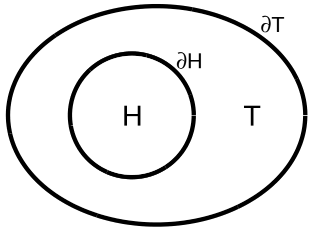
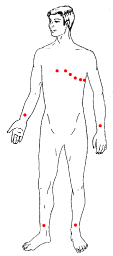
The classical inverse ECG problem

Is it possible to compute the electrical potential at the surface of the heart from body surface measurements?

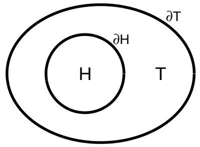




Why?

- Improve traditional ECG recordings
- Better qualitative and quantitative understanding of the heart
- Detect diseases and malfunctions
- ...

The Bidomain model



$$\chi C_m \frac{\partial v}{\partial t} + \chi I_{\text{ion}}(v) = \nabla \cdot (\boldsymbol{M}_i \nabla v) + \nabla \cdot (\boldsymbol{M}_i \nabla u_e) \quad \text{in } H$$
$$\nabla \cdot (\boldsymbol{M}_i \nabla v) + \nabla \cdot ((\boldsymbol{M}_i + \boldsymbol{M}_e) \nabla u_e) = 0 \quad \text{in } H$$
$$\nabla \cdot \boldsymbol{M} \nabla u = 0 \quad \text{in } T$$

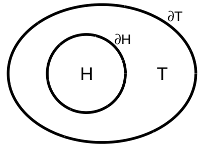
- $v = u_i - u_e$: membrane potential
- I_{ion}: ionic current
- $\boldsymbol{M}_i, \boldsymbol{M}_e$: conductivity tensors

Outside the heart

In T (torso):

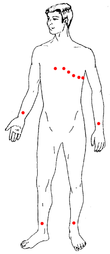
$$\begin{aligned} \nabla \cdot (M \nabla u) &= 0 \quad \text{in } T, \\ (M \nabla u) \cdot n &= 0 \quad \text{along } \partial T. \end{aligned}$$

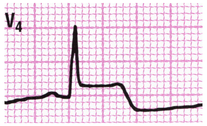
(Not a closed problem!)



ECG (electrocardiogram)

- ECG recording $\to d = d(t)$ along $\Gamma \subset \partial T$
- Focus on one time instance $t = t^*$, $d = d(t^*)$
- Briefly about the time dependent problem



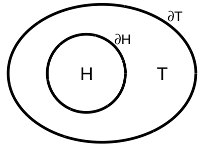


Outside the heart + ECG

In T (torso):

$$\nabla \cdot (M\nabla u) = 0 \quad \text{in } T,$$
$$(M\nabla u) \cdot n = 0 \quad \text{along } \partial T,$$
$$+ \text{ ECG recording of } u \text{ along } \Gamma \subset \partial T.$$

u **along** ∂H**?**



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The Challenge, cont.

Operator $R(g) = u(g)|_\Gamma$, where $u = u(g)$ solves

$$\begin{aligned} \nabla \cdot (M\nabla u) &= 0 \quad \text{in } T, \\ (M\nabla u) \cdot n &= 0 \quad \text{along } \partial T, \\ u &= g \quad \text{along } \partial H. \end{aligned}$$

Find g such that

$$R(g) = d,$$

where d is the data from the ECG recording

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Properties

Solve

$$R(g) = d \tag{1}$$

for g.

- R is a linear operator
- (1) is ill-posed
- If $d \notin \mathrm{Range(R)}$

$$\min_g \|R(g) - d\|^2.$$

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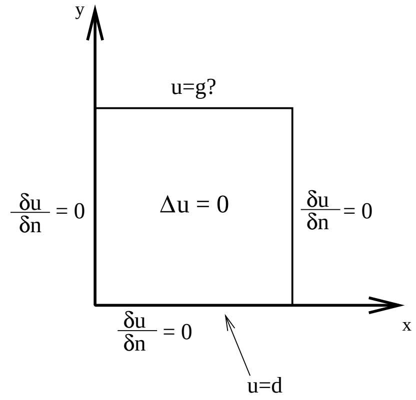
This lecture

- Fourier analysis on the unit square, stationary
- The general case, stationary
- The time dependent problem
- Numerical results

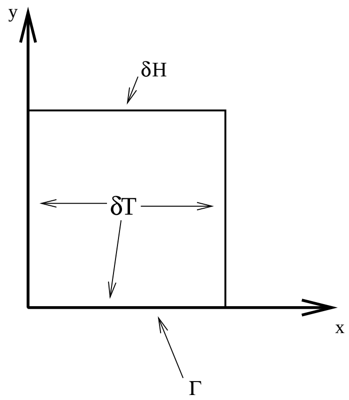
Fourier analysis

Unit square



Fourier analysis

Unit square



The direct problem

Find $u = u(g)$ satisfying

$$\begin{aligned} \Delta u &= 0 \quad \text{in } T, \\ \nabla u \cdot n &= 0 \quad \text{along } \partial T, \\ u &= g \quad \text{along } \partial H. \end{aligned}$$

The direct problem, cont.

Separation of variables:

$$N_k(x,y) = \cos(k\pi x)\cosh(k\pi y), \quad k = 0, 1, \ldots$$

satisfies

$$\begin{aligned} \Delta u &= 0 \quad \text{in } T, \\ \nabla u \cdot n &= 0 \quad \text{along } \partial T. \end{aligned}$$

The direct problem, cont.

Linearity:

$$u(x,y) = \sum_{k=0}^{\infty} c_k \cos(k\pi x)\cosh(k\pi y),$$

where $\{c_k\}$ are constants, satisfies

$$\begin{aligned} \Delta u &= 0 \quad \text{in } T, \\ \nabla u \cdot n &= 0 \quad \text{along } \partial T. \end{aligned}$$

The direct problem, cont.

Fourier cosine series of g:

$$g(x) = \sum_{k=0}^{\infty} p_k \cos(k\pi x)$$

Solution formula for the direct problem

$$u(g)(x,y) = u(x,y) = \sum_{k=0}^{\infty} \frac{p_k}{\cosh(k\pi)} \cos(k\pi x)\cosh(k\pi y).$$

The direct problem, cont.

R: heart surface $\rightarrow$ body surface

$$\begin{aligned} R(g) &= R\left(\sum_{k=0}^{\infty} p_k \cos(k\pi x)\right) = u(g)(x,0) \\ &= \sum_{k=0}^{\infty} \frac{p_k}{\cosh(k\pi)} \cos(k\pi x) \end{aligned}$$

The direct problem, cont.

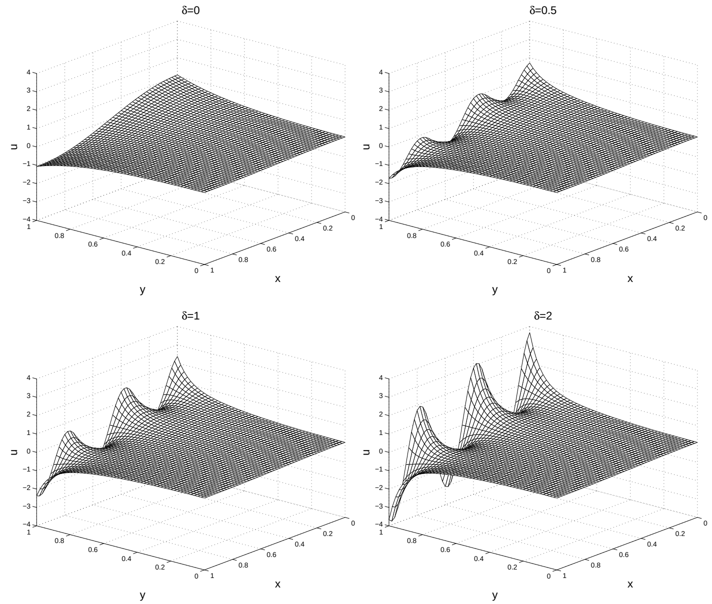
- Fourier coeff.: $p_k \to \frac{p_k}{\cosh(k\pi)}$
- Large k

$$\left|\frac{p_k}{\cosh(k\pi)}\right| \ll |p_k|$$

strong damping effect

- R has a strong smoothing effect

The direct problem, cont.



The inverse problem

- R: heart surface $\to$ body surface
- For a given ECG recording d, find g such that

$$R(g) = d$$

- Recall that

$$R\left(\sum_{k=0}^{\infty} p_k \cos(k\pi x)\right) = \sum_{k=0}^{\infty} \frac{p_k}{\cosh(k\pi)} \cos(k\pi x)$$

The inverse problem, cont

- Consequently

$$R\left(\cos(k\pi x)\right) = \frac{1}{\cosh(k\pi)} \cos(k\pi x)$$

- Eigenvalues

$$\lambda_k = \frac{1}{\cosh(k\pi)} \qquad k = 1, 2, \ldots$$

- Zero is a cluster point for $\{\lambda_k\}$
- R not continuously invertible, R^{-1} <u>not</u> "well-behaved"

The inverse problem, cont.

Fourier expansion

$$d(x) = \sum_{k=0}^{\infty} d_k \cos(k\pi x)$$

Can Easy solve $R(g) = d$ for $g = \sum_{k=0}^{\infty} p_k \cos(k\pi x)$:

$$R(g) = \sum_{k=0}^{\infty} \frac{p_k}{\cosh(k\pi)} \cos(k\pi x) = \sum_{k=0}^{\infty} d_k \cos(k\pi x),$$

yields

$$p_k = d_k \cosh(k\pi) \quad \text{for } k = 0, 1, \ldots.$$

The inverse problem, cont.

Consequently

$$\begin{aligned} g(x) &= R^{-1}(d(x)) = R^{-1}\left(\sum_{k=0}^{\infty} d_k \cos(k\pi x)\right) \\ &= \sum_{k=0}^{\infty} d_k \cosh(k\pi) \cos(k\pi x) \end{aligned}$$

- Fourier coeff.: $d_k \to d_k \cosh(k\pi)$
- Even for small k, $\cosh(k\pi)$ is large, e.g.

$$\cosh(5\pi) \approx 3.32 \cdot 10^6$$

Example 1

- Exact data, $d(x) = \cosh^{-1}(\pi)\cos(\pi x)$
- Error-prone data, $d_\delta(x) = d(x) + \delta \cos(5\pi x)$
- Then

$$R^{-1}(d_\delta) - R^{-1}(d) \approx 3.32 \cdot 10^6\, \delta \cos(5\pi x)$$

- For example, $\|d_\delta - d\|_{L^\infty} = O(10^{-3})$ implies that

$$\|R^{-1}(d_\delta) - R^{-1}(d)\|_{L^\infty} = O(10^3)$$

Regularization

- Output least squares, minimize

$$J(g) = \|R(g) - d\|^2_{L^2(\Gamma)}$$

- Tikhonov regularization

$$J_\epsilon(g) = \|R(g) - d\|^2_{L^2(\Gamma)} + \epsilon\|g\|^2_{L^2(\partial H)}$$

- Second order Tikhonov regularization

$$J_{2,\epsilon}(g) = \|R(g) - d\|^2_{L^2(\Gamma)} + \epsilon\|g_{xx}\|^2_{L^2(\partial H)}$$

- Approximations

$$R_\epsilon^{-1} \approx R^{-1} \quad \text{and} \quad R_{2,\epsilon}^{-1} \approx R^{-1}$$

(derived from $\nabla J_\epsilon = 0$ and $\nabla J_{2,\epsilon} = 0$)

Regularization, cont.

R: heart surface $\to$ body surface

- No regularization

$$R^{-1}\left(\sum_{k=0}^{\infty} d_k \cos(k\pi x)\right) = \sum_{k=0}^{\infty} d_k \cosh(k\pi)\cos(k\pi x)$$

- Tikhonov

$$R_\epsilon^{-1}\left(\sum_{k=0}^{\infty} d_k \cos(k\pi x)\right) = \sum_{k=0}^{\infty} d_k \frac{\cosh(k\pi)}{1+\epsilon\cosh^2(k\pi)}\cos(k\pi x)$$

- Second order Tikhonov

$$R_{2,\epsilon}^{-1}\left(\sum_{k=0}^{\infty} d_k \cos(k\pi x)\right) = \sum_{k=0}^{\infty} d_k \frac{\cosh(k\pi)}{1+\epsilon(k\pi)^4\cosh^2(k\pi)}\cos(k\pi x)$$

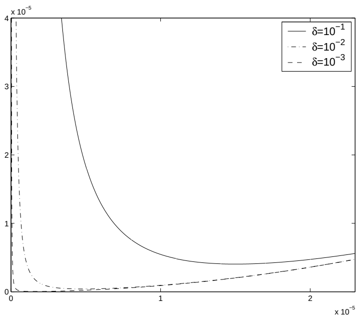
Regularization, cont.

- For the low frequency components of the data d, the action of R^{-1}, R_ϵ^{-1} and $R_{2,\epsilon}^{-1}$ is almost identical, provided that ϵ is small
- The high frequency components of d are damped efficiently by R_ϵ^{-1} and $R_{2,\epsilon}^{-1}$

Example 1, revisited

- Exact data, $d(x) = \cosh^{-1}(\pi)\cos(\pi x)$
- Error-prone data, $d_\delta(x) = d(x) + \delta\cos(5\pi x)$
- Tikhonov, error

$$E(\epsilon,\delta) = \|R^{-1}(d) - R_\epsilon^{-1}(d_\delta)\|^2_{L^2(\partial H)}$$



Example 1, revisited - cont.

L^2 error on the heart surface

- No regularization

$$e(\delta) \approx 2.35 \cdot 10^6 \delta$$

- Tikhonov (optimal regularization)

$$E(\delta) \approx 4.05 \cdot 10^{-5}\delta$$

- Second order Tikhonov (optimal regularization)

$$E_2(\delta) \approx 6.48 \cdot 10^{-8}\delta,$$

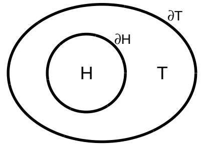
Example 1, revisited - cont.

- Second order works better than plain Tikhonov regularization
- In general, difficult to find an optimal value for the regularization parameter ϵ

The general case

R: heart surface $\to$ (part of the) body surface

- Complex geometry
- Non-constant conductivity M
- Fourier analysis impossible



The general case, cont.

Operator $R(g) = u(g)|_\Gamma$, where $u = u(g)$ solves

$$\begin{aligned} \nabla \cdot (M \nabla u) &= 0 \quad \text{in } T, \\ (M \nabla u) \cdot n &= 0 \quad \text{along } \partial T, \\ u &= g \quad \text{along } \partial H, \end{aligned}$$

and $\Gamma \subset \partial H$.

Find g such that

$$R(g) = d.$$

Linearity

R is a linear operator:

$$R(a_1 g_1 + a_2 g_2) = a_1 R(g_1) + a_2 R(g_2),$$

for any scalars a_1 and a_2 and functions g_1 and g_2 defined on ∂H.

We will use this fact to discretize our inverse problem

Discretization

Linearly independent functions

$$g_1, \ldots, g_n : \partial H \to \mathbb{R},$$

and

$$\begin{aligned} V_n &= \text{span}\{g_1, \ldots, g_n\}, \\ R_n &= R|_{V_n} \end{aligned}$$

Discretization, cont.

$g \in V_n$:

$$g = \sum_{i=1}^{n} p_i g_i,$$

where $\{p_i\}$ are scalars.
Consequently, if

$$r_i = R_n(g_i) \quad \text{for } i = 1, \ldots, n,$$

then the linearity of R_n implies that

$$R_n(g) = \sum_{i=1}^{n} p_i r_i.$$

Discretization, cont.

- Original problem

$$R_n(g) = d$$

- $d \notin \text{Range}(R_n)$

$$\min_{g \in V_n} \|R_n(g) - d\|^2_{L^2(\Gamma)}$$

- Tikhonov

$$\min_{g \in V_n} \left\{ \|R_n(g) - d\|^2_{L^2(\Gamma)} + \epsilon \|g\|^2_{L^2(\partial H)} \right\}$$

Discretization, cont.

$g = \sum_{i=1}^{n} p_i g_i$, thus

$$\begin{aligned} J_\epsilon(g) &= J_\epsilon(p_1, \ldots, p_n) \\ &= \|R_n(g) - d\|^2_{L^2(\Gamma)} + \epsilon \|g\|^2_{L^2(\partial H)} \\ &= \|\sum_{i=1}^{n} p_i r_i - d\|^2_{L^2(\Gamma)} + \epsilon \|\sum_{i=1}^{n} p_i g_i\|^2_{L^2(\partial H)}, \end{aligned}$$

where

$$r_i = R_n(g_i) \quad \text{for } i = 1, \ldots, n,$$

Discretization, cont.

The condition

$$\frac{\partial J_\epsilon}{\partial p_i} = 0 \quad \text{for } i = 1, \dots, n,$$

gives the $n \times n$ system

$$\sum_{j=1}^{n} \left[\int_\Gamma r_j r_i \, dx + \epsilon \int_{\partial H} g_j g_i \, dx \right] p_j = \int_\Gamma d r_i \, dx \quad \text{for } i = 1, \dots, n.$$

Discretization, cont.

Which may be written on the form

$$B_\epsilon p = c,$$

where

$$\begin{aligned} B_\epsilon &= [b_{\epsilon,ij}] \in \mathbf{R}^{n\times n}, \quad b_{\epsilon,ij} = \int_\Gamma r_j r_i \, dx + \epsilon \int_{\partial H} g_j g_i \, dx \\ p &= (p_1, \dots, p_n)^T \in \mathbf{R}^n, \\ c &= \left(\int_\Gamma d r_1 \, dx, \dots, \int_\Gamma d r_n \, dx \right)^T \in \mathbf{R}^n, \end{aligned}$$

An algorithm

a) Pick n linearly independent functions

$$g_1, \dots, g_n : \partial H \to \mathbb{R},$$

defined at the surface ∂H of the heart H

b) For $i = 1, \dots, n$, set $g = g_i$ in the direct problem and solve it for $u = u(g_i)$

c) Compute

$$r_i = u(g_i)|_\Gamma, \quad i = 1, \dots, n$$

An algorithm, cont.

d) Compute the matrix B_ϵ

e) Compute the right hand side c

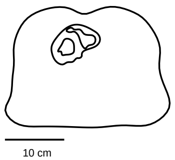
f) Solve the linear system $B_\epsilon p = c$ for p

g) Compute the potential g at the heart surface by

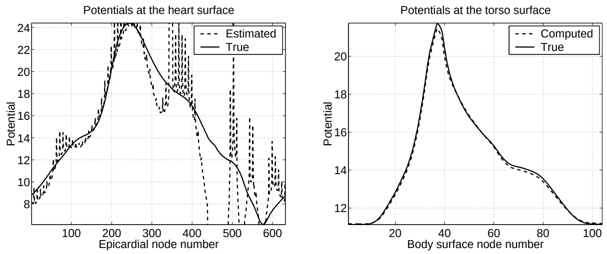
$$g = \sum_{i=1}^{n} p_i g_i$$

For each new observation d, only steps e)-g) have to be carried out. (Important for the time dependent problem)

Example 2

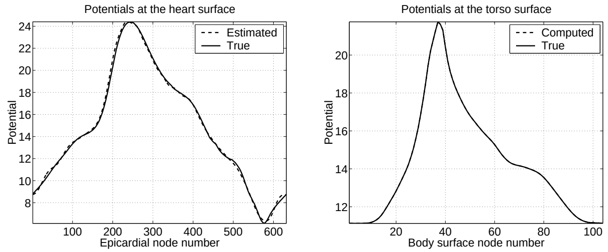


Tikhonov, $\epsilon = 10^{-3}$



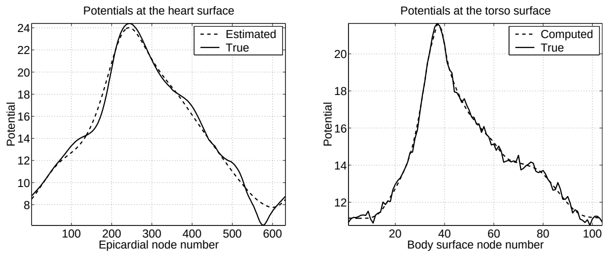
Example 2, cont.

Second order Tikhonov, $\epsilon = 10^{-8}$



Example 2, cont.

Second order Tikhonov, 1% noise, $\epsilon = 1$



The time dependent problem

- Time instances $t_0, \ldots, t_M$ with data

$$d^0, \ldots, d^M \in L^2(\Gamma)$$

  defined at the body surface
- Compute the corresponding potentials at the heart surface

$$g^0, \ldots, g^M$$

Brute force: Solve

$$B_\epsilon p^\tau = c^\tau \quad \text{for } \tau = 0, \ldots, M$$

The time dependent problem, cont.

- Ensure that the change in the epicardial potential is small from one time step to the next

$$\min_{g^\tau \in V_n} \left[\|R_n(g^\tau) - d^\tau\|^2_{L^2(\Gamma)} + \epsilon \|g^\tau - g^{\tau-1}\|^2_{L^2(\partial H)} \right]$$

for $\tau = 1, \ldots, M$

- Hybrid scheme

$$\min_{g^\tau \in V_n} \left[\|R_n(g^\tau) - d^\tau\|^2_{L^2(\Gamma)} + \epsilon \|g^\tau - g^{\tau-1}\|^2_{L^2(\partial H)} + \beta \|\Delta_{\partial H} g^\tau\|^2_{L^2(\partial}$$

($\Delta_{\partial H} g^\tau = \mathrm{curl}_{\partial H}\, \vec{\mathrm{curl}}_{\partial H}\, g^\tau$ - Laplace-Beltrami operator)

- More advanced schemes (F. Greensite)

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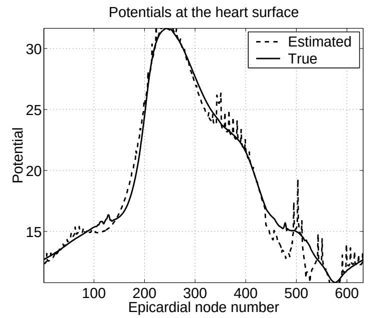
Example 3

$$\min_{g^\tau \in V_n} \left[\|R_n(g^\tau) - d^\tau\|^2_{L^2(\Gamma)} + \epsilon \|g^\tau - g^{\tau-1}\|^2_{L^2(\partial H)} \right]$$

$\epsilon = 0.01$



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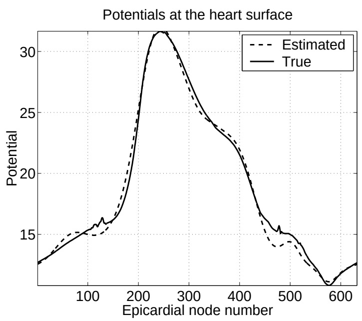
Example 3, cont.

$$\min_{g^\tau \in V_n} \left[\|R_n(g^\tau) - d^\tau\|^2_{L^2(\Gamma)} + \epsilon \|g^\tau - g^{\tau-1}\|^2_{L^2(\partial H)} + \beta \|\Delta_{\partial H} g^\tau\|^2_{L^2(\partial H)} \right]$$

$\epsilon = 0.01$ and $\beta = 1$



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Summary

Aim: To compute the potential at the heart surface from body surface measurements (ECGs)

- Leads to a linear problem $R(g) = d$
- Ill-posed
- From a mathematical point of view, fairly simple
- Second order Tikhonov regularization works well
- Main practical problems:
  - Noisy ECG data
  - High quality geometrical models of the body required