Simulating electromechanical delay across the scales – relating the behavior of single sarcomeres on a sub-cellular scale and the muscle-tendon system on the organ scale

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The time lag between the activation of a muscle and the development of force is commonly denoted as electromechanical delay (EMD). Within this work, a multi-scale model of an idealized muscle-tendon system is used to analyze EMD on different characteristic anatomical length scales. Thereby, the simulated EMD-stretch curves for a complete muscle-tendon system and a single sarcomere are significantly different. While for an isolated muscle muscle EMD is shown to be strongly determined by excitation-contraction coupling (ECC), the EMD-stretch curve for a complete muscle-tendon system is influenced by additional factors, such as, e.g., the tendon. Further, it is shown that the action potential conduction velocity (APCV) has minor influence on EMD.

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1 Introduction

Electromechanical delay (EMD) denotes the time lag between the activation of a muscle and the development of measurable force [1]. Thus, EMD is associated with injuries such as, e.g., chronic ankle instability [2]. Among other factors, EMD is assumed to depend on the action potential conduction velocity (APCV) and the mechanical material behavior of various structures within the muscle-tendon system [1]. While it is hardly feasible to quantify the contribution of specific properties on EMD experimentally, physiologically detailed in silico models have the capability to characterize EMD. For example, a recent simulation study based on Hill-type muscle models could show that EMD depends on the stretch of the muscle-tendon system [3]. However, Hill-type models are spatially lumped and thus cannot resolve spatial heterogeneities, the propagation of action potentials (APs) or relate the microscopic to the macroscopic system behavior. Thus, in this study a continuum mechanical multi-scale model of an idealized muscle-tendon system is used to analyze EMD in individual sarcomeres, i.e. on the microscale, and for the muscle-tendon system, i.e. on the organ scale.

2 Methods

The applied multi-scale skeletal muscle model (cf. [4, 5]) solves for macroscopic deformations of the tissue while taking into account the chemo-electro-mechanical behavior of embedded computational muscle fibers, i.e. resolving the propagation of APs and excitation-contraction coupling (ECC). Thereby, the continuum mechanical constitutive material description of muscle tissue is based on the linear superposition of a passive contribution \( P_{\text{passive}} \) and the activation modulated (sarcomere based) contributions \( P_{\text{active}} \) and \( P_{\text{titin}} \), i.e.

\[
P = P_{\text{passive}} + P_{\text{active}} + P_{\text{titin}} = pF^{-T}.
\]

Assuming incompressibility, the hydrostatic pressure \( p \) enters Eqn. (1) as a Lagrange multiplier, whereby \( F^{-T} \) is the transposed inverse of the deformation gradient tensor. The tendon tissue is modeled as incompressible, isotropic, hyper-elastic material. Thereby, the characteristic J-like stress-stretch relation of both passive muscle and tendon tissue can be well described by an isotropic hyper-elastic Ogden-type material [6]. The corresponding material parameters are given in Tab. 1. The APCV can be adjusted by modulating the capacitance of the muscle fiber membranes \( C_{\text{mem}} \), (cf. Tab. 1).

EMD is simulated for an idealized cuboid muscle-tendon system, i.e. consisting of a muscle fiber bundle which is attached to a tendon (see Tab. 1), and different initial lengths of the muscle-tendon system, quantified as stretch \( \lambda \) with respect to the reference length. To induce an isometric contraction, the muscle is stimulated by applying a current density of 90 µA cm\(^{-2}\) in the middle of each computational muscle fiber. For each numerical experiment, EMD is calculated as the time difference between the event of the stimulus and the instant when the stress at the end of the sample has changed by 1% of the maximum active stress. Accordingly, EMD is determined for a single sarcomere by evaluating the (microscopic) active stress on the stimulation point of an arbitrarily chosen muscle fiber.
Fig. 1: Left: EMD-stretch curve for an isolated muscle applying different APCVs (×) and a corresponding sarcomere (○). Right: EMD-stretch curve for a muscle-tendon system applying an APCV of 3.5 m s⁻¹ (△) and a corresponding sarcomere (○).

### Table 1: Model parameters that are not taken from [4].

| Parameter                        | Value                  |
|----------------------------------|------------------------|
| **Reference geometry**           |                        |
| Muscle length                    | l₀ (m)                 |
| Tendon length                    | l₀ (m)                 |
| Width                            | w₀ (m)                 |
| Height                           | h₀ (m)                 |
| **Material parameters**          |                        |
| Muscle                           | µₘ, 2.22 N cm⁻²         |
| Tendon                           | µₜ, 0.04 N cm⁻²         |
| Maximum active stress            | pₘax, 10 N cm⁻²        |
| Membrane capacitance             | C₀, 0.58 µF cm⁻²       |
| APCV 2 m s⁻¹                     | C₀, 0.58 µF cm⁻²       |
| APCV 3.5 m s⁻¹                   | C₀, 1 µF cm⁻²          |
| APCV 5.5 m s⁻¹                   | C₀, 1.98 µF cm⁻²       |

### 3 Results

Considering an isolated muscle, the EMD-stretch curve for a single sarcomere and the whole muscle have a similar shape (cf. Fig. 1, left). In detail, given an APCV of 5.5 m s⁻¹, the muscle and the corresponding sarcomere show the same EMD values, except for λ = 1.15 and λ = 1.2 where EMD for the muscle is 0.1 ms lower than for the sarcomere. Further, with decreasing APCV, EMD increases in the muscle while qualitatively maintaining the shape of the EMD-stretch curve. Thereby, the observed changes are smaller than 0.6 ms. Simulating EMD for a muscle-tendon system (APCV = 3.5 m s⁻¹) yields a different shape of the EMD-stretch curve, i.e. the highest value of 32.2 ms is reached for λ = 1.05 from where a steep decrease in EMD that plateaus for higher stretches and reaches its minimum value of 8.6 ms for λ = 1.3 (cf. Fig. 1, right) can be observed. In contrast, EMD for a single sarcomere within the muscle-tendon system is nearly invariant with respect to the applied stretch.

### 4 Discussion

The simulated EMD-stretch curve of the muscle-tendon system (cf. Fig. 1, left) well reflects experimental findings (e.g. unpublished evaluation of data from [7]). Thus, it can be concluded that the applied multi-scale model resolves the major properties determining EMD and can be used for an in silico characterization of EMD. While EMD for an isolated muscle is mainly determined by ECC within the sarcomeres (cf. Fig. 1, left), the results suggest that additional factors contribute to EMD for a muscle-tendon system. Considering a muscle-tendon system, the numerical experiments indicate that the characteristic EMD-stretch curve is strongly related to the nonlinear material behavior of the tendon. A lower APCV yields higher EMD in the isolated muscle, however, the observed changes are within a range of 0.5 ms and thus, for the muscle-tendon system only one APCV is shown. The observation of lower EMD values in the muscle than in the sarcomere (cf. Fig. 1, left) can potentially be explained by the fast activation of serial arranged sarcomeres. However, due to the chosen time discretization, i.e. yielding a sampling frequency of 10 kHz, this observation could also be a numerical artefact. Though negligible in the presented scenario, the APCV is believed to contribute to EMD in longer muscles, which will be examined in further studies. Moreover, the influence of additional structural and chemo-electro-mechanical properties of the muscle-tendon system on EMD will be addressed in future works.

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