Computing sensitivity coefficients in Brownian dynamics simulations by Malliavin weight sampling

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We present a method for computing parameter sensitivities and response coefficients in Brownian dynamics simulations. The method involves tracking auxiliary variables (Malliavin weights) in addition to the usual particle positions, in an unperturbed simulation. The Malliavin weights sample the derivatives of the probability density with respect to the parameters of interest and are also interesting dynamical objects in themselves. Malliavin weight sampling is simple to implement, applies to equilibrium or nonequilibrium, steady state or time-dependent systems, and scales more efficiently than standard finite difference methods.

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The response of a system to infinitesimal changes in an external field provides important insights into its underlying physics. Divergences in such response functions can indicate the presence of phase transitions, while their relation to fluctuations in unperturbed systems via fluctuation-dissipation theorems (FDTs) provides a key diagnostic of the difference between equilibrium and nonequilibrium systems\([1]\). Knowledge of the response of a system to changes in internal parameters (e.g., those controlling inter-particle forces) is also of great importance, since it has the potential greatly to accelerate the fitting of force fields to experimental data. For equilibrium systems, responses to perturbations can often be computed from the properties of unperturbed systems via known statistical mechanical relations\([2, 3]\). However, for systems which are far from steady-state, and/or whose dynamics does not obey detailed balance, one is generally forced to resort to finite differencing: explicitly taking the difference between simulation trajectories generated at slightly different parameter values\([3]\). While finite differencing can be made more efficient by reuse of random number streams\([6, 7]\), one still has to re-simulate the perturbed system for each parameter of interest.

In this Letter, we present a simple and generic method for computing responses to infinitesimal changes in internal or external parameters in stochastic Brownian dynamics simulations, which may be in or out of equilibrium. The method does not require simulation of the perturbed system; instead, it involves tracking, in an unperturbed system, auxiliary stochastic variables which sample the derivatives of the probability density with respect to the parameters of interest. We term these auxiliary variables ‘Malliavin weights’ as the method has close links to the Malliavin calculus programme\([8]\), used in quantitative finance for deriving price sensitivities (i.e., ‘Greeks’)\([9]\). Our method extends approaches previously proposed for kinetic Monte-Carlo simulations\([10, 11]\) to a much wider set of problems. It also has interesting links to molecular dynamics methods in which response coefficients are computed via the integration of adjunct equations of motion for individual particles\([5, 10]\). Since Brownian dynamics is very widely used\([13]\) in the study of non-equilibrium statistical physics problems such as driven steady states, active soft matter, and modeling sub-cellular processes in biology, we anticipate that our method should prove widely applicable.

We begin by considering a collection of \(i = 1, \ldots, N\) interacting particles undergoing overdamped Brownian motion, described by the coupled Langevin equations

\[
\frac{d\vec{r}_i}{dt} = \frac{D\vec{f}_i}{k_B T} + \vec{\eta}_i. \tag{1}
\]

Here \(\vec{r}_i\) and \(\vec{f}_i\) are the position of the \(i\)th particle and the force acting on it, respectively, \(D\) is the diffusion coefficient (which for simplicity we here assume to be constant and the same for all particles), \(k_B\) is Boltzmann’s constant, \(T\) is temperature, and the \(\vec{\eta}_i\) are independent vectors of Gaussian white noise of amplitude \(2D\). We now add an extra variable \(q_\lambda\) (a Malliavin weight) which evolves according to

\[
\frac{dq_\lambda}{dt} = \frac{1}{2k_B T} \sum_{i=1}^{N} \frac{\partial \vec{f}_i}{\partial \lambda} \cdot \vec{\eta}_i. \tag{2}
\]

where \(\lambda\) is a parameter of interest for which the only requirement is that \(\partial \vec{f}_i/\partial \lambda\) is known. Note that \(q_\lambda\) does not perturb the dynamics of the particles; it merely acts as a ‘readout’ and should be initialised to \(q_\lambda = 0\). The interpretation of Eq. (2) as a stochastic differential equation is straightforward and uniquely defined—the practical implementation is described in Supplementary Material\([13]\). The noise vector \(\vec{\eta}_i\) is identical in Eqs. (1) and (2)—in each Brownian dynamics timestep, \(q_\lambda\) is updated using the same set of random numbers that were chosen in the update of the particle positions. Our central claim...
is that for any function of the particle positions $A(\{\vec{r}_i\})$

$$\frac{\partial(A)}{\partial \lambda} = \langle A q_\lambda \rangle,$$

(3)

i.e. the response of $A$ to the parameter $\lambda$ is given by the average of $A$ in the unperturbed system, weighted by the appropriate Malliavin weight $q_\lambda$. Eq. (3) has important practical implications. Since the computation of $q_\lambda$ via Eq. (2) is independent of $A$, the same $q_\lambda$ can be used to compute the sensitivity of multiple system properties to the parameter $\lambda$. Moreover, one can track multiple weights corresponding to different choices of $\lambda$, with marginal additional cost.

Eq. (3) is the key result of this Letter. It can be proved by taking moments of a Chapman-Kolmogorov equation for the evolution of the joint probability distribution $P(\{\vec{r}_i\}, q_\lambda; t)$ for the set of particle positions $\{\vec{r}_i\}$ and the Malliavin weight $q_\lambda$. The details are given in Supplementary Material. A crucial intermediate result is that the conditional average of $q_\lambda$ for a given set of particle positions $\{\vec{r}_i\}$, which we denote $\langle q_\lambda \rangle_{\{\vec{r}_i\}}$, is given by

$$\langle q_\lambda \rangle_{\{\vec{r}_i\}} \equiv \frac{\int dq_\lambda P(\{\vec{r}_i\}, q_\lambda; t)}{\int dq_\lambda P(\{\vec{r}_i\}, q_\lambda; t)} = \frac{\partial \ln P(\{\vec{r}_i\}; t)}{\partial \lambda}$$

(4)

where $P(\{\vec{r}_i\}; t)$ is the probability distribution for the particle positions. Thus the Malliavin weight in fact samples the conjugate variable $\partial \ln P/\partial \lambda$.

The proof makes no assumptions about the system being in steady state or obeying detailed balance; thus our method is valid for systems far from steady state, or in driven steady states, as well as for those at equilibrium. Moreover, as we show in Supplementary Material, our approach can easily be extended to systems undergoing underdamped Brownian motion and to the computation of higher-order derivatives.

To illustrate the method, we turn to a simple example for which analytical results are available: a single particle in a one-dimensional harmonic trap described by a potential $U = \frac{1}{2} \kappa x^2 - h x$. To make contact with linear response theory, we take the parameter of interest to be the strength of the applied external force $h$. We set the particle mobility to unity so that the diffusion constant $D = T$ where the temperature $T$ is in units of $\kappa$. At equilibrium, $P_{eq}(x) \sim e^{-U/T}$, so that $\partial \ln P_{eq}/\partial h = (x - \langle x \rangle)/T$ [1], and the FDT holds: $\partial \langle x \rangle/\partial h = (\langle x^2 \rangle - \langle x \rangle^2)/T$. We now apply Malliavin weight sampling to the time-dependent situation in which the particle starts from $x = x_0$ at $t = 0$ and relaxes towards its equilibrium position. Eqs. (1) and (2) become

$$\frac{dx}{dt} = -\kappa x + h + \eta, \quad \frac{dq_h}{dt} = \frac{\eta}{2T}.$$  

(5)

These equations can be solved exactly [17] to give $P(x, q_h; t)$ as a bivariate Gaussian with

$$\langle x \rangle = x_0 e^{-\kappa t} + (h/\kappa)(1 - e^{-\kappa t}), \quad \langle q_h \rangle = 0,$$

$$\langle x^2 \rangle - \langle x \rangle^2 = (T/\kappa)(1 - e^{-2\kappa t}),$$

$$\langle x q_h \rangle = (1 - e^{-\kappa t})/\kappa, \quad \langle q_h^2 \rangle = t/2T.$$  

(6)

This result allows us to verify directly that Eq. (4) is satisfied, that is to say $\langle q_h \rangle_x = \int dx q_h P(x, q_h; t) = \partial \ln P(x; t)/\partial h$, where $P(x; t) = \int dq_h P(x, q_h; t)$. Fig. 1 shows simulation results for $\partial \langle x \rangle/\partial h$, computed by Malliavin weight sampling (MWS) and by forward finite differencing; the inset shows trajectories for $q_h$ from replicate simulation runs. The Malliavin weight $q_h$ behaves as a random walk with zero mean and a diffusion coefficient $1/4T$. Eq. (6) shows that, by analogy with the equilibrium FDT, one can define a time-dependent effective temperature $T_{eff} = (1 - e^{-2\kappa t})/(1 - e^{-\kappa t})$ such that $\partial \langle x \rangle/\partial h = ((\langle x^2 \rangle - \langle x \rangle^2))/T_{eff}$. Calculating the conditional average of the Malliavin weight gives $\langle q_h \rangle_x = (x - \langle x \rangle)/T_{eff}$. Interestingly this has the same form as the equilibrium case but again features $T_{eff}$.

Thus the effective temperature has a wider relevance than would be apparent from the time-dependent FDT since $\partial \langle A \rangle/\partial h = (\langle Ax \rangle - \langle A \rangle x)/T_{eff}$, where $A(x)$ is any function of the particle position.

An important practical issue is raised by the fact that $q_\lambda(t)$ behaves as a random walk (inset to Figure 1) to compute responses to parameter perturbations for systems in steady state, we cannot simply monitor $q_\lambda$ for longer and longer times until the system reaches its steady state. This is because replicate trajectories of $q_\lambda$ diverge at long times and measurements of $\langle A(t)q_\lambda(t) \rangle$
The energy of the cluster is then $U = \frac{1}{2} \sum_{i>j} U(x_i, x_j)$. For a two-dimensional harmonic trap, the energy is given by $U = \frac{1}{2} \sum_{i} \kappa y_i^2$, where $\kappa$ is the spring constant of the trap. This energy is parameterized by the shear rate $\dot{\gamma}$.

To compute the correlation function $\langle xy \rangle / \partial \gamma$ for the system in steady-state, we use the correlation function approach outlined above. Fig. 2 shows that, for $\dot{\gamma} = 0$, $C(\Delta t) = \langle (1/N) \sum_{i=1}^{N} x_i(t) y_i(t) \rangle$ tends to $\partial \langle xy \rangle / \partial \gamma = 0$ as $\Delta t$ increases, where $\partial \langle xy \rangle / \partial \gamma = 0$ (the dashed line) is calculated by finite differencing. In fact the Malliavin weight $q_\gamma$ turns out to be an interesting physical quantity in itself. By splitting the sum in Eq. (8) into individual particle contributions, one can track Malliavin weights $q_{\gamma,i}$ for each individual particle. These provide insight into the response to shear of the one-particle probability distribution $P(x_i, y_i)$. As shown in the inset to Fig. 2b, the individual contributions to the Malliavin weight are biased towards being positive in the first and third quadrants and negative in the second and fourth quadrants, corresponding to the distortion of the particle cloud by the shear.

An important feature of MWS is that, from a single simulation run, one can compute the sensitivities of any function of the particle coordinates, to any parameter of the system. One simply needs to track the Malliavin weights corresponding to all the parameters that are of interest, using the appropriate dynamical rules as derived from Eq. (2). For example in this problem $q_T$ obeys

$$\frac{dq_T}{dt} = -\frac{1}{2k_B T} \sum_{i=1}^{N} \left( \frac{\partial^2 U}{\partial x_i \partial x_i} \eta_{x,i} + \frac{\partial^2 U}{\partial y_i \partial y_i} \eta_{y,i} \right).$$

and an analogous equation for $q_y$ is easily written down. Fig. 3 shows the full panoply of responses of the cluster morphology parameters $\langle xy \rangle$ and $\langle x^2 y^2 \rangle$ to the parameters of the problem, for $\Gamma = 25$, obtained from a single simulation run. Second order derivatives were computed as described in Supplementary Material [17].

We now demonstrate how MWS can reveal subtle details of how the response to shear, $\partial \langle xy \rangle / \partial \gamma |_{\gamma=0}$, depends on $\langle x^2 y^2 \rangle^{1/2}$, which provides a representative measure of the area of the particle cloud. For non-interacting particles one can obtain analytically [17] the intriguing quasi-FDT result $\partial \langle xy \rangle / \partial \gamma |_{\gamma=0} = \langle x^2 y^2 \rangle / 2T$, which holds at $\Gamma = \dot{\gamma} = 0$ and for all values of $\gamma$. The case of interacting particles, however, cannot be solved analytically. We therefore simulated the cloud at a series of increasing values of $\Gamma$ (i.e. increasing cluster size) keeping $\kappa = 10$. The results shown in Fig 3 suggest that $\partial \langle xy \rangle / \partial \gamma |_{\gamma=0}$ is quite accurately proportional to $\langle x^2 y^2 \rangle^{1/2}$. More generally we can define an effective exponent $\beta = d \ln(\langle xy \rangle / \partial \gamma |_{\gamma=0}) / d \ln(\langle x^2 y^2 \rangle^{1/2})$. This can be evaluated as $\Gamma$ varies at fixed $\kappa$, or vice versa. In the former
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ter universality.

than the non-interacting one, and there is apparently lit-
latter case (fixed $\Gamma$ varying
lence is also apparent. An analogous calculation for the
size of the cluster, as the interaction strength $\Gamma$ is vari-
ed $\Gamma = 0$). The inset shows the effective
from the main plot,
We used MWS to compute the derivatives in Eq. (10),
expansion of the derivatives gives

\[
\beta = \frac{\langle x^2y^2 \rangle}{\partial \langle x^2y^2 \rangle / \partial \gamma} \times \frac{\partial^2 \langle xy \rangle / \partial \gamma^2 \partial \Gamma}{\partial \langle xy \rangle / \partial \gamma}. \quad (10)
\]

We used MWS to compute the derivatives in Eq. (10),
with results shown in the inset in Fig. 3b. As expected
from the main plot, $\beta \approx 0.5$, but a more subtle depen-
dence is also apparent. An analogous calculation for the
latter case (fixed $\Gamma$ varying $\kappa$) shows that the correspond-
effective exponent increases from $\beta = 1$ at $\Gamma = 0$ (the
 quasi-FDT result) to $\beta \approx 1.3$ at $\Gamma = 25$. Hence the in-
acting particle case shows considerably more complexity
than the non-interacting one, and there is apparently lit-
tle universality.

These examples demonstrate that MWS provides a
simple and easy-to-implement alternative to finite dif-
erencing, for Brownian dynamics problems that may be
time-dependent or in steady state, in or out of equilib-
rium. Let us now discuss the question of efficiency. As
highlighted above, in MWS one has access to response
coefficients for all parameters of the problem (for which
the derivatives $\partial f_i / \partial \lambda$ in Eq. (2) are known), with little
additional cost, since integrating the equations of motion
for the $q_{\lambda}$ requires no new random numbers and also typ-
ically does not require recalculation of the forces. MWS
also scales more efficiently with the computational effort
than does standard finite differencing. For MWS, the
error in a computation of $\partial \langle A(t) \rangle / \partial \lambda$ scales as $M^{-1/2}$,
where $M$ is the number of replicate simulation runs used
to compute the averages (this follows from the usual scal-
ing of the standard error in the mean with the number of
samples). For finite differencing, there is an inherent
tradeoff between the systematic error introduced by using
a too-large perturbation and the random sampling error
that arises when the perturbation is very small.

One can show [6] that the best possible choice of the per-
turbation size results in an error that scales as $M^{-1/4}$
for a forward finite differencing scheme, and $M^{-1/3}$ for a
centered scheme. Although the scaling can be improved
to $M^{-1/2}$ by using a common random number scheme
[6, 7], even here we expect MWS to be more efficient,
since it does not require the perturbed system to be ex-
plicitly simulated. For example we note that more than
six times as many force evaluations were used to calcu-
late $\partial \langle xy \rangle / \partial \gamma$ in Fig. 2 by finite differencing, compared
to calculating the same quantity to comparable accuracy
by the MWS correlation function method.

MWS has the potential greatly to facilitate the param-
eterization of force fields, when combined with gradient-
based search and optimisation algorithms. This should
be especially relevant for mesoscale problems where
Brownian dynamics algorithms such as dissipative parti-
dle dynamics (DPD) are often the method of choice [16]
(note that the application to DPD should take account of
the fact that the noise terms are pairwise central random
forces). An equally important application of MWS is in
the computation of response functions to external fields—
example in the context of dynamical phase transi-
tions. Interestingly, while we have focused here only on
its long-time limit, the time-correlation function $C(\Delta t)$
is actually equivalent to the time-dependent response to
a step perturbation. This point will be explored in more
detail in future work. A particularly interesting question
concerns the extent to which the Malliavin weight itself
can be used as an autonomous order parameter. For in-
stance in the 1d trap problem the conditional average
$\langle q_{\lambda} \rangle_q$ features the time-dependent effective tempera-
ture $T_{eq}$, generalising the linear response result. Certainly
for glassy systems we expect that the correlation func-
tions $\langle A \Delta q_{\lambda} \rangle$ will show typical non-ergodic memory
and aging phenomenology [10]: it is interesting to speculate
whether the behaviour of $q_{\lambda}$ itself could be used as an
alternative signature of glassy behaviour.

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Proof of Eqs. (3) and (4) in the main text

We start by introducing the probability distribution $P(\{\vec{r}_i\}; t)$ for the particle positions, and the joint probability distribution $P(\{\vec{r}_i\}, q_\lambda; t)$ for the combination of the particle positions and the Malliavin weight. The two are related by

$$P(\{\vec{r}_i\}; t) = \int dq_\lambda P(\{\vec{r}_i\}, q_\lambda; t).$$

We also define the conjugate variable

$$Q_\lambda(\{\vec{r}_i\}; t) = \frac{\partial \ln P(\{\vec{r}_i\}; t)}{\partial \lambda} = \frac{1}{P(\{\vec{r}_i\}; t)} \frac{\partial P(\{\vec{r}_i\}; t)}{\partial \lambda},$$

and the conditional average

$$\langle q_\lambda(\vec{r}_i) \rangle = \frac{\int dq_\lambda q_\lambda P(\{\vec{r}_i\}, q_\lambda; t)}{\int dq_\lambda P(\{\vec{r}_i\}, q_\lambda; t)}.$$

The first goal is to show the equivalence of $Q_\lambda$ and $\langle q_\lambda(\vec{r}_i) \rangle$—Eq. (1) in the main text. We do this by showing that they both obey the same evolution equation.

As hinted at in the main text, we introduce an explicit Euler-type scheme for updating the particle positions. This also makes explicit the updating rule associated with the Malliavin weight. We therefore write

$$\vec{r}_i' = \vec{r}_i + \frac{D \vec{f}_i}{k_B T} \delta t + \xi_i,$$

where $\vec{r}_i'$ is the updated position of the $i$th particle at time $t + \delta t$, $\delta t$ is the time step, and the $\xi_i$ are a set of $3N$ Gaussian random variates of zero mean and variance $2D \delta t$. The corresponding updating rule for the Malliavin weight is

$$q_\lambda' = q_\lambda + \frac{1}{2k_B T} \sum_{i=1}^N \frac{\partial f_i}{\partial \lambda} \cdot \xi_i.$$

Note that the exact same sequence of random variates $\xi_i$ is used for updating the particle positions and the Malliavin weight. In this Euler scheme $P(\{\vec{r}_i\}; t)$ obeys a Chapman-Kolmogorov equation

$$P(\{\vec{r}_i\}; t + \delta t) = \int d^3 \vec{r}_i P(\{\vec{r}_i\}; t) \times W(\{\vec{r}_i\}' | \{\vec{r}_i\})$$

where the propagator is

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[17] As an alternative approach one can describe the Langevin dynamics as a hopping problem in $3N$-dimensional configuration space, using a master equation with a constant total hopping rate. Computation of sensitivity coefficients and response functions in master equation problems has been studied by Plyasunov and Arkin using the Girasol measure transform [11], by ourselves using the notion of trajectory weights [12]; and by Berthier in the context of Monte-Carlo simulations [10].
To establish Eq. (3) in the main text we use Eq. (S1) and the second half of Eq. (S2) to rearrange Eq. (S14) into the
\[ W(\{\tilde{r}'_i\}|\{\tilde{r}_i\}) = (4\pi D \delta t)^{-3N/2} \exp\left(-\sum_{i=1}^{N}(\tilde{r}'_i - \tilde{r}_i - Df_i \delta t/k_B T)^2/4D \delta t\right). \] (S7)

Differentiating the Chapman-Kolmogorov equation with respect to \( \lambda \) leads to an adjoint equation for the conjugate variable \( Q_\lambda \),
\[ Q_\lambda(\{\tilde{r}'_i\}; t + \delta t) P(\{\tilde{r}'_i\}; t + \delta t) = \int \prod_i d^3q_i Q_\lambda(\{\tilde{r}_i\}; t) + \frac{\partial \ln W}{\partial q_i} P(\{\tilde{r}_i\}; t) W(\{\tilde{r}'_i\}|\{\tilde{r}_i\}). \] (S8)

The second quantity in the square brackets in Eq. (S8) is
\[ \frac{\partial \ln W}{\partial q_i} = \frac{1}{2k_B T} \sum_{i=1}^{N} \frac{\partial f_i}{\partial q_i} \left( \tilde{r}'_i - \tilde{r}_i - Df_i \delta t/k_B T \right). \] (S9)

We now show that Eq. (S8) for the evolution of \( Q_\lambda \) is replicated by the evolution equation for the Malliavin weight. The joint probability distribution function \( P(\{\tilde{r}_i\}, q_\lambda; t) \) obeys an extended Chapman-Kolmogorov equation
\[ P(\{\tilde{r}'_i\}, q'_\lambda; t + \delta t) = \int \prod_i d^3r_i d^3\tilde{\xi}_i dq_i P(\{\tilde{r}_i\}, q_\lambda; t) P(\{\tilde{\xi}_i\}) \delta(q'_\lambda - q_\lambda - \Delta_q) \] (S10)
where
\[ \Delta_i(\tilde{r}_i, \tilde{\xi}_i) = \frac{Df_i \delta t/k_B T + \tilde{\xi}_i}{}, \quad \Delta_q(\tilde{r}_i, \tilde{\xi}_i) = \frac{1}{2k_B T} \sum_{i=1}^{N} \frac{\partial f_i}{\partial q_i} \tilde{\xi}_i \] (S11)
give the discrete increments to the particle positions and Malliavin weight. The two \( \delta \)-functions in Eq. (S10) enforce these updating rules. The function \( P(\{\tilde{\xi}_i\}) \) is a 3N-dimensional Gaussian. The 3N random variates \( \tilde{\xi}_i \) are uncorrelated and have zero mean and variance \( 2D \delta t \).

With the definitions in Eqs. (S2) and (S3) in hand we take the first moment of Eq. (S10) with respect to \( q_\lambda \) to get
\[ \langle q_\lambda(\tilde{r}'_i), t + \delta t \rangle P((\tilde{r}'_i); t + \delta t) = \int dq'_\lambda q'_\lambda P((\tilde{r}'_i); q'_\lambda; t + \delta t) \] (S12a)
\[ = \int \prod_i d^3r_i d^3\tilde{\xi}_i dq_i P(\{\tilde{r}_i\}, q_\lambda; t) P(\{\tilde{\xi}_i\}) \delta(q'_\lambda - q_\lambda - \Delta_q) \] (S12b)
\[ = \int \prod_i d^3r_i d^3\tilde{\xi}_i dq_\lambda \delta(q_\lambda + \Delta_q) P(\{\tilde{r}_i\}, q_\lambda; t) P(\{\tilde{\xi}_i\}) \delta(q'_\lambda - q_\lambda - \Delta_q) \] (S12c)
\[ = \int \prod_i d^3r_i dq_\lambda \delta(q_\lambda + \Delta_q) P(\{\tilde{r}_i\}, q_\lambda; t) W(\{\tilde{r}'_i\}|\{\tilde{r}_i\}) \] (S12d)
\[ = \int \prod_i d^3r_i (\delta(q_\lambda; \tilde{r}_i) + \Delta_q) P(\{\tilde{r}_i\}; t) W(\{\tilde{r}'_i\}|\{\tilde{r}_i\}). \] (S12e)

To progress from Eq. (S12b) to (S12e) we do successively the \( q'_\lambda \) integral, the \( \tilde{\xi}_i \) integrals, and the \( q_\lambda \) integral; using first the \( \delta \)-functions then the definition of the conditional average for the final step. In doing the \( \tilde{\xi}_i \) integrations, we recover the propagator \( W(\tilde{r}'_i|\tilde{r}_i) \) given by Eq. (S7) and the \( q_\lambda \) increment becomes
\[ \Delta_q(\tilde{r}_i, \tilde{r}'_i) = \frac{1}{2k_B T} \sum_{i=1}^{N} \frac{\partial f_i}{\partial q_i}. \] (S13)

This is identical to Eq. (S9) therefore we conclude that Eq. (S12e) for updating \( \langle q_\lambda(\tilde{r}_i) \rangle \) is identical to Eq. (S8) for updating the conjugate variable \( Q_\lambda \). By choice these two quantities can be given the same initial values, thus establishing their equivalence, in other words
\[ \int dq_\lambda P((\tilde{r}_i); q_\lambda; t) = \frac{\partial \ln P((\tilde{r}_i); t)}{\partial \lambda}. \] (S14)

To establish Eq. (S3) in the main text we use Eq. (S1) and the second half of Eq. (S2) to rearrange Eq. (S14) into the alternative form \( \int dq_\lambda P((\tilde{r}_i); q_\lambda; t) = \partial P((\tilde{r}_i); t)/\partial \lambda \). Eq. (S3) follows from this since
\[ \langle A q_\lambda \rangle = \int \prod_i d^3r_i dq_\lambda A(\{\tilde{r}_i\}) q_\lambda P(\{\tilde{r}_i\}, q_\lambda; t) \]
\[ = \int \prod_i d^3r_i A(\{\tilde{r}_i\}) \frac{\partial P((\tilde{r}_i); t)}{\partial \lambda} = \langle A \rangle \frac{\partial \langle P((\tilde{r}_i); t) \rangle}{\partial \lambda} = \frac{\partial \langle A \rangle}{\partial \lambda}. \] (S15)
Practical implementation

The implementation of MWS in a Brownian dynamics code is quite straightforward. The main point is that for efficiency one may want to update the Malliavin weight(s) according to Eq. (S5) at the same time as calculating the forces. This requires that the set of random variates \( \xi_i \) be computed and stored at the start of the step, as in the following schematic algorithm:

- generate the \( 3N \) random variates \( \xi_i \),
- compute the forces \( \vec{f}_i(\{\vec{r}_i\}) \) and the quantity \( \sum_{i=1}^N (\partial \vec{f}_i / \partial \lambda) \cdot \vec{\xi}_i \),
- update the particle positions according to Eq. (S5),
- update the Malliavin weight(s) according to Eq. (S1),
- record any quantities of interest, i.e. \( A(\{\vec{r}_i\}) \), and the value of the Malliavin weight(s).

The last item does not necessarily have to be done every time step of course. As indicated in the main text, the algorithm is initialised by setting the particle positions to their initial values and the Malliavin weights to zero. For steady state problems there are two approaches to the use of the MWS correlation function method. The simplest is to choose a set of equally spaced reference points \( t_0 = nT \) for the calculation of \( \Delta q_\lambda = q_\lambda(t) - q_\lambda(t_0) \), where \( T \) is a time period longer than the expected relaxation time of the system (which may have to be determined by trial and error). In this approach, every \( n \) timesteps the current values of \( q_\lambda(t) \) and \( A(t) \) are recorded. The running value of \( q_\lambda \) is then set to zero and the simulation continued. The time average of the stored values of \( q_\lambda A \) gives \( \partial(A) / \partial \lambda \). More efficient is to use a sliding window to calculate the correlation function. Block averaging can be used for error estimates.

Underdamped Brownian dynamics

The extension of MWS to underdamped Brownian dynamics is fairly simple. We denote the particle positions by \( \vec{r}_i \) and velocities by \( \vec{v}_i \). The dynamical equations are

\[
d\vec{r}_i = \vec{v}_i \quad \text{and} \quad m \frac{d\vec{v}_i}{dt} = \vec{f}_i - \gamma \vec{v}_i + \vec{\eta}_i
\]  

(S16)

where \( m \) is the mass, \( \gamma \) is the frictional drag coefficient, and \( \vec{\eta}_i \) are white noise terms of amplitude \( 2\gamma k_B T \). An Euler-type scheme for Eqs. (S16) is

\[
\vec{r}_i' = \vec{r}_i + \vec{v}_i \delta t \quad \vec{v}_i' = \vec{v}_i + \left( \frac{\vec{f}_i - \gamma \vec{v}_i}{m} \right) \delta t + \xi_i
\]  

(S17)

where the \( \xi_i \) are \( 3N \) Gaussian random variates of zero mean and variance \( 2\gamma k_B T \delta t / m^2 \) (note that we divided the velocity equations through by \( m \)). It follows that the probability distribution function \( P(\{\vec{r}_i\}, \{\vec{v}_i\}; t) \) evolves according to the Chapman-Kolmogorov equation

\[
P(\{\vec{r}_i'\}, \{\vec{v}_i'\}; t + \delta t) = \int \prod_i d^3\vec{r}_i d^3\vec{v}_i P(\{\vec{r}_i\}, \{\vec{v}_i\}; t) \delta(\vec{r}_i' - \vec{r}_i - \vec{v}_i \delta t) W(\{\vec{v}_i'\}|\{\vec{v}_i\}, \{\vec{r}_i\})
\]  

(S18)

where the partial propagator is

\[
W(\{\vec{v}_i'\}|\{\vec{v}_i\}, \{\vec{r}_i\}) = (4\pi \gamma k_B T \delta t / m^2)^{-3N/2} \exp\left( -\frac{\sum_{i=1}^N (\vec{v}_i' - \vec{v}_i - (\vec{f}_i - \gamma \vec{v}_i) \delta t / m)^2}{4\gamma k_B T \delta t / m^2} \right).
\]  

(S19)

If we differentiate Eq. (S18) with respect to some parameter \( \lambda \) we obtain

\[
Q_\lambda(\{\vec{r}_i'\}, \{\vec{v}_i'\}; t + \delta t) P(\{\vec{r}_i'\}, \{\vec{v}_i'\}; t + \delta t) = \int \prod_i d^3\vec{r}_i d^3\vec{v}_i \left[ Q_\lambda(\{\vec{r}_i\}, \{\vec{v}_i\}; t) + \partial \ln W / \partial \lambda \right] 
\]  

\[
\times \delta(\vec{r}_i' - \vec{r}_i - \vec{v}_i \delta t) W(\{\vec{v}_i'\}|\{\vec{v}_i\}, \{\vec{r}_i\}) P(\{\vec{r}_i\}, \{\vec{v}_i\}; t)
\]  

(S20)

where \( Q_\lambda(\{\vec{r}_i\}, \{\vec{v}_i\}; t) \equiv \partial \ln P(\{\vec{r}_i\}, \{\vec{v}_i\}; t) / \partial \lambda \). This again suggests the updating rule for the Malliavin weight, \( \dot{q}_\lambda = q_\lambda + \partial \ln W / \partial \lambda \), in other words the derivation is impervious to the presence of a \( \delta \)-function in the full propagator. Inserting the explicit expression for \( W \), and assuming the parameter of interest features only in the force law, gives the Langevin equation

\[
\frac{dq_\lambda}{dt} = \frac{m}{2\gamma k_B T} \sum_{i=1}^N \frac{\partial f_i}{\partial \lambda} \vec{\eta}_i.
\]  

(S21)
This result is very similar to the overdamped case. As a demonstration let us revisit the example of Brownian motion in a one-dimensional trap, but this time consider the underdamped case. The Langevin equations are

\[
\frac{dx}{dt} = v, \quad m \frac{dv}{dt} = -\gamma v - \kappa x + \eta,
\]

and

\[
\frac{dq_h}{dt} = \frac{mv}{\kappa^2}. \tag{S23}
\]

Fig. S1 shows simulation results confirming that \( \langle q_h(x) \rangle = \partial(x)/\partial h \).

Higher-order derivatives

We next demonstrate how MWS extends to the computation of higher-order derivatives. A double application of Eq. (3) in the main text, for two parameters \(\lambda\) and \(\mu\), gives

\[
\frac{\partial^2(A(q^\lambda)})}{\partial \lambda \partial \mu} = \langle A(q^\lambda) \rangle \langle q_{\lambda \mu} \rangle \tag{S24}
\]

where \(q_{\lambda \mu} = \partial q_\lambda / \partial \mu\). Differentiating the discrete updating rule \(q'_\lambda = q_\lambda + \partial \ln W / \partial \lambda\) with respect to \(\mu\) gives

\[
q'_{\lambda \mu} = q_{\lambda \mu} + \partial^2 \ln W / \partial \lambda \partial \mu.
\]

We insert the expression for \(W\) from Eq. S27 into this, and simplify, to find the corresponding Langevin equation

\[
\frac{dq_{\lambda \mu}}{dt} = \frac{1}{2k_B T} \sum_{i=1}^N \left[ \frac{\partial^2 f_i}{\partial \lambda \partial \mu} \right] \eta_i - \frac{D}{k_B T} \frac{\partial f_i}{\partial \lambda} \frac{\partial f_i}{\partial \mu}. \tag{S25}
\]

The new feature in this is a drift term (the last term) which has the consequence that \(\langle q_{\lambda \mu} \rangle = -\langle q_{\lambda \mu} \rangle\). This ensures that \(\partial^2 A / \partial \lambda \partial \mu = 0\) if \(A\) is a constant.

Note that, as a result of the peculiar properties of the stochastic differential calculus, Eq. (S25) is not simply found by differentiating Eq. (2) in the main text; rather one has to proceed via the discrete updating rules. Also note that the second-order Malliavin weight \(q_{\lambda \mu}\) defined in Eq. S24 must be combined with the two first-order Malliavin weights \(q_\lambda\) and \(q_\mu\) to obtain the correct weighted average in Eq. (S24). We have tested the second-order MWS scheme for the trapped interacting particle cloud under shear, see for example Fig 3 in the main text.

One-dimensional trap

Here we derive the expressions in Eqs. (4) for the transient behaviour of a particle in a one-dimensional harmonic trap. Eqs. (4) in the main text are

\[
\frac{dx}{dt} = -\kappa x + \eta, \quad \frac{dq_h}{dt} = \frac{\eta}{2T}. \tag{S26}
\]

These can be integrated to find

\[
x(t) = x_0 e^{-\kappa t} + \frac{h}{\kappa} (1 - e^{-\kappa t}) + \int_0^t dt' e^{-\kappa(t-t')} \eta(t'),
\]

\[
q_h(t) = \frac{1}{2T} \int_0^t dt' \eta(t'). \tag{S27}
\]

Since \(x\) and \(q_h\) are summed Gaussian random noises, it follows that \(P(x, q_h; t)\) is a Gaussian—cf. §3.5.2 in The Theory of Polymer Dynamics M. Doi and S. F. Edwards (OUP, 1986). To characterise this Gaussian, it suffices to calculate the first and second moments. The first moments follow immediately from Eqs. (S27) and are \(x = x_0 e^{-\kappa t} + (h/\kappa)(1 - e^{-\kappa t})\) and \(q_h = 0\), as given in the first line of Eqs. (4). Therefore \(x = \langle x \rangle = \int_0^t dt' e^{-\kappa(t-t')} \eta(t')\).

The second moment of \(x\) (the second line of Eqs. 4) is

\[
\langle x^2 \rangle - \langle x \rangle^2 = \int_0^t dt' \int_0^{t'} dt'' e^{-\kappa(t-t')} e^{-\kappa(t-t'')} \times 2T \delta(t' - t'') = \frac{T}{\kappa} (1 - e^{-2\kappa t}) \tag{S28}
\]
where we have used $\langle \eta(t')\eta(t'') \rangle = 2T \delta(t' - t'')$. Likewise the cross correlation term and the second moment of $q_h$ (the third line of Eqs. S3) are

$$\langle q_h \rangle = \frac{1}{2T} \int_0^t dt' \int_0^t dt'' e^{-\kappa(t-t') \times 2T \delta(t' - t'')} = \frac{1}{\kappa} (1 - e^{-\kappa t})$$

$$\langle q_h^2 \rangle = \frac{1}{(2T)^2} \int_0^t dt' \int_0^t dt'' \times 2T \delta(t' - t'') = \frac{t}{2T}$$ \hspace{1cm} (S29)

Two-dimensional trap in shear

The quasi-FDT result in the main text follows from the steady state probability distribution $P_{ss}(x, y)$ for a particle in a two-dimensional trap under shear, which can be solved in closed form. Let us recall the Langevin equations for this problem,

$$\frac{dx}{dt} = -\kappa x + \dot{\gamma} y + \eta_x, \quad \frac{dy}{dt} = -\kappa y + \eta_y, \hspace{1cm} \text{(S30)}$$

where $\kappa$ is the trap strength and $\dot{\gamma}$ is the shear rate. In common with the main text we set the particle mobility to unity and write temperature in terms of Boltzmann’s constant, so that we can write $D = T$ for the diffusion coefficient.

From the Smoluchowski equation, the steady-state distribution function corresponding to these Langevin equations satisfies

$$\frac{\partial J_x}{\partial x} + \frac{\partial J_y}{\partial y} = 0 \hspace{1cm} \text{(S31)}$$

where the components of the probability current (flux) are

$$J_x = (-\kappa x + \dot{\gamma} y)P_{ss} - T \frac{\partial P_{ss}}{\partial x}, \hspace{1cm} \text{(S32)}$$

$$J_y = -\kappa y P_{ss} - T \frac{\partial P_{ss}}{\partial y}.$$ 

Since the Langevin equations are linear, we expect that $P_{ss}$ will be a bivariate Gaussian so we write

$$P_{ss} \sim \exp(-\frac{1}{2}Ax^2 - \frac{1}{2}By^2 - Cxy) \hspace{1cm} \text{(S33)}$$

where $A$, $B$, and $C$ are coefficients, to be determined. The simplest way to proceed is to insert this as an ansatz into Eqs. S31 and S32, to find that the coefficients have to satisfy

$$2\kappa = (A + B)T, \hspace{1cm} A\kappa = (A^2 + C^2)T, \hspace{1cm} B\kappa = C\dot{\gamma} + (B^2 + C^2)T, \hspace{1cm} C\kappa = A\dot{\gamma}/2 + (A + B)CT.$$ \hspace{1cm} (S34)

These four conditions arise from equating to zero the constant term and the coefficients of $x^2$, $y^2$ and $xy$ in Eq. S31. Although there are only three unknowns, Eqs. S31 and S32 are interdependent and admit the unique solution,

$$A = \frac{4\kappa^3}{(\dot{\gamma}^2 + 4\kappa^2)T}, \quad B = \frac{4\kappa^3 + 2\kappa \dot{\gamma}^2}{(\dot{\gamma}^2 + 4\kappa^2)T}, \quad C = -\frac{2\dot{\gamma} \kappa^2}{(\dot{\gamma}^2 + 4\kappa^2)T}.$$ \hspace{1cm} (S35)

Hence the complete steady state distribution function is

$$P_{ss} = \frac{\kappa^2}{\pi T \sqrt{\dot{\gamma}^2 + 4\kappa^2}} \times \exp \left[ - \frac{2\kappa^3 x^2 + (2\kappa^3 + \kappa \dot{\gamma}^2) y^2 - 2\dot{\gamma} \kappa^2 xy}{(\dot{\gamma}^2 + 4\kappa^2)T} \right].$$ \hspace{1cm} (S36)

For reference, the associated moments are

$$\langle x^2 \rangle_{ss} = \frac{T}{\kappa} \left(1 + \frac{\dot{\gamma}^2}{2\kappa^2}\right), \quad \langle y^2 \rangle_{ss} = \frac{T}{\kappa}, \hspace{1cm} \text{(S37)}$$

$$\langle xy \rangle_{ss} = \frac{\dot{\gamma} T}{2\kappa^2}.$$ 

Differentiating the steady state distribution with respect to the shear rate yields

$$\langle q_{xy} \rangle = \frac{\partial \ln P_{ss}}{\partial \dot{\gamma}}$$

$$= \frac{2\kappa^2(2\kappa x - \dot{\gamma} y)(\dot{\gamma} x + 2\kappa y)}{(\dot{\gamma}^2 + 4\kappa^2)T} - \frac{\dot{\gamma}}{\dot{\gamma}^2 + 4\kappa^2}.$$ \hspace{1cm} (S38)

In the limit $\dot{\gamma} \to 0$ this reduces to $\langle q_{xy} \rangle = xy/2T$. An immediate application of this is to deduce the quasi-FDT result in the main text:

$$\frac{\partial \langle xy \rangle}{\partial \dot{\gamma}} \bigg|_{\dot{\gamma} = 0} = \frac{(x^2y^2)}{2T}.$$ \hspace{1cm} (S39)