DPA PICTURE ALLIANCE/ALAMY

signals free of charge to smartphones and other receivers in December 2016.

Researchers also combine signals and use them in an array of scientific applications, including the monitoring of movements in Earth's crust and for the study of the atmosphere.

The Galileo programme is building another 12 satellites as in-orbit spares and to replace older machinery. It is also starting to build a next-generation system. The EU opened the first of the tenders for building these craft in June. Total costs for the Galileo programme are estimated at around €13 billion (US$15 billion) to €15 billion to the end of 2020.

How would Brexit change the United Kingdom's participation in Galileo, and why is the UK government unhappy?

Brexit would have no effect on the availability of Galileo signals to scientists and other UK citizens — the service is freely available to anyone on the planet.

But a UK-based company, Surrey Satellite Technology in Guildford, a subsidiary of the aerospace giant Airbus, built all the satellites made so far (although many components, such as the satellites' atomic clocks, are sourced from suppliers in Europe).

However, the EU has already effectively excluded UK companies from bidding for the lucrative tender for the next-generation satellites. The British government has complained that this treatment is unfair, given its contributions so far.

After Britain leaves the bloc on 29 March 2019, it will also automatically stop being involved in the defence-related aspects of the Galileo programme — something the government was pushing to stay a part of.

What are Galileo's defence applications?

The system's secure service, scheduled to be fully operational by around 2026, will be restricted to government-authorized users, including the military and essential services such as energy supplies and telecoms. The signals are encrypted to stop interference or malicious jamming.

"Spending £3 billion to £5 billion on a UK system would be grotesquely wasteful."

The United Kingdom has been closely involved in the secure system's development. It had argued that this close participation, and its significant role in EU defence matters, mean it should be given special treatment that would allow it a full role in the inner workings of Galileo's defence aspects. But EU rules do not allow a non-member state to be involved in the development of such security aspects.

The United Kingdom said that this is unacceptable, leading May to say on 1 December that the government would abandon plans to use Galileo for defence and critical national infrastructure. She also confirmed that the United Kingdom was looking at options for building its own global system.

Is that proposal credible?

It might be technically feasible, say experts — Britain has the science and engineering skills to build such a system — but it probably isn't affordable. Widely cited estimates put the construction cost at somewhere between £3 billion (US$4 billion) and £5 billion. That doesn't include the running costs, which amount to about €800 million a year for Galileo. For comparison, the UK space agency's budget this year is £402 million, and Britain's defence research budget will be about £1.9 billion next year.

"Spending £3 billion to £5 billion on a UK system would be grotesquely wasteful," says Robert Massey, deputy executive director of the UK Royal Astronomical Society in London.

And even if Britain were to build its own system, there could be a crucial technical limitation: the lack of available space on the radio spectrum.

What's the issue with the radio spectrum?

The four existing global satnav systems already take up the part of the spectrum allocated for satellite navigation by the International Telecommunication Union (ITU), says Alexandre Vallet, head of the ITU's Space Services Department in Geneva, Switzerland. Squeezing in a new global system might require novel radio-signal designs that don't interfere with other systems, says Vallet. And these would need to be endorsed by international agreements — so it would be a challenge, he says. ■

CANCER RESEARCH

'Super' DNA targeted by drugs

DNA segments that amplify gene activity might represent a new form of gene regulation.

BY HEIDI LEDFORD

Experimental cancer treatments that harness souped-up segments of DNA called super-enhancers to activate genes are working their way to the clinic for the first time. But scientists are still debating how these elements work — and whether they represent a fundamentally new way of regulating genes.

Preliminary data suggest that screening for a particular super-enhancer can identify people with acute myeloid leukaemia who might benefit from a drug called tamibarotene. The data were presented by the drug's maker, Syros Pharmaceuticals, on 2 December at a meeting of the American Society of Hematology in San Diego, California. And on 15 November, the company debuted data from another preliminary trial, in which people with solid tumours were given a drug that targets a protein called CDK7. Laboratory tests have shown that inhibiting this protein can reduce the activity of a super-enhancer that has been linked to some cancers (E. Chipumuro *et al. Cell* **159**, 1126–1139; 2014).

The trials are the first attempts to target super-enhancers to treat human disease. But it is still unclear whether these DNA segments are truly stronger versions of better-known gene-regulating sequences called enhancers. "The word is still out," says Lothar Hennighausen, a geneticist at the US National Institute of Diabetes and Digestive and Kidney Diseases in Bethesda, Maryland. "I'm inclined to think that they are not."

Researchers have long known that enhancers are important for regulating when and how strongly genes are expressed. But in 2013, a group found that some enhancers, called super-enhancers, cluster together near genes that help to determine a cell's unique identity — whether it becomes a mammary or a muscle cell, for instance (D. Hnisz *et al. Cell* **155**, 934–947; 2013).

Super-enhancers seem to be particularly important in embryonic stem cells, and they are sometimes hijacked by cancer cells to drive the aberrant gene activity that fuels tumour growth.

And super-enhancers also attract unusually large numbers of the proteins required to activate the genes they control. These clusters of enhancers and proteins might allow cells to tightly regulate important genes, ensuring that they will be turned on exactly when needed and in precisely the right amount, says Christopher Vakoc, who studies gene expression at Cold Spring Harbor Laboratory in New York and has advised Syros.

"It's all about precision," says Vakoc. "When the cell goes to that much effort to control a gene, it's because the product of that gene is pivotal in biology."

Although mammalian cells have ▶

thousands of enhancers, they typically have only a few hundred super-enhancers. As a result, researchers now use super-enhancers as a signpost for important genes, says Hennighausen. Understanding how they work could shed light on how cells adopt their identities. But researchers don't know whether the enhancers in a cluster act independently, or whether they work together in a new form of gene regulation.

That question arose right from the start, says Richard Young, a biologist at the Whitehead Institute for Biomedical Research and a co-founder of Syros — both in Cambridge, Massachusetts. "There were investigators who questioned whether or not they should have the term 'super', because it implied some function that typical enhancers didn't have," he says. "To be frank, at the time we didn't know if they had some special function."

Since then, researchers have scrutinized a few super-enhancers, studying the function of each enhancer in the cluster. But the results are inconclusive: some enhancers show signs of working together, whereas others seem to work independently. "It's a very intense debate," says Denes Hnisz, a molecular biologist at the Max Planck Institute for Molecular Genetics in Berlin.

Hnisz notes that the discrepancy might arise in part from the algorithms used to identify enhancers in genomic data: the algorithms could be mislabelling some sequences as super-enhancers. And different labs use different assays to test for super-enhancer activity, he adds, which could introduce another source of conflict.

Resolving the debate might have to wait until more scientists have studied more super-enhancers, says Douglas Higgs, a haematologist at the University of Oxford, UK. "At the current time, it is hard to be sure if they represent a new type of fundamental regulatory element."

For Syros, the debate is largely academic, says Nancy Simonian, the company's president and chief executive. "From our point of view, it doesn't really matter," she says. "We're just saying it's a marker for a hotspot that we know is associated with genes that are really important for controlling the cell."

The next few years could bring some answers. Studies of enhancers fell out of favour in the early 2000s, says Hennighausen. But technological advances are bringing them back into fashion. The ability to use relatively simple gene-editing tools, such as CRISPR–Cas9, to alter enhancer sequences has made it easier to study their function, he notes. An experiment that once took two years can now be done in a few months for much less money.

"The questions were always there, but the technology was needed to answer them," he says. "The whole field is emerging right now." ■

EPIDEMIOLOGY

Scientists seek hidden sources of Ebola

Two-thirds of new infections in the Democratic Republic of the Congo cannot be linked to known cases.

GORAN TOMASEVIC/REUTERS

An Ebola health worker carries a child at a hospital in the Democratic Republic of the Congo.

BY AMY MAXMEN

As the epicentre of the Ebola outbreak in the Democratic Republic of the Congo (DRC) shifts into the war-weary city of Butembo, public-health workers are trying to stamp out new infections from an unforeseen source: unregulated health centres.

Decades of political instability in the north-eastern DRC, the site of the epidemic, have fostered an increase in informal clinics that offer traditional and modern medicine. These centres treat people for malaria and other common illnesses, filling the vacuum left by the lack of a functional health system. But they are not designed to prevent the spread of a virus as dangerous as Ebola — which has put their patrons at high risk, according to the World Health Organization (WHO). Health officials have begun trying to lessen the centres' load by pre-emptively giving out malaria medication.

The push highlights a central challenge to ending the epidemic, which is now the second-largest on record: although experimental drugs and a vaccine have helped to limit Ebola's reach, two-thirds of new infections cannot be linked to existing cases. That has left epidemiologists racing to identify overlooked routes of infection. And conventional prevention measures have been thwarted by conditions in the north-eastern DRC, where decades of severe conflict have left millions of people dead, and millions more traumatized and homeless.

"I have lived through many outbreaks, but this is the worst one," says Jean-Jacques Muyembe-Tamfum, director-general of the National Institute for Biomedical Research in Kinshasa.

Already, 494 people have been infected with the virus, and 283 of those have died, the WHO said on 10 December. "This is as tough and complex as it gets," says Peter Salama, head of the WHO's health-emergency programme in Geneva, Switzerland.

In the city of Beni in North Kivu province, health workers have been struggling to identify and monitor people who might have been touched by someone in the throes of an