Coupled Systems of Differential-Algebraic and Kinetic Equations with Application to the Mathematical Modelling of Muscle Tissue.

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Abstract We consider a coupled system composed of a differential-algebraic equation and a large-scale ordinary differential equation where the latter stands for the dynamics of numerous identical particles. Replacing the discrete particles by a kinetic equation in terms of the particle density, we obtain a new class of models that we refer to as partially kinetic systems. We investigate the influence of constraints on the kinetic theory of those systems and present necessary adjustments. An essential tool from kinetic theory, the mean-field limit, also applies to partially kinetic systems as well, which yields a rigorous link between the kinetic equations and their underlying particle dynamics.

Our research is inspired by the mathematical models for muscle tissue where the macroscopic behavior is governed by the equations of continuum mechanics, often discretized by the finite element method, and the microscopic muscle contraction process is described by Huxley’s sliding filament theory. The latter represents a kinetic equation that characterizes the state of the actin-myosin bindings in the muscle filaments. As a prime example, we analyse the influence of constraints on the kinetic theory of a simplified version of Huxley’s sliding filament model.

The general theory of partially kinetic systems is in its early stages. We introduce the equations of motions for partially kinetic systems, which is family of differential-algebraic equations. We conjecture that classical proofs from kinetic theory for global existence and Dobrushin’s stability estimate can be adjusted for partially kinetic systems.

Keywords kinetic theory · statistical physics · differential-algebraic equations · mathematical modelling · skeletal muscle tissue

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1 Introduction

Differential-algebraic equations (DAEs) and kinetic equations are usually considered as separate and quite independent topics. While DAEs stem from models that are in some sense constrained, kinetic theory deals with identical particles such as atoms or molecules and their mutual interaction, leading eventually to the characterization of macroscopic quantities such as density and pressure. In this work, we introduce a problem class that combines these two mathematical structures. More precisely, we study how a large number of identical subsystems or particles acts on a macroscopic component and how the particle system and its coupling with this component behave when a mean-field limit process is applied. Our goal is a kinetic theory where the coupling is taken into account from the beginning and not added after the mean-field limit.

Using a mechanical framework to make the different models more specific, we identify the macroscopic system – the heavy or slow part – with either a rigid body or an elastic body that has been discretized in space by, e.g., the finite element method. The microscopic particles are viewed as mass points, and their coupling with the heavy part is expressed in terms of constraint equations. In this way, we can employ Lagrangian mechanics to set up the equations of motion and profit from the available underlying structure. Standard tools from the theory of DAEs allow then to eliminate the Lagrange multipliers and pass to a system of ordinary differential equations for the subsequent treatment. It turns out that the established results on the mean-field limit and also corresponding stability estimates carry over under certain assumptions.

In classical kinetic theory for interacting particle systems [24], the derivation of macroscopic equations from microscopic particle dynamics is commonly split into two steps: the introduction of particle densities via the mean-field limit and averaging over the momentum variables to obtain macroscopic equations. As a result of these steps, the complete system is transformed into a description where all state variables are replaced by a density (or measure). For more background on the mean-field limit we refer to, e.g., [6,16,23]. In contrast to this well-established theory, we study here the situation where the heavy part is uniformly coupled to numerous identical particles and where only the particles are replaced by a kinetic description. This selective application of the mean-field approach leads to a new system of mixed type, which we call partially kinetic system.

An important example for a partially kinetic system are mathematical models for muscle contraction. Muscle tissue, with all its supporting tissue (heavy parts), contracts due to the accumulated force of numerous actin-myosin cross-bridges (particles). In this specific case, the kinetic theory of cross-bridges without the coupling is already well studied and lead to the famous Huxley model [15,17,27]. On the other hand, models from continuum mechanics are today in use to simulate the muscle contraction at the macro-scale in combination with the finite element method. For the coupling of both scales, simplifications and ad-hoc procedures are used so far [23,10,11] that call for a theoretical foundation.

An important feature of partially kinetic systems lies in the possibility to reduce the dimension since the mean-field equations for partially kinetic systems describe the state of the particles by a measure in the particle positions. The velocities are already determined by the constraint. Therefore, an extra averaging step is not required to reduce the dimension of the system.

This article is organized as follows: In Section 2, a strongly simplified muscle model for the coupling of the microscopic actin-myosin binding with the macroscopic muscle force is presented. This introductory example for partially kinetic systems is discussed both from the differential-algebraic and the kinetic viewpoints. Next, Section 3 generalizes the framework...
to the class of partially kinetic systems and summarizes the properties known so far, along with open issues. Numerical results for the simplified muscle model are finally reported and analyzed in Section 4. It turns out that the limit process of the mean-field limit can be nicely observed numerically. A closer look at the results, however, shows that the numerical treatment of a large number of particles by standard DAE integrators provides asymptotic energy conservation while the upwind discretization in the kinetic equation introduces significant numerical diffusion.

2 An Introductory Example: Muscle Cells as Partially Kinetic Systems

This section presents a linear example for partially kinetic systems, which is also closely related to existing models for muscle tissue and the dynamics of cross-bridges. The central question that we address here is: How should the kinetic theory for cross-bridges be adjusted such that it remains valid given additional constraints that model the coupling with a macroscopic motion?

The emergence of macroscopic effects from microscopic properties is a central theme in kinetic theory. In laymen terms, emergence describes how the big picture arises from the laws that govern the model at a smaller scale. Understanding this transition is essential in many biological applications. Muscle tissue consists of millions of small contractible molecules called actin-myosin cross-bridges. Kinetic theory allows the up-scaling of these microscopic units to the organ level and provides a means to derive macroscopic models for muscle tissue. Almost all such macroscopic models focus on the emergence of a contraction force as the result of the synchronization between all muscle cells. But there are applications where more than just the macroscopic contraction force is of interest.

One example is vibrational medicine, in particular the medical therapy concept called [21] that treats diseased muscle tissue by vibrational stimulation in a certain frequency range. In order to understand this therapy approach, it is important to study how the mechanical stimulation influences the physiological health of cells. In laymen terms: How does the big picture influence the small scale? A first mathematical model for the interplay between mechanics and the physiology of muscle cells was proposed in [22].

We extend this work in the direction of more detailed physiological models for muscle cells that are based on the sliding filament theory for cross-bridges. In mathematical terms, this requires an understanding of muscles at both, the micro and the macro scale. To study the influence of mechanics on the physiology of muscle cells, the coupling between mechanical properties and physiological models is essential. In the following we will therefore study a prototype of a system which couples a physiological model for cross-bridges with a prototypical mechanical system. We mention that in [28], models for the interaction of continuum mechanics and cross-bridge theory have already been proposed.

2.1 A Differential-Algebraic Model for Attached Cross-Bridges

Compared to many other biological phenomena, the contraction of muscles cells is a relatively well studied field [14-17]. For a mathematical introduction to muscle models, we refer to [14-17]. The mainstream theory to explain muscle contraction is called [12-15].

In its simplest form, sliding filament theory suggests that muscle cells consist of parallel myosin- and actin-filaments, as visualized in Fig. 1. On each actin-filament, small binding sides allow myosin heads to attach and to form a bridge between both filaments, a so called
Due to the molecular configuration of newly attached cross-bridges, they pull the two filaments such that they slide alongside each other, which causes a shortening of the muscle cell. This is called a power stroke. After each power stroke, the myosin head can unbind from the binding side, release the ADP (adenosine diphosphate) molecule and obtain new free energy by hydrolyzing another ATP (adenosine triphosphate) molecule.

The cycling of binding, power stroke, unbinding and resetting of myosin heads is called the cross-bridge cycle. Since numerous muscle cells contract due to this mechanism, the whole muscle tissue contracts on the macroscopic scale. The contraction strength is controlled by the rate at which cross-bridge cycles take place. This process depends on the type of muscle tissue, but is always based on a mechanism of blocking or unblocking the binding sides at the actin filaments. In skeletal muscle tissue, the periodic release of calcium ions unblocks the binding sides. A higher frequency of calcium ion bursts leads to a stronger contraction.

Fig. 1 Sketch of the parallel actin-filaments (purple, outside) and myosin-filaments (orange, center). The myosin heads (red) are able to attach to binding sides at the actin filament, which forms a so called cross-bridge.

From the variety of available mathematical models, we extract the common core, which is given by the sliding filament theory with cross-bridges modelled as linear springs. We also simplify the model radically by considering only the attached cross-bridges. Hence, the actual cross-bridge cycling does not take place in the system we present. However, Remark 2.2 below discusses possible extensions, which are neglected for most of the exposition since they distract too much from the main mathematical ideas.

Fig. 2 Model for a single myosin filament (orange), the corresponding pair of actin filaments (purple) and a coupled linear spring (blue).
Without further ado, we present the mathematical model for with the presence of constraints. Our goal is to model a muscle cell which is coupled to a macroscopic linear spring, as displayed in Fig. 2. The attached cross-bridges are represented by microscopic linear springs, and we consider only one half of the contractible unit, as displayed in Fig. 3.

In this section we will study the one-dimensional case. Therefore, we define the dimensions \( n_r = n_q = 1 \). However, throughout the section we will continue to distinguish between \( \mathbb{R} \), \( \mathbb{R}^{n_r} \) and \( \mathbb{R}^{n_q} \) to indicate real numbers and position variables in the according spaces. Later, this will help to relate this simple model to the general case in Section 3. The reader is welcome to read this section with \( n_q \neq n_r \) in mind.

Let \( r \in \mathbb{R}^{n_r} \) denote the extension of a linear spring with mass \( M_r \) and force \( F_r(r) = -\gamma_r r \). We call it the heavy or slow linear spring. We label the attached cross-bridges with \( j = 1, \ldots, N \). The extension of a single cross-bridge is denoted by \( Q_j \in \mathbb{R}^{n_q} \) and each cross-bridge is modelled as a linear spring with mass \( M_q \) and force \( F_q(Q_j) = -\gamma_q Q_j \).

For some constant matrix \( G_r \in \mathbb{R}^{n_q \times n_r} \), we define the function

\[
g(r, Q_j) := G_r r + Q_j.
\]

The linear spring and the myosin filament are considered to be fixed to the walls at both sides, as displayed in Fig. 3. Therefore, we require the total length to remain constant and pick \( G_r = -1 \). For each cross-bridge, we define the constraint as

\[
g(r, Q_j) = g(r_{in}, Q_{in}) \quad \text{for} \quad j = 1, \ldots, N.
\]

The corresponding Lagrangian multipliers are denoted by \( \lambda_1, \ldots, \lambda_N \in \mathbb{R}^{n_r} \). Overall, we arrive at the following differential-algebraic system that models a linear spring coupled to a sliding actin-myosin filament pair with \( N \) cross-bridges:

\[
M_r \ddot{r} = -\gamma_r r - \sum_{i=1}^{N} G_r^T \dot{\lambda}_i,
\]

\[
M_q \ddot{Q}_j = -\gamma_q Q_j - \lambda_j \quad \text{for} \quad j = 1, \ldots, N,
\]

\[
g(r, Q_j) = g(r_{in}, Q_{in}) \quad \text{for} \quad j = 1, \ldots, N
\]

with initial conditions

\[
r(0) = r_{in} \in \mathbb{R}^{n_r}, \quad \dot{r}(0) = \dot{s}_{in} \in \mathbb{R}^{n_r} \quad \text{and} \quad Q_j(0) = Q_{in}^j \in \mathbb{R}^{n_q} \quad \text{for} \quad j = 1, \ldots, N.
\]

There is no initial condition for the velocities \( \dot{Q}_j \), since the constraint implies the compatibility condition

\[
\dot{Q}_j(0) = -G_r \dot{s}_{in} \quad \text{for} \quad j = 1, \ldots, N.
\]
The system (2.1) to (2.3) has differential index 3 [3]. Due to the special structure it is possible to eliminate the Lagrange multipliers and derive an explicit formulation. Differentiating (2.3) twice with respect to time yields

\[ \ddot{Q}_j = -G_r \dot{r} \]  

(2.4)

and

\[ \dddot{Q}_j = -G_r \ddot{r}. \]  

(2.5)

Using (2.5), we solve (2.2) for \( \lambda_j \) and insert the result into (2.1), which leads to

\[ M_r \ddot{r} = -\gamma_r \dot{r} - \sum_{i=1}^{N} G^T_{ri} \left( -\gamma_q Q_i - M_q \ddot{Q}_i \right) \]  

(2.6)

\[ = -\gamma_r \dot{r} - \sum_{i=1}^{N} G^T_{ri} \left( -\gamma_q Q_i + M_q G_r \ddot{r} \right). \]  

(2.7)

After collecting the acceleration terms on the left hand side, one obtains

\[ \begin{align*} 
&M_r \dddot{r} = -\gamma_r \dot{r} + \sum_{i=1}^{N} G^T_{ri} \gamma_q Q_i. \\
&= M_{eff}(N) \dot{r} = F_{eff}(N)(r, Q_1, ..., Q_N). 
\end{align*} \]  

(2.8)

This system of ordinary differential equations describes the effective balance of forces after elimination of the constraint equation, and thus we use the subscript \( \text{eff} \).

In (2.8) the Lagrangian multipliers are eliminated, but the equation is not closed, since \( Q_i \) is needed to compute \( F_{eff}(N) \). We employ (2.9) to generate a first order differential equation for all \( Q_j \), i.e.

\[ \dot{Q}_j = -G_r \dot{r} \quad \text{for } j = 1, \ldots, N. \]  

(2.9)

This closes the system, and (2.8) and (2.9) form now a linear ordinary differential equation. The conceptually quite simple calculation already quantifies the influence of the cross-bridges on the linear springs. Recall that \( N \) denotes the number of cross-bridges, which is in practice of the order \( 10^3 \) to \( 10^6 \). This motivates the application of kinetic theory to this equation.

A numerical simulation of (2.8) and (2.9) is presented in Fig. 4. For the simulation, the initial conditions of the cross-bridge extensions \( Q_i \) are chosen as samples of a normal distribution. For details on the numerical method we refer to Section 4.

2.2 Kinetic Theory forAttached Cross-Bridges with Constraints

started as the mathematical theory to derive macroscopic laws for gas and fluids from their underlying microscopic dynamics. Equations like the Navier-Stokes equation or the heat equation were known before, but their derivation was historically based on conservation laws and macroscopic principles. Kinetic theory allows to derive these laws from microscopic particle models, which are based on atomic laws for the interaction of atoms and molecules. In this sense, kinetic theory is a branch of mathematics with aims at providing answers for Hilbert’s sixth problem, which asked for a derivation of equations for continua by means
The main achievement of kinetic theory is therefore often the proof of macroscopic laws based on fundamental axioms, rather than the discovery of new laws. Nowadays, kinetic theory is not exclusive anymore for atoms, but also applied to other large scale systems of particles in biology and many other fields [1].

The was investigated already in the early eighties [15]. The first approaches suggested to model attached cross-bridges as linear springs, while many refinements have been introduced later on and are still today subject of current research [13]. To compute the contraction force, all models known to us assume implicitly that the kinetic equations remain valid without modification in the presence of constraints. Moreover, the mass of the cross-bridges is assumed to add no kinetic energy to the macroscopic system. These two assumptions are very reasonable and lead to successful models. In the following we want to compute explicitly how the kinetic equations look like in the presence of constraints and give a mathematical quantification for common modelling assumptions.

We remark that this section comprises also a short outline of the fundamentals of kinetic theory. For this purpose, it is preferable to use the ordinary differential equation (2.8) and (2.9) instead of the index-3 formulation (2.1) to (2.3). However, in Section 3 the same ideas will be applied directly to an index-3 system.

As the number of cross-bridges is large, we want to study the limit of infinitely many cross-bridges \( N \to \infty \). A naive limit \( N \to \infty \) leads to a trivial state in equilibrium or to an infinite force. The force term in (2.8)

\[
\sum_{j=1}^{N} G r_j \gamma Q_j
\]

will either be divergent or the cross-bridge positions form a zero sequence. Therefor the naive limit is mathematically and physically boring or unreasonable, since it describes either states close to equilibrium or with infinite energy.

To avoid the energy explosion from the naive limit, we fix a number \( N_{\text{real}} \), which describes a realistic number of cross-bridges. In the mean-field approach, the mathematical limit \( N \to \infty \) is not a statement about how many cross-bridges the system has in reality,

\[^1\] “As to the axioms of the theory of probabilities, it seems to me desirable that their logical investigation should be accompanied by [...] a rigorous and satisfactory development of the method of mean values in mathematical physics, and in particular in the kinetic theory of gases. [...] Boltzmann’s work on the principles of mechanics suggests the problem of developing mathematically the limiting processes, there merely indicated, which lead from the atomistic view to the laws of motion of continua.”
rather it is a statement that the cross-bridge distribution are well approximated by a continuous distribution. Therefore, we increase the number of cross-bridges and also scale the mass and force of each cross-bridge at the same time, such that the energy remains constant. Hence, we multiply the mass \( M_q \) of one cross-bridge and the force \( F_q = \gamma_q Q_j \) with the realistic number of particles \( N_{\text{real}} \) and divide the contribution of one cross-bridge by the number of particles \( N \), i.e.

\[
M_q := \frac{N_{\text{real}}}{N} M_q \quad \text{and} \quad F_q(Q_j) := -\frac{N_{\text{real}}}{N} \gamma_q Q_j,
\]

Accordingly, we replace (2.2) by

\[
N_{\text{real}} \frac{M_q}{N} Q_j = -\frac{N_{\text{real}}}{N} \gamma_q Q_j - \lambda_j.
\]

Now we can consider \( N \to \infty \), i.e. increase the number of cross-bridges, but the magnitude of the accumulated force will be in \( O(N_{\text{real}}) \) and hence not explode.

After this modification, (2.8) takes the form

\[
\left( M_r + N_{\text{real}} \frac{1}{N} \sum_{i=1}^{N} G_{i}^{T} M_{r} G_{i} \right) r = -\gamma_r r + N_{\text{real}} \frac{1}{N} \sum_{i=1}^{N} G_{i}^{T} \gamma_q Q_i. \tag{2.10}
\]

For the mathematical discussion, we could assume without lost of generality \( N_{\text{real}} = 1 \). This is a typical simplification in kinetic theory \([6,16]\), since usually only particles are present in the systems and scaling cancels out in the balance law. However, for partially kinetic systems, this is not the case, since the correct ratio between masses and forces of both systems is relevant. Therefore, different values of \( N_{\text{real}} \) change the properties of the system.

A key observation in equation (2.10) is that only the mean value of the cross-bridge forces is relevant. In other words, we are just interested in the statistics of \( Q_1, Q_2, \ldots \) but not in the concrete states. This motivates the use of a probability measure to quantify the distribution of the cross-bridges.

Let us denote the space of probability measures as \( \mathcal{P}(\mathbb{R}^n) \). The space of probability measures \( \mu \in \mathcal{P}(\mathbb{R}^n) \) with finite first moments is denoted by \( \mathcal{P}^1(\mathbb{R}^n) \), i.e. for \( \mu \in \mathcal{P}^1(\mathbb{R}^n) \) the additional bound \( \int_{\mathbb{R}^n} q \, d\mu(q) < \infty \) holds. For a moment, we assume that for each fixed time \( t \), there is a probability measure \( \mu_t \in \mathcal{P}^1(\mathbb{R}^n) \), such that the cross-bridge extensions \( Q_j(t) \) are random variables, which are independent, identical distributed with probability law \( \mu_t \). We use the notation

\[
Q_j(t) \sim \mu_t \quad :\Rightarrow \quad \mathbb{P}(Q_j(t) \in A) = \mu_t(A), \quad \text{for all} \ A \in \mathcal{B}(\mathbb{R}^n).
\]

We call \( \mu_t \) also the cross-bridge distribution\(^2\) Our goal is to approximate the limit \( N \to \infty \) of (2.10) by an expression in the cross-bridge distribution \( \mu_t \).

Application of the yields

\[
\lim_{N \to \infty} \int_{\mathbb{R}^n} q \, d\mu_t(q) \quad \text{almost surely}. \quad (2.11)
\]

\(^2\) It is not trivial to argue why all cross-bridges \( Q_j \) are well described by one common probability measure \( \mu_t \). This property is related to the concept of propagation of chaos \([16]\). The mean-field limit, which we will discuss later, is one possibility to overcome this issue.
The sum converges almost surely (a.s.), i.e. with probability one the first equality holds. The second relation is just a consequence of $Q_t(t) \sim \mu_t$. This central stochastic convergence theorem motivates to replace the discrete mean force in (2.10) by the so-called mean-field force

$$f_{\text{mean}}(\mu_t) = \int_{\mathbb{R}^n} G_r \gamma q \, d\mu_t(q).$$

This leads to the formal definition of the kinetic equation for (2.8) as

$$(M_r + N_{\text{real}} \int_{\mathbb{R}^n} G_r^T M_r G_r \, d\mu_t(q)) \dot{r} = -\gamma r + N_{\text{real}} G_r^T \gamma q \int_{\mathbb{R}^n} q \, d\mu_t(q).$$

(2.12)

We remark, that for linear constraints the effective mass is constant. For nonlinear constraints, the mean-field mass will depend on the cross-bridge state $\mu_t$. If $\mu_t$ is known, then (2.12) is the effective balance law for the linear spring. However, we are once again left with the task for finding a closing equation for the effective balance law.

We assume that just the initial cross-bridge distribution $\mu^{in} \in \mathcal{P}(\mathbb{R}^n_q)$ is known, i.e.

$$Q^{in}_j \sim \mu^{in}, \quad \text{for all } j = 1, \ldots, N.$$  

As in the discrete case, we utilize the velocity constraint once more. We interpret the velocity constraint (2.9) as a first order differential equation and denote its flow by $Q(t, q^{in})$, i.e. $Q$ satisfies for all $q^{in} \in \mathbb{R}^n_q$

$$\dot{Q}(t, q^{in}) = -G_r r(t), \quad (2.13)$$

$$Q(0, q^{in}) = q^{in}. \quad (2.14)$$

After a time $t$, the discrete cross-bridge state would be given by

$$Q_j(t) = Q(t, Q^{in}_j).$$

The law of $Q_j(t)$ is therefore given by the distribution $\mu^{in}$ after the transformation $Q(t, \cdot): \mathbb{R}^n_q \rightarrow \mathbb{R}^n_q$. This is visualized in Fig. 5. To measure how many cross-bridges have extensions in $A \in \mathcal{B}(\mathbb{R}^n_q)$, we can count how many cross-bridges have an initial extension that is element of $(Q(t, \cdot))^{-1}(A)$, i.e.

$$Q_j(t) \in A \iff Q^{in}_j \in (Q(t, \cdot))^{-1}(A).$$

This relation characterizes the pushforward of a measure [6,10]. For a map $\varphi: \mathbb{R}^n_q \rightarrow \mathbb{R}^n_q$, the pushforward of $\mu^{in}$ under $\varphi$ is defined as

$$\varphi#\mu^{in}(A) := \mu^{in}(\varphi^{-1}(A)), \quad \text{for all } A \in \mathcal{B}(\mathbb{R}^n_q).$$

Applied to our situation, the cross-bridge distribution at time $t$ is given as the pushforward of $\mu^{in}$ under $Q(t, \cdot)$, i.e.

$$\mu_t := Q(t, \cdot)#\mu^{in} \quad (2.15)$$

where # denotes the pushforward. This yields

$$Q_j(t) \sim \mu_t, \quad \text{for all } j = 1, \ldots, N.$$  

The situation is sketched in Fig. 5.
A kinetic description of (2.1) to (2.3) is therefore given by the combination of (2.12), (2.14) and (2.15)

\[
\begin{aligned}
  &\frac{d}{dt} M_r + N_{\text{real}} \int_{\mathbb{R}^q} G^T_r M_q G_r \, d \mu(q) = -\gamma_r r + N_{\text{real}} G^T_r \gamma_q \int_{\mathbb{R}^q} q \, d \mu(q), \\
  &\dot{Q}(\cdot, q^{in}) = -G_r \dot{r}, \quad \text{for all } q^{in} \in \mathbb{R}^{n_q}, \\
  &\mu_t := Q(t, \cdot) \# \mu^{in}
\end{aligned}
\]  

with initial conditions

\[
\begin{aligned}
  &r(0) = r^{in} \in \mathbb{R}^{n_r}, \quad \dot{r}(0) = s^{in} \in \mathbb{R}^{n_r} \quad \text{and} \quad Q(0, q^{in}) = q^{in}
\end{aligned}
\]

and initial cross-bridge distribution \( \mu^{in} \in \mathcal{P}(\mathbb{R}^q) \). In kinetic theory, systems of the form (2.16) to (2.18) are called the equations, since \( Q(t, \cdot) \) describes the flow of the cross-bridge distribution and the forces are replaced by the mean-field force.

The cross-bridge distribution \( \mu_t \) is usually modelled as a continuous measure. However, a first validity check of (2.16) to (2.18) is given by inserting a so called empirical measure for \( \mu_t \). We define the as

\[
\mu^{(\text{emp})}_{Q_1, \ldots, Q_N} := \frac{1}{N} \sum_{j=1}^{N} \delta_{Q_j},
\]

where \( \delta_{Q_j} \) denotes the Dirac measure which assigns unit mass to the position \( Q_j \in \mathbb{R}^{n_q} \). This measure allows us to treat the discrete system (2.8) and (2.9) as a special case of (2.16) to (2.18).

**Lemma 2.1 (Consistency with the discrete system)** For each fixed \( N \in \mathbb{N} \) and \( N_{\text{real}} := N \), inserting \( \mu = \mu^{(\text{emp})}_{Q_1, \ldots, Q_N} \) into the mean-field characteristic flow equations (2.16) to (2.18) yields exactly the underlying discrete system (2.8) and (2.9).

In this sense the discrete system is a special case of the kinetic equations. This validity check does not prove anything for the limit \( N \to \infty \), but it will allow us to define a concept of convergence that relates the limit \( N \to \infty \) to continuity with respect to the initial data.
2.3 Partially Kinetic Mean-Field PDE for Attached Cross-Bridges

The mean-field characteristic flow equations in (2.16) to (2.18) are analytically attractive, but not typical for modelling purposes, as they contain an infinite family of differential equations (2.17).

The method of characteristics allows us to relate the family of ODE in (2.17) to a first order transport equation. We assume that \( \mu^{in} \) has a probability density, i.e. there exists a function \( u(t,q') \) such that

\[
u(t,q') \, dq' = d\mu_t(q') \quad \text{for all } t \in [0, \infty), \, q' \in \mathbb{R}^n\]

where \( dq' \) denotes the Lebesgue measure on \( \mathbb{R}^n \) with variable \( q' \). Then, (2.18) implies that the value of \( u(t,q') \) is constant along the characteristic curves

\[t \mapsto Q(t,q^{in}).\]

Using this invariance, we can compute

\[
0 = \frac{du(t,Q(t,q^{in}))}{dt} = \frac{\partial u}{\partial t} + \frac{\partial u}{\partial q} \dot{Q} \quad \iff \quad 0 = \frac{\partial u}{\partial t} - \frac{\partial u}{\partial q} G_t \dot{r}.
\]

(2.19)

This yields another kinetic description for attached cross-bridges, which is closer to the formulations found in the literature. A numerical simulation of (2.9) and (2.19) is presented in Fig. 6. For details we refer to Section 4. A first comparison of the discrete and the kinetic description is presented in Fig. 7.

![Fig. 6 Trajectory of the heavy system (left) and particles (right). The intensity of the colour represents the density \( u(t,q) \).](image)

2.4 The Mean-Field Limit for Attached Cross-Bridges

Until now, we have just derived different equations for a kinetic description. In (2.11), the strong law of large numbers motivates the use of mean-field force but it is not sufficient to show that the kinetic description is a good approximation for systems with many cross-bridges. Usually, however, only the statistical distribution of cross-bridges is known, which raises the question of how different samples of one distribution are related to each other.
In these plots we compare the simulations for Fig. 4 and Fig. 6. The results for 250 cross-bridges are very well approximated by the corresponding mean-field equation.

In Fig. 8 we perform numerical simulations of the discrete system (2.8) and (2.9), with the initial conditions $r(0) = r^{in} \in \mathbb{R}^n$ and $\dot{r}(t) = s^{in} \in \mathbb{R}^n$ and for a fixed initial distribution
\[
\text{d} \mu^{in}(q) = \frac{1}{\sqrt{2\pi\sigma}} \exp\left(-\frac{(q-m)^2}{2\sigma^2}\right)\]
we sampled $n_{\text{samples}} = 250$ samples of cross-bridge extensions $Q_{i,m}^{in}, \ldots, Q_{N,m}^{in} \in \mathbb{R}^n$, with $Q_{i,m}^{in} \sim \mu^{in}$ for all $i = 1, \ldots, N$ and $m = 1, \ldots, n_{\text{samples}}$. This yields $n_{\text{samples}}$ different initial conditions and therefore $n_{\text{samples}}$ trajectories of the heavy system and the cross-bridges. The trajectories of the heavy system are plotted in Fig. 8.

We estimate the variance of $r(t)$ with respect to the initial conditions, to quantify how the distance of single trajectories from the mean trajectory. In the simulation, the variance reduces asymptotically as $\frac{1}{N}$, which is displayed in Fig. 8. Therefore, even single trajectories are close to the mean trajectory. The mean trajectory converges against the trajectory of the kinetic system.

Now we want to provide analytical tools to prove the observed convergence in Fig. 8. Gronwall’s inequality allows to estimate the influence of perturbations in the initial data for ordinary differential equations [6]. For kinetic systems, Dobrunshin’s stability estimate [6] is a useful generalization of Gronwall’s inequality, since it allows to estimate the influence of perturbations in the initial distribution $\mu^{in}$. To measure the perturbation in the initial distributions, the Monge-Kantorovich metric $W_1: \mathcal{P}(\mathbb{R}^n) \times \mathcal{P}(\mathbb{R}^n) \to [0, \infty)$ is used. The definition can be found below in Definition 3.7.

We consider two initial distributions $\mu_1^{in}, \mu_2^{in} \in \mathcal{P}(\mathbb{R}^n)$ and the corresponding solutions $(r_1, q_1(t, \cdot), \mu_1^{in})$ and $(r_2, q_2(t, \cdot), \mu_2^{in})$ of (2.16) and (2.17) on a finite time interval $[0, T]$. Then there exists a constant $L$ such that the difference between the two solutions can be estimated as
\[
\|r_1(t) - r_2(t)\| + \|\dot{r}_1(t) - \dot{r}_2(t)\| + W_1(\mu_1^{in}, \mu_2^{in}) \leq e^{Lt} \left(\|r_1^{in} - r_2^{in}\| + \|\dot{s}_1^{in} - \dot{s}_2^{in}\| + W_1(\mu_1^{in}, \mu_2^{in})\right). \tag{2.20}
\]
This is an adapted version of Dobrunshin’s stability estimate, which includes the coupling to the heavy system. In Section 3.4, we will state details and general assumptions for which this
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Fig. 8 Samples of trajectories $r(t; \omega)$ for a linear system with different number of particles $n$ (top and bottom right). For increasing number of particles $n$, the estimated variance of $r(t)$ decreases as $\frac{1}{n}$. (bottom left).

adapted version for partially kinetic systems holds. The inequality (2.20) provides a concrete answer to the approximation quality of the kinetic description. By Lemma 2.1, we know that for the choice of an discrete empirical measure $\mu_{Q_1}^{\text{emp}}, \ldots, \mu_{Q_N}^{\text{emp}}$, the trajectories correspond to those of the discrete system (2.1) to (2.3). If

$$W_1(\mu_{Q_1}^{\text{emp}}, \ldots, \mu_{Q_N}^{\text{emp}}; \mu_{\text{in}}) \to 0, \quad \text{for } N \to \infty,$$

then (2.20) provides a bound for the error of the kinetic description for each fixed $N$ and for $t \in [0, T]$ we get the convergence

$$W_1(\mu_{Q_1(t)}^{\text{emp}}, \ldots, Q_{Q_N(t)}, \mu_{\text{in}}) \to 0, \quad \text{for } N \to \infty.$$

This estimate provides a rigorous argument for the use of kinetic models. If the distribution of $N$ particles is very close to to a continuous distribution $\mu_{\text{in}}$, then the kinetic description has a bounded approximation error.

Using tools from probability theory and functional analysis, the topology for this convergence analysis can be refined to the concept of convergence in distribution for probability measures [5]. This leads to the precise definition of mean-field convergence. We omit these details here as they are out of the scope of the present paper.

2.5 Relation to Established Muscle Models

The kinetic theory of cross-bridges (without coupling to another system) is well studied and far more complex than outlined in this section.
In particular, we neglected a fundamental part of cross-bridge dynamics: Cross-bridges can attach and detach. The repeated attachment and detachment leads to a so called cross-bridge cycle. Only with this mechanism the muscle can contract far beyond the working range of a single cross-bridge. The precise nature of the cross-bridge cycle leads to phenomena which can not be easily explained with simpler, non-physiological models [17].

Remark 2.2 (Kinetic Modelling of the Cross-Bridge Cycle) Cross-bridge cycling can be seen as a switched system, where the laws of motion change discontinuously at certain random times. Such phenomena can be modelled with piece-wise deterministic Markov processes [5].

We only sketch a possible approach. Let \( N \) be the number of myosin heads and let \( A(t) \subset \{1, \ldots, N\} \) denote the indices of all myosin heads which form an attached cross-bridge.

- Between jumps a differential-algebraic equation for attached cross-bridges as discussed in this section holds for all \( j \in A(t) \), whereas another differential equation is applied for all \( j \notin A(t) \).
- For each myosin head, a Poisson (waiting) process models the time at which a myosin head changes its state between being an attached cross-bridge or an unattached myosin head. The rate of the Poisson process might depend on state of the complete system!

On the discrete level, a detailed model for the rate of jumps would be required. In particular, additional modelling questions arise, for example how binding sides at the actin-filament are distributed and how many are not blocked by attached cross-bridges. Also, a model for the dynamics of unattached cross-bridges would be required for such a refinement. We did not perform this modelling neither are we aware of any mathematical model of the cross-bridge cycle which models the cycle for each single myosin head.

A similar, but simpler kinetic system can be used for the description of chemical reactions [4, Section 3.3]. Here jumps take place at each chemical reaction between atoms. As a rule of thumb, systems with jumps still admit a kinetic description if the time between two jumps is sufficiently large. Therefore, a lower bound for the time between jumps is usually assumed to obtain theoretical results.

Finally, we want to point towards more applicable and realistic models for muscle tissue.

Remark 2.3 (Comparison with established cross-bridge models) Usually, the notation and derivation of kinetic models for cross-bridges is different and easier than displayed in this section. Let \( u(t, q) \) denote the density of the cross-bridge distribution at time \( t \), as in Section 2.3. Instead of using a fixed the number \( N_{\text{real}} \), it is common to allow \( u \) to be not normalized. The number

\[
N_{\text{real}} = \int_{\mathbb{R}^n} u(t, q) \, dq
\]

then describes the number of attached cross-bridges. It is intuitively clear that the contraction speed of cross-bridges has to match the external contraction speed \( v_{\text{contraction}} \). This leads directly to a transport equation like (2.19).

To include cross-bridge cycling, source terms are added to the transport equation, which allow the creation and annihilation of cross-bridges. Let \( h_{\text{attach}}(q, u(t, q)) \) denote the probability of a cross-bridge with extension \( q \) to be created and let \( h_{\text{detach}}(q, u(t, q)) \) denote the probability of an existing cross-bridge with extension \( q \) to detach. The biochemical properties of myosin heads suggest that new cross-bridges have usually a positive extension and cross-bridges with a negative extension are very likely to detach.
This leads to a so called two state model, with the defining equation

\[
\frac{\partial u}{\partial t}(t, q) + v_{\text{contraction}}(t) \cdot \frac{\partial u}{\partial q}(t, q) = h_{\text{attach}}(q, u(t, q)) - h_{\text{detach}}(q, u(t, q))
\]

The contribution of these cross-bridges to the contraction of the muscle is then computed by

\[
F_{\text{contraction}} = -\int \gamma_q u(t, q) \, dq.
\]

If the external system is a linear spring, as in (2.1), the influence of cross-bridges is modelled as

\[
M_r \ddot{r} = -\gamma r + F_{\text{contraction}}.
\]

The effective balance law for partially kinetic systems (2.8) almost coincides with this balance law, but the mass matrix differs, since (2.8) is of the form

\[
(M_r + N_{\text{real}} M_q) \ddot{r} = -\gamma r + F_{\text{contraction}}.
\]

Also, due to the attachment and detachment, the number \( N_{\text{real}} \) is not constant anymore, which yields a time dependent effective mass for the heavy system.

A hidden modelling assumption of all muscle models known to us is therefore the assumption

\[
\|M_r\| \gg N_{\text{real}} \|M_q\|.
\]

We conclude this remark by a short list of comments on more detailed models.

- The attachment and detachment of cross-bridges is complex. On the kinetic level, there are many different models available [17]. On the discrete level, a mathematically precise model is, up to our knowledge, missing. A possible approach is outlined in Remark 2.2.
- Since cross-bridges are molecules, the dynamics are just approximated by a linear spring. In fact, refined models are essential to explain common behaviour of muscles. Usually this is modelled by the introduction of additional states for attached cross-bridges. This leads again to extensions like in Remark 2.2.
- In many cases, only the mean-field force \( f_{\text{eff}} \) is of interest. Since this only requires knowledge of the first moment of the cross-bridge distribution, reduced models were developed that approximate \( \mu_t \) only by the first moments [27].

Finally, despite the lack of complexity, the simplified model presented in this section provides some details, which are commonly not taken into account.

- The mean-field limit provides a rigorous link between the discrete model (2.1) to (2.3) and the kinetic model (2.16) and (2.17).
- The mass matrix of the heavy system \( M_r \) is replaced by the effective mass matrix \( m_{\text{eff}} \). Moreover, for nonlinear constraints or in the presence of source terms the effective mass matrix is not constant in \( \mu_t \).
- An adapted version of Dobrunshin’s stability estimate (2.20) provides a concrete bound for the approximation error.
3 General Case: Partially Kinetic Systems

This section generalizes and extends the theory of Section 2. A particular focus lies on ideas and generalizations with are inspired by the theory of differential-algebraic equations. In Section 2, we first applied index reduction and then performed the mean-field limit since this approach did allow us to first eliminate Lagrangian multipliers and then motivate the mean-field limit on the level of forces. For the discussion in this section, we will first apply the mean-field limit directly to the differential-algebraic equation and afterwards apply index reduction. This leads to the commutative diagram in Fig. 9.

![Diagram](Diagram.png)

Fig. 9 Different paths to derive the mean-field characteristic flow equations.

We proceed in the following way. First, partially kinetic equations for a general class of couplings between differential-algebraic equations and large-scale particle systems are introduced. This leads to the new concept of mean-field characteristic flows with constraints. Next, we discuss how perturbations in the initial conditions influence the solutions. It turns out that the Monge-Kantorovich metric (also called Wasserstein distance) provides the right metric to measure the influence of perturbations. Derivations and proofs are skipped to avoid technical and notational complexity. Instead we continue the example from Section 2.

3.1 Formal Derivation of Mean-Field Characteristic Flows with Constraints

As a starting point, we generalise the discrete model from (2.1) to (2.3) as follows.

We consider two coupled mechanical systems in their Newtonian formulation. The model in Fig. 3 serves as an example, where the linear spring on the left represents a heavy or slow system and the tiny springs on the right are now considered as tiny mass points representing particles in general. The coupling links each particle in the same way with the motion of the heavy system while there is no direct interaction between the particles. Note that in general the heavy system may be a mechanical multibody system or a discretized elastic body, and the coupling may be a nonlinear kinematic constraint. Our model below covers these situations as well.

We use the state variables \((r, \dot{r}) \in T^{\mathbb{R}^n_r}\), the mass \(M_r\) and internal forces \(F_i(r)\) for the equations of motion of the heavy system. The second system is called the particle system where the variables \((Q_j, \dot{Q}_j) \in T^{\mathbb{R}^n_q}\) denote the state of the \(j\)th particle. All \(N\) particles have the same mass \(M_q\) and the same internal force function \(F_q(Q_j)\) is acting on them.

The constraint function

\[ g : \mathbb{R}^n_r \times \mathbb{R}^{n_q} \to \mathbb{R}^n_q : (r, Q_j) \mapsto g(r, Q_j) \]
couples the heavy system with each individual particle. The constraints are uniform in \( j \) in the sense that up to a constant initial offset, one function acts as the constraint for all particles.

We assume that \( g \) is twice continuously differentiable, i.e. \( g \in C^2 \) and it is locally invertible w.r.t. \( q \), i.e.

\[
\text{rank} \left( \frac{\partial g}{\partial Q_j}(r, Q_j) \right) = n_q, \quad (H1)
\]

for all \( r \in \mathbb{R}^{n_r} \) and \( q_j \in \mathbb{R}^{n_q} \). Obviously, this assumption is strong and allows us, at least locally, to compute the position \( Q_j \) of each particle from the position \( r \) of the heavy system. The equations of motion in Newtonian form are given by

\[
M_r \ddot{r} = F_r(r) - \sum_{j=1}^{N} \frac{\partial g}{\partial r}(r, Q_j) \lambda_j, \quad (3.1)
\]

\[
M_q \ddot{Q}_j = F_q(Q_j) - \frac{\partial g}{\partial Q_j}(r, Q_j) \lambda_j, \quad (3.2)
\]

\[
g(r, Q_j) = g(r(0), Q_j(0)), \quad \text{for all } j = 1, \ldots, N. \quad (3.3)
\]

The algebraic variables of this system are the Lagrangian multipliers \( \lambda_j \in \mathbb{R}^{n_q} \), \( j = 1, \ldots, N \) that correspond to the constraints in (3.3). Again, we point out that up to a constant only one identical constraint function is used for all particles. Moreover, all particles are independent in the sense that there are no direct interactions between them.

The system (3.1) to (3.3) forms a differential-algebraic system with differential index 3 \([3]\). It would now be possible to apply the same steps as in Section 2. However, using the intuition from Section 2.2 we can apply the mean-field limit directly to the DAE by means of the following steps:

1. We assume that the all particles \( Q_j \) are initially independent and identically distributed with probability law \( \mu_\text{in} \in \mathcal{P}^1(\mathbb{R}^{n_q}) \), hence

\[
Q_j^{\text{in}} \sim \mu_\text{in}, \quad \text{for all } j = 1, \ldots, n.
\]

The realistic number of particles is given by the constant \( N_{\text{real}} \in \mathbb{N} \).

2. We use the equations for the particle positions (3.2) and (3.3) to define a characteristic flow

\[
Q(t, \cdot) : \mathbb{R}^{n_q} \to \mathbb{R}^{n_q}.
\]

In this case, the equations for the characteristic flow are given by a infinite family of differential-algebraic equations for \( Q(\cdot, q^{\text{in}}) \) and \( \lambda(\cdot, q^{\text{in}}) \). For each \( q^{\text{in}} \in \mathbb{R}^{n_q} \) the characteristic flow has to satisfy

\[
M_q \dot{Q}(t, q^{\text{in}}) = F_q(Q(t, q^{\text{in}})) - \frac{\partial g}{\partial Q}(r, Q(t, q^{\text{in}})) \lambda(t, Q(t, q^{\text{in}})), \quad (3.4)
\]

\[
g(r, Q(t, q^{\text{in}})) = g(r^{\text{in}}, q^{\text{in}}). \quad (3.5)
\]

We refer to these equations as the mean-field characteristic flow equations with constraints. This allows us to conclude that the statistics of the particles is the pushforward of the initial measure under the characteristics flow

\[
Q_j(t) \sim \mu_t := Q(t, \cdot) \# \mu_\text{in}.
\]
3. Motivated by the strong law of large numbers, we replace the influence of the particles on the heavy system by the corresponding mean-field constraint force, i.e.,

\[
\frac{1}{N} \sum_{i=1}^{\infty} \frac{\partial g}{\partial r}(r, Q_i) \lambda_i \sim \int_{\mathbb{R}^n} \frac{\partial g}{\partial r}(r, q) \lambda(t, q) \, d\mu(q).
\]

(3.6)

The results of steps 1 to 3 yield the system

\[
M_r \ddot{r} = F_r - \int_{\mathbb{R}^n} \frac{\partial g}{\partial r}(r, q) \lambda(t, q) \, d\mu(q),
\]

(3.7)

\[
M_q \ddot{Q} = F_q - \frac{\partial g}{\partial Q}(r, Q(t, q)) \lambda(t, q(t, q^{in})),
\]

(3.8)

\[
g(r, Q(t, q^{in})) = g(r^{in}, q^{in}),
\]

(3.9)

\[
\mu : = Q(t, \cdot)\#\mu^{in}
\]

(3.10)

with initial conditions

\[
r(0) = r^{in}, \quad \dot{r}(0) = s^{in}
\]

and initial particle measure

\[
\mu^{in} \in \mathcal{P}^1(\mathbb{R}^n).
\]

(3.11)

We call (3.7) to (3.9) the mean-field characteristic flow equations with constraints. They are one possibility to characterise the equations of motion for partially kinetic systems.

Example 3.1 (Mean-field characteristic flow with constraints for attached cross-bridges)

As a continuation of the discussion in Section 2, we can compute the corresponding constrained kinetic system, which is given by

\[
M_r \ddot{r} = -\gamma r - \int_{\mathbb{R}^n} G_r^T \lambda(t, q) \, d\mu(q),
\]

(3.13)

\[
M_q \ddot{Q} = -\gamma Q(t, q^{in}) - \lambda(t, Q(t, q^{in})),
\]

(3.14)

\[
G_r r + Q(t, q^{in}) = G_r r^{in} + q^{in},
\]

(3.15)

\[
\mu : = Q(t, \cdot)\#\mu^{in}.
\]

(3.16)

To show energy conservation for constrained physical system, it is in general instructive to use the DAE formulation instead of a formulation with eliminated Lagrangian multipliers.

Lemma 3.2 (Energy conservation for partially kinetic systems) If there exists a Lagrangian function for the heavy system

\[
L_r(r, \dot{r}) = \frac{1}{2} \dot{r}^T M_r \dot{r} - U_r(r)
\]

and a uniform Lagrangian for all single particles

\[
L_q(Q_j, \dot{Q}_j) = \frac{1}{2} \dot{Q}_j^T M_q \dot{Q}_j - U_q(Q_j),
\]

for the right scale, if would be required to multiply this by an factor \(L\), where \(L\) describes the physically realistic number of particles of the system, as explained in Section 2.2.
then the kinetic system has the Lagrangian

\[ L(r, \dot{r}, Q, \dot{Q}) = L_r(r, \dot{r}) + \int_{\mathbb{R}^n_q} L_q(Q(t, q^m(\cdot)), \dot{Q}(t, q^m)) \, d\mu^m(q^m). \]

In particular, the following energy is conserved

\[ E = \frac{1}{2} r^T M_r \dot{r} + U_r(r) + \int_{\mathbb{R}^n_q} \frac{1}{2} \dot{Q}(t, q^m)^T M_q \dot{Q}(t, q^m) + U_q(Q(t, q^m)) \, d\mu^m(q^m). \]

**Proof** We use the splitting \( E = E_r + E_q \) with

\[ E_r = T_r(\dot{r}) + U_r(r) \quad \text{and} \quad E_q = \int_{\mathbb{R}^n_q} T_q(\dot{Q}(t, q^m)) + U_q(Q(t, q^m)) \, d\mu^m(q^m) \]

where \( T_r(\dot{r}) = \frac{1}{2} r^T M_r \dot{r} \) and \( T_q(\dot{Q}_j) = \frac{1}{2} \dot{Q}_j^T M_q \dot{Q}_j \) denote the kinetic energies. We compute

\[
\frac{dE_q}{dt} = \int_{\mathbb{R}^n_q} \dot{Q}(t, q^m)^T M_q \dot{Q}(t, q^m) - F_q^T \dot{Q}(t, q^m) \, d\mu^m(q^m) \\
= - \int_{\mathbb{R}^n_q} \dot{Q}(t, q^m)^T \frac{\partial g^T}{\partial q} \lambda(Q(t, q^m)) \, d\mu^m(q^m).
\]

In the last equations the balance law for the heavy system \([3.1]\) was used. The time derivative of \( E_q \) is

\[
\frac{dE_q}{dt} = \int_{\mathbb{R}^n_q} \dot{Q}(t, q^m)^T M_q \dot{Q}(t, q^m) - F_q^T \dot{Q}(t, q^m) \, d\mu^m(q^m) \\
= - \int_{\mathbb{R}^n_q} \dot{Q}(t, q^m)^T \frac{\partial g^T}{\partial q} \lambda(Q(t, q^m)) \, d\mu^m(q^m).
\]

Here, \([3.2]\) was applied in the last line. Using the time derivative of \([3.8]\) we obtain

\[
\frac{dE}{dt} = - \int_{\mathbb{R}^n_q} \dot{Q}(t, q^m)^T \frac{\partial g^T}{\partial q} \lambda(Q(t, q^m)) + Q(t, q^m)^T \frac{\partial g^T}{\partial q} \lambda(Q(t, q^m)) \, d\mu^m(q^m) \]

\[
= - \int_{\mathbb{R}^n_q} \left( \dot{r}^T \frac{\partial g^T}{\partial r} + \dot{Q}(t, q^m)^T \frac{\partial g^T}{\partial q} \right) \lambda(Q(t, q^m)) \, d\mu^m(q^m) \]

\[
= 0,
\]

which concludes the proof.

**Remark 3.3 (Mean-field characteristic flow for general DAE)** The steps [7] to 2 are also applicable to derive the mean-field characteristic flow of a general DAE with uniform, but not necessarily full-rank, constraints. For this purpose, consider the system of constrained interacting particles

\[
\dot{Q}_j = \sum_{i=1}^N K(Q_j, Q_i) \frac{\partial g^T}{\partial Q_j}(Q_i) \lambda_j, \quad \text{for all} \ j = 1, \ldots, N,
\]

\[
g(Q) = g(Q^m), \quad \text{for all} \ j = 1, \ldots, N.
\]
Here, \( K : \mathbb{R}^n \times \mathbb{R}^n \to \mathbb{R}^n \) represents the pairwise interaction force between two particles. The resulting mean-field characteristic flow with constraints is given by the family of DAEs

\[
\dot{Q}(t,q^m) = \int_{\mathbb{R}^n} K(Q(t,q^m),q) - \frac{\partial g^T}{\partial Q}(q)\lambda(q) \, dq, \\
g(Q(t,q^m)) = g(q^m), \\
\mu := Q(t,\cdot)\#\mu^m
\]

for all \( q^m \in \mathbb{R}^n \). We are not aware of other references to this system from a DAE perspective, but it is a quite natural construction. The corresponding mean-field PDE in the unconstrained case is known as the Jens-Vlaslov equation [6,16].

### 3.2 Index Reduction for Partially Kinetic Systems

For each fixed \( q^m \in \mathbb{R}^n \) the equations (3.8) and (3.9) form a DAE of differential index 3. The index reduction can therefore be performed simultaneously in \( q^m \in \mathbb{R}^n \) for all DAEs of the infinite family of DAE.

Another approach would be that the index reduction of the discrete system is performed in a finite space with vectors \((Q_j)_{j=1,\ldots,N} \in (\mathbb{R}^n)^N\) and the index reduction for the kinetic system applies the same transformations to infinite-dimensional vectors \(Q(t,\cdot) \in C(\mathbb{R}^n,\mathbb{R}^n)\).

We demonstrate the index reduction for the example from Section 2.

**Example 3.4 (Index reduction for attached cross-bridges)** Equation (3.19) directly yields a formula for the Lagrangian multiplier

\[
\lambda(t,Q(t,q^m)) = -\gamma_q Q(t,q^m) - M_q \ddot{Q}(t,q^m), \\
= -\gamma_q Q(t,q^m) + M_q \ddot{G}_r \tilde{r}(t).
\]

In the last line, we used the second time derivative of the constraint (3.15), i.e. \( \ddot{Q}(t,q^m) = -\gamma_q \ddot{r}(t) \). To insert the expression for \( \lambda \) into (3.13) requires a pull-back of the measure \( \mu \) to \( \mu^m \). This yields

\[
\int_{\mathbb{R}^n} G^T_r \lambda(t,q) \, d\mu(q) = \int_{\mathbb{R}^n} G^T_r \lambda(t,Q(t,q^m)) \, d\mu^m(q^m). 
\]

Now we can insert (3.24) into (3.13), which gives

\[
M_r \ddot{r} = -\gamma_q \ddot{r} - \int_{\mathbb{R}^n} G^T_r (-\gamma_q Q(t,q^m) + M_q \ddot{G}_r \tilde{r}(t)) \, d\mu^m(q^m) \\
= -\gamma \ddot{r} + \int_{\mathbb{R}^n} G^T_r \gamma_q q \, dq \, d\mu(q) - \left( \int_{\mathbb{R}^n} G^T_r M_q G_r \, d\mu^m(q^m) \right) \tilde{r}(t).
\]

This is exactly the previously derived force balance law for the heavy system in (2.16).

The steps of Example 3.4 can be generalized. The only additional difficulty are the presence of mixed second order derivatives of the constraint. Therefore we just state the resulting equations of the general mean-field characteristic flow for partially kinetic systems

\[
m_{\text{eff}}(\mu)(\cdot) = f_{\text{eff}}(r,\cdot,\mu), \\
\dot{Q}(t,q^m) = v_{\text{eff}}(r,\cdot, q^m), \\
\mu := Q(t,\cdot)\#\mu^m
\]

for all \( q^m \in \mathbb{R}^n \).
with the lengthy definitions
\[ m_{\text{eff}}(r, \mu_q) := M_r + \int (G_q(r,q))^T M_q(G_q(r,q))^{-1} G_q(r,q) \, d\mu_q(q), \]
(3.31)
\[ f_{\text{eff}}(r, \dot{r}, \mu_q) := F_r + \int (G_q(r,q))^T (G_q(r,q))^{-1} (F_q(q) + M_qG_q^{-1}\kappa(r, \dot{r}, q)) \, d\mu_q(q), \]
(3.32)
\[ v_{\text{eff}}(r, \dot{r}, q) := (G_q(r,q))^{-1} G_r(r,q) \dot{r}. \]
(3.33)

Here, we additionally use the notation \( G_r := \frac{\partial g}{\partial r} \) and \( G_q := \frac{\partial g}{\partial q} \). The term \( \kappa \) collects all mixed derivatives of the constraint, i.e.
\[ \kappa(r, \dot{r}, q) := \frac{\partial^2 g}{\partial t^2}(r,q)[\dot{r}, \dot{r}] + \frac{\partial^2 g}{\partial r\partial q}(r,q)[\dot{r}, \dot{v}_{\text{eff}}(r, \dot{r}, q)] + \frac{\partial^2 g}{\partial q^2}(r,q)[v_{\text{eff}}(r, \dot{r}, q), v_{\text{eff}}(r, \dot{r}, q)]. \]
(3.34)

Moreover, it is possible to reconstruct the value of the Lagrange multiplier depending on \( r(t) \) as
\[ \lambda(t,q) := (G_q(r,q))^{-T}(F_q(q) + M_q(G_q(r,q))^{-1}(G_r(r,q)\dot{r} + \kappa(r, \dot{r}, q))). \]
(3.35)

This allows to construct a solution for the mean-field characteristic flow with constraints (3.37) to (3.39) from a solution of the above system (3.28) and (3.29). Since this result is still preliminary, we formulate it in terms of a hypothesis.

**Hypothesis 3.5 (Existence theorem)** The existence theory for the kinetic model of interacting particle systems [6, Section 1.3] can be adapted to partially kinetic equations. With the norm
\[ \|Q(t, \cdot)\|_\kappa := \sup_{q \in \mathbb{R}^n} \|Q(t, q')\|_{\sup_{q'}}, \]
the equations (3.28) and (3.29) form a differential equation \( \dot{x} = f(x) \) in the Banach space \( \mathbb{R}^n \times \mathbb{R}^n \times C([\mathbb{R}^n \times \mathbb{R}^n]) \) with the above norm for the flow component. If \( H1 \) and Assumptions 7 to 9 are satisfied, an iteration of the right-hand side, i.e. \( f^n = f \circ f \circ \cdots \circ f \), is a contraction on the Banach space, which is sufficient to prove the global existence of solutions.

### 3.3 Mean-Field PDE for Partially Kinetic Systems

In Section 2.3 a mean-field PDE was derived from the mean-field characteristic flow without constraints. The link between the family of ODEs and the first order PDE is provided by the method of characteristics. Using the same approach, we can also derive the mean-field equation for partially kinetic systems, which is given by
\[ m_{\text{eff}}(r, \mu_q) \ddot{r} = f_{\text{eff}}(r, \dot{r}, \mu_q), \]
(3.36)
\[ \frac{\partial u}{\partial t}(t,q) + v_{\text{eff}}(r, \dot{r}, q) \cdot \frac{\partial u}{\partial q}(t,q) = 0, \quad \text{for all } q \in \mathbb{R}^n, \]
(3.37)
with initial conditions
\[ r(0) = r^0 \in \mathbb{R}^n, \quad \dot{r}(0) = s^0 \in \mathbb{R}^n, \quad \text{and} \quad u(t,q) = u^0(q) \quad \text{for all } q \in \mathbb{R}^n \]

This equation is the most useful formulation of partial kinetic systems for numerical simulations. We will present some numerical examples in Section 4.
3.4 Stability Results

The perturbation index provides a tool to measure the numerical difficulty of certain DAE formulations. This requires in particular to choose a norm for the state space of the differential-algebraic system, with the Euclidean norm being a common candidate. In the following, we also use the Euclidean norm on $\mathbb{R}^{n_r}$ and $\mathbb{R}^{n_q}$.

A similar analysis for (3.7), (3.8) and (3.9) requires a choice of a particular norm or metric to measure perturbations of the particle state. In kinetic theory the Monge-Kantorovich metric (also called Wasserstein distance) is a very useful choice. In the following we want to motivate this choice and present a stability estimate for partially kinetic systems.

**Remark 3.6 (Discussion of alternative norms for particle systems.)** A naive choice of a norm for the particle state would be to apply the sup norm on the characteristic flow, i.e.

$$
\|Q(t, \cdot)\|_{\text{sup}} := \sup_{q' \in \mathbb{R}^{n_q}} \|Q(t, q')\|.
$$

But this would forbid many reasonable flows, for example a rotation of the space $\mathbb{R}^{n_q}$ would have infinite sup norm. A slightly better choice, which allows in particular, rotations of the space, is a weighted sup norm, namely

$$
\|Q(t, \cdot)\|_{X} := \sup_{q' \in \mathbb{R}^{n_q}} \frac{\|Q(t, q')\|}{1 + \|q'\|}.
$$

In [6] this norm is used to show global existence of solutions for the mean-field characteristic flow of a system of interacting particles. However, both norms $\|\cdot\|_{\text{sup}}$ and $\|\cdot\|_{X}$ ignore the distribution of particles, i.e. they are independent of $\mu_t$. Moreover, they are unrelated to the mean-field limit.

A metric which does not suffer from the disadvantages stated in Remark 3.6 is the Monge-Kantorovich metric, which intuitively measures the length of the optimal transport of one measure to the mass distribution of the other one, as visualized in Fig. 10.

It is instructive to understand the distance between two discrete measures. For the Monge-Kantorovich metric, particles are interchangeable, in the sense that the labeling of $Q_1, \ldots, Q_N$ is not respected. The Monge-Kantorovich metric tries to find the sum of paths on which the particles must be transported, such that all all particles from one distribution are transported to positions of the other distribution, as visualized in Figs. 10 and 11.

The measure theoretic definition of the Monge-Kantorovich metric does not directly relate to this picture, but provides a useful formulation for analysis. We define the set of coupling measures $\Pi(\mu_1, \mu_2)$ to be the set of all Borel probability measures $\pi : \mathcal{B}(\mathbb{R}^{n_q} \times \mathbb{R}^{n_q}) \to [0, 1]$ with first and second marginals to be $\mu_1$ and $\mu_2$. Equivalently, for each $\pi \in \mathcal{P}(\mathbb{R}^{n_q} \times \mathbb{R}^{n_q})$ we have

$$
\pi \in \Pi(\mu_1, \mu_2) \quad \Leftrightarrow \quad \int_{\mathbb{R}^{n_q} \times \mathbb{R}^{n_q}} (\phi_1(x) + \phi_2(y)) \pi(dx, dy) = \int_{\mathbb{R}^{n_q}} \phi_1(x) \mu_1(dx) + \int_{\mathbb{R}^{n_q}} \phi_2(y) \mu_2(dy)
$$

for all $\phi_1, \phi_2 \in C(\mathbb{R}^{n_q})$ such that $\phi_1, \phi_2 \in O(\|q\|^\gamma)$ as $\|q\| \to \infty$.
The distance between two points in $\mathbb{R}^n$ might be considered to be the length of the shortest line between those points (right). For highly concentrated distributions $\mu_t, \tilde{\mu}_t \in P_1(\mathbb{R}^n)$ is desirable that the distance is similar. This can be achieved by using the Monge-Kantorovich distance, which is related to the optimal gradient flow which transforms $\mu_t$ into $\tilde{\mu}_t$. In the right figure, this is indicated by some intermediate state of the transformation.

The Monge-Kantorovich metric considers interchangeable particles, i.e., the optimal transport from one state to another could lead to different paths.

**Definition 3.7** ([6, Definition 1.4.1]) We define the Monge-Kantorovich distance (with exponent 1) via

$$W_1(\mu, \nu) := \inf_{\pi \in \Pi(\mu, \nu)} \int_{\mathbb{R}^n \times \mathbb{R}^n} \|x - y\| \pi(dx, dy).$$

The Monge-Kantorovich distance is also called Wasserstein distance. The map $W_1$ is a metric on the space $P_1(\mathbb{R}^n)$. For a detailed exposition, we refer to [25]. Note that the metric is related to optimal flows from $\mu$ to $\nu$ with respect to a cost functional implied by the norm $\|\cdot\|$ on $\mathbb{R}^n$.

With Definition 3.7, we have collected all theoretical tools to state an adapted version of Dobrushin’s stability estimate for partially kinetic systems. This theorem is inspired by Dobrushin’s stability estimate for interacting particle systems [6, Theorem 1.4.3].
Hypothesis 3.8 (Dobrushin’s stability estimate for partially kinetic systems) Let $\mu_1^{in}, \mu_2^{in} \in \mathcal{P}(\mathbb{R}^n)$ be initial particle distributions and $(r_1^{in}, \sigma_1^{in}), (r_2^{in}, \sigma_2^{in}) \in \mathbb{R}^{n_r} \times \mathbb{R}^{n_\sigma}$ be initial states for the heavy system. For all $t \in [0, T]$, we define

$$
\mu^1_t := Q(t, \cdot, r_1^{in}, \mu_1^{in}) \# \mu_1^{in} \quad (3.40)
$$

$$
\mu^2_t := Q(t, \cdot, r_2^{in}, \mu_2^{in}) \# \mu_2^{in} \quad (3.41)
$$

where $Q(t, \cdot, r^{in}, \sigma^{in}, \mu^{in})$ denotes the solution of the mean-field characteristic flow equations (3.28) and (3.29) for the given initial conditions $(r_1^{in}, \sigma_1^{in}, \mu_1^{in})$.

Let (H1) and Assumptions 7 to 9 (see Appendix) hold. Then for a fixed initial condition $(r_1^{in}, \sigma_1^{in}, \mu_1^{in})$, for arbitrary initial conditions $(r_1^{in}, \sigma_1^{in}, \mu_1^{in})$ and for all $t \in [0, T]$ one has

$$
\left\| r_1(t) - r_2(t) \right\| + \left\| \sigma_1(t) - \sigma_2(t) \right\| + W_1(\mu_1^t, \mu_2^t) \leq e^{Lt} \left( \left\| r_1^{in} - r_2^{in} \right\| + \left\| \sigma_1^{in} - \sigma_2^{in} \right\| + W_1(\mu_1^{in}, \mu_2^{in}) \right). \quad (3.42)
$$

The constant $L$ depends on $(r_1^{in}, \sigma_1^{in}, \mu_1^{in})$ and on the end of the time interval $T$.

The inequality (3.42) has far reaching consequences and can be considered as one possible cornerstone of rigorous proofs on mean-field convergence [5]. The perturbation index of a DAE also measures the influence of perturbations on the system, not only with respect to perturbation on the initial data, but also in the differential and algebraic equations.

In Section 3.2, we will shortly explain which numerical challenges appear in the simulation of partially kinetic systems. The difficulties motivate to work on the existence and stability analysis of partially kinetic systems. Therefore a perturbation index for the mean-field PDE of partially kinetic systems (3.36) and (3.37) is desirable.

As in kinetic theory [16], we assume that Dobrushin’s stability estimate for partially kinetic systems in Hypothesis 3.8 might play a similar role as Gronwall’s inequality in the classical analysis of ODE and DAE. One indicator is the consistency with the mean-field limit. For discrete states the Mongo-Kantorovich metric is similar to the finite dimensional metric, in the sense

$$
W_1(\mu_1^{emp}, \mu_2^{emp}) \approx \frac{1}{N} \sum_{j=1}^{N} \left\| Q_j - \bar{Q}_{\sigma(j)} \right\|
$$

where $\sigma : \{1, \ldots, N\} \rightarrow \{1, \ldots, N\}$ is a permutation of the labels such that the sum of norms is minimal. Therefore, the metric provides a useful tool to study numerical effects and to lift properties of the discrete to the kinetic system.

3.5 Coupling with Nonlinear Elasticity

Muscle models as presented in Section 2 provide an example with linear constraints. This is clearly not sufficient for multi-scale models. On a large scale, muscles can be modelled as nonlinear, quasi-incompressible, hyperelastic solids [22].

Using the framework of partially kinetic systems, the link between the hyperelastic model at the large scale for the muscle tissue and the cross-bridge model at the physiological scale is given by a nonlinear constraint. The constraint is linear with respect to the extension of cross-bridges but nonlinear with respect to the deformation of the tissue. In this sense, the situation is still similar to Section 2. Additional complexity arises since the heavy system in
this setting is described by the PDEs of elasticity, which results in an infinite-dimensional system already at the discrete case. We can assume that most material points of the muscle are occupied by sarcomeres, which are single units of actin and myosin filaments as modelled in Section 2. This leads mathematically to an infinite family of cross-bridge models at each spatial point of the muscle. A formal derivation is possible and not very different from the theory presented in this article. Analytical results, however, are far more challenging in this setting. Even more, the cross-bridges of sarcomeres at neighbouring spacial points can be in very different states. A mathematical rigorous approach therefore requires a justification for spatial averaging over the cross-bridge states.

4 Numerical Examples of Partially Kinetic Systems

Partially kinetic systems are mixed systems involving Newton’s equations of motion for the heavy components (3.28) and a non-linear transport equation for the particle density (3.37). Therefore, a perfect numerical scheme for such a system should not only nearly conserve energy and momentum, but also the mass of the particle density. It is an open issue if such a scheme exists.

In the literature on sliding filament theory a method that is often used is the distributed moment method [27]. In this method, the particle distributions are parametrised by the first moments of a scaled Gaussian distribution. For specific cases, it is possible to derive a closed set of differential equations for these first moments and thus approximate the solution of a transport equation with source terms by a three dimensional ODE. The problem of conservation of statistical and physical invariances is partially addressed in [19]. This method is successfully used in multi-scale simulations [2, 11]. However, distributed moment methods do not yield a numerically convergent discretization of (3.36) and (3.37). This is acceptable for most applications but not for a mathematically rigorous theory.

4.1 Implementation Details

The numerical simulations in this article are preformed in a straightforward way. More advanced and adapted methods are out of scope for this article.

For numerical time integration, the methods RADAU [9, Section IV.8.] and LSODA [20] from the python package scipy.integrate [26] were used. For all examples in this article, the time integration was successful without any indicators for numerical instabilities in the regular case (H1) with linear constraint.

For space discretisation of the transport equation (3.37), the standard upwind discretisation was used [18, Section 10.4]. For simplicity we assumed zero boundary conditions for the numerical spatial domain. The grid was chosen sufficiently wide such that the boundary conditions do not influence the simulation results.

For systems with linear constraints, the use of the upwind method might appear exaggerated. Instead, it would be sufficient to approximate the shift between $\mu$ and the initial measure $\mu_0$, which is given by $\int G_{\mu_0} \tau d\tau$. If the transport equation (3.37) has no source terms, this numerical scheme is fast and stable. In the presence of source terms, the resulting numerical scheme contains stiff differential equations. However since source terms are essential for realistic muscle models, we neglect this specialised method here and focus on the upwind discretization instead.
4.2 Attached Cross-Bridges with Constraints

Simulation results of the discrete description (2.1), (2.2) and (2.5) and of the corresponding mean-field PDE (2.12) and (2.19) have been presented in Figs. 4, 6 and 7. Linear constraints are numerically pleasant and the kinetic description leads to a good approximation of the discrete system.

In Fig. 12, we compare the energies of both systems with the same data as in Fig. 7. This demonstrates an essential drawback of the kinetic description. The discrete system (2.1), (2.2) and (2.5) is a DAE for which numerical schemes with asymptotic energy conservation exist [7]. In this particular linear example, the numerical conservation of energy is not very difficult for the discrete system. However, due to numerical diffusion of the upwind discretisation, the conservation of energy is lost in the partially kinetic description, even if the same time integration methods are used as in the discrete case. We are not aware of a method which conserves the total energy numerically and at the same time works in the presence of source terms.

5 Conclusion

In this article, we have presented the new framework of partially kinetic systems. We have motivated this abstract class by generalising the kinetic models for the cross-bridge dynamics in skeletal muscles in a manner which allows us to add constraints. Thus, we have provided a rigorous link between existing physiological models at different scales. It can be argued that so far, the coupling is restricted to a rather simple model scenario. Thus, there is a need to generalize the model. At the same time there are theoretical issues that call for a profound analysis.

With probability theory at their core, kinetic equations are quite different to handle than DAEs, and this applies to the numerical schemes as well. In our experience, the differential-algebraic perspective allows a very explicit form of the equations and is therefore more applicable than an alternative abstract differential geometric theory. This means that the methodology of index reduction applies seamlessly to partially kinetic systems. Based on this approach, we are currently working on the transfer of fundamental results such as energy conservation from the particle system to the kinetic description.
Finally, numerical methods for partially kinetic systems are still in their infancy. We have presented an example in which the conservation of energy is violated, which already indicates the limitations of a naive discretization.

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A Assumptions for Dobrushin’s Theorem for Partially Kinetic Systems

We state the assumptions for Dobrushin’s stability estimates for partially kinetic systems Hypothesis 3.8. The proof is not published yet, therefore a critical view is encouraged.

Assumption 1 (Coercive mass) The particle mass is always semi-positive definite, i.e. $M_q$ is symmetric and $\forall M_q > 0$, for all $v \in \mathbb{R}^n$.

The mass of the heavy system symmetric and coercive, i.e. there exists a constant $\delta_m$, such that

$$w^T M_w \geq \frac{1}{\delta_m} \|w\|^2, \quad \text{for all } w \in \mathbb{R}^n.$$

Assumption 2 (Lipschitz continuous terms) There are constants $L_1, L_f, L_m$ such that

$$\left|v_{\text{eff}}(r_1, s_1, q_1) - v_{\text{eff}}(r_2, s_2, q_2)\right| \leq L_1 (\|r_1 - r_2\| + \|s_1 - s_2\| + \|q_1 - q_2\|) \quad (H3.a)$$

$$\left|F_{\text{eff}}^{(1)}(r_1, s_1, q_1) - F_{\text{eff}}^{(1)}(r_2, s_2, q_2)\right| \leq L_f (\|r_1 - r_2\| + \|s_1 - s_2\| + \|q_1 - q_2\|) \quad (H3.b)$$

$$\left|M_{\text{eff}}^{(1)}(r_1, q_1) - M_{\text{eff}}^{(1)}(r_2, q_2)\right| \leq L_m (\|r_1 - r_2\| + \|q_1 - q_2\|) \quad (H3.c)$$

holds for all $(r_1, s_1), (r_2, s_2) \in T^* \mathbb{R}^n$ and $q_1, q_2 \in \mathbb{R}^n$. Notice, that here only the effective force and mass of one particle have to be Lipschitz. The definitions of $M_{\text{eff}}^{(1)}(\cdot)$ and $F_{\text{eff}}^{(1)}(\cdot)$ are given in (2.8) or for the general case by

$$M_{\text{eff}}^{(1)}(r, q) := m_{\text{eff}}(r, \delta_q) \quad \text{and} \quad F_{\text{eff}}^{(1)}(r, q) := f_{\text{eff}}(r, q, \delta_q) \quad (A.1)$$

where $\delta_q$ denote the Dirac delta measure with unit mass at the point $q \in \mathbb{R}^n$.

Assumption 3 (Existence of a total energy) We assume that the total energy of the discrete system is of the form

$$E = T_i(r) + U_i(r) + \sum_{j=1}^{n} T_q(Q_j) + U_q(Q_j).$$

and $E$ is continuous. The forces are given by $F_i = -\nabla U_i$ and $F_q = -\nabla U_q$ and kinetic energies are bilinear $T_i(r) = \frac{1}{2} r^T M_i r$ and $T_q(Q) = \frac{1}{2} Q^T M_q Q$.

Assumption 4 (Bounded force on convex sets) For each constant $E_{\text{max}}$, the force $F_{\text{eff}}^{(1)}$ is linearly bounded w.r.t. $q$ on the convex hull

$$B_{E_{\text{max}}} = \text{conv}(\{(r, q) \in \mathbb{R}^n \times \mathbb{R}^n \mid E(r, q, v_{\text{eff}}(r, q)) \leq C, \text{ for some } q \in \mathbb{R}^n\}).$$

We denote the upper bound for linear rate of increase of $F_{\text{eff}}^{(1)}$ by

$$F_{\text{max}}(E_{\text{max}}) := \sup_{(r, q) \in B_{E_{\text{max}}}} \sup_{q \in \mathbb{R}^n} \frac{\|F_{\text{eff}}^{(1)}(r, q, q)\|}{1 + \|q\|} < \infty. \quad (A.2)$$

The factor is motivated by the norm defined during the existence proof, as explained in Hypothesis 3.8.
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