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Supporting Information

Dynamics of the Glycosidic Bond: Conformational Space of Lactose

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chem_201100854_sm_miscellaneous_information.pdf

S1: Computational conformation analysis.

S2: NMR analysis (PCS and RDC data).

S3: Error analysis of the PCS and RDC data.

S4: Computational treatment of RDCs and PCSs.

S5: The dihedral angles and populations of the conformations derived from Monte Carlo conformational search.

S6: RDC and PCS analysis using the program relax.

S7: The HSQC pulse sequence used in this study.

S8: The global and local minima of the Monte Carlo sampling ensemble.

S1: Computational conformation analysis.

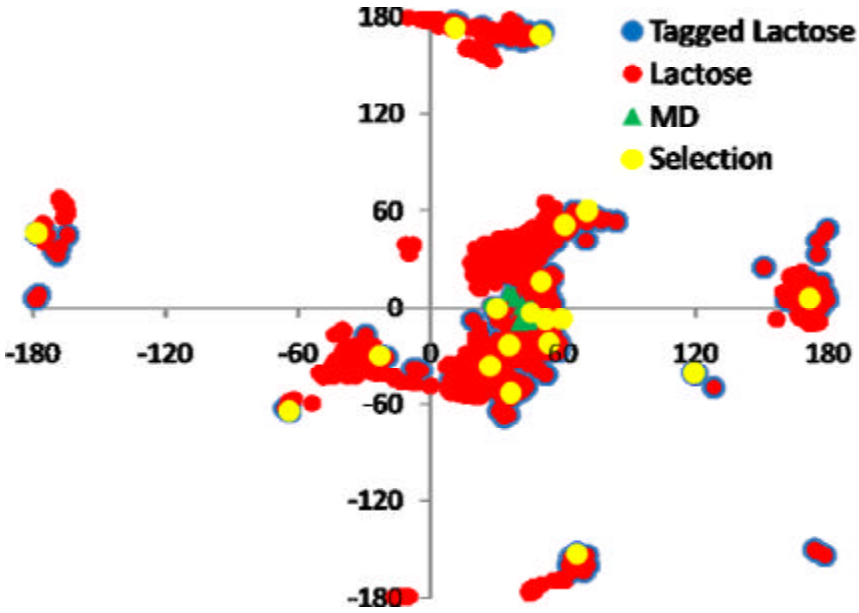


Figure S1. Comparison of the orientations of the glycosidic bond in free (red) and tagged (blue) Lactose as derived from Monte Carlo conformational searches. The dihedral angles of the ensemble reported as almost exclusive energy minima (> 97%) based on external alignment media induced RDC data is shown in green, whereas the conformations used in the relax protocol in yellow. These conformations were selected from the low energy regions on the potential energy surface.

S2: NMR analysis (RDC and PCS data)

Measured pseudocontact shifts

Name		Dy^{3+}	Tb^{3+}	Tm^{3+}	Er^{3+}	Yb^{3+}	Eu^{3+}
Galactose							
C1		0.004	0.040	0.103	0.037	0.0478	0.066
C2		0.008	0.045	0.083	0.045	0.0283	0.061
C3		0.021	0.050	0.079	0.048	0.0385	0.065
C4		0.009	0.014	0.080	0.046	0.0285	0.048
C5		0.016	0.013	0.091	0.030	0.0510	0.078
C6		0.010	0.021	0.101	0.038	0.0408	0.083
H1		0.010	0.045	0.093	0.041	0.0412	0.053
H2		0.021	0.060	0.079	0.044	0.0397	0.038
H3		0.006	0.017	0.092	0.041	0.0355	0.037
H4		0.003	0.007	0.095	0.045	0.0350	0.033
H5		0.014	0.011	0.105	0.039	0.0410	0.044
H6		0.005	0.017	0.114	0.019	0.0467	0.038
H7		0.001	0.048	0.115	0.061	0.0442	0.037
Glucose							
C7	(C1)	0.061	0.087	0.308	0.138	0.0590	0.107
C8	(C2)	None*	None*	None*	None*	0.0890	0.089
C9	(C3)	0.064	0.062	None*	0.035	0.0735	0.081
C10	(C4)	0.025	0.080	0.140	0.049	0.0455	0.077
C11	(C5)	0.042	0.141	0.064	0.097	0.0175	0.087
C12	(C6)	0.049	0.160	None*	0.065	0.0185	0.091
H12	(H1)	0.065	0.073	0.334	0.167	0.0670	0.112
H13	(H2)	None*	None*	None*	None*	0.0617	0.084
H14	(H3)	0.064	0.062	None*	0.054	0.0430	0.070
H15	(H4)	0.015	0.080	0.094	0.051	0.0448	0.075
H16	(H5)	0.098	0.137	0.111	0.105	0.0210	0.079
H17	(H6a)	0.060	0.012	None*	0.044	-0.0242	0.062
H18	(H6b)	0.120	0.098	None*	0.067	0.0275	0.058

Measured residual dipolar couplings (hsqcetgpsisp2.2): The measurement error is 2.4 Hz.

Name		Dy^{3+}	Tb^{3+}	Tm^{3+}	Er^{3+}	Yb^{3+}	Eu^{3+}
Galactose							
C1	H1	-0.3	-0.4	1.1	2.5	1.0	1.8
C2	H2	-2.3	-4.2	4.1	3.3	1.8	2.9
C3	H3	-2.7	-3.9	4.1	3.8	2.0	1.7
C4	H4	0.1	0.0	1.6	1.0	0.5	0.1
C5	H5	-1.8	-2.9	6.7	3.0	1.6	3.0
C6	H6	-1.2	1.2	-2.9	1.8	0.7	0.8
C6	H7	-0.5	-0.6	-1.0	0.4	0.2	0.2
Glucose							
C7 (C1)	H12(H1)	-0.9	-2.8	2.9	-3.0	1.8	0.6
C8 (C2)	H13(H2)	None*	None*	None*	None*	2.4	0.4
C9 (C3)	H14(H3)	-2.7	-3.8	None*	-1.3	3.5	0.8
C10(C4)	H15(H4)	-2.7	-4.4	2.5	-2.6	0.7	0.7
C11(C5)	H16(H5)	-3.3	-3.9	-2.5	-3.2	1.1	0.8
C12(C6)	H17(H6a)	None*	None*	None*	None*	-8.5	1.9
C12(C6)	H18(H6b)	-2.3	-1.2	None*	None*	1.30	0.2

The source and amplitudes of the errors are presented in the main text. Assignation follows the literature conventions (*J. Am.Chem.Soc.* **2005**, *127*, 3589). *****None – excluded because of overlap or line broadening.

S3: Error analysis of the PCS and RDC data.

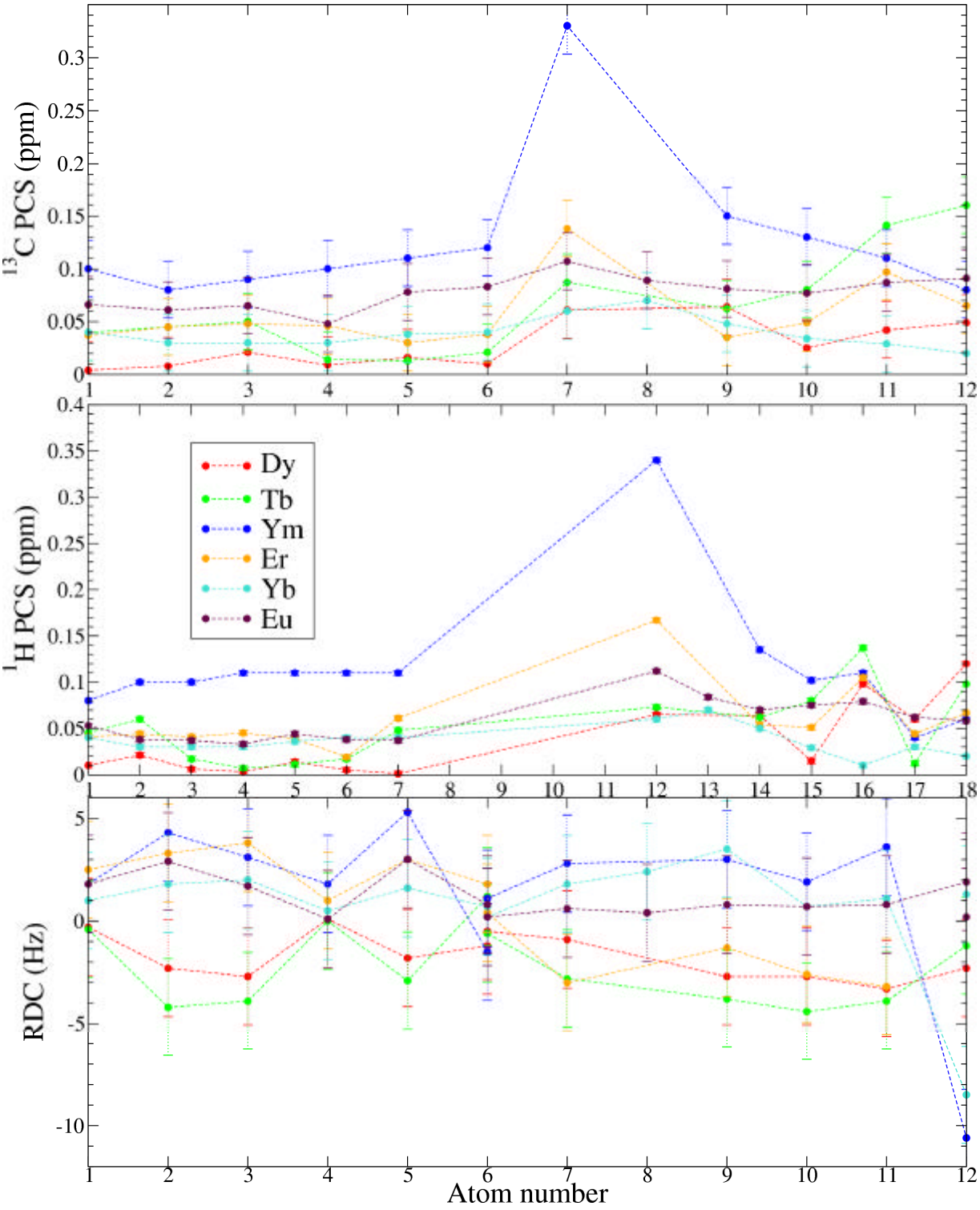


Figure S2. The PCS and RDC data plotted with errors. The low statistical significance of the RDC data is clear. The errors include both the measured peak position uncertainties together with an uncertainty term due to the rCSA, as described in the main text.

S4: Computational treatment of RDCs and PCSs.

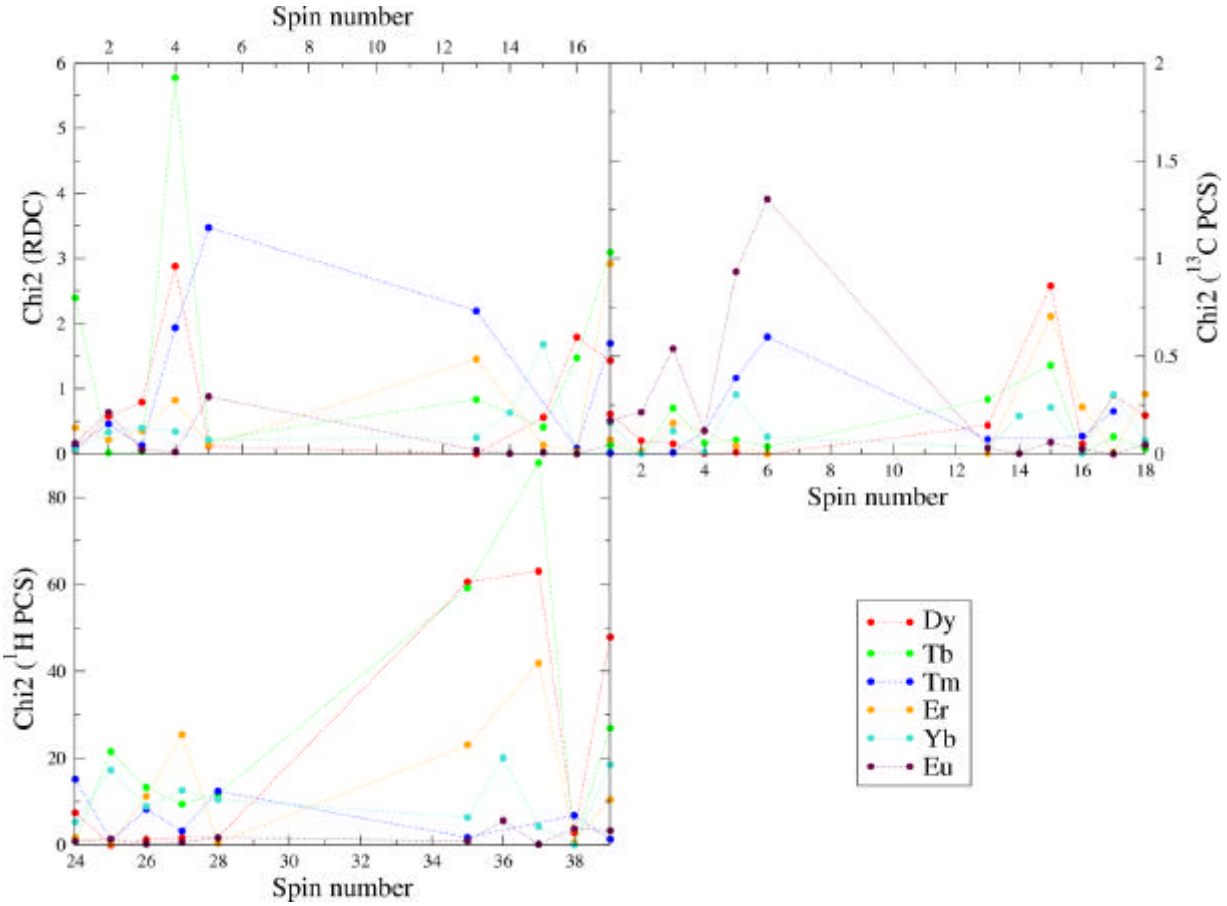


Figure S3. The optimised chi-squared statistic for the Monte Carlo conformation search ensemble, broken down into the individual spin contributions. This plot shows that the ^{1}H PCS is the major contributor to the chi-squared statistic and hence the final result. The RDC data contribution is an order of magnitude less. And the ^{13}C PCS contributes the least. There are no significant outlying points indicating bad data.

S5: The dihedral angles and populations of the conformations derived from Monte Carlo conformational search.

Table S1. The dihedral angles and populations for the best solution of the Monte Carlo conformer search (Entry h in Table 1 and depicted in Fig. 3).

Structure	Dihedral angle Φ (H1'-C1'-O-C4)	Dihedral angle ψ (H4-C4-O-C1')	Probability (%)
1	171.9	5.8	3.8
2	-178.3	46.5	-
3	49.8	168.8	-
4	53.8	-22.3	32
5	36.4	-52.9	24
6	66.3	-152.8	6.1
7	-22.8	-29.9	0.7
8	-63.9	-64.4	18
9	45.6	-3.4	-
10	35.9	-23.2	-
11	11.2	173.3	14
12	27.0	-36.3	-
13	50.1	16.2	-
14	60.7	51.4	-
15	30.3	-0.5	1.6

S6: RDC and PCS analysis using the program relax.

The analysis was implemented using the following relax scripts:

```
# Script for determining populations for lactose conformations using RDCs and
PCSs.

# Python imports.
from os import getcwd, listdir
from re import search

# relax imports.
from data import Relax_data_store; ds = Relax_data_store()
from specific_fns.setup import n_state_model_obj


# Create the data pipe.
pipe.create('lactose', 'N-state')

# Load the structures.
files = listdir(getcwd())
num = 1
for file in files:
    print file
    if search('.pdb$', file):
        structure.read_pdb(file=file,  parser='internal',  set_model_num=num,
set_mol_name='conf')
        num += 1
NUM_STR = num - 1

# Load the sequence information.
structure.load_spins(spin_id=':900@C*', ave_pos=False)
structure.load_spins(spin_id=':900@H*', ave_pos=False)

# Deselect the CH2 protons (the rotation of these doesn't work in the model,
but the carbon doesn't move).
deselect.spin(spin_id=':900@H6')
deselect.spin(spin_id=':900@H7')
deselect.spin(spin_id=':900@H17')
deselect.spin(spin_id=':900@H18')

# Load the CH vectors for the C atoms.
structure.vectors(spin_id='@C*', attached='H*', ave=False)

# Set the values needed to calculate the dipolar constant.
value.set(1.10 * 1e-10, 'bond_length', spin_id="@C*")
value.set('13C', 'heteronucleus', spin_id="@C*")
value.set('1H', 'proton', spin_id="@C*")

# File list.
align_list = ['Dy', 'Tb', 'Tm', 'Er', 'Yb', 'Eu']

# Load the RDCs and PCSs.
for i in xrange(len(align_list)):
    # The RDC.
```

```
    rdc.read(align_id=align_list[i],                file='rdc_Series1_G.txt',
dir='../../../align_data', mol_name_col=None, res_num_col=None, res_name_c
    rdc.read(align_id=align_list[i],             file='rdc_err_measured.txt',
dir='../../../align_data', mol_name_col=None, res_num_col=None, res_nam
    rdc.display(align_id=align_list[i])

    # The PCS.
    pcs.read(align_id=align_list[i],                file='pcs_Series1_G.txt',
dir='../../../align_data', mol_name_col=None, res_num_col=None, res_name_c
    pcs.read(align_id=align_list[i],         file='pcs_err_measured+rcsa.txt',
dir='../../../align_data', mol_name_col=None, res_num_col=None, re
    pcs.display(align_id=align_list[i])

    # The weights.
    rdc.weight(align_id=align_list[i], spin_id=None)
    pcs.weight(align_id=align_list[i], spin_id='@C*')
    pcs.weight(align_id=align_list[i], spin_id='@H*')

    # The temperature.
    temperature(id=align_list[i], temp=298)

    # The frequency.
    frq.set(id=align_list[i], frq=900.015 * 1e6)

# Tag.
######

# Create a data pipe for the aligned tag structures.
pipe.create('tag', 'N-state')

# Load all the tag structures.
NUM_TAG = 1000
for i in range(NUM_TAG):
    structure.read_pdb(file='LactoseMCMM4_'+`i+1`,
dir='../../../structures/tag_1000/080704_MCMM4_aligned-forEd1000',
parser='internal',

# Load the lanthanide atoms.
structure.load_spins(spin_id=':4@C1', combine_models=False, ave_pos=False)

# Switch back to the main analysis data pipe.
pipe.switch('lactose')

# Calculate the paramagnetic centre (from the structures in the 'tag' data
pipe).
paramag.centre(atom_id=':4@C1', pipe='tag')


# Fixed model.
##############

# Set up the model.
n_state_model.select_model(model='fixed')

# Minimisation.
minimise('newton')

# Calculate the AIC value.
```

```
k, n, chi2 = n_state_model_obj.model_statistics()
ds[ds.current_pipe].aic = chi2 + 2.0*k

# Write out a results file.
results.write('results_fixed_rdc+pcs', dir=None, force=True)


# Population model.
###################

# Set up the model.
n_state_model.select_model(model='population')

# Set to equal probabilities.
for j in xrange(NUM_STR):
    value.set(1.0/NUM_STR, 'p'+`j`)

# Minimisation.
minimise('bfgs', constraints=True)

# Calculate the AIC value.
k, n, chi2 = n_state_model_obj.model_statistics()
ds[ds.current_pipe].aic = chi2 + 2.0*k

# Write out a results file.
results.write('results_population_rdc+pcs', dir=None, force=True)

# Show the tensors.
align_tensor.display()

# Show the populations.
for i in range(len(cdp.structure.structural_data)):
    if abs(cdp.probs[i]) > 1e-7:
        print          "%16.10f          %s"          %          (cdp.probs[i],
cdp.structure.structural_data[i].mol[0].file_name)
```

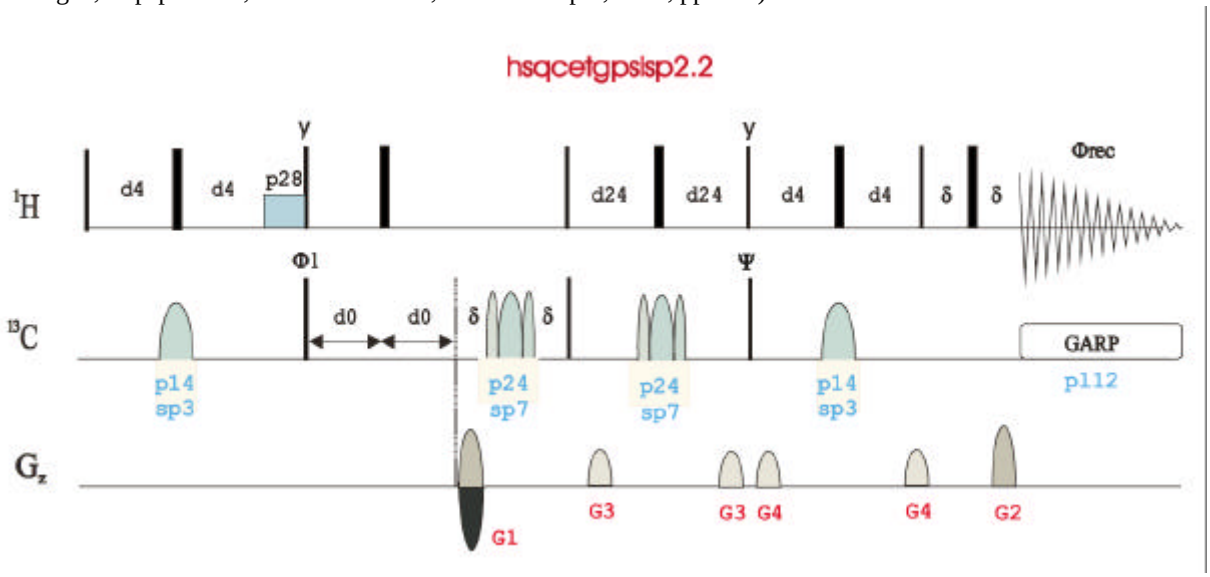
The relax script for finding the multiple local minima, using the results from the previous script is:

```
"""Script for determining local populations for lactose conformations using
RDCs and PCSs (multi-minima search)."""

from specific_fns.setup import n_state_model_obj


# Loop over random positions.
for rand_index in range(200):
    # Reset.
    reset()

    # Create the datapipe.
    pipe.create('lactose', 'N-state')

    # Read the results file.
    results.read('results_fixed_rdc+pcs')
```

```
    # Random starts.
    ################

    # Set up the model.
    n_state_model.select_model(model='population')

    # Random array.
    probs = zeros(cdp.N, float64)
    for j in xrange(cdp.N):
        probs[j] = uniform(0, 1)
    probs = probs / norm(probs)

    # Set the random probabilities.
    for j in xrange(cdp.N):
        value.set(probs[j], 'p'+`j`)

    # Reset the tensors.
    #for i in range(len(cdp.align_tensors)):
    #    cdp.align_tensors[i].Axx = 0.0
    #    cdp.align_tensors[i].Ayy = 0.0
    #    cdp.align_tensors[i].Axy = 0.0
    #    cdp.align_tensors[i].Axz = 0.0
    #    cdp.align_tensors[i].Ayz = 0.0

    # Minimisation.
    minimise('bfgs', constraints=True)

    # Calculate the AIC value.
    k, n, chi2 = n_state_model_obj.model_statistics()
    ds[ds.current_pipe].aic = chi2 + 2.0*k

    # Write out a results file.
    results.write('results_population_rdc+pcs_rand%i' % rand_index, dir=None,
force=True)

    # Show the tensors.
    align_tensor.display()

    # Show the populations.
    for i in range(len(cdp.structure.structural_data)):
        if abs(cdp.probs[i]) > 1e-7:
            print "%16.10f %s" % (cdp.probs[i],
cdp.structure.structural_data[i].mol[0].file_name)
```

S7: The HSQC pulse sequence used in this study.

For acquisition of the coupled $^{1}H,^{13}C$-HSQC spectra the phase-sensitive ge-2D HSQC using PEP and adiabatic pulses for inversion and refocusing with gradients in back-inept and presaturation (T. Parella, Pulse program catalogue, Topspin v1.2, NMRGuide v4.0, Bruker Biospin, 2004, pp 153.) was used.




```
# 1 "/opt/topspin/exp/stan/nmr/lists/pp/hsqcetgpsisp2.2"
;hsqcetgpsisp2.2
;avance-version (02/12/09)
;HSQC
;2D H-1/X correlation via double inept transfer
;   using sensitivity improvement
;phase sensitive using Echo/Antiecho-TPPI gradient selection
;with decoupling during acquisition
;using trim pulses in inept transfer
;using shaped pulses for all 180degree pulses on f2 - channel
;with gradients in back-inept
;
;A.G. Palmer III, J. Cavanagh, P.E. Wright & M. Rance, J. Magn.
;   Reson. 93, 151-170 (1991)
;L.E. Kay, P. Keifer & T. Saarinen, J. Am. Chem. Soc. 114,
;   10663-5 (1992)
;J. Schleucher, M. Schwendinger, M. Sattler, P. Schmidt, O. Schedletzky,
;   S.J. Glaser, O.W. Sorensen & C. Griesinger, J. Biomol. NMR 4,
;   301-306 (1994)

# 1 "/opt/topspin/exp/stan/nmr/lists/pp/Avance.incl" 1
;Avance2.incl
;   for 1
;
;avance-version (03/02/17)

;$Id: Avance2.incl,v 1.10 2003/02/25 14:46:08 ber Exp $
# 21 "/opt/topspin/exp/stan/nmr/lists/pp/hsqcetgpsisp2.2" 2

# 1 "/opt/topspin/exp/stan/nmr/lists/pp/Grad.incl" 1
;Grad2.incl  -  include file for Gradient Spectroscopy
;   for 1
;
```

```
;avance-version (02/05/31)

define list<gradient> EA=<EA>

;$Id: Grad2.incl,v 1.7 2002/06/12 09:04:22 ber Exp $
# 22 "/opt/topspin/exp/stan/nmr/lists/pp/hsqcetgpsisp2.2" 2

# 1 "/opt/topspin/exp/stan/nmr/lists/pp/Delay.incl" 1
;Delay.incl  -  include file for commonly used delays
;
;version 00/02/07

;general delays

define delay DELTA
define delay DELTA1
define delay DELTA2
define delay DELTA3
define delay DELTA4
define delay DELTA5
define delay DELTA6
define delay DELTA7
define delay DELTA8

define delay TAU
define delay TAU1
define delay TAU2
define delay TAU3
define delay TAU4
define delay TAU5


;delays for centering pulses

define delay CEN_HN1
define delay CEN_HN2
define delay CEN_HN3
define delay CEN_HC1
define delay CEN_HC2
define delay CEN_HC3
define delay CEN_HC4
define delay CEN_HP1
define delay CEN_HP2
define delay CEN_CN1
define delay CEN_CN2
define delay CEN_CN3
define delay CEN_CN4
define delay CEN_CP1
define delay CEN_CP2

;loop counters

define loopcounter COUNTER
define loopcounter SCALEF
define loopcounter FACTOR1
define loopcounter FACTOR2
define loopcounter FACTOR3
```

```
;$Id: Delay.incl,v 1.11 2002/06/12 09:04:22 ber Exp $
# 23 "/opt/topspin/exp/stan/nmr/lists/pp/hsqcetgpsisp2.2" 2

"p2=p1*2"

"d0=3u"

"d4=1s/(cnst2*4)"

"d11=30m"

"DELTA=p16+d16+p2+d0*2-4u"
"DELTA1=p16+d16+8u"
"DELTA2=d4-larger(p2,p14)/2-4u"
"DELTA3=d24-cnst17*p24/2-p19-d16-4u"
"DELTA4=d4-larger(p2,p14)/2-p16-d16-4u"

#  1  "mc_line  43  file  /opt/topspin/exp/stan/nmr/lists/pp/hsqcetgpsisp2.2
expanding definition part of mc command before ze"
define delay MCWRK
define delay MCREST
define loopcounter ST1CNT
"ST1CNT = td1 / (2)"
"MCWRK = 0.166667*d1"
"MCREST = d1 - d1"
# 43 "/opt/topspin/exp/stan/nmr/lists/pp/hsqcetgpsisp2.2"
1 ze
#  1  "mc_line  43  file  /opt/topspin/exp/stan/nmr/lists/pp/hsqcetgpsisp2.2
expanding definition of mc command after ze"
# 44 "/opt/topspin/exp/stan/nmr/lists/pp/hsqcetgpsisp2.2"
  d11 pl12:f2
#  1  "mc_line  45  file  /opt/topspin/exp/stan/nmr/lists/pp/hsqcetgpsisp2.2
expanding start label for mc command"
2 MCWRK  * 2 do:f2
LBLSTS1, MCWRK  * 4
LBLF1, MCREST
# 46 "/opt/topspin/exp/stan/nmr/lists/pp/hsqcetgpsisp2.2"
3 (p1 ph1)
  DELTA2 pl0:f2
  4u
  (center (p2 ph1) (p14:sp3 ph6):f2 )
  4u
  DELTA2 pl2:f2 setnmr3|0 setnmr0|34|32|33
  p28 ph1
  4u
  (p1 ph2) (p3 ph3):f2
  d0
  (p2 ph7)
  d0
  p16:gp1*EA
  d16 pl0:f2
  (p24:sp7 ph8:r):f2
  4u
  DELTA pl2:f2
  (center (p1 ph1) (p3 ph4):f2 )
  4u
  p19:gp3
  d16
```

```
  DELTA3 pl0:f2
  (center (p2 ph1) (p24:sp7 ph9:r):f2 )
  4u
  DELTA3 pl2:f2
  p19:gp3
  d16
  (center (p1 ph2) (p3 ph5):f2 )
  4u
  p16:gp4
  d16
  DELTA4 pl0:f2
  (center (p2 ph1) (p14:sp3 ph1):f2 )
  4u
  DELTA4
  p16:gp4
  d16
  (p1 ph1)
  DELTA1
  (p2 ph1)
  4u
  p16:gp2
  d16 pl12:f2
  4u setnmr3^0 setnmr0^34^32^33
  go=2 ph31 cpd2:f2
#  1  "mc_line  91  file  /opt/topspin/exp/stan/nmr/lists/pp/hsqcetgpsisp2.2
expanding mc command in line"
  MCWRK  do:f2 wr #0 if #0 zd igrad EA  MCWRK  ip5*2
  lo to LBLSTS1 times 2
  MCWRK id0  MCWRK  ip3*2  MCWRK  ip6*2  MCWRK  ip31*2
  lo to LBLF1 times ST1CNT
# 93 "/opt/topspin/exp/stan/nmr/lists/pp/hsqcetgpsisp2.2"
exit

ph1=0
ph2=1
ph3=0 2
ph4=0 0 2 2
ph5=1 1 3 3
ph6=0
ph7=0 0 2 2
ph8=0 0 2 2
ph9=0
ph31=0 2 2 0

;pl0 : 120dB
;pl1 : f1 channel - power level for pulse (default)
;pl2 : f2 channel - power level for pulse (default)
;pl3 : f3 channel - power level for pulse (default)
;pl12: f2 channel - power level for CPD/BB decoupling
;sp3: f2 channel - shaped pulse (180degree inversion)
;spnam3: Crp60,0.5,20.1
;sp7: f2 channel - shaped pulse (180degree refocussing)
;spnam7: Crp60comp.4
;p1 : f1 channel -  90 degree high power pulse
;p2 : f1 channel - 180 degree high power pulse
;p3 : f2 channel -  90 degree high power pulse
;p14: f2 channel - 180 degree shaped pulse for inversion
;     = 500usec for Crp60,0.5,20.1
```

```
;p16: homospoil/gradient pulse                          [1 msec]
;p19: gradient pulse 2                                  [500 usec]
;p22: f3 channel - 180 degree high power pulse
;p24: f2 channel - 180 degree shaped pulse for refocussing
;     = 2msec for Crp60comp.4
;p28: f1 channel - trim pulse
;d0 : incremented delay (2D)                            [3 usec]
;d1 : relaxation delay; 1-5 * T1
;d4 : 1/(4J)XH
;d11: delay for disk I/O                                [30 msec]
;d16: delay for homospoil/gradient recovery
;d24: 1/(8J)XH for all multiplicities
;     1/(4J)XH for XH
;cnst2: = J(XH)
;cnst17: = -0.5 for Crp60comp.4
;in0: 1/(2 * SW(X)) = DW(X)
;nd0: 2
;NS: 1 * n
;DS: >= 16
;td1: number of experiments
;FnMODE: echo-antiecho
;cpd2: decoupling according to sequence defined by cpdprg2
;pcpd2: f2 channel - 90 degree pulse for decoupling sequence

;use gradient ratio:  gp 1 : gp 2 : gp 3 : gp 4
;                       80 : 20.1 :   11 :   -5    for C-13
;                       80 :  8.1 :   11 :   -5    for N-15

;for z-only gradients:
;gpz1: 80%
;gpz2: 20.1% for C-13, 8.1% for N-15
;gpz3: 11%
;gpz4: -5%

;use gradient files:
;gpnam1: SINE.100
;gpnam2: SINE.100
;gpnam3: SINE.100
;gpnam4: SINE.100

;cnst17: Factor to compensate for coupling evolution during a pulse
;       (usually +1). A positive factor indicates that coupling
;       evolution continues during the pulse, whereas a negative
;       factor is necessary if the coupling is (partially) refocused.

;$Id: hsqcetgpsisp2.2,v 1.1 2003/01/02 16:31:23 ber Exp $
```

S8: The global and local minima of the Monte Carlo sampling ensemble

Table S2. The top 20 results of 200 relax minimisations starting from random positions is shown. Since the optimisation space is complex and contains numerous local minima we ran the relax algorithm given above 200 times in order to ensure that we found the global minimum. Several local minima close to the global minimum was found as shown below. It should be noted that the populations of these local minima are close to that of the global minimum.

Optimization	chi2	Q(RDC)	Q(PCS)	6	8	4	12	11	9	10	14	13	5	1	7	3	2	15
rand 125	759.562	0.502	0.248	0.061	0.181	0.321	0.000	0.139	0.000	0.000	0.000	0.000	0.236	0.038	0.008	0.000	0.000	0.016
rand 134	760.173	0.510	0.248	0.074	0.192	0.306	0.000	0.127	0.000	0.000	0.000	0.000	0.216	0.051	0.000	0.000	0.000	0.034
rand 12	760.271	0.500	0.248	0.036	0.192	0.281	0.000	0.154	0.000	0.000	-0.000	0.000	0.242	0.034	0.004	0.000	0.000	0.057
rand 10	760.496	0.505	0.249	0.084	0.213	0.365	0.019	0.136	0.000	0.000	0.000	0.000	0.148	0.029	0.000	0.000	0.000	0.006
rand 136	761.035	0.500	0.248	0.010	0.186	0.294	0.000	0.168	0.000	0.000	0.000	0.000	0.230	0.019	0.029	0.000	0.000	0.064
rand 172	761.703	0.504	0.248	0.022	0.201	0.273	0.009	0.161	0.000	0.003	-0.000	0.000	0.218	0.031	0.000	0.000	0.000	0.082
rand 153	761.856	0.508	0.248	0.020	0.186	0.260	0.061	0.174	0.000	0.000	0.000	0.000	0.226	0.020	0.000	0.000	0.000	0.051
rand 18	761.896	0.507	0.247	0.040	0.164	0.269	0.000	0.152	0.000	0.000	0.000	0.000	0.265	0.043	0.000	0.000	0.000	0.067
rand 185	762.288	0.496	0.246	0.007	0.181	0.218	0.000	0.146	0.000	0.000	0.000	0.000	0.344	0.048	0.000	0.000	-0.000	0.054
rand 109	762.339	0.499	0.247	0.000	0.180	0.223	0.034	0.188	0.000	0.000	0.000	0.000	0.275	0.014	0.006	0.000	0.000	0.079
rand 138	762.478	0.498	0.246	0.000	0.185	0.208	0.000	0.171	0.011	0.000	0.000	-0.000	0.352	0.046	0.000	0.000	0.000	0.026
rand 97	762.689	0.514	0.248	0.051	0.205	0.280	0.024	0.142	0.000	0.000	0.000	0.000	0.191	0.029	0.001	0.000	0.000	0.077
rand 25	763.462	0.512	0.248	0.046	0.196	0.248	0.000	0.161	0.000	0.000	0.000	0.000	0.200	0.037	0.000	0.000	0.000	0.112
rand 26	764.059	0.526	0.249	0.084	0.180	0.272	0.000	0.146	0.000	0.015	0.000	0.000	0.164	0.047	0.000	0.000	0.000	0.092
rand 69	764.077	0.532	0.249	0.071	0.160	0.268	0.001	0.146	0.000	0.080	0.000	0.000	0.229	0.045	0.000	-0.000	0.000	0.000
rand 106	764.222	0.518	0.248	0.011	0.191	0.243	0.044	0.179	0.000	0.031	0.000	0.000	0.211	0.026	0.000	0.000	-0.000	0.064
rand 165	764.821	0.516	0.248	0.078	0.160	0.229	0.000	0.138	0.000	0.000	0.000	0.000	0.223	0.082	0.000	0.000	-0.000	0.091
rand 9	764.828	0.530	0.248	0.048	0.182	0.251	0.064	0.155	0.000	0.000	0.000	0.000	0.175	0.045	0.000	0.000	0.000	0.080
rand 190	764.949	0.472	0.249	0.159	0.148	0.260	0.000	0.073	0.000	0.000	0.000	0.016	0.231	0.103	0.000	0.000	0.000	0.011
rand 87	765.039	0.529	0.249	0.057	0.171	0.247	0.011	0.158	0.000	0.033	0.000	0.000	0.190	0.044	0.008	0.000	0.000	0.081

Table S3. Statistics of the top 20 optimisation results.

Structure	Global minimum	Average	Standard deviation
1	3.8%	4.2%	2.01%
2	0.0%	0.0%	0.00%
3	0.0%	0.0%	0.00%
4	32.0%	26.6%	3.61%
5	24.0%	22.8%	5.01%
6	6.1%	4.8%	3.75%
7	0.7%	0.3%	0.66%
8	18.0%	18.3%	1.57%
9	0.0%	0.1%	0.24%
10	0.0%	0.8%	1.92%
11	14.0%	15.1%	2.35%
12	0.0%	1.3%	2.06%
13	0.0%	0.1%	0.35%
14	0.0%	0.0%	0.00%
15	1.6%	5.7%	3.11%