ALGEBRA, AUTOMATA, ALGORITHMS, BIOLOGY & BEYOND

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In this extended abstract, I will examine algebraic approaches to modeling dynamics of biological systems and its relations to certain problems in differential algebra, automata theory and algorithmics.

1. Introduction

Guiseppa (Pina) Carrà's interest was in differential algebra. The best I can recall, she was the first person to introduce me to Ritt-Kolchin's Differential Algebra in the 80's. I tried to work on some hard problems in differential algebra, (like Ritt's problem) and made some progress, but found it too hard.

Pina continued working on many topics in the areas related to differential algebra:

- Differential Gröbner bases and differential dimension,

- Dimensional and probabilistic methods for automatic deduction in elementary and differential geometry,

- Differential resultants,

- Univariate and multivariate Hilbert polynomials,

- Applications of computational differential algebra to analog circuit design, dynamical systems and statistics, and

- Relations between numerical and symbolic methods.

I think that some of these ideas could be applied to problems that arise in systems biology.

2.   S-Systems, Canonical Forms & Differential Algebra

Using a system of first order differential equations (in explicit form), one can construct a general model of a rather complex biochemical reaction involving many genes and proteins. One such model is Savageau-Voit S-system, whose ingredients are n dependent variables $X_1, \ldots, X_n$, and m independent variables $X_{n+1}, \ldots, X_m$ with these $n+m$ variables taking values respectively in $n+m$ domains $D_1, \ldots, D_{n+m}$. In addition the differential equations, the system may need to be constrained by algebraic equations corresponding to stoichiometric constraints, or conserved rates for concentrations.

The basic differential equations of the system are of the form:

$$\dot{X}_i(t) = V_i^+(X_1(t), \ldots, X_{n+m}(t)) - V_i^-(X_1(t), \ldots, X_{n+m}(t)), \qquad (1)$$

for each dependent variable X_i (see [4]). The functions V^+ and V^- are arbitrary rational functions over $\mathbb{R}$. The set of algebraic constraints takes the form

$$\left\{ C_j(X_1(t), \ldots, X_{n+m}(t)) = 0 \right\} \qquad (2)$$

Theorem 1   *Every bio-chemical system arising from an S-system model can be expressed in a canonical form involving $r > n+m$ variables $Z_1, Z_2, \ldots, Z_r$:*

$$
\begin{bmatrix} \dot{Z}_1 \\ \dot{Z}_2 \\ \vdots \\ \dot{Z}_r \end{bmatrix} =
\begin{bmatrix} m_1^+(\mathbf{Z}) - m_1^-(\mathbf{Z}) \\ m_2^+(\mathbf{Z}) - m_2^-(\mathbf{Z}) \\ \vdots \\ m_r^+(\mathbf{Z}) - m_r^-(\mathbf{Z}) \end{bmatrix},
\quad
\begin{bmatrix} a_{11} & a_{12} & \cdots & a_{1r} \\ a_{21} & a_{22} & \cdots & a_{2r} \\ \vdots & \vdots & \ddots & \vdots \\ a_{s1} & a_{s2} & \cdots & a_{sr} \end{bmatrix}
\begin{bmatrix} Z_1 \\ Z_2 \\ \vdots \\ Z_r \end{bmatrix} =
\begin{bmatrix} 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix},
$$

where the m_i^+'s and m_i^-'s are ratios of monomials and the a_{ij}'s are constants in $\mathbb{R}[Z_1, \ldots, Z_r]$ with positive coefficients.

I have not been able to show if such a constrained system would always admit nice decidable procedures for differential ideal membership, for comparing differential ideals, etc. If these systems can be shown to be isobarizable, most of these questions would be decidable. So perhaps, a simple question could focus on isobarizability. For alternative approaches such as AAMC (Algorithmic Algebraic Model Checking), see [3].

3. Postscript

It is interesting to ask why it is that traditionally biology has not explored techniques in mathematics (especially differential algebra). I am reminded of a strange quotation from Eric Ponder, a director of Long Island Biology Association (now called, Cold Spring Harbor Laboratory):

> "Work on the mathematics [for biology] seems to me to have developed along two equally unprofitable lines .... It is futile to conjure up in the imagination a system of differential equations for the purpose of accounting facts, which are not only very complex, but largely unknown."

While there are still a few holdouts in biology simultaneously fighting senility and mathematics, it is heartening to see young biologists embracing and developing new mathematical approaches. They will be inspired by Pina's examples.

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