Reviewer #3: I consider that the authors addressed all my previous points. After reading the new version of the manuscript I find it significantly improved. I am in favor of publishing the manuscript after the following points are being addressed:

1) On the page 7, last subsection of the Results section, the authors wrote "We now fed an agent-based model, implemented in the Morpheus toolbox". This sentence omits the modelling class that the model has, which is definitely more important than the software that the authors used to implement the model. Along the manuscript there is no reference to the fact that the authors use a Cellular Potts Model. This modelling class should be acknowledged in the text of the manuscript, together with an argument of why they favored this modelling class. In fact, they could have chosen Cellular Automata or Vertex model, among others. But CPM has some advantages that the authors used and some disadvantages that the authors circumvented. Hence, it is important to at least briefly elaborate on this.

We agree that the modelling class is an important point to discuss. We thus revised the Results, writing

“To model cell shape kinetics, cellular potts models (Graner and Glazier 1992), vertex models (Alt et al. 2017) and cellular automata (Manukyan et al. 2017) have been used in the past. We chose a cellular potts model, since it allows for arbitrary shapes and stochasticity in cell movement, and is easily applicable as the default implementation in the Morpheus environment (Starruß et al., 2014).”

and the Methods, where we now write:

“To assess the contribution of re-division events to the emerging spatial patterns of NSCs in S-phase, we simulated an NSC population using a cellular Potts model as implemented in Morpheus (Starruß et al., 2014).”

2) In the Supplementary Figure 4B, the authors show that cells divide immediately after S-phase. Nevertheless, this implies that G2-phase is nonexistent. Why is that? Did the authors have an estimation of the length of this phase and know that it is negligible compared to the others? If this is the case, this should be acknowledged in the manuscript.

Following the reviewer’s point, we revised the caption of Supplement Figure 4, where we now write:

“Note that we do not have any information about the length of G2 and thus do neither model nor visualize this phase in the graphs.”

3) The authors experimentally detected that the probability of re-division was ~.15. Yet, the fitting of the simple model after the ABC fitting returned a probability of ~0.38. What is the posterior distribution of this parameter? The authors mentioned in the methods section, subsection "Cell division model" that they used .15 as a lower boundary. Thus, the experimental value and the model estimate are not significantly different from each other? If the authors fix this parameter in 0.15 in the model and repeat the ABC fitting, would they obtain similar results? The authors mentioned in the legend of Supp. Fig. 4 B this difference, but I think this point should be acknowledged in the results section. The authors should at least discuss why there is this discrepancy.

We thank the reviewer for raising this important point. In the revised Results section of the manuscript, we now state clearer that these are two different parameters by writing::

“Note that while the re-division probability is a parameter of our model, the re-division fraction is an experimental observable, which depends on the measurement method. Using snapshot measurements, we found a re-division fraction of 15% re-divisions, which is considerably lower than the re-division probability of 38% (see S4B Fig for a detailed explanation).”

Regarding the question about fixing the re-division parameter to 0.15: We simulated patterns with various re-division probabilities. We found that already for a re-division probability of 0.20 aggregated pattern can no longer be significantly detected.

4) In Legend of Fig. 4 A, there is a grammar problem. Please re-write. Also, what is the meaning of grey and black in Fig. 4 C, D, G and H?

We revised the caption to Fig 4A where we now write:

“We use an agent-based cellular Potts model model to simulate NSC divisions with a re-division probability of $p_{re\text{-}div}$=0.38 and perform virtual measurements with labelling intervals Δt between 9h and 72h (here shown for Δt = 48h).“

We added the missing information about the black and gray coloring by writing:

“Labelling intervals that are also available from experimental data (see Fig 2C) are shown in black, all others in gray.”

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