BioTechMed-Graz

***Bio**medical Basics-**Tech**nological Developments-**Med**ical Implementation*

Research for Health

Quantitative Biomedicine & Modelling

Computational Cardiology – MUG

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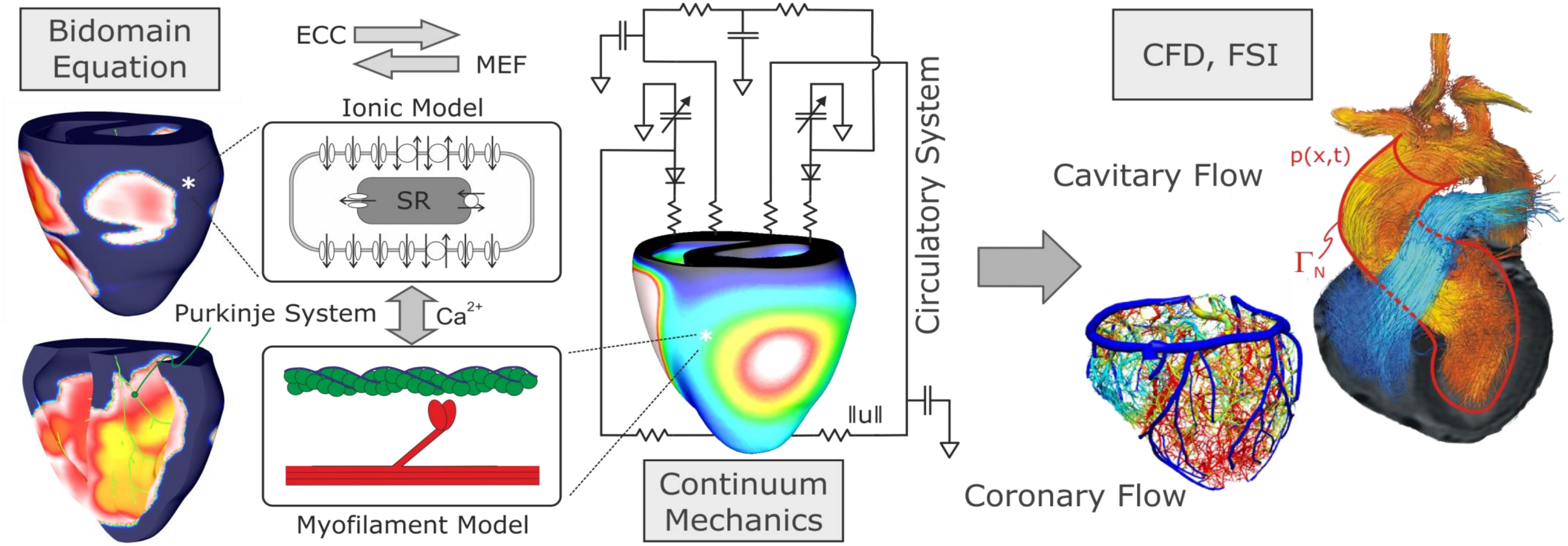
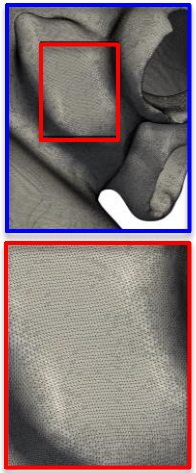
Computing a heart beat



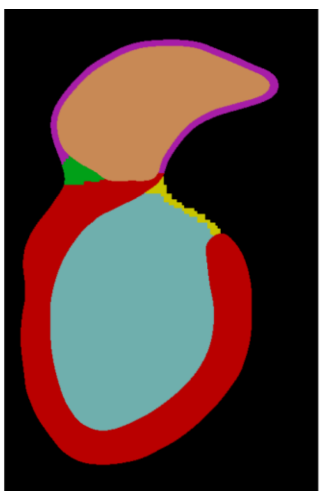
- **Modeling and Computing**
  - Electrophysiology (EP)
  - Non-linear Elasticity
  - Fluid Flow
  - Porous Media Flow
- **EP Applications**
  - Arrhythmogenesis & Defibrillation
- **Mechanics Applications**
  - Heart Failure and CRT
- **Flow Applications**
  - Aortic Valve Disease and Coarctations

Model Building and Computing

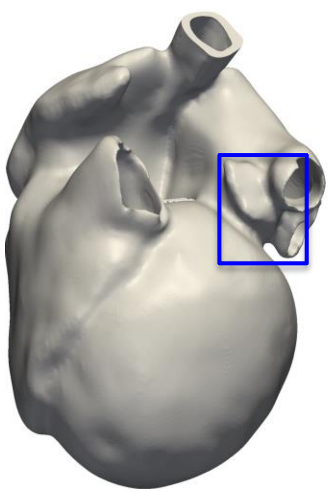
Imaging



Segmentation

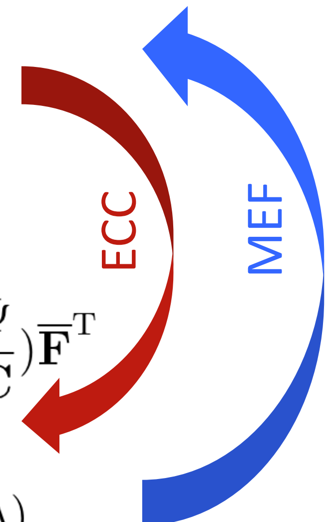


FE Meshing



Mathematical Description

$$
\begin{aligned}
\nabla \cdot (\boldsymbol{\sigma}_i + \boldsymbol{\sigma}_e)\, \mathbf{C}^{-1} \nabla \phi_e &= -\nabla \cdot \boldsymbol{\sigma}_i\, \mathbf{C}^{-1} \nabla V_m - I_e \\
\nabla \cdot \boldsymbol{\sigma}_i\, \mathbf{C}^{-1} \nabla V_m &= -\nabla \cdot \boldsymbol{\sigma}_i\, \mathbf{C}^{-1} \nabla \phi_e + \beta \;\, I_m \\
I_m &= C_m \frac{\partial V_m}{\partial t} + I_{\mathrm{ion}}(V_m, \boldsymbol{\eta}) \\
V_m &= \Phi_i - \Phi_e \\
\frac{\partial \boldsymbol{\eta}}{\partial t} &= f(\boldsymbol{\eta}, V_m, \sigma_a) \\
\mathrm{div}\, \boldsymbol{\sigma}(\boldsymbol{u}) &= \mathrm{b}, \\
\boldsymbol{\sigma} &= \boldsymbol{\sigma}_p + \boldsymbol{\sigma}_a \\
\boldsymbol{\sigma}_p &= J^{-1/3} \overline{\mathbf{F}} (2 \frac{\partial \Psi}{\partial \mathbf{C}}) \overline{\mathbf{F}}^{\mathrm{T}} \\
\boldsymbol{\sigma}_a &= \sigma_a (\overline{\mathbf{f}} \otimes \overline{\mathbf{f}}) \\
\sigma_a &= h(V_m, \boldsymbol{\eta}, \lambda, \dot{\lambda})
\end{aligned}
$$



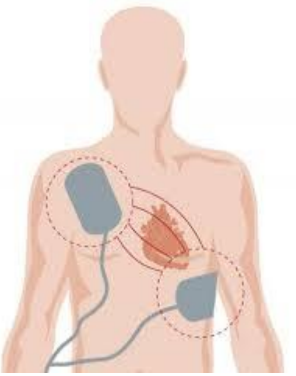
EP

Deformation

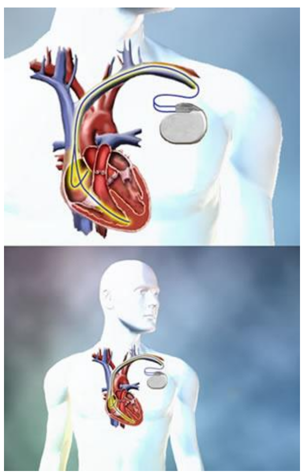
EP and mechanics are bidirectionally coupled through excitation-contraction coupling (ECC) and mechano-electric feedback (MEF)

Electrical Defibrillation

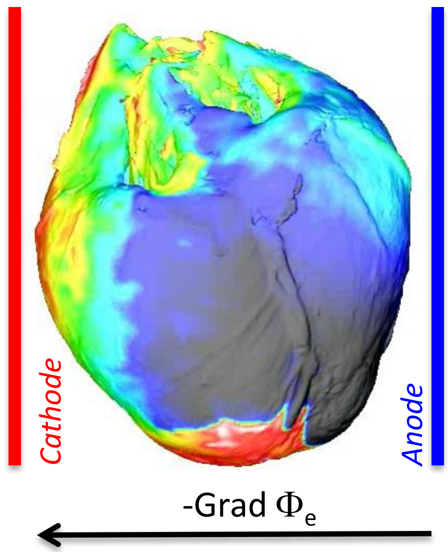
„External“



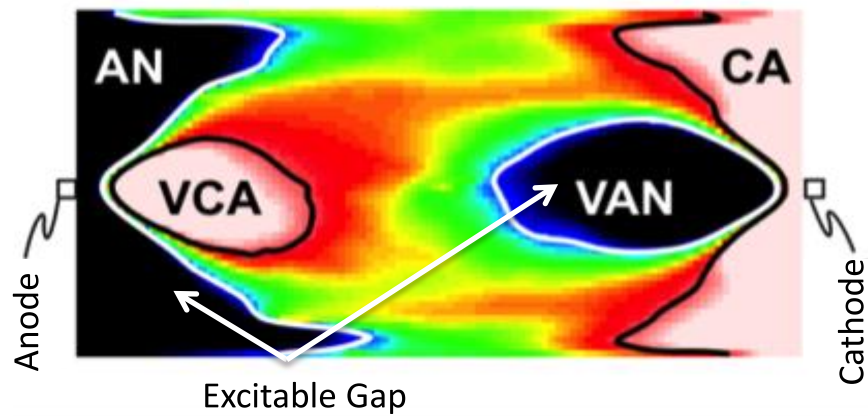
„Internal“



Shock Delivery



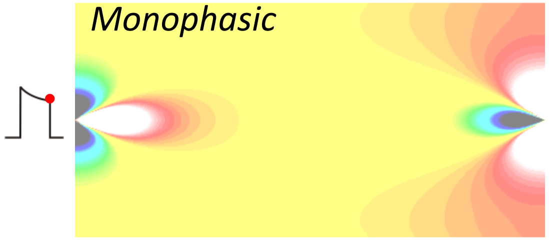
Postshock Virtual Electrode Polarization



- Only reliable therapy to prevent Sudd Cardiac Death
- Detrimental effects affect Quality of Life (Pain Perception)
- Stochastic phenomenom, success depends on strength, location, timing, polarity and pulse shape of shock

Optimal Control Approach

Tissue Response to Defibrillation Shock – Dependency on Shock Waveform

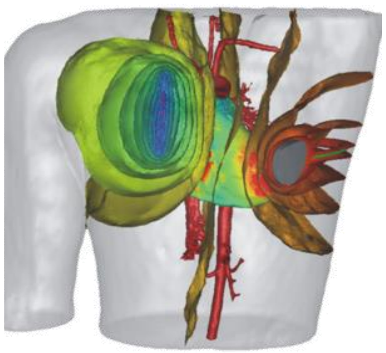


PDE Constrained Optimization

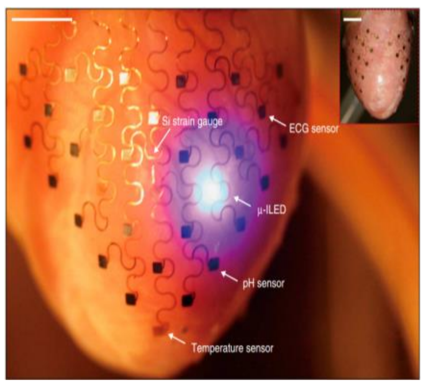
$$\mathcal{L}(V_m, w, I_e, p, q) = J(V_m, I_e) + \langle e(V_m, w, I_e), (p, q) \rangle$$

$$J(V_m, I_e) = \frac{1}{2} \int_0^T \left(\int_{\Omega_{obs}} |V_m - V_d|^2 \, \mathrm{d}\Omega_{obs} + \alpha \int_{\Omega_{con}} |I_e|^2 \, \mathrm{d}\Omega_{con} \right) \mathrm{d}t$$

Optimize Lead Placement



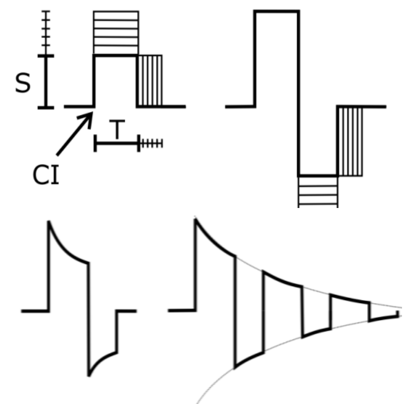
Subcutaneous ICD



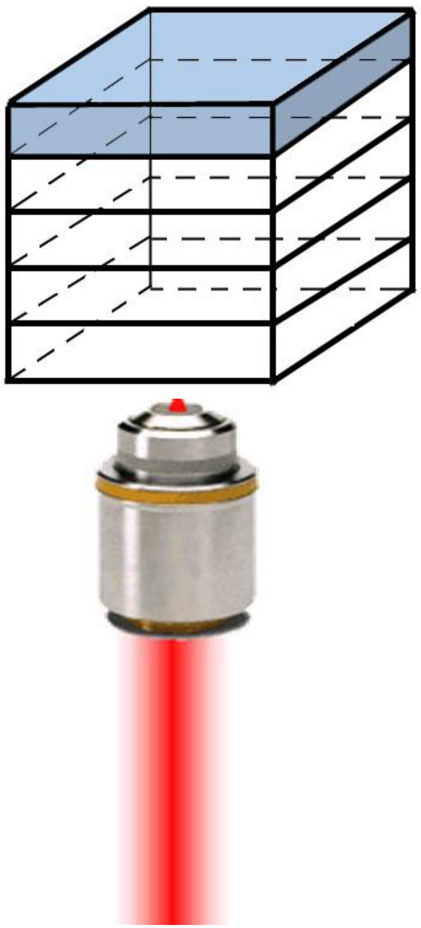
Wide Area Defibrillation

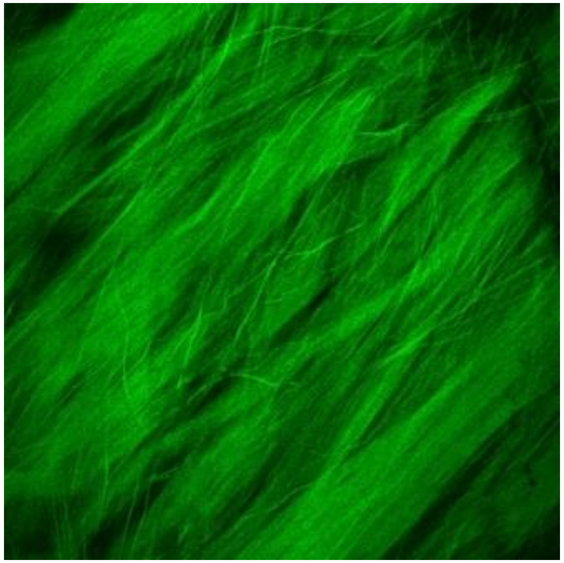
Xu et al, 5:3329, Nature Comm

Optimize Timing/Pulse Shape



- Image stack (z-stack)



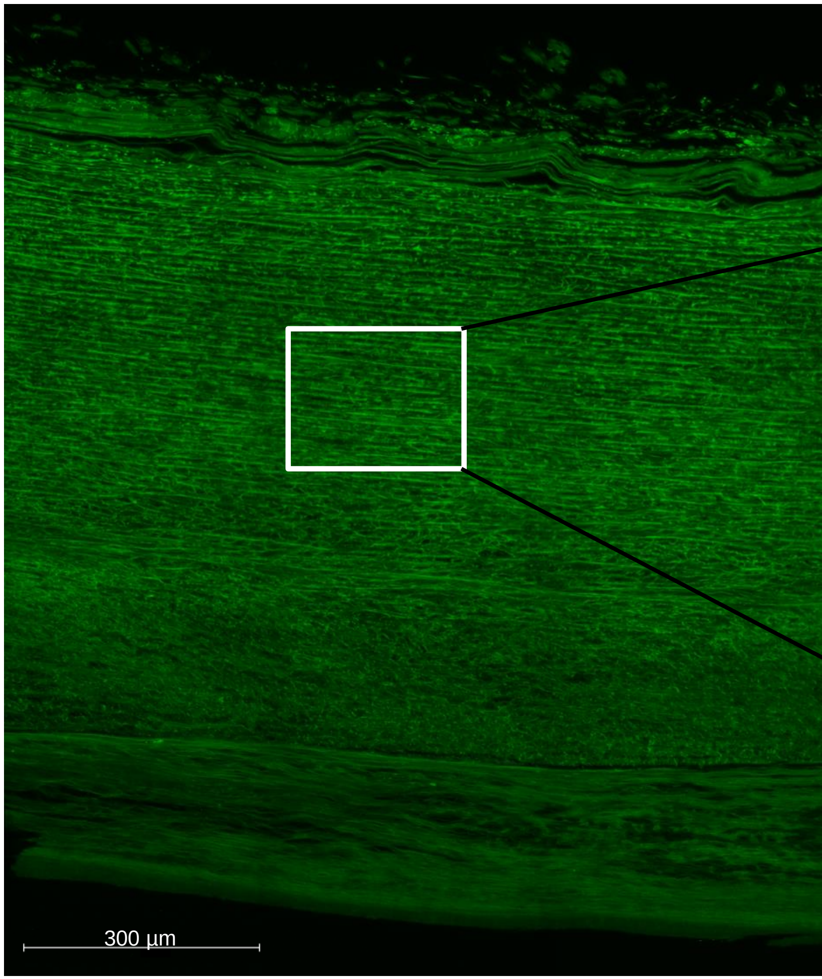


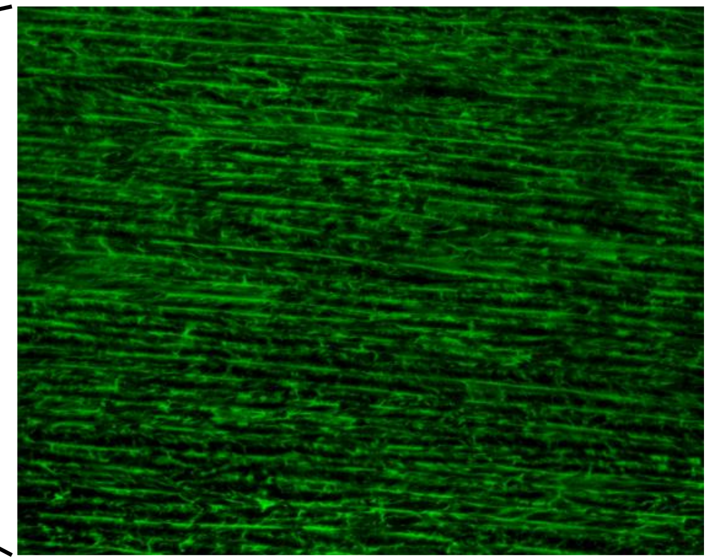
Collagen fibers in the human adventita

- Image size (25x water objective)
  - 534 x 534µm
- Image depth
  - 300nm
- Distance between images
  - 1µm

Human abdominal aorta before and after optical clearing Schriefl et al. [RSI], 2013

- In-plane collagen fibers in the human media





Cross section of a healthy arterial wall
p = 120 mmHg, axial pre-stretch: 12%

- **Material and structural modeling**

- Strain-energy function of the artery wall

$$\Psi_{\text{iso}} = \Psi_{\text{g}}(\bar{\mathbf{C}}) + \sum_{i=4,6} \Psi_{\text{f}i}(\bar{\mathbf{C}}, \mathbf{H}_i)$$

- Energy stored in the two families of dispersed collagen fibers

$$\Psi_{\text{f}i}(\bar{\mathbf{C}}, \mathbf{H}_i) = \frac{k_1}{2k_2}[\exp(k_2\bar{E}_i^2) - 1], \quad i = 4, 6$$

- Green–Lagrange strain-like quantity

$$\bar{E}_i = A\bar{I}_1 + B\bar{I}_i + (1 - 3A - B)\bar{I}_{\text{n}} - 1$$

A and *B* consider the measured **structure** of the collagen fibers

General Goal of MR Research at IME

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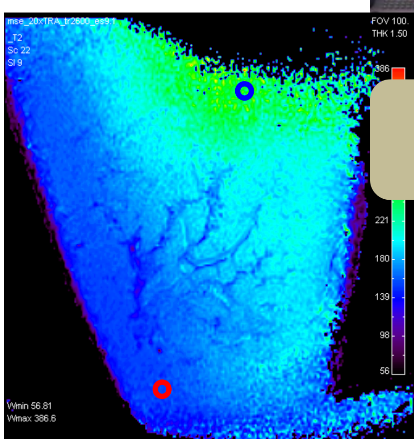
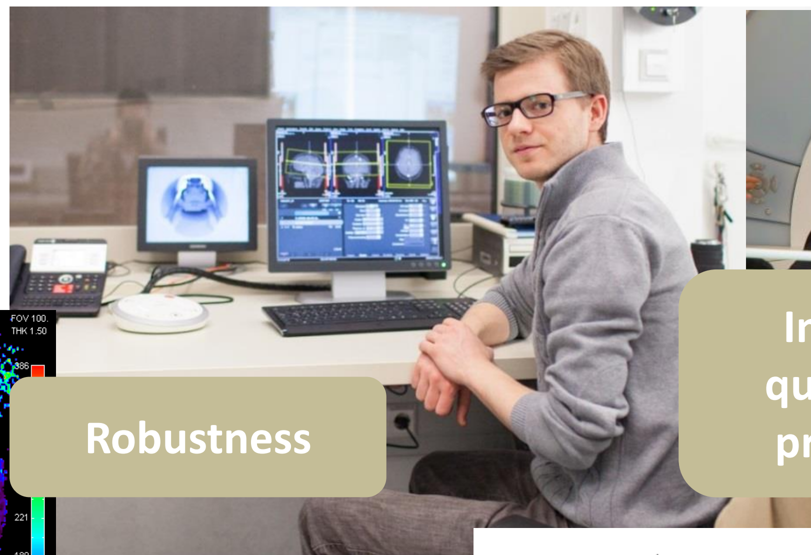
- **The development of MRI towards a biomarker imaging technique by the application of advanced MR principles and mathematical methods.** (SFB Mobis).

Speed



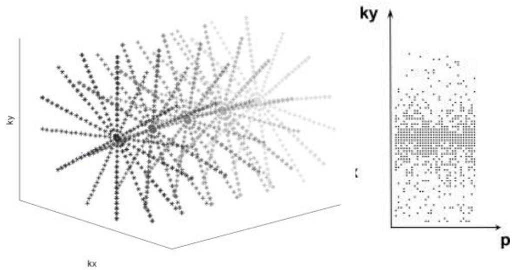


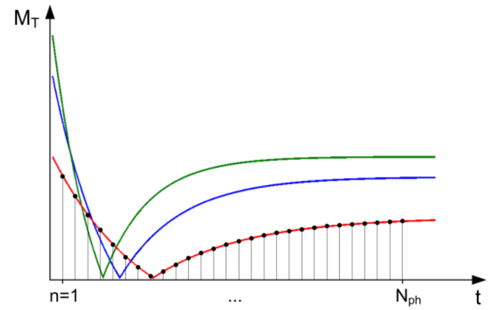
Robustness

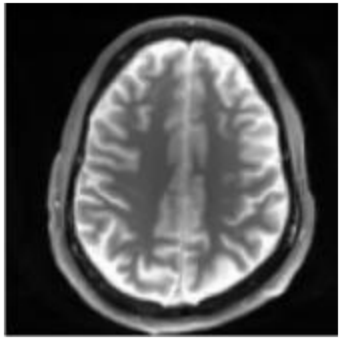
Integrated quantitative procedures

$$F(z) = \frac{M_0}{2}\left(1 + \sqrt{\frac{(1+zE_2)[1 - z(E_1+E_2)\cos\alpha + z^2E_1E_2]}{(-1+zE_2)[-1+z(E_1-E_2)\cos\alpha + z^2E_1E_2]}}\right)$$

Integrated Proc: Multiparameter MRI (mpMRI)







mpMRI:

1. Multiple parameter encoding

$$s_n(T) = \|\vec{M}_n(x,y)\|$$

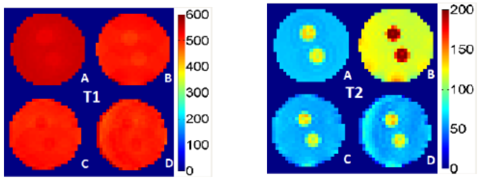
$$\vec{M}_n = \frac{1}{K}\sum_{k=1}^{K} \mathbf{E}\mathbf{R}_x(\alpha_{n,k})\,\mathbf{R}_z(\pi)\left(\mathbf{E}\vec{M}_{n-1} + \vec{e}\right) + \vec{e}$$

2. Generating function for transient sequences

3. Model based reconstruction

$$\min_{T=\{T_1,T_2,M_0\}} \frac{1}{2}\sum_{c,n} \|\mathcal{P}_n\mathcal{F}(c_c s_n(T)) - d_{n,c}\|_2^2 + \lambda \mathrm{TGV}(T)$$

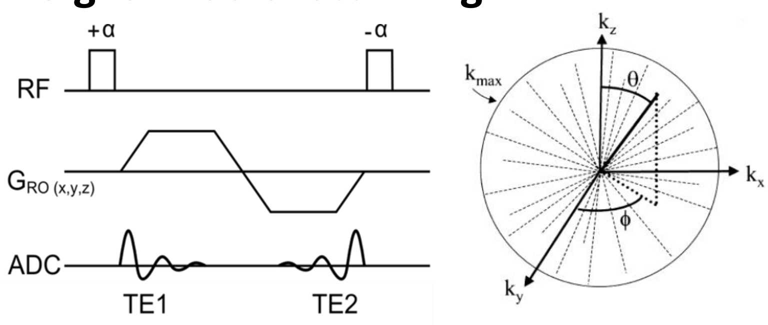
Visibility study
Phantom T1,T2



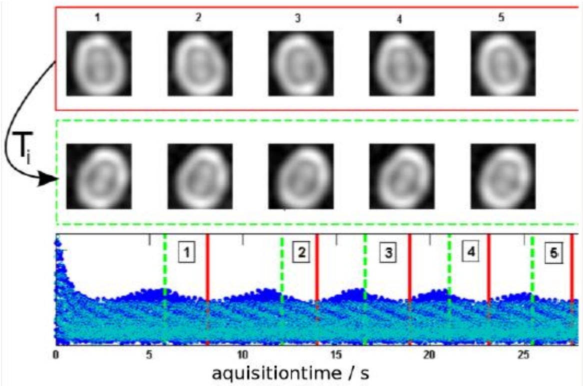
Robustness:
Image Sequences and Motion Correction

- Body motion is still a problem for MRI
- **Goal: retrospective motion correction**

e.g. 3D radial scanning



Low resolution Subsets ⇒



Forward operator model with mapping of motion dependent position to k-space data

$$K : u \mapsto \sum_{t=1}^{N} \mathcal{F}_t(b_j T_t u)$$

Challenges and research objective:

- Motion correction of time-resolved 3D radial acquisitions for free-breathing dynamic MRI
- Motion correction high resolution 3D
- Investigation new math. Approaches

Available Infrastructure

- 3T MRI (Research System)

  Siemens Skyra, 45mT Gradient, different Array coils, Head Coils with 20 and 32 channels, Mouse & Rat coil., fMRI equipment, Elastography unit.

- Pulse programming capabilities
- Advanced signal modelling
- Fast offline reconstruction for new algorithms

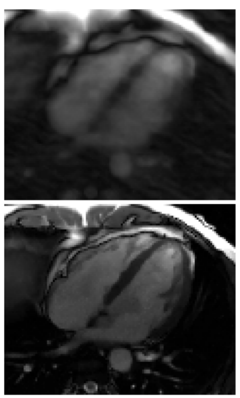
Research Grup

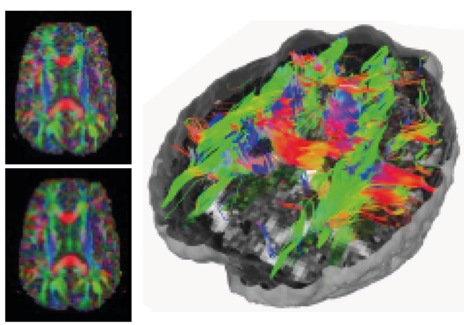
Inverse Problems & Mathematical Imaging
Institute for Mathematics and Scientific Computing

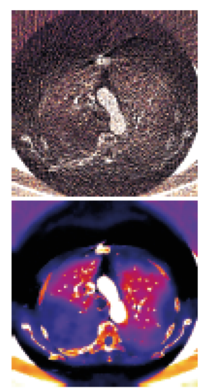
Fields of research

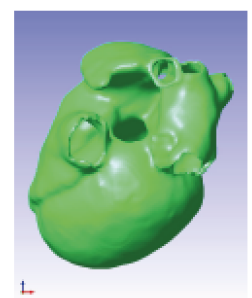
- Variational modelling and optimization for advanced reconstruction and quantification of image data
- Application to medical imaging (MRI/CT), microscopy, and beyond

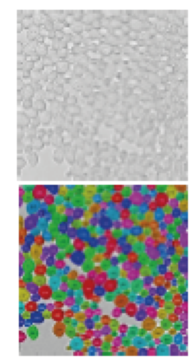
SFB Research Center Mathematical Optimization & Applications in Biomedical Sciences


Dynamic MRI


Regularized DTI


Dual-Energy CT


Binary surface smoothing


Cell segmentation

Involved Researchers

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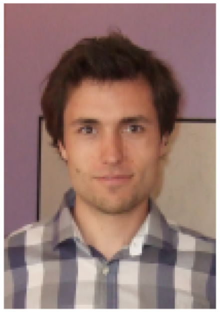
Inverse Problems & Mathematical Imaging

Univ.-Prof. Dr. Kristian Bredies

Head of group

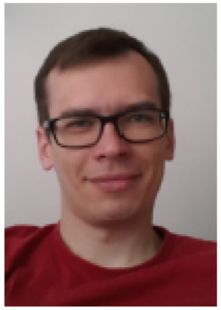
- Advanced imaging techniques/Inverse problems
- Optimization and variational approaches



Dr. Martin Holler

Postdoctoral researcher

- Dynamic imaging and reconstruction
- Image/Video compression techniques

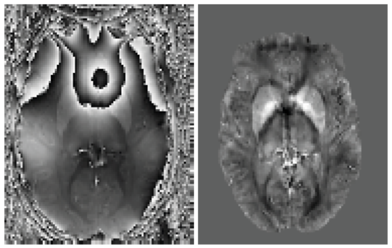


Dr. Kamil Kazimierski

Postdoctoral researcher

- Image data analysis and quantification
- Regularization approaches for inverse problems

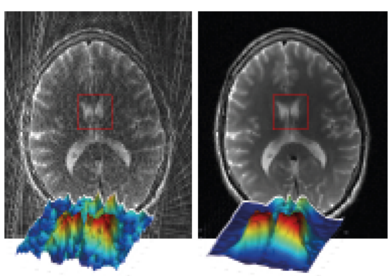
Research Question and Trends



Inverse Problem: Quantitative susceptibility mapping

$$\mathrm{TGV}^2_\alpha(u) = \min_{w\in \mathrm{BD}} \alpha_1\|\nabla u - w\|_{\mathcal{M}} + \alpha_0\|\mathcal{E} w\|_{\mathcal{M}}$$

Advanced regularization



Compressed sensing in MRI (10% of the data)

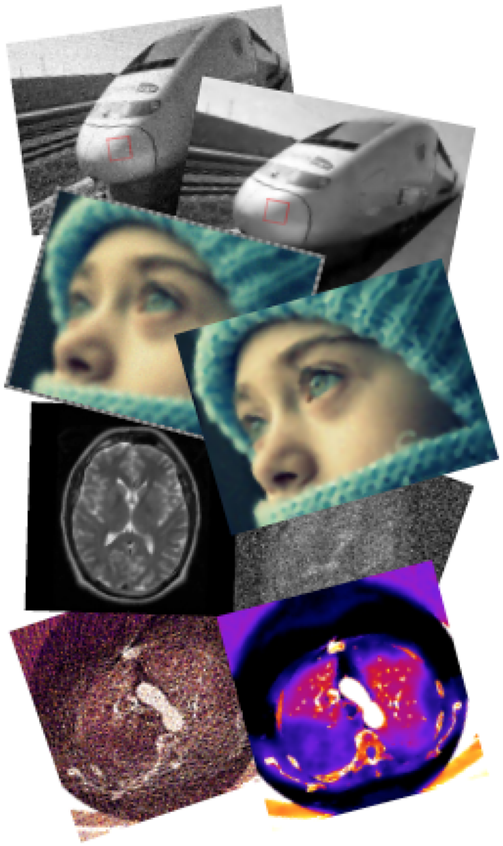
Inverse problems:
How to reconstruct from measurements?

- Modelling: Describe measurements process
- Inversion: Find solution explaining given measurements
- Regularization: Make solution reasonable
- Optimization: Find best of out many solutions

Recent developments

- Inverse problem paradigm becomes established in medical imaging
- Development of advanced regularization approaches
- Compressed sensing: Reconstruction from few measurements
- Availability of powerful optimization algorithms

Cooperation Potential



Available expertise

- Image enhancement:
  Denoising, deblurring & beyond
- Modelling and realization of reconstruction strategies
- Reconstruction from incomplete data
- 2D/3D image data & image sequences

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- Strengthen cooperations with practitioners
- Improve mathematical models
- Enhance efficiency of numerical algorithms

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Medizinische Universität Graz