

POINT OF CARE SAMPLE PROCESSING DEVICE**Technical field**

- 5 The present invention relates, in general terms, to sample processing devices, and more particularly to a portable point of care device for collection and sequential processing of liquid samples.

Background

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Point of care testing (POCT) enables diagnostic information to be obtained at or near the site of patient care, avoiding delays associated with centralised laboratory processing. This capability is particularly important in situations where time-critical treatment decisions can significantly impact patient outcomes, such as in emergency settings and in resource-limited

15 situations.

Blood is a preferred sample type for clinical decision making because it is easily collected and contains a wide array of clinically relevant biomarkers and analytes, including hormones, electrolytes, antibodies, proteins, nucleic acids, and pathogens. However, the

20 complex composition of blood poses challenges for POCT. Components such as haemoglobin and blood cells can interfere with optical assays, mask target biomarkers, and inhibit molecular techniques such as PCR. These interfering components need to be removed prior to analyte testing, yet conventional separation methods rely on centrifugation, which is impractical in portable formats, and also performs inadequately with small sample

25 volumes typical of fingerstick or heel-prick collection. In addition, sensitive and accurate detection frequently requires isolation and concentration of target biomolecules (e.g., nucleic acids, proteins, or other molecular analytes). Isolation typically involves additional reagents and devices, further increasing the complexity and cost of POCT workflows.

- 30 Accordingly, there is thus a need for integrated solutions that combine sample collection and processing in a portable and user-friendly device for POC testing. It would be desirable to overcome or alleviate at least one of the above-described problems.

Summary

Disclosed herein is a device for processing a liquid sample, comprising: a syringe barrel having a body, the body comprising a proximal end, a distal end for receiving a liquid sample, and a plurality of holding chambers formed in the body for holding a plurality of sample processing materials; and at least one stopper slidably disposed within the body of the syringe barrel and configured to fluidically seal the plurality of holding chambers; wherein the at least one stopper is operable to sequentially unseal the plurality of holding chambers to bring the liquid sample received at the distal end of the syringe barrel into contact with the plurality of sample processing materials in the plurality of holding chambers.

Disclosed herein is a method for processing a liquid sample using a device as disclosed herein, the method comprising the steps of: a) receiving a volume of liquid sample at the distal end of the syringe barrel of the device; and b) moving the at least one stopper to sequentially unseal the plurality of holding chambers in the device to bring the liquid sample into contact with a plurality of sample processing materials in the plurality of holding chambers.

Disclosed herein is a kit of parts for a device as disclosed herein, the kit comprising: a syringe barrel having a body, the body comprising a proximal end, a distal end for receiving a liquid sample, and a plurality of holding chambers formed in the body for holding a plurality of sample processing materials; and at least one stopper receivable within the body of the syringe barrel and configured to fluidically seal the plurality of holding chambers.

Disclosed herein is a device for processing a liquid sample, comprising: a syringe barrel having a body, the body comprising a proximal end, a distal end for receiving a liquid sample, and a plurality of holding chambers integrally formed in the body for holding a plurality of sample processing materials; and at least one stopper slidably disposed within the body of the syringe barrel and configured to fluidically seal the plurality of holding chambers; wherein moving the at least one stopper towards the proximal end of the device sequentially unseals the plurality of holding chambers to bring the liquid sample received at the distal end of the syringe barrel into contact with the plurality of sample processing materials in the plurality of holding chambers.

Disclosed herein is a device for processing a liquid sample, comprising: a syringe barrel having a body, the body comprising a proximal end, a distal end for receiving a liquid sample, and a plurality of holding chambers formed in the body for holding a plurality of sample processing materials; a plurality of stoppers slidably disposed within the body of the syringe barrel and forming a fluid-tight seal within the body to isolate the plurality of holding chambers, the plurality of stoppers comprising a distal-most stopper and a proximal-most stopper; and a plunger assembly for controlling relative positioning of the plurality of stoppers within the syringe barrel, the plunger assembly comprising an inner plunger rod fixedly coupled to the distal-most stopper, and an outer plunger rod fixedly coupled to the proximal-most stopper, the inner plunger rod telescopically receivable within the outer plunger rod; wherein the plunger assembly is operable to move the plurality of stoppers to sequentially unseal the plurality of holding chambers such that a liquid sample received at the distal end of the syringe barrel is brought into contact with the plurality of sample processing materials in the plurality of holding chambers.

Brief description of the drawings

Embodiments of the present invention will now be described, by way of non-limiting example, with reference to the drawings in which:

Figure 1 shows the components of a first embodiment of a first type of syringe device with four chambers and a single stopper.

Figure 2 is a schematic showing stepwise sample processing using the assembled syringe device of Figure 1.

Figure 3 shows the components of a second embodiment of the first type syringe device that has three chambers and a single stopper.

Figure 4 is a schematic showing stepwise sample processing using the assembled syringe device of Figure 3.

Figure 5 shows stepwise sample preparation of a blood sample using the syringe device of Figure 1.

Figure 6 shows processed product from different stages of the preparation in Figure 5. (1) Whole blood sample; (2) Following cell lysis with TNT buffer; (3) Following extraction using MPs; (4) Plasma sample obtained after centrifugation (control).

Figure 7 shows processed product from different stages of the preparation in Figure 5. (1) Whole blood sample; (2) Following cell lysis with T6 buffer; (3) Following extraction using MPs; (4) Plasma sample obtained after centrifugation (control).

Figure 8 shows agarose gel electrophoresis of amplified human DNA in blood samples processed using the device of Figure 1. The band at 158 bp corresponds to the p53 gene. (1) Lysis using T6 buffer; (2) Lysis using TNT buffer; (3) Negative control.

Figure 9 shows agarose gel electrophoresis of amplified bacteria DNA in blood samples containing *Brucella* that have processed using the device of Figure 1. The band at 224 bp corresponds to the BCSP31 gene. (1) Lysis using T6 buffer; (2) Lysis using TNT buffer; (3) Negative control.

Figure 10 shows CRISPR-Cas12a detection using samples prepared by the device of Figure 1. Samples processed with TNT buffer were amplified via RPA and monitored in real time, with fluorescence measured at 1-minute intervals over 60 minutes. Background-subtracted fluorescence values are shown as mean $\pm$ SD ($n = 3$), highlighting both the sensitivity and speed of detection.

Figure 11 is a TSH standard curve. Triangle, square, and diamond symbols represent plasma obtained by centrifugation (control), device of Figure 1 with TNT buffer, and device of Figure 1 with T6 buffer, respectively.

Figure 12 shows the components of a first embodiment of a second type of syringe device with two mixing chambers and seven stoppers defining five holding chambers.

Figure 13 shows cross-sectional views at different sections of the device of Figure 12 taken along planes AA', BB', CC' and DD'.

Figure 14 is a schematic showing stepwise assembly of the device of Figure 12.

Figure 15 is a schematic showing stepwise sample processing using the assembled syringe device of Figure 12.

Figure 16 shows a second embodiment of the second type syringe device that has a single mixing chamber and three holding chambers defined by five stoppers.

Figure 17 is a schematic showing stepwise sample processing using the device of Figure 16.

Figure 18 shows a third embodiment of the second type syringe device that has a single mixing chamber, two side chambers, and five holding chambers defined by seven stoppers. Shown on the right are cross-sectional views at different sections of the device taken along planes AA', BB', CC' and DD'.

Figure 19 is a schematic showing stepwise sample processing using the device of Figure 18.

Figure 20 shows stepwise sample preparation of a blood sample using the syringe device of

Figure 12.

Figure 21 shows processed product from different stages of the preparation in Figure 20. (1) Whole blood sample; (2) Eluted product containing extracted DNA.

Figure 22 shows processed product from different stages of the preparation in Figure 5. (1) Whole blood sample; (2) Following cell lysis with T6 buffer; (3) Following extraction using MPs; (4) Plasma sample obtained after centrifugation (control).

Figure 23 shows agarose gel electrophoresis of amplified human DNA in blood samples processed using the device of Figure 12. The band at 158 bp corresponds to the p53 gene. (1) Eluted product; (NC) Negative control.

Figure 24 shows agarose gel electrophoresis of amplified bacterial DNA in blood samples containing *Brucella* processed using the device of Figure 12. The band at 224 bp corresponds to the BCSP31 gene. (1) Eluted product; (NC) Negative control.

Detailed description

Provided herein is a syringe-based point of care testing (POCT) device designed for integrated sample collection and preparation without the need for additional lab equipment or sample transfer. The device comprises a syringe barrel with a proximal end and a distal end for receiving a liquid sample. The distal end of the barrel can be connected to conventional sample collection aids (such as needles or lancets) to collect liquid samples. A plurality of holding chambers (for holding a material, or separation and/or mixing) formed in the body of the barrel can be loaded with various sample processing materials, such as lysis buffers or reagents for isolating particular components from the samples. The holding chambers are initially fluidically sealed by one or more stoppers within the syringe barrel to prevent cross-contamination of the contents of the holding chambers. The one or more stoppers is slidable within the body of the barrel (via an action on a plunger) to sequentially unseal the plurality of holding chambers so that a liquid sample received in the barrel is brought into contact with the processing material in the holding chambers for sample processing. Processed sample can be discharged for further downstream assays. The device thus allows for self-contained, controllable and sequential processing of a fluid sample with a series of processing reagents.

The device simplifies sample collection and preparation workflows, reduces sample loss during processing, shortens processing time, and requires minimal operator training since it

operates like a syringe. It can be used to process a variety of liquid samples for *in vitro* diagnostics, including biological fluids (such as, but not limited to, blood, plasma, serum, lymph, cerebrospinal fluid, synovial fluid, amniotic fluid, sweat, tears, saliva, stool, urine, sputum, mucous, ascites, pleural effusion, seroma, and pus) and environmental samples
5 (such as, but not limited to, food samples, beverage samples, mud samples, freshwater samples, wastewater samples, and seawater samples). In some embodiments, magnetic particles can be loaded into the chambers to remove sample components that can interfere with downstream assays (such as haemoglobin, haematin or immunoglobulins), or to extract and concentrate target analytes of interest from the sample (such as nucleic acids, proteins
10 or metabolites). A magnet attachable to an external surface of the device may be used to immobilise the magnetic particles while subsequent assay steps are carried out in the device, including elution of the target analytes from the magnetic particles, or detection of targets bound to the magnetic particles.

15 The present disclosure also provides a kit to assembling a device as disclosed herein. The kit may further comprise a sample acquisition component, a magnet, and/or at least one sample processing material.

The present disclosure also provides a method of processing a liquid sample using the device
20 as disclosed herein.

In one embodiment of the device, also referred to as a BioSyringe in this disclosure, the device comprises: (a) a syringe barrel having a body with a proximal end, a distal end for receiving a liquid sample, and a plurality of holding chambers integrally formed in the body
25 for holding a plurality of sample processing materials; and (b) at least one stopper slidably disposed within the body of the syringe barrel and forming a fluid-tight seal within the body to isolate the plurality of holding chambers; wherein the at least one stopper is movable to bring a liquid sample received at the distal end of the barrel into sequential contact with sample processing material of the chambers.

30 Figures 1 and 2 show an embodiment of the BioSyringe device herein. Shown in Figure 1 is a kit of parts that can be assembled into a Biosyringe device. The assembled device **100** is shown in Figure 2. Referring to Figure 1, the device comprises a hollow syringe barrel **102** with proximal end **106** through which a stopper **108** can be inserted, and a distal end **104** to

which a sample collection device such as a needle **114** can be attached. A series of holding chambers **118** are integrally formed along the body of the barrel for holding sample processing material. The holding chambers extend outwardly relative to the barrel body and have an opening **124** to an interior surface of the body that is dimensioned for sealing by a stopper. Sample processing material may be loaded through the interior opening **124**. Alternatively, an external opening or port **126** may be formed in each holding chamber for chamber loading. The external port **126** is secured with a cap **128** to prevent leakage of the contents and to keep the interior of the barrel air-tight.

Shown in Figure 1 are annular holding chambers that extend circumferentially around the barrel, but other chamber geometries are also possible, including hemispherical chambers, and chambers that formed are form in only one section of the barrel wall. In general, the holding chambers are arranged at different positions along the barrel body such that each chamber is unsealed in turn when the stopper **108** is moved from distal towards proximal end of the barrel.

The number of holding chambers can be tailored to the sample processing workflow. In preferred embodiments, at least two holding chambers are included to enable at least two sequential processing operations. For example, a first holding chamber may contain material for cell lysis while a second holding chamber contains material for component capture. Additional holding chambers may hold material for component release, component detection, sample dilution or sample washing. In one embodiment, the device includes two holding chambers to contain material for, e.g., lysis and component capture; component capture and component release; or component capture and component detection. In one embodiment, the device includes three holding chambers to contain material for, e.g., lysis, component capture and washing; lysis, component capture and component release; or lysis, component capture and component detection. In one embodiment, the device includes four holding chambers to contain material for, e.g., lysis, component capture, washing, and component release or detection.

The holding chambers may be individually sized to accommodate the required quantities and types of processing material for each processing step. For example, a holding chamber designed to hold solid processing material such as particles or lyophilised reagents, which are generally more compact, may have a smaller volume than a holding chamber designed

to hold liquid material such as buffers and wash solutions. The internal volume of the chambers may range from 100 μ l to 10 ml.

5 A cylindrical stopper **128** inserted into the body of the barrel forms a fluid-tight seal with an interior wall of the barrel body to keep the holding chambers fluidically isolated. The stopper can have varying lengths to provide different sealing capabilities within the syringe barrel. In one embodiment, the stopper has a length sufficient to span and simultaneously seal all of the holding chambers, as shown in Figures 1 and 2. Alternatively, the stopper may have a length that only spans and seals a subset of the holding chambers. The choice of stopper
10 length may depend on the specific application requirements, such as the number of processing steps required for an assay.

The stopper is slidable along the interior length of the barrel. Movement and positioning of the stopper may be controlled using a plunger rod **110** attached to the stopper. The plunger
15 rod **110** may be flanged at a proximal end thereof or may be provided with a handle **112** at the proximal end to facilitate pulling and pushing actions by a user. In the assembled device **100** in Figure 2, pulling on stopper **108** using plunger rod **110** generates a vacuum within the barrel to draw in a liquid sample at the distal end.

20 The device may include a locking mechanism for securing the stopper in place within the syringe barrel. This is advantageous for preventing unintended displacement of the stopper before sample collection or during a processing step. In one embodiment, the locking mechanism uses a bayonet-style configuration in which the plunger rod may be provided with two or more radial pins that project outwardly from the rod surface. The pins are aligned
25 with and engage corresponding vertical slots formed in the inner barrel wall during initial assembly of the device. The pins slide within the slot when the rod is moved axially along the length of the barrel body. At predetermined positions along the barrel wall where rod immobilisation is desired, horizontal grooves extend perpendicularly from each vertical slot, creating a T-shaped configuration. Rotating the plunger rod about its longitudinal axis at
30 these positions causes the pins to move laterally into the horizontal grooves, effectively locking the rod in position. In an alternative embodiment, a magnetic element such as a permanent magnet or ferromagnetic material may be embedded in the stopper or plunger rod, and opposing magnetic elements embedded in or attached to the barrel wall at predetermined positions to secure the stopper or rod in place through magnetic attraction.

A sample acquisition component configured to draw a liquid sample may be attached to the distal end of the barrel for sample collection. The sample acquisition component may comprise one or more piercing elements for exposing and/or aspirating liquids from a biological tissue, a solid matrix (e.g., food or environmental matrix), or a sealed vial or container. Shown in Figure 1 is a hypodermic needle **114** for venous blood collection. The needle may be of varying gauges and lengths depending on the type of sample and mode of sample collection, and may be provided with a protective cap or sheath. Alternatively, a lancet or capillary tube may be used to draw smaller volumes of liquids. The sample acquisition component may also be a needle or microneedle array for less invasive interstitial fluid sampling.

The stopper is preferably made of an elastic material that permits controlled deformation upon insertion into the barrel to ensure a fluid-tight seal. Exemplary materials for stopper fabrication include pliable rubber, thermoplastic rubber, silicone elastomers, and pliable plastics such as thermoplastic polyurethane (TPU).

The syringe barrel may be fabricated from a rigid transparent or translucent material that permits visual monitoring of sample collection and processing. Calibration marks may be printed, etched or molded onto the exterior surface of the barrel for to indicate liquid volumes in the barrel. The plunger rod may likewise be fabricated from a rigid material.

The barrel and stopper are preferably constructed from materials that can withstand standard sterilisation procedures, so that the device may be sterilised prior to use. Suitable sterilisation procedures include steam sterilisation (autoclaving) at temperatures of 121–134°C; chemical sterilisation using ethylene oxide, hydrogen peroxide, chlorine dioxide, or other gases; and radiation sterilisation using gamma rays, X-rays or electron beams.

In one embodiment, the barrel, stopper and plunger rod are fabricated from a thermoplastic material, non-limiting examples of which include thermoplastic polyurethane (TPU), polylactic acid (PLA), polypropylene, poly(methyl methacrylate) (PMMA), and polycarbonate.

Manufacture of the various parts of the device may be carried out by a variety of methods known in the art, depending on the selected materials. Exemplary techniques include but are not limited to injection molding, extrusion, and layer-by-layer assembly (3D printing) using fused deposition modelling (FDM), stereolithography or selective laser sintering (SLS). In
5 a preferred embodiment, the syringe barrel, stopper and plunger rod are 3D printed using fused deposition modelling (FDM) of a thermoplastic material.

The device may be prefilled with sample processing material in one or more holding chambers to provide a ready-to-use assembly for sample preparation. The processing
10 material can be a liquid, a solid matrix such as powders, crystals, granules, lyophilisate, films, nanoparticles, microparticles or beads, or a suspension, emulsion or gel. Examples of sample processing materials include, but are not limited to, binding reagents for binding a component in the liquid sample, cell lysis buffers, lyophilised reagents, water or aqueous buffers for reconstituting lyophilised reagents, wash reagents for washing component-bound
15 binding reagents, elution reagents for releasing a component bound to the binding reagents, and detection reagents for detecting a component bound to the binding reagents.

A variety of ways to fill the holding chambers are contemplated. By way of example, sample processing material may be introduced sequentially into the holding chambers through the
20 internal opening **124** of the holding chambers, beginning with the most distal chamber, before the stopper is inserted to seal the holding chambers. Alternatively, the device may be provided with external loading ports **126**, and the material is introduced through the external ports. The ports are sealed with caps **128** to prevent leakage of the material. In another embodiment, the stopper may be provided with micro-channels or capillary conduits that
25 permit loading of each holding chamber independently. In yet another embodiment, chamber filling may be integrated into the fabrication process. For example, the holding chambers may be filled with processing material immediately after plastic molding or 3D printing of one or more barrel sections, after which the sections are sealed or bonded together to complete the barrel body. In another embodiment, molecular reagents such as antibodies,
30 enzymes, proteins or nucleic acids may be chemically bonded to an internal wall of the holding chambers during or following device fabrication.

In a preferred embodiment, the sample processing material includes magnetic particles (MPs) that have been functionalised to enable removal of one or more components in the

sample. MPs are advantageous for POC processing and testing as they are readily mixed with liquid samples and can be rapidly and selectively immobilised using an external magnet without the need for centrifugation, filtration or other physical separation methods. The MPs can be held in a place at a selected location in the device using the magnet while performing
5 subsequent washing, elution and/or detection steps. MPs are also easily recovered for reuse.

Magnetic particles typically have a core constructed from magnetite (Fe_3O_4), maghemite ($\gamma\text{-Fe}_2\text{O}_3$), ferrites (such as cobalt ferrite, nickel ferrite, manganese ferrite, zinc ferrite, or cadmium ferrite), iron alloys (such as Fe/Au or Fe/Co alloys), magnetic composites (such as
10 copper or gold-doped iron oxides), or metal organic frameworks (such as magnetic zirconium organic frameworks). A polymer matrix is coated around the core to enable further functionalisation. Alternatively, the MPs may be a core-shell MP, such as an MP with iron oxide core and a copper shell ($\text{Fe}_3\text{O}_4@\text{Cu}$) or a gold shell ($\text{Fe}_3\text{O}_4@\text{Au}$). The MPs can range in size from nanometres to a few micrometres, and are not restricted in shape (e.g.,
15 they can be nanoparticles, microparticles, nanorods, nanowires, or nanotubes). Submicron-sized superparamagnetic particles are particularly advantageous as they do not retain residual magnetism after removal of magnetic field, which prevents particle aggregation during storage and handling.

20 The magnetic core is typically coated with a shell material that provides structural integrity, prevents oxidation of the core, and serves as a platform for surface functionalisation. Common shell material include silica (SiO_2), silanes (e.g., γ -methacryloxypropyltrimethoxysilane (MPS), chlorophenylsilane), synthetic polymers (e.g., polyethylene glycol, polyvinyl alcohol (PVA), polystyrene, polyethyleneimine,
25 polydopamine, poly(acrylic acid), poly(2-hydroxyethylmethacrylate) (PHEMA), polyacrylamide, polyvinylpyrrolidone (PVP), poly(glycidyl methacrylate-triallyl isocyanurate-divinylbenzene), poly(N-isopropylacrylamide) (PNIPAM), poly(EGDMA-MAH), poly(MAA-co-EGDMA), poly[2-(methacryloyloxy)ethyl]trimethylammonium chloride (PMAC), poly(3-thienylboronic acid), and poly(8-hydroxyquinoline)), and
30 biopolymers (e.g., dextran, gelatin, carboxymethyl cellulose, agarose, chitosan, carrageenan, and gum arabic). The polymer shell may also incorporate additional functional groups or linkers (e.g., carboxyls, amines, aldehydes, phosphates, hydroxyls, oxiranes, cyclodextrins, 3-chloropropyltrimethoxysilane (CPTMS), olcic acid, streptavidin, or biotin) to facilitate subsequent surface modification and target molecule attachment.

The outer surface of the MPs can be functionalised with various chemical groups, ligands or biomolecules to enable specific capture and removal of target components from the samples. Examples of such binding agents include antibodies and other antigen-binding molecules
5 including aptamers; nucleic acids (for hybridising to target nucleic acid sequences); lectins (for binding to carbohydrate moieties, glycans and glycosylated biomolecules); hydrophobic groups (to capture hydrophobic molecules); affinity ligands that specifically bind certain proteins or peptides; charged groups for capturing oppositely charged ions or molecules; chelating groups for binding to metals or metal-binding molecules; and polymer networks
10 or matrices that have been molecularly-imprinted with a target molecule.

In a preferred embodiment, at least one holding chamber of the device is pre-loaded with magnetic particles (MPs). Each MP may be capable of binding a single or a plurality of components in the sample. A mixture of different MPs may be loaded into a chamber to
15 capture different components.

The MPs may serve different roles depending on the sample processing requirements. In one embodiment, the MPs are functionalised to remove interfering components in the sample that can negatively impact the accuracy or sensitivity of downstream analytical procedures.
20 These interfering components include haem-containing compounds that can cause optical interference in colorimetric or spectrophotometric assays, and immunoglobulins that can inhibit nucleic acid amplification reactions. In another embodiment, the MPs are functionalised to selectively capture and concentrate target analytes of interest (e.g., proteins, nucleic acids, lipids, metabolites, drugs, pathogens, etc.) from the sample for
25 subsequent analysis. Both applications can be combined within a single device, where different chambers contain MPs functionalised for different purposes (removal of interfering components, or extraction of target analytes).

The MPs may be functionalised to bind a target component selected from a nucleic acid, a polypeptide, an antigen, an antibody, a carbohydrate, a lipid, a metabolite, a pigment, a drug,
30 an exosome, or a microvesicle. In particular, MPs binding to pollutants, heavy metals, antibodies, antigens, endotoxins, metabolites, enzymes, proteins, glycoproteins, glycopeptides, phosphopeptides, lectins, low-density lipoproteins, and cancer markers in blood may be used with the device for blood processing.

Preferably, the MPs are functionalised to bind: a) a nucleic acid selected from virus DNA, cell-free DNA (cfDNA), short-stranded DNA, pseudo virus DNA, genomic DNA, chromosomal DNA, chloroplast DNA, plasmid DNA, mitochondrial DNA, recombinant DNA, single-stranded DNA (ssDNA), double-stranded DNA (dsDNA), mRNA, rRNA, tRNA, miRNA, single-stranded RNA (ssRNA), double-stranded RNA (dsRNA), and DNA/RNA hybrids; b) a protein or peptide selected from an isolation antibody, an immunoglobulin, a prion, a fructosyllysine-specific binding protein, a receptor, an enzyme, a phosphopeptide, a synthetic peptide, a digest product of proteins, a lectin, a hormone, a tumour marker, and a DNA-binding protein, c) an exosome or a microvesicle; d) a drug selected from a cardiovascular drug, a steroid hormone, a mycotoxin, a toxin, an antidepressant drug, an anti-HIV drug, a nonsteroidal anti-inflammatory drug (NSAID), an adrenergic agonist (e.g., natural neurotransmitters like adrenaline, noradrenaline, and dopamine), a tyrosine kinase inhibitor (e.g., sunitinib malate), a nicotinic acetylcholine receptor agonist (e.g., nicotine), a benzodiazepine (e.g., Diazepam), a selective serotonin reuptake inhibitor (e.g., Sertraline), a serotonin-norepinephrine reuptake inhibitor (e.g., Duloxetine), a tricyclic antidepressant, a beta-blocker, a chemotherapy drug (e.g., epirubicin hydrochloride), an NMDA receptor antagonist (e.g., ketamine), an opioid, a central nervous system stimulant (e.g., amphetamines, synthetic cathinones), an antibiotic (e.g., chloramphenicol), and a metabolite of the foregoing; e) a carbohydrate, a glycan, a glycoprotein or a glycopeptide; f) a lipid or a lipoprotein (e.g., low-density lipoprotein); g) a cell; or h) haem, haematin, haemosiderin, haemoglobin, myoglobin, bilirubin, or carotene.

By way of non-limiting example, to remove haem, haematin or haemoglobin from a sample, MPs with a copper-doped iron oxide core or a copper shell ($\text{Fe}_3\text{O}_4@\text{Cu}$) may be used. $\text{Fe}_3\text{O}_4@\text{Cu}$ core-shell particles are synthesised in two steps. First, Fe_3O_4 MPs are synthesised by a facile solvothermal method, then obtained Fe_3O_4 particles are dispersed in an aqueous solution of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$, and the product is collected by centrifugation and washed with highly purified water and dried under vacuum to obtain the $\text{Fe}_3\text{O}_4@\text{Cu}$ MPs. The MPs may additionally be functionalised haem-specific binding agents, including but not limited to polyhistidine moieties, polyimidazole moieties, porphyrin moieties, imidazolium ionic liquids, anti-haemoglobin antibodies, haptoglobin, haemopexin, metal chelating groups such as nitrilotriacetic acid (NTA), iminodiacetic acid (IDA) or ethylenediaminetetraacetic acid (EDTA), and haemoglobin-imprinted polymers. In one embodiment, the MPs are

Cu@Fe₃O₄ MPs, core-shell dual-template molecularly imprinted MPs, or MPs functionalised with anti-haemoglobin for binding to haem, haematin or haemoglobin.

In another example, MPs functionalised with Protein A or Protein G can be used to selectively binding immunoglobulins (e.g., IgG) or immune complexes. MPs coated with a poly(N-methacryloyl-L-aspartic acid-hydroxyethyl methacrylate) shell (Fe₃O₄@SiO₂@MAsp-HEMA) have also been shown to selectively adsorb and remove IgG from blood samples. In one embodiment, the MPs are Protein A or Protein G conjugated MPs for binding immunoglobulins such as IgG.

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The MPs may be formed on, conjugated to, or embedded within a molecule, polymer network, organic framework, or porous material to form magnetic composites, non-limiting examples of which include porous organic polymers (MOPs), magnetic molecularly imprinted polymers, magnetic carbon nanotubes, magnetic carbon graphite (e.g., cubic SnFe₂O₄/graphitic carbon nitride), and magnetic zeolites.

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As shown in Figure 1, the device may be provided with a magnet **116** attachable to the syringe barrel for immobilising magnetic particles contained in a holding chamber of the barrel. Immobilisation of the particles facilitates separation of unbound components, particle washing, and subsequent elution and detection steps. The magnet may be configured for selective positioning at a particular section of the barrel, such as around a chamber, to localise particles within that section or chamber. In another embodiment, the magnet may be slidably mounted on the syringe barrel and movable along a length of the syringe barrel to collect particles in different chambers. In other embodiments, two or more magnets may be provided to immobilise MPs at different positions (e.g., in different holding chambers) of the device.

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A C-ring magnet **116** is shown in Figure 1, but other magnet geometries are also contemplated, such as a ring magnet that completely encircles the barrel. The magnet may be provided with a grip to facilitate repositioning along the syringe barrel, or with a locking mechanism to maintain its position at a desired location along the syringe barrel.

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Component-bound MPs may be washed with an aqueous solvent such as water or a wash buffer contained in a chamber, in preparation for component elution or detection. In a non-

limiting example, the wash buffer may be a Tris-HCl buffer (10–50 mM) containing 70–80% ethanol. For immunodetection of components bound to the MPs, the MPs may be washed with a buffer containing a small amount of detergent (e.g., 0.05–0.1% v/v Tween-20) and a blocking agent such as bovine serum albumin (BSA) or non-fat dry milk.

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In one embodiment, an elution reagent is provided a holding chamber to release one or more components bound to the MPs. The composition of the elution reagent may be selected to disrupt the interaction between target components and the MPs. For example, the elution reagent may be a buffer of a different pH to modify surface charges to facilitate desorption (e.g., a low-pH buffer for eluting proteins from Protein A/G conjugated MPs), or may be a high-salt buffer (e.g., >1 M sodium or potassium chloride) to disrupt ionic interactions, or may contain mild surfactants (e.g., Triton X-100 or SDS) to disrupt hydrophobic interactions, or may contain a competitive ligand to displace bound analytes by binding competitively to the MPs. Alternatively, the elution reagent may contain an enzyme or reagent to cleave a linker joining the capture molecule to the MPs, thereby releasing the component-bound capture molecule.

In one embodiment, a detection reagent is provided a holding chamber to detect one or more components bound to the MPs. The detection reagent is capable of generating a detectable signal, such a colorimetric, fluorescent, or luminescent signal, to indicate the presence of the component. In a non-limiting example, the detection reagent is a labelled detection antibody that binds specifically to an antigen or an antibody captured on the MPs. If the antigen is bound to a capture antibody on the MPs, the detection antibody is selected to bind to a different epitope on the antigen from the capture antibody.

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The detection antibody may be conjugated to a fluorescent label (e.g., a fluorescent dye, fluorescent protein or quantum dots) or a colorimetric label (e.g., a dye or plasmonic nanoparticles like gold nanoparticles) for direct detection. Alternatively, an enzyme label (such as horseradish peroxidase, alkaline phosphatase or luciferase) may be used along with a substrate provided in another chamber for detection. The substrate may be TMB (3,3',5,5'-tetramethylbenzidine), ABTS (2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) or OPD (O-phenylenediamine dihydrochloride)) for horseradish peroxidase; p-nitrophenyl phosphate (pNPP) or BCIP/NBT (5-bromo-4-chloro-3-indolyl phosphate/nitroblue tetrazolium) for alkaline phosphatase (AP); and luciferin for luciferase. A quenching agent

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may be included in the substrate composition to minimise background fluorescence or prevent signal decay. Instead of directly detecting the detection antibody, a labelled secondary antibody may be provided in an additional holding chamber for detecting the detection antibody.

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The sample processing material may include a cell lysis composition for lysing cells in the samples to release target analytes. The cell lysis composition may include one or more of an ionic, non-ionic or zwitterionic surfactant (e.g., SDS, Triton X-100, Tween, or cetyltrimethylammonium bromide (CTAB)), a chaotrope (e.g., urea, thiourea, or a
10 guanidinium salt), a cell wall digesting enzyme (e.g., lysozyme or mutanolysin), a protease (e.g., proteinase K or trypsin), a metal chelating agent (e.g., EDTA or EGTA), a disulphide reducing agent (e.g., dithiothreitol, β -mercaptoethanol or tris(2-carboxyethyl)phosphine (TCEP)), and/or an osmotic agent (e.g., ammonium chloride) to disrupt cell walls and cell
15 membranes to facilitate lysis. The composition may be varied according to the cell type to be lysed. For example, microbial cells such as bacteria and fungi often have a robust cell wall that requires enzymatic digestion in combination with surfactant or chaotrope treatment.

In some embodiments, the cell lysis composition comprises one or more of: an alkaline buffer (e.g., 10–100 mM Tris-HCl for maintaining a pH between 7.4 and 8.5), a chelating
20 agent (e.g., 1–100 mM EDTA), a surfactant (e.g., 0.1–2% w/v SDS, 0.1–2% v/v Triton X-100 or Tween, or 0.1–2% w/v CTAB), a chaotrope (e.g., 2–10 M guanidine hydrochloride, guanidine thiocyanate, urea or thiourea), a protease (e.g., about 0.1–1 mg/ml Proteinase K), phenylmethylsulfonyl fluoride (PMSF), 1–10 mM dithiothreitol (DTT), about 50 mM β -mercaptoethanol, ammonium acetate, and/or 50–70% ethanol.

25

In some embodiments, the cell lysis composition is selected from an alkaline surfactant lysis buffer, a neutral pH lysis solution, an erythrocyte lysis buffer, an ammonium chloride potassium (ACK) lysis buffer, an ammonium acetate lysis buffer, a guanidine-based lysis
buffer, a saponin-based lysis buffer, a urea or thiourea-based lysis buffer, and a lysis buffer
30 containing proteinase K and/or lysozyme.

The sample processing material may be provided in a liquid form, or in a dry form (such as lyophilised powder or film) for reconstitution in the syringe device. The dry composition may be reconstituted upon contact with the liquid sample. Alternatively, two holding

chambers may be provided, one containing a dried composition and the other containing a reconstitution solvent (such as a water or an aqueous buffer). The contents of the two chambers are mixed to reconstitute the dried composition before adding to the sample.

- 5 In one embodiment of the BioSyringe device, the device is provided with two holding chambers arranged in series from distal to proximal end of the barrel and containing, respectively, (i) an aqueous solvent; and (ii) lyophilised processing material (such as a lyophilised cell lysis composition). The aqueous solvent may be water or a suitable reconstitution buffer. The device may contain additional holding chambers with reagents or
10 buffers for component capture, washing, or elution/detection.

- In one embodiment of the BioSyringe device, the device is provided with two holding chambers arranged in series from distal to proximal end of the barrel and containing, respectively, (i) a cell lysis composition; and (ii) MPs. Such a device may be used for
15 sequential sample lysis and component capture. The device may contain additional holding chambers with reagents or buffers for washing or elution/detection.

- In one embodiment of the BioSyringe device, the device is provided with two holding chambers arranged in series from distal to proximal end of the barrel and containing,
20 respectively, (i) MPs; and (ii) an aqueous solvent. Such a device may be used for sequential component capture and washing of MPs in preparation for further processing (e.g., component elution/detection). The device may contain additional holding chambers with reagents or buffers for lysis or elution/detection.

- 25 In one embodiment of the BioSyringe device, the device is provided with two holding chambers arranged in series from distal to proximal end of the barrel and containing, respectively, (i) MPs; and (ii) an elution reagent. Such a device may be used for sequential component capture and component release for detection. The device may contain additional holding chambers with reagents or buffers for lysis, washing or detection.

- 30 In one embodiment of the BioSyringe device, the device is provided with two holding chambers arranged in series from distal to proximal end of the barrel and containing, respectively, (i) MPs; and (ii) a detection reagent. Such a device may be used for sequential

component capture and detection of the captured component. The device may contain additional holding chambers with reagents or buffers for lysis, washing or elution.

5 In use, the assembled BioSyringe is pre-loaded with sample processing material in the various holding chambers, and the stopper is moved towards the proximal end of the barrel to draw in a sample (e.g., a biological fluid or environmental fluid) at the distal end and to sequentially contact the sample with the contents of the chambers.

10 Sample processing may comprise one or more of the following steps: i) contacting the sample with a cell lysis composition in a holding chamber to lyse cells in the sample; ii) contacting the sample with magnetic particles (MPs) in a holding chamber to bind a component in the sample to the MPs; iii) contacting component-bound MPs with an aqueous solvent in a holding chamber to wash component-bound MPs; iv) contacting component-bound MPs with an elution reagent in a holding chamber to release a component bound to the MPs; and/or v) contacting component-bound MPs with a detection reagent in a holding chamber to detect a component bound to the MPs.

20 In one embodiment, a dried or lyophilised reagent (e.g., lyophilised lysis buffer) and a solvent for reconstitution are provided in separate holding chambers, and sample processing comprises contacting the two materials to reconstitute the reagent.

Following component capture by the MPs, one or more magnets may be attached to the syringe barrel to immobilise the MPs for subsequent washing, elution and/or detection steps, or to retain the MPs during sample discharge.

25 In embodiments where MPs are used to remove interfering or undesirable components from the sample, following capture of these interfering or undesirable components by the MPs, the processed sample may be discharged from the device and collected for subsequent processing.

30 In other embodiments where the MPs are used for selective capture of target analytes of interest, following capture of the targets by the MPs, the sample containing unbound components may be discarded, and the target-bound MPs may then be subjected to further processing depending on the analytical requirements. In one processing approach, the

captured targets are released from the MPs using an elution reagent contained in a syringe chamber, and the eluate containing the concentrated targets is collected for analysis. In another approach, the captured targets are detected directly using detection reagents in a syringe chamber while still bound to the MPs.

5

Operation of the BioSyringe to remove components from blood is illustrated in Figure 2. The assembled BioSyringe device in Figure 2 contains: (i) lysis buffer **132** in a first holding chamber at the distal end for lysing red blood cells, with volume variable from 10 µl to 1 ml; (ii) and (iii) MPs (**134**, **136**) for removing one or more blood components, in second and
 10 third holding chambers from the distal end, with volume variable from 10 µl to 1 ml (MPs are suspended in water or buffer); and (iv) nuclease-free, sterile, and ultrapure water **138** in the proximal-most holding chamber, with volume variable from 50 µl to 10 ml.

Stepwise operation according to Figure 2:

- 15 I. A sample acquisition component such as a needle **114** is used to draw the required volume of sample into the syringe barrel.
- II. Plunger rod **110** is pulled proximally to mix the sample with lysis buffer in the distal-most holding chamber (**132**) to lyse red blood cells.
- III. Plunger rod **110** is pulled further to mix with MPs in the next holding chamber in the
 20 series (**134**).
- IV. After adsorption of the components by the MPs, ring magnet **116** is placed around this holding chamber to immobilise the MPs.
- V. Plunger rod **110** is pulled further to mix with another set of MPs in the next holding chamber (**136**).
- 25 VI. The ring magnet **116** is placed on this holding chamber to immobilise the MPs.
- VII. Plunger rod **110** is pulled further to mix with sample diluent in the next holding chamber (**138**). This step is for diluting the prepared extract and can be omitted, as dilution can be performed after removing the extract from the syringe.
- VIII. With magnet **116** in place holding the MPs, plunger rod **110** is pushed distally to
 30 discharge the processed sample for subsequent biochemical and molecular diagnostics application.

Another embodiment of the BioSyringe device is shown in Figures 3 and 4. The device has a syringe barrel **202** with four integrally formed holding chambers **218** which are sealed by

a stopper **208** when the device is assembled. Plunger rod **210** is used to control movement of the stopper **208**. A needle **214** at the distal end facilitates liquid collection. Ring magnet **216** is provided for immobilising MPs within the barrel.

- 5 Holding chambers **218** of the device are loaded through the interior of the barrel. The holding chambers contain (from distal-most to proximal-most chambers): i) nuclease-free, sterile, and ultrapure water **232** in the first holding chamber from the distal end for reconstituting lyophilised lysis buffer, with volume variable between 50 µl to 10 ml; ii) lyophilised lysis buffer **234** in the second holding chamber in the series for lysing red blood cells (volume
10 can vary from 10 µl to 1 ml); and iii) MPs **236** in the third holding chamber in the series, suspended in water or a buffer and functionalised for removing a component from blood (volume can vary from 10 µl to 1 ml).

Operation of this device is shown in Figure 4:

- 15 I. A volume of blood is drawn into the syringe barrel.
II. Plunger rod **210** is pulled proximally to mix water in the first holding chamber (**232**) with lyophilised lysis buffer in the second holding chamber (**234**) to reconstitute the buffer, and to mix the lysis solution with the blood sample.
III. Plunger rod **210** is pulled further to mix the lysate with MPs in the third holding
20 chamber (**236**).
IV. After adsorption of sample components by the MPs **236**, the ring magnet **216** is placed around this holding chamber to immobilise the MPs.
V. With magnet in place, the plunger rod **210** is pushed distally to discharge the sample for further processing.

25

- In another embodiment of the device, also referred to as a DnaSyringe in this disclosure, the device comprises: (a) a syringe barrel with a body comprising a proximal end, a distal end for receiving a liquid sample, and a plurality of holding chambers integrally formed in the body for holding a plurality of sample processing materials; (b) a plurality of stoppers
30 slidably disposed within the body of the syringe barrel and forming a fluid-tight seal within the body to isolate the plurality of the holding chambers, the plurality of stoppers comprising a distal-most stopper and a proximal-most stopper; and (c) a plunger assembly for controlling relative positioning of the plurality of stoppers within the syringe barrel, the plunger assembly comprising an inner plunger rod fixedly coupled to the distal-most stopper,

and an outer plunger rod fixedly coupled to the proximal-most stopper, the inner plunger rod telescopically receivable within the outer plunger rod. In use, the plunger assembly is operated to move the plurality of stoppers to sequentially unseal the plurality of holding chambers such that a liquid sample received at the distal end of the syringe barrel is brought
5 into contact with the plurality of sample processing materials in the plurality of holding chambers.

Figure 12 shows a kit of parts that can be assembled into a DnaSyringe device. The assembled device **300** is shown in Figure 14. Referring to Figure 12, the device comprises a
10 hollow syringe barrel **302** with proximal end **306** and distal end **304**. A sample collection device such as a needle **318** can be attached to the syringe at the distal end. The barrel has a proximal section **306** and distal section **304** which couple together at respective ends thereof to form a complete barrel body **302**. The two sections may be joined by an interference fit, by threaded engagement or any suitable coupling means that ensures a fluid-tight fit. In
15 alternative embodiments, the barrel body may be formed as a unibody structure.

Stoppers **322, 324, 326, 330, 332, 334** and **336** are positioned in the barrel body to divide the interior space into a series of fluidically sealed holding chambers (**344, 346** and **348**) for containing sample processing material (see Figure 14). Each stopper is dimensioned to form
20 a fluid-tight seal against the interior wall of the barrel body while maintaining slidable movement along the length of the barrel.

In this arrangement, a holding chamber may be defined between two adjacent spaced-apart stoppers in the barrel body. This is shown with stoppers **322** and **324**, which define between
25 them a fluidically sealed holding chamber **344**, and also with stoppers **324** and **326**, which define holding chamber **346** therebetween.

Alternatively, a stopper may have two adjacent spaced-apart sealing elements each forming a fluid-tight seal with an interior wall of the barrel body, and a holding chamber is defined
30 in the space between the two sealing elements. This is shown with stoppers **326, 330, 332** and **334**, each of which are flanged stoppers having two spaced apart sealing elements **328** that form a fluid-tight seal within the barrel. When positioned within the syringe barrel, the space defined between the two sealing elements and the barrel wall forms a holding chamber **348** for containing sample processing materials.

In another embodiment, the device may include one or more chambers that are integrally formed in the barrel body with a wall portion which extends outwardly relative to the barrel body, each chamber having an opening into the interior of the body that is dimensioned for sealing by a stopper to form a fluidically sealed holding chamber. Holding chambers **558** in Figure 18 are examples of such holding chambers. These holding chambers may be configured to have smaller internal volumes (ranging from 100 μ l to 1 ml), and can be used to contain smaller quantities of sample processing material. Holding chambers **558** are dimensioned and positioned such that each chamber is fluidically sealed by one of the stoppers. Upon axial movement of the stoppers, holding chambers **558** are unsealed allowing their contents to mix with the contents of an adjacent holding chamber.

Referring to Figure 14, distal-most stopper **322** (which is adjacent the distal end) and proximal-most stopper **336** (which is adjacent the proximal end) define respective ends of the series of holding chambers. Variable number and types of stoppers may be used to generate the holding chambers within the barrel. The mixing chambers may have internal volumes ranging from 100 μ l to 1 ml.

Stoppers **322** and **324**, positioned at the distal end of the barrel, are thin disc-shaped stoppers. The disc geometry enables controlled deformation under rotational pressure to allow the stopper to lock against the barrel wall during sample processing (this is further described below). Intermediate stoppers **326**, **330**, **332**, **334**, positioned between distal-most stopper **322** and proximal-most stopper **336**, are flanged stoppers having two spaced apart disc-shaped sealing elements **328** that form a fluid-tight seal within the barrel. The sealing elements are connected by a cylindrical connector portion which has a smaller diameter than the sealing elements. When positioned within the syringe barrel, the annular space defined between the two sealing elements and the barrel wall forms a holding chamber for containing sample processing reagents. Proximal-most stopper **336**, positioned near the proximal end of the barrel, has a cylindrical geometry which provides structural rigidity when outer plunger rod **314** is urged against this stopper to advance the entire series of stoppers during operation.

The device is provided with mixing chambers in which the liquid sample is contacted with sample processing material in the holding chambers. The mixing chambers are configured

to break a fluid seal provided by a stopper when the stopper is positioned in the mixing chamber, thus allowing fluid communication between holding chambers or regions in the barrel body that are otherwise fluidically isolated by the stopper. In one embodiment, the mixing chamber is sized to have a larger internal diameter than the diameter of the stoppers, such that a gap exists around the exterior of a stopper that is positioned in the mixing chamber that allows fluid to flow past the stopper. The mixing chambers may have internal volumes ranging from 1 ml to 10 ml.

Referring to Figure 14, holding chambers **344** and **346** double as mixing chambers. Chamber **344** has an internal diameter that is larger than the diameter of stopper **322**, thereby forming a gap around the exterior of stopper **322** that breaks the fluid seal provided the stopper when stopper **322** is moved within chamber **344**. This is shown in Step II of Figure 15. Similarly, Chamber **346** has an internal diameter that is larger than the diameter of stoppers **324**, **326**, **330**, **332** and **334**, such that when stoppers **324**, **326**, **330**, **332** and **334** are sequentially moved into chamber **346**, the contents of holding chambers **344** and **348** can be sequentially delivered into chamber **346** for mixing the sample. This shown in Steps III, VII, IX, XI and XIII in Figure 15.

Multiple mixing chambers having different volumes may be provided along the barrel to create distinct processing zones tailored to the processing workflow. For example, a proximal mixing chamber may be used to mix a series of processing material contained in proximal holding chambers, before the mixture is advanced into a distal mixing chamber for sample processing. In another example, the sample may be mixed with a first series of processing material in a distal mixing chamber, before being moved to a proximal mixing chamber and contacted with a second series of processing material. Alternatively, the barrel may be provided with a single mixing chamber, and the stoppers are sequentially advanced into the mixing chamber for sample processing.

In a preferred embodiment, loading ports **338** opening to the exterior of the barrel are arranged along the barrel body corresponding to the positions of the holding chambers to allow buffers, dry reagents and other processing material to be loaded into the holding chambers. The ports are secured with caps **340** to keep the holding chambers fluid-tight.

The device includes a plunger assembly configured to be received within the barrel body and controlling relative positioning of the stoppers within the barrel. The plunger assembly includes an inner plunger rod **312** that is telescopically receivable within an outer plunger rod **314**. The inner plunger rod **312** is coupled to the distal-most stopper **322** in the barrel body, while the outer plunger rod **314** is coupled to the proximal-most stopper **336** (see Figure 14). Intermediate stoppers **324**, **326**, **330**, **332** and **334**, which are positioned between the distal-most and proximal-most stoppers, are slidably mounted on the inner plunger rod **312**. The distal stopper **322** may be fixedly mounted on the inner rod **312** so that its axial movement is directly controlled by movement of the inner rod. Similarly, the proximal stopper **336** may be fixedly mounted on the outer rod **314** so that its axial movement is directly controlled by movement of the outer rod.

A single plunger rod configuration moves all stoppers in tandem along one axial direction (either proximally or distally). The dual-rod system is advantageous in providing greater control over stopper movement by enabling independent or coordinated movement of different groups of stoppers. In particular, the dual-rod configuration allows the series of stoppers to be sequentially moved (along either axial direction) into a mixing chamber to break the fluidic seal provided by the stoppers and allow the contents of the holding chambers to be contacted with each other and with the liquid sample.

In some embodiments, the inner and outer plunger rods are coupled such that axial movement of the outer plunger rod causes corresponding axial movement of the inner plunger rod in the same direction. Alternatively or additionally, the inner and outer plunger rods may be rotatably coupled such that rotation of the outer plunger rod about its longitudinal axis causes corresponding rotation of the inner plunger rod in the same rotational direction.

In the embodiment shown in Figure 14, the inner and outer plunger rods are coupled at their respective ends through a retention mechanism. The inner rod **312** has a radial protrusion or flange **313** at one end that is sized so that it cannot pass through a corresponding restriction **315** at an opening at an end of the outer rod **314**. This coupling prevents the inner rod **312** from completely separating from the outer rod **314** while permitting relative sliding of the two rods.

The coupling provides means for controlling both axial and rotational movement of the inner rod through manipulation of the outer rod. In the extended configuration of the plunger assembly shown on the far right of Figure 14, pulling the outer rod **314** in a proximal direction causes the inner rod **312** to move proximally in unison. Similarly, rotating the outer rod **314** about its longitudinal axis causes corresponding axial rotation of the inner rod **312**, enabling rotational positioning control. This coupled arrangement simplifies operation of the syringe device by allowing the outer rod to serve as the primary control for movement and positioning of the entire stopper assembly. The device may include a plunger lever or handle **342** attached to the outer plunger rod **314** to facilitate manual manipulation of the rod during operation.

In an alternative embodiment, the inner and outer rods are not coupled and are configured for independent push/pull operation to provide separate control over different stopper groups. Both plunger rods may be provided with separate plunger levers or handles for independent manual manipulation.

The device comprises a releasable locking mechanism for securing the distal stopper **322** in place within the barrel. The locking mechanism is implemented by the cross-sectional geometries of the stopper and the barrel body, which are shaped to allow selective jamming engagement. Specifically, both the stopper and barrel body have an asymmetric cross-sectional profile, such that one dimension (e.g., a major axis) is longer than another dimension (e.g., a minor axis) (see Figure 15). When the stopper is rotated about a longitudinal axis of the barrel, the major axis of the stopper is urged into contact with the minor axis of the barrel interior, thereby creating a jamming effect that prevents axial displacement of the stopper. Rotating the stopper in the opposite direction returns the stopper to its original (unlocked) orientation.

The distal stopper **322** may be configured as a deformable disc to allow it to undergo partial elastic deformation during rotation, thereby facilitating its transition into and out of the locked configuration. The distal stopper **322** is further rotatably coupled to the outer plunger rod **314** through the mechanical coupling of the outer and inner plunger rods. This arrangement permits engagement and disengagement of the locking mechanism by rotating the outer plunger rod.

In certain embodiments, additional stoppers may also be provided with cross-sectional geometries that allow locking engagement with the barrel wall. These stoppers may be fixedly mounted on the inner plunger rod **312** and rotationally coupled to the outer plunger rod **314** for rotational locking. The locking mechanism allows the inner rod to be held
5 stationary while the outer rod is manipulated to position the rest of the stoppers.

In some embodiments of the device, an unsealing mechanism may be provided to unseal a stopper while the stopper remains axially positioned within the barrel. The unsealing mechanism may comprise rotational coupling between a plunger rod and the stopper, the
10 stopper being rotatable between a sealing configuration in which the stopper forms a fluid-tight seal with an interior wall of the barrel body, and an open configuration in which fluid flow past the stopper is permitted, upon rotation of the plunger rod about a longitudinal axis. The stopper may have a non-circular cross-sectional shape, such as an oval, elliptical or polygonal geometry that provides different sealing characteristics depending on its rotational
15 orientation relative to the barrel wall. When in the sealing configuration, the stopper's cross-sectional dimensions match or slightly exceed the barrel's internal diameter at that location, creating the fluid-tight seal. When rotated to the open configuration, the stopper's reduced dimension in at least one direction creates the gap that allows fluid passage.

20 In the embodiment shown in Figure 15, when distal stopper **322** is locked in place, gaps are formed between the stopper periphery and the interior barrel wall, allowing fluid to flow around the stopper. This arrangement enables the contents of a mixing chamber to be discharged without requiring stopper displacement. Alternatively, liquid can be discharged by advancing the distal stopper into a mixing chamber, allowing the chamber contents to
25 drain past the stopper.

As with the BioSyringe, the number of holding chambers can be tailored to the sample processing workflow. In one embodiment, the device includes at least two holding chambers to contain material for, e.g., lysis and component capture; component capture and component
30 release; or component capture and component detection. In one embodiment, the device includes at least three holding chambers to contain material for, e.g., lysis, component capture, and washing; lysis, component capture, and component release; or lysis, component capture, and component detection. In one embodiment, the device includes at least four

holding chambers to contain material for, e.g., lysis, component capture, washing, and component release or detection.

In one embodiment of the DnaSyringe device, the device is provided with two holding chambers arranged in series from distal to proximal end of the barrel and containing, respectively, (i) an aqueous solvent; and (ii) lyophilised cell lysis composition. The aqueous solvent may be water or a reconstitution buffer. Such a device may be used for reconstitution of the cell lysis composition and subsequent mixing with the sample. The device may contain additional holding chambers with reagents or buffers for component capture, washing, or elution/detection.

In one embodiment of the DnaSyringe device, the device is provided with two holding chambers arranged in series from distal to proximal end of the barrel and containing, respectively, (i) a cell lysis composition; and (ii) MPs. Such a device may be used for sequential sample lysis and component capture. The device may contain additional holding chambers with reagents or buffers for washing or elution/detection.

In one embodiment of the DnaSyringe device, the device is provided with two holding chambers arranged in series from distal to proximal end of the barrel and containing, respectively, (i) MPs; and (ii) an aqueous solvent. Such a device may be used for sequential component capture and washing of MPs in preparation for further processing (e.g., component elution/detection). The device may contain additional holding chambers with reagents or buffers for lysis or elution/detection.

In one embodiment of the DnaSyringe device, the device is provided with two holding chambers arranged in series from distal to proximal end of the barrel and containing, respectively, (i) MPs; and (ii) an elution reagent. Such a device may be used for sequential component capture and component release for detection. The device may contain additional holding chambers with reagents or buffers for lysis, washing or detection.

In one embodiment of the DnaSyringe device, the device is provided with two holding chambers arranged in series from distal to proximal end of the barrel and containing, respectively, (i) MPs; and (ii) a detection reagent. Such a device may be used for sequential

component capture and detection of the captured component. The device may contain additional holding chambers with reagents or buffers for lysis, washing or elution.

- 5 A sample acquisition component comprising one or more piercing elements may be attached to the distal end of the barrel for sample collection. This component may be a needle, lancet capillary tube, or needle array. Furthermore, a magnet **320** may be provided with the device to immobilise magnetic particles (MPs) within the barrel. The magnet may be a ring magnet or a C-ring magnet that can slide along the barrel.
- 10 The same material and process used to fabricate the BioSyringe (described above) may be used for the DnaSyringe.

Assembly of the plunger assembly and the syringe device is shown in Figure 14:

- 15 I. The outer plunger rod **314** is aligned coaxially and mounted over one end of the inner plunger rod **312** to form a complete plunger unit.
- II. The outer rod **314** is pulled towards the other end of the inner rod **312** to give an extended plunger configuration.
- III. The inner plunger rod **312** is fitted sequentially with proximal stopper **336** and intermediate stoppers **334**, **332**, **330** and **326**. The proximal stopper is fixed to outer
20 plunger rod **314**.
- IV. Oval cross-sectioned stoppers **324** and **322** are fitted onto the inner plunger rod **312**. Distal stopper **322** is fixed to the inner plunger rod **312**.
- V. Once the stoppers are properly seated, the assembled plunger unit is introduced into the proximal section **306** of the syringe barrel.
- 25 VI. A plunger lever **342** is attached to the proximal end of outer plunger rod **314**.
- VII. The distal section **304** of the barrel, containing the sample collection port, is attached to proximal section **306**.
- VIII. The stoppers, properly positioned, define six holding chambers **344**, **346**, **348** located proximal to the two mixing chambers **344**, **346**.
- 30 IX. At this point, sample processing material may be loaded into the holding chambers through the loading ports, which are then secured with respective caps **340**.
- X. The fully assembled DnaSyringe **300** is tested for plunger mobility and airtight sealing. A needle **318** may be mounted at the distal tip of barrel body for collecting a sample.

In use, the assembled DnaSyringe is pre-loaded with sample processing material in the holding chambers. Exemplary processing material is described above. In the embodiment shown in Figure 15, the holding chambers are loaded as follow (from distal end to proximal end): (i) lysis buffer **360** in a first holding chamber (volume can vary from 10 μ l to 1 ml);

5 (ii) MPs **362** in a second holding chamber, suspended in water or buffer (volume can vary from 10 μ l to 5 ml); (iii) washing buffer in third, fourth and fifth holding chambers (**364**, **366**, **368**) (volume can vary between 50 μ l to 1 ml); and (iv) elution buffer **370** in a sixth holding chamber to detach the molecule of interest from the MPs (volume can vary from 50 μ l to 10 ml).

10

Figure 15 shows the stepwise operation of the DnaSyringe for processing of a blood sample:

- I. The required volume of blood is drawn into the syringe barrel by pulling the outer plunger rod **314**, thus pulling on the inner plunger rod **312**.
- 15 II. Outer plunger rod **314** is pulled proximally to mix sample with lysis buffer **360** in the distal holding chamber **344** to lyse the cells in blood.
- III. Outer plunger rod **314** is pulled proximally to mix lysate with MPs **362** in holding mixing chamber **346**.
- IV. Outer plunger rod **314** is rotated 90 degrees. This rotates stoppers **322**, **324**. Outer rod
20 **314** is then pushed distally so that the distal stopper **322** is fixed in place at the distal end of holding chamber **346**. Rotating stopper **322** opens up two spaces on the sides of the stopper for fluid to flow out of the syringe barrel.
- V. After binding of analytes of interest by the MPs, a ring magnet **320** is placed around holding chamber **346** to immobilise the MPs within the chamber.
- 25 VI. The syringe is inverted to allow the processed sample in the holding chamber **346** to be discharged, while the particles remain immobilised by the magnet.
- VII. The syringe is inverted again, and outer plunger rod **314** is pushed distally to transfer washing buffer **364** in the third holding chamber into holding chamber **346**.
- VIII. The syringe is inverted to discharge used washing buffer in mixing chamber **346**.
- 30 IX. The syringe is inverted again, and outer plunger rod **314** is pushed distally to transfer washing buffer **366** in the fourth holding chamber into holding chamber **346**.
- X. The syringe is inverted to discharge used washing buffer in holding chamber **346**.
- XI. The syringe is inverted again, and outer plunger rod **314** is pushed distally to transfer washing buffer **368** in the fifth holding chamber into holding chamber **346**.

XII. The syringe is inverted to discharge used washing buffer in holding chamber **346**.

XIII. The syringe is inverted again, and outer plunger rod **314** is rotated 90 degrees so that stoppers **322** and **324** are returned to the unlocked configuration. Outer plunger rod **314** is then pushed distally to transfer elution buffer **370** in the sixth holding chamber into holding chamber **346**.

XIV. Finally, outer plunger rod **314** is pushed distally to discharge the eluate in holding chamber **346**.

A second embodiment of the DnaSyringe is shown in Figure 16. This device has a unibody syringe barrel **404**, containing holding chamber **444** integrally formed in the barrel body. The holding chamber **444** has a wider diameter than sections of the barrel adjacent the holding chamber, and may also be used as a mixing chamber. The distal-most section of the barrel (which accommodates stoppers **422** and **424**) and the holding chamber **444** have oval cross-sections. The remainder of the barrel body has a circular cross-section. A needle **418** is attached to the distal end of the barrel for sample collection.

A series of stoppers are slidably arranged within the barrel, including distal stopper **422**, proximal stopper **436** and 3 intermediate stoppers **424**, **426** and **430**. Stoppers **422**, **424**, **426** and **430** are disc stoppers, while stopper **436** at the proximal end is a cylindrical stopper. The stoppers form fluid-tight seals within the barrel body to section the body into three isolated holding chambers (**452**), defined between adjacent stoppers.

The stoppers are coupled to a plunger assembly that includes inner plunger rod **412** and outer plunger rod **414**. Inner plunger rod **412** can telescope within outer plunger rod **414**. Distal stopper **422** is fixed to inner plunger rod **412**, and proximal stopper **436** is fixed to outer plunger rod **414**. Intermediate stoppers **424**, **426** and **430** can slide along inner plunger rod **412**. The rods are arranged such that pulling and pushing the rods allows positioning of the stoppers within the body of the syringe barrel and in particular within chamber **444**.

The holding chambers of the device are loaded as follow (from distal end to proximal end): (i) water **460** in the first holding chamber for reconstituting a lyophilised lysis buffer (volume can vary from 10 µl to 1 ml); MPs and lyophilised lysis buffer **462** in the second holding chamber (volume can vary from 2 µl to 1 ml); (iii) wash buffer **464** in the third holding chamber (volume can vary between 50 µl to 1 ml); and (iv) elution buffer **466** in the fourth

holding chamber to detach the molecule of interest from the magnetic particles (volume can vary from 50 μ l to 10 ml).

Figure 17 shows the stepwise operation of the DnaSyringe of Figure 16:

- 5 I. The required volume of blood is drawn into the syringe barrel by pulling outer plunger rod **414** in a proximal direction. This pulls on inner plunger rod **412** and moves all stoppers proximally. Concurrently, water **460** in the first holding chamber is mixed with lyophilised lysis buffer and MPs in mixing chamber **444**.
- II. Outer plunger rod **414** is pulled proximally to mix sample with the reconstituted lysis
10 buffer and MPs in chamber **444**.
- III. Outer plunger rod **414** is rotated 90 degrees. This rotates and locks stoppers **422**, **424**. The outer rod **414** is pushed distally so that distal stopper **422** is fixed in place at the distal end of chamber **444**. Rotating stopper **422** opens up two spaces on the sides of the stopper for fluid in chamber **444** to flow out of the syringe barrel.
- 15 IV. After binding of molecule of interest by the MPs, ring magnet **420** is placed around chamber **444** to immobilise the MPs within the chamber.
- V. Outer plunger rod **414** is pushed distally to transfer wash buffer **464** into chamber **444** to wash the MPs while the MPs are immobilised by the magnet.
- VI. Outer plunger rod **414** is pushed distally to discharge the used wash buffer.
- 20 VII. Outer plunger rod **414** is pushed distally to transfer elution buffer **466** into chamber **444** to release an analyte of interest from the MPs while the MPs are immobilised by the magnet.
- VIII. Outer plunger rod **414** is rotated 90 degrees so that stoppers **422** and **424** are returned to the unlocked configuration.
- 25 IX. Outer plunger rod **414** is pushed distally to discharge the eluate in chamber **444**.

A third embodiment of the DnaSyringe is shown in Figure 18. The device has a unibody syringe barrel **504** containing holding chamber **544** integrally formed in the barrel body. Holding chamber **544** is an annular chamber formed around the circumference of the barrel
30 body and has a wider diameter than sections of the barrel adjacent the chamber, and also functions as a mixing chamber in this embodiment. The distal-most section of the barrel (which accommodates stoppers **522** and **524**) and holding chamber **544** have oval cross-sections. The remainder of the barrel body has a circular cross-section. A needle **518** is attached to the distal end of the barrel for sample collection.

A series of stoppers are slidably arranged within the barrel, including distal stopper **522**, proximal stopper **536**, and 5 intermediate stoppers **524**, **526**, **530**, **532** and **534**. The distal and intermediate stoppers are disc stoppers, while the proximal stopper is a cylindrical stopper. The stoppers form fluid-tight seals within the barrel body to section the body into five additional fluidically isolated holding chambers **552**, defined between adjacent stoppers.

Two additional holding chambers **558** with smaller internal volumes are integrally formed in the wall of the barrel body. The holding chambers **558** open into the interior of the barrel and the opening is initially sealed by stoppers **530** and **532** to prevent cross-contamination of the contents of the holding chambers.

The device has a plunger assembly that includes inner plunger rod **512** and outer plunger rod **514**. Inner plunger rod **512** can telescope within outer plunger rod **514**. Distal stopper **522** is fixed to inner plunger rod **512**, and proximal stopper **536** is fixed to outer plunger rod **514**. Intermediates stoppers **524**, **526**, **530**, **532** and **534** can slide along inner plunger rod **512**. The rods arranged such that pulling and pushing the rods allows positioning of the stoppers within the body of the syringe barrel and in particular within chamber **444** (which functions as mixing chamber).

20

The holding chambers of the syringe are loaded as follow (from distal end to proximal end): (i) water **560** in the first holding chamber for reconstituting lyophilised lysis buffer (volume can vary from 10 μ l to 1 ml); (ii) lyophilised lysis buffer **562** in the second holding chamber **544** (volume can vary from 10 μ l to 1 ml); (iii) water **564** in the third holding chamber for reconstituting lyophilised binding buffer (volume can vary from 10 μ l to 1 ml); (iv) MPs coated with antigens (for antibody detection) or antibodies (for antigen detection), along with lyophilised binding buffer **572** in the fourth side chamber (with a smaller internal volume); (v) water **566** in the fifth holding chamber for reconstituting lyophilised antibody (volume can vary from 10 μ l to 1 ml); (vi) lyophilised detection antibody **574** in the sixth holding chamber (also with a smaller internal volume); (vii) immunoassay wash buffer **568** in the seventh holding chamber (volume can vary between 50 μ l to 1 ml); (viii) detection reagent **570** in the eighth holding chamber for detecting the detection antibody bound to MPs (volume can vary from 50 μ l to 10 ml). Where the detection antibody is conjugated to an enzyme, the detection reagent can be a substrate for the enzyme which generates a

30

colorimetric, fluorescent or luminescent signal when acted on by the enzyme. Where the antibody is not labelled, the detection reagent can be a fluorophore-labelled secondary antibody to detect the detection antibody.

- 5 Figure 19 shows the stepwise operation of the DnaSyringe of Figure 18 to perform an immunoassay:
- I. The required volume of sample is drawn into the syringe barrel by pulling outer plunger rod **514** in a proximal direction. This pulls on inner plunger rod **512** and moves all stoppers in tandem proximally. Concurrently, water **560** in the first holding chamber is mixed with lyophilised lysis buffer in second holding chamber / mixing chamber **544**, water **564** in the third holding chamber is mixed with MPs and lyophilised binding buffer **572** in the fourth holding chamber, and water **566** in the fifth holding chamber is mixed with lyophilised detection antibody in the sixth holding chamber.
10
 - II. Outer plunger rod **514** is pulled proximally to mix sample with the reconstituted lysis buffer **561** in mixing chamber **544** for cell lysis.
15
 - III. Outer plunger rod **514** is rotated 90 degrees. This rotates and locks stoppers **522**, **524**. The outer rod **514** is pushed distally so that distal stopper **522** is fixed in place at the distal end of mixing chamber **544**. Rotating stopper **522** opens up two spaces on the sides of the stopper for fluid in mixing chamber **544** to flow out of the syringe barrel.
20
 - IV. Outer plunger rod **514** is pushed distally to transfer MPs in reconstituted binding buffer **563** into mixing chamber **544** to bind one or more analytes of interest to the MPs.
 - V. Ring magnet **520** is placed around mixing chamber **544** to immobilise the MPs within the chamber. The lysate can be discharged from the device with the magnet in place.
 - 25 VI. Outer plunger rod **514** is pushed distally to transfer reconstituted detection antibody **565** into mixing chamber **544** to bind to analytes on the MPs. Excess liquid is discharged from the device with the magnet in place.
 - VII. Outer plunger rod **514** is pushed distally to transfer immunoassay wash buffer **568** into mixing chamber **544** to wash the MPs. Excess liquid containing unbound material is discharged from the device with the magnet in place.
30
 - VIII. Outer plunger rod **414** is pushed distally to transfer detection reagent **570** into mixing chamber **544**. The detection reagent generates a signal (e.g., a colorimetric, fluorescent or luminescent signal) which can be detected optically or spectrophotometrically.

- IX. Outer plunger rod **514** is rotated 90 degrees so that stoppers **522** and **524** are returned to the unlocked configuration.
- X. Outer plunger rod **514** is pushed forward to discharge the detection reagent from mixing chamber **544**.

5

The term “plurality” herein refers to two or more.

As used herein, the term “proximal” refers to a position or direction with respect to a device that, during normal use, is closer to the user of the device. Conversely, the term “distal” refers to a position or direction with respect to the device that, during normal use, is farther from the user of the device.

The term “coupled”, as used herein, means connected, either directly or indirectly, and includes mechanical, electrical, magnetic, fluidic and other forms of connection.

As used herein, “and/or” refers to and encompasses any and all possible combinations of one or more of the associated listed items, as well as the lack of combinations when interpreted in the alternative (or).

20

As used in this application, the singular form “a,” “an,” and “the” include plural references unless the context clearly dictates otherwise. For example, the term “an agent” includes a plurality of agents, including mixtures thereof.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word “comprise”, and variations such as “comprises” and “comprising”, will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

Throughout this specification and the claims which follow, unless the context requires otherwise, the phrase “consisting essentially of”, and variations such as “consists essentially of” will be understood to indicate that the recited element(s) is/are essential i.e. necessary elements of the invention. The phrase allows for the presence of other non-recited elements which do not materially affect the characteristics of the invention but excludes additional

unspecified elements which would affect the basic and novel characteristics of the method defined.

Certain embodiments of the invention will now be described with reference to the following
5 examples which are intended for the purpose of illustration only and are not intended to limit the scope of the generality hereinbefore described.

Example 1: BioSyringe for sequential sample lysis and preparation

10 A kit for the assembly of an embodiment of the BioSyringe is shown in Figure 1, and the assembled BioSyringe is shown in Figure 5.

Fabrication and assembly of BioSyringe

15 The BioSyringe was fabricated using fused deposition modelling (FDM) 3D printing. Transparent polylactic acid (PLA) filament with a diameter of 1.75 mm was used for the barrel and nozzle, while thermoplastic polyurethane (TPU) filament of the same diameter was used for the plunger and sealing elements. All components were designed in SolidWorks, and STL files were generated for each part. These STL files were processed
20 using slicing software to produce G-code. Printing was carried out under controlled laboratory conditions at an ambient temperature of 22–26°C and relative humidity of 40–55%.

The BioSyringe components, including the barrel, plunger, and sealing elements, were first
25 modelled in SolidWorks, with dimensions selected to ensure correct assembly and fluid-tight sealing. STL files for each part were then generated and imported into slicing software, where G-code was created. The printing parameters included a layer thickness of 0.15–0.25 mm, an infill density of 100% for PLA and 50–70% for TPU, nozzle temperatures of 200–220 °C for PLA and 220–240 °C for TPU, and a bed temperature of 55–65°C. Printing speeds
30 were set at 40–60 mm/s for PLA and 20–30 mm/s for TPU. Support structures were automatically generated for overhangs greater than 45°.

Using the prepared G-code, the barrel and nozzle were printed with PLA, while the plunger and sealing fins were produced with TPU. Each component was built layer by layer, and

after printing, the parts were allowed to cool to room temperature before being removed from the build platform (Figure 1).

Following printing, support structures were mechanically removed, and the internal surfaces of the barrel were polished to reduce friction. The TPU plunger was checked for smooth movement and proper sealing, after which it was inserted into the barrel to complete assembly of the syringe.

The BioSyringe was filled with a series of specific compounds including 600 µl of lysis buffer (TNT or T6 buffer) in a first chamber from the distal end, 1 mg Cu-magnetic particles in second and third chambers from the distal end, and TE buffer (10 mM Tris-HCl, 1 mM EDTA, pH 8.0) for dilution of plasma in a fourth chamber from the distal end. The TNT buffer was prepared by combining 50 mM Tris-HCl (pH 7.6), 150 mM NaCl, and 1% Triton X-100. The T6 buffer was prepared by dissolving 472.75 g of guanidine thiocyanate in 400 mL of 50 mM Tris-HCl buffer (pH 7.6) with heating at 65°C. The solution volume was then adjusted to 750 mL with additional Tris-HCl buffer. Subsequently, 30 mL of 0.5 M EDTA (pH 8) and 30 mL of Triton X-100 were added. The final volume was brought to 1000 mL with distilled water.

Preparation of blood sample using the BioSyringe

Human blood was collected from a donor for the experiments. Blood samples of 4 mL each were taken into tubes containing EDTA and stored at 4°C. To evaluate the performance of the BioSyringe under conditions that more closely resemble clinically relevant bacterial loads, whole blood was spiked with 10^5 CFU of *Brucella* cells (Rev.1 vaccination, Razi Vaccine and Serum Research Institute of Iran) per 200 µL (equivalent to 5×10^5 CFU/mL). 0.2 mg of *Brucella melitensis* vaccine was added to 1 mL of the blood sample.

Figure 5 shows the series of steps to lyse leukocytes, erythrocytes, and bacterial cells in the sample to remove haemoglobin.

Initially, 200 µL of whole blood was introduced into the first chamber of the Biosyringe and mixed with lysis buffer (Figure 5, Stage I) by gently rolling the syringe between the palms for 10 min to ensure complete lysis. The resulting mixture was then transferred into the

second chamber by retracting the plunger (Figure 5, Stage II). To achieve homogeneous distribution, the syringe was gently rolled between the hands for 10–20 s, then repeated several times over a total of 3 minutes to facilitate optimal interaction between the sample and the magnetic particles.

5

A magnet was positioned alongside the syringe (Figure 5, Stage III) until the magnetic particles were fully attracted to the inner wall. The supernatant was then transferred into the third chamber, and the heme removal step was repeated using the magnetic particles. Subsequently, the magnet was again applied to the syringe (Figure 5, Stage IV) until the particles accumulated along the wall, after which the solution was transferred into the fourth chamber and mixed with TE buffer. The volume of TE buffer can be adjusted according to the desired target dilution.

10

Finally, the magnet was repositioned to the second chamber, where the magnetic particles remained, allowing the extracted plasma to be recovered from the syringe (Figure 5, Stage V).

15

Analysis of processed blood sample

PCR of BioSyringe output was performed using primers specific to exon 8 of the P53 gene (Table 1). The PCR reaction was carried out in a 20 µl total volume, which included 10 µl of Taq DNA Polymerase 2x Master Mix RED (Ampliqon, Denmark), 10 µl of forward primer, 10 µl of reverse primer, and 1 µl of BioSyringe output that was diluted in TE buffer at ratio of 1:8. A negative control was included by substituting the BioSyringe output with distilled water.

25

The cycling conditions for amplifying the target gene were as follows: an initial denaturation at 94°C for 5 minutes, followed by 45 cycles of 94°C for 30 seconds, 56°C for 30 seconds, and 72°C for 30 seconds. The reaction concluded with a final extension at 72°C for 5 minutes. The PCR products were electrophoresed on 1% agarose gels.

30

PCR of blood containing *Brucella miltensis* was conducted using primers specific to the *Brucella* BCSP31 gene (see Table 1). The PCR reaction was carried out in a 20 µl total volume, which included 10 µl of Taq DNA Polymerase 2x Master Mix RED (Ampliqon,

Denmark), 1 µl of forward primer, 1 µl of reverse primer, and 1 µl of BioSyringe output that was diluted in TE buffer at ratio of 1:8. A negative control was included by substituting the extracted DNA with 1 µl of distilled water.

- 5 The cycling conditions for amplifying the target gene were as follows: an initial denaturation at 94°C for 5 minutes, followed by 40 cycles of 94°C for 30 sec, 60°C for 30 sec, 72°C for 30 sec, and the last extension being 72°C for 5 min. The PCR products were electrophoresed on 1% agarose gels.

- 10 **Table 1:** Sequence of primers (5'–3') for the human p53 gene and *Brucella melitensis* BCSP31 gene

Human p53 gene	exon8-F	GGTAATCTACTGGGACGGAAC (SEQ ID NO: 1)
	exon8-R	GCTTCTTGTCCTGCTTGCTT (SEQ ID NO: 2)
Brucella BCSP31 gene	BCSP31-spF	TGGCTCGGTTGCCAATATCAA (SEQ ID NO: 3)
	BCSP31-spR	CGCGCTTGCCTTTCAGGTCTG (SEQ ID NO: 4)

- Figures 6 and 7 illustrate the performance of the BioSyringe following cell lysis with two different buffers. In Figure 6, whole blood was lysed using TNT buffer. The plasma obtained after subsequent centrifugation is shown as item (4), demonstrating the effective separation of plasma from the cellular components. In Figure 7, cell lysis was performed using T6 buffer. The sample obtained using buffer TNT exhibited a color more similar to that of the plasma sample (pale orange hue), while the sample treated with buffer T6 displayed a pale olive-green hue. The plasma obtained via centrifugation is also shown as item (4), indicating that both buffer systems are capable of producing clear plasma suitable for downstream nucleic acid detection and molecular analysis. These figures collectively demonstrate the functionality of the BioSyringe in preparing plasma from whole blood with effective heme clearance, regardless of the buffer used.

- 25 Plasma extracted using BioSyringe and the two lysis buffers were tested by looking at the PCR output of two genes: p53 and BCSP31. The resulting amplicons were verified through electrophoresis on 1% agarose gels.

- The observed bands at 158 base pairs correspond to exon 8 of the human p53 gene (Figure 8). Lanes 1 and 2 represent the plasma samples obtained with the TNT and T6 buffer,

respectively. This indicates that the output contains genomic DNA that is suitable for amplification.

In Figure 9, a band at 224 bp confirms the successful amplification of the *Brucella* BCSP31 gene via PCR. Lanes 1 and 2 represent the plasma samples obtained with the TNT and T6 buffer, respectively. A comparison of the amplified bands indicates that using a T6 lysis buffer significantly enhanced the amplification of gene fragments compared to a TNT lysis buffer under the same conditions. Since *Brucella* is a Gram-negative bacterium, the use of a more robust lysis buffer led to the release of a greater amount of bacterial DNA.

Example 2: CRISPR-Cas12a-based POCT using BioSyringe-prepared samples

Rapid and sensitive detection of nucleic acids is essential for timely diagnosis of infectious diseases and other genetic conditions. CRISPR-Cas-based diagnostics have emerged as a powerful tool due to their high specificity, programmability, and potential for rapid readout. However, efficient sample preparation remains a critical bottleneck, often requiring centrifugation, pipetting, or heat incubation, which limits POCT applications. The BioSyringe offers a streamlined solution by integrating sample lysis, nucleic acid extraction, and plasma separation into a single, user-friendly device. By minimising equipment requirement, the BioSyringe enables rapid preparation of samples suitable for CRISPR-Cas detection, even in decentralised or resource-limited settings.

In this study, samples were prepared with BioSyringe using TNT or T6 lysis buffers as described in Example 1. The prepared samples were analysed using RPA amplification and Cas12a enzymes.

Methods

In this experiment, the Bp26 gene was selected as the target sequence and then Oligo7 software was used to design RPA forward and reverse primers (Table 2).

Table 2. RPA Primer sequences

Gene	Name	Sequence (5'–3')
------	------	------------------

BP26	F	ATGACGGCCTCGCCCGATATGGCCATTCTC (SEQ ID NO: 5)
	R	TGTCATGGCTTCATTATTCGCGGTCATGGC (SEQ ID NO: 6)

RPA reaction assay was performed in a 50 µL final reaction volume, with 10 µL target BioSyringe output (RBS free plasma lysed samples), 10 µL plasmid DNA (109 copy/µL) as a positive control and 10µL nuclease free water as a negative control. The RPA compounds were added to the lyophilised plate at the bottom of the RPA vial in such a way that first 29.5 µL of primer-free rehydration buffer was added than 2.4µL (of 10 µM/µL) of each RPA forward -and-reverse-direction primers F and R (Table 2), 10 µL of target BioSyringe output, 2.5 mM of MgOAc and RNase-free water was replenished to 50 µL. The mixture was incubated in a conventional water bath at 39 °C for 60 min.

The complete DNA sequences of BP26 from *Brucella melitensis* (SEQ ID NO: 7) was used as a positive control. The sequence was obtained from NCBI and then synthesized and cloned into the pUC19 vector (Genscript, USA). The resulting pUC19 plasmid carrying Bp26 gene were transformed into DH5-alpha-competent E. coli cells. Plasmid extraction was performed following the protocol described in the GeneJET Plasmid Miniprep Kit (Thermo Fisher Scientific Inc, USA). A 5µl aliquot of the purified plasmids was subjected to electrophoresis on a 1% agarose gel. The concentrations of the plasmids were determined using the Qubit 4 Fluorometer (Thermo Fisher Scientific Inc, USA).

Collateral cleavage assays involving SrmCas12a enzymes were conducted in a final reaction volume of 20 µL. Initially, Cas12a proteins and crRNAs were combined to form ribonucleoprotein (RNP) complexes by mixing 400 nM purified SrmCas12a with 400 nM BP3 crRNA, 5'-AAAAUUUCUACUGUUGUAGAUCCUGGCGUAGCACCGAGAGA-3' (SEQ ID NO: 8) in 2 µL of 10X NEBuffer™ r2.1 with followed by incubation at room temperature for 15 min. Subsequently, 400 nM of the assembled RNP was mixed with 1 µl of the RPA amplified product and 400nM ssDNA reporter, /56-FAM/CCCCCCCC/3IABkFQ/ (SEQ ID NO: 9) from Integrated DNA Technologies, and the reactions were incubated for 1 h at 37°C in Step One ABI Real-time PCR (Applied Biosystems, CA, USA). Real-time fluorescence measurements were collected at 1 min intervals for a total of 60 min. To allow comparisons between different conditions, fluorescence for background conditions (no target) were subtracted from samples to generate

background subtracted fluorescence. The measurement of real-time background subtracted fluorescence output are shown in the graphs as means (n = 3).

bp26 (Accession # OQ378327)

5 ATGAACACTCGTGCTAGCAATTTTCTCGCAGCCTCATTTTCCACAATCATGCTC
GTCGGCGCTTTCAGCCTGCCCCGCTTTCGCACAGGAGAATCAGATGACGACGCA
GCCCCGCGCGCATCGCCGTCACCGGGGAAGGCATGATGACGGCCTCGCCCGATA
TGGCCATTCTCAATCTCTCGGTGCTACGCCAGGCAAAGACCGCGCGCGAAGCC
ATGACCGCGAATAATGAAGCCATGACAAAAGTGCTCGAGCCATGAAGAAGGC
10 CGGCATCGAAGATCGCGATCTCCAGACAGGCGGCATCAATATCCAGCCGATTT
ATGTCTATCCTGACGACAAGAACAACCTGAAAGAGCCTACCATCACCGGCTAT
TCTGTATCCACCAGTCTCACGGTTCGCGTGCGCGAACTGGCCAATGTTGGAAA
AATTTTGATGAATCCGTCACGCTCGGTGTTAATCAGGGCGGTGATTTGAACCT
GGTCAATGATAATCCCTCCGCCGTGATCAACGAGGCGCGCAAGCGCGCAGTGG
15 CCAATGCCATTGCCAAGGCGAAGACGCTTGCCGACGCTGCAGGCGTG GGGGCTT
GGCCGTGTGGTGGAAATCAGTGAAGTGAAGCCGCGCCCGCCCATGCCGATGCCAAT
TGCGCGCGGACAGTTCAGAACCATGCTAGCAGCCGCACCGGACAATTCCGTGC
CGATTGCCGCAGGCGAAAACAGCTATAACGTATCGGTCAATGTCGTTTTTGAA
ATCAAGTAA (SEQ ID NO: 7)

20

Results

The sensitivity of RPA amplification in combination with Cas12a enzyme was evaluated using samples prepared with the BioSyringe and two different lysis buffers (Figure 10).

25 Samples processed with TNT buffer consistently produced a very strong signal, with fluorescence reaching approximately 800,000 at minute 1, demonstrating both the efficiency of nucleic acid extraction and the rapid detection capability of the system. This result highlights the potential of the BioSyringe to accelerate CRISPR-Cas-based diagnostics while maintaining high sensitivity.

30

In addition to performance, the BioSyringe provides significant advantages for POCT. The device enables complete sample preparation without the need for centrifugation, pipetting, or heat incubation. By integrating blood collection, lysis, and nucleic acid extraction within a single device, the BioSyringe simplifies the workflow, reduces potential for user error, and

minimises cross-contamination. Its compact, user-friendly design allows operation by personnel with minimal training, making it suitable for decentralised, field, or resource-limited settings.

- 5 The BioSyringe successfully enabled the detection of *Brucella* DNA, demonstrating its capability to handle pathogen-containing samples. This indicates that the syringe-based platform is not limited to host DNA isolation but can also process blood samples contaminated with pathogens, providing a dual-function approach. Such versatility underscores its potential for use in clinical and field diagnostics, where rapid and reliable
- 10 detection of both host and pathogen nucleic acids is critical, particularly in POCT settings. Overall, the combination of rapid sample processing at POC level and minimal equipment requirements positions the BioSyringe as a practical and efficient tool for on-site CRISPR-Cas-based diagnostics. The strong signal observed within the first minute further underscores its potential for rapid and reliable detection in clinical and field application.

15

Example 3: ELISA-based POCT using BioSyringe-prepared samples

- Accurate measurement of thyroid-stimulating hormone (TSH) is critical for the diagnosis and management of thyroid disorders, which are among the most common endocrine
- 20 conditions worldwide. Traditional methods for preparing plasma samples for ELISA often require centrifugation and multiple handling steps, limiting their applicability in point-of-care settings. The BioSyringe provides a streamlined approach for blood sample preparation, enabling rapid and efficient lysis and plasma separation without the need for centrifugation, pipetting, or heat treatment. By simplifying sample handling and preserving analyte
- 25 integrity, the BioSyringe facilitates reliable ELISA measurements, offering a practical solution for decentralized and rapid diagnostics. This study evaluates the performance of TNT and T6 buffers in combination with the BioSyringe for TSH detection, highlighting its potential to improve sample preparation for point-of-care applications.

Methods

The TSH MonoKIT was used for all experiments, with known TSH standards at 0, 0.5, 2.5, 5, and 10 $\mu\text{IU/mL}$ to establish a standard curve. For each assay, 50 μL of calibrator, centrifuged plasma as a control, or sample processed using TNT or T6 buffer was added to

the wells of the ELISA plate. Subsequently, 100 μL of enzyme-conjugated solution was added to each well, and the plate was gently shaken for 30 seconds to ensure thorough mixing. The plate was then covered and incubated at room temperature for 60 minutes.

- 5 After incubation, the solutions were removed, and each well was washed with 300 μL of washing solution to remove unbound substances. Then, 100 μL of substrate solution, which produces a color reaction, was added to each well. The plate was incubated in the dark at room temperature for 15 minutes. After incubation, 50 μL of stop solution was added to terminate the enzymatic reaction, and the plate was gently shaken for 30 seconds.
- 10 Absorbance was measured at 450 nm using a microplate reader (Epoch, BioTek Instruments, Inc.) within 15 minutes of adding the stop solution. Each assay was performed in triplicate. A standard curve was generated by plotting TSH concentrations against their optical densities (ODs). Linear regression analysis was used to determine the coefficient of determination (R^2), indicating the linearity and precision of the assay. Based on the OD of
- 15 the samples, TSH concentrations were calculated using the derived linear equation.

Results

- The standard curves demonstrated high linearity, confirming the reliability of the method for quantifying TSH (Figure 11). The TSH concentration in plasma obtained by centrifugation
- 20 was $3.39 \pm 0.024 \mu\text{IU/mL}$. Samples processed with TNT buffer had a concentration of $3.18 \pm 0.031 \mu\text{IU/mL}$, closely matching the control, whereas samples processed with T6 buffer showed $5.87 \pm 0.045 \mu\text{IU/mL}$, deviating further from the control. These results indicate that the TNT buffer provides a more accurate and reliable sample for ELISA testing.

- 25 The BioSyringe, particularly when used with TNT buffer, enables reliable TSH quantification comparable to conventional centrifuged plasma, demonstrating its suitability for ELISA-based assays. By eliminating centrifugation, pipetting, and heat steps, the device simplifies sample preparation, reduces user error, and facilitates rapid testing in
- 30 decentralized or resource-limited settings.

Beyond TSH measurement, this approach highlights the broader potential of the BioSyringe for POC diagnostics, supporting on-site detection of diverse biomarkers in blood or other biological fluids. The combination of ease of use, reproducibility, and accurate analyte

recovery positions the BioSyringe as a versatile tool for clinical, field, and emergency testing applications, advancing accessible and timely diagnostics across multiple healthcare contexts.

5 **Example 4: DnaSyringe for preparation of blood sample**

Methods

To evaluate the DNA extraction performance of the DnaSyringe, magnetic particles and the
10 corresponding lysis, wash, and elution buffers from the MagBic gDNA Extraction Kit (Ronash Technology Pars, Cat. No. 100100) were utilised.

DnaSyringe was preloaded with reagents arranged sequentially from top to bottom: 600 μ L of lysis buffer (GDLB) in first mixing chamber, 100 μ L of GDM II suspension containing
15 magnetic beads in second mixing chamber, 500 μ L of wash buffer (GDW) in first holding chamber, 500 μ L of wash buffer (GDWI) in second holding chamber, an additional 500 μ L of GDWI in third holding chamber, and 100 μ L of elution buffer (GDE) in fourth holding chamber (Figure 20).

20 For sample processing, 200 μ L of blood spiked with Brucella bacteria was introduced into the first mixing chamber (Figure 20, stage I) and mixed with lysis buffer. The DnaSyringe was gently rolled between the hands to ensure complete lysis of blood and bacterial cells, followed by incubation for 10 minutes. The lysate was then transferred into the second mixing chamber containing magnetic particles (Figure 20, stage II) and gently rolled for 10–
25 20 seconds to ensure homogeneous distribution. This rolling was repeated every 2 minutes for a total of 12 minutes to promote efficient DNA binding to the magnetic beads. The out plunger rod was then rotated 90 degrees (Figure 20, stage IV).

A ring magnet was positioned adjacent to the second mixing chamber to capture the
30 magnetic beads (Figure 20, stage III) until the beads were immobilised to the syringe wall. The supernatant was subsequently discarded (Figure 20, stage VI).

For bead washing, 500 μ L of GDW buffer was pushed into the compartment containing the beads (Figure 20, stage IV) and the DnaSyringe was rolled 15–20 times to remove residual

contaminants. The wash solution was expelled. This was followed by two sequential washes using 500 μ L of GDWI buffer each (Figure 20, stages V, VI), with 15–20 gentle rolls per wash to eliminate nonspecific interactions. If the wash buffer contained alcohol, a 3–5 minute pause was optionally applied to allow evaporation and optimise the washing process.

5 Subsequently, the plunger was rotated 90 degrees to restore the distal stoppers to their original positions. The plunger was then advanced to transfer 100 μ L of GDE elution buffer from the fourth holding chamber into the second mixing chamber (Figure 20, stage VII), followed by a 10-minute incubation to elute DNA from the beads. The eluted genomic DNA

10 was then recovered from the DnaSyringe and stored at -20°C until downstream PCR amplification.

Results

The output of the DnaSyringe is shown in Figure 21. A clear and noticeable color difference

15 is observed between the original whole blood sample and the processed DNA-containing solution. The blood, which initially appears red and opaque due to the presence of cells and hemoglobin, is transformed into a pale, translucent solution after processing with the syringe. This transparency indicates effective removal of cellular debris and hemoglobin,

20 demonstrating that the DnaSyringe can yield a clarified nucleic acid solution suitable for downstream applications, such as PCR or other molecular assays, without requiring additional centrifugation or filtration steps.

PCR analysis was performed as described in Example 4. To assess the quality and amplifiability of the DNA extracted using the DnaSyringe, samples were subjected to 1%

25 agarose gel electrophoresis. As shown in Figure 22, a distinct band at 158 base pairs was observed in lane 1, corresponding to human exon 8 of the p53 gene. This result confirms that human genomic DNA isolated via the DnaSyringe was intact and suitable for PCR amplification, demonstrating the efficiency of the DnaSyringe-based extraction method for recovering high-quality DNA from whole blood samples.

30 Furthermore, Figure 23 shows PCR amplification of the Brucella BCSP31 gene. Lane 1 displays a clear band at 224 base pairs, indicating successful amplification of the bacterial genomic DNA. Lane 2 represents the negative control (NC), which shows no detectable band, confirming the specificity of the amplification. These findings collectively

demonstrate that the syringe-extracted genomic DNA contains both human and bacterial DNA that can be reliably amplified without nonspecific products or degradation, highlighting the versatility and effectiveness of the syringe system for simultaneous detection of host and pathogen DNA.

5

The successful detection of Brucella BCSP31 in addition to human p53 DNA highlights that the DnaSyringe can simultaneously process blood DNA and pathogen-contaminated samples. The clear and specific bands, along with the absence of bands in negative controls, confirm the reliability and specificity of the method. These findings emphasize the potential
10 of the DnaSyringe for instrument-free sample preparation, making it particularly well-suited for POCT or field-based diagnostics where minimal equipment and user intervention are available.

The reference in this specification to any prior publication (or information derived from it),
15 or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

20 Those skilled in the art will appreciate that the invention described herein is susceptible to variations and modifications other than those specifically described. It is to be understood that the invention includes all such variations and modifications, which fall within the spirit and scope. The invention also includes all of the steps, features, compositions and compounds referred to or indicated in this specification, individually or collectively, and any
25 and all combinations of any two or more of said steps or features.

Unless otherwise defined, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs.

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It will be appreciated that many further modifications and permutations of various aspects of the described embodiments are possible. Accordingly, the described aspects are intended to embrace all such alterations, modifications, and variations that fall within the spirit and scope of the appended claims.

CLAIMS

1. A device for processing a liquid sample, comprising:
a syringe barrel having a body, the body comprising a proximal end, a distal end for receiving a liquid sample, and a plurality of holding chambers formed in the body for holding a plurality of sample processing materials; and
at least one stopper slidably disposed within the body of the syringe barrel and configured to fluidically seal the plurality of holding chambers;
wherein the at least one stopper is operable to sequentially unseal the plurality of holding chambers to bring the liquid sample received at the distal end of the syringe barrel into contact with the plurality of sample processing materials in the plurality of holding chambers.
2. The device of claim 1, wherein the plurality of holding chambers are arranged in series.
3. The device of claim 1 or 2, wherein one or more of the holding chambers each independently comprises a wall portion which extends outwardly relative to the barrel body.
4. The device of claim 2 or 3, wherein the at least one stopper forms a fluid-tight seal with an interior wall of the barrel body to fluidically seal the plurality of holding chambers.
5. The device of any one of claims 1 to 4, wherein the plurality of holding chambers each independently has an opening.
6. The device of any one of claims 1 to 5, wherein the at least one stopper comprises two or more stoppers that are configured to move in tandem along the barrel body.
7. The device of any one of claims 1 to 5, wherein the device comprises one stopper forming a fluid-tight seal with an interior wall of the barrel body to fluidically seal the plurality of holding chambers.

8. The device of claim 7, wherein moving the stopper towards the proximal end of the barrel sequentially unseals the plurality of holding chambers and contacts the liquid sample with sample processing material in the plurality of holding chambers.
9. The device of claim 7 or 8, wherein the device comprises a plunger rod coupled to the stopper for moving the stopper.
10. The device of any one of claims 1 to 6, wherein at least one of the plurality of holding chambers is a mixing chamber.
11. The device of claim 10, wherein the mixing chamber is sized to break a fluid seal provided by the stopper when the stopper is positioned in the mixing chamber.
12. The device of claim 11, wherein the mixing chamber has an internal diameter that is larger than a diameter of the stopper.
13. The device of any one of claims 10 to 12, wherein the at least one stopper comprises two or more stoppers.
14. The device of claim 13, wherein the device comprises a plunger assembly for controlling relative positioning of the two or more stoppers within the syringe barrel, the plunger assembly comprising an inner plunger rod and an outer plunger rod, the inner plunger rod telescopically receivable within the outer plunger rod.
15. The device of claim 14, wherein the inner plunger rod is fixedly coupled to a distal-most stopper of the two or more stoppers.
16. The device of claim 14 or 15, wherein the outer plunger rod is fixedly coupled to a proximal-most stopper of the two or more stoppers.
17. The device of claim 15 or 16, wherein the device comprises one or more intermediate stoppers disposed between the distal-most and proximal-most stoppers and slidably mounted on the inner plunger rod.
18. The device of any one of claims 14 to 17, wherein the inner and outer plunger rods are coupled such that axial movement of the outer plunger rod causes corresponding axial movement of the inner plunger rod in the same direction.

19. The device of any one of claims 14 to 18, wherein the inner and outer plunger rods are rotatably coupled such that rotation of the outer plunger rod about its longitudinal axis causes corresponding rotation of the inner plunger rod in the same rotational direction.
20. The device of any one of 10 to 19, wherein the device comprises a releasable locking mechanism for securing a stopper in place within the syringe barrel.
21. The device of claim 20, wherein the releasable locking mechanism comprises rotational coupling between the outer plunger rod and the stopper, the stopper being rotatable between unlocked and locked configurations upon rotation of the outer plunger rod about a longitudinal axis, wherein the stopper has a shape that jams against an interior wall of the barrel body in the locked configuration to prevent movement.
22. The device of any one of claims 1 to 21, wherein the device comprises two holding chambers.
23. The device of any one of claims 1 to 21, wherein the device comprises at least three holding chambers.
24. The device of any one of claims 1 to 21, wherein the device comprises at least four holding chambers.
25. The device of any one of claims 1 to 24, further comprising a magnet attached to the body of the syringe barrel.
26. The device of claim 25, wherein the magnet is configured to move along a length of the barrel body.
27. The device of claim 25 or 26, wherein the magnet is a ring or a C-ring magnet.
28. The device of any one of claims 1 to 27, further comprising a sample acquisition component attached to the distal end of the barrel, the sample acquisition component configured to draw a liquid sample.
29. The device of any one of claims 1 to 28, wherein one or more of the syringe barrel, stopper and/or plunger rod is made of a thermoplastic material.

30. The device of any one of claims 1 to 29, wherein the syringe barrel comprises calibration marks indicating liquid volume contained within the barrel.
31. The device of any one of claims 1 to 30, wherein the syringe barrel is made of a transparent or translucent material.
32. The device of any one of claims 1 to 31, further comprising a sample processing material in at least one of the holding chambers.
33. The device of claim 32, wherein the sample processing material is selected from magnetic particles (MPs) for binding a component in the liquid sample, a cell lysis composition, an aqueous solvent, an elution reagent for releasing a component bound to the MPs, and a detection reagent for detecting a component bound to the MPs.
34. The device of claim 33, wherein the cell lysis composition is a liquid or lyophilised composition.
35. The device of claim 33 or 34, wherein the cell lysis composition comprises one or more of a surfactant, a chaotrope, a cell wall digesting enzyme, a protease, a metal chelating agent, a disulphide reducing agent, and/or an osmotic agent.
36. The device of any one of claims 33 to 35, wherein the MPs are capable of binding a component selected from a nucleic acid, a polypeptide, an antigen, an antibody, a carbohydrate, a lipid, a metabolite, a pigment, a drug, an exosome, and a microvesicle.
37. The device of claim 36, wherein the MPs are capable of binding a component selected from haemoglobin, haematin, and an immunoglobulin.
38. The device of any one of claims 33 to 37, wherein at least one of the holding chambers contains magnetic particles (MPs).

39. The device of any one of claims 1 to 38, wherein the plurality of holding chambers comprises two holding chambers arranged in series from distal to proximal end of the barrel and containing, respectively, (i) a cell lysis composition; and (ii) MPs.
40. The device of any one of claims 1 to 39, wherein the plurality of holding chambers comprises two holding chambers arranged in series from distal to proximal end of the barrel and containing, respectively, (i) MPs; and (ii) an aqueous solvent.
41. The device of any one of claims 1 to 40, wherein the plurality of holding chambers comprises two holding chambers arranged in series from distal to proximal end of the barrel and containing, respectively, (i) MPs; and (ii) an elution reagent.
42. The device of any one of claims 1 to 41, wherein the plurality of holding chambers comprises two holding chambers arranged in series from distal to proximal end of the barrel and containing, respectively, (i) MPs; (ii) a detection reagent.
43. A method for processing a liquid sample using a device of any one of claims 1 to 42, comprising the steps of:
 - a) receiving a volume of liquid sample at the distal end of the syringe barrel of the device; and
 - b) moving the at least one stopper to sequentially unseal the plurality of holding chambers in the device to bring the liquid sample into contact with a plurality of sample processing materials in the plurality of holding chambers.
44. The method of claim 43, wherein the plurality of sample processing materials is selected from magnetic particles (MPs) for binding a component in the liquid sample, a cell lysis composition, an aqueous solvent, an elution reagent for releasing a component bound to the MPs, and a detection reagent for detecting a component bound to the MPs.
45. The method of claim 43 or 44, further comprising a step of attaching a magnet to an exterior of the syringe barrel.

46. The method of any one of claims 43 to 45, further comprising a step of discharging processed sample at the distal end of the syringe barrel.
47. A kit for a device of any one of claims 1 to 42, comprising:
a syringe barrel having a body, the body comprising a proximal end, a distal end for receiving a liquid sample, and a plurality of holding chambers formed in the body for holding a plurality of sample processing materials; and
at least one stopper receivable within the body of the syringe barrel and configured to fluidically seal the plurality of holding chambers.
48. The kit of claim 47, further comprising a plunger rod attachable to the at least one stopper for moving the stopper.
49. The kit of claim 47 or 48, further comprising a sample acquisition component attachable to the distal end of the barrel, the sample acquisition component configured to draw a liquid sample.
50. The kit of any one of claims 47 to 49, further comprising a magnet attachable to the body of the syringe barrel.
51. The kit of any one of claims 47 to 50, further comprising a sample processing material for loading into a holding chamber of the device, wherein the sample processing material is selected from magnetic particles (MPs) for binding a component in the liquid sample, a cell lysis composition, an aqueous solvent, an elution reagent for releasing a component bound to the MPs, and a detection reagent for detecting a component bound to the MPs.
52. A device for processing a liquid sample, comprising:
a syringe barrel having a body, the body comprising a proximal end, a distal end for receiving a liquid sample, and a plurality of holding chambers integrally formed in the body for holding a plurality of sample processing materials; and
at least one stopper slidably disposed within the body of the syringe barrel and configured to fluidically seal the plurality of holding chambers;

wherein moving the at least one stopper towards the proximal end of the device sequentially unseals the plurality of holding chambers to bring the liquid sample received at the distal end of the syringe barrel into contact with the plurality of sample processing materials in the plurality of holding chambers.

53. A device for processing a liquid sample, comprising:

a syringe barrel having a body, the body comprising a proximal end, a distal end for receiving a liquid sample, and a plurality of holding chambers formed in the body for holding a plurality of sample processing materials;

a plurality of stoppers slidably disposed within the body of the syringe barrel and forming a fluid-tight seal within the body to isolate the plurality of holding chambers, the plurality of stoppers comprising a distal-most stopper and a proximal-most stopper; and

a plunger assembly for controlling relative positioning of the plurality of stoppers within the syringe barrel, the plunger assembly comprising an inner plunger rod fixedly coupled to the distal-most stopper, and an outer plunger rod fixedly coupled to the proximal-most stopper, the inner plunger rod telescopically receivable within the outer plunger rod;

wherein the plunger assembly is operable to move the plurality of stoppers to sequentially unseal the plurality of holding chambers such that a liquid sample received at the distal end of the syringe barrel is brought into contact with the plurality of sample processing materials in the plurality of holding chambers.