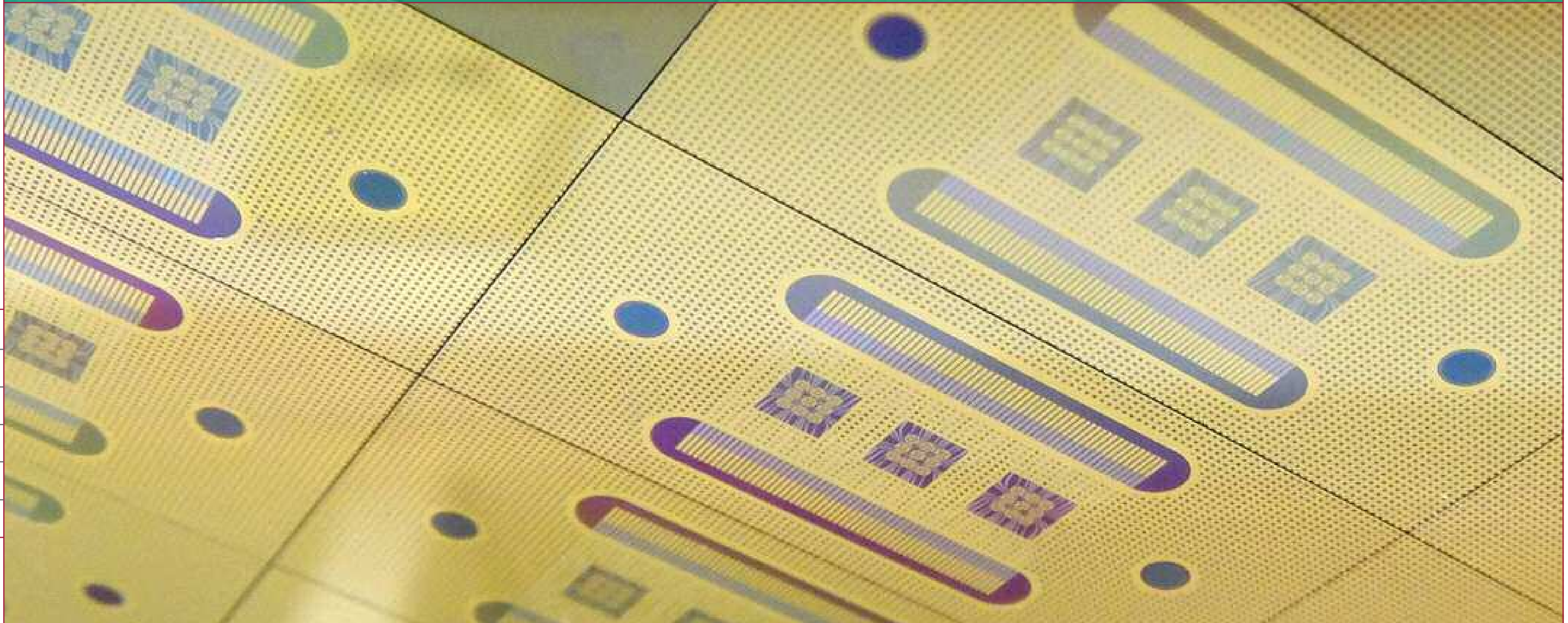
Evonetix

Gene synthesis production at scale

Evonetix is developing an approach to DNA synthesis which could be as revolutionary as the earlier revolution in DNA sequencing.



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Key facts/data:

Evonetix Ltd

Technology: Gene synthesis

Established: 2016

Type: Start-up

Location: Cambridge

Employees: 14

CEO: Dr Tim Brears

Previously Tim Brears served as CEO of a number of bioscience companies, including Xention, a biopharmaceutical company, and Gendaq, a company focused on the development of zinc finger proteins for gene regulation. He spent ten years in the US, initially at Rockefeller University, New York, and then as Director of Licensing at Ciba-Geigy (later Novartis) Agribusiness. He is a graduate of Oxford University and holds a PhD in molecular biology from Cambridge University. He also has an MBA from Duke University's Fuqua School of Business.

A Next-Gen Solexa

Evonetix has ambitions of achieving the same market dominance achieved by Solexa, the gene sequencing pioneer, which span out from the University of Cambridge in 1998, before it was acquired by Illumina Inc. of San Diego for $600m in 2007; at the time it was one of the largest venture capital transactions in the UK bioscience field. Illumina has since used the acquisition to leverage Solexa's world-leading sequencing capability for the analysis of an individual's genetic make-up as well as a myriad of other applications.

Hermann Hauser

The sale of Solexa was a landmark transaction for Hermann Hauser's Amadeus Capital Partners' fund, which had led Solexa's B round in 2004. Since the sale, the cost of DNA sequencing has declined steadily as the market has expanded. That made Hauser think how it could be possible to apply the learning from Next-generation Sequencing (NGS) to the emerging field of gene synthesis; in short, how to do for gene-synthesis what Solexa had done for gene sequencing.

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Gene synthesis and synthetic biology

Gene synthesis represents a potentially larger market even with the huge increase in DNA sequence information available to mankind over the past ten years (facilitated by the Solexa / Illumina approach), it creates an unprecedented opportunity to make DNA materials which can be used to engineer metabolic pathways and organisms, improve industrial processes, create new processes, engineer genomes with new and improved traits and use DNA as a medium for data storage. Known as synthetic biology, it is expected to have a massive impact across many industries.

Disruptive solution

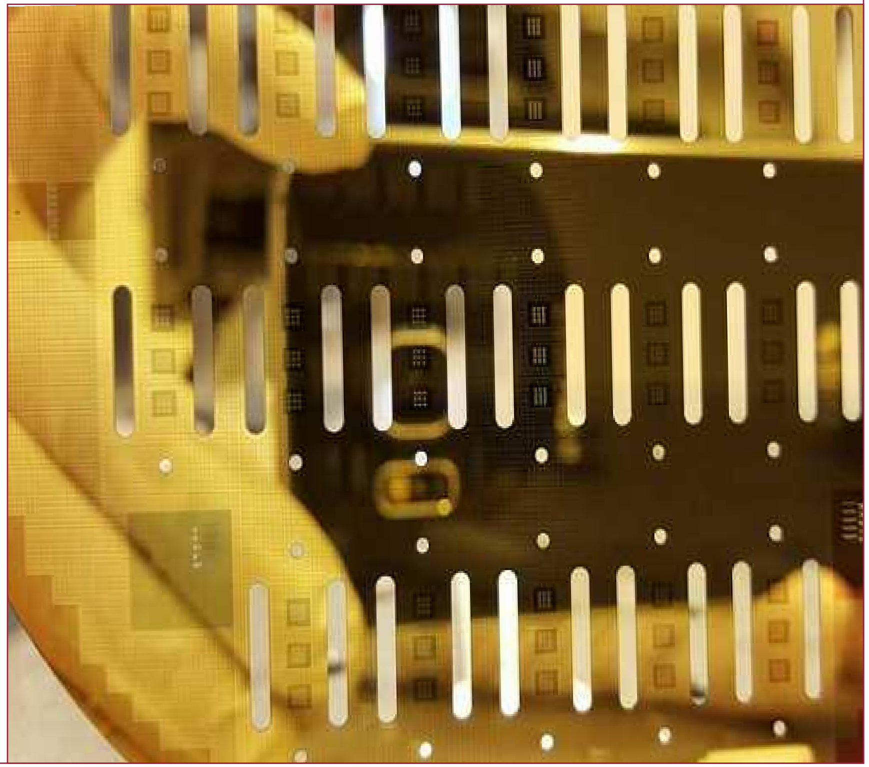
However, a highly disruptive technology is needed to achieve the significant improvements in DNA synthesis required to enable and facilitate these opportunities. Current DNA synthesis methods are relatively slow and inaccurate making them unsuitable to realise ambitious synthetic biology goals. The Holy Grail, therefore, is to find a method that is fast enough to be commercially viable and is error-free. Evonetix, by promising to provide high-fidelity DNA, at scale, without the need for post-synthesis error correction, places itself in the strongest position to enable these opportunities and thereby capture a significant part of the growing synthetic biology opportunity.

Opportunities for synthetic biology

Opportunities include: in materials science, using variants of silk genes for biodegradable, high-performance novel materials; in industrial biotech, creating new enzymes to use biological starting materials and replace the use of petrochemicals; in agriculture, to achieve durable plant disease resistance; and in pharmaceuticals research, by generating greater diversity in drug molecules to address significant unmet medical needs.

Rapid gene printing

Hauser envisaged a gene-sequencing ‘printer’ which would enable biological engineers to ‘write’ new genes and genetic pathways similar to a typesetter creating words with metal type. Together with Cambridge Consultants, he inspired former members of the Solexa team to come together to build the new Evonetix chip and to develop the associated chemistry and biology, and doing so “do to writing DNA what Solexa did to reading DNA” says its CEO, Tim Brears. For a period of 15 months after this the technology was incubated at Cambridge Consultants before being spun out into a company funded jointly by Cambridge Consultants and Providence Investment Company.



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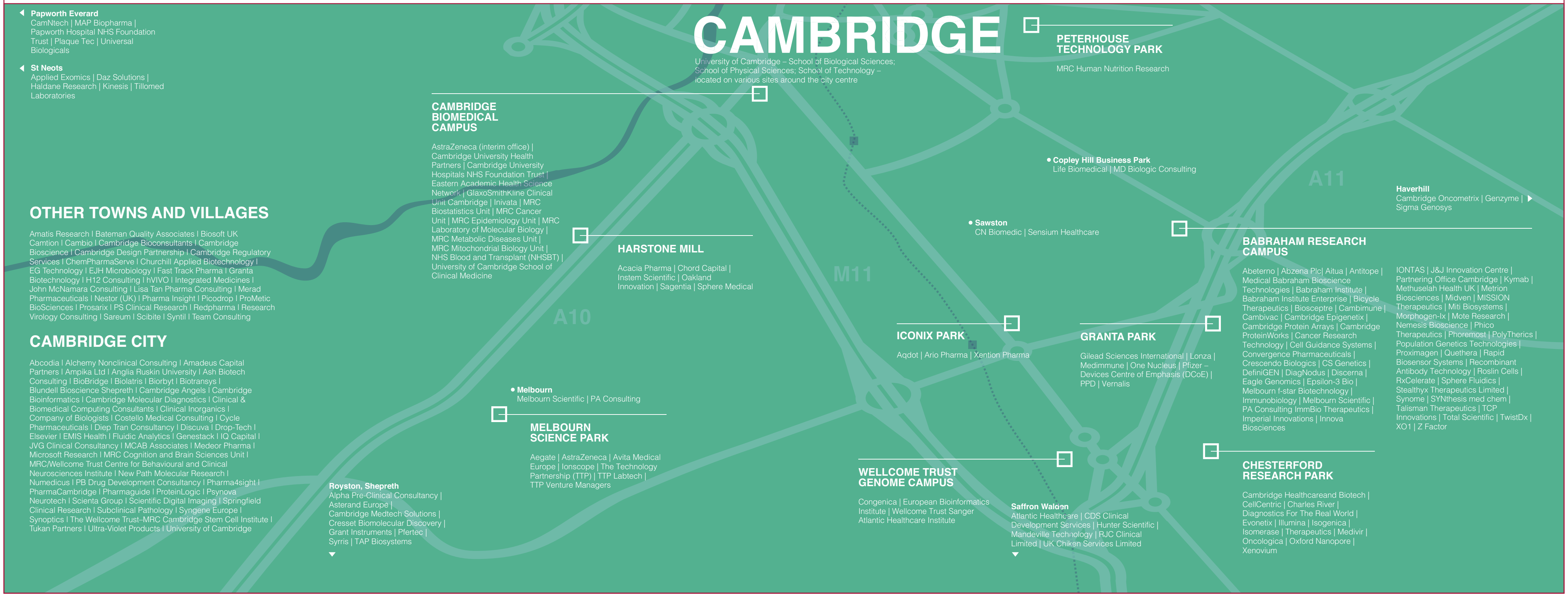
The Cambridge ecosystem

The new company was established on the Chesterford Science Park, south of Cambridge, where Solexa (now Illumina) are based. The scientific inventors of Solexa's technology, Prof Shankar Balasubramanian and David Klenerman, remain in the area, still working at the Chemistry Department of Cambridge University. Cambridge is also home to a world leading bio-informatics community, located at the European Bioinformatics Institute, on the Wellcome Trust Genome Campus, co-located with the Sanger Institute, all of who were the key players in the Human Genome Project, which completed in 2003.

New CEO

In May 2017, Dr Tim Brears joined the company as CEO with the task of raising a Series A round of external finance. The round closed in January 2018 having raised £9m. It was led by DCVC of Silicon Valley and European-based Draper Esprit, and included several further new investors. The funding will allow Evonetix to increase the engineering and research teams from 14 people to around 40 over the course of the year.



Map showing the south Cambridge BioCluster.

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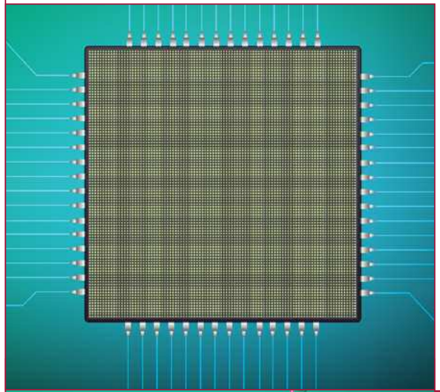
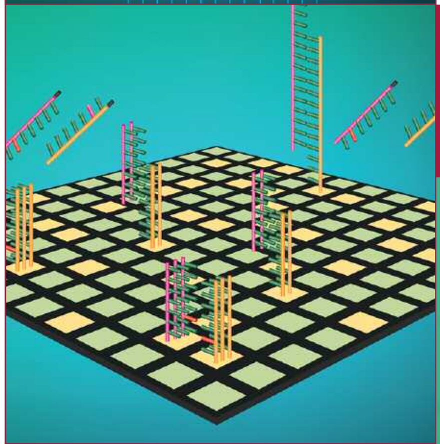
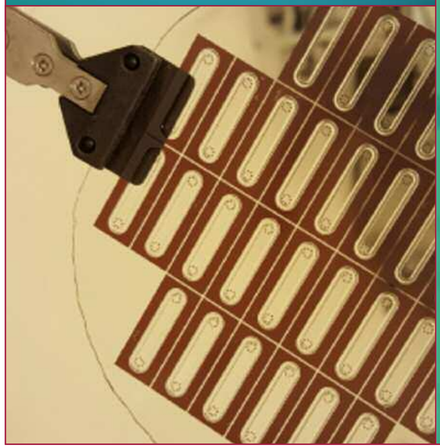






Challenge

The Evonetix technology addresses the challenge of how to make long lengths of DNA accurately and at speed. Whereas current approaches are able to manufacture DNA reasonably accurately at fairly short lengths, it becomes very problematic to maintain accuracy once lengths of 2kb (kilobases) or more are made. The promise of Evonetix's technology says Brears is that it should be possible to produce high-fidelity genes of 'any length' at significantly reduced cost and speed.

USP

The key to the technology is a combination of massive parallelism and high fidelity.

Key aspects include:

- Finely addressable silicon arrays, made using silicon microfabrication techniques, with 10,000 sites at which DNA can be synthesized
- Synergistic control chemistry enabling DNA to be made at each of the sites in a bespoke fashion
- On-chip assembly in conjunction with error detection allowing the generation of high-fidelity DNA
- No physical separation between sites allowing miniaturisation of the process

The solution will enable as a result:

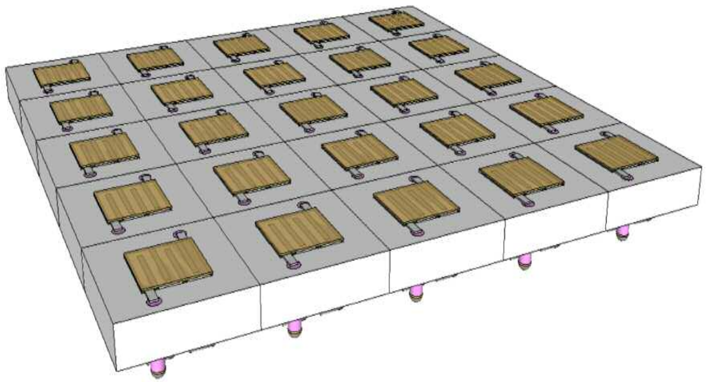
- Sequences of much greater length to be synthesized
- High-fidelity synthesis
- No sequence limitations (GC-rich sequences, repeats etc.)
- A highly scalable platform

Micro-array device

The 'architectural breakthrough', says Brears, is how the microchip-based arrays are configured and controlled. Each chip will carry 10,000 miniaturised reaction sites, each of which is independently controlled, thereby allowing massive parallelism in the DNA synthesis process, permitting many different DNA molecules to be synthesized simultaneously.

Development work

The silicon array is manufactured by semiconductor microfabrication techniques. The company has a prototype chip which it is currently integrating with fluidics to demonstrate the principles of the approach and provide an experimental platform for chemistry integration. Ongoing development work includes the electronics and corresponding software to allow the control of many sites in parallel.



An addressable silicon array capable of independent control of multiple reaction sites (or 'virtual wells').

- Miniaturised for massive parallelism
- Continuous flow for simple fluidics
- Permits good control of chemistry

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Synthesis platform

Evonetix's synthesis platform is compatible with conventional chemical and potentially future enzymatic DNA synthesis. With 'exquisite' control at each of 10,000 sites of synthesis, it will be possible to build any required DNA molecule at any of the sites.

Intellectual property

Brears describes the company's IP position as 'open territory' due to the novelty of the chip design and on-board chemistry. To date, seven patent applications have been filed covering various aspects of the approach.

Business model

Initially, Evonetix will supply high-fidelity genes synthesized in-house to a range of end customers working in fields such as industrial and agricultural biotechnology, pharmaceuticals and clean energy. In digital information storage it will engage with partners who wish to explore the long-term potential of using DNA as a storage medium. Later it will supply the gene synthesis instrumentation to customers and provide the chips and reagents as consumables.

Ambitious plans

During 2018 it plans to move to a larger facility in the Cambridge area in order to accommodate the growing headcount. Within two years, says Brears, it aims to complete a first demonstration of the synthesis unit for customer validation. Long-term, the goal is to have an Evonetix gene synthesizer on every lab bench in the world. ■

www.evonetix.com