COLOR CODE :
YELLOW background = ToDoList as suggested by the reviewer.
GREEN = our reply to the reviewer comments.

Comments and Suggestions for Authors

The authors presented the manuscript entitled: "Molecular dynamics and docking simulations of homologous RsmE methyltransferases hints at a general mechanism for substrate release upon uridine methylation on 16S rRNA". In this manuscript, the authors applied molecular dynamics and docking simulations on the crystal structure of Neisseria Gonorrhoeae RsmE compared to *Escherichia coli* and *Aquifex aeolicus*. The authors proposed for the first time a general catalytic mechanism for bacterial RsmE and a computational approach to analyze the exit mechanism of S-adenosylhomocysteine by molecular dynamics simulations.

In my opinion, this is a valuable work and will be an interesting source for the scientific community.

I suggest the following corrections:

1)

>>In some figures amino acids and numbers overlap and therefore can't be seen clearly. Please revise and modify.

We inspected the Figures 6, 7 and 9 which constitute the main figures with labels. Any annotation in an illustration is a compromise in letter size. But a trade-off was made between it and visibility of model parts at atomic scale. We are convinced that future readers could amplify the figure size in electronic platforms to see all details. Moreover, all residues are named and identifiable in the text, too. We hope that the reviewer could accept it, too. The present solution, to our conviction, best reflects aforementioned trade-off: with letter size getting larger, much of the atomic scale scenery would be hidden, by shrinking the letter size some readers might find it difficult to decipher. So, the best solution is what we have here.

Upon inspection we noticed that the figure numbers must be re-arranged to have an increasing number in the text. We left the numbering scheme of the first = original version here in case the reviewer states them in the comments. In the new version all numbers were updates. This holds also for the reference numbering.

2)

>>Use the mdpi rules for the references. Any reference has a DOI.

We inspected the reference list and we fixed the problem.

Upon insertion of more references (as requested by a second reviewer) need arose to renumber them to show consecutive, increasing REF numbers in the text, too.

We also inspected the web-based information at MDPI to help improving this list.

**https://www.mdpi.com/authors/layout#_bookmark93:**

**A section of *International Journal of Molecular Sciences* (ISSN 1422-0067).**

**https://www.mdpi.com/journal/ijms/instructions#preparation**

**The entire text was revised for spelling errors and modifications are visible because the text parts are colored while black color means unchanged text.**

**Finally, we feel much beholden of the constructive comments helping us to improve the manuscript for successful publication.**

**Of note, the Fig numbers and Ref numbers are those of the original version. And now at the end of revision the Fig numbers and Ref numbers have to be changed for the new version to follow the consecutive order in the text, this as my apologies for any inconvenience this may cause.**