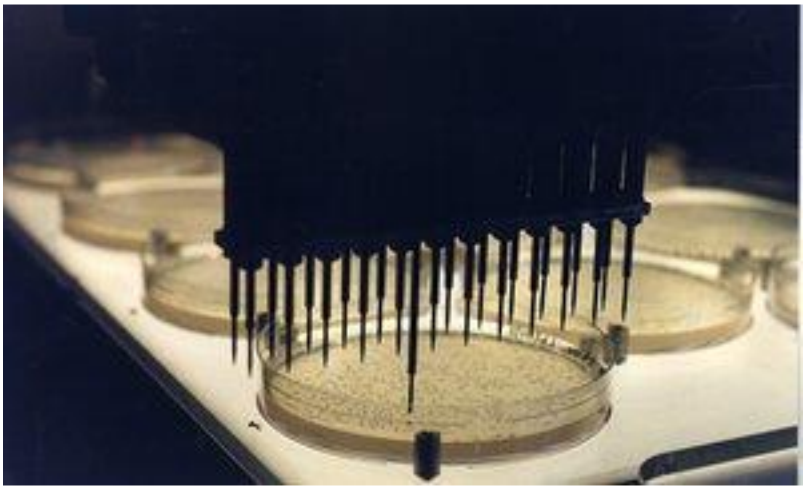
Synthetic genome nearly complete, paving way for bespoke organisms

Human-designed organisms could produce drugs and vaccines, convert waste into energy or grow organs for human transplant operations



The work on yeast marks a substantial advance in researchers' ability to manufacture the code of life. Photograph: Martin Godwin for the Guardian

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75

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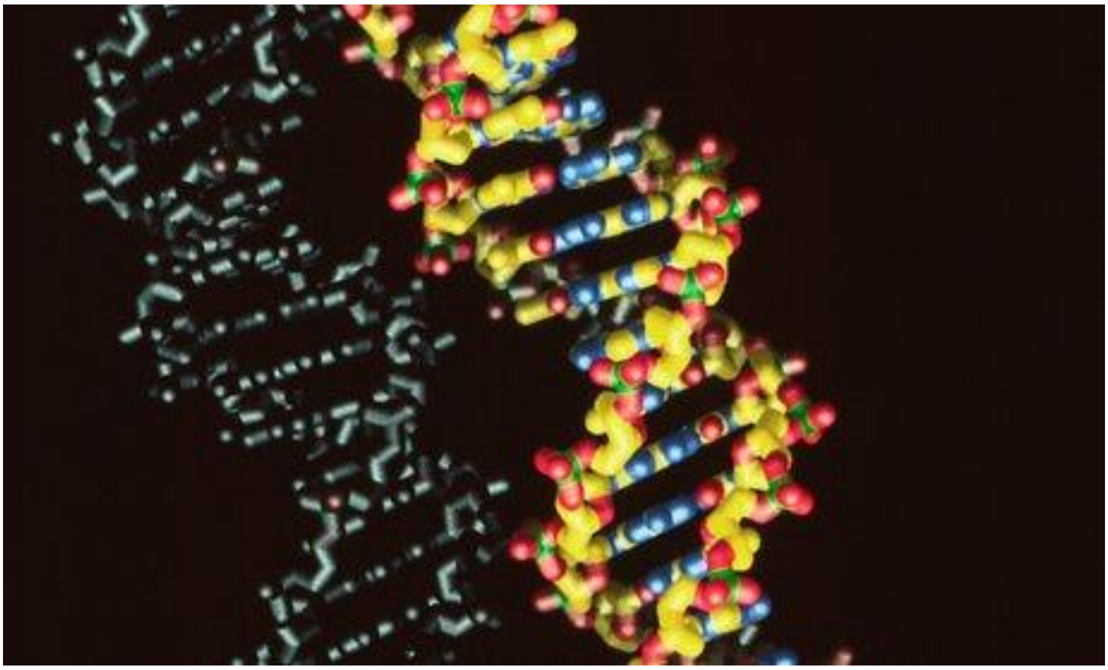
Scientists are close to completing an entire synthetic genome for a microbe that has been used in bread, beer and wine making for more than five thousand years, paving the way for a realm of new organisms designed by the human hand.

The work on baker's yeast marks a substantial advance in researchers' ability to manufacture the code of life. While genetic modification alters only small numbers of genes at a time, the new approach allows scientists to rewrite entire genomes. In doing so, they can strip out excess genetic baggage and unstable regions that have accumulated over millions of years of evolution and add fresh DNA on the way.

The research gives scientists a deeper insight into the basic question of how DNA works in living organisms, but the technology is poised to deliver bespoke microbes, plants and animals too. These would be created to fulfill specific human needs, with genomes that make them produce drugs and vaccines, convert waste into energy, and even grow organs suitable for human transplant operations.

In a series of papers published in Science on Thursday, an international team of scientists from the Synthetic Yeast Project led by Jef Boeke at New York University describe how they used a computer to design each of the 16 chromosomes that natural baker's yeast carries. To do this, they took the sequence of Gs, Ts, Cs and As and made thousands of changes to remove strands they considered unnecessary. The final genome was 8% shorter than that found in nature.



Organisms created with synthetic DNA pave way for entirely new life forms

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The scientists then built five of the chromosomes from chemicals in the lab. Since the papers were submitted to the journal, at least 10 of the bug's chromosomes have been constructed, amounting to more than half of the microbe's genome. One of the chromosomes contains more than a million genetic letters and is the longest chromosome ever synthesised.

Patrick Yizhi Cai, a geneticist on the team at Edinburgh University, said the chromosomes were created from chunks of DNA that were added one by one to natural yeast cells to test whether they worked. In time, all of the natural DNA on a chromosome was replaced with synthetic DNA. Cai likens the process to replacing paragraphs in a book one by one, until eventually a whole chapter has been changed.

Today, the technology to design and build genomes is costly and time consuming. To synthesise all of the DNA in baker's yeast will cost at least $1.25m and each chromosome takes at least a year to manufacture. But researchers expect the price to fall dramatically, in the same way that the cost of gene sequencing has plummeted since the first human genome was read in 2003.

Boeke said that all 16 baker's yeast chromosomes should be built and tested in cells by the end of the year. Yeast cells operating with the full complement of synthetic chromosomes are expected in 2018. The final design includes an extra 17th chromosome made from scratch which will bundle important protein-making parts into one location.

While scientists have previously built genomes for bacteria and viruses, the latest work focuses on more a complex organism that has a clearly defined nucleus. These cells belong to a group called the "eukaryotes", which include plants, animals and humans.

One feature the scientists have built into the baker's yeast DNA allows the cell's genome to be scrambled at will. The researchers will use this to produce yeast cells with completely new DNA codes, some of which may have useful properties, such as improved growth, or an ability to survive higher temperatures.

Paul Freemont, who studies synthetic biology at Imperial College, London, called the work “an amazing advance in our ability to chemically synthesise the blueprint of life.”

“This is a transformative step in the scale and magnitude of what we can assemble and get working in a cell. We are going to have yeast cells powered by human-designed chromosomes,” he said.

Researchers have already begun talking about what organism to build genomes for next. On the cards are nematode worms, plants and even mammalian cells. Eventually, animals such as pigs could have genomes designed to make their organs suitable for human transplant operations. Mammalian cells are already used to produce medical products such as insulin for diabetics.

In May, Boeke and other researchers will hold a public meeting to discuss creating human genomes in the hope of learning more about how they work. If scientists can master the manufacture of human genomes, they could potentially create batches of human cells for medical therapies that are resistant to viruses.

Tom Ellis, another researcher at Imperial College, said the latest batch of papers showed that an entire synthetic eukaryote genome was on the way. “We will learn a lot about biology along the way, but we can also build superpowers – features you don’t see in nature – into the design,” he said. “It’s the ultimate fast lane for evolution.”

Eventually, researchers hope to understand genomes well enough to build new ones that are honed for specific roles. “It will get to the point where the bottleneck is not about how to print the book, but what do you want to write,” said Cai. “Ideally what you want to do is write a new book from scratch.”

https://www.theguardian.com/science/2017/mar/09/synthetic-yeast-genome-nearly-complete-paving-way-for-bespoke-organisms