A note on the dynamics of an HIV infection model using Padé approximants

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Abstract: In this work, we use Padé's approaches in solving a system of ordinary nonlinear differential equations which arises in the model for HIV infection of $CD4^{+}T$ cells. Some graphs are presented to show the reliability and simplicity of this method as well as the algorithms implemented in the analysis of the model.

Key-Words: Padé approximants, Model for HIV of $CD4^{+}T$ cells, Semi-Analytical Method, Normal Padé Table.

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1 Introduction

The non-linear problems form a major line of research in the sciences in general since many phenomena are modeled using nonlinear equations. It is also true that in most cases, it is not possible to find analytical solutions to such models and therefore knowledge of efficient numerical methods to approximate them is essential. Thus, there are several semi-analytical methods that allow us to approximate the solutions numerically, such as the ADM, the DTM and the Padé approximant method [1].

For this reason, the Padé method is used in the resolution of non-linear problems due to its excellent convergence. This method has proven to be very useful in obtaining quantitative information about the solution of many interesting problems in sciences. The applications of Padé approximants are divided into two classes:

- The provision of efficient rational approaches to special mathematical functions.
- The acquisition of quantitative information about a function.

We can say then that the Padé approaches are the basis of several non-linear techniques which have a connection with the well known ϵ algorithm. In the specialized literature, several methods are known to find the Padé approximations, so the fundamental objective of this work is to pay special attention to this type of fractions in which the method is applicable presenting the most relevant properties in the applications.

Now, by way of introduction, it is important to note that HIV is a retrovirus that targets the $CD4^{+}T$ lymphocytes, which are the most abundant white blood cells of the immune system. Although HIV infects other cells also, it wreaks the most havoc on the $CD4^{+}T$ cells by causing their decline and destruction, thus decreasing the resistance of the immune system.

2 Padé approximant mehod

From elemental analysis, divergence in a series of powers is essential to talk about the presence of singularities. This type of divergence shows the problem that polynomials have to approach a function around that singularity, where the basic idea is to represent any function $f(z)$ by a convergent expression [2]. One of the most used techniques that requires as input a finite number of terms is the approximation of Padé. In this method proposed by Padé, this series [13]

$$f(z) = \sum_{i=0}^{\infty} c_i z_i, \tag{1}$$

is replaced by a succession of rational functions of the form:

$$R_N^M(z) = \frac{\sum_{i=0}^{M} a_i z_i}{\sum_{i=0}^{N} b_i z_i}. \tag{2}$$

Therefore, we use the standardization $b_0 = 1$ and the remaining $M+N+1$ coefficients $a_0, \ldots, a_M$ and $b_1, \ldots, b_N$ in Eq.(2) are chosen such that $M + N + 1$

is the coefficient in the power series expansion (see Eq.(1)). Thay is,

$$f(z) - R_N^M(z) = \mathcal{O}\left(Z^{M+N+1}\right), \tag{3}$$

then

$$f(z)\sum_{i=0}^{M} b_i z_i - \sum_{i=0}^{M} a_i z_i = \mathcal{O}\left(Z^{M+N+1}\right). \tag{4}$$

If $\sum a_i z_i$ is a series representation of $f(z)$, then many cases $R_N^M(z) \to f(z)$ when $M, N \to \infty$, even if $\sum a_i z_i$ is divergent. Generally, we consider the convergent succession $R_0^J, R_0^{J+1}, \ldots,$ where $M = N + J$ with J fixed and $N \to \infty$.

Therefore, we get

- Case 1: $M \geq N$. Developing the expression (4) we have:

$$\begin{aligned}
&c_0 + c_1 z + c_2 z^2 + \ldots + c_N z^N + \ldots + c_M z^M + \ldots + c_{M+N} z^{M+N} \\
&+ c_0 b_1 z + c_1 b_1 z^2 + \ldots + c_{N-1} b_1 z^N + \ldots + c_{M-1} b_1 z^M + \ldots + c_{M+N-1} b_1 z^{M+N} \\
&+ c_0 b_2 z^2 + \ldots + c_{N-2} b_2 z^N + \ldots + c_{M-2} b_2 z^M + \ldots + c_{M+N-2} b_2 z^{M+N} \\
&\vdots \\
&+ c_0 b_N z^N + \ldots + c_{M-N} b_N z^M + \ldots + c_M b_N z^{M+N} \\
&= a_0 + a_1 z + a_2 z^2 + \ldots + a_N z^N + \ldots + a_M z^M
\end{aligned}$$

Then, equating coefficients we obtain:

$$\begin{cases}
c_M b_1 + c_{M-1} b_2 + \ldots + c_{M-N+1} b_N = -c_{M+1} \\
c_{M+1} b_1 + c_M b_2 + \ldots + c_{M-N+2} b_N = -c_{M+2} \\
\vdots \\
c_{M+N-1} b_1 + c_{M+N-2} b_2 + \ldots + c_M b_N = -c_{M+N}
\end{cases}$$

and

$$\begin{cases}
a_0 = c_0 \\
a_1 = c_1 + c_0 b_1 \\
a_2 = c_2 + c_1 b_1 + c_0 b_2 \\
\vdots \\
a_N = c_N + c_{N-1} b_1 + c_{N-2} b_2 + \ldots + c_0 b_N \\
\vdots \\
a_M = c_M + c_{M-1} b_1 + c_{M-2} b_2 + \ldots + c_{M-N} b_N
\end{cases}$$

- Case 2: $M < N$.

  In this case and after matching coefficients we get:

$$\begin{aligned}
&c_0 + c_1 z + c_2 z^2 + \ldots + c_M z^M + \ldots + c_N z^N + \ldots + c_{M+N} z^{M+N} \\
&+ c_0 b_1 z + c_1 b_1 z^2 + \ldots + c_{M-1} b_1 z^M + \ldots + c_{N-1} b_1 z^N + \ldots + c_{M+N-1} b_1 z^{M+N} \\
&+ c_0 b_2 z^2 + \ldots + c_{M-2} b_2 z^M + \ldots + c_{N-2} b_2 z^N + \ldots + c_{M+N-2} b_2 z^{M+N} \\
&\vdots \\
&+ c_0 b_M z^M + \ldots + c_{N-M} b_M z^N + \ldots + c_N b_M z^{M+N} \\
&\vdots \\
&+ c_0 b_N z^N + \ldots + c_M b_N z^{M+N} \\
&= a_0 + a_1 z + a_2 z^2 + \ldots + a_M z^M
\end{aligned}$$

$$\begin{cases}
c_M b_1 + c_{M-1} b_2 + \ldots + c_0 b_{M+1} = -c_{M+1} \\
c_{M+1} b_1 + c_M b_2 + \ldots + c_1 b_{M+1} + c_0 b_{M+2} = -c_{M+2} \\
\vdots \\
c_{N-1} b_1 + c_{N-2} b_2 + \ldots + c_{N-M-1} b_{M+1} + c_{N-M-2} b_{M+2} + \ldots + c_0 b_N = -c_N \\
\vdots \\
c_{M+N-1} b_1 + c_{M+N-2} b_2 + \ldots + c_{N-1} b_{M+1} + c_{N-2} b_{M+2} + \ldots + c_M b_N = -c_{M+N}
\end{cases}$$

$$\begin{cases}
a_0 = c_0 \\
a_1 = c_1 + c_0 b_1 \\
a_2 = c_2 + c_1 b_1 + c_0 b_2 \\
\vdots \\
a_M = c_M + c_{M-1} b_1 + c_{M-2} b_2 + \ldots + c_0 b_M
\end{cases}$$

$$\mathcal{A}\begin{bmatrix} b_1 \\ b_2 \\ \vdots \\ b_N \end{bmatrix} = -\begin{bmatrix} c_{M+1} \\ c_{M+2} \\ \vdots \\ c_{M+N} \end{bmatrix}$$

Now, solving these systems we get:

where $\mathcal{A}$ is a matrix $n \times n$ whose entries are given by $A_{ij} = c_{M+i-j}$ with $a_k = 0$ if $k < 0$. Therefore, the coefficients $a_0, a_1 \ldots,$ are determined by using Eq.(5)

$$a_j = \sum_{k=0}^{j} c_{j-k} b_k, \quad 0 \leq j \leq M, \tag{5}$$

where $b_k = 0$ for $k > N$. Here, the resulting rational function $R_N^M(z)$ is called a Padé approximation.

2.1 Modified algorithm

Semi-analytical techniques to solve nonlinear models require an initial vision to determine the solutions as well as the calculation of one or more parameters that fit the initial system. When the parameters are chosen correctly, the results can be very precise, but it is important to emphasize that there is no method for initially choosing this choice. In this work, we suggest to use directly the serial solution for a nonlinear model to find Padé's approximation with highly efficient results [3, 4].

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```
function [P,Q] = fraccion_continuaV2(M,N,y)
    J = M - N; t = 0;
    if(J<0)
        t = N; N = M; M = t; J = abs(J);
    end
    M = M + N - J; A = zeros(M+1); B = zeros(M+1); d = zeros(M+1,1);
    A(1,:) = y(J+1:end);
    B(1,1) = 1; d(1) = A(1,1); P0 = d(1); P1 = d(1);  Q0 = 1;
    for k = 1:M
        l = k-1;
        for i = 1:k
            A(i+1,l+1) = A(i,1)*B(i,l+2)-B(i,1)*A(i,l+2);
            B(i+1,l+1) = B(i,1)*A(i,l+1); l = l - 1;
        end
        d(k+1) = A(k+1,1)/B(k+1,1);
        if(k>1)
            P = suma_pol(P1,conv([d(k+1) 0],P0)); P0 = P1; P1 = P;
            Q = suma_pol(Q1,conv([d(k+1) 0],Q0)); Q0 = Q1; Q1 = Q;
        else

            Q1 = [d(2) 1];
        end
    end
    if(J>0)
        P = suma_pol(conv(fliplr(eval(y(1:J))),Q),conv([1 zeros(1,J)],P));
    end
    if(t~=0)
        t = P; P = Q; Q = t;
    end
 end
```

Algorithm 1. Modified algorithm.

The method receives as input parameters, in addition to the degrees of numerator and denominator of the Padé approximation, the coefficients of the series expansion instead of the function explicitly [5, 6].

3 Dynamics of an HIV infection model

Below we analyze the dynamics for a model of HIV infection from $CD4^{+}T$ cells. The components of this basic model are the concentration of $CD4^{+}T$ cells, $CD4^{+}T$ cells infected with HIV and the HIV-free particles, which we will denote by $T(t)$, $I(t)$ and $V(t)$ respectively [7]. These amounts satisfy the following relationship:

$$\begin{cases} T' &= s - \alpha T + rT\left(1 - \frac{T+I}{T_{max}}\right) - \lambda VT \\ I' &= \lambda VT - \beta I \\ V' &= \eta\beta I - \gamma V \end{cases} \quad (6)$$

with initial conditions $T(0) = r_1, I(0) = r_2$ and $V(0) = r_3$. In this case, we use the values $s = 0.1, \alpha = 0.02, \beta = 0.3, r = 3, \gamma = 2.4, \lambda = 0.0027, T_{max} = 1500, \eta = 10, r_1 = 0.1, r_2 = 0$ and $r_3 = 0.1$.

Now, we assume

$$T(t) = \sum_{n=0}^{\infty} c_n^{(1)} t^n, \quad I(t) = \sum_{n=0}^{\infty} c_n^{(2)} t^n$$

$$V(t) = \sum_{n=0}^{\infty} c_n^{(3)} t^n \quad (7)$$

whence

$$T'(t) = \sum_{n=0}^{\infty} (n+1) c_{n+1}^{(1)} t^n, \quad V'(t) = \sum_{n=0}^{\infty} (n+1) c_{n+1}^{(3)} t^n \quad (8)$$

then, replacing (7) and (8) in (6) we have:

and we get for $n = 0$

Now, for $n > 0$ we get and finally for $n \geq 0$

We now solve the system of non-linear equations to obtain the coefficients $c_n^{(i)}, k = 1, 2, 3, n = 0, 1, \ldots$ of the series approximation. Then, with these coefficients we find the Padé approximation corresponding to each variable of the model (6) and finally we make the corresponding graph.

The procedure proposed in this work [8, 9]. , compared to the method of Homotope developed by Merdan, is much simpler from the algebraic point of view, since we find directly the coefficients of the series expansion of $T(t)$, $I(t)$ and $V(t)$ with very similar results.

We can see in Tab. 1 and 2 the rapid convergence of the method for the calculation of the coefficients

Supongamos

$$T(t) = \sum_{n=0}^{\infty} c_n^{(1)} t^n, \quad I(t) = \sum_{n=0}^{\infty} c_n^{(2)} t^n, \quad V(t) = \sum_{n=0}^{\infty} c_n^{(3)} t^n \quad (4.24)$$

de donde,

$$T'(t) = \sum_{n=0}^{\infty} (n+1) c_{n+1}^{(1)} t^n$$

$$V'(t) = \sum_{n=0}^{\infty} (n+1) c_{n+1}^{(3)} t^n$$

$$T(t)I(t) = \sum_{n=0}^{\infty} \left(\sum_{k=0}^{n} c_k^{(1)} c_{n-k}^{(2)}\right) t^n \quad V(t)T(t) = \sum_{n=0}^{\infty} \left(\sum_{k=0}^{n} c_k^{(1)} c_{n-k}^{(3)}\right) t^n \quad (4.25)$$

Luego, reemplazando (4.24) y (4.25) en (4.23) se tiene

$$\sum_{n=0}^{\infty} (n+1) c_{n+1}^{(1)} t^n + (\alpha - r) \sum_{n=0}^{\infty} c_n^{(1)} t^n + \frac{r}{T_{max}} \sum_{n=0}^{\infty} \left(\sum_{k=0}^{n} c_k^{(1)} c_{n-k}^{(1)}\right) t^n + \ldots + \lambda \sum_{n=0}^{\infty} \left(\sum_{k=0}^{n} c_k^{(1)} c_{n-k}^{(3)}\right) t^n = s \quad (4.26)$$

$$\sum_{n=0}^{\infty} (n+1) c_{n+1}^{(2)} t^n - \lambda \sum_{n=0}^{\infty} \left(\sum_{k=0}^{n} c_k^{(1)} c_{n-k}^{(3)}\right) t^n + \beta \sum_{n=0}^{\infty} c_n^{(2)} t^n = 0 \quad (4.27)$$

$$\sum_{n=0}^{\infty} (n+1) c_{n+1}^{(3)} t^n - \beta\eta \sum_{n=0}^{\infty} c_n^{(2)} t^n + \gamma \sum_{n=0}^{\infty} c_n^{(3)} t^n = 0 \quad (4.28)$$

Y por tanto, de (4.26):

Para $n = 0$:

$$c_1^{(1)} + (\alpha - r) c_0^{(1)} + \frac{r}{T_{max}} \left(c_0^{(1)}\right)^2 + \frac{r}{T_{max}} c_0^{(1)} c_0^{(2)} + \lambda c_0^{(1)} c_0^{(3)} = s \quad (4.29)$$

Para $n > 0$:

$$(n+1) c_{n+1}^{(1)} + (\alpha - r) c_n^{(1)} + \sum_{k=0}^{n} \left(\frac{r}{T_{max}} c_k^{(1)} c_{n-k}^{(1)} + \frac{r}{T_{max}} c_k^{(1)} c_{n-k}^{(2)} + \lambda c_k^{(1)} c_{n-k}^{(3)}\right) = 0 \quad (4.30)$$

De (4.27) y (4.28), para $n \geq 0$, se tiene:

$$(n+1) c_{n+1}^{(2)} - \lambda \sum_{k=0}^{n} c_k^{(1)} c_{n-k}^{(3)} + \beta c_n^{(2)} = 0$$

$$(n+1) c_{n+1}^{(3)} - \beta\eta c_n^{(2)} + \gamma c_n^{(3)} = 0$$

Resolviendo el sistema de ecuaciones no lineales dado por (4.29), (4.30), (4.31) y (4.3 los coeficientes $c_n^{(k)}$, $k = 1, 2, 3, n = 0, 1, \ldots$ de la aproximación en serie dada en estos coeficientes se usan para hallar el aproximante de Padé correspondiente a cad modelo (4.23) y finalmente se realiza la gráfica de las aproximaciones.

Algoritmo 13: vih.m

```
clear all; global N s alpha r Tm lambda beta eta gamma r1 r2 r3
clc; N = 5; s = 0.1; alpha = 0.02; beta = 0.3; r = 3; gamma = 2.4;
lambda = 0.0027; Tm = 1500; eta = 10; r1 = 0.1; r2 = 0; r3 = 0.1;
fun = @sistema3; y0 = zeros(1,3*N+6); y = fsolve(fun,y0);
for k=0:N+1
    ct(k+1) = y(3*k+1);
    ci(k+1) = y(3*k+2);
    cv(k+1) = y(3*k+3);
end
[Pt,Qt] = pade3(ct,3,3);
[Pi,Qi] = pade3(ci,3,3);
```

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procedure established in this work applies directly the algorithm to find the approximate of Padé order (3,3) (see Fig. 1-3) [12].

```
clear all; global N s alpha r Tm lambda beta eta gamma r1 r2 r3
clc; N = 5; s = 0.1; alpha = 0.02; beta = 0.3; r = 3; gamma = 2.4;
lambda = 0.0027; Tm = 1500; eta = 10; r1 = 0.1; r2 = 0; r3 = 0.1;
fun = @sistema3; y0 = zeros(1,3*N+6); y = fsolve(fun,y0);
for k=0:N+1
    ct(k+1) = y(3*k+1);
    ci(k+1) = y(3*k+2);
    cv(k+1) = y(3*k+3);
end
[Pt,Qt] = pade3(ct,3,3);
[Pi,Qi] = pade3(ci,3,3);
[Pv,Qv] = pade3(cv,3,3);
x=0:0.001:1;
R(1,:) = polyval(Pt,x)./polyval(Qt,x);
R(2,:) = polyval(Pi,x)./polyval(Qi,x);
R(3,:) = polyval(Pv,x)./polyval(Qv,x);
plot(x,R)
------------------------------------------------------------
function F = sistema3(c)
global N s alpha r Tm lambda beta eta gamma r1 r2 r3
    F(1) = c(4)+(alpha-r)*c(1)+r/Tm*c(1)^2+r/Tm*c(1)*c(2)+lambda*c(1)*c(3)-s;
    F(2) = c(5)-lambda*c(1)*c(3)+beta*c(2);
    F(3) = c(6)-beta*eta*c(2)+gamma*c(3);
    for n = 1:N
        F(3*n+1) = (n+1)*c(3*(n+1)+1)+(alpha-r)*c(3*n+1);
        F(3*n+2) = (n+1)*c(3*(n+1)+2)+beta*c(3*n+2);
        F(3*n+3) = (n+1)*c(3*(n+1)+3)-beta*eta*c(3*n+2)+gamma*c(3*n+3);
        for k = 0:n
            F(3*n+1) = F(3*n+1)+r/Tm*c(3*k+1)*c(3*(n-k)+1) ...
                +r/Tm*c(3*k+1)*c(3*(n-k)+2)+lambda*c(3*k+1)*c(3*(n-k)+3);
            F(3*n+2) = F(3*n+2)-lambda*c(3*k+1)*c(3*(n-k)+3);
        end
    end
    F(3*N+4) = c(1)-r1;
    F(3*N+5) = c(2)-r2;
    F(3*N+6) = c(3)-r3;
end
```

Algorithm 2. Modified algorithm for model (6).

Al igual que en el problema de Troesch, el procedimiento propuesto en este trabajo, comparado con el método de la Perturbación Homotópica desarrollado por Merdan en [20], es mucho más sencillo desde el punto de vista algebraico, puesto que se hallan directamente los coeficientes de la expansión en serie de $T(t)$, $I(t)$ y $V(t)$ con resultados muy similares, veamos:

n	Este trabajo $T(t)$	$I(t)$	$V(t)$	Merdan [20] $T(t)$	$I(t)$	$V(t)$
0	0.1000000000	0.0000000000	0.1000000000	0.1000000000	0.0000000000	0.1000000000
1	0.3979530000	0.0000270000	-0.2400000000	0.3979530000	0.0000270000	-0.2400000000
2	0.5928490530	0.0000172737	0.2880405000	0.5928490535	0.0000172737	0.2880405000
3	0.5887187712	-0.0000084052	-0.2304151263	0.5887187713	-0.0000084052	-0.2304151263
4	0.4382951587	0.0000061473	0.1382427719	0.4382951585	0.0000061473	0.1382427719
5	0.2608632947	-0.0000028359	-0.0663528422	0.2608632944	-0.0000028359	-0.0663528422
6	0.1291947328	0.0000011533	0.0265397189	0.1291947326	0.0000011533	0.0265397189

Tabla 4.3: Coeficientes $c_n^{(k)}$ de las expansiones en serie dadas en (4.24)

Table 1. Expansion coefficients $c_n^{(k)}$ given in (5) for this work.

Con los coeficientes antes determinados, Merdan en [20], aplica la transformada de Laplace, luego la aproximación de Padé a dicha expresión y finalmente la transformada inversa de Laplace para hallar soluciones aproximadas de $T(t)$, $I(t)$ y $V(t)$. El procedimiento establecido en este trabajo aplica directamente el algoritmo 1 para hallar el aproximante de Padé de orden $(3,3)$

$$T(t)=\frac{0{,}03694657t^3+0{,}08896283t^2+0{,}24903817t+0{,}1}{-0{,}22015132t^3+0{,}88724827t^2-1{,}48914834t+1{,}0} \quad (4.33)$$

$$I(t)=\frac{0{,}00000502t^3+0{,}00003579t^2+0{,}00002700t}{-0{,}05150697t^3+0{,}05835649t^2+0{,}68584349t+1} \quad (4.34)$$

$$V(t)=\frac{-0{,}01144501t^3+0{,}05756449t^2-0{,}11994476t+0{,}1}{0{,}11538176t^3+0{,}57656577t^2+1{,}20055244t+1{,}0} \quad (4.35)$$

Table 2. Expansion coefficients $c_n^{(k)}$ given in (6) using Laplace transform.

With the previously determined coefficients, Merdan in [7] applies the Laplace transform, then Padé approximation to that expression and finally the inverse Laplace transform to find approximate solutions of $T(t)$, $I(t)$ and $V(t)$ [10, 11]. The

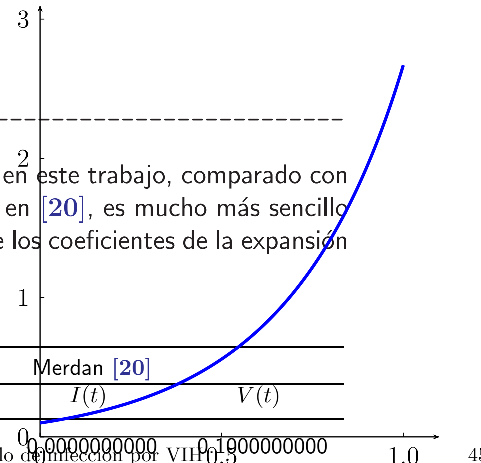

Figura 4.3: Aproximaciones de Padé para $T(t)$

Figure 1: Padé approximants for $T(t)$.

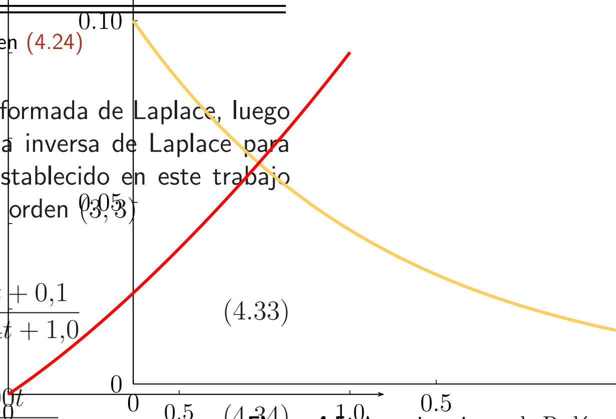

Figura 4.4: Aproximaciones de Padé para $I(t)$

Figure 2: Padé approximants for $I(t)$.

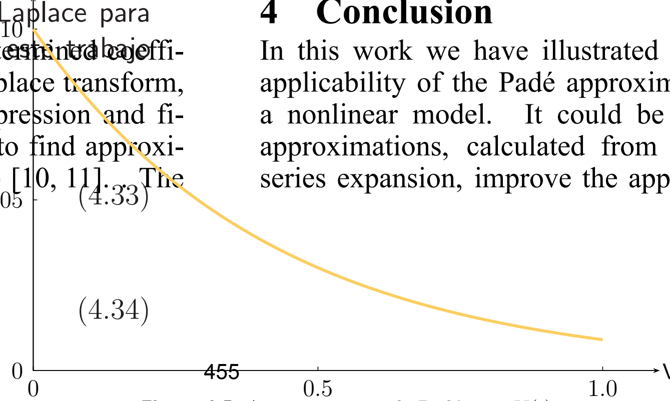

Figura 4.5: Aproximaciones de Padé para $V(t)$

4 Conclusion

In this work we have illustrated the accuracy and applicability of the Padé approximation method for a nonlinear model. It could be seen that Padé's approximations, calculated from the terms of the series expansion, improve the approximation of the

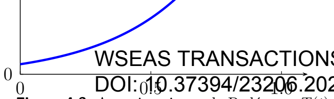

Figura 4.3: Aproximaciones de Padé para $T(t)$

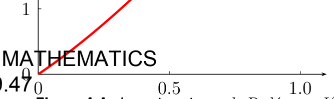

Figura 4.4: Aproximaciones de Padé para $I(t)$

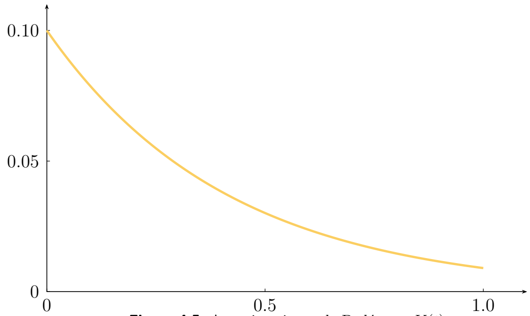

Figura 4.5: Aproximaciones de Padé para $V(t)$

Figure 3: Padé approximants for $V(t)$.

series with respect to the series calculated by other techniques.

Two algorithms were designed to calculate the coefficients of the rational expression corresponding to Padé's approximations of the order (M, N): the first one was calculated by solving a system of linear equations in which the matrix of coefficients is a Toeplitz matrix, which gave very efficient results numerically; the second algorithm developed is much more efficient than the previous one since it uses properties of continuous fractions in which Padé's approximations correspond to any order under the condition of normality of succession.

Finally, it was verified that the results obtained with the algorithms of this work, gave the same results that those obtained with other methods. Therefore, from the algebraic point of view, the procedure is much simpler and efficient, since the expansion coefficients of the series of $T(t)$, $I(t)$ and $V(t)$ were found in a direct way for the initial model.

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