Review on Diploma Thesis of

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Influence of phosphorylation on the conformation of peptides and proteins

The main theme of presented thesis is the analysis of effect of phosphorylation on the conformation of several model systems ranging from simple dipeptides to full proteins. Thesis is written in excellent English language with only minor typos and misspellings. It reads well. It consists of rather short but concise introduction into the field of study (6 pages). Computational methodology section (19 pages) present well both used methods and systems. Results section (30 pages) in a sufficient detail both describe and discuss the results of numerous simulations and finally the conclusions from the results are well compared to the literature. Thesis is reasonably sourced with 60 citations and 77 pages in total.

However, the inconsistencies in the literature about the effect of phosphorylation between individual methods should still be discussed in larger detail. The notation in the equations should stay the same thorough the manuscript and do not change in between the individual equations (c.f. use of ω in eq. 2.8 and 2.14). Also, several figures have almost unreadable units (typically Ramachandran plots, e.g. Figure 3.11). Finally, the statistical significance of the detected trends could be demonstrated.

Nevertheless, I would like to highlight the clarity of the thesis writing. The carefully selected combinations of the model systems help to crosscheck the key findings about different phosphorylation effects of serine in contrast to threonine and tyrosine. I expect to find those results published in impact journal soon.

In summary, after careful reading of the thesis, I recommend to accept the submitted thesis as a part of the procedure of awarding Mgr. degree and I suggest mark A.

Olomouc 1. 9. 2017

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I have several questions on candidate:

1. While I appreciate the analysis of the different levels of dissociation of phosphorylated amino acids, I lack their pKa values. What charge will those phosphorylated groups bear under physiological conditions?
2. What charge was used for phosphate group in the study of the disordered peptides?
3. Haven't you tried another force field(s) on any of your model systems to evaluate how big will be its effect on the backbone conformation propensities of phosphorylated amino acids?
4. Can you estimate the error in the Ramachandran plot area assignment in simulations and compare it to the experiments?
5. What exactly is the source of those large RMSD values for these rather small proteins? Which part of protein is responsible?