods and natural systems to the design of engineering systems and modern technology. In short, replicating and improving what nature does electronically and mechanically. Joseph Archer, Cameron Funnell, Lizy Gill, Lara McMurray, Ellen Strangeway and Toby Willson explore some of the latest advancements that have shown this exciting area of science to have the potential to lead the future of medicine.

In the UK, epilepsy, a neurological condition characterised by seizures, affects 600,000 people. Sudden surges of electrical activity in the brain result in a seizure which can cause extreme convulsions in the person affected. Typically, epilepsy is treated with medication but recent research has shown a microchip can be inserted directly into the skull and detect irregular pre-seizure brain activity and trigger preventative measures with no ill effects. The potential preventative measures include cooling of the brain cells to 22°C or direct release of antiepileptic drugs into the affected brain tissue. These autonomous responses prevent the need for daily medication but control seizure activity without affecting daily routine.

Recently, amputees have gained new levels of control of prosthetics by the implantation of small sensors into the brain. Studies revealed that bursts of electrical signals in the brain were translated into commands for the arm, leaving patients capable of using their robotic arm to control mouse cursors on a screen and serve themselves a drink. However, it has proved harder to generate a robotic hand or limb that provides feedback to the brain. Researchers in

the U.S. have shown a paralysed 28 year old's ability to sense and identify which mechanical finger on his prosthetic hand is being touched.

Neurosurgeons have disclosed that they believe in the foreseeable future a 'living bridge' between the peripheral nervous system and the prosthetic limb will be introduced, allowing signals to flow bi-directionally between the spinal cord, brain and prosthetic limb. Ultimately, this could result in a two way bionic arm that can interpret signals as if they were incoming from a natural forearm, hand or fingers.

In Harefield Hospital, a promising new ventilation support device called the Novalung is being used. Attached via tubes to the leg or directly to the patient's heart, it bypasses their respiratory system, removing carbon dioxide from the blood and then reoxygenating it. Unlike other ventilator systems, which rely on heavy external engines, the Novalung uses the patient's own blood pressure to drive this process and, being about the size and weight of a book, patients are able to remain mobile and awake, meaning prognosis is greatly improved.

Tiny robots made entirely of DNA could be swimming through the blood stream in the next step in the fight against cancer, helping to deliver chemotherapy 1000 times more powerful than current drugs and without the side-effects. Designed to function as normal white blood cells, they would be able to target and destroy disease pathogens and bacteria without harming the body's own healthy cells. At the current stage of research and testing, the nanobots are able to identify 12 different types of cells in humans including the abnormal white blood cells associated with leukaemia and solid tumours. Although testing is currently only cell cultures and animal studies, the hope this year is that a leukaemia patient can be saved by these DNA robots in a process that would take a few weeks.

Bionics could bring about a new age of treating life-threatening illnesses and debilitating conditions which millions of people suffer worldwide. Maybe, one day in the future, your life will be saved by its powerful applications.  $\Delta$ 

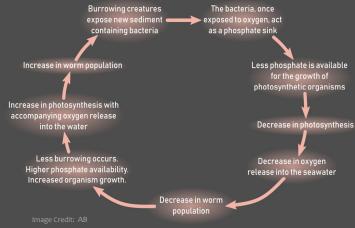
## The Burrowers



New evidence suggests that ancient creatures, some thought to be worm-like, played a key role in the formation of life on Earth. Darwin once stated, "Worms have played a more important role in the history of the world than most persons would at first suppose" and his words stand the test of time. These oceanic creatures are believed to have regulated oxygen levels through their burrowing, creating a negative feedback loop that gradually changed environmental conditions.

It is thought that the 'Cambrian explosion', a burst of diversification beginning 542 million years ago, was made possible by this. Prior to this, most organisms were comprised of single cells collected in colonies. The explosion of diversification led to life resembling that of today and to important changes in the environment. Whilst described as an explosion in geological timeframes, this process took place over 13-25 mil-

Worm-like oceanic creatures developed bio-mineralised skeletons rich in calcium such as shells and spines to guard against predation. These evolutionary



## **Evolutions Little Helpers**

Reporting by Ruth Hodge, Victoria Luck, Lucy Nicholls, Lewis Rose, Jasmine Smith, & Hannah Stewart

organisms being able to burrow into the previously smooth sea floor, creating safe havens beneath the sediment. Predators then evolved digging techniques, causing further perturbation. It has previously been suggested that the construction of skeletons and hard body parts became possible following a sudden, massive expulsion of calcium rich material from volcanically active

Prior to the evolution of these ancient marine creatures, oxygen levels were continuously rising due to the activity of simple organisms such as cyanobacteria. These increasingly high levels would have resulted in lightning strikes and catastrophic fires, threatening terrestrial life if it were not for the evolution of these ancient worms. Fossilised worm casts found in ancient rock sediments show that these multicellular organisms performed a burrowing action down into the ocean floor, exposing new sediment layers to the oceans. This action is believed to have triggered the stabilisation of global oxygen concentrations, as bacteria contained within these layers began extracting phosphates from the water, which reduces

This could have led to a runaway reduction in oxygen levels were it not for a built-in control mechanism. As the organisms continued to disturb the ocean sediment, more phosphate was stored, found in the seawater. Phosphate is an isms, and with less available in the seawater, photosynthesis rates, and therefore oxygen concentrations, began to

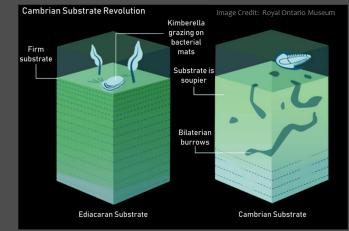
defence mechanisms resulted in the drop. The lack of oxygen caused worm numbers to decrease, reducing the perturbation. This system of negative feedback served to stabilise oxygen concentrations and decrease the density of

> their new lower level, the more stable conditions allowed organisms to adapt and new life to evolve during the Cambrian explosion. This event saw the appearance of more complex life and most of the major animal groups around today. So did these events enable the perfect balance in the Earth's

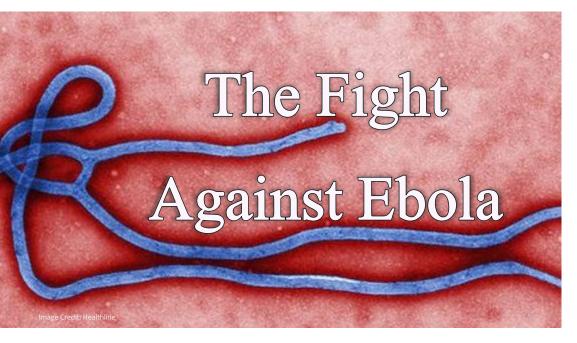
The Cambrian explosion has generated extensive scientific debate. Even as early as 1859, Darwin knew that this explosion was a main objection to the theory of evolution by natural selection as interpretation of the data from the

period is difficult due to an incomplete

The group responsible for this new theory point out that current redox proxies - the data used to see whether oxygen is free in the ocean or locked up in As oxygen levels began to stabilise at sediments – do indicate the presence of such creatures. There is concern, however, that the lack of detail in such records is hiding crucial information. Other scientists believe there is also a possibility that even if they did exist, the effect on oxygen would not have been global. There is still very little known about the early oceans, their structure and how they interacted with evolving life. Δ



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Believed to have its primary case in a two-year-old boy who died in Guinea on 28th Dec 2013, the current outbreak of the Ebola virus that is ravaging western Africa has been described as 'the most severe acute public health emergency seen in modern times'. So what are the facts behind the fear? Molly Butler, Fiona Cantlay, Marta Granatir, Sarah Rosen, Joe Verity-Legg, Robert Wilmot investigate.

In the short time since Ebola haemorrhagic fever was first reported in Guinea, it has spread to Sierra Leone and Liberia, with subsidiary cases in Nigeria, Senegal, Spain and the US. The disease has now claimed 4,033 out of the known 8,400 lives it has threatened. This high fatality rate and the visceral manner in which it kills has gripped Western Civilisation with fear. Fear which, buoyed by frequent, factless media reports - now approaches a psychological pandemic in its own right. With concern over personal safety growing; what are the socio-economic and environmental factors underlying the outbreak, what is being done to combat the disease and how at risk are we in reality?

With the three worst affected nations involved in recent regional civil wars, due in part to high levels of corrupt exploitation of natural resources, these

nations are some of the poorest upon Earth. Unchecked deforestation has resulted in translocation and concentration of species thought to be the natural sink of the virus, spreading and localising virions. With poverty rife, bushmeat is a common source of sustenance and is often obtained from these potentially infected species. Epidemiological research is still on-going, but this is believed to have been the starting point for the current outbreak within West Africa.

Once the outbreak had begun, diagnosis was slow, in part due to it having a similar symptomology with other infectious diseases prevalent in the area and in part due to local inability to conduct thorough assessments. This eventually led to the US CDC creating unnecessary delay before isolation measures were implemented. Furthermore, there is a lack of education, employment or trust for health workers within many of the displaced communities scattered about

the region. Thus, migration and medical mistrust aided the spread of infection. With urban growth rates some of the highest in the world over the last 20 years but growth in public services still lagging, the region provides an ideal breeding ground for the virus.

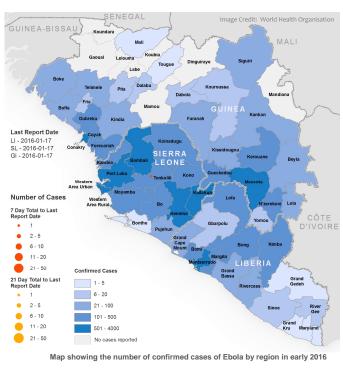
So the question now becomes: what can be done to bring about an end to the crisis and what measures can we take to protect ourselves in the UK? With the media focusing on vaccines, what therapeutic treatments are currently available? While several anti-viral drugs are being developed, notably the ZMapp drug, other practices to help combat the disease — such as maintenance of oxygen levels, blood pressure, IV fluids to balance the body's salt content, and treating opportunistic infections — are proving to be effective.

ZMapp is a combination of 3 monoclonal antibodies, c13C6, c2G4 and c4G7, which are derived from existing antibody cocktails. These antibodies produce a neutralising effect, inhibiting the ability of the virus to replicate. Evidence suggests this treatment method could be effective as it has been reported that, once administered, the viral load of the patient drops dramatically, although significant statistical foundation is still lacking. X-ray structure analysis shows that the antibodies are capable of binding to critical sites on the virus' surface.

Studies involving non-human primates displayed an increased survival rate from 0 in the control group, to 2/3 of infected subjects, provided treatment was administered within 48 hours of infection. Despite the lack of previous human clinical trials, due to the severity of the outbreak, ZMapp was approved by the US FDA for use on Ebola patients in October 2014. The WHO later also deemed use of such drugs as ethical during the epidemic and approved their use.

A randomised clinical trial was begun during the epidemic and treated 72 individuals. Although there was a 40% lower risk of death for those who received ZMapp, the results were not statistically significant and the trial was halted without reaching the target number of participants due to the waning of the outbreak. In the cases where ZMapp has been used, relevant antibody levels within the subject remain high after recovery, providing immunity to future exposure to the pathogen. However, there is evidence to suggest that the mechanism of the Ebola virus involves antibody enhanced binding to target cells, essentially a hijacking of the body's natural defences to the virus' own ends. For this reason, further research into the optimum combination of synergistic antibodies would be ad-

Despite World Health Organisation projections for the number of infected reaching as high as 20,000 by November, thankfully in the UK, we have access to a health service capable of providing these treatments, so an outbreak within the UK would carry a reduced fatality rate. While the recent



cases of transmittance within the US and Europe are causing panic to rise, Prof Jonathan Ball, infectious diseases expert at the University of Nottingham stated:

It would seem that realistically there is a limited threat to a western populace;

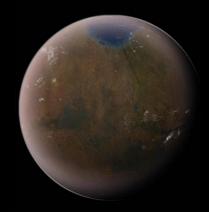
'What Ebola clearly does is cause anxiety. Anxiety partly born from popular culture, especially films, but stepping away from the Hollywood image we need to keep in mind what Ebola is: it isn't particularly contagious, it is inefficient in the method in which it spreads and it is relatively easy to get a hold of provided you have the correct infrastructure.'

as these societies are characterized by high levels of sanitation and health care facilities with access to advanced medicines that are generally lacking in West Africa. Therefore, exit testing for those returning from risk related areas is likely only to be effective against the psychological pandemic this disease pro-

duces, as it is unlikely to positively identify many cases. However, even though the threat to the UK populace is minimal, it is arguable that British Colonialism was a factor in generating the political and environmental climate that enabled this disease to become widespread. Therefore perhaps the UK should bear an elevated responsibility to these countries and provide greater medical assistance and measures to control the increasing number of deaths in Western Africa.

Given the current state of the virus, it can be assumed that the greatest risk Ebola poses is a more efficient method of viral transfer, which would enable it to become endemic within Western Africa. However with on-going clinical trials for drug therapies and vaccinations, it would seem that the fight against Ebola can and will be won. The increased awareness of this virus and it's treatment should also act to reduce the impact of any future epidemics. Δ





## TERRAFORMING

### MAKING THE UNINHABITABLE, HABITABLE

As a neighbouring planet, Mars has been an important part of human cultures worldwide for over 4000 years, from the belief it was a god to the recent scientific explorations with the Mars Rover. Mars is now even more significant to our future, due to the discovery of liquid water near the planet's surface. With Earth's ever growing population, and Mars' potential to sustain life, knowledge about the planet and its future in space colonisation is more sought after than ever.

> Reporting by Aviva Caller, Abigail Lundie, Elspeth Meakin, Oliver Milton, Adam Patrick, Milo Racadio & Chris Tuckwell-Smith

With an average temperature of -62°C (plummeting to -153°C at the poles), and an atmosphere drastically thinner than Earth's - composed almost entirely of carbon dioxide with only traces of oxygen, Mars is not currently suitable for humans. Moreover, Mars is subjected to regular dust storms made of oxidised iron as well as frozen carbon dioxide snowfall, resulting in a hostile climate.

One proposed method of raising Mars' temperature is to send large mirrors into its orbit; these would reflect sunlight towards the planet increasing the average temperature. By focusing on Mars' poles the ice caps would begin to melt, releasing the frozen carbon diox-

ide and water trapped within them, helping to warm the planet. Alternately, propelling icy, ammonia rich asteroids at Mars using nuclear thermal rocket engines could raise the temperature of the entire planet by a few degrees with each impact and release greenhouse gases such as water vapour, in addition to the ammonia released nitrating the soil and thickening the atmosphere.

However, this warming method would take missions over several decades to cover a quarter of the planet's surface in water thus delaying human settlement by centuries. Introduction on the planet of genetically modified single celled organisms, capable of surviving the brutal climate of Mars, would produce the building blocks required for sustaining multicellular life forms in a similar manner to the evolution of life on Earth. One of the possible candidates for this, Cyanobacteria, uses energy from the sun and carbon dioxide from the atmosphere as a food source. releasing oxygen and adding nitrogen and carbon to the iron oxide heavy Martian soil. These changes are essential for life, and would allow bacteria and other organisms to survive on Mars.

As the first foreign organisms on Mars, with no predation at all, the population of these cyanobacteria would have to be tightly controlled to prevent overcrowding. For this reason, the introduction of a 'suicide gene', a gene causing cell death under certain conditions, is initially necessary. Such precautions





could be removed once a balance is reached, through a new food chain created by the introduction of selected and modified animals. This food chain would have to be maintained by humans, as even small changes could result in the eradication of species.

The strength of gravity on Mars is approximately one third of that on Earth and cannot reasonably be altered through human intervention. In some respects this is helpful, for example less support is required for plants and buildings, however it would cause serious health problems within the bodies of larger organisms. It is known that during long term space missions, astronauts lose on average 1.5% of bone mass and 2% of calf muscle volume eve-

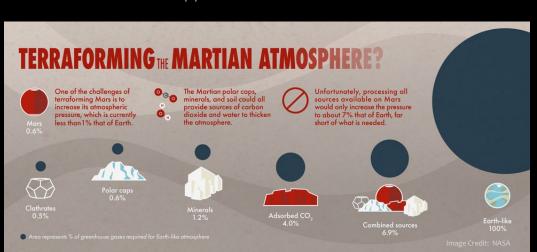
ry month, even when strict exercise regimes are followed. Alongside this, astronauts' slow twitch muscle tissue changes composition to form fast twitch (rapid response) muscle, causing a significant lack of strength and endurance. These are effects from a year long space journey and the effects of longer low-gravity exposure are not known. These problems will affect both humans and livestock as low bone density hugely increases the risk of bone fractures and breaks in all skeletal organisms.

As most livestock on Earth must be put down when suffering from a broken bone, this would result in a huge waste of time, resources, and life. The hormone glucose-dependent insulin-tropic peptide has been found to affect the

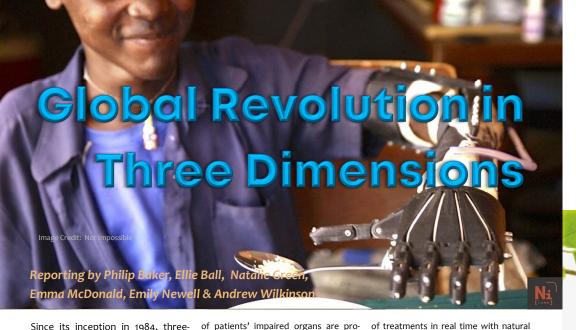
breaking down and production of bone, which could potentially be investigated as a way of combatting the loss of bone matter during the journey to, and life

The problems caused by atmosphere and composition described are merely a few of the main concerns surrounding the potential for life on Mars, many of which may not be resolved for thousands of years. The effort put in now will support the important initial steps of terraforming and further research could lead to the discovery of better solutions to these and currently unasked questions in the future.  $\Delta$ 





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Since its inception in 1984, threedimensional (3D) printing has evolved from an expensive rarity in specialised industry to a much talked about and readily accessible commodity. This 'additive manufacturing' technology creates objects by layering solid matter into predetermined shapes. By solidifying layers of photocurable resin with a laser beam, Charles Hull created the prototype 3D printer and subsequently multiple versions of the device have emerged.

The range of products generated using this process is broad, from simple plastic and household goods to the more recent 'bio-printing' of human tissue and organs for medical purposes. With the simpler devices available to the public from as little as £300 and opensource designs available online, this pioneering concept continues to garner publicity as the range of potential applications becomes apparent.

One area that has captured the media's attention is the use of this technology in the field of medicine. Current applications include customised surgical implants, prosthetics and organ modeling. In the case of the latter, 3D models

duced in silicone gel using data from computerised tomography and magnetic resonance imaging; allowing for presurgical planning, which reduces operating time and patient risk. Printing has revolutionised the manufacture of prosthetics, allowing patient specific customisation and design. Replacement limbs can be printed as a collection of modular components (from as little as £19) and assembled at home.

More recent innovations have included the technique of 'bio-printing', the manufacture of entire sheets of human tissue. Stem cells or cells taken from biopsies are cultured in a growth medium that provides the nutrients needed to multiply and grow into 3D cell colonies called spheroids. These are collected to make 'BioInk' and are injected into a scaffold of hydrogel (an inert water based gel), providing structural support and protection. This is repeated layer upon layer until the desired size of tissue is reached. Following a period of maturation, the spheroids autonomously fuse, innately mirroring embryonic development, using cell signalling to migrate naturally, filling any gaps. The hydrogel dissolves away or is removed, leaving the bio-printed tissue intact.

Made-to-order 3D tissues can be used for medical trials, allowing observation

cell interactions monitored, reducing the need for animal testing. Additionally, therapies can be designed to graft sections of newly printed tissue onto pre-existing organs or tissue to repair damage. Eventually the hope is that entire organs could be synthesised, reducing the likelihood of rejection and removing the need for transplant waiting lists, saving countless lives. This industry continues to grow; currently valued at over £88m it is expected to exceed £544m by 2025.

Specialised and custom manufacture is only the tip of the iceberg. If 3D printing were to even partially replace current industrial processes, it could offer a sustainable method of manufacturing a variety of goods. Plastic requires far less energy than metal to transform into usable material without compromising the quality of the final product, making it an ideal target for industrial application.

Companies have begun to develop this idea further by moving away from traditional oil-based plastics. In partnership with 3Dom Filaments, Biome Bioplastics have developed a plant-based, biodegradable plastic called Biome3D which is not only more environmentally friendly but also outperforms its original counterpart.

Similarly, 'Solar Sinter' is a completely green 3D printer developed by Markus Kayser. Harnessing sunlight, the printer fuses desert sand into glass, making this device 100% renewable using only non-toxic, locally abundant source materials. This creates a demand for silica and could provide a viable source of income. With localised manufacturing, fuel emissions and transport costs are reduced. This new manufacturing model not only supports local economies, with products designed for local needs, but has the potential to lift some of the

world's poorest people from poverty, allowing them to compete in a global market.

Hull postulated that within 30 years 3D printers would be an everyday household item. With the printer fast becoming a mainstream and accessible product, this prediction seems imminent. The development of 3D printing enables products to be digitalised in a similar way to text, audio and video. Indeed, 3D printing may do for physical objects what the Internet has already

done for information, allowing universal access, technological communication and collaboration across the globe.

The rapid development and innovation of this technology was made possible by the open source nature of its design. With schematics freely available online for anyone with the knowledge and ability to construct them, the 3D printer is available to all. A true product for a global society, we are witnessing a global paradigm shift towards a future of almost limitless possibility.  $\Delta$ 

# The Bionie Leaf

Solar energy — an energy source with such potential that evolution has spent the past 3.4 billion years trying to perfect organisms to utilize it. Today, over 3 trillion trees stand to carry out this process of photosynthesis. Could we find a way to use the photosynthetic cycle to solve our own energy needs?

Image Credit: Jessica Polka

# Photosynthesis, at its root means to 'put together' using light. It uses solar energy to manufacture food in the form of glucose. There are two main reactions that happen in photosynthesis, these are light dependent reactions and light independent reactions.

Light dependent, requires photons from sunlight. These photons kick-start the reaction by triggering the release of electrons from chlorophyll molecules. This causes water to break down into more stable hydrogen and oxygen. The subsequent accumulation of hydrogen is then involved in a potential driven reaction which results in the formation of ATP. ATP is a universal energy source used by all cells and utilized by plant cells to produce glucose in this process.

Light independent reactions take place in the chloroplast through a the Calvin cycle. Here, sugars are synthesized from carbon dioxide using the ATP and charge carrying molecules formed in the light dependent reactions.

### Reporting by: Mohini Bhagalia, James Merley, Amar Patel, Joanna Raymond, Kiran Richards & Adam Shephard

In 2009, chemist Daniel Nocera developed a photovoltaic cell that uses sunlight to create an electrical current by separating water into hydrogen and oxygen gases, which relied upon a revolutionary cobalt-phosphate catalyst. This method is analogous to the light dependent reaction. The hydrogen produced is an excellent alternative fuel source and, despite its storage limitations, its story does not end here. Extending the photosynthesis analogy, scientists sought to then mimic the light independent reaction.

This year, a team at Harvard University achieved this by interfacing photovoltaic cells on to a biological platform. They used specialized bacteria, R. eutropha, which consume hydrogen produced by the photovoltaic cell along with carbon dioxide from the atmosphere to produce isopropanol, a type of alcohol, which can be used as a fuel by cars. So here, the bionic leaf came to exist.

When developing technologies, one variable is paramount to—efficiency. Studies have been carried out comparing real leaves to the bionic leaf. The results are promising. Natural photosynthesis is highly inefficient: it evolved for ancient earth's conditions therefore many plants convert sunlight to biomass at an efficiency of about 1%.

H<sub>2</sub>O

Despite its recent creation, the bionic leaf already exceeds this with an efficiency of 3.2%. By optimizing the catalyst and bacterium, continued biological engineering should allow scientists to reach their target efficiency of 5%.

With the Sun producing enough energy in one hour to power all human activity on Earth for a year, utilising this source should be seen as the future for sustainable energy. Adapting a biological process to do so is an avenue that we have only just begun to explore.  $\Delta$ 

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GLUTAMATE GIVES FOODS AN 'UMAMI' FLAVOUR. FOODS WHICH NATURALLY CONTAIN FREE GLUTAMATE INCLUDE:













### **0.55 GRAMS PER DAY**

Amount of MSG ngested by the average consumer in the USA

### 3 GRAMS

Amount of MSG, without food, needed to observe mild symptoms in a small number of people.

DAILY, WE INGEST **20-40 TIMES MORE** 

THAN WE DO MSG

## erous or Delicious

Monosodium Glutamate (MSG) is a white crystalline solid that was first isolated in 1908 by Kidunae Ikeda in Japan. It is the sodium salt of glutamic acid, a non-essential amino acid. When added to food it enhances the savoury flavour, thereby giving it more 'deliciousness' or the 'Umami' taste. But is it merely adding taste or is it adding potential health risks to your food?

Concerns were first raised about MSG. in 1968, by Dr Kwok through a letter to the New England Journal of Medicine, and its potential health impact has been debated ever since. In the letter, Kwok coined the term Chinese Restaurant Syndrome (CRS) after experiencing symptoms such as numbness of the neck and back, general weakness and palpitations, which persisted for up to 2 American Societies for Experimental hours after eating Chinese food.

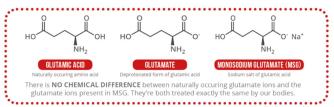
A study in 1969 showed that MSG injection in mice led to obesity and brain lesions; death was the result for ten litters of baby mice within 48 hours of MSG injection. A more recent study in 2002 showed that rats fed on high MSG diets suffered retinal thinning and vision loss. Nutrition therapy practitioner Patrick Holford has raised the issue of hyperactivity in children being associated with MSG intake although this is not the mainstream view.

MSG is often described as an 'excitotoxin' that can overstimulate neurons and lead to nervous disorders. There is also a potential link between MSG and asthma. Two patients who had asthma attacks after eating Chinese food were tested again by ingesting 2.5g of MSG, resulting in asthma attacks once more. The Federation of Biology noted there was 'evidence to support the existence of a subgroup of asthmatic responders to MSG'.

Kwok did not directly attribute CRS to sults that are not easily applied to hu-

MSG and suggested it could instead be due to the generous use of cooking wine or the high sodium content of Chinese food. MSG occurs naturally as glutamate in many foods such as: cheese, tomatoes, soy sauce and potatoes. Manufactured foods also contain glutamate, with marmite containing some of the highest levels. Furthermore, humans naturally produce it and can tolerate considerably higher levels of glutamate than rodents, making the latter an unreliable testing specimen.

However, it is important to note that The MSG studies carried out gave re-



Reporting by Henry Bradford, Parum Cheema, Richard Dickinson, Imogen Player, **Matthew Simpson & Angelica Too** 

mans, as MSG is not normally injected and the animals were given excess amounts relative to their total diet. A Double-Blind Placebo- Controlled study is considered one of the most dependable and unbiased means of testing. There is a lack of these studies that support any negative side effects of MSG. Most studies claiming that MSG is harmful to health have been single blind. The study that found a causal link between MSG and asthma only involved two women and was single blind; the study lacked both quantity of subjects and scientific objectivity. Other recent DBPC trials have failed to reproduce consistent results that match the earlier single blind studies.

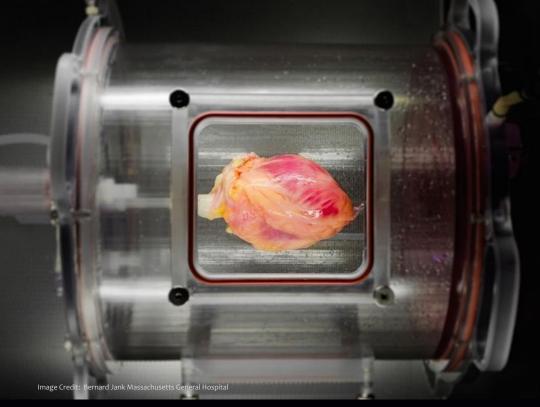
In food labelling, MSG is given a variety of names such as glutamate, yeast extract, texturised vegetable protein and natural flavours, both reflecting the variety of sources for this molecule and manufacturers desire to escape the bad press surrounding it. Usage is expected to increase in South East Asia and West Africa due to improvements in both living standards and the food processing industry, alongside increased urbanisation. However in Western Europe and North America, demand for foodstuffs that contain little or no additives are expected to restrain consumption growth. Currently MSG is classified as safe by the European Union and the Food and Drug Administration. It is unlikely that this will change in the foreseeable future, as there has been insufficient evidence to show that it negatively affects public health.

The studies discussed here show that research into the negative effects of MSG have often involved unrealistic representations of MSG consumption in humans. Ultimately, it will continue to be used as a taste enhancer across the globe, despite the inaccurate negative attention it has received.  $\Delta$ 

#### MSG — The Science

- Originally isolated from seaweed but now generally produced by the fermentation of wheat or molasses.
- MSG, glutamate and glutamic acid are all molecules that only differ in structure by one atom.
- It is a salt of a non-essential amino acid, non-essential meaning it is made naturally by the body from other amino acids and substances.
- Humans digest both glutamate and MSG in exactly the same way.

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In the past, people who have suffered organ failure have been required to wait, potentially for years, for a replacement organ and have risked rejection, infection and death. But increasingly technology is developing new methods which may make this long wait and poor prognosis a thing of the past. Jonathan Stubbs, Giles Whiting, Charlotte Whittick, Carys Wilson & Michael Wood investigate.

Over recent years, the growth of or- organ is decellularised either by perfugans in vitro has seen significant development for use in transplantation and drugs testing. For example, dating back to 2006, bladders have been grown for transplantation into children with spina bifida. There are two main lines of research that show potential for the growth of new organs: the scaffold method and bio-printing.

The scaffold method, which is the older of the two, relies on the use of a preexisting organ from a donor, cadaver or even a similar animal species (usually a new tissues complementary to the recipient are grown. First, the desired

sion (in which the detergent is pumped through the organ) or immersion in a detergent, typically SDS (sodium dodecyl sulphate). This degrades all cells, leaving only the extracellular matrix, a protein scaffold of the organ. Multipotent progenitor cells are then transferred onto the scaffold where they proliferate and develop into a complete organ. This method has been used successfully in developing many different tissues and simple organs such as tracheae, bone tissue and cartilage.

pig) to create a scaffold upon which In the bio-printing method there is no need for an existing organ. The process involves developing an architectural and compositional blueprint of the or-

gan or tissue to be grown. Bio-ink (a solution of living cells suspended in a printable gel) is then created from the cells needed to build the organ or tissue, which is assembled using a 3D printer. A bio-inert hydrogel provides the 3D structure, giving stability and creating channels. This technique allows for the production of organs designed and sized for the target patient.

Both methods allow organs to be grown from cells of the intended recipient, which ensures compatibility. This confers many advantages, including removing the requirement for immunosuppressant drugs for the patient, reducing the likelihood of infection and speeding the patient's recovery time.

# Un break my

### An alternative to transplant that can offer a new hope for hundreds of thousands of patients

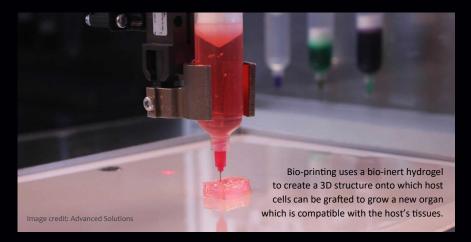
Organs can be grown on demand which Il shorten waiting lists and remove e associated problems with extended spital stays.

However, issues still remain with both methods. Both are relatively expensive, although the cost is constantly decreasing as the technology advances. Complex tissues are difficult to develop due to cell mass and multicellular growth, which will remain a problem but may be overcome through technological devel-

opments. Another problem may arise in the transfer of tissue grown in a sterile environment into the more complex body environment.

Out of the two techniques, the scaffold method is less complex and lower cost than the bio-printing method. However, bio-printing is a quicker and safer process as it is highly controlled and creates a more precise product. It also has the advantage of not requiring a source organ as a template.

These comparisons need to be weighed up before deciding on the most appropriate method to use. As we look to the future, these types of procedure will become more commonplace as the technology improves, demand increases and costs decrease. The culmination of these factors will see the need for organ donors fade away and the long time period spent on waiting lists disappear completely.  $\Delta$ 



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# The Pharmaceutical Paradox: helping others or helping themselves?

A US pharmaceutical company made international headlines by increasing the price of a drug by 5500% igniting the debate on the role of pharmaceutical companies in society and whether they should be a greater power for good.

Reporting by Caroline Adlam, Andrew Bullock, Jack Elsdon, Sabrina Lester, Delina Pereira & Sarah Roberts

The details of the case in question are thus: Turing Pharmaceuticals purchased the rights to Daraprim in August 2015, and subsequently raised the price from \$13.50 to \$750 per pill. Rightly, this has prompted questions about current drug legislation in the US.

Daraprim is the most effective drug currently in use to treat toxoplasmosis — a parasitic infection caused by Toxoplasma gondii. Spread by exposure to cat faeces or ingested via poorly cooked food, it lies dormant within a third of the world's population, causing no symptoms. However, for those with weakened immune systems (such as HIV/AIDS and cancer patients) it can lead to life threatening complications.

This vitally important drug is now monopolised by Turing Pharmaceuticals. As there are no profit caps, they have total control over the pricing. This is not how the drug industry was planned to work. During the drug development process, new compounds are patented by the manufacturers, preventing competitors from producing the drug and taking the profit without the risk of the drug development. Usu-

"This cost is unjustifiable for the medically vulnerable patient population in need of this medication"

- Infectious Diseases Society of America

ally when a patent runs out (after around twenty years), the market is flooded with competition from cheaper, generic alternatives. However, in the case of Daraprim, only a small number of prescriptions are written each year, giving no incentive for other manufacturers to produce it, removing any market competition which usually drives down pricing.

Martin Shkreli, CEO of Turing Pharmaceuticals, defends the price hike, arguing that the current price of the drug is not profitable and that "Daraprim is still underpriced relative to [other cancer drugs]". He also claimed the profits will fund the development of a better drug with fewer side effects, despite doctors stating that the current treatment is already effective, and the increased cost will leave medically vulnerable patients unable to afford treatment.

Can the 5500% price increase therefore be justified? The American business publication Forbes released data on the Research & Development expenditure of 100 pharmaceutical companies over a 10 year period, with

averages showing that the process to take a drug from inception to market could cost a company in the region of \$2 bn; a figure in close agreement with the \$1.74 bn (£1.15 bn) stated by the Association of British Pharmaceuticals Industry.

In 2014, there were 8821 American prescriptions of Daraprim, excluding hospital inpatients, and a minimum of 29 pills are required per patient per course. At the increased \$750 per pill, Turing would be earning at least \$192 m per annum for a product that they did not invent. Moreover, the \$2 bn research cost could be covered in as little as 10 years, with all subsequent years producing pure profit.

There are now calls for pharmaceutical companies to be more transparent with the public about the costs of their drugs and to redesign their drug pricing policies. As a result, the future of the US Pharmaceutical industry may be set to change to include bonus-caps for companies and more market competition.

Following the public backlash, Martin Shkreli has promised to reduce the price increase to an undisclosed amount.  $\boldsymbol{\Delta}$ 



Image Credit: CNN



It's no mystery that the rising levels of CO<sub>2</sub> are a problem. The volume of greenhouse gases humans are releasing into the atmosphere have led to well-known problems including the melting ice caps, rising sea levels, and freak weather. But there is another frightening concern, hidden in the corners of science news articles, with potentially devastating consequences: ocean acidification.

#### Reporting by Thomas Ashford,

#### Charlotte Day, Rachel Fernandes, Lewis Giles, Kirsty Linton & Emily Skinner

Chemistry is fundamental to life. Carbon dioxide plays a vital role in plant respiration and in the regulation of breathing in humans. The rate of increase of CO<sub>2</sub> in the atmosphere is now ten times greater than it has been in the past 10 years, with the consequences passed directly to our seas. The atmosphere is composed of different gases, including CO<sub>2</sub> at approximately 400 ppm by volume. The gases in the atmosphere dissolve into seawater so changes in the composition of the atmosphere cause the composition of

the seawater to change. When CO<sub>2</sub> enters the ocean, it reacts with water to produce hydrogen ions, which in turn react with carbonate ions to form acidic carbonates. This CO<sub>2</sub> and water reaction is the same reason carbonated drinks are more acidic than water.

Ocean pH has fallen by 0.1 since the industrial revolution began. This may not sound like a lot, but if a human's blood pH were to drop by the same amount it would cause severe health problems beginning with headaches and tremors and eventually causing the person to fall into a coma.

But how is this acidification happening? It comes as no surprise that the amount of carbon dioxide released into the atmosphere is more than the planet can handle. But it has to go somewhere, and one third of all atmospheric carbon dioxide is dissolved into the oceans. Normally this would be fine, as it is part of the carbon cycle, where carbon leaves and enters the atmosphere through different processes. However, the rate at which it enters the water is greater than the rate of exchange of the gas back into the atmosphere, causing a net increase of CO<sub>2</sub> in the oceans.

The obvious victim of ocean acidification is marine life. Calcifying organisms are important to the ocean's carefully balanced food web. Everything from coral to shellfish are susceptible to ocean acidification because they require carbonates to form their skeletons and protective shells. Not only are there less carbonate ions for the marine life to use as building blocks, but the acidic form of the carbonates are dissolving the skeletons and shells of marine animals.

But it's not just small creatures that are affected, larger animals are too. The acidification of body fluids causes metabolic rates and immune responses to slow down. If smaller animals, like plankton, have been dissolved away, they will not be able to feed the bigger animals, disrupting ecosystems and possibly leading to mass extinction.

What can the world do? The biggest goal needs to be to reduce the amount of CO2 released into the atmosphere. Governments are working on strategies including climate engineering as well as the implementation of carbon-neutral fuels.

An example of a potential climate engineering solution is iron fertilisation which is a CO<sub>2</sub> removal method where iron is deposited into the ocean stimulating photosynthesis in plankton. Photosynthesis absorbs CO2 from the ocean and produces oxygen, hence reducing ocean acidity. When the plankton die, they fall to the bottom of the ocean and trap the absorbed CO2 in the ocean floor as sediment. There are a couple of flaws to this method. It is economically inefficient, and creating a large volume of plankton could deprive the ocean of oxygen in certain areas, which is damaging to other species.

The simpler option is to reduce the input of CO<sub>2</sub> into the atmosphere. A useful tool to achieve this is the use of carbon-neutral fuels. Carbon-neutral fuels have no carbon footprint or net greenhouse gas emissions. These come in the form of synthetic fuels, such as methane or ammonia, as well as from renewable energy sources such solar and wind power. These options are necessary to reduce the world's CO<sub>2</sub> levels, which will otherwise rise and intensify the already dangerous effects.

There's no doubt that climate change is one of the most pressing problems for the planet, but it's only by looking at the various effects of the excess  $CO_2$  in the atmosphere that we can understand the problem fully. Ocean acidification may not be making headline news but, if we don't start paying more attention now, the effects of it could overtake its better known siblings.  $\Delta$ 

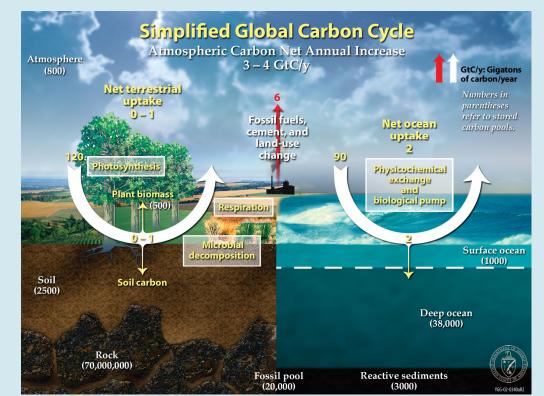


Image Credit: US Department of Energy - Genomic Science Program

# Whot?

quantity of mud on a farmer's boot could spread the infection between both farms and continents.

A major fear is that the fungus could potentially spread to developing countries where bananas are the fourth major food crop. In addition, 400 million people are reliant on bananas for income. In Costa Rica, for example, 100,000 jobs are dependent on the banana trade: 8% of the total jobs in the country. Countries like Costa Rica rely on bananas, as 85% of the fruit produced within the country is eaten there. With such a large potential impact on the people, why are governments not focusing on this issue?

selling, and eating bananas, everyone is expecting someone else to develop a solution. Furthermore the people growing bananas don't have the resources to invest in research, for example, create new fungicides. Those in the Western hemisphere who do have the re-

very difficult to do this without including certain negative aspects of the issue. It could be presented as improving the quality of life of farmers by reducing exposure to fungicides as currently the plants are sprayed up to fifty times a year in an attempt to ward off TR4. The farmers could then keep their jobs and maintain their income. It would be difficult to communicate the issue via negative messaging, for instance by saying that bananas are dying out. This would be likely to cause a selfish panic among the West, resulting in a mass buying of the fruit; a similar panic in farmers may persuade them to grow other crops instead. Neither of their reactions provide a long term solution to the problem.

They say that history repeats itself. The preferred 1950's variety of banana, the Gros Michel, was all but eradicated by a fungal infection. Now the Cavendish looks to be heading the same way. Alex Berrill, Bradley Catt, Callum Green, James Lindsay, Laura McCluskey & Kayleigh Withers investigate.

After the destruction of the Gros Michel banana variety by Fusarium oxysporum f. sp. Cubense, a type of fungal infection that causes wilt, there was a great shift in the market from the Gros Michel variety to the resistant Cavendish banana. This resulted in a loss of research into the fungus - the price of which we are now paying. A new strain of the fungus, Tropical Race 4 (TR4), has since been discovered, to which the Cavendish is vulnerable. This time however, there is no back-up banana!

The fruit, which is sexually sterile, is cultivated by cutting growths off mature plants and replanting them. This is a form of cloning, ensuring that all of the plants produce marketable fruit, with the downside that gain of resistance to disease is much slower to develop within the species. At this time, no Cavendish banana plant has been found to be resistant to TR4. TR4 triggers a self-defence mechanism in the banana plants. Much like mucus in the human respiratory system, a gel-like substance is produced in the xylem vessels to block the spread of the fungus; this prevents water flow to the leaves, causing them to wilt and eventually leading to the plant's death.

The fungus has proved difficult to eliminate as not only is it resistant to fungicides, its spores remain in the soil for 8-10 years and are spread primarily by infected soil and water. This is particularly a problem in countries where infected material can be spread far and wide, for example by cyclones or tsunamis. Previous attempts to eliminate TR4 through other means have been unsuccessful: the funigant methyl bromide is a temporary fix and tissue culture is an expensive technique. Moreover, a tiny

# No bananast

Media coverage surrounding this issue is minimal; other topics are currently more popular amongst the public. Additionally, most British and American bananas are bought from Latin American countries which are currently unaffected by TR4, so this does not greatly impact on the primary export markets.

Why are we not actively pursuing something that will eventually directly affect us? Perhaps it is because of social loafing: the idea that people are less motivated to contribute when others are involved in the situation. With countless people involved in growing,

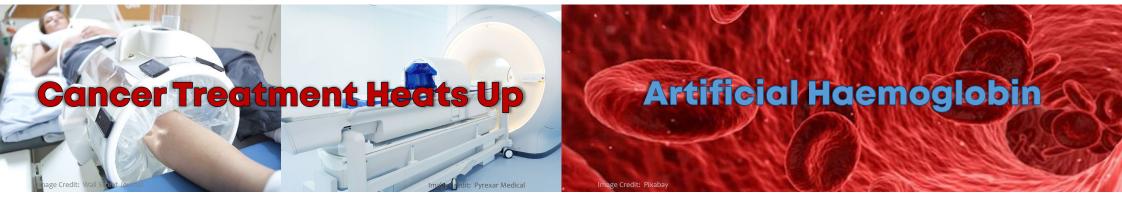
sources are distanced from the farms and are not aware of the seriousness of the situation.

Would it be possible to change people's attitudes towards this issue? It has been suggested to do so by changing their frame of mind. Positive messages spur action to change, although it would be

With over 100 billion bananas eaten every year, TR4

presents an unrecognised global issue. With the fungus on the march, the Cavendish banana may itself follow in the footsteps of the Gros Michel and find itself consigned to the history books. And maybe one day, the answer will be 'yes, we have no bananas'.  $\Delta$ 

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### Reporting by Gus Bonnington, Georgia Gorham, Andrew Kuribayashi-Coleman, William Malewicz, Shannon Round & Benjamin Thrussell

Cancer remains a tumour in modern medicine. A new centre for the treatment of childrens' cancer has just opened at the Charité University Hospital in Berlin, following success in clinical trials. The Centre for Treatment of Children with Hyperthermia & Chemotherapy (CTCHC) is practising innovative techniques, previously neglected by modern medicine, to treat recurring tumours using hyperthermia therapy, alongside conventional treatments. The new centre is practising this innovative technique to help treat some of the 7.6 million people who die globally from cancer each year, focusing on the treatment of recurring tumours.

Hyperthermia occurs when a core region of the body is heated above the normal body temperature of 37°C, aiding in the destruction of tumorous cells. There are two ways that hyperthermia can kill cancerous cells. Firstly, the heating of affected cells to between 41°C and 43°C causes them to undergo a natural process of cell death (apoptosis), whilst leaving healthy cells relatively unharmed. The increase in temperature causes a breakdown in the essential biochemical reactions of cells as their

enzymes cannot work efficiently in high temperatures. Cancerous cells in tumours often have complicated, disorganised structures, making heat loss difficult. This makes these cells more susceptible to apoptosis as a result of increased temperatures. Secondly, hyperthermia can be used to weaken tumours. Even if cancerous cells do not die completely, there is often an additional effect of dilating the blood vessels in the tumorous growth as a result of the heat applied. This increased blood supply to the tumour increases its susceptibility to traditional cancer treatments. It is this technology that will be used by the new centre.

The opening of the CTCHC is a result of successful trials by Düsseldorf University medical school, achieving an 86% positive response to the treatment, alongside a 72% five-year survival rate. 44 participants aged between 7 months and 21 years of age took part in the trials, all of whom had failed to respond to initial treatment or had relapsed once or several times since. As of the end of the study, 46% were in full remission (no signs of cancer remaining) and a further 40% were in partial remission (50% or greater reduction in their tumours).

Originally, hyperthermia therapy was achieved by heating the entire body. but localised methods are preferred. The centre in Berlin uses the BSD-2000 (manufactured by BSD Medical), which directs radio waves, at a frequency of 75 to 120 MHz, to the affected region to be absorbed by the cells, increasing the temperature of the tumour. This is similar to how food is heated in a microwave oven. The BSD-2000 uses multiple sources of electromagnetic waves that constructively interfere, increasing the peak height when they overlap. By targeting the waves so maximum interference occurs at the heart of the tumour, maximum heat is applied to the tumour with minimal temperature change to nearby healthy cells.

This new treatment is rapidly becoming widely practiced with treatment centres now opening across America. Research continues to look at developing hyperthermia therapy for more effective treatments with fewer side effects by methods such as heating the cells using nanoparticles or ultrasound. As cancer remains a primary concern within our society, hyperthermia therapy offers medics a new tool in the fight against cancer.  $\Delta$ 

### Reporting by Sam Gaughan, Gopikaa Kanthasamy, Oliver Martin, Stanley Rawlings & Jacob Townsend

Oxygen has been an intrinsic part of the evolution of life on our planet since it first started to become a major component of our atmosphere 2.5 billion years ago. Along with most living organisms, humans require oxygen to carry out life processes that fuel our existence — without it the majority of life on earth would die out.

Now a new crystal has been created with the ability to store oxygen molecules at concentrations much higher than in air with the ability to later release them - this could be a crucial discovery. Structurally similar to haemoglobin, the crystals are composed of a metal centre (cobalt rather than iron) surrounded by ions that can absorb oxygen at levels 160 times greater than air in a given volume. The absorption can take place at room temperature and pressure over a period of between 24-48 hours which results in the crystals becoming saturated (holding as much oxygen as they can). Releasing the oxygen from these crystals is almost instantaneous upon heating to just under 1000°C, or when depressurised.

During the experiments to synthesise these crystals, researchers began with solid reactants which needed to be heated to progress the reaction. Since the heating of solids is commonly hazardous, they used a solution to heat instead. This meant that the crystal synthesis was more complicated than expected, which may lead to further complications when upscaling the reaction for mass production.

When testing for oxygen releasing conditions, the group discovered that placing the crystals in a near vacuum had the same releasing effect as heating. However, a serious limitation is that due to the reabsorption rate, the crystals would have to spend time "recharging" and eventually would need to be replaced as they lose their structure after multiple cycles of absorbing and releasing oxygen.

Currently hospitals, scuba divers, and fire fighters use heavy, cumbersome oxygen tanks. The creation of a device that uses these crystals, could replace these tanks with a smaller, lightweight and more convenient alternative. After further research, reabsorption times could be reduced and we may be able to use these crystals in fire suppression systems. This would involve the rapid removal of oxygen from a room where a fire has broken out, providing a great solution to use where electronics are present and water is not appropriate.

They would be more effective at sucking oxygen out of the room, thus withdrawing the fire's fuel, than the currently used rapid pumps.

Another potential area where the crystals could be beneficial is in deep space travel; oxygen storage is currently a major issue for space agencies and the use of such crystals may make longer flights in lighter weight aircraft and spacecraft possible, with the side benefit of being able to carry more fuel if the weight and space occupied by oxygen tanks is reduced.

Research into this oxygen crystal and materials like it has rocketed recently since their potential uses were realised. If properly harnessed, this could lead to advancements in oxygen tank technology, which will be hugely beneficial for users by reducing weight and increasing efficiency.

Further uses for the crystal may become evident as research continues, with the crystals' high affinity for oxygen presenting possible applications for gas separation and purification. This is an exciting new area of scientific exploration that could lead us to new frontiers and technologies.  $\Delta$ 

21 | Natural Scientist | January 2016 heated to progress the reaction. Since present and water is not appropriate. 22 | Natural Scientist | January 2016

### Biggest stories of 2016



The World Health Organisation predicts worldwide meat consumption will **double** by 2050. Increasing demand for meat comes with serious implications for the environment and our health. But science may have the answer. Professor Mark Post at Maastrict University has developed a hamburger which can be grown from stem cells in a laboratory, a process using 99% less land, 96% less greenhouse gases and 45% less energy than conventional farming.

The discovery of stem cells in mice, in 1981, was a huge step towards realising the dream of *in vitro* meat as it was for regenerative medicine. These 'master' cells, found in all animals, have the ability to divide almost endlessly and develop into various types of tissues. The 5oz cultured beef-burger Professor Post created was grown in a laboratory using the myosatellite (muscle) stem cells

of a slaughtered cow. Myosatellite cells are used by the cow to repair damaged cells and they multiply and differentiate easily, making them ideal for the project's aims.

To grow the burger, the cells were encouraged to multiply in a growth medium, before being placed in one with a reduced nutrient content to stop multiplication and allow the cells to merge to

become muscle fibres. These fibres were attached to a biodegradable micro-scaffold which provided tension, allowing the fibres to contract and exercise as if in a living cow. This muscle makes up the main component of the burger.

Although this technique was effective, it was not the most economically viable; the first *in vitro* burger cost around

£220,000. Recently, an advance has been made to replace the microscaffolding, the most expensive element of the process, and instead the cells are placed in a special gel around a central column. The resulting ring of tissue allows the cells to provide their own tension, eliminating the need of the micro-scaffold entirely. This process is more efficient and far cheaper than previously. The resulting burger — 20,000 tiny strips of cultured muscle tissue — was added to fatty tissue and other nutrients to make a synthetic meat as nutritious as the real thing. The meat was also stained with beetroot juice to give it the classic 'meaty' colour, as the fibres were initially yellow, due to the lack of blood and myoglobin in the in vitro production.

Health wise, the in vitro burger has extraordinary potential. Regular consumption of normal meat tends to lead to an increased chance of heart disease and other problems associated with a high fat diet. Joan Salge Blake, spokesperson for the Academy of Nutrition and Dietetics claims: "If they are going to make their own fats, they will be able to replace the saturated fatty acids with, for example, omega-3 fatty acids". This would make artificial meat healthier than its more 'natural' predecessor. It doesn't stop at the fat either, in future versions we could see meat lacking cholesterol or laced with essential vitamins normally lacking in meat products.

In addition to the dietary advantages, the sterile lab environment means there is a much lower risk of livestock borne bacteria, such as Salmonella. Similarly, compounds such as growth hormones, pesticide residues, tranquilizer remnants and traces of de-worming chemicals would have no chance of being consumed.

It is widely agreed that lab-grown meat does have a major 'YUCK' factor. How-

ever, food critics have given generally favourable reviews for this burger. Food critic Josh Schonwald stated, "The general bite feels like a hamburger - what was consistently different was the flavour." However, Helen Breewood, a colleague of Professor Post, believes that, "If [people] consider what goes into producing normal meat in a slaughterhouse, I think they would also find it repulsive." If mankind were to overcome this revulsion, there could be enormous benefits for the environment both in the reduction of harm to animals and in the accompanying reduction in antibiotic use. People for the Ethical Treatment of Animals (PETA) are huge advocates of the research, having offered \$1 million to whoever can produce a marketable in

Although cultured meat sounds like an effective alternative to conventional meat, there is still a way to go in its production on an affordable scale. Myosatellite cells have a division limit meaning

a constant supply of muscle tissue is needed. This makes the burger production not entirely slaughter-free. This has led other researchers attempt to use different types of stem cells with fewer limitations. Nicholas Genovese at the University of Missouri is developing a stem cell made from a regular adult cell which might be able to reproduce indefinitely. As organ printing also becomes a leading area of research, many potential new procedures are in the pipe line that are just as applicable to producing sustainable meat as to producing human organs.

In vitro meat may not be the answer to all the world's problems but it may help to solve some of them. Although currently priced out of the reach of the general public, the technique is ready to be significantly scaled up. Only time will tell the true impact of the 'test-tube' burger. A



Professor Mark Post holding a tray of growing medium for muscle cells in 2011.