BULLETIN OF THE
AMERICAN MATHEMATICAL SOCIETY
Volume 82, Number 1, January 1976

A DIRECTION OF BIFURCATION FORMULA IN THE THEORY OF THE IMMUNE RESPONSE[1]

BY GEORGE H. PIMBLEY, JR.

Communicated by A. H. Householder, September 7, 1975

In previous work [1], I derived by biological reasoning and mathematical reduction the following system, attributable to G. I. Bell:

$$du/ds = u[\lambda_1 + k\lambda_1 u - k(\alpha_1 - \lambda_1)v + kn\lambda_1 w], \tag{1a}$$

$$dv/ds = \beta\{v[-\lambda_2 - k(\alpha_2 + \lambda_2)u - k\lambda_2 v - kn\lambda_2 w] + k\gamma uw\}, \tag{1b}$$

$$dw/ds = w[-\lambda_3 + k(\alpha_3 - \lambda_3)u - k\lambda_3 v - kn\lambda_3 w - (k\alpha_3/\theta)uw]. \tag{1c}$$

Equations (1) simulate the immune response of an organism to antigen invasion. The dependent variables u, v, w are, respectively the concentrations of antigens, antibodies, and antibody-producing cells. The meanings of all parameters and constants are found in [1, pp. 93–96].

Equations (1) have two nontrivial rest points. The one nearest the origin, (u_f, v_f, w_f), is stable or unstable according to whether $\beta > \beta_c$ or $\beta < \beta_c$, where $\beta_c > 0$ is a critical value of the parameter β in equation (1b). It is shown [1, Theorem 1] that at $\beta = \beta_c$, a continuous family of periodic solutions bifurcates from (u_f, v_f, w_f). I was able to obtain a direction of bifurcation formula only in the special case where $\lambda_3 = 0$. Namely, periodic solutions bifurcate to the left (right) of β_c, and are stable (unstable) if

$$\beta_c > (\alpha_1 - \lambda_1)\lambda_1/((\alpha_1 - \lambda_1)(\alpha_2 + \lambda_2) + 2\lambda_1\lambda_2), \quad (<). \tag{2}$$

Herein I announce the development of a general formula for direction of bifurcation in equations (1), which approaches condition (2) as $\lambda_3 \longrightarrow 0$. An analytic direction of bifurcation formula will be important in developing the global theory of these bifurcated families of periodic solutions, and in ascribing possible biomedical implications. I describe the new formula.

First we substitute $u = u_f + u^0$, $v = v_f + v^0$, $w = w_f + w^0$ into equations (1), and thus obtain equations centered at (u_f, v_f, w_f). Then we let A_{β_c} be the matrix of the linear part of these centered DE's, with $\beta = \beta_c$. The matrix A_{β_c} has the three linearly independent eigenvectors represented symbolically as

$$(\xi_1, \eta_1, \zeta_1), \quad (\bar{\xi}_1, \bar{\eta}_1, \bar{\zeta}_1), \quad (\xi, \eta, \zeta). \tag{3}$$

AMS (MOS) subject classifications (1970). Primary 92A05; Secondary 34C05.

[1]Work performed under the auspices of the U. S. Energy Research and Development Administration.

Equations (1) also have an invariant surface passing through (u_f, v_f, w_f), represented as follows:

$$z = \phi(x, y) = a_{20}x^2 + a_{11}xy + a_{02}y^2 + o(x^2 + y^2), \tag{4}$$

where x, y, z are new dependent variables obtained from (u^0, v^0, w^0) through a principal axis transformation.

We must define the following quantities:

$$\begin{aligned} &C = is_{12}^{-1}\beta_c\lambda_2, \quad D = is_{12}^{-1}\beta_c(\alpha_2 + \lambda_2) + is_{11}^{-1}(\alpha_1 - \lambda_1), \\ &E = is_{12}^{-1}\beta_c\lambda_2 n + is_{13}^{-1}\lambda_3, \\ &F = -is_{12}^{-1}\beta_c\gamma - is_{11}^{-1}\lambda_1 n - s_{13}^{-1}(\alpha_3 - \lambda_3 - (2\alpha_3/\theta)w_f), \\ &G = -is_{11}^{-1}\lambda_1, \quad H = is_{13}^{-1}(n\lambda_3 + (\alpha_3/\theta)v_f), \quad I = is_{13}^{-1}\alpha_3/\theta, \end{aligned} \tag{5}$$

where

$$s_{11}^{-1} = \frac{\zeta\bar{\eta}_1 - \bar{\zeta}_1\eta}{\Delta}, \quad s_{12}^{-1} = \frac{-\zeta\bar{\xi}_1 + \bar{\zeta}_1\xi}{\Delta}, \quad s_{13}^{-1} = \frac{\eta\bar{\xi}_1 - \bar{\eta}_1\xi}{\Delta}$$

with

$$\Delta = 2i[\xi \operatorname{Im}(\eta_1\bar{\zeta}_1) - \eta \operatorname{Im}(\xi_1\bar{\zeta}_1) + \zeta_1 \operatorname{Im}(\xi_1\bar{\eta}_1)].$$

We make the realistic assumption that $\alpha_1 > \lambda_1$, $\alpha_3 > \lambda_3$.

Also we need the constant $l = \sqrt{\operatorname{trace} A_{\beta_c}^c}$ where $A_{\beta_c}^c$ is the first compound of the matrix A_{β_c}.

Using the constants defined in (4), I put forward the following direction of bifurcation criterion: Define

$$\begin{aligned} \kappa = \frac{1}{l} \operatorname{Re}\{&i(a_{20} - a_{02} + ia_{11})[2\eta\bar{\eta}_1 C + (\xi\bar{\eta}_1 + \eta\bar{\xi}_1)D + (\eta\bar{\zeta}_1 + \zeta\bar{\eta}_1)E \\ &\qquad + (\xi\bar{\zeta}_1 + \zeta\bar{\xi}_1)F + 2\xi\bar{\xi}_1 G + 2\zeta\bar{\zeta}_1 H] \\ &+ 2i(a_{20} + a_{02})[2\eta\eta_1 C + (\xi\eta_1 + \eta\xi_1)D + (\eta\zeta_1 + \zeta\eta_1)E \\ &\qquad + (\xi\zeta_1 + \zeta\xi_1)F + 2\xi\xi_1 G + 2\zeta\zeta_1 H] \\ &\qquad + i\xi_1\zeta_1^2 I + 2i\xi_1|\zeta_1|^2 I\} \\ + \frac{2}{l^2} \operatorname{Re}\{&-(i/2)[2|\eta_1|^2\bar{C} + (\xi_1\bar{\eta}_1 + \bar{\xi}_1\eta_1)\bar{D} + (\eta_1\bar{\zeta}_1 + \bar{\eta}_1\zeta_1)\bar{E} \\ &\qquad + (\xi_1\bar{\zeta}_1 + \bar{\xi}_1\zeta_1)\bar{F} + 2|\xi_1|^2\bar{G} + 2|\zeta_1|^2 H] \\ &\times [\bar{\eta}_1^2\bar{C} + \bar{\xi}_1\bar{\eta}_1\bar{D} + \bar{\eta}_1\bar{\zeta}_1\bar{E} + \bar{\xi}_1\bar{\zeta}_1\bar{F} + \xi_1^2\bar{G} + \bar{\zeta}_1^2\bar{H}]\}. \end{aligned} \tag{6}$$

The criterion is as follows: If κ is negative (positive), then the bifurcation periodic solutions of equations (1) exist in a left (right) neighborhood of $\beta = \beta_c$, and are stable (unstable).

As can be seen in (5), the quantities C, D, E, F are linear in the critical value β_c. Therefore formula (6) gives a representation that is a quadratic function of β_c. Moreover it turns out that the quadratic equation $\kappa = 0$ has a largest positive root when $\lambda_3 \geqslant 0$. We call this root β_{cc}.

Then the criterion for direction of bifurcation can be interpreted as follows: If $\beta_c > \beta_{cc}$, $(<)$, the bifurcated periodic solutions emanating from $\beta = \beta_c$ exist in a left (right) interval of β_c and are stable (unstable).

The quantity on the right in inequality (2) is, in fact, the greatest positive root of $\kappa = 0$ when $\lambda_3 = 0$.

The proof utilizes the focal point-saddle point type of analysis that goes back to Poincaré [2, pp. 167–181].

REFERENCES

1. G. H. Pimbley, Jr., *Periodic solutions of third order predator-prey equations simulating an immune response,* Arch. Rational Mech. Anal. **55** (1974), 93–123.

2. H. Poincaré, *Collected works.* Vol. I, Gauthier-Villars, Paris, 1951.

THEORETICAL DIVISION, UNIVERSITY OF CALIFORNIA, LOS ALAMOS SCIENTIFIC LABORATORY, LOS ALAMOS, NEW MEXICO 87545