First report on the assessment of maximum acceptable daily intake (MADI) of pesticides for humans using intelligent consensus predictions

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Fig.S1. VIP plot of model M1

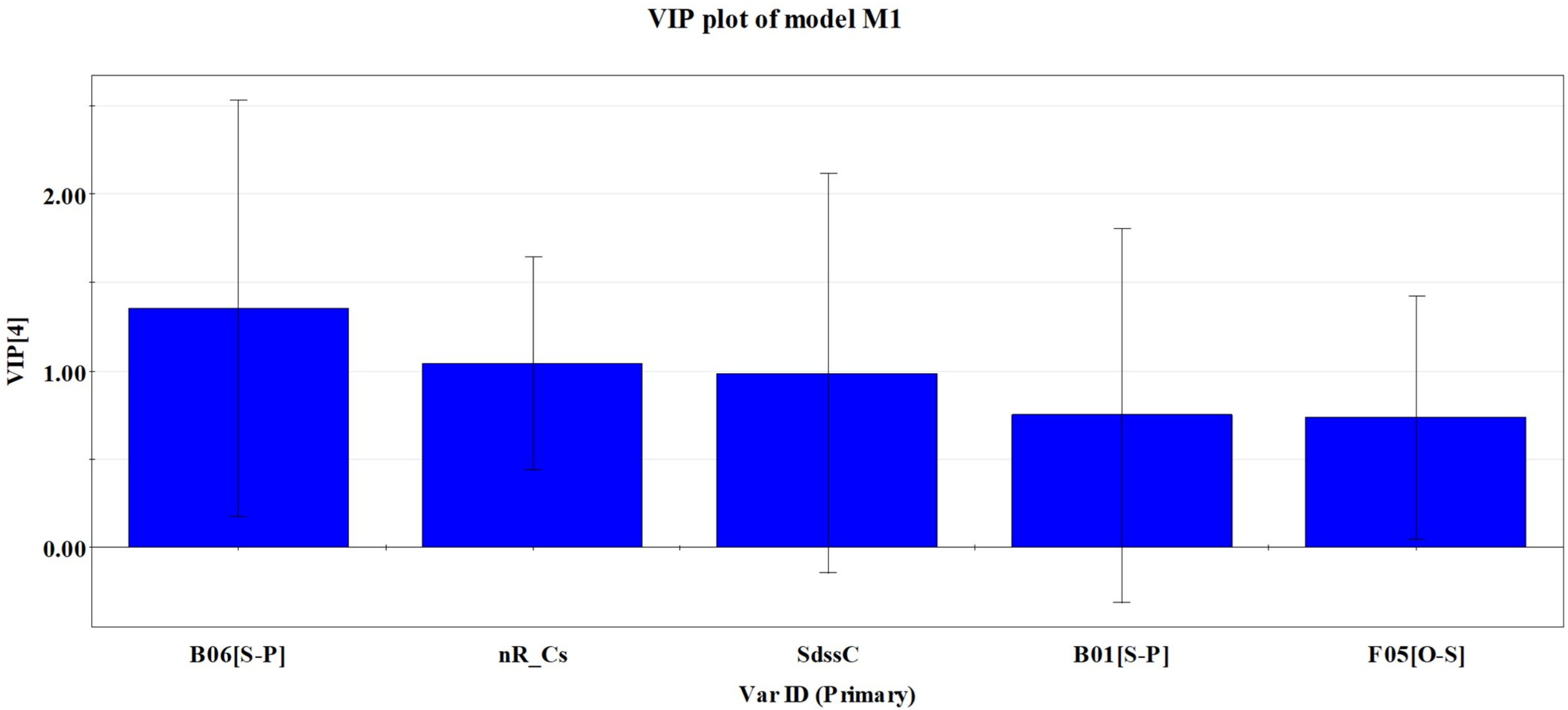

Fig.S2. VIP plot of model M2

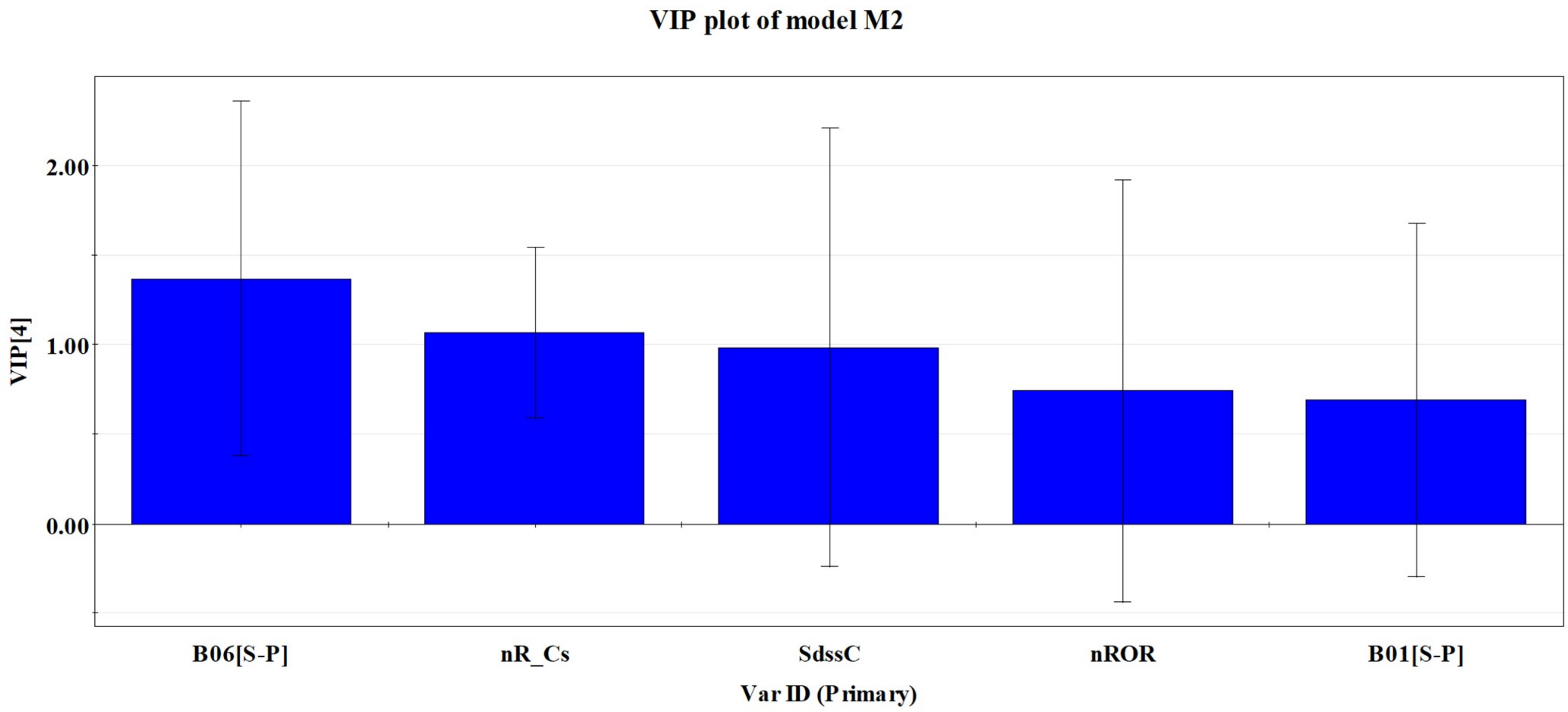

Fig.S3. VIP plot of model M3

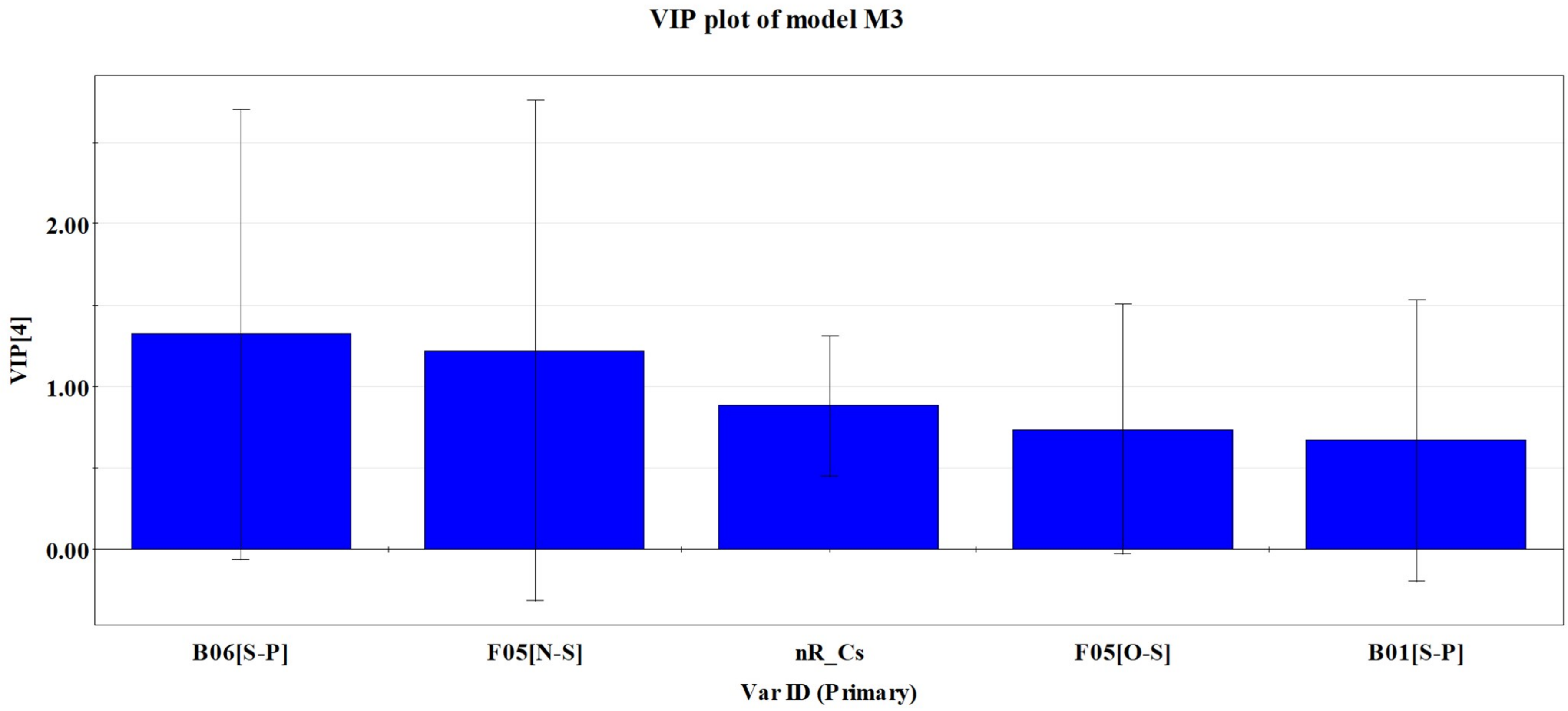

Fig.S4. VIP plot of model M4

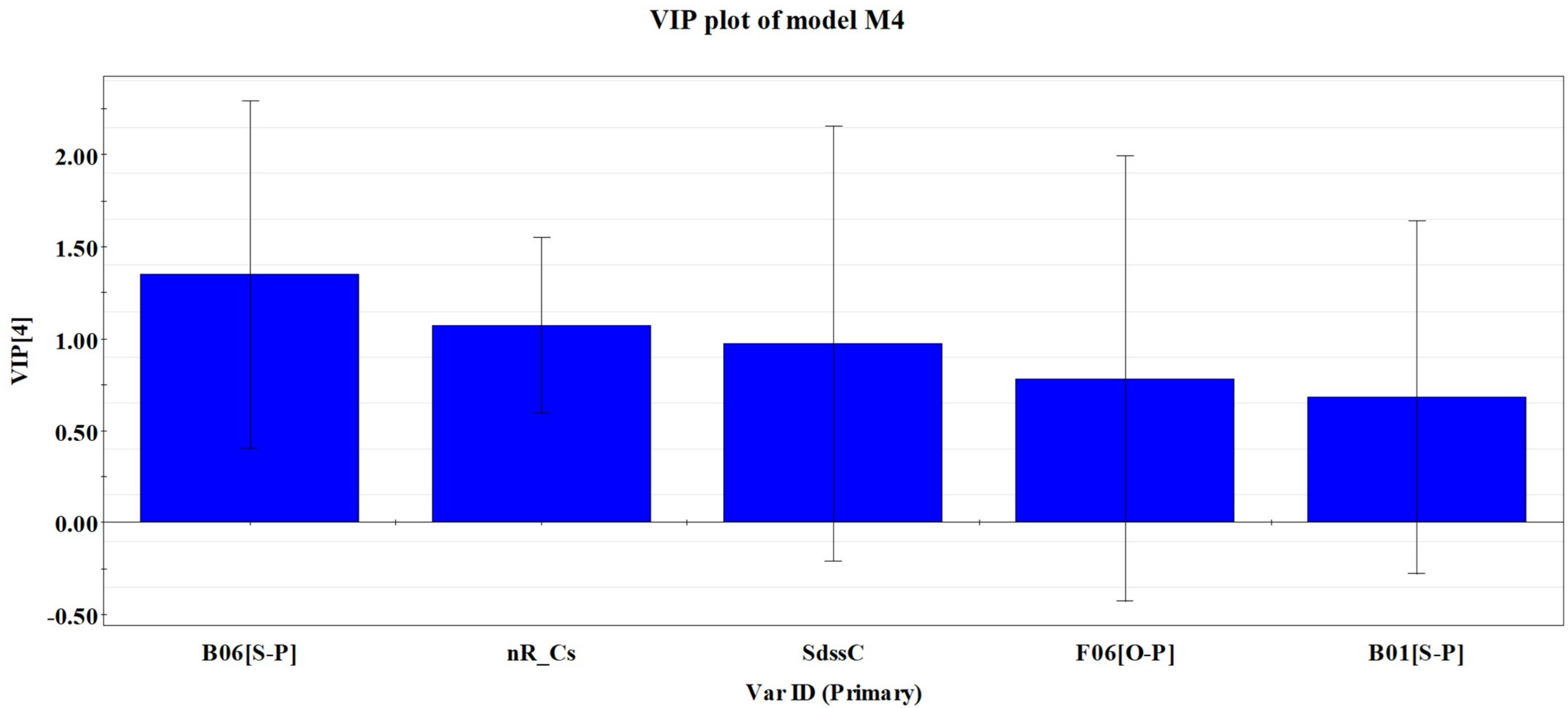

Fig.S5. VIP plot of model M5

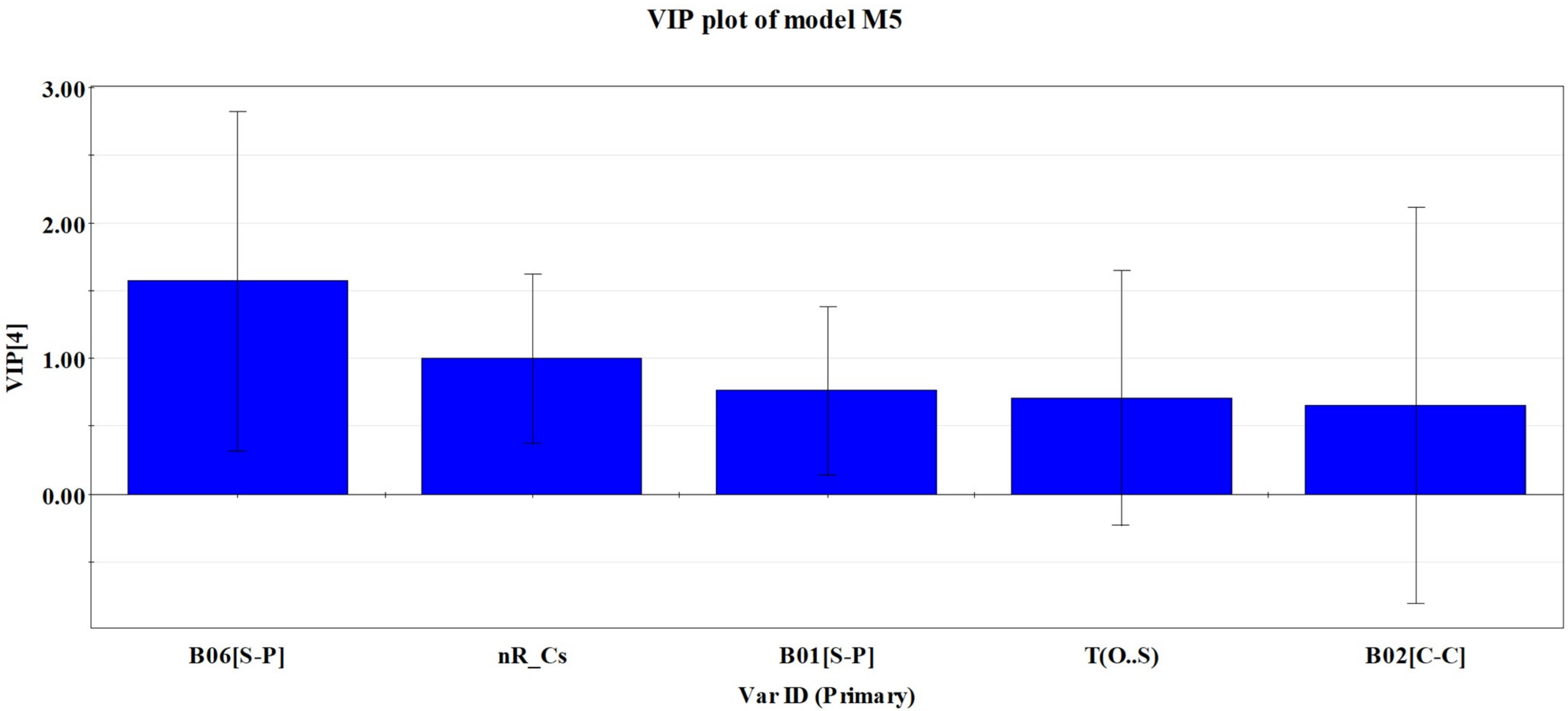

Fig.S6. Regression coefficient plot of model M1

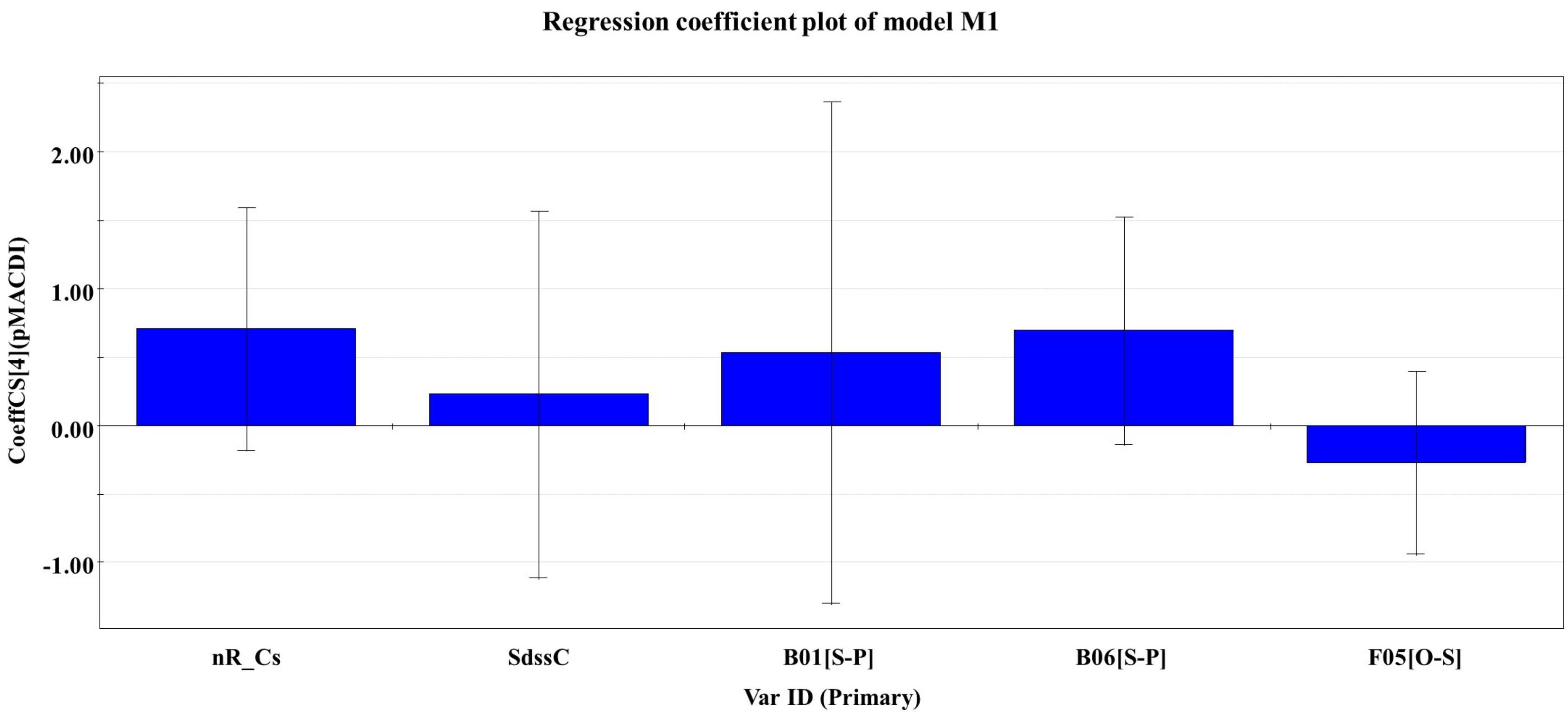

Fig.S7. Regression coefficient plot of model M2

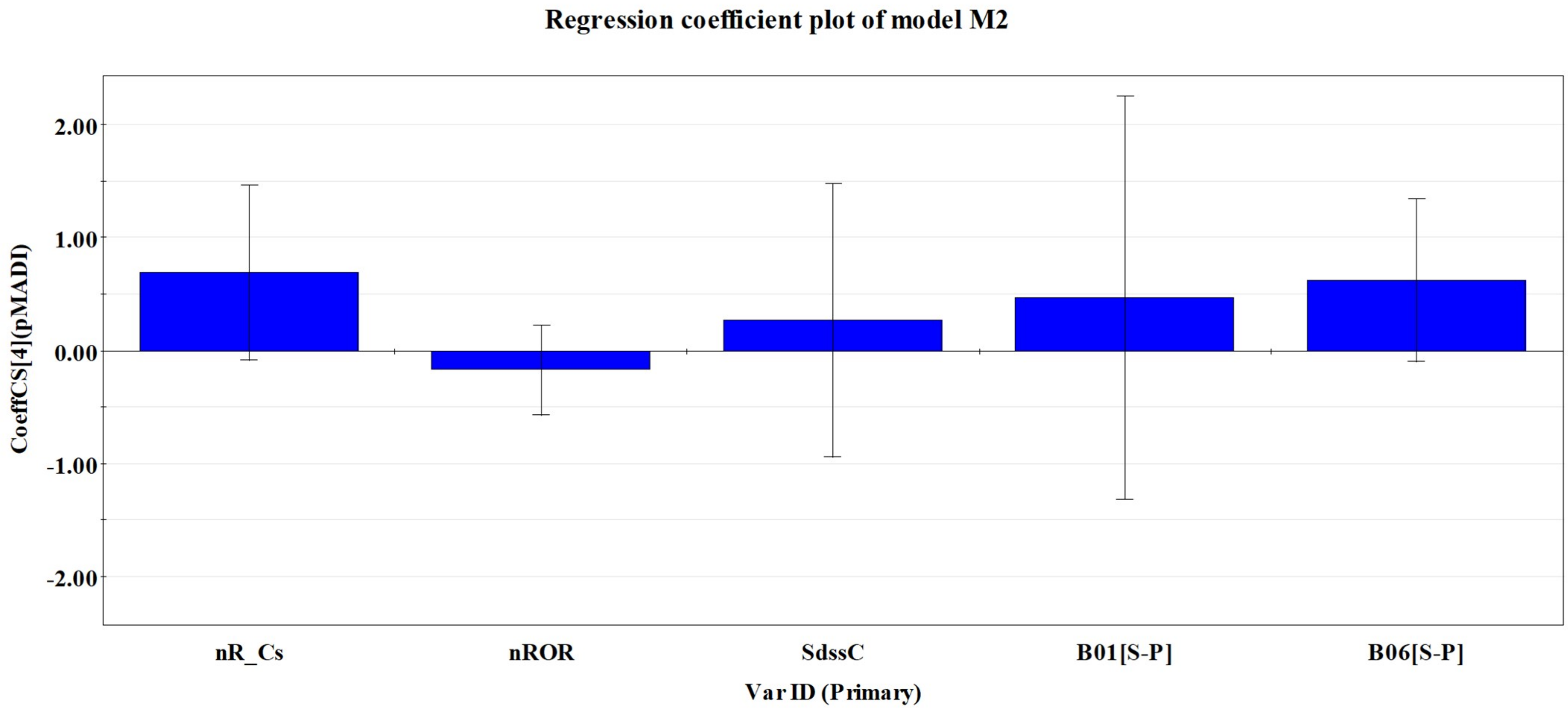

Fig.S8. Regression coefficient plot of model M3

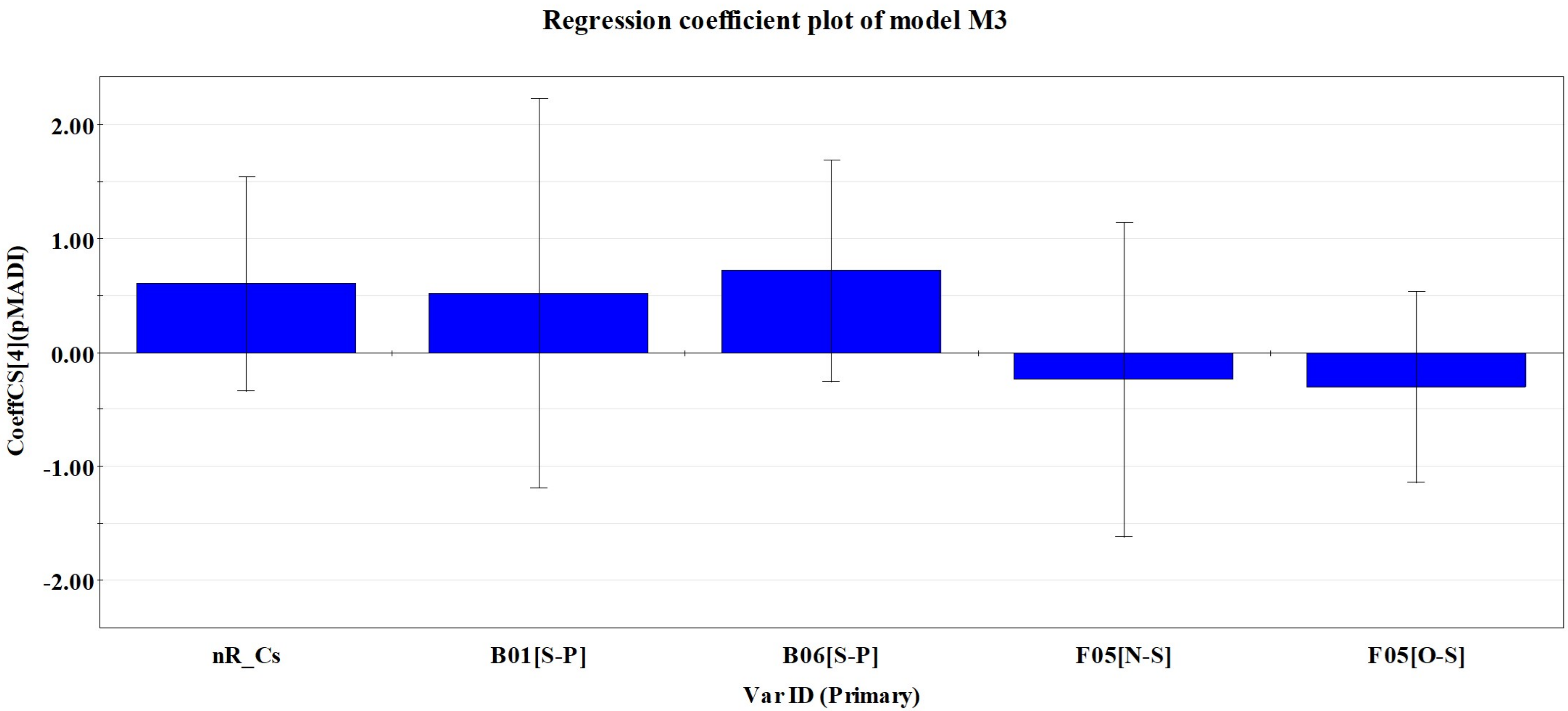

Fig.S9. Regression coefficient plot of model M4

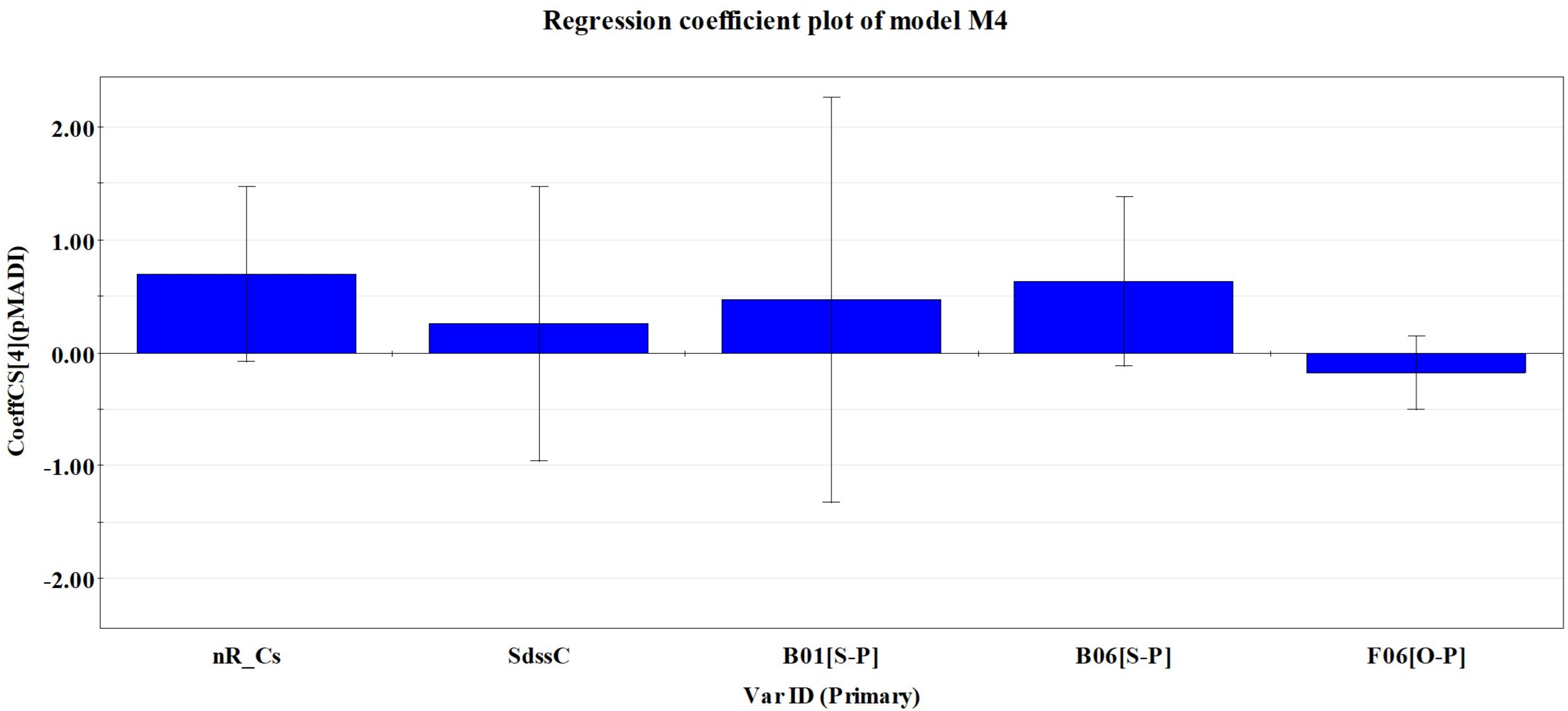

Fig.S10. Regression coefficient plot of model M5

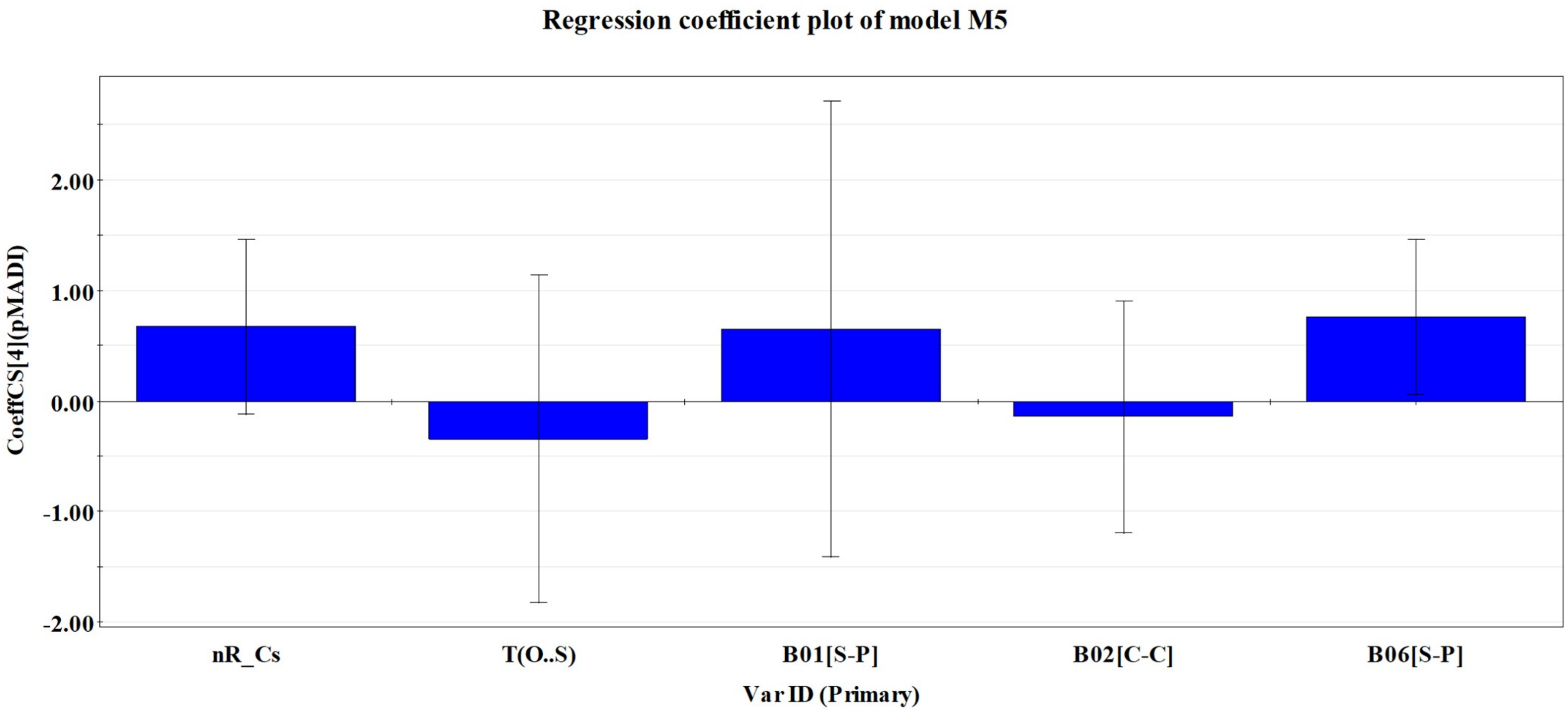

Fig.S11. Loading plot of model M1

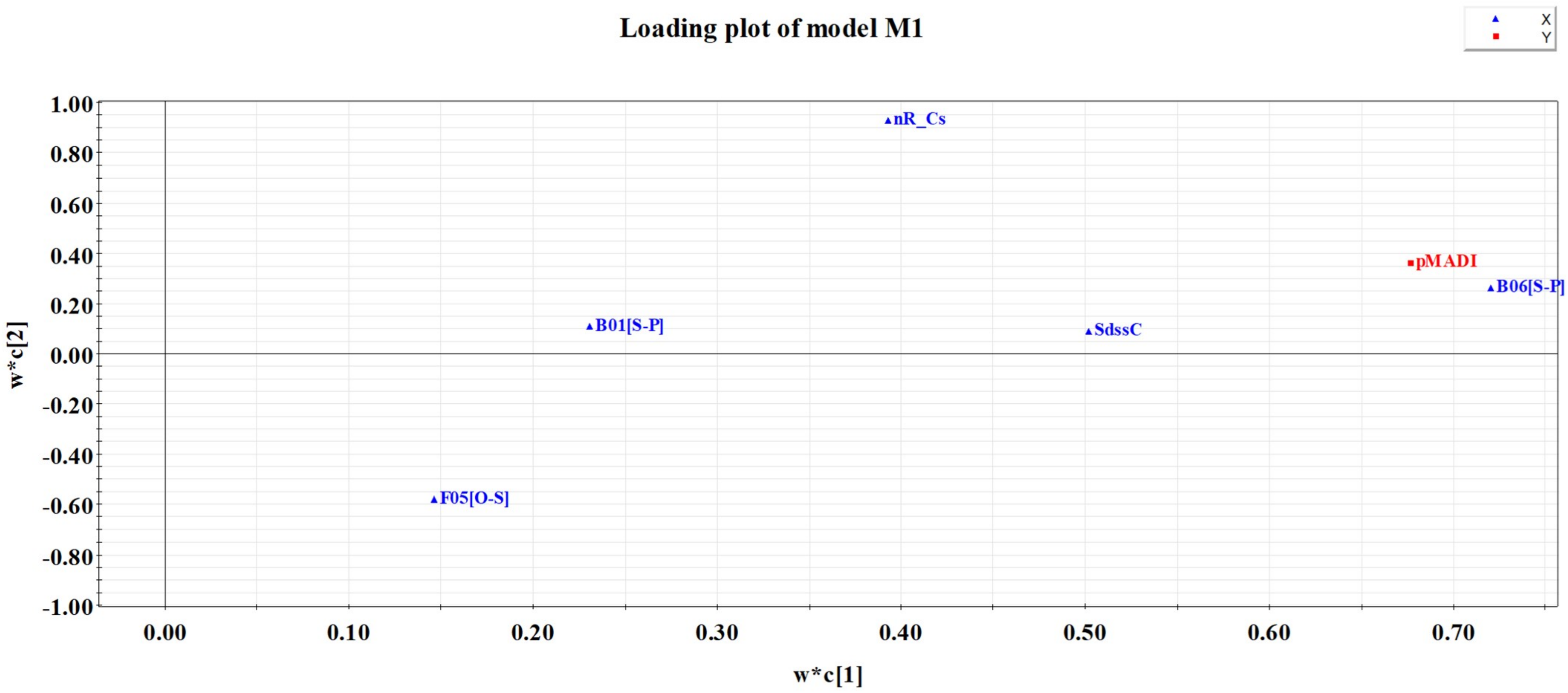

Fig.S12. Loading plot of model M2

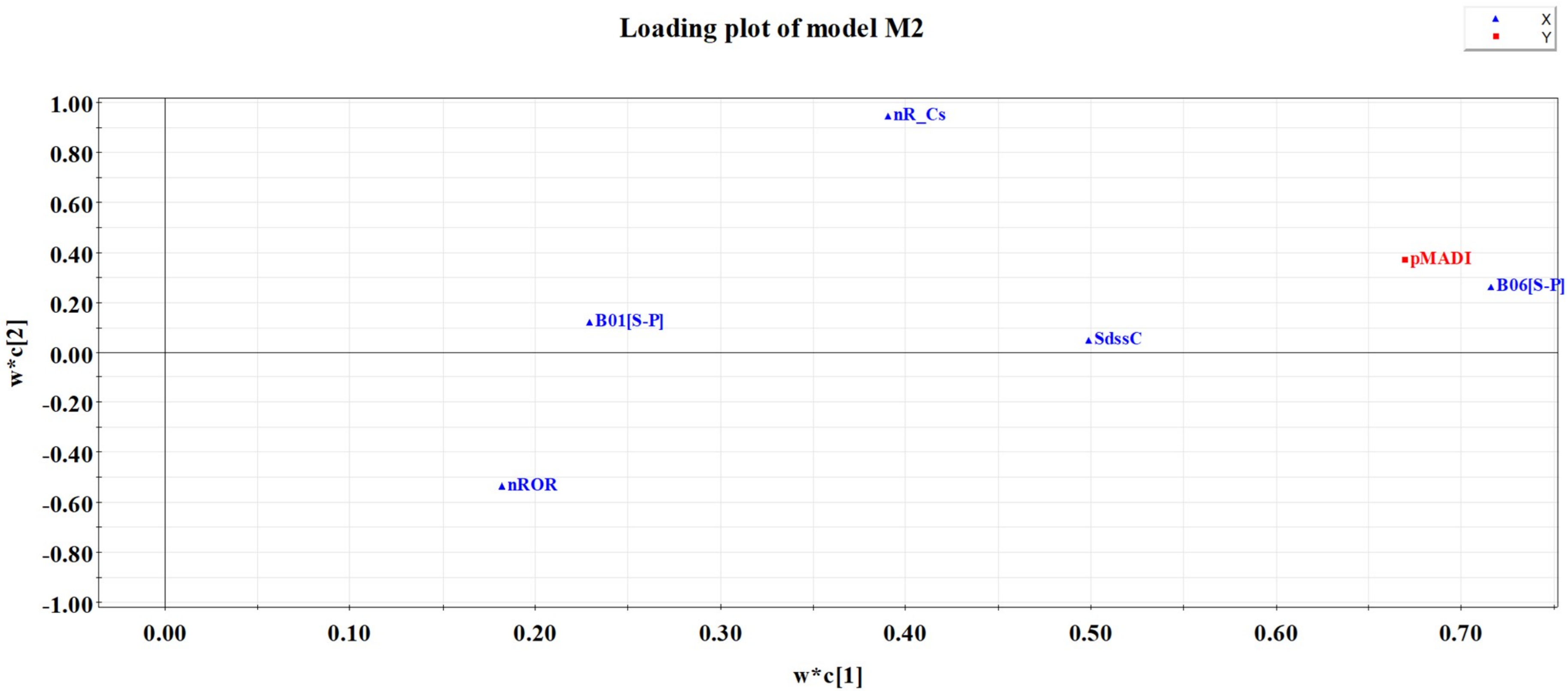

Fig.S13. Loading plot of model M3

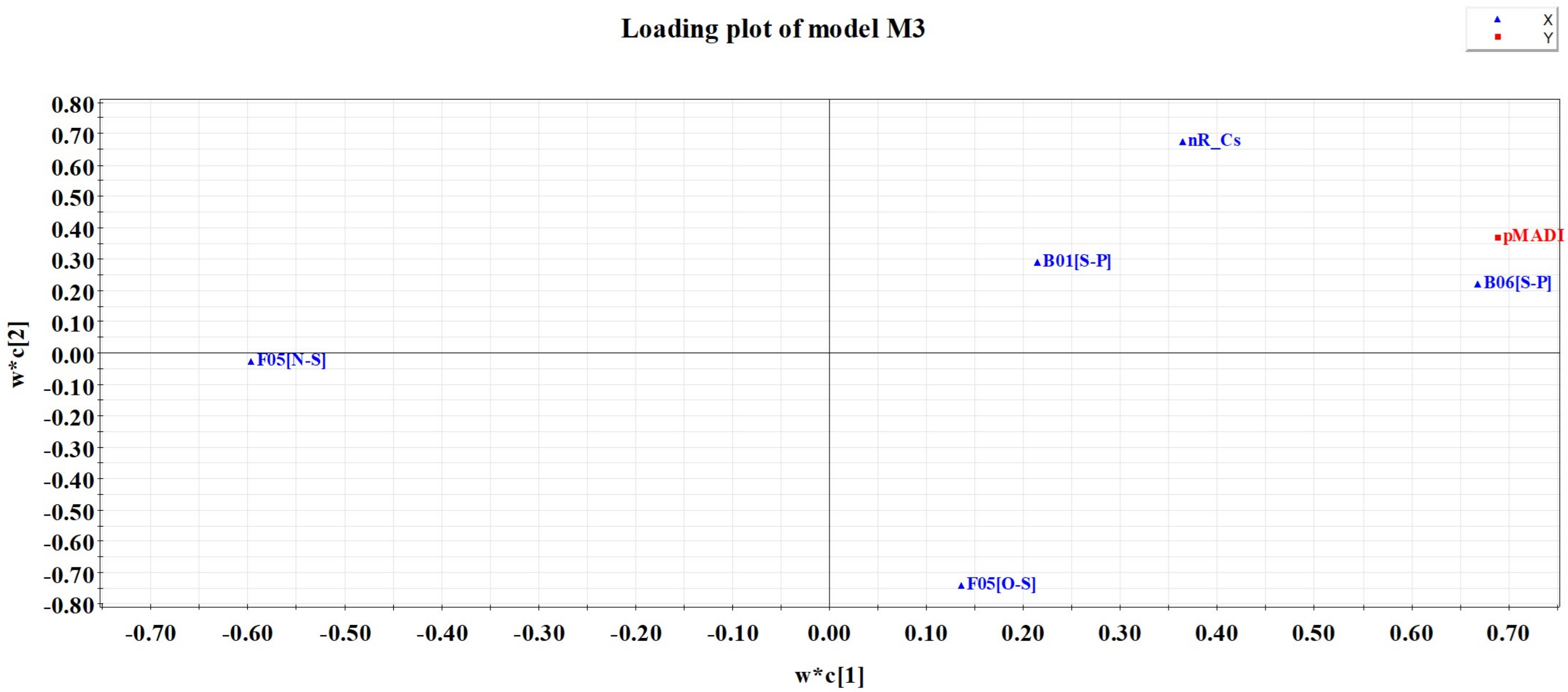

Fig.S14. Loading plot of model M4

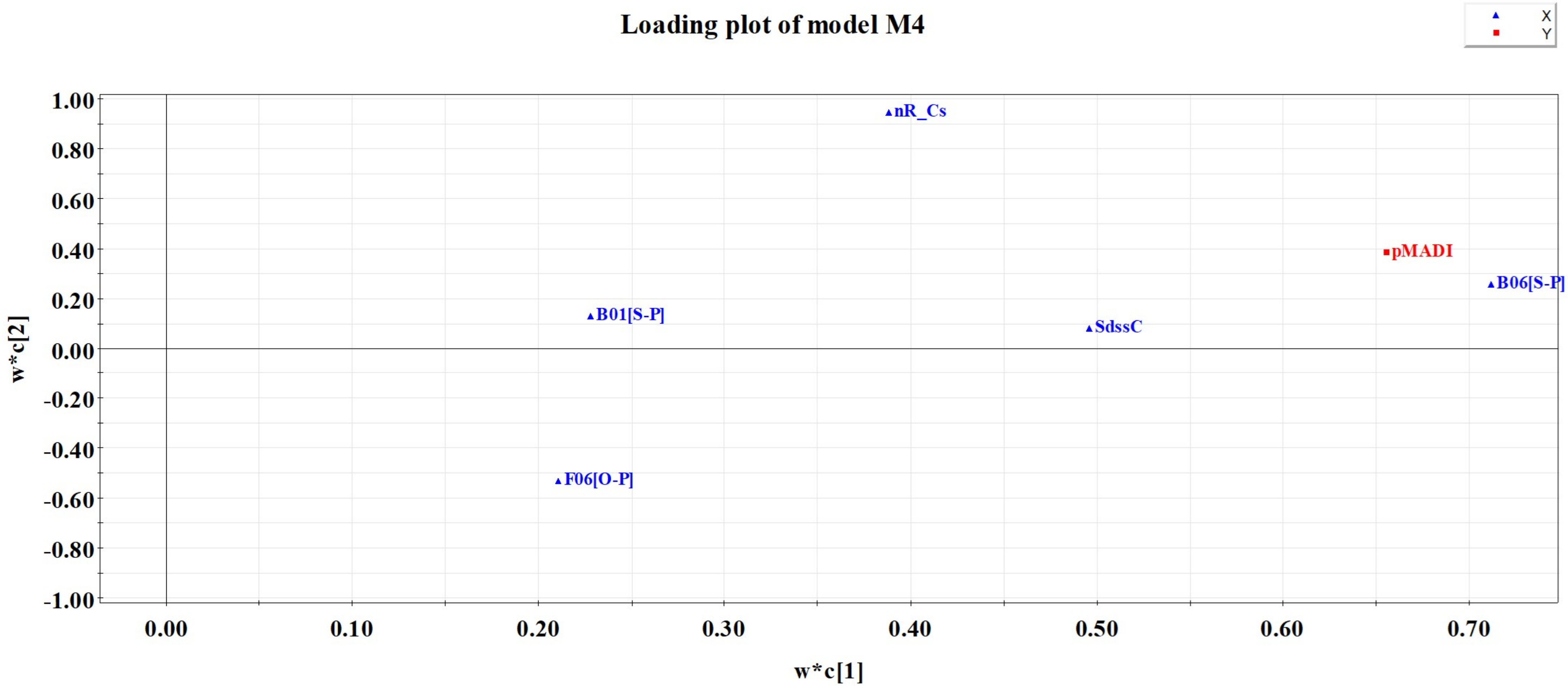

Fig.S15. Loading plot of model M5

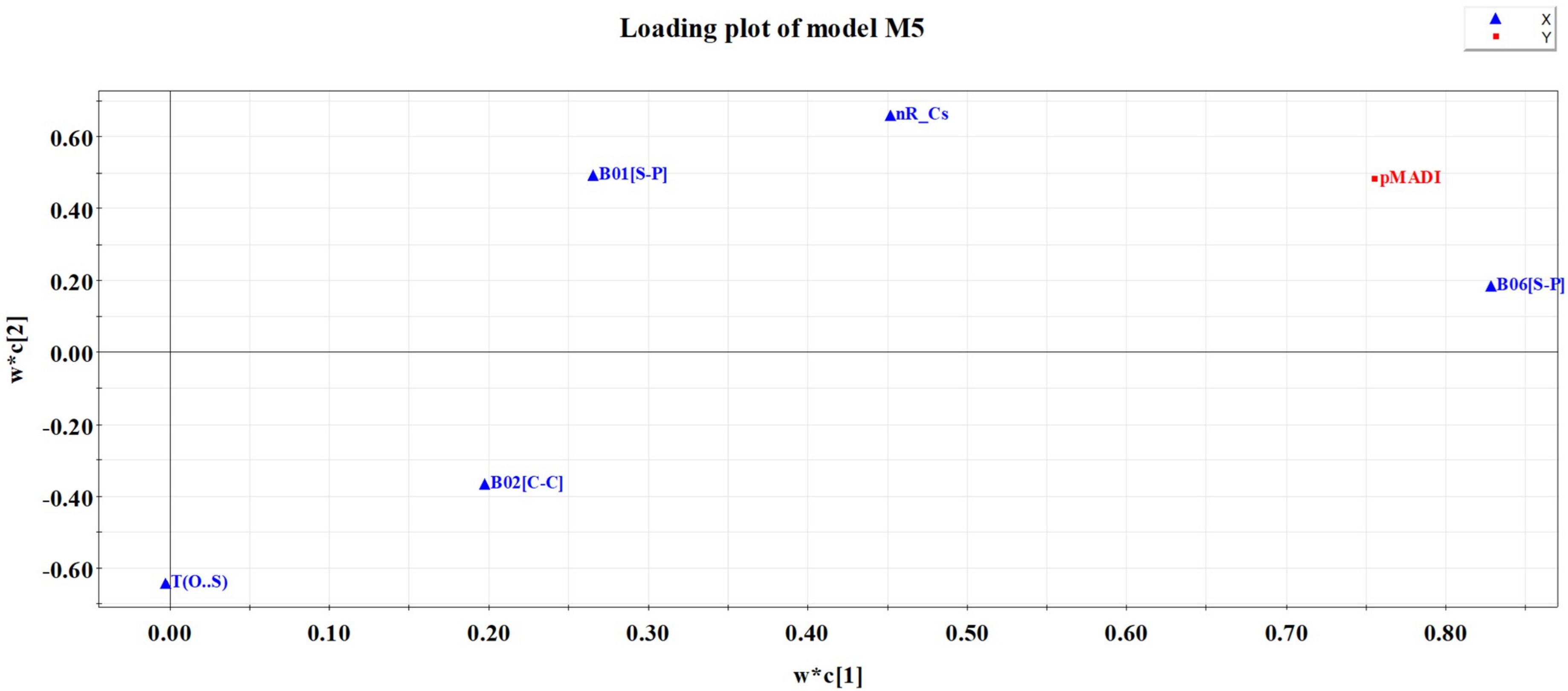

Fig.S16. Score plot of model M1

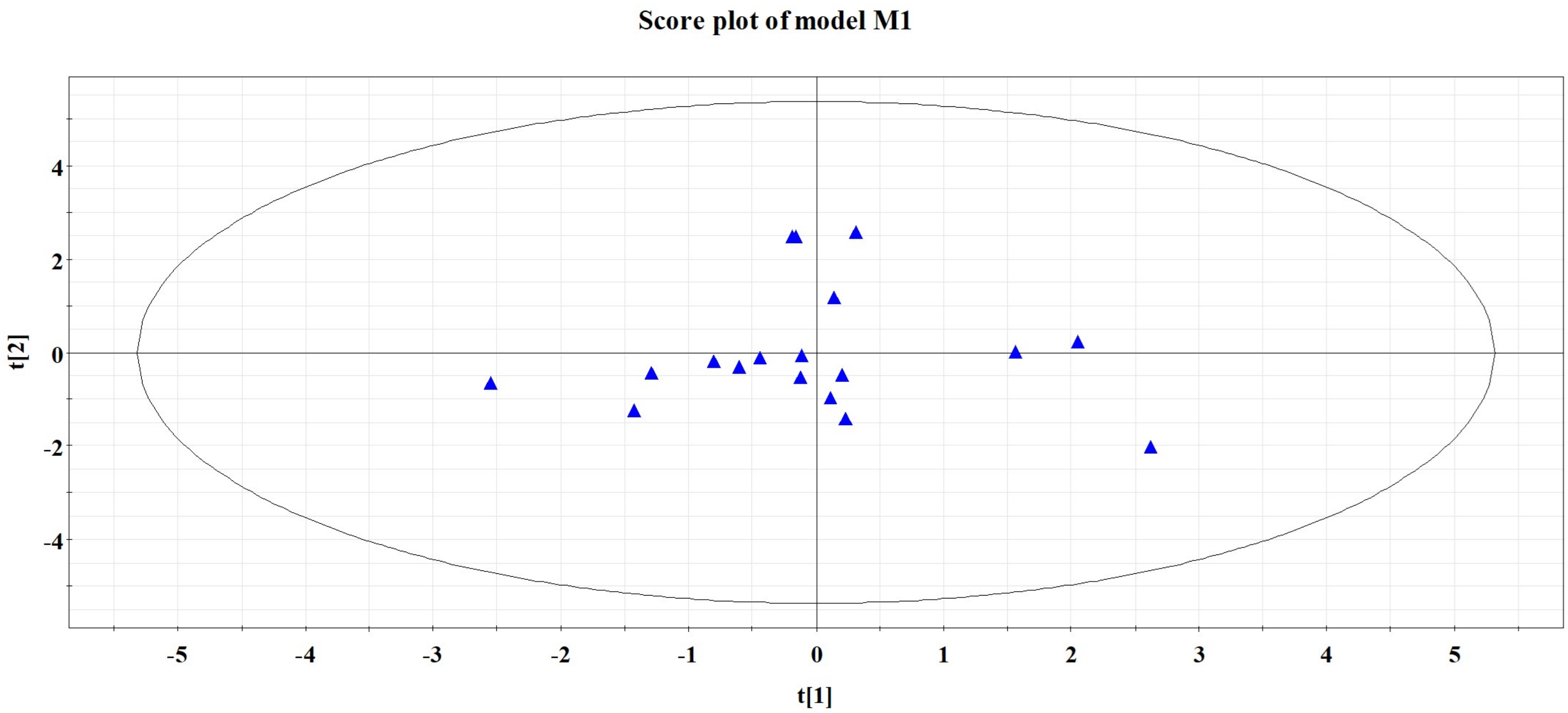

Fig.S17. Loading plot of model M2

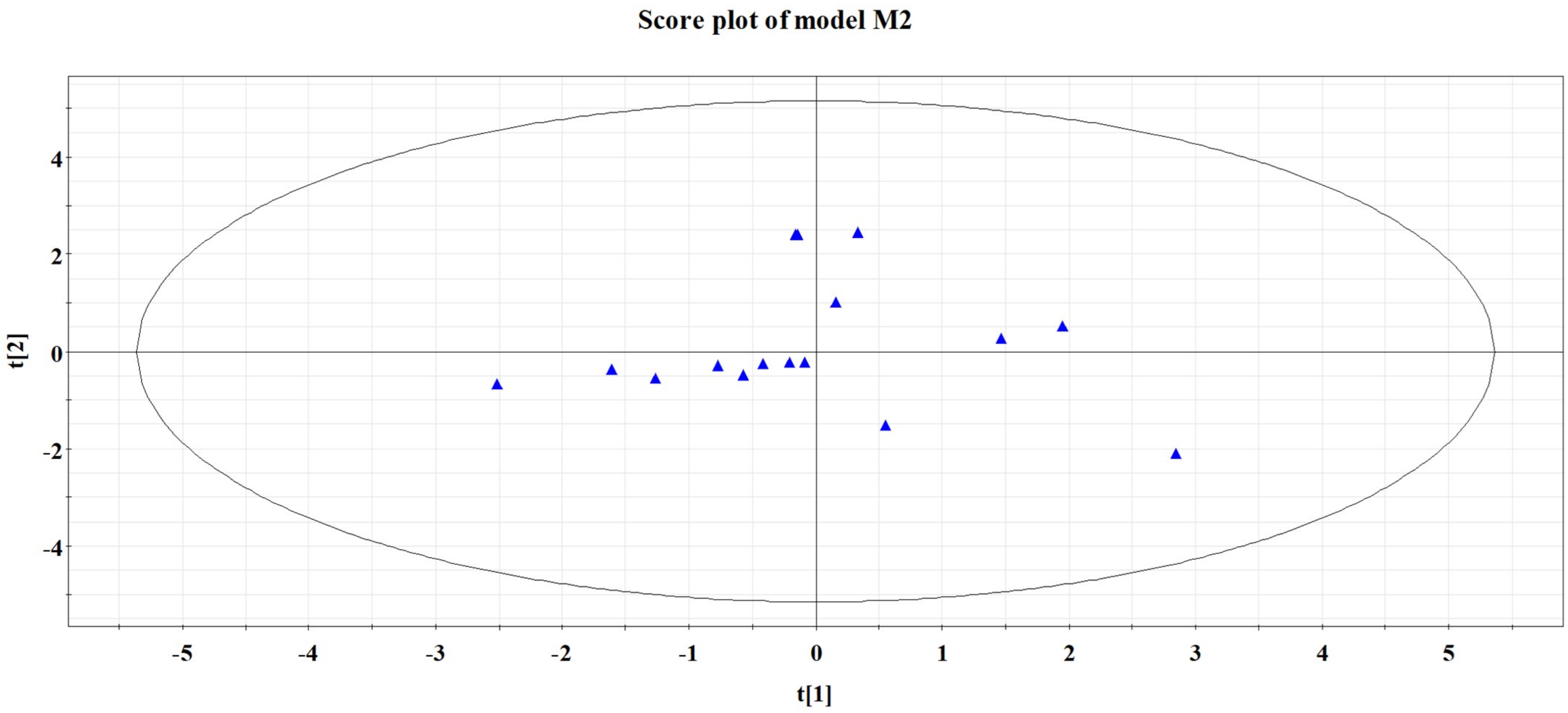

Fig.S18. Loading plot of model M3

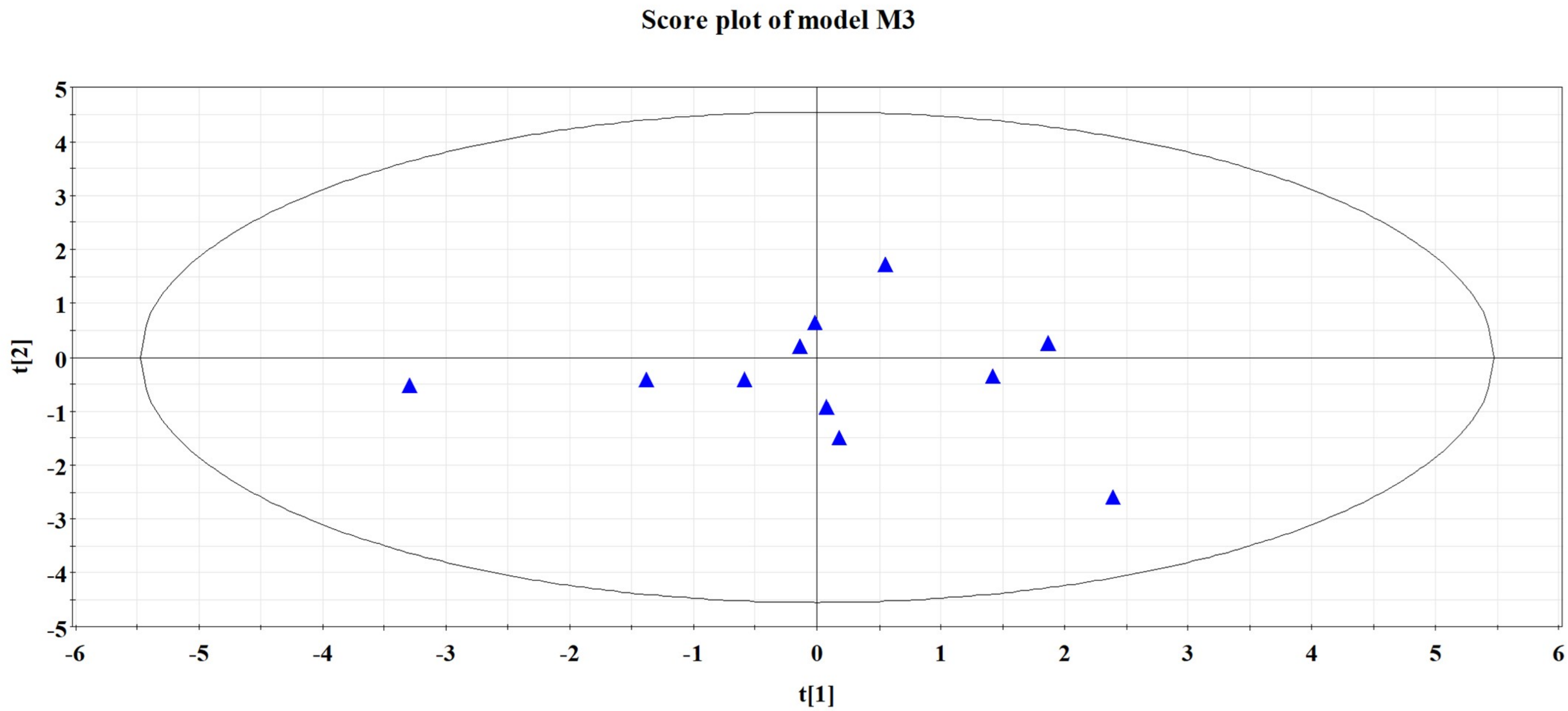

Fig.S19. Loading plot of model M4

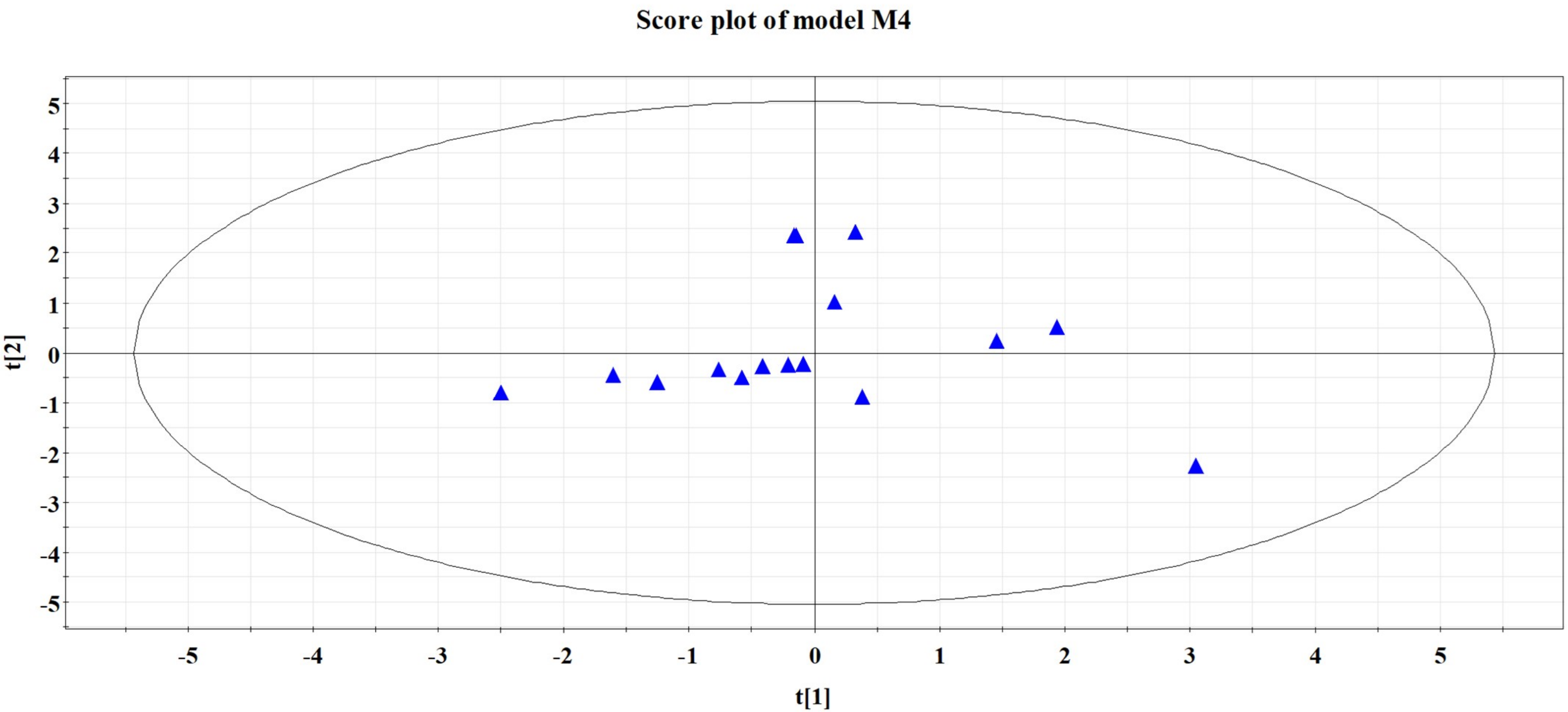

Fig.S20. Loading plot of model M5

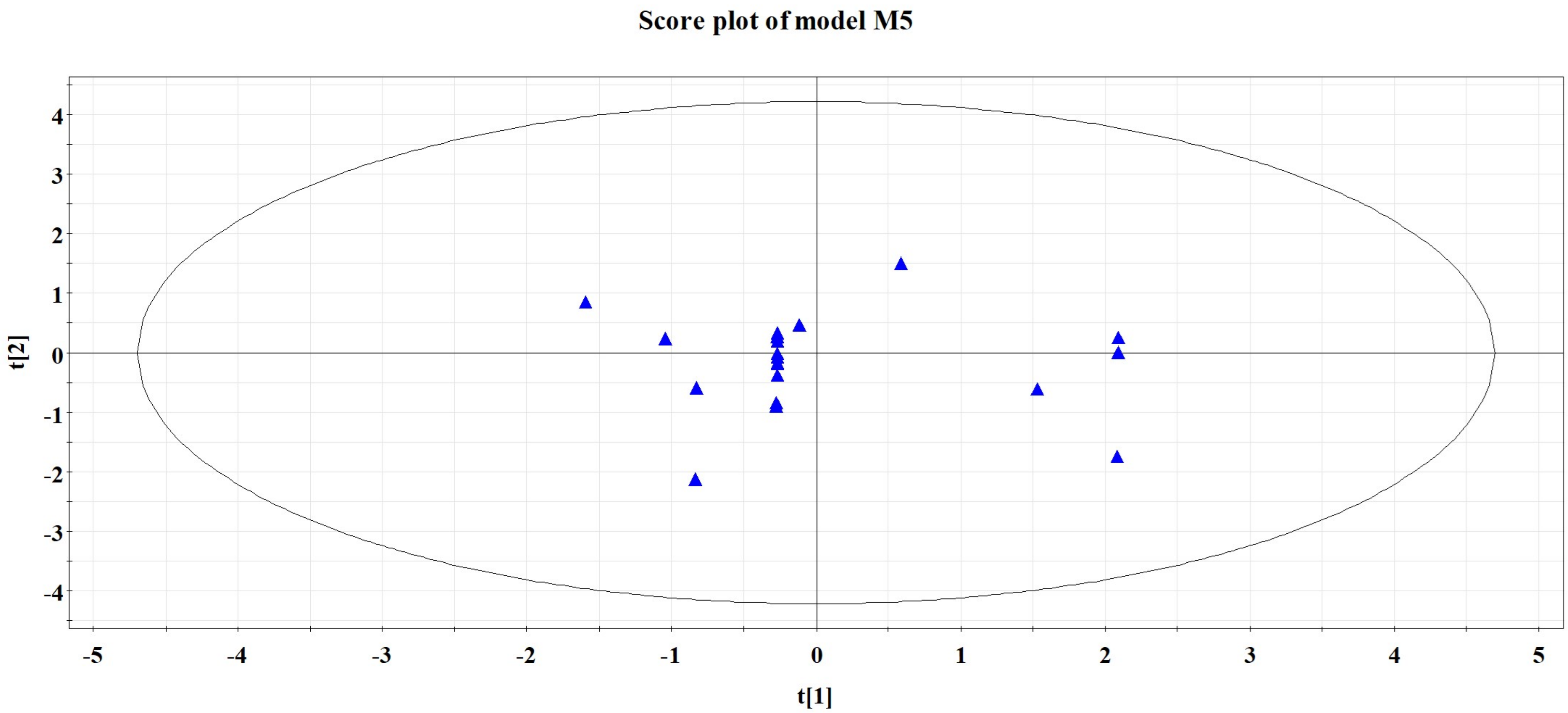

Fig.S21. DModx plot (training set) of model M1

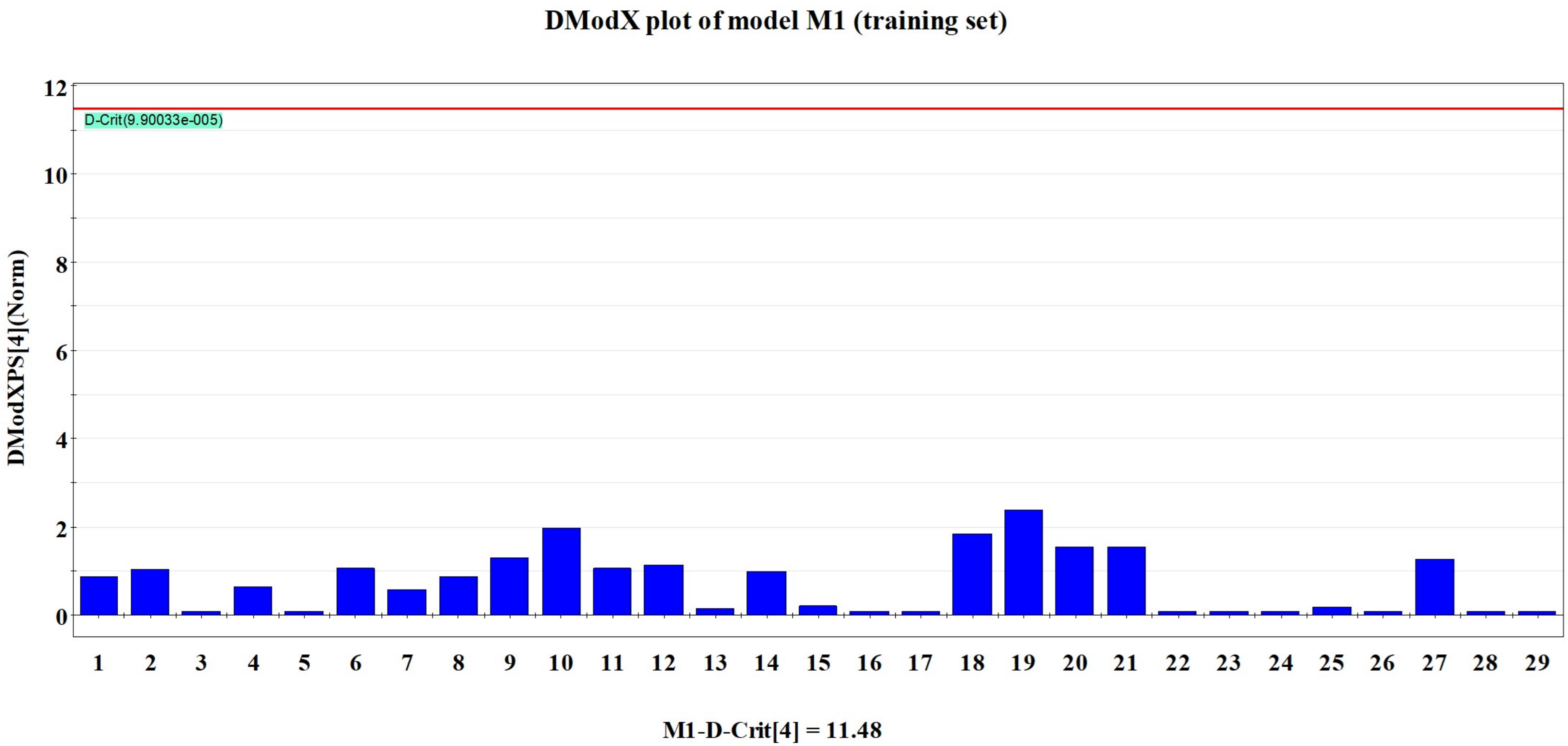

Fig.S22. DModx plot (test set) of model M1

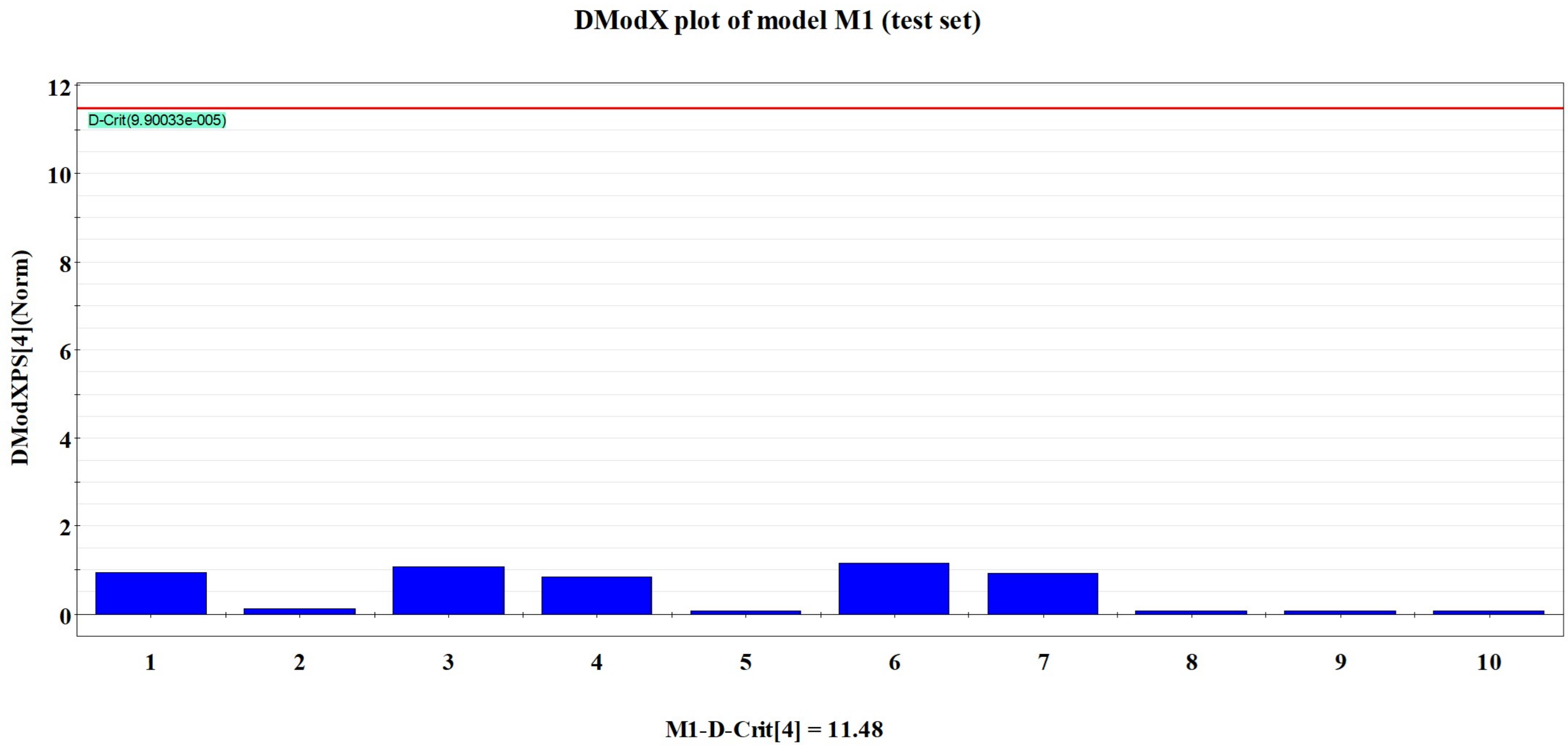

Fig.S23. DModx plot (training set) of model M2

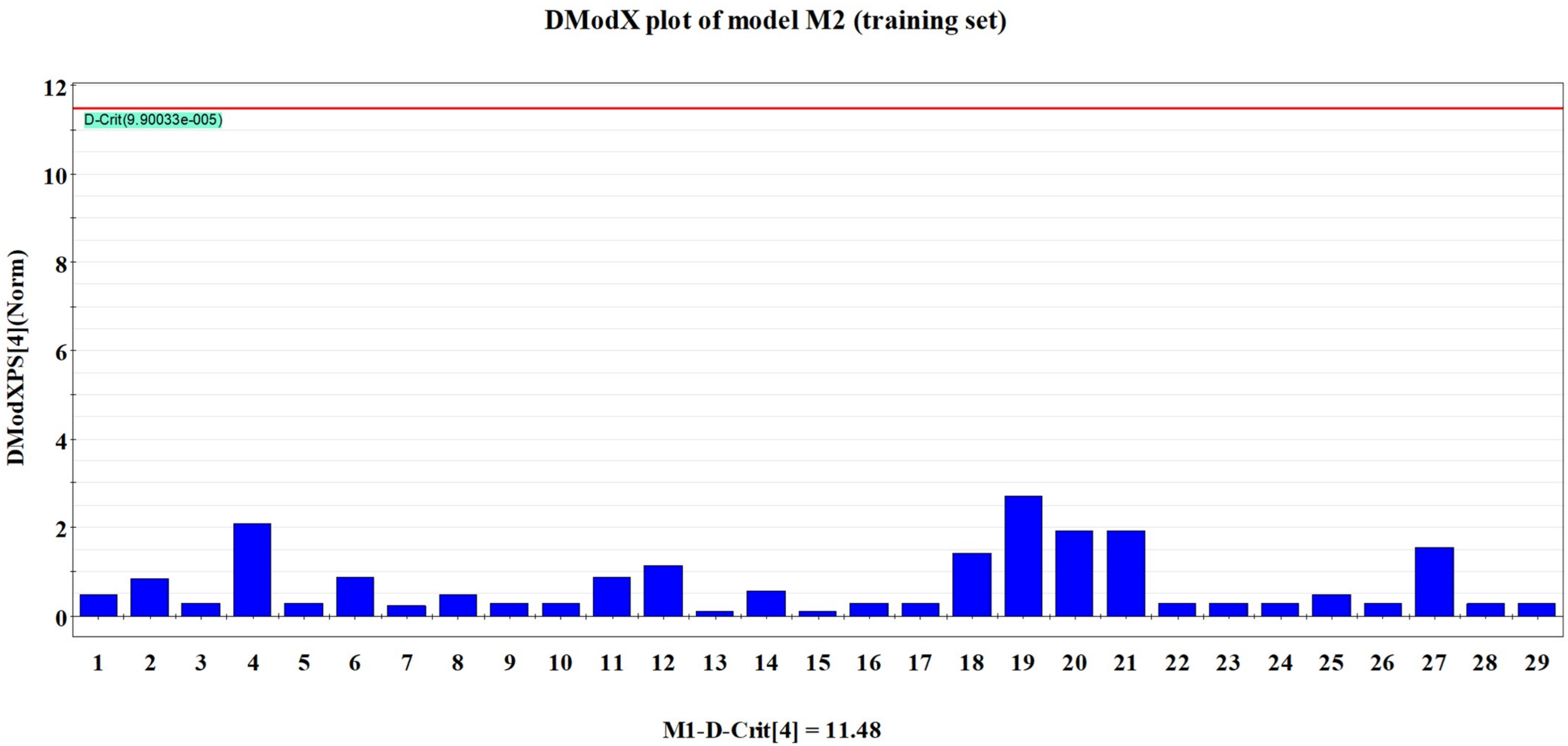

Fig.S24. DModx plot (test set) of model M2

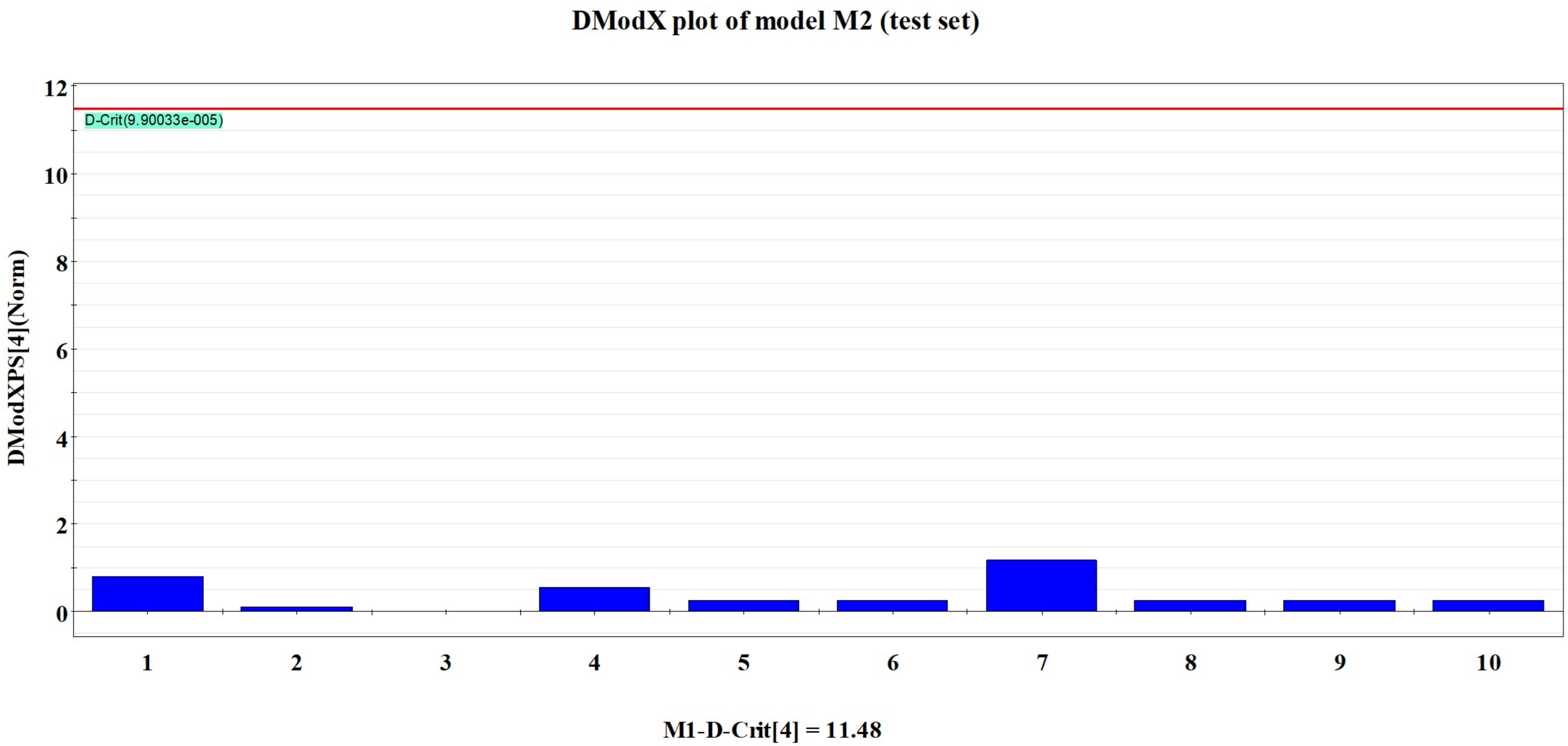

Fig.S25. DModx plot (training set) of model M3

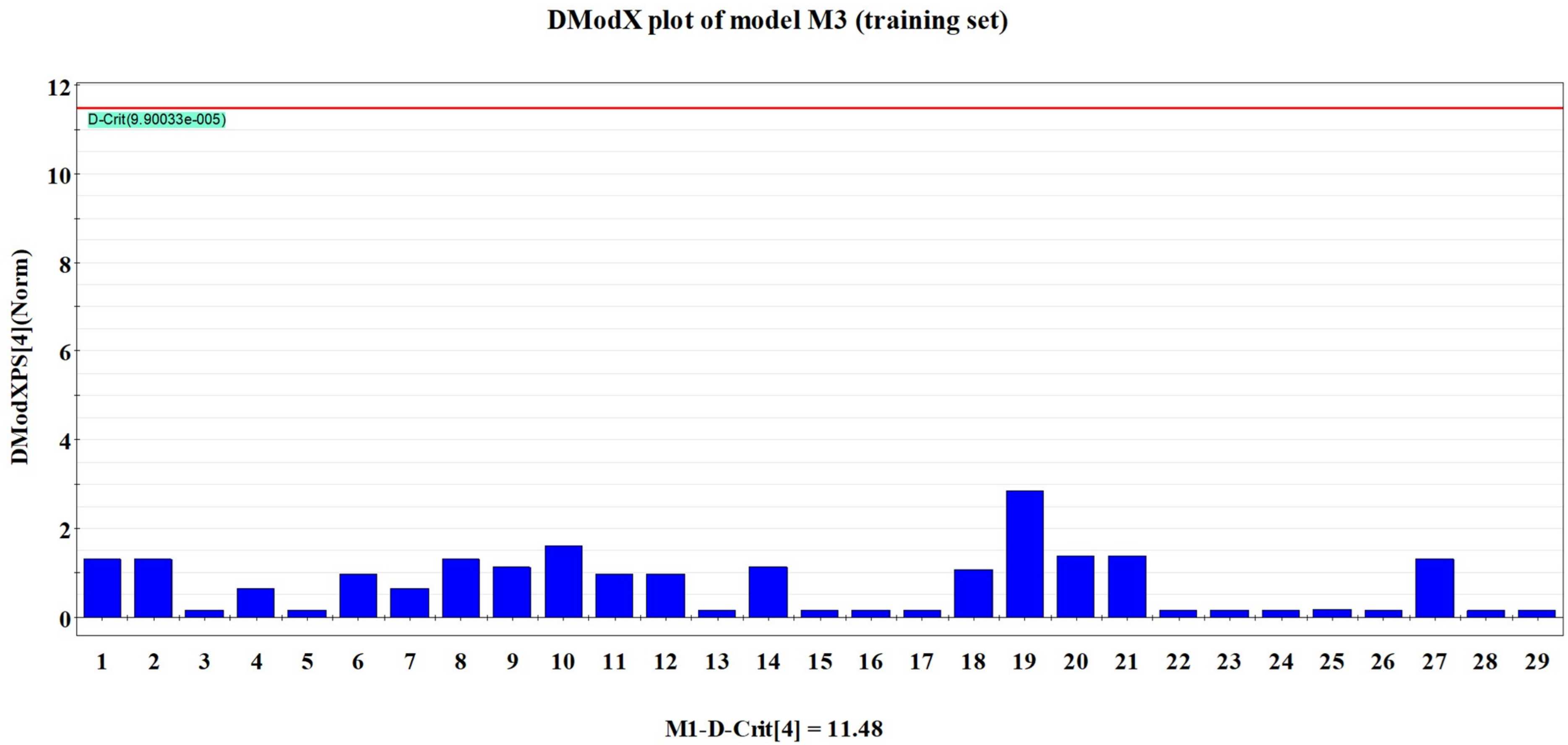

Fig.S26. DModx plot (test set) of model M3

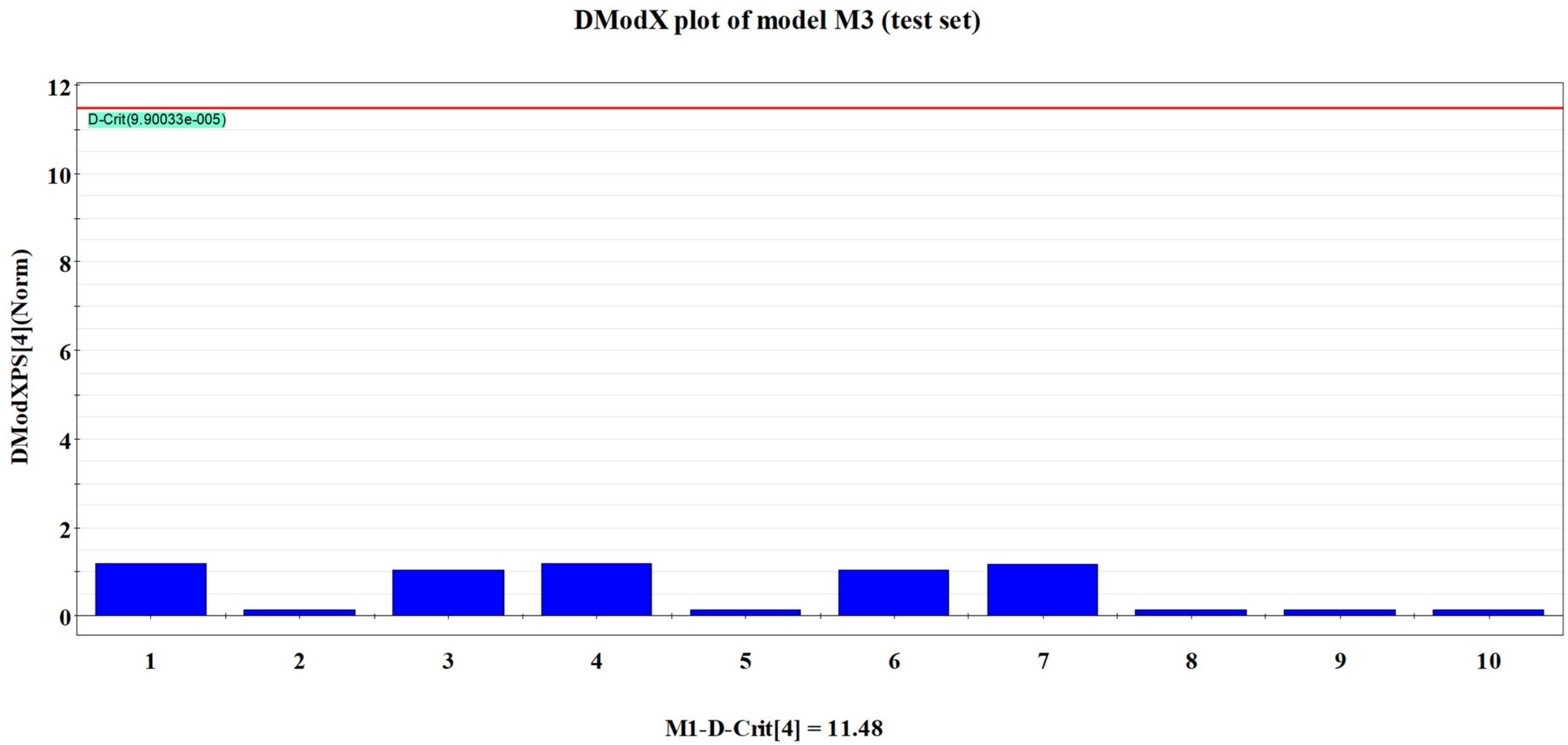

Fig.S27. DModx plot (training set) of model M4

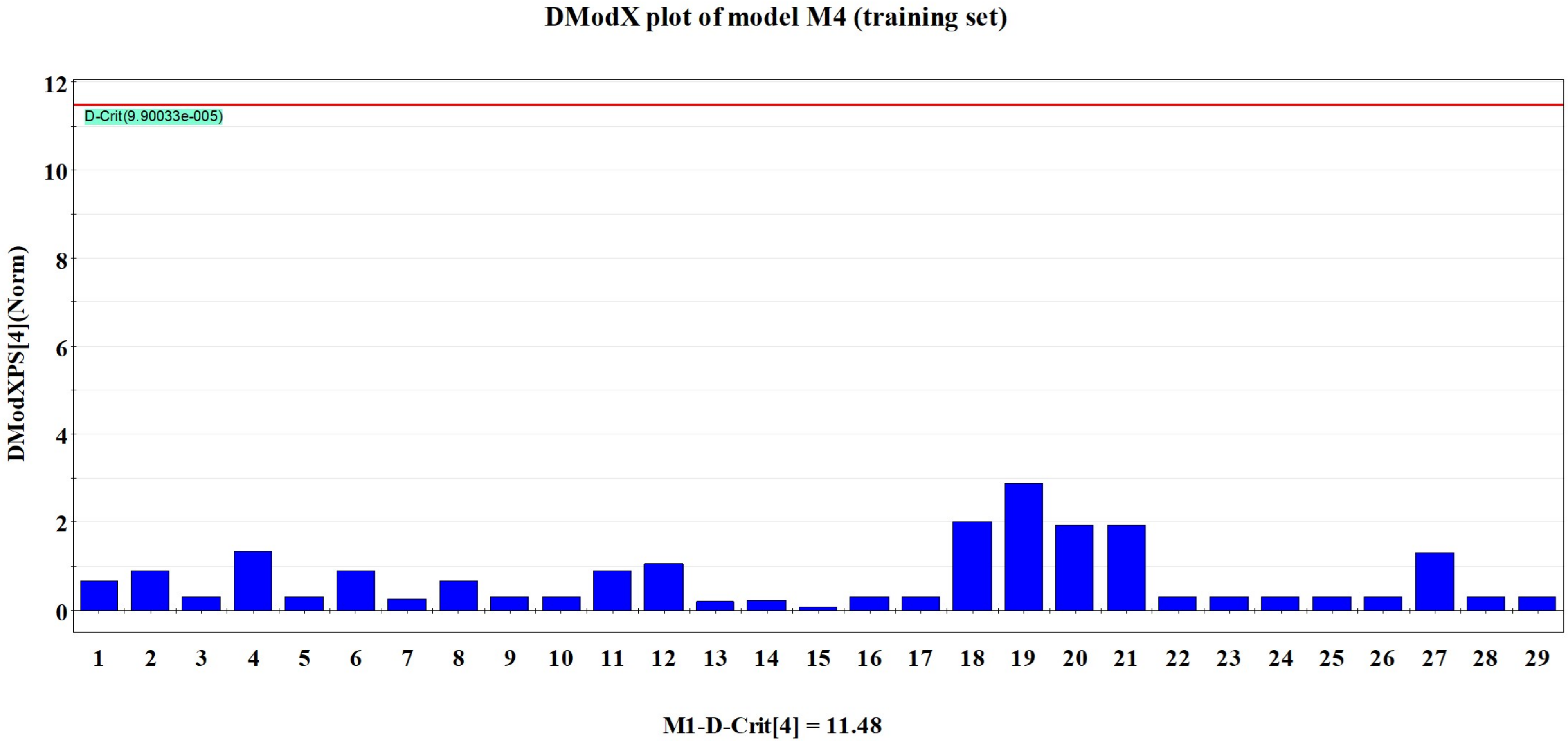

Fig.S28. DModx plot (test set) of model M4

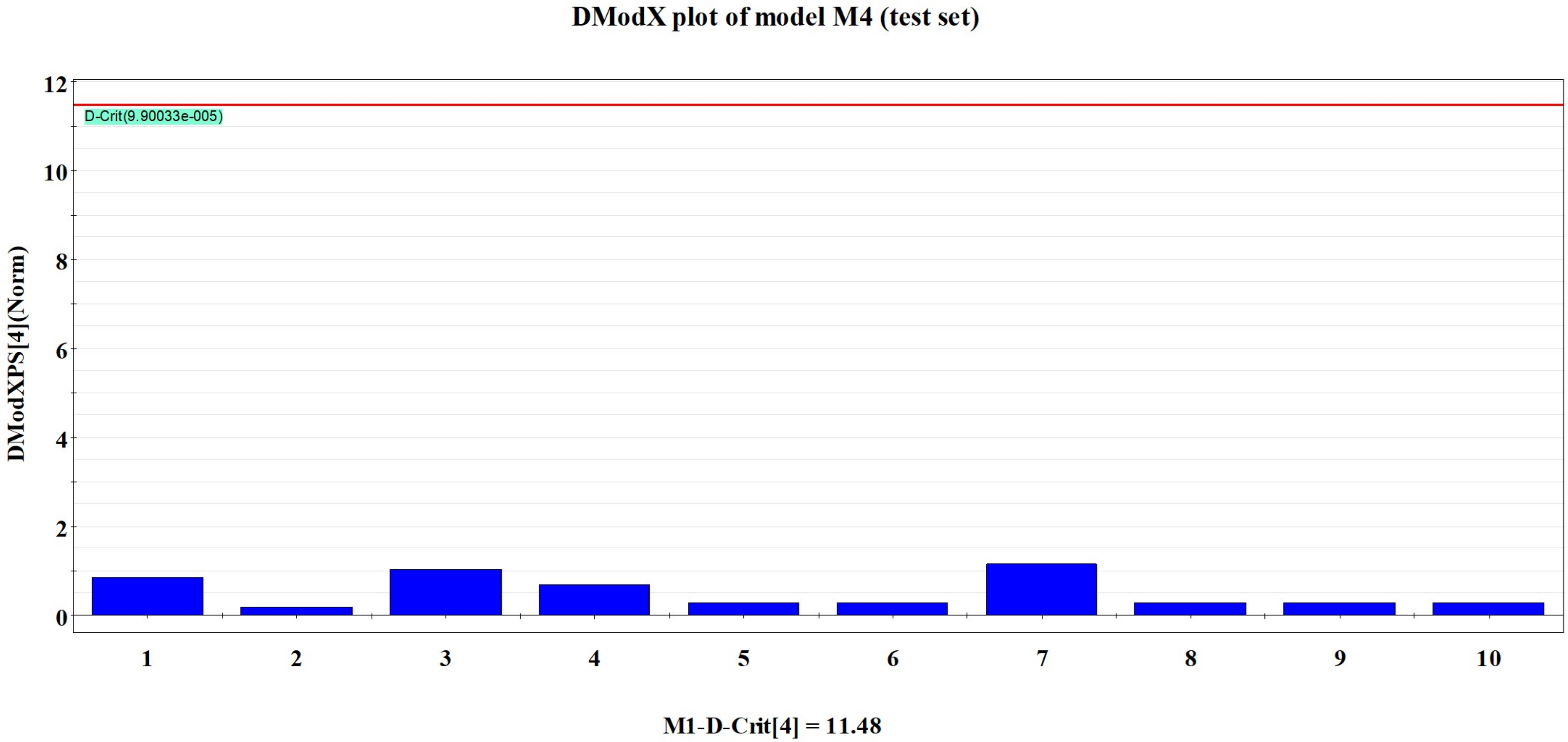

Fig.S29. DModx plot (training set) of model M5

DModX plot of model M5 (training set)

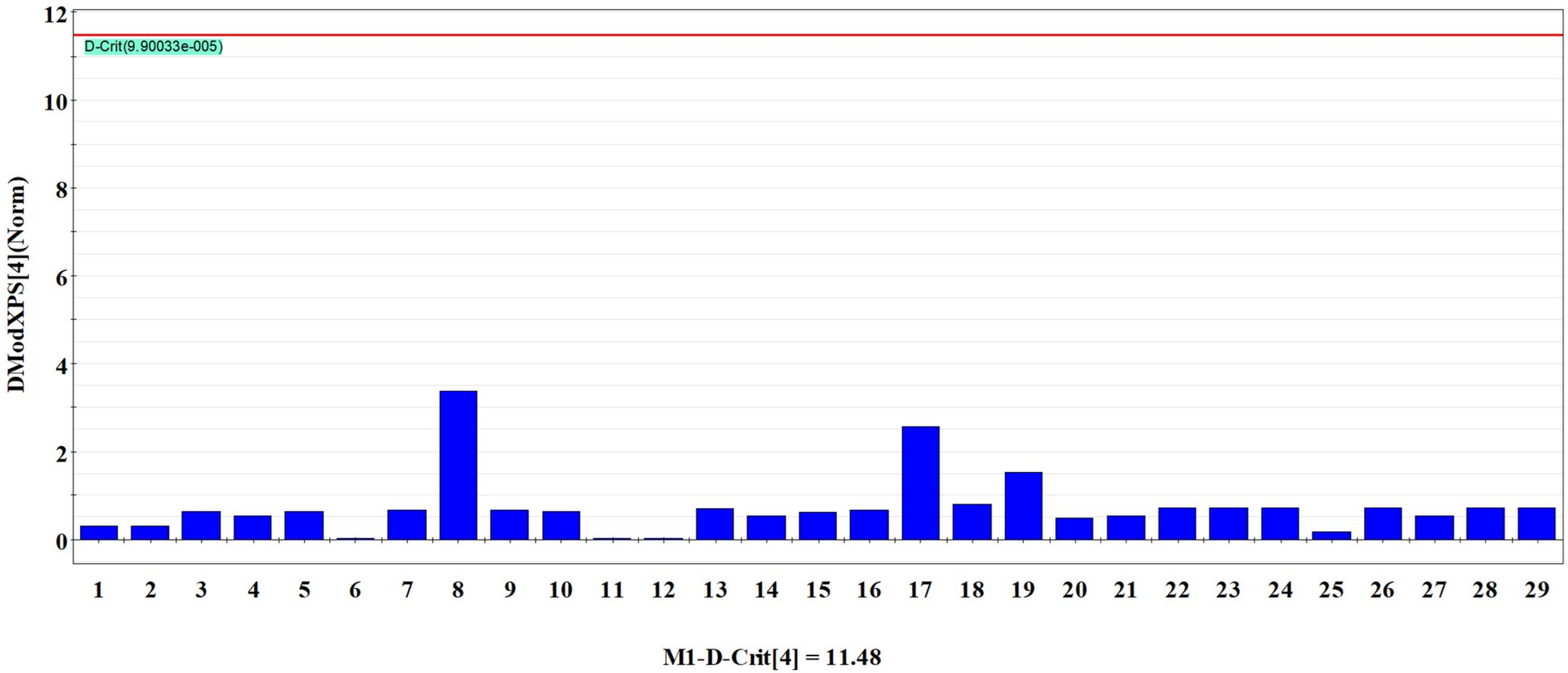

Fig.S30. DModx plot (test set) of model M5

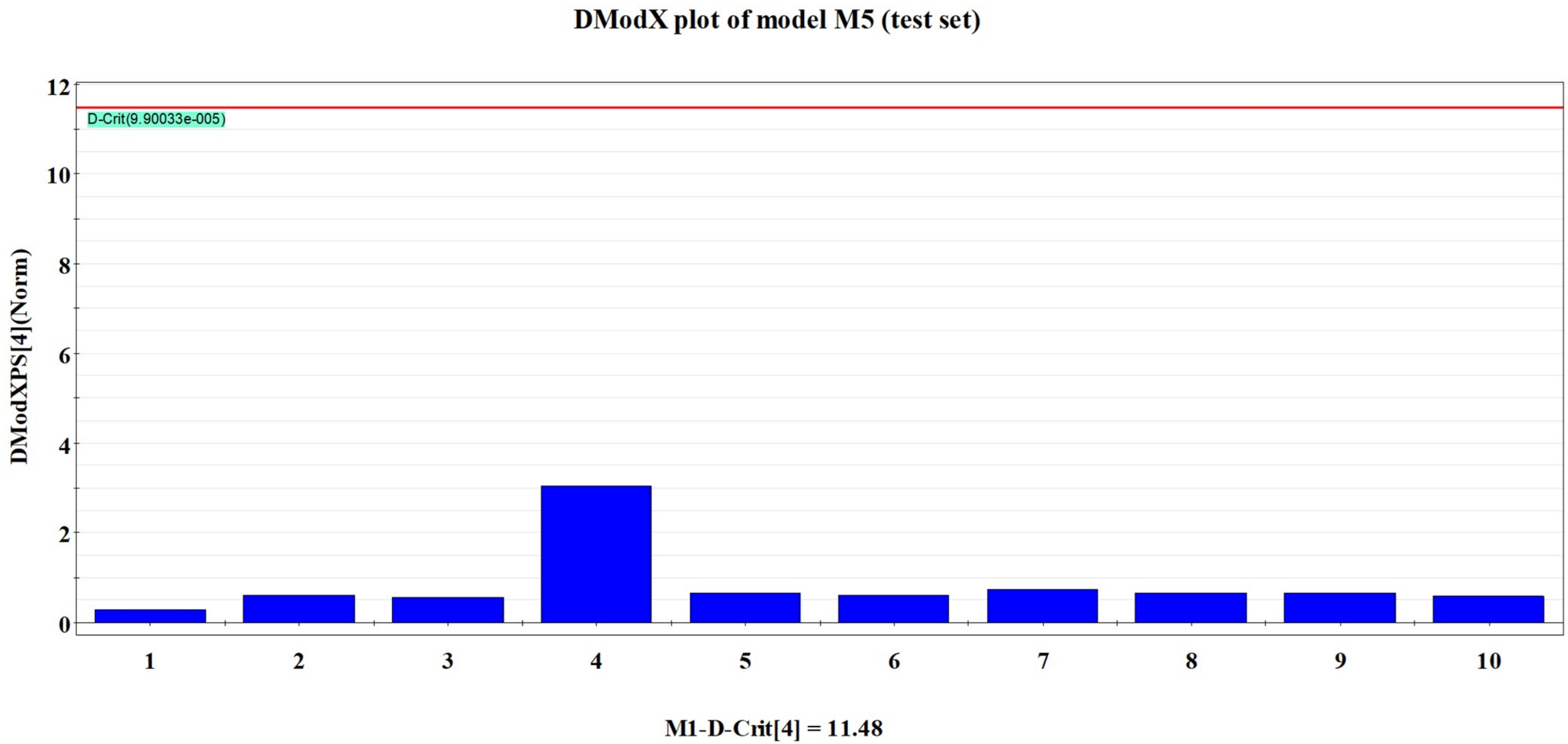

Fig.S31. Y randomization plot of model M1

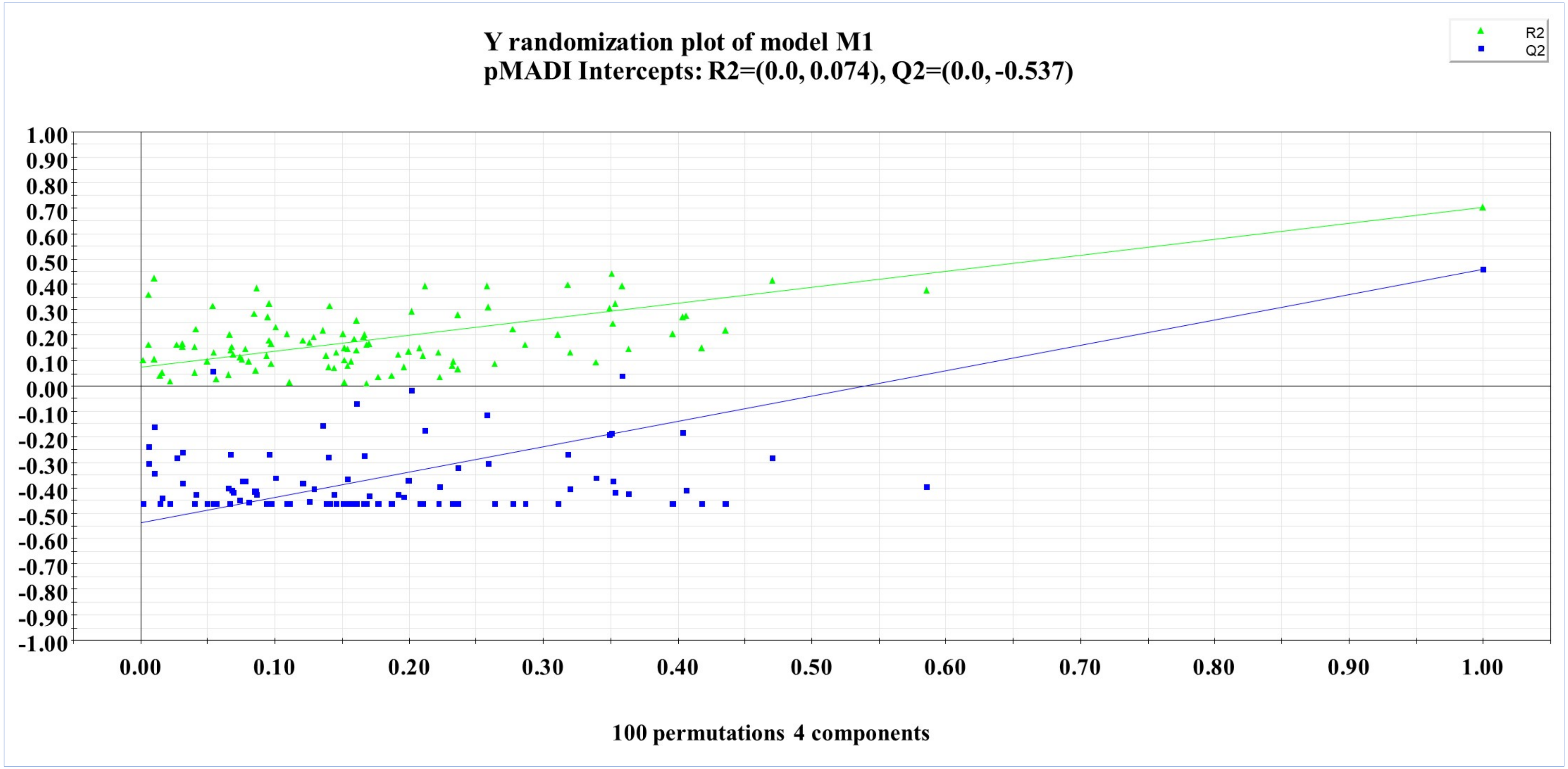

Fig.S32. Y randomization plot of model M2

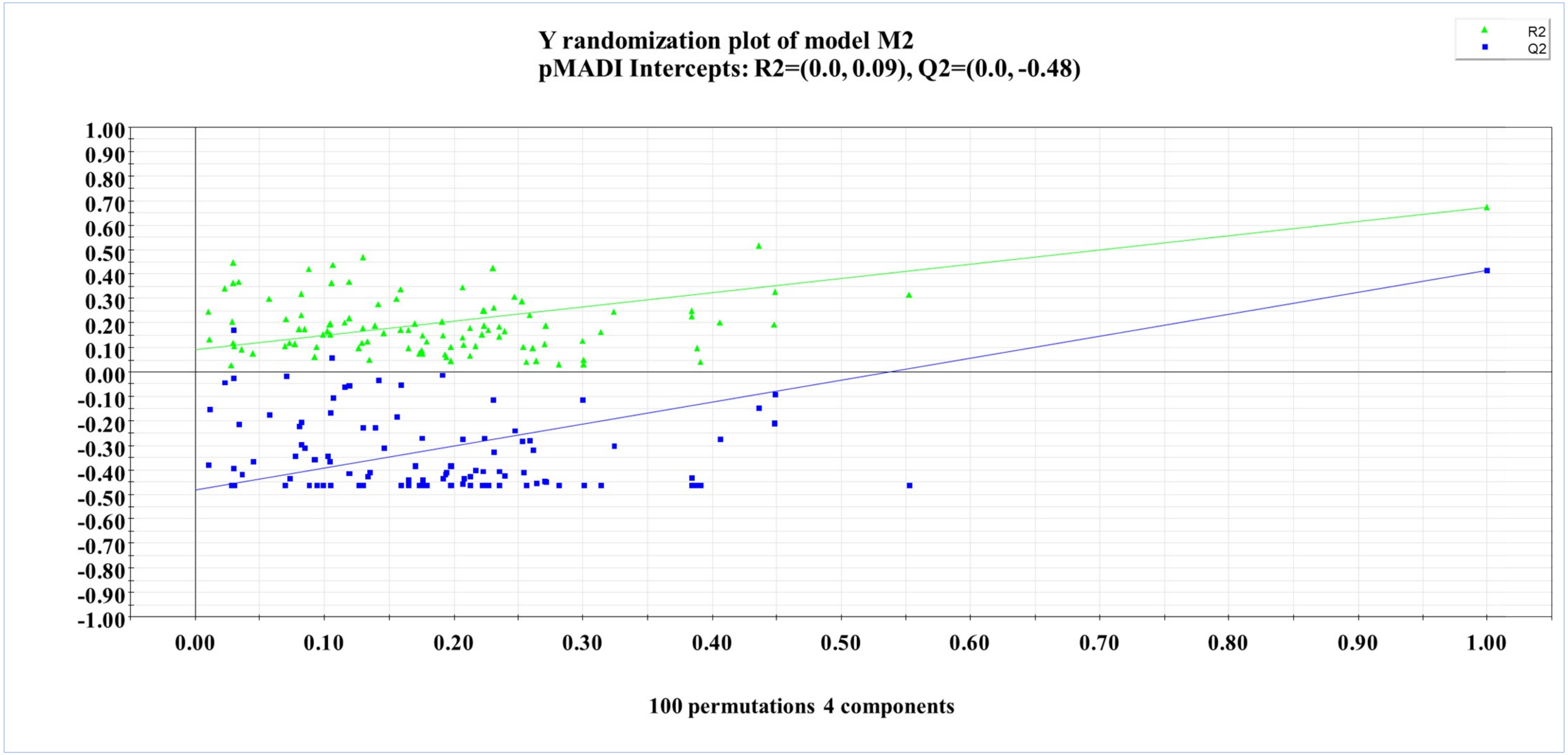

Fig.S33. Y randomization plot of model M3

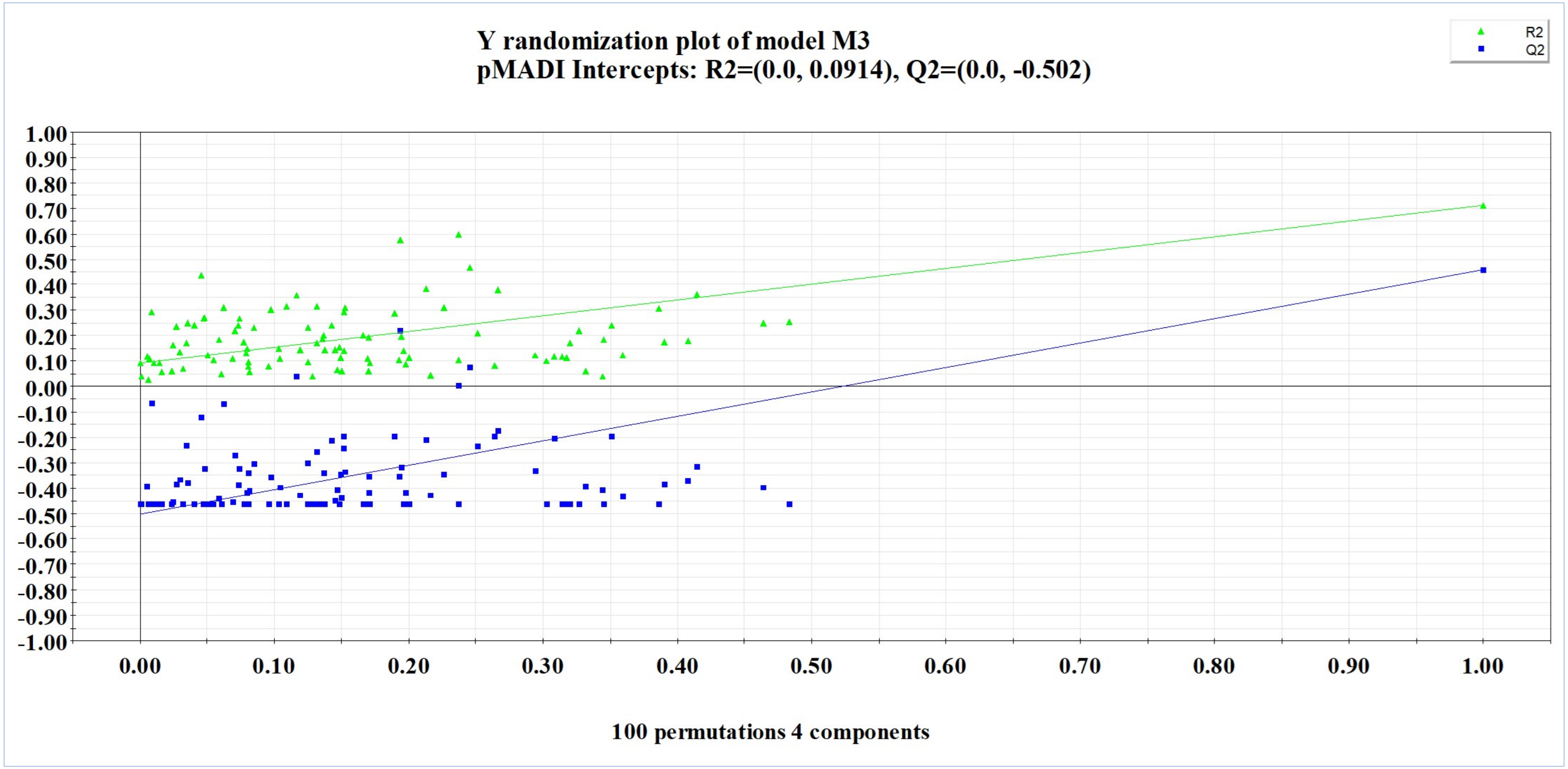

Fig.S34. Y randomization plot of model M4

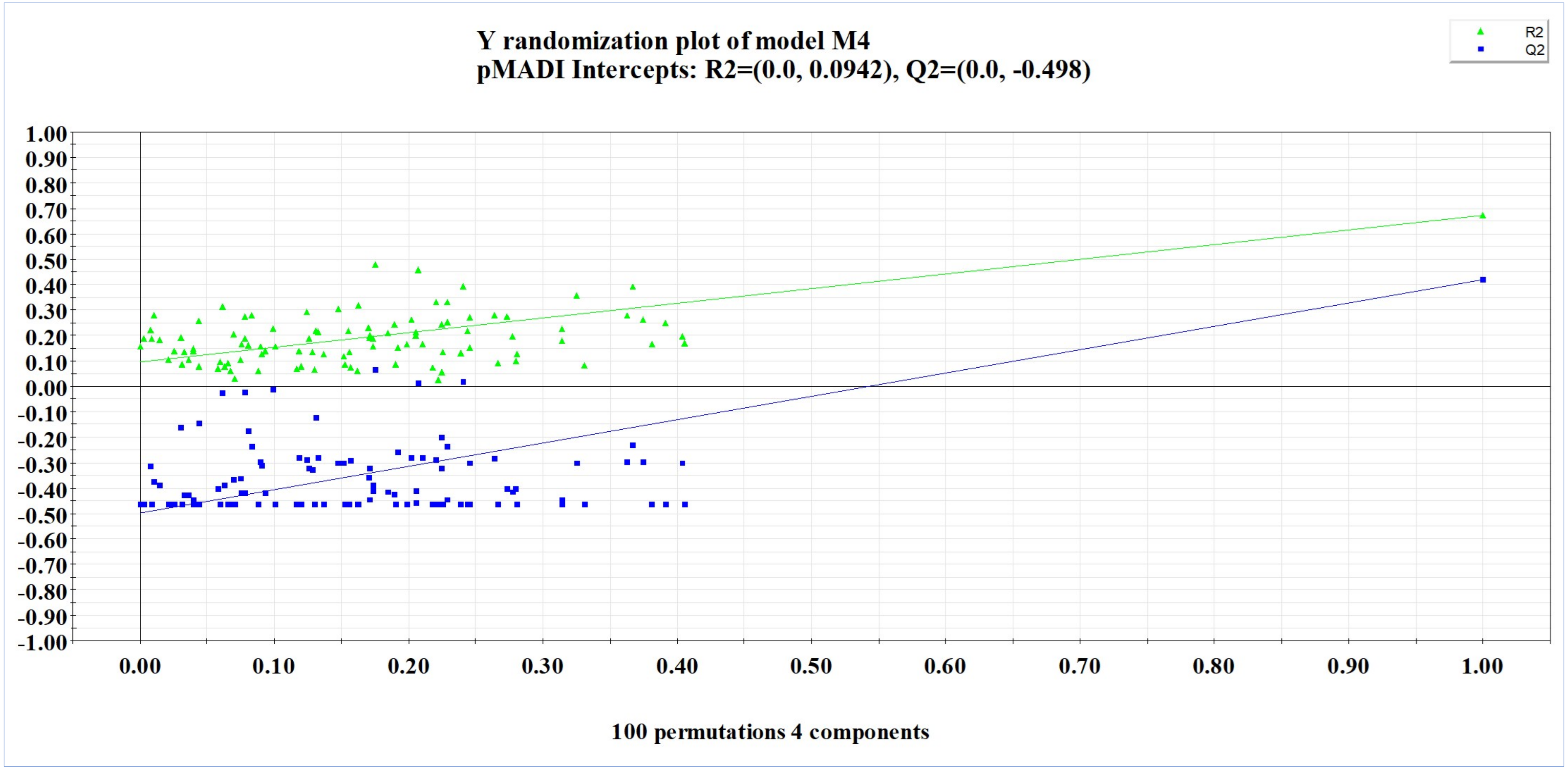

Fig.S35. Y randomization plot of model M5

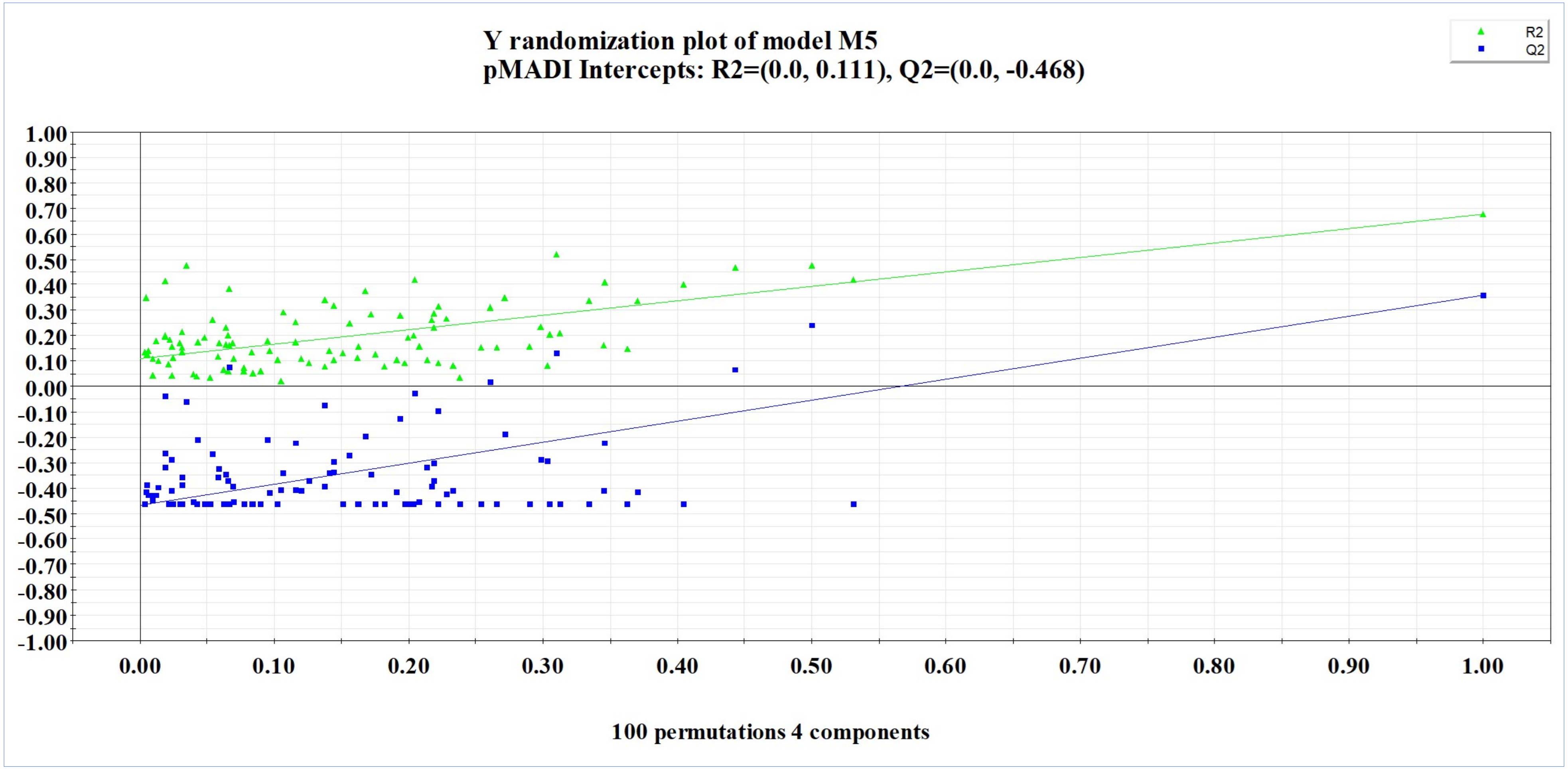
Y randomization plot of model M5
pMADI Intercepts: R2=(0.0, 0.111), Q2=(0.0, -0.468)
R2
Q2
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
-0.10
-0.20
-0.30
-0.40
-0.50
-0.60
-0.70
-0.80
-0.90
-1.00
0.00
0.10
0.20
0.30
0.40
0.50
0.60
0.70
0.80
0.90
1.00
100 permutations 4 components

Table S1. List of top 20 and least 20 toxic pesticides according to the developed models.

S.no.	chemical	Smile	Safety and hazardous
		Top 20 most toxic pesticides	
1	Propetamphos	CCNP(=S)(OC)OC(=CC(=O)OC(C)C)C	Acute toxic, Environmental hazards[1]
2	Pyridafenthion	CCOP(=S)(OCC)OC1=NN(C(=O)C=C1)C2=CC=CC=C2	Irritant[1]
3	Amidothioate	CCNP(=S)(OC)OC1=C(C=C(C=C1)SC)Cl	Human health and protection; High Cramer Class : (class III) [https://sitem.herts.ac.uk/aeru/ppdb/]
4	Sulprofos	CCCSP(=S)(OCC)OC1=CC=C(C=C1)SC	Acute toxic, Environmental hazards[1]
5	Fenthion	CC1=C(C=CC(=C1)OP(=S)(OC)OC)SC	Acute toxic, health hazards environmental hazards[1]
6	Fenthion-ethyl	CCOP(=S)(OCC)OC1=CC(=C(C=C1)SC)C	Acute toxic, Environmental hazards[1]
7	Fensulfothion	CCOP(=S)(OCC)OC1=CC=C(C=C1)S(=O)C	Acute toxic, Environmental hazards[1]
8	Fenthion sulfoxide	CC1=C(C=CC(=C1)OP(=S)(OC)OC)S(=O)C	Acute toxic[1]
9	Pyridaben	CC(C)(C)C1=CC=C(C=C1)CSC2=C(C(=O)N(N=C2)C(C)(C)C)Cl	Acute toxic, Environmental hazards[1]
10	Uniconazole	CC(C)(C)C(C(=CC1=CC=C(C=C1)Cl)N2C=NC=N2)O	Irritant[1]
11	Cloproxydim	CCCC(=C1C(=O)CC(CC1=O)CC(C)SCC)NOCC=CCl]	Human health and protection; High Cramer Class : (class III) [https://sitem.herts.ac.uk/aeru/ppdb/
12	Diniconazole	CC(C)(C)C(C(=CC1=C(C=C(C=C1)Cl)Cl)N2C=NC=N2)O	Irritant, Environmental hazards[1]
13	Diniconazole-M	CC(C)(C)C(C(=CC1=C(C=C(C=C1)Cl)Cl)N2C=NC=N2)O	Irritant, health hazards, Environmental hazards[1]
14	Clethodim	CCC(=C1C(=O)CC(CC1=O)CC(C)SCC)NOCC=CCl	Irritant[1]
15	Bromocyclen	C1C(C2(C(=C(C1(C2(Cl)Cl)Cl)Cl)Cl)Cl)CBr	Suspected poison
16	Tepraloxydim	CCC(=C1C(=O)CC(CC1=O)C2CCOCC2)NOCC=CCl	Health hazards[2]
17	Dieldrin	C1C2C3C(C1C4C2O4)C5(C(=C(C3(C5(Cl)Cl)Cl)Cl)Cl)Cl	Acute toxic, health hazards, Environmental[1]
18	Endrin	C1C2C3C(C1C4C2O4)C5(C(=C(C3(C5(Cl)Cl)Cl)Cl)Cl)Cl	Acute toxic, Environmental hazards[1]
19	Hymexazol	CC1=CC(=O)NO1	Corrosive, Irritant, health hazards, Environmental hazards[1]
20	Fenaminstrobi	CC(=NOCC1=CC=CC=C1C(=NOC)C(=O)NC)C=CC2=C(C=CC=C2Cl)	Irritant[1]

	n	Cl	
Least 20 toxic pesticides			
1	Metcamifen	CNC(=O)NC1=CC=C(C=C1)S(=O)(=O)NC(=O)C2=CC=CC=C2OC	Very low acute toxicity [https://www.tga.gov.au/]
2	Tripyrasulfone	CC1=CC(=NN1CC2=C(C=CC(=C2Cl)C(=O)C3=C(N(N=C3C)C)OC(=O)C4=CN(N=C4C)C)S(=O)(=O)C)C	Low acute toxicity [https://www.apvma.gov.au/]
3	Fomesafen	CS(=O)(=O)NC(=O)C1=C(C=CC(=C1)OC2=C(C=C(C=C2)C(F)(F)F)Cl)[N+](=O)[O-]	Low order of acute toxicity [https://www3.epa.gov/pesticides/]
4	Mecarbinzid	COC(=O)NC1=NC2=CC=CC=C2N1C(=O)NCCSC	No indication of carcinogenicity in humans (not listed by IARC) [1]
5	Triafamone	CN(C1=C(C=CC=C1F)C(=O)C2=NC(=NC(=N2)OC)OC)S(=O)(=O)C(F)F	Low-toxic[1]
6	Asulam	COC(=O)NS(=O)(=O)C1=CC=C(C=C1)N	Low acute toxicity [https://www3.epa.gov/pesticides/]
7	Cyprosulfamide	COC1=CC=CC=C1C(=O)NS(=O)(=O)C2=CC=C(C=C2)C(=O)NC3CC3	Low toxicity in acute toxicity [https://www.federalregister.gov/]
8	Benthiavalicarb-isopropyl	CC(C)C(C(=O)NC(C)C1=NC2=C(S1)C=C(C=C2)F)NC(=O)OC(C)C	Low mammalian oral toxicity [http://sitem.herts.ac.uk/aeru/ppdb/]
9	Bispyribac	COC1=CC(=NC(=N1)OC2=C(C(=CC=C2)OC3=NC(=CC(=N3)OC)OC)C(=O)O)OC	Low acute toxicity [https://www.federalregister.gov/d/2011-2266]
10	Picloram	C1(=C(C(=NC(=C1Cl)Cl)C(=O)O)Cl)N	Slightly toxic [https://www3.epa.gov/pesticides/]
11	Chlorflurenol	C1=CC=C2C(=C1)C3=C(C2(C(=O)O)O)C=C(C=C3)Cl	Low mammalian oral toxicity [https://sitem.herts.ac.uk/aeru/ppdb/].
12	Aminopyralid	NC1=CC(Cl)=NC(C(O)=O)=C1Cl	Low to moderate toxicity [https://sitem.herts.ac.uk/aeru/ppdb/]
13	Aminopyralid	C1=C(C(=C(N=C1Cl)C(=O)O)Cl)N	Non-toxic to mammals [https://wsdot.wa.gov/]
14	Fluroxypyr	C(C(=O)O)OC1=NC(=C(C(=C1Cl)N)Cl)F	Low toxicity [https://wsdot.wa.gov/]
15	Tricamba	COc1c(Cl)cc(Cl)c(Cl)c1C(=O)O	Low for aquatic organisms, mammals [https://www.mda.state.mn.us/]
16	Daminozide	CN(C)NC(=O)CCC(=O)O]	Practically non-toxic to mammals [https://www3.epa.gov/pesticides/
17	Famoxadone	CC1(C(=O)N(C(=O)O1)NC2=CC=CC=C2)C3=CC=C(C=C3)OC4=CC=	Minimal to moderate acute toxicity

		CC=C4	[https://www3.epa.gov/pesticides/]
18	Fluoxapiprolin	CS(=O)(=O)OC1=C(C(=CC=C1)Cl)C2CC(=NO2)C3=CSC(=N3)C4CCN(CC4)C(=O)CN5C(=CC(=N5)C(F)F)C(F)F	Low toxicity [https://www.apvma.gov.au/]
19	Benazolin-ethyl	CCOC(=O)CN1C2=C(C=CC=C2Cl)SC1=O	Slightly toxic by oral exposure. [http://extoxnet.orst.edu/pips/quizalof.htm.]
20	Thifluzamide	CC1=NC(=C(S1)C(=O)NC2=C(C=C(C=C2Br)OC(F)(F)F)Br)C(F)(F)F	Might cause a potential toxicity for the earthworm (Eisenia fetida) [3].

References:

1. S. Kim, J. Chen, T. Cheng, A. Gindulyte, J. He, S. He, Q. Li, B. A. Shoemaker, P. A. Thiessen, B. Yu, L. Zaslavsky, J. Zhang, & E. E. Bolton, PubChem 2023 update, *Nucleic Acids Res.*, 2023, **51**, D1373–D1380, DOI: 10.1093/nar/gkac956. Available from https://pubchem.ncbi.nlm.nih.gov/.
2. MP. Quick, Suspected cases of bromocyclen poisoning., *Vet. Hum. Toxico*. 1992, **34**, 455-457. PMID: 1455619.
3. X. Yao, F. Zhang, Z. Qiao, H. Yu, S. Sun, X. Li, J. Zhang, and X. Jiang, Toxicity of thifluzamide in earthworm (Eisenia fetida), *Ecotoxicol. Environ. Saf.*, 2020, **188**, 109880, DOI: 10.1016/j.ecoenv.2019.109880.

Table S2: Comparative statistical results of the developed models with other models developed using different dataset ratio.

Dataset division ratio	Model	LVs	N_{train}/N_{test}	descriptors	Training set				Test set		
					R^2	Q^2_{LOO}	MAE_{TRAIN}	MAE_{LOO}	$Q^2_{(F1)}$	$Q^2_{(F2)}$	MAE_{TEST}
Present study Training: test=75:25 (approx.)	M1	4	29/10	5	0.704	0.580	0.248	0.303	0.576	0.564	0.306
	M2	4	29/10	5	0.674	0.553	0.255	0.306	0.557	0.544	0.302
	M3	4	29/10	5	0.712	0.568	0.263	0.327	0.544	0.531	0.342
	M4	4	29/10	5	0.674	0.544	0.255	0.314	0.611	0.599	0.288
	M5	4	29/10	5	0.676	0.546	0.261	0.318	0.593	0.581	0.301
Training: test=65:35 (approx.)	M1	4	31/8	5	0.696	0.523	0.279	0.347	0.531	0.505	0.215
	M2	4	31/8	5	0.677	-	0.278	-	0.432	0.420	0.222
	M3	4	31/8	5	0.689	0.527	0.301	0.373	0.463	0.432	0.300
	M4	4	31/8	5	0.711	-	0.268	-	-2.19	-3.13	0.538
	M5	4	31/8	5	0.700	0.562	0.280	0.346	0301	0.261	0.285
Training: test=80:20 (approx.)	M1	4	25/14	5	0.542	0.303	0.262	0.337	0.684	0.461	0.370
	M2	4	25/14	5	-	-	-	-	-	-	-
	M3	4	25/14	5	0.736	0.530	0.306	0.403	-0.06	-0.367	0.344
	M4	4	25/14	5	0.771	-	0.259	-	-2.97	-4.49	0.513
	M5	4	25/14	5	0.546	0.105	0.260	0.371	0.632	0.373	0.419