Genetic Algorithm Optimization of Point Charges in Force Field Development: Challenges and Insights

Supporting Information

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1. GA Convergence: The Population Size Effect

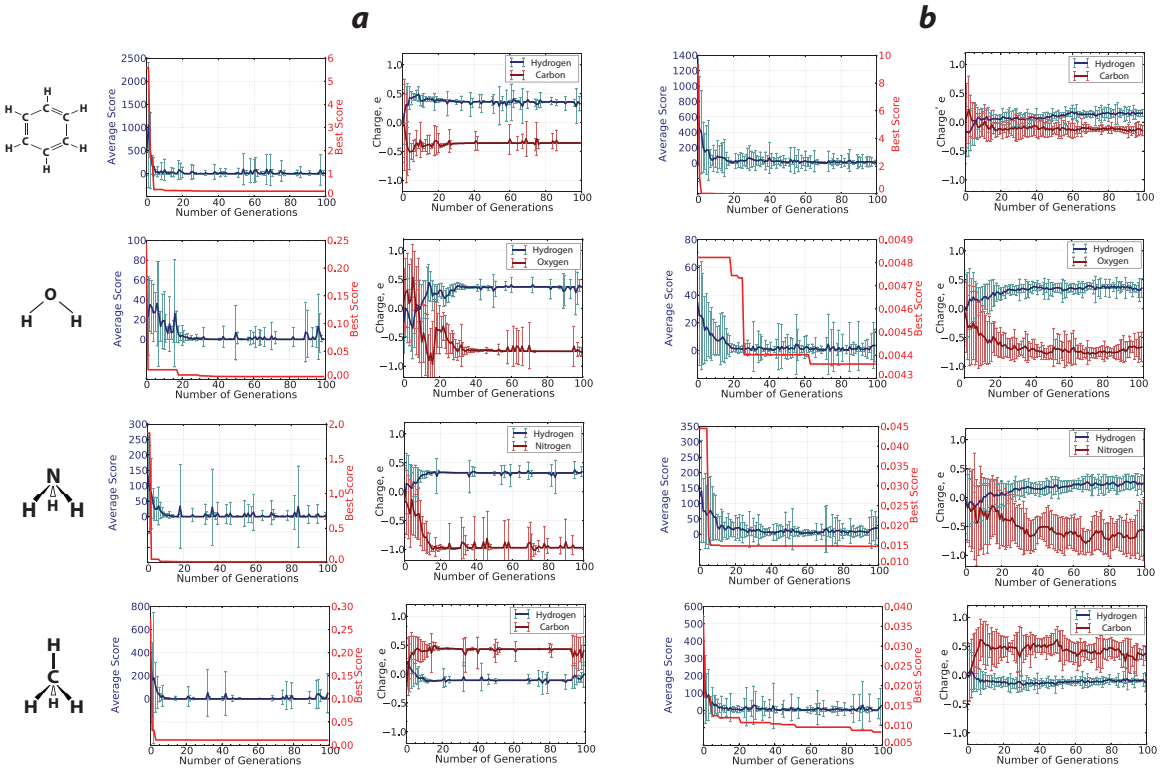

Figure S1. GA convergence with 20 chromosomes in the population (*a*) as compared to 50 chromosomes in the population (*b*).

2. GA Convergence: Binary vs. Real-Number Chromosome Coding

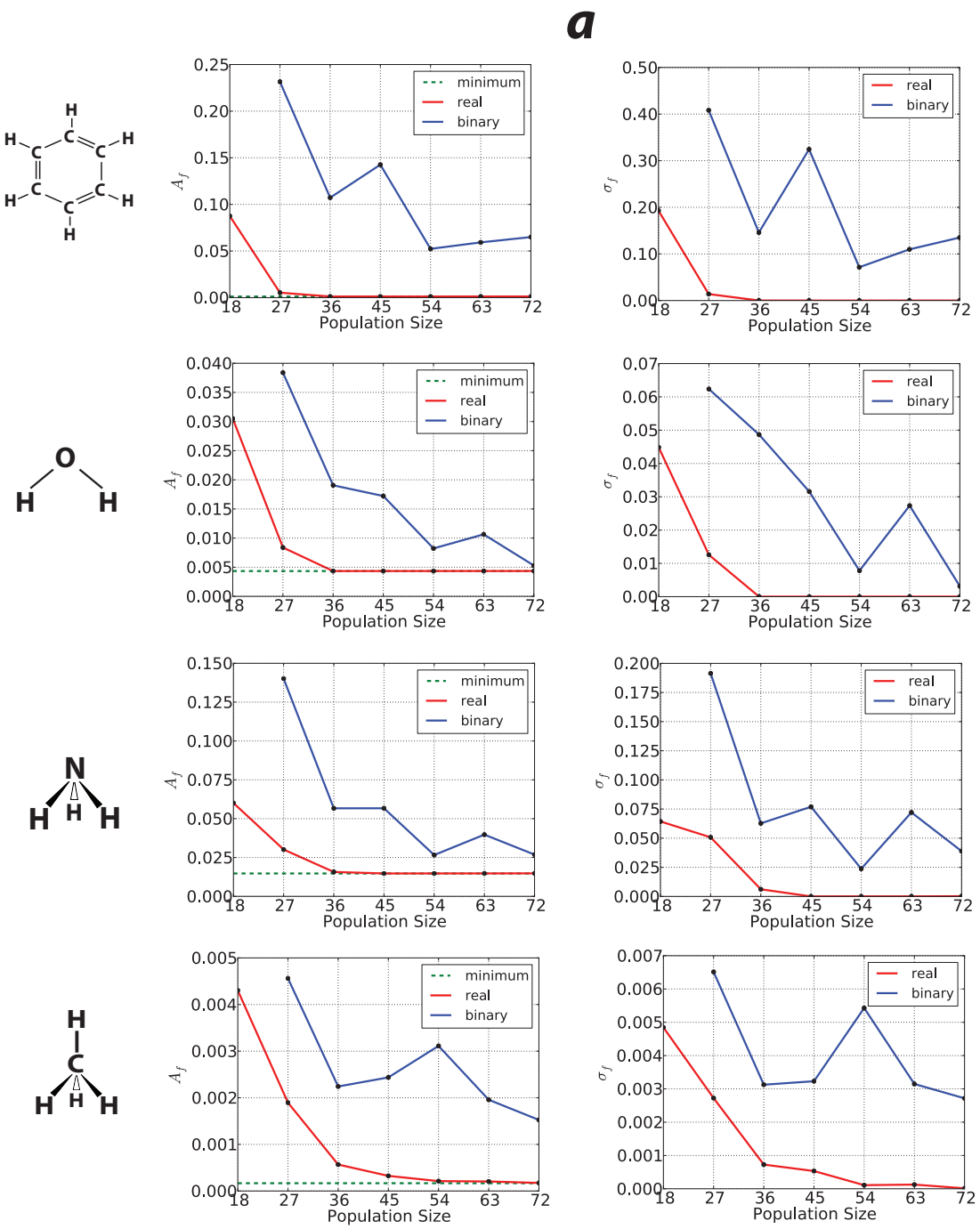

Figure S2a. Average fitness scores A_f and their standard deviations σ_f for 200 GA runs as functions of the population size f the model molecules with two symmetry independent charges. Real-number representation is compared with binary representation of chromosomes. Green dashed line corresponds to the solution found by ESP method.

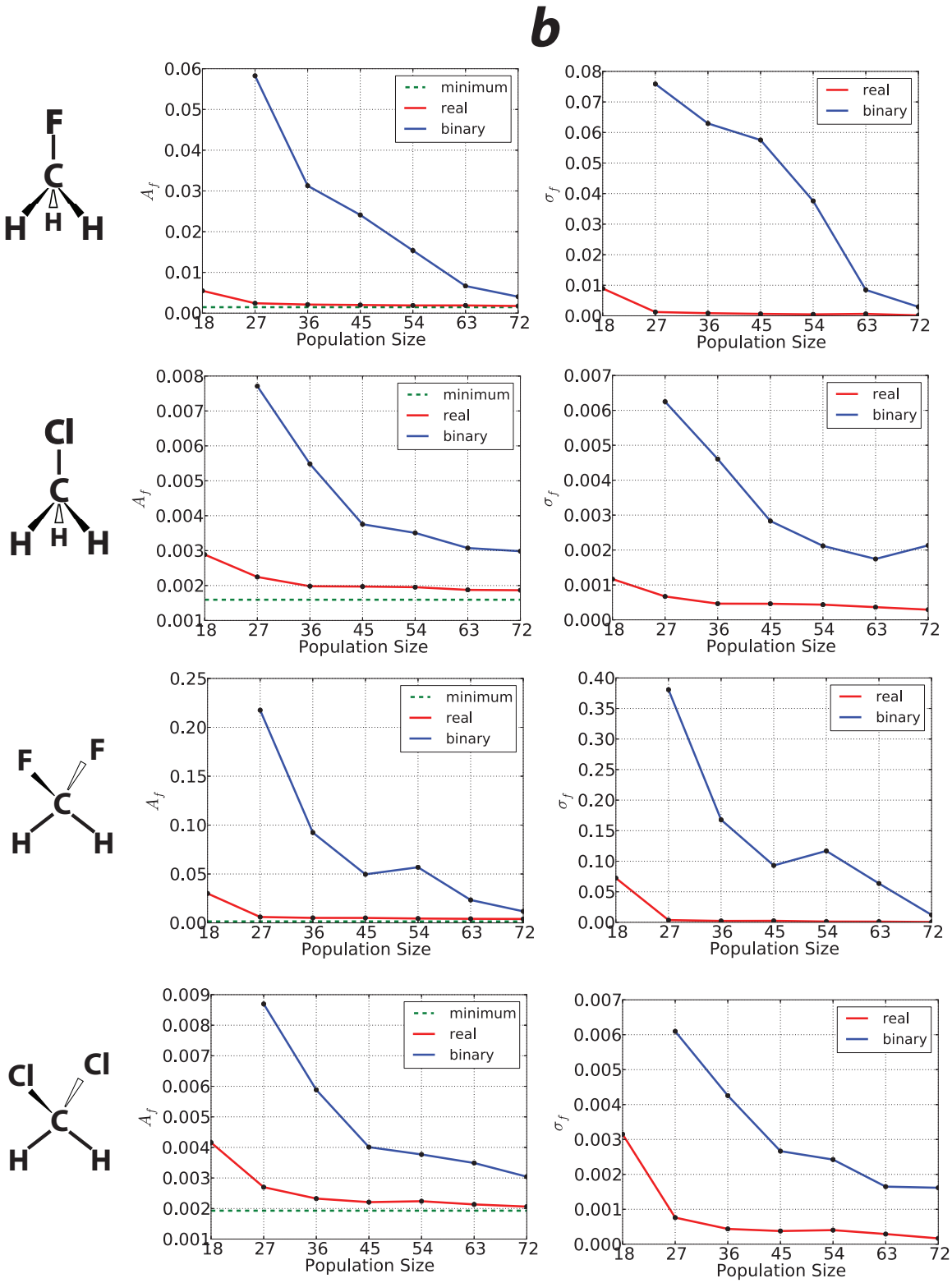

Figure S2b. Average fitness scores A_f and their standard deviations σ_f for 200 GA runs as functions of the population size for the model molecules with three symmetry independent charges. Real-number representation is compared with binary representation of chromosomes. Green dashed line corresponds to the solution found by ESP method.

3. Analysis of the GA Point-Charge Fitting Results

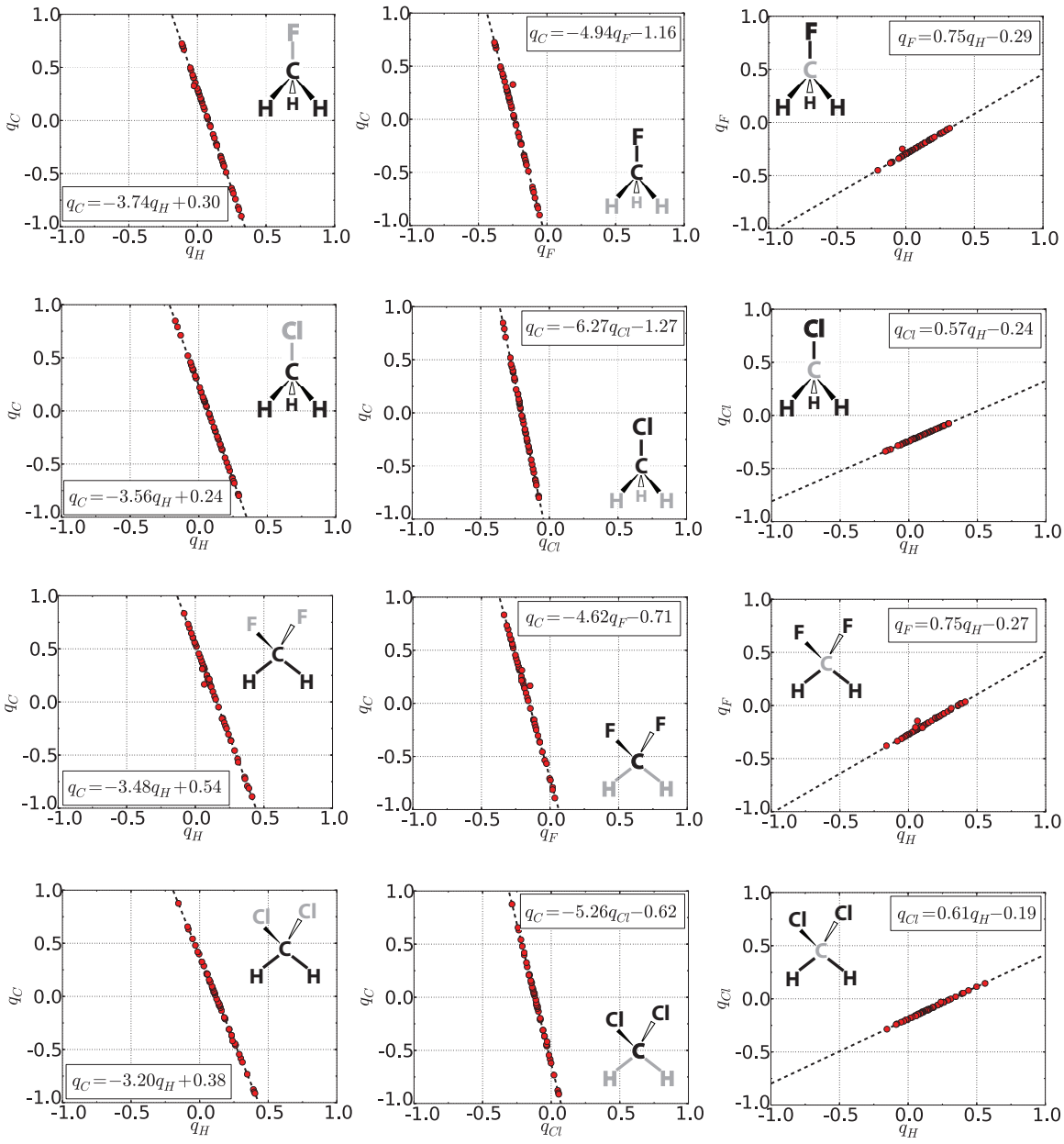

Figure S3. Correlations between the GA-optimized charges in CH_3X, CH_2X_2 (X = F, Cl) molecules obtained from 200 independent GA runs. All trend lines have correlation coefficient R^2 = 1.00. All optimizations were performed with 30 chromosomes in the population.

Table S1. Best and average <q> values with corresponding standard deviations σ of point charges and their fitness scores f obtained from 200 GA runs using charges and Hessian eigenvectors as optimization coordinates. Results are compared with the solutions found by ESP method. All values are in atomic units.

			200 GA Runs					
			Point-Charge Coordinates			Eigenvector Coordinates		
Molecule		ESP	Best	<q>	σ	Best	<q>	σ
H_2O	q_O	-0.758	-0.758	-0.529	0.256	-0.758	-0.758	0.000
	q_H	0.379	0.379	0.264	0.129	0.379	0.379	0.001
	$f \times 10^3$	2.935	2.935	7.582	5.523	2.935	0.000	0.000
NH_3	q_N	-0.970	-0.970	-0.588	0.413	-0.970	-0.970	0.001
	q_H	0.324	0.324	0.196	0.139	0.324	0.324	0.001
	$f \times 10^3$	3.686	3.686	8.494	5.126	3.686	3.694	0.039
C_6H_6	q_C	-0.125	-0.124	-0.099	0.215	-0.125	-0.121	0.009
	q_H	0.125	0.125	0.098	0.219	0.125	0.121	0.009
	$f \times 10^4$	9.577	9.580	92.772	91.687	9.577	12.163	5.208
CH_4	q_C	-0.616	-0.615	-0.024	0.535	-0.616	-0.602	0.026
	q_H	0.154	0.154	0.006	0.134	0.154	0.151	0.007
	$f \times 10^4$	3.387	3.387	16.757	12.480	3.387	3.805	0.848
CH_3F	q_C	-0.038	0.026	0.129	0.476	-0.038	-0.039	0.007
	q_H	0.090	0.072	0.045	0.127	0.090	0.090	0.002
	q_F	-0.229	-0.242	-0.263	0.097	-0.229	-0.228	0.003
	$f \times 10^3$	1.462	1.473	1.965	0.538	1.462	1.468	0.042
CH_3Cl	q_C	-0.560	-0.554	-0.030	0.483	-0.560	-0.560	0.000
	q_H	0.225	0.223	0.077	0.136	0.225	0.225	0.001
	q_{Cl}	-0.114	-0.115	-0.200	0.076	-0.114	-0.114	0.000
	$f \times 10^3$	1.593	1.593	2.309	0.716	1.593	1.593	0.000
CH_2F_2	q_C	0.251	0.261	0.023	0.127	0.251	0.129	0.039
	q_H	0.084	0.080	0.148	0.441	0.084	0.100	0.220
	q_F	-0.209	-0.210	-0.158	0.097	-0.209	-0.163	0.078
	$f \times 10^3$	1.482	1.484	2.254	1.141	1.482	2.830	2.472
CH_2Cl_2	q_C	-0.599	-0.553	-0.042	0.500	-0.599	-0.599	0.001
	q_H	0.305	0.291	0.131	0.155	0.305	0.305	0.000
	q_{Cl}	-0.005	-0.014	-0.111	0.096	-0.005	-0.005	0.000
	$f \times 10^3$	1.930	1.934	2.699	0.739	1.930	1.930	0.000

Table S2. Pairwise linear correlations between the point charges obtained from 200 GA optimizations for the CH_3X, CH_2X_2 (X = F, Cl) and CH_3O^- molecules compared with the analytically derived relationships (eqs. 18-19 in the main text). All values are in atomic units.

Molecule	From GA	Analytical
CH_3F	$q_C = -3.74q_H + 0.30$	$q_C = -3.75q_H + 0.29$
	$q_C = -4.94q_F - 1.16$	$q_C = -4.99q_F - 1.17$
	$q_F = 0.75q_H - 0.29$	$q_F = 0.76q_H - 0.29$
CH_3Cl	$q_C = -3.56q_H + 0.24$	$q_C = -3.55q_H + 0.23$
	$q_C = -6.27q_{Cl} - 1.27$	$q_C = -6.41q_{Cl} - 1.26$
	$q_{Cl} = 0.57q_H - 0.24$	$q_{Cl} = 0.56q_H - 0.23$
CH_2F_2	$q_C = -3.48q_H + 0.54$	$q_C = -3.50q_H + 0.53$
	$q_C = -4.62q_F - 0.71$	$q_C = -4.67q_F + 0.71$
	$q_F = 0.75q_H - 0.27$	$q_F = 0.75q_H - 0.27$
CH_2Cl_2	$q_C = -3.20q_H + 0.38$	$q_C = -3.22q_H + 0.36$
	$q_C = -5.26q_{Cl} - 0.62$	$q_C = -5.28q_{Cl} - 0.59$
	$q_{Cl} = 0.61q_H - 0.19$	$q_{Cl} = 0.61q_H - 0.18$
CH_3O^-	$q_C = -4.07q_H - 0.24$	$q_C = -4.11q_H - 0.29$
	$q_C = -3.69q_O - 2.92$	$q_C = -3.71q_O - 2.92$
	$q_H = 0.91q_O + 0.66$	$q_H = 0.90q_O + 0.64$

Table S3. Numerical equivalence between the eigenbasis of the covariance matrix calculated for 200 independent 20-chromosome GA runs , $\widetilde{\boldsymbol{\Sigma}}$, the eigenbasis of the LS-sum Hessian matrix, and the analytically generated orthonormal basis $\widetilde{\mathbf{U}}$ (eq. 28 in the main text). Eigenvalues of the covariance matrix correspond to the variance (in atomic units, e^2) along each eigenvectors; eigenvalues of the Hessian correspond to the curvatures (in atomic units, $1/a_0^2$) along corresponding eigenvectors.

	Methane		Ammonia		Water		Benzene	
				$\widetilde{\boldsymbol{\Sigma}}$				
Variance	5.75E-09	0.19	7.18E-07	0.13	1.15E-06	0.07	1.85E-07	0.06
q_X	0.244	0.970	0.319	0.948	0.450	0.893	-0.717	0.697
q_H	0.970	-0.244	0.948	-0.319	0.893	-0.450	-0.697	-0.717
				$\widetilde{\mathbf{H}}$				
Curvature	2094.94	0.07	1116.93	1.05	570.33	2.13	9470.55	22.29
q_X	0.244	0.970	0.318	0.948	0.447	0.894	-0.718	0.696
q_H	0.970	-0.244	0.948	-0.318	0.894	-0.447	-0.696	-0.718
				$\widetilde{\mathbf{U}}$				
q_X	0.243	0.970	0.316	0.949	0.447	0.894	0.707	0.707
q_H	0.970	-0.243	0.949	-0.316	0.894	-0.447	0.707	-0.707

4. GA Point Charge Fitting in Terms of the Rotated/Eigenvector Coordinates

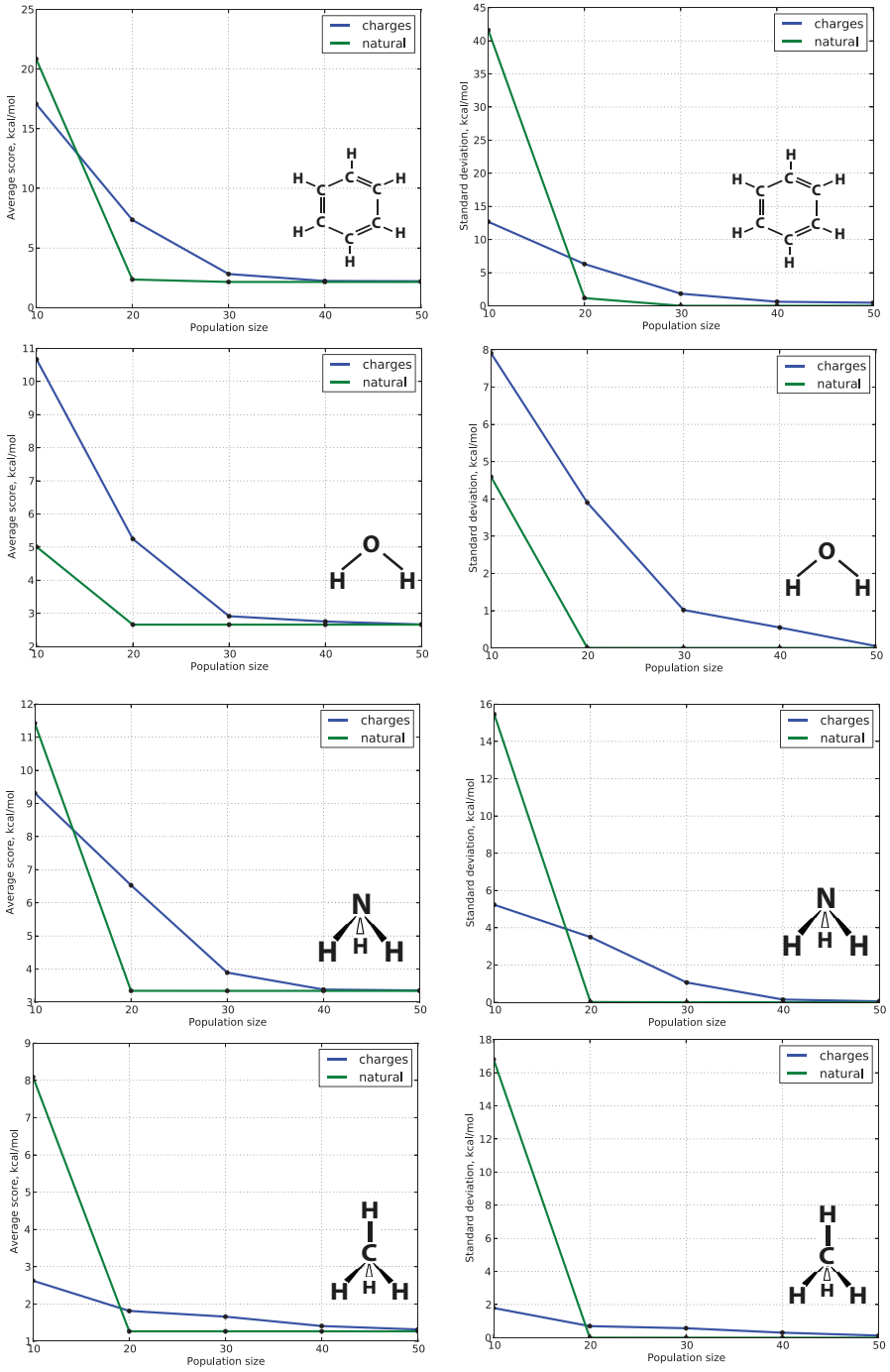

Figure S4a. Average fitness score and its standard deviation for 200 GA runs performed using the point charge values as the optimization coordinates vs. the coordinates defined by the eigenbasis of the LS-sum Hessian matrix; two-charge models.

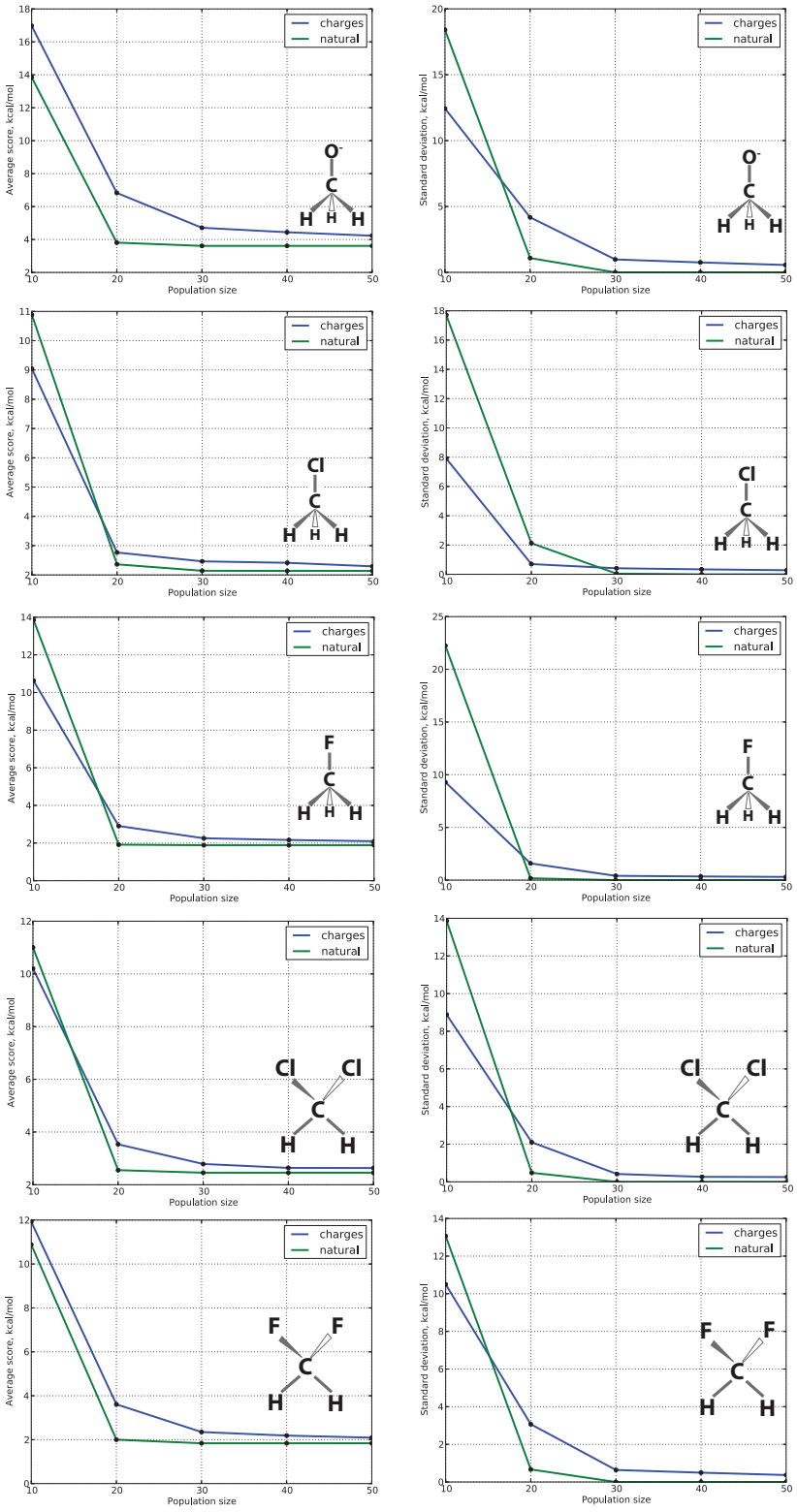

Figure S4b. Average fitness score and its standard deviation for 200 GA runs performed using the point charge values as the optimization coordinates vs. the coordinates defined by the eigenbasis of the LS-sum Hessian matrix; three-charge models.

Table S4. Covariance matrix and Hessian matrix eigenbases $\widetilde{\boldsymbol{\Sigma}}$ and $\widetilde{\mathbf{H}}$ compared with the orthonormal basis $\widetilde{\mathbf{U}}$ (eqs. 28-29 in the main text) . Eigenvalues of the covariance matrix correspond to the variance (in atomic units, e^2) along each eigenvectors; eigenvalues of the Hessian correspond to the curvatures (in atomic units, $1/a_0^2$) along the corresponding eigenvectors. Covariance matrices are calculated for 200 GA runs with 30 chromosomes in the population.

	Chloromethane			Fluoromethane			Methoxide			Dichloromethane			Difluoromethane		
							$\widetilde{\mathbf{H}}$								
Curvature	1555.96	18.23	0.10	1374.20	14.45	0.09	1375.88	15.79	0.12	1382.94	27.35	0.14	1125.74	22.21	0
q_C	0.303	0.059	0.951	0.303	0.101	0.948	0.302	0.165	0.939	0.337	-0.074	0.939	0.336	-0.043	0.
q_X	0.292	0.944	-0.151	0.293	0.936	-0.194	0.293	0.921	-0.256	0.657	0.732	-0.178	0.662	0.722	-0
q_H	0.907	-0.324	-0.269	0.907	-0.336	-0.254	0.907	-0.352	-0.230	0.674	-0.677	-0.296	0.670	-0.691	-0
							$\widetilde{\boldsymbol{\Sigma}}$								
Variance	8.40E-08	8.73E-06	0.12	6.63E-08	5.95E-06	0.11	3.69E-07	4.55E-05	0.14	1.62E-07	8.59E-06	0.11	9.79E-08	9.30E-06	0
q_C	0.302	0.064	0.951	0.302	0.102	0.948	0.303	0.163	0.939	0.335	-0.084	0.938	0.336	-0.043	0.
q_X	0.274	0.950	-0.151	0.288	0.938	-0.193	0.291	0.922	-0.254	0.676	0.715	-0.177	0.664	0.719	-0
q_H	0.913	-0.306	-0.269	0.909	-0.331	-0.254	0.908	-0.350	-0.232	0.656	-0.694	-0.297	0.668	-0.694	-0
							$\widetilde{\mathbf{U}}$								
q_C	0.3015	0.058	0.9519	0.3015	0.0968	0.9488	0.3015	0.1511	0.9399	0.3333	-0.0604	0.9398	0.3333	-0.041	0.9
q_X	0.3015	0.9785	-0.1497	0.3015	0.9397	-0.1884	0.3015	0.9206	-0.2534	0.6667	0.7603	-0.1781	0.6667	0.7098	-0.
q_H	0.9045	-0.3213	-0.2674	0.9045	-0.369	-0.2535	0.9045	-0.3514	-0.2288	0.6667	-0.6362	-0.2918	0.6667	-0.688	-0.

5. 1-Chlorobutane Point Charge Fitting

Chart 1. 1-Chlorobutane Conformers Considered, with Atom Numbering

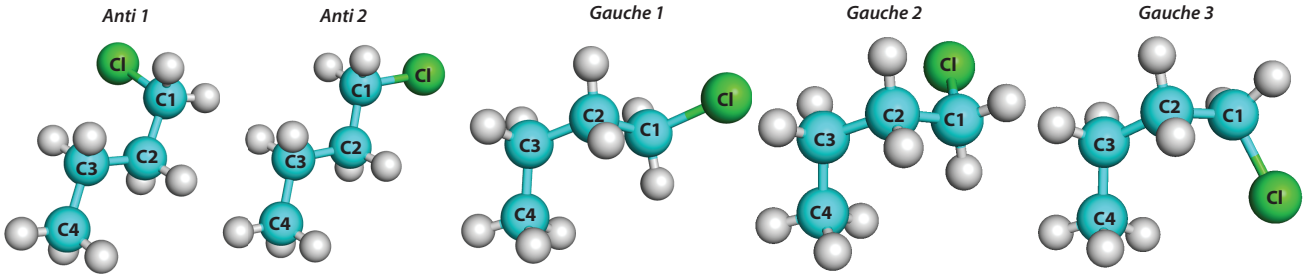

Table S5. Point charges with corresponding dipole moment and total charge obtained with CMA-ES/ESP methods as compared with the average and the standard deviation σ of the point charges, total charge and dipole moment obtained from 200 independent runs for the five conformers of 1-chlorobutane in point charge coordinates and Hessian eigenvectors coordinates.

	q_{C4}	q_{H4}	q_{C3}	q_{H3}	q_{C2}	q_{H2}	q_{C1}	q_{H1}	q_{Cl}	Dipole moment, au	Total charge, au	Fitness, kcal/mol
						CMA-ES/ESP						
Anti 1	-0.257	0.058	0.186	-0.024	0.052	0.014	-0.141	0.105	-0.193	0.918	0.009	2.094
Anti 2	-0.229	0.054	0.163	-0.027	0.051	0.015	-0.104	0.096	-0.206	0.995	0.008	2.126
Gauche 1	-0.134	0.032	0.110	-0.018	0.050	0.011	-0.060	0.088	-0.216	1.006	0.008	2.119
Gauche 2	-0.203	0.047	0.172	-0.027	0.015	0.007	0.005	0.066	-0.213	0.903	0.009	2.136
Gauche 3	-0.119	0.027	0.148	-0.038	0.094	-0.010	-0.030	0.072	-0.211	0.906	0.009	2.143

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Table S5, Continued.

		q_{C4}	q_{H4}	q_{C3}	q_{H3}	q_{C2}	q_{H2}	q_{C1}	q_{H1}	q_{Cl}	Dipole moment, au	Total charge, au	Score, kcal/mol
Point-Charge Coordinates													
Anti 1	<A>	-0.030	0.004	0.037	0.009	0.002	0.026	0.005	0.064	-0.215	0.922	0.008	3.054
	σ	0.380	0.100	0.365	0.113	0.369	0.116	0.371	0.113	0.065	0.087	0.008	0.435
Anti 2	<A>	-0.030	0.008	0.025	0.003	0.027	0.021	0.001	0.069	-0.225	1.015	0.007	3.016
	σ	0.371	0.100	0.341	0.107	0.384	0.123	0.352	0.110	0.060	0.108	0.008	0.405
Gauche 1	<A>	-0.028	0.006	0.058	-0.007	0.007	0.025	-0.017	0.078	-0.223	1.010	0.008	3.059
	σ	0.379	0.103	0.354	0.106	0.370	0.114	0.364	0.114	0.063	0.110	0.008	0.446
Gauche 2	<A>	-0.006	0.000	0.036	0.002	0.022	0.011	0.022	0.061	-0.214	0.905	0.009	3.079
	σ	0.374	0.101	0.367	0.111	0.355	0.107	0.351	0.109	0.063	0.081	0.008	0.455
Gauche 3	<A>	0.041	-0.007	-0.016	0.006	0.036	0.015	0.008	0.065	-0.212	0.921	0.010	3.148
	σ	0.378	0.101	0.360	0.109	0.344	0.106	0.375	0.118	0.062	0.096	0.009	0.489
Eigenvector Coordinates													
Anti 1	<A>	-0.224	0.051	0.138	-0.014	0.081	0.009	-0.147	0.106	-0.192	0.921	0.009	2.576
	σ	0.237	0.059	0.242	0.066	0.243	0.063	0.243	0.069	0.039	0.068	0.006	0.196
Anti 2	<A>	-0.224	0.053	0.153	-0.024	0.062	0.013	-0.116	0.099	-0.204	1.003	0.008	2.574
	σ	0.254	0.063	0.254	0.064	0.238	0.069	0.207	0.062	0.037	0.082	0.006	0.194
Gauche 1	<A>	-0.121	0.030	0.091	-0.013	0.046	0.013	-0.060	0.088	-0.214	1.009	0.009	2.605
	σ	0.257	0.064	0.252	0.065	0.240	0.065	0.210	0.064	0.035	0.080	0.006	0.207
Gauche 2	<A>	-0.225	0.059	0.370	-0.100	-0.276	0.026	0.056	-0.166	-0.290	0.902	0.130	2.394
	σ	0.285	0.071	0.295	0.077	0.266	0.074	0.090	0.065	0.042	0.113	0.046	0.141
Gauche 3	<A>	-0.081	0.017	0.123	-0.033	0.107	-0.013	-0.035	0.074	-0.213	0.922	0.009	2.621
	σ	0.253	0.063	0.238	0.060	0.246	0.063	0.213	0.061	0.036	0.076	0.006	0.178

Table S6. Numerical representation of the eigenbases of the LS-sum Hessian and the covariance matrix for the 200 GA runs for the five conformers of 1-chlorobutane. Eigenvalues of the covariance matrix correspond to the variance (in atomic units, e^2) along each eigenvector; eigenvalues of the Hessian correspond to the curvatures (in atomic units, $1/a_0^2$) along the corresponding eigenvectors.

Anti 1

					$\widetilde{\mathbf{H}}$				
Curvature	3612.01	231.01	58.41	31.07	15.20	0.20	0.15	0.06	0.04
q_{C4}	-0.197	-0.182	-0.004	-0.048	-0.005	0.348	-0.463	0.575	0.510
q_{H4}	-0.582	-0.656	-0.150	-0.367	0.048	-0.132	0.149	-0.141	-0.110
q_{C3}	-0.202	-0.021	0.175	0.165	-0.054	0.644	-0.311	-0.171	-0.598
q_{H3}	-0.404	-0.004	0.723	0.416	-0.188	-0.289	0.079	0.033	0.117
q_{C2}	-0.200	0.106	-0.128	0.187	0.013	0.492	0.406	-0.460	0.528
q_{H2}	-0.400	0.191	-0.605	0.574	0.061	-0.246	-0.147	0.099	-0.112
q_{C1}	-0.194	0.252	0.000	-0.118	0.036	0.219	0.637	0.606	-0.249
q_{H1}	-0.382	0.599	-0.026	-0.515	-0.377	-0.097	-0.226	-0.156	0.050
q_{Cl}	-0.189	0.258	0.201	-0.137	0.901	-0.053	-0.129	-0.082	0.029
					$\widetilde{\mathbf{\Sigma}}$				
Variance	1.24E-06	1.81E-05	8.78E-05	1.53E-04	3.00E-04	2.27E-02	3.05E-02	8.06E-02	1.18E-01
q_{C4}	0.196	-0.181	0.006	0.053	-0.011	-0.533	0.314	0.672	-0.303
q_{H4}	0.580	-0.652	-0.098	0.395	0.019	0.190	-0.090	-0.156	0.057
q_{C3}	0.202	-0.024	0.157	-0.183	-0.039	-0.658	0.095	-0.363	0.570
q_{H3}	0.404	-0.005	0.671	-0.515	-0.129	0.286	0.019	0.072	-0.130
q_{C2}	0.202	0.102	-0.144	-0.158	0.036	-0.362	-0.602	-0.282	-0.573
q_{H2}	0.406	0.182	-0.663	-0.493	0.143	0.179	0.229	0.060	0.104
q_{C1}	0.193	0.252	0.014	0.118	0.012	0.033	-0.629	0.529	0.457
q_{H1}	0.381	0.595	0.017	0.455	-0.454	0.017	0.236	-0.140	-0.109
q_{Cl}	0.180	0.284	0.234	0.231	0.868	-0.004	0.133	-0.072	-0.055

Table S6, Continued.

	Anti 2								
Curvature	3614.47	230.35	64.53	30.14	9.96	0.19	0.14	0.03	0.06
					$\tilde{\mathbf{H}}$				
q_{C4}	0.195	-0.184	-0.005	-0.046	0.012	0.355	0.417	0.539	-0.579
q_{H4}	0.578	-0.666	0.092	-0.374	-0.046	-0.134	-0.137	-0.116	0.145
q_{C3}	0.200	-0.017	-0.149	0.184	0.052	0.628	0.337	-0.616	0.115
q_{H3}	0.398	0.008	-0.634	0.499	0.300	-0.274	-0.096	0.122	-0.019
q_{C2}	0.201	0.105	0.145	0.169	-0.062	0.507	-0.367	0.485	0.517
q_{H2}	0.405	0.184	0.637	0.502	-0.186	-0.256	0.143	-0.097	-0.116
q_{C1}	0.196	0.252	0.001	-0.126	-0.011	0.222	-0.675	-0.231	-0.569
q_{H1}	0.389	0.562	-0.269	-0.425	-0.433	-0.115	0.242	0.052	0.132
q_{Cl}	0.185	0.312	0.259	-0.312	0.824	-0.029	0.123	0.019	0.091
					$\tilde{\mathbf{\Sigma}}$				
Variance	1.23E-06	1.96E-05	7.95E-05	1.29E-04	4.07E-04	2.31E-02	3.43E-02	1.27E-01	6.31E-02
q_{C4}	0.196	0.184	-0.002	0.043	-0.008	-0.480	0.384	-0.561	0.483
q_{H4}	0.580	0.672	-0.143	0.345	0.029	0.165	-0.127	0.121	-0.116
q_{C3}	0.203	0.005	0.177	-0.154	-0.028	-0.614	0.299	0.635	-0.182
q_{H3}	0.408	-0.037	0.713	-0.386	-0.282	0.267	-0.071	-0.128	0.054
q_{C2}	0.201	-0.107	-0.118	-0.192	0.079	-0.404	-0.420	-0.438	-0.599
q_{H2}	0.401	-0.180	-0.541	-0.593	0.219	0.235	0.168	0.083	0.155
q_{C1}	0.193	-0.250	-0.033	0.124	0.004	-0.246	-0.680	0.221	0.558
q_{H1}	0.384	-0.569	0.159	0.508	0.391	0.118	0.244	-0.058	-0.121
q_{Cl}	0.177	-0.288	-0.327	0.210	-0.844	0.019	0.120	-0.014	-0.090

Table S6, Continued.

	Gauche 1								
Curvature	3635.17	179.83	82.72	38.41	10.68	0.23	0.13	0.03	0.07
					$\tilde{\mathbf{H}}$				
q_{C4}	0.196	-0.185	0.036	-0.032	0.016	0.404	0.412	0.516	-0.570
q_{H4}	0.585	-0.663	0.280	-0.253	0.038	-0.154	-0.137	-0.111	0.141
q_{C3}	0.198	-0.028	-0.185	0.144	0.005	0.552	0.424	-0.618	0.196
q_{H3}	0.391	-0.074	-0.589	0.604	0.193	-0.234	-0.136	0.126	-0.058
q_{C2}	0.199	0.155	-0.122	-0.120	-0.097	0.493	-0.305	0.479	0.576
q_{H2}	0.396	0.397	-0.411	-0.587	-0.260	-0.240	0.121	-0.088	-0.155
q_{C1}	0.197	0.223	0.168	0.060	0.001	0.345	-0.663	-0.285	-0.489
q_{H1}	0.397	0.406	0.536	0.406	-0.356	-0.178	0.226	0.069	0.106
q_{Cl}	0.186	0.351	0.201	-0.146	0.870	-0.042	0.121	0.027	0.078
					$\tilde{\mathbf{\Sigma}}$				
Variance	1.28E-06	2.55E-05	7.25E-05	1.24E-04	4.32E-04	2.06E-02	3.47E-02	6.61E-02	1.28E-01
q_{C4}	0.195	0.185	0.037	0.034	0.014	0.389	-0.439	0.541	-0.538
q_{H4}	0.578	0.662	0.295	0.253	0.054	-0.141	0.150	-0.118	0.132
q_{C3}	0.199	0.029	-0.190	-0.137	0.013	0.494	-0.497	-0.606	0.214
q_{H3}	0.399	0.076	-0.599	-0.580	0.216	-0.214	0.166	0.123	-0.068
q_{C2}	0.200	-0.155	-0.119	0.122	-0.109	0.503	0.288	0.450	0.597
q_{H2}	0.396	-0.385	-0.398	0.595	-0.275	-0.252	-0.106	-0.079	-0.161
q_{C1}	0.198	-0.223	0.168	-0.066	-0.028	0.420	0.601	-0.308	-0.494
q_{H1}	0.397	-0.386	0.515	-0.428	-0.374	-0.209	-0.209	0.078	0.107
q_{Cl}	0.190	-0.387	0.224	0.150	0.850	-0.046	-0.106	0.033	0.071

Table S6, Continued.

	Gauche 2								
Curvature	3620.41	171.98	84.31	39.25	7.82	0.29	0.13	0.07	0.04
					$\widetilde{\mathbf{H}}$				
q_{C4}	0.198	-0.184	0.031	-0.034	-0.021	-0.278	-0.525	-0.491	0.575
q_{H4}	0.589	-0.667	0.259	-0.255	-0.022	0.124	0.171	0.124	-0.125
q_{C3}	0.199	-0.022	-0.183	0.143	-0.012	-0.436	-0.538	0.144	-0.636
q_{H3}	0.396	-0.055	-0.576	0.620	-0.178	0.181	0.200	-0.059	0.127
q_{C2}	0.197	0.161	-0.121	-0.129	0.064	-0.436	0.080	0.707	0.451
q_{H2}	0.390	0.411	-0.412	-0.576	0.278	0.228	-0.024	-0.202	-0.090
q_{C1}	0.195	0.228	0.173	-0.002	-0.158	-0.602	0.554	-0.406	-0.142
q_{H1}	0.390	0.400	0.556	0.405	0.405	0.182	-0.122	0.047	0.020
q_{Cl}	0.189	0.334	0.209	-0.131	-0.835	0.216	-0.192	0.106	0.012
					$\widetilde{\mathbf{\Sigma}}$				
Variance	1.49E-06	3.26E-05	6.07E-05	1.60E-04	8.51E-04	2.18E-02	4.63E-02	7.51E-02	1.55E-01
q_{C4}	-0.203	-0.180	0.026	-0.026	-0.010	-0.244	-0.592	-0.445	0.563
q_{H4}	-0.611	-0.657	0.242	-0.248	-0.029	0.112	0.187	0.112	-0.120
q_{C3}	-0.198	-0.012	-0.180	0.155	0.009	-0.407	-0.518	0.134	-0.673
q_{H3}	-0.394	-0.023	-0.561	0.638	-0.174	0.166	0.203	-0.056	0.143
q_{C2}	-0.191	0.164	-0.120	-0.129	0.082	-0.447	0.060	0.719	0.423
q_{H2}	-0.373	0.408	-0.429	-0.572	0.283	0.234	-0.015	-0.204	-0.081
q_{C1}	-0.190	0.231	0.170	-0.016	-0.154	-0.632	0.506	-0.439	-0.095
q_{H1}	-0.382	0.420	0.577	0.375	0.388	0.200	-0.104	0.049	0.010
q_{Cl}	-0.183	0.335	0.184	-0.150	-0.841	0.204	-0.187	0.120	-0.004

Table S6, Continued.

	Gauche 3								
Curvature	3613.95	196.26	79.13	37.21	10.82	0.29	0.13	0.07	0.03
					$\tilde{\mathbf{H}}$				
q_{C4}	0.199	0.182	-0.042	0.004	0.030	0.301	0.512	-0.568	0.499
q_{H4}	0.594	0.654	-0.310	0.133	0.177	-0.131	-0.162	0.139	-0.109
q_{C3}	0.198	0.028	0.193	-0.121	-0.071	0.554	0.453	0.262	-0.569
q_{H3}	0.392	0.061	0.623	-0.554	-0.225	-0.238	-0.153	-0.074	0.108
q_{C2}	0.197	-0.141	0.112	0.159	-0.007	0.524	-0.321	0.481	0.543
q_{H2}	0.391	-0.351	0.371	0.698	0.060	-0.239	0.109	-0.121	-0.112
q_{C1}	0.195	-0.227	-0.161	-0.057	-0.026	0.397	-0.565	-0.559	-0.303
q_{H1}	0.385	-0.567	-0.397	-0.376	0.373	-0.170	0.198	0.144	0.064
q_{Cl}	0.193	-0.136	-0.379	0.067	-0.877	-0.105	0.099	0.072	0.037
					$\tilde{\mathbf{\Sigma}}$				
Variance	1.35E-06	2.25E-05	6.83E-05	1.30E-04	3.82E-04	1.38E-02	3.63E-02	5.75E-02	1.36E-01
q_{C4}	0.201	0.176	0.045	-0.014	0.031	0.291	-0.502	-0.579	0.504
q_{H4}	0.603	0.635	0.306	-0.162	0.199	-0.128	0.163	0.136	-0.114
q_{C3}	0.197	0.031	-0.179	0.134	-0.072	0.508	-0.523	0.305	-0.530
q_{H3}	0.389	0.083	-0.548	0.613	-0.270	-0.212	0.176	-0.084	0.100
q_{C2}	0.196	-0.144	-0.135	-0.150	0.011	0.523	0.311	0.484	0.543
q_{H2}	0.389	-0.349	-0.460	-0.641	0.064	-0.250	-0.094	-0.130	-0.113
q_{C1}	0.192	-0.236	0.160	0.042	-0.017	0.460	0.519	-0.522	-0.355
q_{H1}	0.377	-0.582	0.406	0.354	0.365	-0.196	-0.187	0.130	0.080
q_{Cl}	0.195	-0.145	0.391	-0.141	-0.863	-0.098	-0.085	0.073	0.045

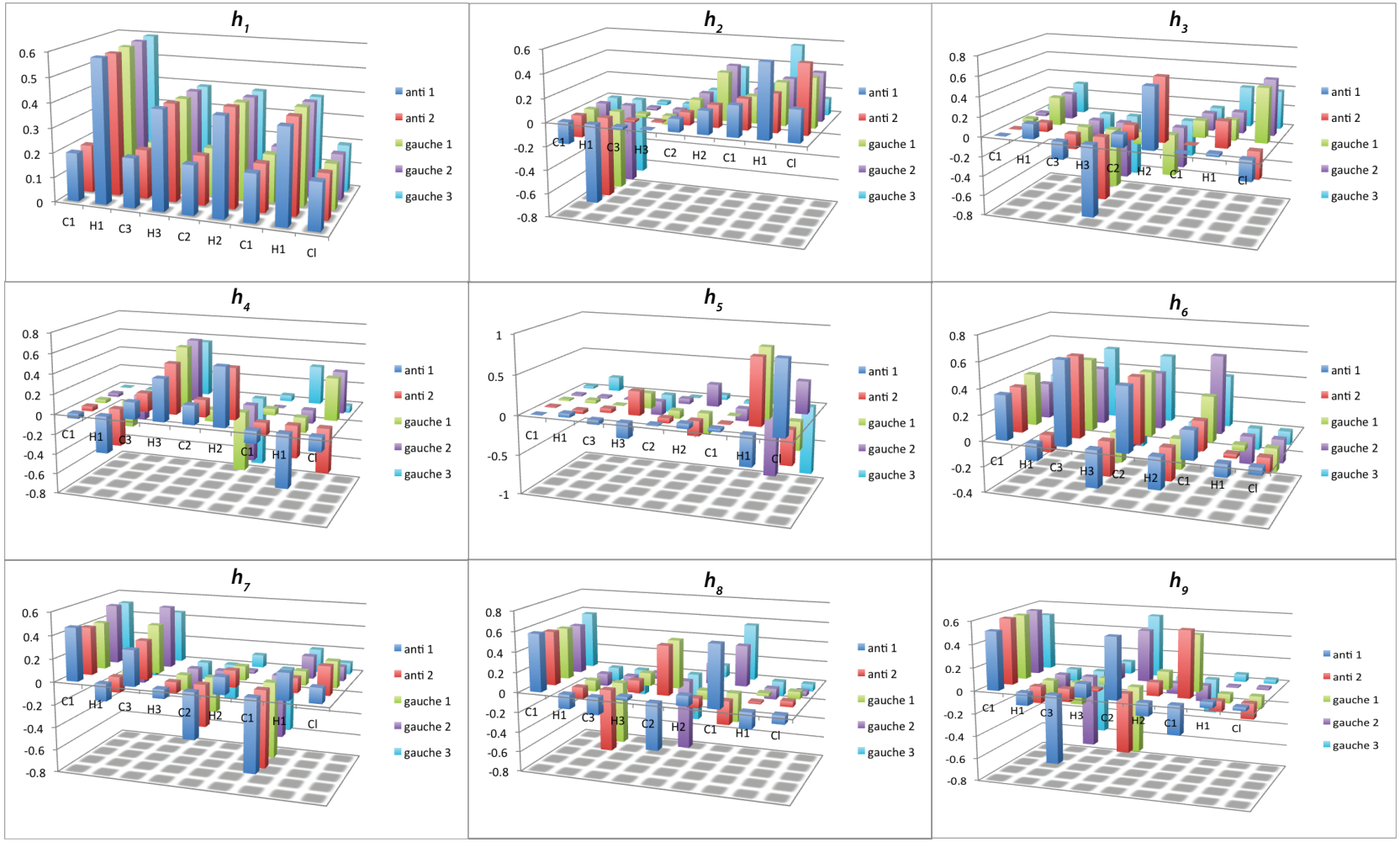

Figure S5. Bar-chart representation of the eigenvectors of the Hessian matrix for five conformers of 1-chlorobutane.

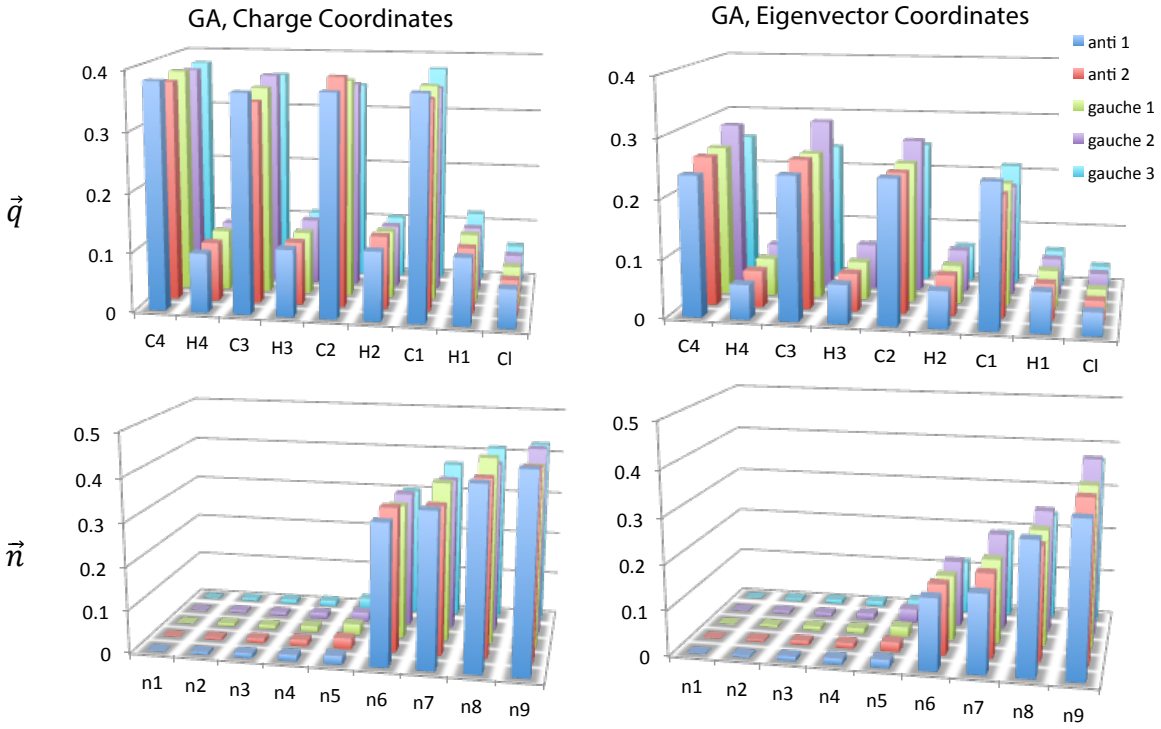

Figure S6. Standard deviations σ of the charges $\vec{q}$ and the corresponding coordinates defined by the LS-sum Hessian eigenvectors $\vec{n}$ obtained from the solutions of 200 GA performed in terms of the charge coordinates, and in terms of the LS-sum Hessian eigenvector coordinates (right).