Response to Referees’ Comments

**The authors would like to thank the editor and referees for their helpful comments and suggestions for changes. For clarity, all corrections made to the manuscript have been highlighted using bold text. We have given details of these alterations below (bold blue text).**

**Reviewer Comments**

**Reviewer 1 (Anonymous)**

**Basic reporting**

According to PeerJ policies, the submitted manuscript should be accompanied by a code used to implement the mathematical model - this requirement has not been fulfilled.

**We have submitted the MATLAB code for the individual-based model and the spatial moment approximation alongside our revised manuscript.**

**Experimental design**

No comments

**Validity of the findings**

When comparing all IBM images in the figure insets (except of panels D in Figs. 2 and 3), all simulated cell distributions look qualitatively similar, thus this is not clear whether the proposed C\_IBM and C\_SM can distinguish between these cell configurations. Some quantitative comparison between the obtained numerical results should be included to validate the techniques that have been presented.

**In Figures 2-3, we use our individual-based model (IBM) to simulate a moving population of cells and explore to what extent spatial structure is generated for different strengths of interaction between cells. We also explore the performance of the spatial moment model as an approximation to our IBM.**

**The pair-correlation function (PCF) CIBM(r), shown in each sub-figure, is a direct quantitative measure of the spatial pattern in the simulated cell populations at a particular time t (computed by averaging results over 500 repeated simulations). However, for ease of visualising the spatial pattern we show an example configuration of cells (taken from one of the 500 simulations at time t) in the inset. Therefore, while the patterns shown in some insets may appear qualitatively similar, the PCF CIBM(r) allows a quantitative comparison to be made and shows systematic differences in the simulated cell distributions, e.g. Poisson (Fig. 2A), regular (Fig. 2B) or clustered (Fig. 2C/D) patterns.**

**We have reworded the captions of Figures 2-3 and have included a sentence on p8, line 260-262, to clarify this.**

**Comments for the author**

The supplemental material (over 50 individual images) is impossible to review -- this should be collected in one file with proper annotations or legends.

**We have collated the 30 individual supplementary figures into 2 figures with appropriate captions.**

**Reviewer 2 (Jacob Scott)**

**Basic reporting**

Pass.

This is a clearly and thoughtfully written piece of scholarship that describes the authors step toward a comprehensive method of understanding collective cell movement. In this manuscript the authors utilize an individual based model and analytic methods to predict the eventual structure (after movement with graded levels of interaction with neighbors) of cellular populations.

They show that without the effect of nearby cells, the structure that they observe in their experimental construct does not match the theoretical predictions. This work stands alone as a single piece of scholarship, but also moves forward nicely from their earlier work in 1-dimensional movement.

**Experimental design**

Pass.

The experimental design was clearly described, as were the mathematical methods. Where there were gaps in the explanation, there were clear references to earlier work where these could be filled in. There were no ethical issues with this research.

**Validity of the findings**

I have no doubt that the findings in this work were reported dutifully, and that the methods were carried out as described.

There was discussion of neglecting the edge effects, and in particular only using a (relatively) small field of view - further, in the analytic methods, periodic boundary conditions were employed. I do wonder how the application of an edge correction method would (if at all) change the analysis.

**Thank you for raising this point – the use of edge corrections with our data was a key point of discussion during the data analysis stage of our work. Because the application of an edge correction can sometimes lead to an unknown extent of bias in the resulting distribution of distances (e.g. Haase, 1995), we made the decision to neglect edge effects in our data, prior to carrying out our analysis. However, our manuscript would indeed benefit from further discussion on this topic - we have included a paragraph to better motivate our decision not to employ an edge correction method in the discussion section (p12, lines 408-416) along with references to the relevant literature.**

**Haase, P. 1995. Spatial pattern analysis in ecology based on Ripley' s K-function : Introduction and methods of edge correction*. Journal of Vegetation Science,* 6(4): 575-582.**