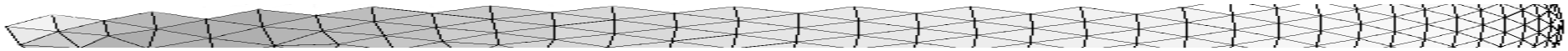
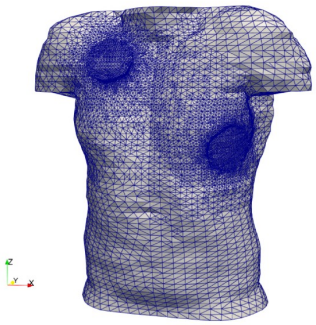
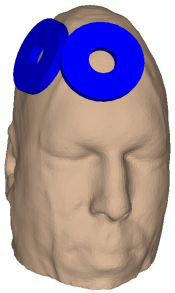
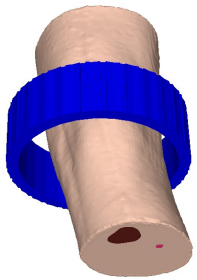
Seminarium CSZ i CI PW, 7 października 2014

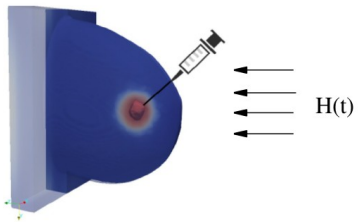


Wyzwania numerycznego modelowania problemów bioelektromagnetyzmu





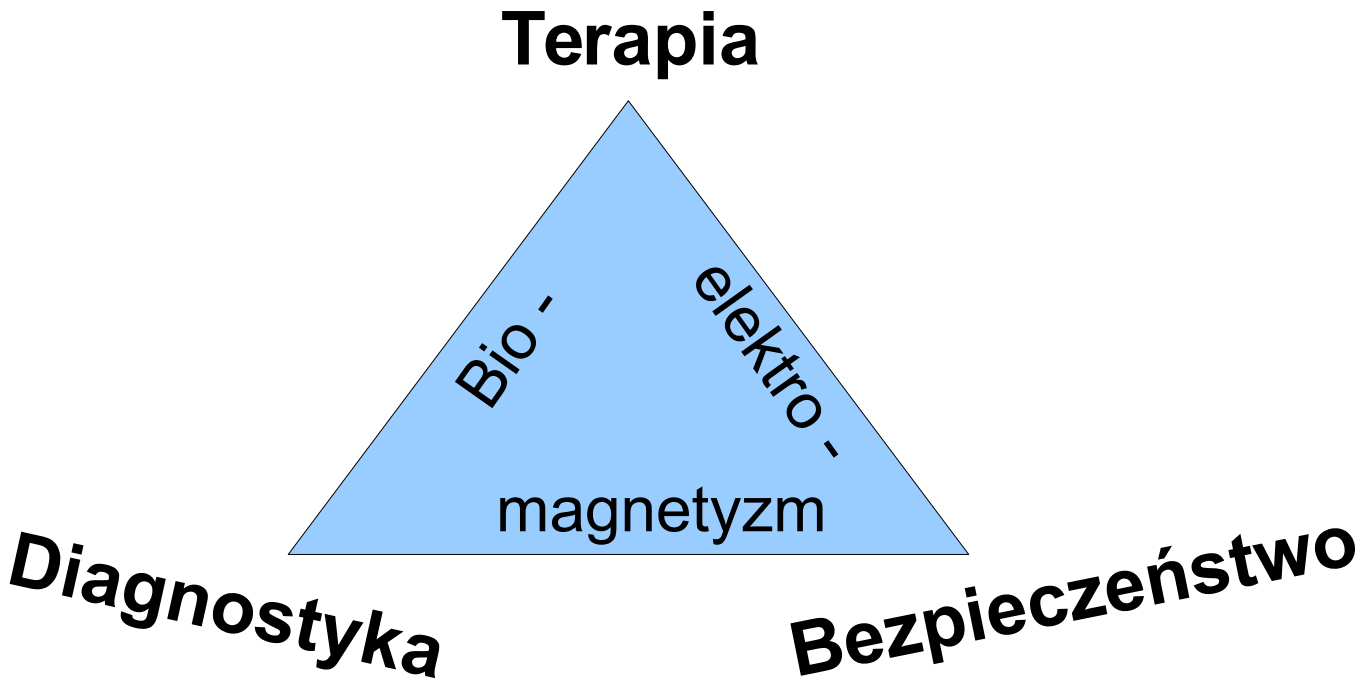




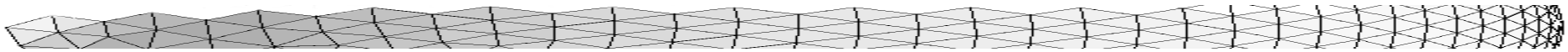
Bartosz Sawicki
Politechnika Warszawska
Wydział Elektryczny

Bioelektromagnetyzm

Oddziaływanie pola elektrycznego i magnetycznego
na organizmy żywe



Bioelektromagnetyzm obliczeniowy

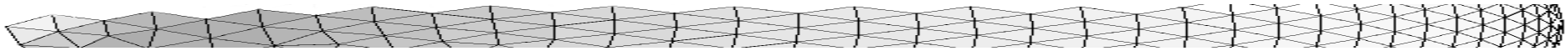


Wykorzystanie **metod komputerowych** do modelowania problemów bioelektromagnetyzmu.

Szeroko stosowane, ma wiele zalet:

+ Mniej problemów etycznych
+ Możliwość zajrzenia do wnętrza ciała
+ Niskie koszty
+ Szybkie eksperymenty

Plan seminarium



- Wyzwania – krok po kroku, na przykładach
  - Opis medyczny i fizyczny problemu
  - Opis matematyczny zjawiska
  - Model obiektu biologicznego
  - Rozwiązanie numeryczne
  - Analiza wyników
- Wyzwanie główne – wiarygodność wyników

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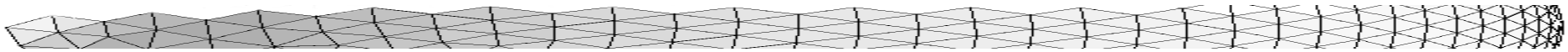

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TMS vs ECT

Transcranial Magnetic Stimulation (TMS) is a replacement for ElectroConvulsive Therapy (ECT)

Therapy for clinical depressions, migraine, epilepsy and others.

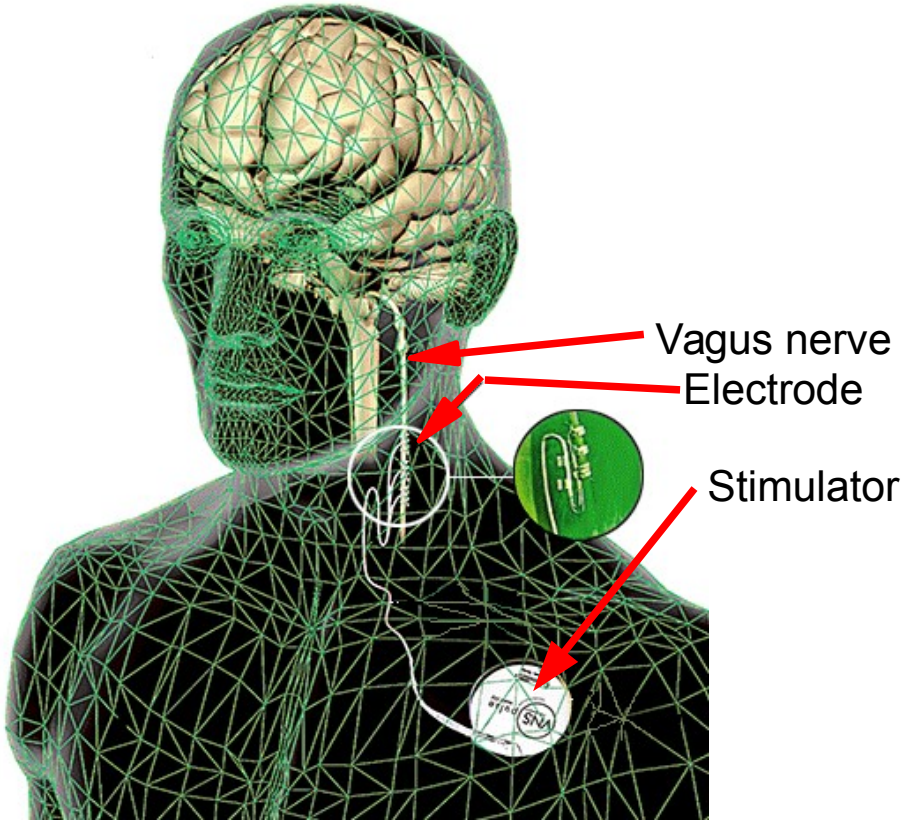
ECT is used since 1930, despite of strong side effects

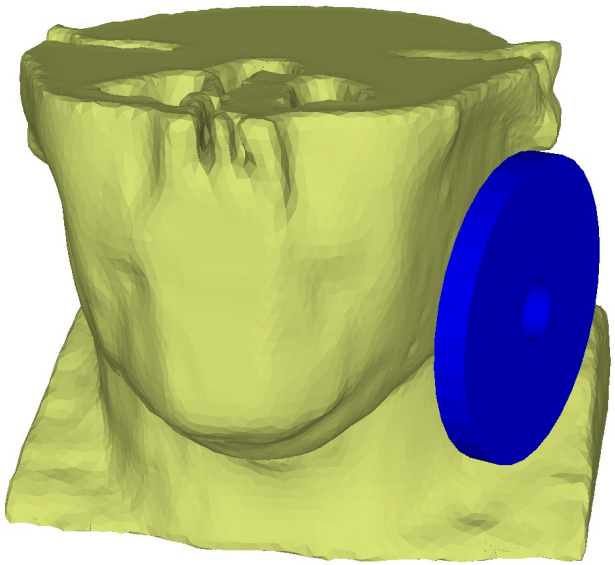
[MRDI webpage]

[Princeton University webpage]

Vagus Nerve Stimulation

Vagus Nerve Stimulation is a therapy for: **epilepsy**, clinical depressions, heart diseases.

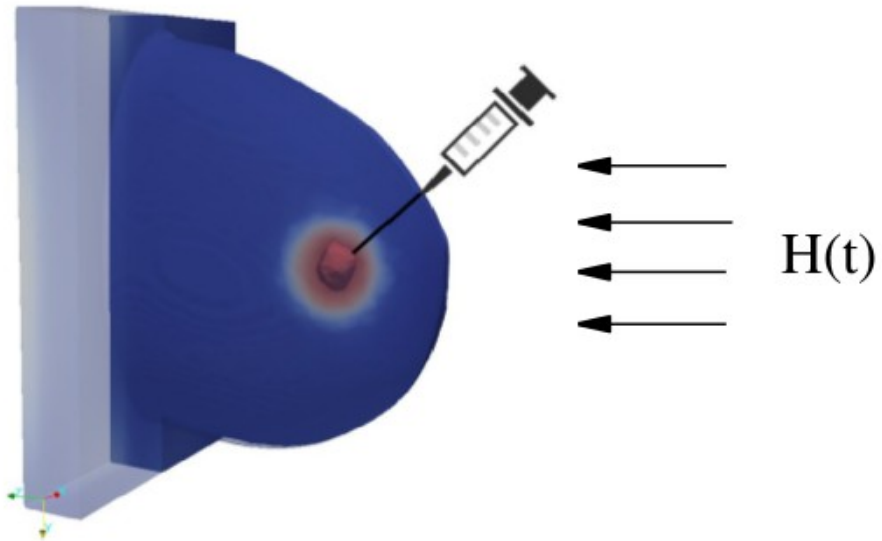




[conceptual device]

Magnetic Fluid Hyperthermia

Hyperthermia is treatment based on overheating (T > 43 C) malicious tissues, which lead to self-destruction (aptopsis).

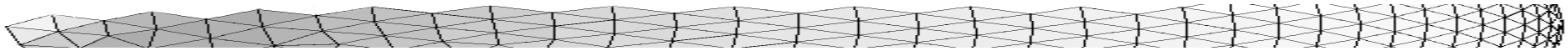


MFH procedure:

1. Magnetic fluid is injected into the tumor.
2. Body is exposed to the low frequency magnetic field.
3. Tumor is precisely overheated.

Based on superparamagnetic heat phenomenon.

Plan seminarium



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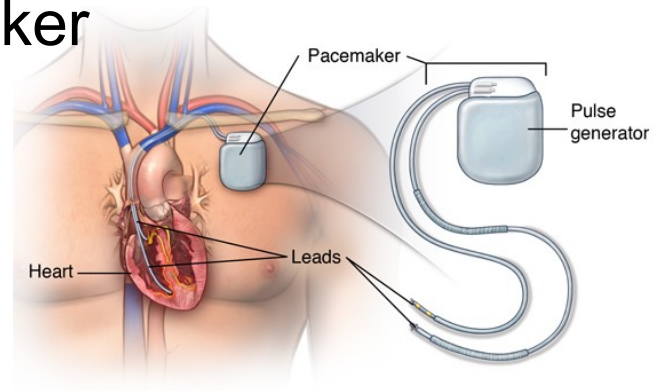
Electric stimulation

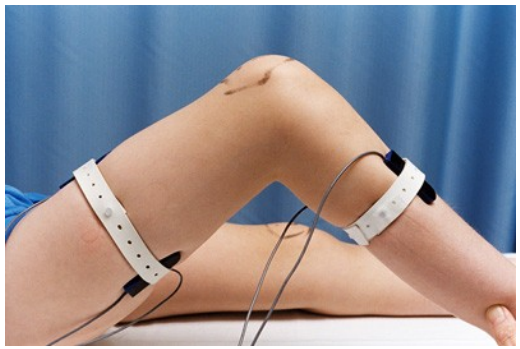
ECT

Pacemaker

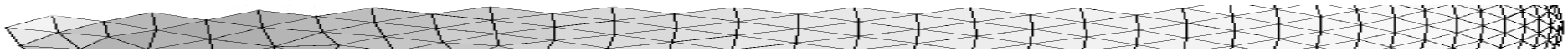


Defibrillation

Muscle stimulation



Electric stimulation



Low frequency (< 2kHz), direct current stimulation

Simple Laplace equation:

$$\nabla \cdot \underline{\sigma} \nabla \varphi = 0$$

Electric scalar potential

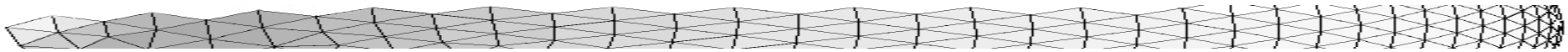
Anisotropic conductivity

$$\vec{J} = -\underline{\sigma} \nabla \varphi$$

Boundary condition:

Source electrode as a Dirichlet BC (fixed potential) is far from reality.

Electrode model



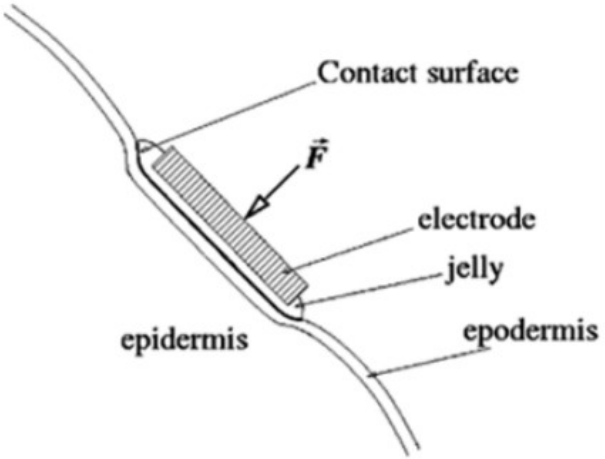
Complete electrode model:

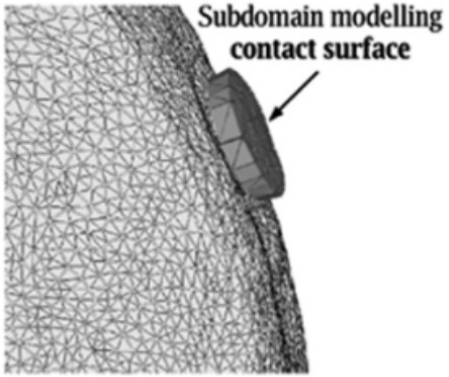
All electrodes:

$$\phi + z_\ell \frac{\partial \phi}{\partial \mathbf{n}} = V_\ell$$

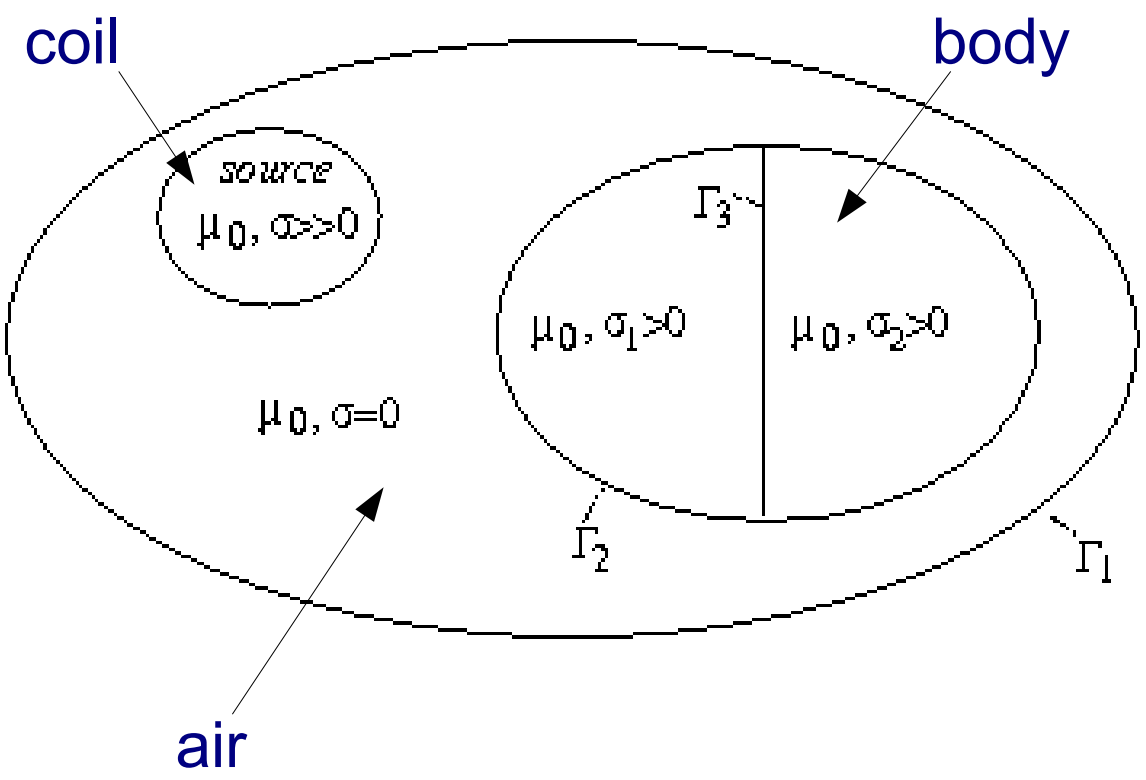
Active electrodes:

$$\int_{S_\ell} \sigma \frac{\partial \phi}{\partial \mathbf{n}} ds = I_\ell$$





Magnetic stimulation

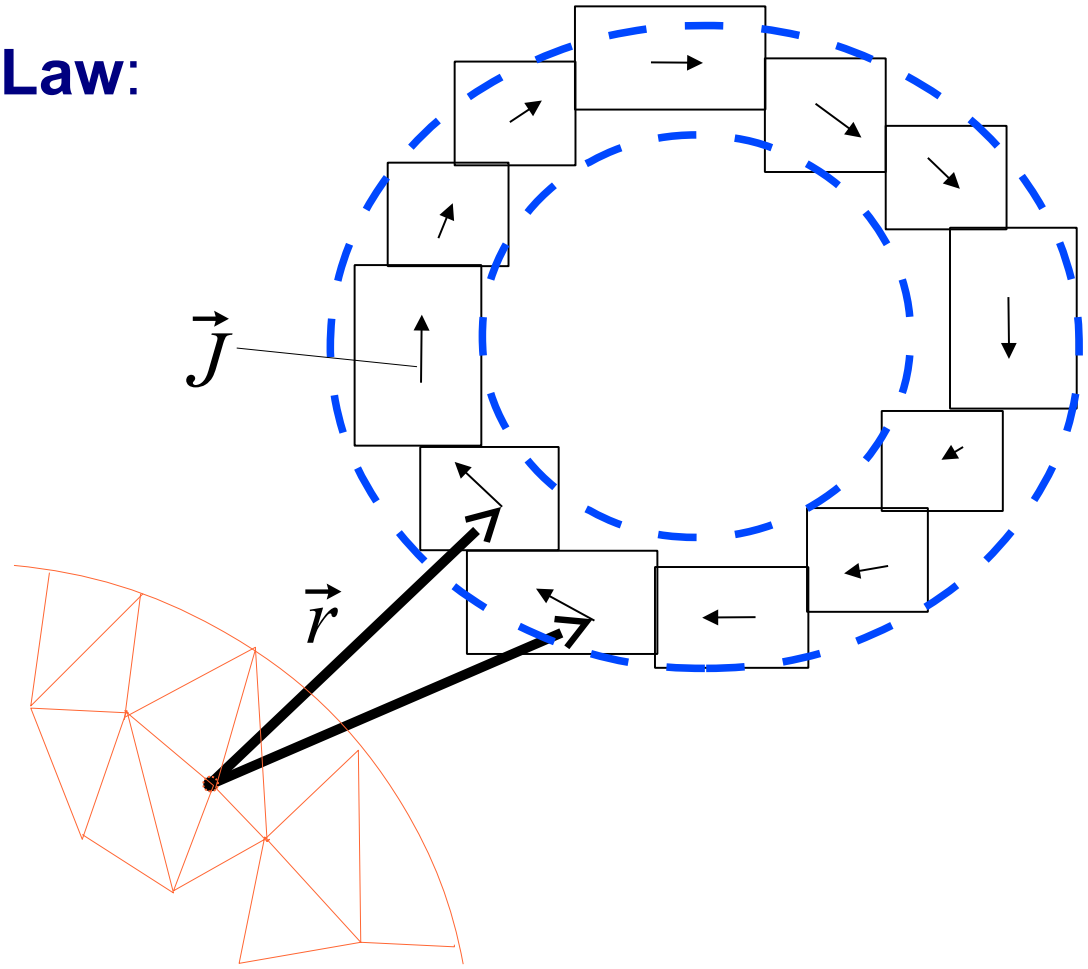


Assumptions:
- source is separated from the body
- body is low conducting (< 1 S/m)
- exciting field is ELF (< 2kHz)
- magnetic permittivity is constant

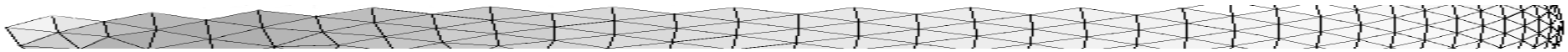
External magnetic field 1

Calculated using **Biot-Savarte Law**:

$$\vec{B} = \frac{\mu_0}{4\pi} \int \frac{\vec{J} \times \vec{r}}{r^3} dv$$



External magnetic field 2



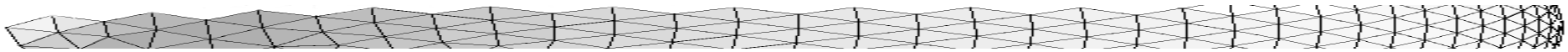
Magnetic field produced by the coil is solved using vector Laplace operator for magnetic vector potential $\mathbf{A}$:

$$-\nabla^2 \mathbf{A} = \mu_0 \mathbf{J}_c$$

$$\mathbf{H} = \frac{1}{\mu_0} \nabla \times \mathbf{A}$$

where $\mathbf{J}_c$ is excitating coil current density vector.

Eddy currents model



Eddy currents in low conducting media can be described by **Faraday's Induction Law**:

$$\nabla \times \vec{E} = -\frac{\partial \vec{B}}{\partial t}$$

We **introduce potentials** for simple BC and smooth solution:

	electric	magnetic
scalar potentials:	φ	Ω
vector potentials:	$\nabla \times \vec{T} = \vec{J}$	$\nabla \times \vec{A} = \vec{B}$

Electric scalar potential

Eddy currents described using **electric scalar potential**:

$$\nabla \times \vec{E} = -\frac{\partial \vec{B}}{\partial t}$$

$$\nabla \times \vec{A} = \vec{B}$$

$$\nabla \times \nabla \varphi = 0$$

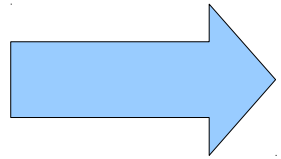
$$\Rightarrow \quad \vec{E} = -\nabla \varphi - \frac{\partial \vec{A}}{\partial t}$$

Electric scalar potential

$$\vec{E} = -\nabla \phi - \frac{\partial \vec{A}}{\partial t}$$

$$\vec{J} = \sigma \vec{E}$$

$$\nabla \cdot \vec{J} = 0$$



Main PDE:

$$\nabla \cdot \sigma \nabla \varphi = -\nabla \cdot \sigma \frac{\partial \vec{A}}{\partial t}$$

Boundary conditions:

$$\frac{\partial \varphi}{\partial n} = -\frac{\partial \vec{A}_n}{\partial t}$$

Electric vector potential

Eddy currents described using **electric vector potential**:

$$\nabla \times \vec{E} = -\frac{\partial \vec{B}}{\partial t}$$
$$\vec{J} = \nabla \times \vec{T}$$
$$\vec{J} = \sigma \vec{E}$$

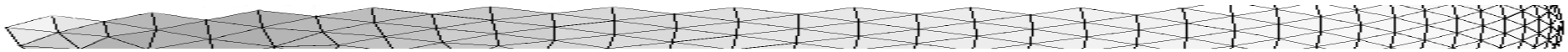
Main PDE:

$$\nabla \times \frac{1}{\sigma} \nabla \times \vec{T} = -\frac{\partial \vec{B}}{\partial t}$$

$$\nabla \times \frac{1}{\sigma} \nabla \times \vec{T} - \nabla\left(\frac{1}{\sigma} \nabla \cdot \vec{T}\right) = -\frac{\partial \vec{B}}{\partial t}$$

Coulomb gauge term
(for uniqueness and robustness)

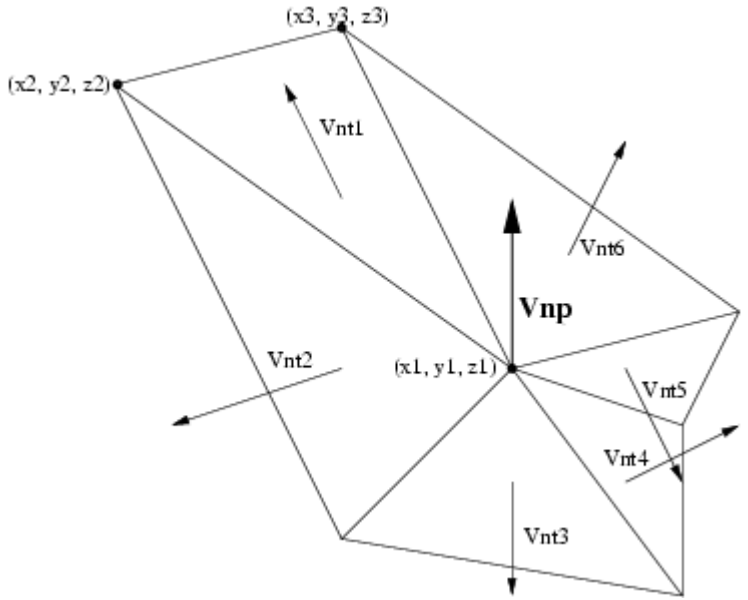
Electric vector potential



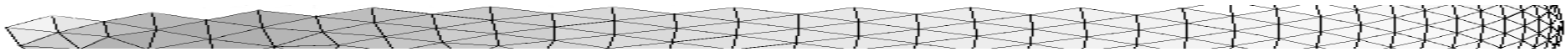
Boundary conditions:

$$\vec{J}\cdot\vec{n}=0 \qquad \nabla\cdot\vec{T}=0$$

$$T_t = T_w = 0, \quad \frac{\partial T_n}{\partial n}=0$$



Scalar potential vs. vector potential



Scalar potential:

1 DOF per node

problems on material boundary

Vector potential:

3 DOF per node

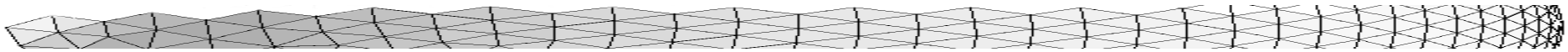
problems on material boundary

ready for magnetic field calculation:

$$\vec{H} = \vec{H}_s + \vec{T} - \nabla \Omega$$

The same eddy currents results.

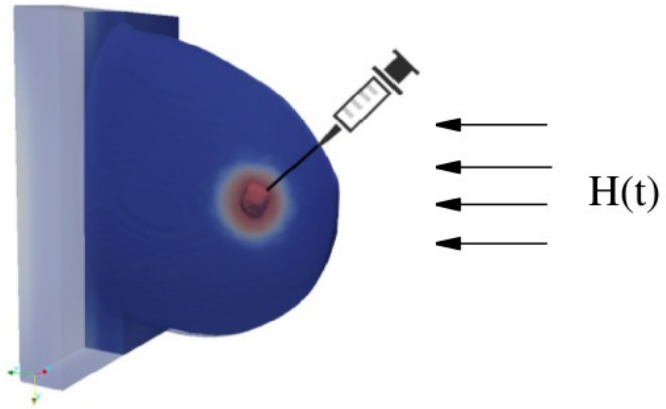
Magnetic Fluid Hyperthermia



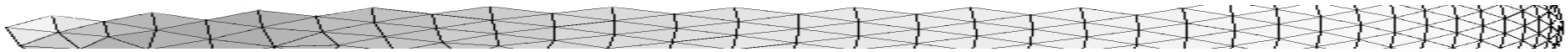
Superparamagnetic heat phenomenon

The superparamagnetic heat phenomenon is essential base of MFH. Power dissipation from magnetic nanoparticles could be expressed as:

$$Q = \pi \mu_0 \chi_0 \mathbf{H}^2 f \frac{2\pi f \tau}{1 + (2\pi f \tau)^2}, \qquad (1)$$



Magnetic Fluid Hyperthermia



Pennes equation

Heat transfer equation for human body (H. Pennes, 1948):

$$\rho c \frac{\partial T}{\partial t} = \nabla \cdot (k \nabla T) + \rho_b c_b \omega (T_b - T) + Q_{met} + Q_{ext} \quad (7)$$

Boundary condition

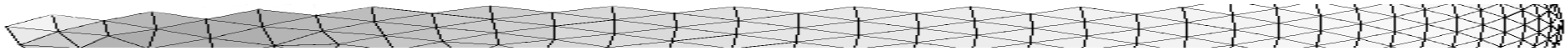
Skin heat exchange could be described by a convection and imposed in the form of Robin boundary condition:

$$\frac{\partial T}{\partial n} = h(T_{ext} - T), \quad (8)$$

where h is heat transfer coefficient and T_{ext} is external temperature.

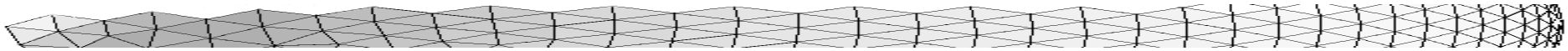
for skin, $h \approx 9.5\ [W/m^2/K]$.

Wyzwania



- Uwzględnienie istotnych zjawisk
  - Które są istotne, a które można pominąć?
- Wybór odpowiedniego, efektywnego opisu matematycznego
  - Dobry opis potrafi znacznie przyspieszyć i ułatwić modelowanie.

Plan seminarium



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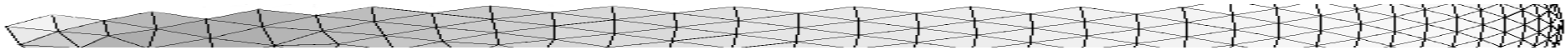
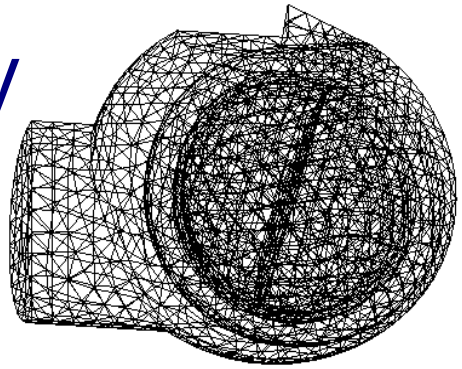
3D Models

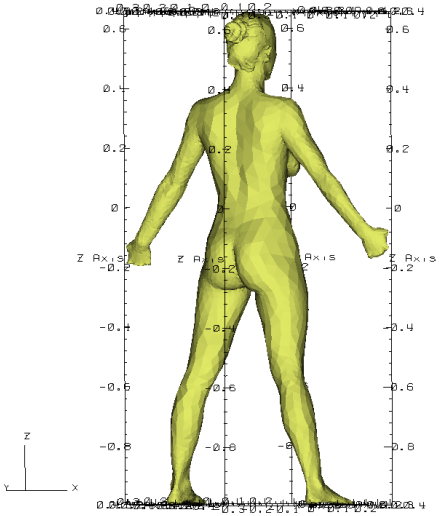


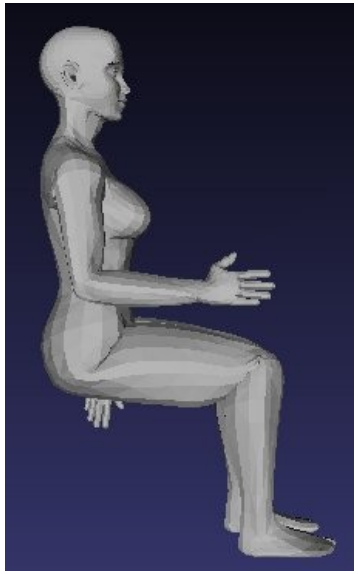
CSG – Constructive Solid Geometry



BR – Boundary Representations

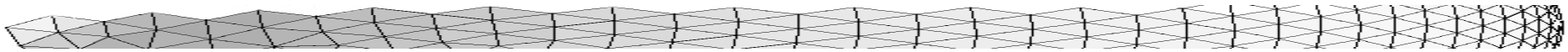
- 3D Scanners
- 3D Graphics Modelers





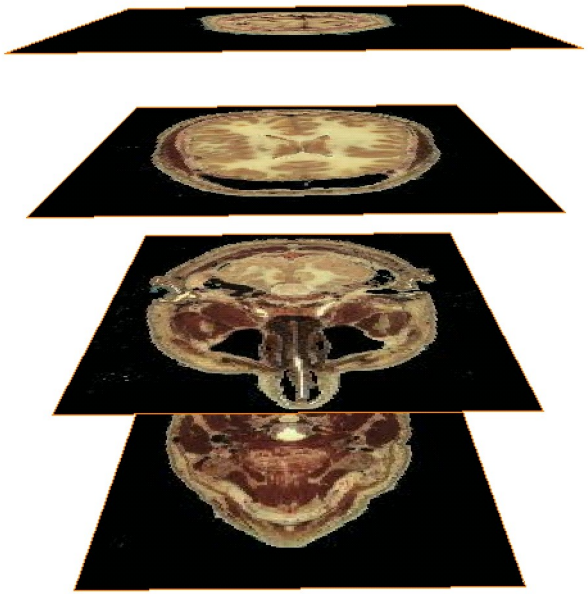
Volume models, voxels

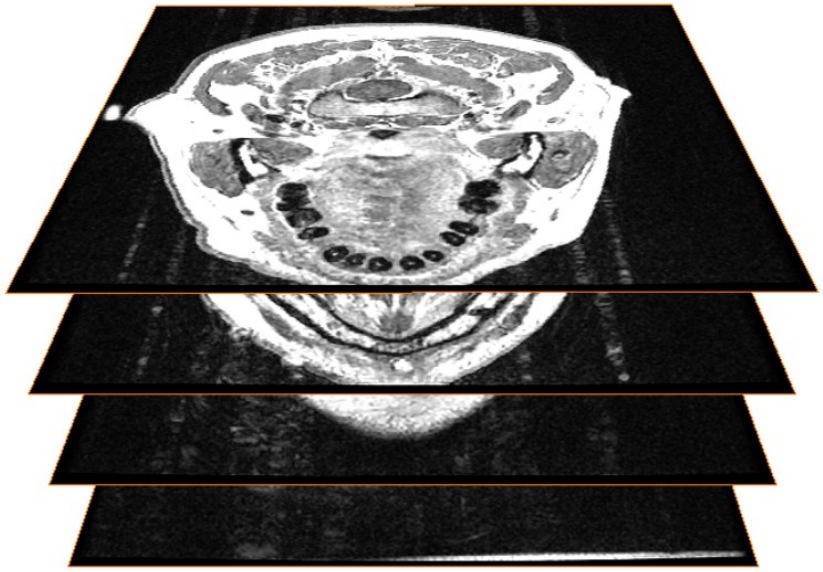
3D Models



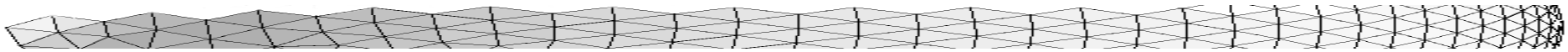
Data acquisition (slides sets):

MRI, CT, Anatomical



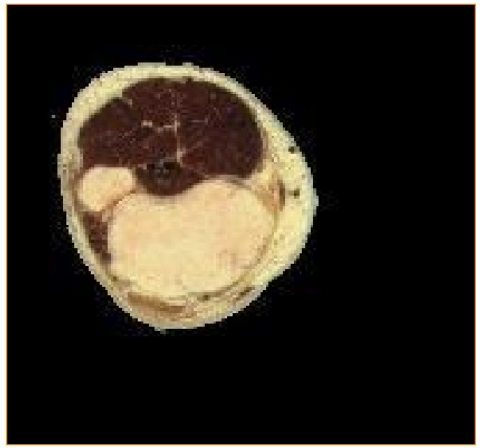


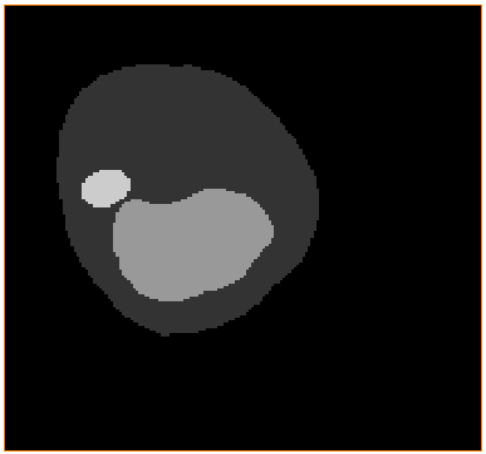
3D Models



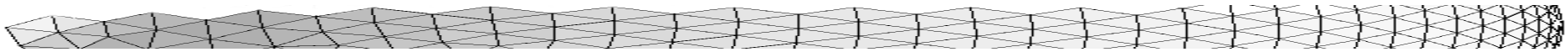
Segmentation:

- the aim is to mark subdomains with different tissues,
- lack of fully automated methods





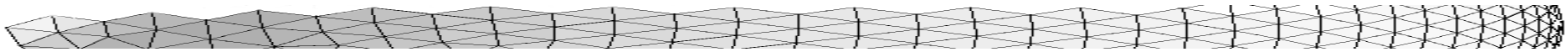
3D Models

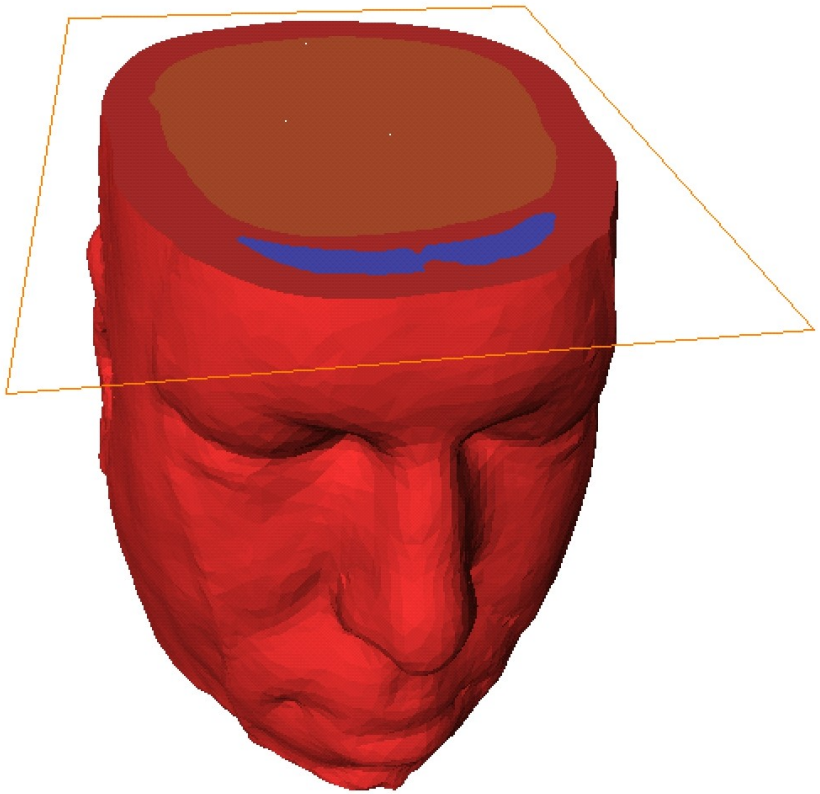


3D volume mesh generation (for FEM):

- Subdomain boundary detection
  - smooth and generate surface meshes (eg. using alg. MarchingCubes)
- Mesh generation in each subdomain
- Mesh quality improvement.

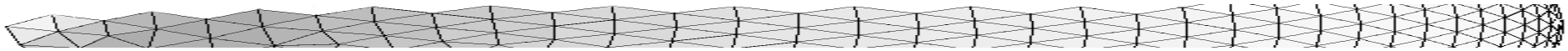
Realistic 3D meshes

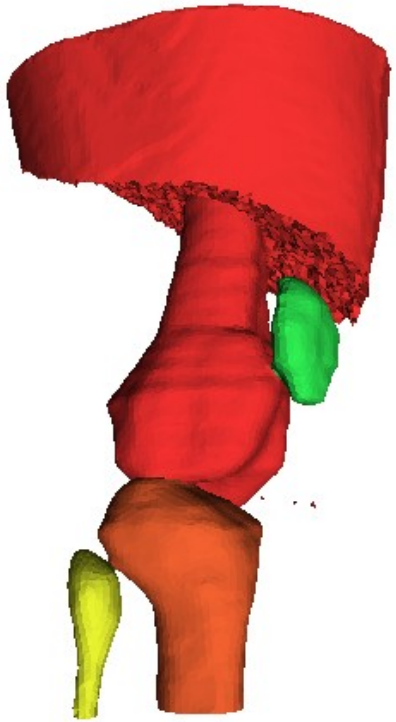




Head model:
120 000 nodes
670 000 tetrahedral
5 tissues

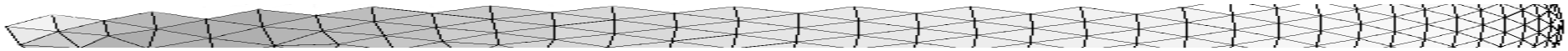
Realistic 3D meshes

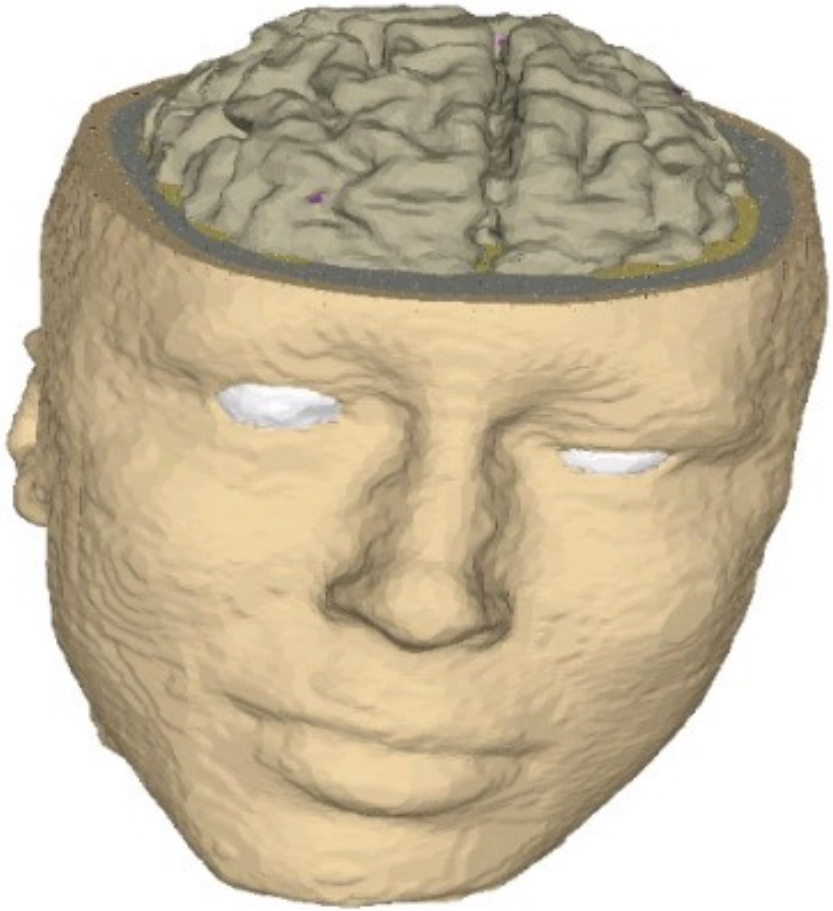




Knee joint model:
160 000 nodes
930 000 tetrahedral
5 subdomains

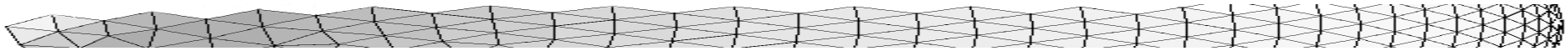
Realistic 3D meshes





Brain model:
470 000 nodes
2 700 000 tetrahedral
7 tissues

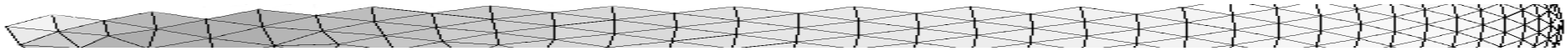
Realistic breasts models



From UWCEM Numerical Breast Phantoms Repository

- class 1 - mostly fatty
- class 2 - scattered fibroglandular
- class 3 - heterogeneously dense
- class 4 - very dense

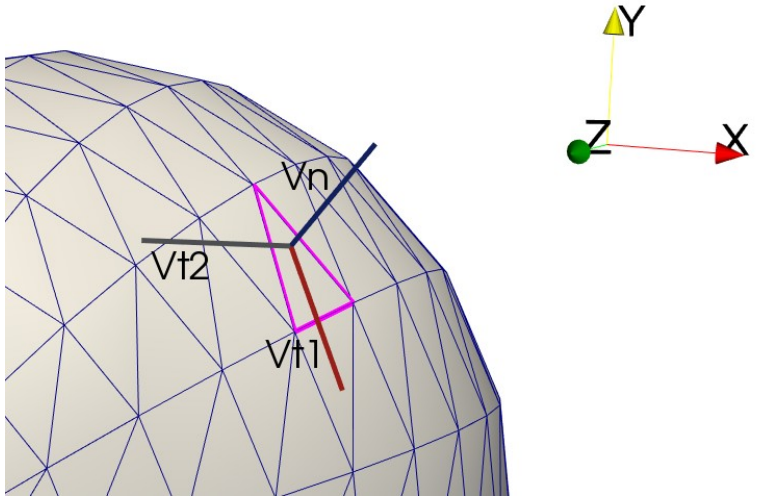
Anisotropic conductivity [S/m]



Isotropic material:

$$\underline{\sigma} = 0.4\, \boldsymbol{I}_3 = \begin{bmatrix} 0.4 & 0 & 0 \\ 0 & 0.4 & 0 \\ 0 & 0 & 0.4 \end{bmatrix}$$

(brain)



Anisotropic material:

$$\underline{\sigma} = \mathbf{V}\mathbf{S}\mathbf{V}^T$$

$$\boldsymbol{S} = \begin{bmatrix} 0.0057 & 0 & 0 \\ 0 & 0.057 & 0 \\ 0 & 0 & 0.057 \end{bmatrix}$$

(bones, skull)

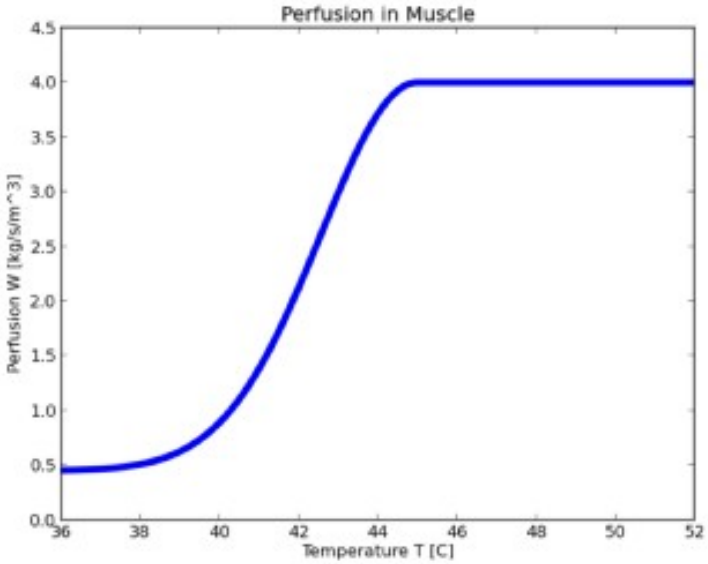
$$\boldsymbol{V} = \begin{bmatrix} vn_x & vn_y & vn_z \\ vt1_x & vt1_y & vt1_z \\ vt2_x & vt2_y & vt2_z \end{bmatrix}$$

Nonlinear blood perfusion

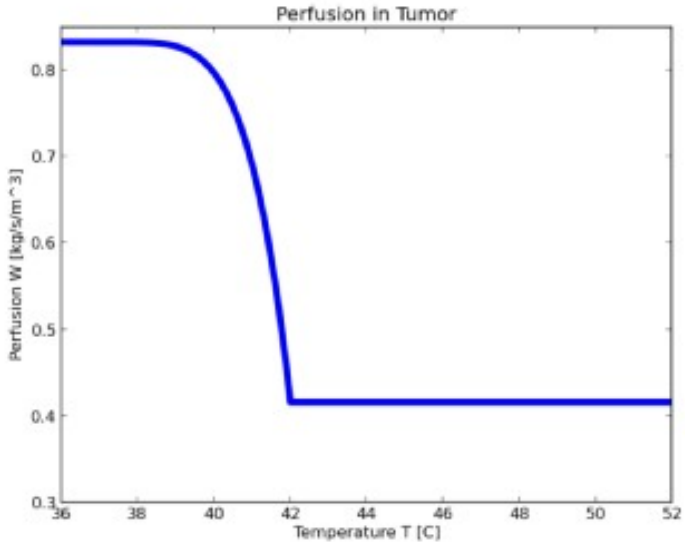
Blood perfusion (cooling factor) is nonlinear, tissue dependent.

$$W_{\text{muscle}} = \begin{cases} 0.45 + 3.55\exp\left(-\frac{(T-45.0)^2}{12.0}\right), & T \le 45.0 \\ 4.00, & T > 45.0. \end{cases}$$

$$W_{\text{tumor}} = \begin{cases} 0.833, & T < 37.0 \\ 0.833 - (T-37.0)^{4.8}/5.438E+3, & 37.0 \le T \le 42.0 \\ 0.416, & T > 42.0. \end{cases}$$

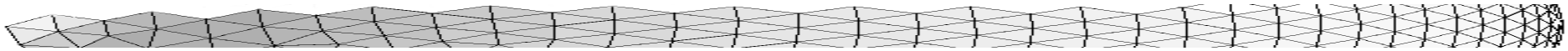


Healthy muscle tissue



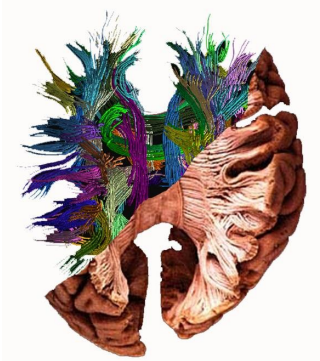
Tumorous tissue

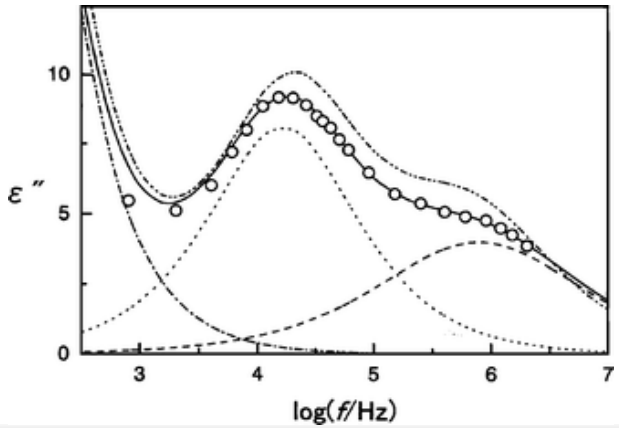
Wyzwania



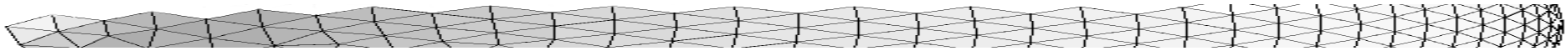
- Skomplikowane kształty i struktura ciała ludzkiego

- Parametry materiałowe tkanek żywych:
  - Anizotropowe, nieliniowe, zmienne w czasie, ...



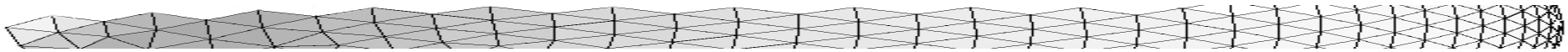


Plan seminarium



- Wyzwania – krok po kroku, na przykładach
  - Opis medyczny i fizyczny problemu
  - Opis matematyczny zjawiska
  - Model obiektu biologicznego
  - Rozwiązanie numeryczne
  - Analiza wyników
- Wyzwanie główne – wiarygodność wyników

Finite Element Method



Finite Element (FEM) was chosen:

- very flexible mesh geometry and element size,
- low frequency field, quasi-static problem,

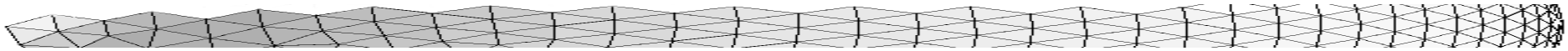
Other popular is Finite Difference (FDM, FDTD, SPFD)

- natural for voxel/cubic mesh,
- time-domain calculations, high frequency.

Main difference:

FEM is an approximation to the solution,
FDM is an approximation to the differential equation.

FEM: Poisson's equation



$$\nabla^2 u = f$$

Weighted residual

$$\hat{u} = \sum_{j=1}^{M} u_j N_j(x)$$

$$\int_\Omega N_i(\nabla^2 u - f)\, dx = 0$$

Variational spaces

$$\int_\Omega \nabla v \cdot \nabla u\, dx = \int_\Omega v\, f\, dx$$

$$\hat{u} = \sum_{j=1}^{M} u_j N_j(x),\ \hat{v} = \sum_{i=1}^{M} v_i N_i(x)$$

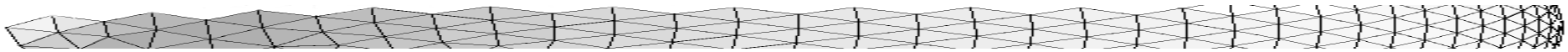
Linear eqn. system

$$\boldsymbol{A}\,\boldsymbol{u} = \boldsymbol{b}$$

$$A_{ij} = \int_\Omega \nabla N_i \cdot \nabla N_j\, dx$$

$$b_i = \int_\Omega N_i\, f\, dx$$

Linear solvers



$$A\,u = b$$

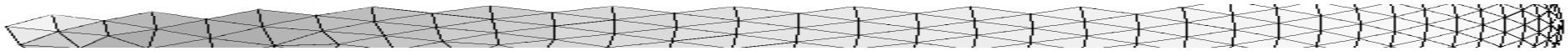
Preconditioners:

Jacobi, ILU, SSOR, AMG

Solvers:

Iterative (Krylov): BiConjugate Gradients, GMRES

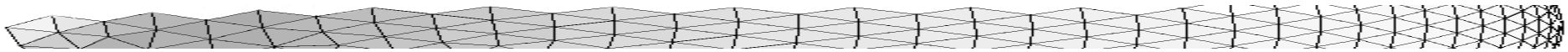
Adaptive Mesh Refinement



- Solve problem with initial mesh
- Estimate error
- Until (satisfied or limited):
  - Mark cells for refinement
  - Refine mesh
  - Solve problem for refined mesh
  - Estimate error

$$e_i = \sum_{j=0}^{3} s_j (\mathbf{J}_i \cdot \mathbf{n}_j)$$

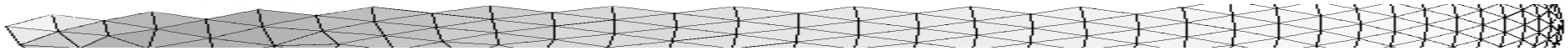
Mesh refinement



Three ways to improve the mesh:

- h-refinement -- split elements
  - Computational geometry problem
- p-refinement -- higher order elements
  - Difficulties with local refinement
- r-refinement -- move vertices, smooth mesh
  - Problem with material boundaries

Mesh quality

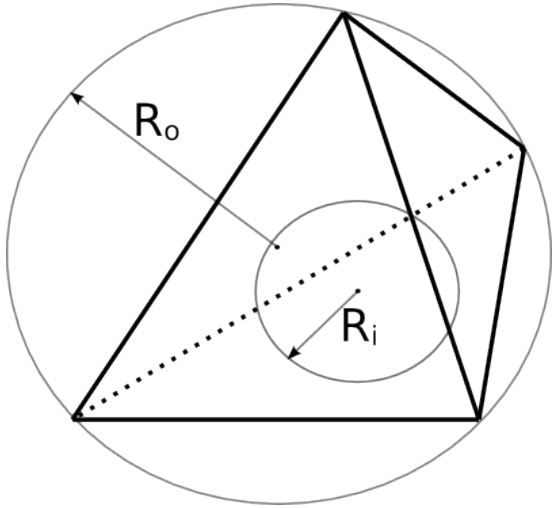


Thin elements lead to errors in solution:

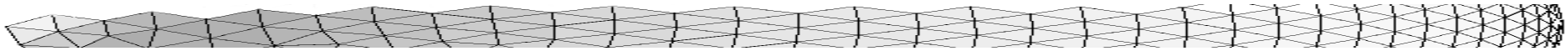
Element quality measured by:

- Inscribed to circumscribed sphere radii ratio
- Maximum/minimum angle, ...

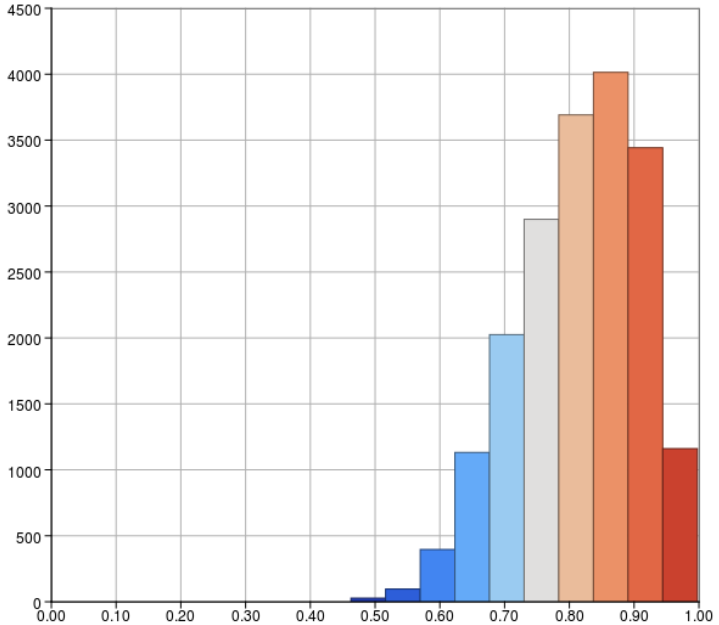
$$q = \frac{R_i}{R_o}$$



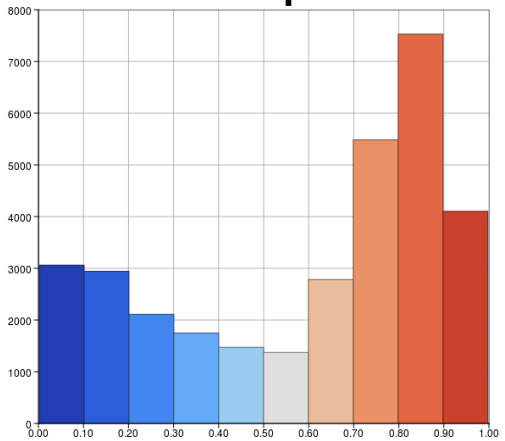
Mesh quality



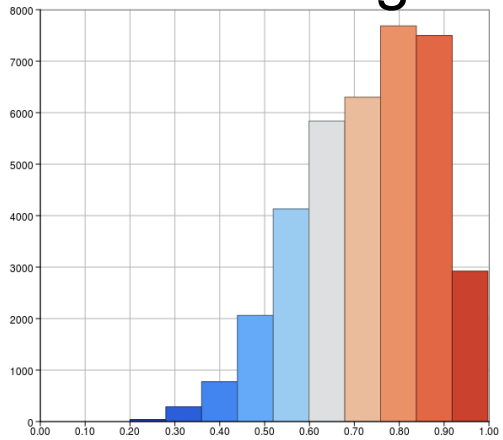
Original mesh histogram



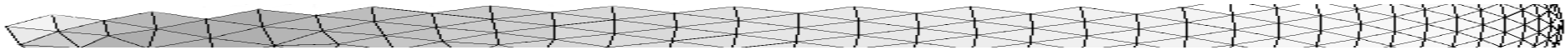
After simple bisection

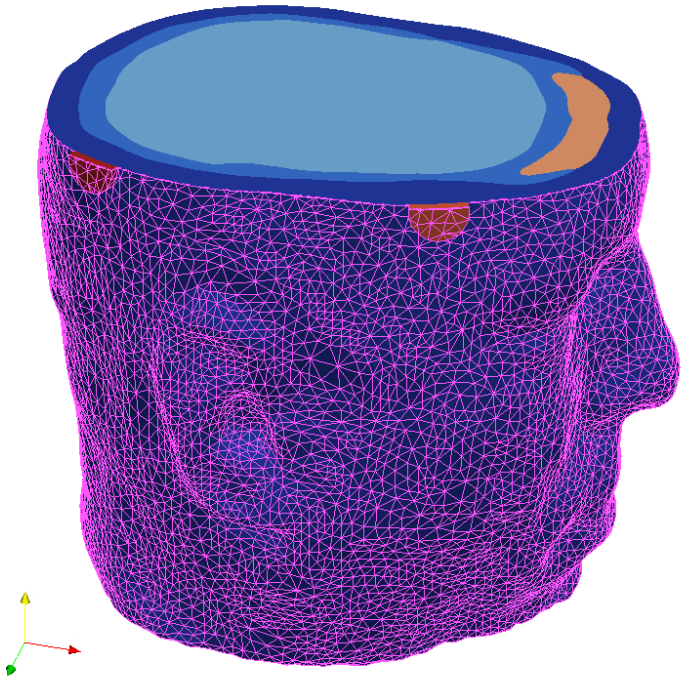


After LEPP algorithm



Head electrodes

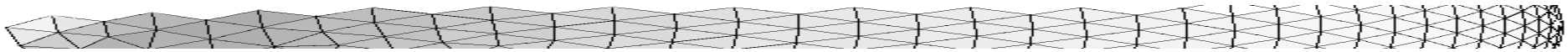




Head model:
- from VisibleHuman dataset,
- 600k elements,
- 5 tissues

Electrodes:
1. active current electrode (5 mA, 30 [A/m^2])
2. grounding electrode (zero Dirichlet BC)

Solvers

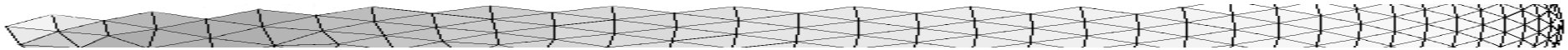


Solver comparison:

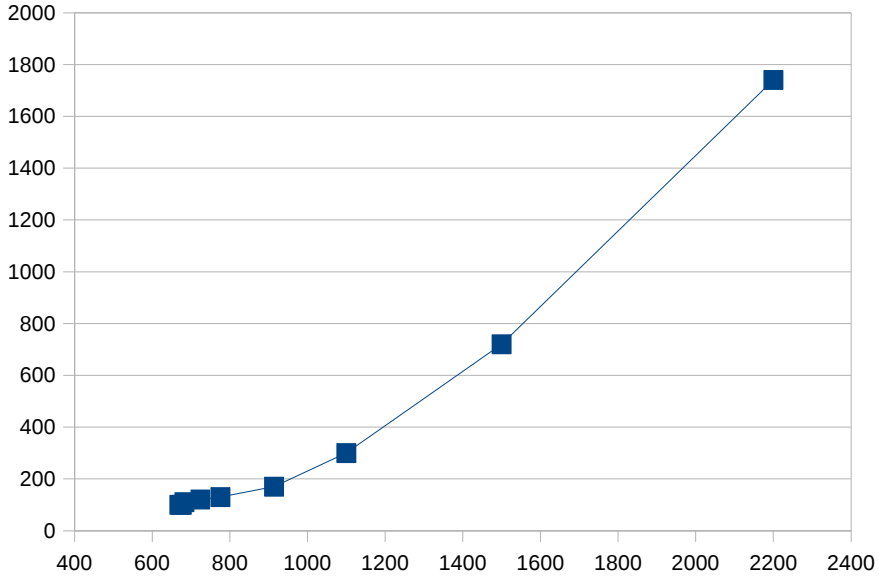
- Laplace equation, 300k unknowns

Summary of timings	Average time	Iterations
Petsc: gmres, ilu	42.46	1534
Petsc: bicgtab, ilu	11.40	255
Petsc: bicgtab, icc	10.03	268
Petsc: bicgtab, sor	8.19	195
Petsc: cg, ilu	7.29	323
Petsc: cg, sor	5.86	276
Petsc: cg, AMG	14.96	11

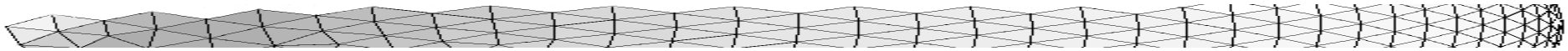
Solver timings



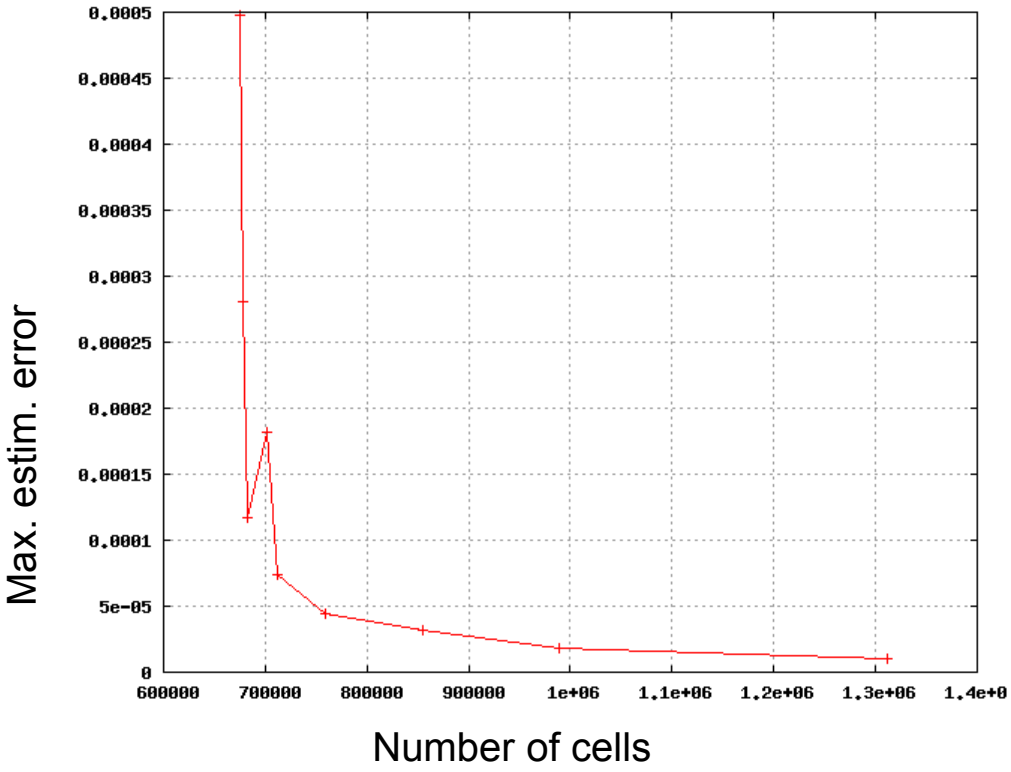
	No. cells	Total iter.-time
Iteration 0	670k	100s
Iteration 1	676k	100s
Iteration 2	683k	110s
Iteration 3	724k	120s
Iteration 4	776k	130s
Iteration 5	914k	170s
Iteration 6	1100k	300s
Iteration 7	1500k	720s
Iteration 8	2200k	1740s
		3490s



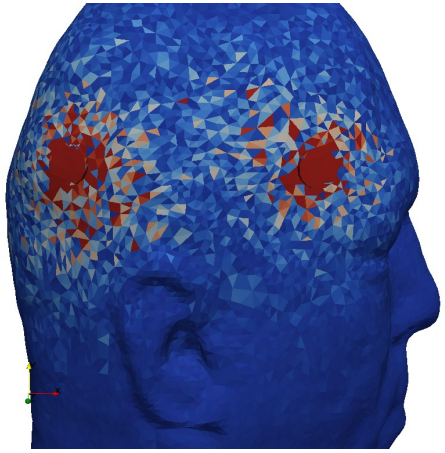
AMR convergence



Estimated error convergence:

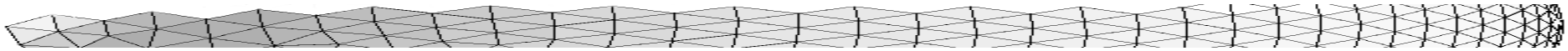


Before:



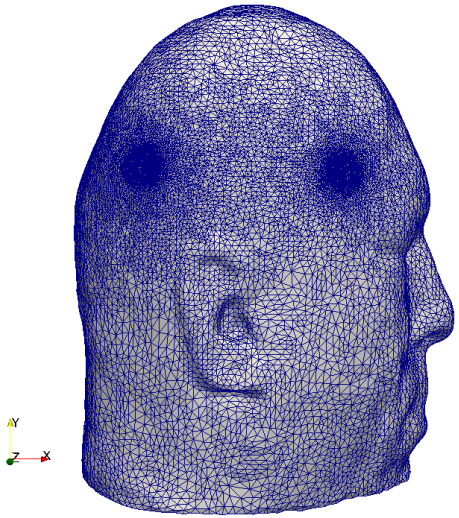
After:

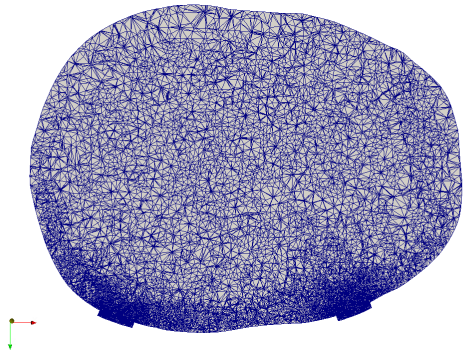
Refined mesh

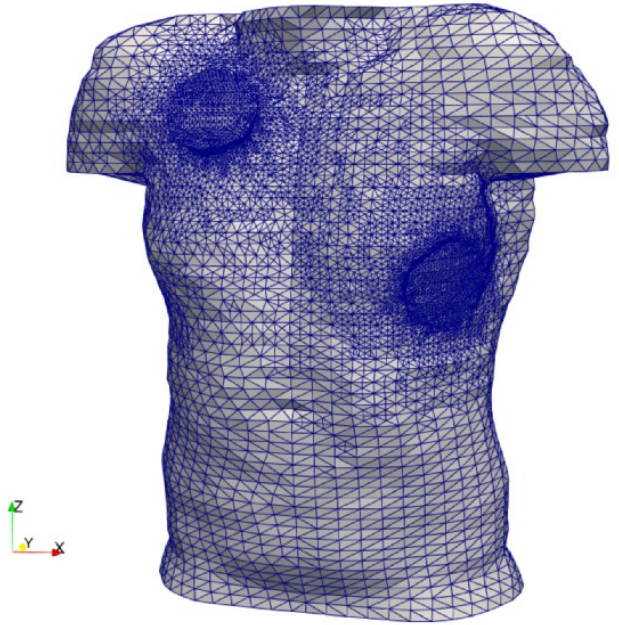


Refined mesh

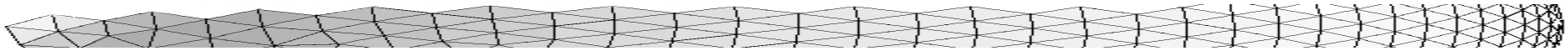
400k vertices, 2 mln cells







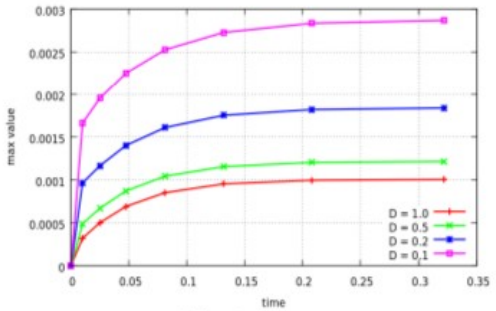
Transient solutions



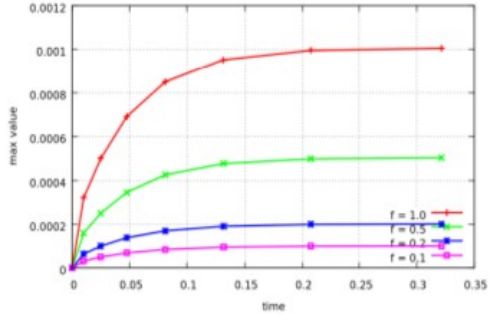
Stiff problem

$$\frac{\partial u}{\partial t} = \nabla \cdot (D \nabla u) - E(u)u + f, \qquad -\frac{\partial u}{\partial n} = -Hu$$

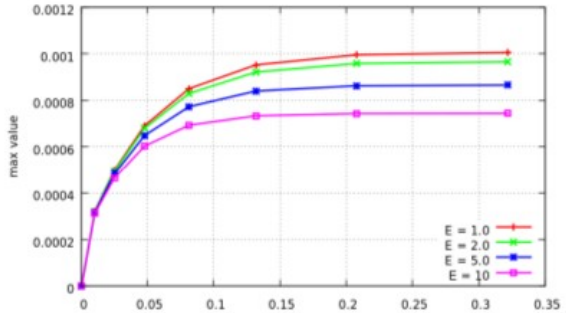
Trial solutions for unified coefficients:



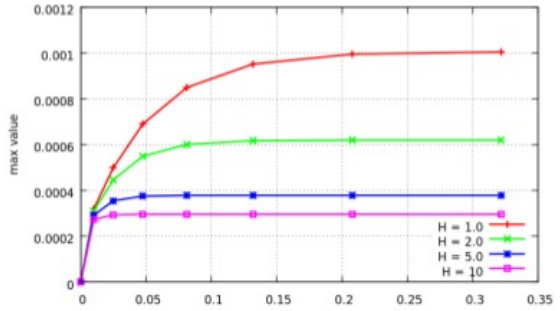
Diffusivity (D)



Source (f)

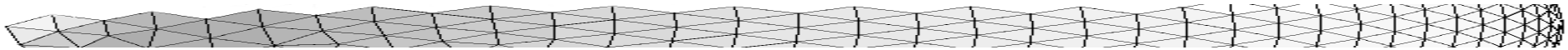


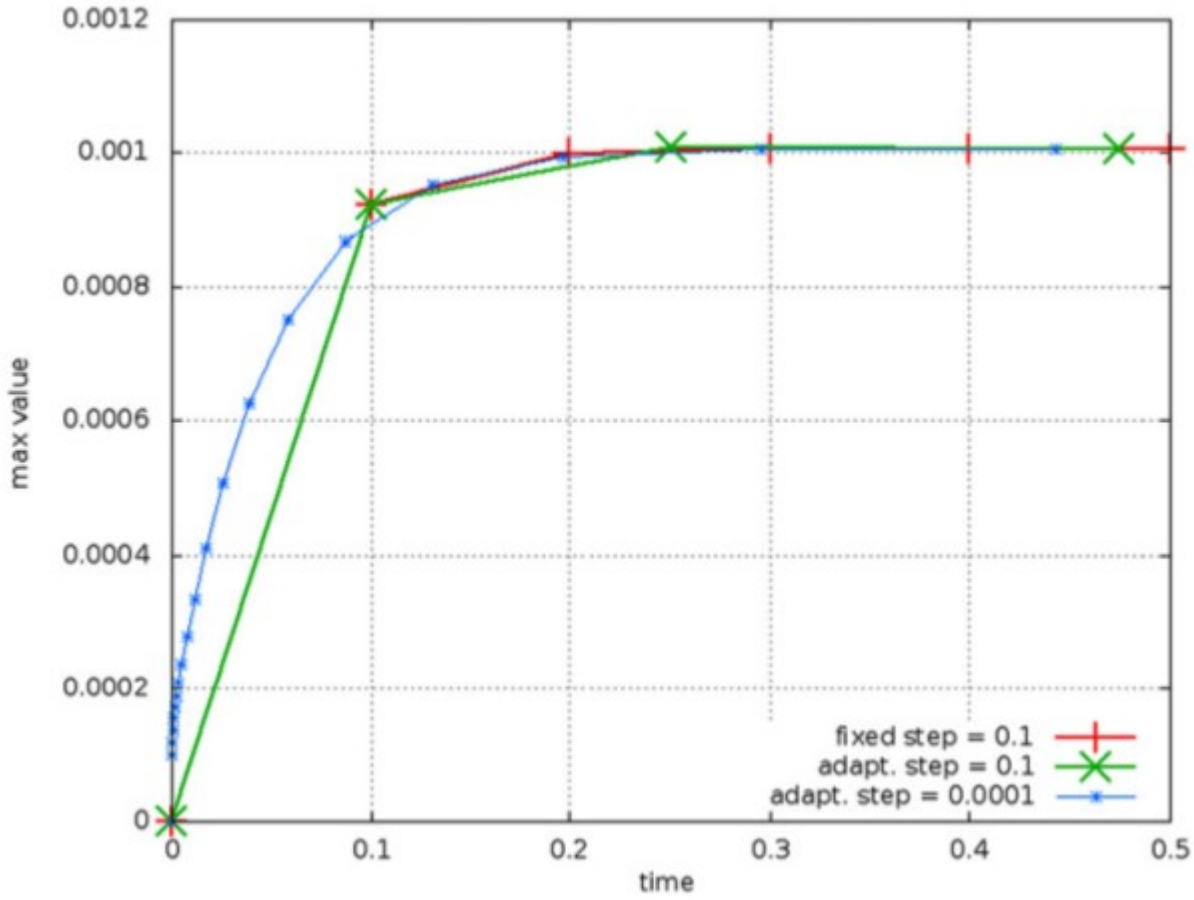
Perfusion (E)



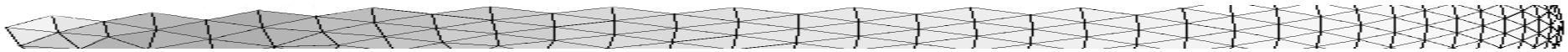
Convection (H)

Time adaptivity



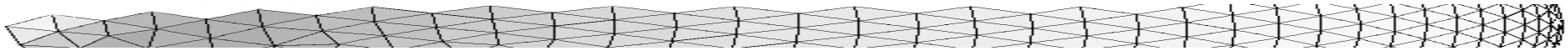


Wyzwania



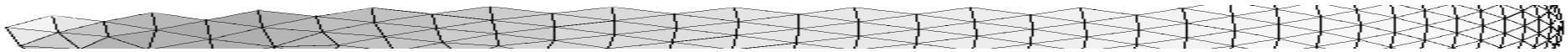
- Wydajne metody do układów równań liniowych
- Zmiejszanie błędu rozwiązania poprzez metody adaptacyjne
- Iteracyjne algorytmy dla problemów nieliniowych
- Rozwiązanie po czasie
  - metody wielokrokowe, zmienny krok

Plan seminarium

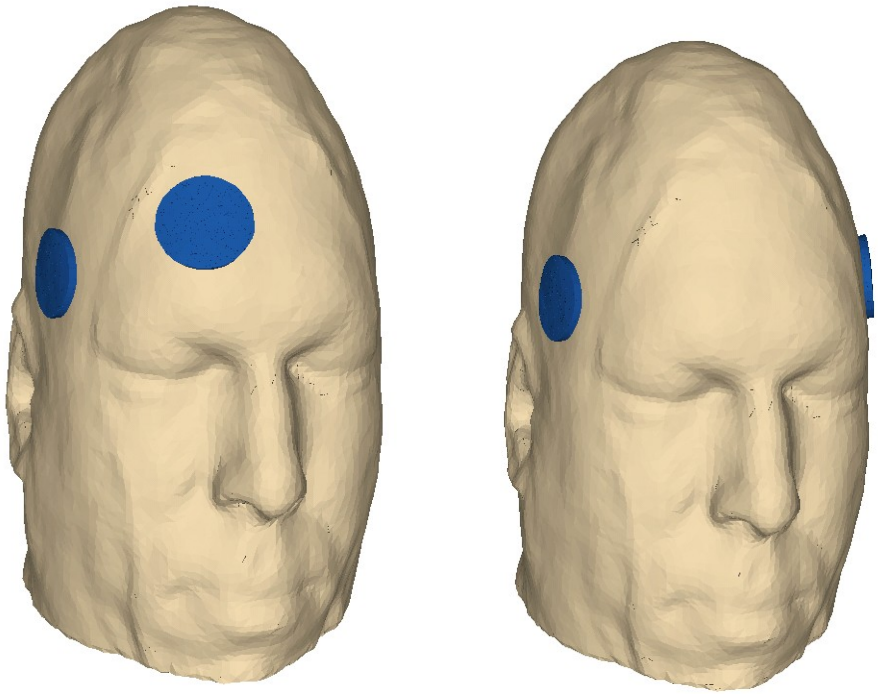


- Wyzwania – krok po kroku, na przykładach
  - Opis medyczny i fizyczny problemu
  - Opis matematyczny zjawiska
  - Model obiektu biologicznego
  - Rozwiązanie numeryczne
  - Analiza wyników
- Wyzwanie główne – wiarygodność wyników

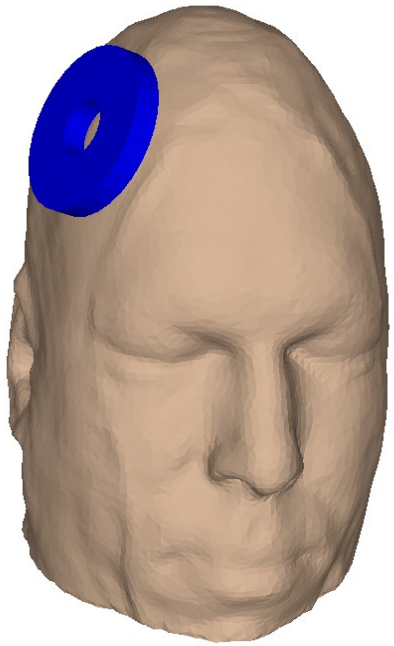
Transcranial Magnetic Stimulation



Can TMS replace controversial ETC?

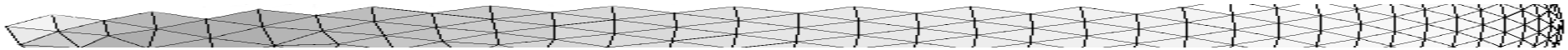


ECT

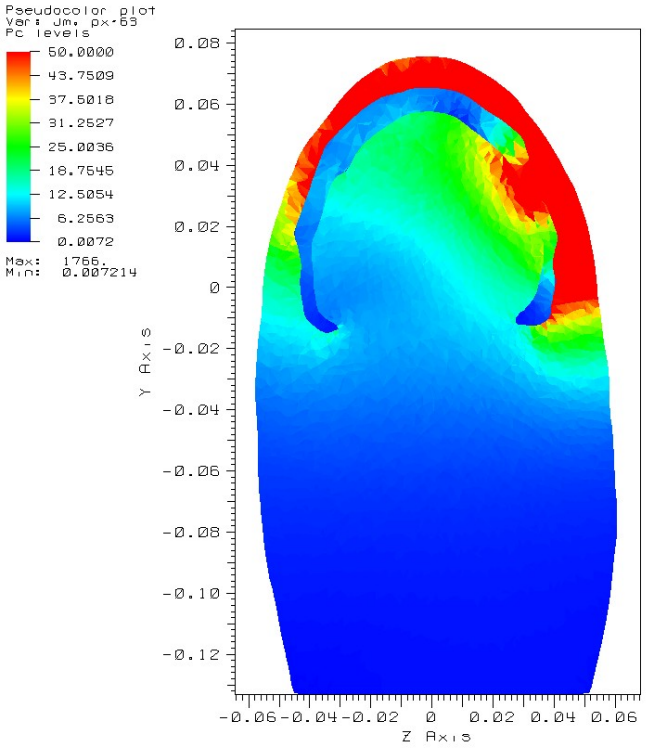


TMS

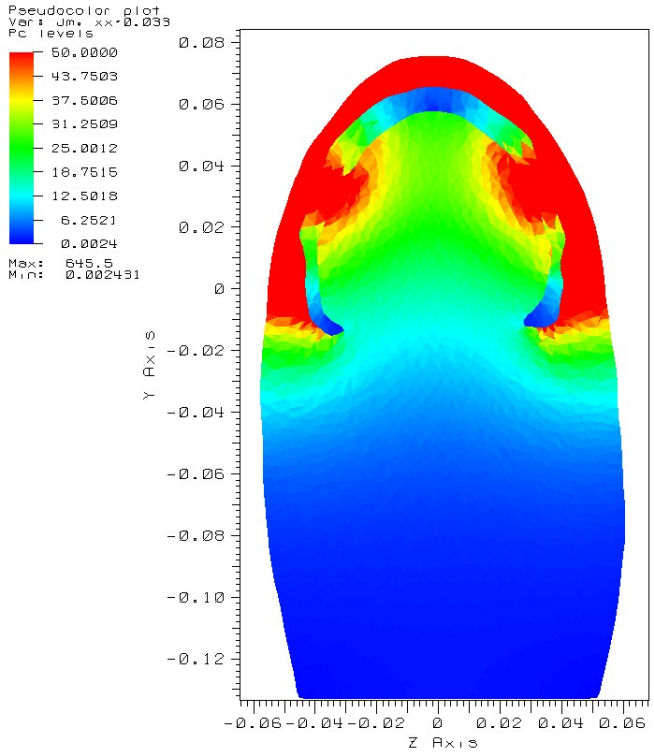
Transcranial Magnetic Stimulation



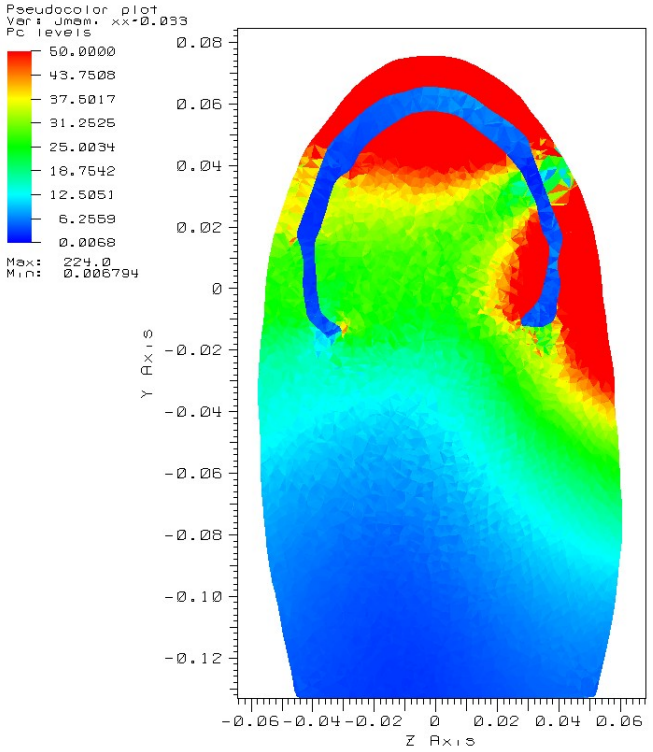
ECT (min):
forehead-temple



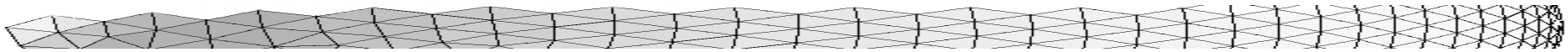
ECT (min):
temple-temple



TMS (max):



Transcranial Magnetic Stimulation



Maximal eddy current density for each tissue:

		ECT-FT			ECT-TT			TMS-1		
		min	**avg**	**max**	**min**	**avg**	**max**	**min**	**avg**	**max**
Skin	J_{max}[A/m^2]	917	3778	7557	604	2416	4843	9	50	210
Scull		129	517	1034	75	296	933	0,7	4	20
Brain		70	287	575	101	443	1538	3	10	120

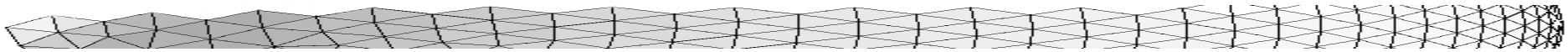
Observations:

ECT produce much (10-100 times) **stronger field**

Similar values of current density are observed only for minimal ECT and maximal TMS. (marked with yellow)

Safety limits are below **0.1** [A/m2]

Transcranial Magnetic Stimulation



Comparison with other authors results:

[1] M. Nadeem et al.: *Computation of Electric and Magnetic Stimulation in Human Head Using the 3-D Impedance Method*, IEEE TM, 2003

ECT: 140-570 A/m^2, TMS: 30-130 A/m^2

[2] M. Sekino, S. Ueno: *Comparison of current distributions in electroconvulsive therapy and transcranial magnetic stimulation,* Journal of Applied Physics, 2002

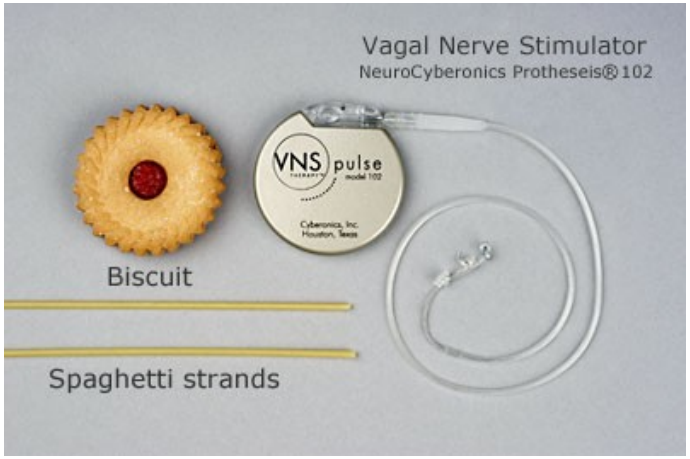
ECT: 266 A/m^2, TMS: 322 A/m^2

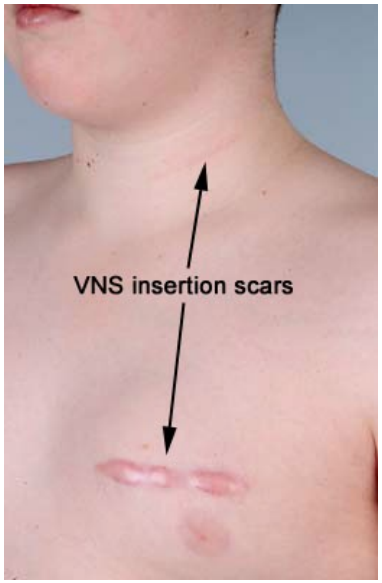
Our results from previous slide:

ECT: 70-1500 A/m^2, TMS: 3-120 A/m^2

Vagus Nerve Stimulation

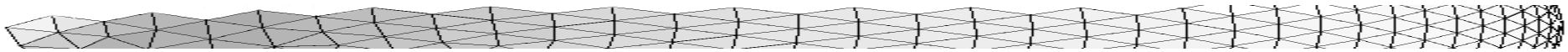
Can we replace electric VNS by magnetic stimulation?

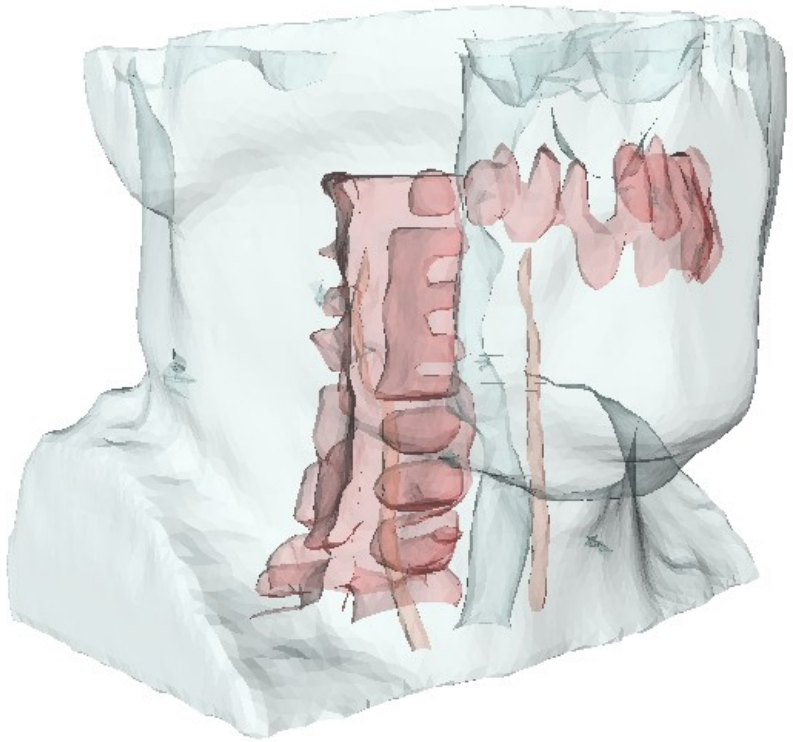




The VNS is a modern treatment (approved in 1994).
Magnetic VNS is just a concept.

Vagus Nerve Stimulation





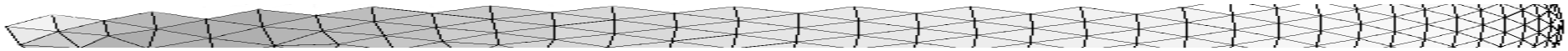
Neck model:

110,000 nodes
620,000 elements

Stimulation :

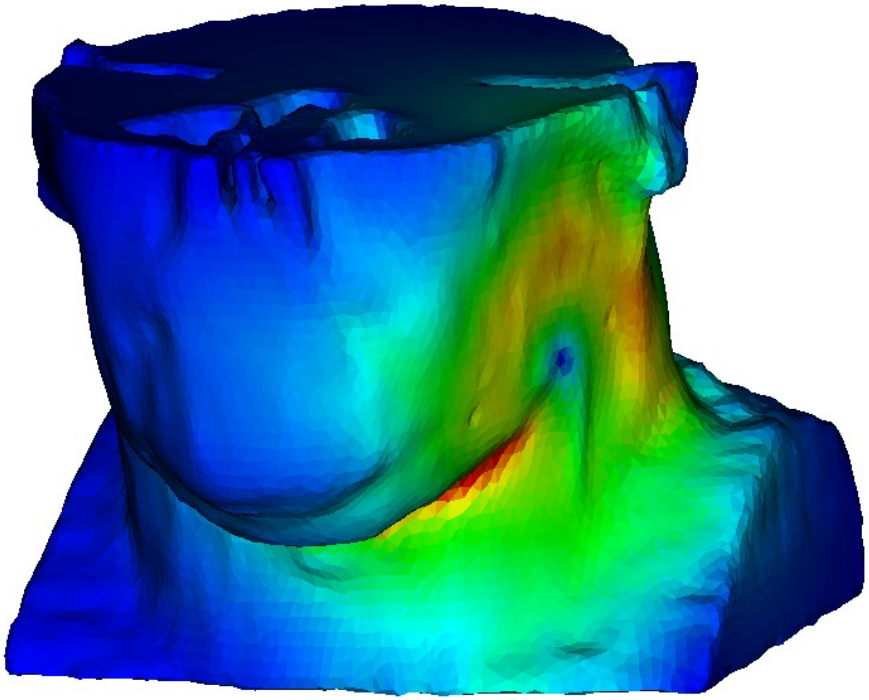
Number of terms - 7
Current - 7 kA
Raise time – 100 μs

Vagus Nerve Stimulation



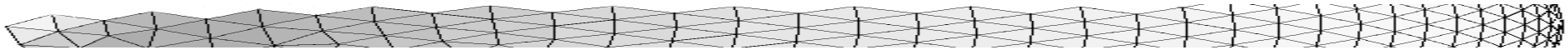
Stimulation by electrodes

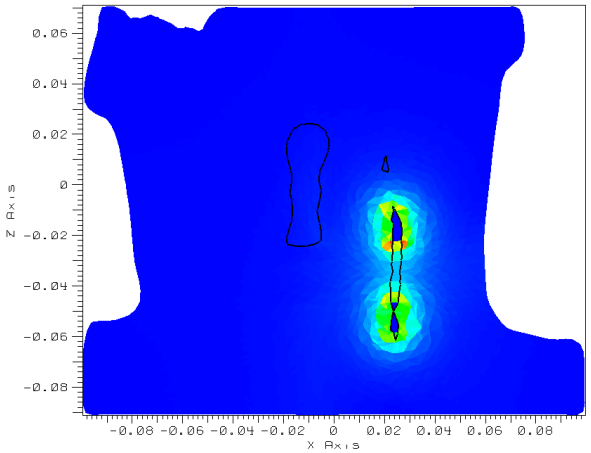
Stimulation by coil

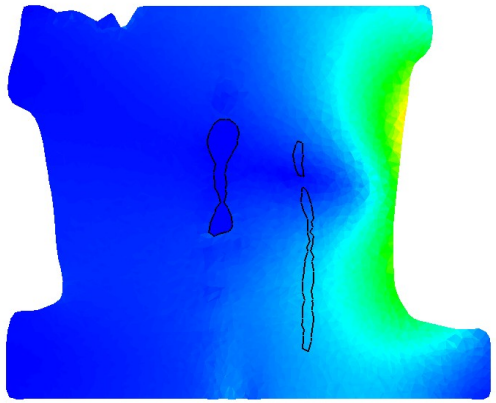


Eddy currents magnitude on the skin surface.

Vagus Nerve Stimulation





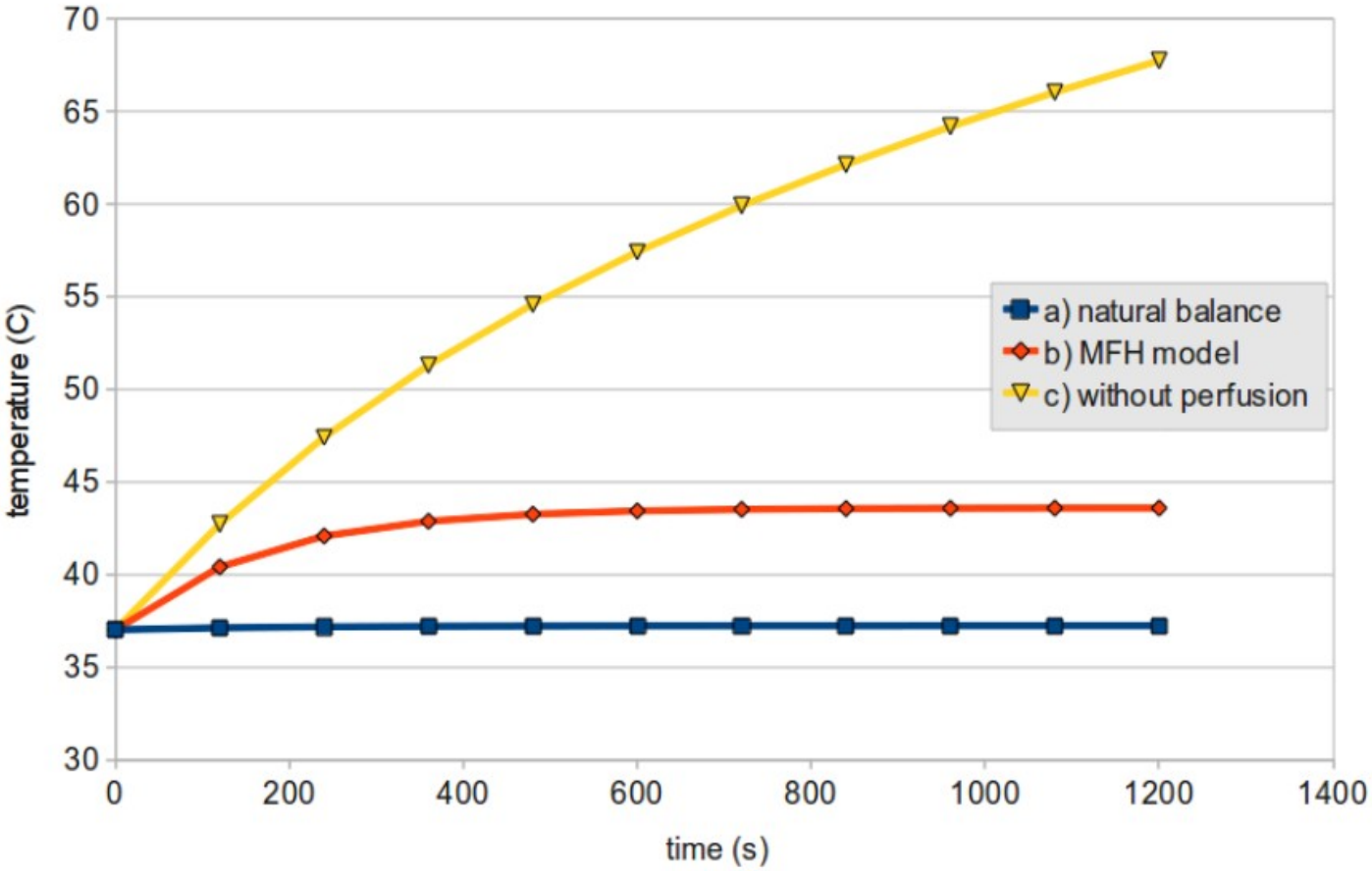


Maximal current density magnitude:

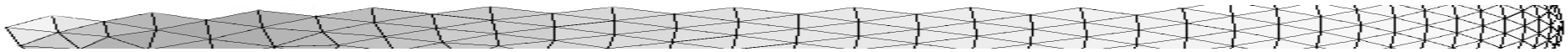
	Electr.	Magn.
Vagus nerve	330	150
Whole neck model	335	500

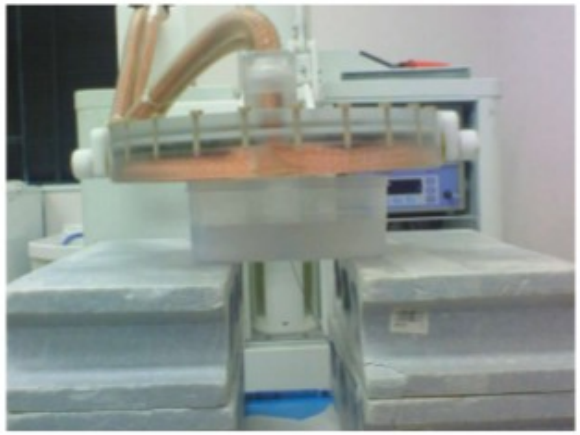
$$\left[\frac{A}{m^2}\right]$$

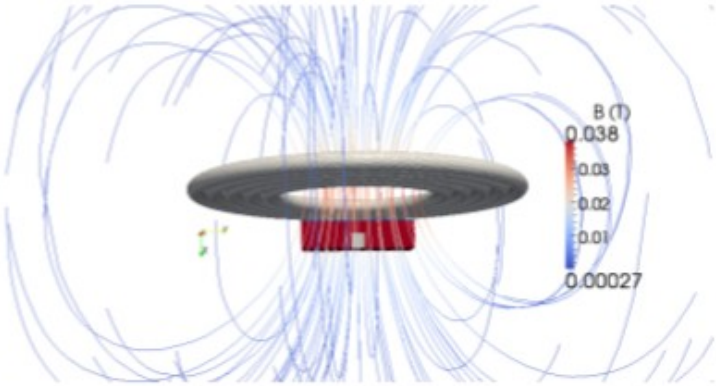
Magnetic Fluid Hyperthermia

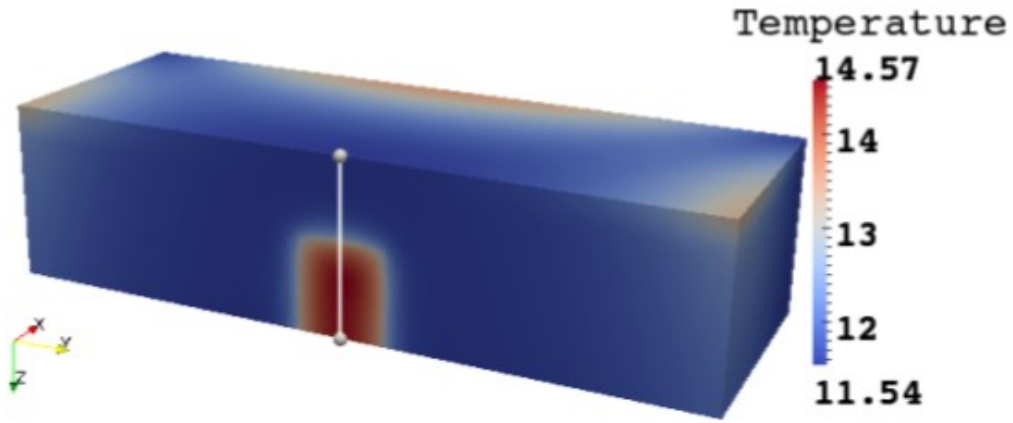


Magnetic Fluid Hyperthermia

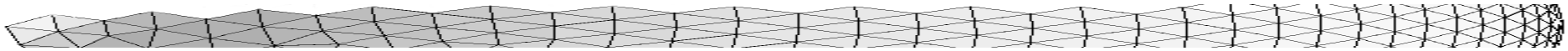








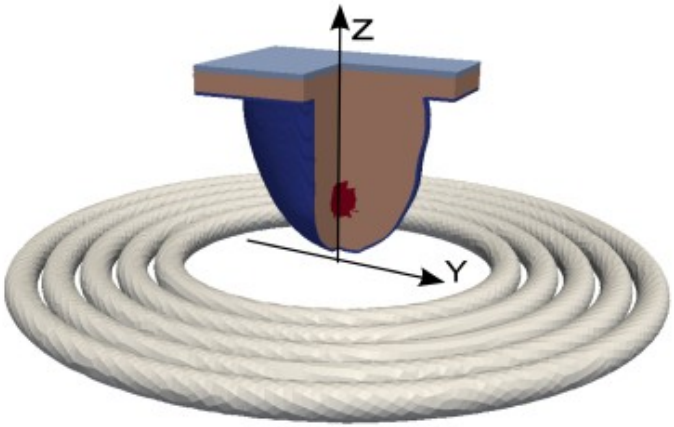
Magnetic Fluid Hyperthermia

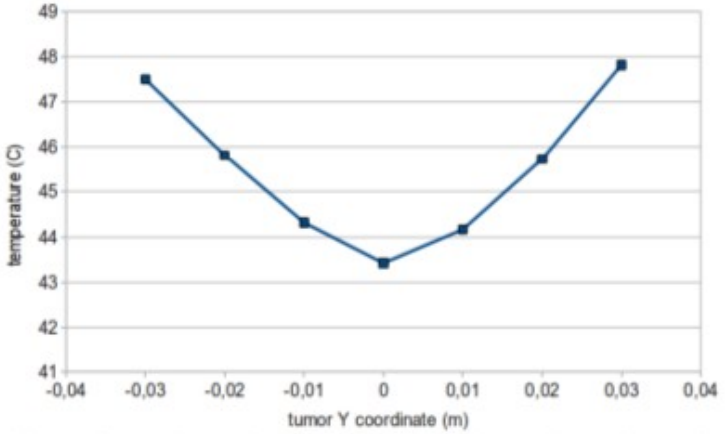


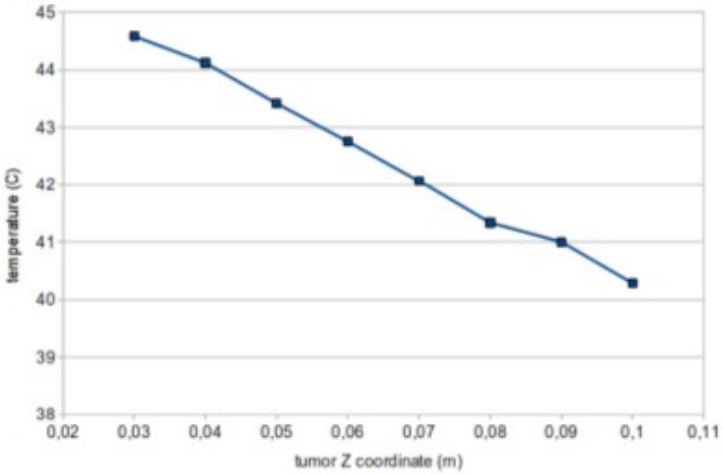
Temperature after 30 minutes exposition: max. 43.6 C

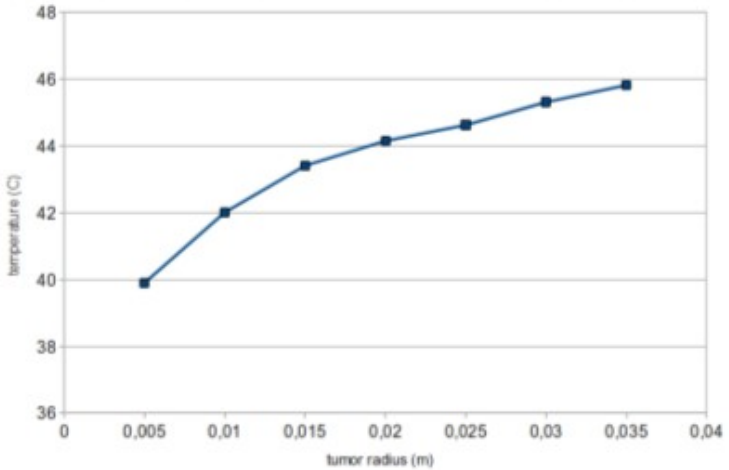
Conclusion:
Therapy is unaffected by breast class and shape.

Magnetic Fluid Hyperthermia

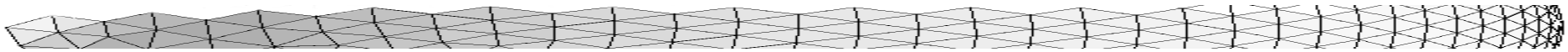






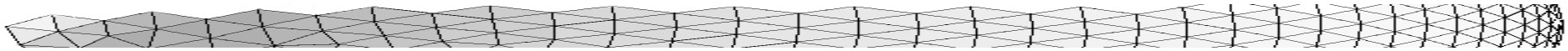


Wyzwania



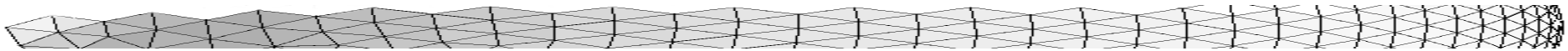
- Eksperymentalne potwierdzenie wyników
  - Trudności z pomiarami rzeczywistych wartości
- Interpretacja wyników
  - Niezbędna wiedza i doświadczenie medyczne

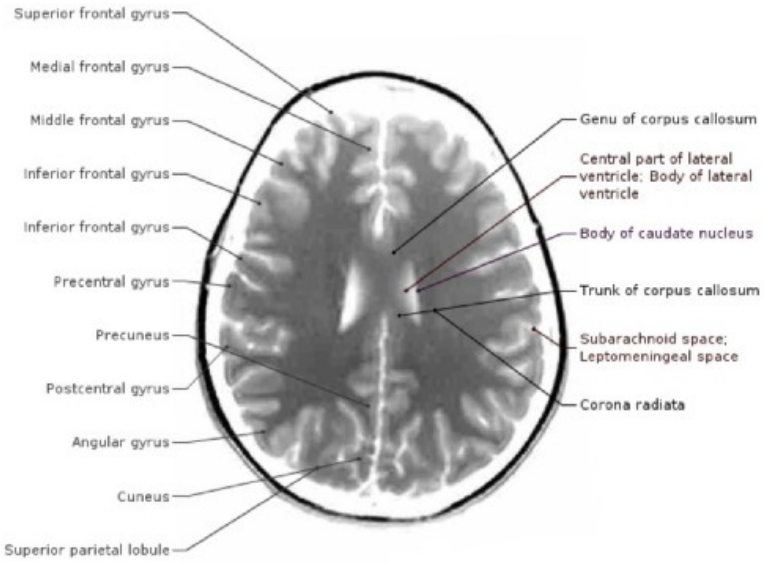
Plan seminarium

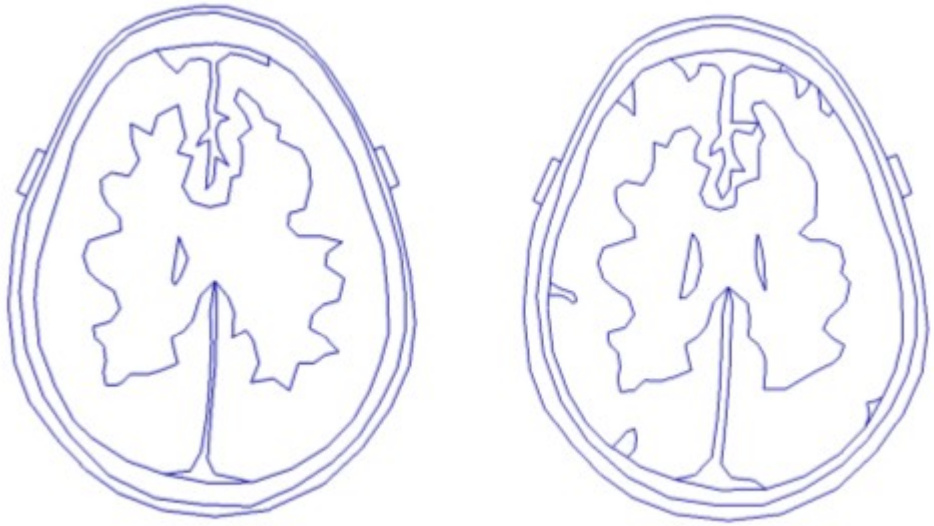


- Wyzwania – krok po kroku, na przykładach
  - Opis medyczny i fizyczny problemu
  - Opis matematyczny zjawiska
  - Model obiektu biologicznego
  - Rozwiązanie numeryczne
  - Analiza wyników
- Wyzwanie główne – wiarygodność wyników

Segmentation uncertainty

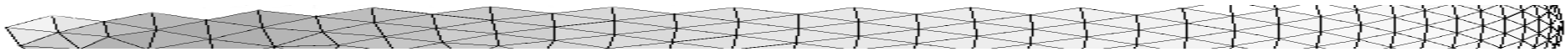






Two different segmentations of the same MRI head scan.

Tissue uncertainty

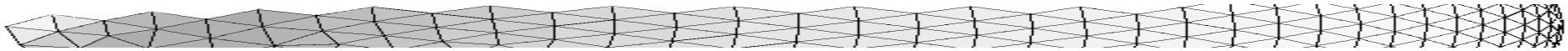


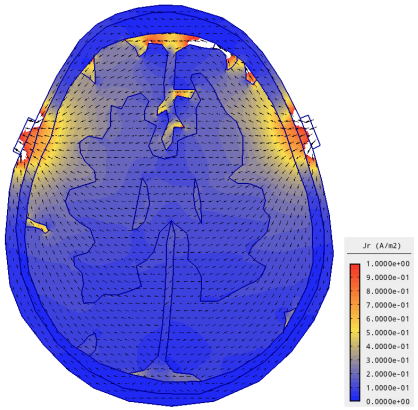
Tissue properties:
inhomogeneous, time-varying, patient specific, non-linear, ...

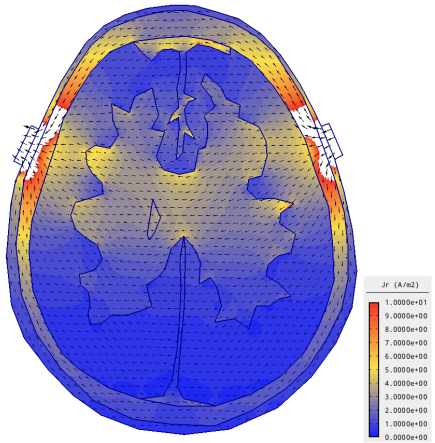
Conductivity [S/m]	Average	Std. dev.	Min	Max
Brain (White Matter)	0.37	0.34	0.05	1.12
Brain (Grey Matter)	0.19	1	0.08	0.26
Bone	0.1	1	0.02	1.17
Skin	0.00121	0.000078	0.00043	0.002
Cerebrospinal Fluid	1.80	0.21	1.59	2.00
Muscle	0.29	0.18	0.04	0.60

Low frequency values from IT'IS literature review published on 01.08.2014.

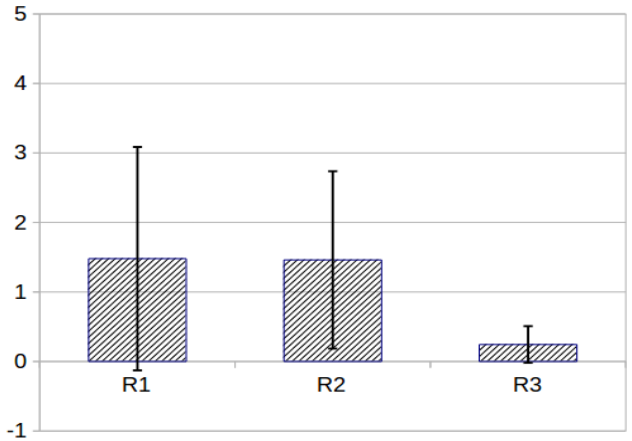
Sensitivity analysis



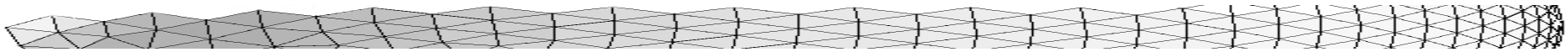




Result	Average	Std. dev.
J in the center of the brain [A/m2]	1.47	1.61
J in the vicinity of electrode [A/m2]	1.46	1.28
Total power loss [W]	0.24	0.26

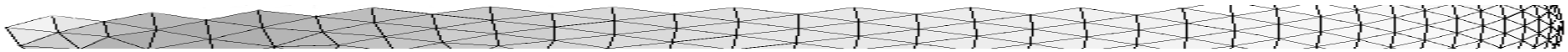


Sources of uncertainty



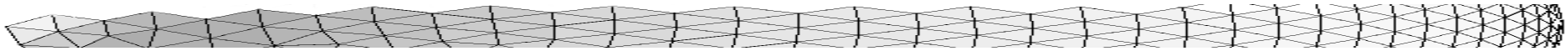
Source of uncertainty	Level	Type	How to reduce?
Mathematical & physical model	unknown	cognitive	Develop advanced mathematical models.
Tissue properties	1000% - 3000%	cognitive and stochastic	Measurements of in-vivo tissue parameters are nearly impossible.
Geometry	10-50%	stochastic and cognitive	Improve techniques for internal imaging and segmentation algorithms.
Numerical errors	1-5%	stochastic	Apply advanced numerical techniques.

Podsumowanie



- Modelowanie numeryczne jest **szeroko stosowane** w bioelektromagnetyzmie.
- Techniki obliczeniowe szybko dają precyzyjne wyniki, jednak ich **wiarygodność jest ograniczona**.
- Wysoka zmienność parametrów ciała ludzkiego wymusza **podejście stochastyczne** i statystyczną analizę wyników.

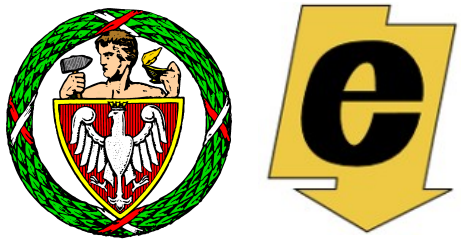
Dziekuję

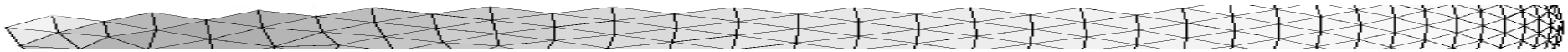


Współpraca (w latach 2003-2014):

- Michał Chojnowski, Arkadiusz Miaskowski, Michal Okoniewski, Przemysław Płonecki, Jacek Starzyński, Robert Szmurło, Stanisław Wincenciak
- Andrzej Rysz, Tomasz Zyss

Politechnika Warszawska
Wydział Elektryczny
Instytut Elektrotechniki Teoretycznej i Systemów Informacyjno-Pomiarowych





KONIEC