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PARAMETER EVALUATION FOR BIOCONCENTRATION MODEL, USING CELLULAR EXCLUSION METHOD

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Abstract We consider a class of biological phenomena described by ordinary differential equations (ODEs) for which certain physical parameters are unknown and very difficult (if not impossible) to be measured. Focusing on the problem of determining "the best fitting parameters" for given observable data, we report on a method for finding the set of parameters that minimizes a cost function associated to the problem. This technique uses the "*Cellular Exclusion Algorithm*" [3] as a fast locating tool of its critical points. We also emphasize how a carefully chosen dominant function can improve the efficiency and reduce the cost of such method.

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1. A BIOCONCENTRATION MODEL

1.1. INTRODUCTION

We consider an environment contaminated by a certain substance (a metal, by example) with uniform concentration c_w. The environment is populated by N species $S_1, S_2, \ldots, S_N$. Each species S_r is characterized by a concentration C_r of the contaminant, for $r = 1, \ldots, N$. The toxic substance flows from the environment into the species and circulates between species, obeying the following linear transfer rules: the uptake flux from environment into the species S_r is $k_r^u c_w$, the release flux for the species S_r is $k_r^e C_r$ (for $r = 1, 2, \ldots, N$) and the uptake flux from species S_p ($p = 1, 2, \ldots, r-1$) into the species S_r ($r = 2, 3, \ldots, N$) is $k_{rp}^u C_p$. It is assumed that there is no uptake flux form species S_p into the species S_r for $p > r$. Such models can be found in [1], [2], for example.

This model is described by the following linear system of differential equations

$$\frac{dC_r}{dt} = k_r^u c_w - k_r^e C_r + \sum_{p=1}^{r-1} k_{rp}^u C_p, \quad \text{for} \quad \text{r} = 1, \ldots, \text{N}. \tag{1}$$

We also assume that all k_r^u are pairwise different each other. This is a natural hypothesis for the known real cases covered by this model. Under the last assumption, the general analytic solution of the Cauchy problem associated to (1) and the initial data $C_r(0) = C_{r,0}$ $(r = 1, 2, \ldots, N)$ has the following form:

$$C_r(t) = \sum_{m=1}^{r} a_{rm}\, e^{-k_m^e t} + c_r, \quad r = 1, \ldots, N, \tag{2}$$

where the coefficients a_{rm} and c_r can be recursively expressed by using the relations

$$\begin{aligned}
a_{rr} &= C_{r,0} + \sum_{m=1}^{r-1} \frac{\sum_{s=m}^{r-1} k_{rs}^u a_{sm}}{k_r^e - k_m^e} + \frac{k_r^u c_w + \sum_{s=1}^{r-1} k_{rs}^u c_s}{k_r^e}, \\
a_{rm} &= -\frac{\sum_{s=m}^{r-1} k_{rs}^u a_{sm}}{k_r^e - k_m^e}, \quad m = 1, \ldots, r-1, \\
c_r &= -\frac{k_r^u c_w + \sum_{s=1}^{r-1} k_{rs}^u c_s}{k_r^e}, \\
a_{11} &:= C_{1,0} - \frac{k_1^u}{k_1^e} c_w, \qquad c_1 := \frac{k_1^u}{k_1^e} c_w.
\end{aligned} \tag{3}$$

1.2. THE PROBLEM

Assume that a set $\{y_1, \ldots, y_n\}$ of measurements on the contaminant concentration C_r performed at the moments of time $\{t_1, \ldots, t_n\}$, respectively is given. We take the concentration c_w and the values of the parameters k_m^e for all $m = 1, \ldots, r-1$ as known.

Our purpose is to determine the parameters k_r^e, a_{rp} for $m = 1, \ldots, r$, and c_r using the information obtained from the above mentioned experimental measurements, using the general form (2) for the solution of (1) (the parameters $k_1^e, \ldots, k_{r-1}^e$ can be determined using the procedure described bellow for experimental measurements on $C_1, \ldots, C_{r-1}$, respectively).

In the following, consider n and r to be fixed. For simplification, we use the notations:

$a_p := a_{rp}$, for $p = 1, \ldots, r$,
$k_p^e := -b_p$, for $p = 1, \ldots, r$,
$a := a_r$, $b := a_{r+1} := b_r$, $c := a_{r+2} := c_r$.

Note that, for the convenience of notations, we alternatively use a or a_r, as well as b or b_r or a_{r+1}, as well as c or a_{r+2}. Also denote

$$\overrightarrow{\boldsymbol{a}} := (a_1, \ldots, a_{r+2})$$

and define $h : \mathbb{R} \times \mathbb{R}^{r+2} \to \mathbb{R}$ by

$$h(t, \overrightarrow{\boldsymbol{a}}) := \sum_{m=1}^{r} a_m \, e^{tb_m} + c. \tag{4}$$

In order to determinate the parameters a_m for $m = 1, \ldots, r+2$, we look for the minimum of the function

$$H : \mathbb{R}^{r+2} \to \mathbb{R}_+, \quad H(\overrightarrow{\boldsymbol{a}}) := \sum_{s=1}^{n} (h(t_s, \overrightarrow{\boldsymbol{a}}) - y_s)^2 \tag{5}$$

within the set of its critical points defined by the solutions of

$$\frac{\partial H}{\partial a_m}(\overrightarrow{\boldsymbol{a}}) = 0, \quad m = 1, \ldots, r+2. \tag{6}$$

1.3. THE EQUATIONS

Let $E : \mathbb{R}^2 \to \mathbb{R}$ with $E(t, \beta) := e^{t\beta}$.

We introduce the notations

$$\begin{cases} f_m(t, y, \overrightarrow{\boldsymbol{a}}) := [h(t, \overrightarrow{\boldsymbol{a}}) - y] E(t, b_m), \quad m = 1, \ldots, r, \\ f_a(t, y, \overrightarrow{\boldsymbol{a}}) := f_r(t, y, \overrightarrow{\boldsymbol{a}}), \\ f_b(t, y, \overrightarrow{\boldsymbol{a}}) := f_{r+1}(t, y, \overrightarrow{\boldsymbol{a}}) := [h(t, \overrightarrow{\boldsymbol{a}}) - y] t a E(t, b), \\ f_c(t, y, \overrightarrow{\boldsymbol{a}}) := f_{r+2}(t, y, \overrightarrow{\boldsymbol{a}}) := h(t, \overrightarrow{\boldsymbol{a}}) - y, \end{cases} \tag{7}$$

and let $F = F(\overrightarrow{\boldsymbol{a}})$ be defined by components as

$$F_m(\overrightarrow{\boldsymbol{a}}) := \sum_{s=1}^{n} f_m(t_s, y_s, \overrightarrow{\boldsymbol{a}}), \quad m = 1, \ldots, r+2. \tag{8}$$

Now, (6) takes the form

$$F(\overrightarrow{\boldsymbol{a}}) = 0. \tag{9}$$

2. CELLULAR EXCLUSION PRINCIPLE

We briefly present here the method used in the present paper for numerically finding the zeros of a nonlinear algebraic systems of equations. This very efficient tool is called *Cellular Exclusion Algorithm* and will be applied to solve (9).

Essentially, the method allows us to locate *all* the solutions of

$$F(\boldsymbol{x}) = 0, \tag{10}$$

where $F : \Omega \subset \mathbb{R}^n \to \mathbb{R}^n$ is a non-degenerate smooth function. More precisely, the method provides a number of "small" disjoint subsets $\Omega_l \subset \Omega$ such that (10) has no solutions inside $\Omega \backslash (\cup \Omega_l)$ (see [3], [11], [12], for example).

We call a *box-interval* centered in $\boldsymbol{\mu} \in \mathbb{R}^n$, of radius $\boldsymbol{\rho} \in \mathbb{R}^n_+$, a set of the form

$$\boldsymbol{\sigma} = [\boldsymbol{\mu} - \boldsymbol{\rho}, \boldsymbol{\mu} + \boldsymbol{\rho}] := \left\{ \boldsymbol{x} \in \mathbb{R}^n \,\middle|\, \boldsymbol{\mu} - \boldsymbol{\rho} \leq \boldsymbol{x} \leq \boldsymbol{\mu} + \boldsymbol{\rho} \right\},$$

where we use the standard componentwise "$\leq$" as a partial ordering in $\mathbb{R}^n$.

For any multi-index $\boldsymbol{\alpha} := (\alpha_1, \ldots, \alpha_n) \in \mathbb{N}^n$ and a variable $\boldsymbol{x} := (x_1, \ldots, x_n) \in \mathbb{R}^n$, we associate the notations:

$$|\boldsymbol{\alpha}| := \sum_i \alpha_i, \quad \boldsymbol{\alpha}! := \prod_i \alpha_i, \quad \boldsymbol{x}^{\boldsymbol{\alpha}} := \prod_i x_i^{\alpha_i}, \quad \partial^{\boldsymbol{\alpha}} := \prod_i \partial^{\alpha_i}.$$

Also, for any box-interval $\boldsymbol{\sigma} \subset \mathbb{R}^n$, let us denote $|\boldsymbol{\sigma}| := \{ \boldsymbol{y} \mid \boldsymbol{y} = |\boldsymbol{x}|, \ \boldsymbol{x} \in \boldsymbol{\sigma} \} \subset \mathbb{R}^n_+$, where $|\boldsymbol{x}| := (|x_1|, \ldots, |x_n|) \in \mathbb{R}^n$.

Definition 1. *Let $q \in \mathbb{N}^*$ and $F : \boldsymbol{\sigma} \to \mathbb{R}^n$ a smooth function defined on a box-interval $\boldsymbol{\sigma} \subset \mathbb{R}^n$. A function $\Lambda_F : |\boldsymbol{\sigma}| \to \mathbb{R}_+$ dominates F of order q on $\boldsymbol{\sigma}$ (denoted by $F \prec_q \Lambda_F$) if the following properties hold:*

1. *$\partial^{\boldsymbol{\alpha}} F$ and $\partial^{\boldsymbol{\alpha}} \Lambda_F$ are absolutely continuous for all $0 \leq |\boldsymbol{a}| < q$.*
2. *$\partial^{\boldsymbol{\alpha}} \Lambda_F(\boldsymbol{x}) \leq \partial^{\boldsymbol{\alpha}} \Lambda_F(\boldsymbol{y})$, for all $\boldsymbol{x}, \boldsymbol{y} \in |\boldsymbol{\sigma}|$, with $\boldsymbol{x} \leq \boldsymbol{y}$ and for all $0 \leq |\boldsymbol{a}| \leq q$.*
3. *$|\partial^{\boldsymbol{\alpha}} F(\boldsymbol{x})| \leq \partial^{\boldsymbol{\alpha}} \Lambda_F(|\boldsymbol{x}|)$, for all $\boldsymbol{x} \in \boldsymbol{\sigma}$ and for all $0 \leq |\boldsymbol{a}| \leq q$.*

Let $q \in \mathbb{N}^*$ and $\boldsymbol{\sigma} = [\boldsymbol{\mu} - \boldsymbol{\rho}, \boldsymbol{\mu} + \boldsymbol{\rho}] \subset \mathbb{R}^n$ a box-interval. The following statement represents the fundamental result in the *Cellular Exclusion Algorithm* based on dominant functions.

Theorem 2.1. [3] *Let $F \prec_q \Lambda_F$ on $\boldsymbol{\sigma}$. If $F = 0$ has solution in $\boldsymbol{\sigma}$, then the following inequality holds:*

$$0 \leq \Lambda_F(|\boldsymbol{\mu}| + \boldsymbol{\rho}) - \Lambda_F(|\boldsymbol{\mu}|) - |F(\boldsymbol{\mu})| - \sum_{0 < |\boldsymbol{\alpha}| < q} \left[\partial^{\boldsymbol{\alpha}} \Lambda_F(|\boldsymbol{\mu}|) - |\partial^{\boldsymbol{\alpha}} F(\boldsymbol{\mu})| \right] \cdot \frac{\boldsymbol{\rho}^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!}. \tag{11}$$

Note that a good choice of the dominant function is the key for improving the numerical efficiency of this algorithm. The following properties [3] can be useful in constructing dominant functions.

Proposition 1. *Let $p, q \in \mathbb{N}^*$ be arbitrarily chosen.*

1. *If $F \prec_q \Lambda_F$ then $F(\boldsymbol{m} + \cdot) \prec_q \Lambda_F(|\boldsymbol{m}| + \cdot)$.*
2. *If $F \prec_1 \Lambda_F$, then $|F| \prec_1 \Lambda_F$.*
3. *If $F \prec_q \Lambda_F$, then $a \cdot F \prec_q |a| \cdot \Lambda_F$, for any $a \in \mathbb{R}$.*

4. If $F_i \prec_q \Lambda_{F_i}$ *for* $i = \overline{1,p}$ *, then* $\sum_{i=1}^{p} F_i \prec_q \sum_{i=1}^{p} \Lambda_{F_i}$.
5. If $F_i \prec_q \Lambda_{F_i}$ *for* $i = \overline{1,p}$ *, then* $\prod_{i=1}^{p} F_i \prec_q \prod_{i=1}^{p} \Lambda_{F_i}$.
6. Let $F = f(f_1, \ldots, f_p)$ *and* $\Lambda_F = \Lambda_f(\Lambda_{f_1}, \ldots, \Lambda_{f_p})$. *If* $f \prec_q \Lambda_f$ *and* $f_i \prec_q \Lambda_{f_i}$ *for* $i = \overline{1,p}$ *, then* $F \prec_q \Lambda_F$.

For supplementary information concerning the cellular exclusion algorithm, the reader is referred to [4], [7], [8], [9], [10], [13].

3. PARTIAL DERIVATIVES OF THE COMPONENTS OF F

We return to the problem of finding all the zeros of (9), where the components of F are described by (8).

For the beginning, it is convenient to write $h(t, \overrightarrow{\mathbf{a}}) = \tilde{h}(t, \overrightarrow{\boldsymbol{a}}) + aE(t,b)$, where

$$\tilde{h}(t, \overrightarrow{\boldsymbol{a}}) := \sum_{m=1}^{r-1} a_m \, E(t, b_m) + c.$$

Consider the convention $\partial_m^p := \frac{\partial^p}{\partial (a_m)^p}$, for all $m = 1, \ldots, r+2$ and all $p \in \mathbb{N}$. Let $\partial^{\tilde{\alpha}} := \partial_1^{\alpha_1} \ldots \partial_{r-1}^{\alpha_{r-1}}$ for any multi-index $\tilde{\boldsymbol{\alpha}} = (\alpha_1, \ldots, \alpha_{r-1})$. The following tables present only the non-zero symbolic derivatives for $t > 0$ of f_m, for $m = 1, \ldots, r-1$, f_a, f_b, f_c

$\partial^{\tilde{\alpha}} \partial_a^i \partial_b^j \partial_c^k f_m$	$\lvert\tilde{\boldsymbol{\alpha}}\rvert$	i	j	k
$\partial_p f_m = E(t, b_p + b_m)$	1	0	0	0
$\partial_a \partial_b^n f_m = t^n E(t, b_m + b)$	0	1	$n \geq 0$	0
$\partial_b^n f_m = t^n a E(t, b_m + b)$	0	0	$n \geq 1$	0
$\partial_c f_m = E(t, b_m)$	0	0	0	1

(12)

$\partial^{\tilde{\alpha}} \partial_a^i \partial_b^j \partial_c^k f_a$	$\lvert\tilde{\boldsymbol{\alpha}}\rvert$	i	j	k
$\partial_p \partial_b^n f_a = t^n E(t, b_p + b)$	1	0	$n \geq 0$	0
$\partial_a \partial_b^n f_a = (2t)^n E(2t, b)$	0	1	$n \geq 0$	0
$\partial_b^n f_a = (\tilde{h} - y) t^n E(t, b) + a(2t)^n E(2t, b)$	0	0	$n \geq 1$	0
$\partial_b^n \partial_c f_a = t^n E(t, b)$	0	0	$n \geq 0$	1

(13)

$\partial^{\tilde{\alpha}}\partial_a^i\partial_b^j\partial_c^k f_b$	$\lvert\tilde{\alpha}\rvert$	i	j	k
$\partial_p\partial_b^n f_b = t^{n+1}aE(t, b_p + b)$	1	0	$n \geq 0$	0
$\partial_p\partial_a\partial_b^n f_b = t^{n+1}E(t, b_p + b)$	1	1	$n \geq 0$	0
$\partial_a\partial_b^n f_b = t^{n+1}(\tilde{h} - y)E(t, b)+ +(2t)^{n+1}aE(2t, b)$	0	1	$n \geq 0$	0
$\partial_b^n f_b = t^{n+1}a(\tilde{h} - y)E(t, b)+ +2^n t^{n+1}a^2E(2t, b)$	0	0	$n \geq 1$	0
$\partial_a^2\partial_b^n f_b = (2t)^{n+1}E(2t, b)$	0	2	$n \geq 0$	0
$\partial_b^n\partial_c f_b = t^{n+1}aE(t, b)$	0	0	$n \geq 0$	1
$\partial_a\partial_b^n\partial_c f_b = t^{n+1}E(t, b)$	0	1	$n \geq 0$	1

(14)

$\partial^{\tilde{\alpha}}\partial_a^i\partial_b^j\partial_c^k f_c$	$\lvert\tilde{\alpha}\rvert$	i	j	k
$\partial_p f_c = E(t, b_p)$	1	0	0	0
$\partial_b^n f_c = t^n aE(t, b)$	0	0	$n \geq 1$	0
$\partial_a\partial_b^n f_c = t^n E(t, b)$	0	1	$n \geq 0$	0
$\partial_c f_c = 1$	0	0	0	1

(15)

where $\partial_p := \frac{\partial}{\partial a_p}$, for all $p = 1, \ldots, r-1$.

Using these derivatives, we can immediately write the ones for F_m:

$$\partial^{\alpha} F_m(\overrightarrow{\boldsymbol{a}}) = \sum_{s=1}^{n} \partial^{\alpha} f_m(t_s, y_s, \overrightarrow{\boldsymbol{a}}), \quad m = 1, \ldots, r+2, \tag{16}$$

where $\boldsymbol{\alpha}$ is the $r+2$ component multi-index $(\alpha_1, \ldots, \alpha_{r+2})$.

4. DOMINANT FUNCTIONS

4.1. THE DOMINANT FUNCTION Λ_E OF E

For the exponential $E(t, x)$ considered as function depending on the variable x, one usually uses the following dominant function of order q "around b"

$$\Gamma_E(t, b, x, \rho, q) := \sum_{k=0}^{q-1} \frac{(xt)^k}{k!} + \frac{(xt)^q}{q!} E(t, b + \rho), \tag{17}$$

for $x \in [b-\rho, b+\rho]$, see [4] for example.

In the present work, we propose another dominant function of order q, namely $\Lambda_E(t,b,x,\rho,q)$ of $E(t,b+x)$ w.r.t. x, introduced by

$$\Lambda_E(t,b,x,\rho,q) := E(t,b)\left[\sum_{k=0}^{q-1}\frac{(xt)^k}{k!} + \frac{(xt)^q}{q!}E(t,\rho)\right], \tag{18}$$

for $x \in [-\rho,\rho]$ and some fixed $\rho > 0$.

Remark 1. *We have replaced the dominant function Γ_E by Λ_E due to the following reasons:*

1. One can prove by induction on j that

$$\left.\frac{\partial^j \Lambda_E(t,b,z,\rho,q)}{\partial z^j}\right|_{z=|x|} \le \left.\frac{\partial^j \Gamma_E(t,b,z,\rho,q)}{\partial z^j}\right|_{z=|b|+|x|}, \tag{19}$$

for all $j = 0,1,\ldots,q$. Using the above property and following the proof of the exclusion criterion in [3] one can immediately show that the inequality (11) is tighter when using Λ_E instead of Γ_E.

2. The r.h.s. of (11) has a much simpler expression when one uses Λ_E as dominant function of E instead of Γ_E.

Consequently, the exclusion criterion works in a more efficient way for Λ_E than for Γ_E.

4.2. DOMINANT FUNCTIONS ASSOCIATED TO THE COMPONENTS OF F

For $t > 0$, we associate the dominant functions of order q w.r.t. the variables $a_1, a_2, \ldots, a_{r+2}$ to the functions f_m, for $m = 1,\ldots,r+2$ (for $x_b \in [-\rho_b,\rho_b]$).

$$\begin{cases}
\Lambda_{f_m}(t,y,\overrightarrow{a},x_b,\rho_b,q) := \\
\qquad := [\tilde{h}(t,\overrightarrow{a}) + |y|]E(t,b_m) + aE(t,b_m)\Lambda_E(t,b,x_b,\rho_b,q) \\
\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad m = 1,\ldots,r-1 \\
\Lambda_{f_a}(t,y,\overrightarrow{a},x_b,\rho_b,q) := \Lambda_{f_r}(t,y,\overrightarrow{a},x_b,\rho_b,q) := \\
\qquad := [\tilde{h}(t,\overrightarrow{a}) + |y|]\Lambda_E(t,b,x_b,\rho_b,q) + a\Lambda_E(2t,b,x_b,\rho_b,q) \\
\Lambda_{f_b}(t,y,\overrightarrow{a},x_b,\rho_b,q) := \Lambda_{f_{r+1}}(t,y,\overrightarrow{a},x_b,\rho_b,q) := \\
\qquad := [\tilde{h}(t,\overrightarrow{a}) + |y|]ta\Lambda_E(t,b,x_b,\rho_b,q) + ta^2\Lambda_E(2t,b,x_b,\rho_b,q) \\
\Lambda_{f_c}(t,y,\overrightarrow{a},x_b,\rho_b,q) := \Lambda_{f_{r+2}}(t,y,\overrightarrow{a},x_b,\rho_b,q) := \\
\qquad := [\tilde{h}(t,\overrightarrow{a}) + |y|] + a\Lambda_E(t,b,x_b,\rho_b,q).
\end{cases} \tag{20}$$

Correspondingly, $\Lambda_F = \Lambda_F(t, y, \overrightarrow{a}, x_b, \rho_b, q)$ are defined on components for $m = 1, 2, \ldots, r+2$ by

$$\Lambda_{F_m}(\overrightarrow{a}, x_b, \rho_b, q) := \sum_{s=1}^{n} \Lambda_{f_m}(t_s, y_s, \overrightarrow{a}, x_b, \rho_b, q). \tag{21}$$

Note that, when using Γ_E as dominant function for E instead of Λ_E, the corresponding dominant functions Γ_{F_m} of F_m ($m = 1, 2, \ldots, r+2$) are formally obtained by simply replacing Λ_E with Γ_E into the expressions of Λ_{F_m}.

4.3. THE DERIVATIVES OF Λ_F,

Let $\boldsymbol{x} = (x_1, \ldots, x_{r+2})$ and $\overrightarrow{\boldsymbol{\rho}} = (\rho_1, \rho_2, \ldots, \rho_{r+2}) \in \mathbb{R}_+^{r+2}$. Denote also by $\rho_a := \rho_r$, $\rho_b := \rho_{r+1}$, $\rho_c := \rho_{r+2}$ and let

$$\begin{aligned} &\Delta\Lambda_{F_m}(\overrightarrow{a}, \overrightarrow{\boldsymbol{\rho}}, q) := \\ &:= \Lambda_{F_m}(|\overrightarrow{a}| + (\rho_1, \rho_2, \ldots, \rho_r, 0, \rho_{r+2}), \rho_b, \rho_b, q) - \Lambda_{F_m}(|\overrightarrow{a}|, 0, \rho_b, q), \end{aligned} \tag{22}$$

$$\begin{aligned} &D^{\boldsymbol{\alpha}}\Lambda_{F_m}(\overrightarrow{a}, \overrightarrow{\boldsymbol{\rho}}, q) := \\ &:= \partial^{\boldsymbol{\alpha}}\Lambda_{F_m}(x_1, \ldots, x_r, b, x_{r+2}, x_{r+1}, \rho_b, q)|_{\boldsymbol{x}=(|a_1|,\ldots,|a_{r-1}|,|a|,0,|c|)}, \end{aligned} \tag{23}$$

where $\boldsymbol{\alpha} := (\alpha_1, \ldots, \alpha_{r+2})$ and the derivatives $\partial^{\boldsymbol{\alpha}}$ in the r.h.s. of (23) are w.r.t. the variables $x_1, \ldots, x_{r+2}$.

In our case, inequalities (11) for the *"investigated exclusion"* box-interval

$$\boldsymbol{\sigma} = [(a_1 - \rho_1, \ldots, a - \rho_a, -\rho_b, c - \rho_c), (a_1 + \rho_1, \ldots, a + \rho_a, \rho_b, c + \rho_c)]$$

take the following particular form

$$\begin{aligned} &0 \le \Delta\Lambda_{F_m}(\overrightarrow{a}, \overrightarrow{\boldsymbol{\rho}}, q) - |F_m(\overrightarrow{a})| - \\ &- \sum_{0<|\boldsymbol{\alpha}|<q} \left[D^{\boldsymbol{\alpha}}\Lambda_{F_m}(\overrightarrow{a}, \overrightarrow{\boldsymbol{\rho}}, q) - |\partial^{\boldsymbol{\alpha}}F_m(\overrightarrow{a})|\right] \cdot \frac{\overrightarrow{\boldsymbol{\rho}}^{\boldsymbol{\alpha}}}{\boldsymbol{\alpha}!}, \end{aligned} \tag{24}$$

where $m = 1, \ldots, r+2$ and the derivatives are understood w.r.t. $\mathbf{x} \in \boldsymbol{\sigma}$.

Therefore, in order to verify them, one has to compute the derivatives

$$\frac{\partial^{\boldsymbol{\alpha}}\Lambda_{f_m}}{\partial \boldsymbol{x}^{\boldsymbol{\alpha}}}(t, y, x_1, \ldots, x_r, b, x_{r+2}, x_{r+1}, \rho_b, q)$$

of the dominant functions Λ_{f_m}, for $m = 1, 2, \ldots, r+2$, only at the points of the form $\boldsymbol{x} = (|a_1|, \ldots, |a_{r-1}|, |a|, 0, |c|)$. The following tables present only the non-zero

symbolic derivatives

$\partial^{\tilde{\alpha}}\partial_a^i\partial_x^j\partial_c^k\Lambda_{f_m}$	$\lvert\tilde{\alpha}\rvert$	i	j	k
$\partial_p\Lambda_{f_m} = E(t, b_p + b_m)$	1	0	0	0
$\partial_a\partial_x^n\Lambda_{f_m} = t^n E(t, b_m + b)$	0	1	$n = \overline{0, q'}$	0
$\partial_x^n\Lambda_{f_m} = t^n a E(t, b_m + b)$	0	0	$n = \overline{1, q'}$	0
$\partial_c\Lambda_{f_m} = E(t, b_m)$	0	0	0	1

(25)

$\partial^{\tilde{\alpha}}\partial_a^i\partial_x^j\partial_c^k\Lambda_{f_a}$	$\lvert\tilde{\alpha}\rvert$	i	j	k
$\partial_p\partial_x^n\Lambda_{f_a} = t^n E(t, b_p + b)$	1	0	$n = \overline{0, q'}$	0
$\partial_a\partial_x^n\Lambda_{f_a} = (2t)^n E(2t, b)$	0	1	$n = \overline{0, q'}$	0
$\partial_x^n\Lambda_{f_a} = (\tilde{h} + \lvert y\rvert)t^n E(t, b) + a(2t)^n E(2t, b)$	0	0	$n = \overline{1, q'}$	0
$\partial_x^n\partial_c\Lambda_{f_a} = t^n E(t, b)$	0	0	$n = \overline{0, q'}$	1

(26)

$\partial^{\tilde{\alpha}}\partial_a^i\partial_x^j\partial_c^k\Lambda_{f_b}$	$\lvert\tilde{\alpha}\rvert$	i	j	k
$\partial_p\partial_x^n\Lambda_{f_b} = t^{n+1} a E(t, b_p + b)$	1	0	$n = \overline{0, q'}$	0
$\partial_p\partial_a\partial_x^n\Lambda_{f_b} = t^{n+1} E(t, b_p + b)$	1	1	$n = \overline{0, q'}$	0
$\partial_a\partial_x^n\Lambda_{f_b} = t^{n+1}(\tilde{h} + \lvert y\rvert)E(t, b) + (2t)^{n+1} a E(2t, b)$	0	1	$n = \overline{0, q'}$	0
$\partial_x^n\Lambda_{f_b} = t^{n+1} a(\tilde{h} + \lvert y\rvert)E(t, b) + 2^n t^{n+1} a^2 E(2t, b)$	0	0	$n = \overline{1, q'}$	0
$\partial_a^2\partial_x^n\Lambda_{f_b} = (2t)^{n+1} E(2t, b)$	0	2	$n = \overline{0, q'}$	0
$\partial_x^n\partial_c\Lambda_{f_b} = t^{n+1} a E(t, b)$	0	0	$n = \overline{0, q'}$	1
$\partial_a\partial_x^n\partial_c\Lambda_{f_b} = t^{n+1} E(t, b)$	0	1	$n = \overline{0, q'}$	1

(27)

$\partial^{\tilde{\alpha}}\partial_a^i\partial_x^j\partial_c^k\Lambda_{f_c}$	$\lvert\tilde{\alpha}\rvert$	i	j	k
$\partial_p\Lambda_{f_c} = E(t, b_p)$	1	0	0	0
$\partial_x^n\Lambda_{f_c} = t^n aE(t, b)$	0	0	$n = \overline{1, q'}$	0
$\partial_a\partial_x^n\Lambda_{f_c} = t^n E(t, b)$	0	1	$n = \overline{0, q'}$	0
$\partial_c\Lambda_{f_c} = 1$	0	0	0	1

(28)

for all $m = 1, \ldots, r-1$ and $p = 1, \ldots, r-1$, where $q' := q - 1$.

We remark that, in comparison to Γ_{f_m}, the use of these new dominant functions will bring considerable simplifications for the computations and the final form of the exclusion inequalities (11).

5. THE EXCLUSION CRITERION

Comparing the derivatives of f_m from (12-15) with the derivatives of Λ_{f_m} (25-28), one can see that "almost all" the terms of the sum in (24) containing differences between these derivatives vanish. In order to explicitly rewrite the inequalities (24), we introduce some notations for the non-null differences:

$$\Theta_a^j(\overrightarrow{\boldsymbol{a}}) := \sum_{s=1}^{n}[(\tilde{h}(t_s, |\overrightarrow{\boldsymbol{a}}|) + |y_s|)t_s^j E(t_s, b) + |a|(2t_s)^j E(2t_s, b)] - \\ - \left|\sum_{s=1}^{n}[(\tilde{h}(t_s, \overrightarrow{\boldsymbol{a}}) - y_s)t_s^j E(t_s, b) + a(2t_s)^j E(2t_s, b)]\right|, \tag{29}$$

$$\Theta_b^{0,j}(\overrightarrow{\boldsymbol{a}}) := \sum_{s=1}^{n}[(\tilde{h}(t_s, |\overrightarrow{\boldsymbol{a}}|) + |y_s|)t_s^{j+1}|a|E(t_s, b) + (2t_s)^j t_s a^2 E(2t_s, b)] - \\ - \left|\sum_{s=1}^{n}[(\tilde{h}(t_s, \overrightarrow{\boldsymbol{a}}) - y_s)t_s^{j+1} aE(t_s, b) + (2t_s)^j t_s a^2 E(2t_s, b)]\right|, \tag{30}$$

$$\Theta_b^{1,j}(\overrightarrow{\boldsymbol{a}}) := \sum_{s=1}^{n}[(\tilde{h}(t_s, |\overrightarrow{\boldsymbol{a}}|) + |y_s|)t_s^{j+1} E(t_s, b) + (2t_s)^{j+1}|a|E(2t_s, b)] - \\ - \left|\sum_{s=1}^{n}[(\tilde{h}(t_s, \overrightarrow{\boldsymbol{a}}) - y_s)t_s^{j+1} E(t_s, b) + (2t_s)^{j+1} aE(2t_s, b)]\right|, \tag{31}$$

for all $j > 0$.

Now, the exclusion inequalities (24) take the form

$$\begin{cases} 0 \le \Delta\Lambda_{F_m}(\overrightarrow{\boldsymbol{a}}, \overrightarrow{\boldsymbol{\rho}}, q) - |F_m(\overrightarrow{\boldsymbol{a}})|, \qquad m = 1, \dots, r-1, \\ 0 \le \Delta\Lambda_{F_a}(\overrightarrow{\boldsymbol{a}}, \overrightarrow{\boldsymbol{\rho}}, q) - |F_a(\overrightarrow{\boldsymbol{a}})| - \displaystyle\sum_{j=1}^{q-1} \Theta_a^j(\overrightarrow{\boldsymbol{a}}) \frac{\rho_b^j}{j!}, \\ 0 \le \Delta\Lambda_{F_b}(\overrightarrow{\boldsymbol{a}}, \overrightarrow{\boldsymbol{\rho}}, q) - |F_b(\overrightarrow{\boldsymbol{a}})| - \displaystyle\sum_{j=1}^{q-1} \Theta_b^{0,j}(\overrightarrow{\boldsymbol{a}}) \frac{\rho_b^j}{j!} - \\ \qquad\qquad - \displaystyle\sum_{j=0}^{q-2} \Theta_b^{1,j}(\overrightarrow{\boldsymbol{a}}) \frac{\rho_a \rho_b^j}{j!}, \\ 0 \le \Delta\Lambda_{F_c}(\overrightarrow{\boldsymbol{a}}, \overrightarrow{\boldsymbol{\rho}}, q) - |F_c(\overrightarrow{\boldsymbol{a}})|. \end{cases} \tag{32}$$

Remark. *These inequalities represent the base relations used in the exclusion cellular algorithm for solving (9).*

6. NUMERICAL RESULTS AND CONCLUSIONS

6.1. NON-PERTURBED DATA

Using $(a, b, c) = (3.5, -1, 0.5)$, we have generated a set of n non-perturbed data $\{y_s\}_{s=1}^n$ corresponding to some arbitrary moments of time $\{t_s\}_{s=1}^n \subset [0, T]$, with $T = 10$ and $n = 250$. Then, we have used our algorithm starting with an initial box-interval $\boldsymbol{\sigma}$ defined by $\boldsymbol{\mu}_{\boldsymbol{\sigma}} = (4, -2, 3)$ and $\boldsymbol{\rho}_{\boldsymbol{\sigma}} = (3.5, 1.5, 3)$. The results are of very good precision. For example, at the iteration level $l = 30$, there are 41 remaining box-intervals of radius $\boldsymbol{\rho} = (3.259629, 1.3969839, 2.7939677) \cdot 10^{-9}$, having the centers inside a set of the form

$$\mathcal{J} = [a_m - \delta_a, a_m + \delta_a] \times [b_m - \delta_b, b_m + \delta_b] \times [c_m - \delta_c, c_m + \delta_c] \tag{33}$$

where $a_m = 3.5$, $b_m = 1 - 10^{-8}$, $c_m = 0.5$, $\delta_a = 5 \cdot 10^{-8}$, $\delta_b = 1.5 \cdot 10^{-8}$, $\delta_c = 10^{-8}$.

Table 1 presents the number $\#I$ of retained intervals at each iteration level l. We mention $\#I$ stabilizes around 42 after $l = 7$.

Table 1: Number of retained intervals for different iteration levels (non-perturbed data)

l	0	1	2	3	...	7	...	15	...	20	...	28	29	30
$\#I$	1	6	14	18	...	44	...	44	...	41	...	42	43	41

6.2. PERTURBED DATA

Starting from (a, b, c), we have simulated in this section different sets of $n = 250$ data affected by measurement errors: each exact datum was perturbed with a random error between $[-p\%, p\%]$ of itself. Beginning with an initial box-interval defined by $\boldsymbol{\mu_\sigma}$ and $\boldsymbol{\rho_\sigma}$, we have estimated the parameters (a_m, b_m, c_m) at the resolution level $l = 30$, where the radius of the remaining box-intervals is $\boldsymbol{\rho} = \boldsymbol{\rho_\sigma}/2^{30}$. The results are summarized in Table 2, where σ and σ_m are the standard deviations corresponding to (a, b, c) and (a_m, b_m, c_m), respectively.

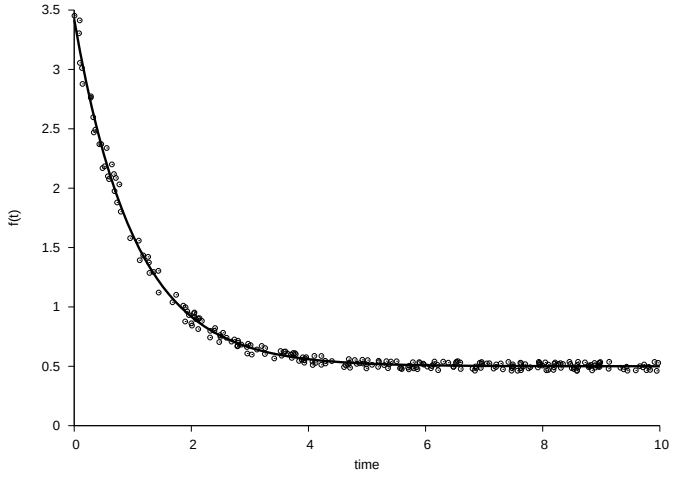
Table 2: Results for the perturbed data.

(a, b, c)	$(3, -1, 0.5)$		$(10^6, -10, 10)$	
$\boldsymbol{\mu_\sigma}$	$(4, -2, 3)$		$(8 \cdot 10^5, -20, 0)$	
$\boldsymbol{\rho_\sigma}$	$(3.5, 1.5, 3)$		$(5 \cdot 10^5, 15, 3 \cdot 10^5)$	
p	2	8	2	8
a_m	2.9803021	2.92152865	$0.99854295 \cdot 10^6$	$0.9941609 \cdot 10^6$
b_m	−0.993202395	−0.972655765	−10.011508	−10.046069
c_m	0.500071955	0.500203925	5.9855171	−6.2855892
δ_a	$5 \cdot 10^{-8}$	10^{-7}	$5 \cdot 10^{-3}$	$5 \cdot 10^{-3}$
δ_b	$3 \cdot 10^{-8}$	$3 \cdot 10^{-8}$	10^{-7}	$3 \cdot 10^{-8}$
δ_c	10^{-8}	10^{-8}	10^{-8}	10^{-8}
σ	0.011475	0.045900	38130.783263	37773.259856
σ_m	0.010993	0.043971	568.922142	2275.735147

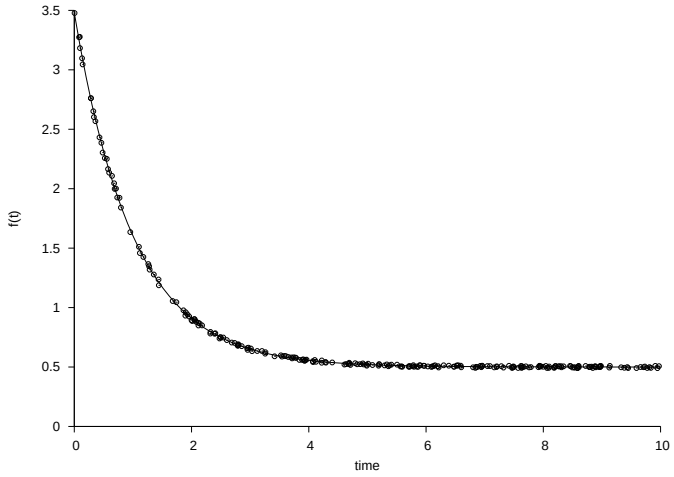
6.3. GRAPHICS

In this section, we graphically illustrate the perturbed data generated with $(a, b, c) = (3, -1, 0.5)$ and the best fitting function, i.e. that function associated to the estimated parameters (a_m, b_m, c_m).

Figure 1: Graphical representation for the perturbed data and the function corresponding to (a_m, b_m, c_m).



8% perturbations, $(a_m, b_m, c_m) = (2.92152865, -0.972655765, 0.500203925)$



2% perturbations, $(a_m, b_m, c_m) = (2.9803021, -0.993202395, 0.500071955)$

6.4. FINAL REMARKS

The accuracy of the estimated parameters increases with the precision of the perturbed data; this is emphasized by the decrease of the standard deviation σ_m associated to these parameters as the maximal relative error p gets smaller.

The fact that $\sigma_m \leq \sigma$ in Table 2 tells us that the estimated parameters fit the perturbed data set in a better way than the initial parameters. We have expected this since data obtained from the initial values of the parameters (a, b, c) were perturbed

and therefore, the global minima of the function H in (5) will now be attained for other values of these parameters.

Also, it has been observed that the accuracy as well as the efficiency are improved when the range time interval $[0, T]$ of the measurements is larger.

We mention that the centers of the remaining box-intervals are concentrated around (a_m, b_m, c_m) with a tolerance $(\delta_a, \delta_b, \delta_c)$. Since $\delta_u << |u_m|$ and $\rho_u << |u_m|$, for all $u \in \{a, b, c\}$, one can consider that (a_m, b_m, c_m) is the estimated solution of (6). We also observed [5] that the numerical effort of getting these values is bigger when the number n of measurements is small.

Another remark relates to the efficiency of the method based on the new dominant which strongly simplifies the numerical code. As compared to the case of using Γ_{F_m}, the running times of the algorithm are much smaller (up to 10 times) when using Λ_{F_m} (see [6] for an example).

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