Division of Translational Molecular Imaging
A Physics-Based Approach to Boost MRI

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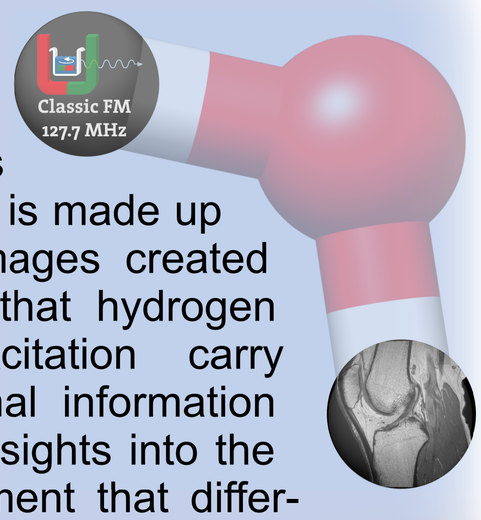
Research for a Life without Cancer

Challenges of Conventional MRI

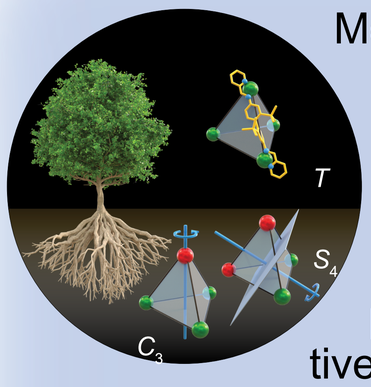
Conventional MR relies on the tiny magnetization of abundant molecules and works only because the body is made up of 70% water. The images created from the radio signal that hydrogen nuclei emit after excitation carry anatomical and functional information but give rather limited insights into the molecular microenvironment that differentiates tumor from healthy tissue.



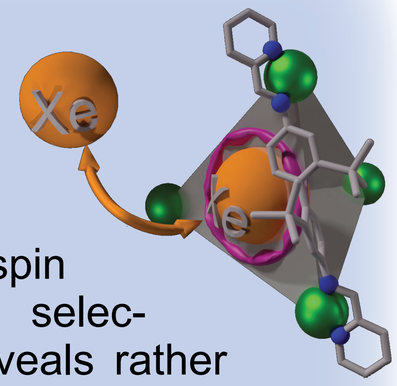
The most significant limitations are:

- 99.9997% of the molecules effectively do not send a signal
- water is not tumor specific
- a tumor at initial diagnosis typically measures 1 cm in size and contains 1 billion cells

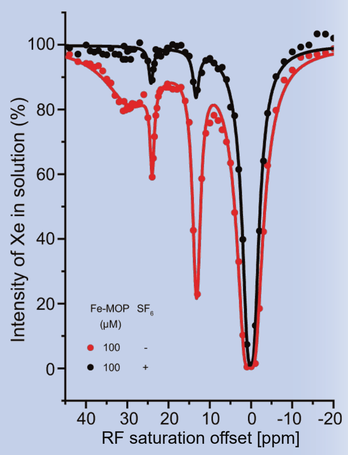
Molecular Hosts as Switchable Spin Gates



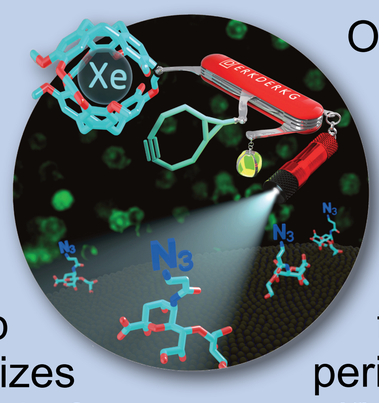
Molecular host structures are investigated for transient trapping of highly polarized ^{129}Xe spins. The spin polarization can be selectively destroyed and reveals rather dilute and "hidden" molecular structures through highly efficient chemical exchange with unbound Xe.



Some of these hosts can be functionalized with a tergeting unit (e.g., an antibody) that provides affinity for a molecular target and enables MRI scans with switchable contrast.



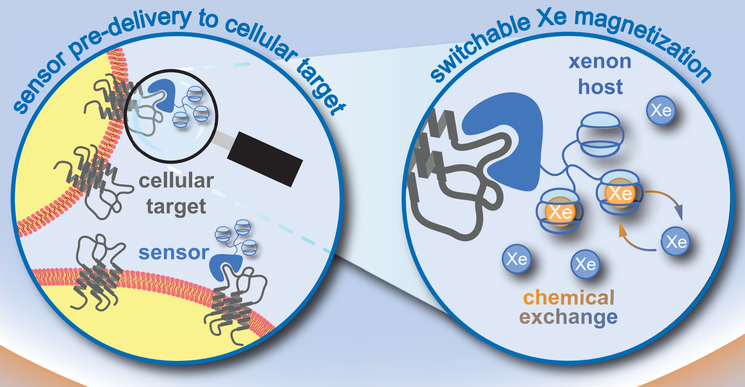
Biosensor Concept



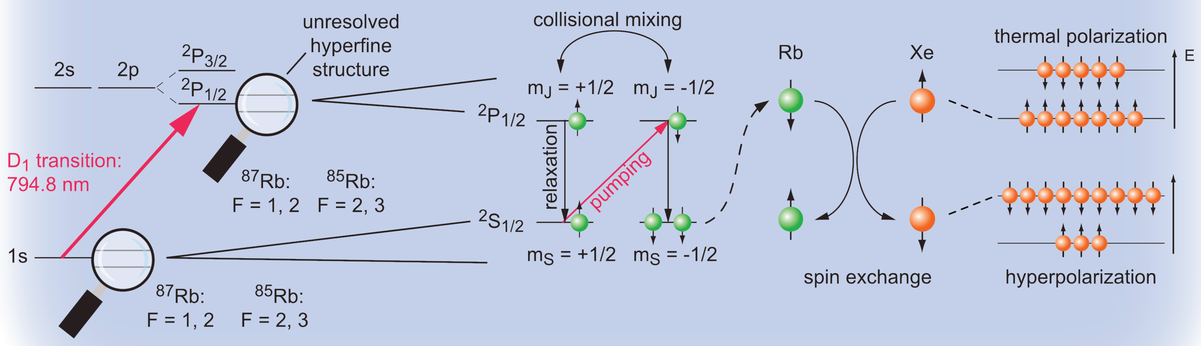
We develop molecular reporters to track specific markers like cell surface glycans or transmembrane proteins in deep tissue. This visualizes tumor-specific alterations before these would cause any changes in the tissue water signal.

Our approach relies on the concept that we detect either actively driven or intrinsic changes that the magnetization experiences upon entering a specific molecular environment. Methods are primarily developed for ^{1}H, ^{129}Xe, and ^{19}F MRI.

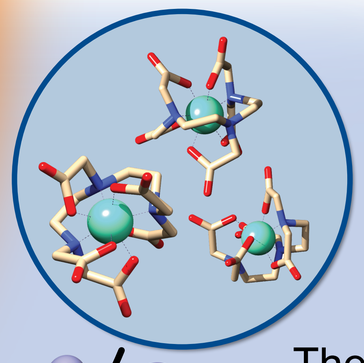
To achieve outstanding sensitivity, we make optimum use of the spin-carrying units. Hyperpolarization is an emerging technique that provides 10^4-fold enhancement of the magnetization. We combine this with another 10^3-fold boost from chemical exchange saturation transfer (CEST). This enables HyperCEST MRI with sensors that spontaneously self-assembe in situ to track targets beyond the limited lifetime of hyperpolarization.



The interaction of circularly polarized infrared light with rubidium vapor in the presence of a magnetic field generates highly polarized Rb electron spins. These are brought in contact with ^{129}Xe to obtain a strongly magnetized, harmless noble gas outside the MRI magnet. This can be dispersed into solutions or be delivered via lung inhalation. Such hyperpolarized ^{129}Xe in solution can be detected at ca. 1.8-million-fold dilution compared to water protons used in conventional MRI.

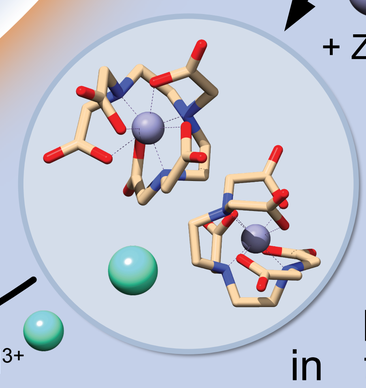


Hyperpolarized Spin Systems



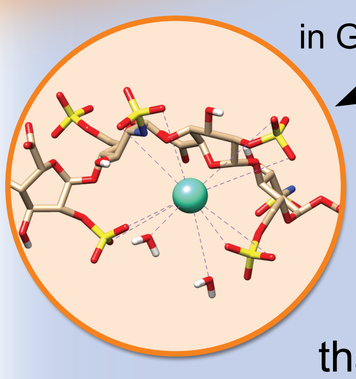
trans-metallation

+ Zn^{2+}



re-chelation in GAGs

Gd^{3+}



There is increasing evidence in MRI exams that the dissociation of contrast agents in vivo can lead to long-term depositions of Gd^{3+} in tissue. New insights into kinetics and thermodynamic equilibria of underlying processes are needed.

We apply time-resolved MRI relaxometry that exploits distinct relaxivities of Gd^{3+} in different molecular environments. Opposing indirect impacts of alternative chelators like polysaccharides on increasing the kinetic stability but reducing the thermodynamic stability of GBCAs could be identified.

Molecular Interactions of Paramagnetic Ions

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