This is a preprint of: "On Darboux integrability of Edelstein's reaction system in  $\mathbb{R}^3$ ", Antoni Ferragut, Clàudia Valls, Carsten Wiuf, Chaos Solitons Fractals, vol. 108, 129–135, 2018. DOI: [10.1016/j.chaos.2018.01.029]

# On Darboux integrability of Edelstein's reaction system in $\mathbb{R}^3$

A Ferragut  $^a$ , C Valls  $^b$ , C Wiuf  $^{c,*}$ 

<sup>a</sup> Institut de Matemàtiques i Aplicacions de Castelló and Departament de Matemàtiques, Universitat Jaume I, Castelló de la Plana, Spain Email: ferraqut@uji.es

<sup>b</sup> Departamento de Matemática, Instituto Superior Técnico, Lisboa, Portugal Email: cvalls@math.tecnico.ulisboa.pt

<sup>c</sup> Department of Mathematical Sciences, University of Copenhagen, Denmark Email: wiuf@math.ku.dk, Phone: +45 5131 9991 ORCID ID: 0000-0002-1302-4445

\* Corresponding author

**Keywords:** Reaction network, polynomial system, exponential factor, first integral, deficiency theorem, multi-stationarity

Classification: Prim34, 37F10, 37N25, 34C14

### Abstract

We consider Edelstein's dynamical system of three reversible reactions in  $\mathbb{R}^3$  and show that it is not Darboux integrable. To do so we characterize its polynomial first integrals, Darboux polynomials and exponential factors.

### 1 Introduction

We consider Edelstein's system of three reversible biochemical reactions among three molecular species [4]:

$$A \xrightarrow{\alpha_{1}} 2 A$$

$$A + B \xrightarrow{\beta_{1}} C \xrightarrow{\gamma_{1}} B,$$
(1)

where  $\alpha_1, \alpha_2, \beta_1, \beta_2, \gamma_1, \gamma_2$  are positive reaction rate constants. Under mass-action kinetics the evolution of the species concentrations is described by the following ODE system of degree 2,

$$\dot{x} = \alpha_1 x + \beta_2 z - \alpha_2 x^2 - \beta_1 xy 
\dot{y} = -\gamma_2 y + (\gamma_1 + \beta_2) z - \beta_1 xy 
\dot{z} = \gamma_2 y - (\gamma_1 + \beta_2) z + \beta_1 xy,$$
(2)



where x, y, z denote the (non-negative) concentrations of the species A, B, C, respectively. Edelstein designed the system as an example of a system with three steady states, two stable and one unstable, for some choices of reaction rate constants. For other choices there is a single stable steady state. He characterized the region of multiple steady states by computational means.

Furthermore, Edelstein suggested that the system's "analytical simplicity" could serve as a potential model system, although the scheme had not been biochemically demonstrated [4]. Despite its apparent simplicity, many aspects of the system are mathematically hard to analyze. In this paper, we study the Darboux integrability of the system by characterizing its Darboux polynomials and exponential factors.

The Edelstein system is an example of a deficiency one reaction network [3, 2], which implies that it has a unique asymptotically stable steady state for each value of the conserved quantity H = y + z for any parameter value, except (potentially) for set of parameter values of dimension one (the deficiency). This set naturally includes the region of multi-stationarity described by Edelstein. The deficiency theory was developed in the 1970s and hence not available to Edelstein [3, 2].

The use of linear first integrals in reaction network theory is common. Edelstein's system has one such first integral, namely H = y + z. With some exceptions the non-linear first integrals have rarely been considered, see [1, 10, 9] for some general considerations and [8, 6, 7, 12] for specific examples. Non-linear first integral are often useful for studying the dynamics of the system, see for example [12, 9]. However, they are generally hard to find. Here we show that Edelstein's system in  $\mathbb{R}^3$  has no polynomial nor rational first integrals, except for H (and transformations thereof). Additionally, we show that it is not Darboux integrable.

### 2 Main theorems

System (2) has a single linear first integral for any choice of positive rate constants,

$$H = y + z$$

which is a consequence of the graphical structure of the reaction network (1) [3]. Using the fact that the set  $\{(x,y,z) \in \mathbb{R}^3 \mid y+z=w\}$  is invariant under the flow generated by (2) for any  $w \in \mathbb{R}_{\geq 0}$ , we can reduce the state space by one dimension. Hence, letting w=y+z, system (2) is transformed into the system

$$\dot{x} = c_4 w + c_1 x - c_4 y - c_2 x^2 - c_3 x y, 
\dot{y} = c_5 w - c_6 y - c_3 x y, 
\dot{w} = 0,$$
(3)

where the six rate constants  $c_1, \ldots, c_6 > 0$  are defined as

$$c_1 = \alpha_1, \quad c_2 = \alpha_2, \quad c_3 = \beta_1, \quad c_4 = \beta_2, \quad c_5 = \beta_2 + \gamma_1 \quad c_6 = \beta_2 + \gamma_1 + \gamma_2.$$

Note that by definition the constants fulfil  $c_6 > c_5 > c_4$ , but this is not important for the arguments that follow. The system (3) cannot be interpreted as a reaction network with

mass-action kinetics, because of the term  $-c_4y$  in the equation for  $\dot{x}$ . The other terms, like  $c_4w$ , can be interpreted in terms of reactions, for example,  $D \to D + A$  in the case of  $c_4w$ , where D is a species with concentration w.

Since w is a constant, we set w = 0 and consider the planar differential system with only five parameters,

$$\dot{x} = c_1 x - c_4 y - c_2 x^2 - c_3 x y, 
\dot{y} = -c_6 y - c_3 x y.$$
(4)

Note that the condition w=0 is biochemically uninteresting as x,y,z are non-negative concentrations in this context.

We will first prove a theorem for system (4) and then use this result to prove a theorem for the original system. Let  $\mathcal{X}$  be the vector field associated system (4),

$$\mathcal{X} = \dot{x}\frac{\partial}{\partial x} + \dot{y}\frac{\partial}{\partial y}.$$

Then the following holds.

**Theorem 1.** Suppose that  $c_2/c_3 \notin \mathbb{Q}_+$ , where  $\mathbb{Q}_+$  denotes the positive rational numbers. Then the following statements hold for system (4).

- (a) It has no polynomial first integrals.
- (b) It has at most two irreducible Darboux polynomials, all of them of degree one. Indeed,  $F_1 = y$  is a Darboux polynomial with cofactor  $K_1 = -c_6 c_3x$  and either:
  - (b.1)  $F_2 = (c_1 + c_6)x c_4y$  is another Darboux polynomial with cofactor  $K_2 = c_1 c_2x$ , if  $(c_2 c_3)c_4 + c_3(c_1 + c_6) = 0$ ;
  - (b.2) or  $F_3 = c_1c_4c_6 c_3(c_4 c_6)(c_6x c_4y)$  is another Darboux polynomial with cofactor  $K_3 = -c_2x$ , if  $(c_2 c_3)c_4 + c_3c_6 = 0$ ;
  - (b.3) or there are no more Darboux polynomials, otherwise.
- (c) It has no rational first integrals.
- (d) It has no exponential factors.
- (e) It is not Darboux integrable.

We remark that Theorem 1(a) and (b.1) are true for all values of the parameters, and not only for  $c_2/c_3 \notin \mathbb{Q}_+$ . The two conditions in (b.1) and (b.2) cannot be fulfilled at the same time. With the added biochemical constraints on the parameters we observe that the quantity in (b.1)  $(c_2 - c_3)c_4 + c_3(c_1 + c_6) = c_2c_4 + c_1c_3 + c_3(c_6 - c_4)$  and the quantity in (b.2)  $(c_2 - c_3)c_4 + c_3c_6 = c_2c_4 + c_3(c_6 - c_4)$  are always positive. Hence with these restrictions there is a unique irreducible Darboux polynomial  $F_1 = y$  for all parameter values, provided that  $c_2/c_3 \notin \mathbb{Q}_+$ .

As a consequence of Theorem 1 we can state a theorem for system (3).

**Theorem 2.** Suppose that  $c_2/c_3 \notin \mathbb{Q}_+$ . Then the following statements hold for system (3).

- (a) The unique irreducible polynomial first integral is H = y + z. Any other polynomial first integral is a polynomial function of H.
- (b) It has no Darboux polynomials with non-zero cofactor.
- (c) It has no rational first integrals except rational functions of H.
- (d) The unique exponential factors are  $F = e^{p(H)}$ , where  $p \in \mathbb{C}[H]$ .
- (e) It is not Darboux integrable.

Likewise Theorem 2(a) is true for all parameter values and not only for  $c_2/c_3 \notin \mathbb{Q}_+$ . It is possible to show that the results hold for some rational choices of  $c_2/c_3$ . However, we do not have a proof in general.

## 3 Proofs

#### 3.1 Proof of Theorem 1

Statement (c) of Theorem 1 follows directly from statement (b). Statement (e) follows from (a), (b), (c) and (d). Hence, we only need to prove the statements (a), (b) and (d). We prove them separately.

#### 3.1.1 Statement (a)

Let H(x, y) be a polynomial first integral of degree  $m \ge 1$  of system (4). We write  $H = \sum_{i=0}^{m} H_i(x, y)$ , with  $H_i$  being homogeneous polynomials for all i, and split the PDE  $\mathcal{X}(H) = 0$  into a system of m + 2 homogeneous ODEs. The equation of degree m + 1 is

$$-x(c_2x + c_3y)\frac{\partial H_m}{\partial x} - c_3xy\frac{\partial H_m}{\partial y} = 0,$$
(5)

using (4). The solution when  $c_2 \neq c_3$  is

$$H_m(x,y) = y^{c_2m/(c_2-c_3)}((c_2-c_3)x + c_3y)^{-c_3m/(c_2-c_3)}.$$

Since  $m \ge 1$  and  $c_2c_3 > 0$ ,  $H_m$  cannot be a polynomial. If  $c_2 = c_3$  then we get

$$H_m(x,y) = f(y \exp(-x/y)),$$

where f is here an arbitrary function. Again this cannot be a polynomial.

Therefore  $H_m$  is not a polynomial and hence no such H can exist. Statement (a) follows.

**Remark 3.** We note that, in the proof of statement (a), we do not need the restriction  $c_2/c_3 \notin \mathbb{Q}_+$ .

#### 3.1.2 Statement (b)

It is straightforward to check that  $F_1 = y$  is a Darboux polynomial with cofactor  $K_1 = -c_6 - c_3 x$ . It holds for all positive values of the constants.

To show that there is a most one other Darboux polynomial we follow the techniques of [5] and [11]. To system (4), we first apply the change of variables (x, y) = (1, u)/v that sets the line at infinity in the horizontal axis. We obtain the cubic system

$$\dot{u} = u(c_2 - c_3 + c_3 u) - (c_1 + c_6 - c_4 u)uv,$$

$$\dot{v} = (c_2 + c_3 u)v - (c_1 - c_4 u)v^2.$$
(6)

Let  $\mathcal{Y}$  be the associated vector field. We note that u and v are Darboux polynomial of (6) since  $u|\dot{u}$  and  $v|\dot{v}$ . Note also that we have written the expressions of  $\dot{u}$  and  $\dot{v}$  as polynomials in v.

Let f(x, y) be an irreducible Darboux polynomial of degree  $m \ge 1$  of system (4) with cofactor  $k(x, y) = k_0 + k_1 x + k_2 y$ . Then the irreducible polynomial  $g(u, v) = v^m f(1/v, u/v) = \sum_{i=0}^m g_i(u)v^i$  is a Darboux polynomial of system (6), where  $g_i \in \mathbb{C}[u]$ . The cofactor of g is

$$K(u,v) = m\frac{\dot{v}}{v} + vk\left(\frac{1}{v}, \frac{u}{v}\right) = k_1 + c_2m + (k_2 + c_3m)u + (k_0 - c_1m + c_4mu)v.$$

The degree of K is 2. It follows that

$$\mathcal{Y}(g) = \dot{u}\frac{\partial g}{\partial u} + \dot{v}\frac{\partial g}{\partial v} = Kg. \tag{7}$$

This PDE can be transformed into an ODE system by writing it as a polynomial equation in the variable v with coefficients depending on u [5]. The coefficients of the PDE give rise to the equations of the ODE system and these equations can be solved recursively to obtain the polynomials  $g_i$ , i = 0, ..., m, that form g [5]. For the monomial  $v^i$ , i = 0, ..., m, we extract an equation in  $g'_{i-1}, g_{i-1}, g'_i, g_i$  of the form

$$[k_1 + c_2 m + (k_2 + c_3 m)u - i(c_2 + c_3 u)] g_i(u) - u(c_2 - c_3 + c_3 u) g_i'(u) =$$

$$-[k_0 - c_1 m + c_4 m u + (i - 1)(c_1 - c_4 u)] g_{i-1}(u) - (c_1 + c_6 - c_4 u) u g_{i-1}'(u),$$
(8)

where i = 0, ..., m, and  $g_{-1} \equiv 0$ . The key point is that all these ODEs depend only on the variable u.

From equation (8) with i = 0 we have

$$(k_1 + c_2m + k_2u + c_3mu)g_0(u) - u(c_2 - c_3 + c_3u)g_0'(u) = 0,$$

with solution

$$g_0(u) = u^{\frac{k_1 + c_2 m}{c_2 - c_3}} (c_2 - c_3 + c_3 u)^{-\frac{k_1 + c_3 m}{c_2 - c_3} + \frac{k_2}{c_3}}, \text{ for } c_2 \neq c_3,$$

up to a non-zero constant which we might take as one because  $v \nmid g$  (as g is irreducible). We notice that the quotient of the eigenvalues of the Jacobian of (6) at the singular point (0,0) is  $(c_2-c_3)/c_2$ , which by assumption is not rational. Hence Theorem 8 of [11] assures

that only two analytic curves pass through this point. Since u=0 and v=0 are Darboux polynomials of the system (6), g cannot pass through (0,0) and therefore the exponent of u in  $g_0$  must be equal to zero. That is,  $k_1 = -c_2m$ . Now since  $g_0$  is a polynomial, we have  $k_2 = -c_3(m-n)$ , where  $n \in \mathbb{N} \cup \{0\}$ . Consequently,  $g_0(u) = (c_2 - c_3 + c_3u)^n$ . As the degree of g is m, we have  $0 \le n \le m$ .

From equation (8) with i = 1 we obtain

$$g_1(u) = (c_2 - c_3 + c_3 u)^{n-1} \left( \frac{(c_2 - c_3)(k_0 - c_1 m)}{c_2} + \frac{c_2 c_4 m + c_3 (k_0 - (c_1 + c_4) m + (c_1 + c_6) n)}{2c_2 - c_3} u + \Delta \sum_{i \ge 2} \frac{(i-1)! c_3^{i-1}}{\prod_{j=1}^{i} ((j+1)c_2 - jc_3)} u^i \right),$$

where  $(j+1)c_2 - jc_3 \neq 0$ , because  $c_2/c_3 \notin \mathbb{Q}_+$ , and

$$\Delta = c_3 k_0 - (c_1 c_3 + c_2 c_4) m + (2c_2 c_4 + c_3 (c_1 - c_4 + c_6)) n.$$

Since  $g_1$  is a polynomial and  $c_2/c_3$  is not rational, we must have  $\Delta = 0$  to cancel the infinite sum. Hence from this equation we obtain an expression for  $k_0$ . The expression of  $g_1$  becomes

$$g_1(u) = (c_2 - c_3 + c_3 u)^{n-1} \left[ (c_2 - c_3) \left( \frac{c_4}{c_3} (m - 2n) - \frac{n}{c_2} (c_1 - c_4 + c_6) \right) + c_4 (m - n) u \right].$$

From equation (8) with i = 2 we obtain

$$g_2(u) = (c_2 - c_3 + c_3 u)^{n-2} \left[ p_2(u) + \Lambda_2 F_1 \left( 1, 1, 2 + \frac{2c_2}{c_2 - c_3}, -\frac{c_3 x}{c_2 - c_3} \right) \right],$$

where  $p_2$  is a polynomial of degree 2,  $\Lambda$  is a constant depending on m, n and the coefficients of the system, and  ${}_2F_1$  is the hypergeometric function. Since this function is not a polynomial, we must have  $\Lambda = 0$ . This equation provides a well-defined expression for m:

$$m = \frac{n}{c_2 c_4 (c_2 + c_3)(c_1 c_3 + c_2 c_4)} \left[ 2c_2^3 c_4^2 - c_2 c_3^2 (c_4 - c_6)(c_1 - 3c_4 + c_6) + 2c_2^2 c_3 c_4 (c_1 - c_4 + c_6) + c_3^3 (c_4 - c_6)(c_1 - c_4 + c_6) \right].$$
(9)

Of course this expression must be a natural number, but this is not important at this moment for the argument.

From equation (8) with i = 3 we obtain three different situations in order to obtain a polynomial expression for  $g_3$ :

(i 
$$(c_2-c_3)c_4+c_3(c_1+c_6)=0$$
, or  $c_3(c_4-c_6)=c_2c_4+c_1c_3$ ,

(ii) 
$$(c_2-c_3)c_4+c_3c_6=0$$
, or  $c_3(c_4-c_6)=c_2c_4$ ,

(iii) 
$$2c_2(2c_4-c_6)+c_3(c_1-c_4+c_6)=0.$$

In the first two cases we have n = m from (9) by direct computations. Moreover further direct computations show that there is a linear solution  $g(u, v) = (c_1 + c_6 - c_4 u)^m$  in the first case and  $g(u, v) = (c_3(c_4 - c_6)(c_6 - c_4 u) - c_1c_4c_6v)^m$  in the second case. By transforming back to the coordinates (x, y), we obtain the Darboux polynomials  $F_2$  and  $F_3$ , respectively, as given in the theorem. No more Darboux polynomials are obtained in these two cases.

It remains to deal with the third case. We aim to show that this case does not lead to more Darboux polynomials. From equation (8) with i = 4 we obtain two different situations that provide a polynomial expression for  $g_4$ :

(iv)  $2c_4 = c_6$ ,

(v) 
$$c_4(2c_2-c_3)=c_6(c_2-c_3)$$
.

We do not provide the solutions  $g_3$  and  $g_4$  because they are very long and not relevant for the proofs.

Concerning the cases (iv) and (v), we discard the first case because by insertion of (iv) into (iii), we get  $c_1 < 0$ , which is not possible. We study the second case, for which we have m = 2n by insertion of (iii) and (v) into (9).

We claim that under the stated hypotheses system (6) has no Darboux polynomials but the axes. If we prove the claim then statement (b) of the theorem follows.

Assume (iii) and (v) hold. To prove the claim we first show that  $\deg g_i(u) = n$  for all  $0 \le i \le m$ . Using the expressions obtained for  $k_0, k_1, k_2$  that hold generally, and (iii) and (v), the solution of equation (8) can be directly computed;

$$g_i(u) = (c_2 - c_3 + c_3 u)^{n-i} C_i(u),$$

where  $C_i \in \mathbb{R}[u]$  is a polynomial (this is consistent with the expressions obtained for  $g_0, g_1, g_2$ ). Now write  $C_i(u)$  as a power series in u. Plugging this expression into (8) and reducing, then the first i+1 coefficients (corresponding to the monomials  $u^j$ ,  $j=0,\ldots,i$ ) of the power series can be obtained from a determined linear system of equations. The rest of the coefficients of the power series is solved from an infinite homogeneous determined linear system of equations, hence they are all zero. This last step assumes  $c_2/c_3 \notin \mathbb{Q}_+$ , which holds by assumption. Thus  $C_i$  is a polynomial of degree i and therefore  $g_i$  has degree n.

In particular, this implies that  $g(u,v) = \sum_{i=0}^{n} g_i(u)v^i$ , that is  $g_i \equiv 0$  for  $i = n+1, \ldots, m$ . This further implies that (8) for i+1=n becomes

$$(n(c_1 - c_4 u) + (k_0 - c_1 m + c_4 m u))g_n(u) + u(c_1 + c_6 - c_4 u)g'_n(u) = 0,$$

where  $m, k_0, c_1, c_4$  must be substituted by their respective values. From this equation we get

$$g_n(u) = C_n u^{\frac{c_2 n}{3c_2 - c_3}} (3c_2 - c_3 - c_2 u + c_3 u)^{\frac{(2c_2 - c_3)n}{3c_2 - c_3}},$$

where  $C_n$  is a constant. Since this is a polynomial and  $c_2/c_3 \notin \mathbb{Q}_+$ , we must have  $C_n = 0$ , and hence  $g_n \equiv 0$ . However, this contradicts the fact that g has degree m. Therefore no new Darboux polynomials are obtained in this case and hence statement (b) of the theorem follows.

#### 3.1.3 Statement (d)

We divide the proof of statement (d) into different partial results.

**Lemma 4.** System (4) has no exponential factors of the form  $\exp(g)$ , with  $g \in \mathbb{C}[x,y]$ .

*Proof.* Suppose that  $\exp(g)$  is an exponential factor of system (4) with cofactor L and  $\deg g = m \in \mathbb{N}$ . It is clear that g satisfies the equation  $\mathcal{X}(g) = L$ . We can write this equation as a system of homogeneous ODE,  $g(x,y) = \sum_{i=0}^m g_i(x,y)$ , where  $g_i$  is a homogeneous polynomial of degree i in x, y. The equation of degree m+1 is

$$-x(c_2x + c_3y)\frac{\partial g_m}{\partial x} - c_3xy\frac{\partial g_m}{\partial y} = 0.$$

According to the proof of statement (a) in Section 3.1.1, such polynomial g cannot exist and the lemma follows.

**Lemma 5.** System (4) has no exponential factors of the form  $\exp(g/y^n)$ , with  $g \in \mathbb{C}[x,y]$ ,  $y \nmid g$  and  $n \in \mathbb{N}$ .

*Proof.* Suppose that  $\exp(g/y^n)$  is an exponential factor of system (4) with cofactor L. Then

$$\mathcal{X}(g) + n(c_6 + c_3 x)g = Ly^n.$$

Let  $\tilde{g} = g|_{y=0} \not\equiv 0$  (by assumption), which is a polynomial in x. Evaluating the above equation on y = 0 we get

$$x(c_1 - c_2 x)\tilde{g}'(x) + n(c_6 + c_3 x)\tilde{g}(x) = 0.$$

This equation has solution

$$\tilde{q}(x) = \tilde{C}x^{-\frac{c_6}{c_1}n}(c_1 - c_2x)^{\frac{c_3}{c_2}n + \frac{c_6}{c_1}n}$$

where  $\widetilde{C} \neq 0$  is a constant. The function  $\widetilde{g}$  is not a polynomial since it has degree  $nc_3/c_2 \notin \mathbb{Q}_+$  by assumption. Hence the lemma follows.

Proof of statement (d). If  $\exp(g/f)$ , with  $g, f \in \mathbb{C}[x, y]$ , is an exponential factor, then f is a Darboux polynomial. For  $(c_2 - c_3)c_4 + c_3(c_1 + c_6) \neq 0$  and  $(c_2 - c_3)c_4 + c_3c_6 \neq 0$ , system (4) has only the Darboux polynomial  $F_1 = y$ . An exponential factor with  $f = y^n$  for some  $n \in \mathbb{N}$  is excluded by Lemma 5.

Assume that  $(c_2 - c_3)c_4 + c_3(c_1 + c_6) = 0$ . In this case, system (4) has exactly two Darboux polynomials with non-zero cofactor, namely  $F_1 = y$  and  $F_2$ . Consequently, if it has an exponential factor, then it must be of the form  $e^{g/(y^{n_1}F_2^{n_2})}$ , where  $y, F_2 \nmid g$  and with  $n_1 \in \mathbb{N} \cup \{0\}$  and  $n_2 \in \mathbb{N}$ . Proceeding as in the proof of Lemma 5, we have  $n_1 = 0$ . So the exponential factor must be of the form  $e^{g/F_2^n}$ , with  $n \in \mathbb{N}$ . Let L be its cofactor. Since  $F_2^n$  has cofactor of  $nK_2$ , we have

$$\mathcal{X}(g) = LF_2^n + (nK_2)g = LF_2^n + n(c_1 - c_2x)g,$$

where  $K_2 = (c_1 - c_2 x)$  follows from statement (b). We take  $F_2 = 0$ , that is,  $y = (c_1 + c_6)x/c_4$  and let  $\tilde{g} = g|_{F_2=0} \not\equiv 0$ . Then

$$n(c_1 - c_2 x)\tilde{g}(x) + x(c_6 + c_3 x)\tilde{g}'(x) = 0.$$

Solving this equation we obtain

$$\tilde{g}(x) = \tilde{C}x^{-\frac{c_1}{c_6}n}(c_6 + c_3x)^{\frac{c_1}{c_6}n + \frac{c_2}{c_3}n},$$

where  $\widetilde{C} \neq 0$  is a constant. This expression is not a polynomial since the exponent of x is negative, because  $n \neq 0$ , or since it has degree  $nc_2/c_3 \notin \mathbb{Q}$ . Hence we get a contradiction and statement (d) follows in this case.

Finally assume  $(c_2 - c_3)c_4 + c_3c_6 = 0$ . As above, system (4) has exactly two Darboux polynomials with non-zero cofactor, namely,  $F_1 = y$  and  $F_3$ . Consequently, if it has an exponential factor, then it must be of the form  $e^{g/(y^{n_1}F_3^{n_2})}$ , where  $y, F_3 \nmid g$  and with  $n_1 \in \mathbb{N} \cup \{0\}$  and  $n_2 \in \mathbb{N}$ . Proceeding as in the proof of Lemma 5, we have  $n_1 = 0$ . So the exponential factor has the form  $e^{g/F_3^n}$ , with  $n \in \mathbb{N}$ . Let  $m = \deg g \in \mathbb{N}$ . We can assume that m < n. Indeed, if  $m \ge n$ , then there exist polynomials q and r such that  $g = qF_3^n + r$ , with  $\deg r < n$ . Hence  $e^{g/F_3^n} = e^q e^{r/F_3^n}$  and therefore  $e^q$  is an exponential factor, in contradiction with Lemma 4. Thus m < n.

From statement (b) we have that  $nK_3 = -c_2x$  is the cofactor of  $F_3^n$ . Proceeding as in the previous case, this leads to the equation

$$\mathcal{X}(g) = LF_3^n + (nK_3)g = LF_3^n - nc_2xg, \tag{10}$$

where  $L = \ell_0 + \ell_1 x + \ell_2 y$  is the cofactor of the exponential factor. Let  $g = \sum_{i=0}^m g_i(x,y)$ , where  $g_i$  is a homogeneous polynomial of degree i, for all i = 0, ..., m. The homogeneous equation of degree n + 1 is  $(\ell_1 x + \ell_2 y) S^n = 0$ , where  $S = c_6 x - c_4 y$  is, up to a non-zero constant, the homogeneous part of highest degree of  $F_3$ . Since  $S \not\equiv 0$ , we have  $\ell_1 = \ell_2 = 0$ .

We distinguish two cases. If m+1 < n then the homogeneous equation of degree n is  $\ell_0 S^n = 0$ , and therefore  $\ell_0 = 0$ . This implies that L = 0 and hence that  $g/F_3^n$  is a rational first integral of system (4), in contradiction with statement (c) of the theorem.

Now we consider the case m + 1 = n. The homogeneous equation of degree m + 1 of (10) is

$$-x(c_2x+c_3y)\frac{\partial g_m}{\partial x}-c_3xy\frac{\partial g_m}{\partial y}+c_2nxg_m=\ell_0S^n.$$

Since x divides the left hand side of this equation, we must have  $\ell_0 = 0$ . Then again L = 0, and we have reached a contradiction.

All cases have been considered and therefore the proof of statement (d) follows.  $\Box$ 

### 3.2 Proof of Theorem 2

Statement (c) of Theorem 2 follows immediately from statements (a) and (b). Statement (e) follows from (a), (b), (c) and (d). This is because it is not possible to construct rational first integrals nor Darboux first integrals without Darboux polynomials. Hence, we need only prove the statements (a), (b) and (d). We prove them separately. Instead of system (2) we shall consider its equivalent system (3).

#### 3.2.1 Statement (a)

Let H(x, y, w) be an irreducible polynomial first integral of degree  $m \in \mathbb{N}$  of system (3). Since w is also a polynomial first integral of (3) and H is irreducible, we can assume that  $w \nmid H$ . Let  $H_0 = H|_{w=0} \not\equiv 0$ . Clearly,  $H_0(x, y)$  is a polynomial first integral of system (4). Thus by Theorem 1(a) we have  $H_0 \equiv 0$ , which is a contradiction. Therefore statement (a) follows.

**Remark 6.** We note that, in the proof of statement (a), we do not need the restriction  $c_2/c_3 \notin \mathbb{Q}_+$  as the proof only depends on Theorem 1(a).

### 3.2.2 Statement (b)

Let f(x, y, w) be an irreducible Darboux polynomial of degree  $m \in \mathbb{N}$  of system (3) with cofactor  $k = k_0 + k_1 x + k_2 y + k_3 w$ . We write  $f = \sum_{i=0}^m f_i(x, y) w^i$ , with  $f_i \in \mathbb{C}[x, y]$  for all  $i = 0, \ldots, m$ , with deg  $f_i \leq m - i$ .

We first assume that  $(c_2 - c_3)c_4 + c_3(c_1 + c_6) \neq 0$  and  $(c_2 - c_3)c_4 + c_3c_6 \neq 0$ . Clearly  $f_0(x,y) = f|_{w=0}$  is a Darboux polynomial of system (4), which is system (3) with w = 0 fixed. It follows from Theorem 1(b) that  $f_0(x,y) = c_0y^n$  with  $c_0 \in \mathbb{C}$  and  $n \in \mathbb{N} \cup \{0\}$ . Moreover we have  $k = -n(c_6 + c_3x) + k_3w$  from the expression for the cofactor of  $F_1 = y$ , see Theorem 1(b). Note that we can take  $c_0 = 1$  as it cannot be zero because f is irreducible (and in particular  $w \nmid f$ ). Indeed, we must have n = m, otherwise there is a factor w in the highest degree terms of f, and this is not possible because w = 0 is not invariant at infinity (we only have the directions  $xy((c_2 - c_3)x + c_3y) = 0$ , which are fulfilled for singular points). Since f is invariant under the flow of system (3), we have

$$(c_{1}x - c_{4}y - c_{2}x^{2} - c_{3}xy + c_{4}w) \sum_{i=1}^{m} \frac{\partial f_{i}}{\partial x} w^{i} + (-(c_{6} + c_{3}x)y + c_{5}w) \left( my^{m-1} + \sum_{i=1}^{m} \frac{\partial f_{i}}{\partial y} w^{i} \right)$$

$$= (-m(c_{6} + c_{3}x) + k_{3}w) \left( y^{m} + \sum_{i=1}^{m} f_{i}w^{i} \right),$$
(11)

where the terms of system (3) have be reordered and we have used  $f_0 = y^m$ .

The equation of degree i in w obtained from (11) is

$$(c_1x - c_4y - c_2x^2 - c_3xy)\frac{\partial f_i}{\partial x} + c_4\frac{\partial f_{i-1}}{\partial x} - (c_6 + c_3x)y\frac{\partial f_i}{\partial y} + c_5\frac{\partial f_{i-1}}{\partial y} = -m(c_6 + c_3x)f_i + k_3f_{i-1}.$$
(12)

Equation (12) for i = 0 is trivial. Equation (12) for i = 1 writes as

$$(c_1x - c_4y - c_2x^2 - c_3xy)\frac{\partial f_1}{\partial x} - (c_6 + c_3x)y\frac{\partial f_1}{\partial y} + c_5my^{m-1} + m(c_6 + c_3x)f_1 + k_3y^m = 0.$$

Direct computations show that  $f_1|_{y=0} \equiv 0$ . Hence we must have  $f_1 = y^k \widetilde{f}_1$ , for some  $k \in \mathbb{N}$ , k < m, and some  $\widetilde{f}_1$  such that  $y \nmid \widetilde{f}_1$ . Plugging the expression of  $\widetilde{f}_1$  into the previous

equation and simplifying we obtain an ODE with unknown  $\tilde{f}_1$ . Direct computations show that this equation has no polynomial solutions unless k = m - 1. Thus  $f_1 = y^{m-1}\tilde{f}_1$ .

We can repeat this argument to show that  $y^{m-i}|f_i$ , for all i < m. That is,  $f_i = y^{m-i}\widetilde{f_i}$ , with  $y \nmid \widetilde{f_i}$ . Now equation (12) for i = m writes as

$$c_5\widetilde{f}_{m-1} + m(c_6 + c_3x)f_m - k_3\widetilde{f}_{m-1}y = 0,$$

where both  $\bar{f}_{m-1}$  and  $\tilde{f}_m = 0$  are constant. Since  $c_3 > 0$  we must have m = 0. Therefore statement (b) follows in this case.

Now assume that  $(c_2 - c_3)c_4 + c_3(c_1 + c_6) = 0$ . In this case y and  $F_2$  are Darboux polynomials of system (4). It follows from Theorem 1(b) that  $f_0(x,y) = y^{n_1}F_2^{n_2}$  with  $n_1, n_2 \in \mathbb{N} \cup \{0\}$ . It can be proved in a similar way as in the previous case that if  $n_1 > 0$  then we have y|f. Thus we have  $n_1 = 0$ . Hence we can write  $f_0(x,y) = F_2^n$  with  $n \in \mathbb{N} \cup \{0\}$ . Now the same arguments explained above but restricting to  $F_2 = 0$  instead of restricting to y = 0 lead to  $F_2|f$ . Hence no irreducible Darboux polynomial f can exist and statement (b) follows in this case.

The case  $(c_2 - c_3)c_4 + c_3c_6 = 0$  follows using the same arguments, replacing  $F_2$  by  $F_3$ . Hence all cases have been considered and statement (b) is proved.

# 3.3 Proof of statement (d)

It follows from statements (a) and (b) that if system (3) has an exponential factor with cofactor L, then it must be of the form  $\exp(g/w^n)$ , with  $g \in \mathbb{C}[x,y,w]$ ,  $w \nmid g$  and  $n \in \mathbb{N} \cup \{0\}$ . Moreover

$$\mathcal{X}(q) = Lw^n$$
.

Let  $\tilde{g} = g|_{w=0} \not\equiv 0$ . If n > 0 then the above equation on w = 0 writes as  $\mathcal{X}(\tilde{g}) = 0$ , and hence  $\tilde{g}$  is a polynomial first integral of system (4), which is not possible by Theorem 1.

Hence, any exponential factor of system (3) must be of the form  $\exp(g)$ , with  $g \in \mathbb{C}[x,y,w]$ . Now let  $\exp(g)$  be an exponential factor of system (3) with cofactor L and  $\deg g = m \in \mathbb{N}$ , that is,  $\mathcal{X}(g) = L$ . We can write this equation as a system of homogeneous ODEs. Let  $g_m$  be the homogeneous polynomial of degree m of g, and let  $\widetilde{g}_m = g_m|_{w=0}$ . The equation of degree m+1 is

$$-x(c_2x + c_3y)\frac{\partial \widetilde{g}_m}{\partial x} - c_3xy\frac{\partial \widetilde{g}_m}{\partial y} = 0.$$

This equation is identical to equation (5) of the proof of Theorem 1(a). Hence the same conclusions apply. In particular we conclude that it has no polynomial solutions of positive degree. Hence  $\tilde{g}_m \equiv 0$ , which yields  $g = w^j \bar{g}$  with  $j \in \mathbb{N}$  and  $\bar{g} \in \mathbb{C}[x, y, w]$ ,  $w \nmid \bar{g}$ . Moreover since deg  $L \leq 1$  because the system is quadratic we must have  $L = \alpha w$ , where  $\alpha \in \mathbb{C} \setminus \{0\}$ , and then j = 1. We note that L has no constant term because j > 0.

We end the proof by showing that indeed  $\alpha = 0$ . After simplifying by w, we have that  $\bar{g}$  satisfies the equation  $\mathcal{X}(\bar{g}) = \alpha$ . The arguments in the proof of Theorem 1(a) show that  $\bar{g}$  does not depend on x, y, that is  $\bar{g} = \bar{g}(w)$  (because  $\dot{w} = 0$ ), so  $\mathcal{X}(\bar{g}) = 0$ , which means that  $\alpha = 0$ , a contradiction.

# Acknowledgements

AF is partially supported by the MINECO grants MTM2013-40998-P and MTM2016-77278-P and by the Universitat Jaume I grant P1-1B2015-16. CV is partially supported by FCT/Portugal through UID/MAT/04459/2013. CW is supported by the Lundbeck Foundation, Denmark, the Danish Research Council and Dr.phil. Ragna Rask-Nielsen Grundforskningsfond (administered by the Royal Danish Academy of Sciences and Letters). Part of this work was done while CW was visiting Universitat Politècnica de Catalunya in Spring 2017.

# References

- [1] Aybar, I.K., Aybar, O.O., Fercec, B., Romanovski, V.G., Samal, S.S., Weber, A.: Investigation of invariants of a chemical reaction system with algorithms of computer algebra. MATCH Commun. Math. Comput. Chem. **74**, 465–480 (2015)
- [2] Feinberg, M.: Chemical reaction network structure and the stability of complex isothermal reactors. i. the deficiency zero and deficiency one theorems. *Chem. Eng. Sci.* **42**(10), 2229–2268 (1987)
- [3] Feinberg, M., Horn, F.J.M.: Chemical mechanism structure and the coincidence of the stoichiometric and kinetic subspaces. *Arch. Ration. Mech. An.* **66**(1), 83–97 (1977)
- [4] Edelstein, B.B.: Biochemical model with multiple steady states and hysteresis. *J. Theor. Biol.* **29**(1), 57–62 (1970)
- [5] Ferragut, A., Gasull, A.: Seeking Darboux polynomials. *Acta Appl. Math.* **139**(1), 167–186 (2014) DOI:10.1007/s10440-014-9974-0.
- [6] Ferragut, A., Valls, C.: On the Darboux integrability of a cubic CRN model in ℝ<sup>5</sup>. Chaos Soliton.Fract. 82, 131–138 (2016)
- [7] Ferragut, A., Valls, C.: On the complete integrability of the Raychaudhuri differential system in  $\mathbb{R}^4$  and of a CRNT model in  $\mathbb{R}^5$ . Qual. Theory Dyn. Syst. DOI:10.1007/s12346-017-0230-7.
- [8] Llibre, J., Valls, C.: Liouvillian and analytic first integrals for the brusselator system. J. Nonlin. Math. Phys. 19(02) (2012)
- [9] Mahdi, A., Ferragut, A, Valls, C., Wiuf, C.: Conservation laws in biochemical reaction networks, submitted.
- [10] Nagy, I., Tóth, J.: Quadratic first integrals of kinetic differential equations. J. Math. Chem. 52(1), 93–114 (2014)
- [11] Seidenberg, A.: Reduction of singularities of the differential equation ady= bdx. *Amer. J. Math.* **90**, 248–269 (1968)
- [12] Volpert, A.I.: Differential equations on graphs. Mat. Sb. (N.S.) 88(4), 578–588 (1972)