

Curriculum Vitae

Prof. Markus Rudin



Professor of Molecular Imaging and Functional Pharmacology
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Degrees/Higher Education

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| 1981 | Dr. sc. nat. (Physical Chemistry), ETH Zurich |
| 1976 | Diploma in Chemistry, ETH Zurich |

Professional Career

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| 2006–present | Professor of Molecular Imaging and Functional Pharmacology, Institute of Biomedical Engineering, Department of Information Technology and Electrical Engineering, D-ITET, ETH Zurich |
| 2005–present | Professor of Molecular Imaging and Functional Pharmacology, Institute of Biomedical Engineering, University of Zurich |
| 2000–2005 | Head Analytical & Imaging Sciences Unit, Novartis Institute of Biomedical Research, Basel |
| 1996–2000 | Director In vivo Models Unit, Novartis Pharma AG, Basel |
| 1993–1996 | Head Biophysics Unit, Preclinical Research, Sandoz Pharma AG, Basel |
| 1990–1993 | Head MRI Group, Preclinical research, Sandoz AG Basel |
| 1983–1990 | Head MR Laboratory, Preclinical Research, Sandoz AG Basel |

Professional Activities

- Member of the Research Council of the Swiss National Science Foundation
- Member of Program Committee of the International Society of Magnetic Resonance in Medicine 2007-9
- Member Steering Committee Neuroscience Center Zürich
- Co-Chair National Competence Center for Biomedical Imaging
- Advisory Board Singapore Biomed Imaging Center (A*Star)

Honors and Awards

- Fellow of International Society of Magnetic Resonance in Medicine 2011
- Novartis Leading Scientist Award 2003
- ETH Medal (PhD Thesis) 1981

Membership in Societies

- International Society for Magnetic Resonance in Medicine
- European Society for Magnetic Resonance in Medicine and Biology

- World Molecular Imaging Society (Trustee)
- European Society for Molecular Imaging (Council Member)
- Swiss Biomedical Engineering Society

Publications

- 147 Peer-Refereed Journal Publications
- > 200 Conference Publications
- 5 Books (4 as editor and contributor, 1 as author)

Achievements

- Development of small animal MRI and fluorescence molecular tomography methods
- Development of imaging approaches to study fundamental biological processes in vivo
- Integration of structural, functional and molecular imaging in drug discovery process
- Imaging-based functional phenotyping of genetically engineered mice

Committees

- SNF Research Council
- Steering Committee Zurich Neuroscience Center
- Steering Committee Center for Imaging Science and Technology
- Steering Committee National Center for Biomedical Imaging (NCCBI)

Teaching

- Biomedical Engineering A
- Biomedical Engineering B
- Molecular Imaging – Principles and Applications
- Seminars Biomedical Engineering
- Seminars Advanced MRI Methods
- Basic Pharmacology (Dental School)
- Basic Pharmacology (Medical School)
- Seminars in Pharmacology and Toxicology

Facilities and Major Equipment

- Biospec 94/30 (9.4 T) MR scanner with cryo-probe (CP) system
- Pharmascan 47/16 (4.7 T) MR scanner with CP
- Hybrid FMT-MRI system
- Fluorescence reflectance imager
- Fluorescence tomography system
- Animal housing facility

Keywords

- Magnetic Resonance Imaging
- Molecular Imaging
- Reporter Gene Assays
- Neural plasticity and repair
- Systems biology/physiology

Future priority areas

- Multimodal imaging
- Signal transduction pathways

For more information visit www.biomed.ee.ethz.ch

Molecular Imaging and Functional Pharmacology

Focus

The group Molecular Imaging and Functional Pharmacology is part of the Animal Imaging Center of UZH/ETH located at the ETH Hnggerberg campus. The AIC develops imaging technologies and imaging tools (probes, protocols, etc) for studying:

- anatomical structures at high resolution,
- physiological processes and functional imaging,
- study of molecular events such as gene expression, and protein function as reflected by activation of signaling pathways.

The combined use of multiplexed imaging technologies will enable a comprehensive characterization of biological systems.

Increase sensitivity in MR data acquisition using cryogenic detector systems

Studies in small rodents (mice) involve voxel volumes typically three orders of magnitude smaller than for clinical application with corresponding high demands for sensitivity. Therefore, one project of the group deals with increasing signal-to-noise ratios (SNR) per unit time. We have evaluated the performance of a cryogenic MRI probe for mouse brain imaging operating at 200 MHz in collaboration with Bruker BioSpin AG (Fllanden). Consistent sensitivity increases by factors 2-3 were observed for the cryoprobes as compared to matched detector systems operating at room temperature. New probe designs are being explored.

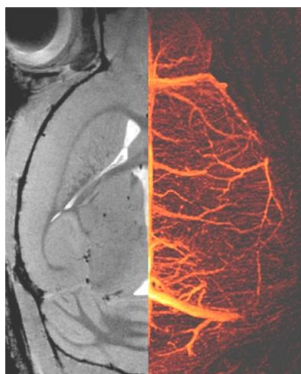


Figure 1:
Horizontal section through mouse brain using cryogenic detection device: gross morphological (left) and vascular anatomy (right) at 60um isotropic resolution

Hybrid MRI-fluorescence molecular tomography

While MRI is capable of providing excellent anatomical and physiological information it suffers from low sensitivity. In contrast, fluorescence displays high sensitivity but suffers from poor spatial confinement due to light scattering by tissue. The combination of MRI and fluorescence molecular tomography (FMT) would allow combining the strengths of the two modalities and is therefore attractive. We are developing hybrid FMT-MRI systems allowing for simultaneous measurement of structural/physiological and molecular information. The system comprises an MR transceiver coil comprising and or multiple optical detector arrays (SPAD or CMOS) for collecting the fluorescence signals. For excitation we adopted a free laser beam approach to allow for maximal flexibility in excitation patterns. Proof of principle has been established in using a murine tumor model, with MRI providing anatomical reference images and FMT assessing the presence of protease degrading enzymes in the tumor. Future developments are the implementation of improved detector systems, development of FMT reconstruction algorithm including anatomical information as priors, and development of multi-wavelengths systems.

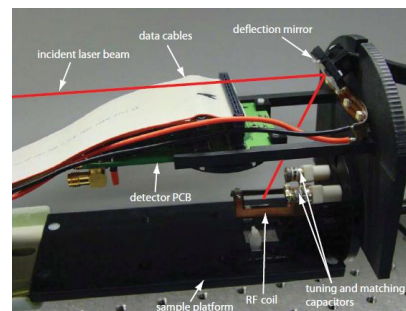


Figure 2: Prototype hybrid FMT-MRI system with an animal support comprising an MRI surface coil transceiver and a SPAD array for FMT.

Neuroscience: Readouts for neuronal activity

Conventional functional MRI (fMRI) measures changes in local blood oxygenation (BOLD contrast) associated with neuronal activation, i.e. a cerebro-vascular response to the stimulus and not the neuronal activation per se. As a consequence, changes in the fMRI response due to a pathological condition or a therapeutic intervention may reflect either a change in neuronal activity, a change in the efficiency of the neurovascular coupling or a combination of the two. Multiple readouts of CNS activity should allow elucidating the underlying mechanisms determining the signal. We have therefore implemented a hybrid setup allowing for the simultaneous measurement of calcium signals using fluorescence readouts and BOLD fMRI *in vivo*.

In collaborations with the neuroscience center fMRI techniques are being used to study structural and functional plasticity of the brain e.g. in response to focal lesions in of the central nervous system or under condition of chronic nociceptive input.

Molecular imaging: Systems physiology/ pathway imaging

The aim of the project is to develop a reporter gene assay that allows visualization and quantification of hypoxia signaling, which is a critical step e.g. in tumor development leading among others to the formation of a tumor vascular network. Hypoxia is triggers the stabilization of hypoxia inducible factor-1 (HIF1), which leads to the expression of more than a hundred genes involved in angiogenesis, glycolysis, inflammatory response, tissue infiltration, etc.. We have developed multiplex PET-FMT-MRI approaches visualizing these processes under *in vivo* conditions (Fig. 3), which led to the surprising finding that hypoxia and 'hypoxia signaling' are not well correlated.

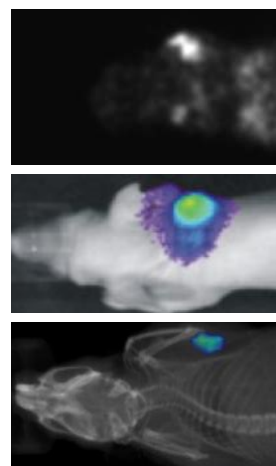


Figure 3: Multimodal imaging of hypoxia signaling. Images reflect three key steps in hypoxia signaling in murine tumor model: assessment of tumor hypoxia as initial trigger using PET (top), stabilization of key regulator of signaling, HIF1, using bioluminescence (middle) and downstream activity of HIF using SPECT imaging (bottom). Simultaneous imaging at various levels of signal transduction cascade will help to elucidate underlying biological mechanisms.