Bio-engineering in the brewery

> An alternative to the hops flower has been found by tweaking the cells of beer yeast

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A bio-engineered alternative has been found for hops, an essential ingredient in beer-making. Hops, the flowers of the hop plant, lend bitterness and the "hoppy" flavour to beer. But hops are difficult to source and the cultivation has a high environment cost. It is not that hops were always used as the ale of early times used a group of herbs, called gruit, to impart the bitter taste. The practice of using hops started in Europe in the 13th century but was resisted in England. In 1471, the city of Norwich banned its use and even half a century later it was described in England as a "wicked and pernicious weed". But adding hops does something to beer that was not to be resisted and all beer is now made with hops.

The world's annual beer production is about 200 billion litres. With a world population of 8 billion, this puts production at 25 litres per capita. With a large part of the world population soon to reach the legal age of drinking, the figure is going to rise. And, as hops are needed for beer-making, the consumption of hops will also increase. Beer-making itself uses only grain and reasonable energy and water, but the production of hops needs resources, particularly, some 100 billion litres of water a year, at current levels, and adds to the cost. And what is more, the essential components of hops are variable from crop to crop and maintaining a steady quality of the beer produced becomes challenging.

As it is only hops that contain specific flavouring agents, no other natural products have been able to take the place of hops, which have commanded high prices since centuries. There is hence interest in finding an alternative to the hops plant, both to contain land and water use as well as to simplify the sourcing and blending of the right material in beer-making. The journal, *Nature Communications*, carries good news in a report by Charles M Denby, Rachel A Li, Van T Vu, Zak Costello, Weiyin Lin, Leanne Jade G Chan, Joseph Williams, Bryan Donaldson, Charles W Bamforth, Christopher J Petzold, Henrik V Scheller, Hector Garcia Martin and Jay D Keasling, from laboratories in California, and in Denmark, that the cells of beer yeast have been engineered to do the work of the most important components of the hops flower!

The process of beer-making is that barley is first sprouted to free its starch content and an enzyme to convert the starch to sugar. When the grain has sprouted to the required degree, sprouting is stopped by roasting the grain. The grain is then crushed and steeped in warm water, when the starch changes to malt sugar. The liquid, called the wort, is boiled and hops are added to impart bitterness. The wort is then fermented by adding beer yeast and the malt sugar is converted into alcohol. At this stage, which is at room temperature, hops are again added, to release "essential oils" which give beer its "hoppy" aroma and flavour.

The *Nature Communications* paper explains that hop flowers have a dense covering that secretes substances that accumulate in the outer skin. The secretion is rich in a substance called terpenes, which give beer its flavour. The composition of the secretion, however, differs from sample to sample and it is difficult to identify which components are active in giving flavour to beer.

Nevertheless, two main ingredients have been isolated and these are the molecules known as linalool and geraniol. Hops are in fact the flowers of the plant, *Humulus lupulu*, a relative of *cannabis indica*, the shrub from which the recreational drug is extracted. And this family of plants, which synthesises terpenes, even cholesterol and the active substance in cannabis, has an intermediary, called GPP, which leads to the products of synthesis. The paper says that the enzymes that help generate linalool and geraniol from GPP in hops have not been identified so far. What has been found, however, are the enzymes that promote the assembly of these molecules in some other plant species.

The group of researchers hence tried out six different candidate enzymes that could bring about the same action in yeast cells, which were designed to have ample GPP. If the yeast cell, which is the agency of fermentation, were itself able to produce linalool and geraniol, this would eliminate the role of hops in imparting aroma and flavour, at any rate.

When the results of trials were not good enough, however, the group checked on the conditions that made efficient creation of the molecules possible in the plant species. But they found that ways to bring about the same conditions in yeast were yet to be perfected. The group hence surveyed other sources and found that the enzyme from *Lycopersicon esculentum,* which is the common tomato, was promising. Once the enzyme was identified, the group used state of the art methods of gene assembly to engineer the yeast strains to create the terpenes required during fermentation.

The method, in fact, allows development of yeast strains with different sets of genetic design by varying the genetic changes in the yeast cells. What this amounts to is hence not just a method to get brewers' yeast to produce flavour molecules that normally come from the addition of hops, but to control the mix of flavour molecules that would be produced.

On the one hand, this is like getting hold of brace of hops strains and being able to fine tune flavour and aroma according to consumer's preference. But then, the paper notes that "the full flavour imparted by traditional hopping is likely to rely on a more diverse bouquet of molecules". But the method, the paper says, "provides a foundation for generating more complex yeast-derived hop flavours, and broadens the possibilities of yeast-biosynthesised flavour molecules to those throughout the plant kingdom."

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Into the mind of God

A week after his demise at the age of 76, here's the foreword to Stephen Hawking's *A Brief History of Time*, written by another celebrated astronomer

CARL SAGAN

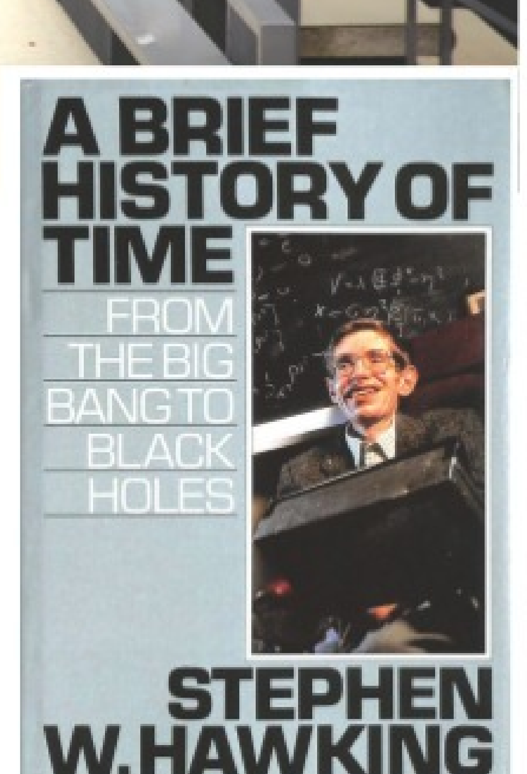
We go about our daily lives understanding almost nothing of the world. We give little thought to the machinery that generates the sunlight that makes life possible, to the gravity that glues us to an Earth that would otherwise send us spinning off into space, or to the atoms of which we are made and on whose stability we fundamentally depend.

Except for children (who don't know enough not to ask the important questions), few of us spend much time wondering why nature is the way it is; where the cosmos came from, or whether it was always here; if time will one day flow backward and effects precede causes; or whether there are ultimate limits to what humans can know.

There are even children, and I have met some of them, who want to know what a black hole looks like; what is the smallest piece of matter; why we remember the past and not the future; how it is, if there was chaos early, that there is, apparently, order today; and why there is a universe.

In our society it is still customary for parents and teachers to answer most of these questions with a shrug, or with an appeal to vaguely recalled religious precepts. Some are uncomfortable with issues like these, because they so vividly expose the limitations of human understanding. But much of philosophy and science has been driven by such enquiries. An increasing number of adults are willing to ask questions of this sort, and occasionally they get some astonishing answers. Equidistant from the atoms and the stars, we are expanding our exploratory horizons to embrace both the very small and the very large.

In the spring of 1974, about two years before the Viking spacecraft landed on Mars, I was at a meeting in England sponsored by the Royal Society… to explore the question of how to search for extra-terrestrial life. During a coffee break, I noticed that a much large meeting was being held in an adjacent hall, which out of curiosity I entered. I soon realised that I was witnessing an ancient rite, the investiture of new fellows into the Royal Society, one of the most ancient scholarly organisations on the planet. In the front row a young man in a wheelchair was, very slowly, signing his name in a book that bore on its earliest pages the signature of Isaac Newton. When at last he finished, there was a stirring ovation. Stephen Hawking was a legend even then.



Hawking is now the Lucasian Professor of Mathematics at Cambridge University, a post once held by Newton and later by Paul Dirac, two celebrated explorers of the very large and the very small. He is their worthy successor. This, Hawking's first book for the non-specialist, holds rewards of many kinds for the lay audience. As interesting as the book's wide-ranging contents is the glimpse it provides into the workings of its author's mind. In this book are lucid revelations on the frontiers of physics, astronomy, cosmology and courage.

This is also a book about God… or perhaps about the absence of God. The word God fills these pages. Hawking embarks on a quest to answer Einstein's famous question about whether God had any choice in creating the universe. Hawking is attempting, as he explicitly states, to understand the mind of God. And this makes all the more unexpected the conclusion of the effort, at least so far — a universe with no edge in space, no beginning or end in time, and nothing for a Creator to do.

Carl Sagan (1934-1996) wrote this introduction for the first edition of *A Brief History of Time* in 1988. Reprinted with permission of the Carl Sagan Estate

The independent

Missing Nobel

Hertog (left) with Hawking

A theory explaining how we might detect parallel universes and a prediction for the end of the world was completed by Stephen Hawking shortly before he died, it has emerged.

The renowned theoretical physicist was working right up until his death last week on his final work, *A Smooth Exit from Eternal Inflation*, which is currently being reviewed by a leading scientific journal. In it he predicted that the universe would eventually end when stars run out of energy.

But Hawking also theorised in his final work that scientists could find alternate universes using probes on space ships, allowing humans to form an even better understanding of our own universe, what else is out there and our place in the cosmos. The physicist's final work was published alongside his co-author, Thomas Hertog of KU Leuven University in Belgium. "He has often been nominated for the Nobel and should have won it. Now he never can," Hertog told *The Sunday Times*, arguing that Hawking could have won that prize for his work on this final paper.

He "would have won a Nobel Prize", Hertog said.

PLUS POINTS

Hearing endangered

Smokers are not just putting themselves at risk of heart disease and cancer but may also be endangering their hearing, Japanese researchers have said.

A new study has found that current smokers were at a higher risk of hearing loss than non-smokers — with that risk apparently increasing with each cigarette smoked. However, kicking the habit appears to reduce this risk again, the scientists said. The authors said the findings provide "strong evidence" of a link, and called for new tobacco control measures to try and prevent or delay hearing loss.

The study, published in the journal *Nicotine and Tobacco Research*, tracked the lifestyle habits and health of more than 50,000 Japanese workers. Using data drawn from records of annual health checks, which include a hearing test, the team looked at how workers' ability to detect both high and low pitch (frequency) sounds changed.

The results show smokers were 60 per cent more likely to develop high-frequency hearing loss, compared to non-smokers, and 20 per cent more likely to lose some ability to hear lower frequency sounds. One in 10 workers developed some form of hearing loss over the eight-year study, and the more cigarettes a worker smoked each day the higher their risk of developing hearing loss, the study found.

"These results suggest that smoking may be a causal factor for hearing loss, although further research would be required to confirm this," the authors write. They point out the study only shows a relationship between smoking and hearing loss, and that it does not prove one causes the other.

They also note that the smoking group was more likely to work in manual and heavy industries, which can increase the likelihood of hearing loss, though they tried to control for this statistically.

Lead scientist Huanhuan Hu, from the National Centre for Global Health and Medicine in Japan, said, "With a large sample size, long follow-up period, and objective assessment of hearing loss, our study provides strong evidence that smoking is an independent risk factor of hearing loss."

The independent

Hot from cold

The mystery of X-ray emissions from comets has been solved by a team of researchers.

The radiation of X-rays from comets has been a long-standing mystery to science, given that X-rays are normally associated with hot objects like the sun but comets are among the coldest objects in the solar system.

When comets travel through the solar system they interact with solar radiation, wind and magnetic field. This produces a visible atmosphere, known as a coma, and the observed cometary tail, as well as, in some cases, X-rays. The X-rays are generated on the sunward side of the comet, where the solar wind impacts the cometary atmosphere forming a bow shock.

A team of scientists from 15 institutes probed the question by carrying out experiments at the LULI laser facility in Paris, in which they replicated the interaction of the solar wind with a comet. The paper has been published in *Nature Physics.*

Bob Bingham from University of Strathclyde's department of physics, who published a theoretical paper on X-rays from comets that formed the basis of the investigation, said, "These experimental results are important as they provide direct laboratory evidence that objects moving through magnetised plasmas can be sites of electron acceleration."

The research also shed light on a cosmic ray mystery known as the injection problem. It is widely recognised that strong shock waves are expected to accelerate particles to very high energies, however, they require a source of particles fast enough to cross the shock. This latest experiment clearly demonstrates that plasma turbulence can provide a source of fast particles, which can overcome the injection problem.