detection module with the addition of the required components; for clarity, these are discussed together.

[0219] The methods include the addition of an amplifier probe, which is hybridized to the target sequence, either directly, or through the use of one or more label extender probes, which serves to allow "generic" amplifier probes to be made. Preferably, the amplifier probe contains a multiplicity of amplification sequences, although in some embodiments, as described below, the amplifier probe may contain only a single amplification sequence, or at least two amplification sequences. The amplifier probe may take on a number of different forms; either a branched conformation, a dendrimer conformation, or a linear "string" of amplification sequences. Label probes then hybridize to the amplification sequences (or in some cases the label probes hybridize directly to the target sequence), and the ETMs are detected, as is more fully outlined below.

[0220] As will be appreciated by those in the art, the systems of the invention may take on a large number of different configurations. In general, there are four types of systems that can be used: (1) "non-sandwich" systems (also referred to herein as "direct" detection) in which the target sequence itself is labeled (again, either because the primers comprise labels or due to the incorporation of labels into the newly synthesized strand); (2) systems in which label probes directly bind to the target analytes; (3) systems in which label probes are indirectly bound to the target sequences, for example through the use of amplifier probes; and (4) labelless electronic methods.

[0221] Detection of the amplification reactions of the invention, including the direct detection of amplification products, indirect detection utilizing label probes (i.e. sandwich assays) or detection of non-amplified targets, is done by detecting assay complexes comprising labels, which can be attached to the assay complex in a variety of ways, as is more fully described below.

[0222] In addition, as described in U.S. Pat. No. 5,587,128, the reaction chamber may comprise a composition, either in solution or adhered to the surface of the reaction chamber, that prevents the inhibition of an amplification reaction by the composition of the well. For example, the wall surfaces may be coated with a silane, for example using a silanization reagent such as dimethylchlorosilane, or coated with a siliconizing reagent such as Aquasil™ or Surfacil™ (Pierce, Rockford, Ill.), which are organosilanes containing a hydrolyzable group. This hydrolyzable group can hydrolyze in solution to form a silanol that can polymerize and form a tightly bonded film over the surface of the chamber. The coating may also include a blocking agent that can react with the film to further reduce inhibition; suitable blocking agents include amino acid polymers and polymers such as polyvinylpyrrolidone, proteins such as BSA, polyadenylic acid and polymaleimide. Alternatively, for silicon substrates, a silicon oxide film may be provided on the walls, or the reaction chamber can be coated with a relatively inert polymer such as a polyvinylchloride. In addition, it may be desirable to add blocking polynucleotides to occupy any binding sites on the surface of the chamber.

[0223] In a preferred embodiment, the biological reaction chamber allows enzymatic cleavage or alteration of the target analyte. For example, restriction endonucleases may be used to cleave target nucleic acids comprising target sequences, for example genomic DNA, into smaller fragments to facilitate either amplification or detection. Alternatively, when the target analyte is a protein, it may be cleaved by a protease. Other types of enzymatic hydrolysis may also be done, depending on the composition of the target analyte. In addition, as outlined herein, the target analyte may comprise an enzyme and the reaction chamber comprises a substrate that is then cleaved to form a detectable product.

[0224] In addition, in one embodiment the reaction module includes a chamber for the physical alteration of all or part of the sample, for example for shearing genomic or large nucleic acids, nuclear lysis, ultrasound, etc.

[0225] In a preferred embodiment, the above-mentioned reactions can be carried out within the magnetic microchannel while the magnetically labeled target analytes are still captured in the channel. Reaction reagents can be introduced into the magnetic microchannel either through a sample inlet port or from a separate fluid inlet port linked directly to the magnetic microchannel. In this embodiment, the magnetic microchannel is properly configured so that it can serve as a reaction chamber. For example, when a PCR reaction will be carried out inside the channel, it is necessary and sometimes essential that a thermal control module as described below is present underneath the channel.

[0226] In a preferred embodiments, a thermal module may be used, that is either part of the different modules or separate but can be brought into spatial proximity to the modules. The thermal module can include both heating and/or cooling capability. Suitable thermal modules are described in U.S. Pat. Nos. 5,498,392 and 5,587,128, and WO 97/16561, incorporated by reference, and may comprise electrical resistance heaters, pulsed lasers or other sources of electromagnetic energy directed to the reaction chamber. It should also be noted that when heating elements are used, it may be desirable to have the reaction chamber be relatively shallow, to facilitate heat transfer; see U.S. Pat. No. 5,587,128. Adequate thermal insulation surrounding the different modules to may also be desired to prevent unintended cross-heating among the modules. Temperature control is useful and sometimes essential for optimizing conditions for various chemical reactions in these modules, as well as binding and elution of target analytes in the magnetic microchannel.

[0227] In a preferred embodiment, the devices of the invention include at least one fluid pump. Pumps generally fall into two categories: "on chip" and "off chip"; that is, the pumps (generally electrode based pumps) can be contained within the device itself, or they can be contained on an apparatus into which the device fits, such that alignment occurs of the required flow channels to allow pumping of fluids.

[0228] In a preferred embodiment, the pumps are contained on the device itself. These pumps are generally electrode based pumps; that is, the application of electric fields can be used to move both charged particles and bulk solvent, depending on the composition of the sample and of the device. Suitable on chip pumps include, but are not limited to, electroosmotic (EO) pumps and electrohydrodynamic (EHD) pumps; these electrode based pumps have sometimes been referred to in the art as "electrokinetic (EK) pumps". All of these pumps rely on configurations of