Supplementary Material

Microfluidic chip for graduated magnetic separation of circulating tumor cells by their EpCAM expression and magnetic nanoparticle binding

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Model of simple dipole magnet

Fig. S1 shows the result of two-dimensional modeling the magnetic field around a simple dipole magnet, with each magnet having a cross section of 1 cm × 1 cm, and the magnets separated by 1 mm. The magnets had opposite directions of magnetization. This is the type of dipole magnet used for cell selection in the CellSearch System [1]. Finite Element Method Magnetics (FEMM 4.2) [2] was used to obtain the solution. The included materials library properties for 52 MGOe NdFeB magnets were assumed, which is the highest grade magnet commonly availabe.

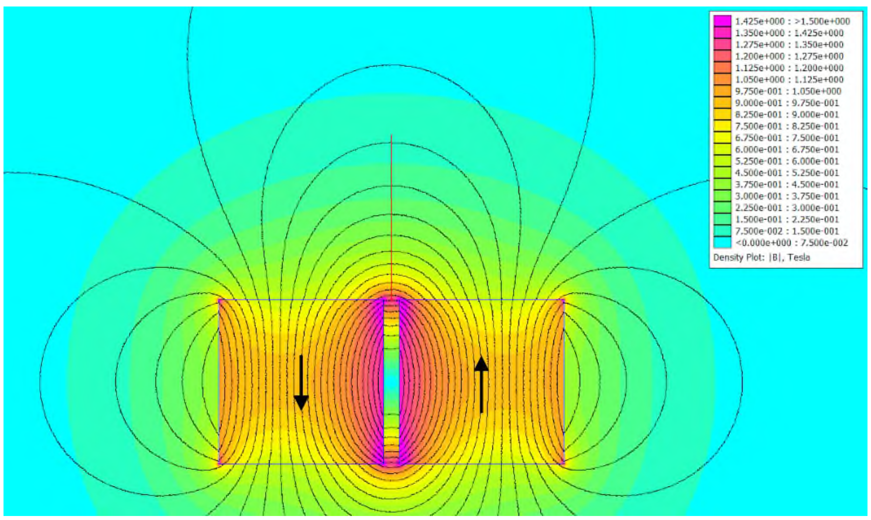

Fig. S1. 2D modelling of a magnetic dipole composed of two magnets of opposing magnetization with cross sections of 1 cm × 1 cm and separated by a 1 mm gap. The flux lines are shown in black and the flux density as a color plot according to the included key. The red vertical line is drawn from the mid-point of the gap to a point 1 cm from the magnets. The magnetic field and field gradient along this line are plotted in Fig. S2.

The magnetic field B (T) and field gradient dB/dx (T/mm) along the vertical red line drawn in Fig. S1 at the midpoint of the gap to a distance of 1 cm from the magnets are shown in Fig. S2. The predicted magnetic field falls from a maximum of about 1.3 T between the magnets to about 0.35 T at 4 mm and less than 0.16 T at 8 mm. The field gradient falls from a maximum of about 0.49 T/mm at 0.5 mm from the magnets to about 0.083 T/mm at 4 mm and only about 0.029 T/mm at 8 mm. Superparamagnetic nanoparticles are magnetically saturated at about 0.4 T [3] and at field strengths greater than 0.4 T magnetophoretic velocities of labeled cells therefore vary with the field gradient. At 4 mm from the magnets the magnetophoretic velocities would therefore be about 15% of the velocities at 0.5 mm. At field strengths lower than 0.4 T, the particles have lower than saturation magnetization so that at 8 mm from the magnets the field gradient is just 6% of the gradient at 0.5 mm, but magnetophoretic velocities would be much lower than 6% of the velocities at 0.5 mm. Such a dipole magnet placed against the wall of a vessel 1 cm in diameter may capture magnetically labelled cells within a few millimeters of the wall, but would be relatively inefficient at capturing cells from greater distances.

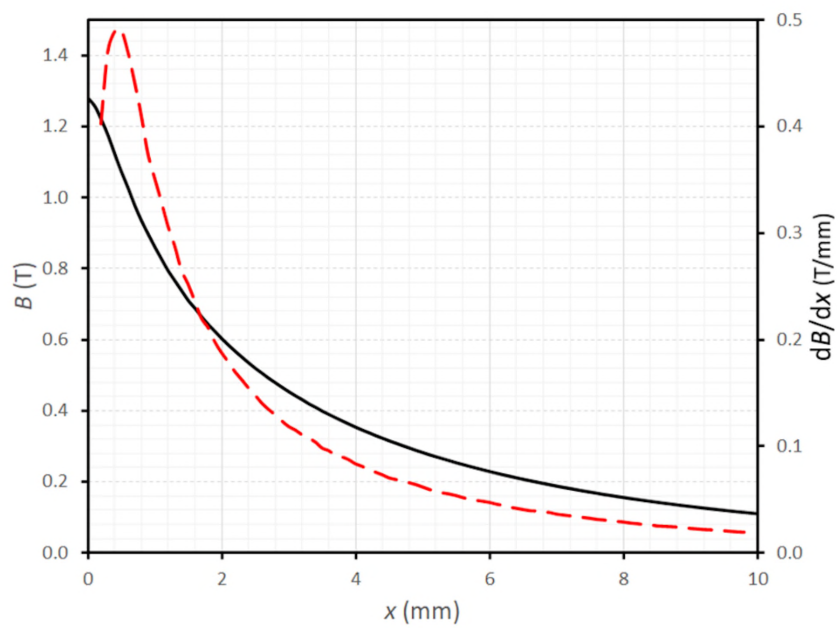

Fig. S2. The magnetic field *B* (T) (black line) and field gradient d*B*/d*x* (T/mm) (dashed red line) along the red vertical line drawn in Fig. S1.

The DMF magnetic field model results

The magnetic fields were modeled using Magneto software (Integrated Engineering Software, Winnipeg, Manitoba, Canada). The model dimensions and material properties assumed are given in the main text. Fig. S3 shows the predicted magnetic field *B* along the center line between the pole pieces as a function of distance from the magnet surface for the two cases considered. The breadth and position for the channel is indicated for each case by the horizontal bars.

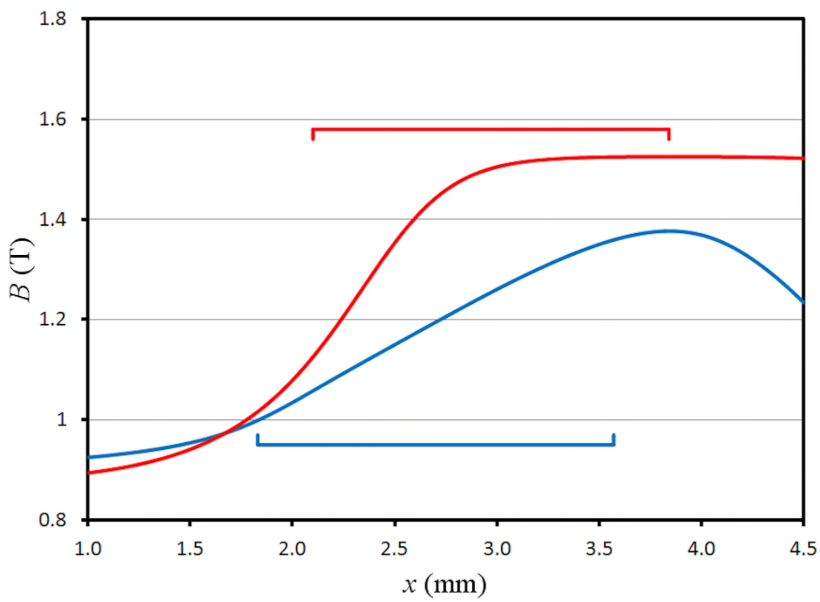

Fig. S3 Magnetic field *B* along the center line between the pole pieces as a function of distance from the surface of the magnet block. The upper red curve corresponds to the case of decreasing field gradient with increasing *x* across the channel breadth (Micro DMF I, upper red bar), and the lower blue curve corresponds to the case of approximately constant field gradient across the channel breadth (Micro DMF II, lower blue bar).

MDM magnet assembly

As explained in the main text, the assembly is made up of 40 NdFeB magnet blocks and four specially-shaped soft iron pieces. The whole assembly is held together in an aluminum structure with non-magnetic nuts and bolts. The arrangement is shown in Fig. S4 and the color contours in field *B* in the region above the magnet arrangement, calculated using Magneto, in Fig. S5. The four regions of high field gradient can be seen around the edges of the 1/16 inch magnet blocks.

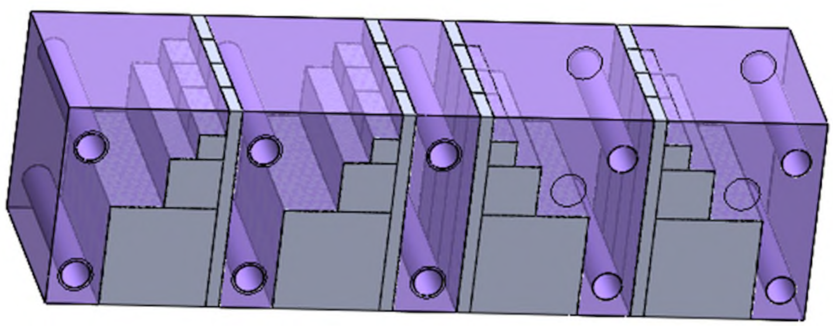

Fig. S4 The arrangement of the magnet blocks (grey) and soft iron pieces (blue) in the MDM magnet assembly

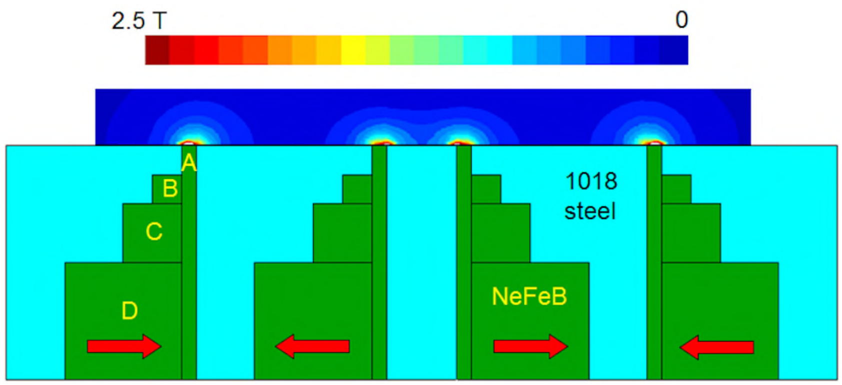

Fig. S5 Color contours in field *B* above the MDM magnet assembly as predicted by Magneto two-dimensional modeling.

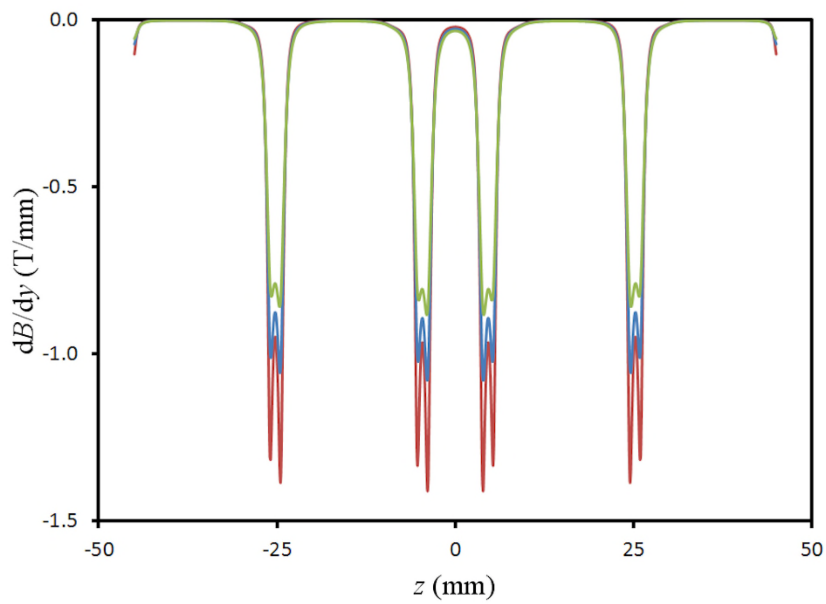

Fig. S6 The gradient in magnetic field *B* in the direction away from the surface of the MDM magnet assembly at distances of 0.400, 0.525, and 0.650 mm from the surface (red, blue, and green curves, respectively) corresponding to the lower internal wall, the center line, and the upper internal wall of the deposition channel.

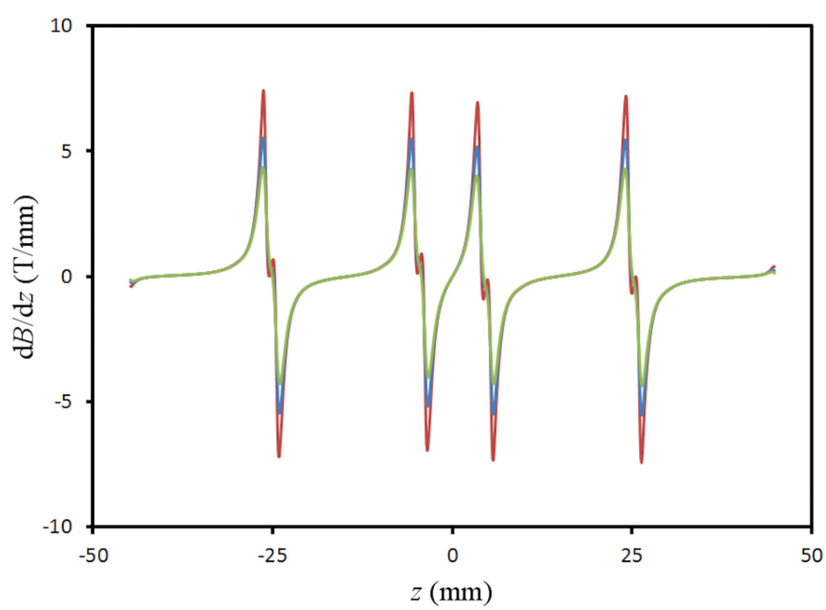

Fig. S7 The gradient in magnetic field *B* in the direction of flow across the surface of the MDM magnet assembly at distances of 0.400, 0.525, and 0.650 mm from the surface (red, blue, and green curves, respectively) corresponding to the lower internal wall, the center line, and the upper internal wall of the deposition channel.

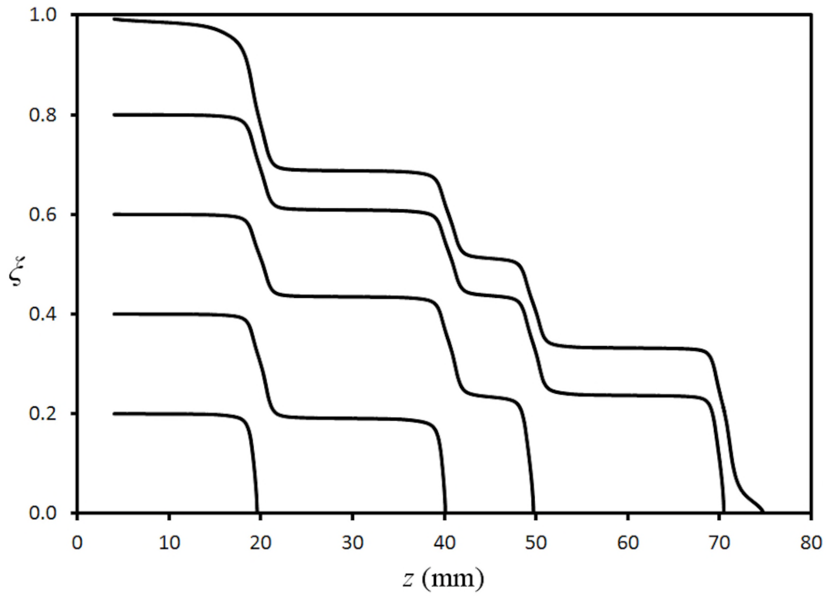

Fig. S8 Trajectories for the limiting condition of $V_{\mathrm{M}}M_{\mathrm{s}} / f \langle v \rangle = 0.00213$ mm/T for initial transverse positions of ξ_0 = 0.992, 0.8. 0.6, 0.4, and 0.2.

References

[1] F. Coumans, L. Terstappen, Detection and characterization of circulating tumor cells by the CellSearch approach, in: T. Kroneis (Ed.), Whole Genome Amplification: Methods and Protocols, Springer New York, New York, NY, 2015, pp. 263-278. https://doi.org/10.1007/978-1-4939-2990-0_18.

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[3] H. Ovadia, P.Y. Paterson, J.R. Hale, Magnetic microspheres as drug carriers: Factors influencing localization at different anatomical sites in rats, Israel Journal of Medical Sciences 19(7) (1983) 631-637.