

loaded in parallel by dipping the array into a bulk solution. Additionally, reactions can be initiated in parallel by stacking two co-registered through-hole arrays one on top of the other. However, the loading and removal of fluids from different through holes in the array is fundamentally a serial process, and the time required to accelerate and de-accelerate a through hole array relative to a dispensing or aspirating tube requires an undue amount of time. Accordingly, moving surface **1** may advantageously take the form of a two-dimensional array when wound, and a one-dimensional array when unwound. Fluids can then be dispensed or removed from the one-dimensional array in a time-sequential (serial) manner, and when desired, the one-dimension array can be reconfigured into a two dimensional array for storage or to conduct parallel operations, such as dip loading, mixing, and optical-based read-out. Additional serial operations, include, but are not limited to, interfacing to an inherently serial analyzer (e.g. mass spectrometer) or interfacing to a compound library stored in microtiter plates.

[0063] In accordance with one embodiment of the invention, moving surface **1** and/or laminate **6** (hereinafter laminate shall be used for this embodiment) can be wound, as a spiral for example, and unwound, acting as an improved microtiter plate. Laminate **6** may be, but is not limited to, a tape, fiber, or belt. The laminate **31** includes through holes **33** perpendicular to its width, which serve as containers to hold sub-microliter volumes of fluid, as shown in **FIG. 2**. Through holes **33** may be machined into the surface, (for example formed from the surface geometry itself, or capillary tubes may be attached at intervals along the length of the surface. Through hole containers **33** are preferably at equally spaced intervals along the length of the surface. Laminate **31** may be wound such that the through holes **33** are perpendicular to the plane of the tape and the through-holes **33** form a known geometric pattern. In a preferred embodiment the through-hole **33** center-to-center spacing is an integral multiple of the well-to-well spacing in a 96-, 384- or 1536-well microtiter plate. Compounds stored as fluids in a microtiter plate are transferred into through-holes **33** by a bank of syringes having a center-to-center spacing an integral multiple of the well spacing in the plate. As shown in **FIG. 3**, the laminate **41** is unwound and passed beneath the syringe dispensing head **42**, whereupon known amounts of fluid are dispensed into each through-hole **43** and laminate **41** is advanced. With two syringe banks and simple automation, fluids can be transferred and loaded into laminate **41** through holes **43** at a rate exceeding one compound per second. Instead of syringes, pins or quills may also be used for the fluid transfer. After fluid loading, laminate **41** may be spooled in a temperature and humidity-controlled chamber to minimize evaporation of the loaded fluids. The high aspect ratio of through-holes **43** serves to slow fluid loss from evaporation because of the small surface area-to-volume ratio.

[0064] As shown in **FIG. 4**, once a compound library is loaded, a two-dimensional array of pins **51** having the same two-dimensional geometry and center-to-center spacing of the through-holes **52** may be dip loaded with reagent, co-registered with respect to the laminate through-hole array **53** and brought into proximity of through-holes **52** such that fluids are transferred from the pins to through-hole **52**. In this manner, reagents are loaded and reactions initiated simultaneously in a massively parallel manner. Cells may also be placed in the through holes and cell-based assays

performed. The laminate through-hole array **53** may be placed in a temperature and humidity-controlled environment for a prescribed length of time after which a stop reagent is added to through-holes **52** in a manner similar to the addition of the reaction reagents. The laminate through-hole array **53** is unwound and the reaction products in each through-hole **52** are sampled and analyzed, for example, by being injected sequentially into a mass spectrometer for analysis. Additionally, if the assay read-out is optical-based then each through-hole **52** is optically analyzed in parallel (i.e. imaged) and then read-out sequentially with the mass spectrometer.

[0065] The Compound Reformatter

[0066] In accordance with one embodiment of the invention, the library compounds to be screened are reformatted from the plates to the surface of the moving surface by a compound reformatter **2**, as shown in **FIG. 1**. Reformatter **2** may include a robotic arm that selects a plate from a storage system and places it within access of the moving surface **1** in a defined location. A microsyringe or a bank of microsyringes on a xyz stage transfers a sample compound from a well to the surface of the tape **6**. In addition to microsyringes, piezo or bubble jet heads, quills or pins may be used to transfer samples to the tape. Repeating this operation results in an array of drops on the moving tape **6**. Because the rate of movement of the tape **6** and/or its position is accurately known, the position and identification of the drop is known, and subsequent reagent additions and analysis can be performed on specific drops later in the high throughput process. The drops are spatially isolated from each other on the tape so that no cross contamination can occur. Preferably, the drops are 1:1 or less to minimize compound usage and so that surface tension forces exceed gravitational forces and the drops stick to the tape **6** regardless of its orientation.

[0067] In a preferred embodiment of the invention, a bank of microsyringes is used instead of one microsyringe. For example, 8 or 12 microsyringes in a row with 9 mm tip-to-tip spacing in a bank can be used to facilitate transfer from commercial 96 and 384-well microtiter plates. A multipipettor approach may be advantageously utilized because it creates time between dispensings that can be used for washing the pipettes and transporting the microtiter plates.

[0068] **FIGS. 5, 6, and 7** show a front view, side view, and top view, respectively, of a syringe bank system **61** in accordance with one embodiment of the invention. A flexible coupling **62** or linkage transmits torque to the plunger drive gear **63**, allowing the torque source, which may be a stepper or servo motor, to be remotely mounted. This greatly reduces the mass of the syringe bank assembly **64** when compared to a design that incorporates the motor onboard. Consequently, the overall assembly has little inertia relative to current designs and therefore requires less power to accelerate when attached to a positioning system. Greater accelerations can also be achieved for a given amount of applied force.

[0069] In various embodiments of the invention, a rack and pinion gearing **63** system is used to transform the rotary motion supplied to the syringe assembly **64** by the motor and coupling into a linear motion, which would then drive the syringe plungers in and out. To combat backlash error a pair of racks attached to the plunger assembly **65** may be used. By mounting the rack gear pieces **66** slightly translated in