Interfacial free energy and the hydrophobic effect

(surface tension/interfacial tension/molecular surface area)

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ABSTRACT   Interfacial free energies demonstrate clearly that the antipathy between hydrocarbon and water rests on the strong attraction of water for itself. However, the unfavorable free energy associated with this antipathy, per unit area of contact between bulk hydrocarbon and water, is about 3-fold larger than a similar figure derived from solubility data per unit area of contact between a single dissolved hydrocarbon molecule and water. The discrepancy illustrates the difficulty in applying macroscopic concepts such as "interfacial surface" at the molecular level and can be formally resolved, at least qualitatively, by the predicted effect of surface curvature on surface tension.

Hildebrand (1), in a paper arguing against the use of the word "hydrophobic" to describe the relative lack of attraction between water and nonpolar substances, has used surface free energy data to point out that the forces between hydrocarbons (or fluorocarbons) and water in contact with each other are attractive and not repulsive. This fact has been understood and pointed out previously by those who have used the word "hydrophobic" in relation to the interaction between hydrocarbon and water (2, 3), but it emerges especially clearly from the data Hildebrand cites. The purpose of the present paper is not to argue for or against the word "hydrophobic" but to reexamine the interaction between hydrocarbon and water on the basis of surface thermodynamics. It will be seen that the special character of hydrocarbon–water antipathy can be demonstrated in this way even more clearly than on the basis of bulk solubility data, which have in recent years been the most common vehicle for introducing the concept of hydrophobicity (3, 4). A more important consequence of the calculations (without which the publication of this exercise would probably not be justified) is that they illustrate forcibly the difficulty on faces when trying to define the surface of a dissolved molecule in aqueous solution and to relate the hydrophobic interaction to the perturbation of the solvent at that surface.

Free energy of interfaces between bulk liquids

Consider a tube of 1 cm² cross-sectional area, containing two immiscible liquids (α and β) with an interface between them (see, for example, ref. 5). The work required to separate the layers and to form 2 cm² of liquid–air surface (one for each liquid) is called the "work of adhesion" and is obtained by the relationship of Dupré (6), $W_{\alpha\beta} = \gamma_a + \gamma_b - \gamma_{ab}$, in which $\gamma_{\alpha\beta}$ is the measured interfacial tension between the two liquids and γ_α and γ_β are the surface tensions at liquid–air surfaces for the pure liquids. If the tube is filled with only a single liquid, the work required to separate the column at any cross-sectional plane to form 2 cm² of identical liquid–air surface is called the "work of cohesion" (7) and is obtained by the relationship $W_{\alpha\alpha} = 2\gamma_\alpha$.

Values for these work functions for hydrocarbon–water

Table 1. Free energy of formation of a liquid–liquid area of contact from surfaces previously exposed to air, in erg/cm² at 25°C

Liquids	Hexane*	Octane†
Hydrocarbon/water	−39.5	−42.0
Hydrocarbon/hydrocarbon	−35.8	−42.4
Water/water	−144.0	−144.0

One erg = 10^{-7} J.
* Data from Linford *et al.* (8).
† Data from Aveyard and Haydon (5), corrected to 25°C.

systems are given in Table 1, with sign reversed to show the free energy of formation of the liquid–liquid contacts. All values are negative, showing that there is attraction between dissimilar as well as between like molecules, but the attractions are unequal and the data show that the disruption of 2 cm² of hydrocarbon–water interface to create 1 cm² each of hydrocarbon–hydrocarbon and water–water contacts is accompanied by a large negative free energy change (numerically equal to $-2\gamma_{\alpha\beta}$) of -102 erg, which amounts to -51 erg per cm² of hydrocarbon–water interface. This process will therefore occur spontaneously if a pathway for alteration of surface contacts exists. Table 1 shows, however, that the underlying cause for the preference for like–like contacts resides almost exclusively in the strong attraction of water for itself. In the case of hexane the attraction between hydrocarbon and water is actually slightly greater than the attraction of hydrocarbon for itself. It is for this reason, and perhaps especially because of the consequences for biological organization (9), that a special term to describe hydrocarbon–water antipathy has proved convenient, which does not mean that "hydrophobic" is a good word for it.

It is pertinent to point out that "solvophobia" is not confined to water. An even more striking example is provided by liquid mercury. The surface tension of liquid mercury is 476 erg/cm (5), and the free energy of attraction of mercury for itself is therefore -952 erg per cm² of contact area. This attraction alone accounts for the lack of solubility of nonmetallic substances in mercury, and all other applicable intermolecular forces must be insignificant in comparison with this attraction.

The interface between solute molecules and solvent

Because the origin of the antipathy between hydrocarbon and water rests on the strong self-attraction of water, it is intuitively reasonable that the favorable free energy of transfer of a hydrocarbon molecule from water to a liquid hydrocarbon solvent should be proportional to the number of water molecules released from contact with the hydrocarbon molecule when the transfer is made (10). This number in turn should be closely related to the surface area of the hydrocarbon molecule, measured at the distance of closest approach of centers of water molecules to that surface (11–13). On this basis it is not unreasonable to equate the free energy of transfer, in unitary units

so as to exclude contributions from the entropy of mixing (3, 4, 14), with the free energy gained by elimination of the hydrocarbon–water interface when a drop of hydrocarbon of molecular dimensions is transferred from water to a hydrocarbon medium. This quantity is formally equal to $-\gamma_{\alpha\beta}$ per cm^2 of surface of the drop; i.e., it is the same as the free energy change for the process discussed above. The unitary free energy of transfer predicted in this way would be -51 erg per cm^2 of molecular area.

This prediction differs substantially from experimental relationships between transfer free energy and molecular surface area, as given by Hermann (11, 12) and by Reynolds *et al.* (13). Both relationships were based on surface areas calculated for the distance of closest approach of the centers of water molecules, but they differ in the precise way in which this was done. Depending on the assumptions made, the incremental free energy change per $Å^2$ of surface, per mol of hydrocarbon transferred, was reported as being between -20 and -33 cal/mol (1 cal = 4.184 J), which corresponds to -14 to -23 erg/cm^2 of actual contact area. There is clearly a large discrepancy between these results and the value of -51 erg/cm^2 derived from the interfacial tension at a larger planar interface, as has been noted previously by Israelachvili *et al.* (15). The discrepancy can be removed to a large extent by altering the location of the "surface" of the solute molecule for the calculation of the surface area, so as to decrease that area to about one-third, but current statistical mechanical theories for solubility of nonpolar solutes in water indicate no theoretical justification for such an arbitrary change (16–18).

The observed discrepancy may be viewed as an illustration of the general difficulty in applying macroscopic concepts of surface chemistry to single molecules. It has been theoretically predicted that the surface tension of a droplet in a large volume of liquid should decrease substantially for very small droplets (19), and it has been claimed that a factor of about 3 is appropriate for small spherical solute molecules in nonpolar solvents (20). A factor of this magnitude would account completely for the discrepancy cited here, but a nonspecific treatment of the problem, purely on the basis of geometry, does not seem entirely satisfactory. A more attractive approach would be one that takes the specific properties of water and hydrocarbon molecules into account, such as is inherent in the statistical mechanical theories cited above. Until a quantitative explanation for the discrep-

ancy becomes available, it would seem realistic to question the validity of applying hydrophobic free energies derived from molecular solubility data to the estimation of the free energy of hydrophobic contacts at the surface of a micelle (21) or a protein molecule (22).

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