# Is the Whole More Than the Sum of Its Parts? A Constituent Based Material Model for Lung Parenchyma.

**S. M. K. Rausch[1], O. Pack[2], C. Martin[2], S. Uhlig[2] and W.A. Wall[1]**

[1]Institute for Computational Mechanics, Technische Universität München, Germany

[2]Institute for Pharmacology and Toxicology, University Hospital Aachen, Germany

Lehrstuhl für Numerische Mechanik

## Introduction

### Ventilator Induced Lung Injuries (VILI)

- Mechanical ventilation of patients with acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) is a life saving treatment.
- Mechanical ventilation can cause VILI.
- VILI occurs due to overstraining of the alveolar tissue.

### Goal: Improvement of mechanical ventilation strategies

The goal of our research is to improve mechanical ventilation, and thus to reduce the frequency and severity of VILI, as well as the associated high mortality rates.

### Aims:

- **Better understanding of mechanical behavior of alveolar tissue**
- **Development of a better material description of lung tissue**

## Alveolar Tissue

### Macro-scale

Lung parenchyma appears as a continuous tissue.

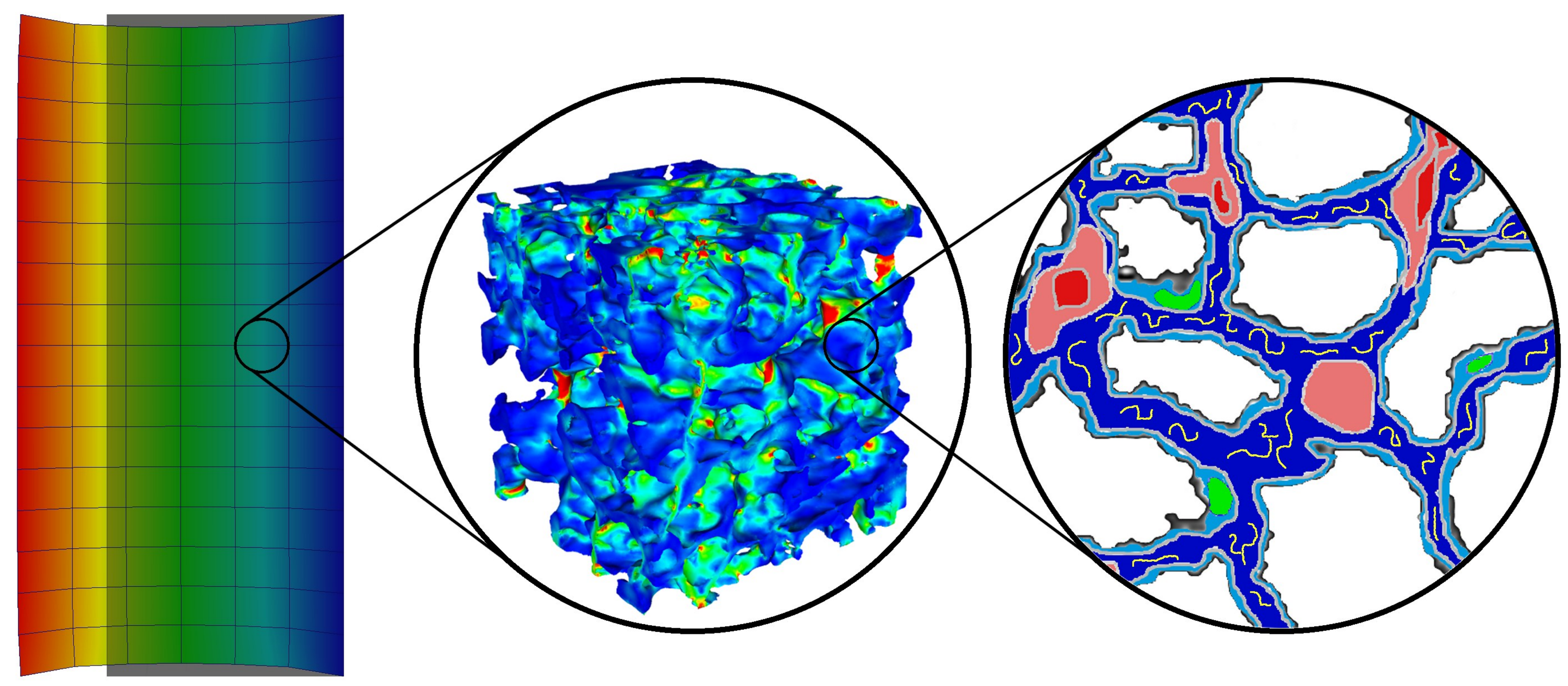
### Meso-scale

Lung parenchyma is a complex sponge-like structure, consisting of 20% tissue and 80% air (for rat lungs).

### Micro-scale:

The parenchyma is further split up into the following components:

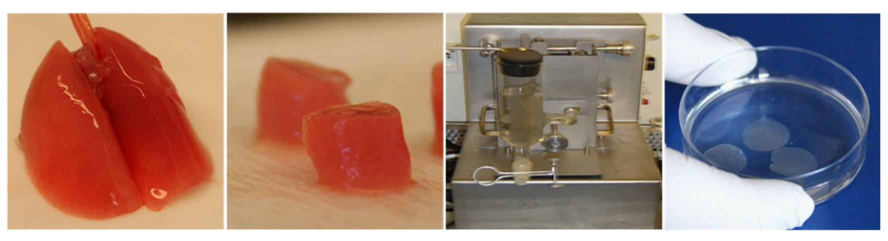
- collagen fibers (CF) and elastin fibers (EF) (yellow)
- interstitium (dark blue)
- basement membrane (light gray)
- epithelial cells (light blue) and their nuclei (green)
- air-tissue interface, covered with a surfactant layer (shades of gray).
- capillaries, filled with blood plasma (light red)
- red blood cells (dark red).
- endothelial cells (not shown) lining the capillary walls.




## Experiments

### Specimens

- Isolated rat lungs
- Precision-cut lung slices (PCLS)
- Viable during testing for at least three days after dissection

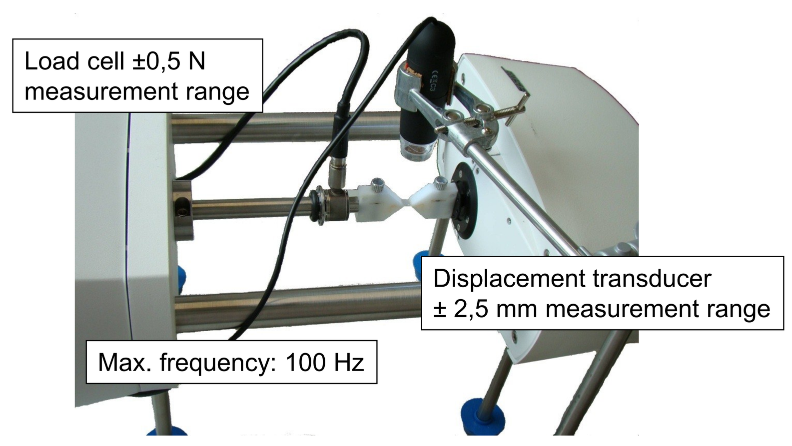


### Testing device

- Bose ElectroForce 3100
- Newly designed tissue clamps

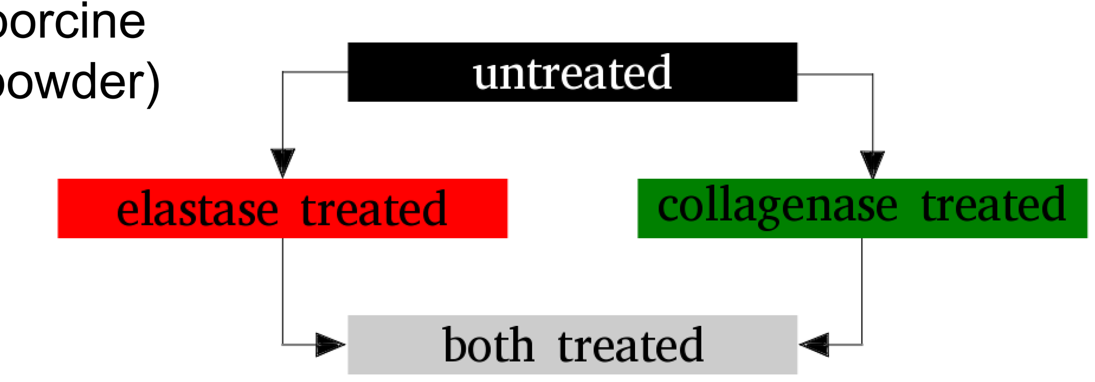
### Material testing

- Preconditioning necessary, due to visco-elastic material properties
- Sinusoidal loading




[Rausch 2011, J Mech Behav Biomed Mater]

- 21 PCLS were examined
  - 10 were treated with collagenase (PCLS were incubated 30 min in collagenase H) prior to elastase
  - 11 were treated with elastase (PCLS were incubated 30 min in E7885 elastase from porcine pancreas-lyophilized powder) prior to collagenase.

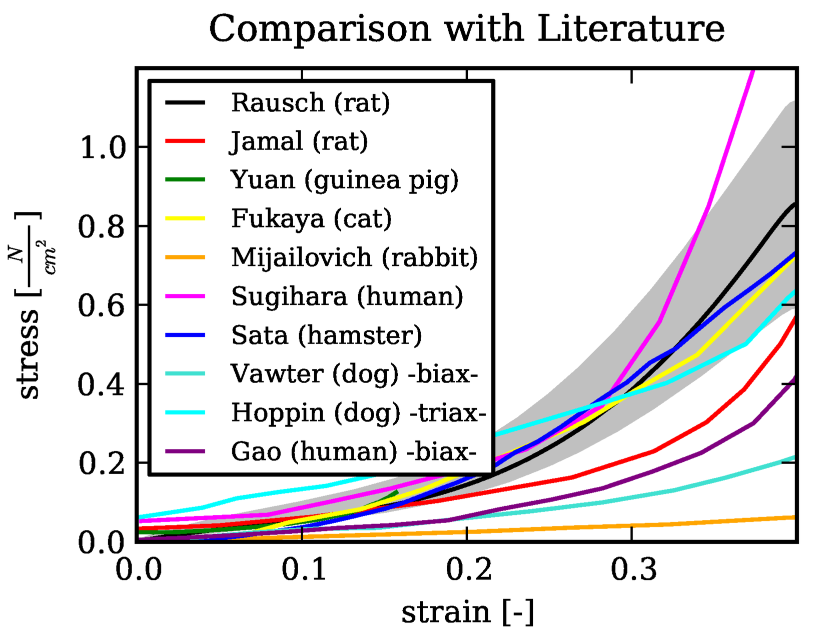



## Experimental Results

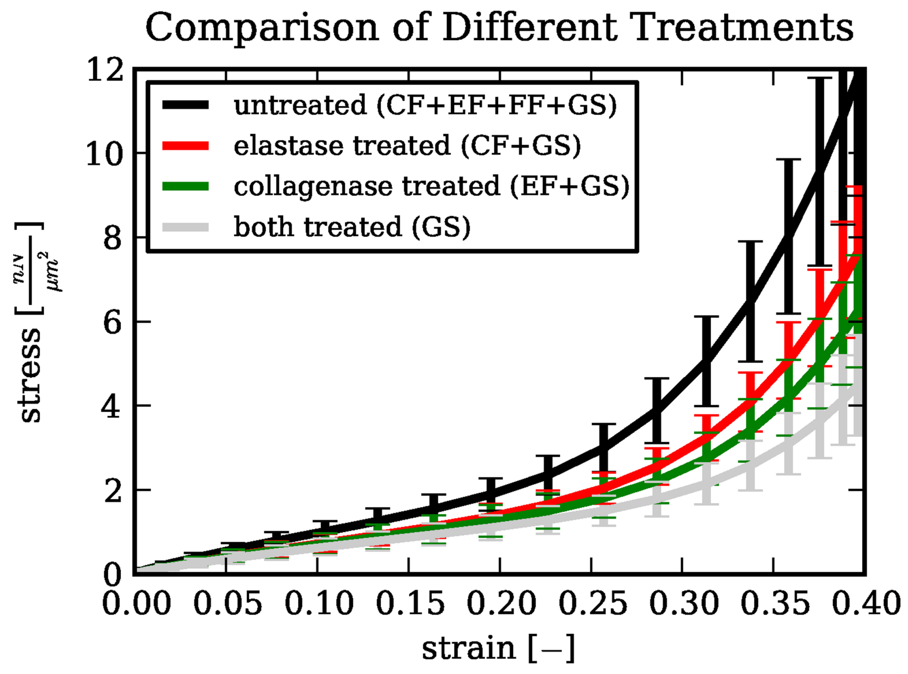
### Comparison with Literature

To test the experimental protocol we compare our experimentally determined curves of the untreated PCLS with the values found in literature. The curves show good agreement of

- the order of magnitude
- and the shape of the curve.



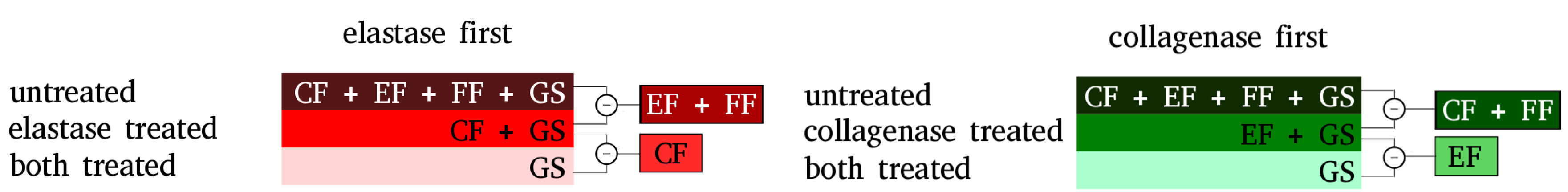

### Experimentally measured curves




- Averaged experimentally determined stress-strain curves
  - untreated PCLS (black),
  - collagenase treated PCLS (green)
  - elastase treated PCLS (red)
  - collagenase as well as elastase treated PCLS (gray).
- Error bars indicate one standard derivation

- The graph shows a clear stress reduction if one, or both of the load-bearing macro-molecules are degenerated.
- Collagenase influences the initial slope as well as the curvature of the stress-strain curve.
- Elastase reduces the initial slope of the curve.

### Determination of the individual constituents

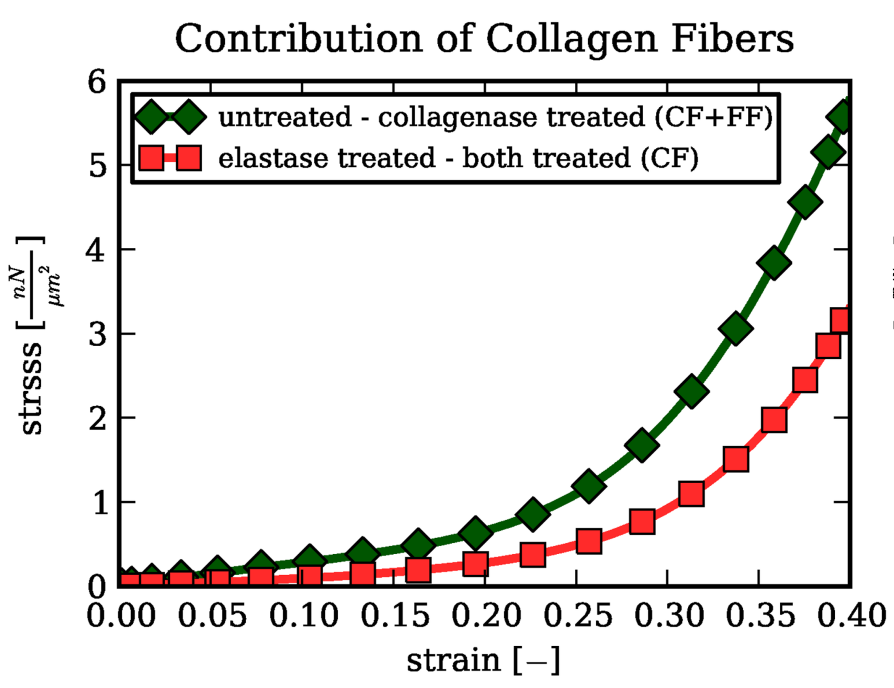


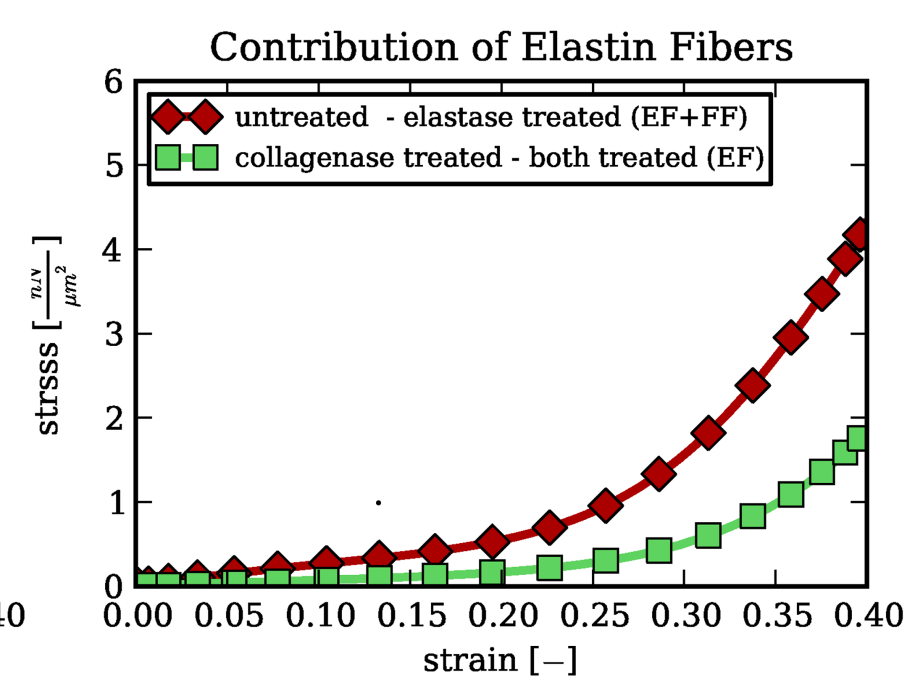

Two ways of calculating the contribution of collagen fibers (CF):

1. Subtracting the curve of collagenase treated PCLS from the curve of untreated PCLS.
2. Subtracting the curve of collagenase and elastase treated PCLS from the curve of elastase treated PCLS.

Two ways of calculating the contribution of elastin fibers (EF):

1. Subtracting the curve of elastase treated PCLS from the curve of untreated PCLS
2. Subtracting the curve of collagenase and elastase treated PCLS from the curves of collagenase treated PCLS.



# Is the Whole More Than the Sum of Its Parts? A Constituent Based Material Model for Lung Parenchyma.

**S. M. K. Rausch[1], O. Pack[2], C. Martin[2], S. Uhlig[2] and W.A. Wall[1]**

[1]Institute for Computational Mechanics, Technische Universität München, Germany

[2]Institute for Pharmacology and Toxicology, University Hospital Aachen, Germany

Lehrstuhl für Numerische Mechanik

## Experimental Conclusion

Difference between the measured curves is the contribution of the fiber-fiber interaction (FF).

$$\Psi = \Psi_{iso}^{GS} + \Psi_{iso}^{CF} + \Psi_{iso}^{EF} + \Psi_{iso}^{FF} + \Psi_{vol}$$

## Material Model Components

### Strain-energy function

- Isotropic, hyperelastic, polyconvex
- split into an isochoric and a volumetric part

$$\Psi = \Psi_{iso}[\bar{I}_1, \bar{I}_2] + \Psi_{vol}[I_3]$$

**The optimal strain energy density functions (SEFs) for each of the constituents is determined, via inverse analysis, from combinations of these summands.**

### Isochoric Parts

Tissue components (elastin, collagen, ground substance, …)

$$\Psi_{neo}^{iso} = c_{lin}(\bar{I}_1 - 3)$$
$$\Psi_{quad}^{iso} = c_{quad}(\bar{I}_1 - 3)^2$$
$$\Psi_{cub}^{iso} = c_{cub}(\bar{I}_1 - 3)^3$$
$$\Psi_{pow4}^{iso} = c_{pow4}(\bar{I}_1 - 3)^4$$
$$\Psi_{pow5}^{iso} = c_{pow5}(\bar{I}_1 - 3)^5$$
$$\Psi_{pow6}^{iso} = c_{pow6}(\bar{I}_1 - 3)^6$$
$$\Psi_{pow7}^{iso} = c_{pow7}(\bar{I}_1 - 3)^7$$
$$\Psi_{mooney}^{iso} = c_1(\bar{I}_1 - 3) + c_2(\bar{I}_2 - 3)$$
$$\Psi_{exp}^{iso} = \frac{k_1}{k_2}\left[\exp\left[k_2\left(\frac{1}{3}\bar{I}_1 - 1\right)\right]^2 - 1\right]$$

### Volumetric Parts

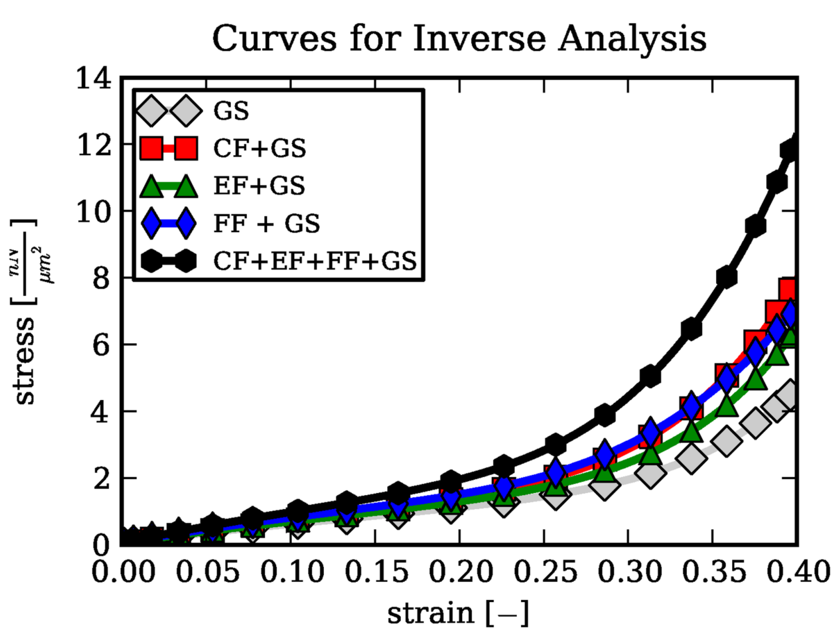
Incompressible alveolar wall and compressible lung parenchyma

$$\Psi_{pen}^{vol} = \epsilon\left(I_3^{\gamma} + \frac{1}{I_3^{\gamma}} - 2\right)$$
$$\Psi_{ogd}^{vol} = \frac{\kappa}{\beta^2}\left(\beta I_3^{1/2} + \frac{1}{I_3^{\beta/2}} - 1\right)$$
$$\Psi_{suss}^{vol} = \kappa\left(I_3^{1/2} - 1\right)^2$$

## Inverse Analysis

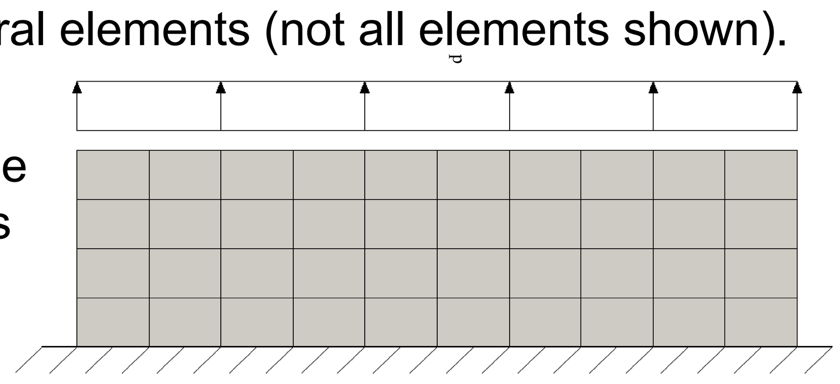
### Fitting the material parameters of the simulation model to experimental results.

- Stress curves from experiment are taken as simulation input.
- Displacement curves from the experiment are taken as criteria for the optimization in the inverse analysis.



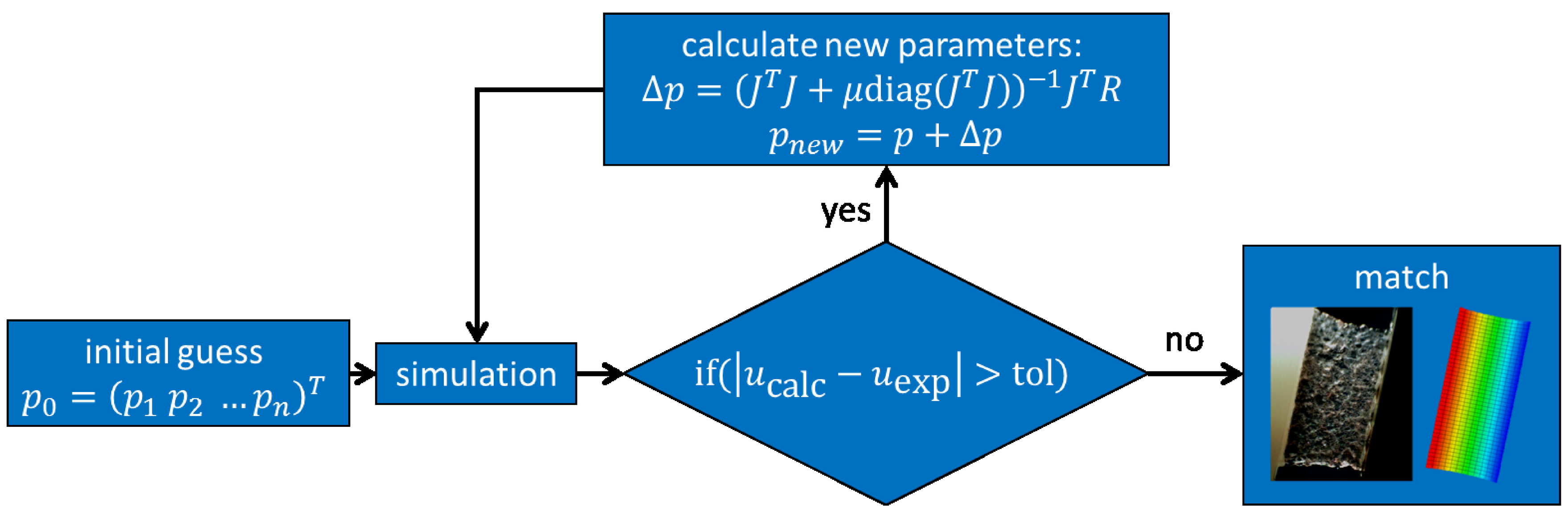

### Simulation model

- The PCLS are discretized with hexahedral elements (not all elements shown).
- One side is fixed (static clamp).
- The other side is loaded equivalent to the experimentally determined stress-curves (moving clamp).



### Fitting algorithm

- Levenberg-Marquardt Algorithm [Marquardt 1963, J Soc Ind Appl Math]




### Data Analysis

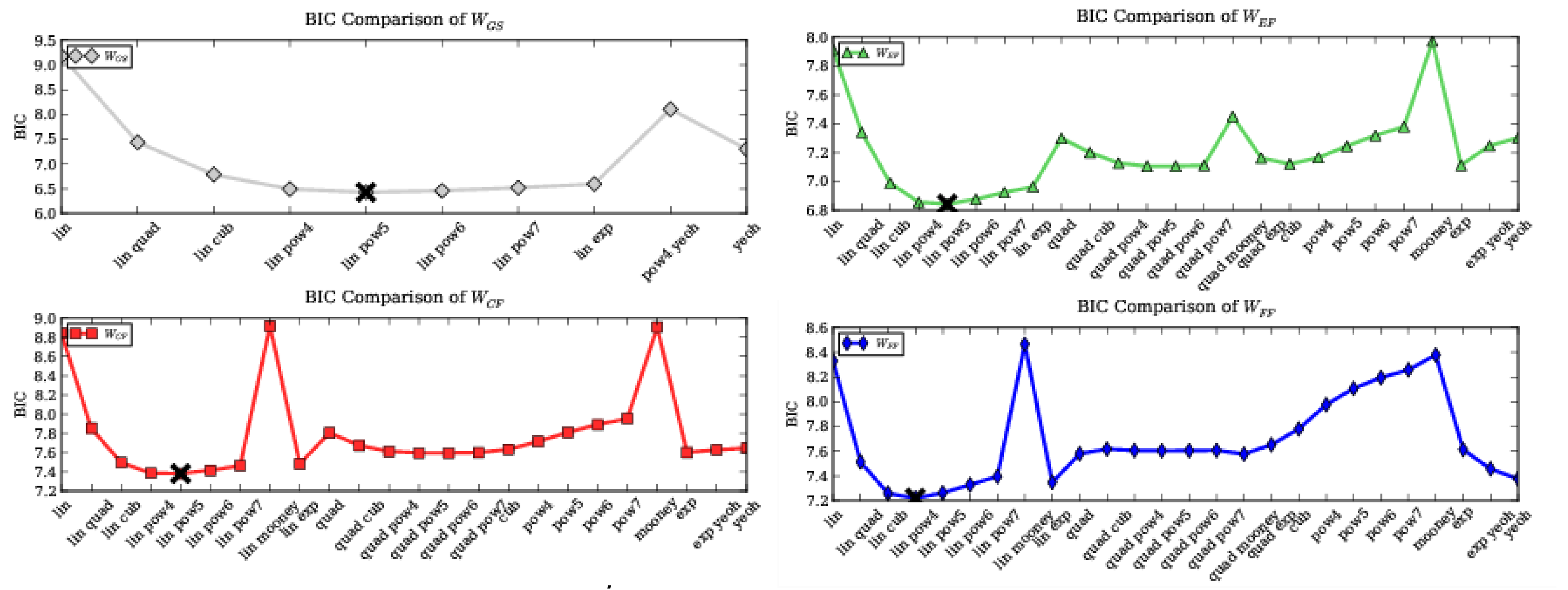
- For comparing the different combinations and recombinations of material models the Bayesian Information Criterion (BIC) is utilized.

### Acknowledgement

Support by the German Science Foundation (DFG) through projects WA 1521/6-2, WA 1521/9-2 and WA 1529/13-1 is gratefully acknowledged.

PAR

## Results




- We found a combination of $\Psi_{neo}^{iso}$ and a higher order term to show the best agreement with the experimental results.
- $\Psi_{iso}^{EF}$ has the lowest material constants, which agrees with the fact that the elastic fibers show the most compliant material behavior.
- The ground substance shows a stiffer behavior for small strains which is reflected by a larger constant within $\Psi_{neo}^{iso}$.

$$\Psi_{CF} = 0{,}565(\bar{I}_1 - 3) + 1186{,}260(\bar{I}_1 - 3)^5$$
$$\Psi_{EF} = 0{,}342(\bar{I}_1 - 3) + 450{,}294(\bar{I}_1 - 3)^5$$
$$\Psi_{FF} = 0{,}789(\bar{I}_1 - 3) + 145{,}782(\bar{I}_1 - 3)^4$$
$$\Psi_{GS} = 1{,}629(\bar{I}_1 - 3) + 174{,}036(\bar{I}_1 - 3)^5 + \frac{8{,}946}{4}(-2\ln J + J^2 - 1)$$

## Conclusion

### Method to determine constituent based material models

The presented method can be applied for every soft biological tissue, containing collagen and elastin fibers.

### Quantification of the contribution of each of the four constituents

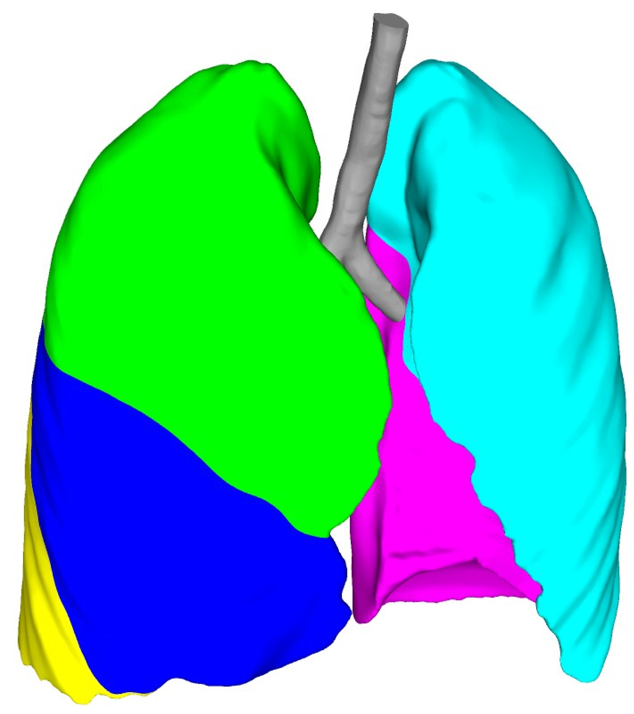
The individual determination, of each constituent, allows us to simulate diseases such as fibrosis, where the fiber content changes.

### Determination of the contribution of the fiber-fiber interaction

It has been shown, that summing up the contributions of the individual components is not enough and that the fiber-fiber interaction has to be included. This interaction was quantified for the first time.

### Application

The determined material model can be utilized in numerical simulations of healthy and diseased lungs [Wall 2010, Int J Num Meth Biomed Eng]. Amongst others these simulations determine the air distribution in mechanically ventilated patients and potential sites of inflammation.



## Future Work

### Determination of alveolar wall material

- Coupling of inverse analysis [Rausch 2011, J Mech Behav Biomed Mater] and multi-scale (FE²) method [Wiechert 2009, Comput Meth Appl Mech Eng]
- Micro-scale: cube with hole
- Optimization of material parameter on micro-scale for experimental results on the macro-scale