METHODS AND SYSTEMS FOR DETERMINING OPTICAL REGIONS OF INTEREST

BACKGROUND

[001] Installation and calibration of laboratory instrumentation can be a time consuming and expensive process. In many cases, engineers from the instrument supplier must be on site to perform these processes. This cost is generally passed on to the user. In some cases, experienced users can successfully calibrate properly manufactured instruments using multi-step procedures. During such calibrations, physical standards and well plates may be used in combination with manual procedures. Manual calibration processing and data inspection is error prone and may rely on ad hoc or subjective measures. While a final system verification step may provide resilience against accepting suboptimal calibrations, automation offers improved objectivity and uniformity during such activities. The present teachings can incorporate expert knowledge into an automated calibration and verification system providing pass/fail status and troubleshooting feedback when a failure is identified. If an instrument should fail the calibration process, then a service engineer can be called. The present teachings can minimize the cost of, and time required for, the installation and calibration procedures.

BRIEF DESCRIPTION OF FIGURES

[002] Fig, 1 illustrates a computer system on which embodiments of the present teachings can be implemented.

[003] Fig. 2 illustrates a laboratory instrument upon which embodiments of the present teachings can be implemented.

[004] Fig. 3 illustrates a sequence of steps used in the calibration of qPCR instruments.

[005] Fig. 4 illustrates the regions-of-interest for a 96 well sample container.

[006] Fig. 5 illustrates the regions-of-interest for a rotated 96 well sample container.

[007] Fig. 6 illustrates a sample array with incorrectly located regions-of-interest.

[008] Fig. 7 illustrates a sample array with correctly located regions-of-interest.

[009] Fig. 8 illustrates a closer view of a sample array with correctly located regions-of-interest.

SUMMARY OF THE INVENTION

[009a] An aspect of the present invention provides a method for the calibration of a laboratory instrument comprising: providing an optical system comprising a light source capable of imaging fluorescence emission from a plurality of biological samples upon excitation by the light source, where each biological sample is contained in one of a plurality of sample wells on a sample well

plate; estimating at least one initial region of interest (ROI) by using the optical system to detect fluorescence emissions at the plurality of sample wells in relation to one or more fluorescence thresholds from each sample well; estimating one or more center locations of each ROI; estimating a size of each ROI; determining an average size of the ROIs from the plurality of sample wells; deriving one or more global gridding models, wherein the global gridding models analyze the estimated center locations of each ROI; applying the global gridding models to improve the precision of the ROI center locations by relating the estimated center locations to one or more location coordinates of a layout of the sample well plate; recovering missing ROIs with one or more mapping functions of the global gridding models; and adjusting the sizes of the ROIs, wherein the adjustment improves the signal-to-noise ratio of the optical system.

[009b] Another aspect of the present invention provides a system for calibrating region of interest (ROI) locations for one or more biological samples in a laboratory instrument, the system comprising: an optical detection system comprising: a plurality of filters; at least one excitation source; at least one detector configured to collect one or more images of fluorescence emissions from the one or more biological samples upon excitation by the at least one excitation source; and a microwell tray comprising a plurality of sample wells where each biological sample is contained in a sample well; and a computer system comprising: at least one processor configured to: set estimates of one or more ROI center locations based on the one or more images of fluorescence emissions from the one or more biological samples, and one or more input parameters received from a user; estimate a size of each ROI; determine an average size of the ROI from a plurality of sample wells; analyze the estimated ROI center locations to find adjacent ROIs; improve the precision of the ROI center locations by applying one or more mapping functions to relate the estimated center locations to one or more location coordinates of a layout of the microwell tray; recover missing ROIs with the one or more mapping functions; and adjust the sizes of the ROIs, wherein the adjustment improves the signal-to-noise ratio of the optical detection system; at least one computer-readable medium; at least one input device coupled to the at least one processor and configured to receive the one or more input parameters from the user; and at least one display.

[0010] The present teachings relate to a method and system for determining a Region of Interest (ROI) for one or more biological samples in a laboratory instrument. In an embodiment, the method comprises an optical system capable of imaging florescence emission from a plurality of sample wells. An initial ROI, its center location and size can be estimated from the fluorescence detected from each well. From this information the average size of the ROIs can be determined and global gridding models can be

CLAIMS

1. A method for the calibration of a laboratory instrument comprising:

providing an optical system comprising a light source capable of imaging fluorescence emission from a plurality of biological samples upon excitation by the light source, where each biological sample is contained in one of a plurality of sample wells on a sample well plate;

estimating at least one initial region of interest (ROI) by using the optical system to detect fluorescence emissions at the plurality of sample wells in relation to one or more fluorescence thresholds from each sample well;

estimating one or more center locations of each ROI;

estimating a size of each ROI;

determining an average size of the ROIs from the plurality of sample wells;

deriving one or more global gridding models, wherein the global gridding models analyze the estimated center locations of each ROI;

applying the global gridding models to improve the precision of the ROI center locations by relating the estimated center locations to one or more location coordinates of a layout of the sample well plate;

recovering missing ROIs with one or more mapping functions of the global gridding models; and

adjusting the sizes of the ROIs, wherein the adjustment improves the signal-to-noise ratio of the optical system.

2. The method of claim 1, wherein each biological sample comprises one or more spectrally distinguishable dyes.

3. The method of claim 2, wherein the one or more spectrally distinguishable dyes comprises at least one of FAM, SYBR Green, VIC, JOE, TAMRA, NED, CY-3, Texas Red, CY-5, Mustang Purple, or ROX.

4. The method of claim 1 wherein the biological sample fluoresces at a predetermined wavelength in response to the excitation.

5. The method of claim 1 wherein the laboratory instrument is configured to analyze the one or more biological samples through the polymerase chain reaction (PCR) process.

6. The method of claim 1 wherein the light source comprises a laser, light emitting diode (LED), or broad spectrum light source.

7. The method of claim 1 wherein the global gridding models comprise comparing the center-to-center distance between ROIs to grid co-ordinates of a well plate layout to determine an X and Y grid co-ordinate for each ROI.

8. The method of claim 7 further comprising determining and applying mapping functions to map each grid co-ordinate to an ROI center.

9. A system for calibrating region of interest (ROI) locations for one or more biological samples in a laboratory instrument, the system comprising:

an optical detection system comprising:

a plurality of filters;

at least one excitation source;

at least one detector configured to collect one or more images of fluorescence emissions from the one or more biological samples upon excitation by the at least one excitation source; and

a microwell tray comprising a plurality of sample wells where each biological sample is contained in a sample well; and

a computer system comprising:

at least one processor configured to: set estimates of one or more ROI center locations based on the one or more images of fluorescence emissions from the one or more biological samples, and one or more input parameters received from a user; estimate a size of each ROI; determine an average size of the ROI from a plurality of sample wells; analyze the estimated ROI center locations to find adjacent ROIs; improve the precision of the ROI center locations by applying one or more mapping functions to relate the estimated center locations to one or more location coordinates of a layout of the microwell tray; recover missing ROIs with the one or more mapping functions; and adjust the sizes of the ROIs, wherein the adjustment improves the signal-to-noise ratio of the optical detection system;

at least one computer-readable medium;

at least one input device coupled to the at least one processor and configured to receive the one or more input parameters from the user; and

at least one display.

10. The system of claim 9 wherein the at least one computer-readable medium is coupled to the processor.

11. The system of claim 10 wherein the computer-readable medium comprises instructions executable by the processor.

12. The system of claim 11 wherein the instructions executed by the processor comprise at least one step for determining ROIs and automating the calibration of the ROI locations.

13. The system of claim 9 wherein the plurality of filters comprises at least one excitation filter, at least one emission filter and at least one beam splitter.

14. The system of claim 9 wherein the at least one biological sample comprises at least one fluorescent dye.

15. The system of claim 9 further comprising a graphical user interface (GUI) configured to enable a user to select the one or more input parameters.

16. The system of claim 9 wherein the one or more input parameters include one or more of: threshold range and step, well size, well center-to-center distance, spacing between sub-arrays, optical pixels per millimeter and plate layout.

17. The system of claim 9 wherein the at least one input device comprises alphanumeric and other keys configured to communicate information to the processor.

18. The system of claim 17 wherein the at least one input device further comprises cursor control to communicate direction information to the processor.

19. The system of claim 9 wherein the plurality of sample wells are arranged in a grid pattern comprising one or more plate layout parameters.

20. The system of claim 19 wherein the one or more plate layout parameters comprise a number of wells, a number of columns, and a number of rows, wherein each well comprises a set of XY coordinates.