

[0131] Techniques of ultraviolet (UV) ablation may also be used in surface tension patterning embodiments. The substrate is functionalized or coated with ablatable material or molecules. UV radiation is used to selectively ablate the coating from regions of the substrate by using a mask, thereby patterning the substrate. Regions from which ablatable material was removed may be further functionalized to create a pattern of interspersed regions of differing surface tension.

[0132] FIG. 8 shows that if two different samples are to be analyzed then one sample is placed in region 1 and another sample is placed in region 2. Areas on the substrate labeled "1" are hydrophobic. Areas on the substrate labeled "2" are hydrophilic. Probe polynucleotide strands are immobilized on the hydrophilic regions of the substrate surface. Liquid droplets comprising potential targets for the probe arrays are localized to the probe regions by surface tension. An anchored cover slip is added to control dispersion of the target liquid. The interaction between the target liquid and the immobilized probes may then be promoted by agitating the substrate slide. Alternately the cover slip itself may be rotated or agitated, optionally by electromagnetic means, to agitate the solution and ensure movement of the target liquid as described below. The surface tension characteristic of the substrate slide inhibits the droplet from dispersing even in light of the relative movements of the substrate slide and the cover slip. The relative movements of the substrate slide and the cover slip can be adjusted to generate less force than the surface tension holding the target liquid on the substrate slide.

[0133] The sample solution can also be further confined by surface tension differential on a cover slip surface. The cover slip can be coated with uniform hydrophobic coating so that the hydrophobic coating enhances the surface tension that holds the liquid sample underneath. The cover slip can also be coated with confined hydrophilic regions surrounded by hydrophobic regions that match the hydrophilic regions on the substrate slide. In this design, an area that is the same size and shape of the sample area on the substrate slide is made hydrophilic, while the area outside is made hydrophobic. The patterning of both the slide and the cover slip will further assist in confining the solution to the sample area. In addition, the hydrophilic area will pull the solution with it during agitation, thus create more effective movement of the sample solution.

[0134] 2. Cover

[0135] In accordance with embodiments of the present invention, a cover is coupled with the substrate to contain the target liquid therebetween. The cover can serve multiple functions. First, it can be used to minimize evaporation of a liquid target sample by reducing the exposure of the target liquid to the environment. Second, by compressing the target liquid, a small amount of target liquid can be spread out to cover a larger probe array area. Finally, the cover can be used to generate movement of the target liquid and thereby promote interaction between the target liquid and the probes on the substrate. The movement of the target liquid can be accomplished by causing relative movement between the cover and the substrate.

[0136] Numerous cover slip designs can be used for the purpose of liquid confinement and movement. In a first example, the cover slip surface may have a uniform hydro-

phobic coating. The hydrophobic coating of the cover slip enhances the effect of the surface tension differentials on the substrate slide for holding a hydrophilic target liquid within the hydrophilic region on the substrate slide. In a second example, the cover slip surface may have a coating with one or more confined hydrophilic regions surrounded by hydrophobic regions that match the hydrophilic/hydrophobic pattern on the substrate slide. In the second example, the patterning of both the substrate slide and the cover slip can further enforce the confinement of a hydrophilic target liquid to the hydrophilic region. In addition, the hydrophilic area will pull the target liquid with it during agitation, thus creating more effective movement of the target liquid. Alternatively, if the target liquid is hydrophobic, the cover slip surface and the substrate surface may have a coating with one or more confined hydrophobic regions surrounded by hydrophilic regions wherein the hydrophobic/hydrophilic pattern on the cover slip matches that on the substrate slide.

[0137] In some embodiments, the cover can be moved by a force, such as magnetic and mechanical force. In addition, to increase the effectiveness of movement of target molecules, protrusions can be engineered on the surface of the cover facing the target liquid. The cover may also have risers which form a container slightly larger than the substrate so that the substrate can be inserted into the cover container during hybridization.

[0138] In the embodiment illustrated in FIG. 9, the cover slip is magnetized, contains magnetized components, or contains magnetically reactive components. This magnetized cover slip can be made by attaching a magnet to a typical glass cover slip or by forming the cover slip out of magnetic glass. A support fixture may be provided to align the cover slip with the substrate slide and to prevent the cover slip from falling off the substrate slide. An example of the support fixture is shown in FIG. 9. This assembly can be placed on a magnetic stirring table similar to a hot plate stirrer commonly used in laboratories. The magnetic driver under the table generates a moving magnetic field, which in turn drives the magnetic cover slip to rotate or move in a circular motion. The motion of the cover slip induces flow and turbulence in the sample liquid sandwiched between the cover slip and the substrate slide, which can enhance the interaction between sample liquid and the probes on the substrate slide.

[0139] In another embodiment, certain surface textures can be engineered on to the surface of the cover slip that is in contact with the sample liquid. This can enhance the capability of the cover slip to induce flow in the sample liquid. The technique can be particularly effective when the target liquid is confined by surface tension differential on either the microarray or cover slip surface. The cover slip should rotate fast enough to generate movement for efficient hybridization but not so fast as to disrupt interactions between target molecules in the sample liquid and probes on the substrate. Alternatively, the cover slip can be agitated at high speeds to enhance mixing, and then slowed or stopped to enable effective interactions.

[0140] In another embodiment, effective movement of the liquid sample can be created using a floating and sliding cover slip. This method combines a rigid cover slip that permits low volumes of target liquids with mechanical movements to achieve dynamic movement of the target