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Optimal Control of the Controlled Lotka-Volterra Equations with Applications-The Permanent Case*

Bernard Bonnard[†] and Jérémy Rouot[‡]

Abstract. In this article motivated by the control of complex microbiota in view to reduce the infection by a pathogenic agent, we introduce the theoretical frame from optimal control to analyze the problem. Two complementary approaches can be applied in the analysis: one is the so-called permanent case, where no digital constraints are concerning the control (taken as a measurable mapping) versus the sampled-data control case taking into account the logistic constraints, e.g. frequency of the medical interventions. The model is the n-dimensional Lotka-Volterra equation controlled using either probiotics or antibiotic agents or transplantation and bactericides. In the permanent case the Maximum principle is used to parameterize the geodesics and the optimal synthesis boils down to analyze mainly the singular trajectories and their concatenation with bang arcs. This analysis is preliminary and complementary to the study of the problem in the frame of optimal sampled-data control, where convergence of the MPC algorithms is related to singular trajectories and non-uniqueness of the optimal dynamics encountered in the permanent case.

Key words. Optimal control in the permanent case, sampled-data control, biomathematics and population dynamics, geometric control theory.

MSC codes. 49K15, 92B05, 93C10, 93C15, 92D25

1. Introduction. The book by Vito Volterra [26] "Leçons sur la théorie mathématique pour la lutte pour la vie" leads to the Lotka-Volterra model to predict in a general frame the evolution on interacting biological species. The problem was studied independently by Lotka which makes the connection with chemical networks. The relation with control systems was already present in the original predator-prey model with two species set by Umberto d'Ancona to explain the evolution of the species in relation with fishing activity during the first World War. The original memoir starts with an interesting discussion about the evolution of the species in relation with integrability properties of the conservative model. It validates Ancona observations and opens the road to analyze different problems of populations dynamics. This leads to extend the model to the non conservative 2d-case in any dimension.

Recently our attention was attracted by the works of Jones et al. [16] based on the model by Stein et al. [25] in an attempt to model and cure a gut mouse microbiota infected by the C-difficile bacteria which leads to a 11-dimensional controlled Lotka-Volterra model, using either fecal transplantation or one antibiotic agent. The problem is analyzed using 2d-reduced (projection) non conservative Lotka-Volterra model. This model validates the effect of a single fecal injection to cure the infection by constructing a separatrix which allows

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to decide about success or failure of the procedure due to delay in the transplantation or insufficient dosing.

To understand this approach let us introduce the Lotka-Volterra dynamics and analyze its limits, already discussed in [26]. The system is given by the equations

40 (1.1)
$$\frac{\mathrm{d}x}{\mathrm{d}t}(t) = (\mathrm{diag}(x(t)))(Ax(t) + r),$$

where $x = (x_1, x_2, \dots, x_n)^{\mathsf{T}}$ belongs to the positive quadrant $x_i \geq 0$ and is the vector of popu-lations of the interacting species, diagx denotes in short the diagonal matrix with coefficients x_i , $A = (a_{ij})$ is the matrix containing the interacting coefficients between the species and $r = (r_1, r_2, \dots, r_n)^{\intercal}$ is the vector describing the individual growth rate without interaction. Assuming the matrix A invertible, the system possesses a unique interior equilibrium (called persistent) given by $x_0 = -A^{-1}r$. The model is only valid provided that each species is contained in an interval $[\varepsilon, M]$, $\varepsilon > 0$ and hence in the model only the so-called persistent trajectories defined for positive times and contained in $[\varepsilon, M]^n$ have physical signification. Therefore the differential equation represents an analytic continuation of the dynamics to the whole euclidean space. But the model in fine describes the interaction between the persistent equilibrium and equilibria of an hierarchy of reduced Lotka-Volterra dynamics associated to extinction of the different species, e.g. extinction of x_1 leads to analyze the reduced model of n-1 interacting species where we substitute in the dynamics $x \to x = (x_2, \dots, x_n)^{\intercal}$ and again we can compute the persistent equilibria of the reduced dynamics. Therefore this leads to interpret the model as a system of interaction between a given number k of equilibria and from this view point different generalizations of the dynamics can be proposed in the frame of dynamical systems.

From this point of view the analysis of [16] is precisely to describe a policy in the experimental setting where a mouse is treated prior to infection by antibiotic and a final fecal injection in order to cure the C-difficile infection. The 2d-reduced model is with a saddle persistent point with stability and unstability domain delimited by separatrixes and the success of the therapy is to reach a stability domain of an healthy (non persistent) equilibrium.

At this time the connection with the network of chemical species pointed by Lotka has to be made in relation with intense research activities in the seventies. They were motivated by the analysis of chemical batch reactors and realized mainly by Feinberg-Horn-Jackson, see for instance the recent book [14]. The study is related to the graph of the reactions using the concept of deficiency. The simplest situation (zero deficiency) being dynamics with no (non trivial) singular point nor periodic trajectory in the irreversible case like the network: $A \to B$, $B \to C$, and a single persistent point with asymptotically stable dynamics in the reversible case like the network: $T + M \to A$, $A \to B$, $B \to T + M$, $A \to T + M$.

Similarly concerning the Lotka–Volterra equations there was an intense research activities due in particular to Zeeman, Smale, Hirsch to analyze the dynamics in the frame of the theory of dynamical systems where again the concept of reduced dynamics is handled using roughly the concept of reduced attractors as the limit behaviors of the trajectories. The mathematical limit of the study is well explained in [15] where such reduction is shown to be useful in the 3d-case in the special case of competitive Lotka–Volterra system that is when A is a matrix with negative entries. The model reduction is associated to a 2d-system with a simplex separatrix

cycle connecting three non persistent (saddle type) equilibria and is surrounding the persistent equilibrium of the model. Without the competing assumption the road to chaos is open using for instance the period doubling bifurcation. Note this leads to consider Generalized Lotka–Volterra dynamics by gluing such simplicia.

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The objective of this paper is to investigate the problem of reducing the infection of a complex microbiote and if the study of the dynamics of the associated Lotka-Volterra model plays a role, the control problem is associated to compute the accessibility set. Indeed from dynamical point of view denoting X the vector field $(\operatorname{diag} x)(Ax + r)$ only this dynamics is studied. But from a control point of view the problem is to assign to each different control action, e.g. antibiotic, probiotic, transplantation or bactericide, an additional vector field Yand to study from geometric point of view the action of the pseudo-semigroup S(D) generated by concatenation of the positive orbits of the vectors fields denoted respectively $\varphi_t = \exp tX$, $\psi_t = \exp tY$, where D is the polysystem $\{X,Y\}$. The accessibility set at time t denoted $A(x_0,t)$ is the orbit when the total time is t and its boundary contains the extremities of the time minimal geodesics. It can be evaluated for small time using Lie brackets computations of X and Y. This boundary can have a complicated structure but an intense research activities at the end of the eighties was devoted to stratify this set under some suitable assumptions in relation with the problem of computing a regular synthesis, see in particular [9], [11]. In this research program the Maximum Principle [23] is a very powerful tool to analyze the optimal solutions since it gives a parametrization of the boundary of the accessibility set, where the geodesics dynamics is the projection of an n-Hamiltonian dynamics that is a differential system in dimension 2n and this system is not smooth.

Let us formulate this principle to analyze for instance the effect of an antibiotic or probiotic treatment only, whence the control system takes the form

$$\frac{\mathrm{d}x}{\mathrm{d}t}(t) = X(x(t)) + u(t)Y(x(t)),$$

where the control $u(\cdot)$ in the permanent case belongs to the set \mathcal{U} of bounded measurable mappings valued in the convex set U = [-1, +1], where u = 0 corresponds to zero dosing that is $X - Y = (\operatorname{diag} x)(Ax + r)$ while to maximal dosing corresponds the dynamics $(\operatorname{diag} x)(Ax + r) + G(x)$, where $G(x) = (\operatorname{diag} x)(\varepsilon_1, \dots, \varepsilon_n)^{\mathsf{T}}$ and $\varepsilon = (\varepsilon_1, \dots, \varepsilon_n)^{\mathsf{T}}$ is the sensitivity vector of the antibiotic or probiotic agent.

Consider the problem of reaching in minimum time a terminal manifold N related to reduce the infected agent x_1 , e.g. reach a small population x_1 in minimal time (a dual formulation of the problem is min x_1 for fixed final time).

Theorem 1.1. The Maximum Principle tells us that if $(x(\cdot), u(\cdot))$ is a time minimal control-trajectory pair on $[0, t_f]$, then there is exists a non vanishing adjoint n-dimensional vector $p(\cdot)$ such that the triple $(z(\cdot), u(\cdot))$, z = (x, p) satisfies the equations that we introduce next.

Denoting $H(z, u) := H_X(z) + uH_Y(z)$ the pseudo-Hamiltonian, where if Z is a vector field, $H_Z(z) = p \cdot Z(x)$ denotes the Hamiltonian lift and M is the maximized or true Hamiltonian $\max_{u \in [-1,+1]} H(z,u)$. Then for almost every t one has

117 (1.2)
$$\frac{\mathrm{d}x}{\mathrm{d}t}(t) = \frac{\partial H}{\partial x}(x(t), p(t), u(t)), \quad \frac{\mathrm{d}p}{\mathrm{d}t}(t) = -\frac{\partial H}{\partial p}(x(t), p(t), u(t)).$$

Moreover the optimal control satisfies the maximization condition a.e.

119 (1.3)
$$H(z(t), u(t)) = M(z(t)),$$

120 and M is a positive constant.

At the terminal time t_f the transversality condition holds

122 (1.4)
$$p(t_f) \perp T_{x(t_f)}^* N.$$

From the maximization condition one deduces that an optimal control is the concatenation of:

- Regular subarcs where $u(t) = \text{sign} H_Y(z(t))$ a.e.
- Singular subarcs defined by the implicit relation $H_Y(z(t)) = 0$.

Such singular arcs define the geodesics solutions when relaxing the control bound to the whole $u \in \mathbb{R}$. They form an Hamiltonian flow constrained to the switching set $\Sigma : H_Y(z) = 0$ in which they filled in general a subset of codimension one. Hence they play an important role in our study, see for instance the reference [5].

The main objective of this article is to analyze geometrically this dynamics in the case of the controlled Lotka–Volterra equations and from the control optimal point of view it is the analogue of the program of classifying the geometric dynamics for the Lotka–Volterra model. The limit being essentially the same that is to handle the curse of dimension and the computational complexity. Making the connection of the problem of minimizing the infection with the problem of maximizing the production of one species for chemical network whose dynamics is given by Arrhenius law, our objective is to use in this frame a series of articles started in the eighties, see for instance [7, 20], aiming to optimize the production of batch chemical reactors and recently pursued in [8]. Besides the study of the geodesics dynamics parameterized by an Hamiltonian system, thanks to the Maximum Principle, a complementary point is to characterize the optimality properties of the geodesics in relation with the concept of conjugate time where the time optimality is lost for the C^1 topology while for a cut point the optimality is lost globally. In this frame the series of results and techniques presented in [5, 1] will be used in their totality.

Moreover in practice our objective is to compute an approximation of the time minimal synthesis that is to reach the terminal manifold for every initial condition determining the closed loop optimal control: $x \to u^*(x)$. Regularity conditions have to be satisfied in order to define the solutions and they are related to the regularity properties of the time minimal value function. Relation with convergence of numerical methods in the sampled-data control case will be pointed in this article but not analyzed due to space restrictions. Also the sampled-data control frame is different since the dynamics of the evolution is given using a MPC method and the controlled Lotka–Volterra dynamics is only an intermediate tool to estimate the effect of the control on a finite horizon on a domain where the Lotka–Volterra model or an extension are valid.

The article is organized as follows. In section 2 the controlled Lotka-Volterra model is introduced and the optimal control problem presented in the frame of permanent controls or sampled-data controls. In the permanent case the Maximum Principle leads to the classification of the geodesics in the context of geometric optimal control and singularity theory using

the seminal earliest contributions of [17, 18, 13]. Some consequences are deduced in the case of a problem with a terminal manifold of codimension one. The section 3 is based on the series of articles [7, 20, 8], which are rather technical and our contribution being to introduce two main concepts. The first one is the notion of Whitney chart to determine in an appropriated coordinates systems the time minimal synthesis in a neighborhood of the terminal manifold using the construction of semi-normal forms to estimate the switching and cut loci up to all cases of codimension two for the C^{∞} -Whitney topology. Secondly the concept of unfolding from singularity theory is introduced in our control frame to reduce the classification to 2d and 3d cases and using their description (dictionary) of the aforementioned references. The final section is devoted to the analysis and the classification of singular arcs in the 2d and 3d cases to deduce the time minimal syntheses. In this program the computation can be automatized in the 2d case using two classical invariants: the collinear set and the singular locus. In dimension 3 the problem is intricate due to the complexity of the singular dynamics. But a program of computations in the general case can be outlined based on gluing Whitney charts as an alternative of programs as for example in [2] to derive patchy feedbacks to approximate the time minimal function, our construction differing by the dominant use of the feedback singular control.

2. Model of Controlled Lotka-Volterra Equation and Optimal Control.

2.1. A quick tour in the 2d-Lotka-Volterra predator-prey model. The original Lotka-Volterra model analyzed in [26] describes, in the frame of (conservative) integrable dynamics, the interaction between two species. More precisely it was constructed to explain the evolution of the averaged populations of two fishing species in relation with diminution of the fishing activity observed by d'Ancona during the first World War and succeeds to explain the observation. From dynamical point of view it concerns the case of a center, the mechanical analogue being the oscillating non linear pendulum and it was extended to the case of an integrable saddle by Volterra himself. The limit of the model are clearly indicated in the memoir and a parallel can be made with the 2d-reduced model of the gut microbiote that we are analyzing in this paper.

We conserve the same notation than in the memoir. In the oscillatory situation the preypredator population $N = (N_1, N_2)$ satisfies the dynamics:

189 (2.1)
$$\frac{dN_1}{dt} = N_1(\varepsilon_1 - \gamma_1 N_2), \quad \frac{dN_2}{dt} = -N_2(\varepsilon_2 - \gamma_2 N_1)$$

where $(\varepsilon_1, \varepsilon_2, \gamma_1, \gamma_2) > 0$, which can be written in a general form as

191 (2.2)
$$\frac{dN_1}{dt} = N_1(\lambda_1 + \mu_1 N_1) \quad \frac{dN_2}{dt} = N_2(\lambda_2 + \mu_2 N_2)$$

192 for real parameters λ_i , μ_i , i = 1, 2.

193 This leads to the equation

194 (2.3)
$$\mu_2 \frac{\mathrm{d}N_1}{\mathrm{d}t} + \lambda_2 \frac{1}{N_1} \frac{\mathrm{d}N_1}{\mathrm{d}t} - \mu_1 \frac{\mathrm{d}N_2}{\mathrm{d}t} - \lambda_1 \frac{1}{N_2} \frac{\mathrm{d}N_2}{\mathrm{d}t} = 0$$

195 and integrating one gets

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$$\mu_2 N_1 + \lambda_2 \ln N_1 - (\mu_1 N_2 + \lambda_1 \ln N_2) = \text{constant}.$$

197 Hence

$$N_1^{\lambda_2} e^{\mu_2 N_1} = C N_2^{\lambda_1} e^{\mu_1 N_2},$$

where C is a constant depending upon the initial conditions $(N_1(0), N_2(0))$.

Volterra describes the solution using the auxiliary curves

201 (2.4)
$$Y = N_1^{-\varepsilon_2} e^{\gamma_2 N_1}, \quad X = N_1^{\varepsilon_1} e^{-\gamma_1 N_2}$$

so that the solution can be locally either represented as a graph Y = CX or X = CY.

203 One denotes

$$\Omega \coloneqq (K_1, K_2) = \left(\frac{\varepsilon_2}{\gamma_2}, \frac{\varepsilon_1}{\gamma_1}\right)$$

the persistent equilibrium. One can use polar coordinates (ρ, ω) centered at Ω and introducing the speed of the area swept by the vector ΩM satisfying the equation

$$\frac{1}{2}\rho^2 \frac{d\omega}{dt} = \frac{1}{2} \left[(N_1 - K_1) \frac{dN_2}{dt} - (N_2 - K_2) \frac{dN_1}{dt} \right] > 0,$$

208 which takes the form

$$\rho^2 \frac{\mathrm{d}\omega}{\mathrm{d}t} = \rho^2 \left[\gamma_1 \sin^2 \omega (K_1 + \rho \cos \omega) + \gamma_2 \cos^2 \omega (K_2 + \rho \sin \omega) \right].$$

210 Hence:

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211 (2.5)
$$t - t_0 = \int_{\omega_0}^{\omega} \frac{d\omega}{\sum_{i=1,2} \left[\gamma_i \sin^2 \omega (K_i + \rho \cos \omega) \right]}.$$

In particular the period is given by the formulae:

213 (2.6)
$$T = \int_0^{2\pi} \frac{\mathrm{d}\omega}{\rho \sin \omega \cos \omega (\gamma_1 \sin \omega + \gamma_2 \cos \omega) + K_1 \gamma_1 \sin^2 \omega + K_2 \gamma_2 \cos^2 \omega}$$

214 while the limit value at Ω is given by

$$\int_0^{2\pi} \frac{\mathrm{d}\omega}{K_1 \gamma_1 \sin^2 \omega + K_2 \gamma_2 \cos^2 \omega} = \frac{2\pi}{\sqrt{\varepsilon_1 \varepsilon_2}}$$

and this gives the analog with the nonlinear pendulum oscillation but the transcendence of the period is different.

Similar formulae gives the time evolution of the population $t \mapsto N_i(t)$. But from physical point of view, what matters is the averaged population $\langle N_i \rangle$ and a simple computation gives the following.

Theorem 2.1. The averaged populations are given by:

$$\langle N_i \rangle = \frac{1}{T} \int_0^{\mathsf{T}} N_i(t) \mathrm{d}t = K_i, i = 1, 2,$$

which are not depending upon the initial conditions but only from the equilibrium Ω .

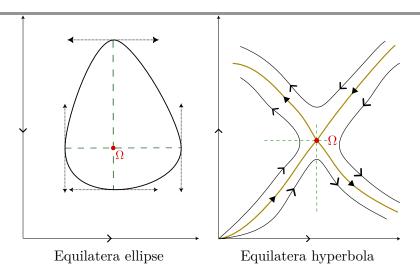


Figure 1. Volterra memoir.

224 The Lotka–Volterra model can be normalized in the same category using the dimensionless

225 variables:

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$$n_1 \coloneqq \frac{N_1}{K_1}, \quad n_2 \coloneqq \frac{N_2}{K_2}$$

227 and we get

228 (2.7)
$$\frac{dn_1}{dt} = \varepsilon_1 n_1 (1 - n_2), \quad \frac{dn_2}{dt} = -\varepsilon_2 n_2 (1 - n_1)$$

229 and the linearized system at Ω takes the form

230 (2.8)
$$\frac{\delta n_1}{\mathrm{d}t} = -\varepsilon_1 \delta n_2, \quad \frac{\delta n_2}{\mathrm{d}t} = \varepsilon_2 \delta n_1.$$

The geometric construction of the dynamics in the memoir is based on the auxiliary curves (2.4) to compute Y = CX.

This opens the path to treat in the same frame the case where $\varepsilon_1 \varepsilon_2 < 0$ so that Ω is a saddle point to get the form XY = C. Volterra gives a geometric representation of the two cases in a single figure, see Fig. 1.

Let us analyze in the oscillatory case the role of the fishing activity, introducing control in the model. The system takes the form:

238 (2.9)
$$\frac{\mathrm{d}N_1}{\mathrm{d}t} = (\varepsilon_1 - \alpha\lambda - \gamma_1 N_2)N_1, \quad \frac{\mathrm{d}N_2}{\mathrm{d}t} = -(\varepsilon_2 + \beta\lambda - \gamma_2 N_1)N_2,$$

where $\alpha, \beta \geq 0$ are the modes of destruction and $\lambda \geq 0$ is the intensity.

Assuming $\varepsilon_1 - \alpha \lambda > 0$ so that the population is still oscillating, the averaged values of N_1, N_2 become

$$\frac{\varepsilon_2 + \beta \lambda}{\gamma_2}, \frac{\varepsilon_1 - \alpha \lambda}{\gamma_1} \quad \text{versus} \quad \frac{\varepsilon_2}{\gamma_2}, \frac{\varepsilon_1}{\gamma_1}$$

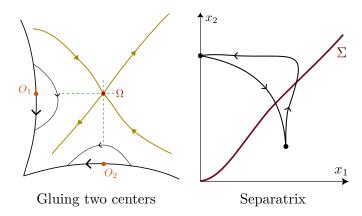


Figure 2. Jones et al. model.

243 without fishing activity (see Theorem 2.1). This confirms the observations by Ancona [2].

This leads to generalize the model to analyze in the same frame controlled populations dynamics introducing dissipation in the model associated to non zero coupling coefficients, to get a 2d-control model of the form

247 (2.10)
$$\frac{\mathrm{d}x}{\mathrm{d}t} = (\mathrm{diag}x)\left[(r+Ax) + u\,\epsilon\right],$$

where A is the interaction matrix, ϵ is the sensitivity vector and the control u is the intensity. Hence, in this frame the role of the constant control u = 1 is to shift the persistent equilibrium and the spectrum of the linearized dynamics.

Lotka–Volterra and Jones et al. The previous discussion clarifies the construction by Jones et al. of a 2d–Lotka–Volterra model to describe a complex microbiote with an interior saddle point and the interaction between the C-difficile population x_1 and the healthy microbiote population aggregated into a single population x_2 . Noting again $\Omega = (K_1, K_2)$ the persistent saddle equilibrium and normalizing: $x_1 \to \frac{x_1}{K_1}$, $x_2 \to \frac{x_2}{K_2}$, this leads to a system with four equilibria: Ω , the origin and two non persistent equilibria O_1, O_2 associated respectively to the reduced dynamics with x_1 or x_2 equal zero. This can be interpreted as gluing together two prey-predators models (see Fig. 2).

The model simulates the following medical protocol:

$$\begin{array}{ccccc} \text{day 0} & \longrightarrow & \text{day } k & \longrightarrow & \text{day } k' > k, \\ \text{(healthy mouse} & \text{(C-difficile infection)} & & \text{(fecal transplantation)} \\ & \& \text{ antibiotic)}, \end{array}$$

where the control actions are the choice of the day of the transplantation and the composition of the fecal injection.

The final state posterior to the fecal injection is either the healthy state O_1 or the infected state O_2 .

A separatrix Σ is constructed in the 2*d*-model indicating the success or the failure of the transplantation therapy. This yields decision algorithms based on the computations of the parameters of the reduced models using the observations. The infection has to be compensated

Figure 3. Generalized Controlled Lotka-Volterra model.

by the fecal transplantation. The mathematical limit of the model being that each species population shall satisfies $M \geq x_i \geq \varepsilon$, in particular if the x_2 population becomes too small the model is not valid. Also from medical point of view a probiotic injection versus antibiotic injection increases the healthy population aiming to struggle against infection.

Since Lotka–Volterra model has to be understood as interaction between a set of computable non persistent singularities with computable domains of attraction with a persistent singular point Ω , the dynamics being restricted to an open set U centered at Ω representing the viability domain of the mathematical model, this opens the road to more complicated models.

For instance, a normalized dynamics of the form

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278 (2.11)
$$\frac{dx}{dt} = x(1-x) - \frac{axy}{d+x}, \quad \frac{dy}{dt} = by(1-\frac{y}{x}),$$

279 where the persistent equilibrium is given by the intersection of a straight-line and a parabola

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$$x = y, \quad ay = (1 - x)(d + x)$$

allows to construct dynamics with a limit cycle obtained by Hopf bifurcation, which is not possible for a 2d-Lotka-Volterra model. The limit of the construction being to analyze stability.

More complicated constructions lead to consider systems with a single interior equilibria with a simplex formed by a polycycle of separatrixes connecting three non persistent saddle equilibria with one or more interior limit cycles generated by Hopf bifurcation, see Fig. 3.

2.2. Some remarks about constructing general controlled Lotka–Volterra models. In the original memoir starting from the integrable case, one considers the interaction between the persistent equilibrium Ω and the origin O which is not persistent. But the distinction between the center case of the elliptic situation and the saddle case of the hyperbolic situation can be deduced from the nature of O only which can be either saddle or a node. Then conversely this leads to construct a model where the persistent singularity Ω can be identified

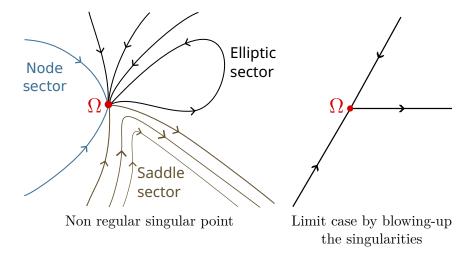


Figure 4. Generalized Controlled Lotka-Volterra model.

by confluence to the origin which is the only equilibrium point but with a linear system which is degenerated.

This construction leads to consider persistent singular point Ω with multiple sectors: node sector, saddle sector and a new type of sector called an elliptic sector, see Fig. 4.

This leads to consider polynomial dynamics: $\frac{dx}{dt} = H(x)$, where at the limit, H is homogeneous with degree k: $H(\lambda x) = \lambda^k H(x)$ and the separatrixes of the different domains are lines.

In the polynomial category the system can be compactified using the Poincaré compactification, identifying the Euclidean plane to the plane (x, z = 1) where the system reads

$$\frac{\mathrm{d}x}{\mathrm{d}t} = H(x, z), \quad \frac{\mathrm{d}z}{\mathrm{d}t} = 0,$$

and H(x,z) is homogeneous with respect to (x,z). Such a system gives us a differential equation, which a can be projected on the two-sphere S^2 . The construction is similar in the n-dimensional case.

From control point of view, one considers a pair of vectors fields (X, Y), where X is the Lotka–Volterra model or a generalization of this model, with a single persistent equilibrium Ω , while Y corresponds to the controlled vector field. It can be of two types:

- antibiotic or probiotics which belongs to the same category: $Y(x) = (\operatorname{diag} x) \epsilon$.
- transplantation or bactericide: in this case this leads to a jump in the initial condition: $x(0) \to x(0) + \lambda v$.

The second case has to be interpreted as the response to a Dirac $t \mapsto \delta(t - t')$ generated as the limit of an unbounded control sequence: $u_n = \lambda n$, $t \in [0, 1/n]$, while the control vector direction is given by the constant vector field Y = v.

In particular this relates our study to the general frame of control systems of the following forms.

Bilinear systems.

$$\frac{\mathrm{d}x}{\mathrm{d}t}(t) = Ax(t) + u(t)(Bx(t) + b),$$

where A, B are constant matrices and b is a constant vector.

Homogeneous systems.

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$$\frac{\mathrm{d}x}{\mathrm{d}t}(t) = H(x(t)) + u(t)b,$$

where H is a polynomic homogeneous vector field and b is a constant vector field.

2.3. Accessibility problem for 2d-systems. The affine case. In this section, we make a complete study of the accessibility problem for 2d-affine systems, in relation with the action of the antibiotic-probiotic agent near the saddle point as in Jones et al. model reduction.

Definitions and Notations. We work in the \mathbb{C}^{ω} (real analytic) category and M denotes a (regular) connected manifold. The set of (local) diffeomorphisms φ denoted by $\mathrm{Diff}(M)$ and let $\Xi(M)$ be the set of vector fields on M. If $X \in \Xi(M)$, one denotes by $\varphi_t = \exp tX$ the one-parameter pseudo-group of local diffeomorphisms: $\varphi_t(x_0) = x(t,x_0), \ x(\cdot)$ being the solution at time t of the Cauchy problem: $\frac{\mathrm{d}x}{\mathrm{d}t}(t) = X(x(t)), \ x(0) = x_0$. A special case is the case of linear vector fields X(x) = Ax, A being a constant matrix, $\varphi_t = \exp tA$ being the exponential matrix and moreover X is complete so that $\exp tA$ is a one-parameter group acting linearly.

Definition 2.2. Let $D = \{X\}$ be a family of $\Xi(M)$ called a polysystem. We denote by S(D) the pseudo-semigroup generated by the family $\exp tX$, $X \in D$, that is:

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$$S(D) = \{ \exp t_1 X_1 \circ \cdots \circ \exp t_k X_k, X_i \in D, t_i > 0 \},$$

and we denote by $t = t_1 + t_2 + \cdots + t_k$ the total transfer time. The pseudo-group S(D) can be extended to the whole group G(D) by taking t_i positive or negative.

Let $x, y \in M$, then y is called accessible from x if there exists $X_i \in D$ and $t_i > 0$ such that

338 (2.12)
$$y = \exp t_1 X_1 \circ \cdots \circ \exp t_k X_k(x)$$

and y is said normally accessible to x if the mapping $(s_1, \ldots, s_k) \mapsto \exp s_1 X_1 \circ \cdots \circ \exp s_k X_k(x)$ is of rank $n = \dim M$ at (t_1, \ldots, t_k) . Fixing x, the set of accessible points is denoted $A^+(x)$ and it is the orbit of S(D).

If y is accessible to x this means that x can be steered to y and the set of points which can be steered to y is denoted $A^{-}(y)$.

Let $D = \{X\}$ be a polysystem, then Sym(D) is the symmetric set $\{\pm X\}$ and we called orbit of x the orbit of the pseudo-group G(D).

The polysystem D is called (normally) controllable on a subset $P \subset M$ if for each pair $(x,y) \in P$, y is (normally) accessible to y. If P = M, the system is said (normally) controllable on M.

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Definition 2.3. Let $X, Y \in \Xi(M)$, the Lie bracket in local coordinates x is calculated with the convention: $[X,Y](x) = \frac{\partial X}{\partial x}(x)Y(x) - \frac{\partial Y}{\partial x}(x)X(x)$. Let $D = \{X\}$ be a polysystem, we denote $D_{L.A.}$ the Lie algebra generated by D. It can be computed introducing:

$$D^1 = D, \ D^2 = D \cup [D, D], \dots, D^k = D^{k-1} \cup [D^{k-1}, D]$$

353 and $D_{L.A.} = \text{span} \cup_{k>1} D^k$.

Theorem 2.4. The following assertions are equivalent:

- 1. For every $x, y \in M$, the Lie algebra $D_{L.A.}(x)$ is of maximal rank = dim M.
- 356 2. For every $x \in M$ and every neighborhood U of x, there exists y in U normally accessible to x.
 - 3. The symmetric system $\{\pm X\}$ is controllable.

359 The third assertion is Chow-Rashevskii theorem [12].

2.3.1. The case of Lie groups. Let G be a Lie group and $\mathfrak g$ its Lie algebra identified to the set of right-invariant vector fields on G. Take $G = Gl(n,\mathbb R)$ be the set of $n \times n$ invertible matrices, $Gl^+(n,\mathbb R)$ the subset of matrices with positive determinant. The Lie algebra $\mathfrak{gl}(n,\mathbb R)$ is the set of $n \times n$ matrices and the Lie bracket of two matrices is [A,B] = AB - BA. If $A \in \mathfrak{gl}(n,\mathbb R)$ the one-parameter group $\exp tA$ is given by the series $\exp A = \sum_{n \geq 0} \frac{A^n}{n!}$.

The group $Gl(n,\mathbb{R})$ acts transitively on $\mathbb{R}^n \setminus \{0\}$ and the action defines linear vector fields $X^+(x) = Ax$. The affine group is the subgroup of $Gl(n,\mathbb{R})$ of matrices $\begin{pmatrix} 1 & 0 \\ v & S \end{pmatrix}$,

where $v \in \mathbb{R}^n$, $S \in Gl(n,\mathbb{R})$ and its Lie algebra is the set of matrices $\begin{pmatrix} 0 & 0 \\ a & A \end{pmatrix}$, $a \in \mathbb{R}^n$,

368 $A \in \mathfrak{gl}(n,\mathbb{R})$. It acts transitively on \mathbb{R}^n identified to $\begin{pmatrix} 1 \\ \mathbb{R}^n \end{pmatrix}$. This induced action defines

affine vector fields $X^+ = Ax + a$. We denote by $\mathfrak{gl}(n,\mathbb{R}) \oplus_s \mathbb{R}^n$ the semi-direct Lie algebra where the Lie bracket is: [(A,a),(B,b)] = ([A,B] = AB - BA, Ab - Ba).

2.3.2. Accessibility results for 2d-affine systems. The Lie algebra $\mathfrak{gl}(n,\mathbb{R})$ decomposes into the direct sum $c \oplus \mathfrak{sl}(n,\mathbb{R})$, where c is the center formed by diagonal matrices cI_n , I_n being the $n \times n$ identity matrix, while $\mathfrak{sl}(n,\mathbb{R})$ is the set of matrices with zero trace associated to linear conservative vector fields. We denote by $Sl(n,\mathbb{R})$ the special linear group of matrices with determinant one. Note that for n = 2, $\mathfrak{sl}(2,\mathbb{R}) = \mathfrak{sp}(1,\mathbb{R})$ the second being associated to planar linear Hamiltonian vector fields and with the identification $Sl(2,\mathbb{R}) = Sp(1,\mathbb{R})$.

We shall restrict our study to the case of conservative vector fields, extension to the non conservative case being straightforward.

Definition 2.5. Let A be a non zero element of $\mathfrak{sp}(1,\mathbb{R})$. Then:

- A is elliptic if the eigenvalues are imaginary: $\{\pm i\sigma\}, \sigma \in \mathbb{R},$
- A is parabolic if 0 is an eigenvalue,
- A is hyperbolic if the eigenvalues are real numbers: $\{\pm \lambda\}$, $\lambda \in \mathbb{R}$.

Lemma 2.6. $A, A' \in \mathfrak{sp}(1, \mathbb{R})$ are called (symplectically) equivalent: $A \sim A'$ if there exists $P \in Sp(1, \mathbb{R})$ such that $P^{-1}AP = A'$. One has:

• A is elliptic if and only if $A \sim \begin{bmatrix} 0 & \alpha \\ -\alpha & 0 \end{bmatrix}$, $\alpha \in \mathbb{R}$.

- A is parabolic if and only if $A \sim \begin{pmatrix} 0 & \varepsilon \\ 0 & 0 \end{pmatrix}$, $\varepsilon = \pm 1$.
- A is hyperbolic if and only if $A \sim \begin{pmatrix} \lambda & 0 \\ 0 & -\lambda \end{pmatrix}$.
- Only in the third case, the equivalent class is given by the spectrum.
- Next we introduce the normal forms of pairs $\{A, B\}$ of vector fields in $\mathfrak{sp}(1, \mathbb{R})$ to study controllability.
- Definition 2.7. Let $D = \{A, B\}$ and $D' = \{A', B'\}$ be two pairs of vector fields in $\mathfrak{sp}(1, \mathbb{R})$.

 They are called equivalent if there exists $a, b \in \mathbb{R}$, ab > 0 such that: $aA \sim A'$, $bB \sim B'$.
- We shall analyze controllability properties using normal forms for pairs $D = \{A, B\}$.
- Lemma 2.8. Let $D = \{A, B\}$ be a polysystem on $\mathfrak{sp}(1, \mathbb{R})$. One has $D_{L.A.}(x) = \mathbb{R}^2$ for $x \neq 0$ if and only if A, B are non proportional and with distinct eigenvectors.
- 2.3.3. Criteria of controllability. From general properties of nonlinear systems we have the following.
- Criteria. Let $A, B \in \mathfrak{sp}(1, \mathbb{R})$ non proportional and with distinct eigenspaces. Then the system is controllable if and only if for every x non zero there exists an element $\varphi = \exp t_1 X_1 \circ \cdots \circ \exp t_k X_k$ of S(D), $\varphi(x)$ forming a periodic path surrounding the point 0.
- Corollary 2.9. Assume A elliptic. Then $D = \{A, B\}$ is controllable if and only if they are non proportional.
- Corollary 2.10. Assume A parabolic and B hyperbolic so that $D_{L.A.}(x) = \mathbb{R}^2$ for $x \neq 0$.

 Then only one polysystem among $\{Ax, Bx\}$ and $\{Ax, -Bx\}$ is controllable. Moreover D is

 controllable if and only if $D \sim \left\{ \begin{pmatrix} 0 & 1 \\ 0 & 0 \end{pmatrix}, \begin{pmatrix} 0 & -1 \\ -1 & 0 \end{pmatrix} \right\}$.
- Corollary 2.11. Take $D = \{A, B\}$ with A and B hyperbolic. Let a > 0 and -a denotes the eigenvalues of A and b > 0 and -b the eigenvalues of B. Let M_1 one intersection of the eigenspace of a with the unit circle and using the positive orientation starting from M_1 denotes M_2, M_3, M_4 the first intersection with the unit circle of the eigenspaces associated respectively to -a, b, -b. Then the only controllable polysystems are associated to (M_1, M_2, M_3, M_4) or (M_1, M_4, M_3, M_2) .
- 2.3.4. Necessary and sufficient conditions results on $Sp(1,\mathbb{R})$. A very interesting result is that the previous controllability analysis can be lifted on the 3d-manifold $Sp(1,\mathbb{R})$ in relation with the action on the Poincaré half-plane. One needs some technical results.
- Lemma 2.12. Let SO(2) be the group of rotations with determinant one given by

$$\left\{ \exp t \begin{pmatrix} 0 & 1 \\ -1 & 0 \end{pmatrix}, t \in [0, 2\pi] \right\}.$$

Let K be a maximal compact subgroup of $Sp(1,\mathbb{R})$. Then there exists a symplectic matrix P such that $K = PSO(2)P^{-1}$.

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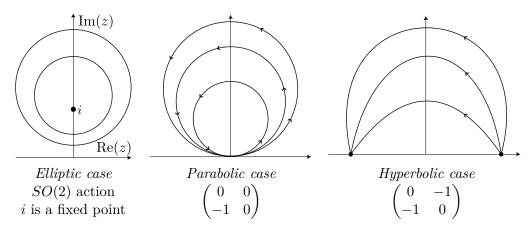


Figure 5. One-parameter dynamics in Poincaré upper plane.

Poincaré half-plane. The Poincaré half-space \mathcal{P} is the set of complex numbers z such that Imz > 0. Then $Sp(1,\mathbb{R})$ acts transitively on \mathcal{P} with the action:

$$S \cdot z = \frac{az+b}{cz+d}, \ z \in P, S = \begin{pmatrix} a & b \\ c & d \end{pmatrix} \in Sp(1,\mathbb{R}).$$

Hence for every one-parameter subgroup $\exp tA$, $A \in Sp(1,\mathbb{R})$ one can associate on \mathcal{P} the vector field $X^+(z) = \frac{\mathrm{d}}{\mathrm{d}t}|_{t=0}(\exp tA) \cdot z$.

One has the following characterization of maximal compact subgroup K:

- SO(2) is the set of matrices S in $Sp(1,\mathbb{R})$ so that $S \cdot i = i$.
- $K = PSO(2)P^{-1}$ is the set of matrices so that $S \cdot z = z$ with $z = P \cdot i$.

This action gives the key to determine the controllability of pairs $D = \{A, B\}$ on $Sp(1, \mathbb{R})$.

Indeed one must find elements of S(D) associated to compact elements of K. They can be

seen as periodic paths in the Poincaré half-space leaving fixed a point. See Fig. 5 illustrating this action.

One deduces the following, see [4] for the details.

Theorem 2.13. Let $D = \{A, B\}$ be a pair of right-invariant vectors fields on $Sp(1, \mathbb{R})$. Then the following conditions are equivalent:

- 1. The polysystem D is controllable on $Sp(1,\mathbb{R})$.
- 2. The polysystem $D = \{Ax, Bx\}$ is controllable on $\mathbb{R}^2 \setminus \{0\}$.

This is a strong controllability result which can be translated to affine pairs $\{(A, a), (B, b)\}$ where $A, B \in \mathfrak{sp}(1, \mathbb{R})$. This comes from [3].

Lemma 2.14. Assume $\{A, B\}$ controllable on $\mathbb{R}^2 \setminus \{0\}$. Then there exists R > 0 large enough such that $\{(A, a), (B, b)\}$ is controllable for |x| > R.

Proposition 2.15. Assume $\{A, B\}$ controllable on $\mathbb{R}^2 \setminus \{0\}$. Then the polysystem $\{(A, a), (B, b)\}$ is controllable on \mathbb{R}^2 if and only if Ax + a and Bx + b have no common equilibrium point.

2.4. Controlled Lotka–Volterra model and optimal control. Next we introduce the definitions and concepts in a general frame.

Definition 2.16. Let $x = (x_1, ..., x_n)^{\mathsf{T}} \in \mathbb{R}^n_+$ be the state of interacting species, x_1 being the infected agent, $x' = (x_2, ..., x_n)^{\mathsf{T}}$ being the state of healthy agents. The dynamics is described by

448 (2.13)
$$\frac{\mathrm{d}x}{\mathrm{d}t} = (\mathrm{diag}x)(Ax + r)$$

- 449 the matrix $A = (a_{ij})$ being the matrix of coefficients of interaction and $r = (r_1, \ldots, r_n)^{\mathsf{T}}$ is
- 450 the vector of individual growth rate. We denote by $M^+ = \mathbb{R}^n_+$ the invariant domain $x_i > 0$
- 451 and M^{\sim} the union of M^{+} with its boundary. The dynamics is called regular if A is invertible.
- The interior or persistent equilibrium is the point $\Omega = (K_1, \dots, K_n)$ given by $x = -A^{-1}r$.
- We note $n = (n_1, \dots, n_n)^{\mathsf{T}}$ the dimensionless coordinates so that Ω is identified to $(1, \dots, 454 \ 1)^{\mathsf{T}}$.

One can associate to (2.13) an hierarchy of dynamics replacing $x \to x' = (x_2, \dots, x_n)^{\mathsf{T}}$ and this leads to up to 2^n equilibria for the dynamics in the physical space, which can be easily computed by recurrence.

The dynamics can be compactified using Poincaré compactification, identifying \mathbb{R}^n to the hyperplane (x, z = 1) in \mathbb{R}^{n+1} to define the system:

$$\frac{\mathrm{d}x}{\mathrm{d}t} = (\mathrm{diag}x)(Ax + r), \quad \frac{\mathrm{d}z}{\mathrm{d}t} = 0,$$

where the right-member can be homogenized to define an homogeneous vector field which can be projected on the n-sphere S^n .

Each equilibrium of the hierarchy of dynamics can be classified according to the L-(linear) stability status associated to the linearized dynamics at equilibrium.

Our study is related to the entanglement of k non persistent equilibria interacting with the persistent equilibrium and one can introduce a model reduction consisting in a polynomic dynamics of the form: $\frac{dx}{dt} = P(x)$.

Introducing the ln-coordinates $x = e^y$ so that the system takes the form:

469 (2.14)
$$\frac{\mathrm{d}y}{\mathrm{d}t} = (Ae^y + r),$$

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- where $y \in \ln M^+$ and the non persistent equilibria are at the infinity.
- We denote by X(x) the vector field defined by (1.1) where x can be taken as the normalized coordinates.
- **2.4.1. Antibiotic or probiotic agent.** For a single antibiotic or probiotic agent the control system takes the form

$$\frac{\mathrm{d}x}{\mathrm{d}t} = X(x) + uY(x),$$

- with $Y(x) = (\operatorname{diag} x)(\varepsilon_1, \dots, \varepsilon_n)^{\mathsf{T}}$ is the sensitivity vector and the control u(t) describes the dosing regimen. Note that u can be restricted to domain [0, 1] using normalizations.
- This notation can be applied to the hierarchy of models so that this leads to an hierarchy of control problems which can be analyzed independently. For instance, prior to infection one

can analyze the effect of probiotics agents where $\varepsilon_i > 0$, while posterior to infection one can consider the effect of antibiotic treatment.

The set of admissible controls fits in the frame of permanent control, where $u(\cdot)$ is a measurable mapping on $[0, t_f]$ valued in [0, 1]. Each measurable bounded mapping can be approximated by a sequence of piecewise constant mappings in the L^{∞} -topology and accessibility can be studied restricting to this class. This is the point of view of geometric control which leads to introduce the polysystem: $D = \{X + uY; u \text{ constant in the interval } [0, 1]\}$.

2.4.2. Fecal transplantation and bactericide. In the case of transplantation or bactericide the control system takes the form:

$$\frac{\mathrm{d}x}{\mathrm{d}t} = X(x) + uY(x),$$

where $Y = (v_1, \ldots, v_n)^{\mathsf{T}}$ is a constant vector field and u takes it values in the whole \mathbb{R}^+ , where the action being to get Dirac pulse $\delta(t-t')$, defined as the limit of controls sequence: $u_n = \lambda n$ on [t', t' + 1/n].

2.4.3. Optimal control problems: the permanent case versus the sampled-data frame. Resuming the previous discussion, one can write the general control system in the form:

$$\frac{\mathrm{d}x}{\mathrm{d}t}(t) = X(x(t)) + \sum_{ant.,pro.} u_i(t)Y_i(x(t)) + \sum_{transp.bac.} u_i'(t)Y'(x(t)),$$

where the two sums are related respectively to probiotic, antibiotic agents and transplantations and bactericides. Moreover discontinuity in the state $x = (x_1, ..., x_n)^{\intercal} \to x' = (x_2, ..., x_n)^{\intercal}$ can be understood as the jump action $x \to x'$. Hence this leads in the general case to a mixture of permanent and sampled-data control systems. The first action is related to permanent control, but due to logistic medical constraints it can fit in the sampled-data frame, e.g. a finite number of medical interventions at some predefined times: $0 < t_1 < \cdots < t_k < t_f$ to modify the treatment. The second action fits in the sampled-data frame, since in particular it corresponds to invasive therapies.

Hence from a general context, the problem is associated to the following optimal control problems related to successive use of the different treatments.

OCP1 in the permanent case. The problem is either to reduce the x_1 -infection or to increase the production or ratio of healthy agents, prior to infection. This leads to consider in a dual formulation problems of the form:

• Reach in minimum time t_f a given terminal manifold N of codimension one for the control system written as: $\frac{\mathrm{d}x}{\mathrm{d}t} = X(x) + uY(x)$, Y being associated to a specific treatment.

This formulation leads to analyze the candidates as computing minimizers in the permanent case using the Maximum Principle, stated in the introduction.

OCP2 in the sampled-data control frame. In the sampled-data control context, one introduces a finite dimensional input-output mapping: $E: (\lambda \in C \subset \mathbb{R}^m, t) \to \mathbb{R}$ where the output is the time response x(t) of the dynamics. One denote by $0 < t_1 < t_2 < \cdots < t_p < t_f$ the sampling times.

In this formulation the problem is analyzed using a Model Predictive Control (MPC) technique:

- Start at time t = 0 from x(0) and fix an horizon of length k in the sampling times. Compute the optimized (finite dimensional) control on this horizon.
- Replace t = 0 by $t = t_1$, where on $[0, t_1]$ the control is the restriction on this interval of the optimized control computed on the whole given horizon. This leads to replace x(0) by $x(t_1)$. Then go to the first step.

In this algorithm, the dynamics is used to estimate over an horizon of length k the effect of the control action. It can be understood as a non causal approach to the problem, since the state-evolution is governed by the optimization algorithm, where the dynamics is used to make the prediction only.

In this article we shall concentrate on the permanent case. But convergence of the algorithm in the sampled-data case is related to the properties of the optimal control in the permanent case.

2.5. Singular trajectories and time optimal control. In this section, we make a brief recap of the properties of singular trajectories, crucial in our analysis, for full details see [5].

Definition 2.17. Let (X,Y) the pairs of C^{ω} vector fields on M associated to control system: $\frac{\mathrm{d}x}{\mathrm{d}t} = X(x) + uY(x)$. The feedback group G_f is the set of triples (φ, α, β) , where φ is a local diffeomorphism and $u = \alpha(x) + \beta(x)v$, $\beta \neq 0$ is a feedback, the group structure being induced by the actions:

- local diffeomorphism $\varphi:(X,Y)\to(\varphi*X,\varphi*Y)$, where $\varphi*Z=d\varphi(Zo\varphi^{-1})$ denotes the image of a vector field Z.
- feedback: $u = \alpha(x) + \beta(x)v \colon (X,Y) \to (X + Y\alpha, Y\beta).$

The control system can be lifted on the cotangent bundle T^*M with symplectic structure defined by $d\omega$, where $\omega = p dx$ is the Liouville form. The Hamiltonians $H_X(z) = p \cdot X(x)$, $H_Y(z) = p \cdot Y(x)$, where z = (x, p) are the symplectic coordinates, are the Hamiltonian lifts of X, Y. The system lift takes the form: $\frac{dz}{dt} = H_X(z) + uH_Y(z)$, and $H_X(z) + uH_Y(z)$ is the pseudo or non maximized Hamiltonian. One can lift every local diffeomorphism φ into a Matthieu symplectomorphism φ defined by: $x = \varphi(y)$, $p = q \frac{\partial \varphi^{-1}}{\partial x}$, where p, q are row vectors. This induces an action of G_f on the pairs (H_X, H_Y) .

Computations of singular extremals. Relaxing the control bound to $u \in \mathbb{R}$, from the Maximum Principle the candidates as time minimizers are the so-called singular extremals control-trajectory pairs written shortly (z,u) solutions of the constrained Hamiltonian dynamics: $\frac{\mathrm{d}z}{\mathrm{d}t}(t) = \mathbf{H}(z(t))$, \mathbf{H} being the Hamiltonian vector field, the constraints coming from the maximization condition: $\frac{\partial H}{\partial u} = H_Y(z) = 0$.

Hence they are solutions contained in the switching set $\Sigma: H_Y(z(t))=0$. They can be computed, deriving this equation with respect to t. Introducing the Poisson bracket of $H_{Z_1}(z)=p\cdot Z_1(x),\ H_{Z_2}(z)=p\cdot Z_2(x),$ by $\{H_{Z_1},H_{Z_2}\}(z)=p\cdot [Z_1,Z_2](x).$

Hence we deduce:

557 (2.16)
$$H_Y(z(t)) = \{H_Y, H_X\}(z(t)) = 0, \\ \{\{H_Y, H_X\}, H_X\}(z(t)) + u(t)\{\{H_Y, H_X\}, H_Y\}(z(t)) = 0.$$

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We introduce the following.

Definition 2.18. The Generalized Legendre-Clebsch condition (GLC) along a singular extremal $(z(\cdot), u(\cdot))$ on $(0, t_f]$ is given by:

$$\frac{\partial}{\partial u} \frac{\mathrm{d}^2}{\mathrm{d}t^2} \frac{\partial H}{\partial u}(z(t)) = \{ \{ H_Y, H_X, \}, H_Y \}(z(t)) \neq 0,$$

562 for every t in $[0, t_f]$. The switching surface is $\Sigma : H_Y(z) = 0$ and we denote Σ' the sub-563 set: $H_Y(z) = \{H_Y, H_X\}(z) = 0$. Then outside the collinear set of Y(x) and [Y, X](x), if 564 $\{\{H_Y, H_X\}, H_Y\} \neq 0$, the restriction of the symplectic form $d\omega$ to Σ' defines a symplectic 565 manifold $(M', \omega_{|M'})$.

This gives the following.

Proposition 2.19. Assume that the GLC-condition holds along (z(t), u(t)) then the extremal is called of minimal order. We have:

- then of minimal order. We have.

 1. The singular control $u_s(.)$ is the dynamic feedback: $u_s(z) = -\frac{\{\{H_Y, H_X\}, H_X\}(z)}{\{\{H_Y, H_X\}, H_Y\}(z)}$.
- 2. Introduce the true Hamiltonian $\mathbf{H}_s(z) := H_X(z) + u_s(z) H_Y(z)$, the singular extremals of minimal order are the solutions of $\mathbf{H}_s(z)$ contained in the set Σ' .
- 572 They are the solutions of $H_s(z)$ restricted to the symplectic manifold M'.

 573 Higher-order singular extremals can be determined at any order using the following algo- 574 rithm. If

$$\{\{H_Y, H_X\}, H_Y\}(z(t)) = 0,$$

576 Then additionally

$$\{\{H_Y, H_X\}, H_X\}(z(t)) = 0.$$

578 Deriving both relations one gets:

$$\{\{\{H_Y, H_X\}, H_Y\}, H_X\}(z(t)) + u(t) \{\{\{H_Y, H_X\}, H_Y\}, H_Y\}(z(t)) = 0, \\ \{\{\{H_Y, H_X\}, H_X\}, H_X\}(z(t)) + u(t) \{\{\{H_Y, H_X\}, H_X\}, H_Y\}(z(t)) = 0.$$

If the control cannot be derived from the previous equations, we repeat the derivation procedure.

2.5.1. Singular extremals as feedback invariants.

Definition 2.20. Let E, F be two vector spaces and G a group acting linearly on E, F. An homomorphism $\chi \colon G \to \mathbb{R} \setminus \{0\}$ is called a character. Let χ be a character, a semi-invariant of weight χ is a map $\lambda \colon E \to \mathbb{R}$ such that for all $x \in E, g \in G, \lambda(g \cdot x) = \chi(g)\lambda(x)$. It is called an invariant if $\chi = 1$. A map $\lambda \colon E \to F$ is a semi-covariant of weight χ if for all $x \in E, g \in G, \lambda(g \cdot x) = \chi(g)g \cdot \lambda(x)$. It is called a covariant if $\chi = 1$.

Theorem 2.21. Denote by λ_s the map which associates to the pair (X,Y) the Hamiltonian vector field \mathbf{H}_s restricted to Σ' . Then it is a covariant for the respective actions of the feedback group. In particular singular extremals are feedback invariants.

Proof. Direct computations give us:

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$$D^{\phi*X,\phi*Y}(x) = \det\left(\frac{\partial\phi}{\partial x}\right) D^{X,Y}(\phi^{-1}(x)), \quad D^{X+\alpha Y,\beta Y}(x) = \beta^4 D^{X,Y}(x),$$
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$$D'^{\phi*X,\phi*Y}(x) = \det\left(\frac{\partial\phi}{\partial x}\right) D'^{X,Y}(\phi^{-1}(x)), \quad D'^{X+\alpha Y,\beta Y}(x) = \beta^3 \left(D'^{X,Y}(x) + \alpha D^{X,Y}(x)\right),$$
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$$D''^{\phi*X,\phi*Y}(x) = \det\left(\frac{\partial\phi}{\partial x}\right) D''^{X,Y}(\phi^{-1}(x)), \quad D''^{X+\alpha Y,\beta Y}(x) = \beta^2 D''^{X,Y}(x).$$

Hence λ_s is a covariant.

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2.5.2. High order Maximum Principle [19].

Proposition 2.22. Assume p is oriented using the convention of the Maximum Principle along the singular extremal $z(\cdot)$: $H_X(z(t)) \geq 0$. Then a necessary time optimality condition on $[0, t_f]$ is given by

$$\frac{\partial}{\partial u} \frac{\mathrm{d}^2}{\mathrm{d}t^2} \frac{\partial H}{\partial u}(z(t)) = \{\{H_Y, H_X\}, H_Y\}(z(t)) \ge 0.$$

Definition 2.23. The singular extremal $z(t) = (x(t), p(t)), t \in [0, t_f]$ is called strict if p is unique up to a scalar.

Corollary 2.24. Assume the strict case. Then the singular trajectories projections of singular extremals of minimal order are stratified according to the following:

- Hyperbolic case: $H_X \cdot \{\{H_Y, H_X\}, H_Y\}(z) > 0$,
- Elliptic case: $H_X \cdot \{\{H_Y, H_X\}, H_Y\}(z) < 0$,
- Abnormal or exceptional case: $H_X(z) = 0$.

2.5.3. Applications.

2d-case. Singular extremals satisfy $H_Y = \{H_Y, H_X\} = 0$ so that singular trajectories are located on the set \mathscr{S} : $\det(Y(x), [Y, X](x)) = 0$. Outside the collinear set \mathscr{C} : $\det(Y(x), X(x)) = 0$ one can takes Y, X as a frame and writing $[[Y, X], Y](x) = \alpha(x)X(x) + \beta(x)Y(x)$. The singular control is given by: $[[Y, X], X](x) + u_s(x)[[Y, X], Y](x) = 0$. Hyperbolic case corresponds to $\alpha(x) > 0$ and elliptic case to $\alpha(x) < 0$.

3d-case. The 3d-case is already a very rich situation to analyze the singular extremals and the program goes as follows.

Introduce the following determinants:

$$D(x) = \det(Y(x), [Y, X](x), [[Y, X], Y](x)),$$

$$D'(x) = \det(Y(x), [Y, X](x), [[Y, X], X](x)),$$

$$D''(x) = \det(Y(x), [Y, X](x), X(x)),$$

620 and using the relations

621 (2.18)
$$H_Y(z) = \{H_Y, H_X\}(z) = 0, \\ \{\{H_Y, H_X\}, H_X\}(z) + u_s\{\{H_Y, H_X\}, H_Y\}(z) = 0,$$

622 We can eliminate p and the singular control is given by the feedback:

$$u_s(x) = -\frac{D'(x)}{D(x)}.$$

Defining the vector field:

625 (2.19)
$$X_s(x) := X(x) + u_s(x)Y(x)$$
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we have: 626

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Proposition 2.25. Singular trajectories of minimal order stratified the dynamics into:

- Hyperbolic arcs in DD'' > 0,
 - Elliptic arcs in DD'' < 0,
 - Exceptional or abnormal arcs in D'' = 0.

Proposition 2.26. For the action of the feedback group $G_f = \{(\varphi, \alpha, \beta)\}$ reducing to φ changes of coordinates on vector fields X_s , the map $\lambda_s:(X,Y)\to X_s$ is a covariant. Hence this allows to generate feedback invariants using the dynamics (2.19).

Equilibria of this dynamics split into two types:

- If $D \neq 0$, they are given by the solutions of $X_s(x) = 0$.
- If D=0, one can reparameterize the dynamics to get the vector field D(x)X(x) D'(x)Y(x) and additional (non isolated) singular points are located on D(x) = D'(x) = D'(x)
- Exceptional trajectories are contained in the invariant set D''(x) = 0 for the dynamics. 639
- **2.6.** Conclusion. In the case of controlled Lotka–Volterra model, the first step in our study 640 is to classify the singular trajectories using the previous stratified dynamics into hyperbolic, 641 642 elliptic and exceptional trajectories.
- 3. Extremals classification and local time minimal syntheses near a terminal manifold 644 of codimension one.
- 3.1. Introduction and definitions. In this section we consider the time minimal con-645 trol problem for the system: $\frac{dx}{dt} = X(x) + uY(x), |u| \leq 1$, with terminal manifold N of 646 codimension one. We denote by $H(z,u) = H_X(z) + u H_Y(z)$ the pseudo-Hamiltonian and $M(z) = \max_{|u| < 1} H(z, u)$ the true or maximized Hamiltonian. In this setting the control 648 domain is taken as U = [-1, +1], where extreme control value is either X(x) - Y(x) or 649 650 X(x) + Y(x) that is the maximal dosing regimen.
- Definition 3.1. The extremals are concatenation of regular extremals for which almost eve-651 rywhere 652

$$u(t) = \operatorname{sign} H_Y(z(t))$$

and singular extremals if 654

$$H_Y(z(t)) = 0$$

holds identically. 656

An extremal is called exceptional if the maximized Hamiltonian is such that M(z) = 0. 657 A BC-extremal is an extremal satisfying the transversality condition. A switching time is 658

an instant such that the extremal control is discontinuous. A bang-bang extremal is a regular extremal with a finite number of switches.

Since the control domain is U = [-1, +1], a singular extremal is called strictly feasible (admissible) if $|u_s| < 1$ and saturating at time t if $|u_s(t)| = 1$. A regular or singular extremal is called strict if p is unique up to a scalar. In the strict case singular extremals can be classified into hyperbolic, elliptic and exceptional extremals. We denote by σ_+, σ_- bang arcs associated respectively to u = +1 or u = -1, σ_s is a singular arc associated to u_s . We denote by $\sigma_1 \sigma_2$ an arc σ_1 followed by σ_2 .

Definition 3.2. Taking an open set V of M, the problem is called geodesically complete on V if for each $x_0, x_1 \in V$ there exists a time minimizing geodesic in V joining x_0 to x_1 . Fixing the target to N (= $N \cap V$), a time minimal synthesis is a discontinuous feedback $x \to u^*(x)$ so that the solutions of $\frac{dx}{dt} = X(x) + u^*(x)Y(x)$ are well defined and $u^*(x)$ is the optimal feedback solution to steer x to the target in minimum time.

3.2. Small time classification of regular extremals. In this section we recall some basic properties of regular extremals, see [17] but also [18] for the analysis of the Fuller phenomenon as a recommended reading.

The surface Σ : $H_Y(z) = 0$ is called the switching surface and we denote by Σ' the set 675 $H_Y(z) = \{H_Y, H_X\}(z) = 0$. Let $z(\cdot) = (x(\cdot), p(\cdot))$ be a reference extremal on $[0, t_f]$. We note 676 $\Phi(t) := H_Y(z(t))$ the switching function coding the switching times. 677

Deriving twice Φ with respect to times, one gets: 678

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$$\frac{\mathrm{d}\Phi}{\mathrm{d}t}(t) = \{H_Y, H_X\}(z(t)),$$

$$\frac{\mathrm{d}^2\Phi}{\mathrm{d}t^2}(t) = \{\{H_Y, H_X\}, H_X\}(z(t)) + u(t)\{\{H_Y, H_X\}, H_Y\}(z(t)).$$

Definition 3.3. The time t is called an ordinary switching time time if $\Phi(t) = 0$ and $\frac{d\Phi}{dt}(t) \neq 0$ 682 0. 683

684 Lemma 3.4. Assume t be an ordinary switching time, then near z(t) every extremal projects 685

- $\sigma_{+}\sigma_{-}$ if $\frac{d\Phi}{dt}(t) > 0$, $\sigma_{-}\sigma_{+}$ if $\frac{d\Phi}{dt}(t) < 0$.
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Definition 3.5. Let $z(\cdot)$ be a bang extremal on $[0,t_f]$ with $u=\varepsilon\in\{-1,+1\}$. We note 688 by $\frac{d^2\Phi_{\varepsilon}}{dt^2}$ the expression (3.1) in which $u \equiv \varepsilon$. The point z(t) is called a fold point if $\Phi(t) =$ $\frac{d\Phi}{dt}(t) = 0$ and $\frac{d^2\Phi_{\varepsilon}}{dt^2}(t) \neq 0$. Assume that Σ' is a regular surface of codimension two. We have 690 691

- e cases:

 Parabolic case: $\frac{\mathrm{d}^2\Phi_+}{\mathrm{d}t^2}(t) \frac{\mathrm{d}^2\Phi_-}{\mathrm{d}t^2}(t) > 0,$ Hyperbolic case: $\frac{\mathrm{d}^2\Phi_+}{\mathrm{d}t^2}(t) > 0 \text{ and } \frac{\mathrm{d}^2\Phi_-}{\mathrm{d}t^2}(t) < 0,$ Elliptic case: $\frac{\mathrm{d}^2\Phi_+}{\mathrm{d}t^2}(t) < 0 \text{ and } \frac{\mathrm{d}^2\Phi_-}{\mathrm{d}t^2}(t) > 0.$
- 694
- This leads to: 695

Proposition 3.6. In the neighborhood of a fold point every extremal projects onto: 696

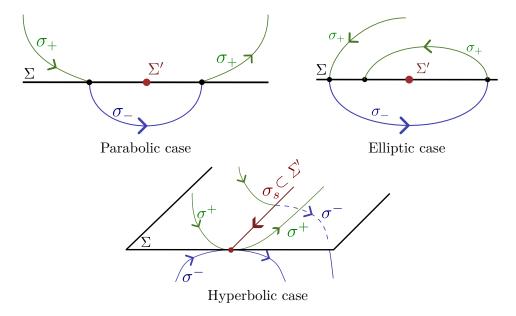


Figure 6. Fold case.

- In the parabolic case: $\sigma_+\sigma_-\sigma_+$ or $\sigma_-\sigma_+\sigma_-$.
- In the hyperbolic case $\sigma_{\pm}\sigma_{s}\sigma_{\pm}$.
- In the elliptic case, every extremal is bang-bang but the number of switches is not uniformly bounded.

This is illustrated in Fig. 6.

Note that in the elliptic case, there is a foliation by a cylinder of the regular extremal dynamics and the number of switches is related to the distance to Σ' versus the Fuller phenomenon, where the sequence of regular arcs is not bang-bang and converges to Σ' .

Application to the 3d-case. Consider the case where Y, [Y, X] and X form a frame i.e.

$$D'' = \det(Y, [Y, X], X)$$

is not vanishing. The problem is strict for singular extremals since Y and [Y, X] are independent. Hyperbolic trajectories are small time minimizing trajectories, while elliptic trajectories are small time maximizing, this up to the first conjugate time t_{1c} computed in [6] if they are strictly admissible (even in the limit case with no constraints on the control). In the parabolic case, they can be absent or not feasible. Consider the separating case where the singular arc is exceptional (abnormal) and assume that it is strictly admissible (for instance relaxing the control bound to the whole \mathbb{R}). In this case using again [6] an exceptional arc σ_s is time minimizing and time maximizing, up to the first conjugate time t_{1c} . Such a point is absent in the 3d-case. Such an arc can be lifted into two extremals $(\pm p, \sigma_s)$ and it corresponds either to an hyperbolic or elliptic situation in Σ' . One contribution of [20] is to analyze the time minimal syntheses near the terminal manifold in this situation.

3.3. General concepts of regular synthesis with a terminal manifold of codimension one. Take a triple (X, Y, N) and let $x_0 \in N$ which can be identified to 0 while N is the plane

 $x_1 = 0$. Let U be a neighborhood of 0, which divides the space into neighborhoods V and W contained respectively in $x_1 < 0$ and $x_1 > 0$ so that $U = V \cup W$. The problem is to compute the time minimal regular synthesis to steer each point of U to the terminal manifold.

N can be taken locally as $f^{-1}(0)$ where f is a submersion from U into a neighborhood of 0 in \mathbb{R} . The set of triples (X, Y, f) is endowed with the C^{∞} -Whitney topology and we denote by $j^k X$ (resp. $j^k Y, j^k f$) the k-jet of X (resp. Y, f) obtained by taking the Taylor expansion at $x_0 = 0$ up to order k. We say that the triple (X, Y, f) has at 0 a singularity of codimension i if $(j^k X, j^k Y, j^k f)$ belongs to a semi-algebraic set of codimension i in the jet space.

Our aim is to make a short presentation of the results of [7, 20, 8] to classify local syntheses up to an homeomorphims preserving the target N for all cases of codimension ≤ 2 , by considering two cases occurring in the application that we introduce next.

Definition 3.7. When Y is everywhere tangent to the target N, the control u is indirect and this case is called the flat case. In the non flat case, the action of the control is direct and the set of points where Y is tangent to N is of codimension ≥ 1 .

Stratified synthesis. Our aim is to describe the local time minimal synthesis in a neighborhood of N by estimating at any order the different strata. Actually, the optimal control feedback $u^*(x)$ is not always defined on the whole subset V of U in the domain $x_1 < 0$, since for some $x \in V$ the target N is not accessible.

In fact we can reduce our study to two cases:

- The case when the convex cone C generated by $\{X \pm Y\}$ is strict and the set of admissible directions points towards the space $x_1 > 0$.
- The exceptional case where the set of admissible directions are tangent to the terminal manifold.

This leads to introduce the exceptional locus in the construction of the stratification of N.

Definition 3.8. Let n be the normal to N oriented toward $x_1 > 0$. The exceptional locus (restricted to N) & is the set of points of N such that: $n(x) \cdot Y(x) = n(x) \cdot X(x) = 0$.

The second part of the stratification amounts to introduce the singular locus.

Definition 3.9. The singular locus (restricted to N) $\mathscr S$ is the set of points of N such that: $n(x) \cdot Y(x) = n(x) \cdot [Y, X](x) = 0$.

Definition 3.10. A stratified synthesis amounts to find a partition of V (or a partition of U in the exceptional case) into V^+ (resp. U^+) where $u^*(x) = +1$ and V^- (resp. U^-) where $u^*(x) = -1$ and a stratified surface separating V^+ and V^- (resp. U^+, U^-) with three kind of strata:

- Switching locus. It is the closure of the set or ordinary switching points and forming the set $W_{\sharp}(\sharp \in \{-1, +1\})$ where W_{+} is associated to $\sigma_{+}\sigma_{-}$ and W_{-} to $\sigma_{-}\sigma_{+}$.
- Cut locus. Let σ : [t_f, 0] → M be a minimizing curve, integrating backwards from N so
 that σ(0) ∈ N, t_f < 0. The cut-locus is the closure of the set of points where optimality
 is lost. It is denoted C and contains the splitting locus L where the optimal feedback
 is not unique.
- Switching singular locus. It is foliated by optimal singular arcs and is denoted Γ_s . Recall that if $u_s \in]-1,+1[$ the singular arc is strictly feasible but it can be saturated if $u_s^*(x) \in \{-1,+1\}$.

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To estimate the different strata we use semi-normal forms restricting the action of the feedback group to local diffeomorphisms φ preserving 0 and feedbacks $u \to -u$ so that σ_+ and σ_- can be inverted in the classification.

This leads to the following important concept.

Definition 3.11. Let $x_0 \in N$ which can be identified to 0. A Whitney chart is a pair (U, φ) where U is a neighborhood and φ a system of coordinates $(x, y, y_1, \dots, y_{n-3}, z)$ such that:

- 1. $Y = \frac{\partial}{\partial z}$, 2. $N \sim (\frac{1}{2}ks^2, w, w_1, ..., w_{n-3}, s)$,
- 3. The time minimal synthesis in U is C^0 described with foliations by 2d or 3d syntheses with triples $(X^{\flat}(x), Y^{\flat}(x), N^{\flat}(x)), x \in \mathbb{R}^2$ or \mathbb{R}^3 where the 3d-cases occur only in the exceptional case if n > 3.

Moreover in U, one can construct the stratified optimal synthesis, where each strata can be estimated at any order.

Definition 3.12. In the previous construction the restriction from n to n-1 decomposing $x=(x',\lambda), N=\cup_{\lambda}N'(\lambda), \text{ where } \lambda\in\mathbb{R}, \text{ is a parameter is called a one dimensional unfolding.}$

The previous definitions will be clarified in the examples we present next.

Main points of the geometric and analytic construction. Let n(x) be the normal to N, oriented towards $x_1 > 0$. We denote by N^{\perp} the symplectic lift of N: $N^{\perp} = \{(x,p); x \in A \}$ N, p = n(x). The stratification of N by the conditions $n(x) \cdot Y(x) = 0$ and $n(x) \cdot [Y, X](x) = 0$ selects ordinary switching points or fold points classified in Proposition 3.6.

- Ordinary switching locus W: One can restrict for simplicity the analysis to the 2d non flat case. Let $x_0 \in N$ such that $n \cdot Y(x_0) = 0$ and both $n \cdot X(x_0)$ and $n \cdot [Y, X](x_0)$ non zero. This leads to compute a switching locus K terminating at x_0 . Such a switching locus is part of W if the corresponding bang-bang extremal crosses the switching locus versus reflects on the switching locus. This leads to estimate the slope of W.
- Singular locus Γ_s : Consider again the non flat case. Let x_0 such that $(n(x_0), x_0)$ is a fold point hence $n \cdot Y(x_0) = n \cdot [Y, X](x_0) = 0$. Moreover assume that $n \cdot X(x_0) \neq 0$ (non exceptional case) and that the singular arc σ_s terminating at x_0 is strictly admissible, such an arc being small time minimizing for the problem with fixed extremities (assuming the condition $n \cdot [[Y, X], Y](x_0) \neq 0$). One can choose coordinates (x,y) such that $Y = \frac{\partial}{\partial y}$ and N is given by $(\frac{1}{2}ks^2, s)$, while X can be normalized to $(1-y^2X_1(x,y))\frac{\partial}{\partial x} + (u-u_s(x)+yX_2(x,y))\frac{\partial}{\partial y}$, where σ_s is identified to $t \to (t,0)$ and u_s is the singular control. Note that such normalizations were introduced in [6] in a more general context.

In order to decide about optimality one can compare by direct computations in the normalized coordinates the curvature of the boundary of the accessibility set along the singular arc with the curvature of N given by k. This leads to the cases described in Fig. 7. In the first case, there exists a cut locus C with slope $-u_s(0)$.

The 3d-case with an hyperbolic point terminating at $x_0 = 0$ can be obtained by constructing a semi-normal form in coordinates (x, y, z) by unfolding the case k > 0 and this leads to Fig. 8.

The central picture corresponds to Fig. 7 with k > 0. Left we have represented a Whitney

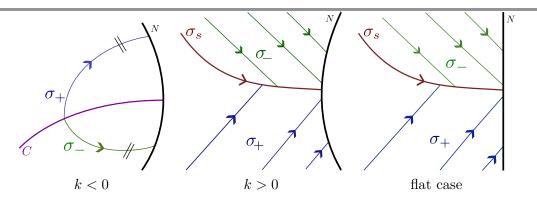


Figure 7. Optimal synthesis in the 2d-hyperbolic case.

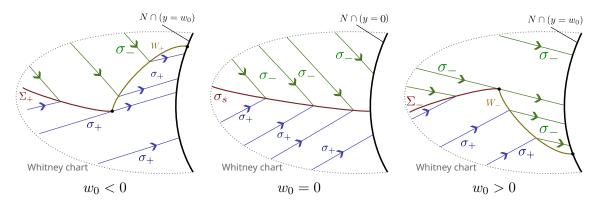


Figure 8. Unfolding in the 2d-hyperbolic case with parameter w_0 .

neighborhood containing the optimal switching locus W_+ intersecting the hyperbolic singular locus. They can be easily computed using the stratification of N^{\perp} into sectors with ordinary switching points and fold points while the singular arc terminating at 0 corresponds to an hyperbolic fold point.

This gives the procedure to compute the optimal syntheses using [7] in the non exceptional case as unfolding of 2d—cases. The procedure fails in the exceptional case where $n \geq 3$, where the following example from [20] shows why it cannot be reduced to 2d-foliations.

An exceptional 3d-case not 2d-reducible. One take a flat case so that N can be identified to (0, w, s) in (x, y, z) coordinates and $Y = \frac{\partial}{\partial z}$. In the construction the main point is to take a bang arc σ_- which is optimal in the domain $x \geq 0$ with a contact of order 3 at 0 with the surface N. Hence this gives birth in the domain x > 0 to arcs σ_- intersecting three times the target N, thanks to contact analysis.

Such a situation occurs for instance for the model which in fine is a C^0 -normal form describing the situation:

$$\frac{\mathrm{d}x}{\mathrm{d}t} = z, \quad \frac{\mathrm{d}y}{\mathrm{d}t} = b, \quad \frac{\mathrm{d}z}{\mathrm{d}t} = 1 + u + y,$$

819 the target N given by $(w,s) \to (0,w,s)$.

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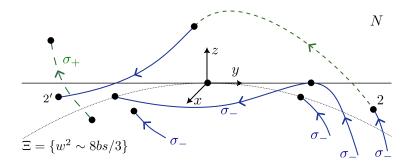


Figure 9. Synthesis exceptional case when b < 0. σ_- has a contact of order 3 with N.

One consider the situation with b > 0 where each point of the neighborhood U can be steered to the target.

In the domain x < 0, every time optimal trajectory is of the form σ_+ and the contact of σ_+ at 0 with N is of order 2.

Optimal arcs $\sigma_{-}(t)$ included in $x \geq 0$ are satisfying:

825 (3.2)
$$x_{-}(t) = t(s + wt/2 + bt^{2}/6 + ...),$$

where the weight of s is one and the weight of w is two, neglected having weights greater than 3.

The curve Ξ is the set of points (0, w, s) N of such that: $\frac{x_-(t)}{t} = \frac{d}{dt} \left(\frac{x_-(t)}{t}\right)$ have a common zero and is given using (3.2) by: $w^2 \sim \frac{8bs}{3}$.

The optimal synthesis is represented on Fig. 9. Optimal arcs σ_{-} in the domain $x \geq 0$ are cutting twice N in the subsets of the target denoted 2 and 2' and have two subarcs which are optimal in x > 0, but the subarc in x < 0 is not optimal.

4. Computations and preliminary results on the Controlled Lotka–Volterra model. The aim of this section is to present the geometric study of the controlled Lotka–Volterra model:

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$$\frac{\mathrm{d}x}{\mathrm{d}t}(t) = X(x(t)) + u(t)Y(x(t)),$$

with $X(x) = (\operatorname{diag} x)(Ax+r)$ and $Y(x) = (\operatorname{diag} x)\epsilon$, where $x = (x_1, \dots, x_n)^{\mathsf{T}}$ is the population species, x_1 represents the infected species and $\epsilon = (\epsilon_1, \dots, \epsilon_n)^{\mathsf{T}}$. The system can be written in ln-coordinates: $y = \ln x$ and it takes the form:

839 (4.1)
$$\frac{\mathrm{d}y}{\mathrm{d}t} = (Ae^y + r) + u \,\epsilon.$$

4.1. Equilibria and the collinear set. The collinear set \mathscr{C} is one of the main feedback invariant, related to computations of the free equilibria of the system for the hierarchy of models with no treatment u=0 or maximal dosing treatment u=1, but also for all intermediate dosing.

This set is a one dimensional algebraic variety and is the projection of the set:

845 (4.2)
$$\{(x_e, u_e) \in \mathbb{R}^n \times \mathbb{R}; \exists u_e, X(x_e) + u_e Y(x_e) = 0\}.$$

At such a point introduce the Jacobian matrix:

$$J(x_e, u_e) = \frac{\partial}{\partial x_{|(x_e, u_e)}} (X(x) + u_e Y(x)).$$

The following dimensionless coordinates are useful in the computations. The system can be written:

850 (4.3)
$$\frac{\mathrm{d}x_i}{\mathrm{d}t} = x_i r_i - x_i \sum_{i=1}^n a_{ij} x_j + u \, x_i \varepsilon_i$$

and denotes by x^* the free equilibrium given by:

$$r_i - \sum_{j=1}^n a_{ij} x_j^* = 0, i = 1, \dots, n.$$

One sets $v_i = \frac{x_i}{x_i^*}$ so that the dynamics takes the form:

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$$\frac{\mathrm{d}v_i}{\mathrm{d}t} = v_i r_i - v_i \sum_{j=1}^n a_{ij} x_j^* v_j + u \, v_i \varepsilon_i,$$

and denoting $a_{ij}^* = a_{ij}x_j^*$, one has $r_i = \sum_{j=1}^n a_{ij}^*$ since the persistent equilibrium is normalized to $\Omega = (1, ..., 1)$.

If we set: $x_i = v_i - 1$, the dynamics is given by:

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$$\frac{\mathrm{d}x_i}{\mathrm{d}t} = (x_i + 1) \sum_{j=1}^n a_{ij}^* - (x_i + 1) \sum_{j=1}^n a_{ij}^* (x_j + 1) + u(x_i + 1)\varepsilon_i.$$

859 Hence we have:

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Proposition 4.1. In the dimensionless coordinates the controlled Lotka-Volterra model is given:

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$$\frac{\mathrm{d}x_i}{\mathrm{d}t} = -(x_i + 1) \sum_{j=1}^n a_{ij} x_j + u(x_i + 1) \varepsilon_i,$$

so that Ω is identified to 0 and the Jacobian matrix at (0,0) is $A=(a_{ij})$.

Similarly one can make the same computation for the forced persistent equilibrium Ω' with maximal dosing $u_e = 1$. Hence one can associate two affine coordinates systems so that

- at $u_e = 0$, the system is given by: $-(x+1)A_0x$,
- at $u_e = 1$, the system is given by: $-(x+1)A_1x$.

This validates the accessibility discussion of section 2.3, where the separatrixes are approximated by lines. In the Volterra model they can be exactly computed thanks to integrability.

The controllability conditions discussed in 2.3 can be generalized to this case.

4.1.1. Computations in the 2d-case. We consider the regular 2-dimensional dynamics given in Proposition 4.1.

Collinear set and classification of equilibria. The collinear set is one of the main feedback invariant related to the computations of free equilibria with no treatment u = 0 and forced equilibria with maximal dosing u = 1.

The collinear set is given by the determinantal variety: det(X(x), Y(x)) = 0:

$$(x_1+1)(x_2+1)(x_1\kappa_2-x_2\kappa_1)=0,$$

- where $\kappa_1 = \varepsilon_1 a_{22} \varepsilon_2 a_{12}$ and $\kappa_2 = \varepsilon_2 a_{11} \varepsilon_1 a_{21}$.
- Alternatively, it can be viewed as the one dimensional algebraic variety projection of the set

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$$\{(x,u) \in \mathbb{R}^2 \times \mathbb{R}, \exists u \text{ such that } X(x) + u Y(x) = 0\}.$$

The condition $u_e \in [0, 1]$ selects a segment of persistent equilibria located on the line:

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$$C := \left\{ x_2 = u_e(x_1) \frac{\kappa_2}{\det A}, \ u_e(x_1) = x_1 \frac{\det A}{\kappa_1} \in [0, 1] \right\}.$$

- In particular, introduce $x_e = (x_{1e}, x_{2e}) \in \mathcal{C}$, the origin $x_e = 0$ is associated to the control $u_e = 0$ while $x_e = (\kappa_1/\det A, \kappa_2/\det A)$ is associated to the control $u_e = 1$.
- For $u_e \in [0, 1]$, define the Jacobian matrix

$$J(x_e, u_e) = \frac{\partial}{\partial x} (X(x) + u_e Y(x))_{|x=x_e},$$

888 we have:

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Lemma 4.2. Let $x_e \in \mathcal{C}$ associated to the control u_e , the spectrum of J is:

spec
$$(J(x_e, u_e)) = \left\{ \left(k_1(x_e) \pm \sqrt{k_1(x_e)^2 + k_1'(x_e)} \right) / 2 \right\},$$

- 891 where $k_1(x_e) = x_{1e}a_{22}\kappa_2/\kappa_1 a_{22} a_{11}(x_{1e}+1)$ and $k_1'(x_e) = -4 \det A(x_{1e}+1)(1 + x_{1e}\kappa_2/\kappa_1)$.
 - 4.2. Computation of the collinearity locus and properties-Construction of a normal form in \ln -coordinates.

Computations about \mathcal{C} in the n-dimensional case. We have the following algorithm, taking the system represented in the x-coordinates.

- Step 1. The collinear set is the projection of the algebraic curve defined by: There exists u_e constant such that $X(x_e) = -u_e Y(x_e)$. This gives n-equations depending upon (n+1) variables (x_e, u_e) .
- Step 2. Take such a pair (x_e, u_e) so that x_e is a forced equilibrium for $u = u_e$ and they form a set with extreme points associated to $u_e = 0$ and $u_e = 1$, when restricting to $u_e \in [0, 1]$.
- 902 The linear dynamics at the point x_e is characterized by the Jacobian matrix:

$$J(x_e, u_e) = \frac{\partial}{\partial x_{|(x_e, u_e)}} (X(x) + u_e Y(x))$$

904 the spectrum being $\sigma(J) = (\lambda_1, \dots, \lambda_n)$ with associated generalized eigenspaces E_{λ_i} , $i = 905 \quad 1, \dots, n$.

The linear stability is determined by this spectrum, thanks to Lyapunov linear stability theory.

- Step 3. From control point of view we have three cases:
- 1. $u_e \notin [0,1]$: u_e is not feasible,

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- 2. $u_e \in]0,1[:u_e \text{ is strictly feasible,}]$
- 3. $u_e = \pm 1$: u_e being feasible but saturating.
- One can discuss the linear controllability of the pair $(J(x_e, u_e), b)$ where $b = Y(x_e)$.
 - Kalman condition: rank $[b, Jb, ..., J^{n-1}] = n$ and the singular point x_e is regular. If the control u_e is strictly feasible local controllability holds [21].
 - If rank $[b, Jb, ..., J^{n-1}] = n k < n$, then the singular point is a singular trajectory (reduced to a point) associated to u_e and k is the codimension of the singularity.
- From linear controllability theory, one can construct a normal form, at a given equilibrium pair (x_e, u_e) .
- We take ln-coordinates so that X(x) takes the form $X^{\flat}(y) = (Ae^y + r)$ and the controlled vector field Y(x) becomes the constant vector field $Y^{\flat} = \epsilon$.
- Let (y_e, u_e) be the selected forced equilibrium in the ln–coordinates and let $z = y y_e$, $v = (u u_e)$ so that the system takes the form:

$$\frac{\mathrm{d}z}{\mathrm{d}t} = J(z) + R(z) + v \,\epsilon,$$

- 924 where J is the Jacobian matrix at (y_e, u_e) .
- 925 One can find coordinates such that the linear dynamics decomposes into

$$\frac{\mathrm{d}z_1}{\mathrm{d}t} = J_{11}z_1 + J_{12}z_2 + v\epsilon$$

$$\frac{dz_2}{\mathrm{d}t} = J_{21}z_2$$

where the restriction to the controllable space $z_2 = 0$ is given by the dynamics:

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$$\frac{\mathrm{d}z_1}{\mathrm{d}t} = J_{11}z_1 + v\,\epsilon.$$

929 The pair (J_{11}, ϵ) can be set in Brunovsky canonical form:

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$$J_{11} = \begin{bmatrix} 0 & \operatorname{Id}_{n-k-1} \\ -a_1 & -a_2 & \dots & -a_{n-k} \end{bmatrix}, \quad \epsilon = \begin{bmatrix} 0 \\ \vdots \\ 0 \\ 1 \end{bmatrix},$$

- where the coefficients (a_1, \ldots, a_{n-k}) are the coefficients of the characteristic polynomial of J_{11} .
- 933 Finally this leads to the construction of a normal form:

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$$\frac{\mathrm{d}z}{\mathrm{d}t} = J(z) + R(z) + v\epsilon,$$

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where the pair $(J(x_e), u_e), \epsilon$ is in linear canonical form. Note in particular that the sensitivity vector ϵ is normalized to $(0,\ldots,0,1)^{\intercal}$ and R(z) is the non-linear part of the dynamics, related 936 to singular trajectories computations. 937

4.3. Singular extremals. Lie brackets can be computed in the original coordinates but 938 the computations are simpler in ln-coordinates, since the control vector field Y^{\flat} is constant. 939 This comes from the following. 940

Proposition 4.3. 941

- 1. If $X = (\operatorname{diag} x)X_1(x)$, $Y = (\operatorname{diag} x)Y_1(x)$, where X_1, Y_1 are polynomic then the iterated Lie brackets are in the same category of polynomic vector fields of the form $(\operatorname{diag} x)P(x)$.
- 2. Let φ be the diffeomorphism: $x = e^y$. Denote by X^{\flat}, Y^{\flat} the images of X, Y by this diffeomorphism. Then by invariance of the Lie bracket: $[X^{\flat}, Y^{\flat}](y) = d\varphi^{-1}[X, Y](e^y)$.

4.3.1. Computations in the 2d-case.

- $X^{\flat} = \left(r_1 + \sum_{j=1,2} a_{1j} e^{x_j}, r_2 + \sum_{j=1,2} a_{2j} e^{x_j}\right),$
- $Y^{\flat} = (\varepsilon_1, \varepsilon_2)$,
- $[X^{\flat},Y^{\flat}]=\Big(\sum_{j=1,2}^{r}\varepsilon_{j}a_{1j}e^{x_{j}},\sum_{j=1,2}\varepsilon_{j}a_{2j}e^{x_{j}}\Big).$ Hence the singular locus:

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$$\mathscr{S}: \det([X,Y](x),Y(x)) = 0$$

953 is given by:

$$x_1 x_2 [x_1(a_{11}\varepsilon_1\varepsilon_2 - \varepsilon_1^2 a_{21}) + x_2(\varepsilon_2^2 a_{12} - \varepsilon_1\varepsilon_2 a_{22})] = 0$$

which stratifies into $x_1 = x_2 = 0$ and a permanent straight-line L. 955

Moreover:

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$$[[X^{\flat}, Y^{\flat}], Y^{\flat}] = (\sum_{j=1,2} \varepsilon_j^2 a_{1j} e^{x_j}, \sum_{j=1,2} \varepsilon_j^2 a_{2j} e^{x_j}).$$

958 Outside the collinear set \mathcal{C}, X, Y form a frame and writing:

$$[[Y, X], X](x) = \alpha(x)X(x) + \beta(x)Y(x),$$

so that: 960

- Hyperbolic (feasible) subarcs are such that $\alpha(x) > 0$,
- Elliptic subarcs are such that $\alpha(x) < 0$.
- At the persistent point intersection of \mathcal{S} and \mathcal{C} , one gets an exceptional point.
- **4.3.2. Computations in the** 3d-case. The Lie brackets computations are as before, ex-964 cept that the index j goes from 1 to 3. So that 965

$$D = \det(Y^{\flat}, [Y^{\flat}, X^{\flat}], [[Y^{\flat}, X^{\flat}], Y^{\flat}])$$

is homogeneous and quadratic with respect to the variable e^{x_i} . 967

Moreover the exceptional locus is given by the relation:

$$D'' = \det(Y^{\flat}, [Y, X]^{\flat}, X^{\flat}) = 0,$$

this set being a quadratic non homogeneous variety with respect to the variables e^{x_i} . 970

Note that the computation of the Lie bracket: $[[Y^{\flat}, X^{\flat}], X^{\flat}]$ is more complex and formal computations are necessary.

This fixes the limit of the computational complexity in the *n*-dimensional case.

4.4. Applications.

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4.4.1. A 2d-working case. In this section, the general techniques from [7, 20] will be applied to analyze a 2d-case study which occurs in the Lotka-Volterra model, see also [10] as a complementary study for the fixed end point problem.

Lie brackets and feedback invariants. The first step is to compute the collinear set C defined by

$$\det(X(x), Y(x)) = 0,$$

981 which takes the form:

982 (4.4)
$$x_1x_2\left(\varepsilon_2(x_1a_{11} + x_2a_{12} + r_1)\right) - \varepsilon_1(x_1a_{21} + x_2a_{22} + r_2) = 0,$$

while the singular locus, defined by S: $\det(Y(x), [Y, X](x)) = 0$, takes the form:

984 (4.5)
$$x_1 x_2 (\varepsilon_2 x_2 (\varepsilon_2 a_{12} - \varepsilon_1 a_{22}) - \varepsilon_1 x_1 (\varepsilon_1 a_{21} - \varepsilon_2 a_{11})) = 0$$

985 and Lie brackets of length 3 are:

$$[[Y, X], Y](x) = -x_1 \left(\varepsilon_1^2 x_1 a_{11} - \varepsilon_2^2 x_2 a_{12}\right) \frac{\partial}{\partial x_1} - x_2 \left(\varepsilon_1^2 x_1 a_{21} + \varepsilon_2^2 x_2 a_{22}\right) \frac{\partial}{\partial x_2},$$
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$$[[Y, X], X](x) = -x_1 \left(\varepsilon_1 x_1 \left(r_1 a_{11} + x_2 a_{12} \left(a_{11} - a_{21}\right)\right) + \varepsilon_2 x_2 a_{12} \left(x_1 \left(a_{21} - a_{11}\right) + r_2\right)\right) \frac{\partial}{\partial x_1}$$

$$-x_2 \left(\varepsilon_2 x_2 \left(r_2 a_{22} + x_1 a_{21} \left(a_{22} - a_{12}\right)\right) + \varepsilon_1 x_1 a_{21} \left(x_2 \left(a_{12} - a_{22}\right) + r_1\right)\right) \frac{\partial}{\partial x_2}.$$

The geometric situation that we analyze in our working example is the exceptional case where we consider the intersection of the collinear locus with the singular locus, which corresponds from (4.4) and (4.5) to intersection of two straight-lines. It corresponds to a generic interaction between an hyperbolic arc and an elliptic arc.

Constructing a semi-normal form. The second step is to construct a semi-normal form for the system. The construction is detailed in [7] but computation are simple in the 2d-case. It consists to choose coordinates such that the intersection is taken as the origin (0,0), Y is identified to the constant vector field $Y = \frac{\partial}{\partial x_2}$ (this amounts mainly to choose ln-coordinates) while the reference singular direction is identified to the straight line $(0x_1)$.

Expanding X in the jet space at (0,0), this leads to analyze the control system:

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$$\dot{x}_1 = -\lambda x_1 + \alpha x_2^2, \qquad \dot{x}_2 = u - u_e$$

998 with $u_e \in]-1,1[, |u| \le 1, \lambda > 0 \text{ and } \alpha > 0.$

Properties of the system. Computing Lie brackets in the new coordinates show relevant simplification with respect to the previous formulae:

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$$X(x) = (-\lambda x_1 + \alpha x_2^2) \frac{\partial}{\partial x_1} - u_e \frac{\partial}{\partial x_2}, \quad Y(x) = \frac{\partial}{\partial x_2},$$

$$[Y, X](x) = -2\alpha x_2 \frac{\partial}{\partial x_1}, \quad [[Y, X], Y](x) = -2\alpha \frac{\partial}{\partial x_1},$$

and the singular line is given by

$$1005$$
 $x_2 = 0.$

1006 Restricting to $x_2 = 0$, one has:

$$X_{|x_2=0} = -\lambda x_1 \frac{\partial}{\partial x_1}, \quad [[Y, X], Y]_{|x_2=0}(x) = -2\alpha \frac{\partial}{\partial x_1}.$$

1009 Hence

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$$[[Y, X], Y]_{|x_2=0}(x) = \frac{2\alpha}{\lambda x_1} X_{|x_2=0}(x)$$

1011 for $x_1 \neq 0$.

Therefore, we obtain the following lemma.

- Lemma 4.4. 1. The origin (0,0) is an abnormal singular arc reduced to a point and the arc $x_1 > 0$ is hyperbolic and the arc $x_1 < 0$ is elliptic.
 - 2. The singular control along the line $x_2 = 0$ is given by $u = u_e$ and is constant and strictly admissible since $u_e \in]-1,+1[$.
- Lemma 4.5. The collinear set C given by det(X,Y) = 0 is the parabola $x_1 = \alpha x_2^2/\lambda$.
- 1018 Clock form. To analyze a 2d-time minimal problem with fixed extremities the standard 1019 technique is to introduce the clock form $\omega = p dx$ defined outside the collinear set by:

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$$p \cdot X(x) = 1, \quad p \cdot Y(x) = 0.$$

Computing one has $\omega = \frac{1}{-\lambda x_1 + \alpha x_2^2} dx_1$ so that

$$d\omega = \frac{2\alpha x_2}{(-\lambda x_1 + \alpha x_2^2)^2} dx_1 \wedge dx_2.$$

- 1023 One can decompose $\mathbb{R}^2 \setminus (\mathcal{C} \cup \mathcal{S})$ in four domains:
- 1024 domain $A: \dot{x}_1 < 0 \cap x_2 > 0$,
 - domain $B: \dot{x}_1 > 0 \cap x_2 > 0$,
- 1026 domain C: $\dot{x}_1 < 0 \cap x_2 < 0$,
- 1027 domain $D: \dot{x}_1 > 0 \cap x_2 < 0$.

On each domain one can compare the time along arcs γ_1, γ_2 joining respectively x_0 to x_1 where $\gamma_1 = \sigma_+ \sigma_-, \gamma_2 = \sigma_- \sigma_+$ using Stokes theorem. One has:

Lemma 4.6. In domain A and D for such arcs the time minimal policy is $\sigma_-\sigma_+$ while in domain B and C the optimal policy us $\sigma_+\sigma_-$.

Proof. Take the case of domain A, one has:

$$\int_{\gamma_1} \omega - \int_{\gamma_2} \omega = \int_{\gamma_1 \vee (-\gamma_2)} d\omega > 0,$$

hence the time along γ_1 is longer than the time along γ_2 . The discussion is similar for the 1035 other cases.

Integrating the extremal curves. The adjoint system takes the form with $p = (p_1, p_2)$: 1036

$$\dot{p}_1 = \lambda p_1, \quad \dot{p}_2 = -2\alpha x_2 p_1.$$

Denoting for $u = \pm 1$, $\beta = u - u_e$, one gets: 1038

Lemma 4.7. The extremal system is characterized by:

- $x_2(t) = x_2(0) + \beta t$, 1040
- $x_1(t) = e^{-\lambda t} \left(x_1(0) + \int_0^t e^{\lambda s} (x_2(0) + \beta s)^2 ds \right)$ 1041
- $\bullet \ p_1(t) = e^{\lambda t} p_1(0),$ 1042

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• $p_2(t) = -2\alpha p_1(0) \int_0^t e^{\lambda s} (x_2(0) + \beta s) ds$ 1043

and they belong to the polynomial exponential category. 1044

The integrals in the expressions of $x_1(t)$ and $p_2(t)$ can be evaluated using: 1045

$$\int_0^t se^{\lambda s} = \frac{te^{\lambda t}}{\lambda} - \frac{1}{\lambda^2} \left(e^{\lambda t} - 1 \right), \qquad \qquad \int_0^t s^2 e^{\lambda s} = \frac{t^2 e^{\lambda t}}{\lambda} - \frac{2}{\lambda} \int_0^t se^{\lambda s} ds.$$

Lemma 4.8. The switching function is $\Phi(t)=p_2(t)$ so that for $u=\pm 1$ and one has: $\ddot{p}_2(t) = -2\alpha p_1 (\lambda x_2 + u - u_e)$ where $p_1(t)$ is of constant sign given by the sign of $p_1(0)$. 1049

Geometric discussion of the synthesis with a terminal manifold N of codimension one. Next we present the discussion of the time minimal synthesis with a terminal manifold N of codimension one by gluing cases discussed in [7].

One takes N as a circle with radius d centered at 0 where the synthesis amounts to glue the hyperbolic and elliptic situation. The circle intersects the hyperbolic arc σ_s at $x_1 = d$ and the elliptic arc σ_s at $x_1 = -d$.

The BC-extremals curves can be parameterized by Lemma 4.7 with $(p_1(0), p_2(0)) = \pm n(0)$ where n(0) is the normal to the circle, n(0) = (x(s), y(s)). Geodesics curves are integrated backwards, geodesics in the interior to the circle are associated to n(0) and geodesics exterior to the circle are associated to -n(0).

Since $Y = \frac{\partial}{\partial x_2}$, from [7] we can at once deduced the synthesis outside the circle, near the hyperbolic point (d,0) and the elliptic point (-d,0), using the curvature of N only at such point which are the images of the curve $(-1/2ks^2, s)$, k > 0 at the hyperbolic point and $(1/2ks^2, s)$ at the elliptic point.

They are represented on Fig.10.

The main properties are

• hyperbolic case: the singular arc is optimal and the optimal policy is -1 for $x_2 > 0$ and +1 for $x_2 < 0$.

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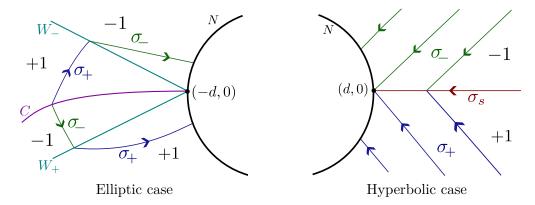


Figure 10. 2d-syntheses.

• elliptic case: The time minimal synthesis is defined by the stratification $W = W_- \cup W_+$ of the switching locus and there exists a cut locus C terminating at (-d, 0).

To complete the analysis one must glue the two syntheses along the target N and consider also geodesics interior to the circle.

To simplify the computations one considers the symmetric case $u = u_e$ which allows to simplify the estimate of the cut locus prolongating the branch at the elliptic point which coincides with the singular line $x_2 = 0$ restricted to the domain $x_1 < -d$.

The synthesis is represented on Fig.11.

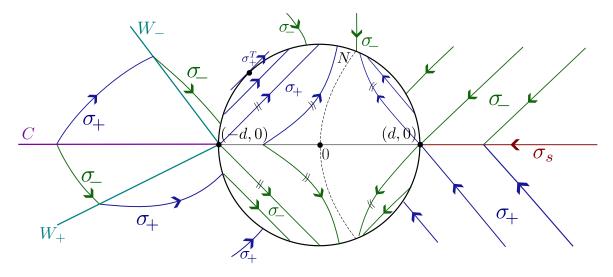


Figure 11. Gluing hyperbolic and elliptic case with N being a circle; the symmetric case $u_e = 0$.

This gives the time minimal synthesis in a neighborhood V of the origin. In general we combine numerical integration using the parameterization of the BC–extremals and the analysis of [7] to glue different Whitney charts.

4.4.2. Complexity if the singular flow in the 3*d***–case.** From dynamical system point of view, the complexity of the Lotka–Volterra model is related to the existence of persistent

equilibrium point, which leads to complicated dynamics related to the hierarchy of dynamics associated to the hierarchy of at most 2^n -equilibria.

Hence, in this section one analyses the same question regarding to existence of permanent equilibria for the singular dynamics associated to the time minimal control problem.

First one must extent the previous 2d—result concerning the existence of (exceptional) singular arc reduced to a point, in the context of controlled Lotka–Volterra model.

Proposition 4.9. Consider the controlled Lotka-Volterra model in the n-dimensional case.

Then there exists (isolated) exceptional arcs reduced to a point.

1089 *Proof.* Consider the pair (X,Y), and choose ln–coordinates so that $Y(x) = \frac{\partial}{\partial x_n}$ with 1090 $X(x) = \sum_{i=1}^n X_i(x) \frac{\partial}{\partial x_i}$, the collinear set is defined by the (n-1)-equations $X_i(x) = 0$,

1091 $i=1,\ldots,n-1$ and let $\lambda=-u_e$ so that $X_n(x)=-\lambda$. Let $\tilde{X}(x)=\sum_{i=1}^{n-1}X_i(x)\frac{\partial}{\partial x_i}+$

 $(X_n(x) + u_e) \frac{\partial}{\partial x_n}$ and by construction there exists x_e on the collinear set so that $\tilde{X}(x_e) = 0$.

Denote by \tilde{J} the Jacobian matrix of \tilde{X} at $x=x_e$ and let $\sigma(\tilde{J})$ be its spectrum.

Denoting by $\operatorname{ad} \tilde{X} \cdot Y = [\tilde{X}, Y]$. Then at x_e the matrix with columns of iterated Lie brackets

$$K = \left(Y, \operatorname{ad}\tilde{X} \cdot Y, \dots, \operatorname{ad}^{n-1}\tilde{X} \cdot Y\right)$$

1096 coincides with the Kalman matrix

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$$\left(b, \tilde{J}b, \dots, \tilde{J}^{n-1}b\right)$$

where b is the constant vector Y(x). The singular point is exceptional if and only if rank $K \le 1099 - n - 1$.

At isolated point, the condition rank = n - 1 can be realized for the controlled Lotka– Volterra model (see Example 4.10 for n = 3).

Example 4.10. In the dimensionless coordinates (see Proposition 4.1), take: $A = \operatorname{diag}(\lambda_1, \lambda_1, \lambda_3)$, $X(x) = -\operatorname{diag}(x+1) Ax$, $Y(x) = \operatorname{diag}(x+1) (\varepsilon_1, \varepsilon_2, \varepsilon_3)^{\mathsf{T}}$ so that the persistent equilibrium is located at $x_e = 0$. The columns of the Kalman matrix K are

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$$Y(0) = (\varepsilon_1, \varepsilon_2, \varepsilon_3)^{\mathsf{T}},$$
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$$[X, Y](0) = (-\varepsilon_1 \lambda_1, -\varepsilon_2 \lambda_1, -\varepsilon_3 \lambda_3)^{\mathsf{T}},$$

$$[X, [X, Y]](0) = (\varepsilon_1 \lambda_1^2, +\varepsilon_2 \lambda_1^2, \varepsilon_3 \lambda_3^2)^{\mathsf{T}},$$

hence rank K < 3 and 0 is a singular exceptional point.

Note that the Jacobian matrix of the singular flow, defined for $\varepsilon_1 \neq \varepsilon_2$, evaluated at 0 is

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$$J = \begin{pmatrix} \frac{\varepsilon_1 \lambda_3}{\varepsilon_1 - \varepsilon_2} - \lambda_1 & \frac{\varepsilon_1 \lambda_3}{\varepsilon_2 - \varepsilon_1} & 0\\ \frac{\varepsilon_2 \lambda_3}{\varepsilon_1 - \varepsilon_2} & \frac{\varepsilon_1 \lambda_3}{\varepsilon_2 - \varepsilon_1} - \lambda_1 + \lambda_3 & 0\\ \frac{\varepsilon_3 \lambda_3}{\varepsilon_1 - \varepsilon_2} & -\frac{\varepsilon_3 \lambda_3}{\varepsilon_1 - \varepsilon_2} & -\lambda_3 \end{pmatrix}$$

and its spectrum $\{\lambda_3 - \lambda_1, -\lambda_3, -\lambda_1\}$ is resonant.

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3d-case. In the 3d-case, the singular trajectories are solutions of the vector field: \dot{x}=1114 X_s(x)=X(x)-u_sY(x), where the singular control feedback is u_s=-D'(x)/D(x) with
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$$D(x) = \det(Y(x), [Y, X](x), [[Y, X], Y](x)), \quad D'(x) = \det(Y(x), [Y, X](x), [[Y, X], X](x)).$$

Moreover exceptional trajectories are located on the exceptional locus D''(x) = 0 with

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$$D''(x) = \det(Y(x), [Y, X](x), X(x)).$$

1118 Computing in the original coordinates leads to complicated expressions:

```
\begin{array}{ll} 1120 & D(x)/x_1x_2x_3 = \left(\varepsilon_1^2x_1a_{21} + \varepsilon_1\left(\varepsilon_2\left(x_2a_{22} - x_1a_{11}\right) + \varepsilon_3x_3a_{23}\right) - \varepsilon_2\left(\varepsilon_2x_2a_{12} + \varepsilon_3x_3a_{13}\right)\right) \\ 1121 & \left(\varepsilon_1^2x_1a_{31} + \varepsilon_2^2x_2a_{32} + \varepsilon_3^2x_3a_{33}\right) + \left(\varepsilon_1^2x_1a_{11} + \varepsilon_2^2x_2a_{12} + \varepsilon_3^2x_3a_{13}\right)\left(\varepsilon_2^2x_2a_{32} + \varepsilon_3\varepsilon_2\left(x_3a_{33} - x_2a_{22}\right)\right) \\ 1122 & -\varepsilon_3^2x_3a_{23} + \varepsilon_1x_1\left(\varepsilon_2a_{31} - \varepsilon_3a_{21}\right)\right) - \left(\varepsilon_1^2x_1a_{21} + \varepsilon_2^2x_2a_{22} + \varepsilon_3^2x_3a_{23}\right) \\ \frac{1123}{1124} & \left(\varepsilon_1^2x_1a_{31} + \varepsilon_1\left(\varepsilon_2x_2a_{32} + \varepsilon_3\left(x_3a_{33} - x_1a_{11}\right)\right) - \varepsilon_3\left(\varepsilon_2x_2a_{12} + \varepsilon_3x_3a_{13}\right)\right), \end{array}
```

$$D'(x)/x_{1}x_{2}x_{3} = \left(-\varepsilon_{1}^{2}x_{1} \ a_{21} + \varepsilon_{1} \left(\varepsilon_{2} \left(x_{1}a_{11} - x_{2}a_{22}\right) - \varepsilon_{3}x_{3}a_{23}\right) + \varepsilon_{2} \left(\varepsilon_{2}x_{2}a_{12} + \varepsilon_{3}x_{3}a_{13}\right)\right)$$

$$\left(\varepsilon_{2}x_{2}\left(x_{1}a_{12}a_{31} - a_{32}\left(x_{1}a_{21} + x_{3}\left(a_{23} - a_{33}\right) + r_{2}\right)\right) - \varepsilon_{1}x_{1}\left(r_{1}a_{31} + x_{3}\left(a_{13} - a_{33}\right)a_{31}\right)\right)$$

$$+ x_{2}\left(a_{12}a_{31} - a_{21}a_{32}\right) + \varepsilon_{3}x_{3}\left(-r_{3}a_{33} + x_{1}a_{31}\left(a_{13} - a_{33}\right) + x_{2}a_{32}\left(a_{23} - a_{33}\right)\right)\right)$$

$$+ \left(\varepsilon_{2}^{2}\left(-x_{2}\right)a_{32} + \varepsilon_{3}\varepsilon_{2}\left(x_{2}a_{22} - x_{3}a_{33}\right) + \varepsilon_{3}^{2}x_{3}a_{23} + \varepsilon_{1}x_{1}\left(\varepsilon_{3}a_{21} - \varepsilon_{2}a_{31}\right)\right)$$

$$+ \left(\varepsilon_{1}x_{1}\left(r_{1}a_{11} + x_{2}a_{12}\left(a_{11} - a_{21}\right) + x_{3}a_{13}\left(a_{11} - a_{31}\right)\right) + \varepsilon_{2}x_{2}\left(x_{3}a_{13}a_{32} - a_{12}\left(x_{1}\left(a_{21} - a_{11}\right)\right)\right)$$

$$+ x_{3}a_{23} + r_{2}\right) - \varepsilon_{3}x_{3}\left(a_{13}\left(x_{1}\left(a_{31} - a_{11}\right) + x_{2}a_{32} + r_{3}\right) - x_{2}a_{12}a_{23}\right)\right)$$

$$- \left(\varepsilon_{1}^{2}\left(-x_{1}\right)a_{31} + \varepsilon_{1}\left(\varepsilon_{3}\left(x_{1}a_{11} - x_{3}a_{33}\right) - \varepsilon_{2}x_{2}a_{32}\right) + \varepsilon_{3}\left(\varepsilon_{2}x_{2}a_{12} + \varepsilon_{3}x_{3}a_{13}\right)\right)$$

$$+ x_{3}a_{23}\left(a_{32} - a_{21}\right) + \varepsilon_{3}x_{3}\left(x_{1}a_{13}a_{21} - a_{23}\left(x_{1}a_{31} + x_{2}\left(a_{32} - a_{22}\right) + r_{3}\right)\right)\right),$$

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$$D''(x)/x_1x_2x_3 = \left(-\varepsilon_1^2x_1a_{21} + \varepsilon_1\left(\varepsilon_2\left(x_1a_{11} - x_2a_{22}\right) - \varepsilon_3x_3a_{23}\right) + \varepsilon_2\left(\varepsilon_2x_2a_{12} + \varepsilon_3x_3a_{13}\right)\right)$$
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$$\left(x_1a_{31} + x_2a_{32} + x_3a_{33} + r_3\right) + \left(-\varepsilon_2^2x_2a_{32} + \varepsilon_3\varepsilon_2\left(x_2a_{22} - x_3a_{33}\right) + \varepsilon_3^2x_3a_{23} + \varepsilon_1x_1\left(\varepsilon_3a_{21}\right)\right)$$
1141
$$-\varepsilon_2a_{31}\right)\left(x_1a_{11} + x_2a_{12} + x_3a_{13} + r_1\right) + \left(\varepsilon_1^2x_1a_{31} + \varepsilon_1\left(\varepsilon_2x_2a_{32} + \varepsilon_3\left(x_3a_{33} - x_1a_{11}\right)\right) - \varepsilon_3\left(\varepsilon_2x_2a_{12} + \varepsilon_3x_3a_{13}\right)\right)\left(x_1a_{21} + x_2a_{22} + x_3a_{23} + r_2\right).$$

Proposition 4.11. If $D(x) \neq 0$, the equilibria of the singular dynamics $\dot{x} = X_s(x)$ are exceptional trajectories reduced to a point. At such a point x_e , the spectrum of $J = \frac{\partial X_s}{\partial x}(x_e)$ is a feedback invariant. Moreover the dynamics is foliated by the invariant set D''(x) = 0 and D(x)D''(x) > 0 or < 0 associated respectively to hyperbolic and elliptic arcs. The singular feedback u_s acts as a geometric pole placement of the dynamics on the collinear set.

1149 *Proof.* The proof is clear following the construction detailed in the proof of Proposition 1150 4.9.

The 4d-case. This gives the road to the n-dimensional case.

The singular exceptional control can be expressed as a feedback using the relation

1153
$$H_X(z) = H_Y(z) = \{H_X, H_Y\}(z) = 0$$

 $\{\{H_X, H_Y\}, H_X\}(z) + u_{se}\{\{H_X, H_Y\}, H_Y\}(z) = 0$

1156 and this leads to

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$$u_{se}(x) = -\frac{D'(x)}{D(x)},$$

1158 where

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$$D(x) = \det(X(x), Y(x), [Y, X](x), [[Y, X], Y](x)),$$

$$D'(x) = \det(X(x), Y(x), [Y, X](x), [[Y, X], X](x)).$$

Similarly to the 3d-case, the singular exceptional dynamics: $\dot{x} = X(x) + u_{se}Y(x)$ can be used to generate feedback invariants.

Remaining singular dynamics are parameterized by a dynamic feedback $u(x, \lambda)$ depending upon a one dimensional coefficient.

5. Conclusion. In this article we have presented the general techniques from geometric control to analyze in the permanent case, the optimal control problem related to vermin reduction in a complex microbiote modelled by the Lotka–Volterra equations.

Our analysis is based on a series of articles classifying the time minimal syntheses for a single—input affine system with terminal manifold of codimension one developed for chemical networks [7, 8, 20]. Using the concepts of Whitney chart and unfolding the explicit computations in a neighbourhood of the terminal manifold can be reduced to problems in dimension 2 or 3 and a dictionary of the time minimal syntheses is described in [7, 20], up to codimension 2 cases. Global syntheses can be described by gluing different Whitney charts.

It can be applied to the controlled Lotka–Volterra model to analyze either the problem of reducing the infection using an antibiotic agent or to reinforce the body prior to infection using a probiotic agent. A case study is given to construct a global optimal synthesis by gluing distinct Whitney charts.

Our article shows the parallel between the analysis of the free dynamics in the frame of dynamical systems and the dynamics of the Hamiltonian dynamics deduced from the Maximum Principle which parameterizes the extremals candidates as minimizers.

The complexity of the Hamiltonian dynamics for nonlinear control systems is related to the existence and their complexity of the singular extremals dynamics. Our contribution is to present preliminary analysis of this complexity, in the frame of the controlled Lotka–Volterra model. It is shown to be related to the collinear set on which are located the equilibrium of the free dynamics where no treatment is applied and the forced equilibrium associated to maximal treatment.

An additional step in our analysis will be to analyze the problem in the sampled–data control frame in relation with the permanent case.

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Barnesiella (Bar.) undefined genus of Lachnospiraceae (Und. Lac.) undefined genus of unclassified Mollicutes (Und. Mol.) unclassified Lachnospiraceae (Uncl. La.) Blautia (Bla.) Other					0.3680 0.3102 0.4706 0.3561 0.7089 0.5400	Akkermansia (Akk.) Coprobacillus (Cop.) Clostridium difficile (C. diff.) Enterococcus (Ent.) undefined genus of Enterobacteriaceae (Und. En.)					0.2297 0.8300 0.3918 0.2907 0.3236
	Bar.	Und. Lac.	Uncl. Lac.	Other	Bla.	Und. Mol.	Akk.	Cop.	Und. En.	Ent.	C. diff.
Bar.	-0.205	0.098	0.167	-0.164	-0.143	0.019	-0.515	-0.391	-0.268	0.008	0.346
Und. Lac.	0.062	-0.104	-0.043	-0.154	-0.187	0.027	-0.459	-0.413	-0.196	0.022	0.301
Uncl. Lac.	0.143	-0.192	-0.101	-0.139	-0.165	0.013	-0.504	-0.772	-0.206	-0.006	0.292
Other	0.224	0.138	0.000	-0.831	-0.223	0.220	-0.205	-1.009	-0400	-0.039	0.666
Bla.	-0.180	-0.051	0.000	-0.054	-0.708	0.016	-0.507	0.553	0.106	0.224	0.157
Und. Mol.	-0.111	-0.037	-0.042	0.041	0.261	-0.422	-0.185	-0.432	-0.264	-0.061	0.164
Akk.	-0.126	-0.185	-0.122	0.380	0.400	-0.160	-1.212	1.389	-0.096	0.191	-0.379
Cop.	-0.071	0.000	0.080	-0.454	-0.503	0.169	-0.562	-4.350	-0.207	-0.223	0.443
Und. Ent.	-0.374	0.278	0.248	-0.168	0.084	0.033	-0.232	-0.395	-0.384	-0.038	0.314
Ent.	-0.042	-0.013	0.024	-0.117	-0.328	0.020	0.054	-2.096	0.023	-0.192	0.111
C. diff.	-0.037	-0.033	-0.049	-0.090	-0.102	0.032	-0.181	-0.303	-0.007	0.014	-0.055

Table 1

(top) Growth rates a_{ij} of each microbial population i of the CDI model. (bottom) Interactions between pairwise microbial populations of the CDI model. Both tables are excerpted from [25].

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