Almost Global Convergence in Singular Perturbations of Strongly Monotone Systems

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Abstract. This paper deals with global convergence to equilibria, and in particular Hirsch's generic convergence theorem for strongly monotone systems, for singular perturbations of monotone systems.

1 Introduction

This paper studies extensions, using geometric singular perturbation theory, of Hirsch's generic convergence theorem for monotone systems ([3, 4, 5, 10]). Informally stated, Hirsch's result says that almost every bounded solution of a strongly monotone system converges to the set of equilibria. There is a rich literature regarding the application of this powerful theorem, as well as of other results dealing with everywhere convergence when equilibria are unique ([10, 1, 6]), to models of biochemical systems. Unfortunately, many models in biology are not monotone. In order to address this drawback (as well as to study properties of large systems which are monotone but which are hard to analyze in their entirety), a recent line of work introduced an input/output approach that is based on the analysis of interconnections of monotone systems. For example, the approach allows one to view a *non*-monotone system as a "negative" feedback loop of monotone open-loop systems, thus leading to results on global stability and the emergence of oscillations under transmission delays, and to the construction of relaxation oscillators by slow adaptation rules on feedback gains. See [11, 12] for expositions and many references. The present paper is in the same character.

Our motivation arose from the observation that time-scale separation may also lead to monotonicity. This point of view is of special interest in the context of biochemical systems; for example, Michaelis Menten kinetics are mathematically justified as singularly perturbed versions of mass action kinetics. A system that is not monotone may become monotone once that fast variables are replaced by their steady-state values. A trivial linear example that illustrates this point is $\dot{x} = -x - y$, $\varepsilon\dot{y} = -y + x$, with $\varepsilon > 0$. This system

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is not monotone with respect to any orthant cone. On the other hand, for $\varepsilon \ll 1$, the fast variable y tracks x, so the slow dynamics is well-approximated by $\dot{x} = -2x$ (which is strongly monotone, because every scalar system is).

We consider systems $\dot{x} = f(x,y)$, $\varepsilon\dot{y} = g(x,y)$ for which the reduced system $\dot{x} = f(x,h(x))$ is strongly monotone (in fact, a slightly stronger technical condition on derivatives is assumed) and the fast system $\dot{y} = g(x,y)$ has a unique globally asymptotically stable steady state $y = h(x)$ for each x, and satisfies an input to state stability type of property with respect to x. One may expect that the original system inherits global (generic) convergence properties, at least for all $\varepsilon>0$ small enough, and this is indeed the object of our study. This question may be approached in several ways. One may view $y-h(x)$ as an input to the slow system, and appeal to the theory of asymptotically autonomous systems. Another approach, the one that we develop here, is through geometric invariant manifold theory ([2, 7, 9]). There is a manifold M_ε, invariant for the full dynamics, which attracts all near-enough solutions, with an asymptotic phase property. The system restricted to the invariant manifold M_ε is a regular perturbation of the fast (ε=0) system. As remarked in Theorem 1.2 in Hirsch's early paper [3], a C^1 regular perturbation of a flow with eventually positive derivatives also has generic convergence. So, solutions in the manifold will be generally well-behaved, and asymptotic phase implies that solutions track solutions in M_ε, and hence also converge to equilibria if solutions on M_ε do. A key technical detail is to establish that the tracking solutions also start from the "good" set of initial conditions, for generic solutions of the large system.

For simplicity, we discuss here only the case of cooperative systems (monotonicity with respect to the main orthant), but proofs in the case of general cones are similar and will be discussed in a paper under preparation.

2 Statement of Main Result

We are interested in systems in singularly perturbed form:

$$\frac{dx}{dt} = f(x,y), \quad \varepsilon\frac{dy}{dt} = g(x,y), \tag{1}$$

where $x \in \mathbb{R}^n$, $y \in \mathbb{R}^m$, $0 < \varepsilon \ll 1$, and f and g are smooth functions. We will present some preliminary results in general, but for our main theorem we will restrict attention to the case when g has the special form $g(x,y) = Ay + h(x)$, where A is a Hurwitz matrix (all eigenvalues have negative real part) and h is a smooth function. That is, we will specialize to systems of the form:

$$\frac{dx}{dt} = f(x,y), \quad \varepsilon\frac{dy}{dt} = Ay + h(x). \tag{2}$$

(We remark later how our results may be extended to a broader class of systems.) Setting ε to zero, we have:

$$\frac{dx}{dt} = f(x, m_0(x)), \tag{3}$$

where $m_0(x) = -A^{-1}h(x)$. As usual in singular perturbation theory, our goal is to use properties of the limiting system (3) in order to derive conclusions about the full system (2) when $0 < \varepsilon \ll 1$. It is helpful to consider the fast system ($\tau = \frac{t}{\varepsilon}$):

$$\frac{dx}{d\tau} = \varepsilon f(x, y), \quad \frac{dy}{d\tau} = Ay + h(x). \tag{4}$$

We will assume given three sets K, $\widetilde{K}$, and L which satisfy the following hypotheses (some technical terms are defined later):

H1 The set $\widetilde{K}$ is an n-dimensional C^∞ simply connected compact manifold with boundary.

H2 The set L is a bounded open subset of $\mathbb{R}^m$, and $M_0 = \{(x, y) \mid y = m_0(x),\ x \in \widetilde{K}\}$, the graph of m_0, is contained in $\widetilde{K} \times L$.

H3 The flow $\{\psi_t\}$ of (3) has eventually positive derivatives on $\widetilde{K}$.

H4 The set $\widetilde{K}$ is convex, and therefore it is p-convex too.

H5 For each $\varepsilon > 0$ sufficiently small, the forward trajectory under (2) of each point in $\widetilde{D} = \mathrm{Int}\widetilde{K} \times L$ is precompact in $\widetilde{D}$.

H6 The equilibrium set $E_0 = \{x \in \mathrm{Int}\widetilde{K} \mid f(x, m_0(x)) = 0\}$ is countable.

H7 The set $K \subset \mathrm{Int}\widetilde{K}$ is compact, and for each $\varepsilon > 0$ sufficiently small, the set $D = K \times L$ is positively invariant.

Note that the equilibria of (2) do not depend on ε, and the ones in $\widetilde{D}$ are in 1-1 correspondence with elements of E_0. The main theorem is:

Theorem 1. *Under assumptions* **H1-H7***, there exists $\varepsilon^* > 0$ such that for each $0 < \varepsilon < \varepsilon^*$, the forward trajectory of (2) starting from almost every point in D converges to some equilibrium.*

Remark: A variant of this result is to assume that the reduced system (3) has a unique equilibrium. In this case, one may improve the conclusions of the theorem to global (not just generic) convergence, by appealing to results of Hirsch and others that apply when equilibria are unique. The proof is simpler in that case, since the foliation structure given by Fenichel's theory (see below) is not required. In the opposite direction, one could drop the assumption of countability and instead provide theorems on generic convergence to the set of equilibria, or even to equilibria if hyperbolicity conditions are satisfied, in the spirit of what is done in the theory of strongly monotone systems.

3 Proof of the Main Theorem

Let us first define some technical terms for any differential equation $\frac{dz}{dt} = F(z)$. Its flow $\{\phi_t\}$ is said to have *eventually positive derivatives on a set* $V \subseteq \mathbb{R}^N$ if there exists t_0 such that $\frac{\partial \phi_t^i}{\partial z_j}(z) > 0$ for all $t \geq t_0$, $z \in V$. When the system is of dimension one, this holds automatically. In general, the following sufficient condition is easier to check. If for all $z \in V$, $\frac{\partial F_i}{\partial z_j}(z) \geq 0$, for all $i \neq j$, and the matrix $\frac{\partial F}{\partial z}(z)$ is irreducible, then $\{\phi_t\}$ has eventually positive derivatives. (This condition is not necessary.)

An open set $W \subseteq \mathbb{R}^N$ is called *p-convex*, if W contains the entire line segment joining x and y whenever $x, y \in V$ and $x \leq y$, where $x \leq y$ means $x_i \leq y_i$ for all $i = 1, \cdots, N$.

Recall the definition of $M_0 = \{(x, y) \mid \ y = m_0(x), x \in \widetilde{K}\}$. It is called *normally hyperbolic* relative to (4), provided all eigenvalues of the matrix A have nonzero real part. This is satisfied in our case as A is Hurwitz. Our proofs are based on Fenichel's theorems [2], in the forms presented and developed by Jones in [7].

Fenichel's First Theorem *Under assumption H1, if M_0 is normally hyperbolic relative to (4), then there exists $\varepsilon_0 > 0$, such that for every $0 < \varepsilon < \varepsilon_0$ and $r > 0$, there is a function $y = m_\varepsilon(x)$, defined on $\widetilde{K}$, of class C^r jointly in x and ε, such that $M_\varepsilon = \{(x, y) \mid y = m_\varepsilon(x),\ x \in \widetilde{K}\}$ is locally invariant under (2).*

We will pick a particular $r > 1$ in the above theorem from now on. Because of **H5**, in our case local invariance implies that $(x(t), y(t))$ satisfies $y(t) = m_\varepsilon(x(t))$ and

$$\frac{dx(t)}{dt} = f\big(x(t), m_\varepsilon(x(t))\big) \tag{5}$$

for all $t \geq 0$. Applying Theorem 1.2 of [4], one can prove

Lemma 1. *Under assumptions* **H1**-**H3***, for each $0 < \varepsilon < \varepsilon_0$, the flow $\{\psi_t\}$ of (5) has eventually positive derivatives on Int$\widetilde{K}$.*

Our assumptions allow us to apply Theorem 4.4 of [4] to obtain:

Lemma 2. *Under assumptions* **H1**-**H6***, for each $0 < \varepsilon < \varepsilon_0$, there exists a set $\mathcal{C}_\varepsilon \subseteq$ Int$\widetilde{K}$ such that the forward trajectory of (5) for every point of $\mathcal{C}_\varepsilon$ converges to some equilibrium, and the measure of Int$\widetilde{K} \setminus \mathcal{C}_\varepsilon$ is zero.*

See [13] for proofs of the above results. Until now, we have discussed the flow only when restricted to the locally invariant manifold M_ε. The next theorem, stated in the form given by [7], deals with more global behavior. In [7], the theorem is stated for $\varepsilon > 0$, but some properties also hold for $\varepsilon = 0$ ([8]). (We will apply this result again with a fixed $r > 1$.) The notation $[-\delta, \delta]$ stands for the cube $\{\ (y_1, \ldots, y_m) \mid\ -\delta \leq |y_i| \leq \delta\ \}$.

Fenichel's Third Theorem *Let ε_0 be as in Fenichel's First Theorem. Under assumption H1, if M_0 is normally hyperbolic relative to (4), then there exists $0 < \varepsilon_1 < \varepsilon_0$ and $\delta > 0$ such that for every $0 \leq \varepsilon < \varepsilon_1$ and $r > 0$, there is a function $h_\varepsilon : \widetilde{K} \times [-\delta, \delta] \to \mathbb{R}^n$ such that the following properties hold:*

1. *For each $x \in \widetilde{K}$, $h_\varepsilon(x, 0) = x$.*

2. *The image of the map* $T_\varepsilon : \widetilde{K} \times [-\delta, \delta] \to \mathbb{R}^n \times \mathbb{R}^m$*, sending* (x, λ) *to* $(h_\varepsilon(x, \lambda), \lambda + m_\varepsilon(h_\varepsilon(x, \lambda)))$*, is defined as the stable manifold* $W^s_\varepsilon(M_\varepsilon)$ *of* M_ε*. For* $p = (x, m_\varepsilon(x)) \in M_\varepsilon$*, the stable fibers* $W^s_\varepsilon(p)$*, defined as* $T_\varepsilon(\{x\} \times [-\delta, \delta])$*, form a "positively invariant" family when* $\varepsilon \neq 0$*, in the sense that* $W^s_\varepsilon(p) \cdot_{W^s_\varepsilon(M_\varepsilon)} t \subseteq W^s_\varepsilon(\phi_t(p))$*.*
3. *"Asymptotic Phase". There are positive constants* k *and* α *such that for any* $p, q \in \mathbb{R}^{n+m}$*, if* $q \in W^s_\varepsilon(p)$*,* $\varepsilon \neq 0$*, then* $|\phi_t(p) - \phi_t(q)| \leq ke^{-\alpha t}$ *for all* $t \geq 0$ *as long as* $\phi_t(p)$ *and* $\phi_t(q)$ *stay in* $W^s_\varepsilon(M_\varepsilon)$*.*
4. *The stable fibers are disjoint, i.e., for* $q_i \in W^s_\varepsilon(p_i)$*,* $i = 1, 2$*, either* $W^s_\varepsilon(p_1) \bigcap W^s_\varepsilon(p_2) = \emptyset$ *or* $W^s_\varepsilon(p_1) = W^s_\varepsilon(p_2)$*.*
5. *The function* $h_\varepsilon(x, \lambda)$ *is* C^r *jointly in* $(\varepsilon, x, \lambda)$*. When* $\varepsilon = 0$*,* $h_{0,\delta}(x, \lambda) = x$*.*

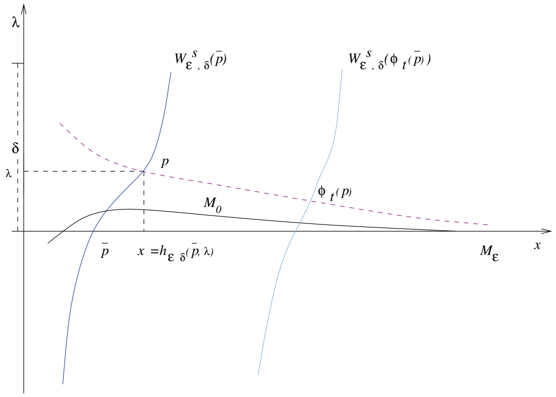

Fig. 1. Sketch of the locally invariant manifold and stable fibers of a system with $n = m = 1$. The critial manifold M_0 is the graph of $m_0(x) - m_\varepsilon(x)$ (black curve), and M_ε is the graph of $\lambda = 0$. They may intersect at some equilibrium points. Through each point $p \in M_\varepsilon$ (x-axis), there is a stable fiber $W^s_\varepsilon(p)$ (blue curve), which consists of the pairs $(h_\varepsilon(x, \lambda), \lambda)$ with $|\lambda| \leq \delta$. If a solution (purple dashed curve) starts on fiber $W^s_\varepsilon(p)$, after a small time t, it evolves to a point on another stable fiber $W^s_\varepsilon(\phi_t(p))$ (light blue curve); this is the "positive invariance" property.

The next lemma gives a sufficient condition to guarantee that a point is on some fiber.

Lemma 3. *Let* ε_1 *and* δ *be as in Fenichel's Third Theorem. There exists* $0 < \varepsilon_2 < \varepsilon_1$*, such that for every* $0 < \varepsilon < \varepsilon_2$*, the set* $\mathcal{A}_\delta := \{(x, y) \mid x \in K,\ |y - m_0(x)| \leq \frac{\delta}{2}\}$ *is a subset of* $W^s_\varepsilon(M_\varepsilon)$*.*

To prove this lemma, we need the following result:

Lemma 4. *Let* U *and* V *be compact, convex subsets of* $\mathbb{R}^n$ *and* $\mathbb{R}^m$ *respectively. Suppose given a continous function* $\phi :\ U \times V \to \mathbb{R}^n \times \mathbb{R}^m$*, it maps* (x, y)

to $(\phi_1(x,y),\phi_2(x,y))$, *and satisfies* $\|\phi_1(x,y)-x\| \le \rho_1$, $\|\phi_2(x,y)-y\| \le \rho_2$ *for some* $\rho_1 > 0$, $\rho_2 > 0$ *and all* $(x,y) \in U \times V$. *Then every point* $(\alpha,\beta) \in U \times V$ *with* $dist(\alpha,\partial U) \ge \rho_1$ *and* $dist(\beta,\partial V) \ge \rho_2$ *is in the image of* ϕ.

See [13] for proofs of Lemma 4 and Lemma 3. The next lemma describes the trajectory of an arbitrary initial point in D.

Lemma 5. *Let* ε_2 *be as in Lemma 3, and* δ *as in Fenichel's Third Theorem. Under assumption* **H7**, *there exists* $0 < \varepsilon_3 < \varepsilon_2$ *such that for each* $0 < \varepsilon < \varepsilon_3$, *if* $p \in D$, *then there exists* $T_0 \ge 0$, *and* $\phi_t(p) \in \mathcal{A}_\delta$ *for all* $t \ge T_0$.

Proof. Setting $z = y - m_0(x)$ (4) becomes

$$\frac{dx}{d\tau} = \varepsilon f(x, z + m_0(x)), \quad \frac{dz}{d\tau} = Az - \varepsilon m_0'(x) f(x, z + m_0(x)).$$

Using the variation of parameters formula for the z equation, together with the fact that A is Hurwitz, one can prove that $z(t)$ eventually becomes smaller than $\delta/2$ for τ large. Back to the slow time scale, there exists T_0 such that $|y - m_\varepsilon(x)| \le \delta$ for $t \ge T_0$, as wanted. □

Remark: Except for the normal hyperbolicity assumption, Lemma 5 is the only place where the special structure (2) was used. Consider a more general system as in (1), and assume that $g(x, m_0(x)) = 0$ on $\widetilde{K}$ for some smooth function m_0. By the same change of variables as in the above proof, (1) is equivalent to $\frac{dx}{d\tau} = \varepsilon f(x, z + m_0(x))$, $\frac{dz}{d\tau} = g(x, z + m_0(x)) - \varepsilon m_0'(x) f(x, z + m_0(x))$. The only property that we need in the lemma is that for any initial condition $(x(0), z(0))$, the solution $(x(t), z(t))$ satisfies $\limsup_{t\to\infty} |z(t)| \le \gamma\left(\limsup_{t\to\infty} d(t)\right)$ where γ is a function of class $\mathcal{K}$, that is to say, a continuous function $[0,\infty) \to [0,\infty)$ with $\gamma(0) = 0$, and $d(t) = \varepsilon m_0'(x(t)) f\big(x(t), z(t) + m_0(x(t))\big)$. In terms of the functions m_0 and g, we may introduce the control system $dz/dt = G(d(t), z) + u(t)$, where d is a compact-valued "disturbance" function and u is an input, and $G(d,z) = g(d, z + m_0(d))$. Then, the property of input-to-state stability with input u (uniformly on d), which can be characterized in several different manners, including by means of Lyapunov functions, provides the desired condition.

Lemma 5 proves that every trajectory in D is attracted to A_δ and therefore is also attracted to M_ε. This will lead to our proof of the main theorem.

Proof of the Main Theorem

Choose $\varepsilon^* = \varepsilon_3$, defined in Lemma 5. For any $p \in D$, there are three cases:

1. $p \in M_\varepsilon$. By Lemma 2, the forward trajectory converges to an equilibrium except for a set of measure zero.
2. $p \in \mathcal{A}_\delta \subset W^s_\varepsilon(M_\varepsilon)$. Then p is on some fiber, say $W^s_\varepsilon(\bar{p})$, where $\bar{p} = (\bar{x}, m_\varepsilon(\bar{x})) \in M_\varepsilon$. If $\bar{x}$ is in $\mathcal{C}_\varepsilon$ (defined in Lemma 2), then $\phi_t(\bar{p}) \to q$, for some $q \in E_0$. By the "asymptotic phase" property of Fenichel's Third

Theorem, $\phi_t(p)$ also converges to q. To deal with the case when $\bar{x} \notin \mathcal{C}_\varepsilon$, it is enough to show that the set $\mathcal{B}_\varepsilon = \bigcup_{\bar{x}\in \mathrm{Int}\widetilde{K}\setminus \mathcal{C}_\varepsilon} W^s_\varepsilon(\bar{p})$ as a subset of $\mathbb{R}^{m+n}$ has measure zero. Define $\mathcal{F}_\varepsilon = (\mathrm{Int}\widetilde{K} \setminus \mathcal{C}_\varepsilon) \times [-\delta, \delta]$. Since $\mathrm{Int}\widetilde{K} \setminus \mathcal{C}_\varepsilon$ has measure zero in $\mathbb{R}^n$, $\mathcal{F}_\varepsilon$ also has measure zero. On the other hand $T_\varepsilon(\mathcal{F}_\varepsilon) = \mathcal{B}_\varepsilon$, and Lipschitz maps send measure zero sets to measure zero sets, we are done.

3. $p \in D \setminus \mathcal{A}_\delta$. By Lemma 5, $\phi_t(p) \in \mathcal{A}_\delta$ for all $t \geq T_0$. Without loss of generality, we assume that T_0 is an integer. If $\phi_{T_0}(p) \in \mathcal{A}_\delta \setminus \mathcal{B}_\varepsilon$, then $\phi_t(p)$ converges to an equilibrium. Otherwise, $p \in \bigcup_{k\geq 0, k\in\mathbb{Z}} \phi_{-k}(\mathcal{B}_\varepsilon)$. Since the set $\mathcal{B}_\varepsilon$ has measure zero and ϕ_{-k} is Lipschitz, $\phi_{-k}(\mathcal{B}_\varepsilon)$ has measure zero for all k, and the countable union of them still has measure zero. □

4 An Example

Consider the following system:

$$\begin{aligned} \frac{dx_i}{dt} &= \gamma_i(y_1, \ldots, y_m) - \beta_i(x_1, \ldots, x_n), \quad i = 1, \ldots, n, \\ \varepsilon \frac{dy_j}{dt} &= -d_j y_j - \alpha_j(x_1, \ldots, x_n), \quad d_j > 0, \quad j = 1, \ldots, m, \end{aligned} \tag{6}$$

where α_j, β_i and γ_i are smooth functions. We assume that

1. When $n > 1$, for all $i, k = 1, \ldots, n$, $i \neq k$, and all $x \in \mathbb{R}^n$, the partial derivatives $\frac{\partial \beta_i}{\partial x_k}(x) < 0$ and $\sum_{l=1}^m \frac{\partial \gamma_i}{\partial y_l}(x)\frac{\partial \alpha_l}{\partial x_k}(x) \leq 0$.
2. The function β_i satisfies that that $\beta_i(x_1, \ldots, x_n) = +\infty$ as all $x_i \to +\infty$ and $\beta_i(x_1, \ldots, x_n) = -\infty$ as all $x_i \to -\infty$.
3. There exists a positive contant M_j such that $|\alpha_j(x)| \leq M_j$ for all $x \in \mathbb{R}^n$.
4. The number of roots of the system of equations $\gamma_i(\alpha_1(x), \ldots, \alpha_m(x)) = \beta_i(x), \quad i = 1, \ldots, m$, is countable.

The conditions are very natural. The condition on the β_i's is satisfied, for example, if there is a linear decay term $-x_i$ in the differential equation for x_i, and all other variables appear saturated in this rate, see an more interesting example in [13].

We are going to show that on any large enough region, and provided that ε is sufficiently small, almost every trajectory converges to an equilibrium. To emphasize the need for small ε, we also show that when $\varepsilon > 1$, a limit cycle could appear.

To apply our main theorem, we take $L = \{ y \in \mathbb{R}^m \mid |y_j| < b_j, \ j = 1, \ldots, m \}$, where b_j is an arbitrary positive number greater than $\frac{M_j}{d_j}$. Picking such b_j assures $y_j \frac{dy_j}{dt} < 0$ for all $x \in \mathbb{R}$ and $|y_j| = b_j$, i.e. the vector field points transverally inside on the boundary of L. Let $K = \{ x \in \mathbb{R}^n \mid -a_{i,2} \leq x_i \leq a_{i,1}, \ i = 1, \ldots, n \}$, where $a_{i,1}$ and $a_{i,2}$ can be any positive numbers such that $\beta_i(x) > N_i := \max_{|y_j|\leq b_j} |\gamma_i(y_1, \ldots, y_m)|$, whenever $x \in \mathbb{R}^n$ satisfies that its ith coordinate $x_i \geq a_{i,1}$; and $\beta_i(x) < -N_i$, whenever $x \in \mathbb{R}^n$ satisfies that its ith coordinate $x_i \leq -a_{i,2}$. All large enough $a_{i,j}$'s satisfy this condition, because of the assumption made on β. So, we have $x_i \frac{dx_i}{dt} < 0$ for all $y \in L$, $x_i = a_{i,1}$ and $x_i = -a_{i,2}$. We then take $\widetilde{K} = \{ x \in \mathbb{R}^n \mid -a_{i,2} - 1 \leq x_i \leq a_{i,1} + 1,\ i = 1, \ldots n \}$, $D = K \times L$ and $\widetilde{D} = \mathrm{Int}\widetilde{K} \times L$. Thus, the vector field will point into the interior of D and $\widetilde{D}$. Hypotheses **H5** and **H7** follow directly from this fact. It is easy to see the other hypotheses also hold. By our main theorem, for sufficiently small ε, the forward trajectory of (6) starting from almost every point in D converges to some equilibrium.

On the other hand, convergence does not hold for large ε. Let $n = 1,\ \beta_1(x_1) = \frac{x_1^3}{3} - x_1,\ m = 1,\ \alpha_1(x_1) = 4\tanh x_1,\ \gamma(y_1) = y_1,\ d_1 = 1$. It is easy to verify that $(0,0)$ is the only equilibrium. When $\varepsilon > 1$, the trace of the Jacobian at $(0,0)$ is $1 - \frac{1}{\varepsilon} > 0$, its determinant is $\frac{15}{\varepsilon} > 0$, so the (only) equilibrium in D is repelling. By the Poincaré-Bendixson Theorem, there exists a limit cycle in D.

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