Email

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Subject:	mSystems00144-16R1 Decision Letter
	January 19, 2017 Prof. Andrés Moya Universidad de Valencia - Instituto Cavanilles Instituto Cavanilles de Biodiversidad y Biología Evolutiva c/ Catedrático José Beltrán 2 Valencia 46071 Spain Re: mSystems00144-16R1 (Health and disease imprinted in the time variability of the human microbiome.) Dear Prof. Andrés Moya: I agree with the reviewer that which ever 'English Language speaker' you used did not do an adequate job editing this manuscript, and they may not have been scientific literate, as they have used some very strange language. Please address this and the other concerns. You want to be proud of the presentation of this work, and this is your opportunity to make sure this article is the best it can be, we do not like to have sloppy presentation in this journal. Below you will find the comments of the reviewers. To submit your modified manuscript, log onto the eJP submission site at Link Not Available . If you cannot remember your password, click the "Can't remember your password?" link and follow the instructions on the screen. Go to Author Tasks and click the appropriate manuscript title to begin the resubmission process. The information that you entered when you first submitted the paper will be displayed. Please update the information as necessary. Provide (1) point-by-point responses to the issues raised by the reviewers as file type "Response to Reviewers," not in your cover letter, and (2) a PDF file that indicates the changes from the original submission (by highlighting or underlining the changes) as file type "Marked Up Manuscript - For Review Only." Please return the manuscript within 60 days; if you cannot complete the modification within this time period, please contact me. If you do not wish to modify the manuscript and prefer to submit it to another journal, please notify me of your decision immediately so that the manuscript may be formally withdrawn from consideration by mSystems. To avoid unnecessary delay in publication should your modified manuscript be accepted, it is important that all elements you upload meet the technical requirements for production. I strongly recommend that you check your digital images using the Rapid Inspector tool at http://rapidinspector.cadmus.com/RapidInspector/zmw/. For a corresponding author who is an active member of ASM at the Contributing or Premium level, the mSystems article processing charge (APC) is $2,250 for Research Articles, Resource Reports, and Methods & Protocols and $1,125 for the shorter Observation and Opinions & Hypotheses formats. For a corresponding author who is a nonmember or Supporting member, the mSystems APC is $3,000 for Research Articles, Resource Reports, and Methods & Protocols and $1,690 for the shorter Observation and Opinions & Hypotheses formats. Nonmember corresponding authors or Supporting members may upgrade or join

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do unhealthy people fall within the healthy range of phase space, and how often does the opposite occur? Would you consider Fig. 2 to be fairly equivalent to Fig. 3?

Specific Comments:

line 90: You seem to be saying that microbial dynamics 'affect' host health status. But I saw no attempt to infer causality in your results section. Be careful about implying causality.

lines 106-105: Are you saying that Taylor's parameters are correlated with an independent measure of community stability? Or that you are assuming they are proxies for stability? Also, you should mention that V is the y-intercept in Fig. 1, while beta is the slope of the line (both in the manuscript and in the figure caption).

lines 113-115: Please provide a reference for this Medicare factoid. Also, delete 'stable such as, for example,' and replace with 'stable, similar to'.

lines 125-126: Label axes with 'beta' and 'V' parameter names, for consistency.

Figure 2: There seems to be a flaw in your zone of health. You've presented a 2-D Gaussian distribution around your 0-centered normalized results. However, I don't think this is correct. Conceptually, there shouldn't be any lower threshold on beta and V where you cross from healthy to unhealthy (just getting more and more stable as those numbers decrease). Very low beta and V are likely to be healthy. I would only expect samples in the upper-right quadrant to be 'unhealthy'. Thus, the boundary of the unhealthy zone should probably look like a rectangle with it's upper right corner rounded.

line 156: Is there precedent in the literature for defining an organism's fitness as it's recovery half-life? If so, please provide reference.

line 158: Are the V and beta parameters from the Langevin equation equivalent to the same parameter from Taylor's law? If so, please state. If not, please give this parameter a different name to avoid confusion. Also, how correlated are the F, V, and beta parameters for each of your model fits?

Figs. 4-5: Describe the panels showing DV and RV (and define these parameters) in the figure caption. How are you defining your medium-ranked stability islands? Quantitatively? Do you see a steady/linear decay in RSI as you move down in average rank? Is there a plateau at medium average ranks? Is there a non-monotonic trend? This is hard to see with just numbers. Maybe try plotting RSI as the width of your average rank colorbar, or show a line-plot with RSI on the y-axis and average rank on the x-axis.

line 214: You say you used the 'largest sampling' time series for Fig. 6. Is this still true after including the paper from David et al.? I think the female time series from the Caporaso paper is shorter than both the time series form the David paper. Also, you mention that you calculated beta and V, but only plot V. Why not show beta as well?