

## **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;

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; and

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.

According to another aspect of the present invention, there is provided 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 the 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;

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;

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; and

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;  
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.

#### Brief Description of the Drawings

Embodiments of the present invention may be better understood from the following detailed description when read in conjunction with the accompanying drawings. Such embodiments, which are for illustrative purposes only, depict novel and non-obvious aspects of the invention. The drawings include the following figures: