

Comparison of Entropic Contributions to Binding in a ‘Hydrophilic’ versus ‘Hydrophobic’ Ligand-Protein Interaction

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Supplementary Information

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Table s1. Amide ^{15}N and ^1H chemical shifts for *apo* and histamine-bound rRaHBP-2(D24R), determined at pH 7.4 and at a temperature of 298 K.

| Residue | Apo | | complex | |
|---------|-----------------------|--------------------|-----------------------|--------------------|
| | ^{15}N (ppm) | ^1H (ppm) | ^{15}N (ppm) | ^1H (ppm) |
| Asn 1 | | | | |
| Gln 2 | | | | |
| Pro 3 | | | | |
| Asp 4 | 121.51 | 8.49 | 121.48 | 8.48 |
| Trp 5 | 110.71 | 6.14 | 110.75 | 6.13 |
| Ala 6 | 130.86 | 7.28 | 130.94 | 7.28 |
| Asp 7 | 124.66 | 7.75 | 124.60 | 7.74 |
| Glu 8 | 128.70 | 8.95 | 128.69 | 8.95 |
| Ala 9 | 122.01 | 8.24 | 121.98 | 8.21 |
| Ala 10 | 117.85 | 7.59 | 117.67 | 7.58 |
| Asn 11 | 112.25 | 8.51 | 112.24 | 8.50 |
| Gly 12 | 111.24 | 8.67 | 111.21 | 8.65 |
| Ala 13 | 122.55 | 8.43 | 122.51 | 8.42 |
| His 14 | 114.15 | 8.07 | 114.12 | 8.05 |
| Gln 15 | 119.56 | 7.59 | | |
| Asp 16 | 121.91 | 8.31 | 121.05 | 8.28 |
| Ala 17 | 127.56 | 8.34 | 127.48 | 8.32 |
| Trp 18 | | | 119.09 | 9.16 |
| Lys 19 | 118.97 | 7.34 | 119.01 | 7.34 |
| Ser 20 | 114.06 | 7.30 | 113.87 | 7.26 |
| Leu 21 | 122.76 | 8.31 | 122.88 | 8.30 |
| Lys 22 | 115.91 | 7.55 | 116.20 | 7.58 |
| Ala 23 | 122.98 | 7.60 | 123.02 | 7.57 |
| Arg 24 | 115.68 | 6.92 | 115.71 | 6.93 |
| Val 25 | 119.63 | 7.52 | | |
| Glu 26 | 116.61 | 7.04 | 116.54 | 7.05 |
| Asn 27 | 115.46 | 7.71 | 115.39 | 7.70 |
| Val 28 | 119.19 | 7.86 | 118.95 | 7.82 |
| Tyr 29 | 124.92 | 8.30 | 125.18 | 8.53 |
| Tyr 30 | 119.48 | 9.05 | 120.37 | 9.02 |
| Met 31 | 125.76 | 8.71 | 125.26 | 8.70 |
| Val 32 | 121.29 | 8.57 | 121.43 | 8.59 |
| Lys 33 | 117.64 | 7.46 | 117.72 | 7.43 |
| Ala 34 | 118.17 | 8.54 | 118.31 | 8.52 |
| Thr 35 | 105.10 | 8.36 | 105.12 | 8.40 |
| Tyr 36 | 116.65 | 7.15 | | |
| Lys 37 | 120.08 | 8.89 | 120.60 | 8.93 |
| Asn 38 | 116.24 | 8.23 | 115.57 | 8.33 |
| Asp 39 | 123.00 | 8.77 | 122.66 | 8.84 |
| Pro 40 | | | | |
| Val 41 | | | 116.80 | 7.89 |
| Trp 42 | | | 120.73 | 8.75 |
| Gly 43 | | | 103.31 | 7.89 |
| Asn 44 | 118.41 | 8.89 | 118.06 | 8.83 |
| Asp 45 | 123.31 | 8.74 | 122.88 | 8.63 |
| Phe 46 | 113.46 | 7.00 | 113.36 | 6.98 |
| Thr 47 | 111.54 | 9.17 | 111.13 | 9.11 |
| Cys 48 | | | 108.02 | 7.74 |
| Val 49 | 115.12 | 6.09 | 115.02 | 6.05 |
| Gly 50 | 115.66 | 9.13 | 115.75 | 8.91 |
| Val 51 | 118.43 | 9.21 | 118.77 | 9.22 |
| Met 52 | 123.13 | 8.13 | 123.58 | 8.23 |
| Ala 53 | 124.38 | 8.03 | 124.64 | 8.09 |
| Asn 54 | 116.86 | 8.90 | 116.99 | 8.96 |
| Asp 55 | | | 117.14 | 8.17 |

| | | | | |
|----------------|--------|-------|--------|-------|
| Val 56 | 119.26 | 8.26 | | |
| Asn 57 | 127.05 | 9.21 | 126.80 | 9.22 |
| Glu 58 | 124.41 | 9.13 | 124.43 | 9.12 |
| Asp 59 | 118.31 | 8.10 | 118.27 | 8.10 |
| Glu 60 | 116.34 | 7.26 | 116.41 | 7.24 |
| Lys 61 | 115.53 | 7.39 | 115.49 | 7.36 |
| Ser 62 | 110.71 | 7.83 | 110.61 | 7.82 |
| Ile 63 | 111.64 | 9.03 | 111.70 | 9.11 |
| Gln 64 | 119.68 | 8.13 | 119.62 | 8.02 |
| Ala 65 | 129.03 | 9.26 | 129.23 | 9.34 |
| Glu 66 | 122.24 | 8.65 | 122.51 | 8.79 |
| Phe 67 | 123.98 | 9.71 | 123.51 | 9.78 |
| Leu 68 | 122.18 | 8.80 | 121.56 | 8.70 |
| Phe 69 | 113.33 | 8.01 | 112.55 | 7.94 |
| Met 70 | 116.37 | 8.49 | 116.63 | 8.47 |
| Asn 71 | 115.50 | 8.63 | 115.68 | 8.58 |
| Asn 72 | 111.27 | 7.93 | 111.76 | 7.93 |
| Ala 73 | 122.48 | 8.84 | 122.74 | 8.80 |
| Asp 74 | 116.75 | 7.72 | 117.37 | 7.73 |
| Thr 75 | 114.68 | 8.43 | 114.73 | 8.38 |
| Asn 76 | 119.66 | 8.22 | | |
| Met 77 | 121.66 | 8.56 | 121.93 | 8.54 |
| Gln 78 | 125.88 | 8.80 | 125.63 | 8.72 |
| Phe 79 | 114.60 | 7.81 | 114.63 | 7.78 |
| Ala 80 | 123.62 | 8.99 | 123.63 | 8.73 |
| Thr 81 | 117.49 | 8.89 | 116.97 | 8.88 |
| Glu 82 | 123.18 | 9.28 | 125.35 | 9.41 |
| Lys 83 | 124.25 | 8.29 | 124.01 | 8.20 |
| Val 84 | 126.91 | 8.82 | 125.81 | 8.84 |
| Thr 85 | 122.05 | 8.77 | 122.34 | 8.67 |
| Ala 86 | 129.58 | 9.03 | 129.69 | 8.97 |
| Val 87 | 115.53 | 8.65 | | |
| Lys 88 | 118.87 | 8.44 | 118.79 | 8.43 |
| Met 89 | 124.65 | 9.86 | 124.65 | 9.87 |
| Tyr 90 | 115.12 | 8.95 | 115.07 | 8.97 |
| Gly 91 | 105.22 | 8.89 | 105.12 | 8.89 |
| Tyr 92 | 123.46 | 7.46 | 123.46 | 7.44 |
| Asn 93 | 120.01 | 11.17 | 120.08 | 11.18 |
| Arg 94 | 122.22 | 8.59 | 122.30 | 8.63 |
| Glu 95 | 124.51 | 10.04 | 124.47 | 10.03 |
| Asn 96 | 123.18 | 9.38 | 123.27 | 9.37 |
| Ala 97 | 125.27 | 8.63 | 125.11 | 8.66 |
| Phe 98 | 119.23 | 9.16 | 119.90 | 9.27 |
| Arg 99 | 123.45 | 9.50 | 122.93 | 9.46 |
| Tyr 100 | | | 130.81 | 10.39 |
| Glu 101 | 120.24 | 9.09 | 120.77 | 9.54 |
| Thr 102 | 115.63 | 8.88 | 116.57 | 8.90 |
| Glu 103 | 122.17 | 9.71 | 122.60 | 9.91 |
| Asp 104 | 114.26 | 8.13 | 114.09 | 8.21 |
| Gly 105 | 107.67 | 7.86 | 107.51 | 7.71 |
| Gln 106 | 119.98 | 7.70 | 120.21 | 7.83 |
| Val 107 | 121.12 | 7.62 | 121.81 | 7.52 |
| Phe 108 | 125.96 | 8.65 | 124.32 | 8.63 |
| Thr 109 | | | 121.06 | 8.92 |
| Asp 110 | | | 127.71 | 8.87 |
| Val 111 | 119.56 | 9.58 | 119.70 | 9.59 |
| Ile 112 | 125.96 | 9.05 | 126.07 | 9.12 |
| Ala 113 | 132.17 | 8.59 | 132.49 | 8.59 |
| Tyr 114 | 118.39 | 8.04 | 118.50 | 8.04 |
| Ser 115 | 124.84 | 8.46 | 124.81 | 8.45 |

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|----------------|--------|-------|--------|-------|
| Asp 116 | 127.56 | 8.98 | 127.54 | 8.99 |
| Asp 117 | 119.70 | 8.96 | 119.59 | 8.93 |
| Asn 118 | 112.11 | 8.37 | 111.91 | 8.33 |
| Cys 119 | 116.08 | 8.02 | 116.11 | 8.01 |
| Asp 120 | 118.89 | 9.59 | 119.14 | 9.69 |
| Val 121 | 123.05 | 10.06 | 123.36 | 10.06 |
| Ile 122 | 129.71 | 9.57 | 129.49 | 9.60 |
| Tyr 123 | 128.59 | 10.07 | 128.78 | 10.13 |
| Val 124 | 131.21 | 8.78 | 131.07 | 8.81 |
| Pro 125 | | | | |
| Gly 126 | 105.40 | 7.75 | 103.92 | 7.67 |
| Thr 127 | 111.12 | 7.95 | 109.55 | 8.34 |
| Asp 128 | | | 124.38 | 7.90 |
| Gly 129 | 107.22 | 8.25 | 107.39 | 8.09 |
| Asn 130 | | | 117.75 | 8.26 |
| Glu 131 | 119.71 | 8.20 | | |
| Glu 132 | | | 124.15 | 8.28 |
| Gly 133 | 111.86 | 8.73 | 112.64 | 8.76 |
| Tyr 134 | 114.89 | 8.98 | 115.12 | 9.08 |
| Glu 135 | 117.75 | 10.00 | 117.81 | 10.04 |
| Leu 136 | 124.15 | 8.48 | 124.27 | 8.51 |
| Trp 137 | 127.42 | 9.93 | 127.55 | 9.97 |
| Thr 138 | 114.00 | 9.76 | 114.44 | 9.80 |
| Thr 139 | 113.70 | 7.38 | 113.83 | 7.35 |
| Asp 140 | 122.73 | 7.84 | 122.93 | 7.83 |
| Tyr 141 | 118.48 | 6.43 | 118.27 | 6.43 |
| Asp 142 | 121.35 | 7.74 | 121.38 | 7.73 |
| Asn 143 | 120.08 | 7.23 | 120.11 | 7.23 |
| Ile 144 | 124.89 | 8.56 | 124.87 | 8.53 |
| Pro 145 | | | | |
| Ala 146 | 128.34 | 8.72 | 128.39 | 8.71 |
| Asn 147 | | | | |
| Cys 148 | 114.41 | 7.46 | 114.48 | 7.45 |
| Leu 149 | 121.69 | 7.98 | 121.67 | 7.99 |
| Asn 150 | 115.85 | 8.66 | 115.91 | 8.65 |
| Lys 151 | 119.46 | 7.18 | 119.47 | 7.18 |
| Phe 152 | 118.92 | 8.31 | 118.95 | 8.31 |
| Asn 153 | 115.49 | 8.47 | 115.51 | 8.47 |
| Glu 154 | 120.43 | 7.73 | 120.46 | 7.73 |
| Tyr 155 | 118.22 | 8.01 | 118.08 | 7.99 |
| Ala 156 | 120.08 | 8.13 | 120.09 | 8.14 |
| Val 157 | 118.58 | 6.48 | 118.55 | 6.47 |
| Gly 158 | | | | |
| Arg 159 | 118.91 | 7.84 | | |
| Glu 160 | 123.39 | 8.92 | 123.43 | 8.92 |
| Thr 161 | | | 117.05 | 8.26 |
| Arg 162 | 122.26 | 8.88 | 122.53 | 8.89 |
| Asp 163 | 121.23 | 8.44 | 121.05 | 8.43 |
| Val 164 | 122.73 | 7.66 | 122.78 | 7.63 |
| Phe 165 | 126.46 | 9.16 | 126.10 | 9.10 |
| Thr 166 | 117.62 | 6.61 | 117.57 | 6.58 |
| Ser 167 | 115.48 | 9.18 | 115.42 | 9.16 |
| Ala 168 | 124.30 | 7.51 | 124.28 | 7.49 |
| Cys 169 | 114.30 | 7.63 | 114.23 | 7.61 |
| Leu 170 | 118.06 | 7.21 | 117.84 | 7.19 |
| Glu 171 | 125.50 | 7.35 | 125.50 | 7.34 |

Table s2. ^{15}N amide R_1 and R_2 and ssNOE values for *apo* rRaHBP-2(D24R) at 500 MHz, 298 K.

The error in the average values is given as the standard deviation.

| Residue | R_1 (1/s) | error | R_2 (1/s) | error | ssNOE | error |
|----------------|-------------------------------|--------------|-------------------------------|--------------|--------------|--------------|
| D4 | 1.64 | 0.08 | 11.41 | 0.44 | 0.87 | 0.08 |
| W5 | 1.56 | 0.04 | 10.29 | 0.16 | 0.78 | 0.04 |
| A6 | 1.72 | 0.03 | 10.61 | 0.24 | 0.82 | 0.04 |
| D7 | 1.30 | 0.03 | 8.56 | 0.12 | 0.63 | 0.04 |
| E8 | 1.73 | 0.07 | 10.27 | 0.12 | 0.80 | 0.04 |
| A9 | 1.79 | 0.02 | 10.54 | 0.17 | 0.73 | 0.03 |
| A10 | 1.62 | 0.03 | 10.34 | 0.15 | 0.76 | 0.04 |
| N11 | 1.60 | 0.05 | 10.34 | 0.22 | 0.76 | 0.05 |
| G12 | 1.71 | 0.05 | 11.48 | 0.17 | 0.76 | 0.05 |
| A13 | 1.89 | 0.10 | 11.67 | 0.49 | 0.83 | 0.07 |
| H14 | | | | | | |
| Q15 | 1.62 | 0.04 | 11.51 | 0.17 | 0.77 | 0.05 |
| D16 | 1.67 | 0.04 | 10.19 | 0.19 | 0.77 | 0.04 |
| A17 | 1.66 | 0.03 | 11.05 | 0.22 | 0.80 | 0.05 |
| K19 | 1.65 | 0.03 | 11.38 | 0.10 | 0.77 | 0.05 |
| S20 | 1.68 | 0.04 | 11.26 | 0.20 | 0.79 | 0.06 |
| L21 | 1.75 | 0.04 | 11.81 | 0.39 | 0.74 | 0.06 |
| K22 | 1.66 | 0.03 | 11.67 | 0.17 | 0.83 | 0.04 |
| A23 | 1.76 | 0.03 | 11.16 | 0.17 | 0.78 | 0.06 |
| R24 | 1.66 | 0.03 | 11.45 | 0.27 | 0.68 | 0.05 |
| V25 | 1.69 | 0.03 | 12.25 | 0.23 | 0.81 | 0.06 |
| E26 | 1.54 | 0.03 | 9.75 | 0.16 | 0.69 | 0.05 |
| N27 | 1.56 | 0.02 | 9.74 | 0.16 | 0.73 | 0.05 |
| V28 | 1.54 | 0.02 | 9.16 | 0.08 | 0.68 | 0.04 |
| Y29 | 1.70 | 0.05 | 10.31 | 0.35 | 0.81 | 0.07 |
| Y30 | 1.73 | 0.05 | 11.07 | 0.30 | 0.75 | 0.07 |
| M31 | 1.73 | 0.05 | 11.06 | 0.32 | 0.78 | 0.06 |
| V32 | 1.72 | 0.08 | 14.15 | 0.68 | 0.68 | 0.10 |
| K33 | 1.71 | 0.06 | 11.48 | 0.19 | 0.77 | 0.07 |
| A34 | 1.72 | 0.03 | 10.88 | 0.27 | 0.79 | 0.05 |
| T35 | 1.69 | 0.09 | 11.07 | 0.46 | 0.81 | 0.10 |
| Y36 | 1.83 | 0.06 | 12.34 | 0.44 | 0.87 | 0.10 |
| K37 | 1.84 | 0.10 | 12.00 | 0.38 | 0.75 | 0.12 |
| N38 | 1.40 | 0.17 | 10.98 | 1.40 | 0.28 | 0.18 |
| D39 | 1.74 | 0.06 | 12.75 | 0.46 | 0.70 | 0.07 |
| N44 | 1.71 | 0.06 | 11.51 | 0.50 | 0.78 | 0.08 |
| D45 | 1.76 | 0.04 | 10.51 | 0.24 | 0.76 | 0.07 |
| F46 | 1.61 | 0.02 | 10.42 | 0.16 | 0.83 | 0.05 |
| T47 | 1.68 | 0.04 | 11.21 | 0.46 | 0.78 | 0.07 |
| V49 | 1.58 | 0.05 | 10.43 | 0.30 | 0.75 | 0.06 |
| G50 | 1.88 | 0.12 | 10.22 | 0.76 | 0.65 | 0.13 |
| V51 | 1.78 | 0.04 | 12.15 | 0.42 | 0.72 | 0.06 |
| M52 | 1.77 | 0.03 | 11.49 | 0.20 | 0.73 | 0.06 |
| A53 | 1.78 | 0.16 | 12.40 | 0.54 | 0.61 | 0.14 |
| N54 | 1.69 | 0.03 | 9.54 | 0.17 | 0.65 | 0.05 |
| V56 | 1.65 | 0.03 | 9.61 | 0.15 | 0.74 | 0.04 |
| N57 | 1.72 | 0.05 | 10.41 | 0.28 | 0.77 | 0.07 |
| E58 | 1.83 | 0.09 | 10.97 | 0.41 | 0.76 | 0.05 |
| D59 | 1.63 | 0.02 | 10.19 | 0.14 | 0.79 | 0.03 |
| E60 | 1.57 | 0.02 | 9.99 | 0.08 | 0.77 | 0.05 |
| K61 | 1.71 | 0.03 | 10.33 | 0.26 | 0.70 | 0.05 |
| S62 | 1.71 | 0.04 | 10.89 | 0.15 | 0.79 | 0.05 |
| I63 | 1.73 | 0.04 | 10.31 | 0.18 | 0.64 | 0.07 |
| Q64 | | | | | | |
| A65 | 1.69 | 0.05 | 9.98 | 0.23 | 0.74 | 0.05 |
| E66 | 1.76 | 0.02 | 10.07 | 0.22 | 0.71 | 0.07 |

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|-------------|------|------|-------|------|------|------|
| F67 | 1.68 | 0.06 | 11.40 | 0.46 | 0.67 | 0.12 |
| L68 | 1.79 | 0.05 | 10.87 | 0.14 | 0.63 | 0.08 |
| F69 | | | | | | |
| M70 | 1.63 | 0.06 | 11.12 | 0.12 | 0.74 | 0.07 |
| N71 | | | | | | |
| N72 | 1.66 | 0.05 | 10.76 | 0.57 | 0.57 | 0.06 |
| A73 | 1.66 | 0.02 | 10.86 | 0.14 | 0.79 | 0.04 |
| D74 | 1.63 | 0.03 | 10.02 | 0.10 | 0.69 | 0.04 |
| T75 | 1.75 | 0.10 | 10.08 | 0.31 | 0.70 | 0.08 |
| N76 | | | | | | |
| M77 | 1.62 | 0.03 | 10.16 | 0.17 | 0.69 | 0.04 |
| Q78 | 1.65 | 0.07 | 11.11 | 0.36 | 0.84 | 0.08 |
| F79 | | | | | | |
| A80 | 1.65 | 0.07 | 10.34 | 0.27 | 0.69 | 0.07 |
| T81 | 1.67 | 0.03 | 10.67 | 0.28 | 0.73 | 0.07 |
| E82 | 1.78 | 0.05 | 10.48 | 0.41 | 0.78 | 0.10 |
| K83 | 1.45 | 0.13 | 10.94 | 0.67 | 0.53 | 0.13 |
| V84 | 1.74 | 0.08 | 13.69 | 0.61 | 0.72 | 0.14 |
| T85 | 1.84 | 0.03 | 11.49 | 0.39 | 0.89 | 0.11 |
| A86 | 1.80 | 0.03 | 10.54 | 0.18 | 0.73 | 0.05 |
| V87 | | | | | | |
| K88 | 1.76 | 0.03 | 10.24 | 0.16 | 0.71 | 0.06 |
| M89 | 1.61 | 0.02 | 10.19 | 0.19 | 0.82 | 0.06 |
| Y90 | | | | | | |
| G91 | 1.97 | 0.07 | 11.87 | 0.27 | 0.76 | 0.06 |
| Y92 | 1.73 | 0.05 | 11.70 | 0.30 | 0.74 | 0.05 |
| N93 | 1.55 | 0.04 | 10.15 | 0.34 | 0.83 | 0.07 |
| R94 | 1.64 | 0.03 | 10.21 | 0.15 | 0.75 | 0.05 |
| E95 | 1.65 | 0.03 | 10.33 | 0.28 | 0.80 | 0.04 |
| N96 | 1.71 | 0.05 | 10.90 | 0.10 | 0.80 | 0.07 |
| A97 | | | | | | |
| F98 | | | | | | |
| R99 | 1.72 | 0.02 | 10.73 | 0.23 | 0.72 | 0.06 |
| E101 | 1.79 | 0.05 | 11.80 | 0.44 | 0.79 | 0.09 |
| T102 | 1.72 | 0.05 | 11.60 | 0.21 | 0.75 | 0.06 |
| E103 | 2.03 | 0.12 | 10.56 | 0.30 | 0.70 | 0.11 |
| D104 | | | | | | |
| G105 | 1.68 | 0.10 | 9.64 | 0.27 | 0.68 | 0.08 |
| Q106 | 1.60 | 0.05 | 9.90 | 0.21 | 0.59 | 0.07 |
| V107 | 1.67 | 0.03 | 9.57 | 0.13 | 0.71 | 0.05 |
| F108 | | | | | | |
| V111 | 1.69 | 0.06 | 16.74 | 0.58 | 0.87 | 0.08 |
| I112 | 1.69 | 0.04 | 11.34 | 0.27 | 0.77 | 0.06 |
| A113 | 1.60 | 0.03 | 11.92 | 0.27 | 0.76 | 0.06 |
| Y114 | | | | | | |
| S115 | 1.61 | 0.03 | 10.68 | 0.16 | 0.78 | 0.05 |
| D116 | 1.69 | 0.05 | 10.79 | 0.13 | 0.79 | 0.06 |
| D117 | 1.89 | 0.11 | 12.98 | 0.47 | 0.70 | 0.07 |
| N118 | 1.70 | 0.06 | 10.43 | 0.26 | 0.65 | 0.06 |
| C119 | 1.74 | 0.04 | 17.75 | 0.98 | 0.82 | 0.07 |
| D120 | 1.59 | 0.24 | 19.56 | 1.55 | 0.53 | 0.19 |
| V121 | 1.60 | 0.03 | 11.71 | 0.28 | 0.70 | 0.06 |
| I122 | 1.60 | 0.04 | 11.87 | 0.35 | 0.76 | 0.06 |
| Y123 | 1.67 | 0.05 | 11.21 | 0.55 | 0.73 | 0.06 |
| V124 | 1.80 | 0.05 | 12.83 | 0.51 | 0.64 | 0.06 |
| G126 | 1.76 | 0.10 | 12.50 | 0.54 | 0.85 | 0.11 |
| T127 | 1.70 | 0.08 | 12.80 | 0.23 | 0.52 | 0.09 |
| G129 | 1.64 | 0.09 | 9.48 | 0.26 | 0.69 | 0.06 |
| E131 | | | | | | |
| G133 | 1.78 | 0.06 | 14.19 | 0.81 | 0.63 | 0.11 |

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|----------------|-------------|-------------|--------------|-------------|-------------|-------------|
| Y134 | 1.67 | 0.03 | 10.69 | 0.28 | 0.76 | 0.05 |
| R135 | 1.57 | 0.04 | 10.91 | 0.35 | 0.82 | 0.07 |
| L136 | 1.64 | 0.04 | 11.65 | 0.34 | 0.73 | 0.06 |
| W137 | 1.65 | 0.04 | 11.02 | 0.52 | 0.72 | 0.07 |
| T138 | 1.74 | 0.05 | 10.77 | 0.19 | 0.84 | 0.06 |
| T139 | 1.67 | 0.04 | 12.62 | 0.45 | 0.73 | 0.07 |
| D140 | 1.66 | 0.03 | 10.47 | 0.21 | 0.59 | 0.05 |
| Y141 | 1.52 | 0.04 | 10.46 | 0.27 | 0.73 | 0.05 |
| D142 | 1.75 | 0.04 | 10.31 | 0.32 | 0.72 | 0.05 |
| N143 | 1.41 | 0.02 | 8.44 | 0.10 | 0.62 | 0.04 |
| I144 | 1.60 | 0.04 | 9.28 | 0.15 | 0.69 | 0.04 |
| A146 | 1.89 | 0.08 | 10.92 | 0.20 | 0.88 | 0.06 |
| C148 | 1.67 | 0.04 | 17.33 | 0.38 | 0.75 | 0.06 |
| L149 | 1.76 | 0.04 | 13.55 | 0.33 | 0.80 | 0.05 |
| N150 | 1.78 | 0.03 | 10.79 | 0.19 | 0.83 | 0.04 |
| K151 | 1.72 | 0.04 | 10.88 | 0.27 | 0.76 | 0.05 |
| F152 | 1.75 | 0.04 | 10.91 | 0.16 | 0.75 | 0.05 |
| N153 | 1.81 | 0.04 | 10.99 | 0.32 | 0.82 | 0.05 |
| E154 | 1.69 | 0.02 | 10.71 | 0.15 | 0.81 | 0.04 |
| Y155 | | | | | | |
| A156 | | | | | | |
| V157 | 1.51 | 0.02 | 10.02 | 0.12 | 0.74 | 0.03 |
| R159 | 1.66 | 0.03 | 9.72 | 0.15 | 0.67 | 0.04 |
| E160 | 1.57 | 0.07 | 9.47 | 0.24 | 0.76 | 0.07 |
| R162 | 1.77 | 0.04 | 10.74 | 0.35 | 0.70 | 0.07 |
| D163 | 1.67 | 0.06 | 10.88 | 0.15 | 0.92 | 0.06 |
| V164 | 1.58 | 0.04 | 10.19 | 0.32 | 0.75 | 0.09 |
| F165 | 1.83 | 0.13 | 10.82 | 0.69 | 0.63 | 0.15 |
| T166 | 1.53 | 0.04 | 9.92 | 0.17 | 0.67 | 0.05 |
| S167 | 1.67 | 0.10 | 10.80 | 0.44 | 0.72 | 0.07 |
| A168 | 1.83 | 0.08 | 11.20 | 0.11 | 0.77 | 0.05 |
| C169 | | | | | | |
| L170 | 1.62 | 0.03 | 9.66 | 0.22 | 0.62 | 0.04 |
| E171 | 1.66 | 0.02 | 4.65 | 0.04 | 0.34 | 0.02 |
| Average | 1.69 | 0.10 | 11.06 | 1.65 | 0.73 | 0.09 |

Table s3. ^{15}N amide R_1 and R_2 and ssNOE values for *apo* rRaHBP2(D24R) at 600 MHz, 298 K.

The error in the average values is given as the standard deviation.

| Residue | R_1 (1/s) | error | R_2 (1/s) | error | ssNOE | error |
|----------------|-------------------------------|--------------|-------------------------------|--------------|--------------|--------------|
| D4 | 1.10 | 0.09 | 12.87 | 0.25 | 0.81 | 0.06 |
| W5 | 1.20 | 0.06 | 12.00 | 0.49 | 0.85 | 0.03 |
| A6 | 1.29 | 0.03 | 11.95 | 0.21 | 0.83 | 0.04 |
| D7 | 0.89 | 0.03 | 9.66 | 0.12 | 0.79 | 0.04 |
| E8 | 1.22 | 0.02 | 12.32 | 0.28 | 0.90 | 0.04 |
| A9 | 1.34 | 0.01 | 12.05 | 0.15 | 0.89 | 0.03 |
| A10 | 1.20 | 0.02 | 11.56 | 0.30 | 0.82 | 0.03 |
| N11 | 1.31 | 0.07 | 12.24 | 0.29 | 0.76 | 0.04 |
| G12 | 1.27 | 0.04 | 13.52 | 0.47 | 0.81 | 0.04 |
| A13 | 1.44 | 0.12 | 13.74 | 0.64 | 0.81 | 0.05 |
| H14 | | | | | | |
| Q15 | 1.18 | 0.03 | 12.64 | 0.49 | 0.86 | 0.04 |
| D16 | 1.28 | 0.03 | 11.77 | 0.20 | 0.84 | 0.04 |
| A17 | 1.21 | 0.02 | 12.97 | 0.43 | 0.89 | 0.04 |
| K19 | 1.22 | 0.03 | 13.19 | 0.26 | 0.81 | 0.04 |
| S20 | 1.20 | 0.03 | 14.04 | 0.36 | 0.76 | 0.05 |
| L21 | 1.35 | 0.03 | 14.25 | 0.79 | 0.79 | 0.05 |
| K22 | 1.24 | 0.02 | 13.06 | 0.21 | 0.90 | 0.04 |
| A23 | 1.27 | 0.05 | 12.92 | 0.33 | 0.77 | 0.05 |
| R24 | 1.26 | 0.06 | 13.06 | 0.33 | 0.79 | 0.05 |
| V25 | 1.24 | 0.03 | 14.20 | 0.31 | 0.80 | 0.05 |
| E26 | 1.18 | 0.03 | 11.49 | 0.24 | 0.69 | 0.04 |
| N27 | 1.19 | 0.04 | 11.59 | 0.15 | 0.70 | 0.04 |
| V28 | 1.17 | 0.02 | 10.79 | 0.22 | 0.81 | 0.04 |
| Y29 | 1.25 | 0.04 | 12.08 | 0.58 | 0.78 | 0.05 |
| Y30 | 1.35 | 0.05 | 11.94 | 0.46 | 0.77 | 0.05 |
| M31 | 1.33 | 0.05 | 11.79 | 0.53 | 0.76 | 0.05 |
| V32 | 1.17 | 0.05 | 15.19 | 2.07 | 0.74 | 0.09 |
| K33 | 1.24 | 0.02 | 13.15 | 0.47 | 0.81 | 0.05 |
| A34 | 1.22 | 0.03 | 12.31 | 0.17 | 0.79 | 0.04 |
| T35 | 1.11 | 0.07 | 11.25 | 0.43 | 0.82 | 0.10 |
| Y36 | 1.28 | 0.09 | 13.10 | 0.95 | 0.80 | 0.10 |
| K37 | 1.21 | 0.07 | 12.03 | 0.63 | 0.78 | 0.10 |
| N38 | 1.53 | 0.82 | 12.85 | 2.00 | 0.50 | 0.27 |
| D39 | 1.19 | 0.07 | 13.73 | 0.53 | 0.73 | 0.06 |
| N44 | 1.40 | 0.10 | 13.67 | 0.79 | 0.84 | 0.09 |
| D45 | 1.29 | 0.04 | 11.58 | 0.81 | 0.92 | 0.06 |
| F46 | 1.23 | 0.03 | 12.42 | 0.28 | 0.92 | 0.04 |
| T47 | 1.30 | 0.07 | 12.77 | 0.67 | 0.73 | 0.06 |
| V49 | 1.26 | 0.06 | 10.73 | 0.49 | 0.80 | 0.05 |
| G50 | 1.42 | 0.14 | | | 0.69 | 0.16 |
| V51 | 1.32 | 0.05 | 14.27 | 0.53 | 0.80 | 0.05 |
| M52 | 1.29 | 0.04 | 12.59 | 0.26 | 0.74 | 0.06 |
| A53 | 1.18 | 0.14 | 13.19 | 1.51 | 0.55 | 0.15 |
| N54 | 1.31 | 0.04 | 11.33 | 0.32 | 0.71 | 0.05 |
| V56 | 1.27 | 0.02 | 10.69 | 0.26 | 0.74 | 0.04 |
| N57 | 1.21 | 0.04 | 12.19 | 0.62 | 0.85 | 0.06 |
| E58 | 1.29 | 0.06 | 12.58 | 0.39 | 0.83 | 0.04 |
| D59 | 1.23 | 0.01 | 11.72 | 0.13 | 0.76 | 0.03 |
| E60 | 1.14 | 0.02 | 11.19 | 0.17 | 0.75 | 0.04 |
| K61 | 1.26 | 0.03 | 11.50 | 0.17 | 0.78 | 0.04 |
| S62 | 1.28 | 0.03 | 12.29 | 0.22 | 0.81 | 0.04 |
| I63 | 1.29 | 0.03 | 11.90 | 0.56 | 0.86 | 0.07 |
| Q64 | | | | | | |

| | | | | | | |
|-------------|------|------|-------|-------|------|------|
| A65 | 1.29 | 0.02 | 11.65 | 0.39 | 0.75 | 0.04 |
| E66 | 1.25 | 0.05 | 11.29 | 0.48 | 0.87 | 0.08 |
| F67 | 1.20 | 0.06 | 11.22 | 0.82 | 1.09 | 0.14 |
| L68 | | | 12.81 | 0.852 | 0.75 | 0.09 |
| F69 | | | | | | |
| M70 | 1.25 | 0.04 | 13.26 | 0.73 | 0.79 | 0.06 |
| N71 | | | | | | |
| N72 | 1.30 | 0.05 | 12.65 | 0.47 | 0.80 | 0.06 |
| A73 | | | 12.05 | 0.22 | 0.82 | 0.03 |
| D74 | 1.22 | 0.02 | 11.26 | 0.22 | 0.83 | 0.04 |
| T75 | 1.28 | 0.12 | 12.68 | 0.46 | 0.71 | 0.07 |
| N76 | | | | | | |
| M77 | 1.24 | 0.02 | 11.92 | 0.30 | 0.81 | 0.04 |
| Q78 | 1.26 | 0.06 | 12.05 | 0.84 | 0.85 | 0.07 |
| F79 | | | | | | |
| A80 | 1.24 | 0.03 | 12.14 | 0.44 | 0.84 | 0.07 |
| T81 | 1.22 | 0.03 | 12.13 | 0.44 | 0.78 | 0.06 |
| E82 | 1.26 | 0.07 | 11.22 | 1.14 | 0.77 | 0.09 |
| K83 | 1.06 | 0.13 | 10.92 | 1.34 | 0.40 | 0.14 |
| V84 | 1.24 | 0.14 | 15.55 | 2.22 | 0.74 | 0.17 |
| T85 | 1.18 | 0.08 | 13.32 | 0.55 | 0.86 | 0.11 |
| A86 | 1.35 | 0.02 | 13.15 | 0.52 | 0.78 | 0.05 |
| V87 | | | | | | |
| K88 | 1.27 | 0.04 | 11.63 | 0.49 | 0.81 | 0.05 |
| M89 | 1.26 | 0.05 | 11.04 | 0.52 | 0.81 | 0.04 |
| Y90 | 1.29 | 0.05 | 11.98 | 0.23 | 0.83 | 0.03 |
| G91 | 1.47 | 0.10 | 12.30 | 0.80 | 0.89 | 0.05 |
| Y92 | 1.23 | 0.04 | 13.28 | 0.34 | 0.90 | 0.04 |
| N93 | 1.11 | 0.06 | 12.17 | 0.60 | 0.78 | 0.06 |
| R94 | 1.19 | 0.04 | 12.10 | 0.33 | 0.79 | 0.04 |
| E95 | 1.24 | 0.03 | 11.76 | 0.19 | 0.79 | 0.03 |
| N96 | 1.30 | 0.06 | 12.34 | 0.92 | 0.86 | 0.07 |
| A97 | | | | | | |
| F98 | | | | | | |
| R99 | 1.26 | 0.03 | 12.51 | 0.28 | 0.82 | 0.05 |
| E101 | 1.31 | 0.05 | 12.77 | 0.49 | 0.67 | 0.07 |
| T102 | 1.29 | 0.04 | 12.83 | 0.57 | 0.68 | 0.05 |
| E103 | 1.34 | 0.09 | 13.98 | 1.12 | 0.67 | 0.10 |
| D104 | | | | | | |
| G105 | 1.26 | 0.12 | 11.90 | 0.58 | 0.76 | 0.11 |
| Q106 | 1.19 | 0.06 | 12.19 | 0.36 | 0.73 | 0.08 |
| V107 | 1.21 | 0.02 | 10.89 | 0.32 | 0.77 | 0.04 |
| F108 | | | | | | |
| V111 | 1.19 | 0.04 | 20.80 | 0.73 | 0.91 | 0.07 |
| I112 | 1.26 | 0.04 | 11.87 | 0.73 | 0.84 | 0.06 |
| A113 | 1.29 | 0.03 | 12.98 | 0.51 | 0.95 | 0.06 |
| Y114 | | | | | | |
| S115 | 1.16 | 0.03 | 12.70 | 0.33 | 0.83 | 0.05 |
| D116 | 1.20 | 0.02 | 13.15 | 0.46 | 0.75 | 0.04 |
| D117 | 1.36 | 0.09 | 15.71 | 0.67 | 0.67 | 0.07 |
| N118 | 1.27 | 0.04 | 11.73 | 0.18 | 0.71 | 0.05 |
| C119 | 1.30 | 0.07 | 24.97 | 1.53 | 0.82 | 0.06 |
| D120 | 1.23 | 0.28 | 18.95 | 4.24 | 0.75 | 0.24 |
| V121 | 1.20 | 0.06 | 12.99 | 0.37 | 0.84 | 0.05 |
| I122 | 1.18 | 0.04 | 13.80 | 0.71 | 0.91 | 0.06 |
| Y123 | 1.25 | 0.04 | 12.77 | 0.47 | 0.90 | 0.05 |
| V124 | 1.28 | 0.06 | 13.44 | 0.77 | 0.80 | 0.06 |
| G126 | 1.24 | 0.09 | 15.47 | 1.39 | 0.64 | 0.10 |
| T127 | 1.41 | 0.10 | 15.96 | 1.47 | 0.58 | 0.10 |
| G129 | 1.40 | 0.14 | 11.27 | 0.30 | 0.59 | 0.05 |

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|----------------|-------------|-------------|--------------|-------------|-------------|-------------|
| E131 | | | | | | |
| G133 | 1.23 | 0.06 | 15.81 | 1.80 | 0.54 | 0.10 |
| Y134 | 1.20 | 0.03 | 12.04 | 0.289 | 0.77 | 0.04 |
| R135 | 1.14 | 0.04 | 13.32 | 0.53 | 0.79 | 0.05 |
| L136 | 1.15 | 0.03 | 12.73 | 0.43 | 0.79 | 0.04 |
| W137 | 1.21 | 0.06 | 12.84 | 0.47 | 0.81 | 0.06 |
| T138 | 1.21 | 0.05 | 13.61 | 0.52 | 0.91 | 0.06 |
| T139 | 1.23 | 0.04 | 14.45 | 0.87 | 0.66 | 0.06 |
| D140 | 1.28 | 0.02 | 12.21 | 0.50 | 0.73 | 0.05 |
| Y141 | 1.18 | 0.05 | 12.06 | 0.46 | 0.73 | 0.04 |
| D142 | 1.26 | 0.02 | 11.47 | 0.30 | 0.84 | 0.04 |
| N143 | 1.06 | 0.01 | 9.74 | 0.15 | 0.68 | 0.03 |
| I144 | 1.23 | 0.01 | 10.74 | 0.31 | 0.76 | 0.04 |
| A146 | 1.40 | 0.05 | 12.72 | 0.37 | 0.84 | 0.04 |
| C148 | 1.31 | 0.05 | 22.43 | 0.72 | 0.72 | 0.05 |
| L149 | 1.30 | 0.04 | 15.44 | 0.56 | 0.76 | 0.05 |
| N150 | 1.30 | 0.03 | 11.80 | 0.23 | 0.83 | 0.04 |
| K151 | 1.27 | 0.03 | 12.42 | 0.47 | 0.82 | 0.05 |
| F152 | 1.25 | 0.03 | 12.37 | 0.21 | 0.83 | 0.05 |
| N153 | 1.34 | 0.02 | 11.93 | 0.25 | 0.80 | 0.04 |
| E154 | 1.24 | 0.03 | 11.48 | 0.30 | 0.82 | 0.04 |
| Y155 | | | | | | |
| A156 | | | | | | |
| V157 | 1.11 | 0.02 | 11.36 | 0.17 | 0.83 | 0.03 |
| R159 | 1.22 | 0.01 | 11.17 | 0.17 | 0.85 | 0.04 |
| E160 | 1.19 | 0.08 | 10.18 | 0.33 | 0.68 | 0.05 |
| R162 | 1.33 | 0.04 | 12.26 | 0.50 | 0.90 | 0.08 |
| D163 | 1.22 | 0.03 | 12.40 | 0.39 | 0.80 | 0.04 |
| V164 | 1.08 | 0.03 | 12.30 | 0.60 | 0.77 | 0.07 |
| F165 | 1.38 | 0.12 | 12.24 | 1.55 | 0.58 | 0.10 |
| T166 | 1.16 | 0.04 | 11.34 | 0.45 | 0.73 | 0.04 |
| S167 | 1.27 | 0.06 | 12.41 | 0.54 | 0.87 | 0.06 |
| A168 | 1.33 | 0.07 | 13.25 | 0.28 | 0.78 | 0.04 |
| C169 | 1.31 | 0.03 | 10.68 | 0.34 | 0.65 | 0.03 |
| L170 | 1.23 | 0.02 | 10.56 | 0.23 | 0.61 | 0.03 |
| E171 | 1.37 | 0.01 | 5.48 | 0.06 | 0.33 | 0.02 |
| Average | 1.25 | 0.08 | 12.64 | 2.12 | 0.78 | 0.10 |

Table s4. ^{15}N amide R_1 and R_2 and ssNOE values for rRaHBP2(D24R) in complex with histamine at 500 MHz, 298 K. The error in the average values is given as the standard deviation.

| Residue | R_1 (1/s) | error | R_2 (1/s) | error | ssNOE | error |
|----------------|-------------------------------|--------------|-------------------------------|--------------|--------------|--------------|
| D4 | 1.74 | 0.12 | 11.55 | 0.60 | 0.80 | 0.08 |
| W5 | 1.52 | 0.05 | 10.64 | 0.15 | 0.78 | 0.04 |
| A6 | 1.82 | 0.03 | 10.79 | 0.13 | 0.77 | 0.04 |
| D7 | 1.30 | 0.04 | 8.57 | 0.10 | 0.69 | 0.05 |
| E8 | 1.72 | 0.02 | 10.31 | 0.25 | 0.80 | 0.05 |
| A9 | 1.82 | 0.03 | 10.71 | 0.23 | 0.86 | 0.04 |
| A10 | 1.62 | 0.03 | 10.17 | 0.16 | 0.77 | 0.04 |
| N11 | 1.70 | 0.04 | 10.56 | 0.31 | 0.81 | 0.06 |
| G12 | 1.72 | 0.06 | 11.38 | 0.21 | 0.74 | 0.05 |
| A13 | 2.01 | 0.09 | 12.83 | 0.14 | 0.90 | 0.08 |
| H14 | 1.64 | 0.04 | 10.53 | 0.29 | 0.84 | 0.06 |
| D16 | 1.68 | 0.03 | 10.29 | 0.21 | 0.74 | 0.04 |
| A17 | 1.75 | 0.02 | 10.88 | 0.17 | 0.73 | 0.04 |
| W18 | 1.68 | 0.02 | 11.49 | 0.17 | 0.90 | 0.06 |
| K19 | 1.67 | 0.02 | 11.32 | 0.17 | 0.78 | 0.04 |
| S20 | 1.63 | 0.01 | 10.79 | 0.20 | 0.73 | 0.04 |
| L21 | 1.72 | 0.03 | 12.09 | 0.15 | 0.75 | 0.04 |
| K22 | 1.66 | 0.04 | 11.57 | 0.16 | 0.88 | 0.05 |
| A23 | 1.72 | 0.02 | 11.23 | 0.21 | 0.82 | 0.04 |
| R24 | | | | | | |
| E26 | | | | | | |
| N27 | 1.56 | 0.02 | 9.99 | 0.16 | 0.68 | 0.05 |
| V28 | | | | | | |
| Y29 | 1.74 | 0.02 | 10.55 | 0.21 | 0.69 | 0.06 |
| Y30 | 1.73 | 0.05 | 10.67 | 0.26 | 0.73 | 0.06 |
| M31 | | | | | | |
| V32 | 1.62 | 0.06 | 12.46 | 0.32 | 0.72 | 0.06 |
| K33 | 1.69 | 0.02 | 11.81 | 0.30 | 0.80 | 0.05 |
| A34 | 1.68 | 0.05 | 11.23 | 0.27 | 0.77 | 0.05 |
| T35 | 1.63 | 0.03 | 11.38 | 0.22 | 0.75 | 0.06 |
| K37 | 1.80 | 0.04 | 10.37 | 0.25 | 0.91 | 0.08 |
| N38 | 1.63 | 0.03 | 11.40 | 0.19 | 0.78 | 0.06 |
| D39 | | | | | | |
| V41 | 1.73 | 0.05 | 11.09 | 0.27 | 0.87 | 0.07 |
| W42 | 1.58 | 0.05 | 11.49 | 0.33 | 0.66 | 0.06 |
| G43 | 1.74 | 0.03 | 12.09 | 0.22 | 0.85 | 0.05 |
| N44 | 1.69 | 0.06 | 10.35 | 0.22 | 0.69 | 0.05 |
| D45 | 1.64 | 0.05 | 11.23 | 0.21 | 0.80 | 0.07 |
| F46 | 1.63 | 0.03 | 10.64 | 0.20 | 0.72 | 0.04 |
| T47 | 1.69 | 0.03 | 10.24 | 0.38 | 0.73 | 0.06 |
| C48 | 1.79 | 0.06 | 10.06 | 0.24 | 0.84 | 0.08 |
| V49 | 1.56 | 0.03 | 10.31 | 0.31 | 0.90 | 0.05 |
| G50 | 1.84 | 0.05 | 10.89 | 0.21 | 0.72 | 0.05 |
| V51 | 1.79 | 0.05 | 10.60 | 0.25 | 0.86 | 0.06 |
| M52 | 1.78 | 0.02 | 10.79 | 0.19 | 0.77 | 0.06 |
| A53 | 1.65 | 0.03 | 9.48 | 0.24 | 0.79 | 0.06 |
| N54 | 1.80 | 0.03 | 9.19 | 0.18 | 0.70 | 0.05 |
| D55 | 1.66 | 0.02 | 8.32 | 0.07 | 0.62 | 0.04 |
| N57 | 1.67 | 0.05 | 9.92 | 0.36 | 0.76 | 0.06 |
| E58 | 1.80 | 0.09 | 10.93 | 0.20 | 0.78 | 0.06 |
| D59 | 1.62 | 0.02 | 10.27 | 0.11 | 0.73 | 0.03 |
| E60 | 1.58 | 0.04 | 10.23 | 0.11 | 0.76 | 0.05 |
| K61 | 1.71 | 0.05 | 10.40 | 0.19 | 0.81 | 0.06 |
| S62 | 1.79 | 0.03 | 10.50 | 0.20 | 0.75 | 0.05 |
| I63 | 1.75 | 0.04 | 10.39 | 0.31 | 0.73 | 0.07 |
| Q64 | 1.50 | 0.04 | 9.62 | 0.16 | 0.65 | 0.04 |

| | | | | | | |
|-------------|------|------|-------|------|------|------|
| A65 | 1.74 | 0.02 | 9.75 | 0.15 | 0.74 | 0.05 |
| E66 | 1.73 | 0.03 | 9.97 | 0.23 | 0.75 | 0.05 |
| F67 | 1.75 | 0.05 | 10.28 | 0.32 | 0.74 | 0.06 |
| L68 | 1.70 | 0.05 | 11.12 | 0.18 | 0.79 | 0.07 |
| F69 | 1.63 | 0.03 | 10.59 | 0.27 | 0.74 | 0.05 |
| M70 | 1.71 | 0.04 | 11.82 | 0.26 | 0.76 | 0.07 |
| N71 | 1.60 | 0.04 | 10.58 | 0.28 | 0.72 | 0.04 |
| N72 | 1.67 | 0.03 | 10.34 | 0.22 | 0.64 | 0.05 |
| A73 | | | | | | |
| D74 | 1.60 | 0.03 | 9.37 | 0.07 | 0.59 | 0.03 |
| T75 | 1.59 | 0.09 | 9.85 | 0.33 | 0.69 | 0.07 |
| M77 | 1.68 | 0.02 | 9.89 | 0.10 | 0.76 | 0.05 |
| Q78 | 1.65 | 0.03 | 10.51 | 0.29 | 0.68 | 0.06 |
| F79 | 1.62 | 0.03 | 9.88 | 0.28 | 0.73 | 0.06 |
| A80 | 1.65 | 0.03 | 10.03 | 0.11 | 0.89 | 0.06 |
| T81 | 1.63 | 0.03 | 9.64 | 0.23 | 0.76 | 0.05 |
| E82 | 1.76 | 0.04 | 10.38 | 0.22 | 0.75 | 0.05 |
| K83 | 1.64 | 0.03 | 10.14 | 0.28 | 0.84 | 0.06 |
| V84 | 1.78 | 0.04 | 10.31 | 0.15 | 0.76 | 0.05 |
| T85 | | | | | | |
| A86 | 1.74 | 0.04 | 10.37 | 0.09 | 0.82 | 0.05 |
| K88 | 1.72 | 0.04 | 10.60 | 0.30 | 0.94 | 0.08 |
| M89 | 1.62 | 0.03 | 9.64 | 0.19 | 0.77 | 0.06 |
| Y90 | | | | | | |
| G91 | 1.91 | 0.07 | 11.91 | 0.23 | 0.79 | 0.06 |
| Y92 | 1.75 | 0.05 | 11.58 | 0.20 | 0.84 | 0.05 |
| N93 | 1.60 | 0.07 | 10.45 | 0.35 | 0.68 | 0.06 |
| R94 | | | | | | |
| E95 | 1.65 | 0.04 | 10.02 | 0.14 | 0.70 | 0.04 |
| N96 | 1.75 | 0.07 | 10.53 | 0.32 | 0.70 | 0.07 |
| A97 | | | | | | |
| F98 | | | | | | |
| R99 | 1.75 | 0.04 | 10.69 | 0.24 | 0.82 | 0.06 |
| Y100 | 1.70 | 0.04 | 10.73 | 0.28 | 0.87 | 0.07 |
| E101 | 1.72 | 0.02 | 10.27 | 0.24 | 0.83 | 0.06 |
| T102 | 1.75 | 0.02 | 10.85 | 0.19 | 0.88 | 0.06 |
| E103 | 1.78 | 0.02 | 10.81 | 0.29 | 0.83 | 0.06 |
| D104 | 1.66 | 0.02 | 9.54 | 0.16 | 0.75 | 0.05 |
| G105 | 1.66 | 0.03 | 9.68 | 0.11 | 0.67 | 0.04 |
| Q106 | 1.69 | 0.03 | 10.72 | 0.14 | 0.69 | 0.05 |
| V107 | 1.60 | 0.04 | 9.63 | 0.17 | 0.71 | 0.05 |
| F108 | 1.72 | 0.04 | 10.55 | 0.18 | 0.86 | 0.06 |
| T109 | 1.71 | 0.06 | 10.33 | 0.23 | 0.78 | 0.06 |
| D110 | 1.73 | 0.05 | 10.13 | 0.25 | 0.81 | 0.05 |
| V111 | 1.70 | 0.03 | 11.08 | 0.31 | 0.75 | 0.05 |
| I112 | | | | | | |
| A113 | 1.70 | 0.04 | 12.48 | 0.42 | 0.69 | 0.06 |
| Y114 | 1.64 | 0.03 | 11.79 | 0.16 | 0.78 | 0.04 |
| S115 | 1.58 | 0.02 | 11.37 | 0.27 | 0.70 | 0.05 |
| D116 | 1.70 | 0.06 | 11.38 | 0.37 | 0.85 | 0.06 |
| D117 | 1.86 | 0.10 | 13.24 | 0.26 | 0.55 | 0.07 |
| N118 | 1.80 | 0.04 | 10.22 | 0.26 | 0.74 | 0.07 |
| C119 | 1.68 | 0.04 | 17.16 | 0.56 | 0.80 | 0.05 |
| D120 | 1.66 | 0.05 | 16.23 | 0.38 | 0.81 | 0.06 |
| V121 | 1.64 | 0.03 | 11.37 | 0.24 | 0.67 | 0.05 |
| I122 | 1.65 | 0.04 | 10.52 | 0.21 | 0.83 | 0.06 |
| Y123 | 1.63 | 0.05 | 10.87 | 0.33 | 0.75 | 0.06 |
| V124 | 1.69 | 0.04 | 11.08 | 0.35 | 0.81 | 0.06 |
| G126 | 1.73 | 0.05 | 10.64 | 0.15 | 0.74 | 0.06 |
| T127 | 1.76 | 0.05 | 9.70 | 0.17 | 0.62 | 0.05 |

| | | | | | | |
|----------------|-------------|-------------|--------------|-------------|-------------|-------------|
| D128 | 1.79 | 0.05 | 9.89 | 0.31 | 0.63 | 0.06 |
| G129 | 1.63 | 0.04 | 10.13 | 0.14 | 0.74 | 0.05 |
| N130 | 1.60 | 0.04 | 10.46 | 0.25 | 0.70 | 0.04 |
| E132 | 1.63 | 0.03 | 9.74 | 0.17 | 0.72 | 0.05 |
| G133 | 1.73 | 0.04 | 11.19 | 0.28 | 0.79 | 0.05 |
| Y134 | 1.72 | 0.03 | 10.56 | 0.28 | 0.83 | 0.06 |
| E135 | 1.56 | 0.04 | 10.65 | 0.18 | 0.74 | 0.06 |
| L136 | 1.64 | 0.03 | 11.62 | 0.24 | 0.73 | 0.05 |
| W137 | 1.67 | 0.05 | 12.20 | 0.31 | 0.71 | 0.06 |
| T138 | 1.59 | 0.04 | 10.95 | 0.15 | 0.74 | 0.04 |
| T139 | 1.66 | 0.03 | 12.49 | 0.25 | 0.80 | 0.07 |
| D140 | 1.67 | 0.03 | 10.75 | 0.20 | 0.63 | 0.05 |
| Y141 | 1.59 | 0.05 | 9.82 | 0.37 | 0.72 | 0.05 |
| D142 | 1.74 | 0.03 | 10.50 | 0.26 | 0.68 | 0.05 |
| N143 | 1.41 | 0.02 | 8.57 | 0.07 | 0.61 | 0.04 |
| I144 | 1.57 | 0.02 | 9.79 | 0.08 | 0.73 | 0.04 |
| A146 | 1.94 | 0.07 | 10.66 | 0.46 | 0.73 | 0.05 |
| C148 | 1.79 | 0.07 | 19.30 | 0.42 | 0.67 | 0.06 |
| L149 | 1.78 | 0.03 | 13.96 | 0.23 | 0.81 | 0.06 |
| N150 | 1.75 | 0.02 | 10.89 | 0.12 | 0.74 | 0.03 |
| K151 | 1.74 | 0.04 | 10.78 | 0.26 | 0.79 | 0.05 |
| F152 | 1.82 | 0.05 | 11.67 | 0.39 | 0.83 | 0.07 |
| N153 | 1.76 | 0.03 | 10.56 | 0.19 | 0.80 | 0.05 |
| E154 | 1.68 | 0.03 | 10.81 | 0.09 | 0.82 | 0.05 |
| Y155 | 1.74 | 0.04 | 11.02 | 0.09 | 0.81 | 0.04 |
| A156 | 1.77 | 0.03 | 10.92 | 0.05 | 0.78 | 0.04 |
| V157 | 1.54 | 0.03 | 10.44 | 0.17 | 0.78 | 0.03 |
| E160 | 1.56 | 0.08 | 9.16 | 0.34 | 0.64 | 0.08 |
| T161 | 1.48 | 0.03 | 7.69 | 0.12 | 0.62 | 0.04 |
| R162 | 1.72 | 0.05 | 10.82 | 0.28 | 0.81 | 0.07 |
| D163 | 1.64 | 0.04 | 10.79 | 0.27 | 0.81 | 0.05 |
| V164 | 1.63 | 0.05 | 10.56 | 0.36 | 0.81 | 0.08 |
| F165 | | | | | | |
| T166 | 1.61 | 0.03 | 10.26 | 0.30 | 0.77 | 0.06 |
| S167 | 1.68 | 0.13 | 11.55 | 0.48 | 0.72 | 0.08 |
| A168 | 1.90 | 0.09 | 11.57 | 0.31 | 0.67 | 0.05 |
| C169 | | | | | | |
| L170 | 1.60 | 0.03 | 9.27 | 0.25 | 0.67 | 0.05 |
| E171 | 1.64 | 0.01 | 4.86 | 0.05 | 0.34 | 0.02 |
| Average | 1.69 | 0.09 | 10.75 | 1.44 | 0.75 | 0.08 |

Table s5. ^{15}N amide R_1 and R_2 and ssNOE values for rRaHBP2(D24R) in complex with histamine at 600 MHz, 298 K. The error in the average values is given as the standard deviation.

| Residue | R_1 (1/s) | error | R_2 (1/s) | error | ssNOE | error |
|----------------|-------------------------------|--------------|-------------------------------|--------------|--------------|--------------|
| D4 | 1.23 | 0.11 | 13.33 | 0.72 | 0.98 | 0.08 |
| W5 | 1.17 | 0.05 | 12.63 | 0.54 | 0.83 | 0.03 |
| A6 | 1.27 | 0.04 | 12.43 | 0.37 | 0.84 | 0.04 |
| D7 | 0.94 | 0.03 | 9.53 | 0.27 | 0.77 | 0.04 |
| E8 | 1.31 | 0.03 | 12.19 | 0.42 | 0.84 | 0.04 |
| A9 | 1.40 | 0.01 | 12.26 | 0.30 | 0.84 | 0.03 |
| A10 | 1.25 | 0.02 | 11.06 | 0.16 | 0.88 | 0.03 |
| N11 | 1.22 | 0.04 | 11.55 | 0.45 | 0.79 | 0.05 |
| G12 | 1.26 | 0.04 | 13.19 | 0.57 | 0.73 | 0.04 |
| A13 | 1.39 | 0.09 | 14.05 | 0.35 | 0.86 | 0.05 |
| H14 | 1.21 | 0.04 | 12.20 | 0.42 | 0.78 | 0.05 |
| D16 | 1.24 | 0.03 | 11.82 | 0.19 | 0.80 | 0.04 |
| A17 | 1.22 | 0.03 | 12.46 | 0.23 | 0.83 | 0.04 |
| W18 | 1.19 | 0.03 | 13.34 | 0.41 | 0.82 | 0.04 |
| K19 | 1.24 | 0.02 | 13.06 | 0.34 | 0.84 | 0.03 |
| S20 | 1.27 | 0.01 | 12.96 | 0.28 | 0.81 | 0.04 |
| L21 | 1.27 | 0.02 | 14.02 | 0.38 | 0.84 | 0.04 |
| K22 | 1.22 | 0.02 | 13.02 | 0.12 | 0.76 | 0.03 |
| A23 | 1.28 | 0.02 | 12.82 | 0.27 | 0.83 | 0.03 |
| R24 | | | | | | |
| E26 | | | | | | |
| N27 | 1.16 | 0.02 | 11.22 | 0.31 | 0.73 | 0.04 |
| V28 | | | | | | |
| Y29 | 1.28 | 0.04 | 11.25 | 0.27 | 0.87 | 0.05 |
| Y30 | 1.23 | 0.05 | 12.40 | 0.36 | 0.77 | 0.05 |
| M31 | 1.23 | 0.02 | 13.00 | 0.36 | 0.82 | 0.04 |
| V32 | 1.21 | 0.06 | 15.68 | 0.42 | 0.85 | 0.06 |
| K33 | 1.25 | 0.03 | 13.03 | 0.23 | 0.87 | 0.04 |
| A34 | 1.24 | 0.02 | 12.61 | 0.20 | 0.77 | 0.03 |
| T35 | 1.26 | 0.02 | 11.44 | 0.66 | 0.83 | 0.05 |
| K37 | 1.32 | 0.02 | 12.83 | 0.41 | 0.73 | 0.05 |
| N38 | 1.21 | 0.03 | 12.40 | 0.36 | 0.79 | 0.05 |
| D39 | 1.20 | 0.02 | 13.41 | 0.62 | 0.76 | 0.04 |
| V41 | 1.26 | 0.04 | 12.09 | 0.21 | 0.87 | 0.05 |
| W42 | 1.16 | 0.04 | 12.99 | 0.68 | 0.67 | 0.04 |
| G43 | 1.25 | 0.04 | 12.88 | 0.59 | 0.84 | 0.04 |
| N44 | 1.25 | 0.05 | 12.16 | 0.61 | 0.82 | 0.04 |
| D45 | 1.29 | 0.04 | 12.58 | 0.29 | 0.73 | 0.05 |
| F46 | 1.22 | 0.04 | 12.08 | 0.62 | 0.84 | 0.04 |
| T47 | 1.30 | 0.03 | 12.36 | 0.49 | 0.81 | 0.04 |
| C48 | 1.19 | 0.04 | 13.47 | 0.21 | 0.90 | 0.07 |
| V49 | 1.19 | 0.10 | 11.66 | 0.74 | 0.79 | 0.03 |
| G50 | 1.35 | 0.05 | 11.84 | 0.27 | 0.87 | 0.05 |
| V51 | 1.30 | 0.03 | 12.35 | 0.33 | 0.87 | 0.05 |
| M52 | 1.37 | 0.01 | 11.75 | 0.31 | 0.85 | 0.04 |
| A53 | 1.24 | 0.02 | 10.86 | 0.24 | 0.70 | 0.04 |
| N54 | 1.40 | 0.02 | 10.46 | 0.08 | 0.73 | 0.04 |
| D55 | 1.25 | 0.03 | 9.65 | 0.32 | 0.65 | 0.03 |
| N57 | 1.25 | 0.03 | 11.50 | 0.33 | 0.87 | 0.05 |
| E58 | 1.30 | 0.03 | 12.95 | 0.21 | 0.82 | 0.04 |
| D59 | 1.23 | 0.01 | 12.13 | 0.25 | 0.77 | 0.03 |
| E60 | 1.13 | 0.02 | 11.87 | 0.27 | 0.81 | 0.04 |
| K61 | 1.27 | 0.02 | 11.27 | 0.38 | 0.75 | 0.04 |
| S62 | 1.30 | 0.03 | 12.42 | 0.33 | 0.81 | 0.04 |

| | | | | | | |
|-------------|------|------|-------|------|------|------|
| I63 | 1.27 | 0.03 | 12.13 | 0.50 | 0.78 | 0.05 |
| Q64 | 1.15 | 0.01 | 11.09 | 0.23 | 0.68 | 0.03 |
| A65 | 1.30 | 0.02 | 12.26 | 0.34 | 0.84 | 0.04 |
| E66 | 1.28 | 0.05 | 11.47 | 0.40 | 0.80 | 0.05 |
| F67 | 1.29 | 0.03 | 12.04 | 0.21 | 0.85 | 0.05 |
| L68 | 1.32 | 0.04 | 12.84 | 0.35 | 0.76 | 0.05 |
| F69 | 1.25 | 0.02 | 11.26 | 0.32 | 0.75 | 0.04 |
| M70 | 1.22 | 0.03 | 12.47 | 0.36 | 0.80 | 0.05 |
| N71 | 1.22 | 0.02 | 12.83 | 0.35 | 0.83 | 0.04 |
| N72 | 1.31 | 0.04 | 11.65 | 0.38 | 0.74 | 0.04 |
| A73 | 1.25 | 0.02 | 12.11 | 0.27 | 0.74 | 0.03 |
| D74 | 1.18 | 0.01 | 11.33 | 0.16 | 0.70 | 0.03 |
| T75 | 1.18 | 0.09 | 11.38 | 0.76 | 0.69 | 0.05 |
| M77 | 1.31 | 0.02 | 11.40 | 0.30 | 0.79 | 0.04 |
| Q78 | 1.31 | 0.04 | 12.03 | 0.54 | 0.84 | 0.05 |
| F79 | 1.27 | 0.03 | 12.00 | 0.45 | 0.85 | 0.05 |
| A80 | 1.32 | 0.02 | 11.10 | 0.35 | 0.80 | 0.04 |
| T81 | 1.19 | 0.02 | 10.84 | 0.30 | 0.77 | 0.04 |
| E82 | 1.25 | 0.04 | 11.46 | 0.20 | 0.86 | 0.04 |
| K83 | 1.27 | 0.04 | 11.99 | 0.33 | 0.88 | 0.05 |
| V84 | 1.29 | 0.03 | 12.10 | 0.29 | 0.79 | 0.04 |
| T85 | | | | | | |
| A86 | 1.31 | 0.03 | 13.16 | 0.40 | 0.80 | 0.04 |
| K88 | 1.29 | 0.03 | 11.31 | 0.32 | 0.84 | 0.05 |
| M89 | 1.18 | 0.02 | 11.57 | 0.38 | 0.81 | 0.04 |
| Y90 | | | | | | |
| G91 | 1.39 | 0.11 | 12.42 | 0.59 | 0.79 | 0.05 |
| Y92 | 1.31 | 0.03 | 13.08 | 0.40 | 0.86 | 0.04 |
| N93 | 1.19 | 0.03 | 11.30 | 0.55 | 0.83 | 0.06 |
| R94 | | | | | | |
| E95 | 1.19 | 0.02 | 11.77 | 0.17 | 0.78 | 0.03 |
| N96 | 1.26 | 0.04 | 12.50 | 0.52 | 0.80 | 0.06 |
| A97 | 1.33 | 0.03 | 12.43 | 0.41 | 0.80 | 0.03 |
| F98 | | | | | | |
| R99 | 1.21 | 0.02 | 11.72 | 0.17 | 0.84 | 0.04 |
| Y100 | 1.22 | 0.05 | 11.84 | 0.48 | 0.90 | 0.06 |
| E101 | 1.18 | 0.03 | 12.14 | 0.52 | 0.83 | 0.04 |
| T102 | 1.26 | 0.02 | 12.12 | 0.46 | 0.87 | 0.05 |
| E103 | 1.41 | 0.03 | 11.65 | 0.44 | 0.74 | 0.04 |
| D104 | 1.29 | 0.04 | 10.89 | 0.20 | 0.73 | 0.04 |
| G105 | 1.24 | 0.03 | 11.97 | 0.36 | 0.74 | 0.04 |
| Q106 | 1.20 | 0.03 | 12.72 | 0.28 | 0.75 | 0.04 |
| V107 | 1.22 | 0.02 | 10.87 | 0.26 | 0.78 | 0.04 |
| F108 | 1.26 | 0.02 | 12.02 | 0.36 | 0.92 | 0.05 |
| T109 | 1.23 | 0.03 | 11.95 | 0.52 | 0.87 | 0.05 |
| D110 | 1.28 | 0.03 | 12.10 | 0.37 | 0.90 | 0.04 |
| V111 | 1.23 | 0.02 | 13.14 | 0.44 | 0.86 | 0.04 |
| I112 | | | | | | |
| A113 | 1.21 | 0.04 | 12.60 | 0.62 | 0.89 | 0.06 |
| Y114 | 1.18 | 0.02 | 13.39 | 0.19 | 0.79 | 0.03 |
| S115 | 1.19 | 0.03 | 13.52 | 0.59 | 0.85 | 0.05 |
| D116 | 1.20 | 0.03 | 13.03 | 0.57 | 0.80 | 0.05 |
| D117 | 1.51 | 0.06 | 17.68 | 0.76 | 0.76 | 0.07 |
| N118 | 1.34 | 0.03 | 11.79 | 0.23 | 0.75 | 0.06 |
| C119 | 1.25 | 0.02 | 25.85 | 0.84 | 0.83 | 0.05 |
| D120 | 1.16 | 0.04 | 20.24 | 0.92 | 0.93 | 0.06 |
| V121 | 1.14 | 0.02 | 12.85 | 0.29 | 0.89 | 0.05 |
| I122 | 1.19 | 0.03 | 13.37 | 0.78 | 0.85 | 0.05 |
| Y123 | 1.29 | 0.04 | 12.73 | 0.93 | 0.83 | 0.05 |
| V124 | 1.27 | 0.03 | 12.43 | 0.50 | 0.79 | 0.05 |

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|----------------|-------------|-------------|--------------|-------------|-------------|-------------|
| G126 | 1.24 | 0.02 | 11.31 | 0.47 | 0.71 | 0.05 |
| T127 | 1.28 | 0.03 | 11.62 | 0.35 | 0.78 | 0.05 |
| D128 | 1.36 | 0.04 | 11.99 | 0.37 | 0.86 | 0.05 |
| G129 | 1.25 | 0.05 | 12.49 | 0.25 | 0.70 | 0.04 |
| N130 | 1.21 | 0.03 | 12.90 | 0.39 | 0.77 | 0.04 |
| E132 | 1.18 | 0.04 | 11.35 | 0.17 | 0.76 | 0.04 |
| G133 | 1.31 | 0.04 | 12.49 | 0.29 | 0.88 | 0.04 |
| Y134 | 1.16 | 0.05 | 12.75 | 0.46 | 0.91 | 0.05 |
| E135 | 1.13 | 0.03 | 12.77 | 0.36 | 0.79 | 0.05 |
| L136 | 1.20 | 0.03 | 12.76 | 0.56 | 0.84 | 0.04 |
| W137 | 1.17 | 0.03 | 12.95 | 0.28 | 0.86 | 0.05 |
| T138 | 1.19 | 0.03 | 11.93 | 0.34 | 0.82 | 0.04 |
| T139 | 1.21 | 0.03 | 15.72 | 0.51 | 0.78 | 0.05 |
| D140 | 1.25 | 0.03 | 12.39 | 0.31 | 0.71 | 0.04 |
| Y141 | 1.11 | 0.03 | 11.20 | 0.42 | 0.73 | 0.04 |
| D142 | 1.26 | 0.03 | 12.69 | 0.40 | 0.76 | 0.04 |
| N143 | 1.07 | 0.01 | 9.89 | 0.12 | 0.68 | 0.03 |
| I144 | 1.22 | 0.02 | 11.15 | 0.32 | 0.72 | 0.03 |
| A146 | 1.44 | 0.07 | 13.49 | 0.13 | 0.82 | 0.04 |
| C148 | 1.31 | 0.03 | 22.55 | 0.73 | 0.87 | 0.06 |
| L149 | 1.38 | 0.03 | 16.04 | 0.67 | 0.87 | 0.05 |
| N150 | | | | | | |
| K151 | 1.24 | 0.03 | 13.06 | 0.14 | 0.88 | 0.05 |
| F152 | 1.26 | 0.04 | 12.98 | 0.47 | 0.84 | 0.06 |
| N153 | 1.33 | 0.03 | 12.14 | 0.20 | 0.85 | 0.04 |
| E154 | 1.24 | 0.03 | 12.32 | 0.28 | 0.83 | 0.04 |
| Y155 | 1.28 | 0.03 | 12.33 | 0.23 | 0.88 | 0.04 |
| A156 | 1.29 | 0.02 | 12.29 | 0.27 | 0.79 | 0.03 |
| V157 | 1.10 | 0.02 | 11.80 | 0.24 | 0.81 | 0.03 |
| E160 | 1.24 | 0.09 | 11.18 | 0.51 | 0.74 | 0.06 |
| T161 | 1.13 | 0.02 | 9.08 | 0.18 | 0.64 | 0.03 |
| R162 | 1.32 | 0.05 | 13.39 | 0.34 | 0.84 | 0.05 |
| D163 | 1.22 | 0.03 | 12.41 | 0.31 | 0.86 | 0.04 |
| V164 | 1.23 | 0.03 | 11.53 | 0.46 | 0.82 | 0.06 |
| F165 | | | | | | |
| T166 | 1.17 | 0.04 | 11.67 | 0.40 | 0.81 | 0.04 |
| S167 | 1.24 | 0.14 | 13.65 | 1.04 | 0.67 | 0.06 |
| A168 | 1.42 | 0.08 | 13.69 | 0.42 | 0.92 | 0.05 |
| C169 | | | | | | |
| L170 | 1.21 | 0.02 | 10.42 | 0.17 | 0.68 | 0.03 |
| E171 | 1.41 | 0.01 | 5.67 | 0.06 | 0.34 | 0.02 |
| Average | 1.25 | 0.07 | 12.44 | 1.98 | 0.80 | 0.07 |

Table s6. ^{15}N amide model-free parameters for *apo* rRaHBP2(D24R) calculated from NMR relaxation data acquired at 298 K.

| Residue | m | S^2 | error | S_f^2 | error | S_s^2 | error | τ_e (ps) | error | τ_s (ps) | error | R_{ex} (1/s) 500 MHz | error | Chi ² |
|---------|---|-------|-------|---------|-------|---------|-------|---------------|--------|---------------|---------|---------------------------------|-------|------------------|
| D4 | 3 | 0.80 | 0.03 | | | | | | | | | 1.44 | 0.35 | 3.52 |
| W5 | 3 | 0.79 | 0.02 | | | | | | | | | 0.38 | 0.24 | 4.26 |
| A6 | 1 | 0.87 | 0.01 | | | | | | | | | | | 5.95 |
| D7 | 4 | 0.62 | 0.01 | | | | | 10.82 | 3.18 | | | 0.85 | 0.16 | 21.83 |
| E8 | 3 | 0.80 | 0.01 | | | | | | | | | 0.36 | 0.18 | 25.82 |
| A9 | 1 | 0.88 | 0.00 | | | | | | | | | | | 37.05 |
| A10 | 3 | 0.80 | 0.01 | | | | | | | | | 0.27 | 0.16 | 7.32 |
| N11 | 4 | 0.80 | 0.02 | | | | | 17.69 | 9.04 | | | 0.59 | 0.28 | 8.65 |
| G12 | 3 | 0.85 | 0.02 | | | | | | | | | 0.87 | 0.26 | 6.17 |
| A13 | 1 | 0.96 | 0.03 | | | | | | | | | | | 2.86 |
| H14 | | | | | | | | | | | | | | |
| Q15 | 3 | 0.80 | 0.01 | | | | | | | | | 1.34 | 0.23 | 4.90 |
| D16 | 1 | 0.84 | 0.01 | | | | | | | | | | | 12.06 |
| A17 | 3 | 0.82 | 0.01 | | | | | | | | | 0.94 | 0.22 | 13.17 |
| W19 | 3 | 0.82 | 0.01 | | | | | | | | | 1.07 | 0.18 | 9.82 |
| S20 | 3 | 0.81 | 0.01 | | | | | | | | | 1.40 | 0.21 | 22.26 |
| L21 | 3 | 0.89 | 0.02 | | | | | | | | | 0.88 | 0.36 | 4.15 |
| K22 | 3 | 0.83 | 0.01 | | | | | | | | | 1.25 | 0.15 | 7.27 |
| A23 | 1 | 0.89 | 0.01 | | | | | | | | | | | 12.86 |
| R24 | 4 | 0.83 | 0.02 | | | | | 26.33 | 12.52 | | | 1.11 | 0.22 | 3.87 |
| V25 | 3 | 0.84 | 0.01 | | | | | | | | | 1.77 | 0.21 | 6.08 |
| E26 | 4 | 0.75 | 0.01 | | | | | 28.58 | 6.45 | | | 0.51 | 0.17 | 11.15 |
| N27 | 4 | 0.77 | 0.01 | | | | | 27.39 | 7.24 | | | 0.55 | 0.15 | 22.19 |
| V28 | 5 | 0.72 | 0.01 | 0.77 | 0.01 | 0.94 | 0.01 | | | 1118.65 | 745.451 | | | 26.88 |
| Y29 | 1 | 0.84 | 0.01 | | | | | | | | | | | 5.35 |
| Y30 | 1 | 0.88 | 0.02 | | | | | | | | | | | 2.05 |
| M31 | 1 | 0.88 | 0.01 | | | | | | | | | | | 2.08 |
| V32 | 3 | 0.81 | 0.02 | | | | | | | | | 3.68 | 0.69 | 7.36 |
| K33 | 3 | 0.82 | 0.01 | | | | | | | | | 1.15 | 0.22 | 4.68 |
| A34 | 3 | 0.85 | 0.01 | | | | | | | | | 0.53 | 0.15 | 13.60 |
| T35 | 1 | 0.83 | 0.02 | | | | | | | | | | | 6.85 |
| Y36 | 1 | 0.94 | 0.02 | | | | | | | | | | | 4.47 |
| K37 | 1 | 0.91 | 0.02 | | | | | | | | | | | 8.72 |
| N38 | 4 | 0.65 | 0.08 | | | | | 73.85 | 66.82 | | | 2.63 | 1.37 | 1.08 |
| D39 | 4 | 0.84 | 0.03 | | | | | 34.84 | 17.08 | | | 1.79 | 0.42 | 4.91 |
| N44 | 3 | 0.88 | 0.02 | | | | | | | | | 0.77 | 0.47 | 1.96 |
| D45 | 1 | 0.86 | 0.01 | | | | | | | | | | | 9.71 |
| F46 | 3 | 0.82 | 0.01 | | | | | | | | | 0.44 | 0.15 | 19.52 |
| T47 | 4 | 0.84 | 0.02 | | | | | 26.53 | 16.14 | | | 0.70 | 0.39 | 0.90 |
| V49 | 1 | 0.81 | 0.01 | | | | | | | | | | | 1.66 |
| G50 | | | | | | | | | | | | | | |
| V51 | 3 | 0.90 | 0.02 | | | | | | | | | 1.20 | 0.35 | 5.30 |
| M52 | 4 | 0.87 | 0.02 | | | | | 37.77 | 19.75 | | | 0.46 | 0.21 | 4.67 |
| A53 | 4 | 0.81 | 0.06 | | | | | 75.41 | 131.42 | | | 1.95 | 0.88 | 1.69 |
| N54 | 5 | 0.76 | 0.01 | 0.85 | 0.01 | 0.89 | 0.02 | | | 1081.44 | 287.88 | | | 11.61 |
| D56 | 5 | 0.76 | 0.01 | 0.81 | 0.01 | 0.93 | 0.01 | | | 1326.39 | 1756.68 | | | 4.85 |
| V57 | 1 | 0.84 | 0.01 | | | | | | | | | | | 8.51 |
| E58 | 1 | 0.90 | 0.02 | | | | | | | | | | | 5.66 |
| D59 | 4 | 0.80 | 0.01 | | | | | 12.73 | 5.55 | | | 0.42 | 0.10 | 20.41 |
| E60 | 4 | 0.77 | 0.01 | | | | | 13.56 | 6.18 | | | 0.33 | 0.12 | 17.87 |
| K61 | 2 | 0.84 | 0.01 | | | | | 23.40 | 11.74 | | | | | 8.12 |
| S62 | 3 | 0.85 | 0.01 | | | | | | | | | 0.34 | 0.17 | 6.59 |
| I63 | 5 | 0.82 | 0.03 | 0.86 | 0.04 | 0.95 | 0.04 | | | 948.383 | 5077.24 | | | 9.31 |

| | | | | | | | | | | | | | | | | | | | | |
|-------------|---|------|------|------|------|------|------|--|--------|--------|---------|---------|--|--|--|--|------|------|------|-------|
| Q64 | | | | | | | | | | | | | | | | | | | | |
| A65 | 2 | 0.82 | 0.01 | | | | | | 26.87 | 9.59 | | | | | | | | | | 7.73 |
| E66 | 2 | 0.85 | 0.01 | | | | | | 47.46 | 20.58 | | | | | | | | | | 28.00 |
| F67 | 1 | 0.85 | 0.02 | | | | | | | | | | | | | | | | | 9.33 |
| L68 | | | | | | | | | | | | | | | | | | | | |
| F69 | | | | | | | | | | | | | | | | | | | | |
| M70 | 3 | 0.82 | 0.02 | | | | | | | | | | | | | | 0.74 | 0.28 | | 3.80 |
| N71 | | | | | | | | | | | | | | | | | | | | |
| N72 | 4 | 0.83 | 0.02 | | | | | | 41.08 | 15.04 | | | | | | | 0.83 | 0.32 | | 9.29 |
| A73 | | | | | | | | | | | | | | | | | | | | |
| D74 | 2 | 0.80 | 0.01 | | | | | | 14.30 | 7.71 | | | | | | | | | | 15.00 |
| T75 | 2 | 0.84 | 0.02 | | | | | | 43.73 | 21.70 | | | | | | | | | | 12.54 |
| N76 | | | | | | | | | | | | | | | | | | | | |
| M77 | 2 | 0.81 | 0.01 | | | | | | 15.60 | 7.44 | | | | | | | | | | 15.56 |
| Q78 | 1 | 0.86 | 0.02 | | | | | | | | | | | | | | | | | 1.81 |
| F79 | | | | | | | | | | | | | | | | | | | | |
| A80 | 1 | 0.83 | 0.01 | | | | | | | | | | | | | | | | | 8.62 |
| T81 | 1 | 0.84 | 0.01 | | | | | | | | | | | | | | | | | 9.84 |
| E82 | 1 | 0.87 | 0.02 | | | | | | | | | | | | | | | | | 5.86 |
| K83 | 4 | 0.67 | 0.05 | | | | | | 55.91 | 22.22 | | | | | | | 1.92 | 0.78 | | 1.41 |
| V84 | 3 | 0.88 | 0.04 | | | | | | | | | | | | | | 2.56 | 0.73 | | 1.20 |
| T85 | 1 | 0.93 | 0.01 | | | | | | | | | | | | | | | | | 12.59 |
| A86 | 5 | 0.85 | 0.02 | 0.89 | 0.03 | 0.95 | 0.03 | | | | 1053.44 | 4683.41 | | | | | | | | 17.97 |
| V87 | | | | | | | | | | | | | | | | | | | | |
| K88 | 5 | 0.80 | 0.03 | 0.85 | 0.01 | 0.94 | 0.03 | | | | 2140.27 | 6002.84 | | | | | | | | 10.78 |
| M89 | 1 | 0.82 | 0.01 | | | | | | | | | | | | | | | | | 1.53 |
| Y90 | | | | | | | | | | | | | | | | | | | | |
| G91 | 1 | 0.95 | 0.02 | | | | | | | | | | | | | | | | | 5.68 |
| Y92 | 3 | 0.84 | 0.02 | | | | | | | | | | | | | | | 1.19 | 0.27 | 10.31 |
| N93 | 3 | 0.78 | 0.02 | | | | | | | | | | | | | | 0.66 | 0.31 | | 5.48 |
| R94 | 1 | 0.82 | 0.01 | | | | | | | | | | | | | | | | | 17.07 |
| E95 | 3 | 0.83 | 0.01 | | | | | | | | | | | | | | | 0.29 | 0.15 | 6.56 |
| N96 | 1 | 0.86 | 0.01 | | | | | | | | | | | | | | | | | 1.22 |
| A97 | | | | | | | | | | | | | | | | | | | | |
| F98 | | | | | | | | | | | | | | | | | | | | |
| R99 | 1 | 0.87 | 0.01 | | | | | | | | | | | | | | | | | 16.97 |
| E101 | 4 | 0.87 | 0.02 | | | | | | 50.82 | 26.94 | | | | | | | 0.66 | 0.35 | | 3.25 |
| T102 | 4 | 0.84 | 0.02 | | | | | | 41.68 | 13.00 | | | | | | | 0.92 | 0.35 | | 1.90 |
| E103 | 2 | 0.86 | 0.02 | | | | | | 76.13 | 90.58 | | | | | | | | | | 12.28 |
| D104 | | | | | | | | | | | | | | | | | | | | |
| G105 | 2 | 0.79 | 0.02 | | | | | | 31.92 | 19.59 | | | | | | | | | | 8.10 |
| Q106 | 4 | 0.76 | 0.02 | | | | | | 40.01 | 12.06 | | | | | | | | 0.63 | 0.31 | 15.19 |
| V107 | 5 | 0.76 | 0.01 | 0.8 | 0.03 | 0.94 | 0.03 | | | | 1053.94 | 3044.5 | | | | | | | | 17.93 |
| F108 | | | | | | | | | | | | | | | | | | | | |
| V111 | 3 | 0.82 | 0.02 | | | | | | | | | | | | | | | 6.63 | 0.40 | 6.65 |
| I112 | 3 | 0.85 | 0.02 | | | | | | | | | | | | | | | 0.49 | 0.30 | 1.90 |
| A113 | 3 | 0.83 | 0.01 | | | | | | | | | | | | | | | 1.34 | 0.27 | 6.23 |
| Y114 | | | | | | | | | | | | | | | | | | | | |
| S115 | 3 | 0.79 | 0.01 | | | | | | | | | | | | | | | 0.85 | 0.19 | 14.30 |
| D116 | 4 | 0.79 | 0.01 | | | | | | 14.93 | 8.27 | | | | | | | | 0.91 | 0.16 | 15.98 |
| D117 | 4 | 0.89 | 0.04 | | | | | | 84.12 | 266.33 | | | | | | | | 2.08 | 0.52 | 2.97 |
| N118 | 4 | 0.82 | 0.02 | | | | | | 41.60 | 12.98 | | | | | | | | 0.38 | 0.23 | 4.28 |
| C119 | 3 | 0.88 | 0.02 | | | | | | | | | | | | | | | 7.71 | 0.72 | 3.62 |
| D120 | 3 | 0.82 | 0.10 | | | | | | | | | | | | | | | 8.33 | 1.92 | 3.43 |
| V121 | 3 | 0.81 | 0.01 | | | | | | | | | | | | | | | 1.39 | 0.26 | 3.67 |
| I122 | 3 | 0.80 | 0.02 | | | | | | | | | | | | | | | 1.84 | 0.37 | 4.63 |
| Y123 | 3 | 0.84 | 0.02 | | | | | | | | | | | | | | | 0.92 | 0.38 | 5.05 |
| V124 | 4 | 0.88 | 0.02 | | | | | | 44.27 | 23.86 | | | | | | | | 1.34 | 0.38 | 7.49 |
| G126 | 3 | 0.86 | 0.04 | | | | | | | | | | | | | | | 1.87 | 0.70 | 5.84 |
| T127 | 4 | 0.83 | 0.03 | | | | | | 109.04 | 46.90 | | | | | | | | 2.24 | 0.43 | 1.79 |

| | | | | | | | | | | | | | | | | | | |
|-------------|---|------|------|------|------|------|------|--|--------|--------|--|---------|---------|------|--|--|--|--------|
| G129 | 2 | 0.79 | 0.02 | | | | | | 53.20 | 12.01 | | | | | | | | 10.71 |
| E131 | | | | | | | | | | | | | | | | | | |
| G133 | 4 | 0.83 | 0.03 | | | | | | 83.90 | 28.30 | | | 3.49 | 0.80 | | | | 5.63 |
| Y134 | 4 | 0.82 | 0.01 | | | | | | 14.81 | 8.05 | | | 0.55 | 0.20 | | | | 8.97 |
| E135 | 3 | 0.78 | 0.02 | | | | | | | | | | 1.47 | 0.30 | | | | 6.62 |
| L136 | 3 | 0.80 | 0.01 | | | | | | | | | | 1.46 | 0.26 | | | | 11.30 |
| W137 | 3 | 0.83 | 0.02 | | | | | | | | | | 0.94 | 0.30 | | | | 3.94 |
| T138 | 1 | 0.86 | 0.01 | | | | | | | | | | | | | | | 22.95 |
| T139 | 4 | 0.81 | 0.02 | | | | | | 39.14 | 13.82 | | | 2.31 | 0.44 | | | | 3.07 |
| D140 | 2 | 0.82 | 0.01 | | | | | | 45.06 | 11.27 | | | | | | | | 10.42 |
| Y141 | 4 | 0.76 | 0.02 | | | | | | 19.49 | 6.02 | | | 0.98 | 0.29 | | | | 1.16 |
| D142 | 1 | 0.84 | 0.01 | | | | | | | | | | | | | | | 12.52 |
| N143 | 2 | 0.68 | 0.00 | | | | | | 21.94 | 2.86 | | | | | | | | 26.64 |
| I144 | 5 | 0.74 | 0.01 | 0.79 | 0.01 | 0.93 | 0.01 | | | | | 1042.66 | 1737.98 | | | | | 8.25 |
| A146 | 1 | 0.89 | 0.01 | | | | | | | | | | | | | | | 12.95 |
| N148 | 4 | 0.84 | 0.02 | | | | | | 32.06 | 13.49 | | | 7.06 | 0.39 | | | | 2.85 |
| C149 | 3 | 0.88 | 0.02 | | | | | | | | | | 2.40 | 0.28 | | | | 3.79 |
| N150 | 1 | 0.87 | 0.01 | | | | | | | | | | | | | | | 9.58 |
| K151 | 1 | 0.86 | 0.01 | | | | | | | | | | | | | | | 6.53 |
| F152 | 3 | 0.85 | 0.01 | | | | | | | | | | 0.41 | 0.18 | | | | 13.60 |
| N153 | 1 | 0.89 | 0.01 | | | | | | | | | | | | | | | 5.12 |
| E154 | 1 | 0.85 | 0.01 | | | | | | | | | | | | | | | 5.63 |
| Y155 | | | | | | | | | | | | | | | | | | |
| A156 | | | | | | | | | | | | | | | | | | |
| V157 | 3 | 0.75 | 0.01 | | | | | | | | | | 0.65 | 0.12 | | | | 16.44 |
| R159 | 2 | 0.80 | 0.01 | | | | | | 12.21 | 6.43 | | | | | | | | 31.30 |
| E160 | 2 | 0.75 | 0.01 | | | | | | 25.67 | 8.29 | | | | | | | | 1.81 |
| R162 | 1 | 0.88 | 0.01 | | | | | | | | | | | | | | | 6.62 |
| D163 | 3 | 0.81 | 0.02 | | | | | | | | | | 0.68 | 0.26 | | | | 8.18 |
| V164 | 3 | 0.75 | 0.01 | | | | | | | | | | 0.94 | 0.36 | | | | 15.91 |
| F165 | 2 | 0.87 | 0.03 | | | | | | 119.51 | 212.22 | | | | | | | | 0.46 |
| T166 | 4 | 0.75 | 0.02 | | | | | | 23.13 | 7.15 | | | 0.44 | 0.25 | | | | 3.36 |
| S167 | 1 | 0.86 | 0.02 | | | | | | | | | | | | | | | 4.72 |
| A168 | 4 | 0.85 | 0.03 | | | | | | 19.02 | 11.64 | | | 0.62 | 0.35 | | | | 17.28 |
| C169 | | | | | | | | | | | | | | | | | | |
| L170 | 2 | 0.77 | 0.01 | | | | | | 51.23 | 6.36 | | | | | | | | 3.75 |
| E171 | 5 | 0.29 | 0.00 | 0.69 | 0.01 | 0.42 | 0.00 | | | | | 1449.54 | 33.74 | | | | | 143.40 |

Table s7. ^{15}N amide model-free parameters for rRaHBP2(D24R) in complex with histamine calculated from NMR relaxation data acquired at 298 K.

| Residue | m | S^2 | error | S^2_f | error | S^2_s | error | τ_e (ps) | error | τ_s (ps) | error | R_{ex} (1/s) 500 MHz | error | Chi ² |
|---------|---|-------|-------|---------|-------|---------|-------|---------------|-------|---------------|---------|---------------------------------|-------|------------------|
| D4 | 3 | 0.84 | 0.04 | | | | | | | | | 1.40 | 0.60 | 4.83 |
| W5 | 3 | 0.76 | 0.02 | | | | | | | | | 1.31 | 0.31 | 2.67 |
| A6 | 1 | 0.88 | 0.01 | | | | | | | | | | | 18.17 |
| D7 | 4 | 0.62 | 0.02 | | | | | 8.19 | 3.56 | | | 0.88 | 0.18 | 4.86 |
| E8 | 1 | 0.86 | 0.01 | | | | | | | | | | | 7.28 |
| A9 | 1 | 0.90 | 0.01 | | | | | | | | | | | 9.28 |
| A10 | 3 | 0.81 | 0.01 | | | | | | | | | 0.20 | 0.14 | 4.81 |
| N11 | 1 | 0.84 | 0.01 | | | | | | | | | | | 6.43 |
| G12 | 4 | 0.82 | 0.02 | | | | | 26.11 | 8.46 | | | 1.29 | 0.29 | 3.13 |
| A13 | 3 | 0.96 | 0.03 | | | | | | | | | 0.85 | 0.35 | 4.43 |
| H14 | 3 | 0.80 | 0.02 | | | | | | | | | 0.79 | 0.30 | 5.01 |
| D16 | 4 | 0.82 | 0.01 | | | | | 13.40 | 8.04 | | | 0.54 | 0.15 | 10.21 |
| A17 | 3 | 0.86 | 0.01 | | | | | | | | | 0.50 | 0.14 | 28.03 |
| W18 | 3 | 0.83 | 0.01 | | | | | | | | | 1.31 | 0.20 | 17.43 |
| K19 | 3 | 0.82 | 0.01 | | | | | | | | | 1.21 | 0.14 | 9.06 |
| S20 | 4 | 0.81 | 0.01 | | | | | 13.17 | 7.40 | | | 1.12 | 0.13 | 11.16 |
| L21 | 3 | 0.84 | 0.01 | | | | | | | | | 1.76 | 0.18 | 9.00 |
| K22 | 3 | 0.80 | 0.01 | | | | | | | | | 1.67 | 0.13 | 11.42 |
| A23 | 3 | 0.85 | 0.01 | | | | | | | | | 0.90 | 0.16 | 8.67 |
| R24 | | | | | | | | | | | | | | |
| N27 | 4 | 0.75 | 0.01 | | | | | 21.30 | 6.15 | | | 0.67 | 0.17 | 8.23 |
| Y29 | 1 | 0.86 | 0.01 | | | | | | | | | | | 9.31 |
| Y30 | 4 | 0.82 | 0.02 | | | | | 20.15 | 11.83 | | | 0.72 | 0.26 | 7.23 |
| M31 | | | | | | | | | | | | | | |
| V32 | 3 | 0.79 | 0.02 | | | | | | | | | 3.15 | 0.32 | 8.24 |
| K33 | 3 | 0.84 | 0.01 | | | | | | | | | 1.33 | 0.14 | 5.39 |
| A34 | 4 | 0.80 | 0.01 | | | | | 13.16 | 6.99 | | | 1.37 | 0.18 | 3.14 |
| T35 | 3 | 0.82 | 0.01 | | | | | | | | | 1.07 | 0.21 | 3.30 |
| K37 | 1 | 0.87 | 0.01 | | | | | | | | | | | 24.40 |
| N38 | 3 | 0.81 | 0.01 | | | | | | | | | 1.31 | 0.20 | 3.60 |
| D39 | | | | | | | | | | | | | | |
| V41 | 3 | 0.84 | 0.02 | | | | | | | | | 0.65 | 0.23 | 4.30 |
| W42 | 4 | 0.75 | 0.02 | | | | | 31.03 | 7.68 | | | 2.14 | 0.32 | 2.36 |
| G43 | 3 | 0.86 | 0.01 | | | | | | | | | 1.32 | 0.22 | 6.96 |
| N44 | 1 | 0.84 | 0.01 | | | | | | | | | | | 9.60 |
| D45 | 4 | 0.81 | 0.02 | | | | | 21.29 | 12.13 | | | 1.17 | 0.23 | 1.11 |
| F46 | 3 | 0.81 | 0.01 | | | | | | | | | 0.62 | 0.23 | 6.49 |
| T47 | 1 | 0.85 | 0.01 | | | | | | | | | | | 8.00 |
| C48 | 3 | 0.79 | 0.02 | | | | | | | | | 1.55 | 0.24 | 59.78 |
| V49 | 3 | 0.78 | 0.01 | | | | | | | | | 0.65 | 0.32 | 5.48 |
| G50 | 1 | 0.89 | 0.01 | | | | | | | | | 0.00 | 0.00 | 6.87 |
| V51 | 3 | 0.86 | 0.02 | | | | | | | | | 0.36 | 0.21 | 10.76 |
| M52 | 1 | 0.88 | 0.01 | | | | | | | | | | | 3.32 |
| A53 | 2 | 0.79 | 0.01 | | | | | 25.03 | 7.85 | | | | | 9.81 |
| N54 | 5 | 0.76 | 0.02 | 0.86 | 0.01 | 0.89 | 0.02 | | | 1559.29 | 1654.77 | | | 14.61 |
| D55 | 5 | 0.64 | 0.01 | 0.79 | 0.01 | 0.81 | 0.01 | | | 1372.31 | 146.24 | | | 18.83 |
| N57 | 1 | 0.83 | 0.01 | | | | | | | | | | | 6.72 |
| E58 | 3 | 0.83 | 0.02 | | | | | | | | | 1.04 | 0.21 | 12.68 |
| D59 | 4 | 0.79 | 0.01 | | | | | 16.59 | 5.72 | | | 0.68 | 0.12 | 17.46 |
| E60 | 3 | 0.74 | 0.01 | | | | | | | | | 1.08 | 0.15 | 12.83 |
| K61 | 1 | 0.83 | 0.01 | | | | | | | | | | | 6.41 |
| S62 | 1 | 0.87 | 0.01 | | | | | | | | | | | 18.18 |
| I63 | 1 | 0.85 | 0.01 | | | | | | | | | | | 10.31 |

| | | | | | | | | | | | | | | |
|-------------|---|------|------|------|------|------|------|--------|--------|---------|---------|------|------|-------|
| Q64 | 4 | 0.71 | 0.01 | | | | | 26.42 | 3.83 | | | 0.89 | 0.13 | 5.13 |
| A65 | 2 | 0.84 | 0.01 | | | | | 15.21 | 9.49 | | | | | 45.41 |
| E66 | 5 | 0.81 | 0.03 | 0.85 | 0.04 | 0.96 | 0.04 | | | 1506.76 | 6514.47 | | | 6.20 |
| F67 | 3 | 0.84 | 0.01 | | | | | | | | | 0.46 | 0.21 | 9.48 |
| L68 | 3 | 0.85 | 0.02 | | | | | | | | | 0.78 | 0.25 | 5.28 |
| F69 | 4 | 0.80 | 0.01 | | | | | 19.04 | 7.95 | | | 0.52 | 0.18 | 1.01 |
| M70 | 3 | 0.82 | 0.01 | | | | | | | | | 1.31 | 0.25 | 9.40 |
| N71 | 3 | 0.79 | 0.01 | | | | | | | | | 1.27 | 0.24 | 11.00 |
| N72 | 2 | 0.83 | 0.01 | | | | | 36.37 | 10.33 | | | | | 5.80 |
| A73 | | | | | | | | | | | | | | |
| D74 | 4 | 0.73 | 0.01 | | | | | 34.38 | 3.51 | | | 0.50 | 0.11 | 66.15 |
| T75 | 2 | 0.79 | 0.02 | | | | | 32.32 | 10.29 | | | | | 2.31 |
| M77 | 5 | 0.79 | 0.02 | 0.83 | 0.01 | 0.96 | 0.02 | | | 1578.33 | 5165.22 | | | 8.44 |
| Q78 | 1 | 0.84 | 0.01 | | | | | | | | | | | 7.69 |
| F79 | 1 | 0.82 | 0.01 | | | | | | | | | | | 9.76 |
| A80 | 5 | 0.80 | 0.02 | 0.82 | 0.02 | 0.97 | 0.03 | | | 4488.27 | 7651.16 | | | 4.70 |
| T81 | 1 | 0.79 | 0.01 | | | | | | | | | | | 12.17 |
| E82 | 1 | 0.85 | 0.01 | | | | | | | | | | | 9.77 |
| K83 | 3 | 0.82 | 0.01 | | | | | | | | | 0.45 | 0.22 | 7.30 |
| V84 | 1 | 0.85 | 0.01 | | | | | | | | | | | 19.34 |
| T85 | | | | | | | | | | | | | | |
| A86 | 1 | 0.84 | 0.01 | | | | | | | | | | | 30.00 |
| K88 | 1 | 0.85 | 0.01 | | | | | | | | | | | 4.50 |
| M89 | 1 | 0.79 | 0.01 | | | | | | | | | | | 17.98 |
| G91 | 1 | 0.95 | 0.02 | | | | | | | | | | | 1.40 |
| Y92 | 3 | 0.86 | 0.01 | | | | | | | | | 1.02 | 0.24 | 3.29 |
| N93 | 3 | 0.78 | 0.02 | | | | | | | | | 0.75 | 0.35 | 5.18 |
| R94 | | | | | | | | | | | | | | |
| E95 | 4 | 0.77 | 0.01 | | | | | 14.87 | 5.69 | | | 0.85 | 0.15 | 23.13 |
| N96 | 3 | 0.83 | 0.02 | | | | | | | | | 0.56 | 0.33 | 8.06 |
| A97 | | | | | | | | | | | | | | |
| R99 | 3 | 0.81 | 0.01 | | | | | | | | | 0.69 | 0.13 | 17.94 |
| Y100 | 3 | 0.83 | 0.02 | | | | | | | | | 0.42 | 0.29 | 5.95 |
| E101 | 1 | 0.84 | 0.01 | | | | | | | | | | | 27.69 |
| T102 | 3 | 0.85 | 0.01 | | | | | | | | | 0.31 | 0.18 | 20.65 |
| E103 | 2 | 0.88 | 0.01 | | | | | 33.49 | 15.56 | | | | | 2.83 |
| D104 | 5 | 0.78 | 0.01 | 0.83 | 0.03 | 0.94 | 0.03 | | | 1004.56 | 1719.23 | | | 9.26 |
| G105 | 2 | 0.79 | 0.01 | | | | | 31.07 | 7.81 | | | | | 25.37 |
| Q106 | 4 | 0.80 | 0.01 | | | | | 24.58 | 8.39 | | | 0.98 | 0.18 | 21.26 |
| V107 | 2 | 0.78 | 0.01 | | | | | 14.00 | 8.24 | | | | | 5.97 |
| F108 | 3 | 0.83 | 0.01 | | | | | | | | | 0.44 | 0.21 | 11.91 |
| T109 | 3 | 0.81 | 0.02 | | | | | | | | | 0.42 | 0.27 | 6.53 |
| D110 | 1 | 0.84 | 0.01 | | | | | | | | | | | 14.12 |
| V111 | 3 | 0.82 | 0.01 | | | | | | | | | 1.26 | 0.27 | 14.45 |
| I112 | | | | | | | | | | | | | | |
| A113 | 3 | 0.83 | 0.02 | | | | | | | | | 1.66 | 0.35 | 13.00 |
| Y114 | 3 | 0.79 | 0.01 | | | | | | | | | 2.03 | 0.13 | 12.41 |
| S115 | 3 | 0.79 | 0.01 | | | | | | | | | 1.73 | 0.25 | 7.63 |
| D116 | 3 | 0.80 | 0.02 | | | | | | | | | 1.59 | 0.30 | 6.28 |
| D117 | 4 | 0.91 | 0.03 | | | | | 146.03 | 199.93 | | | 2.25 | 0.37 | 17.03 |
| N118 | 2 | 0.86 | 0.01 | | | | | 33.03 | 16.94 | | | | | 9.55 |
| C119 | 3 | 0.81 | 0.01 | | | | | | | | | 8.66 | 0.46 | 20.94 |
| D120 | 3 | 0.79 | 0.02 | | | | | | | | | 6.48 | 0.37 | 9.22 |
| V121 | 3 | 0.77 | 0.01 | | | | | | | | | 1.79 | 0.19 | 29.53 |
| I122 | 3 | 0.79 | 0.01 | | | | | | | | | 0.80 | 0.25 | 10.99 |
| Y123 | 3 | 0.82 | 0.02 | | | | | | | | | 0.74 | 0.34 | 1.75 |
| V124 | 3 | 0.83 | 0.02 | | | | | | | | | 0.84 | 0.31 | 2.09 |
| G126 | 4 | 0.80 | 0.01 | | | | | 24.60 | 9.97 | | | 0.66 | 0.21 | 7.56 |
| T127 | 5 | 0.79 | 0.01 | 0.85 | 0.05 | 0.94 | 0.05 | | | 672.87 | 1737.95 | | | 19.66 |
| D128 | 5 | 0.84 | 0.03 | 0.88 | 0.03 | 0.95 | 0.03 | | | 1187.31 | 4014.00 | | | 16.56 |

| | | | | | | | | | | | | | | |
|-------------|---|------|------|------|------|------|------|-------|-------|---------|--------|------|------|-------|
| G129 | 4 | 0.78 | 0.02 | | | | | 27.99 | 6.55 | | | 0.85 | 0.23 | 25.78 |
| N130 | 4 | 0.77 | 0.01 | | | | | 19.09 | 7.47 | | | 1.28 | 0.24 | 10.34 |
| E132 | 4 | 0.78 | 0.01 | | | | | 19.03 | 8.03 | | | 0.44 | 0.16 | 16.75 |
| G133 | 3 | 0.86 | 0.02 | | | | | | | | | 0.69 | 0.26 | 3.24 |
| Y134 | 3 | 0.84 | 0.01 | | | | | | | | | 0.54 | 0.26 | 19.94 |
| E135 | 3 | 0.75 | 0.01 | | | | | | | | | 1.53 | 0.21 | 10.50 |
| L136 | 3 | 0.81 | 0.01 | | | | | | | | | 1.55 | 0.26 | 6.81 |
| W137 | 3 | 0.79 | 0.01 | | | | | | | | | 1.91 | 0.20 | 13.31 |
| T138 | 3 | 0.78 | 0.01 | | | | | | | | | 1.16 | 0.22 | 4.12 |
| T139 | 3 | 0.81 | 0.01 | | | | | | | | | 2.74 | 0.24 | 12.04 |
| D140 | 4 | 0.80 | 0.01 | | | | | 38.65 | 7.80 | | | 0.96 | 0.19 | 7.45 |
| Y141 | 4 | 0.73 | 0.02 | | | | | 16.71 | 5.41 | | | 0.91 | 0.25 | 8.34 |
| D142 | 4 | 0.83 | 0.01 | | | | | 29.00 | 10.07 | | | 0.59 | 0.25 | 16.55 |
| N143 | 4 | 0.66 | 0.01 | | | | | 23.41 | 3.09 | | | 0.45 | 0.09 | 27.65 |
| I144 | 4 | 0.77 | 0.01 | | | | | 22.72 | 5.92 | | | 0.22 | 0.13 | 4.33 |
| A146 | 3 | 0.94 | 0.03 | | | | | | | | | 0.68 | 0.26 | 17.60 |
| C148 | 3 | 0.86 | 0.02 | | | | | | | | | 8.26 | 0.38 | 9.13 |
| L149 | 3 | 0.89 | 0.01 | | | | | | | | | 2.86 | 0.23 | 0.89 |
| N150 | 3 | 0.86 | 0.01 | | | | | | | | | 0.30 | 0.13 | 19.27 |
| K151 | 3 | 0.83 | 0.01 | | | | | | | | | 1.34 | 0.17 | 21.67 |
| F152 | 3 | 0.86 | 0.02 | | | | | | | | | 1.00 | 0.30 | 8.53 |
| N153 | 1 | 0.88 | 0.01 | | | | | | | | | | | 12.30 |
| E154 | 3 | 0.82 | 0.01 | | | | | | | | | 0.63 | 0.18 | 7.76 |
| Y155 | 3 | 0.84 | 0.01 | | | | | | | | | 0.59 | 0.17 | 7.82 |
| A156 | 3 | 0.85 | 0.01 | | | | | | | | | 0.32 | 0.11 | 14.82 |
| V157 | 3 | 0.74 | 0.01 | | | | | | | | | 1.35 | 0.16 | 12.27 |
| E160 | 2 | 0.77 | 0.02 | | | | | 25.81 | 12.10 | | | | | 6.44 |
| T161 | 5 | 0.63 | 0.01 | 0.72 | 0.01 | 0.87 | 0.01 | | | 923.73 | 120.83 | | | 21.71 |
| R162 | 3 | 0.85 | 0.02 | | | | | | | | | 0.99 | 0.29 | 12.08 |
| D163 | 3 | 0.80 | 0.02 | | | | | | | | | 1.07 | 0.25 | 4.35 |
| V164 | 3 | 0.80 | 0.01 | | | | | | | | | 0.60 | 0.29 | 0.76 |
| F165 | | | | | | | | | | | | | | |
| T166 | 3 | 0.79 | 0.01 | | | | | | | | | 0.60 | 0.28 | 5.09 |
| S167 | 4 | 0.80 | 0.05 | | | | | 37.77 | 26.47 | | | 1.72 | 0.77 | 0.81 |
| A168 | 3 | 0.92 | 0.03 | | | | | | | | | 0.62 | 0.39 | 16.22 |
| C169 | | | | | | | | | | | | | | |
| L170 | 2 | 0.77 | 0.01 | | | | | 31.71 | 5.81 | | | | | 6.04 |
| E171 | 5 | 0.32 | 0.00 | 0.72 | 0.01 | 0.44 | 0.01 | | | 1426.07 | 30.09 | | | 107.6 |

Table s8 $T\Delta S_{conf}$ values for backbone amide groups between *apo* rRaHBP-2(D24R) and the histamine bound complex. Residues with an absolute $T\Delta S_{conf}$ value greater than the error are shown in bold.

| <i>complex - apo</i> | | |
|----------------------|---|--------------|
| Residue | $T\Delta S_{conf}$ (kJ/mol) | error |
| Asp 4 | -0.55 | 1.48 |
| Trp 5 | 0.42 | 0.62 |
| Ala 6 | -0.30 | 0.44 |
| Asp 7 | -0.01 | 0.30 |
| Glu 8 | -0.91 | 0.39 |
| Ala 9 | -0.44 | 0.33 |
| Ala 10 | -0.07 | 0.34 |
| Asn 11 | -0.56 | 0.67 |
| Gly 12 | 0.52 | 0.78 |
| Ala 13 | -0.27 | 4.43 |
| Gln 15 | | |
| Asp 16 | 0.40 | 0.38 |
| Ala 17 | -0.68 | 0.41 |
| Trp 18 | | |
| Lys 19 | -0.02 | 0.41 |
| Ser 20 | 0.05 | 0.41 |
| Leu 21 | 1.00 | 0.71 |
| Lys 22 | 0.40 | 0.42 |
| Ala 23 | 0.92 | 0.47 |
| Arg 24 | | |
| Val 25 | | |
| Asn 27 | 0.19 | 0.30 |
| Tyr 29 | -0.34 | 0.46 |
| Tyr 30 | 1.03 | 0.87 |
| Val 32 | 0.28 | 0.82 |
| Lys 33 | -0.29 | 0.39 |
| Ala 34 | 0.73 | 0.49 |
| Thr 35 | 0.23 | 0.62 |
| Lys 37 | 0.85 | 1.17 |
| Asn 38 | -1.61 | 1.22 |
| Asn 44 | 0.76 | 1.05 |
| Asp 45 | 0.73 | 0.56 |
| Phe 46 | 0.08 | 0.42 |

| | | |
|---------------|--------------|-------------|
| Thr 47 | -0.09 | 0.68 |
| Val 49 | 0.41 | 0.50 |
| Val 51 | 0.84 | 0.94 |
| Met 52 | -0.21 | 0.62 |
| Ala 53 | 0.22 | 1.51 |
| Asn 54 | -0.02 | 0.42 |
| Val 56 | | |
| Asn 57 | 0.17 | 0.52 |
| Glu 58 | 1.21 | 0.90 |
| Asp 59 | 0.24 | 0.22 |
| Glu 60 | 0.28 | 0.27 |
| Lys 61 | 0.17 | 0.37 |
| Ser 62 | -0.46 | 0.54 |
| Ile 63 | -0.57 | 0.83 |
| Gln 64 | | |
| Ala 65 | -0.22 | 0.36 |
| Glu 66 | 0.63 | 0.91 |
| Phe 67 | 0.11 | 0.70 |
| Leu 69 | | |
| Met 70 | -0.03 | 0.66 |
| Asn 71 | | |
| Asn 72 | -0.07 | 0.64 |
| Asp 74 | 0.83 | 0.20 |
| Thr 75 | 0.81 | 0.75 |
| Met 77 | 0.30 | 0.45 |
| Gln 78 | 0.29 | 0.70 |
| Ala 80 | 0.48 | 0.57 |
| Thr 81 | 0.75 | 0.38 |
| Glu 82 | 0.28 | 0.73 |
| Lys 83 | -1.63 | 0.86 |
| Val 84 | 0.47 | 1.50 |
| Thr 85 | | |
| Ala 86 | 0.02 | 0.71 |
| Lys 88 | -0.75 | 0.78 |
| Met 89 | 0.41 | 0.29 |
| Gly 91 | -0.03 | 2.19 |
| Tyr 92 | -0.20 | 0.74 |
| Asn 93 | 0.00 | 0.62 |
| Arg 94 | | |
| Glu 95 | 0.85 | 0.39 |

| | | |
|---------|--------------|-------------|
| Asn 96 | 0.52 | 0.67 |
| Ala 99 | 1.07 | 0.40 |
| Glu 101 | 0.58 | 0.86 |
| Thr 102 | -0.22 | 0.67 |
| Glu 103 | -0.46 | 0.73 |
| Asp 104 | | |
| Gly 105 | -0.03 | 0.47 |
| Gln 106 | -0.46 | 0.56 |
| Val 107 | -0.30 | 0.34 |
| Val 111 | -0.04 | 0.58 |
| Ile 112 | | |
| Ala 113 | 0.01 | 0.61 |
| Ser 115 | 0.09 | 0.38 |
| Asp 116 | -0.10 | 0.48 |
| Asp 117 | -0.44 | 2.15 |
| Asn 118 | -0.80 | 0.68 |
| Cys 119 | 1.19 | 0.81 |
| Asp 120 | 0.43 | 2.79 |
| Val 121 | 0.55 | 0.43 |
| Ile 122 | 0.08 | 0.53 |
| Tyr 123 | 0.19 | 0.72 |
| Val 124 | 0.91 | 0.96 |
| Gly 126 | 0.96 | 1.48 |
| Thr 127 | 0.49 | 0.93 |
| Gly 129 | 0.14 | 0.54 |
| Gly 133 | -0.52 | 0.94 |
| Tyr 134 | -0.34 | 0.54 |
| Glu 135 | 0.33 | 0.46 |
| Leu 136 | -0.13 | 0.47 |
| Trp 137 | 0.59 | 0.61 |
| Thr 138 | 1.25 | 0.47 |
| Thr 139 | 0.02 | 0.60 |
| Asp 140 | 0.31 | 0.41 |
| Tyr 141 | 0.32 | 0.45 |
| Asp 142 | 0.16 | 0.48 |
| Asn 143 | 0.13 | 0.12 |
| Ile 144 | -0.38 | 0.32 |
| Ala 146 | -1.35 | 1.97 |
| Cys 148 | -0.38 | 0.82 |
| Leu 149 | -0.25 | 0.81 |

| | | |
|----------------------------------|--------------|-------------|
| Asn 150 | 0.19 | 0.40 |
| Lys 151 | 0.60 | 0.60 |
| Phe 152 | -0.28 | 0.71 |
| Asn 153 | 0.19 | 0.50 |
| Glu 154 | 0.44 | 0.43 |
| Ala 156 | | |
| Val 157 | 0.19 | 0.24 |
| Glu 160 | -0.20 | 0.45 |
| Arg 162 | 0.72 | 0.86 |
| Asp 163 | 0.14 | 0.60 |
| Val 164 | -0.59 | 0.44 |
| Phe 165 | | |
| Thr 166 | -0.49 | 0.47 |
| Ser 167 | 1.04 | 1.48 |
| Ala 168 | -1.61 | 2.15 |
| Leu 170 | 0.06 | 0.24 |
| Glu 171 | -0.15 | 0.05 |
| <hr/> <i>TΔS_{amide}</i> | 12.37 | 9.76 |