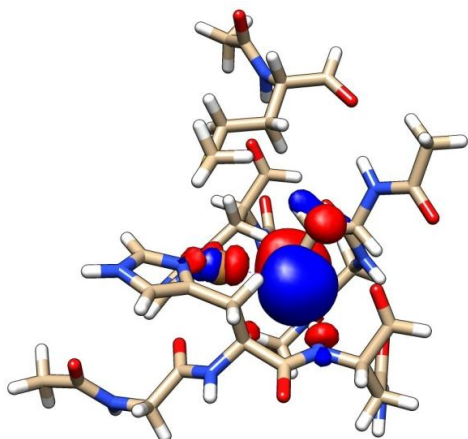
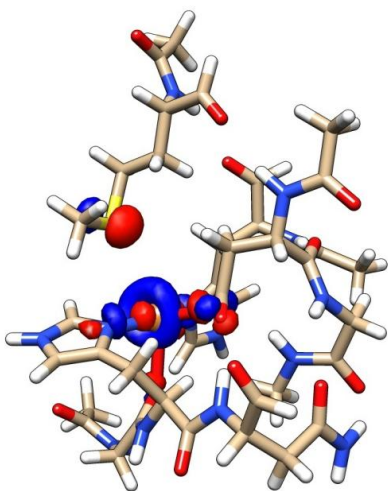


**SUPPORTING INFORMATION**

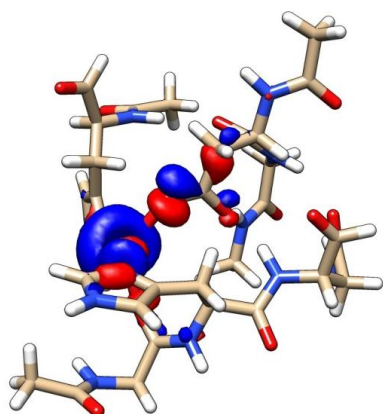
**Figure S1. Highest occupied molecular orbital (M06-2X functional) of reduced copper proteins.**



**(a) Native**



**(b) Cys112Asp**



**(c) Cys112Asp/Met121Leu**

Table S1. Computed Mülliken Spin populations (a.u) of synthetic models at the copper centre using different functionals

<b>Method</b>	$[\text{Cu}(\text{NCS})_2]^0$	$[\text{Cu}(\text{SCH}_3)_2]^0$
BP86/B2//BP86/B1	0.193	0.212
B3LYP/B2//B3LYP/B1	0.206	0.224
B3LYP-D3BJ/B2//B3LYP-D3BJ/B1	0.206	0.224
M06-L/B2//M06-L/B1	0.231	0.245
M06-2X/B2//M06-2X/B1	0.610	0.524

Table S2. Computed Mülliken Spin populations (a.u) of big models of copper proteins at the copper centre using M06-2X functional.

<b>Method</b>	M06-2X	QM/MM <sup>29</sup>
Native	0.728	0.508
Cys112Asp	0.805	0.670
Cys112Asp/Met121Leu	0.824	0.643