# A Modified Fixed Point Method for Biochemical Transport

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ABSTRACT: This work is devoted to a modified fixed point method applied to the bio-chemical transport equation. To have a good accuracy for the solution we treat, we apply an implicit scheme to this equation and use a modified fixed point technique to linearize the problem of transport equation with a generalized nonlinear reaction and diffusion equation. Next, we apply this methods in particular to the the dynamical system of a bio-chemical process.
Eventually, we accelerate these algorithms by the optimized domain decomposition methods.
Several test-cases of analytical problems illustrate this approach and show the efficiency of the proposed new method.

Key Words: Bio-chemical transport, Modified fixed point method, Optimal control.

## Contents

## 1. Introduction

Our general equation of bio-chemical transport equation, could be written as:

$$\begin{cases} \frac{\partial u}{\partial t} + -div\left(D(u)\nabla u\right) + \nabla vu + F(u) & = & f(x,y) \text{ on } \Omega \\ u & = & h \text{ on } \partial\Omega \\ u & = & h_o \text{ on } t = 0 \end{cases} \tag{1.1}$$

Where $u = (u_i)$ the concentration (dispersal) of reactant, F is the reaction model and D is the diffusion flux. The lists of bio-chemical model is too wide to cite in this paper, but our boundary equation (1.1), generalizes a lot of bi-chemicals models (with second order derivative). As concerned biochemical models, we cite the Fisher equation (for tumors model [5], [15]), Murray Model [6], Keller and Segel( for Chemotaxis process [7]) and FitzHugh-Nagumo (for the simulation of electric propagation in nerves [8]),...
The use of Hopf biffurcation or continuation methods are insufficient for modeling in general these type biochemical dynamic and solving these models cost heavy time. Then, the use of accurate numerical methods is necessary to solve the dynamics. Notice, the use of the Newton type methods is ineffective for solving nonlinear equation of dynamics because the dimension of variables in these equations is large (more than 3 variables). Also, the use of explicit scheme to solve these equations is not accurate, stable and efficient in general . So In order to make ours bio-chemicals simulations fast, stable and efficient, we apply in this paper, the modified fixed point (we propose in [1], [2],[4]) to solve problem (1.1) type. Modifying the treated equations someway to make the global energy of the system contracting at each step of time, we guarantee that our method converge quickly to the stationary solution and the time step size is realistic compared to an explicit method (because of the CFL condition impose a very small time step size for explicit scheme). Also, modifying the equations of dynamics give stable solutions: The use

of finite element or finite volume discretization is sensitive to the anisotropic and convective equations: modifying equations by q relaxation procedure solves this issue and we show the weak formulation of problem (1.1), has one and unique solution.

In the first part of this paper, we will present the modified fixed point method applied to our equation (1.1). In the second part we apply this method to the particular case of a dynamical reaction equation without a diffusion or convection term. We are interested in this section, because the equations type we treat, model a lot of bio-chemical process (the Michaleis-Menton for Enzyme kinetics [9], [16], Hill Kinetics [10], Goldbeter-Koshland for switch phenomena [11], Tyson Model for cell cycles [12], Burgos Fang Model [13] ...). The equations we treat in this paper in general are unstable and hard to solve by classical methods, so we apply the modified fixed point to make the solutions robust and stables.

Finally, we give some numerical results and implementation that prove the efficiency of the method.

## 2. Nonlinear reaction diffusion equation

By a full implicit scheme, equation (1.1) becomes

$$\begin{cases} cu - div\, D(u)\nabla u + vu &= f(x,y) \text{ on } \Omega \\ u &= h \text{ on } \partial\Omega \end{cases} \tag{2.1}$$

The fixed point method is constructed successively as:

$$\begin{cases} cu_{n+1} - div\, D(u_n)\nabla u_{n+1} + \nabla vu_{n+1} + F(u_{n+1}) &= f(x,y) \text{ on } \Omega \\ u_{n+1} &= o \text{ on } \partial\Omega \end{cases} \tag{2.2}$$

Where $u_0$ is an initial function value.

Let

$$V = \{u \in H(\Omega)/\ D(u) \in L^1(\Omega)\ and\ \|u\|_H < M\}$$

H is the specific Sobolev space adopted for problem (1) (we take $H(\Omega) = H_0^1(\Omega)$ for a dirichlet condition on the boundary and $H(\Omega) = H^1(\Omega)$ for a Neuman condition) and $\|u\|_H$ is the norm on the Sobolev space H ($\|u\|_H = \|\nabla u\|$ in the case of dirichlet condition and $\|u\|_H = \|u\| + \|\nabla u\|$ in the case of neumann condition). M is a positive constant that we choose to make the solution of the variational formula of equation (2.1) to be bounded (for physical reason). The energy of equation (2.1) is:

$$E(u) = \int_\Omega cu\, u + \int_\Omega u\, \nabla vu + \frac{1}{2}\int_\Omega D(u)\nabla u\, \nabla u - \int_\Omega fu$$

Equation (2.1) is equivalent to the global minimization of the Energy E on the space H with some constraints. We can prove that E is a K contraction on V for a small number M (see [1], [2] for prove and explanation in the case of nonlinear diffusion). This method is local and could diverge for an initial sequence departure is $u_0 = h_0$. the same thing could be said if we apply a Newton type method. As a solution to this problem we make some modifications to the equation to have successive sequences that are not distant from the initial value $u_0 = h_0$. As in [2] where, we proposed a modified fixed point to a just a semi linear equation, and in [1] where, we applied a modified fixed point to a nonlinear equation, we generalize this method to our equation by mean of solving the following iterative equations:

$$\begin{cases} cu_{n+1} - div((D(u_n) + r(u_n)), \nabla u_n)\nabla u_{n+1}) + (u_{n+1}) &= f(x,y) - div(r(u_n), \nabla u_n)\nabla u_n) + K(u_n) \text{ on } \Omega \\ u_{n+1} &= o \text{ on } \partial\Omega \end{cases}$$

$$(2.3)$$

the function r and K are selected such a way that the valuational energy of this equation is a K contraction where, K is very small for reasonable choice of bound M (Generally M Must be less than $\|u_0\|_H$). This small K make the convergence of the method fast and reduce the number of successive iterations in time compared to Newton or Fixed method ones. Also, the convergence to the solution is stable because the energy is a contraction (there is one and only one solution for the problem and the error is controlled).

## 3. Dynamical reaction model

In this section, we treat a particular case of equation (1.1): We eliminate the convective and diffusive term and take into account a non linear reaction: Without the transport term in equation, we obtain a dynamical equation:

$$\frac{dy}{dt} = F(y), \quad y(0) = u_0 \tag{3.1}$$

F is non linear function that could have many roots, which make the equation unstable and accurate using classical model from initial value $u_0$.
An implicit scheme of this equation could be writing as:

$$y_{n+1} = F(y_{n+1}) + K y_n \ \ y_0 = u_0 \tag{3.2}$$

We do the same job of section 2 and apply a modified fixed point method to the problem (instead of a continuation method that make a lot of time to process):

$$y_{n+1} = F(y_n) + c_n y_{n+1} + (K - c_n) y_n \tag{3.3}$$

$c_n$ is choose such a way that the energy of y, should be a contraction.
We can take for example::

$$c_n = \nabla F(y_n) + \frac{1}{2} y_n . Hess F(y_n)$$

Hess is the matrix hessian for the function F.

## 4. Numerical simulation

We treat first the simulation of equation 1.1 where $\Omega$ is a squared domain, we take different values for the diffusion D and the convection v, the functions f, h and $h_0$ are given by taking an exact solution $u_{exact}$ to the problem 1.1 on the square $\Omega$. We implemented the modified fixed point method to several academic solution $u_{exact}$. We take in this paper in the case of function of two variable:

$$u_{exact}(x, y, t) = ((2x - y)e^{-t(x^2 + y^2 +} + x sin(\pi y), (2x + y)e^{-t(x^2 + y^2)} + y cos(\pi x) + 1)$$

The next figures show the error between the approximate solution by a finite element method and the analytical solution of equations 2.3: $u_{exact}(., t)$ in the given step t for different value D, F, v=(a,b), $\Delta t$, the step t and the mesh h of the finite element.
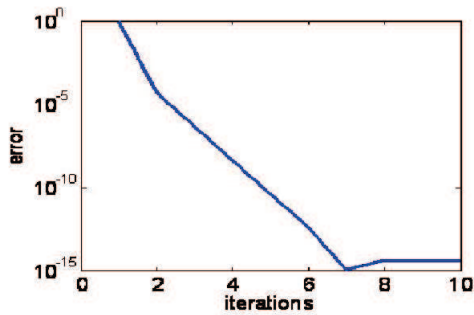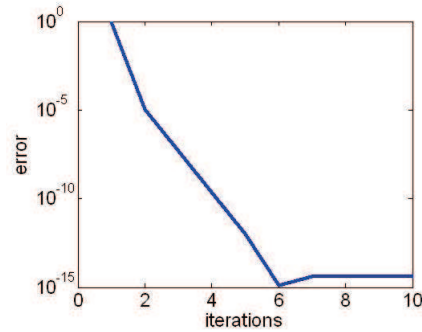


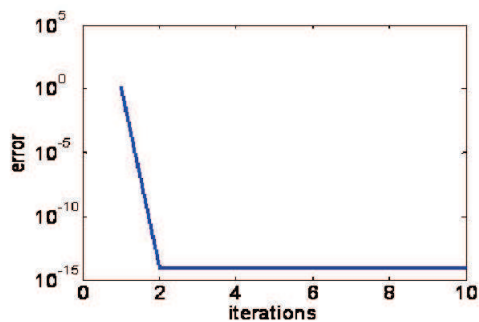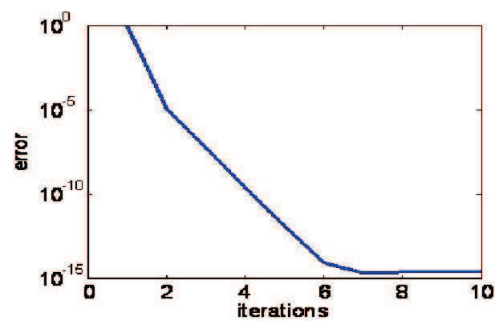Figure 1: case1.



Figure 2: case2.

Figure 3: case3



Figure 4: case4

Figures 1,2,3,4 showing the spatial error at a given time $t$ in ms between the approximate solution by the fixed point method and the given exact solution of the problem (1.1) in terms of the given iterations.

case1: $\Delta t$=0.1, t=0.1,D=I,a=b=0   h=0,025.$F(u,v) = (u*v - v, u)^t$.
case2: $\Delta t$=0.1, t=0.5, D=0,1I,a=-2,b=1 and h=0,001.$F(u) = a/(b + \|u\|)(1,1)^t$
case3: $\Delta t$=0.1,t=10,$D = [1, 1 - e^{-(x+y)}; -1, 2]$,a=-1,b=0 and h=0,001.$F(u) = (u, u^3 - vu)^t$,
case4: $\Delta t$=0.5,t=1, $D$=0.5I, a=2, b=-1,5 and h=0,001.$F(u) = (\frac{u}{1+u^2}, \frac{v}{1+u^2})^t$.
h is the mesh grid and I is the matrix identity.

These figures shows that the modified fixed point method converge quickly to the solution and give a good accuracy. To reduce time computation due to the implicit scheme, we have combined this method an optimized wave domain decomposition method to accelerate the algorithm.
For the dynamical system (Equation (3.2))we give the simulation of a reaction with four reactant the bio-chemical equation (Equation (3.1)).

$$X_1 + E \rightleftharpoons X_2 + \frac{1}{2}X_3 \rightleftharpoons X_4 + F$$
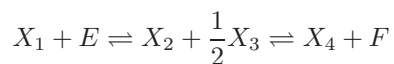
We take for F a polynomial function as for the Michaleis-Menton model for enzymes ([16]). We take for the initial value $[X_1] = 1$ and $[X_i] = 0$ for i=2,3,4. the next figure show the result of concentration species by solving the equation using the proposed modified fixed method in section 3.
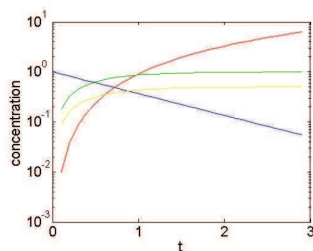


Figure 5: Evolution of the concentrations per time

These results are close to a simulation with a benchmark of biochemical simulation (PyMol).

## 5. Conclusion

We have applied a modified fixed point method to resolve the general nonlinear transport equation, then we applied the method to a dynamical system. We assume that we can prove by theory the fast convergence of the method applied to this equation.

Several test-cases show the efficiency of the modified Fixed point method.
As a perspective of this article about modified fixed point method we can treat:

- Applying the method to the Groundwater equations

- Applying the Fick and Darcy equations

- Comparing results with realistic experiments.

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