

Reviewer Report

Title: High-Resolution Computational Modeling of Immune Responses in the Gut

Version: Revision 3 **Date: 3/21/2019**

Reviewer name: Paul Macklin, Ph.D.

Reviewer Comments to Author:

I appreciate the authors' efforts to revise their manuscript to address the editorial and review concerns. However, I'm a little concerned.

This is the second time the authors have "redefined" what their lattice sites represent.

This is not just a matter of crossing out micrometers and writing millimeters. Either the original simulations were actually 30 mm x 10 mm and they just mislabeled twice, or the original simulation was performed on the wrong domain size and the simulations now need to be rerun on the correct 30 mm x 10 mm grid.

I'd like the authors to clearly answer which correction matches reality for this submission:

A) The simulations were originally performed on a 30 nm x 10 nm domain as in the original simulation, but they have now re-run all simulations on a correct 30 mm x 10 mm grid and updated all the results, figures, and as needed, conclusions.

B) The simulations were originally performed on a 30 micron x 10 micron domain as in the resubmission, but they have now re-run all simulations on a correct 30 mm x 10 mm grid and updated all the results, figures, and as needed, conclusions.

C) The simulations were originally performed on a 30 mm x 10 mm domain, and they were mislabeled twice but at last are correctly labeled now. They have verified and rechecked all code and configuration settings that the simulation runs truly correspond mathematically to a 30 mm x 10 mm domain.

D) Something else that they 100% clearly state, rather than thanking us and redefining axes again.

The reason we need to be careful on this is that in numerics packages, changing a simulation previously run on a small domain to one now corresponding to a big domain is almost never a simple matter of relabeling the prior plots. Rescaling axes without changing the data is equivalent to changing the diffusion coefficient (and other parameters).

Either the original and resubmitted labels were wrong, and they have now corrected. Or their original units were correctly stated, the domain size was wrong, and they must correct by rerunning the simulations on the correct domain. Or space was nondimensionalized, and all the parameters were internally represented in units of lattice sites instead of physical units. (e.g., diffusion coefficients in length units² / time units). (But this strikes me as less likely.)

If I simulate a city block with unrealistic parameters, it doesn't automatically become a correct simulation of the entire city by just relabeling axes. The statements about just relabeling units, as well as relying upon "configurable run parameters", gives me pause to be a little cautious before accepting.

An explicit clarification on (A)-(D) (or other) will be helpful. I think the results are probably fine. But I want to be sure, and not just probably fine.

Also, now that I'm looking through the GitHub repo for the project, I'd like to see a clearer statement on

which parameter files to use when running to reproduce the specific results in this paper. If any additional scripts or configuration files are needed to create the figures in this paper (e.g., parameter sweeps), they should include them somewhere in the github repo with clear instructions. (The instructions are presently a bit vague.)

Thank you. I think with a little more clarification, this paper will be acceptable for publication and a great contribution. But relabeling plot axes twice without rerunning anything makes me nervous, and I need more clarity to give a green light.

Methods

Are the methods appropriate to the aims of the study, are they well described, and are necessary controls included? Choose an item.

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