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Multiscale derivation of an augmented Smoluchowski equation

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ABSTRACT

Smoluchowski and Fokker–Planck equations for the stochastic dynamics of order parameters have been derived previously. The question of the validity of the truncated perturbation series and the initial data for which these equations exist remains unexplored. To address these questions, we take a simple example, a nanoparticle in a host medium. A perturbation parameter ε, the ratio of the mass of a typical atom to that of the nanoparticle, is introduced and the Liouville equation is solved to $O\left(\varepsilon^2\right)$. Via a general kinematic equation for the reduced probability W of the location of the center-of-mass of the nanoparticle, the $O\left(\varepsilon^2\right)$ solution of the Liouville equation yields an equation for W to $O\left(\varepsilon^3\right)$. An augmented Smoluchowski equation for W is obtained from the $O\left(\varepsilon^2\right)$ analysis of the Liouville equation for a particular class of initial data. However, for a less restricted assumption, analysis of the Liouville equation to higher order is required to obtain closure.

1. Introduction

Smoluchowski and Fokker–Planck equations for the stochastic dynamics of slow variables have been derived from the Liouville equation via several multiscale approaches [1–13]. These studies introduce a perturbation parameter ε such as a characteristic mass, length, or time ratio and then derive the aforementioned stochastic equations via an expansion in ε. In general, the stochastic equations emerge in the $O\left(\varepsilon^2\right)$ analysis of the Liouville equation used to construct the N-atom probability density [1–11].

In the course of re-examining this work, several questions emerge. The Fokker–Planck and Smoluchowski equations yield the evolution of the reduced probability density W for a set of slow variables (order parameters). These variables evolve on timescales much longer than that of individual atomic vibrations and collisions. Examples of these slow variables include the center-of-mass (CM) and overall structure of a nanoparticle. The equations for W of the aforementioned types are closed in W and only involve evolution on long timescales. It was shown [12,13] on general grounds from the Liouville equation that W is conserved (i.e. obeys a conservation equation), and to $O\left(\varepsilon^2\right)$ is closed given restrictions on the initial data for the N-atom probability density to first order. In addition, the resultant $O\left(\varepsilon^2\right)$ equation was derived from the $O\left(\varepsilon\right)$ analysis of the Liouville equation and the general conservation law for W. Questions arise regarding (1) whether there is more general initial data for which the resulting stochastic equation is closed in W, (2) whether it would still be closed if the analysis is carried out to higher order and what are the associated necessary conditions on the initial data, and (3) whether a perturbation scheme in ε would breakdown in higher order.

The specific aim of this study is to conduct a multiscale analysis of the Liouville equation as represented earlier [12,13] and continue the analysis up to $O\left(\varepsilon^3\right)$ truncation of the equation for W. We also present a more general set of solutions/choices of the initial data required to close the resulting stochastic equation for W for both the $O\left(\varepsilon^2\right)$ and $O\left(\varepsilon^3\right)$ truncations.

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2. Formulation

Our demonstration system is a single nanoparticle in a host medium. Key variables used are as follows. The CM of the nanoparticle, $\vec{\Phi}$, is defined as

$$\vec{\Phi} = \sum_{i=1}^{N} \frac{m_i}{M} \vec{r}_i \Theta_i, \tag{2.1}$$

where m_i is the mass of atom i, N is the total number of atoms in the system (nanoparticle plus host medium), $\vec{r}_i$ is the position of atom i, $M = \sum_{i=1}^{N} m_i \Theta_i$ is the total mass of the nanoparticle, and Θ_i is 1 when i is in the nanoparticle and 0 otherwise. The total momentum $\vec{\Pi}$ of the nanoparticle is given by

$$\vec{\Pi} = \sum_{i=1}^{N} \vec{p}_i \Theta_i, \tag{2.2}$$

where $\vec{p}_i$ is the momentum of atom i. Here, $\vec{\Pi}$ is not assumed to be slowly varying and is thus not considered an order parameter (see Refs. [12,13] for other cases and further discussion). Define ε via

$$\varepsilon = \frac{m}{M} \ll 1, \tag{2.3}$$

where m is the mass of a typical atom in the nanoparticle.

The state of the N-atom system is denoted $\Gamma = \left\{\vec{r}_1, \vec{p}_1, \ldots \vec{r}_N, \vec{p}_N\right\}$. The probability density $\rho\left(\Gamma, t\right)$ at time t satisfies the Liouville equation:

$$\frac{\partial \rho}{\partial t} = -\sum_{i=1}^{N} \left(\frac{\vec{p}_i}{m_i} \cdot \frac{\partial \rho}{\partial \vec{p}_i} + \vec{F}_i \cdot \frac{\partial \rho}{\partial \vec{p}_i} \right) \equiv \mathcal{L}\rho, \tag{2.4}$$

where $\vec{F}_i$ is the force on atom i and $\mathcal{L}$ is the Liouville operator.

The reduced probability density W is defined via

$$W\left(\vec{\varphi}, t\right) = \int \mathrm{d}\Gamma^* \delta\left(\vec{\varphi} - \vec{\Phi}\left(\Gamma^*\right)\right) \rho\left(\Gamma^*, t\right), \tag{2.5}$$

where $\vec{\varphi}$ is a value of the CM of interest.

Using Eqs. (2.4) and (2.5), and proceeding as in Pankavich et al. [12,13], one obtains the conservation equation

$$\frac{\partial W}{\partial t} = -\varepsilon \frac{\partial}{\partial \vec{\Phi}} \cdot \left(\int \mathrm{d}\Gamma^* \delta\left(\vec{\Phi} - \vec{\Phi}^*\right) \rho \frac{\vec{\Pi}^*}{m} \right), \tag{2.6}$$

where the superscript * on $\vec{\Phi}$ and $\vec{\Pi}$ indicates $\vec{\Phi}\left(\Gamma^*\right)$ and $\vec{\Pi}\left(\Gamma^*\right)$. Following arguments presented earlier [8–13], the N-atom probability density is expressed as a function of both Γ and $\vec{\Phi}$. In other words, $\rho\left(\Gamma, \vec{\Phi}, t\right)$ depends on the set of atomic positions and momenta, both directly and indirectly through $\vec{\Phi}$. With this and the chain rule, one finds

$$\frac{\partial \rho}{\partial t} = \left(\mathcal{L}_0 + \varepsilon \mathcal{L}_1\right) \rho \tag{2.7}$$

$$\mathcal{L}_0 = -\sum_{i=1}^{N} \left(\frac{\vec{p}_i}{m_i} \cdot \frac{\partial}{\partial \vec{r}_i} + \vec{F}_i \cdot \frac{\partial}{\partial \vec{p}_i} \right) \tag{2.8}$$

$$\mathcal{L}_1 = -\frac{\vec{\Pi}}{m} \cdot \frac{\partial}{\partial \vec{\Phi}}. \tag{2.9}$$

Note that derivatives with respect to Γ in $\mathcal{L}_0$ are at constant $\vec{\Phi}$, while those with respect to $\vec{\Phi}$ in $\mathcal{L}_1$ are at constant Γ. The next step in the multiscale analysis is to construct a perturbative solution of the Liouville equation (2.4) such that

$$\rho = \sum_{n=0}^{\infty} \varepsilon^n \rho_n. \tag{2.10}$$

A set of scaled times, $t_n = \varepsilon^n t$ $(n = 0, 1, \ldots)$, is introduced to capture the various ways in which ρ depends on time; i.e. $\rho\left(\Gamma, \vec{\Phi}, t_0, \underline{t}\right)$, where $\underline{t} = \{t_1, t_2, \ldots\}$ represents the set of long-time variables. With this, using the chain rule, and proceeding as earlier [12,13], one finds

$$\Lambda_0 \rho_0 = 0 \tag{2.11}$$

and for $n > 0$,

$$\Lambda_0 \rho_n = -\sum_{i=1}^{n} \Lambda_i \rho_{n-i} \tag{2.12}$$

where $\Lambda_n = \frac{\partial}{\partial t_n} - \mathcal{L}_n$ and $\mathcal{L}_n = 0$ for $n > 1$.

While Pankavich et al. [13] explore a variety of ensembles, we choose here the case of a closed, isothermal system. This leads to the following solution for the lowest order probability distribution:

$$\rho_0 = \frac{e^{-\beta H} W_0\left(\vec{\Phi}, \underline{t}\right)}{Q} \equiv \hat{\rho} W_0 \tag{2.13}$$

where $Q\left(\beta, \vec{\Phi}\right) = \int d\Gamma^* \delta\left(\vec{\Phi} - \vec{\Phi}^*\right) e^{-\beta H^*}$, $H(\Gamma) = \sum_{i=1}^{N} \frac{p_i^2}{2m_i} + V(\Gamma_r)$, $\Gamma_r = \left\{\vec{r}_1, \vec{r}_2, \ldots \vec{r}_N\right\}$, and W_0 is the lowest order reduced probability density $\left(W = \sum_{n=0}^{\infty} \varepsilon^n W_n\right)$.

To $O(\varepsilon)$, Eq. (2.12) admits the solution

$$\rho_1 = e^{\mathcal{L}_0 t_0} A_1 - \int_0^{t_0} dt_0' e^{\mathcal{L}_0 (t_0 - t_0')} \Lambda_1 \rho_0 \tag{2.14}$$

where $A_n\left(\Gamma, \vec{\Phi}, \underline{t}\right)$ is the nth order initial condition $(n = 1, 2, \ldots)$.

Inserting (2.9) and (2.13) in (2.14), using the Gibbs hypothesis, and removing the secular behavior in ρ_1, one finds

$$\frac{\partial W_0}{\partial t_1} = 0. \tag{2.15}$$

Thus,

$$\rho_1 = A_1 + \hat{\rho}\left(\beta \vec{f}^{th} W_0 - \frac{\partial W_0}{\partial \vec{\Phi}}\right) \cdot \int_{-t_0}^{0} ds e^{-\mathcal{L}_0 s} \frac{\vec{\Pi}}{m}, \tag{2.16}$$

where $s = t_0' - t_0$. As $Q = e^{-\beta F}$ for free energy F, one finds

$$\vec{f}^{th} = -\partial F / \partial \vec{\Phi}. \tag{2.17}$$

To obtain Eq. (2.16), the assumption that the first order initial data resides in the nullspace of $\mathcal{L}_0$ (i.e. $\mathcal{L}_0 A_1 = 0$) was used. In what follows, we extend this assumption to include all orders, i.e. for $n > 0$

$$\mathcal{L}_0 A_n = 0, \tag{2.18}$$

and explore the implications for an augmented Smoluchowski equation. To stop the analysis at this point would yield the Smoluchowski equation as earlier [12,13]. In the next section, we continue the analysis to higher orders and explore the implication of the theory, especially on the choice of the initial statistical state of the system.

3. Initial data, closure, and the augmented Smoluchowski equation

On physical grounds, we expect that not all initial data should lead to the Smoluchowski equation. In this section, we investigate the types of initial data that are consistent with the Smoluchowski equation and explore the implications of multiscale analysis for generalized equations when the perturbation series solution of the Liouville equation is carried out to $O(\varepsilon^2)$. The result is a generalized equation for the reduced probability valid to $O(\varepsilon^3)$. Pankavich et al. [12] showed that up to $O(\varepsilon^2)$ the resultant stochastic equation (of the Smoluchowski or Fokker–Planck type) is closed if $A_1 = 0$. This implies the first order correction to the reduced probability density W_1 is zero, since it is related to A_1 via

$$W_1 = \int d\Gamma^* \delta\left(\vec{\Phi} - \vec{\Phi}^*\right) A_1\left(\Gamma^*, \vec{\Phi}^*, \underline{t}\right). \tag{3.1}$$

In what follows, we consider a more general choice for A_1 that is consistent with (3.1), i.e.

$$A_1 = \hat{\rho} W_1. \tag{3.2}$$

To $O(\varepsilon^2)$, one finds

$$\Lambda_0 \rho_2 = -\left(\Lambda_1 \rho_1 + \Lambda_2 \rho_0\right). \tag{3.3}$$

This admits the solution

$$\rho_2 = A_2 - \int_{-t_0}^{0} ds e^{-\mathcal{L}_0 s} \left\{\frac{\partial \rho_0}{\partial t_2} + \frac{\partial \rho_1}{\partial t_1} + \frac{\vec{\Pi}}{m} \cdot \frac{\partial \rho_1}{\partial \vec{\Phi}}\right\}, \tag{3.4}$$

recalling that A_2 is taken to be in the nullspace of $\mathcal{L}_0$.

Inserting (2.13) and (2.16) in (3.4), one obtains

$$\rho_2 = A_2 - \int_{-t_0}^{0} \mathrm{d}s\mathrm{e}^{-\mathcal{L}_0 s}\left\{\hat{\rho}\frac{\partial W_0}{\partial t_2} + \frac{\partial A_1}{\partial t_1} + \hat{\rho}\left[\left(\beta\vec{f}^{th} - \frac{\partial}{\partial\vec{\Phi}}\right)\frac{\partial W_0}{\partial t_1}\right]\cdot\left(\int_{-(s+t_0)}^{0}\mathrm{d}s'\mathrm{e}^{-\mathcal{L}_0 s'}\frac{\vec{\Pi}}{m}\right)\right.$$
$$\left. + \frac{\vec{\Pi}}{m}\cdot\frac{\partial A_1}{\partial\vec{\Phi}} + \frac{\vec{\Pi}}{m}\cdot\frac{\partial}{\partial\vec{\Phi}}\left[\hat{\rho}\left(\beta\vec{f}^{th}W_0 - \frac{\partial W_0}{\partial\vec{\Phi}}\right)\cdot\left(\int_{-(s+t_0)}^{0}\mathrm{d}s'\mathrm{e}^{-\mathcal{L}_0 s'}\frac{\vec{\Pi}}{m}\right)\right]\right\}. \tag{3.5}$$

Using (2.15) and (3.2), and rearranging terms, (3.5) becomes

$$\rho_2 = A_2 - t_0\hat{\rho}\left(\frac{\partial W_0}{\partial t_2} + \frac{\partial W_1}{\partial t_1}\right) - \hat{\rho}\left(\frac{\partial W_1}{\partial\vec{\Phi}} - \beta\vec{f}^{th}W_1\right)\cdot\left(\int_{-t_0}^{0}\mathrm{d}s\mathrm{e}^{-\mathcal{L}_0 s}\frac{\vec{\Pi}}{m}\right)$$
$$+ \frac{\hat{\rho}}{m^2}\left(\frac{\partial}{\partial\vec{\Phi}} - \beta\vec{f}^{th}\right)\left(\frac{\partial}{\partial\vec{\Phi}} - \beta\vec{f}^{th}\right)W_0\left(\int_{-t_0}^{0}\mathrm{d}s\mathrm{e}^{-\mathcal{L}_0 s}\vec{\Pi}\int_{-(s+t_0)}^{0}\mathrm{d}s'\mathrm{e}^{-\mathcal{L}_0 s'}\vec{\Pi}\right)$$
$$+ \frac{\hat{\rho}}{m^2}\left(\frac{\partial W_0}{\partial\vec{\Phi}} - \beta\vec{f}^{th}W_0\right)\cdot\left\{\int_{-t_0}^{0}\mathrm{d}s\mathrm{e}^{-\mathcal{L}_0 s}\vec{\Pi}\cdot\frac{\partial}{\partial\vec{\Phi}}\left(\int_{-(s+t_0)}^{0}\mathrm{d}s'\mathrm{e}^{-\mathcal{L}_0 s'}\vec{\Pi}\right)\right\}. \tag{3.6}$$

Multiplying both sides of (3.6), evaluated at Γ^*, by Δ (where $\Delta = \delta\left(\vec{\Phi} - \vec{\Phi}^*\right)$) and integrating over Γ^*, one obtains

$$\int \mathrm{d}\Gamma^*\Delta\rho_2 = \int \mathrm{d}\Gamma^*\Delta A_2 - t_0\int \mathrm{d}\Gamma^*\delta\left(\vec{\Phi} - \vec{\Phi}^*\right)\hat{\rho}\left(\frac{\partial W_0}{\partial t_2} + \frac{\partial W_1}{\partial t_1}\right)$$
$$- \frac{1}{m}\int \mathrm{d}\Gamma^*\Delta\hat{\rho}\left(\frac{\partial W_1}{\partial\vec{\Phi}} - \beta\vec{f}^{th}W_1\right)\cdot\left(\int_{-t_0}^{0}\mathrm{d}s\mathrm{e}^{-\mathcal{L}_0 s}\vec{\Pi}^*\right)$$
$$+ \frac{1}{m^2}\int \mathrm{d}\Gamma^*\Delta\hat{\rho}\left(\frac{\partial}{\partial\vec{\Phi}} - \beta\vec{f}^{th}\right)\left(\frac{\partial}{\partial\vec{\Phi}} - \beta\vec{f}^{th}\right)W_0\left(\int_{-t_0}^{0}\mathrm{d}s\mathrm{e}^{-\mathcal{L}_0 s}\vec{\Pi}^*\int_{-(s+t_0)}^{0}\mathrm{d}s'\mathrm{e}^{-\mathcal{L}_0 s'}\vec{\Pi}^*\right)$$
$$+ \frac{1}{m^2}\int \mathrm{d}\Gamma^*\Delta\hat{\rho}\left(\frac{\partial W_0}{\partial\vec{\Phi}} - \beta\vec{f}^{th}W_0\right)\cdot\left\{\int_{-t_0}^{0}\mathrm{d}s\mathrm{e}^{-\mathcal{L}_0 s}\vec{\Pi}^*\cdot\frac{\partial}{\partial\vec{\Phi}}\left(\int_{-(s+t_0)}^{0}\mathrm{d}s'\mathrm{e}^{-\mathcal{L}_0 s'}\vec{\Pi}^*\right)\right\}. \tag{3.7}$$

We remove secular behavior in ρ_2, i.e. we impose the condition that ρ_2 must be bounded as $t_0 \to \infty$. This implies

$$\lim_{t_0\to\infty}\frac{1}{t_0}\int \mathrm{d}\Gamma^*\delta\left(\vec{\Phi} - \vec{\Phi}^*\right)\rho_2 = 0. \tag{3.8}$$

With this, using (3.8), and applying $\frac{1}{t_0}\lim_{t_0\to\infty}$ to both sides of (3.7) yields

$$\left(\frac{\partial W_0}{\partial t_2} + \frac{\partial W_1}{\partial t_1}\right) = \frac{\gamma^{(2)}_{\alpha\alpha'}}{m^2}\left(\frac{\partial}{\partial\Phi_\alpha} - \beta f^{th}_\alpha\right)\left(\frac{\partial}{\partial\Phi_{\alpha'}} - \beta f^{th}_{\alpha'}\right)W_0 + \frac{\lambda^{(2)}_{\alpha\alpha'}}{m^2}\left(\frac{\partial}{\partial\Phi_{\alpha'}} - \beta f^{th}_{\alpha'}\right)W_0, \tag{3.9}$$

where the summation over repeated indices is implicit, following the Einstein convention, and

$$\gamma^{(2)}_{\alpha\alpha'} = \left\langle \Pi_\alpha\int_{-t}^{0}\mathrm{d}s\mathrm{e}^{-\mathcal{L}_0 s}\Pi_{\alpha'}\right\rangle \tag{3.10}$$

$$\lambda^{(2)}_{\alpha\alpha'} = \left\langle \Pi_\alpha\int_{-t}^{0}\mathrm{d}s\frac{\partial}{\partial\Phi_\alpha}\left(\mathrm{e}^{-\mathcal{L}_0 s}\Pi_{\alpha'}\right)\right\rangle, \tag{3.11}$$

where

$$\langle Y\rangle = \int \mathrm{d}\Gamma^*\delta\left(\vec{\Phi} - \vec{\Phi}^*\right)\hat{\rho}Y \tag{3.12}$$

for any dynamical variable $Y\ (\Gamma)$. Also, recall that the statistical mechanical postulate "the longtime and ensemble averages for equilibrium systems are equal" implies

$$\langle Y\rangle \equiv \int \mathrm{d}\Gamma^*\delta\left(\vec{\Phi} - \vec{\Phi}^*\right)\hat{\rho}Y\left(\Gamma^*\right) = Y^{th} = \lim_{t\to\infty}\frac{1}{t}\int_{-t}^{0}\mathrm{d}s\mathrm{e}^{-\mathcal{L}_0 s}Y. \tag{3.13}$$

With this, (3.6) becomes

$$\rho_2 = A_2 - \hat{\rho} t_0 \left[\frac{\gamma^{(2)}_{\alpha\alpha'}}{m^2} \left(\frac{\partial}{\partial \Phi_\alpha} - \beta f^{th}_\alpha \right) \left(\frac{\partial}{\partial \Phi_{\alpha'}} - \beta f^{th}_{\alpha'} \right) W_0 + \frac{\lambda^{(2)}_{\alpha\alpha'}}{m^2} \left(\frac{\partial}{\partial \Phi_{\alpha'}} - \beta f^{th}_{\alpha'} \right) W_0 \right]$$
$$- \hat{\rho} \left(\frac{\partial W_1}{\partial \Phi_\alpha} - \beta f^{th}_\alpha W_1 \right) \int_{-t_0}^{0} \mathrm{d}s \mathrm{e}^{-\mathcal{L}_0 s} \frac{\Pi_\alpha}{m}$$
$$+ \frac{\hat{\rho}}{m^2} \left(\int_{-t_0}^{0} \mathrm{d}s \mathrm{e}^{-\mathcal{L}_0 s} \Pi_\alpha \int_{-(s+t_0)}^{0} \mathrm{d}s' \mathrm{e}^{-\mathcal{L}_0 s'} \Pi_{\alpha'} \right) \left(\frac{\partial}{\partial \Phi_\alpha} - \beta f^{th}_\alpha \right) \left(\frac{\partial}{\partial \Phi_{\alpha'}} - \beta f^{th}_{\alpha'} \right) W_0$$
$$+ \frac{\hat{\rho}}{m^2} \left\{ \int_{-t_0}^{0} \mathrm{d}s \mathrm{e}^{-\mathcal{L}_0 s} \Pi_{\alpha'} \frac{\partial}{\partial \Phi_{\alpha'}} \left(\int_{-(s+t_0)}^{0} \mathrm{d}s' \mathrm{e}^{-\mathcal{L}_0 s'} \Pi_\alpha \right) \right\} \left(\frac{\partial W_0}{\partial \Phi_\alpha} - \beta f^{th}_\alpha W_0 \right). \tag{3.14}$$

Using (3.13) and the definition of W in (2.5), (3.7) becomes

$$W_2 \equiv \int \mathrm{d}\Gamma^* \delta \left(\vec{\Phi} - \vec{\Phi}^* \right) \rho_2 = \int \mathrm{d}\Gamma^* \delta \left(\vec{\Phi} - \vec{\Phi}^* \right) A_2. \tag{3.15}$$

Similar to the argument yielding (3.2), we choose the initial data for ρ_2 as

$$A_2 = \hat{\rho} W_2 \tag{3.16}$$

and investigate the consequences for closure. This means that as long as the first and second order initial conditions can be written as a function of Γ and $\vec{\Phi}$ in the separable form such that the atomic variables Γ satisfy the ensemble generated by the conditional probability $\hat{\rho}$, the first and second order corrections for the reduced probability density can be found from (3.2) and (3.16). One can envision that this might be generalized to higher orders; however, this requires further analysis.

Inserting (2.13), (2.16) and (3.14) in the RHS of (2.6), and using (3.2) and (3.16), one gets

$$\int \mathrm{d}\Gamma^* \Delta \frac{\Pi^*_{\alpha_1}}{m} \rho = \int \mathrm{d}\Gamma^* \Delta \frac{\Pi^*_{\alpha_1}}{m} \left(\rho_0 + \varepsilon \rho_1 + \varepsilon^2 \rho_2 \right)$$
$$= \int \mathrm{d}\Gamma^* \Delta \hat{\rho} \frac{\Pi^*_{\alpha_1}}{m} W_0 + \varepsilon \int \mathrm{d}\Gamma^* \Delta \hat{\rho} \frac{\Pi^*_{\alpha_1}}{m} W_1$$
$$+ \varepsilon \int \mathrm{d}\Gamma^* \Delta \hat{\rho} \frac{\Pi^*_{\alpha_1}}{m} \left(\int_{-t_0}^{0} \mathrm{d}s \mathrm{e}^{-\mathcal{L}_0 s} \frac{\Pi^*_{\alpha_2}}{m} \right) \left(\beta f^{th}_{\alpha_2} W_0 - \frac{\partial W_0}{\partial \Phi_{\alpha_2}} \right) + \varepsilon^2 \int \mathrm{d}\Gamma^* \Delta \hat{\rho} \frac{\Pi^*_{\alpha_1}}{m} W_2$$
$$-\varepsilon^2 \int \mathrm{d}\Gamma^* \Delta \hat{\rho} \frac{\Pi^*_{\alpha_1}}{m} \left(\frac{\partial W_0}{\partial t_2} + \frac{\partial W_1}{\partial t_1} \right)$$
$$-\varepsilon^2 \int \mathrm{d}\Gamma^* \Delta \hat{\rho} \frac{\Pi^*_{\alpha_1}}{m} \left(\int_{-t_0}^{0} \mathrm{d}s \mathrm{e}^{-\mathcal{L}_0 s} \frac{\Pi^*_{\alpha_2}}{m} \right) \left(\frac{\partial W_1}{\partial \Phi_{\alpha_2}} - \beta f^{th}_{\alpha_2} W_1 \right)$$
$$+ \varepsilon^2 \int \mathrm{d}\Gamma^* \Delta \hat{\rho} \frac{\Pi^*_{\alpha_1}}{m} \left[\int_{-t_0}^{0} \mathrm{d}s \mathrm{e}^{-\mathcal{L}_0 s} \frac{\Pi^*_{\alpha_2}}{m} \left(\int_{-(s+t_0)}^{0} \mathrm{d}s' \mathrm{e}^{-\mathcal{L}_0 s'} \frac{\Pi^*_{\alpha_3}}{m} \right) \right]$$
$$\times \left(\frac{\partial}{\partial \Phi_{\alpha_2}} - \beta f^{th}_{\alpha_2} \right) \left(\frac{\partial}{\partial \Phi_{\alpha_3}} - \beta f^{th}_{\alpha_3} \right) W_0$$
$$+ \varepsilon^2 \int \mathrm{d}\Gamma^* \Delta \hat{\rho} \frac{\Pi^*_{\alpha_1}}{m} \left\{ \int_{-t_0}^{0} \mathrm{d}s \mathrm{e}^{-\mathcal{L}_0 s} \frac{\Pi^*_{\alpha_2}}{m} \left[\int_{-(s+t_0)}^{0} \mathrm{d}s' \frac{\partial}{\partial \Phi_{\alpha_2}} \left(\mathrm{e}^{-\mathcal{L}_0 s'} \frac{\Pi^*_{\alpha_3}}{m} \right) \right] \right\}$$
$$\times \left(\frac{\partial W_0}{\partial \Phi_{\alpha_3}} - \beta f^{th}_{\alpha_3} W_0 \right). \tag{3.17}$$

Define the coefficients $\gamma^{(3)}$ and $\lambda^{(3)}$ as

$$\gamma^{(3)}_{\alpha_1\alpha_2\alpha_3} = \left\langle \Pi_{\alpha_1} \int_{-t}^{0} \mathrm{d}s \mathrm{e}^{-\mathcal{L}_0 s} \Pi_{\alpha_2} \int_{-(s+t)}^{0} \mathrm{d}s' \mathrm{e}^{-\mathcal{L}_0 s'} \Pi_{\alpha_3} \right\rangle \tag{3.18}$$

$$\lambda^{(3)}_{\alpha_1\alpha_2\alpha_3} = \left\langle \Pi_{\alpha_1} \int_{-t}^{0} \mathrm{d}s \mathrm{e}^{-\mathcal{L}_0 s} \Pi_{\alpha_2} \int_{-(s+t)}^{0} \mathrm{d}s' \frac{\partial}{\partial \Phi_{\alpha_2}} \left(\mathrm{e}^{-\mathcal{L}_0 s'} \Pi_{\alpha_3} \right) \right\rangle. \tag{3.19}$$

With this, and noting that $\langle \vec{\Pi}^* \rangle = 0$, (3.17) becomes

$$\int \mathrm{d}\Gamma^* \Delta \frac{\Pi^*_{\alpha_1}}{m}\rho = +\varepsilon \frac{\gamma^{(2)}_{\alpha_1\alpha_2}}{m^2}\left(\beta f^{th}_{\alpha_2} - \frac{\partial}{\partial \Phi_{\alpha_2}}\right) W_0 + \varepsilon^2 \frac{\gamma^{(2)}_{\alpha_1\alpha_2}}{m^2}\left(\beta f^{th}_{\alpha_2} - \frac{\partial}{\partial \Phi_{\alpha_2}}\right) W_1 + \varepsilon^2 \frac{\gamma^{(3)}_{\alpha_1\alpha_2\alpha_3}}{m^3}\left(\frac{\partial}{\partial \Phi_{\alpha_2}} - \beta f^{th}_{\alpha_2}\right)\left(\frac{\partial}{\partial \Phi_{\alpha_3}} - \beta f^{th}_{\alpha_3}\right) W_0 + \varepsilon^2 \frac{\lambda^{(3)}_{\alpha_1\alpha_2\alpha_3}}{m^3}\left(\frac{\partial}{\partial \Phi_{\alpha_3}} - \beta f^{th}_{\alpha_3}\right) W_0. \tag{3.20}$$

Inserting (3.20) in (2.6) yields

$$\frac{\partial W}{\partial t} = \varepsilon^2 \frac{\partial}{\partial \Phi_{\alpha_1}}\left\{\frac{\gamma^{(2)}_{\alpha_1\alpha_2}}{m^2}\left(\frac{\partial}{\partial \Phi_{\alpha_2}} - \beta f^{th}_{\alpha_2}\right)(W_0 + \varepsilon W_1)\right\} - \varepsilon^3 \frac{\partial}{\partial \Phi_{\alpha_1}}\left\{\frac{\gamma^{(3)}_{\alpha_1\alpha_2\alpha_3}}{m^3}\left(\frac{\partial}{\partial \Phi_{\alpha_2}} - \beta f^{th}_{\alpha_2}\right)\left(\frac{\partial}{\partial \Phi_{\alpha_3}} - \beta f^{th}_{\alpha_3}\right) W_0\right\} - \varepsilon^3 \frac{\partial}{\partial \Phi_{\alpha_1}}\left\{\frac{\lambda^{(3)}_{\alpha_1\alpha_2\alpha_3}}{m^3}\left(\frac{\partial}{\partial \Phi_{\alpha_3}} - \beta f^{th}_{\alpha_3}\right) W_0\right\}. \tag{3.21}$$

For the above equation to be closed, the first and second order reduced probability densities W_1 and W_2 need to be zero. However, note that to $O(\varepsilon^2)$

$$\frac{\partial W}{\partial t} = \varepsilon^2 \frac{\partial}{\partial \Phi_{\alpha_1}}\left\{\frac{\gamma^{(2)}_{\alpha_1\alpha_2}}{m^2}\left(\frac{\partial}{\partial \Phi_{\alpha_2}} - \beta f^{th}_{\alpha_2}\right)(W_0 + \varepsilon W_1)\right\}, \tag{3.22}$$

which is closed regardless of the value of W_1, i.e. replacing $W_0 + \varepsilon W_1$ by W.

In what follows, we continue the analysis of the Liouville equation up to $O(\varepsilon^3)$ and $O(\varepsilon^4)$, the aim being to discover hidden terms that are required in the $O(\varepsilon^3)$ stochastic equation to yield closure in W in a manner similar to the way the W_1 term was brought from the $O(\varepsilon^2)$ analysis of the Liouville equation to bring closure to the $O(\varepsilon^2)$ equation of W.

To $O(\varepsilon^3)$, one gets

$$\Lambda_0 \rho_3 = -(\Lambda_1 \rho_2 + \Lambda_2 \rho_1 + \Lambda_3 \rho_0). \tag{3.23}$$

Therefore

$$\rho_3 = A_3 - \int_{-t_0}^{0} \mathrm{d}s \mathrm{e}^{-\mathcal{L}_0 s}\left\{\frac{\partial \rho_0}{\partial t_3} + \frac{\partial \rho_1}{\partial t_2} + \frac{\partial \rho_2}{\partial t_1} + \frac{\vec{\Pi}}{m}\cdot\frac{\partial \rho_2}{\partial \vec{\Phi}}\right\} \tag{3.24}$$

where A_3 is taken to be in the nullspace of $\mathcal{L}_0$, as stated in (2.18).

Inserting (2.13), (2.16) and (3.14) in (3.24), one gets

$$\rho_3 = A_3 - \hat{\rho}\int_{-t_0}^{0} \mathrm{d}s \mathrm{e}^{-\mathcal{L}_0 s}\left\{\frac{\partial W_0}{\partial t_3} + \frac{\partial W_1}{\partial t_2} + \frac{\partial W_2}{\partial t_1} - \left(\int_{-(s+t_0)}^{0} \mathrm{d}s' \mathrm{e}^{-\mathcal{L}_0 s'}\frac{\Pi_\alpha}{m}\right)\left(\frac{\partial}{\partial \Phi_\alpha} - \beta f^{th}_\alpha\right) \times \left[\frac{\gamma^{(2)}_{\alpha_1\alpha_2}}{m^2}\left(\frac{\partial}{\partial \Phi_\alpha} - \beta f^{th}_\alpha\right)\left(\frac{\partial}{\partial \Phi_{\alpha'}} - \beta f^{th}_{\alpha'}\right) + \frac{\lambda^{(2)}_{\alpha_1\alpha_2}}{m^2}\left(\frac{\partial}{\partial \Phi_{\alpha'}} - \beta f^{th}_{\alpha'}\right)\right] W_0 + \frac{\Pi_{\alpha_1}}{m}\left(\frac{\partial}{\partial \Phi_{\alpha_1}} - \beta f^{th}_{\alpha_1}\right) W_2 - \frac{\Pi_{\alpha_1}}{m}\left(\frac{\partial}{\partial \Phi_{\alpha_1}} - \beta f^{th}_{\alpha_1}\right)\int_{-(s+t_0)}^{0} \mathrm{d}s' \mathrm{e}^{-\mathcal{L}_0 s'}\rho^*_{\alpha_2\alpha_3}\right\}, \tag{3.25}$$

where

$$\rho^*_{\alpha\alpha'} = \frac{\gamma^{(2)}_{\alpha_1\alpha_2}}{m^2}\left(\frac{\partial}{\partial \Phi_\alpha} - \beta f^{th}_\alpha\right)\left(\frac{\partial}{\partial \Phi_{\alpha'}} - \beta f^{th}_{\alpha'}\right) W_0 + \frac{\lambda^{(2)}_{\alpha_1\alpha_2}}{m^2}\left(\frac{\partial}{\partial \Phi_{\alpha'}} - \beta f^{th}_{\alpha'}\right) W_0 + \frac{\Pi_\alpha}{m}\left(\frac{\partial W_1}{\partial \Phi_\alpha} - \beta f^{th}_\alpha W_1\right) + \frac{1}{m^2}\left(\Pi_\alpha \int_{-(s+s'+t_0)}^{0} \mathrm{d}s'' \mathrm{e}^{-\mathcal{L}_0 s''}\Pi_{\alpha'}\right)\left(\frac{\partial}{\partial \Phi_\alpha} - \beta f^{th}_\alpha\right)\left(\frac{\partial}{\partial \Phi_{\alpha'}} - \beta f^{th}_{\alpha'}\right) W_0 \times \frac{1}{m^2}\left[\Pi_{\alpha'}\frac{\partial}{\partial \Phi_{\alpha'}}\left(\int_{-(s+s'+t_0)}^{0} \mathrm{d}s'' \mathrm{e}^{-\mathcal{L}_0 s'' \Pi_\alpha}\right)\right]\left(\frac{\partial W_0}{\partial \Phi_\alpha} - \beta f^{th}_\alpha W_0\right). \tag{3.26}$$

$\int \mathrm{d}\Gamma^* \Delta \frac{\Pi^*_{\alpha_1}}{m}\rho$ is now equal to the right hand side of (3.20) plus $\varepsilon^3 \int \mathrm{d}\Gamma^* \Delta \frac{\Pi^*_{\alpha_1}}{m}\rho_3$. However, as our objective is to construct a rate equation for W to $O(\varepsilon^3)$, we are only interested in the ε and ε^2 terms appearing in the second integrand. As can be seen from (2.6), these will contribute to the $O(\varepsilon^2)$ and $O(\varepsilon^3)$ parts of the final stochastic equation, while the ε^3 terms will contribute to the $O(\varepsilon^4)$ part. Thus, all the W_0 terms will have $O(\varepsilon^3)$ contribution to (3.20) while the W_1 and W_2 terms will have $O(\varepsilon^2)$ and $O(\varepsilon)$ contributions to (3.20). To further clarify this last statement, take for example a general equation for W, $\partial W/\partial t = \varepsilon JW$; this translates into $\partial W/\partial t = \varepsilon^2 J\left(W_0 + \varepsilon W_1 + \varepsilon^2 W_2\right)$ to $O(\varepsilon^2)$. With this, we can see that the W_1 and W_2 terms needed to close the W conservation equation to $O(\varepsilon^2)$ are $\varepsilon^3 W_1$ and $\varepsilon^4 W_2$ and thus can only be found from the $O(\varepsilon^3)$ and $O(\varepsilon^4)$ analysis of the Liouville equation.

With this, neglecting terms higher than $O(\varepsilon^2)$ yields

$$\varepsilon^3 \int \mathrm{d}\Gamma^* \Delta \frac{\Pi^*_{\alpha_1}}{m} \rho_3 = -\varepsilon \frac{\gamma^{(2)}_{\alpha_1\alpha_2}}{m^2}\left(\frac{\partial}{\partial \Phi_{\alpha_2}} - \beta f^{th}_{\alpha_2}\right)\left(\varepsilon^2 W_2\right) + \varepsilon^2 \frac{\gamma^{(3)}_{\alpha_1\alpha_2\alpha_3}}{m^3}\left(\frac{\partial}{\partial \Phi_{\alpha_2}} - \beta f^{th}_{\alpha_2}\right)\left(\frac{\partial}{\partial \Phi_{\alpha_3}} - \beta f^{th}_{\alpha_3}\right)(\varepsilon W_1) + \varepsilon^2 \frac{\lambda^{(3)}_{\alpha_1\alpha_2\alpha_3}}{m^3}\left(\frac{\partial}{\partial \Phi_{\alpha_3}} - \beta f^{th}_{\alpha_3}\right)(\varepsilon W_1) \tag{3.27}$$

noting that $W_3 \equiv \int \mathrm{d}\Gamma^* \delta\left(\vec{\Phi} - \vec{\Phi}^*\right)\rho_3 = \int \mathrm{d}\Gamma^* \delta\left(\vec{\Phi} - \vec{\Phi}^*\right) A_3$ which is shown in a similar manner as done for (3.15).

To $O(\varepsilon^4)$, one gets

$$\Lambda_0 \rho_4 = -\left(\Lambda_1 \rho_3 + \Lambda_2 \rho_2 + \Lambda_3 \rho_1 + \Lambda_4 \rho_0\right). \tag{3.28}$$

As the contribution of ρ_4 to $\int \mathrm{d}\Gamma^* \Delta \frac{\Pi^*_{\alpha_1}}{m}\rho$ is of $O(\varepsilon^4)$ $\left(as \rho = \rho_0 + \varepsilon\rho_1 + \varepsilon^2\rho_2 + \varepsilon^3\rho_3 + \varepsilon^4\rho_4\right)$, only the W_2 and higher order correction terms will have $O(\varepsilon^2)$ or lower order contributions to (3.20). Thus, neglecting the W_0 and W_1 terms in ρ_4, (3.28) admits the solution

$$\rho_4 = A_4 - \hat{\rho}\frac{\partial W_3}{\partial t_1} + \hat{\rho}\left(\frac{\partial}{\partial \Phi_\alpha} - \beta f^{th}_\alpha\right) W_3 + \frac{\Pi_{\alpha_1}}{m}\frac{\partial}{\partial \Phi_{\alpha_1}}\left\{\hat{\rho}\int_{-t_0}^{0} \mathrm{d}s e^{-\mathcal{L}_0 s}\frac{\Pi_{\alpha_2}}{m}\left(\frac{\partial}{\partial \Phi_{\alpha_2}} - \beta f^{th}_{\alpha_2}\right) W_2\right\}. \tag{3.29}$$

With this and neglecting all terms higher than $O(\varepsilon^2)$,

$$\varepsilon^4 \int \mathrm{d}\Gamma^* \Delta \frac{\Pi^*_{\alpha_1}}{m}\rho_4 = \varepsilon^2 \frac{\gamma^{(3)}_{\alpha_1\alpha_2\alpha_3}}{m^3}\left(\frac{\partial}{\partial \Phi_{\alpha_2}} - \beta f^{th}_{\alpha_2}\right)\left(\frac{\partial}{\partial \Phi_{\alpha_3}} - \beta f^{th}_{\alpha_3}\right)\left(\varepsilon^2 W_2\right) + \varepsilon^2 \frac{\lambda^{(3)}_{\alpha_1\alpha_2\alpha_3}}{m^3}\left(\frac{\partial}{\partial \Phi_{\alpha_3}} - \beta f^{th}_{\alpha_3}\right)\left(\varepsilon^2 W_2\right). \tag{3.30}$$

Inserting the RHS of (3.20), (3.27) and (3.30) in (2.6), yields to $O(\varepsilon^3)$

$$\frac{\partial W}{\partial t} = \varepsilon^2 \frac{\partial}{\partial \Phi_{\alpha_1}}\left\{\frac{\gamma^{(2)}_{\alpha_1\alpha_2}}{m^2}\left(\frac{\partial}{\partial \Phi_{\alpha_2}} - \beta f^{th}_{\alpha_2}\right) W\right\} - \varepsilon^3 \frac{\partial}{\partial \Phi_{\alpha_1}}\left\{\frac{\gamma^{(3)}_{\alpha_1\alpha_2\alpha_3}}{m^3}\left(\frac{\partial}{\partial \Phi_{\alpha_2}} - \beta f^{th}_{\alpha_2}\right)\left(\frac{\partial}{\partial \Phi_{\alpha_3}} - \beta f^{th}_{\alpha_3}\right) W\right\} - \varepsilon^3 \frac{\partial}{\partial \Phi_{\alpha_1}}\left\{\frac{\lambda^{(3)}_{\alpha_1\alpha_2\alpha_3}}{m^3}\left(\frac{\partial}{\partial \Phi_{\alpha_3}} - \beta f^{th}_{\alpha_3}\right) W\right\}. \tag{3.31}$$

We term (3.31) the augmented Smoluchowski equation.

4. Conclusions

We have shown that one can obtain an augmentation of the Smoluchowski equation. As expected, such a closed equation only exists for initial data on ρ that is quasi-equilibrium in character (i.e. $\mathcal{L}_0 A_n = 0$). Unless initial conditions are set to zero, closure of the stochastic equation in W is found only when the perturbative solution of the Liouville equation is examined to $O(\varepsilon^4)$. The higher order terms are used to imply the specific form of the augmented Fokker–Planck equation and to obtain expressions for the parameters in them that can be computed via molecular dynamics.

The form of the augmented Smoluchowski equation (3.31) satisfies certain general criteria. First, conservation of W was built in due to the use of the generalized conservation equation (2.6). Second, Eq. (3.31) contains the equilibrium solution. In particular, if Q is expressed in terms of the free energy F, i.e. $Q = e^{-\beta F}$, then $f^{th}_\alpha = -\partial F/\partial \Phi_\alpha$. Hence, the equilibrium solution $W \propto e^{-\beta F}$ satisfies (3.31) for $\partial W/\partial t = 0$. Third, as (3.31) yields the reduced dynamics to $O(\varepsilon^3)$, it can be used for systems wherein ε is larger than appropriate for the Smoluchowski equation, i.e. the separation of time scales is not large enough (for example, a small nanoparticle or short protein). Furthermore, the approach could account for systems where intermediate scales (for which ε would be larger) are important. Examples include proteins with side branches and the various stages of viral structural transitions or infection. In the case of enveloped viruses such as HIV, the fusion stage of infection involves the overall behavior of both membranes and the interaction of the glycoproteins attached to the virus surface with the target cell protein receptors. Glycoproteins anchor the virus to the target cell and trigger subsequent conformational changes that allow the final fusion. These proteins are smaller than the overall size of the virus but are bigger than the atomic scale which also need to be taken into consideration. However, allowing various levels of coarse-graining is achieved at the expense of needing the additional friction coefficients $\gamma^{(3)}$ and $\lambda^{(3)}$. As for $\gamma^{(2)}$, these need to be calculated via correlation functions.

The above results warrant further examination. (1) What other kinds of equations arise for different initial data? (2) If the initial state of the system is quasi-equilibrium in character, will subsequent evolution leave the system in a quasi-equilibrium state for all time? (3) Otherwise, if the initial conditions are not in the null space of $\mathcal{L}_0$, does that imply that to higher order W will depend on t_0? (4) What is the most general set of initial data that can be used to make the stochastic equation closed in W or will W be coupled to other variables through additional equations? (5) As direct simulation of the augmented Smoluchowski equation is not practical, what is the Langevin-like equation that, via a Monte Carlo approach, is equivalent to the augmented Smoluchowski equation?

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References

[1] R.I. Cukier, J.M. Deutch, Microscopic theory of Brownian motion: The multiple-time-scale point of view, Physical Review 177 (1) (1968) 240–244.
[2] J.E. Shea, I. Oppenheim, Fokker–Planck equation and Langevin equation for one Brownian particle in a nonequilibrium bath, Journal of Physical Chemistry 100 (49) (1996) 19035–19042.
[3] J.E. Shea, I. Oppenheim, Fokker–Planck equation and non-linear hydrodynamic equations of a system of several Brownian particles in a non-equilibrium bath, Physica A 247 (1–4) (1997) 417–443.
[4] M.H. Peters, Fokker–Planck equation, molecular friction, and molecular dynamics for Brownian particle transport near external solid surfaces, Journal of Statistical Physics 94 (3/4) (1999) 557–586.
[5] M.H. Peters, Fokker–Planck equation and the grand molecular friction tensor for coupled rotational and translational motions of structured Brownian particles near structured surfaces, Journal of Chemical Physics 110 (1) (1999) 528–538.
[6] M.H. Peters, The Smoluchowski diffusion equation for structured macromolecules near structured surfaces, Journal of Chemical Physics 112 (12) (2000) 5488–5498.
[7] P.J. Ortoleva, Nanoparticle dynamics: A multiscale analysis of the Liouville equation, Journal of Physical Chemistry B 109 (45) (2005) 21258–21266.
[8] Y. Miao, P. Ortoleva, All-atom multiscaling and new ensembles for dynamical nanoparticles, Journal of Chemical Physics 125 (4) (2006) 044901.
[9] Y. Miao, P. Ortoleva, Viral structural transitions: An all-atom multiscale theory, Journal of Chemical Physics 125 (21) (2006) 214901.
[10] Z. Shreif, P. Ortoleva, Curvilinear All-Atom Multiscale (CAM) Theory of Macromolecular Dynamics, Journal of Statistical Physics 130 (4) (2008) 669–685.
[11] Z. Shreif, P. Ortoleva, Computer-aided design of nanocapsules for therapeutic delivery, Computational and Mathematical Methods in Medicine (2008) (in press).
[12] S. Pankavich, Z. Shreif, P. Ortoleva, Multiscaling for classical nanosystems: Derivation of Smoluchowski and Fokker–Planck equations, Physica A 387 (16–17) (2008) 4053–4069.
[13] S. Pankavich, Y. Miao, J. Ortoleva, Z. Shreif, P. Ortoleva, Stochastic dynamics of bionanosystems: Multiscale analysis and specialized ensembles, Journal of Chemical Physics 128 (2008) 234908.