Explanation of NMR mobility of peptide dendrimers using distributed computing

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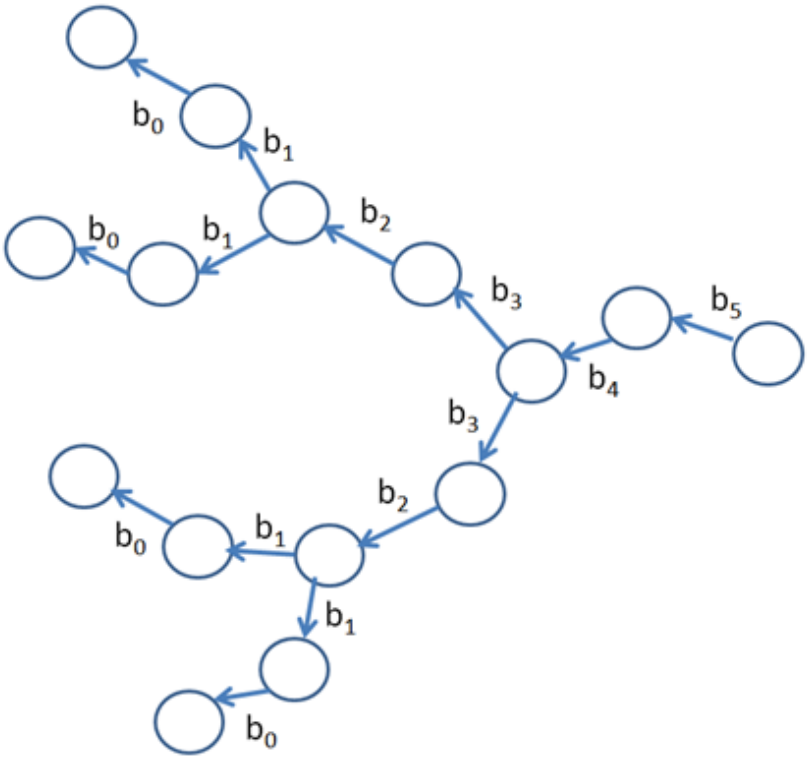
The schematic structure of the dendrimer



1. People need to improve quality of life (health and etc.)

2. The development of biocompatible nanocontainers for the delivery of drugs and genes (cancer, viral diseases, brain diseases, etc)

3. Dendrimers are unique macromolecules that are well suited for the role of such nanocontainers

The distributed computing

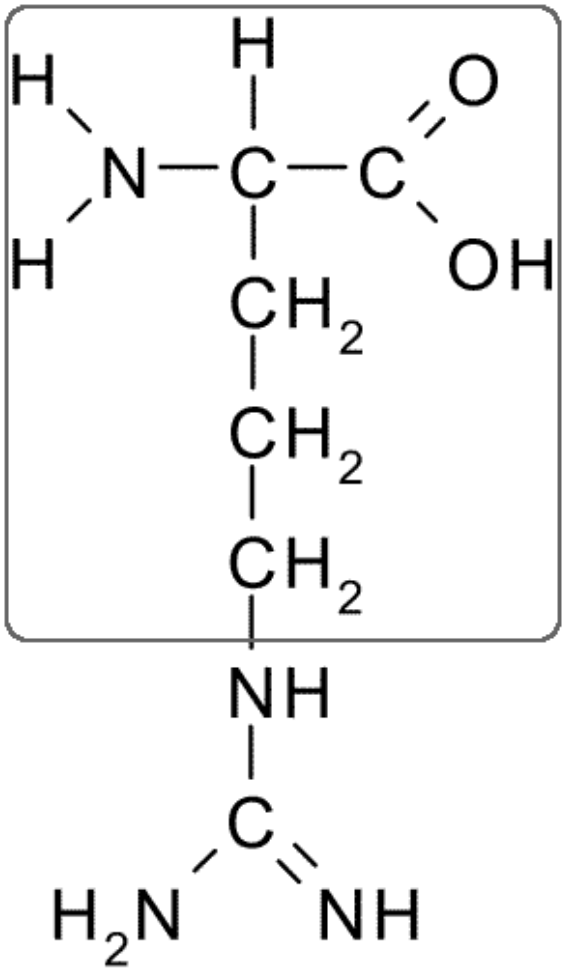
- We used the computer simulation for study of nanocontainers
- Ordinary computing resources are not enough and we used the technology of distributed computing

Scientific problem

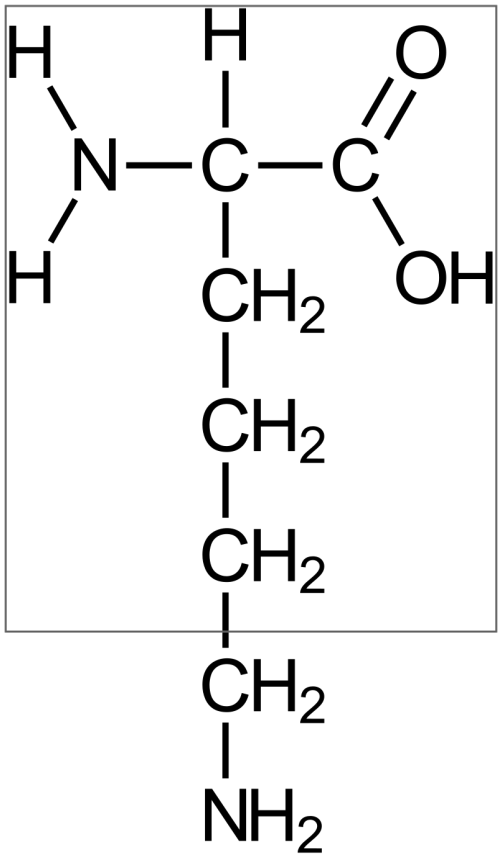
1. Dendrimer with Lys-2Arg repeat units is better suited for biomedical applications then dendrimer with Lys-2Lys repeat units
2. NMR experiment showed that the mobility in the side groups of argenine is slower than in lysines. Two hypotheses:
   - Argenines in the dendrimer are hooked to each other and form a "net", this leads to a slowdown in mobility
   - In argenine, the group observed in NMR is farther from the end than in lysine.

The task: to simulate these dendrimers, to study their properties and to give an explanation of what is observed in the experiment.

Arginine vs Lysine

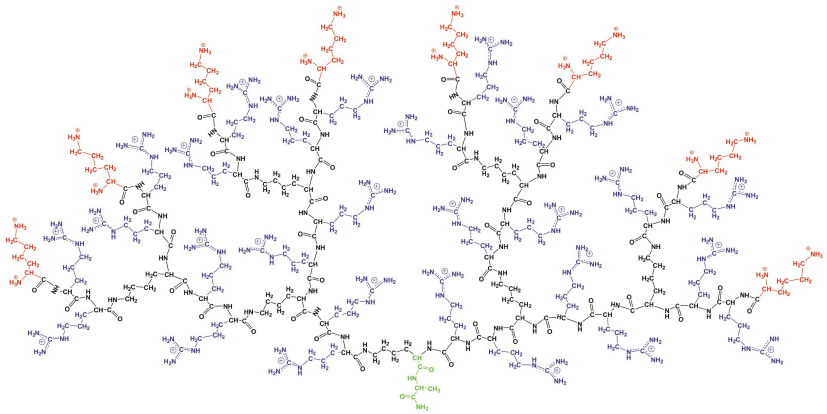


Arg

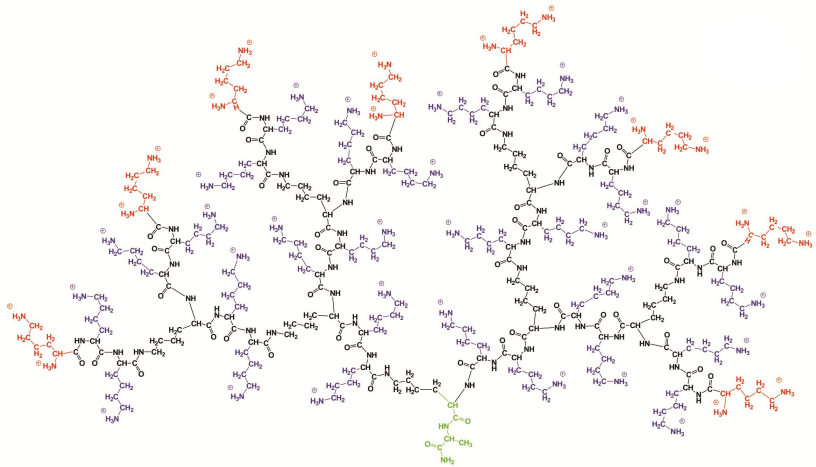


Lys

The chemical structure of novel peptide dendrimers



Lys-2Arg



Lys-2Lys

2Arg and 2Lys mean a linear fragments between the branch points in dendrimers

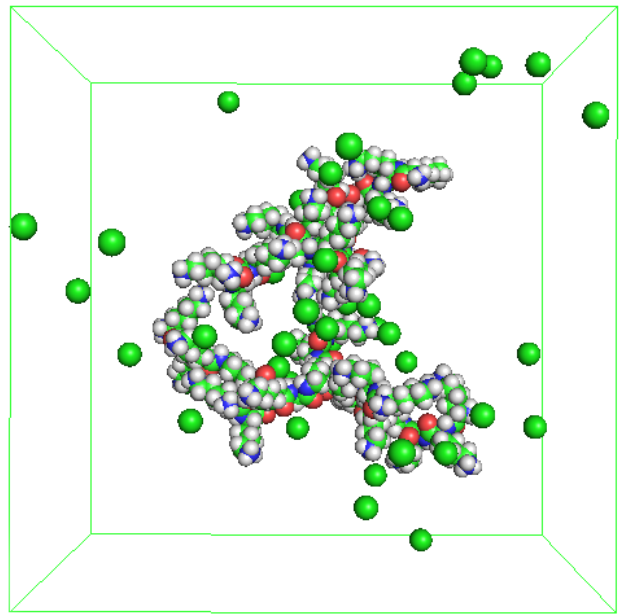
The molecular dynamics simulation

Each dendrimer with their counterions was placed in a cubic cell

The molecular dynamics (MD) was applied for simulation

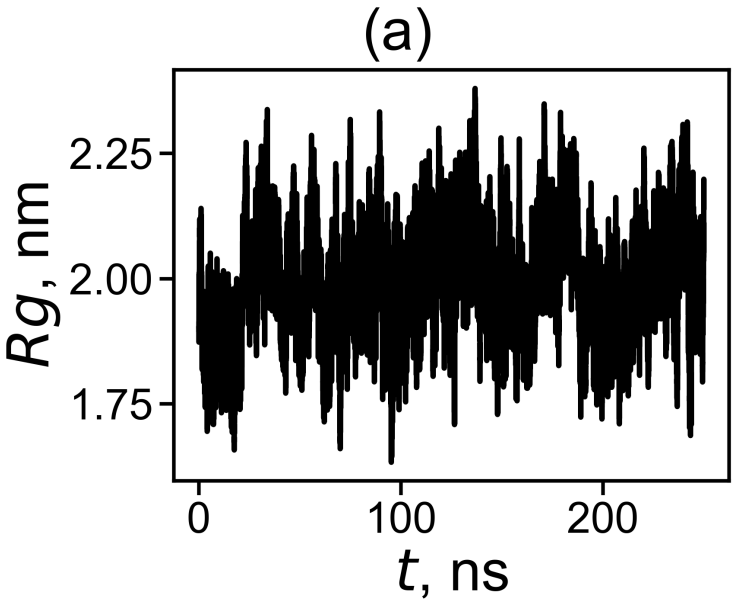
We used:
- Gromacs software package
- the amber force field

Parallel calculations were performed on CPU and GPU



The molecular dynamics simulation

$$R_g = \sqrt{\frac{1}{M}\sum_i m_i r_i^2}, \quad (1)$$

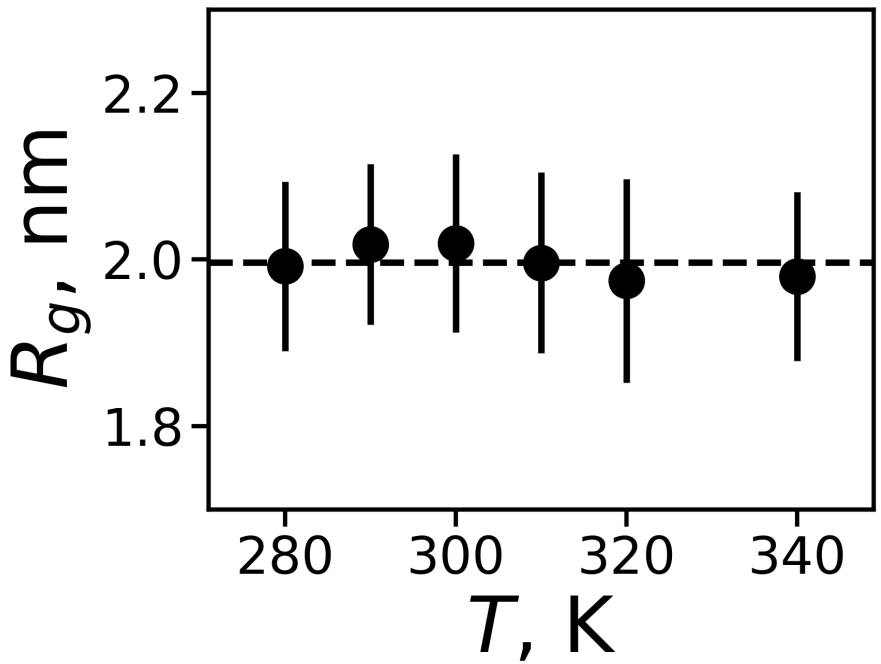


r_i - the distance from center of mass of dendrimer

m_i - mol. weight of i-th atom
M - mol. weight of dendrimer

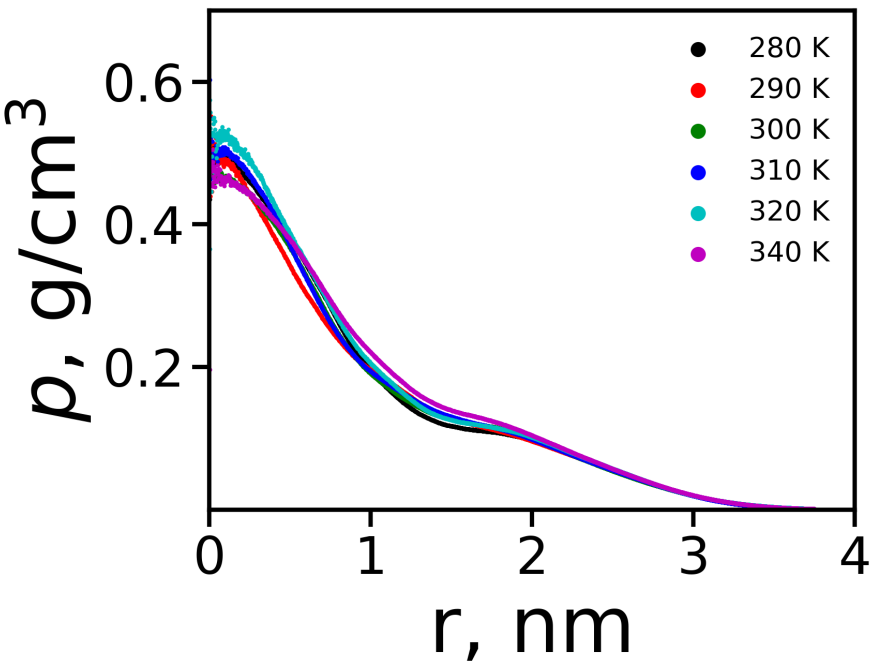
t - simulation time

The average size



It was obtained that size and shape of Lys-2Lys and Lys-2Arg dendrimers are similar.

The radial density profile



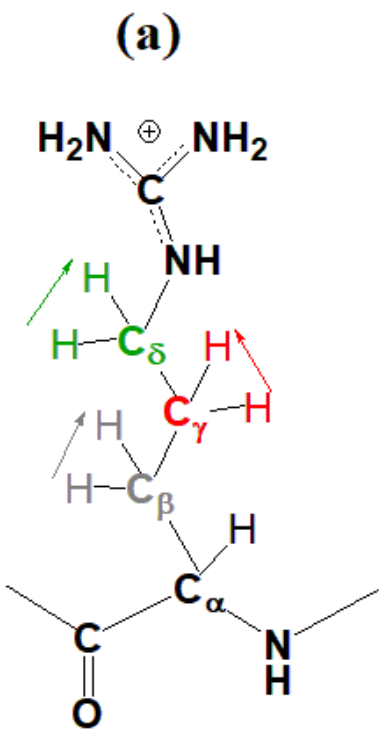
All other structural characteristics, including radial density and radial charge profiles are also similar.

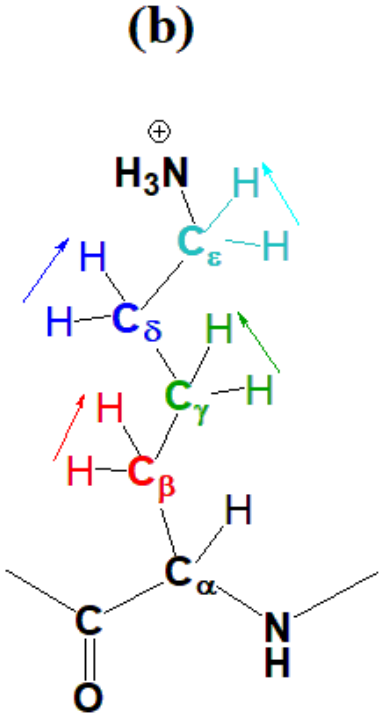
H-H vectors in NMR experiment

NMR - nuclear magnetic resonance

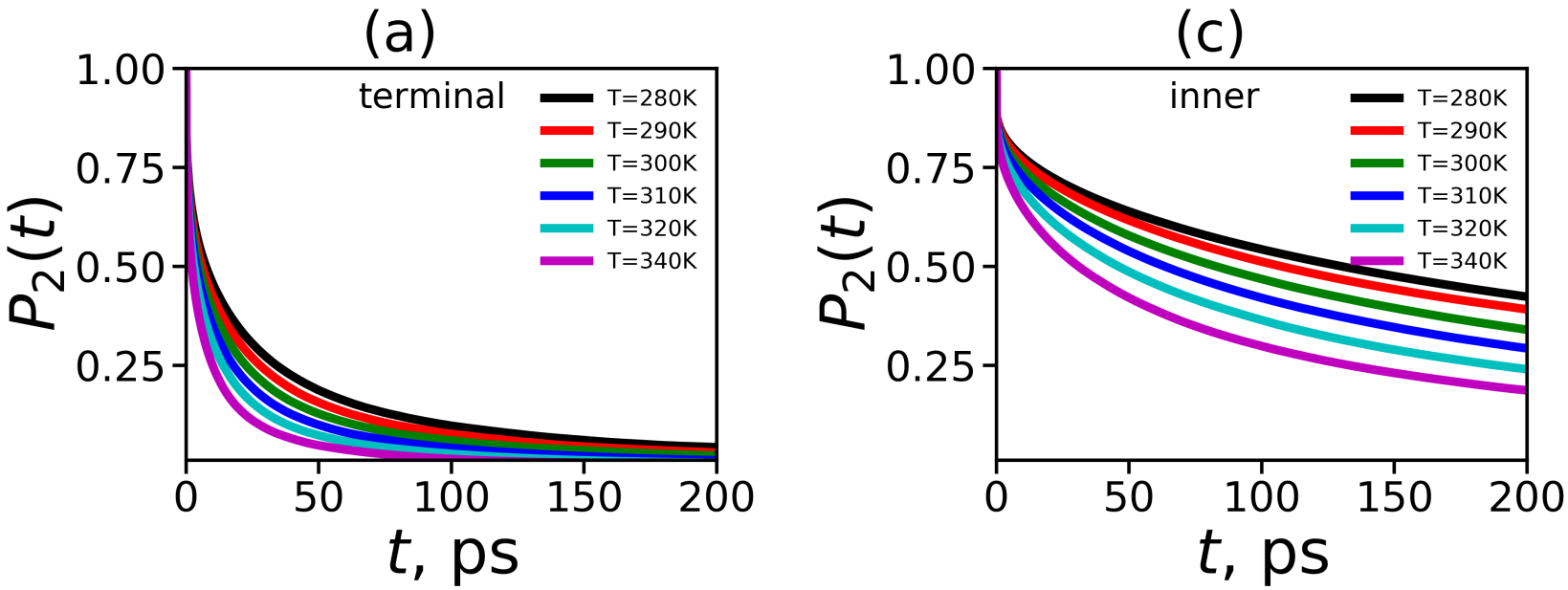
In an NMR experiment, the mobility of vectors formed by two hydrogens in one hydrocarbon group is measured.

In the experiment, inner and terminal groups can be distinguished.





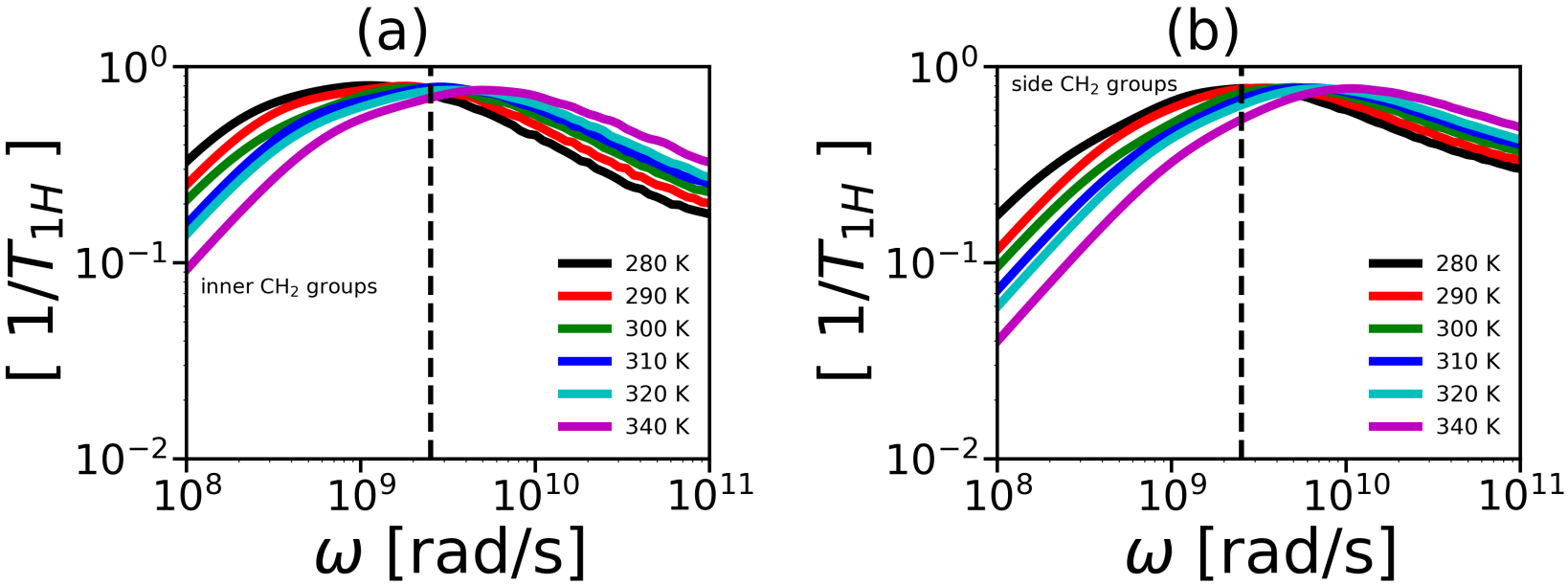
The second-order orientational ACF



the second-order orientational ACF

$$P_2(t) = \frac{3}{2}\left\langle \frac{\left(\mathrm{r}(t)\cdot\mathrm{r}(0)\right)^2}{|\mathrm{r}(t)|^2\,|\mathrm{r}(0)|^2}\right\rangle - \frac{1}{2} \qquad (2)$$

The frequency dependencies of $[1/T_{1H}]$

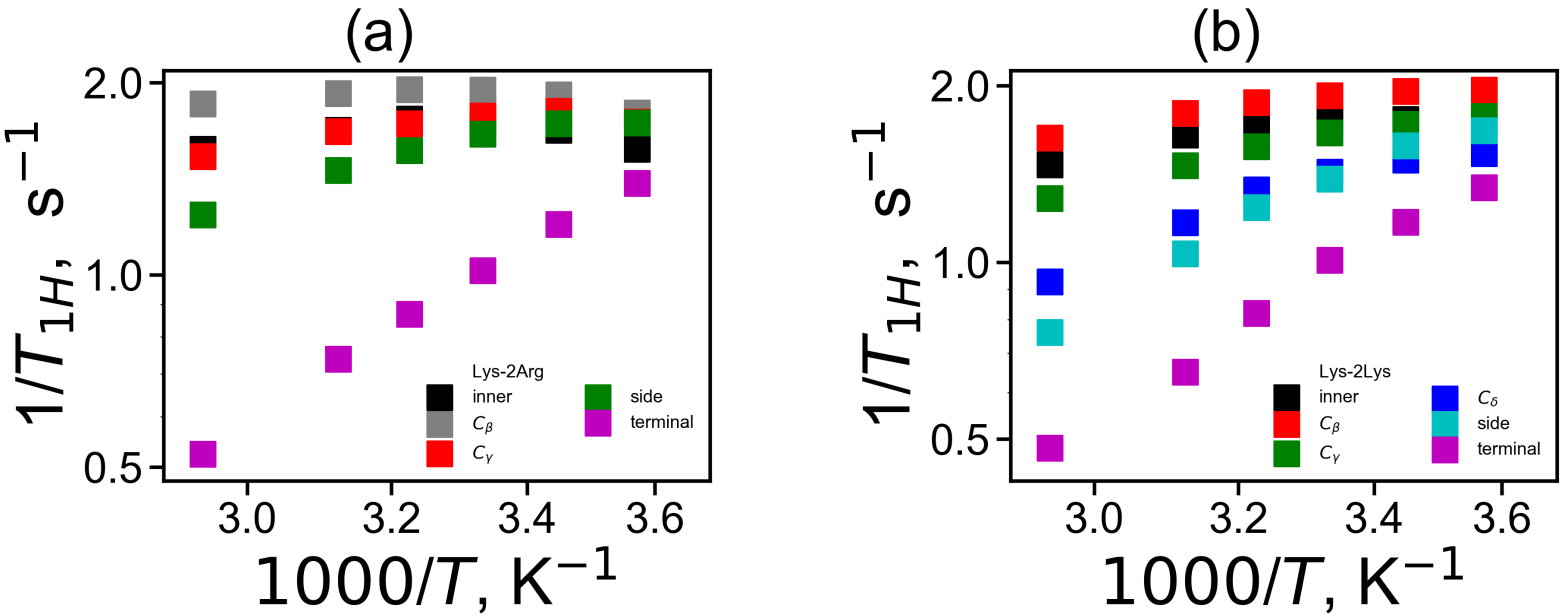


$$\left[\frac{1}{T_{1H}}\right](\omega) = \omega\Big(J(\omega) + 4J(2\omega)\Big) \tag{3}$$

The spectral density is calculated by the cosine Fourier transform

$$J(\omega) = 2\int_0^\infty P_2(t)\cos(\omega t)\,dt \tag{4}$$

The ^{1}H NMR spin-lattice relaxation rate $1/T_{1H}$



the conversion to experimental points at the spectrometer frequency

$$\frac{1}{T_{1H}} = \frac{A_0}{\omega_H}\left[\frac{1}{T_{1H}}\right] \tag{5}$$

Conclusions

1. We performed MD simulation of the novel peptide dendrimers using distributed computing.
2. Most of the structural and electrostatic properties of both dendrimers are the same and independent of temperature, i.e. these dendrimers form similar stable nanocontainers.
3. Our MD simulation confirms the significant difference in the mobility of he side CH_2-N groups in the Lys-2Arg dendrimer in comparison with the same CH_2-N groups in the Lys-2Lys dendrimer.
4. We have revealed that this difference is due to the larger distance from the NMR active side CH_2-N group to the end of the side segment in the 2Arg spacer than the distance from a similar group in 2Lys spacer.

Peptide dendrimers for good quality of life

Articles of our scientific group on this topic

1. Sheveleva, N.N. et.al. Sci. Rep. 2018, 8, 1. **IF 3.998**
2. Sheveleva, N.N. et.al. RSC Advances 2019, 9. **IF 3.119**
3. Mikhtaniuk, S.E. et.al. Polymers 2020, 12, 1657. **IF 4.329**
4. Bezrodnyi, V.V. et.al. Int.J.Mol.Sci. 2020, 21, 9749. **IF 4.556**

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Thank you for attention!