

# Method of Matrices Operations in H2 Control for Calcium Ion Channel on the Biological Membrane as a Closed Circuit.

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あらまし

I have proposed an h2 control principle for bio chemical noise filtering function of the calcium in channel on the excitable cellular membrane. The Calcium channel is composed of four identical subunits. Each of which contains a helical segment which contains a lot of electrical charge that acts as a membrane voltage sensor. The opening and closing of the channel pore are facilitated by the activating positionings of the voltage sensor. The temporal changes in the system were described by ten differential equations under the condition that minimizes the 2 norm of the transfer function of the system from the noise input the out put. The computed temporal changes in the open and closed states are significantly influenced by the changes in the amounts of the control inputs. The present methods, when extended will be available for evaluating the filtering function of the bio membranes.

和文キーワード Bio membrane, calcium in, Channel, Subunits, Voltage sensor, H2 control, Noise, 2 norm.

## 閉回路としてのカルシウムイオンチャンネルのH2制御

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Abstract

カルシウムイオンを選択的に通過させるカルシウムイオンチャンネルの機能特性を雑音フィルターの視点からH2制御を用いて解析する方法を提唱した。カルシウムイオンチャンネルは4個の相同性の高いサブユニットから構成されている。また膜電位感受性を有するタンパク分子がそれぞれのサブユニットに付属し、その空間内の位置が変化することでチャンネル開閉が加速される。本研究では10個のチャンネル構造を10個の状態方程式で表示し、雑音が出力されるまでの系の伝達関数の2ノルムを最少にする場合のチャンネルの状態の過渡的状況を数値計算で決定した。制御入力の変化によって開状態、閉状態のチャンネルの時間経過を大きく影響された。本研究を発展させることで生体膜チャンネルの生化学的雑音低減効果を評価できる可能性を示唆した。

英文 key words 生体膜. カルシウムイオン. チャンネル. H2制御. 雑音. 伝達関数 2ノルム

**1. Introduction.**

Calcium channel ( Fig 1 ) on the excitable membrane filters only Calcium ion though there are a lot of agonist and antagonist that compete the channel with Calcium ion. Hence, the mechanism can be described by the H2 control principle. The dynamical action of the Calcium channel is characterized by four identical subunits (Fig 2) that act concertedly. The channel opening and closing are strongly influenced by a particular segment named S4 ( Fig 3 ) which has a high voltage sensing property in each subunits. S4 contains a lot of charges on its surface. When it takes the activating position in the subunit, the transitions among the open states are facilitated. By the spatial consideration of the activating positionings of the voltage sensor, we have ten conformations of one Calcium channel. (Fig 4-a and Fig 4-b).

In the present work, we present a detailed matrix expansion for computing the H2 controlled temporal change of the amounts of the Calcium channel states.

**2. Mathematical method.**

The state equations for these ten conformation states are given by linear combination of weighted control inputs.

Fig 1

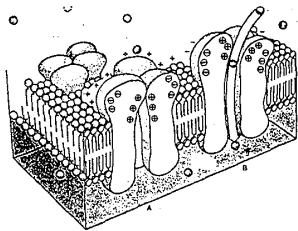


Fig 2



Fig 3

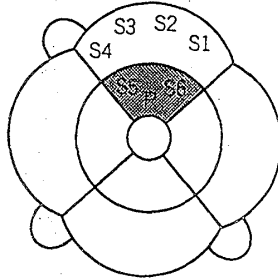
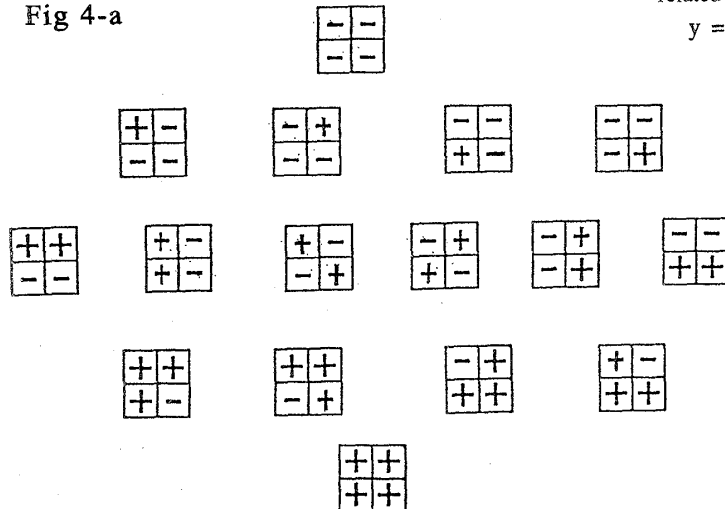


Fig 4-a



$$\partial C_0 / \partial t = k_c C_1 + k_L / f_4 O_0 - (4 k_c + k_L f_4) C_0 + p_9' u_3 + p_1' u_1 \quad \text{-----(1)}$$

$$\partial C_1 / \partial t = 4 k_c C_0 + 2 k_c C_2 + k_L / f_3 O_1 - (k_c + 3 k_c + k_L f_3) C_1 + p_1 u_1 + p_{10}' u_3 + p_2' u_1 \quad \text{-----(2)}$$

$$\partial C_2 / \partial t = 3 k_c C_1 + 3 k_c C_3 + k_L / f_2 O_2 - (2 k_c + 2 k_c + k_L f_2) C_2 + p_2 u_1 + p_{11}' u_3 + p_3' u_1 \quad \text{-----(3)}$$

$$\partial C_3 / \partial t = 2 k_c C_2 + 4 k_c C_4 + k_L / f O_3 - (3 k_c + k_c + k_L f) C_3 + p_3 u_1 + p_{12}' u_3 + p_4' u_1 \quad \text{-----(4)}$$

$$\partial C_4 / \partial t = k_c C_3 + k_L O_4 - (4 k_c + k_L) C_4 + p_4 u_1 + p_{13}' u_3 \quad \text{-----(5)}$$

$$\partial O_0 / \partial t = f_4 k_L C_0 + k_c f O_1 - (k_L / f_4 + 4 k_c / f) O_0 + p_9 u_3 + p_5' u_2 \quad \text{-----(6)}$$

$$\partial O_1 / \partial t = 4 k_c / f O_0 + k_L f_3 C_1 + 2 k_c f_2 O_2 - (k_c f + k_L / f_3 + 3 k_c / f_2) O_1 + p_{10} u_3 + p_6' u_2 \quad \text{----(7)}$$

$$\partial O_2 / \partial t = 3 k_c / f_2 O_1 + k_L f_2 C_2 + 3 k_c f_3 O_3 - (2 f_2 k_c + k_L / f_2 + 2 k_c / f_3) O_2 + p_{11} u_3 + p_7' u_2 \quad \text{----(8)}$$

$$\partial O_3 / \partial t = 2 k_c / f_3 O_2 + k_L f C_3 + 4 k_c f_4 O_4 - (3 k_c f_3 + k_L / f + k_c / f_4) O_3 + p_7 u_2 + p_{12} u_3 + p_8' u_2 \quad \text{----(9)}$$

$$\partial O_4 / \partial t = k_c / f_4 O_3 + k_L C_4 - (4 k_c f_4 + k_L) O_4 + p_8 u_2 + p_{13} u_3 \quad \text{----(10)}$$

The vector form

$$\partial \mathbf{x}'(t) / \partial t = \mathbf{A} \mathbf{x} + \mathbf{B} \mathbf{1} \mathbf{w} + \mathbf{B} \mathbf{2} \mathbf{u}$$

Vector form of the equation for the estimator Z

$$\mathbf{Z} = \mathbf{C} \mathbf{1} \mathbf{x} + \mathbf{D} \mathbf{1} \mathbf{2} \mathbf{u}$$

Vector form of the equation for the observer out put y

$$\mathbf{y} = \mathbf{C} \mathbf{2} \mathbf{x} + \mathbf{D} \mathbf{2} \mathbf{1} \mathbf{w}$$

The vector for of the optimized control u^ is given by the product of B2, X and x^

$$\mathbf{u}^ = - \mathbf{B} \mathbf{2} \mathbf{T} \mathbf{X} \mathbf{x}^$$

where x^ is the state vector of the observers and T denotes transpose.

$\mathbf{x}^ \mathbf{T} = [ X_{10}, X_{11}, X_{12}, X_{13}, X_{14}, X_{15}, X_{16}, X_{17}, X_{18} ] \mathbf{T}$  which correspond to state variables. X is the solution of related algebraic Riccati equation.

$$\mathbf{A} \mathbf{T} \mathbf{X} + \mathbf{X} \mathbf{A} - \mathbf{X} \mathbf{B} \mathbf{2} \mathbf{B} \mathbf{2} \mathbf{T} \mathbf{X} + \mathbf{C} \mathbf{1} \mathbf{T} \mathbf{C} \mathbf{1} = 0$$

The vector equation of observer x^ is given by

$$\partial \mathbf{x}^ / \partial t = \mathbf{A} \mathbf{x}^ + \mathbf{B} \mathbf{2} \mathbf{u} + \mathbf{Y} \mathbf{C} \mathbf{2} \mathbf{T} (\mathbf{y} - \mathbf{C} \mathbf{2} \mathbf{x}^)$$

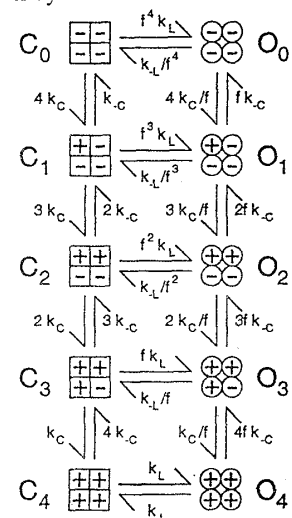
where Y is the solution of adjoint algebraic Riccati equation

$$\mathbf{A} \mathbf{Y} + \mathbf{Y} \mathbf{A} \mathbf{T} - \mathbf{Y} \mathbf{C} \mathbf{2} \mathbf{T} \mathbf{C} \mathbf{2} \mathbf{Y} + \mathbf{B} \mathbf{1} \mathbf{B} \mathbf{1} \mathbf{T} = 0$$

To close the feed back loop of the system, y can be related to state variable x by

$$\mathbf{y} = \mathbf{x} \mathbf{d} - \mathbf{C} \mathbf{2} \mathbf{x}$$

Fig 4-b



$$A = \begin{bmatrix} a11 & a12 & a13 & a14 & a15 & a16 & a17 & a18 & a19 \\ a21 & 0 & a23 & 0 & 0 & 0 & 0 & 0 & a29 \\ 0 & a32 & 0 & a34 & 0 & 0 & 0 & a38 & 0 \\ 0 & 0 & a43 & 0 & a45 & 0 & a47 & 0 & 0 \\ 0 & 0 & 0 & a54 & 0 & a56 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & a65 & 0 & a67 & 0 & 0 \\ 0 & 0 & 0 & a74 & 0 & a76 & 0 & a78 & 0 \\ 0 & 0 & a83 & 0 & 0 & 0 & a87 & 0 & a89 \\ a91 & a92 & a93 & a94 & a95 & a96 & a97 & a98 & a99 \end{bmatrix};$$

$$B_2^T = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & b11 & b13 & b15 & b17 \\ b1 & b3 & b5 & b7 & b9 & 0 & 0 & 0 & 0 \\ b2 & b4 & b6 & b8 & b10 & b12 & b14 & b16 & b18 \end{bmatrix}$$

Matrix form of the Riccati solution X is

$$X = \begin{bmatrix} X11 & X12 & X13 & X14 & X15 & X16 & X17 & X18 & X19 \\ X12 & X22 & X23 & X24 & X25 & X26 & X27 & X28 & X29 \\ X13 & X23 & X33 & X34 & X35 & X36 & X37 & X38 & X39 \\ X14 & X24 & X34 & X44 & X45 & X46 & X47 & X48 & X49 \\ X15 & X25 & X35 & X45 & X55 & X56 & X57 & X58 & X59 \\ X16 & X26 & X36 & X46 & X56 & X66 & X67 & X68 & X69 \\ X17 & X27 & X37 & X47 & X57 & X67 & X77 & X78 & X79 \\ X18 & X28 & X38 & X48 & X58 & X68 & X78 & X88 & X89 \\ X19 & X29 & X39 & X49 & X59 & X69 & X79 & X89 & X99 \end{bmatrix}$$

The control input is

$$u^{\wedge} = -B_2^T X x^{\wedge}$$

$$B_2^T X = \begin{bmatrix} X11 & X12 & X13 & X14 & X15 & X16 & X17 & X18 & X19 \\ 0 & 0 & 0 & 0 & 0 & b11 & b13 & b15 & b17 \\ b1 & b3 & b5 & b7 & b9 & 0 & 0 & 0 & 0 \\ b2 & b4 & b6 & b8 & b10 & b12 & b14 & b16 & b18 \end{bmatrix}$$

$$= \begin{bmatrix} b11 X16 + b13 X17 + b15 X18 + b17 X19 & : & Xb11 \\ b1 X11 + b3 X12 + b5 X13 + b7 X14 + b9 X15 & : & Xb21 \\ b2 X11 + b4 X12 + b6 X13 + b8 X14 + b10 X15 + \\ + b12 X16 + b14 X17 + b16 X18 + b18 X19 & : & Xb31 \end{bmatrix}$$

$$\begin{bmatrix} X12 & X22 & X23 & X24 & X25 & X26 & X27 & X28 & X29 \\ 0 & 0 & 0 & 0 & 0 & b11 & b13 & b15 & b17 \\ b1 & b3 & b5 & b7 & b9 & 0 & 0 & 0 & 0 \\ b2 & b4 & b6 & b8 & b10 & b12 & b14 & b16 & b18 \end{bmatrix}$$

$$=$$

$$\begin{bmatrix} b11 X36 + b13 X37 + b15 X38 + b17 X39 & : & Xb13 \\ b1 X13 + b3 X23 + b5 X33 + b7 X34 + b9 X35 & : & Xb23 \\ b2 X13 + b4 X23 + b6 X33 + b8 X34 + b10 X35 \\ + b12 X36 + b14 X37 + b16 X38 + b18 X39 & : & Xb33 \end{bmatrix}$$

$$= \begin{bmatrix} X14 & X24 & X34 & X44 & X45 & X46 & X47 & X48 & X49 \\ 0 & 0 & 0 & 0 & 0 & b11 & b13 & b15 & b17 \\ b1 & b3 & b5 & b7 & b9 & 0 & 0 & 0 & 0 \\ b2 & b4 & b6 & b8 & b10 & b12 & b14 & b16 & b18 \end{bmatrix}$$

$$= \begin{bmatrix} b11 X46 + b13 X47 + b15 X48 + b17 X49 & : & Xb14 \\ b1 X14 + b3 X24 + b5 X34 + b7 X44 + b9 X45 & : & Xb24 \\ b2 X14 + b4 X24 + b6 X34 + b8 X44 + b10 X45 \\ + b12 X46 + b14 X47 + b16 X48 + b18 X49 & : & Xb34 \end{bmatrix}$$

$$= \begin{bmatrix} X15 & X25 & X35 & X45 & X55 & X56 & X57 & X58 & X59 \\ 0 & 0 & 0 & 0 & 0 & b11 & b13 & b15 & b17 \\ b1 & b3 & b5 & b7 & b9 & 0 & 0 & 0 & 0 \\ b2 & b4 & b6 & b8 & b10 & b12 & b14 & b16 & b18 \end{bmatrix}$$

$$= \begin{bmatrix} b11 X56 + b13 X57 + b15 X58 + b17 X59 & : & Xb15 \\ b1 X15 + b3 X25 + b5 X35 + b7 X45 + b9 X55 & : & Xb25 \\ b2 X15 + b4 X25 + b6 X35 + b8 X45 + b10 X55 \\ + b12 X56 + b14 X57 + b16 X58 + b18 X59 & : & Xb35 \end{bmatrix}$$

$$= \begin{bmatrix} X16 & X26 & X36 & X46 & X56 & X66 & X67 & X68 & X69 \\ 0 & 0 & 0 & 0 & 0 & b11 & b13 & b15 & b17 \\ b1 & b3 & b5 & b7 & b9 & 0 & 0 & 0 & 0 \\ b2 & b4 & b6 & b8 & b10 & b12 & b14 & b16 & b18 \end{bmatrix}$$

$$= \begin{bmatrix} b11 X66 + b13 X67 + b15 X68 + b17 X69 & : & Xb16 \\ b1 X16 + b3 X26 + b5 X36 + b7 X46 + b9 X56 & : & Xb26 \\ b2 X16 + b4 X26 + b6 X36 + b8 X46 + b10 X56 \\ + b12 X66 + b14 X67 + b16 X68 + b18 X69 & : & Xb36 \end{bmatrix}$$

$$= \begin{bmatrix} X17 & X27 & X37 & X47 & X57 & X67 & X77 & X78 & X79 \\ 0 & 0 & 0 & 0 & 0 & b11 & b13 & b15 & b17 \\ b1 & b3 & b5 & b7 & b9 & 0 & 0 & 0 & 0 \\ b2 & b4 & b6 & b8 & b10 & b12 & b14 & b16 & b18 \end{bmatrix}$$

$$= \begin{bmatrix} b11 X67 + b13 X77 + b15 X78 + b17 X79 & : & Xb17 \\ b1 X17 + b3 X27 + b5 X37 + b7 X47 + b9 X57 & : & Xb27 \\ b2 X17 + b4 X27 + b6 X37 + b8 X47 + b10 X57 \\ + b12 X67 + b14 X77 + b16 X78 + b18 X79 & : & Xb37 \end{bmatrix}$$

$$\begin{bmatrix}
 X_{19} & X_{29} & X_{39} & X_{49} & X_{59} & X_{69} & X_{79} & X_{89} & X_{99} \\
 0 & 0 & 0 & 0 & 0 & b_{11} & b_{13} & b_{15} & b_{17} \\
 b_1 & b_3 & b_5 & b_7 & b_9 & 0 & 0 & 0 & 0 \\
 b_2 & b_4 & b_6 & b_8 & b_{10} & b_{12} & b_{14} & b_{16} & b_{18}
 \end{bmatrix}$$

=

$$\begin{aligned}
 & b_{11} X_{69} + b_{13} X_{79} + b_{15} X_{89} + b_{17} X_{99} && : X_{b19} \\
 & b_1 X_{19} + b_3 X_{29} + b_5 X_{39} + b_7 X_{49} + b_9 X_{59} && : X_{b29} \\
 & b_2 X_{19} + b_4 X_{29} + b_6 X_{39} + b_8 X_{49} + b_{10} X_{59} \\
 & + b_{12} X_{69} + b_{14} X_{79} + b_{16} X_{89} + b_{18} X_{99} && : X_{b39}
 \end{aligned}$$

Them,we have

$$u = - B_2^T X x^{\wedge}$$

$$\begin{aligned}
 &= \\
 & [X_{b11} \quad X_{b12} \quad X_{b13} \quad X_{b14} \quad X_{b15} \quad X_{b16} \quad X_{b17} \quad X_{b18} \quad X_{b19} \\
 & X_{b21} \quad X_{b22} \quad X_{b23} \quad X_{b24} \quad X_{b25} \quad X_{b26} \quad X_{b27} \quad X_{b28} \quad X_{b29} \\
 & X_{b31} \quad X_{32} \quad X_{b33} \quad X_{b34} \quad X_{b35} \quad X_{b36} \quad X_{b37} \quad X_{b38} \quad X_{b39} ] \\
 & [ x_{10} \ x_{11} \ x_{12} \ x_{13} \ x_{14} \ x_{15} \ x_{16} \ x_{17} \ x_{18} ]^T \\
 &= \\
 & - [X_{b11}X_{10} + \quad X_{b12} X_{11} + \quad X_{b13} X_{12} + \quad X_{b14} X_{13}+ \quad X_{b15} X_{14}+ \quad X_{b16} X_{15}+ \quad X_{b17} X_{16} + X_{b18} X_{17} + X_{b19} X_{18} \\
 & X_{b21} X_{10} + \quad X_{b22} X_{11} + \quad X_{b23} X_{12} + \quad X_{b24} X_{13}+ \quad X_{b25} X_{14} + \quad X_{b26} X_{15}+ \quad X_{b27} X_{16} + X_{b28} X_{17} + X_{b29} X_{18} \\
 & X_{b31} X_{10} + \quad X_{b32} X_{11} + \quad X_{b33} X_{12}+ \quad X_{b34} X_{13}+ \quad X_{b35} X_{14} + \quad X_{b36} X_{15} + \quad X_{b37} X_{16} + X_{b38} X_{17} + X_{b39} X_{18} ]
 \end{aligned}$$

$$B_2 \begin{bmatrix}
 0 & b_1 & b_2 \\
 0 & b_3 & b_4 \\
 0 & b_5 & b_6 \\
 0 & b_7 & b_8 \\
 0 & b_9 & b_{10} \\
 b_{11} & 0 & b_{12} \\
 b_{13} & 0 & b_{14} \\
 b_{15} & 0 & b_{16} \\
 b_{17} & 0 & b_{18}
 \end{bmatrix}$$

$$\begin{aligned}
 B_2 u = & \\
 & b_1 (X_{b21} X_{10} + X_{b22} X_{11} + X_{b23} X_{12} + X_{b24} X_{13} + X_{b25} X_{14} + X_{b26} X_{15} + X_{b27} X_{16} + X_{b28} X_{17} + X_{b29} X_{18}) \\
 & + b_2 (X_{b31} X_{10} + X_{b32} X_{11} + X_{b33} X_{12} + X_{b34} X_{13} + X_{b35} X_{14} + X_{b36} X_{15} + X_{b37} X_{16} + X_{b38} X_{17} + X_{b39} X_{18}) \\
 & b_3 (X_{b21} X_{10} + X_{b22} X_{11} + X_{b23} X_{12} + X_{b24} X_{13} + X_{b25} X_{14} + X_{b26} X_{15} + X_{b27} X_{16} + X_{b28} X_{17} + X_{b29} X_{18}) \\
 & + b_4 (X_{b31} X_{10} + X_{b32} X_{11} + X_{b33} X_{12} + X_{b34} X_{13} + X_{b35} X_{14} + X_{b36} X_{15} + X_{b37} X_{16} + X_{b38} X_{17} + X_{b39} X_{18}) \\
 & b_5 (X_{b21} X_{10} + X_{b22} X_{11} + X_{b23} X_{12} + X_{b24} X_{13} + X_{b25} X_{14} + X_{b26} X_{15} + X_{b27} X_{16} + X_{b28} X_{17} + X_{b29} X_{18}) \\
 & + b_6 (X_{b31} X_{10} + X_{b32} X_{11} + X_{b33} X_{12} + X_{b34} X_{13} + X_{b35} X_{14} + X_{b36} X_{15} + X_{b37} X_{16} + X_{b38} X_{17} + X_{b39} X_{18}) \\
 & b_7 (X_{b21} X_{10} + X_{b22} X_{11} + X_{b23} X_{12} + X_{b24} X_{13} + X_{b25} X_{14} + X_{b26} X_{15} + X_{b27} X_{16} + X_{b28} X_{17} + X_{b29} X_{18}) \\
 & + b_8 (X_{b31} X_{10} + X_{b32} X_{11} + X_{b33} X_{12} + X_{b34} X_{13} + X_{b35} X_{14} + X_{b36} X_{15} + X_{b37} X_{16} + X_{b38} X_{17} + X_{b39} X_{18}) \\
 & b_9 (X_{b21} X_{10} + X_{b22} X_{11} + X_{b23} X_{12} + X_{b24} X_{13} + X_{b25} X_{14} + X_{b26} X_{15} + X_{b27} X_{16} + X_{b28} X_{17} + X_{b29} X_{18}) \\
 & + b_{10} (X_{b31} X_{10} + X_{b32} X_{11} + X_{b33} X_{12} + X_{b34} X_{13} + X_{b35} X_{14} + X_{b36} X_{15} + X_{b37} X_{16} + X_{b38} X_{17} + X_{b39} X_{18}) \\
 & b_{11} (X_{b11} X_{10} + X_{b12} X_{11} + X_{b13} X_{12} + X_{b14} X_{13} + X_{b15} X_{14} + X_{b16} X_{15} + X_{b17} X_{16} + X_{b18} X_{17} + X_{b19} X_{18}) \\
 & + b_{12} (X_{b31} X_{10} + X_{b32} X_{11} + X_{b33} X_{12} + X_{b34} X_{13} + X_{b35} X_{14} + X_{b36} X_{15} + X_{b37} X_{16} + X_{b38} X_{17} + X_{b39} X_{18})
 \end{aligned}$$

$$b13(Xb11X10 + Xb12 X11 + Xb13 X12 + Xb14 X13 + Xb15 X14 + Xb16 X15 + Xb17 X16 + Xb18 X17 + Xb19 X18 + b14(Xb31 X10 + Xb32 X11 + Xb33 X12 + Xb34 X13 + Xb35 X14 + Xb36 X15 + Xb37 X16 + Xb38 X17 + Xb39 X18)$$

$$b15(Xb11X10 + Xb12 X11 + Xb13 X12 + Xb14 X13 + Xb15 X14 + Xb16 X15 + Xb17 X16 + Xb18 X17 + Xb19 X18 + b16(Xb31 X10 + Xb32 X11 + Xb33 X12 + Xb34 X13 + Xb35 X14 + Xb36 X15 + Xb37 X16 + Xb38 X17 + Xb39 X18)$$

$$b17(Xb11X10 + Xb12 X11 + Xb13 X12 + Xb14 X13 + Xb15 X14 + Xb16 X15 + Xb17 X16 + Xb18 X17 + Xb19 X18 + b18(Xb31 X10 + Xb32 X11 + Xb33 X12 + Xb34 X13 + Xb35 X14 + Xb36 X15 + Xb37 X16 + Xb38 X17 + Xb39 X18)$$

setting

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$b1 Xb21 + b2 Xb31 = Xa1,$	$b3 Xb21 + b4 Xb31 = Xa10,$	$b5 Xb21 + b6 Xb31 = Xa19,$
$b1 Xb22 + b2 Xb32 = Xa2,$	$b3 Xb22 + b4 Xb32 = Xa11,$	$b5 Xb22 + b6 Xb32 = Xa20,$
$b1 Xb23 + b2 Xb33 = Xa3,$	$b3 Xb23 + b4 Xb33 = Xa12,$	$b5 Xb23 + b6 Xb33 = Xa21,$
$b1 Xb24 + b2 Xb34 = Xa4,$	$b3 Xb24 + b4 Xb34 = Xa13,$	$b5 Xb24 + b6 Xb34 = Xa22,$
$b1 Xb25 + b2 Xb35 = Xa5,$	$b3 Xb25 + b4 Xb35 = Xa14,$	$b5 Xb25 + b6 Xb35 = Xa23,$
$b1 Xb26 + b2 Xb36 = Xa6,$	$b3 Xb26 + b4 Xb36 = Xa15,$	$b5 Xb26 + b6 Xb36 = Xa24,$
$b1 Xb27 + b2 Xb37 = Xa7,$	$b3 Xb27 + b4 Xb37 = Xa16,$	$b5 Xb27 + b6 Xb37 = Xa25,$
$b1 Xb28 + b2 Xb38 = Xa8,$	$b3 Xb28 + b4 Xb38 = Xa17,$	$b5 Xb28 + b6 Xb38 = Xa26,$
$b1 Xb29 + b2 Xb39 = Xa9,$	$b3 Xb29 + b4 Xb39 = Xa18,$	$b5 Xb29 + b6 Xb39 = Xa27,$

$b9 Xb21 + b10 Xb31 = Xa37,$	$b11 Xb11 + b12 Xb31 = Xa46,$	$b7 Xb21 + b8 Xb31 = Xa28,$
$b9 Xb22 + b10 Xb32 = Xa38,$	$b11 Xb12 + b12 Xb32 = Xa47,$	$b7 Xb22 + b8 Xb32 = Xa29,$
$b9 Xb23 + b10 Xb33 = Xa39,$	$b11 Xb13 + b12 Xb33 = Xa48,$	$b7 Xb23 + b8 Xb33 = Xa30,$
$b9 Xb24 + b10 Xb34 = Xa40,$	$b11 Xb14 + b12 Xb34 = Xa49,$	$b7 Xb24 + b8 Xb34 = Xa31,$
$b9 Xb25 + b10 Xb35 = Xa41,$	$b11 Xb15 + b12 Xb35 = Xa50,$	$b7 Xb25 + b8 Xb35 = Xa32,$
$b9 Xb26 + b10 Xb36 = Xa42,$	$b11 Xb16 + b12 Xb36 = Xa51,$	$b7 Xb26 + b8 Xb36 = Xa33,$
$b9 Xb27 + b10 Xb37 = Xa43,$	$b11 Xb17 + b12 Xb37 = Xa52,$	$b7 Xb27 + b8 Xb37 = Xa34,$
$b9 Xb28 + b10 Xb38 = Xa44,$	$b11 Xb18 + b12 Xb38 = Xa53,$	$b7 Xb28 + b8 Xb38 = Xa35,$
$b9 Xb29 + b10 Xb39 = Xa45,$	$b11 Xb19 + b12 Xb39 = Xa54,$	$b7 Xb29 + b8 Xb39 = Xa36,$

$b13 Xb11 + b14 Xb31 = Xa55,$	$b15 Xb11 + b16 Xb31 = Xa64,$	$b17 Xb11 + b18 Xb31 = Xa73,$
$b13 Xb12 + b14 Xb32 = Xa56,$	$b15 Xb12 + b16 Xb32 = Xa65,$	$b17 Xb12 + b18 Xb32 = Xa74,$
$b13 Xb13 + b14 Xb33 = Xa57,$	$b15 Xb13 + b16 Xb33 = Xa66,$	$b17 Xb13 + b18 Xb33 = Xa75,$
$b13 Xb14 + b14 Xb34 = Xa58,$	$b15 Xb14 + b16 Xb34 = Xa67,$	$b17 Xb14 + b18 Xb34 = Xa76,$
$b13 Xb15 + b14 Xb35 = Xa59,$	$b15 Xb15 + b16 Xb35 = Xa68,$	$b17 Xb15 + b18 Xb35 = Xa77,$
$b13 Xb16 + b14 Xb36 = Xa60,$	$b15 Xb16 + b16 Xb36 = Xa69,$	$b17 Xb16 + b18 Xb36 = Xa78,$
$b13 Xb17 + b14 Xb37 = Xa61,$	$b15 Xb17 + b16 Xb37 = Xa70,$	$b17 Xb17 + b18 Xb37 = Xa79,$
$b13 Xb18 + b14 Xb38 = Xa62,$	$b15 Xb18 + b16 Xb38 = Xa71,$	$b17 Xb18 + b18 Xb38 = Xa80,$
$b13 Xb19 + b14 Xb39 = Xa63,$	$b15 Xb19 + b16 Xb39 = Xa72,$	$b17 Xb19 + b18 Xb39 = Xa81,$

B2 u =

$$Xa1 X10 + Xa2 X11 + Xa3 X12 + Xa4 X13 + Xa5 X14 + Xa6 X15 + Xa7 X16 + Xa8 X17 + Xa9 X18$$

$$Xa10 X10 + Xa11 X11 + Xa12 X12 + Xa13 X13 + Xa14 X14 + Xa15 X15 + Xa16 X16 + Xa17 X17 + Xa18 X18$$

$$Xa19 X10 + Xa20 X11 + Xa21 X12 + Xa22 X13 + Xa23 X14 + Xa24 X15 + Xa25 X16 + Xa26 X17 + Xa27 X18$$

$$Xa28 X10 + Xa29 X11 + Xa30 X12 + Xa31 X13 + Xa32 X14 + Xa33 X15 + Xa34 X16 + Xa35 X17 + Xa36 X18$$

$$Xa37 X10 + Xa38 X11 + Xa39 X12 + Xa40 X13 + Xa41 X14 + Xa42 X15 + Xa43 X16 + Xa44 X17 + Xa45 X18$$

$$Xa46 X10 + Xa47 X11 + Xa48 X12 + Xa49 X13 + Xa50 X14 + Xa51 X15 + Xa52 X16 + Xa53 X17 + Xa54 X18$$

$$Xa55 X10 + Xa56 X11 + Xa57 X12 + Xa58 X13 + Xa59 X14 + Xa60 X15 + Xa61 X16 + Xa62 X17 + Xa63 X18$$

$$Xa64 X10 + Xa65 X11 + Xa66 X12 + Xa67 X13 + Xa68 X14 + Xa69 X15 + Xa70 X16 + Xa71 X17 + Xa72 X18$$

$$Xa73 X10 + Xa74 X11 + Xa75 X12 + Xa76 X13 + Xa77 X14 + Xa78 X15 + Xa79 X16 + Xa80 X17 + Xa81 X18$$



Ob1 = ( a11 - Xa1 - Y(1,1) )	Ob28=( 0 - Xa28 - Y(1,4) )	Ob55=( 0 - Xa55 - Y(1,7) )
Ob2 = ( a12 - Xa2 - Y(1,2) )	Ob29=( 0 - Xa29 - Y(2,4) )	Ob56=( 0 - Xa56 - Y(2,7) )
Ob3 = ( a13 - Xa3 - Y(1,3) )	Ob30=( a43 - Xa30 - Y(3,4) )	Ob57=( 0 - Xa57 - Y(3,7) )
Ob4 = ( a14 - Xa4 - Y(1,4) )	Ob31=( 0 - Xa31 - Y(4,4) )	Ob58=( a74 - Xa58 - Y(4,7) )
Ob5 = ( a15 - Xa5 - Y(1,5) )	Ob32=( a45 - Xa32 - Y(4,5) )	Ob59=( 0 - Xa59 - Y(5,7) )
Ob6 = ( a16 - Xa6 - Y(1,6) )	Ob33=( 0 - Xa33 - Y(4,6) )	Ob60=( a76 - Xa60 - Y(6,7) )
Ob7 = ( a17 - Xa7 - Y(1,7) )	Ob34=( a47 - Xa34 - Y(4,7) )	Ob61=( 0 - Xa61 - Y(7,7) )
Ob8 = ( a18 - Xa8 - Y(1,8) )	Ob35=( 0 - Xa35 - Y(4,8) )	Ob62=( a78 - Xa62 - Y(7,8) )
Ob9 = ( a19 - Xa9 - Y(1,9) )	Ob36=( 0 - Xa36 - Y(4,9) )	Ob63=( 0 - Xa63 - Y(7,9) )
%-----		
Ob1s = -Y(1,1)	Ob16s = -Y(1,4)	Ob31s = -Y(1,7)
Ob2s = -Y(1,2)	Ob17s = -Y(2,4)	Ob32s = -Y(2,7)
Ob3s = -Y(1,3)	Ob18s = -Y(3,4)	Ob33s = -Y(3,7)
Ob4s = -Y(1,4)	Ob19s = -Y(4,4)	Ob34s = -Y(4,7)
Ob5s = -Y(1,5)	Ob20s = -Y(4,5)	Ob35s = -Y(5,7)
Ob1ss = - Y(1,6)	Ob16ss =- Y(4,6)	Ob31ss =- Y(6,7)
Ob2ss =- Y(1,7)	Ob17ss =- Y(4,7)	Ob32ss =- Y(7,7)
Ob3ss =- Y(1,8)	Ob18ss =- Y(4,8)	Ob33ss =- Y(7,8)
Ob4ss =- Y(1,9)	Ob19ss =- Y(4,9)	Ob34ss =- Y(7,9)
%-----		
Ob10=( a21 - Xa10 - Y(1,2) )	Ob37=( 0 - Xa37 - Y(1,5) )	Ob64=( 0 - Xa64 - Y(1,8) )
Ob11=( 0 - Xa11 - Y(2,2) )	Ob38=( 0 - Xa38 - Y(2,5) )	Ob65=( 0 - Xa65 - Y(2,8) )
Ob12=( a23 - Xa12 - Y(2,3) )	Ob39=( 0 - Xa39 - Y(3,5) )	Ob66=( a83 - Xa66 - Y(3,8) )
Ob13=( 0 - Xa13 - Y(2,4) )	Ob40=( a54 - Xa40 - Y(4,5) )	Ob67=( 0 - Xa67 - Y(4,8) )
Ob14=( 0 - Xa14 - Y(2,5) )	Ob41=( 0 - Xa41 - Y(5,5) )	Ob68=( 0 - Xa68 - Y(5,8) )
Ob15=( 0 - Xa15 - Y(2,6) )	Ob42=( a56 - Xa42 - Y(5,6) )	Ob69=( 0 - Xa69 - Y(6,8) )
Ob16=( 0 - Xa16 - Y(2,7) )	Ob43=( 0 - Xa43 - Y(5,7) )	Ob70=( a87 - Xa70 - Y(7,8) )
Ob17=( 0 - Xa17 - Y(2,8) )	Ob44=( 0 - Xa44 - Y(5,8) )	Ob71=( 0 - Xa71 - Y(8,8) )
Ob18=( a29 - Xa18 - Y(2,9) )	Ob45=( 0 - Xa45 - Y(5,9) )	Ob72=( a89 - Xa72 - Y(8,9) )
%-----		
Ob6s = -Y(1,2)	Ob21s = -Y(1,5)	Ob36s = -Y(1,8)
Ob7s = -Y(2,2)	Ob22s = -Y(2,5)	Ob37s = -Y(2,8)
Ob8s = -Y(2,3)	Ob23s = -Y(3,5)	Ob38s = -Y(3,8)
Ob9s = -Y(2,4)	Ob24s = -Y(4,5)	Ob39s = -Y(4,8)
Ob10s =- Y(2,5)	Ob25s = -Y(5,5)	Ob40s = -Y(5,8)
Ob6ss =- Y(2,6)	Ob21ss =- Y(5,6)	Ob36ss =- Y(6,8)
Ob7ss =- Y(2,7)	Ob22ss =- Y(5,7)	Ob37ss =- Y(7,8)
Ob8ss =- Y(2,8)	Ob23ss =- Y(5,8)	Ob38ss =- Y(8,8)
Ob9ss =- Y(2,9)	Ob24ss =- Y(5,9)	Ob39ss =- Y(8,9)
%-----		
Ob19=( 0 - Xa19 - Y(1,3) )	Ob46=( 0 - Xa46 - Y(1,6) )	Ob73=( a91 - Xa73 - Y(1,9) )
Ob20=( a32 - Xa20 - Y(2,3) )	Ob47=( 0 - Xa47 - Y(2,6) )	Ob74=( a92 - Xa74 - Y(2,9) )
Ob21=( 0 - Xa21 - Y(3,3) )	Ob48=( 0 - Xa48 - Y(3,6) )	Ob75=( a93 - Xa75 - Y(3,9) )
Ob22=( a34 - Xa22 - Y(3,4) )	Ob49=( 0 - Xa49 - Y(4,6) )	Ob76=( a94 - Xa76 - Y(4,9) )
Ob23=( 0 - Xa23 - Y(3,5) )	Ob50=( a65 - Xa50 - Y(5,6) )	Ob77=( a95 - Xa77 - Y(5,9) )
Ob24=( 0 - Xa24 - Y(3,6) )	Ob51=( 0 - Xa51 - Y(6,6) )	Ob78=( a96 - Xa78 - Y(6,9) )
Ob25=( 0 - Xa25 - Y(3,7) )	Ob52=( a67 - Xa52 - Y(6,7) )	Ob79=( a97 - Xa79 - Y(7,9) )
Ob26=( a38 - Xa26 - Y(3,8) )	Ob53=( 0 - Xa53 - Y(6,8) )	Ob80=( a98 - Xa80 - Y(8,9) )
Ob27=( 0 - Xa27 - Y(3,9) )	Ob54=( 0 - Xa54 - Y(6,9) )	Ob81=( a99 - Xa81 - Y(9,9) )
%-----		
Ob11s = -Y(1,3)	Ob26s = -Y(1,6)	Ob41s = -Y(1,9)
Ob12s = -Y(2,3)	Ob27s = -Y(2,6)	Ob42s = -Y(2,9)
Ob13s = -Y(3,3)	Ob28s = -Y(3,6)	Ob43s = -Y(3,9)
Ob14s = -Y(3,4)	Ob29s = -Y(4,6)	Ob44s = -Y(4,9)
Ob15s = -Y(3,5)	Ob30s = -Y(5,6)	Ob45s = -Y(5,9)
Ob11ss =- Y(3,6)	Ob26ss =- Y(6,6)	Ob41ss =- Y(6,9)
Ob12ss =- Y(3,7)	Ob27ss =- Y(6,7)	Ob42ss =- Y(7,9)
Ob13ss =- Y(3,8)	Ob28ss =- Y(6,8)	Ob43ss =- Y(8,9)
Ob14ss =- Y(3,9)	Ob29ss =- Y(6,9)	Ob44ss =- Y(9,9)
%-----		

$$\begin{aligned}
 \text{xdot}(1) &= a11*x(1) + a12*x(2) + a13*x(3) + a14*x(4) + a15*x(5) + a16*x(6) + a17*x(7) + a18*x(8) + a19*x(9) \\
 &+ Xa1*x(10) + Xa2*x(11) + Xa3*x(12) + Xa4*x(13) + Xa5*x(14) + Xa6*x(15) + Xa7*x(16) + Xa8*x(17) + Xa9*x(18) \\
 \text{xdot}(2) &= a21*x(1) + a23*x(3) + a29*x(9) \\
 &+ Xa10*x(10) + Xa11*x(11) + Xa12*x(12) + Xa13*x(13) + Xa14*x(14) + Xa15*x(15) + Xa16*x(16) + Xa17*x(17) + Xa18*x(18) \\
 \text{xdot}(3) &= a32*x(2) + a34*x(4) + a38*x(8) \\
 &+ Xa19*x(10) + Xa20*x(11) + Xa21*x(12) + Xa22*x(13) + Xa23*x(14) + Xa24*x(15) + Xa25*x(16) + Xa26*x(17) + Xa27*x(18) \\
 \text{xdot}(4) &= a43*x(3) + a45*x(5) + a47*a7 \\
 &+ Xa28*x(10) + Xa29*x(11) + Xa30*x(12) + Xa31*x(13) + Xa32*x(14) + Xa33*x(15) + Xa34*x(16) + Xa35*x(17) + Xa36*x(18) \\
 \text{xdot}(5) &= a54*x(4) + a56*x(6) \\
 &+ Xa37*x(10) + Xa38*x(11) + Xa39*x(12) + Xa40*x(13) + Xa41*x(14) + Xa42*x(15) + Xa43*x(16) + Xa44*x(17) + Xa45*x(18) \\
 \text{xdot}(6) &= a65*x(5) + a67*x(7) \\
 &+ Xa46*x(10) + Xa47*x(11) + Xa48*x(12) + Xa49*x(13) + Xa50*x(14) + Xa51*x(15) + Xa52*x(16) + Xa53*x(17) + Xa54*x(18) \\
 \text{xdot}(7) &= a74*x(4) + a76*x(6) + a78*x(8) \\
 &+ Xa55*x(10) + Xa56*x(11) + Xa57*x(12) + Xa58*x(13) + Xa59*x(14) + Xa60*x(15) + Xa61*x(16) + Xa62*x(17) + Xa63*x(18) \\
 \text{xdot}(8) &= a83*x(3) + a87*x(7) + a89*x(9) \\
 &+ Xa64*x(10) + Xa65*x(11) + Xa66*x(12) + Xa67*x(13) + Xa68*x(14) + Xa69*x(15) + Xa70*x(16) + Xa71*x(17) + Xa72*x(18) \\
 \text{xdot}(9) &= a91*x(1) + a92*x(2) + a93*x(3) + a94*x(4) + a95*x(5) + a96*x(6) + a97*x(7) + a98*x(8) + a99*x(9) \\
 &+ Xa73*x(10) + Xa74*x(11) + Xa75*x(12) + Xa76*x(13) + Xa77*x(14) + Xa78*x(15) + Xa79*x(16) + Xa80*x(17) + Xa81*x(18) \\
 \text{xdot}(10) &= Ob1*x(10) + Ob2*x(11) + Ob3*x(12) + Ob4*x(13) + Ob5*x(14) + Ob6*x(15) + Ob7*x(16) + Ob8*x(17) + Ob9*x(18) \\
 &+ Ob1s*x(1) + Ob2s*x(2) + Ob3s*x(3) + Ob4s*x(4) + Ob5s*x(5) + Ob1ss*x(6) + Ob2ss*x(7) + Ob3ss*x(8) + Ob4ss*x(9) \\
 \text{xdot}(11) &= Ob10*x(10) + Ob11*x(11) + Ob12*x(12) + Ob13*x(13) + Ob14*x(14) + Ob15*x(15) + Ob16*x(16) + Ob17*x(17) + Ob18*x(18) \\
 &+ Ob6s*x(1) + Ob7s*x(2) + Ob8s*x(3) + Ob9s*x(4) + Ob10s*x(5) + Ob6ss*x(6) + Ob7ss*x(7) + Ob8ss*x(8) + Ob9ss*x(9) \\
 \text{xdot}(12) &= Ob19*x(10) + Ob20*x(11) + Ob21*x(12) + Ob22*x(13) + Ob23*x(14) + Ob24*x(15) + Ob25*x(16) + Ob26*x(17) \\
 &+ Ob27*x(18) + Ob11s*x(1) + Ob12s*x(2) + Ob13s*x(3) + Ob14s*x(4) + Ob15s*x(5) + Ob11ss*x(6) + Ob12ss*x(7) \\
 &+ Ob13ss*x(8) + Ob14ss*x(9) \\
 \text{xdot}(13) &= Ob28*x(10) + Ob29*x(11) + Ob30*x(12) + Ob31*x(13) + Ob32*x(14) + Ob33*x(15) + Ob34*x(16) + Ob35*x(17) + Ob36*x(18) \\
 &+ Ob16s*x(1) + Ob17s*x(2) + Ob18s*x(3) + Ob19s*x(4) + Ob20s*x(5) + Ob16ss*x(6) + Ob17ss*x(7) + Ob18ss*x(8) + Ob19ss*x(9) \\
 \text{xdot}(14) &= Ob37*x(10) + Ob38*x(11) + Ob39*x(12) + Ob40*x(13) + Ob41*x(14) + Ob42*x(15) + Ob43*x(16) \\
 &+ Ob44*x(17) + Ob45*x(18) + Ob21s*x(1) + Ob22s*x(2) + Ob23s*x(3) + Ob24s*x(4) + Ob25s*x(5) + Ob21ss*x(6) \\
 &+ Ob22ss*x(7) + Ob23ss*x(8) + Ob24ss*x(9) \\
 \text{xdot}(15) &= Ob46*x(10) + Ob47*x(11) + Ob48*x(12) + Ob49*x(13) + Ob50*x(14) + Ob51*x(15) + Ob52*x(16) + Ob53*x(17) + Ob54*x(18) \\
 &+ Ob26s*x(1) + Ob27s*x(2) + Ob28s*x(3) + Ob29s*x(4) + Ob30s*x(5) + Ob26ss*x(6) + Ob27ss*x(7) + Ob28ss*x(8) + Ob29ss*x(9) \\
 \text{xdot}(16) &= Ob55*x(10) + Ob56*x(11) + Ob57*x(12) + Ob58*x(13) + Ob59*x(14) + Ob60*x(15) + Ob61*x(16) + Ob62*x(17) + Ob63*x(18) \\
 &+ Ob31s*x(1) + Ob32s*x(2) + Ob33s*x(3) + Ob34s*x(4) + Ob35s*x(5) + Ob31ss*x(6) + Ob32ss*x(7) + Ob33ss*x(8) + Ob34ss*x(9) \\
 \text{xdot}(17) &= Ob64*x(10) + Ob65*x(11) + Ob66*x(12) + Ob67*x(13) + Ob68*x(14) + Ob69*x(15) + Ob70*x(16) + Ob71*x(17) + Ob72*x(18) \\
 &+ Ob36s*x(1) + Ob37s*x(2) + Ob38s*x(3) + Ob39s*x(4) + Ob40s*x(5) + Ob36ss*x(6) + Ob37ss*x(7) + Ob38ss*x(8) + Ob39ss*x(9) \\
 \text{xdot}(18) &= Ob73*x(10) + Ob74*x(11) + Ob75*x(12) + Ob76*x(13) + Ob77*x(14) + Ob78*x(15) + Ob79*x(16) + Ob80*x(17) + Ob81*x(18) \\
 &+ Ob41s*x(1) + Ob42s*x(2) + Ob43s*x(3) + Ob44s*x(4) + Ob45s*x(5) + Ob41ss*x(6) + Ob42ss*x(7) + Ob43ss*x(8) + Ob44ss*x(9)
 \end{aligned}$$

To close the loop, we set the negative feed back as

$$\begin{aligned}
 y1 &= -x1, \\
 y2 &= -x2 \\
 y3 &= -x3, \\
 y4 &= -x4 \\
 y5 &= -x5, \\
 y6 &= -x6 \\
 y7 &= -x7, \\
 y8 &= -x8 \\
 y9 &= -x9.
 \end{aligned}$$

We can obtain the coefficients Obn and Obnss

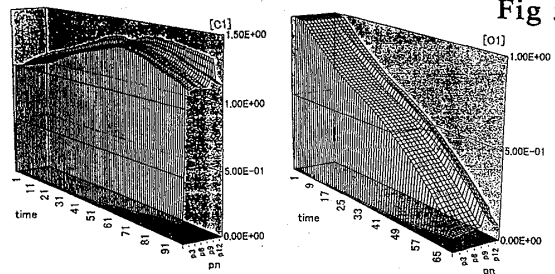


Fig 5

## 2. Results.

Fig 5 shows the temporal changes in [C1] and [O1] with changes in weighting coefficients for the control inputs un. Significant changes can be observed at particular pn. The present evaluation when extended will be available for predicting the noise filtering function of biomembranes.

## 3.Reference

1. Matkes.T.N and Jones.W. J.Gen. Phys. vol 99. pp 367. 1992.