7. Summary

Model reduction for molecular problems is mainly understood as the identification of suitable reaction coordinates and the calculation of free energy profiles along these. This thesis addresses model reduction for both mechanical models and stochastic differential equation from the unifying viewpoint of geometric mechanics, thereby reviewing and extending available techniques (e.g., from celestial mechanics or climate modelling) to dynamical molecular problems.

We present a systematic elaboration of the transformation properties of such different molecular models as mechanical models, Brownian motion or hypo-elliptic Langevin equations. Regarding the latter we take advantage of the close relationship with Hamiltonian systems and demonstrate that the Itô-Stratonovich ambiguity vanishes, if we confine our attention to point transformations (i.e., symplectic lifts of transformations of the configuration variables). A central paradigm in reduced modelling is the (thermodynamical) free energy. We give a detailed and concise analysis of different notions of free energy (standard and geometric free energy) and develop a generalized version of the famous Blue Moon Ensemble method which does not make any reference to the underlying dynamical system. Most notably, we gain precise understanding of the notion *free energy as the potential of mean (constraint) force* which allows for designing novel and efficient algorithms for the calculation of free energy profiles; a schematic overview of the various concepts can be found in Appendix A. For both diffusion and mechanical models we derive reduced models that are structure-preserving and covariant with regard to transformations of the reaction coordinate. As a common feature, we recognize that the reduced models contain the geometric free energy as an effective potential, which casts geometric free energy a fundamental dynamical quantity. In particular we show that the optimal prediction Hamiltonian can be written as a sum of kinetic energy and geometric free energy, where the kinetic energy is defined with respect to an averaged Riemannian metric that is induced by the reaction coordinate and which is easily computed numerically. (A brief survey over the various reduction schemes is given in Section 3.5.)

Since reduced modelling essentially boils down to the calculation of geometric free energy, sampling free energy landscapes becomes a problem of its own. We solve this problem in the context of Thermodynamic Integration by introducing two novel sampling algorithms that can handle reaction coordinate constraints: First of all, we introduce a robust hybrid Monte-Carlo scheme for constrained mechanical systems, for which a strong Law of Large Numbers is proved. Additionally, we derive a constrained Langevin equation that preserves the canonical distribution. Both algorithms prove useful for the calculation of free energy profiles, and we propose a very simple Thermodynamic Integration scheme for the Langevin equation that does without Blue Moon reweighting and without the evaluation of second derivatives. We illustrate the performance of the reduction strategies by means of two paradigmatic model systems: n-butane and glycine dipeptide analogue. With regard to the former we do rather detailed numerical simulations of the reduced models comparing them against the full system. We observe that both averaged Brownian motion and optimal prediction perform remarkably well in terms of dynamical observables such as decay of correlations or transition rates between *cis* and *trans* conformations (which was rather unexpected in the case of optimal prediction). Both systems exhibit the common feature that the (extrinsic) geometry of the reaction coordinate has significant dynamical effects on the conformation dynamics that compete with the effects

induced by the potential energy (geometric free energy). Moreover optimal prediction reveals an interesting physical mechanism: the kinetic energy tends to stabilize the extended *trans* conformation by slightly increasing the total energy of the bulky *cis* transformations. Since the conformational change is actuated by an internal rotation of the molecule we have termed this effect *internal centripetal force*. For glycine the calculations confirm the former observation, namely, that the kinetic energy stabilizes the extended C5 conformations by slightly lowering their energy as compared to the C7 conformations. We moreover recognize that the kinetic energy preserves the molecular potential's symmetry under parity transformations in the Ramachandran plane of the two central backbone angles, while exhibiting even a higher symmetry. Both the configuration dependence of the effective mass and possible symmetry-breaking may lead to interesting physical effects and demand for systematic studies in the future.