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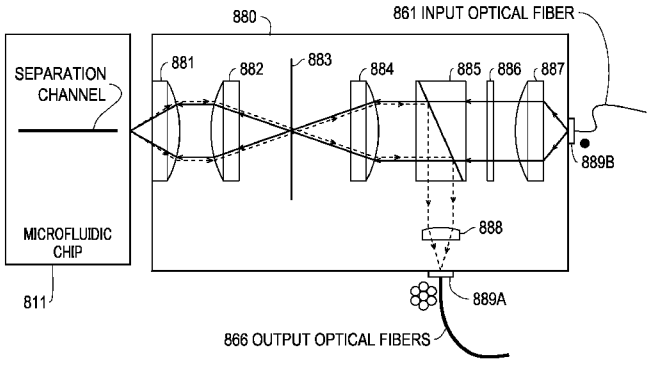

FIG. 8

(57) Abstract: Aspects of the disclosure provide a DNA analyzer. The DNA analyzer includes an interface for coupling a microfluidic chip to the DNA analyzer. The microfluidic chip includes a first separation channel for electrophoretic separation of DNA fragments in a first sample. Further, the DNA analyzer includes a first optical device. The first optical device includes an illuminating path and a detecting path. The illuminating path directs a first input light beam received from a light source to a first separation channel of the microfluidic chip. The first input light beam causes fluorescent labels attached on DNA fragments in the first separation channel to emit a first fluorescence light. The detecting path collects and directs the first fluorescent light to a first plurality of optical fibers. Further, the DNA analyzer includes a spectrometer configured to receive the first fluorescent light from the plurality of optical fibers and detect fluorescent components in the first fluorescent light. Further, in an embodiment, the illuminating path is configured to receive the first input light beam from the light source via a first input optical fiber.

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MICRO FLUIDIC OPTIC DESIGN

INCORPORATION BY REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No.6 1/393,574, "Micro Fiuidic Optic Design" filed on October 15, 2010, which is incorporated herein by reference in its entirety.

BACKGROUND

[0002] The background description provided herein is for the purpose of generally presenting the context of the disclosure. Work of the presently named inventors, to the extent the work is described in this background section, as well as aspects of the description that may not otherwise qualify as prior art at the time of filing, are neither expressly nor impliedly admitted as prior art against the present disclosure.

[0003] DNA is recognized as the "ultimate biometric" for human identification. DNA analysis can provide evidence for solving forensic and medical cases, such as in areas of criminal justice, identifications of human remains, paternity testing, pathogen detection, disease detection, and the like.

SUMMARY

[0004] Aspects of the disclosure provide a DNA analyzer. The DNA analyzer includes an interface for coupling a microfluidic chip to the DNA analyzer. The microfluidic chip includes a first separation channel for eiectrophoretic separation of DNA fragments in a first sample. Further, the DNA analyzer includes a first optical device. The first optical device includes an illuminating path and a detecting path. The illuminating path directs a first input light beam received from a light source to a first separation channel of the microfluidic chip. The first input light beam causes fluorescent labels attached on DNA fragments in the first separation channel to emit a first fluorescence light. The detecting path collects and directs the first fluorescent light to a first plurality of optical fibers. Further, the DNA analyzer includes a spectrometer configured to receive the first fluorescent light from the plurality of optical fibers and detect fluorescent components in the first fluorescent light. Further, in an embodiment, the illuminating path is configured to receive the first input light beam from the light source via a first input optical fiber.

[0005] In an embodiment, the first optical device includes a first set of optic elements and a first motion control module configured to adjust the first set of optic elements to align the first set of optic elements to the first separation channel. In an example, the first motion control module is configured to adjust the first set of optic elements based on detection output of the spectrometer. In another example, the first optical device includes an objective lens configured to focus the first input light beam to the first separation channel based on detection output of the spectrometer.

[0006] According to an aspect of the disclosure, the first optical device includes an optical fiber connector configured to connect the first input optical fiber and the first plurality of output fibers with the first optical device. For example, the optical fiber connector is configured to connect the first input optical fiber at a center position, and connect the first plurality of output fibers around the center position.

[0007] According to another aspect of the disclosure, the first optical device includes an input optical fiber connector configured to connect the first input optical fiber with the first optical device, and an output optical fiber connector configured to connect the first plurality of output fibers with the first optical device. In an example, the first optical device includes a dichroic splitter configured split the first input light beam and the first output light beam to pass at least one different optic element. Further, the first optical device includes a filter configured to filter out fluorescence in the first input light beam.

[0008] Further, according to an aspect of the disclosure, the spectrometer includes an optical fiber connector configured to connect the first plurality of output optical fibers to the spectrometer. Then, the spectrometer includes a dispersive element, such as a grating module, configured to spatially separate the fluorescent components, and an array of photo detection units configured to detect the spatially separated fluorescent components. In an example, the array of photo detection units is within a charge coupled device (CCD).

[0009] In an embodiment, the microfluidic chip includes a second separation channel for electrophoretic separation of DNA fragments in a second sample. The DNA analyzer includes a second optical device. The second optical device also includes an illuminating path and detecting path. The illuminating path directs a second input light beam received from the light source to the second separation channel. The second input light beam causes fluorescent labels attached on DNA fragments in the second separation channel to emit a second fluorescence light. The detecting path collects and directs the second fluorescent light to a second plurality of optical fibers. Further, the spectrometer includes an optical fiber

connector configured to connect the first plurality of output optical fibers and the second plurality of output optical fibers with the spectrometer. In an example, the optical fiber connector is configured to stack the first plurality of output optical fibers and the second plurality of output optical fibers in a line.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010) Various embodiments of this disclosure that are proposed as examples will be described in detail with reference to the following figures, wherein like numerals reference like elements, and wherein:

[0011] Fig 1 shows a block diagram of an exemplary DNA analyzer according to an embodiment of the disclosure;

[0012] Figs. 2A-2C show a swab example and a sample cartridge example according to an embodiment of the disclosure;

[0013] Fig. 3 shows a schematic diagram of a microfluidic chip example according to an embodiment of the disclosure;

[0014] Fig. 4 shows an implementation of a DNA analyzer according to an embodiment of the disclosure;

[0015] Fig. 5 shows a flow chart outlining a process example for using a DNA analyzer to perform DNA analysis according to an embodiment of the disclosure;

[0016] Fig. 6 shows a flow chart outlining a process example for a DNA analyzer to perform DNA analysis according to an embodiment of the disclosure;

[0017] Fig. 7 shows a block diagram of a detection module 750 according to an embodiment of the disclosure;

[0018] Fig. 8 shows a block diagram of a set of optic components example 880 according to an embodiment of the disclosure;

[0019] Fig. 9 shows a block diagram of a set of optic components example 980 according to an embodiment of the disclosure;

[0020] Fig. 10 shows a block diagram of a detector example 1090 according to an embodiment of the disclosure;

[0021] Fig. 11 shows a schematic diagram of a multiple-sample microfluidic chip 1100 example according to an embodiment of the disclosure; and

[0022] Fig. 12 shows a block diagram of a detection module 1250 according to an embodiment of the disclosure.

DETAILED DESCRIPTION OF EMBODIMENTS

[0023] Fig. 1 shows a block diagram of an exemplary DNA analyzer 100 according to an embodiment of the disclosure. The DNA analyzer 100 includes a microfluidic chip module 110, a thermal module 120, a pressure module 130, a high voltage module 140, a detection module 150, a power module 160, a computing module 170, and a controller module 180. Additionally, the DNA analyzer 100 can include a magnetic module 190. These elements can be coupled together as shown in Fig. **1.**

[0024] The DNA analyzer 100 is capable of processing sample-to-answer DNA analysis on an integrated single-chip. Thus, using the DNA analyzer 100 to perform DNA analysis does not need substantial experience and knowledge of DNA processes. In an example, the appropriate procedures to use the DNA analyzer 100 to perform DNA analysis can be learned quickly. Additionally, the integrated single-chip DNA analysis requires a reduced volume of reagents, for example, in the order of a micro-liter. Further, the reduced volume of reagents can reduce thermal inputs for inducing thermal cycles in the DNA analysis, and thus reduce the time for DNA analysis.

[0025] The microfluidic chip module 110 includes a microfluidic chip 111. The microfluidic chip 111 can be suitably coupled with other elements of the DNA analyzer 100 to perform integrated single-chip DNA analysis. In an example, the microfluidic chip module 110 is implemented as a disposable cartridge, and a cartridge interface that can couple the disposable cartridge with other components of the DNA analyzer 100 that are not included as part of the disposable cartridge. The disposable cartridge includes the microfluidic chip 111 and a micro-to-macro interface. The micro-to-macro interface couples the microfluidic chip 111 to macro structures on the disposable cartridge. The disposable cartridge can be separately stored, and can be installed in the DNA analyzer 100 at a time of DNA analysis. After the DNA analysis, the disposable cartridge can be suitably thrown away.

[0026] The microfluidic chip 111 includes various domains that can be suitably configured to enable the integrated single-chip DNA analysis. In an embodiment, DNA analysis generally includes a step of PCR amplification, and a step of electrophoretic separation. The microfluidic chip 111 can include a first domain 111a for the PCR amplification and a second domain 111b for the electrophoretic separation. In addition, the microfluidic chip 111 can include other domains that are suitably integrated with the first domain 111a and the second domain 111b. In an example, the microfluidic chip 111 includes a purification domain fluidically coupled with the first domain 111a. The purification domain

can be used to extract and purify a template DNA. It is noted that any suitable techniques, such as solid-phase extraction, liquid-phase extraction, and the like, can be used to purify the template DNA in the purification domain.

[0027] In another example, the microfluidic chip 111 includes a post-PCR clean-up/dilution domain that is fluidically coupled with the first domain 111a and the second domain 111b. The post-PCR clean-up/dilution domain can be used for any suitable process after the PCR amplification and before the electrophoretic separation.

[0028] The first domain 111a includes a reservoir configured for PCR amplification. In an embodiment, the first domain 111a includes multiple separated reservoirs to enable simultaneous PCR amplification for multiple DNA samples. The temperature at the first domain 111a can be controlled by the thermal module 120 to enable the PCR amplification. According to an embodiment of the disclosure, the PCR amplification on the microfluidic chip 111 requires only a small volume of reagents, and the PCR amplification can achieve rapid thermal cycling. In an example, the volume of reagents used for the PCR amplification can be in the order of sub-micro-liter, and the time required for the PCR amplification can be under 20 minutes.

[0029] The second domain 111b can include a plurality of micro channels. The plurality of micro channels can be configured for electrophoretic separation. More specifically, each micro channel can be filled with, for example, polymer sieving matrix. Further, an electric field can be induced in the micro channel. Thus, when DNA fragments are injected in the micro channel, the DNA fragments can migrate by force of the electric field at different speeds based on the sizes of the DNA fragments.

[0030] Additionally, the second domain 111b can be configured to facilitate DNA fragments detection in the DNA analysis. In an example, DNA fragments are tagged with fluorescent labels during PCR, before being injected in the micro channels. The fluorescent labels can emit fluorescence of pre-known wavelength when excited by a laser beam. The second domain 111b includes a detection window configured for detection. The laser beam can be directed to pass through the detection window to excite the fluorescent labels in the micro channels. The emitted fluorescence can pass through the detection window to be collected and detected.

[0031] The microfluidic chip 111 can include additional structures to facilitate the integrated single-chip DNA analysis. For example, the microfluidic chip 111 can include microfluidic channels that can direct DNA fragments from the first domain 111a to the

second domain 111b. Through the microfluidic channels, the DNA fragments flow in a solution from the first domain 111a to the second domain 111b. In addition, the microfluidic chip 111 can include inlets for receiving reagents and the template DNA. The microfluidic chip 111 can also include additional reservoirs for additional processing steps, such as dilution, cleanup, and the like.

[0032] The microfluidic chip 111 can be constructed from any suitable material. In an example, the microfluidic chip 111 is constructed from glass. In another example, the microfluidic chip 111 is constructed from plastic or polymeric material.

[0033] In addition to the microfluidic chip 111, the disposable cartridge can include a sample acceptor and a reagent carrier. In an example, the sample acceptor accepts a swab used for taking DNA sample, such as from saliva, bloodstains, cigarettes, and the like. Further, the sample acceptor extracts a template DNA from the swab. The sample acceptor can use any suitable mechanism, such as solid-phase extraction, liquid-phase extraction, and the like to obtain and/or purify the template DNA from the swab. In an embodiment, the sample acceptor uses a solid-phase DNA extraction method, such as silica beads based DNA extraction.

[0034] In another embodiment, the sample acceptor uses a liquid-phase DNA extraction method. The liquid-phase DNA extraction method can simplify the purification and extraction process, and reduce a total cost of the DNA analyzer 100. In an example, the sample acceptor uses an enzymatic DNA-isolation method to extract and purify the template DNA . The enzymatic DNA-isolation method can achieve liquid phase purification without a need of centrifugation. In addition, the sample acceptor can be suitably designed to maintain sample integrity.

[0035] More specifically, the sample acceptor can include a plurality of separated wells for taking swabs, for example. Thus, the DNA analysis can simultaneously process multiple DNA samples. Each well includes a liquid phase mixture that is sealed by a membrane at a bottom portion of the well. The liquid phase mixture can conduct enzymatic digestion of all proteins and other cellular interferences, with the exception of DNA. For example, the liquid phase mixture can include thermostable proteinases from thermophilic Bacillus species, such as disclosed in U.S. Patent Application Publication No. 2004/0197788, which is incorporated herein by reference in its entirety. Thus, the liquid phase mixture can perform DNA extraction and purification when a swab is immersed in the liquid phase mixture. The liquid phase method can achieve comparable DNA quality to other

methodologies in both DNA concentration and purity. In an example, a final DNA concentration by the liquid phase method is in a range of 0.5-2 ng/pL.

[0036] Further, using the liquid phase extraction method instead of the silica solid phase method can reduce the overall hydraulic pressure requirement to induce solution flow through the microfluidic chip 111. In an embodiment, the liquid phase extraction can enable a valveless design for the microfluidic chip 111. Thus, the liquid phase extraction can simplify the DNA analyzer 100 and simplify the manufacturing and testing steps in association with the solid-phase extraction.

[0037] Before taking DNA sample, a swab can be sealed in a hard case to avoid contamination. The swab can be attached to a seal cap that can seal the hard case. The swab can be identified by various mechanisms. In an example, a barcode label is attached to the hard case to identify the swab. In another example, the seal cap has a radio frequency identification (RFID) tag implanted. The RFID tag can identify the swab attached to the seal cap throughout the process. After the swab is used to take DNA sample, the swab can be placed in one of the plurality of separated wells, and can be sealed in the well, for example, by the seal cap attached to the sampled swab. In an embodiment, the seal cap is a stepped seal cap that can seal the well in a first step, and a second step. When the seal cap seals the well in the first step, the swab does not puncture the membrane. When the seal cap seals the well in the second step, the swab punctures the membrane and is immersed in the liquid phase mixture. The liquid phase mixture can then extract template DNA from the swab.

[0038] The reagent carrier can house a plurality of reagents for DNA analysis, such as reagents for polymerase chain reaction (PCR) amplification, solutions for electrophoretic separation, and the like. In an STR typing example, the reagent carrier houses reagents for multiplexed STR amplification. The reagents can perform multiplexed STR amplification and can use multiple fluorescent dyes to label STR alleles. The reagents can be commercially available reagent kits or can be tailored to the micro-scale chip environment to further facilitate the integrated single-chip DNA analysis.

[0039] In addition, the reagent carrier houses solutions that are suitable for electrophoretic separation in the micro-scale chip environment. For example, the reagent carrier houses a coating solution, such as poly-N-hydroxyethylacrylamide, and the like. The coating solution can be used to coat micro channel walls prior to the separation to reduce electro osmotic flow and enable single base pair resolution of amplified DNA fragments. In another example, the reagent carrier houses a dilution solution, such as water and/or

Formamide, and the like. The dilution solution can be used to reduce the ionic strength of the sample in order to promote better electro-kinetic injection. In another example, the reagent carrier houses an internal lane standard (ILS). The ILS can be used for accurate size measurements. The reagent carrier also houses a polymer solution for electrophoretic separation in the micro-scale chip environment. The polymer solution is used as gels to provide a physical separation of DNA fragments according to chain length. For example, the polymer solution can include a sieving or non-sieving matrix, such as that disclosed in U.S. Patents No. 7,531,073, No. 7,399,396, No. 7,371,533, No. 7,026,414, No. 6,81 1,977 and No. 6,455,682, which are incorporated herein by reference in their entirety. In an example, a polymer-sieving matrix can be used to yield a single-base resolution in a total separation length of 8 cm and in less than 400 seconds.

[0040] The thermal module 120 receives control signals from the controller module 180, and induces suitable temperatures for DNA analysis, such as a temperature for DNA extraction, thermal cycles for the PGR amplification, a temperature for electrophoretic separation, and the like. In an example, the thermal module 120 includes a resistance heater to control a temperature in the wells of the sample acceptor for the DNA extraction and purification. In another example, the thermal module 120 includes another resistance heater to control a temperature at the second domain 111b.

[0041] In another example, the thermal module 120 includes a heating unit, a cooling unit and a sensing unit to induce the thermal cycles for the PCR amplification at the first domain 111a. The heating unit can direct heat to the first domain 11ia, the cooling unit can disperse heat from the first domain 111a, and the sensing unit can measure a temperature at the first domain 11ia. The controller module 180 can control the heating unit and the cooling unit based on the temperature measured by the sensing unit.

[0042] In an embodiment, the thermal module 120 performs non-contact thermal controls. For example, the thermal module 120 includes an infrared light source as the heating unit, a cooling fan as the cooling unit, and an infrared pyrometer as the temperature sensing unit. The infrared light source, such as a halogen light bulb, can excite, for example, the 1.7 μm vibrational band of liquid. Thus, the infrared light source can heat a small volume of solution within a reservoir in the first domain 111a independent of the reservoir to achieve rapid heating and cooling. The infrared pyrometer measures blackbody radiation from an outside of the reservoir. In an example, the reservoir is designed to have a thinner side for the infrared pyrometer measurements. The infrared pyrometer measurements at the thinner side

can more accurately reflect the temperature of solution within the reservoir. Thus, the DNA analyzer 100 can achieve a precise temperature control along with rapid thermal cycles. In an example, the DNA analyzer 100 can achieve a temperature fluctuation of less than ±0.1°C, and a time of the thermal cycles for the PCR amplification can be less than 20 minutes.

[0043] The pressure module 130 receives control signals from the controller module 180, and applies suitable pressures to the microfluidic chip module 110 to enable fluid movement. In an embodiment, the pressure module 130 receives a sensing signal that is indicative of a pressure applied to the microfluidic chip module 110, and suitably adjusts its operation to maintain the suitable pressure to the microfluidic chip module 110.

[0044] The pressure module 130 can include a plurality of pumps. The plurality of pumps control the injection of the various reagents and the template DNA solutions into the microfluidic chip 111. According to an embodiment of the disclosure, the plurality of pumps can be individually controlled to achieve any possible timing sequence.

[0045] The pressure module 130 may include other pressure components to suit the integrated single-chip integrated DNA analysis. In an embodiment, the microfluidic chip 111 has membrane valves. The pressure module 130 can include a hydrodynamic pressure/vacuum system to suitably control the closing and opening of the membrane valves to enable fluid movement through the microfluidic chip 111.

[0046] In another embodiment, the microfluidic chip 111 is valveless. For example, the DNA analyzer 100 uses a liquid phase DNA extraction instead of a silica solid phase DNA extraction. The liquid phase DNA extraction can be integrated with following DNA processes on a valveless microfluidic chip. Thus, the hydrodynamic pressure/vacuum system is not needed. The pressure module 130 can be simplified to reduce the footprint, the weight, the cost, and the complexity of the DNA analyzer 100.

[0047] The power module 160 receives a main power, and generates various operation powers for various components of the DNA analyzer 100. In an example, the DNA analyzer 100 is implemented using a modular design. Each module of the DNA analyzer 100 needs an operation power supply, which can be different from other modules. The power module 160 receives an AC power input, such as 100-240 V, 50-60 Hz, single phase AC power from a power outlet. Then, the power module 160 generates 5 V, 12 V, 24 V, and the like, to provide operation powers for the various components of the DNA analyzer 100.

[0048] In addition, the power module 160 generates high voltages, such as 1000 V, 2000 V, and the like, for suitable DNA processes on the microfluidic chip 111, such as electro- kinetic injection, electrophoretic separation, and the like.

[0049] Further, the power module 160 can implement various protection techniques, such as power outrage protection, graceful shut-down, and the like, to protect the various components and data against power failure. It is noted that the power module 160 may include a back-up power, such as a battery module, to support, for example, graceful shut¬ down.

[0050] The high voltage module 140 can receive the high voltages from the power module 160 and suitably apply the high voltages on the microfluidic chip 111. For example, the high voltage module 140 includes interfaces that apply the high voltages to suitable electrodes on the microfluidic chip 111 to induce electro-kinetic injection and/or electrophoretic separation.

[0051] The detection module 150 includes components configured to suit the integrated single-chip DNA analysis. In an embodiment, the detection module 150 is configured for multicolor fluorescence detection. The detection module 150 includes a light source, a set of optic elements and a detector unit.

[0052] The light source unit emits a light beam. In an example, the light source includes an argon-ion laser unit. In another example, the light source includes a solid state laser, such as a Coherent Sapphire optically pumped semiconductor laser unit. The solid state laser has the advantages of reduced size, weight and power consumption. In another example, the light source includes a splitter configured to split one light beam into a plurality of light beams. In another example, the light source includes a plurality of light emitting diodes (LEDs) to emit a plurality of light beams. Further, the light source includes a filter to select a suitable spectral range.

[0053] The set of optic elements can direct the laser beam to pass through the detection window at the second domain 111b of the microfluidic chip 111. The laser beam can excite fluorescent labels attached to DNA fragments to emit fluorescence. Further, the set of optic elements can collect and direct the emitted fluorescence to the detector unit for detection. In an STR typing example, STR alleles are separated in the second domain 111b according to sizes. STR alleles of different sizes pass the detection window at different times. In addition, STR alleles of overlapping sizes can be tagged with fluorescent labels of different colors. The detector unit can be configured to detect an STR allele having a

fluorescent label based on a time of fluorescence emitted by the fluorescent label and a color of the emitted fluorescence.

[0054] In another example, internal lane standard (ILS) is added to migrate in the micro channel with the STR alleles. The ILS includes DNA fragments of known sizes, and can be tagged with a pre-determined fluorescent dye. The detector unit detects fluorescence emitted from the ILS to set up a size scale. In addition, the detector unit detects fluorescence emitted from the STR alleles. The detector unit can suitably convert the detected fluorescence into electrical signals. The electrical signals can be suitably stored and/or analyzed. In an example, a processor executes DNA analysis software instructions to identify the STR alleles by their sizes and emitted fluorescence colors (wavelengths).

[0055] The computing module 170 includes computing and communication units. In an example, the computing module 170 includes a personal computer. The personal computer can be coupled with the controller module 180 to provide a user interface. The user interface can inform the status of the DNA analyzer 100, and can receive user instructions for controlling the operation of the DNA analyzer 100. The personal computer includes various storage media to store software instruction and data. The personal computer can include DNA analysis software that can perform data processing based on raw data obtained from the detection module 150. In addition, the personal computer can be coupled to external processing units, such as a database, a server, and the like to further process the data obtained from the DNA analyzer 100.

[0056] The magnetic module 190 can enable a magnetic solid phase for the integrated single chip DNA analysis. In an embodiment, the magnetic solid phase can be suitably incorporated in the integrated single chip DNA analysis to facilitate a volume reduction to suit for low copy numbers of template DNAs. In another embodiment, the magnetic solid phase can be suitably incorporated into an integrated single chip sequencing DNA analysis.

[0057] The controller module 180 can receive status signals and feedback signals from the various components, and provide control signals to the various components according to a control procedure. In addition, the controller module 180 can provide the status signals to, for example, the personal computer, to inform the user. Further, the controller module 180 can receive user instructions from the personal computer, and may provide the control signals to the various components based on the user instructions.

[0058] During operation, the controller module 180 receives user instructions from the personal computer to perform a STR typing analysis, for example. The controller module 180 then monitors the microfluidic chip module 110 to check whether a suitable disposable cartridge has been installed, and whether swabs have been identified and suitably immersed in the liquid phase mixture to extract template DNA. When the controller module 180 confirms the proper status at the microfluidic chip module 110, the controller module 180 starts a control procedure corresponding to the STR typing analysis. In an example, the controller module 180 can control the thermal module 120 to maintain an appropriate temperature at the wells of the sample acceptor for a predetermined time. The liquid phase mixture in the wells can extract template DNAs from the swabs. Then, the controller module 180 can control the pressure module 130 to pump the extracted template DNAs into the first domain 111a of the microfluidic chip 111. In addition, the controller module 180 can control the pressure module 130 to pump reagents for multiplexed STR amplification into the first domain 111a.

[0059] Further, the controller module 180 can control the thermal module 120 to induce thermal cycling for the multiplexed STR amplification at the first domain 111a. The reagents and the thermal cycling can cause DNA amplification. In addition, the DNA amplicons can be suitably tagged with fluorescent labels.

[0060] Subsequently, the controller module 180 can control the pressure module 130 to flow the DNA amplicons to the second domain 111b. The controller module 180 may control the pressure module 130 to pump a dilution solution into the microfluidic chip 111 to mix with the DNA amplicons. In addition, the controller module 180 may control the pressure module 130 to pump an ILS into the microfluidic chip 111 to mix with the DNA amplicons.

[0061] Further, the controller module 180 controls the high voltage module 140 to induce electro-kinetic injection to inject DNA fragments into the micro channels. The DNA fragments include the amplified targets, and the ILS. Then, the controller module 180 controls the high voltage module 140 to induce electrophoretic separation in the micro channels. Additionally, the controller module 180 can control the thermal module 120 to maintain a suitable temperature at the second domain 111b during separation, for example, to maintain the temperature for denaturing separation of the DNA fragments.

[0062] The controller module 180 then controls the detection module 150 to detect the labeled DNA fragments. The detection module 150 can emit and direct a laser beam to the micro channels to excite the fluorescent labels to emit fluorescence. Further, the detection

module 150 can detect the emitted fluorescence and store detection data in a memory. The detection data can include a detection time, and a detected color (wavelength), along with a detected intensity, such as a relative magnitude of the detected fluorescence. The detection data can be transmitted to the personal computer for storage. Additionally, the controller module 180 can provide control statuses to the personal computer to inform the user. For example, the controller module 180 can send an analysis completed status to the personal computer when the control procedure is completed.

[0063] The DNA analyzer 100 can be suitably configured for various DNA analyses by suitably adjusting the reagents housed by the reagent carrier and the control procedure executed by the controller module 180.

[0064] It should be understood that the DNA analyzer 100 can be suitably modified. For example, multiple modules may be used to perform the functions of one module in the Fig. 1. In another example, a module in Fig. 1 may be removed if it is not needed anymore. In another example, functions of multiple modules in the Fig. 1 may be combined and performed by a different module.

[0065] Fig. 2A shows a swab storage example 212, and Figs. 2B-2C show a side elevation view and a front elevation view of a sample cartridge example 215 according to an embodiment of the disclosure. The swab storage 212 includes a case 203, a seal cap 202 and a swab 205. The seal cap 202 and the swab 205 are attached together. In addition, the swab storage 212 includes an identifier, such as a barcode label 204 that can be attached to the case 203, an RFID tag 201 that can be implanted in the seal cap 202, and the like.

[0066] Before taking DNA sample, the swab 205 is safely stored in the case 203 to avoid contamination. After taking DNA sample, the swab 205 can be placed in the sample cartridge 215.

[0067] The sample cartridge 215 can include a microfluidic chip 211, a sample acceptor 207 and a reagent carrier 206. The sample acceptor 207 includes a plurality of separated wells 207A-207D for taking swabs. Each well includes a liquid phase mixture 214 that is sealed by a membrane 208 at a bottom portion of the well. The liquid phase mixture 214 can conduct enzymatic digestion of all proteins and other cellular interferences, with the exception of DNA, and thus can perform DNA extraction and purification when a swab with DNA sample is inserted in the liquid phase mixture 214.

[0068] While the sample cartridge 215 is described in the context of swabs, it should be understood that the sample cartridge 215 can be suitably adjusted to suit other DNA

gathering methods, such as blood stain cards, airborne samples, fingerprints samples, and the like.

[0069] In an embodiment, the seal cap 202 is a stepped seal cap that can seal the well in a first step, and a second step. When the seal cap 202 seals the well in the first step, the swab 205 does not puncture the membrane 208, and can be safely sealed in the well to maintain sample integrity. When the seal cap 202 seals the well in the second step, the swab 205 punctures the membrane 208 and is immersed in the liquid phase mixture 214.

[0070] The reagent carrier 206 houses various solutions for DNA analysis. In an STR typing example, the reagent carrier houses reagents for multiplexed STR amplification. In addition, the reagent carrier houses a coating solution, such as poly~N-hydroxyethylacrylamide, and the like. The coating solution can be used to coat micro channel walls prior to the separation. Further, the reagent carrier houses a dilution solution, such as water, formamide, and the like. The dilution solution can be used to reduce the ionic strength in order to promote better electro-kinetic injection. In an embodiment, the reagent carrier houses an internal lane standard (ILS). The 1LS can be used for size measurement. The reagent carrier also houses a polymer solution for electrophoretic separation in the micro-scale chip environment.

[0071] During operation, for example, a new disposable cartridge 215 is taken from a storage package, and installed in a DNA analyzer, such as the DNA analyzer 100. Then, a swab 205 can be used to take a DNA sample. The swab 205 is then identified and inserted into one of the wells 207A-207D and sealed in the first step. Additional swabs 205 can be used to take DNA samples, and then identified and inserted into the un-used wells 207A-207D. Further, the DNA analyzer 100 can include a mechanism that can push the seal caps 202 to seal the wells 207A-207D in the second step, thus the swabs 205 can puncture the membrane 208, and immerse in the liquid phase mixture 214.

[0072] Fig. 3 shows a schematic diagram of a microfluidic chip example 311 according to an embodiment of the disclosure. The microfluidic chip 311 includes various micro structures, such as inlets 312-314, reaction reservoirs 315-316, channels 317a-317b, electrode reservoirs 318, outlets (not shown), and the like, that are integrated for single-chip DNA analysis. It is noted that the various micro structures can be designed and integrated to suit for various DNA analyses, such as STR typing, sequencing, and the like. Further, while in the embodiment shown in Fig. 3, reagents and solutions are introduced to the microfluidic

chip 311 from an external supply, it should be understood that storing such reagents and solutions on or in the microfluidic chip 311 is envisioned.

[0073] The inlets 312-314 can be coupled to a pressure module to inject solutions in the microfluidic chip 311. As described above, the connection can be made via a micro-macro interface. In an example, the inlet 312 is for injecting a template DNA solution from a well of the sample acceptor 207, and the inlet 313 is for injecting PCR reagents from the reagent carrier 206. In addition, the inlet 313 can be used for injecting dilution solution and ILS from the reagent carrier 206.

[0074] The reaction reservoirs 315-316 are configured for various purposes. In an example, the reaction reservoir 315 is configured for the PCR amplification, and the reaction reservoir 316 is configured for the post-PCR processes, such as dilution, and the like. More specifically, the reaction reservoir 315 is located in a first domain 311a, which is a thermal control domain. The temperature within the thermal control domain 311a can be precisely controlled. In an example, an infrared heating unit directs heat to the thermal control domain 311a, a cooling fan disperses heat from the thermal control domain 311a, and an infrared sensing unit measures a temperature in the thermal control domain 311a. The infrared heating unit and the cooling fan can be controlled based on the temperature measured by the infrared sensing unit. The infrared heating unit, the cooling fan, and the infrared sensing unit can perform thermal control without contacting the thermal control domain 311a.

[0075] In another example, the temperature in the thermal control domain 311a is measured by a thermal coupling technique. More specifically, the microfluidic chip 311 includes a thermal-coupler reservoir 319 within the first domain 311a. Thus, the solution temperature within the reaction reservoir 315 and the thermal-coupler reservoir 319 can be closely related. The solution temperature within the thermal-coupler reservoir 319 can be measured by any suitable technique. Based on the measured solution temperature within the thermal-coupler reservoir 319, the solution temperature within the reaction reservoir 315 can be determined. Then, the infrared heating unit and the cooling fan can be controlled based on the temperature measured by the thermal coupling technique in order to control the solution temperature in the reaction reservoir 315.

[0076] In an embodiment, after the PCR amplification, the PCR mixture is fluidically directed from the reaction reservoir 315 to a post-PCR clean-up/dilution domain, such as the reaction reservoir 316. In the reaction reservoir 316, the PCR mixture is diluted. In an example, the PCR mixture and a dilutant solution are mixed together according to a

ratio from 1:5 to 1:20 (1 part of PCR mixture to 5-20 parts of dilutant). Further, ILS can be added in the reaction reservoir 316 to mix with the PCR mixture.

[0077] The channels 317a-317b are located in a second domain 311b. Electric fields can be suitably applied onto the channels 317a-317b. In an example, the channels 317a~317b are configured according to a cross-T design, having a short channel 317a and a long channel 317b.

[0078] The electrode reservoirs 318 can be used to apply suitable electric fields over the short channel 317a and the long channel 317b. Thus, the short channel 317a is configured for electro-kinetic injection, and the long channel 317b is configured for electrophoretic separation. For example, when a high voltage is applied to the short channel 317a, DNA fragments can be injected from the reaction reservoir 316 into the short channel 317a at the intersection of the short channel 317a and the long channel 317b. The long channel 317b can be filed with sieving matrix. When a high voltage is applied to the long channel 317b, the injected DNA fragments can migrate in the long channel 317b to the positive side of the electric field induced by the high voltage, in the presence of the sieving matrix. In an example, the length of the long channel 317b is about 8.8 cm with detection at about 8 cm from the intersection.

[0079] It should be understood that the microfiuidic chip 311 can include other structures to assist DNA analysis. In an example, the microfiuidic chip 311 includes an alignment mark 321. The alignment mark 321 can assist a detection module to align to the long channel 317b.

[0080] During operation, for example, the inlet 312 can input a template DNA into the reaction reservoir 315, and the inlet 313 can input PCR reagents into the reaction reservoir 315. Then, thermal-cycling can be induced at the first domain 311a, and PCR amplification can be conducted in the reaction reservoir 315 to amplify DNA fragments based on the template DNA and the PCR reagents. After the PCR amplification, the DNA amplicons in the reaction reservoir 315 can be mobilized into the reaction reservoir 316 in a liquid flow. In the reaction reservoir 316, a dilution solution and ILS can be input to mix with the DNA fragments. Further, the DNA fragments in the reaction reservoir 316 can be injected across the short channel 317a by electro-kinetic injection. The DNA fragments then migrate in the long channel 31.7b under the force of electric field applied over the long channel 317b. The speed of migration depends on the sizes of the DNA amplicons, in the presence of the sieving

matrix. Thus, the DNA fragments are separated in the long channel 317b according to their sizes.

[0081] Fig. 4 shows an exemplary DNA analyzer 400 according to an embodiment of the disclosure. The DNA analyzer 400 is packaged in a box. The box includes handles, wheels and the like, to facilitate transportation of the DNA analyzer 400. In an implementation, the total weight of the DNA analyzer 400 is less than 70 lb, and is appropriate for two persons to carry.

[0082] The DNA analyzer 400 is implemented in a modular manner. Each module can be individually packaged, arid can include an interface for inter-module couplings. Thus, each module can be easily removed and replaced. The modular design can facilitate assembly, troubleshooting, repair, and the like.

[0083] The DNA analyzer 400 includes a user module (UM) 410, an active pressure module (APM) 430, a detection module 450, a power module (PM) 460, a computing module 470, and a controller module (CM) 480. In addition, the DNA analyzer 400 includes a sample cartridge storage 415 and a swab storage 412.

[0084] The UM 410 includes a holder to hold a sample cartridge, such as the sample cartridge 215, at an appropriate position when the sample cartridge is inserted by a user. Further, the UM 410 includes interface components to couple the sample cartridge 215 with, for example, the APM 430, the detection module 450, and the like. The UM 410 includes thermal components, such as resistance heaters 421, a cooling fan 422, an infrared heating unit 423, and the like. The thermal components can be suitably positioned corresponding to the sample cartridge 215. For example, a resistance heater 421 is situated at a position that can effectively control a temperature of the liquid phase mixture within the plurality of separated wells on the sample cartridge 215. The temperature can be determined to optimize enzyme activities of the liquid phase mixture to conduct enzymatic digestion of all proteins and other cellular interferences, with the exception of DNA. Another resistance heater 421 is at a position that can effectively control a temperature of the separation channel on the microfluidic chip 211. The infrared heating unit is at a position that can direct heat to the thermal control domain of the microfluidic chip 211 on the sample cartridge 215. The cooling fan is at a position that can effectively disperse heat from the thermal control domain. Further, the UM 410 includes a high voltage module that can apply suitable high voltages via the electrode reservoirs of the microfluidic chip 211.

[0085] It is noted that the UM 410 can include other suitable components. In an embodiment, the UM 410 includes a magnetic module that can suitably apply magnetic control over a domain of the microfluidic chip 211.

[0086] The APM 430 includes suitably components, such as pumps, vacuums, and the like, to apply suitable pressures to the microfluidic chip 211 to enable fluid movement.

[0087] The PM 460 receives an input main power, and generates various operation powers, such as 6 V, 12 V, 24 V, 1000V, 2000V, and the like, for various components of the DNA analyzer 400.

[0088] The detection module 450 can include a laser module (LM) 451, a passive optics module (POM) 452, and an active optics module (AOM) 453. The LM 451 can include any suitable device to emit a laser beam. In an embodiment, the LM 451 includes an argon-ion laser. In another example, the LM 451 includes a diode laser. In another embodiment, the LM 451 includes a solid state laser, such as a Coherent Sapphire optically pumped semiconductor laser. The solid state laser can have a reduced size and weight, and can consume less power than the argon-ion laser. In addition, the solid state laser generates less waste heat, such that fan size can be reduced to reduce footprint of the DNA analyzer 400.

[0089] The AOM 453 includes optical elements that may need to be adjusted with regard to each inserted microfluidic chip. In an example, the AOM 453 includes motion control module to align the optical elements to one separation channel on the microfluidic chip. Further, in an example, the motion control module can align the optical elements based on detection results. In an embodiment, the DNA analyzer 400 performs an optical calibration procedure after an microfluidic chip is inserted in the DNA analyzer 400. During the optical calibration procedure, a specific dye is sent to a separation channel. Then, the motion control module adjusts the AOM 453 to maximize a detection signal.

[0090] The POM 452 includes various optical elements, such as lens, splitters, photo-detectors, and the like, that do not need to be adjusted with regard to each inserted microfluidic chip. In an example, the POM 452 is calibrated and adjusted with regard to the LM 451 and the AOM 453 when the detection module 450 is assembled. Then, the optical elements within the POM 452 are situated at relatively fixed positions, and generally do not need to be adjusted with regard to each inserted microfluidic chip.

[0091] In another embodiment, the LM 451, the POM 452, and the AOM 453 are optically coupled via optical fibers. In an example, an optical fiber transmits a light beam

emitted by the LM 451 to the AOM 453, and a plurality of optical fibers transmit the fluorescence light beam collected by the AOM 453 to the POM 452. Using optical fibers improves layout flexibility.

[0092] The controller module 480 is coupled to the various components of the DNA analyzer 400 to provide control signals for DNA analysis. The controller module 480 includes a control procedure that determines sequences and timings of the control signals.

[0093] The computing module 470 is implemented as a personal computer. The personal computer includes a processor, a memory storing suitable software, a keyboard, a display, and a communication interface. The computing module 470 can provide a user interface to ease user control and monitor of the DNA analysis by the DNA analyzer 400.

[0094] It should be understood that the DNA analyzer 400 can be suitably modified. For example, multiple modules may be used to perform the functions of one module in the Fig. 4. In another example, a module may be removed if it is not needed anymore. In another example, functions of multiple modules in the Fig. 4 may be combined and performed by a different module.

[0095] Fig. 5 shows a flow chart outlining a process example for using a DNA analyzer, such as the DNA analyzer 400, to perform DNA analysis according to an embodiment of the disclosure. The process starts at S501, and proceeds to S510.

[0096] At S510, a user of the DNA analyzer 400 plugs in a main power supply. In an embodiment, the main power supply can be a 110 V, 50 Hz, AC power supply, or can be a 220V, 60 Hz, AC power supply. The power module 460 can convert the main power supply to a plurality of operation powers, and provide the plurality of operation powers to the various modules of the DNA analyzer 400. Then, the process proceeds to S515.

[0097] At S515, the user starts up a user control interface. For example, the user turns on the personal computer 470, and starts a software package that interacts with the user and the controller module 480. The software package enables the personal computer 470 to provide a user control interface on the display. Further, the software package enables the personal computer 470 to receive user instructions via the keyboard or mouse. The software packages can also enable the personal computer 470 to communicate with the controller module 480. Then, the process proceeds to S520.

[0098] At S520, the user instructs the DNA analyzer 400 to initialize. The user control interface receives the initialization instruction, and the software package enables the personal computer 470 to send the initialization instruction to the controller module 480. The

controller module 480 can then initialize the various components of the DNA analyzer 400. For example, the controller module 480 can power on the various components, check the status and reset the status if needed. Then, the process proceeds to S525.

(0099] At S525, the user inserts a sample cartridge 215 in the UM 410. The sample cartridge 215 can be positioned by a holder. The interface components can suitably couple the sample cartridge 215 to other components of the DNA analyzer 400. Then, the process proceeds to S530.

[0100] At S530, the user takes a swab 205, and lets the DNA analyzer 400 to identify the swab 205. In an example, the DNA analyzer 400 includes a barcode reader that can read the barcode label 204 attached to the case 203 for storing the swab 205. In another example, the DNA analyzer 400 excites the RFID 201 implanted in the seal cap 202 of the swab 205 to obtain a unique serial number of the swab 205. Then, the process proceeds to S535.

[0101] At S535, the user uses the swab 205 to take a DNA sample and inserts the swab 205 into a well of the sample cartridge 215. The user may repeat the steps S530 and S535 to insert multiple swabs 205 into the separated wells of the sample cartridge 215. Then, the process proceeds to S540.

[0102] At S540, the user instructs the DNA analyzer 400 to start a DNA analysis. The user control interface receives the start instruction, and the software package enables the personal computer 470 to send the start instruction to the controller module 480. The controller module 480 can start a control procedure corresponding to the DNA analysis. In an example, the controller module 480 starts an STR typing procedure corresponding to a multiplexed STR typing analysis. In another example, the controller module 480 starts a sequencing procedure corresponding to DNA sequencing analysis. It is noted that, in an embodiment, the control procedure includes an optical calibration step that suitably aligns the optical elements the DNA analyzer 400, such as the AOM 453, and the like, to a suitable detection zone, such as a separation channel on a microfluidic chip of the sample cartridge 215. Then, the process proceeds to S545.

[0103] At S545, the user waits and monitors the status of the DNA analysis. The control procedure can specify sequences and timings of control signals to various components of the DNA analyzer 400 corresponding to the DNA analysis. Then, the controller module 480 automatically sends the control signals according to the sequences and the timings specified in the control procedure. In addition, the controller module 480 receives status and

feedback signals from the various components, and sends them to the personal computer 470. The personal computer 470 then provides the analysis status for the user to monitor. Then, the process proceeds to S550.

(0104] At S550, the controller module 480 finishes executing the control procedure, and sends an analysis-completed status to the personal computer 470. The personal computer 470 can inform the user of the analysis-completed status via the user control interface. Then, the process proceeds to S555.

[0105] At S555, the user performs post data processing. The user can store the raw data of the DNA analysis, or transmit the raw data to a remote receiver. In addition, the user may start a software package for post data processing. Alternatively, the software package for post data processing can be suitably integrated with the control procedure. Thus, after the control procedure is successfully executed, the software package for post data processing is executed automatically to perform post data processing. The process then proceeds to S599 and terminates.

[0106] It is noted that to perform another DNA analysis, the user may throw away the sample cartridge and repeat S520-S550. It is also noted that the sequence of the DNA analysis steps can be suitably adjusted. For example, S535 and S530 can be swapped, thus a swab can be first used to take a DNA sample, and then identified by the DNA analyzer 400.

[0107] Fig. 6 shows a flow chart outlining a process example 600 for a DNA analyzer to perform multiplexed STR typing according to an embodiment of the disclosure. The process starts at S601 and proceeds to S605.

[0108] At S605, the DNA analyzer performs optical calibration. In an embodiment, the AOM 453 includes a motion control module coupled with the optical elements. After a new sample cartridge 215 is installed in the DAN analyzer, the motion control module aligns the optical elements to a separation channel on a microfluidic chip within the sample cartridge 215. In an example, a specific dye that does not interfere the fluorescent labels is used. For example, the fluorescent labels emit fluorescence in the wavelength range of 530 nm to 650 num, and the specific dye emits light of about 700 μm wavelength. The dye is sent to the separation channel, the detection module 450 is activated to detect the light intensity. In an embodiment, the motion control module is configured to position the optical elements to maximize the detected light intensity. In another embodiment, the motion control module is configured to position the optical elements, such that the detected light intensity is larger than a threshold.

[0109] At S610, the controller module 480 controls the resistance heater 421 to maintain a temperature for template DNA extraction and purification. More specifically, the resistance heater 421 is positioned corresponding to the plurality of wells on the sample cartridge 215. A well can accept a swab 205. The swab 205 can puncture the membrane that seals the liquid phase mixture at the bottom of the well, thus the swab 205 is immersed into the liquid phase mixture. The liquid phase mixture can extract and purify a template DNA from the swab at the temperature according to enzymatic DNA isolation method. In an embodiment, the liquid phase mixture can achieve a compatible DNA concentration and purity to silica based solid phase extraction method in about 6 minutes. Then, the process proceeds to S620.

[0110] At S620, the controller module 480 controls the APM 430 to flow the extracted template DNA and reagents to a reaction reservoir for the PCR amplification. For example, the reagent carrier 206 houses reagents for multiplexed STR amplification. The controller module 480 sends control signals to the APM 430. In response to the control signals, a pump pumps the liquid phase mixture from the well to the reaction reservoir, and another pump pumps the reagents from the reagent carrier 206 to the reaction reservoir. Then, the process proceeds to S630.

[0111] At S630, the controller module 480 controls the cooling fan 422 and the infrared heating unit 423 to induce thermal cycling in the reaction reservoir for the multiplexed STR amplification. In addition, the reagents can attach fluorescent labels to the DNA amplicons during the STR amplification process. The process then proceeds to S640.

[0112] At S640, after the PCR amplification, the solution can be diluted. More specifically, the controller module 480 sends control signals to the APM 430 after the PCR amplification. In response to the control signals, the APM 430 flows the DNA amplicons into a dilution reservoir. In addition, the APM 430 flows a dilution solution from the reagent carrier into the dilution reservoir. The process then proceeds to S650.

[0113] At S650, the controller module 480 sends control signals to the high voltage module in the UM 410 to inject the DNA amplicons across the injection arm (the short channel 317a). Then, the process proceeds to S660.

[0114] At S660, the controller module 480 sends control signals to the high voltage module in the UM 410 to apply appropriate high voltage over the separation channel (the long channel 317b) to separate the DNA amplicons based on sizes. The process then proceeds to S670.

[0115] At S670, the controller module 480 sends control signals to the detection module 450 to excite the fluorescent labels to emit fluorescence and detect the emitted fluorescence. The raw detection data can be sent to the personal computer 470 for storage and post-processing. The process then proceeds to S699, and terminates.

[0116] It is noted that some process steps in the process 600 can be executed in parallel. For example, the step S660 and the step S670 can be executed in parallel. The controller module 480 sends control signals to both the high voltage module in the UM 410 and the detection module 450 at about the same time. The control signals to the high voltage module in the UM 410 cause the electrophoretic separation in the separation channel, while the control signals to the detection module 450 cause fluorescence detection. In another example, the optical calibration step S605 can be executed any time before the DNA amplicons are injected into the separation channel.

[0117] It is noted that the process 600 can be suitably adjusted along with reagents adjustments for other DNA analysis, such as qPCR DNA quantitation, sequencing, and the like.

[0118] In a qPCR DNA quantitation example, step S601 to S630 are executed, and step S640 to S670 can be deleted. In addition, in step S630, when thermal cycles are induced in a qPCR reservoir for PCR amplification, the controller module 480 sends control signals to the detection module 450 to detect fluorescence emitted by the fluorescent labels in the qPCR reservoir.

[0119] It is also noted that a magnetic solid phase purification process step can be suitably added into the process 600 to facilitate further volume reduction, thus the process 600 can be adjusted for DNA sequencing.

[0120] Fig. 7 shows a block diagram of an exemplary detection module 750 coupled with an exemplary sample cartridge 715 having a microfluidic chip 711 according to an embodiment of the disclosure. The detection module 750 can be suitably installed in a DNA analyzer, such as the DNA analyzer 100, or the DNA analyzer 400. Further, the detection module 750 can be coupled with other components, such as a processor 771. The processor 771 processes signals received from the detection module 750 and provides processed signals to the detection module 750. The detection module 750 includes a light source module 751, an active optics module 753, and a detector 790. These elements are coupled together using optical fibers 761 and 766 as shown in Fig. 7.

[0121] In an embodiment, the microfluidic chip 711 includes generally identical or equivalent components as the exemplary microfluidic chip 311. For example, the microfluidic chip 711 includes a first domain configured for PGR amplification and a second domain having a separation channel configured for electrophoretic separation. In another embodiment, the microfluidic chip 711 includes one or more separation channel configured for electrophoretic separation, and the microfluidic chip 711 does not necessarily include the first domain.

[0122] The detection module 750 is optically coupled to the microfluidic chip 711. As described above, the microfluidic chip 711 includes a separation channel configured for electrophoretic separation of DNA fragments. The DNA fragments migrate in the separation channel based on their sizes. The DNA fragments can be suitably tagged with fluorescent labels. The fluorescent labels can be optically detected by the detection module 750. Based on the detected fluorescent labels, DNA analyses, such as identification, sequencing, and the like, can be suitably performed.

[0123] More specifically, the detection module 750 directs a light beam to a location of the separation channel along the migration direction of the DNA fragments. The light beam can excite the fluorescent labels attached to the DNA fragments to emit fluorescence when the DNA fragments migrate through the location. The detection module 750 collects the emitted fluorescence and detects properties of the fluorescence, such as intensity, wavelength, timing, and the like. The detected properties can be suitably stored and analyzed.

[0124] The light source module 751 can include any suitable light emitting device, such as an argon-ion laser device, a solid state laser, a laser diode (LD), and the like, to generate the light beam. In an example, the light source module 751 includes a Coherent Sapphire optically pumped semiconductor laser (OPSL) that outputs a laser beam of 488 nm wavelength, and has an output power of 200 mW. The light source module 751 provides the laser beam to the active optics module 753 via the input optical fiber 761.

[0125] In another example, the light source module 751 includes an LD that emits light in a wavelength range, such as in the wavelength range of 472 nrn to 495 nm. Further, the light source module 751 includes a collimating lens (not shown), a filter (not shown), and a coupling lens (not shown). The collimating lens collimates the emitted light from the LD. Then, the filter, such as a low pass filter, blocks a portion of the spectra that overlaps with fluorescent labels in use. Further, the coupling lens couples the filtered light to the input

optical fiber 761. The input optical fiber 761 provides an input light beam to the active optics module 753

[0126] It is noted that, in an embodiment, the input optical fiber 761 and the light beam transmitted by the input optical fiber 761 are suitably configured to keep a relatively small numerical aperture. In an example, the input optical fiber 761 and the light beam transmitted are configured to keep the numerical aperture smaller than 0.1, such that the input light beam is at a center of the active optics module 753 to minimize aberration.

[0127] The active optics module 753 includes optical elements that may need to be adjusted for each sample cartridge 715. In the Fig. 7 example, the active optics module 753 includes an optic assembly that includes a set of optic elements 780 and a motion control module 756 coupled to the set of optic elements 780 to move all or a portion of the modular component. The set of optic elements 780 is configured to receive the input light beam from the input optical fiber 761, and suitably directs the input light beam to the separation channel on the microfluidic chip 711. The set of optic elements 780 is also configured to collect fluorescence emitted by the fluorescent labels into an output light beam, and transmit the output light beam to the detector 790 via the output optical fibers 766. The motion control module 756 can adjust the set of optic elements 780 to align the set of optic elements 780 to the separation channel on the microfluidic chip 711.

[0128] In the Fig. 7 example, the motion control module 756 receives signals from the processor 771 to move the set of optic elements 780. Thus, in an example, the set of optic elements 780, the detector 790, the processor 771 and the motion control module 756 form a loop during an optical calibration to align the set of optic elements 780 to the separation channel. For example, during an exemplary optical calibration process, a specific dye, such as a dye emitting light about 700 μm wavelength can be sent to a detection zone of the separation channel. The 700 μm wavelength is much larger than the fluorescent labels wavelength range (e.g., 530 nm to 650 nm), thus the dye does not interfere the fluorescent labels. The set of optic elements 780 directs the input light beam to the separation channel to stimulate the dye to emit light, and collects the resultant light emitted by the dye. The set of optic elements sends the emitted light to the detector 790 via the output optical fibers 766. In this exemplary optical calibration process, the detector 790 generates electrical signals corresponding to the light intensity of the emitted light. The processor 771 then signals the motion control module 756 to position the set of optic elements 780 to maximize the amount of emitted light that the set of optic elements 780 receives.

[0129] In another example, a portion of the set of optic elements 780 has adjustable features. For example, an objective lens of the set of optic elements 780 has adjustable focus. In an embodiment, the objective lens is adjusted based on signals from the processor 771 to focus the input light beam onto the separation channel on the microfluidic chip 711.

[0130] The detector 790 is configured to detect light properties of the output light beam, such as wavelength components, intensities corresponding to the wavelength components, and the like. In an embodiment, the detector 790 includes various optical elements (not shown) configured to cause spectral dispersion to spatially separate the wavelength components in the output light beam. Further, the detector 790 includes an array of photo detection units to detect the spatially separated wavelength components. In an example, the optical elements include a dispersive element, such as a grating element, to cause spectral dispersion, and the detector 790 includes a charge coupled device (CCD) system to detect light intensities at different locations.

[0131] Generally, the light source module 751, and the detector 790 are situated at substantially fixed positions. In an example, the optical elements within the detector 790 are pre-calibrated and fixed at their calibrated positions by the manufacture. Then, the optical elements are situated at their calibrated positions, and do not need to be adjusted for every sample cartridge 715.

[0132] As shown, the detection module 750 can be implemented in a modular manner. Each of the light source module 751, the detector 790 and the active optics module 753 can be individually handled, such as manufactured, purchased, tested, and calibrated. Further, the light source module 751, the detector 790 and the active optics module 753 can be suitably coupled together using the input optical fiber 761 and the output optical fibers 766, and assembled in a DNA analyzer. During operation, when a new sample cartridge 715 is installed in the DNA analyzer, the active optics module 753 is calibrated with regard to a microfluidic chip 711 on the sample cartridge 715. The light source module 751 and the detector 790 do not need to be adjusted for every sample cartridge 715.

[0133] In an example, when a new sample cartridge 715 is installed in a DNA analyzer having the detection module 750, the DNA analyzer can start an optical calibration procedure to calibrate the detection module 750 with regard to a microfluidic chip 711 on the sample cartridge 715. During the calibration procedure, the motion control module 756 aligns the set of optic elements 780 to a separation channel on the microfluidic chip 711. In an embodiment, a specific dye is sent into the separation channel to assist the alignment. In

another example, the microfluidic chip 711 includes an alignment mark to assist the set of optic elements 780 to align to a desired location along the separation channel.

[0134] In an embodiment, the DNA analyzer starts a control procedure to control the various components of the DNA analyzer to act on the microfluidic chip 711 in order to perform an integrated single-chip DNA analysis. For example, template DNA can be suitably extracted and fluidically directed to the first domain of the microfluidic chip 711; a PCR amplification can be suitably induced in the first domain of the microfluidic chip 711 to amplify DNA fragments; then the amplified DNA fragments are suitably injected into the separation channel of the microfluidic chip 711; and then electrophoretic separation can be suitably induced in the separation channel. In addition, the detection module 750 can be controlled to direct an input light beam to the separation channel to excite fluorescent labels used to tag the DNA fragments. The fluorescent labels emit fluorescence. The detection module 750 collects the fluorescence into an output light beam, and detects fluorescence information in the output light beam. The detected fluorescence information can be suitably stored, and further processed by the DNA analyzer, or can be transmitted to other device for further processing.

[0135] Fig. 8 shows an exemplary block diagram of a set of optic elements 880 according to an embodiment of the disclosure. The set of optic elements 880 includes a first lens 881, a second lens 882, a pinhole 883, a third lens 884, a dichroic mirror 885, a short pass filter 886, a fourth lens 887 and a fifth lens 888 configured in a confocal optical system. The second lens 882, the pinhole 883 and the third lens 884 form a spatial filter. Further, the set of optic elements 880 are assembled together into an optic assembly. The optic assembly includes interfaces for coupling optical fibers with the set of optic elements 880. In the Fig. 8 example, the optic assembly includes a connector 889A for coupling output optical fibers 866, and a connector 889B for coupling an input optical fiber 861. As shown, the exemplary connector 889A accepts seven optical fibers, arranges one optical fiber in the center, and arranges the other six optical fibers around the center optical fiber to form a hexagon shape. The connector 889B accepts one optical fiber. It should be understood that the connector 889B can include more than one optical fiber, and the connector 889A can include other numbers of optical fibers, and can arrange the optical fibers in various different shape.

[0136] The set of optic elements 880 forms an input optical path (illuminating path) and an output optical path (detecting path). The input optical path includes the input optical fiber 861, the fourth lens 887, the short pass filter 886, the dichroic mirror 885, the third lens

884, the pinhole 883, the second lens 882, and the first lens 881. The output optical path includes the first lens 881, the second lens 882, the pinhole 883, the third lens 884, the dichroic mirror 885, and the fifth lens 888.

[0137] On the input optical path, the input optical fiber 861 emits the input light beam into the set of optic elements 880. The fourth lens 887 forms the input light beam into a substantially collimated light beam. The short pass filter 886 reduces fluorescence components in the collimated input light beam. In an embodiment, the input optical fiber 861 generates auto-fluorescence. The auto-fluorescence is a relatively large portion of noise to the whole system. The short pass filter 886 reduces the auto-fluorescence in the collimated input light beam to improve signal to noise ratio.

[0138] The dichroic mirror 885 is configured to allow the filtered collimated input light beam to pass. Then, the third lens 881 forms the filtered collimated light beam into a narrowing conical input beam that is focused to pass the pinhole 883.

[0139] Then, the conical input beam passes the second lens 882 and the first lens 881. The second lens 882 collimates the conical input light beam, and the first lens 881 focuses the input light beam onto a detection zone of the separation channel.

[0140] When DNA fragments migrate to the detection zone of the separation channel, the fluorescence labels attached on the DNA fragments absorb the input light beam, and emit fluorescence.

[0141] On the output optical path, the first lens 881 collects the fluorescence emitted from the fluorescence labels, and forms collimated output light beam. Then, the second lens 882 forms the collimated output light beam into a narrowing conical output beam that is focused to pass the pinhole 883. The spatial filter formed by the second lens 882, the pinhole 883 and the third lens 884 rejects scattered light from surrounding surfaces into the microfluidic chip. Then, third lens 884 collimates the conical output light beam. The dichroic mirror 885 reflects the collimated output light beam to direct the output light beam to the fifth lens 888. The fifth lens 888 focuses the output light beam to the output optical fibers 866 connected on the connector 889A.

[0142] It is noted that, in the Fig. 8 example, the input optical path and the output optical path do not completely overlap due to the dichroic mirror 885. Thus, different optical elements can be used on the input optical path and the output optical path to suit for different needs of the two optical paths. This configuration provides flexibility, and different optics can be added on the two optical paths to improve performance. For example, the short pass

filter 886 is used on the input optical path to reduce auto-fluorescence generated by input optical fiber 861.

[0143] Fig. 9 shows a block diagram of another set of optic elements example 980 according to an exemplary embodiment of the disclosure. The set of optic elements 980 includes a first lens 981, a second lens 982, a pinhole 983, a third lens 984, and a fourth lens 987 configured in a confocal optical system. The second lens 982, the pinhole 983 and the third lens 984 form a spatial filter. Further, the set of optic elements 980 includes a connector 989 for coupling both an input optical fiber 961 and output optical fibers 966. The connector 989 is configured to arranges the input optical fiber 961 in the center, and arranges six output optical fibers 966 around the center optical fiber to form a hexagon shape.

[0144] The set of optic elements 980 forms an input optical path (illuminating path) and an output optical path (detecting path) using the same optics. The input optical path follows the input optical fiber 961, the fourth lens 987, the third lens 984, the pinhole 983, the second lens 982, and the first lens 981. The output optical path follows the first lens 981, the second lens 982, the pinhole 983, the third lens 984, and the fourth lens 987.

[0145] On the input optical path, the input optical fiber 961 emits the input light beam into the set of optic elements 980. In an example, the input optical fiber 961 and the light transmitted in the input optical fiber 961 are configured to have a relatively small numerical aperture, such as smaller than 0.1. Thus, the input light emitted by the input optical fiber 961 keeps in the center of the optics in the set of optic elements 980 to reduce aberration.

[0146] The fourth lens 987 forms the input light beam into a substantially collimated light beam. Then, the third lens 981 forms the filtered collimated light beam into a narrowing conical input beam that is focused to pass the pinhole 983.

[0147] Then, the conical input beam passes the second lens 982 and the first lens 981. The second lens 982 collimates the conical input beam, and the first lens 981 focuses the input light beam onto a detection zone of the separation channel.

[0148] When DNA fragments migrate to the detection zone of the separation channel, the fluorescence labels attached to the DNA fragments absorb the input light beam, and emit fluorescence.

[0149] On the output optical path, the first lens 981 collects the fluorescence emitted from the fluorescence labels, and forms collimated output light beam. It is noted that the fluorescence labels may emit the fluorescence in all directions. In an embodiment, the

first lens 981 has a relatively large numerical aperture, such as greater than 0.5 to collect a relatively large portion of the fluorescence. Then, the second lens 982 forms the collimated output light beam into a narrowing conical output light beam that is focused to pass the pinhole 983. The spatial filter formed by the second lens 982, the pinhole 983 and the third lens 984 rejects scattered light from surrounding surfaces. Then, third lens 984 collimates the conical output light beam. The fourth lens 987 focuses the output light beam to the optical fibers 966 and 961 attached to the connector 989.

[0150] It is noted that, in an embodiment, the fourth lens 987 can be suitably configured that a relatively larger portion of the output light beam, such as more than 50% of the output light beam, can be aberrated onto the output optical fibers 966.

[0151] Fig. 10 shows a block diagram of a detector example 1090 according to an exemplary embodiment of the disclosure. The detector 1090 includes first lenses 1092, a dispersive element 1093, second lenses 1094, and a CCD system 1098. Further, the detector 1090 includes a connector 1091 configured to couple optical fibers 1066 with the detector 1090.

[0152] In an embodiment, the optical fibers 1066 include two ends. Each end is attached to a suitable connector. In the Fig. 10 example, one end of the optical fibers 1066 is attached to the connector 1091 and the other end of the optical fibers 1066 is attached to a connector 1089. The connector 1089 and the connector 1091 are in different configurations. In the Fig. 10 example, the optical fibers 1066 are in the form of a bundle of seven optical fibers. The connector 1089 arranges one optical fiber in the center, and arranges the other six optical fibers around the center optical fiber to form a hexagon shape. The connector 1091 stacks the seven optical fibers vertically to form a vertical slit.

[0153] During operation, the optical fibers 1066 transmit a light beam having the collected fluorescence from the connector 1089 to the connector 1091. The optical fibers 1066 emit the light beam in the form of a vertical line. The first lenses 1092 collectively collimate the light beam. In an example, the dispersive element 1093 is a grating element that has a large number of closely spaced vertical slits constituting a grating. The dispersive element 1093 causes spectral dispersion to spatially spread the fluorescence components by wavelengths. It is noted that, for ease of illustration, the spectral dispersion onto a detection surface of the CCD system 1098 is shown in the horizontal direction. The second lenses 1094 collectively focus the spread fluorescence components onto the CCD system 1098 at different horizontal locations. The CCD system 1098 includes an array of photo sensitive

devices configured to detect light intensities at the different horizontal locations. The light intensities, and the location information can be used to identity fluorescence labels, and identify DNA fragments.

[0154] Fig. 11 shows a schematic diagram of a multiple-sample microfluidic chip example 1100 according to an embodiment of the disclosure. The multiple-sample microfluidic chip 1100 can be used to simultaneously perform DNA analysis for multiple samples. Similar to the microfluidic chip 311 in Fig. 3, the multiple-sample microfluidic chip 1100 includes various micro structures, such as inlets 1121-1124, reaction reservoirs 1152, 1162 and 1172, connection channels 1151,1161, 1171, 1181, 1153, 1163 and 1173, injection channels 1154, 1164, 1174 and 1184, separation channels 1155, 1165, 1175 and 1185 (separation channel-A to separation channel-D), electrode reservoirs 1131-1140, waste reservoirs 1124 and 1125, and the like. These micro structures can be similarly configured as their corresponding micro structures in Fig. 3 and can operate similarly as their corresponding micro structures in Fig. 3.

[0155] In addition, similar to the microfluidic chip 311, the multiple-sample microfluidic chip **1100** includes a first domain 1111a, and a second domain 1111b. The first domain 1111a is a thermal control domain, and the temperature within the first domain 1111a can be controlled in a similar manner as the thermal control domain 311a.

[0156] The first domain 1111a can include multiple reaction reservoirs that are respectively designated to multiple samples to perform simultaneous PCR amplification for the multiple samples. In the Fig. 11 example, the reaction reservoirs 1152, 1162 and 1172 are located within the first domain 1111a. During a PCR amplification step, for example, the reaction reservoir 1152 includes a first liquid mixture of a first template DNA extracted from a first sample and first reagents, the reaction reservoir 1162 includes a second liquid mixture of a second template DNA extracted from a second sample and second reagents, and the reaction reservoir 1172 includes a third liquid mixture of a third template DNA extracted from a third sample and third reagents. Then, when thermal cycles are generated within the first domain 1111a, for example, by an infrared light source and a cooling fan, PCR amplifications can be simultaneously performed in the reaction reservoirs 1152, 1162 and 1172.

[0157] In an embodiment, the first domain 1111a includes a thermal coupler reservoir (not shown) for measuring a temperature within the first domain 1111a. In another embodiment, the temperature measurement is performed by an infrared sensing unit.

[0158] The second domain 1111b includes multiple separation units that are respectively designated to multiple samples. In an embodiment, each separation unit includes a separation channel and an injection channel coupled together. In addition, the separation unit includes electrode reservoirs that are in association with the injection channel and the separation channel to provide electric fields for electro-kinetic injection and electrophoretic separation. It is noted that separation units may share electrode reservoirs. In the Fig. 11 example, the second domain 1111b includes four separation units. The first separation unit includes the injection channel 1154 and the separation channel 1155. The second separation unit includes the injection channel 1164 and the separation channel 1165. The third separation unit includes the injection channel 1174 and the separation channel 1175. The fourth separation unit includes the injection channel 1184 and the separation channel 1185.

[0159] It is noted that the multiple-sample microfluidic chip 1100 can include other domains, such as post-PCR clean-up/dilution domain, and the like. Alternatively, a domain can be configured to be a multi-purpose domain. For example, the first domain 1111a can be suitably configured for purification and/or post-PCR processing. Thus, the reaction reservoirs 1152, 1162 and 1172 can also be purification reservoirs and/or post-PCR reservoirs.

[0160] In another example, the electrode reservoirs 1131, 1133 and 1136 are suitably configured for diluting PCR mixtures. Specifically, the electrode reservoir 1131 dilutes a first PCR mixture received from the reaction reservoir 1152 with a first dilutant, and prepares the first PCR mixture for electrophoretic separation in the separation channel 1155. The electrode reservoir 1133 dilutes a second PCR mixture received from the reaction reservoir 1162 with a second dilutant, and prepares the second PCR mixture for electrophoretic separation in the separation channel 1165. The electrode reservoir 1136 dilutes a third PCR mixture received from the reaction reservoir 1172 with a third dilutant, and prepares the third PCR mixture for electrophoretic separation in the separation channel 1175. In an embodiment, respective dilution ratios are used in the electrode reservoirs 1131, 1133 and 1136. The dilution ratios are from 1:5 to 1:20 (one part of PCR mixture to 5-20 parts of dilutant).

[0161] The various micro structures can be suitably coupled together to form multiple processing units for multiple-sample DNA analysis. In Fig. 11 example, the multiple-sample microfluidic chip 1100 includes four processing units. The first processing unit includes the inlets 1121, the connection channel 1151, the reaction reservoir 1152, the connection channel 1153, the injection channel 1154, and the separation channel 1155. The

second processing unit includes the inlets 1122, the connection channel 1161, the reaction reservoir 1162, the connection channel 1163, the injection channel 1164, and the separation channel 1165. The third processing unit includes the inlets 1123, the connection channel 1171, the reaction reservoir 1172, the connection channel 1173, the injection channel 1174, and the separation channel 1175. The fourth processing unit includes the inlet 1124, the connection channel 1181, the injection channel 1184, and the separation channel 1185.

[0162] The micro structures of a processing unit can be fluidically coupled together to enable liquid flow. Using the first processing unit as an example, the inlets 1121 are suitably coupled to a pump module. The pump module can input the first template DNA and the first reagents into the reaction reservoir 1152 via the connection channel. 1151 by a pressure force. In the reaction reservoir 1152, PCR amplification is performed based on the first template DNA and the first reagents. After the PCR amplification, the DNA amplicons flow through the connection channel 1153 by a pressure force. Further, the DNA amplicons are injected into the separation channel 1155 via the injection channel 1154 by an electro-kinetic force. Then, electrophoretic separation can be performed in the separation channel 1155.

[0163] The multiple processing units can be configured to fluidically separated from each other on the same multiple-sample microfiuidic chip 1100. Thus, the multiple processing units can be respectively used to perform DNA analysis for multiple samples using a single microfiuidic chip.

[0164] It is noted that the processing units can be suitably configured to include branches. The branches can be suitably enabled or disabled. Using the first processing unit in Fig. 11 as an example, in addition to the connection channel 1153, the reaction reservoir 1152 is also coupled to a connection channel 1156 directing to the waste reservoir 1124. In an embodiment, the connection channel 1153 has a higher resistance than the connection channel 1156, for example, by having a smaller cross-section area than the connection channel 1156. However, the connection channel 1156 includes a valve 1157. When the valve 1157 is closed, the connection channel 1156 is closed, then liquid can be forced to the higher resistance connection channel 1153. When the valve 1157 is open, liquid can flow through the connection channel 1156 to the waste reservoir 1124.

[0165] It is also noted that the four processing units can be configured in a same manner or can be configured in different manners. In the Fig. 11 example, the first, second and third processing units are configured in a same manner, and the fourth processing unit is

configured differently from the other processing units. For example, each of the first, second and third processing units includes a reaction reservoir in the first domain 1111a. In addition, corresponding connection channels, such as the connection channels 1153, 1163 and 1173, are suitably routed, such as zigzagged, to have substantially the same length. Thus, the first, second and third processing units can be used to perform DNA analysis for three samples simultaneously. The fourth processing unit does not include a reaction reservoir in the first domain 1111a. Thus, the fourth processing unit can be used to perform DNA analysis for a sample that does not need PCR amplification, or the PCR amplification for the sample is suitably performed previously.

[0166] It is also noted that a multiple-sample microfluidic chip can include multiple first domains, and/or second domains. In an example, a multiple-sample microfluidic chip may suitably include four sets of the schematic diagram in Fig. 11. Then, the multiple-sample microfluidic chip can be used to simultaneously perform DNA analysis for twelve samples, or can be used to simultaneously perform electrophoretic separation for sixteen samples.

[0167] Of course, a multiple-sample microfluidic chip can be configured to repeat the structure in a single sample microfluidic chip, such as the microfluidic chip 311. The repeated structures may be coupled together, or may be independent of each other. In an example, two structures are thermally coupled together. For example, the PCR reaction reservoirs of the two structures are thermally coupled together. In another example, two structures are fluidically coupled together. For example, the two structures share a same inlet. In another example, the repeated structures are independent of each other. For example, the PCR reaction reservoirs of the repeated structures are thermally isolated, thus thermal cycles can be independently induced for the PCR reaction reservoirs.

[0168] Accordingly, a DNA analyzer can be suitably configured for multiple-sample DNA analysis. For example, a thermal module of the DNA analyzer has a capability to generate thermal cycles within multiple first domains on a multiple-sample microfluidic chip, and the thermal module can be suitably configured to suit a multiple-sample microfluidic chip in use. In an embodiment, a thermal module of the DNA analyzer includes a halogen light bulb to direct heat to a first domain, such as the first domain 1111a, including multiple thermally coupled reaction reservoirs for PCR amplification. In another embodiment, a thermal module of the DNA analyzer includes multiple heat sources that can independently direct heat to thermally isolated reaction reservoirs. In another example, a detection module of the DNA analyzer has a capability to detect fluorescence from sixteen separation channels.

The detection module can be suitably configured to suit a multiple-sample microfluidic chip in use.

(0169] Fig. 12 shows a block diagram of an exemplary detection module 1250 coupled with an exemplaiy sample cartridge 1215 having a microfluidic chip 1200 according to an embodiment of the disclosure. The detection module 1250 can be suitably installed in a DNA analyzer, such as the DNA analyzer 100, or the DNA analyzer 400. Further, the detection module 1250 can be coupled with other components, such as a processor 1271. The detection module 1250 includes a light source module 1251, an active optics module 1253, and a detector 1290. These elements are coupled together using optical fibers.

[0170] The microfluidic chip 1200 includes multiple separation channels, for example, separation channel-A to separation channel-D. The multiple separation channels can be configured to perform, in parallel, electrophoretic separation of multiple DNA samples. In an embodiment, the microfluidic chip 1200 is configured identically or equivalently to the microfluidic chip 1100 to simultaneously perform integrated DNA analysis for multiple samples; the description of these components has been provided above and will be omitted here for clarity purposes. In another embodiment, the microfluidic chip 1200 includes the multiple separation channels and other suitable structures to merely perform electrophoretic separation of multiple DNA samples.

[0171] The detection module 1250 utilizes certain components that are identical or equivalent to those used in the detection module 750; the description of these components has been provided above and will be omitted here for clarity purposes. However, in this embodiment, the active optics module 1253 includes multiple optic assemblies, and each optic assembly includes a set of optic elements and a motion control module. For example, a first optic assembly includes a set of optical elements 1280-A and a motion control module 1256-A; a second optic assembly includes a set of optical elements 1280-B and a motion control module 1256-B; a third optic assembly includes a set of optical elements 1280-C and a motion control module 1256-C; and a fourth optic assembly includes a set of optical elements 1280-D and a motion control module 1256-D.

[0172] The light source module 1251 can include any suitably light emitting device, such as an argon-ion laser device, a solid state laser, a laser diode (LD), and the like, to provide light beams to the multiple optic assemblies. In an example, the light source module 1251 includes a laser module, such as a Coherent Sapphire optically pumped semiconductor laser (OPSL) outputting a laser beam of 488 nm wavelength. Further, the light source module

1251 includes a splitter configured to split the laser beam into multiple laser beams. The multiple laser beams are respectively provided to the multiple optic assemblies via the input optical fiber-A to input optical fiber-D.

[0173] In another example, the light source module 1251 includes multiple sets of LDs coupled with suitable optic elements to generate the multiple input light beams. The multiple light beams are respectively provided to the multiple optic assemblies via the input optical fiber-A to input optical fiber~D.

[0174] Each optic assembly in Fig. 12 utilizes certain components that are identical or equivalent to those used in the optic assembly in Fig. 7; the description of these components has been provided above and will be omitted here for clarity purposes. Each optic assembly receives an input light beam from the light source module 1251 via an input optical fiber, and provides an output light beam to the detector 1290 via a group of output optical fibers.

[0175] The detector 1290 utilizes certain components that are identical or equivalent to those used in the detector 1090; the description of these components has been provided above and will be omitted here for clarity purposes. However, in an embodiment, the connector 1291 stacks all the output optical fibers in the four groups of output optical fibers vertically with space between groups to form a broken vertical slit. Specifically, the connector 1291 stacks optical fibers within a group together vertically as the connector 1091, and stacks the four groups vertically with space between groups. Thus, each section in the broken vertical slit corresponds to an output light beam collected from a separation channel. In an example, the dispersive element 1293 is a grating element that has a large number of closely spaced vertical slits constituting a grating. The dispersive element 1293 causes spectral dispersion to spatially spread fluorescence components in the broken vertical slit by wavelengths. It is noted that, for ease of illustration, the spectral dispersion onto a detection surface of the CCD system 1298 is shown in the horizontal direction. The spread fluorescence components are imaged onto the CCD system 1298 at different horizontal locations. The CCD system 1298 includes an array of photo sensitive devices configured to detect light intensities at the different horizontal locations and vertical regions. The vertical region information can be used to identical separation channels, and the light intensities, and the horizontal location information can be used to identify fluorescence labels and to identify DNA fragments.

[0176] It is noted that, in another embodiment, the connector 1291 may stack all the output optical fibers in the four groups of output optical fibers vertically in a line without any space between the groups.

[0177] While the invention has been described in conjunction with the specific embodiments thereof that are proposed as examples, it is evident that many alternatives, modifications, and variations will be apparent to those skilled in the art. Accordingly, embodiments of the invention as set forth herein are intended to be illustrative, not limiting. There are changes that may be made without departing from the scope of the invention.

WHAT IS CLAIMED IS:

1. An apparatus, comprising:

a first optical device comprising:

an illuminating path that directs a first input light beam received from a light source to a first separation channel of a microfluidic chip, the first input light beam causing fluorescent labels attached on DNA fragments in the first separation channel to emit a first fluorescence light; and

a detecting path that collects and directs the first fluorescent light to a first plurality of optical fibers; and

a spectrometer configured to receive the first fluorescent light from the plurality of optical fibers and detect fluorescent components in the first fluorescent light.

2. The apparatus of claim 1, wherein:

the illuminating path is configured to receive the first input light beam from the light source via an input optical fiber.

3. The apparatus of claim 1, wherein the first optical device further comprises:

a first set of optic elements; and

a first motion control module configured to align the first set of optic elements to the first separation channel.

4. The apparatus of claim 3, wherein the first motion control module is configured to align the first set of optic elements based on detection output of the spectrometer.

5. The apparatus of claim 1, wherein the first optical device further comprises:

an objective lens configured to focus the first input light beam to the first separation channel based on detection output of the spectrometer.

6. The apparatus of claim 2, wherein the first optical device comprises:

an optical fiber connector configured to connect the first input optical fiber and the first plurality of output fibers with the first optical device.

7. The apparatus of claim 6, wherein

the optical fiber connector is configured to connect the first input optical fiber at a center position, and the first plurality of output fibers around the center position.

8. The apparatus of claim 2, wherein the first optical device comprises:

an input optical fiber connector configured to connect the first input optical fiber with the first optic assembly; and

an output optical fiber connector configured to connect the first plurality of output fibers with the first optic assembly.

9. The apparatus of claim 8, wherein the first optical device comprises:

a dichroic splitter configured split the first input light beam and the first fluorescent light.

10. The apparatus of claim 9, wherein the first optical device comprises:

a filter configured to filter out fluorescence in the first input light beam.

11. The apparatus of claim 1, wherein the spectrometer further comprises:

an optical fiber connector configured to connect the first plurality of output optical fibers to the spectrometer.

12. The apparatus of claim 1, wherein the spectrometer further comprises:

a dispersive element configured to spatially separate the fluorescent components; and

an array of photo detection units configured to detect the spatially separated fluorescent components.

13. The apparatus of claim 12, wherein the array of photo detection units is within a charge-coupled device (CCD) system.

14. The apparatus of claim 2, further comprising:

a second optical device comprising:

an illuminating path that directs a second input light beam received from the light source to a second separation channel of the microfluidic chip, the second input light beam causing fluorescent labels attached on DNA fragments in the second separation channel to emit a second fluorescent light; and

a detecting path that collects and directs the second fluorescent light to a second plurality of optical fibers.

15. The apparatus of claim 14, wherein the spectrometer comprises:

an optical fiber connector configured to connect the first plurality of output optical fibers and the second plurality of output optical fibers with the spectrometer.

16. The apparatus of claim 15, wherein

the optical fiber connector is configured to stack the first plurality of output optical fibers and the second plurality of output optical fibers in a line.

17. A method, comprising:

directing, by an illuminating path, a first input light beam to a first separation channel of a microfluidic chip, the first input light beam causing fluorescent labels attached on DNA fragments in the first separation channel to emit a first fluorescent light;

collecting the first fluorescent light;

transmitting, by a first plurality of output optical fibers, the first fluorescent light to a spectrometer; and

detecting, by the spectrometer, fluorescent components in the first fluorescent light.

18. The method of claim 17, further comprising:

aligning a first set of optic elements to the first separation channel based on detection output of the spectrometer.

19. The method of claim 17, further comprising:

transmitting, by a first input optical fiber, the first input light beam from a light source to the illuminating path.

20. The method of claim 17, further comprising:

splitting the first input light beam and the first output light beam to pass at least one different optic element.

21. The method of claim 17, further comprising:

filtering out fluorescence in the first input light beam.

22. The method of claim 17, wherein detecting, by the spectrometer, the fluorescent components in the first output light beam further comprises:

spatially separating the fluorescent components;

detecting, by an array of photo detection units, the spatially separated fluorescent components.

23. A DNA analyzer, comprising:

an interface for coupling a microfluidic chip to the DNA analyzer, wherein the microfluidic chip includes a first separation channel for electrophoretic separation of DNA fragments in a first sample;

a first optical device comprising:

an illuminating path that directs a first input light beam received from a light source to the first separation channel of the microfluidic chip, the first input light beam causing fluorescent labels attached on DNA fragments in the first separation channel to emit a first fluorescence light; and

a detecting path that collects and directs the first fluorescent light to a first plurality of optical fibers; and

a spectrometer configured to receive the first fluorescent light from the plurality of optical fibers and detect fluorescent components in the first fluorescent light.

24. The DNA analyzer of claim. 23, wherein

the illuminating path is configured to receive the first input light beam from the light source via a first input optical fiber.

25. The DNA analyzer of claim 23, wherein the first optical device further comprises:

a first set of optic elements; and

a first motion control module configured to adjust the first set of optic elements to align the first set of optic elements to the first separation channel.

26. The DNA analyzer of claim 25, wherein the first motion control module is configured to adjust the first set of optic elements based on detection output of the spectrometer.

27. The DNA analyzer of claim 23, wherein the first optical device further comprises:

an objective lens configured to focus the first input light beam to the first separation channel based on detection output of the spectrometer.

28. The DNA analyzer of claim 24, wherein the first optical device comprises:

an optical fiber connector configured to connect the first input optical fiber and the first plurality of output fibers with the first optical device.

29. The DNA analyzer of claim 28, wherein

the optical fiber connector is configured to connect the first input optical fiber at a center position, and connect the first plurality of output fibers around the center position.

30. The DNA analyzer of claim 24, wherein the first optical device comprises:

an input optical fiber connector configured to connect the first input optical fiber with the first optical device; and

an output optical fiber connector configured to connect the first plurality of output fibers with the first optical device.

31. The DNA analyzer of claim 30, wherein the first optical device comprises;

a dichroic splitter configured split the first input light beam and the first output light beam to pass at least one different optic element.

32. The DNA analyzer of claim 31, wherein the first optical device comprises:

a filter configured to filter out fluorescence in the first input light beam.

33. The DNA analyzer of claim 23, wherein the spectrometer further comprises:

an optical fiber connector configured to connect the first plurality of output optical fibers to the spectrometer.

34. The DNA analyzer of claim 23, wherein the spectrometer further comprises:

a dispersive element configured to spatially separate the fluorescent components; and

an array of photo detection units configured to detect the spatially separated fluorescent components.

35. The DNA analyzer of claim 34, wherein the array of photo detection units is within a charge coupled device (CCD) system.

36. The DNA analyzer of claim 24, further comprising:

a second optical device comprising:

an illuminating path that directs a second input light beam received from the light source to a second separation channel of the microfluidic chip, the second input light beam causing fluorescent labels attached on DNA fragments in the second separation channel to emit a second fluorescence light; and

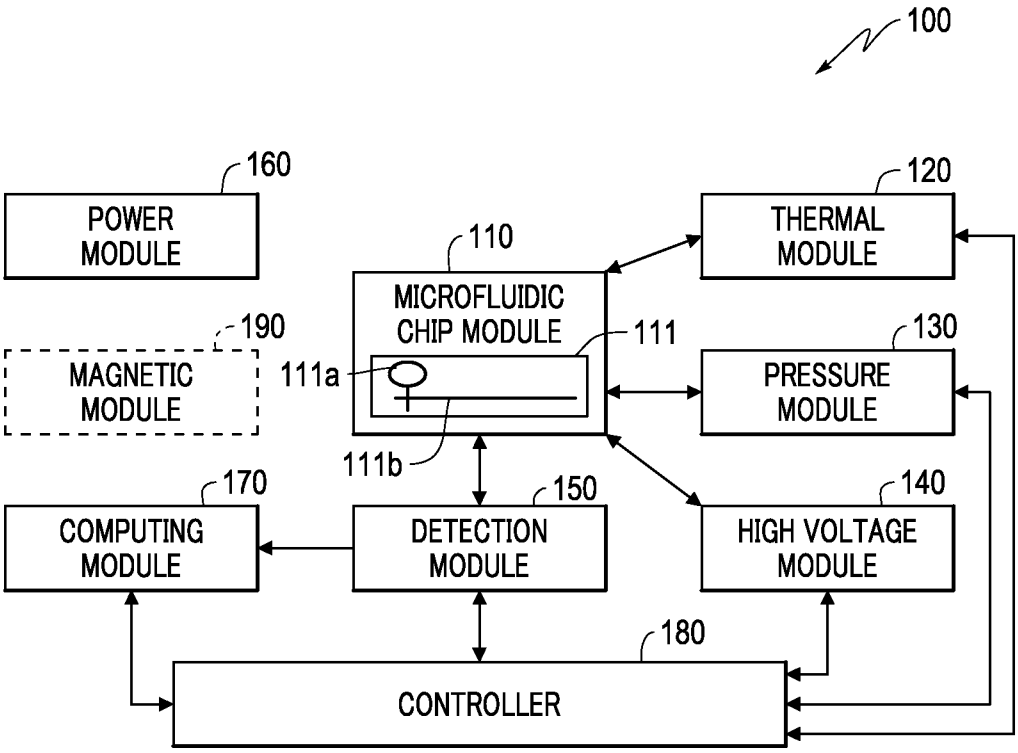
a detecting path that collects and directs the second fluorescent light to a second plurality of optical fibers.

. 37. The DNA analyzer of claim 36, wherein the spectrometer comprises:

an optical fiber connector configured to connect the first plurality of output optical fibers and the second plurality of output optical fibers with the spectrometer.

38. The DNA analyzer of claim 37, wherein

the optical fiber connector is configured to stack the first plurality of output optical fibers and the second plurality of output optical fibers in a line.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120
THERMAL MODULE
110
MICROFLUIDIC CHIP MODULE
111
190
MAGNETIC MODULE
111a
130
PRESSURE MODULE
111b
170
150
140
COMPUTING MODULE
DETECTION MODULE
HIGH VOLTAGE MODULE
180
CONTROLLER

FIG. 1

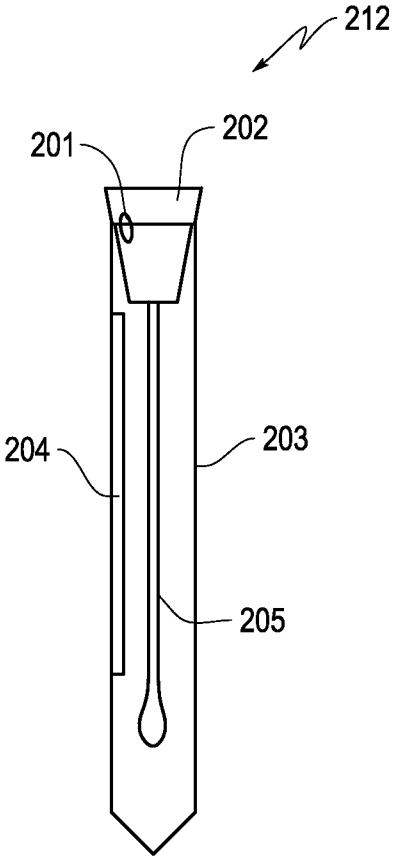
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FIG. 2A

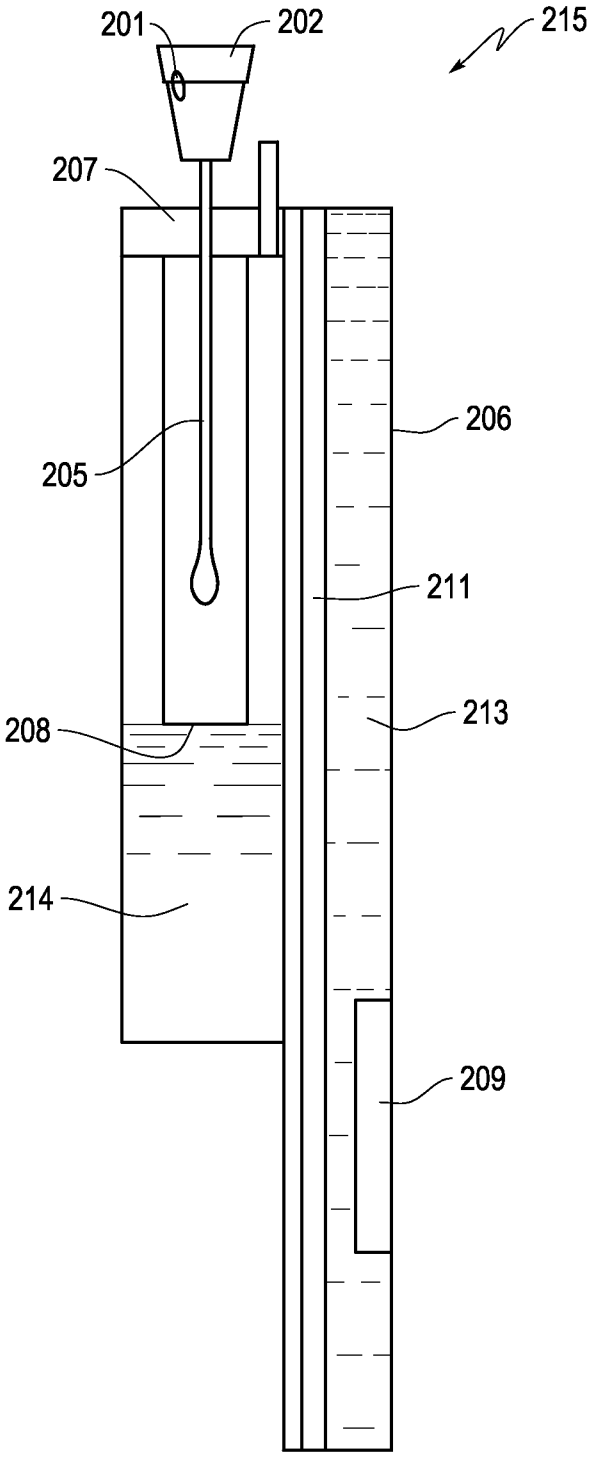
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FIG. 2B

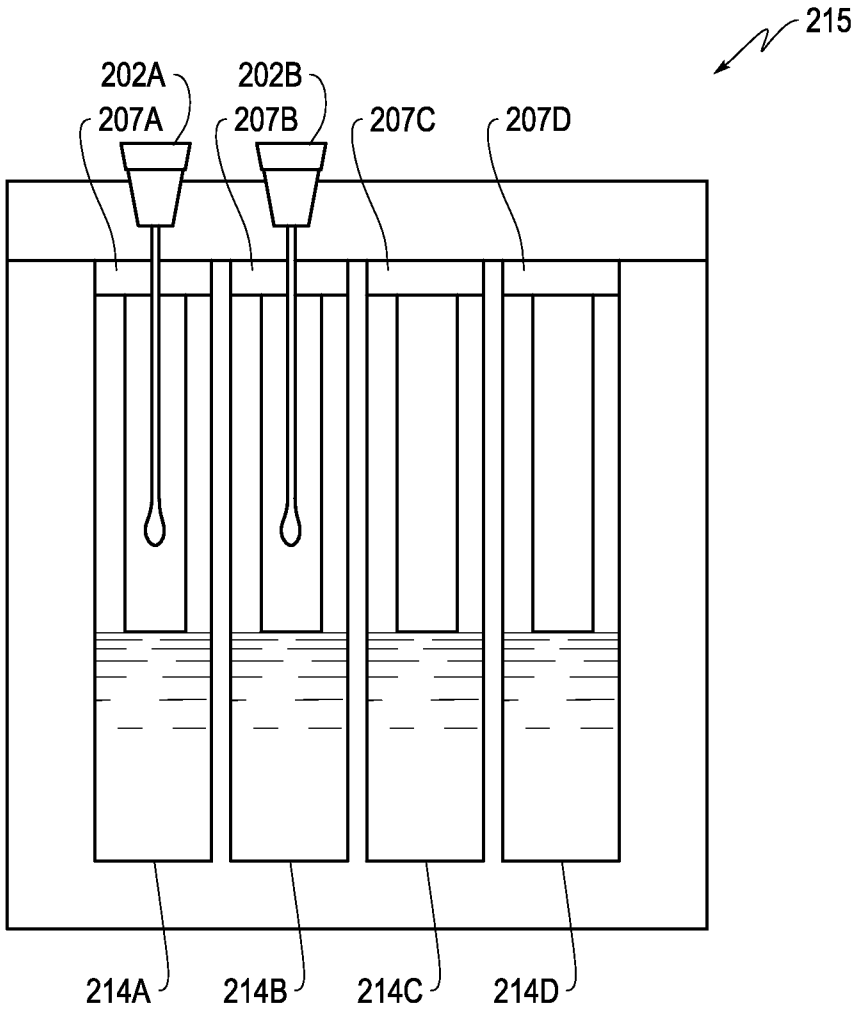

FIG. 2C

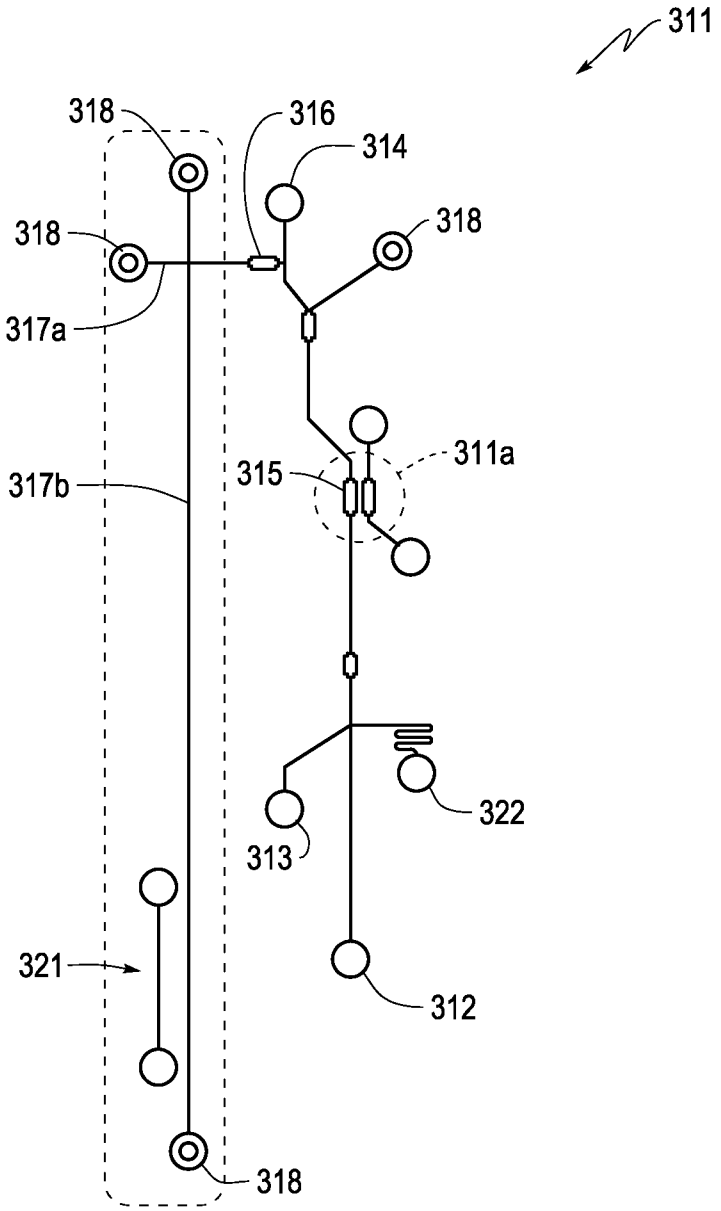

FIG. 3

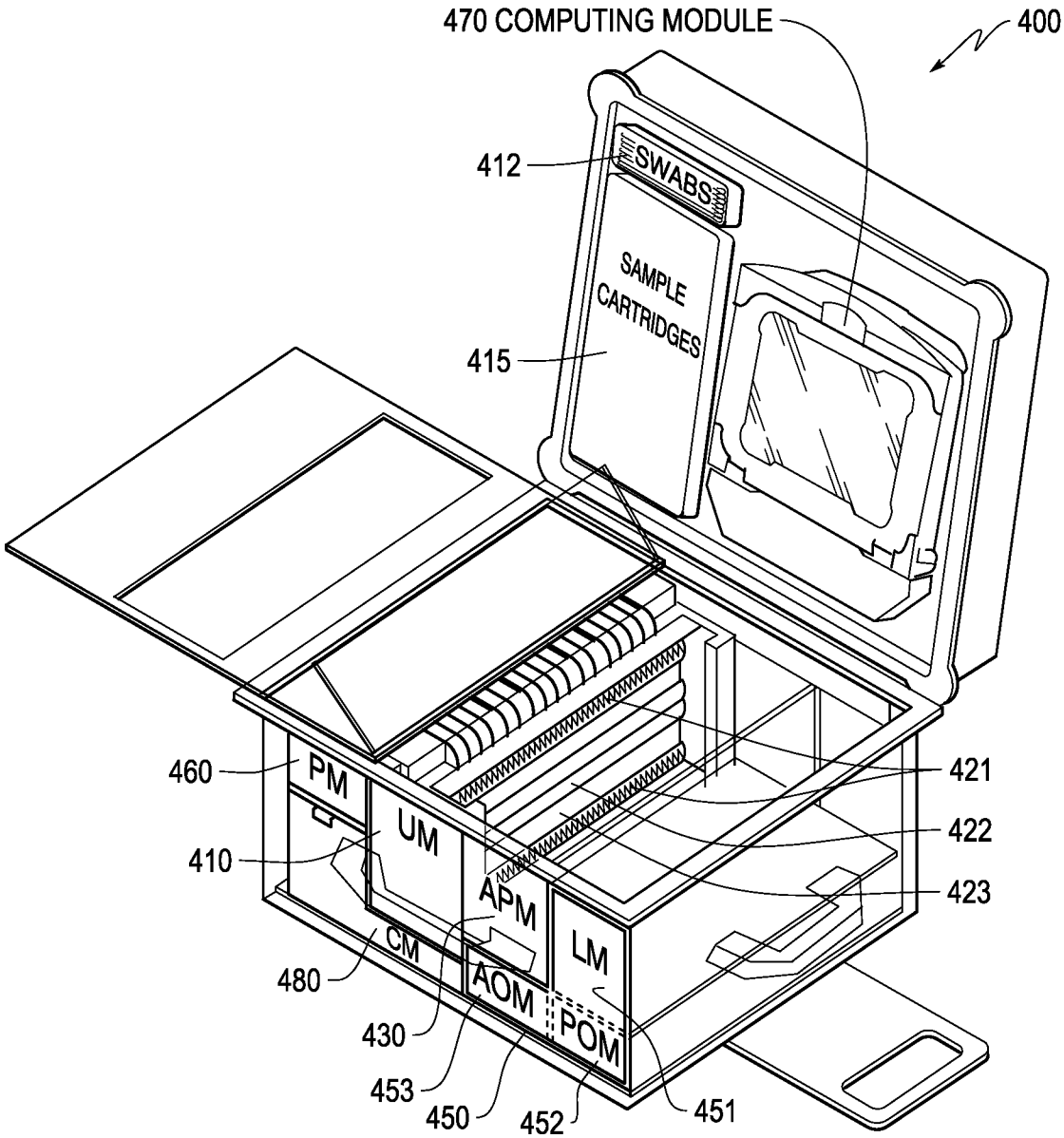
470 COMPUTING MODULE
400
412
SWABS
SAMPLE CARTRIDGES
415
460
PM
410
UM
APM
CM
480
AOM
LM
POM
430
453
450
452
451
421
422
423

FIG. 4

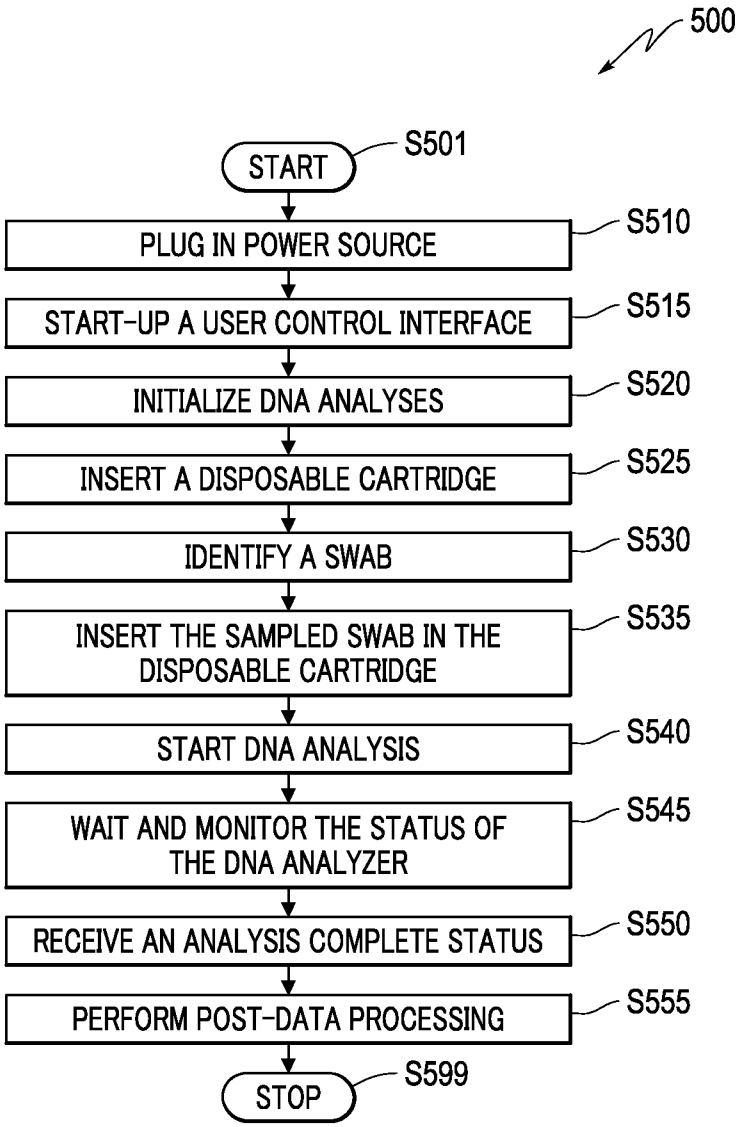
500
START
S501
PLUG IN POWER SOURCE
S510
START-UP A USER CONTROL INTERFACE
S515
INITIALIZE DNA ANALYSES
S520
INSERT A DISPOSABLE CARTRIDGE
S525
IDENTIFY A SWAB
S530
INSERT THE SAMPLED SWAB IN THE DISPOSABLE CARTRIDGE
S535
START DNA ANALYSIS
S540
WAIT AND MONITOR THE STATUS OF THE DNA ANALYZER
S545
RECEIVE AN ANALYSIS COMPLETE STATUS
S550
PERFORM POST-DATA PROCESSING
S555
STOP
S599

FIG. 5

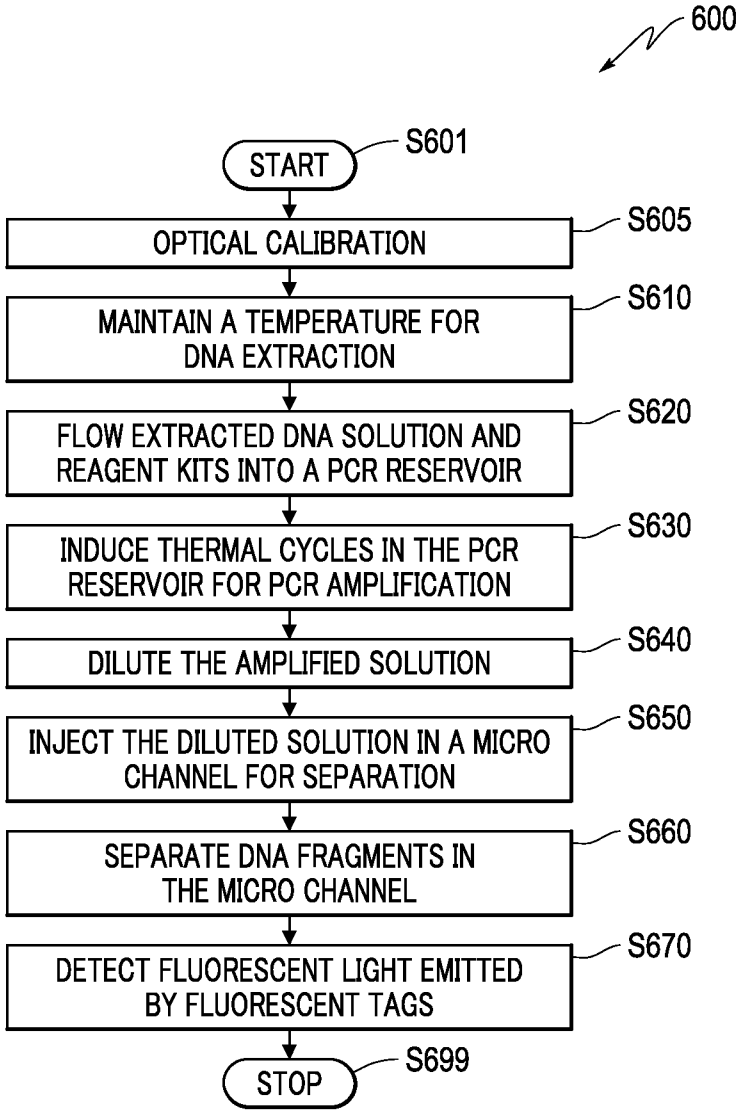
600
START
S601
OPTICAL CALIBRATION
S605
MAINTAIN A TEMPERATURE FOR DNA EXTRACTION
S610
FLOW EXTRACTED DNA SOLUTION AND REAGENT KITS INTO A PCR RESERVOIR
S620
INDUCE THERMAL CYCLES IN THE PCR RESERVOIR FOR PCR AMPLIFICATION
S630
DILUTE THE AMPLIFIED SOLUTION
S640
INJECT THE DILUTED SOLUTION IN A MICRO CHANNEL FOR SEPARATION
S650
SEPARATE DNA FRAGMENTS IN THE MICRO CHANNEL
S660
DETECT FLUORESCENT LIGHT EMITTED BY FLUORESCENT TAGS
S670
STOP
S699

FIG. 6

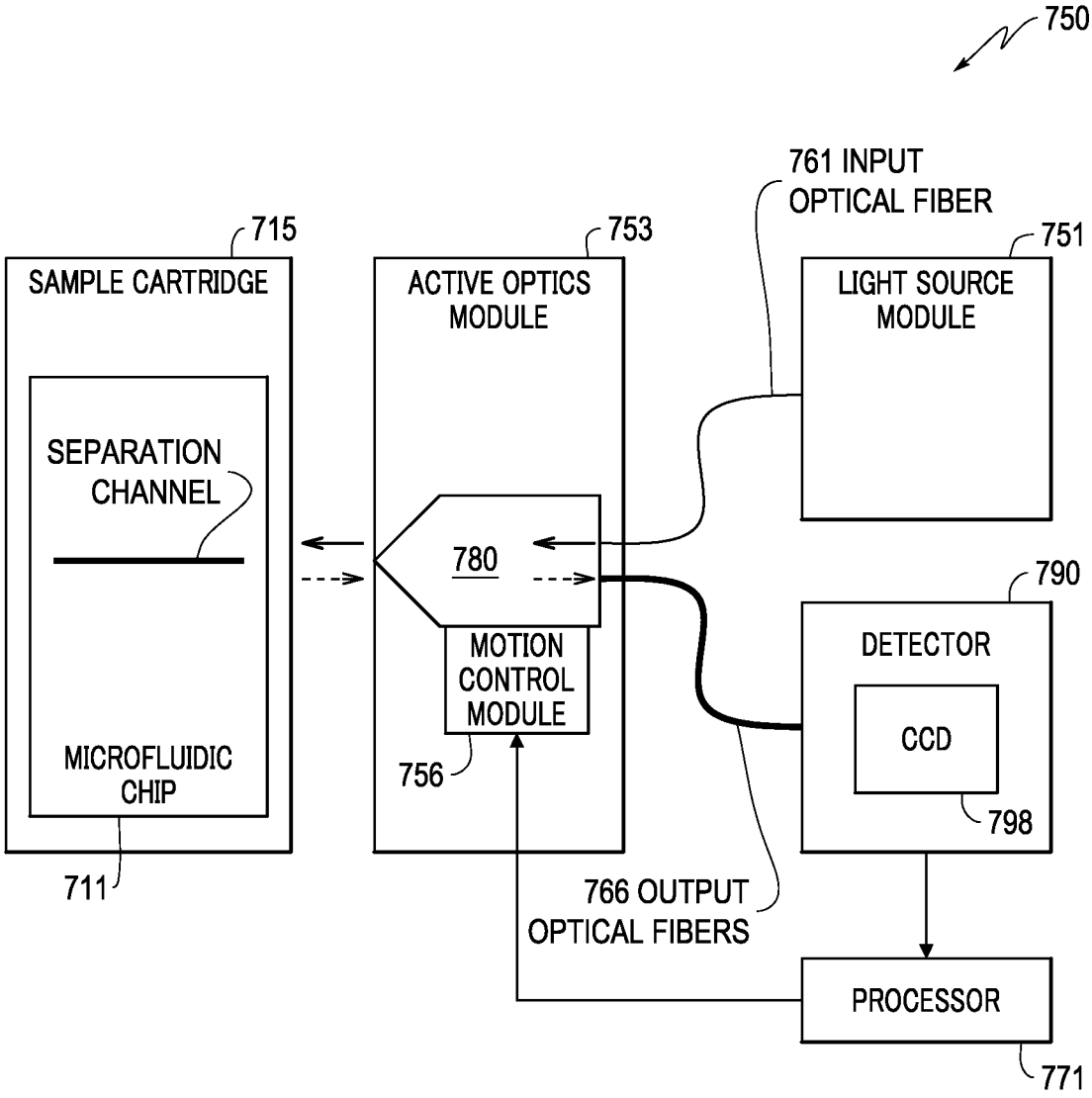
750
761 INPUT OPTICAL FIBER
715
SAMPLE CARTRIDGE
753
ACTIVE OPTICS MODULE
751
LIGHT SOURCE MODULE
SEPARATION CHANNEL
780
790
DETECTOR
MOTION CONTROL MODULE
CCD
MICROFLUIDIC CHIP
756
798
711
766 OUTPUT OPTICAL FIBERS
PROCESSOR
771

FIG. 7

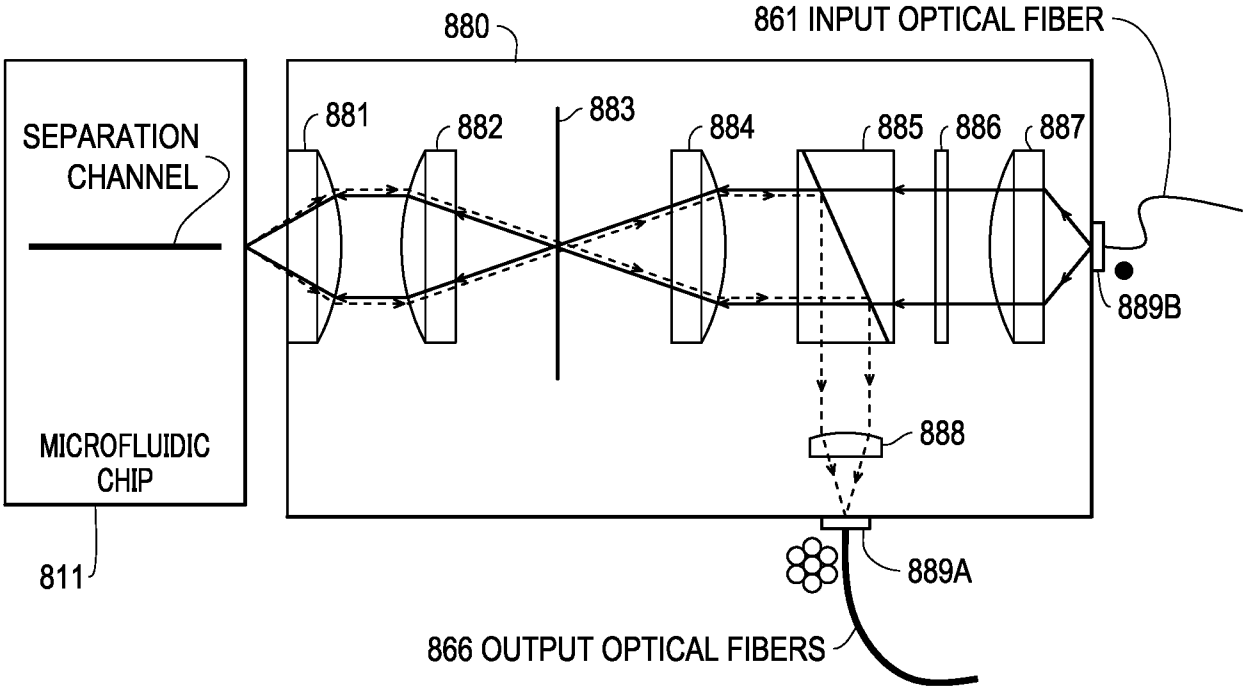
880
861 INPUT OPTICAL FIBER
SEPARATION CHANNEL
881
882
883
884
885
886
887
889B
888
MICROFLUIDIC CHIP
811
889A
866 OUTPUT OPTICAL FIBERS

FIG. 8

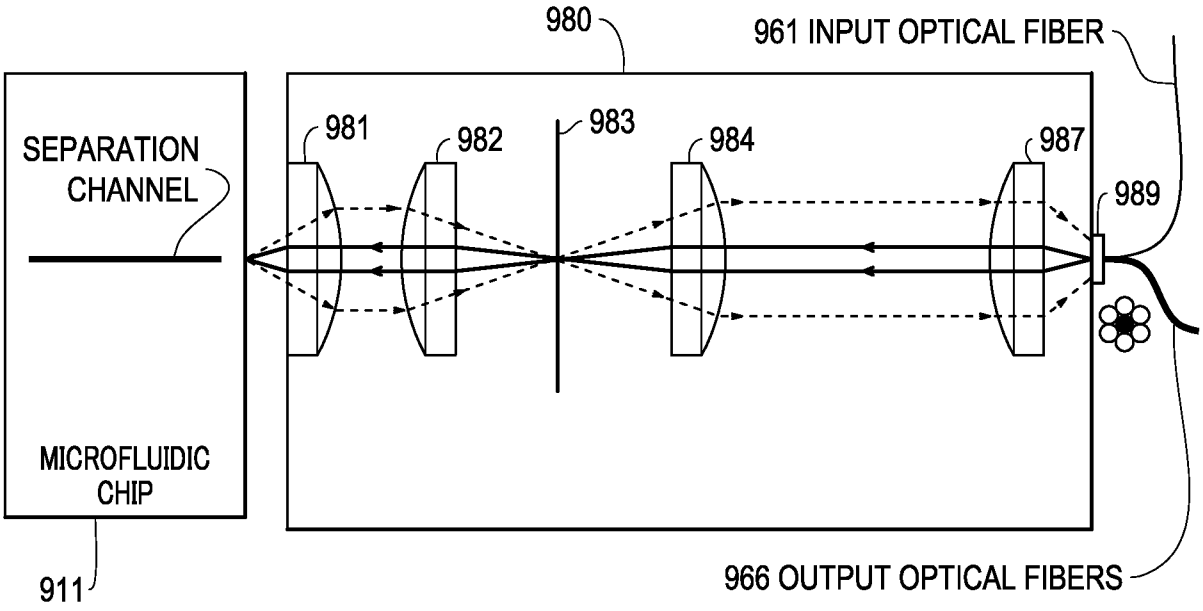
980
961 INPUT OPTICAL FIBER
SEPARATION CHANNEL
981
982
983
984
987
989
MICROFLUIDIC CHIP
911
966 OUTPUT OPTICAL FIBERS

FIG. 9

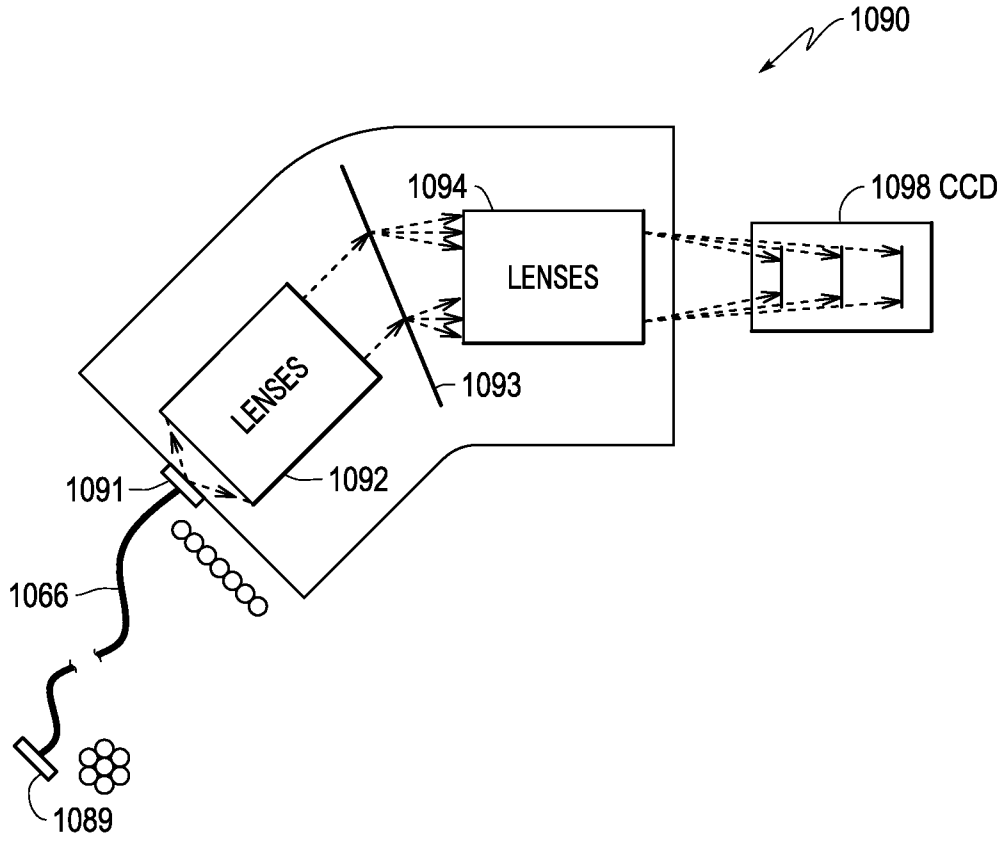

FIG. 10

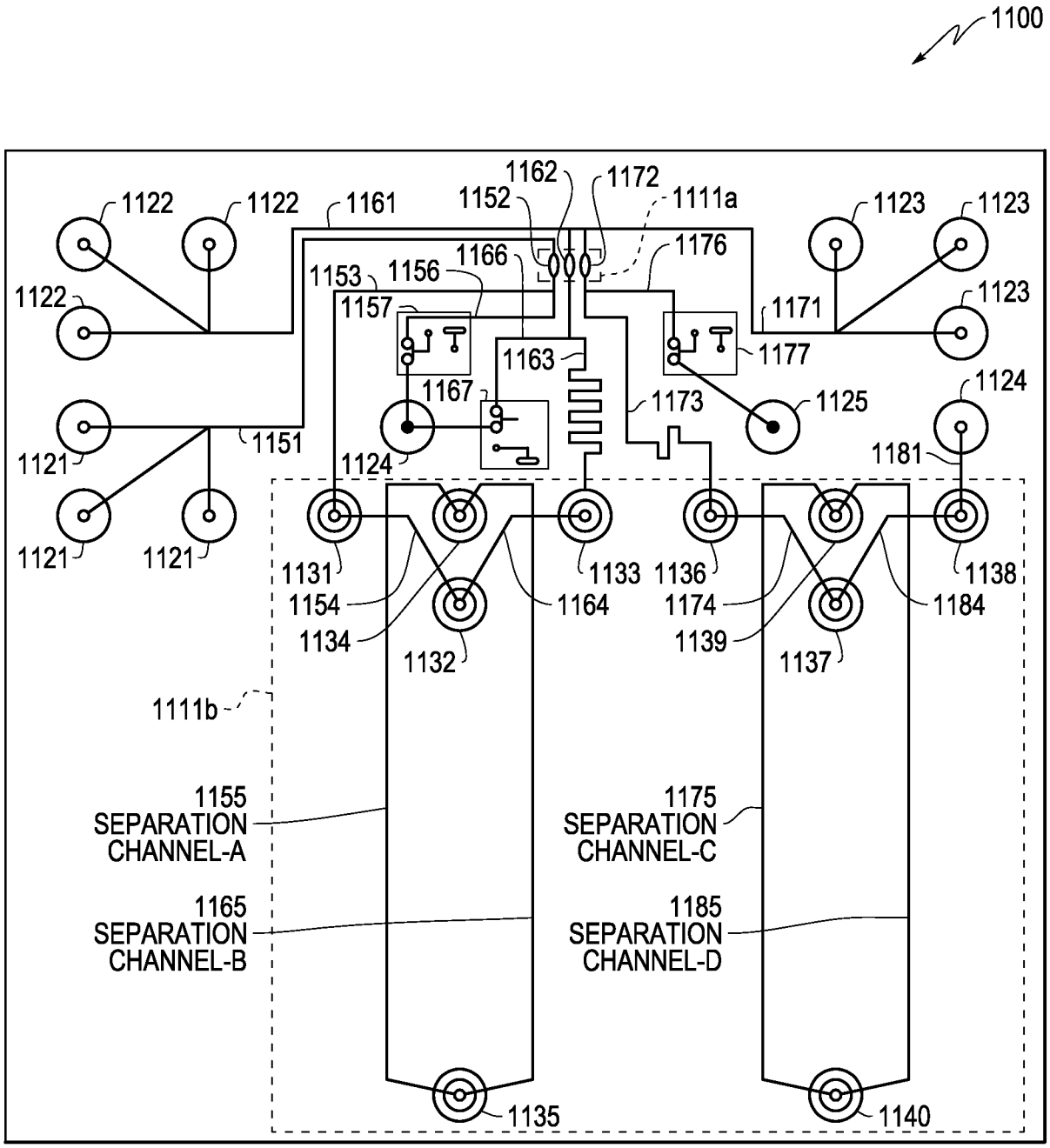
1100
1162
1172
1152
1111a
1122
1122
1161
1123
1123
1176
1166
1153
1156
1122
1157
1171
1123
1163
1177
1167
1173
1125
1124
1151
1181
1121
1124
1121
1121
1131
1133
1136
1138
1154
1164
1174
1184
1134
1132
1139
1137
1111b
1155
SEPARATION
CHANNEL-A
1175
SEPARATION
CHANNEL-C
1165
SEPARATION
CHANNEL-B
1185
SEPARATION
CHANNEL-D
1135
1140

FIG. 11

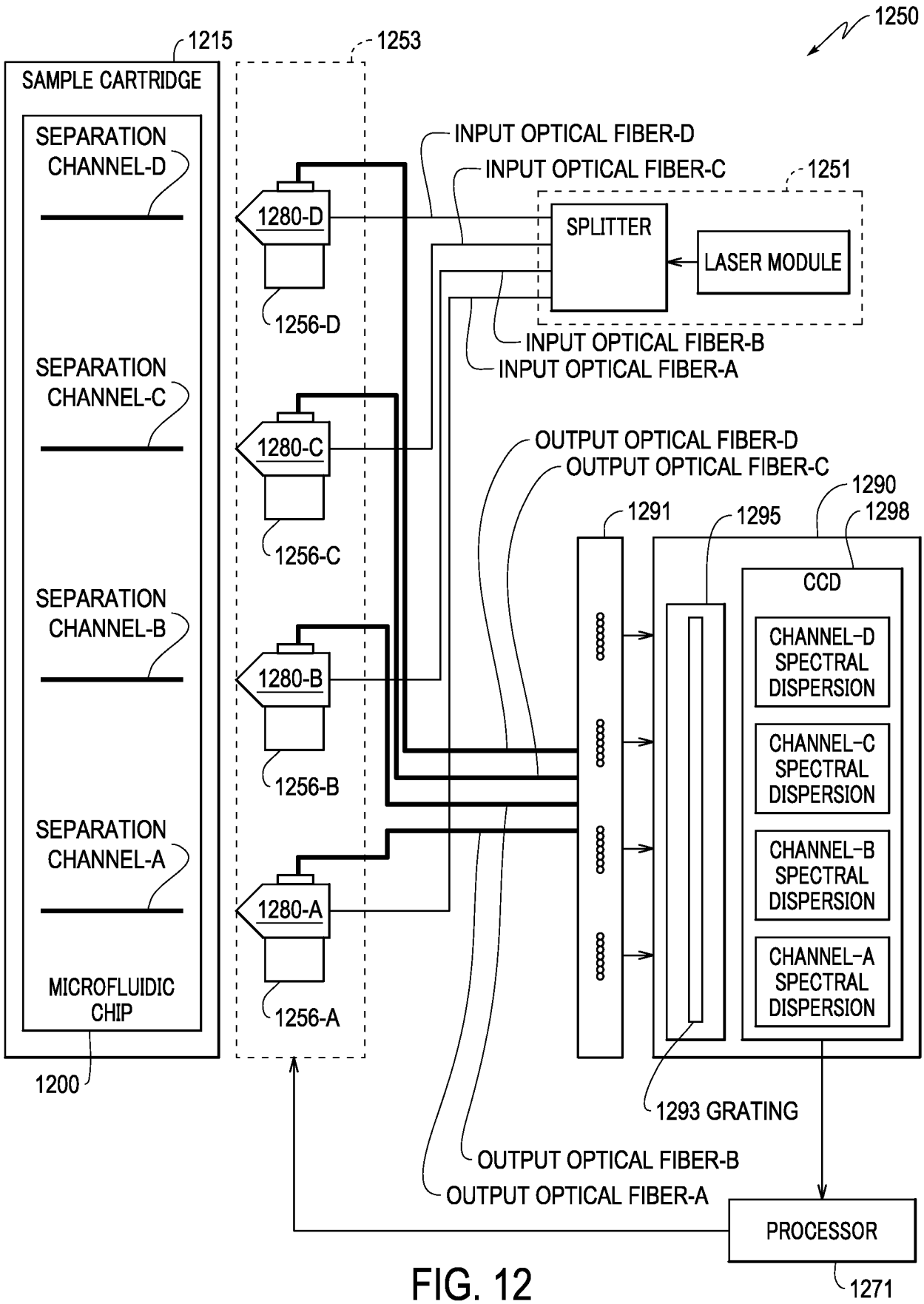
1250
1215
1253
SAMPLE CARTRIDGE
SEPARATION CHANNEL-D
SEPARATION CHANNEL-C
SEPARATION CHANNEL-B
SEPARATION CHANNEL-A
MICROFLUIDIC CHIP
1200
1280-D
1256-D
1280-C
1256-C
1280-B
1256-B
1280-A
1256-A
INPUT OPTICAL FIBER-D
INPUT OPTICAL FIBER-C
1251
SPLITTER
LASER MODULE
INPUT OPTICAL FIBER-B
INPUT OPTICAL FIBER-A
OUTPUT OPTICAL FIBER-D
OUTPUT OPTICAL FIBER-C
1290
1291
1295
1298
CCD
CHANNEL-D SPECTRAL DISPERSION
CHANNEL-C SPECTRAL DISPERSION
CHANNEL-B SPECTRAL DISPERSION
CHANNEL-A SPECTRAL DISPERSION
1293 GRATING
OUTPUT OPTICAL FIBER-B
OUTPUT OPTICAL FIBER-A
PROCESSOR
1271

FIG. 12

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2011/056357

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N21/64 G01J3/00 G01N27/447
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01N G01J BOIL

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal , BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2004/245445 Al (SUZUKI M0T0HI K0 [JP]) 9 December 2004 (2004-12-09) paragraphs [0003] , [0029] , [0031] , [0032] , [0033] , [0034] f i gure 1	1,5, 12, 13,22, 27,34,35
X	US 2010/243916 Al (MAURER SCOTT [US] ET AL) 30 September 2010 (2010-09-30)	1-3,6, 8-13, 17, 19-21, 23-25, 28,30-35
Y	f i gure 1 paragraphs [0024] , [0026] , [0031] , [0027] , [0029] , [0038] , [0039]	4,5, 7, 14-16, 18,26, 27,29, 36-38

-/--

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 January 2012	31/01/2012

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	D'Al essandro, Davi de

3

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PHILLIPS TERRY M: "Analysis of single-cell cultures by immunoaffinity capillary electrophoresis with laser-induced fluorescence detection", LUMINESCENCE (CHICHESTER), vol. 16, no. 2, March 2001 (2001-03), pages 145-152, XP55016910, ISSN: 1522-7235 figure 2 page 147, right-hand column, last paragraph --- MALCIK N ET AL: "The performance of a microchip-based fiber optic detection technique for the determination of Ca<2+> ions in urine", SENSORS AND ACTUATORS B: CHEMICAL: INTERNATIONAL JOURNAL DEVOTED TO RESEARCH AND DEVELOPMENT OF PHYSICAL AND CHEMICAL TRANSDUCERS, ELSEVIER S.A, SWITZERLAND, vol. 107, no. 1, 27 May 2005 (2005-05-27), pages 24-31, XP025328330, ISSN: 0925-4005, D0I: 10.1016/J.SNB.2004.09.049 [retrieved on 2005-05-27]	1,13,14, 17,22, 34,35
Y		7,29
A	page 26, right-hand column, last paragraph figure 1 --- US 2010/032582 Al (XIA HUA [US] ET AL) 11 February 2010 (2010-02-11) paragraphs [0036], [0046], [0051] figures 1,2,4 --- US 2003/038248 Al (MAHER KEVIN [US] ET AL) 27 February 2003 (2003-02-27) paragraphs [0008], [0011], [0055] figure 2 --- W0 99/61894 Al (ANALYTIC0N AG BI0TECHN0L0GIE P [DE]; GOD RALF [DE]; MUELLER KUHRT LUTZ) 2 December 1999 (1999-12-02) page 2, line 32 - page 3, line 9 page 8, line 9 - line 24 --- -/--	12,22 4,5,7, 18,26, 27,29 14-16, 36-38 15,16, 37,38
Y		

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BELLON V ET AL: "FEASIBILITY AND PERFORMANCES OF A NEW, MULTIPLEXED, FAST AND LOW-COST FIBER-OPTIC NIR SPECTROMETER FOR THE ON-LINE MEASUREMENT OF SUGAR IN FRUITS" APPLIED SPECTROSCOPY, THE SOCIETY FOR APPLIED SPECTROSCOPY. BALTIMORE, US, **vol.** 47, **no.** 7, 1 **July** 1993 (1993-07-01), **pages** 1079 - 1083, XP000382930, ISSN: 0003-7028, DOI: 10.1366/00037029344 15255 **figure** 1 **page** 1082, **right-hand column, last line** -----	15,16, 37,38

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2011/056357

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us 2003038248 A1	27-02-2003	NONE	
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