Triangular Decompositions for Solving Parametric Polynomial Systems

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Motivation

Stability analysis of (polynomial) dynamical systems leads to manipulate the solution sets of systems of equations, inequations or inequalities, so-called semi-algebraic sets. We generalize comprehensive triangular decomposition (CTD) to these sets and apply this new tool to a concrete example.

Laurent Model for Prion Diseases

Mad cow disease is a transmissible disease of the central nervous system, thought to be caused by prion proteins. Prion proteins exist in normal form $\mathrm{PrP}^{\mathrm{C}}$ and pathogenic form $\mathrm{PrP}^{\mathrm{Sc}}$. The former is harmless while the latter can multiply by converting $\mathrm{PrP}^{\mathrm{C}}$ into $\mathrm{PrP}^{\mathrm{Sc}}$. An excess of $\mathrm{PrP}^{\mathrm{Sc}}$ causes prion diseases. Can a small amount of $\mathrm{PrP}^{\mathrm{Sc}}$ cause prion disease? The model of Laurent reduces this question to the dynamical system below, where x and y are the concentrations of $\mathrm{PrP}^{\mathrm{C}}$ and $\mathrm{PrP}^{\mathrm{Sc}}$:

$$\begin{cases} \frac{\mathrm{d}x}{\mathrm{d}t} = k_1 - k_2 x - x\frac{a(1+by^n)}{1+cy^n} \\ \frac{\mathrm{d}y}{\mathrm{d}t} = x\frac{a(1+by^n)}{1+cy^n} - k_4 y \end{cases}$$

where experiments suggest to set $b = 2$, $c = 1/20$, $n = 4$, $a = 1/10$, $k_4 = 50$ and $k_1 = 800$. Now we have:

$$\begin{cases} \frac{\mathrm{d}x}{\mathrm{d}t} = f_1 \\ \frac{\mathrm{d}y}{\mathrm{d}t} = f_2 \end{cases} \text{with} \begin{cases} f_1 = \frac{16000+800y^4-20k_2x-k_2xy^4-2x-4xy^4}{20+y^4} \\ f_2 = \frac{2(x+2xy^4-500y-25y^5)}{20+y^4} \end{cases}. \quad (1)$$

A constant solution of the above differential equations is called an equilibrium, that is a point $(x, y) \in \mathbb{R}^2$ at which the right hand side equations vanish. An equilibrium (x, y) is asymptotically stable if any solution of (1) starting near (x, y) become arbitrarily close to it. By Routh-Hurwitz criterion (x, y) is asymptotically stable if

$$\Delta_1 = -(\frac{\partial f_1}{\partial x} + \frac{\partial f_2}{\partial y}) > 0 \text{ and } \Delta_2 = \frac{\partial f_1}{\partial x} \cdot \frac{\partial f_2}{\partial y} - \frac{\partial f_1}{\partial y} + \frac{\partial f_2}{\partial x} > 0.$$

Thus, determining the (asymptotically stable) equilibria of system (1) leads to solving semi-algebraic sets.

Basic Definitions

- A semi-algebraic set of $\mathbb{R}^n$ is a finite union of sets of form:
  $$\{(u, x) \in \mathbb{R}^n \mid (\forall f \in F) f(u, x) = 0 \,\&\, (\forall g \in G)\, g(u, x) > 0\},$$
  where F and G are any finite polynomial sets of $\mathbb{R}[U, X]$.
- A pair $[T, G+]$ is called a regular semi-algebraic system if
  - T is a squarefree regular chain of $\mathbb{R}[U, X]$,
  - $G+$ is a finite set of strict polynomial inequalities $\{g > 0\}$,
  - each g is regular w.r.t the saturated ideal of $\langle T \rangle$.
- A regular semi-algebraic system $[T, G+]$ separates well at $u \in \mathbb{R}^d$ if $[T(u), G(u)+]$ is a regular semi-algebraic system of $\mathbb{R}[X]$ after specialization and no initials of polynomials in T vanish during the specialization.

CTD of Semi-algebraic Sets

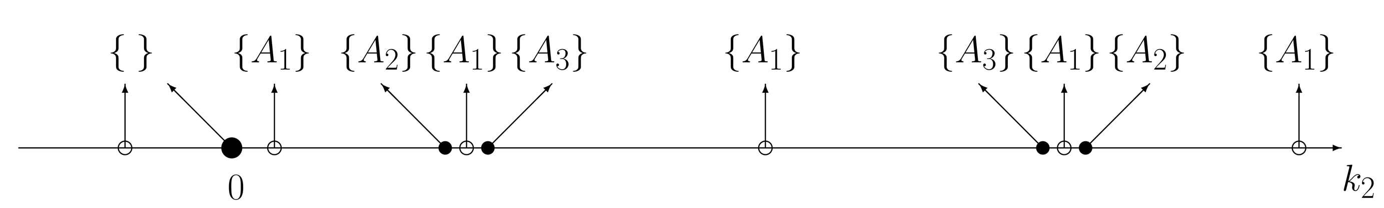
Let $\mathcal{S}$ be a parametric semi-algebraic set of $\mathbb{R}[U, X]$. A comprehensive triangular decomposition of $\mathcal{S}$ is given by :

- a finite partition $\mathcal{C}$ of the parameter space $\mathbb{R}^d$ into connected semi-algebraic sets,
- for each $C \in \mathcal{C}$, an associated sample point $s \in C$,
- for each $C \in \mathcal{C}$ a set of regular semi-algebraic systems $\mathcal{A}_C$ of $\mathbb{R}[U, X]$ such that for each $u \in C$: each $A \in \mathcal{A}_C$ separates well at u; the solutions sets of the systems $A(u)$, for $A \in \mathcal{A}_C$, are pairwise disjoint and their union is exactly the set of points of $\mathcal{S}$ whose $U-$coordinates are equal to u.

In system (1), let p_1 and p_2 be respectively the numerators of f_1 and f_2. The parametric semi-algebraic set

$$\mathcal{S} : \{p_1 = p_2 = 0, k_2 > 0, \Delta_1 > 0, \Delta_2 > 0\}$$

encodes exactly the asymptotically hyperbolic equilibria of system (1). A comprehensive triangular decomposition of $\mathcal{S}$ is illustrated as follows:



Equilibria Analysis

With CTD at hand, we can count the number of (asymptotically stable) equilibria of (1) depending on parameters. Let

$$\begin{aligned} R_1 = {} & 100000k_2^8 + 1250000k_2^7 + 5410000k_2^6 + 8921000k_2^5 \\ & - 9161219950k_2^4 - 5038824999k_2^3 - 1665203348k_2^2 \\ & - 882897744k_2 + 1099528405056. \end{aligned}$$

If $R_1 > 0$ (Figures 1 and 3), then the system has one equilibrium, which is asymptotically stable. If $R_1 < 0$ (Figure 2), then the system has three equilibria, two of which are asymptotically stable. If $R_1 = 0$, the system experiences a bifurcation.

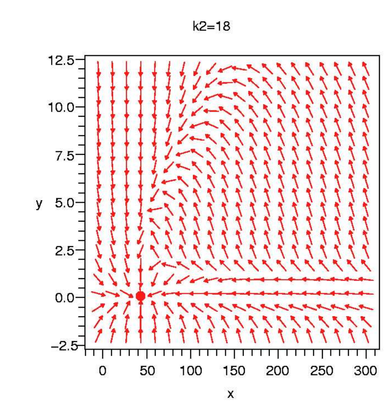


Figure 1

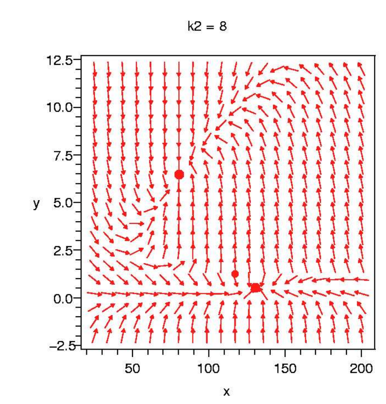


Figure 2

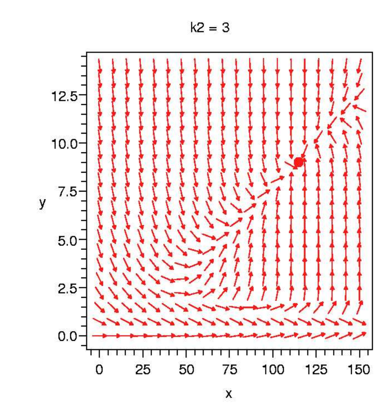


Figure 3

From these figures, we also observe that: In Figure 1, the concentration of $\mathrm{PrP}^{\mathrm{Sc}}$ (y-coordinate) finally becomes low and thus the system enters a harmless state. Conversely, in Figure 3 the concentration of $\mathrm{PrP}^{\mathrm{Sc}}$ goes high and thus the systems enters a pathogenic state. In Figure 2, the system exhibits bistability, the initial concentrations of $\mathrm{PrP}^{\mathrm{Sc}}$ determines whether the final state pathogenic or not. We thus deduce the following facts:

- The turnover rate k_2 determines whether it is possible for a pathogenic state to occur.
- As an answer to our question, a small amount of $\mathrm{PrP}^{\mathrm{Sc}}$ does not lead to a pathogenic state when k_2 is large.
- Compounds that inhibit addition of $\mathrm{PrP}^{\mathrm{Sc}}$ can be seen as a possible therapy against prion diseases. However, compounds that increase the turnover rate k_2 would be the best therapeutic strategy against prion diseases.