MICROFLUIDIC PLATFORM OF ARRAYED SWITCHABLE SPIN-VALVE ELEMENTS FOR HIGH-THROUGHPUT SORTING AND MANIPULATION OF MAGNETIC PARTICLES AND BIOMOLECULES

TECHNICAL FIELD

[0001] The present invention relates to systems and processes for trapping, manipulating and releasing magnetic particles and biological or chemical species that are coupled to or tagged with magnetic particles. More particularly, the present invention is directed to microfluidic platforms that include one or more spin-valve elements in an array that can be operated to trap, manipulate and release various biological or chemical species.

BACKGROUND ART

[0002] The ability to manipulate chemical and biological species on a microscale is an important tool that enables a variety of applications in the fields of biotechnology, microanalysis, microsynthesis, and similar technologies. Depending on the application, useful manipulations may involve separating, transposting, positioning and/or storing various chemical and biological species.

[0003] Conventional microfluidic systems that have been used to manipulate chemical and/or biological species have involved controlling fluid flow on a microscale. Chemical or biological species that are suspended in the fluid may thus be manipulated. In some microfluidic systems, pumps and/or valves are used to control fluid flow through a series of physical microchannels formed within a substrate. Such systems are not easily fabricated, have complex structures, and are not easily reconfigured for different operations or dynamica.

[0004] High gradient magnetic separation is a long established procedure for selectively retaining magnetic materials in a chamber or column disposed in a magnetic field. This technique has also been applied to non-magnetic targets such as biological materials that are labeled or tagged with magnetic particles. In high gradient magnetic separation a target analyte within a complex sample is labeled with a magnetic material through association with a specific binding ligand that is conjugated to a coating on the particle. The target analyte coupled to the magnetic label is suspended in a fluid which is placed in a chamber or passed through a column and a magnetic gradient is applied to the chamber or column. In the presence of the magnetic gradient the magnetically labeled target analyte is retained while materials that do not have magnetic labels pass through the chamber or column. The retained target analyte can then be eluted by changing the strength of, or eliminating, the magnetic field.

[0005] High gradient magnetic separation chambers or columns typically contain a matrix of magnetically susceptible material such as steel wool or wire matrix. When a magnetic field is applied across the chamber, a high magnetic field gradient will be locally induced within the chamber close to the surface of the matrix, permitting retention of the fairly weakly magnetized analytes.

[0006] Typical magnetic particle sorting applications include separation of biological analytes such as cells, proteins, and DNA. The premise of the sorting is to attach a chemically functionalized magnetic particle to a desired biological specimen and then apply a magnetic field gradient to pull the magnetic particles away from the solution, thereby leaving the unwanted molecules behind. In this case, sorting is done as an ensemble and single particle location specificity as an end result is not achievable. Single particle sorting techniques have recently been demonstrated based on magnetic wires or domain wall tips. The limitations of these techniques are power consumption and the particles cannot be sorted into an array for long periods of time without causing local heating and hence, possible damage to the samples.

[0007] In addition to techniques that are used to sort biological and chemical particles, there are techniques that allow for the manipulation of such particles. Such techniques allow for altering the physical or chemical reaction pathways that occur in biological organisms at the most fundamental level.

[0008] The application of lateral and torsional forces to biomolecules by tethered magnetic particles has been an essential method for revealing information about molecular motors, protein-DNA interactions, and the forces associated with folding and unfolding dynamics of DNA. In these experiments, one end of the biological molecule is immobilized onto a microscope slide while the other is attached to a magnetic particle that follows the field gradients generated by macroscopic rare earth magnets. These techniques are generally limited by the fact that the sample must be immobilized and the information obtained is via constant force on the magnetic particle.

[0009] There are many different approaches to single molecule measurement and manipulation: atomic force microscopy, micropipettes, electrophoretic translocation, and optical and magnetic tweezers. The geometry that is characteristic to each technique limits the throughput capabilities of the technique as well as the type of biological or chemical system which can be studied. Among the many techniques, tweezers technologies have proven amenable to studying a variety of systems ranging from DNA elasticity to molecular motor dynamics while preserving throughput capabilities, thereby making it one of the more powerful single molecule techniques currently available.

[0010] Single molecule tweezers technologies have been developed and widely used to study information about the behavior of individual biological molecules that is otherwise obscured by the statistics of ensemble measurements. A few examples include: 1) how the recognition of protein binding sites and enzymatic work on DNA is affected by the physical conformation (i.e. supercoiling) of DNA; 2) how the function that DNA plays in living cells is directly related to the torsional stress it undergoes in them (altering this conformation often proves lethal to the cells functions); 3) the ability to apply torsional force to molecular motors can lead to information about the energy production of the motor and its enzymatic role in a cell; and 4) rotation of DNA during transcription by RNA polymerase opens the possibility of resolving individual transcription steps.

[0011] The more versatile tweezers technologies include optical and magnetic tweezers. Optical tweezers involve tethering biological molecules to dielectric spheres (i.e. handles) and then capturing the spheres at the focal point of an electric field gradient. These tweezers can selectively