



SDI FINAL EVALUATION FORM 1.1

PART 1:

Journal Name:	British Journal of Mathematics & Computer Science
Manuscript Number:	2013_BJMCS_7800
Title of the Manuscript:	Constrained Stochastic Space Search Method for Parameter Estimation in Biological Networks

PART 2:

FINAL EVALUATOR'S comments on revised paper (if any)	Authors' response to final evaluator's comments
Although the author(s) answered majority of the questions and made revision regarding the suggested corrections, I consider that the paper needs just few additional corrections. Indeed those corrections were already listed in the first version of the manuscript as well. But probably the author(s) did not reply them strongly. Hereby my suggestion about the paper is to accept it after the following comments are added to the final version of the draft. - As the reply of the 4th item, on page 10, the author(s) added some explanation. I consider that still a small example related to different initialization and getting the same results would be very useful. This example can be an additional plot related to this situation or relevant reference studies that were already conducted about this issue. - I agreed the author(s)' reply about item 5. Whereas still it is not clear for me whether the current system has such types of oscillatory behaviour or higher ordered reactions. If the selected small system indicates these behaviours, the author(s) should explain under which interactions, we observe such relations clearly. Otherwise I consider that the authors still need to show how the results would change under $\Delta t=1.5$ or 2 or higher jump in time and finally in the end the outputs need to be briefly discussed.	- The initialization vector takes into consideration the regulatory effect between any two transcripts, hence, the choice: $\omega_i^{(0)} \in \{-1, +1\}$. The parameter scaling in line 11 of the pseudo-code (Table 1, page 7) ensures a faster convergence of the CSSS. If other parameters other than this domain (e.g. $\omega_i^{(0)} \in \{-5, +5\}$ where the -5 and +5 correspond to repression and activation) are considered, then the convergence of both CSSS and ICRS/DS are marginally slower but the overall convergence pattern is invariant of that reported in Fig. 4 (page 10). - The (small) system under consideration does not exhibit higher order dynamics. It also does not have oscillatory behaviour. In this manuscript, systems of higher order dynamics that exhibit oscillatory behaviour are not considered but rather systems with lower order dynamic without oscillatory behaviour. However, it is foreseeable that an increase in the order of dynamics, having oscillatory behaviour and high levels of measurement noise in data might only further complicate the network inference. In such a case, another follow up study might be warranted to investigate such situations.