DEVICE, SYSTEM AND METHOD FOR ISOLATING A BIOLOGICAL MATERIAL

TECHNICAL FIELD

[0001] The present disclosure relates broadly, but not exclusively, to devices, systems and methods for isolating a biological material, such as a nucleic acid.

BACKGROUND

[0002] Nucleic acid isolation is the first step that needs to be performed for many modern genomics techniques and applications. After lysis of cells, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) need to be isolated and purified for subsequent downstream processing and analysis, such as PCR and sequencing.

[0003] Automated nucleic acid extraction systems have the potential to improve workflow and decrease variability in the basic research as well as in the clinical laboratory. While many automated systems are commercially available, most of the systems are based on automatic liquid handling technology that involves pipetting and dispensing of samples and bio-reagents, which can be prone to cross-contamination and require vigorous maintenance such as pre- and post- clean-up by end-users.

[0004] A need therefore exists to provide devices, systems and methods that can address at least some of the above problems.

SUMMARY

[0005] An aspect of the present disclosure provides a device for isolating a biological material from a sample. The device comprises a housing defining a plurality of compartments and a plurality of fluid channels, wherein each compartment is configured to be fluidically connected to a respective fluid channel, and wherein each fluid channel comprises a respective end terminating at a track

disposed on the housing; a slider movable along the track, the slider comprising a plurality of connecting channels extending therethrough, wherein a selected one of the connecting channels is configured to connect ends of selected ones of the fluid channels based on a position of the slider along the track; and a dry reagent capsule configured to be mounted to the housing, the dry reagent capsule comprising at least one dry reagent for mixing with the sample, wherein the dry reagent capsule is further configured to be fluidically connected to a respective fluid channel *in-situ*.

[0006] The housing may comprise a first housing member securely joined to a second housing member, and the first housing member may comprise grooves arranged to form the respective fluid channels.

[0007] The plurality of compartments may comprise a sample compartment configured to receive the sample, a plurality of liquid reagent compartments and a waste compartment.

[0008] Each of the sample and liquid reagent compartments may comprise a respective inlet configured to be connected to pneumatic source for controlling a fluid flow to or from said compartment.

[0009] The device may further comprise a first pneumatic vent disposed in one of the liquid reagent compartments and a second pneumatic vent disposed in the waste compartment.

[0010] The plurality of liquid reagent compartments may be preloaded with respective liquid reagents.

[0011] In a first position, the slider may be configured to connect a first liquid reagent compartment containing a hydration buffer with a first chamber of the dry reagent capsule, the first chamber containing a first dry reagent, for mixing the hydration buffer with the first dry reagent to form a first solution.

[0012] In a second position, the slider may be configured to connect the first liquid reagent compartment with a second liquid reagent compartment containing a lysis buffer, for mixing the first solution with the lysis buffer to form a second solution.

[0013] In a third position, the slider may be configured to:

connect the second liquid reagent compartment with a second chamber of the dry reagent capsule, the second chamber containing a second dry reagent, for mixing the second solution with the second dry reagent to form a third solution; and

connect the second chamber of the dry reagent capsule with the sample compartment for mixing the third solution with the sample to form a fourth solution.

[0014] The fluid channels may comprise a binding channel, and in a fourth position, the slider may be configured to connect the sample compartment with the binding channel to store the fourth solution in the binding channel for a predetermined period for extracting the biological material from the fourth solution and binding the extracted biological material to a surface of the binding channel.

[0015] In a fifth position, the slider may be configured to:

connect a third liquid reagent compartment containing a first wash buffer with the binding channel to wash the biological material bound to the surface of the binding channel; and

connect the binding channel with the waste compartment for discarding a first waste solution without the biological material to the waste compartment.

[0016] In a sixth position, the slider may be configured to:

connect a fourth liquid reagent compartment containing a second wash buffer with the binding channel to wash the biological material bound to the surface of the binding channel; and

connect the binding channel with the waste compartment for discarding a second waste solution without the biological material to the waste compartment.

[0017] In a seventh position, the slider may be configured to:

connect a fifth liquid reagent compartment containing an elution buffer with the binding channel to elute the biological material from the surface of the binding channel; and

connect the binding channel with an outlet for collecting the eluted biological material.

[0018] In an alternate first position, the slider is configured to:

connect a first liquid reagent compartment containing a lysis buffer with a chamber of the dry reagent capsule, the chamber containing the at least one dry

reagent, for mixing the lysis buffer with the at least one dry reagent to form a reagent solution; and

connect the chamber of the dry reagent capsule with the sample compartment for mixing the reagent solution with the sample to form a sample solution.

[0019] The fluid channels may comprise a binding channel, and in an alternate second position, the slider may be configured to connect the sample compartment with the binding channel to store the sample solution in the binding channel for a predetermined period for extracting the biological material from the sample solution and binding the extracted biological material to a surface of the binding channel.

[0020] In an alternate third position, the slider may be configured to:

connect a second liquid reagent compartment containing a first wash buffer with the binding channel to wash the biological material bound to the surface of the binding channel; and

connect the binding channel with the waste compartment for discarding a first waste solution without the biological material to the waste compartment.

[0021] In an alternate fourth position, the slider may be configured to:

connect a third liquid reagent compartment containing a second wash buffer with the binding channel to wash the biological material bound to the surface of the binding channel; and

connect the binding channel with the waste compartment for discarding a second waste solution without the biological material to the waste compartment.

[0022] In an alternate fifth position, the slider may be configured to:

connect a fourth liquid reagent compartment containing a third wash buffer with the binding channel to wash the biological material bound to the surface of the binding channel; and

connect the binding channel with the waste compartment for discarding a third waste solution without the biological material to the waste compartment.

[0023] In an alternate sixth position, the slider may be configured to:

connect a fifth liquid reagent compartment containing an elution buffer with the binding channel to elute the biological material from the surface of the binding channel; and

connect the binding channel with an outlet for collecting the eluted biological material.

[0024] The at least one dry reagent may comprise lyophilized beads containing a crosslinker selected to attach to the biological material, and the surface of the binding channel may be coated with a functional group selected to attach to the crosslinker.

[0025] The biological material may comprise a nucleic acid.

[0026] Another aspect of the disclosure provides an automated biological material extraction system comprising:

a receptacle configured to receive the device as described above;

a pressure source configured to control a fluid flow to and from a selected compartment of the sample compartment and liquid reagent compartments; and

an actuator configured to move the slider of the device to predetermined positions along the track.

[0027] The system may further comprise a mechanism configured to exert a force on the dry reagent capsule to break a seal covering at least one chamber of the capsule to fluidically connect the capsule with the respective fluid channel *in-situ*.

[0028] The biological material may comprise a nucleic acid.

[0029] Another aspect of the present disclosure provides a method of isolating a biological material from a sample, the method comprising:

disposing the sample in the sample compartment of the device as described above;

breaking a seal covering at least one chamber of the dry reagent capsule to fluidically connect the capsule with the respective fluid channel *in-situ*; and

moving the slider to predetermined positions along the track to:

mix the liquid reagents and the at least one dry reagent with the sample for extracting the biological material from the sample;

bind the extracted biological material to a surface of a binding channel disposed in the device;

purify the biological material bound to the surface of the binding channel; and

elute the purified biological material.

[0030] The biological material may comprise a nucleic acid.

BRIEF DESCRIPTION OF THE DRAWINGS

[0031] Embodiments will be better understood and readily apparent to one of ordinary skill in the art from the following written description, by way of example only, and in conjunction with the drawings, in which:

[0032] Figure 1A shows a top perspective view of a device for isolating a biological material according to an example embodiment.

[0033] Figure 1B shows a bottom perspective view of the device of Figure 1A.

[0034] Figure 1C shows an exploded top view of the device of Figure 1A.

[0035] Figure 1D shows an exploded bottom view of the device of Figure 1A.

[0036] Figure 2A shows a perspective view of a first housing member of the device of Figure 1A.

[0037] Figure 2B shows a top view of the first housing member of Figure 2A.

[0038] Figure 2C shows a first bottom view of the first housing member of Figure 2A.

[0039] Figure 2D shows a second bottom view of the first housing member of Figure 2A.

[0040] Figure 2E shows a third bottom view of the first housing member of Figure 2A.

[0041] Figure 3A shows a top view of the second housing member of the device of Figure 1A.

[0042] Figure 3B shows a bottom view of the second housing member of Figure 3A.

[0043] Figure 4 shows various views of a dry agent capsule of the device of Figure 1A.

[0044] Figure 5 shows top and bottom views of a slider of the device of Figure 1A.

[0045] Figures 6A-6J show various positions of the slider of Figure 5 along a track and respective fluid flows.

[0046] Figure 7A shows a top perspective view of a device for isolating a biological material according to another example embodiment.

[0047] Figure 7B shows a bottom perspective view of the device of Figure 7A.

[0048] Figure 8A shows a perspective view of a first housing member of the device of Figure 7A.

[0049] Figure 8B shows a bottom view of the first housing member of Figure 8A.

[0050] Figure 9 shows a top perspective view of the second housing member of the device of Figure 7A.

[0051] Figure 10 shows a bottom view of a slider of the device of Figure 7A.

[0052] Figure 11 shows various views of a dry agent capsule of the device of Figure 7A.

[0053] Figure 12 shows a flow chart illustrating a method of isolating a biological material from a sample according to an example embodiment.

DETAILED DESCRIPTION

[0054] The present disclosure provides a device for performing extraction and purification of a biological material, e.g. nucleic acids such as deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), from a sample in a closed system. An example of the device is a disposable cartridge containing a sliding valve. Reagent fluids are stored onboard, along with foil sealed capsules that isolate lyophilized beads from any potential fluids/fluid vapors. When the cartridge is loaded onto an instrument, the instrument actuates the sliding valve to align unique channels with outlets from the reagent well. The valve is configured to have an “off” position at the beginning

and end of travel. Air nozzles are placed in each reagent well and connected to an external pressure source/actuator to control a fluid flow. Vented air nozzles are sealed with a hydrophobic filter to prevent leaking of liquid reagents and then with a foil to dead end the chimney, preventing any fluid from saturating a protective hydrophobic vent. The instrument pierces this foil when the cartridge is inserted. A foil-sealed capsule contains lyophilized bead or dry reagent. The capsule is retained on the cartridge by press fit posts. As the instrument actuates downward, the bottom foil of the capsule is pierced by drafted posts that then seal on vertical channels. These are isolated by the sliding valve until it is moved to a position that allows fluid to flow into the capsule.

[0055] The device is configured to process the extraction and isolation of nucleic acids from samples, such as biological samples, environment samples, etc. The cartridge is configured to mix reagents with a sample for extracting nucleic acids from the sample, to bind/isolate nucleic acids in the fluidic channel and to elute nucleic acids.

[0056] In an example, the fluidic channel is coated with a chemical functional group (e.g. amino (-NH_2) group) to capture extracted nucleic acids using cross-linking agents (e.g. homobifunctional imidoesters). The device is configured to wash away cell and protein residues, any other contaminants while nucleic acids are bound to the surface and to store liquid waste in an on-board waste well. The device is configured to elute purified nucleic acids by treating the fluidic channel with an elution buffer (e.g. a buffer solution with pH > 10.6) that releases nucleic acids from the fluidic channel. The eluted nucleic acid is then dispensed into an external container, such as an Eppendorf tube, to be used for the downstream process and/or analysis.

[0057] In the description that follow, the device and method are described in relation to the isolation of a nucleic acid from a sample, but it will be appreciated that the structure of the device and its working principles can be applied to the isolation of other biological materials.

[0058] Figures 1A-1D show various views of a device for isolating a biological material, in the form of a nucleic acid (NA) extraction cartridge **1**, according to an example embodiment. The NA extraction cartridge **1** comprises a first housing member **10** (hereinafter also referred to as main body **10**), a second housing member **20** (hereinafter also referred to as lid plate **20**), a slider **30** (hereinafter also referred to as

sliding valve **30**), and a dry reagent capsule **40**. These parts are typically made of plastic including, but not limited to, acrylonitrile Butadiene Styrene (ABS), polyethylene (HDPE or LDPE), polycarbonate (PC), polypropylene (PP), polyamide, Cyclic olefin copolymer (COC), thermoplastic elastomer, Polyethylene terephthalate (PET), Polyethylene terephthalate glycol (PETG), SMMA, polymethyl methacrylate (PMMA), etc.

[0059] The main body **10** includes a sample compartment **11**, a reagent reservoir **12** and a waste compartment **13**. A cap **14,** which is configured to seal the sample compartment **11** in a fluid-tight manner, is attached to the main body **10** of the cartridge **1** via a hinge **16**. Reagent compartments of the reagent reservoir **12** contain various liquid reagents for extracting and purifying NA molecules from a sample (as described in further details below) and are sealed with foil **60**. The foil **60** includes a moisture-impermeable membrane, which is typically a heat-sealable moisture barrier film, such as mylar foil and metalized plastic film. An outlet **50** is configured to dispense eluted NA to a container, such as an Eppendorf tube.

[0060] As discussed below with reference to Figures 6A-6J, the sliding valve **30** can move laterally along the sliding valve channel or track **15** to different positions to allow fluidic connection for different stages of NA extraction/purification process.

[0061] A NA binding channel **18** is formed by a NA binding groove **17** of main body **10** and a corresponding NA binding ridge **22** of the lid plate **20**. The channel is formed by bonding the lid plate **20** to the bottom side of main cartridge **10**. Various bonding methods such as chemical (adhesive) bonding, solvent bonding, laser welding, ultrasonic welding can be used to bond the two parts. In alternate embodiments, the NA binding channel **18** may be formed on either the main body **10** or the lid plate **20**.

[0062] Vented air inlets are covered with a respective liquid-impermeable membrane **70-72**, which includes a hydrophobic filter to prevent leaking of liquid reagents, and then sealed with foil **63, 64** to prevent any fluid from saturating a protective hydrophobic vent during storage. The instrument pierces the foil **63, 64** when the cartridge **1** is inserted.

[0063] In the embodiment shown in Figs. 1A-1D, the dry reagent capsule **40** has two columns to store lyophilized beads. Bottom and top sides of the dry reagent capsule **40** are covered with foil **61** and **62**, respectively, to provide a moisture barrier to protect dry reagents during storage. Once the cartridge is inserted in the instrument, the

instrument actuates downward, and the bottom foil **61** of the capsule **40** is pierced by posts that then seal on vertical channels.

[0064] Figures 2A-2E show various views of the first housing member or main body **10** of the NA extraction cartridge **1**, and Figures 3A-3B show various views of the second housing member or lid plate **20** of the cartridge **1**. Reagent reservoir **12** is divided into a plurality of compartments or wells **12a-12f** that contain various liquid reagents which are preloaded. In an example, compartment **12a** contains a hydration buffer for dry beads, compartment **12b** contains a lysis buffer, compartment **12c** contains DNase, compartment **12d** contains wash buffer 1, compartment **12e** contains wash buffer 2, and compartment **12f** contains an elution buffer, respectively. In some applications, compartment **12c** may be empty and not in use, but it will be appreciated that the end-user can optionally add a desired reagent.

[0065] As shown in Figures 2A and 2E, an air nozzle **80a** is disposed in the sample compartment **11**, and an air nozzle **80b**-**80f** is placed in each reagent well of the reagent reservoir **12**. Air nozzles **80a**-**80f** span the extraction cartridge **1** from the top side through the bottom side of the main body **10** then the top side of the lid plate **20** to the bottom side of the lid plate **20** (Figures 3A and 3B). While not shown in the drawings, air nozzles **80a**-**80f** are connected to an external pressure source/actuator, such as syringe pumps or a suitable pneumatic source, to control a fluid flow to or from the associated well, thereby pushing or pulling liquid from/to the sample compartment, reagent compartments and NA binding channel. Further, an air vent **81a** is disposed in one of reagent wells of the reagent reservoir **12** and another air vent **81b** is disposed in the waste compartment **13**, respectively, to allow the fluidic movement.

[0066] As also described with reference to Figure 1, vertical channels **41a – 41c** in the form of hollow posts are provided on the main body **10** for connection with dry reagent capsule **40**. When the cartridge **1** is inserted in the instrument, the instrument actuates downward, the bottom foil of the capsule **40** is pierced by these hollow posts that then seal on vertical channels **41a – 41c**. In other words, the dry reagent capsule **40** in the example embodiments is fluidically connected to a respective fluid channel *in-situ*.

[0067] With reference to Figure 4, the dry reagent capsule **40** in this example includes chambers **51**, **52** each configured to contain a respective dry reagent in the form of lyophilized beads. A different number of chambers may be used in alternate embodiments. Further, holes **53**, **54**, and **55** are provided at the bottom of the

chambers **51**, **52** for connection with the vertical channels **41a**, **41b** and **41c**, respectively.

[0068] The placement of vertical channels is shown in Figures 2B and 2C. A plurality of vertical channels **90a-90y** span from the top side to the bottom of the main body **10**. In addition, as shown in Figure 2D, a plurality of horizontal grooves **100a-100l** are defined in the bottom side of the main body **10**, while a horizontal groove **100m** (Figure 2B) is defined in the top side of the main body **10**. Horizontal fluid channels are formed by bonding the lid plate **20** to the bottom side of main body **10**. Each groove **100a**-**100m** is configured to connect a selected one of the vertical channels **90a-90k** to a selected one of the vertical channels **90l-90y** and NA outlet **50**. For example, groove **100a** connects vertical channel **90a** with vertical channel **90l**.

[0069] It can also be seen from Figures 2A-2E that the sample compartment **11** and each compartment of the reagent reservoir are configured to be fluidically connected to respective fluid channels, and each fluid channel has a respective end terminating at the groove or track **15** disposed on main body **10**. For example, vertical channels **90l – 90y** are located underneath the sliding valve **30** when the sliding valve **30** is disposed in the track **15**.

[0070] Figure 5 shows various views of the sliding valve **30** according to an example embodiment. The sliding valve **30** has a plurality of different channels **120** which align with a plurality of vertical channels (**90l – 90y**)**.** The sliding valve **30** can slide from one end of the track **15** to the other by pulling by the holder **121**. For example, in an automated system, an actuator can be used to drive the sliding valve **30** through precise distances such that a selected one of the connecting channels **120** can connect ends of selected ones of the fluid channels formed by the horizontal grooves **100a-100l** based on a position of the slider **30** along the track **15**.

[0071] With reference to Figures 6A-6J, an example operation of the cartridge **1** for nucleic acid extraction and purification is now described. A sample is disposed in the sample compartment **11**. In this operation, an external pneumatic/pressure source, which is connected to air nozzles **80a-80f** (Figures 3A-3B), can be used to effect fluid flows. It will be appreciated that the device can also be used for the isolation of other biological materials, e.g. by appropriate changes to the reagents.

[0072] In Figure 6A (position A), the slider or sliding valve **30** is in the initial or reference position, in which all channels are closed. For example, the cartridge **1** may

be inserted into an instrument or system with the slider **30** being in this position. From this position, the slider **30** can be moved to other positions in a series of discrete steps.

[0073] During the subsequent operation, air pressure is equally applied to reagent wells or compartments via air nozzles **80a-80f**. However, the liquid/reagent only flows along certain fluidic channels opened up by moving the sliding valve **30**.

[0074] In Figures 6B1 and 6B2 (positions B1 and B2), the sliding valve **30** is positioned to make a channel between vertical channel **90l** and vertical channel **90m** such that a fluidic passage is formed between the compartment **12a** and dry reagent chamber **51**. A hydration buffer is pushed from compartment **12a** to dry reagent chamber **51** through horizontal channel **100a** (connected to vertical channel **90a** and vertical channel **90l**), horizontal channel **100b** (connected to vertical channel **90m** and vertical channel **90b**) and hole **53** (Figure 4) at the bottom of the dry reagent capsule chambers **51** to dissolve a first dry reagent in the form of lyophilized beads (preferably dimethyl adipimidate (DMA) or a suitable homobifunctional imidoester crosslinker) in the chamber **51** then pull back to compartment **12a**. For example, when the hydration buffer reaches the chamber **51**, a combination of positive and negative pressures applied by the external source via air nozzle **80b** can result in mixing of the hydration buffer with the dry reagent, before the solution is withdrawn to compartment **12a**.

[0075] In Figure 6C (position C), the sliding valve **30** is positioned to make a channel between vertical channel **90l** and vertical channel **90n** such that a fluidic passage is formed between compartment **12a** and compartment **12b**. The crosslinker solution is pushed from compartment **12a** to compartment **12b**, which contains a lysis buffer, through horizontal channel **100a** (connected to vertical channel **90a** and vertical channel **90l**) and horizontal channel **100c** (connected to vertical channel **90c** and vertical channel **90n**) to mix with the lysis buffer. The external pressure is provided via air nozzle **80b** and the air vent **81a** can promote fluidic movement by releasing the pressure inside compartment **12b**.

[0076] In Figure 6D (position D), the sliding valve **30** is positioned to make a channel between vertical channels **90n** and **90o** and between vertical channels **90p** and **90q** such that a fluidic passage is formed between the compartment **12b**, the dry reagent chamber **52**, and the sample compartment **11**. The crosslinker solution + lysis buffer from compartment **12b** is pushed to dry reagent chamber **52** through horizontal channel **100c** (connected to vertical channel **90c** and vertical channel **90n**), horizontal channel **100d** (connected to vertical channel **90o** and vertical channel **90d**) and hole **54**

(Figure 4) at the bottom of the dry reagent capsule chamber **52** to dissolve a second dry reagent in the form of lyophilized beads (preferably proteinase K). Then, the mixed solution is pushed from dry reagent chamber **52** to sample compartment **11** through hole **55** (Figure 4), horizontal channel **100e** (connected to vertical channel **90e** and vertical channel **90p**) and horizontal channel **100f** (connected to vertical channel **90f** and vertical channel **90q**) to mix with a sample contained in the sample compartment **11**. At this position, the external pressure is applied via air nozzle **80a**.

[0077] In Figure 6E (position E), the sliding valve **30** is positioned to make a channel between vertical channels **90q** and **90r** and between vertical channels **90s** and **90t** such that a fluidic passage is formed between the sample compartment **11** and the NA binding channel **18**. The mixed solution of lysis buffer + sample is pushed from sample compartment **11** to NA binding channel **18** through horizontal channel **100f** (connected to vertical channel **90f** and vertical channel **90q**) then via vertical channel **90r**. NA binding channel **18** is connected to waste compartment **13** via vertical channel **90s** then through horizontal channel **100g** (connected to vertical channel **90t** and waste compartment **13**). At this position, the external pressure is applied via air nozzle **80a**. The air vent **81b** promotes fluidic movement by releasing the pressure inside sample compartment **11**. Then, the external pressure source is switched off, therefore no liquid is moving to the waste compartment **13** and the sample solution is incubated for a predetermined time (e.g. 10 minutes) to lyse the cells and to bind extracted NA to a surface of the NA binding channel **18**. The channel **18** can be optionally heated by a heater positioned underneath the cartridge **1** and provided with the instrument into which the cartridge **1** is inserted. The incubation period may vary in alternate embodiments, e.g. depending on the material of the sample.

[0078] In Figure 6F (position F), the sliding valve **30** is positioned to make a channel between vertical channels **90u** and **90r** and between vertical channels **90s** and **90t** such that a fluidic passage is formed between the reagent compartment **12c**, NA binding channel **18** and waste compartment **13**. A liquid reagent (DNase) from reagent compartment **12c** is pushed to NA binding channel **18** through horizontal channel **100h** (connected to vertical channel **90g** and vertical channel **90u**) then via vertical channel **90r** to react with the surface-bound NA. The left-over sample solution (lysed sample minus NA molecules) is pushed from NA binding channel **18** to waste compartment **13** via vertical channel **90s** then through horizontal channel **100g** (connected to vertical channel **90t** and waste well **13**). At this position, the external pressure is applied via air

nozzle **80c**. In some embodiments, the use of the DNase treatment may be optional and can be skipped.

[0079] In Figure 6G (position G), the sliding valve is **30** positioned to make a channel between vertical channels **90v** and **90r** and between vertical channels **90s** and **90t** such that a fluidic passage is formed between reagent compartment **12d**, NA binding channel **18** and waste compartment **13**. A first wash buffer is pushed from reagent compartment **12d** to NA binding channel **18** through horizontal channel **100i** (connected to vertical channel **90h** and vertical channel **90v**) then via vertical channel **90r** to wash the surface-bound NA. The left-over sample solution (lysed sample minus NA molecules) from NA binding channel **18** is pushed to waste compartment **13** via vertical channel **90s** then through horizontal channel **100g** (connected to vertical channel **90t** and waste well **13**). At this position, the external pressure is applied via air nozzle **80d**.

[0080] In Figure 6H (position H), the sliding valve **30** is positioned to make a channel between vertical channels **90w** and **90r** and between vertical channels **90s** and **90t** such that a fluidic passage is formed between reagent compartment **12e**, NA binding channel **18** and waste compartment **13**. A second wash buffer is pushed from reagent compartment **12e** to NA binding channel **18** through horizontal channel **100j** (connected to vertical channel **90i** and vertical channel **90w**) then via vertical channel **90r** to wash the surface-bound NA. The left-over sample solution (lysed sample minus NA molecules) from NA binding channel **18** is pushed to waste compartment **13** via vertical channel **90s** then through horizontal channel **100g** (connected to vertical channel **90t** and waste well **13**). At this position, the external pressure is applied via air nozzle **80e**.

[0081] In Figure 6I (position I), the sliding valve **30** is positioned to make a channel between vertical channels **90x** and **90r** and between vertical channels **90s** and **90y** such that a fluidic passage is formed between reagent compartment **12f**, NA binding channel **18** and outlet **50**. An elution buffer is pushed from reagent compartment **12f** to NA binding channel **18** through horizontal channel **100k** (connected to vertical channel **90j** and vertical channel **90x**) then via vertical channel **90r** to elute NA from the binding channel **18**. Then, the eluted NA from NA binding channel **18** is pushed to NA outlet **50** via vertical channel **90s** then through horizontal channel **100l** (connected to vertical channel **90k** and vertical channel **90y**) and horizontal channel **100m** (connected vertical channel **90k** and NA outlet **50**). The eluted NA can be collected at the outlet **50** by suitable means. At this position, the external pressure is applied via air nozzle **80f**.

[0082] In Figure 6J (position J), which is at the end of the process, the sliding valve **30** is position to close all vertical channels. In this position, the cartridge **1** can be withdrawn from the instrument and suitably disposed.

[0083] Figures 7A-7B show top and bottom perspective views of a device for isolating a biological material, in the form of a nucleic acid (NA) extraction cartridge **700**, according to an alternate embodiment. The NA extraction cartridge **700** is largely similar to the NA extraction cartridge described above with reference to Figures 1-6, and comprises a first housing member **710** (hereinafter also referred to as main body **710**), a second housing member **720** (hereinafter also referred to as lid plate **720**), a slider **730** (hereinafter also referred to as sliding valve **730**), a dry reagent capsule **740**, and a cap **750**. Figure 8A-8B shows perspective and bottom views of the first housing member **710**. Figure 9 shows a top perspective view of the second housing member **720**. Figure 10 shows a bottom view of the slider **730**, and Figure 11 shows various views of the dry agent capsule **740**.

[0084] With reference to Figures 8A, the first housing member **710** differs from the first housing member **10** described above in a number of features. Firstly, the number of reagent compartments or wells of the first housing member **710** is reduced to five. In an example, compartment **712a** contains a lysis buffer, compartment **712b** contains a 1st wash buffer, compartment **712c** contains a 2nd wash buffer, compartment **712d** contains 3rd wash buffer, and compartment **712e** contains an elution buffer, respectively. In other words, a hydration buffer chamber is not required in this embodiment. Secondly, the number of vertical channels in the form of hollow posts provided on the first housing member **710** for connection with dry reagent capsule **740** is reduced from three to two (see **741a** and **741b** in Figure 8A), since the number of dry reagent chambers of the dry reagent capsule **740** is one (see **751** in Figure 10). For example, the chamber **751** can contain the at least one dry reagent (e.g. both first and second dry reagents) in the form of lyophilized beads. Accordingly, the number and positions of the horizontal channels of the first housing member **710** and connecting channels of the slider **730** are adapted to accommodate the above changes.

[0085] Other changes in the NA extraction cartridge **700** compared to the NA extraction cartridge **10** include forming the NA binding channel **718** by groove **722** in the second housing member **720** (see Figure 9) instead of a ridge.

[0086] Operation of the NA extraction cartridge **700** is similar to that of the NA extraction cartridge **10**, except that the steps as described above with reference to Figures 6B1-6B2, 6C and 6D are combined into a single step. In this step, the lysis buffer from compartment **712a** is pushed through respective fluid channels and connecting channel therebetween to the dry reagent chamber **751** where the lysis buffer can dissolve the one or multiple dry reagents present in the chamber. For example, when the lysis buffer reaches the chamber **751**, a combination of positive and negative pressures applied by the external source via an air nozzle can result in mixing of the lysis buffer with the dry reagents, before the solution is withdrawn to the sample compartment **711** to mix with the sample contained in the sample compartment **711**. One of the vertical channel **741a**, **741b** is used for injecting the lysis buffer into the chamber **751** while the other is used for withdrawing the mixed solution from the chamber **751**. The lysis buffer in this embodiment can be, for example, a mixture of the lysis buffer and hydration buffer of the embodiment in Figures 1-6, or a new recipe capable of dissolving lyophilized beads and lysing the biomolecules in the sample. In other words, this embodiment can simplify the preparation of the reagent solution by selecting the appropriate combination of the lysis buffer and dry reagents, resulting in a reduction of two steps.

[0087] Thereafter, the NA extraction cartridge **700** can be operated in the same way as the NA extraction cartridge **10**. In this embodiment, the DNase treatment step (as discussed above with reference to Figure 6F) can be skipped, and replaced with an additional washing step as desired, i.e. 3 washing steps using the 1st, 2nd, and 3rd wash buffers respectively. The composition of the wash buffers can differ depending on the target molecules and the bodily fluids present in the sample. The wash buffers are interchangeable between this embodiment and the first embodiment of Figures 1-6, especially when the sample compartment for DNase treatment step in the first embodiment is used to contain a wash buffer instead. For the sake of brevity, the washing and elution steps are not repeated here.

[0088] Figure 12 shows a flow chart **1200** illustrating a method of isolating a biological material from a sample according to an example embodiment. At step **1202**, the sample is disposed in the sample compartment of the device as described above. At step **1204**, a seal covering at least one chamber of the dry reagent capsule is broken to fluidically connect the capsule with the respective fluid channel *in-situ*. At step **1206**, the slider is moved to predetermined positions along the track to successively mix at least one liquid reagents and the at least one dry reagent with

the sample for extracting the biological material from the sample, bind the extracted biological material to a surface of a binding channel disposed in the device, purify the biological material bound to the surface of the binding channel, and elute the purified biological material.

[0089] As described, the isolation of nucleic acid can be performed using a compact and self-containing device which is in the form of a cartridge that can be inserted into an instrument before the process and removed from the instrument once the process is completed. In other words, the relevant liquid and dry reagents are already present in the device and external liquid handling is not necessary. Cross-contamination and maintenance can be significantly reduced. Furthermore, the use of a single slider with integrated connecting channels, together with linear movements of the slider, to selectively connect fluid channels of the device can reduce the number of moving parts and enable automated operation.

[0090] It will be appreciated by a person skilled in the art that numerous variations and/or modifications may be made to the present invention as shown in the specific embodiments without departing from the scope of the invention as broadly described. For example, suitable adjustments can be made to the reagents or sequence of operations to adapt the device for isolation of a different type of biological material. The present embodiments are, therefore, to be considered in all respects to be illustrative and not restrictive.

CLAIMS

1. A device for isolating a biological material from a sample, the device comprising:

a housing defining a plurality of compartments and a plurality of fluid channels, wherein each compartment is configured to be fluidically connected to a respective fluid channel, and wherein each fluid channel comprises a respective end terminating at a track disposed on the housing;

a slider movable along the track, the slider comprising a plurality of connecting channels extending therethrough, wherein a selected one of the connecting channels is configured to connect ends of selected ones of the fluid channels based on a position of the slider along the track; and

a dry reagent capsule configured to be mounted to the housing, the dry reagent capsule comprising at least one dry reagent for mixing with the sample, wherein the dry reagent capsule is further configured to be fluidically connected to a respective fluid channel *in-situ*.

2. The device as claimed in claim 1, wherein the housing comprises a first housing member securely joined to a second housing member, and wherein the first housing member comprises grooves arranged to form the respective fluid channels.

3. The device as claimed in claim 1, wherein the plurality of compartments comprises a sample compartment configured to receive the sample, a plurality of liquid reagent compartments and a waste compartment.

4. The device as claimed in claim 3, wherein each of the sample and liquid reagent compartments comprises a respective inlet configured to be connected to pneumatic source for controlling a fluid flow to or from said compartment.

5. The device as claimed in claim 4, further comprising a first pneumatic vent disposed in one of the liquid reagent compartments and a second pneumatic vent disposed in the waste compartment.

6. The device as claimed in claim 3, wherein the plurality of liquid reagent compartments are preloaded with respective liquid reagents.

7. The device as claimed in claim 3, wherein, in a first position, the slider is configured to connect a first liquid reagent compartment containing a hydration buffer with a first chamber of the dry reagent capsule, the first chamber containing a first dry reagent, for mixing the hydration buffer with the first dry reagent to form a first solution.

8. The device as claimed in claim 7, wherein, in a second position, the slider is configured to connect the first liquid reagent compartment with a second liquid reagent compartment containing a lysis buffer, for mixing the first solution with the lysis buffer to form a second solution.

9. The device as claimed in claim 8, wherein, in a third position, the slider is configured to:

connect the second liquid reagent compartment with a second chamber of the dry reagent capsule, the second chamber containing a second dry reagent, for mixing the second solution with the second dry reagent to form a third solution; and

connect the second chamber of the dry reagent capsule with the sample compartment for mixing the third solution with the sample to form a fourth solution.

10. The device as claimed in claim 9, wherein the fluid channels comprise a binding channel, and wherein, in a fourth position, the slider is configured to connect the sample compartment with the binding channel to store the fourth solution in the binding channel for a predetermined period for extracting the biological material from the fourth solution and binding the extracted biological material to a surface of the binding channel.

11. The device as claimed in claim 10, wherein, in a fifth position, the slider is configured to:

connect a third liquid reagent compartment containing a first wash buffer with the binding channel to wash the biological material bound to the surface of the binding channel; and

connect the binding channel with the waste compartment for discarding a first waste solution without the biological material to the waste compartment.

12. The device as claimed in claim 11, wherein, in a sixth position, the slider is configured to:

connect a fourth liquid reagent compartment containing a second wash buffer with the binding channel to wash the biological material bound to the surface of the binding channel; and

connect the binding channel with the waste compartment for discarding a second waste solution without the biological material to the waste compartment.

13. The device as claimed in claim 12, wherein, in a seventh position, the slider is configured to:

connect a fifth liquid reagent compartment containing an elution buffer with the binding channel to elute the biological material from the surface of the binding channel; and

connect the binding channel with an outlet for collecting the eluted biological material.

14. The device as claimed in claim 3, wherein, in a first position, the slider is configured to:

connect a first liquid reagent compartment containing a lysis buffer with a chamber of the dry reagent capsule, the chamber containing the at least one dry reagent, for mixing the lysis buffer with the at least one dry reagent to form a reagent solution; and

connect the chamber of the dry reagent capsule with the sample compartment for mixing the reagent solution with the sample to form a sample solution.

15. The device as claimed in claim 14, wherein the fluid channels comprise a binding channel, and wherein, in a second position, the slider is configured to connect the sample compartment with the binding channel to store the sample solution in the binding channel for a predetermined period for extracting the biological material from the sample solution and binding the extracted biological material to a surface of the binding channel.

16. The device as claimed in claim 15, wherein, in a third position, the slider is configured to:

connect a second liquid reagent compartment containing a first wash buffer with the binding channel to wash the biological material bound to the surface of the binding channel; and

connect the binding channel with the waste compartment for discarding a first waste solution without the biological material to the waste compartment.

17. The device as claimed in claim 16, wherein, in a fourth position, the slider is configured to:

connect a third liquid reagent compartment containing a second wash buffer with the binding channel to wash the biological material bound to the surface of the binding channel; and

connect the binding channel with the waste compartment for discarding a second waste solution without the biological material to the waste compartment.

18. The device as claimed in claim 17, wherein, in a fifth position, the slider is configured to:

connect a fourth liquid reagent compartment containing a third wash buffer with the binding channel to wash the biological material bound to the surface of the binding channel; and

connect the binding channel with the waste compartment for discarding a third waste solution without the biological material to the waste compartment.

19. The device as claimed in claim 18, wherein, in a sixth position, the slider is configured to:

connect a fifth liquid reagent compartment containing an elution buffer with the binding channel to elute the biological material from the surface of the binding channel; and

connect the binding channel with an outlet for collecting the eluted biological material.

20. The device as claimed in claim 10 or 15, wherein the at least one dry reagent comprises lyophilized beads containing a crosslinker selected to attach to the biological material, and wherein the surface of the binding channel is coated with a functional group selected to attach to the crosslinker.

21. The device as claimed in claim 1, wherein the biological material comprises a nucleic acid.

22. An automated biological material extraction system comprising:

a receptacle configured to receive the device as claimed in claim 3;

a pressure source configured to control a fluid flow to and from a selected compartment of the sample compartment and liquid reagent compartments; and

an actuator configured to move the slider of the device to predetermined positions along the track.

23. The system as claimed in claim 22, further comprising a mechanism configured to exert a force on the dry reagent capsule to break a seal covering at least one chamber of the capsule to fluidically connect the capsule with the respective fluid channel *in-situ*.

24. The system as claimed in claim 23, wherein the biological material comprises a nucleic acid.

25. A method of isolating a biological material from a sample, the method comprising:

disposing the sample in the sample compartment of the device as claimed in claim 6;

breaking a seal covering at least one chamber of the dry reagent capsule to fluidically connect the capsule with the respective fluid channel *in-situ*; and

moving the slider to predetermined positions along the track to:

mix the liquid reagents and the at least one dry reagent with the sample for extracting the biological material from the sample;

bind the extracted biological material to a surface of a binding channel disposed in the device;

purify the biological material bound to the surface of the binding channel; and

elute the purified biological material.

26. The method as claimed in claim 25, wherein the biological material comprises a nucleic acid.