Supporting information

Computational Details:

Calculations were undertaken using the Amsterdam Density Functional 2013 (ADF2013.01) suite at a GGA BP86/TZP all-electron level of theory in the spin-unrestricted formalism. Calculations were performed in an unrestricted fashion using the GGA Becke-Perdew density functional and the TZP all-electron basis set. Relativistic corrections using the Zeroth-Order Regular Approximation (ZORA) were applied to the strontium basis set. SCF and geometry optimisation was achieved using the ADF default criteria.

Structural Model:

Calculations proceeded from a model derived from the first listed Mn4CaO5 cluster of RCSB PDB 4IL6 and coordinating amino acids D1-Tyr161, D1-Asp170, D1-Glu189, D1-His190, D1-His332, D1-Glu333, D1-His337, D1-Asp342, D1-Ala344, CP43-Glu354 and CP43-Arg357 and the optional presence of D1-Gln165. Three attendant noncovalent waters proximal to W3 were incorporated at their crystallographic positions with their oxygen atoms constrained in Cartesian space but were otherwise rotable. Carboxylate-terminal amino acids (Ala, Asp, Glu) coordinating the cluster were truncated to ethanoate ions and their terminal methyl carbons pinned in Cartesian space. Histidine residues were similarly modelled as 4-methylimidazole in either neutral or cationic forms with their terminal methyl carbons pinned in Cartesian space. CP43-Arg357 was truncated to N-methylguanidinium. Dihedrals relating the carbonyl oxygens of D1-Asp170, D1-Glu180 and D1-Ala344, the manganese ions to which these residues were connected and the strontium ion were constrained to their crystallographic values. Protonation of the D1-His337 simulant was enforced by constraint of the N-H distances to 1.10 Å. D1-Tyr161 was modelled as a 4-methylphenol molecule, whilst D1-Gln165 was modelled as ethanamide. Due to the conformational flexibility of non-covalently interacting residues D1-Tyr161, D1-Gln165 and D1-His190, all non-hydrogen atoms of these residues were constrained at their crystallographic positions.

In light of the typical inability of X-ray crystallography to resolve hydrogen atoms, automatic saturation of models was achieved in either PyMOL or ADFInput. Due to the arbitrary orientation of hydroxide and water protons resultant from this technique, where necessary water and hydroxide molecules were rotated about their oxygen atoms into realistic orientations with respect to likely hydrogen bonding partners, prior to optimisation.

Electronic Model:

Model total charge was selected to be consistent with an expected $4\times Mn^{III}$ oxidation state configuration. Manganese ions were spin polarised corresponding to an 'ABBA' Ms=0 spin-coupling configuration, analogous to earlier calculations which modelled the Ca structure. While both the ABBA and ABAB coupling patterns give rise to the lowest energy structures, alternative coupling patterns that satisfy the total spin are not precluded by calculations. In general, the calculations do not exhibit significant variation of interatomic distances with different spin-coupling patterns, except in those cases where a given spin-coupling pattern elicits an Mn oxidation state configuration that is not {III,III,III,III}.

Optimised coordinates of model structure:

These coordinates have been normalised against the non-mass-weighted molecular

centroid and rounded to 4 decimal places for convenience. Cartesian displacements with respect to the origin are given in Å.

	-4.5178	4.9518	6.5593	C	2.7992	0.2148	-5.7027
C	-3.4378	4.6978	5.5413	C	2.2154	-0.5400	-4.5417
C	-2.9248	5.7418	4.7643	O	0.9506	-0.7138	-4.5239
C	-2.9528	3.4078	5.3213	O	3.0589	-0.9266	-3.6709
C	-1.9478	5.5058	3.8023	H	2.9708	1.2509	-5.3739
C	-1.9738	3.1628	4.3723	H	2.1181	0.2400	-6.5620
C	-1.4678	4.2118	3.6213	H	3.7727	-0.2029	-5.9888
O	-0.4978	3.9498	2.6803	C	-2.7898	1.9478	-3.7837
H	-0.1167	4.8093	2.2599	C	-2.2403	0.7887	-2.9665
H	-4.6834	6.0276	6.7088	O	-2.2601	0.8875	-1.7042
H	-3.2918	6.7595	4.9241	O	-1.8119	-0.2316	-3.6247
H	-3.3451	2.5746	5.9097	H	-1.9643	2.3917	-4.3587
H	-1.5358	6.3263	3.2149	H	-3.2188	2.7085	-3.1235
H	-1.5968	2.1581	4.1809	H	-3.5264	1.5836	-4.5144
H	-4.2653	4.5166	7.5382	O	0.9438	-0.0605	-1.8271
H	-5.4801	4.5104	6.2534	O	-1.0066	-1.8200	-1.3552
C	-3.5638	-0.5682	3.5623	O	1.3842	-2.6979	-2.0441
C	-2.6620	-1.2186	2.4989	O	-1.1731	-3.7076	0.5213
O	-2.6494	-0.7744	1.3333	O	1.6913	-1.2591	1.2608
O	-1.9268	-2.2089	2.9425	Sr	-0.5465	0.3075	0.2733
H	-4.0794	0.2933	3.1292	Mn	2.3936	-1.0699	-1.6489
H	-2.9404	-0.2634	4.4129	Mn	-0.1412	-1.2210	-2.8797
H	-4.2915	-1.3043	3.9326	Mn	-0.0433	-3.3396	-0.8914
C	4.0702	2.6018	-0.4167	Mn	-0.5142	-3.3274	2.1613
C	3.2220	1.3685	-0.0938	H	2.0216	-0.3245	1.2933
O	2.2518	1.4951	0.6925	H	1.4221	-1.5150	2.1879
O	3.5512	0.2433	-0.6557	O	-0.4211	2.5958	0.0618
H	4.2161	3.2055	0.4868	H	-1.2028	2.9904	-0.3706
H	3.4947	3.2061	-1.1331	O	-1.7872	-5.4919	2.4441
H	5.0306	2.3238	-0.8650	H	-1.8208	-5.1567	1.5069
C	3.3742	8.5298	2.2623	H	-0.9769	-6.0364	2.4468
C	2.2012	7.6338	1.9473	O	1.7912	2.6688	3.1073
C	1.8262	6.4048	2.4773	H	0.9386	3.1752	2.9587
N	1.2922	7.9338	0.9993	H	2.0479	2.3658	2.1910
C	0.3762	6.9538	0.9373	O	-0.2555	0.6454	2.8571
N	0.7082	6.0178	1.8383	H	0.4563	1.3139	2.9991
H	1.3114	8.7662	0.4186	H	-0.3428	0.1773	3.7368
H	3.9781	8.0746	3.0553	O	0.6707	-2.5903	3.5018
H	2.2982	5.8086	3.2508	H	1.4005	-3.2181	3.6598
H	-0.4520	6.9062	0.2435	O	-0.3258	-0.5002	5.3473
H	3.0533	9.5226	2.6140	H	0.4899	0.0348	5.5355
H	4.0268	8.6747	1.3873	H	0.0134	-1.3314	4.9268
C	6.6032	-3.7862	0.8013	O	1.7972	1.3318	5.6053
C	5.7353	-3.2125	-0.2467	H	1.8587	1.7745	4.7123
C	4.4559	-2.7278	-0.1787	H	1.4202	2.0275	6.1727
N	6.1351	-3.0068	-1.5623	C	-1.5348	-5.1232	-4.6297
C	5.1107	-2.4070	-2.2308	C	-1.0611	-4.1093	-3.5987
N	4.0878	-2.2373	-1.4110	O	-0.7795	-2.9461	-4.0248
H	7.0436	-3.2314	-1.9516	O	-0.9552	-4.5513	-2.4041
H	6.9404	-4.8079	0.5624	H	-2.0883	-5.9400	-4.1521
H	3.7846	-2.6509	0.6717	H	-0.6525	-5.5520	-5.1308
H	5.1403	-2.0887	-3.2649	H	-2.1442	-4.6371	-5.4019
H	6.0533	-3.8319	1.7483	C	-7.0298	-1.7602	-2.4417
H	7.5029	-3.1740	0.9735	N	-5.8274	-2.4707	-2.0033
C	2.5042	-6.4522	0.7973	C	-4.6513	-1.8297	-1.6776
C	1.4939	-5.2932	0.7597	N	-4.6503	-0.4982	-1.5245
O	1.1974	-4.8963	-0.4129	N	-3.5569	-2.5392	-1.4562
O	1.0559	-4.8163	1.8641	H	-2.5666	-2.1286	-1.3630
H	2.1147	-7.2893	0.2033	H	-7.8299	-2.4948	-2.5801
H	2.6987	-6.7828	1.8232	H	-5.6887	-3.3874	-2.4166
H	3.4403	-6.1107	0.3352	H	-5.3693	0.0391	-1.9953
C	3.0632	-5.6982	-7.2347	H	-3.6164	-3.5474	-1.3636
C	2.7091	-5.2627	-5.8326	H	-6.8873	-1.2128	-3.3891
C	2.3557	-4.0463	-5.2875	H	-3.7366	-0.0054	-1.3890
N	2.6881	-6.1463	-4.7504	H	-7.3558	-1.0593	-1.6619
C	2.3413	-5.4806	-3.6230	C	-4.0038	3.6018	1.3793
N	2.1434	-4.2057	-3.9282	C	-3.4698	4.4188	0.2163
H	1.8248	-3.4876	-3.1582	N	-3.5928	5.7418	0.3083
H	2.9887	-4.8411	-7.9128	O	-2.9588	3.8658	-0.7597
H	2.2125	-3.0851	-5.7661	H	-4.3184	4.1958	2.2474
H	2.2121	-5.8996	-2.6306	H	-3.2078	2.9078	1.6774
H	2.3785	-6.4785	-7.5976	H	-4.8508	3.0027	1.0170
H	4.0906	-6.0873	-7.2877	H	-3.8591	6.1856	1.1801
H	2.8847	-7.1408	-4.7951	H	-3.1981	6.3107	-0.4338