Numerical Solution of an Inverse Problem in a Cell Division Equation

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Abstract

The comprehension of the cellular division is fundamental in the study of many phenomenon like the growth of a tumor or of the cancer. Many models have been proposed to describe the evolution of cell density: Model of Bell and Anderson in 1967 [1], model of Sino and Streifer in 1967 and 1971. Many natural phenomenon have long been represented by ordinary differential equations, but it is more realistic for cell division to consider the time and size dependent equation. We obtain a system of hyperbolic partial differential equation not easy to solve analytically. For the cell evolution, the problem in laboratories is generally to find the cell division rate, from an experimental measure of cell density. The problem under consideration is ill-posed in Hadamard’s sense and we aim to determine the solution numerically. Of course, it is convenient to solve the direct problem before tracking the inverse one.

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1 Introduction

Most problems we encounter are direct problems in the sense that these problems are well-posed in Hadamard’s sense. But many important problems to be solved are ill-posed in Hadamard’s sense, like the problem of determining the cell division rate from an experimental data of cell density. Many author have explored the resolution of this problem: Benoit Perthame, George Zubelli,
Marie Douminic [2], [4], [5], [6]. Here we will deeply explain and give an amelioration to the numerical determination of the solution. We clearly pose the problem under consideration: In laboratories, it is generally just an experimental measure of cell density is available (experimental measure of a stable distribution of cell density). From the experimental data, we show that it is possible to reconstruct the cell division rate. Let us notice how benefit it is to know the cell division rate: in fact, it is possible to influence the cell division rate to control human heath. So, our paper is organized as followed: We firstly present the model and make some assumption for simplicity. Then we formulate an eigenvalue problem to be solved. Afterward, we use a fixed point theory to prove the existence of a stable distribution, an then we solve the direct problem numerically and finally we attack the inverse problem. Numerical simulations are provided to illustrate our results.

2 The model

Models for cell division equations are generally structured by one variable which is generally the cell size. It could have been cell age. The original model had been presented by Bell and Anderson in 1967 [1]. The following model presented in [2] represents the evolution of cell density:

\[
\begin{aligned}
&\frac{\partial n(t, x)}{\partial t} + \frac{\partial}{\partial x} \left[ g(x)n(t, x) \right] + b(x)n(t, x) + \mu(x)n(t, x) = \int_0^1 \frac{1}{\sigma^2} \beta\left(\frac{x}{\sigma}, \sigma\right) dx \\
n(t, 0) &= 0
\end{aligned}
\]  

(1)

where

- \( n(t, x) \) represents the cell of size \( x \) at time \( t \).
- \( \beta(x, \sigma) \) represents the division rate of the mother cells of size \( x \) into daughter cells of size \( \sigma x \) and \( (1 - \sigma)x \) after mitosis. We have \( \beta(y, \sigma) = \beta(y, 1 - \sigma) \ \forall \sigma \)
- \( g(x) \) denotes the individual growth rate of cells of size \( x \).
- \( \mu(x) \) denotes the death rate, or the chance (per time unit) that cells of size \( x \) dies

We choose simplicity and make the following assumptions:

- All cells of a micro-parasite class growth according to a deterministic rule.
- All cells after having reached a certain size (mother cell) divide into two part, just in two, giving birth to two identical daughter cells: it is called equal mitosis.
- Cell age does not influence the growth law and the preferred size of the division.
• There is a negligible number of death during a normal growth.

• We assume $g = 1$. In fact, $g(x)$ denotes the individual growth rate of cells of size $x$ and we have

$$\frac{dx}{dt} = g(x)$$

(assuming that there is not fission) and for $g$ equal to a constant $a$, one finds

$$x(t) = x_0 + at$$

where $x_0$ is the initial size of cells and we obtain the linear model. We then choose $a = 1$ just for simplicity. In fact, other cases are studied likewise.

Taking into account the above hypothesis, equation (1) becomes:

$$\begin{aligned}
\frac{\partial n}{\partial x}(t, x) + \frac{\partial n}{\partial t}(t, x) + b(x)n(t, x) &= 4b(2x)n(t, 2x) \quad x > 0, \ t \geq 0 \\
n(t, 0) &= 0
\end{aligned}$$

(2) which is the partial differential equation of hyperbolic kind we are going to study.

Solutions to the above equation could be determined using characteristic methods, but quantities available for measure in a laboratory is a stable distribution $N$ of cell density and the problem is to determine the cell division rate numerically. The problem under consideration is ill-posed in Hadamard’s sense, so a regularization method is needed transform the initial problem into a well-posed problem. It is necessary to formulate the problem to be solved clearly.

3 Existence of the stable distribution

Proposition 3.1 If we look for solutions of equation (2) in the form $\Psi(t)N(t)$ (we separate variables), then:

• $N$ must satisfy an eigenvalue problem :

$$\begin{aligned}
-\frac{dN}{dx}(x) - b(x)N(x) + 4b(2x)N(2x) &= \lambda N(x) \\
\text{with } \lambda &= \frac{\Psi'}{\Psi} \text{ constant, independent of } x \text{ and } t
\end{aligned}$$

• $\Psi(t) = e^{\lambda t}$

• The adjoint equation of the eigenvalue problem is given by:

$$\begin{aligned}
\frac{d\Phi}{dx}(x) - b(x)\Phi(x) + 2b(x)\Phi\left(\frac{x}{2}\right) &= \lambda\Phi(x), \ x \geq 0 \\
\Phi(x) &> 0, \ \forall x > 0
\end{aligned}$$

(3)
Proof 3.1 Let’s set \( t, x \in \mathbb{R}^+ \) \( n(t, x) = \Psi(t)N(x) \). then,
\[
\frac{\partial n}{\partial x}(t, x) + \frac{\partial n}{\partial t}(t, x) + b(x)n(t, x) = 4b(2x)n(t, 2x)
\]

imply that:
\[
\Psi'(t)N(x) + \Psi(t)\frac{dN}{dx}(x) + b(x)\Psi(t)N(x) = 4\Psi(t)b(2x)N(2x) \tag{4}
\]

dividing both members by \( \Psi(t) \) we obtain
\[
\frac{\Psi'(t)}{\Psi(t)}N(x) + \frac{dN}{dx}(x) + b(x)N(x) = 4b(2x)N(2x)
\]

which gives
\[
\frac{\Psi'(t)}{\Psi(t)} = \frac{-\frac{dN}{dx}(x) - b(x)N(x) + 4b(2x)N(2x)}{N(x)} = \lambda, \quad \lambda \in \mathbb{R}
\]

\( \lambda \) is an independent constant of \( t \) and of \( x \)

\( \Psi \) is then given by
\[
\Psi(t) = ce^{\lambda t}, \quad c \in \mathbb{R}
\]

Replacing \( \Psi \) by this value in equation (4), \( N \) must satisfy the following eigenvalue equation:
\[
-\frac{dN}{dx}(x) - b(x)N(x) + 4b(2x)N(2x) = \lambda N(x)
\]

Considering the operator \( H \):
\[
H : L^2(\mathbb{R}^+, dx) \rightarrow L^2(\mathbb{R}^+, dx)
\]
\[
N \mapsto HN,
\]

where for \( x > 0 \),
\[
HN(x) = -\frac{dN}{dx}(x) - b(x)N(x) + 4b(2x)N(2x).
\]

Then, the adjoint operator \( A^* \) is defined on the same spaces. And for \( x > 0 \) by
\[
H^*\Phi(x) = \frac{d\Phi}{dx}(x) - b(x)\Phi(x) + 2b(x)\Phi\left(\frac{x}{2}\right).
\]

The parameter \( \lambda \) which is the dominant eigenvalue is generally called Malthus parameter ([6])

If we add the condition of normalization to the eigenvalue equation, we obtain the following equation:
\[
\begin{cases}
-\frac{dN}{dx}(x) - b(x)N(x) + 4b(2x)N(2x) = \lambda N(x), & x \geq 0 \\
N(x) > 0, \forall x > 0 , \\
N(0) = 0 \\
\int_{0}^{+\infty} N(x)dx = 1
\end{cases}
\]
3.1 Analysis of fixed points

A fixed point of system (2) is given by:

\[ n^*(x) = 4 \int_0^{2x} b(u)n^*(u)e^{-\int_x^u b(\sigma)d\sigma} du \]  

(6)

We define the following operator:

\[ (\Phi)(\Psi)(x) = 4 \int_0^A 1_{[0,2A]}(u)b(u)\Psi(u)e^{-\int_x^u b(\sigma)d\sigma} du \]

\[ = \int_0^A \Psi(u)\lambda(x,u)du \]

\[ \Psi \in E = L^1([0,A]) \]

We study the fixed points of \( \Phi \) using the theory of positive operators defined on a cone in a Banach space.

\[ \lambda(x,u) = 41_{[0,2A]}(u)b(u)e^{-\int_x^u b(\sigma)d\sigma} \]

where \( A \) is the maximal size. Each fixed point of \( \Phi \) in the positive cone is a cell density that satisfies (6)

**Proposition 3.2** Let \( E = L^1([0,A]) \) with the positive cone \( E_+ = \{ \Psi \in E : \Psi \geq 0, a.e. \} \), and let de

There exists a unique non-zero positive fixed point of the operator \( \Phi \)

**Proof 3.2** For the proof of this proposition, we will prove that the operator \( \Phi \) is compact, Non-supporting,

**Lemma 3.1** the following assumptions are held:

1. \( \lambda \in L^\infty_+((0,A] \times [0,A]) \)

2. \( \lim_{h \to 0} \int_0^A |\lambda(x + h,\xi) - \lambda(x,\xi)|dx = 0 \), where \( \lambda \) is extended by \( \lambda(x,\xi) = 0 \) for \( x, \xi \in \] - \infty, A[\bigcup]A, +\infty[ \]

3. There exist numbers \( \alpha \) with \( A > \alpha > 0 \) and \( \epsilon > 0 \) such that \( \lambda(x,\xi) \geq \epsilon \) for almost all \( (x,\xi) \in ]0,A[\bigtimes]A - \alpha, A[ \)

**Proof 3.3** the proof of the above lemma comes from the definition of \( \lambda \)

**Lemma 3.2** Under the assumptions of the above lemma, the operator \( \Phi : E \longrightarrow E \) is non-supporting and compact.
Proof 3.4 Let us define the positive linear functional $f_0 \in E_+^*$ by

$$\langle f_0, \Psi \rangle = \int_0^A s(u)b_m \exp\left(-\int_x^y b(\sigma)d\sigma\right)\Psi(u)du, \Psi \in E$$

where

there exist $b_m > 0$ and $b_M < +\infty$ such that $b_m < b(x) < b_M$ for all $x > 0$.

the function $s(\xi)$ is defined as $s(\xi) = 0$, $\xi \in [0, A - \alpha]$; $s(\xi) = \epsilon$, $\epsilon \in ]A - \alpha, A]$. Hence, $\lambda(x, \xi) \geq s(\xi)$ for almost all $(x, \xi) \in [0, A] \times [0, A]$. It is easy to see that the functional $f_0$ is strictly positive and

$$\Phi^{n+1}\Psi \geq (f_0, \Psi)\epsilon, \epsilon = 1 \in E_+, \Psi \in E_+$$

Then for any integer $n$ we have

$$\Phi^n\Psi \geq (f_0, \Psi)\epsilon, \epsilon = 1 \in E_+, \Psi \in E_+$$

Therefore we obtain $(F, \Phi^n\Psi) > 0$, $n \geq 0$ for every pair $\Psi \in E_+/\{0\}$, $F \in E_+^*/\{0\}$, that is, $\Phi$ is nonsupporting. Next, it is easy to see that the operator $\Phi$ is compact.

In [3] the following lemma was proved:

Lemma 3.3 Let $r(\Phi)$ be the spectral radius of the operator $\Phi$. Then the following holds:

1. If $r(\Phi) \leq 1$, the only nonnegative solution of the equation $\Phi\Psi = \Psi$ is the trivial solution $\Psi = 0$

2. If $r(\Phi) > 1$, the equation $\Phi\Psi = \Psi$ has at least one non-zero positive solution.

Remark 3.1 For uniqueness, it has also been proved that if $\lambda(x, y)$ can be factorized and majorized by $u(x)v(y)$ (which is called the proportionate mixing assumption), it is easily seen that there always exists a unique non trivial steady state under the condition

$$r(T) = \int_0^A \lambda_T(\sigma, \sigma)d\sigma > 1$$

with

$$T(\Psi)(x) = \int_0^A \Psi(u)\lambda_T(x, u)du$$

$\Psi \in E = L^1([0, A])$ with $\lambda_T(x, y) = u(x)v(y)$

In this case, $u(x)$ is the eigenvector of the operator $T$ corresponding to the spectral radius $r(T)$. In our case, it is easy to see that $\lambda(x, y) \leq \lambda_T(x, y)$ and $\lambda_T(x, y)$ satisfy the proportionate mixing assumption.
4 Numerical solution of the cell division equation

To solve the problem numerically, we have to ensure that the problem is well posed in Hadamard's sense. Else, the numerical solution would have nothing in common with the real data. The following theorems had been proved in [5]

**Theorem 4.1 (Existence and uniqueness of solution)**

Let us admit the following hypothesis:

- $b \in C(\mathbb{R}^+) $
- $b_m > 0 \text{ et } b_M < +\infty$ such that $b_m < b(x) < b_M \forall \ x > 0.$

Then there exists a unique $(\lambda, N, \Phi)$ to the equations (5) and (3) with $\Phi, N \in C^1(\mathbb{R}^+)$ such that $N$ positive

$$\begin{cases} 
    b_m \leq \lambda \leq b_M \\
    \frac{c}{(1 + x)^k} \leq \Phi(x) \leq C(1 + x^k)
\end{cases}$$

where $c, C \text{ and } k$ are 3 positive constant such that

$$2^k b_m > b_M$$

$N$ and its derivative vanish at 0 and $+\infty$

**Theorem 4.2** Let us consider the above hypothesis:

- $b \in C(\mathbb{R}^+) $
- $b_m > 0 \text{ et } b_M < +\infty$ tel que $b_m < b(x) < b_M \forall \ x > 0,$

The application

$$\Gamma : b \rightarrow (\lambda, N)$$

is

1. continue en $b$ de $L^\infty(\mathbb{R}^+)$ in $[b_m, b_M] \times L^1 \cap L^\infty(\mathbb{R}^+)$ under the weak topology of $L^\infty(\mathbb{R}^+)$
2. Locally lipscht-continuous in $b$ under the strong topology of $L^2(\mathbb{R}^+)$ in $[b_m, b_M] \times L^2(\mathbb{R}^+)$
3. of class $C^1$ from $L^2(\mathbb{R}^+)$ to $[b_m, b_M] \times L^2(\mathbb{R}^+)$

We are now going to solve the general problem (Equation (1)) numerically. Then we will solve the eigenvalue problem and then compare the numerical result and confirm the long term convergence of the cell density to a stable distribution.
4.1 General equation

We solve our equation on the rectangle \([0; T] \times [0; L]\).

The closed intervalle \([0; L]\) is discretised in \(m + 1\) nodules \(x_i\) for \(i = 0, ..., m\) with a regular amplitude. Let us denote \(\Delta x\) the time amplitude. The same is done with the time intervalle and we denote \(\Delta t\) the time amplitude (\([0, T]\) is divided into \(n\) points). Let’s \(n_i^k\) The cell density at \(x_i = i\Delta x\) at time \(t_k = k\Delta t\). We use the following scheme

\[
(1 + \beta + \Delta t b_i)n_i^{k+1} - \beta n_i^{k+1} - 4\Delta t b_2 n_{2i}^{k+1} = n_i^k \quad 1 \leq i \leq m
\]  

(11)

with \(\beta = \frac{\Delta t}{\Delta x}\)

which is consistent, stable without condition. We then obtain a linear system to be solved. We just want to stress on the method we used to store the matrix of the linear system in order to optimize the memory space: the storage method of Moorse whose principle is: This data structure has three tables with the following functions:

1. A table containing the non-zero element values of the matrix, given line by line. We denote this table AA. Its dimension (length) is \(n_z\), representing the number of non-zero elements of the matrix \(B\) of the linear system

2. A table of integer containing the index of colon corresponding to the elements of table by AA. We denote this table by \(J\)

3. A table of integer containing a pointer on the position where each line begins in the table AA and \(J\). Its i-th element, \(I(i)\) will thus contain for \(i = 1, ..., m\), the position where begins the i-th line in tables AA and \(J\). Its dimension will be \(m + 1\) with a convention that \(I(m + 1) = n_z + 1\). Ie the address of the beginning of a fictive \((n + 1) - th\) line in tables AA and \(J\).

4.2 Numerical solution of the eigenvalue problem

The problem under consideration is the eigenvalue problem that we solve on the interval \([0, L]\):

\[ AX = \lambda X \]

After discretization we obtain \(A_n Y_h = \lambda_n Y_h\).

The direct problem being well posed, let us solve it by a stable numerical method.

We solve the problem on the finite interval \([0, L]\)

let us consider equation (5) on \([0, L]\) and assume that the cell density is known and verify the following conditions:

- \(b \in C(\mathbb{R}^+)\)

- \(\exists \ b_m > 0 \ et \ b_M < +\infty \ tel \ que \ b_m < b(x) < b_M \ \ \forall \ x > 0\).
Let \( ([x_i, x_{i+1}])_{0 \leq i \leq m} \) a subdivision of the interval \([0, L]\) in \(m\) interval of same amplitude 
\[ h = \frac{L}{m}, \quad x_{i+1} = x_i + h, \quad i = 0 \ldots m. \]
we obtain the following discreet equation:
\[
\begin{align*}
N_i - N_{i-1} \frac{1}{h} + (\lambda + b_i)N_i + 4b_{2i}N_{2i,1} \leq \frac{L}{h} = \lambda_i N_i, \quad 1 \leq i \leq \frac{L}{h}
\end{align*}
\] (12)

with \( N_i = N(x_i) \)
This equation leads us to the following equation:
\[
A_h Y_h = \lambda_h Y_h
\] (13)

with \( A_h = (a_{i,j}), i, j \in \{1 \ldots m\} \) defined as followed:
\[
\begin{align*}
.a_{i,i} &= -\frac{1}{h} - b_i, \quad i = 1 \ldots m; \\
a_{i,i-1} &= \frac{1}{h}, \quad i = 2 \ldots m; \\
a_{i,2i} &= 4b_{2i}, \quad i = 1 \ldots \left\lfloor \frac{m}{2} \right\rfloor; \\
a_{i,j} &= 0, \quad \text{si } j \neq i, 2i, i - 1.
\end{align*}
\]

Then we use a MATLAB function to determine the dominant eigenvalue that the eigenvector
is the stable distribution.

4.3 Long term behavior of the evolution equation
We will draw figures that compare the solution of the evolution equation and the numerical
solution to the eigenvalue problem

4.3.1 Observation and Interpretation of numerical results
Figure (4.3),(4.3), (4.3),(4.3) represent the approximated solution to the direct problem: de-
termination of the cell density for the non-perturbed division rate \( b = 1 \). This passes through
the resolution of an eigenvalue equation that we have represented the solution. Observing the
curve representing the surface of density, we notice that after a certain time \( T \) high enough,
the surface takes a stable form that we have also represented: It is the said stable distribution.
We also notice that \( n(T, \cdot) \) has the same form with \( N \), solution to the eigenvalue equation. The
representation of both quantities in the same frame permits to verify that \( n(T, \cdot) \) is a multiple
of \( N \). This illustrate the said convergence of cell density to a stable distribution. This is an
important result: In fact, in laboratories the quantity available for measure is the stable dis-
btribution. Or, mathematically we can solve the eigenvalue equation and effectively deduce the
stable distribution.

Figure (4.3),(4.3),(4.3),(4.3) represent the approximated solution of the said direct problem
for a random perturbation of the cell division rate. The curve obtained are practically identic to
those without perturbation: A small perturbation of data has not greatly changed the solution.
[Long term behavior of the cell density for $b=1$]
Numerical solution of an inverse problem

Solution of the eigenvalue problem for $b=1$

Comparison of solutions for $b=1$

Figure 1: *Approximated cell density for the non perturbed division rate*
[surface of cell density for $b=1+0.001*\max(\text{rand}(1,5))/\text{norm}(\text{rand}(1,5))$]

[Long term behavior of the cell density for $b=1+0.001*\max(\text{rand}(1,5))/\text{norm}(\text{rand}(1,5))$]
Figure 2: Approximated cell density for a random perturbation of division rate
[surface of cell density for $b=1+\exp(-8(x-2)^2)$]

[Long term behavior of the cell density for $b=1+\exp(-8(x-2)^2)$]
Numerical solution of an inverse problem

Figure 3: Approximated cell density for a variable perturbation of the division rate
Figure (4.3), (4.3), (4.3), (4.3) represents also the above quantities, with a variable perturbation of cell division rate. The conclusion is the same. This illustrates the well-posedness of the direct problem: the problem of determining the cell density from an experimental measure of cell division rate.

5 Numerical solution of the inverse problem

The inverse problem we have said consists of determining the division rate $b$ from a noisy measure of the stable distribution $(\lambda, N)$. We have to inverse the application

$$\Gamma : b \rightarrow (\lambda, N)$$

in suitable spaces, where $b$, $N$, $\lambda$ are linked by the following eigenvalue equation:

$$\begin{aligned}
&-\frac{dN(x)}{dx}(x) - b(x)N(x) + 4b(2x)N(2x) = \lambda N(x), \quad x \geq 0 \\
&N(x) > 0, \quad \forall x > 0 , \\
&N(0) = 0 \\
&\int_{0}^{+\infty} N(x)dx = 1
\end{aligned}$$

(15)

It was shown in [4] that

$$\Gamma^{-1} : [b_m, b_M] \times L^1 \cap L^\infty(\mathbb{R}^+) \rightarrow \mathbb{L}^\infty(\mathbb{R}^+),$$

(16)

is not continuous. Thus, the problem under consideration is ill-posed in Hadamard’s sense. So regularization is needed. It was also proved [5] that

$$\begin{aligned}
&\alpha \frac{d}{dy} \left( b_\alpha N \right)(y) + 4 b_\alpha(y) N(y) = b_\alpha \left( \frac{y}{2} \right) N \left( \frac{y}{2} \right) + \lambda N \left( \frac{y}{2} \right) + 2 \frac{dN}{dy} \left( \frac{y}{2} \right), \quad y > 0
\end{aligned}$$

(16)

(where $0 < \alpha < 1$ is the regularization parameter)

is a well-posed equation in Hadamard’s sense. And the solution $b_\alpha$ of the above equation is closed to the solution $b$ of equation (5). We are going to concentrate on numerical simulations.

Before simulations, we notice that instead of observing the stable distribution $(\lambda, N)$, it is a noisy $N_\epsilon$ that is observed, and we deduce from the combination of equation (16) and (5) that

$$\lambda_{\lambda, \epsilon} = \frac{\int_{0}^{+\infty} N_\epsilon dx}{\int_{0}^{+\infty} x N_\epsilon dx + \frac{\alpha}{4} \int_{0}^{+\infty} N_\epsilon dx}$$

(17)
Before presenting numerical results, we note that we firstly represent the product $bN$ before deducing $b$. We notice that data we use to solve the inverse problem are the results obtained from the direct problem and we tries to reconstruct the initial data: with known division rate, we found a stable distribution numerically, we then use the stable distribution obtained numerically to reconstruct the initial division rate. We notice that there are two major source of error: The error from the experimental measure of the stable distribution and the error due to regularization.

5.0.2 Observations and interpretation

Figure (5) and (5) reconstruct the cell division rate $b$ used to solve the direct problem. Taking the regularization parameter near to 0, we notice that the product $bN$ is practically equal to $N$. Thus, $b$ is almost 1 and the reconstruction is very good (Almost perfect). It is in this manner that in laboratories, a single observation of the stable distribution of cell density enables to reconstruct the cell division rate satisfactorily.

We have the same conclusions with figure (5) and (5) since the rate to reconstruct is near 1.

6 Conclusion

It has been question to solve a ill-posed problem in Hadamard’s sense numerically: determination of cell division from a noisy data of a stable distribution of cell density. It has been necessary to consider the direct problem before numerical solution to the inverse problem to prove that the reconstruction of cell division rate could be obtained from an experimental data of cell density. Numerical solutions obtained are quite satisfactory, noting both source of error.
[Reconstruction of the division rate for $b=1$, $\alpha = 0.001$]

[Product $bN$ for $b=1+0.001\times\max(\text{rand}(1,5))/\text{norm(\text{rand}(1,5))}$]
Numerical solution of an inverse problem

[Reconstruction of the division rate for b=1+0.001*max(rand(1,5))/norm(rand(1,5)),

\[ \alpha = 0.0001 \]

Figure 4: Reconstruction of the cell division rate

7 Discussion

The model studied in this paper is a simplified model with the hypothesis we made. Also, the regularization used here (In the same sense as Tikhonov method is quite good, but could be ameliorated. We propose ourselves in the near future to study the general model of cell density and propose a new regularization method for the inverse problem). We have not stressed on the regularization parameter, but the regularization plays a urge role on the numerical solution. In our next work in the near future we shall attack that problem.

References


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