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Analysis of robust pattern formation in the developing *Drosophila* eye using two mathematical models

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Motivation and Aim: *Drosophila* larval development is characterized by the formation of an ordered pattern of light sensitive units (ommatidia) in the presumptive eye structure, called eye imaginal disc. This pattern is initially determined by the precise spatial arrangement of R8 cells, future R8 photoreceptors. The mechanisms of formation and maintenance of the correct R8 cell arrangement, despite variability in expression of main regulators, remain elusive. Here, we use an *in silico* approach to study the regulatory mechanisms underlying the robust spatial pattern of R8 cells.

Methods and Algorithms: We implemented two mathematical models using the approach first introduced in [1, 2]. Previously developed mathematical models mostly include 'generalized' regulators that summarize the activating and repressive inputs of several gene products. Our approach provides incorporation of individual regulators into the model. The numerical simulations of cell differentiation process were visualized on the two-dimensional grid consisting of 2600 cells. To analyze the robustness of pattern formation, we randomly introduced noise into the model parameters.

Results: The spatial patterning of R8 cells comprises several steps, which are manifested in the expression of major proneural gene *atonal.* At the first step, the proneural clusters, including several R8 cells, are formed. Next, a single R8 cell is selected within each cluster to become the R8 photoreceptor. There are several concepts regarding the R8 cell selection, however, all of them involve a classic mechanism of lateral inhibition by the Notch-Delta pathway at a certain stage of pattern formation [3]. We studied the behavior of two models that differently implement the mechanism of local activation of *atonal* in the R8 cells and inhibition of its activity in the surrounding cells [1, 2]. The first model used the mechanism of local *atonal* activation by *scabrous* gene. In the second model, *scabrous* played a role of an indirect activator, acting through the inhibition of repression by the Notch-Delta pathway. We analyzed the response of the pattern structure to parameter perturbations within the two models. As a result, we characterized the features of stable pattern formation associated with each activation mechanism.

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