

understood that any fluid or fluids may be used and that any component or species or combination of components or species in the fluid may be determined, detected or measured.

[0107] One embodiment of the invention is illustrated in **FIGS. 27 and 28**. Depicted in each figure is a fluidic device that can be used to titrate a sample and a reagent. The device includes eleven essentially parallel microchannels that are formed in a serpentine pattern on a substrate. The eleven microchannels are fed by two inlets **344** and **346** that receive fluid from reservoirs **340** and **342**. Fluid entering inlet **344** is directed to the first channel on the left. Fluid entering via inlet **346** is distributed to an upper portion of each of the remaining 10 channels. The first channel joins the second channel at region **348**, which may be a mixing region. If flow rates of the two fluids are about equal and if the volume of the combined channels is equal to about twice the volume of each of the individual channels, then the combined fluid in the mixing region may be about 50% by volume of each of the original fluids. Of course, if the fluids or components in the fluids interact or change, then the composition of the combined fluids may be different than one or both of the original two fluids. The process may be repeated downstream where the 50/50 fluid from the second channel is combined with pure fluid in the third channel (from inlet **346**). If the same ratios are used in this mixing region, then the resulting fluid will be about 25/75 of first fluid to second fluid. These ratios can, of course, vary depending upon a number of factors, for example, viscosity, specific gravity, backpressure, surface tension and channel geometry. Mixing may be aided by a mixing device such as a CAM shown in the enlarged portion of **FIG. 28**.

[0108] The end of each of the channels may be joined at point **350** which may be a waste stream or other stream composed of the combined fluids. Prior to joining, each channel may pass an area proximate to a sensor such as one of electrodes **364** or reference electrode **368**. Therefore, each dilution of the two fluids (in 10 of the channels) may be analyzed by a different detector. Each sensor may be monitored separately, or the sensors may be monitored in parallel. In this manner, fluids comprising multiple different pre-determined solutions may be analyzed in parallel. For example, if each successive channel is diluted 50/50 with pure fluid from inlet **346**, the channels may include, for instance, fluids having ratios of the second fluid to the first fluid of 1:1, 3:1, 8:1, 16:1, 32:1, 64:1, 128:1, etc. The components of each stream may react concurrently and may be analyzed concurrently. Using the methods described herein, devices may be designed with any number of different dilution ratios. The dilutions need not be linear and may be, for example, logarithmic or second order functions.

[0109] In one embodiment, a titration platform may be provided that includes one or more sensors. A sensor is a device that can detect a physical or chemical condition of a fluid. Examples of sensors include, for example, electrodes, ion-specific electrodes, photocells, spectrometers, chips, electrochemical detectors, light scattering detectors, fluorescence detectors, sulfur detectors, nitrogen detectors, BOD detectors, gas sensors, UV detectors, radioactivity detectors, immunosensors, diode arrays, conductivity detectors, refractive index detectors, polarity detectors, etc. Sensors may be either qualitative or quantitative. Each sensor may be associated with a channel, such as a microchannel in a microfluidic

device. Using methods and structures described herein, different ratios of reagent to analyte may be flowed through different channels. For example, a microfluidic device may include 10 microchannels, and each successive microchannel may include a fluid having a reagent to analyte ratio that is greater than that of a fluid in a previous microchannel. For example, the ratio of reagent to analyte may increase by a specific factor, such as, for example, 2, 4 or 10, with each successive microchannel. Titrations may be run with any amount of fluid and in some embodiments only small amounts of sample are required. For example, in some embodiments, less than 1 mL, less than 100  $\mu\text{L}$ , or less than 10  $\mu\text{L}$  of sample and/or titrant can be used. Fluids exhibiting different ratios may flow through a sensor placed in position so as to be able to determine a characteristic of a fluid in one or more channels, e.g., at a point in, near, or aligned with each microchannel. The sensor may be placed at or near a point along the channel where reagent and analyte have been allowed to interact to an extent adequate to allow substantially complete reaction between the two. For example, a sensor may be placed downstream of a mixing region.

[0110] Many types of titrations can be carried out in accordance with the invention. For example, titrations may be based on precipitation (Ag(I) with  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{I}^-$ ,  $\text{SCN}^-$ , or  $\text{S}^{2-}$ ), complex formation (Ag(I) forming complexes with ligands such as  $\text{CN}^-$  or  $\text{S}_2\text{O}_3^{2-}$ ), redox (Fe(II)/Fe(III) with Ce(III)/Ce(IV)), and acid-base. The course of the titration can be followed using many types of sensors. Some examples of techniques that can be used with titrations are potentiometry, amperometry, spectrophotometry, turbidometry, fluorimetry, and calorimetry.

[0111] An end point for the titration may be determined, for example, by monitoring the sensors and recording which sensor is associated with a microchannel that provides the lowest ratio of reagent to analyte and that indicates all of the reagent has been reacted. Sensors may also measure excess reagent, excess sample, or both. In similar embodiments, different ratios of reagent to analyte can be used to assure that at least one of the sensors will be measuring in a "preferred" range. For example, a preferred range may be a range where response is linear or the titration has a low limit of detection or standard deviation.

[0112] In another embodiment, measurement of reaction conditions may be measured in parallel using multiple sensors. Parallel readings may result, for example, in significant time savings. A series of dilutions in various channels may be used to provide different reagent to analyte ratios, but the varying ratio fluids may be delivered concurrently, rather than sequentially over time. Thus, one test sample may be analyzed at any number of reagent to analyte ratios and may be analyzed in parallel. A microprocessor may be used to record data from multiple sensors. The ratios may be pre-determined and may be controlled, for example, by the geometry of the device or by flow rates of the sample, titrant, or both. Such parallel measurements may be useful, for example, in monitoring chemical processes in real time. Continuous data for any number of reagent to analyte ratios may be obtained for a single sample and may be obtained at any point in time. When used in a microfluidic device, sample use rates for continuous monitoring may be small, for example, less than one microliter of sample per second or less than 10  $\mu\text{L}$  per titration. Microfluidic devices may also provide for fast reaction times, minimizing the time