Author's response to reviews

Title: Fuzzy Cognitive Map Technique for Meningitis Diagnosis Support Among Infants and Children

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Author's response to reviews: see over
Editorial Requests:

1. We recommend that you ask a native English speaking colleague to help you copyedit the paper. If this is not possible, you may need to use a professional language editing service. For authors who wish to have the language in their manuscript edited by a native-English speaker with scientific expertise, BioMed Central recommends Edanz (www.edanzediting.com/bmc1). BioMed Central has negotiated a 10% discount to the fee charged to BioMed Central authors by Edanz. Use of an editing service is neither a requirement nor a guarantee of acceptance for publication. For more information, see our FAQ on language editing services at http://www.biomedcentral.com/authors/authorfaq/editing.

Response: An native English speaker has copy edited the whole paper.

2. Ethics - Experimental research that is reported in the manuscript must have been performed with the approval of an appropriate ethics committee. Research carried out on humans must be in compliance with the Helsinki Declaration (http://www.wma.net/en/30publications/10policies/b3/index.html), and any experimental research on animals must follow internationally recognized guidelines. A statement to this effect must appear in the Methods section of the manuscript, including the name of the body which gave approval, with a reference number where appropriate.

Response: The necessary statement has been added in the methods section.

3. Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals). It is important that your files are correctly formatted.

Response: The manuscript has been designed using the LaTeX template.

Responses to Reviewers

We would like to thank the Associate Editor for handling the reviewing process and the two Referees for their very detailed comments and suggestions which have helped us to significantly improve the quality of our paper. All the concerns and questions raised by the Referees have been answered and the paper has been revised accordingly.
Reviewer's report
Title: Fuzzy Cognitive Map Technique for Meningitis Diagnosis Support Among Infants and Children
Version: 1 Date: 1 February 2012

Reviewer 1: Neli R S Ortega
Reviewer's report:
Major Compulsory Revisions:
The manuscript titled “Fuzzy cognitive map technique for meningitis diagnosis support among infants and children” addresses the application of cognitive maps, which is a tool that has proved very useful in control systems, in medical decision making. The subject is certainly interesting, although not exactly original. The text is reasonably organized, but very redundant. There are figures and tables that can be deleted. The aim of the work costs to get the course. Also, there are laboratory tests reasonably quick, although invasive, to assess the type of meningitis. In this sense, how the system might actually be useful? It is a cost-benefit situation or availability of these tests? These issues must be discussed once the novelty of the paper is the application and not a model or theory used.

Response 1.1: We agree with this reviewer’s comment and have revised the manuscript to address the issues. The novelty of the proposed work is the application of the FCM methodology for modelling meningitis diagnosis for children living in semi-urban areas of India, where individuals typically experience barriers when presenting with meningitis (costs of blood tests and time taken to analyse the results). The model addresses these concerns by having a readily available tool which is easy to apply within the everyday clinical practice of physicians and potentially obviating the need for further tests if not required. This tool has the potential to be applied within communities, for example, by mobile healthcare professionals, to address the access barrier that many Indians are confronted with when living in more remote communities. These issues have been included within the revised manuscript.

In addition, some theoretical and philosophical aspects are relevant:
1) Fuzzy relations between signs and diagnoses in a FCM describe associations between these conditions and not necessarily causality. Causal relationships are complex to establish in health, demanding depth studies about the dynamics of the disease and the use of various epidemiological techniques. Therefore, it is essential to be careful when establishing causal conditions, or even with the use of the word causality.

Response 1.2: We agree with this reviewer’s comment about the causal relations and have revised the paper. We now refer to associations between the concepts/conditions and not causality.
2) The MCF, as proposed by Kosko and implemented in this study, is useful in control system precisely because, depending on the transformation function and the parameters used, they converge to a fixed point or a cycle. This feature provides robustness to the system allowing it to adapt to changes in initial conditions. However, the use of these systems in the differential diagnosis of disease requires further attention. It is unclear how the system can converge to different values depending on the initial conditions, i.e., for different patients in the case of application in health. You should also discuss what it would mean changing the values of FCM status in relation to patient status.

Response 1.3: The differential diagnosis is a different case than the control systems and this is a first trial using FCMs to diagnose meningitis. Our goal was to implement a new methodology (FCMs), to develop a preliminary system for diagnosis which is transparent and easy to use. In the revised manuscript we have added: “The principal objective of the study described in this paper was to provide a decision making tool to the physicians working within infrastructural and economical constraints i.e., within a real world environment where solutions are sought to address external limitations that cause inefficiencies in the system; in this case the prohibitive costs to the patient of undergoing laboratory tests to detect meningitis and costly delays in the system which increase the likelihood of poorer outcomes.”.

We have discussed in the revised manuscript how the values of concepts change in FCM in relation to patient status (presented in Table 4). “…each patient state is represented as a vector of 19 concepts, where each concept is a sign or symptom or risk factor. Each one concept takes an initial value (activated value); if it is for example the Brudzinski’s sign “ON”, the concept takes the value 1, or in the case of “OFF”, it takes the value 0. The paediatrician can provide any value between 0 and 1. Then a concept vector is produced with the concept values and it is used in the FCM simulation algorithm (presented in [20]). A new (final) concept vector is produced after the system convergence (actually a system’s equilibrium point). The final value of the decision node Men is the value which is presented in Table A of Appendix and assessed for the system decision. The system converges to a different final state, if the initial patient conditions are different. An analytical description of how the values of FCM status change in relation to patient status is presented in previous works of Papageorgiou 2011 [54].”

3) On these maps in general the weight matrix is fixed in time, even as indicated in equations 1 and 2, however, in the text the authors indicate that the system takes as input an “initial matrix”. This matrix changes in time? According to that dynamic? If the weights change it seems very strange from the viewpoint of application of the MCF in health.

Response 1.4: The weight matrix does not change during the system simulation. The weights remain fixed in time during FCM simulation process. We have corrected it in the text and thus a weight matrix is used.

4) The lambda value should also be fixed and the model for the diagnosis is completed only when a value of lambda is chosen as the most appropriate.
Response 1.5: We considered a set of lambda values in order to choose the most appropriate one. When we select a lambda value then this value is fixed in the evaluation of the model for the meningitis diagnosis. The necessary explanation is presented in section 3 (Analysis of Results).

5) In establishing the weight matrix specialists work with discrete values (linguistic terms defined), why not use a system based on rules with Sugeno type inference? In this case it seems more appropriate.

Response 1.6: In the revised manuscript in section 2.3 (before Figure 5) we explain this issue. In our case, to make it more understandable for our expert users, we felt it is more appropriate to define the relationships between concepts using simple rules. We opted to use a simple inference mechanism suggested by Mamdani, given that there cannot be more than four rules per edge, as represented in columns 5-8 of Table 2. An edge is represented by a row. This inference mechanism performs efficiently with a limited number of rules, otherwise the Sugeno algorithm [53] is a more suitable choice as the consequent part of the rules is presented by an equation as opposed to fuzzy sets.

6) The authors seem to have used the same database to study the values of lambda and to evaluate the accuracy of the system, which would be a mistake. It is also not clear how is the values of the state of the patients. What are the values of the array of states? They are classical or fuzzy measures? What is coding used?

Response 1.7: In the revised manuscript we used different data sets for training and testing, for the evaluation of the accuracy of the system. The necessary explanation is provided in section 3.

7) The evaluation of the cases was performed by expert consensus? Were those who worked to produce the model?

Response 1.8: This issue is discussed in section 2.4 and section 3 (Analysis of the Results). We used the dataset provided by the same experts who helped in designing the FCM model.

8) The system was not evaluated using statistical tools. Since there is a gold standard can be used, for example, a ROC curve to evaluate the system performance.

Response 1.9: For the evaluation of the system performance, we calculate the Positive and Negative Predicted values and the Sensitivity and Specificity of the system for the 16 new patient cases. The table in Appendix A has not been deleted as the other reviewer had conducted the statistical test.
Minor Essential Revisions:
1) Revise the text in order to be more objective and not repetitive.
2) it is necessary to review the notation.
3) The equations of the membership functions are unnecessary since there are graphics. I think the graphics are more interesting than the equations given the profile of the magazine readers.
4) There are errors in the numbering of tables and columns.
5) The algorithm presented on page 13 is unnecessary since the system is quite simple.
6) Tables A and B of the appendix may be deleted. In fact, they seem to be not part of the document.
7) Table 1 is unnecessary, the symptoms may be described in the text.
8) Table 5 is unnecessary, since the values are shown in Figure 7.
9) Figures 3 and 4 must be redone because it is unethical to use graphics directly extracted by Print Screen of the fuzzy toolbox frame of the Matlab. Moreover, they have very bad quality.
10) Figures 5 and 6 are totally unnecessary.

Response 1.10: Thank you for the above suggestions. In the revised manuscript we have corrected all these issues and deleted unnecessary figures and tables.

Level of interest: An article of importance in its field
Quality of written English: Not suitable for publication unless extensively edited
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests.

Reviewer 2: Faith-Michael Uzoka
Reviewer's report:
General Comments
Overall grammar of the paper needs improvement. Paper lacks good organization especially in the early sections. The model development should focus on the fuzzy cognitive map and the fuzzy cognitive map modeling of meningitis symptoms and diagnosis. Sections need to be properly numbered. Graphs and figures need to be drawn in a publishable form and clearly labeled. They are currently not showing nicely
Response 2.1: Thank you for the above comments. We have revised our manuscript accordingly. The paper has been re-structured and an English-speaking proof reader has amended all grammatical errors. Sections, graphs and figures have been redone.

Specific Comments
Pages 10 and 11: The authors need to clearly show how the numbers 0.232, 0.464, 0.696, etc.
Response 2.2: We have revised the manuscript and in section 2 we have deleted the equations and added more information in the text about the selection of the fuzzy sets. Figures 3 and 4, which illustrate the related fuzzy regions.

Page 12: The authors need to explain why a bi-value evaluation of the symptoms (ON and OFF). There is no accounting for degree of manifestation (existence) of each symptom in a patient. The authors utilized a set of rules determined by some physicians. It would be nice to show a portion of the rule base (at least 20 rules). What is the basis of rule multiplication by 0.75 and 0.25? How did the authors arrive at the crisp weights based on ‘max’ aggregation, centroid defuzzification, and mamdani inference methods.
Response 2.3: Agreed. This issue has been addressed in the revised manuscript in section 2.3. A specific example is also provided.

Page 14: Why should lambda exceed 1? This tends to contradict the preamble that precedes the actual FCM algorithm.
Response 2.4: We revised the text to remove this anomaly. Now, lambda value does not exceed 1. In the training phase with physicians we used a number of different lambda values in order to select the most appropriate value. We explain this issue and how the lambda values perform in the FCM simulation process. Section 3 has been revised accordingly to address the above issue.

Page 15: Lambda = 0.3 is identified as the most accurate predictive lambda value. What are the implications of this to practice? There is need for a thorough discussion on this. Why is this most accurate lambda value? Discuss the relevance of the results as it relates to other lambda values.
Response 2.5: In the revised manuscript, in section 3 for analysis of results, we have discussed the selection of lambda values and the implications of this to practice. In Appendix A, we gather the results from all lambda values. When we arrange high values of lambda, near to one, then we do not have any differentiation of the results. We had the same output for all patient cases. The best differentiation on our results was accomplished for a specific lambda value, \( \lambda = 0.3 \).

Page 16: Surely, this study is not without limitations. Authors need to clearly discuss the limitations of the work.
Response 2.6: In the revised manuscript, in section 4 (Discussion and Conclusion) a number of limitations are discussed.

Page 20: Table 3 (on page 21) tends to make Table 1 redundant.
Response 2.7: Agreed. This has been corrected in the revised manuscript.

Page 21: There is a significant confusion about the difference between symptoms of meningitis and lifestyle issues that can increase risk of meningitis. Table 3 tends to imply that high economic status and good nutrition have some
direct relationship with meningitis diagnosis. This is questionable, and authors need to clearly show the validity of this or redo the analysis (separating symptoms from risk factors).

**Response 2.8:** In the revised manuscript, in section 4, we discuss this issues and the shortcomings of this paper. We have also clearly differentiated symptoms from risk factors within the paper. Low economic status as a risk factor in meningitis has been highlighted in the supporting literature within the introduction.

Furthermore, how does Table 3 show the strength of connection among concepts (as indicated in the body of the paper)? It only shows causal weights with respect to meningitis.

**Response 2.9:** Maybe there is a misunderstanding in the clarity of the strength of connections among concepts. The weights in our examined case are not causal, but they represent the strength of the connection among concepts. This issue has been corrected in the revised manuscript. Also, in Response 1.2, we refer to it.

Figure 2: What is the difference between the pair-wise causal relationship analysis shown here and the use of analytical hierarchy process (Saaty 1981)? See Uzoka et al - An experimental comparison of fuzzy logic and analytic hierarchy process for medical decision support systems.

**Response 2.10:** According to our previous response, the weights between concepts represents the strength of the connection between the concepts. There is no hierarchy among concepts or any pair-wise causal relationship analysis as described in Saaty (1981). The FCM model constructed by our experts uses a different methodological approach (ground up expert opinion) than the approach typically used in AHP and fuzzy logic.

We have provided an explanation in section 2.3. “This approach enables pediatricians to identify the weight of association between two concepts using readily understandable linguistic terms, and the FCM inference mechanism allows the various concepts to be interpreted in their entirety. Within this interpretation, there is no hierarchy among concepts, unlike that suggested by [51] and used by [52] to diagnose malaria”.

The textbox shown in the appendix is not necessary.

**Response 2.11:** Following the reviewer’s suggestion, we have deleted it. In the revised manuscript, we have added in the Appendix a table with the final values of decision concept $Mn$ for a number of different lambda $= \{0.9; 0.8; 0.7; 0.6; 0.5; 0.45; 0.4; 0.3; 0.2; 0.1\}$. The accuracy for each lambda value is calculated.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
No competing interests.