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Hydrodynamic Effect on the Coagulation of Porous Biopolymers

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ABSTRACT: The rate of diffusional coagulation of globular macromolecules vanishes in hydrodynamic calculations which employ stick boundary conditions at the solvent–macromolecule surface. We show that finite coagulation rates are predicted by a theory which recognizes the porous or rough character of polymer surfaces. Approximate rates for the coagulation of neutral proteins are calculated. The theory is relevant to other macromolecular rate processes, such as large-scale internal motions in proteins.

Many biochemical processes involve the association of large subunits or the relative motion of two subunits in close proximity.[2a] The diffusion equations describing the kinetics of these processes contain diffusion constants which depend on the relative positions of the subunits.[2b] These diffusion constants are inversely related to the hydrodynamic drag coefficients for relative motion of the subunits.[3,4] It is well known that the ordinary hydrodynamics of impenetrable bodies with stick boundary conditions predict that the hydrodynamic drag coefficients diverge strongly as the bodies come into contact.[5] As noted by Honig, Roebersen, and Wiersema this leads to the unphysical result that the coagulation rate of colloids vanishes, if one does not assume infinitely strong attractive forces near contact.

Recently, it has been noted by several authors that the porous nature of biopolymers affects their hydrodynamic properties.[6] Porosity may arise from either the imperfect packing of subunits or the surface irregularities of otherwise close-packed structures, such as globular proteins. Here, we note that biopolymer porosity is of key importance in the hydrodynamics of relative motion of subunits. When protein porosity is taken into account the hydrodynamic drag coefficients are only weakly singular when the bodies are in contact and the coagulation rate, predicted from diffusion-controlled reaction rate theory, is nonvanishing.

Consider the coagulation of two equal-sized spherical particles with radius a and interaction potential $U(r)$. Diffusion-controlled reaction theory relates the rate constant k for coagulation and the position-dependent relative diffusion constant $D(r)$ where r is the distance between particle centers:[3]

$$k = 4\pi \left[\int_{2a}^{\infty} \frac{e^{U(r)/k_{\mathrm{B}}T}}{r^2 D(r)} \, \mathrm{d}r \right]^{-1} \tag{1}$$

If there were no hydrodynamic interactions between the particles $D(r)$ would be twice the free translational diffusion constant of the particles. Then the rate constant for coagulation of particles with no interaction potential is given by the Smoluchowski expression:

$$k_{\mathrm{SM}} = 4\pi(2D)(2a) \tag{2}$$

The relative diffusion constant $D(r)$ is related by an Einstein relation to the drag coefficient for relative motion of the particles $f(r)$

$$D(r) = k_{\mathrm{B}}T/f(r) \tag{3}$$

An exact series expansion of $f(r)$ has been obtained by Brenner for the case of relative motion of impenetrable spheres with stick boundary conditions. Honig, Roebersen, and Wiersema have shown that this exact result is very closely approximated by a rational function which fits the series expansion exactly at large and small separations. At large separations $f(r)$ can be obtained by the use of the Oseen tensor[3]

$$f(r) = \tfrac{1}{2} f_{\mathrm{d}} \left(1 + \frac{3}{2u} + \ldots\right) \tag{4}$$

where $u = (r - 2a)/a$ and f_{d} is the translational friction constant of the particle. At small separations most of the drag is due to the large velocity gradients in the gap between the particles and lubrication theory gives[4]

$$f(r) \simeq f_{\mathrm{lub}}(r) = \tfrac{1}{2} f_{\mathrm{d}}(1/2u) \tag{5}$$

It is this strong divergence at small separations which leads to the vanishing coagulation rate of impenetrable spheres with stick boundary conditions. The approximant developed by Honig, Roebersen, and Wiersema fits eq 4 at large separation and equation 5 at small separations:

$$f_{\mathrm{HRW}} = \tfrac{1}{2} f_{\mathrm{d}} \frac{6u^2 + 13u + 2}{6u^2 + 4u} \tag{6}$$

Rather than calculating exactly the drag on approaching porous spheres, we will develop an approximant analogous to that of Honig, Roebersen, and Wiersema which fits the drag at large and small separations.

The translational friction constant for a porous biopolymer is less than the Stokes value $6\pi\eta a$. We may define an effective hydrodynamic radius $a' = f_{\mathrm{d}}/6\pi\eta$. McCammon, Deutch, and Felderhof[6] have shown how one can determine a' from the porosity structure of the biopolymer.

When the two biopolymers are far apart Oseen tensor arguments indicate that the drag is asymptotically:

$$f = \tfrac{1}{2} f_{\mathrm{d}} \left(1 + \frac{3}{2}\frac{\alpha}{u} + \ldots\right) \tag{7}$$

where $\alpha = a'/a$.

It is the small separation behavior of f which is substantially modified by porosity. The porous biopolymer is not as effective as a solid sphere in slowing down the solvent and therefore such large velocity gradients are not generated in the gap. We note that in the gap the ejected fluid flows almost tangential to the spheres, and it is the large gradients of this tangential velocity which contribute most to f. One approach to flows across porous media,[7] which we can therefore utilize for the flow in the gap, mimics the effect of porosity by replacing the stick boundary conditions by a slip boundary condition

$$V_{\tan} = \zeta \frac{\partial V_{\tan}}{\partial n} \tag{8}$$

which relates the tangential velocity to its normal derivative. The quantity ζ is called the slipping length. Of course, the possible normal flow of fluid from the gap into the porous polymer can only act to reduce the total drag.

The effective hydrodynamic radius of a sphere with this boundary condition is[5]

$$a' = a \frac{1 + 2\zeta/a}{1 + 3\zeta/a} \tag{9}$$

Thus we can determine ζ from the effective hydrodynamic radius of the protein. Using lubrication theory, Hocking has determined the drag on spheres with partial slip at small separations.[8] He finds

$$f \simeq f_{\mathrm{lub}} = \tfrac{1}{2} f_{\mathrm{d}} \frac{1}{\alpha u} \times \left[\frac{(1 + [6\zeta/au]) \ln (1 + [6\zeta/au]) - (6\zeta/au)}{(6\zeta/au)^2}\right] \tag{10}$$

When ζ vanishes, this reduces to the result for stick spheres eq 5. However, for any finite ζ the limiting form for small u is

$$f = \tfrac{1}{2} f_{\mathrm{d}}(-\gamma \ln u) \tag{11}$$

where $\gamma = a^2/6\zeta a'$. For finite ζ, the divergence at small separations is much weaker than the $1/u$ dependence of stick spheres. Because this divergence is so weak, the integral in eq 1 is finite and the rate constant is nonvanishing.

An adequate approximant for f to be used to find the hydrodynamic effect on coagulation rate can be obtained, fitting eq 10 at small separations and equation 7 at large separations:

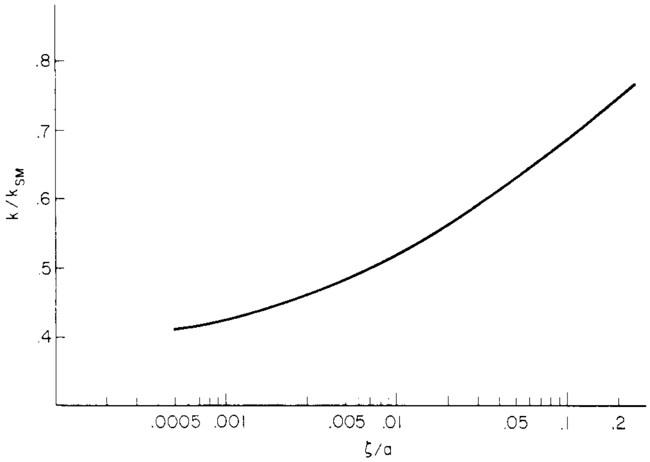

Figure 1. The hydrodynamic effect on coagulation rate of biopolymers. A typical value of the slipping length to radius ratio ζ/a is 0.15 for small proteins and smaller for larger subunits.

$$f = \frac{f_{\mathrm{d}}}{2} \frac{u^2 + \tfrac{3}{2}\alpha u + f_{\mathrm{lub}}/(f_{\mathrm{d}}/2)}{u^2 + 1} \tag{12}$$

No exact formula for the drag on approaching porous spheres is available at present; therefore, the accuracy of this approximant at intermediate separations is unknown. However, for the stick case ($\zeta = 0$) this approximate result does not differ greatly from that used by Honig et al.[4]

In Figure 1 we graph k/k_{SM} for the coagulation of neutral porous spheres as a function of the slipping length ζ. It is easy to see analytically that k vanishes rather weakly as $-1/\ln(\zeta/a)$ as the spheres become less porous. A typical value of ζ/a for a porous protein is about 0.15; the hydrodynamic effect for this value is $k/k_{\mathrm{SM}} = 0.72$. When the slipping length becomes very large, the lubrication theory results in equation 10 break down. A detailed analysis of the pure slip, $\zeta = \infty$, case is presented in another publication.[9]

In summary, taking biopolymer porosity into account removes the unsatisfactory features of stick hydrodynamic calculations of the hydrodynamic effect on diffusion-controlled reaction rates. We point out that many other phenomena, such as large-scale motions in proteins, involve hydrodynamic interactions between macromolecular structures in close proximity.[10] Unsatisfactory features of stick hydrodynamic calculations on the motions should be removed by including the effect of protein porosity.

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