sample under a first set of conditions (e.g., a first temperature and/or a first pH) and to release the polynucleotides under a second set of conditions (e.g., a second, higher temperature and/or a second, more basic, pH). Typically, the polynucleotides are retained preferentially as compared to inhibitors that may be present in the sample. Particles **218** are confined by a retention member **216** (e.g., a column) through which polynucleotide molecules must pass when moving between the inlet **265** and outlet **267**.

[**0106**] Typically, the ligands on the particles **218** retain polynucleotides from liquids having a pH about 9.5 or less (e.g., about 9.0 or less, about 8.75 or less, about 8.5 or less, but preferably more than 7.0). As a sample solution moves through filtration element **250**, polynucleotides are retained while the liquid and other solution components (e.g., inhibitors) are less retained (e.g., not retained) and exit the filtration element. In general, the ligands release polynucleotides when the pH is about 10 or greater (e.g., about 10.5 or greater, about 11.0 or greater). Consequently, polynucleotides can be released from the ligand modified particles into the surrounding liquid.

[**0107**] A filter **219**, typically made of polycarbonate and typically having a pore size about 1-2 μm smaller than the smallest particles used, prevents particles **218** from passing downstream of the filtration element. A channel **287** connects filter **219** with outlet **267**. Filter **219** has a surface area that is larger than the cross-sectional area of inlet **265**. For example, in some embodiments, the ratio of the surface area of filter **219** to the cross-sectional area of inlet **265** (which cross-sectional area is typically about the same as the cross-sectional area of channel **214**) is at least about 5 (e.g., at least about 10, at least about 20, at least about 50) μm^2. In some embodiments, the surface area of filter **219** is at least about 1 mm^2 (e.g., at least about 2 mm^2, at least about 3 mm^2).

[**0108**] In some embodiments, the cross-sectional area of inlet **265** and/or channel **214** is about 0.25 mm^2 or less (e.g., about 0.2 mm^2 or less, about 0.15 mm^2 or less, about 0.1 mm^2 or less). The larger surface area presented by filter **219** to material flowing through the filtration element helps prevent clogging while avoiding significant increases in the void volume (discussed hereinbelow) of the processing region.

[**0109**] Typically, the total volume (including particles **218**) between inlet **265** and filter **219** is about 15 microliters or less (e.g., about 10 microliters or less, about 5 microliters or less, about 2.5 microliters or less, about 2 microliters or less). In an exemplary embodiment, the total volume is about 2.3 microliters. In some embodiments, particles **218** occupy at least about 10 percent (e.g., at least about 15 percent) of the total volume of the filtration element. In some embodiments, particles **218** occupy about 75 percent or less (e.g., about 50 percent or less, about 35 percent or less) of the total volume of processing chamber **220**.

[**0110**] In some embodiments, the volume of the filtration element that is free to be occupied by liquid (e.g., the void volume of processing region **220** including interstices between particles **218**) is about equal to the total volume minus the volume occupied by the particles. Typically, the void volume of the filtration element is about 10 microliters or less (e.g., about 7.5 microliters or less, about 5 microliters or less, about 2.5 microliters or less, about 2 microliters or less). In some embodiments, the void volume is about 50 nanoliters or more (e.g., about 100 nanoliters or more, about 250 nanoliters or more). In an exemplary embodiment, the total volume of the filtration element is about 2.3 microliters. For example, in an exemplary embodiment, the total volume of the filtration element is about 2.3 microliters, the volume occupied by particles is about 0.3 microliters, and the volume free to be occupied by liquid (void volume) is about 2 microliters.

[**0111**] In some embodiments, a volume of channel **287** between filter **219** and outlet **267** is substantially smaller than the void volume of the filtration element. For example, in some embodiments, the volume of channel **287** between filter **219** and outlet **267** is about 35% or less (e.g., about 25% or less, about 20% or less) of the void volume. In an exemplary embodiment, the volume of channel **287** between filter **219** and outlet **267** is about 500 nanoliters.

[**0112**] Filter **219** typically has pores with a width smaller than the diameter of particles **218**. In an exemplary embodiment, filter **219** has pores having an average width of about 8 microns, and particles **218** have an average diameter of about 10 microns.

[**0113**] While the filtration element has been described as having a retention member formed of multiple surface-modified particles, other configurations can be used. For example, in some embodiments, filtration element includes a retention member configured as a porous member (e.g., a filter, a porous membrane, or a gel matrix) having multiple openings (e.g., pores and/or channels) through which polynucleotides pass. Surfaces of the porous member are modified to preferentially retain polynucleotides. Filter membranes available from, for example, Osmonics, are formed of polymers that may be surface-modified and used to retain polynucleotides within processing region **220**. In some embodiments, processing region **220** includes a retention member configured as a plurality of surfaces (e.g., walls or baffles) through which a sample passes. The walls or baffles are modified to preferentially retain polynucleotides.

Channels

[**0114**] Channels of microfluidic component **201** typically have at least one sub-millimeter cross-sectional dimension. For example, channels of network **201** may have a width and/or a depth of about 1 mm or less (e.g., about 750 microns or less, about 500 microns, or less, about 250 microns or less) and are at least 1 μm thick, preferably at least 10 μm think, and more preferably at least 100 μm thick. Channels of component **201** typically hold at least about 0.375 microliters of liquid (e.g., at least about 0.750 microliters, at least about 1.25 microliters, at least about 2.5 microliters). In some embodiments, channels hold about 7.5 microliters or less of liquid (e.g., about 5 microliters or less, about 4 microliters or less, about 3 microliters or less).

Valves

[**0115**] A valve is a component that has a normally open state, allowing material to pass along a channel from a position on one side of the valve (e.g., upstream of the valve) to a position on the other side of the valve (e.g., downstream of the valve). Upon actuation, the valve transitions to a closed state that prevents material from passing along the channel from one side of the valve to the other. For example, valve V1 depicted in FIG. **12** is a single valve that includes