commonly used in many laboratory applications and settings and are well known to those in the art.

[0166] Another optional embodiment of the present invention comprises a charge coupled device. CCD cameras are very useful in that they can detect even very small amounts of electromagnetic energy (e.g., such that emitted by fluorophores in the present invention). CCD cameras are made from semi-conducting silicon wafers that release free electrons when light photons strike the wafers. The output of electrons is linearly directly proportional to the amount of photons that strike the wafer. This allows the correlation between the image brightness and the actual brightness of the event observed. CCD cameras are very well suited for imaging of fluorescence emissions since they can detect even extremely faint events, can work over a broad range of spectrum, and can detect both very bright and very weak events. CCD cameras are well know to those in the art and several suitable examples include those made by: Stratagene (La Jolla, Calif.), Alpha-Innotech (San Leandro, Calif.), and Apogee Instruments (Tucson, Ariz.) among others.

[0167] Yet another optional embodiment of the present invention comprises use of a photodiode to detect fluorescence from the molecules in the microfluidic device. Photodiodes absorb incident photons that cause electrons in the photodiode to diffuse across a region in the diode thus causing a measurable potential difference across the device. This potential can be measured and is directly related to the intensity of the incident light.

[0168] In some aspects, the detector measures an amount of light emitted from the material, such as a fluorescent or chemiluminescent material. As such, the detection system will typically include collection optics for gathering a light based signal transmitted through the detection window or zone, and transmitting that signal to an appropriate light detector. Microscope objectives of varying power, field diameter, and focal length are readily utilized as at least a portion of this optical train. The detection system is typically coupled to a computer (described in greater detail below), via an analog to digital or digital to analog converter, for transmitting detected light data to the computer for analysis, storage and data manipulation.

[0169] In the case of fluorescent materials such as labeled cells or fluorescence indicator dyes or molecules, the detector optionally includes a light source which produces light at an appropriate wavelength for activating the fluorescent material, as well as optics for directing the light source to the material contained in the channel or chamber. The light source can be any number of light sources that provides an appropriate wavelength, including lasers, laser diodes and LEDs. Other light sources are optionally utilized for other detection systems. For example, broad band light sources for light scattering/transmissivity detection schemes, and the like. Typically, light selection parameters are well known to those of skill in the art.

[0170] The detector can exist as a separate unit, but is preferably integrated with the controller system, into a single instrument. Integration of these functions into a single unit facilitates connection of these instruments with a computer (described below), by permitting the use of few or a single communication port(s) for transmitting information between the controller, the detector and the computer. Integration of the detection system with a computer system typically includes software for converting detector signal information into assay result information, e.g., concentration of a substrate, concentration of a product, presence of a compound of interest, or the like.

[0171] In another aspect of the current invention, monitoring of the physical changes in molecules in the invention is achieved using a calorimetric detection system. In calorimetric assays, a change in heat capacity is measured as molecules undergo unfolding due to changes in temperature. Titration calorimetry and/or differential scanning calorimetry is optionally used to determine the thermal parameters of a test molecule for a target molecule in the invention. See, e.g., Brandts, J. et al. (1990) "Study of strong to ultratight protein interactions using differential scanning calorimetry" Biochem 29(29):6927-6940. Calorimetric measurement devices are available from a number of sources and their calibration and use are well known to those versed in the art.

[0172] Computer

[0173] As noted above, either or both of the fluid direction system and/or the detection system are coupled to an appropriately programmed processor or computer that functions to instruct the operation of these instruments in accordance with preprogrammed or user input instructions, receive data and information from these instruments, and interpret, manipulate and report this information to the user. As such, the computer is typically appropriately coupled to one or both of these instruments (e.g., including an analog to digital or digital to analog converter as needed).

[0174] The computer optionally includes appropriate software for receiving user instructions, either in the form of user input into set parameter fields, e.g., in a GUI, or in the form of preprogrammed instructions, e.g., preprogrammed for a variety of different specific operations. The software then converts these instructions to appropriate language for instructing the operation of the fluid direction and transport controller to carry out the desired operation.

[0175] For example, the computer is optionally used to direct a fluid direction system to control fluid flow, e.g., through a variety of interconnected channels. The fluid direction system optionally directs the movement of at least a first member of a plurality of molecules into a first member of a plurality of channels concurrent with directing the movement of at least a second member of the plurality of molecules into one or more detection channel regions. The fluid direction system also directs the movement of at least a first member of the plurality of molecules into the plurality of channels concurrent with incubating at least a second member of the plurality of molecules. It also directs movement of at least a first member of the plurality of molecules into the one or more detection channel regions concurrent with incubating at least a second member of the plurality of molecules.

[0176] By coordinating channel switching, the system directs the movement of at least one member of the plurality of molecules into the plurality of microchannels and/or one member into a detection region at a desired time interval, e.g., greater than 1 minute, about every 60 seconds or less, about every 30 seconds or less, about every 10 seconds or less, about every 1.0 seconds or less, or about every 0.1 seconds or less. Each sample, with appropriate channel switching as described above, remains in the plurality of channels for a desired period of time, e.g., between about 0.1 minutes or less and about 60 minutes or more. For example the samples optionally remain in the channels for a selected incubation time of, e.g., 20 minutes.