Pattern selection by dynamical paths

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During embryonic development isogenic cells acquire distinct traits, becoming differentiated into different cell types. Differentiation commonly involves spatial coupling through signaling gradients or cell-to-cell communication, and it is usually related to pattern formation. The selection of a specific pattern, with a characteristic number and location of each cell type, is crucial for tissue formation. Therefore, this selection is reliable done. Yet, the dynamics underlying developmental programs are highly complex, nonlinear and involve stochasticity. The stochasticity partially arises from the low copy number of the reactants involved in these genetic reactions. These dynamics can potentially drive multiple stable patterns. This raises the issue of how pattern selection can occur and how reliable selections can arise.

Herein we make use of a model[2] that mediates cell-to-cell communication through an intercellular mutual inhibition and includes a cell-autonomous negative feedback loop[3] to address these issues. drive several different stable pattern solutions[3]: homogeneous solutions – all cells are the same cell type (H in FIG. 1) –, *salt-and-pepper* patterns – periodic patterns composed of two cell types, one completely surrounding the other one (P and I in FIG. 1) –, and the stripped pattern – two cell types forming rows of cells (S in FIG. 1). This dynamics have been used to characterize the interaction between cells through the Notch pathway, which is one of the main signaling pathways acting during animal development. This pathway relies on a transmembrane receptor, Notch, that can bind to a ligand, Delta, anchored on an adjacent cell.

We consider the dynamical process of reaching a spatio–temporal pattern through the dynamical change of a control parameter (signal, Fig.1). Therefore, the pattern which is finally selected and the reliability of this selection depends on the dynamical evolution of this control parameter. Changes on parameters are translated into dynamical paths on the parameter space, where different regions are identified according to the pattern solutions that are stable. Hence, the characteristics of these dynamical paths are crucial for selecting a certain pattern under a scenario in which different solutions coexist.

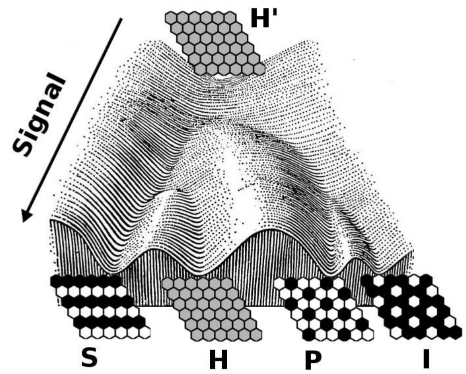

FIG. 1. Modification of the figure of Waddington's epigenetic landscape[5]. The system starts in a homogeneous solution (H) and, after a parameter modification (signal), it can select among four different patterns: S, H, P, I.

Our study shows the dependency of the pattern finally selected and the characteristics of the chosen dynamical path. These characteristics consist on (i) the existence of a pattern and its stability in the different regions crossed by the path, (ii) the velocity of the parameter changes, and (iii) whether the dynamical path simultaneously occurs in all cells or it sequentially occurs along the tissue through a propagating wave. Among others, we show that the pattern of stripes, which does not correspond to the fastest growing mode, can be selected if the parameter change propagates with an optimal velocity[5].

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[2] Collier JR, Monk NA, Maini PK, and Lewis JH (1996) *Pattern formation by lateral inhibition with feedback: a mathematical model of Delta-Notch intercellular signalling.* J Theor Biol 183: 429–446.

[3] Formosa-Jordan P, Ibanes M (2013) Competition in Notch signaling with cis enriches cell fate decisions. Submitted.

[4] Waddington CH (1942) *Canalisation of development and the inheritance of acquired characters.* Nature 150: 563–564

[5] Palau–Ortin D, Formosa–Jordan P, Sancho JM, and Ibañes M (2014) *Pattern selection by dynamical paths.* Preprint