

# Nanoparticle Dynamics: A Multiscale Analysis of the Liouville Equation<sup>†</sup>

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A theory of nanoparticle dynamics based on scaling arguments and the Liouville equation is presented. We start with a delineation of the scales characterizing the behavior of the nanoparticle/host fluid system. Asymptotic expansions, multiple time and space scale techniques, the resulting coarse-grained dynamics of the probability densities of the Fokker–Planck–Chandrasekhar (FPC) type for the nanoparticle(s), and the hydrodynamic models of the host medium are obtained. Collections of nanoparticles are considered so that problems such as viral self-assembly and the transition from a particle suspension to a solid porous matrix can be addressed via a deductive approach that starts with the Liouville equation and a calibrated atomic force field, and yields a generalized FPC equation. Extensions allowing for the investigation of the rotation and deformation of the nanoparticles are considered in the context of the space-warping formalism. Thermodynamic forces and dissipative effects are accounted for. The notion of configuration-dependent drag coefficients and their implications for coagulation and consolidation are shown to be natural consequences of the analysis. All results are obtained via formal asymptotic expansions in mass, size, and other physical and kinetic parameter ratios.

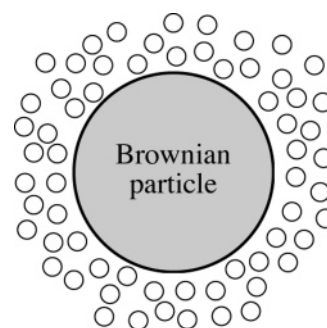
## I. Introduction

Nanoparticles of natural and engineered origin present a grand challenge for statistical mechanics. They lie at the boundary between the macroscopic and microscopic regimes; multiscale techniques are thus required to gain a fundamental understanding of their behavior.

Examples of important bionanoparticles and the phenomena they display abound. Virus self-assembly: this and other aspects of their life cycle involve millions to hundreds of millions of atoms simultaneously and therefore cannot readily be analyzed by a straightforward microscopic approach. The formation and functioning of mitochondria, ribosomes, and other intracellular structures and molecular machines are other systems wherein nanoparticles interact with a host medium via the interplay of fluctuating and macroscopic forces. Delivery of drugs by functionalized particles, magnetically directed migration and heating of drug-bearing particles, and light-detectible imaging systems seem to have great medical potential. Also nanoparticles can be combined to form composite materials with interesting engineering characteristics. The transport of gold and other particles is key to the formation of deposits, whereas other particles carry pollutants.

Although atomic-scale systems are dominated by fluctuations, macroscopic systems can be well-characterized by a reduced set of average variables. Therefore, a challenge of nanoscience is that the phenomena of interest can only be understood via a nesting of atomistic (fluctuating) variables and more macroscopic ones.

There is great value in developing a rigorous theory of nanosystem kinetics starting from the Liouville equation. Unlike phenomenological approaches, such a deductive approach results in universal equations in which the only parameters are those of the atomic force field. The theme of this study is that an understanding of nanosystems should follow from a delineation

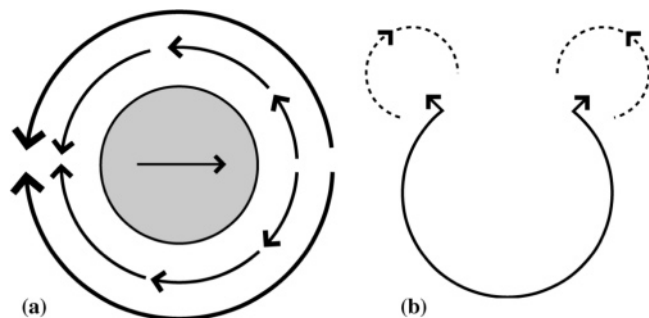


**Figure 1.** A massive and geometrically large Brownian particle immersed in a host medium experiences many collisions with the small host particles. If this BP is slow, these collisions tend to cancel an average, suggesting that the BP only experiences a fluctuating force that averages out in time and across the BP surface.

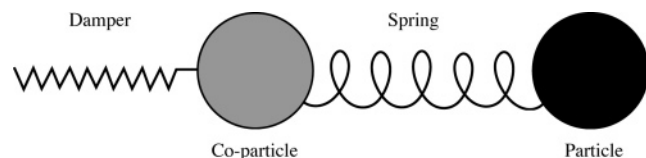
of the space and time scales involved in the system of interest. The classic example of a nanoparticle phenomenon is the fluctuating motion of a Brownian particle (BP) in a host medium of small particles.<sup>1</sup> It is shown here that the migration of such a BP can be understood via an analysis of the Liouville equation in terms of space and time scales that are natural for its large mass and size. These factors imply the slowness of the BP relative to the motion of the host particles due to both inertia and a spatial averaging (Figure 1). An understanding of the composite BP/host medium system also must account for the slow hydrodynamic behavior of the host medium.

Another aspect of the behavior of a nanoparticle is the dressing of its dynamics as by the vortex of Figure 2. Such phenomena impart memory and dissipation to the dynamics; elastic properties of the medium impart rebound and oscillatory effects (Figure 3) wherein the concept of a co-particle is introduced. Another facet of this dressing is the effective force between nanoparticles introduced by their individual interactions with the host medium (Figure 4). The forces between nanoparticles, and hence the manner in which the multiple nanoparticle

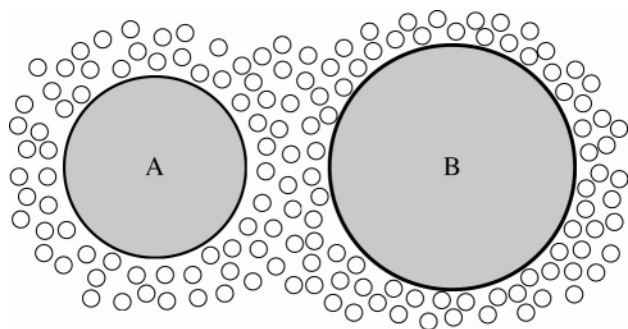
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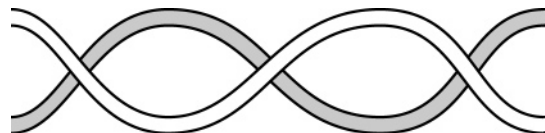
**Figure 2.** (a) A moving nanostructure can induce a vortex in the host medium that feeds back to the dynamics of the structure, creating a dressed particle with modified behavior. (b) The fluctuating structure of a polymer can create a set of vortices that implies an effective hydrodynamic interaction between its ends. Thus, there are three types of forces on a nanostructure: (1) direct inter- or intraparticle forces; (2) thermodynamic forces caused by equilibrium changes in the host fluid properties induced by the instantaneous configuration of the nanostructure; and (3) effective time-delayed interaction from the exchange of phonons or vortices with the host medium.



**Figure 3.** In effect, a nanostructure in a host medium creates a virtual (correlate) particle with which it interacts to yield a dressing of the nanostructure's dynamics by the medium. The spring and resistance represent the elastic and viscous responses of the host medium.



**Figure 4.** BPs A and B interact through shared host particles as well as the direct forces between them, yielding a net effective force.



**Figure 5.** The configuration of a pair of nanostructures that, when compared to Figure 4, suggests the strong geometry-dependence of the contact area and hence the strength and scaling of the interaction between the nanostructures and with the host medium. These geometrical considerations imply the scaling of various contributions to the Liouville operator.

system scales, depend strongly on the geometry of the nanoparticles (Figure 5). It is shown here how these effects result from the many-body dynamics of a composite nanoparticle/host medium system.

The multiple scale understanding of nanosystems dates back to Einstein, Langevin, Smolokowski, Chandrasekhar, and others.<sup>1–4</sup> Deutch and Oppenheim<sup>5</sup> presented an approach to nanoparticle dynamics based on projection operators and a perturbation scheme in the nanoparticle/host particle mass ratio.

This set the stage for a series of analyses of nanoparticle dynamics based on the Liouville equation. Shea and Oppenheim<sup>6</sup> derived FPC and Langevin equations for a single nanoparticle in a host medium using projection operators and perturbation techniques using the mass ratio and macroscopic gradients in the host medium as perturbation parameters. The present approach is based on a formal multiple space–time scaling approach integrated with a statistical argument derived from the nanoparticle/host particle size ratio that allows for a united asymptotic expansion to directly arrive at FPC equations for single and multiple nanoparticle and intra-nanoparticle structural dynamics. When the slow hydrodynamics of the composite nanoparticle/host medium system is accounted for, it is shown formally that the treatment leads to a set of coupled FPC equations, one for each mode. Shea and Oppenheim<sup>6</sup> extended their work to the case of multiple nanoparticles, introducing a number of smallness parameters. Here we provide a unified asymptotic expansion and a seven-time scale formulation that allows one to capture transitional behaviors (e.g., when the time scale switches as nanoparticle density increases and the behavior becomes more like a solid porous matrix than a suspension). We also introduce the notion of space warping to treat nanoparticle deformation and rotation, thereby separating the slow and fast features of these processes.

Nanosystem phenomena can impart a scaling of operators; we show that a nanoparticle of large surface area tends to average out individual bombardments of the host medium when the nanoparticle is slowly moving. This implies that an operator used to compute the force on the nanoparticle by the host medium must have a specific scaling property when applied to functions in Liouville space that correspond to near-equilibrium behaviors. This is distinct from a perturbation scheme in the ratio of the host/nanoparticle mass. Such a notion of operator scaling has also been used to derive reaction rates from a Liouville equation formulation of the reacting hard sphere model.<sup>7–10</sup>

## II. Multiple Scale Unfolding and Recomposition

A formal analysis is now presented by which mesoscopic equations bridging two or more scales are derived. The method is based on an unfolding of the Liouville equation to reveal its multiple time and space scale character, followed by a recomposition of the equation via a perturbation method to arrive at a coarse-grained equation that captures the mesoscopic phenomenon and averages out the shorter scale variations in a way that preserves their effect on the long-scale dynamics. The method allows for a hierarchical treatment leading to progressively coarser grained equations.

If a system evolves on several time scales, it is appropriate to introduce distinct time variables.<sup>11</sup> Let  $t_0 = t$  be the fundamental (i.e., shortest) time variable. If  $t_0$  changes by one unit, then a typical atomic vibration or collision of a host medium particle with another or with a nanoparticle takes place. Because of its mesoscopic nature, the system also evolves on one or more longer time scales. If the time scales are separated by an order of magnitude or more, then a parameter  $\epsilon$  ( $\ll 1$ ) can be introduced that reflects the ratio of the characteristic time of the fundamental scale to that of the next (longer) scale. The natural time variable for this first long scale is  $t_1 = \epsilon t$ . As time changes by a large interval (e.g.,  $\epsilon^{-1}$  fundamental time units),  $t_1$  changes by one unit. This concept can be generalized to a sequence of times,  $t_n = \epsilon^n t$ , that are presumed to be ordered with increasing integer powers of  $\epsilon$ . There could be other

sequences: for example,  $t_0 = t$ ,  $t_1 = -(\epsilon^2 \ln \epsilon)t$ ,  $t_2 = \epsilon^3 t$ , etc. Only integer power sequences are considered here.

As a mesoscopic system can be described in terms of multiple time scales, it may similarly involve a number of well-separated spatial scales. For example, let  $\vec{r}_0 = \vec{r}$  define a position such that the average nearest-neighbor distance between molecules in the host medium is one unit. However, there may be other spatial scales natural to the system. There are lengths characterizing the size of a nanoparticle or the average distance between the latter. Other scales that have no direct reflection in the Liouville equation, such as the width of interfaces in a two-phase host medium or the Debye length for an electrolyte host medium, may enter the problem. In analogy to the multiple times, a set of spatial variables,  $\vec{r}_n = \epsilon^n \vec{r}$ ,  $n = 0, 1, \dots$ , that characterize the atomic, mesoscopic, and longer scale behaviors, can be introduced.

Underlying these kinematic aspects of a mesoscopic system are physical factors. For example, the ratio of the mass of a host medium molecule to that of a nanoparticle can be small. Expressing this ratio as a power of  $\epsilon$  allows one to see how the separations of physical scales (associated with mass or the strength/range of interaction potentials) imply the kinematic scales.

As the above time and space variables are natural for describing a mesoscopic system, the probability  $\rho$  for the state of the many-body system should be written as a function of these variables. If  $\rho$  depends independently on two times  $t_0$  and  $t_1$ , then  $\partial\rho/\partial t = \partial\rho/\partial t_0 + \epsilon\partial\rho/\partial t_1$  (on the basis of the chain rule). Similar considerations follow for spatial derivatives. As shown more explicitly in later sections, the spatio-temporal scaling and the separation of the magnitudes of physical factors imply that the Liouville operator  $\mathcal{L}$  may be written as a sum of terms of the form  $\epsilon^n \mathcal{L}_n$  in which  $\mathcal{L}_n$  is an operator with respect to the momenta and the various scaled spatial variables for each particle. With this, the Liouville equation takes the form

$$\sum_{n=0}^{\infty} \epsilon^n \frac{\partial \rho}{\partial t_n} = \sum_{n=0}^{\infty} \epsilon^n \mathcal{L}_n \rho \quad (\text{II.1})$$

The multiple scale analysis of these systems reflects the phenomenon of interest. For example, a theory can be developed for the slow overall conformational changes of a nanoparticle in an aqueous medium: for the result of interest, one averages out the short time scale vibrational/collisional behavior. This suggests a physical picture in which the lowest order  $\rho$  reflects a state of equilibrium for the fast host medium and intranoparticle modes. Mesoscopic theory then takes the form of an equation for the slow variables evolving in the presence of rapidly fluctuating ones. Specifically, one obtains an FPC equation for the slow variable reduced probability distribution. Deriving such results directly from the Liouville equation is the objective of this and later sections.

For cases in which  $\epsilon \ll 1$ , an expansion for  $\rho$ ,

$$\rho = \sum_{n=0}^{\infty} \rho_n \epsilon^n \quad (\text{II.2})$$

can be attempted. This is not a straightforward Taylor series for  $\rho$ . Rather, the postulated dependence of the  $\rho_n$  on the multiple space and time variables introduces a type of infinite resummation that ensures that the expansion is valid for all times, including  $t \rightarrow \infty$ .

In many phenomena in nanoscience, one is interested in behaviors wherein the fast processes are at equilibrium. In this

case the leading term  $\rho_0$  does not depend on  $t_0$ . Thus  $\rho_0$  evolves slowly in time, for example, on mesoscopic or longer scales, and hence the  $O(\epsilon^0)$  term in eq II.1 implies

$$\mathcal{L}_0 \rho_0 = 0 \quad (\text{II.3})$$

In the simplest case,  $\rho_0$  is thus taken to have the equilibrium form  $\rho_0 = W \exp(-\beta H_0)/Q$  in which  $H_0$  is the Hamiltonian from which  $\mathcal{L}_0$  is constructed. If  $\langle \dots \rangle$  indicates an integration over all variables on which  $\mathcal{L}_0$  operates, then the partition function  $Q = \langle e^{-\beta H_0} \rangle$  is independent of these variables. In many problems of interest, the host medium supports multiple phases (e.g., liquid vs gas). The resulting interfaces are configured, for example, with gas over liquid in a weak gravitational field. The latter field plays no significant role energetically because the multiphase configuration results from the cooperativity due to host molecule/host molecule interaction. Hence, although  $H_0$  may not have any appreciable, explicit dependence on the position of the nanoparticle, nanoparticle position dependence can appear in  $Q$  as a consequence of the choice of the ensemble (i.e., gas overlying liquid).

There are more general solutions of eq II.3, that is,  $\rho_0$  is expressed as a linear combination of null vectors of  $\mathcal{L}_0$ . These are discussed further in the appendix in the context of the hydrodynamic modes of the host fluid/nanoparticle system.

From the form of  $\rho_0$ ,  $W$  is seen as the probability distribution for the variables describing the longer scale behavior of the system.

Collecting  $O(\epsilon)$  terms in eq II.1 yields

$$\left( \frac{\partial}{\partial t_0} - \mathcal{L}_0 \right) \rho_1 = - \frac{\partial \rho_0}{\partial t_1} + \mathcal{L}_1 \rho_0 \quad (\text{II.4})$$

This equation has the formal solution

$$\rho_1 = e^{\mathcal{L}_0 t_0} \rho_1^0 + \int_0^{t_0} dt'_0 \exp[\mathcal{L}_0(t_0 - t'_0)] \left[ - \frac{\partial \rho_0}{\partial t_1} + \mathcal{L}_1 \rho_0 \right] \quad (\text{II.5})$$

in which  $\rho_1^0$  is  $\rho_1$  at  $t_0 = 0$ . The fact that  $\mathcal{L}_0 H_0 = 0$  implies

$$\rho_1 = e^{\mathcal{L}_0 t_0} \rho_1^0 - t_0 \frac{e^{-\beta H_0}}{Q} \frac{\partial W}{\partial t_1} + \int_0^{t_0} dt'_0 \exp[\mathcal{L}_0(t_0 - t'_0)] \mathcal{L}_1 \frac{e^{-\beta H_0}}{Q} W \quad (\text{II.6})$$

The second term on the right-hand side (RHS) appears to diverge as  $t_0 \rightarrow \infty$ . For  $\rho_1$  to be well-behaved, this term must be balanced by a contribution from the last term. This is the case if

$$\frac{\partial W}{\partial t_1} = \mathcal{D}_1 W \quad (\text{II.7})$$

$$\mathcal{D}_1 W \equiv \lim_{t_0 \rightarrow \infty} \frac{1}{t_0} \int_0^{t_0} dt'_0 \left\langle \exp[\mathcal{L}_0(t_0 - t'_0)] \mathcal{L}_1 W \frac{e^{-\beta H_0}}{Q} \right\rangle \quad (\text{II.8})$$

The  $\mathcal{D}_1$  operator simplifies in many cases because  $\langle \mathcal{L}_0 A \rangle$  for any function  $A$  frequently vanishes.

To  $O(\epsilon^2)$  one obtains

$$\left( \frac{\partial}{\partial t_0} - \mathcal{L}_0 \right) \rho_2 = - \frac{\partial \rho_0}{\partial t_2} - \frac{\partial \rho_1}{\partial t_1} + \mathcal{L}_2 \rho_0 + \mathcal{L}_1 \rho_1 \quad (\text{II.9})$$

Using arguments as those for  $O(\epsilon)$ , one may derive an equation



of the form  $\partial W/\partial t_2 = \mathcal{D}_2 W$  in which  $\mathcal{D}_2$  is a linear operator. In obtaining this result, the term  $\partial W/\partial t_1$  is replaced by  $\mathcal{D}_1 W$  and is bundled into  $\mathcal{D}_2 W$ .

Generalizing the above arguments to  $O(\epsilon^n)$  and introducing linear operators  $\mathcal{D}_n$  ( $n = 1, 2, \dots$ ) yields

$$\frac{\partial W}{\partial t_n} = \mathcal{D}_n W \quad (\text{II.10})$$

Suppose that only the behavior on time scales greater than  $t_0$  but shorter than  $t_{m+1}$  is sought ( $m \geq 1$ ). In this case,  $t_1$  can be thought of as the new fundamental time appropriate for the  $t_1$  and slower behavior. Letting  $\tau = t_1$ , multiplying eq II.10 by  $\epsilon^{n-1}$ , summing from  $n = 1$  to  $n = m$ , and using the chain rule yields the FPC equation

$$\frac{\partial W}{\partial \tau} = \mathcal{D} W \quad (\text{II.11})$$

$$\mathcal{D} = \sum_{n=1}^m \mathcal{D}_n \epsilon^{n-1} \quad (\text{II.12})$$

This recomposed Liouville equation serves as the basis for a rigorous theory of the slow (i.e.,  $t_1, \dots, t_m$ -dependent) dynamics of a multiscale system. The level  $m$  at which the development is truncated depends on the phenomenon of interest: for example, the latter is presumed to only involve dynamics on the  $t_m$  scale or shorter. The remainder of this paper is focused on implementing this unfolding/recomposition prescription for nanoparticles in a host medium. Generalized FPC equations for slow behavior are obtained. The above unfolding of the Liouville equation and recomposition into coarse-grained equations can be repeated, yielding a hierarchy of theories for the longer and longer space–time scale behaviors.

A challenge for the theory of mesoscopic systems is the tendency of these systems to transition from one space–time scaling behavior to another. For example, interacting nanoparticles evolve on a number of scales that depend on their individual conformation and that relative to others. As these nanoparticles can experience large conformational changes or approach each other, such a system may switch between slow and fast behavior due to collision or self-assembly into complex structures. This switching is captured by eq II.11, as shown more explicitly in later sections.

### III. A Structureless Nanoparticle in a Host Fluid

Consider a system of  $N$  host particles, labeled  $1, \dots, N$ , and a nanoparticle, labeled  $N + 1$ . Let the ratio of the mass of a typical host particle ( $m$ ) to that of the nanoparticle be  $\epsilon^2$  for  $\epsilon \ll 1$  (i.e.,  $m_{N+1} = \epsilon^{-2} m$ ). Other scalings could be adopted as appropriate and would evoke different behavioral regimes. Assuming that the momentum distribution is near equilibrium, the typical kinetic energy of a particle is  $3/2 k_B T$ . Hence, the typical momentum of the nanoparticle is of the order  $\sqrt{m_{N+1} k_B T}$ , so that  $\vec{p}_{N+1} = \epsilon^{-1} \vec{P}$  introduces a momentum  $\vec{P}$  that is appropriate for the nanoparticle. With this, the typical velocity of the nanoparticle is  $O(\epsilon)$ , and in a time characteristic of that for collisions between, or with, the host particles, the nanoparticle only moves a distance of  $O(\epsilon)$ . This suggests that the short time scale host dynamics could reach equilibrium with the instantaneous nanoparticle configuration. Long time and length scale variables are needed to capture the overall nanoparticle migration of interest here. These are found to be  $t_4 = \epsilon^4 t$  and  $\vec{R}$

$= \epsilon^3 \vec{r}_{N+1}$ . The latter assumptions are found to be natural at a later stage in the development and, in effect, imply a choice of the phenomenon of interest (i.e., Brownian motion).

It is convenient to define relative coordinates  $\vec{s}_i = \vec{r}_i - \vec{r}_{N+1}$  for the  $N$  host particles. With this, the probability density  $\rho(\vec{p}_1, \vec{s}_1, \dots, \vec{p}_N, \vec{s}_N, \vec{P}, \vec{R}, t_0, t_1, t_2, t_3, t_4; \epsilon)$  satisfies

$$\sum_{n=0}^4 \epsilon^n \frac{\partial \rho}{\partial t_n} = (\mathcal{L}_0 + \epsilon^2 \mathcal{L}_1 + \epsilon^4 \mathcal{L}_2) \rho \quad (\text{III.1})$$

$$\mathcal{L}_0 = - \sum_{i=1}^N \left\{ \frac{\vec{p}_i}{m_i} \cdot \frac{\partial}{\partial \vec{s}_i} - \frac{\partial V}{\partial \vec{s}_i} \cdot \frac{\partial}{\partial \vec{p}_i} \right\} \quad (\text{III.2})$$

$$\mathcal{L}_1 = - \frac{\vec{P}}{m} \cdot \vec{\Xi} - \vec{F} \cdot \frac{\partial}{\partial \vec{P}} \quad (\text{III.3})$$

$$\mathcal{L}_2 = - \frac{\vec{P}}{m} \cdot \frac{\partial}{\partial \vec{R}} \quad (\text{III.4})$$

The factors  $\vec{\Xi}$  and  $\vec{F}$  are defined via

$$\vec{\Xi} = - \frac{1}{\epsilon} \sum_{i=1}^N \frac{\partial}{\partial \vec{s}_i}, \quad \vec{F} = - \frac{1}{\epsilon} \frac{\partial V}{\partial \vec{r}_{N+1}} = \vec{\Xi} V \quad (\text{III.5})$$

Here,  $V$  is the  $(N + 1)$ -body potential and is assumed to only depend on the relative configuration. The operator  $\vec{\Xi}$  is assumed to be  $O(\epsilon^0)$  when applied to any quasi-equilibrium probability under the notion that it involves many vector contributions, which tend to cancel. A notable exception is extreme regions of configuration space associated with shock waves or vortices in the host medium induced by a high-velocity nanoparticle (Figure 2). The scaling adopted here is valid for the quasi-equilibrium host medium relevant for classic Brownian motion, however.

To examine the  $\vec{\Xi}$ -scaling ansatz more closely, let the host particles have a radius  $R_h$  such that  $R_B \approx \epsilon^{-1} R_h$  for a nanoparticle of size  $R_B$ . The number  $N_h$  of host particles in a monolayer around the nanoparticle is then  $4\pi R_B^2$  times  $2R_h$  times the density of host particles  $\{\sim [(4/3)\pi R_h^3]^{-1}$  for a liquid host}. Thus,  $N_h$  is  $O(\epsilon^{-2})$ . For nanoparticle motion only driven by fluctuations of the host, in the large  $R_B$  ( $\epsilon \rightarrow 0$ ) limit, the net force on the nanoparticle imposed by the host is due to the residual fluctuations from the large but finite  $N_h$  statistics. The central limit theorem suggests that the net force on the nanoparticle by the host particles (assuming short-range forces) is of the order  $N_h^{-1/2}$ , that is,  $O(\epsilon)$ . This is taken as a justification for the scaling implied in eq III.5.

With this,  $\epsilon^2$  is seen as a natural parameter in terms in which  $\rho$  can be expanded. From eq III.1 it is seen that times  $t_1$  and  $t_3$  can be ignored as the RHS has no explicit  $\epsilon$  and  $\epsilon^3$  terms. Thus, the present treatment is a three-time theory. Note that initial data, host medium hydrodynamic modes, or space and time scales arising from host multiphase behaviors could evoke  $\epsilon$  and  $\epsilon^3$  behavior, however. Thus, we assume that  $\rho$  can be constructed as an asymptotic expansion in  $\epsilon^2$ :

$$\rho = \sum_{n=0}^{\infty} \rho_n(\vec{p}_1, \vec{s}_1, \dots, \vec{p}_N, \vec{s}_N, \vec{P}, \vec{R}, t_0, t_2, t_4) \epsilon^{2n} \quad (\text{III.6})$$

At  $O(\epsilon^0)$ , the Liouville equation allows for solutions  $\rho_0$  that are independent of the microscopic time  $t_0$  so that  $\mathcal{L}_0 \rho_0 = 0$ .

This has the quasi-equilibrium solution

$$\rho_0 = \frac{\exp(-\beta H_0)}{Q} W(\vec{P}, \vec{R}, t_2, t_4) = \hat{\rho} W \quad (\text{III.7})$$

The Hamiltonian for the medium in the force field of the nanoparticle is denoted  $H_0$  and  $Q$  is the partition function:

$$Q = \int d^3 p_1 d^3 s_1 \dots d^3 p_N d^3 s_N \exp\{-\beta H_0\} = \langle e^{-\beta H_0} \rangle \quad (\text{III.8})$$

The function  $W$  depends only on the large-scale variables describing the state of the nanoparticle.

To  $O(\epsilon^2)$

$$\left(\frac{\partial}{\partial t} - \mathcal{L}_0\right)\rho_1 = -\frac{\partial \rho_0}{\partial t_2} + \mathcal{L}_1 \rho_0 \quad (\text{III.9})$$

in which we henceforth drop the 0 on  $t_0$  for simplicity. Equation III.9 yields the solution

$$\rho_1 = e^{\mathcal{L}_0 t} \rho_1^0 + \int_0^t dt' \exp[\mathcal{L}_0(t-t')] \mathcal{L}_1 \rho_0 - t \frac{\partial W}{\partial t_2} \hat{\rho} \quad (\text{III.10})$$

in which  $\rho_1^0$  is the value of  $\rho_1$  at  $t = 0$ . Because it involves the evolution operator  $\exp(\mathcal{L}_0 t)$ ,  $\rho_1$  involves short time scale, fluctuating host dynamics.

The secular (divergent as  $t \rightarrow \infty$ ) behavior in  $\rho_1$  must be removed if the asymptotic expansion is to be well-behaved. The removal of the secular behavior in  $\rho_1$  implies

$$\frac{\partial W}{\partial t_2} = \langle \mathcal{L}_1 \rho_0 \rangle = 0 \quad (\text{III.11})$$

Use has been made of the fact that (1)  $\langle \partial A / \partial \vec{p}_i \rangle = \vec{0}$  for any factor  $A$  that vanishes at large  $\vec{p}_i$  and (2) periodic boundary conditions on  $\rho$  with respect to the  $\vec{s}_i$  are imposed. It is concluded that  $W$  has no  $t_2$ -dependence, which implies that  $\rho_1$  has no such dependence either.

The  $O(\epsilon^4)$  terms yield

$$\left(\frac{\partial}{\partial t} - \mathcal{L}_0\right)\rho_2 = -\frac{\partial \rho_0}{\partial t_4} + \mathcal{L}_1 \rho_1 - \frac{\vec{P}}{m} \cdot \left[ \frac{\partial W}{\partial \vec{R}} \hat{\rho} + W \frac{\partial \hat{\rho}}{\partial \vec{R}} \right] \quad (\text{III.12})$$

Applying  $\langle \dots \rangle$  to eq III.12 yields

$$\begin{aligned} \frac{\partial}{\partial t} \langle \rho_2 \rangle &= -\frac{\partial W}{\partial t_4} + \langle \mathcal{L}_1 e^{\mathcal{L}_0 t} \rho_1^0 \rangle + \\ &\int_0^t dt' \langle \mathcal{L}_1 \exp[\mathcal{L}_0(t-t')] \mathcal{L}_1 \rho_0 \rangle - \frac{\vec{P}}{m} \cdot \left[ \frac{\partial W}{\partial \vec{R}} + \beta W \frac{\partial \mathcal{F}}{\partial \vec{R}} \right] \end{aligned} \quad (\text{III.13})$$

in which  $\beta \mathcal{F} = -\ln Q$  introduces the host medium for energy  $\mathcal{F}$  (for further discussion see Section VI). In the above equation, the fact that  $\langle \partial A / \partial \vec{s}_i \rangle = \vec{0}$  and  $\langle \partial A / \partial \vec{p}_i \rangle = \vec{0}$  for any relevant  $A$  has again been used.

The final result of this computation, an equation for  $W$ , arises out of an examination of the large  $t$  behavior of  $\rho_2$ . Assuming that all the initial data for  $\rho$  are captured in  $\rho_0$ , that is, the fast variables are in equilibrium and  $\rho_1^0$  is zero, integrating eq III.13 with respect to  $t$  from 0 to  $t_{\max}$  yields  $\langle \rho_2 \rangle(t_{\max})$ , which has to be finite at all times for the self-consistency of the asymptotic expansion. The sum of all of the terms in  $\langle \rho_2 \rangle$  that are found to diverge as  $t_{\max} \rightarrow \infty$  must thus balance, yielding

$$\frac{\partial W}{\partial t_4} + \frac{\vec{P}}{m} \cdot \frac{\partial W}{\partial \vec{R}} = \frac{\gamma}{m} \nabla_{\vec{P}} \cdot (\vec{P} W) + \frac{\gamma}{\beta} \nabla_{\vec{P}}^2 W - \frac{\beta \vec{P}}{m} \cdot \frac{\partial \mathcal{F}}{\partial \vec{R}} W \quad (\text{III.14})$$

in which  $\gamma$  is the drag coefficient that can be expressed in terms of the force autocorrelation function

$$\gamma = \frac{\beta}{6} \int_{-\infty}^{\infty} \langle \hat{\rho} \vec{F}(0) \cdot \vec{F}(\tau) \rangle d\tau \quad (\text{III.15})$$

with  $\vec{F}(\tau) = \exp(-\mathcal{L}_0 \tau) \vec{F}(0)$ . Thus, the FPC equation with thermodynamic force  $-\partial \mathcal{F} / \partial \vec{R}$  follows from a scaling analysis of the Liouville equation directly. The present derivation clarifies the quantitative relations among the scales and their physical origins and provides the expected expression for the drag coefficient. Certain issues remain open, however, some of which are addressed in the following sections and in the appendix.

#### IV. Multiple Nanoparticles on Seven-Time Scales

As two nanoparticles approach each other, the behavior may switch from a slow random walk to a rapid acceleration as strong, short-range forces dominate. A conformational change of a given nanoparticle can decrease its effective surface area and, hence, the scalings of the averaging of fluctuating forces imposed by the host medium or its interaction with other nanoparticles (Figures 4 and 5). The behavior of a large number of nanoparticles in a host fluid can transition from that of a low viscosity suspension to that of a rigid, fluid-filled porous matrix as density (and hence congestion) increases beyond a critical level. Because of the importance of the large number of time scales that can arise in the multiple nanoparticle problem, the unfolding/recomposition method of Section II is ideally suited.

Consider the dynamics of a multiple nanoparticle system in which (1) the structures are strongly affected by the host medium, and (2) several spatial scales must be accounted for because of the direct and indirect interactions between the nanoparticles (Figures 4 and 5). As suggested in Figure 5, several scalings are possible depending on the geometries of each nanoparticle and the strength of the coarse-grained interaction these geometries imply.

A collection of  $N_B$  spherical nanoparticles in a host medium of  $N$  particles ( $N \gg N_B$ ) is used to illustrate the approach. Let the nanoparticles be at positions  $\vec{x}_k$ , and, in analogy to the single nanoparticle case, have masses  $\epsilon^{-2} M_k$  and momenta  $\epsilon^{-1} \vec{P}_k$ , in which  $k = 1, \dots, N_B$  (for  $\epsilon \ll 1$ ). The host particles are described by their positions  $\vec{r}_i$ , momenta  $\vec{p}_i$ , and masses  $m_i$ , in which  $i = 1, \dots, N$ . The goal is to identify the time and length scales characterizing the dynamics of the multiple interacting nanoparticle/host fluid system. To understand the range of possible effects, first we limit the description of the nanoparticles to their location, ignoring their internal structure and orientation (however, see Section V).

In addition to the variables introduced above, let  $\vec{X}_k = \epsilon \vec{x}_k$ ,  $\vec{Y}_k = \epsilon^3 \vec{x}_k$ ,  $\vec{R}_i^{(1)} = \epsilon \vec{r}_i$ ,  $\vec{R}_i^{(3)} = \epsilon^3 \vec{r}_i$ , and  $t_n = \epsilon^n t$  for integer  $n$ .

Assume that the potential energy of the system can be written as

$$\begin{aligned} V(\vec{r}_1 \dots \vec{r}_N, \vec{x}_1 \dots \vec{x}_{N_B}) &= V_0(\vec{r}_1 \dots \vec{r}_N, \vec{x}_1 \dots \vec{x}_{N_B}) + \epsilon^2 V_{BB}^S \\ &(\vec{X}_1 \dots \vec{X}_{N_B}) + \epsilon^5 V_{BB}^L(\vec{R}_1^{(1)} \dots \vec{R}_N^{(1)}, \vec{X}_1 \dots \vec{X}_{N_B}) \end{aligned} \quad (\text{IV.1})$$

$$V_0 = V_h(\vec{r}_1 \dots \vec{r}_N) + \sum_{k=1}^{N_B} U_k^S(\vec{s}_{1k} \dots \vec{s}_{Nk})$$

$$V_{Bh}^L = \sum_{k=1}^{N_B} \sum_{i=1}^N U_{ik}^L(\vec{S}_{ik}) = \sum_{k=1}^{N_B} V_k^L(\vec{S}_{1k}, \dots, \vec{S}_{Nk}) \quad (\text{IV.2})$$

in which  $\vec{s}_{ik} = \vec{r}_i - \vec{x}_k$  and  $\vec{S}_{ik} = \vec{R}_i^{(1)} - \vec{X}_k$ . In this expression,  $V_h$  is the interaction of host particles in the absence of any nanoparticles,  $U_k^S$  is the strong, short-range nanoparticle–host interaction,  $U_{ik}^L$  is the weak, long-range nanoparticle–host interaction, and  $V_{BB}$  is a direct interaction between nanoparticles. In what follows, an FPC equation for a reduced probability density is constructed: it accounts for the fluctuating forces the host medium exerts on the nanoparticles that are taken to scale with a power of  $\epsilon$  reflecting nanoparticle size. The ansatz of eq IV.1 is only one of the possible scaling approaches. The idea that the direct inter-nanoparticle interaction scales as  $\epsilon^2$  is meant to imply that the strong attractive nanoparticle–host interaction forbids the nanoparticles from coming into direct contact. Other scalings must be used if this is not the case.

Once the physical picture has been set forth (i.e., the ansatz of eq IV.1), the formal unfolding/recomposition analysis of Section II can be carried out. The Hamiltonian describing the system is written as

$$H = H_0 + H_B \quad (\text{IV.3})$$

$$H_0 = \sum_{i=1}^N \frac{p_i^2}{2m_i} + V_0,$$

$$H_B = \sum_{k=1}^{N_B} \frac{P_k^2}{2M_k} + \epsilon^2 V_{BB}^S + \epsilon^5 V_{Bh}^L \quad (\text{IV.4})$$

With this, the  $(N + N_B)$ -body probability distribution  $\rho(\vec{p}_i, \vec{r}_i, \vec{R}_i^{(1)}, \vec{R}_i^{(3)}; i = 1, \dots, N; \vec{P}_k, \vec{x}_k, \vec{X}_k, \vec{Y}_k; k = 1, \dots, N_B; t_n, n \geq 0; \epsilon)$  evolves via

$$\sum_{n=0}^{\infty} \epsilon^n \left[ \frac{\partial}{\partial t_n} - \mathcal{L}_n \right] \rho = 0 \quad (\text{IV.5})$$

$$\mathcal{L}_0 = - \sum_{i=1}^N \left( \frac{\vec{p}_i}{m_i} \cdot \frac{\partial}{\partial \vec{r}_i} - \frac{\partial V_0}{\partial \vec{r}_i} \cdot \frac{\partial}{\partial \vec{p}_i} \right) \quad (\text{IV.6})$$

$$\mathcal{L}_2 = - \sum_{k=1}^{N_B} \left( \frac{\vec{P}_k}{M_k} \cdot \frac{\partial}{\partial \vec{X}_k} \right) \quad (\text{IV.7})$$

$$\mathcal{L}_n = - \sum_{i=1}^N \frac{\vec{p}_i}{m_i} \cdot \frac{\partial}{\partial \vec{R}_i^{(n)}}, \quad n = 1, 3 \quad (\text{IV.8})$$

$$\mathcal{L}_4 = - \sum_{k=1}^{N_B} \left( \frac{\vec{P}_k}{M_k} \cdot \frac{\partial}{\partial \vec{Y}_k} - \frac{\partial V_{BB}^S}{\partial \vec{X}_k} \cdot \frac{\partial}{\partial \vec{P}_k} - \frac{\partial V_k^L}{\partial \vec{X}_k} \cdot \frac{\partial}{\partial \vec{P}_k} \right) \quad (\text{IV.9})$$

$$\mathcal{L}_6 = \sum_{i=1}^N \sum_{k=1}^{N_B} \frac{\partial U_{ik}^L}{\partial \vec{R}_i^{(1)}} \cdot \frac{\partial}{\partial \vec{p}_i} \quad (\text{IV.10})$$

and  $\mathcal{L}_7$  is the same as  $\mathcal{L}_6$  with  $\partial/\partial \vec{R}_i^{(1)}$  and  $\partial/\partial \vec{p}_i$  replaced by  $\partial/\partial \vec{X}_k$  and  $\partial/\partial \vec{P}_k$ . Note that

$$\frac{\partial V_k^L}{\partial \vec{X}_k} = \epsilon^3 \sum_{i=1}^N \frac{\partial U_{ik}^L}{\partial \vec{X}_k} \quad (\text{IV.11})$$

is  $O(\epsilon^0)$  if within the range of  $U_k^L$  there are  $O(\epsilon^{-3})$  host particles. Finally,  $\mathcal{L}_5, \mathcal{L}_8, \mathcal{L}_9 \dots = 0$ .

To  $O(\epsilon^0)$ , the Liouville equation allows for the  $t_0$ -independent solution

$$\rho_0 = \frac{\exp(-\beta H_0) W}{Q} \quad (\text{IV.12})$$

in which  $W$  depends on the  $\vec{P}_k, \vec{x}_k, \vec{X}_k, \vec{Y}_k, \vec{R}_i^{(1)}, \vec{R}_i^{(3)}$ , and  $t_n$  for  $n > 0$ . The partition function  $Q$  is given by

$$Q = \int d^3 p_1 d^3 r_1 \dots d^3 p_N d^3 r_N \exp(-\beta H_0) \quad (\text{IV.13})$$

In principle,  $Q$  depends on all spatial variables except  $\vec{r}_i$ . With this partition function, associate a free energy  $\mathcal{F}$  via  $Q = \exp(-\beta \mathcal{F})$ . From Figure 5 it is seen that the forces induced on one nanoparticle by another depend on the geometry of the contact zone. Thus, the host average {i.e., as weighted by  $\exp[-\beta(H_0 - \mathcal{F})]$ } depends on the configuration  $\{\vec{x}_k; k = 1 \dots N_B\}$  of the nanoparticles, their contact areas (not addressed explicitly here), and possibly the  $\vec{X}_k$  and  $\vec{Y}_k$  in ways that depend on the scales of spatial variations in the host medium (i.e., due to phase interfaces).

A variety of scaling behaviors and associated thermodynamic forces may arise from the gradients of  $\mathcal{F}$  with respect to the nanoparticle configuration. For example, there could be a long-range ordering induced in the host medium by  $U_k^S$ . Thus, a nanoparticle pair could experience long-range thermodynamic forces induced by the host medium. Such effects depend on temperature and the mean density of the host (e.g., the proximity to the host medium critical point). For example, in a liquid/gas coexistence-supporting system, a cluster of nanoparticles could be bound in a host duplet, implying that  $\mathcal{F}$  could depend on the longer scale variables  $\vec{X}_k, \vec{Y}_k, \vec{R}_i^{(1)}$ , and  $\vec{R}_i^{(3)}$  in ways that depend on the size and shape of the host droplet and the width of the liquid/gas interface. Scaling of the multiple nanoparticle system is seen to allow one to capture both long- and short-range thermodynamic forces including more subtle effects not seen directly in the Hamiltonian (e.g., phase boundaries and droplets). The theory outline above may be closed in  $O(\epsilon^7)$  to yield a recomposed equation for the dependence of  $W$  on the  $\vec{P}_k, \vec{x}_k, \vec{X}_k, \vec{Y}_k, \vec{R}_i^{(1)}$ , and  $\vec{R}_i^{(3)}$ , and on the scaled times  $t_1, \dots, t_7$ . This formalism allows one to analyze a full range of phenomena, from the self-assembly of a virus to the dynamics of a deformable porous medium, that accounts for the fluctuating and coherent forces imposed by the host medium.

The viscous drag factors that arise depend on the configuration of the nanoparticle array. One expects that theories of virus self-assembly based on Langevin equations for the interacting units should contain such configuration-dependent drag coefficients. The interaction between units of a self-assembling structure, as mediated by a fluctuating host fluid, is taken into account by the present formalism.

## V. Conformational and Rotational Dynamics

A nanoparticle experiences continuous rotational and internal vibrational/conformational fluctuations. In this section it is shown that mesoscopic behavior emerges not only from both the large mass and the size of a nanoparticle, but also from the

collective behavior of a large number of its constituent atoms or molecules bound as a deformable structure (e.g., a viral envelope).

Consider a nanoparticle made of  $N^*$  particles, labeled  $j = 1, \dots, N^*$ , immersed in a host medium of  $N$  particles, labeled  $i = 1, \dots, N$ . The center of mass  $\vec{r}^{\text{com}}$  of the nanoparticle is given by

$$\vec{r}^{\text{com}} = \frac{1}{M} \sum_{j=1}^{N^*} M_j \vec{r}_j^* \quad (\text{V.1})$$

in which  $\vec{r}_j^*$  is the location of particle  $j$  in the nanoparticle, and  $M_j$  is its mass ( $M = M_1 + \dots + M_{N^*}$ ). Define  $N^*$  displacements via  $\vec{\sigma}_j = \vec{r}_j^* - \vec{r}^{\text{com}}$ . In analogy to the scaling ansatz of Section III, assume that  $M = m/\epsilon^2$  for a typical mass  $m$  of a host particle. With Jaqaman and Ortoleva<sup>12</sup> it is convenient to introduce a set of collective coordinates  $\Gamma_1, \dots, \Gamma_{3N^*-3}$  such that

$$\vec{\sigma}_j = \sum_{n=1}^{3N^*-3} \Gamma_n \vec{f}_n(\vec{\sigma}_j^0) \quad (\text{V.2})$$

in which  $\vec{\sigma}_j^0$  is a reference configuration, and  $\vec{f}_n$  is a basis function. With these coordinates and their time derivatives  $\dot{\Gamma}_n$ , one may rewrite the Liouville equation. The advantage is that one can choose the  $\vec{f}_n$  so that a relatively small subset of the  $\Gamma_n$  captures the slow dynamics of the nanostructure, and thereby one may carry out a multiple scale analysis involving the dynamics of the slow internal modes of the nanoparticle coupled to the Brownian motion of the center of mass and the host medium.

The amplitudes of the modes defined in eq V.2 provide a starting point for a multiple scale treatment of the deforming, rotating structure. Assuming that the  $\Gamma_n$  of eq V.2 can be divided into fast and slow groups, the lowest order solution of the Liouville equation in the multiple scale formalism involves an equilibrium factor that consists of the potential of the host particles and the nanoparticle–host interaction. As the latter involves the slow as well as the fast mode amplitudes, there is a nontrivial coupling between the slow modes of the nanoparticle and the host medium. The result is a recomposed equation for the probability  $W$  of the long-time behavior of the coupled slow migration, rotation, and deformation of the nanoparticle. This equation involves thermodynamic and drag forces for the dynamics of migration, rotation, and slow deformation modes. All these effects depend on partition functions and fluctuating force correlation functions from the host and internal mode dynamics.

For a rigid structure, only the rotational modes of eq V.2 are needed, that is,

$$\vec{\sigma}_j = \vec{\Gamma} \vec{\sigma}_j^0 \quad (\text{V.3})$$

for a  $3 \times 3$  rotation matrix  $\vec{\Gamma}$  that can be expressed in terms of three Euler angles. With this, one can recast the Liouville equation in terms of the Euler angles and their time derivatives, the position and momentum of the center of mass, and the state of the  $N$  host particles. As with the large BP asymptotics of previous sections, one may analyze large moment-of-inertia asymptotics (and similarly for slow bending, dilatation, torsion, or other large-scale, slow modes of a nonrigid structure). As the frequencies of these modes can imply a large range of time scales, a variety of scaling behaviors and asymptotic analyses can emerge.

To illustrate the range of possibilities, reconsider the scaling of the net force acting on the center of mass. This scaling depends on the surface area of the nanostructure. Let  $\lambda$  be the longest length characterizing the size of the nanostructure. If the structure is spherical and compact (e.g., not an empty shell), then  $\lambda^3$  scales as the total mass  $M$  and, hence, as  $\epsilon^{-2}$  so that surface area scales as  $\epsilon^{-4/3}$ . If the nanostructure is a hollow sphere, circular disk, or a rod, then surface area scales as  $\epsilon^{-2}$ . With this, it is seen that the statistics of the random force scales with a power of  $\epsilon$  that depends on the geometry of the structure, which is also the case for the moment of inertia.

A distinct class of considerations arises when the internal dynamics of the nanostructure is considered. Although the overall migration and rotation of a nanostructure can be slow, its internal dynamics can be considered on the same level as that of the host medium. Hence, the lowest order solution of the Liouville equation is that which is for the nanostructure at a given position and orientation, but, like the host medium, all other internal degrees of freedom are at equilibrium. Thus, one may investigate a variety of distinct scalings for the fluctuating dynamics of a nanostructure.

## VI. Further Developments

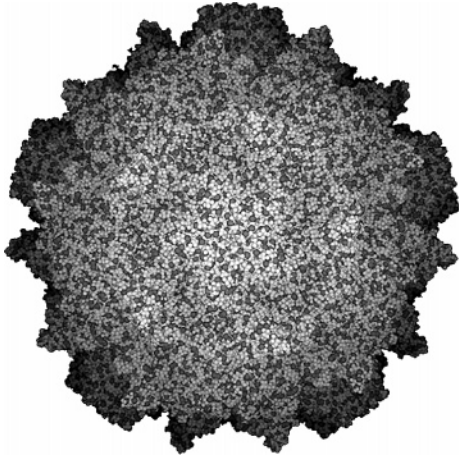
A scaling approach for deriving FPC-type equations has been presented. These equations yield the dynamics of the slow variable reduced probability density. Computer molecular dynamics and Monte Carlo methods can be used to provide values of generalized drag coefficients and thermodynamic forces. In this way mesoscopic dynamics is derived from an atomic force field to arrive at a parameter-free theory. The FPC equations obtained capture the richness of mesoscopic phenomena, which, by definition, follow from the interplay of deterministic and stochastic behaviors.

Practical considerations limit the direct numerical solution of FPC equations. However, such equations are equivalent to Langevin equations<sup>2</sup>. Thus, a promising approach is to set forth the Langevin equation corresponding to a given FPC equation and then proceed in a Monte Carlo fashion.

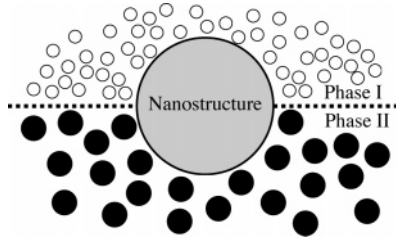
The interaction of a nanoparticle with a nonuniform host medium is accounted for in the present formalism. Applications include the traversal of the outer cell membrane by a virus and the dynamics of nanoparticles at oil/water or other phase boundaries, which are common features of natural and engineered systems. The transport of gold colloids to form gold deposits or the process of mineral particle transport during petroleum production are other examples. For these systems, the partition function of Sections III–V depends on the position and orientation of the nanoparticles. The partition function is that for the host medium equilibrated with the instantaneous nanoparticle configuration. It can be written as  $\exp(-\beta\mathcal{F})$  in which the free energy  $\mathcal{F}$  depends on the configuration of the nanoparticles. In this case, the nanoparticles are driven by the gradient of  $\mathcal{F}$  with respect to the state of the nanoparticles. This thermodynamic force appears in the FPC equation for the nanoparticles (e.g., eq III.13).

Estimates of the dependence of  $\mathcal{F}$  on nanoparticle configuration can be obtained. Consider the situation of Figure 7 in which a structure is passing between two phases (e.g., a virus entering a host cell membrane). Let  $\mathcal{A}^I$  and  $\mathcal{A}^{II}$  be the surface areas of the particle exposed to Phases I and II, respectively. Let  $\sigma^I$  and  $\sigma^{II}$  be the interaction free energies (energy/area of the nanoparticle/medium contact). If these surface energies are the same for all points on the surface of the nanoparticle, and  $\mathcal{F}^I$  is the free energy of the system when the particle is





**Figure 6.** Poliovirus proteins self-assemble into a capsid. The shape and fluctuations of the proteins mediate their hierarchical self-assembly into protomers, then into pentamers, and finally into a capsid. The stability of the capsid depends on the composition and temperature of the host fluid as well as the structure of the proteins.



**Figure 7.** A nanoparticle shown passing from Phase I to Phase II because of the difference in its interaction with the light and dark host particles. The dynamics of the structure is driven by both random fluctuating forces and the thermodynamic effect of the fraction of the nanoparticle's surface exposed to Phase I vs Phase II.

completely immersed in Phase I, far from the interface, then

$$\mathcal{F}(\vec{R}, \underline{\omega}) = \mathcal{F}^I - (\mathcal{A}^I + \mathcal{A}^{II})\sigma^I + \mathcal{A}^I \sigma^I + \mathcal{A}^{II} \sigma^{II} \quad (\text{VI.1})$$

in which the areas depend on the nanoparticle position  $\vec{R}$  and the orientation (specified by Euler angles  $\underline{\omega}$ ). In this manner one may formulate the FPC equation to simulate a virus or other particle as it interacts with an interface. This provides a guideline for developing the more rigorous approaches of Sections III–V.

An outstanding challenge is continuous scaling. For example, as a nanostructure propagates through a host medium it may interact with the phonons or varieties the medium supports. These disturbances have a continuous range of characteristic times that span many orders of magnitude. Thus, there may not be a well-defined separation of scales or a natural small parameter. However, dimensional analysis suggests that the size of a nanoparticle divided by its speed is a characteristic time that is likely selected from the spectrum of time scales for the composite host/nanoparticle system. Other characteristic times can be constructed from particle size and host medium viscosity. Thus, there may be ways to select relevant subsets of host modes from the continuum so that continuously scaled systems could be treated rigorously by a multiscale approach. The co-particle model of Figure 3 could be a basis for an approach to vortices (Figure 2) and phonons. In the appendix it is shown how the introduction of discrete host modes results in a set of coupled FPC equations, one for each eigenfunction of the host medium Liouville operator. Each of the probability functions that arise

in this theory describes the evolution of the nanoparticles as influenced by a given host mode.

In conclusion, rigorous approaches to the dynamics of nanosystems can be developed for obtaining parameter-free or few-parameter models. Therefore, predictive modeling of nanosystems can be achieved.

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## Appendix: Slow Host and Intrastructural Modes

Slow modes in the composite nanoparticle/host medium system warrant care in a multiple scale analysis. Neglect of the effects of these modes results in the omission of host vortex phenomena as shown in Figure 2 or the slow compressional, bending, twisting, or other large-scale dynamics of the nanoparticles. A formal analysis, based on the spectrum of the Liouville operator, is now set forth. In the main body of this work, it was assumed that the smallness of the host particles relative to the nanoparticle implied that the host dynamics is fast relative to that of the nanostructure. However, as suggested in Figure 2, the motion of a nanoparticle can create long-lived, large spatial scale hydrodynamic disturbances in the host. This implies that the Liouville operator  $\mathcal{L}_h$  for the nanostructure-free host medium has small eigenvalues. This causes a breakdown of the multiscale development set forth in Sections III–V. The origin of this breakdown is a feedback wherein the large-scale motion of the nanoparticle induces hydrodynamic motion in the host which, in turn, pushes on the nanoparticle. Because of the large number of host particles involved, the induced host medium disturbance has a large cumulative mass, and the time scale of the host hydrodynamic disturbances can be comparable to that of the motion and deformation of the nanoparticle.

If the nanoparticle is imparted a kinetic energy on the order of  $k_B T$ , then its velocity (and, for the phenomena of interest, the velocity induced in the disturbed host medium) is of  $O(\epsilon)$  when the nanoparticle has a mass of  $O(\epsilon^{-2})$ . Thus, the term  $m_i^{-1} \vec{p}_i \cdot \partial/\partial \vec{r}_i$  in  $\mathcal{L}_h$  consists of a factor,  $O(\epsilon)$ , from  $\vec{p}_i/m_i$  divided by a length that is roughly the size of the nanoparticle [e.g.,  $O(\epsilon^{-1})$ ], yielding an effective  $O(\epsilon^2)$  contribution to  $\mathcal{L}_h$ . This suggests that the motion of the nanoparticle excites modes of  $\mathcal{L}_h$  with eigenvalues of  $O(\epsilon^2)$ . An alternative argument is that a vortex acts as a correlate particle (Figure 3): like the nanoparticle, the correlate has a velocity of  $O(\epsilon)$  and it operates on the lengthscale of the size of the nanoparticle [e.g.,  $O(\epsilon^{-1})$ ]. Assuming that these modes contribute a term in  $\mathcal{L}_h$  that is of the magnitude of an effective velocity [here  $O(\epsilon)$ ] divided by a characteristic length [here  $O(\epsilon^{-1})$ ], then such a term is  $O(\epsilon^2)$ . In summary, it is expected that the relevant eigenvalues of the interacting nanoparticle/host system are of  $O(\epsilon^2)$ . In the above arguments we have assumed that the length scale of the disturbance in the host fluid is the same as the size of the nanoparticle. In reality it can be quite different, being related to the velocity of the particle and the viscosity of the host fluid.

Let  $|n\rangle$  be the  $n$ th eigenfunction of  $\mathcal{L}_h$  with eigenvalue  $\lambda_n$ :

$$\mathcal{L}_h |n\rangle = \lambda_n |n\rangle \quad (1)$$

In what follows, it is assumed that the eigenfunctions are



orthonormal ( $\langle n' | n \rangle = \delta_{nn'}$ ) and that the spectrum of  $\mathcal{L}_h$  is discrete. There is a wide range of eigenvalues: some correspond to slow conservation-derived modes ( $\lambda_n$  small); others are fast, localized, or particle-like modes ( $\lambda_n$  large). On the basis of the above arguments, assume that the modes that are relevant to the phenomena of interest can be divided into two well-defined groups:

$$\lambda_n = \begin{cases} \lambda_n^*, & \text{fast modes} \\ \lambda_n^* \epsilon^2, & \text{slow modes} \end{cases} \quad (2)$$

for  $\lambda_n^*$  constant as  $\epsilon \rightarrow 0$ . With this,  $\mathcal{L}_h$  may be divided into fast and slow parts via a spectral decomposition. The introduction of projection operators  $|n\rangle\langle n|$  yields

$$\begin{aligned} \mathcal{L}_h &= \mathcal{L}_f + \epsilon^2 \mathcal{L}_s \\ \mathcal{L}_s &= \sum_n^{(s)} \lambda_n^* |n\rangle\langle n| \end{aligned} \quad (3)$$

For  $\mathcal{L}_s$ , the sum is restricted to modes with eigenvalues that scale as  $\epsilon^2$ , and similarly  $\mathcal{L}_f$ .

With the above equation and the formalism of Section II, one may reexamine Brownian motion by now allowing for the effects of slow behavior induced in the host medium.

With the above equation, the Liouville equation for the composite nanoparticle/host medium system is assumed to be

$$\frac{\partial \rho}{\partial t} = [\mathcal{L}_f + \epsilon \mathcal{L}_1 + \epsilon^2 (\mathcal{L}_s + \mathcal{L}_2)] \rho \quad (4)$$

Unlike in Section III,  $\mathcal{L}_h$  now has an  $O(\epsilon^2)$  contribution  $\mathcal{L}_s$ , whereas  $\mathcal{L}_2$  is from the motion of the nanoparticle itself. An expansion of  $\rho$  in  $\epsilon$  implies that if  $H_f$  is the Hamiltonian generating  $\mathcal{L}_f$ , then to  $O(\epsilon^0)$

$$\rho_0 = \frac{\exp(-\beta H_f)}{Q} \sum_n^{(s)} W_n(\vec{P}, \vec{X}, t_1, t_2) |n\rangle \quad (5)$$

for a set of functions  $W_n$  that depend on the slow times  $t_1 = \epsilon t$  and  $t_2 = \epsilon^2 t$ , the scaled nanoparticle coordinate, and momentum  $\vec{P}$ . The higher order problems are similar to those discussed in Section III. Using a solubility condition, one finds that the  $t_1$ -dependence of the  $W_n$  is generated by

$$\frac{\partial W_n}{\partial t_1} = \sum_{n'} \mathcal{D}_{nn'}^{(1)} W_{n'} \quad (6)$$

for operators  $\mathcal{D}_{nn'}^{(1)}$  related to  $\mathcal{L}_f$ . To  $O(\epsilon^2)$  one has

$$\left( \mathcal{L}_f - \frac{\partial}{\partial t_0} \right) \rho_2 = \frac{\partial \rho_0}{\partial t_2} + \frac{\partial \rho_1}{\partial t_1} - \mathcal{L}_1 \rho_1 - (\mathcal{L}_2 + \mathcal{L}_s) \rho_0 \quad (7)$$

From this equation one may extract a set of coupled linear equations for the  $t_2$ -scale evolution of the  $W_n$ . The resulting equations for  $\partial W_n / \partial t_1$  and  $\partial W_n / \partial t_2$  can be recomposed into a single, long-time equation as shown in Section II. This formal construction of the coupled nanoparticle/host medium equations suggests the scenarios by which the host medium hydrodynamic modes can be excited, allowing for a wide range of behaviors for nanoparticle motion.

The above results do not make the detailed connection between the vortices and the  $W_n$ . This would follow from a detailed examination of the properties of the eigenfunctions  $|n\rangle$  that correspond to hydrodynamic behavior.

The lowest order probability (5) accounts for the slow nanoparticle/hydrodynamic behavior in terms of a joint probability that is expressed as a sum of slow modes  $|n\rangle$ . This suggests a phenomenological approach wherein the nanoparticle/host system is modeled via a Langevin equation for the nanoparticle coupled to the host fluid via a mesoscopic fluid mechanical model with fluctuating forces and fluxes, and is subjected to boundary conditions at the surface of the nanoparticle or body forces within the host continuum imposed by the nanoparticle. However, the results obtained above show that one must cast the problem in terms of a joint coarse-grained probability (i.e., the sum of the  $W_n |n\rangle$  terms) and not as a product of  $W$  and host hydrodynamic factors.

## References and Notes

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