

Racing through the DNA

Wageningen scientists are able to decipher genetic material in no time thanks to two new DNA sequencers. One of them operates 25 thousand times faster than the equipment of fifteen years ago.

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Today, I sequenced more DNA than I managed in the last six years put together', realized researcher Elio Schijlen after working with the Illumina HiSeq 2000 for the first time. This new sequencer is able to unravel an entire human genome in an afternoon. In the late nineteen nineties, this operation required several machines and took fifteen years, says Schijlen, an expert in next-generation sequencing at Plant Research International, part of Wageningen UR. 'I personally started deciphering DNA in 2004 and even that was the Stone Age compared to today.'

Things have changed now, thanks to two brand-new sequencers - worth 1.7 million euros between them - which Wageningen UR has purchased through CAT-AgroFood, an initiative of the Ministry of Economic Affairs, Agriculture and Innovation, the province of Gelderland and Wageningen UR. At present the sequencers are used mainly by Wageningen UR and the biotech firm KeyGene. Other firms are also able to make use of the facilities, which were presented to interested parties on 16 February.

SCRUTINIZED

At first glance a non-expert would think the Illumina HiSeq 2000 was an ultramodern photocopier. It is a plastic box with a screen showing a black surface and green flickering

specks. Those specks represent the four base pairs - A, T, C and G - that are the building blocks of DNA. DNA sequencers decipher the order in which these building blocks are put together. The fragments of DNA that are being scrutinized are on a microscopically small slide and they are invisible to the human eye. They are read by a tiny camera and a laser in hundreds of millions of simultaneous reactions.

A little further along is a more primitive machine, a precursor to the speedy new one. 'It's an ABI from the end of the 1990s, when it was state of the art', says Schijlen. 'We still use the ABI to verify small pieces of material.' The ABI is able to decipher nearly 1 million base pairs a day while the new Illumina can get through 25 billion base pairs in the same time. The model that came between those two is still there too: a sequencer from 2007, capable of processing 500 million base pairs a day.

FITTING JIGSAW PIECES

Schijlen is now using the speedy Illumina to unravel the genomes of 150 tomato varieties. 'That was simply not possible before; it would have taken years and have cost far too much.' The scientists are using the sequenced DNA to look for genetic variations that affect the taste or the resistance to disease and drought. This knowledge will speed up tomato breeding in

future and make it more effective.

However, the problem with tomatoes is that the hereditary material consists of many repeated bits of DNA. A genome can only be deciphered in pieces, after which computers try to put the unravelled pieces back together again. Schijlen: 'Sequencing is a lot like doing a jigsaw puzzle. It takes you longer to do a puzzle consisting of thousands of tiny, similar pieces than a puzzle with a hundred large, distinct pieces.'

The second new sequencer - the PacBio RS - is the ideal solution for the large jigsaw pieces. It uses an entirely new method to analyse DNA sequences. While the Illumina is only able to read DNA pieces with up to 100 base pairs, the PacBio can unravel fragments with several thousand base pairs. So it is doing larger pieces. On the other hand, the PacBio is only able to decipher 50 thousand fragments in a single analysis rather than hundreds of millions.

That is what makes the combination with the high-speed Illumina so powerful, says Schijlen. 'The best option is to have several different technologies available so that you can exploit the best aspects of each technology.'

The PacBio RS is still in the test phase. Schijlen will be trying it out with the known but still incomplete tomato genome. Then it will probably be possible to fit the jigsaw pieces that are still missing. ■



PHOTO BART DE GOUW

A researcher places a slide with DNA in the sequencer.

SCANNED BASE PAIRS PER DAY

1,000,000 in 1997

500,000,000 in 2007

25,000,000,000 in 2012

25,000 x faster
15 years on