

A toolkit for dynamics *relaxing* the BMRB



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General overview of relax

The program *relax* [1,2,3] (<http://nmr-relax.com>) is designed for the study of the dynamics of proteins and other macromolecules through the analysis of NMR relaxation data. It is a flexible open source toolkit focused on experimental molecular dynamics, as investigated by NMR. *relax* is controlled via special user functions either by the built in python prompt or by powerful python scripting.

Supported NMR theories

A number of data analysis techniques are supported by *relax* including:

- Exponential curve fitting (for finding the R_1 and R_2 relaxation rates) and steady-state NOE calculation
- Reduced spectral density mapping
- Lipari-Szabo model-free analysis

The power of open source

The *relax* source code is licensed under the GNU General Public License (GPL). This ensures that the program will never disappear, all resources will be permanently reachable at <http://gna.org/projects/relax>. It also allows everyone to modify, fix, or expand the code to suit their needs. The benefits include a solid framework and toolkit for rapid development using one the simplest programming languages for non-coders to learn. As the program is freely available to all NMR spectroscopists on all operating systems (including Linux, OS X and Windows), the new analysis will be easily accessible for others to test and use, maximising its distribution and use.

Interfacing with the *minfx* optimisation library

relax uses the *minfx* optimisation library for numerical optimisation. Its many built in algorithms are all available within *relax*. These include line search, trust region and conjugate gradient methods, step selection subalgorithms, hessian modifications, as well as grid search, Levenberg-Marquardt and simplex algorithms.

General overview of relax (continued)

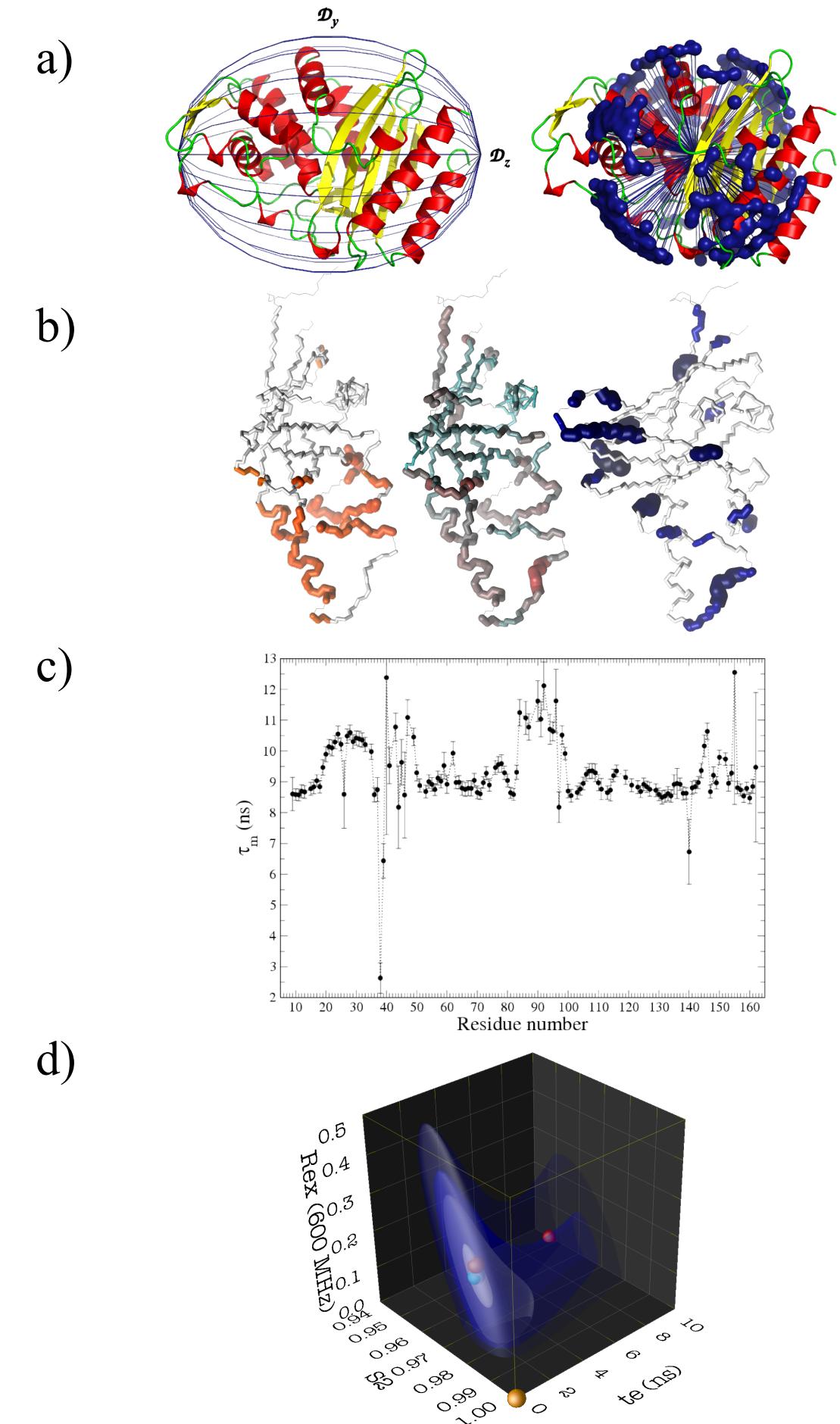
Data visualization

The results of an analysis, or any data input in *relax*, can be visualised using a number of programs:

- a) [PyMOL](#)
(for geometric objects, such as the diffusion tensor)
- b) [MOLMOL](#)
(for 1D data, such as S₂ values)
- c) [Grace](#)
(for 2D data, such as local τ_m as a function of residue number)
- d) [OpenDX](#)
(for 3D data, such as the χ^2 space for optimisation surface visualisation)

Interfacing with other model-free analysis programs

relax can create the input files, execute in-line, and then read the output of both [ModelFree4](#) and [Dasha](#) effectively using these as replacement model-free optimisation engines.



Relaxation data consistency

The open source framework has allowed a new data analysis type to be added by Sébastien Morin [4].

This analysis checks the consistency of experimentally measured, multiple-field spin relaxation data, allowing the quality of the data to be assessed prior to model-free analysis.

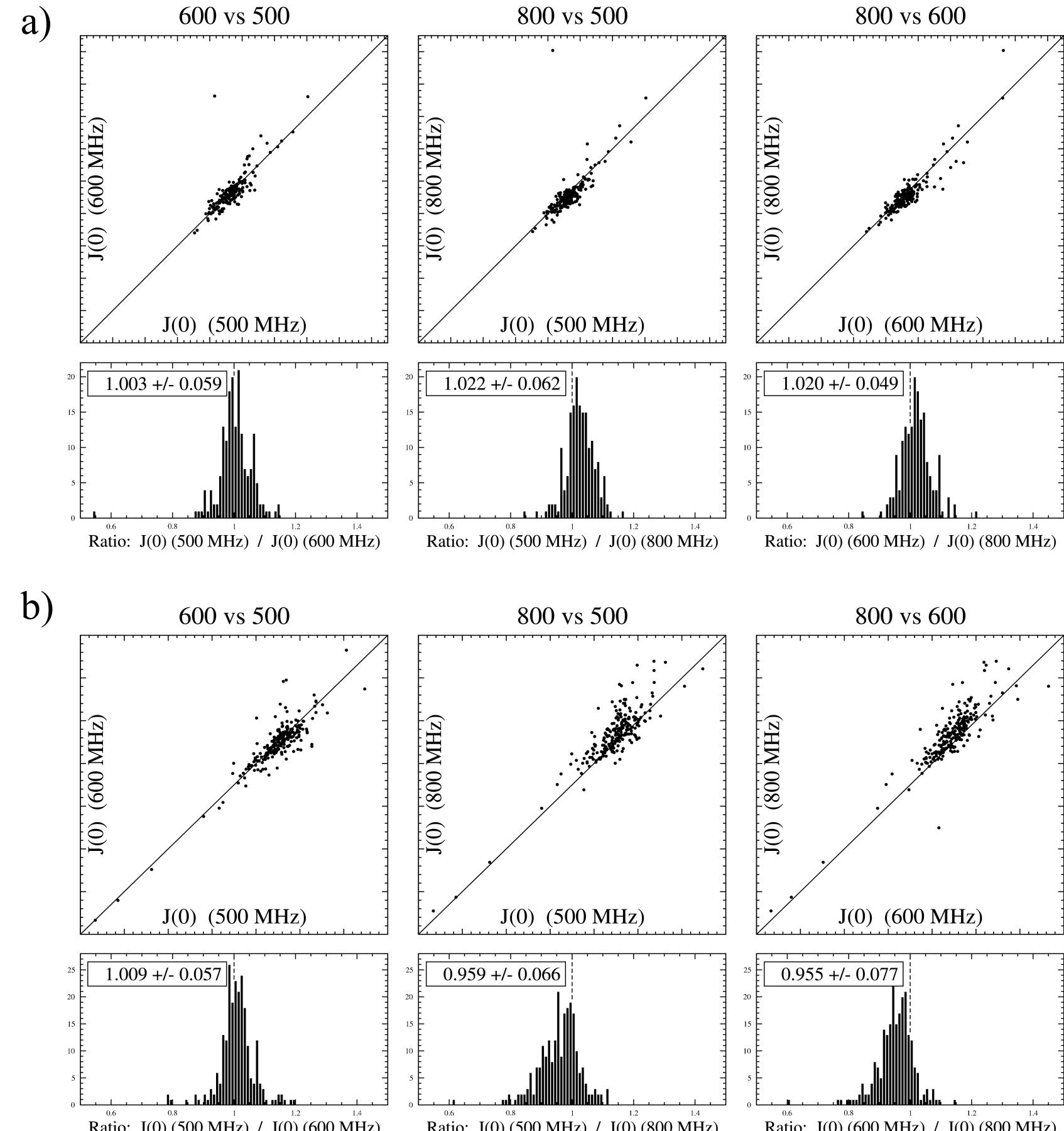
More specifically, it is the R_2 data quality that is being probed by these $J(0)$, F_{R_2} and F_η tests.

Excluding inconsistent R_2 data from a model-free analysis yields improved results since R_2 affects diffusion tensor optimisation as well as model selection, especially when inconsistencies introduce artificial conformational exchange (R_{ex}) terms.

The figure shows $J(0)$ consistency tests results for two different situations:

a) A three-field dataset of high consistency.

b) A three-field dataset of lower consistency, with problems arising from inconsistent 800 MHz R_2 data.



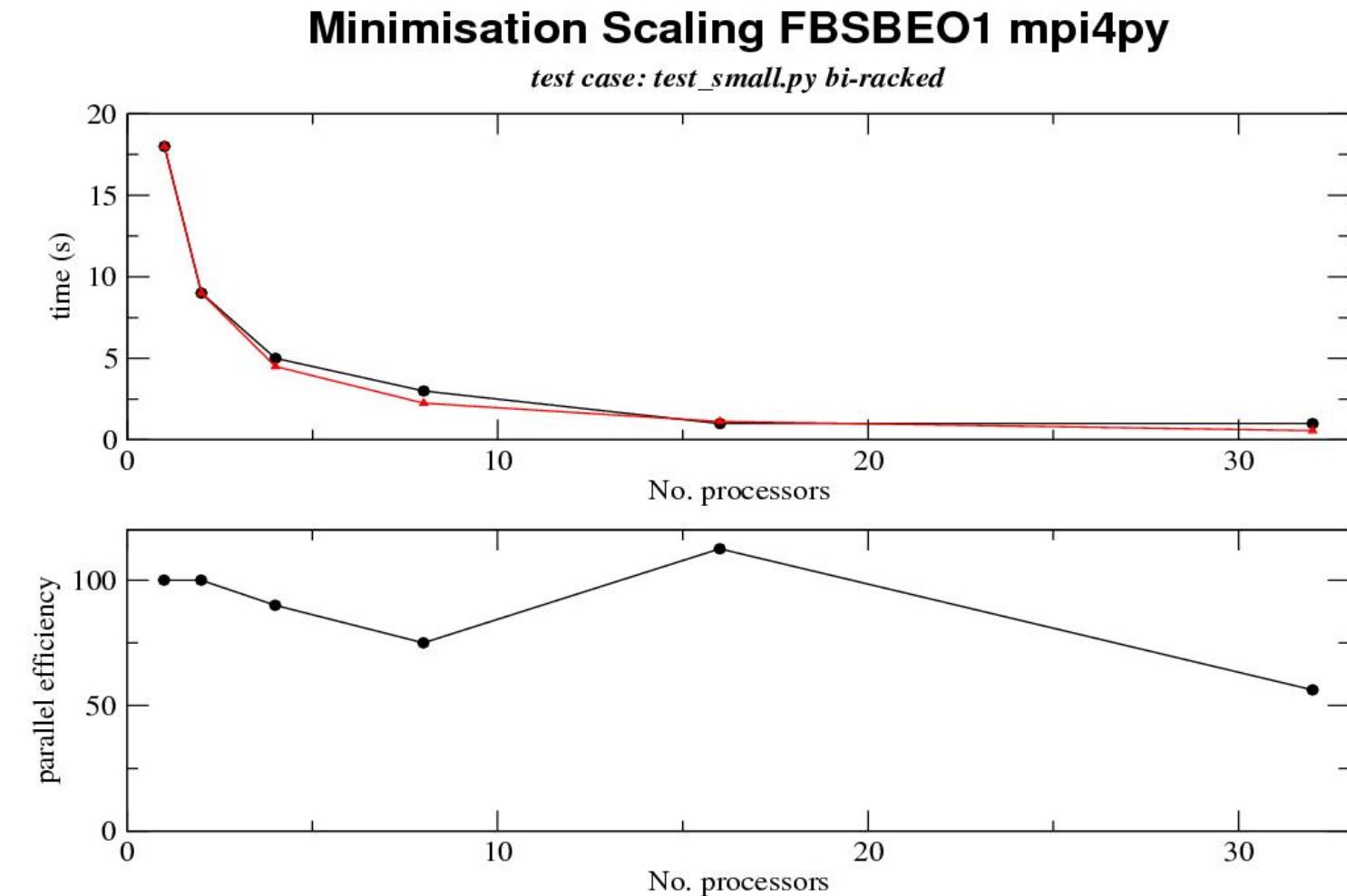
The multi-processor development branch

Sitting within the *relax* source code repository is a special branch developed by Gary Thompson.

This is the fully functional multi-processor code allowing *relax* to execute on clusters through the Message Passing Interface (MPI).

The figure demonstrates the scaling efficiency where the red line is the expected run times with perfect scaling efficiency and the black line is *relax*'s scaling efficiency.

This branch can be accessed from the code repository at <http://svn.gna.org/svn/relax>.



The rhombic chemical shift tensor (CST) development branch

Still a work in progress, another branch is being developed by Pavel Kadeřávek and Petr Novák for handling the non-colinearity of the rhombic chemical shift tensor and the multiple dipolar interaction mechanisms in RNA and DNA.

The relaxation dispersion development branch

Finally, another branch is being developed by Sébastien Morin for analysis of relaxation dispersion data for probing the slow μ s-ms-s motions known as conformational (or chemical) exchange. The aim is to support both CPMG and $R_{1\rho}$ data to be analysed as either slow, intermediate or fast exchange.

Making dynamics data useful

A real problem with dynamics data from NMR, specifically fast ps-ns motions, is understanding the link between motions and molecular function.

One cause of this problem is an absence of access to basic data preventing further analysis to be performed. In contrast to dynamics, the utility of chemical shifts and macromolecular 3D structures is assured by their presence in the BMRB (<http://www.bmrb.wisc.edu>) and PDB (<http://www.pdb.org>) databases, respectively. Without this required deposition, published structures and chemical shifts would practically be simply pretty pictures.

Compared to the 100% deposition rates for shifts and structures, the deposition of dynamics data is relatively meager.

Hence, there is a real need for dynamics data deposition.



relaxing the BMRB

A collaboration between the BMRB and *relax* is in progress with the goals of simplifying the BMRB deposition process for NMR relaxation data and of improving the flexibility and completeness of the NMR-STAR data model.

BMRB NMR-STAR dictionary v3.1

The NMR-STAR dictionary (ontology) is being redesigned on the basis of theory to better represent NMR relaxation and model-free dynamics data in a software independent way. Changes include the creation of new data categories (e.g. 'General_relaxation') for better deposition, archiving, and distribution of new types of relaxation data, and the renaming of the old saveframe 'Order_parameter' to 'Model_free' to allow for SRLS theory and the Jens Meiler model-free order parameters of RDC data, and numerous other additions to improve the value and utility of the deposited data.

The changes and additions will be released soon as v3.1 of the NMR-STAR dictionary.

The modifications to *relax*

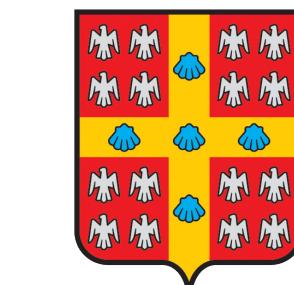
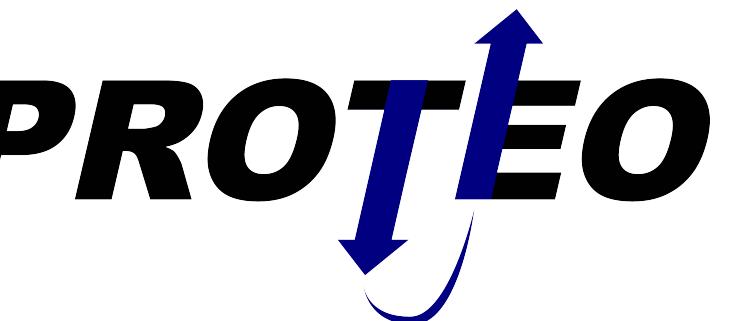
A number of changes within *relax* are being introduced by Edward d'Auvergne to facilitate data deposition.

Once a model-free analysis has been performed, creating a single file for BMRB submission containing all relaxation and model-free data will be as simple as loading the final results into the program and then executing a single user function called `bmrblib.write()`. Missing data, such as information about temperature control settings, etc., will be identified in the process. To support this simplicity, a new python API (`bmrblib`) between *relax* and the NMR-STAR parsing library `pystarlib` (<http://code.google.com/p/pystarlib>) is being created to support the NMR-STAR dictionary.

With *relax*'s support for reading `ModelFree4` and `Dasha` outputs, together with support for the creation of NMR-STAR v3.1 files, deposition of relaxation and model-free data to the BMRB will become a very quick and simple operation.

References

- (1) d'Auvergne, EJ & Gooley, PR (2008). Optimisation of NMR dynamic models I. Minimisation algorithms and their performance within the model-free and Brownian rotational diffusion spaces. *J. Biomol. NMR*, **40**(2), 107-119. → reprint available
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- (3) d'Auvergne, EJ (2006). Protein dynamics: a study of the model-free analysis of NMR relaxation data. Ph.D. thesis, Biochemistry and Molecular Biology, University of Melbourne. (*Available in paperback form from amazon.com*).
- (4) Morin, S & Gagné, SM (in press) Simple tests for the validation of multiple field spin relaxation data. *J. Biomol. NMR*. (DOI 10.1007/s10858-009-9381-4) → reprint available



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