

Supporting Information

Table S1. Natural electron configuration of Zn and the ligating atoms for Cys₂His₂, Cys₃His and Cys₄ zinc finger models obtained through natural population analysis (NPA).

Atom	Natural electron configuration
[Zn(Cys) ₂ (His) ₂]	
Zn	[core] 4s(0.50) 3d(9.94) 4p(0.01)
S(1)	[core] 3s(1.78) 3p(4.79) 3d(0.05) 5s(0.01) 5p(0.01)
S(2)	[core] 3s(1.78) 3p(4.81) 3d(0.05) 5s(0.01) 5p(0.01)
N(1)	[core] 2s(1.39) 2p(4.25) 3p(0.03) 3d(0.02)
N(2)	[core] 2s(1.39) 2p(4.24) 3p(0.02) 3d(0.02)
[Zn(Cys) ₃ (His)] ⁻	
Zn	[core] 4s(0.54) 3d(9.95) 4p(0.01)
S(1)	[core] 3s(1.78) 3p(4.82) 3d(0.04) 4p(0.01) 5s(0.01) 5p(0.01)
S(2)	[core] 3s(1.78) 3p(4.80) 3d(0.04) 5s(0.01) 5p(0.01)
S(3)	[core] 3s(1.78) 3p(4.83) 3d(0.04) 4p(0.01) 5s(0.01) 5p(0.01)
N(1)	[core] 2s(1.39) 2p(4.20) 3p(0.02) 3d(0.02)
[Zn(Cys) ₄] ²⁻	
Zn	[core] 4s(0.56) 3d(9.95) 4p(0.01)
S(1)	[core] 3s(1.79) 3p(4.82) 3d(0.04) 4p(0.01) 5s(0.01) 5p(0.01)
S(2)	[core] 3s(1.79) 3p(4.81) 3d(0.04) 5s(0.01) 5p(0.01)
S(3)	[core] 3s(1.79) 3p(4.81) 3d(0.04) 4p(0.01) 5s(0.01) 5p(0.01)
S(4)	[core] 3s(1.79) 3p(4.81) 3d(0.04) 4p(0.01) 5s(0.01) 5p(0.02)

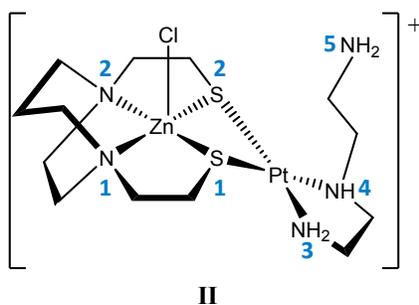


Fig. S1. Structures of [(Zn(bme-dach)Cl)(Pt(dien))]⁺, used as a standard in the benchmarking process discussed below.

Benchmarking of DFT methods. Based on recommendations from previous studies,^{1,2-4} two GGA functionals: G96LYP^{5,6} and PBE⁷ and five hybrid GGA functionals: B3LYP,^{8,6} MPWLYP1M,⁴ PBE0,⁹ B3PW91^{8,10} and MPW1PW91¹¹ were selected for benchmarking. Bonding parameters (Table S2) from the x-ray crystal structure of [(Zn(bme-dach)Cl)(Pt(dien))]⁺ (Fig. S1, **II**) was used as the standard in the process. The computations are performed using Gaussian03 suite of programs.¹² Geometry optimization was performed for the complexes using various functional and basis set combinations. Lan12DZ basis set was used for Pt with effective core potential in all calculations involving Pt. When using 6-311G basis set for the computations, Gaussian03 implements the Wachters-Hay all electron basis set^{13,14} for Zn.

Table S2. Bond parameters of II: Comparison of the performance of select density functionals

Method	Bond lengths (Å)								
	Zn-Cl	Zn-S(1)	Zn-S(2)	Zn-N(1)	Zn-N(2)	Pt-S(1)	Pt-S(2)	Pt-N(3)	Pt-N(4)
Experimental	2.258	2.457	2.421	2.148	2.167	2.308	2.311	2.069	2.103
B3LYP/6-311++G(d,p)	2.220	2.500	2.497	2.256	2.256	2.368	2.369	2.151	2.187
G96LYP/6-311++G(d,p)	2.236	2.503	2.508	2.274	2.267	2.379	2.380	2.169	2.208
MPWLYP1M/6-311++G(d,p)	2.231	2.519	2.514	2.278	2.277	2.383	2.383	2.172	2.211
B3PW91/6-311++G(d,p)	2.206	2.473	2.472	2.228	2.229	2.344	2.344	2.128	2.159
MPW1PW91/6-311++G(d,p)	2.202	2.469	2.467	2.220	2.222	2.339	2.339	2.120	2.150
PBE/6-311++G(d,p)	2.202	2.469	2.467	2.220	2.222	2.339	2.339	2.120	2.150
PBE0/6-311++G(d,p)	2.201	2.468	2.465	2.219	2.222	2.336	2.336	2.117	2.147

Method	Bond angles (deg)							
	N(1)-Zn-N(2)	S(1)-Zn-S(2)	N(1)-Zn-S(1)	N(2)-Zn-S(2)	Cl-Zn-N(1)	Cl-Zn-N(2)	Cl-Zn-S(1)	Cl-Zn-S(2)
Experimental	75.1	82.3	84.6	85.5	109.0	108.6	115.8	114.3
B3LYP/6-311++G(d,p)	72.5	81.9	84.5	84.6	109.9	109.8	116.8	116.5
G96LYP/6-311++G(d,p)	72.3	82.5	85.3	85.6	110.2	110.6	114.8	114.5
MPWLYP1M/6-311++G(d,p)	72.2	81.9	84.6	84.7	109.8	109.8	116.8	116.5
B3PW91/6-311++G(d,p)	73.0	81.8	84.7	84.8	109.7	109.5	116.6	116.3
MPW1PW91/6-311++G(d,p)	73.0	81.8	84.6	84.6	109.5	109.2	116.9	116.6
PBE/6-311++G(d,p)	72.8	81.8	85.0	85.0	109.2	109.0	116.8	116.4
PBE0/6-311++G(d,p)	73.0	81.7	84.5	84.5	109.3	109.0	117.3	116.9

Benchmarking the Performance of Select DFT functionals. The structure of **II** was optimized with each of the selected seven functionals using 6-311G++(d,p) basis set. The bond lengths and bond angles of the optimized structures are summarized in Table S2. The difference in bond angles is little and does not provide useful information. However, clear trends can be noticed by studying the variations in the bond lengths. Firstly, except in the case of the Zn-Cl bond distance, the functionals that use the LYP correlation functional produce bond lengths longer by an average 0.06 Å for Zn-S bonds and 0.10 Å for Zn-N bonds and similar trends are observed at the Pt centre. Given that an accuracy of 0.02 Å can be reached by DFT methods, there is certainly room for improvement. By comparing B3LYP, G96LYP and MPWLYP1M, it can be inferred that the inaccuracy is largely due to the correlation functional, as variation in the exchange functional seem to have little influence on the trends of bond lengths. On the other hand, the PW91 and PBE correlation functionals performed better overall. The average deviations from experimental values for bond distances are: 0.06 Å for Zn-Cl, 0.03 Å for Zn-S and 0.05 Å for Zn-N bonds. No big difference in the performance is observed between PBE and its hybrid version, PBE0. Further MPW1PW91 and PBE0, which share the basic functional form,⁹ perform a little better than B3PW91. Nevertheless, none of these functional/basis set combinations produced a satisfactory accuracy.

Table S3. Comparison of optimized bond lengths (Å) of II using B3LYP with double- ζ and triple- ζ basis functions with and without diffuse functions

Method	Zn-Cl	Zn-S(1)	Zn-S(2)	Zn-N(1)	Zn-N(2)	Pt-S(1)	Pt-S(2)	Pt-N(3)	Pt-N(4)
Experimental	2.258	2.457	2.421	2.148	2.167	2.308	2.311	2.069	2.103
B3LYP/6-31G(d,p)	2.222	2.529	2.522	2.176	2.178	2.364	2.364	2.149	2.187
B3LYP/6-31++G(d,p)	2.221	2.505	2.499	2.246	2.246	2.367	2.367	2.151	2.189
B3LYP/6-311G(d,p)	2.242	2.522	2.518	2.197	2.195	2.370	2.366	2.147	2.179
B3LYP/6-311++G(d,p)	2.220	2.500	2.497	2.256	2.256	2.368	2.369	2.151	2.187

Benchmarking Variations of Basis Functions. Other than the exchange-correlation functional, basis sets are the essential part that determines the outcomes of the computation. In fact, the above deviations could be due to inadequacy in the basis functions. Hence we decided to test variations of the Pople basis set, by changing number of basis, polarization and diffuse functions. In an effort to check whether the performance of the commonly used functional, B3LYP, can be improved just by tuning the basis functions, we opted to use it as the invariant in the benchmarking process. Additionally, since the deviation from experimental bond lengths is significant in the case of B3LYP, any change in performance could be tracked easily.

At first we tested the effect of varying the number of basis and diffuse functions. For this purpose, geometry optimization was carried out on **II** using B3LYP functional with 6-31G(d,p) and 6-311G(d,p) basis sets and the same with added diffuse functions on all atoms. The optimized bond lengths are listed in Table S3. Since comparison of bond angles is not very useful, from here on only bond lengths will be discussed. Here, an observable trend is that the addition of diffuse functions results in improvement of Zn-S bond lengths, while the same worsened Zn-N bond lengths. Further the triple-zeta basis function results only in a little improvement over the double-zeta basis function. Hence in the following benchmarks, in order to save computation time and resources, only Zn and the ligating atoms (N, S and Cl) will be treated at triple- ζ quality while double- ζ quality basis functions will be used for C and H.

Table S4. Comparison of optimized bond lengths (Å) for **II using B3LYP with mixed basis functions – using diffuse functions only on anionic ligands and variations in polarization functions.**

Method	Zn-Cl	Zn-S(1)	Zn-S(2)	Zn-N(1)	Zn-N(2)	Pt-S(1)	Pt-S(2)	Pt-N(3)	Pt-N(4)
Experimental	2.258	2.457	2.421	2.148	2.167	2.308	2.311	2.069	2.103
B3LYP/6-311++G(d,p)	2.220	2.500	2.497	2.256	2.256	2.368	2.369	2.151	2.187
B3LYP/mBS1 ^a	2.234	2.515	2.511	2.200	2.201	2.366	2.365	2.152	2.185
B3LYP/mBS2 ^b	2.230	2.516	2.511	2.197	2.198	2.365	2.365	2.152	2.185
B3LYP/mBS3 ^c	2.209	2.486	2.482	2.212	2.213	2.348	2.347	2.162	2.195
B3LYP/mBS4 ^d	2.244	2.464	2.457	2.199	2.200	2.339	2.339	2.144	2.177
B3LYP/mBS5 ^e	2.243	2.466	2.460	2.202	2.204	2.338	2.337	2.145	2.178

^a mBS1 = C, H: 6-31G(d,p); N, Zn: 6-311G(f); S, Cl: 6-311+G(d)

^b mBS2 = C, H: 6-31G(d,p); N: 6-311G(d); Zn: 6-311G(3fg); S, Cl: 6-311+G(d)

^c mBS3 = C, H: 6-31G(d,p); N: 6-311G(d); Zn: 6-311G(3fg); S, Cl: 6-311+G(2d)

^d mBS4 = C, H: 6-31G(d,p); N: 6-311G(3df); Zn: 6-311G(3fg); S: 6-311+G(3df); Cl: 6-311+G(d)

^e mBS5 = C, H: 6-311G(d,p); N: 6-311G(3df); Zn: 6-311G(3fg); S: 6-311+G(3df); Cl: 6-311+G(d)

Diffuse functions are essential to describe systems with loosely bound electrons such as anionic ligands. However it is not required on all atoms to properly describe a given molecule. Therefore in the next step, a mixed basis set (mBS1) with diffuse functions only on S and Cl atoms was used. A comparison of the results with the experimental values and the values from 6-311++G(d,p) on all atoms is presented in Table S4. Avoiding the use of diffuse functions on N and Zn led to a dramatic improvement in Zn-N bond distance. Since Pt-N bond distances are not affected by this change, it can be deduced that the improvement is mostly from better definition of Zn orbitals. However, diffuse functions on N in this case may just be redundant hence may be omitted. As a consequence of the tighter binding of N to Zn, the Zn-S and Zn-Cl bonds are affected, which is seen as elongation of the respective bond lengths.

Given the complex nature of compound **II**, we considered that increasing the polarization functions may lead to further improvement. Therefore the effect of including higher order polarization functions on various atoms was attempted in the next step. Representative examples from several computations that were performed for this purpose are summarized in Table S4. Higher order polarization functions on Zn alone produces little improvement as seen from the results of mBS2 basis set. But this, in combination with higher order polarization functions on the ligand atoms proved to be beneficial, which can be observed in the results from mBS3 and mBS4. However, using higher order polarization functions on Cl led to shortening of Zn-Cl bond distance which is not desirable. Hence just the basic polarization was used on Cl. The result from using mBS4 for the basis set shows great improvements in Zn-Cl and Zn-S bond distances; their deviations from experimental values is well within the DFT accuracy range. The Pt-S bond lengths improved too. Although there is considerable improvement in Zn-N and Pt-N bond lengths, they still deviate from the experimental values by average 0.05 Å and 0.08 Å respectively. From the benchmarking process, it can be seen that the performance of B3LYP functional can be significantly improved by complimenting with proper basis functions. However at this stage it seems that no further improvement is possible for this level of theory. In order to maintain consistency in the

quality of basis sets on all atoms, in mBS5, the basis functions on C and H were improved to triple- ζ quality. This resulted in minor changes in bond lengths. We chose to use this mixed basis set for our calculations.

Table S5. Comparison of optimized bond lengths (Å) for II using B3LYP and MPW1PW91 functionals with 6-311++G(d,p) and mBS5 basis sets.

Method	Zn-Cl	Zn-S(1)	Zn-S(2)	Zn-N(1)	Zn-N(2)	Pt-S(1)	Pt-S(2)	Pt-N(3)	Pt-N(4)
Experimental	2.258	2.457	2.421	2.148	2.167	2.308	2.311	2.069	2.103
B3LYP/6-311++G(d,p)	2.220	2.500	2.497	2.256	2.256	2.368	2.369	2.151	2.187
B3LYP/mBS5	2.243	2.466	2.460	2.202	2.204	2.338	2.337	2.145	2.178
MPW1PW91/6-311++G(d,p)	2.202	2.469	2.467	2.220	2.222	2.339	2.339	2.120	2.150
MPW1PW91/mBS5	2.224	2.437	2.434	2.172	2.174	2.310	2.309	2.115	2.143

The Chosen DFT Method. Further, we tested combination of the optimal basis set, mBS5, with the better performing hybrid DFT functionals, MPW1PW91 and PBE0. The geometry optimization of II at these levels led to desirable results. The optimized M-L bond lengths of II at MPW1PW91/mBS5 level are listed in Table S5. At this level, the deviation of Zn-Cl bond from the experimental data was 0.03 Å. The average Zn-S bond distance measured 2.436 Å which is almost identical with the corresponding experimental average. The average Zn-N bond distance was 2.173 Å, which deviates from the experimental average by 0.02 Å. The Pt-S distances were again very close to experimental values and Pt-N bond distance was longer by an average 0.04 Å, which is the largest deviation. We chose to use MPW1PW91/mBS5 level to investigate coordination sphere expansion in structural zinc sites. However, similar results were obtained for the PBE0 functional.

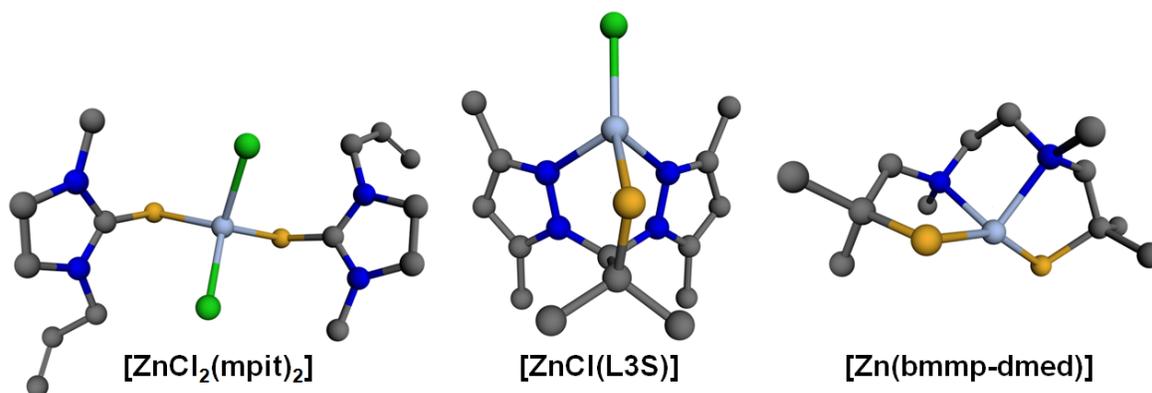


Fig. S2. Optimized structures of the complexes used for validation of MPW1PW91/mBS5 level of theory. The M-L bond lengths are listed in Table S5. Here, mpit = 1-methyl-3-(prop-2-enyl)-imidazole-2(3H)-thione-S;¹⁵ L3SH = bis(3,5-dimethylpyrazolyl)(1-methyl-1-sulfanylethyl)-methane¹⁶ and bmmp-dmed = N,N'-bis-2-methyl-mercaptopropyl-N,N'-dimethylethylene-diamine.¹⁷

Table S6. Comparison of optimized bond lengths (Å) of zinc complexes for validation of MPW1PW91/mBS5 level of theory.

[ZnCl ₂ (mpit) ₂]				
Method	Zn-Cl(1)	Zn-Cl(2)	Zn-S(1)	Zn-S(2)
Experimental	2.264	2.254	2.374	2.370
B3LYP/6-311++G(d,p)	2.289	2.289	2.461	2.458
B3LYP/mBS5 ^a	2.315	2.313	2.389	2.389
MPW1PW91/6-311++G(d,p)	2.269	2.269	2.422	2.420
MPW1PW91/mBS5	2.290	2.292	2.360	2.359

[ZnCl(L3S)]				
Method	Zn-Cl	Zn-N(1)	Zn-N(2)	Zn-S
Experimental	2.191	2.079	2.079	2.248
B3LYP/6-311++G(d,p)	2.213	2.147	2.155	2.282
B3LYP/mBS5	2.220	2.091	2.097	2.248
MPW1PW91/6-311++G(d,p)	2.194	2.120	2.125	2.264
MPW1PW91/mBS5	2.200	2.070	2.074	2.232

[Zn(bmmp-dmed)]				
Method	Zn-N(1)	Zn-N(2)	Zn-S(1)	Zn-S(2)
Experimental	2.130	2.130	2.237	2.237
B3LYP/6-311++G(d,p)	2.250	2.250	2.271	2.271
B3LYP/mBS5	2.205	2.205	2.244	2.244
MPW1PW91/6-311++G(d,p)	2.207	2.207	2.255	2.255
MPW1PW91/mBS5	2.169	2.169	2.231	2.231

Validation of Choice. The outcome of the benchmarking process indicates that the chosen DFT method is sufficient to describe the system of interest. However, in order to test the general applicability of the method to zinc model complexes, we assessed its performance on three other zinc complexes for which crystal structure data was available. The chosen complexes were all tetra-coordinate representing various coordination sphere with combinations of N, S, and Cl ligands (Fig. S2). The complexes are [ZnCl₂(mpit)₂], consisting of only Cl and neutral S ligands¹⁵; [ZnCl(L3S)], where L3S is a tridentate ligand with two nitrogen and one sulphur donor atom¹⁶ and [Zn(bmmp-dmed)], a Cys₂His₂ type zinc finger model compound¹⁷ (See Fig. S2).

These complexes were geometry optimized at B3LYP/6-311++G(d,p), B3LYP/mBS5, MPW1PW91/6-311++G(d,p) and MPW1PW91/mBS5 levels to compare the performances of the methods. The optimized structures of these complexes at MPW1PW91/mBS5 level are shown in Fig. S2. The experimental and computed bond lengths of the complexes are given in Table S6. From these values it is obvious that MPW1PW91/mBS5 strikes a balance between the types of Zn-L bonds and easily outperforms other methods. Thus we conclude that MPW1PW91/mBS5 is a suitable method in general for DFT modelling of structural zinc sites that are made of histidine and cysteine ligands. With further benchmarking, which takes into account the oxygen ligands, the method can be extended to all biological zinc sites.

References

- 1 C. J. Cramer and D. G. Truhlar, *Phys. Chem. Chem. Phys.*, 2009, **11**, 10757.
- 2 G. Frison and G. Ohanessian, *J. Comput. Chem.*, 2008, **29**, 416-433.
- 3 V. M. Rayón, H. Valdés, N. Díaz and D. Suárez, *J. Chem. Theory Comput.*, 2008, **4**, 243-256.
- 4 N. E. Schultz, Y. Zhao and D. G. Truhlar, *J. Phys. Chem. A*, 2005, **109**, 11127-11143.
- 5 P. M. W. Gill, *Mol. Phys.*, 1996, **89**, 433-445.
- 6 C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B*, 1988, **37**, 785-789.
- 7 J. P. Perdew, K. Burke and M. Ernzerhof, *Phys. Rev. Lett.*, 1996, **77**, 3865-3868.
- 8 A. D. Becke, *J. Chem. Phys.*, 1993, **98**, 5648.
- 9 C. Adamo and V. Barone, *J. Chem. Phys.*, 1999, **110**, 6158.
- 10 J. P. Perdew, K. A. Jackson, M. R. Pederson, D. J. Singh and C. Fiolhais, *Phys. Rev. B*, 1992, **46**, 6671-6687.

- 11 C. Adamo and V. Barone, *J. Chem. Phys.*, 1998, **108**, 664.
- 12 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. Montgomery J. A., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez and J. A. and Pople, *Gaussian 03, Revision D.02*, Gaussian, Inc., Wallingford CT, 2004.
- 13 A. J. H. Wachters, *J. Chem. Phys.*, 2003, **52**, 1033-1036.
- 14 P. J. Hay, *J. Chem. Phys.*, 2008, **66**, 4377-4384.
- 15 D. J. Williams, T. A. Ly, J. W. Mudge, W. T. Pennington and G. L. Schimek, *Acta Crystallogr.*, 1997, **53**, 415-416.
- 16 B. S. Hammes and C. J. Carrano, *J. Chem. Soc. Dalton Trans.*, 2000, 3304-3309.
- 17 C. A. Grapperhaus, C. S. Mullins, P. M. Kozlowski and M. S. Mashuta, *Inorg. Chem.*, 2004, **43**, 2859-2866.