The potential of using magnetic fields in separation: Magnetic Chromatography?

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Why am I here addressing you?

- Along with my collaborator, Dr. Maciej Zborowski, a biophysicist at the Cleveland Clinic, we have been conducting magnetic cell separation research since 1995.
- Continuously funded by NIH, and approximately ¾ of this time by NSF, plus some VC and commercialization money...
- DARPA project (2008-2012): *Large-scale human placenta progenitor cell-derived erythrocyte production – continuous red blood cell production*. Our part was to separate red blood cells, RBCs, based totally on the *intrinsic* magnetic susceptibility of deoxygenated RBCs...
  - VERY weak signal, but clear difference between oxygenated and deoxygenated RBCs..
  - this started us on our “quest” to push the limits of permanent magnet power and “engineering design”
Examples of “weak”

Begs the question: Can we extend this to molecules??

Fundamentals governing magnetic separation

\[ m = \frac{u_m}{S_m} = \frac{(\chi_{RBC} - \chi_f)V_{RBC}}{3\pi \eta D_{RBC}} \]

\[ S_m = H \nabla B_0 \]

\[ \chi_{RBC} = F\left(\text{number of Fe atoms, Bohr magnetons per Fe}\right) \]

H = magnetic field strength
B_0 = magnetic flux density
Even more basic: $F_{mag} = (\chi_p - \chi_f) V H V B_0$

Intrinsic

Human ingenuity
Demonstration of particle magnetophoresis by CTV in gadolinium solution such that \( \kappa_1 < \kappa_{\text{medium}} < \kappa_2 \)

\[
\Delta \kappa_1 = \kappa_1 - \kappa_{\text{medium}} < 0 \quad \Rightarrow \quad m_1 < 0 \quad \text{Duke beads (polystyrene)}
\]

\[
\Delta \kappa_2 = \kappa_2 - \kappa_{\text{medium}} > 0 \quad \Rightarrow \quad m_2 > 0 \quad \text{Margel MMC3 beads}
\]

Date performed: 6/06/01
Composition: Duke 8.1 μm (16% CV) and Margel MMC3 5.2 μm beads
Concentration: not provided
Solution: 1:10 Magnevist (Berlex Labs) in 0.1% Pluronic F-68
Gd\(^{3+}\) concentration: 0.05M
Solution mag. susceptibility (SI):
\(-0.821 \times 10^{-5}\)
Solution viscosity: \(1.04 \times 10^{-3}\) kg/m s

Keep Video Clip “MMC3_Duke8” in the same folder for moving images
\[ \nabla \left( \frac{1}{2} \mathbf{H} \cdot \mathbf{B} \right) = \text{const} \]
Duke 8.1 & MMC3
100 images: 20 frames/sec
So, why am I here?
Can we separate molecules with magnetism??

- Conventional wisdom says: No!
- Randomizing thermal energy to great for entities smaller than 0.5 microns

\[
\frac{\text{thermal energy}}{\text{magnetic energy}} = \frac{k_B T}{\mu_0 MHV} > 1
\]

Ferrohydrodynamics, by R.E. Rosensweg (1985)
Number of assumptions/problems with this analysis/approach

• New, relative to 1985, more powerful magnets available, relatively inexpensive
• While submicron particles were considered in the previous “rule of thumb” analysis, distances for very high magnetic fields were considered on the order of cm.
• Assumed that to separate, you had to **move** the entity..
How about magnetic “chromatography”?

- We do not expect molecules to “move” to binding/active sites in chromatography! Let diffusion do the moving...
- Magnetic forces are highly Non-linear, with very high forces at very short distances!
- The “magnetic energy” calculation above was made not taking into consideration these very high, non-linear forces next to the magnetic dipole

\[
\frac{\text{thermal energy}}{\text{magnetic energy}} = \frac{k_B T}{\mu_0 MHV} > 1
\]

\[
F_{mag} = (\chi_p - \chi_f) V H V B_0
\]
The relationship between magnetic induction $B$ and magnetic field strength $H$ is given by $B = \mu_0(H + M)$, where $\mu_0$ is the permeability of vacuum. The graph shows the magnetic induction $B$ (in Tesla) plotted against magnetic field strength $H$ (in A/m) for different materials:

- 1010 steel
- 1018 steel
- cast Fe
- VanPer
- M19 transformer steel
- Carpenter 49 (Ni Steel)

Each material line is color-coded for easy identification.
Now consider the $\mathbf{H \nabla B}$ term in:

$$F_{mag} = (\chi_p - \chi_f) V H \nabla B_0$$

- This is where the “engineering design” comes in!
3.2 by 25 mm needle magnet
(N42 NdFeB magnet)

- Rapid drop in field
- Localized gradients
- Symmetry
Density Plot: $|B|$, Tesla

$1.330 \times 10^0$ : $>1.400 \times 10^0$
$1.261 \times 10^0$ : $1.330 \times 10^0$
$1.191 \times 10^0$ : $1.261 \times 10^0$
$1.122 \times 10^0$ : $1.191 \times 10^0$
$1.053 \times 10^0$ : $1.122 \times 10^0$
$9.830 \times 10^{-1}$ : $1.053 \times 10^0$
$9.135 \times 10^{-1}$ : $9.830 \times 10^{-1}$
$8.440 \times 10^{-1}$ : $9.135 \times 10^{-1}$
$7.745 \times 10^{-1}$ : $8.440 \times 10^{-1}$
$7.050 \times 10^{-1}$ : $7.745 \times 10^{-1}$
$6.355 \times 10^{-1}$ : $7.050 \times 10^{-1}$
$5.660 \times 10^{-1}$ : $6.355 \times 10^{-1}$
$4.965 \times 10^{-1}$ : $5.660 \times 10^{-1}$
$4.270 \times 10^{-1}$ : $4.965 \times 10^{-1}$
$3.575 \times 10^{-1}$ : $4.270 \times 10^{-1}$
$2.880 \times 10^{-1}$ : $3.575 \times 10^{-1}$
$2.185 \times 10^{-1}$ : $2.880 \times 10^{-1}$
$1.490 \times 10^{-1}$ : $2.185 \times 10^{-1}$
$7.950 \times 10^{-2}$ : $1.490 \times 10^{-1}$
$<1.000 \times 10^{-2}$ : $7.950 \times 10^{-2}$

Length, mm

1.6 mm

$7.5 \times 10^4 \text{ T/m}$

$1.5 \times 10^4$

$3.0 \times 10^3$
Consider a Hallback array (developed mid 90’s)

• Notice how field extends out on one side!
• Non-symmetry in the “z-direction”
Electrospun fiber

200 nm

4 \times 10^7 \text{T/m}

3.6 \times 10^6 \text{T/m}
Some Sample Calculations

• Consider Hemoglobin, O₂

• Hb, four “hemes”; one Fe each
  - 5-9 nm diameter, 381 nm³
  - volumetric magnetic susceptibility of 6.11x 10⁻³ (deoxy form)
  - for reference, RBC (deoxy) is 2.8 x 10⁻⁵

• O₂ well documented paramagnetic properties
  - 8.2 x 10⁻³ nm³
  - volumetric magnetic susceptibility of 1.91 x 10⁻⁶
Magnetic forces as a function of $\frac{1}{2} B \delta B$
“Energy” as a function of $\frac{1}{2} B \delta B$

- Hb
- RBC
- O2

Boltzmann thermal, 298 K

Boltzmann thermal, liquid N2

Van der Waals energies

Measured charged amino acid interactions

Antibody-Antigen
Summary

• On small scale, we can move very weakly paramagnetic entities (on the order of microns)
• On small scale, we can separate very weakly paramagnetic entities (on order of micron)
• A couple of reports exist of systems to enrich O₂ from air.
• Advances in the power of permanent magnets has been significant over the last couple of decades.
• Advances/application in computer modeling, nanoparticle supply, magnet designs, and microfluids, allows for potential to scale up systems that have the potential to separate molecules from liquid and gas.