Summary:

This study utilized openmm software to conduct molecular dynamics simulations of Boltorn G4, a dendrimer-like polymer, in a water environment. The project involved the creation of a pdb file and the determination of appropriate parameters for the amber force field, utilizing MOPAC and ABALONE packages. The research findings have contributed to the understanding of Boltorn, dendrimers, hyper-branched polymers, and hydroxy-terminated polymers, which have potential for use in nanoscale applications. The simulations revealed that the Boltorn polymer experienced compression and breathing over time when solvated in water, with the compression occurring in the middle of the polymer chain.

Background:

BoltornG4 is a fourth-generation dendritic polymer that possesses favorable properties such as bio-compatibility, biodegradability, and the ability to form covalent bonds, making it a promising material for a wide range of applications, including medical devices, drug delivery, and environmental remediation. To study the behavior of BoltornG4 when solvated in water, a pdb file was created to make the polymer look like a protein to introduced to the OpenMM program, which is a free, open-source, and flexible tool used to simulate molecular dynamics at the atomic-level resolution. To simulate the behavior of BoltornG4, the Assisted Model Building with Energy Refinement (AMBER) force field was used, with the General AMBER force field (GAFF) as an extension to the AMBER force field to account for the limitations of the traditional AMBER force field for organic molecules. The AMBER force field is a mathematical model that describes the potential energy of a molecule in terms of the positions of the atoms, taking into account the interactions between atoms that are close to each other and those that are far apart. The model includes the stretching, angle bending, angle torsion, and electrostatic and van der Waal's forces, as well as the equilibration structural parameters, force constants, and torsional angle parameters. The OpenMM program uses different integrators and algorithms to compute the evolution of the system over time, and it can run simulations on various hardware platforms, including CPUs, GPUs, and FPGAs. To extract the data from the output of OpenMM, the coordinates of the output structures were obtained. Other software programs, such as Mopac and Abalone, which are used to adjust the parameters of the force field, which is essential to run the simulation into OpenMM. The use of the pdb file to make the polymer look like a protein to be introduced to the OpenMM program, is important because it allows for the simulation of the behavior of the polymer at the atomic-level resolution, providing insights into its behavior that cannot be obtained through experimental methods alone. The model is illustrated in Figure 1, which shows the stretching, angle bending, angle torsion, and electrostatic and van der Waals forces.

$$E_{\text{pair}} = \sum_{\text{bonds}} k_r(r - r_{\text{eq}})^2 + \sum_{\text{angles}} k_\theta(\theta - \theta_{\text{eq}})^2 + \sum_{\text{dihedrals}} \frac{v_n}{2} \times [1 + \cos(n\phi - \gamma)] + \sum_{i<j} \left[\frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^{6}} + \frac{q_i q_j}{\varepsilon R_{ij}}\right]$$

Figure 1 shows the mathematical model of the Amber force field, which is used in molecular dynamics simulations to predict the behavior of a molecule over time.

It consists of the equations that describe the potential energy of the molecule in terms of the positions of the atoms. The equations take into account the interactions between atoms that are close to each other, as well as the interactions between atoms that are far apart. The model includes the stretching, angle bending, angle torsion, and electrostatic and van der Waal's forces, as well as the equilibration structural parameters, force constants, and torsional angle parameters. The non-bonded potentials are characterized by the A, B, and q parameters. The dihedral angle, φ, and the phase angle, γ, are also included in the model.

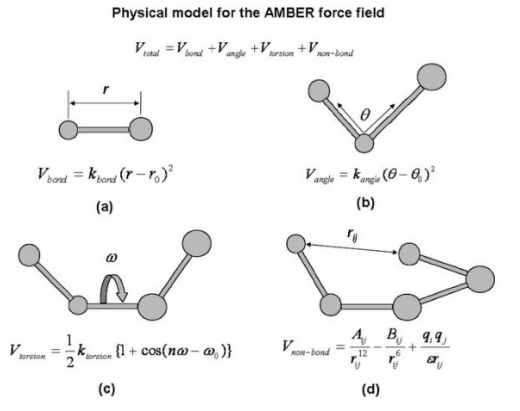

Figure2, the physical model of the Amber force field.

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URLS of used software:

OpenMM: https://openmm.org/

SAMSON: https://www.samson-connect.net/

MOPAC: http://openmopac.net/

ABALONE: http://www.biomolecular-modeling.com/Abalone/abalone-ii.html

Methods:

The methods employed in this research involved the use of molecular dynamics simulation through the OpenMM software. To construct the model of the BoltornG4 material, the SAMSON software was utilized, and a protein data bank (.pdb) file was created. The file was optimized and minimized to ensure a reliable and realistic simulation.

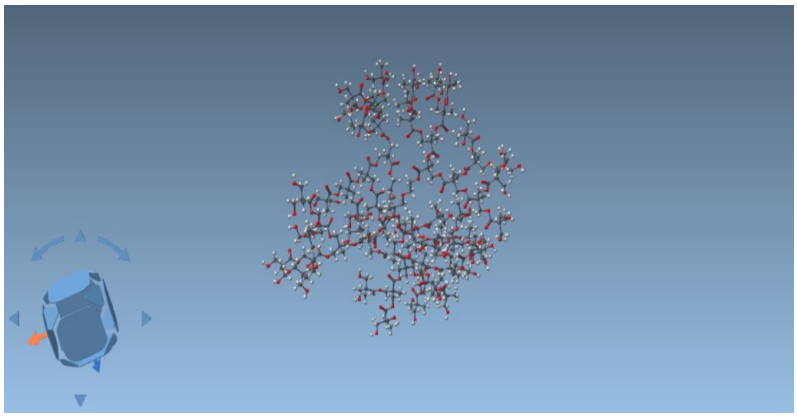

Figure 3 shows a screenshot of the PDB visualization with SAMSON software.

A modified force field was created to accurately describe the atoms in the Boltorn molecule, as the Boltorn molecule fragments were optimized in the MOPAC-PM6 software, and charge distributions were added to the AMBER force field. The force field parameters were adjusted to reflect the physical properties of the system, as some parameters necessary to describe the Boltorn structure were taken from the GAFF-force field and manually added to the Amber force field. Python scripts were used to load the model as PDB file and force field as an XML file into OpenMM.

The simulation results were obtained using the TIP3 water model in OpenMM, which is a model of water molecules that includes a partial charge distribution on the atoms of the water molecule. A simulation time refers to the length of time that the simulation is run. The simulation time used in a simulation depends on the system being simulated and the desired level of accuracy, and for this simulation a 55 seconds was consumed to run 100000 steps. A time-step of 0.002 picoseconds, which refers to the time interval used to update the positions and velocities of the atoms in the simulation. The LangevinMiddleIntegrator as the integration method, which is method used in the simulation, and it is a numerical integration method as the Verlet integration method that is used to update the positions and velocities of the atoms in the simulation. The LangevinMiddle Integrator is utilized in simulations that involve a heat pathway. The simulation was run, with the temperature of the simulation set to 300 Kelvin and a friction coefficient of 1/picosecond, which represents the amount of resistance or friction that the particles in the simulation experience as they move. The simulation was conducted in a 6.0 x 6.0 x 6.0 nm box, which contained approximately 7000 water molecules. The simulation was run on the OpenMM software on a GPU platform, and the properties of the system, such as energy, temperature, size, and dynamics, were monitored. The results were expressed using the matplotlib package through graphs, and using the built in commands in the OpenMM, which helped to extract coordinates from the output files.

Results:

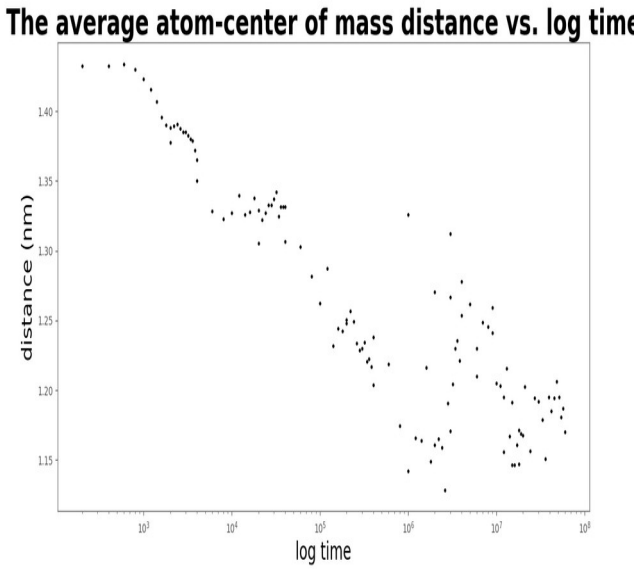

figure 4: The average distance between each atom and the center of mass of its chain vs log time for 120 structures at 1K,10K,100K,1M,10M and 30M steps, the compression of the distance by time is clear, the chain seem to deviate from compression, after long time, due to chain breathing.

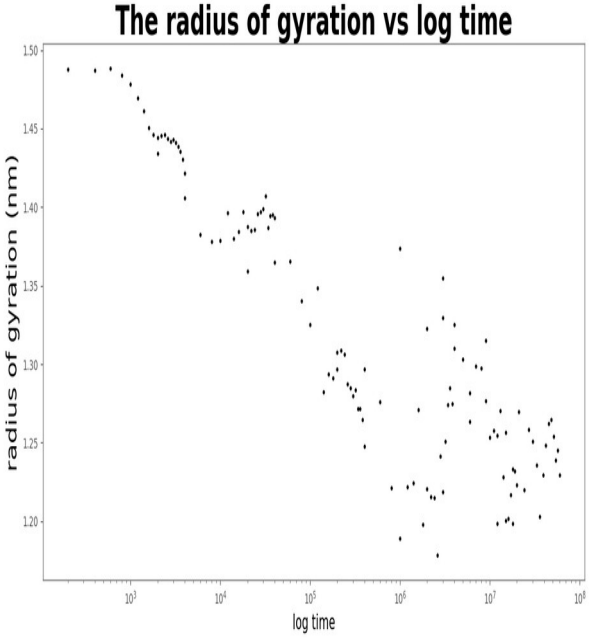

figure 5: The radii of gyration vs log time for the 120 structures, same behavior was detected as expected as the radius of gyration depends on the squared distance between atom and center of mass, and the masses.

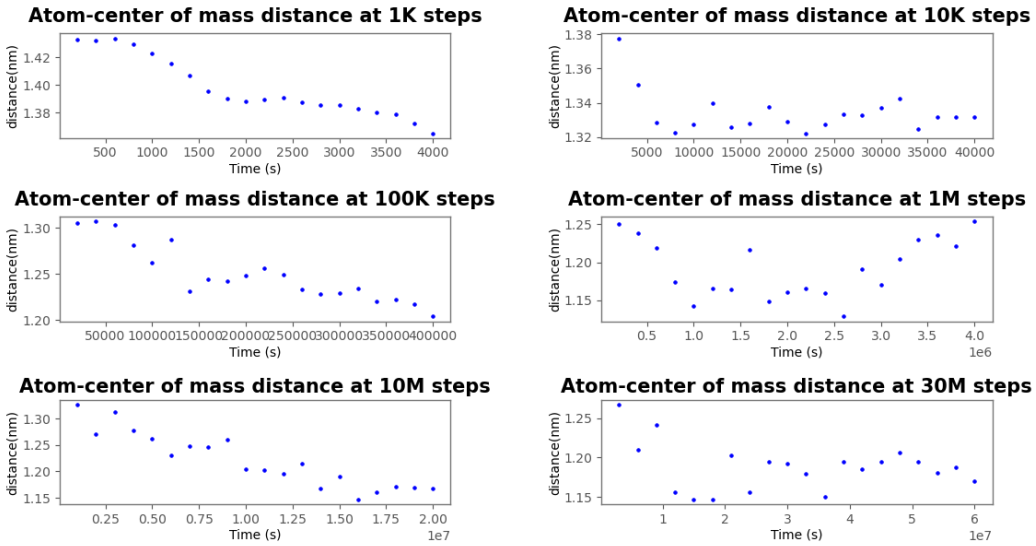

figure 6: 6 plots show how atom-center of mass distance is varying with the simulation time, generally, these curves show the compression behavior,the breathing is clear at 1M steps.

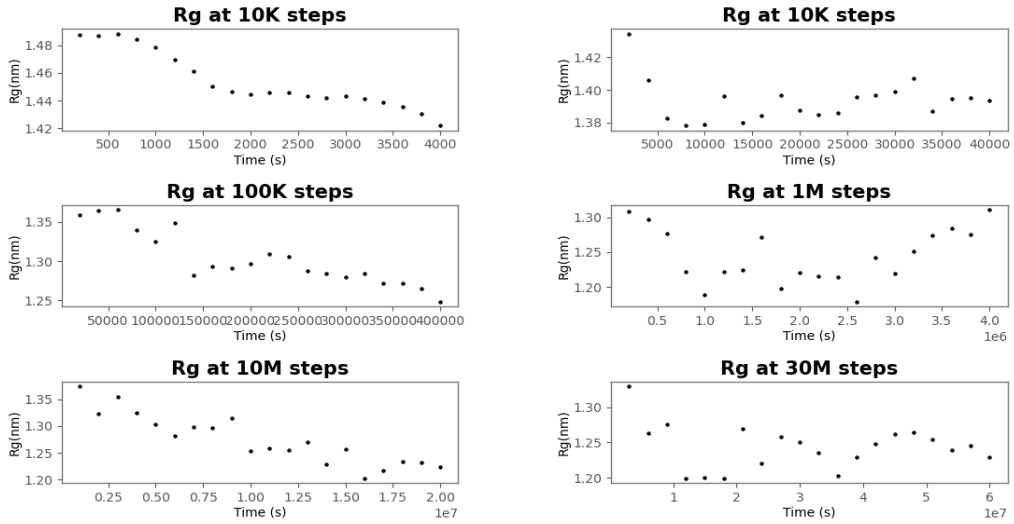

figure 7: 6 plots show how radius of gyration is varying with the simulation time, generally, these curves show the compression behavior,the breathing is clear at 1M steps.

We divide the molecule into ten shells, to study the atoms distribution and the density of every shell, to get closer view in the monomers distribution.

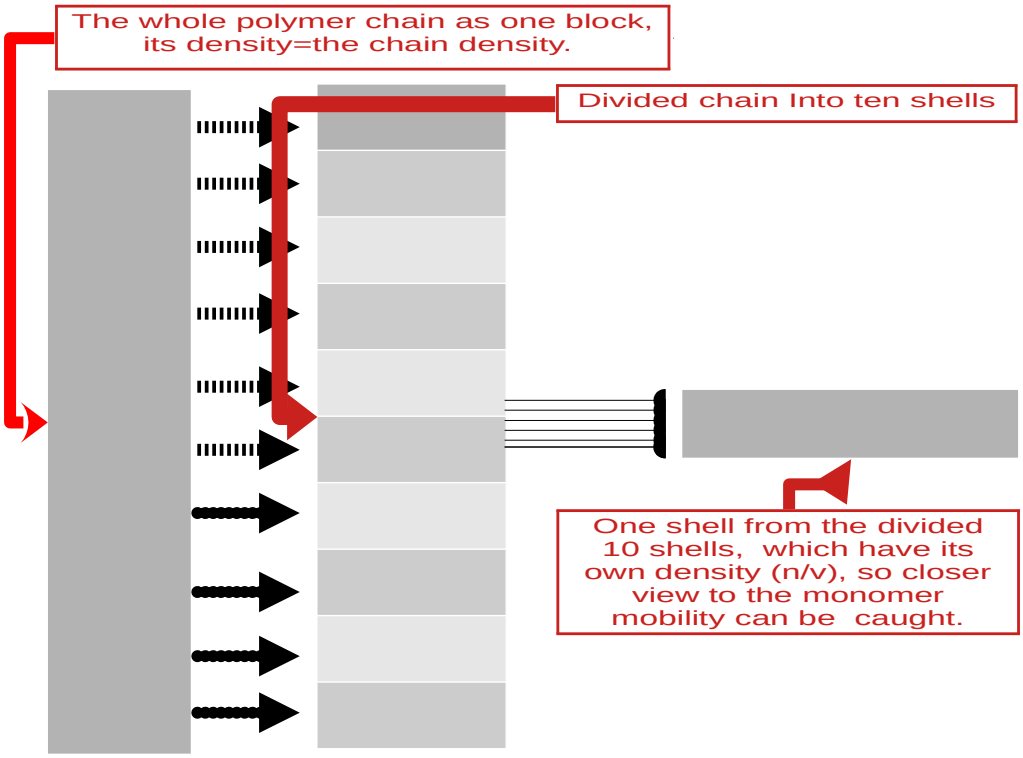

Figure 8: Explanation of dividing a molecule into shells.

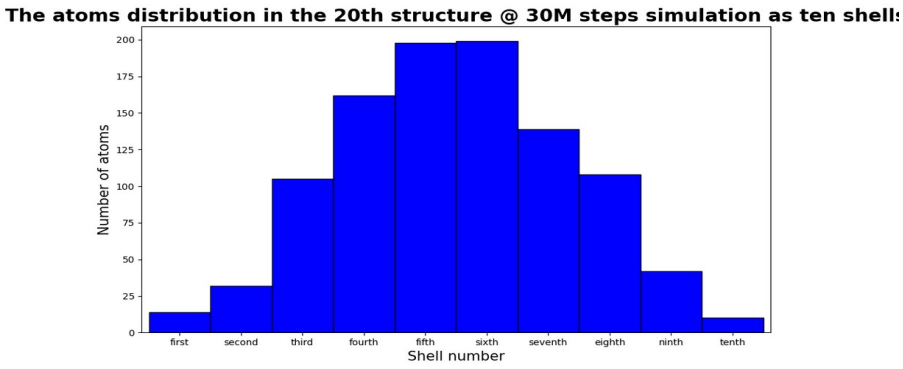

figure 9: shows histogram of the 20th structure after 0.06 milliseconds in water, divided into 10 shells, every shell represents the distance atom-center of mass, we know from the previous figure that the atoms tend to compressed in the middle, it means that there is a lot of atom distributed in a small distance in the middle. Every value of these distances is atom-center of mass, it means that is represents one atom so the y axis is number of atoms.

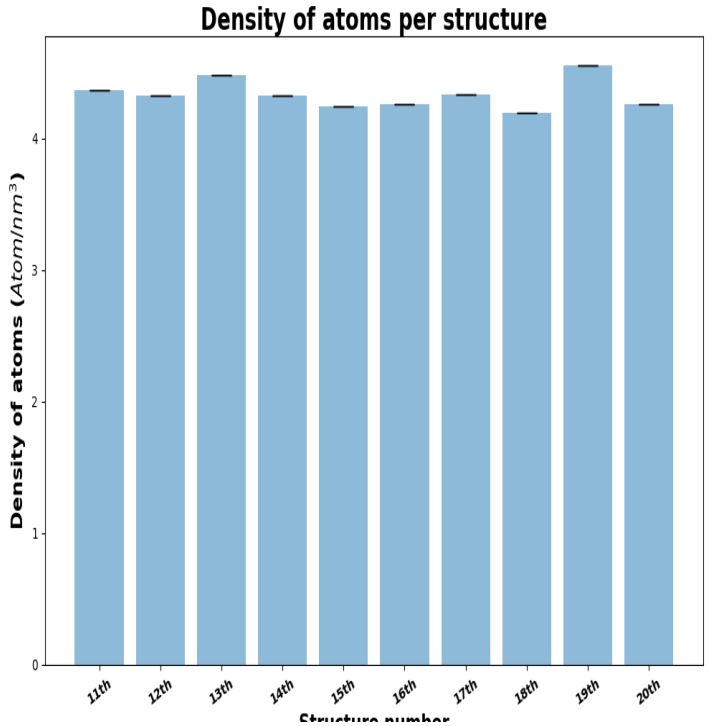

figure10: shows the densities of the whole structure, and it shows that the atom density has little fluctuations.

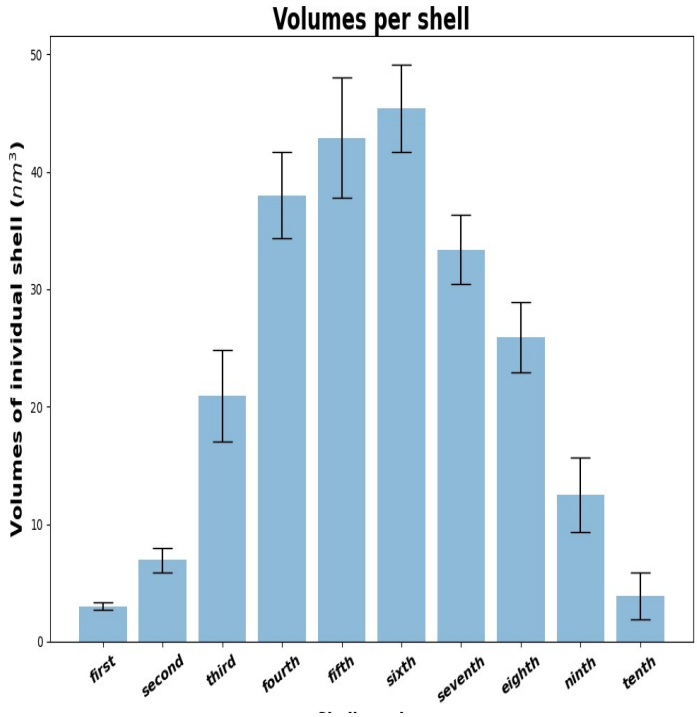

figure11: shows the mean volumes per shell, and it shows that the volume increases by the shell number until the sixth shell, then it starts to decreases. The maximum volume is a shell number 6

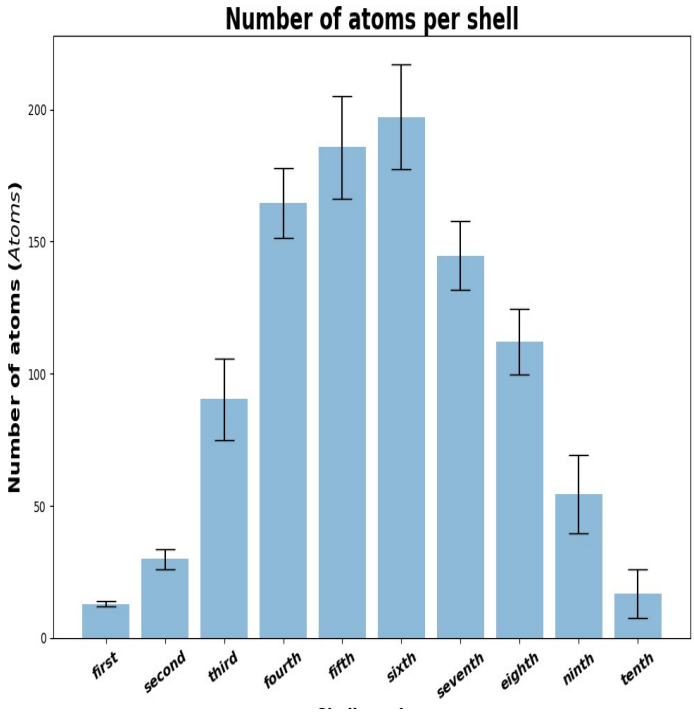

figure12: shows the number of atoms per shell, it increases by shell number, until shell number 6, then starts to decrease, as the volumes. That give reason why the density of shells is constant while there is a mobility of monomers towards mid-shells.

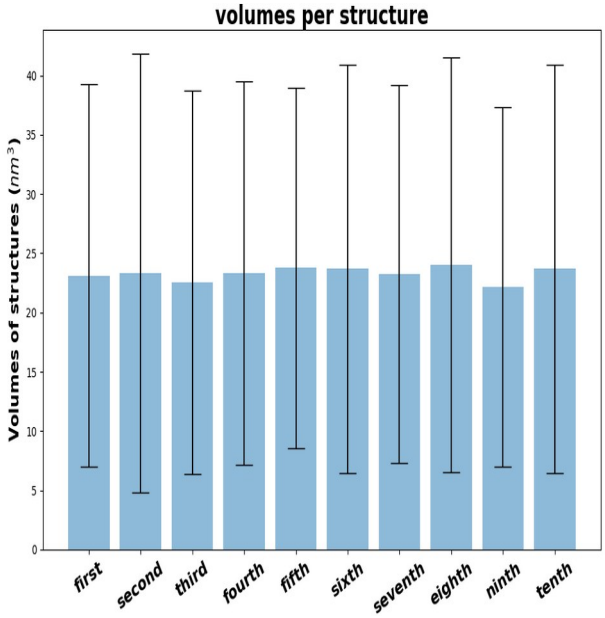

figure13: shows the volume of structure, it shows little fluctuations of the volumes of structure during the simulation.

The number of atoms in the shell number 1 in the last ten structures respectively = [13, 14, 13, 13, 13, 14, 13, 13, 10, 14]

The number of atoms in the shell number 2 in the last ten structures respectively = [26, 29, 22, 32, 34, 31, 30, 35, 29, 32]

The number of atoms in the shell number 3 in the last ten structures respectively = [94, 80, 69, 89, 121, 77, 92, 99, 78, 105]

The number of atoms in the shell number 4 in the last ten structures respectively = [176, 181, 152, 165, 158, 165, 156, 186, 144, 162]

The number of atoms in the shell number 5 in the last ten structures respectively = [174, 215, 169, 200, 174, 207, 176, 189, 154, 198]

The number of atoms in the shell number 6 in the last ten structures respectively = [193, 202, 215, 199, 169, 171, 189, 197, 238, 199]

The number of atoms in the shell number 7 in the last ten structures respectively = [145, 139, 165, 119, 148, 157, 158, 137, 140, 139]

The number of atoms in the shell number 8 in the last ten structures respectively = [118, 108, 118, 106, 117, 132, 126, 96, 93, 108]

The number of atoms in the shell number 9 in the last ten structures respectively = [56, 35, 64, 66, 60, 40, 57, 42, 83, 42]

The number of atoms in the shell number 10 in the last ten structures respectively = [14, 6, 22, 20, 15, 15, 12, 15, 40, 10]

Discussion:

The analysis of the simulation data revealed the chain started in an extended conformotion, as shown in figures 3, 4, 5, and 6. The compression is evident in the decreasing distance between the atoms and the center of mass of the chain, as well as in the decreasing radius of gyration, until the time of 4 nanoseconds. The chain starts to relax as it exhibited breathing behavior, as shown in figures 3 and 6, where the compression fluctuating after a long time, the extended conformation starts again. A dividing of the molecule into ten shells is a good method to give a closer view on atom distribution through the chain. We find the volume changes with the number of atoms, thats why the density curve has a little fluctuating figure 9.

Overall, the analysis of the simulation data provided insights into the atom distribution, density mobility, and compression behavior of the chain over time, and fluctuation in the conformations after about 250K picoseconds as time-steps.

Conclusions:

The simulations revealed that the Boltorn polymer has then reached a dynamic equilibrium and is sampling physically relevant conformations.

Appendix:

Revision history:

Version	Changes	Date	Initials	Sign
v1	New			