

Biological pattern formation: an eye on neurogenic wavefronts

Pau Formosa-Jordan*^(1,2), Marta Ibañes Miguez⁽¹⁾, Saúl Ares^(2,3) and José María Frade⁽⁴⁾

⁽¹⁾ *Departament d'Estructura i Constituents de la Matèria, Facultat de Física, Universitat de Barcelona, Spain*

⁽²⁾ *Max Planck Institute for the Physics of Complex Systems, Dresden, Germany*

⁽³⁾ *Logic of Genomic Systems Laboratory, Spanish National Biotechnology Centre CNB-CSIC, Madrid, Spain; and GISC*

⁽⁴⁾ *Instituto Cajal, CSIC, Madrid, Spain*

Pattern formation is an essential part of embryonic development. When an organism develops, cells become distinct from each other creating robust patterns. Neurogenesis is an example of such a process in which individual cells single out to become neurons from a group of equivalent progenitor cells.

Pattern formation during neurogenesis has two features that strongly differ from those common in Physics pattern formation processes: it drives a spatially discrete fine-grained pattern (composed of two cell types) and it does not involve any transport of a chemical but just short-range cell-to-cell communication. In addition, pattern formation during neurogenesis often does not occur through pattern nucleation at different spatial locations or through spontaneous propagation over a less stable state. Instead, the neurogenic pattern grows regularly from a single expanding domain (Fig. 1) and its spreading is both externally and internally regulated. Pattern expansion requires a diffusing molecule (morphogen) that enables the dynamics of patterning to occur and whose production is, in turn, controlled by the pattern itself. Note that this morphogen is not involved itself in the pattern formation. This scenario is what we call a self-regulated wavefront.

How this propagation and the pattern left behind depend on the state of the invaded tissue? We have addressed this question combining both theory and experiments¹. First, we have provided evidence of the molecular state of the invaded tissue in the vertebrate embryonic retina. Second, we have evaluated computationally the implications of such a state. To this end, we have modelled the neurogenic wavefront in terms of four variables: the morphogen, two variables that set the spatial interaction between cells, and a fourth variable that is a readout of the state of differentiation. Since this process is the result of biochemical interactions, we have extended our description to Langevin dynamics in which a multiplicative noise takes into account the intrinsic randomness of such reactions. Finally, we have also

included the irregular shape and arrangement of cells in tissues.

Our results predict that a change in the state of the invaded tissue from the normal wild type conditions strongly alters pattern formation and wavefront propagation, frequently yielding irregular growing patterns. These results are consistent with previous experimental observations² and provide a potential explanation. Moreover, we have extended our conclusions to the context of neurogenesis in the fruit fly's eye, by first mimicking computationally experimental data previously reported³.

Altogether, our work exemplifies the complexity of biological pattern formation and the benefit of using hybrid computational-experimental strategies.

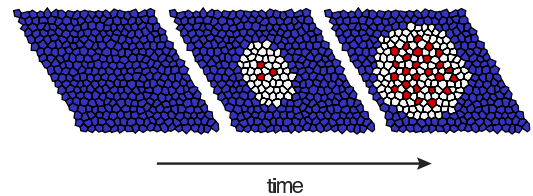


FIG. 1. Snapshots from simulation results, showing a growing pattern of different cell types, mimicking the neurogenic wavefront in the vertebrate eye. Red cells are newly differentiated neural cells, white cells have the potential to commit to the neural fate, and blue cells correspond to non-neural tissue invaded by the neurogenic wavefront.

* pformosa@ecm.ub.es

¹ P. Formosa-Jordan, M. Ibañes, S. Ares and J.M. Frade. *Development*, in press.

² S.F. Rocha, S.S. Lopes, A. Gossler, and D. Henrique. *Dev. Biol.* **328**, 54 (2009).

³ N.L. Brown, C.A. Sattler, S.W. Paddock and S.B. Carroll. *Cell* **80**, 879 (1995).