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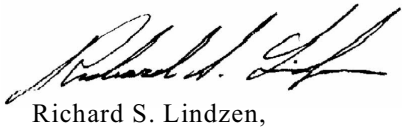
Randy Schekman, PhD
Editor-in-Chief, PNAS
University of California, Berkeley
Department of Molecular and Cell Biology
626 Barker Hall
Berkeley, CA

Dear Dr. Schekman:

Thank you for your efforts. The reviews were helpful in clarifying our paper. Unfortunately, the revision no longer adheres to the space restrictions of PNAS, and we will have to publish the revised paper elsewhere. However, we have prepared (and attached) our detailed response to all the reviews. We have also attached the revised manuscript. We feel it is necessary for us to do this simply because we found comments on the rejection of our paper on the internet even before receiving your official decision. I feel it is, therefore, necessary for us to make the reviews of our PNAS contribution and our response to them public.

As to your quote from one of the board members, the answer is straightforward. We clarify in Section 4 (Methodology) of the revised paper the use of a simple model to generate time series with specified feedbacks to test various analysis methods. The use of simple regression over the entire record (as is the procedure in Trenberth et al, 2010 and Dessler, 2010) is shown to severely understate negative feedbacks and exaggerate positive feedbacks – and even to produce significant positive feedback for the case where no feedbacks were actually present (viz Figure 7 and Table 1 of the revised paper) . Our method, while hardly ideal, fairly accurately replicates negative feedbacks and only modestly understates positive feedbacks. Equally important, the simple regression approach leads to extraordinarily small values of the correlation (r^2) on the order of 0.02. Such values would, in normal scientific fields, lead to the immediate rejection of the results of Trenberth et al and Dessler as insignificant. We show that the appropriate use of objectively determined segments that adhere to the normal requirement that segments be short compared to equilibration times while long compared to the time scales associated with feedback processes, greatly increases the signal to noise ration, eliminates biases due to equilibration, and greatly increases r^2 – despite reducing the degrees of freedom (viz Figure 9 of the revised manuscript). I hope that you will agree that holding such unjustified and insignificant analyses as those by Trenberth et al and Dessler to be standards for comparison to be disturbing to say the least.

Sincerely yours,



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