Reviewer #1 (Comments to the Author):  
  
Pantoja-Hernandez et al. reframed and analysed the PORD model from Coterell et al.  
which models the determination of segment size by the oscillating genes of the segmentation clock. They found that in this model the components "A" and "R" oscillate around an unstable limit cycle when initiated in an spatially uniform state, a perturbation at the most anterior side drives the whole system unstable. The diffusive coupling makes that each spatial point leaves progressively this limit cycle to another stable steady state. The new steady state consist of a static spatial pattern with a characteristic wavelength. With the existence of this unstable limit cycle the model would be unstable to external noise, which is an essential ingredient in models of gene expression. The authors found that by varying the parameter "beta" this limit cycle can be driven between stable and unstable regimes. In this way the authors propose a receding morphogen gradient driving this transition, making the system robust to noise. This manuscript is very valuable as the authors clarified the mechanism of the original PORD model (missing in the original paper), the system has an interesting spatial instability and it is also an interesting proposal for a simplified mechanism of the segmentation clock.  
  
I have the following points that should be addressed  
  
Major points:  
  
1. In the analysis of the equations (A1) I could not see in figure 6 (a) the point where the limit cycle became unstable and the new stable fixed points in the diagram. This is vital for the manuscript as it is the main mechanism for patterning.

2. To further understand the phase space portrait equations (A1) when "beta" is low enough, it must be shown the stability and type of fixed points coexisting, if the oscillation is perturbed at a given phase, to which fixed point the system will land on?

3. The introduction of the diffusion constant "D\_a" is unnecessary as it only introduces confusion on how this system works. Two diffusion constants are only necessary if the patterning emerged from an instability due to the spatial coupling (Turing type), and indeed the most interesting part of this model is that the patterning emerges from a different mechanism. The spatial analysis should be done by having only the diffusion constant "D\_r".

4. A plot showing the relationship between segment size and velocity is necessary, as it is one of the central parameters in models of the segmentation clock. The following paper should be cited (doi.org/10.2976/1.3027088). Also it should be cited when mentioning the slowing of oscillations that generate the traveling waves.

5. In equations 6 a and b, the white noise term is "dW/dt" and not "dW", as W is the Wiener process which is the time integral of white noise.  
  
  
Minor points:  
  
6. Wnt and Fgf oscillate in chicken and mouse, but it does not oscillate in zebrafish.  
  
7. The word "substance" is used when the authors mean "morphogen".  
  
8. In equations 6 a and b, what is the exact meaning of "a bar" and "r bar" are the mean values of the deterministic oscillation? or is the value of the unstable fixed point?

9. In page 10, k^2 = 0 is mentioned, but it is not mentioned explicitly that k is the Fourier mode.  
  
10. In equation (8) the letter "K" should be omitted as it can be confused with a dissociation constant.  
  
11. When the coefficient of variation C\_v = 0.1 the segments are irregular, can you explain why?  
  
  
  
Reviewer #2 Evaluations:  
Overall Rating: Reconsider based on responses to issues raised by reviewers  
  
Reviewer #2 (Comments to the Author):  
  
This paper revisits a model proposed by Cotterell et al a few years ago (the "PORD" model) and aims at modifying it to make it essentially more robust. The PORD model is slightly modified, then a parameter is assumed to act as a wavefront. It is argued that this model explains better some experiments.  
  
In my opinion, the change is a relatively incremental discussion compared to the PORD model. But before I get to this, there is another issue, primarily due in fact to Cotterell et al : the PORD model is not fundamentally different from another classical model, the Meinhardt model for segmentation, which patterns in the absence of a wavefront exactly as described by the author of the current paper. This connection of the PORD to the Meinhardt model is [briefly] discussed in Francois et al, Curr Op Syst Biology, 2018, with some mathematical derivations in Supplement of the paper, showing e.g. that the system in absence of diffusion is a relaxation oscillator, etc... . As an illustration, Fig 2B of that paper is virtually identical to the present Fig 1, and while the precise terms/details of the equations are different, both the structures of the equations (nuclines, etc...) and the properties (autoactivation + repression, initial conditions, mechanism of stabilization) appear very similar to me. I would invite the authors to make more explicit this connection, or to explain in which ways those models are fundamentally different. This is not a minor issue since, again, many properties of the PORD model discussed here are virtually identical to Meinhardt's model, and of course Meinhardt himself discussed limitations and fixes of his segmentation model (e.g. in his 1982 book, see also his 1992 review in Reports on Progress of Physics).  
  
Now going back to the new model, this kind of models classically stabilize because of diffusion, which explains why there can be irregular patterns if initial conditions are randomized. The authors then add an extra « Wavefront » parameter to induce a transition from a cycle to the pattern, arguing that this would stabilize the system. This adds "some" robustness.  
  
Overall, I find the idea potentially interesting, but the novelty of the idea is not entirely clear to me. But on top of the important theoretical discussion, better connections to biology and explanations about what happens would be really welcome in my opinion.  
I have some detailed comments.  
  
Major comments:  
1. My major recommendation is to discuss better the connections to the current model (and to the PORD) to other existing models. Some of my comments below relate to this issue because the authors do not give all the details needed to understand how their model practically work (in my opinon).

2. Meinhardt discussed how morphogens can bias reaction diffusion based patterning in his own model, I am wondering if the authors could compare their work to his.

3. A general question is what defines a somite. For instance, when p11 it is said that when "the limit cycle turns unstable, a somite is formed", so I gather that implicitly the authors assume that a somite is defined by a steady state. But part of the discussion (in the biological literature as well as in Meinhardt's papers already) is that the definition of a proper somite includes not one but two states. Meinhardt argues that the alternation of two steady states A/B is necessary to define a segment. In the biology papers, rostral caudal markers have been argued to be necessary to define somites, so that somites without markers are not "proper" somites. So in the authors' model, what defines a somite, for instance in Fig 3B ? Are boundaries stabilized by diffusion ? If we switch off diffusion, what happens and how realistic is it ?

4. I suspect that in the authors' mind, the pattern is clearly defined by two « states » (the yellow and blue region). Is it a bistable system (possibly "blurred" by diffusion) ? Then, the idea to have a transition from oscillation to bistablility fits several other models of somitogenesis, that should be mentioned. In fact those models precisely have a wavefront inducing a bifurcation, just like what the authors build here, so it is a bit unclear to me what the fundamental difference is with such models. For instance, the "irregular" pattern could also just be a bistable system stabilizing with random initial conditions.

5. Another related point is the size of the pattern. If the speed is multiplied by 2 (on Fig 5), it seems the pattern size is also multiplied by 2, which fits the expectation of the clock and wavefront model (size of the pattern = period times speed). Is it correct ?

6. the authors argue that the modified model includes some "robustness". But there is no real metric of this robustness, just simulations in presence of noise compared for instance to Fig 2 where irregular patterns are shown due to very specific initial conditions. What happens if one uses the initial conditions of Fig 2 for Fig 5 ? More generally, the notion of robustness is a bit fuzzy and I am wondering if the authors could find a way to quantify their model vs the PORD model in terms of robustness (to noise ? to initial conditions ?)

7. Lastly, again coming back to other model and classical experiment on somitogenesis, it is generally argued that the system creates essentially two kinds of stripes, or equal size (possibly corresponding to rostra-caudal markers in somites). But then, on Fig 4 and Fig 6 the blue region is much smaller than the yellow region. How realistic is it ? In general, more connections to biology and possible predictions of the current model not present in the PORD model would be welcome...