Biomedical Array Processing:

Array processing for Early Recognition and Treatment of Atrial Fibrillation

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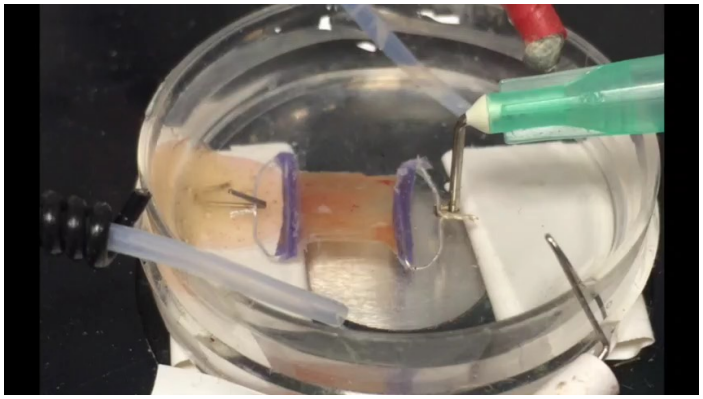
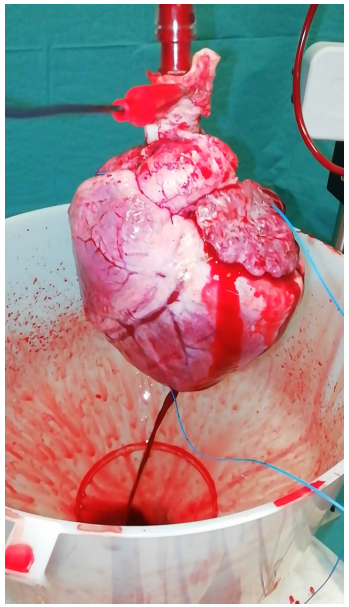


Living myocardial slices



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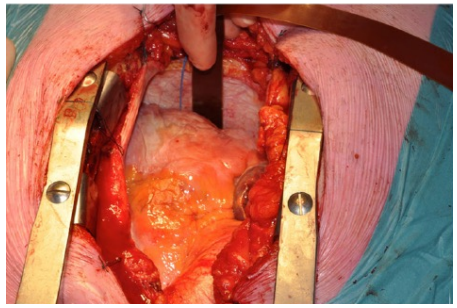

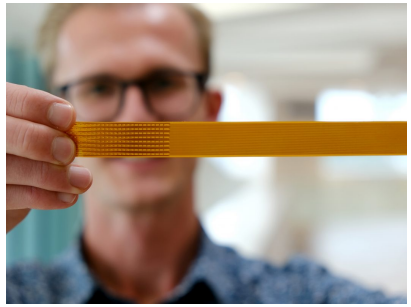

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Atrial Fibrillation

Atrial fibrillation:

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

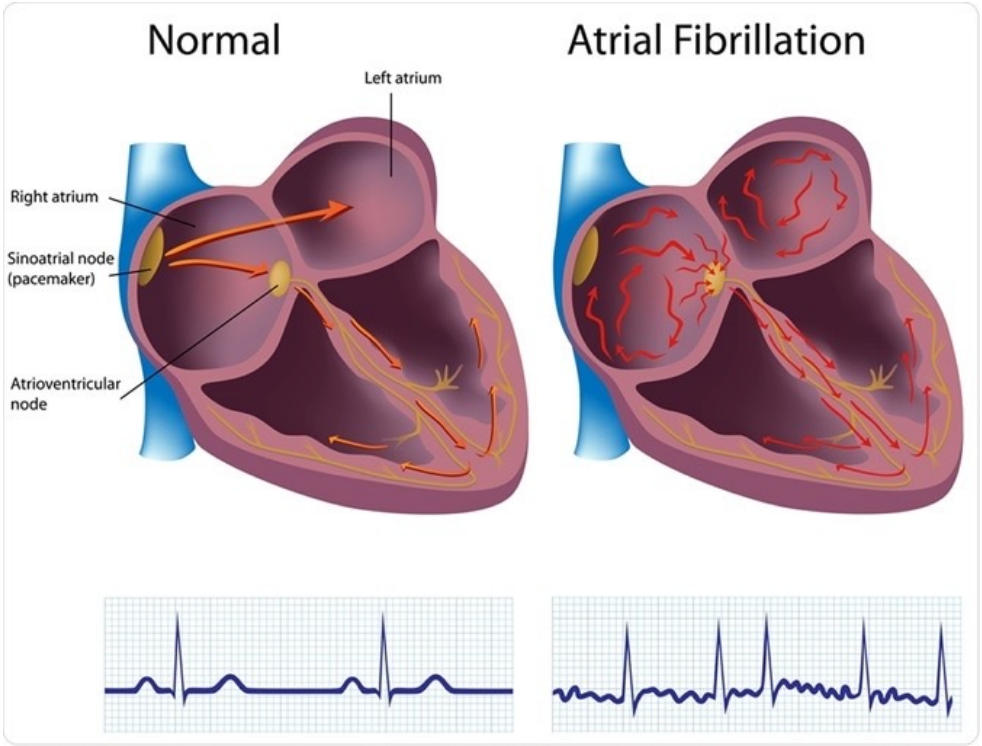
stroke or heart-related hospitalizations

Prevalence:

- Most common sustained cardiac

arrhythmia

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



Atrial fibrillation. Image Credit: Alila Medical Media / Shutterstock

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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.

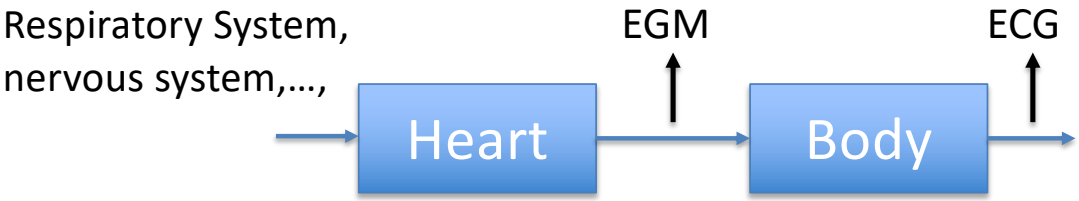
Atrial Fibrillation – Main Issues

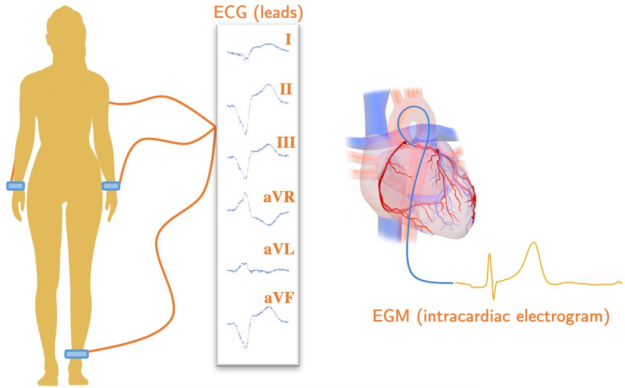
- Origin and exact mechanism of AF not (yet) well understood
- When understood…what to do?
- Non-invasive (ECG) detection (and differentiation from other arrhythmias) of AF is very challenging
- Early detection is challenging, but important (AF is progressive)

Today

- Atrial signal estimation
- Parameter estimation for cardiac tissue cells

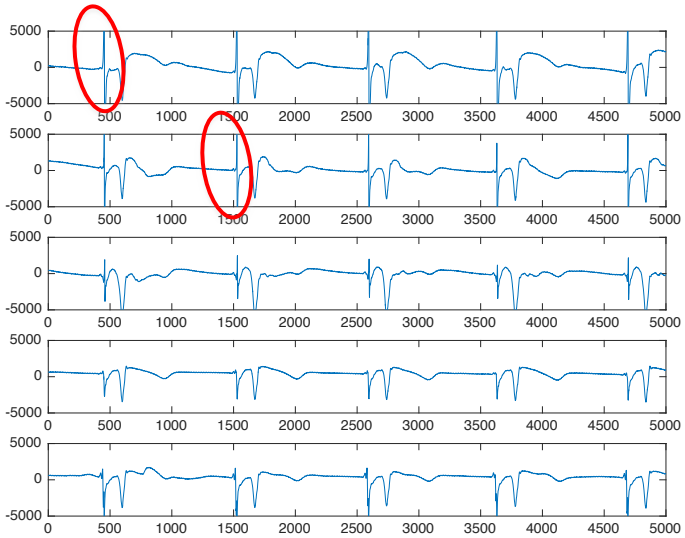
High level problem formulation



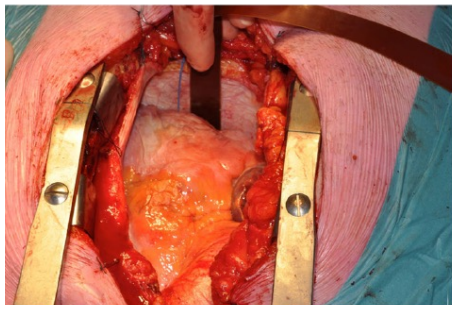


From L. Bote-Curiel et. Al, Deep Learning and Big Data in Healthcare: A Double Review for Critical Beginners. *Appl. Sci.* **2019**, *9*, 2331.

Atrial Component Estimation for EGMs



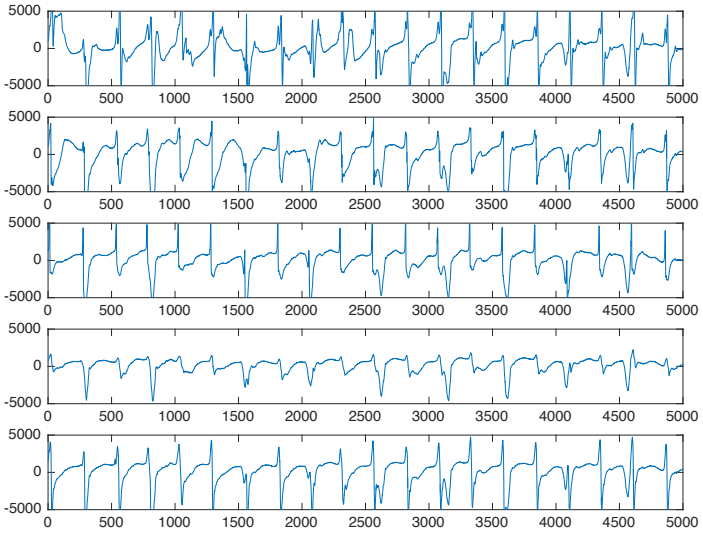
time samples ($fs = 10$ kHz)



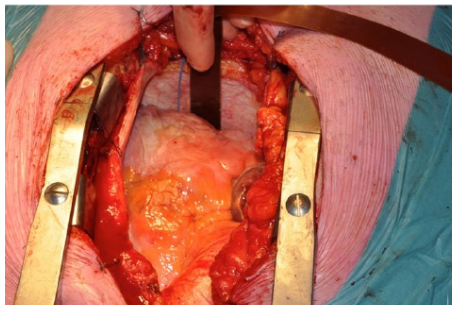
Response at 5 different positions of the sensor without atrial fibrillation.

- Inspection of atrial component by cardiologist.
- EGM also contains disturbing ventricular components.

Atrial Component Estimation for EGMs



time samples ($fs = 10$ kHz)



Response at 5 different positions of the sensor with atrial fibrillation.

- During atrial fibrillation, inspection of the atrial components is complicated due to overlap in time with ventricular component.
- How to estimate the atrial component?

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Atrial Component Estimation for EGMs

- Often a "bipolar electrode" is used in clinic.
- Bipolar electrode consists of two closely spaced sensors where the responses are subtracted.

$$EGM_{BP}[t] = EGM_m[t] - EGM_n[t]$$

- Obviously, this removes components that are common in $EGM_m[t]$ and $EGM_n[t]$ (i.e., that arrive at the same time)
- However, it also makes the response very sensitive to orientation of the array and direction of arrival of the atrial wavefront.
- Hence, the atrial component will be distorted.

EGMs – Signal model (Time)

Let the EGM at sensor m by given by

$$x_m[t] = s_{a,m}[t] + s_{v,m}[t] + n_m[t],$$

where $s_{a,m}[t]$, $s_{v,m}[t]$ and $n_m[t]$ are stochastic mutually uncorrelated processes of the atrial, ventricular and sensor self noise components respectively.

Assuming all cells generate the same action potential ("source") s_a, $s_{a,m}[t] = (s_a * a_m)[t]$ and $s_{v,m}[t] = (s_v * v_m)[t]$:

$$x_m[t] = \underbrace{(s_a * a_m)[t]}_{s_{a,m}[t]} + \underbrace{(s_v * v_m)[t]}_{s_{v,m}[t]} + n_m[t],$$

EGMs – Signal model (STFT)

Transforming to STFT domain:

$$x_m[f,\, k] = \mathcal{F}\left\{x_m[t,\, k]\right\} = s_a[f,\, k]a_m[f,\, k] + s_v[f,\, k]v_m[f,\, k] + n_m[f,\, k],$$

Stacking data across sensors per frequency f and per time frame k in vector form:

$$\mathbf{x} = s_a\mathbf{a} + s_v\mathbf{v} + \mathbf{n}.$$

Problem formulation:

Find a spatial filter $\mathbf{w}$ such that $\hat{s}_{a,m} = \mathbf{w}^H\mathbf{x}$.

EGMs – Signal model (STFT)

- Spatial cross correlation: $\mathbf{R_x} = \mathrm{E}\left[\mathbf{x}\mathbf{x}^{\mathrm{H}}\right] = \mathbf{R_A} + \mathbf{R_V} + \mathbf{R_N}$.
- Spatially uncorrelated sensor self noise: $\mathbf{R_N} = \sigma_n^2\mathbf{I}$.
- Assuming all cells generate an action potential s_a, $\mathbf{R_a} = E\left[|s_a|^2\mathbf{a}\mathbf{a}^{\mathrm{H}}\right] = \sigma_a^2\mathbf{a}\mathbf{a}^{\mathrm{H}}$
- $\mathbf{R_v} = \sigma_v^2\mathbf{v}\mathbf{v}^{\mathrm{H}}$
- $\mathbf{R_x} = \sigma_a^2\mathbf{a}\mathbf{a}^{\mathrm{H}} + \sigma_v^2\mathbf{v}\mathbf{v}^{\mathrm{H}} + \sigma_n^2\mathbf{I}$.

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Ventricular Transfer function

Ventricular transfer function $\mathbf{v}$:

- ventricular component originates from relatively far away and reaches the sensors instantaneously, meaning the phase differences are negligible and the magnitude differences are small
- $\mathbf{v} \approx \frac{1}{\sqrt{M}}\mathbf{1}$
- Remember the Bi-polar electrode: $\mathbf{w}_{BP} = [1, -1]^T$:
  - If $\mathbf{v} = \frac{1}{\sqrt{M}}\mathbf{1}$, $\mathbf{x} = s_a\mathbf{a} + s_v\frac{1}{\sqrt{M}}\mathbf{1} + \mathbf{n}$.
  - Hence, $\hat{s}_{a,m} = \mathbf{w}_{BP}^H\mathbf{x} = \mathbf{w}_{BP}^H s_a\mathbf{a} + \mathbf{w}_{BP}^H\mathbf{n}$
  - Perfectly cancellation of ventricular components
  - Distortion of the atrial components.

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Ventricular Transfer function

More accurate estimates of the ventricular transfer function can be obtained by using EVD of $\mathbf{R_x}$:

- $\mathbf{R_x} = \mathbf{U}\mathbf{\Lambda}\mathbf{U}^{\mathrm{H}}$
- Assume that the ventricular component is one of the dominant eigenvectors.
- $\hat{\mathbf{v}} = \arg\max \mathbf{U}^{\mathrm{H}}\mathbf{1}$.

The interference cross-correlation matrix then is fully described by as

$$\mathbf{R_{v+n}} = \sigma_v^2 \hat{\mathbf{v}}\hat{\mathbf{v}}^{\mathrm{H}} + \sigma_n^2 \mathbf{I}. \tag{1}$$

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Atrial Transfer Function

Using the GEVD:

$$\mathbf{U}^{\mathrm{H}}\mathbf{R_a}\mathbf{U} = \mathbf{\Lambda}, \text{ and } \mathbf{U}^{\mathrm{H}}\mathbf{R_{v+n}}\mathbf{U} = \mathbf{I}.$$

Setting $\mathbf{Q} = \mathbf{U}^{-\mathrm{H}}$, gives

$$\mathbf{R_a} = \mathbf{Q}\mathbf{\Lambda}\mathbf{Q}^{\mathrm{H}}, \text{ and } \mathbf{R_{v+n}} = \mathbf{Q}\mathbf{Q}^{\mathrm{H}}.$$

Leading to:

$$\mathbf{R_x} = \mathbf{R_a} + \mathbf{R_{v+n}} = \mathbf{Q}\left(\mathbf{\Lambda} + \mathbf{I}\right)\mathbf{Q}^{\mathrm{H}},$$

$$\mathbf{U}^{\mathrm{H}}\mathbf{R_x}\mathbf{U} = \mathbf{\Lambda} + \mathbf{I}.$$

Assuming rank $r = 1$ for $\mathbf{R_a}$, the estimated atrial transfer function is then given by

$$\hat{\mathbf{a}} = \mathbf{Q}\mathbf{e}_1.$$

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Atrial Component Estimation

Using the MVDR beanforner:

$$\begin{aligned} \min_{\mathbf{w}^{\mathrm{H}}} \quad & \mathbf{w}^{\mathrm{H}}\mathbf{R}_{\mathbf{v}+\mathbf{n}}\mathbf{w} \\ \text{s.t.} \quad & \mathbf{w}^{\mathrm{H}}\mathbf{a} = 1. \end{aligned}$$

Assuming $\mathbf{a}$ is normalized for the mth electrode,

$$\hat{s}_m = \mathbf{w}^{\mathrm{H}}\mathbf{x}$$

and

$$\hat{\mathbf{s}} = \hat{s}_m\mathbf{a} = (\mathbf{w}^{\mathrm{H}}\mathbf{x})\mathbf{a}$$

Results – Bipolar vs. Proposed

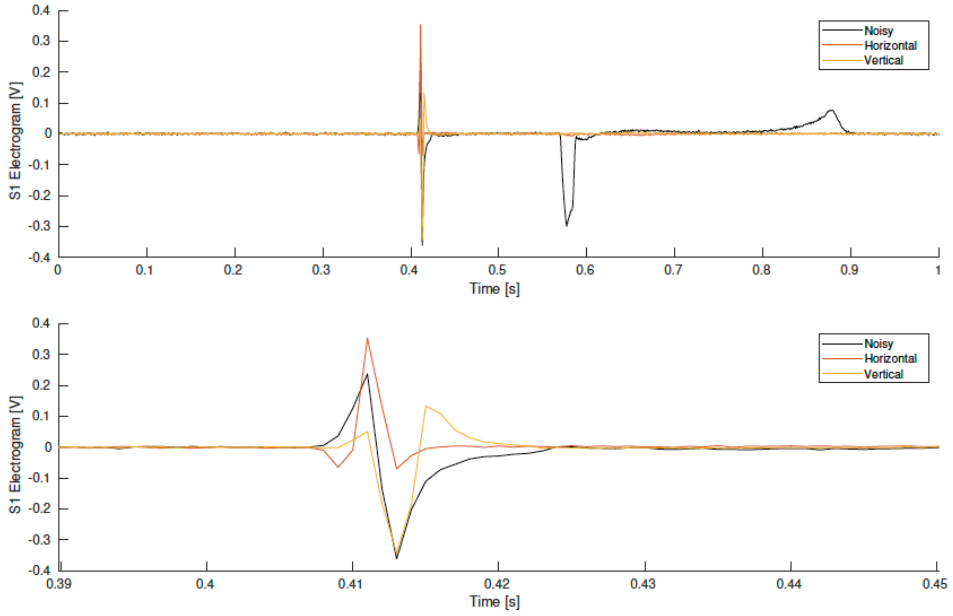

Figure 3.5: A comparison of two different orientations of bipolar electrodes against the noisy EGM of S1, where the bottom plot is a zoomed version of the top one. The EGMs have been composed with an SNR of 20 dB.

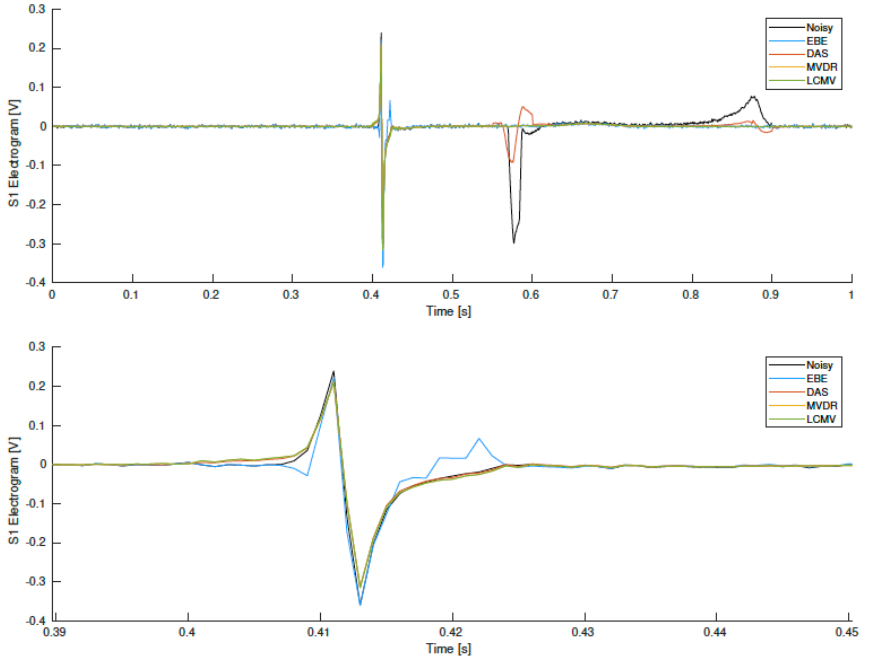

Figure 3.7: A comparison of the four beamformers using V2 against the noisy EGM of S1 using all $M = 25$ electrodes, where the bottom plot is a zoomed version of the top one. The EGMs have been composed with an SNR of 20 dB.

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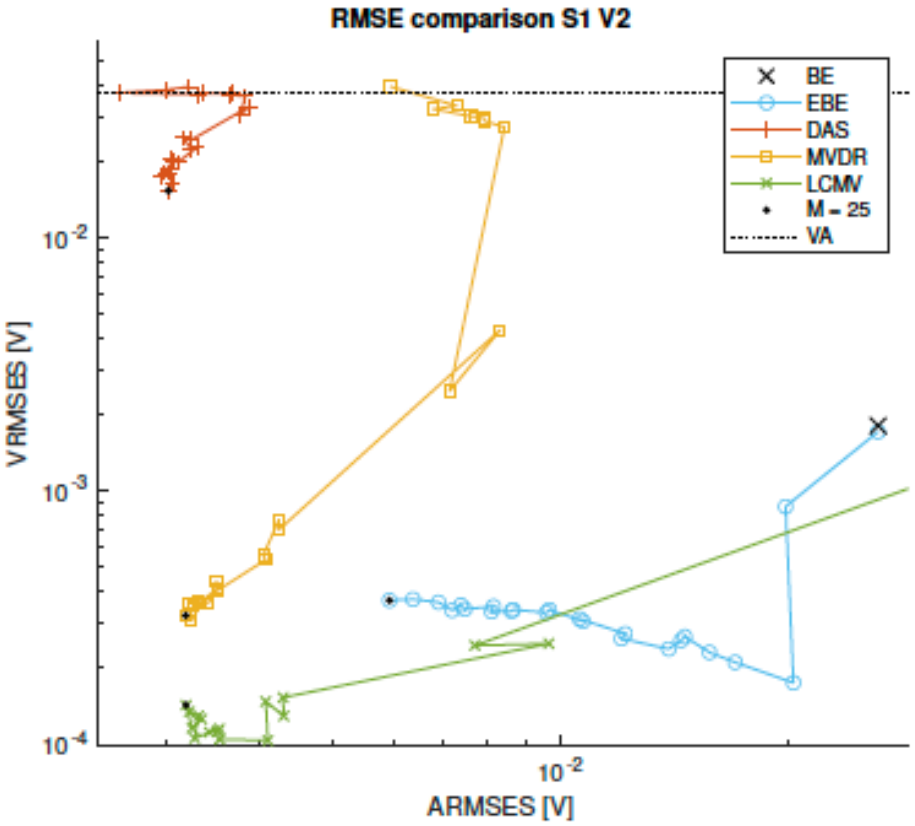
Results – Bipolar vs. Proposed



- Propose estimators can use any number of electrodes.
- Given atrial transfer fuction, target is undistorted.
- Current limitation: Rank-1 is assumed for target correlation matrix $\mathbf{R_a}$
- Instead of using $\hat{\mathbf{a}} = \mathbf{Q}\mathbf{e}_1$ assume rank $r > 1$ and use complete signal subspace.

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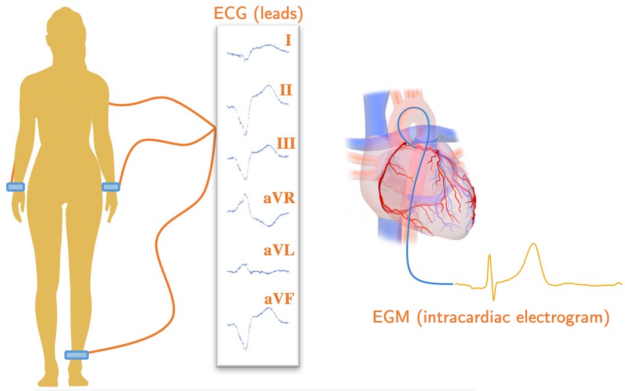
High level problem formulation

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



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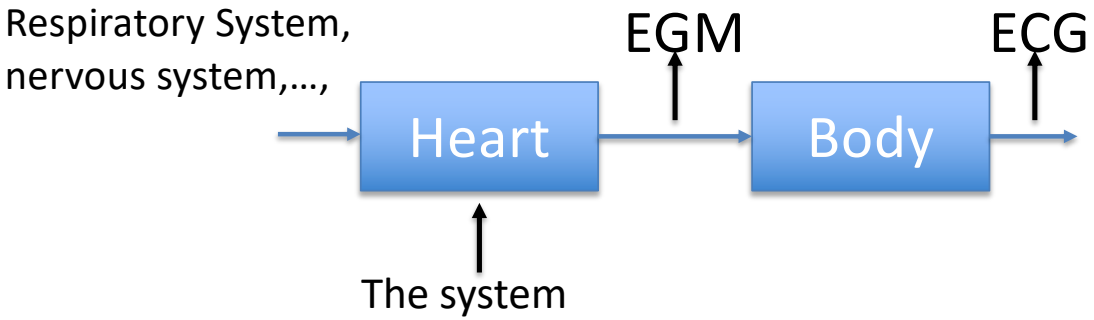

My philosophy: Given EGM/ECG realizations, try to infer the system that generated these.

- 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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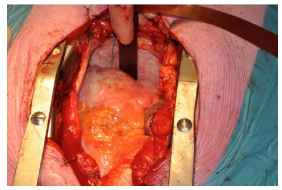
High level overview of projects



Respiratory System,
nervous system,…,

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

- Find transfer functions from

EGM <=> ECG

1 Early non-invasive ECG-based AF detection

- How to characterize AF (features)?
- How to differentiate the different stages of AF?
- How to differentiate from other arrhythmias?

Given EGM signals, can we learn what to look for in the ECG?
Can we extract EGM/atrial parameters from the ECG?

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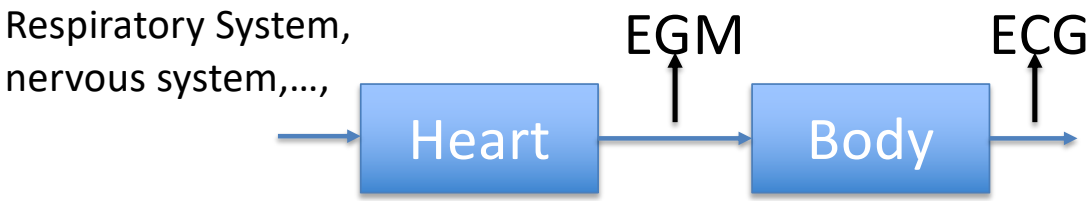
High level overview of projects

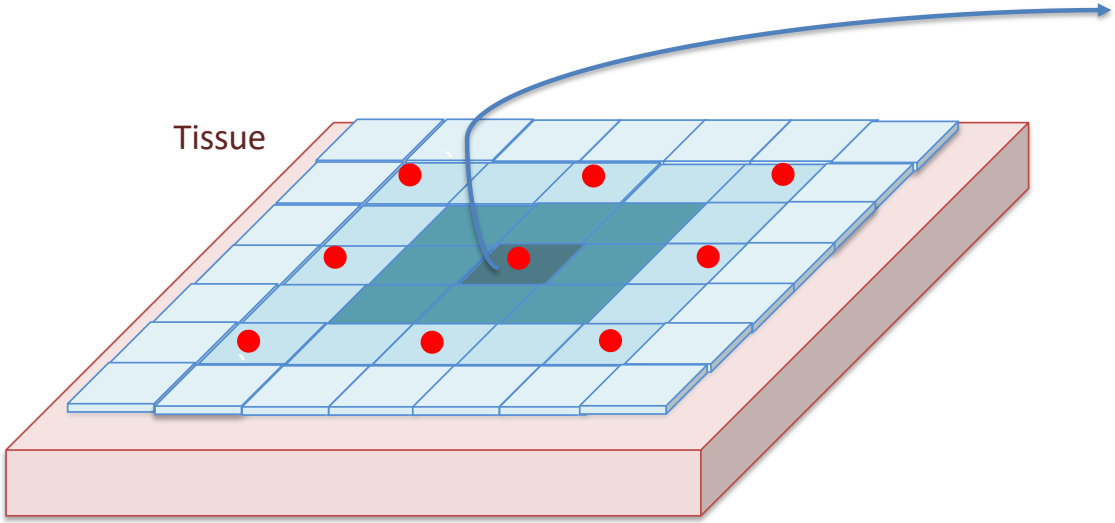
1 Early non-invasive ECG-based AF detection



2 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

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

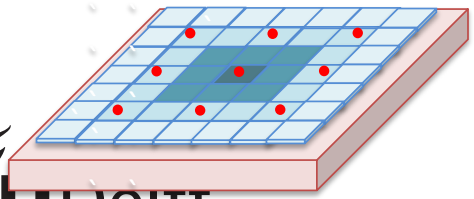
Let the EGM at sensor m, at coordinates $\mathbf{y}_m$ and time t be given by $\phi_m(\mathbf{y}_m, t)$

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

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 $\boldsymbol{\delta}(t) = [\delta(t - \tau_0), \delta(t - \tau_1), ..., \delta(t - \tau_{N-1})]^T$.



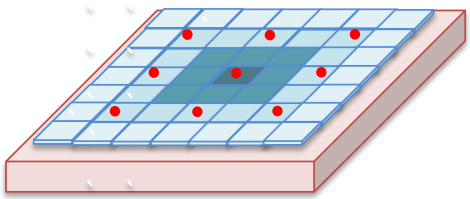
Altogether we have:

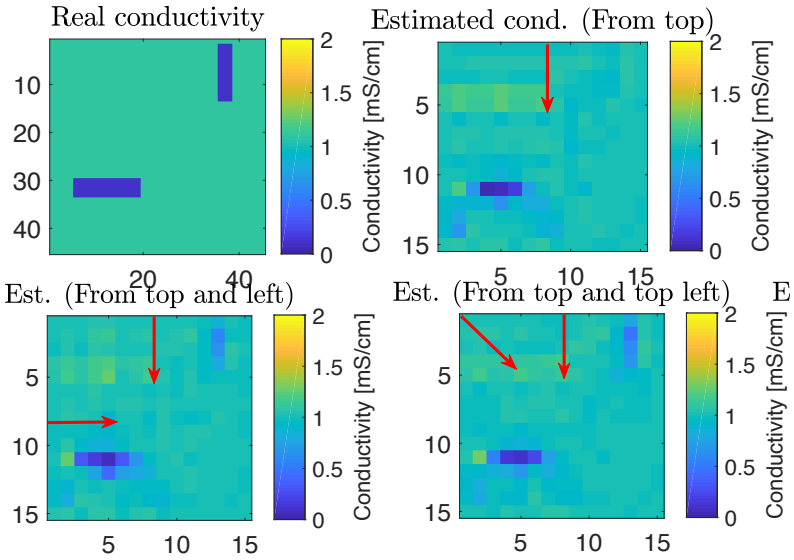
$$\phi_m(t) = a_m(t) * v_0(t)$$

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.

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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.

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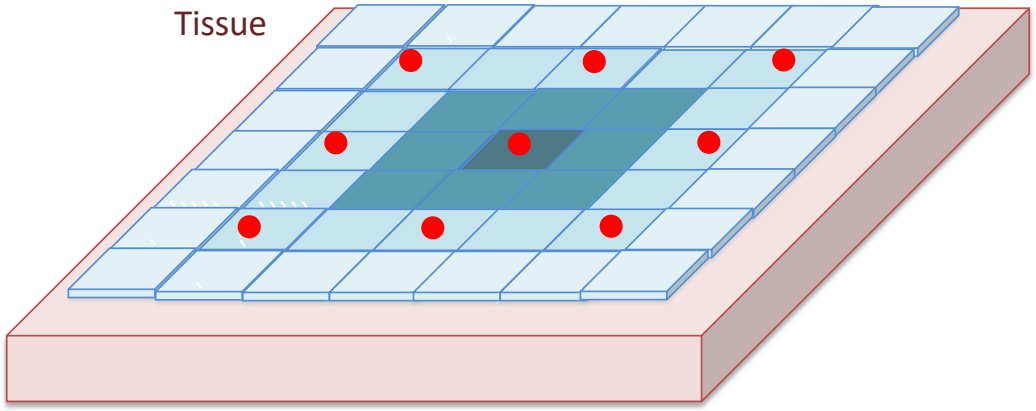
Confirmatory Factor Analysis

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

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

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

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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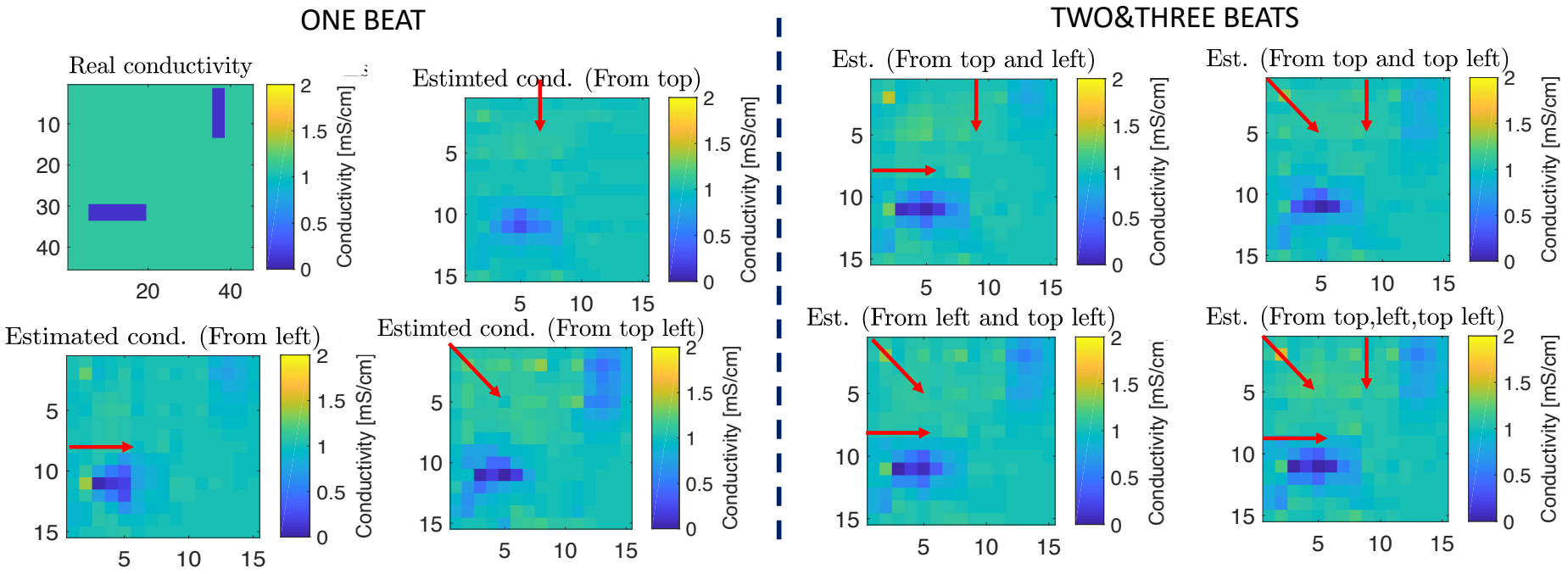
Experiments with Simulated Data



Estimating “cell” properties - Open questions…

- How to estimate parameters for deeper layers?
- How to take the sensor height into account?
- What if we measure on a (small) distance? => catheter
- Current method for confirmatory factor analysis is complex (and non-convex). Can we develop less complex methods?
- How to do this less/non invasive based on ECG or catheter?
- The assumption of a single action potential shape is not always valid. How to generalize this?
- How to use this information to guide the surgeon during ablation or other techniques?

Some Example Graduation topics

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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 $\hat{\mathbf{R}}_N$)

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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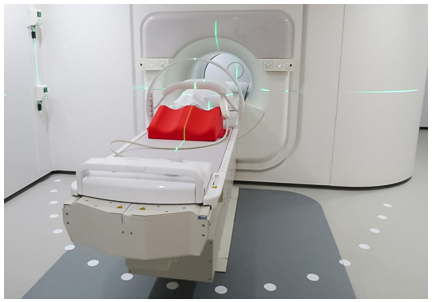
Some Possible Topics (usually custom made)

Speech & Audio processing:

- Estimation of RTFs using machine learning
- Active Noise Reduction for MRIs



Biomedical:

- Imaging of the heart using microphones
- Local activation time estimation
- Staging and detection of AF using ECG measurements
- Atrial transfer function estimation
- ECG inversion: Can we estimate parameters from the atrial cells from (many) ECG signals.
- Estimation of tissue properties from EGMs
- Through the skull Doppler ultrasound imaging
- …

GSP

- Dynamic graph topology identification with applications to brain science and recommender systems
- Lifetime optimization in IoT networks using graph signal processing

Localization:

- Acoustic vector sensors for acoustic imaging and source localization

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Some hints for project 2

Constructing the noisy signal:

- For sources s_p and microphone m: $x_m[t] = (s_1 * h_{1,m})[n] + \sum_{p=2}^{P}(s_p * h_{p,m})[t]$
- Processing using STFT (i.e., using short time frames of 20 ms): window and FFT the samples $x_m[\text{overlap}(l-1)+1 : \text{overlap}(l-1)+\text{frsize}]$

Estimating Correlation matrices: $\mathbf{R_n}(k,l) = E[\mathbf{n}(k,l)\mathbf{n}^H(k,l)]$ and $\mathbf{R_x}(k,l) = E[\mathbf{x}(k,l)\mathbf{x}^H(k,l)]$

- Assuming ergodicity (sources are spatially invariant) you can estimate $\mathbf{R_n}(k,l)$ e.g. as

$$\hat{\mathbf{R}}_\mathbf{n}(k,l) = \frac{1}{N}\sum_{p=l-M_1}^{l+M_2}\mathbf{n}(k,p)\mathbf{n}^H(k,p)$$

or as

$$\begin{aligned}\hat{\mathbf{R}}_\mathbf{n}(k,l) &= \begin{cases}\hat{\mathbf{R}}_\mathbf{n}(k,l-1)\alpha + \mathbf{n}(k,l)\mathbf{n}^H(k,l)(1-\alpha) & \text{target not present}\\ \hat{\mathbf{R}}_\mathbf{n}(k,l-1) & \text{target is present}\end{cases}\\ \hat{\mathbf{R}}_\mathbf{x}(k,l) &= \hat{\mathbf{R}}_\mathbf{x}(k,l-1)\alpha + \mathbf{x}(k,l)\mathbf{x}^H(k,l)(1-\alpha)\end{aligned}$$

- How to know whether the target is present or not? Either cheat by using directly the mix of interferers, or build a detector.