4. Conclusions

To conclude, in my Thesis I found that ligands with phosphorus acid pedant arm substituting carboxylate in DOTA structure are endowed with several favorable features like a water residence lifetime optimal for a preparation of high-relaxivity covalent conjugates. Importantly, these promising properties were proved to persist even after the conjugation as was demonstrated on a symmetrical ditopic model compound for the first time. Importantly, the following study of low-generation PAMAM conjugate proved that, unlike most of the published studies, the relaxivity of these macromolecular systems is not exchange-limited. This has allowed me to investigate in detail the limiting effects on the relaxivity of the internal rotation of the complex in the conjugates. In addition, I shown that the local motions of the dendrimer backbone and of the conjugated complexes can be slowed down by a formation of supramolecular adducts with cationic polyaminoacids. Also, I was able to quantitatively evaluate the effects of the local motions and to effectively reduce them. As a result, the efficacy of these systems as relaxation agents is the highest so far reported for this class of compounds that can find a variety of potential biomedical/bioinorganic applications.

For the close future, we plan *in vivo* tests of these conjugated Gd(III) complexes on mice to explore their pharmacokinetics, stability and distribution in organism. In ligand design, the negative impact of the internal mobility needs to be urgently addressed. The research currently under way in our group, is focused on a preparation of a fast-exchanging Gd(III) chelate able to be covalently conjugated to a macromolecular carrier in a ditopic fashion. That should, in theory, avoid the internal mobility substantially and, in turn, allow achieving really high relaxivities.