$$\in \partial h(v^\varepsilon(s)) + v^\varepsilon - v^* \quad a.e.\ s \in ]0,T[.$$

Relations (12), (13) and (20) represent the Euler-Lagrange optimality equations for the approximate control problem $(P^\varepsilon)$. Passing to the limit in these equations for $\varepsilon \to 0$, we obtain (8),(9), (10).

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*Department of Mathematics*
*Polytechnic Institute*
*R - 6600, Iasi*
*ROMANIA*

ANALELE STIINTIFICE ALE UNIVERSITATII "AL.I.CUZA" IASI
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# ON STABILITY AND BIFURCATION OF IMMUNE SYSTEM

BY

M.M.A. El-SHEIKH and A.A.SOLIMAN

**1.Introduction**. The immunity process of an organism to infection where devised in mathematical models as a two-component system of ordinary differential equations by B e l l [2],[3]. Recently P r i m b l e y [11], [12], improved Bell's model and discussed oscillation and stability of steady states using L e f s c h e t z approach [8]. Moreover he introduced in [11],[12],[13],[14], a 3-component model describing the immunity process of an organism to infection, the interaction between the produce of antibodies when stimulated by antigen. During his papers, P i m b l e y has been studied oscillation of steady states solutions using an artificial parameter on both the two and three-dimension systems. In this paper, we consider both the two and three-component immune systems introduced by [11],[12]. We discuss the stability and bifurcation of periodic solutions and then we use the technique of [7],[9] to apply the centre manifold theory.

In section 2 we use a very simple technique introduced by P o o r e [15] depends on monotonicity of one of the natural parameters given in the immune 2-component system to discuss existence, index and stability of steady states. In section 3 we study the Pimbley 3-component immune system, Hopf's bifurcation and center manifold theories are considered our approach depends on the improved technique of [6],[9]. Finally in section 4, we use Poincare-Andronov substitution ([1],[16]) to discuss the global stability by discussing the behaviour of path at infinity.

**2.Bell's immune 2-component system**. In this section we discuss a 2-component immune system recently introduced by [2],[3]. Using a very simple monotonicity technique of [15], we study in details the existence, index and stability of steady states.

Consider the 2-component system

$$(2.1) \qquad \begin{aligned} u' &= uf(u,v) \\ v' &= vg(u,v) \end{aligned}$$

where

$$f(u,v) = -\lambda_2 - k\lambda_2 u + k(\alpha_2 - \lambda_2)\bar{v} - k\frac{\alpha_2}{\theta}uv$$

$$g(u,v) = \lambda_1 - k(\alpha_1 - \lambda_1)u + k\lambda_1 v.$$

Here, $u$ and $v$ denote the concentration of antibody and antigen respectively, $\alpha_1$ denotes the elimination rate of antigen when antigen bounded to antibody, $\lambda_1$ is the increasing rate of antigen when antibody is absent, $\alpha_2$ denotes the rate production of antibody which stimulates binding of antigen to antibody, and $\lambda_2$ denotes the decreasing rate of antibody when antigen is absent.

The steady states $(\bar{u},\bar{v})$ of the 2-component system (2.1) are the solution of the equations

$$(2.2) \qquad -\lambda_2 - k\lambda_2\bar{u} + k(\alpha_2 - \lambda_2)\bar{v} - k\frac{\alpha_2}{\theta}\bar{u}\bar{v} = 0$$

$$\lambda_1 - k(\alpha_1 - \lambda_1)\bar{u} + k\lambda_1\bar{v} = 0$$

We shall use the monotonicity techinique introduced by P o o r e [15] to study the existence, index and stability of steady states of (2.2) by drawing the relation between the parameter $\alpha_2$ against $\bar{u}$, assuming that all other parameters be fixed.

Solving the two equations in (2.2) simultaneously in $\bar{v}$ and $\alpha_2$ , we get

$$(2.3) \qquad \bar{v} = \frac{k(\alpha_1 - \lambda_1)\bar{u} - \lambda_1}{k\lambda_1}$$

$$(2.4) \qquad \alpha_2 = \frac{k\alpha_1\lambda_2\theta\bar{u}}{(\theta - \bar{u})[k(\alpha_1 - \lambda_1)\bar{u} - \lambda_1]}$$

Thus the relation between $\alpha_2$ and $\bar{u}$ may look like Fig.(1)

Now, the coefficient matrix $A$ of the linearized problem

$$y' = Ay$$

is corresponding to (3.3.1), where

$$(2.5) \qquad A = \begin{pmatrix} uf_u + f & uf_v \\ vg_u & vg_v + g \end{pmatrix} =$$

$$= \begin{pmatrix} -\lambda_2 - k[2\bar{u}(\lambda_2 + \alpha_2\bar{v}) + (\alpha_2 - \lambda_2)\bar{v}] & k\bar{u}(\alpha_2 - \lambda_2 - \frac{\alpha_2}{\theta}\bar{u}) \\ -k\bar{v}(\alpha_1 - \lambda_1) & \lambda_1 - k(\alpha_1 - \lambda_1)\bar{u} + 2k\lambda_1\bar{v} \end{pmatrix}$$

Thus, by using (2.3) and (2.4), it is easy to see that

$$(2.6) \qquad \Delta = \det A = M\frac{d\alpha_2}{d\bar{u}} + N$$

where

$$M = [(k+1)(\alpha_1 - \lambda_1) + k\frac{(\alpha_1 - \lambda_1)^2}{\lambda_1}\bar{u}]\{\frac{\bar{u}^2(\theta - \bar{u})[k(\alpha_1 - \lambda_1)\bar{u} - \lambda_1]}{k(\alpha_1 - \lambda_1)\bar{u}^2 - \lambda_1\theta}\}$$



$$N = k(\alpha_1 - \lambda_1)\bar{u}\{3k\lambda_2\bar{u} - k\frac{\alpha_1}{\lambda_1}(\lambda_2 + 2\bar{u}) + 2\bar{u}(k\bar{u} + 1)\} +$$

$$+ \frac{\bar{u}}{\lambda_1}(\alpha_1 - \lambda_1)(\lambda_2 + \frac{\bar{u}}{\theta})[k(\alpha_1 - \lambda_1)\bar{u} - \lambda_1]^2,$$

$$M > 0, N > 0 \; for \; \theta > \bar{u}, \frac{\alpha_1(2\bar{u} + \lambda_2)}{3\lambda_2\bar{u}} < \lambda_1 < \frac{k(\alpha_1 - \lambda_1)\bar{u}^2}{\theta}.$$

By the above discussion and Fig.(1) we can obtain the following result.

**Lemma 2.1**: *Let $\alpha_1 > \lambda_1$ , $\theta > \bar{u}$, and*

$$\frac{\alpha_1(2\bar{u} + \lambda_2)}{3\lambda_2\bar{u}} < \lambda_1 < \frac{k(\alpha_1 - \lambda_1)\bar{u}^2}{\theta}.$$

*If trace $A \neq 0$, then*

(i) *there exists a unique positive nontrivial steady state for $\bar{u}$ in $(0, \frac{\lambda_1}{k(\alpha_1 - \lambda_1)})U(\frac{\lambda_1}{k(\alpha_1 - \lambda_1)}, \theta)$,*

(ii) *the nontrivial steady state is a node with index*

$$I = \frac{\det A}{|\det A|} = \Delta / |\Delta| = +1.$$

By (2.5) the characteristic roots obey the characteristic equation

$$(2.7) \qquad \nu^2 - \sigma\nu + \Delta = 0$$

where

$$\sigma = \lambda_1 - \lambda_2 + k[(\alpha_2 + 2\lambda_1 - \lambda_2)\bar{v} - (2\lambda_2 + \frac{\alpha_2\bar{v}}{\theta} + \alpha_1 - \lambda_1)\bar{u}]$$

and

$$\bar{\Delta} = 2k^2\bar{u}\bar{v}(\alpha_1 - \lambda_1)(\alpha_2 - \lambda_2) + k(\alpha_1 - \lambda_1)[\lambda_2\bar{u} + 2k\bar{u}^2(\lambda_2 + \frac{\alpha_2\bar{v}}{\theta} - \lambda_1\bar{v}] -$$

$$- \lambda_1\{\lambda_2(1 + 2k\bar{v}) + 2\bar{u}k(1 + k\bar{v})(\lambda_2 + \frac{\alpha_2}{\theta}) + k^2\bar{v}[2(\alpha_2 - \lambda_2)\bar{v} + \frac{\alpha_2}{\lambda_1\theta}\bar{u}^2]\}$$

We denote by the R o u t h - H e r w i t z ([4]) that necessary and sufficient conditions for the steady states $(\bar{u},\bar{v})$ of (2.1) to be asymptotically stable are

$$\lambda_1\frac{\bar{v}}{\bar{u}} < \lambda_2 < \frac{\alpha_2}{\alpha_1}(\alpha_1 - \lambda_1), \quad \alpha_2 < [\frac{1}{2}(\lambda_1\bar{v} - \lambda_2\bar{u})]^2 - \alpha_1\lambda_2(\alpha_1 - \lambda_1)$$

provided that

$$\sqrt{\lambda_2} < \sqrt{\lambda_1} < \sqrt{\alpha_1} < \frac{1}{2}\frac{\lambda_1\bar{v} - \lambda_2\bar{u}}{\sqrt{\lambda_2}}$$

and $\theta$ is sufficiently large.

Now to discuss global asymptotic stability of the null steady state , we consider the Liapunov function

$$E = a^* u^2 + (b^* + c^*)uv + d^* v^2 \tag{2.8}$$

where

$$a^* = \frac{1}{2}[k(\alpha_2^2 + 1) + \lambda_2]^{-1} > 0,$$

$$b^* = \frac{\lambda_1}{2R}[\lambda_2 + k(2 + 2\alpha_2^2 + \lambda_2 - \alpha_2)] > 0,$$

$$c^* = \frac{1}{2R}[k\alpha_2(\alpha_2\lambda_2 - 1) + \lambda_2(k + \lambda_2)] > 0,$$

$$d^* = \frac{k}{2R}(\alpha_2 - \lambda_2)[(\lambda_2 + k\alpha_2^2) + (k\alpha_2\lambda_1 - k(\alpha_2 - \lambda_2)],$$

Here

$$R = \lambda_1\lambda_2[\lambda_1 - \lambda_2 + k(\alpha_2^2 - 1)][k(\alpha_2^2 + 1) + \lambda_2] > 0.$$

Then, its derivative is given by

$$E' = 2a^* uu' + (b^* + c^*)(f + g)uv + 2d^* vv' =$$

$$= [2a_0^*(\lambda_2 + k\alpha_2^2)]u^2 + (b^* + c^*)[\lambda_1 - \lambda_2 + k\alpha_2(\frac{1}{\lambda_2} - \alpha_2)]uv+ \tag{2.9}$$

$$+ [2d^*\lambda_1(1 + k\frac{\alpha_2}{\lambda_2})]v^2 \quad where\ a_0^* = -a^* ,$$

thus for $\lambda_2 < \lambda_1 < 1$ and $\alpha_2 < 1/\lambda_2$, $E'$ is positive-definite function, consequently $(\bar{u}, \bar{v})$ is unstable.

**3.Pimbley three-component immune system.** In 1974 P i m b l e y [12], [13] introduced the 3-component sytem.

$$u' = uf(u, v, w)$$

$$v' = vg(u, v, w) + k\gamma uw \tag{3.1}$$

$$w' = wh(u, v, w) + s[1 + k(u + v + nw)]$$

where

$$f(u, v, w) = \lambda_1 - k\lambda_1 u - k(\alpha_1 - \lambda_1)v + kn\lambda_1 w$$

$$g(u, v, w) = -\lambda_2 - k(\alpha_2 + \lambda_2)u - k\lambda_2 v + kn\lambda_2 w$$



$$h(u, v, w) = -\lambda_3 + k(\alpha_3 - \lambda_3)u - k\lambda_3 v - kn\lambda_3 w - k\frac{\alpha_3}{\theta}uw$$

Here $u, v$ and $w$ denote the concentrations of antigen, antibody and antibody producing cells respectively, $\lambda_3$ denotes the rate of the elimination of antibody producing cells on the absence of antigens, $\alpha_2$ denotes the rate of expanding anti-bodies, $\alpha_3$ denotes the rate constant of binding the antigen to receptors of the cells (which produce antibody) stimulates the producing of cells, $\theta$ denotes the concentration level that can be exceeded, $S$ is constant source term and $n$ is the number of receptors per cell, and $\alpha_1, \lambda_1$ and $\lambda_2$ be as defined in section 3.3.

We first note that, when $k\gamma$ and $S$ are sufficiently small, (3.1) is equivalent to the Gauss Lotka-Volterra type

$$U'_i = U_i(\lambda_i + \sum_{ij} a_{ij}U_j) \quad i, j = 1, 2, 3 \tag{3.2}$$

i.e., (3.1) takes the form

$$u' = u[\lambda_1 + k\lambda_1 u - k(\alpha_1 - \lambda_1)v + kn\lambda_1 w]$$

$$v' = v[-\lambda_2 - k(\alpha_2 + \lambda_2)u - k\lambda_2 v - kn\lambda_2 w] \tag{3.3}$$

$$w' = w[-\lambda_3 + k(\alpha_3 - \lambda_3)u - k\lambda_3 v - kn\lambda_3 w - k\frac{\alpha_3}{\theta}uw]$$

It is clear that the four fixed points on the boundary of $\mathbf{R}^3$ are $(0,0,0)$, $(-\frac{1}{k}, 0, 0)$ , $(0, -\frac{1}{k}, 0)$ and $(0, 0, -\frac{1}{kn})$.

Now we consider the case when $\theta$ is large enough (i.e., when the antibody production is limited ).

For the plane $w = 0$ in the half plane $u' = 0$ on the segment joint $(0, \frac{\lambda_1}{k(\alpha_1 - \lambda_1)})$ to $(-\frac{1}{k}, 0)$ and $v' = 0$ on the segment between $(0, -\frac{1}{k})$ and $(-\frac{\lambda_2}{k(\alpha_2 + \lambda_2)}, 0)$.

It is clear that (0,0), $(-\frac{\lambda_2}{k(\alpha_2 + \lambda_2)}, 0)$ and $(0, -\frac{1}{k})$ are sources while $(0, \frac{\lambda_1}{k(\alpha_1 - \lambda_1)})$ and $(-\frac{1}{k}, 0)$ are sinks (see Fig.(2)).

Thus , for the plane $w' = 0$ , there is an orbit $O_3$ in the third quadrant from $(0, -\frac{1}{k})$ to $(-\frac{1}{k}, 0)$, (see Fig.(3)).

Now using the transformations

$$u = \bar{u} + \varepsilon X_1, v = \bar{v} + \varepsilon X_2, w = \bar{w} + \varepsilon X_3, \tag{3.4}$$

the system (3.3) takes the form

$$X' = AX + R(X) \tag{3.5}$$

where $X$ is the column vector $(X_1 X_2 X_3)^T$ and $A$ is the Jacobian matrix

$$A = \begin{pmatrix} k\lambda_1\bar{u} & -k(\alpha_1 - \lambda_1)\bar{u} & kn\lambda_1\bar{u} \\ -k(\alpha_2 + \lambda_2)\bar{v} & -k\lambda_2\bar{v} & -kn\lambda_2\bar{v} \\ k(\alpha_3 - \lambda_3)\bar{w} & -k\lambda_3\bar{w} & -kn\lambda_3\bar{w} \end{pmatrix} \tag{3.6}$$

and $R(X)$ is the nonlinear part

$$R(X) = K\varepsilon \begin{pmatrix} X_1[\lambda_1 X_1 - (\alpha_1 - \lambda_1)X_2 + n\lambda_1 X_3] \\ X_2[-(\alpha_2 + \lambda_2)X_1 - \lambda_2 X_2 - n\lambda_2 X_3] \\ X_3[(\alpha_3 - \lambda_3)X_1 - \lambda_3 X_2 - n\lambda_3 X_3] \end{pmatrix}$$

It is known [4] that according to the Routh Hurwitz criteria a necessary and sufficient condition for steady states of (3.5) to be asymptomatically stable is.

$$\sigma = trace\ A < 0,\ \Delta = \det A < 0\ and\ C = \sigma\hat{\sigma} - \Delta < 0 \tag{3.7}$$

Here, since by (3.6) we have

$$\sigma = k(\lambda_1 \bar{u} - \lambda_2 \bar{v} - n\lambda_3 \bar{w})$$

$$\hat{\sigma} = k^2\{[\alpha_2\lambda_1 - \alpha_1(\alpha_2 + \lambda_2)]\bar{u}\bar{v} + n\alpha_3\lambda_1\bar{u}\bar{w}\} \tag{3.8}$$

$$\Delta = k^3 n\{\alpha_1(\alpha_2\lambda_3 + \alpha_3\lambda_2) - 2\lambda_1\lambda_2\alpha_3)\bar{u}\bar{v}\bar{w}\}$$

and

$$\begin{aligned} C = k^3\{&\lambda_1^2(\alpha_2\bar{v} + \alpha_3 n\bar{w})\bar{u}^2 + n\alpha_1\lambda_3(\alpha_2 + \lambda_2)\bar{u}\bar{v}\bar{w} + \\ &+ \alpha_1\lambda_2(\alpha_2 + \lambda_2)\bar{u}^2\bar{v}\} - k^3\{\alpha_1\lambda_1(\alpha_2 + \lambda_2)\bar{u}^2\bar{v} + \\ &+ \lambda_1\lambda_2(\alpha_2\bar{v} + 3n\alpha_3\bar{w})\bar{u}\bar{v} + \alpha_2\lambda_3 n(\alpha_1 + \lambda_1)\bar{u}\bar{v}\bar{w} + \\ &+ n^2\alpha_3\lambda_1\lambda_3\bar{u}\bar{w}^2\} \end{aligned}$$

Thus the steady states $(\bar{u}, \bar{v})$ are asymptotically stable if and only if

$$\lambda_1 < \frac{1}{\bar{u}}(\lambda_2\bar{v} + n\lambda_3\bar{w}),\ \alpha_1 < \frac{\lambda_1(\alpha_2\bar{v} + n\alpha_3\bar{w})}{(\alpha_2 + \lambda_2)\bar{v}}$$

and

$$\begin{aligned} \lambda_3 < \frac{1}{\delta_1}\{&\lambda_1\lambda_2(\alpha_2\bar{v} + 3n\alpha_3\bar{w})\bar{u}\bar{v} + \alpha_1\lambda_1(\alpha_2 + \lambda_2)(\lambda_2 - \lambda_1)\bar{u}^2\bar{v} + \\ &+ \lambda_1^2(\alpha_2\bar{v} + \alpha_3 n\bar{w})\bar{u}^2\} \end{aligned}$$

where

$$\delta_1 = n\bar{u}\bar{w}[(\lambda_2 - \lambda_1)\bar{v} + n\alpha_3\lambda_1\bar{w}].$$

Now, as it is well known ([1], [9]), the quantity $C$ is important in determining the stability of the trivial equilibrium and accurance of Hopf's bifurcation. Since the characteristic equation (3.6) is

$$\nu^3 - \sigma\nu^2 + \hat{\sigma}\nu - \Delta = 0, \tag{3.9}$$



There exists at least one real eigenvalue $\nu_0$ say, then we have the factorization

$$(\nu - \nu_0)\{\nu^2 + (\nu_0 - \sigma)\nu + (\nu_0^2 - \sigma\nu_0 + \hat{\sigma})\} = 0 \tag{3.10}$$

Thus, at $\nu = \sigma$, then there exist pure imaginary eigenvalues $\nu_1$ and $\nu_2$, $\nu_1 = -\bar{\nu}_2$. Now, the equation

$$C = \sigma\sigma - \Delta = 0$$

with the algebric calculations takes the form.

$$C(\lambda_3) = a_1\lambda_3 + b_1 \tag{3.11}$$

where

$$a_1 = k^3 n\{[\alpha_1(\alpha_2 + \lambda_2) + \alpha_2(\alpha_1 + \lambda_1)]\bar{v} - n\alpha_3\lambda_1\}\bar{u}\bar{w}$$

$$\begin{aligned} b_1 = k^3\{&\alpha_1\bar{u}^2\bar{v}(\alpha_2 + \lambda_2)(\lambda_2 - \lambda_1) + \lambda_1\bar{u}[\alpha_2\bar{u}\bar{v}(\lambda_1\bar{u} - \lambda_2\bar{v}) - \\ &- \lambda_2\bar{v} + n\alpha_3\bar{u}\bar{w}(\lambda_1\bar{u} - 3\lambda_2\bar{v})]\} \end{aligned}$$

Equation (3.11) is clearly a straight line with the slope $C'$.

$$C' = \frac{\partial C}{\partial\lambda_3} > 0\ for\ \alpha_3 < [\frac{\alpha_1(2\alpha_2 + \lambda_2) + \alpha_2\lambda_1}{n\lambda_1}]\bar{v}$$

and crosses the C-axis at $b_1$, where $b_1 < 0$ provided that $\lambda_2 < \lambda_1 < \lambda_2\frac{\bar{v}}{\bar{u}}$ (see Fig.4).

Thus $\lambda_3^c$ is uniquely determined. Suppose $\lambda_3 > \lambda_3^C$. Then, by equation (3.4.11) we see that $C(\lambda_3) > 0$. On the other hand, if $\lambda_3 < \lambda_3^C$, then $C(\lambda_3) < 0$. Thus at $\lambda = \lambda_3^c$ there exists a change of sign for the quantity $C$. This gives rise to Hopf bifurcation to occur (see [22]) and we have the following bifurcation result:

**Theorem 3.1** : *The system* (3.1) *with the substitutions* (3.4) *provided that* $\lambda_2 < \lambda_1 < \lambda_2\frac{\bar{v}}{\bar{u}}$, $\alpha_3 < \frac{[\alpha_1(2\alpha_2+\lambda_2)+\alpha_2\lambda_1]\bar{v}}{n\lambda_1}$, *$\theta$ is large enough, $k\gamma$ and $S$ are sufficiently small, give rise to the occurrence of one parameter family of periodic solutions of* (3.1) *which tend continuosly to* $(\bar{u}, \bar{v}, \bar{w})$ *as* $\lambda_3 \to \lambda_3^C$, *with period $T$ which tends to* $T_0 = \frac{2\pi}{\sigma}$ *as* $\lambda_3 \to \lambda_3^C$.

Now, to apply the centre manifold theory [10], we return back to (3.5). Following [1] we use transformation

$$X = Ty \tag{3.12}$$

where

$$T = \begin{pmatrix} t_{11} & t_{12} & t_{13} \\ t_{21} & t_{22} & t_{23} \\ t_{31} & t_{32} & t_{33} \end{pmatrix} = \begin{pmatrix} \frac{1}{2}(\zeta_1 - \bar{\zeta}_1) & \frac{1}{2}(\zeta_1 + \bar{\zeta}_1) & \zeta \\ \frac{1}{2}(\xi_1 - \bar{\xi}_1) & \frac{1}{2}(\xi_1 + \bar{\xi}_1) & \xi \\ \frac{1}{2}(\xi_{01} - \bar{\xi}_{01}) & \frac{1}{2}(\xi_{01} + \bar{\xi}_{01}) & \xi \end{pmatrix} \tag{3.13}$$

$$\begin{pmatrix}\zeta_1\\ \xi_1\\ \xi_{01}\end{pmatrix}, \begin{pmatrix}\bar{\zeta}_1\\ \bar{\xi}_1\\ \bar{\xi}_{01}\end{pmatrix} \text{ and } \begin{pmatrix}\zeta\\ \xi\\ \xi_0\end{pmatrix}$$

are the eigenvectors of $A$.

When the Hopf bifurcation occurs, $A$ has a negative real part eigenvalue $\sigma$ and a pair of pure imaginary eigenvalues $\pm i\omega$ , where for

$$\frac{\alpha_1}{2\alpha_3\lambda_2}[\alpha_2\lambda_3+\alpha_3\lambda_2] < \lambda_1 < \frac{1}{\bar{u}}[\lambda_2\bar{v}+n\lambda_3\bar{w}]$$

$$\sigma = \text{trace } A = k[\lambda_1\bar{u}-\lambda_2\bar{v}-\lambda_3 n\bar{w}] < 0$$

and

$$\omega = \sqrt{\hat{\sigma}} = \sqrt{\Delta/\sigma} =$$

$$= [\frac{k^2 n\{\alpha_1(\alpha_2\lambda_3+\alpha_3\lambda_2)-2\alpha_3\lambda_1\lambda_2\}\bar{u}\bar{v}\bar{w}}{\lambda_1\bar{u}-\lambda_2\bar{v}-n\lambda_3\bar{w}]}^{\frac{1}{2}}$$

If the eigenvectors of $A$ associated with $\sigma$ is $\nu_1$ and that associated with $i\omega$ is $\nu_2+i\nu_3$, where $\nu_1,\nu_2$ and $\nu_3$ are real vectors, then it is clear ( see [14]) that the matrix

$$T = (\nu_3,\nu_2,\nu_1)$$

is nonsingular. Moreover, the diagonalized matrix is given by

$$T^{-1}AT = \begin{pmatrix}0 & -\omega & 0\\ \omega & 0 & 0\\ 0 & 0 & \sigma\end{pmatrix} \tag{3.14}$$

By (3.12) the system (3.5) takes the form

$$\begin{pmatrix}y_1\\ y_2\\ y_3\end{pmatrix} = \begin{pmatrix}0 & -\omega & 0\\ \omega & 0 & 0\\ 0 & 0 & \sigma\end{pmatrix}\begin{pmatrix}y_1\\ y_2\\ y_3\end{pmatrix} + T^{-1}\begin{pmatrix}R_1(Ty)\\ R_2(Ty)\\ R_3(Ty)\end{pmatrix} \tag{3.15}$$

where

$$R_1(Ty) = k\varepsilon[t_{11}N_1y_1^2+t_{12}N_2y_2^2+t_{13}N_3y_3^2+(t_{11}N_2+t_{12}N_1)y_1y_2+$$
$$+(t_{11}N_3+t_{13}N_1)y_1y_3+(t_{12}N_3+t_{13}N_2)y_2y_3],$$
$$R_2(Ty) = k\varepsilon[t_{21}S_1y_1^2+t_{22}S_2y_2^2+t_{23}S_3y_3^2+(t_{21}S_2+t_{22}S_1)y_1y_2+$$
$$+(t_{21}S_3+t_{23}S_1)y_1y_3+(t_{23}S_2+t_{22}S_3)y_2y_3],$$

and

$$R_3(Ty) = k\varepsilon[t_{31}D_2y_1^2+t_{32}D_2y_2^2+t_{33}D_3y_3^2+(t_{31}D_2+D_{32}D_1)y_1y_2+$$



$$+(t_{32}D_3+t_{33}D_2)y_2y_3+(t_{31}D_3+t_{33}D_1)y_1y_3],$$

where

$$N_j = \lambda_1 t_{1j}-(\alpha_1-\lambda_1)t_{2j}+n\lambda_1 t_{3j},$$
$$S_j = [(\alpha_2+\lambda_2)t_{1j}+\lambda_2 t_{2j}+n\lambda_2 t_{3j}]$$
$$D_j = (\alpha_3-\lambda_3)t_{1j}-\lambda_3 t_{2j}-n\lambda_3 t_{3j}, \quad j=1,2,3.$$

If the first column of the inverse of the matrix $T$ is

$$q = \begin{pmatrix}q_1\\ q_2\\ q_3\end{pmatrix}$$

then (3.15) becomes

$$\frac{d}{dt}\begin{pmatrix}y_1\\ y_2\\ y_3\end{pmatrix} = \begin{pmatrix}0 & -\omega & 0\\ \omega & 0 & 0\\ 0 & 0 & \sigma\end{pmatrix}\begin{pmatrix}y_1\\ y_2\\ y_3\end{pmatrix} + R_1(TY)q \tag{3.16}$$

where

$$T^{-1} = \begin{pmatrix}q_1 & b_1^0 & c_1^0\\ q_2 & b_2^0 & c_2^0\\ q_3 & b_3^0 & c_3^0\end{pmatrix}$$

Now, following G u c k e n h e i m e r and H o l m e s [6] and L i u et al [9], we assume that the center manifold at the origin of $(y_1,y_2,y_3)$ - space is

$$y_3 = f(y_1,y_2) \tag{3.17}$$

Then, $y_3$ satisfies

$$\frac{dy_3}{dt} = \frac{\partial f}{\partial y_1}\cdot\frac{dy_1}{dt}+\frac{\partial f}{\partial y_2}\cdot\frac{dy_2}{dt}$$

such that

$$y_3(0,0) = 0$$

In the center manifold $y_3 = f(y_1,y_2)$, the stability of the priodic solution generated from Hopf bifurcation is determinated by the sign of the quantity $B$ ( see [9]),

$$B = F_{111}+G_{112}+G_{222}+[F_{12}(F_{11}+F_{22})- \tag{3.18}$$
$$-G_{12}(G_{11}+G_{22})-F_{11}G_{11}+F_{22}G_{22}]/\omega$$

where

$$F(y_1,y_2) = q_1 g(y_1,y_2,f(y_1,y_2))$$

$$G(y_1, y_2) = q_2 g(y_1, y_2, f(y_1, y_2))$$

$$g(y_1, y_2, f) = R(Ty)$$

$$F_j = \frac{\partial F}{\partial y_j}, \quad F_{ij} = \frac{\partial^2 F}{\partial y_j \partial y_i}, \quad F_{ijj} = \frac{\partial^3 F}{\partial^2 y_j \partial y_i},$$

$$F_{iij} = \frac{\partial^3 F}{\partial y_j \partial^2 y_i}, \quad F_{jjj} = \frac{\partial^3 F}{\partial y_j^3}, \quad \ldots, \quad i, j = 1, 2$$

In fact, $A$ is given by

$$B = \frac{\xi k \varepsilon}{2\Delta}\Big[\{2z_3[(\xi_1 + \bar{\xi}_1)(3f_1 \cdot f_{11} + f \cdot f_{111} + 2f_2 \cdot f_{21} +$$

$$+ f_1 \cdot f_{22} + f \cdot f_{122}) + (\zeta_1 + \bar{\zeta}_1)(2f_1 \cdot f_{12} + f_{11} \cdot f_2 +$$

$$+ f \cdot f_{112} + 3f_2 \cdot f_{22} + f \cdot f_{222})] +$$

$$+ z_5[(\xi_1 + \bar{\xi}_1)(3f_{11} + y_1 \cdot f_{111} + f_{22} + y_1 \cdot f_{122} +$$

$$+ (\zeta_1 + \bar{\zeta}_1)(y_1 \cdot f_{222} + y_1 \cdot f_{211} + 2f_{21})] +$$

$$+ z_6[(\xi_1 + \bar{\xi}_1)(y_2 \cdot f_{111} + y_2 \cdot f_{221} + 2f_{21}) +$$

$$+ (\zeta_1 + \bar{\zeta}_1)(3f_{22} + y_2 \cdot f_{222} + y_2 \cdot f_{211} + f_{11})]\} +$$

$$+ \frac{\xi k \varepsilon}{2}[(\xi_1 + \bar{\xi}_1)^2 - (\zeta_1 + \bar{\zeta}_1)^2]\{2(z_1 + z_2) +$$

$$+ 2z_3[f_1^2 + f_2^2 + f(f_{11} + f_{22})] + z_5[y_1(f_{11} + f_{22}) + 2f_1] +$$

$$+ z_6[2f_2 + y_2(f_{11} + f_{22})]\}\{2z_3[f_1 \cdot f_2 + f \cdot f_{21}] + z_4 +$$

$$+ z_5[f_2 + y_1 \cdot f_{21}] + z_6[y_2 \cdot f_{21} + f_1]\}\Big],$$

where

$$z_1 = \frac{1}{4}[\lambda_1(\xi_1 - \bar{\xi}_1)^2 + n\lambda_1(\xi_0 + \bar{\xi}_{01})(\xi_1 + \bar{\xi}_1) - (\alpha_1 - \lambda_1)(\zeta_1 + \bar{\zeta}_1)(\xi_1 + \bar{\xi}_1)],$$

$$z_2 = \frac{1}{4}[\lambda_1(\xi_1 - \bar{\xi}_1{}^2 + n\lambda_1(\xi_1 - \bar{\xi}_1)(\xi - \bar{\xi}_1) - (\alpha_1 - \lambda_1)(\zeta_1 - \bar{\zeta}_1)(\xi_1 - \bar{\xi}_1)],$$

$$z_3 = \frac{1}{2}[\lambda_1 \xi^2 + n\lambda_1 \xi \xi_0 - (\alpha_1 - \lambda_1)\xi_0 \zeta$$

$$z_4 = \frac{1}{4}[2\lambda_1(\xi_1 + \bar{\xi}_1)(\xi_1 - \bar{\xi}_1) + n\lambda_1(\xi_{01} - \xi_{01})(\xi_1 - \bar{\xi}_1) - (\alpha_1 - \lambda_1)(\zeta_1 - \bar{\zeta}_1)(\xi_1 + \bar{\xi}_1)],$$

$$z_5 = \frac{1}{2}[2\lambda_1 \xi(\xi_1 + \bar{\xi}_1) - \zeta(\alpha_1 - \lambda_1)(\xi_1 - \bar{\xi}_1) + n\lambda_1 \xi_0(\xi_1 + \bar{\xi}_1) +$$



$$+ n\lambda_1 \xi(\xi_{01} + \bar{\xi}_{01}) - (\alpha_1 - \lambda_1)(\zeta_1 + \zeta_1)(\xi_1 - \bar{\xi}_1)], \tag{3.19}$$

$$z_6 = \frac{1}{2}[2\lambda_1 \xi(\xi_1 - \bar{\xi}_1) + n\lambda_1 \xi_0(\xi_1 - \bar{\xi}_1) - (\alpha_1 - \lambda_1)\zeta(\xi_1 - \bar{\xi}_1)] -$$

$$- \xi(\alpha_1 - \lambda_1)(\zeta_1 - \zeta_1) - n\lambda_1 \xi(\xi_{01} - \bar{\xi}_{01})]$$

Thus, clearly if $\alpha_1 \to \lambda_1$, ( i.e. when the difference between the rates of increasing and elimination of the antigen is sufficiently small ) then $B > 0$, and consequently the periodic solution is unstable.

**4.Poincare - Andronov substitutions ([1],[16]).** Now, to study the behaviour of paths at infinity, we use the Poincare substitution [1], [16].

$$u_1 = u/w \quad , \quad u_2 = v/w \quad , \quad u_3 = 1/w \quad ,$$

in (3.4.1), ( $\theta$ is large enough), we get

$$u'_1 = \frac{u_1}{u_3}\{k(\lambda_1 + \lambda_3 - \alpha_3)u_1 + k(\lambda_1 + \lambda_3 - \alpha_1)u_2 + (\lambda_1 + \lambda_3)u_3 + nk(\lambda_1 + \lambda_3)\}$$

$$u'_2 = \frac{u_2}{u_3}\{-k(\alpha_2 + \alpha_3 + \lambda_2 - \lambda_3)u_1 + k(\lambda_3 - \lambda_2)u_2 + (\lambda_3 - \lambda_2)u_3 + nk\lambda_3\} \tag{4.1}$$

$$u'_3 = \{-k(\alpha_3 - \lambda_3)u_1 + k\lambda_3 u_2 + \lambda_3 u_3 + nk\lambda_3\}$$

Following R o y and S o l i m a n o ([16]), we use the additional change of variables

$$u_3 d\tau = dt \tag{4.2}$$

Then, we have for $\lambda_3 > \lambda_2, \alpha_i > \lambda_i, \; i = 1, 2, 3,$

$$\frac{du_1}{d\tau} = u_1[k(\lambda_1 + \lambda_3 - \alpha_3)u_1 + k(\lambda_1 + \lambda_3 - \alpha_1)u_2 + (\lambda_3 + \lambda_2)u_3 + nk(\lambda_1 + \lambda_3)],$$

$$\frac{du_2}{d\tau} = u_2[-k(\alpha_2 + \alpha_3 + \lambda_2 - \lambda_3)u_1 + k(\lambda_3 - \lambda_2)u_2 + (\lambda_3 - \lambda_2)u_3 + nk\lambda_3], \tag{4.3}$$

$$\frac{du_3}{d\tau} = u_3[-k(\alpha_3 - \lambda_3)u_1 + k\lambda_3 u_2 + \lambda_3 u_3 + nk\lambda_3].$$

On $u_1 = 0$ plane, we have

$$(4.4)\qquad \frac{du_2}{d\tau} = u_2[k(\lambda_3-\lambda_2)u_2 + (\lambda_3-\lambda_2)u_3 + kn\lambda_3],$$

$$\frac{du_3}{d\tau} = u_3[k\lambda_3 u_2 + \lambda_3 u_3 + nk\lambda_3]$$

The system (4.4) has the critical points $(0,0,0)$ and $(0,\bar{u}_2,\bar{u}_3)$, where

$$\bar{u}_2 = \frac{k(\lambda_3-\lambda_2)-1}{kn\lambda_2}\ ,\ \bar{u}_3 = \frac{k}{n\lambda_2}[\lambda_2(n^2-1)+\lambda_3-1]$$

The variational matrix $A$ at the critical point $(0,0,0)$ is

$$A_1 = \begin{pmatrix} 0 & 0 & 0 \\ 0 & nk\lambda_3 & 0 \\ 0 & 0 & nk\lambda_3 \end{pmatrix}$$

The characteristic eigenvalues of $A_1$ is a solution of (3.9), where

$$\sigma = \mathrm{trace\ A_1} = 2\mathrm{nk}\lambda_3, \hat{\sigma} = \mathrm{k^2n^2}\lambda_3^2, \Delta = 0,$$

that namely $\nu_1 = 0$, $\nu_2 = \nu_3 = nk\lambda_3$, are all positive, consequently, the critical point (0,0,0) is unstable.

By the same way for the critical point $(0,\bar{u}_2,\bar{u}_3)$, the variational matrix of $(0,\bar{u}_2,\bar{u}_3)$ is

$$A_2 = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 2k(\lambda_3-\lambda_2)\bar{u}_2 + (\lambda_3-\lambda_2)\bar{u}_3 + nk\lambda_3 & (\lambda_3-\lambda_2)\bar{u}_2 \\ 0 & k\lambda_3\bar{u}_3 & k\lambda_3\bar{u}_2 + 2\lambda_3\bar{u}_3 + nk\lambda_3 \end{pmatrix}$$

$$\sigma = \mathrm{trace\ A_2} = \frac{1}{\mathrm{n}\lambda_2}\{\mathrm{k}[3(\lambda_3-\lambda_2)^2 + 2\mathrm{n}^2\lambda_2\lambda_3] -$$

$$-\lambda_3 - (\lambda_3-\lambda_2)[k(n^2\lambda_2 + 3\lambda_3 - 1) - 2]\} > 0$$

$$\hat{\sigma} = [2k(\lambda_3-\lambda_2)\bar{u}_2 + (\lambda_3-\lambda_2)\bar{u}_3 + kn\lambda_3][k\lambda_3\bar{u}_2 +$$

$$+ 2\lambda_3\bar{u}_3 + kn\lambda_3] - k\lambda_3(\lambda_3-\lambda_2)\bar{u}_2\bar{u}_3.$$

Since $\sigma > 0$, for $\lambda_3 > \lambda_2$, the critical point $(0,\bar{u}_2,\bar{u}_3)$ is unstable.

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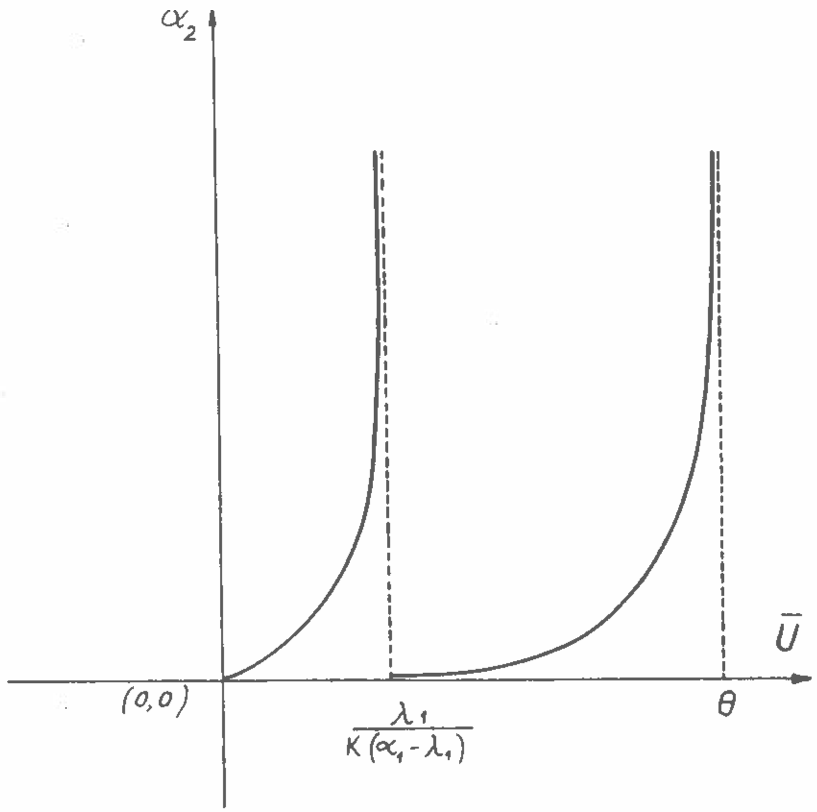
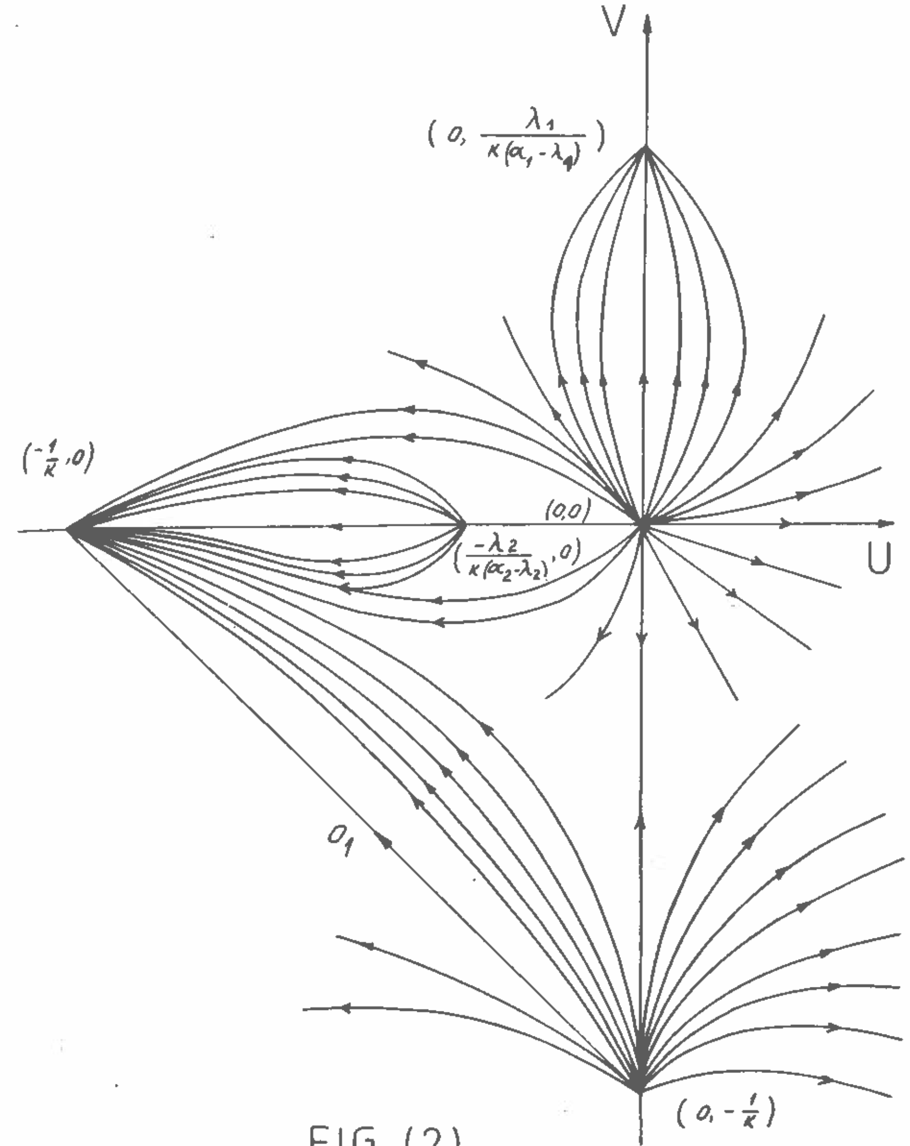
*Department of Mathematics*
*Faculty of Sciences*
*Monoufia University*
*Shibin El-Koom*
*EGYPT*



$\alpha_2$
$\bar{U}$
(0,0)
$\frac{\lambda_1}{K(\alpha_1-\lambda_1)}$
$\theta$


FIG. (1)





V
U
$(0, \frac{\lambda_1}{K(\alpha_1-\lambda_1)})$
$(-\frac{1}{K},0)$
(0,0)
$(\frac{-\lambda_2}{K(\alpha_2-\lambda_2)},0)$
$0_1$
$(0,-\frac{1}{K})$


FIG (2)

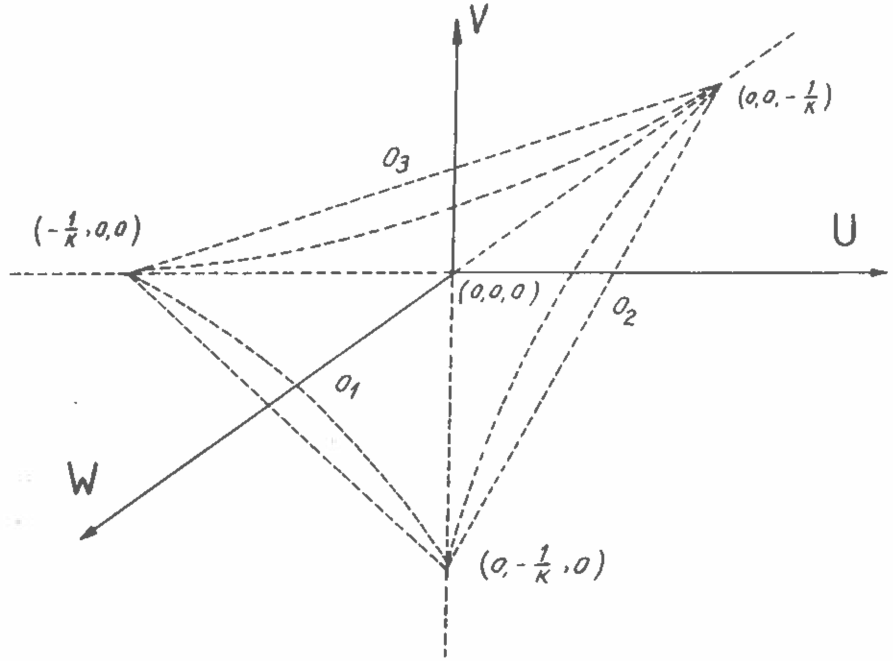



FIG. (3)

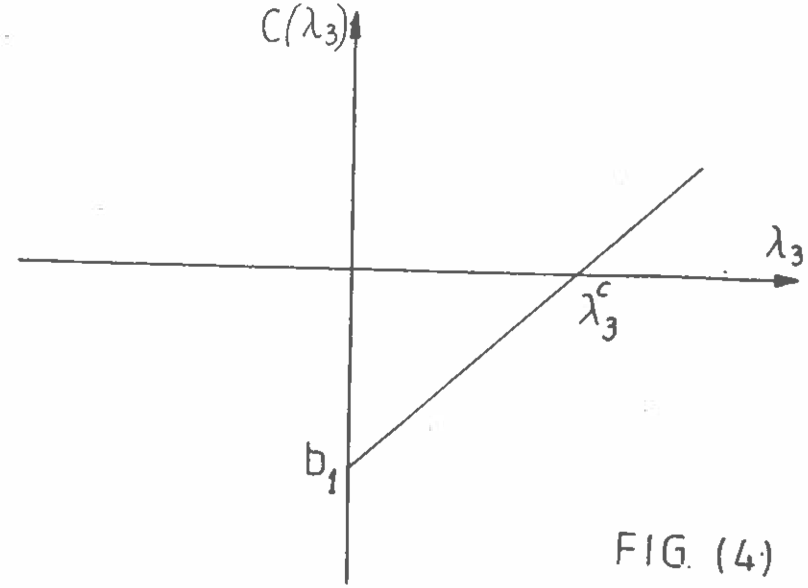



FIG. (4)

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# STABILITY CRITERIA FOR NONLINEAR VOLTERRA TYPE DIFFERENCE EQUATIONS

BY

PAVEL TALPALARU

**1.Introduction.** Difference equations occur in many branches of applied mathematics: numerical analysis, physics, control theory and optimization. In recent years, considerable attention has been paid to the development of the qualitative theory for difference equations.

In order to discuss the asymptotic problems for difference equations, generally speaking, the analogous methods to those for differential and functional-differential equations are aplicable.

The purpose of this pair is to extend a part of the results of T. H a r a, T.Y ö n e y a m a and T.I t o h [3] concerning the asymptotic properties of an integro-differential system to the case of corresponding discrete system of the form

$$x(n+1) = A(n)\,x(n) + \sum_{m=0}^{n-1} B(n,m,x(m)) \tag{V}$$

where $A(n)$ is a $q\times q$ matrix on $N$ and $B(n,m,x)$ is a $q$ vector for $n,m\in N, m<n$ and $x\in \mathbf{R}^q$.

The discrete analogue of an integro-differential system has been studied in a particular case , by Ja.V.B y k o v and V.G. L i n e n k o [1] who have obtained interesting results concerning the boundedness and stability of the solutions of such systems, N.L u c a and P.T a l p a l a r u [4] who have considered the discrete analogue of an integro-differential system of the convolution type of the form

$$x(n+1) = Ax(n) + \sum_{m=0}^{n-1} C(n-m-1)x(m) + h(n,x(\cdot)), \tag{1.1}$$

where $A$ and $C$ are constant $q\times q$ matrices and $h(n,x(\cdot))$ is an operator, $n\in N$. In the study of equation (1.1) were used a technique based on the discrete analogue of the variation of constants formula, the method of the difference resolvent associated with the linear system

$$y(n+1) = Ay(n) + \sum_{m=0}^{n-1} C(n-m-1)y(m) \tag{1.2}$$