Systems and Methods for Assessing of Biological Samples

Background of the Invention

Field of the Invention

The present invention relates generally to devices, systems, and methods for assessing biological samples, and more specifically to devices, systems, and methods for simultaneously assessing a plurality of biological samples.

Description of the Related Art

Optical systems for biological and biochemical reactions have been used to monitor, measure, and/or analyze such reactions. Such systems are commonly used in sequencing, genotyping, polymerase chain reactions (PCR), and other biochemical reactions to monitor progress and provide quantitative data. For example, an optical excitation beam may be used during real-time PCR (qPCR) processes to illuminate fluorescent DNA-binding dyes or fluorescent probes to produce fluorescent signals indicative of the amount of a target gene or other nucleotide sequence. Increasing demands to provide greater numbers of reactions per test or experiment have resulted in instruments that are able to conduct large numbers of reactions simultaneously.

The increase in the number sample sites in a single test or experiment has led to microtiter plates and other sample formats that provide ever smaller sample volumes. In addition, techniques such as digital PCR (dPCR) have increased the demand for smaller sample volumes that contain either zero or one target nucleotide sequence in a majority of a large number of test samples. There is a need for systems and sample format that will provide reliable data in even high-density sample format with sample sites having volumes on the order of nanoliters or picoliters.

Summary of the Invention

According to an aspect of the present invention, there is provided a system for determining the number of target nucleotide molecules in a sample, the system comprising:

a sample holder configured to receive an article comprising at least 20,000 separate reaction sites, the reaction sites having a non-circular cross-section;

an excitation optical system comprising a light source configured to simultaneously illuminate the at least 20,000 separate reaction sites;

an optical sensor comprising a predetermined number of pixels, the predetermined number of pixels being at least 20 times the number of reaction sites;

an emission optical system comprises a system working distance from the sample holder, wherein the system working distance is less than or equal to 60 millimeters; and

a beamsplitter configured to reflect excitation light from the excitation optical system to the sample and to transmit emission light from the sample to the optical sensor.

~~According to another aspect of the present invention, t~~There is ~~provided~~ also disclosed a system for determining the number of target nucleotide molecules in a sample, comprising:

a sample holder configured to receive an article comprising a plurality of separate reaction sites;

an image recording system comprising an optical sensor; and

a housing comprising:

an excitation optical system comprising a light source configured to simultaneously illuminate the separate reaction sites;

an emission optical system configured to transfer radiation from the article to the image recording system; and

a beamsplitter configured to reflect excitation light from the excitation optical system to the sample and to transmit emission light from the sample to the optical sensor;

wherein the image recording system is detachably mounted to the housing.

According to another aspect of the present invention, there is provided a method of measuring an amount of a target nucleotide in one or more samples, the method comprising:

providing a system comprising:

a sample holder configured to receive an article comprising at least 20,000 separate reaction sites, the reaction sites having a non-circular cross-section;

an excitation optical system comprising a light source configured to simultaneously illuminate the at least 20,000 separate reaction sites;

WHAT IS CLAIMED IS:

1. A system for determining the number of target nucleotide molecules in a sample, the system comprising:

a sample holder configured to receive an article comprising at least 20,000 separate reaction sites, the reaction sites having a non-circular cross-section;

an excitation optical system comprising a light source configured to simultaneously illuminate the at least 20,000 separate reaction sites;

an optical sensor comprising a predetermined number of pixels, the predetermined number of pixels being at least 20 times the number of reaction sites;

an emission optical system comprises a system working distance from the sample holder, wherein the system working distance is less than or equal to 60 millimeters; and

a beamsplitter configured to reflect excitation light from the excitation optical system to the sample and to transmit emission light from the sample to the optical sensor.

2. The system of claim 1, further comprising a computer including a processor and an electronic memory in communication with the processor, wherein:

the computer receives images from the optical sensor of the at least 20,000 separate reaction sites;

the memory comprises instructions for performing a digital PCR calculation; and

the computer is configured to calculate, based on the instructions and received images, a number of target nucleotide particles contained in at least some of the at least 20,000 separate reaction sites.

3. The system of claim 1, further comprising:

a housing containing excitation optical system and the emission optical system; and

an image recording system comprising the optical sensor;

wherein the image recording system is detachably mounted to the housing.

4. The system of claim 3, wherein the image recording system is a camera phone or a smartphone

~~5. The system of claim 3, wherein the image recording system is an iPhone.~~

6.5. The system of claim 3, wherein the image recording system comprises a processor configured to acquire images from the optical sensor and to process the images to provide biochemical information of the sample.

~~7. A system for determining the number of target nucleotide molecules in a sample, comprising:~~

~~a sample holder configured to receive an article comprising a plurality of separate reaction sites;~~

~~an image recording system comprising an optical sensor; and~~

~~a housing comprising:~~

~~an excitation optical system comprising a light source configured to simultaneously illuminate the separate reaction sites;~~

~~an emission optical system configured to transfer radiation from the article to the image recording system; and~~

~~a beamsplitter configured to reflect excitation light from the excitation optical system to the sample and to transmit emission light from the sample to the optical sensor;~~

~~wherein the image recording system is detachably mounted to the housing.~~

~~8. The system of claim 7, wherein the image recording system is a camera phone or a smartphone.~~

~~9. The system of claim 7, wherein the image recording system is an iPhone.~~

~~10. The system of claim 7, wherein image recording system comprises a processor configured to acquire images from the optical sensor and to process the images to provide biochemical information of the sample.~~

~~11.~~6. A method of measuring an amount of a target nucleotide in one or more samples, the method comprising:

providing a system comprising:

a sample holder configured to receive an article comprising at least 20,000 separate reaction sites, the reaction sites having a non-circular cross-section;

an excitation optical system comprising a light source configured to simultaneously illuminate the at least 20,000 separate reaction sites;

an optical sensor comprising a predetermined number of pixels, the predetermined number of pixels being at least 20 times the number of reaction sites;

an emission optical system comprises a system working distance from the sample holder, wherein the system working distance is less than or equal to 60 millimeters; and

a beamsplitter configured to reflect excitation light from the excitation optical system to the sample and to transmit emission light from the sample to the optical sensor;

providing the article;

performing an amplification assay on at least some of the at least 20,000 reaction sites;

placing the article in the sample holder;

illuminating the article using the excitation optical system;

measuring emission radiation from at least some of the at least 20,000 separate reaction sites; and

determining an amount of the target nucleotide.

~~12.~~7. The method of claim ~~11~~6, further comprising:

dividing at least a portion of a sample solution containing the target nucleotide between at least some of the at least 20,000 reaction sites;

determining an amount of the target nucleotide in the solution by measuring emission radiation from at least some of the at least 20,000 reaction sites.

~~13.~~8. The method of claim ~~12~~7, further comprising

dividing at least a portion of a sample solution containing the target nucleotide between the reaction sites of a plurality of articles, each article comprising the at least 20,000 reaction sites;

determining an amount of the target nucleotide in the solution by measuring emission radiation from at least some of reaction sites of each of the plurality of articles.

~~14.~~9. The method of claim ~~12~~7, further comprising

dividing at least a portion of a sample solution containing the target nucleotide between the reaction sites of a plurality of articles, each article comprising the at least 20,000 reaction sites;

sequentially placing each article of the plurality of articles in the sample holder and measuring emission radiation from at least some of the at least 20,000 separate reaction sites of each article;

determining an amount of the target nucleotide in the solution based on measured emission radiation all of the plurality of articles.