sources, fluctuations in the aerosol size distribution are governed by the nearby sources and coherence near unity between b_s and nearly all ECI channels may be found for a fairly broad low-frequency band, although again the coherence is greatest and the band broadest for ECI channels 5 and 6.

The ECI has enabled us to carry out aircraft studies of fluctuations in the size distribution of tropospheric aerosol and of the relation of these fluctuations to those of trace gas concentrations and light scattering coefficients over Buffalo and Houston. Spectral analysis of the crosswind flight data upwind of industrial and urban sources in Buffalo indicates that most of the observed fluctuations were associated with atmospheric turbulence. Similar analysis of data from Houston suggests, among other features, secondary aerosol formation associated with ozone.

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6. This work was supported by the Aerosol Research Branch, U.S. Environmental Protection Agency. We thank E. J. Powers and Y. C. Kim for their advice and assistance with the spectral analysis.

13 January 1981; revised 17 April 1981

Isolation of Biological Materials by Use of Erbium (III)–Induced Magnetic Susceptibilities

Abstract. *Positive magnetic susceptibilities can be introduced into biological materials by their sequestration of erbium (III) ions. Particles of such material may then be manipulated under the influence of an external magnetic field.*

With the increasing use of magnetism for analysis, separation, and purification and the prospect of directing drugs to specific body locations under the influence of a magnetic field (*1*), ways of artificially introducing positive magnetic susceptibilities in otherwise diamagnetic materials warrant attention. The ability to do this selectively and in a predictable, controlled manner is especially desirable. Magnetic techniques have been used to separate red cells from whole blood (*2, 3*), recover specific cell types from heterogeneous mixtures with magnetic antibody complexes (*4, 5*), and rapidly purify enzymes by use of affinity ligands bound to magnetic beads (*6*). Here we report the effectiveness of Er^{3+} as a magnetizing agent.

Preliminary observations by Westcott (*7*) indicated that large positive susceptibilities can be introduced in biological particles by their adsorption of magnetic cations (*8*). Such "magnetized" particles can then be easily manipulated by magnetic fields. The trivalent cations of the lanthanide series are especially effective in this respect. Owing to the presence of unpaired *f* electrons, these cations have some of the highest magnetic moments of any individual ions (Er^{3+}, 9.5 Bohr magnetons; Ho^{3+}, 10.3 Bohr magnetons). In addition, their large charge-to-radius ratio results in strong affinities for suitable negatively charged ligands. In the work reported here we magnetized a variety of substances by binding Er^{3+} to anionic moieties in the target material. Particles of materials that have been magnetized in this way can be retrieved from suspension under the influence of an external magnetic field.

The principles underlying such magnetic separations can be easily demonstrated by adding a small quantity of beaded cation-binding resin to a solution of 1 to 10 m*M* $ErCl_3$. In the absence of Er^{3+}, the beads show no magnetic behavior. With Er^{3+} in the solution, they are strongly attracted to a magnet placed against the sides of the container.

The forces on a particle suspended in a magnetic field involve complex mathematics, even for relatively simple geometries. Such expressions may, however, be generalized for a particle in a medium where the magnetization of neither the particle nor the medium is large compared to the magnetic field strength, H. Computation is simplified by considering only the z component of force due to the z component of the field gradient. With these assumptions, the force in the direction of the magnetic gradient on a particle immersed in a fluid can be adequately described by

$$F_z = (\psi_f - \psi_p) H_z \frac{\delta H_z}{\delta z} \qquad (1)$$

where ψ_p and ψ_f are the magnetic susceptibilities of the particle and the fluid, respectively, and H_z $(\delta H_z/\delta z)$ is the volume average of the corresponding product (*9*). Thus, neglecting any hydrodynamic and gravitational forces, a particle with a magnetic susceptibility ψ will experience a force equal to the difference between the ψ of the medium and that of the particle, times H, times the gradient of the field strength over the volume of the particle.

In the simple demonstration described above, the cation-binding particles are normally diamagnetic. Hence the positive magnetic susceptibilities observed must arise from adsorption of paramagnetic Er^{3+} ions from solution. Considering Eq. 1, the attraction of these particles by magnetic fields indicates that the concentration of Er^{3+} cations about the particles is greater than that of a corresponding volume of solution. Preliminary experiments with a torsion magnetometer have indicated that mutual alignment of the electron spins of adsorbed Er^{3+}, which would produce domains of pseudoferromagnetism, does not occur. The resulting positive magnetic moment should therefore be proportional to the sum of the moments of the individual Er^{3+} ions bound to each particle.

The relation between magnetic forces and adsorbed paramagnetic cations can be explored, without complex mathematical treatments, by ferrography, a well-characterized technique for magnetic separations (*10*). The principles of the ferrographic method are illustrated in Fig. 1. The relative volume magnetic susceptibility of a particle can be determined by the distance (millimeters) it travels along a glass slide in the presence of a restraining perpendicular magnetic force. In this fashion, the relative magnetic susceptibility of each component of a mixture of particles can be assessed while separating the components on the basis of their magnetic behavior.

In the application described here, the adsorption of the paramagnetic cation Er^{3+} by several types of cation-binding material was employed to demonstrate the principles of induced magnetic moments. Hydroxyapatite, Dowex 50W, and carboxymethyl cellulose were selected as model particles. Cellulose particles served as a reference, since their Er^{3+} binding would be minimal under the conditions used. The extent of Er^{3+} binding by equal weights of each material in 150 m*M* KCl, *p*H 6.0, was determined by the murexide technique over a range of initial Er^{3+} concentrations from

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Table 1. Relative magnetization of standard particles compared to their binding of Er^{3+} and theoretical volume magnetic susceptibilities ψ_{th}. Suspensions of the particles were treated with Er^{3+} at pH 6.0, and their relative volume magnetic susceptibilities measured, as magnetic path length, by the technique of ferrography. Scatchard analyses were performed to derive the affinity, K, and concentration of binding sites, n, for Er^{3+} on the particles. The volume (microliters) of 0.1 mg of each particle was determined to be 1.13 for hydroxyapatite, 0.098 for Dowex 50W, and 1.2 for carboxymethyl cellulose.

Particle	Functional group	Size (μm)	K (mM^{-1})	n (mM)	Ψ_{th}	Magnetic path length (mm)
Hydroxyapatite	$-PO_4$	2 to 80	4.6	0.43	1.75	5
Dowex 50W	$-SO_3H$	10 to 80	3.5	0.35	1.34	23
Carboxymethyl cellulose	$-COOH$	10 to 150	2.5	0.07	0.15	58
Cellulose	None	10 to 150	0	0	0	∞

0.1 to 10 mM. The affinities for Er^{3+} in this concentration range are hydroxyapatite > Dowex 50W > carboxymethyl cellulose. As anticipated, cellulose bound no Er^{3+} under these conditions (Table 1).

Small amounts (0.1 mg) of each material were then suspended in solutions of 150 mM KCl, pH 6.0, containing 0.1 to 10 mM Er^{3+} (1 ml) and the relative magnetic susceptibility of each was determined by ferrography. Measurements of the distance traveled by particles of each material before contacting the glass slide at any of the Er^{3+} concentrations showed the order of magnetization to be the same as the relative affinity for Er^{3+}: hydroxyapatite > Dowex 50W > carboxymethyl cellulose. Cellulose was not magnetized (Table 1).

Scatchard analysis (*11*) of the Er^{3+} binding data permit calculation of an effective binding affinity, K, and the concentration of binding sites, n, per 0.1 mg of each type of particle (Table 1). With these figures, it is possible to relate the extent of Er^{3+} binding to an effective volume magnetic susceptibility. The paramagnetic susceptibility of a particle can be expressed as

$$\Psi_p \propto \frac{Kn}{V} \qquad (2)$$

where V is the volume occupied by the particle. When theoretical volume susceptibilities for 0.1 mg of each type of particle (Table 1) are compared to the degree of magnetization, the observed susceptibilities of the particles can be predicted by Eq. 2.

In principle, these concepts can be extended qualitatively to the magnetic separation of particles of biological origin. At present, Er^{3+} adsorption and magnetic separation is employed in arthritis research (*12*). Magnetic retrieval and separation of small wear particles of bone and cartilage from synovial fluid aspirates has shown promise as a tool for investigating the biomechanical degradation of cartilage and bone in a number of arthritides. Bone and cartilage adsorb considerable quantities of Er^{3+} and can be readily recovered by magnetic techniques.

We have demonstrated that yeast cells, bacteria, and Visna virus can be magnetically recovered from Er^{3+}-containing solutions with an efficiency greater than 80 percent (*13*).

These preliminary studies suggest that magnetic precipitation may provide solutions to problems in isolation and separation that are not available with more traditional techniques. Moreover, the potential for recovering a specific material from heterogeneous mixtures offers interesting possibilities. Since the binding of Er^{3+} to a negatively charged group is affected by such physical factors as the pK_a of the binding group, pH, and ionic strength, it may be possible to use variations in any of these parameters to magnetize preferentially a specific material. For example, separation of Dowex 50W from carboxymethyl cellulose can be achieved by increasing the ionic strength of the medium, so that the weaker binding of Er^{3+} to carboxymethyl cellulose is reduced below that required for magnetic retrieval and only the Dowex 50W is precipitated by the magnetic field. Similarly, selective recovery of bone particles from mixtures of cartilage and bone may be achieved by treating the mixture with Alcian blue, a histological dye that binds tightly to the anionic sites of cartilage. Under these conditions, only the mineralized material will bind Er^{3+} and be magnetically precipitated. Using these approaches, it may be possible to modify the degree of magnetization, depending on physical and chemical properties of the substance being magnetized and the presence or absence of selective agents that modulate the binding of Er^{3+} and hence magnetization.

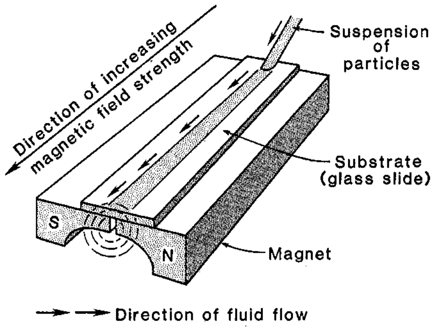

Fig. 1. The ferrographic technique constrains a liquid, in which the particles are suspended, to flow over a glass slide (the substrate) placed above the poles of a strongly divergent magnetic field. A particle with a volume magnetic susceptibility that is positive with regard to the fluid will be attracted to the surface of the substrate by the magnetic field. In this configuration, a particle suspended in the liquid enters the magnetic field moving parallel to the surface of the slide. As fluid flows down the slide, this particle will experience a magnetic force perpendicular to the fluid flow. Complete mathematical descriptions of the effects of hydrodynamic, gravitational, and magnetic forces on such a particle can be found in (*14*)

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30 January 1981; revised 5 May 1981