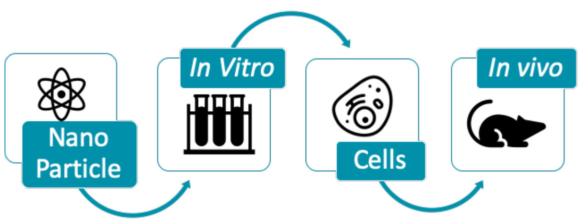
RELAX: Particle Relaxometry Module

The RELAX Module

The RELAX package for the MOMENTUM™ Magnetic Particle Imaging (MPI) system, is a tool developed for researchers designing new nanoparticles and tracers specific to MPI applications.

It runs using the same magnetic properties as MOMENTUM to give an indication of how magnetic nanoparticles will behave during imaging. By measuring the magnetic relaxation properties of novel nano-systems, researchers can predict and fine-tune properties like resolution or sensitivity before starting expensive *in vivo* investigations.

RELAX is the perfect tool to stage experiments from particle development to *in vivo* acquisitions on the same system, ensuring success at every step.



What is relaxometry?

Superparamagnetic iron oxide particles (SPIOs) used in MPI follow two distinct modes of relaxation: Néel and Brownian.

Néel relaxation: This describes the internal net magnetization change of a particle to from one orientation to another without physical rotation of the particle. This parameter is mostly affected by the particle's composition and temperature and occurs on a timescale of nanoseconds.

Brownian relaxation: This represent the physical rotation of the particle in space and is dependent on temperature, the particle size, and the viscosity of the surrounding. This rotation happens on a scale of microseconds.

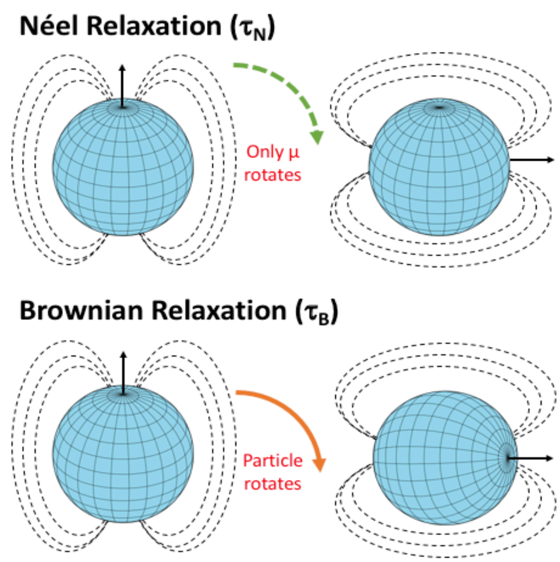


Figure 1 - Difference between Néel and Brownian ***relaxation.*** *Néel relaxation is a change in the magnetization of the particle (without movement), while Brownian relaxation is a physical rotation of the particle without a change in the internal magnetization of the particle. (adapted from [1]).*

A relaxometer is a device that is used to measure the actual magnetic relaxation (composite of both Néel and Brownian relaxations) for a specific sample. The device measures the net magnetization (M) of the sample in presence of a varying applied magnetic field (H) as it runs from negative to positive and back (Figure 2).

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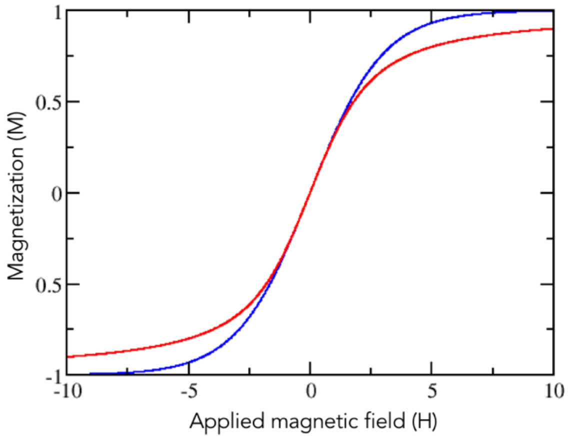

Figure 2 – Langevin curve for the RELAX experiment. When H is highly negative, the magnetization M starts in a saturated state. As H in increased (from left to right), M desaturates to reach a linear transition with H around 0. As H continues to increase, M re-saturates to the same intensity with opposite polarization. The same process occurs when H decreases (from right to left). Image from [2].

For high negative values of the applied field H, the magnetization of the sample is saturated at a low value (left side of the curve). The field is then increased towards 0 mT. As the applied magnetic field is close to 0, there is a linear transition where the magnetization measured is proportional to the applied field. Past a certain threshold, the magnetization starts to saturate again, aligning itself to the applied field. This experiment traces the Langevin function specific to the particle tested.

The RELAX module measures the net magnetization for a field sweep (H) between -100 and 100 mT and a 20 mT excitation field, the same parameters that are used on the MOMENTUM MPI system during image acquisition. The output of RELAX is the derivative of the Langevin function seen in Figure 3, which is also called the point spread function (PSF).

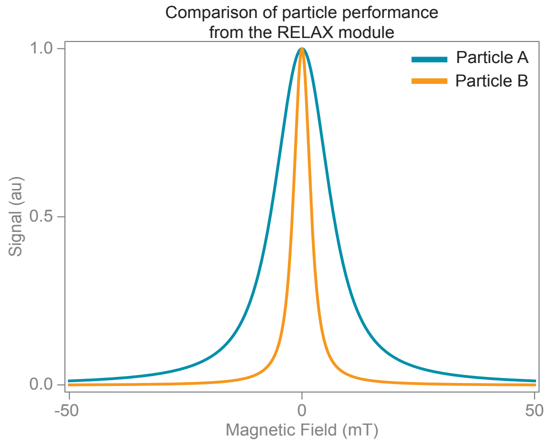

Figure 3 – Peak-height normalized RELAX curve for 2 different particles. In this case, particle B has a much greater intrinsic resolution because of its smaller FWHM.

How to read a PSF

There are two important parameters to consider when looking at a point spread function: the signal intensity (height), which reflects the sensitivity of the particle, and the full-width half-maximum (FWHM), which is related to the resolution for that particle.

A specific particle is said to be more sensitive when it gives a higher signal for the same amount of iron. To compare the FWHM for two different particles, it is necessary to normalize the signal obtained by the concentration of the sample, since the more iron there is in the sample, the higher the signal will be.

For a homogenous population of purely Néel-relaxing small particles, the transition is close to a step function. The point-spread function is broadened by the variations in particle size, the apparition of core sub-domains, and the particle's Brownian relaxation motion. The FWHM of the PSF is measured in Tesla (T). The MPI image resolution in millimetres can be

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estimated by dividing the FWHM of the PSF by the imaging gradient strength (Typically 5.7 T/m on a MOMENTUM system using default mode scanning).

Ideal Particle size

According to Langevin model theory, the bigger the particle with a single core, the smaller the FWHM of the point-spread function.

Unfortunately, as cores get bigger, their Brownian relaxation also increases. In addition, cores can start showing multiple domains which will not transition at the same time. Both phenomena will increase the FWHM and affect the intrinsic resolution. An empirical ideal core size was estimated around 27 nm and was described as the Langevin wall [3] but this is highly dependent on particle design. This is why RELAX is a useful tool for new particle optimization before *in vivo* testing.

Potential Applications

In addition to being useful for nanoparticle development, RELAX can also be used to measure the effects of the nanoparticle environment on relaxation. Brownian relaxation will be affected by changes in the environment surrounding the nanoparticle (viscosity, temperature, hydrogen bonding, etc). RELAX can also be used to investigate particles that are designed to bind, as their motion and therefore their Brownian relaxation properties will change. This can be used to assess *ex vivo* or *in vivo* binding to a target, or even percentage of effective biding.

When developing new particles, it is recommended to use RELAX on the particles and their potential substrates, and in cells or organoids, to best predict the particles behavior *in vivo*.

Summary

The RELAX module measures the net magnetization of a sample with varying applied filed. This is used to predict the image sensitivity and contrast that will be attainable when imaging new particles in the MOMENTUM MPI system.

Furthermore, RELAX can help design new experiments *in vitro* to probe microenvironment and binding properties before translating them *in vivo* successfully.

References

[1] M. H. Pablico-Lansigan et al. Nanoscale, 2013
[2] L. M. Bauer et al. J. Phys. Chem. Lett., 2015
[3] Z. W. Tay et al. Biomed Phys Eng 2018

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