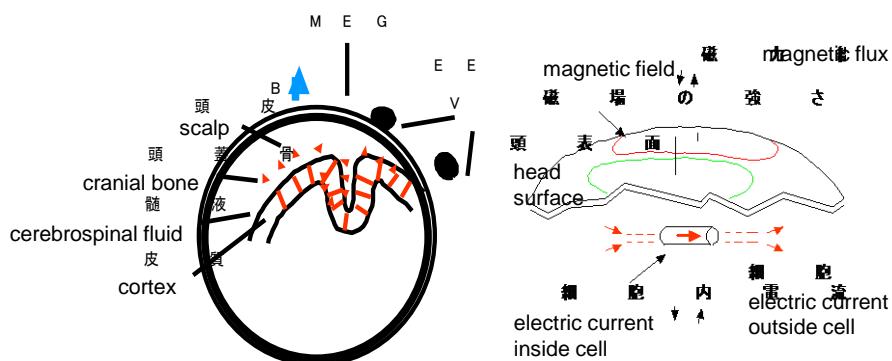


Practical Aspects of Some Bio-magnetic Inverse Problems

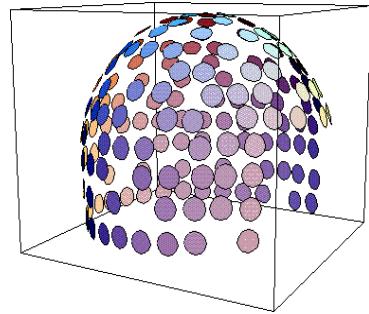
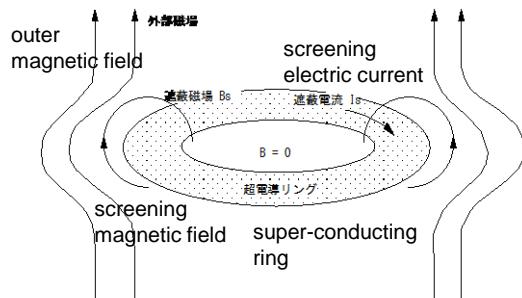
Takashi Suzuki

Magneto- Encephalography

脳磁図分析



超伝導量子干渉素子 SUperconducting Quantum Interference Device



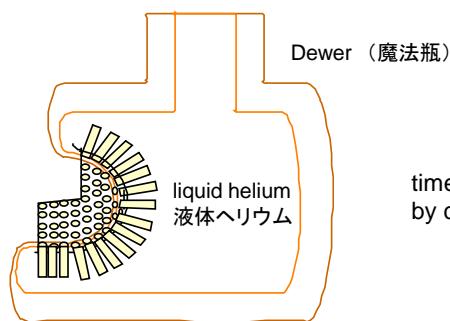
Josephson効果

リングを二つ並列につなぐと電流の位相差が干渉して
量子化した磁束が電圧から測定できる

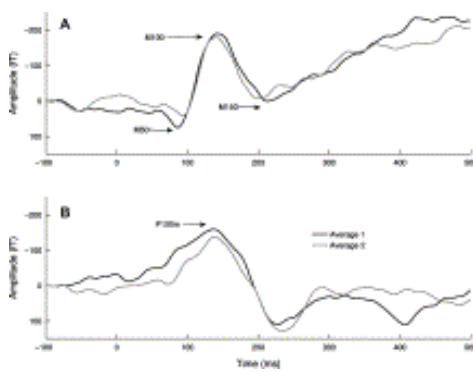
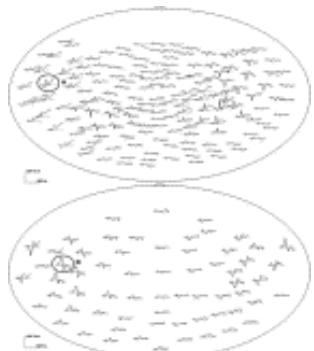
critical current level

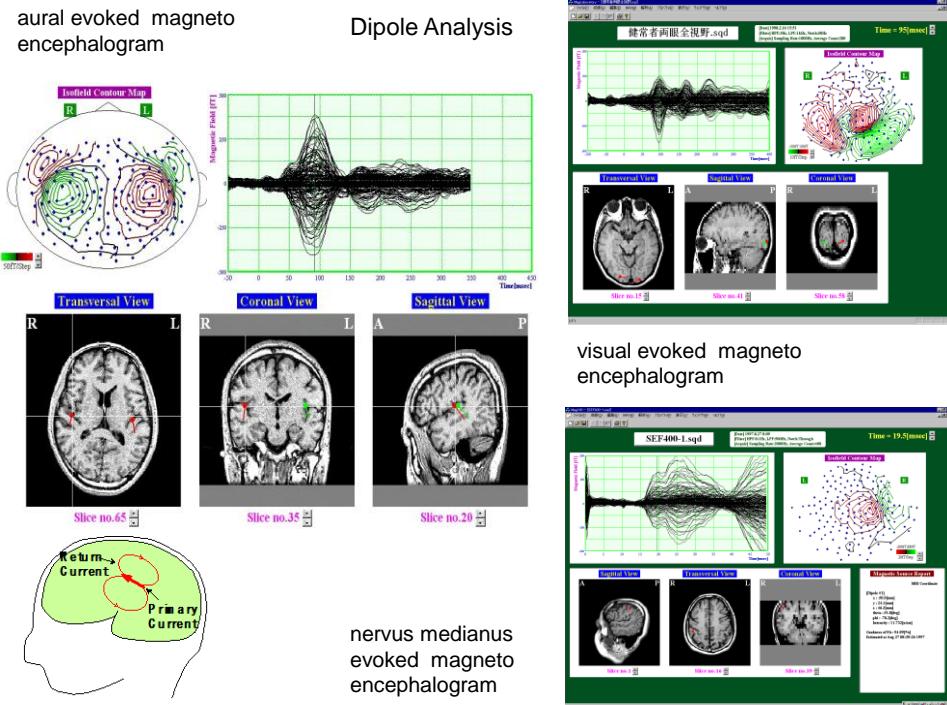
↓
electric voltage
↓
quantized
measurement of
magnetic fields

超電導リングに細い部分を作り込む。
細い部分を流れる電流が超電導の臨界電流を超えると電圧が生じる。
リングを貫く遮蔽磁場が量子化される



time series data
by channels





standard theory (direct problem)

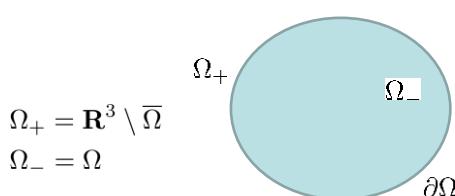
Ω volume conductor

$\mu_0 > 0$ permeability

$$\nabla \times B = \mu_0 J, \quad \nabla \cdot B = 0$$

$$J = J^p - \sigma(x) \nabla V$$

$$\sigma(x) = \begin{cases} \sigma, & x \in \Omega \\ 0, & x \notin \Omega \end{cases}$$



B magnetic field

J total current density

$J^p(x)$ primary current

$\sigma(x)$ conductivity (one layer model)

distribution theory

$$B \in C^1(\overline{\Omega_{\pm}}), \mu_o J \in L^1_{loc}(\mathbf{R}^3)$$

\Rightarrow

$$\nabla \times B = \mu_0 J, \quad \nabla \cdot B = 0 \text{ in } \mathbf{R}^3 \setminus \partial\Omega$$

$$[n \times B]_+^+ = 0, [n \cdot B]_+^+ = 0 \text{ on } \partial\Omega$$

\Rightarrow

$$B \in C(\mathbf{R}^3)$$

1. compatibility condition

$$\nabla \cdot (\sigma(x) \nabla V) = \nabla \cdot J^p \text{ in } \mathbf{R}^3 \setminus \partial\Omega$$

$$\left[\sigma(x) \frac{\partial V}{\partial n} \right]_-^+ = 0 \text{ on } \partial\Omega$$

2. interface regularity

$$[\nabla(n \cdot B)]_-^+ = 0 \text{ on } \partial\Omega$$

Kobayashi-S.-Watanabe 06

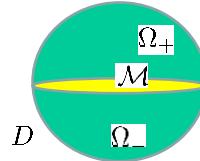
\mathcal{M} , $C^{1,1}$ interface, $D \subset \mathbf{R}^3$

$B \in H^1(D)^3$, $J \in H(\text{rot}, \Omega_{\pm})$

$\nabla \times B = J \in L^2(D)^3$

$\nabla \cdot B = 0 \in L^2(D)$

$\Rightarrow n \cdot B \in H_{loc}^2(D)$



well-posedness (distributional solution)

$J^p(x), \sigma(x) \mapsto B(x), V(x)$

$\nabla \times B = \mu_0 J, \quad \nabla \cdot B = 0$

$J = J^p - \sigma(x) \nabla V$

$$\sigma(x) = \begin{cases} \sigma, & x \in \Omega \\ 0, & x \notin \Omega \end{cases}$$

$B, V \in C^1(\overline{\Omega_{\pm}})$

$B(\infty) = 0, V(\infty) = 0$

$J^p \in C^1(\overline{\Omega_-}), J^p = 0$ in Ω_+

standard regularity

$J^p \in C^{1+\theta}(\overline{\Omega_-}), \partial\Omega, C^{2+\theta}$

$\Rightarrow B, V \in C^{2+\theta}(\overline{\Omega_{\pm}})$

layer potential

\Rightarrow Geselowitz equation 67, 70

$$\Gamma(x) = \frac{1}{4\pi|x|} \text{ Newton potential}$$

$$\frac{\sigma}{2}V(\xi) = - \int_{\Omega} \nabla \cdot J^p(y) \Gamma(\xi - y) dy$$

$$-\sigma \int_{\partial\Omega} V(y) \frac{\partial}{\partial \nu_y} \Gamma(\xi - y) dS_y, \quad \xi \in \partial\Omega$$

$$B(x) = -\mu_0 \int_{\Omega} J^p(y) \times \nabla \Gamma(x - y) dy$$

$$+ \mu_0 \sigma \int_{\partial\Omega} V(y) \nu_y \times \nabla \Gamma(x - y) dS_y$$

$x \notin \partial\Omega$

spherical model

Grynszpan - Geselowitz 73

1. $\sigma(x) = 0$ in Ω_+

\Rightarrow

$\exists U = U(x)$

$B = \mu_0 \nabla U$ in Ω_+

2. Ω ball

\Rightarrow

$\nu_y = y/|y|$

$$B(x) \cdot \frac{x}{|x|}$$

$$= -\frac{\mu_0}{4\pi} \int_{\Omega} \frac{J^p(y) \times y}{|x - y|^3} dy \cdot \frac{x}{|x|}$$

$x \notin \partial\Omega$

3. $U(\infty) = 0, \hat{x} = x/|x|$

\Rightarrow

$$\begin{aligned} U(x) &= - \int_0^\infty \frac{d}{dt} U(x + t\hat{x}) dt \\ &= - \int_0^\infty \nabla U(x + t\hat{x}) \cdot \hat{x} dt \\ &= -\frac{1}{\mu_0} \int_0^\infty B(x + t\hat{x}) \cdot \hat{x} dt \end{aligned}$$

$$\frac{x}{|x|} = \frac{x + t\hat{x}}{|x + t\hat{x}|} = \hat{x} \Rightarrow$$

$$B(x + t\hat{x}) \cdot \hat{x}$$

$$= -\frac{\mu_0}{4\pi} \int_{\Omega} \frac{J^p(y) \times y}{|x + t\hat{x} - y|^3} dy \cdot \hat{x}$$

$$\begin{aligned} U(x) &= \frac{1}{4\pi} \\ &\int_{\Omega} \frac{J^p(y) \times y dy}{|x - y|(|x| |x - y| + x \cdot (x - y))} \cdot x \\ &x \in \Omega_+ \end{aligned}$$

standard theory (inverse problem)

$q_1, \dots, q_m \in \partial\Omega$ channels

$(B \cdot \nu)(q_1), \dots, (B \cdot \nu)(q_m)$ data

ν unit normal vector

dipole hypothesis, Sarvas 87

$$J^p(x) = \sum_{k=1}^N Q_k \delta(x - a_k)$$

$a_k \in \mathbf{R}^3$ position, $Q_k \in \mathbf{R}^3$ moment

direct mapping

$$\varphi : x = (a_1, Q_1, \dots, a_N, Q_N) \in \mathbf{R}^{6N}$$

$$\mapsto ((B \cdot \nu)(q_1), \dots, (B \cdot \nu)(q_m)) \in \mathbf{R}^m$$

Dipole moving method

1. over-determined problem
2. number of dipoles prescribed
3. local minima

Inverse problem

Find $x \in \mathbf{R}^n$, $\varphi(x) = z$, $n = 6N$

$z \in \mathbf{R}^m$ observed data

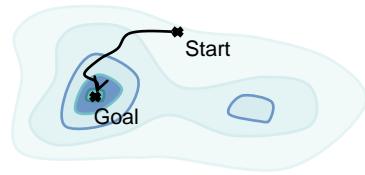
$N = 1$ or $N = 2$

\Rightarrow

$$\varphi : \mathbf{R}^n \rightarrow \mathbf{R}^m$$

$n = 6$ or $n = 12$, $m \approx 100$

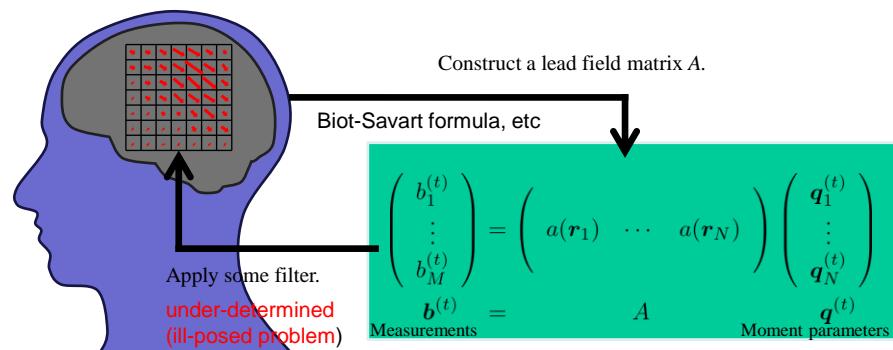
1. initial guess
2. parameter perturbation
3. gof check



spatial filtering method

A method to reconstruct distributed magnetic sources

1. Subdivide the solution space into some small regions (**voxels**)
2. Place a point source (current dipole) to each voxels
3. Describe the measurements by linear combination of magnetic fields derived by each sources
4. Calculate the orientation and magnitude of each sources



Various spatial filters

- Non-adaptive filter

– Weighting positional relationship between sensors and solution space

- Minimum norm filter
- sLORETA

Minimum norm filter

$$Q = {}^t A (A^t A)^{-1} B$$

Moore-Penrose quasi-inverse

normalized equation

$B = (\mathbf{b}^{(1)}, \dots, \mathbf{b}^{(T)})$: Time series measurements data

$Q = (\mathbf{q}^{(1)}, \dots, \mathbf{q}^{(T)})$: Time series moment parameters

- Adaptive filter

– Varying weights by time variation of measurements

- Minimum variance filter
- MUSIC filter

Minimum variance filter

$$Q_j = \frac{(B^t B)^{-1} A_j}{{}^t A_j (B^t B)^{-1} A_j} B$$

Q_j : j th row of Q

A_j : j th column of A

MUSIC method

- Multiple Signal Classification (MUSIC)
 - An algorithm to provide asymptotically unbiased estimates of locations and parameters of multiple signal sources

- MUSIC algorithm applied to MSI

1. eigen-decomposition of the covariance matrix of the measurements

$$R = \text{Cov}(B) = \Phi \Lambda^t \Phi \quad B: \text{time series measurements matrix}$$

$$\text{Cov}(B) = (1/T) B^t B$$

$\Phi = (\varphi_1, \dots, \varphi_M)$: Eigenvectors

$\Lambda = \text{diag}(\lambda_1, \dots, \lambda_M)$: Diagonal matrix of eigenvalues

2. Select the dimension r of the signal eigen-space

$(\lambda_1, \dots, \lambda_r), \Phi_s$: Signal eigenvalues and eigenvectors.
 $(\lambda_{r+1}, \dots, \lambda_M), \Phi_n$: Noise eigenvalues and eigenvectors.

$$a(r_i) = U_i \Sigma_i^t V_i, \quad \mathcal{J}_i = \lambda_{\min} \{ {}^t U_i \Phi_n^t \Phi_n U_i \}$$

$$\lambda_1 \geq \dots \geq \lambda_r \gg \lambda_{r+1} \approx \dots \approx \lambda_M$$

Minimum eigenvalues of R

Source Identification

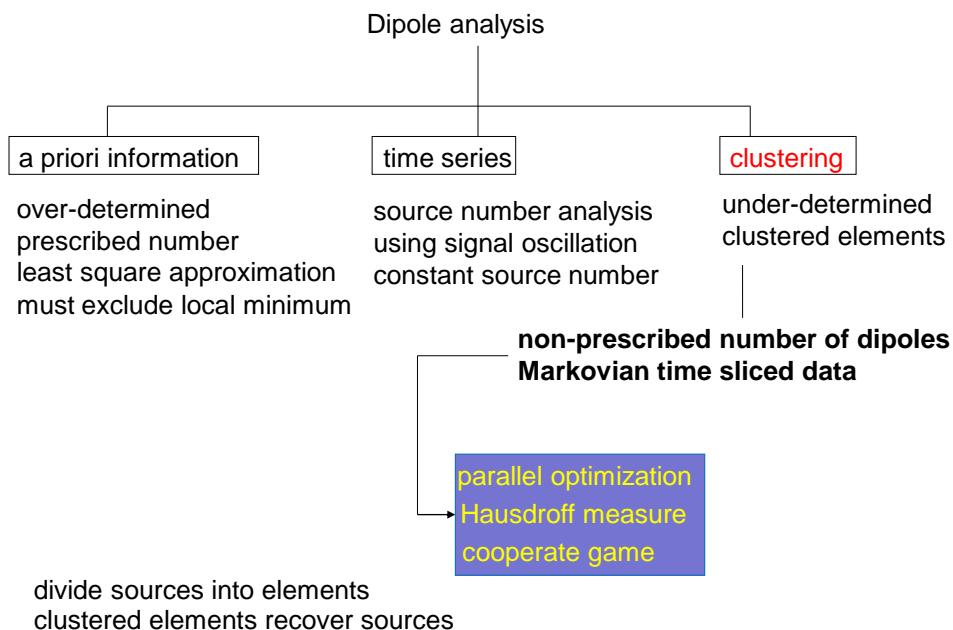
$A : \mathbf{R}^n \rightarrow \mathbf{R}^m$, matrix $A = (a_{ij})$, (m, n)

$$\begin{aligned} Ax = y &\Leftrightarrow \\ a_{11}x_1 + a_{12}x_2 + \dots + a_{1n}x_n &= y_1 \\ a_{21}x_1 + a_{22}x_2 + \dots + a_{2n}x_n &= y_2 \\ \dots \\ a_{m1}x_1 + a_{m2}x_2 + \dots + a_{mn}x_n &= y_m \end{aligned}$$

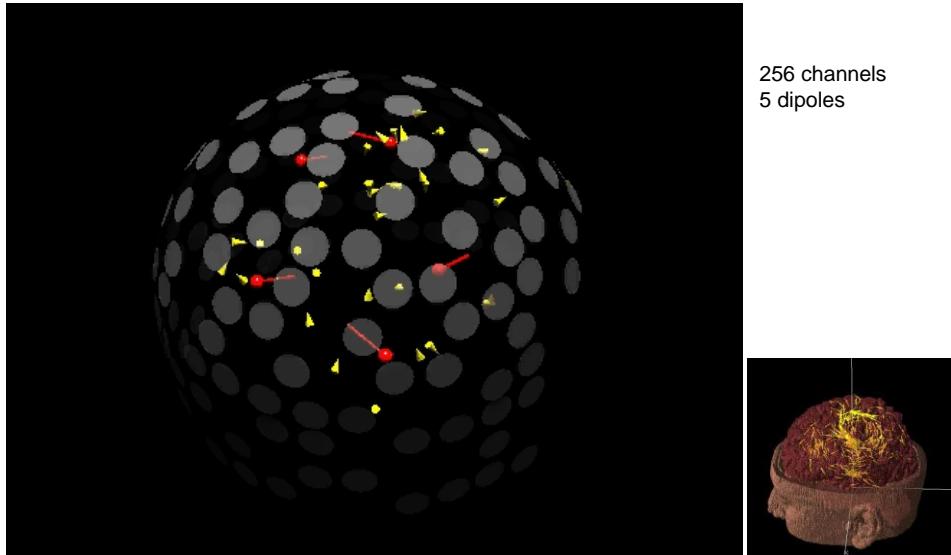
$m > n \Rightarrow$ overdetermined \Rightarrow non-existence
 \Rightarrow least square approximation

$n > m \Rightarrow$ underdetermined \Rightarrow non-uniqueness
 \Rightarrow selection of the solution

Many unknowns admit many solutions



Numerical experiment



digitization of bio-functions → diagnosis, pathology prediction, therapy

Parallel optimization

$x \in \mathbf{R}^n \mapsto \varphi(x) \in \mathbf{R}^m$ direct mapping

$z \in \mathbf{R}^m$ observed data

$\varphi(x) = z$, $x \in \mathbf{R}^n$ unknown source

$m > n$ under-determined

$\mathcal{M} = \{x \in \mathbf{R}^n \mid \varphi(x) = z\}$

⇒

($m - n$)-dimensional manifold

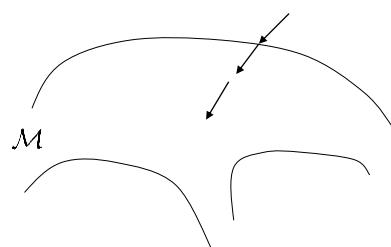
Iterative sequence having reached the manifold leaves there with the probability 1

$$J(x) = \frac{1}{2} |\varphi(x) - z|^2 \text{ accuracy}$$

$\{x_\ell\}$ iterative sequence

$$J(x_\ell) \downarrow 0$$

Approaching improves accuracy with the probability 1/2



Iterative sequence with high-accuracy freezes in under-determined system because n -dimensional volume of \mathcal{M} is zero

melting makes frozen sequence move → how and where?

$$\Delta x_\ell = x_{\ell+1} - x_\ell$$

$$J(x) = \frac{1}{2} |\varphi(x) - z|^2$$

⇒

$$\Delta J_\ell \equiv J(x_{\ell+1}) - J(x_\ell)$$

$$= (\varphi'(x_\ell) \Delta x_\ell, \varphi(x_\ell) - z) + o(|\Delta x_\ell|)$$

freezing zone

$$|\varphi'(x_\ell) \Delta x_\ell| \approx J(x_\ell)^{1/2}$$

parallel optimization

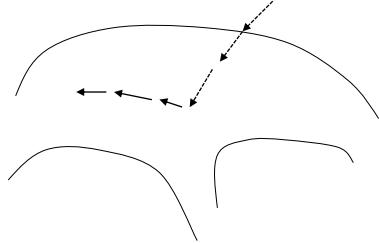
outside freezing zone ... approaching
inside freezing zone ... melting

$$\Delta x_\ell \in \text{Ker}(\varphi'(x_\ell))$$

⇒ $|\Delta J_\ell| \ll 1$ “melting”

$$\Delta x_\ell \in \{\text{Ker} \varphi'(x_\ell)\}^\perp = \text{Ran} \varphi'(x_\ell)^t$$

⇒ $|\Delta J_\ell| \approx 1$ “approaching”



How? ... singular decomposition of matrix

$$\Delta x_\ell \in \text{Ker}(\varphi'(x_\ell))$$

⇒ $|\Delta J_\ell| \ll 1$ approaching

$$\Delta x_\ell \in \{\text{Ker} \varphi'(x_\ell)\}^\perp = \text{Ran} \varphi'(x_\ell)^t$$

⇒ $|\Delta J_\ell| \approx 1$ melting

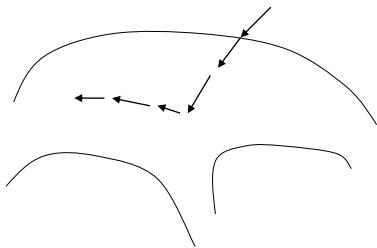
$$\varphi'(x_\ell)^t = Q \Sigma W$$

$$= (q_1, \dots, q_n) \begin{pmatrix} \lambda_1 & 0 & \dots & 0 \\ 0 & \lambda_2 & \dots & 0 \\ \cdot & \cdot & \dots & \cdot \\ \cdot & \cdot & \dots & \lambda_m \\ \cdot & \cdot & \dots & \cdot \\ 0 & 0 & \dots & 0 \end{pmatrix} \begin{pmatrix} w_1 \\ w_2 \\ \vdots \\ w_m \end{pmatrix}$$

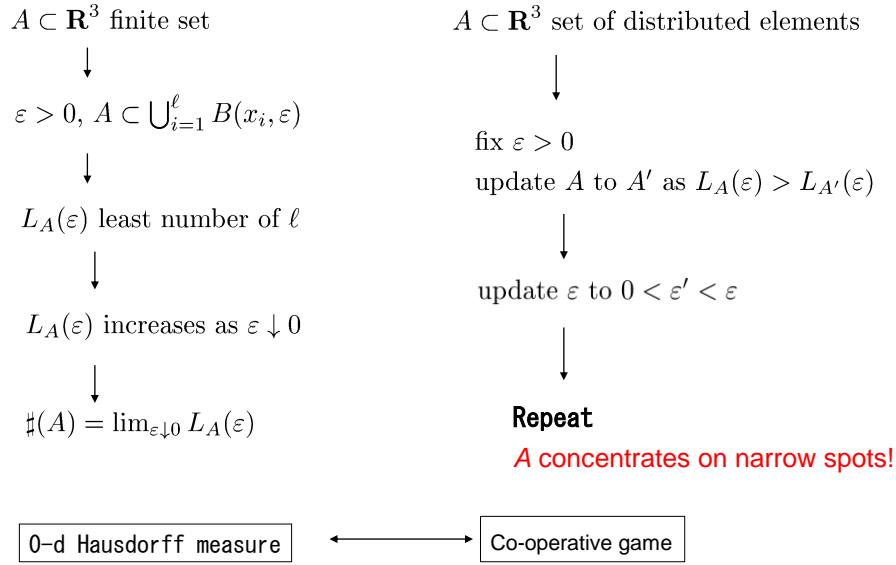
$$Q \in O(n), W \in O(m)$$

q_1, \dots, q_m : basis of $\text{Ran} \varphi'(x_\ell)^t$

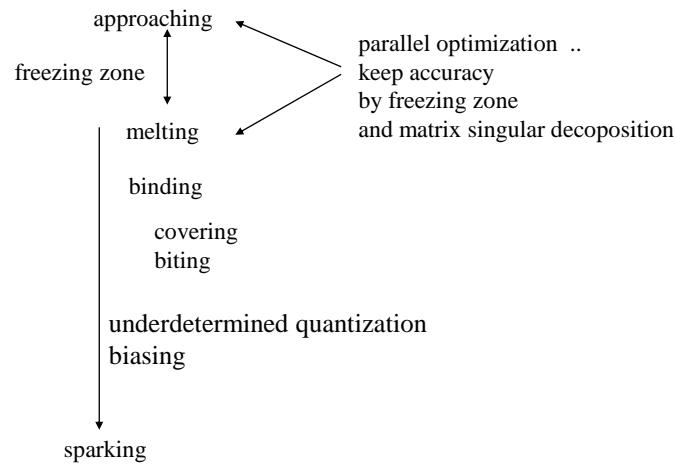
q_{m+1}^t, \dots, q_n^t : basis of $\text{Ker} \varphi'(x_\ell)$



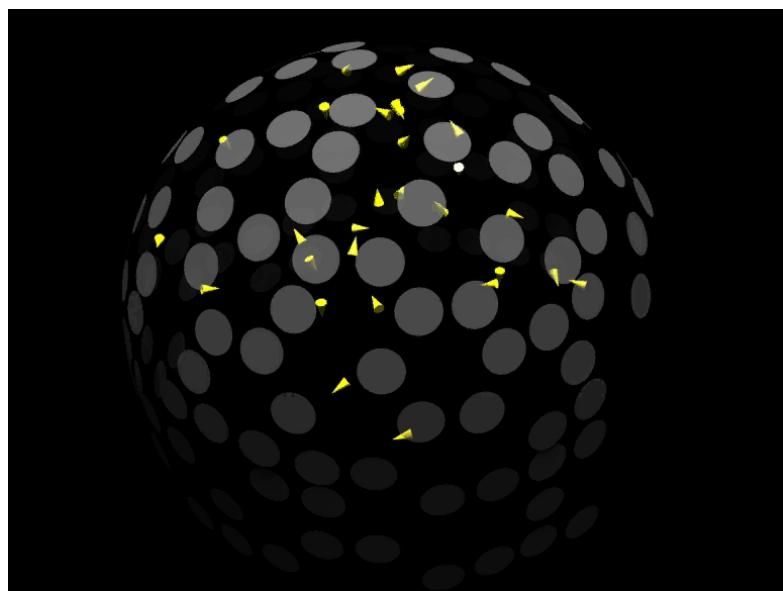
Where?...Binding ~Principal policy of melting in source identification



Program integrates sub-routines

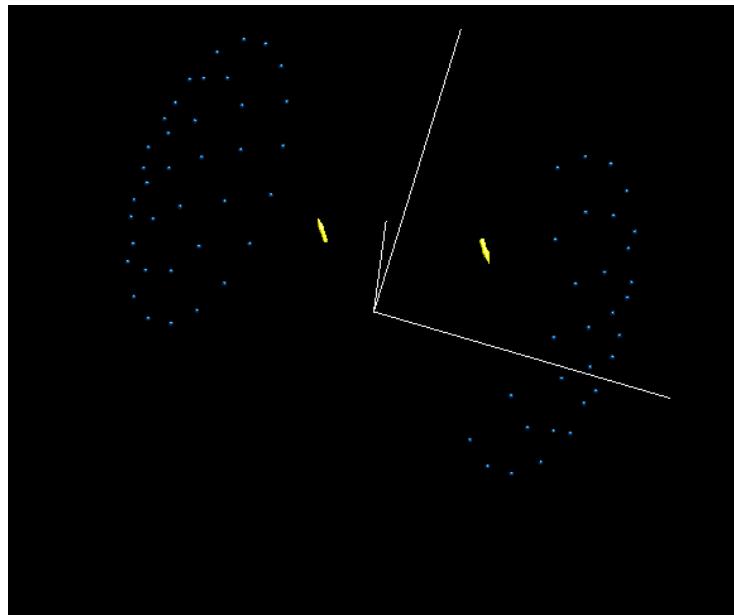


clustering



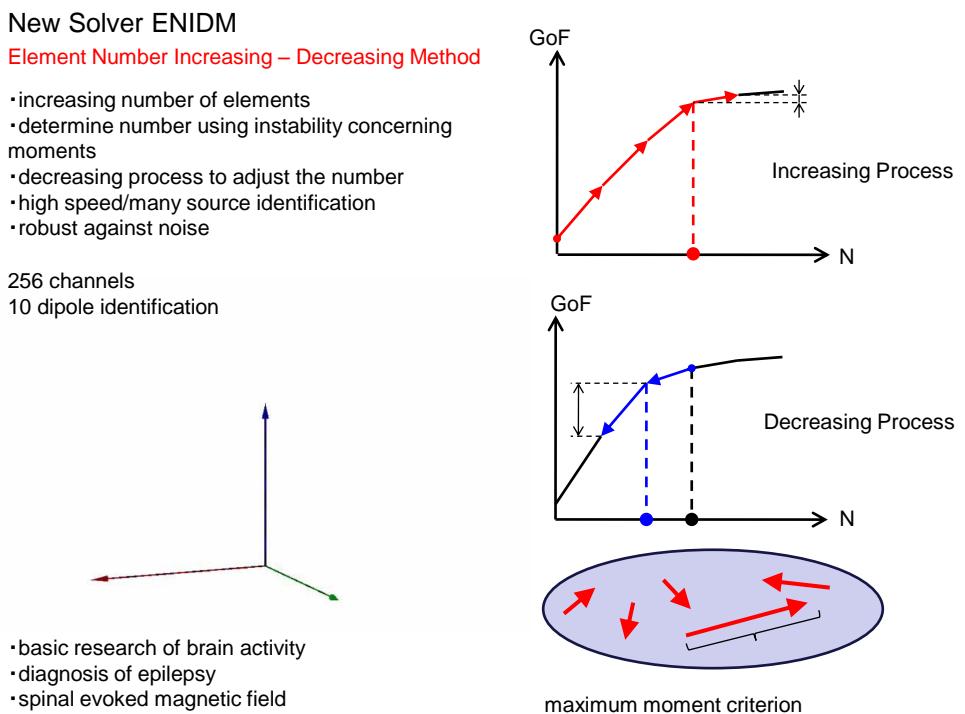
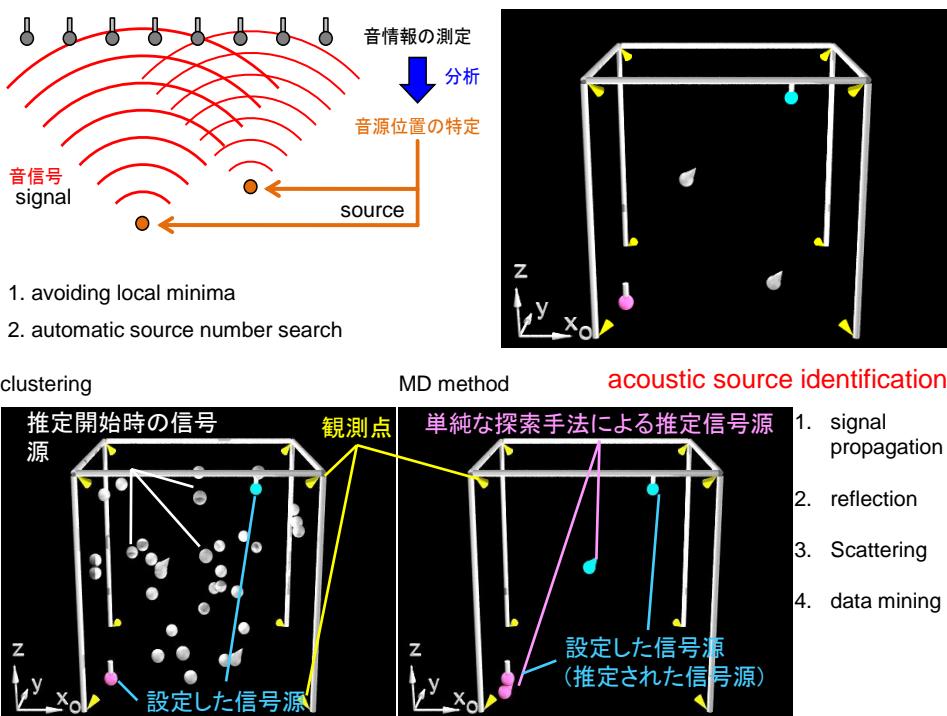
Aural evoked current
measured by 128chnnels

1- time sliced
real data analysis



nervus medianus **time series data analysis**
using 32×32 channels

moving, separating, annihilating,
binding dipoles



- basic research of brain activity
- diagnosis of epilepsy
- spinal evoked magnetic field

Spinal cord dysfunction (脊髄機能障害)

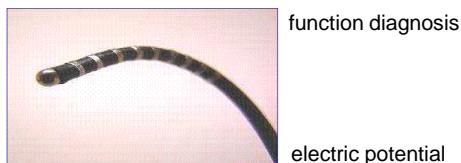
spinal cord oppression by intervertebral disk (椎間板)

signal transmission abnormality (信号伝達異常)

paralysis (麻痺) dyskinesia (運動障害)

medication (投薬) excision (切除)

form diagnosis



spinal evoked magnetic field

non-invasive measurement

bio-magnetic source identification

high quality time resolution

primary current

... evoked by electric action of spinal cord

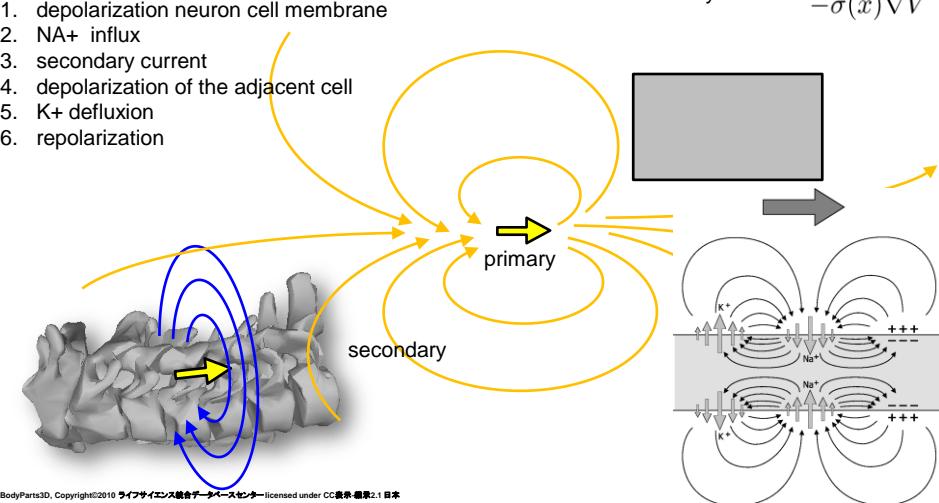
J^p

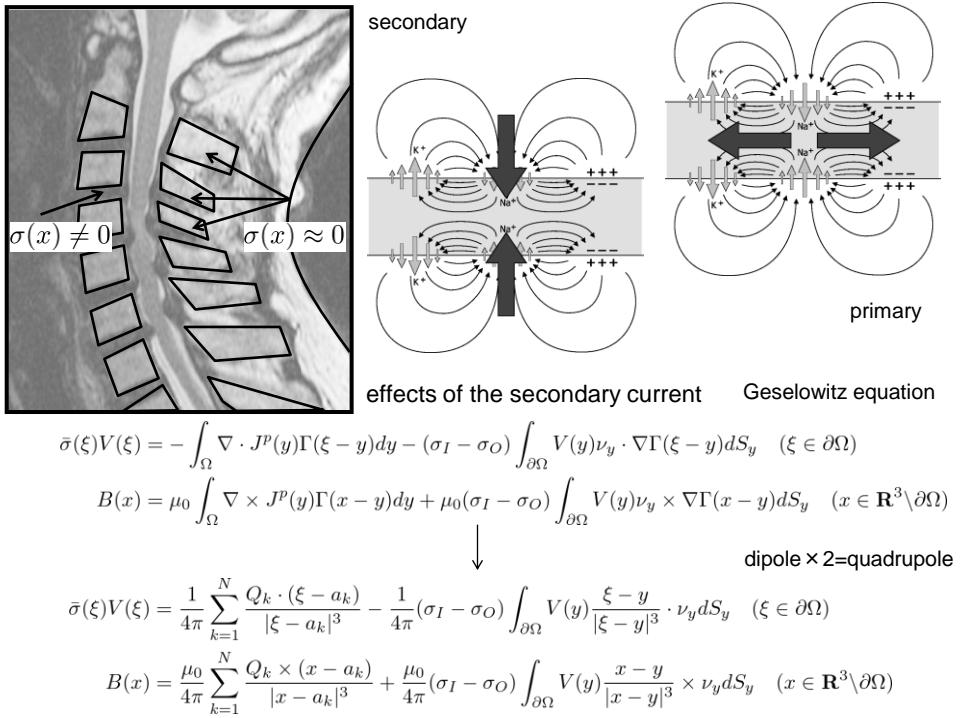
secondary current

.. evoked by the primary current subject to the conductivity

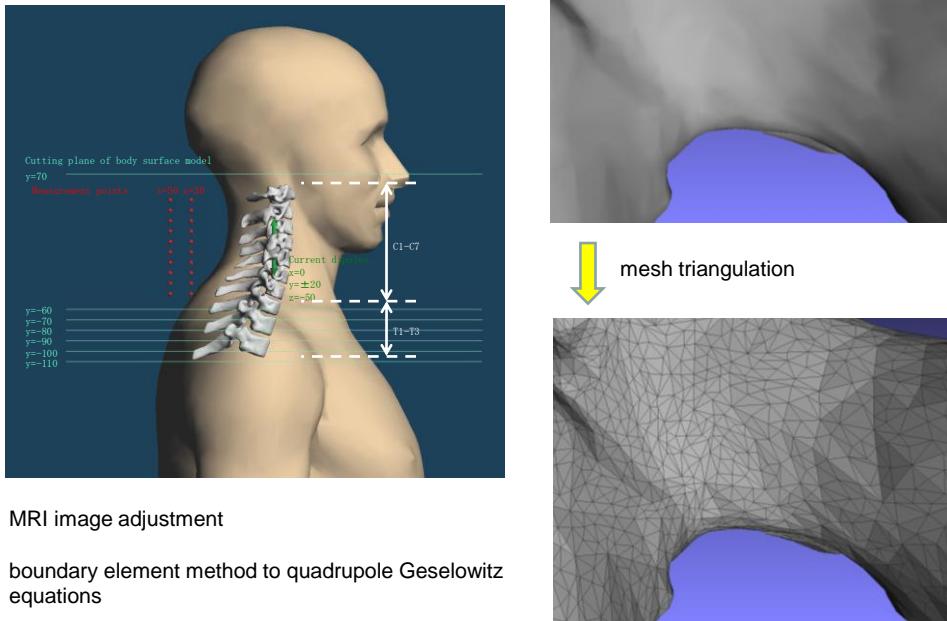
$$-\sigma(x)\nabla V$$

1. depolarization neuron cell membrane
2. NA⁺ influx
3. secondary current
4. depolarization of the adjacent cell
5. K⁺ defluxion
6. repolarization

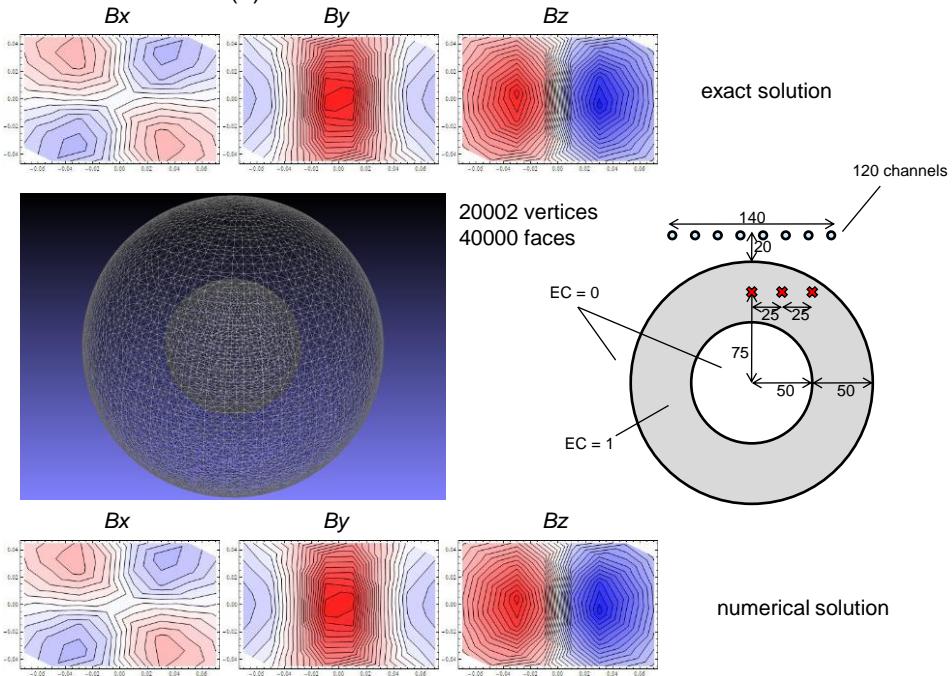




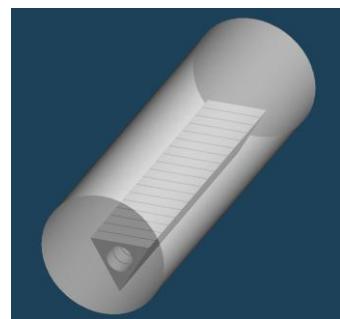
standard model of human body
(Japanese adults, male/female)



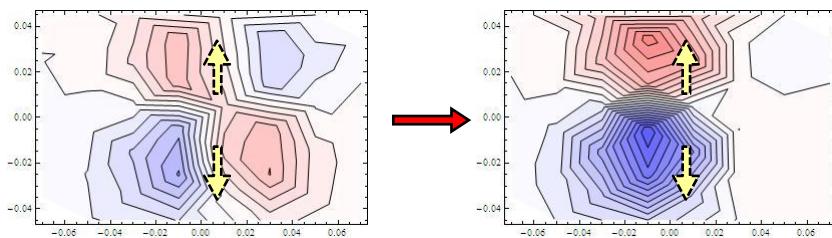
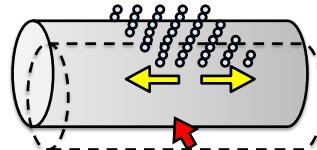
Simulation check (1)

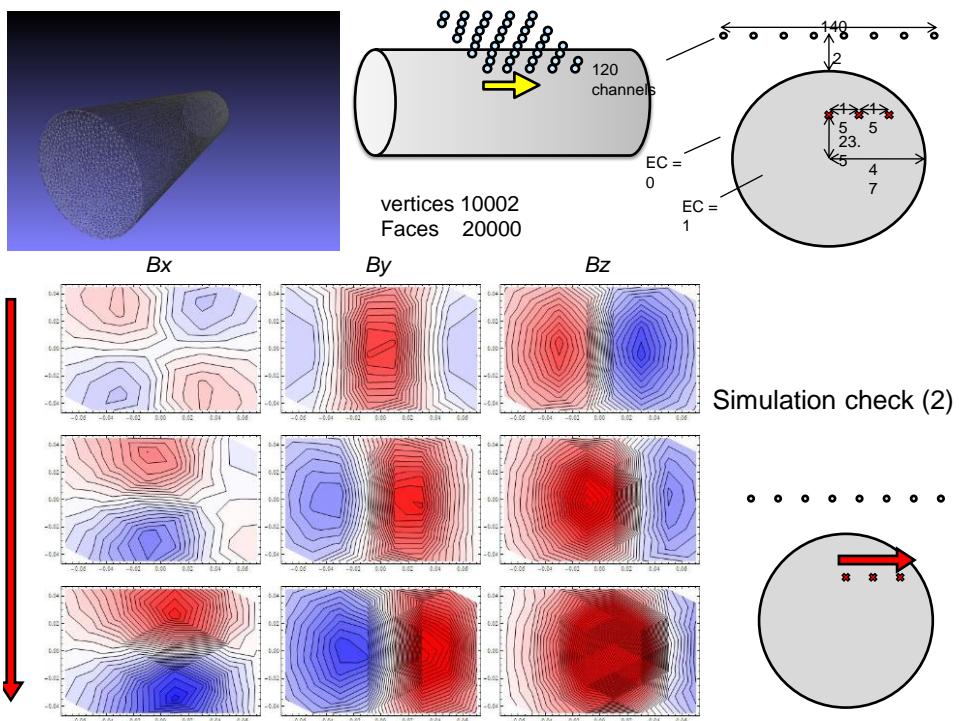


phantom data – secondary current



quadrupole approaching circular cylinder face causes magnetic field crush



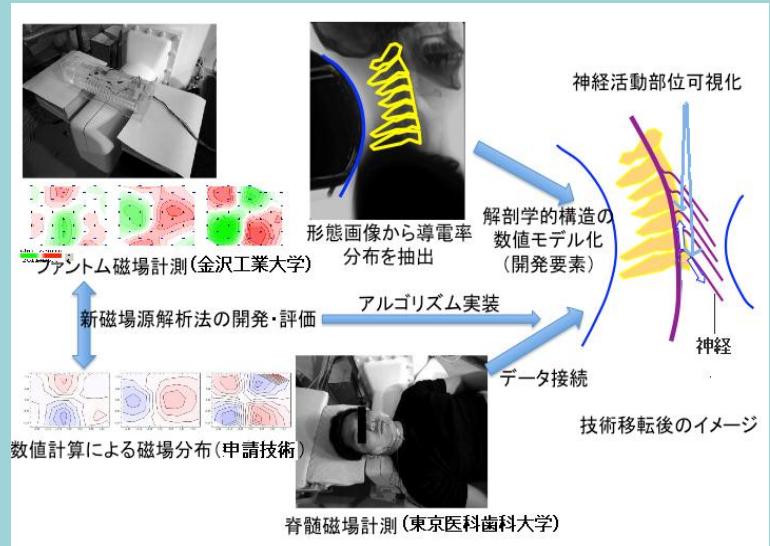


Magneto-Spinography

A-step 採択、音源定位への展開
イノベーションジャパン出展(9月21日-22日)
新技術説明会報告(11月22日)

数理モデルの構築

境界要素法による順問題シミュレーション
瞬間データから未知数ソースを探索(国内特許申請)
ファントムデータとの照合
実データ分析準備



Summary

1. Mathematical medicine is a new field provided with many targets where several approaches and formulations are possible
2. Among others brain activity analysis is an important issue. Electro-magnetic theories may formulate some aspects
3. A mathematical method to clinical medicine is presented, dipole bio-magnetic data analysis for spinal cord

References

1. 佐藤真, 脊髄誘発磁場分析における磁場源の考察, 日本応用数理学会論文誌, 2011, in press
2. 鈴木貴, 脳磁図分析-医学における逆問題, 「数学の楽しみ」, 日本評論社, 東京, 2007, pp. 68-103
3. T. Kobayashi, S. K. Watanabe, Interface vanishing for solutions to Maxwell and Stokes Systems, J. Mathematical Fluid Mechanics 8 (2006) 382-397