CALIFORNIA INSTITUTE OF TECHNOLOGY
BioEngineering

Bi 250

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Problem Set #8

Issued: 5 Mar 12
Due: 14 Mar 12

1. *Pattern formation by lateral inhibition. Based on Collier et al., Journal of theoretical biology, 1996*

   The Notch-Delta signaling pathway allows communication between neighboring cells during development. It has a critical role in the formation of 'fine-grained' patterns, generating distinct cell fates among groups of initially equivalent neighboring cells and sharply delineating neighboring regions in developing tissues. In this problem, we investigate the pattern-forming potential and temporal behavior of the Collier model.

   The dynamics of Notch (n_p) and Delta (d_p) for each individual cell p are governed by:

   $$\dot{n_p} = f(\bar{d_p}) - n_p$$

   $$\dot{d_p} = \nu(g(n_p) - d_p)$$

   where $\bar{d_p}$ denotes the mean of the levels of Delta activity in the cells adjacent to cell p, and

   $$f(x) = \frac{x^k}{a + x^k}, g(x) = \frac{1}{1 + bx^h}$$

   (a) Describe the model and state its assumptions. Describe what the steady state will look like in a simulation of this model.

   (b) What is the main feature of the model that allows fine grain patterning? Comment on its properties.

2. *Scaling of morphogen gradients. Based on Ben-Zvi, Barkai, PNAS, 2010*

   Consider the feedback "expansion-repression" model for morphogen gradient scaling in which the range of the morphogen gradient, [M] increases with the abundance of some diffusible molecule [E], whose production, in turn, is repressed by morphogen signaling. The partial differential equations

   $$\frac{d[M]}{dt} = D_M \nabla^2[M] - (1 + [E])^{-1_1} \alpha_M^1 [M] - (1 + [E])^{-1} \alpha_M^2 [M]^2$$

   $$\frac{d[E]}{dt} = D_E \nabla^2[E] - \alpha_E^1 [E] + \beta_E \frac{1}{1 + ([M]/T_{rep})^h}$$

   and boundary conditions:

   $$D_M \nabla[M]_{x=0} = -\eta_M$$

$$D_M \nabla [M]_{x=L} = 0$$
$$D_E \nabla [E]_{x=0} = 0$$
$$D_E \nabla [E]_{x=L} = 0$$

represent the dynamics of morphogen/expander concentrations with respect to position and time.

a) Explain the dynamics of the expansion-repression mechanism at three different times: when the morphogen gradient is sharp, when the gradient expands, and at steady state.

b) What is the condition on the diffusion of the expander that allows for scaling of the gradient?