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Cite this: *Lab Chip*, 2017, **17**, 2539

Perspective on droplet-based single-cell sequencing

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DOI: 10.1039/c7lc90069d

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Published on 19 July 2017. Downloaded on 11/9/2020 6:50:24 PM.

Sequence information provides one of the key windows into the type, state and nature of a cell. However, all cells are not alike, and it has become increasingly recognized that the differences between cells can provide much greater information and deeper insight into their behavior. These differences can arise from the heterogeneity of cells or from the differences in cell state. However, to truly elucidate these differences, it is essential to probe the properties of individual cells and to compare these properties among a large number of cells.

This has become feasible with the advent of single-cell sequencing. Today, this is primarily performed using the mRNA of the cells, providing a proxy for the gene expression level of the cells. Performing RNA-seq at the single-cell level demands that the cells be compartmentalized in a volume that is of comparable size to that of the cell itself. This is most conveniently accomplished using some type of microfluidic device. Early devices using valves to define and control the volume established the general feasibility of single-cell sequencing and commercial devices facilitated numerous published studies that established the value of information at the level of a single cell. However, a demand remained for a simpler method that could extend the sequencing to far greater numbers of cells while still providing single-cell resolution.

One route to meet this demand is to use droplet microfluidics. Individual cells can be encapsulated in the drops and genomic barcodes, unique to each drop, can be linked to the mRNA. These barcodes provide an identifier that is read during the sequencing and allows the sequence information to be decoded to the individual cell from which it came. These techniques provide a low cost means of sequencing thousands of cells simultaneously with single-cell resolution. The use of droplet microfluidics for single-cell RNA-seq was introduced in two recent papers (DOI: 10.1016/j.cell.2015.04.044, DOI: 10.1016/j.cell.2015.05.002) that established the basic concepts. This was rapidly followed by several commercial implementations of these, or similar droplet-microfluidics-based methods that have brought this technology to a large number of users.

The field is now advancing very rapidly. Large numbers of studies are underway to collect and explore the new information that is now accessible with single-cell RNA-seq. Improvements to the microfluidics are also advancing rapidly. And, extensions to other sequencing methods are also being developed, extending the investigations to probe information beyond mRNA alone. This has rapidly become a burgeoning field, where microfluidic techniques are essential and where droplet-based microfluidics has enabled a major advance.

In this thematic collection, *Lab on a Chip* aims to highlight the new advances in this growing field with an emphasis on the interface between the technological advancements and high impact applications of droplet-based single-cell sequencing.

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