On Symbolic Approaches to Integro-Differential Equations

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Abstract Recent progress in computer algebra has opened new opportunities for the parameter estimation problem in nonlinear control theory, by means of integro-differential input-output equations. This paper recalls the origin of integro-differential equations. It presents new opportunities in nonlinear control theory. Finally, it reviews related recent theoretical approaches on integro-differential algebras, illustrating what an integro-differential elimination method might be and what benefits the parameter estimation problem would gain from it.

1 Introduction

Under the impulse of the founding papers of Fliess [25], a school of researchers developed an approach of nonlinear control theory formulated within the framework of Ritt and Kolchin differential algebra [34, 48]. This approach led to various constructive methods which were implemented on computer algebra software dedicated for differential algebra [10, 11]. In this context, the present paper is concerned with a parameter estimation method, which is connected to an algorithmic

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structural identifiability test, based on the computation of the so-called input-output equation of the parametric nonlinear dynamical system under investigation [20, 41]. Since numerical integration is often much less sensitive to noisy data than numerical differentiation, the parameter estimation step of this method provides more reliable estimates of parameters, by first transforming the input-output equation into an integro-differential equation. This idea has been tested on a range of examples [21, 22, 26, 40, 58, 59]. This important transformation of nonlinear differential equations to integro-differential ones, which so far has required some human skill, can now be achieved algorithmically [8, 13].

Integral equations have other advantages as compared to differential ones. First, they permit to handle non smooth functions, in particular, piecewise constant inputs [21, 22, 26]. Second, they may naturally depend on initial conditions: a feature which may be important for the parameter estimation problem. In both cases, it may be interesting to bypass differential elimination in order to compute the desired equation.

These results and this research were at least partially motivated by purely theoretical studies of the algebraic properties of integro-differential algebras and their operator rings [3–5, 27, 29, 45, 52]. In turn, they raise the fascinating and difficult task of extending the Ritt-Kolchin theory known as *differential algebra* to the broader theory *integro-differential algebra* since integral or integro-differential equations are not allowed within the framework of differential algebra. One important goal would be an elimination theory for integro-differential algebra. It would allow the computation of integro-differential input-output equations using a wider set of operations than in differential algebra, hence possibly faster computations as well as a greater variety of formulations for the input-output equations.

This paper is structured as follows. Section 2 recalls the origin of integro-differential equations. Here, the term “origin” carries two meanings: what are the first historic examples of integro-differential models? and what kind of modelling processes lead to such models? This section will prove interesting for readers who discover integro-differential equations and for algebraists who are not aware of the needs of modellers. Section 3 sketches the application to parameter estimation for nonlinear dynamical systems that motivated this new interest for integro-differential equations. This section will be interesting for applied researchers who are not aware of some key properties of Ritt and Kolchin differential algebra: properties that need not generalize to the integro-differential framework. Last, Section 4 reviews some attempts to design algebraic theories of integro-differential equations and some of the many issues that need to be addressed. It illustrates also, via two examples, what an integro-differential elimination method could be and what would be the benefit to the parameter estimation problem.

2 Origin of Integro-Differential Models

One of the simplest nonlinear integro-differential models studied in the literature is the Volterra-Kostitzin model [35, pages 66-69], which may be used for describing the evolution of a population, in a closed environment, intoxicated by its own metabolic products (other applications of the same model are considered in Kostitzin's book). It is an integro-differential equation since the unknown function $y(t)$ appears both differentiated and under some integral sign.

$$\frac{\mathrm{d}y}{\mathrm{d}t}(t) = \varepsilon\, y(t) - k\, y(t)^2 - c\, y(t) \int_{t-T}^{t} K(t-\tau)\, y(\tau)\, \mathrm{d}\tau\,.$$

The independent variable t is time. The dependent variable $y(t)$ is the population, varying with time. The symbols ε, k, c and T denote parameters. The *kernel* (or *nucleus*) $K(t,\tau) = K(t-\tau)$ is the *residual action function*. For instance, it could be very similar to a "survival function" in population dynamics [31, page 3]: a decreasing function, starting at $K(0) = 1$, equal to 0 outside the interval $[0, T]$. Then $K(t-\tau)$ would represent the "toxicity factor" of metabolic products which are the most toxic when produced, at $t = \tau$, become less toxic with the time, and have a negligible toxic effect at time $t = \tau + T$.

As we shall see later, nontrivial kernels introduce difficulties in the symbolic treatment of integro-differential equations. It is thus interesting to remark that a simplified version of the Volterra-Kostitzin model, with a trivial kernel $K(t,\tau) = 1$, was studied by Kostitzin himself (the model is then equivalent to a differential equation of order two). It was more recently reconsidered in [17] and [43, chapter 4] and fitted against experimental data, in order to validate its pertinence.

2.1 Hereditary Theories

In integral or integro-differential models, integral terms depend on kernels of the very special form $K(t,\tau) = K(t-\tau)$. Such kernels permit to express "hereditary", "historical" or "plastic" effects, i.e. the idea that the evolution of the current state of the system being modelled, depends not only on the current state but also on its past. The original qualifier is "hereditary". The qualifier "historical" was suggested by Volterra [62, page 300] to avoid any confusion with biological notions. The qualifier "plastic" (by opposition to "elastic") is used in structural mechanics [38, page 59].

2.1.1 Historical Origin

It is interesting to remark that biology is one of the first scientific domains where hereditary modelling was considered to be promising. In [60, page 295], Volterra claims to have coined the expression "integro-differential equation". A few lines further, he refers to an article by Picard [44], which contains the following paragraph (page 194), translated from French:

> But heredity plays especially a major role in life sciences and we do not know if we will ever be able to use the mathematical tool for the intimate study of biological phenomena, and if we will not always need to restrict ourselves to rough averages and frequency curves. We should not, however, reduce in advance our mathematical conception of the world, and we can dream of functional equations more complicated than the former [differential] ones because they will involve, in addition, integrals taken between a very distant past and the present time, integrals which will bring their part of heredity.

The study of hereditary models is strongly connected with the theory of functionals, i.e. functions z that depend on all the values that some other function $y(t)$ may take over some range $a \leq t \leq b$. This was investigated in detail by Volterra [63], who sketched hereditary formulations of magnetism, electricity, elasticity, $\ldots$ It is intimately related to the theory of the convolution product, which arises in distribution theory [24], and whose algebraic properties were much studied by Volterra, as a special case of the "composition" of two functions. See [63] for the theory and [16, pages 293-294] for more on the history.

2.2 *Some Classical Integro-Differential Models*

2.2.1 A Predator-Prey Model

The following integro-differential system [62, pages 328-329] models two populations: one of them feeds on the other. It enhances a classical Volterra model of population dynamics. Volterra models here the fact that the increase of population does not depend only on the current amount of food available but also on the food which was available in the past.

$$
\begin{aligned}
\frac{\mathrm{d}y_1}{\mathrm{d}t}(t) &= y_1(t)\,\left(\varepsilon_1 - \gamma_1\, y_2(t) - \int_0^t f_1(t-\tau)\, y_2(\tau)\,\mathrm{d}\tau\right)\,,\\
\frac{\mathrm{d}y_2}{\mathrm{d}t}(t) &= y_2(t)\,\left(-\varepsilon_2 + \gamma_2\, y_1(t) + \int_0^t f_2(t-\tau)\, y_1(\tau)\,\mathrm{d}\tau\right)\,.
\end{aligned}
\tag{1}
$$

2.2.2 Elastic Torsion of a Wire

This example is borrowed from [63, chapter V, pages 147-149]. To a first approximation the connection between the moment m of the torsional couple and the corresponding angle of torsion ω is given, in the case of static equilibrium, by the linear relation $\omega = k\,m$ where k is a constant depending on the characteristics of the wire. Let $m(\tau)$ denote the torsional moment acting on the wire at time τ. In order to find the angle of torsion $\omega(t)$ at time t we must add to the right-hand side of $\omega(t) = k\,m(t)$ a corrective term depending on all the values of $m(\tau)$ for τ prior to t, and therefore a *functional* of $m(\tau)$. Assume the hereditary effects modelled by this functional is linear. One then obtains the following relation between $\omega(t)$ and $m(t)$:

$$\omega(t) = k\, m(t) + \int_{-\infty}^{t} f(t,\tau)\, m(\tau)\,\mathrm{d}\tau\,. \tag{2}$$

Solving this Volterra integral equation [63, chapter II, page 44] with respect to $m(t)$, denoting the reciprocal kernel of $\frac{1}{k}\, f(t,\tau)$ by $\varphi(t,\tau)$ and assuming the hereditary effects prior to $t = 0$ are negligible, we get

$$m(t) = \frac{1}{k}\,\omega(t) + \int_{0}^{t} \varphi(t,\tau)\,\omega(\tau)\,\mathrm{d}\tau\,. \tag{3}$$

Let us pass now from the static to the dynamic case and try to study the oscillations of the wire. For this, suppose that the angular velocity and acceleration are no longer negligible. The equation of motion of the wire is obtained from (3) by means of d'Alembert's principle, by substituting

$$m(t) - \mu\,\frac{\mathrm{d}^2\omega}{\mathrm{d}t^2}(t) \quad (\mu \text{ constant})$$

for $m(t)$. We then get an integro-differential equation giving $\omega(t)$ in terms of $m(t)$:

$$m(t) - \mu\,\frac{\mathrm{d}^2\omega}{\mathrm{d}t^2}(t) = h\,\omega(t) + \int_{0}^{t} \varphi(t,\tau)\,\omega(\tau)\,\mathrm{d}\tau\,. \tag{4}$$

2.2.3 Propagation of a Nervous Impulse

This model is borrowed from [46, chapter XXXV, eq (32), page 426]. See also [31, chapter 1, page 5]. This nonpolynomial integral model is interesting because it has a trivial kernel and is equivalent to a polynomial system of integro-differential equations.

It is currently widely admitted that nervous impulses are propagated as follows in neurons: differences of ionic concentrations between the inside and the outside of axons make their membranes polarized. The occurence of an electric current in the neighborhood of some region of interest opens ionic channels, causing changes of ionic concentrations, hence an electric current in the region itself. The nervous influx is obtained by repeating this phenomenon along the whole axon. The details of the ionic activities, *at a fixed position* of the axon, are described by the famous Hodgkin-Huxley nonlinear differential model [33, chapter 5, pages 205-206].

The following model is probably older than the Hodgkin-Huxley model [30]. It is built on quite similar biological hypotheses and is concerned by the distance $u(t)$ traveled by an influx along a nerve (an axon, possibly). The parameter I represents an electric current suddenly established in the neighborhood region at $t = 0$. The parameter h is a concentration threshold above which a nerve excitation is triggered [46, eq (6), page 379]. It is assumed that the ionic concentration and the electric current satisfy a linear differential equation of first order, depending on two parameters K and k [46, eq (18), page 423]. The time t_1 at which the region of interest releases an influx is then a function of k, K, h and I. The parameter α is a constant depending on physical properties of the nerve: radius, specific resistances of the core of the nerve and its surrounding sheaths [46, eq (10), page 421]. The integral term of the model comes here from the fact that the distance is an integral of the speed [46, eq (21), page 424]. Since it is not motivated by any hereditary consideration, the absence of any nontrivial kernel is not surprising:

$$h\, e^{\alpha\, u(t)+k\, t} = \frac{h\, K\, I}{K\, I - k\, h} + K\, I \int_{t_1}^{t} e^{\alpha\, u(\tau)+k\, \tau}\, \mathrm{d}\tau\,. \tag{5}$$

Let now $v(t)$ be the exponential. The nonpolynomial integral equation (5) can be encoded by the following polynomial integro-differential system:

$$\begin{aligned} \frac{\mathrm{d}v}{\mathrm{d}t}(t) &= \left(\alpha\, \frac{\mathrm{d}u}{\mathrm{d}t}(t) + k\right)\, v(t)\,, \\ h\, v(t) &= \frac{h\, K\, I}{K\, I - k\, h} + K\, I \int_{t_1}^{t} v(\tau)\, \mathrm{d}\tau\,. \end{aligned} \tag{6}$$

Of course, the equation (5) can also easily be transformed to differential form, by simple differentiations. However, this is no longer true when considering a time-varying (possibly non-smooth) current $I(t)$.

3 Integro-Differential Equations for Parameter Estimation

In this section, we present the application to parameters estimation for nonlinear dynamical systems that motivated our interest for integro-differential algebra. Together with the application, we introduce key concepts of differential algebra. In the next section, we will discuss issues raised by their generalization to integro-differential algebra.

3.1 Statement of the Estimation Problem

The academic two-compartment model depicted in Figure 1 is a close variant of [59, (1), page 517] endowed with an input $u(t)$. Compartment 1 represents the blood system and compartment 2 represents some organ. Both compartments are supposed to have unit volumes. The function $u(t)$, which has the dimension of a flow, represents a medical drug, injected in compartment 1. The drug diffuses between the two

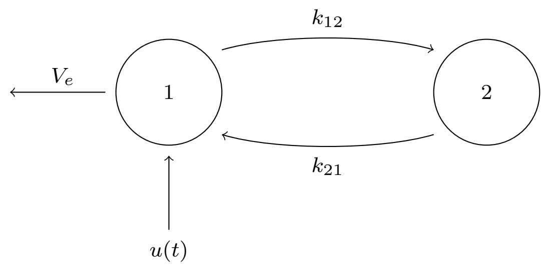

Fig. 1 A two-compartment model featuring three parameters.

compartments, following linear laws: the proportionality constants are named k_{12} and k_{21}. The drug exits compartment 1, following a law of Michaelis-Menten type. Such a law indicates a hidden enzymatic reaction. In general, it depends on two constants V_e and k_e. For the sake of simplicity, it is assumed that $k_e = 1$. The state variables in this system are $x_1(t)$ and $x_2(t)$. They represent the concentrations of drug in each compartment. This information is sufficient to write the two first equations of the mathematical model (7). The last equation of (7) states that the output, denoted $y(t)$, is equal to $x_1(t)$. This means that only $x_1(t)$ is observed: some numerical data are available for $x_1(t)$ but not for $x_2(t)$. The problem addressed here then consists in estimating the three parameters k_{12}, k_{21} and V_e from these data and the knowledge of $u(t)$.

$$\begin{aligned} \dot{x}_1(t) &= -k_{12}\, x_1(t) + k_{21}\, x_2(t) - \frac{V_e\, x_1(t)}{1 + x_1(t)} + u(t)\,, \\ \dot{x}_2(t) &= k_{12}\, x_1(t) - k_{21}\, x_2(t)\,, \\ y(t) &= x_1(t)\,. \end{aligned} \tag{7}$$

3.2 The Algebraic Setting

3.2.1 On the Solutions

Ritt and Kolchin *differential algebra* provides an algebraic framework for polynomial differential systems. Differential systems involving rational fractions, such as (7), are easily handled. Other kinds of nonlinearities are not directly covered by the theory but many nonpolynomial systems can be transformed into polynomial ones, using techniques similar to the one we used for the propagation model of nervous impulses. Differential algebra imposes, however, another restriction, which is more important to us, since it reduces its applicability to control theory: the solutions of the systems under study are supposed to belong to integral domains (e.g. an equation such as $u(t)\,v(t) = 0$ would imply that $u(t) = 0$ or $v(t) = 0$) and must be differentiable infinitely many times. The input $u(t)$ of (7) must then be smooth. One cannot study the case of a piecewise constant function $u(t)$ without leaving the realm of differential algebra.

3.2.2 Differential Polynomial Ideal

Subtract right-hand sides from left-hand sides of (7). Multiply the first equation by its denominator and state that this latter is nonzero. One obtains a system of three differential polynomial equations and one inequation:

$$p_1 = p_2 = p_3 = 0\,, \quad 1 + x_1 \neq 0\,. \tag{8}$$

The left-hand sides of (8) belong to the *differential polynomial ring*

$$\mathscr{R} = \mathbb{Q}(k_{12}, k_{21}, V_e)\{u, y, x_1, x_2\}\,.$$

The three symbols y, x_1, x_2 are *differential indeterminates*. To this system, one associates a *differential ideal*

$$\mathfrak{A} = [p_1, p_2, p_3] : (1 + x_1)^\infty.$$

Technically, the ideal $\mathfrak{A}$ is defined as the ideal of $\mathscr{R}$ generated by the three differential polynomials and their derivatives up to any order, *saturated* by the multiplicative family generated by $1 + x_1$. This means that if any differential polynomial of the form $(1 + x_1)\,g$ belongs to $\mathfrak{A}$, then g itself belongs to $\mathfrak{A}$. It can be proved that $\mathfrak{A}$ is a *prime* (hence *radical*) differential ideal.

3.2.3 Theorem of Zeros

As already pointed out, in differential algebra, solutions are sought in differential rings that are free of zero-divisors. This restriction has some drawbacks for applications in control theory. Algebraically, it has a big advantage: the differential ideal $\mathfrak{A}$ is then the set of all differential polynomials that annihilate over the whole solution set of (7). In particular, a Theorem of Zeros [48, chapter I, 16] holds in differential algebra:

Theorem 1. *A differential polynomial g annihilates over all the solutions of a system of differential polynomial equations $f_1 = f_2 = \cdots = f_n = 0$ if, and only if, a power of g belongs to the differential ideal generated by $f_1, f_2, \ldots, f_n$.*

The formulation above is not completely precise since the algebraic structure $\mathscr{S}$ which is supposed to contain the solutions is not given. Many precise variants could be given: $\mathscr{S}$ could be some *differential field*, an algebra of formal power series, a field of meromorphic functions ... See [9] for more details on this question.

3.2.4 Elimination Theory

An *elimination theory* has been available in differential algebra from its very beginning [48, 57]. Some algorithms such as [39, diffgrob], [14, 15, RosenfeldGroebner], [47, rif], [2, 36, 49, Thomas algorithm] are implemented in computer algebra systems. In the sequel, we concentrate on RosenfeldGroebner and its most recent implementation in the MAPLE package [10, DifferentialAlgebra]. The first argument of such an algorithm is a system of differential polynomial equations and inequations. The second argument is a *ranking*, i.e. a total ordering on the set

$$\{k_{12}, k_{21}, V_e\} \cup \{w^{(r)} \mid r \geq 0,\, w \text{ differential indeterminate}\}\,.$$

For an example such as (8), the output of the software is a *regular differential chain* — a notion slightly more general than Ritt's *characteristic set* [7, Definition 3.1] — of the differential ideal $\mathfrak{A}$ w.r.t. the ranking. Regular differential chains are finite sets of differential polynomials. By choosing a suitable ranking such as

$$\text{(the derivatives of } x_1, x_2) \gg \text{(the derivatives of } y, u) \gg \text{(the parameters)}\,,$$

one can directly read in the output of the software the differential polynomial of $\mathfrak{A}$ which has the *lowest rank* w.r.t. the ranking. This differential polynomial is the so-called *differential input-output equation* of (7). It depends only on y, u, their derivatives, and the parameters to be estimated.

3.3 The Input-Output Equation of the Problem

A pretty-printed form of the differential input-output equation of (7) is:

$$\begin{aligned} -\theta_1\, u(t) + \theta_2\, \frac{y(t)}{y(t)+1} + \theta_3\, \frac{\mathrm{d}}{\mathrm{d}t} \left(\frac{y(t)^2}{y(t)+1} \right) & \\ - \theta_4\, \frac{\mathrm{d}}{\mathrm{d}t} \left(\frac{1}{y(t)+1} \right) &= \dot{u}(t) - \ddot{y}(t)\,, \end{aligned} \tag{9}$$

where the θ_i stand for the following *blocks of parameters*:

$$\theta_1 = k_{21}\,, \quad \theta_2 = k_{21}\, V_e\,, \quad \theta_3 = k_{12} + k_{21}\,, \quad \theta_4 = k_{12} + k_{21} + V_e\,. \tag{10}$$

3.3.1 Structural Identifiability Study

The *structural identifiability study* is a preliminary study of the input-output equation. It can be viewed as a theoretical parameter estimation process, where the observed function $y(t)$, the input $u(t)$, and their derivatives up to any order are supposed to be as "generic" as possible and perfectly known.

A huge amount of literature is devoted to this question. See [1, 23, 37, 41, 42, 56, 59] and the references therein.

In our example, the structural identifiability study leads in a straightforward way to the desired conclusion of the global structural identifiability for this model. The essential argument is as follows:

1. Evaluating (9) at (at least) four different values of t, it is possible to build an invertible linear system whose unknowns are the blocks of parameters θ_i.
2. Knowing the blocks of parameters θ_i, it is easy to recover the values of the model parameters k_{12}, k_{21}, V_e, by solving the polynomial system (10).

It is worth noticing that step 1 of this argument eventually relies on the assumption that (9) is the equation of minimal order and degree constraining $y(t), u(t)$ and the parameters to be estimated. Ultimately, this argument relies on the Theorem of Zeros.

Indeed, on some other example, a non-minimal input-output equation could be artificially obtained by adding a polynomial of the form $\theta\, m$ (θ any parameter block, m belonging to the differential ideal $\mathfrak{A}$) to the minimal equation. At step 1, such a polynomial m would always evaluate to zero, yielding a linear system that would always be singular. The whole argument would then collapse.

3.3.2 Integro-Differential Form of the Input-Output Equation

A parameter estimation method can be designed by implementing "numerically" the steps 1 and 2 above, using the available numerical data for the observed function $y(t)$ and the input $u(t)$. If the data is noisy (but not only then), a straightforward implementation is however very likely to produce useless results since the second derivative of $y(t)$ then needs to be estimated numerically. In order to obtain more accurate results, it is desirable to convert the differential input-output equation (9) to integral form since numerical integration is less sensitive to noise than numerical differentiation. There are different ways to do it. Some methods are given in [12]. One possibility consists in applying twice the integration operator on (9). On our example, the result is the nonlinear Volterra integral equation (11). This formula still involves a derivative of the output, but evaluated at $t = a$. Viewing this derivative as an extra parameter θ_5, to be estimated, Equation (11) does not involve any derivative of the output:

$$
\begin{aligned}
&- \theta_1 \int_a^t \int_a^{\tau_1} u(\tau_2)\,\mathrm{d}\tau_2\,\mathrm{d}\tau_1 \\
&+ \theta_2 \int_a^t \int_a^{\tau_1} \frac{y(\tau_2)}{y(\tau_2)+1}\,\mathrm{d}\tau_2\,\mathrm{d}\tau_1 \\
&+ \theta_3 \left(\int_a^t \frac{y(\tau)^2}{y(\tau)+1}\,\mathrm{d}\tau - \frac{y(a)^2}{y(a)+1}\,(t-a) \right) \\
&- \theta_4 \left(\int_a^t \frac{1}{y(\tau)+1}\,\mathrm{d}\tau - \frac{1}{y(a)+1}\,(t-a) \right) \\
&- \dot{y}(a)\,(t-a) \\
&= \int_a^t u(\tau)\,\mathrm{d}\tau - u(a)\,(t-a) - y(t) + y(a)\,.
\end{aligned}
\tag{11}
$$

In general, the resulting formula is an integro-differential equation. The method outlined here always produces formulas with trivial kernels. It can be completely automated, thanks to recent progresses in computer algebra [8, 12, 13].

3.3.3 Actual Parameter Estimation

An integro-differential input-output equation such as (11) is used to build an overdetermined[1] linear system, whose unknowns are the parameter blocks θ_i. Its solutions, obtained by linear least squares, may be used as a first guess for nonlinear least squares such as the Levenberg-Marquardt method or Linear Matrix Inequalities. See [19, 20, 41, 59].

Recovering the initial model parameters from refined estimates of the parameter blocks θ_i is usually a difficult problem for which no satisfactory general solution is known. An important difficulty is raised by possible algebraic relations between blocks of parameters. In our example, we have such a relation:

$$\theta_1\,(\theta_3 - \theta_4) + \theta_2 = 0\,. \tag{12}$$

3.4 *Algorithmic Transformation to Integro-Differential Form*

Transforming (9) into the integral equation (11) is very easy because the former equation has the special form

$$\sum \theta_i\, \frac{\mathrm{d}}{\mathrm{d}t}\, F_i\,,$$

where the θ_i are constant expressions (their derivatives are zero) and the F_i are order zero fractions. However, the input-output equations returned by differential

[1] A square linear system is sufficient for the identifiability study, which is of theoretical nature. On real, possibly noisy, data, it is preferable to evaluate the input-output equations at much more values of t, and thereby obtain an overdetermined linear system.

elimination algorithms do not always have this shape. Instead, they have the form of polynomials in the derivatives of the differential indeterminates, which implies that the $\frac{\mathrm{d}}{\mathrm{d}t} F_i$ expressions are expanded. A first algorithm for converting this raw form into (9) is published in [8], with a flaw fixed in [12]. An enhanced version, with a canonical output, is published in [13].

4 Towards Algebraic Theories

The systematic treatment of integral operators in algebra—usually under the name of Rota-Baxter operators—has been inaugurated with Glen Baxter's seminal paper [6]. While originally viewed in a probability context, Rota-Baxter operators have soon found interest in broader areas of algebra, especially through Gian-Carlo Rota's well-known papers [54, 55]. For a modern survey on Rota-Baxter algebra we refer to the monograph [28].

The notion of Rota-Baxter operator was combined with differential algebra structures in [50, 53] for creating an algebraic framework that allows a constructive treatment of boundary problems for linear ordinary differential equations. In particular, the Green's operator (resolvent operator), which maps the forcing function to the solution of the boundary problem, is expressed as a Fredholm integral operator that belongs to a suitable operator ring.

Let us explain this in some more detail. We start from an *integro-differential algebra* $(\mathcal{F}, \partial, \int)$, meaning an algebra over some field K with two K-linear operators $\partial, \int \colon \mathcal{F} \to \mathcal{F}$ that are supposed to capture differentiation and integration in an algebraic context. Hence the derivation ∂ is required to satisfy the Leibniz axiom (= product rule for differentiation) while $\int$ must satisfy the Rota-Baxter axiom (= integration by parts); moreover we stipulate $\partial \circ \int = 1_{\mathcal{F}}$ for tying the two notions together, just as the fundamental theorem of calculus does in the case $\mathcal{F} = C^\infty(\mathbb{R})$; note that this is a special case of the generalized Leibniz integral rule (14). It turns out that the other composition is not quite the identity but $\int \circ \, \partial = 1_{\mathcal{F}} - E$, where $E \colon \mathcal{F} \to \mathcal{F}$ is a multiplicative linear map that may be thought as the evaluation at the initialization point of the integral operator $\int$. Indeed, this is what happens in the most important example $\mathcal{F} = C^\infty(\mathbb{R})$ where $\partial f(x) = df/dx$ and $\int f(x) = \int_a^x f(\xi)\, d\xi$ for some initialization point $a \in \mathbb{R}$; consequently, here $E \colon \mathcal{F} \to \mathbb{R}$ is the evaluation $f(x) \mapsto f(a)$. Of course $C^\infty(\mathbb{R})$ contains many other integro-differential algebras, for example the polynomials $\mathbb{R}[x]$ or the analytic functions $C^\omega(\mathbb{R})$, and various intermediate algebras like the exponential polynomials (real or complex linear combinations of $x^k e^{\lambda x}$ for any $k \in \mathbb{N}$ and $\lambda \in \mathbb{R}$).

Each integro-differential algebra $(\mathcal{F}, \partial, \int)$ now gives rise to an operator ring $\mathcal{F}[\partial, \int]$ that contains both differential operators such as $a(x)\,\partial^2 + b(x)\,\partial + c(x)$ for coefficient functions $a(x), b(x), c(x) \in \mathcal{F}$ and integral operators such as $x^2 e^x \int e^{-2x}$, as well as evaluation operators E_a for various points $a \in \mathbb{R}$. Note that the integral operator $x^2 e^x \int e^{-2x}$ is here understood as a non-commutative operator composition, acting as $f(x) \mapsto \int_a^x x^2 e^{x-2\xi} f(\xi)$. We refer to $\mathcal{F}[\partial, \int]$ as the *integro-differential* *operator ring* over $\mathcal{F}$. One can prove that every boundary problem over $\mathcal{F}$ has a Green's operator $G \in \mathcal{F}[\partial, \int]$, which can be determined algorithmically if one has a fundamental system of solutions for the underlying homogeneous differential equation [53, Thm. 26].

The treatment of *linear partial differential equations* is considerably more difficult. Of course one will replace $(\mathcal{F}, \partial, \int)$ by a structure $(\mathcal{F}, \partial_x, \partial_y, \int^x, \int^y)$, where $\mathcal{F}$ is an algebraic structure describing multivariate (for simplicity here: bivariate) functions with two derivations ∂_x, ∂_y and two Rota-Baxter operators $\int^x, \int^y$. However, this would not lead us very far since even very simple examples like $u_x - u_y = f$ cannot be solved in terms of these basic building blocks. One crucial missing piece is a structure for *substitutions*. For treating linear partial differential equations, it is sufficient to allow only linear substitutions like $u(x, y) \mapsto u(ax + by, cx + dy)$ for $a, b, c, d \in \mathbb{R}$. The resulting algebraic structure, a so-called *Rota-Baxter hierarchy*, is surprisingly complex and has been described in [51]. In fact, the current setup omits the derivations ∂_x, ∂_y for keeping the complications to a minimum (derivations are comparatively easy to add since their algebraic relations are far less complex than those connected with the Rota-Baxter operators).

Similar to the case of plain integro-differential algebras, every Rota-Baxter hierarchy comes with a *multivariate operator ring* that we could provisionally denote by $\mathcal{F}[\int^x, \int^y]$ or by $\mathcal{F}[\partial_x, \partial_y, \int^x, \int^y]$ if the derivations are added in. The main innovation from the ordinary case is that substitution operators $M^* = \left(\begin{smallmatrix} a & b \\ c & d \end{smallmatrix}\right)^*$, acting as described above for a matrix $M \in \mathbb{R}^{2\times 2}$, are also part of the basic building blocks. Their interaction with the Rota-Baxter operators is complicated, but normal forms have been deduced [51, Thm 4.10], for the case of arbitrarily many variables.

Describing the nature of those operator relations would lead us too far afield for the present paper. It will suffice to mention just one special case of Axiom (7) of [51, Def. 2.3], namely

$$\int^x M^* \int^x = M^* \int^x \int^y - \int^x M^* \int^y,$$

where $M \in \mathbb{R}^{2\times 2}$ is the substitution matrix with $a = c = 1, b = d = 0$, acting by $u(x, y) \mapsto u(x, x)$. Written in the usual notation, this is exactly *Dirichlet's rule* to be mentioned in Section 4.1.3. However, the great advantage of the operator-ring framework is that there is a normal form (namely the right-hand side). In fact, we are confident that these normal forms are in fact canonical (meaning every simplification can only lead to a single normal form), which is equivalent to the algebraic statement that the chosen identities are a non-commutative Gröbner basis for the ideal of operator relations. This is work in progress, more than half of the proof is completed but there the derivations are very long.

Up to now we have spoken about linear differential and integral equations, both ordinary and partial (of course this includes also the mixed integro-differential cases). For passing to nonlinear equations, one can pass to the ring of *integro-differential polynomials*. In the univariate case, this has been introduced in [52]. Essentially the same structure—but extended to the partial case as well as differential fractions—was subsequently treated in [8, 13]. The basic idea in all case is that nested integrals like $\int u^2 u'^3 \int u' u''^2 \int u'' (u''')^5$ or $\int u'^2 \int u'' \int u u''^4$, or linear combinations of these, are in canonical form only if the highest derivative of u appears nonlinearly in each of the nested integrands. Hence the first example above is canonical, but the second is not.

While the algebraic investigation of the linear case (univariate and multivariate integro-differential operator rings) are now gradually maturing to some extent, the nonlinear case of *integro-differential polynomials/fractions* is wide open. In the last two sections we will only address two prominent issues that appear to pose considerable difficulties and, by the same token, a highly interesting arena of algebraic research.

4.1 Computational Issues

4.1.1 The Generalized Leibniz Integral Rule

Though there does exist applications of integro-differential equations which only need trivial kernels, this is certainly not the case of equations arising from hereditary modelling, which have the form:

$$\int_a^t K(t,\tau)\, f(\tau)\, \mathrm{d}\tau\,.$$

Over such expressions, the formula

$$\frac{\mathrm{d}}{\mathrm{d}t} \int_a^t = \text{the identity operator} \tag{13}$$

does not hold anymore. Instead, one must apply the general form of Leibniz integral rule, which gives:

$$\frac{\mathrm{d}}{\mathrm{d}t} \int_a^t K(t,\tau)\, f(\tau)\, \mathrm{d}\tau = \int_a^t \frac{\mathrm{d}K}{\mathrm{d}t}(t,\tau)\, f(\tau)\, \mathrm{d}\tau + K(t,t)\, f(t)\,. \tag{14}$$

However, this formula raises a computational problem, in the case of singular kernels. Let us quote Volterra [63, chapter II, page 54]:

> It is rather curious to note that it was precisely these singular cases that were the first in order of time to arise; the first integral equation considered goes back to Abel and is as follows:
>
> $$\sqrt{2\,g}\, z(t) = \int_0^t \frac{y(\tau)}{(t-\tau)^{\frac{1}{2}}}\, \mathrm{d}\tau\,, \tag{15}$$
>
> and the kernel $(t-\tau)^{-\frac{1}{2}}$ becomes infinite at $\tau = t$.

Differentiating (15) causes a division by zero. In particular, we see that, contrarily to what happens in differential algebra, differentiation of integro-differential expressions is not always defined.

4.1.2 Integration by Change of Variable

The change of variable formula is:

$$\int_a^b F(\varphi(t))\,\frac{\mathrm{d}\varphi}{\mathrm{d}t}(t)\,\mathrm{d}t = \int_{\varphi(a)}^{\varphi(b)} F(t)\,\mathrm{d}t\,.$$

Kostitzin applies it [35, page 68] for studying the Volterra-Kostitzin model in the case of a trivial kernel. Having proven that

$$\frac{\mathrm{d}y}{\mathrm{d}t}(t) = F(y(t))\,,$$

he deduces that

$$t = \int_{y(0)}^{y(t)} \frac{1}{F(\tau)}\,\mathrm{d}\tau\,.$$

This identity shows that, in an integro-differential algebra theory in which integration operators with general bounds would be allowed, the equality test between two expressions might be a difficult problem.

4.1.3 Dirichlet's Rule

Volterra attributes this formula to Dirichlet in [61, page 36] and often uses it:

$$\int_a^t \int_a^\tau F(\tau_2,\tau)\,\mathrm{d}\tau_2\,\mathrm{d}\tau = \int_a^t \int_{\tau_2}^t F(\tau_2,\tau)\,\mathrm{d}\tau\,\mathrm{d}\tau_2\,.$$

In the parameter estimation problem described in Section 3, this formula could have been used in order to produce another form of the integral equation (11), which would have involved a non trivial kernel. Indeed:

$$\int_a^t \int_a^\tau F(\tau_2)\,\mathrm{d}\tau_2\,\mathrm{d}\tau = \int_a^t (t-\tau)\,F(\tau)\,\mathrm{d}\tau\,.$$

This formula illustrates another difficulty that arises when testing equality between two integro-differential expressions. Recent progresses on this issue are given in [51].

4.2 On Generalizations of the Theorem of Zeros

As pointed out in Section 3, the Theorem of Zeros is implicitly used in the structural identifiability test based on the input-output equation. This section shows that it might not generalize in the integro-differential framework. Observe a similar difficulty occurs in other theories such as difference algebra [18].

Let us define an integro-differential ring $\mathscr{R} = \mathbb{Q}\{u\}$ as the smallest ring containing the integro-differential indeterminate u, the rational numbers, stable under derivation and integration. For simplicity, let us restrict ourselves to the case of a derivation δ being the left inverse of the integration $\int$, i.e. an abstract form of (13). Let us denote $x = \int 1$.

Given any $p \in \mathscr{R}$, let us define the integro-differential ideal generated by p as the smallest ideal of the ring $\mathscr{R}$, containing p, stable under derivation and integration. Let us denote it $[p]$. Consider now

$$p = u - \int u\,, \tag{16}$$

which is meant to be an abstract form of the left-hand side of the integral equation

$$u(t) - \int_0^t u(\tau)\,\mathrm{d}\tau = 0\,.$$

This equation admits $u(t) = 0$ for unique solution. However, we prove below that $u^m \notin [p]$ for any non-negative integer m, i.e. that, in the algebraic framework sketched above, the Theorem of Zeros does not hold.

Proposition 1. *Take $p \in \mathscr{R}$. Then, any element q of $[p]$ can be written as $q = \sum_{i=1}^{s} a_i\, M_i$ where $a_i \in \mathbb{Q}$ and each M_i has the form*

$$M_i = m_{i,0} \int m_{i,1} \int \cdots \int m_{i,k-1} \int m_{i,k}(\delta^{b_i} p) \int m_{i,k+1} \int \cdots \int m_{i,t_i}\,, \tag{17}$$

where b_i is a non-negative integer, the $m_{i,j}$ are monomials in x, and u and its derivatives.

Proof. Admitted.

Let us denote by $w(M_i)$ the *weight in u* of any M_i of the form of (17), with $w(M_i) = 1 + \sum_{j=0}^{t_i} \deg(m_{i,j}, [u, \delta u, \ldots])$, where $\deg(m_{i,j}, [u, \delta u, \ldots])$ denotes the total degree of $m_{i,j}$ in the variables u, δu, …

Lemma 1. *Take $p = u - \int u$ and consider some M_i in the form of (17). Then replacing u by $\alpha\, u$ in M_i yields $\alpha^{w(M_i)} M_i$, for any $\alpha \in \mathbb{Q}$. Moreover, replacing u by e^x in M_i yields 0 if $b_i > 0$, or a polynomial in x and e^x whose degree in e^x is at most $w(M_i) - 1$ otherwise.*

Proof. Immediate.

Proposition 2. *Take $p = u - \int u$. Then $u^m \notin [p]$ for any non-negative integer m.*

Proof. Assume that $u^m \in [p]$ for some m. Let us prove that this yields a contradiction. By Proposition 1, we have $u^m = \sum_{i=1}^{s} a_i\, M_i$ where the a_i are in $\mathbb{Q}$ and the M_i have the form of (17). The monomial u^m is homogeneous of degree m. By an homogeneity argument and by Lemma 1, all M_i have the same weights $w(M_i) = m$ in u.

Substituting $u = e^x$ in u^m yields e^{mx}. However, substituting $u = e^x$ in any M_i either yields 0 if $b_i > 0$, or a polynomial in x and e^x whose degree in e^x is at most $m - 1$ by Lemma 1. This yields a contradiction since e^x, e^{2x}, …, e^{mx} are linearly independent over $\mathbb{Q}[x]$.

4.3 On Derivation-Free Elimination

The most challenging theoretical issue would consist in developing an elimination theory for integro-differential equations that would permit to bypass differential algebra methods. To our knowledge, such a derivation-free elimination theory has not been considered yet. To illustrate what it could ideally do, we show that Equation (11) can be obtained from Equation (7) without performing any differentiation. Let us slighty rewrite Equation (7) as

$$
\begin{aligned}
f_1(t) &:= -\dot{y}(t) - k_{12}\, y(t) + k_{21}\, x_2(t) - V_e\, \frac{y(t)}{1 + y(t)} + u(t)\,,\\
f_2(t) &:= -\dot{x}_2(t) + k_{12}\, y(t) - k_{21}\, x_2(t)\,.
\end{aligned}
$$

Since $f_1(t)$ and $f_2(t)$ are identically zero, we obtain the equation

$$
0 = k_{21} \int_a^t \int_a^\tau f_1(\tau_2) + f_2(\tau_2)\, \mathrm{d}\tau_2\, \mathrm{d}\tau + \int_a^t f_1(\tau)\, \mathrm{d}\tau\,.
$$

Simplifying the previous equation yields

$$
\begin{aligned}
k_{21} \int_a^t \int_a^\tau u(\tau_2)\, \mathrm{d}\tau_2\, \mathrm{d}\tau - k_{21}\, V_e \int_a^t \int_a^\tau \frac{y(\tau_2)}{1 + y(\tau_2)}\, \mathrm{d}\tau_2\, \mathrm{d}\tau \\
- (k_{21} + k_{12}) \int_a^t y(\tau)\, \mathrm{d}\tau - V_e \int_a^t \frac{y(\tau)}{1 + y(\tau)}\, \mathrm{d}\tau + k_{21}\, (y(a) + x_2(a))\, (t - a) \\
= y(t) - y(a) - \int_a^t u(\tau)\, \mathrm{d}\tau\,.
\end{aligned}
$$

From $f_1(a) = 0$, one has

$$
k_{21}\, x_2(a) = \dot{y}(a) + k_{12}\, y(a) + V_e\, \frac{y(a)}{1 + y(a)} - u(a)\,.
$$

Replace $k_{21}\, x_2(a)$ by its value in the last equation. Simple computations show that

$$
\begin{aligned}
k_{21}\left(\int_a^t\int_a^\tau u(\tau_2)\,\mathrm{d}\tau_2\,\mathrm{d}\tau + y(a)\,(t-a) - \int_a^t y(\tau)\,\mathrm{d}\tau\right)\\
-\,k_{21}\,V_e\int_a^t\int_a^\tau \frac{y(\tau_2)}{1+y(\tau_2)}\,\mathrm{d}\tau_2\,\mathrm{d}\tau - V_e\left(\int_a^t \frac{y(\tau)}{1+y(\tau)}\,\mathrm{d}\tau - \frac{y(a)}{1+y(a)}\right)\\
+\,k_{12}\left(y(a)\,(t-a) - \int_a^t y(\tau)\,\mathrm{d}\tau\right) + \dot y(a)\,(t-a)\\
= y(t) - y(a) - \int_a^t u(\tau)\,\mathrm{d}\tau + u(a)\,(t-a)\,.
\end{aligned}
$$

This last equation is equivalent (up to the sign) to (11), by using the properties $y^2/(1+y) = y - 1 + 1/(1+y)$ and $1/(y+1) = 1 - y/(y+1)$.

4.4 On Alternative Input-Output Equations

A structural identifiability study, based on the differential input-output equation, was sketched in Section 3.3.1. Since this equation is computed in the strict framework of differential algebra, it does not feature any initial value of any non-observed variable. In some cases, however, the initial conditions of some non-observed variables are known, and their knowledge is necessary to prove the structural identifiability of the model. A first approach to overcome this difficulty is presented in [21, 22]: the integration of the input-output equations followed by some further manipulations yields expressions involving the initial conditions of the non-observed variables, permitting to prove the structural identifiability. We show in this section that integro-differential elimination offers another approach since it permits to compute integral input-output equations featuring naturally these important initial values. The system Σ under study is inspired from [32]:

$$
\dot x_1(t) = \theta_1\,x_2(t) + u(t)\,, \tag{18}
$$

$$
\dot x_2(t) = \theta_2\,x_1(t)\,x_2(t) + \theta_3\,x_2(t) + u(t)\,, \tag{19}
$$

together with the assumptions

- $x_1(0) = x_{10}$ is known,
- $x_2(t)$ and $u(t)$ are observed on some interval $[0, t_0]$,
- $x_1(t)$ is *not* observed on $]0, t_0]$.

The parameters to be estimated are θ_1, θ_2 and θ_3. Differential elimination methods permit to compute the following differential input-output equation:

$$
\ddot x_2(t)\,x_2(t) - \dot x_2^2(t) + \dot x_2(t)\,u(t) - x_2(t)\,\dot u(t) - \theta_1\,\theta_2\,x_2^3(t) - \theta_2\,u(t)\,x_2^2(t)\,.
$$

The structural identifiability study sketched in Section 3.3.1 would conclude to the non-identifiability of Σ since θ_3 does not even appear in this equation. Converting this equation to integro-differential form would obviously not change this conclusion. Now, it is interesting to observe that one can obtain an expression depending on θ_3 by evaluating (19) at $t = 0$, provided that $x_2(0) \neq 0$. Another expression can be obtained if $x_2(0) = 0$ and $\dot{x}_2(0) \neq 0$: differentiating (19) and rewriting the term $\dot{x_1}(t)$ using (18) yields

$$\ddot{x}_2(t) = \theta_2 \Big((\theta_1 \, x_2(t) + u(t)) \, x_2(t) + x_1(t) \, \dot{x}_2(t) \Big) + \theta_3 \, \dot{x}_2(t) + \dot{u}(t) \,. \qquad (20)$$

Evaluating this expression at $t = 0$ provides an expression for θ_3 as a function of $x_1(0)$, $x_2(0)$, $\dot{x_2}(0)$, $\ddot{x}_2(0)$, $u(0)$, $\dot{u}(0)$, θ_1 and θ_2. More generally, a formula can be obtained provided that some derivative of $x_2(t)$ does not vanish at $t = 0$.

Let us now compute an integral input-output equation, using the integration operator from the beginning. First put Σ in an integral form:

$$x_1(t) = x_{10} + \int_0^t \theta_1 \, x_2(\tau) + u(\tau) \, \mathrm{d}\tau \,, \qquad (21)$$

$$x_2(t) = x_{20} + \int_0^t \theta_2 \, x_1(\tau) \, x_2(\tau) + \theta_3 \, x_2(\tau) + u(\tau) \, \mathrm{d}\tau \,. \qquad (22)$$

Using (21) for replacing $x_1(t)$ by its value in (22) yields

$$\begin{aligned} x_2(t) = x_{20} + \int_0^t \theta_2 \, \left(x_{10} + \int_0^\tau \theta_1 \, x_2(\tau_2) + u(\tau_2) \, \mathrm{d}\tau_2 \right) x_2(\tau) \\ + \theta_3 \, x_2(\tau) + u(\tau) \, \mathrm{d}\tau \,. \end{aligned} \qquad (23)$$

Expanding (23) yields

$$x_2(t) = I_0(t) + (x_{10} \, \theta_2 + \theta_3) \, I_1(t) + \theta_2 \, I_2(t) + \theta_1 \, \theta_2 \, I_3(t) \qquad (24)$$

with

$$I_0(t) = x_{20} + \int_0^t u(\tau) \, \mathrm{d}\tau \,, \qquad I_1(t) = \int_0^t x_2(\tau) \, \mathrm{d}\tau \,,$$

$$I_2(t) = \int_0^t x_2(\tau) \int_0^\tau u(\tau_2) \, \mathrm{d}\tau_2 \, \mathrm{d}\tau \,, \qquad I_3(t) = \int_0^t x_2(\tau) \int_0^\tau x_2(\tau_2) \, \mathrm{d}\tau_2 \, \mathrm{d}\tau \,.$$

Let us now follow the structural identifiability study sketched in Section 3.3.1 on (24). The linear system considered at step 1 is invertible since the three terms $I_1(t)$, $I_2(t)$ and $I_3(t)$ are linearly independent[2]. Thus the structural identifiability study would infer the global structural identifiability of Σ. The input-output equa-

[2] Indeed, if the three terms were linearly dependent, there would exist three constants A, B, C such that $A \, I_1(t) + B \, I_2(t) + C \, I_3(t) = 0$ modulo the prime differential ideal $\mathfrak{A}$ generated by Σ. Differentiate this equation. Divide it by $x_2(t)$. Differentiate again. One gets $B \, u(t) + C \, x_2(t) = 0$. However, $B \, u(t) + C \, x_2(t)$ is not reduced to zero by Σ, viewed as a regular differential chain (or a characteristic set) of $\mathfrak{A}$. This contradiction proves the linear independence of the three terms.

tion obtained by integro-differential elimination is therefore not equivalent to the one obtained by plain differential elimination.

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