

Computing diffusion coefficients in macromolecular simulations: the Diffusion Coefficient Tool for VMD

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Software

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Summary

Computing diffusion coefficients from classical molecular dynamics (MD) simulations is a common task when assessing solvent and lipid dynamics both in bulk and in confined regions. Solute-modulated lateral diffusion of lipids is especially interesting in biological membranes, where it plays a role in receptor activity and raft formation (Dainese et al., 2014).

The Diffusion Coefficient Tool is an analysis plugin for the Visual Molecular Dynamics (VMD) analysis environment (Humphrey, Dalke, & Schulten, 1996), which computes various types of diffusion coefficients for a molecular species from simulated trajectories.

Method

Diffusion coefficients are computed on the basis of time- and ensemble-averaged squared displacement (MSD) of the chosen molecular species. The MSD $M(\tau)$ is defined by fixing an arbitrary time origin and a *lag time* τ as the mean displacement over that interval:

$$M(\tau) = \langle |\mathbf{r}(\tau) - \mathbf{r}(0)|^2 \rangle$$

where $\mathbf{r}(t)$ indicates the position of a particle at time t , and the angle brackets indicate an average over all particles of the species under analysis. In practice, to improve convergence, the MSD analysis is repeated using different time origins, under the equilibrium assumption. If the system is in a diffusive regime and the position measurement error is negligible, the diffusion coefficient can be obtained through Einstein's relation:

$$D(\tau) = M(\tau)/2E\tau$$

where E is the dimensionality of the system (integer, $1 \leq E \leq 3$). In general, MSD values at multiple lag times are computed from the same trajectory to check their linearity and asymptotic slope in τ to check diffusivity and average out measurement errors (Martin, Forstner, & Käs, 2002).

Implementation

After installation, the plugin is accessible from VMD in the *Extensions - Analysis - Diffusion Coefficient Tool* menu. The analysis is run on the currently loaded trajectory in the *top* molecule (Figure 1). The diffusion coefficient tool can be used either interactively with its

graphical user interface (GUI, Figure 1), or calling the `diffusion_coefficient` procedure in VMD's embedded TCL language.

The tool can compute the following quantities:

- $M(\tau)$ ("MSD displacement" GUI button, or procedure argument `-msd`)
- "Instantaneous" $D(\tau) = M(\tau)/2E\tau$, valid as long as diffusivity holds and position errors are small (button "Diffusion coefficient", argument `-d`)
- D (and its standard error) through least-squares fitting of $M(\tau)$ to $2ED\tau + \sigma$ (button "Linear fit", argument `-fitD`).

The results are either plotted (GUI) or returned as a list (procedure call). The following table lists the correspondence between the GUI and procedure arguments.

GUI text	Procedure argument	Default value
Selection	<code>-selection</code>	water and noh
Diffusion along	<code>-alongx</code> , etc.	3D
Subtract drift	<code>-remove_drift</code>	Enabled
τ from	<code>-from</code>	Trajectory length / 10
τ to	<code>-to</code>	Trajectory length / 2
τ step	<code>-step</code>	Trajectory length / 50
Analysis from	<code>-interval_from</code>	Trajectory start
Analysis to	<code>-interval_to</code>	Trajectory end
Analysis step	<code>-interval_step</code>	All frames
Time between frames	<code>-dt</code>	1 ns

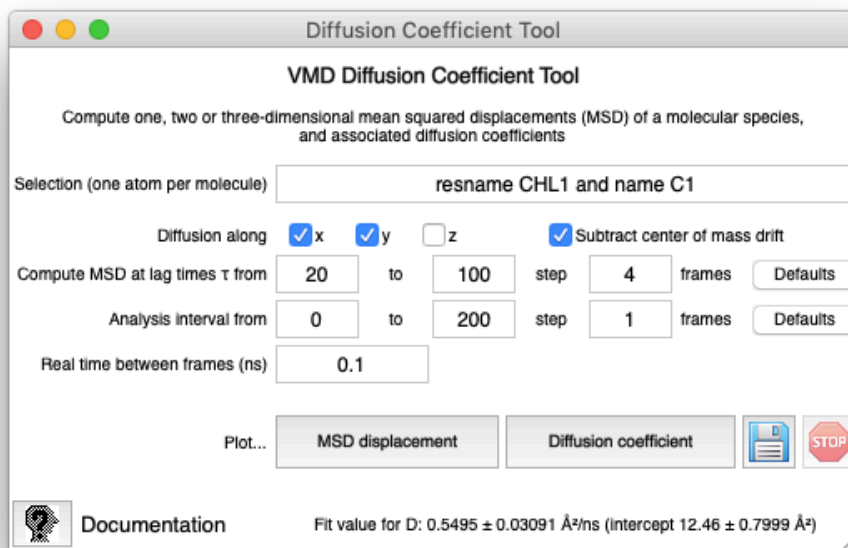


Figure 1: The main window of Diffusion Coefficient Tool

The time averaging scheme and interpretation of the interval window parameters is shown

in Figure 2: averaging occurs over the windows of span τ that can be constructed in the analysis interval, strided by an *interval step*. The analysis is repeated for the chosen values of τ , ranging from a minimum to a maximum, again with a stride.

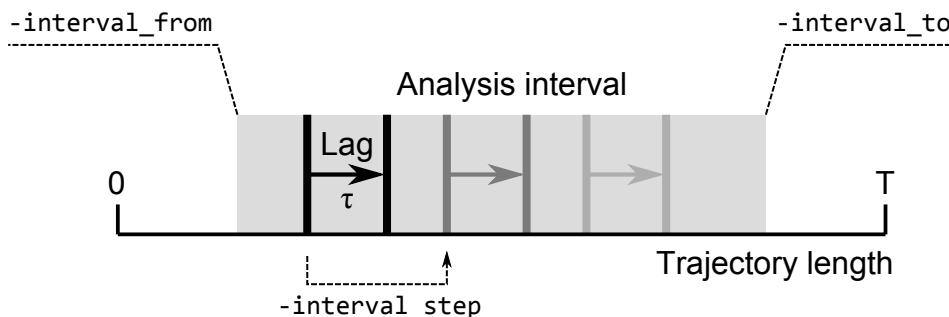


Figure 2: The interval selection parameters and time-averaging scheme. The MSD samples being averaged are indicated by shades of grey.

Note that obtaining *converged* MSD values from MD simulations requires an aggregated sampling much larger than the characteristic time τ . In common MD regimes such sampling can only be achieved as long as several equivalent atoms are available for averaging. For this reason, the plugin provides an atom selection, which must match one atom per diffusing molecule, for MSD values to be averaged over.

Related tools

MEMBPLUGIN is a VMD plugin which implements additional analysis types specifically for quasi-planar bilayer simulations (Guixà-González et al., 2014). This tool's regression test is based on the case study trajectories provided with MEMBPLUGIN. The `gmx msd` utility is distributed with GROMACS and performs a similar MSD calculation from the command line shell (Lemkul, 2019).

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