

not only to move samples as discussed above in Section II, but also to determine the position of the sample (e.g., to facilitate imaging).

[0150] For example, conducting samples have circulating currents induced by an RF field that in turn produce their own magnetic field, and interact strongly with an applied field. This interaction can be used to move samples and also detect their presence. In one mechanism discussed in greater detail below, magnetic polarization of a sample changes the inductance of a coil (e.g., a microcoil of an array) in proximity to the sample and, in turn, this inductance change can be detected using high frequency signals. In yet another example, electrical polarization of a sample gives rise to the forces responsible for dielectrophoresis (DEP). This polarization can be detected via a change in capacitance between the sample and the electrodes of an electric-field generating device (e.g., a micropost or microcoil with an applied voltage) with no dissipation, or by a change in damping due to the oscillating electric polarization in the sample.

[0151] The foregoing examples provide various mechanisms by which the location of a sample can be detected. Based on the capability to detect the position of a sample relative to a given field generating component, in one embodiment each of the field generating components 200 is analogous to an imaging pixel (e.g., consider a two-dimensional CCD array) that provides valuable information toward constructing a comprehensive image of a sample distribution suspended in a microfluidic system. In another embodiment, images of sample distributions in turn may be used as feedback to manipulate one or more samples according to a prescribed algorithm.

[0152] In one embodiment based on magnetic bead-bound samples, the effect of the bead's magnetism on the inductance of a microcoil is exploited to facilitate sample detection. For example, the inductance L of a given microcoil is proportional to an effective magnetic permeability μ_{eff} . Without any magnetic particles in the vicinity of the microcoil, μ_{eff} is equal to the magnetic permeability of a vacuum μ_0 , but in the presence of a magnetic bead (e.g., a paramagnetic particle, or PMP) having some magnetic permeability μ_{bead} , the effective permeability associated with the microcoil is $\mu_{\text{eff}} = (1-a)\mu_0 + a\mu_{\text{bead}}$ (where $a \ll 1$) thereby altering the inductance of the microcoil by some amount ΔL . Accordingly, by monitoring the inductance L of a microcoil via high frequency signals applied to the microcoil, such changes ΔL in the microcoil's inductance may be detected, thereby indicating the presence of a bead-bound sample in the vicinity of the microcoil.

[0153] Depending on the size and hence inductance of the microcoil and the magnetic permeability of the bead, changes in inductance ΔL may range from approximately 0.1% of L to 1% of L (e.g., a Dynabead having a diameter of approximately 4.5 to 5 micrometers and a magnetic permeability μ_{bead} of approximately $1.25\mu_0$ can cause a change in inductance ΔL on the order of 0.1% of L). Also, the frequency response of the bead's magnetic permeability also should be taken into consideration; in particular, for the Dynabead example, μ_{bead} has a real value for frequencies below approximately 100 MHz. Hence, in one exemplary implementation, RF signals below or approximately 100 MHz are employed in the detection scheme.

[0154] FIG. 17 is a diagram illustrating an arrangement of RF/detection components 480 that forms a "frequency

locked loop," according to one embodiment of the present disclosure, for facilitating sample detection. In the embodiment of FIG. 17, an exemplary microcoil 212 is shown in terms of its variable inductance L (which changes in the presence of a magnetic sample) and its associated coil resistance R_L . In one aspect of this embodiment, the variable inductance L and coil resistance R_L form part of a bridge circuit 485, which also includes a known predetermined capacitance C_{RF} (having a parasitic resistance R_C) and two known resistances R_1 and R_2 .

[0155] For ease of illustration and to facilitate the following discussion, the remaining components in FIG. 17 are shown directly connected to the microcoil 212; it should be appreciated, however, that in other embodiments, the remaining RF/detection components 480 shown in FIG. 17 may be shared amongst multiple microcoils of a microcoil array in a multiplexed fashion, along with other circuitry providing DC current to the microcoils for purposes of sample manipulation as discussed above. For example, another signal similar to the direction signal 472 may be used, together with the row and column select signals and additional switches as appropriate (e.g., in a manner similar to that discussed above in connection with FIGS. 13-15), to facilitate operation of microcoils for both manipulation and detection purposes using multiplexed RF and DC signals.

[0156] As mentioned above, in the embodiment of FIG. 17 a "frequency locked loop" is formed by the bridge circuit 485, a phase detector 482, a low pass filter 484, and a voltage controlled oscillator (VCO) 486. Generally speaking, the phase detector, low pass filter and voltage controlled oscillator are similar to well-known components conventionally found in phase locked loop configurations. However, the combination of a uniquely arranged bridge circuit including the microcoil 212, together with the other indicated components, results in a locking circuit based on frequency rather than phase, wherein the locking frequency varies in direct relationship to changes in the inductance L due to the presence of a sample. Accordingly, by monitoring changes in the locking frequency of the circuit shown in FIG. 17, the presence of a sample in proximity to the microcoil may be detected.

[0157] To explain the operation of the circuit shown in FIG. 17, we first consider an exemplary implementation in which the output $V(\omega)$ of the VCO 486 is a sinusoidally varying voltage having an angular frequency ω that is a function of a control voltage V_c input to the VCO. Using the phasor notation $Ae^{j\theta}$ to express sinusoidal voltages (where A represents amplitude and θ represents phase), and expressing all phases relative to the output of the VCO 486, the voltages $V_1(\omega)$ and $V_2(\omega)$ taken from the bridge circuit 485 may be expressed as $V_1e^{j\theta_1}$ and $V_2e^{j\theta_2}$, where

$$\theta_1 = -\arctan \frac{\omega L}{R_1 + R_L} \quad \text{and} \quad (4)$$

$$\theta_2 = \arctan \frac{1}{\omega C_{\text{RF}}(R_2 + R_C)}. \quad (5)$$

As discussed in further detail below, the frequency locked loop is configured such that the control voltage V_c stabilizes at some DC value when $\theta_1 = \theta_2$. Accordingly, from the above