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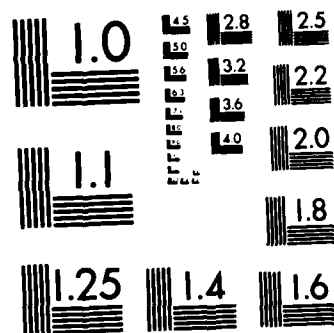
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Contribution to:
<div align="center">

Proceedings of the International Topical Conference on
KINETICS OF AGGREGATION AND GELATION
University of Georgia, April 2-4, 1984: Edited by F. Family and D.P. Landau

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EXPERIMENTAL MEASUREMENTS OF THE KINETIC EVOLUTION OF CLUSTER SIZE DISTRIBUTIONS WITH APPLICATIONS TO THE FRACTAL STRUCTURE OF ANTIGEN-ANTIBODY CLUSTERS

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1. INTRODUCTION

In previous work [1,2] we have used a Nanopar resistive pulse analyzer to determine the temporal evolution of the distribution of clusters formed by antigen coated latex microspheres cross linked by the complementary antibody. This antigen-antibody system is conceptually isomorphic to an organic polymer reaction involving RA_f units (latex microspheres with f active antigens) cross linked by B_2 units (complementary antibody) with only A-B bonding allowed.

The form of the cluster size distribution was studied as a function of the time, concentration of RA_f units, and concentration of B_2 units. The experimental results were interpreted theoretically in terms of solutions of the unidirectional Smoluchowski equations. These equations are

$$\frac{dX_n}{dt} = \frac{1}{2} \sum_{n=1}^{n-1} a_{n-n',n'} X_{n-n'} X_{n'}$$

(1)

$$\sum_{n'=1} a_{nn'} X_n X_{n'}.$$

Here, X_n is the mole fraction of clusters containing n monomers, and the $a_{nn'}$'s are the bimolecular reaction rate coefficients. These coefficients contain the information which fully determine detailed kinetic evolution of the cluster size distribution. To be specific we have found that it is theoretically convenient and experimentally acceptable to regard the structure of the matrix element $a_{nn'}$ as separable into two factors viz

$$a_{nn'} = g F(n,n'). \qquad (2)$$

Here $F(n,n')$ describes the dependence of a on the numbers n, and n' of units in each pair of interacting clusters. F is dimensionless, and can be normalized for convenience by the condition

$$F(1,1)=1. \qquad (2a)$$

We shall denote $F(n,n')$ as the cluster reaction factor. The factor g is independent of the size of the interacting clusters and is a measure of the "stickiness" associated with the binding of one single unit (in a cluster of n) to a single complementary monomer (in a cluster n'). The binding factor g is a reflection of the specific properties of the antigen-antibody bond, and the conditions of the solution and the coated spheres which can be experimentally varied. These conditions include the initial number (f) of antigenic sites on each sphere, the antibody concentration $[ab_0]$, the concentration of microspheres initially placed in solution $[C_0]$ and the pH and salt concentration of the reaction mixture. Thus the bimolecular reaction rate coefficient $a_{nn'}$ is a rich source of information on the basic physical factors which control the process of aggregation. The factor $F(n,n')$ provides information on how the size of clusters at the present time results from the aggregating smaller clusters at earlier times. Furthermore, as we shall see, $F(n,n')$ contains information on the Hausdorff dimensionability (D) of the evolving clusters. Here we can regard the clusters as fractals, and the factor F is a measure of the topological and dynamical factors which describe the coalescence of developed clusters.

The factor g on the other hand is of great practical importance. For in the use of latex immunoassays [3,4,5,6] it provides a quantitative means for optimizing the reagents so as to maximize the sensitivity and the speed of the agglutination reaction. It also enables the immunologist to determine such useful parameters as the binding constant [7] for the interaction between antibody in solution, and the antigen bound to the microsphere. It also permits a determination of the antibody lifetime [2], and the degree of coverage of the sphere by antigen [2,7].
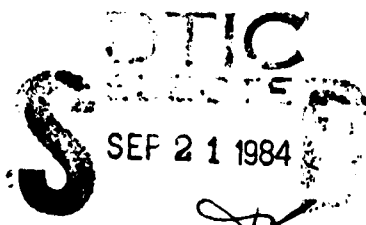
Our prior work [1,2] established the form of the cluster size distributions. Within the experimental error the distribution was consistent with the form:

$$(X_n/X) = \frac{(1-b)e^{-nb}(nb)^{n-1}}{n!}. \qquad (3)$$

Here X is the total mole fraction of monomer

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We have enclosed ~~six (6)~~ copies of the final report on our Grant
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initially added to the solution, and

$$b = (1 - \frac{\Sigma X_n}{X})$$ (4a)

is a measure of the degree of reaction. For our system

$$0 < b < 1.$$ (4b)

We also showed that asymptotically as $b \to 1$ (X_n/X) takes the form

$$\frac{X_n}{n} \to \frac{1}{\sqrt{\pi}} \frac{(1-b)}{b} \frac{1}{n^\tau}$$ (5a)

with $\tau = 3/2$ (5b)

Finally by investigating the form of known analytic solutions of the Smoluchowski equation we reported that the data found experimentally could be produced if the factor F had the form

$$F(n,n') = \frac{n+n'}{2}.$$ (6)

In the present communication we report that we have obtained [7] computer solutions of the Smoluchowski equations. These solutions permit us to investigate the effects of a much broader class of forms for the cluster reaction factor $F(n,n')$ upon the distribution of cluster sizes. Also we have shown that physical consideration of the processes of coalescence of clusters enables us to make a theoretical connection between the form of F and the topological characterization of the clusters. This argument permits a deduction of the Hausdorff dimensionality of these clusters of latex microspheres cross linked by antibody.

2. DETERMINATION OF POSSIBLE FORMS OF CLUSTER REACTION FACTOR: CONNECTION WITH HAUSDORFF DIMENSIONALITY

Previous analytic solutions of the unidirectional Smoluchowski equations have been obtained using the following forms for $a_{nn'}$ [7,8]

$$a_{nn'} = A \quad \text{(a)}$$
$$= B(n+n') \quad \text{(b)} \quad (7)$$
$$= Cnn' \quad \text{(c)}$$

We have broadened the class of such forms by considering as well the following three functions

$$a_{nn'} = g(n^\omega + n'^\omega) \quad \text{(a)}$$
or
$$a_{nn'} = g(n^{\omega/2} + n'^{\omega/2})^2 \quad \text{(b)} \quad (8)$$
or
$$a_{nn'} = g(nn')^{\omega/2} \quad \text{(c)}$$

Using the procedures described briefly below we found that any of these choices for $a_{nn'}$ could fit the data within experimental error provided that an appropriate choice was

made for the value of the exponential ω. The best values of ω found in each case were as follows:

Eqn 8(a) $\omega = 1.05 \pm 0.04$
Eqn 8(b) $\omega = 1.02 \pm 0.05$ (9)
Eqn 8(c) $\omega = 0.99 \pm 0.05$

It is interesting to observe that each of these three forms for the $a_{nn'}$'s are quite different when $n \neq n'$ however their diagonal terms depend upon n in an identical manner viz

$$a_{nn} \sim n^\omega.$$ (10)

It is possible to obtain a physical interpretation of the form of Eqn 8c in the following manner. Let us regard each cluster as a fractal whose Hausdorff dimensionality is D. Thus, the relationship between number n of units in a cluster and the effective radius R of the cluster is given by

$$n \sim R^D.$$ (11)

Let us now assume that two clusters, each having n and n' units respectively, can only interact and bind with one another by cross linking of those units near the surface of each cluster. Suppose that those units on the surface are contained within a thickness ΔR around the radius R and that ΔR is independent of R. Then the number of units (Δn) in the cluster of n available for bonding is

$$\Delta n \sim \frac{\partial n}{\partial R} \Delta R$$ (12a)

or $\Delta n \sim R^{D-1} \Delta R$ (12b)

or using Eqn 11 we can write

$$\Delta n \sim n^{(D-1)/D} \Delta R.$$ (13)

Similarly the number available for bonding on the n' cluster is

$$\Delta n' \sim n'^{(D-1)/D} \Delta R.$$

Since $a_{nn'}$ is expected to be proportional to $\Delta n \Delta n'$ it follows at once that

$$a_{nn'} \sim (nn')^{D-1)/D}.$$ (14)

On comparing this with Eqn 8c we find

$$\frac{\omega}{2} = \frac{D-1}{D}.$$ (15)

This then provides a relationship between the experimental parameter ω and the Hausdorff dimensionality D.

Using $\omega = 0.99 \pm 0.05$ we conclude that for our system that

$$D = 2.0 \pm 0.1 \qquad\qquad (16)$$

Theoretical calculations based on equilibrium considerations by Parisi and Sourlas [10] and F. Family [11] have shown that in the case of lattice animals the scaling exponent ν defined by the Eqn $R \sim n^\nu$ has the value $1/2$. Since $D=1/\nu$ for lattice animals our present finding is in agreement with their result.

The argument above is, of course, a crude one in that it regards a cluster of n particles as having an active region ΔR which is independent of both the size of that cluster (n) and of the size of the cluster (n') with which it interacts. In general this may not be the case. In our view, however, it seems likely that at least for large clusters the active region for cluster-cluster penetration may indeed satisfy our assumption. The work of M. Plischke and I. Racz reported that this conference is relevant to this issue in the case of the Eden model and DLA in two dimensions. Clearly it would be most desirable to investigate theoretically the size ΔR of the interaction zone for large clusters using computer simulation for three-dimensional model systems.

Finally we discuss the manner in which we deduced the best value of ω for each of the three choices for $a_{nn'}$ as given in 8a,b,c. The determination of ω based on the fact that the experimentally measurable quantity $b(6)$ as defined by,

$$b(6) = 1 - \frac{\sum\limits^{6} c_i}{\sum i c_i}$$

remains below a maximum value which is a function of ω. The behavior of $b(6)$ as a function of a dimensionless time T is shown in Figure 1 from which it can be seen that, for each ω, $b(6)$ does not monotonically increase as a function of T but instead reaches a distinct maximum value. This maximum value of $b(6)$ is a well behaved function of ω as is shown in Figure 2. This figure shows $b(6)_{max}$ as a function of ω for each of the functional forms of the coefficients for which numerical solutions of the Smoluchowski equations were obtained. This functional relationship between ω and $b(6)_{max}$ was used to deduce ω from an experimental measurement of $b(6)_{max}$.

The experimental value of $b(6)_{max}$ was determined from roughly 800 measurements made of the cluster size distributions under a wide variety of experimental conditions.

It was found from a frequency histogram of the number of measurements made of given values of $b(6)$, shown here as Figure 3, that the number of times values of $b(6)$ were observed drops dramatically as $b(6)$ increases beyond .49. This data set included a substantial fraction of measurements at large values of T, hence this drop constitutes an experimental measurement of $b(6)_{max}$:

$$b(6)_{max} = .49 \pm .01 .$$

Figure 4 is a detailed view of Figure 2 was used to convert this measurement $b(6)_{max}$ into measurements of ω:

$\omega = 1.05 \pm .04$ for $i^\omega + j^\omega$

$\omega = 1.02 \pm .05$ for $(i^\omega/2 + j^\omega/2)^2$

$\omega = .99 \pm .05$ for $(ij)^{\omega/2}$.

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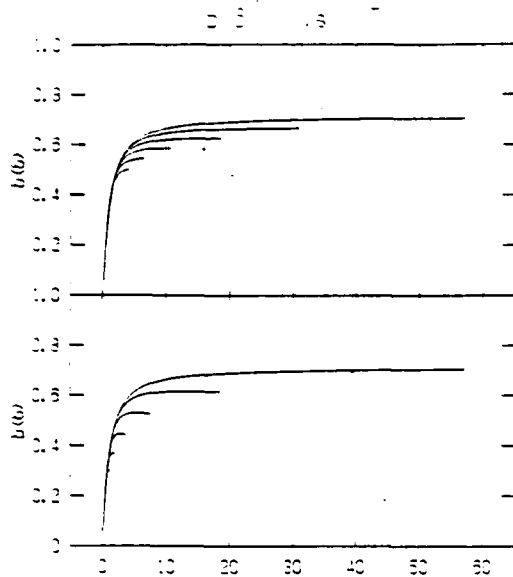
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FIGURE 1

The maximum values of b(6) are shown through graphs of b(6) versus T from kinetic coefficients of the form $i^\omega + j^\omega$ (top) and ij^ω (bottom) with values of ω ranging from 0.0 (highest curve) to 1.0 (lowest curve) in increments of 0.2. For each form of the coefficients and each value of ω these curves exhibit a maximum, above which no value of b(6) should be observed.
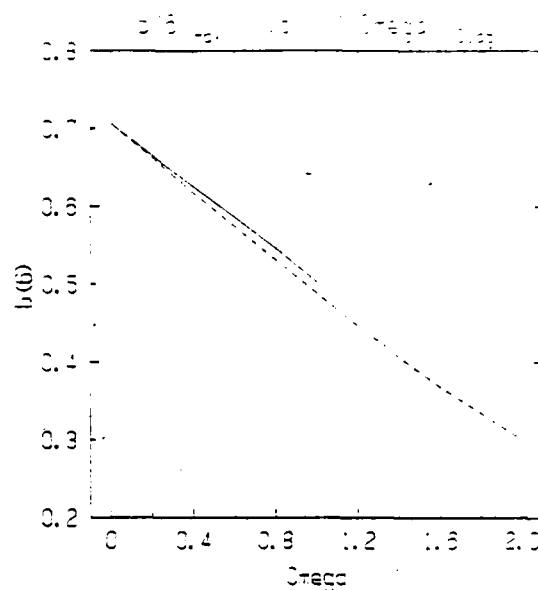
FIGURE 2

The similarity for asymptotic shape of the distributions as predicted by three different forms of the kinetic coefficients is shown by a graph of $b(6)_{max}$ versus ω_d. The three forms of the coefficients are $i^\omega + j^\omega$ (solid line), $(ij)^{\omega/2}$ (dashed line), and $(i^{\omega/2} + j^{\omega/2})^2$ (dotted line).
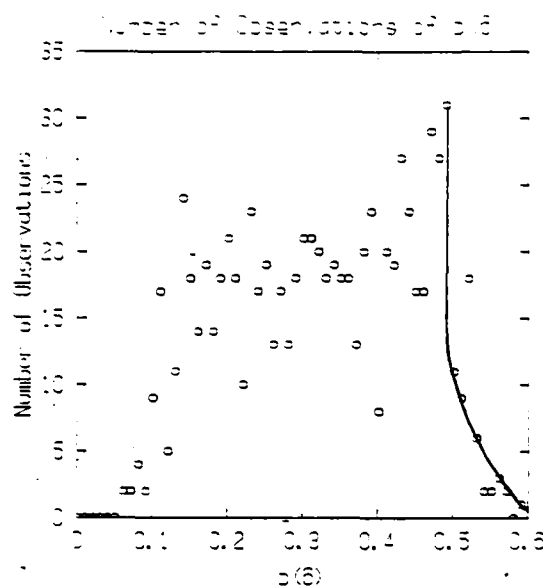
FIGURE 3

The number of observations of values of $b(6)$ between $x-.005$ and $x+.005$ is drawn as a function of x, for x ranging from 0.0 to 0.6 by increments of .01. The tail of this histogram is drawn as a solid line.
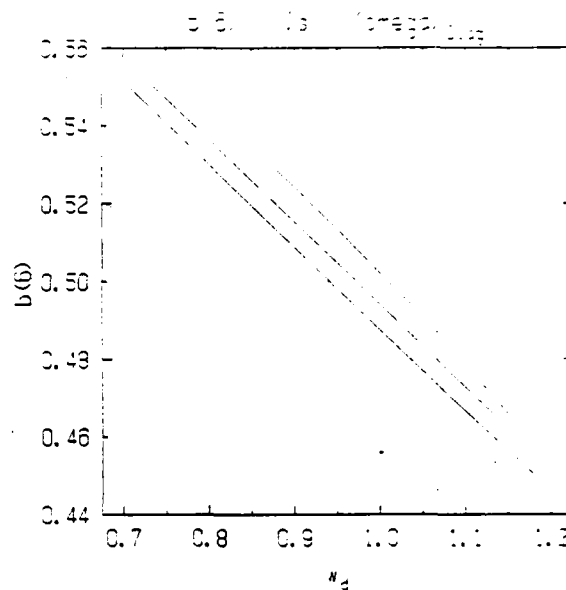
FIGURE 4

The curves used for the determination of ω_d from $b(6)_{max}$ is shown for three forms of the kinetic coefficients. The three forms of the coefficients are $i^\omega + j^\omega$ (top line), $(i^{\omega/2} + j^{\omega/2})^2$ (middle line), and $(ij)^{\omega/2}$ (bottom line).