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Editorial

Digital PCR, a technique for the future

We are very pleased to be able to bring you this special issue of Biomolecular Detection and Quantification which focuses on digital PCR (dPCR). The underpinning method of dPCR, which was coined in 1999 [1], actually predates qPCR [2] and is a powerful technique that could offer improved sensitivity, precision and reproducibility [3]. Now is an exciting time for this method and there are numerous examples of where the improved reproducibility can be applied clinically and where the superior sensitivity and precision could enable measurements to be performed that are simply not possible using PCR or, in many cases, sequencing.

In this special issue we have selected seven manuscripts that discuss and present dPCR in a variety of subjects. Dhillon et al. present a new application of dPCR in the form of a proximity ligation assay (PLA) opening the possibility of using limiting dilution to improve the detection and quantification of proteins which, in this case focussed on *Clostridium difficile* toxins, are important markers for disease. Matthew Butchbach presents a review on the application of dPCR as a robust method to identify genes associated with paediatric-onset disorders. This review also highlights how dPCR can offer a powerful technology to track changes in genomic biomarkers with disease progression. He also argues that dPCR has the potential to become the tool of choice for the verification of mutations identified by next generation sequencing, copy number determination and also for non-invasive prenatal screening.

The next four manuscripts deal with the application and analysis dPCR. Whale et al. discuss multiplexing by dPCR and describe the different approaches that can be applied highlighting the unique approaches on offer by dPCR. They also report and name a characteristic of dPCR, namely partition specific competition (PSC), that must be considered when applying thresholds to multiplex assays that use the same primers but different probes, as is common when measuring single nucleotide variants or polymorphisms. Debski and Garstecki describe how to design dPCR experiments to ensure desired precision is achieved when dealing with patient samples. This is an important and frequently neglected consideration when discussing the performance of any molecular method. Jones and colleagues present a short report that investigates the dynamic range of dPCR, which is often reported as being at a disadvantage when compared with qPCR. In this study they demonstrate that if you have enough partitions it is possible to perform dPCR with a dynamic range of up to six orders of magnitude, which is approaching that of qPCR. Finally the manuscript by Madic et al. describes application of the first three colour dPCR instrument for multiplex analysis of three mutations of the *EGFR* gene. This droplet-based platform applies a unique sample partition format by employing a "2D droplet array" that can be directly imaged following the PCR reaction.

The last article deals with accuracy, reliability and reproducibility in the context of nucleic acid quantification and highlights how dPCR could be used to quantify reference materials. Bhat and Emslie also discuss how the use of reference materials and certified reference materials, already established when measuring many biochemical analytes, could support the traceable analysis of molecular targets such as BCR-ABL1 [4]. While dPCR is already being used to quantify such materials, they highlight the fact that further work is required to better understand sources of bias and uncertainty.

We hope you enjoy these articles which illustrate the potential of this fairly new and unique molecular method. We are of the opinion that dPCR offers considerable potential as a method that will advance clinical research and routine diagnosis and could become the method of choice in areas such as precision and personalised healthcare. This special issue will add to the increasing body of literature reporting on the use of digital PCR in every day laboratory practises and offer solutions to some of remaining challenges and pitfalls that could be encountered.

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