THE FUTURE OF MAGNETIC BEAD RESUSPENSION

DEVICE FOR MAGNETIC BEAD RESUSPENSION IN A REAGENT TROUGH

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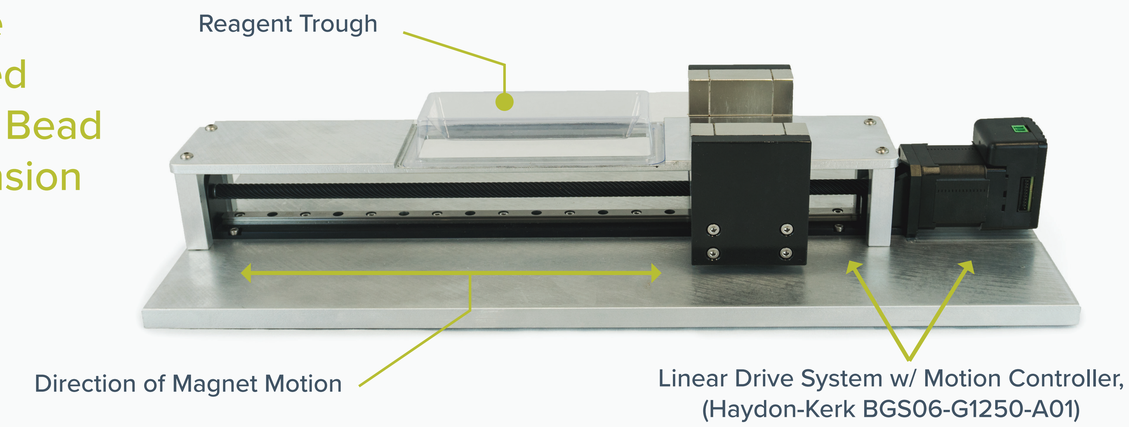
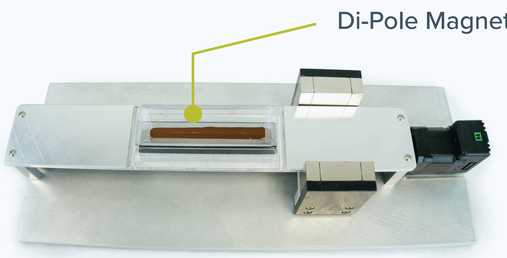
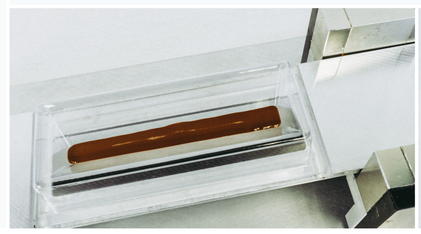
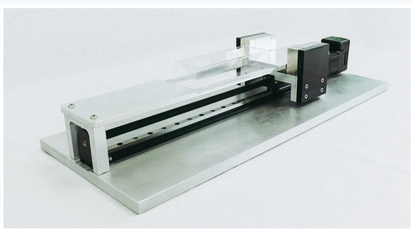
Prototype Automated Magnetic Bead Resuspension Device









ABSTRACT

The use of high gradient magnetic fields for the separation of particles is commonplace in the fields of immunology, proteogenomics, molecular biology, and other bio-medical industries. Target particles, comprising entities such as DNA, RNA, proteins, and other bio-molecules, may be isolated from a solution by the use of magnetic beads. These beads are stored in an open reagent trough until they are aspirated via pipette to the microtiter tray used to run the assay. During this time, which can last a few minutes, the beads will fall out of solution, which results in and incorrect bead concentration, that will negatively affect the assay results. This incorrect concentration will also lead to waste, as the bottom one-third of the trough will have a very high bead density which may not be able to be used. Therefore, the beads may need to be resuspended at various times throughout the procedure. Methods to accomplish this include shaking of the reagent trough or pipette tip mixing, both of which can be inconsistent and increase overall assay time. In addition, mechanisms to verify that the magnetic beads have been suspended into solution are very uncertain. Verification has mostly consisted of subjective techniques, such as visual observation or by choosing a tip mixing duration time based on the successful results of the protocol, which was derived during assay development.

A prototype device has been developed to automatically keep the bead solution homogenous in a reagent trough and allows for the bead concentrations to be quantitatively verified. The device consists of a base which holds a reagent trough containing the magnetic beads in solution. A magnet assembly is mounted to a carriage that is axially movable along a track, which is in line with the reagent trough. As the magnet assembly moves back and forth along the outside of the reagent trough, a magnetic field and field gradient moves along with the magnet, causing agitation of the beads. This agitation causes the magnetic beads to remain in suspension in the reagent trough, or it resuspends them if they have already begun to fall out of solution. The device is self-contained and can mount on the deck of, (and be integrated to), an automated liquid handling system. It can easily be modified to accommodate a variety of reagent troughs used throughout the life sciences field. The movement of the magnet assembly is automated and electronically controlled, so that unique motion protocols can be developed based on particle size and concentration. The device can verify that the beads are properly suspended through the use of a sensor, which is integrated to electronic controller.

MATERIALS & METHODS

- To prove the feasibility of this concept, a study was run using four different bead solutions. The device was evaluated on the following parameters:

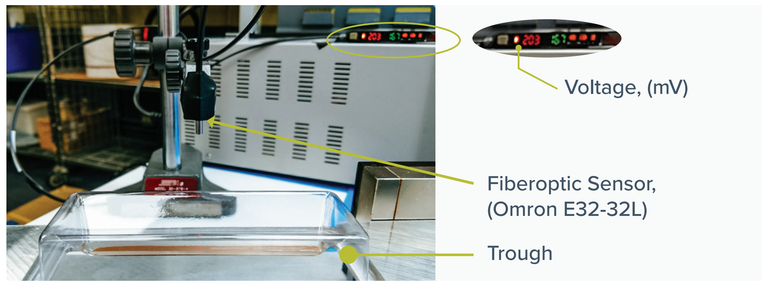
+ It's ability to resuspend the beads once they have fallen out of solution, (aggregated to the bottom of the trough).

+ It's ability of the device to keep the beads in solution once they were added to the reagent trough.

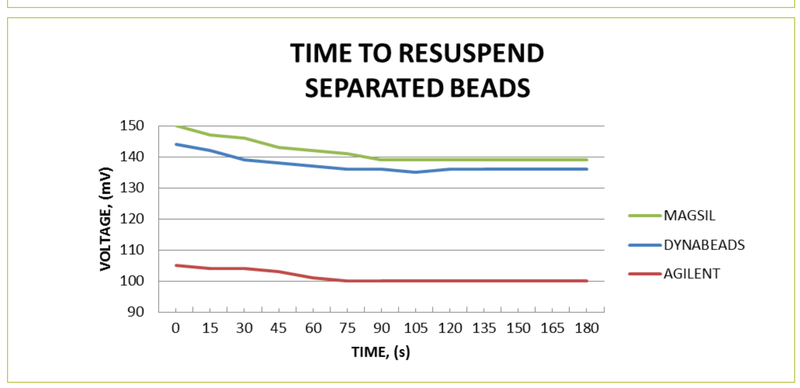
- The Bead Types evaluated were as follows:

BEAD TYPE	PARTICLE SIZE	SOLUTION DENSITY
Dynabeads M-270 Carboxylic Acid	2.8µm	100mg/mL
Agilent PL6604-0090AB Carboxyl Microspheres	4.6µm	20mg/Ml
Promega MagneSil Blue	5.6µm	1.1mg/mL

- All bead solutions were mixed in their bottles before they were added to the trough.
- The troughs were placed on a Dexter LifeSep® 96F magnetic separator to get them to fall out of solution.
- Verification of the two evaluation parameters was accomplished using a digital amplifier with a fiberoptic sensor. The sensor was positioned over the reagent trough. The amplifier provided an output in milli-volts, (mV). A reading was taken when the mixed bead solution was added to the trough, and at various times throughout the test.



RESULTS



- The study indicated that the device is able to keep all three bead types suspended in solution for at least 3 hours.
- The study indicated that the device was able to successfully resuspend all three bead types, when the beads fell out of solution.
- The resuspension time was between 75s, (Agilent), to 90s, (MagSil and Dynabeads).

CONCLUSION

The device is able to keep the solutions resuspended for an extended period of time.

The ability to resuspend magnetic particle solutions in a trough using a device with a moving magnet assembly was shown to be possible. The device was also able to keep the solutions resuspended for an extended period of time.

Furthermore, verification of proper magnetic bead solution homogeneity was demonstrated through the use of a sensor.

We feel that such a device could provide a distinct advantage in reducing assay time and solution waste, when integrated into an automated liquid handling system.

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