**Supporting Information**

**Table S1:** Equilibration points for simulations of Fe\_1, Fe\_2, Fe\_3, Cu and Zn

|  |  |  |  |
| --- | --- | --- | --- |
| **System** | **Equilibration point / ns** | | |
|  | **A** | **B** | **C** |
| Fe\_1 | 200 | 300 | 100 |
| Fe\_2 | 150 | 250 | 100 |
| Fe\_3 | 300 | 150 | 100 |
| Cu | 250 | 300 | 100 |
| Zn | 200 | 200 | 100 |

**Table S2**: Post-equilibration RMSD and Rg values (Å) for three different Fe coordination modes

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **System** | **RMSD** | | | | **Rg** | | | |
|  | **Ave** | **SD** | **Min** | **Max** | **Ave** | **SD** | **Min** | **Max** |
| Fe\_1 | 2.04 | 0.35 | 1.23 | 4.32 | 7.20 | 0.15 | 6.70 | 8.06 |
| Fe\_2 | 3.80 | 0.45 | 2.29 | 5.82 | 7.40 | 0.20 | 6.70 | 8.95 |
| Fe\_3 | 3.66 | 0.26 | 2.50 | 4.78 | 7.59 | 0.15 | 6.87 | 8.25 |

**Table S3**: RMSF values (Å) by residue

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **RMSF** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** |
| Fe\_1 | 3.725 | 4.520 | 7.107 | 8.047 | 8.178 | 4.821 | 6.509 | 8.015 | 6.043 | 8.312 | 7.381 | 8.464 | 6.263 | 3.387 | 7.256 | 7.726 |
| SD | 0.115 | 0.192 | 0.162 | 0.158 | 0.157 | 0.088 | 0.131 | 0.198 | 0.239 | 0.280 | 0.066 | 0.115 | 0.090 | 0.023 | 0.045 | 0.074 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fe\_2 | 5.043 | 4.824 | 7.966 | 9.397 | 7.133 | 4.352 | 7.875 | 8.581 | 7.014 | 7.807 | 5.198 | 5.949 | 4.339 | 7.195 | 9.183 | 9.054 |
| SD | 0.173 | 0.147 | 1.101 | 0.531 | 1.065 | 0.619 | 0.153 | 0.586 | 0.118 | 1.175 | 1.338 | 0.282 | 0.765 | 0.088 | 0.611 | 1.079 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fe\_3 | 3.185 | 5.647 | 5.774 | 9.808 | 9.157 | 5.269 | 6.089 | 6.741 | 6.083 | 8.663 | 5.313 | 6.818 | 7.848 | 5.056 | 7.063 | 10.520 |
| SD | 0.412 | 0.586 | 0.504 | 0.156 | 0.180 | 0.197 | 0.463 | 0.650 | 0.495 | 0.180 | 0.498 | 0.641 | 0.075 | 0.334 | 0.167 | 0.037 |

**Table S4**: Post-equilibration RMSD and Rg values (Å)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **System** | **RMSD** | | | | **Rg** | | | |
|  | **Ave** | **SD** | **Min** | **Max** | **Ave** | **SD** | **Min** | **Max** |
| Cu | 2.83 | 0.21 | 1.86 | 4.01 | 7.62 | 0.17 | 7.03 | 8.56 |
| Fe\_1 | 2.04 | 0.35 | 1.23 | 4.32 | 7.20 | 0.15 | 6.70 | 8.06 |
| Zn | 3.34 | 0.25 | 1.11 | 4.84 | 8.09 | 0.21 | 7.23 | 8.83 |

**Table S5a**: Bond length data averaged over equilibrated trajectories

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Fe\_1** | **Asp1\_O-Fe** | **Asp1\_N-Fe** | **His6\_O-Fe** | **His6\_N-Fe** | **His14\_N-Fe** |
| Ave | 1.977 | 2.049 | 1.991 | 1.980 | 2.014 |
| SD | 0.056 | 0.065 | 0.057 | 0.054 | 0.056 |
|  |  |  |  |  |  |
| **Cu** | **Asp1\_O-Cu** | **Asp1\_N-Cu** | **His6\_N-Cu** | **His14\_N-Cu** |  |
| Ave | 1.980 | 2.061 | 1.961 | 1.976 |  |
| SD | 0.058 | 0.068 | 0.055 | 0.058 |  |
|  |  |  |  |  |  |
| **Zn** | **Asp1\_O-Zn** | **His6\_N-Zn** | **Glu11\_O-Zn** | **His14\_N-Zn** |  |
| Ave | 2.095 | 2.079 | 2.261 | 2.047 |  |
| SD | 0.127 | 0.063 | 0.355 | 0.064 |  |

**Table S5b**: Bond Angle data averaged over equilibrated trajectories

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Fe\_1** | **Asp1\_O-Fe-Asp1\_N** | **Asp1\_O-Fe-His6\_N** | **Asp1\_O-Fe-His6\_O** | **Asp1\_O-Fe-His14\_N** |
| Ave | 80.8 | 91.9 | 161.9 | 106.2 |
| SD | 1.9 | 2.2 | 2.6 | 2.6 |
|  |  |  |  |  |
| **Cu** | **Asp1\_O-Cu-Asp1\_N** | **Asp1\_O-Cu-His6\_N** | **Asp1\_O-Cu-His14\_N** |  |
| Ave | 80.8 | 89.5 | 168.5 |  |
| SD | 2.2 | 3.0 | 3.1 |  |
|  |  |  |  |  |
| **Zn** | **Asp1\_O-Zn-His6\_N** | **Asp1\_O-Zn-Glu11\_O** | **Asp1\_O-Zn-His14\_N** |  |
| Ave | 98.3 | 98.7 | 103.5 |  |
| SD | 4.3 | 7.6 | 4.6 |  |

**Table S6**: RMSF values (Å) by residue

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **RMSF** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** |
| Cu | 5.512 | 7.017 | 9.480 | 7.367 | 9.149 | 4.164 | 7.756 | 6.796 | 6.287 | 8.836 | 7.976 | 8.350 | 6.167 | 3.813 | 7.407 | 7.402 |
| SD | 1.789 | 1.326 | 0.853 | 0.110 | 1.180 | 1.187 | 1.071 | 0.984 | 1.036 | 1.036 | 0.541 | 0.988 | 1.355 | 0.069 | 0.228 | 0.862 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fe\_1 | 3.725 | 4.520 | 7.107 | 8.047 | 8.178 | 4.821 | 6.509 | 8.015 | 6.043 | 8.312 | 7.381 | 8.464 | 6.263 | 3.387 | 7.256 | 7.726 |
| SD | 0.115 | 0.192 | 0.162 | 0.158 | 0.157 | 0.088 | 0.131 | 0.198 | 0.239 | 0.280 | 0.066 | 0.115 | 0.090 | 0.023 | 0.045 | 0.074 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Zn | 4.853 | 8.349 | 11.241 | 8.682 | 8.162 | 4.675 | 8.521 | 7.612 | 6.595 | 8.007 | 3.935 | 8.222 | 8.614 | 4.728 | 8.133 | 10.487 |
| SD | 0.212 | 0.084 | 0.101 | 0.162 | 0.189 | 0.371 | 0.367 | 0.333 | 0.743 | 0.103 | 0.069 | 0.253 | 0.105 | 0.182 | 0.655 | 0.850 |

**Table S7:** Salt bridge interaction matrix (%) for Cu simulation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cu** | **Asp1** | **Glu3** | **Asp7** | **Glu11** |
| **Arg5** | 0.00 | 37.78 | 76.96 | 0.00 |
| **Lys16** | 1.00 | 1.25 | 13.70 | 0.00 |

**Table S8:** Salt bridge interaction matrix (%) for Fe\_1 simulation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Fe\_1** | **Asp1** | **Glu3** | **Asp7** | **Glu11** |
| **Arg5** | 1.82 | 0.00 | 96.66 | 1.00 |
| **Lys16** | 1.00 | 91.09 | 1.00 | 1.00 |

**Table S9:** Salt bridge interaction matrix (%) for Zn simulation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Zn** | **Asp1** | **Glu3** | **Asp7** | **Glu11** |
| **Arg5** | 0.00 | 10.46 | 82.14 | 1.00 |
| **Lys16** | 2.57 | 1.00 | 2.29 | 1.00 |

**Table S10:** Breakdown of MM energy of minimised representative clusters

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **BOND** | **ANGLE** | **DIHED** | **VDW** | **EEL** | **EGB** | **1-4 VDW** | **1-4 EEL** | **Combined**  **EL/GB** | **Combined**  **VDW** |
| **Cu** | 11.71 | 86.28 | 153.25 | -95.75 | -1206.49 | -335.77 | 45.86 | 735.64 | -806.62 | -49.89 |
| **Fe** | 11.78 | 88.22 | 155.49 | -101.86 | -1165.03 | -258.88 | 47.59 | 676.09 | -747.81 | -54.27 |
| **Zn** | 10.34 | 87.11 | 170.08 | -95.96 | -962.35 | -396.22 | 45.56 | 554.88 | -803.69 | -50.4 |

**Figure S1:** Overlay of frames from 350 and 369.15 ns (tan and blue, respectively) from Fe\_1C.

