Reviewer’s report

Title: Computational Dynamic Approaches for Temporal Omics Data with Applications to Systems Medicine

Version: 0  Date: 05 Jan 2017

Reviewer: Fabio Stella

Reviewer's report:

The paper is about an extremely important problem in biological data anaysis. Time course data, and manipulation data, are extremely important to discover complex mechanism and causation which rule P4.

I fully agree that a review paper on the subject is needed and extremely useful for those researchers who want to start working in this extremely challenging research area.

However, I think that the structure of the paper is not optimal, I found the paper to be poorly structured when presenting different important issues connected with the research area.

I would have expected for example that some summary concerning the state-of-the art performances depending on different specific mining tasks to be presented and critically discussed. I would have hoped for a part of the paper presenting which are the main challenges for the next years. I would have expected to have specific informations concerning the software platforms to analyze any specific problem type.

Furthermore, I have the following concerns:

Pag 5, line 7

In my humble opinion there are few and quite old references, i.e. many citations are missing.

I kindly suggest the following

Acerbi, E., Viganò, E., Poidinger, M., Mortellaro, A., Zelante, T., Stella, F. (2016). "Continuous time Bayesian networks identify Prdm1 as a negative regulator of TH17 cell differentiation in humans". Scientific Reports, 6, 23128


and the references therein.
Pag 5, line 17

I kindly suggest to consider the following paper


Analysis of time course Omics datasets.

Grigorov MG1.

which could provide some useful information

Pag 6, line 21

I miss the reason why you mention data reduction, I think the venn diagram to be useful independently from data reduction or feature selection/generation. Could you be so kind to help me understand?

Pag 6, line 34

I kindly ask to take into account the following papers


doi:10.1038/nbt1205-1499

How does gene expression clustering work?

Patrik D'haeseleer

Pag 6, line 56

I suggest to take into account the following papers

Biostatistics. 2013 Jan; 14(1): 87-98.

Published online 2012 Aug 27. doi: 10.1093/biostatistics/kxs027
Classification of patients from time-course gene expression

Yuping Zhang
Robert Tibshirani
Ronald Davis

http://biostatistics.oxfordjournals.org/content/8/3/507.full.pdf+html

Pag 6, line 56 and 57
I miss the meaning of this sentence.

Pag 7, line 43-51
sorry but I miss the meaning of this sentence. Could you please help me to understand?

Pag 8, line 26, you write "evolution of a probability system"
maybe probabilistic system?

Pag 8, line 41
I wonder how fundamental contributions from the Granger causality theory are not mentioned.

To mention just a few papers
http://link.springer.com/chapter/10.1007%2F978-3-642-02466-5_17

Pag 9, line 7-22
could you be that kind to explain what you mean by balanced and unbalanced?
I find this sentence too long to be properly understood.

Pag 10, line 10
Also in this context I suggest the Garnger causality approach to be taken into account. In particular, the papers which applied and developed Granger causality for gene regulatory network reconstruction.

Pag 10, line 29-31
Maybe you can also mention the ill-conditioning problem which is stringly associated with the kind of data used here.

Pag 10, line 46
I suggest to read and include also more recent papers in this direction, for example
http://link.springer.com/article/10.1007/s10994-012-5311-x
https://bmcbioinformatics.biomedcentral.com/articles/10.1186/1471-2105-10-122

Pag 10, line 51
If you mention knowledge elicitation, as I think, you should mention some paper of the many related to Bayesian structural knowledge elicitation for example.

Pag 11, line 4, you wrote "observed data"
this is typically refereed to as the evidence

Pag 11, line 7
I think it is more correct to write that parameters are assumed to be random variables and they are associated with some probability distribution
I kindly suggest to split this sentence, in my humble opinion it is too long and thus the reader may get lost.

I kindly suggest to take into proper account also the following papers:

http://link.springer.com/article/10.1007/s10994-012-5311-x
http://bmcsystbiol.biomedcentral.com/articles/10.1186/1752-0509-4-130
http://www.jair.org/papers/paper5126.html

I suggest also to read some of the papers of Dana Pe'er on the subject of Bayesian networks for gene analysis.

https://www.c2b2.columbia.edu/danapeerlab/html/

maybe it could be better to move to the software section.

I suggest to cite the authors of these packages.

I was under the impression that software tools, and languages were to be discussed here. However, I found this part not that informative as I hoped.
**Level of interest**
Please indicate how interesting you found the manuscript:

An article of limited interest

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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