

To whom it may concern
Chaos, Editorial Office:

Through this letter, I am resubmitting the manuscript entitled “Hybrid reaction-diffusion and clock-and-wavefront model for the arrest of oscillations in the somitogenesis segmentation clock”, with reference number CHA21-AR-00106, to be considered for publication in Chaos. We have modified the manuscript taking into consideration all the Reviewers’ comments and criticism. Please find below our response to the Reviewers.

Sincerely

Moisés Santillán

Reviewer 1

1. I am satisfied with the clarifications that the authors in explaining the proposed mechanism. I still have a couple of issues.
[We are grateful to Reviewer 1 for thoroughly reviewing our manuscript. His/her suggestions have greatly helped us to improve it.](#)
2. In my first iteration I mentioned that Wnt and Fgf oscillated in mouse but not in zebrafish, but there is no mention of other cyclic genes in the manuscript like hes/her genes which oscillate in all vertebrates, please mention them. (Here is a suggestion doe: [10.1371/journal.pbio.1001364](https://doi.org/10.1371/journal.pbio.1001364)).
[We have included the correction suggested by the Reviewer.](#)
3. In the manuscript the words wavefront and morphogen gradients are interchanged as if they are the same. In the field there are ongoing discussions on what is the "wavefront", is it an internal timer as observed in neuroblasts? Are the receding morphogen gradients as Retinoic-Acid, Fgf or Wnt? and so on. Please be very specific and mention that you are visualising a wavefront generated by a receding morphogen gradient.
[We have carefully revised our manuscript to make clear that, in our case, by a wavefront we mean a receding morphogen gradient.](#)
4. In section V it is mentioned the theoretical need for an AP identity in the somites. This identity indeed has been observed experimentally, Fig. 3G of this paper ([doi: 10.1242/dev.009266](https://doi.org/10.1242/dev.009266)) is a beautiful example, please cite.
[Thanks a lot for suggesting this reference \(we were not aware of it\). We have included it in our manuscript.](#)
5. In figure 5 A, a straight line $L_{\text{bar}} = v_o T$ must be plotted, where T is the oscillation period in the anterior part. This would show if the numerics deviate from this relation.
[We have modified Fig. 5 as suggested by the Reviewer.](#)
6. In Figures 6 and 8, the mean value of CV_L is shown. I find this weird as the CV is a measure of the ratio of standard deviation and the mean, the correct way to proceed is to pull all the numerical data together for an specific value of the control parameter (CV_noise or IC) and then obtain a single value of the coefficient of variation. This is because the aim is to converge to the probability distribution behind the stochastic process.
[We thank the reviewer for his/her suggestion. We have computed the value of CV and modified](#)

Figs. 6 and 8 accordingly.

Reviewer 2

1. The authors have addressed my questions/concerns. I only have a few minor comments on what has been added.

We are grateful to Reviewer 2 for his/her suggestions, which greatly helped us to improve it.

2. The authors study in detail noise influence, and at the end of p15, the authors comment on the advantage of changing the β parameter, namely that it prevents sensitivity from initial condition and adds a « control » on homogeneity. But I am wondering now if it is completely fair to contrast this mechanism with « random » inhomogeneity. One could totally imagine a mechanism where the inhomogeneities would not in fact be random, and it seems to me that fundamentally it is not very different from a controlled β . Similarly, if β were to be random, one would not gain much. So I am not entirely convinced that the main interest of β is to fight against noise. I guess a way to turn this is that β essentially introduces an external control of the instability, for instance to modulate the size of the pattern. I am wondering if the authors could comment on this.

We agree with the Reviewer, and we have modified the corresponding paragraph as suggested.

3. A related point is that it would be good to more explicitly tell in conclusion that β is probably related to morphogens gradient (such as FGF). Again there are predictions here on the influence of FGF on the homogeneity of the pattern for instance.

We have made clear in the conclusion that β is probably related to a morphogen gradient (like FGF)

4. P16, I agree with the observation that most simple models deal with the observed period gradients in a rather ad-hoc way and that there is room for better explanations. The authors might mention this recent paper where the same issue is discussed and where a rather significant period gradient naturally emerges from a simple interplay between enhancers

<https://elifesciences.org/articles/55778> .

We have included and discussed the suggested reference. Thank you for bringing it to our attention.

5. P 13 : speculate->speculate

We have corrected this typo. Thank you for pointing it out.