

MATERIAL CONVEYING SYSTEMS, COMPUTER PROGRAM PRODUCTS, AND METHODS

COPYRIGHT NOTIFICATION

- 5 [0001] Pursuant to 37 C.F.R. § 1.71(e), Applicants note that a portion of this disclosure contains material which is subject to copyright protection. The copyright owner has no objection to the facsimile reproduction by anyone of the patent document or patent disclosure, as it appears in the Patent and Trademark Office patent file or records, but otherwise reserves all copyright rights whatsoever.

CROSS-REFERENCES TO RELATED APPLICATIONS

- 10 [0002] This application claims the benefit of U.S. Provisional Application No. 60/527,125, filed December 4, 2003, the disclosure of which is incorporated by reference in its entirety for all purposes.

FIELD OF THE INVENTION

- 15 [0003] The invention generally provides material conveying systems and related methods for accurately conveying selected quantities of material to and/or from material sites.

BACKGROUND OF THE INVENTION

- [0004] Rotary peristaltic pumps are utilized to convey material in a wide variety
20 of applications including in the production of pharmaceuticals, chemicals, foods, and beverages. In a typical rotary peristaltic pump system, a series of rollers or shoes are rotated in a circular path into contact with one or more material conduits, e.g., flexible tubes or hoses, such that the conduits are compressed against a compression surface, such as a curved wall. This generates moving regions of compression along a length of
25 the conduit, which pull material in the conduit that is upstream from the moving regions and pushes material in the conduit that is downstream from the moving regions to effect conveyance of the material through the conduit. One advantage of peristaltic pumps is the ability to convey material through conduits in the absence of contact between internal pump components and the material being conveyed. For example, this
30 tends to reduce the risk of contaminating the conveyed material.

[0005] Periodic variations in the quantity of material conveyed by a rotary peristaltic pump are typically observed and can lead to inaccurately conveyed quantities of material, especially when multiple uniform quantities are sought to be conveyed. More specifically, there is generally a substantially linear relationship between angular displacement and the quantity of material conveyed during a displacement cycle when the lead roller (i.e., the roller whose contact with a material conduit is furthest advanced in a particular displacement cycle) applies constant pressure on the material conduit. However, this relationship tends to become non-linear as the lead roller undergoes a disengagement event during which the pressure applied by the lead roller on the material conduit decreases to zero. This produces a repeatable aberration or periodic variation in the function relating displaced quantity of material with angular displacement of the pump, which when unaccounted for can lead to inaccurately dispensed quantities of material.

[0006] Accordingly, it is apparent that systems that account for periodic variations in the quantities of material conveyed by rotary peristaltic pumps are desirable. These and a variety of additional features of the present invention will become evident upon complete review of the following disclosure.

SUMMARY OF THE INVENTION

[0007] The invention generally relates to material conveying systems and methods that reliably convey selected quantities of material using peristaltic pumps, including microliter volumes of fluidic material. The approaches to reproducibly conveying desired quantities of material described herein readily account for periodic variations that are commonly observed in quantities of material conveyed with peristaltic pumps, and are typically less complex to implement than many pre-existing conveyance techniques. According to certain embodiments, for example, the systems of the invention are configured to effect substantially identical roller disengagement events for each quantity of material conveyed to minimize roller disengagement as a source of variation among conveyed quantities. In certain embodiments, the systems and methods of the invention further provide for the synchronous and accurate conveyance of multiple quantities of material to achieve elevated levels of throughput. Embodiments of the invention also include methods to minimize the carryover of material between material sites, such as between wells disposed in a multi-well

container, to reduce, e.g., the risk of cross-contaminating those sites or conveying inaccurate amounts of material. The invention also provides related computer program products that can be used to implement the methods and systems described herein.

[0008] In one aspect, the invention provides a material conveying system. The system includes at least one peristaltic pump having a rotatable roller support that supports at least two rollers (e.g., fixed rollers, rotatable rollers, or combinations thereof), and at least one motor that is operably connected to the peristaltic pump to rotate the roller support. The system also includes at least one controller that is operably connected to the motor. The controller is configured to effect rotation of at least the roller support in at least one rotational increment that substantially corresponds to an integral multiple of an angular distance disposed between adjacent rollers supported by the roller support such that when one or more material conduits are operably connected to the peristaltic pump and the peristaltic pump conveys material through the material conduits, quantities of material that correspond to the rotational increment are conveyed to or from at least one material site (e.g., a material container, a substrate surface, etc.). Identical rotational increments generally convey substantially uniform quantities of material to or from the material site. Moreover, the rotational increment is typically uncompensated for flow rate characteristics of the system. In some embodiments, the system further includes at least one material conduit that is operably connected to the peristaltic pump. Typically, the controller is configured to effect substantially identical roller disengagements from the material conduit for each conveyed quantity of material to minimize periodic variation among the conveyed quantities of material. Optionally, the system also includes at least one detector operably connected to the controller. The detector is configured to detect detectable signals produced at one or more material sites.

[0009] In certain embodiments, the system further includes at least one positioning component that is operably connected to the controller. The positioning component is structured to moveably position at least one material conduit and/or one or more material sites relative to one another. The positioning component typically comprises at least one object holder that is structured to support the material sites. In some embodiments, the system further includes the material conduit operably connected to the positioning component and to the peristaltic pump. Optionally, the

system further includes at least one cleaning component operably connected to the controller. The cleaning component is structured to clean the material conduit when the material conduit is operably connected at least to the positioning component, and the positioning component moves the material conduit at least proximal to the cleaning
5 component. In certain embodiments, the system further includes at least one mounting component that mounts at least the peristaltic pump, the motor, and the positioning component relative to one another.

[0010] In another aspect, the invention provides a material conveying system that includes at least one material conduit and at least one peristaltic pump that is
10 operably connected to the material conduit. The peristaltic pump includes a rotatable roller support that supports at least two rollers. The material conveying system is typically automated. The system also includes at least one feedback component that is operably connected to the peristaltic pump. The feedback component comprises at least one motor that rotates the roller support. In addition, the system also includes at
15 least one controller that is operably connected to the feedback component, which controller is configured to effect rotation of at least the roller support in at least one rotational increment that substantially corresponds to an integral multiple of an angular distance disposed between adjacent rollers supported by the roller support such that quantities of material conveyed through the material conduit to or from at least one
20 material site correspond to the rotational increment. The rotational increment generally corresponds to at least a 0.1 μ l material volume. Further, identical rotational increments generally convey substantially uniform material volumes to or from the material site. Typically, the rotational increment is uncompensated for flow rate characteristics of the system. In some embodiments, the material conveying system
25 further comprises at least one detector operably connected to the controller. The detector is configured to detect detectable signals produced at one or more material sites.

[0011] The peristaltic pumps that are included in the material conveying systems of the invention include various embodiments. In some embodiments, for
30 example, the peristaltic pump comprises a multi-channel peristaltic pump. Typically, the peristaltic pump is configured to reversibly convey the quantities of material to or from the material site. In addition, the peristaltic pump typically generates sufficient

material flow rates at least proximal to a terminus of the material conduit to effect non-contact material dispensing from the terminus. Further, the roller support typically supports, e.g., 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 30, or more rollers. The moment of inertia of the roller support is generally minimized to prevent a quantity of material from adhering to an external portion of the material conduit when the peristaltic pump conveys material through the material conduit. Moreover, angular distances disposed between pairs of adjacent rollers supported by the roller support are typically substantially equal to one another. For example, adjacent rollers supported by the roller support are generally disposed at most 180° apart from one another. In some embodiments, the roller support is interchangeable with at least one other roller support. In embodiments where the rollers are rotatable, the peristaltic pump optionally includes a gear mechanism that effects rotation of the rotatable rollers when the motor rotates the roller support, e.g., to minimize material conduit wear.

[0012] In some embodiments, the feedback component comprises at least one drive mechanism that is operably connected to the motor. The drive mechanism typically includes at least one control component that effects position feedback control of the motor. The motor generally includes at least one position encoder and at least one gear reduction component. For example, the motor typically comprises a servo motor or a stepper motor. In certain embodiments, the feedback component further comprises one or more weight scales that are operably connected to the controller. The weight scales detect weights of materials disposed at one or more material sites.

[0013] The controller is generally configured to effect substantially identical roller disengagements from the material conduit for each conveyed quantity of material to minimize periodic variation among the conveyed quantities of material. In embodiments where the rollers are rotatable, the controller is optionally further configured to effect rotation of at least one of the rollers supported by the roller support. In these embodiments, the rollers typically rotate in a direction that is opposite from a direction of rotation of the roller support to minimize material conduit wear. For example, the rollers and the roller support typically rotate at velocities that have substantially equal absolute values. In certain embodiments, the controller effects at least one negative pressure pulse at least proximal to a terminus of the material conduit after effecting rotation of the roller support in the rotational increment to prevent a

quantity of material from adhering to an external portion of the material conduit. The moment of inertia of the roller support is generally minimized to further prevent the quantity of material from adhering to the external portion of the material conduit.

[0014] The material conduits included in the systems of the invention also
5 include various embodiments. In some embodiments, for example, a cavity disposed through the material conduit includes a cross-sectional dimension of between 1 mm and 10^5 μ m. Typically, the material conveying system comprises a plurality of material conduits in which termini of at least two of the material conduits are spaced at a distance from one another to simultaneously communicate with different wells disposed
10 in at least one multi-well container. In some embodiments, the material conveying system comprises a plurality of material conduits in which two or more of the material conduits communicate with different material sources.

[0015] In some embodiments, at least one terminus of the material conduit comprises at least one tip. In these embodiments, the tip is optionally integral with the
15 terminus. In certain embodiments, a cavity disposed through the tip comprises at least two different cross-sectional dimensions. Typically, at least a portion of the tip is tapered. In some embodiments, at least a portion of the material conduit proximal to the terminus is substantially linear. The substantially linear portion of the material conduit comprises a length of at least 60 mm. In some embodiments, the terminus of
20 the material conduit and the tip are connected by an insert, e.g., such that the conduit and tip communicate with one another. In some of these embodiments, portions of the insert are inserted into portions of the terminus and the tip, whereas in other embodiments, portions of the terminus and the tip are inserted into portions of the insert. The insert is generally fabricated from a less flexible material than at least the
25 material conduit.

[0016] In certain embodiments, the material conveying system further includes at least one positioning component that is operably connected to the controller. The positioning component is generally structured to moveably position the material conduit and/or the material site relative to one another. For example, the positioning
30 component optionally includes at least one object holder that is structured to support the material site. In addition, the controller is typically configured to simultaneously effect rotation of the roller support and moveably position the material conduit and/or

the material site relative to one another such that the quantities of material are conveyed to or from the material site synchronous with the relative movement of the material conduit and/or the material site.

[0017] In some embodiments, the positioning component comprises at least one
5 X/Y-axis linear motion table operably connected to at least one position feedback control drive that controls movement of the X/Y-axis linear motion table along an X-axis and a Y-axis. Typically, the positioning component comprises at least one object holder operably connected to the X/Y-axis linear motion table, which object holder is structured to support the material site. In certain embodiments, the positioning
10 component includes at least one Z-axis linear motion component comprising at least one material conduit support head that supports at least a portion of the material conduit and that moves along a Z-axis. The Z-axis linear motion component generally comprises at least one solenoid. The positioning component is typically configured to move the material conduit support head with sufficient velocity to eject adherent
15 material that adheres to an external portion of the material conduit.

[0018] In certain embodiments, the material conveying system further includes at least one cleaning component operably connected to the controller, which cleaning component is structured to clean the material conduit when the positioning component moves the material conduit at least proximal to the cleaning component. In some of
20 these embodiments, for example, the cleaning component comprises a vacuum chamber comprising at least one orifice into or proximal to which the positioning component moves the material conduit such that an applied vacuum removes adherent material from an external surface of the material conduit. An outer cross-sectional dimension of the material conduit is typically smaller than a cross-sectional dimension of the orifice.

25 [0019] In some embodiments, the material conveying system further includes at least one mounting component that mounts at least the peristaltic pump, the feedback component, and the positioning component relative to one another. The mounting component is typically substantially rigid.

[0020] In another aspect, the invention provides a computer program product
30 comprising a computer readable medium having one or more logic instructions for receiving one or more input parameters selected from the group consisting of: (i) a rotational increment that substantially corresponds to an integral multiple of an angular

distance disposed between adjacent rollers supported by a roller support of a peristaltic pump; (ii) a cross-sectional dimension of a material conduit; (iii) a quantity of material to be conveyed to or from a material site; and (iv) an angular distance disposed between adjacent rollers supported by a roller support of a peristaltic pump. The computer
5 program product also includes one or more logic instructions for rotating a roller support of a peristaltic pump in rotational increments that substantially correspond to integral multiples of an angular distance disposed between adjacent rollers supported by the roller support of the peristaltic pump such that when one or more material conduits are operably connected to the peristaltic pump and the peristaltic pump
10 conveys material through the material conduits, quantities of material that correspond to the rotational increments are conveyed to or from at least one material site. In certain embodiments, the computer program product further includes at least one logic instruction for moving an X/Y-axis linear motion table and a Z-axis motion component synchronous with rotating the roller support.

15 [0021] In another aspect, the invention relates to a method of conveying material. The method includes providing a material conveying system comprising at least one controller that is operably connected to at least one motor that is operably connected to at least one peristaltic pump. The peristaltic pump comprises a rotatable roller support that supports at least two rollers and is operably connected to at least one
20 material conduit. The system is typically automated. The method also includes conveying the material (e.g., a cell suspension, a reagent, a buffer, a solid support suspension, etc.) through the material conduit in which the controller effects rotation of the roller support in at least one rotational increment that substantially corresponds to an integral multiple of an angular distance disposed between adjacent rollers supported
25 by the roller support such that quantities of material conveyed to or from at least one material site correspond to the rotational increment. The controller typically effects rotation of the roller support such that shearing effects on material (e.g., cells or the like) conveyed in the material are minimized. Typically, the material is conveyed to the material site without the material conduit contacting the material site. The
30 quantities of material generally comprise at least 0.1 μ l of the material. In some embodiments, the system further comprises at least one feedback component that is operably connected to the motor, which feedback component effects position feedback control of the peristaltic pump. The controller generally effects substantially identical

roller disengagements from the material conduit for each conveyed quantity of material to minimize periodic variation among the conveyed quantities of material. The rotational increment is generally uncompensated for flow rate characteristics of the system. Identical rotational increments typically convey substantially uniform quantities of material to or from the material site. In certain embodiments, the method further includes effecting at least one negative pressure pulse at least proximal to a terminus of the material conduit with the controller after effecting rotation of the roller support in the rotational increment to prevent a quantity of material from adhering to an external portion of the material conduit.

10 [0022] In some embodiments, the system further comprises at least one positioning component that is operably connected to the controller, which positioning component is structured to moveably position the material conduit and/or the material site relative to one another. The positioning component typically moves the material conduit with sufficient velocity to eject adherent material, if any, that adheres to an external portion of the material conduit. Typically, the method includes moving the material conduit with sufficient velocity to eject adherent material, if any, that adheres to an external portion of the material conduit. In some embodiments, the positioning component moves the material conduit such that adherent material, if any, that adheres to an external portion of the material conduit contacts at least one other object to remove the adherent material from the external portion of the material conduit. For example, the other object optionally comprises a portion of a well of a multi-well container.

[0023] In certain embodiments, the material site comprises at least one multi-well container and the method comprises conveying at least a first quantity of material into at least a first well of the multi-well container, moving the material conduit and/or the material site relative to one another, e.g., with the positioning component such that the material conduit is in communication with at least a second well of the multi-well container, and conveying at least a second quantity of material into the second well of the multi-well container. The moving step and at least one conveying step are typically substantially simultaneous with one another. Typically, the moving step comprises positioning a portion of the material conduit above or in the second well.

[0024] In some embodiments, the system includes a plurality of material conduits that are operably connected to the peristaltic pump and the method comprises conveying multiple quantities of material to or from the material site through the material conduits. In these embodiments, two or more of the material conduits
5 generally materially communicate with different material sources. Typically, the multiple quantities of material are conveyed substantially simultaneously. In some embodiments, the material site comprises at least one multi-well container and termini of at least two of the material conduits are spaced at a distance that corresponds to a distance between at least two wells disposed in the multi-well container. In these
10 embodiments, the method generally comprises simultaneously conveying the material through the two material conduits to or from the two wells. The material site generally comprises at least one material container and/or at least one substrate surface. The material container typically comprises a multi-well material container having, e.g., 6, 12, 24, 48, 96, 192, 384, 768, 1536, or more wells. The substrate surface optionally
15 comprises a membrane surface.

[0025] In another aspect, the invention provides a method of conveying material to a material site. The method includes providing a material conveying system comprising at least one material conduit, and at least one pump that is operably connected to the material conduit, which pump conveys the material through the
20 material conduit. The material conveying system also includes at least one positioning component that is operably connected to the material conduit, which positioning component moves the material conduit. In addition, the material conveying system also includes at least one controller that is operably connected to the pump and the positioning component. The controller effects the pump to convey the material through
25 the material conduit and the positioning component to move the material conduit. The method also includes conveying the material (e.g., fluidic material, etc.) through the material conduit such that a quantity of the material adheres to a terminal portion of the material conduit, thereby forming an adherent material quantity. In addition, the method also includes accelerating at least the terminal portion of the material conduit
30 towards the material site with the positioning component, and decelerating the terminal portion of the material conduit with the positioning component such that the adherent material quantity is conveyed from the terminal portion of the material conduit to the material site. The material site generally comprises at least one well of a multi-well

container. The decelerating step typically comprises ejecting the adherent material quantity from the terminal portion of the material conduit. Typically, the adherent material quantity is conveyed to the material site without contacting the terminal portion of the material conduit and the material site. In some embodiments, the material comprises a cell suspension and the method minimizes shearing effects on conveyed cells.

BRIEF DESCRIPTION OF THE DRAWINGS

- [0026] Figures 1 A and B schematically illustrate a peristaltic pump roller disengagement event.
- 10 [0027] Figures 2A-C schematically illustrate various exemplary angular distances.
- [0028] Figure 3 schematically depicts a material conveying system from a perspective view according to one embodiment of the invention.
- [0029] Figure 4 schematically shows a detailed perspective view of a peristaltic pump from the material conveying system of Figure 3.
- 15 [0030] Figure 5 schematically shows a cross-sectional view through a roller support that supports passively rotatable rollers as the roller support rotates the rollers into contact with a material conduit.
- [0031] Figure 6 schematically illustrates a passively rotatable roller contacting a material conduit.
- 20 [0032] Figure 7 schematically depicts a portion of a roller support that supports actively rotatable rollers from a front elevational view.
- [0033] Figure 8 schematically shows a cross-sectional view of a volume of fluid wicking or adhering to the tip of a conduit.
- 25 [0034] Figure 9 is a graph that schematically illustrates a conduit tip velocity profile according to one embodiment of the invention.
- [0035] Figure 10 schematically depicts a cross-sectional view of a volume of fluid being dispensed from a tip of a conduit in the absence of fluid wicking.

[0036] Figure 11 schematically illustrates a detailed perspective view of a drive motor having a position encoder and gear reduction from the material conveying system of Figure 3.

5 [0037] Figure 12 schematically shows X- and Y-axis linear motion table and position feedback control drives according to one embodiment of the invention.

[0038] Figure 13 schematically depicts a detailed perspective view of an object holder from the material conveying system of Figure 3.

[0039] Figure 14A schematically shows a top view of a microtiter plate.

10 [0040] Figure 14B schematically illustrates a bottom view of the microtiter plate shown in Figure 14A.

[0041] Figure 14C schematically depicts a cross-sectional view of the microtiter plate shown in Figure 14A.

15 [0042] Figure 15A schematically shows a partially transparent perspective view of a vacuum chamber of a cleaning component according to one embodiment of the invention.

[0043] Figure 15B schematically illustrates a detailed cross-sectional view of a material conduit tip disposed proximal to an orifice of a portion of the vacuum chamber of Figure 15A.

20 [0044] Figures 16A-D schematically illustrate various material conduit tips according to certain embodiments of the invention.

[0045] Figure 17 is a block diagram showing a representative example logic device in which various aspects of the present invention may be embodied.

[0046] Figure 18A illustrates fluid volumes dispensed from a system when the rotational increment was 12° per volume dispensed.

25 [0047] Figure 18B illustrates fluid volumes dispensed from a system when the rotational increment was 18° per volume dispensed.

[0048] Figure 18C illustrates fluid volumes dispensed from a system when the rotational increment was 30° per volume dispensed.

[0049] Figure 18D illustrates fluid volumes dispensed from a system when the rotational increment was 42° per volume dispensed.

DETAILED DESCRIPTION

I. DEFINITIONS

5 [0050] Before describing the present invention in detail, it is to be understood that this invention is not limited to particular systems or methods, which naturally can vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting. Further, unless defined otherwise, all technical and scientific terms used herein have the same
10 meaning as commonly understood by one of ordinary skill in the art to which this invention pertains. In describing and claiming the present invention, the following terminology and grammatical variants will be used in accordance with the definitions set out below.

[0051] The term “**material**” refers to matter in essentially any physical state.
15 For example, material can be in the form of gases, liquids, semi-liquids, pastes, powders, and combinations thereof. To further illustrate, material comprises cell and/or reagent suspensions in certain embodiments of the invention.

[0052] The term “**angular distance**” or “**angular displacement**” refers to an angle that a rotating body rotates through. In some embodiments of the present
20 invention, for example, a rotatable roller support of a peristaltic pump rotates in rotational increments that substantially correspond to integral multiples of angular distances disposed between adjacent rollers supported by the roller support.

[0053] The term “**moment of inertia**” refers to a measure of the resistance of a body to angular acceleration about a given axis that is equal to the sum of the products
25 of each element of mass in the body and the square of the element’s distance from the axis.

[0054] The term “**reversibly convey**” refers to a process of conveying material in which the material or portions thereof are capable of being, e.g., removed from a material site after being dispensed at the site, dispensed at one material site after being
30 removed from another material site, and/or the like. In certain embodiments of the invention, for example, fluidic materials are aspirated from material sites (e.g., wells of

a micro-well plate or other fluidic material source) and dispensed at other sites (e.g., wells of a micro-well plate, surfaces of substrates, fluidic material waste containers, etc.). Reversible material conveyance is typically effected by rotating the peristaltic pump roller support in a direction that is opposite from the direction the roller support is rotated to convey the material to the particular material site from which the material is removed.

[0055] The term “**non-contact material dispensing**” refers to a process of material dispensing in which material conduits of a material conveying system do not contact material sites or material disposed at material sites when the material is dispensed from the conduits.

[0056] The term “**feedback component**” refers to a component of a system that provides information about one or more other components of the system. In certain embodiments, for example, the material conveying systems of the invention include feedback components comprising motors that rotate roller supports of peristaltic pumps. In these embodiments, the feedback components generally provide, e.g., information relating to roller support position to controllers to which the feedback components are typically operably connected such that the controllers can effect rotation of the roller supports in selected rotational increments. In some embodiments, feedback components provide information such as the weight of material present at a particular material site. Additional details relating to these types of feedback components, which are optionally adapted for use in the material conveying systems of the invention, are described further in, e.g., U.S. Patent Application No. 10/350,905, entitled “FLUID HANDLING METHODS AND SYSTEMS,” filed January 24, 2003 by Micklash II et al., which is incorporated by reference.

[0057] The term “**rotational increment**” refers to an angular displacement of a roller support. For example, controllers of the systems of the invention are typically configured to effect rotation of roller supports in rotational increments that substantially correspond to integral multiples of angular distances disposed between adjacent rollers supported by the roller supports, e.g., such that substantially identical roller disengagements are effected for each quantity of material conveyed. In certain embodiments, for example, a user directly selects the rotational increment in which a roller support rotates, whereas in other embodiments, a system controller is configured

to select an appropriate rotational increment, e.g., based upon an input quantity of material that a user desires to be conveyed.

[0058] The term “**roller disengagement**” or “**disengagement event**” refers to a process in which a roller of a roller support is removed from contact with a material conduit during operation of a peristaltic pump. The disengagement event typically corresponds to a change in pressure applied by the roller undergoing the disengagement from approximately a maximum to substantially zero.

[0059] The phrase “**integral multiple of an angular distance disposed between adjacent rollers**” refers to the product of the angular distance disposed between adjacent rollers supported by a roller support of a peristaltic pump by an integer, that is, any of the natural numbers, the negatives of these numbers, or zero. The controllers of the systems described herein are typically configured to effect rotation of roller supports in rotational increments that substantially correspond to integral multiples of angular distances disposed between adjacent rollers supported by the roller supports. To illustrate, if a roller support includes three rollers disposed 120° apart from one another and the selected integer is +2, then the rotational increment of the roller support will be 240°, whereas if the selected integer is +4 for the same roller support, then the rotational increment of the roller support will be 480°, and so forth. Positive and negative signs before the selected integer generally refer to the relative direction of rotation of the roller support, e.g., forward or reverse.

[0060] A material conduit “**communicates**” with a material site when material can be translocated to and/or from the material site through the conduit, e.g., under an applied pressure a peristaltic pump.

[0061] The term “**periodic variation**” refers to a recurrent change in output or other characteristic of a given device or system. To illustrate, there is typically a periodic variation in the quantity of material conveyed by a rotary peristaltic pump, e.g., when a roller disengages from a material conduit during a displacement cycle. More specifically, there is generally a substantially linear relationship between angular displacement and the quantity of material conveyed during a displacement cycle when the lead roller (i.e., the roller whose contact with a material conduit is furthest advanced in a particular displacement cycle) applies constant pressure on the material conduit. However, this relationship tends to become non-linear as the lead roller undergoes a

disengagement event during which the pressure applied by the lead roller on the material conduit decreases to zero. This produces a repeatable aberration or periodic variation in the function relating displaced quantity of material with angular displacement of the pump.

- 5 [0062] The term “**top**” refers to the highest point, level, surface, or part of a device or system, or device or system component, when oriented for typical designed or intended operational use, such as conveying material from a source to a destination. In contrast, the term “**bottom**” refers to the lowest point, level, surface, or part of a device or system, or device or system component, when oriented for typical designed or
10 intended operational use.

II. INTRODUCTION

- [0063] While the present invention will be described with reference to a few specific embodiments, the description is illustrative of the invention and is not to be construed as limiting the invention. Various modifications can be made to the
15 embodiments of the invention described herein by those skilled in the art without departing from the true scope of the invention as defined by the appended claims. For example, although the conveyance of relatively small quantities or volumes of material (e.g., on the scale of milliliters, microliters, etc.) is emphasized herein primarily for clarity of illustration, it will be appreciated that the systems and methods of the
20 invention can be adapted to accurately convey essentially any quantity of material. It is also noted here that for a better understanding, certain like components are designated by like reference letters and/or numerals throughout the various figures.

- [0064] The systems and methods of conveying materials of the present invention generally include rotating peristaltic pumps with precisely regulated
25 accelerations, velocities, and decelerations to effect accurate angular displacements. Moreover, the systems and methods described herein typically account for periodic variations produced, e.g., by roller disengagement events such that accurate and repeatable conveyance of material is achieved using rotary peristaltic pumps. In certain embodiments, for example, material conveying systems are configured such that
30 substantially identical roller disengagement events occur for each conveyed quantity of

material, thereby minimizing roller disengagement as a source of variation among conveyed quantities of material.

[0065] To illustrate, there is generally a substantially linear relationship between angular displacement of a pump roller support and the quantity (e.g., volume) of material conveyed when the lead pump roller begins and ends a displacement cycle applying constant pressure to a material conduit. Further, as the lead roller begins to disengage from the material conduit, e.g., while another roller begins to engage the conduit (e.g., tubing or the like), there is typically a period where the conveyed quantity becomes at least partially negative as a function of angular displacement as at least some material in the conduit is sucked backwards to fill the gap left by the lead roller coming out of contact with the conduit. This is further illustrated in Figures 1 A and B, which schematically show pump roller support 100 supporting four rollers 102. In Figures 1 A and B, Ω and Ω' are the same magnitude. As shown, rollers 102 compress conduit 104 against compression surface 106 to effect conveyance of material through conduit 104. Arrow 108 shows the direction of rotation of roller support 100, while arrows 110 show the direction material conveyance through conduit 104. Figure 1B shows the change in state of conduit 104 after the pump has rotated roller support 100 the displacement Ω shown in Figure 1A. The progression from Figure 1A to Figure 1B shows that when the exiting or disengaging lead roller comes out of contact with conduit 104, that roller pulls away from conduit 104 causing material (e.g., fluid, gas, paste, etc.) in conduit 104 to at least momentarily to be sucked backwards. This causes a repeatable aberration or periodic variation in the function relating displaced quantity of material with angular displacement of the pump roller support.

[0066] Accordingly, aspects of the invention disclosed herein relate to systems and methodologies that readily account for this periodic variation such that selected quantities of material (e.g., fluidic material, etc.) are accurately conveyed using rotary peristaltic pumps. In certain embodiments, for example, the invention provides a control system configured to convey quantities of material (e.g., fluid volumes) that correspond to an angular pump rotation or rotational increment that is equal to an integral multiple of the angular distance disposed between adjacent rollers. Various exemplary angular distances are schematically illustrated in Figures 2A-C. More specifically, Figure 2A schematically shows roller support 200 supporting two rollers

202 disposed at an angular distance, θ , of 180°, Figure 2B schematically illustrates roller support 200 supporting three rollers 202 disposed such that θ equals 120°, and Figure 2C schematically depicts roller support 200 supporting four rollers 202 disposed such that θ equals 90°. Essentially any angular distance is optionally utilized. For example, minimum dispense quantities can be reduced by increasing the number of pump rollers. The angle θ is given by the equation:

$$\theta = S/r$$

where S is the distance along the circumference of the circular path disposed between the axes of rotation of adjacent rollers 202 (i.e., the arc length subtended by the angle θ) and r is the distance from the axis of rotation of roller support 200 to the axis of rotation of roller 202. In this manner, the methods and systems described herein ensure that the same roller disengagement events occur for each dispense/aspiration, thereby eliminating the roller disengagement as a source of variation in dispense/aspiration quantities between dispenses/aspirations.

[0067] To further illustrate aspects of the invention, Figure 3 schematically depicts a material conveying system according to one embodiment of the invention. The material conveying systems of the invention are generally highly automated such that material conveyance processes can be performed with higher throughput in addition to greater accuracy and simplicity than many pre-existing systems. As shown, material conveying system 300 includes peristaltic pump 302 (e.g., a multi-channel low volume peristaltic pump) mounted on mounting component 304 (shown as a rigid frame). Material conveying system 300 also includes a feedback component that comprises drive motor 306, which includes a position encoder and gear reduction, and which is operably connected to peristaltic pump 302 to effect precisely controlled rotation of the rotatable roller support of peristaltic pump 302. The feedback component also includes a control system for drive motor 306 (not shown in Figure 3) that is capable of position feedback control.

[0068] Material conduits 308 are disposed between the compression surfaces and rollers of peristaltic pump 302. In addition, one set of termini of material conduits 308 communicate with the same or different material sources (not within view), while the other set of termini are operably connected to material conduit support head 310 via

tips 311. Material conduit support head 310 is attached to arm 318 via Z-axis linear motion component 312 (e.g., a compact, high speed, short travel Z-axis motion component or system). Arm 318 suspends material conduit support head 310 above object holder 314. A motor (not shown), such as a solenoid motor or the like, is typically operably connected to Z-axis linear motion component 312 to effect Z-axis translation of material conduit support head 310 relative to material sites (e.g., multi-well plates, membranes, etc.) disposed on object holder 314. Object holder 314 is operably connected to X/Y-axis linear motion tables 320, which move object holder 314 relative to material conduit support head 310 along the X- and Y-axes. X/Y-axis linear motion tables 320 are also mounted on mounting component 304. One or more motors (e.g., solenoid motors, etc.) are generally operably connected to the material conveying systems of the invention to effect motion of object holders on X/Y-axis linear motion tables. For example, solenoid motor 316 effects motion of object holder 314 in material conveying system 300. Although not within view in Figure 3, material conveying system 300 also generally includes control drives, e.g., for X/Y-axis linear motion tables 320 and position feedback for drive motor 306. Exemplary control drives are schematically illustrated in Figure 12. The material conveying systems of the invention also typically include controllers (also not shown in Figure 3) that are configured to effect rotation of peristaltic pump roller supports in selected rotational increments. The rotational increments typically substantially correspond to integral multiples of angular distances disposed between adjacent rollers supported by the roller supports to thereby account for periodic variation as described herein. These and other aspects of the invention are described in greater detail below.

III. PERISTALTIC PUMPS

25 [0069] Among the advantages of the systems and methods described herein is that identical rotational increments convey substantially (i.e., approximately or exactly) uniform quantities of material (e.g., material volumes, etc.) to or from the material site. Moreover, rotational increments are typically uncompensated for flow rate characteristics of the particular system utilized unlike certain pre-existing systems, such as the apparatus alleged in, e.g., U.S. Pat. No. 6,393,338, entitled "APPARATUS AND
30 CONTROL METHOD FOR ACCURATE ROTARY PERISTALTIC PUMP FILLING," issued May 12, 2002 to Kemnitz, which is incorporated by reference.

Accordingly, the systems and methods of the present invention are typically easier or less complex to implement than many of these pre-existing methods and systems.

[0070] Essentially any rotary peristaltic pump can be used in the systems of the present invention. Peristaltic pumps typically use a turning mechanism to move material through a tube or other conduit that is compressed at a number of points in contact with, e.g., rollers, shoes, etc. of the pump such that the material is moved through the tube with each rotating motion. Typically, peristaltic pumps are configured to reversibly convey quantities of material to or from selected material sites (e.g., microtiter plates, surfaces of substrates, or the like). Peristaltic pumps generally include rotatable roller carriers or supports that support at least two rollers (e.g., 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 30, or more rollers). In certain embodiments, roller supports may be interchanged with one another, e.g., roller supports having different numbers of rollers. To further illustrate, roller supports typically support between about 2 and about 50 rollers, more typically between about 3 and about 40 rollers, and still more typically between about 4 and about 30 rollers. Generally, the greater the number of rollers supported on a given roller support, the smaller the quantity of material the peristaltic pump will be capable of conveying, since the controllers of the invention are typically configured to rotate roller supports in rotational increments that substantially correspond to integral multiples of angular distances disposed between adjacent rollers supported on the roller supports.

[0071] Adjacent rollers supported by a roller support are generally disposed at most 180° apart from one another. Moreover, angular distances disposed between pairs of adjacent rollers supported by roller supports are typically substantially (i.e., approximately or exactly) equal to one another. For example, adjacent rollers supported by a roller support are optionally positioned such that rotational increments substantially correspond to angular displacements selected from, e.g., about 12° (e.g., corresponding to 30 substantially equally spaced rollers), about 18° (e.g., corresponding to 20 substantially equally spaced rollers), about 22.5° (e.g., corresponding to 16 substantially equally spaced rollers), about 24° (e.g., corresponding to 15 substantially equally spaced rollers), about 25.7° (e.g., corresponding to 14 substantially equally spaced rollers), about 27.7° (e.g., corresponding to 13 substantially equally spaced rollers), about 30° (e.g.,

corresponding to 12 substantially equally spaced rollers), about 32.7° (e.g.,
corresponding to 11 substantially equally spaced rollers), about 36° (e.g.,
corresponding to 10 substantially equally spaced rollers), about 40° (e.g.,
corresponding to 9 substantially equally spaced rollers), about 45° (e.g., corresponding
5 to 8 substantially equally spaced rollers), about 51.4° (e.g., corresponding to 7
substantially equally spaced rollers), about 60° (e.g., corresponding to 6 substantially
equally spaced rollers), about 72° (e.g., corresponding to 5 substantially equally spaced
rollers), about 90° (e.g., corresponding to 4 substantially equally spaced rollers), about
120° (e.g., corresponding to 3 substantially equally spaced rollers), about 180° (e.g.,
10 corresponding to 2 substantially equally spaced rollers), or the like. Optionally, angular
distances disposed between pairs of adjacent rollers supported by a given roller support
are not equal to one another.

[0072] Although other fluidic material volumes may be conveyed using the
systems described herein, rotational increments generally correspond to at least about a
15 0.1 μ l volume of fluidic material. Microliter volumes are generally desirable, e.g.,
when conveying fluidic materials to and/or from high-density multi-well plates, such as
1536-well plates having total volume capacities that are typically between about 10 to
about 15 μ l/well, with the systems of the present invention. Larger volumes of fluidic
material (e.g., milliliter volumes, liter volumes, etc.) are also optionally conveyed using
20 the systems of the present invention. A user can typically select the desired quantities
of material (e.g., volumes or aliquots of fluidic material) conveyed with the systems of
the invention by varying such parameters as the number of rollers supported by a roller
support of the peristaltic pump, the rotational increments selected, the inner cross-
sectional dimensions (e.g., diameter, etc.) of the material conduits utilized, the depth or
25 extent of contact between rollers and material conduits when the rollers compress the
materials conduits against the compression surface of the peristaltic pump, and the like.

[0073] In some embodiments, for example, the peristaltic pump comprises a
multi-channel peristaltic pump such that multiple quantities of material can be
conveyed simultaneously. To illustrate, Figure 4 schematically shows a detailed
30 perspective view of peristaltic pump 302 from material conveying system 300. In the
embodiment shown, peristaltic pump 302 comprises five channels 400. Optionally,
additional channels 400 are added to peristaltic pump 302, or one or more of channels

400 are removed from peristaltic pump 302. Typically, the number of channels is selected according to the type of material site utilized in a particular application. For example, the number of channels can be selected to correspond to a given number of rows or columns of wells in a multi-well plate. Rollers 402 of the roller support of peristaltic pump 302 are also schematically shown in Figure 4.

[0074] Although rotatable rollers (e.g., passively or actively rotatable) that rotate relative to roller supports are typically utilized in the systems of the invention, non-rotatable functionally equivalent components, such as fixed rollers or shoes are also optionally used. However, rotatable rollers generally produce less wear on material conduits (e.g., flexible tubing or the like) than non-rotatable equivalents for comparable amounts of usage. Conduit wear is typically initially observed primarily at or near the regions of initial contact between the rollers and conduits. To illustrate this type of wear, Figure 5 schematically shows a cross-sectional view through roller support or carrier 500 that supports passively rotatable rollers 502 as roller support 500 rotates rollers 502 into contact with material conduit 504. Arrow 506 represents the angular velocity of roller carrier 500, ω_C , and arrow 508 represents the direction of material conveyance through material conduit 504. Wear region 510 is shown proximal to the region of initial contact between rollers 502 and material conduit 504 for the direction of roller support 500 rotation indicated. For example, if a roller carrier or support is spinning at velocity, V_C , a passively rotatable roller supported by the roller support generally will have a roller velocity, V_R , equal to zero before contacting the conduit. When the roller contacts the conduit, friction will typically cause the rotatable roller to accelerate from $V_R = 0$ to $V_R = -V_C \cos \theta$ instantaneously. The derivation of $V_R = -V_C \cos \theta$ is described further below. This acceleration is generally too large to achieve. Instead, the roller typically skids on the conduit producing wear at or near the initial region of contact, such as wear region 510 schematically illustrated in Figure 5. To further illustrate, Figure 6 schematically illustrates roller carrier arm 600 supporting passively rotatable roller 602 as rotatable roller 602 contacts material conduit 604. As referred to above, $V_R = -V_C \cos \theta$, which with reference to Figure 6 is derived as follows:

$$V_R = -V_C \sin \phi$$

$$\phi = 180^\circ - 90^\circ - \theta \text{ or } 90^\circ - \theta, \text{ so}$$

$$V_R = -V_C \sin (90^\circ - \theta)$$

$$V_R = -V_C (\sin 90^\circ \cos \theta - \cos 90^\circ \sin \theta)$$

$\sin 90^\circ = 1$ and $\cos 90^\circ = 0$, so

$$V_R = -V_C \cos \theta$$

- 5 and $\cos \theta$ is 1 when the conduit wrapped around the rollers. Accordingly, to minimize this type of conduit wear, rollers are optionally actively rotated such that they have initial velocities that are substantially equal to $-V_C$ in certain embodiments of the invention. In some of these embodiments, for example, a planetary gear transmission produces this rotation of the rollers, which rotation is in a direction opposite from or
- 10 counter to the rotation of the roller support. In particular, a spur gear or the like is attached coaxially to each roller. The pitch curve of the gears is substantially equal to the radius of the rollers. In addition, a fixed ring gear or the like surrounds the spur gears. The transmission is driven by spinning the roller support or carrier. To illustrate, Figure 7 schematically depicts a portion of a roller support that supports
- 15 actively rotatable rollers from a front elevational view. As shown, roller support **700** supports rollers **702**. As also shown, spur gears **704** are coaxially attached to each roller **702** and ring gears **706** surround spur gears **704** such that when roller support **700** is rotated via drive shaft **708**, rollers **702** rotate substantially with $-V_C$ by gear transmission.
- 20 **[0075]** More gradual wear is also generally observed over time at all points of contact along the particular conduit. As described further below, the rollers are typically accelerated and decelerated at rates that are sufficient to achieve clean conveyances of material from material conduits, e.g., without significant adherence or carryover of fluidic materials to material conduit surfaces proximal to dispense termini
- 25 (e.g., dispense tips, nozzles, etc.) of the material conduits. If the force from the acceleration is greater than the frictional force between the rollers and the conduit, the surfaces of the rollers and the conduit will slide across one another causing the material conduit to wear. This more gradual wear can also be minimized by giving the rollers an initial velocity that equals $-V_C$ by, e.g., the gear transmission mechanism described
- 30 above.

[0076] A peristaltic pump utilized in a system of the present invention typically generates sufficient material conveyance or flow rates at least proximal to a terminus a material conduit to effect non-contact material dispensing from the terminus. Non-contact dispensing minimizes the risk of cross-contaminating material sites, such as the wells disposed in multi-well plates. Moreover, non-contact material dispensing also typically enhances system throughput as material can be conveyed from material conduits "on-the-fly", such as when materials are dispensed as material conduits and material sites are moved relative to one another.

[0077] To convey uniformly sized quantities of material (e.g., uniform volumes of fluidic material in the range of about 0.1 to about 10 μ l, etc.), carryover, adherence, or wicking of material on outer surfaces of material conduits, e.g., proximal to dispense termini should avoided. For example, Figure 8 schematically shows a cross-sectional view of a volume of fluidic material **800** wicking or adhering to the tip of material conduit **802**. Such material wicking typically occurs when the quantity of material being conveyed from a conduit is at conveyance rates that are too low to prevent the material from adhering to outer surfaces of the conduit. Accordingly, the peristaltic pumps of the invention are optionally configured to decelerate at rates that are sufficient to "throw off", expel, or eject the selected quantity of the particular material being conveyed from material conduit termini without the material wicking on the outer surfaces of material conduit termini. To illustrate, Figure 9 is a graph (ordinate is velocity, V, and abscissa is time, t) that schematically illustrates a conduit tip velocity profile according to one embodiment of the invention. More specifically, Figure 9 depicts a generalized type of steep deceleration **900** that is utilized to expel aliquots of material from conduits without material wicking. To further illustrate, Figure 10 schematically depicts a cross-sectional view of volume of fluid **1000** being dispensed from a tip of material conduit **1002** without fluid wicking. In certain embodiments, for example, the moment of inertia of a roller support is minimized to prevent a quantity of material from adhering to an external portion of a material conduit when the peristaltic pump flows material through the material conduit. The moment of inertia can be minimized, for example, by minimizing the weight of the roller support. In addition, system controllers are typically configured to decelerate peristaltic pump drive motors at rates sufficient to prevent material wicking. Drive motors are described further below.

[0078] Peristaltic pumps that can be adapted for use in the systems of the invention are available from a wide variety of commercial suppliers including, e.g., ABO Industries Inc. (San Diego, CA, USA), Analox Instruments Ltd. (London, UK), ASF Thomas Industries GmbH (Puchheim, Germany), Barnant Co. (Barrington, IL, USA), Cole-Parmer Instrument Company (Vernon Hills, IL, USA), Fluid Metering Inc. (Syosset, NY, USA), Gorman-Rupp Industries (Bellville, OH, USA), I & J Fisnar Inc. (Fair Lawn, NJ, USA), Möller Feinmechanik GmbH & Co. (Fulda, Germany), PerkinElmer Instruments (Shelton, CT, USA), Terra Universal Inc. (Anaheim, CA, USA), and the like. Additional details relating to rotary pumps are described in, e.g., Karassik et al. (Eds.), Pump Handbook, The McGraw-Hill Companies (2000) and Nelik, Centrifugal and Rotary Pumps: Fundamentals with Applications, CRC Press (1999), which are both incorporated by reference.

IV. MOTION CONTROL

[0079] The motion control systems of the invention typically include matched components such as controllers, motor drives, motors, encoders and resolvers, user interfaces and software. Controllers, user interfaces, and software are described in greater detail below. Peristaltic pump drive motors generally include at least one position encoder and at least one gear reduction component. Exemplary motors utilized in the systems of the invention typically include, e.g., servo motors, stepper motors, or the like. In some embodiments, feedback components of the systems of the invention include at least one drive mechanism that is operably connected to the motor. The drive mechanism typically includes at least one control component that effects position feedback control of the motor.

[0080] As referred to above, the movement of peristaltic pump roller supports is typically effected by a motor operably connected to the pump. Exemplary motors that are optionally utilized in the systems of the invention include, e.g., DC servomotors (e.g., brushless or gear motor types), AC servomotors (e.g., induction or gearmotor types), stepper motors, linear motors, or the like. Servomotors typically have an output shaft that can be positioned by sending a coded signal to the motor. As the input to the motor changes, the angular position of the output shaft changes as well. Stepper motors generally use a magnetic field to move a rotor. Stepping can typically be performed in full step, half step, or other fractional step increments. Voltage is applied to poles

around the rotor. The voltage changes the polarity of each pole, and the resulting magnetic interaction between the poles and the rotor causes the rotor to move. To further illustrate, Figure 11 schematically illustrates a detailed perspective view of drive motor 306 that includes a position encoder and gear reduction from the material
5 conveying system of Figure 3.

[0081] The systems of the invention also generally include motor drives (e.g., AC motor drives, DC motor drives, servo drives, stepper drives, etc.), which act as interfaces between controllers and motors. In certain embodiments, motor drives include integrated motion control features. For example, servo drives typically provide
10 electrical drive output to servo motors in closed-loop motion control systems, where position feedback and corrective signals optimize position and speed accuracy. Servo drives with integrated motion control circuitry and/or software that accept feedback, provide compensation and corrective signals, and optimizes position, velocity, and acceleration. Figure 12 schematically shows X- and Y-axis linear motion table and
15 position feedback control drives 1200 according to one embodiment of the invention. X/Y-axis linear motion tables are described in greater detail below.

[0082] Suitable motors and motor drives are generally available from many different commercial suppliers including, e.g., Yaskawa Electric America, Inc. (Waukegan , IL, USA), AMK Drives & Controls, Inc. (Richmond, VA, USA),
20 Enprotech Automation Services (Ann Arbor, MI, USA), Aerotech, Inc. (Pittsburgh , PA, USA), Quicksilver Controls, Inc. (Covina , CA, USA), NC Servo Technology Corp. (Westland, MI, USA), HD Systems Inc. (Hauppauge , NY, USA), ISL Products International, Ltd. (Syosset , NY, USA), and the like. Additional detail relating to motors and motor drives are described in, e.g., Polka, Motors and Drives, ISA (2002)
25 and Hendershot et al., Design of Brushless Permanent-Magnet Motors, Magna Physics Publishing (1994), which are both incorporated by reference.

V. POSITIONING AND MOUNTING COMPONENTS

[0083] In some embodiments, the material conveying systems of the invention further include a positioning component that is operably connected to a controller.
30 Controllers are described in greater detail below. The positioning component is generally structured to moveably position material conduits and/or material sites

relative to one another. Positioning components typically include at least one object holder that is structured to support the material site (e.g., a multi-well plate, a substrate, etc.). In addition, the controller is typically configured to simultaneously effect rotation of the roller support and moveably position the material conduits and/or material sites
5 relative to one another such that the material volumes are conveyed to or from the material site synchronous with the relative movement of the material conduits and/or the material sites, e.g., to effect high throughput "on-the-fly" material dispensing.

[0084] For positioning along two different axes, the object holders of the invention generally have one or more alignment members positioned to receive, e.g.,
10 each of the two axes of a multi-well container. For example, Figure 13 shows a detailed perspective view of object holder 314 from material conveying system 300 of Figure 3. As shown, container station 1300 is disposed on support structure 1302 of object holder 314. Support structure 1302 supports vacuum plate 1304. Protrusions 1306 and 1308 function as alignment members. The illustrated embodiment of the
15 container station 1300 has two x-axis protrusions 1308 and one y-axis protrusion 1306 extending from support structure 1302. Accordingly, x-axis protrusions 1308 and y-axis protrusion 1306 are fixedly positioned relative to the vacuum plate 1304, which, in this embodiment, acts to hold a multi-well container in position once it has been positioned. X-axis locating protrusions 1308 are constructed to cooperate with an x-
20 axis surface of a multi-well container (e.g., a y-axis wall of a microtiter plate), while y-axis protrusion 1306 is constructed to cooperate with an y-axis surface of the container (e.g., a y-axis wall of a microtiter plate).

[0085] The alignment members can be, for example, locating pins, tabs, ridges, recesses, or a wall surface, and the like. In preferred embodiments, an alignment
25 member includes a curved surface that contacts a properly positioned multi-well container. The use of a curved surface minimizes the effect of, for example, roughness of the container surface that contacts the alignment member. The use of two alignment members along one axis and one alignment member along the second axis, as shown in Figure 13, is another approach to minimize the effect of surface irregularities on the
30 proper positioning of the container. The multi-well container contacts three points along the surface of the container, so proper alignment is not dependent upon the entire container surface being regular.

[0086] Certain embodiments of the invention apply specifically to the positioning of microtiter plates when used as the material sites. To illustrate, microtiter plate 1400 is shown in Figures 14A-C. As shown, microtiter plate 1400 comprises well area 1402 which has many individual sample wells for holding samples and reagents.

5 Microtiter plates are available in a wide variety of sample well configurations, including commonly available plates with 6, 12, 24, 48, 96, 192, 384, 768, 1536, or more wells. It will be appreciated that microtiter plates are available from a various manufacturers including, e.g., Greiner America Corp. (Lake Mary, FL, USA), Nalge Nunc International (Rochester, NY, USA), and the like. Microtiter plate 1400 has outer

10 wall 1404 having registration edge 1406 at its bottom. In addition, microtiter plate 1400 includes bottom surface 1408 below the well area on the plate's bottom side. Bottom surface 1408 is separated from outer wall 1404 by alignment member receiving area 1410. Alignment member receiving area 1410 is bounded by a surface of outer wall 1404 and by inner wall 1412 at the edge of bottom surface 1408. Although there

15 may be some lateral supports 1414 in alignment member receiving area 1410, these areas are generally open between inner wall 1412 and an inner surface of the outer wall 1404.

[0087] According to the invention, to position a microtiter plate the alignment members of the container station are optionally arranged to cooperate with inner wall

20 1412 of the microtiter plate. Inner wall 1412 is advantageously used, as inner wall 1412 is typically more accurately formed and is more closely associated with the perimeter of the sample well area, as compared to an outer wall of plate 1400, such as wall 1404. Accordingly, aligning an inner wall (e.g., inner wall 1412) of a microtiter plate relative to alignment members is generally preferred to aligning with an outer

25 wall, such as wall 1404. The increased positioning precision that is obtained by using an inner wall as the alignment surface makes possible the use of high-density microtiter plates, such as 1536-well plates. Further, by having the alignment members (e.g., alignment protrusions 1306 and 1308) cooperate with an inner wall 1412 of plate 1400, minimal structures are needed adjacent the outside of the plate. In such a manner, a

30 robotic arm or other transport device is able to readily access plate 1400. Having the protrusions positioned adjacent inner wall 1412 thereby facilitates translocating plate 1400. However, it will be appreciated that the alignment members or protrusions can be placed in alternative positions and still facilitate the precise positioning of the plate.

[0088] The object holders of the invention generally include one or more movable members. The movable members function to move a container against one or more alignment members. For example, once a multi-well container is placed in the general location of the alignment members, the movable members (termed "pushers" herein) move the container so that an alignment surface of the container is in contact with one or more of the alignment members of the positioning device. The positioning device can have pushers for positioning of the container along one or more axes. For example, a positioning device will often have one or more pushers that position a container along an x-axis, and one or more additional pushers that position the container along a y-axis. The pushers can be moved by means known to those of skill in the art. For example, air cylinders, springs, pistons, elastic members, electromagnets or other magnets, gear drives, and the like, or combinations thereof, are suitable for moving the pushers so as to move containers into a desired position.

[0089] One embodiment of a container station of an object holder having pushers for positioning a microtiter plate along both the x-axis and the y-axis is shown in Figure 13. When the microtiter plate is generally positioned adjacent the x- and y-axis protrusions, the bottom surface of the microtiter plate is directly above top surface 1310 of vacuum plate 1304. Y-axis pusher 1312, which extends through slot 1314 in support structure 1302, is used to apply pressure to a y-axis side wall of the microtiter plate. Sufficient force is applied to the plate to push the microtiter plate against y-axis protrusion 1306. When the microtiter plate is pushed against y-axis protrusion 1306, x-axis pusher 1318, which extends through slot 1320 of support structure 1302, is used to push an x-axis wall of the microtiter plate towards x-axis protrusions 1308. In this manner, the microtiter plate is accurately and precisely positioned relative both the x-axis and y-axis protrusions. It is sometimes advantageous, although not necessary, to have one or more of the pushers contact an inner wall of a microtiter plate rather than an outer wall. With this arrangement, the alignment members and pushers are underneath the microtiter plate. This leaves the area surrounding the exterior of the plate free of protrusions that could otherwise interfere with other devices that, for example, place the microtiter plate on the support.

[0090] As referred to above, the object holder embodiment shown in Figure 13 includes vacuum plate 1304 that functions as a retaining device to hold a properly

positioned container in a desired position. With both y-axis pusher **1312** and x-axis pusher **1318** applying sufficient force to precisely place the microtiter plate, a vacuum source (not shown) applies a vacuum through vacuum line **1322** into vacuum openings or holes **1324**. Air source (not shown) applies air pressure through an air line (not shown) to effect movement of the pushers.

[0091] In certain embodiments, positioning components also include X/Y-axis linear motion tables operably connected to position feedback control drives that control movement of the X/Y-axis linear motion tables along X- and Y-axes. In certain embodiments, linear motion tables are configured to move only along a single axis, such as an X-axis or a Y-axis. Typically, object holders are mounted on, e.g., X/Y-axis linear motion tables. As an example, Figure 3 schematically shows object holder **314** mounted on X/Y-axis linear motion table **320**. Positioning components also generally include Z-axis linear motion components that include material conduit support heads (see, e.g., material conduit support head **310** schematically shown in Figure 3) that supports portions of material conduits and that move along the Z-axis. The Z-axis linear motion components generally include a solenoid motor or the like to effect movement of the material conduit support heads along the z-axis. As described herein, positioning components are typically configured to move the material conduit support heads with sufficient velocity to eject adherent material that adheres to external portions of material conduits. In certain embodiments, Z-axis linear motion components also include material removal heads, e.g., mounted proximal to material conduit support heads. For example, certain material removal heads are configured to noninvasively remove materials from the wells of multi-well plates, e.g., to effect plate washing during certain applications. Material removal heads are typically structured to prevent cross-contamination among wells of multi-well plates as materials are removed from the plates. Additional details relating to material removal heads, systems and related methods, that are optionally adapted for use with the systems of the present invention are provided in, e.g., U.S. Provisional Pat. Appl. No. 60/461,638, entitled "MATERIAL REMOVAL DEVICES, SYSTEMS, AND METHODS," filed April 8, 2003 by Micklash II et al., which is incorporated by reference.

[0092] Various other positioning components or portions thereof can be utilized in the systems of the invention. In certain embodiments, for example, detectable

signals produced at material sites (e.g., multi-well plates, substrate surfaces, etc.) disposed on the object holders of the systems described herein are detected. In some of these embodiments, orifices are disposed through object holders to facilitate such detection. To further illustrate, object holders optionally comprise nests in which

5 multi-well plates or other material sites can be positioned in some embodiments of the invention. These or other types of object holders that can be utilized in the systems of the present invention are described in, e.g., International Publication No. WO 01/96880, entitled "AUTOMATED PRECISION OBJECT HOLDER," filed June 15, 2001 by Mainquist et al., U.S. Provisional Pat. Appl. No. 60/492,586, entitled

10 "MULTI-WELL CONTAINER POSITIONING DEVICES AND RELATED SYSTEMS AND METHODS," filed August 4, 2003 by Evans, and U.S. Provisional Pat. Appl. No. 60/492,629, entitled "NON-PRESSURE BASED FLUID TRANSFER IN ASSAY DETECTION SYSTEMS AND RELATED METHODS," filed August 4, 2003 by Evans et al., which are each incorporated by reference.

15 [0093] In some embodiments, the material conveying system further includes at least one mounting component that mounts at least the peristaltic pump, the feedback component, and the positioning component relative to one another. The mounting component is typically substantially rigid, e.g., fabricated from steel or other materials that can adequately support the other system components during operation of the

20 system.

VI. CLEANING COMPONENTS

[0094] The material conveying systems of the invention optionally also include cleaning components that are structured to clean material conduits (e.g., tips thereof), e.g., when positioning components move the material conduits at least proximal to the

25 cleaning components. As described above, for example, as fluidic materials are dispensed, some fluid typically wicks up the outer surface of material conduit tips. This generally leads to additional wicking if the adherent fluid is not removed from the tips, because as the surface finish of a tip becomes coated with fluid it tends to attract more fluid, e.g., during subsequent dispensing steps. Moreover, this also typically

30 leads to inaccurate quantities of material being dispensed, since wicked materials are not dispensed at the selected material sites and/or are dispensed at non-selected sites. This inaccuracy may be compounded when multiple quantities of material are

simultaneously dispensed from multiple material conduits, because material wicking tends to occur at different rates at the material conduit tips. Accordingly, wicked material is generally cleaned from material conduit tips, e.g., between dispensing steps using a cleaning component in certain embodiments of the invention.

- 5 [0095] In some embodiments, for example, cleaning components include vacuum chambers that comprise at least one orifice into or proximal to which the positioning component moves the material conduits such that an applied vacuum removes wicked or otherwise adherent material from external surfaces of the material conduits. Typically, outer cross-sectional dimensions of the material conduits are
10 smaller than cross-sectional dimensions of the orifices. To illustrate, Figure 15A schematically shows a partially transparent perspective view of vacuum chamber 1502 of cleaning component 1500 according to one embodiment of the invention. As shown, multiple orifices 1504 are disposed in cleaning component 1500 and communicate with outlet 1506, which is typically operably connected to a vacuum source (not shown).
15 Also shown is material conduit support head 1508 is disposed over cleaning component 1500. Orifices 1504 are structured to correspond to material conduit tips 1510 of material conduit support head 1508 such that material conduit tips 1510 can be lowered at least partially into orifices 1504 to effect removal of adherent materials from material conduit tips 1510 under an applied vacuum. Figure 15B schematically illustrates a
20 detailed cross-sectional view of material conduit tip 1510 disposed proximal to orifice 1504. Arrows 1512 represent the velocity of the air, V_A , flowing through orifice 1504. As material conduit tip 1510 is lowered into orifice 1504, the area of orifice 1504 is decreased such that V_A increases in the gap that remains between vacuum chamber 1502 and material conduit tip 1510 and pulls or otherwise removes adherent material
25 from the outer surfaces of material conduit tip 1510. Vacuum chambers are optionally disposed, e.g., on surfaces of object holders of the positioning components of the systems of the invention.

- [0096] As cross-sectional dimensions of vacuum chamber orifices decrease, the risk of contacting vacuum chambers and thereby damaging material conduit tips as the
30 tips are lowered into the orifices increases. Accordingly, compliant materials, such as certain tapes, are optionally disposed over the orifices of vacuum chambers having orifice cross-sectional dimensions that are too large to otherwise produce sufficiently

high V_A to remove adherent materials from material conduit tips when those tips are disposed in the orifices. The tape acts to seal the orifices. In these embodiments, as the tips are lowered, they puncture the tape creating holes that are typically slightly larger than that cross-sectional dimensions of the tips. Sufficiently high V_A can typically be
5 achieved through the gaps between the tips and edges of the holes in the tape to effect removal of adherent materials from the outer surfaces of the tips.

VII. MATERIAL CONDUITS

[0097] The material conduits used in the systems of the invention include various embodiments. In some embodiments, for example, a terminus of a material
10 conduit includes a tip (e.g., a tapered tip, such as a nozzle or the like) that is fabricated integral with the conduit or is connected to the conduit, e.g., via an insert. The size (e.g., internal cross-sectional dimension) of the material conduit (e.g., pump tubing, etc.) and/or tip utilized is typically dependent, at least in part, on, e.g., the desired dispense volume, the viscosity of the material being conveyed, and the like. Although
15 larger sizes are optionally utilized, cavities disposed through material conduits and/or tips typically include, e.g., cross-sectional dimensions of between about 100 μm and about 10^5 mm, more typically between about 500 μm and about 10^4 mm, and still more typically between about 1 mm and about 10^3 mm. Optionally, cavities disposed through material conduits or tips include at least two different cross-sectional
20 dimensions. In certain embodiments, cavities disposed through material conduits and/or tips include cross-sectional dimensions that differ from one another. Generally, the optimum tubing size (e.g., internal diameter) is such that it is large enough to allow the dispense volume to be delivered rapid enough to generate high velocities at the dispense tips, but small enough so that the angular displacement of the pump is
25 sufficiently large to make hysteresis and other mechanical/hydraulic variations nebulous. As described herein, when significantly high tip velocities are attained, the fluid or other material can be ejected at a distance great enough to allow dispensing without entering, e.g., the target well of a multi-well container with the dispenser tip. Moving the target material site or tip along the x- and y-axes synchronous with the
30 pump delivery timing produces an automated system for rapidly and accurately dispensing fluids at material sites. Pumps and X/Y-axis linear motion tables are described in greater detail above. Moreover, increasing the number of pump channels

and delivery tips to 2, 4, 8, 16, etc. correspondingly reduces the delivery times by 1/2, 1/4, 1/8, 1/16, etc., respectively.

[0098] To further illustrate, there are many instances where delicate living cells are dispensed into micro-well plates or other material sites. These cells can be
5 damaged by the shear forces associated with being forced through delivery tips with very small inside diameters (e.g., less than 200 μm). If the internal tip diameter utilized for dispensing these cells is so large that high tip velocities cannot be attained, the fluid may form a drop on the tip during the dispense cycle rather than forming a stream. Material wicking is also described above. In some embodiments of the invention,
10 accurate dispensing is further achieved by moving the tips down into the selected wells along the Z-axis far enough such that after the fluid is dispensed, the fluid level in the well will be slightly above the end of the delivery tips. This also allows the fluid to be dispensed into wells with smaller cross-sectional areas than fluid drops that would form on the tips during, e.g., a non-contact dispense condition. When the dispensing is
15 complete, the tips are raised and/or the material site is lowered along the Z-axis such that a wet touch off condition is created which eliminates any residual drops from forming on the delivery tips. Optionally, the tips are contacted with, e.g., dry sides of the wells to wick-off the droplets.

[0099] In certain embodiments, the systems of the invention are configured to
20 propel droplets, which are formed on the ends of dispense tips, off using mechanical inertia principals. In this configuration, the fluid is dispensed to form a droplet on the end of the dispense tip. At this point, the pump typically stops flowing material through the material conduits and the dispense tips are typically accelerated at a sufficient rate downward along the Z-axis to accelerate the drops without moving or
25 significantly deforming them. Once an adequate velocity is reached, dispense tips are rapidly decelerated to propel the droplets off the end of the dispense tips. The shapes of the moving droplets are typically more columnar, and with smaller diameters, than the original droplets formed on the tips. This allows the droplets to enter, e.g., wells with small cross-sectional areas. This approach provides another method for non-
30 contact dispensing.

[0100] In some embodiments, the systems of the invention generate initial positive pressure pulses followed by negative pressure pulses as described herein. The

negative pressure pulses are produced by large negative flow rate changes that occur at the end of a given dispense cycle to prevent droplets from forming on the tip. More specifically, at the start of a particular dispense cycle a high flow rate is typically achieved in a small amount of time, because the dispense volumes are generally small and the volume dispensed at low velocity is typically minimized. A large negative flow rate change typically occurs when the high flow rate is abruptly stopped. These abrupt flow rate changes, or pressure pulses, are transmitted from the pump to the dispense tip outlet as efficiently as possible to prevent the dispensing performance from being compromised. The flow path downstream of the pump roller support generally should not have any features that add accumulator or flow restricting properties to the fluid system. In some embodiments, for example, flow paths have the following attributes:

1. Minimal volume between the pump and the dispense tip;
2. Maximal tubing stiffness (e.g., 1/16" outer diameter fluorinated ethylene propylene (FEP) tubing, etc.) and minimized length of peristaltic tubing on the outlet side of the pump;
3. Optimized tubing connectors or inserts for connecting the peristaltic/FEP and FEP/dispense tip connections. Exemplary connections have the following attributes:
 - (i) greater stiffness than the tubing and tips;
 - (ii) constant internal cross-sectional dimensions with smooth walls;
 - (iii) similar internal cross-sectional dimensions for the tubing, tips, and inserts; and
 - (iv) lack compliant seals; and,
4. Tubing should be straight to within about 60 mm from the exit of the dispense tip.

[0101] To illustrate, Figures 16A-D schematically illustrate various material conduit tips according to certain embodiment of the invention. More specifically, Figure 16A schematically shows pump tubing 1600 and dispense tip 1602 connected to one another by being inserted into insert 1604. O-rings 1606 attach pump tubing 1600 and dispense tip 1602 to insert 1604. Figure 16B schematically shows pump tubing

1600 and dispense tip 1602 connected to one another by being inserted into insert 1608 (shown as a compliant sleeve). Figure 16C schematically depicts insert 1610 inserted into pump tubing 1600 and dispense tip 1602 to connect pump tubing 1600 and dispense tip 1602 to one another. Insert 1610 typically comprises greater stiffness than either pump tubing 1600 or dispense tip 1602. Figure 16D schematically illustrates pump tubing 1600 fabricated with an integral dispense tip.

[0102] Material conduits, tips, and inserts are optionally fabricated from a wide variety of materials. Exemplary materials used to fabricate material conduits include fluorinated ethylene propylene (FEP), polytetrafluoroethylene (PTFE), perfluoroalkoxy (PFA), autoprene, C-FLEX® (a styrene-ethylene-butylene (SEBS) modified block copolymer with silicone oil), NORPRENE® (a polypropylene-based material), PHARMED® (a polypropylene-based material), silicon, TYGON®, VITON® (includes a range of fluoropolymer elastomers), and the like. Material conduit tips and inserts can be fabricated from, e.g., various polymeric materials such as, polytetrafluoroethylene (TEFLON™), polypropylene, polystyrene, polysulfone, polyethylene, polymethylpentene, polydimethylsiloxane (PDMS), polycarbonate, polyvinylchloride (PVC), polymethylmethacrylate (PMMA), and the like. Material conduit tips and inserts are also optionally fabricated from other materials including glass and various metals. Materials for fabricating material conduits, tips, and inserts are typically readily available from many different commercial suppliers including, e.g., Saint-Gobain Performance Plastics (Garden Grove, CA, USA), DuPont Dow Elastomers L.L.C. (Wilmington, DE, USA), and the like.

VIII. MATERIAL SITES

[0103] The systems and methods of the present invention can be adapted for use with essentially any type of material site. Typical material sites used in the systems of the invention include material containers, substrate surfaces, and the like. Exemplary material containers include multi-well material containers, such as micro-well plates, reaction blocks, and other containers used, e.g., to perform multiple assays, synthesis reactions, or other processes in parallel. Multi-well material containers such as these typically include, e.g., 6, 12, 24, 48, 96, 192, 384, 768, 1536, or more wells, and are generally available from various commercial suppliers including, e.g., Greiner America Corp. (Lake Mary, FL, USA), Nalge Nunc International (Rochester, NY, USA), H+P

Labortechnik AG (Oberschleißheim, Germany), and the like. Additional details relating to reaction blocks that are suitable for use in the systems of the invention are provided in, e.g., International Publication No. WO 03/020426, entitled "PARALLEL REACTION DEVICES," filed September 5, 2002 by Micklash II, et al., which is

5 incorporated by reference.

[0104] To further illustrate, the systems of the invention are also optionally configured to dispense material on substrate surfaces. For example, the systems described herein can be utilized to produce dot arrays or the like on substrate surfaces at various different densities. Arrayed materials are commonly used in, e.g., clinical testing (e.g., blood cholesterol tests, blood glucose tests, pregnancy tests, ovulation tests, etc.) in addition to many other applications known in the art. Essentially any substrate material is optionally adapted for use with the systems of the invention. In certain embodiments, for example, substrates are fabricated from silicon, glass, or polymeric materials (e.g., glass or polymeric microscope slides, silicon wafers, etc.).

10 Suitable glass or polymeric substrates, including microscope slides, are available from various commercial suppliers, such as Fisher Scientific (Pittsburgh, PA, USA) or the like. Optionally, substrates utilized in the systems of the invention are membranes. Suitable membrane materials are optionally selected from, e.g. polyaramide membranes, polycarbonate membranes, porous plastic matrix membranes (e.g.,

20 POREX® Porous Plastic, etc.), porous metal matrix membranes, polyethylene membranes, poly(vinylidene difluoride) membranes, polyamide membranes, nylon membranes, ceramic membranes, polyester membranes, polytetrafluoroethylene (TEFLON™) membranes, woven mesh membranes, microfiltration membranes, nanofiltration membranes, ultrafiltration membranes, dialysis membranes, composite

25 membranes, hydrophilic membranes, hydrophobic membranes, polymer-based membranes, a non-polymer-based membranes, powdered activated carbon membranes, polypropylene membranes, glass fiber membranes, glass membranes, nitrocellulose membranes, cellulose membranes, cellulose nitrate membranes, cellulose acetate membranes, polysulfone membranes, polyethersulfone membranes, polyolefin

30 membranes, or the like. Many of these membranous materials are widely available from various commercial suppliers, such as, P.J. Cobert Associates, Inc. (St. Louis, MO, USA), Millipore Corporation (Bedford, MA, USA), or the like.

IX. CONTROLLERS, COMPUTER PROGRAM PRODUCTS, AND ADDITIONAL SYSTEM COMPONENTS

[0105] The controllers of the automated systems of the present invention are generally configured to effect substantially identical roller disengagements from
5 material conduits for each conveyed quantity of material to minimize periodic variation among the conveyed quantities of material. Controllers are typically operably connected to one or more system components, such as motors (e.g., via motor drives), positioning components (e.g., X/Y-axis linear motion tables, Z-axis motion
10 components, etc.), cleaning components, detectors, fluid sensors, robotic translocation devices, or the like, to control operation of these components. More specifically, controllers are generally included either as separate or integral system components that are utilized, e.g., to effect roller support rotation in selected rotational increments, the movement of positioning components, the detection and/or analysis of detectable signals received from sample containers by detectors, etc. Controllers and/or other
15 system components is/are optionally coupled to an appropriately programmed processor, computer, digital device, or other logic device or information appliance (e.g., including an analog to digital or digital to analog converter as needed), which functions to instruct the operation of these instruments in accordance with preprogrammed or user input instructions (e.g., material conduit cross-sectional dimensions, rotational
20 increments, volumes to be conveyed, etc.), receive data and information from these instruments, and interpret, manipulate and report this information to the user.

[0106] A controller or computer optionally includes a monitor which is often a cathode ray tube ("CRT") display, a flat panel display (e.g., active matrix liquid crystal display, liquid crystal display, etc.), or others. Computer circuitry is often placed in a
25 box, which includes numerous integrated circuit chips, such as a microprocessor, memory, interface circuits, and others. The box also optionally includes a hard disk drive, a floppy disk drive, a high capacity removable drive such as a writeable CD-ROM, and other common peripheral elements. Inputting devices such as a keyboard or mouse optionally provide for input from a user. An exemplary system comprising a
30 computer is schematically illustrated in Figure 17.

[0107] The computer typically includes appropriate software for receiving user instructions, either in the form of user input into a set of parameter fields, e.g., in a

GUI, or in the form of preprogrammed instructions, e.g., preprogrammed for a variety of different specific operations. The software then converts these instructions to appropriate language for instructing the operation of one or more controllers to carry out the desired operation, e.g., varying or selecting the rate or mode of movement of various system components, directing translation of positioning components, or the like. The computer then receives the data from, e.g., sensors/detectors included within the system, and interprets the data, either provides it in a user understood format, or uses that data to initiate further controller instructions, in accordance with the programming, e.g., such as in monitoring detectable signal intensity, multi-well container positioning, or the like.

[0108] More specifically, the software utilized to control the operation of the systems of the invention typically includes logic instructions that direct, e.g., the system to convey material (e.g., fluidic material) to material sites, the pushers of an object holder of a positioning component to push containers into contact with alignment members when the containers are positioned on the object holder, a robotic handling device to translocate containers, and/or the like. To further illustrate, the invention provides control software, or computer program products that include computer readable media, having one or more logic instructions for receiving one or more input parameters selected from the group consisting of: (i) a rotational increment that substantially corresponds to an integral multiple of an angular distance disposed between adjacent rollers supported by a roller support of a peristaltic pump; (ii) a cross-sectional dimension of a material conduit; (iii) a quantity of material to be conveyed to or from a material site; and (iv) an angular distance disposed between adjacent rollers supported by a roller support of a peristaltic pump. The software or computer program product also includes one or more logic instructions for rotating a roller support of a peristaltic pump in rotational increments that substantially correspond to integral multiples of an angular distance disposed between adjacent rollers supported by the roller support of the peristaltic pump such that when one or more material conduits are operably connected to the peristaltic pump and the peristaltic pump conveys material through the material conduits, quantities of material that correspond to the rotational increments are conveyed to or from material sites. In certain embodiments, the software or computer program product further includes at least one logic instruction for moving an X/Y-axis linear motion table and a Z-axis motion component synchronous

with rotating the roller support. The computer readable medium of, e.g., the computer program product optionally includes one or more of: a CD-ROM, a floppy disk, a tape, a flash memory device or component, a system memory device or component, a hard drive, a data signal embodied in a carrier wave, or the like.

- 5 **[0109]** The computer can be, e.g., a PC (Intel x86 or Pentium chip-compatible DOS™, OS2™, WINDOWS™, WINDOWS NT™, WINDOWS95™, WINDOWS98™, WINDOWS2000™, WINDOWS XP™, LINUX-based machine, a MACINTOSH™, Power PC, or a UNIX-based (e.g., SUN™ work station) machine) or other common commercially available computer which is known to one of skill.
- 10 Standard desktop applications such as word processing software (e.g., Microsoft Word™ or Corel WordPerfect™) and database software (e.g., spreadsheet software such as Microsoft Excel™, Corel Quattro Pro™, or database programs such as Microsoft Access™ or Paradox™) can be adapted to the present invention. Software for performing, e.g., material conveyance to selected wells of a multi-well plate, assay
- 15 detection, and data deconvolution is optionally constructed by one of skill using a standard programming language such as Visual basic, C, C++, Fortran, Basic, Java, or the like.

- [0110]** The automated systems of the invention are optionally further configured to detect and quantify absorbance, transmission, and/or emission (e.g.,
- 20 luminescence, fluorescence, etc.) of light, and/or changes in those properties in samples that are arrayed in the wells of a multi-well container, on a substrate surface, or at other material sites. Alternatively, or simultaneously, detectors can quantify any of a variety of other signals from multi-well containers or other material sites including chemical signals (e.g., pH, ionic conditions, or the like), heat (e.g., for monitoring endothermic or
- 25 exothermic reactions, e.g., using thermal sensors) or any other suitable physical phenomenon. In addition to other system components described herein, the material conveying systems of the invention optionally also include illumination or electromagnetic radiation sources, optical systems, and detectors. Because the systems and methods of the invention are flexible and allow essentially any chemistry to be
- 30 assayed, they can be used for all phases of assay development, including prototyping and mass screening.

[0111] In some embodiments, the systems of the invention are configured for area imaging, but can also be configured for other formats including as a scanning imager or as a nonimaging counting system. An area imaging system typically places an entire multi-well container or other specimen onto the detector plane at one time.

5 Accordingly, there is typically no need to move photomultiplier tubes (PMTs), to scan a laser, or the like, because the detector images the entire container onto many small detector elements (e.g., charge-coupled devices (CCDs), etc.) in parallel. This parallel acquisition phase is typically followed by a serial process of reading out the entire image from the detector. Scanning imagers typically pass a laser or other light beam

10 over the specimen, to excite fluorescence, reflectance, or the like in a point-by-point or line-by-line fashion. In certain cases, confocal-optics are used to minimize out of focus fluorescence. The image is constructed over time by accumulating the points or lines in series. Nonimaging counting systems typically use PMTs or light sensing diodes to detect alterations in the transmission or emission of light, e.g., within wells of a multi-

15 well container. These systems then typically integrate the light output from each well into a single data point.

[0112] A wide variety of illumination or electromagnetic sources and optical systems can be adapted for use in the systems of the present invention. Accordingly, no attempt is made herein to describe all of the possible variations that can be utilized

20 in the systems of the invention and which will be apparent to one skilled in the art. Exemplary electromagnetic radiation sources that are optionally utilized in the systems of the invention include, e.g., lasers, laser diodes, electroluminescence devices, light-emitting diodes, incandescent lamps, arc lamps, flash lamps, fluorescent lamps, and the like. One preferred type of laser used in the assaying systems of the invention are

25 argon-ion lasers. Exemplary optical systems that conduct electromagnetic radiation from electromagnetic radiation sources to sample containers and/or from multi-well containers to detectors typically include one or more lenses and/or mirrors to focus and/or direct the electromagnetic radiation as desired. Many optical systems also include fiber optic bundles, optical couplers, filters (e.g., filter wheels, etc.), and the

30 like.

[0113] Suitable signal detectors that are optionally utilized in these systems detect, e.g., emission, luminescence, transmission, fluorescence, phosphorescence,

absorbance, or the like. In some embodiments, the detector monitors a plurality of optical signals, which correspond in position to "real time" results. Example detectors or sensors include PMTs, CCDs, intensified CCDs, photodiodes, avalanche photodiodes, optical sensors, scanning detectors, or the like. Each of these as well as
5 other types of sensors is optionally readily incorporated into the systems described herein. The detector optionally moves relative to material sites, such as multi-well plates or other assay components, or alternatively, multi-well plates or other assay components move relative to the detector. In certain embodiments, for example, detection components are coupled to translation components that move the detection
10 components relative to material sites positioned on container positioning devices of the systems described herein. Optionally, the systems of the present invention include multiple detectors. In these systems, such detectors are typically placed either in or adjacent to, e.g., a multi-well plate or other vessel, such that the detector is in sensory communication with the multi-well plate or other vessel (i.e., the detector is capable of
15 detecting the property of the plate or vessel or portion thereof, the contents of a portion of the plate or vessel, or the like, for which that detector is intended). In certain embodiments, detectors are configured to detect electromagnetic radiation originating in the wells of a multi-well container.

[0114] The detector optionally includes or is operably linked to a computer,
20 e.g., which has system software for converting detector signal information into assay result information or the like. For example, detectors optionally exist as separate units, or are integrated with controllers into a single instrument. Integration of these functions into a single unit facilitates connection of these instruments with the computer, by permitting the use of a few or even a single communication port for
25 transmitting information between system components. Detection components that are optionally included in the systems of the invention are described further in, e.g., Skoog et al., Principles of Instrumental Analysis, 5th Ed., Harcourt Brace College Publishers (1998) and Currell, Analytical Instrumentation: Performance Characteristics and Quality, John Wiley & Sons, Inc. (2000), which are both incorporated by reference.

30 [0115] The systems of the invention optionally also include at least one robotic translocation or gripping component that is structured to grip and translocate material sites, such as multi-well plates between components of the automated systems and/or

between the systems and other locations (e.g., other work stations, etc.). In certain embodiments, for example, systems further include gripping components that move multi-well plates between positioning components, incubation or storage components, etc. A variety of available robotic elements (robotic arms, movable platforms, etc.) can
5 be used or modified for use with these systems, which robotic elements are typically operably connected to controllers that control their movement and other functions. Exemplary robotic gripping devices that are optionally adapted for use in the systems of the invention are described further in, e.g., U.S. Pat. No. 6,592,324, entitled
10 "GRIPPER MECHANISM," issued July 15, 2003 to Downs et al., and International Publication No. WO 02/068157, entitled "GRIPPING MECHANISMS, APPARATUS, AND METHODS," filed February 26, 2002 by Downs et al., which are both incorporated by reference.

[0116] Figure 17 is a schematic showing a representative example material removal system including an information appliance in which various aspects of the
15 present invention may be embodied. As will be understood by practitioners in the art from the teachings provided herein, the invention is optionally implemented in hardware and software. In some embodiments, different aspects of the invention are implemented in either client-side logic or server-side logic. As will also be understood in the art, the invention or components thereof may be embodied in a media program
20 component (e.g., a fixed media component) containing logic instructions and/or data that, when loaded into an appropriately configured computing device, cause that apparatus or system to perform according to the invention. As will additionally be understood in the art, a fixed media containing logic instructions may be delivered to a viewer on a fixed media for physically loading into a viewer's computer or a fixed
25 media containing logic instructions may reside on a remote server that a viewer accesses through a communication medium in order to download a program component.

[0117] Figure 17 shows information appliance or digital device 1700 that may be understood as a logical apparatus (e.g., a computer, etc.) that can read instructions
30 from media 1717 and/or network port 1719, which can optionally be connected to server 1720 having fixed media 1722. Information appliance 1700 can thereafter use those instructions to direct server or client logic, as understood in the art, to embody

aspects of the invention. One type of logical apparatus that may embody the invention is a computer system as illustrated in 1700, containing CPU 1707, optional input devices 1709 and 1711, disk drives 1715 and optional monitor 1705. Fixed media 1717, or fixed media 1722 over port 1719, may be used to program such a system and
5 may represent a disk-type optical or magnetic media, magnetic tape, solid state dynamic or static memory, or the like. In specific embodiments, the aspects of the invention may be embodied in whole or in part as software recorded on this fixed media. An exemplary computer program product is described further above. Communication port 1719 may also be used to initially receive instructions that are
10 used to program such a system and may represent any type of communication connection. Optionally, aspects of the invention are embodied in whole or in part within the circuitry of an application specific integrated circuit (ACIS) or a programmable logic device (PLD). In such a case, aspects of the invention may be embodied in a computer understandable descriptor language, which may be used to
15 create an ASIC, or PLD. Figure 17 also includes material conveying system 300, which is operably connected to information appliance 1700 via server 1720. Optionally, material conveying system 300 is directly connected to information appliance 1700. During operation, material conveying system 300 typically conveys materials to and/or from selected material sites on a positioning component of material
20 conveying system 300, e.g., as part of an assay or other process. Figure 17 also shows detector 1724, which is optionally included in the systems of the invention. As shown, detector 1724 is operably connected to information appliance 1700 via server 1720. In some embodiments, detector 1724 is directly connected to information appliance 1700. In certain embodiments, detector 1724 is configured to detect detectable signals
25 produced at material sites positioned on the positioning component of material conveying system 300. In other embodiments, material sites (e.g., multi-well containers, etc.) are transferred (e.g., manually or using a robotic translocation device) to detector 1724 before and/or after material is conveyed to and/or from the material sites on the positioning component of material conveying system 300.

30 X. SYSTEM COMPONENT FABRICATION

[0118] System components (e.g., positioning components, cleaning components, etc.) are optionally formed by various fabrication techniques or

- combinations of such techniques including, e.g., machining, stamping, engraving, injection molding, cast molding, embossing, extrusion, etching (e.g., electrochemical etching, etc.), or other techniques. These and other suitable fabrication techniques are generally known in the art and described in, e.g., Altintas, Manufacturing Automation: Metal Cutting Mechanics, Machine Tool Vibrations, and CNC Design, Cambridge University Press (2000), Molinari et al. (Eds.), Metal Cutting and High Speed Machining, Kluwer Academic Publishers (2002), Stephenson et al., Metal Cutting Theory and Practice, Marcel Dekker (1997), Rosato, Injection Molding Handbook, 3rd Ed., Kluwer Academic Publishers (2000), Fundamentals of Injection Molding, W. J. T. Associates (2000), Whelan, Injection Molding of Thermoplastics Materials, Vol. 2, Chapman & Hall (1991), Fisher, Extrusion of Plastics, Halsted Press (1976), and Chung, Extrusion of Polymers: Theory and Practice, Hanser-Gardner Publications (2000), which are each incorporated by reference. In certain embodiments, following fabrication, system components are optionally further processed, e.g., by coating surfaces with a hydrophilic coating, a hydrophobic coating (e.g., a Xylan 1010DF/870 Black coating available from Whitford Corporation (West Chester, PA), etc.), or the like, e.g., to prevent interactions between component surfaces and reagents, samples, or the like.

XI. MATERIAL CONVEYING METHODS

- [0119] In addition to the systems and computer program products described herein, the invention also relates to methods of conveying material. For example, one method includes conveying material (e.g., a cell suspension, a reagent, a buffer, a solid support suspension, etc.) through one or more material conduits of a system described herein in which the controller effects rotation of the roller support in at least one rotational increment that substantially corresponds to an integral multiple of an angular distance disposed between adjacent rollers supported by the roller support such that quantities of material conveyed to or from a material site correspond to the rotational increment. Essentially any rotational increment can be selected including, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, 50, or more times an angular distance disposed between adjacent rollers of a given roller support. As described herein, the controller typically effects rotation of the roller support such that shearing effects on the conveyed material (e.g., cells or the like) are minimized. The controller generally effects

substantially identical roller disengagements from material conduits for each conveyed quantity of material, e.g., to minimize periodic variation among the conveyed quantities of material. Further, identical rotational increments generally convey substantially uniform material volumes to or from material sites. Moreover, the rotational
5 increments utilized as described herein are typically uncompensated for flow rate characteristics of the particular system. This simplifies the implementation of the systems and methods of the invention relative to many pre-existing approaches.

[0120] In some embodiments, material is conveyed to material sites without material conduits contacting the material site (i.e., non-contact material dispensing).
10 For example, these methods optionally include effecting negative pressure pulses proximal to termini of material conduits with the controller after effecting rotation of the roller support in the selected rotational increment, e.g., to prevent quantities of material from adhering to external portions of material conduits. Optionally, the methods include moving material conduits with sufficient velocity to eject adherent
15 material that adheres to external portions of the material conduits, e.g., to convey the material to a material site or to clean the external portions of the material conduits. In some embodiments, the methods include contacting adherent material that adheres to external portions of material conduits with another object (e.g., the edge of a well of a multi-well container, etc.) to remove the adherent material from the external portions of
20 the material conduits.

[0121] As described herein, material sites optionally comprise multi-well containers (e.g., microtiter plates, etc.). In these embodiments, methods of conveying material optionally include conveying a first quantity of material into a first well of a multi-well container, moving a material conduit and/or the multi-well container relative
25 to one another, e.g., with the positioning component such that the multi-well container is in communication with a second well of the multi-well container, conveying a second quantity of material into the second well of the multi-well container, and so forth. The moving and conveying steps are typically substantially simultaneous with one another, e.g., to effect "on-the-fly" material dispensing.

30 [0122] Other methods of the invention include conveying material through a material conduit such that a quantity of the material adheres to a terminal portion of the material conduit to form an adherent quantity of material. Thereafter, these methods

also generally include accelerating at least the terminal portion of the material conduit towards the material site, and decelerating the terminal portion of the material conduit such that the adherent quantity of material is conveyed (e.g., ejected) from the terminal portion of the material conduit to the material site.

- 5 [0123] Essentially any biochemical or cellular assay, or synthesis reaction, can be adapted for performance in the systems and according to the methods of the invention. To illustrate, common types of assays performed in, e.g., multi-well plates include those relating to signal transduction, cell adhesion, apoptosis, cell migration, GPCR, cell permeability, receptor/ligand binding, intracellular calcium flux, membrane potential, nucleic acid hybridization, cell growth/proliferation, among many others that are known in the art. Additional details relating to certain of these and other assays involving multi-well plates are described in, e.g., Parker et al. (2000) "Development of high throughput screening assays using fluorescence polarization: nuclear receptor-ligand binding and kinase/phosphatase assays," J. Biomolecular Screening 5(2):77-88, 10 Asa (2001) "Automating cell permeability assays," Screening 1:36-37, Norrington (1999) "Automation of the drug discovery process," Innovations in Pharmaceutical Technology 1(2):34-39, Fukushima et al. (2001) "Induction of reduced endothelial permeability to horseradish peroxidase by factor(s) of human astrocytes and bladder carcinoma cells: detection in multi-well plate culture," Methods Cell Sci. 23(4):211-9, 15 Neumayer (1998) "Fluorescence ELISA, a comparison between two fluorogenic and one chromogenic enzyme substrate," BPI 10(Nr. 5), Graeff et al. (2002) "A novel cycling assay for nicotinic acid-adenine dinucleotide phosphate with nanomolar sensitivity," Biochem J. 367(Pt 1):163-8, Rogers et al. (2002) "Fluorescence detection of plant extracts that affect neuronal voltage-gated Ca^{2+} channels," Eur. J. Pharm. Sci. 25 15(4):321-30, and Rappaport et al. (2002) "New perfluorocarbon system for multilayer growth of anchorage-dependent mammalian cells," Biotechniques 32(1):142-51, which are each incorporated by reference. Additional details relating to various methods that are optionally performed using the systems of the present invention are also described in, e.g., U.S. Patent Application No. 60/492,629, entitled "NON-PRESSURE BASED FLUID TRANSFER IN ASSAY DETECTION SYSTEMS AND RELATED METHODS," filed August 4, 2003 by Evans et al., which is incorporated by reference. 30

XII. EXAMPLE

[0124] It is understood that the example and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and scope of the appended claims.

[0125] This example illustrates various dispenses using an 8 tip system in which the peristaltic pump had a roller support that supported 12 rollers in which the angular distance disposed between each pair of adjacent rollers was 30°. Figure 18A shows a series of dispenses in which the system was set to an angular displacement of 12° per dispense. As shown, it is apparent that there was a repeating pattern of varying dispense volumes. In fact, some dispense volumes were essentially zero. Figure 18B shows a series of dispenses in which the system was set to an angular displacement of 18° per dispense. While there were no zero volume dispenses, periodic variation in dispense volumes was still observed. Figure 18C shows a series of dispenses in which the system was set to an angular displacement of 30° per dispense. As shown, there was essentially no variation in dispense volumes at this angular displacement setting. As the angular distance disposed between each pair of adjacent rollers was 30° for this system, rotational increments that are integral multiples of 30° are typically optimal for this system. Figure 18D shows a series of dispenses in which the system was set to an angular displacement of 42° per dispense. While the percentage variation between dispenses may have expected to be less due to the higher dispense volumes, close examination of the droplet sizes shows that, once again, periodic variation was present.

[0126] While the foregoing invention has been described in some detail for purposes of clarity and understanding, it will be clear to one skilled in the art from a reading of this disclosure that various changes in form and detail can be made without departing from the true scope of the invention. For example, all the techniques and apparatus described above can be used in various combinations. All publications, patents, patent applications, and/or other documents cited in this application are incorporated by reference in their entirety for all purposes to the same extent as if each individual publication, patent, patent application, and/or other document were individually indicated to be incorporated by reference for all purposes.

CLAIMS

WHAT IS CLAIMED IS:

1. A material conveying system, comprising:
 - at least one peristaltic pump having a rotatable roller support that
 - 5 supports at least two rollers;
 - at least one motor that is operably connected to the peristaltic pump to rotate the roller support; and,
 - at least one controller that is operably connected to the motor, which controller is configured to effect rotation of at least the roller support in at least one
 - 10 rotational increment that substantially corresponds to an integral multiple of an angular distance disposed between adjacent rollers supported by the roller support such that when one or more material conduits are operably connected to the peristaltic pump and the peristaltic pump conveys material through the material conduits, quantities of material that correspond to the rotational increment are conveyed to or from at least one
 - 15 material site.
2. The material conveying system of claim 1, wherein identical rotational increments convey substantially uniform quantities of material to or from the material site.
3. The material conveying system of claim 1, wherein the rotational increment
- 20 is uncompensated for flow rate characteristics of the system.
4. The material conveying system of claim 1, further comprising:
 - at least one detector operably connected to the controller, which detector is configured to detect detectable signals produced at one or more material sites.
5. The material conveying system of claim 1, further comprising:
- 25 at least one material conduit that is operably connected to the peristaltic pump.
6. The material conveying system of claim 5, wherein the controller is configured to effect substantially identical roller disengagements from the material conduit for each conveyed quantity of material to minimize periodic variation among
- 30 the conveyed quantities of material.

7. The material conveying system of claim 1, further comprising:

at least one positioning component that is operably connected to the controller, which positioning component is structured to moveably position at least one material conduit and/or one or more material sites relative to one another.

5 8. The material conveying system of claim 7, wherein the positioning component comprises at least one object holder that is structured to support the material sites.

9. The material conveying system of claim 7, further comprising the material conduit operably connected to the positioning component and to the peristaltic pump.

10 10. The material conveying system of claim 7, further comprising:
at least one cleaning component operably connected to the controller, which cleaning component is structured to clean the material conduit when the material conduit is operably connected at least to the positioning component, and the positioning component moves the material conduit at least proximal to the cleaning component.

15 11. The material conveying system of claim 7, further comprising:
at least one mounting component that mounts at least the peristaltic pump, the motor, and the positioning component relative to one another.

12. The computer program product of claim 1, further comprising at least one logic instruction for:

20 moving an X/Y-axis linear motion table and a Z-axis motion component synchronous with rotating the roller support.

25

30