

Reviewer's report

Title: ADAM: Analysis of Discrete Models of Biological Systems Using Computer Algebra

Version: 4 **Date:** 16 May 2011

Reviewer number: 2

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The authors have taken some care to address some of the comments made by the reviewers in the previous round of the review process, and the paper is undoubtedly improved. In particular, the abstract and the Background section have benefited from the revisions and are now much clearer, making the context of the paper clear to the reader from the start. The Mathematical Background is also now more accessible.

Nevertheless I still find that in some parts the presentation of the paper seems rather muddled and needs to be improved.

These concerns are listed below.

- Major Compulsory Revisions

- 1) The order and presentation of the material in the Results and Discussion section is not the most helpful to the reader. The authors launch into a comparison with related techniques before they have adequately presented their own tool. I would suggest that the comparisons with other tools should be postponed until the application subsection, which makes it clear what ADAM can do.
- 2) Similarly within the Comparison to Other Systems subsection the presentation still needs to be improved. At the start of subsection the authors explain why the basis of their comparison is not runtime. But they do not make explicit what criteria they are using for the comparison. The reader gets to work this out from the text and the table, Table 1, but it would be much better to state the basis for the comparison clearly to start with. Moreover Table 1 is very difficult to read.
- 3) It is not clear to me why Petri nets and the Snoopy tool are given the prominent position in the paper that they are. As I previously stated if the authors wish to compare with a Petri net tool, it should be a tool which is similarly focused towards logical/Boolean networks such as Ruths Signalling Petri nets, rather than a general Petri net toolset like Snoopy. Although the paper now mentions Ruth's tool in PathwayOracle, this is extremely superficial and a really minimal attempt to address the suggestion previously made. I would suggest that Petri nets should be dropped from the list of input formulations for ADAM given in the second paragraph of General Features. The authors could then make a comment after the list saying that Petri nets can be converted to polynomial dynamical systems but not currently analyzed after the list. This seems to be more

straightforward the present arrangement of caveats.

4) In the subsection Remarks about Logical Models, the authors state that models with sequential updates can be converted into synchronous models with identical state space. This implies that the outcome of updates in the same time-step is deterministic, and the sequential ordering cannot make any difference. If this is indeed the case it is not clear why sequential ordering is needed and why synchronous updates are not always used. If that is not the case, and in most concurrent systems, the ordering of the interleaving can have a profound impact on the outcome, the authors should explain what they mean by the statement above.

- Minor Essential Revisions

1) In the Abstract, the first sentence of the Results paragraph is not currently a sentence – this needs to be fixed.

2) Background, paragraph 5: “allows to apply tools” should be “allows us to apply tools” or “allows the application of tools” (the verb “to allow” takes a noun as subject not another verb).

3) Last sentence before subsection General Features: “basis” should be “bases”

4) General Features, second paragraph: “ADAM can analyze discrete models” – this sentence seems misplaced.

5) Comparison to Other Systems, line 9: since the use of continuous here is non-standard it should be in quotation marks or italics (as done later).

6) Table 1: the presentation of this material must be improved.

7) The comparison with GenYsis-P Toolbox seems rather superficial.

8) Penultimate sentence of Comparison to Other Systems: it seems rather nonsensical to compare the running time of your algorithm to the number of words used to describe another’s procedure.

9) Remarks about Logical Models, line 5: “as it is common” -# “as is common”

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.