

tion state since the minimum field required to flip the state of the spin-valve was 15 Oe. FIGS. 9A-9I depict a sequence of a magnetic particle confined by the field gradient produced by a spin-valve element during rotation of the magnets about the platform. To visually demonstrate the rotation of the magnetic particles, a strand of particles **28** was used instead of individual particles in FIGS. 9A-9I. The length of the strands was four particles, the first of which is trapped in the field gradient to the right of the spin-valve element. As the magnetic field was rotated, the line of particles followed the field. For angles of 135° to 270°, the length of the strand of magnetic particles appears shorter. This is due to the fact that the trapped particle remains in its initial location and the strand of particles overlap the spin-valve element and are obscured by it.

The experiments which were conducted to provide the results depicted in FIGS. 8 and 9 above demonstrate that bistable spin-valve elements, in the absence of applied magnetic fields, are capable of confining magnetic particles that are separated from the traps by a membrane and that with the application of a rotating magnetic field gradient, it is possible to rotate magnetic particles while they are confined to a specific location. This ability to rotate confined particles can be used to apply torsional forces to arrays of DNA molecules and other biological specimens, chemical compounds, etc. This ability allows for high-throughput and low power consumption measurement and control of biological and chemical processes on a single molecule level.

According to another aspect of the present invention, which will now be discussed, the microfluidic magnetic trap platform is used with an applied magnetic force microscope (MFM) cantilever. The MFM cantilever tip serves as a magnetorobotic arm that provides a translatable local magnetic field gradient to capture and move magnetic particles with nanometer precision. The MFM electronics can be programmed to sort an initially random distribution of particles by moving them within an array of magnetic trapping elements. The system permits a particle sorting rate of approximately 5500 particles/minute. Release of the particles from the MFM tip is made possible by the membrane that separates the arm and magnetic trap elements from the particle solution. This platform has potential applications for magnetic based sorting, manipulation and probing of biological molecules in a constant displacement or a constant force mode.

In initial experiments using a commercially available cobalt coated MFM tip with a radius of 90 nm, a height of 15 μm, and width at the top of the tip of 10 μm it was discovered that the particles were not strongly attracted to the tip field gradients and did not translate with the tip. This was attributed to the fact that the tip slope was sufficiently large to allow for a diminished interaction between the magnetic material on the sidewall of the tip and the particles. To increase the area of interaction between the tip and the particle, the tip was sanded by scanning it rapidly on a hard surface such as vicinal yttria stabilized cubic zirconia. Scanning electron microscopy images show a sanded tip had a 0.8 μm wide sanded plateau. With this geometry, the magnetic material that produces the field gradient to capture the particles consists of a ring having a 60 nm width and a radius of approximately 400 nm.

Size sorting experiments were conducted by injecting a solution of 2.8 μm and 5 μm diameter iron and iron oxide embedded polystyrene particles suspended in water into the wells of the microfluidic magnetic trap platform so that the particles were . FIG. 10A depicts an initial random distribution of particles including transit particle **30** and held particles **31**, and FIG. 10B depicts the particles after being sorted as all being held. The tip provides the translatable magnetic field

gradient while the PERMALLOY™ elements of the spin-valve traps are used to spatially confine the sorted particles. The particles are placed into each sorted position by approaching the surface of the membrane over where the particle to be moved is located. Since the tip field gradients die off as r^{-3} , it is necessary to bring the tip as close to the particle to be moved as possible. The minimum distance is limited by the thickness of the membrane which in one experiment was 200 nm; however, it is possible to decrease the thickness of the membrane to 100 nm without damaging the resilience of the membrane. Once the tip contacts the surface, the particle is moved to a predetermined trapping element. To release the particle from the tip field gradient, the tip is retracted from the surface to suitable distance, for example about 9 μm or greater. At this height, the tip then moves to the next particle to be sorted. FIG. 11A depicts how a particle can be moved into a desired portion using a magnetic tipped probe. In FIG. 11A, the particle **33** is moved from an initial position **34** to a new position **35** manipulating the tip **36** of the probe **37** as illustrated and discussed above. FIG. 11B depicts the magnetic tipped probe and microfluidic magnetic trap platform of FIG. 11A in perspective.

Once the particles are placed into desired positions in the array, each particle can be annotated for future manipulation and analysis. Sorting of various sized particles can be accomplished by tailoring of the tip geometry for specific size ranges.

In the case of a tip size of 800 nm, the geometry was optimized for 1 micrometer particles, although larger particles could also be sorted with less efficiency. The maximum velocity at which the particles are translated was measured by rastering the tip in incremental velocities and recording the point at which the magnetic microparticle no longer follows the tip. A maximum translation velocity of 2.2 mm/sec±0.1 mm/sec for a 1 μm particle was measured in this manner. To determine the maximum sorting rate, it was assumed that with an average translation distance of 20 μm, a tip repositioning time of 2 ms and a computer interface time of 1 ms. These approximations were used to calculate a maximum sorting rate of approximately 5500 individual particles can be sorted per minute.

The magnetic homogeneity and smaller size of the 1 micrometer magnetic particles made them a typical choice for magnetic tweezers experiments. To implement a magnetic tweezers platform, a comparison was needed between the forces acting on the particles to conventional tweezers instruments. To determine the force acting on the particles velocity was measured. However, since the particles are near the surface of the membrane, a simple treatment using the Stoke's Law for viscous drag is not appropriate in determining the force acting on the particle. Using the relationship for hydrodynamic drag on a particle positioned at a surface, the force is expressed as $F=1.7005 \times 6\pi\eta r^2 G$, here η is the viscosity of the medium, which in this case is water, r the radius of the sphere and G the shear rate of the fluid flow. For this equation to be valid, it must be proven that the test system is under laminar flow conditions. For laminar flow the Reynold's number (Re) for the system must be less than 1, and for the present system Re was calculated as $Re=2.3 \times 10^{-6} \pm 0.1 \times 10^{-6}$ from the velocity measurements made by scanning the tip. Therefore, the shear rate can be calculated under the condition of a uniform velocity gradient by using the velocity of at the center of the sphere, which, in this case, corresponds to the distance from the surface to the center of the sphere. Under these conditions, a shear rate of $4.6 \pm 0.1 \times 10^3 \text{ sec}^{-1}$ was calculated which corresponds to a force of $35.3 \pm 2.0 \text{ pN}$.