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Supporting Information

NOAH: NMR Supersequences for Small Molecule Analysis and Structure Elucidation

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Supporting Information

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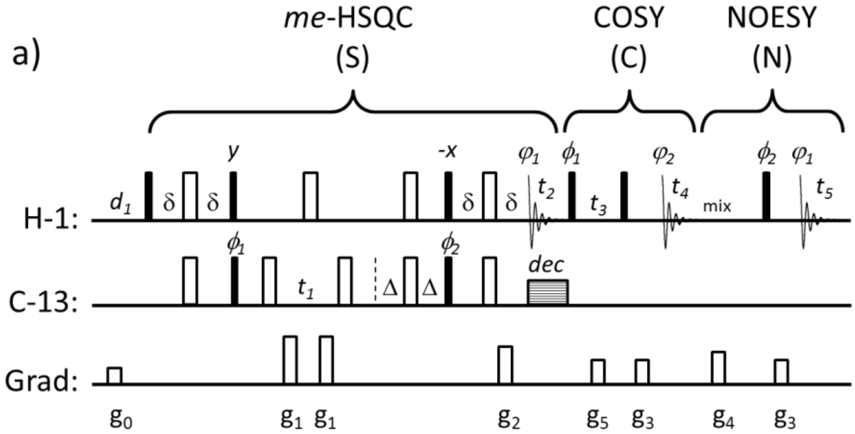
Description of example NOAH-3 and NOAH-5 supersequences

Many variants of the NOAH supersequences may be created by arranging appropriately the component modules, as suggested in Tables 1 (main text) and S1 below. The maximum number of experiments combined into one NOAH experiment that we have achieved so far is five. The representative pulse sequences for the NOAH-3, SCN and NOAH-5, MSBCN experiments are shown in Figure S1 and described here.



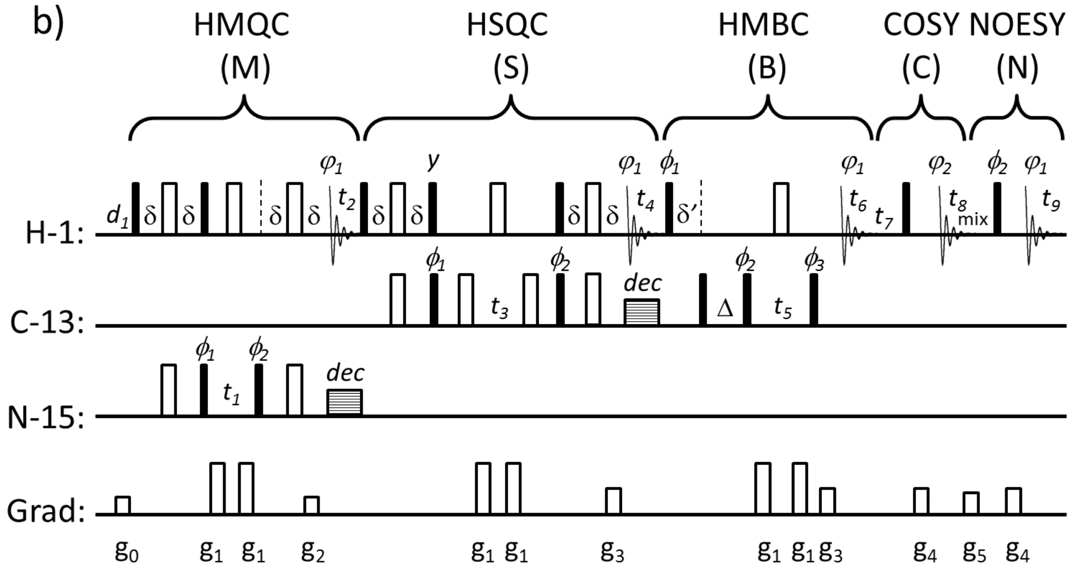


Fig. S1. (a) The NOAH-3 (SCN) pulse sequence combining 2D ^{13}C multiplicity edited HSQC, 2D COSY and 2D NOESY experiments. All pulses are applied with phase *x* unless indicated otherwise. Phase cycles: ϕ_1=x,-x, ϕ_2=x,x,-x,-x, receiver phases: φ_1=x,-x,-x,x, φ_2=x,-x; gradients (ms, G/cm): g_0=(1, 7), g_1=(1, 40), g_2=(1, 20.1), g_3=g_5=(1, 10), g_4=(1, 17). The polarity of gradient pulses, g_1, g_3 and all receiver phases are inverted for all even increments. The 180 degree C-13 pulses are constant adiabaticity WURST pulses. The δ delays are the J-evolution delays set to $1/4J_{CH}$, the delay Δ is set to $1/2J_{CH}$ for multiplicity editing, d_1 is the common recovery delay and *mix* defines the NOESY mixing delay. (b) The NOAH-5 (MSBCN) pulse sequence combining 2D ^{15}N HMQC, 2D ^{13}C HSQC, 2D ^{13}C HMBC, 2D COSY and 2D NOESY experiments. All pulses are applied with phase *x* unless indicated otherwise. Phase cycles: ϕ_1=x,-x, ϕ_2=x,x,-x,-x, ϕ_3=x, receiver phases: φ_1=x,-x,-x,x, φ_2=x,-x; gradients (ms, G/cm): g_0=(1, 7), g_1=(1,40), g_2=(1,10), g_3=g_4=(1,20), g_5=(1,17). The polarity of gradient pulses, g_1, g_4 and all receiver phases are inverted for all even increments. The 180 degree C-13 pulses are constant adiabaticity WURST pulses. The δ delays are the J-evolution delays set to $1/4J_{NH}$ and $1/4J_{CH}$ in the ^{15}N HMQC and ^{13}C HSQC modules respectively. The δ' delay serves for low-pass filtration for residual one-bond correlations and is set to $1/2J_{CH}$ for the one-bond J_{CH} couplings, Δ is set to $1/2^nJ_{CH}$ for the long-range J_{CH} couplings, d_1 is the common recovery delay and *mix* defines the NOESY mixing delay.

The NOAH-3 experiment (Fig. S1a) begins with the multiplicity edited version of the ^{13}C HSQC module where the phase cycle and gradients are arranged in such a way as to keep the magnetization of protons that are not directly coupled to ^{13}C along the +z axis at the end of this module. The bulk ^{1}H magnetization that is preserved in the HSQC experiment is then used by the following COSY and NOESY modules as described in detail in the main text. The spectra recorded with this pulse sequence are shown in Fig S4.

The NOAH-5 experiment (Fig. S1b) starts with the ^{15}N HMQC pulse sequence. The magnetization from protons that are not directly bound to ^{15}N nuclei is preserved and kept along the +z-axis at the end of this pulse sequence module. This is followed by the ^{13}C HSQC module where the phase cycle and gradients are arranged in such a way as to keep the magnetization of protons that are not directly coupled to ^{13}C along the +z axis. Multiplicity editing may be incorporated through addition of a spin-echo prior to the reverse-INEPT step, as for the standard implementation of the edited HSQC experiment (see Fig. S1a). HSQC is followed by the HMBC pulse sequence, which is essentially equivalent to the basic HMBC pulse sequence with the echo-anti-echo gradient selection scheme. We use the version of the HMBC pulse sequence that preserves the magnetization of the protons that are not coupled to ^{13}C nuclei via long range ^{13}C-^{1}H couplings. This magnetization is de-phased by the decoding gradient at the end of the HMBC block before the ^{13}C HMBC FID is acquired. This last gradient in the HMBC block that refocuses the ^{1}H magnetization of protons coupled to ^{13}C at the same time serves also as the encoding gradient for the following H-H COSY experiment. The encoded ^{1}H magnetization of the COSY experiment is allowed to evolve during the t_7-evolution delay just after the 2D HMBC spectrum is recorded. Note that both the $^{n}J_{CH}$ and J_{HH} couplings evolve during the HMBC experiment. This allows reduction of the relatively long t_1-evolution period that is typically required for the conventional 2D H-H COSY experiments. In fact, it can be beneficial to set the conventional COSY t_1 evolution delay to a fixed starting delay to allow the J_{HH} couplings to evolve before the first FID is recorded so as to enhance crosspeak intensities. On the other hand, a too long initial J_{HH} evolution tends to emphasize correlations via small, long range couplings that are not always deemed to be useful. Therefore, some compromise between the duration of the HMBC acquisition time and J_{HH} evolution period may be necessary for this particular combination of the two NOAH modules. At the end of the t_7 (COSY t_1) evolution period a 90˚ proton read pulse transfers the frequency encoded magnetization to coupled proton sites. Following this read pulse half of the magnetization is stored along the z-axis while the other half is refocused by the decoding gradient and observed during the free induction decay, t_8 providing the 2D COSY spectrum. The COSY acquisition period, t_8 serves also as the first part of the NOESY mixing period. As in the NOAH-MSCN experiment (see Fig. 1 in the main text) both the COSY and NOESY experiments in this NOAH-MSBCN pulse sequence share the same t_1 evolution period (here t_7). The COSY acquisition is appended with a delay (*mix*) to meet the requirements of the total duration of the NOESY mixing period (t_8 + *mix)*. The NOESY block ends with a read pulse and a decoding gradient before the 2D NOESY spectrum is acquired (t_9). Thus all five 2D spectra in this version of the NOAH-MSBCN experiment are recorded starting from a single d_1 recovery delay, providing substantial time savings. The spectra recorded with this pulse sequence are shown in Fig. 3 of the main text.

Comparison with the conventionally acquired 2D spectra

The quality of the NOAH-4 (MSCN) spectra is compared with that of the corresponding conventionally acquired 2D spectra in Figs S2 and S3. Both data sets were recorded with a single scan per increment to emphasize the speed factor and the quality of the NOAH spectra that can be obtained without extensive phase cycling. The total experiment time is reduced approximately three-fold, from ~27 minutes for the four conventionally acquired data sets to 8 minutes and 38 seconds for NOAH. While a slight increase in the t_1-noise was observed in the COSY and NOESY modules of the NOAH-4 data, this can easily be overcome by symmetrization. For low concentration / low sensitivity samples the number of scans can be increased as required. As usual, this also helps with the artefact suppression from phase cycling. Likewise the resolution of the spectra can be improved by increasing the number of t_1 increments in more demanding samples with no reduction in the efficiency of the NOAH experiments.

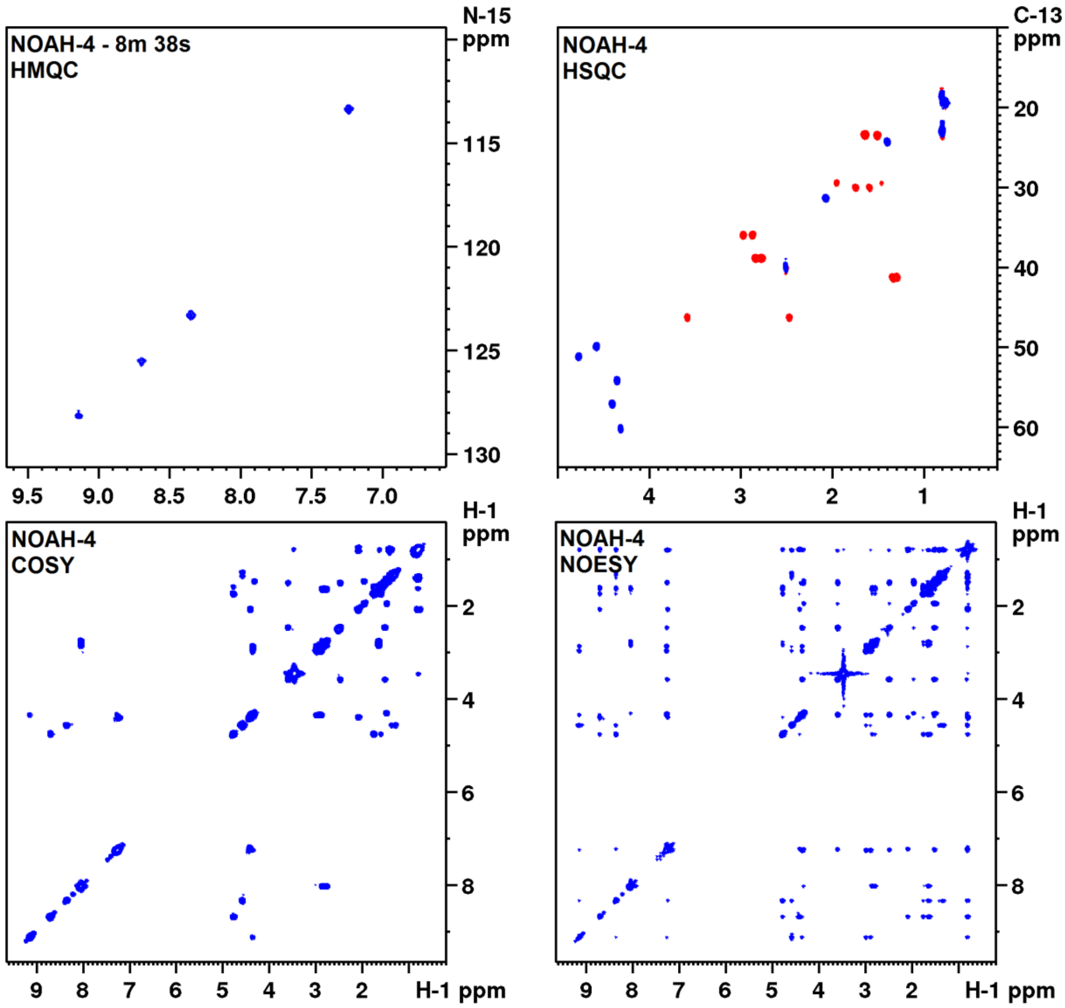


Fig. S2. NOAH-4 (MSCN), spectra of 50 mM gramicidin S in DMSO-d_6 at 298K, to be compared with the corresponding conventional 2D experiments shown in Fig. S3; d1=1.3 s, ns=1, the NOESY mixing time was 350 ms, raw data size=1k x 1k (256 x 4), sw=7002 x 3501 Hz (^{15}N HMQC), 7002 x 35014 (^{13}C HSQC) and 7002 x 7002 Hz (^{1}H COSY and NOESY), the total experiment duration was 8 min 38s.

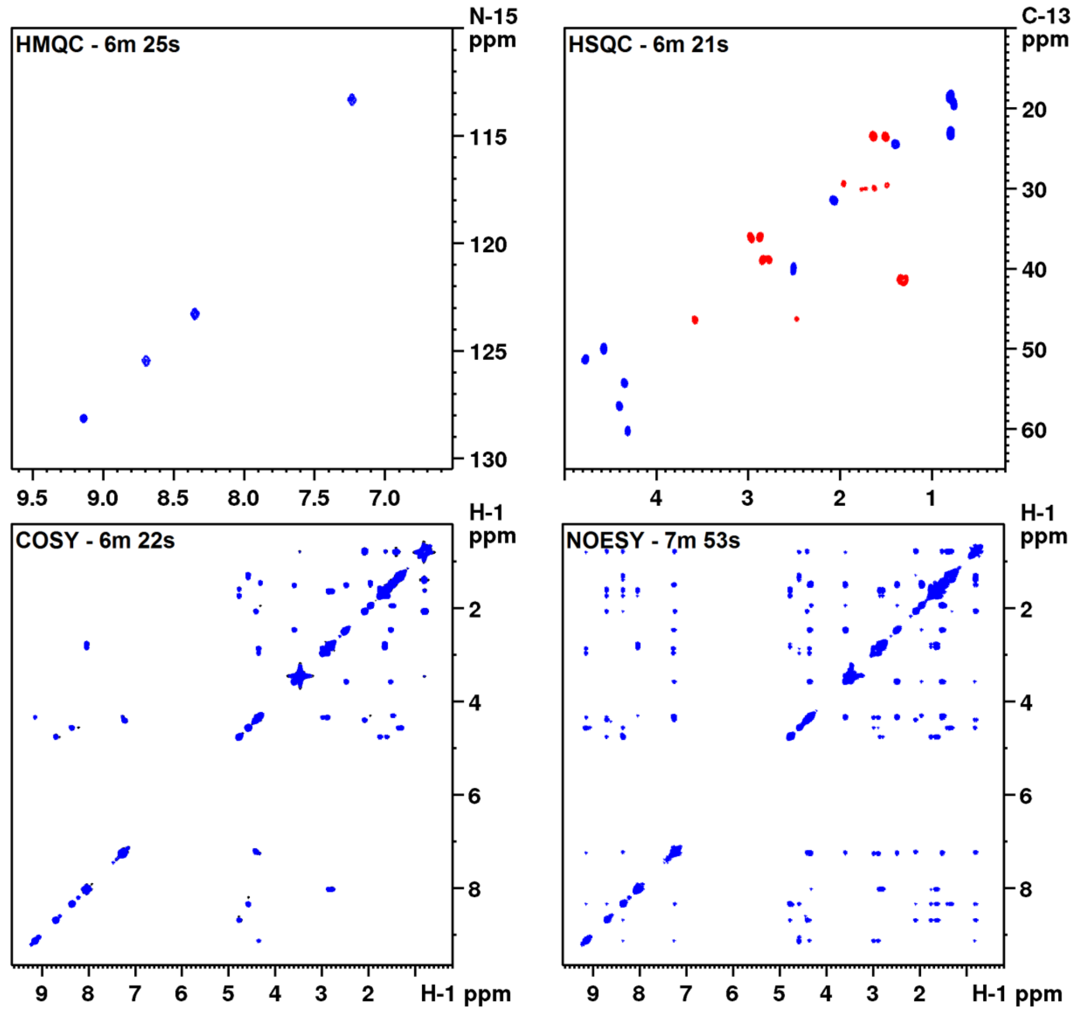


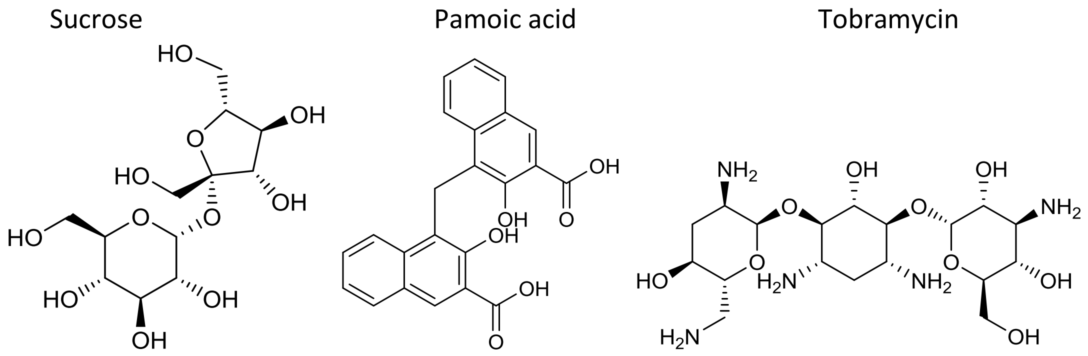
Fig. S3. Individual conventionally acquired 2D spectra of 50 mM gramicidin S in DMSO-d_6 at 298K recorded with similar parameters to the corresponding modules in the NOAH-4 experiment shown in Fig S2, d1=1.3 s, ns=1, raw data size=1k x 256, sw=7002 x 3501 Hz (^{15}N HMQC), 7002 x 35014 (^{13}C HSQC) and 7002 x 7002 Hz (^{1}H COSY and NOESY), the NOESY mixing time was 350 ms; the individual experiment times were 6m 25 s (HMQC), 6m 21s (HSQC), 6m 22s (COSY) and 7m 53s (NOESY), the total experiment duration for all four 2D experiments was 27 min 21s.

Illustrative NOAH spectra

So far out of the 285 possible supersequences outlined in Table 1 (main text) and Table S1 we have successfully tested the following 12 experiments:

NOAH-2: **SB** Fig. S4, **SC** Fig. S5, **BC** Fig. S8, **MC** Fig. S9, **MB** Fig. S10;
NOAH-3: **SCN** Fig. S6, **MCN** Fig. S11, **SBD** Fig. S12, **SBT** Fig. S13;
NOAH-4: **MSCN** Fig. 2 (main text), **SBCN** Fig. S7;
NOAH-5: **MSBCN** Fig. 3 (main text).

The sequences are illustrated below using the following compounds:



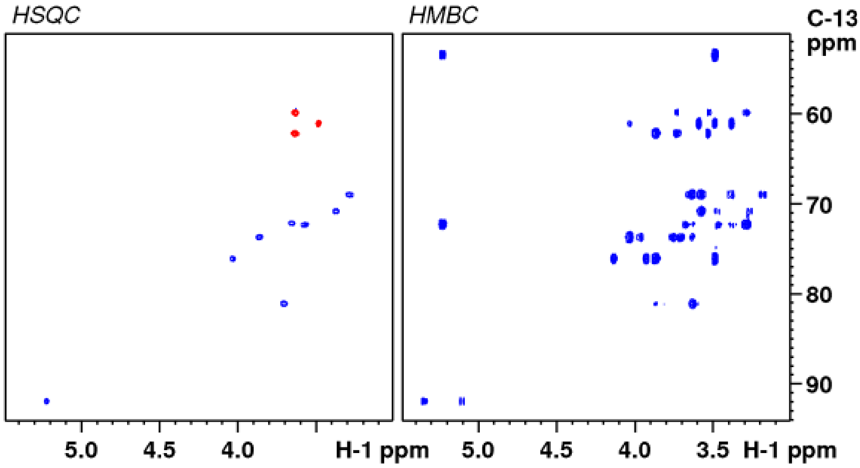


Fig. S4. NOAH-2 (SB), multiplicity edited ^{13}C HSQC+^{13}C HMBC, the sample is 2 mM sucrose in D_2O, d1=1.2 s, ns=1, raw data size=1k x 256, sw=3200 x 8800 Hz (^{13}C), the total experiment duration was 3 min 50 sec. Note, the peak that appears at 53.5 ppm is folded from 103.5 ppm in the HMBC spectrum.

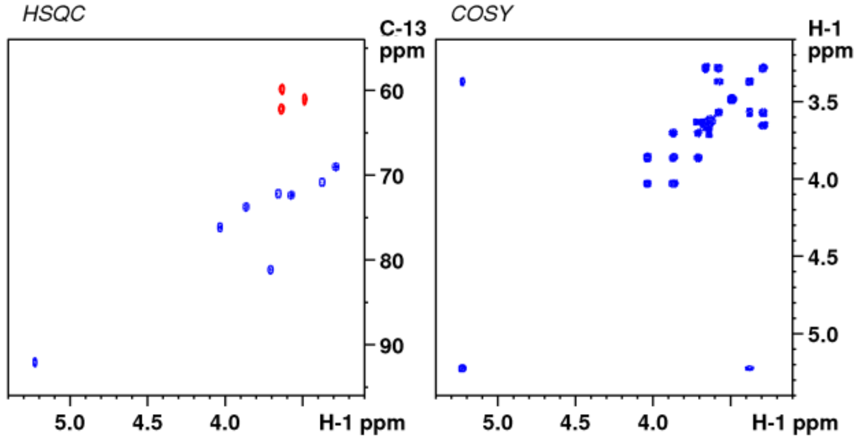


Fig. S5. NOAH-2 (SC), multiplicity edited ^{13}C HSQC+COSY, the sample is 2 mM sucrose in D_2O, d1=1.2 s, ns=1, raw data size=1k x 512, sw=3200 x 35200 Hz (^{13}C) and 3200 x 3200 Hz (^{1}H), the total experiment duration was 7 min.

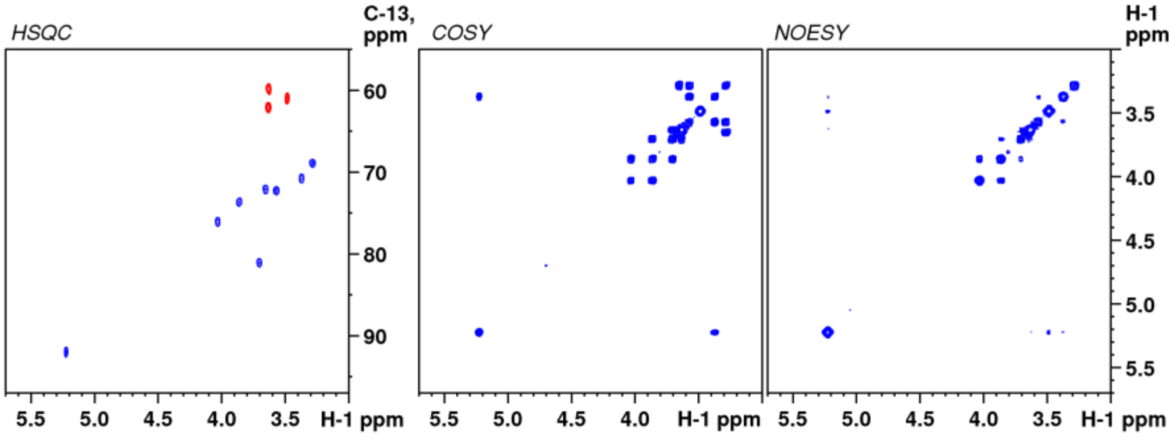


Fig. S6. NOAH-3 (SCN), multiplicity edited ^{13}C HSQC+COSY+NOESY, the sample is 2 mM sucrose in D_2O, d1=1.2 s, ns=1, raw data size=1k x 768, sw=3200 x 35200 Hz (^{13}C) and 3200 x 3200 Hz (^{1}H), the total experiment duration was 10 min. The relatively long duration of the experiment is partially due to the long NOESY mixing delay of 700 ms.

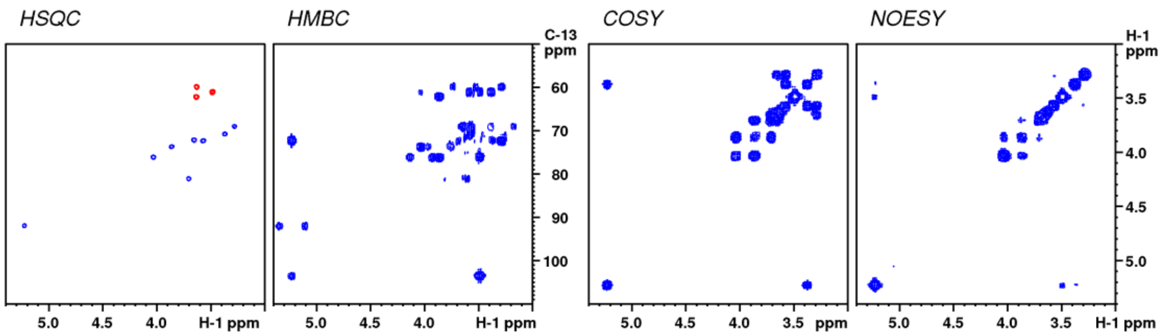


Fig. S7. NOAH-4 (SBCN), multiplicity edited ^{13}C HSQC+^{13}C HMBC+COSY+NOESY, the sample is 2 mM sucrose in D_2O, d1=1.5 s, ns=1, raw data size=512 x 1024, sw=3200 x 35200 Hz (^{13}C) and 3200 x 3200 Hz (^{1}H), the total experiment duration was 12 min. The relatively long duration of the experiment is partially due to the long NOESY mixing delay of 700 ms.

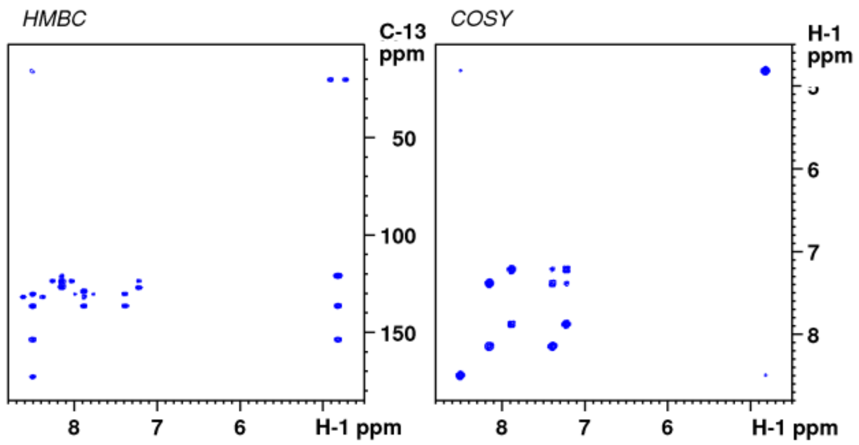


Fig. S8. NOAH-2 (BC), ^{13}C HMBC+COSY, the sample is 10 mM pamoic acid in DMSO-d_6, d1=2 s, ns=1, raw data size=512 x 512, sw=3200 x 35200 Hz (^{13}C) and 3200 x 3200 Hz (^{1}H), the total experiment duration was 10 min.

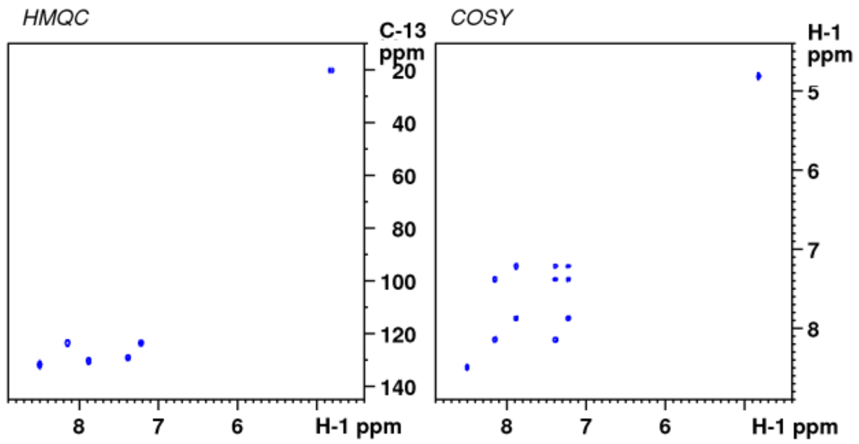


Fig. S9. NOAH-2 (MC), ^{13}C HMQC+COSY, the sample is 10 mM pamoic acid in DMSO-d_6, d1=1.2 s, ns=1, raw data size=1k x 512, sw=3200 x 35200 Hz (^{13}C) and 3200 x 3200 Hz (^{1}H), the total experiment duration was 7 min.

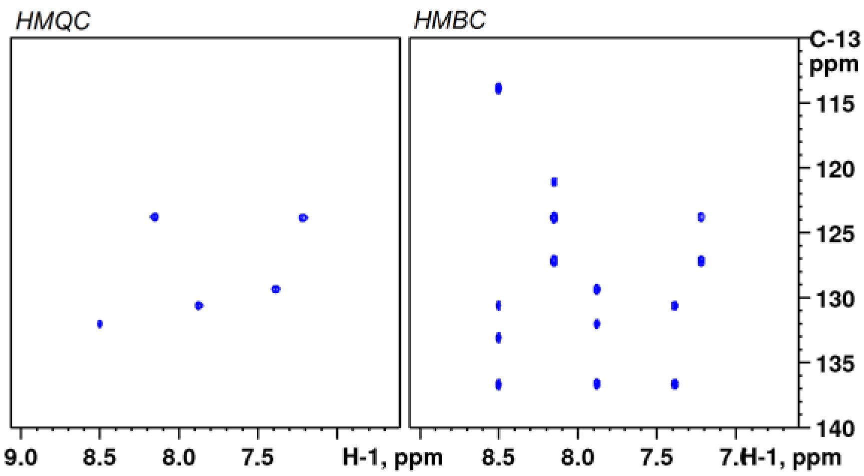


Fig. S10. NOAH-2 (MB), ^{13}C HMQC+^{13}C HMBC, the sample is 10 mM pamoic acid in DMSO-d_6, d1=1.2 s, ns=1, raw data size=1k x 256, sw=3200 x 35200 Hz (^{13}C), the total experiment duration was 3 min. 20 sec. Only the aromatic part of the spectrum is shown. The peak that appears at 114 ppm is folded (CH_2 group).

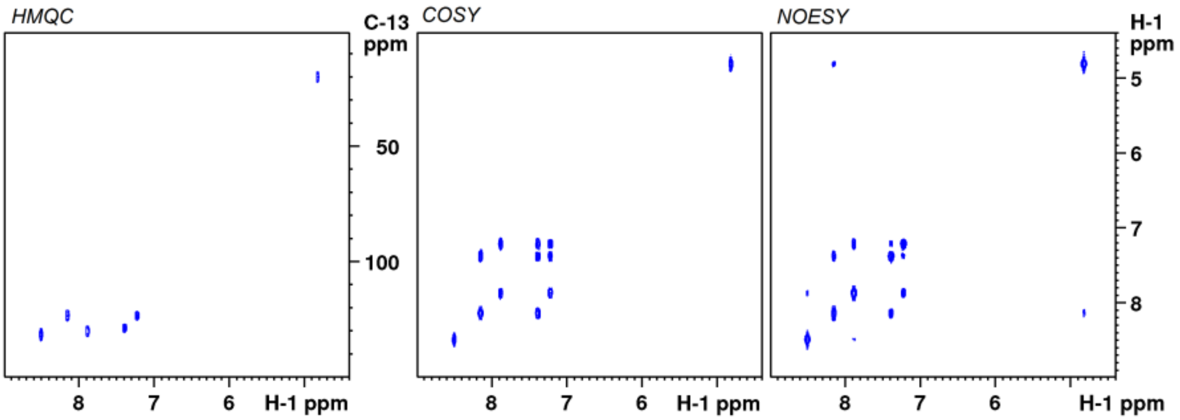


Fig. S11. NOAH-3 (MCN), [13]C HMQC+COSY+NOESY, the sample is 10 mM pamoic acid in DMSO-d_6, d1=2 s, ns=1, raw data size=1k x 384, sw=3200 x 35200 Hz ([13]C) and 3200 x 3200 Hz ([1]H), the total experiment duration was 11 min.

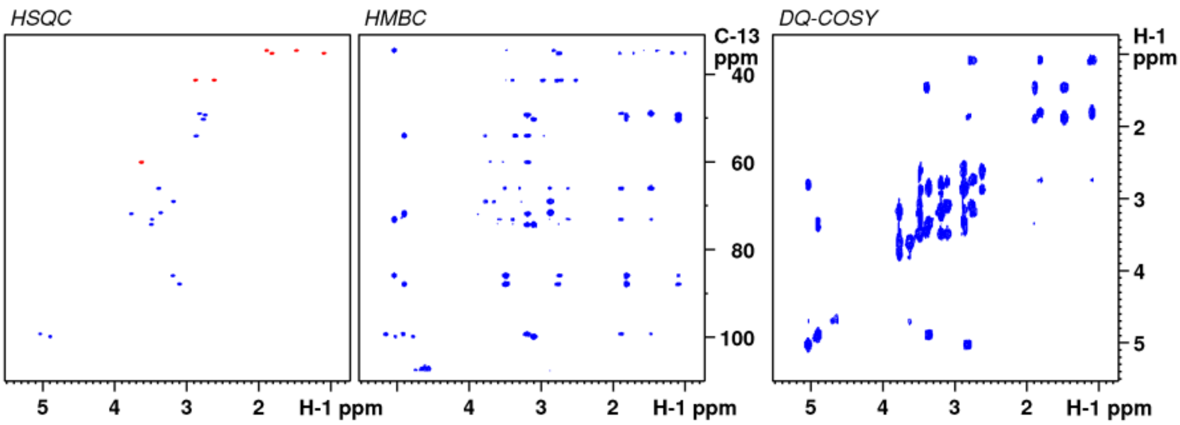


Fig. S12. NOAH-3 (SBD), multiplicity edited [13]C HSQC+[13]C HMBC+DQFCOSY, the sample is 2 mM tobramycin in D_2O, d1=1.0 s, ns=1, raw data size=1k x 768, sw=7002 x 14005 Hz ([13]C) and 7002 x 7002 Hz ([1]H), the total experiment duration was 7 min.

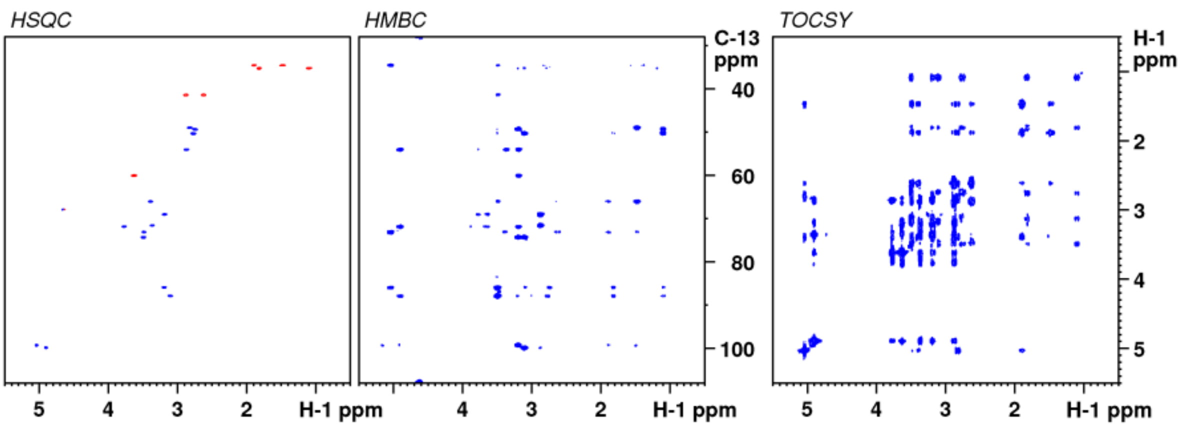


Fig. S13. NOAH-3 (SBT), multiplicity edited [13]C HSQC+ [13]C HMBC+TOCSY, the sample is 2 mM tobramycin in D_2O, d1=1.5 s, ns=1, raw data size=1k x 768, sw=7002 x 14005 Hz ([13]C) and 7002 x 7002 Hz ([1]H), the total experiment duration was 8 min 40s.

Table S1: Further examples of NOAH supersequences (continued from main text Table 1).

”me” denotes multiplicity edited pulse sequences.

NOAH-2:

25) ^{13}C HSQC-^{15}N HMBC
26) ^{13}C HSQC-^{15}N HMQC
27) ^{13}C HSQC-^{15}N HSQC
28) ^{13}C HSQC-^{15}N meHSQC
29) ^{13}C HMQC-^{15}N HMBC
30) ^{13}C HMQC-^{15}N HMQC
31) ^{13}C HMQC-^{15}N HSQC
32) ^{13}C HMQC-^{15}N meHSQC
33) ^{13}C meHSQC-COSY (Fig. S5)
34) ^{13}C meHSQC-NOESY
35) ^{13}C meHSQC-TOCSY
36) ^{13}C meHSQC-DQFCOSY
37) ^{13}C meHSQC-^{13}C HMBC (Fig. S4)
38) ^{13}C meHSQC-^{15}N HMBC
39) ^{13}C meHSQC-^{15}N HMQC
40) ^{13}C meHSQC-^{15}N HSQC
41) ^{13}C meHSQC-^{15}N meHSQC
42) ^{15}N HSQC-COSY
43) ^{15}N HSQC-NOESY
44) ^{15}N HSQC-TOCSY
45) ^{15}N HSQC-DQFCOSY
46) ^{15}N HSQC-^{15}N HMBC
47) ^{15}N HSQC-^{13}C HMQC
48) ^{15}N HSQC-^{13}C HMBC
49) ^{15}N HSQC-^{13}C HSQC
50) ^{15}N HSQC-^{13}C meHSQC
51) ^{15}N HMQC-COSY
52) ^{15}N HMQC-NOESY
53) ^{15}N HMQC-TOCSY
54) ^{15}N HMQC-DQFCOSY
55) ^{15}N HMQC-^{15}N HMBC
56) ^{15}N HMQC-^{13}C HMQC
57) ^{15}N HMQC-^{13}C HMBC
58) ^{15}N HMQC-^{13}C HSQC
59) ^{15}N HMQC-^{13}C meHSQC
60) ^{15}N meHSQC-COSY
61) ^{15}N meHSQC-NOESY
62) ^{15}N meHSQC-TOCSY
63) ^{15}N meHSQC-DQFCOSY
64) ^{15}N meHSQC-^{15}N HMBC
65) ^{15}N meHSQC-^{13}C HMQC
66) ^{15}N meHSQC-^{13}C HMBC
67) ^{15}N meHSQC-^{13}C HSQC
68) ^{15}N meHSQC-^{13}C meHSQC
69) ^{13}C HMBC-COSY (Fig. S8)

70) ^{13}C HMBC-DQFCOSY
71) ^{13}C HMBC-TOCSY
72) ^{13}C HMBC-NOESY
73) ^{15}N HMBC- COSY
74) ^{15}N HMBC-DQFCOSY
75) ^{15}N HMBC-TOCSY
76) ^{15}N HMBC-NOESY

NOAH-3:

77) ^{13}C HSQC-^{15}N HMBC-COSY
78) ^{13}C HSQC-^{15}N HMQC-COSY
79) ^{13}C HSQC-^{15}N HSQC-COSY
80) ^{13}C HSQC-^{15}N meHSQC-COSY
81) ^{13}C HMQC-^{15}N HMBC-COSY
82) ^{13}C HMQC-^{15}N HMQC-COSY
83) ^{13}C HMQC-^{15}N HSQC-COSY
84) ^{13}C HMQC-^{15}N meHSQC-COSY
85) ^{13}C meHSQC-^{13}C HMBC-COSY
86) ^{13}C meHSQC-^{15}N HMBC-COSY
87) ^{13}C meHSQC-^{15}N HMQC-COSY
88) ^{13}C meHSQC-^{15}N HSQC-COSY
89) ^{13}C meHSQC-^{15}N meHSQC-COSY
90) ^{15}N HSQC-^{15}N HMBC-COSY
91) ^{15}N HSQC-^{13}C HMQC-COSY
92) ^{15}N HSQC-^{13}C HMBC-COSY
93) ^{15}N HSQC-^{13}C HSQC-COSY
94) ^{15}N HSQC-^{13}C meHSQC-COSY
95) ^{15}N HMQC-^{15}N HMBC-COSY
96) ^{15}N HMQC-^{13}C HMQC-COSY
97) ^{15}N HMQC-^{13}C HMBC-COSY
98) ^{15}N HMQC-^{13}C HSQC-COSY
99) ^{15}N HMQC-^{13}C meHSQC-COSY
100) ^{15}N meHSQC-^{15}N HMBC-COSY
101) ^{15}N meHSQC-^{13}C HMQC-COSY
102) ^{15}N meHSQC-^{13}C HMBC-COSY
103) ^{15}N meHSQC-^{13}C HSQC-COSY
104) ^{15}N meHSQC-^{13}C meHSQC-COSY
105) ^{13}C HSQC-^{15}N HMBC-DQFCOSY
106) ^{13}C HSQC-^{15}N HMQC-DQFCOSY
107) ^{13}C HSQC-^{15}N HSQC-DQFCOSY
108) ^{13}C HSQC-^{15}N meHSQC-DQFCOSY
109) ^{13}C HMQC-^{15}N HMBC-DQFCOSY
110) ^{13}C HMQC-^{15}N HMQC-DQFCOSY
111) ^{13}C HMQC-^{15}N HSQC-DQFCOSY
112) ^{13}C HMQC-^{15}N meHSQC-DQFCOSY
113) ^{13}C meHSQC-^{13}C HMBC-DQFCOSY (Fig. S12)
114) ^{13}C meHSQC-^{15}N HMBC-DQFCOSY
115) ^{13}C meHSQC-^{15}N HMQC-DQFCOSY
116) ^{13}C meHSQC-^{15}N HSQC-DQFCOSY
117) ^{13}C meHSQC-^{15}N meHSQC-DQFCOSY

118) ^{15}N HSQC-^{15}N HMBC-DQFCOSY
119) ^{15}N HSQC-^{13}C HMQC-DQFCOSY
120) ^{15}N HSQC-^{13}C HMBC-DQFCOSY
121) ^{15}N HSQC-^{13}C HSQC-DQFCOSY
122) ^{15}N HSQC-^{13}C meHSQC-DQFCOSY
123) ^{15}N HMQC-^{15}N HMBC-DQFCOSY
124) ^{15}N HMQC-^{13}C HMQC-DQFCOSY
125) ^{15}N HMQC-^{13}C HMBC-DQFCOSY
126) ^{15}N HMQC-^{13}C HSQC-DQFCOSY
127) ^{15}N HMQC-^{13}C meHSQC-DQFCOSY
128) ^{15}N meHSQC-^{15}N HMBC-DQFCOSY
129) ^{15}N meHSQC-^{13}C HMQC-DQFCOSY
130) ^{15}N meHSQC-^{13}C HMBC-DQFCOSY
131) ^{15}N meHSQC-^{13}C HSQC-DQFCOSY
132) ^{15}N meHSQC-^{13}C meHSQC-DQFCOSY
133) ^{13}C HSQC-^{15}N HMBC-TOCSY
134) ^{13}C HSQC-^{15}N HMQC-TOCSY
135) ^{13}C HSQC-^{15}N HSQC-TOCSY
136) ^{13}C HSQC-^{15}N meHSQC-TOCSY
137) ^{13}C HMQC-^{15}N HMBC-TOCSY
138) ^{13}C HMQC-^{15}N HMQC-TOCSY
139) ^{13}C HMQC-^{15}N HSQC-TOCSY
140) ^{13}C HMQC-^{15}N meHSQC-TOCSY
141) ^{13}C meHSQC-^{13}C HMBC-TOCSY (Fig. S13)
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143) ^{13}C meHSQC-^{15}N HMQC-TOCSY
144) ^{13}C meHSQC-^{15}N HSQC-TOCSY
145) ^{13}C meHSQC-^{15}N meHSQC-TOCSY
146) ^{15}N HSQC-^{15}N HMBC-TOCSY
147) ^{15}N HSQC-^{13}C HMQC-TOCSY
148) ^{15}N HSQC-^{13}C HMBC-TOCSY
149) ^{15}N HSQC-^{13}C HSQC-TOCSY
150) ^{15}N HSQC-^{13}C meHSQC-TOCSY
151) ^{15}N HMQC-^{15}N HMBC-TOCSY
152) ^{15}N HMQC-^{13}C HMQC-TOCSY
153) ^{15}N HMQC-^{13}C HMBC-TOCSY
154) ^{15}N HMQC-^{13}C HSQC-TOCSY
155) ^{15}N HMQC-^{13}C meHSQC-TOCSY
156) ^{15}N meHSQC-^{15}N HMBC-TOCSY
157) ^{15}N meHSQC-^{13}C HMQC-TOCSY
158) ^{15}N meHSQC-^{13}C HMBC-TOCSY
159) ^{15}N meHSQC-^{13}C HSQC-TOCSY
160) ^{15}N meHSQC-^{13}C meHSQC-TOCSY
161) ^{13}C HSQC-^{15}N HMBC-NOESY
162) ^{13}C HSQC-^{15}N HMQC-NOESY
163) ^{13}C HSQC-^{15}N HSQC-NOESY
164) ^{13}C HSQC-^{15}N meHSQC-NOESY
165) ^{13}C HMQC-^{15}N HMBC-NOESY
166) ^{13}C HMQC-^{15}N HMQC-NOESY
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173) ^{13}C meHSQC-^{15}N meHSQC-NOESY
174) ^{15}N HSQC-^{15}N HMBC-NOESY
175) ^{15}N HSQC-^{13}C HMQC-NOESY
176) ^{15}N HSQC-^{13}C HMBC-NOESY
177) ^{15}N HSQC-^{13}C HSQC-NOESY
178) ^{15}N HSQC-^{13}C meHSQC-NOESY
179) ^{15}N HMQC-^{15}N HMBC-NOESY
180) ^{15}N HMQC-^{13}C HMQC-NOESY
181) ^{15}N HMQC-^{13}C HMBC-NOESY
182) ^{15}N HMQC-^{13}C HSQC-NOESY
183) ^{15}N HMQC-^{13}C meHSQC-NOESY
184) ^{15}N meHSQC-^{15}N HMBC-NOESY
185) ^{15}N meHSQC-^{13}C HMQC-NOESY
186) ^{15}N meHSQC-^{13}C HMBC-NOESY
187) ^{15}N meHSQC-^{13}C HSQC-NOESY
188) ^{15}N meHSQC-^{13}C meHSQC-NOESY
189) ^{13}C HMQC- COSY-NOESY (Fig. S11)
190) ^{13}C meHSQC- COSY-NOESY (Fig. S6)
191) ^{15}N HSQC- COSY-NOESY
192) ^{15}N meHSQC- COSY-NOESY

NOAH-4:

193) ^{13}C HSQC-^{15}N HMBC-COSY-NOESY
194) ^{13}C HSQC-^{15}N HMQC-COSY-NOESY
195) ^{13}C HSQC-^{15}N HSQC-COSY-NOESY
196) ^{13}C HSQC-^{15}N meHSQC-COSY-NOESY
197) ^{13}C HMQC-^{15}N HMBC-COSY-NOESY
198) ^{13}C HMQC-^{15}N HMQC-COSY-NOESY
199) ^{13}C HMQC-^{15}N HSQC-COSY-NOESY
200) ^{13}C HMQC-^{15}N meHSQC-COSY-NOESY
201) ^{13}C meHSQC-^{13}C HMBC-COSY-NOESY (Fig. S7)
202) ^{13}C meHSQC-^{15}N HMBC-COSY-NOESY
203) ^{13}C meHSQC-^{15}N HMQC-COSY-NOESY
204) ^{13}C meHSQC-^{15}N HSQC-COSY-NOESY
205) ^{13}C meHSQC-^{15}N meHSQC-COSY-NOESY
206) ^{15}N HSQC-^{15}N HMBC-COSY-NOESY
207) ^{15}N HSQC-^{13}C HMQC-COSY-NOESY
208) ^{15}N HSQC-^{13}C HMBC-COSY-NOESY
209) ^{15}N HSQC-^{13}C HSQC-COSY-NOESY
210) ^{15}N HSQC-^{13}C meHSQC-COSY-NOESY
211) ^{15}N HMQC-^{15}N HMBC-COSY-NOESY
212) ^{15}N HMQC-^{13}C HMQC-COSY-NOESY
213) ^{15}N HMQC-^{13}C HMBC-COSY-NOESY
214) ^{15}N HMQC-^{13}C meHSQC-COSY-NOESY
215) ^{15}N meHSQC-^{15}N HMBC-COSY-NOESY
216) ^{15}N meHSQC-^{13}C HMQC-COSY-NOESY

217) ^{15}N meHSQC-^{13}C HMBC-COSY-NOESY
218) ^{15}N meHSQC-^{13}C HSQC-COSY-NOESY
219) ^{15}N meHSQC-^{13}C meHSQC-COSY-NOESY
220) ^{13}C HSQC-^{15}N HMQC-^{13}C HMBC-NOESY
221) ^{13}C HSQC-^{15}N HSQC-^{13}C HMBC-NOESY
222) ^{13}C HSQC-^{15}N meHSQC-^{13}C HMBC-NOESY
223) ^{13}C HMQC-^{15}N HMQC-^{13}C HMBC-NOESY
224) ^{13}C HMQC-^{15}N HSQC-^{13}C HMBC-NOESY
225) ^{13}C HMQC-^{15}N meHSQC-^{13}C HMBC-NOESY
226) ^{13}C meHSQC-^{15}N HMQC-^{13}C C HMBC-NOESY
227) ^{13}C meHSQC-^{15}N HSQC-^{13}C HMBC-NOESY
228) ^{13}C meHSQC-^{15}N meHSQC-^{13}C HMBC-NOESY
229) ^{15}N HSQC-^{13}C HMQC-^{13}C HMBC-NOESY
230) ^{15}N HSQC-^{13}C HSQC-^{13}C HMBC-NOESY
231) ^{15}N HSQC-^{13}C meHSQC-^{13}C HMBC-NOESY
232) ^{15}N HMQC-^{13}C HMQC-^{13}C HMBC-NOESY
233) ^{15}N HMQC-^{13}C meHSQC-^{13}C HMBC-NOESY
234) ^{15}N meHSQC-^{13}C HMQC-^{13}C HMBC-NOESY
235) ^{15}N meHSQC-^{13}C HSQC-^{13}C HMBC-NOESY
236) ^{15}N meHSQC-^{13}C meHSQC-^{13}C HMBC-NOESY
237) ^{13}C HSQC-^{15}N HMQC-^{13}C HMBC-COSY
238) ^{13}C HSQC-^{15}N HSQC-^{13}C HMBC-COSY
239) ^{13}C HSQC-^{15}N meHSQC-^{13}C HMBC-COSY
240) ^{13}C HMQC-^{15}N HMQC-^{13}C HMBC-COSY
241) ^{13}C HMQC-^{15}N HSQC-^{13}C HMBC-COSY
242) ^{13}C HMQC-^{15}N meHSQC-^{13}C HMBC-COSY
243) ^{13}C meHSQC-^{15}N HMQC-^{13}C C HMBC-COSY
244) ^{13}C meHSQC-^{15}N HSQC-^{13}C HMBC-COSY
245) ^{13}C meHSQC-^{15}N meHSQC-^{13}C HMBC-COSY
246) ^{15}N HSQC-^{13}C HMQC-^{13}C HMBC-COSY
247) ^{15}N HSQC-^{13}C HSQC-^{13}C HMBC-COSY
248) ^{15}N HSQC-^{13}C meHSQC-^{13}C HMBC-COSY
249) ^{15}N HMQC-^{13}C HMQC-^{13}C HMBC-COSY
250) ^{15}N HMQC-^{13}C meHSQC-^{13}C HMBC-COSY
251) ^{15}N meHSQC-^{13}C HMQC-^{13}C HMBC-COSY
252) ^{15}N meHSQC-^{13}C HSQC-^{13}C HMBC-COSY
253) ^{15}N meHSQC-^{13}C meHSQC-^{13}C HMBC-COSY

NOAH-5:

254) ^{13}C HSQC-^{15}N HMQC-^{13}C HMBC-COSY-NOESY
255) ^{13}C HSQC-^{15}N HSQC-^{13}C HMBC-COSY-NOESY
256) ^{13}C HSQC-^{15}N meHSQC-^{13}C HMBC-COSY-NOESY
257) ^{13}C HMQC-^{15}N HMQC-^{13}C HMBC-COSY-NOESY
258) ^{13}C HMQC-^{15}N HSQC-^{13}C HMBC-COSY-NOESY
259) ^{13}C HMQC-^{15}N meHSQC-^{13}C HMBC-COSY-NOESY
260) ^{13}C meHSQC-^{15}N HMQC-^{13}C HMBC-COSY-NOESY
261) ^{13}C meHSQC-^{15}N HSQC-^{13}C HMBC-COSY-NOESY
262) ^{13}C meHSQC-^{15}N meHSQC-^{13}C HMBC-COSY-NOESY
263) ^{15}N HSQC-^{13}C HMQC-^{13}C HMBC-COSY-NOESY
264) ^{15}N HSQC-^{13}C HSQC-^{13}C HMBC-COSY-NOESY

265) ^{15}N HSQC-^{13}C meHSQC-^{13}C HMBC-COSY-NOESY
266) ^{15}N HMQC-^{13}C HMQC-^{13}C HMBC-COSY-NOESY
267) ^{15}N HMQC-^{13}C meHSQC-^{13}C HMBC-COSY-NOESY
268) ^{15}N meHSQC-^{13}C HMQC-^{13}C HMBC-COSY-NOESY
269) ^{15}N meHSQC-^{13}C HSQC-^{13}C HMBC-COSY-NOESY
270) ^{15}N meHSQC-^{13}C meHSQC-^{13}C HMBC-COSY-NOESY
271) ^{13}C HSQC-^{15}N meHSQC-^{15}N HMBC-COSY-NOESY
272) ^{13}C HMQC-^{15}N HMQC-^{15}N HMBC-COSY-NOESY
273) ^{13}C HMQC-^{15}N HSQC-^{15}N HMBC-COSY-NOESY
274) ^{13}C HMQC-^{15}N meHSQC-^{15}N HMBC-COSY-NOESY
275) ^{13}C meHSQC-^{15}N HMQC-^{15}N HMBC-COSY-NOESY
276) ^{13}C meHSQC-^{15}N HSQC-^{15}N HMBC-COSY-NOESY
277) ^{13}C meHSQC-^{15}N meHSQC-^{15}N HMBC-COSY-NOESY
278) ^{15}N HSQC-^{13}C HMQC-^{15}N HMBC-COSY-NOESY
279) ^{15}N HSQC-^{13}C HSQC-^{15}N HMBC-COSY-NOESY
280) ^{15}N HSQC-^{13}C meHSQC-^{15}N HMBC-COSY-NOESY
281) ^{15}N HMQC-^{13}C HMQC-^{15}N HMBC-COSY-NOESY
282) ^{15}N HMQC-^{13}C meHSQC-^{15}N HMBC-COSY-NOESY
283) ^{15}N meHSQC-^{13}C HMQC-^{15}N HMBC-COSY-NOESY
284) ^{15}N meHSQC-^{13}C HSQC-^{15}N HMBC-COSY-NOESY
285) ^{15}N meHSQC-^{13}C meHSQC-^{15}N HMBC-COSY-NOESY

Experimental setup

The NOAH experiments are setup in a manner similar to conventional 2D heteronuclear ^{13}C experiments, but with the following specific requirements:

- The number of memory blocks used for data acquisition must be defined with the acquisition parameter *NBL.* This must be set equal to the number of NOAH modules in the sequence eg NBL=4 for a NOAH-4 experiment.
- The TD1 data size must be increased (scaled) according to the number of NOAH modules in the sequence. Thus, a NOAH-4 requiring 256 t_1 points for each NOAH module dictates that TD1 be set to 256*4 = 1024 points.
- Since only a single F1 frequency domain is explicitly defined (typically for the ^{13}C dimension) the scaling constants for the F1 spectral widths for all other F1 dimensions (^{15}N and/or ^{1}H) must be set for the correct definition of these frequencies in the final data sets.
  - *cnst10* defines the ^{13}C:^{1}H spectral width (as Hz) ratio
  - *cnst20* defines the ^{13}C:^{15}N spectral width (as Hz) ratio (if ^{15}N experiments are used)

Data processing makes use of the following AU processing scripts (which are provided below):

- **spiltx**: splits the single NOAH data set into *NBL* individual data sets for processing as separate experiments. For a NOAH experiment acquired in EXPNO ***X***, **splitx** will produce data sets numbered ***X001***, ***X002***, ***X003*** …etc according to the number of NOAH modules.
- **fixF1**: corrects the F1 chemical shift axis for ^{1}H (ie homonuclear experiments). Requires *cnst10* as input.
- **fixF1n**: corrects the F1 chemical shift axis for ^{15}N. Requires *cnst20* as input.

Pulse Programs

Pulse programs are provided here for the NOAH-4 MSCN and NOAH-5 MSBCN experiments reported in the main text. Other variants are available on request from the authors.

NOAH-4 MSCN

```
;noah4_MSCN - NOAH-4: 15N-HMQC + me-HSQC + COSY + NOESY
;Topspin 3 version 2013/10/03
;WaveMaker supported version
;
;$CLASS=HighRes
;$DIM=2D
;$TYPE=
;$SUBTYPE=
;$COMMENT=

#include <Avance.incl>
#include <Grad.incl>
#include <Delay.incl>


"p2=p1*2"
"p4=p3*2"
"p22=p21*2"
"d3=0.25s/cnst2"
"d2=d3*2.0"
"d14=0.5s/cnst3"
"d21=0.25s/cnst4"
"d22=p16+d16"
"d0=3u"
"d10=3u"
"d20=3u"
"in0=inf1/2"
"in10=inf1*cnst10"
"in20=in0*cnst20"
"l0=td1/8"

"DELTA=d22+p1+d0-2.0*p4/3.14159"
"DELTA1=d3-p14/2"
"DELTA2=d3+p14/2"
"DELTA3=d16+p2/2+d0-p21*2/3.1416-4u"
"DELTA4=d4-p2*2"
"DELTA8=d8-d22-3m-aq-p3-p16-62u"  ; adjusts noe mixing time
"DELTA12=DELTA2-p16-p3-de-p2/3.14-8u"
"DELTA13=d21-p16-8u"
"DELTA14=d16+p16+4u-d10"

"acqt0=0"
baseopt_echo

1 ze
  30m
2 30m
3 5m  do:f2
4 50u UNBLKGRAD  ; purge pulses
  4u pl3:f3
  4u pl2:f2
  (p21 ph1):f3
  (p3 ph1):f2
```

```
  4u pl1:f1
  p16:gp0
  4u
  (p1 ph1)
  4u
  p16:gp0*-1.37
  4u
  (p1 ph2)
  4u
  p16:gp0*0.77
  50u BLKGRAD
  d1 st0
5 p1 ph7
  d21
  (center (p2 ph1):f1 (p22 ph1):f3)
  d21 UNBLKGRAD
  (p1 ph7):f1
  (p21 ph3):f3
  4u
  p16:gp1*-1*EA
  DELTA3
  (p22 ph3):f3
  d20
  p16:gp1*EA
  d16
  (p2 ph4)
  p16:gp1*EA
  d16
  d20
  (p22 ph5):f3
  4u
  p16:gp1*-1*EA
  DELTA3
  (p21 ph5):f3
  d21
  (center (p2 ph1):f1 (p22 ph1):f3)
  4u
  p16:gp5
  DELTA13 4u pl16:f3
  4u  BLKGRAD
  goscnp ph30 cpd3:f3  ; acquire 15N HMQC
  4u do:f3

  4u pl3:f3
  4u pl2:f2
  (p21 ph1):f3
  (p3 ph1):f2
  50u  UNBLKGRAD
  p16:gp0*1.77
  2m st

  (p1 ph1)
  DELTA1
  (p14:sp3 ph1):f2
  (p2 ph1):f1
  DELTA2 pl2:f2
  (p1 ph2):f1
  (p3 ph3):f2
  DELTA
  (p14:sp3 ph1):f2
  4u
```

```
p16:gp1*EA
d16
d0
(p2 ph1)
d0
4u
p16:gp1*EA
d16
(p14:sp3 ph1):f2
if "d4>0.0"   ;optional HSQC multiplicity editing
{
  DELTA
  (p2 ph1):f1
  (p14:sp3 ph1):f2
  DELTA4
  (p2 ph1):f1
  (p14:sp3 ph1):f2
  d4 pl2:f2
}
else
{
  DELTA pl2:f2
}
(p3 ph5):f2
(p1 ph1):f1
DELTA1
(p14:sp3 ph1):f2
(p2 ph1):f1
p16:gp2
DELTA12 pl2:f2
4u BLKGRAD
(p3 ph1):f2
4u pl12:f2
goscnp ph30 cpd2:f2      ; acquire C-13 HSQC
4u do:f2
4u pl2:f2
(p3 ph1):f2
50u UNBLKGRAD
p16:gp0*0.77
2m st
(p1 ph28)
DELTA14
(p2 ph1)
4u
p16:gp3
d16
d10
(p1 ph1)
4u
p16:gp3*EA
d16 BLKGRAD
goscnp ph28   ; acquire H-H COSY
4u
(p3 ph1):f2
4u
50u UNBLKGRAD
p16:gp4
DELTA8 st
p1 ph5
d22
de
```

```
  4u
  (p2 ph5)
  4u
  p16:gp3*EA
  d16 BLKGRAD
  go=2 ph29    ; acquire H-H NOESY

  30m wr #0 if #0 zd igrad EA

  lo to 3 times 2

  1m id0
  1m id10
  1m id20
  1m ip6*2
  1m ip28*2
  1m ip29*2

  lo to 4 times l0

  50u BLKGRAD
exit

ph1=0
ph2=1
ph3=0 2
ph4=0 0 0 0 2 2 2 2
ph5=0 0 2 2
ph6=0
ph7=2
ph8=0 2
ph28=0 2
ph29=0 2 2 0
ph30=0 2 2 0
ph31=0 2

;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
;pl16: f3 channel - power level for CPD/BB decoupling
;sp3: f2 channel - shaped pulse 180 degree
;p1 : f1 channel -  90 degree high power pulse
;p2 : f1 channel - 180 degree high power pulse
;p3 : f2 channel -  90 degree high power pulse
;p4 : f2 channel - 180 degree high power pulse
;p14: f2 channel - 180 degree shaped pulse for inversion
;p16: homospoil/gradient pulse
;p21: f3 channel -  90 degree high power pulse
;p22: f3 channel - 180 degree high power pulse
;d0 : incremented delay (2D)                          [3 usec]
;d1 : relaxation delay
;d4: delay for HSQC multiplicity editing 1/2J(XH)     [~3.45 msec]
;d8: delay for NOE buildup
;d11: delay for disk I/O                              [5 msec]
;d16: delay for homospoil/gradient recovery
;aq: acquisition time
;cnst2: = J(CH)
;cnst4: = 1J(NH)
;cnst10: = scaling factor swC/swH for COSY/NOESY
;cnst20: = scaling factor swC/swN for 15N HMQC
```

```
;inf1: 1/SW(X) = 2 * DW(X)
;in0: 1/(2 * SW(X)) = DW(X)
;nd0: 2
;ns: 1 * n
;ds: >= 16
;td1: number of experiments - multiple of NBL
;NBL: = 4 number of blocks (NOAH modules)
;FnMODE: echo-antiecho
;cpd2: decoupling according to sequence defined by cpdprg2
;pcpd2: f2 channel - 90 degree pulse for decoupling sequence
; ~~~~~~~~~~~~~~~~ WaveMaker Definitions ~~~~~~~~~~~~~~~~~~~~
;sp3:wvm:wu180C13: cawurst-20(260 ppm, 0.5 ms)
;cpd2:wvm:C13dec: cawurst_d-20(260 ppm, 1.4 ms)

;use gradient ratios:
;                   80 : 20.1*2  for C-13
;                   80 :  8.1*4  for N-15

;for z-only gradients:
;gpz0: 17 %
;gpz1: 80 %
;gpz2: 40.2%
;gpz3: 23%
;gpz4: 33%
;gpz5: 32.4 %

;use gradient files:
;gpnam0: SMSQ10.100
;gpnam1: SMSQ10.100
;gpnam2: SMSQ10.100
;gpnam3: SMSQ10.100
;gpnam4: SMSQ10.100
;gpnam5: SMSQ10.100
```

NOAH-5 MSBCN

```
;noah5_MSBCN - NOAH5: 15N-HMQC + meHSQC + HMBC + COSY + NOESY
;Topspin 3 version 2013/10/03
;WaveMaker supported version;
;
;$CLASS=HighRes
;$DIM=2D
;$TYPE=
;$SUBTYPE=
;$COMMENT=

#include <Avance.incl>
#include <Grad.incl>
#include <Delay.incl>

"p2=p1*2"
"p4=p3*2"
"p22=p21*2"
"d3=0.25s/cnst2"
"d2=d3*2.0"
"d14=0.5s/cnst13"
"d21=0.25s/cnst4"
"d22=p16+d16"
"d0=3u"
"d10=3u"
"d20=3u"
"in0=inf1/2"
"in10=inf1*cnst10"
"in20=in0*cnst20"
"l0=td1/10"

"DELTA=d22+p1+4u+d0-p4/3.14159"
"DELTA1=d3-p14/2"
"DELTA2=d3+p14/2"
"DELTA3=d16+p2/2+d0-p21*2/3.1416-4u"
"DELTA4=d4-p2*2"
"DELTA8=d8/2-100u-d22-p3-aq-3m-4u"  ; adjusts noe mixing time
"DELTA9=d8/2-p16"
"DELTA12=DELTA2-p16-p3-de-p2/3.14-8u"
"DELTA13=d21-p16-8u"

"acqt0=0"
baseopt_echo

1 ze
  30m pl12:f2
2 30m
3 5m do:f2
4 50u UNBLKGRAD  ; purge pulses
  4u pl3:f3
  4u pl2:f2
  (p21 ph1):f3
  (p3 ph1):f2
  4u pl1:f1
  p16:gp0
  4u
  (p1 ph1)
  4u
  p16:gp0*-1.37
```

```
  4u
  (p1 ph2)
  4u
  p16:gp0*0.77
  50u BLKGRAD
  d1 st0
5 p1 ph7
  d21
  (center (p2 ph1):f1 (p22 ph1):f3)
  d21 UNBLKGRAD
  (p1 ph7):f1
  (p21 ph3):f3
  4u
  p16:gp1*-1*EA
  DELTA3
  (p22 ph3):f3
  d20
  p16:gp1*EA
  d16
  (p2 ph4)
  p16:gp1*EA
  d16
  d20
  (p22 ph5):f3
  4u
  p16:gp1*-1*EA
  DELTA3
  (p21 ph5):f3
  d21
  (center (p2 ph1):f1 (p22 ph1):f3)
  4u
  p16:gp5
  DELTA13 4u pl16:f3
  4u BLKGRAD
  goscnp ph30 cpd3:f3  ; acquire 15N HMQC
  4u do:f3

  4u pl3:f3
  4u pl2:f2
  (p21 ph1):f3
  (p3 ph1):f2
  50u UNBLKGRAD
  p16:gp0*1.77
  2m st

  (p1 ph1)
  DELTA1
  (p14:sp3 ph1):f2
  (p2 ph1):f1
  DELTA2 pl2:f2
  (p1 ph2):f1
  (p3 ph3):f2
  DELTA
  (p14:sp3 ph1):f2
  4u
  p16:gp1*EA
  d16
  d0
  (p2 ph4)
  d0
  4u
```

```
p16:gp1*EA
d16
(p14:sp3 ph1):f2
if "d4>0.0"   ;optional HSQC multiplicity editing
{
  DELTA
  (p2 ph1):f1
  (p14:sp3 ph1):f2
  d4
  (p2 ph1):f1
  (p14:sp3 ph1):f2
  d4 pl2:f2
}
else
{
  DELTA pl2:f2
}
(p3 ph5):f2
(p1 ph1):f1
DELTA1
(p14:sp3 ph1):f2
(p2 ph1):f1
p16:gp2
DELTA12 pl2:f2
4u BLKGRAD  ;
(p3 ph1):f2
4u pl12:f2
goscnp ph30 cpd2:f2      ; acquire C-13 HSQC
4u do:f2
4u pl2:f2
(p3 ph1):f2
50u UNBLKGRAD
p16:gp0*0.77
2m st
(p1 ph3)
d2
(p3 ph3):f2
d14
(p3 ph5):f2
DELTA
(p14:sp3 ph1):f2
4u
p16:gp1*EA
d16
d0
(p2 ph1)
d0
4u
p16:gp1*EA
d16
(p14:sp3 ph1):f2
DELTA pl2:f2
(p3 ph6):f2
4u
p16:gp2
d16 BLKGRAD
goscnp ph29  ; acquire C-13 HMBC
4u
(p3 ph1):f2
2m st
d10
```

```
   (p1 ph1)
   50u UNBLKGRAD
   p16:gp2*EA
   (p3 ph1):f2
   d16 BLKGRAD
   goscnp ph31   ; acquire H-H COSY
   4u
   DELTA8 st
   50u UNBLKGRAD
   p16:gp4
   DELTA9
   p1 ph5
   p16:gp2*EA
   d16 BLKGRAD
   go=2 ph30     ; acquire H-H NOESY

   30m wr #0 if #0 zd igrad EA

   lo to 3 times 2

   1m id0
   1m id10
   1m id20
   1m ip6*2
   1m ip29*2

   lo to 4 times l0

exit

ph1=0
ph2=1
ph3=0 2
ph4=0 0 0 0 2 2 2 2
ph5=0 0 2 2
ph6=0
ph7=2
ph29=0 2 2 0
ph30=0 2 2 0
ph31=0 2

;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
;pl16: f3 channel - power level for CPD/BB decoupling
;sp3: f2 channel - adiabatic pulse 180 degree
;p1 : f1 channel -  90 degree high power pulse
;p2 : f1 channel - 180 degree high power pulse
;p3 : f2 channel -  90 degree high power pulse
;p4 : f2 channel - 180 degree high power pulse
;p14: f2 channel - 180 degree shaped pulse for inversion
;p16: homospoil/gradient pulse
;p21: f3 channel -  90 degree high power pulse
;p22: f3 channel - 180 degree high power pulse
;d0 : incremented delay (2D)                          [3 usec]
;d1 : relaxation delay; [e.g. 60ms]
;d4: delay for HSQC multiplicity editing 1/2J(XH)    [~3.45 msec]
;d8: delay for NOE buildup
;d11: delay for disk I/O                              [5 msec]
;d16: delay for homospoil/gradient recovery
```

```
;aq: acquisition time
;cnst2: = J(CH)
;cnst4: = 1J(NH)
;cnst13: = nJ(CH)
;cnst10: = scaling factor swC/swH for COSY/NOESY
;cnst20: = scaling factor swC/swN for 15N HMQC
;inf1: 1/SW(X) = 2 * DW(X)
;in0: 1/(2 * SW(X)) = DW(X)
;nd0: 2
;ns: 1 * n
;ds: >= 16
;td1: number of experiments - multiple of NBL
;NBL: = 5 number of blocks (NOAH modules)
;FnMODE: echo-antiecho
;cpd2: decoupling according to sequence defined by cpdprg2
;pcpd2: f2 channel - 90 degree pulse for decoupling sequence
; ~~~~~~~~~~~~~~~~ WaveMaker Definitions ~~~~~~~~~~~~~~~~~~~
;sp3:wvm:wu180C13: cawurst-20(220 ppm, 0.5 ms)
;cpd2:wvm:C13dec: cawurst_d-20(220 ppm, 1.4 ms)

;use gradient ratios:
;                   80 : 20.1*2  for C-13
;                   80 :  8.1*4  for N-15

;for z-only gradients:
;gpz0: 17 %
;gpz1: 80 %
;gpz2: 40.2%
;gpz4: 33%
;gpz5: 32.4 %

;use gradient files:
;gpnam0: SMSQ10.100
;gpnam1: SMSQ10.100
;gpnam2: SMSQ10.100
;gpnam4: SMSQ10.100
;gpnam5: SMSQ10.100
```

AU processing scripts

The following AU programs are used for data processing after acquisition of the complete NOAH experiment, as described above.

splitx

```
/************************************************/
/*      splitx - based on nbl        21.11.2015  */
/************************************************/

  int size[3];
  int *row;
  int i, j, k, td, td1, tds, td1s, tdx;
  int oexpno, nexpno, byteorder, parmode;
  int nbl = 0, fntype = 0;
  char path[PATH_MAX + 64];
  FILE **fp;

  /***** get dataset and parameters *****/

  FETCHPAR("PARMODE", &parmode)
  FETCHPAR("NBL", &nbl)

  if (parmode != 1) STOPMSG("Program is only suitable for 2D")
  if ((nbl<2) || (nbl>8)) STOPMSG("Program is only suitable for 8 > NBL >
1")

  FETCHPARS("BYTORDA", &byteorder)
  FETCHPARS("TD", &tds)
  FETCHPAR1("TD", &td1)
  FETCHPAR1S("TD", &td1s)

  td = ((tds + 255) / 256) * 256;
  if (td <= 0  ||  td > 64 * 1024 * 1024)
    STOPMSG("TD{F2} out of range")
  if (td1s <= 0  ||  td1s > 64 * 1024 * 1024)
    STOPMSG("TD{F1} out of range")
  tdx = nbl*td;
  if ((double) tdx >= 2. * 1024 * 1024 * 1024 / sizeof(int))
    STOPMSG("amount of memory requested too large")

  /***** get input *****/

  oexpno = expno;
  nexpno = expno * 1000 + 1;
  GETINT("Enter EXPNO to store new dataset:", nexpno)
  if (nexpno <= 0)
    STOPMSG("invalid expno value")

  /***** check files *****/

  for(i=0; i<nbl; i++)
  {
    WRAPARAM(nexpno+i)
    ERRORABORT
  }

  fp = (FILE **) calloc(nbl+1, sizeof(FILE *));
```

```
(void)strcpy(path, ACQUPATH("ser"));
if ((fp[nbl] = fopen(path, "rb")) == 0)
  STOPMSG(strcat(path, " - cannot open file for reading"))

for(i=0; i<nbl; i++)
{
  expno = nexpno+i;
  (void)strcpy(path, ACQUPATH("ser"));
  if ((fp[i] = fopen(path, "wb")) == 0)
    STOPMSG(strcat(path, " - cannot open file for writing"))
}

expno = oexpno;

/***** allocate memory *****/

if((row = (int*)malloc(tdx * sizeof(int))) == 0)
  STOPMSG("cannot get enough memory")

/***** split *****/

Show_status("splitting data");   // tdi ????

k = td1s / nbl;
for (i = 0; i < k; i ++)
{
  if (fread(row, sizeof(int), tdx, fp[nbl]) != (size_t)(tdx))
    STOPMSG("read failed")

  local_swap4(row, tdx * sizeof(int), byteorder);

  for (j = 0; j < nbl; j++)
  {
    if (fwrite(row+j*td, sizeof(int), td, fp[j]) != (size_t)(td))
      STOPMSG("write failed")
  }
}

/***** free resources *****/

for(i=0; i<nbl; i++) fclose(fp[i]);
fclose(fp[i]);
free(row);

/***** store parameters and generate audit entry ***/

td1  /= nbl;
td1s /= nbl;

strcpy(path, ACQUPATH(0));
byteorder = local_endian();
size[0] = td;
size[1] = td1s;
i = 0;
do
{
  double ymin, ymax;
  char  autext[PATH_MAX + 256];
  char* hashbuf = autext + sprintf(autext, "created by splitx");

  hashbuf += sprintf(hashbuf, " %d", nbl);
```

```
    hashbuf += sprintf(hashbuf, " %d. dataset from\n       %s", i + 1,
path);

    DATASET(name, nexpno + i, procno, disk, user)

    STOREPAR("NBL", 1)
    STOREPARS("NBL", 1)
    STOREPARS("BYTORDA", byteorder)
    STOREPAR1("TD", td1)
    STOREPAR1S("TD", td1s)

    if (CheckSumFileMax(ACQUPATH("ser"), 0, hashbuf, 0, 0, byteorder, 0,
                  parmode + 1, tds, size, size, &ymin, &ymax) > 0)
    {
      (void)AuditCreate(ACQUPATH("audita.txt"), autext);
      STOREPARS("YMIN_a", ymin)
      STOREPARS("YMAX_a", ymax)
    }

    REFRESHDATA
  }
  while (++i < nbl);

  QUIT
```

fixF1

```
/* fixF1 fix F1 axis for NOAH HH correlation spectra */
/* requires cnst10 - C/H scaling factor              */
/* Eriks Kupce: eriks.kupce@bruker.com               */

int    eno, ceno;
double a1=0.0, sw1=0.0, sf1=0.0;
float x1=0.0;
char  c1[8];


      FETCHPAR("CNST 10", &x1);   GETFLOAT("cnst10 :", x1);

  if(x1 < 1.1)
  {
    sprintf(text, "scaling factor = %.4f. \Aborting...", x1);
    STOPMSG(text);
  }

  FETCHPARS("SFO1", &sf1);
  STOREPAR1S("SFO1", sf1);

  FETCHPARS("NUC1", c1);
  STOREPAR1S("NUC1", c1);

  FETCHPARS("BF1", &a1);
  STOREPAR1S("BF1", a1);

  FETCHPAR1S("SW_h", &sw1);

  sw1 = sw1/x1;
  STOREPAR1S("SW_h", sw1);
  STOREPAR1S("SW", sw1/sf1);

  FETCHPARS("O1", &a1);
  STOREPARS("O2", a1);
  STOREPAR1S("O1", a1);

  XFB
  XCMD("1 SR 0")

QUIT
```

fixF1n

```
/* fixF1n fix F1 axis for NOAH 15N HMQC */
/* requires cnst20 - C/N scaling factor */
/* Eriks Kupce: eriks.kupce@bruker.com  */

int    eno, ceno;
double a1=0.0, sw1=0.0, sf1=0.0;
float x1=0.0;
char  c1[8];


      FETCHPAR("CNST 20", &x1);   GETFLOAT("cnst20 :", x1);

  if(x1 < 1.1)
  {
    sprintf(text, "scaling factor = %.4f. \Aborting...", x1);
    STOPMSG(text);
  }

  FETCHPARS("SFO3", &sf1);
  STOREPAR1S("SFO1", sf1);

  FETCHPARS("NUC3", c1);
  STOREPAR1S("NUC1", c1);

  FETCHPARS("BF3", &a1);
  STOREPAR1S("BF1", a1);

  FETCHPAR1S("SW_h", &sw1);

  sw1 = sw1/x1;
  STOREPAR1S("SW_h", sw1);
  STOREPAR1S("SW", sw1/sf1);

  FETCHPARS("O3", &a1);
  STOREPAR1S("O1", a1);

  XFB
  XCMD("1 SR 0")

QUIT
```