On the Parameter Estimation Problem for Integro-Differential Models

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This talk summarizes a joint work with modelers and biologists [2]. It deals with the parameter estimation problem for dynamical systems presented by explicit systems of polynomial integro-differential equations (IDE).

Models formulated by means of IDE are very interesting because they are much more expressive than their ODE counterparts: they naturally permit to express delays (IDE are viewed as continuous delay differential equations in [9]), to take into account the age of populations (typical motivation for integral equations in population dynamics), to incorporate curves obtained by interpolating experimental data as integral kernels (an important feature for modeling processes interacting with complicated environment) and to handle non smooth (e.g. piecewise defined) inputs. See [6] and references therein.

The rest of this abstract is essentially borrowed from the introduction of [2].

IDE modeling raises, in turn, the problem of estimating parameters from experimental data. This talk focuses on a particular method, called the "input-output (IO) ideal" method, which is available in the nonlinear ODE case. Its principle consists in computing an equation (called the "IO equation") which is a consequence of the model equations and only depends on the model inputs, outputs and parameters. In the nonlinear ODE case, it is known since [8] that it can serve to decide the identifiability property of the model. It is known since [7] that it can also be used to determine a first guess of the parameters from experimental data. This first guess may then be refined by means of a nonlinear fitting algorithm (of type Levenberg-Marquardt) which requires many different numerical integrations of the model.

Designing analogue theories and algorithms in the IDE case is almost a completely open problem. The talk presents two contributions:

- 1. a symbolic method for computing an IO equation from a given nonlinear IDE model. This method is incomplete but it is likely to apply over an important class of models that are interesting for modelers. It relies on the elimination theory for differential algebra [4, 5] and on an algorithm for integrating differential fractions [3];
- an algorithm for the numerical integration of IDE systems, implemented within a new open source C library [1]. The library does not seem to have any available equivalent. Our algorithm is an explicit Runge-Kutta method which is restricted to Butcher tableaux specifically designed in order to avoid solving integral equations at each step.

Keywords: nonlinear integro-differential, input-output equation, parameter estimation, numerical integration

References

[1] FRANÇOIS BOULIER AND AL, *BLINEIDE*. http://cristal.univ-lille.fr/~boulier/BLINEIDE.

- [2] François Boulier, Hélène Castel, Nathalie Corson, Valentina Lanza, François Lemaire, Adrien Poteaux, Alban Quadrat, and Nathalie Verdière, *Symbolic-Numeric Methods for Nonlinear Integro-Differential Modeling*. Submitted to CASC (2018), http://hal.archives-ouvertes.fr/hal-01765409.
- [3] François Boulier, Joseph Lallemand, François Lemaire, Georg Regens-Burger, and Markus Rosenkranz, *Additive normal forms and integration of differential fractions. JSC* 77, 77-38 (2016).
- [4] François Boulier, Daniel Lazard, François Ollivier, and Michel Petitot, Representation for the radical of a finitely generated differential ideal. In Proceedings of ISSAC'95, Montreal, 1995.
- [5] François Boulier, Daniel Lazard, François Ollivier, and Michel Petitot, Computing representations for radicals of finitely generated differential ideals. *AAECC* **20**(1), 73–121 (2009).
- [6] FRANÇOIS BOULIER, FRANÇOIS LEMAIRE, MARKUS ROSENKRANZ, ROSANE USHIROBIRA, AND NATHALIE VERDIÈRE, On Symbolic Approaches to Integro-Differential Equations. In Advances in Delays and Dynamics (2017), https://hal.archives-ouvertes.fr/hal-01367138.
- [7] LILIANNE DENIS-VIDAL, GHISLAINE JOLY-BLANCHARD, AND CÉLINE NOIRET, System identifiability (symbolic computation) and parameter estimation (numerical computation). In Numerical Algorithms 34 282–292 (2003).
- [8] LENNART LJUNG AND TORKEL GLAD. On global identifiability for arbitrary model parametrisations. Automatica **30** 265–276 (1994).
- [9] WIKIPEDIA. *Delay Differential Equations*. https://en.wikipedia.org/wiki/Delay_differential_equation.

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