

NUCLEIC ACID PURIFICATION DEVICE AND SYSTEM

Cross References to Related Applications

- [0001] The present application claims the benefit of the Singapore Patent Application No. 10202009183S filed on 18 September 2020, the entire contents of which are incorporated herein by reference for all purposes.

Technical Field

- [0002] Various embodiments generally relate to a nucleic acid purification device, and a nucleic acid purification system. In particular, various embodiments generally relate to a nucleic acid purification device for a diagnostic system performing nucleic acid based analysis, and a nucleic acid purification system for the diagnostic system.

Background

- [0003] Conventionally, nucleic acid based analysis can provide accurate and early detection for infectious disease diagnosis in clinical laboratories. The analysis procedure generally starts from sample preparation. Sample preparation typically involves extraction of nucleic acids from raw samples such as blood, sputum, feces, etc. This is a critical step in the whole analysis workflow, which will directly affect the performance and/or outcome of the analysis. It is generally known to be difficult to efficiently extract DNA (Deoxyribonucleic acid) from semi-solid and solid samples (i.e. sputum, feces) due to the high viscosity of sample and existence of fibres/particles within samples. Common methods for isolating nucleic acids, such as solvent precipitation, silica membrane based adsorption, magnetic beads extraction, etc., typically rely on skilled laboratory technicians and the whole process usually involves many manual operations such as adding/removing various reagents, centrifugation, mixing, etc. Thus, conventional methods are dependent on highly skilled technicians and consistent results may be hard to achieve due to the numerous manual operations.

- [0004] Further, the timely diagnosis and precise identification of infectious agents remain an ever-present challenge for healthcare and biosecurity professionals. Detection of such agents is possible through a range of assays including culture-based tests and immunoassays.

However, (polymerase chain reaction) PCR-based assays are often used for the fast, sensitive, and specific detection of pathogens. Short time-to-result is of paramount importance as delays can have serious consequences with regards to both the appropriate treatment of the infected and the containment of secondary spread. The drive for point-of-care (POC) diagnostic systems demands results to be made available within minutes. Traditional nucleic acid extraction or purification usually includes many steps such as cell lysis, DNA capturing, washing, elution, etc., which is tedious, time consuming and needs trained or highly skilled professional operators or technicians. Further, such laboratory scale practices and processes restrict the implementation of nucleic acid based diagnosis in point-of-care (POC) settings, such as general clinics, resource-limited situations, on-site environments, etc. It will be desirable to develop a fast sample-in, result-out POC method and device to address and solve the above issues. However, on the other hand, fast and efficient cell lysis from semi-solid and solid samples are always challenging. For example, beads beating to process such samples is known to take a long time. In particular, if a large volume of such samples is required, the time for cell lysis through beads beating is expected to be even longer.

[0005] In addition, human error, contamination, low purity quality, and inconsistent yield are major problems associated with manual sample preparation for nucleic acid purification. These issues can cause inaccuracies in data and experiments, which would be discarded with all relevant reagents, should data errors occur.

[0006] In recent years, the demand for more accurate data, the desire to eliminate costly errors, and the need to keep standards consistent across samples are driving more laboratory to seek and develop automated sample preparation devices/instruments in laboratory settings.

[0007] There are a few automated sample preparation devices/instruments currently available in the market, such as SPRI-TE from BECKMAN COULTER INC., CHEMAGIC PREPITO from PERKINELMER and MAGNA PURE LC from ROCHE. However, one problem with these automated sample preparation devices/instruments are the utilization of liquid handler workstation, which significantly increases both the cost of the device/instrument and the sample processing time. Further, reagent rack and tip/tube rack would still have to be manually loaded into the device/instrument. The liquid handler workstation appears to be capable of simulating some of the manual sample preparation processes, except processes such as the centrifugation process, etc. For samples like blood,

urine and saliva, centrifugation may not be necessary and may be replaced by filtration process. However, for processing feces sample, centrifugation is necessary such that feces supernatant can be obtained for further DNA extraction. Otherwise small feces debris will block the pipette tip, the immobilization column (for example, in the SPRI-TE device) and even the surface of magnetic beads to inhibit DNA extraction. Since centrifugation is not able or too difficult to be integrated into the automated sample preparation processes, these automated sample preparation devices/instruments usually cannot process feces samples or can only process feces supernatant after centrifugation processing is performed separately. [0008] Accordingly, there is a need for a more effective and versatile device/system for nucleic acid extraction or purification, in particular for semi-solid and solid samples.

Summary

[0009] According to various embodiments, there is provided a nucleic acid purification device including a support structure having a head-assembly-support portion; and a head assembly supported by the head-assembly-support portion of the support structure. The head assembly including a frame member; an elongated magnetizable member supported by the frame member, the elongated magnetizable member having a central axis extending longitudinally through the elongated magnetizable member, wherein the elongated magnetizable member is rotatable about the central axis relative to the frame member, wherein the elongated magnetizable member is longitudinally translatable along the central axis with respect to the head-assembly-support portion of the support structure so as to be moveable towards and away from the head-assembly-support portion; and a permanent magnet moveable towards and away from the elongated magnetizable member so as to engage with or disengage from the elongated magnetizable member. The head assembly is operable to engage the permanent magnet with the elongated magnetizable member to induce magnetism in the elongated magnetizable member and move the elongated magnetizable member with induced magnetism to translate along the central axis with respect to the head-assembly-support portion. The head assembly is operable to disengage the permanent magnet from the elongated magnetizable member to lose its induced magnetism and rotate the elongated magnetizable member without induced magnetism about the central axis relative to the frame member.

[00010] According to various embodiments, there is provided a nucleic acid purification system including a nucleic acid purification device and a microfluidic chip. The nucleic acid purification device including a support structure having a head-assembly-support portion and a stage portion spaced apart and opposing the head-assembly-support portion, and a head assembly supported by the head-assembly-support portion of the support structure. The head assembly including a frame member; an elongated magnetizable member supported by the frame member, the elongated magnetizable member having a central axis extending longitudinal through the elongated magnetizable member, wherein the elongated magnetizable member is rotatable about the central axis relative to the frame member, wherein the elongated magnetizable member is longitudinally translatable along the central axis with respect to the head-assembly-support portion of the support structure so as to be moveable towards and away from the head-assembly-support portion; and a permanent magnet moveable relative to the frame member towards and away from the elongated magnetizable member so as to engage with or disengage from the elongated magnetizable member. The microfluidic chip is for placing on the stage portion of the support structure of the nucleic acid purification device. The microfluidic chip including a plurality of wells, wherein at least one well of the microfluidic chip contains a plurality of magnetic particles. The head assembly of the nucleic acid purification device is operable to engage the permanent magnet with the elongated magnetizable member to induce magnetism in the elongated magnetizable member and move the elongated magnetizable member with induced magnetism to translate along the central axis so as to move a tip of the elongated magnetizable member towards the stage portion for inserting into the at least one well of the microfluidic chip placed on the stage portion to capture the plurality of magnetic particles in the at least one well and subsequently move the tip of the elongated magnetizable member away from the stage portion for removing the plurality of magnetic particles magnetically attached to the tip of the elongated magnetizable member from the at least one well. When the tip of the elongated magnetizable member and the plurality of magnetic particles magnetically attached thereto are inserted into one other well of the microfluidic chip, the head assembly of the nucleic acid purification device is operable to disengage the permanent magnet from the elongated magnetizable member to lose its induced magnetism and rotate the elongated magnetizable member without induced magnetism about the central axis relative to the frame member in a manner so as to disperse

the plurality of magnetic particles from the tip of the elongated magnetizable member into the one other well.

Brief description of the drawings

- 5 [00011] In the drawings, like reference characters generally refer to the same parts throughout the different views. The drawings are not necessarily to scale, emphasis instead generally being placed upon illustrating the principles of the invention. In the following description, various embodiments are described with reference to the following drawings, in which:
- 10 [00012] FIG. 1 shows a schematic diagram of a nucleic acid purification system including a nucleic acid purification device and a microfluidic chip according to various embodiments.
- [00013] FIG. 2 shows the microfluidic chip according to various embodiments.
- [00014] FIG. 3 shows another view of the microfluidic chip of FIG. 2 according to various embodiments.
- 15 [00015] FIG. 4 shows experimental observation for 10 seconds and 2 seconds lysis based on on-chip ultrasonic cell lysis according to various embodiments conducted using rabbit blood.
- [00016] FIG. 5 shows higher magnet gradient may be obtained when placing a permanent magnet of the nucleic acid purification device closer to a beads capturing tip of a soft-iron
- 20 bar (i.e. a tip of an elongated magnetizable member) of the nucleic acid purification device according to various embodiments.
- [00017] FIG. 6 shows a cut-in (e.g. the flat side surface) on a round soft-iron bar (i.e. an elongated magnetizable member) of the nucleic acid purification device will give higher localized magnetic gradient at the beads capturing tip of the soft-iron bar (i.e. the tip of the
- 25 elongated magnetizable member) of the nucleic acid purification device according to various embodiments.
- [00018] FIG. 7A shows the permanent magnet being detached from a hexagon shaped soft iron bar (i.e. the elongated magnetizable member) of the nucleic acid purification device according to various embodiments.
- 30 [00019] FIG. 7B shows the permanent magnet of the nucleic acid purification device being attached to the soft iron bar (i.e. elongated magnetizable member) of the nucleic acid purification device according to various embodiments.

[00020] FIG. 8A shows a cone (i.e. a cap) pre-loaded on-chip to be loaded onto the soft iron bar (i.e. the elongated magnetizable member 124) of the nucleic acid purification device automatically by lowering down the tip of the soft iron bar (i.e. the tip of the elongated magnetizable member) according to various embodiments.

5 [00021] FIG. 8B shows the cone (i.e. the cap) being loaded onto the soft iron bar (i.e. the elongated magnetizable member) according to various embodiments.

[00022] FIG. 9 shows an example of specific dimension for the cone (i.e. the cap) according to various embodiments.

10 [00023] FIG. 10 shows the nucleic acid purification system, the nucleic acid purification device, and the microfluidic chip according to various embodiments.

[00024] FIG. 11 shows a top view of the microfluidic chip according to various embodiments.

15 [00025] FIG. 12(a) to FIG. 12(d) shows step-by-step operation to detach the cone (i.e. the cap) from the beads manipulation bar (i.e. the elongated magnetizable member) according to various embodiments.

[00026] FIG. 13A and FIG. 13B shows the unique sensor arrangement to control area-to-area contact between the soft iron bar (i.e. the elongated magnetizable member) and the permanent magnet for auto alignment when approaching to each other according to various embodiments.

20 [00027] FIG. 14 shows the operation of a sliding plate of the microfluidic chip for sealing or establishing channel connection according to various embodiments.

[00028] FIG. 15 shows the microfluidic chip with the pre-stored cone (i.e. the cap) according to various embodiments.

25 [00029] FIG. 16(a) shows an initial position of the cone (i.e. the cap) and the soft-iron tip (i.e. the tip of the elongated magnetizable member) at the first end when the head assembly is going down or moving down according to various embodiments.

30 [00030] FIG. 16(b) shows the cone (i.e. the cap) and the soft-iron tip (i.e. the tip of the elongated magnetizable member) being moved to the other end of the cone disposing well (e.g. the arcuate opening) after the head assembly is rotated before the cone (i.e. the cap) is going to be detached from the soft-iron tip (i.e. the tip of the elongated magnetizable member) by moving the head assembly up according to various embodiments.

Detailed description

[00031] Embodiments described below in the context of the apparatus are analogously valid for the respective methods, and vice versa. Furthermore, it will be understood that the embodiments described below may be combined, for example, a part of one embodiment
5 may be combined with a part of another embodiment.

[00032] It should be understood that the terms “on”, “over”, “top”, “bottom”, “down”, “side”, “back”, “left”, “right”, “front”, “lateral”, “side”, “up”, “down” etc., when used in the following description are used for convenience and to aid understanding of relative positions or directions, and not intended to limit the orientation of any device, or structure or any part
10 of any device or structure. In addition, the singular terms “a”, “an”, and “the” include plural references unless context clearly indicates otherwise. Similarly, the word “or” is intended to include “and” unless the context clearly indicates otherwise.

[00033] Various embodiments generally relate to a nucleic acid purification device, and a nucleic acid purification system. In particular, various embodiments generally relate to a
15 nucleic acid purification device for a diagnostic system performing nucleic acid based analysis, and a nucleic acid purification system for the diagnostic system. According to various embodiments, the diagnostic system may be a point of care (POC) diagnostic system for performing nucleic acid based analysis, including, but not limited to, infectious disease diagnosis.

[00034] Various embodiments seek to provide a solution for fast nucleic acid purification (or nucleic acid extraction or nucleic acid sample preparation) from semi-solid and solid samples for used in the diagnostic system. According to various embodiments, samples such as sputum, feces may be processed into purified nucleic acids within minutes. In various
20 embodiments, effective nucleic acid purification/extraction/preparation and transfer may be achieved by combining and/or integrating acoustic energy, mechanical motion and/or magnetic interaction into a single setup to boost bio-reaction.

[00035] Various embodiments may seek to employ the use of magnetic particles for nucleic acid purification/extraction/preparation and transfer. According to various
25 embodiments, the magnetic particles may include, but not limited to, magnetic beads, superparamagnetic beads, superparamagnetic particles, or other particles suitable for magnetic bead DNA (Deoxyribonucleic acid) extraction. According to various
30 embodiments, DNA may bind with the magnetic particles. According to various

embodiments, the nucleic acid purification device may be configured to collect the magnetic particles (with or without DNA being bound) from a first location (for example, a well in a microfluidic chip), transfer the magnetic particles to a second location (for example, one other well in the microfluidic chip), and release the magnetic particles at the second location.

- 5 According to various embodiments, the nucleic acid purification device may be configured to automatically perform the steps of collection, transfer, and release so as to remove and/or eliminate human intervention in order to reduce and/or eliminate human error, requirement of skilled technician, contamination, low purity, and/or inconsistent yield when transferring the magnetic particles between various processes during the nucleic acid
10 purification/extraction/preparation process.

[00036] Various embodiments also seek to provide a nucleic acid purification system for processing semi-solids or solids samples, such as feces, at high speed, high efficiency and free of contamination. According to various embodiments, the nucleic acid purification system may be configured to enable contamination free and effective sample lysis, fast fluid
15 transfer, fast DNA binding to magnetic particles, and effective magnetic particles collection/transfer/release to obtain purified nucleic acids. According to various embodiments, the nucleic acid purification system may be configured to perform sample lysis in an enclosed chamber so as to be free of contamination, to flush and filter the lysed sample to extract the lysis solution for fast fluid transfer into a well with magnetic particles
20 for DNA binding to the magnetic particles, and automated transferring of magnetic particles with bound DNA between different solutions for washing, purification and elution. According to various embodiments, the nucleic acid purification system may be configured to automatically perform the various steps in order to reduce and/or eliminate human error, requirement of skilled technician, contamination, low purity, and/or inconsistent yield.

25 [00037] Various embodiments also seek to provide a microfluidic chip for the nucleic acid purification system which complements the nucleic acid purification device for enhancing the efficiency, reliability and versatility of the nucleic acid purification system to be used in point of care diagnostic system. According to various embodiments, the microfluidic chip may include, but not limited to, the enclosed lysis chamber, a filter for filtering lysed sample,
30 an embedded channel for fluid transfer, a pre-loaded well with binding solutions and magnetic particles, pre-loaded wells with washing, purification and/or elution solutions, and a cap for the nucleic acid purification device to facilitate contamination free transfer of the

magnetic particles. According to various embodiments, the microfluidic chip may be a single-use disposable microfluidic chip for processing a single sample.

- [00038]** FIG. 1 shows a schematic diagram of a nucleic acid purification system 100 according to various embodiments. According to various embodiments, the nucleic acid purification system 100 may be configured for performing nucleic acid purification (or nucleic acid extraction or nucleic acid sample preparation). According to various embodiments, nucleic acid purification system 100 may be configured for processing semi-solid and/or solid. According to various embodiments, the nucleic acid purification system 100 may include a nucleic acid purification device 102 and a microfluidic chip 104.
- Accordingly, various embodiments seek to provide the nucleic acid purification system 100, the nucleic acid purification device 102, and/or the microfluidic chip 104. According to various embodiments, the nucleic acid purification device 102 may be configured to collect magnetic particles 170 from a first location (for example, a well 173 in the microfluidic chip 104), transfer the magnetic particle to a second location (for example, one other well 174 in the microfluidic chip 104), and release the magnetic particle at the second location. According to various embodiments, the magnetic particles 170 may include, but not limited to, magnetic beads, superparamagnetic beads, superparamagnetic particles, or other particles suitable for magnetic bead DNA (Deoxyribonucleic acid) extraction. According to various embodiments, the microfluidic chip 104 may be configured to complement the nucleic acid purification device 102 for completing the nucleic acid purification system 100 to perform nucleic acid purification (or nucleic acid extraction or nucleic acid sample preparation) from a sample. According to various embodiments, the microfluidic chip 104 may be configured to be a single-use disposable microfluidic chip for processing a single sample.
- [00039]** According to various embodiments, the nucleic acid purification device 102 may include a support structure 110 (for example, see FIG. 10). Accordingly, the support structure 110 may provide the framework for the disposition of the various components and elements of the nucleic acid purification device 102 and/or to give an overall physical form to the nucleic acid purification device 102. According to various embodiments, the support structure 110 of the nucleic acid purification device 102 may include a head-assembly-support portion 112. According to various embodiments, the head-assembly-support portion 112 may be configured to hold or carry a head assembly 120.

[00040] According to various embodiments, nucleic acid purification device 102 may include a head assembly 120. According to various embodiments, the head assembly 120 may be supported by the head-assembly-support portion 112 of the support structure 110. According to various embodiments, the head assembly 120 may be held or carried by the head-assembly-support portion 112 in a manner so as to be suspended or hung from the head-assembly-support portion 112 of the support structure 110.

[00041] According to various embodiments, the head assembly 120 of the nucleic acid purification device 102 may include a frame member 122. According to various embodiments, the frame member 122 may be a structure to connect or join or hold various elements/components of the head assembly 120 together to form an assembled unit. Accordingly, the frame member 122 may be configured or customised into various shapes and sizes so as to accommodate the various elements/components of the head assembly 120 such that these elements/components of the head assembly 120 may be fitted or mounted to the frame member 122.

[00042] According to various embodiments, the head assembly 120 of the nucleic acid purification device 102 may include an elongated magnetizable member 124. According to various embodiments, the elongated magnetizable member 124 may be supported by the frame member 122. Accordingly, the frame member 122 may hold or carry the elongated magnetizable member 124. Hence, the elongated magnetizable member 124 may be coupled or attached to the frame member 122.

[00043] According to various embodiments, the elongated magnetizable member 124 may have a central axis 125 (or longitudinal axis) extending longitudinally through the elongated magnetizable member 124. Accordingly, the central axis 125 of the elongated magnetizable member 124 may be extending through the elongated magnetizable member 124 along a centerline running through the center of the elongated magnetizable member 124 lengthwise from end to end. According to various embodiments, the elongated magnetizable member 124 may be rotatable about the central axis 125 relative to the frame member 122. Accordingly, the rotational axis of the elongated magnetizable member 124 coincides with the central axis of the elongated magnetizable member 124. According to various embodiments, the elongated magnetizable member 124 may be rotatably coupled to the frame member 122 so as to be rotatable about the central axis 125 relative to the frame member 122.

[00044] According to various embodiments, the elongated magnetizable member 124 may be longitudinally translatable along the central axis 125 with respect to the head-assembly-support portion 112 of the support structure 110 so as to be moveable towards and away from the head-assembly-support portion 112. Accordingly, the elongated magnetizable member 124 may be operated to move longitudinally in two opposite longitudinal directions along the central axis 125, a first direction being towards the head-assembly-support portion 112 and a second direction being away from the head-assembly-support portion 112. Hence, the elongated magnetizable member 124 may be selectively moved upwards towards the head-assembly-support portion 112 or downwards away from the head-assembly-support portion 112. Thus, the elongated magnetizable member 124 may be capable of two different longitudinal translation motions along the central axis 125, a first being translating longitudinally upwards towards the head-assembly-support portion 112 and a second being translating longitudinally downwards away from the head-assembly-support portion 112.

[00045] For example (see FIG. 10), according to various embodiments, the frame member 122 of the head assembly 120 may be moveable along the central axis 125 with respect to the head-assembly-support portion 112 of the support structure 110 so as to move the elongated magnetizable member 124 relative to the head-assembly-support portion 112. Accordingly, the elongated magnetizable member 124 may remain stationary with respect to the frame member 122 of the head assembly 120 along the central axis 125 so as to be moveable together along the central axis 125 relative to the head-assembly-support portion 112 of the support structure 110 for moving the elongated magnetizable member 124 relative to the head-assembly-support portion 112. Hence, the elongated magnetizable member 124 and the frame member 122 may be non-moveable relative to each other along the central axis 125. According to various embodiments, the elongated magnetizable member 124 may be coupled to the frame member 122 in a manner so as to be non-moveable relative to each other along the central axis 125 and still rotatable relative to each other about the central axis 125.

[00046] As another example, according to various embodiments (not shown), the frame member 122 of the head assembly 120 may be stationary with respect to the head-assembly-support portion 112 of the support structure 110 along the central axis 125 and the elongated magnetizable member 124 may be longitudinally translatable along the central axis 125 with respect to the frame member 122 of the head assembly 120 so as to be moveable towards and away from the head-assembly-support portion 112 of the support structure 110.

Accordingly, the frame member 122 of the head assembly 120 and the head-assembly-support portion 112 of the support structure 110 may be non-moveable relative to each other along the central axis 125, while the elongated magnetizable member 124 may be moveable relative to the frame member 122 along the central axis 125. Hence, the elongated magnetizable member 124 may translate longitudinally along the central axis with respect to the frame member 122 so as to be moveable towards and away from the head-assembly-support portion 112 of the support structure 110, whereby the disposition of the frame member 122 of the head assembly 120 and the head-assembly-support portion 112 of the support structure 110 may be fixed along the central axis 125.

10 [00047] According to various embodiments, the head assembly 120 of the nucleic acid purification device 102 may include a permanent magnet (or magnet) 126. According to various embodiments, the permanent magnet 126 may be moveable towards and away from the elongated magnetizable member 124 so as to engage with or disengage from the elongated magnetizable member 124. According to various embodiments, the permanent magnet 126 may be moveable relative to the elongated magnetizable member 124. Accordingly, the permanent magnet 126 may be operated to move in two different motions, a first motion being towards the elongated magnetizable member 124 for engagement with the elongated magnetizable member 124 and a second motion being away from the elongated magnetizable member 124 for disengaging with the elongated magnetizable member 124. Hence, the permanent magnet 126 may be selectively moved towards the elongated magnetizable member 124 or away from the elongated magnetizable member 124. Accordingly, the permanent magnet 126 may be moved between an engagement position in which the permanent magnet 126 is engaged or in contact with the elongated magnetizable member 124 and a retracted position in which the permanent magnet 126 is disengaged or spaced apart from the elongated magnetizable member 124. According to various embodiments, when the permanent magnet 126 is engaged or in contact with the elongated magnetizable member 124, the elongated magnetizable member 124 may be induced with magnetism.

30 [00048] According to various embodiments, the permanent magnet 126 may also be moveable relative to the frame member 122 of the head assembly 120 and/or the head-assembly-support portion 112 of the support structure 110.

[00049] For example (see FIG. 7A, FIG. 7B and FIG. 10), according to various embodiments, the permanent magnet 126 may be coupled to the frame member 122 of the

head assembly 120 in a manner so as to be moveable relative to the frame member 122 and the elongated magnetizable member 124 such that permanent magnet 126 may be moved towards the elongated magnetizable member 124 for engagement with the elongated magnetizable member 124 and moved away from the elongated magnetizable member 124 to disengage from the elongated magnetizable member 124. According to various embodiments, various mechanisms imparting movements or motions may couple the permanent magnet 126 to the frame member 122 of the head assembly 120 such that the permanent magnet 126 may be moveable relative to the frame member 122 and the elongated magnetizable member 124. According to various embodiments, the engagement position and the retracted position of the permanent magnet 126 may be fixed with reference to the frame member 122 of the head assembly 120 such that the permanent magnet 126 may be moveable between the engagement position and the retracted position.

[00050] As another example, according to various embodiments (not shown), the permanent magnet 126 may be coupled to the support structure 110 in a manner so as to be moveable relative to the support structure 110 and the elongated magnetizable member 124 such that permanent magnet 126 may be moved towards the elongated magnetizable member 124 for engagement with the elongated magnetizable member 124 and moved away from the elongated magnetizable member 124 to disengage from the elongated magnetizable member 124. According to various embodiments, the permanent magnet may be coupled to any portion of the support structure 110, including, but not limited to, the head-assembly-support portion 112, the column portion, the base portion, or the stage portion 114. According to various embodiments, various mechanisms imparting movements or motions may couple the permanent magnet 126 to support structure 110 such that the permanent magnet 126 may be moveable relative to the support structure 110 and the elongated magnetizable member 124. According to various embodiments, the engagement position and the retracted position of the permanent magnet 126 may be fixed with reference to the support structure 110 such that the permanent magnet 126 may be moveable between the engagement position and the retracted position.

[00051] According to various embodiments, the head assembly 120 of the nucleic acid purification device 102 may be operable to engage the permanent magnet 126 with the elongated magnetizable member 124 to induce magnetism in the elongated magnetizable member 124 and move the elongated magnetizable member 124 with induced magnetism to translate along the central axis 125 with respect to the head-assembly-support portion 112

of the support structure 110. Accordingly, by moving the elongated magnetizable member 124 with induced magnetism downwards and upwards with respect to the head-assembly-support portion 112 of the support structure 110, a tip 124a of the elongated magnetizable member 124 may be inserted into a well 173 of the microfluidic chip 104 for attracting (or capturing) the magnetic particles 170 within the well 173 to the tip 124a of the elongated magnetizable member 124 for collection during the downward movement and subsequently remove the magnetic particles 170 from the well 173 during the upward movement. Subsequently, by moving the elongated magnetizable member 124 with induced magnetism downwards again with respect to the head-assembly-support portion 112 of the support structure 110, the tip 124a of the elongated magnetizable member 124 may be inserted into one other well 174 of the microfluidic chip 104 for transferring the magnetic particles 170 into the one other well 174. According to various embodiments, the tip 124a of the elongated magnetizable member 124 may be a distal end of the elongated magnetizable member 124 farthest from the head-assembly-support portion 112 of the support structure 110 and/or the frame member 122 of the head assembly 120.

[00052] According to various embodiments, the head assembly 120 of the nucleic acid purification device 102 may be operable to disengage the permanent magnet 126 from the elongated magnetizable member 124 to cause the elongated magnetizable member 124 to lose its induced magnetism and rotate the elongated magnetizable member 124 without induced magnetism about the central axis 125 relative to the frame member 122. Accordingly, when the tip 124a of the elongated magnetizable member 124 is inserted into the one other well 174 of the microfluidic chip 104, disengagement the permanent magnet 126 may remove the induced magnetism from the elongated magnetizable member 124. Hence, the magnetic particles 170 may no longer be attracted to the tip 124a of the elongated magnetizable member 124 and, thus, may be released into the one other well 174 of the microfluidic chip 104. Further, by rotate the elongated magnetizable member 124 without induced magnetism about the central axis 125 relative to the frame member 122, the tip 124a of the elongated magnetizable member 124 may turn or spin or stir or swirl within the one other well of the microfluidic chip 104. The rotation of the elongated magnetizable member 124 may promote the dislodgement of the magnetic particles 170 from the tip 124a of the elongated magnetizable member 124 and may also agitate a solution in the one other well 174 of the microfluidic chip 104 to enhance mixing of the magnetic particles 170 with the solution of the one other well 174.

[00053] According to various embodiments, the permanent magnet 126 of the head assembly 120 of the nucleic acid purification device 102 may be moveable along a trajectory or a path intersecting the central axis 125 of the elongated magnetizable member 124. Accordingly, the trajectory or the path of the permanent magnet 126 may converge with the
5 central axis 125 of the elongated magnetizable member 124. Hence, the trajectory or the path of the permanent magnet 126 may lead the permanent magnet 126 into contact or engagement with the elongated magnetizable member 124 such that magnetism may be induced in the elongated magnetizable member 124 by the permanent magnet 126.

[00054] According to various embodiments (for example see FIG. 7A, FIG. 7B and FIG.
10 10), the trajectory or the path of the permanent magnet 126 may be perpendicular to the central axis 125 of the elongated magnetizable member 124 (or radial with respect to the central axis 125 of the elongated magnetizable member 124). According to various embodiments (not shown), the trajectory or the path of the permanent magnet 126 may be inclined with respect to the central axis 125 of the elongated magnetizable member 124.
15 Hence, the trajectory or the path of the permanent magnet 126 and the central axis 125 of the elongated magnetizable member 124 may form a non-perpendicular angle (i.e. that is less than 90° or more than 90°).

[00055] According to various embodiments, the permanent magnet 126 may be moveable towards and away from a side of the elongated magnetizable member 124 so as to engage
20 with or disengage from the side of the elongated magnetizable member 124. According to various embodiments, the side of the elongated magnetizable member 124 may be a segment of a longitudinal side of the elongated magnetizable member 124. According to various embodiments, the segment of the longitudinal side of the elongated magnetizable member 124 may be adjacent to the tip 124a of the elongated magnetizable member 124. According
25 to various embodiments, the segment of the longitudinal side of the elongated magnetizable member 124 may be between the frame member 122 of the head assembly 120 and the tip 124a of the elongated magnetizable member 124.

[00056] According to various embodiments, the elongated magnetizable member 124 may include a flat side surface 124b. According to various embodiments, the flat side surface
30 124b may be along the segment of the longitudinal side of the elongated magnetizable member 124. Accordingly, the flat side surface 124b may be extending longitudinally along the segment of the longitudinal side of the elongated magnetizable member 124. According to various embodiments, the flat side surface 124b of the elongated magnetizable member

124 may be adjacent to the tip 124a of the elongated magnetizable member 124. According to various embodiments, the flat side surface 124b of the elongated magnetizable member 124 may be between the frame member 122 of the head assembly 120 and the tip 124a of the elongated magnetizable member 124. According to various embodiments, the permanent magnet 126 may be moveable towards and away from the flat side surface 124b of the elongated magnetizable member 124 so as to engage with or disengage from the flat side surface 124b of the elongated magnetizable member 124.

[00057] According to various embodiments, the permanent magnet 126 may include a flat contact surface 126a. According to various embodiments, the flat contact surface 126a of the permanent magnet 126 may be facing or directed towards the elongated magnetizable member 124. According to various embodiments, the permanent magnet 126 may be moveable towards and away from the flat side surface 124b of the elongated magnetizable member 124 so as to engage the flat contact surface 126a of the permanent magnet 126 with the flat side surface 124b of the elongated magnetizable member 124 or disengage the flat contact surface 126b of the permanent magnet 126 from the flat side surface 124b of the elongated magnetizable member 124.

[00058] According to various embodiments, the head assembly 120 may be operated such that the flat contact surface 126a of the permanent magnet 126 and the flat side surface 124b of the elongated magnetizable member 124 may be flatly engaged to each other to maximise contact with each other so as to optimise the induced magnetism in the elongated magnetizable member 124. According to various embodiments, the shapes and sizes of the flat contact surface 126a of the permanent magnet 126 and the flat side surface 124b of the elongated magnetizable member 124 may be configured to maximise the contact area with each other for optimising induced magnetism in the elongated magnetizable member 124. According to various embodiments, a distance of the flat side surface 124b of the elongated magnetizable member 124 from the tip 124a of the elongated magnetizable member 124 may be configured to optimise the induced magnetism in the elongated magnetizable member 124.

[00059] According to various embodiments, the head assembly 120 may be operable such that the elongated magnetizable member 124 may be freely rotatable about the central axis 125 relative to the frame member 122 when the permanent magnet 126 is operated to move towards the flat side surface 126b of the elongated magnetizable member 124 for engagement. Accordingly, with the elongated magnetizable member 124 being free to rotate

about the central axis 125 when the permanent magnet 126 is operated to move towards the flat side surface 126b of the elongated magnetizable member 124 for engagement, the flat contact surface 126a of the permanent magnet 126 urging or pushing against the flat side surface 124b of the elongated magnetizable member 124 may corresponding rotate the elongated magnetizable member 124 about the central axis 125 relative to the frame member 122 such that the flat contact surface 126a of the permanent magnet 126 and the flat side surface 124b of the elongated magnetizable member 124 may be aligned and oriented to flatly engage to each other. Hence, being freely rotatable about the central axis 125 enable the elongated magnetizable member 124 to rotate in compliance based on the flat contact surface 126a of the permanent magnet 126 urging or pushing against the flat side surface 124b of the elongated magnetizable member 124. Thus, the free rotation of the elongated magnetizable member 124 about the central axis 125 relative to the frame member 122 when the permanent magnet 126 is moved towards the flat side surface 126b of the elongated magnetizable member 124 may allow automatic alignment of the flat contact surface 126a of the permanent magnet 126 and the flat side surface 124b of the elongated magnetizable member 124 for flatly engaging with each other.

[00060] According to various embodiments, the head assembly 120 may further include a sensor arrangement 140 (for example, see FIG 13A and FIG. 13B). According to various embodiments, the sensor arrangement 140 may be configured to determine relative positions between the flat contact surface 126a of the permanent magnet 126 and the flat side surface 124b of the elongated magnetizable member 124 for controlling the permanent magnet 126 to engage with the elongated magnetizable member 124 such that the flat contact surface 126a of the permanent magnet 126 and the flat side surface 124b of the elongated magnetizable member 124 may be flatly engaged to each other. Accordingly, the sensor arrangement 140 may provide feedback control to move the permanent magnet 126 for engagement with the elongated magnetizable member 124. For example, according to various embodiments, the sensor arrangement 140 may include a first sensor 142 configured to determine a relative distance between the flat contact surface 126a of the permanent magnet 126 and the elongated magnetizable member 124 such that a speed of movement of the permanent magnet 126 may be controlled based on the relative distance. According to various embodiments, the speed of movement of the permanent magnet 126 may be reduced when the first sensor 142 detects that the relative distance is below a predetermined threshold such that the permanent magnet 126 may move slower as the flat contact surface

126a of the permanent magnet 126 urges or pushes against the flat side surface 124b of the elongated magnetizable member 124 to fully engage flatly against each other. Further, according to various embodiments, the sensor arrangement 140 may include a second sensor 144 configured to determine whether the flat contact surface 126a of the permanent magnet 126 and the flat side surface 124b of the elongated magnetizable member 124 are flatly engaged with each other. Accordingly, the movement of the permanent magnet 126 may be stopped when the second sensor 144 detects that the required engagement is achieved. Furthermore, according to various embodiments, the second sensor 144 of the sensor arrangement 140 may also be configured to determine if the flat side surface 124b of the elongated magnetizable member 124 is aligned to the flat contact surface 126a of the permanent magnet 126 for flatly engaging with each other. According to various embodiments, if the second sensor 44 detects that the flat side surface 124b of the elongated magnetizable member 124 and the flat contact surface 126a of the permanent magnet 126 are not aligned, the elongated magnetizable member 124 may be rotated such that the flat side surface 124b of the elongated magnetizable member 124 and the flat contact surface 126a of the permanent magnet 126 are aligned before the permanent magnet 126 is moved to fully engage with the elongated magnetizable member 124.

[00061] According to various embodiments, the elongated magnetizable member 124 may include a polygonal cross-sectional profile. According to various embodiments, the polygonal cross-sectional profile may include, but not limited to, a triangular cross-sectional profile, a quadrilateral cross-sectional profile, a pentagonal cross-sectional profile, a hexagonal cross-sectional profile, a heptagonal cross-sectional profile, an octagonal cross-sectional profile, etc. According to various embodiments, a longitudinal segment of the elongated magnetizable member 124 may include the polygonal cross-sectional profile (for example, see FIG. 7A, FIG. 7B, FIG. 8A, FIG. 8B). According to various embodiments, the longitudinal segment of the elongated magnetizable member 124 may be adjacent to the tip 124a of the elongated magnetizable member 124. According to various embodiments, the longitudinal segment of the elongated magnetizable member 124 may be between the frame member 122 of the head assembly 120 and the tip 124a of the elongated magnetizable member 124. According to various embodiments, each side surfaces of the longitudinal segment of the elongated magnetizable member 124 with the polygonal cross-sectional profile may serve as the flat side surface 124b of the elongated magnetizable member 124 for engagement with the flat contact surface 126a of the permanent magnet 126.

Accordingly, each side surfaces of the longitudinal segment of the elongated magnetizable member 124 with the polygonal cross-sectional profile may be a corresponding longitudinal side of the elongated magnetizable member 124.

[00062] According to various embodiments, the tip 124a of the elongated magnetizable member 124 may be shaped or configured to maximise localised magnetic gradient at the tip 124a when the permanent magnet 126 is engaged with the elongated magnetizable member 124. According to various embodiments, the tip 124a of the elongated magnetizable member 124 may be of a sharp or tapered or pointed shape to maximise the localised magnetic gradient. According to various embodiments, the tip 124a of the elongated magnetizable member 124 may also be shaped or configured to eliminate or minimise spillage when the elongated magnetizable member 124 is rotated with the tip 124a of the elongated magnetizable member 124 inserted in the well 173, 174 of the microfluidic chip 104 containing solutions. According to various embodiments, the tip 124a of the elongated magnetizable member 124 may be of a sharp or tapered or pointed shape to eliminate or minimise spillage. For example, according to various embodiments, the tip 124a of the elongated magnetizable member 124 may be a pointed tip or a conical tip.

[00063] According to various embodiments, the elongated magnetizable member 124 may be made of magnetizable material. According to various embodiments, the elongated magnetizable member 124 may be made of soft magnetic materials. For example, according to various embodiments, the elongated magnetizable member 124 may be made of, including but not limited to, soft iron, soft ferrites, iron-silicon alloy, or nickel-iron alloy. According to various embodiments, the elongated magnetizable member 124 may be in the form of, including but not limited to, a bar, a rod, or a pole.

[00064] According to various embodiments, the head assembly 120 may be rotatable about a rotational axis 135 with respect to the support structure 110. According to various embodiments, the rotational axis 135 may be parallel to the central axis 125 of the elongated magnetizable member 124 of the head assembly 120. According to various embodiments, rotating the head assembly 120 about the rotational axis 135 with respect to the support structure 110 may rotate the head assembly 120 relative to the support structure 110 in a manner so as to move the elongated magnetizable member 124 laterally along a circular arc path. Accordingly, when the head assembly 120 rotates about the rotational axis 135 relative to the support structure 110, the elongated magnetizable member 124 may be moved sideways along the circular path such that the central axis 125 of the elongated magnetizable

member 124 remains parallel to the rotational axis 135 in all positions along the circular arc path. According to various embodiments, the circular arc path has a radius corresponding to a direct distance between the rotational axis 135 and the central axis 125 of the elongated magnetizable member 124.

- 5 [00065] For example, according to various embodiments, the head assembly 120 may be rotatable about the rotational axis 135 with respect to the head-assembly-support portion 112 of the support structure 110 (for example, see FIG. 10). Accordingly, the head assembly 120 may be rotated about the rotational axis 135 relative to the head-assembly-support portion 112 of the support structure 110 for moving the elongated magnetizable member
- 10 124 laterally along the circular arc path with respect to the head-assembly-support portion 112 of the support structure 110. According to various embodiments, the head-assembly-support portion 112 of the support structure 110 may remain stationary and the head assembly 120 may be moved in a manner so as to rotate about the rotational axis 135. According to various embodiments, the elongated magnetizable member 124 and the frame
- 15 member 122 of the head assembly 120 may be non-moveable relative to each other along a plane perpendicular to the central axis 125 of the elongated magnetizable member 124. According to various embodiments, rotating the head assembly 120 about the rotational axis 135 relative to the head-assembly-support portion 112 of the support structure 110 may rotate the frame member 122 about the rotational axis 135 relative to the head-assembly-
- 20 support portion 112 and along the plane perpendicular to the central axis 125 of the elongated magnetizable member 124. Accordingly, the elongated magnetizable member 124 may be rotated together with the frame member 122 about the rotational axis 135 relative to the head-assembly-support portion 112 of the support structure 110 as the frame member 122 is rotated about the rotational axis 135 relative to the head-assembly-support portion
- 25 112. Since the rotational axis 135 and the central axis 125 of the elongated magnetizable member 124 are parallel to each other, rotating the elongated magnetizable member 124 about the rotational axis 135 relative to the head-assembly-support portion 112 may move the elongated magnetizable member 124 about the rotational axis 135 with a constant distance between the elongated magnetizable member 124 and the rotational axis 135 such
- 30 that the elongated magnetizable member 124 is moving laterally along the circular arc path.
- [00066] As another example, according to various embodiments (not shown), the head-assembly-support portion 112 of the support structure 110 may be in the form of an arm with the rotational axis 135 passing through a first end of the arm and the head assembly

120 being coupled to a second end of the arm. According to various embodiments, the head-assembly-support portion 112 in the form of the arm may have its first end rotatably coupled to a column portion of the support structure 110 such that the head-assembly-support portion 112 in the form of the arm may be rotatable about the rotational axis 135 relative to the column portion. Accordingly, rotating the head-assembly-support portion 112 in the form of the arm about the rotational axis 135 at the first end thereof may rotate the head assembly 120 at the second thereof about the rotational axis 135 relative to the column portion. According to various embodiments, the elongated magnetizable member 124 and the frame member 122 of the head assembly 120 may be non-moveable relative to each other along a plane perpendicular to the central axis 125 of the elongated magnetizable member 124. According to various embodiments, rotating the head assembly 120 about the rotational axis 135, as a result of rotating the head-assembly-support portion 112 in the form of the arm about the rotational axis 135 relative to the column portion, may rotate the frame member 122 about the rotational axis 135 relative to the column portion and along the plane perpendicular to the central axis 125 of the elongated magnetizable member 124. Accordingly, the elongated magnetizable member 124 may be rotated together with the frame member 122 about the rotational axis 135 relative to the column portion as the frame member 122 is rotated about the rotational axis 135 relative to the column portion. Since the rotational axis 135 and the central axis 125 of the elongated magnetizable member 124 are parallel to each other, rotating the elongated magnetizable member 124 about the rotational axis 135 relative to the column portion may move the elongated magnetizable member 124 about the rotational axis 135 with a constant distance between the elongated magnetizable member 124 and the rotational axis 135 such that the elongated magnetizable member 124 is moving laterally along the circular arc path.

[00067] According to various embodiments, the relative movements between the various elements/components of the nucleic acid purification device 102 (i.e. the rotation of the elongated magnetizable member 124 relative to the frame member 122 about the central axis 125, the longitudinal translation of the elongated magnetizable member 124 relative to head-assembly-support portion 112 of the support structure 110 along the central axis, the movement of the permanent magnet 126 towards and away from the elongated magnetizable member 124, and/or the rotation of the head assembly 120 relative to the support structure 110 about the rotational axis 135) may be actuated by a suitable actuator including, but not

limited to, a mechanical actuator, a hydraulic actuator, a pneumatic actuator, or an electric actuator.

- [00068] According to various embodiments (for example see FIG. 7A, FIG. 7B, FIG. 10), the head assembly 120 may include a rotary actuator 132 coupled to the elongated magnetizable member 124 for rotating the elongated magnetizable member 124 about the central axis 125 relative to the frame member 122. The rotary actuator 132 may produce a rotary motion to rotate the elongated magnetizable member 124 relative to the frame member 122 about the central axis 125. According to various embodiments, the rotary actuator 132 may be coupled between the elongated magnetizable member 124 and the frame member 122 so as to rotate the elongated magnetizable member 124 relative to the frame member 122 about the central axis 125 of the elongated magnetizable member 124. According to various embodiments, a body of the rotary actuator 132 may be coupled to the frame member 122 and an output shaft of the rotary actuator 132 may be coupled to the elongated magnetizable member 124. As an example, the output shaft of the rotary actuator 132 may be coupled to an end portion of the elongated magnetizable member 124 opposite the tip 124a of the elongated magnetizable member 124. According to various embodiments, the rotary actuator 132 may include, but not limited to, a direct current (DC) motor, an alternating current (AC) motor, induction motor, asynchronous motor, synchronous motor, fluid power actuators, or vacuum actuators.
- [00069] According to various embodiments, the head assembly 120 may include a linear actuator 134 (see FIG. 10) for translating the elongated magnetizable member 124 longitudinally along the central axis 125 of the elongated magnetizable member 124. The linear actuator 134 may generate a motion in a straight line for moving the elongated magnetizable member 124 longitudinally along the central axis 125. According to various embodiments, the linear actuator 134 may be disposed and/or coupled in a manner such that the elongated magnetizable member 124 is longitudinally translatable along the central axis 125 with respect to the support structure 110. According to various embodiments, the linear actuator 134 may include, but not limited to, a screw type linear actuator (e.g. a leadscrew, a ball and roller screw), a wheel and axle type linear actuator (e.g. a rack and pinion, a chain drive, a belt drive, a crank and slider), a cam type linear actuator, a hydraulic linear actuator, a pneumatic linear actuator, an electro-mechanical linear actuator, a linear motor, or a telescoping linear actuator.

[00070] For example, according to various embodiments, the linear actuator 134 may be coupled between the head-assembly-support portion 112 of the support structure 110 and the frame member 122 of the head assembly 120 to move the frame member 122 of the head assembly 120 with respect to the head-assembly-support portion 112 of the support structure 110 in a direction parallel to the central axis 125 of the elongated magnetizable member 124 so as to translate the elongated magnetizable member 124 longitudinally along the central axis 125 towards and away from the head-assembly-support portion 112. Accordingly, the linear actuator 134 may move the frame member 122 of the head assembly 120 relative to the head-assembly-support portion 112 of the support structure 110 so as to move the elongated magnetizable member 124, which is non-moveable relative to the frame member 122 along the central axis 125, with respect to the head-assembly-support portion 112 of the support structure 110. According to various embodiments, a body of the linear actuator 134 may be coupled to the head-assembly-support portion 112 of the support structure 110 and an output movement part of the linear actuator 134 may be coupled to the frame member 122 of the head assembly 120.

[00071] As another example (not shown), according to various embodiments, linear actuator 134 may be coupled between the frame member 122 of the head assembly 120 and the elongated magnetizable member 124 so as to translate the elongated magnetizable member 124 longitudinally along the central axis 125 relative to the frame member 122 for moving the elongated magnetizable member 124 towards and away from the head-assembly-support portion 112. According to various embodiments, a body of the linear actuator 134 may be coupled to the frame member 122 of the head assembly 120 and an output movement part of the linear actuator 134 may be coupled to the elongated magnetizable member 124 so as to directly move the elongated magnetizable member 124 relative to the frame member 122.

[00072] According to various embodiments, the head assembly 120 may include an actuation unit 150 (for example, see FIG. 7A, FIG. 7B and FIG. 10) coupled to the permanent magnet 126 for moving the permanent magnet 126 towards and away from the elongated magnetizable member 124. Accordingly, the actuation unit 150 may serve as the mechanism imparting movements or motions to the permanent magnet 126 for moving the permanent magnet 126 relative to the frame member the elongated magnetizable member 124. According to various embodiments, the actuation unit 150 may include, but not limited

to, a linear actuator, a rotary to linear actuating mechanism, a robotic arm, a manipulator, or a Cartesian coordinate robot arrangement.

[00073] According to various embodiments, the actuation unit 150 may include an extendable mechanism 152 and an actuating mechanism 154. According to various
5 embodiments, the permanent magnet 126 may be mounted to an end (or output end) of the extendable mechanism 152. According to various embodiments, the actuating mechanism 154 may be coupled to the extendable mechanism to control an extension or a retraction of the extendable mechanism 152 for moving the permanent magnet 126 towards and away from the elongated magnetizable member 124. According to various embodiments, the
10 extendable mechanism 152 may include, but not limited to a telescopic mechanism, a slidable mechanism, an extendable bellow mechanism, or a scissor type extension mechanism. According to various embodiments, the actuating mechanism 154 may include any suitable actuator including, but not limited to, a mechanical actuator, a hydraulic actuator, a pneumatic actuator, or an electric actuator. According to various embodiments,
15 the actuating mechanism 154 may include suitable motion convertor to convert driving motion of the actuator into suitable output motion for moving the extendable mechanism.

[00074] According to various embodiments, the nucleic acid purification device 102 may include a rotary actuator 136 (see FIG. 10) for rotating the head assembly 120 relative to the support structure 110 about the rotational axis 135. The rotary actuator 136 may produce a
20 rotary motion to rotate the head assembly 120 relative to the support structure 110 about the rotational axis 135. According to various embodiments, the rotary motion may be in a stepwise manner, whereby the rotary actuator 136 is capable of dividing the angular rotation into steps. According to various embodiments, the rotary actuator 136 may be coupled between the head assembly 120 and the support structure 110 so as to rotate the head
25 assembly 120 relative to the support structure 110 about the rotational axis 135. According to various embodiments, the rotary actuator 136 may be a stepper rotary actuator including, but not limited to, a stepper motor or a servomotor.

[00075] For example as shown in FIG. 10, according to various embodiments, the head assembly 120 may be rotatable about the rotational axis 135 with respect to the head-
30 assembly-support portion 112 of the support structure 110 for moving the elongated magnetizable member 124 laterally along the circular arc path with respect to the head-assembly-support portion 112 of the support structure 110. According to various embodiments, the rotary actuator 136 may be coupled between the head assembly 120 and

the head-assembly-support portion 112 of the support structure 110 in a manner so as to rotate the head assembly 120 about the rotational axis 135 with respect to the head-assembly-support portion 112 of the support structure 110. According to various embodiments, a body of the rotary actuator 136 may be coupled to the head-assembly-support portion 112 of the support structure 110 and an output shaft of the rotary actuator 136 may be coupled to the head assembly 120. For example, according to various embodiments, the output shaft of the rotary actuator 136 may be coupled to the body of the linear actuator 134 which is for translating the elongated magnetizable member 124 longitudinally along the central axis 125 of the elongated magnetizable member 124.

10 [00076] As another example (not shown), according to various embodiments, the head-assembly-support portion 112 of the support structure 110 may be in the form of the arm with the first end thereof rotatably coupled to the column portion of the support structure 110 and the head assembly 120 coupled to the second end thereof such that the head assembly 120 is rotatable about the rotational axis 135. According to various embodiments, 15 the rotary actuator 136 may be coupled between the head-assembly-support portion 112 of the support structure 110 and the column portion of the support structure 110 so as to rotate the head-assembly-support portion 112 in the form of the arm about the rotational axis 135 for rotating the head assembly 120 about the rotational axis 135.

[00077] According to various embodiments, the nucleic acid purification device 102 may include a controller. According to various embodiments, the controller may be electrically connected to the various actuator and/or actuation unit for controlling and coordinating the various movements of the various elements. For example, according to various embodiments, the controller may be configured to control the rotary actuator 132 for rotating the elongated magnetizable member 124 about the central axis 125 relative to the frame member 122, the linear actuator 134 for translating the elongated magnetizable member 124 longitudinally along the central axis 125, actuation unit 150 for moving the permanent magnet 126 towards and away from the elongated magnetizable member 124, and/or the rotary actuator 136 for rotating the head assembly 120 relative to the support structure 110 about the rotational axis 135.

25 30 [00078] In various embodiments, the "controller" may be understood as any kind of a logic implementing entity, which may be special purpose circuitry or a processor executing software stored in a memory, firmware, or any combination thereof. Thus, in an embodiment, the "controller" may be a hard-wired logic circuit or a programmable logic

circuit such as a programmable processor, e.g. a microprocessor (e.g. a Complex Instruction Set Computer (CISC) processor or a Reduced Instruction Set Computer (RISC) processor). The "controller" may also be a processor executing software, e.g. any kind of computer program, e.g. a computer program using a virtual machine code such as e.g. Java. Any other
5 kind of implementation of the respective functions which are described in more detail throughout may also be understood as the "controller" in accordance with various embodiments. In various embodiments, the "controller" may be part of a computing system or a controller or a microcontroller or any other system providing a processing capability. According to various embodiments, such systems may include a memory which is for
10 example used in the processing carried out by the device or system. A memory used in the embodiments may be a volatile memory, for example a DRAM (Dynamic Random Access Memory) or a non-volatile memory, for example a PROM (Programmable Read Only Memory), an EPROM (Erasable PROM), EEPROM (Electrically Erasable PROM), or a flash memory, e.g., a floating gate memory, a charge trapping memory, an MRAM
15 (Magnetoresistive Random Access Memory) or a PCRAM (Phase Change Random Access Memory).

[00079] According to various embodiments, the support structure 110 of the nucleic acid purification device 102 may include a stage portion 114 for supporting the microfluidic chip 104. According to various embodiments, the stage portion 114 may be spaced apart from
20 the head-assembly-support portion 112. According to various embodiments, the stage portion 114 may be opposing the head-assembly-support portion 112. Accordingly, the elongated magnetizable member 124 may be moved away from the stage portion 114 when the elongated magnetizable member 124 of the head assembly 120 translates longitudinally along the central axis 125 to move towards the head-assembly-support portion 112. Further,
25 the elongated magnetizable member 124 may be moved towards the stage portion 114 as the elongated magnetizable member 124 of the head assembly 120 translates longitudinally along the central axis 125 to move away from the head-assembly-support portion 112. Therefore, the elongated magnetizable member 124 may be translatable longitudinally along the central axis 125 to move between the head-assembly-support portion 112 and the stage
30 portion 114.

[00080] According to various embodiments, the nucleic acid purification device 102 may include a sonication component 160. The sonication component 160 may provide acoustic energy to agitate samples. According to various embodiments, the sonication component

160 may include a acoustic energy output surface 162. According to various embodiments, the sonication component 160 may be coupled to the stage portion 114 of the support structure 110 in a manner so as to contact the microfluidic chip 104 when the microfluidic chip 104 is supported on the stage portion 114. Accordingly, the sonication component 160 may impart acoustic energy to the microfluidic chip 104 for agitating a sample contained in the microfluidic chip 104. According to various embodiments, the sonication component 160 may be coupled to the stage portion 114 in a manner such that the acoustic energy output surface 162 of the sonication component 160 may flush with a support surface of the stage portion 114. Accordingly, when the microfluidic chip 104 is placed onto the stage portion 114, the acoustic energy output surface 162 of the sonication component 160 may be in direct contact or abutting a bottom surface 104a of the microfluidic chip 104 such that the acoustic energy may be directly projected into the microfluidic chip 104 to optimise the effect of the acoustic energy for agitating the sample.

[00081] According to various embodiments, the microfluidic chip 104 may include a plurality of wells 173,174, 175, 176, 177, 178 (for example, see FIG. 2 and FIG. 3). According to various embodiments, each well 173,174, 175, 176, 177, 178 may be a recess in the microfluidic chip 104 with an opening at a top surface 104b of the microfluidic chip 104 providing access into the well 173,174, 175, 176, 177, 178. The top surface of the microfluidic chip 104 may be the surface facing upwards (or directed towards the head-assembly-support portion 112) when the microfluidic chip 104 is placed onto the stage portion 114.

[00082] According to various embodiments, at least one well 173,174, 175, 176, 177, 178 of the microfluidic chip 104 may contain the plurality of magnetic particles 170. According to various embodiments, the head assembly 120 of the nucleic acid purification device 102 may be operable to engage the permanent magnet 126 with the elongated magnetizable member 124 to induce magnetism in the elongated magnetizable member 124. According to various embodiments, the head assembly 120 may then move the elongated magnetizable member 124 with induced magnetism to translate along the central axis 124 so as to move the tip 124a of the elongated magnetizable member 124 towards the stage portion 114 for inserting into the at least one well 173,174, 175, 176, 177, 178 of the microfluidic chip 104 placed on the stage portion 114 to capture the plurality of magnetic particles 170 in the at least one well 173,174, 175, 176, 177, 178. According to various embodiments, the head assembly 120 may subsequently move the tip 124a of the elongated magnetizable member

124 away from the stage portion 114 for removing the plurality of magnetic particles 170 magnetically attached to the tip 124a of the elongated magnetizable member 124 from the at least one well 173,174, 175, 176, 177, 178.

[00083] Further, according to various embodiments, when the tip 124a of the elongated magnetizable member 124 and the plurality of magnetic particles 170 magnetically attached thereto are inserted into one other well 173,174, 175, 176, 177, 178 of the microfluidic chip 104, the head assembly 120 of the nucleic acid purification device 102 may be operable to disengage the permanent magnet 126 from the elongated magnetizable member 124 to cause the elongated magnetizable member 124 to lose its induced magnetism. Accordingly, the head assembly 120 may then rotate the elongated magnetizable member 124 without induced magnetism about the central axis 125 relative to the frame member 122 in a manner so as to disperse the plurality of magnetic particles 170 from the tip 124a of the elongated magnetizable member 124 into the one other well 173,174, 175, 176, 177, 178.

[00084] According to various embodiments, the plurality of wells 173,174, 175, 176, 177, 178 of the microfluidic chip 104 may be arranged in a circular arc corresponding to the circular arc path of the elongated magnetizable member 124 when the head assembly 120 is rotated about the rotational axis 135. Accordingly, the head assembly 120 of the nucleic acid purification device 102 may be operable to rotate the head assembly 120 for moving the elongated magnetizable member 124 along the circular arc path to transfer the plurality of magnetic particles 170 magnetically attached to the tip 124a of the elongated magnetizable member 124 from the at least one well 173,174, 175, 176, 177, 178 to the one other well 173,174, 175, 176, 177, 178.

[00085] According to various embodiments, the microfluidic chip 104 may include a removable cap 180 (for example see FIG. 15) held in the microfluidic chip 104. According to various embodiments, the cap 180 may be configured for fitting onto the tip 124a of the elongated magnetizable member 124. According to various embodiments, the cap 180 may serve as a barrier between the plurality of magnetic particles 170 and the tip 124a of the elongated magnetizable member 124 to prevent contamination. According to various embodiments, the cap 180 may be shaped and dimensioned for interference fit with the tip 124a of the elongated magnetizable member 124 so as to ensure that the cap 180 may not fall off during transfer of the plurality of magnetic particles 170 and/or rotation of the elongated magnetizable member 124 about the central axis 125. According to various embodiments, a thickness of the wall of the cap may be configured to maximise the magnetic

force of the tip 124a of the elongated magnetizable member 124 passing through the cap. According to various embodiments, as an example, the cap 180 may be in the form of a cone.

[00086] According to various embodiments, the head assembly 120 of the nucleic acid purification device 102 may be operable to move the elongated magnetizable member 124 to translate along the central axis 125 so as to move the tip 124a of the elongated magnetizable member 124 towards the stage portion 114 for inserting into the cap 180 of the microfluidic chip 104 placed on the stage portion 114 so as to fit the cap 180 over the tip 124a of the elongated magnetizable member 124. According to various embodiments, the head assembly 120 may subsequently be operated to move the tip 124a of the elongated magnetizable member 124 away from the stage portion 114 for removing the cap 180 from the microfluidic chip 104 with the cap 180 fitted to the tip 124a of the elongated magnetizable member 124.

[00087] According to various embodiments, the microfluidic chip 104 may include an arcuate opening 182 (for example see FIG. 15). According to various embodiments, the arcuate opening 182 may be configured to cooperate with the movement of the elongated magnetizable member 124 for the removal of the cap 180 from the tip 124a of the elongated magnetizable member 124. According to various embodiments, the arcuate opening 182 may be an opening having a curve shape or an arc shape. According to various embodiments, a width of a first end 182a of the arcuate opening 182 may be wider than a width at a second end 182b of the arcuate opening 182.

[00088] According to various embodiments, the head assembly 120 of the nucleic acid purification device 102 may be operable to move the elongated magnetizable member 124 to translate along the central axis 125 so as to move the tip 124a of the elongated magnetizable member 124 with the cap 180 fitted thereto towards the stage portion 114 for inserting into the arcuate opening 182 of the microfluidic chip 104 placed on the stage portion 114 via the first end 182a of the arcuate opening 182. According to various embodiments, the head assembly 120 may then be operated to rotate the head assembly 120 about the rotational axis 135 with respect to the support structure 110 so as to move the elongated magnetizable member 124 laterally along the circular arc path to the second end 182a of the arcuate opening 182. According to various embodiments, the head assembly 120 may subsequently be operated to move the tip 124a of the elongated magnetizable member 124 away from the stage portion 114 for removing the cap 180 from the tip 124a of the

elongated magnetizable member 124 as the cap 180 is held by the narrower width at the second end 182a of the arcuate opening 182.

[00089] According to various embodiments, the width of the first end 182a of the arcuate opening 182 of the microfluidic chip may be configured such that the tip 124a of the elongated magnetizable member 124 together with the cap 180 fitted thereon may be inserted through the first end 182a of the arcuate opening 182. Accordingly, the width of the first end 182a of the arcuate opening 182 may be equal or larger than a diameter/width of the outermost (or largest overall) perimeter of the cap 180. According to various embodiments, the width of the second end 182b of the arcuate opening 182 of the microfluidic chip may be equal or larger than a diameter/width of the outermost (or largest overall) perimeter of the tip 124a of the elongated magnetizable member 124 alone, and smaller than the diameter/width of the outermost (or largest overall) perimeter of the cap 180. Accordingly, the tip 124a of the elongated magnetizable member 124 together with the cap 180 fitted thereon may be inserted through the first end 182a of the arcuate opening 182 while the smaller width of the second end 182b of the arcuate opening 182 may block or obstruct the cap 180 and still allowing the tip 124a of the elongated magnetizable member 124 to pass therethrough. For example, according to various embodiments, the second end 182b of the arcuate opening 182 of the microfluidic chip 104 may include an inward protruding collar or flange forming a constriction such that the width at the second end 182b of the arcuate opening 182 may be smaller than the width at the first end 182a of the arcuate opening 182. Accordingly, the inward protruding collar or flange may block or obstruct the cap 180 as the tip 124a of the elongated magnetizable member 124 is being drawn out from the second end 182b of the arcuate opening 182 such that the cap 180 may be removed.

[00090] According to various embodiments, the microfluidic chip 104 may include an enclosed lysis chamber 171 (for example see FIG. 3 and FIG. 15). According to various embodiments, the enclosed lysis chamber 171 may include an inlet port 171a. According to various embodiments, sample may be introduced into the enclosed lysis chamber 171 via the inlet port 171a. For example, according to various embodiments, the inlet port 171a may be an opening at the top surface of the 104b of the microfluidic chip 104 or a short tube extending from the top surface of the 104b of the microfluidic chip 104 into the enclosed lysis chamber 171. According to various embodiments, the enclosed lysis chamber 171 may be arranged or disposed within the microfluidic chip 104 in a manner such that the enclosed lysis chamber 171 may lie on the acoustic energy output surface 162 of the sonication

component 160 when the microfluidic chip 104 is placed on the stage portion 114 of the nucleic acid purification device 102.

[00091] According to various embodiments, the enclosed lysis chamber 171 may include a filter 171b (for example see FIG. 3) partitioning the enclosed lysis chamber into an upper sub-chamber and a lower sub-chamber. According to various embodiments, the filter 171b may be disposed along a height of the enclosed lysis chamber 171 between the bottom surface 104a and the top surface 104b of the microfluidic chip 104. According to various embodiments, the enclosed lysis chamber 171 may contain lysis solution and the filter 171b may be immersed in the lysis solution. According to various embodiments, the sample being introduced into the enclosed lysis chamber 171 may be retained in the upper sub-chamber. After the sample is being subjected to lysis, the filter may filter the fibre/debris and keep them within the upper sub-chamber while the lysis processed solution to flow into the lower sub-chamber.

[00092] According to various embodiments, the microfluidic chip 104 may include a discharge tube 184 (for example see FIG. 3). According to various embodiments, the discharge tube 184 may extend from the lower sub-chamber of the enclosed lysis chamber 171 to an exterior surface of the microfluidic chip 104. According to various embodiments, a first end opening 184a of the discharge tube 184 may be located within the lower sub-chamber of the enclosed lysis chamber 171 and a second end opening 184b of the discharge tube 184 may be exposed from the exterior surface (e.g. the top surface 104b) of the microfluidic chip 104. Accordingly, the lysis processed solution may be discharge from the lower sub-chamber of the enclosed lysis chamber 171 via the discharge tube 184. According to various embodiments, discharging of the lysis processed solution may be via fluid purging or air purging via the inlet port 171a of the enclosed lysis chamber 171.

[00093] According to various embodiments, the microfluidic chip 104 may include a sliding plate 186 (for example see FIG. 3, FIG. 14 and FIG. 15). According to various embodiments, the sliding plate 186 may be slidable along the exterior surface (e.g. the top surface 104b) of the microfluidic chip 104. According to various embodiments, the sliding plate 186 may include an embedded channel 188. According to various embodiments, a first end opening 188a of the embedded channel 188 and a second end opening 188b of the embedded channel 188 may be exposed from a surface 186a of the sliding plate 186. The surface 186a of the sliding plate 186 may be one of the two broad flat surfaces of the sliding plate 186. Accordingly, the a first end opening 188a of the embedded channel 188 and a

second end opening 188b of the embedded channel 188 may be exposed from the same surface 186a of the sliding plate 186. According to various embodiments, the surface 186a of the sliding plate 186 may be facing (or directed towards) the top surface 104b of the microfluidic chip 104. According to various embodiments, the surface 186a of the sliding plate 186 may be in sliding engagement with the exterior surface (e.g. the top surface 104b) of the microfluidic chip 104.

[00094] According to various embodiments, the sliding plate 186 may be slidable along the top surface 104b of the microfluidic chip 104. According to various embodiments, the sliding plate 186 may be slidable into an aligned position to align the first end opening 188a of the embedded channel 188 of the sliding plate 186 with the second end opening 184b of the discharge tube 184 and to align the second end opening 188b of the embedded channel 188 of the sliding plate 186 with the at least one well 173 of the microfluidic chip 104 for transferring fluid from the enclosed lysis chamber 171 into the at least one well 173. Accordingly, by sliding the sliding plate 186 into the aligned position, the lysis processed solution may be from the enclosed lysis chamber 171 via the discharge tube 184, through the embedded channel 188 and into the at least one well 173. Subsequently, the lysis processed solution may be mixed with the plurality of magnetic particles in the at least one well 173 and be transferred to the other wells 174, 175, 176, 177, 178 using the nucleic acid purification device 102 from one well to another in a step by step manner so as to perform the nucleic acid purification/extraction/preparation process.

[00095] In the following, the nucleic acid purification system 100, the nucleic acid purification device 102 and the microfluidic chip 104 according to the various embodiments will be described in further details with reference to the more detailed embodiments as shown in the subsequent figures. The detailed embodiments described in the following include all features and limitations as previously described unless indicated otherwise.

[00096] According to various embodiments, there is provided the nucleic acid purification device 102 (or an integrated microfluidic device) and the microfluidic chip 104 (or a chip). FIG. 2 shows a microfluidic chip 104 according to various embodiments. According to various embodiments, the microfluidic chip 104 may be developed for automated sample preparation for DNA extraction from semi-solid or solid samples. As shown in FIG. 2, the microfluidic chip 104 (or chip) may be formed by a rigid plate containing micro-channels (e.g. the embedded channel 188) and seven main reaction chambers/wells 171, 173, 174, 175, 176, 177, 178, which may be pre-stored with different types of reagents for DNA

purification/extraction/preparation. An additional movable plate (e.g. the sliding plate 186) may be utilized to disconnect a first chamber (e.g. the enclosed lysis chamber 171) and a first well 173, and only establish connection between the two when ready to start the process. Reagents in the seven main reaction chambers/wells 171, 173, 174, 175, 176, 177, 178 may be sealed with plastic film 105 through lamination. Instead of using additional device/pipettes to manipulate different reagents for lysis, binding, washing, elution, etc., various embodiments utilized a bio-reaction booster setup (e.g. the nucleic acid purification device 102) to enable contamination free cell lysis, fast DNA/RNA binding to the magnetic beads (or magnetic particles 170), the magnetic beads (or magnetic particles 170) collection/transfer/release to obtain purified nucleic acids. In one way, fast and efficient cell lysis may be realized through coupling ultrasonic wave into the samples. In another way, the lysis may be implemented through agitating samples in a vessel.

[00097] According to various embodiments, the following protocol or process flow was developed for the nucleic acid purification system 100, the nucleic acid purification device 102 and the microfluidic chip 104 according to the various embodiments, and verified via *Clostridium difficile* DNA detection through on-chip feces sample processing using the nucleic acid purification system 100, the nucleic acid purification device 102 and the microfluidic chip 104 according to the various embodiments.

[00098] Step 1: Suspend feces in provided solution in a container, e.g. ~ Feces 0.5 g in 1.5 mL solution in the container.

[00099] Step 2: approximately 200 μ L sample is introduced into first chamber (e.g. the enclosed lysis chamber 171) of the microfluidic chip 104 which contains pre-stored solution for lysis.

[00100] Step 3: Ultrasonic lysis of cells in sample according to optimized protocol.

[00101] Step 4: Through the micro-channel (e.g. the embedded channel 188), the lysis processed sample is flushed into the first well 173 which contains pre-stored solution optimized for DNA seizing by magnetic beads (or magnetic particles 170).

[00102] Step 5: The magnetic beads (or magnetic particles 170) with seized DNA are captured by a magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) and transferred to the second well 174; the magnetic field on the magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) is removed; the magnetic beads (or magnetic particles 170) are re-dispersed into solution through rotating of the magnetic bar (i.e. the elongated magnetizable member 124

of the nucleic acid purification device 102); the magnetic field on magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) is regenerated; the magnetic beads are re-captured by the magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) and transferred to the
5 third well 175.

[000103] Step 6: the magnetic field on magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) is removed; the magnetic beads (or magnetic particles 170) are re-dispersed into solution through rotating of the magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102);
10 the magnetic field on magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) is regenerated; magnetic beads (or magnetic particles 170) are re-captured by the magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) and transferred to the fourth well 176.

[000104] Step 7: the magnetic field on magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) is removed; the magnetic beads (or magnetic particles 170) are re-dispersed into solution through rotating of magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102); the magnetic field on magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) is regenerated; magnetic beads (or magnetic particles 170) are
20 re-captured by the magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) and transferred to the fifth well 177.

[000105] Step 8: the magnetic field on magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) is removed; the magnetic beads (or magnetic particles 170) are re-dispersed into solution through rotating of magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102); the magnetic field on magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) is regenerated; the magnetic beads (or magnetic particles 170) are re-captured by the magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) and transferred to sixth well 178.

30 **[000106]** Step 9: the magnetic field on magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) is removed; the magnetic beads (or magnetic particles 170) are re-dispersed into solution through rotating of magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102); the

magnetic field on magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) is regenerated; the magnetic beads (or magnetic particles 170) are re-captured by the magnetic bar (i.e. the elongated magnetizable member 124 of the nucleic acid purification device 102) and transferred to cone unloading chamber (e.g. the arcuate opening 182).

[000107] Step 10: Purified DNA is ready for collection in the sixth well 178.

[000108] According to various embodiments, several parts of the the nucleic acid purification system 100, the nucleic acid purification device 102 and/or the microfluidic chip 104 have been configured to ensure the successful processing of semi-solid samples such as feces at high speed, high efficiency and free of contamination.

[000109] FIG. 3 shows another view of the microfluidic chip 104 according to various embodiments. According to various embodiments, the overall configuration of the microfluidic chip 104 may be integrated with pre-storage of reagents, fast fluid transfer between chambers, effective beads capturing and sonication coupling for cell lysis in semi-solid/solid (e.g. feces).

[000110] According to various embodiments, the microfluidic chip may be designed to have pre-stored reagents for nucleic acid purification/extraction/preparation. According to various embodiments, the reagents are determined such that all reagents may be stored at room temperature instead of 4⁰C or -20⁰C. According to various embodiments, the reagents stored in the seven main reaction chambers/wells 171, 173, 174, 175, 176, 177, 178 may be sealed through a plastic lamination process and the user may just peel off the lamination layer (e.g. the plastic film 105) to get the microfluidic chip 104 ready to be used. According to various embodiments, the enclosed lysis chamber 171 and a spare chamber 172 (i.e. a chamber used as a backup chamber for additional function) may be sealed with the sliding plate 186 which will be described in more details later. According to various embodiments, the chamber 171 for cell lysis may be shaped as shown in FIG. 3 such that fluid may be fully purged first before air is purged into the channel (e.g. the embedded channel 188) so as to eliminate or minimise sample loss.

[000111] In general, DNA purification/extraction/preparation is to disrupt cells and collect DNA for subsequent molecular analysis. Cell lysis is typically the most time consuming part in the sample preparation and it is usually done through either chemical lysis (e.g. sodium dodecyl sulfate - SDS, cetyltrimethyl ammonium bromide - CTAB, enzyme) or mechanical lysis (e.g. grinding, beads beating). In various embodiments,

ultrasonic energy from an external ultrasonic horn (i.e. the sonication component 160) may be coupled to a specifically configured chamber (e.g. the enclosed lysis chamber 171) containing both sample and lysis reagents for cell lysis. According to various embodiments, when ultrasonic wave propagate in the solution, localized pressure gradient may be generated and the cells may then be subjected to high shear stress which may be utilized for lysis. The lysis microfluidic chamber (e.g. the enclosed lysis chamber 171) in contact with horn (i.e. the sonication component 160) may be made of the material of PMMA (polymethyl methacrylate) which has an acoustic impedance of $3.2 (10^6 \text{ kg}/(\text{m}^2\text{s}))$ close to acoustic impedance of water ($1.5 (10^6 \text{ kg}/(\text{m}^2\text{s}))$). In this way, the efficiency of acoustic energy (or sound energy) transfer is calculated as

$$100\% - \frac{(3.2 - 1.5)^2}{(3.2 + 1.5)^2} \cong 87\%$$

[000112] To ensure a good energy transfer from the horn (i.e. the sonication component 160) to the microfluidic chip 104, a $500 \mu\text{m}$ thick PDMS (polydimethylsiloxane) membrane (with an acoustic impedance of $1.1 (10^6 \text{ kg}/(\text{m}^2\text{s}))$) may be utilized in between the horn (i.e. the sonication component 160) and the microfluidic chip 104 to have the energy transfer efficiency as

$$100\% - \frac{(1.5 - 1.1)^2}{(1.5 + 1.1)^2} \cong 98\%$$

[000113] According to various embodiments, an additional advantage of the PDMS membrane is that it may be pressed, deformed such that a gapless coupling or in-contact of horn (i.e. the sonication component 160) to the microfluidic chip 104 may be obtained. FIG. 4 shows experimental observation for 10 seconds and 2 seconds lysis based on on-chip ultrasonic cell lysis conducted using rabbit blood. The experiments have showed that at least 0.5 Kg contact force may be needed to be applied for achieving good cell lysis. In the experiments, on-chip ultrasonic cell lysis is validated using rabbit blood. As shown in FIG. 4, 10 seconds lysis or sonication time may lead to nearly 100% cell lysis while 2 seconds lysis time may already lead to 80% cell lysis. In this way, the cell lysis time according to the various embodiments have been significantly reduced from 15 minutes (required for conventional methods) to a few seconds with the microfluidic chip 104 configuration, microfluidic chip 104 material selection, as well as coupling of the sonication horn (i.e. the sonication component 160) to the microfluidic chip 104 according to the various embodiments. Most importantly, the sonication in the various embodiments may be remote

from microfluidic chip 104 (i.e. no direct contact with sample/reagents) and, thus, there may be no concern of contamination.

[000114] According to various embodiments, the microfluidic chip 104 may include sandwiched filter (or filter 171b) to have effective lysis of semi-solid/solid sample (e.g. feces) while prevent flowing of semi-solid/solid debris (e.g. feces debris) to downstream so as to eliminate or minimise blockage of the micro-channel (e.g. the embedded channel 188) and/or inhibition of DNA seizing by magnetic beads (or magnetic particles 170).

[000115] Feces sample is known to be one of the most difficult to-be-processed sample types since it is semi-solid. It is difficult to be dissolved and is fibre/debris rich after dissolving in solution. It is also difficult to be handled using pipettes due to the blockage of pipette tips by fibre/debris. On-chip processing of feces sample is even more challenging since microchannel is much easier to be blocked by the fibre/debris and thus lead to sample loss. Besides channel blockage, sticky debris may inhibit DNA capturing by magnetic beads (or magnetic particles 170). In various embodiments, a fine mesh filter embedded in the lysis chamber on-chip (or enclosed lysis chamber 171 of the microfluidic chip 104 as shown in FIG. 3) to effectively filter fibre/debris after lysis while allowing only lysis processed solution to flow to downstream. According to various embodiments, the filter 171b may be positioned in such a way that it may be fully immersed in lysis solution before adding in the sample. After sample loading, all feces may be in the lysis solution and subjected to ultrasonic based lysis. So the filter 171b may ensure proper lysis of sample while prevent the flowing of fibre/debris to downstream.

[000116] Various embodiments may be provided with an effective and contamination free bio-reaction booster setup (e.g. the nucleic acid purification device 102) to create disturbance in the chamber/wells 171, 173, 174, 175, 176, 177, 178 of the microfluidic chip 104 with liquid containing bio samples and reactance.

[000117] In magnetic beads based DNA capturing, micron sized surface coated/treated superparamagnetic beads are mixed with DNA solution followed by separation from the solution. During the separation, usually a space varying magnetic field is generated from an electromagnet and the superparamagnetic beads will move along the magnetic field gradient. However a few drawbacks are encountered when electromagnet is implemented for such separation: excessive heat generated due to high current applied for effective separation; inconsistent magnetic field/force generated due to temperature fluctuation of coil and soft

magnetic rod placed in the center of coil; and/or maximum generated magnetic force is limited by the maximum current the coil can be fed for a fixed coil turns.

[000118] There may be less concern on the above problems when utilizing a permanent magnet instead of an electromagnet. This is because the permanent magnet is not powered
5 by electricity, its magnetic field does not depend on current and, thus, there may be no concern on excessive heat generated. However, the magnetic field of permanent magnet is not amenable. Hence, the use of permanent magnet may not be directly applied in magnetic beads based DNA capturing.

[000119] In contrast to conventional methods, according to various embodiments, the
10 permanent magnet 126 may be attached to/detached from a soft iron rod (i.e. the elongated magnetizable member 124) so as to turn on/off a magnetic field generated. According to various embodiment, the coupling or engagement may be configured to ensure high magnetic field may be generated for beads capturing and an auto alignment between a permanent magnet 126 and a magnetizable bar (i.e. the elongated magnetizable member 124)
15 for area-to-area contact. The following are more details on the configuration.

[000120] According to various embodiments, the end of soft iron rod (i.e. the tip 124a of the elongated magnetizable member 124) may be in a shape of sharp end so that the localized magnetic gradient at tip 124a may be maximized.

[000121] According to various embodiments, the permanent magnet may be put as close
20 to the beads capturing tip of soft-iron bar (i.e. the tip 124a of the elongated magnetizable member 124) as possible as validated through simulation (see FIG. 5). FIG. 5 shows higher magnet gradient may be obtained when placing the permanent magnet 126 closer to the beads capturing tip of soft-iron bar (i.e. the tip 124a of the elongated magnetizable member 124) according to various embodiments.

[000122] According to various embodiments, a cut-in (e.g. the flat side surface 124b), for
25 ensuring area-to-area contact, on the soft iron bar (i.e. the elongated magnetizable member 124) may give higher localized magnetic gradient at the beads capturing tip of soft-iron bar (i.e. the tip 124a of the elongated magnetizable member 124) as shown in FIG. 6. FIG. 6 shows a cut-in (e.g. the flat side surface 124b) on a round soft-iron bar (i.e. the elongated
30 magnetizable member 124) will give higher localized magnetic gradient at the beads capturing tip of soft-iron bar (i.e. the tip 124a of the elongated magnetizable member 124) according to various embodiments.

[000123] According to various embodiment, a hexagon shape of the soft iron rod (i.e. the elongated magnetizable member 124), as shown as in FIG. 7A, may be utilized for improved magnetic beads (or magnetic particles 170) capturing. When the permanent magnet 126 in a holder (e.g. the extendable mechanism 152) moves close to the soft iron bar (i.e. the elongated magnetizable member 124), the soft iron rod (i.e. the elongated magnetizable member 124) may be magnetized and rotated to be aligned to the permanent magnetic field according to various embodiments. According to various embodiments, the permanent magnet 126 and/or the edge of permanent magnet holder (e.g. the extendable mechanism 152) may push and cause the rotation of the hexagonal shape soft iron rod (i.e. the elongated magnetizable member 124) and eventually bring the surface of the permanent magnet (e.g. the flat contact surface 126a of the permanent magnet 126) and the soft iron rod (e.g. flat side surface 124b of the elongated magnetizable member 124) together. According to various embodiments, such configuration may ensure a smooth detaching of the permanent magnet 126 from the soft iron rod (i.e. the elongated magnetizable member 124) as shown in FIG. 7B. FIG. 7A shows the permanent magnet 126 being detached from the hexagon shaped soft iron bar (i.e. the elongated magnetizable member 124) according to various embodiments. FIG. 7B shows the permanent magnet 126 being attached to soft iron bar (i.e. the elongated magnetizable member 124) according to various embodiments. According to various embodiments, the soft iron bar (i.e. the elongated magnetizable member 124) and permanent magnet 126 may be automatically aligned for area to area contact.

[000124] In various embodiments, contamination free bio-reaction may be achieved through an attached cone (i.e. the cap 180) to the able-to-spin soft iron rod (i.e. the elongated magnetizable member 124). The configuration in the various embodiments may ensure the cone (i.e. the cap 180) may remain attached to the soft iron bar tip (i.e. the tip 124a of the elongated magnetizable member 124) throughout the process such that cone (i.e. the cap 180) handling time may be saved.

[000125] According to various embodiments, during the purification/extraction/preparation process, the magnetic beads (or magnetic particles 170) captured with DNA/RNA may be attached to the cone (i.e. the cap 180) instead of the soft iron rod (i.e. the tip 124a of the elongated magnetizable member 124). Since the magnetic beads (or magnetic particles 170) may be super tiny (approximately 2 um in diameter) and light, they may remain sticking to the surface of cone (i.e. the cap 180) after the soft iron rod (i.e. the elongated magnetizable member 124) is demagnetized. Thus an active beads

detaching method may be needed. The configuration in the various embodiments ensure a controlled spinning of the soft iron rod (i.e. the elongated magnetizable member 124) and the cone (i.e. the cap 180) to actively disperse the magnetic beads (or magnetic particles 170) into the solution. The beauty of this configuration is that a high detaching force may be applied by applying a higher spinning speed. Thus a shorter bio-reaction time may be achieved.

[000126] On the other hand, the various embodiments may enable both clockwise and anti-clockwise spinning of cone (i.e. the cap 180) at controlled speed (revolution per minute, rpm) in solution. By applying such optimized spinning to the cone (i.e. the cap 180), an active mixing may applied to the solution and the samples such that effective reaction may be done in a shorter time.

[000127] According to various embodiments, the cone (i.e. the cap 180) may prevent contamination, the cone shape (i.e. the shape of the cap 180) may be configured for fast/effective DNA extraction and the cone (i.e. the cap 180) may be manipulated for fast/effective DNA extraction.

[000128] Contamination is always a concern for molecular detection especially for polymerase chain reaction, PCR, based detection since theoretically millions or billions of DNA molecules can be synthesized after 32 cycles of amplification starting from a single DNA molecule. To prevent direct contact of the soft iron bar (i.e. the elongated magnetizable member 124) of the various embodiments with the reagents, the plastic cone (i.e. the cap 180) may be configured to be attached to the soft iron bar (i.e. the elongated magnetizable member 124) as shown in FIG. 8A and FIG. 8B. FIG. 8A shows the cone (i.e. the cap 180) pre-loaded on-chip to be loaded onto soft iron bar (i.e. the elongated magnetizable member 124) automatically by lowering down the tip of soft iron bar (i.e. the tip 124a of the elongated magnetizable member 124) according to various embodiments. FIG. 8B shows the cone (i.e. the cap 180) being loaded onto soft iron bar (i.e. the elongated magnetizable member 124) according to various embodiments. Such cone (i.e. the cap 180) may be pre-stored on the microfluidic chip 104, picked up by the soft iron bar (i.e. the elongated magnetizable member 124) through tight fit and discarded onto the microfluidic chip 104 through the movement of soft iron bar (i.e. the elongated magnetizable member 124) against a U-shape structure on the system (e.g. the nucleic acid purification device 102) or the microfluidic chip 104. According to various embodiments, the cone (i.e. the cap 108) may be spun in solution to boost up bio-reactions.

[000129] According to various embodiments, the shape of the cone (i.e. the cap 180), for example as shown in the FIG. 9, may be configured such that a tight fit between the bar (i.e. the elongated magnetizable member 124) and the cone (i.e. the cap 180) may be achieved. FIG. 9 shows an example of specific dimension for the cone (i.e. the cap 180) according to various embodiments. For example, the bar (i.e. the elongated magnetizable member 124) with $\varnothing 5.5 \pm 0.1\text{mm}$ matching with $\varnothing 5.5 \pm 0.1\text{mm}$ on the cone (i.e. the cap 180). According to various embodiments, the cone (i.e. the cap 180) may have a very thin wall thickness (approximately 0.2-0.3 mm) around its tip such that maximum magnetic force may be generated for fast capturing of magnetic beads (or magnetic particles 170). On the other hand, the cone (i.e. the cap 180) may have a sharp tip angle (approximately 22°) such that at high spinning rate (e.g. approximately 600 rpm), the solution in the well 173,174, 175, 176, 177, 178 may not be spilled out. Thus, a high spinning rate may always be applied for magnetic beads dispersing to ensure a fast beads release from the surface of the cone (i.e. the cap 180). According to various embodiments, as short as a few seconds of spinning may be enough for effectively beads release.

[000130] FIG. 10 shows the nucleic acid purification system 100, the nucleic acid purification device 102, and the microfluidic chip 104 according to various embodiments

[000131] According to various embodiments, the microfluidic chip 104 may be configured to have a unique layout and shape.

[000132] According to various embodiments, the wells 173,174, 175, 176, 177, 178 on the microfluidic chip 104 may be arranged in a semicircle (e.g. an arc shape) and such layout may significantly simplify system operation mechanism and steps. Accordingly, a super-fast DNA/RNA purification/extraction/preparation on a small foot print of the microfluidic chip 104 may be achieved. As shown in FIG. 10, a single stepper motor (e.g. the rotary actuator 136) may rotate the head assembly 120 carrying the beads manipulation bar (i.e. the elongated magnetizable member 124) to cover all the wells 173,174, 175, 176, 177, 178 on the microfluidic chip 104. When the beads manipulation bar (i.e. the elongated magnetizable member 124) moves out of wells 173,174, 175, 176, 177, 178, a single step rotation of the head assembly 120 may be triggered immediately. Without complicated operations by a 3-axis (XYZ) robot arm or manipulator, the single step rotation from well 173,174, 175, 176, 177, 178 to well 173,174, 175, 176, 177, 178 may take only a very short period (e.g. a single second as achieved in the prototype). Furthermore, such layout may allow more wells 173,174, 175, 176, 177, 178 as well as cones (i.e. the cap 180) packed on

a small footprint of microfluidic chip 104, thereby reducing the cost of the microfluidic chip 104.

5 [000133] According to various embodiments, the nucleic acid purification device 102 and the microfluidic chip 104 may be configured with a robust mechanism for the cone (i.e. the cap 108) unloading operation.

[000134] FIG. 11 shows a top view of the microfluidic chip 104 according to various embodiments. FIG. 12(a) to FIG. 12(d) shows step-by-step operation to detach the cone (i.e. the cap 180) from the beads manipulation bar (i.e. the elongated magnetizable member 124) according to various embodiments. According to various embodiments, with the semicircle
10 (or arc shape) arrangement of wells 173, 174, 175, 176, 177, 178 and the rotating operation of beads manipulation bar (i.e. the elongated magnetizable member 124), the cone (i.e. the cap 180) may be unloaded into a cone unloading chamber (e.g. the arcuate opening 182 of the microfluidic chip 104) through a simple rotation and lift-up step (see FIG. 12(a) to FIG. 12(d)). When the cone (i.e. the cap 180) moves/rotates to the top of the cone unloading
15 chamber (e.g. the second end 182b of the arcuate opening 182), a U-shape holder (e.g. an inward protruding collar or flange) may abut a base (or a rim or an edge) of the cone (i.e. the cap 180). When the bar (i.e. the elongated magnetizable member 124) moves up, the U-shaped holder may block the cone (i.e. the cap 180) from moving-up, thus detaching the cone (i.e. the cap 180) from the bar (i.e. the elongated magnetizable member 124) and
20 eventually the cone (i.e. the cap 180) may be deposited into the cone unloading chamber. It can be seen that in various embodiments, the semicircle (or arc shape) arrangement of the wells 173, 174, 175, 176, 177, 178 and the rotating operation of the bar (i.e. the elongated magnetizable member 124) may enable a simple yet fast cone detachment to be implemented. Further, with the direction of pressing force to insert the bar (i.e. the elongated magnetizable
25 member 124) into cone (i.e. the cap 180) aligned and parallel to the center direction of motor rotation, a large pressing force may be applied and thus a tight fit between cone (i.e. the cap 180) and bar (i.e. the elongated magnetizable member 124) may be achieved.

[000135] According to various embodiments, the nucleic acid purification device 102 may include a unique sensor arrangement 140 to control area-to-area contact between the soft
30 iron bar (i.e. the elongated magnetizable member 124) and the permanent magnet 126 for auto alignment when approaching to each other. FIG. 13A and FIG. 13B shows the unique sensor arrangement 140 to control area-to-area contact between the soft iron bar (i.e. the

elongated magnetizable member 124) and the permanent magnet 126 for auto alignment when approaching to each other according to various embodiments.

5 [000136] As shown in FIG. 6, the area-to-area contact between the permanent magnet 126 and soft iron bar (i.e. the elongated magnetizable member 124) may ensure high magnetic field generated at the tip of soft iron bar (i.e. the tip 124a of the elongated magnetizable member 124). With such engagement, the magnetic beads (or magnetic particles 170) may be quickly and effectively attracted so that high yield and fast DNA extraction may be achieved. In various embodiments, the unique sensor arrangement 140 as implemented, as shown in FIG. 13A and FIG. 13B, may determine how to bring the permanent magnet 126
10 to the soft iron bar (i.e. the elongated magnetizable member 124) and how to establish the area-to-area contact between them.

[000137] According to various embodiments, the first sensor 142 of the sensor arrangement 140 may be utilized to determine the reference position of the permanent magnet 126. According to various embodiment, movements of the permanent magnet 126
15 from the reference position may be controlled such that one surface of the soft iron bar (i.e. the flat side surface 124b of the elongated magnetizable member 124) may be fully in-contact with the permanent magnet 126. When the permanent magnet 126 moves close to the soft iron bar (i.e. the elongated magnetizable member 124), the speed of movement of the permanent magnet 126 may be reduced such that soft iron bar (i.e. the elongated
20 magnetizable member 124) may slowly auto-align with the permanent magnet 126. Further, the second sensor 144 of the sensor arrangement 140 may be utilized to determine whether area-to-area contact has been achieved or whether the soft iron bar (e.g. the flat side surface 124b of the elongated magnetizable member 124) is in perfect area facing towards the permanent magnet 126 where the permanent magnet 126 is located.

25 [000138] According to various embodiments, the second sensor 144 of the sensor arrangement 140 may be positioned such that when area-to-area contact is achieved, it may not be blocked and triggered. On the other hand, it may be triggered when area-to-area contact is not achieved. Thus, the sensor arrangement 140 may be utilized to determine the alignment of the soft iron rod (i.e. the elongated magnetizable member 124) so as to control
30 the rotation of the soft iron rod (i.e. the elongated magnetizable member 124) for alignment, as well as to determine whether area-to-area contact is established.

[000139] According to various embodiments, the microfluidic chip 104 may include the sliding plate 186 for either establishing channel connection or sealing pre-stored reagents.

[000140] According to various embodiments, the sliding plate 186 may have the embedded channel 188. When the sliding plate 186 is in the “not pushed-in” position, the two ends 188a, 188b of embedded channel 188 are not aligned with the opening holes of the enclosed lysis chamber 171 and the first well 173. The elastic rubber connectors in the enclosed lysis chamber 171 and the first well 173 may be firmly attached to the flat surface 186a (dead-end) of the sliding plate 186. In this way, good sealing by rubber connector may be obtained. When the sliding plate 186 is fully pushed in as shown in FIG. 14, the two ends 188a, 188b of the embedded channel 188 on the sliding plate 186 may be aligned with the opening holes of the enclosed lysis chamber 171 and the first well 173. Thus, a channel connection between the enclosed lysis chamber 171 and the first well 173 may be established and ready for fluid transfer. According to various embodiments, operation of the sliding plate 186 may be a single-step and easy to operate by users. FIG. 14 shows the operation of the sliding plate 186 for sealing or establishing channel connection according to various embodiments.

[000141] According to various embodiments, additional unique system configuration of the various embodiments may include into the following few parts: the overall concept of arranging the wells 173,174, 175, 176, 177, 178 in a semicircle (or an arc shape); the mechanism and operation of the bio-reaction booster (e.g. the nucleic acid purification device 102) to implement lysis; promote localized reaction in chamber/wells 171, 173,174, 175, 176, 177, 178; integrate the cone (i.e. the cap 180) or cover for the soft-iron tip (i.e. the tip 124a of the elongated magnetizable member 124) to achieve active mixing and contamination free DNA extraction; the mechanism and operation to integrate specifically configured permanent magnet 126 and soft-iron (i.e. the elongated magnetizable member 124) to achieve effective capturing of magnetic beads (or magnetic particles 170) and re-disperse of magnetic beads (or magnetic particles 170), and the coupling of ultrasonic power to the microfluidic chip 104 for fast cell lysis.

[000142] Firstly, according to various embodiments, the wells 173,174, 175, 176, 177, 178 arranged in the semicircle (or the arc shape) may be easily reached and covered by a simple rotating mechanism which is cost effective, small in terms of footprint. More importantly, two microfluidic chips 104 may be processed side by side when needed or additional PCR (including reagent manipulation) chip may be arranged side by side. Further, such arrangement may allow easy implementation of the cone (i.e. the cap 180) loading/unloading as shown in FIG. 11 and FIG. 12(a) to FIG 12(d).

[000143] Secondly, as shown in FIG. 15, a cone (i.e. the cap 180) may be pre-sealed on-chip in one of the wells on-chip. FIG. 15 shows the microfluidic chip 104 with the pre-stored cone (i.e. the cap 180) according to various embodiments. According to various embodiments, the shape of the soft-iron tip (i.e. the tip 124a of the elongated magnetizable member 124) may be configured to be perfectly matched with the inner shape of cone (i.e. the cap 180) such that the cone (i.e. the cap 180) may be tight fit to the tip of soft-iron bar (i.e. the tip 124a of the elongated magnetizable member 124) when the soft-iron tip (i.e. the tip 124a of the elongated magnetizable member 124) is pressing against the cone (i.e. the cap 180). After that, the soft-iron bar (i.e. the elongated magnetizable member 124) may be lifted up together with the cone (i.e. the cap 180) as shown in the FIG. 8B. According to various embodiments, the pressing force of the soft-iron bar (i.e. the elongated magnetizable member 124) against the cone (i.e. the cap 180) may be controlled by a force (e.g. a pneumatic pressure) driving the head assembly 120 carrying the soft-iron bar (i.e. the elongated magnetizable member 124) up and down as shown in FIG. 8A.

[000144] According to various embodiments, after the sample processing, the cone (i.e. the cap 180) may be discarded. According to various embodiments, the cone (i.e. the cap 180) may be configured to be discarded onto microfluidic chip 104. According to various embodiments, during cone unloading, the head assembly 120 carrying the soft-iron tip (i.e. the tip 124a of the elongated magnetizable member 124) with the cone (i.e. the cap 180) may rotate such that the cone (i.e. the cap 180) in the unloading well (e.g. the arcuate opening 182) may move from one end 182a (see FIG. 16(a) to the other end 182b (see FIG. 16(b)). When the soft-iron tip (i.e. the tip 124a of the elongated magnetizable member 124) at the other end 182b is moved up, a U-shape blocking structure on jig at the other end 182b may stop the cone (i.e. the cap 180) from moving up and detach the cone (i.e. the cap 180) from the soft-iron tip (i.e. the tip 124a of the elongated magnetizable member 124) and leave the cone (i.e. the cap 180) in a cone disposing well (e.g. below the arcuate opening 182). FIG. 16(a) shows an initial position of the cone (i.e. the cap 180) and the soft-iron tip (i.e. the tip 124a of the elongated magnetizable member 124) at the first end 182a when head assembly 120 is going down or moving down according to various embodiments. FIG. 16(b) shows the cone (i.e. the cap 180) and the soft-iron tip (i.e. the tip 124a of the elongated magnetizable member 124) being moved to the other end 182b of the cone disposing well (e.g. the arcuate opening 182) after the head assembly 120 is rotated before the cone (i.e. the cap 180) is going to be detached from the soft-iron tip (i.e. the tip 124a of the elongated

magnetizable member 124) by moving the head assembly 120 up according to various embodiments.

[000145] Thirdly, effective DNA capturing and release may be very much dependent on how effective the magnetic beads (or magnetic particles 170) may be collected and dispersed, and this is uniquely implemented in various embodiments through the integration of actuation, the soft iron bar (i.e. the elongated magnetizable member 124) and the permanent magnet 126. As shown in FIG. 7A, the soft-iron bar (i.e. the elongated magnetizable member 124) may be attached to the rotary actuator 132 (e.g. a motor) and the spinning pattern (speed, directions, duration and so on) may be programmed to achieve idea fluid/sample/beads mixing in the wells 173,174, 175, 176, 177, 178 of the microfluidic chip 104. Such spinning of the soft-iron bar (i.e. the elongated magnetizable member 124) may only be started when the permanent magnet 126 is not in contact (or free from contact) with soft-iron bar (i.e. the elongated magnetizable member 124). During magnetic beads collection, the permanent magnet 126 may be moved by a motoring mechanism (e.g. the actuation unit 150) to get into contact with the soft-iron bar (i.e. the elongated magnetizable member 124) as shown in FIG. 7B. According to various embodiments, such configuration, together with the implementation of the cone (i.e. the cap 180), may ensure high and consistent magnetic field gradient at the soft-iron tip (i.e. the tip 124a of the elongated magnetizable member 124) compared to the conventional use of electromagnet, allow effective mixing for efficient DNA purification/extraction/preparation, and enable contamination free operations.

[000146] With the above configuration for effective and contamination free mixing, the time needed for single round of mixing in each well 173,174, 175, 176, 177, 178 of the microfluidic chip 104 may be as short as a few seconds only and several rounds of magnetic beads (or magnetic particles 170) capturing and re-dispersal may be implemented for more efficient DNA purification/extraction/preparation. Together with the effective coupling of ultrasonic power onto the microfluidic chip 104 through contact and interface control for super-fast cell lysis (in seconds) as described earlier, various embodiments may ensure very fast DNA purification/extraction/preparation, e.g. as short as within 8 minutes. According to various embodiments, with further system optimization, the DNA purification/extraction/preparation time may be reduced to as short as 5 minutes.

[000147] Based on experiments conducted, a sample of DNA purification result for a detection of E. coli in human feces, the result obtained for on-chip sample preparation based

on the various embodiments is 8 minutes as compared with manual sample preparation based on conventional protocol which requires approximately 30 minutes.

[000148] According to various embodiments, there is provided a nucleic acid purification device (or a magnetic particles transfer and bio-reaction booster device) for a diagnostic apparatus, the device including: a bio-reaction booster including a magnetizable bar (i.e. the elongated magnetizable member) which may be rotated about its longitudinally axis at controllable rotational speed to create disturbance in a well of a microfluidic chip with liquid containing bio samples and reactance.

[000149] According to various embodiments, the shape and layout of the reagent chip (or the microfluidic chip) may ensure the super-fast DNA/RNA purification/extraction/preparation on a small foot print of the chip assisted by a simple system mechanism (e.g. the nucleic acid purification device).

[000150] Various embodiments may include a unique cone (i.e. the cap) concept to prevent contamination with specific shape configuration for fast/effective DNA purification/extraction/preparation and a unique mechanism (e.g. the nucleic acid purification device) to manipulate the cone (i.e. the cap) for fast/effective DNA purification/extraction/preparation as well as the cone (i.e. the cap) unloading.

[000151] According to various embodiments, the nucleic acid purification device may be configured to ensure area-to-area contact between the permanent magnet and the soft iron bar (i.e. the elongated magnetizable member) to maximise magnetic field coupling, while achieving easy attachment/detachment and automated alignment of the permanent magnet and the soft iron bar (i.e. the elongated magnetizable member). When the permanent magnet and the soft iron bar (i.e. the elongated magnetizable member) are detached, controlled rotation of the cone (i.e. the cap) attached to soft iron bar tip (i.e. the tip of the elongated magnetizable member) in terms of speed/directions may be implemented such that bio-reactions may be boosted.

[000152] According to various embodiments, a unique sensor arrangement and relevant control may be provided to ensure area-to-area contact between the soft iron bar (i.e. the elongated magnetizable member) and the permanent magnet when they approach each other.

[000153] Various embodiments may be configured to perform sonication lysis of semi-solid/solid samples in an enclosed chamber of a microfluidic chip, manipulate the semi-solid samples in the microfluidic chip that is pre-stored with fluid, move the fluid internally, and/or capture/transfer/release magnetic beads (or magnetic particles) between open wells

of the microfluidic chip arranged in semicircle (or arc shape) through a soft-iron tip (i.e. the tip of the elongated magnetizable member) covered with a cone (i.e. the cap) pre-stored on the microfluidic chip.

[000154] Various embodiments may pre-store the cone (i.e. the cap) on the microfluidic chip and automatically, via the nucleic acid purification device, load the cone (i.e. the cap) onto the soft-iron tip (i.e. the tip of the elongated magnetizable member), or unload the cone (i.e. the cap) from the soft-iron tip (i.e. the tip of the elongated magnetizable member) for contamination-free mixing of the fluid containing the magnetic beads (or magnetic particles) or spinning-off of the magnetic beads (or magnetic particles) from the cone surface (i.e. surface of the cap) for magnetic beads (or magnetic particles) dispersion.

[000155] According to various embodiments, the microfluidic chip may be configured to integrate a customized cone into the microfluidic chip for contamination free on-chip manipulation of the fluid and the semi-solid samples.

[000156] Various embodiments may provide the cone (i.e. the cap) as part of the microfluidic chip for easy unloading via a simple operation exploiting the semicircle (or arc shape) layout of all the open wells of the microfluidic chip.

[000157] Various embodiments may utilize a cut-in (or flat side surface) of a polygonal (e.g. hexagonal) shaped soft-iron bar (i.e. elongated magnetizable member) for auto alignment of the soft-iron bar (i.e. elongated magnetizable member) to an approaching permanent magnet to obtain area-to-area contact between the soft-iron bar (i.e. elongated magnetizable member) and permanent magnet.

[000158] Various embodiments may be operated for on-demand coupling and decoupling of the permanent magnet to the cut-in (or flat side surface) of the soft-iron bar (i.e. elongated magnetizable member) to obtain high magnetic gradient at the sharp tip of soft-iron bar (i.e. the tip of the elongated magnetizable member), or free the soft-iron bar (i.e. elongated magnetizable member) for spinning at pre-set patterns (direction, speed, duration).

[000159] Various embodiments may utilize an on-chip plastic sliding plate (with built-in channel and hooked up to the main part of the microfluidic chip) for a single step of switching from reagents sealing in separated chambers/wells to chamber-to-well connection through the built-in channel built-in of the plastic sliding plate.

[000160] Various embodiments may provide the plastic sliding plate as part of the microfluidic chip which is hooked up to the main body of microfluidic chip for the ability to enable on-demand sealing of reagents loading chamber.

[000161] Various embodiments may utilize a built-in filter immersed in the semi-solid samples in a plastic chamber of the microfluidic chip sonicated by an ultrasonic source for cell lysis and prevention of big sized particles to be transferred to downstream after sample lysis.

- 5 [000162] While the invention has been particularly shown and described with reference to specific embodiments, it should be understood by those skilled in the art that various changes, modification, variation in form and detail may be made therein without departing from the scope of the invention as defined by the appended claims. The scope of the invention is thus indicated by the appended claims and all changes which come within the
- 10 meaning and range of equivalency of the claims are therefore intended to be embraced.

Claims

1. A nucleic acid purification device comprising
 - a support structure having a head-assembly-support portion; and
 - a head assembly supported by the head-assembly-support portion of the support structure, the head assembly comprising
 - a frame member,
 - an elongated magnetizable member supported by the frame member, the elongated magnetizable member having a central axis extending longitudinally through the elongated magnetizable member, wherein the elongated magnetizable member is rotatable about the central axis relative to the frame member, wherein the elongated magnetizable member is longitudinally translatable along the central axis with respect to the head-assembly-support portion of the support structure so as to be moveable towards and away from the head-assembly-support portion, and
 - a permanent magnet moveable towards and away from the elongated magnetizable member so as to engage with or disengage from the elongated magnetizable member,
 - wherein the head assembly is operable to engage the permanent magnet with the elongated magnetizable member to induce magnetism in the elongated magnetizable member and move the elongated magnetizable member with induced magnetism to translate along the central axis with respect to the head-assembly-support portion, and
 - wherein the head assembly is operable to disengage the permanent magnet from the elongated magnetizable member to lose its induced magnetism and rotate the elongated magnetizable member without induced magnetism about the central axis relative to the frame member,
 - wherein the elongated magnetizable member comprises a flat side surface and the permanent magnet comprises a flat contact surface, wherein the permanent magnet is moveable towards and away from the flat side surface of the elongated magnetizable member so as to engage the flat contact surface of the permanent magnet with the flat side surface of the elongated magnetizable member or disengage the flat contact surface of the permanent magnet from the flat side surface of the elongated magnetizable member,
 - wherein an engagement between the flat side surface of the elongated magnetizable member and the flat contact surface of the permanent magnet optimises the induced

magnetism in the elongated magnetizable member to maximise localized magnetic gradient at a tip of the elongated magnetizable member.

2. The device as claimed in claim 1, wherein the permanent magnet is moveable along a trajectory intersecting the central axis of the elongated magnetizable member.

3. The device as claimed in claim 1, wherein the head assembly further comprises a sensor arrangement to determine relative positions between the flat contact surface of the permanent magnet and the flat side surface of the elongated magnetizable member for controlling the permanent magnet to engage with the elongated magnetizable member such that the flat contact surface of the permanent magnet and the flat side surface of the elongated magnetizable member are flatly engaged to each other.

4. The device as claimed in claim 1, wherein the head assembly further comprises a rotary actuator coupled to the elongated magnetizable member for rotating the elongated magnetizable member about the central axis relative to the frame member and a linear actuator for translating the elongated magnetizable member longitudinally along the central axis.

5. The device as claimed in claim 4, wherein the linear actuator is coupled between the head-assembly-support portion of the support structure and the frame member of the head assembly to move the frame member of the head assembly with respect to the head-assembly-support portion of the support structure in a direction parallel to the central axis of the elongated magnetizable member so as to translate the elongated magnetizable member longitudinally along the central axis towards and away from the head-assembly-support portion.

6. The device as claimed in claim 5,
wherein the head assembly further comprises an actuation unit coupled to the permanent magnet for moving the permanent magnet towards and away from the elongated magnetizable member,
wherein the actuation unit comprises

an extendable mechanism with the permanent magnet mounted to an end of the extendable mechanism, and

an actuating mechanism coupled to the extendable mechanism to control an extension or a retraction of the extendable mechanism for moving the permanent magnet towards and away from the elongated magnetizable member.

7. The device as claimed in claim 1, wherein the head assembly is rotatable about a rotational axis with respect to the support structure, wherein the rotational axis is parallel to the central axis of the elongated magnetizable member of the head assembly such that rotating the head assembly about the rotational axis with respect to the support structure moves the elongated magnetizable member laterally along a circular arc path.

8. The device as claimed in claim 7, wherein the head assembly is rotatable about the rotational axis with respect to the head-assembly-support portion of the support structure for moving the elongated magnetizable member laterally along the circular arc path with respect to the head-assembly-support portion of the support structure.

9. The device as claimed in claim 8, further comprising
a further rotary actuator coupled between the head assembly and the head-assembly-support portion of the support structure in a manner so as to rotate the head assembly about the rotational axis with respect to the head-assembly-support portion of the support structure.

10. The device as claimed in claim 1, wherein the support structure have a stage portion for supporting a microfluidic chip, the stage portion being spaced apart and opposing the head-assembly-support portion such that the elongated magnetizable member moves away from the stage portion as the elongated magnetizable member of the head assembly translates longitudinally along the central axis to move towards the head-assembly-support portion and the elongated magnetizable member moves towards the stage portion as the elongated magnetizable member of the head assembly translates longitudinally along the central axis to move away from the head-assembly-support portion.

11. The device as claimed in claim 10, further comprising a sonication component having a acoustic energy output surface, wherein the sonication component is coupled to the stage portion in a manner such that the acoustic energy output surface contacts the microfluidic chip when the microfluidic chip is supported on the stage portion.

12. A nucleic acid purification system comprising,
 a nucleic acid purification device comprising
 a support structure having a head-assembly-support portion and a stage portion spaced apart and opposing the head-assembly-support portion, and
 a head assembly supported by the head-assembly-support portion of the support structure, the head assembly comprising
 a frame member,
 an elongated magnetizable member supported by the frame member, the elongated magnetizable member having a central axis extending longitudinal through the elongated magnetizable member, wherein the elongated magnetizable member is rotatable about the central axis relative to the frame member, the elongated magnetizable member having a flat side surface, wherein the elongated magnetizable member is longitudinally translatable along the central axis with respect to the head-assembly-support portion of the support structure so as to be moveable towards and away from the head-assembly-support portion, and
 a permanent magnet moveable relative to the frame member towards and away from the elongated magnetizable member so as to engage with or disengage from the elongated magnetizable member, the permanent magnet having a flat contact surface; and
 a microfluidic chip for placing on the stage portion of the support structure of the nucleic acid purification device, the microfluidic chip comprising a plurality of wells, wherein at least one well of the microfluidic chip contains a plurality of magnetic particles,
 wherein the head assembly of the nucleic acid purification device is operable to engage the permanent magnet with the elongated magnetizable member such that the flat contact surface of the permanent magnet is engaged to the flat side surface of the elongated magnetizable member to induce magnetism in the elongated magnetizable

member and move the elongated magnetizable member with induced magnetism to translate along the central axis so as to move a tip of the elongated magnetizable member towards the stage portion for inserting into the at least one well of the microfluidic chip placed on the stage portion to capture the plurality of magnetic particles in the at least one well and subsequently move the tip of the elongated magnetizable member away from the stage portion for removing the plurality of magnetic particles magnetically attached to the tip of the elongated magnetizable member from the at least one well, wherein an engagement between the flat side surface of the elongated magnetizable member and the flat contact surface of the permanent magnet optimises the induced magnetism in the elongated magnetizable member to maximise localized magnetic gradient at the tip of the elongated magnetizable member and

wherein, when the tip of the elongated magnetizable member and the plurality of magnetic particles magnetically attached thereto are inserted into one other well of the microfluidic chip, the head assembly of the nucleic acid purification device is operable to disengage the permanent magnet from the elongated magnetizable member to lose its induced magnetism and rotate the elongated magnetizable member without induced magnetism about the central axis relative to the frame member in a manner so as to disperse the plurality of magnetic particles from the tip of the elongated magnetizable member into the one other well.

13. The system as claimed in claim 12,

wherein the microfluidic chip comprises a removable cap held in the microfluidic chip,

wherein the head assembly of the nucleic acid purification device is operable to move the elongated magnetizable member to translate along the central axis so as to move the tip of the elongated magnetizable member towards the stage portion for inserting into the cap of the microfluidic chip placed on the stage portion to fit the cap over the tip of the elongated magnetizable member and subsequently move the tip of the elongated magnetizable member away from the stage portion for removing the cap from the microfluidic chip.

14. The system as claimed in claim 13, wherein the cap is shaped and dimensioned for interference fit with the tip of the elongated magnetizable member.

15. The system as claimed in claim 12,

wherein the head assembly of the nucleic acid purification device is rotatable about a rotational axis with respect to the head-assembly-support portion of the support structure, the rotational axis being parallel to the central axis of the elongated magnetizable member of the head assembly such that rotating the head assembly about the rotational axis with respect to the head-assembly-support portion of the support structure moves the elongated magnetizable member laterally along a circular arc path,

wherein the plurality of wells of the microfluidic chip is arranged in a circular arc corresponding to the circular arc path of the elongated magnetizable member in a manner such that the head assembly of the nucleic acid purification device is operable to rotate the head assembly for moving the elongated magnetizable member along the circular arc path to transfer the plurality of magnetic particles magnetically attached to the tip of the elongated magnetizable member from the at least one well to the one other well.

16. The system as claimed in claim 15,

wherein the microfluidic chip comprises an arcuate opening, wherein a width of a first end of the arcuate opening is wider than a width at a second end of the arcuate opening,

wherein the head assembly of the nucleic acid purification device is operable to move the elongated magnetizable member to translate along the central axis so as to move the tip of the elongated magnetizable member with a cap fitted thereto towards the stage portion for inserting into the arcuate opening of the microfluidic chip placed on the stage portion via the first end thereof, rotate the head assembly about the rotational axis with respect to the head-assembly-support portion of the support structure to move the elongated magnetizable member laterally along the circular arc path to the second end of the arcuate opening, and subsequently move the tip of the elongated magnetizable member away from the stage portion for removing the cap from the tip of the elongated magnetizable member as the cap is held by the narrower width at the second end of the arcuate opening.

17. The system as claimed in claim 12,

wherein the microfluidic chip comprises an enclosed lysis chamber with an inlet port,

wherein the nucleic acid purification device further comprises a sonication component having a acoustic energy output surface, wherein the sonication component is coupled to the stage portion in a manner so as to contact the microfluidic chip for transmitting the acoustic energy to the enclosed lysis chamber when the microfluidic chip is supported on the stage portion.

18. The system as claimed in claim 17, wherein the enclosed lysis chamber of the microfluidic chip comprises

a filter partitioning the enclosed lysis chamber into an upper sub-chamber and a lower sub-chamber, and

a discharge tube extending from the lower sub-chamber to an exterior surface of the microfluidic chip, wherein a first end opening of the discharge tube is within the lower sub-chamber and a second end opening of the discharge tube is exposed from the exterior surface of the microfluidic chip.

19. The system as claimed in claim 18,

wherein the microfluidic chip comprises a sliding plate having an embedded channel with a first end opening of the embedded channel and a second end opening of the embedded channel exposed from a surface of the sliding plate,

wherein the sliding plate is in sliding engagement with the exterior surface of the microfluidic chip in a manner so as to be slidable into an aligned position to align the first end opening of the embedded channel of the sliding plate with the second end opening of the discharge tube and to align the second end opening of the embedded channel of the sliding plate with the at least one well of the microfluidic chip for transferring fluid from the enclosed lysis chamber into the at least one well.