Nature Reviews Genetics | Published online 16 Aug 2016

IN BRIEF

DNA SEQUENCING

Real-time prioritization of sequencing output

One limitation of DNA sequencing platforms is that a proportion of sequencing capacity is often 'wasted' on uninformative sequence reads. Loose *et al.* developed 'Read Until' software for use with the Oxford Nanopore Technologies MinION DNA sequencer. In nanopore sequencing, a DNA strand translocates through a protein pore as electrical current is passed through, and the resulting shifts in the current (known as squiggles) are decoded into DNA sequence. The Read Until software analyses, in real time, the squiggle data generated from each pore in the machine, comparing them with simulated squiggle data of the known species of DNA being sequenced. Based on whether the first 250 squiggle events represent predetermined regions of interest, the pores can be individually controlled to continue sequencing or to have their current switched to reject that DNA molecule ready for a different one. For phage λ DNA, Read Until allowed selective sequencing of chosen regions, and it normalized sequencing coverage by rejecting regions that became over-represented during sequencing.

ORIGINAL ARTICLE Loose, M., Malla, S. & Stout, M. Real-time selective sequencing using nanopore technology. *Nat. Methods* http://dx.doi.org/10.1038/nmeth.3930 (2016)

GENETIC INTERACTIONS

Leveraging context-dependent essentiality

To identify genes for which essentiality is dependent on the genetic background, Chen *et al.* used a library of 80 *Saccharomyces cerevisiae* strains, each of which represses an essential gene following doxycycline treatment. After exposing 60 million cells of each strain to doxycycline, they used genome sequencing on the rare surviving cells to identify naturally occurring mutations that rescued the lethality of the repressed essential gene. Overall, 17 gene pairs were identified across 5 conditionally essential genes. The lethal effects of the loss of *ADE13* — which encodes adenylosuccinate lyase (ADSL), mutations of which cause the human metabolic disorder ADSL deficiency — could be rescued by mutations in five different genes. In *Caenorhabditis elegans*, knockdown of one of these genes (phosphoribosylaminoimidazole carboxylase) substantially reduced the pathological effects of ADSL knockdown. Such strategies might enable human therapeutics, by targeting the genetic interactions contributing to pathology rather than attempting functional replacement of a primary genetic defect.

ORIGINAL ARTICLE Chen, P. *et al.* The non-essentiality of essential genes in yeast provides therapeutic insights into a human disease. *Genome Res.* http://dx.doi.org/10.1101/gr.205955.116 (2016)

TECHNOLOGY

Enabling accurate single-cell genome amplification

Multiple displacement amplification (MDA) is a method for whole-genome amplification, but a challenge is to amplify genomes evenly and accurately from single cells. Two new studies report accessible alternatives to current specialized microfluidics instrumentation. Leung *et al.* used a commercially available piezoelectric dispenser to process single cells in liquid droplets on a solid surface and showed robust MDA across >100 single human cells. In an alternative method, Xu *et al.* used a polyethylene glycol hydrogel to compartmentalize single-cell reactions and demonstrated high-fidelity MDA for cultured bacterial cells and human microbiome samples.

ORIGINAL ARTICLES Leung, K. *et al.* Robust high-performance nanoliter-volume single-cell multiple displacement amplification on planar substrates. *Proc. Natl Acad. Sci. USA* **113**, 8484–8489 (2016) | Xu, L. *et al.* Virtual microfluidics for digital quantification and single-cell sequencing. *Nat. Methods* http://dx.doi.org/10.1038/nmeth.3955 (2016)