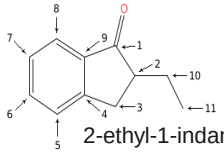
NMR Applications
Biological Science

http://nmr.vuw.ac.nz

Chemical structure analyses

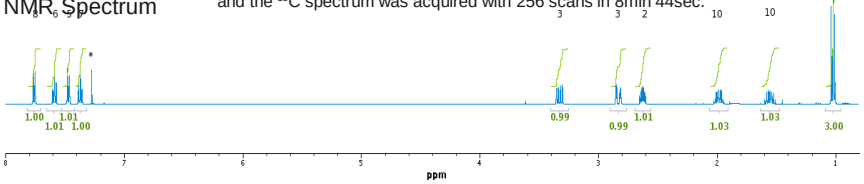


2-ethyl-1-indanone

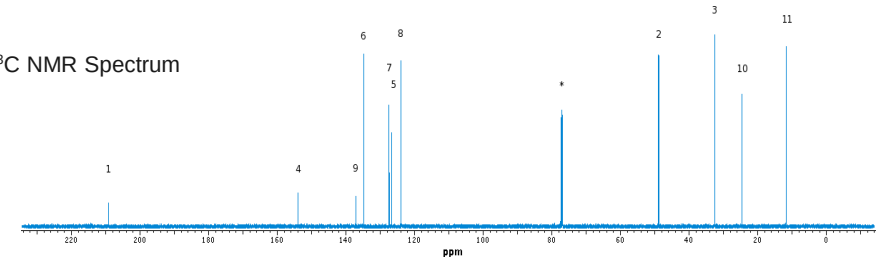
A sample of 2% 2-ethyl-1-indanone in $CDCl_3$ was used to acquire all these examples.

The 1D spectra on this sample were easily acquired, as the sample is quite concentrated (~128mM). The ^1H spectrum was acquired with a single scan, and the ^{13}C spectrum was acquired with 256 scans in 8min 44sec.

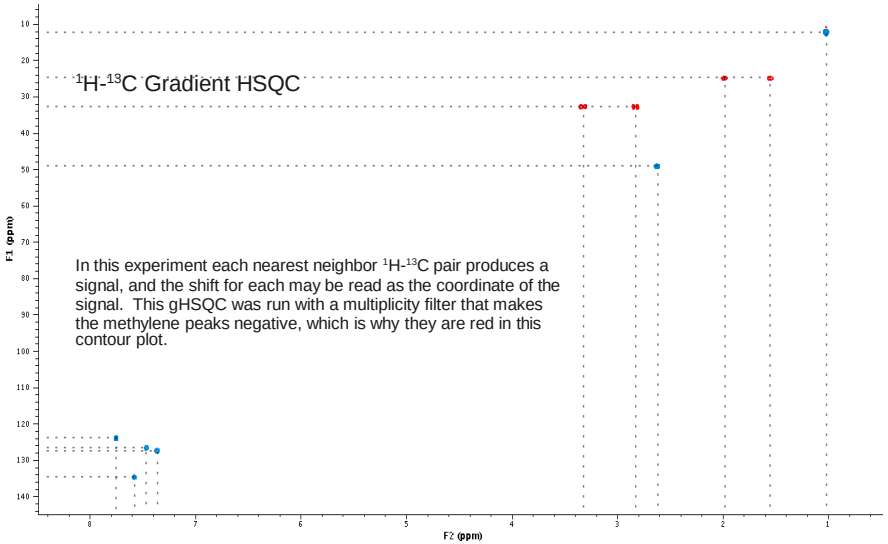
^1H NMR Spectrum



^{13}C NMR Spectrum



^1H-^{13}C Gradient HSQC



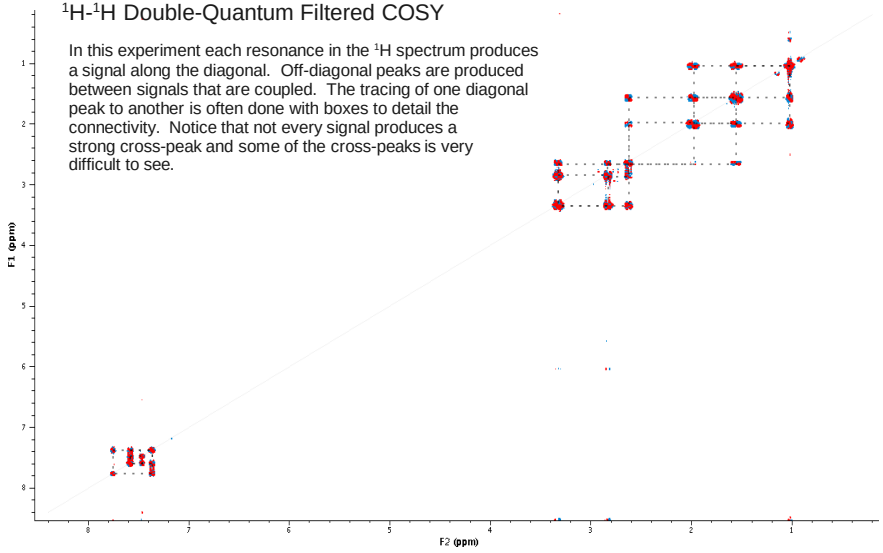
In this experiment each nearest neighbor ^1H-^{13}C pair produces a signal, and the shift for each may be read as the coordinate of the signal. This gHSQC was run with a multiplicity filter that makes the methylene peaks negative, which is why they are red in this contour plot.

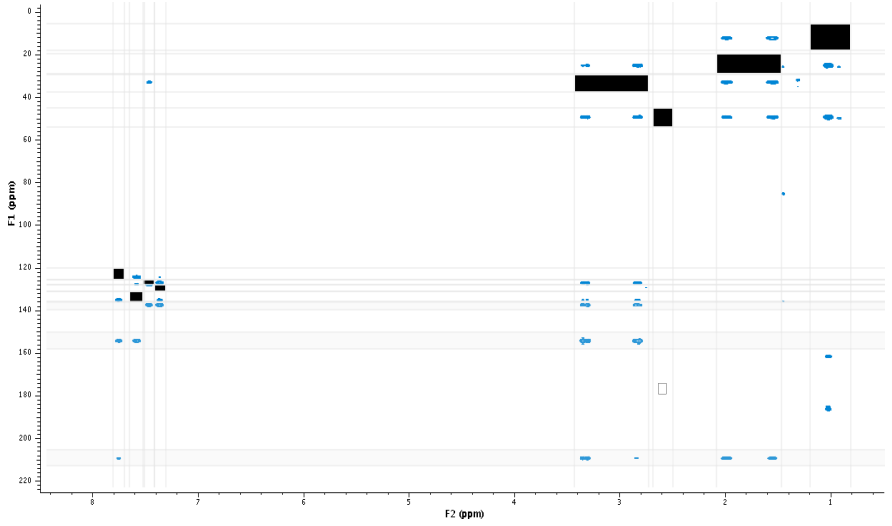
^1H-^{13}C Gradient HMBC

In this experiment signals are produced by ^{13}C atoms coupled to ^1H that are not directly attached. Typically, the experiment is set up to show couplings between next nearest neighbors (^2J couplings). The spectrum is deciphered below with intersecting boxes, the black fields have no signal as they would are where a nearest neighbor (^1J) coupling would exist. Notice that the quaternary carbons, which produced no signal in the HSQC above, do show up here and are highlighted in gray.

^1H-^1H Double-Quantum Filtered COSY

In this experiment each resonance in the ^1H spectrum produces a signal along the diagonal. Off-diagonal peaks are produced between signals that are coupled. The tracing of one diagonal peak to another is often done with boxes to detail the connectivity. Notice that not every signal produces a strong cross-peak and some of the cross-peaks is very difficult to see.





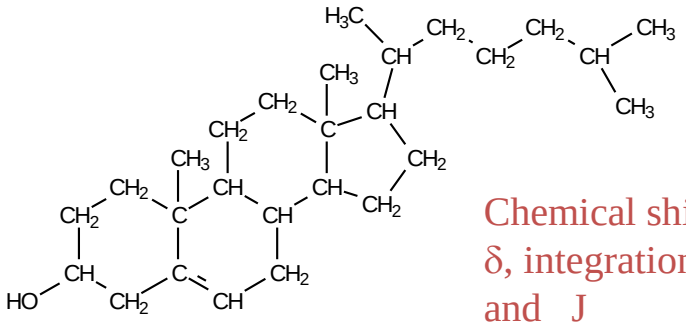
Stereo Chemistry

Because NOE can reveal 1H spins that are in proximity in 3D space, it is often used to assist research on the stereochemistry of organic compounds

Chemical structure

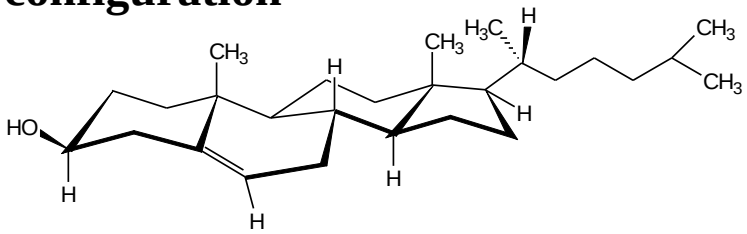
^{1}H: 46 hydrogen atoms

^{13}C: 27 carbon atoms.



Chemical shift δ, integration, and J correlations

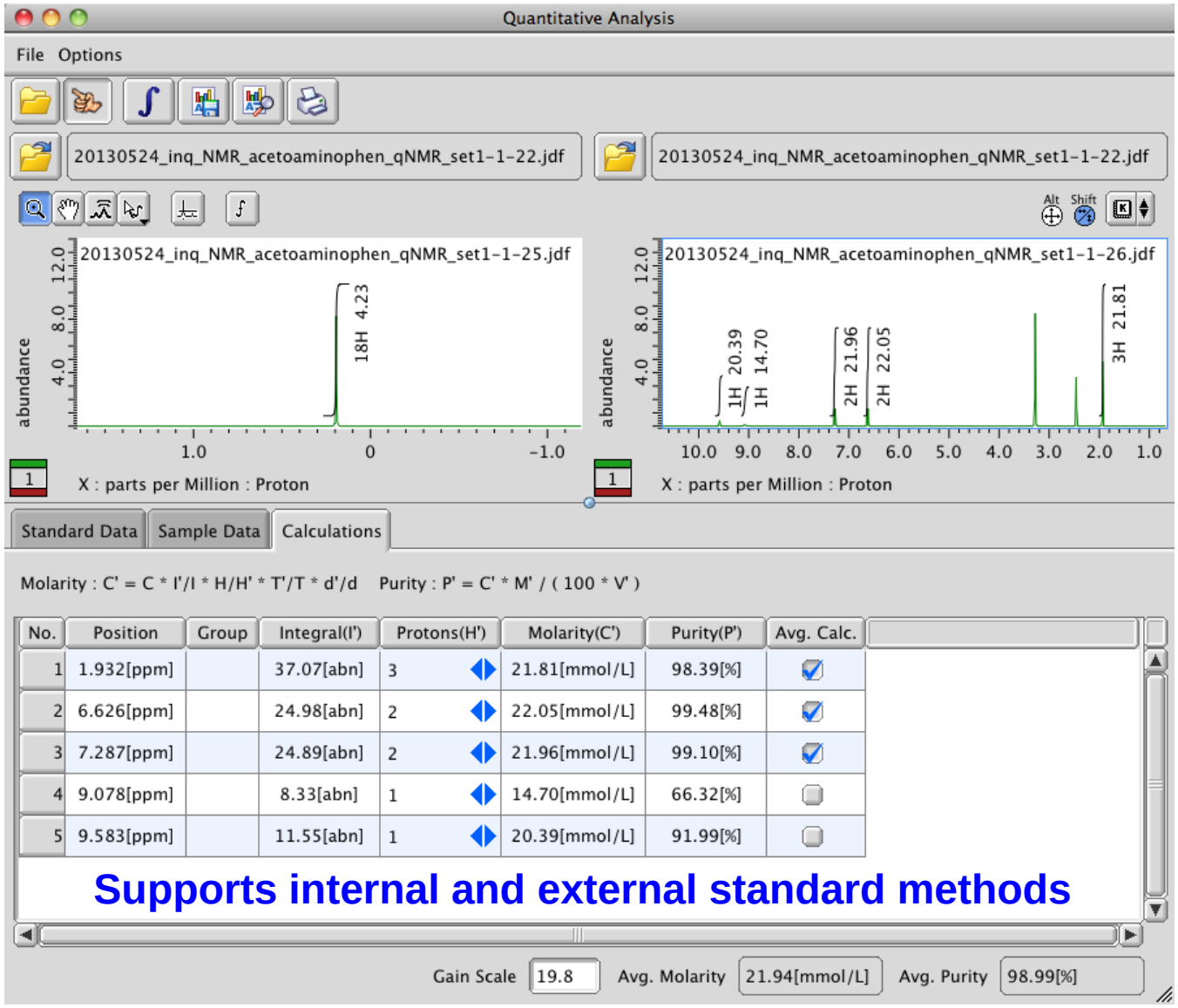
Relative configuration



^{1}H-^{1}H splitting and NOE

A BEGINNER'S PRIMER ON NOE MEASUREMENT INSIGHTS INTO 3D STRUCTURE.

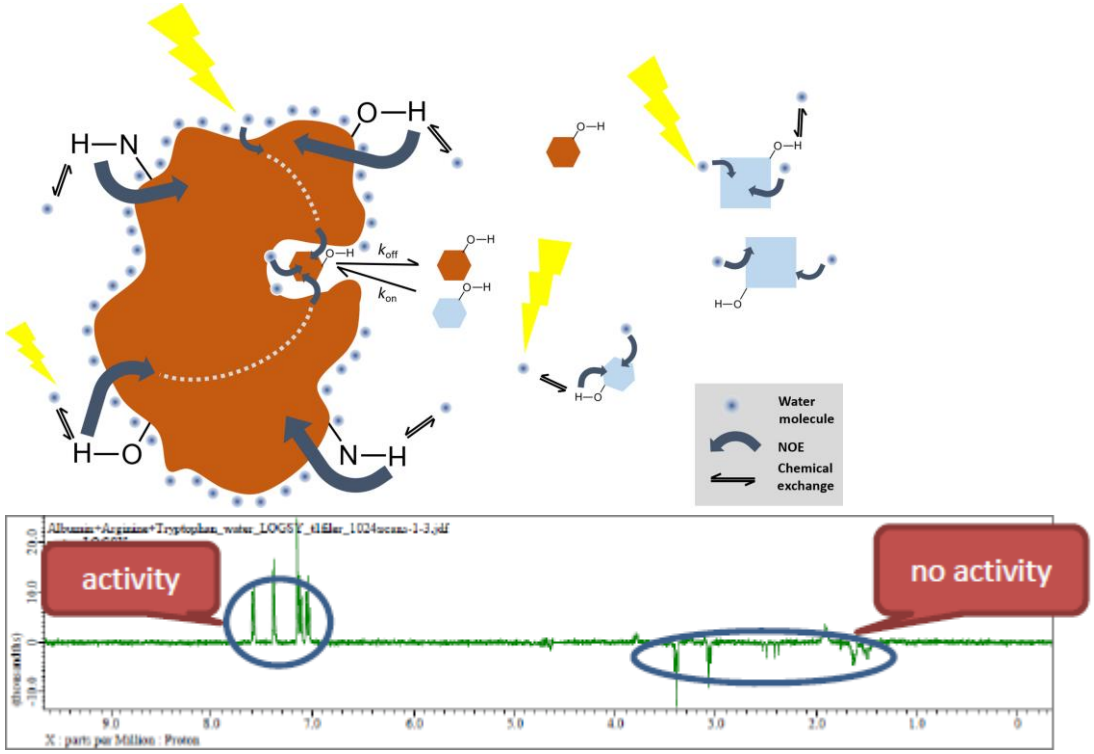
Quantitative Analyses - qNMR



Quantitative Analyses – qNMR, Adolfo Botana, Jeol Inc.

Saturation Transfer Differences

WaterLOGSY pulse sequence is a sensitive ligand-observed for detection of interaction between macromolecules, such as a ligand and a protein and DNA or RNA fragments.

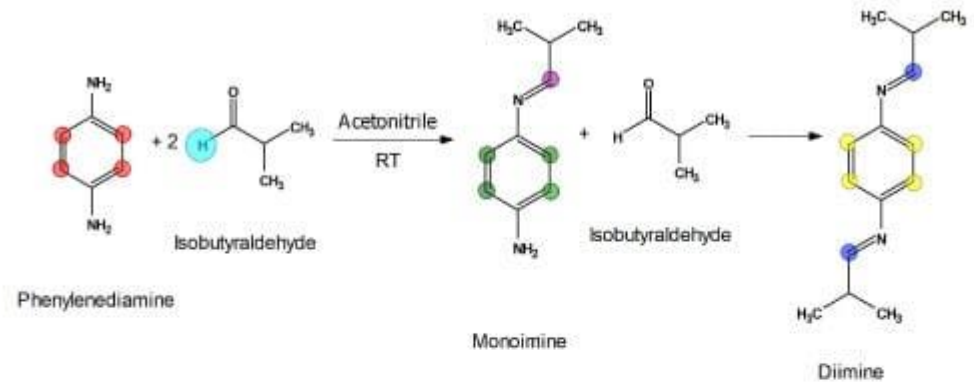


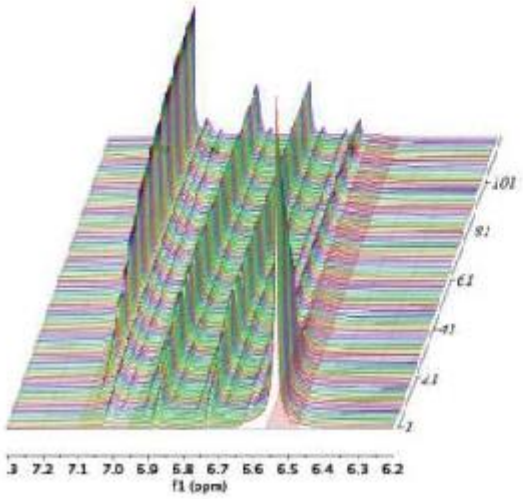
[NMR waterLOGSY as An Assay in Drug Development Programmes for Detecting Protein-Ligand Interactions]

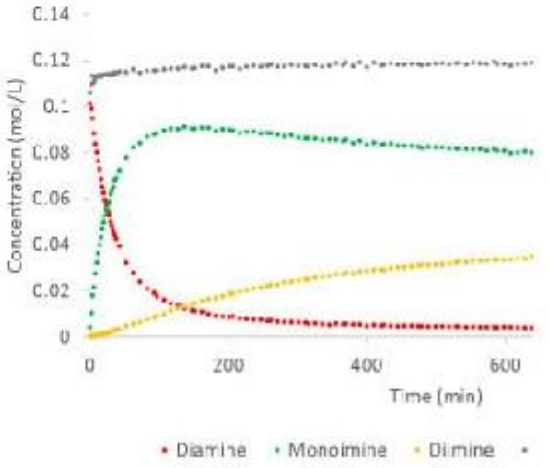
[WaterLOGSY as a method for primary NMR screening: Practical aspects and range of applicability]

[The discovery of novel antitrypanosomal 4-phenyl-6-(pyridin-3-yl)pyrimidines]

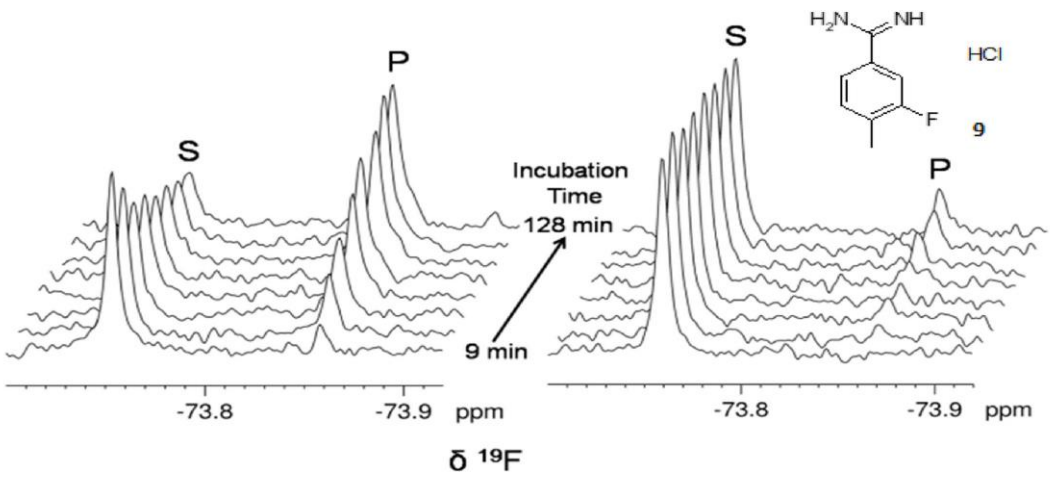
Reaction Monitoring and Kinetic analyses

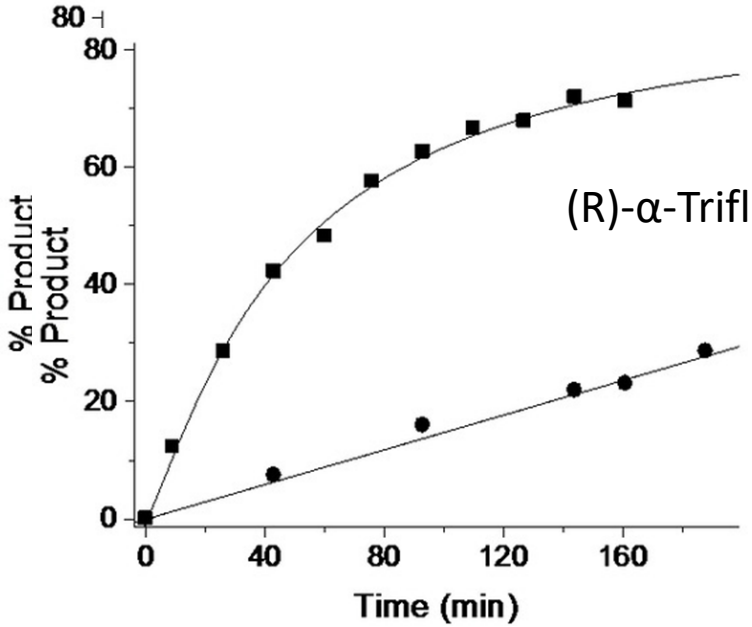






19F NMR for the Monitoring of Protease Digestion of Peptides

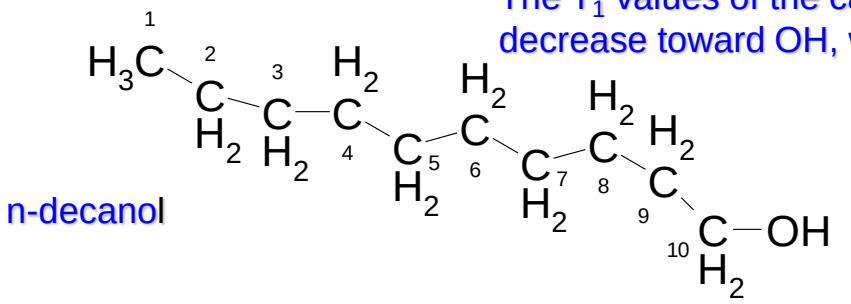




(R)-α-Trifluoromethylalanine.

ChemBioChem, Volume: 23, Issue: 1, 04 November 2021, DOI: (10.1002/cbic.202100470)
https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/cbic.202100470

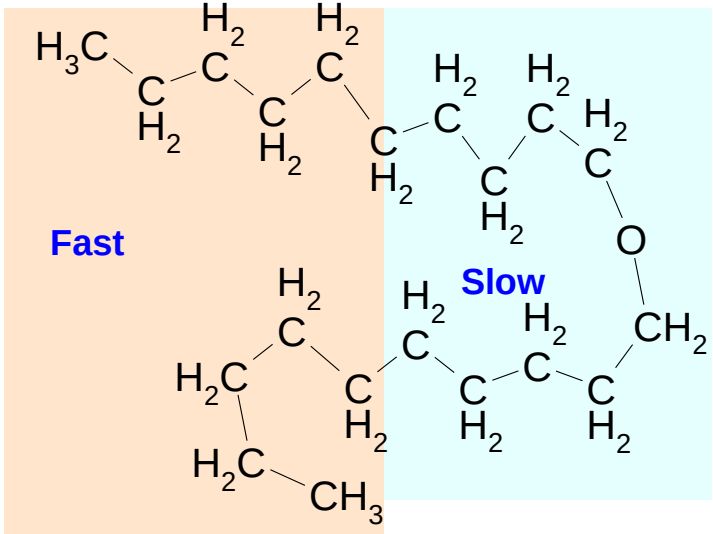
Structural Information from T_1



n-decanol

The T_1 values of the carbons decrease toward OH, why?

Carbon	T_1/sec
1	3.1
2	2.2
3	1.6
4	1.1
5	0.84
6	0.84
7	0.84
8	0.77
9	0.77
10	0.65



Those T_1 values prove the two molecular complex by hydrogen bound

Biological samples analysis

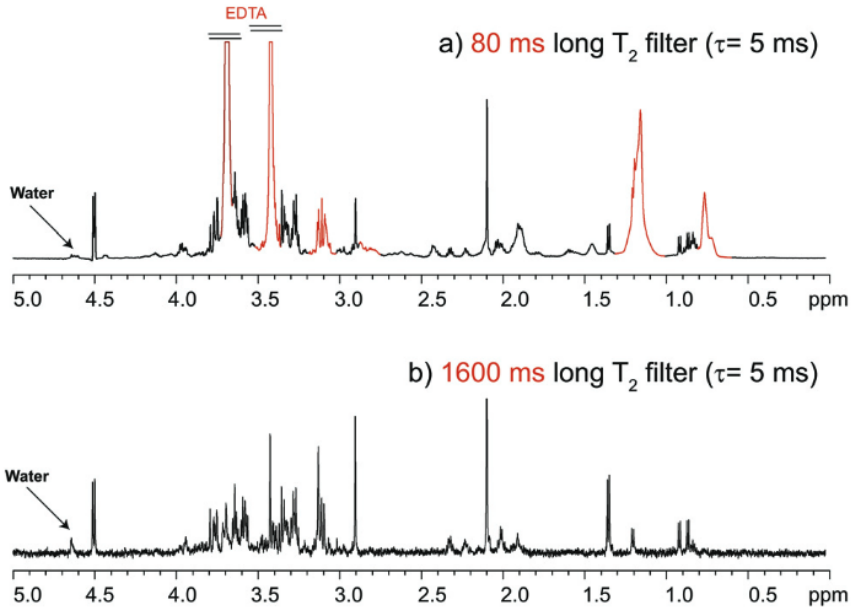


Fig. 5 Wasted pulse sequences allow the use of T_2 filters of a length impossible to use achieve with presat-CPMG. This allows the introduction of T_2 encoding to distinguish between different metabolite populations. Compare (b), in which a 1600 ms long filter has been made possible by Wasted-II, with (a) in which an 80 ms filter has been used (also using Wasted-II). Note that the suppression of the water signal is excellent even when using these long filters. The sample is human blood with non-deuterated EDTA.

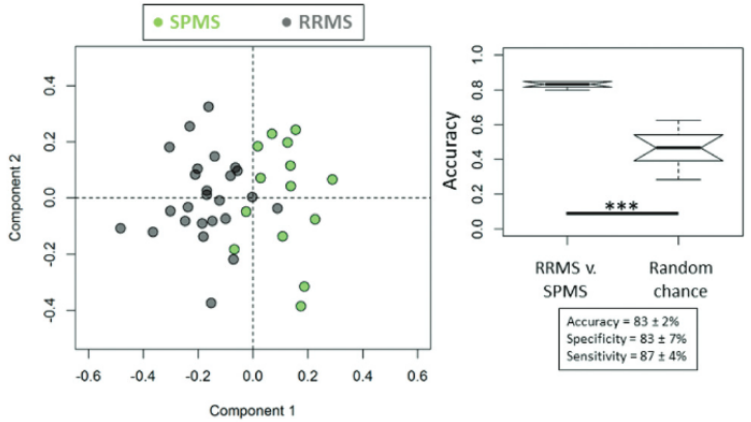
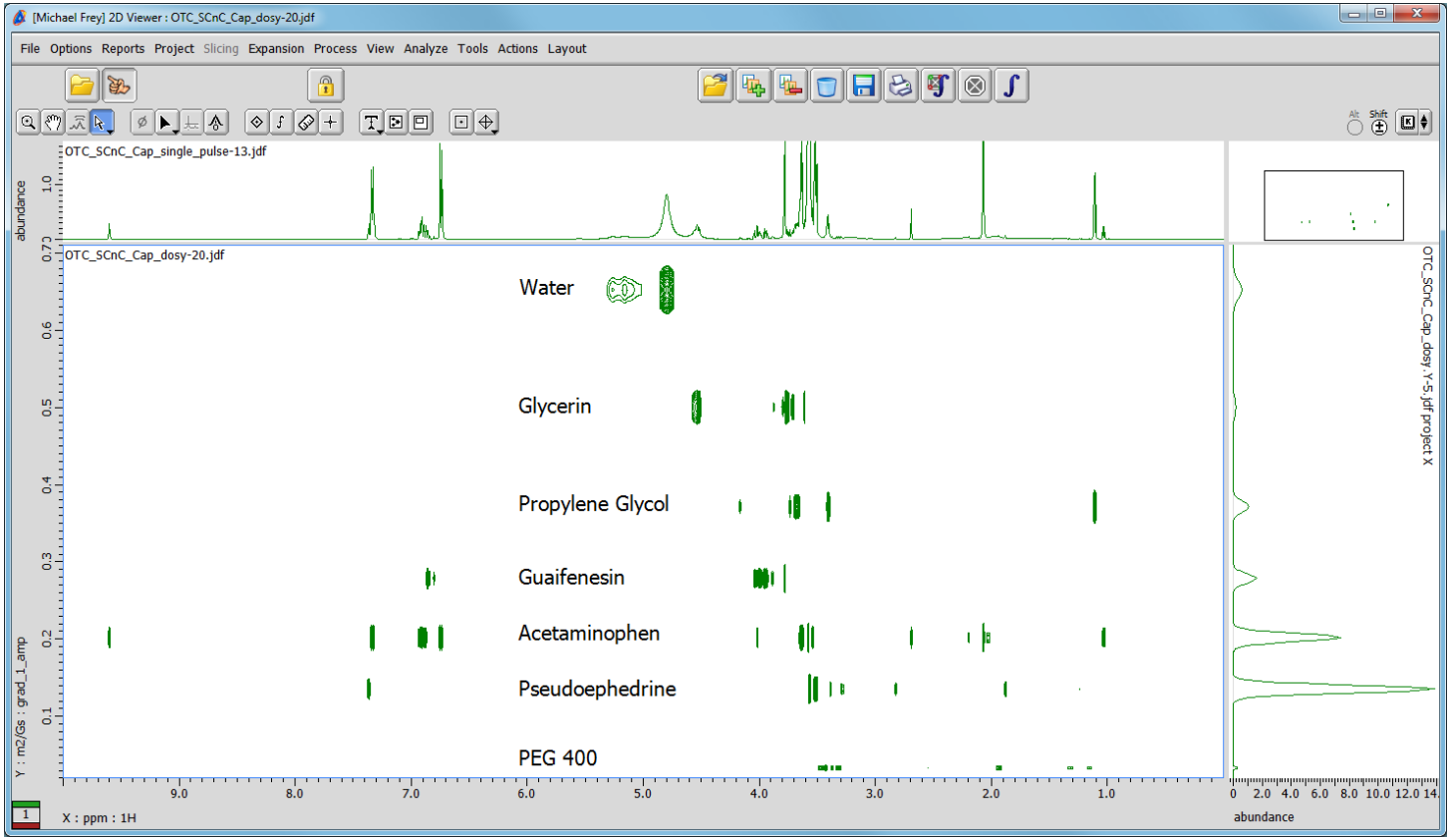


Fig. 6 OPLS-DA results from blood plasma Wasted-II ^{1}H NMR data discriminating SP from RR multiple sclerosis patients. Left, a representative scores plots illustrating separation between SPMS and RRMS plasma spectra in the multivariate models, and right, the accuracy of the cross-validated ensemble of OPLS-DA models is significantly better than random chance. Kolmogorov–Smirnov test *p*-values <0.001 are represented by ***.

https://doi.org/10.1039/C9AN01005J

DOSY NMR of paracetamol tablet

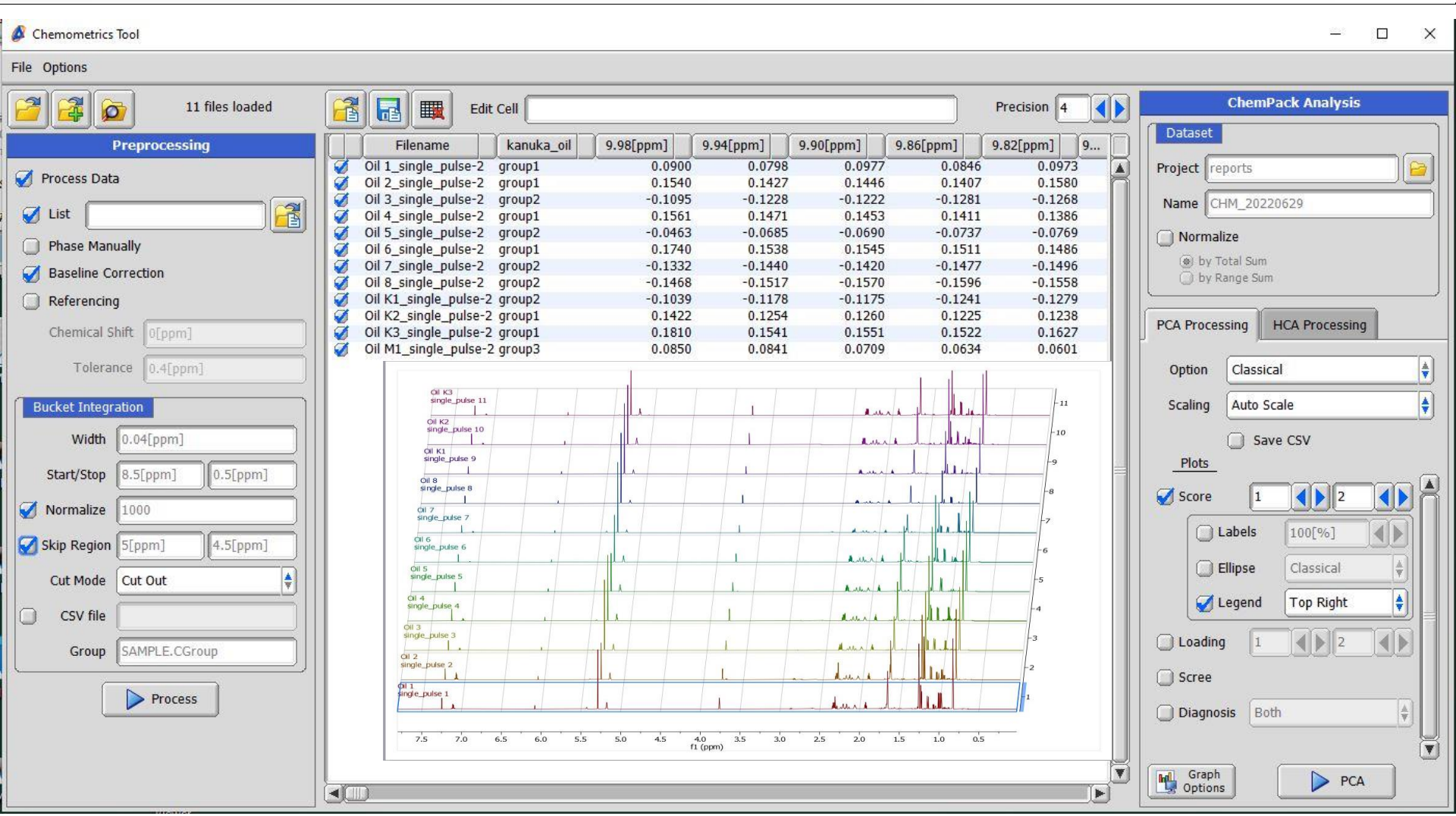
[Practical Introduction to DOSY]



Solvent Methanol-d_4

https://nmr.chemistry.manchester.ac.uk/?q=node/432

Metabolomics

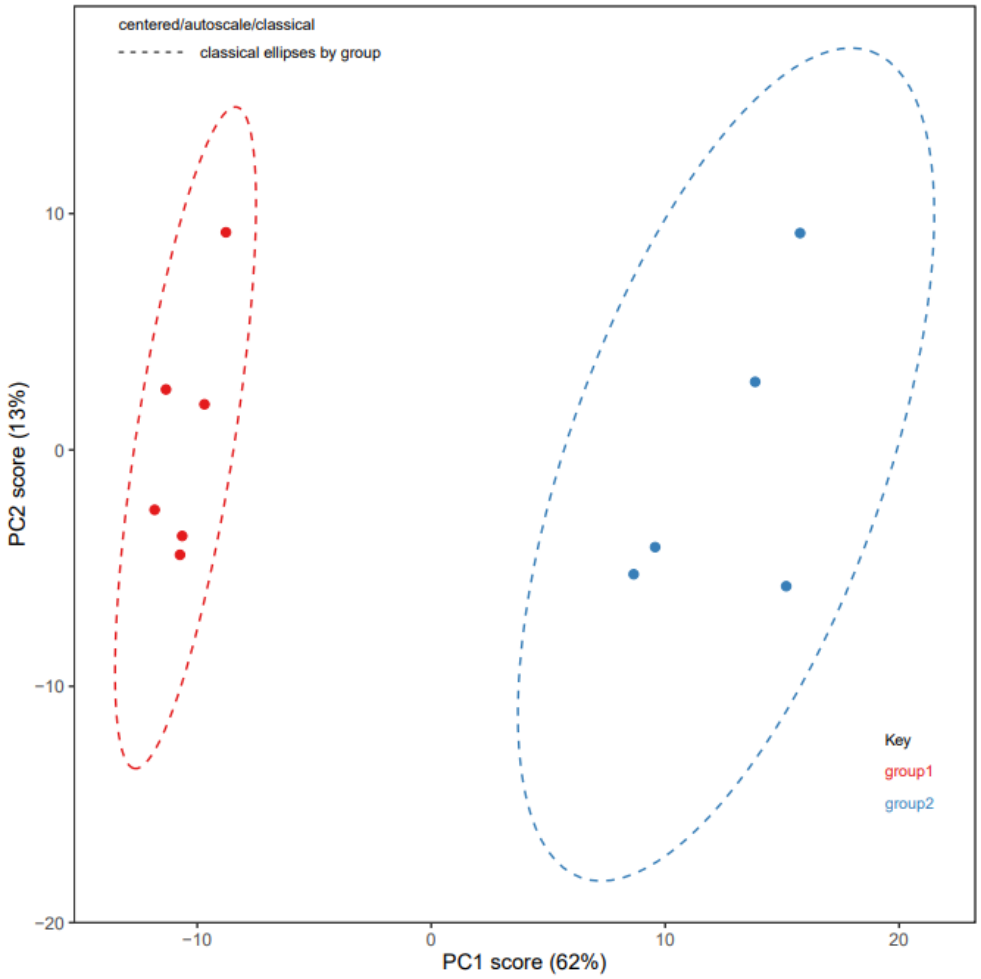


http://nmr.vuw.ac.nz/nmr/wp-content/uploads/presentations/Metabolomics.pdf

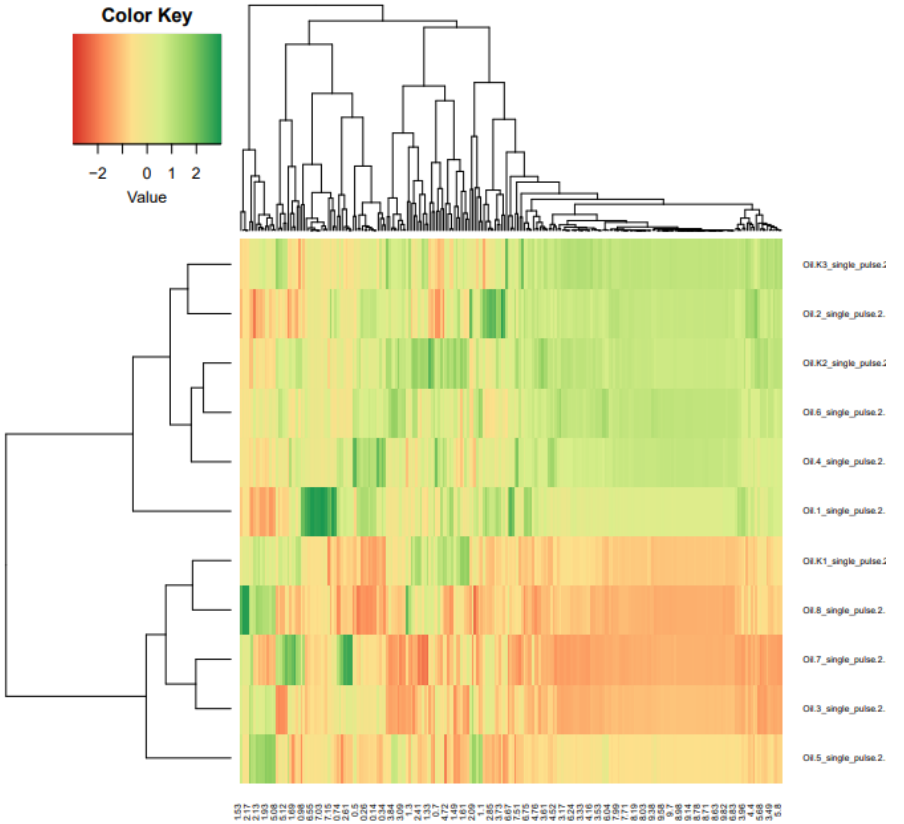
http://nmr.vuw.ac.nz/wunmr/wp-content/uploads/webinars/NMR_chemometrics_Jeol.pdf

Chemometrics Tool in Delta

PCA- Principal Component Analyses

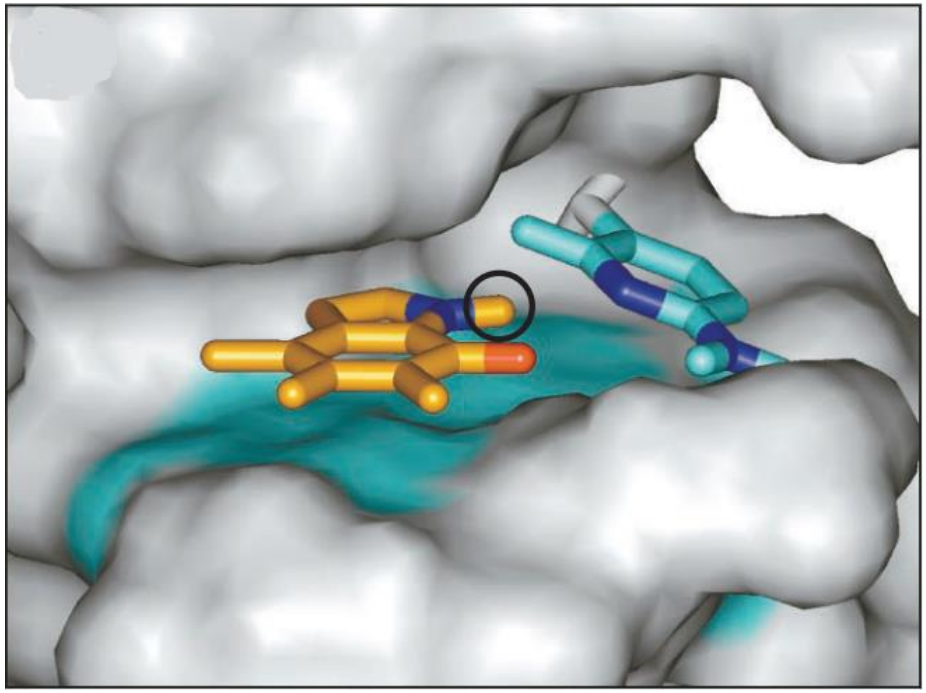


HCA- Hierarchical Cluster Analyses

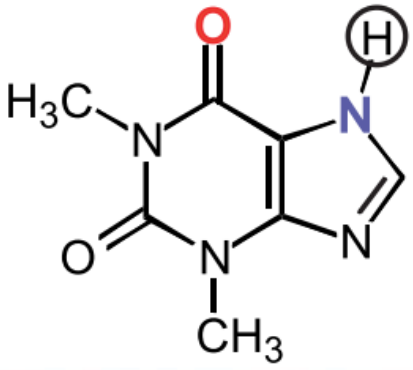


http://nmr.vuw.ac.nz/nmr/wp-content/uploads/presentations/Metabolomics.pdf
http://nmr.vuw.ac.nz/wunmr/wp-content/uploads/webinars/NMR_chemometrics_Jeol.pdf

Molecular investigation of the interaction target-aptamer: where does the binding event takes place ?



Stacking and hydrogen bond interaction !
RNA structural interactions in a ligand binding site proved by NMR spectroscopy



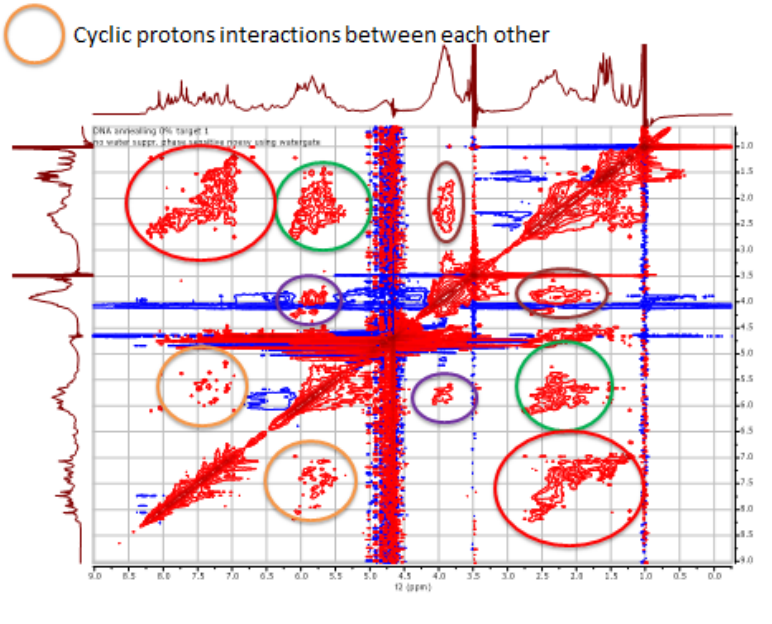
Caffeine differs by a methyl group (encircled H replaced by a CH_3)

Displays affinity for theophylline 10,000 times that of caffeine

Hermann, T. and D. J. Patel (2000). "Adaptive Recognition by Nucleic Acid Aptamers." Science **287**(5454): 820-825.
Zimmermann, G. R., et al. (1997). "Interlocking structural motifs mediate molecular discrimination by a theophylline-binding RNA." Nature Structural Biology **4**(8): 644-649.

Noesy-Nuclear Overhauser Effect

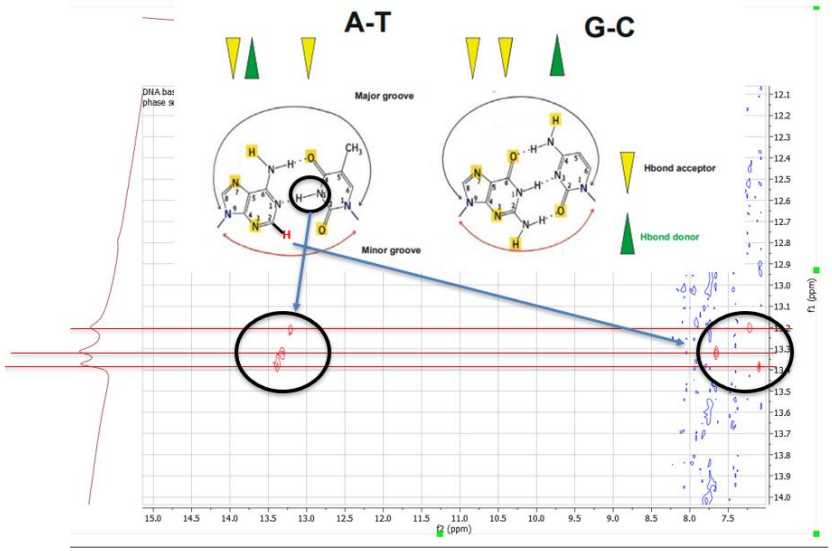
http://nmr.vuw.ac.nz/wunmr/wp-content/uploads/applications/Aptemer_NMR.pdf



Sugar protons interactions **in space** with other protons from nucleotides or from sugars

Sugar protons and cyclic protons interactions **in space** with other protons from nucleotides or from sugars

2D NOESY from 12 to 15ppm



Unraveling the binding mode of a methamphetamine aptamer: a spec-troscopic and calorimetric investigation
Clement Sester,†,‡ Jordan AJ McCone,‖ Ian Vorster,‡ Joanne E Harvey,‖ and Justin M Hodgkiss*,†,‡

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