Conformational and transport properties of small circular DNA molecules in dilute solution: A detailed molecular dynamics simulation study

Terpsichori Alexiou,[1] Dimitrios G. Tsalikis,[1] Panagiotis V. Alatas,[1] Vlasis G. Mavrantzas[1,2]

[1]*Department of Chemical Engineering, University of Patras & FORTH/ICE-HT, Patras, GR 26504, Greece*

[2]*Particle Technology Laboratory, Department of Mechanical and Process Engineering, ETH-Z, CH-8092 Zurich, Switzerland*

Bio-polymers such as DNA or chromosomes present immense biological and technological interest, being involved in numerous applications, such as electrophoretic separation and enzymology, structural stabilization of proteins, as well as targeted drug delivery. In recent years, significant research interest is emerging towards the understanding of the role of the molecular architecture in the dynamic and rheological properties of DNA solutions. Despite the significant progress in experimental visualization techniques, inherent experimental difficulties in studying the detailed structure of DNA at an atomistic level persist, and consequently, simulations offer an appealing alternative for the study of these systems at an atomistic resolution.

The objective of the work presented here is to explore high fidelity molecular simulations as a tool for understanding the structural and dynamic properties of solvated circular DNA molecules and how these are influenced by parameters such as concentration and molecular length. To this end, we performed detailed atomistic molecular dynamics (MD) simulations of dilute aqueous solutions of short DNA circles, also called minicircles, i.e. micro-cyclic structures that are comprised of up to a few hundred base pairs and are amenable to detailed atomistic simulations. Last generation force fields of the AMBER family have been implemented, taking into account the most recent PARMBSC1 modifications specifically developed for DNA[1]. A high computational load is required for these systems, because the number of structural units of the system (DNA and water molecules) can reach to the order of millions. The GROMACS[2] simulation package was employed to perform equilibrium MD calculations, and the resulting MD trajectories from relatively long simulations are thoroughly analyzed for the calculation of local conformational properties and (segmental and terminal) dynamics. Very good agreement of the predicted values of backbone torsion angles is observed compared to relevant experimental data. In our work, special emphasis is placed on the estimation of the mean radius-of-gyration, center-of-mass self-diffusion coefficient, and zero-shear rate viscosity, and their dependence on molecular size, ionic strength and solution concentration. The computational results presented here constitute an important stepping stone for the derivation of reliable scaling laws for describing the conformational, dynamic and rheological properties of longer circular DNA molecules.

References

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2. van der Spoel, et al. *J. Comput. Chem.* **26:** 1701-1718 (2005).