SYSTEM AND METHOD FOR HIGH THROUGHPUT PROCESSING OF DROPLETS

PRIORITY

[0001] This application is a continuation-in-part of U.S. application Ser. No. 09/081,700, entitled "Apparatus and Method for Droplet Microchemistry", having a filing date of Nov. 20, 2000, which is a continued prosecution of U.S. application Ser. No. 09/081,700, entitled "Apparatus and Method for Droplet Microchemistry" having a filing date of May 20, 1998, which claims priority from U.S. provisional application No. 60/057,734, filed Aug. 28, 1997, each of which is herein incorporated by reference.

TECHNICAL FIELD

[0002] The present invention pertains to a system and method for dispensing, transporting, tracking, and analyzing a massive number of droplets of liquid, where the analyzing may include mass spectrometry and optical interrogation, such as fluorescence spectrometry, Raman spectroscopy, and UV absorption, and for performing microchemical operations on these droplets, the operations including mixing, dilution, concentration, heating, cooling, and filtering.

BACKGROUND OF THE INVENTION

[0003] Chemistry on the micro-scale, involving the reaction and subsequent analysis of quantities of reagents or analytes of order microliters or smaller, is an increasingly important aspect of the development of new substances in the pharmaceutical and other industries (e.g., synthesis and analysis of new conductive polymers, phosphors, superconductors, etc.). Such reaction and analysis must accommodate vast libraries of compounds to be reacted and analyzed under various conditions.

[0004] Significant problems associated with current technologies dealing with chemical analysis of vast numbers of compounds (potentially on the order of hundreds of thousands or millions per day) include the problem of tracking and identifying each droplet as it moves through a high throughput processing system. Furthermore, the surface upon which the droplets are dispensed is typically unsuitable or not optimized for high throughput processing of droplets. These surface properties, include, but are not limited, to cleanliness, biocompatibility, surface energy, binding affinity, porosity, chemical interaction, chemical addition, sample information encoding, and tracking. Additionally, the processing of the droplets may necessitate transporting droplets through a controlled environment for large periods of time.

SUMMARY OF INVENTION

[0005] In accordance with one embodiment of the invention, a method and system are provided for high throughput processing of a plurality of droplets. The method includes dispensing the plurality of droplets onto a substantially unperforated surface. The surface is moved through a delay line such that each droplet hangs from the surface for at least a period of time, the droplet adhering to the surface by virtue, at least in part, of surface attraction.

[0006] In further related embodiments, the step of dispensing each droplet includes limiting each droplet to a specified volume smaller than one microliter. Each droplet may be dispensed onto the surface while the surface is moving. Motion of the surface may be delayed through a delay line. Delaying the motion may include moving the surface via a pulley system, or moving the surface around a drum. Delaying the motion may include hanging each droplet beneath the surface, exposing each droplet to a controlled environment, and analyzing a characteristic of each droplet.

[0007] In accordance with another embodiment of the invention, a method and system for high throughput processing of a plurality of droplets includes dispensing each droplet onto a moving surface and tracking each droplet's position. The moving surface may move continuously or in a discontinuous start/stop action. One or more microtiter plates may be provided to a microtiter plate handling system. Data is provided that identifies each microtiter plate's position to the microtiter plate handling system. The microtiter plate handling system is then commanded to retrieve a particular microtiter plate, the particular plate presented by the microtiter plate handling system for dispensing. Each droplet's position may be measured and recorded on the moving surface using a position sensor, such that each droplet is associated with a fiducial position on the moving surface. The position sensor may be a rotary encoder. Each droplet's position on the moving surface may be measured and recorded at substantially the same time each droplet is dispensed onto the moving surface. Each droplet's position may be saved in random-access memory. Each droplet may be detected using a drop sensor, the drop sensor at a known position relative to the position sensor. The known position is then verified with each droplet's position based on the fiducial position and position information obtained from the position sensor at each droplet's time of detection. The drop sensor may be located at an interface to an analyzer, substrate station, or a reactant station. A failure may be recorded if the known position does not correspond to each droplet's position based on the fiducial position and position information obtained from the position sensor at time of detection. A particular droplet may be dispensed onto the moving surface with known analytical properties. The particular droplet's position and identity can then be verified by analyzing the particular droplet at a known position relative to the fiducial position so as to obtain analyzed properties; comparing the particular droplet's analyzed properties with the particular droplet's known analytical properties; and comparing the known position against the particular droplet's position as derived from the position sensor.

[0008] In additional related embodiments, each droplet may be subjected to a controlled environment, which may include hanging the droplet from the moving surface for at least a specified minimum period of time, the droplet adhering to the moving surface through, at least in part, surface attraction. Each droplet may be transported, via the moving surface, through an environmentally controlled delay line.

[0009] In other related embodiments, at least one operation may be performed on each droplet from the group of operations consisting of mixing, diluting, concentrating, filtering, and analyzing. Analyzing may include performing at least one operation from the group of operations consisting of optical interrogation and mass spectrometry. Optical interrogation may include at least one of fluorescence spectrometry, Raman spectroscopy and UV absorption. Analyzing the content of each droplet may include aspirating each droplet into a dispensing unit and presenting each droplet for