Math 19. Lecture 31
Switches

T. Judson

Fall 2005

1 Pocket Gophers and Mite Parasites

Consider the co-evolution of pocket gophers and their mice parasites. Suppose that $g(t)$ represents the fraction of gophers of a certain blood type and $m(t)$ the fraction of lice that like to feed on gophers of that blood type.

- This interaction might be governed by the following system.

$$\frac{dg}{dt} = F(g, m) \tag{1}$$

$$\frac{dm}{dt} = H(g, m). \tag{2}$$

- Since the parasites reproduce at a much faster rate than the gophers, (1) must be the slow moving system and (2) must be the fast moving system. This dictates that $|F(g, m)|$ should be much smaller than $|H(g, m)|$ except near those values of (g, m) where is $H = 0$.

- The requirement that $|F| \ll |H|$ says that for most values of (g, m) the function $g(t)$ is changing at a much slower rate that $m(t)$.

- For any given initial value for m, a good first approximation to (1) and (2) can be obtained by regarding g as a constant in (2) and using it as a parameter for m. Using this approximation,

$$\frac{dm}{dt} = H(g, m)$$

predicts that $m(t)$ will be found equal to one of the solutions to the equation

$$H(g, m) = 0, \tag{3}$$

where

$$\frac{\partial H}{\partial m}(g, \cdot)|_m < 0. \tag{4}$$

The condition in (3) says that m is an equilibrium point to

$$\frac{dm}{dt} = H(g, m).$$

The condition in (4) says that this equilibrium point is stable.

- In general, g will not be truly constant as its motion is controlled by

  $$\frac{dg}{dt} = F(g, m).$$

  That is, g will change slowly and thus the conditions in (3) and (4) that depend on g will change slowly, and thus m will change slowly even as it stays close to obeying (3) for each value of t.

- An exception occurs when g evolves in

  $$H(g, m) = 0$$

  so as to make one of the stable equilibria of the m equation disappear. In the figure below, we get a sudden switching from 0.1 to 0.7. Such switches are sometimes called *catastrophes*.

2 Thresholds in Development

A fundamental application of these fast-slow ideas can be seen in the article *Thresholds in Development*.[1] The point of the article is to present and give evidence for a model that explains how nearest neighbor cells in an embryo might naturally develop in drastically different ways. Lewis, Slack, and Wolpert sought a mechanism that was compatible with the notion that development is determined by relative concentrations of ambient chemicals (e.g. morphogens).

[1] Lewis, Slack, and Wolpert. "Thresholds in Development," *Journal of Theoretical Biology* **65** (1977) 579–590. See Reading 26.1 (pp. 421–428).

2.1 The Historical Context of the Article

The proposed explanations for such catastrophic difference in offspring fate had two fundamental flaws.

- They required drastic and unrealistic changes in the size of the morphogen concentration over very small distances.
- They couldn't explain how cells "remember" morphogen signals after the morphogen dissipates.

2.2 The Proposed Model

Lewis, Slack, and Wolpert considered the activation of a gene G by a signaling substance S.

- The amount of G's product at time t is denoted by $g(t)$.
- The amount of S at time t is given by S(t).
- Lewis, Slack, and Wolpert proposed that the rate of change of g depends linearly on the amount of S, there are feedbacks so that relatively small concentrations of g promote g's growth, while large concentrations inhibit it.
- They considered the following equation for g:

$$\frac{dg}{dt} = k_1 S + \frac{k_2 g^2}{k_3 + g^2} - k_4 g, \tag{5}$$

  where the k_i's are constants.

2.3 The Analysis of the Model

Lewis, Slack, and Wolpert considered the behavior of g for different values of S. The plot of the right-hand side of (5) has different numbers of stable equilibrium points.

When $S < S_c$, there are two stable equilibria, one near $g = 0$ and one with g much larger than zero. There is also one unstable equilibrium point between the two stable ones. Thus, as $S \to S_c$, the small g stable equilibrium point cancels against the unstable one so that when $S > S_c$, there is only one stable equilibrium point, and this one is where g is relatively large.

2.4 An Explanation

This model explains how two adjoining cells can have different values of g even though they are close together. All we need is that S is near S_c at these two cells but with S slightly larger than S_c in one cell and slightly smaller that S_c in the other cell. the result is that the former cell has g near zero while the latter cell has relatively large g. Moreover, if S subsequently decreases to zero (because the signaling cells are no longer active), then the drastic difference in g output by these two neighboring cells still remains.

Readings and References

- C. Taubes. *Modeling Differential Equations in Biology.* Prentice Hall, Upper Saddle River, NJ, 2001. Chapter 26.
- "Thresholds in Development," pp. 421–428.