Positive and negative circuits in dynamical systems

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Abstract. We state precisely and demonstrate two conjectures of R. Thomas following which a) the existence of a positive circuit in the oriented interaction graph of a differential system is a necessary condition for the existence of several steady states, and b) the existence of a negative non-oriented circuit of length at least two is a necessary condition for the existence of a stable periodic orbit.

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1. Introduction

R. Thomas has conjectured in [12] that a positive feedback loop in the graph of interaction of a differential system is a necessary condition for multistationarity (the existence of several equilibria). This conjecture is important as multistationarity is related, from a biological point of view, to differentiation of the cells; for the discussion, we refer the reader to [12, 11], to the introduction in this journal of J. Demongeot, and to the paper in this journal of Snoussi [9].

The second conjecture of R. Thomas [12] is that a negative loop is a necessary condition for a stable periodic behavior. The possibility of sustained oscillations is also very important for living systems (cf. oscillations of the glycolysis [12]), and we refer the reader to the same papers for the biological background. What is fascinating in these two conjectures is that they depend very weakly on the precise formulation of the underlying dynamical systems: in fact, they have just to follow some conditions on the signs of their Jacobian matrix, i.e., on the way each variable influences (positively or negatively) the time variation of another variable.

We present here a more precise formulation and a simple proof of these conjectures ; see also ([10, 11, 6]), and the paper of Snoussi. The proof depends strongly on theorems of graph and matrix theory.

2. Notations and definitions

We consider a differential system

$$\dot{x} = f(x)$$

defined for $x \in D$, where D is an open convex set of $\mathbf{R}^n$ and f is at least C^1 on D. We suppose that the Jacobian matrix $Df(x)$ has elements of fixed signs (i.e., positive, zero, or negative) in D. We associate with this matrix the directed (oriented) interaction graph, with n vertices, where there is an edge from i to j if $f_j(x)$ depends on x_i. This edge will be positive (negative) if the associated element of the Jacobian matrix is. The hypothesis on the sign of the Jacobian matrix implies therefore that the signed graph is the same everywhere in D. We will also speak of the "signed Jacobian matrix" to designate the matrix of signs.

For the definition of circuits (or loops) in this graph (or in the matrix), we refer to [4]. A circuit will be positive (negative) if the product of its edges is positive (negative). We define also the semicircuit, that is the same concept on the non-oriented interaction graph ([2]).

3. Proof of the first conjecture

We show that the function f is in fact injective if the circuits are nonpositive.

Theorem 1 *If all circuits of the interaction graph are nonpositive, and if there is at least one non-zero term in the expansion of the determinant of the signed Jacobian matrix, then the function f is injective on D.*

By non-zero term, we mean that there is a signed product in the expansion of the determinant which is non-zero, and therefore negative on D (see the formula in [4, p.33]).

Corollary 1 *If all circuits of the interaction graph are nonpositive, and if there is at least one non-zero term in the expansion of the determinant of the signed Jacobian matrix, then there is at most one equilibrium in D.*

Corollary 2 *If all circuits of the interaction graph are nonpositive, and if all the main diagonal elements (the circuits of length one) are negative, then there is at most one equilibrium in D.*

Let us remark that, if all circuits are nonpositive, but the signed determinant cancels (has no non-zero term in its expansion), there can be multiple equilibria. Consider the following system in dimension two:

$$\begin{cases} \dot{x} = y - x \\ \dot{y} = 0 \end{cases}$$

then there is no positive loop, and yet there is an infinite number of (non-isolated) equilibria, given by $x = y$.

Proof : Suppose that x_1 and x_2 are two distinct points in D such that $f(x_1) = f(x_2)$. Then, by a Taylor-type formula:

$$f(x_1) - f(x_2) = 0 = \int_0^1 Df((1-\alpha)x_1 + \alpha x_2)(x_2 - x_1)d\alpha = A(x_1, x_2)(x_2 - x_1)$$

It implies that $A(x_1, x_2)$ is singular. The matrix $A(x_1, x_2)$ has elements with the same signs as $Df(x)$ because it integrates the elements of $Df(x)$ on the straight line from x_1 to x_2, and that this line belongs to the convex set D: therefore it has the same graph. From the hypothesis, all the circuits in $A(x_1, x_2)$ are nonpositive, and we deduce, using a known result from ([4, p. 34]) that all the nonzero terms in the expansion of the determinant have the same sign. If one at least of this term is nonzero, then the determinant is nonzero, and this contradicts the singularity of $A(x_1, x_2)$.

The first corollary is trivial, and the second comes from the fact, that, if all the diagonal elements are negative, then the term "product of the elements on the main diagonal" will be nonzero in the expansion of the determinant (see [4, p. 34]). Then the corollary one applies.

Remark. The convex set D can be only a region of the domain of definition of f, and the elements of the Jacobian matrix may change their signs outside D. The theorem says that, in that region D, they will be at most one steady state.

4. Proof of the second conjecture

It is easy to see that, if all the circuits are nonnegative, then the steady states cannot be asymptotically stable, nor the periodic trajectories (asymptotic stability meaning here orbital asymptotic stability, see [5]). In fact, it is enough that the diagonal elements (the circuits of length one) are nonnegative, and at least one positive, on D. It implies that the trace of the Jacobian matrix is positive, and precludes any stability (for the periodic trajectories, see the theorem in [5, p. 212]). The easy following proposition follows:

Property 1 *If all the circuits of length one (the diagonal elements) are nonnegative, and one at least is positive, then the steady states and the periodic solution cannot be asymptotically stable*

In the following, we will therefore make hypotheses only on the circuits of length greater than one. In fact, we will use the semicircuits (called semicycles in [2]), that is the closed paths in the non-oriented graph. We recall that a nonnegative matrix is irreducible if and only if its oriented graph is irreducible ([1]). We will also make use of the well-developed theory of cooperative systems ([3, 7]).

Theorem 2 *Suppose that the semicircuits of length p, $2 \leq p \leq n$ are nonnegative. Then the dynamical system is similar (by a change of the signs of some variables) to a cooperative system.*

Corollary 3 *Suppose that all the semicircuits of length p, $2 \leq p \leq n$ are nonnegative. Then there is no attracting (and therefore no asymptotically stable) periodic trajectory.*

Corollary 4 *Suppose that all the semicircuits of length p, $2 \leq p \leq n$ are nonnegative; suppose moreover that the oriented graph is strongly connected. Then almost every trajectory converge towards an equilibrium or is unbounded.*

Corollary 5 *Suppose that all the semicircuits of length p, $2 \leq p \leq n$ are nonnegative, that the oriented graph is strongly connected, and that every trajectory is bounded. Then almost every trajectory converge towards an equilibrium.*

From a practical point of view, it means that every trajectory goes towards an equilibrium. In the biological systems for example, it is often easy to obtain bounds on the variables. The result is rather strong then, because it says that, if some condition on a qualitative graph is fulfilled, then almost every trajectory goes to equilibrium.

Proof: The proof is simple and almost contained in [7]. If all the semicircuits of length p, $2 \leq p \leq n$ are nonnegative, then a theorem of graph theory ([2], see also the results in [4, p. 37]) says that it is possible to subdivide the n variables into two groups (one group can be empty), such that, in each group, the signs of the (non-oriented) vertices is positive, and the signs of the vertices between the two groups are negative. Thus the Jacobian matrix is of the form (after a possible re-indexing of the variables):

$$\begin{pmatrix} A & -B \\ -C & D \end{pmatrix}$$

where, if the variables have been partitioned into two groups having q and $(n-q)$ elements, the matrix A is $q \times q$, D is $(n-q) \times (n-q)$, B is $q \times (n-q)$, and C is $(n-q) \times q$. The matrices B and C are nonnegative, and the matrices A and D are nonnegative outside of the main diagonal (the circuits of length one can be of any sign, and even unsigned). Then, if we make the following change of variables (we simply change the signs of the variable of the second group)

$$\begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix} \begin{pmatrix} A & -B \\ -C & D \end{pmatrix} \begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix} = \begin{pmatrix} A & B \\ C & D \end{pmatrix}$$

we obtained a cooperative system (the off-diagonal term of the Jacobian matrix are nonnegative on D), and the corollaries are deduced from the known properties of these systems ([3, 7, 8]; see for example [3, p. 431, p. 435]). Let us recall that the key property of these systems is that they have a monotonous flow, with respect to the partial ordering in $\mathbf{R}^n$.

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