The (parametric) Voice of Your Heart

Towards Parametric Cardiac Modelling for Early Recognition and Treatment of AF

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TU Delft

Signal Processing for Cardiac Applications

- Appointment at EMC, Cardiology, Electrophysiology
- The team:







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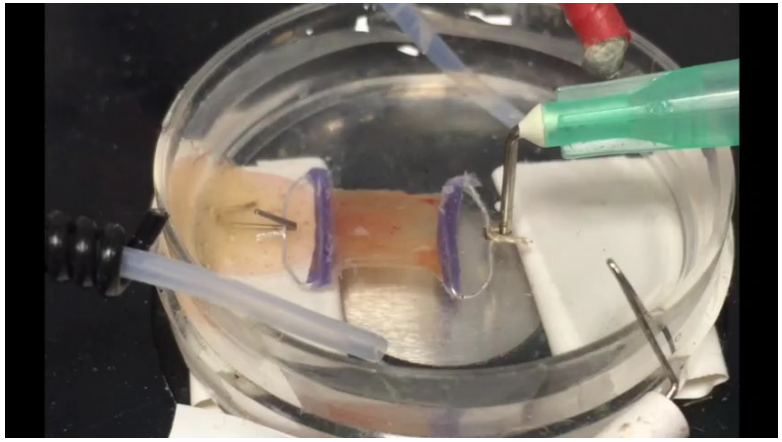
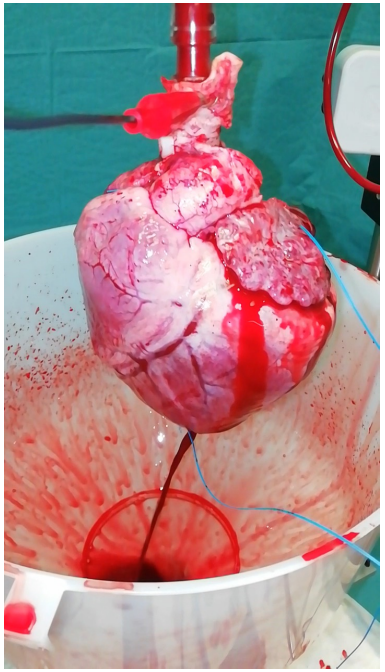
EMC, unit Electrophysiology - the lab



Living myocardial slices



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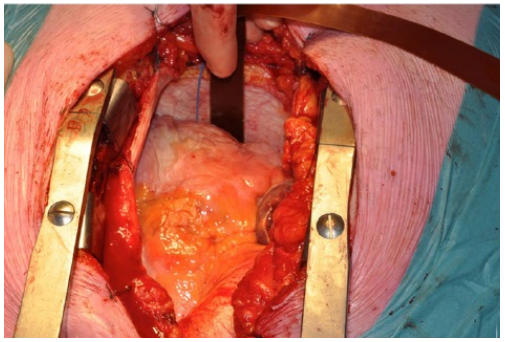

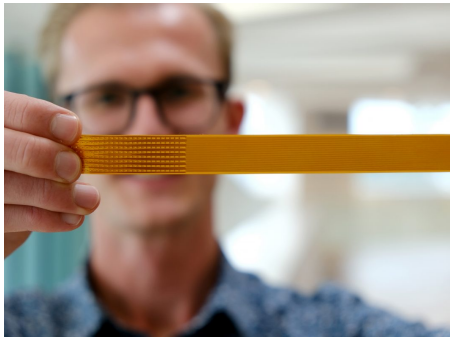

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Atrial Fibrillation

Atrial fibrillation:

- rapid and irregular beating of the atria
- increases risk for heart failure,

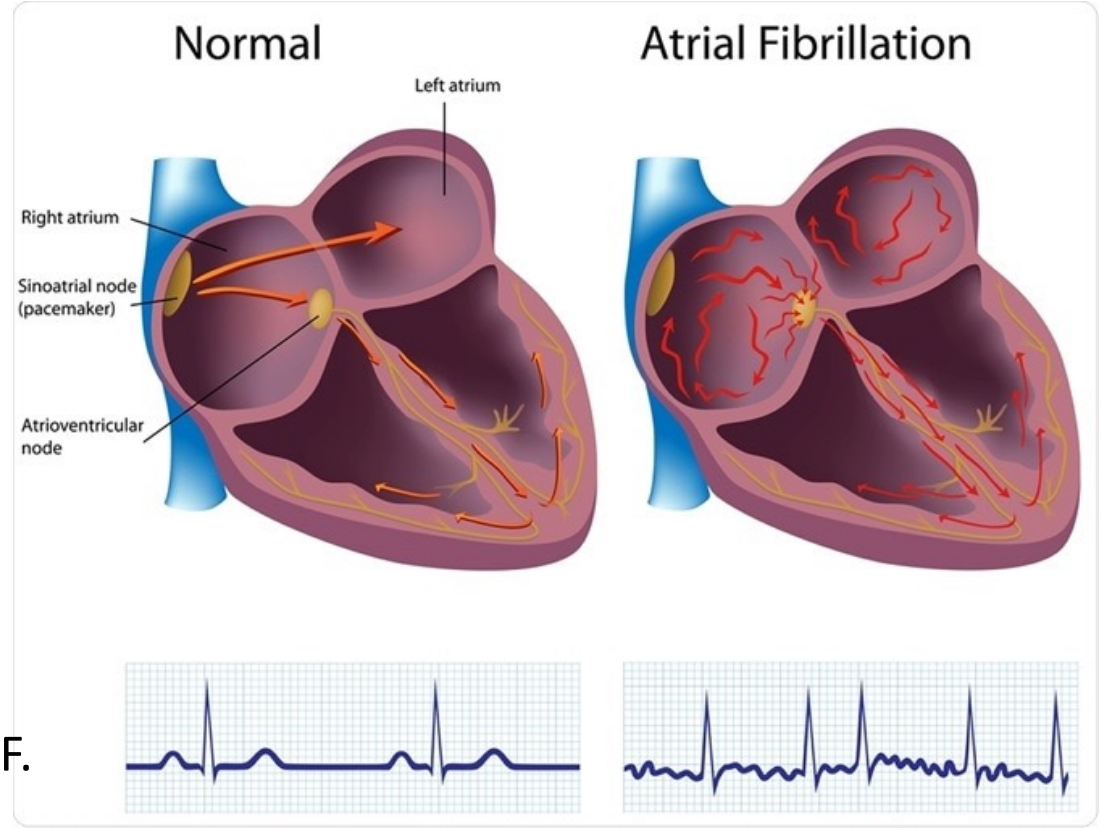
stroke or heart-related hospitalizations

Prevalence:

- Most common sustained cardiac

arrhythmia

- People of 40+ have risk of 25 % to develop AF.



Atrial fibrillation. Image Credit: Alila Medical Media / Shutterstock

Atrial Fibrillation – Existing Therapies

Trigger + Substrate = AF

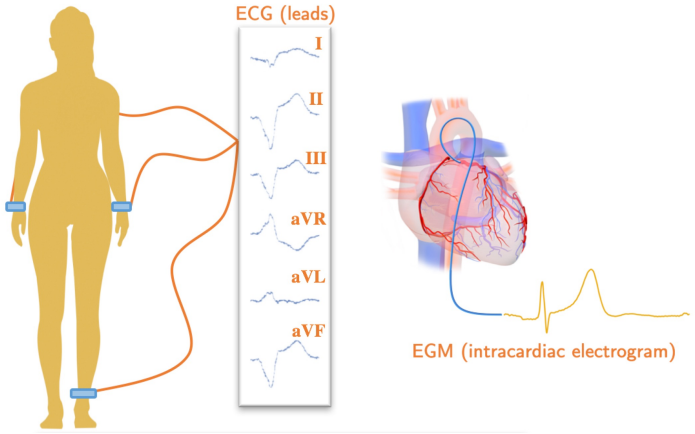
- Anti-arrhythmic drug (Rhythm control, lowers heart-rate), reoccurs with 70 % of patients within 1 year.
- Electrical cardioversion (reset), reoccurs with 67 % of patients in 1 year.
- Ablation. Reoccurrence: 35 %, 44 % and 49 % within 1, 3 and 5 year.

Atrial Fibrillation – Main Issues

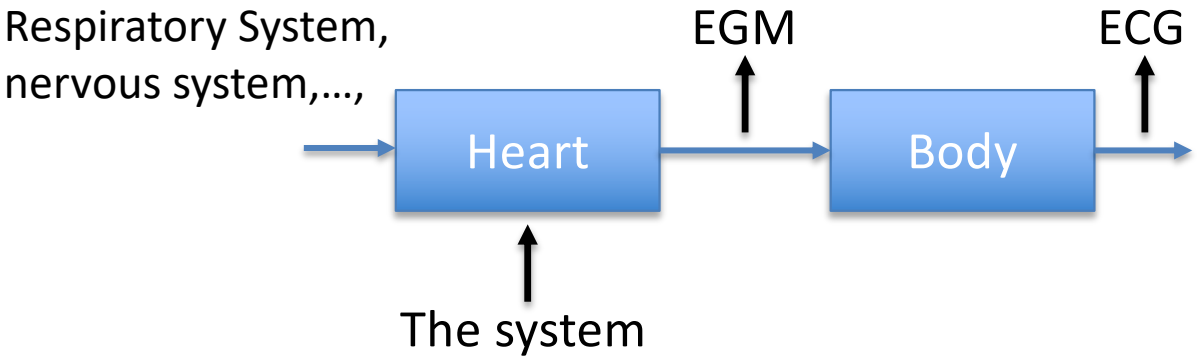
- Origin and exact mechanism of AF not (yet) well understood
- When understood…what to do?
- Non-invasive (ECG) detection (and differentiation from other arrhythmias) of AF is very challenging
- Early detection is challenging, but important (AF is progressive)

High level problem formulation

Typical approach: Draw conclusions based on the (output) realizations of the (human) system



From L. Bote-Curiel et. Al, Deep Learning and Big Data in Healthcare: A Double Review for Critical Beginners. *Appl. Sci.* **2019**, *9*, 2331.



My philosophy: Given EGM/ECG realizations, try to infer the system that generated these.

- How to model the atrium from a signal processing point of view?
- How to infer the model parameters from the EGM or ECG measurements?

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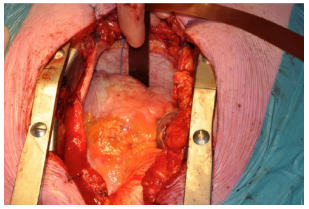
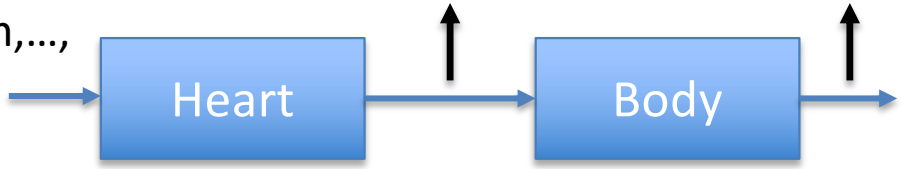
High level overview of projects

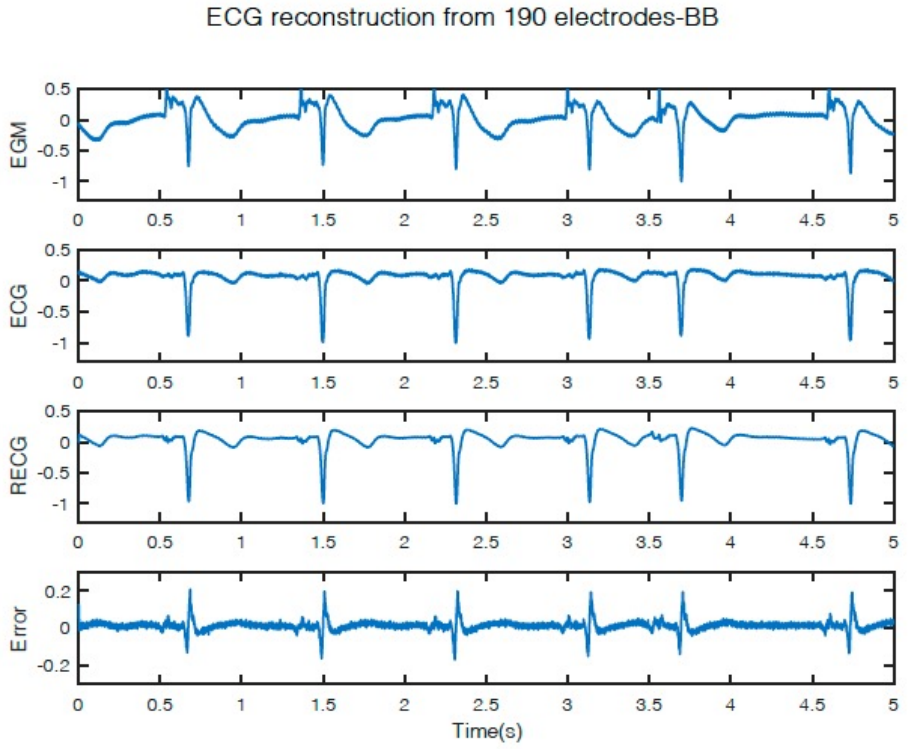


Respiratory System, nervous system,…,



1 Early non-invasive ECG-based AF detection

- How to characterize AF



- Unique combination of data: EGM &
- Measure how AF characterizes itself EGMs and transform this to ECG leve

- Find transfer functions from EGM <=> ECG

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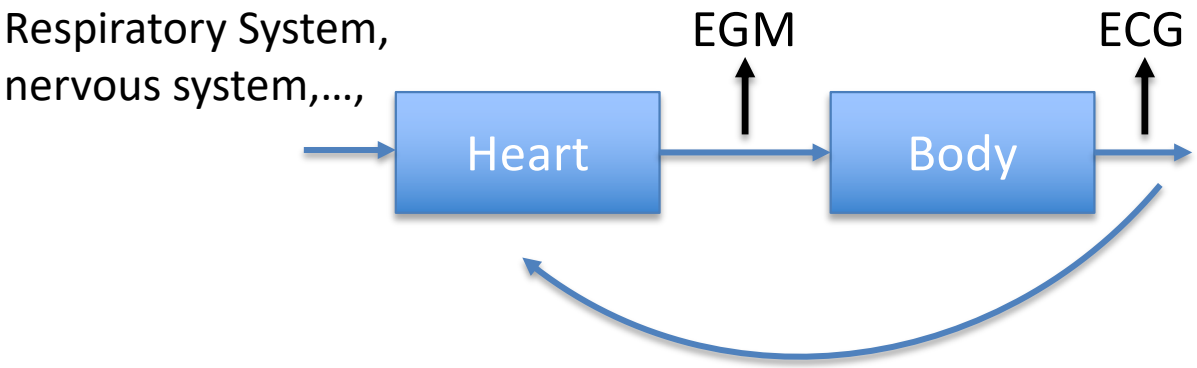
High level overview of projects



1 Early non-invasive ECG-based AF detection

2 Interpretable ECG-based parametric modelling of the heart

- Given the ECG, can we derive a parametric desciption, where the parameters physically relate to the heart?
- Can we, from the parameters, infer the condition of the heart (e.g., degree of AF)?

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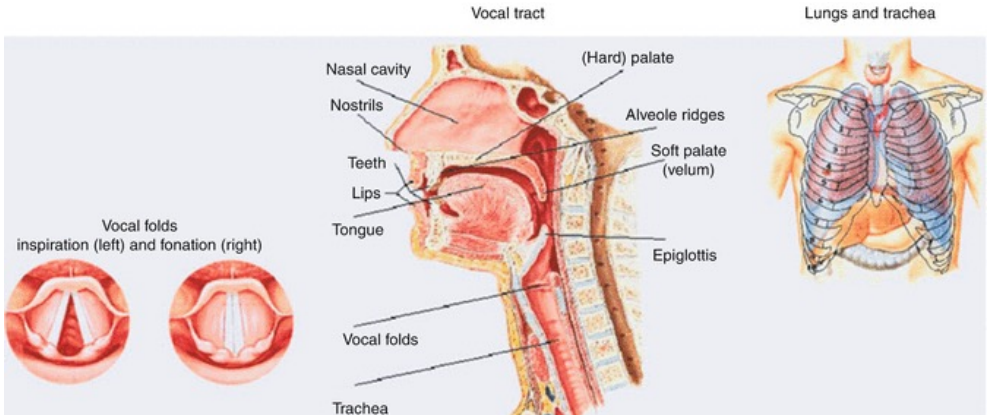
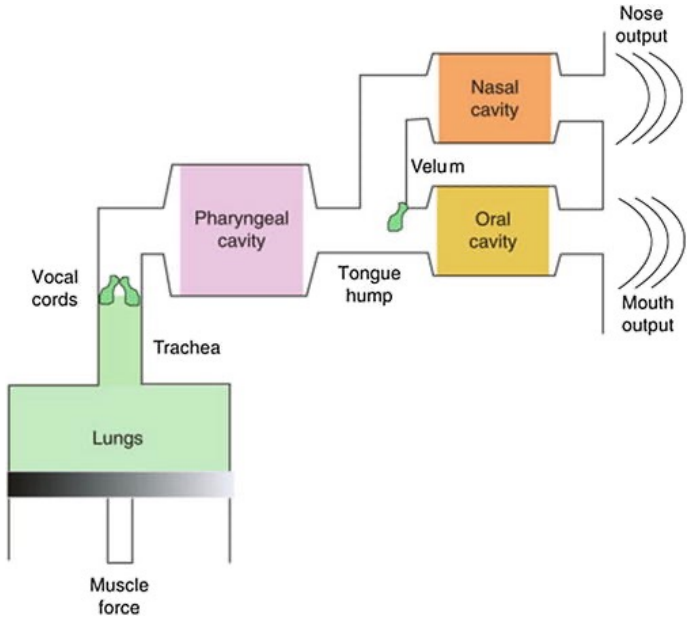
Speech Production - Anatomy

Overview of speech production system:

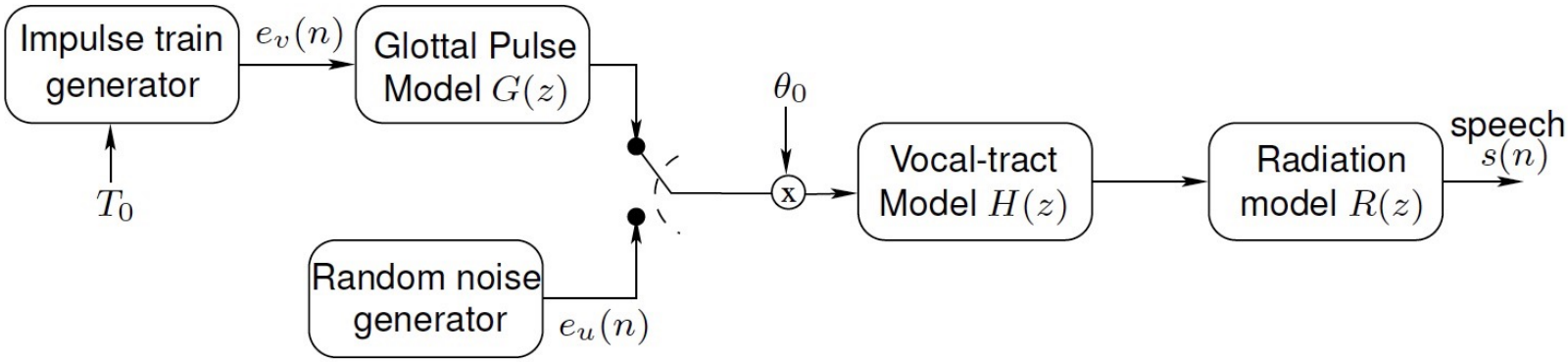
- Lungs
- Larynx (organ of voice production).
- Vocal Tract
  - throat (pharyngeal cavity).
  - oral+nasal cavity.





From *Docio-Fernandez L., García Mateo C. Speech Production. In: Li S.Z., Jain A.K. (eds) Encyclopedia of Biometrics. Springer, Boston, MA, 2015.*

Speech Production - Source-Filter Model



$$S(z) = \begin{cases} \theta_0 E_v(z) G(z) H(z) R(z) & \text{if voiced} \\ \theta_0 E_u(z) H(z) R(z) & \text{if unvoiced} \end{cases}$$

Filters $H(z)$, $G(z)$, and $R(z)$ are/can be approximated as all-pole.

- Decoupling of complete system into:
  - Excitation (input)
  - Filters representing differrent cavities in speech production system
- Filter coefficients have a direct physical meaning and are interpretable.

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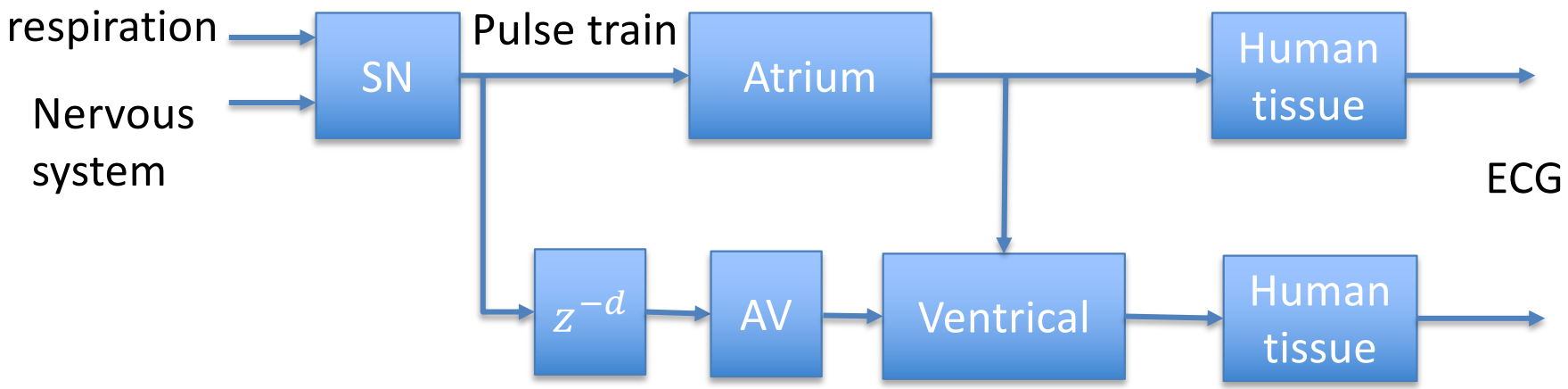
Interpretable ECG-based parametric modelling of the heart



- AR/ARMA models describing Atrium and Ventrical
- Decouple input (Sinus and AV nodes) from atrial and ventricular response
- Filter coefficients physically interpretable and related to arrythmias
- ECG=> filter coefficients => Arrythmia detection/localization, staging of degree

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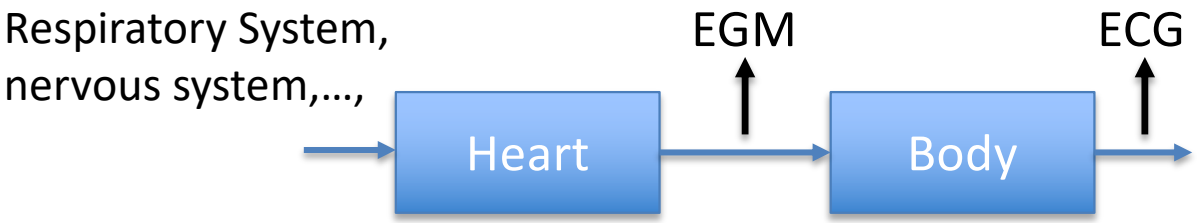
High level overview of projects



1 Early non-invasive ECG-based AF detection

2 Interpretable ECG-based parametric modelling of the heart

3 Determine cardiac tissue properties at cell level from EGM measurements

Cell properties like conductivity and anisotropy are believed to play an important role in Atrial Fibrillation

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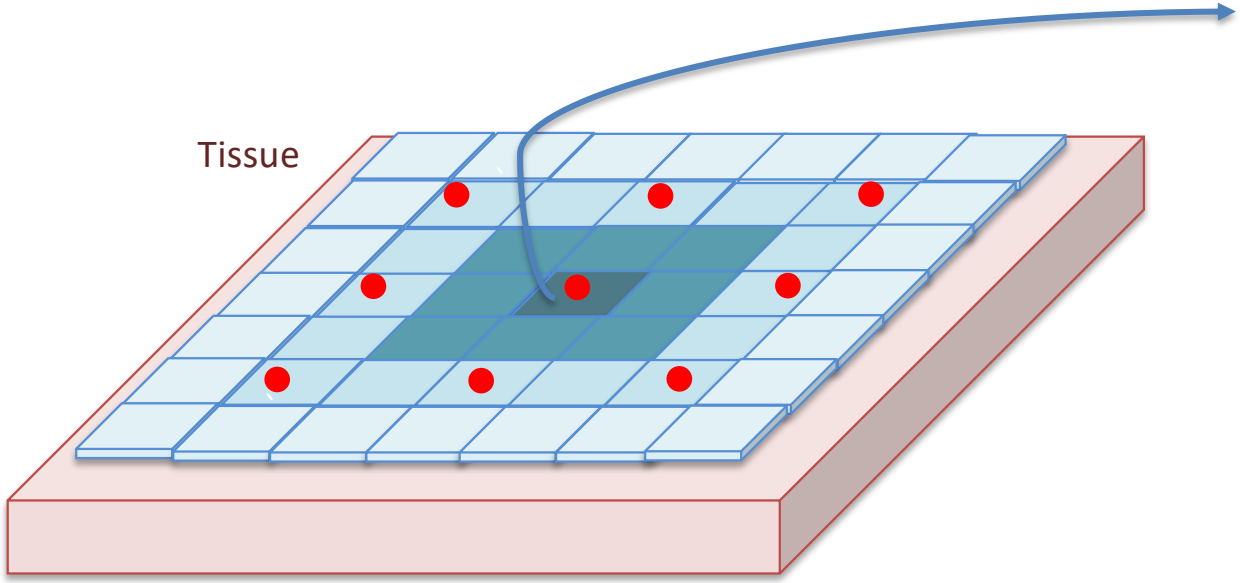
Estimating “cell” properties



- Many cells, very few electrodes.
- Many parameters to be estimated
  - Cell conductivity σ
  - Anisotropy ratio α
  - Activation time of the cell.

Challenge: An ill posed problem to estimate parameters for many cells with few electrodes ($N \gg M$).

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Estimating “cell” properties

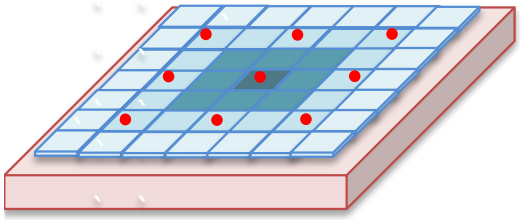
Let the EGM at sensor m, at coordinates $\mathbf{y}_m$ and time t be given by $\phi_m(\mathbf{y}_m, t)$

$$\phi_m(\mathbf{y}_m, t) = \frac{a}{4\pi\sigma_e} \sum_{n=1}^{N} \frac{I_{tm}(\mathbf{x}_n, t)}{\sqrt{\|\mathbf{y}_m - \mathbf{x}_n\|^2 + z_0^2}} = \frac{a}{4\pi\sigma_e} \mathbf{r}_m^T \mathbf{I}_{tm}(t)$$

with transmembrane currents $\mathbf{I}_{tm}(t) = S_v^{-1} \mathbf{D}_\sigma \mathbf{v}(t)$, with

$$\mathbf{D}_\sigma = \mathbf{D}_x \mathrm{Diag}(\boldsymbol{\sigma}) \mathbf{D}_x + \mathbf{D}_y \mathrm{Diag}(\boldsymbol{\alpha}) \mathrm{Diag}(\boldsymbol{\sigma}) \mathbf{D}_y$$

and $\mathbf{v}(t) = \boldsymbol{\delta}(t) * v_0(t)$, where $\boldsymbol{\delta}(t) = [\delta(t - \tau_0), \delta(t - \tau_1), ..., \delta(t - \tau_{N-1})]^T$.



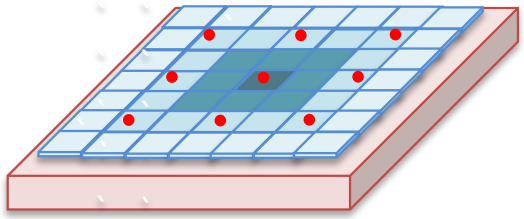
Altogether we have:

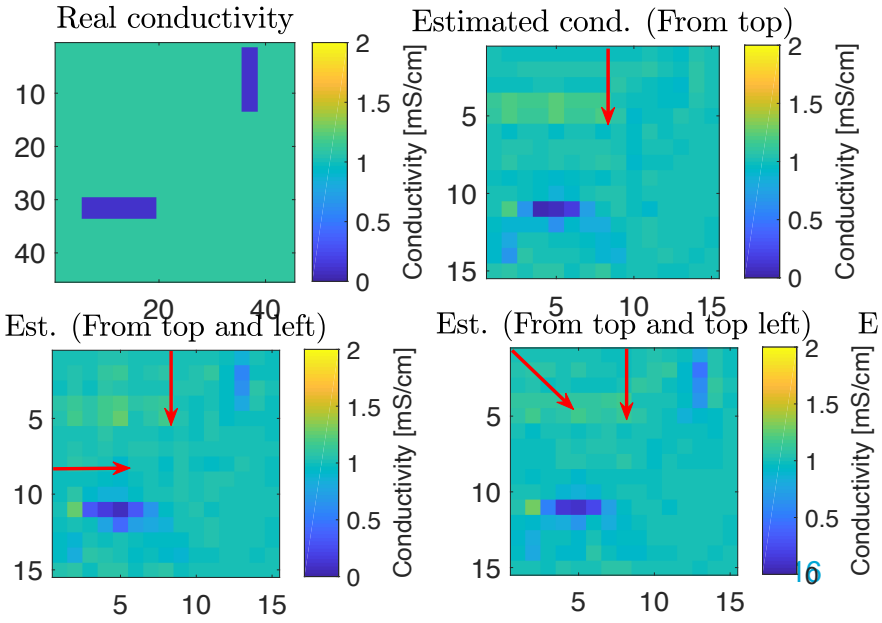
$$\phi_m(t) = a_m(t) * v_0(t)$$

where $a_m(t) = \frac{a S_v^{-1}}{4\pi\sigma_e} \mathbf{r}_m^T \mathbf{D}_{\sigma,\alpha} \boldsymbol{\delta}$.

Problem Formulation

- # cells $N \gg$ # electrodes M
- Can we estimate all model parameters α_n, σ_n and τ_n $\forall n$ jointly?
- Use multiple frequency bands and multiple heartbeats to increase the number of knowns.
- Can we involve multiple heartbeats and "illuminate" the tissue from different direction?





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Factor Analysis & CSPDM

- **EGM model in the time domain:** $\phi_m(t) = a_m(t) * v_0(t) + u_m(t)$
- **EGM model in STFT domain:** $\widetilde{\phi}_m(l,k) = \widetilde{a}_m(l,k)\widetilde{v}_0(l,k) + \widetilde{u}_m(l,k)$
- Use stacked vector notation: $\widetilde{\boldsymbol{\phi}}(l,k) = [\widetilde{\phi}_1(l,k), ..., \widetilde{\phi}_M(l,k)]^T$
- Calculate the cross power spectral density matrix (CPSDM) of the EGM in the lth frame and the kth frequency band:

$$\begin{aligned}\mathbf{P}_\phi(l,k) &= E[\widetilde{\boldsymbol{\phi}}(l,k)\widetilde{\boldsymbol{\phi}}(l,k)^H] \\ &= E[\widetilde{v}_0^2(l,k)]\widetilde{\mathbf{a}}(l,k)\widetilde{\mathbf{a}}(l,k)^H + \mathbf{P}_u(l,k),\end{aligned}$$

- where $\mathbf{P}_u(l,k) = \text{Diag}([q_1, \cdots, q_M]^T)$: with the mth diagonal element $q_m = E[\widetilde{u}_i^2(l,k)]$ the PSD of the sensor-self noise of the mth sensor.

Confirmatory Factor Analysis

$$\mathbf{P}_{\phi}(l,k) = E[\widetilde{v}_0^2(l,k)]\widetilde{\mathbf{a}}(l,k)\widetilde{\mathbf{a}}(l,k)^H + \mathbf{P}_u(l,k)$$

- **General confirmatory factor analysis (CFA) problem**

  CFA methods have been proposed to estimate the parameters of the following model

$$\boldsymbol{P}_{\mathbf{y}} = \mathbf{A}\boldsymbol{\Phi}\mathbf{A}^H + \boldsymbol{P}_{\mathbf{u}} \in \mathbb{C}^{M\times M}$$

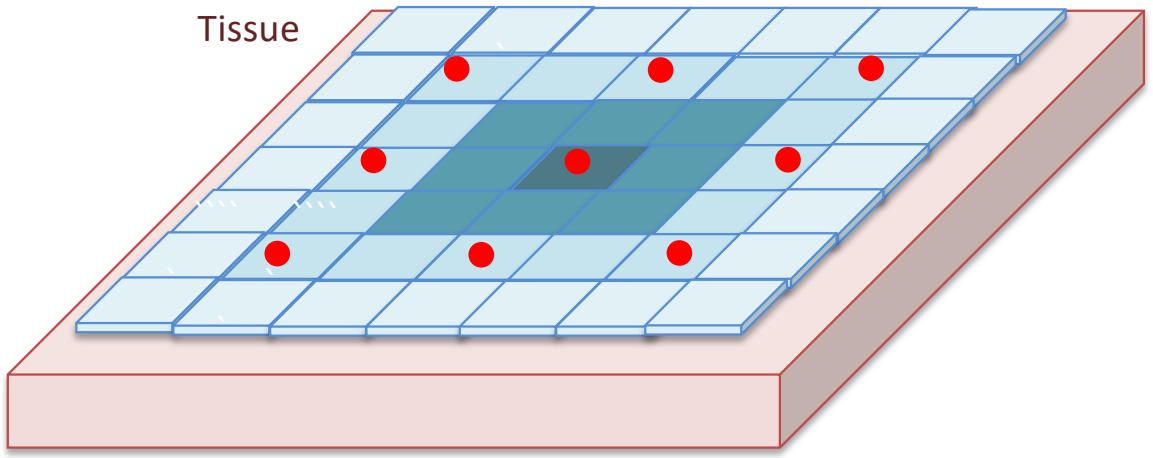
  where

  - $\boldsymbol{P}_{\mathbf{y}}$: $M \times M$ variance-covariance matrix of the measurements,
  - $\mathbf{A}$: $M \times r$: matrix of unknown factor loadings,
  - $\boldsymbol{P}$: $r \times r$ variance-covariance matrix of the r common factors
  - $\boldsymbol{P}_{\mathbf{u}}$: $M \times M$variance-covariance matrix of the residuals.

Confirmatory Factor Analysis

Apply Simultaneous confirmatory factor analysis to

- Use multiple Frequencies and multiple heartbeats
- Estimate the conductivity σ for all cells,
- Estimate the anisotropy ratio α for all cells,
- The local activation time of τ_n for all cells.



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Confirmatory Factor Analysis

$$\min_{\substack{\boldsymbol{\sigma},\boldsymbol{\alpha},\{\mathbf{P}_u(k,l)\},\\ \{\tau_n(l)\},n=0,\cdots,N-1}} \sum_{\forall k\in S_f,\forall l\in S_l} F(\hat{\mathbf{P}}_\phi(k,l),\mathbf{P}_\phi(k,l))$$

$$\begin{aligned}
\text{s.t.}\quad & \mathbf{P}_\phi(k,l) = \widetilde{\mathbf{a}}(k,l)P(k,l)\widetilde{\mathbf{a}}(k,l)^H + \mathbf{P}_u(k,l),\\
& \widetilde{\mathbf{a}}(k,l) = [Q\mathbf{r}_1^T\mathbf{D}_\sigma\widetilde{\boldsymbol{\delta}}(k,l),\cdots,Q\mathbf{r}_M^T\mathbf{D}_\sigma\widetilde{\boldsymbol{\delta}}(k,l)]^T,\\
& \mathbf{D}_\sigma = \mathbf{D}_x\mathrm{Diag}(\boldsymbol{\sigma})\mathbf{D}_x + \mathbf{D}_y\mathrm{Diag}(\boldsymbol{\alpha})\mathrm{Diag}(\boldsymbol{\sigma})\mathbf{D}_y,\\
& \widetilde{\boldsymbol{\delta}}(k,l) = [\exp(-\frac{j2\pi f_s k}{K}\tau_0(l)),\ldots,\exp(-\frac{j2\pi f_s k}{K}\tau_{N-1}(l))]\\
& \mathbf{P}_u(k,l) = \mathrm{Diag}[q_1(k,l),q_2(k,l),\cdots,q_M(k,l)],\\
& q_m(k,l)\geq 0, m=1,2,\cdots,M,\\
& P(k,l) = \widetilde{v_0}(k,l),\\
& \tau_0 = 0,
\end{aligned}$$

for $\forall k \in S_f, \forall l \in S_l$, where $S_f = \{k_1,\cdots,k_N\}$ is the set of the frequency indices and $S_l = \{l_1,\cdots,l_N\}$ is the set of the heartbeats for conductivity and activation time estimation.

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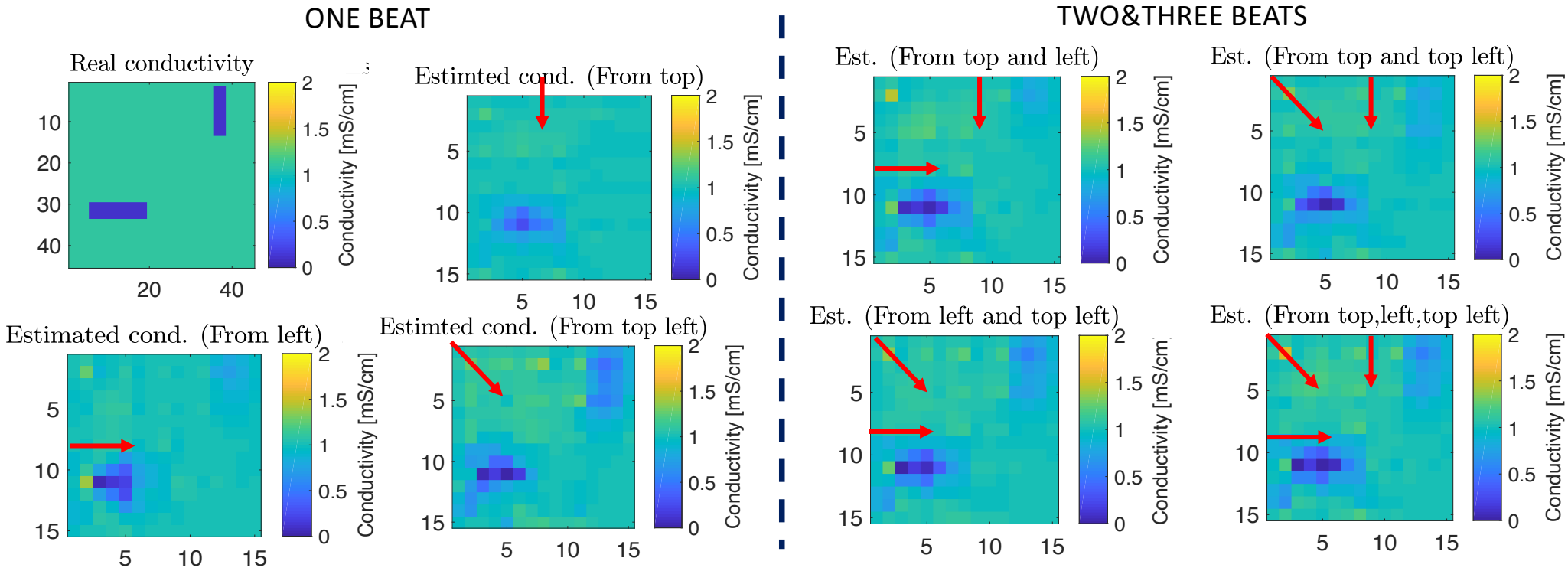
Experiments with Simulated Data



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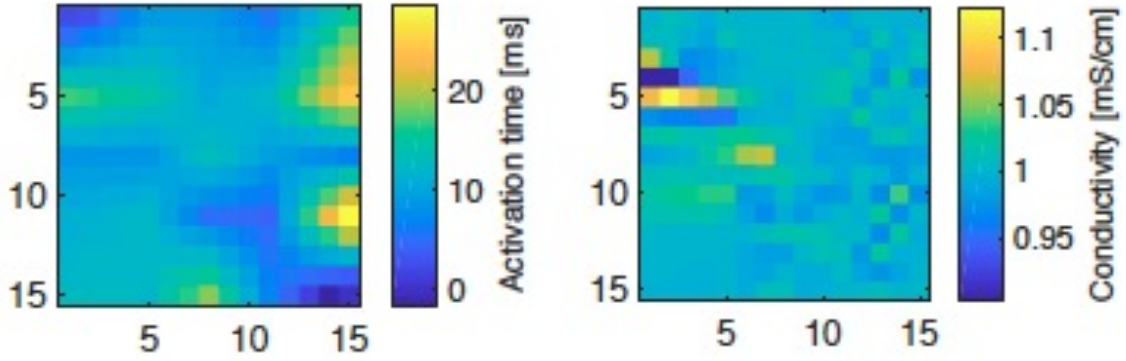
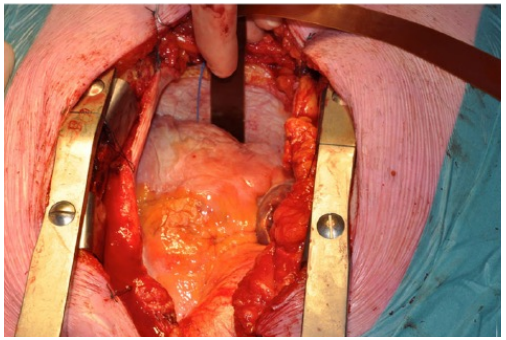
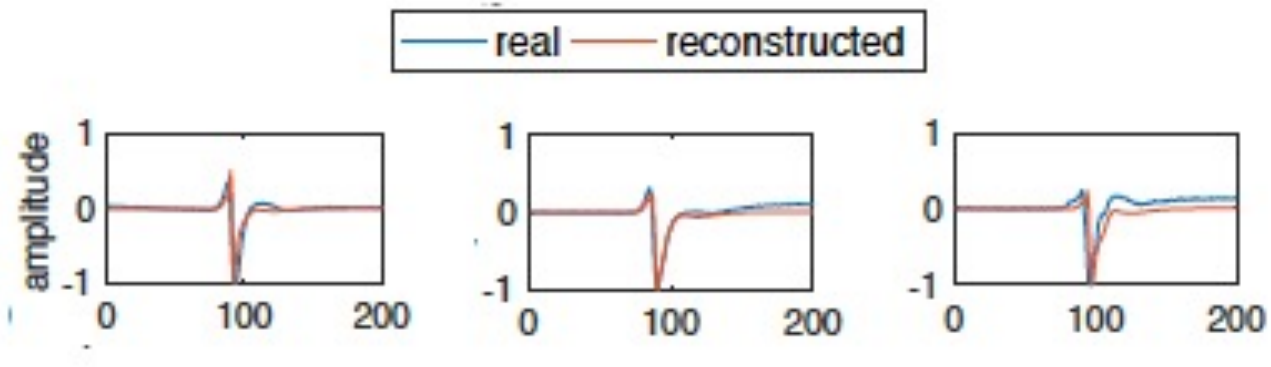
Experiments with measured Data





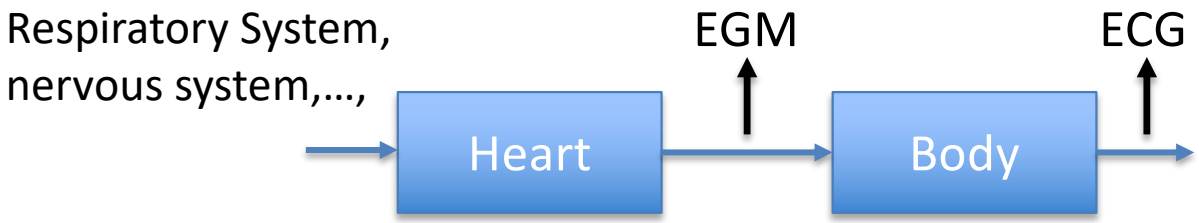


Open questions…

1 Early non-invasive ECG-based AF detection

2 Interpretable ECG-based parametric modelling of the heart

3 Determine cardiac tissue properties at cell level from EGM/ECG measurements



We can estimate tissue properties from EGMs, but

- How to estimate parameters for deeper layers?
- What if we measure on a (small) distance? => catheter
- How to do this less/non invasive based on ECG or catheter?
- How to use this information for to guide the surgeon during ablation or other techniques?

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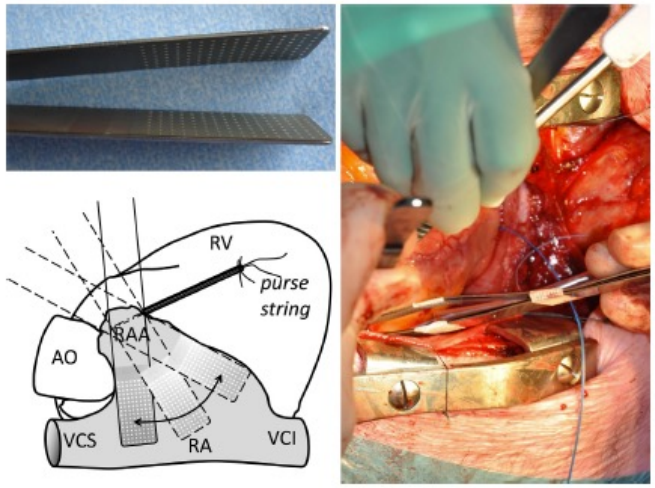
Future



Future:

- Can we extend our models to 3d tissue ?
  - Model multiple cell layers
  - Take distance into account
  - Epicardiac combined with endocardiac measurements
- Inversion problem: From heart to body surface
- How to help the surgeon? Based on Measurements, estimate model parameters and predict the effect of ablations?

Graduation topics – Biomedical SP & Audio

Multi-Microphone Noise reduction

- Delay and sum beamformer

$$\mathbf{w}_k(l) = \frac{\mathbf{d}_k}{\mathbf{d}_k^H \mathbf{d}_k}$$

- MVDR beamformer

$$\mathbf{w}_k(l) = \frac{\left(\mathbf{R}_{Y,k}(l)\right)^{-1}\mathbf{d}_k}{\mathbf{d}_k^H\left(\mathbf{R}_{Y,k}(l)\right)^{-1}\mathbf{d}_k} = \frac{\left(\mathbf{R}_{N,k}(l)\right)^{-1}\mathbf{d}_k}{\mathbf{d}_k^H\left(\mathbf{R}_{N,k}(l)\right)^{-1}\mathbf{d}_k}$$

- Multi-Channel Wiener

$$\mathbf{w}_k = \underbrace{\frac{\sigma_{S,k}^2(l)}{\sigma_{S,k}^2(l) + (\mathbf{d}_k^H(l)R_{\mathbf{N}_k}^{-1}\mathbf{d}_k(l))^{-1}}}_{\text{Single-channel Wiener}} \underbrace{\frac{R_{\mathbf{N}_k}^{-1}(l)\mathbf{d}_k(l)}{\mathbf{d}_k^H(l)R_{\mathbf{N}_k}^{-1}\mathbf{d}_k(l)}}_{MVDR}$$

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Multi-Microphone Noise reduction

- All beamformers depend on the ATF $\mathbf{d}_k$
- How to estimate the ATF $\mathbf{d}_k$?
  - EVD of $\mathbf{R}_X = \mathbf{R}_Y - \mathbf{R}_N$, or, GEVD of $(\mathbf{R}_Y, \mathbf{R}_N)$
  - This is accurate when ($\mathbf{R}_Y$ and $\mathbf{R}_N$) are known. However, estimation errors severely affect results.
- Graduation topic: Can we obtain better estimators for $\mathbf{d}_k$ by combining the GEVD and machine learning approaches to take into account estimation errors in ($\hat{\mathbf{R}}_Y$ and $\hat{\mathbf{R}}_N$)

Multi-Microphone Noise reduction

- Beamformers and estimation of ATF depends on knowing $\mathbf{R}_N$.
- Typically $\mathbf{R}_N$ is estimated using a VAD, which implies that updates cannot be made dusing speech presence.
- Graduation topic: Can we obtain better estimators for $\mathbf{R}_N$?

Acoustic Imaging of the Heart Using Microphones

- Imaging (Xray, MRI, Ultrsound, etc.) techniques are relatively expensive and not always available in developing countries.
- Can we develop a simple imaging technique to visualize the different parts of the human heart using an array of microphones.
- Applications:
  - Imaging on the basis of sound of heart and lungs.
  - Store the recordings, and perform offline beamforming to "zoom" in to certain areas.
  - In developing countries, more advanced imaging techniques are not always available in local medical centers and difficult to maintain. This should become a device which is easy to make and maintain, and give first indications of what can be wrong.

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Some Possible Topics (usually custom made)

Speech:

- Estimation of RTFs using machine learning
- Estimation of RTFs using EVD/GEVD
- …

Biomedical:

- Imaging of the heart using microphones
- Local activation time estimation
- Staging of AF
- Atrial transfer function estimation
- ECG-based early detection of AF using knowledge from EGMs.
- …