Effective 2D model does not account for geometry sensing by self-organized proteins patterns

By means of a computational model analysis accompanying intriguing experiments, Schweizer et al. (1) claim to show that MinE membrane binding is responsible for self-organized geometry sensing.

We investigated the simulation files provided by the authors and found that the model neither accounts for actual MinE membrane interactions nor for any observed MinDE protein patterns. A detailed discussion of our analysis can be found in the supplementary document hosted at http://arxiv.org/abs/1403.5934. It does not reproduce any of the computational data presented in the article (1). For the published parameters, pattern formation is restricted to very small cytosol/membrane ratios. Cytosolic volume is not accounted for, and total densities indicate an effective bulk height less than 6 μm. We find that scaling the cytosolic dynamics by a small factor $\mathcal{O}(1)$ or increasing the gold layer size eliminates the instability. Hence, the model configuration deviates from the experiment by orders of magnitude. In striking contradiction to the accompanying experiments and to the claim in the article, bulk volume has a severe effect on the computational model. The authors compensate for this system size dependence by adjusting intrinsic system parameters (MinE/MinD ratio) without mentioning it. Moreover, the adjusted parameters deviate from the experimental value, whereas the published parameters do not.

Even with these adjustments, the model relies on simulation artifacts to reproduce the experimental data. Alignment to the aspect ratio requires periodic boundaries at the gold layer. The alignment angle is controlled by cross-boundary coupling in horizontal and vertical directions. The aspect ratio of the patch has a negligible effect on alignment. Alignment ceases and waves become disordered blobs if periodic boundary conditions are removed, or if the gold layer size is increased to match the experiment. This invalidates the model on a conceptual level.

The model is claimed to extend and supersede previous models by incorporating experimental evidence regarding MinE membrane interactions (2, 3). We note that MinE membrane binding was already proposed and analyzed by Arjunan and Tomita (4). Moreover, the model contradicts the experimental references in several aspects. Park et al. (3) have shown that unmasking the anti-MinCD domains in $MinE^{F7E/I24N}$ restores the WT phenotype without membrane binding. In contrast, computational patterns are lost if MinE membrane binding is reduced and cannot be recovered by adjusting MinE recruitment. Hence, the model actually implies that MinE membrane binding is required for pattern formation in the first place and not for geometry sensing in particular as the paper claims. The ratio of MinE/MinD residence times quantifies the relative strength of the MinE membrane binding. It has been quantified experimentally by Loose et al. (2). The value in the computational model exceeds the experimental value by an order of magnitude. As a consequence, MinDE waves contain about 10 times more MinE than MinD, in contradiction with experiments (2, 5). In particular, we note that the computational data in their figure 5*C* cannot be reproduced. We find a 16-fold increased MinE/MinD ratio, which represents a 23-fold deviation from the cited experiments (2).

We conclude that the computational model is invalid, and any conclusions drawn from it are void.

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4 Arjunan SN, Tomita M (2010) A new multicompartmental reaction-diffusion modeling method links transient membrane attachment of E. coli MinE to E-ring formation. *Syst Synth Biol* 4(1): 35–53.

5 Loose M, Fischer-Friedrich E, Ries J, Kruse K, Schwille P (2008) Spatial regulators for bacterial cell division self-organize into surface waves in vitro. *Science* 320(5877):789–792.

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The authors declare no conflict of interest.

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