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# The Mechanism of Partition in Aqueous Media

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## Abstract

From the quantitative determination of the polar surface tension parameters of Dextran 150 (DEX) and polyethylene glycol 6,000 (PEG), it is shown that both polymers are pronounced monopolar Lewis bases. By means of the theory of short-range (SR) (polar or hydrogen bonding) interactions, and also taking into account the influence of long-range Lifshitz-van der Waals (LW) interactions, it is demonstrated that DEX and PEG, immersed in water, repel each other with a sizable repulsion energy. That repulsion energy is highest when the polymers are most strongly dehydrated. Thus it becomes clear why a certain concentration of each polymer must be reached before phase separation can occur. Monopolar repulsion also accounts for the occurrence of the formation of multiple phases, provided the participating polymers all are monopoles of the same sign. The mechanism for the preferential migration of biopolymers or particles to one or the other phase is also elucidated. While in some cases (e.g., affinity partition) the preferential migration is due to a specific attraction to one of the phases, in many other cases the preference for one phase appears to be rather due to the fact that a biopolymer is more strongly repelled by the other phase; this repulsion is enhanced: a) by an increase in $M_w$ of the biopolymer and/or b) by an increase in $M_w$ of the polymer in the repelling phase.

## INTRODUCTION

Separation of solutes by partition in immiscible (usually organic) solvents was pioneered by Lyman C. Craig (*1*), mainly using partition in the countercurrent distribution mode. For the development of the partition chromatography mode, Martin and Synge (*2*) were awarded a Nobel prize in 1952.

Following a number of observations by Beijerinck (*3, 4*) on the phase separation or coacervation (*5*) between water-soluble polymers dissolved in water, such as gelatin and agar, and gelatin and soluble starch, Albertsson pioneered the use of other water-soluble systems during the late 1950s (*6, 7*). Of these, the dextran-polyethylene glycol system is typical and now also the best known example.

Nevertheless, as Albertsson stated in the most recent edition of his work (*7*): "The mechanism governing [aqueous phase] partition is largely unknown" (p. 3).

We have demonstrated earlier that the phase separation frequently observed in solutions of two different (largely apolar) polymers in organic solvents is generally due to a van der Waals repulsion (*8*). However, with water-soluble polymers the mechanism is not nearly as obvious.

The experimental observation is that with dextran and polyethylene glycol in water, phase separation occurs when the two polymers are present at concentrations of above $\simeq$8% (w/v) each or $\simeq$8% total polymer (*6, 7*). Now, a van der Waals repulsion will not exist between dextran and polyethylene glycol (PEG) dissolved or suspended in water, because the van der Waals-Lifshitz surface tension ($\gamma^{LW}$) of water is only 21.8 mJ/m$^2$ (9), while the $\gamma^{LW}$ of both dextran and PEG is of the order of 42 to 43 mJ/m$^2$ (see below), so that *nonhydrated* dextran and PEG would *attract* each other (in water) with an energy of about 7 mJ/m$^2$. Second, dextran is one of the biopolymers endowed with a remarkably low surface charge (when dissolved in water): by Tiselius electrophoresis, the electrophoretic mobility of Dextran (T-40) at $\mu$ = 0.15 was $-0.002$ μm/s/V/cm (*10*), corresponding to $\zeta$-potentials of $-0.06$ and $-0.7$ mV respectively for the lower molecular weight dextrans, and 33% less than those values for the higher molecular weight dextrans (*11*). Thus in systems containing dextran as one of the repelling partners, electrostatic repulsion may also be ruled out.

However, recently it has become clear that many biopolymers, including various proteins, poly- and oligosaccharides, as well as RNA, when measured in the dried state, are monopolar, i.e., they are mainly, or solely, Lewis bases (or electron donors) (*12–14*) (see below). Not only dextran, but also PEG belongs to this class. It can readily be demonstrated that two monopolar substances of the same type will repel each other (see below). If that monopolar repulsion energy is stronger than the van der Waals energy of attraction (of about 7 mJ/m$^2$, see above), a net repulsion will ensue, resulting in phase separation.

## THEORY

### Lifshitz-van der Waals Interactions

Lifshitz-van der Waals (LW) or long-range interactions comprise dispersion (London), orientation (Keesom), and induction (Debye) forces (*15, 16*). LW interfacial tensions can be obtained from LW surface tensions via

$$\gamma_{12}^{LW} = (\gamma_1^{LW} - \gamma_2^{LW})^2 \tag{1}$$

LW surface tension of a solid 1 can be measured by contact angle ($\theta$) determinations (*17*) with LW liquids 3 by using a variant of the Young-Good-Firifalco-Fowkes equation (*9, 18*):

$$1 + \cos\theta = 2\sqrt{\gamma_1^{LW}/\gamma_3} \tag{2A}$$

or

$$\gamma_1^{LW} = \frac{\gamma_3(1 + \cos\theta)^2}{4} \tag{2B}$$

The values of $\gamma^{LW}$ of LW liquids are known for many liquids (*19*) or can easily be measured by various standard methods.

### Short-Range Interactions

In water and many other polar liquid media, hydrogen bonds play a considerable role. For instance, 70% of the energy of cohesion of liquid water is due to hydrogen bonds (*15, 16*). Therefore, when a solid or a solute that have hydrogen donor and/or hydrogen acceptor capacities is immersed in water (which has strong hydrogen donor *and* hydrogen acceptor capacties), a stronger attraction will ensue than can be accounted for by just the LW attraction. The additional attraction, due to the formation of hydrogen bonds with the water molecules, has essentially a very short-range (SR) character, i.e., *in vacuo*, unlike LW interactions, its energy decays to close to zero within 3 to 4 Å (*16*).

We can express $\gamma^{SR}$ in a rigorous manner (*12, 17*) by first introducing its parameters:

$$\gamma_i^{SR} = 2\sqrt{\gamma_i^{\oplus}\gamma_i^{\ominus}} \tag{3}$$

Here, $\gamma^{\oplus}$ stands for the electron acceptor (Lewis acid) parameter of Compound *i*, and $\gamma_i^{\ominus}$ for its electron donor (Lewis base) parameter. Since Compounds 1 and 2 may each have both electron donor and electron acceptor capabilities, the free energy of SR interaction between Substances 1 and 2 may be described as

$$\Delta G_{12}^{SR} = -2(\sqrt{\gamma_1^{\oplus}\gamma_1{}^{\ominus}} + \sqrt{\gamma_1^{\ominus}\gamma_2^{\oplus}}) \tag{4}$$

Now, the Dupré equation for the free energy of adhesion:

$$\Delta G_{12}^{\mathrm{adh}} = \gamma_{12} - \gamma_1 - \gamma_2 \tag{5}$$

is also valid with respect to the SR component of free energy

$$\Delta G_{12}^{SR} = \gamma_{12}^{SR} - \gamma_1^{SR} - \gamma_2^{SR} \tag{6}$$

or, rearranged,

$$\gamma_{12}^{SR} = \Delta G_{12}^{SR} + \gamma_1^{SR} + {}_2^{SR} \tag{6A}$$

Combining Eqs. (3), (4), and (6A) (*12, 17*):

$$\gamma_{12}^{SR} = 2(\sqrt{\gamma_1^{\oplus}\gamma_1^{\ominus}} + \sqrt{\gamma_2^{\oplus}\gamma_2^{\ominus}} - \sqrt{\gamma_1^{\oplus}\gamma_2^{\ominus}} - \sqrt{\gamma_1^{\oplus}\gamma_2^{\ominus}}) \tag{7}$$

From the Young-Dupré equation:

$$\Delta G_{SL} = \gamma_L(1 + \cos\theta) \tag{8}$$

Also:

$$\Delta G_{SL} = \Delta G_{SL}^{LW} + \Delta G_{SL}^{SR} \tag{9}$$

Thus, using Eqs. (7) and (8), the complete Young-Dupré equation in terms of (LW + SR) can now be established:

$$1 + \cos\theta = \frac{-1}{\gamma_L^{TOT}}(\Delta G_{SL}^{LW} + \Delta G_{SL}^{SR}) \tag{10}$$

or

$$1 + \cos\theta = \frac{2}{\gamma_L^{TOT}} \left(\sqrt{\gamma_S^{LW}\gamma_L^{LW}} + \sqrt{\gamma_S^{\oplus}\gamma_L^{\ominus}} + \sqrt{\gamma_S^{\ominus}\gamma_L^{\oplus}}\right) \quad (10A)$$

where

$$\gamma_l^{TOT} = \gamma_l^{SR} + \gamma_l^{LW} \quad (11)$$

If the $\gamma^{LW}$, $\gamma^{\oplus}$, and $\gamma^{\ominus}$ values of a number of liquids are known by contact angle measurements with three suitable liquids (see Eq. 10A), these parameters can all be determined for a given polar solid. The total interaction energy between two such polar solids (1 and 2), immersed in Liquid 3, can than be derived from the generalized Dupré equation:

$$\Delta G_{132} = \gamma_{12} + \gamma_{13} + \gamma_{23} \quad (12)$$

combining Eq. (12) with Eq. (7), we obtain (*15, 17*):

$$\Delta G_{132}^{SR} = 2\,[\sqrt{\gamma_3^{\oplus}}(\sqrt{\gamma_1^{\ominus}} + \sqrt{\gamma_2^{\ominus}} - \sqrt{\gamma_3^{\ominus}}) + \sqrt{\gamma_3^{\ominus}}(\sqrt{\gamma_1^{\oplus}} + \sqrt{\gamma_2^{\oplus}} - \sqrt{\gamma_3^{\oplus}}) - \sqrt{\gamma_1^{\oplus}\gamma_2^{\ominus}} - \sqrt{\gamma_1^{\ominus}\gamma_2^{\oplus}}] \quad (13)$$

## EXPERIMENTAL

Five percent (w/v) aqueous solutions of DEX (Dextran 150; $M_w \simeq 150{,}000$, Pharmacia, Uppsala, Sweden) and of PEG (polyethylene glycol 6,000, $M_w \simeq 8{,}000$, Sigma, St. Louis, Missouri) were deposited on clean new glass microscope slides (1″ × 3″) and air-dried for several days. After drying, the slides were kept in a vacuum desiccator over $CaSO_4$. PEG solutions contract strongly on glass and thus yield only a very small surface area, once dried; barely enough for 1 or 2 contact angle measurements. Thus, as an alternative, molten PEG was poured into a glass Petri dish (2″ diameter) and, after solidification, stored in a vacuum desiccator. Advancing contact angles (Table 1) were then measured on the flat dry surfaces of DEX and PEG with the liquids listed in Table 2. The water used was triple distilled; the other liquids were analytical and/or highest quality.

One of the impediments to preparing hydrated layers of PEG or concentrating PEG on ultrafiltration membranes for measuring contact angles, as in our previous work with other polymers (*13, 16*), is the

TABLE 1
Contact Angles (θ) Measured on Dried Dextran T-150 and PEG 6,000 with Various Liquids

| Liquid used | Dextran T-150 | PEG 6,000 |
|---|---|---|
| $H_2O$ | 30° | 18.25° |
| DMSO | 16° | 13.75° |
| α-Bromonaphthalene | 16° | 10° |
| Diiodomethane | 29° | 26° |

TABLE 2
Surface Thermodynamic Properties (in $mJ/m^2$) of the Liquids Used in the Contact Angle Determination (see Table 1)

| Liquids | $\gamma^{LW}$ | $\gamma^{\oplus}$ | $\gamma^{\ominus}$ | $g^{SR}$ | $\gamma^{TOT}$ |
|---|---|---|---|---|---|
| $H_2O$ | 21.8 | 36[a] | 18[a] | 51 | 72.8 |
| DMSO | 44 | 0 | 30[a] | 0 | 44 |
| α-Bromonaphthalene | 43.6 | 0.44[a] | 0.44[a] | 0.9 | 44.4 |
| Diiodomethane | 50.8 | 1.0[a] | 0 | 0 | 50.8 |

[a] Ref. *12*.

unusually strong, virtually asymptotic decrease in flux due to membrane fouling and/or to membrane repulsion. One difficulty with DEX is that, once a highly concentrated layer of hydrated DEX is built up on a cellulose acetate membrane, the entire layer of hydrated polymer tends to detach from the membrane. This may be due to the strong repulsion between two $\gamma^{\ominus}$ monopoles; see below.

## RESULTS AND DISCUSSION

### Repulsion between DEX and PEG

In Table 1 the contact angles are given, measured on dried layers of Dextran T-150 and of PEG 6,000, with a number of liquids, of which the surface thermodynamic properties are listed in Table 2. As the contact angles found for the two materials are somewhat higher with DMSO than with α-bromonaphthalene, we may consider both of them to be monopolar Lewis acids (i.e., polar surfaces having only $\gamma^{\ominus}$ and no $\gamma^{\oplus}$ parameters) (*12–14*). Thus, DMSO, which also has a $\gamma^{\ominus}$ and little or no $\gamma^{\oplus}$ component (*20*), is best used for the contact angle determination of the

$\gamma^{LW}$ components of both materials, see Table 3. If these $\gamma^{LW}$ components are derived (via Eq. 2B) from the contact angles obtained with diiodomethane, no enormous error would occur, but a value for $\gamma^{LW}$ would be found that is 5 to 7% too high, due to the small but not negligible $\gamma^{\oplus}$ parameter of diiodomethane, which allows it to engage in a polar interaction with the strongly ($\gamma^{\ominus}$) monopolar DEX and PEG surfaces. Once the $\gamma^{LW}$ values are established, the $\gamma^{\ominus}$ values for DEX and PEG can be derived via Eq. (10A) from the contact angles determined with water, given in Table 1.

Using Eq. (13) and the data from Tables 2 and 3, the total interaction energy $\Delta G_{132}^{TOT}$ between (dry) DEX and PEG, immersed in water, is found to equal +46.7 mJ/m$^2$. This, of course, signifies a strong repulsion. However, we must not lose sight of the fact that, when dissolved in water, DEX and PEG are not dry but strongly hydrated. Contact angles are not as easily measured on hydrated DEX or PEG as on, e.g., hydrated proteins. However, only a negligible error would be made in assuming the surface tension parameters of DEX and PEG to be close to those of a typical hydrated protein (*13*) or, e.g., RNA (*14*). It has been found (*13, 14*) that the $\Delta G_{132}^{SR}$ of two such hydrated materials that are originally monopolar (and both of the same sign) in the dry state is invariably zero due to the orientation of the dipoles of the water of hydration. That leaves $\Delta G_{132}^{LW}$. With all hydrated biopolymers, $\gamma^{LW}$ is around 25 to 27 mJ/m$^2$ (*13, 14, 16*); the $\Delta G_{132}^{LW}$ of two such hydrated materials in water is then of the order of −0.1 to −0.6 mJ/m$^2$, which in this case is equal to the total hydrated $\Delta G_{132}^{TOT}$. This value, compared to the $\Delta G_{132}^{TOT}$ value for the *dry* materials (immersed in water) of +46.7 mJ/m$^2$ (see above), is very close to zero.

TABLE 3
Surface Thermodynamic Parameters (in mJ/m$^2$) of (dry) Dextran T-150 and (dry) PEG 6,000, Obtained from the Data in Tables 1 and 2

| | $\gamma^{LW}$ | $\gamma^{\oplus}$ | $\gamma^{\ominus}$ |
|---|---|---|---|
| Dextran T-150 | 42[a] | 0 | 39 |
| PEG 6,000 | 43[a] | 0 | 45 |

[a] From $\theta^{DMSO}$ (see Table 1); the $\gamma^{LW}$ values that would be obtained from the contact angles measured with α-bromonaphthalene and diiodomethane are consistently somewhat on the high side (44–46 mJ/m$^2$) on account of the interaction of the $\gamma^{\oplus}$ components of these liquids with the $\gamma^{\ominus}$ components of the two solids.

## Influence of Polymer Concentration

Figure 1 is a graph of the concentration of these polymers in water vs the $\Delta G_{132}^{TOT}$ value (in mJ/m$^2$). The straight line is based on the assumption that total dehydration is attained at 100% polymer concentration, and that the degree of dehydration is linearly proportional to the total concentration of the polymers dissolved in water. This may, of course, be a considerable oversimplification, but for lack of more precise data we assume for the moment that we may use this interpolation on a straight line. In particular, we use it very close to the origin and at relatively low concentrations. It can be seen that around 8% (w/v) of both polymers (i.e., at an 8% total polymer concentration), an interpolated $\Delta G_{132}^{TOT}$ of +3 mJ/m$^2$ is found. We thus note that at the approximate concentration at which phase separation usually sets in (*6, 7*), a mutual repulsion energy is reached which (if we take the mutual contactable surface area for the two polymers to be of the order of 200 Å$^2$) is approximately +1.5 kT. This corresponds to the energy level that begins to exceed the Brownian motion (*21*).

Thus the reason why aqueous phase separation, e.g., the repulsion between DEX and PEG molecules, becomes effective only above a given polymer concentration (*6, 7*) appears to lie in the fact that a minimum degree of dehydration of both polymers must first be reached in order to raise their repulsion energy to a high enough level to overcome the Brownian energy that favors remixing.

## Multiple Phase Separation

While phase separations brought about by two different apolar polymers dissolved in the same solvent are extremely common, dissolving three or more apolar polymers in one (apolar) solvent will not give rise to more than two phases. The reason for this is easily understood by realizing that apolar phase separations only will occur when the $\gamma^{LW}$ of the solvent has a value in between the $\gamma^{LW}$'s of the two polymers (*8*). A third polymer added to this mixture usually either has a lower or a higher $\gamma^{LW}$ than the solvent. In either case, a third polymer will join one or the other phase without creating a new one.

In polar systems, however, the occurrence of multiple phases in one solvent due to the presence of several different polymers is well documented (*6, 7*). From the combining rule for $\Delta G_{132}^{SR}$ (Eq. 13) it can easily be shown that a pair of monopolar (e.g., both $\gamma^{\ominus}$) polymers will repel each other in water when their $\gamma^{\ominus}$ values average about 20.5 mJ/m$^2$ (supposing their $\gamma^{LW}$ values to be around 40 mJ/m$^2$). This, however, is not

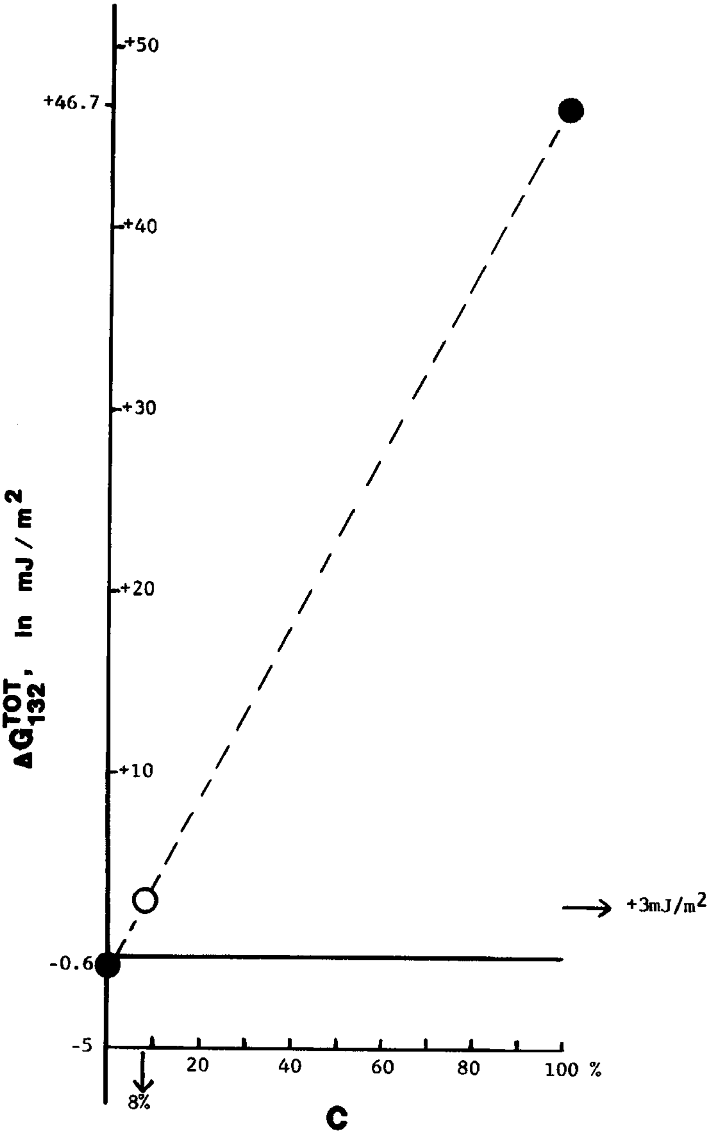

FIG. 1. Interaction energy $\Delta G_{132}^{\mathrm{TOT}}$ (in mJ/m$^2$) between DEX and PEG in water, as a function of the degree of dehydration, which is taken to be proportional to the total polymer concentration. Only the solid circles indicate data points; the open circle stands for the interpolation at $C \simeq 8\%$ total polymer concentration (and thus also for 8% dehydration); corresponding to a repulsion of +3 mJ/m$^2$ between two (still partly hydrated) molecules of DEX and PEG, a value that is of the order of magnitude of +1.5 kT.

taking their hydration into account. For two hydrated monopolar (e.g., $\gamma^{\ominus}$) polymers, *each* present in concentrations no higher than $\simeq 10\%$ (w/v), a $\Delta G_{132}^{TOT}$ of $\simeq +17.5$ mJ/m$^2$ will be attained, which should lead to effective repulsion (see Fig. 1). Keeping in mind that in the dry state, $\Delta G_{132}^{LW} \simeq -6.9$ mJ/m$^2$, $\Delta G_{132}^{SR}$ should then be at least $+24.4$ mJ/m$^2$, which can be attained if the *average* $\gamma^{\ominus}$ of each member of a polymer pair is $\simeq$ 27.7 mJ/m$^2$. This also holds true of more than two polymers, again provided that the total polymer concentration reaches 20%, to assure a sufficient degree of dehydration of each polymer. For a *total* polymer concentration of only 8%, the average $\gamma^{\ominus}$ value for all polymers involved should be higher, i.e., $\simeq$42 mJ/m$^2$ to achieve phase separation. This condition is realized for PEG and dextran.

In any event, as long as all polymers mixed together in aqueous solution are largely monopolar and of the same sign, and as long as each pair has a sufficiently high average $\gamma^{\ominus}$ value (or $\gamma^{\oplus}$, as the case may be) and finally, as long as they all have different densities in the separated, dissolved status (*6, 7*), they will separate into different phases, in each one of which a given polymer will be the preponderant species.

These general rules fit in well with the observations of Albertsson (*6, 7*), Beijerinck (*3, 4*), and Ostwald and Hertel (*22*).

## Surface and Interfacial Tensions of DEX and PEG Solutions

Surface tensions of DEX and PEG solutions can be measured, but the results obtained are largely meaningless due to the fact that both polymers behave as surfactants in aqueous solution, i.e., they tend to concentrate at the air/water interface (*23*). For instance, by the Wilhelmy-plate method, the $\gamma$ value for 6.2% PEG 6,000 in water was found to be 57.7 mJ/m$^2$, and for 8% DEX T-500, 59.0 mJ/m$^2$. After mixing and phase separation, the $\gamma_1$ value for the top phase (mainly PEG) was 58.1, and for the bottom phase (mainly DEX), 58.7 mJ/m$^2$ (*24*). The lowering of the surface tension of water from 72.8 to about 58 or 59 mJ/m$^2$ by the admixture of only 6.2 to 8% polymers (themselves with a $\gamma^{TOT}$ of 42 to 43) is clearly not possible without some concentration of the polymer at the liquid/air interface.

The interfacial tension between fully hydrated (and between dry) DEX and PEG must be very small. The $\gamma_{12}^{SR}$ in both cases is close to zero (Eq. 7); see above. And the $\gamma_{12}^{LW}$, both in the dry and in the hydrated states, should only be of the order of $10^{-2}$ to $10^{-3}$ mJ/m$^2$, given the closeness of the $\gamma^{LW}$ values of DEX and PEG; see also Albertsson (*6, 7*). Thus, given the low interfacial tension between the phases, they would be able to mix readily if it were not for the positive $\Delta G_{132}$ value and the difference in density.

## Preference of Various Polymers and Particles for One of the Phases

An enormous body of observations has been accumulated by Albertsson and his coworkers over the last 28 years (*6, 7*), and the analysis of the mechanism of the preferential migration of various polymers and particles to one phase or the other will take considerable time, and even if completed could not possibly be described in a single paper. Only a few general cases will therefore be alluded to here.

To begin with, preference of a given biopolymer for phase X could be due to its attraction to phase X or to its repulsion from phase Y. Affinity partition (*6, 7*) clearly is an example of the first mechanism.

In many cases, however, a second pathway is the more probable one. Many biopolymers, such as polysaccharides (*12*), various proteins (*13*), RNA but not DNA (*14*), are mainly monopolar Lewis bases (having mainly or only a $\gamma^{\ominus}$ parameter). These will all be repelled by both DEX and PEG; they will ultimately congregate in the phase containing the polymer that has the smallest energy of repulsion toward them. For instance, a typical protein, human serum albumin (HSA) (*13*), will be repelled by DEX (in the dry state) with $\Delta G_{132} = +13.5$ and by PEG (also dry) with $\Delta G_{132} = +18.8$ mJ/m$^2$. Thus HSA would tend more toward the DEX phase; but a *complete* migration of HSA to the DEX phase is unlikely to ensue, as the total energy of repulsion from PEG would not readily reach a value of +1.5 kT under hydrated conditions, except possibly at very high DEX and/or PEG concentrations. HSA or a similar protein would also flee to the DEX phase, if:

(a) The protein itself has a very high molecular weight (See Ref. *6*, Fig. 4.20. For various data on other proteins and viruses of different molecular weights, see Ref. *7*, Table 5.5.) and/or

(b) The other phase comprises, instead of PEG, a very high molecular weight polymer, such as methylcellulose (See the same data from Albertsson, mentioned under (a) (*6, 7*).).

In both cases, due to the much greater surface area of close approach occurring with larger protein molecules and larger phase-forming polymers, the critical value of $\Delta G_{132} \simeq +1.5$ kT is reached much more readily; and virtually total rejection of, e.g., the largest viruses by the methylcellulose phase, appears easily achieved (*7*, Table 5.5).

## REFERENCES

1. L. C. Craig and D. Craig, in *Techniques of Organic Chemistry,* Vol. 3 (A. Weissberger, ed.), Interscience, New York, 1956, p. 149.
2. A. J. P. Martin and R. L. M. Synge, *Biochem. J., 35,* 1358 (1941).
3. M. W. Beijerinck, *Zbl. Bakt., 2,* 627, 698 (1896).
4. M. W. Beijerinck, *Kolloid Z., 7,* 16 (1910).
5. H. G. Bungenberg de Jong, in *Colloid Science,* Vol. 2 (H. R. Kruyt, ed.), Elsevier, Amsterdam, 1949, p. 255.
6. P. Å. Albertsson, *Partition of Cell Particles and Macromolecules,* 2nd ed., Wiley-Interscience, New York, 1971.
7. P. Å. Albertsson, *Partition of Cell Particles and Macromolecules,* 3rd ed., Wiley-Interscience, New York, 1986.
8. C. J. van Oss, S. N. Omenyi, and A. W. Neumann, *Colloid Polym. Sci., 257,* 737 (1979).
9. F. W. Fowkes, *J. Phys. Chem., 67,* 2538 (1963).
10. C. J. van Oss, R. M. Fike, R. J. Good, and J. M. Reinig, *Anal. Biochem., 60,* 212 (1974).
11. C. J. van Oss, *Sep. Purif. Methods, 4,* 167 (1975).
12. M. K. Chaudhury, C. J. van Oss, and R. J. Good, In Preparation.
13. C. J. van Oss, R. J. Good, and M. K. Chaudhury, *J. Protein Chem., 5,* 585 (1986).
14. C. J. van Oss, R. J. Good, and M. K. Chaudhury, *J. Chromatogr., 391,* 53 (1987).
15. M. K. Chaudhury, "Short Range and Long Range Forces in Colloidal and Macroscopic Systems," PhD Dissertation, State University of New York at Buffalo, 1984.
16. C. J. van Oss, R. J. Good, and M. K. Chaudhury, *J. Colloid Interface Sci., 111,* 378 (1986).
17. C. J. van Oss, R. J. Good, and M. K. Chaudhury, *Sep. Sci. Technol., 22,* 1 (1987).
18. R. J. Good and L. A. Girifalco, *J. Phys. Chem., 64,* 561 (1960).
19. J. J. Jasper, *J. Phys. Chem. Ref. Data, 1,* 841 (1972).
20. C. J. van Oss, R. J. Good, and M. K. Chaudhury, In Preparation.
21. A. Einstein, *Z. Elektrochem., 13,* 41 (1907).
22. W. Ostwald and R. H. Hertel, *Kolloid Z., 47,* 288, 357 (1929).
23. R. J. Good and C. J. van Oss, *Abstracts, 57th Colloid Surface Science Symposium,* Toronto, June 1983.
24. C. J. van Oss and D. R. Absolom, Unpublished Results.

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**Note Added in Proof.** We have hitherto described polar (electron-donor/electron-acceptor, or Lewis acid-base) interactions as short range, designating them with the superscript SR throughout this paper and a few preceding papers (*13, 16, 17*). It should be stressed, however, that these interactions, when not occurring *in vacuo* but in polar liquids, can make their influence felt over distances of several nanometers due to the induction of a change in molecular ordering among the liquid molecules. It will therefore be our practice henceforth to designate polar (Lewis acid-base) interactions as AB instead of SR interactions.