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**On the evolutionary  $\Gamma$ -convergence of gradient systems  
modeling slow and fast chemical reactions**

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**Abstract.** We investigate the limit passage for a system of ordinary differential equations modeling slow and fast chemical reaction of mass-action type, where the rates of fast reactions tend to infinity. We give an elementary proof of convergence to a reduced dynamical system acting in the slow reaction directions on the manifold of fast reaction equilibria. Then we study the entropic gradient structure of these systems and prove an E-convergence result via  $\Gamma$ -convergence of the primary and dual dissipation potentials, which shows that this structure carries over to the fast reaction limit. We recover the limit dynamics as a gradient flow of the entropy with respect to a pseudo-metric.

## 1. INTRODUCTION

We consider reaction equations for the concentrations  $\mathbf{c}(t)$  of  $I$  chemical species in the state space  $\mathbf{X} := [0, \infty)^I$ , where the  $R$  reaction rates can be additively decomposed into a slow and a fast part, viz.

$$\dot{\mathbf{c}} = -\mathbf{R}_\varepsilon(\mathbf{c}) := -\sum_{r=1}^{R_s} k_r (\mathbf{c}^{\alpha_r} - \kappa_r \mathbf{c}^{\beta_r}) (\alpha_r - \beta_r) - \frac{1}{\varepsilon} \sum_{r=R_s+1}^R k_r (\mathbf{c}^{\alpha_r} - \kappa_r \mathbf{c}^{\beta_r}) (\alpha_r - \beta_r) \quad (1.1)$$

where  $k_r > 0$  and  $\kappa_r k_r > 0$  are the forward and backward reaction rates,  $\alpha_r \in \mathbb{N}_0^I$  and  $\beta_r \in \mathbb{N}_0^I$  are the stoichiometric coefficients (with monomial notation  $\mathbf{c}^\alpha = \prod_{i=1}^I c_i^{\alpha_i}$ ), and  $\varepsilon$  is the small parameter which describes the ratio between slow and fast time scales such that the limit  $\varepsilon \searrow 0$  corresponds to infinite reaction speed.

For the limit passage  $\varepsilon \searrow 0$  in (1.1), we show two types of results: the first one is the convergence of the solution curves to a curve satisfying a limit system of ODEs which can be either formulated in  $\mathbb{R}^R$ , including an algebraic constraint to the fast reaction equilibrium manifold, or, alternatively, as a reduced system of ODEs acting only in  $\mathbb{R}^{R_s}$ , the space of “slow” directions, with appropriately modified reaction rates. This limit passage has been widely investigated, as a particular instance of a *quasi-steady-state approximation* (QSSA) for reaction systems. We refer e.g. to [12, 3, 25, 24] and the references therein. We highlight the work of Bothe [4], in which a rigorous justification of a limit passage for (1.1) was previously shown. Our proof is based on Bothe’s techniques but performed in a simpler setting with respect to the “slow” dynamics, so that it becomes much more direct, not requiring higher-order estimates and providing a more explicit dimension reduction.

We perform the limit passage in the transformed variables of stoichiometric vector coordinates rather than concentrations, as a standard approach to QSSA, see Section 2.3. In a series of papers, a group of authors including Goeke, Noethen and Walcher [10, 20, 18, 19, 8, 9] studied QSSA for systems of this type with respect to its justification in a mathematical as well as modeling sense. In addition, they developed qualitative and quantitative tools for the identification of small parameters. Regarding mass-action kinetics, our result generalizes their approach in [10, 9] in that we do not require the linear stability analysis of the limit invariant manifold associated to the Tihonov-Fenichel theory [27]. Instead, we prove local Lipschitz continuity of the *equilibrium map*, which maps the initial data to the the unique equilibrium corresponding to the system of “fast” reactions, and directly perform the singular limit via time-rescaling. In this way, no assumptions in addition to reversibility and the linear independence of the stoichiometric vectors are required.

Our second result concerns the stability of the entropic gradient structure of (1.1) with respect to the limit passage, cf. also [? ]. Following the framework in [14, 15], we say that (1.1) has a gradient structure, if there exists a triple  $(\mathbf{X}, \mathcal{E}, \Psi_\varepsilon)$ , where  $\mathcal{E} : \mathbf{X} \rightarrow \mathbb{R}_\infty$  denotes the relative entropy of the system and  $\Psi_\varepsilon$  is the corresponding *dissipation potential*, such that (1.1) can be written equivalently in the form  $D\mathcal{E}(\mathbf{c}) + D_\varepsilon \Psi_\varepsilon(\mathbf{c}, \dot{\mathbf{c}}) = 0$ . It is shown in [15] that solutions  $\mathbf{c}_\varepsilon$  of (1.1) can in this case be characterized by the *upper energy dissipation*

estimate

$$\mathcal{E}(\mathbf{c}(T)) + \int_0^T \left\{ \Psi_\varepsilon(\mathbf{c}, \dot{\mathbf{c}}) + \Psi_\varepsilon^*(\mathbf{c}, -D\mathcal{E}(\mathbf{c})) \right\} dt \leq \mathcal{E}(\mathbf{c}(0)), \quad (\mathbf{UEDE})$$

where  $\Psi^*(\mathbf{c}, \cdot)$  denotes the Legendre dual of  $\Psi(\mathbf{c}, \cdot)$ . For details, we refer to Subsection 2.2 and Section 4. A crucial point of this characterization is that **(UEDE)** is a scalar inequality, written solely in terms of functionals. Hence, it is possible to apply variational methods such as  $\Gamma$ -convergence. We prove an *evolutionary  $\Gamma$ -convergence* (E-convergence) result in the spirit of the survey [17], showing that a limit triple  $(\mathbf{X}, \mathcal{E}, \Psi_0)$  exists and that the limit curve satisfies the corresponding **(UEDE)**. In our case, the limit dissipation potential  $\Psi_0$  provides a pseudo-metric on  $\mathbf{X}$  only, thus enforcing the equilibrium constraint for the fast reaction. An important feature of our approach is that the limit passage does not require estimates in addition to **(UEDE)**. Our interpretation is that E-convergence provides a natural approach to the quasi-steady state approximation, ensuring thermodynamic consistency of the limiting process. For related works in this direction, we refer to [11, 12].

We note that in contrast to [11], we do not require the (geodesic) convexity of the entropy as a Lyapunov functional for system (1.1), which is in general unknown [14]. This lack of convexity also excludes the use of known stability results for metric gradient flows as in [7]. Our approach provides a new thermodynamically consistent perspective on QSSA in the case of reversible reactions. Our motivation is that it may in the future be helpful for parameter identification and consistent modeling of coupled systems. From an abstract point of view, the result highlights the robustness and flexibility of the notion of E-convergence for a large and natural class of entropic gradient structures, even without the assumption of convexity.

**Outline.** In the next section, we collect preliminary results on reaction systems of type (1.1), including a precise definition of the entropic gradient structure, the change of variables from concentrations to stoichiometric vector coordinates, a priori estimates which hold uniformly in  $\varepsilon > 0$  and properties of the data-to-equilibrium map. In Section 3, we prove the first convergence result as a limit passage in terms of the equations. In Section 4, we introduce the notions associated to the E-convergence of gradient structures and then prove the limit passage for the entropic gradient structure of (1.1) in this sense.

## 2. ASSUMPTIONS AND PRELIMINARY RESULTS ON REACTION KINETICS SATISFYING DETAILED BALANCE

We are interested in the evolution of a system of  $I \in \mathbb{N}$  species undergoing  $R \in \mathbb{N}$  simultaneous reactions of mass-action type. Denoting by  $\mathbf{c}(t) \in [0, \infty)^I =: \mathbf{X}$  the vector of concentrations at time  $t$ , the evolution of the system is given by the ODE system (1.1). It is well-known that for any fixed  $\varepsilon > 0$  the system in (1.1) is globally solvable and solutions converge to an equilibrium as  $t \rightarrow \infty$ , see Theorem 2.1 below.

**2.1. Slow and fast reaction kinetics.** We consider reaction systems with slow and fast reactions, i.e., let  $R_s \in \mathbb{N}$  and  $R_f \in \mathbb{N}$  denote the number of slow and fast reactions, respectively, with  $R := R_s + R_f$ .

We make the following general assumptions:

- (R1)  $R \leq I$  and the vectors  $\boldsymbol{\gamma}_1, \dots, \boldsymbol{\gamma}_R$  are linearly independent.
- (R2) The relative reaction rate constants  $\kappa_r$ ,  $r = 1, \dots, R$ , are independent of  $\varepsilon$ .
- (R3) The absolute reaction rate constants for slow reactions  $k_{r,\varepsilon}^s$ ,  $r = 1, \dots, R_s$  do not depend on  $\varepsilon$ . The absolute reaction rate constants for the fast reactions satisfy  $k_{r,\varepsilon}^f = \frac{1}{\varepsilon} \tilde{k}_r^f$  for  $r = 1, \dots, R_f$ , with  $\tilde{k}_r^f$  independent of  $\varepsilon$ .

We denote by  $\overset{\circ}{\mathbf{X}}$  the interior of the non-negative cone  $\mathbf{X}$ . For a given  $\varepsilon > 0$  and an initial datum  $\mathbf{c}_\varepsilon^0 \in \overset{\circ}{\mathbf{X}}$ , the equations for  $\mathbf{c}_\varepsilon$  read

$$\dot{\mathbf{c}}_\varepsilon = - \sum_{r=1}^{R_S} k_r^S (\mathbf{c}_\varepsilon^{\alpha_r} - \kappa_r \mathbf{c}_\varepsilon^{\beta_r}) \boldsymbol{\gamma}_r - \frac{1}{\varepsilon} \sum_{r=R_S+1}^R \tilde{k}_r^f (\mathbf{c}_\varepsilon^{\alpha_r} - \kappa_r \mathbf{c}_\varepsilon^{\beta_r}) \boldsymbol{\gamma}_r, \quad \mathbf{c}_\varepsilon(0) = \mathbf{c}_\varepsilon^0. \quad (2.1)$$

In the following, we will sometimes write

$$\mathbf{C}_r(\mathbf{c}) := \mathbf{c}^{\alpha_r} - \kappa_r \mathbf{c}^{\beta_r} \quad (2.2)$$

for the state-dependent part of the  $r$ -th reaction rate in (2.1).

Any solution of (1.1) stays in the stoichiometric class  $\mathbf{c}_\varepsilon^0 + \mathbf{S}$ , where  $\mathbf{S} := \text{span}\{\boldsymbol{\gamma}_1, \dots, \boldsymbol{\gamma}_R\}$  is the *stoichiometric subspace*. The orthogonal complement  $\mathbf{S}^\perp$  gives the invariants of the evolution: For each  $\boldsymbol{\zeta} \in \mathbf{S}^\perp$ , one has that  $\boldsymbol{\zeta} \cdot \mathbf{c}(t) = \boldsymbol{\zeta} \cdot \mathbf{c}_\varepsilon^0$  for all  $t > 0$ .

The condition of *detailed balance* for a reaction system means that there exists a positive steady state  $\mathbf{c}_* = (c_i^*)_{i=1, \dots, I}$  such that all reactions are in equilibrium. It is a classical result that system (2.1) satisfies this condition, i.e. there exists  $\mathbf{c}_* > 0$  such that

$$\mathbf{C}_r(\mathbf{c}_*) = 0 \Leftrightarrow \mathbf{c}_*^{\alpha_r - \beta_r} = \kappa_r, \quad \text{for all } r = 1, \dots, R. \quad (2.3)$$

Note that the existence and value of  $\mathbf{c}_*$  is independent of  $\varepsilon > 0$ . We say that a steady state  $\mathbf{c}_{\text{eq}}$  corresponds to the initial datum  $\mathbf{c}^0$  if

$$\boldsymbol{\gamma}_r^c \cdot \mathbf{c}_{\text{eq}} = \boldsymbol{\gamma}_r^c \cdot \mathbf{c}^0 \quad \text{for all } r = 1, \dots, R_c,$$

where  $\boldsymbol{\gamma}_r^c$  is a basis of the orthogonal complement  $\mathbf{S}^\perp$ , the dimension of which is  $R_c = I - R$ .

We summarize the above properties of (2.1) in a theorem and refer to [5, 13] and in particular to [4, Thm. 1].

**Theorem 2.1** (Dynamics of (2.1)). *Let  $\varepsilon > 0$  be fixed, but arbitrary. The following statements hold:*

- (a) *For each initial value  $\mathbf{c}^0 \in \overset{\circ}{\mathbf{X}}$ , there exists a unique steady state  $\mathbf{c}_{\text{eq}} \in (\mathbf{c}^0 + \mathbf{S}) \cap \overset{\circ}{\mathbf{X}}$  of the dynamical system induced by (2.1) corresponding to  $\mathbf{c}^0$ . Moreover,  $\mathbf{c}_{\text{eq}}$  is uniquely determined, independently of the absolute reaction rate constants  $k_r$ .*
- (b) *The solution  $\mathbf{c}_\varepsilon \in C^\infty([0, \infty); \mathbb{R}^I)$  to the initial-value problem (2.1) exists globally in time, it is unique and it satisfies  $\mathbf{c}_\varepsilon(t) \in \overset{\circ}{\mathbf{X}}$  for all  $t \geq 0$ .*

**2.2. Entropic gradient structure of the system.** It was shown in [15] (see also [16]) that systems of the form (2.1) have an entropic *gradient structure* in the following sense. Given a positive steady state  $\mathbf{c}_*$  of (2.1) with detailed balance (2.3), we define the *relative entropy*  $\mathcal{E} : \mathbf{X} \rightarrow \mathbb{R}$  with respect to  $\mathbf{c}_*$  and the Onsager matrices  $\mathbb{K}_\varepsilon(\mathbf{c}) \in \mathbb{R}_{\text{spssd}}^{I \times I}$  (symmetric and positive semidefinite), cf. [21, Eqn. (1.11)] or [22, Eqs. (2-1)–(2-4)], by

$$\mathcal{E}(\mathbf{c}) := \mathcal{H}(\mathbf{c} | \mathbf{c}_*) := \sum_{i=1}^I c_i^* E(c_i / c_i^*), \quad \text{with } E(z) = \begin{cases} z \log z - z + 1 & \text{if } z > 0, \\ 1 & \text{if } z = 0, \end{cases}$$

$$\mathbb{K}_\varepsilon(\mathbf{c}) := \sum_{r=1}^R k_{r,\varepsilon} \Lambda(\mathbf{c}^{\alpha_r}, \kappa_r \mathbf{c}^{\beta_r}) (\boldsymbol{\alpha}_r - \boldsymbol{\beta}_r) \otimes (\boldsymbol{\alpha}_r - \boldsymbol{\beta}_r)$$

with the (nonnegative) *logarithmic mean*

$$\Lambda(a, b) := \begin{cases} 0 & \text{if } a = 0 \text{ or } b = 0, \\ \frac{a-b}{\log b - \log a} & \text{if } a, b > 0, a \neq b, \\ a & \text{if } a = b > 0, \end{cases}$$

and  $\boldsymbol{\gamma} \otimes \boldsymbol{\gamma} \in \mathbb{R}^{I \times I}$  denoting the tensor product, i.e.,  $(\boldsymbol{\gamma} \otimes \boldsymbol{\gamma})_{ij} = \gamma_i \gamma_j$ . Note that  $\mathbb{K}_\varepsilon(\mathbf{c})$  depends on  $\varepsilon > 0$  but not on  $\mathbf{c}_*$ .

Using the detailed-balance condition on  $\mathbf{c}_*$  and the calculation rules for the logarithm, we immediately verify

$$\dot{\mathbf{c}} = -\mathbf{R}_\varepsilon(\mathbf{c}) \iff \dot{\mathbf{c}} = -\mathbb{K}_\varepsilon(\mathbf{c})\mathcal{D}\mathcal{E}(\mathbf{c}). \quad (2.4)$$

Associated with the Onsager operator family  $\mathbb{K}_\varepsilon$ , we define the dual dissipation potentials  $\Psi_\varepsilon^* : \mathbf{X} \times \mathbb{R}^I \rightarrow [0, \infty]$  via

$$\Psi_\varepsilon^*(\mathbf{c}, \boldsymbol{\xi}) = \frac{1}{2} \boldsymbol{\xi} \cdot \mathbb{K}_\varepsilon(\mathbf{c}) \boldsymbol{\xi} = \frac{1}{2} \sum_{r=1}^R k_{r,\varepsilon} \Lambda(\mathbf{c}^{\alpha_r}, \kappa_r \mathbf{c}^{\beta_r}) (\boldsymbol{\xi} \cdot (\boldsymbol{\alpha}_r - \boldsymbol{\beta}_r))^2.$$

Moreover, we introduce the (primal) *dissipation potentials*  $\Psi_\varepsilon : \mathbf{X} \times \mathbb{R}^I \rightarrow [0, \infty]$  as Legendre duals of  $\Psi_\varepsilon^*$  at  $\mathbf{c} \in \mathbf{X}$ , i.e.

$$\Psi_\varepsilon(\mathbf{c}, \mathbf{v}) := \sup_{\boldsymbol{\xi} \in \mathbb{R}^I} \{ \langle \boldsymbol{\xi}, \mathbf{v} \rangle - \Psi_\varepsilon^*(\mathbf{c}, \boldsymbol{\xi}) \}.$$

One of the features of this structure is that by means of the *Young-Fenchel estimate* [6],

$$\Psi_\varepsilon(\mathbf{c}, \mathbf{v}) + \Psi_\varepsilon^*(\mathbf{c}, \boldsymbol{\xi}) \geq \langle \boldsymbol{\xi}, \mathbf{v} \rangle, \quad (2.5)$$

and the chain rule  $\frac{d}{dt}\mathcal{E}(\mathbf{c}) = \langle \mathcal{D}\mathcal{E}(\mathbf{c}), \dot{\mathbf{c}} \rangle$ , it follows that the scalar *energy dissipation balance*

$$\mathcal{E}(\mathbf{c}(T)) + \int_0^T \left\{ \Psi_\varepsilon(\mathbf{c}, \dot{\mathbf{c}}) + \Psi_\varepsilon^*(\mathbf{c}, -\mathcal{D}\mathcal{E}(\mathbf{c})) \right\} dt = \mathcal{E}(\mathbf{c}(0)). \quad (\mathbf{EDB})$$

is an equivalent formulation to the rate equation (2.1). The same argument shows that actually, the equality in **(EDB)** can be replaced by the *upper energy dissipation estimate*

$$\mathcal{E}(\mathbf{c}(T)) + \int_0^T \left\{ \Psi_\varepsilon(\mathbf{c}, \dot{\mathbf{c}}) + \Psi_\varepsilon^*(\mathbf{c}, -\mathcal{D}\mathcal{E}(\mathbf{c})) \right\} dt \leq \mathcal{E}(\mathbf{c}(0)). \quad (\mathbf{UEDE})$$

We further discuss this structure in Section 4 and show it is preserved in the limit, in a suitably generalized sense.

**2.3. Transformation of the system.** An alternative formulation of (2.1) is obtained by a linear change of coordinates in the concentrations  $\mathbf{c}$  to a basis provided by the stoichiometric vectors. Here, for simplicity, we choose an orthonormal basis  $(\boldsymbol{\gamma}_1^c, \dots, \boldsymbol{\gamma}_{R_c}^c)$  of the orthogonal complement  $\mathbf{S}^\perp$  of the stoichiometric subspace. Correspondingly, we write  $\boldsymbol{\gamma}_r^f$ ,  $r = 1, \dots, R_f$ , to indicate the  $r$ -th reaction vector corresponding to a fast reaction and  $\boldsymbol{\gamma}_r^s$ ,  $r = 1, \dots, R_s$ , for the  $r$ -th reaction vector corresponding to a slow reaction. We set

$$\mathbb{T} = (\boldsymbol{\gamma}_1^f, \dots, \boldsymbol{\gamma}_{R_f}^f, \boldsymbol{\gamma}_1^s, \dots, \boldsymbol{\gamma}_{R_s}^s, \boldsymbol{\gamma}_1^c, \dots, \boldsymbol{\gamma}_{R_c}^c) \in \mathbb{R}^{I \times I}$$

the transposed of the extended stoichiometric matrix, which is invertible due to (R1) and introduce the transformed variable  $\mathbf{g} := \mathbb{T}^{-1}\mathbf{c}$ . In the following, we consider the vector  $\mathbf{g} \in \mathbb{R}^I$  as a triple with the three components  $\mathbf{g}^f \in \mathbb{R}^{R_f}$  for the fast,  $\mathbf{g}^s \in \mathbb{R}^{R_s}$  for the slow, and  $\mathbf{g}^c \in \mathbb{R}^{R_c}$  for conserved quantities. More generally, the superscripts ‘‘s’’, ‘‘f’’ and ‘‘c’’ indicate the truncation of a vector in  $\mathbb{R}^I$  to these components. Clearly, the curve  $t \mapsto \mathbf{c}_\varepsilon(t)$  solves (2.1) with  $\mathbf{c}_\varepsilon(0) = \mathbf{c}_\varepsilon^0$ , if and only if the transformed solution  $\mathbf{g}_\varepsilon = \mathbb{T}^{-1}\mathbf{c}_\varepsilon$  satisfies

$$\dot{\mathbf{g}}_{\varepsilon,r} = \begin{cases} -k_{r,\varepsilon} C_r(\mathbb{T}\mathbf{g}_\varepsilon) & \text{for } r = 1, \dots, R, \\ 0 & \text{otherwise,} \end{cases} \quad \mathbf{g}_\varepsilon(0) = \mathbf{g}_\varepsilon^0 := \mathbb{T}^{-1}\mathbf{c}_\varepsilon^0, \quad (2.6)$$

where  $C_r$  is defined as in (2.2).

**2.4. Transformed gradient structure.** The gradient structure for (2.1) introduced in Subsection 2.2 is inherited by the system in (2.6). We set

$$\tilde{\mathbf{X}} = \mathbb{T}^{-1}\mathbf{X} \quad \text{and} \quad \tilde{\mathcal{E}}(\mathbf{g}) = \mathcal{E}(\mathbb{T}\mathbf{g}),$$

and write  $\tilde{\dot{\mathbf{X}}} = \mathbb{T}^{-1}\dot{\mathbf{X}}$ . It follows that  $D_{\mathbf{g}}\tilde{\mathcal{E}}(\mathbf{g}) = \mathbb{T}^{\top}D_{\mathbf{c}}\mathcal{E}(\mathbf{c}) = \mathbb{T}^{\top}\log(\frac{\mathbf{c}}{\mathbf{c}_*})$ . Note that  $\mathcal{E}$  depends implicitly on  $\varepsilon$  if  $\mathbf{c}_*$  depends on  $\varepsilon$ . However, by (R2) the steady state  $\mathbf{c}_*$  can be assumed to be independent of  $\varepsilon$ .

Using the gradient system for the untransformed system, the equations for  $\mathbf{g}_{\varepsilon}$  can be written in the form

$$\dot{\mathbf{g}}_{\varepsilon} = \mathbb{T}^{-1}\dot{\mathbf{c}}_{\varepsilon} = -\mathbb{T}^{-1}\mathbb{K}_{\varepsilon}(\mathbf{c}_{\varepsilon})\mathbb{T}^{-\top}D_{\mathbf{g}}\tilde{\mathcal{E}}(\mathbf{g}_{\varepsilon}). \quad (2.7)$$

Hence, defining the Onsager matrix  $\tilde{\mathbb{K}}_{\varepsilon}(\mathbf{g}_{\varepsilon}) := \mathbb{T}^{-1}\mathbb{K}_{\varepsilon}(\mathbb{T}\mathbf{g}_{\varepsilon})\mathbb{T}^{-\top} \in \mathbb{R}_{\text{spsd}}^{I \times I}$  gives the gradient system  $(\tilde{\mathbf{X}}, \tilde{\mathcal{E}}, \tilde{\Psi}_{\varepsilon}^*)$  for the transformed equation (2.6), where  $\tilde{\Psi}_{\varepsilon}^*$  is the family of quadratic forms associated with  $\tilde{\mathbb{K}}_{\varepsilon}$ . In particular,  $\tilde{\mathbb{K}}_{\varepsilon}(\mathbf{g})$  takes on diagonal form,

$$\tilde{\mathbb{K}}_{\varepsilon}(\mathbf{g}) = \sum_{r=1}^R k_{r,\varepsilon} \tilde{\Lambda}_r(\mathbf{g}) \mathbf{e}_r \otimes \mathbf{e}_r = \text{diag}(k_{r,\varepsilon} \tilde{\Lambda}_r(\mathbf{g}))_{r=1,\dots,R},$$

where  $\mathbf{e}_r \in \mathbb{R}^I$  denotes for all  $r \in R$  the  $r$ -th unit vector and

$$\tilde{\Lambda}_r(\mathbf{g}) := \Lambda(\mathbf{c}^{\alpha_r}, \kappa_r \mathbf{c}^{\beta_r}) \quad \text{for } \mathbf{c} = \mathbb{T}\mathbf{g}. \quad (2.8)$$

Following Subsection 2.2, we obtain that for every  $\varepsilon > 0$  the system (2.7) is equivalent to

$$\tilde{\mathcal{E}}(\mathbf{g}_{\varepsilon}(t)) + \int_s^t \tilde{\Psi}_{\varepsilon}(\mathbf{g}_{\varepsilon}, \dot{\mathbf{g}}_{\varepsilon}) + \tilde{\Psi}_{\varepsilon}^*(\mathbf{g}_{\varepsilon}, -\mathbb{T}^{\top} \log(\frac{\mathbb{T}\mathbf{g}_{\varepsilon}}{\mathbf{c}_*})) \, dr = \tilde{\mathcal{E}}(\mathbf{g}_{\varepsilon}(s)), \quad (\mathbf{EDB}_{\varepsilon})$$

for every  $0 \leq s < t < \infty$ .

Note that the dual dissipation potentials  $\Psi_{\varepsilon}^* : \tilde{\mathbf{X}} \times \mathbb{R}^I \rightarrow [0, \infty]$  can be additively decomposed into

$$\tilde{\Psi}_{\varepsilon}^*(\mathbf{g}, \boldsymbol{\xi}) = \tilde{\Psi}_{\varepsilon}^{s,*}(\mathbf{g}, \boldsymbol{\xi}^s) + \tilde{\Psi}_{\varepsilon}^{f,*}(\mathbf{g}, \boldsymbol{\xi}^f) + \tilde{\Psi}_{\varepsilon}^{c,*}(\mathbf{g}, \boldsymbol{\xi}^c), \quad \text{where}$$

$$\tilde{\Psi}_{\varepsilon}^{s,*}(\mathbf{g}, \boldsymbol{\xi}^s) = \frac{1}{2} \sum_{r=1}^{R_s} k_r \tilde{\Lambda}_r(\mathbf{g}) (\xi_r^s)^2, \quad \tilde{\Psi}_{\varepsilon}^{f,*}(\mathbf{g}, \boldsymbol{\xi}^f) = \frac{1}{2\varepsilon} \sum_{r=1}^{R_f} k_r \tilde{\Lambda}_r(\mathbf{g}) (\xi_r^f)^2, \quad \text{and } \tilde{\Psi}_{\varepsilon}^{c,*}(\mathbf{g}, \boldsymbol{\xi}^c) \equiv 0.$$

Correspondingly, the primal dissipation potentials  $\tilde{\Psi}_{\varepsilon} : \tilde{\mathbf{X}} \times \mathbb{R}^I \rightarrow [0, \infty]$  are given by

$$\tilde{\Psi}_{\varepsilon}(\mathbf{g}, \mathbf{v}) = \tilde{\Psi}_{\varepsilon}^s(\mathbf{g}, \mathbf{v}^s) + \tilde{\Psi}_{\varepsilon}^f(\mathbf{g}, \mathbf{v}^f) + \tilde{\Psi}_{\varepsilon}^c(\mathbf{g}, \mathbf{v}^c), \quad \text{where}$$

$$\tilde{\Psi}_{\varepsilon}^s(\mathbf{g}, \mathbf{v}^s) = \sum_{r=1}^{R_s} \frac{(v_r^s)^2}{2k_r \tilde{\Lambda}_r(\mathbf{g})}, \quad \tilde{\Psi}_{\varepsilon}^f(\mathbf{g}, \mathbf{v}^f) = \varepsilon \sum_{r=1}^{R_f} \frac{(v_r^f)^2}{2k_r \tilde{\Lambda}_r(\mathbf{g})}, \quad \text{and } \tilde{\Psi}_{\varepsilon}^c(\mathbf{g}, \mathbf{v}^c) = \begin{cases} 0 & \text{if } \mathbf{v}^c = 0, \\ \infty & \text{otherwise.} \end{cases}$$

Note that  $\tilde{\Psi}_{\varepsilon}^{s,*}$ ,  $\tilde{\Psi}_{\varepsilon}^{f,*}$  and  $\tilde{\Psi}_{\varepsilon}^{c,*}$  are, for fixed  $\mathbf{g}$ , the Legendre transforms of  $\tilde{\Psi}_{\varepsilon}^s$ ,  $\tilde{\Psi}_{\varepsilon}^f$  and  $\tilde{\Psi}_{\varepsilon}^c$  on the smaller spaces  $\mathbb{R}^{R_s}$ ,  $\mathbb{R}^{R_f}$  and  $\mathbb{R}^{R_c}$ , respectively, whereas  $\tilde{\Psi}_{\varepsilon}^*(\mathbf{g}, \cdot)$  is the Legendre transform of  $\tilde{\Psi}_{\varepsilon}(\mathbf{g}, \cdot)$  on  $\mathbb{R}^I$ . This splitting is possible due to the diagonal structure of the transformed Onsager operator  $\tilde{\mathbb{K}}_{\varepsilon}(\mathbf{g})$ .

**2.5. Uniform estimates based on (EDB<sub>ε</sub>).** Based on the energy-dissipation balance, we obtain a priori estimates. By Theorem 2.1, we can choose  $\mathbf{c}_*$  independently of  $\varepsilon > 0$  such that  $\mathcal{E}$  in (EDB<sub>ε</sub>) does not depend on  $\varepsilon$  either; this provides several  $\varepsilon$ -uniform estimates.

We make the following two assumptions on the initial data  $\mathbf{c}_{\varepsilon}^0$ , stated in terms of  $\mathbf{g}_{\varepsilon}^0$  and  $\mathcal{E}$ , for the remainder of the paper:

(I1) The limits  $\mathbf{g}_0^s = \lim_{\varepsilon \rightarrow 0} (\mathbf{g}_{\varepsilon}^0)^s$  and  $\mathbf{g}_0^c = \lim_{\varepsilon \rightarrow 0} (\mathbf{g}_{\varepsilon}^0)^c$  exist.

(I2) There is a constant  $E_0 > 0$ , such that

$$\sup_{\varepsilon > 0} \tilde{\mathcal{E}}(\mathbf{g}_\varepsilon^0) = \sup_{\varepsilon > 0} \mathcal{E}(\mathbf{c}_\varepsilon^0) = E_0 < \infty.$$

Under these assumptions, we immediately obtain the following.

**Lemma 2.2.** *Let  $(\mathbf{g}_\varepsilon)_{\varepsilon > 0}$  be a family of solutions of  $(\mathbf{EDB}_\varepsilon)$ . The following statements are true:*

(a) *There exists a constant  $C(E_0) > 0$  such that*

$$\sup_{\varepsilon > 0, t \in [0, \infty)} |\mathbf{g}_\varepsilon(t)| \leq C(E_0). \quad (2.9)$$

(b) *There exists a constant  $K_0 > 0$  such that*

$$\sup_{\varepsilon > 0} \|\dot{\mathbf{g}}_\varepsilon^s\|_{L^2(0, \infty)} \leq K_0 E_0. \quad (2.10)$$

(c) *The relative entropy  $\tilde{\mathcal{E}}$  is a strict Lyapunov functional for (2.6). In particular, we have  $\lim_{t \rightarrow \infty} \mathbf{g}_\varepsilon(t) = \mathbf{g}_{\text{eq}, \varepsilon}$  with  $\mathbf{g}_{\text{eq}, \varepsilon} = \mathbb{T}^{-1} \mathbf{c}_{\text{eq}}$  denoting the transformed equilibrium, given by Theorem 2.1.*

*Proof.* Note that for these properties to hold, it is sufficient to replace  $(\mathbf{EDB}_\varepsilon)$  by an upper estimate of type  $(\mathbf{UEDE})$ .

(a) For the proof of (2.9), we combine  $(\mathbf{EDB}_\varepsilon)$  with the elementary estimate

$$E(s) \geq (\sqrt{s} - 1)^2 \quad (s \geq 0)$$

to obtain for all  $t > 0$ :

$$\sup_{\varepsilon > 0} \sum_{i=1}^I \left( \sqrt{c_{\varepsilon, i}(t)} - \sqrt{c_i^*} \right)^2 \leq \sup_{\varepsilon > 0} \mathcal{E}(\mathbf{c}_\varepsilon(t)) \leq \sup_{\varepsilon > 0} \mathcal{E}(\mathbf{c}_\varepsilon^0).$$

The estimate (2.9) follows by Assumption (I2).

(b) Note that by (2.9), there is a constant  $K_0 > 0$  such that

$$\sup_{\varepsilon > 0, t \in [0, \infty)} \tilde{\Lambda}_r(\mathbf{g}_\varepsilon(t)) \leq K_0, \quad \text{for all } r = 1, \dots, R,$$

with  $\tilde{\Lambda}_r$  as in (2.8). By  $(\mathbf{EDB}_\varepsilon)$  with  $s = 0$  and letting  $t \rightarrow +\infty$ , we have

$$\sup_{\varepsilon > 0} \int_0^\infty \Psi_\varepsilon^s(\mathbf{g}_\varepsilon, \dot{\mathbf{g}}_\varepsilon) dt = \sup_{\varepsilon > 0} \int_0^\infty \sum_{r=1}^{R_s} \frac{(\dot{g}_\varepsilon^s(t))^2}{\tilde{\Lambda}_r(\mathbf{g}_\varepsilon(t))} dt \leq E_0$$

and thus (2.10) holds.

(c) The strict Lyapunov property follows from  $(\mathbf{EDB}_\varepsilon)$ , using again that  $\tilde{\Lambda}_r^{-1}$ , ( $r = 1, \dots, R_s$ ) are bounded away from 0 by (2.9). Moreover, by (2.9), orbits are relatively compact, so the convergence to equilibrium follows by LaSalle's Invariance Principle, cf. e.g. also [4]. □

**2.6. The equilibrium map.** In the following lemma, we show elementary properties of the equilibrium map  $\mathbf{eq} : \mathring{\mathbf{X}} \rightarrow \mathring{\mathbf{X}}$ , which maps an initial value of concentrations  $\mathbf{c}^0 > 0$  for (2.1) to the unique corresponding equilibrium  $\mathbf{c}_{\text{eq}} > 0$ . Note that the result is independent of the particular structure and scaling of (2.1), but holds for all systems of reaction kinetics with detailed balance. In particular, we will use the result with respect to the system (3.1) of fast reactions only. Note also that parts of this lemma are well-known and ideas for the proof or similar statements can e.g. be found in [4]. We restate and reprove them to match this setting.

**Lemma 2.3.** *The equilibrium map  $\mathbf{eq} : \mathring{\mathbf{X}} \rightarrow \mathring{\mathbf{X}}$  is locally Lipschitz continuous on  $\mathring{\mathbf{X}}$  and  $\mathbf{eq}(\mathbf{c}^0)$  is uniquely determined by the conserved quantities  $(\mathbf{g}^0)_i^c = \gamma_i^c \cdot \mathbf{c}^0$  only.*

*Proof.* First, note that for  $\mathbf{c}_*$  being a positive steady state of (2.1) and  $\boldsymbol{\eta}_* := \mathbf{log} \mathbf{c}_*$  it follows from (2.3) that

$$\boldsymbol{\gamma}^r \cdot \boldsymbol{\eta} = \log \kappa_r, \quad \text{for all } r = 1, \dots, R. \quad (2.11)$$

Conversely, for every  $\hat{\boldsymbol{\eta}}_* \in \mathbb{R}^I$  satisfying (2.11),  $\hat{\mathbf{c}}_* := \mathbf{e}^{\hat{\boldsymbol{\eta}}_*}$  is a positive steady state of (2.1).

Let  $\mathbf{c}_{\text{eq}}$  and  $\hat{\mathbf{c}}_{\text{eq}}$  be the two equilibrium states of (2.1) corresponding to the initial data  $\mathbf{c}^0 = \mathbb{T}\mathbf{g}^0$  and  $\hat{\mathbf{c}}^0 = \mathbb{T}\hat{\mathbf{g}}^0$ , respectively. Then by (2.11), the corresponding  $\boldsymbol{\eta} = \mathbf{log} \mathbf{c}_{\text{eq}}$  and  $\hat{\boldsymbol{\eta}} = \mathbf{log} \hat{\mathbf{c}}_{\text{eq}}$  satisfy

$$\boldsymbol{\gamma}^r \cdot (\boldsymbol{\eta} - \hat{\boldsymbol{\eta}}) = 0, \quad \text{for all } r = 1, \dots, R,$$

i.e.  $\boldsymbol{\eta} - \hat{\boldsymbol{\eta}} \in \mathbf{S}^\perp$ . Since  $\mathbf{c}_{\text{eq}} - \mathbf{c}^0 \in \mathbf{S}$  and  $\hat{\mathbf{c}}_{\text{eq}} - \hat{\mathbf{c}}^0 \in \mathbf{S}$ , it follows that

$$\begin{aligned} (\mathbf{c}_{\text{eq}} - \hat{\mathbf{c}}_{\text{eq}}) \cdot (\boldsymbol{\eta} - \hat{\boldsymbol{\eta}}) &= (\mathbf{c}^0 - \hat{\mathbf{c}}^0) \cdot (\boldsymbol{\eta} - \hat{\boldsymbol{\eta}}) = (\mathbb{T}(\mathbf{g}^0 - \hat{\mathbf{g}}^0)) \cdot (\boldsymbol{\eta} - \hat{\boldsymbol{\eta}}) \\ &= \sum_{r=1}^{R_c} (g_r^0 - \hat{g}_r^0) (\boldsymbol{\gamma}_r^c \cdot (\boldsymbol{\eta} - \hat{\boldsymbol{\eta}})), \end{aligned} \quad (2.12)$$

where the last identity is due to the orthogonality  $\boldsymbol{\gamma}_r^s \perp \boldsymbol{\eta} - \hat{\boldsymbol{\eta}}$  and  $\boldsymbol{\gamma}_r^f \perp \boldsymbol{\eta} - \hat{\boldsymbol{\eta}}$ . For  $0 < a < b < +\infty$ , let

$$\mathbf{X}_a^b = \{\mathbf{c} \in \mathbf{X} : a < c_i < b \text{ for all } i = 1, \dots, I\} \subset \mathring{\mathbf{X}}.$$

We first show that for all  $\mathbf{c}^0 \in \mathbf{X}_a^b$ , there are constants  $0 < A < B < +\infty$  such that  $\mathbf{c}_{\text{eq}} = \mathbf{eq}(\mathbf{c}^0) \in \mathbf{X}_A^B$ . The upper bound  $B$  follows immediately from Lemma 2.2. To prove the lower bound, consider the initial value  $\mathbf{a} = (a, \dots, a)$  and the positive equilibrium  $\mathbf{c}_{\text{eq}}^a = \mathbf{eq}(\mathbf{a})$ . Then by (2.12), we have

$$0 < \mathcal{H}(\mathbf{c}_{\text{eq}} | \mathbf{c}_{\text{eq}}^a) + \mathcal{H}(\mathbf{c}_{\text{eq}}^a | \mathbf{c}_{\text{eq}}) = (\mathbf{c}_{\text{eq}} - \mathbf{c}_{\text{eq}}^a) \cdot (\boldsymbol{\eta} - \boldsymbol{\eta}^a) = (\mathbf{c}^0 - \mathbf{a}) \cdot (\boldsymbol{\eta} - \boldsymbol{\eta}^a),$$

so  $(\mathbf{c}^0 - \mathbf{a}) \cdot \log \mathbf{c}_{\text{eq}}^a \leq (\mathbf{c}^0 - \mathbf{a}) \cdot \log \mathbf{c}_{\text{eq}}$ . Since  $\max_i c_{\text{eq},i} \leq B$  and  $\mathbf{c}_{\text{eq}}^a$  is bounded from below, it follows that  $\mathbf{c}_{\text{eq}}$  is also bounded from below.

To prove Lipschitz continuity, let again  $\mathbf{c}_{\text{eq}}$  and  $\hat{\mathbf{c}}_{\text{eq}}$  be two equilibrium states in  $\mathbf{X}_A^B$  corresponding to the initial data  $\mathbf{c}^0$  and  $\hat{\mathbf{c}}^0$  in  $\mathbf{X}_a^b$ . Then the logarithmic means  $\Lambda_i = \Lambda(c_{\text{eq},i}, \hat{c}_{\text{eq},i})$  satisfy  $\Lambda_i \in \mathbf{X}_A^B$  for all  $i = 1, \dots, I$ . By (2.12), it follows that

$$\begin{aligned} |\mathbf{c}_{\text{eq}} - \hat{\mathbf{c}}_{\text{eq}}|^2 &\leq B \sum_{i=1}^I \frac{(c_{\text{eq},i} - \hat{c}_{\text{eq},i})^2}{\Lambda_i} = B(\mathbf{c}^0 - \hat{\mathbf{c}}^0) \cdot (\mathbf{log} \mathbf{c}_{\text{eq}} - \mathbf{log} \hat{\mathbf{c}}_{\text{eq}}) \\ &\leq B|\mathbb{T}| |(\mathbf{g}^0)^c - (\hat{\mathbf{g}}^0)^c| |\mathbf{log} \mathbf{c}_{\text{eq}} - \mathbf{log} \hat{\mathbf{c}}_{\text{eq}}| \leq C |(\mathbf{g}^0)^c - (\hat{\mathbf{g}}^0)^c| |\mathbf{c}_{\text{eq}} - \hat{\mathbf{c}}_{\text{eq}}|, \end{aligned}$$

where the constant  $C = C(A, B, \mathbb{T}) > 0$  includes the Lipschitz constant of the logarithm on  $\mathbf{X}_A^B$ .  $\square$

**Remark 2.4.** *Note that existence and Lipschitz continuity of the equilibrium map on compact subsets  $\mathbf{X}_a^b$  of the non-negative cone  $\mathbf{X}$  can also be argued as follows: The equilibrium is the unique minimizer of the relative entropy  $\mathcal{E}$  under the linear constraint  $\mathbf{g}^c = \text{const.}$ , and  $\mathcal{E}$  is strictly convex and analytic on  $\mathbf{X}_a^b$ .*

### 3. CONVERGENCE TO A SYSTEM OF ODES ON THE MANIFOLD OF FAST EQUILIBRIA

The aim of this section is to prove the convergence of solutions  $\mathbf{g}_\varepsilon$  of (2.6) to solutions of a suitable limit system. In terms of the concentrations  $\mathbf{c}$ , we recover the result of [4] under slightly less restrictive conditions on reaction terms and slightly more restrictive conditions on the slow dynamics. In particular, our proof is very simple and short and does not require higher-order estimates. In terms of  $\mathbf{g}$ , we uncover two corresponding formulations of the

limit problem, either as a mixed full system of ODEs and algebraic constraints (3.3), or as a system of ODEs in fewer variables (3.2).

Let  $t \mapsto \mathbf{h}(t) = (\mathbf{h}^f(t), \mathbf{h}^s(t), \mathbf{h}^c(t))$  be a solution of the transformed system of fast reactions only, namely

$$\dot{\mathbf{h}}_r^f(\tau) = -k_r^f \mathbf{C}_r^f(\mathbb{T}\mathbf{h}(\tau)), \quad \text{for all } r = 1, \dots, R_f, \quad \dot{\mathbf{h}}^s = \dot{\mathbf{h}}^c = 0, \quad \mathbf{h}(0) = \mathbf{h}_0, \quad (3.1)$$

and denote by  $\mathbf{h}_{\text{eq}}$  the unique positive equilibrium of this system corresponding to  $\mathbf{h}_0$ . Arguing as in Lemma 2.3, we see that  $\mathbf{h}_{\text{eq}}$  actually only depends on the conserved components  $(\mathbf{h}_0^s, \mathbf{h}_0^c)$ , but not on  $\mathbf{h}_0^f$ . In the following we will write this dependence in the form  $\mathbf{h}_{\text{eq}} = \mathbf{h}_{\text{eq}}[\mathbf{h}_0^s, \mathbf{h}_0^c]$ . In a first step, we prove convergence of solutions using Lemmas 2.2 and 2.3 and a time-rescaling argument.

**Lemma 3.1.** *For every  $t_0 \geq 0$ , we have*

$$\lim_{\varepsilon \rightarrow 0} \mathbf{g}_\varepsilon^f(t_0) = (\mathbf{h}_{\text{eq}}[\mathbf{g}^s(t_0), \mathbf{g}^c(t_0)])^f.$$

*In particular, there is a time  $t^+ > 0$ , such that the limit curve*

$$\lim_{\varepsilon \rightarrow 0} \mathbf{g}_\varepsilon =: \mathbf{g} = (\mathbf{g}^f, \mathbf{g}^s, \mathbf{g}^c) \in C([0, t^+], \overset{\circ}{\mathbf{X}})$$

*with*

$$\lim_{t \searrow 0} \mathbf{g}(t) = \mathbf{g}_0 := (\mathbf{h}_{\text{eq}}^f[\mathbf{g}_0^s, \mathbf{g}_0^c], \mathbf{g}_0^s, \mathbf{g}_0^c) = \mathbf{h}_{\text{eq}}[\mathbf{g}_0^s, \mathbf{g}_0^c]$$

*is continuous and remains in the transformed positive cone.*

*Proof.* By (2.9), for every  $t_0 \geq 0$ , we can choose a convergent subsequence of  $\mathbf{g}_\varepsilon(t_0)$  labeled by  $\varepsilon^j(t_0)$  with  $\varepsilon^j(t_0) \rightarrow 0$  as  $j \rightarrow \infty$  and limit  $\mathbf{g}(t_0) = \lim_{j \rightarrow \infty} \mathbf{g}_{\varepsilon^j(t_0)}(t_0)$ . We use this limit value in the following and show a posteriori that it does not depend on the choice of subsequence  $\varepsilon^j(t_0)$ . Starting from  $t_0$ , we rescale time by  $\varepsilon^j(t_0)$  and define  $\tau = \frac{t}{\varepsilon^j(t_0)}$  and  $\mathbf{h}_{\varepsilon^j(t_0)}(\tau) = \mathbf{g}_{\varepsilon^j(t_0)}(t_0 + \varepsilon^j(t_0)\tau)$ . Then,  $\tau \mapsto \mathbf{h}_{\varepsilon^j(t_0)}(\tau)$  satisfies

$$\begin{aligned} \dot{\mathbf{h}}_{\varepsilon^j(t_0)}^f &= -k^f \mathbf{C}^f(\mathbb{T}\mathbf{h}_{\varepsilon^j(t_0)}), \\ \dot{\mathbf{h}}_{\varepsilon^j(t_0)}^s &= -\varepsilon k^s \mathbf{C}^s(\mathbb{T}\mathbf{h}_{\varepsilon^j(t_0)}), \\ \dot{\mathbf{h}}_{\varepsilon^j(t_0)}^c &= 0 \end{aligned}$$

with initial condition  $\mathbf{h}_{\varepsilon^j(t_0)}(0) = \mathbf{g}_{\varepsilon^j(t_0)}$ .

We first show that as  $j \rightarrow \infty$ , the solution  $\mathbf{h}_{\varepsilon^j(t_0)}$  converges to the solution  $\mathbf{h}$  of (3.1) with  $\mathbf{h}_0 = \mathbf{g}(t_0)$ . Clearly, we have that

$$\mathbf{h}_{\varepsilon^j(t_0)}^c(\tau) - \mathbf{h}^c(\tau) = \mathbf{h}_{\varepsilon^j(t_0)}^c(0) - \mathbf{h}^c(0).$$

Using the uniform bound (2.9) for  $\mathbf{h}_{\varepsilon^j(t_0)}$ , we obtain

$$|\dot{\mathbf{h}}_{\varepsilon^j(t_0)}^s(\tau) - \dot{\mathbf{h}}^s(\tau)| \leq \varepsilon^j(t_0) |k^s \mathbf{C}^s(\mathbb{T}\mathbf{h}_{\varepsilon^j(t_0)}(\tau))| \leq \varepsilon^j(t_0) K_1$$

for some  $K_1 > 0$ . Moreover, using that  $\mathbf{g} \mapsto \mathbf{C}^f(\mathbb{T}\mathbf{g})$  is continuous on the compact set  $|\mathbf{g}| \leq C(E_0)$  with  $C(E_0)$  from Lemma 2.2, we obtain

$$\begin{aligned} &|\dot{\mathbf{h}}_{\varepsilon^j(t_0)}^f(\tau) - \dot{\mathbf{h}}^f(\tau)| \\ &\leq k^f L \left\{ |\mathbf{h}_{\varepsilon^j(t_0)}^f(\tau) - \mathbf{h}^f(\tau)| + \varepsilon^j(t_0) K_1 \tau + |\mathbf{h}_{\varepsilon^j(t_0)}^s(0) - \mathbf{h}^s(0)| + |\mathbf{h}_{\varepsilon^j(t_0)}^c(0) - \mathbf{h}^c(0)| \right\}. \end{aligned}$$

By Gronwall's inequality,

$$|\mathbf{h}_{\varepsilon^j(t_0)}^f(\tau) - \mathbf{h}^f(\tau)| \leq (C|\mathbf{h}_{\varepsilon^j(t_0)}(0) - \mathbf{h}(0)| + \varepsilon^j(t_0) K_1 \tau) e^{k^f L \tau},$$

with a constant  $C = C(L, K_1, k^f) > 0$ . Let now  $\delta > 0$ . By Lemma 2.2, we can choose  $T_\delta > 0$  such that for all  $\tau \geq T_\delta$ ,

$$|\mathbf{h}(\tau) - \mathbf{h}_{\text{eq}}| \leq \frac{\delta}{2}.$$

Choose  $j(\delta)$  sufficiently large to achieve

$$(C|\mathbf{h}_{\varepsilon^j(t_0)}(0) - \mathbf{h}(0)| + \varepsilon^j(t_0)LK_1\tau)e^{k^f L\tau} < \frac{\delta}{2}$$

for all  $\tau \leq 2T_\delta$ . Then, it follows that

$$|\mathbf{g}_{\varepsilon^j(t_0)}^f(t_0+t) - \mathbf{h}_{\text{eq}}^f| = |\mathbf{h}_{\varepsilon^j(t_0)}^f(\tau) - \mathbf{h}_{\text{eq}}^f| \leq |\mathbf{h}_{\varepsilon^j(t_0)}^f(\tau) - \mathbf{h}^f(\tau)| + |\mathbf{h}^f(\tau) - \mathbf{h}_{\text{eq}}^f| \leq \delta,$$

for all  $T_\delta \leq \tau \leq 2T_\delta$ , i.e. for all  $\varepsilon^j(t_0)T_\delta \leq t \leq 2\varepsilon^j(t_0)T_\delta$ . We conclude by Theorem 2.1 that regardless of the choice of subsequence  $\varepsilon^j(t_0)$ ,  $\lim_{j \rightarrow \infty} \mathbf{g}_{\varepsilon^j(t_0)}^f(t_0) = \mathbf{h}_{\text{eq}}^f$ , as  $\mathbf{h}_{\text{eq}}^f$  depends on  $\mathbf{g}^s(t_0)$  and  $\mathbf{g}^c(t_0)$  but not on  $\mathbf{g}^f(t_0)$ .

It remains to show that  $\mathbf{g}$  is continuous and contained in the transformed positive cone up to some  $t^+ > 0$ . By Theorem 2.1,  $\mathbf{g}_0 \in \tilde{\mathbf{X}}_a^b := \mathbb{T}^{-1}\mathbf{X}_a^b$  for some  $0 < a < b < +\infty$ . By continuity of  $\mathbf{g}^s$  and  $\mathbf{g}^c$  ( $\mathbf{g}^c$  is constant), there exists a  $t^+ > 0$  such that  $\tilde{\mathbf{g}}(t) = (\mathbf{g}_0^f, \mathbf{g}^s(t), \mathbf{g}^c(t)) \in \tilde{\mathbf{X}}_{a/2}^{2b}$  for all  $0 \leq t \leq t^+$ . By Lemma 2.3, there are  $0 < A < B < +\infty$  such that  $\mathbf{g} = \mathbf{h}_{\text{eq}} \circ \tilde{\mathbf{g}} \in C([0, t^+], \tilde{\mathbf{X}}_A^B)$ .  $\square$

It remains to characterize the system which is solved by the limit curve  $\mathbf{g}$ . The main result of this section is the following.

**Theorem 3.2.** *The limit curve  $t \mapsto \mathbf{g}(t) = \mathbf{h}_{\text{eq}}[\mathbf{g}^s(t), \mathbf{g}^c(t)]$  obtained in Lemma 3.1 is uniquely determined by the reduced system of  $R_s$  ODEs*

$$\begin{aligned} \dot{\mathbf{g}}^s(t) &= -k^s \mathbf{C}^s(\mathbb{T}\mathbf{h}_{\text{eq}}[\mathbf{g}^s(t), \mathbf{g}_0^c]), & t \in (0, \infty), \\ \mathbf{g}^s(0) &= \mathbf{g}_0^s. \end{aligned} \tag{3.2}$$

*Proof.* The theorem follows straightforwardly from Lemma 3.1. We first show that for  $t \in (0, \infty)$ ,  $\mathbf{g}$  satisfies the mixed system of ODEs and constraints given by

$$\begin{aligned} \dot{\mathbf{g}}^s(t) &= -k^s \mathbf{C}^s(\mathbb{T}\mathbf{g}(t)), & t \in (0, \infty), \\ \mathbf{C}^f(\mathbb{T}\mathbf{g}(t)) &= 0, & t \in (0, \infty), \\ \mathbf{g}(0) &= \mathbf{g}_0. \end{aligned} \tag{3.3}$$

Validity of the second set of equations in (3.3) follows from Lemma 3.1. To verify the first set of equations, note that by Lemma 2.2, possibly after choosing a subsequence, we have  $\dot{\mathbf{g}}_\varepsilon^s \rightharpoonup \dot{\mathbf{g}}^s$  weakly in  $L^2([0, T])$  for every  $T \geq 0$ . In addition,  $\dot{\mathbf{g}}_\varepsilon^s(t) = -k^s \mathbf{C}^s(\mathbb{T}\mathbf{g}_\varepsilon(t))$  with an  $\varepsilon$ -uniform  $L^\infty$ -bound on the right-hand-side, so

$$\mathbf{g}^s(T) - \mathbf{g}^s(0) = \lim_{\varepsilon \rightarrow 0} \int_0^T -k^s \mathbf{C}^s(\mathbb{T}\mathbf{g}_\varepsilon(t)) dt = \int_0^T -k^s \mathbf{C}^s(\mathbb{T}\mathbf{g}(t)) dt,$$

by dominated convergence. In particular,  $\mathbf{g}^s$  is locally absolutely continuous and the first set of equations holds. Again by Lemma 3.1, (3.2) characterizes  $\mathbf{g}$ .  $\square$

**Remark 3.3.** *The merit of system (3.2) depends on the equilibrium map  $\mathbf{h}_{\text{eq}}$  being explicit. It can e.g. be calculated from the Wegscheider conditions combining the  $R_f$  conditions in (2.11) and the  $I - R_f$  conditions in  $\mathbf{c}_{\text{eq}} \in \mathbf{c}^0 + \mathbf{S}_f$ , where  $\mathbf{S}_f$  is the stoichiometric subspace corresponding to fast reactions only, or as the unique minimizer of the (convex) entropy  $\mathcal{E}$  constrained to  $\mathbf{c}_{\text{eq}} \in \mathbf{c}^0 + \mathbf{S}_f$ . Note that regardless of the choice of representation for the limit system, in order to obtain its initial value, the equilibrium map needs to be calculated in at least this instance. We provide a simple example in the next subsection.*

**3.1. Example.** As a simple but illustrative example, we consider the following reaction system for three different species consisting of one slow and one fast reaction, namely



Thus, the stoichiometric vectors are given by  $\boldsymbol{\alpha}^s = (0, 0, 3)^\top$ ,  $\boldsymbol{\beta}^s = (1, 0, 0)^\top$  and  $\boldsymbol{\alpha}^f = (1, 1, 0)^\top$ ,  $\boldsymbol{\beta}^f = (0, 0, 1)^\top$ . In particular, the evolution equations for the concentrations  $\mathbf{c} = (c_1, c_2, c_3)$  read

$$\dot{\mathbf{c}} = -k^s (c_3^3 - \kappa^s c_1) (\boldsymbol{\alpha}^s - \boldsymbol{\beta}^s) - \frac{k^f}{\varepsilon} (c_1 c_2 - \kappa^f c_3) (\boldsymbol{\alpha}^f - \boldsymbol{\beta}^f), \quad (3.4)$$

and their solutions are plotted against the limit concentrations in Figure 3.1.

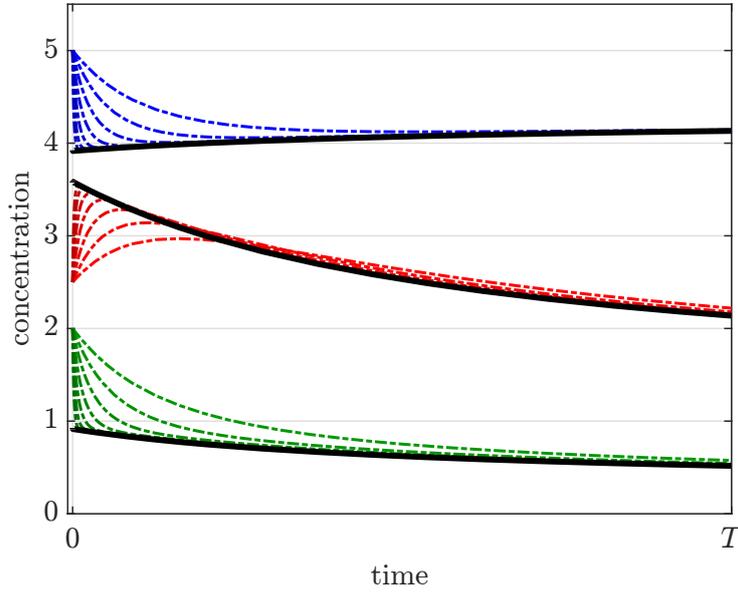


FIGURE 1. Solutions  $\mathbf{c}$  of example system (3.4) for different values of  $\varepsilon$  (dash-dotted) and limit solution (solid).

The transformed quantities  $\mathbf{g} = (\mathbf{g}^s, \mathbf{g}^f, \mathbf{g}^c)$  are three scalars related to the concentrations  $\mathbf{c}$  via  $\mathbf{c} = \mathbb{T}\mathbf{g}$ , where the matrix  $\mathbb{T}$  and its inverse are

$$\mathbb{T} = \begin{pmatrix} -1 & 1 & 3/\sqrt{14} \\ 0 & 1 & -2/\sqrt{14} \\ 3 & -1 & 1/\sqrt{14} \end{pmatrix}, \quad \mathbb{T}^{-1} = \frac{1}{14} \begin{pmatrix} 1 & 4 & 5 \\ 6 & 10 & 2 \\ 3\sqrt{14} & -2\sqrt{14} & \sqrt{14} \end{pmatrix}.$$

For every  $\varepsilon > 0$ ,  $\mathbf{g}_\varepsilon = \mathbb{T}^{-1}\mathbf{c}_\varepsilon$  solves

$$\begin{aligned} \dot{\mathbf{g}}^s &= -k^s \left[ \left( 3\mathbf{g}^s - \mathbf{g}^f + \frac{1}{\sqrt{14}}\mathbf{g}^c \right)^3 - \kappa^s \left( -\mathbf{g}^s + \mathbf{g}^f + \frac{3}{\sqrt{14}}\mathbf{g}^c \right) \right], \\ \dot{\mathbf{g}}^f &= -\frac{1}{\varepsilon} k^f \left[ \left( -\mathbf{g}^s + \mathbf{g}^f + \frac{3}{\sqrt{14}}\mathbf{g}^c \right) \left( \mathbf{g}^f - \frac{2}{\sqrt{14}}\mathbf{g}^c \right) - \kappa^f \left( 3\mathbf{g}^s - \mathbf{g}^f + \frac{1}{\sqrt{14}}\mathbf{g}^c \right) \right], \\ \mathbf{g}^c &= \mu = \text{const.} \end{aligned}$$

Given a fixed  $\mu$ , we calculate the equilibrium map  $\mathbf{eq}_\mu : \mathbf{g}^s \mapsto \mathbf{c}_{\text{eq}}$  with respect to the fast reaction. The three Wegscheider conditions are

$$\begin{aligned} c_{\text{eq},1}c_{\text{eq},2} &= \kappa^f c_{\text{eq},3}, \\ \mu &= \mathbf{g}^c = \sqrt{14}(3c_{\text{eq},1} - 2c_{\text{eq},2} + c_{\text{eq},3}), \\ \mathbf{g}^s &= \frac{1}{14}(c_{\text{eq},1} + 4c_{\text{eq},2} + 5c_{\text{eq},3}). \end{aligned}$$

We solve explicitly to obtain the equilibrium map

$$\begin{aligned} c_{\text{eq},1} &= \frac{1}{2} \left( \psi_{\mu,\kappa^f}(\mathbf{g}^s) - \kappa^f + \frac{5}{\sqrt{14}}\mu - \mathbf{g}^s \right), \\ c_{\text{eq},2} &= \frac{1}{2} \left( \psi_{\mu,\kappa^f}(\mathbf{g}^s) - \kappa^f - \frac{5}{\sqrt{14}}\mu - \mathbf{g}^s \right), \\ c_{\text{eq},3} &= \frac{1}{2} \left( \kappa^f + \frac{3}{\sqrt{14}}\mu + 5\mathbf{g}^s - \psi_{\mu,\kappa^f}(\mathbf{g}^s) \right), \end{aligned}$$

where

$$\psi_{\mu,\kappa^f}(\mathbf{g}^s) = \sqrt{(\kappa^f)^2 + \left( \frac{5}{\sqrt{14}}\mu - \mathbf{g}^s \right)^2 + 2\kappa^f \left( \frac{3}{\sqrt{14}}\mu + 5\mathbf{g}^s \right)}.$$

By Theorem 3.2, the limit dynamics are determined by the well-posed scalar ODE

$$\dot{\mathbf{g}}^s = -k^s \left[ \frac{1}{8} \left( \kappa^f + \frac{3}{\sqrt{14}}\mu + 5\mathbf{g}^s - \psi_{\mu,\kappa^f}(\mathbf{g}^s) \right)^3 - \kappa^s \frac{1}{2} \left( \psi_{\mu,\kappa^f}(\mathbf{g}^s) - \kappa^f + \frac{5}{\sqrt{14}}\mu - \mathbf{g}^s \right) \right].$$

#### 4. E-CONVERGENCE OF THE ENTROPIC GRADIENT STRUCTURE

The aim of this section is to study the limit  $\varepsilon \searrow 0$  for (2.1) in terms of its gradient structure. This will provide a stronger result than Theorem 3.2, in the sense that the limit equations (3.2) receive an additional structure. Moreover, this may be considered a natural approach to the quasi-steady state approximation, as it ensures thermodynamic consistency of the limiting process.

As in Subsection 2.2, we consider a triple  $(\mathbf{X}, \mathcal{E}, \Psi)$ , where  $\mathbf{X}$  is a (suitable) state space,  $\mathcal{E} : \mathbf{X} \rightarrow \mathbb{R}_\infty$  is a driving functional, i.e. an entropy or energy functional, and  $\Psi$  is a suitable *dissipation potential*. The metric gradient flow, cf. e.g. [1], for this structure is given by curves  $u : t \mapsto u(t) \in \mathbf{X}$  which satisfy the upper energy dissipation estimate

$$\mathcal{E}(u(T)) + \int_0^T \left\{ \Psi(u, \dot{u}) + \Psi^*(u, -D\mathcal{E}(u)) \right\} dt \leq \mathcal{E}(u(0)), \quad (\text{UEDE})$$

where  $\Psi(u, \dot{u})$  provides the metric derivative of  $u$  and  $\Psi^*(u, -D\mathcal{E}(u))$  gives the metric slope of the entropy along  $u$ . We show that the limit problem (3.2) still provides an upper energy dissipation estimate, but the limit dissipation functional  $\tilde{\Psi}$  provides only a pseudo-metric on  $\tilde{\mathbf{X}}$ . This structure enforces the equilibrium constraint for the fast reactions.

**4.1. Definition of E-convergence.** Following the notions in the survey [17], we consider families  $(\mathbf{X}, \mathcal{E}_\varepsilon, \Psi_\varepsilon)_{\varepsilon>0}$  depending on a small parameter  $\varepsilon$ . The aim is then to find limits  $\mathcal{E}_0$  and  $\Psi_0$  such that a limit  $u$  of the solutions  $u_\varepsilon$  is a solution for the limit problem given by  $\mathcal{E}_0$  and  $\Psi_0$ . A first systematic study of evolutionary  $\Gamma$ -convergence (or E-convergence) relying on gradient structures was initiated in [23], see also [26]. Here, we prove an E-convergence result based on Theorem 3.2 and the  $\Gamma$ -convergence of the dual and primal dissipation functionals  $\tilde{\Psi}_\varepsilon^*$  and  $\tilde{\Psi}_\varepsilon$ . We recall the definition of (static)  $\Gamma$ -convergence of functionals.

**Definition 4.1** (Gamma- and Mosco convergence). *Let  $(\Phi_\varepsilon)_{\varepsilon>0}$  be a family of functionals  $\Phi_\varepsilon : \mathbf{Y} \rightarrow \mathbb{R}_\infty$ , where  $\mathbf{Y}$  is a Banach space, and let  $\Phi : \mathbf{Y} \rightarrow \mathbb{R}_\infty$ .*

(a)  $(\Phi_\varepsilon)_\varepsilon$  is said to  $\Gamma$ -converge to  $\Phi$  with respect to the strong (weak) convergence in  $\mathbf{Y}$  (write  $\Phi_\varepsilon \xrightarrow{\Gamma} \Phi$  and  $\Phi_\varepsilon \xrightarrow{\Gamma} \Phi$ , respectively) as  $\varepsilon \searrow 0$ , if the following conditions are satisfied:

(i) (Liminf estimate) If  $u_\varepsilon \rightarrow u$  ( $u_\varepsilon \rightharpoonup u$ ), then  $\liminf_{\varepsilon \searrow 0} \Phi_\varepsilon(u_\varepsilon) \geq \Phi(u)$ .

(ii) (Recovery sequences) For all  $u \in \mathbf{Y}$ , there exists a sequence  $(\hat{u}_\varepsilon)_\varepsilon$  with  $\hat{u}_\varepsilon \rightarrow u$  ( $\hat{u}_\varepsilon \rightharpoonup u$ ) and  $\limsup_{\varepsilon \searrow 0} \Phi_\varepsilon(\hat{u}_\varepsilon) \leq \Phi(u)$ .

(b)  $(\Phi_\varepsilon)_\varepsilon$  is said to converge in the sense of Mosco to  $\Phi$  as  $\varepsilon \searrow 0$  (write  $\Phi_\varepsilon \xrightarrow{M} \Phi$ ), if both  $\Phi_\varepsilon \xrightarrow{\Gamma} \Phi$  and  $\Phi_\varepsilon \xrightarrow{\Gamma} \Phi$ .

In our situation,  $\mathbf{Y} = \mathbb{R}^I$  is always finite-dimensional, so Gamma- and Mosco convergence are equivalent.

On grounds of these notions for variational convergence of static functionals, a notion of evolutionary convergence for generalized gradient systems was built (cf. [17, Ch. 2]). We slightly adapt this notion to our setting, as the limit passage creates a boundary layer at time  $t = 0$ , cf. Section 4.3.

**Definition 4.2** (Evolutionary  $\Gamma$ -convergence). *Let a family  $(\mathbf{X}, \mathcal{E}_\varepsilon, \Psi_\varepsilon)_{\varepsilon > 0}$  be given and let  $T > 0$ . We say that  $(\mathbf{X}, \mathcal{E}_\varepsilon, \Psi_\varepsilon)_{\varepsilon > 0}$  (strongly) E-converges to a limit triple  $(\mathbf{X}, \mathcal{E}_0, \Psi_0)$  on  $(0, T]$  as  $\varepsilon \searrow 0$  and write*

$$(\mathbf{X}, \mathcal{E}_\varepsilon, \Psi_\varepsilon) \xrightarrow{E} (\mathbf{X}, \mathcal{E}_0, \Psi_0),$$

if, given a sequence of solutions  $u_\varepsilon : [0, T] \rightarrow \mathbf{X}$  to  $(\mathbf{X}, \mathcal{E}_\varepsilon, \Psi_\varepsilon)$  with a suitable condition on the initial values  $(u_\varepsilon^0)_{\varepsilon > 0}$ , there exists a limit solution  $u : [0, T] \rightarrow \mathbf{X}$  to  $(\mathbf{X}, \mathcal{E}_0, \Psi_0)$  with suitable  $u(0) = u^0$  and a subsequence  $\varepsilon_k \rightarrow 0$  such that for all  $t \in (0, T]$ :

$$u_{\varepsilon_k}(t) \rightarrow u(t) \quad \text{and} \quad \mathcal{E}_{\varepsilon_k}(u_{\varepsilon_k}(t)) \rightarrow \mathcal{E}(u(t)).$$

**4.2. Proof of E-convergence.** As a first step, we prove the Mosco convergence of the primal and dual dissipation potentials  $\tilde{\Psi}_\varepsilon^*(\mathbf{g}_\varepsilon, \cdot)$  and  $\tilde{\Psi}_\varepsilon(\mathbf{g}_\varepsilon, \cdot)$  defined in Subsection 2.4. In view of Lemma 3.1, we may reduce our considerations to the smaller state space  $\tilde{\mathbf{X}}$ .

**Proposition 4.3.** *Let  $\lim_{\varepsilon \rightarrow 0} \mathbf{g}_\varepsilon = \mathbf{g}$  in the cone  $\tilde{\mathbf{X}}$  be given. Then the families of dual and primal dissipation potentials  $(\tilde{\Psi}_\varepsilon^*(\mathbf{g}_\varepsilon, \cdot))_{\varepsilon > 0}$  and  $(\tilde{\Psi}_\varepsilon(\mathbf{g}_\varepsilon, \cdot))_{\varepsilon > 0}$  converge in the sense of Mosco as  $\varepsilon \searrow 0$  to their respective limits  $\tilde{\Psi}_0^*(\mathbf{g}, \cdot)$  and  $\tilde{\Psi}_0(\mathbf{g}, \cdot)$  given by*

$$\tilde{\Psi}_0^*(\mathbf{g}, \boldsymbol{\xi}) = \begin{cases} \tilde{\Psi}^{s,*}(\mathbf{g}, \boldsymbol{\xi}^s) & \text{if } \boldsymbol{\xi}^f = 0, \\ \infty & \text{otherwise,} \end{cases}$$

and, correspondingly,

$$\tilde{\Psi}_0(\mathbf{g}, \mathbf{v}) = \begin{cases} \tilde{\Psi}^s(\mathbf{g}, \mathbf{v}^s) & \text{if } \mathbf{v}^c = 0, \\ \infty & \text{otherwise.} \end{cases}$$

*Proof.* The limit is nontrivial in  $\tilde{\Psi}^f$  and  $\tilde{\Psi}^{f,*}$  only. Clearly, we have  $\lim_{\varepsilon \rightarrow 0} \tilde{\Psi}_\varepsilon^f(\mathbf{g}_\varepsilon, \cdot) = 0$ . By [2, Thm. 3.7], this implies the result for  $\tilde{\Psi}^{f,*}$  as well.  $\square$

The main result of this section is the following.

**Theorem 4.4.** *Under Assumptions (R1)–(R3) and (I1), (I2), we obtain*

$$(\tilde{\mathbf{X}}, \tilde{\mathcal{E}}, \tilde{\Psi}_\varepsilon) \xrightarrow{E} (\tilde{\mathbf{X}}, \tilde{\mathcal{E}}, \tilde{\Psi}_0)$$

in the sense of Definition 4.2. In particular, the limit curve  $\mathbf{g} \in C([0, \infty), \overset{\circ}{\mathbf{X}})$  satisfies the (UEDE)

$$\tilde{\mathcal{E}}(\mathbf{g}(t)) + \int_0^t \left[ \tilde{\Psi}_0(\mathbf{g}, \dot{\mathbf{g}}) + \tilde{\Psi}_0^*(\mathbf{g}, -\mathbb{T}^\top \mathbf{log} \left( \frac{\mathbb{T}\mathbf{g}}{\mathbf{c}_*} \right)) \right] ds \leq \tilde{\mathcal{E}}(\mathbf{g}_0), \quad (4.1)$$

for all  $t \geq 0$ , with  $\mathbf{g}_0$  given by Lemma 3.1.

*Proof.* For all  $0 < s < t < t^+$ , equation (EDB $_\varepsilon$ ),

$$\tilde{\mathcal{E}}_\varepsilon(\mathbf{g}_\varepsilon(t)) + \int_s^t \left[ \tilde{\Psi}_\varepsilon(\mathbf{g}_\varepsilon, \dot{\mathbf{g}}_\varepsilon) + \tilde{\Psi}_\varepsilon^*(\mathbf{g}_\varepsilon, -D\tilde{\mathcal{E}}(\mathbf{g}_\varepsilon)) \right] dr = \tilde{\mathcal{E}}_\varepsilon(\mathbf{g}_\varepsilon(s)),$$

holds for  $\mathbf{g}_\varepsilon$ . We apply the limit  $\varepsilon \rightarrow 0$  on both sides. By Lemma 3.1,  $\lim_{\varepsilon \rightarrow 0} \mathbf{g}_\varepsilon = \mathbf{g}$  in  $C([s, t^+]; \mathbf{X}_A^B)$  for some  $0 < A < B < +\infty$  and by Lemma 2.2,  $\dot{\mathbf{g}}_\varepsilon^s \rightarrow \dot{\mathbf{g}}^s$  in  $L^2((s, t^+); \mathbb{R}^{R_s})$ . By Proposition 4.3, it follows that

$$\liminf_{\varepsilon \rightarrow 0} \tilde{\Psi}_\varepsilon^s(\mathbf{g}_\varepsilon, \dot{\mathbf{g}}_\varepsilon^s) \geq \tilde{\Psi}^s(\mathbf{g}, \dot{\mathbf{g}}^s) \quad \text{and} \quad \liminf_{\varepsilon \rightarrow 0} \tilde{\Psi}_\varepsilon^{s,*}(\mathbf{g}_\varepsilon, -D\tilde{\mathcal{E}}(\mathbf{g}_\varepsilon)^s) \geq \tilde{\Psi}^{s,*}(\mathbf{g}, -D\tilde{\mathcal{E}}(\mathbf{g})^s). \quad (4.2)$$

In particular, we have that

$$\liminf_{\varepsilon \rightarrow 0} \tilde{\Psi}_\varepsilon^{f,*}(\mathbf{g}_\varepsilon, -D\tilde{\mathcal{E}}(\mathbf{g}_\varepsilon)^f) \geq \tilde{\Psi}^{f,*}(\mathbf{g}, -D\tilde{\mathcal{E}}(\mathbf{g})^f), \quad (4.3)$$

so that

$$-D\tilde{\mathcal{E}}(\mathbf{g})_r^f = -\gamma^r \cdot \mathbf{log} \left( \frac{\mathbf{c}}{\mathbf{c}_*} \right) = 0 \quad \text{for all } r = 1, \dots, R_f, \quad (4.4)$$

and  $\tilde{\Psi}^{f,*}(\mathbf{g}, -D\tilde{\mathcal{E}}(\mathbf{g})^f) = 0$ . Note that (4.4) is equivalent to  $\mathbf{c}$  being in equilibrium with respect to the fast reactions. Continuity of  $\tilde{\mathcal{E}}$  and continuity of  $\mathbf{g}$  imply the limit estimate

$$\tilde{\mathcal{E}}(\mathbf{g}(t)) + \int_s^t \left[ \tilde{\Psi}_0(\mathbf{g}, \dot{\mathbf{g}}) + \tilde{\Psi}_0^*(\mathbf{g}, -\mathbb{T}^\top \mathbf{log} \left( \frac{\mathbb{T}\mathbf{g}}{\mathbf{c}_*} \right)) \right] dr \leq \tilde{\mathcal{E}}(\mathbf{g}(s)). \quad (4.5)$$

Performing the limit  $s \rightarrow 0$  on both sides of (4.5) yields (4.1). For the extension of this result from the interval  $(0, t^+]$  to  $(0, \infty)$ , cf. Section 4.3 below.  $\square$

Clearly, the two main theorems 3.2 and 4.4 imply convergence of the curve of concentrations  $\mathbf{c}_\varepsilon = \mathbb{T}\mathbf{g}_\varepsilon \rightarrow \mathbf{c} = \mathbb{T}\mathbf{g}$  on  $(0, \infty)$  with  $\mathbf{c}_0 = \mathbb{T}\mathbf{g}_0$ . In terms of the concentrations  $\mathbf{c}$ , one obtains the following result on the passage to the limit  $\varepsilon \searrow 0$ . We omit its proof for the sake of brevity and refer to [4] and [? ], where similar studies were made directly in the untransformed variables.

**Theorem 4.5.** *Under the Assumptions of Theorem 4.4, we obtain*

$$(\mathbf{X}, \mathcal{E}, \Psi_\varepsilon) \xrightarrow{E} (\mathbf{X}, \mathcal{E}, \Psi_0)$$

in the sense of Definition 4.2, for a suitable limit dissipation functional  $\Psi_0$ . Equivalently to (4.1), the limit curve  $\mathbf{c} \in C((0, \infty); \mathbf{X})$  satisfies  $\lim_{t \searrow 0} \mathbf{c}(t) = \mathbf{c}_0$  and

$$\begin{aligned} \dot{\mathbf{c}} &= - \sum_{r=1}^{R_s} k_r^s \mathbf{C}_r^s(\mathbf{c}) \gamma_r^s - \sum_{\rho=1}^{R_f} \sum_{r=1}^{R_s} \partial_{g_r^s} \mathbf{h}_{\text{eq}}[(\mathbb{T}^{-1}\mathbf{c})^f, (\mathbb{T}^{-1}\mathbf{c}_0)^c]_{\rho} k_r^s \mathbf{C}_r^s(\mathbf{c}) \gamma_r^f \\ &= [\mathbf{1} - \mathbb{T}^f ((\mathbb{T}^f)^\top \mathbf{J}(\mathbf{c}) \mathbb{T})^{-1} (\mathbb{T}^f)^\top \mathbf{J}(\mathbf{c})] \left( \sum_{r=1}^{R_s} k_r^s \mathbf{C}_r^s(\mathbf{c}) \gamma_r^s \right), \end{aligned} \quad (4.6)$$

where  $\mathbb{T}^f := (\gamma_1^f, \dots, \gamma_{R_f}^f) \in \mathbb{R}^{I \times R_f}$  and  $\mathbf{J}(\mathbf{c}) := \text{diag}(c_1^{-1}, \dots, c_I^{-1}) \in \mathbb{R}^{I \times I}$ .

The idea of proof for the second characterization of the limit  $\mathbf{c}$  in (4.6) relies on the fact that along the solution  $\mathbf{c} = \mathbb{T}\mathbf{g}$ , one has

$$\frac{d}{dt}\mathcal{C}^f(\mathbf{c}(t)) = 0,$$

for all  $t > 0$ .

**4.3. Concluding remarks.** We give some remarks concerning Theorems 4.4 and 4.5.

E-convergence in the sense of Definition 4.2 requires continuity of the full limit curve  $\mathbf{g}$ , in particular, of  $\mathbf{g}^f$ . Using Lemma 2.3, this is guaranteed as long as  $\mathbf{g} \in \tilde{\mathbf{X}}_a^b$  for some  $0 < a < b < +\infty$ . As shown in Lemma 3.1, by continuity of  $\mathbf{g}^s$ , this property holds at least up to some  $t^+$ . But this condition is also necessary and sufficient for Lipschitz continuity and thus unique solvability of (3.2). A posteriori, Lemma 2.3 shows that the right-hand side of (3.2) preserves the transformed positive cone  $\tilde{\mathbf{X}}$ , which yields global solvability of (3.2) as well as uniform positivity and thus uniform convergence of  $\mathbf{g}_\varepsilon$  and E-convergence on all compact subsets of  $(0, \infty)$ . For a similar argument in the non-transformed setting, cf. [4] and [?].

The limit system  $(\tilde{\mathbf{X}}, \tilde{\mathcal{E}}, \tilde{\Psi}_0)$  generalizes the concept of a gradient flow on a metric space in the sense that the dissipation potential  $\tilde{\Psi}_0$  only generates a pseudometric on  $\tilde{\mathbf{X}}$  via

$$\text{dist}(\mathbf{g}, \hat{\mathbf{g}}) = \inf \left\{ s \in C^1([0, 1], \tilde{\mathbf{X}}), s(0) = \mathbf{g}, s(1) = \hat{\mathbf{g}} : \int_0^1 \tilde{\Psi}_0(s(t), \dot{s}(t)) dt \right\}.$$

By the definition in Proposition 4.3, all  $\mathbf{g}, \hat{\mathbf{g}} \in \tilde{\mathbf{X}}$  with  $\mathbf{g}^s = \hat{\mathbf{g}}^s$  are at distance 0 from each other. This is consistent with the limiting curve  $t \mapsto \mathbf{g}(t)$  being determined by the reduced system (3.2).

At time  $t = 0$ , an additional amount of energy is dissipated in the limit. Note that, in general,  $\lim_{t \searrow 0} \mathbf{c}(t) = \mathbf{c}_0 \neq \lim_{\varepsilon \rightarrow 0} \mathbf{c}_\varepsilon^0 =: \mathbf{c}_0^0$  and that assumptions (I1) and (I2) do not require the limit on the r.h.s. to exist. If it exists, the amount of dissipated energy is  $\mathcal{E}(\mathbf{c}_0^0) - \mathcal{E}(\mathbf{c}_0)$ . This quantity is non-negative as  $\mathbf{c}_0$  is the unique fast-reaction steady state corresponding to  $\mathbf{c}_0^0$ : indeed,  $\mathcal{E}(\mathbf{c}_0^0) - \mathcal{E}(\mathbf{c}_0)$  is exactly the amount of energy which is dissipated in the (gradient) system (3.1) of only fast reactions over the time interval  $\tau \in [0, \infty)$  along the curve joining  $\mathbb{T}^{-1}\mathbf{c}_0^0$  and its corresponding equilibrium  $\mathbb{T}^{-1}\mathbf{c}_0$  of (3.1). This phenomenon can be viewed as an additional external force which instantaneously brings the system into the fast-reaction equilibrium, acting only at initial time.

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