Reviewer's report

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

Version: 4 **Date:** 23 May 2011

Reviewer number: 1

Reviewer's report:

Authors have answered most of my previous comments. I just have a few more comments that I am sure authors can easily incorporate in order to make this manuscript easy to read.

Minor comments:

(a) I still have some issues with the way authors have addressed my previous comment on Paragraph 4 of background section regarding “lengthy explanations and supplementary material as a basis to undermine other Boolean modeling papers”. I think authors should instead state clearly here that previous methods lack web interface and require local installations, making those tools less approachable to biologists. On the other hand, ADAM provides an alternative as a simple web based tool for steady state computation in comparable run time complexity to previously published methods.

(b) In the subsection “Remarks about Logical Models”, the statement “Models with sequential updates can be converted into synchronous models with identical state space” is probably wrong. In my opinion the state space can be totally different from synchronous update and also depending upon the order in which sequential updates are made.

(c) For the sake of completeness of the paper, authors should provide a table listing mapping of x1 to x60 on gene names in [20] (could be a supplementary table as well). Furthermore, every time authors list a Boolean vector (e.g. in Eq 1, Figure 1, Figure 2 and Boolean vector just above Figure 2), it should be written as a table with a dedicated row to gene Id’s x1 … x60. This will improve readability of the steady states throughout the paper. There is no away I can associate any meaning to Boolean vectors the way they are currently written.

Discretionary Revisions:

(a) Reference to agent-based models in Paragraph 5 of Background is missing.

(b) Reference to Grobner basis in 2nd paragraph of Results and Discussion is missing.

(c) In Figure 1, it is weird to have “Click to view dependency Graph, Running analysis now” in the Figure. Authors might just want to give the table of steady states.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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