A Lagrangian perspective on skeletal muscle models

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FB Mathematik
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Vienna

What I want to do...

simulation of skeletal muscles

What I did so far...

~~simulation of skeletal muscles~~

reformulation of skeletal muscles models

The principle question

$$\begin{cases} H(p, q) & = H_1(q_1, p_1) + H_2^{(n)}(q_2, p_2) \\ g(q_1, q_2) & = 0 \end{cases}$$

for $\dim(q_2) = n \to \infty$, we need statistical ensembles...

	Euler-Lagrange equation	'Partial' Liouville equation	Liouville equation
unknowns	q_1, q_2	q_1, ρ_2	ρ_1, ρ_2
type	Hamiltonian (very big)	Hamiltonian and transport eq.	too complex

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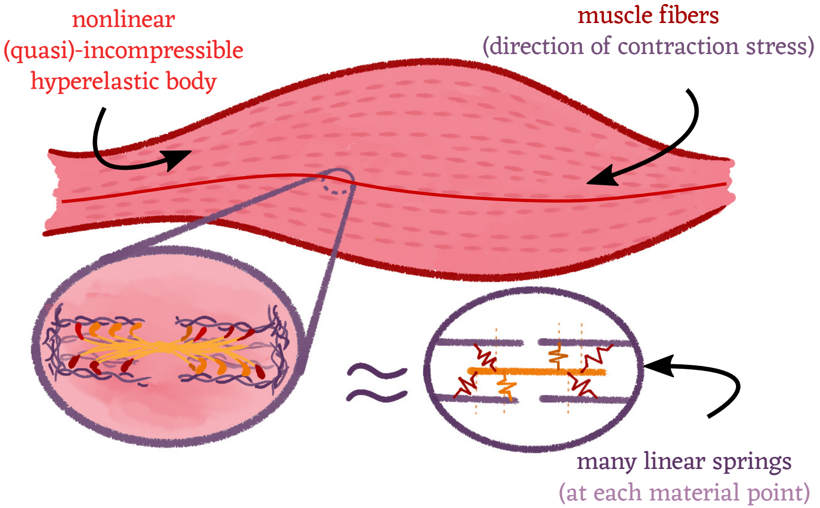
Overview of the model



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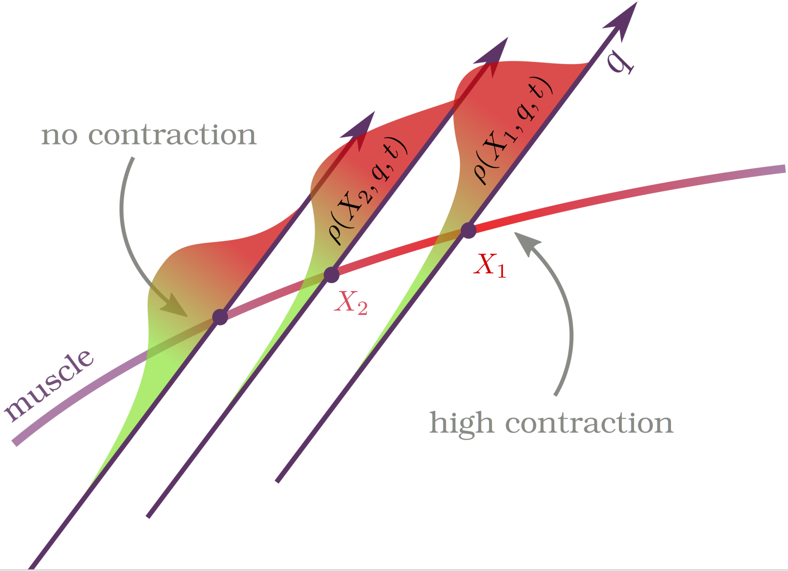

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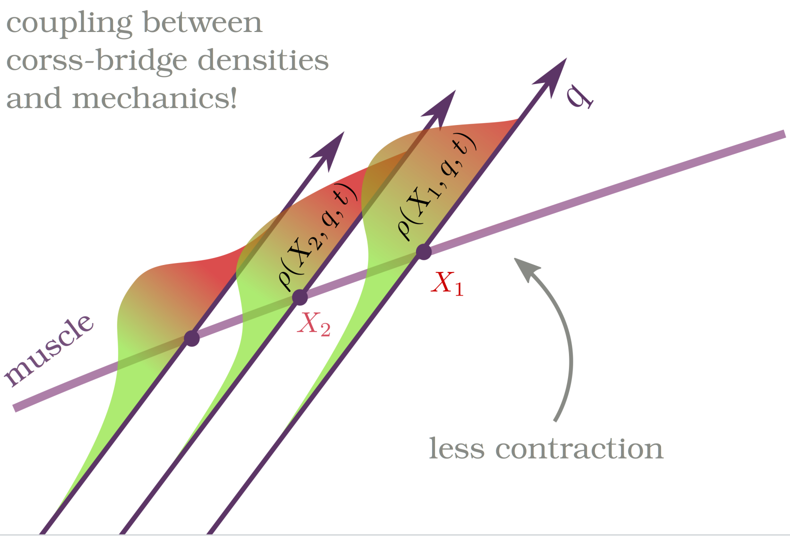

A skeletal muscle model

Combining elasticity and cross-bridge theory yields the model

$$
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\rho\ddot{\varphi} &= \mathrm{Div}\left(\boldsymbol{P}_{\mathrm{active}} + \boldsymbol{P}_{\mathrm{passive}}\right),\\
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p_{\mathrm{act}} &:= \kappa \int_{\mathbb{R}} q \,\mathrm{d}q,\\
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$\rho_q(q,t;X)$ **is different at each material point** $X \in \mathcal{B}$**!**

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$\rho_q(q,t;X)$ **is different at each material point** $X \in \mathcal{B}$**!**

There are smart, but mathematically inconsistent ways to replace the transport equation!

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For $f = g = 0$ the system is conservative!

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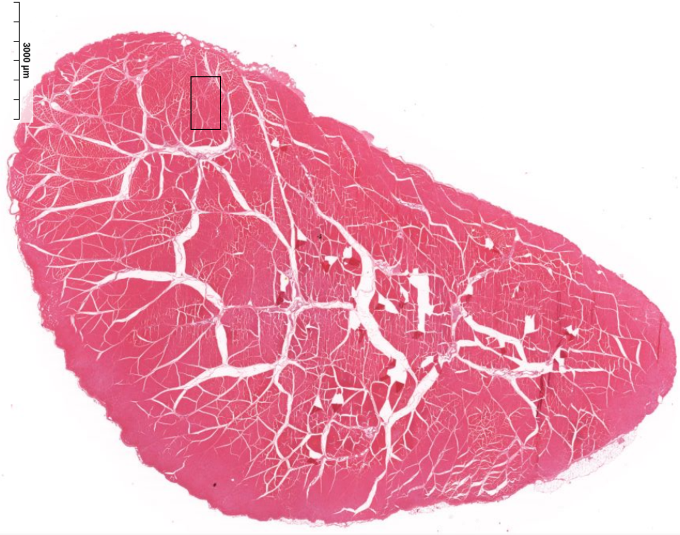
Is the transport equation part of a Hamiltonian system?

Exploration of skeletal muscles



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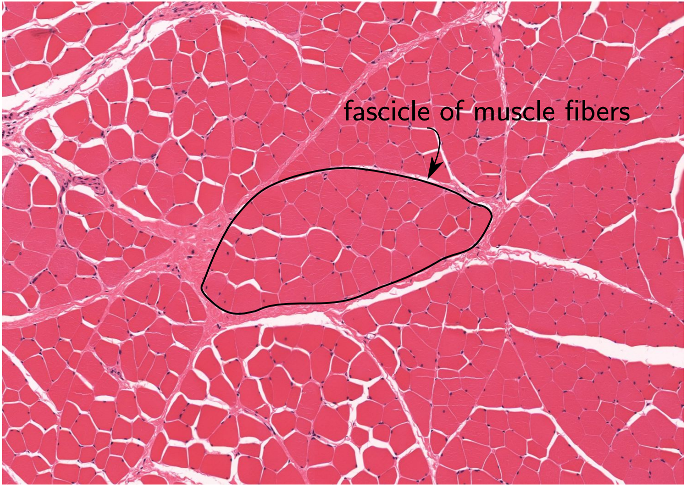

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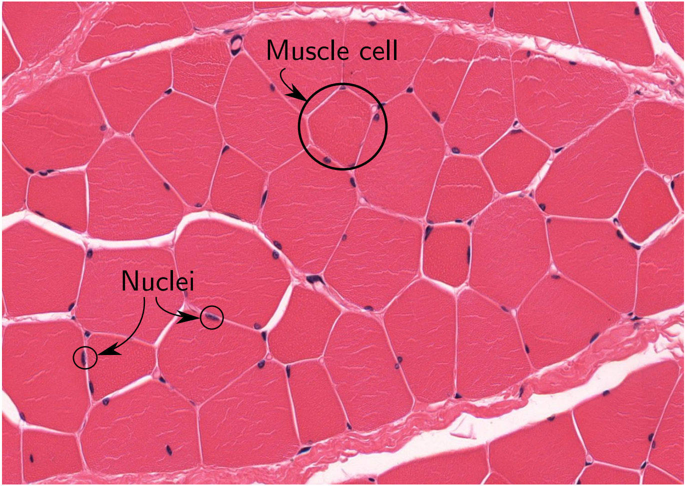
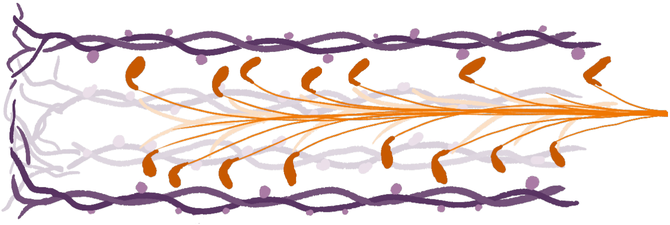


Exploration of skeletal muscles

Many little cross-bridges, taking many little steps. . .



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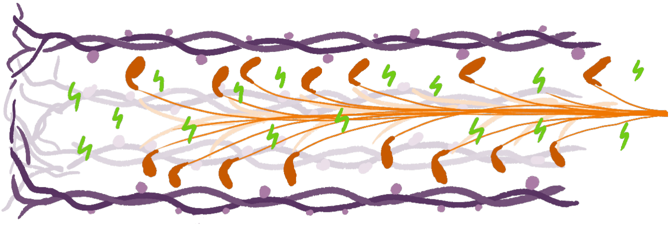

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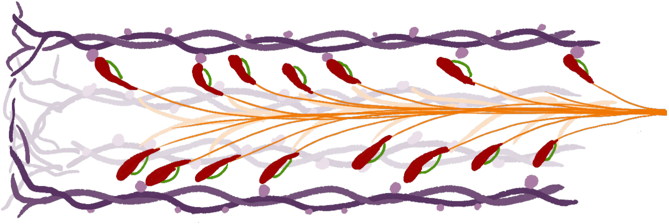

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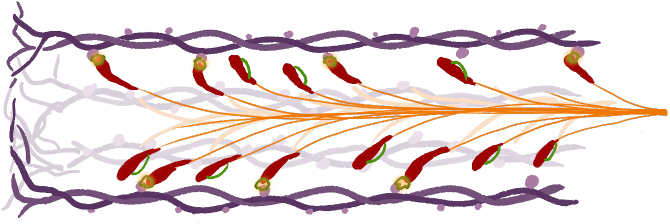

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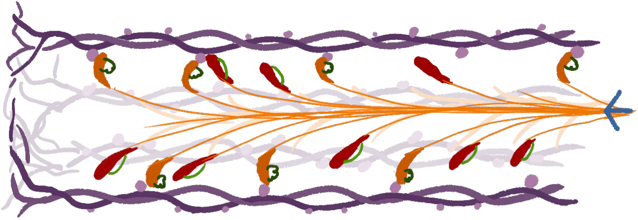

Contraction!

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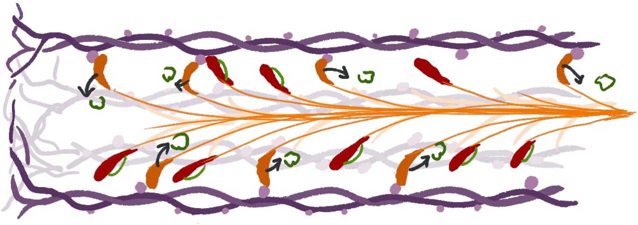

The simplest cross-bridge model possible

We consider attached cross-bridges to act like **linear springs**, i.e.

$$\ddot{q}_i = -\kappa q_i.$$

With q_i being the current displacement of the ith cross-bridge head.

What happens if we ignore attachment and detachment!

Far too restrictive for muscle models!

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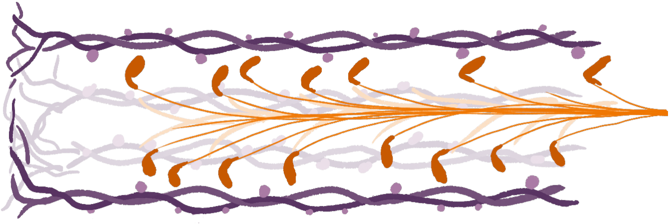
Revisiting the little sarcomere



We do not model this!

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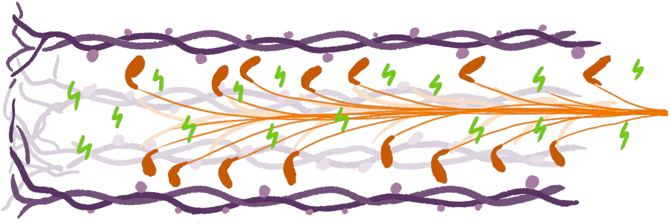

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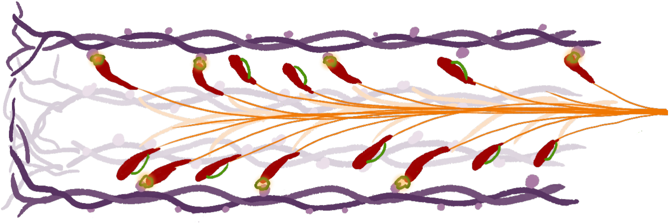
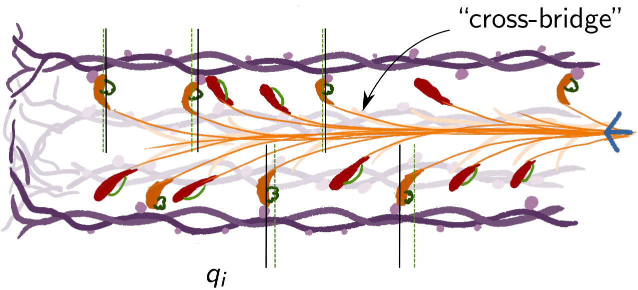


Here our model starts!

Revisiting the little sarcomere



It is just a collection of linear springs!

Revisiting the little sarcomere

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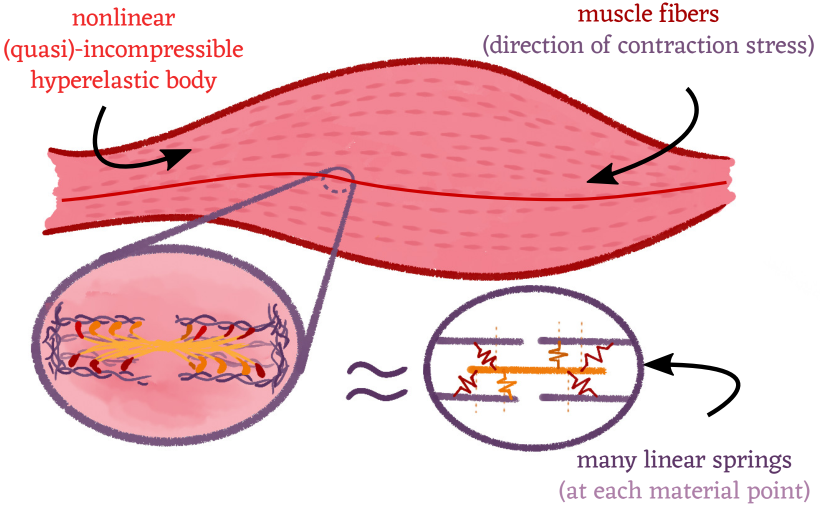
Overview of the model



Using the Lagrangian

$$\widetilde{\mathcal{L}}(\varphi, q_i, \lambda) = \mathcal{L}_{\text{elasticity}}(\varphi) + \mathcal{L}_{\text{linear springs}}(q_i) - \langle \lambda_i, g_i(\varphi, q_i) \rangle$$

we derive the coupled system

$$\begin{aligned} \rho\ddot{\varphi}\,(X,t) &= \operatorname{Div}\left(\boldsymbol{P} - \lambda \boldsymbol{G}\right), \\ m\ddot{q}_i\,(X,t) &= -\kappa q_i\,(X,t) + \lambda_i\,(X,t), \\ g_i\,(X,t) &= 0, \end{aligned}$$

$$\boldsymbol{P} = \frac{\partial \mathcal{L}}{\partial\, \mathrm{D}\varphi}, \quad \boldsymbol{G} = \lambda \frac{\partial g_i}{\partial\, \mathrm{D}\varphi}.$$

How can we derive the transport equation?

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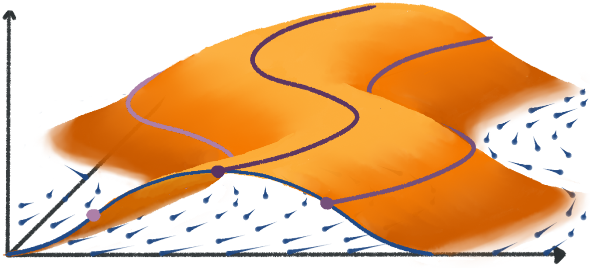
Statistical Ensembles

Key modelling step:



Replacement of the displacements $q_i(t)$ by a density of displacements $\rho_q(q, t)$.

Statistical Ensembles

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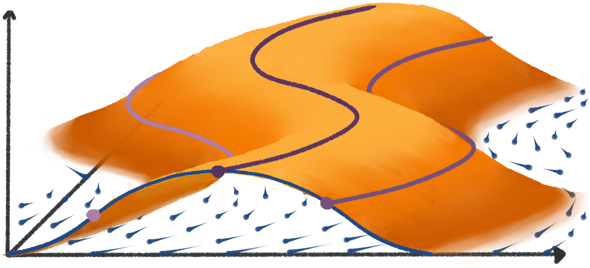

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Statistical Ensembles

We replace the displacements $q_i(t)$ by a density of displacements $\rho_q(q,t)$. The (constraint) equations

$$q_i = \|n_{\text{fiber}}\| + \text{const.}$$

transform to

$$\frac{\partial \rho_q}{\partial t} - v_{\text{fiber}} \frac{\partial \rho_q}{\partial q} = 0.$$

Mathematical tool: Method of characteristics.

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Mathematical tool: Method of characteristics.

The role of the Lagrange multiplier

We can derive a direct formula for the Lagrange multiplier

$$\lambda_i = \kappa q_i - m \frac{\mathrm{d}^2}{\mathrm{d}t^2} \left\| n_{\text{fiber}} \right\| .$$

Since the mass m of a cross-bridge is small

$$\lambda_i \approx \kappa q_i .$$

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A “partial Liouville equation”

We derive the mixed system

$$\rho\ddot{\varphi} = \operatorname{Div}\left(\boldsymbol{P} - \lambda\boldsymbol{G}\right),$$

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Finding good numerics for this equation is my current goal!

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The activation revisited as Lagrangian multiplier

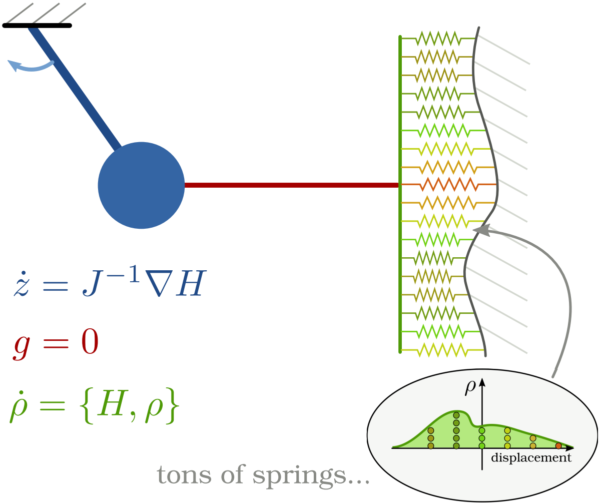
In this Lagrangian framework, we can identify active stress as a coupling term, i.e.

$$\boldsymbol{P}_{\text{active}} = \frac{p_{\text{act}}}{\sqrt{N_f^T \boldsymbol{C} N_f}} N_f \otimes n_f \;\; = \lambda \boldsymbol{G}.$$

If we assume a small mass of myosin heads, both models coincide and we get

$$p_{\text{act}} = \lambda = -\kappa \int \rho(q) q \,\mathrm{d}q$$

A toy example



$$\dot{z} = J^{-1} \nabla H$$

$$g = 0$$

$$\dot{\rho} = \{H, \rho\}$$

tons of springs...

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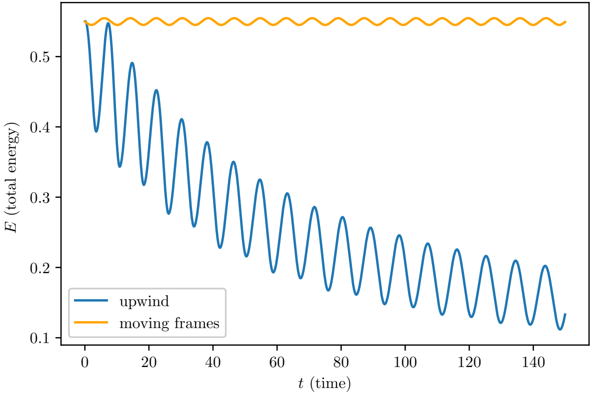

A toy example

Extension to non-conservative case?

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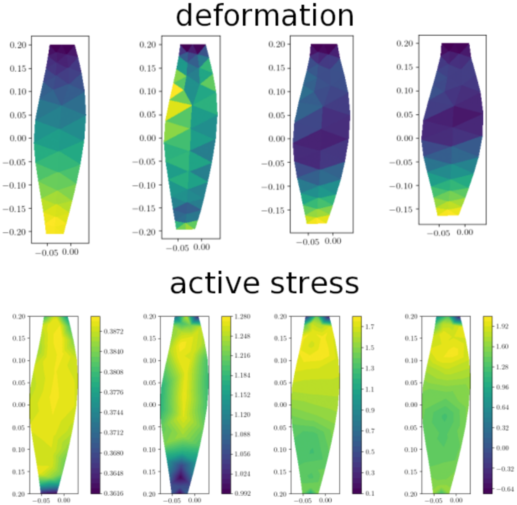
Source terms in the transport equation

$$\frac{\partial \rho_q}{\partial t} - v_{\text{fiber}} \frac{\partial \rho_q}{\partial q} = f \cdot (\rho_q) - g \cdot (1 - \rho_q),$$

lead to stiff equations.

Colourful but unstable for large deformations...



Question I: Stochastic terms?

We just derive the (boring) conservative part of muscle models.

How can we modify the myosin head dynamicsto get contraction?

Mathematical difficulty:

ATP changes the displacement of cross-bridges

$$q \mapsto q + \delta q.$$

This leads to stochastic jump terms!

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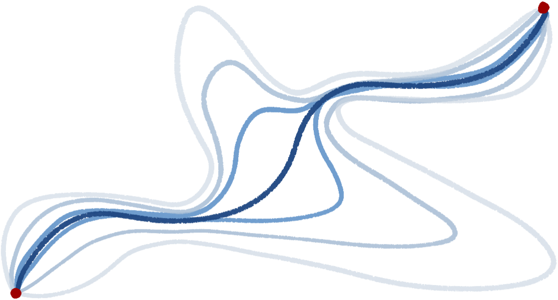
Question II: Variational integration possible?



Variational principle: $\mathrm{d}S(\varphi) = 0.$

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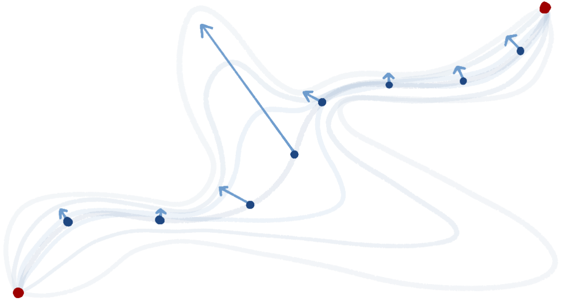

Variational principle: $\mathrm{d}S_h(\varphi_h) = 0.$

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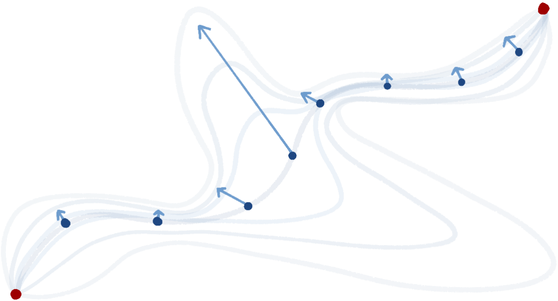

How to integrate the partial Liouville equation (transport equation) and **respect the underlying variational principle?**

Thanks for your attention!