ELECTRONIC SUPPLEMENTARY INFORMATION

TITLE: Solvent Water Interactions Within The Active Site of the Membrane Type I Matrix Metalloproteinase

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S1) Expression and purification of the active catalytic domain of MT1-MMP. For the crystallization of the non-inhibited Zn^{2+}-MT1-MMP, the plasmid containing the catalytic domain of human MT1-MMP together with the hinge linker to the hemopexin-like domain (residues 112–292) as described in Grossman et al.[1] was transformed into Escherichia coli BL21 (DE3) (Novagen). The expression was carried out as previously described in Ogata et al.[1]

For the preparation of Co^{2+}-MT1-MMP, the expression plasmid for the catalytic domain of human MT1-MMP together with the hinge region (residues 112-319) was mutated in (C127S) MT1-MMP (Genscript, USA) to avoid oxidation sensitivity of the Co^{2+} and cloned into the pET3a expression vector with a His-tag at the C-terminus. The plasmid was then expressed into *Escherichia coli* BL21(DE3) (Novagen). Expression of the apo-enzyme and washing of inclusion bodies were carried out as described previously for the wild-type MT1-MMP.[1] No significant difference in activity was observed for the mutant (C127S)-MT1-MMP and the wild type MT1-MMP, and as such only the MT1-MMP label will be hereafter used for simplicity.

S2) Molar extinction coefficient determination for wild type MT1-MMP. An accurate estimation of the molar extinction coefficient of MT1-MMP was required to determine the correct stoichiometry, i.e. the metal/protein ratio. This value was accurately determined by means of MCD spectroscopy at room temperature, which allows the concentration of tryptophan in a protein sample to be obtained.

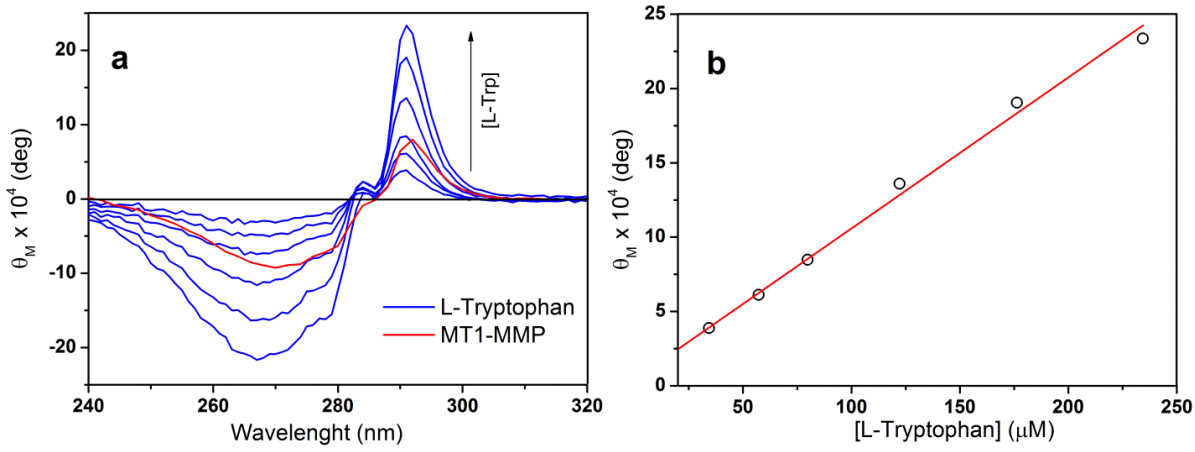

Figure 1 (a): MCD spectra of L-tryptophan at 25, 50, 75, 100, 150, 200 μM (blue lines) and a solution of MT1-MMP with absorbance of 0.635 at 274 nm (red line). **(b)** θ_M at 291 nm versus L-tryptophan concentration were linearly fitted with $R^2 = 0.997$.

In Figure 1-a, the blue curves represent the MCD spectra of different concentration of L-tryptophan. The MCD signal peaks at 291 nm, and it was this data points that was used for the calibration curve shown in Figure 1-b. The spectrum of the wild type MT1-MMP was acquired and the MCD absorption at 295 was $8 \cdot 10^4$ deg. This value corresponded to a concentration of L-tryptophan of 73 μM, determined by means of the calibration curve. Since only four tryptophan are present in the sequence of wild type MT1-MMP, the concentration of the enzyme that generated the red spectrum in Figure 1-a was readily calculated from [MT1-MMP] = [Trp] / 4 = 18 μM.

The corresponding UV absorption of the protein solution at this concentration was measured by means of a UV-VIS spectrometer and corresponded to 0.64 at 274 nm in a quartz cell of 1 cm pathlength. This yieled a molar extinction coefficient of $\varepsilon_{274}=A_{247}/cl = 35280\ M^{-1}cm^{-1}$. This value is similar to the molar extinction coefficient $\varepsilon_{calc} = 35410\ M^{-1}\ cm^{-1}$, calculated using the protein analysis software ProtParam[2] available through the ExPASy server.[3]

S3) Preparation of apo-MT1-MMP (metal-free material) / Preparation of Co^{2+}-MT1-MMP.

Since the presence of extraneous metal can arise from many sources (e.g. reagents, wares, bottles) all materials and buffers were treated to avoid metal contamination. Plastic wares were cleaned with 20% HNO_3 in triple distilled water and extensively rinsed with triple distilled water. All buffers used in experiments were prepared using chemicals of the highest purity available and made metal-free either by extraction with dithizone in CCl_4 [4] or by passage over a Chelex-100 column (Bio-Rad). Solutions were made oxygen-free by blowing argon through for 1h and stored in anaerobic conditions. Dialysis membranes were demetallized by heating up to 80°C in 0.01 M EDTA for 30 min and washed with triple distilled water. This step was repeated without EDTA once again. Quartz sample cells were used and rendered metal-free by soaking overnight in 20% HNO_3 in double triple distilled water and rinsed again with triple distilled water just before the measurements.

There are several strategies for introducing a metal into a protein described in literature.[6,7] Most of them involve the preparation of the apoprotein followed by metal addition[5, 6] or the displacement of the original metal by exposing the native protein to excess concentration of the target metal[7, 8]. Only two examples of cobalt substitution in matrix metalloproteinases have been reported in literature: i) Co^{2+}-MMP-12 was prepared by exhaustive dialysis against cobalt excess in presence of AHA inhibitor [9]; and ii) Co^{2+}-MMP-1 was obtained by removal of the native metal dialyzing against *o*-phenanthroline and successively addition of cobalt salt [10]. We initially attempted method (ii): native MT1-MMP was dialyzed against *o*-phenanthroline resulting in an unstable apoprotein which subsequently aggregated and precipitated out of solution. This is because the protein is subject to autoproteolysis, and thus slow exhaustive dialysis of the zinc form against excess of cobalt (metal exchange) cannot be carried out in

absence of a chemical inhibitor. To obtain uninhibited Co^{2+}-MT1-MMP in the large quantities required for spectroscopic investigations, the addition of the metal was performed during the folding process of the apoprotein. This folding was carried out in anaerobic conditions through dialysis of apo-MT1-MMP (12-14 kDa molecular-weight cutoff) against 10 fold volume of 50 mM Hepes pH 8.5, 100 mM NaCl, 10 mM $CaCl_2$, 0.3 mM $CoCl_2$, 2 M urea (24 h at 25 °C). The solution was then changed to 50 mM Hepes pH 7.4, 100 mM NaCl, 10 mM $CaCl_2$, 0.3 mM $CoCl_2$, 1 M urea (24 h at 4 °C) and finally dialyzed against 50 mM Hepes pH 7.4, 100 mM NaCl, 5 mM $CaCl_2$, 0.3 mM $CoCl_2$ (24 h at 4 °C). The protein was washed by the excess of $CoCl_2$ through several washing cycles with 50 mM Hepes pH 7.4, 100 mM NaCl, 5 mM $CaCl_2$ and concentrated by using Amicon Ultra-15 Centrifugal Filter (Merck Millipore, 10 kDa MW cut-off). The protein concentration was determined at 275 nm, using the extinction coefficient for the wild-type MT1-MMP of 35280 M^{-1} cm^{-1}. This value was calculated by using magnetic circular dichroism spectroscopy (MCD) of tryptophan at room temperature.[11, 12] The quality of the samples was determined by SDS-PAGE. Zinc and cobalt content of the protein samples from three independent preparations was measured by flame atomic absorption spectroscopy (Mikrolab Kolbe GmbH, Mülheim an der Ruhr, Germany). Metals content was found to be 2.1 ± 0.2 mol Co^{2+} / mol protein and 0.0 ± 0.2 mol Zn^{2+} / mol protein. These values suggest that the protein contains a cobalt atom both in the catalytic and in the structural site and that the presence of residual zinc is negligible. Co^{2+}-MT1-MMP preparation results in a pure enzyme as demonstrated by SDS page (Figure 2). The protein has a molecular weight of ~ 21 kDa, which corresponds to the size of the catalytic domain after autoproteolytic cleavage of the hinge region (residues 112-285).[1] 20 µL of protein solution was mixed with 10 µL of reducing sample buffer and heated for 5 min at 70 °C before application to the gel. The composition of the buffer is 20 mM Tris-HCl pH 6.8, 1 mM Na_2EDTA, 20% (v/v) glycerol, 0.025 (w/v) bromophenol blue, 5% (v/v) 2-mercaptoethanol. Dual Color Protein Standard III (Serva Electrophoresis) was used as marker (m).

The purity of the Co^{2+}-MT1-MMP construct was checked by SDS page. Figure 2 shows the detected band of Co-MT1-MMP one day before and right after the last purification dialysis step. The enzyme was characterized by a molecular weight of ≈ 21 kDa, which corresponds to the size of the catalytic domain after autoproteolytic cleavage of the hinge region (residues 112-285).[1]

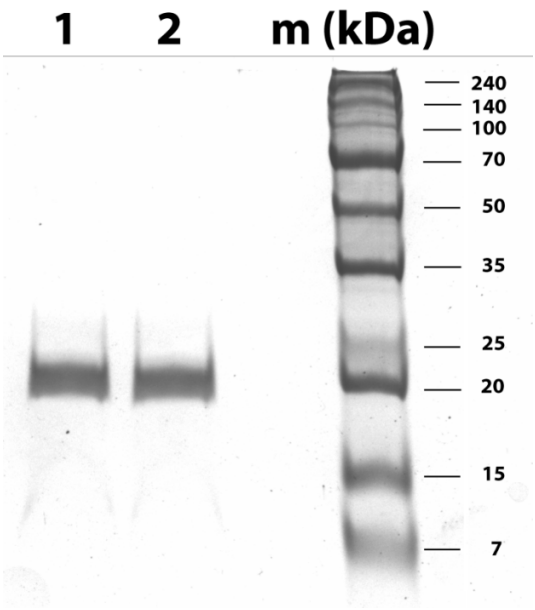

Figure 2: Size and purity of Co^{2+}-MT1-MMP documented by SDS-PAGE (15%). Co^{2+}-MT1-MMP catalytic domain before (lane 1) and after (lane 2) the last dialysis step performed in 50 mM Hepes pH 7.4, 100 mM NaCl and 5 mM $CaCl_2$ for 24 h at 25 °C.

S4) Inhibition of Co^{2+}-MT1-MMP by acetohydroxamic acid (AHA).

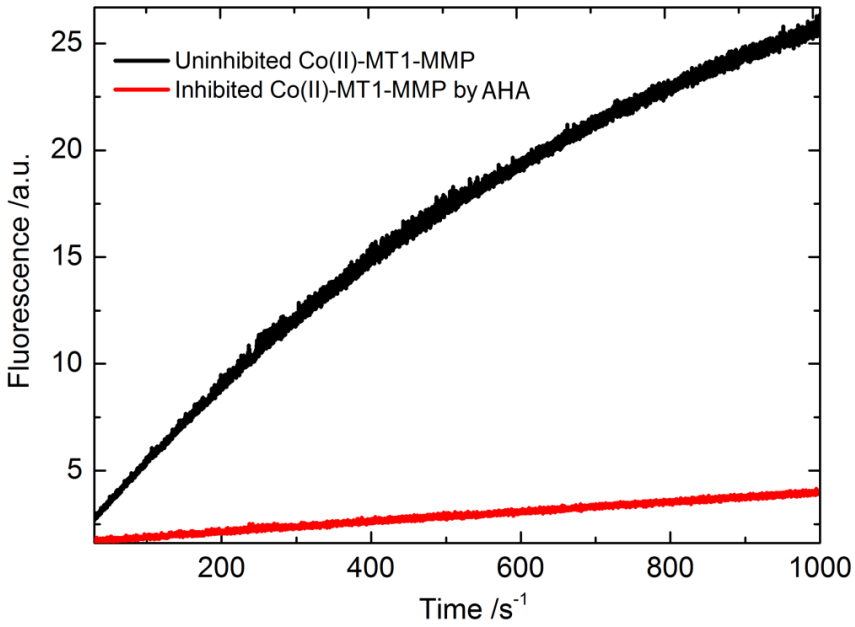

Figure 3: Hydrolysis of a fluorogenic collagen-like peptide by the non-inhibited Co^{2+}-MT1-MMP (black curve) compared to the hydrolysis rate of Co^{2+}-MT1-MMP inhibited by acetohydroxamic acid (AHA, red curve). [Co^{2+}-MT1-MMP] = 0.1 µM, [peptide] = 350 µM, [AHA] = 0.4 M, in 50 mM Hepes pH 7.4, 100 mM NaCl, 5 mM and 5 $CaCl_2$ at 25 °C.

S5) X-ray data collection statistics for MT1-MMP.

Table 1: X-ray data-collection statistics for the catalytic domain of MT1-MMP. The values in parentheses are for the outermost resolution shell.[1]

	Native	Zn-peak	Zn-remote	Ca-peak
Data Collection				
Wavelength (Å)	0.91841	1.24000	1.34000	1.95000
Space group	$P4_32_12$	$P4_32_12$	$P4_32_12$	$P4_32_12$
Unit-cell parameters				
***a* = *b* (Å)**	62.99	63.02	63.05	63.08
***c* (Å)**	122.60	122.64	122,68	122,79
Resolution (Å)	44.54-2.24 (2.37-2.24)	44.56-2.46 (2.61-2.46)	44.59-2.62 (2.78-2.62)	44.61-2.88 (3.05-2.88)
No. of observed reflections	98084	201819	161826	151387
No. of unique reflections	12491	16520	13552	10689
R_{merge}	0.105 (0.998)	0.080 (0.705)	0.065 (0.519)	0.163 (1.145)
Completeness (%)	0.998 (0.993)	0.962 (0.806)	0.952 (0.777)	0.998 (0.989)
$\langle I/\sigma(I)\rangle$	16.8 (2.3)	27.3 (2.3)	31.2 (2.7)	20.4 (1.9)
$CC_{1/2}$	99.8 (70.1)	99.9 (68.4)	99.9 (83.0)	99.7 (68.4)
Refinement				
Resolution (Å)	44.5-2.24			
R/R_{free} **(%)**	19.5/25.4			
No. of reflections	12490			

No. of protein atoms	1431
No. of water molecules	68
Rmsd bond distances (Å)	0.007
Rmsd angles (°)	1.008
Ramachandran plot (%)	
Favored	95.3
Allowed	4.1
Outliers	0.6

S6) Additional crystallographic figures. Comparison of the X-ray structure of MT1-MMP to literature MMP structures.

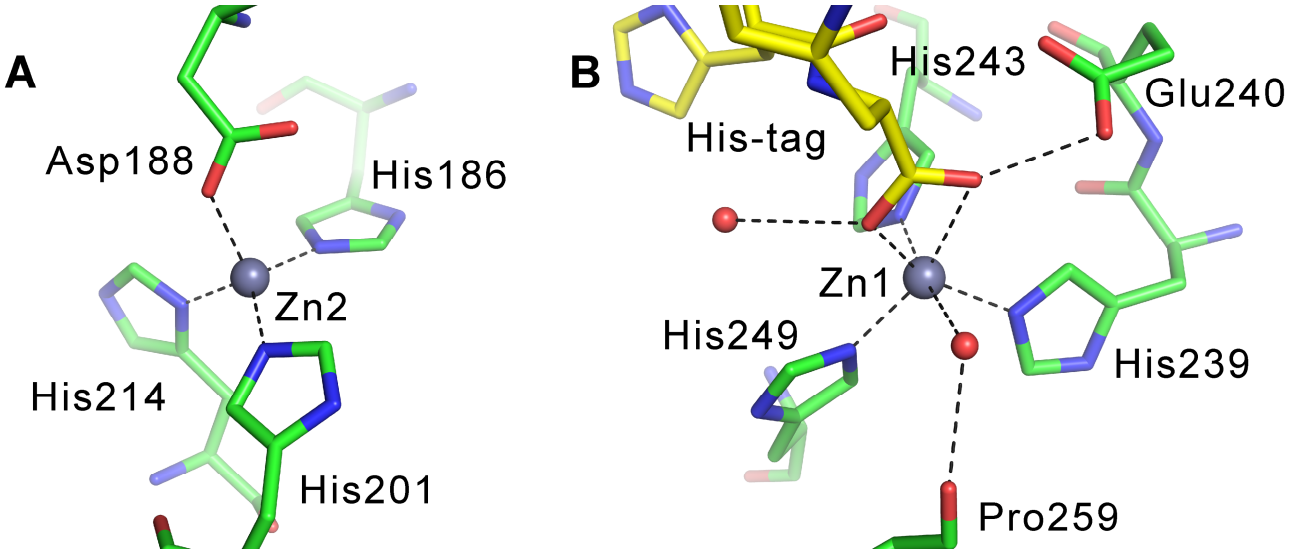

Figure 4: The structural and catalytic site of the catalytic domain of MT1-MMP.

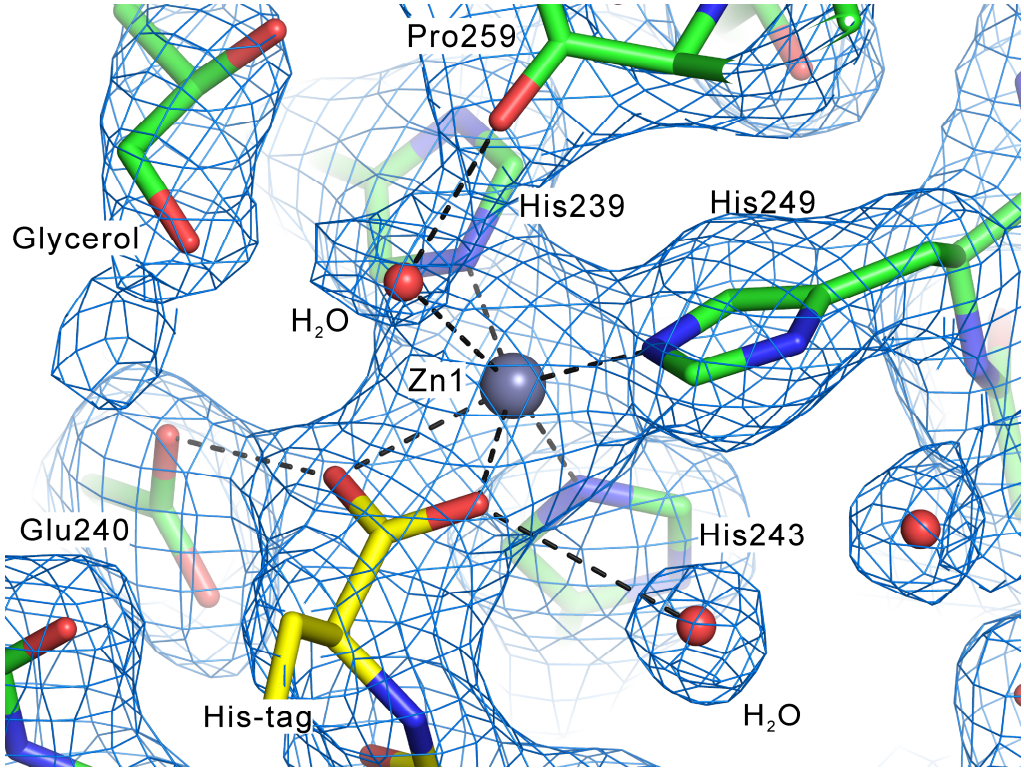

Figure 5: The interaction of the His-tag the catalytic zinc ion in our MT1-MMP construct showing the electron density (2Fo—Fc map).

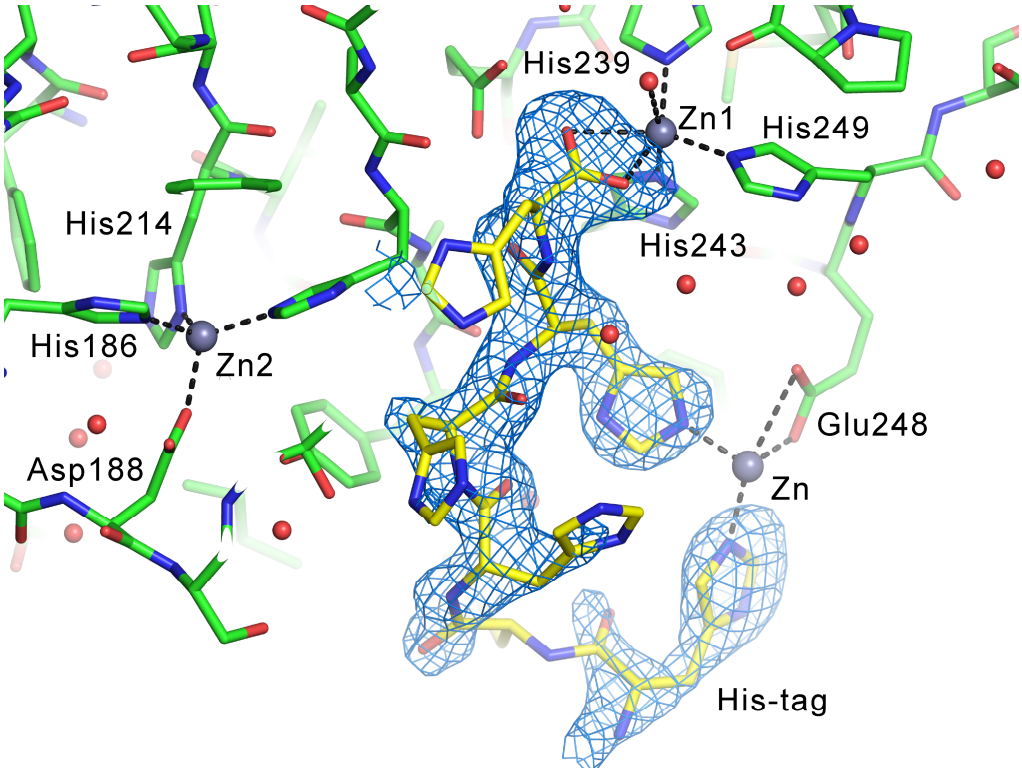

Figure 6: Modeled location of the His-tag of our MT1-MMP construct showing the Fo—Fc omit electron density map (blue mesh).

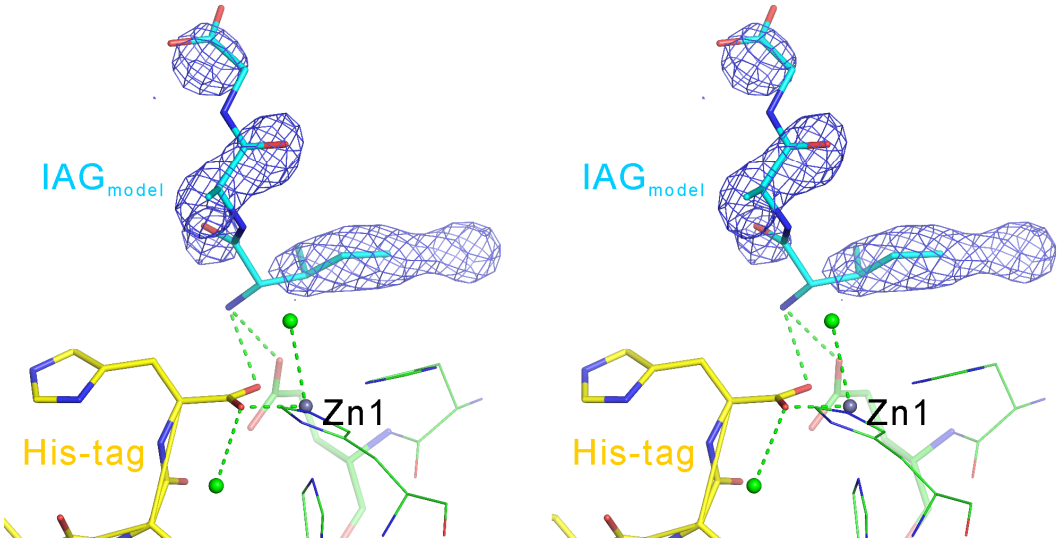

Figure 7: Additional electron density (Fo─Fc omit map, blue mesh) identified in our MT1-MMP crystal structure assigned to two cryoprotectant (glycerol) molecules (See Figure 4 and Supporting information Figure 5). The identified electron density was similar to that seen in the earlier Bertini structures which included the cleaved peptide (N-fragment of Ile-Ala-Gly), suggesting the glycerol molecules have the same surface protein interactions as the substrate and the electron density associated with these small molecules can be used to model the likely conformation of the N-fragment product would take in our crystallographic model.

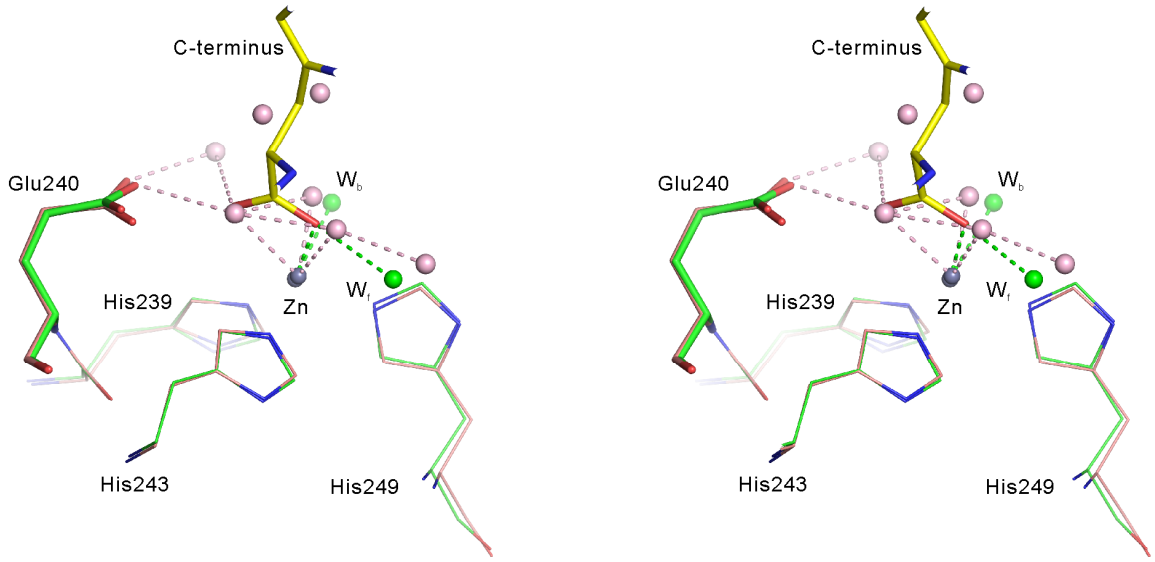

Figure 8: Comparison of the catalytic site of MT1-MMP, with the His-tag bound to the Zn^{2+} ion (PDB entry 5H0U, this study: green) with the resting state of MMP-12 (PDB entry 2OXU: pink) i.e. three number of waters interacting with the Zn.

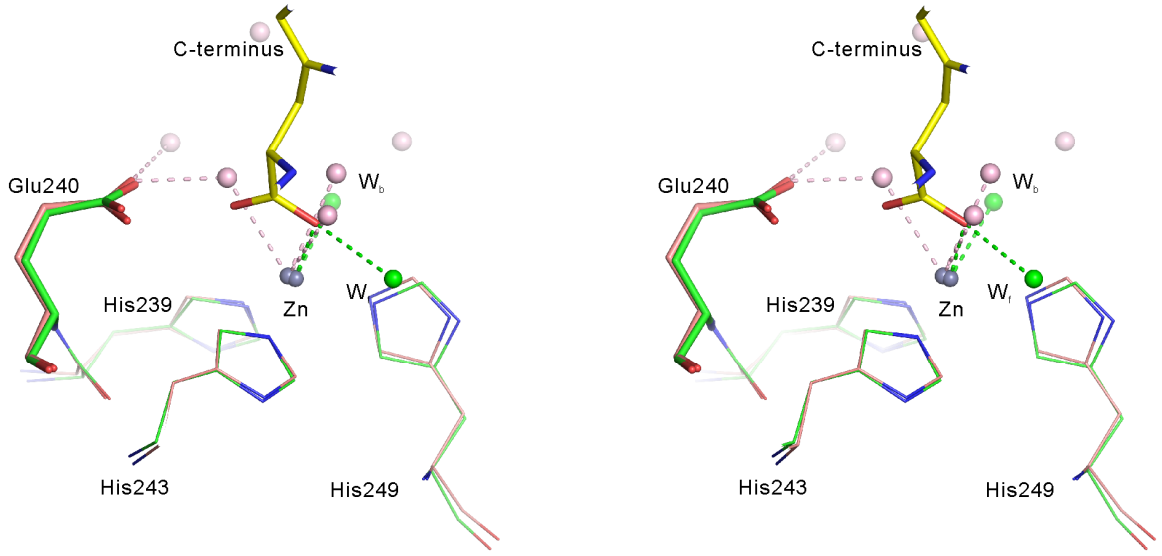

Figure 9: Comparison of the catalytic site of MT1-MMP, with the His-tag bound to the Zn^{2+} ion (PDB entry 5H0U, this study: green) with the resting state of MMP-8 (PDB entry 2OY4: pink) i.e. three number of waters interacting with the Zn.

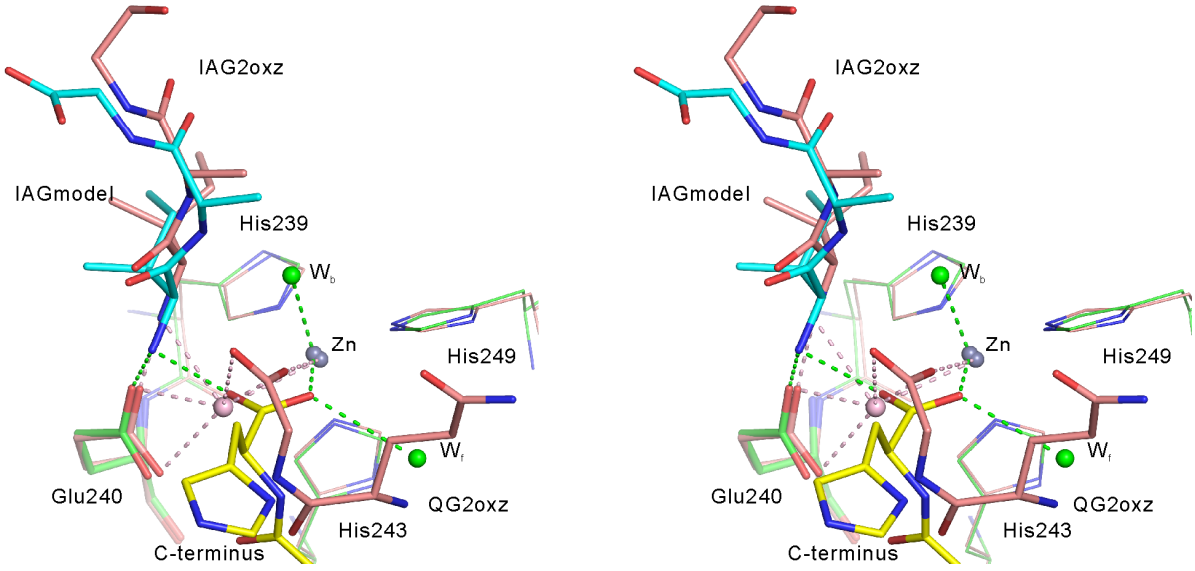

Figure 10: Comparison of the catalytic site of MT1-MMP, with the His-tag bound to the Zn^{2+} ion (PDB entry 5H0U, this study: green) and the modeled peptide (IAG_{model}: light blue), with the cleaved peptide (IAG_{2oxz}: pink) of MMP-12 (PDB entry 2OXZ: pink).

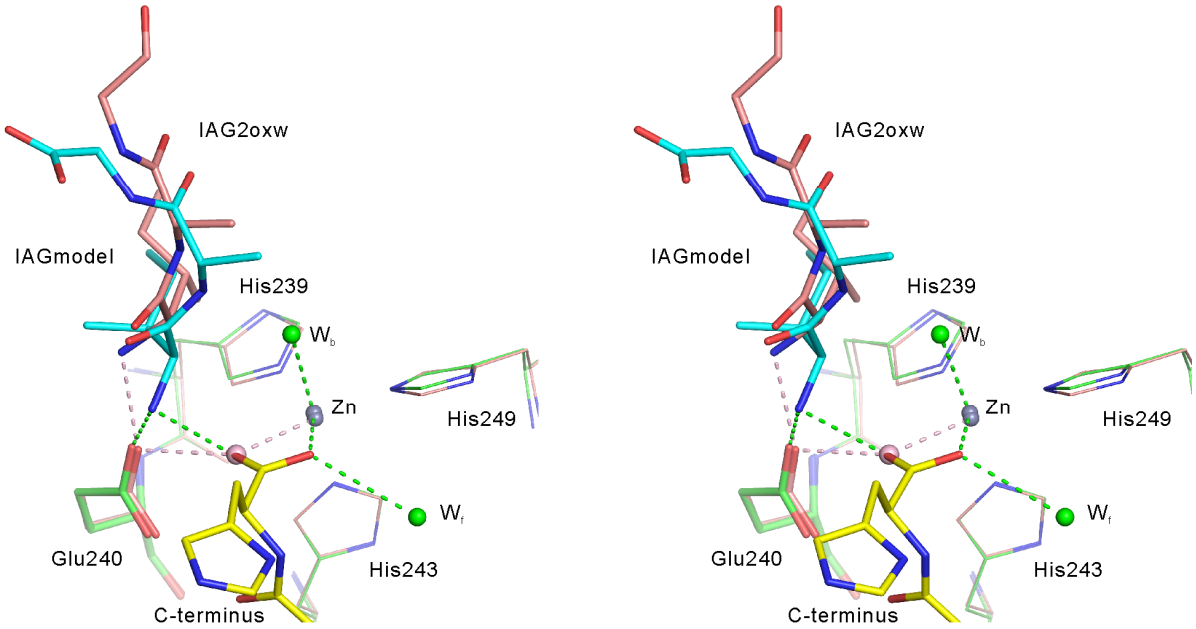

Figure 11: Comparison of the catalytic site of MT1-MMP, with the His-tag bound to the Zn^{2+} ion (PDB entry 5H0U, this study: green) and the modeled peptide (IAG_{model}: light blue), with the cleaved peptide (IAG_{2oxw}: pink) of MMP-12 (PDB entry 2OXW: pink).

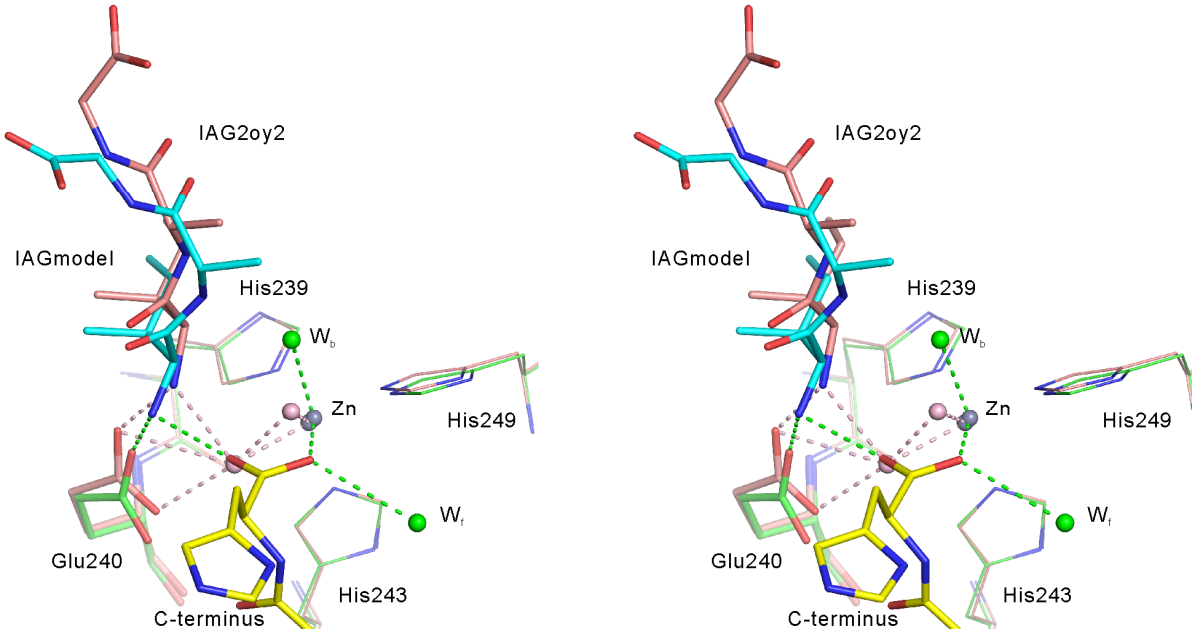

Figure 12: Comparison of the catalytic site of MT1-MMP, with the His-tag bound to the Zn^{2+} ion (PDB entry 5H0U, this study: green) and the modeled peptide (IAG_{model}: light blue), with the cleaved peptide (IAG_{2oxw}: pink) of MMP-8 (PDB entry 2OY2: pink).

Table 2: Geometry of the catalytic Zn^{2+} ion seen in literature MMP structures which have an exogenous carboxylate ligands bound to the Zn.

	PDB	Distances (Å)					Note
		Zn1-W_b	$O_{carboxylate}$-W_f	Zn1-$O_{carboxylate}$		O_{Glu240}-$O_{carboxylate}$	
MMP3	1b3d	-	-	2.00	2.71	2.90	
	1b8y	-	-	2.02	2.85	2.68	
	1caq	-	-	1.99	2.83	2.64	
	1ciz	-	-	2.09	2.62	2.57	
	1hfs	-	-	1.84	2.62	2.69	
	1hy7	-	-	1.93	2.95	2.51	chainB
	1sln	-	-	3.00	1.75	3.59/3.56	
	4dpe	2.58	-	1.88	3.08	2.74	
MMP7	2y6c	-	-	1.95	2.98	2.73	
MMP8	1bzs	-	-	1.97	2.65	2.65	
	3tt4	-	-	2.15	2.68	2.78	
MMP9	2ow0	-	-	2.12	2.55	3.03*	*Nε2(GLN)
	2ow2	-	-	1.78	-	2.75*	*Nε2(GLN)
	4hma	-	-	1.90	2.78	3.31*	*Oε1(GLN)
	5i12	-	-	1.90	2.77	2.56	
MMP12	1i76	-	-	1.99	2.78	2.62	
	1os2	-	2.95	1.99	2.82	-	chainB
	1ros	-	-	1.92	2.59	2.59	
	2oxz	-	-	2.36	-	-	
	2wo8	-	-	2.05	2.08	3.21	
	2wo9	-	-	2.02	2.68	2.63	
	2woa	-	-	2.04	2.71	2.76	
	3ehx	-	-	1.99	2.72	2.50	
	3ehy	-	-	1.88	2.71	2.62	
	3lir	-	-	2.05	2.60	2.74	
	3ts4	-	3.29	2.11	2.48	2.58	
	4efs	-	-	2.18	2.69	2.67	
	4h30	-	-	1.86	2.93	2.70	
	4h84	-	-	1.89	2.84	2.63	
	4i03	-	-	2.39	2.43	-	ALA
	5cxa	-	-	1.91	2.86	2.65	
	5i0l	-	-	1.75	2.72	2.54	
	5i2z	-	3.43	2.08	2.45	2.77*	*Nε2(GLN)
	5i3m	-	-	1.90	2.99	2.67*	*Nε2(GLN)
	5i4o	-	-	1.89	2.84	2.65*	*Nε2(GLN)
	5i43	-	-	1.87	2.56	2.70*	*Nε2(GLN)
MMP13	1ztq	-	-	2.14	2.99	-	
	3elm	-	-	2.12	2.60	2.67	
	3i7g	-	-	2.34	2.26	2.38	
	3tvc	-	-	2.20	2.59	2.71	
	3wv1	-	-	2.06	2.41	2.45	
	3wv3	-	-	2.08	2.43	2.56	
	4l19	-	-	2.17	2.32	2.65	chainB
MMP14	5H0U	2.74	3.15	1.97	2.50	2.59	

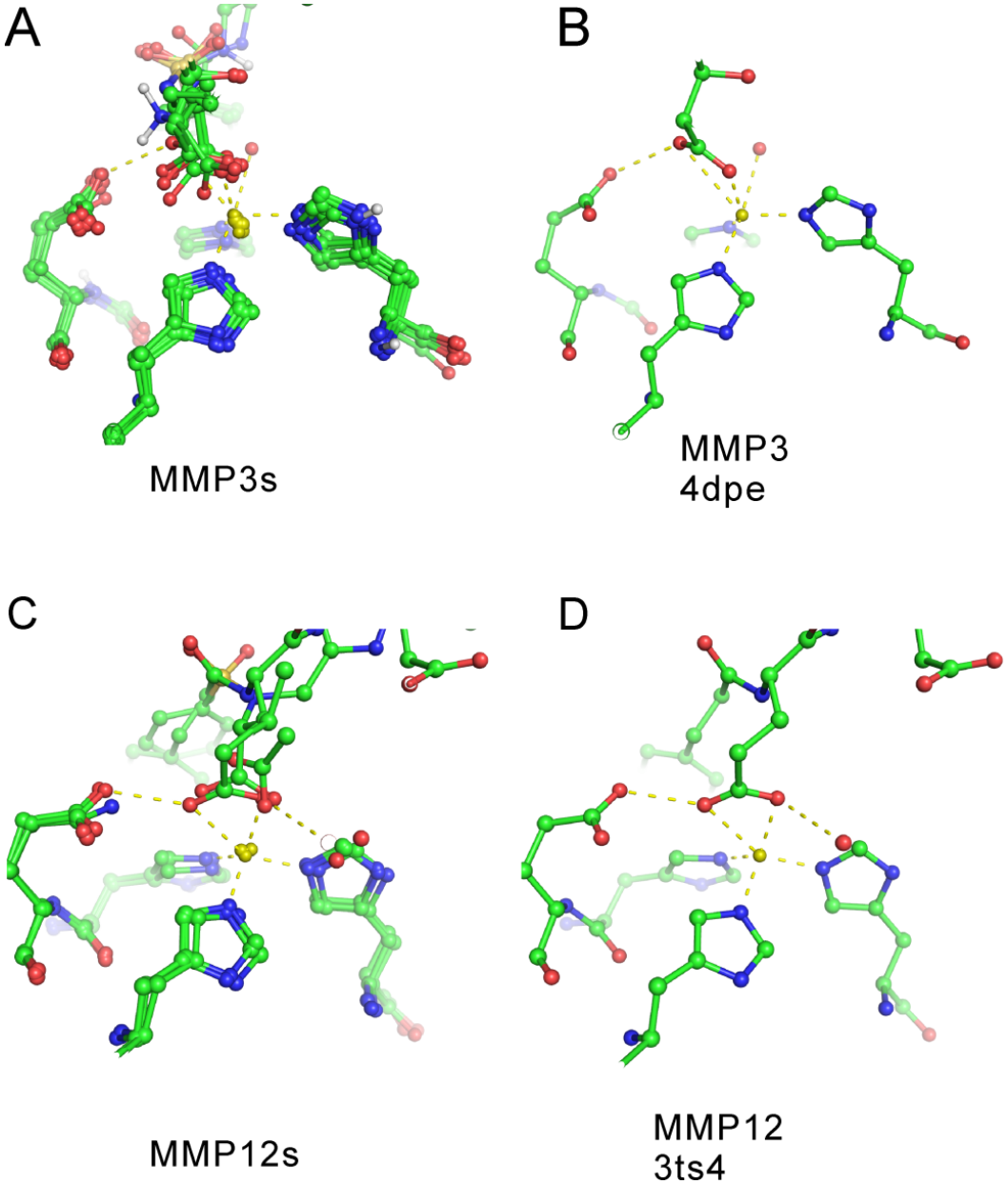

Figure 13: Comparison of the catalytic site of MMPs. (A) Structural alignment with MMP3s with the carboxylate ligands. (B) MMP3 (PDB id 4dpe) with W_b. (C) Structural alignment with MMP12s with the carboxylate ligands. (D) MMP12 (PDB id 3ts4) with W_f.

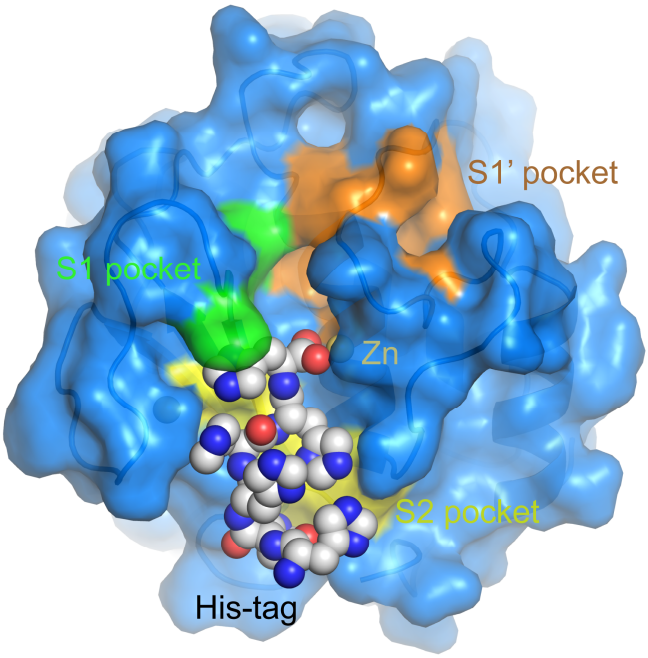

Figure 14: Interaction of the His-tag with the protein cleft. According to the nomenclature of Schechter and Berger (Biochem Biophys Res Commun, 1967), the MMPs active site is characterized by three unprimed pockets (to the left side of the catalytic zinc: S1 to S3) and three primed pockets (to the right side: S1´ to S3´) which drive the binding of the substrates. The main subsite for substrate recognition in MMPs is the specificity pocket S1´ [13] which varies considerably in terms of amino acid sequence, size and shape. The primed pockets thus interact with the N-terminus fragment, while the C-terminus fragment instead interacts with the unprimed pockets.

S7) Analysis of Co^{2+} EPR and MCD spectra from wild type and inhibited Co^{2+}-MT1-MMP.

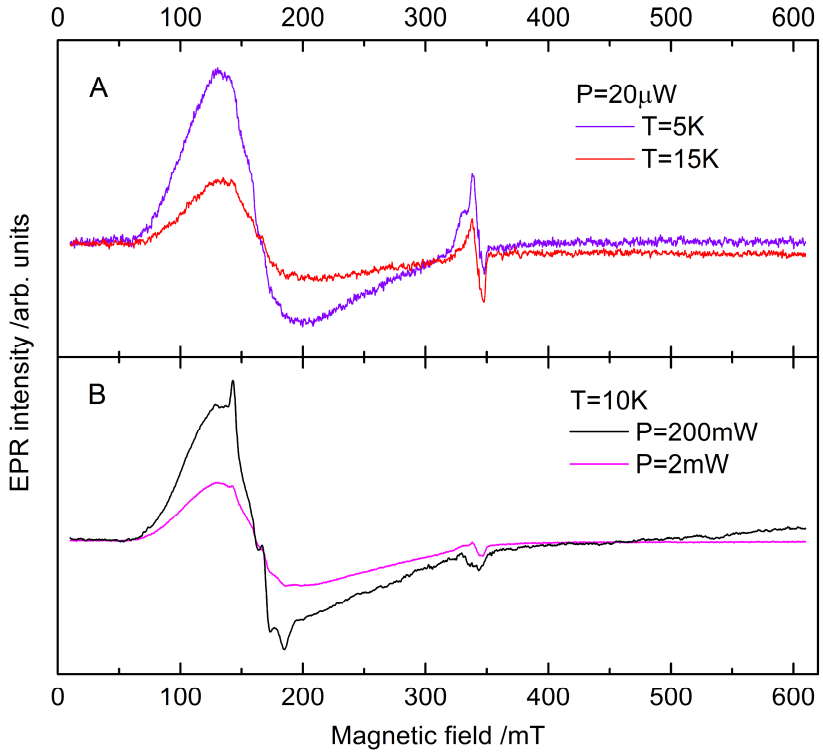

Figure 15: Comparison of CW X-band EPR spectra of Co^{2+}-MT1-MMP recorded at various temperatures and powers: (A) T = 5K, P = 20 μW and T = 15 K, P = 20 μW; (B) T=10K, P=200mW and T=10K, P=2mW. ν_{mw}= 9.638GHz. Within each subplot the signals are shown to scale.

Spectra shown in **Fig. 15A** were measured at low power (P = 20 μW) to minimize the saturation effects at 5 K. In the absence of saturation, the EPR signal intensity is proportional to the inverse of the temperature. We find that the ratio of signal intensities for 5 and 15 K is around 2.6 instead of 3, which indicates that at T = 5 K and P = 20 μW the spectrum is slightly saturated. This behavior is indicative of the zero-field splitting value being D>0. **Fig. 15B** demonstrates that the EPR spectrum at g ≈ 4.3 consists of two components with different saturation properties. The broad main feature assigned to the Co^{2+} ion at the catalytic site saturates more readily than the second component, which shows additional splitting.

Fig. 16 shows the raw MCD data collected at 1.8 K in the absence and presence of the inhibitor AHA. For both datasets, a scatter like background was subtracted from the data, which was suspected to be caused by strain. **Fig. 17** and **18** show global fits of the data in terms of 8 and 4 Gaussian functions respectively, described in the main text.

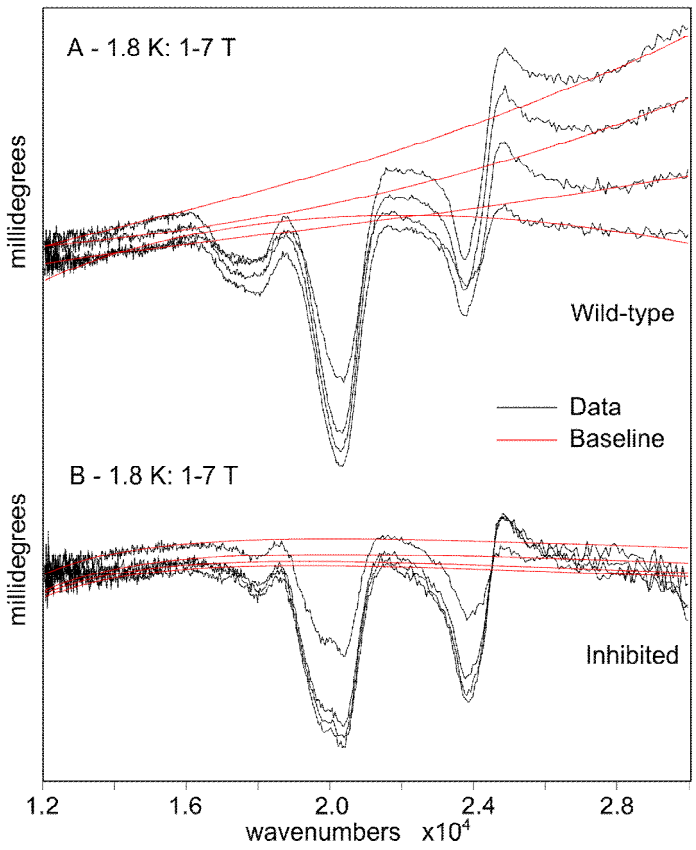

Figure 16: Raw MCD data Co^{2+} substituted MMP-12 in the presence (B) and absence (A) of the inhibitor AHA (100 mM) collected at 1.8 K. A baseline was subtracted from all data to account for a field dependent baseline.

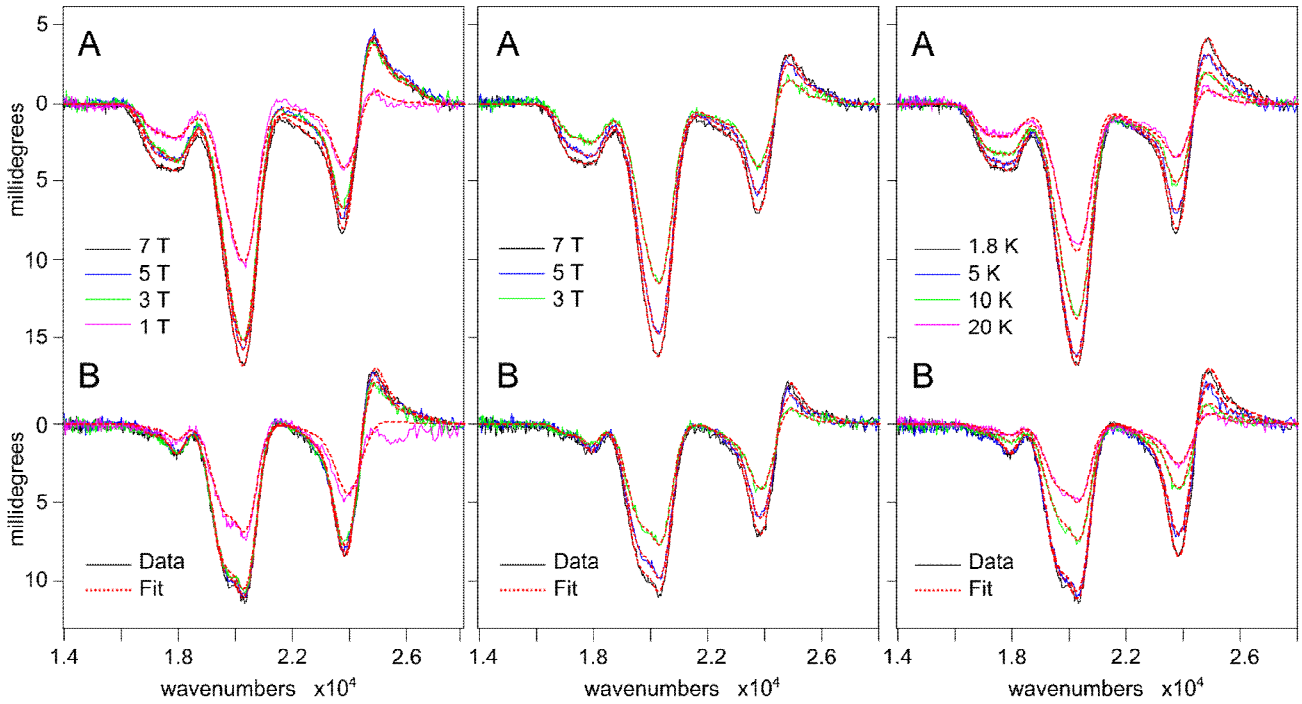

Figure 17: Global MCD fitting of Co^{2+} substituted MT1-MMP in the presence (B) and absence (A) of the inhibitor AHA. Left and middle) Magnetic field dependence measured at 1.8 K and 5K; Right) Temperature dependence measured at 7 T.

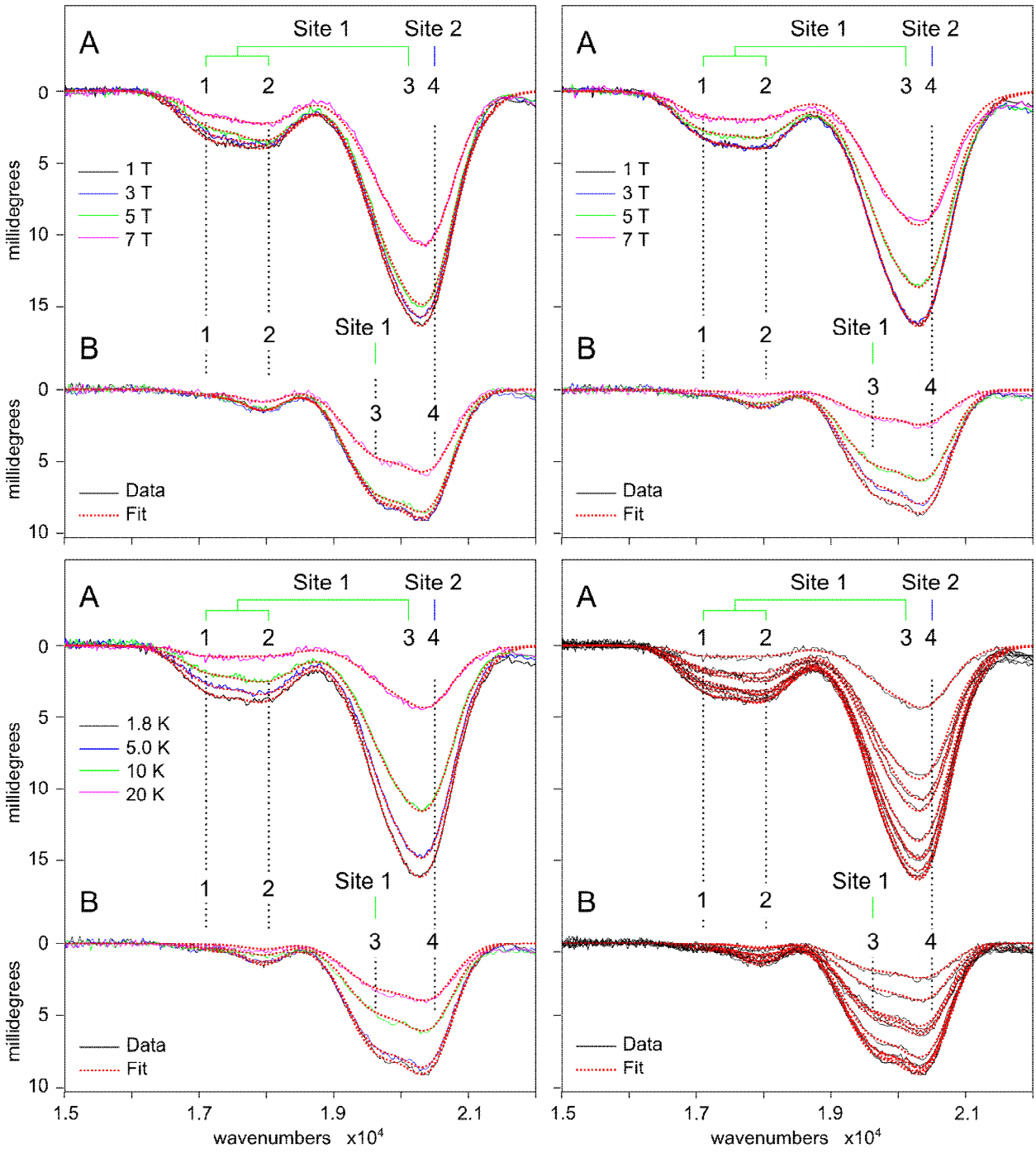

Figure 18: MCD fitting of the low frequency (red) region in terms of four Gaussian functions. (A) without AHA, (B) with AHA. Top) Magnetic Field dependence measured at 1.8 K (LHS) and 5K (RHS); Bottom Temperature dependence measured at 7 T (LHS) and the entire dataset (RHS). A slightly different baseline was subtracted from the raw data in this analysis. These fittings were used to construct the magnetization curves in the main text.

As described in the main text, band assignments were based on the effect of the inhibitor (AHA). Bands 1-4 are all modified by the inhibitor and are thus assigned to the catalytic site: band 1 (17,200) band 2 (18,000) are significantly diminished or completely lost upon inhibitor binding whereas band 3 (20,000) decreases in intensity by 50% and is shifted to the red (500 cm^{-1}) and band 4 doubles in intensity (its position is not well defined in the non-inhibited form). Bands 5-8 are unchanged and thus assigned to the structural site. It is important to note though that the structural site should also have some contribution in the 17,000-21,000 cm^{-1} region and thus the fitted bands should only be considered dominantly one species or the other.

While it is difficult to justify fitting the feature at 20,000 cm^{-1} to two bands on the basis of a single MCD spectrum collected at one temperature and magnetic field, changes in the exact shape of this feature as a function of temperature (see **Fig. 18**), make the inclusion of two bands necessary. It is noted though that the relative intensities of bands 3 and 4 are unlikely to be well constrained.

From this dataset we are unable to constrain the coordination number of the structural site in the Co^{2+} substituted protein. The only feature we can assign to the structural site which does not overlap with the catalytic site is the pseudo-A type MCD feature at 24,000 cm^{-1}. This feature has no clear nesting behavior, suggesting a large zero-field splitting ($D > 100$ cm^{-1}). d-d transitions of high spin Co^{2+} complexes do not generally extend this far to the blue, although there are examples of 5/6 coordinate species in the literature whose highest d-d transition does appear in this region.[14, 15] We hypothesize that the structural site in the Co^{2+} substituted enzyme could adopt a five coordinate, square pyramidal coordination if the mono-dentate carboxylate ligand of the corresponding Zn^{2+} complex favored bi-dentate coordination in the Co^{2+} substituted protein, owing to the higher coordination number preference of Co^{2+}.[15] If this was the case, it could explain the blue shifted MCD signal and also the large D value inferred for the structural site.[14]

Finally we stress that we do not observe any evidence for a 4-coordinate metal site in the Co^{2+} substituted enzyme. Tetrahedral Co^{2+} complexes typically display a strong pseudo-A type MCD transition, i.e. a derivative shaped signal in the 17,000 cm^{-1} region is completely absent in the spectra.

S8) QM/MM geometry optimizations of structural models A-K.

We employed QM/MM geometry optimizations to model the metal coordination spheres in MT1-MMP. The coordination sphere of the structural zinc ion is tetrahedral and consists of three histidine residues (His186, His201, and His214) and one aspartic acid (Asp188). As hydrogen atoms cannot be seen in X-ray experiments, we modeled both protonation states of aspartic acid: deprotonated and protonated. When Asp188 is protonated, the hydrogen bond Asp188-O2H···O-Thr190 appears, which is absent in the crystal structure. Hence, we propose that the structural site of MT1-MMP resembles structure A in **Fig. 19**. Key distances for models A and B are listed in **Table 3**. They confirm the proposed assignment since the computed Asp188-O2···O-Thr190 distance is in the range of the experimental values for model A, but much smaller for model B.

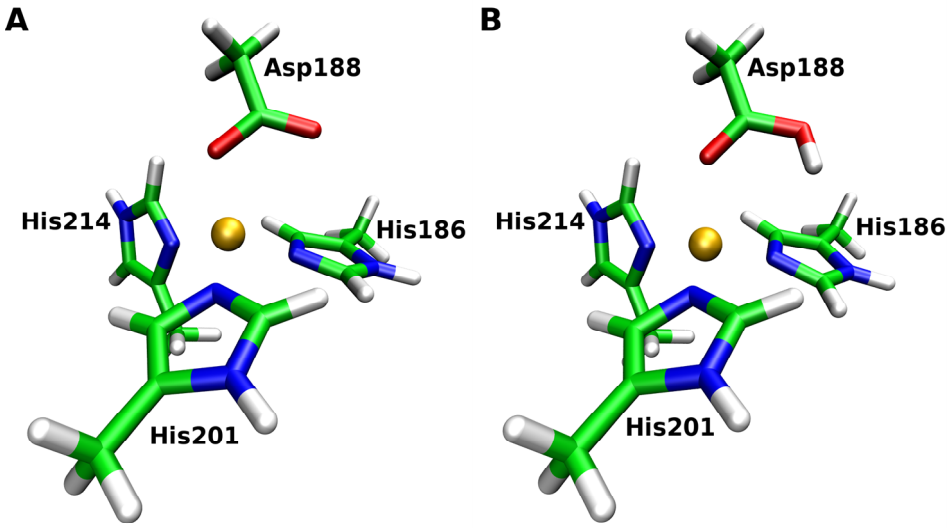

Figure 19: Coordination of zinc at the structural site: models A and B.

The catalytic zinc ion is located in the active site of the enzyme. The X-ray data show three histidine residues (His239, His243, and His249) coordinating this zinc ion, but the exact number of water molecules is not resolved. We prepared models of the catalytic zinc coordination site with 1-3 water ligands (structures C-I in **Fig. 20**). In the tetrahedral models the single water ligand interacts with Glu240 either directly or through an additional water molecule, and it thus represents the nucleophilic water, W_n. In the penta-coordinate models, the same water ligand is present, with a second water, W_b, binding on the back face of Zn^{2+}. We expect back-face binding to be preferred over front-face binding because of the possible interaction with Pro259 on the back, while there are no obvious water-protein interactions on the front face. Key distances for models C-I are listed in **Table 3**.

Table 3: Key distances in crystal structures and QM/MM-optimized coordination spheres of zinc at the structural site of MT1-MMP, in Å.

Distance	exp (this work)	1BUV	3MA2	A	B
$Zn^{2+}\cdots$ O1-Asp188	1.99	2.12	2.04/1.90	1.94	2.04
$Zn^{2+}\cdots$ O2-Asp188	3.25	3.01	3.25/3.22	3.07	3.44
Asp188-O2$\cdots$O-Thr190	3.30	3.82	3.21/3.23	3.30[b]	2.65[c]
$Zn^{2+}\cdots$ N-His186	1.99	1.75	1.92/1.93	2.00	2.00
$Zn^{2+}\cdots$ N-His201	2.12	2.21	2.08/2.06	1.99	1.96
$Zn^{2+}\cdots$ N-His214	1.99	2.60	2.03/2.06	2.04	1.99

[a] a dimer; [b] 3.26 Å with Thr190 in the QM part; [c] 2.44 Å with Thr190 in the QM part.

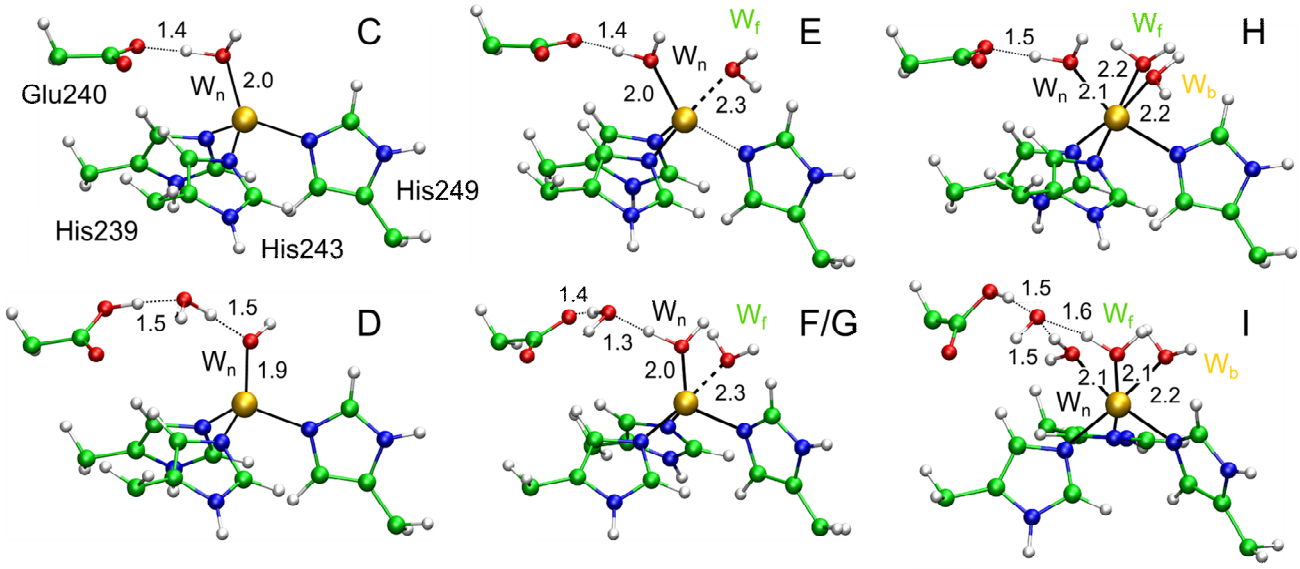

Figure 20: Coordination of zinc at the catalytic site of an uninhibited MT1-MMP: models C-I.

Models C-D with tetrahedral coordination. In structure C a water molecule coordinating zinc forms a hydrogen bond with Glu240, while in structure D a hydroxyl anion coordinates zinc and the side chain of Glu240 is neutral. In structure C the computed distances from zinc to both oxygens of the Glu240 side chain are very short due to a direct H-bond between the coordinating water molecule and Glu240.

Models E-G with 5-fold coordination. In structure E two water molecules coordinate zinc and one of them forms a hydrogen bond with Glu240. In structure F two water molecules coordinate zinc and the side chain of Glu240 is negatively charged. In structure G a hydroxyl anion and a water molecule

coordinate zinc and the side chain of Glu240 is neutral. The computed distances from zinc to both oxygens of the Glu240 side chain increase in the order E < F < G.

Models H-I with octahedral coordination. In structure H three water molecules coordinate zinc and one of them forms a hydrogen bond with Glu240. In structure I three water molecules coordinate zinc, two water molecules form H-bonds with a hydroxyl anion, and the side chain of Glu240 is neutral.

Models J-K of the AHA inhibited catalytic site. The optimized structures are shown in **Fig. 21**. Structure J corresponds to the inhibited complex in the absence of the first coordination sphere water. Structure K represents the 6-coordinated complex with one water molecule.

Table 4: Key distances in the QM/MM-optimized coordination spheres of zinc at the catalytic site of an uninhibited MT1-MMP, in Å.

Distance	C	D	E	F	G	H	I
$Zn^{2+}\cdots$ O1-Glu240	3.76	4.86	3.97	4.49	4.76	4.30	5.00
$Zn^{2+}\cdots$ O2-Glu240	4.50	5.01	4.77	4.99	5.13	4.81	5.10
$Zn^{2+}\cdots$ N-His239	2.01	2.01	2.06	2.03	2.04	2.12	2.14
$Zn^{2+}\cdots$ N-His243	2.03	2.04	2.10	2.09	2.11	2.17	2.15
$Zn^{2+}\cdots$ N-His249	2.01	2.01	2.06	2.04	2.01	2.09	2.08

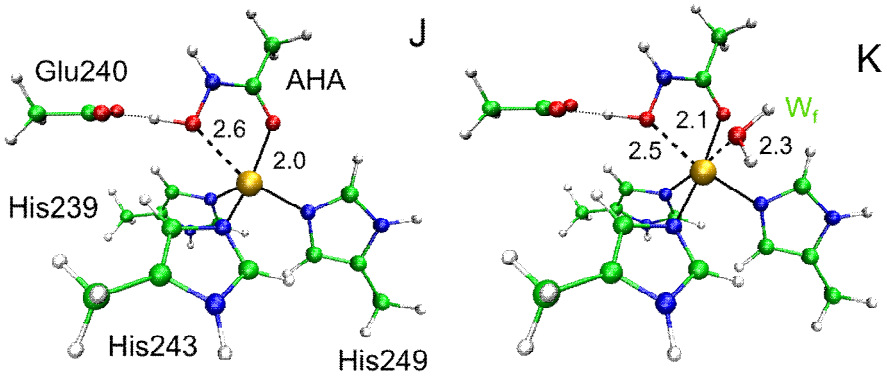

Figure 21: Coordination spheres of zinc at the AHA inhibited catalytic site: models J and K.

S9) Comparison of computed key distances in Co^{2+} and Zn^{2+} QM/MM models.

Table 5: Key distances in the QM/MM-optimized coordination spheres of cobalt and zinc at the structural site of MT1-MMP, in Å.

Distance	A		B	
	Zn	Co	Zn	Co
M^{2+}··· O1-Asp188	1.94	1.95	2.04	2.10
M^{2+}··· O2-Asp188	3.07	3.05	3.44	3.50
M^{2+}··· N-His186	2.00	2.00	2.00	1.99
M^{2+}··· N-His201	1.99	1.98	1.96	1.94
M^{2+}··· N-His214	2.04	2.04	1.99	1.98

Table 6: Key distances in the QM/MM-optimized coordination spheres of cobalt and zinc at the catalytic site of uninhibited MT1-MMP, in Å.

Distance	C		D	
	Zn	Co	Zn	Co
M^{2+}··· O1-Glu240	3.76	3.77	4.86	4.86
M^{2+}··· O2-Glu240	4.50	4.56	5.01	5.01
M^{2+}··· N-His239	2.01	2.02	2.01	2.02
M^{2+}··· N-His243	2.03	2.05	2.04	2.06
M^{2+}··· N-His249	2.01	1.99	2.01	2.02
M^{2+}··· O-Water	1.96	1.95	1.87	1.87

Table 7: Key distances in the QM/MM-optimized coordination spheres of cobalt and zinc at the catalytic site of uninhibited MT1-MMP, in Å.

Distance	E		F		G	
	Zn	Co	Zn	Co	Zn	Co
$M^{2+}\cdots$ O1-Glu240	3.97	3.91	4.49	4.51	4.76	4.78
$M^{2+}\cdots$ O2-Glu240	4.77	4.82	4.99	5.11	5.13	5.22
$M^{2+}\cdots$ N-His239	2.06	2.04	2.03	2.01	2.04	2.02
$M^{2+}\cdots$ N-His243	2.10	2.17	2.09	2.14	2.11	2.16
$M^{2+}\cdots$ N-His249	2.06	2.04	2.04	2.02	2.04	2.02
$M^{2+}\cdots$ O-Water1	2.01	1.98	1.98	1.97	1.90	1.90
$M^{2+}\cdots$ O-Water2	2.29	2.28	2.27	2.32	2.33	2.46

Table 8: Key distances in the QM/MM-optimized coordination spheres of cobalt and zinc at the catalytic site of uninhibited MT1-MMP, in Å.

Distance	H		I	
	Zn	Co	Zn	Co
$M^{2+}\cdots$ O1-Glu240	4.30	4.27	5.00	5.01
$M^{2+}\cdots$ O2-Glu240	4.81	4.79	5.10	5.11
$M^{2+}\cdots$ N-His239	2.12	2.09	2.14	2.12
$M^{2+}\cdots$ N-His243	2.17	2.15	2.15	2.15
$M^{2+}\cdots$ N-His249	2.09	2.07	2.08	2.07
$M^{2+}\cdots$ O-Water1	2.11	2.10	2.13	2.14
$M^{2+}\cdots$ O-Water2	2.21	2.26	2.13	2.18
$M^{2+}\cdots$ O-Water3	2.21	2.32	2.17	2.21

Table 9: Key distances in the QM/MM-optimized coordination spheres of cobalt and zinc at the catalytic site of inhibited MT1-MMP, in Å.

Distance	J		K	
	Zn	Co	Zn	Co
$M^{2+}\cdots$ N-His239	2.02	2.01	2.12	2.09
$M^{2+}\cdots$ N-His243	2.05	2.05	2.12	2.11
$M^{2+}\cdots$ N-His249	2.02	2.02	2.08	2.05
$M^{2+}\cdots$ ON-Inh	2.50	2.55	2.27	2.45
$M^{2+}\cdots$ OC-Inh	2.00	2.00	2.10	2.07
$M^{2+}\cdots$ O-Water	-	-	2.17	2.25

S10) Optimized QM/MM geometries (QM part)

Table 10: Optimized Cartesian coordinates in xyz format.

Structure A – Zn^{II} /Å				Structure B – Zn^{II} /Å			
Atom	x	y	z	Atom	x	y	z
C	-24.3819	23.34711	14.19142	C	-24.5038	23.49052	14.16592
H	-23.6477	24.06265	13.80457	H	-23.7878	24.19904	13.73653
H	-24.8189	22.81328	13.3457	H	-24.9941	22.95922	13.34836
N	-22.6499	22.69272	15.95668	N	-22.6094	22.7884	15.73733
H	-22.1611	23.59222	16.01156	H	-22.1025	23.68088	15.7632
C	-23.7381	22.39225	15.14548	C	-23.8	22.52765	15.0696
C	-22.3788	21.62112	16.73169	C	-22.2689	21.71052	16.47033
H	-21.5983	21.59947	17.47666	H	-21.3693	21.64158	17.06487
N	-23.2195	20.63566	16.45283	N	-23.1784	20.74995	16.30844
C	-24.0646	21.10548	15.4701	C	-24.1272	21.25089	15.43445
H	-24.8763	20.5056	15.10049	H	-24.9862	20.67192	15.14624
C	-27.3281	19.92198	19.05321	C	-27.2165	20.19276	18.93988
H	-27.7745	19.40343	18.19945	H	-27.6708	19.74388	18.05142
H	-27.4573	19.2421	19.90432	H	-27.3075	19.42399	19.71835
C	-25.8344	20.08984	18.73269	C	-25.7404	20.34355	18.6429
O	-25.2547	21.17506	18.70591	O	-25.0656	19.33046	18.39513
O	-25.2648	18.93421	18.49277	O	-25.2002	21.54633	18.68911
C	-19.4073	15.69601	19.08622	H	-24.2147	21.50324	18.72796
H	-18.4851	16.1014	19.5114	C	-19.4191	15.69387	19.06785
H	-19.8275	15.02089	19.83918	H	-18.4959	16.0932	19.49603
N	-20.1086	18.0854	19.32504	H	-19.8488	15.02583	19.82166
H	-19.2526	18.37639	19.83277	N	-20.1228	18.0776	19.34544
C	-20.3478	16.82571	18.80785	H	-19.2813	18.35292	19.89222
C	-21.1232	18.90086	18.99254	C	-20.3463	16.83318	18.78467
H	-21.1991	19.93471	19.30156	C	-21.1009	18.91846	18.98825
N	-22.0287	18.22568	18.28678	H	-21.1689	19.94056	19.33601
C	-21.5596	16.92973	18.17229	N	-21.9821	18.27116	18.21744
H	-22.1273	16.17202	17.65558	C	-21.5235	16.96668	18.09404
C	-22.3583	17.38634	14.46806	H	-22.0793	16.22974	17.53681

H	-22.2406	18.40385	14.07736	C	-22.3373	17.35937	14.39875
H	-21.7695	17.31048	15.3869	H	-22.2164	18.36881	13.98702
N	-24.36	17.67182	15.94681	H	-21.7452	17.29099	15.31723
C	-23.8002	17.11358	14.79777	N	-24.3331	17.71122	15.8665
C	-25.6464	17.32924	15.95751	C	-23.7784	17.09838	14.73794
H	-26.3627	17.66156	16.69179	C	-25.6241	17.3706	15.90271
N	-25.936	16.56333	14.89287	H	-26.3508	17.73046	16.61335
H	-26.8854	16.27315	14.62247	N	-25.9151	16.56026	14.87669
C	-24.7862	16.42142	14.13965	H	-26.8678	16.2535	14.62418
H	-24.779	15.87414	13.20995	C	-24.7726	16.38116	14.12254
Zn	-23.6568	18.92805	17.39627	H	-24.7767	15.79339	13.21773
H	-25.1526	23.95676	14.66303	Zn	-23.4363	18.95413	17.12495
H	-27.9171	20.83239	19.16414	H	-25.2374	24.10608	14.68648
H	-19.0859	15.11784	18.21994	H	-27.8367	21.05921	19.16966
H	-21.9299	16.67981	13.75718	H	-19.0987	15.11185	18.20375
				H	-21.9072	16.64161	13.70025
Structure C – Zn^{II} /Å				Structure D – Zn^{II} /Å			
Atom	x	y	z	Atom	x	y	z
C	-12.9542	8.149636	15.31892	C	-13.0692	8.281257	15.47932
H	-13.1848	9.016244	14.69331	H	-13.3139	9.167511	14.88639
H	-12.0279	7.713087	14.93126	H	-12.1129	7.904544	15.10087
N	-11.8574	8.046369	17.61326	N	-11.9918	8.121861	17.77289
H	-11.1998	7.296524	17.37302	H	-11.2855	7.416818	17.53379
C	-12.7939	8.577453	16.74513	C	-12.9583	8.638766	16.92806
C	-12.0046	8.619881	18.82569	C	-12.1687	8.649153	19.00143
H	-11.3703	8.405694	19.67758	H	-11.5143	8.445711	19.83439
N	-13.0012	9.503449	18.78352	N	-13.2063	9.478303	19.00068
C	-13.4852	9.495468	17.48812	C	-13.6957	9.488648	17.71077
H	-14.2561	10.18428	17.17348	H	-14.5223	10.12033	17.42368
C	-16.521	11.69882	15.21809	C	-16.7973	11.63459	14.94597
H	-16.9035	12.63599	14.79686	H	-17.087	12.52803	14.38065
H	-15.5367	11.51959	14.78081	H	-15.7635	11.42259	14.6623

C	-16.3866	11.87586	16.74269	C	-16.8328	11.98589	16.43085
O	-15.1976	12.12534	17.15007	O	-15.8462	12.80302	16.75912
O	-17.4009	11.78153	17.47513	O	-17.6716	11.58968	17.23947
C	-19.2118	8.097496	19.3874	C	-19.1501	8.006493	19.24543
H	-19.9396	8.504746	20.10167	H	-19.9437	8.425472	19.87934
H	-19.2999	8.65826	18.45502	H	-19.1765	8.526116	18.28418
N	-17.3148	7.713168	21.0637	N	-17.3696	7.665999	21.05
H	-17.7009	6.893535	21.53879	H	-17.7218	6.781592	21.42701
C	-17.8312	8.304501	19.9192	C	-17.8267	8.274939	19.8916
C	-16.114	8.269001	21.32585	C	-16.224	8.271106	21.42798
H	-15.5092	8.004518	22.18161	H	-15.6699	7.99765	22.31523
N	-15.827	9.198358	20.41936	N	-15.9194	9.253061	20.58647
C	-16.894	9.226508	19.53873	C	-16.9185	9.2676	19.62796
H	-16.9497	9.937743	18.72617	H	-16.9583	10.01099	18.8434
C	-12.1545	7.212961	24.40243	C	-12.2064	7.077684	24.70378
H	-11.0678	7.074196	24.32552	H	-11.1228	6.909227	24.65813
H	-12.4017	7.377624	25.45502	H	-12.4816	7.216602	25.75181
N	-12.6436	9.656886	24.0857	N	-12.7089	9.538137	24.38229
H	-12.4057	9.904865	25.05516	H	-12.5074	9.794984	25.34701
C	-12.5822	8.378471	23.57061	C	-12.6036	8.257449	23.87742
C	-13.0241	10.508	23.11411	C	-13.1202	10.36626	23.39769
H	-13.1535	11.56887	23.248	H	-13.3059	11.42353	23.5276
N	-13.2151	9.840788	21.98	N	-13.2723	9.678926	22.27159
C	-12.9307	8.512468	22.2544	C	-12.9439	8.371438	22.55549
H	-12.98	7.751684	21.49075	H	-12.9818	7.601225	21.79925
Zn	-14.1138	10.304435	20.26375	Zn	-14.1548	10.313271	20.57466
O	-14.5503	12.06804	19.55523	O	-14.4576	12.15952	20.68777
H	-15.0378	12.75899	20.05152	H	-15.41	12.8783	19.80509
H	-14.892	12.1186	18.54993	H	-13.6606	12.64218	20.9662
H	-13.7317	7.408557	15.13355	O	-16.1605	13.29624	19.23822
H	-17.2184	10.93059	14.88415	H	-16.9776	12.81747	19.48088
H	-19.481	7.064324	19.16792	H	-15.9349	13.03694	17.76737
H	-12.6673	6.302841	24.0913	H	-13.8023	7.513534	15.23187
				H	-17.4437	10.81903	14.6218

				H	-19.3858	6.961499	19.04418
				H	-12.7472	6.204084	24.33988
Structure E – Zn^{II} /Å				Structure F – Zn^{II} /Å			
Atom	x	y	z	Atom	x	y	z
C	-13.0029	8.201136	15.37083	C	-13.1047	8.232278	15.3253
H	-13.2468	9.072722	14.75733	H	-13.3581	9.114932	14.73207
H	-12.072	7.782556	14.97333	H	-12.1547	7.850373	14.9369
N	-11.9049	8.043292	17.65424	N	-12.0309	8.068218	17.61569
H	-11.2696	7.278656	17.40079	H	-11.3257	7.35932	17.38438
C	-12.8327	8.613561	16.80151	C	-12.99	8.590535	16.76833
C	-12.013	8.621436	18.86895	C	-12.2161	8.592176	18.84486
H	-11.3761	8.377419	19.70938	H	-11.5479	8.409346	19.6726
N	-12.9724	9.54385	18.8461	N	-13.256	9.417632	18.83601
C	-13.4794	9.555152	17.55824	C	-13.7406	9.434255	17.54629
H	-14.2377	10.26461	17.25524	H	-14.5573	10.07898	17.2533
C	-16.5869	11.70448	15.12265	C	-16.8209	11.62319	14.92726
H	-16.9693	12.62881	14.6733	H	-17.1708	12.5248	14.40801
H	-15.5952	11.52051	14.70482	H	-15.8057	11.43718	14.57001
C	-16.4763	11.90656	16.64566	C	-16.7668	11.93801	16.43617
O	-15.2916	12.15203	17.07244	O	-15.6799	12.51287	16.8127
O	-17.5003	11.83337	17.36553	O	-17.7305	11.67877	17.19622
C	-19.1192	8.141378	19.34068	C	-19.0872	8.080198	19.18823
H	-19.8546	8.573105	20.03314	H	-19.8674	8.505108	19.83485
H	-19.1879	8.682919	18.39485	H	-19.1414	8.589932	18.22292
N	-17.2551	7.743917	21.05005	N	-17.248	7.754909	20.93897
H	-17.6505	6.922441	21.51178	H	-17.5878	6.873974	21.33225
C	-17.744	8.344245	19.89766	C	-17.7488	8.369172	19.80171
C	-16.0534	8.296323	21.33496	C	-16.1069	8.3843	21.29446
H	-15.4708	8.016971	22.20019	H	-15.5201	8.101902	22.15666
N	-15.7408	9.232765	20.44819	N	-15.8412	9.385724	20.46147
C	-16.7919	9.26744	19.54909	C	-16.8674	9.386568	19.5276
H	-16.8291	9.983951	18.74182	H	-16.9498	10.13621	18.74941

C	-12.1455	7.152365	24.47567	C	-12.1986	7.168484	24.63554
H	-11.063	7.02703	24.34258	H	-11.1145	7.006449	24.58924
H	-12.3475	7.27409	25.54281	H	-12.4733	7.313632	25.68266
N	-12.8691	9.553333	24.30955	N	-12.8154	9.605063	24.33433
H	-12.6345	9.776922	25.28444	H	-12.7403	9.847765	25.31694
C	-12.6403	8.333994	23.71061	C	-12.598	8.347835	23.80596
C	-13.3127	10.42059	23.378	C	-13.1944	10.43943	23.34395
H	-13.5737	11.44468	23.59309	H	-13.4488	11.47981	23.49038
N	-13.3847	9.819758	22.1951	N	-13.2117	9.78641	22.18711
C	-12.9598	8.521104	22.39204	C	-12.8355	8.4864	22.46307
H	-12.9084	7.810695	21.5814	H	-12.7703	7.736981	21.68843
Zn	-13.9697	10.480781	20.35269	Zn	-13.9698	10.428269	20.42383
O	-12.4039	12.08575	20.77123	O	-14.6943	12.23209	20.75752
H	-12.7169	12.65252	21.51974	H	-15.3958	12.63782	20.02762
H	-11.5883	11.69057	21.11548	H	-14.0844	12.96263	20.99245
O	-14.9921	11.96175	19.53606	O	-16.2659	13.1424	19.15049
H	-15.294	12.78734	19.9668	H	-17.1174	12.66444	19.20534
H	-15.1508	12.07328	18.49654	H	-15.9568	12.93639	18.15075
H	-13.7669	7.448416	15.17644	O	-12.0566	11.65498	19.93342
H	-17.2749	10.92275	14.80067	H	-11.8005	12.06156	20.79821
H	-19.4033	7.108392	19.13985	H	-12.1596	12.40004	19.32668
H	-12.6682	6.254504	24.14592	H	-13.8466	7.466103	15.10034
				H	-17.4769	10.81271	14.60976
				H	-19.3285	7.032251	19.01042
				H	-12.7313	6.285102	24.2835
Structure G – Zn^{II} /Å				Structure H – Zn^{II} /Å			
Atom	x	y	z	Atom	x	y	z
C	-13.0913	8.174253	15.38966	C	-13.0303	8.211861	15.44405
H	-13.3084	9.060241	14.78503	H	-13.2481	9.079779	14.81496
H	-12.1417	7.770232	15.02379	H	-12.0937	7.778915	15.0766
N	-11.9731	8.098246	17.66246	N	-11.9528	8.110989	17.74415
H	-11.2442	7.415648	17.42693	H	-11.2951	7.364533	17.50287

C	-12.9923	8.531754	16.83621	C	-12.8904	8.640064	16.87476
C	-12.1662	8.623025	18.89131	C	-12.0836	8.717412	18.94713
H	-11.4702	8.493076	19.70523	H	-11.4423	8.512948	19.79586
N	-13.2645	9.36617	18.90434	N	-13.0689	9.61061	18.90188
C	-13.7832	9.321665	17.63059	C	-13.566	9.577094	17.61286
H	-14.6765	9.865185	17.36319	H	-14.3402	10.25417	17.2857
C	-16.7985	11.62577	14.8718	C	-16.5968	11.72089	14.93792
H	-17.0734	12.51135	14.28627	H	-16.9743	12.6241	14.44116
H	-15.7577	11.40793	14.62183	H	-15.6257	11.49473	14.49463
C	-16.887	11.98969	16.35131	C	-16.3984	12.02359	16.43576
O	-15.8709	12.74514	16.73827	O	-15.2069	12.37927	16.75162
O	-17.7938	11.65251	17.1105	O	-17.3577	11.92587	17.23899
C	-19.1013	8.056646	19.21674	C	-19.1439	8.145219	19.32597
H	-19.8839	8.477173	19.86361	H	-19.8871	8.578807	20.009
H	-19.1495	8.573738	18.25463	H	-19.2079	8.677816	18.37519
N	-17.2654	7.700894	20.96622	N	-17.2954	7.773971	21.05663
H	-17.6054	6.812985	21.34511	H	-17.6747	6.934923	21.50169
C	-17.764	8.331534	19.8377	C	-17.776	8.361598	19.89359
C	-16.1158	8.317551	21.3237	C	-16.1001	8.339525	21.35012
H	-15.5265	8.020906	22.17967	H	-15.5129	8.060242	22.21286
N	-15.8454	9.324914	20.50374	N	-15.7934	9.279407	20.46533
C	-16.8745	9.34536	19.57777	C	-16.83	9.293641	19.55031
H	-16.9492	10.10753	18.81433	H	-16.8534	9.995587	18.72891
C	-12.2033	7.139555	24.6718	C	-12.1139	7.074328	24.47086
H	-11.1191	6.974813	24.63675	H	-11.0331	6.907789	24.36512
H	-12.4888	7.283247	25.71604	H	-12.3345	7.21721	25.53247
N	-12.8358	9.573424	24.35788	N	-12.5123	9.529206	24.22295
H	-12.7843	9.82245	25.33987	H	-12.2337	9.757577	25.18616
C	-12.5936	8.317477	23.83714	C	-12.5329	8.264489	23.67995
C	-13.2076	10.39864	23.3565	C	-12.9082	10.40779	23.28031
H	-13.4798	11.43638	23.48831	H	-12.9699	11.46786	23.45663
N	-13.1958	9.741081	22.20365	N	-13.1914	9.77663	22.14925
C	-12.8084	8.448861	22.48955	C	-12.9469	8.441216	22.38505
H	-12.72	7.69847	21.71802	H	-13.0699	7.698952	21.61131

Zn	-13.9874	10.425440	20.47036	Zn	-14.077	10.580705	20.45421
O	-14.6752	12.17605	20.72734	O	-12.6041	12.27086	20.71081
H	-15.6081	12.79055	19.8109	H	-13.0197	12.76038	19.98056
H	-14.0545	12.87365	21.00197	H	-12.7926	12.79211	21.51841
O	-16.317	13.22303	19.18708	O	-14.7744	12.13624	19.22233
H	-17.1561	12.76551	19.39434	H	-15.3311	12.79154	19.6917
H	-16.0197	12.98128	17.74342	H	-14.9832	12.23529	18.21503
O	-12.027	11.75298	19.8024	O	-15.3577	11.88707	21.87723
H	-11.7872	12.06585	20.70886	H	-14.8406	12.52112	22.40734
H	-12.4842	12.5154	19.42301	H	-15.9696	11.41432	22.48109
H	-13.8433	7.424428	15.14405	H	-13.7965	7.465839	15.23314
H	-17.4376	10.80653	14.5424	H	-17.3052	10.93027	14.69052
H	-19.3434	7.011069	19.02642	H	-19.4211	7.109463	19.12993
H	-12.7364	6.260569	24.3095	H	-12.6652	6.193462	24.14179
Structure I – Zn^{II} /Å				Structure J – Zn^{II} /Å			
Atom	x	y	z	Atom	x	y	z
C	-13.1048	7.897089	15.54582	C	-13.1372	8.564477	15.4159
H	-13.2022	8.833705	14.98356	H	-13.4307	9.457209	14.85795
H	-12.1861	7.417844	15.19211	H	-12.1867	8.220911	14.9936
N	-11.8264	8.052638	17.71196	N	-12.1304	8.226912	17.71906
H	-11.0088	7.515079	17.41062	H	-11.457	7.499349	17.45414
C	-13.0205	8.148893	17.01849	C	-12.992	8.893196	16.8676
C	-12.0298	8.483234	18.97679	C	-12.2881	8.719108	18.96285
H	-11.2427	8.543956	19.71062	H	-11.7192	8.394576	19.81961
N	-13.287	8.863859	19.14034	N	-13.2111	9.672118	18.96362
C	-13.9139	8.646865	17.93086	C	-13.6505	9.794914	17.66088
H	-14.965	8.858265	17.81227	H	-14.3804	10.53482	17.37694
C	-16.8257	11.62636	14.84344	C	-16.8821	11.84098	14.70597
H	-17.0459	12.49154	14.20721	H	-17.4423	12.75287	14.46128
H	-15.7726	11.38923	14.66504	H	-16.0848	11.74591	13.97028
C	-16.9844	12.05379	16.30304	C	-16.218	12.03781	16.0698
O	-16.1276	13.00484	16.62837	O	-14.9915	12.2823	16.08253

O	-17.7946	11.58218	17.1	O	-16.9408	11.9761	17.13706
C	-19.1691	8.078459	19.19097	C	-19.156	8.093677	19.35403
H	-19.9611	8.496732	19.82788	H	-19.9104	8.518671	20.02882
H	-19.2182	8.584821	18.2233	H	-19.224	8.623363	18.40039
N	-17.3349	7.766902	20.95266	N	-17.3686	7.8101	21.1572
H	-17.6585	6.875759	21.3364	H	-17.7703	7.005946	21.64557
C	-17.8422	8.383024	19.81984	C	-17.8	8.324406	19.94278
C	-16.2081	8.417021	21.3216	C	-16.1996	8.39739	21.48056
H	-15.6163	8.135679	22.18079	H	-15.6598	8.188807	22.39174
N	-15.9594	9.432027	20.50259	N	-15.8488	9.277856	20.54959
C	-16.9807	9.422574	19.56649	C	-16.8325	9.221007	19.57801
H	-17.0654	10.17873	18.79855	H	-16.7957	9.828416	18.68835
C	-12.2105	7.195325	24.61157	C	-12.2215	7.120508	24.72675
H	-11.1249	7.052123	24.54113	H	-11.1336	6.996072	24.65086
H	-12.4663	7.32121	25.66614	H	-12.4706	7.237549	25.784
N	-12.8873	9.622312	24.36178	N	-12.6765	9.595474	24.41257
H	-12.7942	9.854653	25.34455	H	-12.4036	9.896239	25.3579
C	-12.6536	8.378417	23.8089	C	-12.6649	8.304172	23.92256
C	-13.319	10.45796	23.39057	C	-13.0852	10.43037	23.43896
H	-13.6024	11.48693	23.55938	H	-13.1224	11.50337	23.55268
N	-13.3533	9.821415	22.22816	N	-13.3377	9.744914	22.32437
C	-12.9341	8.530508	22.47534	C	-13.0698	8.421703	22.61838
H	-12.8758	7.799333	21.68287	H	-13.1891	7.64264	21.87987
Zn	-14.0514	10.414031	20.37597	C	-13.6644	14.70532	20.6799
O	-14.6617	12.37692	21.0875	H	-13.8024	14.9173	21.74297
H	-15.2536	12.81869	20.39265	H	-14.1805	15.47431	20.10164
H	-14.0486	13.08177	21.38747	H	-12.5928	14.73273	20.46093
O	-14.4112	11.4947	18.56444	C	-14.1791	13.33646	20.38739
H	-15.1995	12.15568	18.72371	O	-13.7013	12.32266	20.96943
H	-14.4972	11.10792	17.68722	N	-15.1504	13.231	19.49575
O	-16.1951	13.14414	19.12436	H	-15.5879	14.01111	19.00122
H	-17.0364	12.69171	19.32267	O	-15.6323	11.96494	19.23035
H	-16.2095	13.20336	17.67788	H	-16.1022	12.00877	18.26677
O	-12.1196	11.37644	19.9239	Zn	-14.1395	10.408500	20.59153

H	-11.8653	11.89773	20.72445	H	-13.8594	7.777112	15.20028
H	-12.4789	12.00606	19.28102	H	-17.5788	11.01319	14.57357
H	-13.9114	7.242461	15.21574	H	-19.4	7.04887	19.16196
H	-17.4425	10.79384	14.50494	H	-12.7306	6.221379	24.37975
H	-19.3985	7.028325	19.0103				
H	-12.7336	6.307284	24.25692				
Structure K – Zn^{II} /Å							
Atom	x	y	z				
C	-13.1486	8.545014	15.50242				
H	-13.4171	9.436793	14.92973				
H	-12.1902	8.189834	15.10828				
N	-12.1787	8.249061	17.83193				
H	-11.4891	7.535023	17.57874				
C	-13.0376	8.886444	16.95626				
C	-12.3637	8.770036	19.06535				
H	-11.7968	8.475135	19.93486				
N	-13.3016	9.707074	19.03759				
C	-13.7188	9.793356	17.72495				
H	-14.4503	10.51772	17.41229				
C	-16.9096	11.8433	14.67739				
H	-17.4841	12.74726	14.43368				
H	-16.1115	11.7608	13.94042				
C	-16.2401	12.05226	16.03846				
O	-15.0179	12.31978	16.03321				
O	-16.9484	11.97812	17.11515				
C	-19.2253	8.077083	19.35726				
H	-19.9793	8.498449	20.03454				
H	-19.2889	8.610992	18.40595				
N	-17.4316	7.730174	21.13746				
H	-17.828	6.90461	21.59681				

C	-17.8662	8.28409	19.94237				
C	-16.2326	8.272426	21.44395				
H	-15.6837	8.025477	22.34104				
N	-15.8771	9.16528	20.53076				
C	-16.8819	9.165743	19.58335				
H	-16.8483	9.804714	18.71486				
C	-12.2284	7.110595	24.70623				
H	-11.141	6.979463	24.62942				
H	-12.4749	7.219913	25.76552				
N	-12.582	9.59825	24.40666				
H	-12.2614	9.88693	25.34159				
C	-12.658	8.309354	23.91622				
C	-12.9815	10.45588	23.44642				
H	-12.9232	11.53169	23.55073				
N	-13.3163	9.788661	22.34423				
C	-13.1097	8.453181	22.62879				
H	-13.2961	7.685033	21.89299				
C	-13.5808	14.81159	20.44158				
H	-13.8127	15.06828	21.47892				
H	-14.0816	15.52761	19.78642				
H	-12.4984	14.88048	20.30668				
C	-14.0068	13.40296	20.18186				
O	-13.4576	12.43638	20.77247				
N	-15.0034	13.23533	19.32503				
H	-15.4922	13.99175	18.84343				
O	-15.4484	11.95185	19.08655				
H	-16.0186	11.99353	18.1916				
Zn	-14.2707	10.531354	20.69125				
O	-15.8569	11.61824	21.86545				
H	-15.6039	12.33491	22.49524				
H	-16.4271	11.02163	22.39622				

H	-13.8718	7.764524	15.26588				
H	-17.5906	11.00288	14.54284				
H	-19.4664	7.032942	19.15806				
H	-12.7402	6.214775	24.35458				

S11) Optimized model geometries used for EPR parameter calculations.

Table 11: Optimized Cartesian coordinates in xyz format

Structure A – Co^{2+} /Å				Structure B – Co^{2+} /Å			
Atom	x	y	z	Atom	x	y	z
C	-24.3798	23.34405	14.19457	C	-24.4966	23.48757	14.16729
H	-23.6451	24.0592	13.80805	H	-23.7822	24.19773	13.73791
H	-24.8165	22.80975	13.3489	H	-24.9867	22.95632	13.34942
N	-22.6485	22.6915	15.96098	N	-22.5991	22.78218	15.73545
H	-22.1607	23.5915	16.01575	H	-22.0916	23.674	15.76242
C	-23.7358	22.38961	15.14886	C	-23.7912	22.52458	15.06967
C	-22.3746	21.61908	16.73444	C	-22.2585	21.70065	16.46527
H	-21.5925	21.59771	17.47786	H	-21.356	21.62765	17.05486
N	-23.2124	20.63043	16.45384	N	-23.1699	20.74141	16.30418
C	-24.0577	21.10099	15.46965	C	-24.1194	21.24732	15.43172
H	-24.866	20.4986	15.09636	H	-24.9791	20.67115	15.13963
C	-27.3325	19.92339	19.05452	C	-27.2356	20.19884	18.94683
H	-27.7769	19.40571	18.19916	H	-27.6963	19.74997	18.0613
H	-27.4632	19.24282	19.90486	H	-27.3255	19.43093	19.72618
C	-25.839	20.09562	18.74024	C	-25.7629	20.34449	18.64069
O	-25.2559	21.17874	18.72532	O	-25.0972	19.32178	18.39257
O	-25.266	18.94098	18.48974	O	-25.214	21.54126	18.67683
C	-19.41	15.69721	19.08633	H	-24.2282	21.4983	18.71279
H	-18.4877	16.10118	19.5127	C	-19.4267	15.70008	19.06039
H	-19.8316	15.02243	19.83883	H	-18.5044	16.09478	19.49458
N	-20.1042	18.08766	19.32568	H	-19.865	15.03566	19.81262
H	-19.2484	18.37485	19.83587	N	-20.122	18.08429	19.34101
C	-20.347	16.82934	18.8066	H	-19.2813	18.35532	19.89067
C	-21.1117	18.90919	18.98552	C	-20.346	16.84453	18.77067
H	-21.1819	19.94409	19.29201	C	-21.096	18.93036	18.98262
N	-22.0176	18.24022	18.27288	H	-21.1616	19.95068	19.33642
C	-21.5542	16.94041	18.16349	N	-21.974	18.29269	18.19948
H	-22.1222	16.18622	17.64188	C	-21.5171	16.98728	18.07082

C	-22.3597	17.38452	14.46679	H	-22.0681	16.25578	17.5021
H	-22.2423	18.40217	14.07656	C	-22.3323	17.36313	14.39658
H	-21.7728	17.30826	15.38666	H	-22.2132	18.37175	13.98259
N	-24.3616	17.66729	15.94543	H	-21.7398	17.29936	15.31455
C	-23.8018	17.11052	14.79449	N	-24.3213	17.69152	15.88068
C	-25.6487	17.32244	15.95486	C	-23.7717	17.0978	14.73865
H	-26.3678	17.65382	16.68666	C	-25.6122	17.34282	15.91686
N	-25.9372	16.55825	14.88862	H	-26.3377	17.68785	16.63612
H	-26.8866	16.26895	14.61725	N	-25.9064	16.54899	14.87949
C	-24.7874	16.41884	14.1353	H	-26.8595	16.24488	14.62605
H	-24.7805	15.87247	13.2051	C	-24.7663	16.38641	14.11721
Co	-23.6669	18.92225	17.39049	H	-24.7728	15.81125	13.20431
H	-25.1507	23.95453	14.66472	Co	-23.4981	18.97171	17.16773
H	-27.9214	20.83382	19.16567	H	-25.2314	24.10149	14.68815
H	-19.0878	15.11868	18.22053	H	-27.8497	21.0692	19.17788
H	-21.9298	16.67849	13.75634	H	-19.1034	15.11517	18.19933
				H	-21.9036	16.6436	13.69903
Structure C – Co^{2+} /Å				Structure D – Co^{2+} /Å			
Atom	x	y	z	Atom	x	y	z
C	-12.9429	8.144842	15.31905	C	-13.0667	8.269616	15.47377
H	-13.1667	9.007634	14.68571	H	-13.3079	9.156002	14.87955
H	-12.0174	7.700526	14.93864	H	-12.1109	7.890438	15.09709
N	-11.8506	8.05861	17.6163	N	-11.9821	8.124715	17.76506
H	-11.1929	7.307274	17.38197	H	-11.2719	7.423672	17.52657
C	-12.7862	8.582315	16.74248	C	-12.9586	8.626589	16.92257
C	-12.0025	8.639645	18.82518	C	-12.1647	8.649102	18.9943
H	-11.3707	8.431853	19.68046	H	-11.5055	8.455014	19.82577
N	-13.0022	9.52066	18.77482	N	-13.217	9.461012	18.99697
C	-13.4819	9.503248	17.47723	C	-13.709	9.462585	17.70696
H	-14.2518	10.18969	17.15575	H	-14.549	10.07712	17.42154
C	-16.5049	11.70172	15.22442	C	-16.7919	11.63388	14.94846
H	-16.8846	12.63928	14.80181	H	-17.0777	12.52655	14.37994

H	-15.523	11.51867	14.78335	H	-15.7574	11.41882	14.66978
C	-16.3615	11.8857	16.74731	C	-16.8326	11.98668	16.43228
O	-15.1716	12.15072	17.14323	O	-15.8442	12.80191	16.76421
O	-17.3681	11.78349	17.48896	O	-17.6747	11.59379	17.23851
C	-19.2154	8.091216	19.39813	C	-19.1548	8.006154	19.24222
H	-19.9429	8.493879	20.11521	H	-19.9491	8.424542	19.87573
H	-19.3065	8.654853	18.46766	H	-19.1836	8.523537	18.27985
N	-17.3184	7.715429	21.07666	N	-17.3772	7.681834	21.05179
H	-17.7024	6.895196	21.55241	H	-17.7282	6.799279	21.43342
C	-17.8354	8.301324	19.92939	C	-17.8321	8.280414	19.88702
C	-16.1202	8.276059	21.33998	C	-16.2353	8.294436	21.42953
H	-15.5144	8.017271	22.19669	H	-15.684	8.031211	22.32172
N	-15.8353	9.204212	20.42964	N	-15.9293	9.270165	20.57941
C	-16.9013	9.224159	19.54543	C	-16.9254	9.272266	19.61662
H	-16.9579	9.930194	18.72826	H	-16.9658	10.00999	18.82684
C	-12.1556	7.209433	24.40088	C	-12.2037	7.08271	24.70247
H	-11.0688	7.069468	24.32786	H	-11.1201	6.914027	24.65541
H	-12.4053	7.379597	25.452	H	-12.4781	7.222109	25.75076
N	-12.6401	9.651813	24.06799	N	-12.7085	9.54244	24.38052
H	-12.4059	9.90465	25.03687	H	-12.5077	9.80069	25.34471
C	-12.5802	8.370511	23.56124	C	-12.6019	8.262253	23.87609
C	-13.0172	10.49705	23.08834	C	-13.123	10.36964	23.39491
H	-13.1435	11.55941	23.21482	H	-13.3125	11.42583	23.52611
N	-13.2076	9.823435	21.95754	N	-13.2754	9.682431	22.26814
C	-12.9251	8.496155	22.24277	C	-12.943	8.375268	22.55414
H	-12.971	7.729474	21.48445	H	-12.9793	7.603975	21.79869
Co	-14.1392	10.296635	20.24432	Co	-14.1596	10.291592	20.568
O	-14.5369	12.08737	19.54979	O	-14.4481	12.13317	20.73252
H	-15.0424	12.77593	20.03379	H	-15.42	12.86442	19.82298
H	-14.8639	12.14049	18.53503	H	-13.6608	12.63842	21.00389
H	-13.7236	7.406665	15.13551	O	-16.1605	13.28398	19.25771
H	-17.2065	10.93596	14.89351	H	-16.9828	12.81168	19.49696
H	-19.4828	7.05834	19.17503	H	-15.9334	13.03273	17.76843
H	-12.6687	6.298402	24.09297	H	-13.8019	7.504007	15.22594

				H	-17.4383	10.81892	14.6229
				H	-19.3884	6.960247	19.04332
				H	-12.7448	6.208955	24.33932
Structure E – Co^{2+} /Å				Structure F – Co^{2+} /Å			
Atom	x	y	z	Atom	x	y	z
C	-13.0031	8.211045	15.38791	C	-13.0982	8.159975	15.34202
H	-13.2456	9.081338	14.77191	H	-13.3225	9.043942	14.73814
H	-12.0707	7.792112	14.99434	H	-12.1491	7.756993	14.97364
N	-11.9019	8.069761	17.67142	N	-11.999	8.072897	17.62498
H	-11.2639	7.307405	17.42074	H	-11.272	7.385804	17.39582
C	-12.8363	8.627711	16.81796	C	-13.002	8.521203	16.78589
C	-12.013	8.656547	18.88381	C	-12.1977	8.601878	18.85037
H	-11.3722	8.421681	19.72394	H	-11.5104	8.470871	19.67183
N	-12.9813	9.56988	18.85944	N	-13.2899	9.357774	18.84828
C	-13.49	9.567059	17.57169	C	-13.7948	9.321562	17.56659
H	-14.2514	10.27003	17.26266	H	-14.6652	9.894249	17.28185
C	-16.5885	11.70935	15.10507	C	-16.788	11.60971	14.97602
H	-16.9723	12.63096	14.65085	H	-17.105	12.51383	14.44085
H	-15.6012	11.52106	14.6787	H	-15.7655	11.40688	14.64816
C	-16.4569	11.92782	16.62486	C	-16.7685	11.94057	16.48332
O	-15.2716	12.20527	17.02572	O	-15.7275	12.59468	16.85914
O	-17.4678	11.83836	17.36341	O	-17.7139	11.62042	17.24291
C	-19.1216	8.141824	19.33916	C	-19.102	8.068182	19.18895
H	-19.8579	8.571622	20.03178	H	-19.8847	8.491051	19.83398
H	-19.1936	8.682317	18.39311	H	-19.1548	8.578687	18.22396
N	-17.2536	7.758265	21.04858	N	-17.264	7.748789	20.94346
H	-17.6425	6.932809	21.50924	H	-17.5991	6.864839	21.33483
C	-17.7482	8.355385	19.89622	C	-17.7666	8.361235	19.8055
C	-16.0626	8.324812	21.34201	C	-16.128	8.383428	21.30269
H	-15.477	8.050578	22.20691	H	-15.5399	8.105552	22.16553
N	-15.7614	9.269578	20.45629	N	-15.868	9.387283	20.46852
C	-16.809	9.291718	19.55029	C	-16.8929	9.384198	19.53192

H	-16.85	10.00798	18.7426	H	-16.984	10.13762	18.75715
C	-12.1374	7.133802	24.48967	C	-12.1984	7.174778	24.62227
H	-11.0552	7.002891	24.35932	H	-11.1141	7.014907	24.57071
H	-12.3421	7.257175	25.55603	H	-12.4686	7.320132	25.67064
N	-12.8426	9.539083	24.31501	N	-12.8172	9.61016	24.32442
H	-12.608	9.765648	25.2893	H	-12.7315	9.854014	25.30569
C	-12.6235	8.316163	23.72129	C	-12.6058	8.353206	23.79506
C	-13.2752	10.40655	23.37772	C	-13.2061	10.44343	23.33421
H	-13.5247	11.43425	23.58863	H	-13.4584	11.48399	23.48317
N	-13.3508	9.802036	22.19638	N	-13.2367	9.790405	22.17806
C	-12.9379	8.49987	22.40084	C	-12.8574	8.490938	22.45398
H	-12.8834	7.787393	21.59203	H	-12.7956	7.741538	21.67865
Co	-14.0406	10.463913	20.37705	Co	-14.0488	10.409577	20.40673
O	-12.3945	12.01261	20.72004	O	-14.6756	12.25311	20.76805
H	-12.694	12.60073	21.45645	H	-15.3984	12.67206	20.0585
H	-11.5998	11.58979	21.07928	H	-14.074	12.98574	21.02128
O	-14.9376	12.03439	19.49134	O	-16.2895	13.17211	19.20924
H	-15.368	12.80211	19.92126	H	-17.1386	12.69355	19.29579
H	-15.0956	12.13744	18.4538	H	-16.0038	12.97983	18.19232
H	-13.7662	7.457745	15.19213	O	-12.0887	11.48369	20.03596
H	-17.2798	10.9257	14.79517	H	-11.8392	11.93757	20.88013
H	-19.4024	7.107646	19.13989	H	-12.1347	12.18767	19.37535
H	-12.6648	6.239571	24.15755	H	-13.8515	7.408839	15.10463
				H	-17.4464	10.80751	14.64262
				H	-19.3403	7.019772	19.00972
				H	-12.7303	6.289589	24.27351
Structure G – Co^{2+} /Å				Structure H – Co^{2+} /Å			
Atom	x	y	z	Atom	x	y	z
C	-13.09	8.106859	15.39901	C	-13.0546	8.214298	15.49114
H	-13.2817	8.994002	14.78673	H	-13.2647	9.087204	14.86574
H	-12.1434	7.683191	15.04836	H	-12.1145	7.783336	15.1307
N	-11.9503	8.100388	17.66134	N	-11.9562	8.131258	17.78104

H	-11.2032	7.438582	17.42589	H	-11.2845	7.401937	17.53059
C	-13.004	8.467042	16.84531	C	-12.9251	8.629964	16.92774
C	-12.1541	8.630114	18.8871	C	-12.0907	8.730078	18.98913
H	-11.4416	8.549573	19.69307	H	-11.4319	8.541214	19.8278
N	-13.2933	9.31027	18.90861	N	-13.1093	9.585675	18.96476
C	-13.8281	9.217382	17.64349	C	-13.6242	9.536243	17.68299
H	-14.7612	9.695836	17.38716	H	-14.4285	10.18328	17.36969
C	-16.7675	11.61168	14.89598	C	-16.6172	11.72488	14.9126
H	-17.0169	12.49898	14.3021	H	-16.9964	12.62457	14.41042
H	-15.7252	11.37799	14.66605	H	-15.6462	11.49722	14.47037
C	-16.8748	11.98364	16.37219	C	-16.4167	12.03528	16.40812
O	-15.8865	12.77745	16.75576	O	-15.2241	12.39077	16.7199
O	-17.7702	11.62047	17.13289	O	-17.3742	11.94313	17.21448
C	-19.109	8.059392	19.21297	C	-19.1442	8.145558	19.3253
H	-19.8949	8.480807	19.85509	H	-19.8875	8.578467	20.00889
H	-19.1543	8.57334	18.24908	H	-19.2104	8.677664	18.37438
N	-17.2791	7.717282	20.9723	N	-17.2875	7.769479	21.0465
H	-17.6155	6.82825	21.35142	H	-17.6624	6.926777	21.48824
C	-17.7762	8.341706	19.83962	C	-17.7752	8.363269	19.89009
C	-16.1373	8.343229	21.33698	C	-16.0896	8.334811	21.33478
H	-15.551	8.054207	22.19771	H	-15.497	8.04898	22.19159
N	-15.8701	9.351036	20.51435	N	-15.7891	9.281457	20.45459
C	-16.8941	9.361533	19.58103	C	-16.834	9.301113	19.54843
H	-16.9736	10.12323	18.81742	H	-16.8619	10.0047	18.72883
C	-12.1957	7.152098	24.6576	C	-12.1093	7.059658	24.46119
H	-11.1113	6.987848	24.61817	H	-11.0292	6.88705	24.35693
H	-12.477	7.293264	25.70359	H	-12.3304	7.207836	25.52212
N	-12.8171	9.588549	24.35211	N	-12.4827	9.514939	24.2047
H	-12.7433	9.836295	25.33289	H	-12.2079	9.742993	25.16894
C	-12.5915	8.332013	23.8278	C	-12.5199	8.248864	23.66515
C	-13.199	10.41675	23.35364	C	-12.8712	10.394	23.26
H	-13.4631	11.45585	23.49206	H	-12.918	11.45567	23.4342
N	-13.2096	9.760553	22.19994	N	-13.1651	9.762637	22.12997
C	-12.8264	8.46572	22.48324	C	-12.9355	8.425338	22.37047

H	-12.7515	7.715043	21.71009	H	-13.0688	7.68395	21.598
Co	-14.0472	10.408221	20.45492	Co	-14.1097	10.657144	20.49929
O	-14.6617	12.18302	20.74501	O	-12.6365	12.29248	20.71451
H	-15.6225	12.80106	19.8322	H	-12.9968	12.80969	19.97433
H	-14.0521	12.89676	21.00892	H	-12.8013	12.82464	21.52133
O	-16.332	13.23477	19.21679	O	-14.8088	12.1465	19.1842
H	-17.171	12.77713	19.4252	H	-15.3279	12.84389	19.63769
H	-16.0373	13.00637	17.75929	H	-15.0124	12.23716	18.17265
O	-12.0457	11.51334	19.99333	O	-15.3243	11.88944	21.87443
H	-11.8132	11.907	20.87175	H	-14.8139	12.51777	22.41961
H	-12.2769	12.28216	19.45503	H	-15.9544	11.41373	22.45997
H	-13.8527	7.370998	15.14432	H	-13.8181	7.469866	15.26528
H	-17.4113	10.79994	14.55726	H	-17.3241	10.93078	14.67211
H	-19.3493	7.01305	19.02457	H	-19.421	7.109638	19.12953
H	-12.7285	6.272225	24.2971	H	-12.665	6.180646	24.13473
Structure I – Co^{2+} /Å				Structure J – Co^{2+} /Å			
Atom	x	y	z	Atom	x	y	z
C	-13.1031	7.882501	15.57955	C	-13.1363	8.553941	15.4209
H	-13.1886	8.823386	15.022	H	-13.4216	9.443671	14.85395
H	-12.1864	7.397426	15.22838	H	-12.1837	8.204284	15.00863
N	-11.82	8.057207	17.73993	N	-12.1414	8.24064	17.73415
H	-10.9973	7.530697	17.43442	H	-11.4628	7.515531	17.47707
C	-13.0215	8.127672	17.0545	C	-13.003	8.892616	16.8714
C	-12.023	8.488492	19.00507	C	-12.311	8.744675	18.97256
H	-11.2335	8.560213	19.73514	H	-11.7423	8.436643	19.8357
N	-13.2861	8.84765	19.17742	N	-13.2435	9.689981	18.95912
C	-13.9169	8.611886	17.97204	C	-13.6742	9.795608	17.65171
H	-14.9738	8.79802	17.86189	H	-14.4082	10.52534	17.35498
C	-16.8298	11.62945	14.83083	C	-16.8824	11.84175	14.71591
H	-17.0503	12.4915	14.19051	H	-17.4459	12.75476	14.48285
H	-15.7753	11.39525	14.65695	H	-16.0909	11.75418	13.97274
C	-16.9959	12.06189	16.28729	C	-16.204	12.033	16.07326

O	-16.1434	13.01876	16.61135	O	-14.9825	12.29674	16.07266
O	-17.8051	11.59114	17.08492	O	-16.9107	11.94808	17.15094
C	-19.1688	8.077961	19.19804	C	-19.1557	8.086738	19.35379
H	-19.9589	8.493223	19.83943	H	-19.9087	8.513046	20.02926
H	-19.2236	8.585721	18.23138	H	-19.2232	8.616611	18.40015
N	-17.313	7.75672	20.93712	N	-17.3726	7.807473	21.16157
H	-17.6328	6.863621	21.32024	H	-17.7759	7.005078	21.65153
C	-17.8375	8.382674	19.81762	C	-17.7993	8.314574	19.94181
C	-16.1786	8.401787	21.2917	C	-16.2032	8.393825	21.48411
H	-15.5717	8.110834	22.13676	H	-15.6651	8.188883	22.39706
N	-15.9423	9.424817	20.47861	N	-15.8454	9.265159	20.54572
C	-16.9808	9.425347	19.56115	C	-16.8275	9.203099	19.57127
H	-17.0762	10.18601	18.79917	H	-16.7864	9.802859	18.6765
C	-12.2123	7.195517	24.60697	C	-12.2227	7.121673	24.72326
H	-11.1265	7.050867	24.54223	H	-11.1346	6.996883	24.65086
H	-12.4724	7.32643	25.65999	H	-12.475	7.242874	25.77944
N	-12.8763	9.623773	24.33802	N	-12.6748	9.595088	24.39987
H	-12.7922	9.861677	25.31998	H	-12.4027	9.898113	25.34462
C	-12.6502	8.374406	23.79515	C	-12.6641	8.302434	23.91345
C	-13.2953	10.45537	23.3571	C	-13.0801	10.4274	23.42207
H	-13.5714	11.48732	23.52001	H	-13.1149	11.50069	23.53325
N	-13.331	9.81128	22.19751	N	-13.3329	9.739106	22.30786
C	-12.9254	8.518109	22.45924	C	-13.0669	8.416191	22.60794
H	-12.8701	7.780109	21.6735	H	-13.1845	7.635247	21.87116
Co	-14.0608	10.454098	20.36248	C	-13.6606	14.71233	20.67538
O	-14.6923	12.36862	21.05107	H	-13.8041	14.93379	21.7357
H	-15.2937	12.80815	20.34964	H	-14.1737	15.47578	20.08738
H	-14.0821	13.07394	21.35663	H	-12.5878	14.73797	20.46202
O	-14.4752	11.44263	18.52673	C	-14.1725	13.34131	20.39234
H	-15.2501	12.1148	18.69307	O	-13.7032	12.3314	20.99101
H	-14.6216	10.99248	17.68896	N	-15.1327	13.22073	19.4912
O	-16.2116	13.13453	19.12222	H	-15.5751	13.99286	18.98811
H	-17.0609	12.6972	19.32231	O	-15.6085	11.94769	19.24039
H	-16.2229	13.21196	17.65193	H	-16.0807	11.98034	18.26849

O	-12.1694	11.43441	19.9391	Co	-14.1622	10.428392	20.59509
H	-11.8804	11.91133	20.75712	H	-13.8603	7.768818	15.20309
H	-12.454	12.11056	19.30753	H	-17.5783	11.01373	14.58117
H	-13.9124	7.236802	15.23872	H	-19.4013	7.042283	19.16171
H	-17.443	10.79328	14.49473	H	-12.7312	6.221371	24.37828
H	-19.397	7.027816	19.01586				
H	-12.7348	6.306288	24.25433				
Structure K – Co^{2+} /Å							
Atom	x	y	z				
C	-13.1465	8.491912	15.5303				
H	-13.3943	9.382955	14.94635				
H	-12.185	8.124365	15.15627				
N	-12.1524	8.266538	17.85917				
H	-11.4379	7.577108	17.60943				
C	-13.056	8.839268	16.98479				
C	-12.3562	8.793163	19.08925				
H	-11.7695	8.540357	19.95814				
N	-13.3511	9.668255	19.06139				
C	-13.786	9.707861	17.75257				
H	-14.5695	10.37334	17.43861				
C	-16.8712	11.82953	14.73727				
H	-17.4378	12.74416	14.51618				
H	-16.0851	11.75113	13.98708				
C	-16.1744	12.01865	16.08553				
O	-14.9621	12.30935	16.06454				
O	-16.8593	11.90662	17.18011				
C	-19.264	8.062584	19.3737				
H	-20.0158	8.475416	20.05867				
H	-19.3347	8.603795	18.42699				
N	-17.4566	7.714355	21.13978				

H	-17.8492	6.888538	21.60214				
C	-17.9019	8.267347	19.94924				
C	-16.2491	8.249784	21.42937				
H	-15.6901	8.001501	22.31988				
N	-15.8988	9.137263	20.50872				
C	-16.9182	9.142874	19.57628				
H	-16.8916	9.776626	18.70347				
C	-12.2436	7.131427	24.65613				
H	-11.1559	7.002736	24.57715				
H	-12.4874	7.249774	25.71554				
N	-12.5998	9.614565	24.34585				
H	-12.275	9.904454	25.27846				
C	-12.6786	8.324157	23.85832				
C	-13.0055	10.46858	23.38417				
H	-12.9483	11.54376	23.49084				
N	-13.3481	9.800738	22.28379				
C	-13.1372	8.465584	22.57217				
H	-13.3266	7.695907	21.83883				
C	-13.5394	14.8292	20.43196				
H	-13.7883	15.1114	21.45879				
H	-14.0299	15.52777	19.75062				
H	-12.4551	14.8939	20.3123				
C	-13.9631	13.41525	20.20282				
O	-13.4077	12.45795	20.80166				
N	-14.9711	13.22913	19.35895				
H	-15.4746	13.97191	18.87213				
O	-15.4231	11.93792	19.15854				
H	-15.9884	11.94193	18.22237				
Co	-14.3789	10.600390	20.66094				
O	-15.8361	11.63035	21.90331				
H	-15.5722	12.33982	22.53874				

H	-16.4179	11.03398	22.42409				
H	-13.8743	7.719492	15.2817				
H	-17.5637	10.99958	14.59673				
H	-19.5002	7.018613	19.16779				
H	-12.7527	6.229569	24.31628				

S12) Calibration of computed cobalt isotropic hyperfine coupling constants

We calibrated the chosen QM(TPSSh/CP(PPP)) level of theory for the calculation of cobalt(II) isotropic hyperfine coupling constants against experimental data. Geometries of $Co(H_2O)_6^{2+}$, $Co(acac)_2(H_2O)_2$ (acac is acetylacetonate), and Co(*N*-MeIz)$_6^{2+}$ (*N*-MeIz is *N*-methylimidazole) were optimized with the B3LYP functional in combination with the 6-31G** basis set. Cobalt(II) isotropic hyperfine constants in these complexes were calculated at the QM(TPSSh/CP(PPP)) level of theory and compared to experimental data to obtain a scaling factor of 1.97 (**Table 11**).

Table 11: Determination of a scaling factor *f* for the isotropic hyperfine coupling constants of cobalt, A_{iso}: comparison between calculated and experiments HFCs of cobalt complexes, in MHz.

Distance	A_{iso} (exp)	A_{iso} (calc)	*f*
$Co(H_2O)_6^{2+}$	278	-151	1.84
$Co(acac)_2(H_2O)_2$	239	-115	2.08
Co(*N*-MeIz)$_6^{2+}$	268[a]	-134	2.00

[a] A_z was calculated, $A_{x,y}$ were observed

S13) References

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