Author’s response to reviews

Title: Bridging the Gap Between Complexity Science and Clinical Practice by Formalizing Idiographic Theories: A Computational Model of Functional Analysis

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(Please note that the correctly formatted letter has been uploaded as a separated document. See file: response to reviewers (second revision).docx)

In this document, points addressed by the associate editor and reviewers are stylized in blue text, and responses are stylized in black text.

Editor

Your manuscript "Bridging the Gap Between Complexity Science and Clinical Practice by Formalizing Idiographic Theories: A Computational Model of Functional Analysis" (BMED-D-19-01710R1) has been assessed by our reviewers. Based on these reports, and my own assessment as Editor, I am pleased to inform you that it is potentially acceptable for publication in BMC Medicine, once you have carried out some essential revisions suggested by our reviewers.

We want to thank the editor and both reviewers to take the time to re-assess the revised manuscript. We are pleased that you consider it potentially acceptable – given some minor revisions suggested by a reviewer. Our response to these suggestions including corresponding changes in the manuscript are presented below.
Reviewer 1: Johannes Zimmermann

This is a revised version of a manuscript I reviewed a few weeks ago. In short, I think the authors have done a very good job in revising the paper. My earlier concerns have been adequately addressed, and the manuscript has been clarified in many places. In summary, I believe that the paper is now ready for publication. Congratulations on this impressive work!

We want to thank reviewer 1 for the positive evaluation of our revision!

Reviewer 3: Günter Schiepek

Thank you for the detailed revision according to the comments of the reviewers (at least to mine). I recognize an important improvement of the MS by the revision, and in consequence, I have only some minor remarks.

1. On concerns the statement on page 26, lines 562-571, that you expect that formalizing idiographic theories (I still have a profound problem with this contradicting concept) can improve the precision of intervention predictions, ... I have severe doubts on this, because in nonlinear systems the prediction is profoundly limited. Indeed high frequency monitoring of change dynamics reveals quite different dynamic patterns or trajectories than those you have modeled and you are showing in your phase space diagrams. Your model is basically linear and it is hypothetical in the sense that no real case with real data on the process are given. This point should be discussed in a more serious way than it was done up to now.

We want to thank reviewer 3 for the overall positive evaluation of our revision. In response to previous requests, we elaborated on the conditions under which intervention predictions can be improved, through clarifying that they heavily depend on the accuracy of the model. We agree with the reviewer that there is another important layer to this elaboration, that is the accuracy also strongly depends on the quality of the processes that we try to capture. If these are of non-linear nature, which indeed has been shown to be the case for many processes in clinical practice, predictions become increasingly difficult. We therefore followed the suggestion of the reviewer (see second point) to include a remark on this issue:

Page 25-26, lines 553 – 567:
Linear versus non-linear dynamics. We introduced two perspectives in constructing idiographic systems: First, a top-down approach in which generic factors are modelled and subsequently personalized through adapting parameters, and second, a bottom-up approach in which personalized factors are modelled directly – extending the search horizon to incorporate any factor that can be related to the patient’s system. In the present paper, we formalized a case conceptualization within the generic framework of functional analysis, using (primarily) linear equations. It is important to note that, especially when following the bottom-up approach of constructing idiographic systems for and with each patient, system dynamics should encompass not only linear, but also non-linear dynamics. Indeed, prior research examining the quality of system dynamics found that processes in therapy are often non-linear and chaotic (41,62). Such dynamics are, by definition, hard to predict and are heavily dependent on the specific set-up of the simulation; slight changes in the set-up of initial conditions and parameters might have dramatic effects on the simulated behavior. In such cases, it may only be possible to make broad predictions about expected behavior, for example, not when a panic attack will occur, but rather whether a system is vulnerable to such attacks. We encourage future research to further investigate how such dynamics should precisely be incorporated in the formalization of theories.
2. However I appreciate your work and I see a future for the mathematization of idiographic models - the important step is indeed to develop the models together with the patient - so, in consequence, there should be further developments which include the criticism not in any discussion, but in practice-based research and in concrete practical work. Here I agree with your optimism, lets do it. We whole-heartedly agree and hope that this paper will do its part in promoting the mathematization of idiographic models.

I suggest to make some minor remarks on this point which is not so much a request for this paper but for the future work on the way you started. Changes as suggested are presented in the box above (remark 1).

We would like to thank both reviewers again for their time and commenting on our manuscript. With kind regards,
Julian Burger (on behalf of all co-authors)