METHODS AND SYSTEMS FOR A DIGITAL PCR EXPERIMENT DESIGNER

BACKGROUND

[0001] Digital PCR (dPCR) is an analytical technique that used to provide absolute quantitation of nucleic acid samples, to detect and quantify the concentration of rare targets, and to measure low fold-changes in nucleic acid concentration.

[0002] In dPCR, a solution containing a relatively small number of a target polynucleotide or nucleotide sequence may be subdivided into a large number of small test samples, such that each sample generally contains either one or more molecule of the target nucleotide sequence or none of the target nucleotide sequence. When the samples are subsequently thermally cycled in a PCR protocol, procedure, or experiment, the samples containing the target nucleotide sequence are amplified and produce a positive detection signal, while the samples containing no target nucleotide sequence are not amplified and produce no detection signal.

[0003] Potentially, a dPCR system may have a very high precision enabling accurate measurement for genetic quantification. The challenge with an unknown sample is to perform the experiment at a dilution that falls within the dynamic range supported by the system.

[0004] Generally, increasing the number of replicates increases the accuracy and reproducibility of dPCR results. The dynamic range depends on the total number of available reaction vessels and on the measurement precision necessary for your application.

SUMMARY

[0005] In one ~~exemplary embodiment~~aspect, a computer-implemented method for designing a digital PCR (dPCR) experiment is provided. The method includes receiving, from a user, a selection of optimization type. ~~The optimization type may be maximizing the dynamic range, minimizing the number of substrates including reaction sites needed for the experiment, determining a dilution factor, or determining the lower limit of detection, for example.~~ The method further includes receiving, from the user, a precision measure for an experiment, and a minimum concentration of a target in a reaction site for the experiment. The method also includes

determining a set of dPCR experiment design factors for the experiment based on the optimization type. The set of dPCR experiment design factors is then displayed to the user.

[0005a] According to another aspect, there is provided a non-transitory computer-readable storage medium encoded with instructions, executable by a processor, the instructions comprising instructions for:

receiving, from a user, a selection of optimization type;

receiving, from the user, a precision measure for an experiment;

receiving, from the user, a minimum concentration of a target in a reaction site for the experiment;

determining a set of dPCR experiment design factors for the experiment based on the optimization type; and

displaying the set of dPCR experiment design factors to the user.

[0005b] According to another aspect, there is provided a system for designing a digital PCR system, the system comprising:

a processor; and

a memory encoded with instructions executable by the processor, the instructions comprising instructions for:

receiving, from a user, a selection of optimization type;

receiving, from the user, a precision measure for an experiment;

receiving, from the user, a minimum concentration of a target in a reaction site for the experiment;

determining a set of dPCR experiment design factors for the experiment based on the optimization type; and

displaying the set of dPCR experiment design factors to the user.

[0005c] According to another aspect, there is provided a method for designing a digital PCR (dPCR) experiment, the method comprising:

receiving, from a user, a selection of concentration data type;

receiving, from the user, genome information for an experiment;

receiving, from the user, a lower limit of detection measure for the experiment;

receiving, from the user, a desired fold change for the experiment;

determining a set of dPCR experiment design factors for the experiment based on the concentration data type; and

displaying the set of dPCR experiment design factors to the user.

DESCRIPTION OF THE FIGURES

[0006] FIGs. 1A and FIG. 1B illustrate graphs showing the relationship of dynamic range, measurement precision, and the lower and upper limits of detection according to various embodiments of the present teachings.

[0007] FIG. 2 illustrates a plot showing the relationship of the lower limit of detection (LLOD) and the upper limit of detection (ULOD) to the number of substrates including reaction sites according to various embodiments described herein.

[0008] FIG. 3 illustrates a plot showing the optimal concentration ranges for dPCR experiments according to various embodiments described herein.

[0009] FIG. 4 illustrates a plot showing how precision improves with a larger number of reactions according to various embodiments described herein.

[0010] FIG. 5 illustrates the effect of total interrogated volume on the lowest limit of detection according to various embodiments described herein.

[0011] FIG. 6 illustrates the relationship of precision with false calls according to various embodiments described herein.

[0012] FIG. 7 illustrates contours showing the desired load for optimal precision under the influence of nonzero false positives and false negatives according to various embodiments described herein.

[0013] FIG. 8 illustrates contours showing the lower limit of detection under the influence of false positive and false negative calls according to various embodiments described herein.

[0014] FIG. 9 illustrates contours showing the desired load concentrations to compensate for positive/negative reaction loss according to various embodiments described herein.