Exposure setups for in vivo experiments using waveguides

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Contents

Experimental design

- 3 studies in cooperation with the International University Bremen (Prof. A. Lerchl):

1. **Influence of 900 MHz electromagnetic fields on spontaneous leukaemia in AKR/J mice**
   160 mice exposed to generic GSM test signal, 400 mW/kg (whole body), 24 hrs / day
   160 mice sham-exposed. Endpoints: leukaemia rate and production of solid tumours. End: 9/2004

2. **In vivo experiments on exposure to the high frequency electromagnetic fields of mobile telecommunication. B. Carcinogenesis**
   same as 1., but generic UMTS test signal. End: 4/2005

3. **Long-term study on the effects of UMTS signals on laboratory rodents**
   Four generations of mice (c. 1200 animals altogether) exposed to generic UMTS test signal, different specific absorption rates (SAR). Endpoints: fertility, development, teratogenic effects. End: 7/2007

⇒ For all studies the biological design was prescribed by the Federal Office for Radiation Protection (BfS) concerning

- exposure of **freely moving** animals
- exposure at **fixed** averaged whole body specific absorption rates (**SAR**)
- exposure by generic **GSM900 or UMTS** test signals

Exposure of non-restrained animals

- The prescribed biological design allows
  - a long-term exposure up to 24 hours per day
  - animals held in cages (i.e. usual laboratory environment)
  - standard animal handling

- but can also introduce variations of the exposure due to
  1. different locations of the animals in the incident field
  2. varying orientations (postures) of the animals with respect to the direction of wave propagation and the polarization of the field vector
  3. the superposition of the original incident field and the scattered field from neighbouring animals
  4. the age-dependent development of body mass

$\Rightarrow$ While points 2. + 4. are inherent to the biological design and can not be avoided, the effects of 1. + 3. can be reduced by a suitable technical design of the exposure device

Reduction of whole body exposure variation

- The technical design should provide a field distribution inside the cage as uniform as possible in order to minimize the variations due to different locations of the moving animals.
- Also, a well-defined stable and reproducible field distribution reduces the effect of scattered fields from neighbouring animals (e.g. the excitation of higher order modes)

These features together with the above mentioned requirement of a very high number of simultaneously exposed animals can be fulfilled with the concept of the radial waveguide

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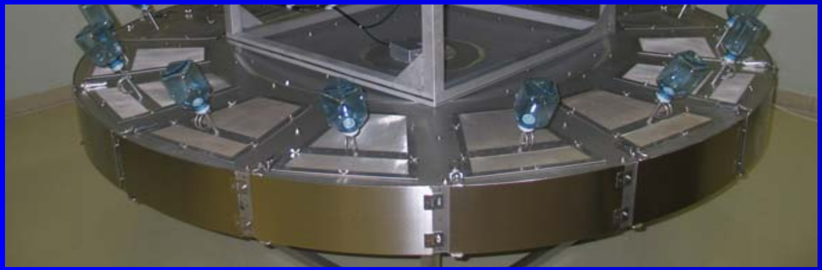
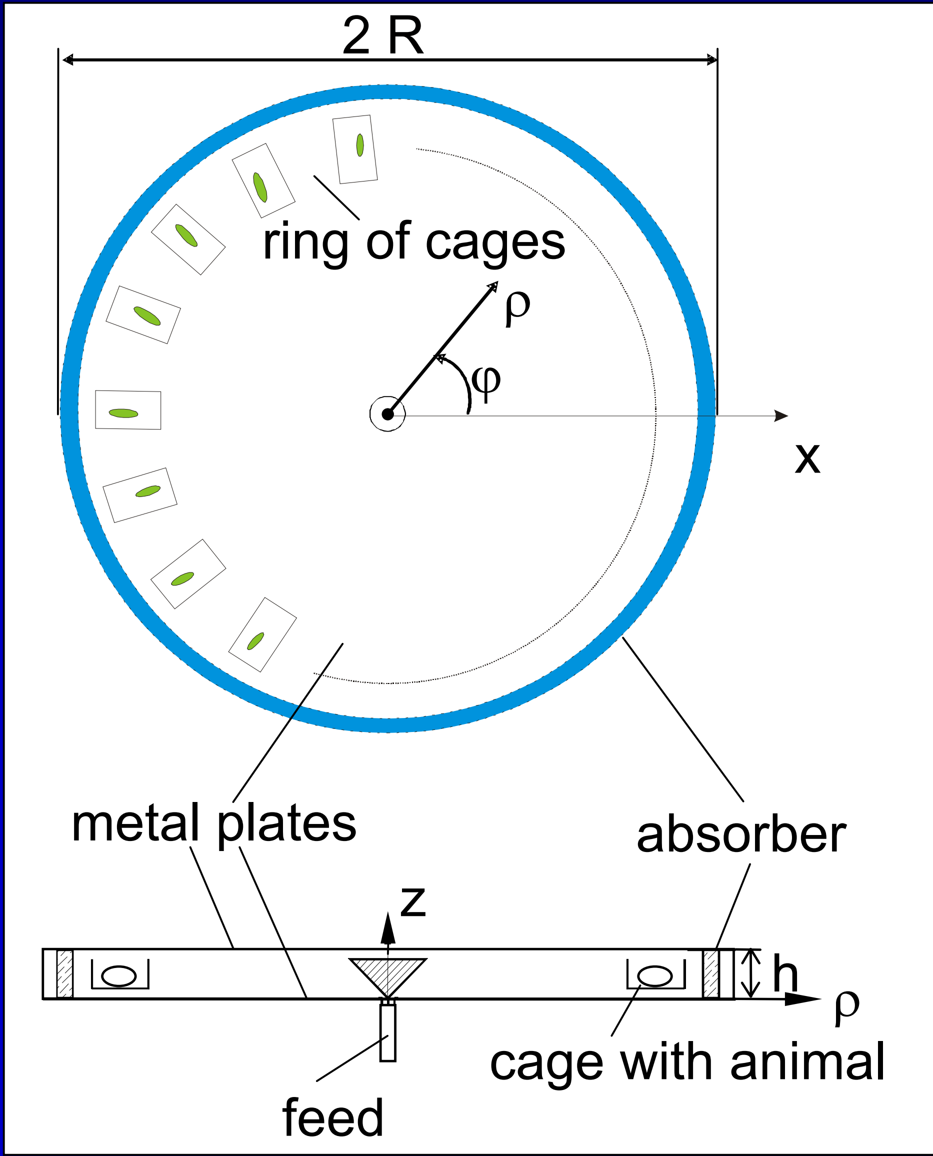
Design of a radial waveguide

- parallel circular metal plates
- absorbing material at radial boundary (mandatory for experiments with free-running animals in order to minimize the SWR)
- feed system: rotational symmetrical cone antenna in the centre exciting radially propagating waves
- cages arranged at constant distance from the centre





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Advantages of radial waveguide exposure chamber

+ simultaneous exposure of numerous biological samples

+ uniform exposure due to highly symmetrical configuration

+ high ratio of power density to generated power

+ electrically closed system
  $\Rightarrow$ no additional shielding of laboratory
  exposed and sham-exposed waveguide can be located close to each other

+ complete numerical analysis feasible
  $\Rightarrow$ modelling one sector with proper boundary conditions
  containing field excitation, exposed animals in the cage and
  termination of the waveguide

Exposure field: fundamental TM^{z}_{00} (TEM) -mode

- waveguide's height < half the wavelength
- rotational symmetrical excitation (empty waveguide)

} only TEM-wave propagating

$$E_z(\rho,\varphi,z) = -jA\frac{k_0^2}{\omega\mu_0\varepsilon_0}H_0^{(2)}(k_0\rho)$$

$$H_\varphi(\rho,\varphi,z) = -A\frac{k_0}{\mu_0}H_0^{(2)\,'}(k_0\rho)$$

- E-field polarized in vertical direction
- field strength constant in the waveguide's cross-section (ρ = const.)
- field decays for large radial distances $\sim\frac{1}{\sqrt{\rho}}$
  - for ordinary arrangements field decay in exposure region rather small
- Therefore, the TEM-mode is well suited for the generation of a uniform exposure field.

Higher order modes

If height of the cages that is prescribed by animal protection authority requires a waveguide's height of h $\geq \lambda/2$

$\Rightarrow$ higher order modes with respect to the vertical direction can propagate in addition to the TEM-mode

- TE^z_{01}-mode:

$$E_\varphi(\rho,\varphi,z) = A_{01}\frac{k_\rho}{\varepsilon}H_0^{(2)\prime}(k_\rho\rho)\sin\left(\frac{\pi}{h}z\right)$$

$$H_\rho(\rho,\varphi,z) = -jA_{01}\frac{k_\rho k_z}{\omega\varepsilon\mu}H_0^{(2)\prime}(k_\rho\rho)\cos\left(\frac{\pi}{h}z\right)$$

$$H_z(\rho,\varphi,z) = -jA_{01}\frac{k_\rho^2}{\omega\varepsilon\mu}H_0^{(2)}(k_\rho\rho)\sin\left(\frac{\pi}{h}z\right)$$

- TM^z_{01}-mode:

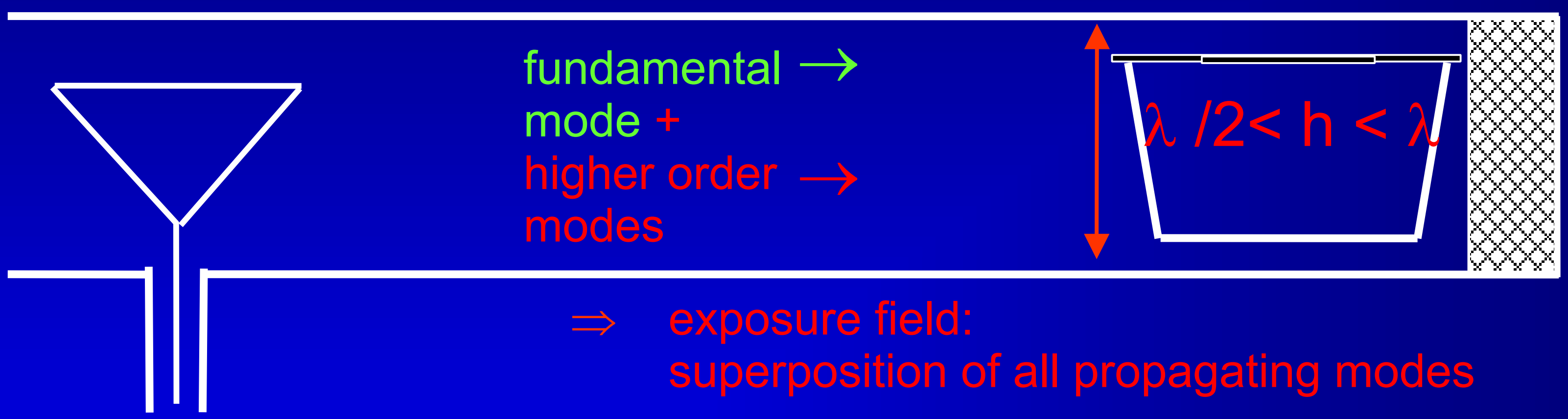
$$E_z(\rho,\varphi,z) = -jB_{01}\frac{k_\rho^2}{\omega\mu\varepsilon}H_0^{(2)}(k_\rho\rho)\cos\left(\frac{\pi}{h}z\right)$$

$$E_\rho(\rho,\varphi,z) = jB_{01}k_\rho\frac{k_z}{\omega\mu\varepsilon}H_0^{(2)\prime}(k_\rho\rho)\sin\left(\frac{\pi}{h}z\right)$$

$$H_\varphi(\rho,\varphi,z) = -B_{01}\frac{k_\rho}{\mu}H_0^{(2)\prime}(k_\rho\rho)\cos\left(\frac{\pi}{h}z\right)$$

Higher order modes have non-uniform field distribution in the waveguide's cross section and different propagation properties compared to the TEM-mode

Single mode excitation of cage region

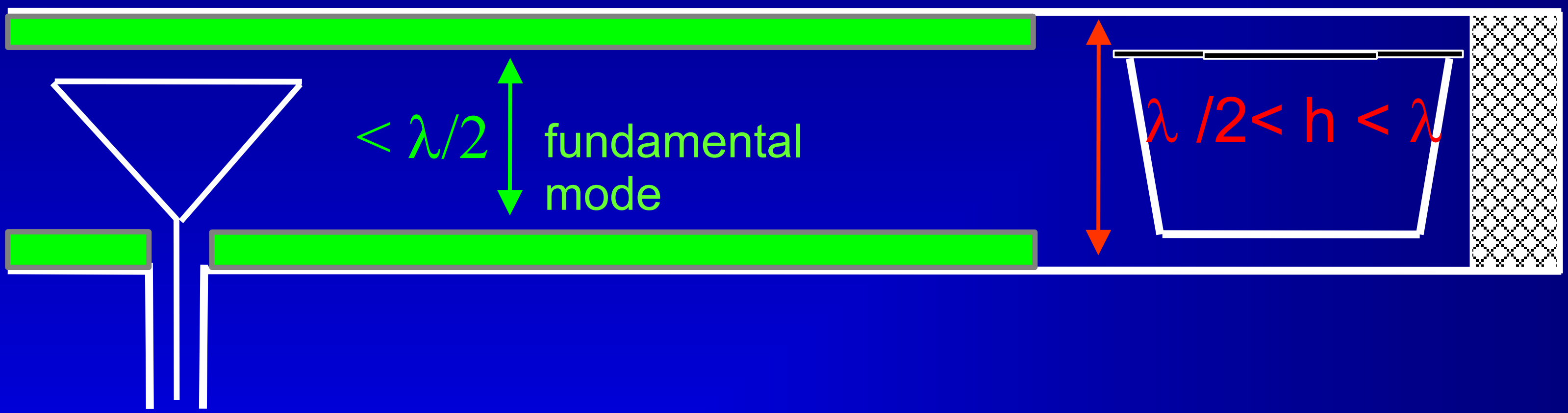


⇒ exposure field:
superposition of all propagating modes

⇒ can lead to non-reproducible exposure (interference effects) due to different propagation properties

⇒ **higher order modes must be suppressed**

Single mode excitation of cage region



counter measure: reduction of waveguide's height for smaller radii

$\Rightarrow$ **single mode excitation of cage region**

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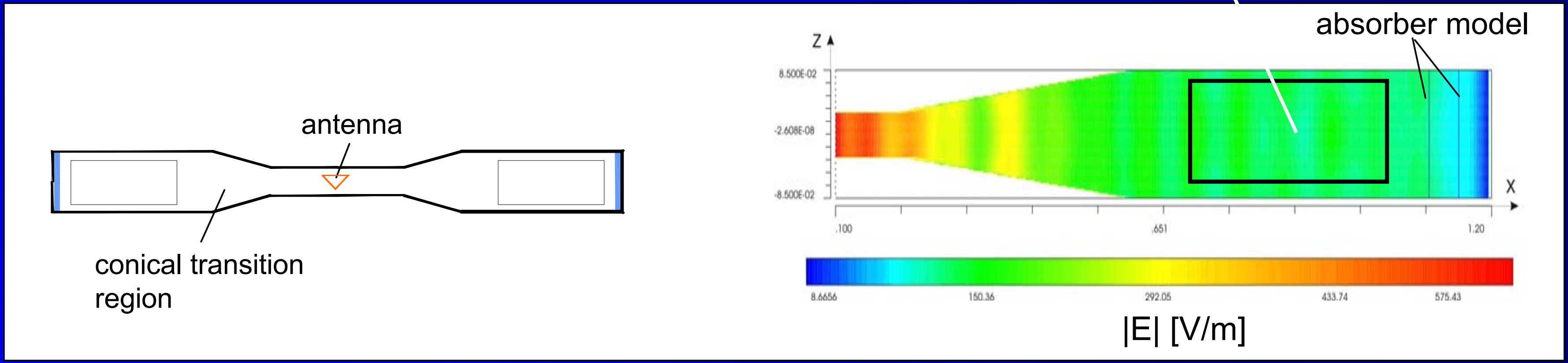
Example: single mode excitation of the cage region

- frequency 2 GHz
- cage height 16 cm ($h = \lambda$)
- height in the cage region: 17cm
  height in the centre: 6cm

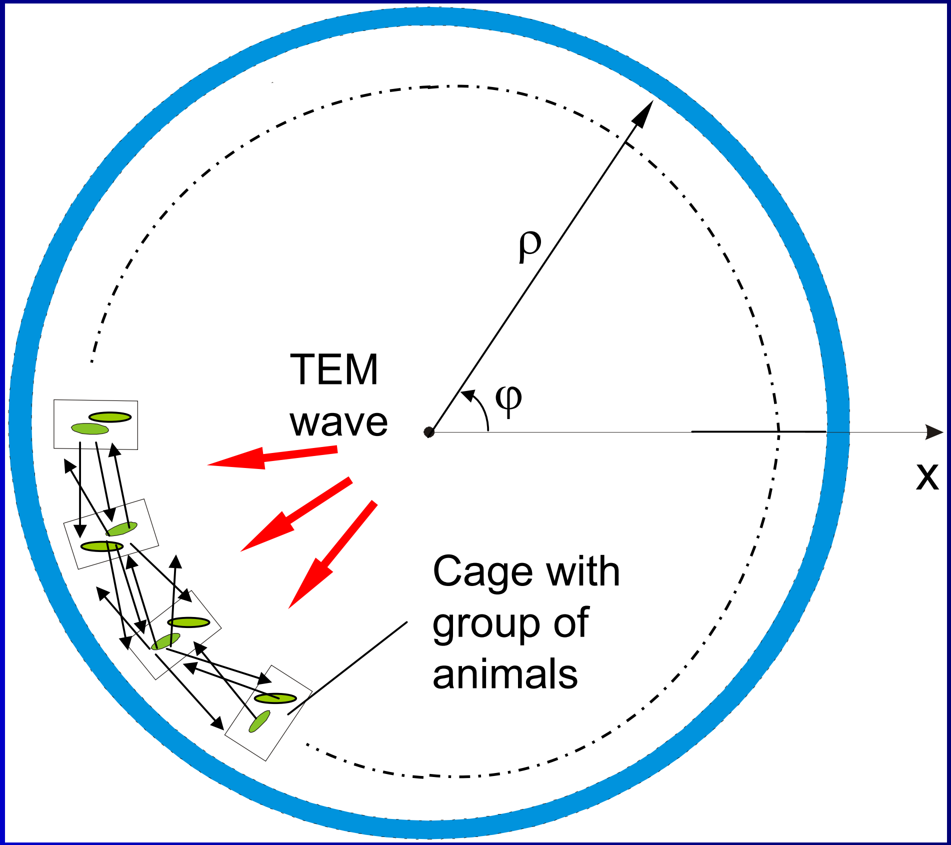
$\Rightarrow$ uniform field distribution in vertical direction, exposure field is given by the TEM-wave



- ➢ unwanted field components in the cage region are negligible as compared to the wanted z-component of the fundamental mode

Exposure of large animals or groups of animals

- For animal or group size in the dimension of wavelength the scattered field is not negligible and can affect the field distribution in neighbouring cages
- Due to the movement of the animals the excitation of higher order modes with circumferential variation can lead to non-reproducible exposure
- Therefore a ‘decoupling’ of adjacent cage regions is necessary in order to keep stable exposure field conditions



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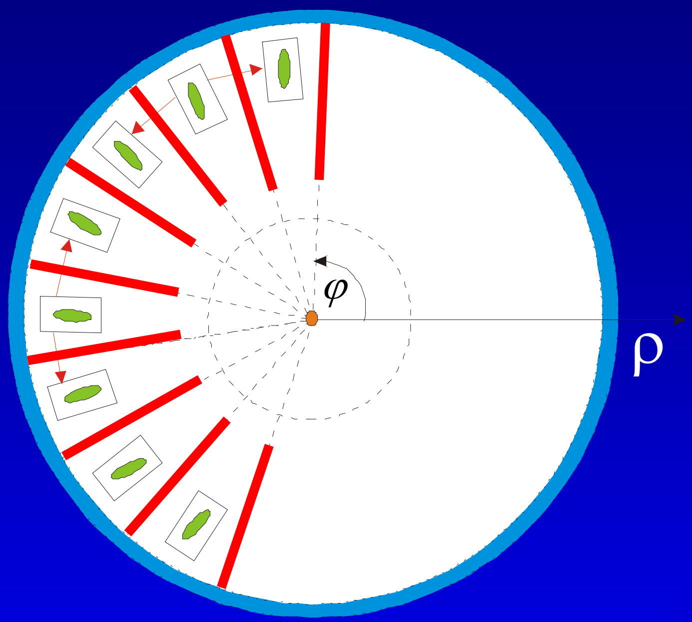
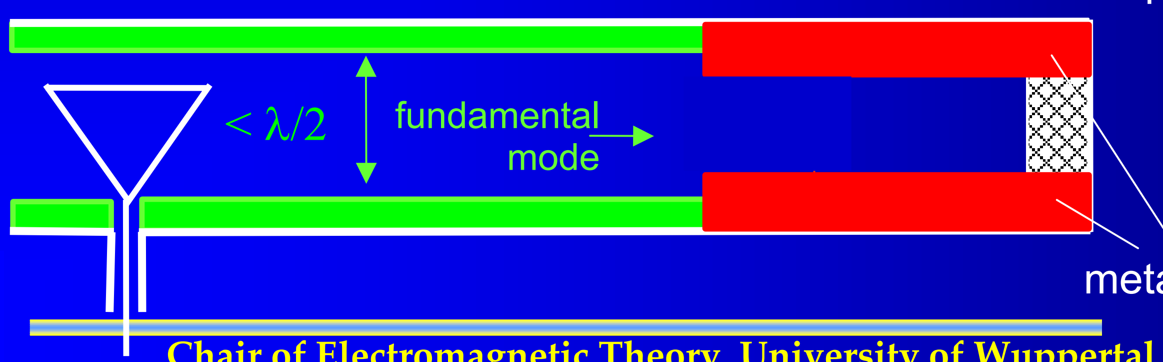
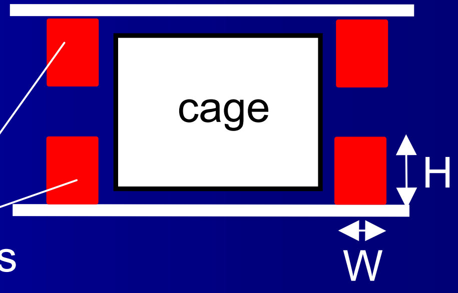
Approach A:
decoupling of adjacent sectors by metal bars



- metal bars attached to the upper and lower plate between the cages
  - bars do not alter the propagation properties of the TEM-mode
  - but shift-up the cut-off frequencies of unwanted higher order modes out of the frequency range of operation
  - height H and width W optimised by numerically solving the eigenvalue problem of the waveguide
  - applicable for waveguide heights $\lambda/2 \leq h \leq \lambda$ and exposure of large animals or larger numbers of mice per cage





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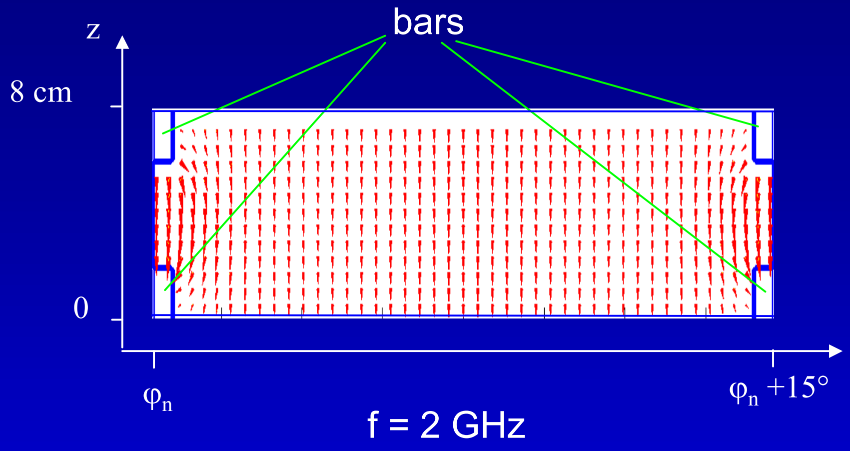
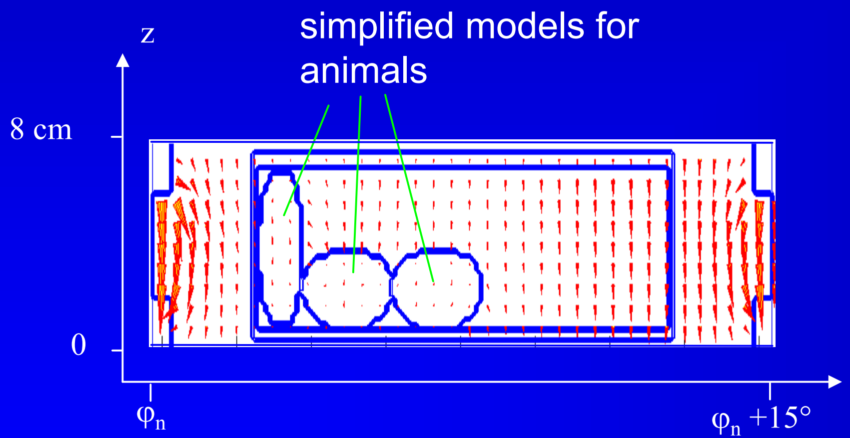
Example: field distribution in cross-section of sector decoupled by metal bars



empty sector with metal bars:

exposure field given by TEM-wave only

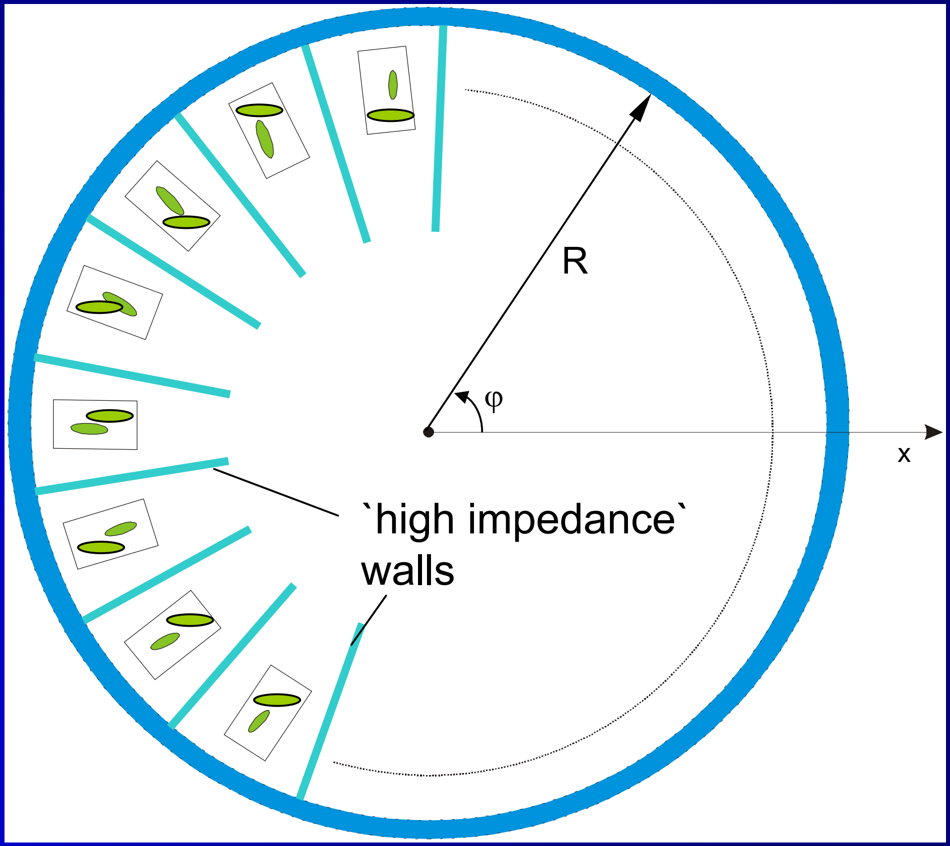


sector with metal bars, cage and simplified models for animals (ellipsoids):

- expected field distortions (scattered fields) caused by animals are restricted to the immediate vicinity of the animals
- neighbouring sectors are decoupled

Approach B: decoupling of adjacent sectors by 'high impedance' walls

- application for waveguide heights h $\geq \lambda$ and exposure of large animals or larger numbers of mice per cage
- `high impedance` walls must not alter the propagation properties of the TEM-mode
- therefore, the wall impedance must tend to infinity $Z_w \rightarrow j \propto$



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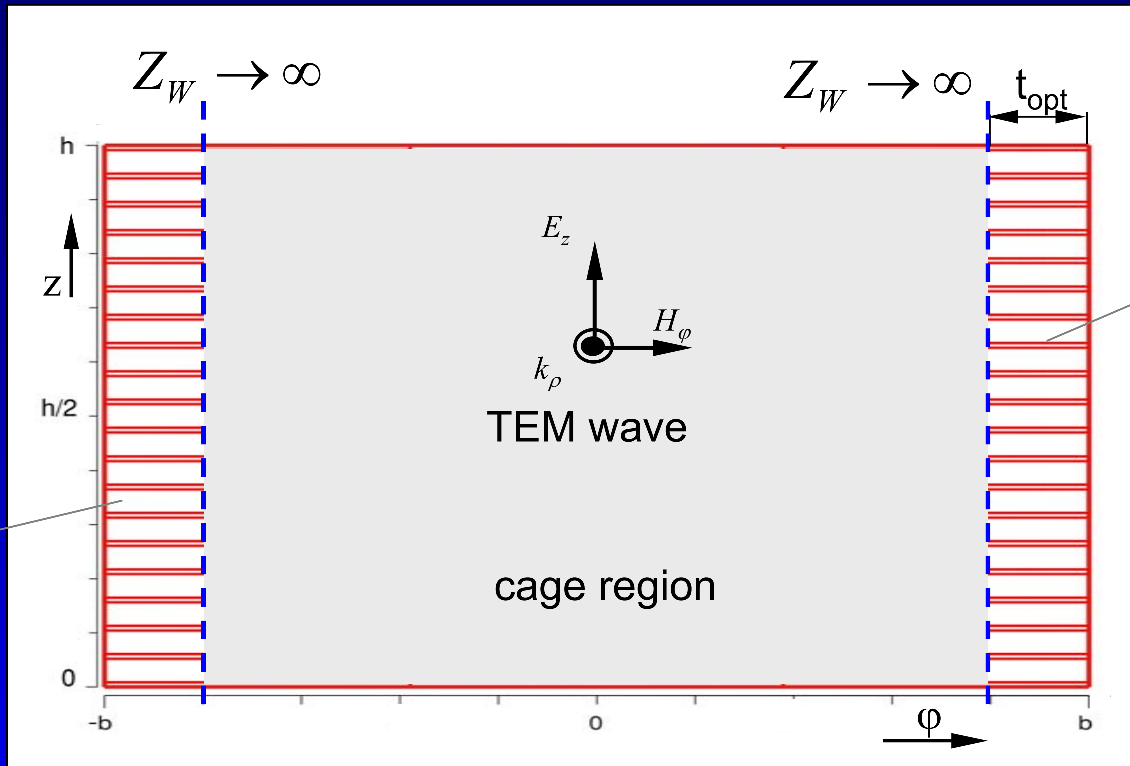
Cross section of sector with high impedance walls



corrugated metal walls with dielectric inserts ε_r

grooves are oriented in parallel to the propagation of the TEM-wave ρ-direction

$$Z_W = \left.\frac{E_z}{H_\rho}\right|_{y=b-t_{opt}} = j\,Z_0\sqrt{\frac{\mu_r}{\varepsilon_r}}\,\frac{\tan\left(\frac{2\pi\,t_{opt}}{\lambda}\sqrt{1-\left(\frac{m\lambda}{2w}\right)^2}\right)}{\sqrt{1-\left(\frac{m\lambda}{2w}\right)^2}} \to j\infty$$

with

$$t_{opt} = \frac{\lambda}{4}\left[\sqrt{\varepsilon_r\,\mu_r - \left(\frac{m\lambda}{2w}\right)^2}\right]^{-1}$$

anisotropic wall impedance tends to infinity for the optimum groove depth

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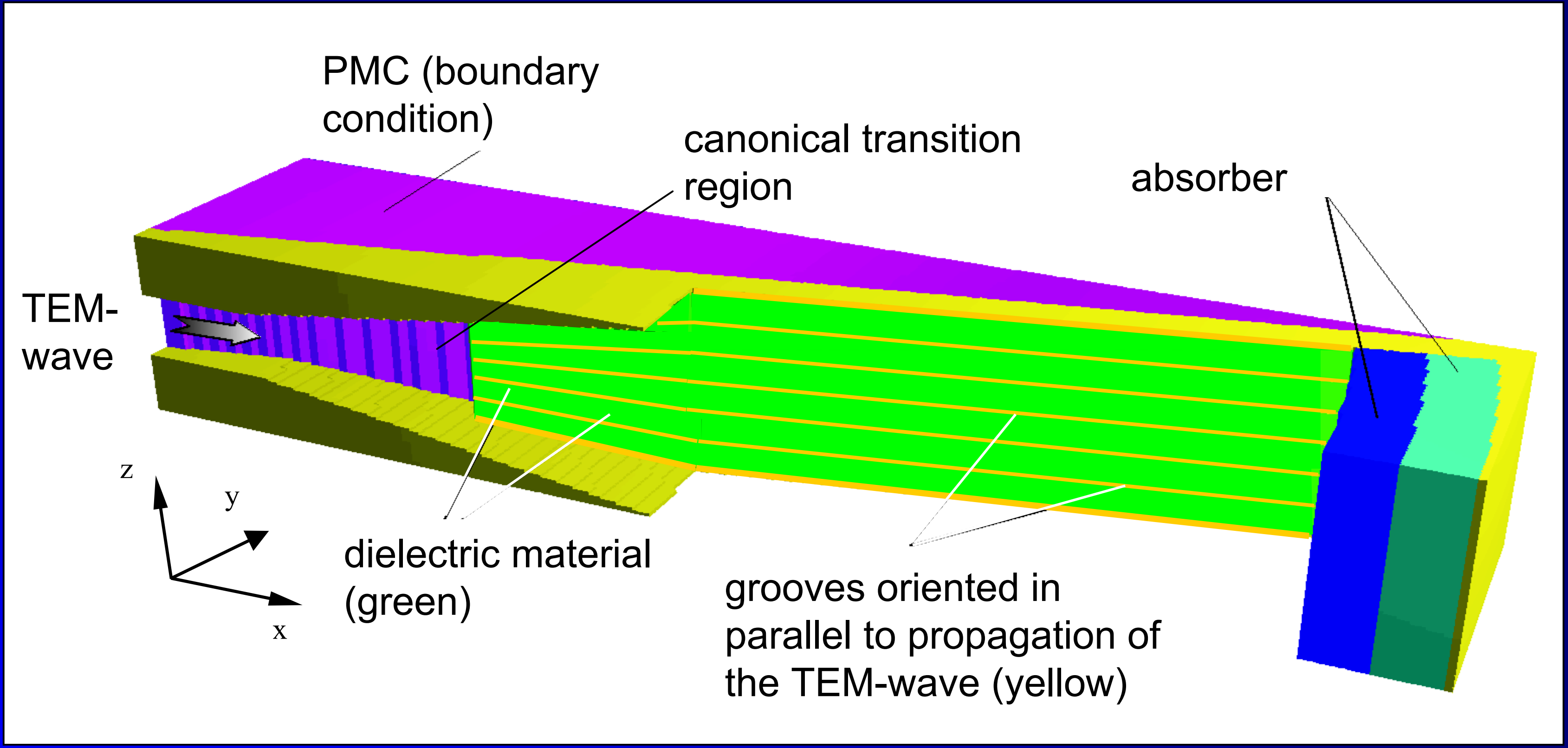
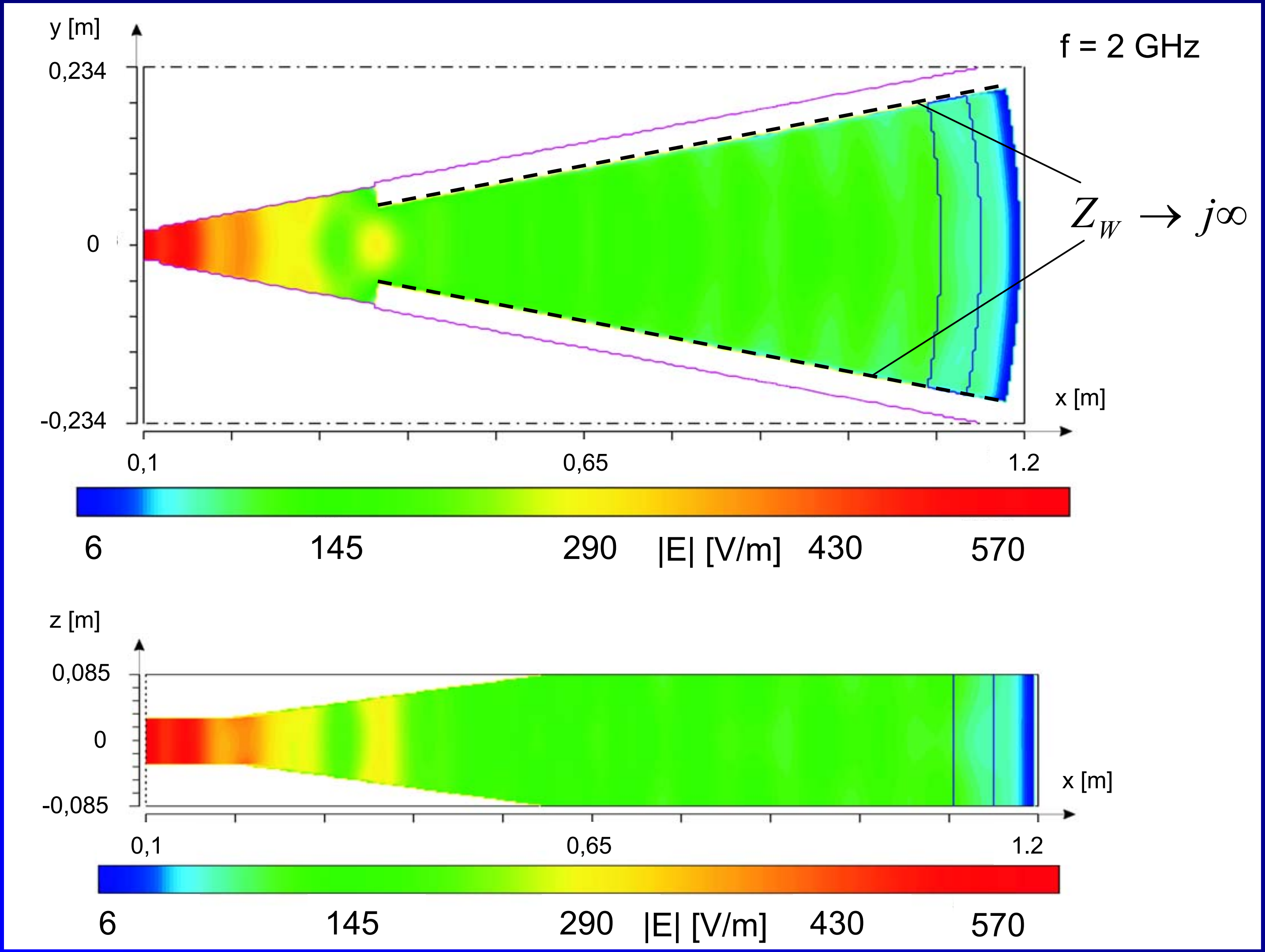
Model for sector with high impedance walls



Computed field distribution with high impedance walls



⇒ uniform field distribution in vertical and azimuthal direction

⇒ exposure field only given by the TEM-wave

Technical implementation

- 3 studies in cooperation with the International University Bremen (Prof. A. Lerchl):

1. **Influence of 900 MHz electromagnetic fields on spontaneous leukaemia in AKR/J mice**
   160 mice exposed to generic GSM test signal, 400 mW/kg (whole body), 24 hrs / day
   160 mice sham-exposed. Endpoints: leukaemia rate and production of solid tumours. End: 9/2004

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   same as 1., but generic UMTS test signal. End: 4/2005

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   Four generations of mice (c. 1200 animals altogether) exposed to generic UMTS test signal, different specific absorption rates (SAR). Endpoints: fertility, development, teratogenic effects. End: 7/2007

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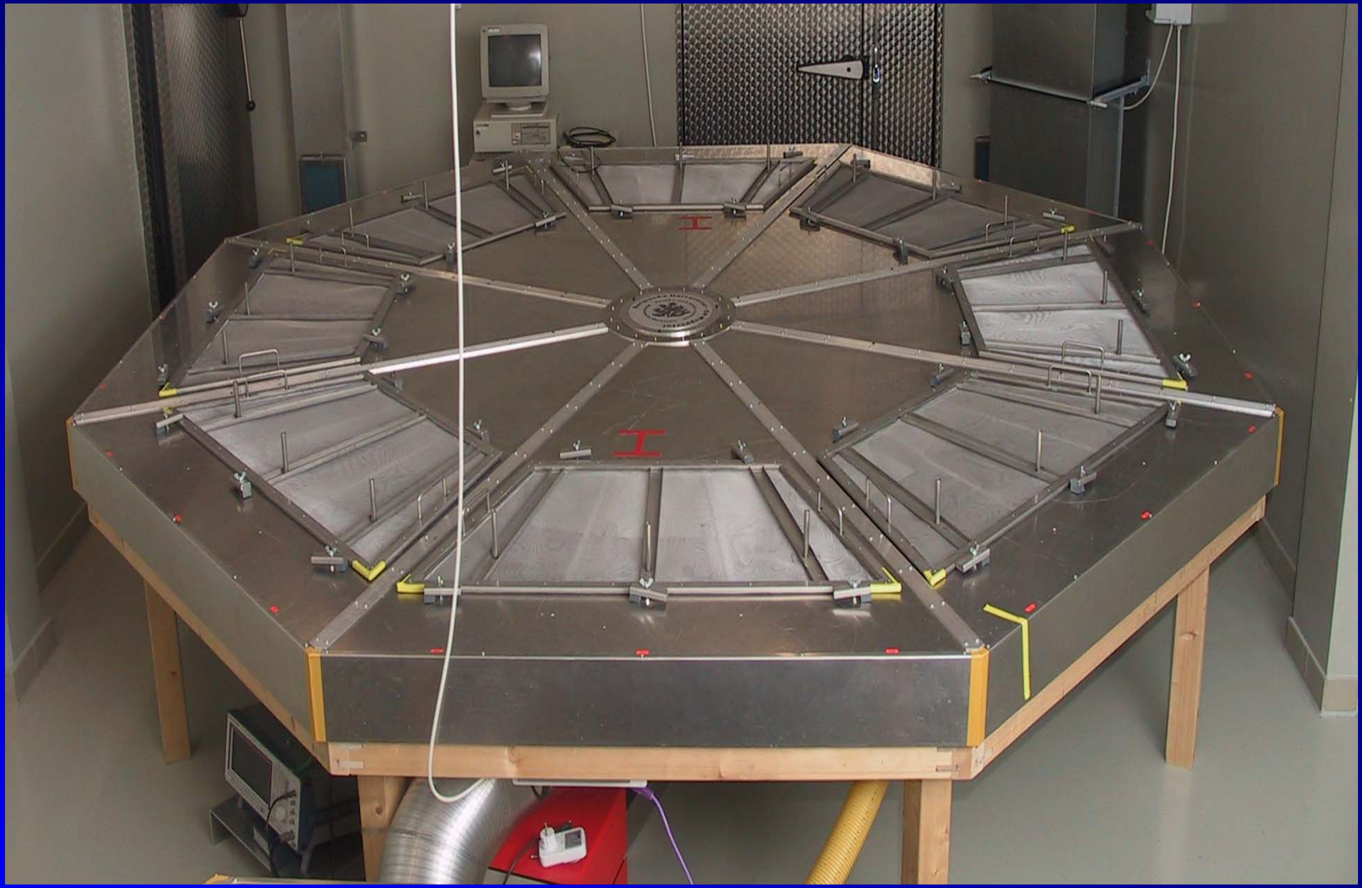
Exposure of AKR/J mice to GSM 900 test signal

- Life-long exposure
- 7 mice per cage (cage height 15.5 cm)
- 24 exposed / 24 sham-exposed cages
- Exposure device:
  2 radial waveguides with diameter of 4 m and height of 17 cm ($\lambda/2 \leq h \leq \lambda$),
  24 sectors decoupled by metal bars

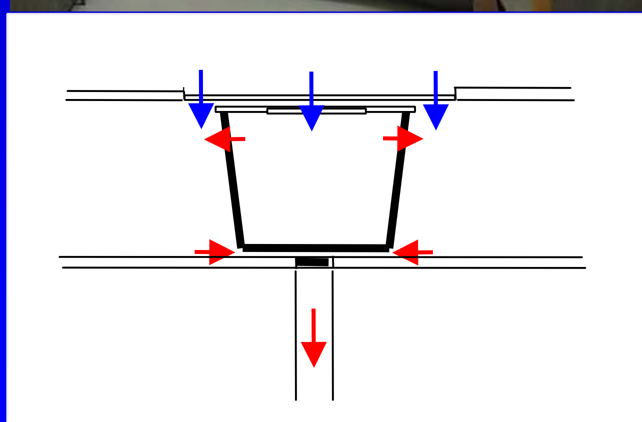
Results already published

- Sommer, A. M., Streckert, J., Bitz, A. K., Hansen, V. W., Lerchl, A.: No effects of GSM-modulated 900 MHz electromagnetic fields on survival rate and spontaneous development of lymphoma in female AKR/J mice. BMC Cancer, 4:77, 2004.
- Sommer, A. M., Bitz, A. K., Streckert, J., Hansen, V. W., Lerchl, A.: No effect from 900 MHz electromagnetic fields on the spontaneous development of lymphoma in female AKR/J mice. 26th BEMS Annual Meeting, Washington, DC, June 2004, 258-259.

GSM 900: exposure system (1/2)



GSM 900: exposure system (2/2)



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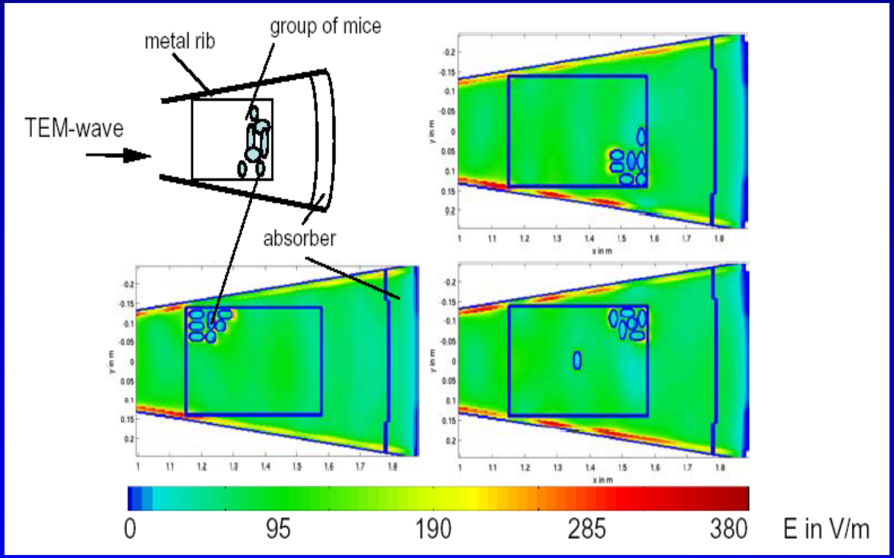
Electric field and SAR distribution

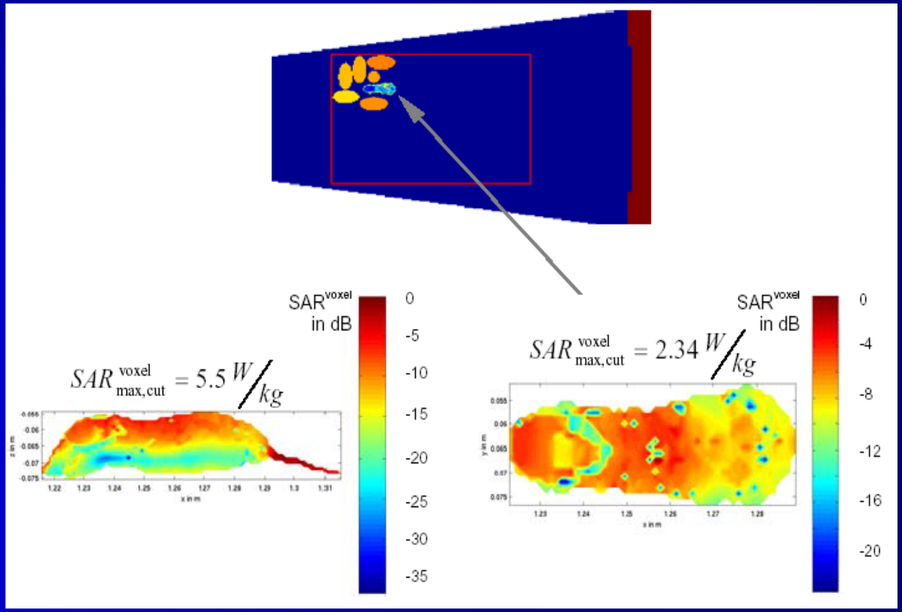
Example of electric field distribution for different configurations of 7 mice per cage



Averaged whole body SAR_{wb} of 0.4 W/kg at P_{in} = 35 W

Standard deviation of SAR_{wb}: $\sigma \approx \pm 40\%$

SAR distribution in detailed mouse model with spatial resolution of (1.2 mm)³, model scaled from a 7-day-old rat (IT'IS, Switzerland)



The evaluation of organ-specificic SAR is not necessary due to the biological endpoints, but the SAR distribution must be checked with respect to possible 'hot spots'.

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Exposure of AKR/J mice to UMTS test signal

- Same exposure condition as for the GSM 900 study, but height of cages reduced from 15.5 cm to 7 cm
- Exposure device: same radial waveguides as for the GSM 900 study, but reduced height of 8 cm ($\lambda/2 \leq h \leq \lambda$)

Results already published

- A.M. Sommer, A. Lerchl, A.K. Bitz, J. Streckert, V.W. Hansen: UMTS-modulated electromagnetic fields do not affect hematological or histological parameters in lymphoma-prone mice. 28th BEMS Annual Meeting, Cancun, Mexico, June 2006, 317-318.
- Lerchl, A., Sommer, A.M., Bitz, A., Streckert, J., Hansen, V.: UMTS-modulated electro-magnetic fields do not influence the development of lymphoma in female AKR/J mice. 27th BEMS Annual Meeting, Dublin, Ireland, June 2005, 177.
- Bitz, A. K., Streckert, J., Sommer, A. M., Lerchl, A., Hansen, V. W.: 2 GHz-exposure of non-restrained AKR/J mice in a slightly over-moded Radial Waveguide. 26th BEMS Annual Meeting, Washington, DC, June 2004, 139.

UMTS: 2 GHz exposure system

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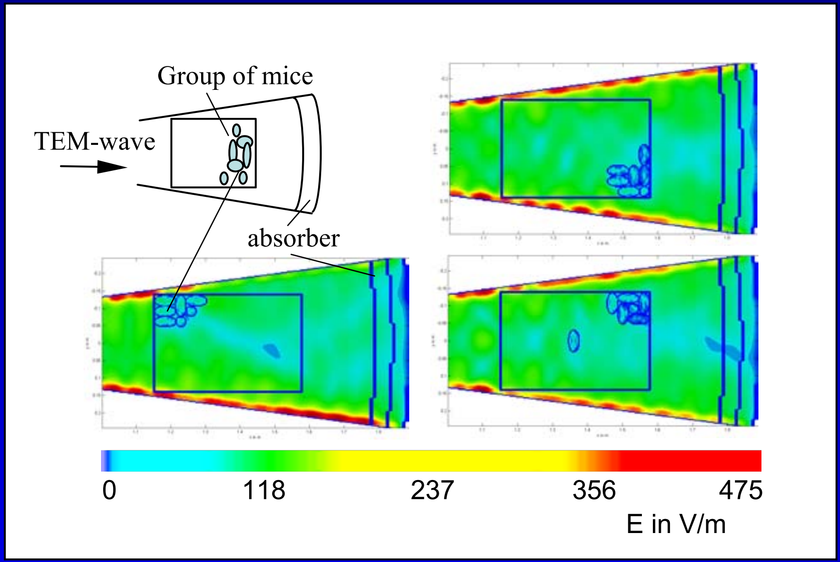
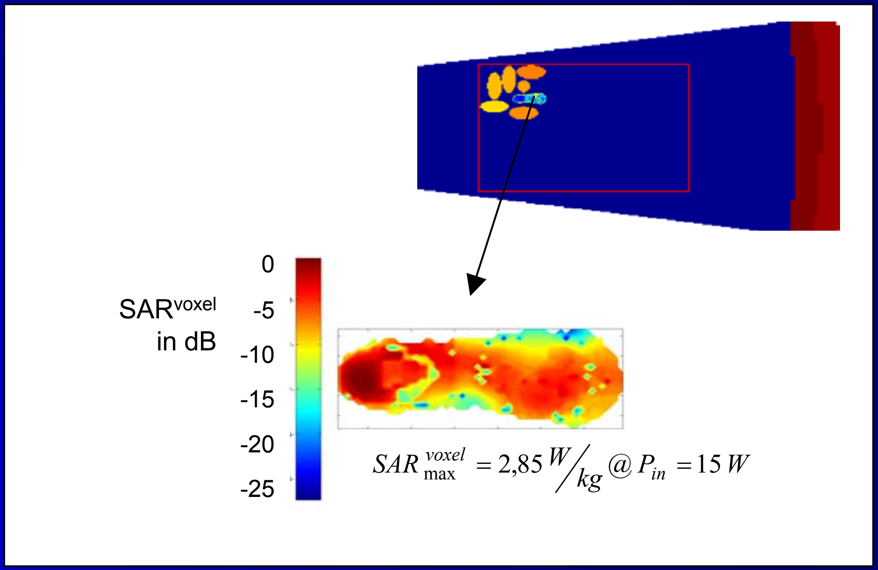
Example of electric field distribution for different configurations of 7 mice per cage



Averaged whole body SAR_{wb} of 0.4 W/kg at P_{in} = 15 W

Standard deviation of SAR_{wb}: $\sigma = \pm 50\%$

SAR distribution in detailed mouse model with spatial resolution of $(1.2\ mm)^3$, model scaled from a 7-day-old rat (IT'IS, Switzerland)



SAR_{wb} = 253 mW/kg at P_{in} = 15 W

The evaluation of organ-specific SAR is not necessary due to the biological endpoints, but the SAR distribution must be checked with respect to possible 'hot spots'.

Technical implementation (3)

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Exposure of strain C57BL mice to UMTS test signal (running project)

- 2688 animals are exposed during the study
- 128 cages in total:
  32 sham-exposed groups / 3x 32 groups exposed with 0.08, 0.4 and 1.3 W/kg

Flowchart of animals per cage:

2 pregnant mice & 1 male mouse
14 days

↓

1 pregnant mouse & 1 male mouse
7 days

↓

1 female mouse (again pregnant), 1 male mouse & 6 pups
21 days

↓

4 young mice per cage

48 days

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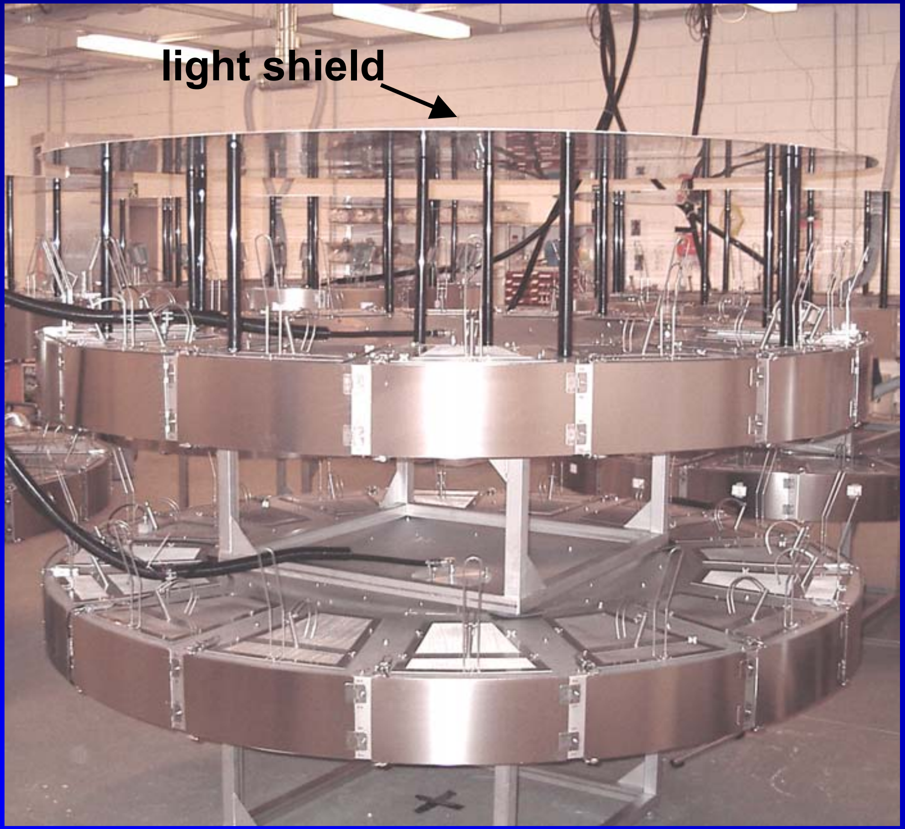
Exposure setup (1/2)

Exposure setup (2/2)

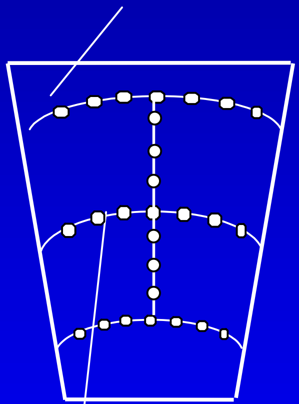


Field measurements in the implemented exposure device

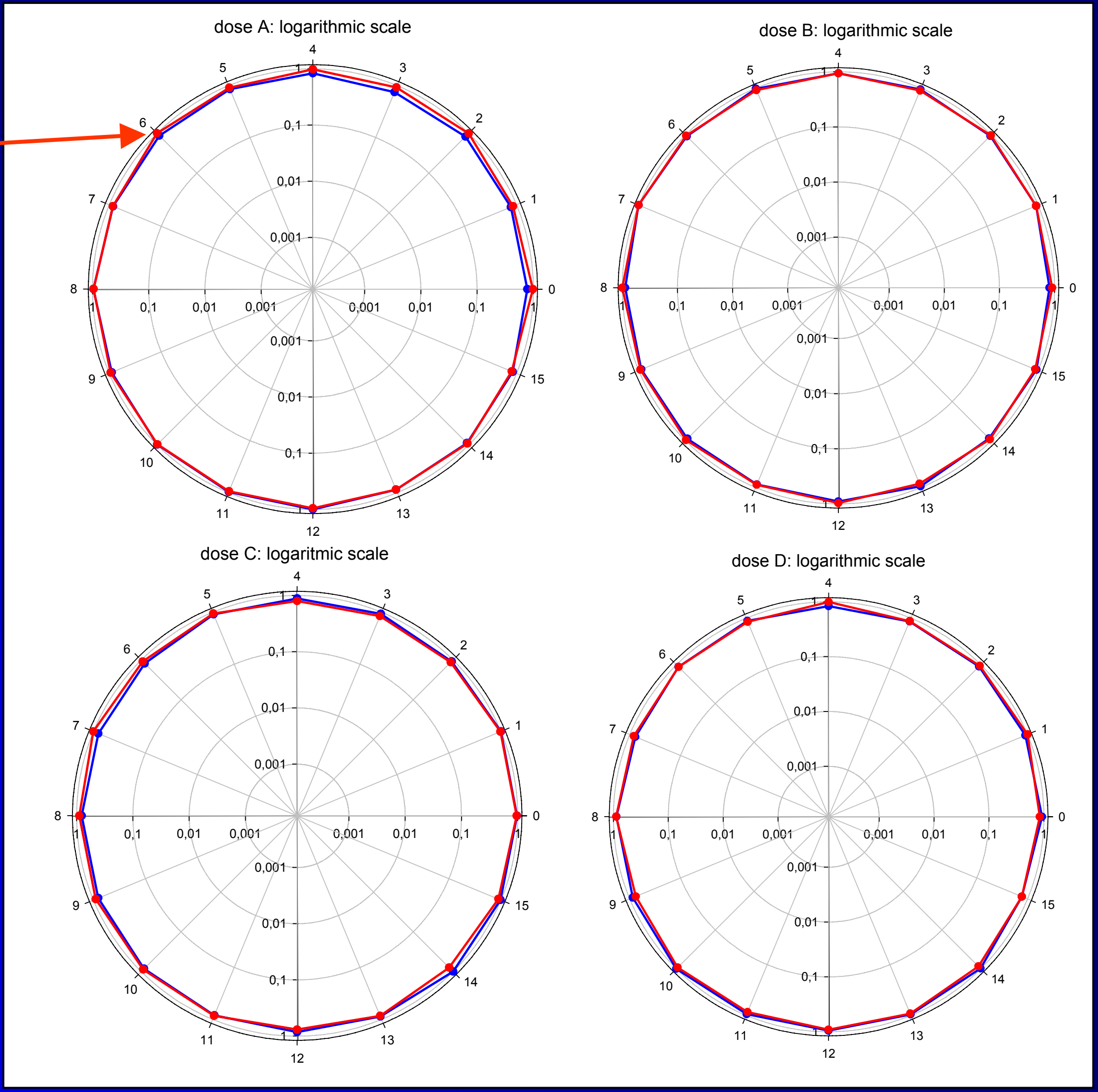
normalized averaged field values for one cage

σ ≈ 25%

cage



measuring points



upper device

lower device

Animal models (1/2)

- 2 models obtained from IT'IS, Zurich, Switzerland
  - 1st model: pregnant rat: 275g, spatial resolution 1mm
  - 2nd model: 7-day-old rat: 17g, spatial resolution 0,5mm

<u>Adult mice (weight between 24g and 34g):</u>

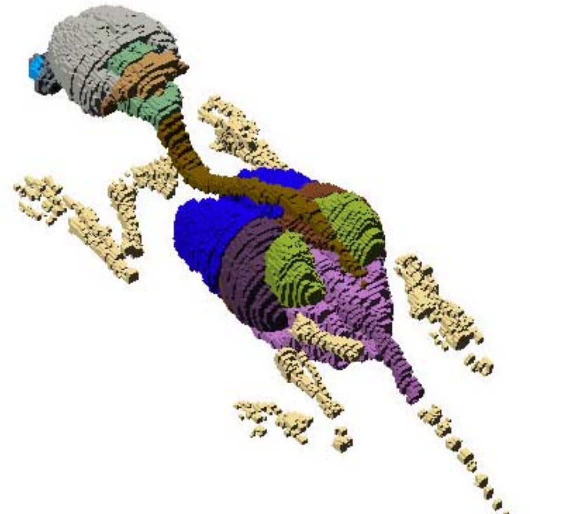
- Scaled from 1st model: spatial resolution 1.2 mm
- Scaled from 2nd model: spatial resolution 0,7 to 1.2mm

<u>young mice 17g:</u>

- Scaled from 2nd model: spatial resolution 0.5 mm

<u>Mouse pup (age: 9 days):</u>

- Ellipsoids were used: weight: 7 g;
- spatial resolution: 0.6 mm



ITIS Zürich

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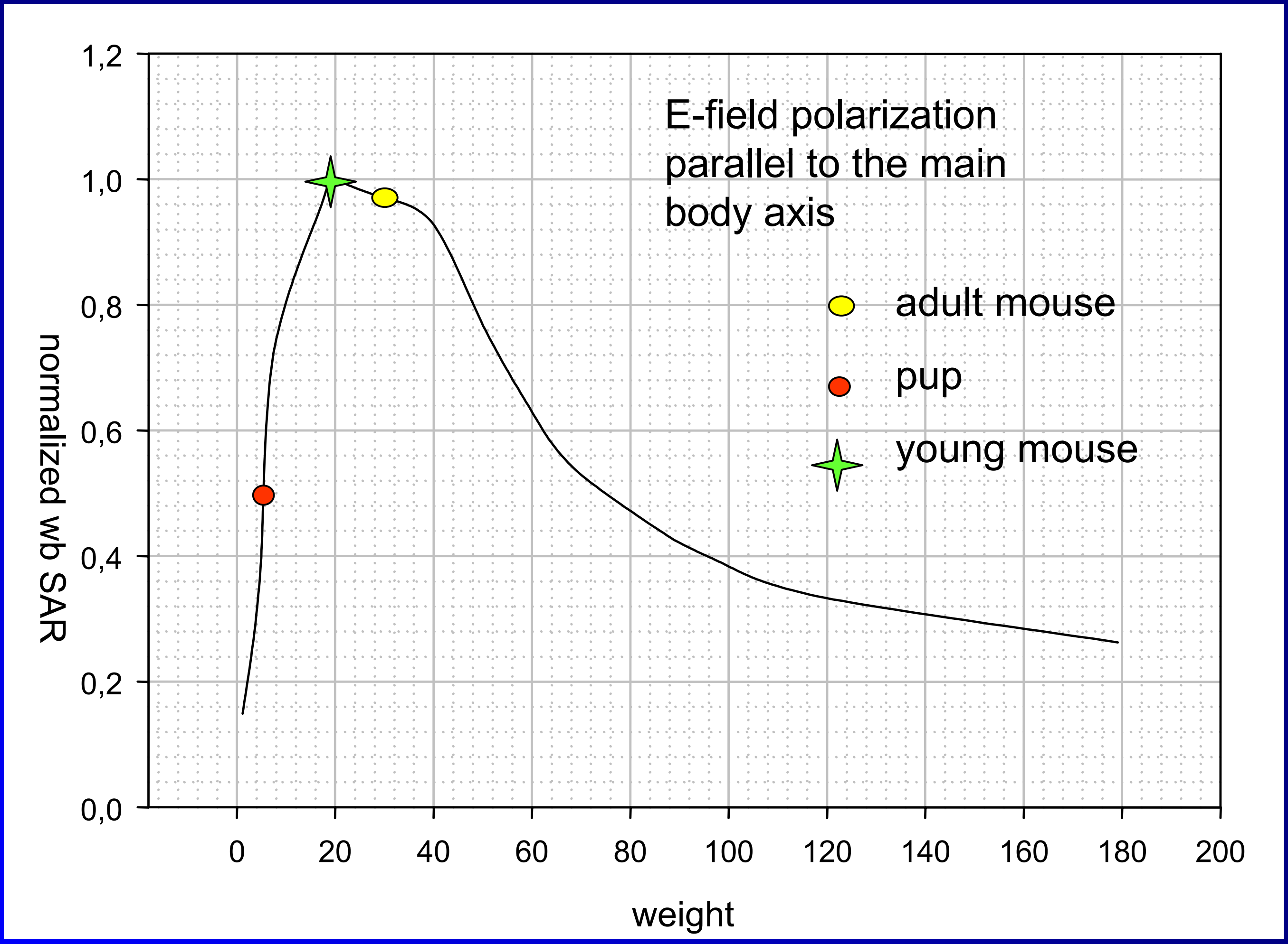
Animal models (2/2)



Electrical material parameters

material	permittivity	conductivity	tissue density
tail/muscle(parallel_fiber)	55,096	1,5417	1040
tail/skin(dry)	38,617	1,251	1158,85
body/air	1	0	1,3
body/avg. Brain	43,266	1,238	1030
body/blood	59,081	2,161	1158,85
body/bone_cortical	11,675	0,304	1600
body/marrow_not_infiltrated	5,352	0,075	1158,85
body/cartilage	39,836	1,399	1158,85
body/cerebro_spinal_fluid	66,96	3,048	1158,85
body/eye_tissiue(sclera)	53,32	1,703	1000
body/fat	5,33	0,085	1100
body/glands	57,899	1,61	1158,85
body/heart	55,899	1,887	1040
body/kidney	53,945	2,066	1158,85
body/large_intestine	54,798	1,686	1040
body/liver	43,885	1,384	1040
body/lung(extrapolated)	34,964	1,026	1040
body/muscle(transverse_fibre)	53,333	1,434	1040
body/nails	11,67	0,304	1158,85
body/nerve	30,666	0,901	1158,85
body/skin(wet)	43,575	1,317	1100
body/small_intestine	55,486	2,81	1040
body/spleen	53,455	1,889	1158,85
body/stomach	62,948	1,818	1158,85
body/teeth	11,67	0,304	1158,85
body/tongue	53,32	1,472	1158,85
body/trachea	40,304	1,193	1158,85
body/uterus	58,636	1,878	1158,85
body/bone_cortical	11,67	0,304	1300
avg. Rat tissue	43,195	1,411	1137,22

material parameters according to Brooks database were used

http://www.fcc.gov/fcc-bin/dielec.sh

uncertanty of the material parameters in literature

- changing the material parameters ± 10%

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Configurations (1)

The decision which constellations of mice in a cage from an infinite number of possibilities are considered for a representative numerical dosimetry is not trivial, since

- the movement of the animals is a dynamic, non-deterministic process
- some constellations are more typical than others
- even small variations of a configuration can change the SAR distribution
- the number of computer runs must be limited to a certain quantum (e.g. < 100)

Configurations (2)

Ideally, many calculations and a weighting of different configurations according to their occurrence might be reasonable.

However, for a reliable statistic the required data are not available.

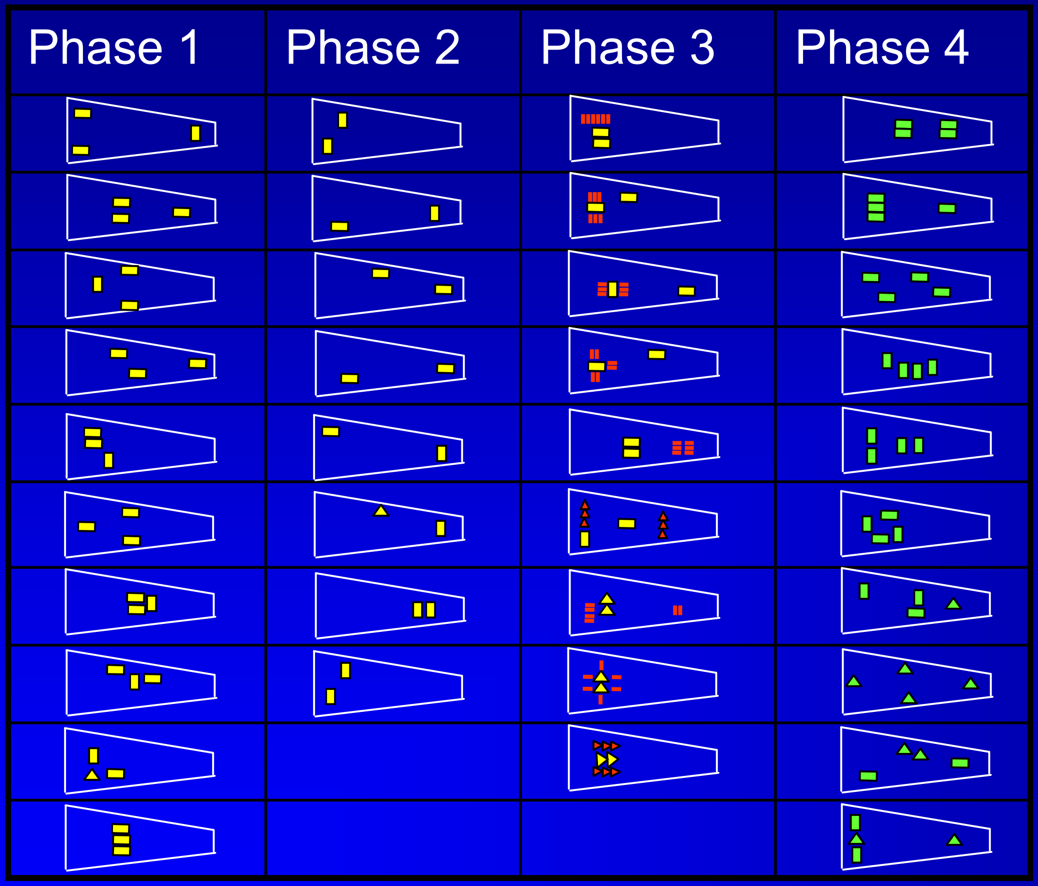
For a practicable assessment of the whole body SAR without weighting

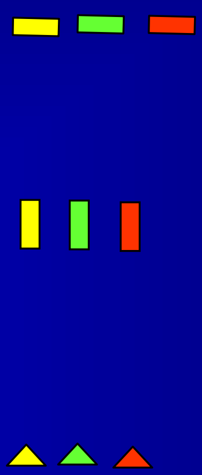
- typical configurations were identified in agreement with the IU Bremen (e.g. (agglomerating mice, pubs close to the dam)
- some configurations known as “worst cases“ were included in order to avoid an underestimation of SAR (e.g. mice erected on the hind legs, isolated animals)

For future investigations a registration of time-varying configurations is planned, but an exhaustive data collection in an animal laboratory must be assigned to a separate project.

Configurations (3)

The following configurations of mice in a cage were analysed:





adult mouse / young mouse / pup lengthwise in the cage

adult mouse / young mouse / pup mouse across in the cage

adult mouse / young mouse / pup in an upright position

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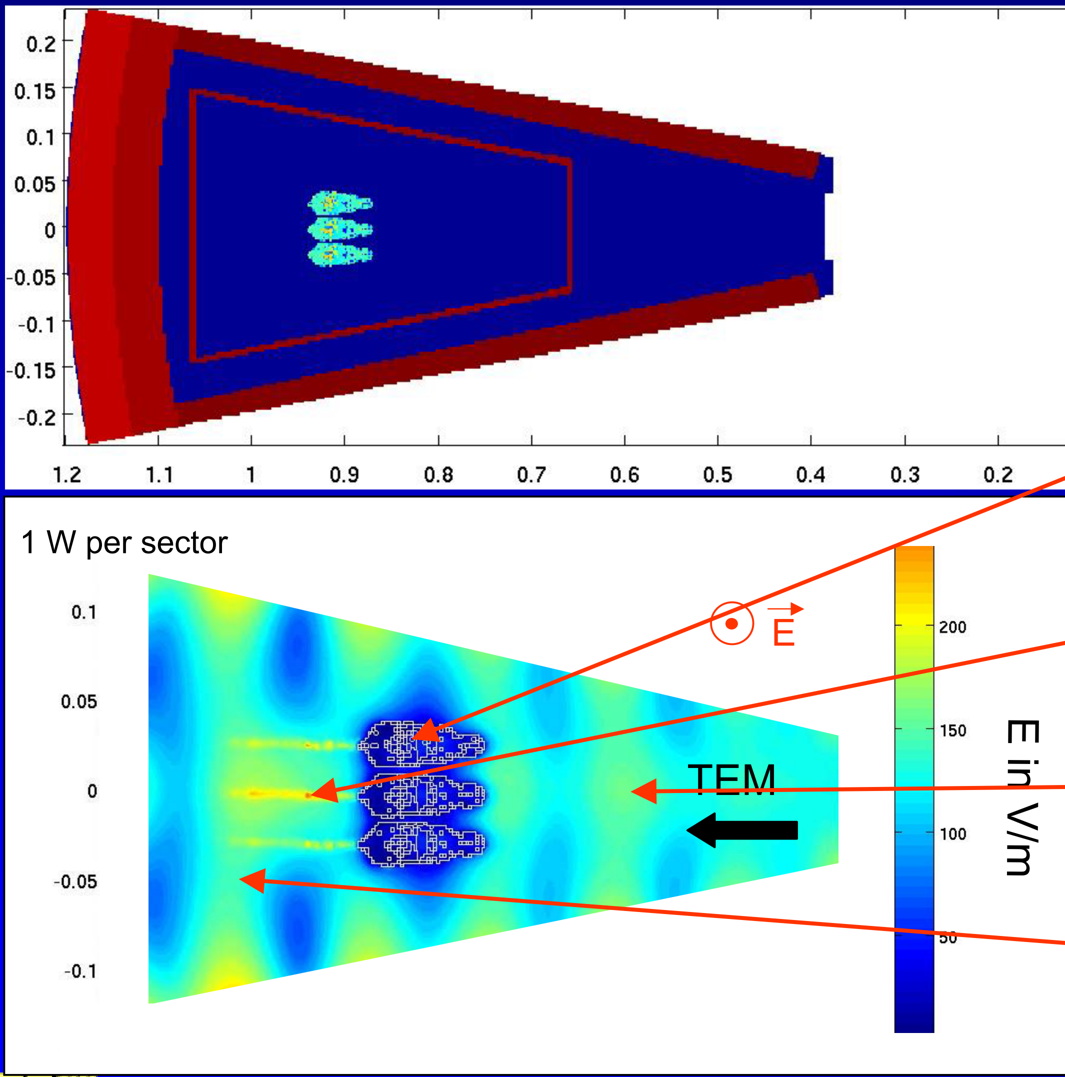
1st stage: exposure field for one configuration



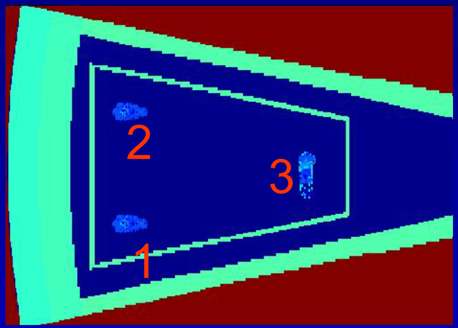
low field inside the biological objects

higher field strength above the tail of the mice

standing waves

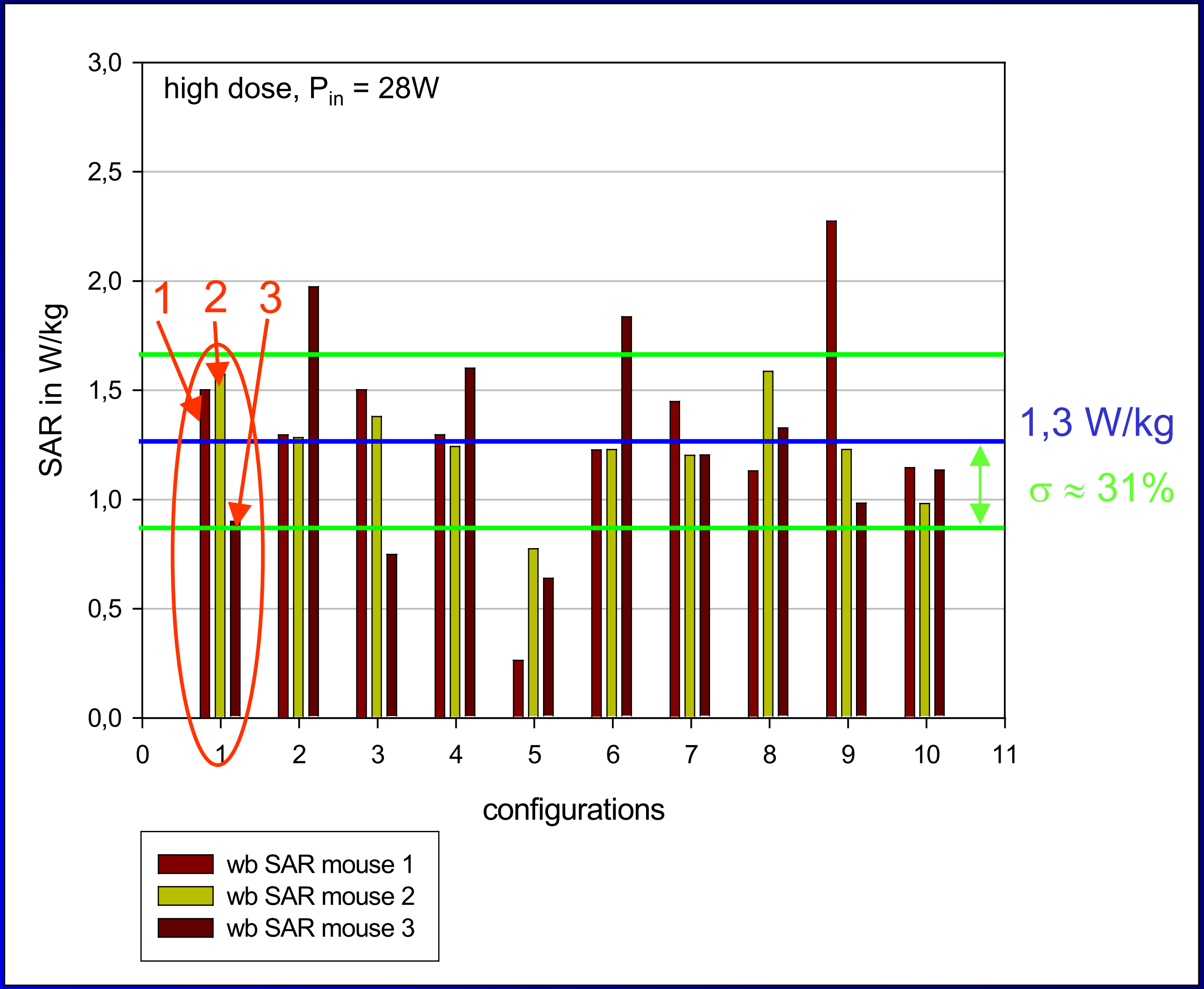
- due to reflections at the mice
- due to reflections at the non-perfect absorber

1st stage: whole body SAR for 3 mice per cage



configuration 1

For more than 1 animal, a simple estimation of the wb-SAR as a function of the location of the models is not always possible.



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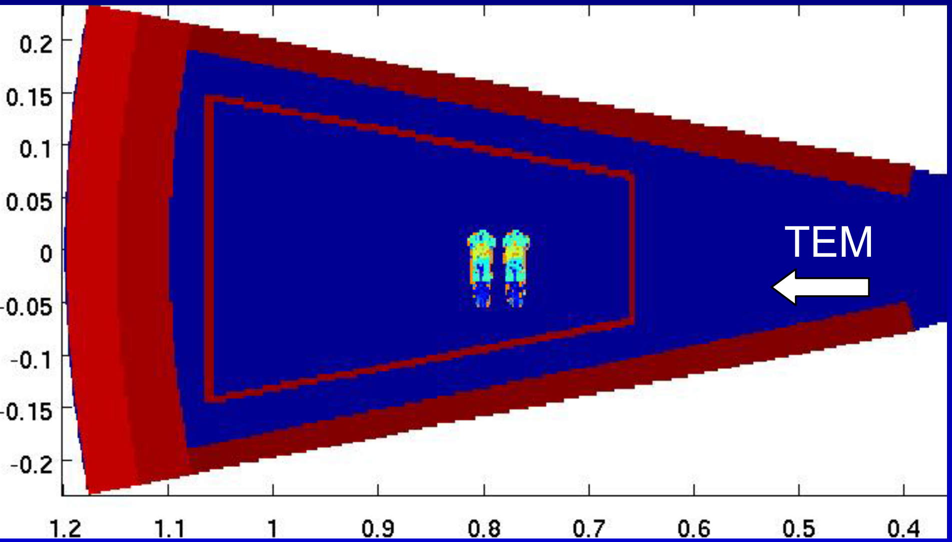
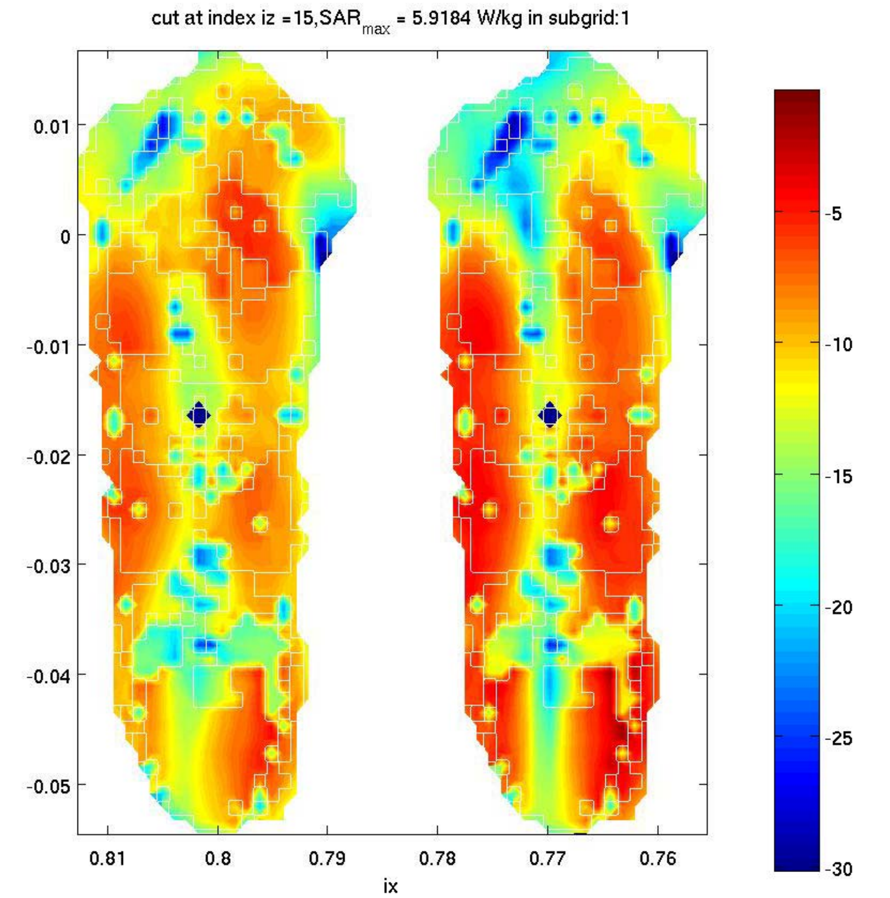
2nd stage: SAR distribution of 2 adult mice

example of 1 configuration



SAR distribution for 1 configuration



logarithmic scale

2nd mouse is shadowed by the first one

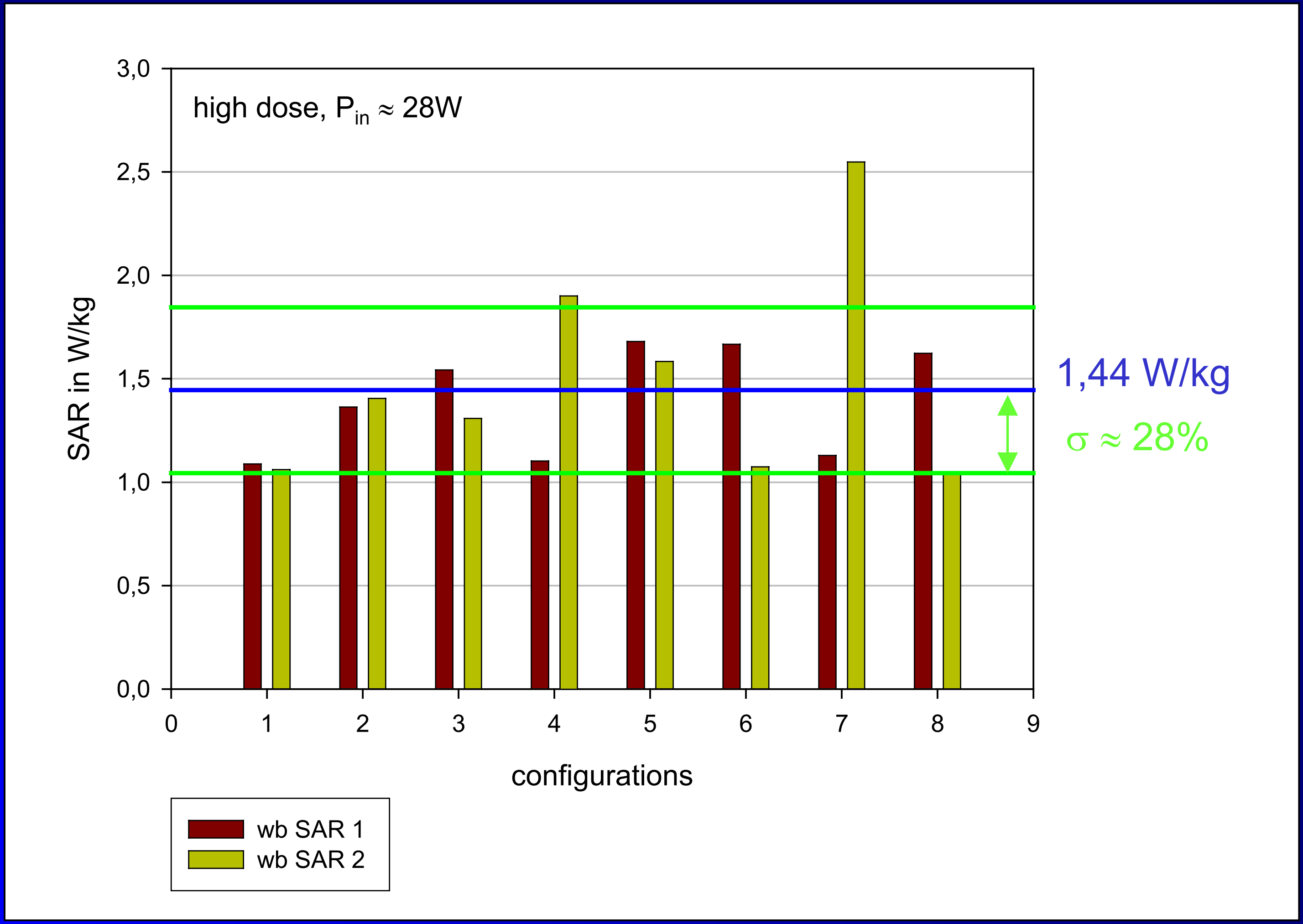
- larger SAR values occur in the 1st mouse

Wb SAR: 1st mouse: 1,18 W/kg

2nd mouse: 0,75 W/kg

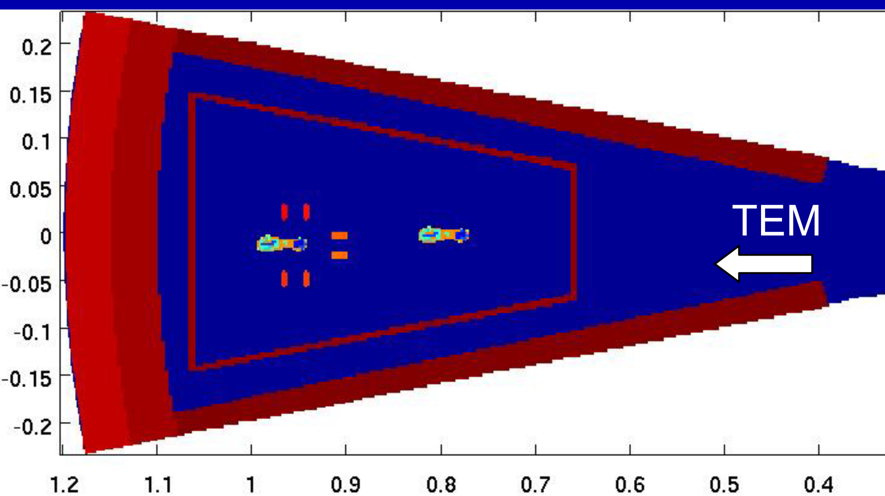
P_{sector} = 1W

2^{nd} stage: whole body SAR for 2 mice per cage

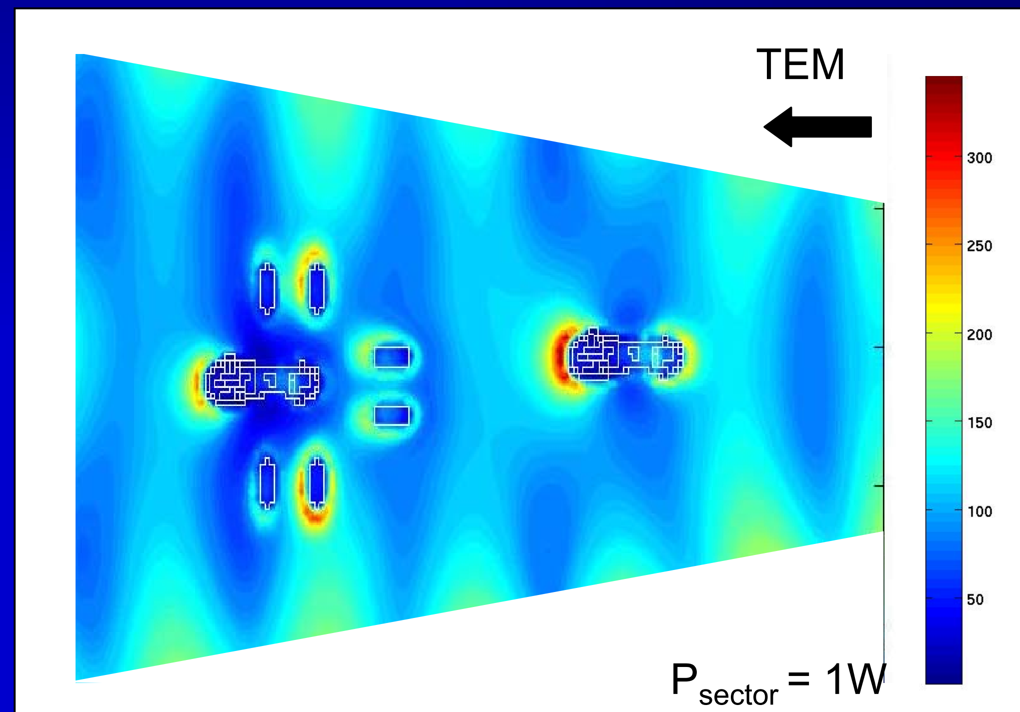


3rd stage: field distribution and SAR distribution (1/2)

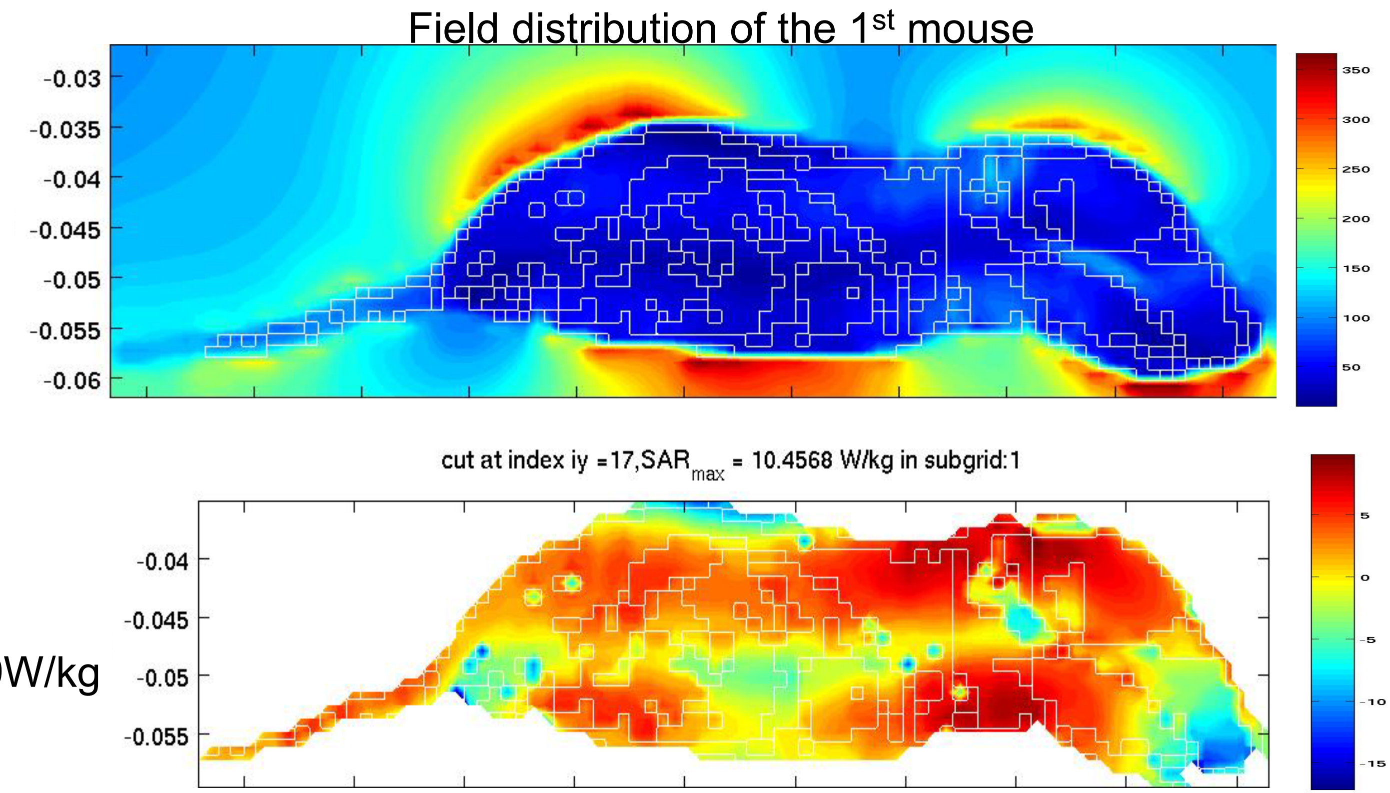
an example of 1 configuration with 8 mice



exposure region



3rd stage: field distribution and SAR distribution (2/2)



Wb SAR: 1,39W/kg

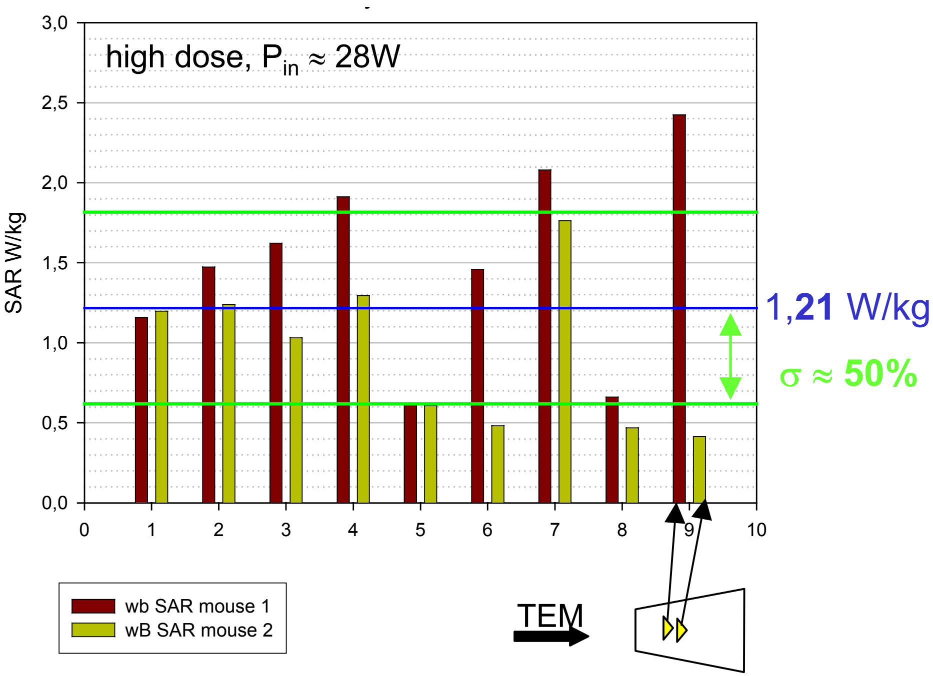
P_{sector}=1W

logarithmic scale

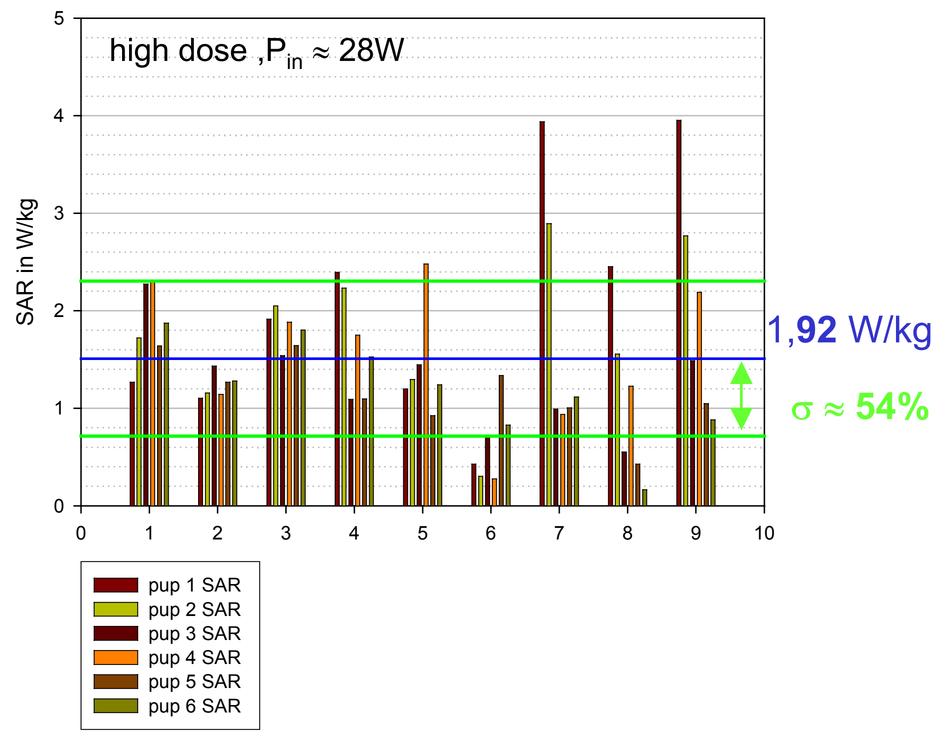
High field values at the outer surface of the animal, do not necessarily lead to high SAR values at the animals surface

3rd stage : whole body SAR for 8 mice per cage

Whole body SAR for the adult mice



Whole body SAR for 6 pups (7g)



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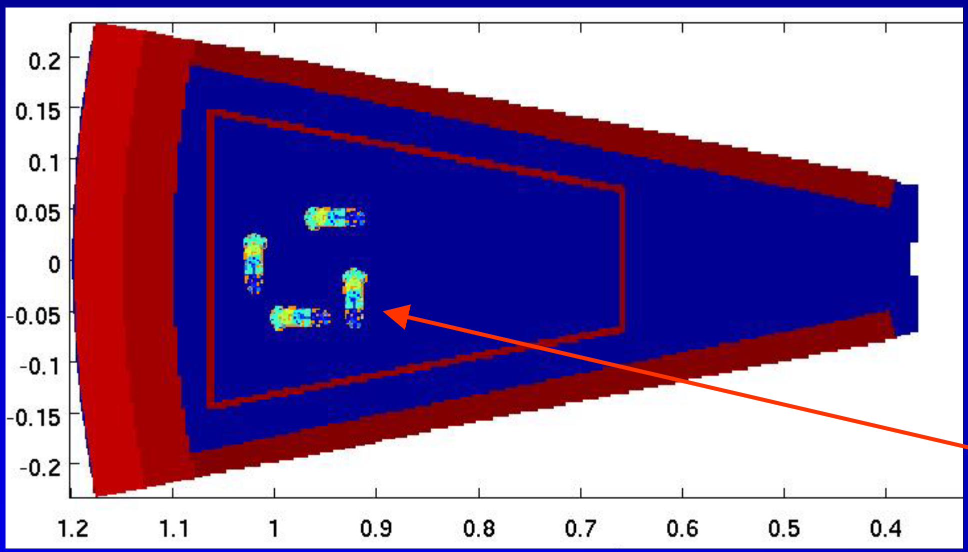
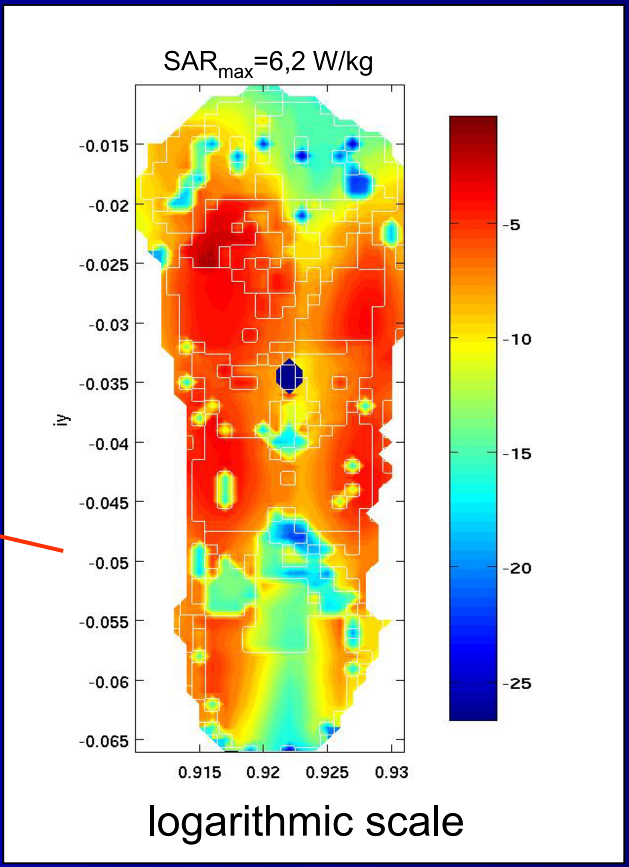
4^{th} stage: 4 young mice per cage; SAR distribution for one mouse

example of 1 configuration

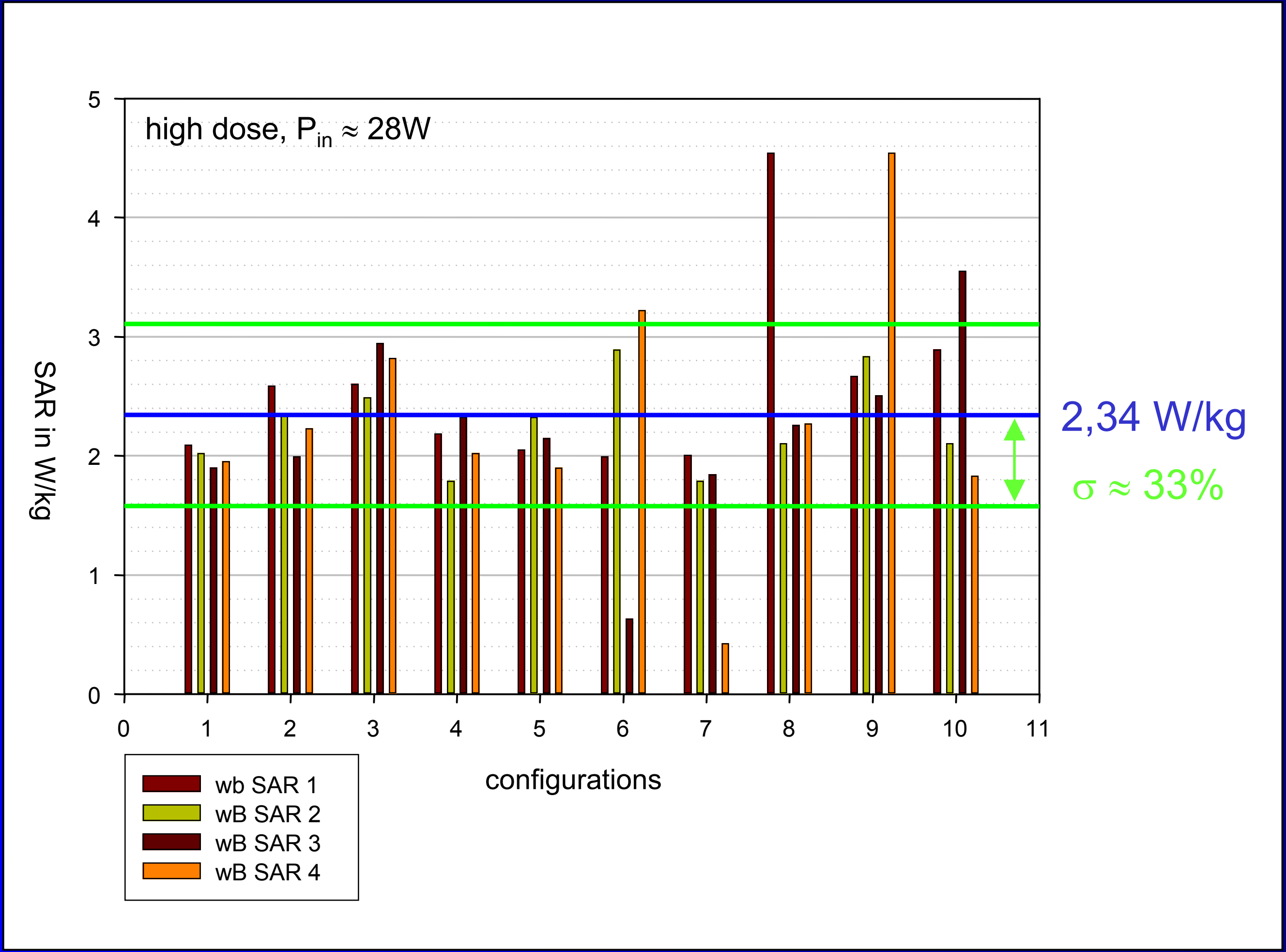




wb.-SAR of the 1^{st} mouse: 1,45 W/kg
Averaged wb-SAR for the configuration: 1,6 W/kg

P_{sector} = 1W

4th stage: whole body SAR for 4 young mice per cage



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Reinhardt, Bitz, El Ouardi, Streckert, Hansen

Conclusion

- With the modified radial waveguide setup we achieved a well defined exposure, merely leaving those variations of the whole body SAR introduced by the biological design.

- The prescribed SAR values of 1.3 W/kg, 0.4 W/kg, 0.08 W/kg were adjusted according to the 1st stage of the study (adult mice). The corresponding input power was kept constant during all stages because of the animals' rapid growth.

P_{in} = 28 W; S = 22 W/m^2	Wb -SAR for high dose in W/kg	Standard deviation
1st configuration	1,3	31%
2nd configuration	1,44	28%
3rd configuration; adult:	1,21	50%
pups:	1,92	54%
4th configuration	2,34	33%

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