Magnetic Separators for Life Sciences

Scalable Magnetic Designs to Achieve Comparable Capture Rates and Capture Efficiency across Multiple Vessel Diameters

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About Magnetic Separators

Magnetic separators are used during a variety of magnetic carrier-based purification and bead coating processes such as protein separations, nucleic acid isolations, and immunodiagnostics. The separators typically contain strong magnets oriented in a geometry set to enhance the magnetic field projected into the container vessel to ensure adequate magnetic bead capture.[1] The purification and bead coating processes are often developed on a small, experimental scale before transfer to a functional process scale for use in industrial and manufacturing settings. In addition, batch size varies as dictated by material need, sales projections, and manufacturing schedules. Accordingly, the strong magnets used for magnetic carrier separation must be scaled to prevent process variation between batch size due to inadequate wash efficiency and discrepant capture rates.

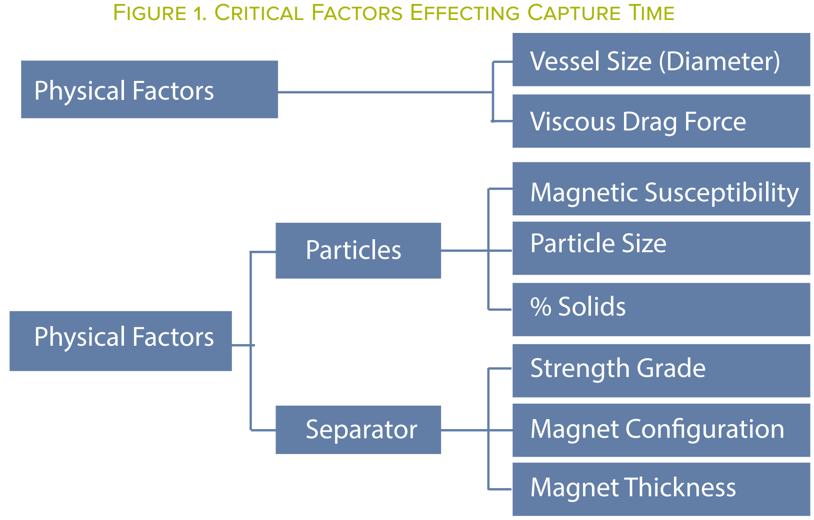
Magnetic Separator Scalability

In the context of this work, magnetic separator scalability is defined as the consistent capture of magnetic particles as measured by capture time and capture efficiency (>99%) independent of reaction vessel diameter.

Critical Factors Effecting Capture Time and Scalability

- Capture time can be effected by physical and magnetic factors as listed in Figure 1.
- Many factors such as particle suspension medium and bead magnetic susceptibility may be held constant while scaling batch sizes to ensure accurate results.
- Magnetic separators are typically designed around commonly available off-the-shelf or standard bottles.
- The diameter of the bottle plays a crucial role in separator scaling because it represents the maximum distance the particles must travel through the fluid to reach the vessel walls.

Figure 1. Critical Factors Effecting Capture Time



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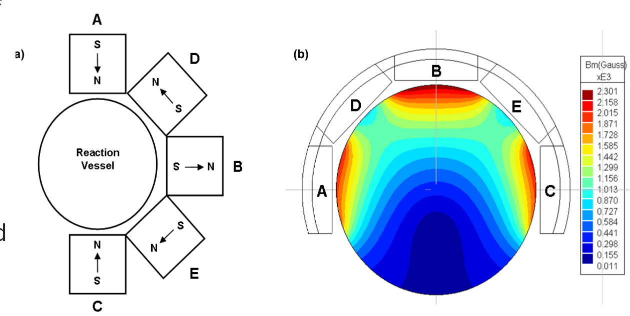
MAGNETIC SEPARATOR SCALING

- A mathematical relationship between the average magnetic field magnitude and the cross sectional vessel area has been devised for magnetic separators with magnets arranged in a quadrature geometry.
- This model was conceived using the following assumptions:
  - Particle size and magnetic susceptibility are held constant.
  - Magnetic particles interact independently of one another.
  - The magnetic circuit created by each separator is similar.
- Figure 2 depicts a schematic representation of the quadrature magnet geometry[2] (a) and the magnetic field gradient induced by the magnetic circuit (b).
- Magnetic separators were designed for consistent capture time by scaling the average magnetic field magnitude in the bottle section surface (calculated as the RMS value) to the area of that surface.
- B_{RMS} and Area Equations

FIGURE 2. QUADRATURE GEOMETRY AND MAGNETIC FIELD

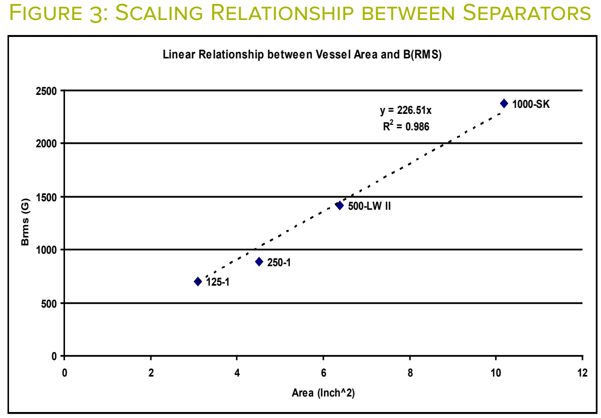


$$B_{RMS} = \sqrt{\frac{B_1^{\,2} + B_2^{\,2} + \ldots + B_n^{\,2}}{n}} \quad \text{versus} \quad Area = \pi r^2$$

TABLE 1. MAGNETIC FIELD MAGNITUDE AND VESSEL AREA

Separator	Radius (in)	Area (in²)	B_{RMS} (G)	BRMS / Area
125-1	0.9925	3.09	702	226.84
250-1	1.2	4.52	891	196.95
500-LW II	1.425	6.38	1420	222.59
1000-SK	1.8	10.18	2380	233.82

FIGURE 3: SCALING RELATIONSHIP BETWEEN SEPARATORS



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METHODS AND RESULTS

- The Dexter Magnetic Technologies, Inc. LifeSep® magnetic separators were built under the premise that magnet thickness and magnetic material could be varied systematically with an emphasis on the mathematical correlation between vessel size and magnetic field to provide scalable separations.
- Four magnetic separators ranging in size from 0.125L to 1L were examined to determine if consistent microparticle capture times and wash efficiencies could be achieved across vessels of increasing diameter using the appropriately scaled magnets.
- Capture Time at 1% Solids and Wash Efficiency at varying % Solids were examined as described.
- Capture Time:
  - Experiments utilized Dynabead M-270 Carboxylic Acid Microparticles; Size: 2.8 µm; Monodispersed in solution[3].
- Capture time was performed at 1% solids for each separator in phosphate buffered saline (PBS), pH 7.2
- A percent solids standard curve was established using solutions of known percent solids prepared gravimetrically with Dynabead M-270 microparticles.
  - The percent solids remaining in solution over time was calculated by comparing the measured solids content of collected aliquots to the percent solids at time 0 using the equation shown below.
  - Viscosity effects were examined for select separators using varying glycerol concentrations in PBS, pH 7.2 (see Table 4 and Figure 6).
- Capture time remained equivalent between the 125-1 and 250-1 separators with increasing liquid medium viscosity.
  - % Solids remaining in solution at time N (T_N).

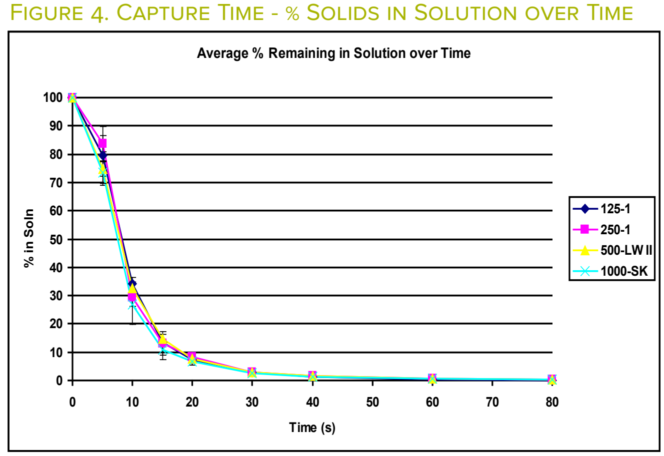
$$\%\,\text{Solids in Soln}\ T_N = 100 * \frac{\%\text{Solids}\ T_N}{\%\text{Solids}\ T_0}$$

TABLE 2. CAPTURE TIME - % SOLIDS IN SOLUTION OVER TIME

Time (s)	0	5	10	15	20	30	40	60	80
125-1	100.0	79.4	34.2	13.5	7.4	2.8	1.3	0.4	0.2
250-1	100.0	83.6	29.3	13.1	8.3	2.9	1.5	0.5	0.2
500-LW II	100.0	74.9	32.7	14.7	7.8	3.0	1.6	0.6	0.2
1000-SK	100.0	73.6	26.9	11.0	6.6	2.6	1.3	0.5	0.2

1% Solids in Phosphate Buffered Saline pH 7.2

FIGURE 4. CAPTURE TIME - % SOLIDS IN SOLUTION OVER TIME



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Methods and Results

- Wash Efficiency:
  - Performed using M-270 microparticles at varying % Solids (1%-10%) in PBS, pH 7.2.
- Wash efficiency was established by determining the weight of the liquid solution remaining in the bottle following aspiration and comparing to the full liquid weight.
- The impact of volume on wash efficiency in a single separator was examined and showed that wash efficiency does not vary significantly from the maximum to minimum separator batch sizes (data not shown).

Figure 5. Wash Efficiency per Separator at 1% Solids

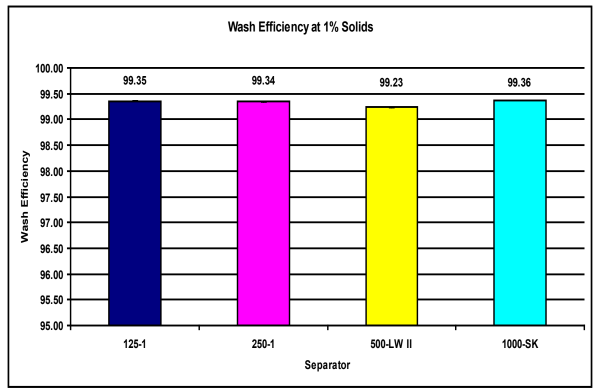


Table 3. Wash Efficiency

% Solids	1%	4%	8%	10%
125-1	99.35	96.57	93.77	92.08
250-1	99.34	97.16	n.t.	n.t.
500-LW II	99.23	97.32*	n.t.	n.t.
1000-SK	99.36	97.19*	n.t.	n.t.

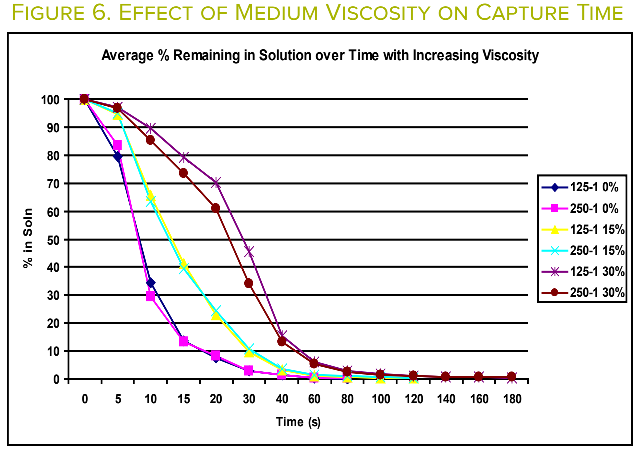
Indicated % Solids in phosphate buffered saline pH 7.2. n.t. - Not Tested
*Performed at the mimum batch volume for the indicated separator

Table 4. Effect of Medium Viscosity on Capture Time

Time (s)	0	5	10	15	20	30	40	60	80
125-1	100.0	94.7	65.7	41.2	22.9	9.7	3.1	1.2	0.7
250-1	100.0	95.0	63.5	39.6	24.4	10.6	3.5	1.6	0.9
500-LW II	100.0	97.2	89.7	79.3	70.2	45.6	15.6	6.0	2.8
1000-SK	100.0	96.8	85.2	73.6	60.8	34.2	13.2	5.2	2.6

Indicated % Solids in phosphate buffered saline pH 7.2. n.t. - Not Tested
*Performed at the mimum batch volume for the indicated separator

Figure 6. Effect of Medium Viscosity on Capture Time



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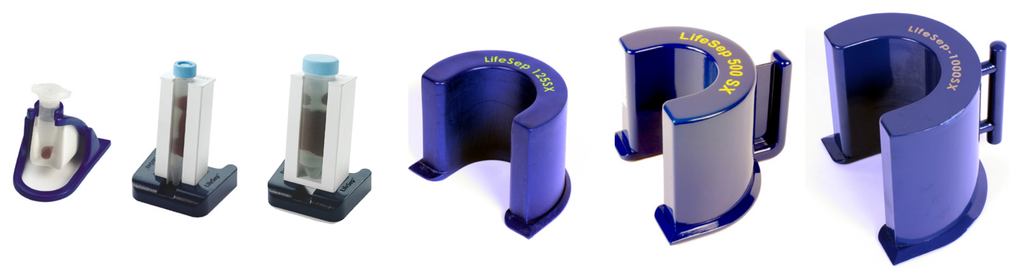
Conclusions

Magnetic separator technology is excellent for use in biotechnology and life science research applications that rely on biomagnetic bead processing such as DNA separation, cell isolation and rare cell detection, development of immunoassays, capture of biomolecules, and protein purification. Separators are typically designed to work with most commercially available superparamagnetic beads, roughly 0.8 μm and above.

Advantages:

- Scalability allows for a seamless transition between research and production phases.
- Open-faced configuration permits clear visibility and easy bottle removal.
- Field strength optimization allows the processing of high % solids (10% solids held by the 125-1 separator).



- A method to develop scalable magnetic separators in a quadrature geometry was proposed by establishing a correlation between the average magnetic field magnitude (B_{RMS}) of the separator and the reaction vessel cross sectional area (A).
- Using this correlation, the magnet thickness and material may be tailored to create the magnetic field gradient required to achieve comparable capture times across different vessel diameters.
- Microparticle capture consistently achieved >99% at 60 seconds for PBS solutions containing 1% solids (Dynabead M-270 particles) for each magnetic separator (0.125 – 1.0 L).
- Wash efficiency reached >99% supernatant removal across all magnetic separators at 1% solids, and varied only 0.75% (96.57% - 97.32%) at 4% solids for each magnetic separator.

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*Footnote Copy™ magnet arrays can be optimized