

Computational Analysis of SAM Analogs as Methyltransferase Inhibitors of nsp16/nsp10 complex from SARS-CoV-2

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Supplementary Materials

Figure S1. Conformations acquired by the nsp16 protein during 200 ns of MD simulations for 1a, 2b and 4c systems. PCA plots (left) from initial (blue) to 200 ns (red) structures. Initial, intermediate, and final 3D conformations are highlighted in orange, green and purple, respectively.

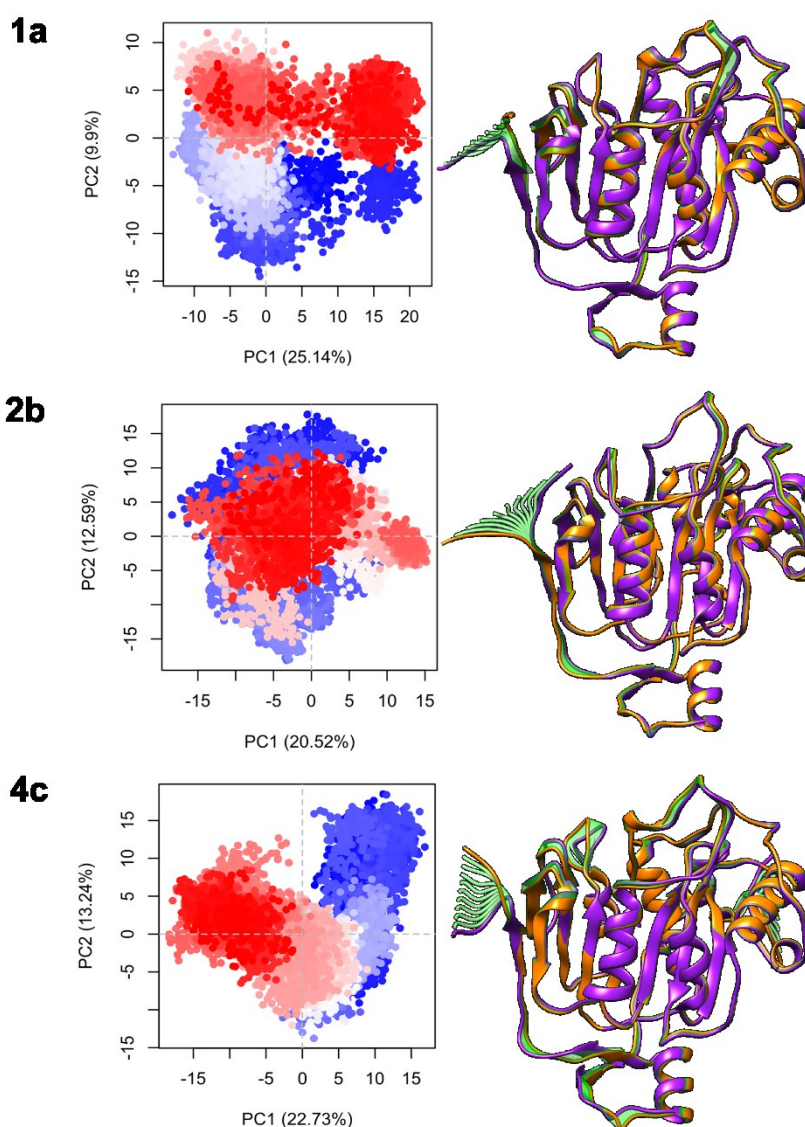


Figure S2. Labeled atoms of 2D structures of simulated compounds.

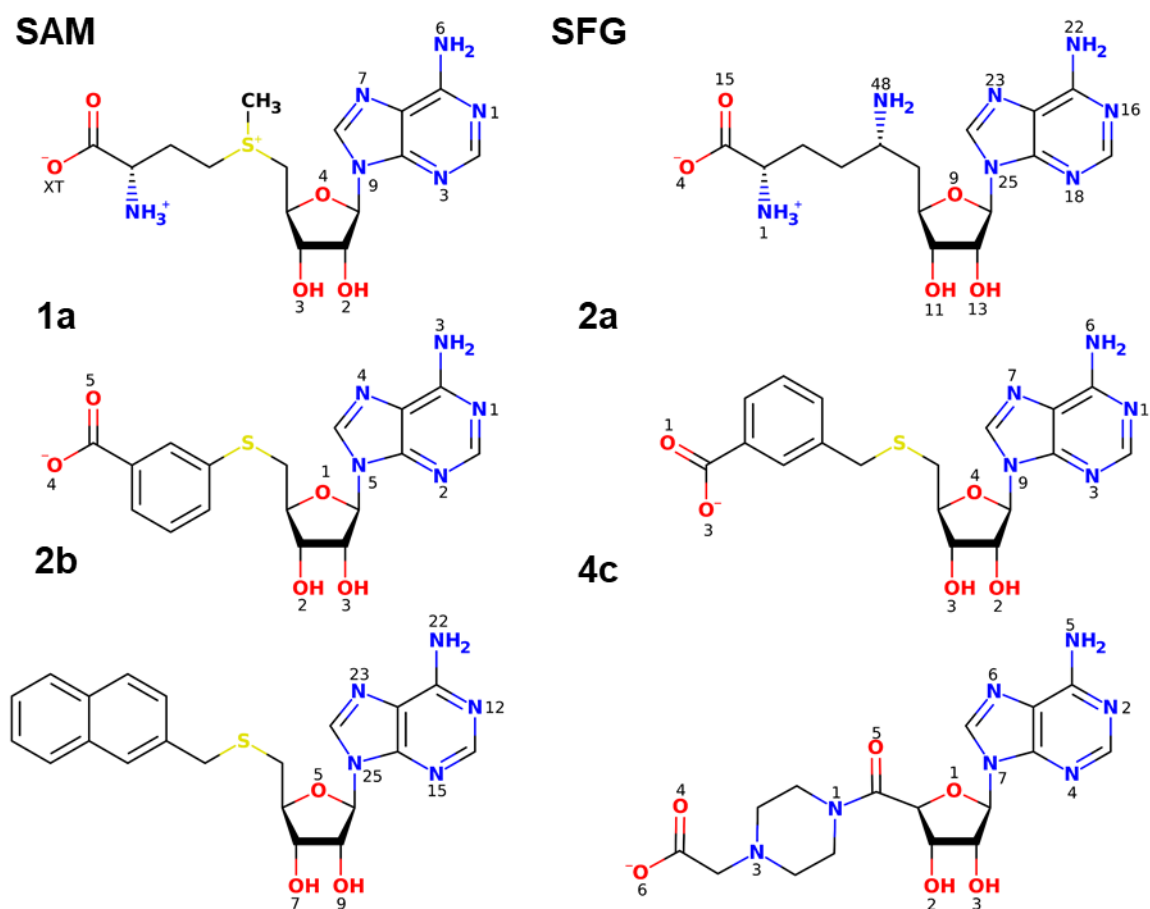


Table S1. RMSF values (in Å) for all nsp16 systems.

| Residue | Index | 1a | 2a | 2b | 4c | SAM | SFG |
|---------|-------|------|------|------|------|------|------|
| SER | 1 | 3.05 | 4.13 | 4.04 | 6.06 | 4.65 | 4.85 |
| SER | 2 | 2.03 | 2.19 | 2.08 | 3.97 | 2.46 | 2.17 |
| GLN | 3 | 1.53 | 1.22 | 1.31 | 3.49 | 1.56 | 1.33 |
| ALA | 4 | 1.24 | 1.03 | 1.09 | 1.22 | 1.13 | 1.05 |
| TRP | 5 | 0.94 | 0.89 | 0.83 | 0.98 | 0.89 | 0.86 |
| GLN | 6 | 0.54 | 0.55 | 0.57 | 0.56 | 0.54 | 0.51 |
| PRO | 7 | 0.42 | 0.44 | 0.45 | 0.42 | 0.41 | 0.41 |
| GLY | 8 | 0.41 | 0.44 | 0.45 | 0.42 | 0.41 | 0.40 |
| VAL | 9 | 0.42 | 0.42 | 0.45 | 0.46 | 0.40 | 0.41 |
| ALA | 10 | 0.47 | 0.48 | 0.47 | 0.50 | 0.45 | 0.45 |
| MET | 11 | 0.43 | 0.46 | 0.44 | 0.43 | 0.43 | 0.42 |
| PRO | 12 | 0.57 | 0.60 | 0.59 | 0.56 | 0.58 | 0.60 |
| ASN | 13 | 0.66 | 0.67 | 0.68 | 0.64 | 0.69 | 0.70 |
| LEU | 14 | 0.72 | 0.81 | 0.74 | 0.69 | 0.81 | 0.79 |
| TYR | 15 | 0.59 | 0.72 | 0.58 | 0.55 | 0.72 | 0.74 |
| LYS | 16 | 0.64 | 0.77 | 0.61 | 0.60 | 0.79 | 0.82 |

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|-----|----|------|------|------|------|------|------|
| MET | 17 | 0.73 | 0.87 | 0.70 | 0.69 | 0.84 | 0.93 |
| GLN | 18 | 0.65 | 0.81 | 0.63 | 0.60 | 0.71 | 0.73 |
| ARG | 19 | 0.65 | 0.69 | 0.65 | 0.62 | 0.69 | 0.71 |
| MET | 20 | 0.61 | 0.63 | 0.61 | 0.59 | 0.64 | 0.61 |
| LEU | 21 | 0.73 | 0.71 | 0.74 | 0.70 | 0.76 | 0.74 |
| LEU | 22 | 0.67 | 0.65 | 0.69 | 0.64 | 0.69 | 0.65 |
| GLU | 23 | 0.71 | 0.68 | 0.76 | 0.68 | 0.81 | 0.66 |
| LYS | 24 | 0.65 | 0.65 | 0.77 | 0.65 | 0.79 | 0.57 |
| CYS | 25 | 0.61 | 0.57 | 0.70 | 0.57 | 0.65 | 0.52 |
| ASP | 26 | 0.66 | 0.63 | 0.70 | 0.56 | 0.60 | 0.60 |
| LEU | 27 | 0.64 | 0.63 | 0.70 | 0.54 | 0.62 | 0.60 |
| GLN | 28 | 1.00 | 0.86 | 0.99 | 0.79 | 0.94 | 0.87 |
| ASN | 29 | 1.06 | 0.72 | 0.80 | 0.65 | 0.85 | 0.58 |
| TYR | 30 | 0.88 | 0.61 | 0.62 | 0.52 | 0.71 | 0.56 |
| GLY | 31 | 1.46 | 0.93 | 1.22 | 0.86 | 1.42 | 0.94 |
| ASP | 32 | 1.18 | 0.74 | 0.91 | 0.76 | 1.03 | 0.75 |
| SER | 33 | 1.19 | 0.86 | 0.93 | 0.81 | 1.02 | 0.87 |
| ALA | 34 | 0.96 | 0.80 | 0.86 | 0.81 | 0.88 | 0.82 |
| THR | 35 | 0.70 | 0.75 | 0.75 | 0.77 | 0.72 | 0.76 |
| LEU | 36 | 0.58 | 0.62 | 0.61 | 0.62 | 0.62 | 0.68 |
| PRO | 37 | 0.72 | 0.84 | 0.79 | 0.81 | 0.84 | 1.00 |
| LYS | 38 | 0.88 | 1.18 | 0.97 | 1.02 | 1.09 | 1.28 |
| GLY | 39 | 0.80 | 1.05 | 0.89 | 0.93 | 0.99 | 1.22 |
| ILE | 40 | 0.51 | 0.54 | 0.54 | 0.64 | 0.58 | 0.71 |
| MET | 41 | 0.51 | 0.51 | 0.55 | 0.67 | 0.59 | 0.68 |
| MET | 42 | 0.42 | 0.52 | 0.47 | 0.54 | 0.45 | 0.53 |
| ASN | 43 | 0.45 | 0.51 | 0.46 | 0.48 | 0.44 | 0.57 |
| VAL | 44 | 0.37 | 0.41 | 0.38 | 0.41 | 0.37 | 0.45 |
| ALA | 45 | 0.37 | 0.43 | 0.39 | 0.44 | 0.37 | 0.40 |
| LYS | 46 | 0.39 | 0.46 | 0.41 | 0.40 | 0.35 | 0.41 |
| TYR | 47 | 0.39 | 0.45 | 0.35 | 0.35 | 0.32 | 0.35 |
| THR | 48 | 0.34 | 0.37 | 0.34 | 0.33 | 0.33 | 0.33 |
| GLN | 49 | 0.34 | 0.37 | 0.35 | 0.32 | 0.33 | 0.32 |
| LEU | 50 | 0.37 | 0.41 | 0.38 | 0.35 | 0.35 | 0.35 |
| CYS | 51 | 0.38 | 0.43 | 0.38 | 0.36 | 0.35 | 0.37 |
| GLN | 52 | 0.39 | 0.42 | 0.40 | 0.37 | 0.36 | 0.38 |
| TYR | 53 | 0.41 | 0.45 | 0.42 | 0.41 | 0.40 | 0.40 |
| LEU | 54 | 0.42 | 0.47 | 0.42 | 0.41 | 0.39 | 0.41 |
| ASN | 55 | 0.45 | 0.54 | 0.47 | 0.45 | 0.42 | 0.47 |
| THR | 56 | 0.49 | 0.58 | 0.49 | 0.50 | 0.46 | 0.47 |
| LEU | 57 | 0.46 | 0.53 | 0.44 | 0.46 | 0.43 | 0.46 |
| THR | 58 | 0.48 | 0.54 | 0.48 | 0.51 | 0.46 | 0.49 |
| LEU | 59 | 0.55 | 0.64 | 0.60 | 0.66 | 0.48 | 0.54 |
| ALA | 60 | 0.52 | 0.60 | 0.49 | 0.52 | 0.44 | 0.54 |
| VAL | 61 | 0.45 | 0.51 | 0.45 | 0.47 | 0.42 | 0.47 |

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|-----|-----|------|------|------|------|------|------|
| PRO | 62 | 0.48 | 0.51 | 0.49 | 0.50 | 0.47 | 0.56 |
| TYR | 63 | 0.55 | 0.59 | 0.65 | 0.62 | 0.57 | 0.65 |
| ASN | 64 | 0.58 | 0.63 | 0.65 | 0.61 | 0.63 | 0.67 |
| MET | 65 | 0.45 | 0.45 | 0.44 | 0.42 | 0.47 | 0.48 |
| ARG | 66 | 0.41 | 0.42 | 0.48 | 0.38 | 0.46 | 0.45 |
| VAL | 67 | 0.36 | 0.37 | 0.34 | 0.34 | 0.36 | 0.37 |
| ILE | 68 | 0.39 | 0.38 | 0.36 | 0.37 | 0.36 | 0.39 |
| HID | 69 | 0.39 | 0.35 | 0.35 | 0.36 | 0.35 | 0.40 |
| PHE | 70 | 0.39 | 0.38 | 0.36 | 0.53 | 0.33 | 0.41 |
| GLY | 71 | 0.48 | 0.48 | 0.43 | 0.68 | 0.35 | 0.49 |
| ALA | 72 | 0.51 | 0.44 | 0.43 | 0.52 | 0.36 | 0.45 |
| GLY | 73 | 0.69 | 0.64 | 0.51 | 0.64 | 0.43 | 0.55 |
| SER | 74 | 0.62 | 0.61 | 0.78 | 0.89 | 0.70 | 0.82 |
| ASP | 75 | 0.66 | 0.79 | 0.97 | 1.12 | 0.82 | 1.11 |
| LYS | 76 | 0.56 | 0.73 | 0.94 | 0.97 | 0.72 | 0.97 |
| GLY | 77 | 0.56 | 0.66 | 0.77 | 1.10 | 0.61 | 0.77 |
| VAL | 78 | 0.46 | 0.55 | 0.55 | 0.63 | 0.52 | 0.55 |
| ALA | 79 | 0.45 | 0.45 | 0.47 | 0.46 | 0.46 | 0.52 |
| PRO | 80 | 0.44 | 0.46 | 0.45 | 0.46 | 0.46 | 0.49 |
| GLY | 81 | 0.45 | 0.45 | 0.43 | 0.42 | 0.40 | 0.45 |
| THR | 82 | 0.41 | 0.43 | 0.39 | 0.36 | 0.37 | 0.42 |
| ALA | 83 | 0.42 | 0.46 | 0.41 | 0.40 | 0.40 | 0.42 |
| VAL | 84 | 0.36 | 0.39 | 0.34 | 0.36 | 0.34 | 0.36 |
| LEU | 85 | 0.38 | 0.43 | 0.36 | 0.35 | 0.36 | 0.37 |
| ARG | 86 | 0.42 | 0.46 | 0.43 | 0.40 | 0.44 | 0.41 |
| GLN | 87 | 0.42 | 0.63 | 0.44 | 0.42 | 0.42 | 0.41 |
| TRP | 88 | 0.37 | 0.40 | 0.38 | 0.37 | 0.38 | 0.38 |
| LEU | 89 | 0.40 | 0.42 | 0.40 | 0.41 | 0.41 | 0.41 |
| PRO | 90 | 0.53 | 0.55 | 0.55 | 0.58 | 0.55 | 0.55 |
| THR | 91 | 0.75 | 0.89 | 0.83 | 0.84 | 0.81 | 0.90 |
| GLY | 92 | 0.70 | 0.97 | 0.85 | 0.89 | 0.81 | 0.82 |
| THR | 93 | 0.48 | 0.55 | 0.50 | 0.51 | 0.51 | 0.51 |
| LEU | 94 | 0.44 | 0.46 | 0.42 | 0.42 | 0.46 | 0.46 |
| LEU | 95 | 0.39 | 0.43 | 0.39 | 0.38 | 0.41 | 0.41 |
| VAL | 96 | 0.41 | 0.43 | 0.38 | 0.39 | 0.41 | 0.41 |
| ASP | 97 | 0.39 | 0.39 | 0.35 | 0.38 | 0.37 | 0.42 |
| SER | 98 | 0.42 | 0.46 | 0.39 | 0.44 | 0.41 | 0.47 |
| ASP | 99 | 0.54 | 0.50 | 0.43 | 0.50 | 0.37 | 0.49 |
| LEU | 100 | 0.73 | 0.61 | 0.60 | 0.66 | 0.49 | 0.62 |
| ASN | 101 | 0.95 | 1.14 | 0.73 | 0.98 | 0.69 | 0.82 |
| ASP | 102 | 0.89 | 1.03 | 0.79 | 0.94 | 0.74 | 0.74 |
| PHE | 103 | 0.53 | 0.67 | 0.60 | 0.59 | 0.51 | 0.58 |
| VAL | 104 | 0.59 | 0.59 | 0.63 | 0.69 | 0.58 | 0.63 |
| SER | 105 | 0.48 | 0.50 | 0.50 | 0.48 | 0.46 | 0.51 |
| ASP | 106 | 0.63 | 0.53 | 0.52 | 0.59 | 0.48 | 0.50 |

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|-----|-----|------|------|------|------|------|------|
| ALA | 107 | 0.46 | 0.48 | 0.45 | 0.46 | 0.45 | 0.47 |
| ASP | 108 | 0.50 | 0.52 | 0.50 | 0.51 | 0.52 | 0.53 |
| SER | 109 | 0.53 | 0.57 | 0.53 | 0.53 | 0.53 | 0.56 |
| THR | 110 | 0.46 | 0.54 | 0.48 | 0.47 | 0.49 | 0.52 |
| LEU | 111 | 0.68 | 0.59 | 0.57 | 0.61 | 0.57 | 0.63 |
| ILE | 112 | 0.78 | 0.89 | 0.59 | 0.70 | 0.54 | 0.66 |
| GLY | 113 | 0.88 | 0.74 | 0.65 | 0.77 | 0.59 | 0.75 |
| ASP | 114 | 0.66 | 0.56 | 0.55 | 0.69 | 0.47 | 0.58 |
| CYS | 115 | 0.64 | 0.65 | 0.58 | 0.73 | 0.50 | 0.61 |
| ALA | 116 | 0.68 | 0.64 | 0.67 | 0.83 | 0.58 | 0.67 |
| THR | 117 | 0.76 | 0.73 | 0.68 | 0.72 | 0.60 | 0.68 |
| VAL | 118 | 0.70 | 0.70 | 0.64 | 0.59 | 0.57 | 0.64 |
| HIP | 119 | 0.65 | 0.71 | 0.70 | 0.62 | 0.61 | 0.66 |
| THR | 120 | 0.58 | 0.57 | 0.54 | 0.52 | 0.53 | 0.57 |
| ALA | 121 | 0.79 | 0.68 | 0.69 | 0.75 | 0.77 | 0.70 |
| ASN | 122 | 0.59 | 0.56 | 0.51 | 0.51 | 0.60 | 0.53 |
| LYS | 123 | 0.56 | 0.49 | 0.45 | 0.45 | 0.55 | 0.47 |
| TRP | 124 | 0.40 | 0.41 | 0.39 | 0.37 | 0.39 | 0.43 |
| ASP | 125 | 0.36 | 0.36 | 0.36 | 0.34 | 0.37 | 0.39 |
| LEU | 126 | 0.36 | 0.36 | 0.35 | 0.33 | 0.35 | 0.36 |
| ILE | 127 | 0.38 | 0.40 | 0.39 | 0.33 | 0.37 | 0.42 |
| ILE | 128 | 0.44 | 0.43 | 0.40 | 0.35 | 0.36 | 0.43 |
| SER | 129 | 0.53 | 0.54 | 0.50 | 0.36 | 0.35 | 0.41 |
| ASP | 130 | 0.52 | 0.51 | 0.58 | 0.39 | 0.33 | 0.44 |
| MET | 131 | 0.63 | 0.48 | 0.57 | 0.44 | 0.36 | 0.40 |
| TYR | 132 | 0.54 | 0.45 | 0.55 | 0.43 | 0.42 | 0.41 |
| ASP | 133 | 0.68 | 0.58 | 0.92 | 0.65 | 0.79 | 0.60 |
| PRO | 134 | 0.75 | 0.77 | 1.45 | 0.79 | 1.26 | 1.06 |
| LYS | 135 | 0.79 | 0.91 | 1.17 | 0.99 | 1.32 | 1.48 |
| THR | 136 | 0.69 | 0.81 | 1.54 | 1.01 | 1.45 | 1.22 |
| LYS | 137 | 0.85 | 1.37 | 1.84 | 1.05 | 1.74 | 1.81 |
| ASN | 138 | 1.17 | 1.36 | 1.89 | 1.29 | 2.34 | 1.75 |
| VAL | 139 | 1.60 | 2.32 | 1.98 | 1.42 | 2.56 | 1.95 |
| THR | 140 | 1.73 | 2.50 | 1.97 | 1.52 | 2.43 | 2.07 |
| LYS | 141 | 1.56 | 1.55 | 1.56 | 1.16 | 1.46 | 1.57 |
| GLU | 142 | 1.19 | 1.02 | 1.05 | 0.93 | 0.99 | 1.07 |
| ASN | 143 | 0.69 | 0.67 | 0.65 | 0.62 | 0.62 | 0.64 |
| ASP | 144 | 0.60 | 0.63 | 0.58 | 0.59 | 0.59 | 0.59 |
| SER | 145 | 0.50 | 0.53 | 0.50 | 0.49 | 0.48 | 0.48 |
| LYS | 146 | 0.53 | 0.53 | 0.49 | 0.46 | 0.46 | 0.45 |
| GLU | 147 | 0.76 | 0.84 | 0.73 | 0.70 | 0.65 | 0.71 |
| GLY | 148 | 0.97 | 1.16 | 0.96 | 1.31 | 0.86 | 0.89 |
| PHE | 149 | 0.65 | 0.64 | 0.60 | 0.56 | 0.49 | 0.51 |
| PHE | 150 | 0.49 | 0.52 | 0.51 | 0.44 | 0.44 | 0.46 |
| THR | 151 | 0.53 | 0.69 | 0.63 | 0.52 | 0.54 | 0.56 |

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|-----|-----|------|------|------|------|------|------|
| TYR | 152 | 0.60 | 0.66 | 0.59 | 0.45 | 0.49 | 0.54 |
| ILE | 153 | 0.63 | 0.61 | 0.53 | 0.44 | 0.44 | 0.48 |
| CYS | 154 | 0.56 | 0.54 | 0.48 | 0.46 | 0.44 | 0.46 |
| GLY | 155 | 0.60 | 0.57 | 0.54 | 0.47 | 0.48 | 0.52 |
| PHE | 156 | 0.69 | 0.66 | 0.59 | 0.46 | 0.50 | 0.54 |
| ILE | 157 | 0.75 | 0.72 | 0.61 | 0.47 | 0.53 | 0.56 |
| GLN | 158 | 0.64 | 0.68 | 0.57 | 0.50 | 0.54 | 0.56 |
| GLN | 159 | 0.61 | 0.61 | 0.56 | 0.52 | 0.54 | 0.56 |
| LYS | 160 | 0.43 | 0.46 | 0.44 | 0.41 | 0.42 | 0.45 |
| LEU | 161 | 0.39 | 0.41 | 0.39 | 0.38 | 0.39 | 0.43 |
| ALA | 162 | 0.40 | 0.44 | 0.40 | 0.39 | 0.39 | 0.44 |
| LEU | 163 | 0.41 | 0.46 | 0.41 | 0.41 | 0.39 | 0.45 |
| GLY | 164 | 0.39 | 0.43 | 0.40 | 0.39 | 0.38 | 0.43 |
| GLY | 165 | 0.42 | 0.42 | 0.42 | 0.43 | 0.37 | 0.43 |
| SER | 166 | 0.34 | 0.35 | 0.34 | 0.34 | 0.33 | 0.35 |
| VAL | 167 | 0.34 | 0.37 | 0.34 | 0.34 | 0.33 | 0.34 |
| ALA | 168 | 0.36 | 0.39 | 0.33 | 0.32 | 0.32 | 0.33 |
| ILE | 169 | 0.35 | 0.38 | 0.35 | 0.32 | 0.33 | 0.33 |
| LYN | 170 | 0.35 | 0.39 | 0.37 | 0.32 | 0.32 | 0.35 |
| ILE | 171 | 0.36 | 0.35 | 0.35 | 0.32 | 0.31 | 0.32 |
| THR | 172 | 0.37 | 0.34 | 0.36 | 0.33 | 0.34 | 0.34 |
| GLU | 173 | 0.43 | 0.41 | 0.40 | 0.40 | 0.40 | 0.37 |
| HID | 174 | 0.44 | 0.47 | 0.42 | 0.42 | 0.42 | 0.38 |
| SER | 175 | 0.48 | 0.43 | 0.39 | 0.37 | 0.36 | 0.36 |
| TRP | 176 | 0.44 | 0.41 | 0.40 | 0.37 | 0.36 | 0.36 |
| ASN | 177 | 0.44 | 0.44 | 0.41 | 0.38 | 0.37 | 0.37 |
| ALA | 178 | 0.47 | 0.47 | 0.45 | 0.43 | 0.42 | 0.43 |
| ASP | 179 | 0.51 | 0.53 | 0.50 | 0.46 | 0.45 | 0.46 |
| LEU | 180 | 0.50 | 0.54 | 0.47 | 0.43 | 0.41 | 0.41 |
| TYR | 181 | 0.43 | 0.46 | 0.43 | 0.41 | 0.40 | 0.40 |
| LYS | 182 | 0.48 | 0.48 | 0.47 | 0.45 | 0.44 | 0.44 |
| LEU | 183 | 0.53 | 0.54 | 0.48 | 0.44 | 0.44 | 0.43 |
| MET | 184 | 0.47 | 0.49 | 0.47 | 0.46 | 0.47 | 0.45 |
| GLY | 185 | 0.55 | 0.60 | 0.55 | 0.53 | 0.55 | 0.52 |
| HID | 186 | 0.50 | 0.52 | 0.47 | 0.45 | 0.45 | 0.44 |
| PHE | 187 | 0.42 | 0.44 | 0.40 | 0.41 | 0.40 | 0.41 |
| ALA | 188 | 0.44 | 0.45 | 0.42 | 0.42 | 0.41 | 0.43 |
| TRP | 189 | 0.46 | 0.47 | 0.45 | 0.45 | 0.44 | 0.44 |
| TRP | 190 | 0.37 | 0.38 | 0.36 | 0.37 | 0.36 | 0.36 |
| THR | 191 | 0.35 | 0.36 | 0.36 | 0.36 | 0.35 | 0.35 |
| ALA | 192 | 0.35 | 0.37 | 0.36 | 0.34 | 0.35 | 0.35 |
| PHE | 193 | 0.35 | 0.37 | 0.38 | 0.35 | 0.37 | 0.35 |
| VAL | 194 | 0.37 | 0.39 | 0.40 | 0.38 | 0.38 | 0.32 |
| THR | 195 | 0.39 | 0.46 | 0.53 | 0.41 | 0.38 | 0.35 |
| ASN | 196 | 0.36 | 0.42 | 0.41 | 0.41 | 0.36 | 0.36 |

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|-----|-----|------|------|------|------|------|------|
| VAL | 197 | 0.42 | 0.44 | 0.40 | 0.41 | 0.38 | 0.41 |
| ASN | 198 | 0.48 | 0.52 | 0.57 | 0.45 | 0.42 | 0.45 |
| ALA | 199 | 0.46 | 0.51 | 0.47 | 0.47 | 0.48 | 0.46 |
| SER | 200 | 0.45 | 0.51 | 0.49 | 0.42 | 0.44 | 0.44 |
| SER | 201 | 0.42 | 0.40 | 0.53 | 0.51 | 0.40 | 0.43 |
| SER | 202 | 0.44 | 0.41 | 0.66 | 0.52 | 0.58 | 0.47 |
| GLU | 203 | 0.43 | 0.47 | 0.46 | 0.44 | 0.39 | 0.45 |
| ALA | 204 | 0.44 | 0.44 | 0.42 | 0.41 | 0.41 | 0.44 |
| PHE | 205 | 0.38 | 0.39 | 0.40 | 0.34 | 0.37 | 0.38 |
| LEU | 206 | 0.37 | 0.38 | 0.36 | 0.35 | 0.34 | 0.37 |
| ILE | 207 | 0.38 | 0.41 | 0.37 | 0.38 | 0.38 | 0.38 |
| GLY | 208 | 0.42 | 0.48 | 0.41 | 0.42 | 0.42 | 0.42 |
| CYS | 209 | 0.40 | 0.43 | 0.39 | 0.41 | 0.39 | 0.40 |
| ASN | 210 | 0.38 | 0.41 | 0.39 | 0.39 | 0.35 | 0.39 |
| TYR | 211 | 0.37 | 0.40 | 0.37 | 0.37 | 0.35 | 0.38 |
| LEU | 212 | 0.45 | 0.46 | 0.44 | 0.43 | 0.42 | 0.45 |
| GLY | 213 | 0.66 | 0.67 | 0.65 | 0.63 | 0.62 | 0.63 |
| LYS | 214 | 0.89 | 0.94 | 0.90 | 0.89 | 0.90 | 0.86 |
| PRO | 215 | 0.83 | 0.90 | 0.87 | 0.79 | 0.83 | 0.80 |
| ARG | 216 | 0.89 | 0.98 | 0.99 | 0.85 | 0.94 | 0.86 |
| GLU | 217 | 0.86 | 0.88 | 0.90 | 0.81 | 0.96 | 0.82 |
| GLN | 218 | 0.89 | 0.95 | 0.98 | 0.88 | 0.98 | 0.85 |
| ILE | 219 | 0.57 | 0.61 | 0.63 | 0.57 | 0.67 | 0.58 |
| ASP | 220 | 0.59 | 0.63 | 0.63 | 0.56 | 0.65 | 0.60 |
| GLY | 221 | 0.58 | 0.63 | 0.66 | 0.58 | 0.66 | 0.61 |
| TYR | 222 | 0.54 | 0.57 | 0.61 | 0.56 | 0.61 | 0.58 |
| VAL | 223 | 0.46 | 0.47 | 0.49 | 0.46 | 0.53 | 0.47 |
| MET | 224 | 0.39 | 0.39 | 0.41 | 0.39 | 0.43 | 0.39 |
| HIE | 225 | 0.38 | 0.38 | 0.40 | 0.38 | 0.39 | 0.38 |
| ALA | 226 | 0.42 | 0.41 | 0.44 | 0.40 | 0.42 | 0.41 |
| ASN | 227 | 0.40 | 0.40 | 0.42 | 0.39 | 0.42 | 0.40 |
| TYR | 228 | 0.37 | 0.38 | 0.41 | 0.36 | 0.39 | 0.38 |
| ILE | 229 | 0.42 | 0.41 | 0.43 | 0.39 | 0.41 | 0.39 |
| PHE | 230 | 0.47 | 0.46 | 0.48 | 0.45 | 0.45 | 0.44 |
| TRP | 231 | 0.45 | 0.44 | 0.48 | 0.42 | 0.45 | 0.42 |
| ARG | 232 | 0.45 | 0.42 | 0.46 | 0.40 | 0.43 | 0.41 |
| ASN | 233 | 0.55 | 0.52 | 0.56 | 0.50 | 0.52 | 0.50 |
| THR | 234 | 0.61 | 0.60 | 0.66 | 0.57 | 0.61 | 0.57 |
| ASN | 235 | 0.69 | 0.72 | 0.75 | 0.62 | 0.71 | 0.64 |
| PRO | 236 | 0.86 | 1.05 | 0.96 | 0.78 | 0.82 | 0.83 |
| ILE | 237 | 0.75 | 0.73 | 0.67 | 0.62 | 0.64 | 0.65 |
| GLN | 238 | 0.84 | 0.81 | 0.77 | 0.71 | 0.77 | 0.75 |
| LEU | 239 | 0.51 | 0.56 | 0.53 | 0.54 | 0.54 | 0.50 |
| SER | 240 | 0.51 | 0.52 | 0.54 | 0.56 | 0.52 | 0.48 |
| SER | 241 | 0.50 | 0.50 | 0.51 | 0.53 | 0.50 | 0.48 |

| | | | | | | | |
|-----|-----|------|------|------|------|------|------|
| TYR | 242 | 0.56 | 0.52 | 0.52 | 0.52 | 0.54 | 0.52 |
| SER | 243 | 0.48 | 0.47 | 0.48 | 0.47 | 0.47 | 0.47 |
| LEU | 244 | 0.47 | 0.49 | 0.51 | 0.52 | 0.51 | 0.52 |
| PHE | 245 | 0.85 | 0.85 | 0.88 | 0.89 | 0.87 | 0.87 |
| ASP | 246 | 1.17 | 1.22 | 1.29 | 1.20 | 1.20 | 1.18 |
| MET | 247 | 0.58 | 0.64 | 0.63 | 0.65 | 0.61 | 0.61 |
| SER | 248 | 0.72 | 0.88 | 0.77 | 0.81 | 0.74 | 0.78 |
| LYS | 249 | 0.77 | 1.00 | 0.82 | 0.87 | 0.81 | 0.82 |
| PHE | 250 | 0.49 | 0.61 | 0.51 | 0.54 | 0.50 | 0.50 |
| PRO | 251 | 0.52 | 0.56 | 0.52 | 0.54 | 0.51 | 0.55 |
| LEU | 252 | 0.51 | 0.52 | 0.50 | 0.50 | 0.50 | 0.53 |
| LYS | 253 | 0.83 | 0.91 | 0.88 | 0.94 | 0.80 | 0.91 |
| LEU | 254 | 1.14 | 1.23 | 1.00 | 1.07 | 1.16 | 1.19 |
| ARG | 255 | 1.21 | 1.36 | 1.18 | 1.24 | 1.23 | 1.32 |
| GLY | 256 | 1.74 | 1.93 | 1.55 | 1.26 | 1.75 | 1.89 |
| THR | 257 | 0.64 | 0.70 | 0.61 | 0.56 | 0.63 | 0.71 |
| ALA | 258 | 0.58 | 0.66 | 0.58 | 0.56 | 0.61 | 0.63 |
| VAL | 259 | 0.56 | 0.61 | 0.58 | 0.58 | 0.62 | 0.63 |
| MET | 260 | 0.68 | 0.77 | 0.77 | 0.73 | 0.75 | 0.77 |
| SER | 261 | 0.91 | 0.98 | 0.86 | 0.88 | 0.91 | 0.88 |
| LEU | 262 | 1.61 | 1.49 | 1.08 | 1.47 | 1.83 | 1.06 |
| LYS | 263 | 1.72 | 1.98 | 1.76 | 1.51 | 1.84 | 1.46 |
| GLU | 264 | 2.46 | 2.99 | 2.26 | 2.03 | 2.27 | 1.82 |
| GLY | 265 | 2.45 | 2.68 | 2.23 | 2.00 | 2.21 | 1.94 |
| GLN | 266 | 1.81 | 2.70 | 1.64 | 1.47 | 2.65 | 1.55 |
| ILE | 267 | 1.27 | 1.20 | 1.11 | 1.04 | 1.17 | 1.10 |
| ASN | 268 | 1.31 | 1.13 | 1.15 | 1.02 | 1.17 | 1.21 |
| ASP | 269 | 1.40 | 1.13 | 1.18 | 1.03 | 1.20 | 1.23 |
| MET | 270 | 1.25 | 1.06 | 1.06 | 0.94 | 1.09 | 1.14 |
| ILE | 271 | 0.79 | 0.79 | 0.76 | 0.69 | 0.76 | 0.86 |
| LEU | 272 | 0.76 | 0.74 | 0.76 | 0.67 | 0.73 | 0.82 |
| SER | 273 | 0.78 | 0.76 | 0.76 | 0.70 | 0.73 | 0.85 |
| LEU | 274 | 0.63 | 0.64 | 0.62 | 0.58 | 0.60 | 0.74 |
| LEU | 275 | 0.55 | 0.54 | 0.53 | 0.50 | 0.55 | 0.60 |
| SER | 276 | 0.68 | 0.65 | 0.64 | 0.60 | 0.66 | 0.68 |
| LYS | 277 | 0.82 | 0.79 | 0.72 | 0.68 | 0.87 | 0.83 |
| GLY | 278 | 0.72 | 0.70 | 0.62 | 0.61 | 0.83 | 0.75 |
| ARG | 279 | 0.61 | 0.65 | 0.56 | 0.55 | 0.60 | 0.66 |
| LEU | 280 | 0.48 | 0.54 | 0.47 | 0.46 | 0.49 | 0.55 |
| ILE | 281 | 0.41 | 0.48 | 0.42 | 0.41 | 0.42 | 0.53 |
| ILE | 282 | 0.45 | 0.54 | 0.52 | 0.48 | 0.54 | 0.60 |
| ARG | 283 | 0.55 | 0.63 | 0.64 | 0.61 | 0.83 | 0.65 |
| GLU | 284 | 0.69 | 0.92 | 0.92 | 0.95 | 1.17 | 0.71 |
| ASN | 285 | 0.88 | 1.29 | 1.56 | 1.51 | 1.84 | 1.06 |
| ASN | 286 | 0.89 | 1.21 | 1.51 | 1.20 | 1.49 | 0.97 |

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|-----|-----|------|------|------|------|------|------|
| ARG | 287 | 0.88 | 1.09 | 1.43 | 1.05 | 1.27 | 0.93 |
| VAL | 288 | 0.68 | 0.70 | 0.74 | 0.73 | 0.86 | 0.65 |
| VAL | 289 | 0.72 | 0.69 | 0.67 | 0.70 | 0.74 | 0.71 |
| ILE | 290 | 0.66 | 0.62 | 0.61 | 0.59 | 0.63 | 0.63 |
| SER | 291 | 0.90 | 0.77 | 0.78 | 0.64 | 0.72 | 0.87 |
| SER | 292 | 0.98 | 0.91 | 0.87 | 0.70 | 0.79 | 1.04 |
| ASP | 293 | 1.33 | 1.50 | 1.30 | 1.01 | 0.97 | 1.50 |
| VAL | 294 | 1.65 | 3.10 | 2.35 | 1.50 | 1.47 | 4.02 |
| LEU | 295 | 3.53 | 4.87 | 4.06 | 3.00 | 3.35 | 6.08 |
| VAL | 296 | 5.12 | 6.74 | 5.49 | 4.45 | 4.82 | 7.77 |
| ASN | 297 | 6.89 | 8.66 | 7.88 | 6.27 | 6.77 | 9.57 |

Table S2. Per-residue decomposition values (kcal/mol) for nsp16 systems.

| Residue | Index | 1a | 2a | 2b | 4c | SAM | SFG |
|---------|-------|-------|------|------|-------|-------|------|
| SER | 1 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| SER | 2 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLN | 3 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ALA | 4 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| TRP | 5 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLN | 6 | 0.00 | 0.00 | 0.01 | 0.01 | 0.01 | 0.00 |
| PRO | 7 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLY | 8 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| VAL | 9 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ALA | 10 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| MET | 11 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PRO | 12 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASN | 13 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 14 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| TYR | 15 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LYS | 16 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 |
| MET | 17 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLN | 18 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ARG | 19 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| MET | 20 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 21 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 22 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLU | 23 | 0.01 | 0.00 | 0.00 | 0.01 | -0.01 | 0.00 |
| LYS | 24 | -0.01 | 0.00 | 0.00 | -0.01 | 0.02 | 0.00 |
| CYS | 25 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASP | 26 | 0.01 | 0.01 | 0.00 | 0.01 | -0.01 | 0.00 |
| LEU | 27 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLN | 28 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASN | 29 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| TYR | 30 | 0.00 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |

| | | | | | | | |
|-----|----|-------|-------|-------|-------|-------|-------|
| GLY | 31 | 0.00 | 0.01 | 0.00 | 0.01 | 0.01 | 0.00 |
| ASP | 32 | 0.02 | 0.02 | 0.00 | 0.02 | -0.01 | 0.01 |
| SER | 33 | 0.00 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |
| ALA | 34 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| THR | 35 | 0.00 | 0.00 | 0.01 | 0.00 | 0.01 | 0.00 |
| LEU | 36 | 0.00 | 0.00 | 0.00 | -0.01 | 0.01 | 0.00 |
| PRO | 37 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LYS | 38 | -0.01 | -0.01 | 0.01 | -0.01 | 0.01 | 0.00 |
| GLY | 39 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |
| ILE | 40 | 0.02 | 0.03 | 0.02 | 0.01 | 0.03 | 0.02 |
| MET | 41 | -0.10 | -0.06 | -0.11 | -0.25 | -0.01 | -0.02 |
| MET | 42 | -0.21 | -0.18 | -0.22 | -0.74 | 0.01 | -0.03 |
| ASN | 43 | -3.42 | -3.49 | -0.88 | -1.06 | -0.73 | -0.32 |
| VAL | 44 | 0.05 | 0.05 | 0.00 | 0.05 | 0.04 | -0.01 |
| ALA | 45 | 0.00 | 0.01 | 0.01 | -0.04 | 0.06 | 0.01 |
| LYS | 46 | -0.49 | -0.40 | -0.65 | -0.57 | 1.12 | -0.14 |
| TYR | 47 | 0.01 | -0.01 | -0.16 | -0.06 | -2.23 | -0.05 |
| THR | 48 | 0.02 | 0.02 | 0.04 | 0.01 | 0.04 | 0.02 |
| GLN | 49 | 0.01 | 0.01 | 0.01 | 0.00 | 0.02 | 0.01 |
| LEU | 50 | 0.00 | 0.00 | 0.00 | -0.02 | 0.04 | 0.00 |
| CYS | 51 | 0.01 | 0.00 | 0.01 | 0.01 | -0.01 | 0.00 |
| GLN | 52 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 | 0.00 |
| TYR | 53 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 |
| LEU | 54 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 |
| ASN | 55 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| THR | 56 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 57 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| THR | 58 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 59 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ALA | 60 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| VAL | 61 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PRO | 62 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| TYR | 63 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASN | 64 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| MET | 65 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 |
| ARG | 66 | 0.00 | 0.00 | 0.01 | 0.00 | 0.02 | 0.01 |
| VAL | 67 | 0.01 | 0.01 | 0.01 | 0.00 | 0.05 | 0.01 |
| ILE | 68 | 0.00 | 0.01 | 0.01 | -0.02 | 0.07 | 0.01 |
| HID | 69 | 0.02 | -0.01 | -0.04 | 0.03 | -1.18 | -0.10 |
| PHE | 70 | -0.25 | -0.25 | -0.27 | -0.23 | -0.13 | -0.26 |
| GLY | 71 | -0.33 | -0.47 | -0.60 | -0.27 | -3.41 | -1.48 |
| ALA | 72 | -0.22 | -0.31 | -0.47 | -0.56 | -0.42 | -0.19 |
| GLY | 73 | 0.02 | 0.62 | 0.04 | -0.80 | -1.84 | -1.17 |
| SER | 74 | -6.23 | -4.84 | -1.04 | -5.13 | -1.03 | -2.05 |
| ASP | 75 | 0.61 | 0.68 | 0.48 | 2.88 | -0.13 | 1.03 |

| | | | | | | | |
|-----|-----|-------|--------|-------|-------|--------|-------|
| LYS | 76 | -4.26 | -10.43 | 0.06 | -6.25 | 0.09 | -0.85 |
| GLY | 77 | 0.00 | -0.01 | 0.02 | -0.04 | 0.08 | 0.06 |
| VAL | 78 | -0.02 | -0.02 | -0.07 | 0.00 | -0.09 | -0.13 |
| ALA | 79 | -0.06 | -0.03 | -0.05 | -0.14 | -0.68 | 0.08 |
| PRO | 80 | -0.02 | -0.01 | -0.30 | -0.18 | -1.21 | -0.07 |
| GLY | 81 | 0.01 | 0.01 | -0.01 | -0.07 | -0.81 | 0.04 |
| THR | 82 | 0.01 | 0.01 | 0.00 | 0.00 | -0.13 | -0.02 |
| ALA | 83 | 0.00 | 0.00 | 0.01 | 0.01 | 0.00 | 0.00 |
| VAL | 84 | 0.01 | 0.01 | 0.01 | -0.03 | 0.08 | 0.02 |
| LEU | 85 | 0.00 | 0.00 | 0.00 | -0.01 | 0.04 | 0.01 |
| ARG | 86 | -0.01 | -0.01 | 0.01 | 0.01 | 0.02 | 0.01 |
| GLN | 87 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |
| TRP | 88 | -0.01 | -0.01 | -0.01 | 0.00 | -0.01 | 0.00 |
| LEU | 89 | 0.00 | 0.00 | 0.01 | 0.00 | 0.01 | 0.00 |
| PRO | 90 | 0.00 | 0.00 | 0.00 | 0.00 | -0.01 | 0.00 |
| THR | 91 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLY | 92 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| THR | 93 | 0.00 | 0.00 | 0.01 | 0.01 | 0.01 | 0.01 |
| LEU | 94 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 |
| LEU | 95 | 0.00 | 0.01 | 0.01 | -0.01 | 0.04 | 0.01 |
| VAL | 96 | 0.00 | 0.01 | 0.01 | -0.01 | 0.05 | 0.01 |
| ASP | 97 | 0.00 | 0.01 | -0.05 | -0.03 | -0.21 | -0.09 |
| SER | 98 | -0.09 | -0.18 | -0.19 | -0.11 | -0.32 | -0.23 |
| ASP | 99 | -5.23 | -2.62 | -4.01 | -8.16 | -12.69 | -6.14 |
| LEU | 100 | -2.32 | -2.30 | -2.58 | -2.62 | -2.60 | -2.86 |
| ASN | 101 | -0.47 | -0.07 | -0.06 | -0.22 | -0.12 | -0.08 |
| ASP | 102 | 0.09 | 0.08 | 0.03 | 0.08 | -0.01 | 0.04 |
| PHE | 103 | -0.04 | -0.04 | -0.07 | -0.05 | -0.31 | -0.13 |
| VAL | 104 | 0.00 | 0.00 | -0.01 | 0.00 | -0.01 | -0.01 |
| SER | 105 | 0.00 | 0.00 | 0.00 | 0.01 | 0.03 | 0.01 |
| ASP | 106 | 0.04 | 0.04 | 0.01 | 0.04 | -0.01 | 0.01 |
| ALA | 107 | 0.00 | 0.00 | 0.00 | 0.01 | 0.02 | 0.01 |
| ASP | 108 | 0.01 | 0.01 | 0.00 | 0.01 | -0.02 | 0.00 |
| SER | 109 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |
| THR | 110 | 0.02 | 0.03 | 0.04 | 0.02 | 0.10 | 0.05 |
| LEU | 111 | 0.00 | -0.01 | -0.02 | -0.01 | -0.02 | -0.01 |
| ILE | 112 | -0.06 | -0.04 | -0.04 | -0.06 | -0.02 | -0.02 |
| GLY | 113 | -0.11 | -0.08 | -0.10 | -0.26 | -0.10 | -0.03 |
| ASP | 114 | -1.32 | -1.19 | -1.01 | -0.94 | -1.80 | -1.60 |
| CYS | 115 | -2.66 | -2.54 | -2.40 | -1.65 | -2.48 | -2.89 |
| ALA | 116 | -0.08 | -0.05 | -0.06 | -0.14 | -0.07 | -0.07 |
| THR | 117 | -0.03 | -0.01 | -0.03 | -0.05 | 0.01 | -0.01 |
| VAL | 118 | -0.01 | -0.01 | -0.02 | -0.03 | -0.01 | -0.02 |
| HIP | 119 | 0.01 | 0.01 | 0.02 | 0.01 | 0.03 | 0.02 |
| THR | 120 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |

| | | | | | | | |
|-----|-----|-------|-------|-------|-------|-------|-------|
| ALA | 121 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASN | 122 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LYS | 123 | 0.00 | 0.00 | 0.01 | 0.00 | 0.02 | 0.01 |
| TRP | 124 | 0.00 | -0.01 | -0.01 | 0.00 | -0.01 | -0.01 |
| ASP | 125 | 0.00 | 0.00 | 0.00 | 0.00 | -0.02 | -0.01 |
| LEU | 126 | 0.01 | 0.01 | 0.01 | 0.00 | 0.03 | 0.01 |
| ILE | 127 | 0.00 | 0.01 | 0.00 | -0.02 | 0.07 | 0.00 |
| ILE | 128 | -0.04 | -0.02 | -0.05 | -0.07 | 0.10 | -0.03 |
| SER | 129 | -0.17 | -0.07 | -0.15 | -0.26 | 0.50 | -0.06 |
| ASP | 130 | 2.69 | 0.74 | 1.21 | 2.09 | -4.42 | 0.33 |
| MET | 131 | -3.03 | -2.89 | -4.09 | -4.73 | -2.42 | -3.45 |
| TYR | 132 | -1.30 | -2.23 | -1.22 | -1.68 | -2.78 | -1.60 |
| ASP | 133 | -0.22 | -1.17 | -0.31 | -0.48 | -1.21 | -0.30 |
| PRO | 134 | -0.23 | -0.65 | -0.21 | -0.32 | -0.81 | -0.41 |
| LYS | 135 | 0.05 | 0.17 | 0.08 | 0.05 | 0.28 | 0.10 |
| THR | 136 | 0.00 | 0.07 | 0.02 | 0.03 | 0.11 | 0.01 |
| LYS | 137 | -0.10 | 0.03 | 0.03 | -0.02 | 0.19 | 0.07 |
| ASN | 138 | 0.02 | 0.02 | 0.01 | 0.00 | 0.01 | 0.01 |
| VAL | 139 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| THR | 140 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LYS | 141 | 0.00 | 0.01 | 0.01 | 0.00 | 0.02 | 0.02 |
| GLU | 142 | 0.01 | 0.01 | 0.00 | 0.01 | -0.01 | 0.00 |
| ASN | 143 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 |
| ASP | 144 | 0.02 | 0.01 | 0.01 | 0.02 | -0.01 | 0.00 |
| SER | 145 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |
| LYS | 146 | 0.01 | 0.02 | 0.03 | 0.01 | 0.06 | 0.04 |
| GLU | 147 | 0.04 | 0.04 | 0.03 | 0.02 | 0.01 | 0.04 |
| GLY | 148 | 0.00 | 0.02 | 0.02 | 0.06 | 0.06 | 0.03 |
| PHE | 149 | -1.51 | -1.54 | -0.94 | -0.41 | -1.28 | -1.33 |
| PHE | 150 | -0.05 | -0.09 | -0.06 | -0.04 | -0.13 | -0.06 |
| THR | 151 | 0.01 | 0.01 | 0.00 | -0.01 | 0.00 | 0.01 |
| TYR | 152 | -0.06 | -0.03 | -0.03 | 0.00 | -0.02 | -0.04 |
| ILE | 153 | -0.07 | -0.06 | -0.03 | -0.02 | -0.02 | -0.03 |
| CYS | 154 | 0.00 | -0.01 | 0.00 | 0.00 | -0.01 | 0.00 |
| GLY | 155 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PHE | 156 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ILE | 157 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLN | 158 | 0.01 | 0.01 | 0.01 | 0.00 | 0.01 | 0.01 |
| GLN | 159 | 0.01 | 0.01 | 0.01 | 0.00 | 0.01 | 0.01 |
| LYS | 160 | 0.00 | 0.00 | 0.01 | 0.00 | 0.02 | 0.01 |
| LEU | 161 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 |
| ALA | 162 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 163 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLY | 164 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLY | 165 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 |

| | | | | | | | |
|-----|-----|-------|-------|-------|-------|-------|-------|
| SER | 166 | 0.00 | 0.00 | 0.01 | 0.00 | 0.01 | 0.00 |
| VAL | 167 | 0.01 | 0.01 | 0.01 | 0.00 | 0.05 | 0.01 |
| ALA | 168 | -0.02 | 0.00 | -0.01 | -0.02 | 0.02 | -0.01 |
| ILE | 169 | -0.05 | -0.01 | -0.05 | -0.06 | 0.08 | -0.05 |
| LYN | 170 | -0.05 | 0.01 | -0.40 | -0.26 | -0.59 | -0.28 |
| ILE | 171 | -0.01 | -0.01 | -0.01 | -0.01 | -0.02 | -0.02 |
| THR | 172 | -0.02 | 0.00 | 0.00 | -0.01 | 0.02 | 0.00 |
| GLU | 173 | 0.02 | 0.03 | 0.02 | 0.03 | 0.00 | 0.01 |
| HID | 174 | -0.01 | 0.01 | 0.00 | 0.00 | 0.05 | 0.01 |
| SER | 175 | 0.00 | 0.02 | 0.02 | 0.01 | 0.06 | 0.01 |
| TRP | 176 | 0.00 | -0.01 | -0.01 | 0.00 | -0.03 | 0.00 |
| ASN | 177 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.01 |
| ALA | 178 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASP | 179 | 0.02 | 0.01 | 0.01 | 0.01 | 0.00 | 0.01 |
| LEU | 180 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 |
| TYR | 181 | 0.00 | 0.00 | 0.00 | 0.00 | -0.01 | 0.00 |
| LYS | 182 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 |
| LEU | 183 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 |
| MET | 184 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLY | 185 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| HID | 186 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PHE | 187 | -0.01 | -0.01 | -0.01 | -0.01 | -0.01 | -0.01 |
| ALA | 188 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| TRP | 189 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| TRP | 190 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| THR | 191 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ALA | 192 | 0.00 | 0.01 | 0.01 | 0.00 | 0.02 | 0.01 |
| PHE | 193 | -0.01 | -0.01 | -0.02 | -0.01 | -0.01 | -0.01 |
| VAL | 194 | 0.00 | 0.01 | 0.01 | -0.01 | 0.02 | 0.01 |
| THR | 195 | 0.00 | 0.01 | 0.00 | -0.03 | 0.02 | 0.00 |
| ASN | 196 | 0.01 | 0.01 | 0.01 | 0.00 | 0.02 | 0.01 |
| VAL | 197 | 0.01 | 0.01 | 0.02 | -0.01 | 0.03 | 0.01 |
| ASN | 198 | -0.05 | -0.02 | -0.02 | -0.07 | 0.02 | 0.01 |
| ALA | 199 | 0.00 | 0.00 | 0.01 | 0.01 | 0.00 | 0.01 |
| SER | 200 | 0.00 | 0.01 | 0.01 | 0.00 | 0.01 | 0.01 |
| SER | 201 | -0.01 | 0.01 | 0.00 | -0.01 | 0.02 | 0.00 |
| SER | 202 | -0.01 | 0.01 | 0.00 | -0.02 | 0.03 | -0.01 |
| GLU | 203 | 0.06 | 0.13 | -0.01 | 0.05 | 0.01 | 0.12 |
| ALA | 204 | 0.00 | 0.00 | -0.01 | -0.02 | 0.00 | -0.01 |
| PHE | 205 | 0.01 | -0.01 | 0.00 | 0.04 | -0.09 | 0.00 |
| LEU | 206 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ILE | 207 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLY | 208 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| CYS | 209 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASN | 210 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |

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|-----|-----|------|------|------|-------|-------|------|
| TYR | 211 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 212 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLY | 213 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LYS | 214 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PRO | 215 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ARG | 216 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLU | 217 | 0.00 | 0.00 | 0.00 | 0.00 | -0.01 | 0.00 |
| GLN | 218 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ILE | 219 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASP | 220 | 0.00 | 0.00 | 0.00 | 0.00 | -0.01 | 0.00 |
| GLY | 221 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| TYR | 222 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| VAL | 223 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| MET | 224 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| HIE | 225 | 0.00 | 0.00 | 0.00 | 0.00 | -0.01 | 0.00 |
| ALA | 226 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASN | 227 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| TYR | 228 | 0.00 | 0.00 | 0.00 | -0.01 | 0.00 | 0.00 |
| ILE | 229 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PHE | 230 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| TRP | 231 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ARG | 232 | 0.00 | 0.01 | 0.03 | 0.00 | 0.06 | 0.03 |
| ASN | 233 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| THR | 234 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASN | 235 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PRO | 236 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ILE | 237 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLN | 238 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 239 | 0.00 | 0.00 | 0.01 | 0.00 | 0.01 | 0.00 |
| SER | 240 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| SER | 241 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| TYR | 242 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| SER | 243 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 244 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PHE | 245 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASP | 246 | 0.01 | 0.01 | 0.00 | 0.01 | 0.00 | 0.00 |
| MET | 247 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| SER | 248 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LYS | 249 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 |
| PHE | 250 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| PRO | 251 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 252 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LYS | 253 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 254 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ARG | 255 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 |

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|-----|-----|------|------|------|------|-------|------|
| GLY | 256 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| THR | 257 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ALA | 258 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| VAL | 259 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| MET | 260 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| SER | 261 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 262 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LYS | 263 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLU | 264 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLY | 265 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLN | 266 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ILE | 267 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASN | 268 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASP | 269 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| MET | 270 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ILE | 271 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 272 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| SER | 273 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 274 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 275 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| SER | 276 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LYS | 277 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| GLY | 278 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ARG | 279 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| LEU | 280 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ILE | 281 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ILE | 282 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ARG | 283 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.01 |
| GLU | 284 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASN | 285 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASN | 286 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ARG | 287 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 |
| VAL | 288 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| VAL | 289 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ILE | 290 | 0.00 | 0.01 | 0.01 | 0.00 | 0.01 | 0.01 |
| SER | 291 | 0.00 | 0.00 | 0.01 | 0.00 | 0.00 | 0.00 |
| SER | 292 | 0.01 | 0.01 | 0.02 | 0.01 | 0.01 | 0.01 |
| ASP | 293 | 0.02 | 0.01 | 0.01 | 0.02 | -0.01 | 0.01 |
| VAL | 294 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.01 |
| LEU | 295 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| VAL | 296 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| ASN | 297 | 0.01 | 0.00 | 0.01 | 0.01 | 0.00 | 0.00 |