

THE PHYSICAL PROPERTIES OF CYTOPLASM. A STUDY BY
MEANS OF THE MAGNETIC PARTICLE METHOD. PART II.
THEORETICAL TREATMENT

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A. INTRODUCTION

IN Part I (1) a method was described for measuring some of the physical properties of the cytoplasm of chick cells in tissue culture by means of magnetic particles. The cells were allowed to phagocytose these particles, which were then acted on by magnetic fields, their movements being observed simultaneously under high magnification.

In this paper the theoretical basis for the experimental methods used has been set out. The results are mainly standard pieces of magnetism and hydrodynamics, but as they are scattered about in the literature it was thought worth while to bring them all together in one place.

The paper has been written for workers who may wish to use the method themselves, or who wish to examine its foundations critically. For those only interested in the results an extended summary of the theoretical conclusions has already been given in Part I. An elementary knowledge of magnetism and hydrodynamics is therefore assumed. There are occasional remarks from a more advanced standpoint, but they are not crucial to the main results.

The experimental methods have been set out in part I. It will suffice here to state the general theoretical problems for which we require solutions. There are three main cases. They are

(1) Twisting: the permanent magnet case.

In this case the magnetic particle is turned into a little permanent magnet by applying a large magnetic field momentarily. It is subsequently twisted by a much smaller field applied in a direction roughly perpendicular to its permanent magnetic moment.

(2) Twisting: the soft iron case.

In this case the material is considered to have no hysteresis. A magnetic field is applied at a small angle to the length of the particle, which is thus twisted.

(3) Dragging.

In this case a large field, with a large field gradient is applied. The magnetic particle is magnetically saturated, and after being twisted into line, is dragged by the field gradient.

We wish to calculate the velocity (or the angular velocity) of the particle in terms of its size, shape, and magnetic properties, and the physical properties and boundaries of the medium in which the particle is embedded.

We tackle the problems in the following order. We first show that we can neglect the effects of inertia, and by elementary arguments find how the forces vary with scale. We then consider the behaviour of the medium, discussing the effects of the shape of the particle, of boundaries, and of non-newtonian and elastic behaviour. Next we give the formulae for the magnetic forces on the particle, and then in section F we show how all the factors can be combined to evaluate the velocity (or angular velocity) of the particle for the three main cases.

Finally we give some brief theoretical notes on the production of large field gradients and a note on some comparative numerical values for the stress.

B. GENERAL CONSIDERATIONS

1. Inertia

Inertia will delay the approach to the steady state and will alter the final velocity distribution. We shall show that both of these effects can be neglected in our experiments mainly because the particles are so small.

There are two problems that can be considered separately. Firstly, the inertia of the fluid, secondly the inertia of the particle.

For the inertia of the fluid the relevant characteristic of the motion is the ratio of the inertia forces to the viscous forces (Reynold's number). It is given by

$$\frac{\sigma \varrho a^2}{\eta}$$

where σ = reciprocal of a characteristic time

ϱ = density of the fluid

η = viscosity of the fluid

a = a characteristic length

(see for example the case of an oscillating sphere, (7), paragraph 354). This formula applies strictly only to short particles.

If the above parameter is $\ll 1$, the inertia of the liquid is negligible. Another use of the parameter is that the value of $\left(\frac{1}{\sigma}\right)$ defined by putting $\frac{\sigma \varrho a^2}{\eta}$ equal to unity, gives the *order* of the time required to approach the steady state.

We shall not be considering particles bigger than 10 μ in diameter, so we

may put $a = 5 \times 10^{-4}$ cm. If we take as a lower bound for η the value for water (0.01 poise), since biological fluids can scarcely be less viscous, and put $\varrho = 1$, we obtain for the upper bound of $\left(\frac{1}{\sigma}\right)$ the value $\frac{1}{40}$ milliseconds.

This is naturally very much smaller than anything we have measured. We should note in passing that if the margin were not so great a more exact treatment would be advisable. Our formula gives the time for the particle to reach a good fraction of its final velocity, but in certain cases the later stages of the asymptotic approach to the final velocity may take much longer than the earlier stages.

These results only apply strictly to the case of an infinite fluid. We can give an argument which suggests that the effect of adding fixed boundaries will usually be to decrease the time to approach the steady state. Consider two cases: firstly a particle in an infinite fluid, secondly the same particle with fixed boundaries added to the fluid. Let the forces applied to the particles be such that the same steady velocity is attained in the two cases. We will assume that as a rough measure of the time to approach equilibrium we may take the ratio of the kinetic energy of the fluid to the rate of dissipation of energy, both *for the steady state*. The effect of fixed boundaries is to increase the resistance and therefore the rate of dissipation of energy. The boundaries also reduce the amount of fluid in motion and over most of the volume¹ decrease the fluid's velocity. The total kinetic energy is thus likely to be reduced. Therefore the ratio referred to above will be decreased.

To estimate the effect of the inertia of the particle we consider the case of the dragging of an iron sphere. The ratio of the inertia to the viscous forces is

$$\frac{4\pi}{3} \frac{a^3 \varrho' \frac{dv}{dt}}{6\pi\eta a v}$$

where v = velocity

ϱ' = density of sphere

If we define the characteristic time $\frac{1}{\sigma}$ by the equation

$$\frac{dv}{dt} \equiv \frac{v}{\left(\frac{1}{\sigma}\right)}$$

¹ This assumes that the boundaries do not force the flow into a very restricted channel, in which case the velocity would be increased considerably.

this ratio becomes

$$\frac{2}{9} \frac{\sigma \rho' a^2}{\eta}$$

which apart from the numerical factor is the same form as before, except that ρ' is now the density of the iron. It can easily be shown that exactly the same type of parameter is involved in the case of rotation. Thus the effects of the inertia of the particle are negligible.

The case for non-newtonian fluids, whose "viscosity" varies with shear is not quite so clear cut. However the margin in our experiments is so big that we can simply consider the extreme case where the inner parts of the liquid move effectively as a solid, and the outer parts as a newtonian liquid. This is clearly similar to the movements of a body of increased radius in water. In our experiments the radius of the body is bounded by the size of the cell, so that we again get a very small value for the time to reach equilibrium.

The case for the visco-elastic medium is given on page 519.

The conclusion is the same. Thus for all possible cases in our experiments the steady state is reached in a time very much smaller than anything we can measure.

2. Scale

We shall next show, by simple dimensional arguments, how the forces involved in dragging and twisting change with scale. We only consider a range of scale over which the magnetic factors (e.g. $\frac{dH}{d\kappa}$) can be considered constant.

(a) Dragging

As before let a = characteristic length of particle
 v = characteristic velocity of particle
 η = viscosity of (newtonian) liquid
 ρ = density of fluid

The density of the particle is clearly not involved in the steady state condition. We restrict ourselves to a range of scale over which the density of the fluid can also be ignored, for the reasons given above.

The magnetic field will produce a force per unit volume given by

$$I \frac{dH}{d\kappa}$$

where I = magnetic induction of the particle

$\frac{dH}{d\kappa}$ = magnetic field gradient producing the force.

A force per unit volume has the dimensions $M L^{-2} T^{-2}$. The only combination of a , v and η which will give this is $\left(\frac{\eta v}{a^2}\right)$.

Whence we obtain

$$v \sim \frac{a^2}{\eta} \cdot I \left(\frac{dH}{d\kappa}\right).$$

Thus, as the scale is reduced, the velocity decreases as the square of the characteristic length. The time for the body to traverse its own length increases linearly with the reciprocal of the characteristic length.

(b) Twisting

Here the magnetic couple per unit volume depends on

$$(IH) f(\theta)$$

where θ is an angle.

This has the dimensions $M L^{-1} T^{-2}$ and from ω (the typical angular velocity), η and a we can only form the combination $\eta \omega$.

Thus

$$\omega \sim \frac{IH}{\eta} \cdot f(\theta).$$

Therefore the angular velocity does not vary with scale.

Note that if the liquid has boundaries they, too, must be scaled for the above results to apply.

If the liquid is non-newtonian comparisons can only be made between conditions under which the shear is the same. For dragging this occurs when the time for the particles to go their own lengths is the same; for twisting, when the angular velocities are the same. The interesting result for twisting, that the angular velocity is independent of scale is therefore also true for the non-newtonian case.

Finally note that the magnetic conditions have *not* been scaled. Scaling the magnets producing the field makes no difference to the value of the field, but does alter the field gradient. This reservation is therefore important in dragging but not in twisting. It is easy to see that if we *do* scale the magnets for the dragging case the time for a particle to be dragged its own length is independent of scale for both the newtonian and the non-newtonian cases.

C. THE FORCES ON A BODY IN A VISCOUS FLUID

1. Variation with shape

The variation with shape is naturally more complicated than the variation with scale, and has only been worked out for special cases, usually in an infinite fluid. It is possible to obtain the result for the general ellipsoid, but we shall only quote those for ovary ellipsoids of revolution, as we require them merely to give some idea of the general behaviour. We consider in this section the formulae for a body immersed in an infinite newtonian liquid, leaving to the two following sections the consideration of boundaries and of non-newtonian behaviour.

We shall use the following notation for the ovary ellipsoid:

major axis = a

minor axes = $b = c$

eccentricity, e , given by $1 - e^2 = \frac{b^2}{a^2}$

We denote

$$\frac{2(1-e^2)}{e^3} \left(\frac{1}{2} \log \frac{1+e}{1-e} - e \right) \text{ by } \alpha_0.$$

$$- \left(\frac{1-e^2}{2e^3} \log \frac{1+e}{1-e} - \frac{1}{e^2} \right) \text{ by } \beta_0.$$

and

$$\frac{b^2}{e} \log \frac{1+e}{1-e} \text{ by } \chi_0.$$

(All logs are natural logs).

(a) *Twisting*

For a sphere: couple = $8\pi\eta a^3\omega$

where ω = angular velocity

(7, para 334)

For an ovary ellipsoid of revolution:

We shall only consider the case of rotation about a minor axis. This has been solved by Edwards (2), but owing to an algebraical slip towards the end he omits the factor $2/3$. The correct result, in his notation, is, for the general ellipsoid,

$$\text{couple} = \frac{32\mu\pi\omega}{5} \left(\frac{b^2 + \frac{2}{3}c^2}{b^2B + c^2C} \right).$$

This being adapted to our notation, and restricted to the case of the ovary ellipsoid, becomes

$$\text{couple} = \frac{32\eta\pi\omega}{5} \left(\frac{a^2 + \frac{2}{3}b^2}{a^2\alpha_0 + b^2\beta_0} \right) a b^2.$$

We express this as couple = $k \cdot 8\pi\eta\omega a^2 b$ and evaluate k numerically for different values of a/b .

Some values are given in Table I.

TABLE I

$\frac{a}{b}$	1.0	2.0	3.0	4.0	5.0	10.0	20.0
k	1.0	0.84	0.91	1.00	1.10	1.60	2.50

In the limit $(a/b) \rightarrow \infty$, $k \rightarrow \frac{2}{5} \left(\frac{a}{b} \right) \frac{1}{\left(\log \frac{2a}{b} - 1 \right)}$.

(b) *Dragging*

For a sphere:

the force is $6\pi\eta a v$ with the usual notation

(7, para 337)

For an ovary ellipsoid of revolution

(i) in the direction of its major axis, a

we have force = $6\pi\eta R v$

where

$$R = \frac{8}{3} \frac{a b^2}{\chi_0 + \alpha_0 a^2}$$

(7, paras 339 and 114)

This reduces to

$$R = \frac{8}{3} \frac{a e}{\left(1 + \frac{1}{e^2} \right) \log \frac{1+e}{1-e} - \frac{2}{e}}$$

For the special case where the ellipsoid is very long, so that $a \gg b$

$$R \rightarrow \frac{4}{3} \frac{a}{\left(2 \log \frac{2a}{b} - 1 \right)}$$

Numerical values are given in Table II below.

(ii) in the direction of its minor axis, b

we have
$$R = \frac{8}{3} \cdot \frac{a b^2}{\chi_0 + \beta_0 b^2}$$

(7, paras 339 and 114)

whence we obtain

$$R = \frac{16}{3} \cdot \frac{a e}{\left(3 - \frac{1}{e^2}\right) \left(\log \frac{1+e}{1-e}\right) + \frac{2}{e}}$$

and when $a \gg b$

$$R \rightarrow \frac{8}{3} \cdot \frac{a}{\left(2 \log \frac{2a}{b} + 1\right)}$$

Numerical values are given in Table II.

TABLE II
Values of a/R for the dragging of an ovary ellipsoid.

b/a	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
a/R (along major axis)	∞	3.764	2.799	2.267	1.914	1.662	1.467	1.314	1.191	1.091	1.000
a/R (along minor axis)	∞	2.617	2.108	1.815	1.606	1.451	1.326	1.224	1.138	1.063	1.000

The numerical values are taken from Gans (4), where the numerical results for a planetary ellipsoid are also given.

2. The effect of boundaries

(a) Boundaries are, in general, more important in dragging than in twisting. This is not surprising when we remember that the viscosity of a viscous fluid through which a sphere is *dragged* falls off as $\frac{1}{r}$ a long way from the sphere (in contrast to the case where the inertia is important and viscosity negligible), while the angular velocity in the fluid round a *rotating* sphere falls off as $\frac{1}{r^3}$.

The following examples illustrate this point. In all cases a is the inner radius, b the outer radius.

(i) translation of a sphere in a fixed cylindrical tube

$$\text{force} = 6 \pi \eta a v \left(1 + 2.104 \frac{a}{b} + \dots\right)$$

(ii) rotation of a sphere in a fixed spherical shell

$$\text{couple} = 8 \pi \eta a^3 \omega \left(\frac{1}{1 - a^3/b^3}\right)$$

(iii) translation of a cylinder in a fixed cylinder

$$\text{Force per unit length} = 2 \pi \eta v \left(\frac{1}{\log a - \log b}\right)$$

(iv) rotation of a cylinder in a fixed cylinder

$$\text{couple per unit length} = 4 \pi \eta a^2 \omega \left(\frac{1}{1 - a^2/b^2}\right)$$

(b) Dragging

For the translation of a sphere along the axis of a fixed cylindrical tube the solution with the higher terms included is

$$\text{force} = \frac{6 \pi \eta a v}{1 - 2.104 \left(\frac{a}{b}\right) + 2.09 \left(\frac{a}{b}\right)^3 - 0.95 \left(\frac{a}{b}\right)^5 \dots}$$

where a = radius of sphere

b = radius of tube.

This formula is for the case when Reynold's number is infinitesimal. (3.)

Thus when $b = 3a$ the formula gives a resistance of 2.7 times that for an infinite fluid, and for $b = 4a$, a factor of about 2.0, so that increases of this sort are very probable in a small cell. Neighbouring inclusions may well have quite a large effect.

For bodies of a shape not greatly different from a sphere, a good approximation is to use the above formula taking for " a " the value for the "equivalent sphere" in the infinite fluid case. This approximation can only be very rough for the case of a very elongated body, or of a wall very close to a body.

(c) *Twisting*

The effect of boundaries on the couple exerted on a compact body of revolution rotating about its axis of symmetry is fairly easily grasped, and is small unless the boundaries are near the equatorial belt of the body.

The effect of the boundaries on less restricted bodies (including our particles) has not been worked out, but below we try to give a rough bound.

(i) *Bodies of revolution.*

These have been treated by Jeffery (6). He gives a general treatment which can be described as follows: for *any* body of revolution rotating in an infinite fluid about its axis of symmetry we can find a family of surfaces each of which rotates with constant angular velocity. We can then always obtain the solution for the body rotating within one of these surfaces, regarded as a fixed wall, by superimposing a uniform counter-rotation on the whole system to bring the "wall" to rest. This explains the form and intimate relationship between the fall-off of angular velocity and the increase of couple due to a boundary in the two simple cases of rotation quoted above.

Jeffery gives the formulae for the case of an ellipsoid of revolution. A typical result, for a planetary ellipsoid with an axial ratio of 2.24, surrounded by a confocal planetary ellipsoidal shell such that the spacing at the equator is 20 per cent of the body's equatorial radius, shows that the shell increases the viscous couple by a factor of 1.9.

Jeffery has also solved another illuminating case; that of a sphere rotating close to a fixed plane perpendicular to the axis of rotation. The results show that the plane has to be extremely close to the pole to have any considerable effect e.g. at a distance of 2 per cent of the radius it increases the resistance by only 17 per cent. This is because the major part of the viscous couple comes from the equatorial belt, where both the arm of the couple and the velocity are big.

We may thus conclude that unless the boundary approaches close to the body at points far from the axis of rotation, the increase in couple is unlikely to be big.

(ii) *Other bodies.*

In general our particles are not bodies of revolution, and even if they were we could not easily distinguish their different angular positions under the microscope. Apparently no case has been solved which helps us here.

We propose to estimate the couple on an ovary ellipsoid of revolution rotating inside a fixed spherical shell, radius d (d not too close to a) as follows: we suspect that such a shell would not increase the couple on the el-

liploid by more than it would increase that of a sphere of radius a . This implies that the couple would be increased by no more than

$$8\pi\eta a^3\omega\left(\frac{a^3}{d^3}\right)$$

neglecting terms higher than $\left(\frac{a^3}{d^3}\right)$

Now we have shown (page 511) that the couple on the ellipsoid in an infinite fluid is approximately given by

$$8\pi\eta a^2 b \omega$$

so that the total couple could be written as

$$8\pi\eta a^2 b \omega \left(1 + p \cdot \frac{a^3}{d^3}\right)$$

where p is probably between (a/b) and 1. However this estimate is little more than a guess.

For a comparatively short particle the boundaries are not likely to cause a large variation in the couple e.g. for d one half greater than a , and for a particle of axial ratio 2 : 1, the couple is probably not more than doubled.

Finally we consider how a fixed obstruction at one end of the particle affects its behaviour. A rough estimate can be made by comparing this case with that of a particle of twice the length, and acted upon by double the magnetic couple, with obstructions near its middle. It is clear that in this second case the motion would hardly be altered at all by the obstructions, as they are so near the axis of rotation. The viscous couple on the second particle in a newtonian fluid is very roughly 4 times that of the first (see page 512). Therefore the angular velocity will be halved.

Thus in an infinite newtonian liquid an obstruction at one end increases the resistance so that about twice the couple needs to be applied to give the same angular velocity. It also, of course, produces a small translation of the particle.

Stated in this way it seems probable that the result would also apply to most non-newtonian liquids.

Note that it is not essential for the obstruction to *touch* the particle, as a very close approach may produce sufficient resistance to reduce the angular velocity appreciably.

3. *Non-newtonian behaviour*

So far we have only considered newtonian liquids. This is sufficient for calibration liquids, but may not be for the cytoplasm.

Consider first the behaviour of a liquid, whose "viscosity" varies with shear, in a concentric cylinder viscometer (neglecting end effects). It can be shown that what we measure is the average value of the fluidity $\left(\frac{1}{\eta}\right)$. In symbols

$$\eta_e = \frac{\int_{s_a}^{s_b} ds}{\int_{s_a}^{s_b} \frac{ds}{\eta}}$$

where η_e = experimental value of the viscosity

s = shearing stress

s_a = shearing stress at inner cylinder

s_b = shearing stress at outer cylinder

That is, if we substitute the experimental values of angular velocity, etc in the usual formula for the viscosity, we obtain the above value of η_e . It is assumed that the "viscosity" is a function of the instantaneous value of the shear only.

This solution is possible because the surfaces in the fluid which retain their shape (i.e. move as if solid) are surfaces of constant stress, and one can therefore give the stress distribution across the annulus irrespective of the curve of $\left(\frac{1}{\eta}\right)$ against s . This condition also applies to the only other case which has been worked out, namely that of the flow through a capillary, although the actual formula given above does not.

We thus see, as is intuitively obvious, that the effect is to slur over the detailed variations in the curve of $\left(\frac{1}{\eta}\right)$ against s , and to give an average value.

The details are usually got by making b only slightly greater than a , so that the average is taken over only a very small portion of the curve on each occasion, and by repeating at different rates of shear to cover a wide range.

We are clearly unable to do anything of this sort in our experiments. Even for a sphere in a non-newtonian liquid the problem is of a different order of

difficulty and does not appear to have been solved. The shear stress varies with latitude from zero to a maximum and it is not at all clear how it distributes itself in the non-newtonian case. The problem of the ellipsoid is even more hopeless.

However it appears extremely plausible that if we substitute the experimental values in the formula, the value of η derived will correspond to some average value; that is, to some point on the curve of η against s between the maximum value of s and some minimum, probably zero. Moreover it seems very likely that the apparent change of η with shear will be less than the maximum change anywhere within this region. Since we cannot rely on our experimental arrangements to measure small differences accurately, we conclude that this method will only show up large changes of "viscosity" with shear, and may conceal small changes.

We note at this point a feature which may be expected in the behaviour of a non-spherical particle in a non-newtonian fluid of the type which becomes very viscous at low shearing stresses. Since the shear near the axis is much less than that near the ends of the particle, the fluid may behave almost as a solid at points near the axis, and also at points far from the particle, so that the flow may take place over a rather restricted region.

D. *The forces on a body in a jelly*

We can apply almost all the previous formulae to the case of a particle in an isotropic elastic medium. Since we are only dealing with feeble jellies we may take Poisson's ratio equal to $\frac{1}{2}$. For *small* strains all the algebraical results for *velocity* in a viscous newtonian fluid apply to the *deflection* in a hookian elastic medium, providing we substitute n , the rigidity modulus, for η the viscosity.

For example, the couple on a sphere rotating in a viscous liquid, which is

$$8 \pi \eta a^3 \omega$$

η = viscosity

ω = angular velocity

a = radius of sphere

enables us to write down the couple on a sphere embedded in an elastic medium as (for small angles)

$$8 \pi n a^3 \theta$$

n = rigidity modulus

θ = angular deflection

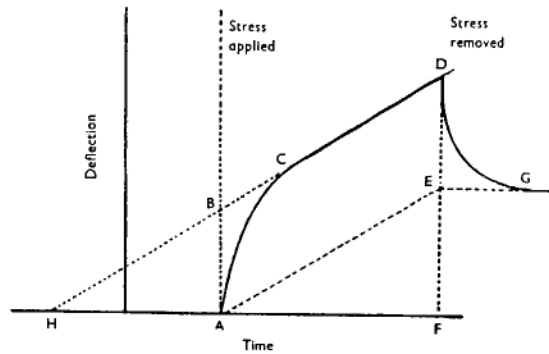


Fig. 1.

To clarify our terms consider next a simple visco-elastic medium, which behaves as shown in figure 1 when a constant stress is suddenly applied and later suddenly removed. In this figure the elastic properties are represented by AB and DE , the viscous damping by the exponential rise AC and fall DG , and the pseudo-viscous yield occurring along CD , by EF . The relaxation time is HA .

If we have a particle embedded in a simple visco-elastic medium whose relaxation time is constant with stress, we can obtain the relaxation time experimentally without knowing any of the details of the particle, boundaries, etc. by simply dividing the elastic deflection (for small strains) by the corresponding pseudo-viscous yield rate for any given applied couple. This follows from the similarity in form of the viscous and elastic coefficients mentioned above. If the relaxation time is a function of the stress, there is no simple solution for the general case.

We have so far neglected inertia. We now take it into account and show that the period of free oscillation is very short, and the damping high, again mainly because the particles are so small.

We first consider a particle in a simple elastic medium without viscosity. Due to the inertia it will be capable of free oscillations of both translation and rotation. It can easily be shown that, neglecting for simplicity the inertia of the medium, the dimensionless parameter for both cases is of the form

$$\frac{\sigma^2 \varrho' a^2}{n}$$

where $\frac{1}{\sigma}$ is the order of the period of free oscillation, and ϱ' is the density of the particle.

Putting $\frac{1}{\sigma} = 1$ millisecond, $a = 5 \mu$, and $\varrho' = 4$, we see that for the parameter to equal unity, n must be 1 dyne/cm². This is extremely feeble (for a normal gelatin gel $n = 10^3$ to 10^5 dynes/cm²). For a stiffer medium the time is of course shorter.

It is clear that for a substance as feeble as this the viscous damping would in practice be important. We will therefore consider a particle in a medium with both viscous and elastic properties, and find the condition for critical damping. We assume that the times involved are so short that we can neglect any pseudo-viscous yield.

If we work through a particular case, such as a sphere undergoing rotary oscillations about its axis, and neglect for simplicity the inertia of the medium, we obtain the condition for critical damping as

$$n \sim \frac{4\eta^2}{\varrho' a^2}$$

ϱ' = density of sphere.

We could have derived this, without the constant, in a rough and ready manner by equating the values of σ^2 which make the two previous dimensionless parameters (page 506 and page 518) equal to unity.

Putting $a = 3 \mu$, $\eta = 0.01$ poise, and $\varrho' = 4$, we obtain $n = 1,100$ dynes/cm². This is not high, but it is rather higher than our estimates. Moreover as already observed it is highly unlikely that the "viscosity" coefficient in biological materials is as low as that of water.

As regards the effects of boundaries, a closer examination shows that since the ratio of the viscous to elastic forces is independent of them, the condition for the damping remaining critical or greater when boundaries are added, reduces to the condition that the ratio of the damping forces to the inertia forces shall not decrease, which we have already shown (page 507) to be probable in most cases.

We thus conclude that the time-period of free oscillation of our particles is less than a milli-second (probably much less) and that the damping is critical or greater unless the rigidity modulus is high and the viscosity low, which is not the case in our experiments.

We have only considered the case of small strains. Large strains may well increase the apparent value of the rigidity modulus, calculated using the simple theory. It is unlikely however in our cases to increase it sufficiently to alter our general conclusions.

We have dealt with this point about critical damping because it is sometimes suggested that a resonance method should be used. Apart from the experimental difficulties due to the very short time periods, it is clear that the extremely low "Q" of the system would make this unprofitable.

It has also been suggested that the restoring force on a particle could be increased by magnetic means, though this would mask any elastic effect due to the medium. The simple theory shows that in the case of a sphere this is equivalent to the medium having a rigidity modulus of

$$\frac{B H}{24 \pi} \text{ dynes/cm}^2.$$

A more exact treatment would be required if the method were seriously contemplated. It is thus not impossible that oscillations could be produced. The envelope of these oscillations is determined by the ratio of the viscous to the inertia forces, and this could be used to measure the former. As has been shown this involves making measurements in a time probably of the order of microseconds. This is not impossible, but it is certainly not easy. The only advantage of such a method is that it is not necessary to know the magnetic forces accurately, although it is essential to know the exact formulae for the viscous and the inertia forces. These could if necessary be checked by calibration experiments in a known liquid. We have not pursued this approach further.

E. THE FORCES ON A BODY IN A MAGNETIC FIELD

1. *Twisting: the permanent magnet case*

Assuming that the particle is magnetically homogeneous we note that the magnetic condition is independent of scale, and therefore the forces per unit volume are also independent of scale, over a range where H and $\frac{dH}{dz}$ can be considered constant.

The variation with shape is more complex. The ellipsoid is the only body for which the magnetic conditions are constant throughout the volume for a uniform applied field. As in the hydrodynamic cases, we will consider only ellipsoids of revolution.

We proceed as follows: we first calculate a factor depending on the shape of the ellipsoid. Using this we find from the B/H curve of the material the relevant value of B for an ellipsoid permanently magnetised along its ma-

ior axis. From this we easily obtain the magnetic moment (M) of the ellipsoid. The couple due to a small applied field, h , perpendicular to the length of the ellipsoid, is then Mh .

The factors which are calculated for ellipsoids are "demagnetising factors." These express the amount by which the magnetisation of the ellipsoid produces a reversed magnetic field acting upon itself, and thus tending to demagnetise itself, and are defined by the equation

$$H' \equiv D I$$

where H' = the demagnetising field produced
 I = the intensity of magnetisation
 D = demagnetisation co-efficient.

D will in general depend upon direction, and will have three different values corresponding to the three axes of the general ellipsoid. The behaviour for other directions can be found by compounding I and H vectorially.

We shall, as usual, only quote the formulae for an ovary ellipsoid of revolution. They are

$$D_1 = 4 \pi \left(\frac{1}{e^2} - 1 \right) \left(\frac{1}{2e} \log \frac{1+e}{1-e} - 1 \right) \text{ for the major axis.}$$

$$D_2 = 2 \pi \left(\frac{1}{e^2} - \frac{1-e^2}{2e^3} \log \frac{1+e}{1-e} \right) \text{ for the minor axes.}$$

(The logs are natural logs)

where a = major axis, $b = c$ = minor axes and $1-e^2 = \frac{b^2}{a^2}$. When $a \gg b$, these formulae become

$$D_1 \simeq 4 \pi \frac{b^2}{a^2} \left(\log \frac{2b}{a} - 1 \right), \quad D_2 \simeq 2 \pi$$

For the particular case of a sphere $D_1 = D_2 = \frac{4 \pi}{3}$

$$\text{that is } \frac{D_1}{D_2} = \frac{4 \pi}{4 \pi} = 3$$

((8). The notation has been altered.)

Thus if we consider the case of b fixed and a increasing, we see that $\left(\frac{4 \pi}{D_1} \right)$

increases rapidly, while $\left(\frac{4\pi}{D_2}\right)$ tends to the value 2. We give a few values in Table III.

TABLE III

$\frac{a}{b}$	1.0	2.0	3.0	4.0	5.0	10.0	20.0
$\frac{4\pi}{D_1}$	3.00	5.71	9.17	13.2	17.9	49.3	148
$\frac{4\pi}{D_2}$	3.00	2.42	2.21	2.16	2.12	2.04	2.02

As is well known there is a simple graphical construction to find the working point on the B/H curve for a body with a given D in a (parallel) external field H_1 . The curve of $(B-H)$ against H is plotted, and a line is drawn from the point H_1 on the H axis with slope $-\left(\frac{4\pi}{D}\right)$. The working point is the point where this line cuts the curve. This construction applies for any value of the applied field H_1 . For a permanent magnet we usually have $H_1 = 0$; in this case we are working in the top left-hand quadrant of the $(B-H)$ against H curve.

Once we have found the working value of $(B-H)$ the magnetic moment (M) of the ellipsoid is simply

$$M = \frac{(B-H)}{4\pi} \cdot V$$

where $V =$ volume of the ellipsoid.

2. Twisting: the soft iron case

We consider the case of an ellipsoid of soft iron in a magnetic field inclined at a small angle to its major axis. By soft iron we mean here a material with no hysteresis. We do not restrict ourselves to the case of constant permeability, and will in fact consider a material which becomes magnetically saturated.

We calculate the case of an ovary ellipsoid of revolution (major axis = a , minor axes = $b = c$) where the applied field, H , makes an angle θ with the major axis, and the intensity of magnetisation, I , makes an angle α with the major axis. In general $\alpha \neq \theta$. I is constant throughout the body

both in magnitude and direction. We solve by splitting into components. We obtain

$$I \cos \alpha = \frac{\mu-1}{4\pi} (H \cos \theta - D_1 I \cos \alpha) \quad \text{along the major axis}$$

$$I \sin \alpha = \frac{\mu-1}{4\pi} (H \sin \theta - D_2 I \sin \alpha) \quad \text{along a minor axis.}$$

We shall only consider the cases where the angles are small. We therefore put $\sin \theta = \theta$ and $\cos \theta = 1$, etc, and eliminating I we obtain

$$\alpha = \theta \left[\frac{\frac{1}{(\mu-1)} + \frac{1}{\left(\frac{4\pi}{D_1}\right)}}{\frac{1}{(\mu-1)} + \frac{1}{\left(\frac{4\pi}{D_2}\right)}} \right]$$

Now to this approximation the couple (C) experienced by the particle is

$$C = I V H (\theta - \alpha)$$

where $V =$ volume of particle.

That is

$$C = I V H \theta \left(1 - \frac{\alpha}{\theta}\right)$$

which we can write

$$C = I V H \theta \left[\frac{\frac{1}{\left(\frac{4\pi}{D_2}\right)} - \frac{1}{\left(\frac{4\pi}{D_1}\right)}}{\frac{1}{(\mu-1)} + \frac{1}{\left(\frac{4\pi}{D_2}\right)}} \right]$$

This is the expression we require.

It follows that

(i) if $(\mu-1) \gg \left(\frac{4\pi}{D_2}\right)$ (the suffix 2 referring to the broadways-on case) the term in the bracket is effectively constant as H varies, and

$$C \text{ varies as } I H$$

as we should expect.

(ii) if we have a material of low permeability, or one which is saturated so that $(\mu-1)$ has become low, we may have $(\mu-1) < \left(\frac{4\pi}{D_2}\right)$. This latter factor varies from 3 for a sphere to 2 for a long ellipsoid (page 522). Writing the expression for the couple as

$$C = IVH(\mu-1)\theta \left[\frac{\frac{1}{\left(\frac{4\pi}{D_2}\right)} - \frac{1}{\left(\frac{4\pi}{D_1}\right)}}{1 + \frac{(\mu-1)}{\left(\frac{4\pi}{D_2}\right)}} \right]$$

we see that C varies as $I H (\mu-1)$ approximately that is C varies as I^2 approximately.

Thus if the material is saturated the couple does not increase with the field indefinitely, but tends to a limit.

(iii) for short ellipsoids the couple is less than might be expected on simple theory by the factor

$$\frac{\left(1 - \frac{D_1}{D_2}\right)}{\left(1 + \frac{\left(\frac{4\pi}{D_2}\right)}{(\mu-1)}\right)}$$

which is always less than 1, and moreover becomes zero for a sphere, for which $D_1 = D_2$.

A moment's thought shows that this latter point is obvious. If a soft iron sphere is subjected to a slowly rotating magnetic field, the magnetism rotates, not the sphere. This is in fact the clue to all the effects. As the magnetic material saturates with increasing field, for example, it becomes easier for the magnetism to rotate. For magnetite, where $(\mu-1)$ can be small these effects may be quite important.

3. Dragging

As we are concerned with obtaining the maximum drag, we will only give the case where the particle is in a magnetic field large enough to saturate it. The magnetic moment (M) will normally be in the direction of the applied field. The force on the particle in the x direction, F_x , is given by

$$F_x = M_x \frac{\partial H_x}{\partial x} + M_y \frac{\partial H_x}{\partial y} + M_z \frac{\partial H_x}{\partial z}$$

where M_x, M_y, M_z are the vectorial components of M and H_x is the x component of the applied field H .

There are similar expressions for F_y and F_z .

The force thus depends on terms of the form $\left(\frac{\partial H_x}{\partial x}\right)$ rather than of the form $\left(H_x \frac{\partial H_x}{\partial x}\right)$ which occur in certain other cases.

The force on the particle is not necessarily along its length. For example, if the particle is in a magnetic field which lies in the y direction ($H_x = H_z = 0$), so that it, too, points in the y direction ($M_x = M_z = 0$), there will nevertheless be a force on the particle in the x direction if $\left(\frac{\partial H_x}{\partial y}\right)$ is not zero.

F. THE VARIATION IN RATE OF MOVEMENT WITH SHAPE

We can now combine the results of the previous sections.

1. Twisting: the permanent magnet case

We assume that an ovary ellipsoid is magnetised parallel to its major axis so that it becomes a permanent magnet, of magnetic moment M , and that it is then acted on by a small magnetic field (h) perpendicular to its length. This will produce a couple Mh and if the ellipsoid is immersed in a newtonian liquid it will rotate with an angular velocity ω . The problem we wish to solve is, how big is ω and how does it vary with shape?

To obtain the value of ω for any particular case we merely have to work out the magnetic and the viscous couples from the formulae given in the previous sections and equate them. However it is useful to get a qualitative idea of how ω changes with shape (we know that it is independent of scale) so we shall suppose that b is kept constant and a allowed to increase. The nature of the variation depends on the nature of the magnetic material.

We take the extreme case first. If the ellipsoid is long, so that the slope of the $(B-H)$ against H curve is much less than $\left(\frac{4\pi}{D_1}\right)$, then $(B-H)$ will effectively be constant, and M will only increase due to the increase in volume, that is proportional to ab^2 . The viscous couple, however, increases at a rate be-

tween a^2b and a^3 . Thus in this range the angular velocity decreases rather faster than $\left(\frac{1}{(a/b)}\right)$.

On the other hand, if the ellipsoid is short, and the magnetic material such that the slope of the $(B-H)$ against H curve is much greater than $\left(\frac{4\pi}{D_1}\right)$, then the angular velocity varies as

$$\frac{a b^2 \left(\frac{4\pi}{D_1}\right)}{k a^2 b}$$

where k is tabulated on page 511.

We thus evaluate $\left(\frac{1}{3} \frac{4\pi}{D_1} \frac{1}{k} \frac{b}{a}\right)$ for various values of a/b .

TABLE IV

$\left(\frac{a}{b}\right)$	1.0	2.0	3.0	4.0	5.0
$\left(\frac{1}{3} \frac{4\pi}{D_1} \frac{1}{k} \frac{b}{a}\right)$	1.00	1.13	1.12	1.10	1.09

It can be seen that the variation with shape is not very great. Eventually the angular velocity will fall off, but by this time the approximation used is unlikely to be still valid. Thus for a real $(B-H)$ against H curve the angular velocity will eventually decrease with increasing (a/b) . It may be roughly constant over a range for (a/b) small, but this depends on the shape of the curve. The exact values can be calculated for any given curve from the formulae given.

The above results apply strictly to the special ellipsoids chosen. It seems reasonable to assume that in the region where the shape of the ellipsoid is making a large difference the approximation for a body of arbitrary shape will not be as good as for ranges where the ellipsoid's shape is having little effect on the angular velocity. However it is not easy to put a figure to the usefulness of the approximation.

We have not pursued this further, as the problem is complicated and we have in any case in our actual experiments taken an average value. If greater accuracy is required the solutions for the viscous forces and the demagnetising co-efficients for the general ellipsoid are available, and might give a better idea of the effects of irregular shape.

2. Twisting: the soft iron case

The qualitative results for the corresponding problem in the soft iron case can easily be seen. For very long ovary ellipsoids the angular velocity will fall off rather faster than $\left(\frac{1}{(a/b)}\right)$ as in the previous case. For almost spherical ones it will again be small. Somewhere in between there will be a maximum, depending on the properties of the material and the size of the applied field. The exact values can be calculated for particular cases from the formulae given.

It seems probable that for actual particles of irregular shape we shall get similar effects to those calculated for the ellipsoid. That is, for very short particles we shall get smaller couples than might be expected on the simple theory, and for larger applied fields the couple tending to a maximum instead of increasing indefinitely. In the case of any particular material the evaluation of a few cases for the ellipsoid should give a good idea of the general behaviour, though the reduction in couple due to shortness is likely to be less important for irregular bodies.

The treatment will not apply to materials which show hysteresis.

3. Dragging

We will only consider the cases of an ovary ellipsoid of revolution being moved either parallel or perpendicular to its length. Other directions can be solved by compounding vectorially. We consider the relevant field gradient as fixed, and investigate how the velocity of movement depends on the dimensions. For our case the magnetic force, for a given value of $(B-H)$ at saturation, depends only on the volume, not on the shape. We have already shown (page 509) that the effect of size is to make the velocity vary as the square of the characteristic length, so that it only remains to investigate shape variations. As before the formulae will give an exact solution for any chosen case.

(a) dragging parallel to the major axis.

The formula for the viscous resistance and a selection of values are given on page 512. These show that for a fixed b , the drag increases with a , initially rather slowly, say as $\sqrt[4]{a}$, and gradually increases to rather slower than a . Taking $\sqrt[4]{a}$ as a typical value, the velocity of the particle will roughly be proportional to

$$\frac{b^2 a}{\sqrt[4]{a} b^2}$$

(b) dragging parallel to a minor axis.

The formula and a selection of the values are given on page 512. These show that if b is fixed and a increased, the drag increases initially a little faster than the previous case, so that we may take \sqrt{a} as typical, giving

$$\text{velocity} \sim \frac{b^2 a}{\sqrt{a} b}$$

What is wanted in fact in both cases is a good estimate of the volume of the particle, plus an approximate estimate of a and b . This conclusion is likely to stand for particles having irregular shapes.

G. PRODUCING FIELD GRADIENTS

We first note that since

$$\frac{\partial H_x}{\partial x} + \frac{\partial H_y}{\partial y} + \frac{\partial H_z}{\partial z} = 0$$

we cannot get a large value of $\frac{\partial H_x}{\partial x}$ without either one or both of the other

two being large, and of opposite sign. This implies that the lines of force cannot be parallel in such a region. They must either diverge or be bent.

It can be shown that a magnetically saturated particle can never be in true stable equilibrium under the influences of magnetic forces *alone*. This follows simply by regarding the particle as having a (fixed) surface distribution of magnetic poles, and applying the appropriate analogue of Earnshaw's Theorem (5, 374 and 167). The particle will in fact be either in unstable equilibrium or be moving towards one of the magnets producing the field.

We next wish to show, quite generally, that a very large field gradient can only be produced (leaving aside electric currents for the moment) by having ferromagnetic material *near* the particle. This is perhaps obvious on dimensional grounds. A magnet of a given *shape* and of a given material will produce the same field at corresponding points, irrespective of scale. Thus, clearly, the smaller the magnet, the greater the field gradient. As there is an upper limit to the size of $(B-H)$ for magnetic materials, there must come a time when the gradient can only be increased by making everything smaller.

We can illustrate this by calculating the result for an ideal pole-piece in

the shape of a truncated cone, semi-angle α , with the particle at the apex of the cone, which we will take as the origin. We will assume that the direction of magnetisation is everywhere parallel to the axis of the cone. The solution of this problem, which is quite straightforward, gives the field gradient at the origin as

$$\left(\frac{\partial H}{\partial x}\right)_{x=0} = \frac{6\pi I}{x_0} \sin^2 \alpha \cos^3 \alpha$$

where I = intensity of magnetisation of the pole-piece, which is assumed to be uniform.

x_0 = distance of pole-piece from the particle at the origin.

There are three points to notice about this answer. Firstly that the expression has a maximum with respect to α at $\cos \alpha = \frac{3}{\sqrt{15}}$. Secondly that we can write this maximum (putting $4\pi I = B-H$) as

$$\frac{(B-H)}{x_0} \frac{18\sqrt{3}}{50\sqrt{5}} \quad (B, H \text{ refer to the polepiece})$$

so that the field gradient at the origin is of the form

$$p \frac{(B-H)}{x_0}$$

where p is a constant a bit less than 1. This form of result is very general.

Thirdly we note that if we had not continued the pole to infinity, but stopped it at the point x_1 , we should have obtained

$$p(B-H) \left(\frac{1}{x_0} - \frac{1}{x_1} \right)$$

which shows that as long as x_1 is several times x_0 , the result is not sensitive to its exact value. This obviously follows from the fact that we are integrating an expression of the form $\left(\frac{B-H}{r^4}\right)$ through a volume. Thus distant contributions have hardly any effect, because of the upper limit to $(B-H)$.

It is not necessary, however, to produce the magnetic gradient *directly* with the primary magnet. We can produce a large uniform field, and consider the gradient near a small body of soft iron placed in this field. For simplicity we will consider the case where this body is a sphere. This is

extremely easy, as for points outside it behaves exactly as a doublet of strength

$$\frac{B-H}{4\pi} \cdot \frac{4\pi}{3} a^3$$

located at its center (a = radius of sphere). Let the particle be a distance r from the centre of the sphere ($r > a$).

If we consider the case where the applied field is parallel to the line joining the particle and the sphere, the force is an *attraction* given by

$$|F| = \frac{B-H}{r} \left(\frac{a}{r}\right)^3 2M$$

(M refers to the particle, B and H to the soft iron sphere.)

For the case where the field is perpendicular to the joining line, we have a *repulsion* of

$$|F| = \frac{B-H}{r} \left(\frac{a}{r}\right)^3 3M$$

It is thus possible to control the direction of the force to some extent by altering the direction of the applied field. It should be noted that the force falls off as $\frac{1}{r^4}$, so that it will vary rapidly with the position of the particle.

To sum up, the maximum gradient will usually be of the form

$$p \frac{(B-H)}{x_0}$$

where $(B-H)$ is the value for the iron in the immediate vicinity, x_0 is the distance of the nearest iron from the particle, and p is a constant depending in a complicated way on the configuration, but approaching a value of the order of 1 in well-designed cases. The more distant parts of the magnetic circuit do not affect the gradient directly, but only in so far as they determine $(B-H)$ in the iron near the particle.

We must consider briefly the possibility of producing high field gradients by electric currents in air-cored coils. We first observe that we require a *sustained* force for our purposes; a short pulse is in general not sufficient. The limitation is therefore the steady heating effect: either the small rise in temperature which the culture will tolerate, which would be important for coils close to, or the rise in temperature of the coil itself for larger, more

distant coils. We will not give a general treatment, but will give one simple example. Consider the conical polepiece of page 529. Instead of a cone of magnetic material, imagine that this cone is a former upon which a coil is wound. What is the current through such a coil which would produce the same field-gradient as the magnet did? By considering the equivalent magnetic shell we arrive at the simple answer that

$$\begin{aligned} ni &= I \text{ where } n = \text{number of turns per cm} \\ i &= \text{current in coil (c.m.u.)} \\ I &= \text{magnetic intensity of the iron.} \end{aligned}$$

Now we can easily make $I = 10^3$, so that if we had 1 turn per mm ($n = 10$) i must be 10^2 , or 10^2 amps. This will clearly give an enormous amount of heat. The margin in the calculation is so big that more precise considerations would not be appropriate. Briefly we note that the heating effect allows (ni) to increase as $1^{3/2}$, where 1 is a characteristic length, so that air-core coils can only compete with magnets if they are both very large, which, as we have shown is the case which produces low field gradients. Thus, in general, magnets are much better than air-cored coils for our purpose.

H. SOME NUMERICAL VALUES FOR THE STRESS

Although we have argued that the method is a very poor one for finding how the "viscosity" of a non-newtonian liquid varies with stress, it is clear that if the range of stresses is very wide indeed we may expect quite considerable differences in behaviour. It is therefore useful to compare the maximum values of the stresses due to twisting and dragging magnetically, and due to gravity. To simplify matters, since we are only concerned with orders of magnitude, we will consider the case of a sphere, taking its radius (r) as 1μ .

1. twisting of a sphere magnetically.

The maximum stress in this case is

$$\frac{BH}{4\pi} \text{ dynes/cm}^2.$$

For $B = 225$ and $H = 45$ oersteds we get

$$\sim 400 \text{ dynes/cm}^2.$$

2. dragging a sphere magnetically.

The maximum stress is

$$\frac{B}{12\pi} \cdot r \left(\frac{dH}{dx} \right) \text{ dynes/cm}^2$$

for $B = 1500$ and $\frac{dH}{dx} = 10^4$ oersteds/cm (say)

$$\text{and } r = 10^{-4} \text{ cm}$$

we get

$$\sim 40 \text{ dynes/cm}^2.$$

3. dragging a sphere due to gravity.

For the general case (as in a centrifuge) where the centrifugal acceleration is ng we have the maximum stress equal to

$$(\rho - \rho_0) \frac{ng}{3} \cdot r$$

where ρ = density of particle

ρ_0 = density of liquid.

There are two cases of interest.

- (a) for magnetic particles under gravity.

Taking $\rho = 4$ $\rho_0 = 1$ $n = 1$ $r = 10^{-4}$ cm
we get

$$= \frac{1}{10} \text{ dynes/cm}^2.$$

- (b) for natural inclusions of the cell, in a centrifuge.

Take, arbitrarily, $(\rho - \rho_0) = 0.1$.

We obtain for the maximum stress

$$\frac{n}{300} \text{ dynes/cm}^2$$

for an acceleration of ng .

The point we wish to bring out is not merely that the stresses produced during magnetic twisting are rather bigger than in magnetic dragging, but that both are enormously bigger than the effect of gravity. Moreover, these

stresses are only equaled when centrifuging natural inclusions of the same size by centrifugal fields of the order of 10^5 times gravity.

Finally we must emphasize that these results only apply for particles of the chosen size, as can be seen from the factor r in the later expressions.

SUMMARY¹

1. The paper gives the theory of the magnetic particle method, in which some of the mechanical properties of a fluid are estimated by observing the movements of magnetic particles in it due to applied fields.

2. For the very small particles likely to be used in biological systems the inertia can be neglected.

3. The effect of scale is derived for particles of irregular shape in a newtonian liquid.

4. Exact formulae are quoted, for the three cases most often encountered, for an ovary ellipsoid of revolution in an infinite newtonian liquid. References to the general ellipsoid are given.

5. The effects of the irregular shape of a particle, of boundaries, and of non-newtonian and elastic behaviour of the fluid are discussed qualitatively.

6. Some theoretical notes are given on producing large gradients of magnetic field.

7. Some comparative numerical values of the stresses in certain biological applications are evaluated.

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¹ A more extended summary has been given in Part I (1, p. 79).