methods can be implemented. One such example environment is that of an optical system, such as that illustrated in FIG. 1A. The example optical system may include a device for obtaining or producing an image of a region. The example outlined in FIG. 1 shows an example imaging configuration of a backlight design implementation.

[0061] As can be seen in the example of FIG. 1A, subject samples are located on sample structure or container 110 (e.g., a flowcell as disclosed herein), which is positioned on a sample stage 170 under an objective lens 142. Light source 160 and associated optics direct a beam of light, such as laser light, to a chosen sample location on the sample container 110. The sample fluoresces and the resultant light is collected by the objective lens 142 and directed to a photo detector 140 to detect the florescence. Sample stage 170 is moved relative to objective lens 142 to position the next sample location on sample container 110 at the focal point of the objective lens 142. Movement of sample stage 170 relative to objective lens 142 can be achieved by moving the sample stage itself, the objective lens, the entire optical stage, or any combination of the foregoing. Further implementations may also include moving the entire imaging system over a stationary sample.

[0062] Fluid delivery module or device 100 directs the flow of reagents (e.g., fluorescent nucleotides, buffers, enzymes, cleavage reagents, etc.) to (and through) sample container 110 and waste valve 120. In particular implementations, the sample container 110 can be implemented as a flowcell that includes clusters of nucleic acid sequences at a plurality of sample locations on the sample container 110. The samples to be sequenced may be attached to the substrate of the flowcell, along with other optional components.

[0063] The system also comprises temperature station actuator 130 and heater/cooler 135 that can optionally regulate the temperature of conditions of the fluids within the sample container 110. Camera system 140 can be included to monitor and track the sequencing of sample container 110. Camera system 140 can be implemented, for example, as a CCD camera, which can interact with various filters within filter switching assembly 145, objective lens 142, and focusing laser/focusing laser assembly 150. Camera system 140 is not limited to a CCD camera and other cameras and image sensor technologies can be used.

[0064] Light source 160 (e.g., an excitation laser within an assembly optionally comprising multiple lasers) or other light source can be included to illuminate fluorescent sequencing reactions within the samples via illumination through fiber optic interface (which can optionally comprise one or more re-imaging lenses, a fiber optic mounting, etc). Low watt lamp 165, focusing laser 150, and reverse dichroic are also presented in the example shown. In some implementations focusing laser 150 may be turned off during imaging. In other implementations, an alternative focus configuration can include a second focusing camera (not shown), which can be a quadrant detector, a Position Sensitive Detector (PSD), or similar detector to measure the location of the scattered beam reflected from the surface concurrent with data collection.

[0065] Although illustrated as a backlit device, other examples may include a light from a laser or other light source that is directed through the objective lens 142 onto the samples on sample container 110. Sample container 110 can be ultimately mounted on a sample stage 170 to provide movement and alignment of the sample container 110 relative to the objective lens 142. The sample stage can have one or more actuators to allow it to move in

For example, the interface baffle may be an aperture shaped to enable light to pass through its center, while obscuring interference from external light sources. EOM 188 may also include an objective, a tube lens, and or other optical components configured to shape, direct, and/or focus fluorescent light excited by the one or more light sources of LGM 182.

[0075] Light passing through EOM 188 may be directed into one of the other adjacent modular subassemblies, for example, CAM 186, through an interface port. CAM 186 may include one or more light sensors. In some implementations, a first light sensor may be configured to detect light from the first light source of LGM 182 (e.g., in a red wavelength), and a second light sensor may be configured to detect light from the second light source of LGM 182 (e.g., a green wavelength). The light sensors of CAM 186 may be positioned within an enclosure in a configuration such as to detect light from two incident light beams wherein the incident light beams may be spaced apart by a predetermined distance (e.g., between 1 mm and 10 mm) based on the pitch of the two sensors. In some examples, the first light sensor and the second light sensor may be spaced apart from each other by between 3 mm and 8 mm. The light sensors may have a detection surface sufficiently sized to allow for beam drift, for example, due to thermal effects or mechanical creep. Output data from the light sensors of CAM 186 may be communicated to a computer processor. The computer processor may then implement computer software program instructions to analyze the data and report or display the characteristics of the beam (e.g., focus, shape, intensity, power, brightness, position) to a graphical user interface (GUI), and/or automatically control actuators and laser output to optimize the laser beam. Beam shape and position may be optimized by actuating internal optics of system 180 (e.g., tilting mirrors, articulating lenses, etc.).

[0076] FTM 184 may also couple to EOM 188 through an interface port. FTM 184 may include instruments to detect and analyze the alignment and focus of all of the optical components in system 180. For example, FTM 184 may include a light source (e.g., a laser), optics, and a light sensor, such as a digital camera or CMOS chip. The laser may be configured to transmit light source and optics may be configured to direct light through optical components in system 180 and the light sensor may be configured to detect light being transmitted through optical components in system 180 and output data to a computer processor. The computer processor may then implement computer software program instructions to analyze the data and report or display the characteristics of the laser beam (e.g., focus, intensity, power, brightness, position) to a graphical user interface (GUI), and/or automatically control actuators and laser output to optimize the laser beam. In some examples, FTM 184 may include a cooling system, such as an air or liquid cooling system as known in the art.

[0077] In some implementations, LGM 182 may include light sources that operate at higher powers to also accommodate for faster scanning speeds (e.g., the lasers in LGM 182 may operate at a five times greater power output). Similarly, the light source of laser module may operate at a higher output power and/or may also include a high resolution optical sensor to achieve nanometer scale focus precision to accommodate for faster scanning speeds. The cooling system of FTM 184 may be enhanced to accommodate the additional heat output from the higher powered laser using cooling techniques known in the art.

[0078] In one example, each modular subassembly may mechanically couple to one or more other modular subassemblies, and/or to a precision mounting plate 190. In some

implementations, precision mounting plate 190 may mechanically couple to a stage assembly 192. Stage assembly 192 may include motion dampers, actuators to actuate one or more components within one or more modular subassemblies, cooling systems, and/or other electronics or mechanical components as known in the art.

[0079] The modular subassemblies may be prefabricated, configured, and internally aligned. In some implementations, a control unit may be electronically coupled to stage assembly 192 and communicatively coupled to a user interface to enable automatic or remote manual alignment of one or more modular subassemblies after they have been coupled to precision mounting plate 190. Each modular subassembly may be a field replaceable unit (FRU), such that it may be removed from precision mounting plate 190 and replaced with another functionally equivalent modular subassembly without disturbing the alignment or configuration of the other modular subassemblies in the system.

[0080] Each module is pre-aligned and pre-qualified before integration into system 180. For example, assembly and configuration of LGM 182 may include the mechanical coupling of one or more lasers or laser diodes into an enclosure, and installation of control electronics to operate the lasers or laser diodes. The entire LGM 182 may then be mounted on a test bed and operated to align the laser diodes within the enclosure, as well as any optics or other components. The LGM enclosure may include external mounting structures, such as mounting pins, datum, notches, tabs, slots, ridges, or other protrusions or indentations configured to align the LGM 182 to the test bed, as well as to precision mounting plate 190 when installed in system 180. Once LGM 182 is configured and tested, it may be either installed in a system 180, or packaged and stored or shipped as a field replaceable unit (FRU).

be used for each light beam. In some examples, the beam shaping lens is a Powell lens, such that the light beams are shaped into line patterns.

[0084] LGM 1182 may further include mirrors 1002 and 1004. A light beam generated by light source 1650 may reflect off mirror 1002 as to be directed through an aperture or semi-reflective surface of mirror 1004, and into EOM 1188 through a single interface port. Similarly, a light beam generated by light source 1660 may reflect off of mirror 1003 and mirror 1004 as to be directed into EOM 1188 through a single interface port. In some examples, an additional set of articulating mirrors may be incorporated adjacent to mirror 1004 to provide additional tuning surfaces, for example, as illustrated in FIG. 1H.

[0085] Both light beams may be combined using dichroic mirror 1004. Both light beams may be directed through line forming optics, such as a Powell lens. Mirrors 1002 and 1004 may each be configured to articulate using manual or automated controls as to align the light beams from light sources 1650 and 1660. The light beams may pass through a shutter element 1006. EOM 1188 may include objective 1404 and a z-stage 1024 which moves objective 1404 longitudinally closer to or further away from a target 1192. For example, target 1192 may include a liquid layer 1550 and a translucent cover plate 1504, and a biological sample may be located at an inside surface of the translucent cover plate as well an inside surface of the substrate layer located below the liquid layer. The z-stage may then move the objective as to focus the light beams onto either inside surface of the flowcell (e.g., focused on the biological sample). The biological sample may be DNA, RNA, proteins, or other biological materials responsive to optical sequencing as known in the art. In some implementations, the

PZT mirrors. Similarly, a red laser module may generate a second laser beam that also reflects off of two PZT mirrors and is combined with the first laser beam. Both laser beams may then pass through a Powell lens to generate a line pattern, and then through a shutter, EOM optics, and an objective lens. In some implementations, the laser beams may be defocused using a defocus lens prior to passing through the objective as to increase the line width of the laser beams. Alternatively, the laser beams may be defocused by articulating the objective in the Z-axis. By focusing the laser beams at a focal point beyond the surfaces of the flowcell, the laser lines may be widened as to disperse energy at the sample and avoid photo-saturation, photo-bleaching, and laser damage at high scanning speeds and high laser powers. In some implementations, the line patterns may be increased in width from less than 5 microns to more than 13 microns.

[0094] The LGM alignment system may include control surfaces to adjust or manipulate relative positioning of mirrors 1002 and 1004, as well as the lenses, lasers, or other components or optics in the LGM. For example, adjustments may be made using manual manipulation of control knobs, screws, or other components. In other implementations, one or more of the optical components may be adjusted or manipulated automatically. Automatic control devices may include a motorized translation stage, an actuation device, one or more piezo stages, and/or one or more automatic switch and flip mirrors and lenses. A software interface may be used to control all the devices, test system, calibration, and test procedure. The alignment system includes a beam profiler (e.g., a 2D imaging sensor), imaging lens (replacing EOM objective lens), attenuator, and/or alignment targets. The software interface may be used to output reports for quality control and product evaluation. For example, the

reports may include data generated by the beam profiler relating to beam intensity and profile relative to each alignment configuration of the optical components of the LGM.

[0095] In some implementations, a method for aligning an LGM using an LGM alignment system may include identifying reasonable alignment positions and tolerances for imaging optics, sensors, and mechanics relative to an LGM alignment system. The LGM alignment system is external to the modular optical analytic system. As such, the internal components of the LGM may be assembled and aligned prior to installation in the modular optical analytic system. The internal components of the LGM may also be aligned during a maintenance activity.

[0096] In some implementations, alignment of the LGM optical components may be accomplished using actuated devices for automatic tracking and adjustment during sequencing or between sequencing cycles/runs. For example, the actuated devices can be a piezo stage, a motorized actuator, or similar devices known in the art. The actuated devices may also compensate for drift caused by temperature changes, as well as decay of optical components including lasers, lens, and mounts.

[0097] Each optical component may mechanically couple to an enclosure or optical frame using a mechanical interface with precision contact pads, dowel pins, stoppers, or other precision mechanical mounting surfaces as known in the art.

[0098] FIGS. 2A and 2B are diagrams illustrating precision mounting structures on EOM 188. In several implementations, EOM 188 may include an EOM enclosure 210. EOM 188 may mechanically and optically couple to LGM 182, FTM 184, and CAM 186 (e.g., the enclosure

other signals capable of being exchanged by a given communications interface 924. These signals may be provided to communications interface 924 via a channel 928. This channel 928 may carry signals and may be implemented using a wired or wireless communication medium. Some examples of a channel may include a phone line, a cellular link, an RF link, an optical link, a network interface, a local or wide area network, and other wired or wireless communications channels.

[00128] In this document, the terms "computer program medium" and "computer usable medium" are used to generally refer to media such as, for example, memory 908, storage unit 922, media 914, and channel 928. These and other various forms of computer program media or computer usable media may be involved in carrying one or more sequences of one or more instructions to a processing device for execution. Such instructions embodied on the medium, are generally referred to as "computer program code" or a "computer program product" (which may be grouped in the form of computer programs or other groupings). When executed, such instructions may enable the computing engine 900 to perform features or functions of the disclosed technology as discussed herein.

[00129] While various implementations of the disclosed technology have been described above, it should be understood that they have been presented by way of example only, and not of limitation. Likewise, the various diagrams may depict an example architectural or other configuration for the disclosed technology, which is done to aid in understanding the features and functionality that can be included in the disclosed technology. The disclosed technology is not restricted to the illustrated example architectures or configurations, but the desired features can be implemented using a variety of alternative architectures and

11. The imaging system of claim 2, further comprising a one or more line widening optics to increase the line width of the first light beam and the line width of the second light beam.

12. The imaging system of claim 11, wherein the one or more line widening optics comprises defocus lens, a prism, or a diffuser.

13. The imaging system of claim 11, wherein the one or more line widening optics comprises a Powell lens positioned after a defocus lens in an optical path from the first light source and second light source to the objective lens.

14. The imaging system of claim 2, wherein the line width of the first light beam is increased to lower overall power density of the first light beam on a surface of the sample such that the power density of the first light beam on the surface of the sample is below a photosaturation threshold of a first dye on the sample, and wherein the line width of the second light beam is increased to lower overall power density of the second light beam on a surface of the sample such that the power density of the second light beam on the surface of the sample is below a photosaturation threshold of a second dye on the sample.

15. The imaging system of claim 7, further comprising: a z-stage for articulating the objective to adjust the line width of the first light beam and to adjust the line width of the second light beam.

16. The imaging system of claim 15, further comprising:

a processor; and

a non-transitory computer readable medium with computer executable instructions embedded thereon, the computer executable instructions configured to cause the imaging system to:

determine a quality of a signal from the TDI sensor; and

articulate the objective in the z-axis to adjust the focal point and optimize the quality of the signal from the TDI sensor.

17. A DNA sequencing system, comprising:

a line generation module and an objective lens;

the line generation module comprising:

a plurality of light sources, each light source to emit a light beam; and

one or more line forming optics to shape each light beam into a line; and

wherein the objective lens or the one or more line forming optics are to increase a width of each line at a first surface or a second surface of a flowcell.

18. The system of claim 17, wherein the objective lens is to focus each light beam at a focal point external to an interior surface of the flowcell as to increase the width of each line at the first surface or the second surface of the flowcell.

19. The system of claim 18, wherein the focal point is above a top interior surface of the flowcell or below a bottom interior surface of the flowcell.

20. The system of claim 19, wherein the focal point is between about 50 μm and about 150 μm below the bottom interior surface of the flowcell or between about 50 μm and about 150 μm above the top interior surface of the flowcell.