QSPR on Estimating of Polychlorinated Biphenyls Relative Response Factor using Molecular Descriptors Family

Lorentz JÄNTSCHI

Technical University of Cluj-Napoca, Romania, http://lori.academicdirect.org

Abstract

The molecular descriptors family methodology was applied on relative response factor of polychlorinated biphenyls in order to obtain quantitative structure-property relationships.

The use of molecular descriptors family allows making of important remarks about nature of the relative response factor property and its causality.

The obtained quantitative structure-property relationships can explain over 62% of polychlorinated biphenyls relative response factors.

Keywords:

polychlorinated biphenyls (PCBs), molecular descriptors family (MDF), multiple linear regression (MLR), quantitative structure-property relationship (QSPR)

Introduction

Polychlorinated biphenyls (PCBs) are a group of 209 synthetic halogenated aromatic hydrocarbons, being a lipophilic group of global pollutants. The PCBs have different toxicity and biological effects including death, birth defects, reproductive failure, liver damage, tumors [1, 2]. The compounds were used in the electricity generating industry as insulating and coolant agents in transformers and capacitors [3, 4] because they do not burn easily and

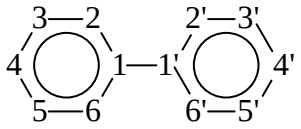
are good insulators. PCBs were produce commercially since 1929, till 1977 in U.S. but they are still present in environmental samples from the polar regions of air, snow, water, and living organisms [5-7] being widely pollutants.

A quantitative structure-property relationship (QSPR) relates a quantitative measurable property of chemical, physical, or even biological property and is a technique used today in many domains, including pharmaceutical, environmental, biological domains. Today, the literature contains a lot of QSPR equations for many parameters used to assess the risk of chemicals in the environment [8-11]. Most of the QSPR equation are based on linear regression analysis [12] or by the artificial neural networks [13-16].

The aim of this paper is to present the ability of the molecular descriptors family (MDF) in estimation of relative response factor of PCBs, using the data from Mullin et al. [17] which synthesized and determined the retention times and response factors relative to a reference standard (octachloronaphthalene) of all 209 congeners (Table 1) by using temperature-programmed, high resolution gas chromatography, and electron-capture detection methods (HRGC/ECD).

Material

All 209 PCBs were included into the study. PCBs are synthetic chlorinated hydrocarbon compounds that consist of two benzene rings linked by a single carbon–carbon bond, with from 1 to all 10 of the hydrogen atoms replaced with chlorines. The generic structure of the PCBs is:



PCBs are produced by chlorination of a biphenyl with anhydrous chlorine in the presence of iron filing or ferric chloride as the catalyst being possible ten degree of chlorination and producing 10 PCBs congener group: mono-, di-, tri-, terta-, penta-, hexa-, hepta-, octa-, nona-, decachlorobiphenyl. Table 1 contains the PBCs number, the structure (chlorine-filled) and the measured property (relative response factor, rrf).

Table 1. Polychlorinated biphenyls relative response factors (rrf)

PCB	Chlorines	rrf	PCB	Chlorines	rrf	PCB	Chlorines	rrf
1	2	0.0251	71	2,3',4',6	0.468	141	2,2',3,4,5,5'	1.352
2	3	0.0393	72	2,3',5,5'	0.5515	142	2,2',3,4,5,6	1.218
3	4	0.04	73	2,3',5',6	0.5805	143	2,2',3,4,5,6'	0.7088
4	2,2'	0.0374	74	2,4,4',5	0.671	144	2,2',3,4,5',6	0.8764
5	2,3	0.119	75	2,4,4',6	0.6461	145	2,2',3,4,6,6'	0.6789
6	2,3'	0.38	76	2',3,4,5	0.5795	146	2,2',3,4',5,5'	0.728
7	2,4	0.69	77	3,3',4,4'	0.3812	147	2,2',3,4',5,6	0.6
8	2,4'	0.206	78	3,3',4,5	1.1151	148	2,2',3,4',5,6'	0.554
9	2,5	0.388	79	3,3',4,5'	0.881	149	2,2',3,4',5',6	0.572
10	2,6	0.262	80	3,3',5,5'	0.7278	150	2,2',3,4',6,6'	0.5676
11	3,3'	0.0449	81	3,4,4',5	0.7159	151	2,2',3,5,5',6	0.785
12	3,4	0.179	82	2,2',3,3',4	0.773	152	2,2',3,5,6,6'	0.5235
13	3,4'	0.2	83	2,2',3,3',5	0.6339	153	2,2',4,4',5,5'	0.688
14	3,5	0.3047	84	2,2',3,3',6	0.386	154	2,2',4,4',5,6'	0.57
15	4,4'	0.107	85	2,2',3,4,4'	0.7396	155	2,2',4,4',6,6'	0.586
16	2,2',3	0.447	86	2,2',3,4,5	0.7968	156	2,3,3',4,4',5	1.389
17	2,2',4	0.412	87	2,2',3,4,5'	1.021	157	2,3,3',4,4',5'	1.1965
18	2,2',5	0.313	88	2,2',3,4,6	0.6892	158	2,3,3',4,4',6	1.132
19	2,2',6	0.3037	89	2,2',3,4,6'	0.561	159	2,3,3',4,5,5'	0.9934
20	2,3,3'	0.7238	90	2,2',3,4',5	0.611	160	2,3,3',4,5,6	1.1914
21	2,3,4	1.0598	91	2,2',3,4',6	0.571	161	2,3,3',4,5',6	0.9672
22	2,3,4'	1.0935	92	2,2',3,5,5'	0.5375	162	2,3,3',4',5,5'	1.0322
23	2,3,5	0.5	93	2,2',3,5,6	0.6676	163	2,3,3',4',5,6	0.9976
24	2,3,6	0.793	94	2,2',3,5,6'	0.4514	164	2,3,3',4',5',6	0.9848
25	2,3',4	0.5	95	2,2',3,5',6	0.443	165	2,3,3',5,5',6	1.0777
26	2,3',5	0.603	96	2,2',3,6,6	0.4308	166	2,3,4,4',5,6	1.0421
27	2,3',6	0.495	97	2,2',3',4,5	0.631	167	2,3',4,4',5,5'	1.0658
28	2,4,4'	0.854	98	2,2',3',4,6	0.6246	168	2,3',4,4',5',6	0.8375
29	2,4,5	0.6339	99	2,2',4,4',5	0.613	169	3,3',4,4',5,5'	0.8355
30	2,4,6	0.8202	100	2,2',4,4',6	0.5871	170	2,2',3,3',4,4',5	0.75
31	2,4',5	0.562	101	2,2',4,5,5'	0.668	171	2,2',3,3',4,4',6	1.1712
32	2,4',6	0.278	102	2,2',4,5,6'	0.4561	172	2,2',3,3',4,5,5'	1.172
33	2',3,4	0.447	103	2,2',4,5',6	0.6068	173	2,2',3,3',4,5,6	2.044
34	2',3,5	0.6092	104	2,2',4,6,6	0.4561	174	2,2',3,3',4,5,6'	0.806
35	3,3',4	0.3746	105	2,3,3',4,4'	0.94	175	2,2',3,3',4,5',6	0.381
36	3,3',5	0.2948	106	2,3,3',4,5	1.0046	176	2,2',3,3',4,6,6'	1.0589

PCB	Chlorines	rrf
37	3,4,4'	0.58
38	3,4,5	0.722
39	3,4',5	0.347
40	2,2',3,3'	0.722
41	2,2',3,4	0.5469
42	2,2',3,4'	0.792
43	2,2',3,5	0.503
44	2,2',3,5'	0.524
45	2,2',3,6	0.54
46	2,2',3,6'	0.468
47	2,2',4,4'	0.848
48	2,2'4,5	0.556
49	2,2',4,5'	0.648
50	2,2',4,6	0.6817
51	2,2',4,6'	0.6
52	2,2',5,5'	0.418
53	2,2',5,6'	0.3606
54	2,2',6,6'	0.3643
55	2,3,3',4	0.829
56	2,3,3',4'	0.829
57	2,3,3',5	0.6
58	2,3,3',5'	0.609
59	2,3,3',6	0.6
60	2,3,4,4'	1.0164
61	2,3,4,5	1.2227
62	2,3,4,6	1.1478
63	2,3,4',5	0.728
64	2,3,4',6	0.607
65	2,3,5,6	0.8408
66	2,3',4,4'	0.646
67	2,3',4,5	0.6
68	2,3',4,5'	0.726
69	2,3',4,6	0.8024
70	2,3',4',5	0.658

PCB	Chlorines	rrf
107	2,3,3',4',5	0.8183
108	2,3,3',4,5'	1.0654
109	2,3,3',4,6	0.9625
110	2,3,3',4',6	0.65
111	2,3,3',5,5'	0.6601
112	2,3,3',5,6	0.8286
113	2,3,3',5',6	0.604
114	2,3,4,4',5	1.0261
115	2,3,4,4',6	1.1328
116	2,3,4,5,6	1.3987
117	2,3,4',5,6	0.8895
118	2,3',4,4',5	0.87
119	2,3',4,4',6	0.8239
120	2,3',4,5,5'	0.7444
121	2,3',4,5',6	0.7659
122	2',3,3',4,5	0.7247
123	2',3,4,4',5	0.6645
124	2',3,4,5,5'	0.848
125	2',3,4,5,6'	0.556
126	3,3',4,4'5	0.4757
127	3,3',4,5,5'	0.5834
128	2,2',3,3',4,4'	1.188
129	2,2',3,3',4,5	0.997
130	2,2',3,3',4,5'	0.952
131	2,2',3,3',4,6	0.8492
132	2,2',3,3',4,6'	0.7303
133	2,2',3,3',5,5'	1.148
134	2,2',3,3',5,6	0.7331
135	2,2',3,3',5,6'	0.7031
136	2,2',3,3',6,6'	0.444
137	2,2',3,4,4',5	1.112
138	2,2',3,4,4',5'	0.827
139	2,2',3,4,4',6	0.7219
140	2,2',3,4,4',6'	0.6732

PCB	Chlorines	rrf
177	2,2',3,3',4',5,6	1.0009
178	2,2',3,3',5,5',6	0.621
179	2,2',3,3',5,6,6'	0.8237
180	2,2',3,4,4',5,5'	1.295
181	2,2',3,4,4',5,6	1.6046
182	2,2',3,4,4',5,6'	1.1272
183	2,2',3,4,4',5',6	0.976
184	2,2',3,4,4',6,6'	1.0046
185	2,2',3,4,5,5',6	1.437
186	2,2',3,4,5,6,6'	1.2236
187	2,2',3,4',5,5',6	1.122
188	2,2',3,4',5,6,6'	0.7337
189	2,3,3',4,4',5,5'	1.5091
190	2,3,3',4,4',5,6	1.31
191	2,3,3',4,4',5',6	1.4741
192	2,3,3',4,5,5',6	1.599
193	2,3,3',4',5,5',6	1.4167
194	2,2',3,3',4,4',5,5'	1.868
195	2,2',3,3',4,4',5,6	0.415
196	2,2',3,3',4,4',5',6	1.2321
197	2,2',3,3',4,4',6,6'	0.9522
198	2,2',3,3',4,5,5',6	1.07
199	2,2',3,3',4,5,6,6'	1.1508
200	2,2',3,3',4,5',6,6'	0.369
201	2,2',3,3',4',5,5',6	0.803
202	2,2',3,3',5,5',6,6'	1.165
203	2,2',3,4,4',5,5',6	1.629
204	2,2',3,4,4',5,6,6'	0.8034
205	2,3,3',4,4',5,5',6	1.406
206	2,2',3,3',4,4',5,5',6	1.673
207	2,2',3,3',4,4',5,6,6'	1.3257
208	2,2',3,3',4,5,5',6,6'	1.1756
209	2,2',3,3',4,4',5,5',6,6'	1.139

Methods

Opposing to the Wiener [18-21], Randic [22], molecular connectivity [23] which consider strictly the topological structure of the molecule as the only structure descriptor, the MDF considers both topological structure and topographical shape of the molecule as essential contributors to the molecular property behavior.

The MDF methodology starts with 3D structure of molecules constructing using a molecular modeling program (such as HyperChem), partial charge distribution calculations (using a method like semi-empirical Extended Hückel Single Point Approach) and calculation of a huge number (787968) of molecular descriptors based on different assumptions [24].

The MDF methodology continues with cleaning of the family by the undefined, trivial and identical values members. For the rrf property of PCBs set a number of 98434 members remain in the MDF.

The measured property and the remained MDF members are stored into a database. A set of client-server programs runs for QSPR findings using a MLR (multiple linear regressions) algorithm.

First are found the member which correlates the best with the measured property. Pairs of members enter into bi-varied findings of QSPRs in the second. Multi-varied findings of QSPRs use heuristic algorithms in place of all possible combinations because all possible combinations are almost impossible to be exhausted in real time.

Finally, a query program search for the best obtained results into the results table from the database, and produce a report.

Results

The procedure of QSPRs findings has runs for mono-, bi- and four-varied models. The best mono-varied MDF QSPR, best bi-varied MDF QSPR, and best found four-varied MDF QSPR are gave and discussed.

The calculated values of the members which appear in the QSPRs of PCBs are in table 2.

Table 2. The molecular descriptors used in the QSPR for polychlorinated biphenyls

PCB	iHMdTHg	10^{-2}imMrFHt	iHDdFHg	10^{-2}imMrFHt	10^{2}iMMMjQg	10^{-1}iAMrVQg
001	1.266	2.031	1.070	2.031	0.470	-0.945
002	1.341	2.102	1.114	2.102	2.878	-2.070
003	1.277	2.102	1.126	2.102	1.490	-2.119
004	1.213	2.102	1.219	2.102	3.409	-1.007
005	1.651	2.102	1.333	2.102	1.010	-1.291
006	1.586	2.102	1.281	2.102	0.657	-1.259
007	1.614	2.102	1.324	2.102	0.638	-1.276
008	1.520	2.102	1.293	2.102	1.231	-1.360
009	1.581	2.102	1.282	2.102	0.684	-1.325
010	1.516	2.102	1.230	2.102	0.747	-0.822
011	1.649	2.176	1.327	2.176	2.527	-2.985
012	1.698	2.176	1.388	2.176	0.613	-3.099
013	1.589	2.176	1.342	2.176	1.957	-3.071
014	1.762	2.176	1.359	2.176	2.648	-2.891
015	1.529	2.176	1.356	2.176	1.327	-3.171
016	1.545	2.176	1.442	2.176	4.344	-1.337
017	1.530	2.176	1.437	2.176	4.330	-1.178
018	1.538	2.176	1.408	2.176	4.759	-1.356
019	1.487	2.176	1.384	2.176	5.485	-1.769
020	1.923	2.176	1.508	2.176	1.321	-1.676
021	2.069	2.176	1.607	2.176	0.966	-1.722
022	1.859	2.176	1.523	2.176	1.299	-1.823
023	2.087	2.176	1.566	2.176	1.771	-1.704
024	1.960	2.176	1.527	2.176	1.821	-0.884
025	1.885	2.176	1.504	2.176	1.023	-1.649
026	1.891	2.176	1.469	2.176	1.344	-1.676
027	1.844	2.176	1.455	2.176	1.827	-0.872
028	1.823	2.176	1.518	2.176	1.130	-1.788
029	2.057	2.176	1.573	2.176	0.966	-1.702
030	1.996	2.176	1.526	2.176	2.667	-0.871
031	1.829	2.176	1.487	2.176	1.313	-1.804
032	1.781	2.176	1.467	2.176	2.167	-0.922
033	1.901	2.176	1.515	2.176	1.316	-1.797
034	1.962	2.176	1.491	2.176	1.318	-1.694
035	1.957	2.250	1.567	2.250	4.231	-4.251
036	2.018	2.250	1.535	2.250	4.223	-3.969
037	1.901	2.250	1.583	2.250	2.737	-4.430
038	2.196	2.250	1.662	2.250	2.557	-4.211
039	1.961	2.250	1.555	2.250	3.848	-4.060

040	1.832	2.250	1.636	2.250	5.775	-1.478
041	1.936	2.250	1.683	2.250	5.440	-2.279
042	1.818	2.250	1.635	2.250	5.459	-1.603
043	1.954	2.250	1.648	2.250	5.503	-0.530
044	1.826	2.250	1.603	2.250	5.612	-1.468
045	1.827	2.250	1.600	2.250	6.229	-0.745
046	1.778	2.250	1.577	2.250	6.301	-1.173
047	1.804	2.250	1.633	2.250	5.598	-1.378
048	1.945	2.250	1.655	2.250	4.751	-2.459
049	1.812	2.250	1.606	2.250	5.040	-1.689
050	1.882	2.250	1.601	2.250	6.338	1.158
051	1.763	2.250	1.573	2.250	6.405	1.058
052	1.818	2.250	1.577	2.250	5.197	-1.411
053	1.776	2.250	1.547	2.250	0.202	-1.160
054	1.436	2.250	1.499	2.250	9.935	-0.246
055	2.296	2.250	1.756	2.250	1.040	-2.184
056	2.196	2.250	1.714	2.250	1.101	-2.369
057	2.312	2.250	1.714	2.250	1.465	-2.177
058	2.253	2.250	1.686	2.250	1.095	-2.218
059	2.190	2.250	1.678	2.250	2.054	-1.100
060	2.296	2.250	1.756	2.250	1.019	-2.184
061	2.615	2.250	1.891	2.250	0.787	-2.251
062	2.492	2.250	1.817	2.250	2.827	-1.113
063	2.252	2.250	1.734	2.250	1.224	-2.358
064	2.130	2.250	1.692	2.250	2.260	-1.168
065	2.467	2.250	1.803	2.250	1.886	-1.123
066	2.159	2.250	1.713	2.250	1.015	-2.314
067	2.282	2.250	1.722	2.250	1.078	-2.170
068	2.216	2.250	1.689	2.250	1.151	-2.158
069	2.223	2.250	1.679	2.250	3.409	-1.082
070	2.165	2.250	1.680	2.250	1.101	-2.354
071	2.120	2.250	1.658	2.250	1.943	-1.161
072	2.221	2.250	1.655	2.250	1.155	-2.199
073	2.182	2.250	1.635	2.250	2.078	-1.081
074	2.222	2.250	1.742	2.250	0.993	-2.351
075	2.163	2.250	1.694	2.250	4.313	-1.146
076	2.358	2.250	1.757	2.250	1.104	-2.411
077	2.225	2.326	1.777	2.326	1.842	-5.733
078	2.406	2.326	1.806	2.326	2.794	-5.413
079	2.281	2.326	1.746	2.326	2.336	-5.259
080	2.337	2.326	1.714	2.326	4.508	-4.883

081	2.353	2.326	1.827	2.326	2.129	-5.627
082	2.182	2.326	1.855	2.326	6.661	-1.884
083	2.199	2.326	1.818	2.326	5.951	-1.198
084	2.078	2.326	1.774	2.326	7.377	-1.196
085	2.169	2.326	1.858	2.326	6.634	5.400
086	2.457	2.326	1.939	2.326	5.637	-2.306
087	2.176	2.326	1.826	2.326	6.510	-1.794
088	2.332	2.326	1.861	2.326	7.219	-1.179
089	2.132	2.326	1.793	2.326	8.010	-1.368
090	2.185	2.326	1.825	2.326	5.760	-1.207
091	2.064	2.326	1.775	2.326	7.017	-1.245
092	2.191	2.326	1.793	2.326	5.862	-0.302
093	2.309	2.326	1.851	2.326	6.592	-1.250
094	2.153	2.326	1.762	2.326	3.889	-1.396
095	2.076	2.326	1.744	2.326	9.502	-1.268
096	1.750	2.326	1.694	2.326	8.815	-0.319
097	2.191	2.326	1.827	2.326	6.693	-3.060
098	2.131	2.326	1.778	2.326	7.552	-1.373
099	2.177	2.326	1.833	2.326	5.638	2.140
100	2.117	2.326	1.778	2.326	8.989	-1.237
101	2.183	2.326	1.806	2.326	6.258	-1.746
102	2.146	2.326	1.767	2.326	0.517	-1.397
103	2.129	2.326	1.751	2.326	1.224	-1.304
104	1.800	2.326	1.695	2.326	8.758	-0.320
105	2.530	2.326	1.940	2.326	1.000	-3.045
106	2.798	2.326	2.013	2.326	0.918	-2.816
107	2.545	2.326	1.900	2.326	1.281	-3.025
108	2.584	2.326	1.911	2.326	1.180	-2.816
109	2.678	2.326	1.948	2.326	3.845	-1.358
110	2.429	2.326	1.861	2.326	2.341	-1.450
111	2.598	2.326	1.871	2.326	1.342	-2.809
112	2.654	2.326	1.929	2.326	2.199	-1.380
113	2.488	2.326	1.834	2.326	2.596	-1.349
114	2.739	2.326	2.035	2.326	0.844	-3.075
115	2.619	2.326	1.965	2.326	4.850	-1.445
116	3.131	2.326	2.162	2.326	3.012	-1.406
117	2.596	2.326	1.951	2.326	2.513	-1.462
118	2.515	2.326	1.910	2.326	1.003	-3.009
119	2.459	2.326	1.865	2.326	4.215	-1.417
120	2.568	2.326	1.885	2.326	1.163	-2.778
121	2.518	2.326	1.842	2.326	4.395	-1.315

122	2.609	2.326	1.925	2.326	1.221	-3.139
123	2.573	2.326	1.932	2.326	1.612	-3.035
124	2.578	2.326	1.898	2.326	1.284	-3.099
125	2.544	2.326	1.871	2.326	2.849	-1.436
126	2.631	2.402	1.991	2.402	1.984	-6.649
127	2.684	2.402	1.959	2.402	2.489	-6.090
128	2.493	2.402	2.059	2.402	11.594	-2.445
129	2.662	2.402	2.088	2.402	9.267	-3.022
130	2.509	2.402	2.023	2.402	6.822	-4.135
131	2.541	2.402	2.018	2.402	12.395	0.694
132	2.394	2.402	1.975	2.402	10.893	-1.278
133	2.523	2.402	1.987	2.402	8.845	-3.576
134	2.520	2.402	2.003	2.402	11.802	-1.441
135	2.414	2.402	1.941	2.402	3.496	-3.441
136	2.025	2.402	1.875	2.402	7.833	-0.414
137	2.501	2.402	2.033	2.402	10.196	-2.647
138	2.501	2.402	2.033	2.402	10.196	-2.647
139	2.527	2.402	2.023	2.402	10.581	-1.938
140	2.445	2.402	1.981	2.402	15.550	-1.603
141	2.655	2.402	2.066	2.402	7.948	1.184
142	2.948	2.402	2.179	2.402	9.178	-4.242
143	2.623	2.402	2.027	2.402	4.458	-2.230
144	2.540	2.402	1.991	2.402	14.219	5.992
145	2.225	2.402	1.932	2.402	7.675	-0.415
146	2.515	2.402	2.001	2.402	7.862	-1.134
147	2.506	2.402	2.012	2.402	8.972	-1.447
148	2.465	2.402	1.951	2.402	4.526	-1.590
149	2.408	2.402	1.948	2.402	11.778	-1.224
150	2.075	2.402	1.879	2.402	7.892	-0.416
151	2.519	2.402	1.980	2.402	4.014	-1.375
152	2.182	2.402	1.922	2.402	7.736	-0.417
153	2.507	2.402	2.016	2.402	8.379	-2.257
154	2.457	2.402	1.958	2.402	2.261	-1.497
155	2.123	2.402	1.883	2.402	7.854	-0.416
156	2.991	2.402	2.178	2.402	0.710	-3.863
157	2.903	2.402	2.130	2.402	0.865	-3.936
158	2.876	2.402	2.115	2.402	3.756	-1.770
159	3.042	2.402	2.148	2.402	0.833	-3.541
160	3.274	2.402	2.267	2.402	3.502	-1.700
161	2.933	2.402	2.086	2.402	4.053	-1.637
162	2.916	2.402	2.092	2.402	0.981	-3.914

163	2.854	2.402	2.096	2.402	1.827	-1.802
164	2.814	2.402	2.051	2.402	1.991	-1.782
165	2.911	2.402	2.067	2.402	2.183	-1.666
166	3.218	2.402	2.293	2.402	5.007	-1.809
167	2.887	2.402	2.107	2.402	0.988	-3.871
168	2.841	2.402	2.061	2.402	4.121	-1.728
169	2.993	2.481	2.180	2.481	2.031	-6.909
170	2.933	2.481	2.276	2.481	2.310	0.139
171	2.817	2.481	2.208	2.481	19.874	-1.436
172	2.946	2.481	2.241	2.481	15.518	-5.458
173	3.117	2.481	2.314	2.481	16.680	-5.029
174	2.847	2.481	2.191	2.481	2.429	-0.753
175	2.837	2.481	2.174	2.481	2.072	-2.424
176	2.461	2.481	2.102	2.481	7.217	-0.548
177	2.797	2.481	2.192	2.481	4.905	-1.999
178	2.817	2.481	2.158	2.481	6.772	-1.425
179	2.419	2.481	2.087	2.481	7.229	-0.555
180	2.939	2.481	2.257	2.481	12.841	-1.478
181	3.103	2.481	2.327	2.481	14.476	5.585
182	2.895	2.481	2.203	2.481	5.638	-1.707
183	2.830	2.481	2.183	2.481	7.556	-1.300
184	2.508	2.481	2.109	2.481	7.160	-0.550
185	3.116	2.481	2.294	2.481	0.402	-3.275
186	2.794	2.481	2.224	2.481	7.032	-0.568
187	2.811	2.481	2.172	2.481	2.801	-1.857
188	2.466	2.481	2.098	2.481	7.158	-0.557
189	3.322	2.481	2.349	2.481	0.936	-4.856
190	3.434	2.481	2.419	2.481	5.219	-2.203
191	3.220	2.481	2.288	2.481	4.672	-2.148
192	3.489	2.481	2.388	2.481	5.306	-2.023
193	3.199	2.481	2.269	2.481	2.275	-2.192
194	3.331	2.560	2.478	2.560	13.923	-9.996
195	3.354	2.560	2.491	2.560	1.815	6.194
196	3.229	2.560	2.411	2.560	1.215	-2.458
197	2.854	2.560	2.322	2.560	6.491	-0.764
198	3.373	2.560	2.456	2.560	4.469	-1.637
199	2.992	2.560	2.378	2.560	6.451	-0.814
200	2.814	2.560	2.305	2.560	6.510	-0.789
201	3.373	2.560	2.456	2.560	4.605	-1.637
202	2.773	2.560	2.289	2.560	6.470	-0.803
203	3.366	2.560	2.473	2.560	6.067	-12.649

204	3.036	2.560	2.392	2.560	6.364	-0.821
205	3.738	2.560	2.574	2.560	4.708	-2.650
206	3.725	2.641	2.680	2.641	2.158	-2.966
207	3.343	2.641	2.587	2.641	5.759	-1.455
208	3.304	2.641	2.569	2.641	5.849	-1.534
209	3.790	2.722	2.841	2.722	5.372	13.418

The best mono-varied MDF QSPR has the equation:

- $\hat{Y} = -5.063 \cdot 10^{-1} + 5.348 \cdot 10^{-1} \cdot iHMdTHg$ (1)

where $\hat{Y}$ is the predicted rrf (Y is the measured rrf), and the *iHMdTHg* is the member used in estimation and the associated statistical results are:

- $r = 0.793$ (correlation coefficient); $r^2 = 0.629$ (squared correlation coefficient); $s = 0.319$ (standard deviation); $F = 351$ (Fisher estimator); $p = 2.01 \cdot 10^{-46}$, (significance of regression model); $r^2_{cv} = 0.619$ (the leave one out square cross validation score). (2)

The graphical representation of the mono-varied MDF QSPR given by the equation (1) is in figure 2.

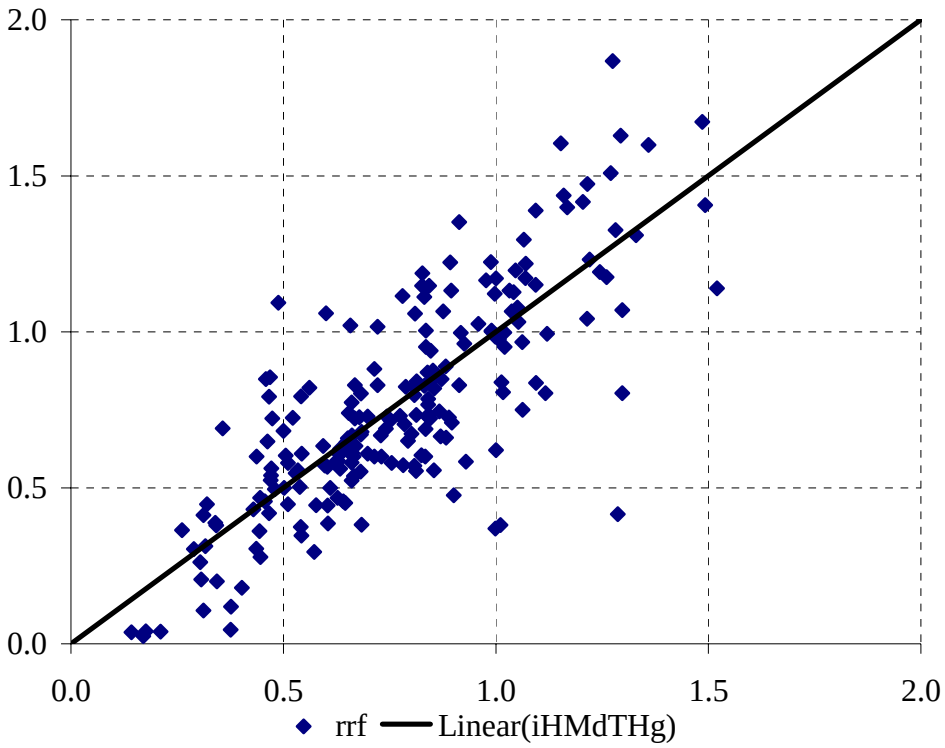


Figure 2. The plot of best mono-varied MDF QSPR

The best bi-varied MDF QSPR is:

- $\hat{Y} = 5.085\text{-}357.29 \cdot imMrFHt + 2.1561 \cdot iHDdFHg$ (3)

and the associated statistical results are:

- $r = 0.832$; $r^2 = 0.693$; $s = 0.1964$; $F = 232$, $p = 1.556 \cdot 10^{-53}$; $r^2(rrf, imMrFHt) = 0.448$; $r^2(rrf, iHDdFHg) = 0.581$; $r^2(imMrFHt, iHDdFHg) = 0.931$; $r^2_{cv} = 0.682$ (4)

The graphical representation of best bi-varied MDF QSPR (equation 3) is in figure 3.

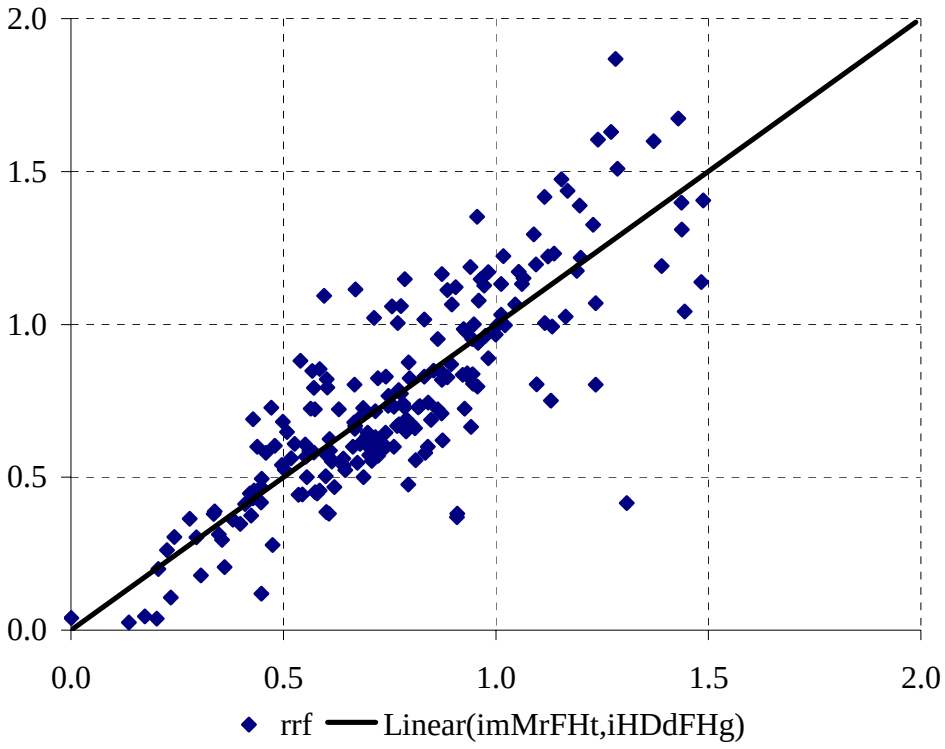


Figure 3. The plot of best bi-varied MDF QSPR

The best found four-varied MDF QSPR is:

- $\hat{Y}=6.055\text{-}416.9 \cdot imMrFHt + 2.314 \cdot iHDdFHg + 1.829 \cdot iMMMjQg - 2.51 \cdot 10^{-3} \cdot iAMrVQg$ (5)

and the associated statistical results for four-varied QSPR are:

- $r = 0.858$; $r^2 = 0.737$; $s = 0.183$; $F = 143$, $p = 5.768 \cdot 10^{-58}$; $r^2(rrf, imMrFHt) = 0.448$; $r^2(rrf, iHDdFHg) = 0.581$; $r^2(rrf, iMMMjQg) = 0.062$; $r^2(rrf, iAMrVQg) = 0.205$; $r^2(imMrFHt, iHDdFHg) = 0.931$; $r^2(imMrFHt, iMMMjQg) = 0.177$; $r^2(imMrFHt, iAMrVQg) = 0.002$; $r^2(iHDdFHg, iMMMjQg) = 0.111$; $r^2(iHDdFHg, iAMrVQg) = 0.0004$; $r^2(iMMMjQg, iAMrVQg) = 0.025$; $r^2_{cv} = 0.717$ (6)

The graphical representation of best found four-varied MDF QSPR (equation 5) is in figure 4.

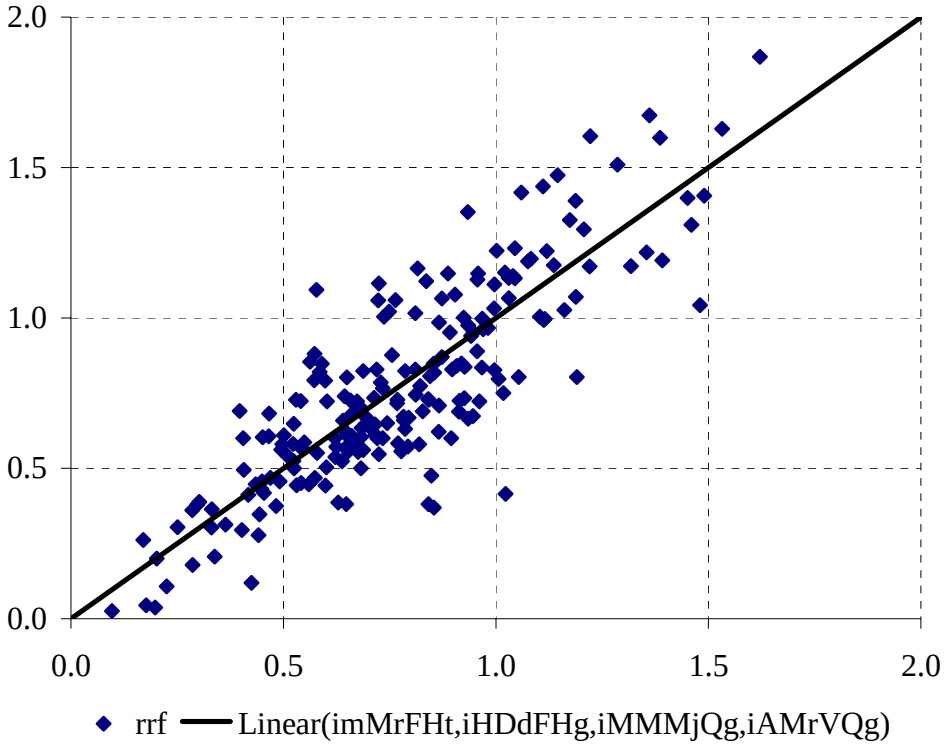


Figure 4. The plot of best found four-varied MDF QSPR

Discussions

The best mono-varied MDF QSPR (equation 1) uses from a total number of 98434 MDF members the *iHMdTHg* member. The used descriptors take into consideration the geometric distance operator computed using Cartesian coordinates of the PCBs (last character from the descriptor name 'g') and the number of directly bonded hydrogen's ('H'). The mono-varied MDF QSPR of relative response factor of PCBs is statistical significant giving us a probability of wrong model equal with $2.01 \cdot 10^{-44}$ % (equation (2)). Looking at the statistical results of the QSPR we can say that almost sixty-three percent of variation in PCBs relative response factor can be explain by its linear relations with the MDF member called *iHMdTHg*. Looking at the leave one out square cross validation score of mono-varied model we can see that this QSPR has good potential of estimation of PCBs relative response factor,

having a score equal with 0.619. The mono-varied model shows us that the variation of relative response factor can be assign to geometric conformation and the directly bonded hydrogen's.

The bi-varied MDF QSPR uses *imMrFHt* and *iHDdFHg* molecular structure descriptors (equation 3). The last letters of the descriptors name denote the use of topological distance (t) as well as the geometrical distance (g) in relative response factor estimation of PCBs. The penultimate letters of the members name highlight the importance of the directly bonded hydrogen's (H) in estimation of the relative response factor of PCBs. Thus, the bi-varied model is a model which takes into consideration the directly bonded hydrogen's as well as the topological and geometrical distance. The probability of a wrong bi-varied model (equation 4) is equal with $1.556 \cdot 10^{-51}$ %. Sixty-nine percent of the variation of PCBs relative response factor is explainable by its linear relation with *imMrFHt* and *iHDdFHg* MDF members. Looking at the statistical result of bi-varied MDF QSPR (equation 4) we can observe that there is a strong linearity between the used MDF members ($r^2 = 0.931$) while the linearity between the relative response factor and each MDF member is a weak one (the r^2(Rf, *imMrFHt*) = 0.448, and respectively r^2(Rf, *iHDdFHg*) = 0.581). The leave one out cross validation score gives us the power of estimation of PCBs relative response factor, which in case of the bi-varied MDF QSPR model is about 0.68.

The four-varied MDF QSPR for relative response factors of PCBs uses the *imMrFHt*, *iHDdFHg*, *iMMMjQg*, and *iAMrVQg* MDF members. If we look at the MDF members names to the last letter, it can be observed that the four-varied MDF QSPR take into consideration one MDF member which use the topologic distance operator (t) and three descriptors which use the geometrical distance operator (g). If we look at the penultimate letters of MDF members implied in the best found four-varied MDF QSPR it can be observed that two MDF members take into account the number of directly bonded hydrogen's (H) and the other two the partial change, semi-empirical Extended Hückel model, Single Point approach (Q). The four-varied MDF QSPR is statistically significant giving us a probability of wrong model equal with $5.768 \cdot 10^{-56}$ %.

Almost seventy-four percent of relative response factor variation is explainable by its linear relation with *imMrFHt*, *iHDdFHg*, *iMMMjQg*, and *iAMrVQg* molecular structure descriptors. The square of correlation coefficient between used MDF members from four-varied MDF QSPR (equation 6) suggest that is no link between using of orthogonal

descriptors (Principal and/or Dominant Component Analysis) in four-varied MDF QSPR modeling of relative response factor of PCBs. The four-varied MDF QSPR have a cross validation score equal with 0.717; thus, this model, compared with the mono and bi-varied models, has the greatest estimation ability of PCBs relative response factor.

Inspecting all best or best found QSPRs, we can take into account the presence of iHMdTHg member in mono-varied MDF QSPR, of imMrFHt and iHDdFHg members in bi-varied MDF QSPR and of imMrFHt, iHDdFHg, iMMMjQg, and iAMrVQg members in four-varied MDF QSPR. All of them use the inverse linearization operator (first letter of the names, i) which suggest that the relative response factor (rrf) property is linear on inverse of molecular structure descriptors. The presence of M (maximal fragments) and D (distance-based fragments) on third position of names suggest that rrf is a global molecular property (all atoms from the molecule contribute in approximately same manner to the rrf and rrf is an inter-atomic distance-based property. The “FH” association from member’s names suggests that the hydrogen’s interact with a force-based descriptor to the stationary phase of high resolution gas chromatograph. The “jQ” and “VQ” associations suggest a conservative inverse of distance based interaction of partial atomic charges (j is 1/p·d and V is p/d) with the stationary phase of high resolution gas chromatograph. The major presence of “g” geometric distance operator in averse of “t” topological distance operator denote that the rrf property is much sensitive to the geometrical shape of the PCBs then molecular topology.

Conclusions

The lower value of squared correlation coefficients of MDF QSPR suggest that the relative response factor property of polychlorinated biphenyls can be explained with at most about 75% using in-vitro molecular structure descriptors, which are a expected result, considering that the elution process are in gas phase, where molecular structure can suffer geometrical conformation changes. The geometrical shape of the molecule is dominant for relative response factor property (three of four descriptors from four-varied MDF model use geometrical distance operator). Atomic partial charge distributions and hydrogen’s play the main role on interactions with the stationary phase of high resolution gas chromatograph.

References

1. Kannan N., Tanabe S., Borrell A., Aguilar A., Focardi S., Tatsukawa. R., *Isomer-specific analysis and toxic evaluation of polychlorinated biphenyls in striped dolphins affected by an epizootic in the western Mediterranean Sea*, Archives of Environmental Contamination and Toxicology, 1993, 25, p. 227-233.

2. Kannan N., Tanabe S., Ono M., Tatsukawa. R., *Critical evaluation of polychlorinated biphenyl toxicity in terrestrial and marine mammals: increasing impact of non-ortho and mono-ortho coplanar polychlorinated biphenyls from land to ocean*, Archives of Environmental Contamination and Toxicology, 1989, 18, p. 850-857.

3. Ronald Eisler, and André A. Belisle, *Planar PCB Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review*, Contaminant Hazard Reviews, 1996, p. 1-96.

4. ToxFAQs™ for Polychlorinated Biphenyls (PCBs), available at http://www.atsdr.cdc.gov/tfacts17.html

5. Hargrave B. T., Vass W. P., Erickson P. E., and Fowler B. R., *Distribution of chlorinated hydrocarbon pesticides and PCBs in the Arctic Ocean*, Canadian Technical Report of Fisheries and Aquatic Sciences, 1989, 1644.

6. Larsson P., Jarnmark C., and Sodergren A., *PCBs and chlorinated pesticides in the atmosphere and aquatic organisms of Ross Island, Antarctica*, Marine Pollution Bulletin, 1992, 25, p. 9-12.

7. Norstrom R. J., Simon M., Muir D. C. G., and Schweinsburg R. E., *Organochlorine contaminants in Arctic marine food chains: identification, geographical distribution, and temporal trends in polar bears*, Environmental Science & Technology, 1988, 22, p. 1063-1071.

8. Niemelä J.R., *Validation of the BIODEG Probability Program*, TemaNord Repost, 1994, 589, p. 153-156.

9. Damborsky J., *A mechanistic approach to deriving quantitative structure-activity relationship models for microbial degradation of organic compounds. SAR and QSAR in*

Environmental Research, Proceedings of the Satellite Workshop on Biodegradation accompanying the 6th International Workshop on QSAR in Environmental Sciences, Italy, September 12, 1994.

10. Blok J., *Classification of biodegradability by growth kinetic parameters*, Ecotoxicology and Environmental Safety, 1994, 27, p. 294-305.

11. Warne M. A., Ebbels T. M. D., Lindon J. C., Nicholson J. K., *Semiempirical Molecular-Orbital Properties of Some Polycyclic Aromatic Hydrocarbons and Correlation with Environmental Toxic Equivalency Factors*, Polycyclic Aromatic Compounds, 2003, 23, 23-74.

12. Schultz T. W., Cronin M. T. D., Walker J. D., Aptula A. O., *Quantitative structure-activity relationships (QSARs) in toxicology: a historical perspective*, Journal of Molecular Structure: THEOCHEM, 2003, 622(1), p. 1-22.

13. Schultz T. W., Cronin M. T. D., Netzeva T. I., *The present status of QSAR in toxicology*, Journal of Molecular Structure: THEOCHEM, 2003, 622, p. 23-38.

14. Sparks T. C., Crouse G. D., Durst G., Natural products as insecticides: the biology, biochemistry and quantitative structure–activity relationships of spinosyns and spinosoids, Pest Management Science, 2001, 10, 896-905.

15. Kompare B. *Estimating environmental pollution by xenobiotic chemicals using QSAR (QSBR) models based on artificial intelligence*, Water Science and Technology, 1998, 37(8), p. 9-18.

16. Marjan Vracko, *Kohonen Artificial Neural Network and Counter Propagation Neural Network in Molecular Structure-Toxicity Studies*, Current Computer - Aided Drug Design, 2005, 1(1), p. 73-78.

17. Mullin M.D., Pochini C.M., McCrindle S., Romkes M., Safe S.H., and Safe L.M., *High resolution PCB analysis: synthesis and chromatographic properties of all 209 PCB congeners*, Environmental Science & Technology, 1984, 18, p. 468-476.

18. Li X., Li Z., Hu M., *A novel set of Wiener indices*, Journal of Molecular Graphics and Modelling, 2003, 22(2), p. 161-172.

19. Li X.H., *The extended hyper-Wiener index*, Canadian Journal of Chemistry, 2003, 81(9), p. 992-996.

20. Li X.H., Lin J.J., *The Overall Hyper-Wiener Index*, Journal of Mathematical Chemistry, 2003, 33(2), 81-89.

21. Cash G.G., *Relationship between the Hosoya polynomial and the hyper-Wiener index*, Applied Mathematics Letters, 2002, 15(7), p. 893-895.

22. Delorme C., Favaron O., Rautenbach D., *On the Randic index*, Discrete Mathematics, 2002, 257(1), p. 29-30.

23. Li X.H., Jalbout A.F., Solimannejad M., *Definition and application of a novel valence molecular connectivity index*, Journal of Molecular Structure: THEOCHEM, 2003, 663(1), p. 81-85.

24. Lorentz JÄNTSCHI, *MDF - A New QSAR/QSPR Molecular Descriptors Family*, Leonardo Journal of Sciences, 2004, Issue 4, p. 67-84.