Computational analysis of neurogenesis in a regenerative neuroepithelium

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The olfactory epithelium (OE) of the mouse has proved to be an exceptional good system for exploring the regulation of neurogenesis. The numbers and arrangements of cells within neural structures are tightly controlled. During OE development and regeneration, ORNs are produced by regulated proliferation of different progenitor cell types. Crucial to this process is a negative feedback loop in which GDF11, a protein produced by ORNs, inhibits proliferation of ORN progenitors. Both ORNs and progenitors also produce a potent GDF11 inhibitor, follistatin, which is secreted additionally by stromal cells underlying OE. The existence of this inhibitor-of-an-inhibitor creates the possibility of positive, as well as negative, feedback control in this system.

A central question is how these interactions create a dynamics that the layered neural structure in the epithelium is formed. Since the same cells are both producers and targets of GDF11 and follistatin, we designed a computational model including reaction-advection-diffusion processes with feedback effects in time and space as well as cells at different stages, with a moving boundary to be determined as part of the solution of the model. This model then is solved numerically by fi nite difference schemes. Simulation results show the dynamics that a synergistic feedback loop induced by signaling molecule GDF11 organizes neural cells into the layered tissue structure.