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A numerical method for linear Volterra integral equations on infinite intervals and its application to the resolution of metastatic tumor growth models



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ABSTRACT

A Nyström method for linear second kind Volterra integral equations on unbounded intervals, with sufficiently smooth kernels, is described. The procedure is based on the use of a truncated Lagrange interpolation process and of a truncated Gaussian quadrature formula. The stability and the convergence of the method in suitable weighted spaces of functions are studied and some numerical examples showing its reliability are presented. In particular, the proposed method has been tested for the numerical resolution of some Volterra integral equations arising from the reformulation of differential models describing metastatic tumor growth whose unknown solutions represent biological observables as the metastatic mass or the number of metastases.

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1. Introduction

In this paper we consider the numerical solution of linear Volterra integral equations (VIEs) of the second kind on the positive semiaxis

$$f(t) - \int_{0}^{t} k(s,t) f(s) \, ds = g(t), \quad t \ge 0, \tag{1}$$

where the kernel k(s, t) is a given function defined on $\Delta = \{(s, t) | t \ge 0, 0 \le s \le t\}$, g(t) is a known function on \mathbb{R}^+ and f(t) is the unknown solution. In the sequel the functions k and g will be assumed sufficiently smooth.

Such kind of integral equations are of interest since they are involved in many applications which include elasticity, semiconductors, scattering theory, seismology, heat conduction, metallurgy, fluid flow, chemical reactions, population dynamics, etc. (see, for example, [3] and the references therein).

The case when *t* belongs to a bounded interval has been extensively studied and a large variety of numerical methods have been developed for an accurate approximation of the solution f(t). A fairly wide and exhaustive bibliography for many existing methods proposed for the solution of linear and nonlinear VIEs both with smooth kernels and with weakly singular ones can be found in [3,8,9]. Also more recent literature is dedicated to the numerical treatment of VIEs by means of collocation methods, Nyström methods, qualocation methods, Sinc methods, global spectral methods

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(see [1,4,5,10,15,18,21-23,30,32]). In particular, the case of weakly singular kernels has been considered in the papers [1,4,5,10,15,21–23,30]. Due to the singular behavior of the solutions, linear or non-linear transformations (see, for instance, [15,22,30]) are often employed in order to improve their smoothness as well as to obtain high orders of convergence.

Here we are interested in the case $t \in [0, +\infty)$, which, according to our knowledge, has not been treated in literature from a numerical point of view.

As a first step of the procedure we propose, by the change of variable $s = te^{-z}$ we write equation (1) as follows

$$f(t) - t \int_{0}^{+\infty} k(te^{-z}, t) f(te^{-z}) e^{-z} dz = g(t), \quad t \ge 0.$$
(2)

Then, introduced the operator

$$(Kf)(t) = t \int_{0}^{+\infty} k(te^{-z}, t) f(te^{-z}) e^{-z} dz$$
(3)

and denoted by I the identity operator, equation (2) can be expressed in the more compact form

$$(I - K) f(t) = g(t), \quad t \ge 0.$$
 (4)

In a second step we aim to apply a Nyström type method for the numerical solution of equation (4). Such method will be based on an approximation of the integral in (3), obtained by replacing the function $f(te^{-z})$ with a truncated Lagrange polynomial interpolating f at some suitable nodes in $[0, +\infty)$. A further discretization is achieved by applying a truncated quadrature rule for the computation of some integrals needed to construct the approximate solution we are looking for.

The stability and the convergence of this method in suitable spaces of functions endowed with weighted uniform norm is addressed and also the well conditioning of the linear systems which it leads to solve is proved. The reliability of the proposed numerical procedure is shown through some tests. In particular, the method is applied for the numerical solution of some Volterra integral equations (see [16,17]) which arise from the reformulation of differential models describing the evolution of tumor metastases by structured population equations (see [19]). The method allows to compute some biological observables of interest as the metastatic mass, the total or cumulative number of metastases, which represent the unknown solutions of these integral equations.

The outline of the paper is as follows. In Section 2 the function spaces are defined and some preliminary results concerning the employed Lagrange interpolation process and quadrature formula are given. Section 3 is devoted to the description of the numerical method and to the analysis of its convergence and stability. In Section 4 several numerical examples are shown, in particular tests concerning the application of the proposed method to the numerical resolution of a metastatic tumor growth model. The proofs of the main results are contained in Section 5.

2. Preliminaries

2.1. Function spaces

We denote by $L\log^+ L$ the set of all measurable functions $f : \mathbb{R}^+ \to \mathbb{R}$ for which

$$\rho(f) = \int_{0}^{+\infty} |f(t)| (1 + \log^{+} |f(t)|) dt < +\infty,$$
(5)

where $\log^+(t) = \log(\max\{1, t\})$, for t > 0, and by L^1 the set of all measurable functions $f: \mathbb{R}^+ \to \mathbb{R}$ such that

$$\|f\|_{1} = \int_{0}^{+\infty} |f(t)| dt < +\infty.$$

With the weight function

$$u(t) = t^{\gamma} (1+t)^{\delta} e^{-\frac{1}{2}}, \quad \gamma, \delta \ge 0, \tag{6}$$

let C_u be the function space defined as

$$C_u = \left\{ f \in C((0, +\infty)) : \lim_{\substack{t \to 0^+ \\ t \to +\infty}} (fu)(t) = 0 \right\}, \quad \text{if} \quad \gamma > 0,$$

or

)

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$$C_u = \left\{ f \in C([0, +\infty)) : \lim_{t \to +\infty} (fu)(t) = 0 \right\}, \quad \text{if} \quad \gamma = 0$$

endowed with the weighted norm

$$||f||_u = \sup_{t \ge 0} |(fu)(t)|$$

In the case of smoother functions, for any positive integer r we introduce the following Sobolev-type spaces

$$W_r(u) = \{ f \in C_u : f^{(r-1)} \in AC((0, +\infty)), \| f^{(r)} \varphi^r \|_u < +\infty \},\$$

where $\varphi(t) = \sqrt{t}$ and AC(A) denotes the collection of all functions which are absolutely continuous on every closed subset $A \subseteq (0, +\infty)$. We equip this space with the norm

$$||f||_{W_r(u)} = ||f||_u + ||f^{(r)}\varphi^r||_u.$$

In what follows W_r will denote the Sobolev-type space corresponding to the weight $u(t) \equiv 1$ and we will set $W_0(u) = C_u$.

Denoting by \mathbb{P}_m the set of all algebraic polynomials of degree at most *m*, for any function $f \in C_u$ we define the weighted error of best polynomial approximation as

$$E_m(f)_u = \inf_{P_m \in \mathbb{P}_m} \|f - P_m\|_u$$

which, as it is well known (see [29]), satisfies the condition

$$\lim_{m} E_m(f)_u = 0, \quad \forall f \in C_u.$$
⁽⁷⁾

The following Favard type inequality holds true [25, (2.4)]

$$E_m(f)_u \le \frac{\mathcal{C}}{m^{\frac{r}{2}}} \| f^{(r)} \varphi^r \|_u, \quad \forall f \in W_r(u),$$
(8)

where C is a positive constant independent of f and m.

In the following we will denote by C a positive constant which may assume different values in different formulas. We will write C(a, b, ...) to say that C depends on the parameters a, b, ... and $C \neq C(a, b, ...)$ to say that C is independent of the parameters a, b, ... Moreover, if $A, B \ge 0$, the symbol $A \sim B$ means that there exists a constant $0 < C \neq C(A, B)$ such that $C^{-1}B \le A \le CB$.

2.2. Truncated Lagrange polynomial

Let

$$w_{\alpha}(t) = t^{\alpha} e^{-t}, \quad \alpha > -1,$$

be a generalized Laguerre weight and let $\{p_m(w_\alpha)\}_m$ be the sequence of the corresponding orthonormal polynomials having positive leading coefficients.

If *f* is a locally continuous function in \mathbb{R}^+ , let $L_{m+1}(f, t)$ be the Lagrange polynomial interpolating the function *f* at the zeros z_1, z_2, \ldots, z_m of $p_m(w_0)$ and at the additional point $z_{m+1} := 4m$. We recall that (see [31, p. 128])

$$0 < z_1 < z_2 < \ldots < z_m < 4m.$$

Then one has

$$L_{m+1}(f,t) = \sum_{k=1}^{m+1} \ell_{m+1,k}(t) f(z_k),$$

where

$$\ell_{m+1,k}(t) = l_{m,k}(t) \frac{4m-t}{4m-z_k}, \quad k = 1, \dots, m,$$

with $l_{m,k}(t) = \frac{p_m(w_0,t)}{p'_m(w_0,z_k)(t-z_k)}$ the *k*-th fundamental Lagrange polynomial associated with the system of interpolation nodes $\{z_1, z_2, \dots, z_m\}$ and

$$\ell_{m+1,m+1}(t) = \frac{p_m(w_0,t)}{p_m(w_0,4m)}.$$

Now, for *m* sufficiently large, let j = j(m) be the integer defined by

$$j = \min_{i=1,\dots,m} \{i : z_i \ge 4\theta m\},\tag{9}$$

where $0 < \theta < 1$ is fixed. With χ_j the characteristic function of the interval $[0, x_j]$, we consider the truncated Lagrange polynomial $L_{m+1}^*(f, t)$ defined as follows

$$L_{m+1}^{*}(f,t) := L_{m+1}(\chi_{j}f,t) = \sum_{k=1}^{j} \ell_{m+1,k}(t)f(z_{k}).$$
(10)

It has been introduced in [24] (see also [11,27]) and satisfies the properties stated in the following two lemmas, with *u* the weight function given in (6), which will be useful for proving our main results.

Lemma 2.1. Let $u(t) = t^{\gamma}(1+t)^{\delta}e^{-\frac{t}{2}}$ with $\frac{1}{4} \leq \gamma \leq \frac{5}{4}$ and $0 \leq \delta \leq 1$. Then, for any $f \in C_u$ we have

$$\|L_{m+1}^*(f)\|_u \le C \log m \|f\|_u, \tag{11}$$

and

$$\|f - L_{m+1}^*(f)\|_u \le C \log m[E_M(f)_u + e^{-Am} \|f\|_u],$$
(12)

where $M = \lfloor \frac{\theta m}{1+\theta} \rfloor$ and the constant A, C are independent of f and m. Moreover, for any $f \in W_r(u)$, $r \ge 1$, we have

$$\|L_{m+1}^{*}(f)^{(r)}\varphi^{r}\|_{u} \le C\log m \|f\|_{W_{r}(u)},$$
(13)

where $C \neq C(m, f)$.

The inequality (12) has been proved in [25, (2.8), Theorem 2.2] in a more general case and inequality (11) is a consequence of it. Moreover, (13) has been proved in [13, (8), Theorem 2.2] in the case $\delta = 0$ and $\alpha > -1$.

With ρ defined in (5), we recall the following

Lemma 2.2. [20, Lemma 9] Let $u(t) = t^{\gamma} (1+t)^{\delta} e^{-\frac{t}{2}}$ with $\gamma \leq \frac{1}{4}$ and $\delta \geq \frac{1}{4} - \gamma$. For all functions $f \in C_u$ and for all g with $\frac{g}{\sqrt{w_0 \varphi}} \in \text{Llog}^+ \mathbf{L}$, there exists a constant $C \neq C(m, f, g)$ such that

$$\int_{0}^{+\infty} |g(t)||L_{m+1}^{*}(f,t)|dt \leq \mathcal{C}\rho\left(\frac{g}{\sqrt{w_{0}\varphi}}\right) ||fu||_{\infty}.$$

Note that the above theorems hold true for any fixed $\theta \in (0, 1)$. A natural choice of θ is done taking into account the vanishing behavior of f u at infinity.

2.3. Truncated quadrature formula

The numerical method we are going to propose for the solution of equation (1) makes use of the following truncated Gauss-Laguerrre quadrature formula

$$\int_{0}^{\infty} f(t)w_{0}(t)dt = \sum_{i=1}^{j} \lambda_{i}f(z_{i}) + R_{m}(f),$$
(14)

where $\lambda_1, \lambda_2, ..., \lambda_m$ are the weights of the classical complete Gauss-Laguerre rule and j is the integer defined in (9) in correspondence with a fixed $\theta \in (0, 1)$.

It has been proved [25, Proposition 2.3] that if $\frac{w_0}{u} \in L^1$ then, for any fixed $\theta \in (0, 1)$ and $\forall f \in C_u$, the remainder term $R_m(f)$ satisfies this estimate

$$|R_m(f)| \le \mathcal{C}\left[E_M(f)_u + e^{-Am} \|f\|_u\right],\tag{15}$$

with C and A not depending on m and f and $M = \lfloor \frac{\theta m}{1+\theta} \rfloor \sim m$.

2.4. Unisolvence

The theorem stated below establishes sufficient conditions ensuring that equation (4), and then (1), is unisolvent. In what follows we will denote by $k_t(s)$ and $k_s(t)$ the function k(s, t) regarded as a function of the only variable *s* or *t*, respectively.

Theorem 2.3. Let $u(t) = t^{\gamma}(1+t)^{\delta}e^{-\frac{t}{2}}$ with $\gamma \leq \frac{1}{4}$ and $\delta \geq \frac{1}{4} - \gamma$. Let us assume that the kernel k(s, t) satisfies

$$\sup_{t\geq 0} u(t) \left\| \frac{k_t}{u} \right\|_1 < +\infty, \tag{16}$$

$$\sup_{t\geq 0} u(t)\rho\left(\frac{k_t}{\sqrt{w_0\varphi}}\right) < +\infty,\tag{17}$$

and

$$\lim_{h \to 0} \sup_{t \ge 0} \rho\left(\frac{u(t+h)k_{t+h} - u(t)k_t}{\sqrt{w_0\varphi}}\right) = 0.$$
(18)

If $\text{Ker}(I - K) = \{0\}$ in C_u , then equation (4) is unisolvent for any $g \in C_u$.

The next lemma gives some smoothing properties of the solution f of (4) (when it exists).

Lemma 2.4. Let us assume that the kernel k(s, t) satisfies (16) and

$$\sup_{t\geq 0}\varphi^{r}(t)u(t)\left\|\frac{1}{u}\frac{\partial^{r}}{\partial t^{r}}k(\cdot,t)\right\|_{1}<+\infty,$$
(19)

$$\sup_{t \ge 0} \varphi^{h}(t) \left| \frac{\partial^{h-1}}{\partial s^{i} \partial t^{h-1-i}} k(s,t) \right|_{|s=t} < +\infty, \quad h = 1, \dots, r, \ i = 0, \dots, h-1,$$
(20)

for some $r \ge 1$. If $g \in W_r(u)$, then

$$f \in W_{r-1}(u) \Rightarrow f \in W_r(u).$$

3. Numerical method

This section will be dedicated to the description of a new method of Nyström type for the numerical solution of the Volterra integral equation (1) and the successive analysis of its stability and convergence. More precisely, the method will approximate the solution of the equivalent integral equation (2) (or (4)). We define the following discrete operator

$$(K_m f)(t) = t \int_0^{+\infty} k(te^{-z}, t) L_{m+1}^*(f, te^{-z}) e^{-z} dz.$$

The method aims to solve the next approximating equation

$$(I - K_m)f_m = g \tag{21}$$

in the unknown f_m . In order to compute the approximating solution f_m the following steps will be carried out.

First, we multiply both sides of the equation (21) by the weight u(t) defined in (6) obtaining

$$(f_m u)(t) - u(t)t \int_0^{+\infty} k(te^{-z}, t) L_{m+1}^*(f, te^{-z}) e^{-z} dz = (gu)(t),$$
(22)

that by (10) becomes

$$(f_m u)(t) - u(t) \sum_{k=1}^{J} \frac{(f_m u)(z_k)}{u(z_k)} c_k(t) = (gu)(t),$$
(23)

where $c_k(t)$, $k = 1, \ldots, j$, are defined as

$$c_k(t) = t \int_{0}^{+\infty} k(te^{-z}, t)\ell_{m+1,k}(te^{-z})e^{-z}dz.$$
(24)

Now, collocating the equation (23) at the knots z_r , r = 1, ..., j, we obtain the linear system of order j

$$\sum_{k=1}^{j} \left[\delta_{r,k} - \frac{u(z_r)}{u(z_k)} c_k(z_r) \right] a_k = b_r, \quad r = 1, \dots, j,$$
(25)

where the unknowns are $a_k = (f_m u)(z_k)$, k = 1, ..., j, and the right-hand sides are $b_r = (gu)(z_r)$, r = 1, ..., j.

Finally, once the linear system (25) has been solved, one can compute the solution of the approximating equation (21). In fact if (a_1, \ldots, a_j) is a solution of the system (25), the Nyström interpolating function

$$f_m(t) = g(t) + \sum_{k=1}^{j} \frac{c_k(t)}{u(z_k)} a_k$$
(26)

is a solution of the equation (21) and vice versa. In this sense the linear system (25) and the finite-dimensional equation (21) can be considered equivalent.

Let us note that the multiplication by the weight u(t) on the both sides of equation (21) allows to avoid numerical problems in the computation of g belonging to the weighted space C_u . We recall that, under this assumption, the solution f of the integral equation (4) (and of equation (1)) also belongs to the space C_u if the hypotheses of Theorem 2.3 are satisfied. Moreover, this choice will be crucial in order to prove the well conditioning of the linear system (25).

The following theorem establishes the stability and convergence of the proposed numerical method.

Theorem 3.1. Under the same assumptions of Theorem 2.3, for all sufficiently large m (say $m \ge m_0$), the approximate inverses $(I - K_m)^{-1} : C_u \to C_u$ exist and are uniformly bounded. Moreover, the Nyström interpolants f_m converge in C_u to the exact solution f of (1). In particular, if $f \in W_r(u)$, for some $r \ge 1$, the following error estimate is fulfilled

$$\|f - f_m\|_u \le \frac{\mathcal{C}}{m^{\frac{r}{2}}} \|f\|_{W_r(u)}, \quad m \ge m_0,$$
(27)

where C does not depend on m and f. Finally, the condition number in uniform norm of the coefficient matrix A_m of system (25) satisfy

$$\sup_{m\geq m_0}\operatorname{cond}(A_m)\leq \mathcal{C},$$

where C is independent of m.

3.1. Computational aspects

As described in the previous subsection, the proposed numerical procedure simply consists in solving the linear system (25) and computing the approximating function given in (26) by using the solution of (25).

However, we note that a difficulty could arise in the practical computation of the integrals $c_k(t)$, k = 1, ..., j, $t \in \mathbb{R}^+$, which is necessary both in computing the entries of the coefficient matrix of the system (25) and in evaluating the Nyström interpolant (26). When their analytical expressions are not available or their computation requires too much effort, we propose to approximate them using the truncated Gauss-Laguerre quadrature rule (14) i.e. we approximate $c_k(t)$ by the quantity

$$c_{k,m}(t) = t \sum_{i=1}^{j} \lambda_i k(te^{-z_i}, t) \ell_{m+1,k}(te^{-z_i}).$$

In this way, we get the following new linear system

$$\sum_{k=1}^{J} \left[\delta_{r,k} - \frac{u(z_r)}{u(z_k)} c_{k,m}(z_r) \right] \bar{a}_k = b_r, \quad r = 1, \dots, j.$$
(28)

If $(\bar{a}_1, \ldots, \bar{a}_j)$ is a solution of the system (28), then the function

$$\bar{f}_m(t) = g(t) + \sum_{k=1}^j \frac{c_{k,m}(t)}{u(z_k)} \bar{a}_k$$
⁽²⁹⁾

is a solution of the finite dimensional equation

$$(I - \bar{K}_m)\bar{f}_m = g,\tag{30}$$

with the operator \bar{K}_m defined as

$$(\bar{K}_m f)(t) = t \sum_{i=1}^{j} \lambda_i k(t e^{-z_i}, t) L_{m+1}^*(f, t e^{-z_i}),$$
(31)

and vice versa.

The following theorem provides a comparison between the condition numbers of systems (25) and (28). Furthermore an estimate for the error $||f - \bar{f}_m||_u$ is given, being f and \bar{f}_m the solutions of (1) and (30), respectively.

Theorem 3.2. Let us assume that the assumptions of Theorem 2.3 are satisfied for $\gamma = \frac{1}{4}$ and $\delta \ge 0$. Further assume that

$$\sup_{t\geq 0} \|k_t\|_{W_r} < +\infty, \tag{32}$$

for any $r \ge 1$. Denoting by A_m and \bar{A}_m the matrices of the coefficients of systems (25) and (28), respectively, then

$$\lim_{m} \frac{\operatorname{cond}(A_m)}{\operatorname{cond}(A_m)} = 1$$

Moreover, if $f, \bar{f}_m \in W_r(u)$, for some $r \ge 1$,

$$\|f - \bar{f}_m\|_u \le C \frac{\log m}{m^{\frac{r}{2}}} \|\bar{f}_m\|_{W_r(u)},$$
(33)

where $C \neq C(m, f)$.

4. Numerical examples

In this section we will show the performances of the proposed numerical method in the resolution of some test integral equations of type (1). Moreover, in Subsection 4.1 we will present the numerical results obtained by applying it for solving some special Volterra integral equations arising in the resolution of a metastatic tumor growth model. All the computations have been performed in double arithmetics.

In particular, in the first example we will take an integral equation whose exact solution f is known and we will compute the weighted error

$$e_m(f)_u = \max_{t \in X} |(f(t) - \bar{f}_m(t))u(t)|,$$

where *X* is a sufficiently large uniform mesh of the interval [0, d]. In the second example, since the solution of the considered integral equation is unknown, we will report the absolute error defined as above but with *f* replaced by \overline{f}_{1024} .

In agreement with Theorems 3.1 and 3.2, the errors $e_m(f)_u$ tend to 0 for increasing values of m and for any choice of the interval [0, d] and the condition numbers in uniform norm are uniformly bounded with respect to m. In particular, the values of the condition numbers, computed using the MatLab function cond.m, are very close to 1.

We point out that even if in the computation of $e_m(f)_u$ the parameter *d* can be arbitrarily chosen, a more efficient choice of *d* can be done taking into account the vanishing behavior of $\overline{f}_m u$ at infinity (see Tables 1 and 3).

The method essentially consists in solving the linear system (25) or (28) of order *j*, where *j* is defined in (9), and in constructing the approximating solution $f_m(t)$ or $\overline{f}_m(t)$ by using (26) or (29), respectively. In our tests we take $\theta = \frac{1}{4}$. In the implementation of the truncated interpolation process defined by (10) and of the truncated quadrature formula given in (14). We point out that this choice of the parameter θ allows us to reduce almost of one half the dimension of the linear systems to solve without any loss of accuracy in the approximation of the solution *f*(*t*). Moreover, we note that the linear systems (25) and (28) do not depend on the point *t* where we would like to compute the approximating solution. Then we need to solve only one linear system of dimension *j* whatever is the number of the evaluation points.

Example 4.1. We consider the following integral equation

$$f(t) - \int_{0}^{t} \frac{e^{-\frac{s}{2}}}{(s+t+10)^{2}} f(s) \, ds = g(t),$$

Table 1			
Example	4.1,	d =	15.

т	j	$e_m(f)_u$	$\operatorname{cond}(\bar{A}_m)$
8	5	2.1874e – 05	1.0108
16	10	2.3863e - 07	1.0120
32	19	2.1852e – 10	1.0278
64	39	3.4416e – 15	1.0132

Table 2 Example 41

Example	- 1.1 .
d	$e_{64}(f)_u$
50	3.6082 <i>e</i> - 15
100	3.2751e – 15
500	2.9976e – 15
1000	2.9976e - 15

Table 3			
Example	4.2,	d =	6

	т	j	$e_m(f)_u$	$\operatorname{cond}(\bar{A}_m)$
Ī	8	5	1.1135e – 04	1.0104
	16	10	3.7856e – 05	1.0140
	32	19	1.5291e – 06	1.0163
	64	39	7.9058e - 08	1.0168
	128	78	5.7575e – 10	1.0171
	256	156	4.1424e – 11	1.0173
	512	312	5.7134e – 12	1.0171

4.2.
$e_{512}(f)_u$
3.6082 <i>e</i> - 12
3.3367 <i>e</i> – 12
5.9852e – 13
1.2632e – 13

with $g(t) = t - \frac{1}{2} \left(-2 + \frac{e^{-\frac{t}{2}}(t+10)}{(t+5)} + e^{5+\frac{t}{2}}(t+12) \left(E_i(-t-5) - E_i\left(-5 - \frac{t}{2}\right) \right) \right)$, where $E_i(t) = -\int_{-t}^{\infty} \frac{e^{-s}}{s} ds$ is the exponential integral function. The exact solution is f(t) = t. In Table 1 we show the absolute errors computed with d = 15 and the condition numbers of the solved linear systems. As one can see, solving a well conditioned linear system of order 39, we can approximate the solution with 14 exact decimal digits in the weighted space C_u , with $\gamma = \frac{1}{4}$ and $\delta = 0$, where the solution lives. Such accuracy is achieved also when larger values of d are considered (see Table 2). According to Theorem 3.2, this fast convergence is due to the fact that the solution is very smooth.

Example 4.2. Let us take the following Volterra integral equation

$$f(t) - \int_{0}^{t} \frac{e^{-\frac{s}{2}} \sin(\log(s^{2} + t + 1))}{(s^{2} + t^{2} + 2)^{4}} f(s) \, ds = \frac{|t - 2|^{\frac{7}{2}}}{(2 + t^{2})^{3}}$$

whose exact solution is unknown. The absolute errors computed with d = 6 along with the condition numbers of the involved linear systems are reported in Table 3. Since in this case the right-hand side is not smooth, it is necessary to increase *m* in order to improve the accuracy of the approximate solution. In particular, solving a linear system of order 312 the solution is approximated with 10 exact decimal digits in the weighted space C_u , with $\gamma = \frac{1}{4}$ and $\delta = 0$. Larger values of *d* are considered in Table 4.

4.1. An application to the resolution of a metastatic tumor growth model

In [19] the following mathematical model describing the dynamics of the metastatic colony size distribution is introduced

$$\begin{cases} \frac{\partial}{\partial t}\rho(x,t) + \frac{\partial}{\partial x}[\sigma(x)\rho(x,t)] = 0, & x \in [1,b), t \ge 0\\ \sigma(1)\rho(1,t) = \beta(x_p(t)) + \int_{1}^{b} \beta(x)\rho(x,t) dx, & t \in (0,+\infty),\\ \rho(x,0) = 0, & x \in [1,b). \end{cases}$$
(34)

In this model *x* represents the tumor size, i.e. the number of cells in the tumor, and b > 1 is the tumor size at the saturated level. The unknown solution is the metastatic density $\rho(x, t)$ i.e. the colony size distribution with cells number *x* at time *t*. Moreover, $x_p(t)$ represents the number of cells in the primary tumor at time *t*. It grows with rate $\sigma(x)$ per unit time and it is assumed to be generated by $x_0 = 1$ cell at time t = 0. The growing tumor emits metastatic cells with the rate

$$\beta(x) = \mu x^{\alpha}$$
,

where μ is the colonization coefficient and α is the fractal dimension of blood vessels infiltrating the tumor.

In many cases, the quantity of interest is a biological observable, as the total metastatic burden M(t), the total number of metastases N(t) or the cumulative number $N_c(t)$ of metastases whose size is larger than c, at time t. They can be represented as a weighted integral of the metastatic density of the following form

$$F_{\phi}(t) = \int_{1}^{b} \phi(x)\rho(x,t) dx$$

and, in particular, one has

t

$$F_{\phi}(t) = \begin{cases} M(t) & \text{if } \phi(x) = x \\ N(t) & \text{if } \phi(x) = 1 \\ N_{c}(t) & \text{if } \phi(x) = \chi_{x \ge c}(x) \end{cases}$$
(35)

with $\chi_{x>c}$ the characteristic function of the interval $[c, +\infty)$.

In [16,17] the PDE model (34) has been reformulated into the following Volterra integral equations whose unknowns are the biological observables given by (35)

$$M(t) - \int_{0}^{1} k(s, t) M(s) \, ds = g_1(t), \quad t \ge 0, \tag{36}$$

$$N(t) - \int_{0}^{t} k(s,t)N(s) \, ds = g_2(t), \quad t \ge 0, \tag{37}$$

and

$$N_{c}(t) - \int_{0}^{t} k(s,t) N_{c}(s) \, ds = g_{3}(t), \quad t \ge 0.$$
(38)

When the Gompertzian growth rate model $\sigma(x) = ax \log(b/x)$ is adopted the known functions involved in (36)-(38) take the following expressions

$$k(s,t) = \mu \left[b \left(\frac{1}{b}\right)^{e^{-a(t-s)}} \right]^{\alpha},$$

$$g_{1}(t) = \int_{0}^{t} b \left(\frac{1}{b}\right)^{e^{-a(t-s)}} \mu \left[b \left(\frac{x_{0}}{b}\right)^{e^{-as}} \right]^{\alpha} ds,$$

$$g_{2}(t) = \int_{0}^{t} \mu \left[b \left(\frac{x_{0}}{b}\right)^{e^{-as}} \right]^{\alpha} ds,$$
(39)

Table 5

_ . . .

Condition numbers of the linear systems arising in the resolution of (36)-(38).

т	j	$cond(\bar{A}_m)$
8	5	1.000006485389099
16	10	1.000010296197991
32	19	1.000014173184103
64	39	1.000016592265398
128	78	1.000018477932370
256	156	1.000019760800370
512	312	1.000022741926087

Table 6			
Approximations of th	e metastatic	mass	M(t).

t (days)	M(t)	$\bar{e}_{256}(M,t)$
10	9.5761540409707e – 07	2.2113e – 16
20	3.43738092921289e - 06	2.4641 <i>e</i> – 16
50	4.76102391692788e - 05	1.4232e – 16
100	1.41371616606773e – 03	6.1353e – 16
200	3.338101325088806e - 01	0
300	2.76657047364006e + 01	1.5409e – 15
400	1.117371320370793 <i>e</i> + 03	2.0348e – 16
500	2.6397724751520e + 04	1.3781e – 15
1000	9.99350249e + 08	4.5073e – 11
1500	2.1098648e + 11	6.3736e – 10
2000	4.95535e + 12	4.2673e - 08

$$g_{3}(t) = \int_{0}^{t+\frac{\log\left(\log_{\frac{1}{b}}\left(\frac{c}{b}\right)\right)}{\int_{0}^{a}}} \mu\left[b\left(\frac{x_{0}}{b}\right)^{e^{-as}}\right]^{\alpha} ds.$$

The values of the four parameters a, b, μ and α involved into the model described above were estimated in [19] in the clinical scenario of a patient having multiple metastatic tumors in the liver with a hepatocellular carcinoma as a primary tumor. Assuming that the primary tumor started from a single cell, i.e. $x_0 = 1$, the results were the following

$$a = 2.86 \cdot 10^{-3} \,\text{day}^{-1}, \qquad b = 7.3 \cdot 10^{10} \,\text{cells},
\mu = 5.3 \cdot 10^{-8} \,(\text{cells day})^{-1}, \qquad \alpha = 0.663.$$
(40)

In order to apply the proposed numerical method for solving integral equations (36)-(38), the integrals $g_1(t)$, $g_2(t)$ and $g_3(t)$ at the right-hand sides have been approximated by means of the truncated Gaussian quadrature rule (14). Since the dependence on the time of the parameters *a* and μ defined in (40) is expressed in days, the method computes all the biological observables M(t), N(t) and $N_c(t)$ as functions of the number of days *t*. If we multiply the parameters *a* and μ by a coefficient \mathcal{K} , in correspondence of the input parameter *t*, the method provides approximations of the observables related to $\mathcal{K}t$ days. A suitable choice of \mathcal{K} let us to improve the performances of the method for larger numbers of days. Indeed, the computation of the approximated solution in an unweighted function space could be affected by loss of accuracy when *t* becomes large enough.

We highlight that we always reduce to solve a very well conditioned linear system, as confirmed by the condition numbers reported in Table 5, where \bar{A}_m is the matrix of coefficients of linear system (28) corresponding to the kernel k(s, t) in (39) common to the integral equations (36)-(38).

In Table 6 we show the approximated values of the metastatic mass M(t), solution of equation (36), for increasing numbers of days t, obtained with j = 156 (m = 256). The approximations are reported with the significative digits that we can consider to be correct according to the relative errors $\bar{e}_{256}(M, t)$, where

$$\bar{e}_m(f,t) = \frac{|\bar{f}_{1024}(t) - \bar{f}_m(t)|}{|\bar{f}_{1024}(t)|}.$$

The metastatic mass growth is showed in Fig. 1 and the behavior of the corresponding relative errors $\bar{e}_m(M, t)$ is illustrated in Fig. 2. In particular one can see that, for $t \le 200$, the relative errors obtained both for j = 78 and for j = 156 are at least of order 10^{-14} (some of the relative errors for j = 156 are also reported in Table 6). By comparing Fig. 2 with Figure 6 (left) in [16], it can be seen that our method allows us to obtain smaller errors than those reported there. In particular, we get relative errors of order 10^{-6} already solving linear systems of dimension j = 39.



Fig. 1. Graphical behavior of the metastatic mass M(t).



Fig. 2. Relative errors $\bar{e}_m(M, t)$ for the approximations of the metastatic mass.

Table 7 Comparisons with the results in [19].						
t (days)	N(t) [19]	N(t)		N(t)	t (days) [19]	t (days)
1100	135	128		135	1100	1110.5
1227	263	249		263	1227	1237
1300	396	373		396	1300	1310.5
1400	712	670		712	1400	1410

Applying the method for solving equation (37), we get the total number N(t) of the metastases after t days. In Fig. 3 we show how N(t) grows for t up to 7000 days and in Fig. 4 the graphs of the corresponding relative errors are presented for different choices of the dimensions j of the solved linear systems.

We compared the results obtained for N(t) with the ones presented in [19] and [6]. In the second and third column of Table 7 on the left we show the values obtained for N(t) in [19, p. 181] and the ones obtained for the same values of t using our method, respectively. Inspecting Table 7 on the right one can see that we get the results predicted for N(t) in [19, p. 181] with a delay of only about 10 days. In Table 8 we made analogous comparisons with the results presented in [6, Table 3, p. 8]. We note that in [6, Table 3, p. 8] the authors make also a comparison with the results obtained in [19, p. 181] and, expressing the time in years, they give the results for 3, 3.4, 3.6 and 3.8 years corresponding to 1095, 1241, 1314 and 1387 days, respectively.

Finally, we applied our method for solving equation (38), obtaining the cumulative number $N_c(t)$ of metastases whose size is larger than *c*. In Fig. 5 we compare the values of $N_c(t)$ for increasing values of the colony size *c* at four successive observation times expressed in days. Our results are in line with the ones showed in [19, Fig. 4 (a)]. Moreover, in Figs. 6–8



Fig. 3. Graphical behavior of the growth of the total number N(t) of metastases.



Fig. 4. Relative errors $\bar{e}_m(N, t)$ for the total number of metastases.

$t (\text{days}) = N(t) \begin{bmatrix} 6 \end{bmatrix} = N(t)$ $N(t) = t (\text{days}) \begin{bmatrix} 6 \end{bmatrix} = t (\text{days})$)
1095 134 124 134 1095 1109	
1241 260 268 260 1241 1235	
1314 396 404 396 1314 1310.5	
1387 718 620 718 1387 1411.5	

we show the evolution of the number of metastases larger than different sizes. In particular, in Fig. 6 we compared the number of the total numbers of metastases and the number of metastases larger than 10^8 cells after 3 years and in Figs. 7 and 8 we compared the number of metastases larger than 10^8 cells and larger than 10^9 cells after 3 and 5 years. A good agreement with the results in [6, Fig. 3 and Fig. 4] can be deduced.

5. Proofs

We first prove Lemma 2.1.

Proof of Lemma 2.1. We have to prove only (13). Denoting by $P_M \in \mathbb{P}_M$ the polynomial of best approximation of f in C_u of degree $M = \lfloor \frac{\theta m}{1+\theta} \rfloor$, we have

$$\|[L_{m+1}^*(f)]^{(r)}\varphi^r\|_{u} \le \|[L_{m+1}^*(f-P_M)]^{(r)}\varphi^r\|_{u} + \|[L_{m+1}^*(P_M)]^{(r)}\varphi^r\|_{u}.$$

Table 8



Fig. 5. Cumulative number $N_c(t)$ of metastases as a function of the colony size *c* (in cells) obtained with j = 156 (m = 256).



Fig. 6. Comparison of the total number of metastases and the number of metastases larger than 10⁸ cells after 3 years.



Fig. 7. Comparison of the number of metastases larger than 10^8 cells and larger than 10^9 cells after 3 years.

In order to estimate the first term at the right hand side we use [28, (26)]

$$\|Q^{(r)}\varphi^r\|_u \leq \mathcal{C}m^{\frac{1}{2}}\|Q\|_u, \quad \forall Q \in \mathbb{P}_m,$$

where $C \neq C(m)$. Concerning the second term we recall [28, Lemma 2.1]



Fig. 8. Comparison of the number of metastases larger than 10^8 cells and larger than 10^9 cells after 5 years.

$$\|[L_{m+1}^{*}(P_{M})]^{(r)}\varphi^{r}\|_{u} \leq Cm^{\frac{r}{2}} \int_{0}^{\frac{1}{\sqrt{m}}} \frac{\Omega_{\varphi}^{r}(f, y)_{u}}{y} \, dy + Ce^{-Am} \|f\|_{u},$$

where $A \neq A(m, f)$, $C \neq C(m, f)$ and

$$\Omega_{\varphi}^{r}(f, y)_{u} = \sup_{0 < y \le h} \sup_{t \in I_{rh}} \left| (\Delta_{h\varphi}^{r} f)(t) u(t) \right|, \quad I_{rh} = [8r^{2}h^{2}, Ch^{-2}],$$

with

$$\Delta_{h\varphi}^r f(t) = \sum_{i=0}^r (-1)^i \binom{r}{i} f\left(t + h\varphi(t)(r-i)\right),$$

the main part of the φ -modulus of smoothness. We get

$$\|[L_{m+1}^*(f)]^{(r)}\varphi^r\|_{u} \leq Cm^{\frac{r}{2}}\|L_{m+1}^*(f-P_M)\|_{u} + Cm^{\frac{r}{2}}\int_{0}^{\frac{1}{\sqrt{m}}}\frac{\Omega_{\varphi}^r(f,y)_{u}}{y}\,dy + Ce^{-Am}\|f\|_{u}.$$

Taking into account (11) and that, for $f \in W_r(u)$, [25, p. 1048]

$$\Omega_{\varphi}^{r}(f, y)_{u} \leq \mathcal{C}y^{r} \| f^{(r)} \varphi^{r} \|_{u}$$

and (8) hold true, we get

$$\begin{aligned} \|[L_{m+1}^*(f)]^{(r)}\varphi^r\|_{u} &\leq \mathcal{C}m^{\frac{r}{2}}\log m E_M(f)_{u} + \mathcal{C}\|f^{(r)}\varphi^r\|_{u} + \mathcal{C}e^{-Am}\|f\|_{u} \\ &\leq \mathcal{C}\log m \|f\|_{W_r(u)}, \end{aligned}$$

i.e. (13).

In order to prove Theorems 2.3 and 3.1, we need the following lemmas.

Lemma 5.1. Let $u(t) = t^{\gamma} (1+t)^{\delta} e^{-\frac{t}{2}}$ with $\gamma \leq \frac{1}{4}$ and $\delta \geq \frac{1}{4} - \gamma$ and let us assume that the kernel k satisfies (17), then we have $\sup_{m} \|K_m\|_{C_u \to C_u} < +\infty.$

$$u(t)|(K_m f)(t)| = u(t) \left| \int_0^t k(s, t) L_{m+1}^*(f, s) ds \right|$$

$$\leq \int_{0}^{+\infty} |u(t)k(s,t)| |L_{m+1}^*(f,s)| ds$$
$$\leq C ||f||_u. \quad \Box$$

Lemma 5.2. Let $u(t) = t^{\gamma} (1+t)^{\delta} e^{-\frac{t}{2}}$ with $\gamma \leq \frac{1}{4}$ and $\delta \geq \frac{1}{4} - \gamma$ and let us assume that the kernel k satisfies (17) and (18), then the sequence $\{K_m\}_m, K_m : C_u \to C_u$, is collectively compact.

Proof. The thesis follows from Lemma 2.2 and the Ascoli-Arzelá theorem. In fact

$$\begin{split} |u(t+h)(K_mf)(t+h) - u(t)(K_mf)(t)| &= \left| \int_0^t \left(u(t+h)k(s,t+h) - u(t)k(s,t) \right) L_{m+1}^*(f,s) ds \right. \\ &+ \int_t^{t+h} \left(u(t+h)k(s,t+h) - u(t)k(s,t) \right) L_{m+1}^*(f,s) ds \\ &+ \int_t^{t+h} u(t)k(s,t) L_{m+1}^*(f,s) ds \right| \\ &\leq \int_0^t |u(t+h)k(s,t+h) - u(t)k(s,t)| |L_{m+1}^*(f,s)| ds \\ &+ \int_t^{t+h} |u(t+h)k(s,t+h) - u(t)k(s,t)| |L_{m+1}^*(f,s)| ds \\ &+ \int_t^{t+h} |u(t)k(s,t)| |L_{m+1}^*(f,s)| ds \\ &\leq 2 \int_0^{+\infty} |u(t+h)k(s,t+h) - u(t)k(s,t)| |L_{m+1}^*(f,s)| ds \\ &+ \int_0^{+\infty} |u(t)k(s,t)\chi_{[t,t+h]}(s)| |L_{m+1}^*(f,s)| ds \\ &+ \int_0^{+\infty} |u(t)k(s,t)\chi_{[t,t+h]}(s)| |L_{m+1}^*(f,s)| ds \\ &+ \int_0^{+\infty} |u(t)k(s,t)\chi_{[t,t+h]}(s)| |L_{m+1}^*(f,s)| ds \\ &\leq 2 \rho \left(\frac{u(t+h)k_{t+h} - u(t)k_t}{\sqrt{w_0\varphi}} \right) \|f\|_u + \rho \left(\frac{u(t)k_t\chi_{[t,t+h]}}{\sqrt{w_0\varphi}} \right) \|f\|_u. \end{split}$$

Taking into account that if $\frac{u(t)k_t}{\sqrt{w_0\varphi}} \in \mathbf{L}\log^+ \mathbf{L}$ then

$$\lim_{h \to 0} \rho\left(\frac{u(t)k_t\chi_{[t,t+h]}}{\sqrt{w_0\varphi}}\right) = \lim_{h \to 0} \int_t^{t+h} \frac{|u(t)k(s,t)|}{\sqrt{w_0(s)\varphi(s)}} \left(1 + \log^+ \frac{|u(t)k(s,t)|}{\sqrt{w_0(s)\varphi(s)}}\right) ds = 0.$$

under the assumptions on k, we get

$$\lim_{h \to 0} \sup_{m} \sup_{\|f\|_{u} = 1} \|u(\cdot + h)(K_{m}f)(\cdot + h) - u(\cdot)(K_{m}f)(\cdot)\|_{\infty} = 0. \quad \Box$$

Lemma 5.3. Let $u(t) = t^{\gamma}(1+t)^{\delta}e^{-\frac{t}{2}}$ with $\gamma \leq \frac{1}{4}$ and $\delta \geq \frac{1}{4} - \gamma$. Assuming that the kernel k satisfies (16) and (17), we have

$$\lim_m \|(K-K_m)f\|_u = 0, \quad \forall f \in C_u.$$

Proof. We have

$$(Kf)(t) - (K_m f)(t) = t \int_0^{+\infty} k(te^{-z}, t) [f(te^{-z}) - L_{m+1}^*(f, te^{-z})]e^{-z}dz$$
$$= \int_0^t k(s, t) [f(s) - L_{m+1}^*(f, s)]ds.$$

Denoting by $P_M \in \mathbb{P}_M$ the polynomial of best approximation of $f \in C_u$ of degree $M = \lfloor \frac{\theta m}{1+\theta} \rfloor$, we get

$$\begin{aligned} |(Kf)(t) - (K_m f)(t)|u(t) &\leq \int_0^{+\infty} \frac{u(t)}{u(s)} |k(s,t)|| f(s) - P_M(s)|u(s)ds \\ &+ \int_0^{+\infty} \frac{u(t)}{u(s)} |k(s,t)|| P_M(s) - L_{m+1}^*(P_M,s)|u(s)ds \\ &+ \int_0^{+\infty} u(t)|k(s,t)|| L_{m+1}^*(P_M - f,s)|ds \\ &= \int_0^{+\infty} \frac{u(t)}{u(s)} |k(s,t)|| f(s) - P_M(s)|u(s)ds \\ &+ \int_0^{+\infty} \frac{u(t)}{u(s)} |k(s,t)|| L_{m+1}(P_M,s) - L_{m+1}^*(P_M,s)|u(s)ds \\ &+ \int_0^{+\infty} u(t)|k(s,t)|| L_{m+1}^*(P_M - f,s)|ds. \end{aligned}$$

Applying Lemma 2.2, under the assumptions on k(s, t), and taking into account [28, (35)], [25, p. 1055-1056]

 $|L_{m+1}(P_M, s) - L_{m+1}^*(P_M, s)|u(s) \le C \log m \, e^{-Am} \|P_M\|_u \le C \log m \, e^{-Am} \|f\|_u,$

where $C \neq C(m, P_M)$, we get

$$\|(K-K_m)f\|_u \leq \mathcal{C}E_M(f)_u.$$

Then, the thesis easily follows, being $M \sim m$. \Box

Now we are able to prove Theorem 2.3.

Proof of Theorem 2.3. Using [2, Lemma 4.1.2 p. 114] and Lemmas 5.1, 5.2 and 5.3, we deduce that the operator $K : C_u \to C_u$ is compact. Consequently, the equation (4) satisfies the Fredholm alternative and, then, under the assumption $\text{Ker}(I - K) = \{0\}$ in C_u , it has a unique solution f in C_u for any right-hand side $g \in C_u$. \Box

Proof of Lemma 2.4. It is easy to prove that the assumption (16) implies

$$\|Kf\|_{u} \leq \mathcal{C}\|f\|_{u}, \quad \mathcal{C} \neq \mathcal{C}(f).$$

Moreover, since for $r \ge 1$ one has

$$(Kf)^{(r)}(t) = \int_{0}^{t} \frac{\partial^{r}}{\partial t^{r}} k(s,t) f(s) ds + \sum_{j=0}^{r-1} f^{(j)}(t) \sum_{i=0}^{r-j-1} \mathcal{C}_{ij} \left. \frac{\partial^{r-j-1}}{\partial s^{i} \partial t^{r-j-1-i}} k(s,t) \right|_{s=t}$$

with C_{ij} positive constants depending only on i and j, we get

(41)

$$|(Kf)^{(r)}(t)\varphi^{r}(t)u(t)| \leq ||f||_{u}\varphi^{r}(t)u(t) \int_{0}^{t} \left| \frac{\partial^{r}}{\partial t^{r}}k(s,t) \right| \frac{ds}{u(s)} + C\sum_{j=0}^{r-1} ||f^{(j)}\varphi^{j}||_{u} \sum_{i=0}^{r-j-1} \varphi^{r-j}(t) \left| \frac{\partial^{r-j-1}}{\partial s^{i}\partial t^{r-j-1-i}}k(s,t) \right|_{s=t}$$

where C is a positive constant independent of f and k. Consequently, under the assumptions (19) and (20) and using an inequality in [13, proof of Lemma 6.3, p. 148], we have

$$||Kf||_{W_r(u)} \leq C ||f||_{W_{r-1}(u)},$$

i.e. if $f \in W_{r-1}(u)$ then $Kf \in W_r(u)$. Taking into account that f = g - Kf, under the assumption $g \in W_r(u)$, we deduce that $f \in W_r(u)$, too. \Box

Proof of Theorem 3.1. Applying [2, Theorem 4.1.1 p. 106] together with [2, Lemma 4.1.2 p. 114] and Lemmas 5.1, 5.2 and 5.3, we deduce that, for sufficiently large *m*, say $m \ge m_0$, the inverse operators $(I - K_m)^{-1}$ exist and are uniformly bounded, i.e. for $m \ge m_0$

$$\|(I - K_m)^{-1}\|_{C_u \to C_u} \le \frac{1 + \|(I - K)^{-1}\|_{C_u \to C_u} \|K_m\|_{C_u \to C_u}}{1 - \|(I - K)^{-1}\|_{C_u \to C_u} \|(K - K_m)K_m\|_{C_u \to C_u}} \le \mathcal{C},$$
(42)

with $C \neq C(m)$, and

$$\|f - f_m\|_u \le \|(I - K_m)^{-1}\|_{\mathcal{C}_u \to \mathcal{C}_u}\|(K - K_m)f\|_u.$$
(43)

Consequently the method is stable and, since, by (41) and (42), (43) becomes

$$\|f - f_m\|_u \le \mathcal{C}E_M(f)_u,\tag{44}$$

from (7) we can deduce that it is also convergent. Furthermore, being $M \sim m$ and taking into account (8), from (44) estimate (27) trivially follows.

Moreover, if A_m is the matrix of the coefficients of system (25), proceeding as in [2, pp. 112-113], by Lemma 5.1 and (42), we deduce that

$$\operatorname{cond}(A_m) \leq \operatorname{cond}(I - K_m) \leq \mathcal{C} < +\infty, \quad \mathcal{C} \neq \mathcal{C}(m). \quad \Box$$

In order to prove Theorem 3.2 we need the following lemmas concerning some properties of the operator \bar{K}_m defined in (31).

Lemma 5.4. Let $u(t) = t^{\gamma}(1+t)^{\delta}e^{-\frac{t}{2}}$ with $\frac{1}{4} \leq \gamma < \frac{1}{2}$ and $0 \leq \delta \leq 1$. Assuming that the kernel k satisfies

```
\sup_{t\geq 0}\|k_t\|_{\infty}<+\infty,
```

we have for the linear operator $\bar{K}_m : C_u \to C_u$

 $\|\bar{K}_m\|_{C_n\to C_n} \leq \mathcal{C}\log m,$

where $C \neq C(m, f)$.

Proof. We have

$$\begin{split} |(\bar{K}_m f)(t)|u(t) &\leq u(t)t \sum_{i=1}^j \lambda_i |k(te^{-z_i}, t)| |L_{m+1}^*(f, te^{-z_i})| \\ &\leq \|k_t\|_{\infty} \sum_{i=1}^j \lambda_i |L_{m+1}^*(f, te^{-z_i})|u(te^{-z_i}) \frac{tu(t)}{u(te^{-z_i})} \\ &\leq \|k_t\|_{\infty} \|L_{m+1}^*(f)\|_u \sum_{i=1}^j \lambda_i \frac{tu(t)}{u(te^{-z_i})}. \end{split}$$

Now, taking into account that [26] $\lambda_i \sim \Delta z_i w_0(z_i)$, i = 1, ..., m, and that [12, Lemma 4.1] (see, also, [28, p. 609]) $w_0(z_i) \sim w_0(z)$ for $z_i < z < z_{i+1}$, for $\delta \ge 0$ we have

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$$\sum_{i=1}^{j} \lambda_i \frac{tu(t)}{u(te^{-z_i})} \le C \sup_{t\ge 0} \int_0^{+\infty} \frac{tu(t)e^{-z}}{u(te^{-z})} dz \le C.$$
(45)

Then, using (11) we get

$$\begin{aligned} |(\bar{K}_m f)(t)|u(t) &\leq \mathcal{C}\log m \, \|k_t\|_{\infty} \|f\|_u \sup_{t\geq 0} \int_0^{+\infty} \frac{tu(t)u(z)}{u(te^{-z})} dz \\ &\leq \mathcal{C}\log m \|k_t\|_{\infty} \|f\|_u. \quad \Box \end{aligned}$$

Lemma 5.5. Let $u(t) = t^{\gamma}(1+t)^{\delta}e^{-\frac{t}{2}}$ with $\frac{1}{4} \leq \gamma < \frac{1}{2}$, $0 \leq \delta \leq 1$ and let $r \geq 1$. For $f \in W_r(u)$ and the kernel k satisfying (32) we have

$$\|K_m f - \bar{K}_m f\|_u \le \frac{\mathcal{C}}{m^{\frac{r}{2}}} \log m \left(\sup_{t \ge 0} \|k_t\|_{W_r} \right) \|f\|_{W_r(u)},$$

where $C \neq C(m, f, k_t)$.

Proof. Since $(\bar{K}_m f)(t)$ is the approximation of $(K_m f)(t)$ by means of the truncated Gaussian rule (14) we have

$$u(t)|(K_m f)(t) - (\bar{K}_m f)(t)| = u(t)t|R_m(H_t)|,$$
(46)

where $H_t(z) = G(te^{-z}, t)$ with $G(s, t) = k(s, t)L_{m+1}^*(f, s)$ and, using estimate (15) for the quadrature error, we get

$$u(t)t|R_m(H_t)| \le C \Big[u(t)tE_M(H_t)_u + e^{-Am}u(t)t||H_t||_u \Big].$$
(47)

Taking into account (11), for $\gamma < \frac{1}{2}$ and $\delta \ge 0$, we get

$$\begin{aligned} u(t)t \|H_t\|_u &= \max_{z \ge 0} \frac{u(t)tu(z)}{u(te^{-z})} |k(te^{-z}, t)L_{m+1}^*(f, te^{-z})u(te^{-z})| \\ &\leq \|k_t\|_{\infty} \|L_{m+1}^*(f)\|_u \max_{z,t \ge 0} \frac{(1+t)^{\delta} te^{-\frac{t}{2}(1-e^{-z})} z^{\gamma}(1+z)^{\delta} e^{-\frac{z}{2}(1-2\gamma)}}{(1+te^{-z})^{\delta}} \\ &\leq \mathcal{C} \log m \|k_t\|_{\infty} \|f\|_u. \end{aligned}$$

$$(48)$$

Applying (8) we obtain

$$u(t)tE_{M}(H_{t})_{u} \leq \frac{\mathcal{C}}{m^{\frac{r}{2}}}u(t)t\|H_{t}^{(r)}\varphi^{r}\|_{u}.$$
(49)

Note that, with $F(z) = f(te^{-z})$ we have

$$|F^{(r)}(z)| \le C(r) \sum_{k=1}^{r} |f^{(k)}(te^{-z})(te^{-z})^{k}|$$

and

$$\begin{split} |F^{(r)}(z)\varphi^{r}(z)u(z)| &\leq \mathcal{C}(r)\frac{\varphi^{r}(z)u(z)}{u(te^{-z})}\sum_{k=1}^{r} \left| f^{(k)}(te^{-z})(te^{-z})^{\frac{k}{2}}u(te^{-z}) \right| (te^{-z})^{\frac{k}{2}} \\ &\leq \mathcal{C}(r)\frac{\varphi^{r}(z)u(z)}{u(te^{-z})}\sum_{k=0}^{r} \left\| f^{(k)}\varphi^{k} \right\|_{u} (te^{-z})^{\frac{k}{2}}. \end{split}$$

By [14, Lemma 2.1], if $0 \le t \le 1$ we get

$$|F^{(r)}(z)\varphi^{r}(z)u(z)| \leq C(r)\frac{t^{\frac{1}{2}}e^{-\frac{z}{2}}\varphi^{r}(z)u(z)}{u(te^{-z})}||f||_{W_{r}(u)}$$

while for $t \ge 1$

$$|F^{(r)}(z)\varphi^{r}(z)u(z)| \leq C(r)\frac{t^{\frac{r}{2}}e^{-\frac{z}{2}}\varphi^{r}(z)u(z)}{u(te^{-z})}||f||_{W_{r}(u)}.$$

Then, for $\gamma < \frac{1}{2}$ and $\delta \ge 0$, being h = 1 for $0 \le t \le 1$ and h = r for $t \ge 1$, we get

$$\begin{split} u(t)t \| H_t^{(r)} \varphi^r \|_u &\leq \mathcal{C} \| G_t \|_{W_r(u)} \max_{z,t \geq 0} \frac{u(t)tt^{\frac{h}{2}} e^{-\frac{z}{2}} \varphi^r(z) u(z)}{u(te^{-z})} \\ &\leq \mathcal{C} \| G_t \|_{W_r(u)} \max_{z,t \geq 0} \frac{(1+t)^{\delta} t^{1+\frac{h}{2}} e^{-\frac{t}{2}(1-e^{-z})} z^{\gamma+\frac{r}{2}} (1+z)^{\delta} e^{-\frac{z}{2}(1-2\gamma)}}{(1+te^{-z})^{\delta}} \\ &\leq \mathcal{C} \| G_t \|_{W_r(u)} \\ &\leq \mathcal{C} \Big[\| G_t \|_u + \| G_t^{(r)} \varphi^r \|_u \Big]. \end{split}$$

Since, by (11), we have

$$\|G_t\|_u \leq \mathcal{C}\log m \|k_t\|_{\infty} \|f\|_u$$

and, by [14, Lemma 2.1], (11) and (13),

$$\|G_t^{(r)}\varphi^r\|_{u} \le C\|L_{m+1}^*(f)\|_{W_r(u)}\|k_t\|_{W_r}$$

$$\le C\log m\|k_t\|_{W_r}\|f\|_{W_r(u)},$$

we obtain

$$u(t)t \|H_t^{(r)}\varphi^r\|_u \leq C \log m \|k_t\|_{W_r} \|f\|_{W_r(u)}.$$

Substituting the last inequality into (49), we deduce

$$u(t)tE_M(H_t)_u \leq \frac{C}{m^{\frac{r}{2}}}\log m ||k_t||_{W_r} ||f||_{W_r(u)}.$$

Finally, combining the last inequality with (48), (47) and (46), the thesis follows. \Box

Now we can prove Theorem 3.2.

Proof of Theorem 3.2. For a sufficiently large *m*, by Theorem 3.1, A_m^{-1} exists, then the identity

$$\bar{A}_m = A_m [I_m + A_m^{-1} (\bar{A}_m - A_m)]$$

holds true. Moreover, proceeding as in [2, pp. 112-113] it is easy to prove that

$$||A_m^{-1}|| \le ||(I-K_m)^{-1}||_{C_u \to C_u} \le C.$$

Now we estimate $||A_m - \bar{A}_m||$. Let $D(t) = \sum_{k=1}^{j} \frac{\ell_{m+1,k}(t)}{u(z_k)}$ and note that $D \in \mathbb{P}_m$. We have

$$\begin{split} \|A_m - \bar{A}_m\| &\leq \max_{1 \leq r \leq j} u(z_r) \left| \sum_{k=1}^{j} \frac{c_k(z_r) - c_{k,m}(z_r)}{u(z_k)} \right| \\ &= \max_{1 \leq r \leq j} u(z_r) \left| z_r \int_{0}^{+\infty} k(z_r e^{-z}, z_r) \left(\sum_{k=1}^{j} \frac{\ell_{m+1,k}(z_r e^{-z})}{u(z_k)} \right) e^{-z} dz \\ &- z_r \sum_{i=1}^{j} \lambda_i k(z_r e^{-z_i}, z_r) \left(\sum_{k=1}^{j} \frac{\ell_{m+1,k}(z_r e^{-z_i})}{u(z_k)} \right) \right| \\ &\leq \max_{t \geq 0} u(t) \left| t \int_{0}^{+\infty} k(t e^{-z}, t) D(t e^{-z}) e^{-z} dz - t \sum_{i=1}^{j} \lambda_i k(t e^{-z_i}, t) D(t e^{-z_i}) \right| \end{split}$$

Adding and subtracting $k(te^{-z}, t)L_{m+1}^*(D, te^{-z})e^{-z}$ in the integral and $\lambda_i k(te^{-z_i}, t)L_{m+1}^*(D, te^{-z_i})$ in the sum, we get

$$\begin{aligned} \|A_m - \bar{A}_m\| &\leq \max_{t \geq 0} u(t) \left| (K_m D)(t) - (\bar{K}_m D)(t) \right| \\ &+ \max_{t \geq 0} u(t) t \int_0^{+\infty} |k(te^{-z}, t)| \left| D(te^{-z}) - L_{m+1}^*(D, te^{-z}) \right| e^{-z} dz \\ &+ \max_{t \geq 0} u(t) t \sum_{i=1}^j \lambda_i |k(te^{-z_i}, t)| \left| D(te^{-z_i}) - L_{m+1}^*(D, te^{-z_i}) \right| \\ &=: B_1 + B_2 + B_3. \end{aligned}$$

Then applying Lemma 5.5 with f = D and r = m + 1 we get

$$B_1 \leq \frac{\mathcal{C}}{m^{\frac{m+1}{2}}} \log m\left(\sup_{t\geq 0} \|k_t\|_{W_{m+1}}\right) \|D\|_{W_{m+1}(u)},$$

and, since under our assumptions $\sup_{t\geq 0} \|k_t\|_{W_r} < +\infty$ for any $r\geq 1$, we deduce

$$B_1 \leq \frac{C}{m^{\frac{m+1}{2}}} \log m \|D\|_{W_{m+1}(u)}.$$

Concerning B_2 and B_3 , we have

$$B_2 \le \|k_t\|_{\infty} \|(D - L_{m+1}^*(D))u\|_{\infty} \int_{0}^{+\infty} \frac{tu(t)e^{-z}}{u(te^{-z})} dz$$

and

$$B_3 \le \|k_t\|_{\infty} \|(D - L_{m+1}^*(D))u\|_{\infty} \sum_{i=1}^j \lambda_i \frac{tu(t)}{u(te^{-z_i})}$$

Recalling (45) and using (12) we get

$$B_2 + B_3 \leq \mathcal{C} \|k_t\|_{\infty} \log m E_M(D)_u$$

and applying (8) with r = m + 1, under the assumptions on k_t , we obtain

$$B_2 + B_3 \le \frac{C}{m^{\frac{m+1}{2}}} \log m \|D\|_{W_{m+1}(u)}$$

Summing up we deduce

$$||A_m - \bar{A}_m|| \le C \frac{\log m}{m^{\frac{m+1}{2}}} ||D||_{W_{m+1}(u)}$$

and taking into account that $D \in \mathbb{P}_m$ we have

$$||A_m - \bar{A}_m|| \le C \frac{\log m}{m^{\frac{m+1}{2}}} \max_{t \ge 0} u(t)|D(t)|.$$

Consequently, using (11)

$$\|A_m - \bar{A}_m\| \le \frac{\mathcal{C}}{m^{\frac{m+1}{2}}} \log m \max_{t \ge 0} \sum_{k=1}^j \frac{u(t)|\ell_{m+1,k}(t)|}{u(z_k)} \le \mathcal{C} \frac{\log^2 m}{m^{\frac{m+1}{2}}}.$$

Therefore $\lim_m \|A_m^{-1}(\bar{A}_m - A_m)\| = 0$. Consequently $(\bar{A}_m)^{-1}$ exists for sufficiently large *m* and

$$\lim_{m} \frac{\operatorname{cond}(\bar{A}_m)}{\operatorname{cond}(A_m)} \leq 1.$$

On the other hand, we use the identity

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$$A_m = \bar{A}_m [I_m + (\bar{A}_m)^{-1} (A_m - \bar{A}_m)]$$

to prove that

$$\lim_{m} \frac{\operatorname{cond}(A_m)}{\operatorname{cond}(\bar{A}_m)} \le 1$$

and, consequently,

$$\lim_{m} \frac{\operatorname{cond}(A_m)}{\operatorname{cond}(A_m)} = 1$$

In order to prove (33), we write

$$||f - \bar{f}_m||_u \le ||f - f_m||_u + ||f_m - \bar{f}_m||_u.$$

For the first term at the right-hand side, using (27) and (8) under the assumption $f \in W_r(u)$, we get

$$||f - f_m||_u \leq \frac{\mathcal{C}}{m^{\frac{r}{2}}} ||f||_{W_r(u)}.$$

For the second term we have

$$||f_m - \bar{f}_m||_u \le ||(I + K_m)^{-1}|| ||(K_m - \bar{K}_m)\bar{f}_m||_u.$$

Then, using Lemma 5.5 and the assumption $\sup_{t>0} ||k_t||_{W_r} < +\infty$ for any $r \ge 1$, we get

$$\|f_m - \bar{f}_m\|_u \le \frac{\mathcal{C}}{m^{\frac{r}{2}}} \log m \left(\sup_{t \ge 0} \|k_t\|_{W_r} \right) \|\bar{f}_m\|_{W_r(u)} \\ \le \frac{\mathcal{C}}{m^{\frac{r}{2}}} \log m \|\bar{f}_m\|_{W_r(u)}.$$

Consequently, (33) follows. \Box

6. Conclusions

In the present paper we describe a new method for the computation of long-time solutions of linear Volterra integral equations of the second kind. By a proper change of variable the original equation is transformed into an equivalent integral equation on the positive semiaxis which is solved in suitable weighted function spaces by applying a Nyström type method. To this aim first we applied a truncated product quadrature rule, based on Gauss-Laguerre nodes along with an additional point, for the discretization of the integral in (2). Then we derive a Nyström interpolant of the solution (see (26)). A fully discretized version of the method is implemented when the so-called modified moments of the kernel (see (24)) cannot be computed analytically or their computation is too much expensive. The evaluation of the approximate solution leads to solve a well conditioned linear system whose dimension is reduced due to the use of a truncated Lagrange interpolation process underlying the construction of the employed product quadrature formula.

The numerical tests confirm the theoretical results. In particular the proposed method has been tested for the numerical resolution of some Volterra integral equations arising from the reformulation of differential models describing metastatic tumor growth where it is assumed that both the primary and the secondary tumors grow according to the Gompertzian growth model and emit metastases with the same emission rate. Hence the application of the proposed procedure allowed us to predict some biological observables as the metastatic mass or the number of metastases also at long times.

A generalization of the Iwata PDE model (34) to the case where primary and secondary tumors have different growths and emission rates can be obtained as well as its reformulation into a Volterra integral equation ([16,17]). In a forthcoming work we are going to apply the proposed procedure to solve the Volterra integral equations reformulating such more general PDE models. The new growth laws included in the study will comprise exponential, power, generalized logistic and von Bertalanffy laws, all of them already introduced in [7].

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