NMR Imaging Facility

double-resonant $^{1}H/^{129}Xe$ probe head

wide bore NMR spectrometer

MRI experiments are prformed on a 400 MHz widebore solid-state NMR spectrometer with an imaging upgrade. The gradient system is able to achieve amplitudes of 100 G/cm.

Several microimaging coils with diameters ranging from 5 to 30 mm are used for rf excitation and detection. All coils are tunable to ^{1}H frequency and some include a second resonator tunable to ^{129}Xe and ^{23}Na. The rf system includes two 300 W amplifiers for proton and X-nuclei excitation, respectively. A VT unit is available to run experiments at different sample temperatures

The group also has access to the 400 MHz animal MRI scanner a the Experimental and Clinical Research Center (ECRC).

head MRI of a newborn mouse

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Research Focus at FMP

FMP at Campus Berlin-Buch

The Leibniz-Institut für Molekulare Pharmakologie (FMP) is located on the Campus Berlin-Buch and maintains close relationship with the various universities of Germany's capital.
FMP research focuses on the structures, functions and interactions of proteins and on the development of new concepts for interfering pharmacologically with their functions.

An interdisciplinary approach is crucial for this work, and a particular strength of the FMP is the close interaction in the fields of chemistry and biology. The unique combination of technology platforms at the FMP, including a state-of-art NMR facility, an open screening unit and a mass spectrometry lab, provides an ideal environment for research projects that strive to discover new biologically active substances.

in-house developments for novel NMR approaches

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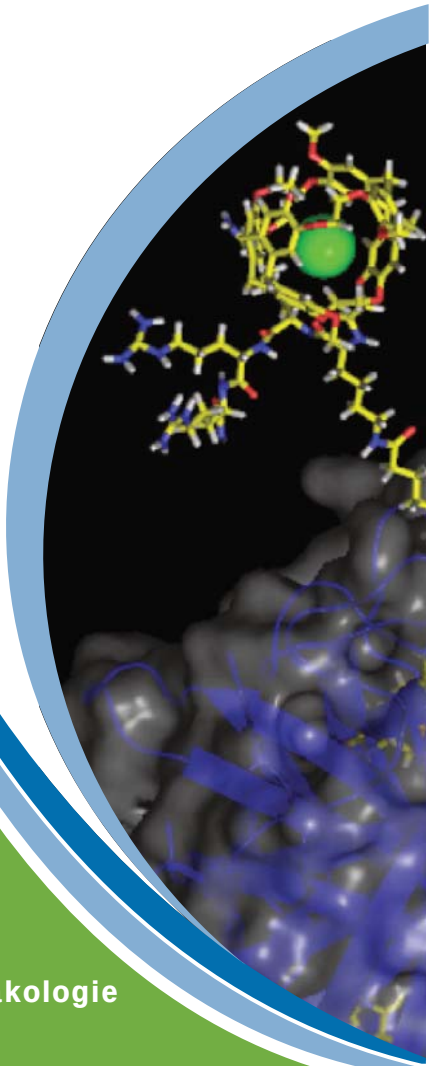
ERC Project

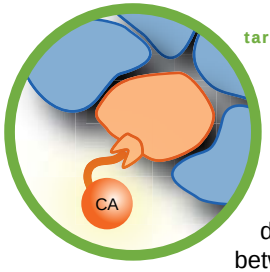
BiosensorImaging

A Novel Approach for Molecular Imaging



Leibniz-Institut für Molekulare Pharmakologie

Magnetic Resonance in Diagnostic Imaging



targeted contrast agent for cellular marker

The focus of pharmacoligical research, i.e., the understanding of drug action, would benefit substantially from imaging modalities that directly visualize interactions that occur between a living organism and chemicals. Conventional diagnostic imaging reveals changes in morphology or organ function that occur much later than impacts on the molecular level. The emerging field of molecular imaging aims to focus on such early responses where the biochemical pathways are well known.

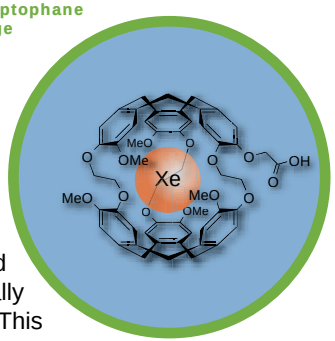
Nuclear Magnetic Resonance Imaging (MRI) is one of the most powerful modalities in biomedical imaging with several advantages over other methods such as fluorescence microscopy or radioactive approaches like PET and SPECT. MRI can contain biochemical information that unambiguously identifies the molecular origin of the signal. However, conventional MRI suffers from intrinsic low sensitivity – an aspect that is usually accounted for by detecting the water proton signal in biological samples. Overcoming these limitations can make MRI an important tool to visualize prosesses investigated in phamacological studies.

The BiosensorImaging project aims to establish a novel approach of molecular MRI detection for improving drug development and therapy monitoring. The combination of conventional proton MRI with its superior soft-tissue contrast for morphological information and the development of targeted contrast agents that reveal the presence of biochemical markers at high sensitivity will allow better understanding of pharmacological processes in the living organisms.

abdomen
MRI of a mouse

Xenon Biosensors

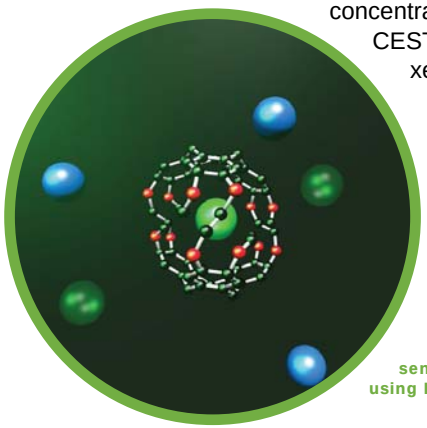
cryptophane cage



NMR signals of the noble gas xenon are extremely sensitive to their molecular environment. In order to make this sensing ability available for NMR contrast agents, xenon can be trapped in functionalized molecular cages that specifically bind to a certain analyte. This combines the high sensitivity from hyperpolarized nuclei with the excellent biochemical specificity of the targeting moiety.

We functionalyze cryptophan cages to enable binding events of these xenon hosts to targets of biochemical relevance such as cell surface receptors. Since the xenon is not bound covalently to the cage, the sensor can be dilivered in advance, independent of the hyperpolarization lifetime.

A novel detection method called Hyper-CEST (chemical exchange staruation transfer with hyperpolarized nuclei) yields a huge sensitivity enhancement and allows to detect target concentrations < 1 pM. Hyper-CEST exploits the fact that xenon is only bound temporarily to the cage, thus allowing to transfer cage-related information onto thousands of nuclei.



sensitivity enhancement using Hyper-CEST detection

"... the work could offer exciting possibilities for biomedical imaging" — **Nature Biotechnology**

"MRI technology breaks new ground in molecular imaging" — **US National Cancer Institute**

"Heat gives 'hyper' MRI jolt of speed and sensitivity" — **R&D News**

Production of Hyperpolarized Xenon

LEIPNIX polarizer

For the flexible production of hyperpolarized xenon we developped a new design for a mobile setup that can be used at different NMR scanners.

Spin exchange optical pumping (SEOP) is performed with a new type of line-narrowed la-ser diodes emitting at high power levels (>100 W) in cw mode. The polarization optics work with a single beam line, achieving a circular polarization degree of 99.99%. This ensures very efficient optical pumping of rubidium vapor.

The relative compact design of the LEIPNIX setup (Laser Enabled Increase of Polarization for Nuclei of Imprisoned Xenon) is optimized for continuous flow applications that allow for permanent production of solutions saturated with hyperpolarized xenon for encapsulation in molecular cages. A xenon spin polarization of ca. 16% is delivered in samples with a signal instability of less than 1%.

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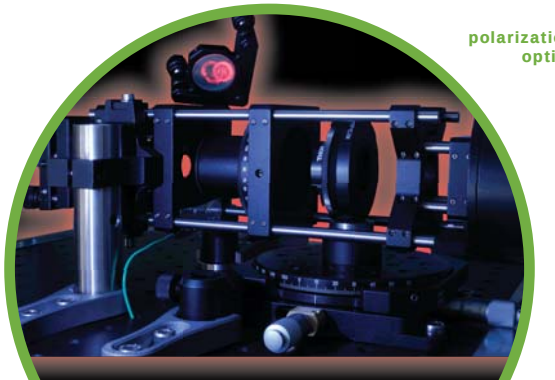

polarization optics