Researchers show novel technique that can 'taste' DNA

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Scientists at The University of Nottingham have demonstrated for the first time that it is possible to selectively sequence fragments of DNA in real time, greatly reducing the time needed to analyse biological samples.

A paper published today in the academic journal *Nature Methods* describes a novel technique for highly selective DNA sequencing, called

'Read Until'. The method, used with real-time nanopore sequencing, enables the user to analyse only DNA strands that contain pre-determined signatures of interest.

Dr Matt Loose, of the Cell and Developmental Biology Research Group in the University's School of Life Sciences, has been working with the MinION, a new portable DNA sequencing technology produced by biotech company Oxford Nanopore Technologies. All sequencing was carried out at The University of Nottingham Next Generation Sequencing Facility, DeepSeq.

"This is the first time that direct selection of specific DNA molecules has been shown on any device," said Dr Loose. "We hope that it will enable many future novel applications, especially for portable sequencing. This makes sequencing as efficient as possible and will provide a viable, informatics based alternative to traditional wet lab enrichment techniques. The application of this approach to a wide number of problems from pathogen detection to sequencing targeted regions of the human genome is now within reach."

The pocket-sized MinION device - the same technology which NASA recently sent to the International Space Station in an effort to investigate whether DNA sequencing is possible in microgravity - employs tiny molecular pores in a membrane that 'sense' the sequence of DNA fragments passing through these nanopores, producing minute fluctuations in a current trace. These current traces, termed 'squiggles' then need to be converted to DNA bases using base caller software, often located in the cloud. The University of Nottingham team used signal processing techniques to map these squiggles to reference sequences, by passing this step.

In the paper, the Nottingham team go further, showing that this squiggle matching technique can be performed at a rate that enables decisions to

be made about the fragment of DNA that is being sequenced before it has completely passed through the nanopore. Depending on the sequence, individual nanopores within the MinION can then be instructed to continue sequencing or to eject the current DNA fragment and start sequencing another. The Nottingham team show that this 'real-time selective sequencing', or as some have called it 'DNA tasting', can reduce the time needed to sequence key DNA fragments or enable the analysis of pathogen samples where there is host and other DNA present in the sample.

The Read Until method/technique was developed by applying dynamic time warping to match short query current traces to references, demonstrating selection of specific regions of small genomes, individual amplicons from a group of targets, or normalisation of amplicons in a set.

More information: Real-time selective sequencing using nanopore technology, *Nature Methods*, DOI: 10.1038/nmeth.3930

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