Getting air to firm up

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The gossamer-thin aerogel is set to gain strength and utility

The aerogel is like a jelly but more delicate. It is delicate because it is a jelly where the water part has been replaced by air. A gel, like jelly, is a liquid in its bulk, with a framework of firm, internal linkages that gives it an extent of rigidity. Now, if we replace the liquid portion with air, then most of the weight disappears while the air-filled, porous, usually transparent framework -- the aerogel -- remains. This lightweight structure has value and use for many purposes. The structure, however, in all aerogels created so far, is brittle and cannot be worked upon. On top of this, aerogels are expensive to produce.

Guoqing Zu, Kazuyoshi Kanamori, Ayaka Maeno, Hironori Kaji and Kazuki Nakanishi from Kyoto University, report in the journal, *Angewandte Chemie*, a technique to create low cost, customisable aerogels, which have greater strength, are elastic and can be rolled, twisted or cut. These aerogels also have a special property of repelling water and are efficient insulators of heat. Mixing graphene in the structure also gives the possibility of electrical conductivity. The electrical properties can be controlled by manipulating the aerogel, which could lead to more applications.

The molecules of a normal liquid are free and in constant motion throughout the body of the liquid. Gels are liquids too but the molecules connect to one another. They do not form crystals, as in solids, but they form chains and "cross links", which provide a three dimensional, honey-comb structure. As the proportion of the liquid material that participates in cross linking is small, the bulk of the material stays fluid and the gel is usually unstable and "jelly-like". The cross linking usually collapses when the gel is heated and the collapse is usually irreversible.

The aerogel derives from a gel. Once the gel has formed and there is a framework, the liquid in the bulk is gently evacuated and replaced with a gas. The liquid is removed by a process called supercritical drying. This is where the liquid is warmed and the pressure is reduced, gradually, so that the liquid stays liquid a little longer than it should, or gets "supercritical". Evaporation can then be regulated so that the framework does not collapse. This kind of drying could be regarded as the opposite of boiling the liquid, which leads to evaporation faster than just drying.

Once the liquid has been removed from a gel, in this way, what remains, in the first place, is a lightweight frame. And then, in the second place, air, or gas, which forms its bulk, is confined to small compartments. This second property makes aerogels powerful insulators.

The way a normal gas conducts heat is that the molecules gain energy when they are in contact with a hot surface. These energetic molecules then communicate, by collisions, with other molecules, so that energy is passed on to the other parts of the container of the gas. In the case of insulators, the fibres of the insulating material confine the air to small pockets, whose dimensions compare with the average distance that gas molecules move before they collide with other molecules. This interferes with passing on energy from one side of an insulator to another.

In the case of an aerogel, although there is no material for support and the structure is fragile, the dimensions of the compartments formed are small indeed. Aerogels are thus excellent insulators both of heat as well as of sound, which also propagates by energy transfer across molecules of gases.

The aerogel was first made, in 1931, from silica gels. Aerogels from different materials, like the oxides of aluminium, chromium, iron and tin, carbon, organic polymers, semiconductor nanostructures, gold and copper have since been developed. As for the cost of supercritical drying, other methods, like drying without reducing the pressure or freeze drying have been used. In freeze drying, the gel is chilled so that the water content freezes. The pressure is then reduced, so that the ice sublimes or evaporates without melting.

The paper in *Angewandte Chemie* says these methods have, however, not been able to overcome fragility, which limits the applications of aerogels. Additives to increase strength are found to reduce the porosity and increase the weight, which takes away from the character. There have been half-way solutions, the paper says, but either poor scope for bending or other processing has limited the success of aerogels developed so far.

The Kyoto University team reports that the impasse now appears to be over. They report that a class of polymers, or chain molecules, that they have been working with show "excellent mechanical properties, such as superflexibility and processability and multi-functionality combining thermal insulation, selective absorption, and strain sensing properties." The team has said that the chain molecules of the aerogels can be made directly using a selected material, called VDMMS, or along with related material, VMDMS. Varying the proportions then results in a range of pore sizes, from 20-100 nm to two-20 microns, which is a thousand times larger.

The paper describes the kind of cross linking that takes place in the process, which leads to great elasticity of the structure. This is a departure from the opposite, which is rigidity and hence fragility of traditional aerogels. They are thus capable of being bent, twisted and cut to different shapes. The aerogels with the finer pore size are more effective insulators than conventional materials like polyurethane foam or mats of glass wool, the paper says.

Another feature of many aerogels is that the material of the structure, once formed, is treated to repel water, for stability. The aerogels created by the Kyoto group also repel water and display selective absorption when exposed to a mixture of water and other liquids, like oils. This property, along with flexibility, would enable their use for the separation of mixtures. The aerogel would selectively absorb the oil, which can then be squeezed out, and the process can be repeated till all the oil has been removed.

Aerogels that conduct electricity have also been developed by introducing slivers of graphene into the structure. These slivers are in better contact when the aerogel is under pressure. Pressure can thus be used as a means of controlling the current passed, with applications in electronics or for use as touchpads.

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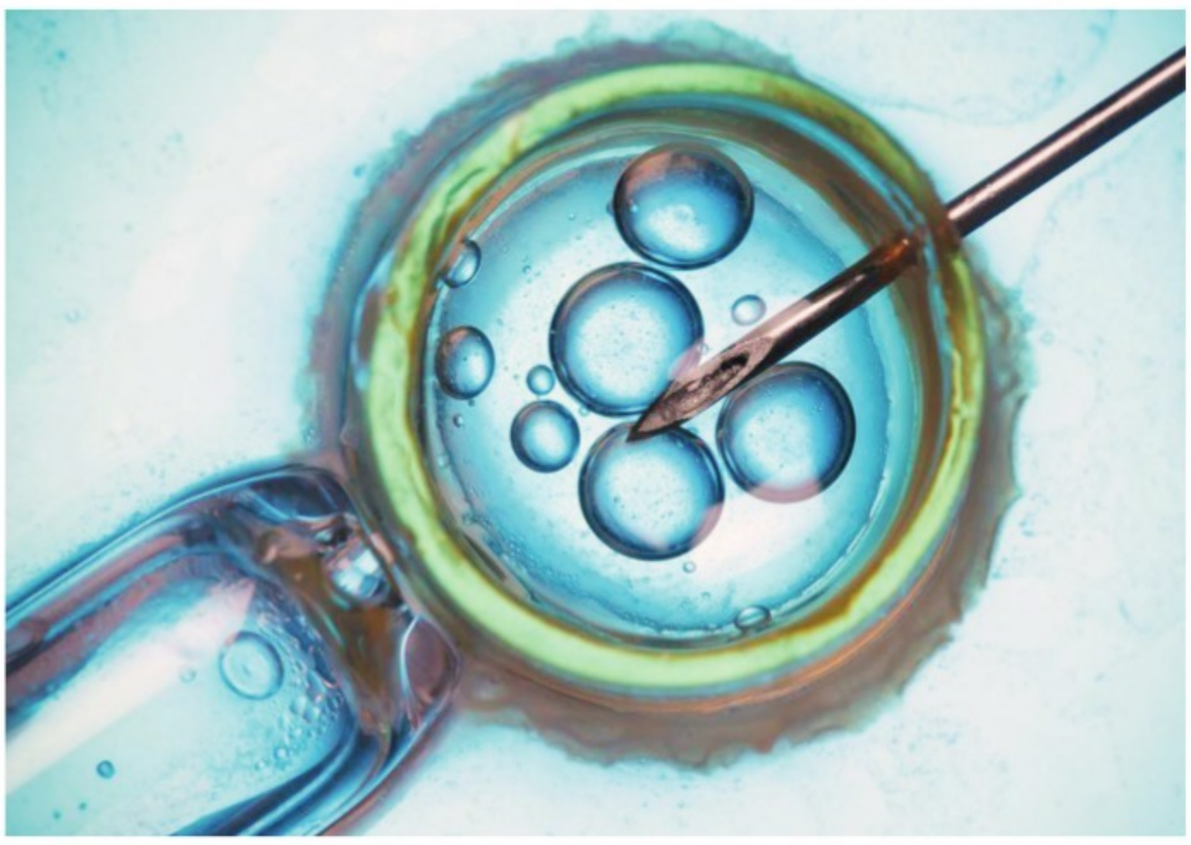
The 'designer baby' debate

The issue of genetically testing human embryos is fraught with ethical and legal complexities — but also at the heart of the matter are contrasting opinions about what makes an acceptable clinical trial



DARREN GRIFFIN, ALAN THORNHILL & CAGRI OGURBUT

Screening embryos for genetic abnormalities in IVF was first successfully performed in 1989, resulting in the birth of the Munday twins. A test to screen for a specific genetic abnormality was later developed; choosing embryos with the correct number of chromosomes and discarding those with too many or too few. This test is widely used in fertility clinics to increase the chance of live birth and a healthy baby. Whether it should be performed at all, however, is hotly debated.

Both egg and sperm cells normally have 23 chromosomes, and after fertilisation a single-celled embryo with 46 chromosomes is formed. A cell with 46 chromosomes is known as "euploid", and an abnormal cell, with fewer or more chromosomes, is known as "aneuploid". Aneuploidy can lead to congenital abnormalities (such as Down syndrome), pregnancy loss, infertility or IVF not resulting in pregnancy.

Embryonic cells continue dividing after fertilisation and, after five or six days, there are about 100 cells, each with 46 chromosomes — if the cells are normal. One group of cells will become a baby and the other the placenta. At this stage a few cells that would later form the placenta can be removed by an embryologist for testing. The test is known as preimplantation genetic testing for aneuploidy or PGT-A.

Trial by error

By only implanting euploid embryos, PGT-A should improve a woman's chances of becoming pregnant. However, the first clinical trials to evaluate the procedure showed the reverse to be true, and authors of those trials remain fierce opponents of the test. But parents who have benefited from PGT-A, and many fertility experts, are enthusiastic advocates. A lively debate has persisted ever since.

Early versions of PGT-A used fluorescent probes to identify specific chromosomes three days after fertilisation when the embryo has just eight cells. However, those methods were prone to misdiagnosis and didn't look at every chromosome in the embryo. So abnormal aneuploid cells could be missed and normal embryos could be mistakenly classed as aneuploid, which partly explains the unfavourable clinical trial results.

As well as changing the embryo biopsy time to five or six days after fertilisation, more accurate and sensitive tests were developed to analyse all chromosomes simultaneously. These new approaches — demonstrated in several clinical trials, observational studies and large national data sets — have improved IVF results, increased pregnancy and birth rates, and reduced miscarriage. As a result, many fertility experts now believe PGT-A can be beneficial, using the right methods, in the right hands and with the right patients.

However, opponents of PGT-A argue there is still not enough high-quality evidence to justify it. They argue that PGT-A should only be used after at least one "properly designed" favourable clinical trial has been published, as they consider the previous trials, showing PGT-A to be of benefit, to be biased, poorly designed and too small.

The debate continues as PGT-A advocates argue there is already enough evidence to support PGT-A and that further clinical trials are unnecessary and too expensive. Also, they argue that many widely used IVF procedures, such as intracytoplasmic sperm injection — where a sperm is directly injected into an egg and fertilised before implantation — were never subjected to clinical trials as their benefits were immediately obvious. At the core of the debate are contrasting opinions of what constitutes a well designed, well conducted clinical trial.

Aside from clinical trial evidence, there are other considerations about the cost of not providing PGT-A — in financial, medical, legal and ethical terms. For instance, ethically, what would be the harm to patients — medical and psychological — if they had an aneuploid pregnancy, assuming PGT-A wasn't on offer?

Mosaicism

Another complicating factor is "mosaic" embryos or embryos containing both euploid and aneuploid cells. The latest technology, called next generation sequencing, is so sensitive it readily detects mosaic embryos. Some fertility experts consider this a benefit, as most mosaic embryos, if transferred, will not result in pregnancy. Others worry that, since healthy babies have been born following mosaic embryo transfer, many mosaic embryos could be unnecessarily discarded if they are classed as "abnormal".

We need more research to understand how chromosomal abnormalities arise in embryos, mosaic or otherwise, and how to prevent them. One new diagnostic approach involves testing the fluid in which the embryo develops, rather than removing cells from the embryo. This fluid is thought to contain DNA from the embryo, and early results are promising.

PGT-A can be improved but it will never be perfect — no test is. The disagreement between PGT-A opponents and advocates is whether this test is good enough now. Unfortunately, when new evidence does emerge, it always seems to further polarise opinion rather than leading to clarity and resolution.

Genetic counsellors are trained to demystify the complexities of issues, such as mosaicism, and explain to patients what the transfer of a mosaic embryo might mean for them. Fertility experts may continue debating the pros and cons of PGT-A but patients can only make an informed choice if provided with all of the available evidence.

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PLUS POINTS

Sullied by our touch

The area of the ocean that remains undamaged by humans is tiny, according to the first ever comprehensive analysis of "marine wilderness". Global shipping, fishing operations and pollution running into the sea from land have all taken their toll on the world's seas, including some of the most remote areas.

Areas of true wilderness are vital as they are some of the most diverse parts of the ocean and the last places on Earth still inhabited by sizeable numbers of large predators like sharks.

Even the few fragments that remain are threatened as advanced fishing technologies and melting sea ice expose them to human activity. Most of the remaining wilderness, which covers no more than 13 per cent of the world's oceans, can be found in the polar regions and around remote Pacific Island nations. The scientists behind the study have called for international agreements to recognise the unique value of these zones.

Kendall Jones of the University of Queensland, who led the research, said they were "astonished by just how little marine wilderness remains". "The ocean is immense, covering over 70 percent of our planet, but we've managed to significantly impact almost the entirety of the vast ecosystem," he said.

Crucially, less than five per cent of the remaining wilderness is officially protected. "This means the vast majority of marine wilderness could be lost at any time, as improvements in technology allow us to fish deeper and ship farther than ever before," explained Jones, "Thanks to a warming climate, even some places that were once safe due to year-round ice cover can now be fished."

The research, published in the journal *Current Biology*, used available data on 19 different human impacts such as fertiliser pollution as well as fishing activities across the world. They defined areas as wilderness if they were in the lowest 10 per cent of these impacts.

The independent

Chronic pain relief

A modified form of botulinum toxin gives long-lasting pain relief without adverse effects and, in time, could replace opioid drugs as a safe and effective way of treating chronic pain, according to new research by the University of Sheffield, University College London and the Hospital for Sick Children, Toronto.

For the study, published recently in Science Translational Medicine and funded by the Medical Research Council, scientists deconstructed the botulinum molecule and reassembled it with an opioid called dermorphin to make Derm-bot — a compound, which successfully targets and silences pain signals from neurons in the spinal cords of mice. Key neurons in the spinal cord are targets for pain management as they directly "sense" pain and send this information to the brain.

Co-corresponding author, Bazbek Davletov from the department of biomedical science at the University of Sheffield, said, "We developed a molecular Lego system, which allows us to link the botulinum 'warhead' to a navigation molecule, in this case, the strong opioid called dermorphin, allowing the creation of widely desired long-lasting pain killers without the side effects of opioids."

Dermorphin targets and binds to opioid receptors on the surface of neurons which allows the Derm-Bot compound to enter the cells where the botulinum 'warhead' then reversibly inhibits the release of neurotransmitter, silencing the cells essential for sending pain signals to the brain.

"It doesn't affect muscles like the botulinum used to reduce wrinkles, but it does block nerve pain for up to four months without affecting normal pain responses. It really could revolutionise how chronic pain is treated if we can translate it into clinic, removing the need for daily opioid intake," explained co-corresponding author, Steve Hunt from UCL's department of cell and developmental biology.