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Force-induced structural changes in non-sulfated carrageenan based oligosaccharides – a theoretical study

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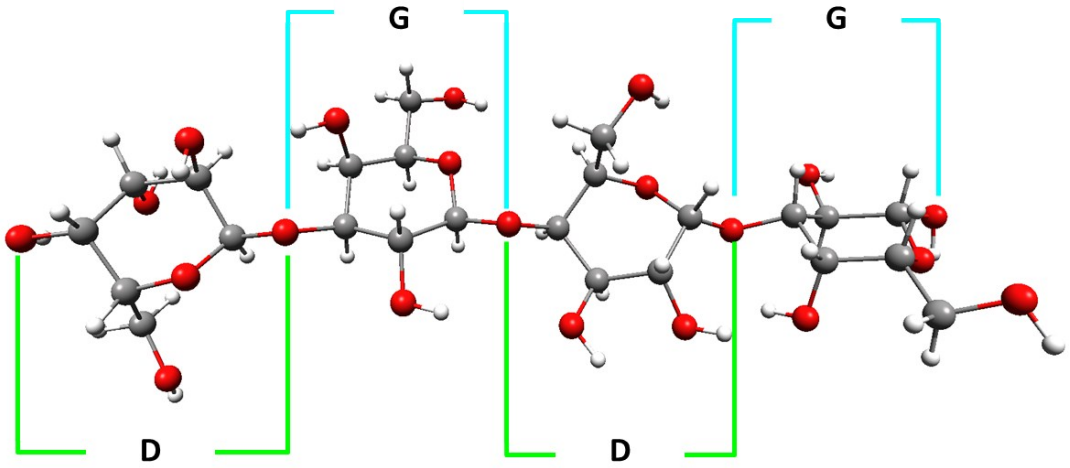
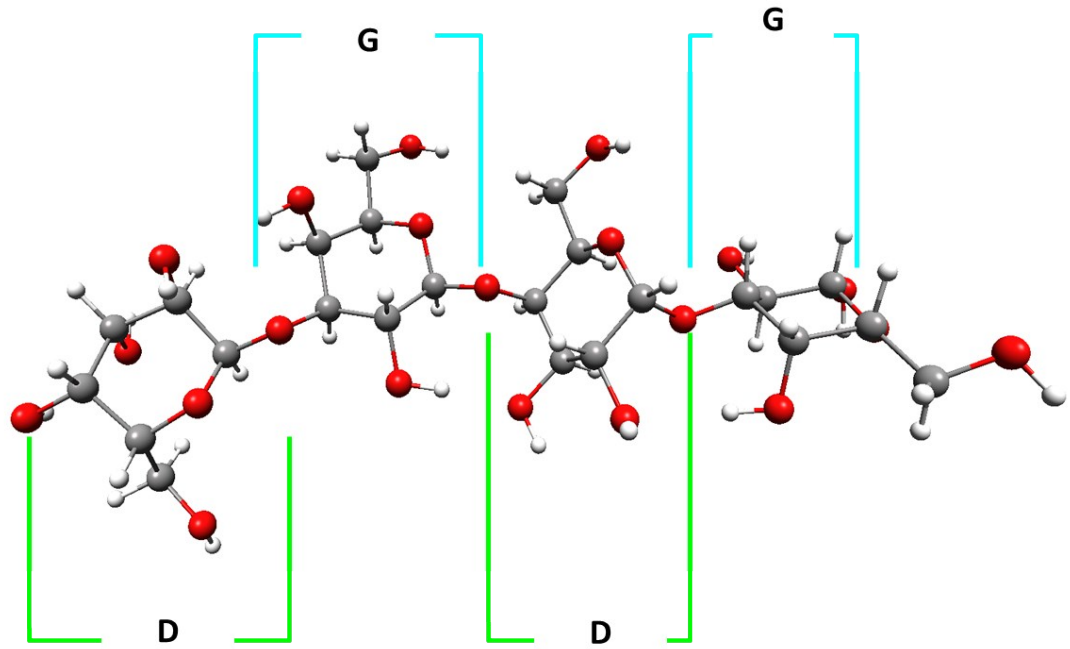
Supplementary Materials

Tab. 1A. Energy values for selected structures (verified as minima and transition states) for the EGO history of optimization for selected forces.

f [au]	Starting structure			TS1			MIN1			TS2			Resulting structure (MIN2)		
	E [au]	v[cm^{-1}]	L [Å]	E [au]	v [cm^{-1}]	L [Å]	E [au]	v [cm^{-1}]	L [Å]	E [au]	v[cm^{-1}]	L [Å]	E [au]	v [cm^{-1}]	L [Å]
0.048				-687.1708672	-86.53	4.856	-687.1719115	+54.24	5.023	-687.1602172	-90.72	5.240	-687.1739643	+64.88	5.490
0.050				-687.1708675	-86.71	4.855	-687.1719118	+54.43	5.023	-687.1602173	-91.19	5.239	-687.1739639	+64.79	5.489
0.056	-687.1851592	+76.57	4.529	-687.1708649	-87.50	4.855	-687.1719115	+54.18	5.023	-687.1602162	-91.42	5.238	-687.1739631	+64.95	5.490
0.060				-687.1708632	-86.20	4.856	-687.1719124	+54.41	5.023	-687.1602199	-90.29	5.236	-687.1739657	+64.87	5.489
0.065				-687.1708644	-86.78	4.856	-687.1719123	+54.43	5.023	-687.160219	-90.00	5.242	-687.1739678	+64.92	5.489



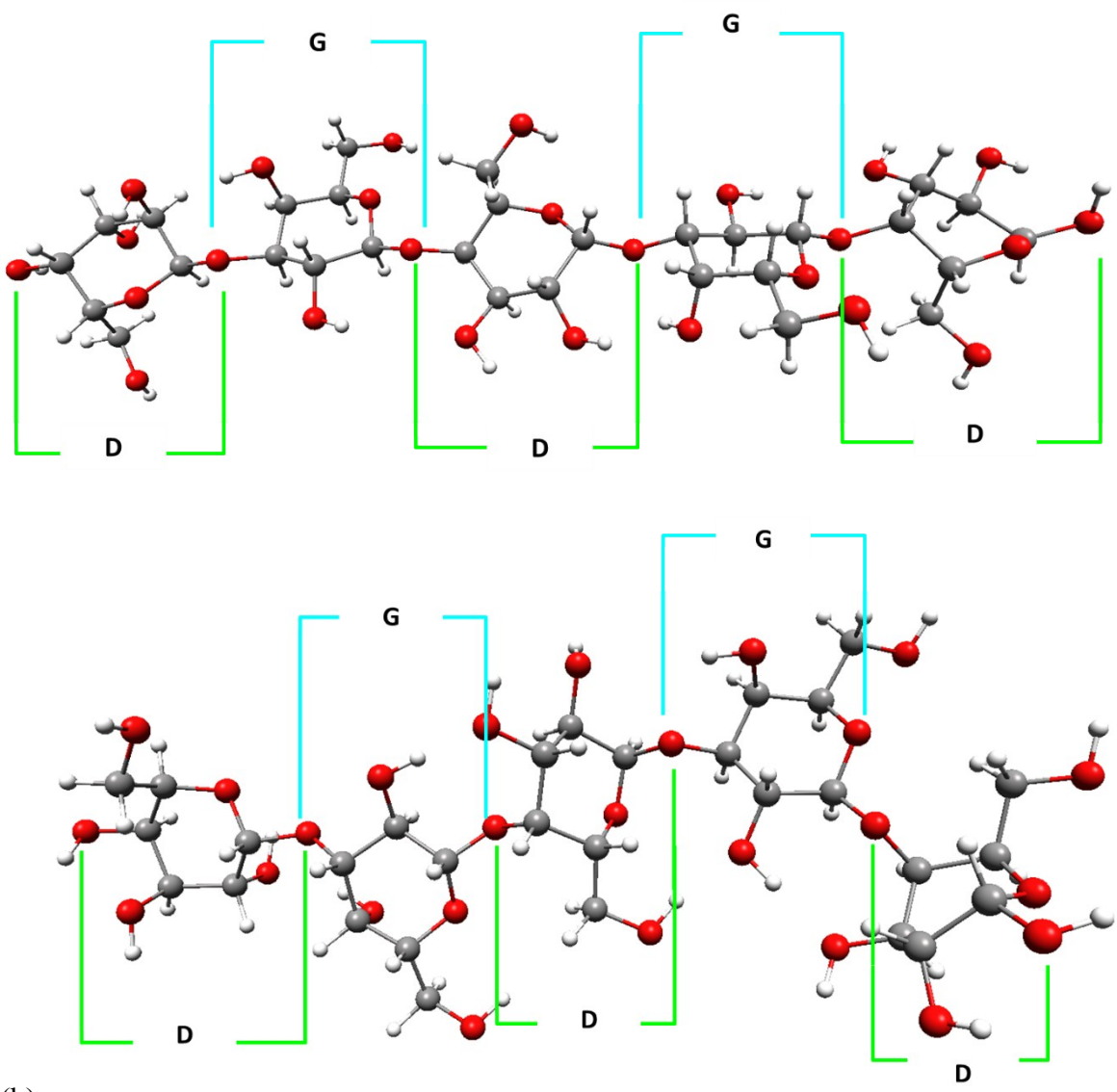
(a)



(b)

Fig. 1A The stretched (a) and relaxed (b) structure of the **DGDG** tetramer for the external force $f = 0.055$ au.

(a)



(b)

Fig. 2A The stretched (a) and relaxed (b) structure of the **DGDGD** pentamer for the external force $f = 0.060$ au.

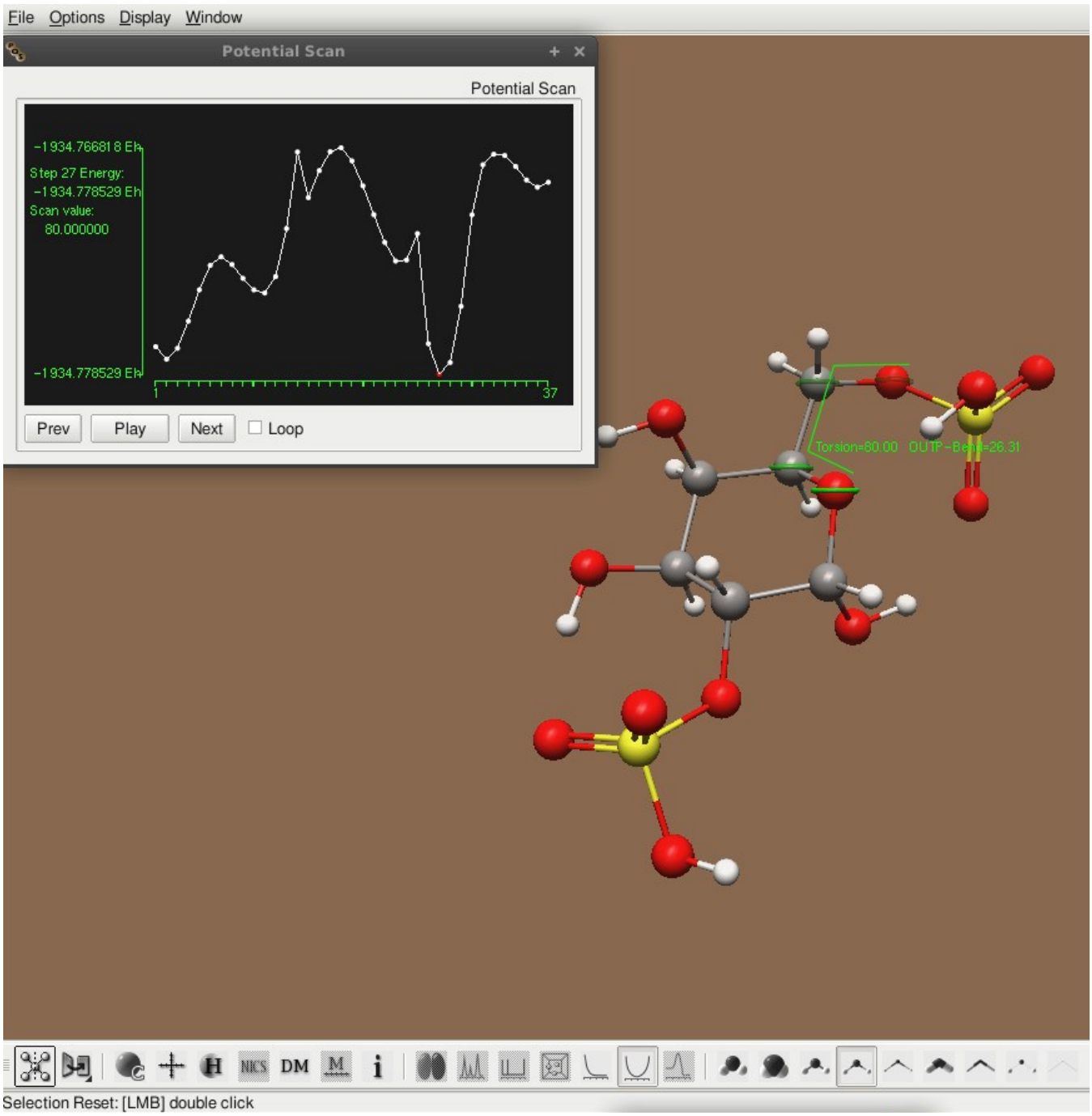


Fig 3A The potential scan along the dihedral angle O6C5C6O in the D2S6S structure

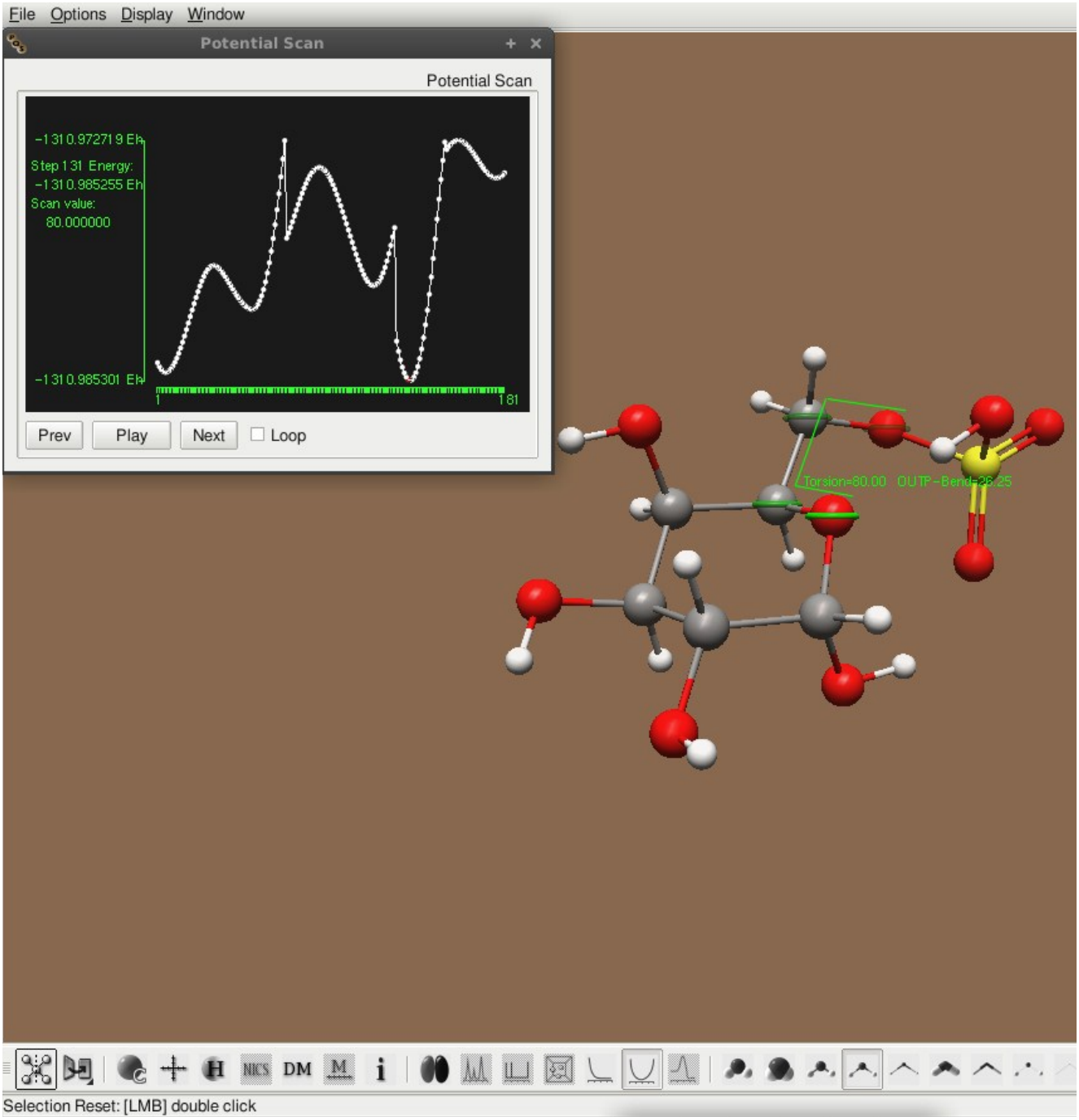


Fig 4A The potential scan along the dihedral angle O6C5C6O in the D6S structure.

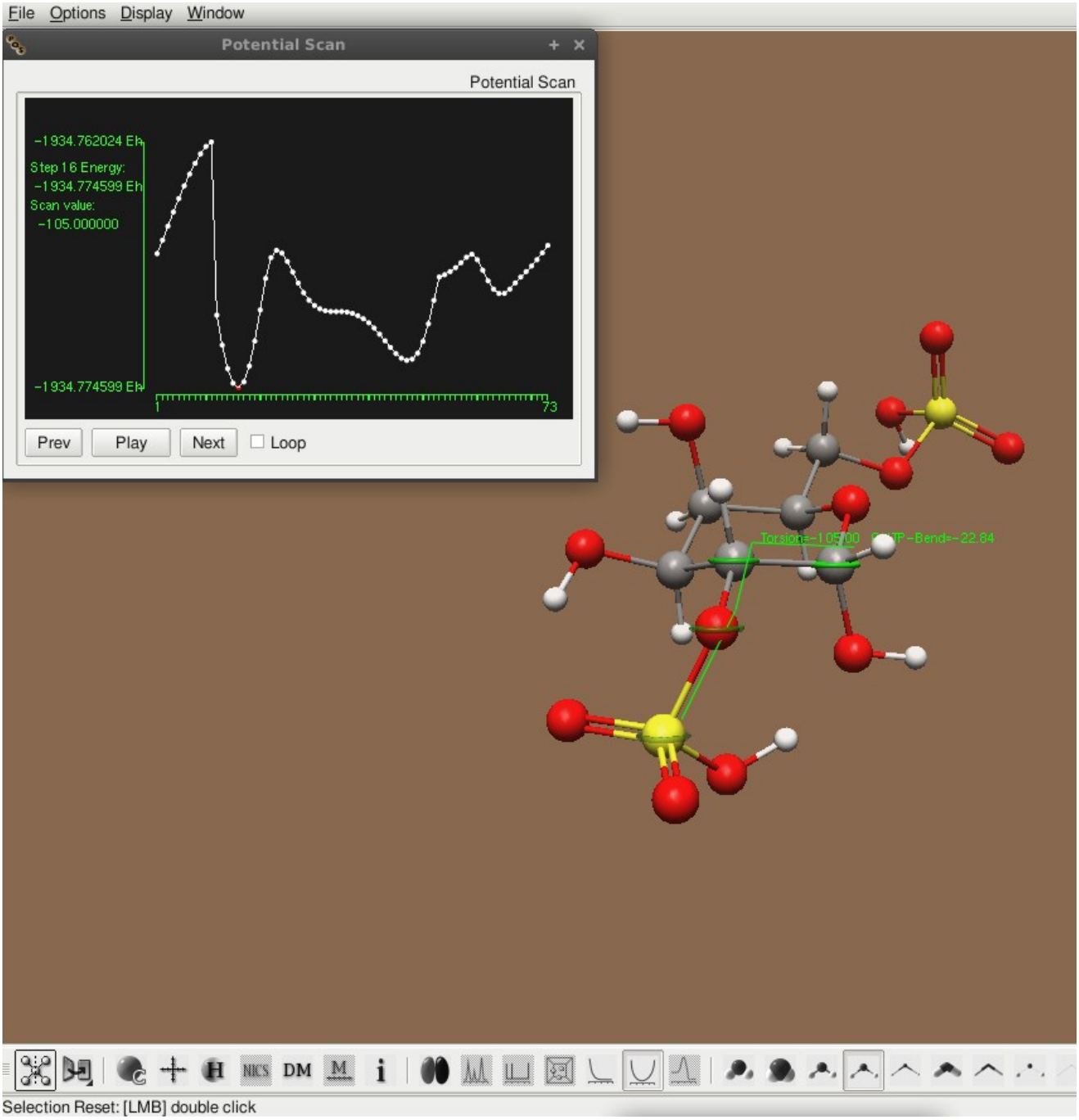


Fig 5A The potential scan along the dihedral angle C1C2OS in the D2S6S structure.

Methods

The molecular systems of interest consisted of single, unfunctionalized monosaccharide molecule (α-D-galactopyranose) either immersed in water or in vacuum. The initial geometries relied on the structures obtained in the results of our previous study [1] and corresponded to the favorable conformations of the α-D-Gal molecule in aqueous solutions [2,3]. This includes the ring conformation in the $^4C_1$ geometry and the hydroxymethyl group in the *trans* position with respect to the C_4 carbon atom. The dimensions of the simulation cell were equal to ~ 3.0 × 3.0 × 3.0 nm^3.

All QM-MM/MD simulations were performed by using the GROMACS 4.5.5 package [4]. The QM (DFT-derived) [5,6] potentials were calculated every step by applying the 6-31G basis set [7] and BLYP functional [8]. The ORCA 2.9 software [9] was used for that purpose. The QM potentials were used to describe the interactions within the selected parts of the system (i.e. the whole saccharide molecule), while the saccharide molecule interacts with its environment (i.e. with the remaining water molecules, if present in the system) *via* 'classical' potentials originating from the classical force fields. The Lennard-Jones parameters and partial charges of saccharide molecules (used only to describe the interactions with classically modelled water molecules) were adopted from the CHARMM36 force field [10]. The CHARMM-compatible TIP3P model [11] was accepted to describe water molecules.

The simulations were carried out under periodic boundary conditions and under the NPT (for condensed-phase simulations) or NVT (vacuum simulations) conditions. The temperature was maintained close to its reference value (298 K) by applying the V-rescale thermostat [12], whereas the Parrinello-Rahman barostat [13] was used to control the pressure (1 bar). The centre of mass motion was removed every step. The equations of motion were integrated using the leapfrog scheme [14] with a time step of 0.5 fs. Nonbonded interactions were computed using plain cutoff at distance of 1.4 nm.

Initially, the system was subjected to the energy minimization (steepest descent algorithm) and short MD (~5 ps) simulation based on the QM/MM protocol. The force-extension curves were then calculated by using the GROMACS-inherent pulling protocol [4]. Either the O_1-O_4 or O_1-O_3 distance was used as the coordinate, which corresponded to pulling the 1-4 or 1-3-linked saccharides, respectively. The pulling relied on applying the parabolic potential with the force constant equal to 5000 kJ/mol/nm^2 and the pulling rate was set to 0.05 nm/ps. The data (forces and distances) were collected every 5 simulation steps.

References

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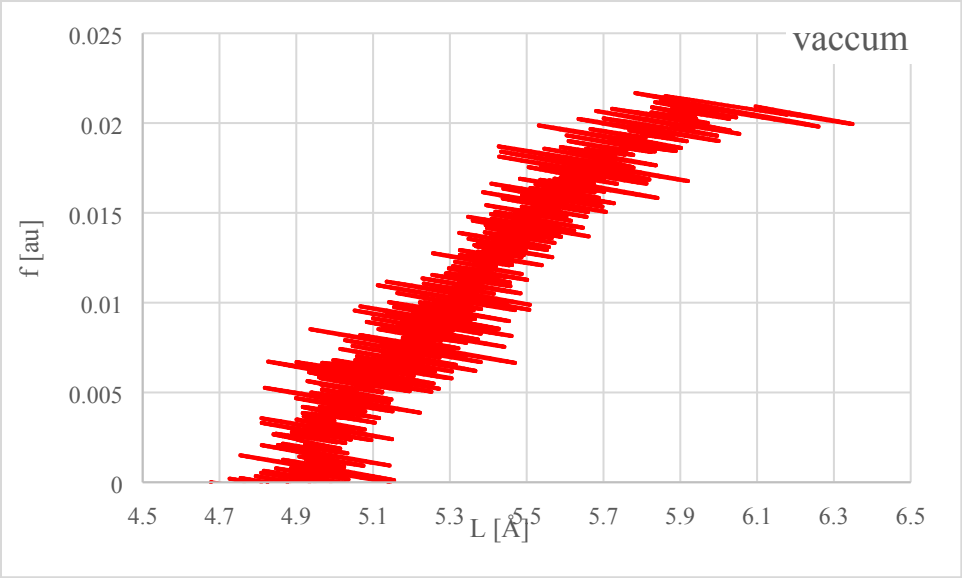

Fig. 6A Theoretical (MD) force-extension curve (i.e. external stretching force vs. elongated molecule length) for the monomer **G** in vacuum.

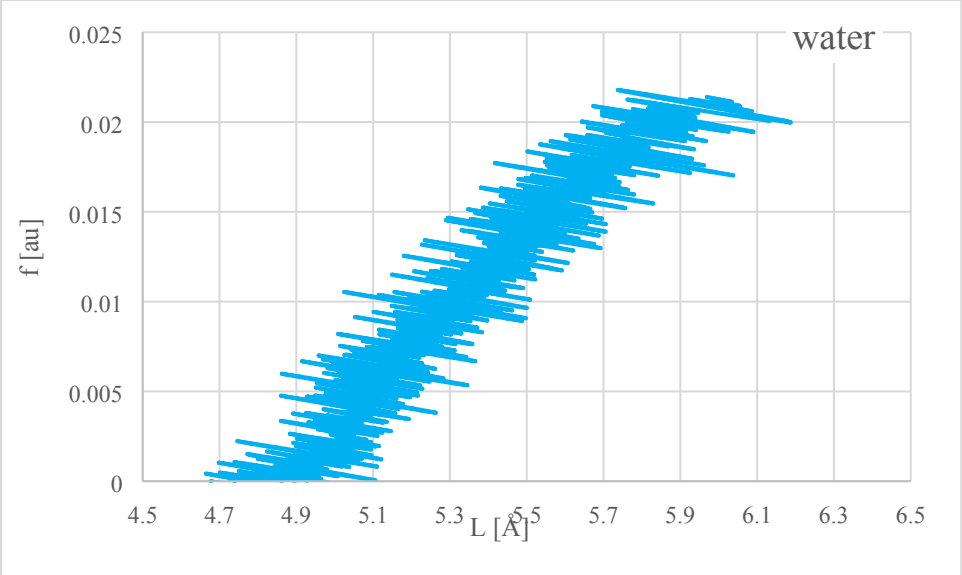

Fig. 7A Theoretical (MD) force-extension curve (i.e. external stretching force vs. elongated molecule length) for the monomer **G** in water.

Tab 2A EGO and CGO results (L in Å)

Oligomer	Method	L1		conformer	L2		conformer	L3		conformer	L4		conformer	L5		conformer	L
D	EGO	5.579	5.624	$^1C_4$													5.624
	CGO		5.489														5.489
G	EGO	5.77**	5.875	$^4C_1$													5.875
	CGO		5.785														5.785
DG	EGO	5.826	5.514	$^1C_4$	5.226	4.775	$^4C_1$										10.257
	CGO		5.513	$^4C_1$		4.773	$^4C_1$										10.259
GD	EGO	5.332	4.790	$^4C_1$	5.858	4.882	$B_{3,O}$										9.342
	CGO		4.790	$^4C_1$		4.885	$B_{3,O}$										9.346
DGD	EGO	5.984	5.515	$^1C_4$	5.284	4.711	$^4C_1$	5.9476	4.386	$^1S_3$							13.784
	CGO		5.515	$^1C_4$		4.711	$^4C1$		4.385	$^1S_3$							13.778
GDG	EGO	5.396	4.792	$^4C_1$	5.810	4.812	$B_{3,O}$	5.4489	4.799	$^4C_1$							13.858
	CGO		4.793	$^1C_4$		4.815	$B_{3,O}$		4.799	$^4C_1$							13.870
DGDG	EGO	5.893	5.514	$^1C_4$	5.172	4.707	$^4C_1$	5.782	4.465	$^4C_1$	5.347	4.787	$^4C_1$				18.946
	CGO		5.514	$^1C_4$		4.706	$^4C_1$		4.465	$^4C_1$		4.787	$^4C_1$				18.953
GDGD	EGO	5.465	4.791	$^4C_1$	5.856	4.868	$B_{3,O}$	5.3332	4.735	$^4C_1$	5.965						17.441
	CGO		4.793	$^4C_1$		4.827	$B_{3,O}$		4.738	$^4C_1$							
DGDGD	EGO	5.876	5.515	$^1C_4$	5.151	4.716	$^4C_1$	5.7553	4.518	$^4C_1$	5.162	4.755	$^4C_1$	5.816	4.393	$^1S_3$	21.119
	CGO		5.515	$^4C_1$		4.716	$^4C_1$		4.518	$^4C_1$		4.754	$^4C_1$		4.393	$^1S_3$	21.140
GDGDG	EGO	5.473	4.791	$^4C_1$	5.863	4.871	$B_{3,O}$	5.3401	4.726	$^4C_1$	5.910	4.957	^2S_O	5.511	4.796	$^4C_1$	23.472
	CGO		4.793	$^4C_1$		4.846	$B_{3,O}$		4.724	$^4C_1$		4.970	^2S_O		4.796	$^4C_1$	23.456