that there is no accumulation of errors for the overall translational and rotational degrees of freedom. When $1/\xi_i$ is small compared to the time scales present in the system, the dynamics will be completely different from MD, but the sampling is still correct.

In GROMACS there are two algorithms to integrate equation (3.108): an efficient one, where the relative error in the temperature is $\frac{1}{2}\Delta t\,\xi$, and a more complex leap-frog algorithm [46], which has third-order accuracy for any value of $\Delta t\,\xi$. In this complex algorithm four Gaussian random number are required per integration step per degree of freedom, and with constraints the coordinates need to be constrained twice per integration step. Depending on the computational cost of the force calculation, this can take a significant part of the simulation time. Exact continuation of a stochastic dynamics simulation is not possible, because the state of the random number generator is not stored. When using SD as a thermostat, an appropriate value for ξ is 0.5 ps^{-1}, since this results in a friction that is lower than the internal friction of water, while it is high enough to remove excess heat (unless plain cut-off or reaction-field electrostatics is used). With this value of ξ the efficient algorithm will usually be accurate enough.

3.9 Brownian Dynamics

In the limit of high friction, stochastic dynamics reduces to Brownian dynamics, also called position Langevin dynamics. This applies to over-damped systems, *i.e.* systems in which the inertia effects are negligible. The equation is:

$$\frac{\mathrm{d}\boldsymbol{r}_i}{\mathrm{d}t} = \frac{1}{\gamma_i}\boldsymbol{F}_i(\boldsymbol{r}) + \mathring{\boldsymbol{r}}_i \tag{3.109}$$

where γ_i is the friction coefficient [amu/ps] and $\mathring{\boldsymbol{r}}_i(t)$ is a noise process with $\langle \mathring{r}_i(t)\ \mathring{r}_j(t+s)\rangle = 2\delta(s)\delta_{ij}k_BT/\gamma_i$. In GROMACS the equations are integrated with a simple, explicit scheme:

$$\boldsymbol{r}_i(t+\Delta t) = \boldsymbol{r}_i(t) + \frac{\Delta t}{\gamma_i}\boldsymbol{F}_i(\boldsymbol{r}(t)) + \sqrt{2k_BT\frac{\Delta t}{\gamma_i}}\,\boldsymbol{r}_i^G \tag{3.110}$$

where $\boldsymbol{r}_i^G$ is Gaussian distributed noise with $\mu = 0$, $\sigma = 1$. The friction coefficients γ_i can be chosen the same for all particles or as $\gamma_i = m_i/\xi_i$, where the friction constants ξ_i can be different for different groups of atoms. Because the system is assumed to be over-damped, large timesteps can be used. LINCS should be used for the constraints since SHAKE will not converge for large atomic displacements. BD is an option of the `mdrun` program.

3.10 Energy Minimization

Energy minimization in GROMACS can be done using steepest descent, conjugate gradients, or l-bfgs (limited-memory Broyden-Fletcher-Goldfarb-Shanno quasi-Newtonian minimizer... we prefer the abbreviation). EM is just an option of the `mdrun` program.