Exposure Setups for In Vitro RF Experiments

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IT'IS FOUNDATION

ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

In Vitro Laboratory Studies with IT'IS Participation

In Vitro Studies

Partner: Institut für klinische Chemie und Pathobiochemie, Universitätsklinikum Benjamin Franklin, Berlin, Germany
Objectives: Investigation of possible genotoxic effects and effects on gene expression due to GSM exposure in the human HL60 cell system
Partner: Klinische Abteilung Arbeitsmedizin, Universitätsklinik Innere Medizin IV, Wien, Austria
Objectives: Investigation of possible direct and indirect genotoxic effects due to ELF magnetic field exposure in several human cell lines
Partner: Institut für Pflanzengenetik und Kulturpflanzenforschung, Gatersleben, Germany
Objectives: Analysis of molecular and cellular responses of embryonic stem cells to RF and ELF electromagnetic field exposure
Partner: Investigacion Bioelectromagnetismo, Hospital Ramon y Cajal, Madrid, Spain
Objectives: Investigation of the influence of RF EMF on differentiation and gene expression of pheochromocytoma PC12 cells and of primary cultures from nucleous striatum of rat foetuses
Partner: Laboratory of Radiobiology, STUK - Radiation and Nuclear Safety Authority, Helsinki, Finland
Objectives: Effects of RF EMF on (1) pattern of expression of genes and their protein products and (2) cell cycle kinetics
Partner: Institut für Biophysik, Universität Hannover, Germany
Objectives: Investigation of cellular responses to ELF EMF of various cell systems on different levels of signal transduction, gene expression and protein targeting
Partner: Department of Physics, University of Bologna, Italy
Objectives: Investigation of possible effects of RF EMF on the human immune system dependent on the age of subjects
Partner: Laboratoire PIOM, Ecole Nationale Superieure de Chimie et de Physique, Cedex, France
Objectives: Determination whether RF EMF are able to act as direct or indirect carcinogens using the standardised rat tracheal epithelial cells transformation assay
Partner: Department of Pharmacology, University of Milan, Italy
Objectives: Investigation of possible ELF EMF effects on the development, composition and function of neuronal nicotinic receptors in human neuronal cells
Partner: Laboratoire PIOM, Ecole Nationale Superieure de Chimie et de Physique, Cedex, France
Objectives: Effects on activation of ODC activity after RF exposure at 1800 and 900 MHz
Partner: Department of Environmental Sciences, University of Kuoppio, Finland
Objectives: Replication study of the effects on activation of ODC activity after RF exposure at 835 MHz
Partner: Ente per le tecnologie, l'Energia e l'Ambiente, Department of Environment, Rome, Italy
Objectives: Replication study of genotoxic effects of RF EMF on lymphocytes at 900 and 1800 MHz
Partner: National Radiological Protection Board, Oxfordshire, UK
Objectives: Replication study of genotoxic effects of RF EMF on lymphocytes at 900 MHz
Partner: Institute for Electromagnetic Sensing of the Environment, Italian National Research Council Naples, Italy
Objectives: Replication study of genotoxic effects due to ELF magnetic field exposure in human diploid fibroblasts
Partner: Institute for Molecular Cancer Research, University of Zurich, Switzerland
Objectives: Replication study of genotoxic effects due to ELF magnetic field exposure in human diploid fibroblasts
Partner: Institut für Krebsforschung Universität Wien, Austria
Objectives: Investigation of possible effects of GSM & UMTS exposure on protein function
Partner: Klinische Abteilung Arbeitsmedizin, Universitätsklinik Innere Medizin IV, Wien, Austria
Objectives: Investigation of possible direct and indirect genotoxic effects of GSM and UMTS exposure in several human cell lines
Partner: Forschungszentrum Seibersdorf, Umwelt & Lebenswissenschaften, Toxikologie, Austria
Objectives: Investigation of possible effects of GSM and UMTS exposure on cells of the human immune system
Partner: Institute for Science & Technology in Medicine, Keele University, Stoke-on-Trent, UK
Objectives: Examination of possible effects of RF emissions from cellular telephones on biogenic magnetite in living cells (magnetotactic bacteria and cell cultures)
Partner: Institute of Cell Biology and Biosystems Technology, University of Rostock, Germany
Objectives: Examination of possible effects of RF EMF on cell activation processes in human cell systems

Contents

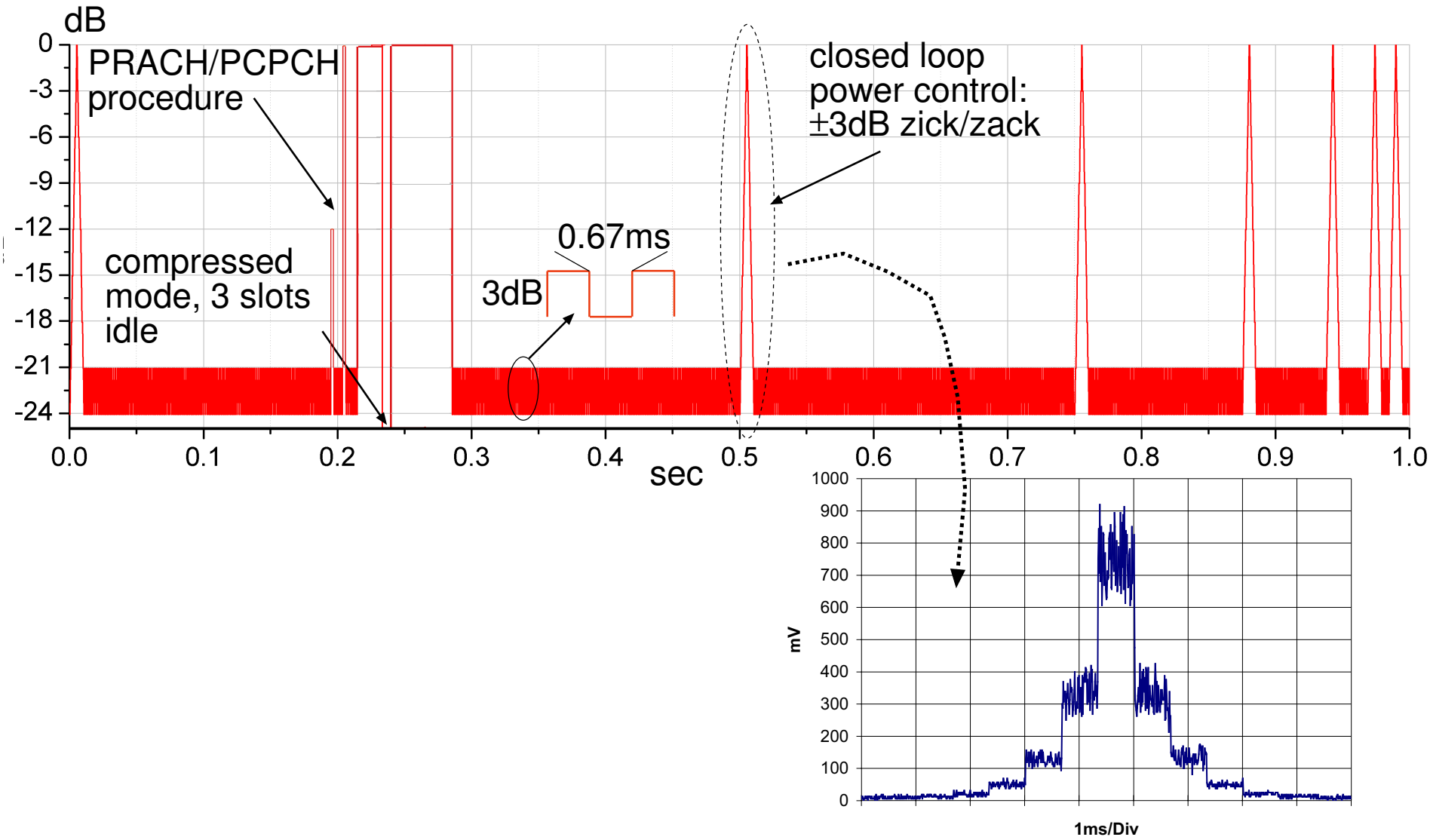
- Requirements
- Solutions
- sXc1800XL8
- Conclusions

Requirements

- **(different) exposures + shame at exactly the same conditions except the induced RF**
- **minimal deviation from a standard biological protocol (flask/petri dish, medium, environment, etc.)**

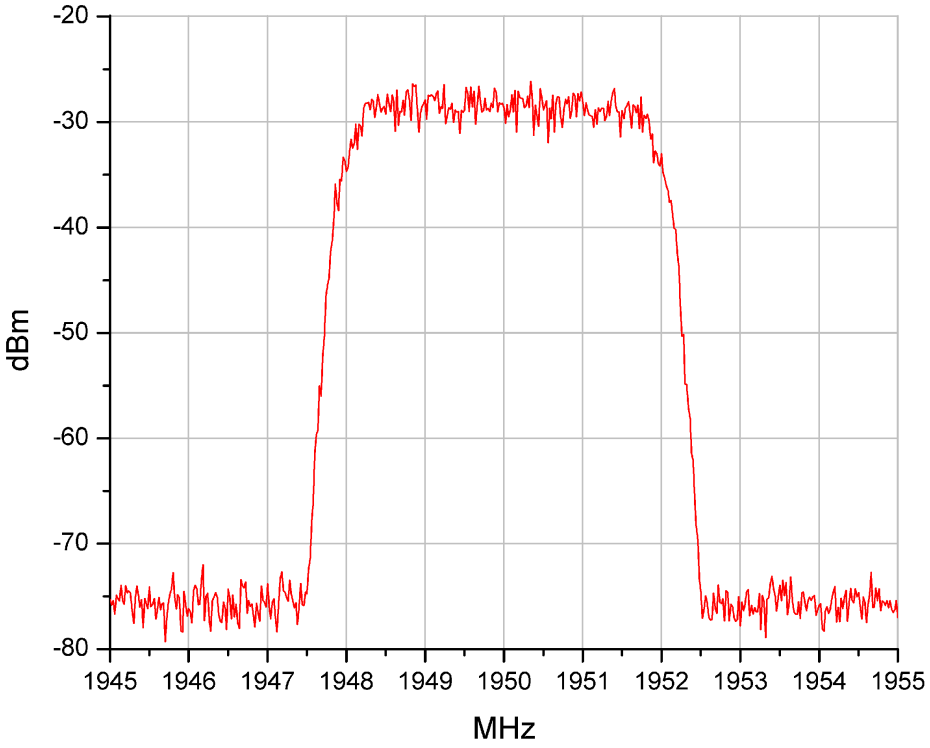
- stable RF carrier (frequency, Pavg, low noise)
- flexible modulation (enable most complex schemes)
- well defined and uniformly induced E- and H-fields (at cell culture)
- well defined environmental conditions
- fully characterized sources of artifacts (e.g., temperature load, vibration, EMC, EMI, etc.)
- all environmental and technical parameters continuously monitored
- uncertainty analysis

UMTS TPC Test Signal

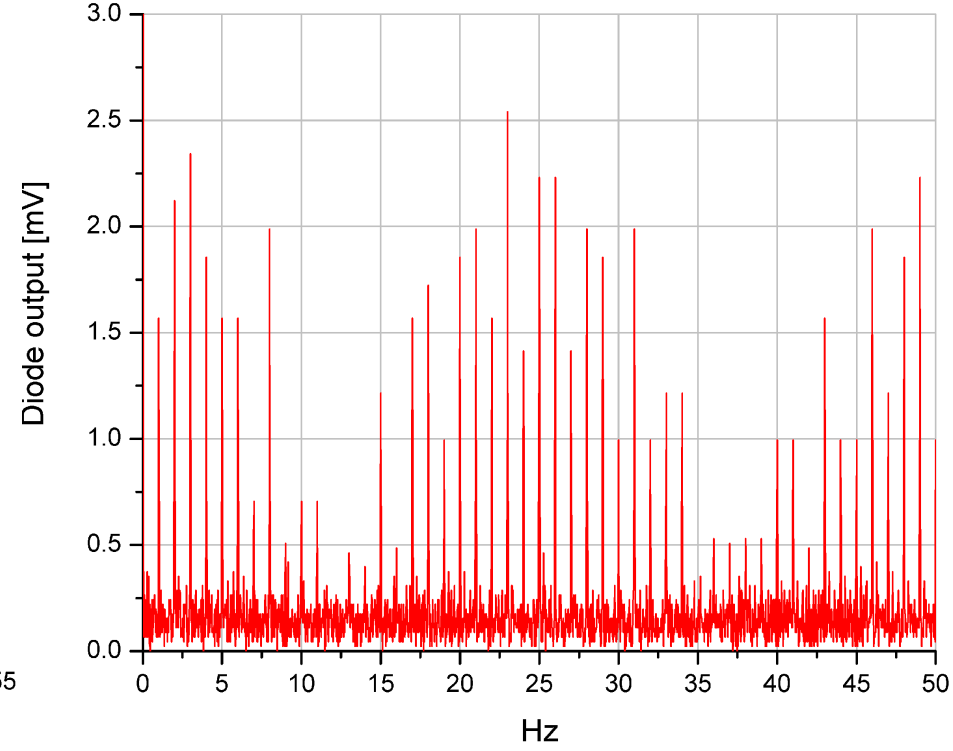


Spectral Content

HF spectrum



ELF envelope spectrum



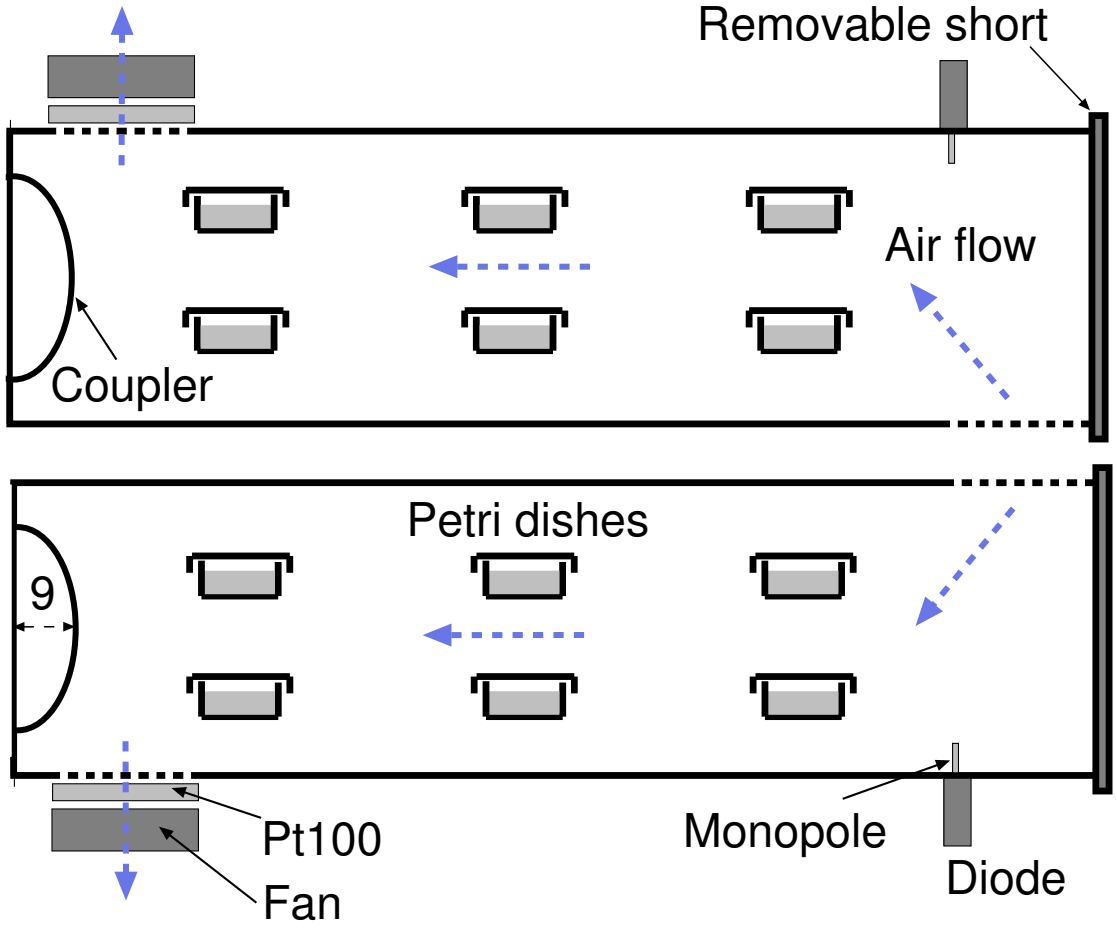
Consequence

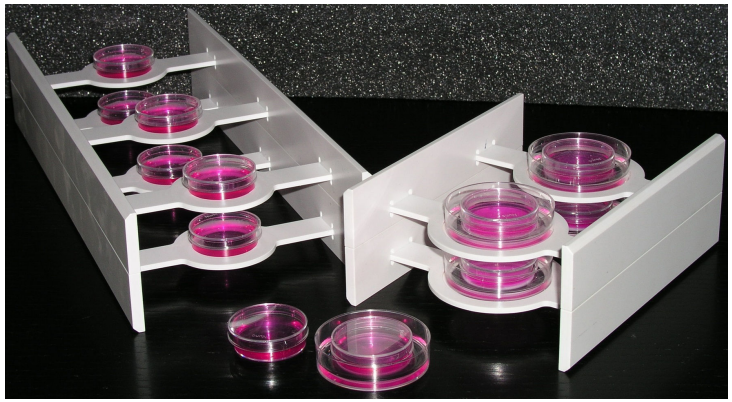
- **(almost) each biological endpoint requires a specific exposure setup**

Current

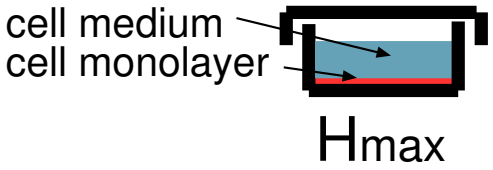
- sXc900 (petri 35mm, monolayer, suspension)
- sXc1800 (petri 35mm, monolayer, suspension)
- sXc1950 (petri 35mm, monolayer, suspension)
- sXcTEM (900MHz, T45 flasks, suspension)
- wirepatch (900MHz, petri 35mm, suspension)

Mechanical Design

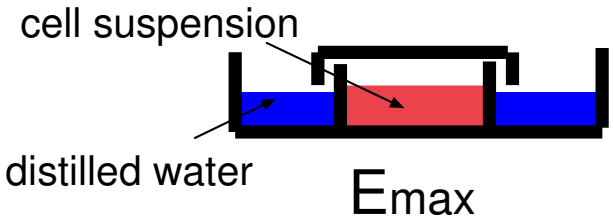




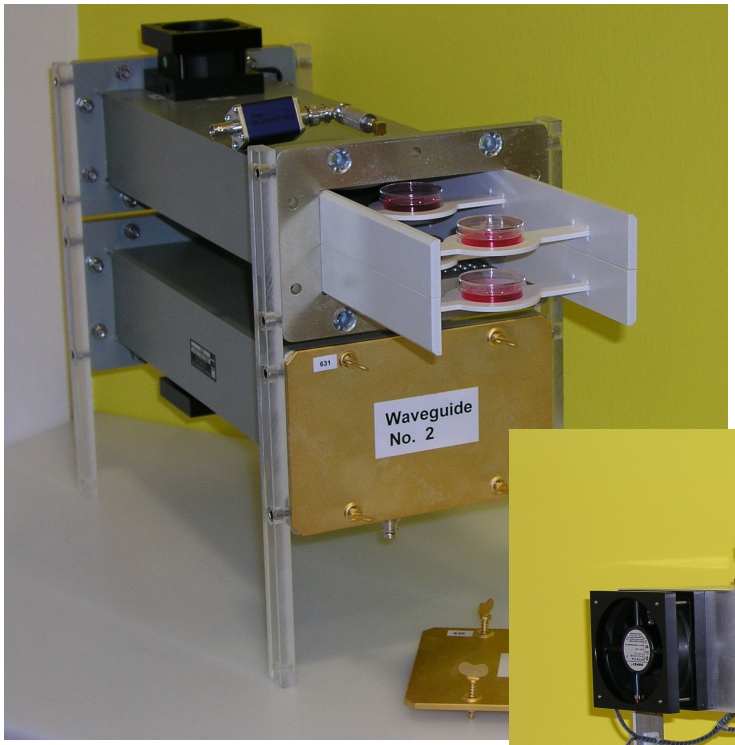
Monolayer exposure



Suspension exposure

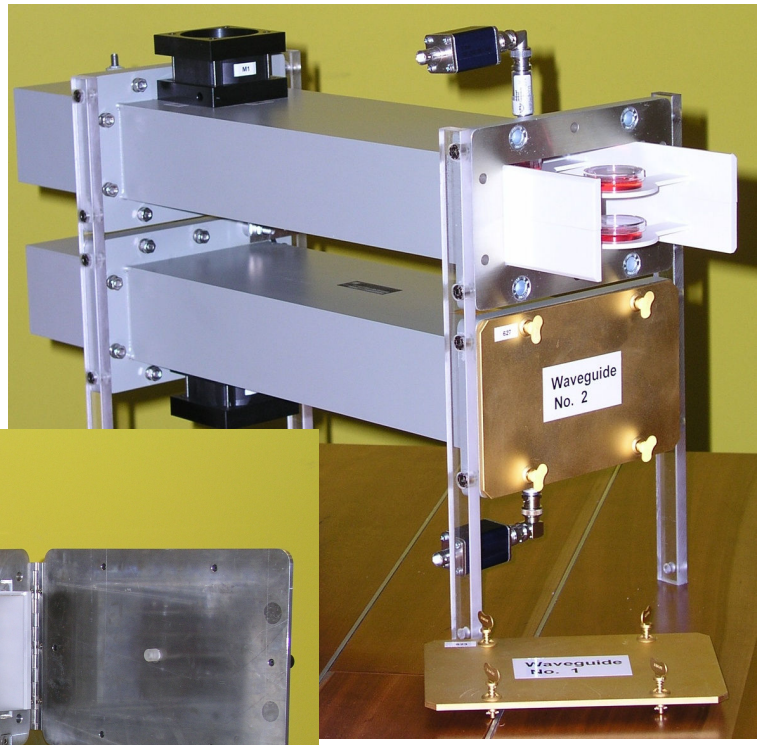


sXc In Vitro Exposure Systems



sXc 1800

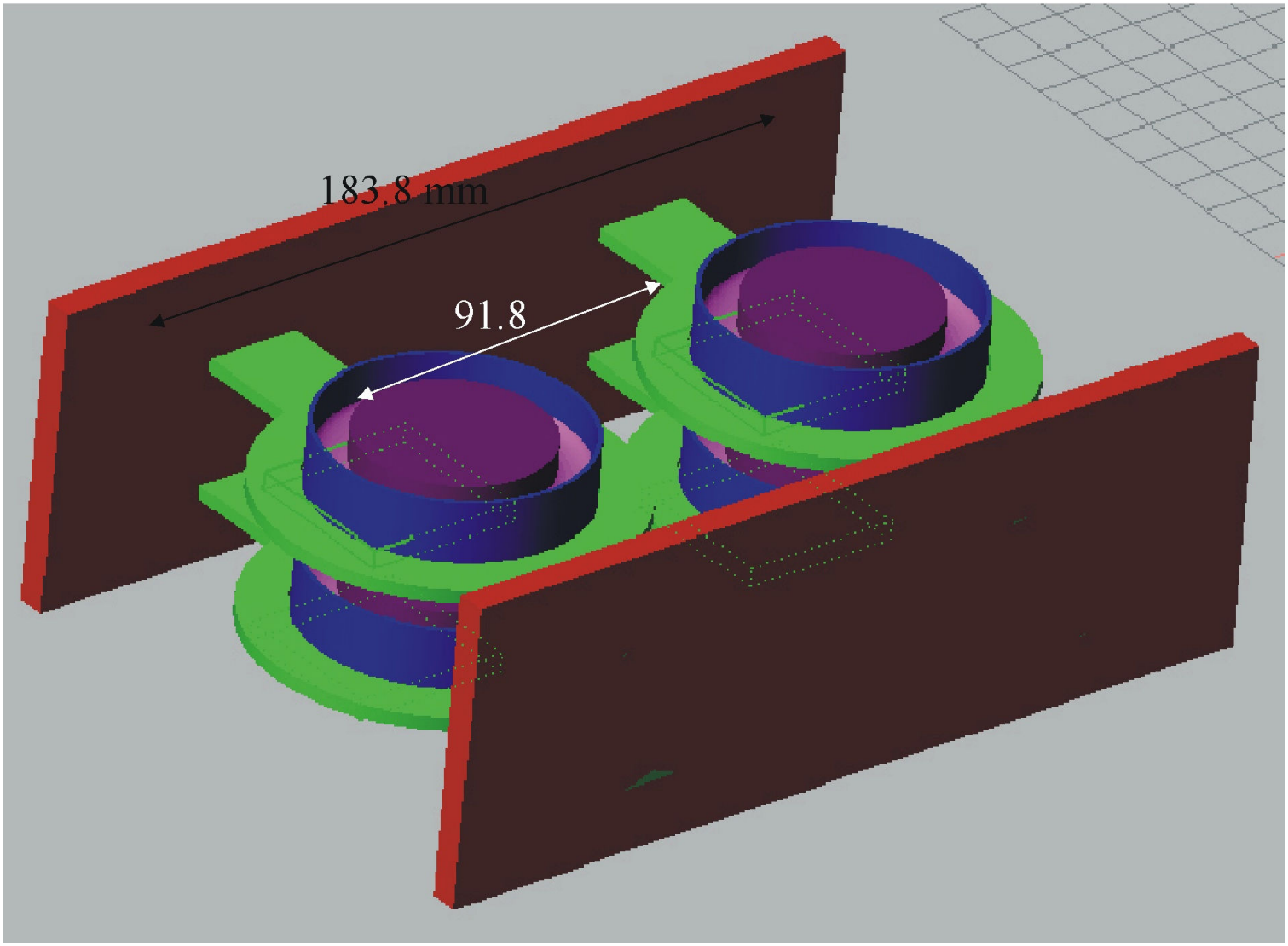
sXc 900



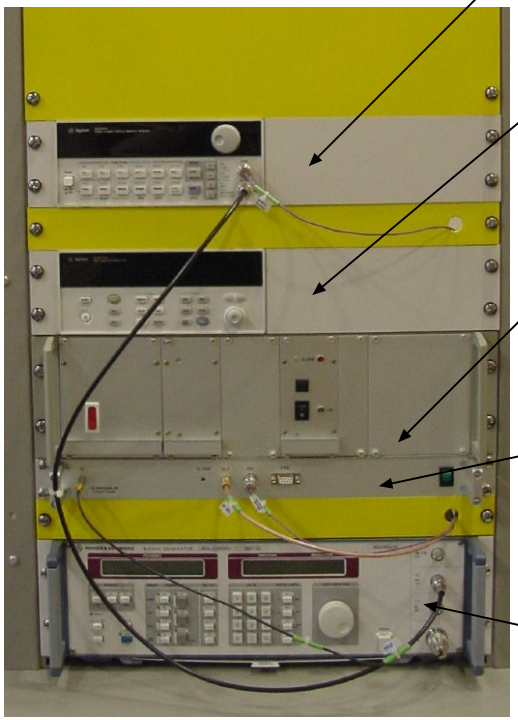
sXc UMTS

Installed Setup

Mechanical Design: Dish Holder Suspension



Signal Generation



PC & Software

Function-generator

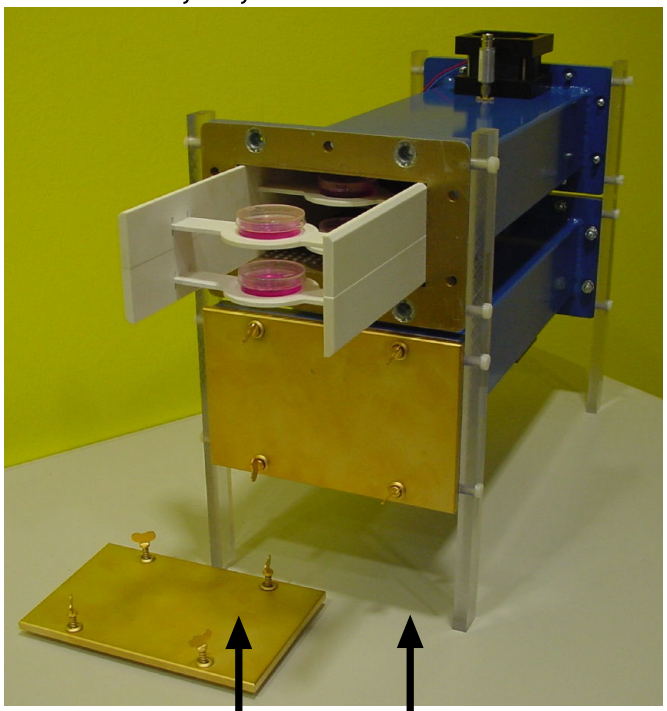
Data-logger

Electronics
DCU

blank
Amplifier
out
in

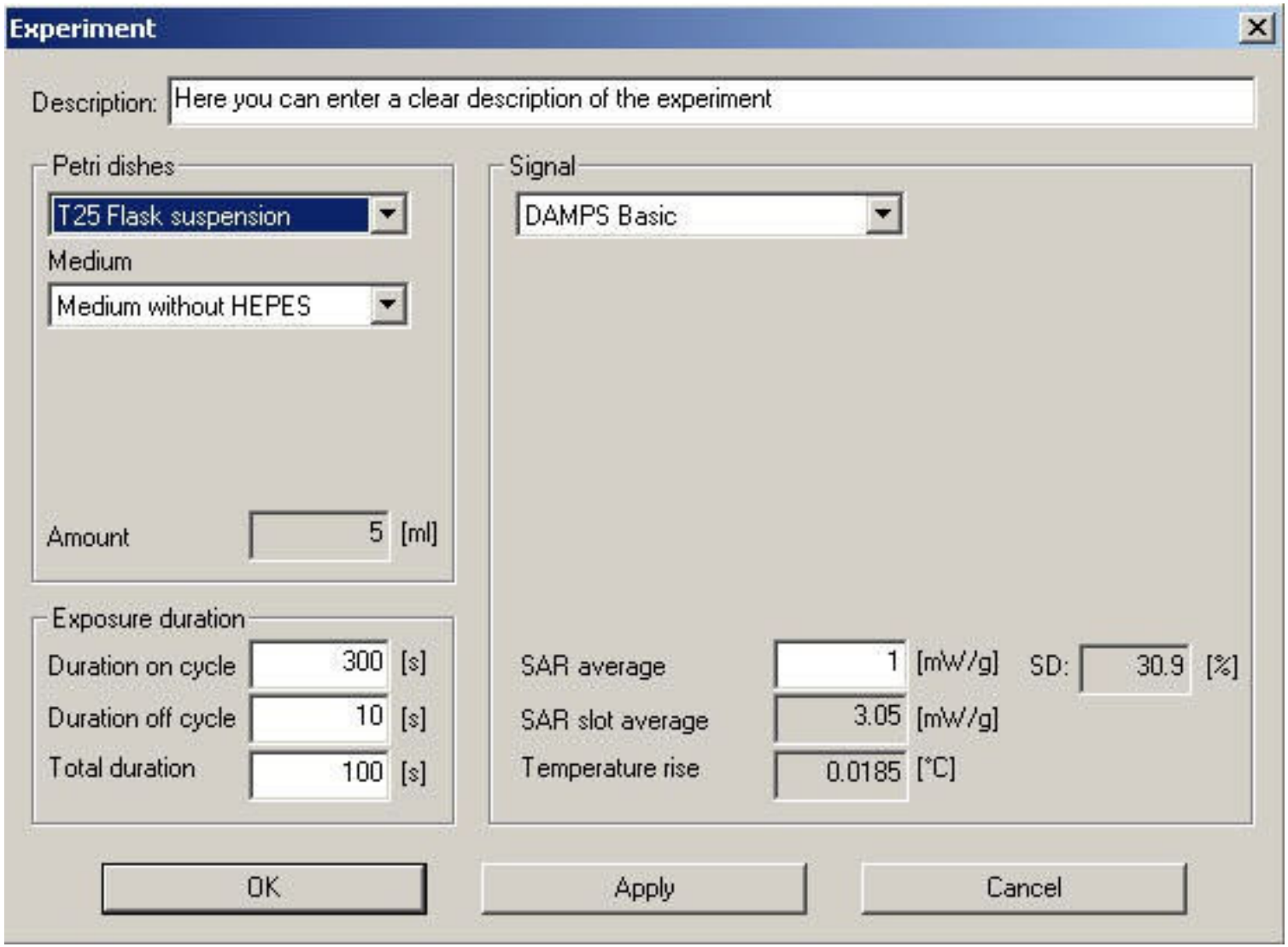
RF-generator
mod

H, T, I_{Fan}

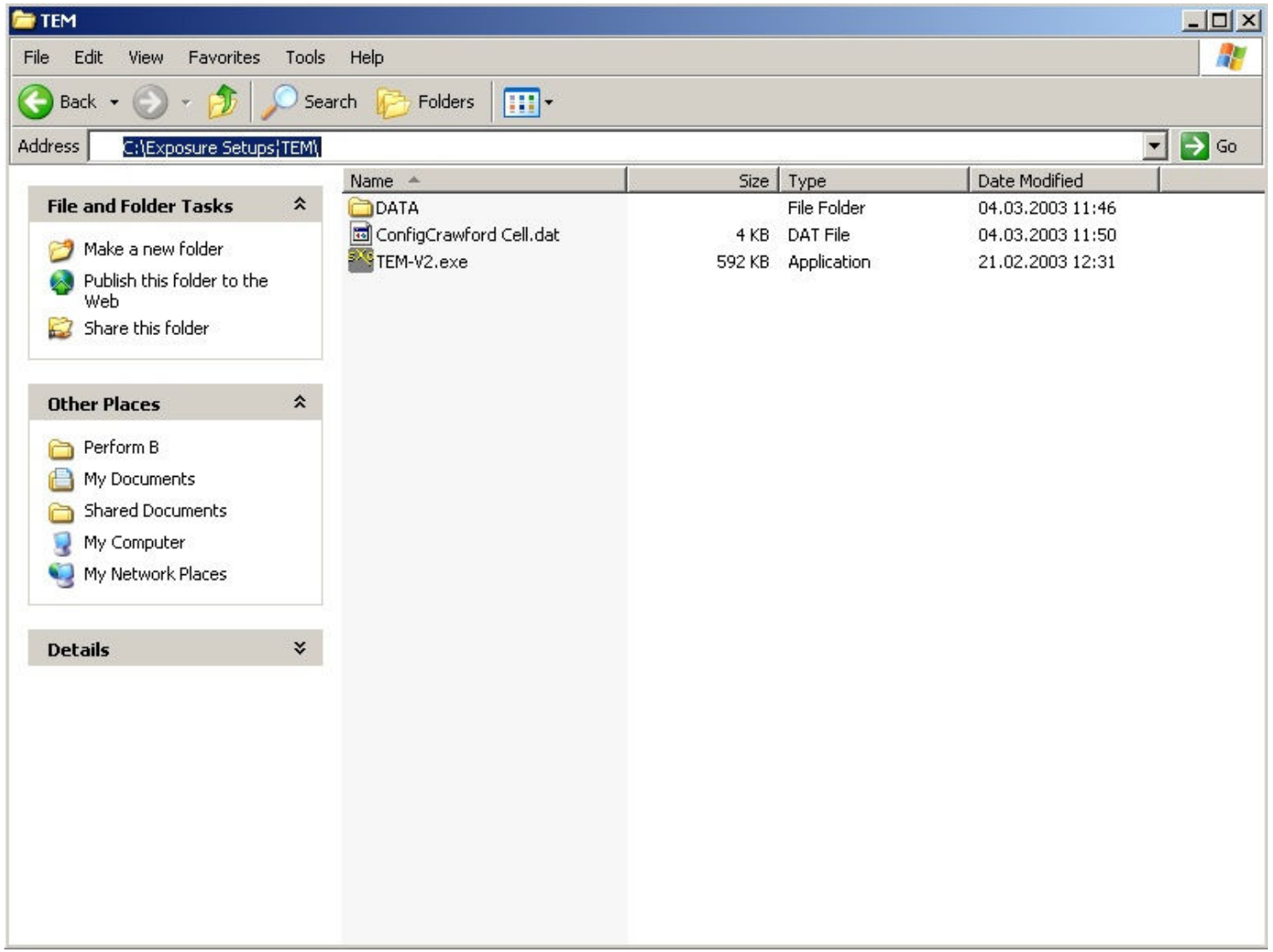


HF-switch

sXc User Software: Signal Choice



sXc User Software: File Structure



Quality Control & Data Security

- Recording of entire experiment history (10s intervals)
- Data security
  - files are read-only
  - binary mode
  - data are faked and encoded using a safe RC4 algorithm
  - data files are stored at 2 different physical locations
- Self-detection of malfunctions (tracing & handling of ~ 60 errors)
- Complete analysis of data stream at IT'IS in case of malfunction
- Provision of evaluation report to the lab by email

Data Analysis

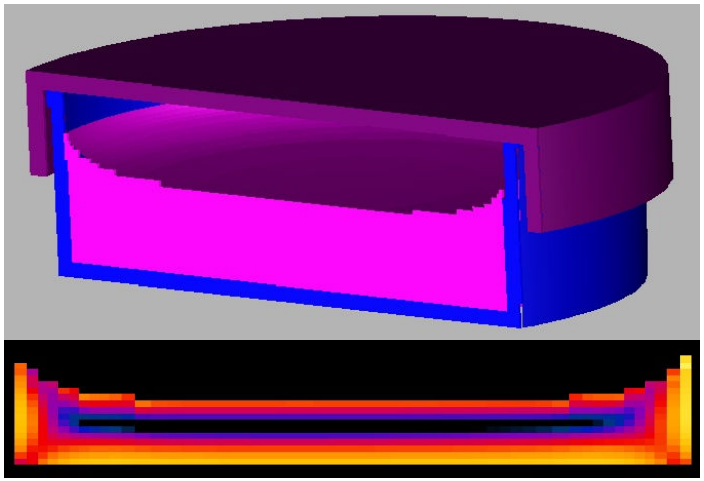
sXc 1800 Experiment Parameters

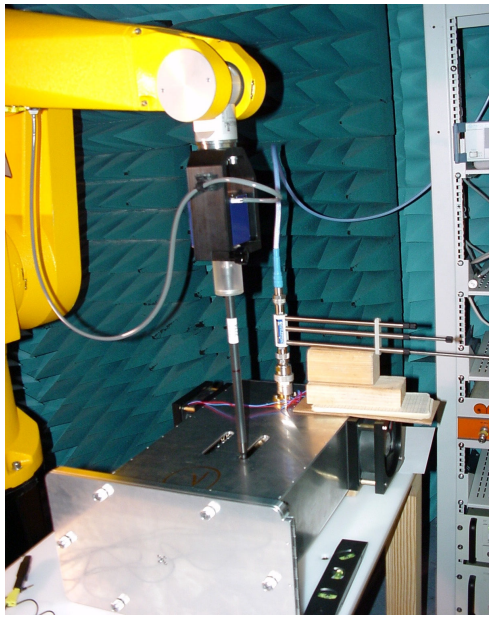
Description	Value	Dimension
Start Date and Time	2002-05-21-12:50:08	
Stop Date and Time	2002-05-23-08:51:15	
Expected Average SAR	2	[mW/g]
Modulation	ON	[]
Frame Structure	ON	[]
DTX	OFF	[]
Talk	ON	[]
Handover	OFF	[]
Environment	OFF	[]
Duration ON	600	[s]
Duration OFF	1200	[s]
Total Duration	44	[h]
Number of Cycles	88	[#]
Expected Temp rise	0.05	[K]

Description	Wave Guide 1	Wave Guide 2	Dimension
Power	OFF	ON	
SAR ± SD (during exposure)	0 ± 0	2.05± 1.17	[mW/g]
SAR (Min, Max) (during exposure)	0 , 0	0.33 , 3.12	[mW/g]
SAR ± SD (during exposure and dtx false)	0 ± 0	2.85± 0.012	[mW/g]
SAR (Min, Max) (during exposure and dtx false)	0 , 0	2.82 , 3.12	[mW/g]
SAR ± SD (during exposure and dtx true)	0 ± 0	0.34± 0.001	[mW/g]
SAR (Min, Max) (during exposure and dtx true)	0 , 0	0.33 , 0.34	[mW/g]
T ± SD	37.14± 0.017	37.05± 0.018	[C°]
T (Min, Max)	36.84 , 37.17	36.7 , 37.07	[C°]
deltaT ± SD	0.09± 0.002	0.09± 0.002	[C°]
deltaT (Min, Max)	0.09 , 0.14	0.09 , 0.14	[C°]
Fan current ± SD	0.259± 0.002	0.237± 0	[A]
Resonance Frequency	n.a.	1817	[MHz]

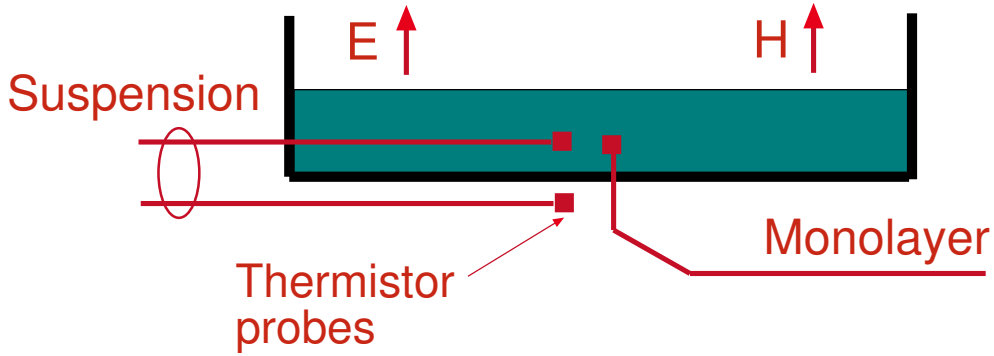
Event	#
Warnings	0
Abortion	0

Dosimetry: Methods





- High resolution FDTD analysis with SEMCAD (numerical models include meniscus and all plastic parts)
- Coupled electro-thermal evaluation
- Field validation with isotropic 3-axis E- and H-field probes
- SAR verification with dosimetric field and temperature probes (DASY4)
- Assessment of the temperature load with flexible thermistor probes

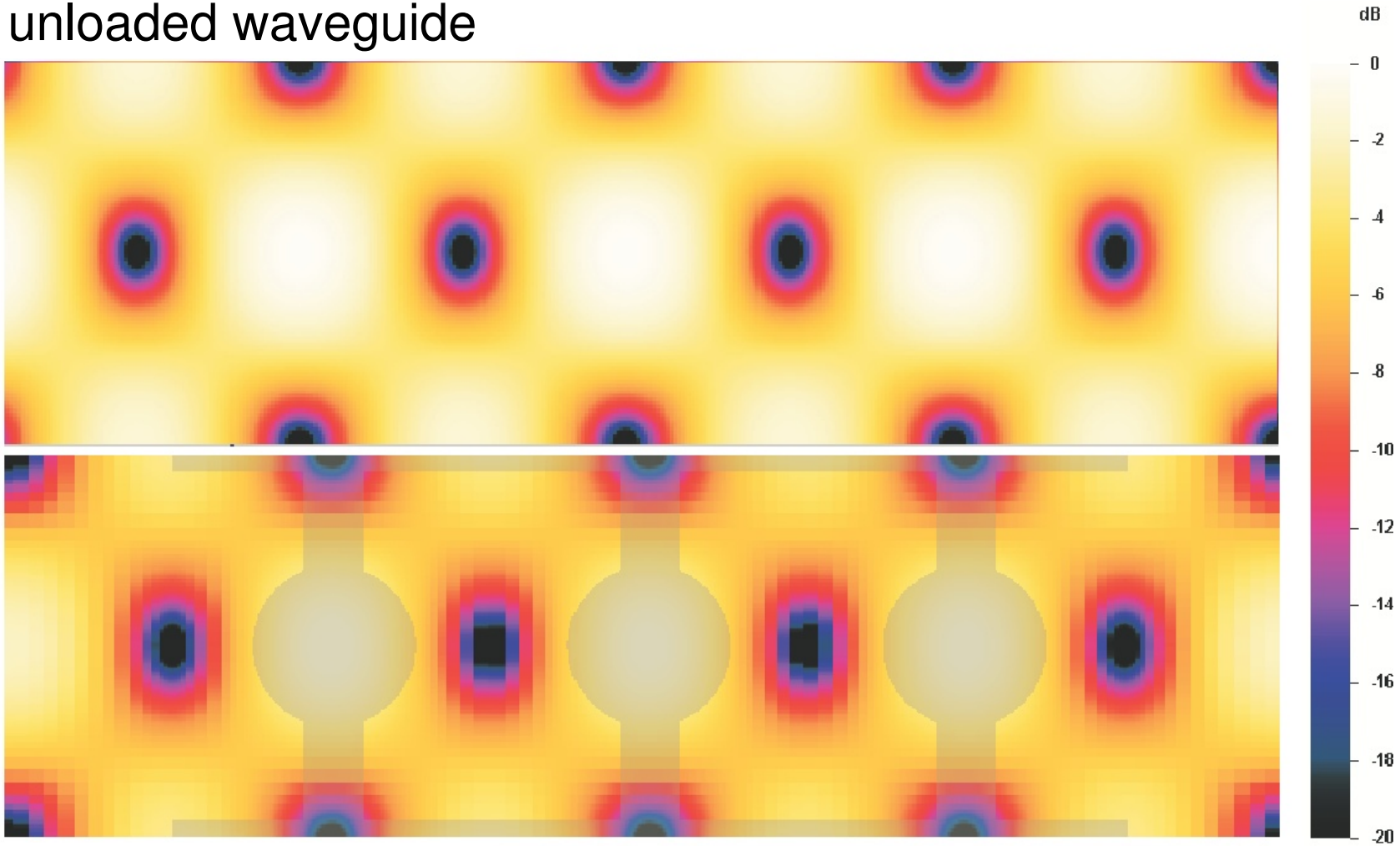


Dosimetric Concept

- numerical optimization of field distributions with respect to maximum uniformity, efficiency and minimized uncertainties
- numerical evaluation of field conditions
- verification of simulations by free field and dosimetric measurements
- determination of temperature rise
- uncertainty and variability analysis

Numerical Optimization of Petri Dish Position

unloaded waveguide



loaded waveguide

Dosimetric Concept

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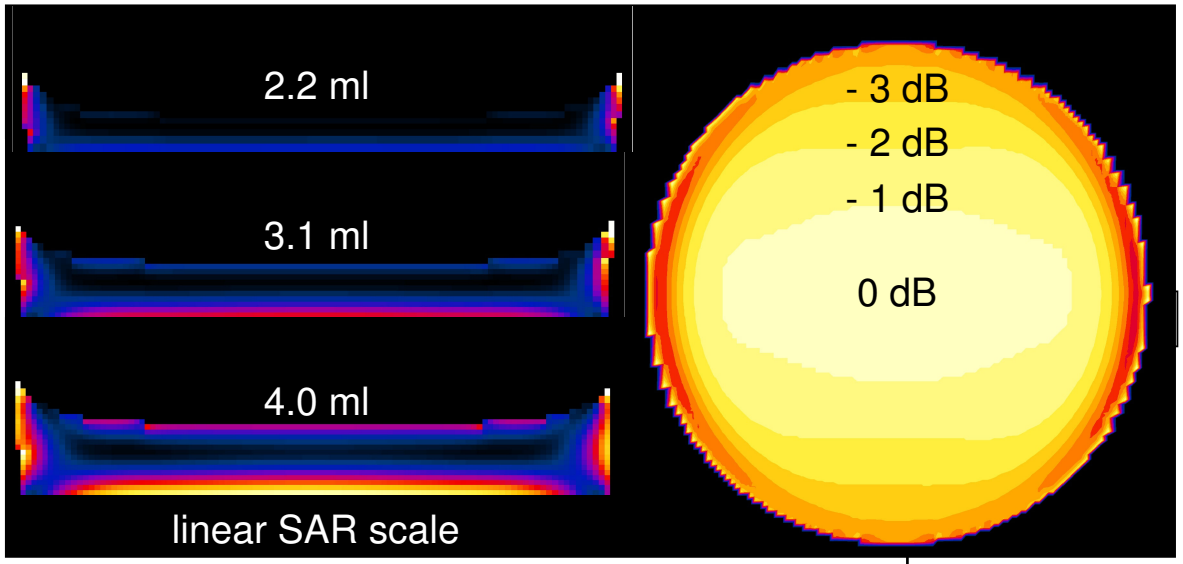
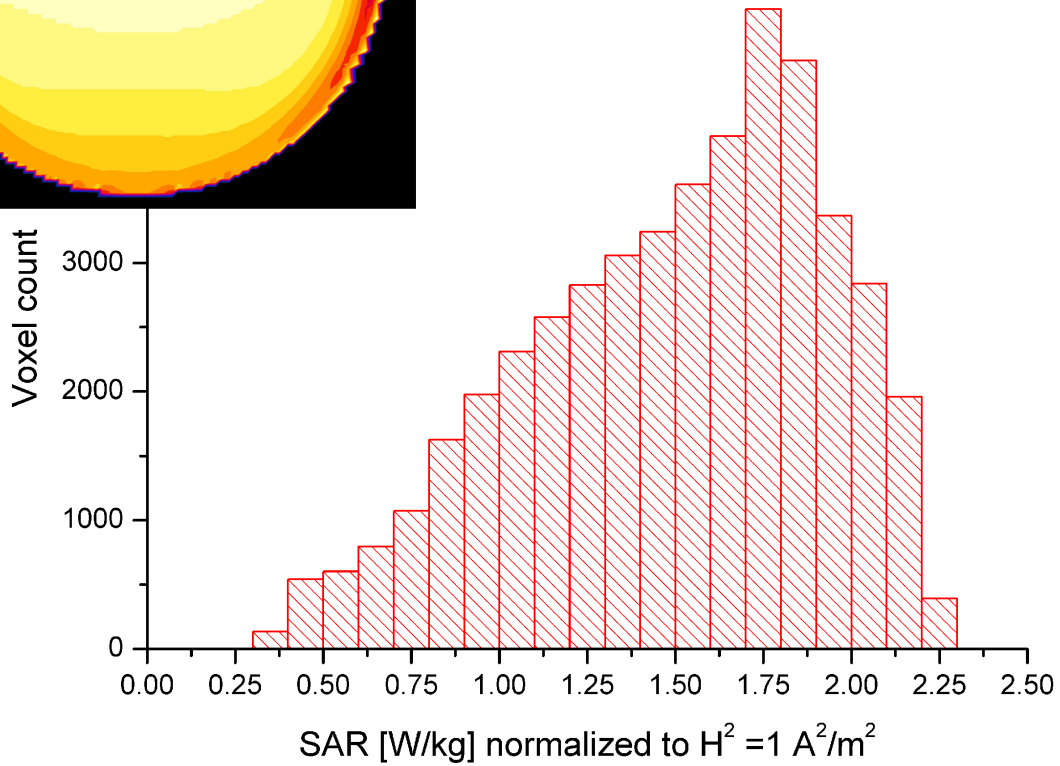
Numerical Evaluation: SAR Evaluation



- FDTD simulation (SEMCAD)
- high resolution numerical models
- several medium levels

3.1 ml DMEM
SD/Avg = 28%



Dosimetric Concept

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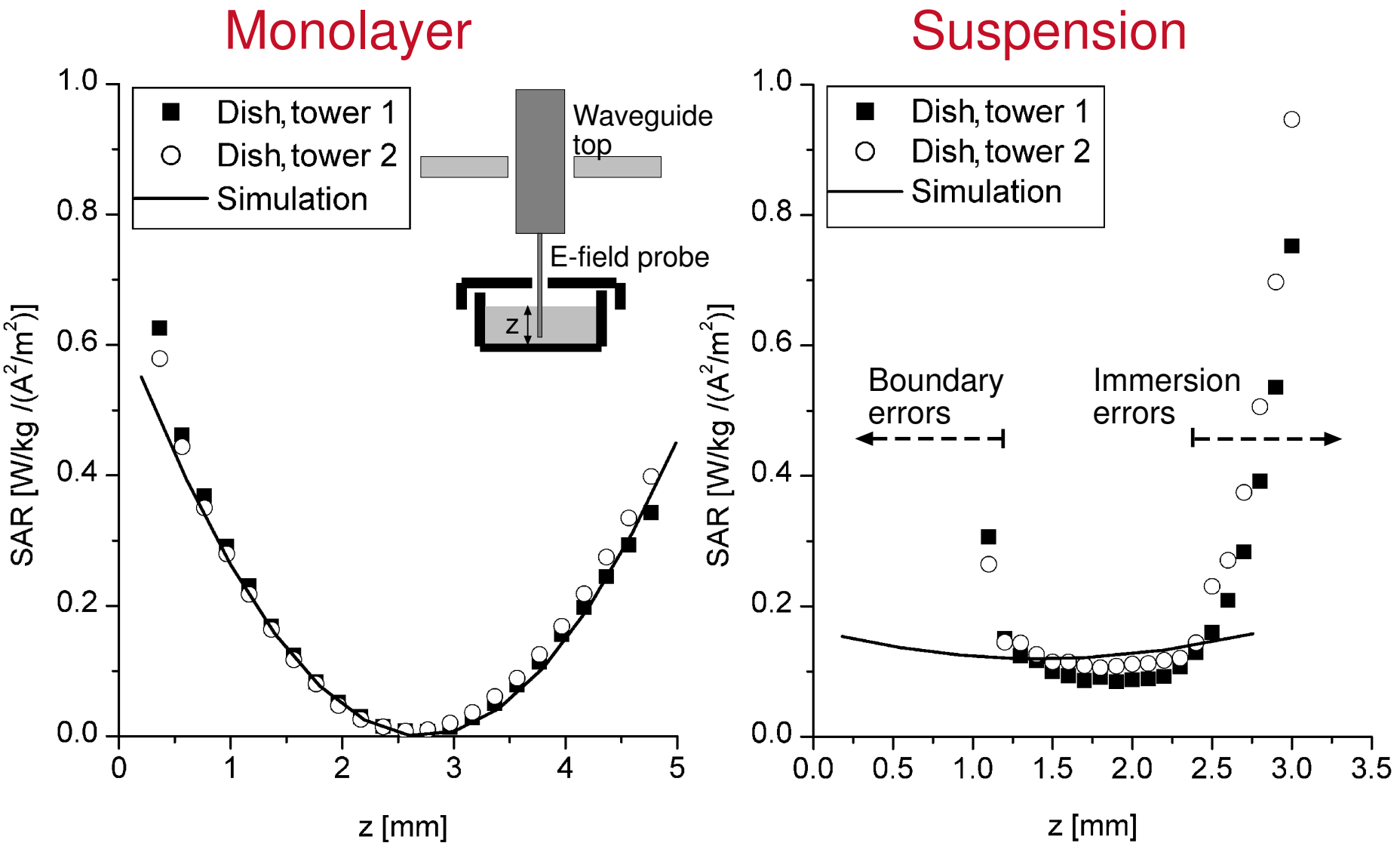
Dosimetry: Experimental Verification



Dosimetric Concept

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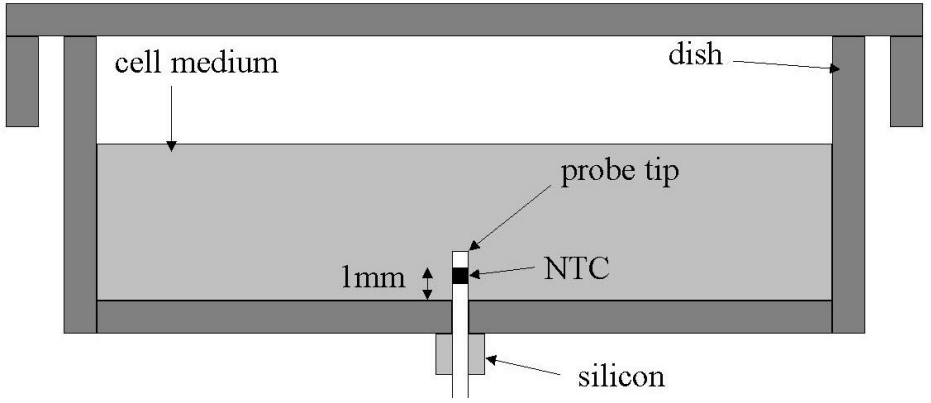
Determination of the Temperature Rise

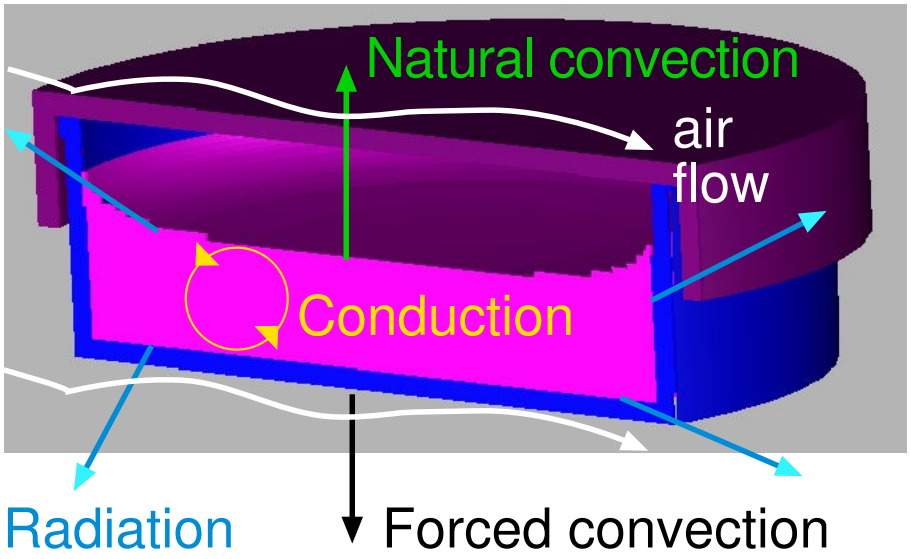
Experimental

- one point measurements in the temperature maximum
- time constants for temperature response dependent upon liquid height, fan speed and signal strength



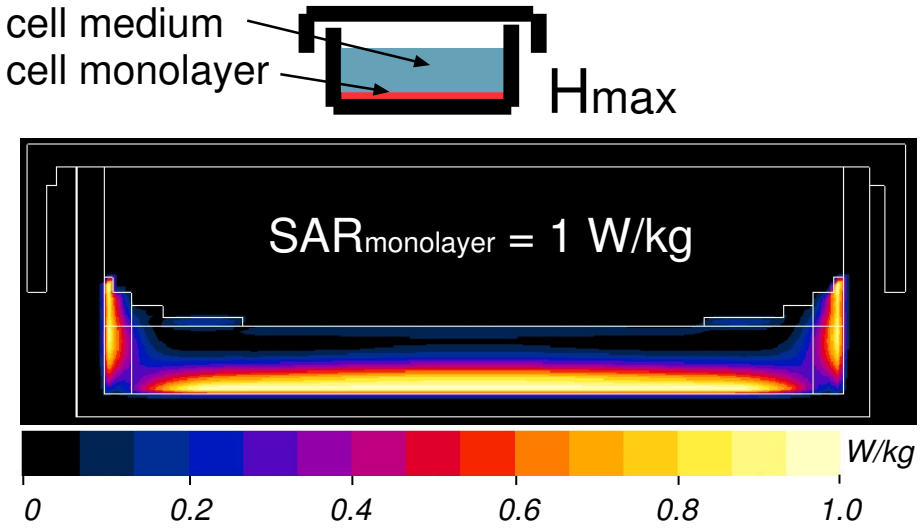
Numerical

- coupled electro-thermal FDTD analysis
- heat transfer due to conduction, convection and radiation
- thin plate approximation for heat transfer coefficients

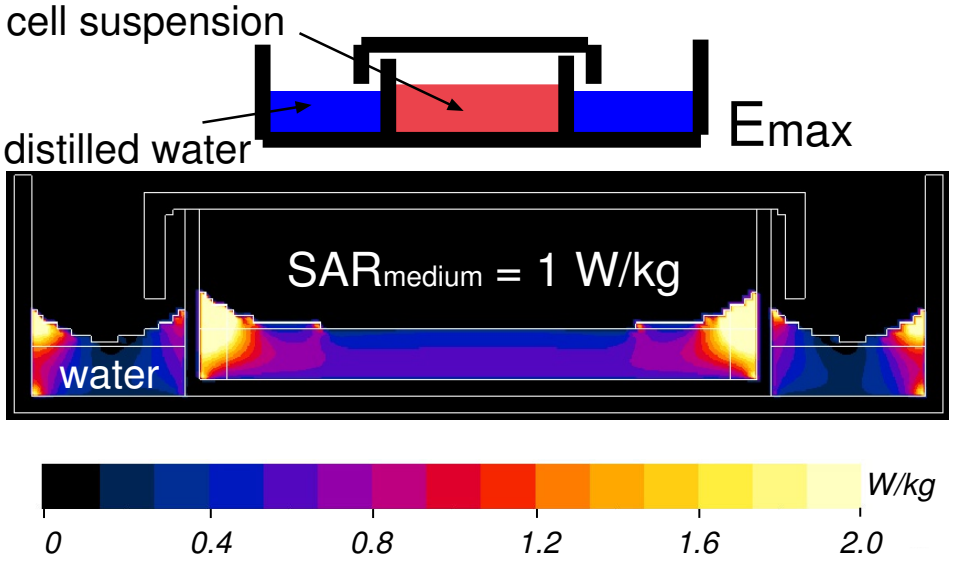


SAR & Temperature Distribution

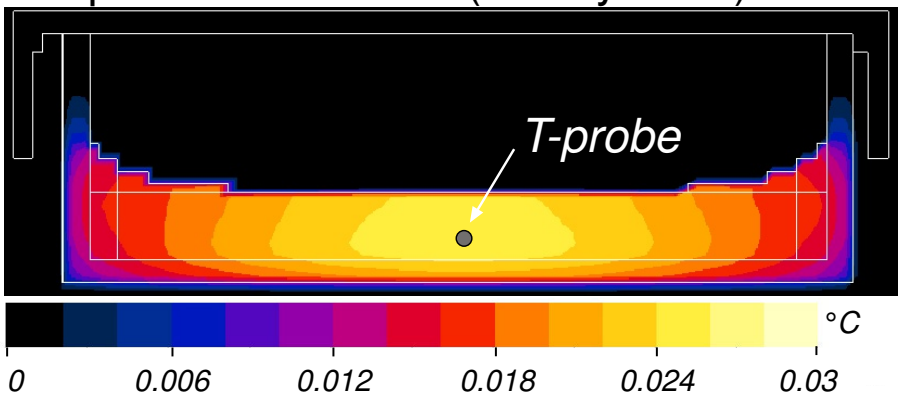
Monolayer exposure

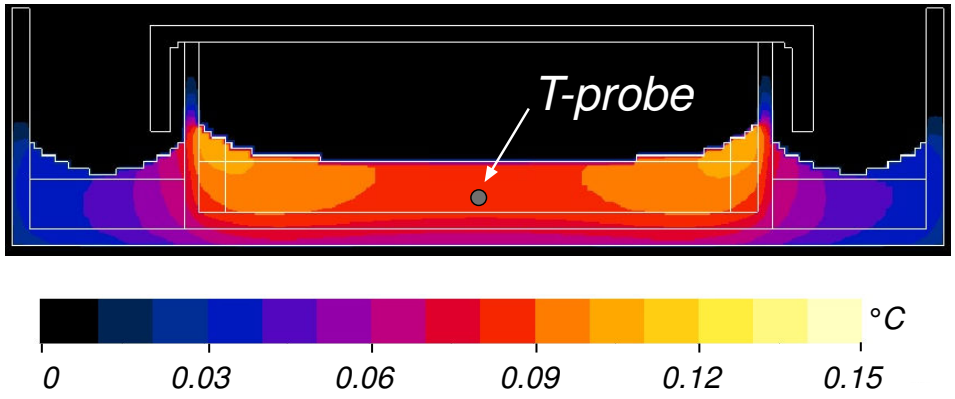


Suspension exposure



Temperature increase (steady state)





Dosimetric Concept

- numerical optimization of field distributions with respect to maximum uniformity, efficiency and minimized uncertainties
- numerical evaluation of field conditions
- verification of simulations by free field and dosimetric measurements
- determination of temperature rise and other artifacts
- uncertainty and variability analysis

Uncertainty & Variability Analysis

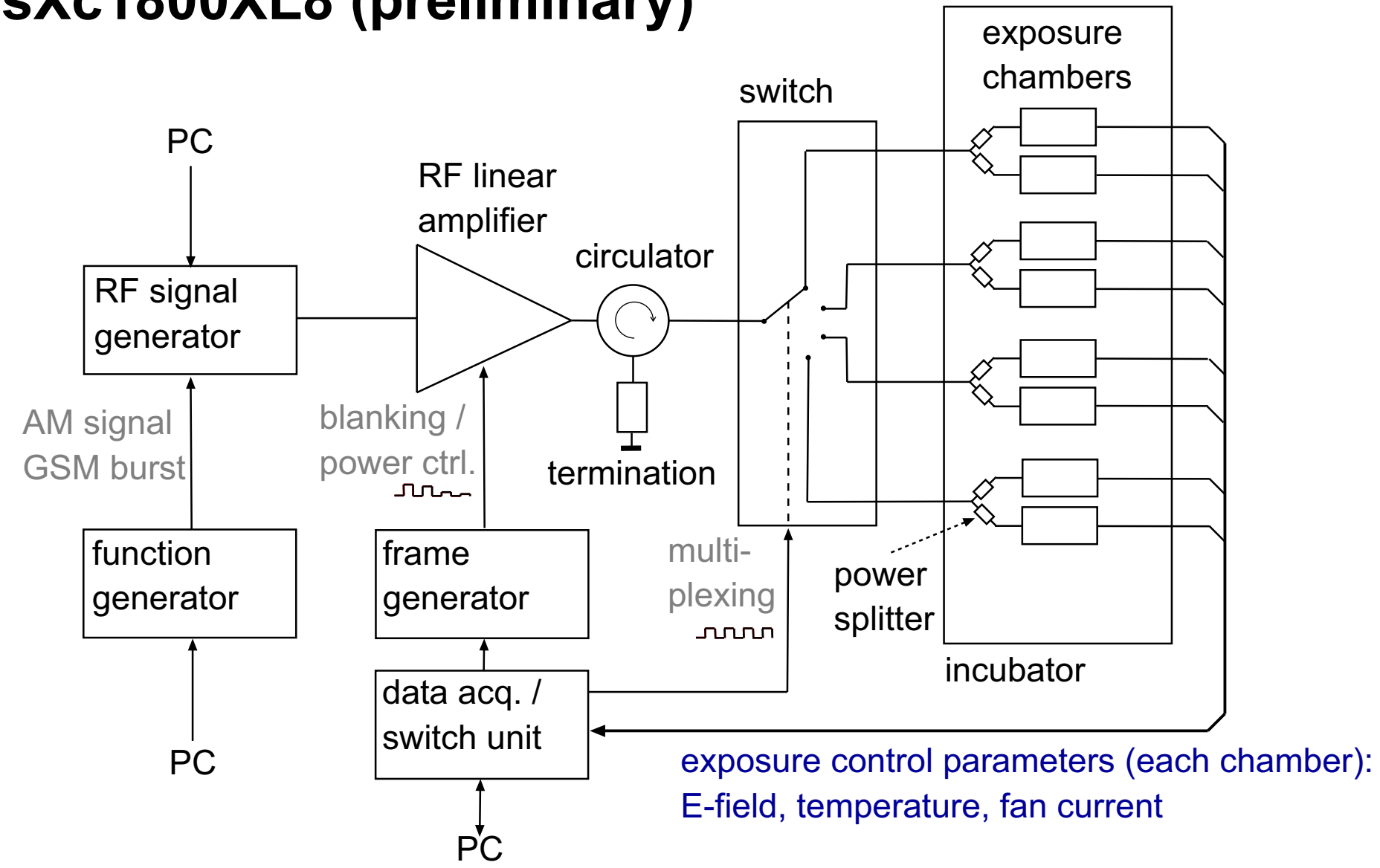
Uncertainty of SAR Assessment	MI.	Su.
Fit for extrapolation to monolayer	2.8%	-
Fit for varying medium volume	1.9%	-
Vertical location of cells	4.8%	-
Numerical discretization (0.1 mm reference)	8.2%	4.9%
Determination of medium volume (± 5 µl)	0.3%	< 0.1%
Dielectric parameters	11%	15%
E-field probe	7.6%	7.6%
Probe positioning	1.6%	1.6%
Sensor calibration for incident fields	11%	11%

Variability Analysis of SAR	MI.	Su.
Frequency dependency of loop coupler	4.5%	4.5%
Evaporation of dist. water (max. 2ml)	-	16%
Use of a large lid on 60 mm Petri dish	-	2.0%
Determination of medium volume (± 5 µl)	0.3%	< 0.1%
Dish holder misplacement (±2 mm)	0.7%	2.4%
Incident field assessment	2.2%	2.2%
Drift	0.5%	0.5%

sXc1800XL8 (preliminary)

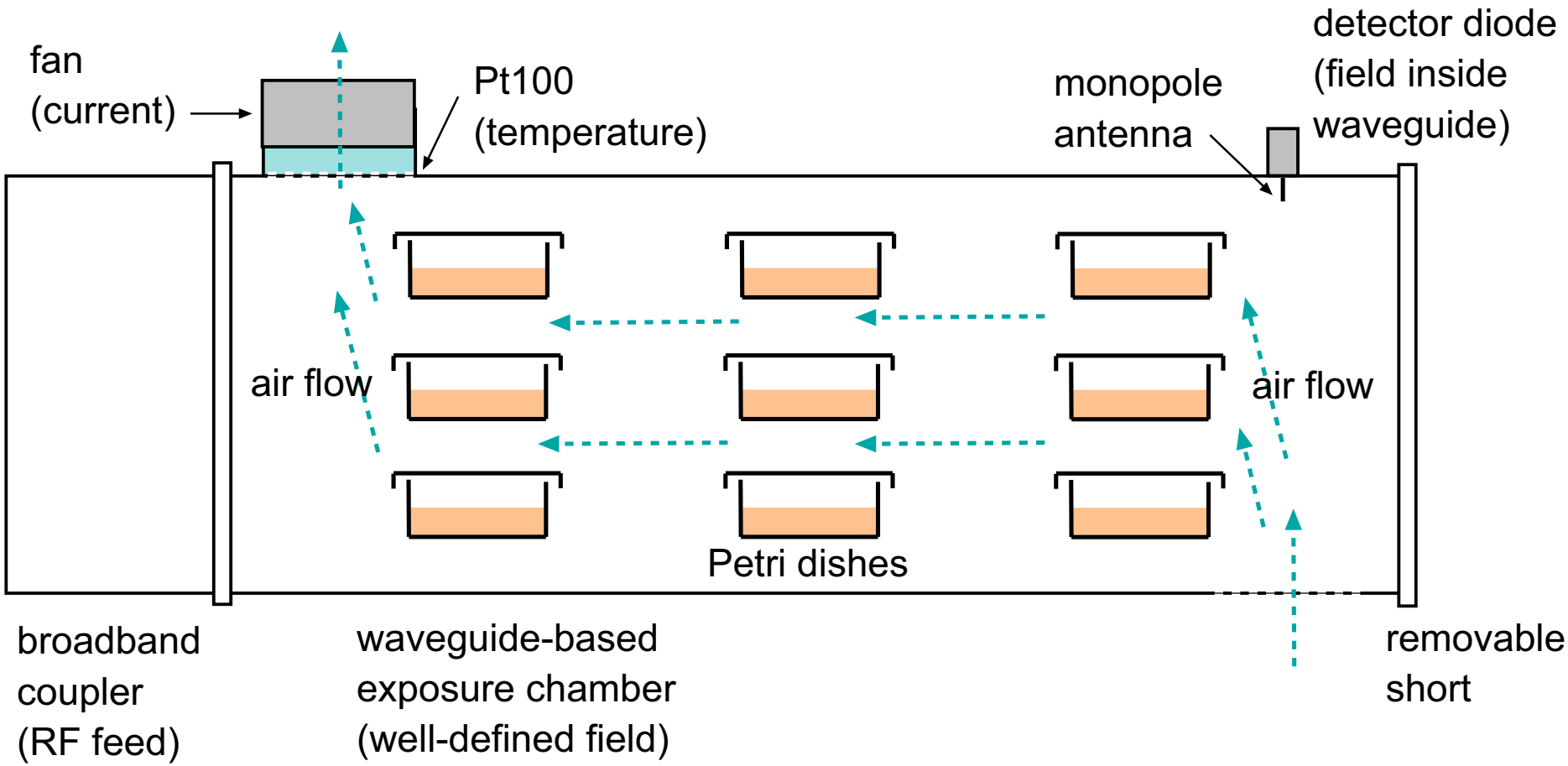
- 1800 MHz, GSM-based signals, 8 chambers in matched pairs
- pair wise exposure: 2 chambers at the same exposure level
- independent monitoring and control of each exposure level
- waveguide-based exposure chambers
- exposure levels: 10 W/kg, 2 W/kg, 0.2 W/kg and sham condition
- random and user setting of exposure levels including sham control
- continuous or intermitted exposure with user defined on/off periods
- designed for the exposure of large sample volumes
- fits in one standard incubator
- monitoring and control of all exposure parameters for each chamber: E-field, temperature and fan currents
- complete uncertainty budget and variation analysis

sXc1800XL8 (preliminary)



exposure control parameters (each chamber):
E-field, temperature, fan current

sXc1800XL8 (preliminary)



Conclusions

- **different exposure systems have been developed for different biological endpoints/protocols that allow to conduct exposure and shame at exactly the same conditions except the induced RF (@ $\Delta T < 0.1^{\circ}C$)**
- stable RF carrier (frequency, Pavg, low noise)
- flexible modulation schemes
- well defined and uniform induced E- and H-fields (at cell culture)
- well defined environmental conditions
- fully characterized and minimized sources of artifacts (e.g., temperature load, vibration, EMC, EMI, etc.)
- all environmental and technical parameters continuously monitored
- uncertainty analysis

Conclusions (Modulations)

- CW
- arbitrary ELF modulations
- GSM:217Hz
- GSM basic
- GSM DTX
- GSM talk: GSM Basic: 66%; DTX: 34%
- GSM environment (Talk + Environment)
- UMTS constant power, i.e. no TPC
- UMTS TPC
- D-AMPS
- IS95
- IMT2000

All signals can be applied intermittent (on/off)!

Conclusions (Exposure Systems)

Current

- sXc900 (petri 35mm, monolayer, suspension)
- sXc1800 (petri 35mm, monolayer, suspension)
- sXc1950 (petri 35mm, monolayer, suspension)
- sXcTEM (900MHz, T45 flasks, suspension)
- wirepatch (900MHz, petri 35mm, suspension)

In Development

- sXc1800XL8
- sXcTEM (27MHz, T45 flasks, suspension)
- sXcTEM (900MHz, petri 35mm, suspension)
- sXcELF-LCI (life cell imaging)
- sXc1950=ICL (life cell imaging)

Acknowledgements

- This study was generously supported by
  - German Radiation Protection Agency (BfS)
  - European Union (5th Framework Program)
  - Swiss Agency for Education and Science (BBW)
  - Mobile Manufacturers Forum (MMF)
  - GSM Association (GSMA)