August 19, 2017

Dr. Brian Matthews  
Editor, Protein Science  
[proteinscience@proteinsociety.org](mailto:proteinscience@proteinsociety.org)

Dear Dr. Matthews:

Thank you for your consideration of our manuscript PRO-17-0207. We’ve revised the manuscript based on the reviewers’ comments and have summarized our changes in this letter.

This is a reasonable paper to (re)acquaint readers with the APBS suite. It does a reasonable job of providing a description of this program. However, the paper could do a better job of telling an eager novice why they want to use this program. If (as suggested in Fig 1) it would be to assign titration states then some more information about this should be provided. Gain the use of the other (APBS only) electrostatic properties should be described briefly. The paper does not describe and specific results so the reviewing questions are not always applicable.

NEED RESPONSE.

The first draft of this paper did not include the figures. I rooted around and found the version with figures in the SI section of the Journal review site. Then this version retains notes between the authors.

NEED RESPONSE.

Generally, when an innovation is introduce that should speed up solution of the problem (eg TABI-PB vs PB or Graph theory vs MC) it would be useful to know how much faster it is. Or to know that the innovation is faster under a certain set of conditions. The authors should also ensure that the references give the necessary comparison of accuracy between older and newer techniques.

NEED RESPONSE.

page 1. Put in a reference for use of explicit electrostatic models.

NEED RESPONSE.

Unclear if the Course-graining in paragraph 1 is the continuum solvent. If so then add a reference and describe the properties that will be effected by this choice.

NEED RESPONSE.

page 4: its useful to know the PQR files simply replaces standard columns to the right of a pdb file with charge and radius, but I’m not sure we need to know this started as a SED script.

NEED RESPONSE.

Page 5: A reference should be given for the debump algorithm.

NEED RESPONSE.

The Monte Carlo methods for finding protonation states as a f(pH) generally converge readily despite the formal problem being O(2N). While N may be large for the whole protein is is modest at any given pH and MC works well. However, having different methods to arrive at a goal is an advantage.

NEED RESPONSE.

Page 6. It should be noted that these force fields are primarily for amino acids. What is done for other ligands found in the structure?

NEED RESPONSE.

Page 7. 3.1 What is the length scales for which each method should be used?

NEED RESPONSE.

3.2 What terms are contained in the nonpolar component? Does this include the implicit van der Waals and the cavity formation terms (which are not so easily separable)? What value is used (kcal/Å2)?

NEED RESPONSE.

Fig 3 should give a standard PB potential surface to compare with the PB-AM model. It would be useful to note when the spherical cow is fine and when it is not. Perhaps combine fig 2, 3 and 4 for one or 2 proteins using the different methods Fig 6 should provide a scale in Å for the proteins. I don’t understand what red and blue mean in this figure. If it is electrostatic potential give the scale and the net charge of each protein.

NEED RESPONSE.

What program is used to make this display (as APBS uses others for the visual interface).

NEED RESPONSE.

Fig 5 and 6. I’m not sure what these figures are trying to show. These are not produced by APBS. In what way does the graphical program use APBS input and not its own surface algorithms.

NEED RESPONSE.

The manuscript describes current status of the popular software APBS and associated resources. The manuscript is clearly written and easy to follow. I have only two minor points:

1. Please, correct DelPhi reference to <https://www.ncbi.nlm.nih.gov/pubmed/22583952>

This has been done.

1. There are some leftovers from the editing as for example “\*\*Dave: please make sure this is true! ⋆⋆”. The manuscript should be proofread.

We apologize for the error; this has been fixed.

Thank you again for your consideration of this manuscript.

Sincerely,



Nathan Baker  
Director  
Advanced Computing, Mathematics, and Data Division