Table 1. Details of GRID (version 11) calculations.

Alignment	Cα atoms of modeled ligand-receptor complexes
Charges	ESP/MNDO
Probes	CH_3 and H^+
Electrostatic cutoff (kcal/mol)	30.0
Van der Waals cutoff (kcal/mol)	30.0
Relative dielectric constant	4
Grid spacing (Å)	2
Box size	26 x 28 x 22
Number of variables	6720

CH_3 = Methyl probe (r=1.95Å; q=0.0e); H^+ = Proton probe (r=0.00Å; q=1.0e)

Table 2. Block unscaled weights for X-matrices with different dielectric models

X-Matrix dielectric model[a]	**Block unscaled weights**	
	steric field	**electrostatic field**
C	1.554	0.796
R	1.548	0.795
W	1.029	0.972
H	1.106	0.919

[a]Dielectric model: C: constant (ε= 4); R: distance dependent; W: Warshel model; H: Hingerty model.

Table 3. Predictive performance for the initial X-matrices without application of variable selection[a].

Method[b]	LV[c]	SDEC(%)	R^2	SDEP(%)	Q^2	Xsel[d]
C-N	2	13.24	0.64	21.19	0.077	4775
C-A	1	20.41	0.14	21.96	0.009	3803
C-B	2	12.42	0.68	20.68	0.121	4775
R-N	1	15.97	0.47	20.64	0.124	4599
R-A	4	7.46	0.88	21.60	0.041	4599
R-B	2	12.03	0.70	21.12	0.083	4599
W-N	2	10.66	0.76	21.16	0.080	4600
W-A	3	11.12	0.74	21.37	0.062	4600
W-B	2	11.06	0.74	21.33	0.065	4600
H-N	2	10.30	0.78	21.03	0.091	4600
H-A	4	7.29	0.89	21.52	0.048	4600
H-B	2	11.44	0.73	21.21	0.072	4600

[a]A minimum standard deviation sigma cutoff of 0.05 was used to filter out variables of very low variance before statistical analysis.

[b]Dielectric model: C: constant ($\varepsilon = 4$); R: distance dependent; W: Warshel; H: Hingerty. Variable scaling procedure: N: No scaling; A: Autoscaling; B: Block scaling.

[c]Number of latent variables

[d]Number of selected X variables in the model

Table 4. Predictive performance of regression models obtained with a cutoff value of 5 kcal/mol for the computed interaction fields[a].

Method	LV	SDEC(%)	R^2	SDEP(%)	Q^2	Xsel
N-T-C	1	20.17	0.16	21.79	0.020	92
	2	16.49	0.44	19.89	0.187	
	3	13.95	0.60	19.42	0.224	
	4	12.22	0.69	18.95	0.261	
	5	10.94	0.79	19.62	0.208	
B-T-C	1	19.23	0.24	21.37	0.061	171
	2	16.82	0.41	20.16	0.164	
	3	15.19	0.52	23.20	-0.105	
	4	12.70	0.66	25.46	-0.331	
	5	9.82	0.80	27.72	-0.579	

[a]Key as for Table 3 with T denoting use of the Q^2-GRS variable selection method.

Table 5. Effect of grid spacing on predictive performance for the Q^2-GRS variable selection method[a].

Spacing[b]	LV	SDEC(%)	R^2	SDEP(%)	Q^2	Xsel
1	0	22.06	0.00	23.10	-0.09	199
	1	16.73	0.42	19.97	0.18	
	2	12.11	0.70	17.69	0.36	
	3	11.08	0.75	16.52	0.44	
	4	10.22	0.78	17.25	0.39	
	5	9.15	0.83	18.59	0.29	
2	0	22.06	0.00	23.10	-0.09	133
	1	14.87	0.54	18.91	0.27	
	2	10.92	0.75	15.43	0.51	
	3	8.78	0.84	14.26	0.58	
	4	7.37	0.89	13.54	0.62	
	5	6.77	0.90	13.44	0.63	

[a] Key as for Tables 3 and 4. The N-T-C matrix was used and the Q^2-cutoff was set to 0.1 for selecting small boxes for the final model.

[b]Grid spacing (in Å) used in the small sub box calculations (see methods for description). In both cases, final PLS models were obtained with a 2 Å grid spacing.

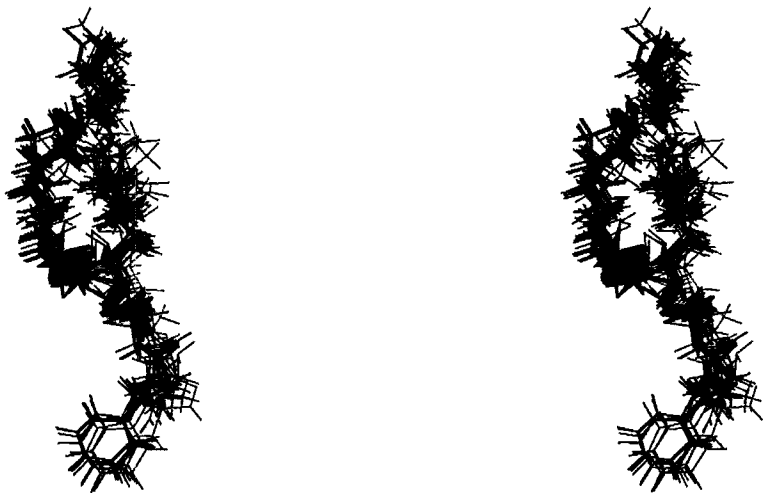

Figure 1. Alignment of the 26 HSF-PLA2 inhibitors used in the CoMFA studies. In the stereo plot, C and H atoms are shown in grey and all other atoms are shown in black.

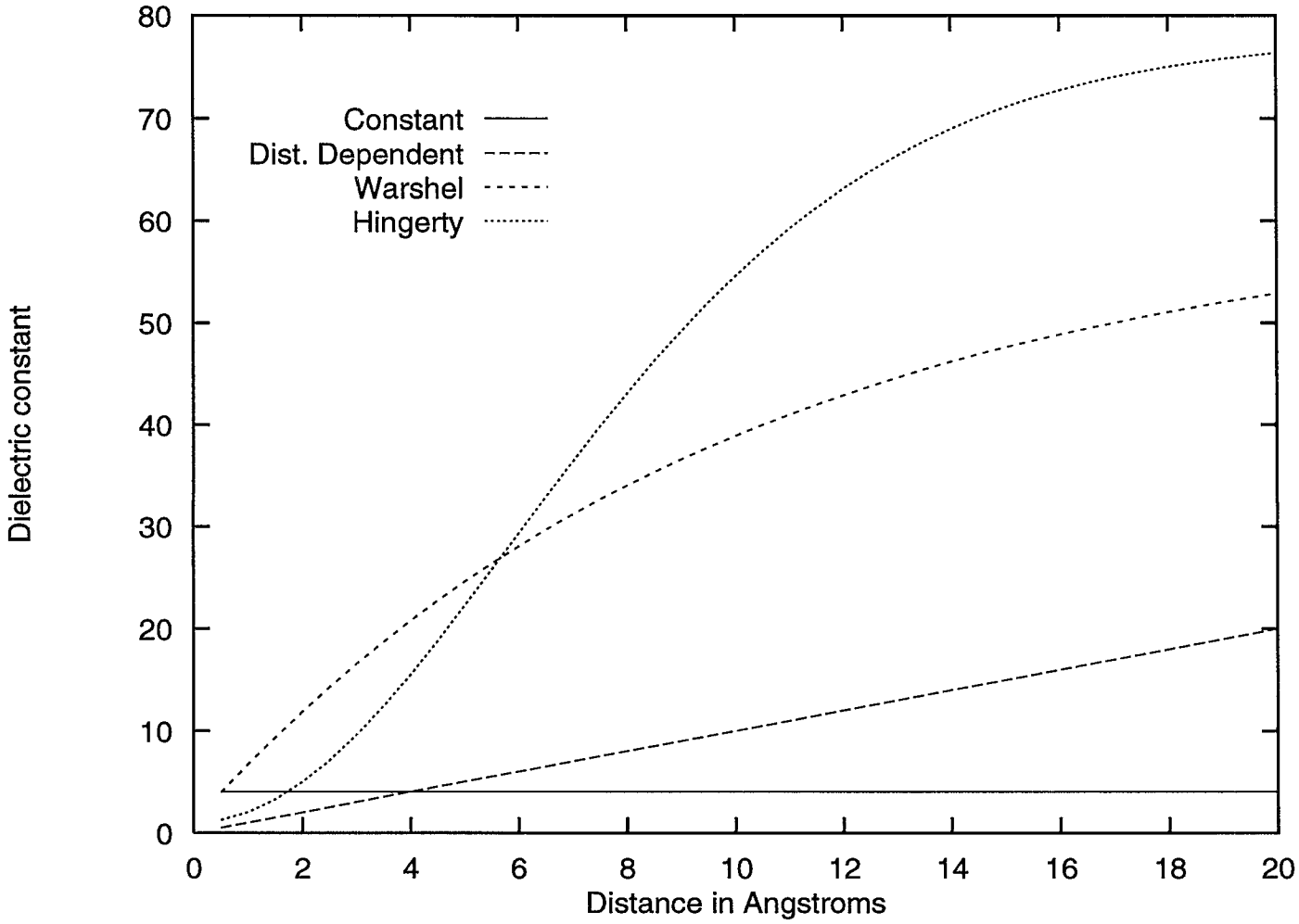

Figure 2. Behaviour of the four different dielectric models tested in the CoMFA studies.

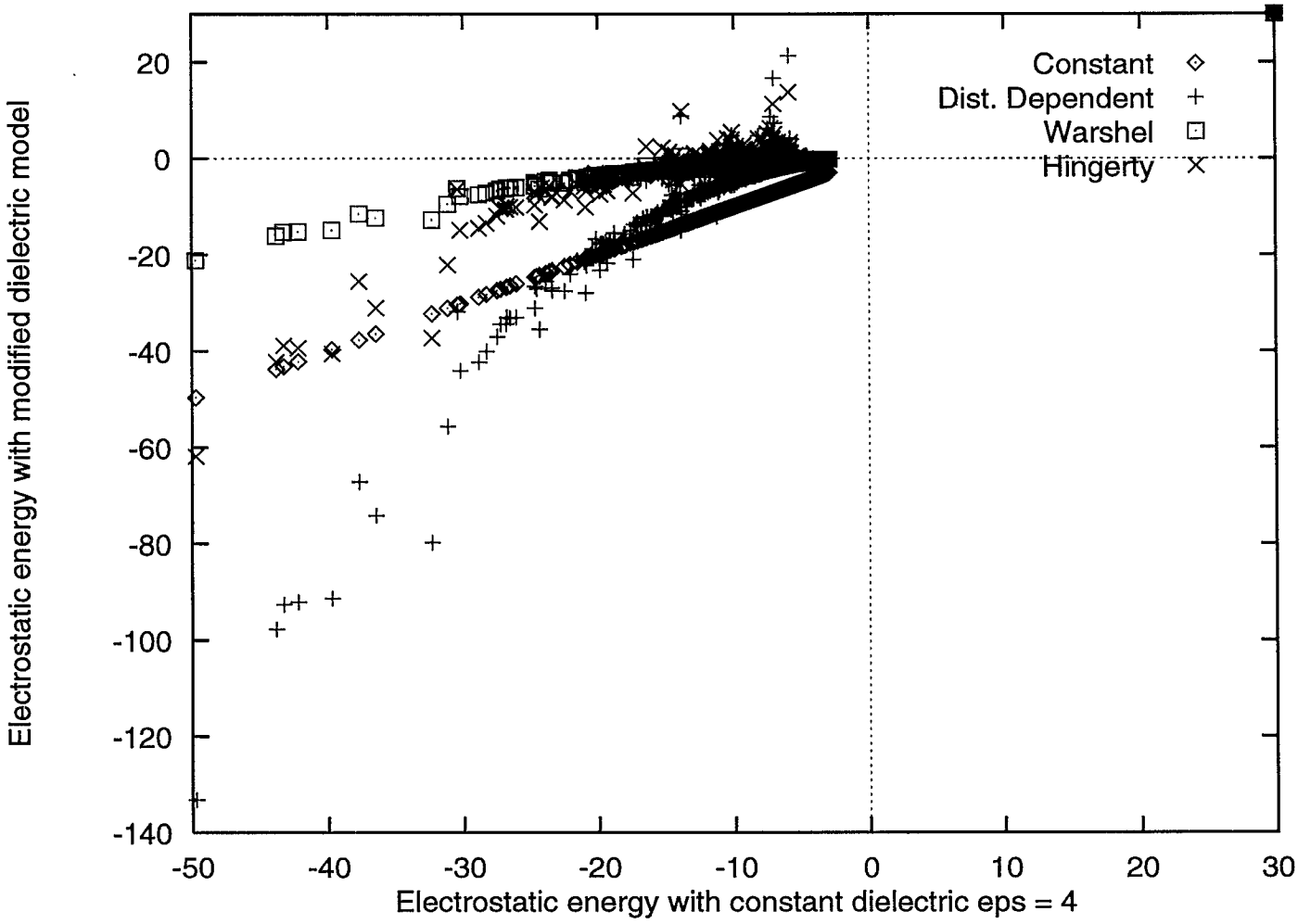

Figure 3. Comparison of the electrostatic energies (in kcal/mol) computed with different dielectric models for a proton probe interacting with a molecules LM1166.

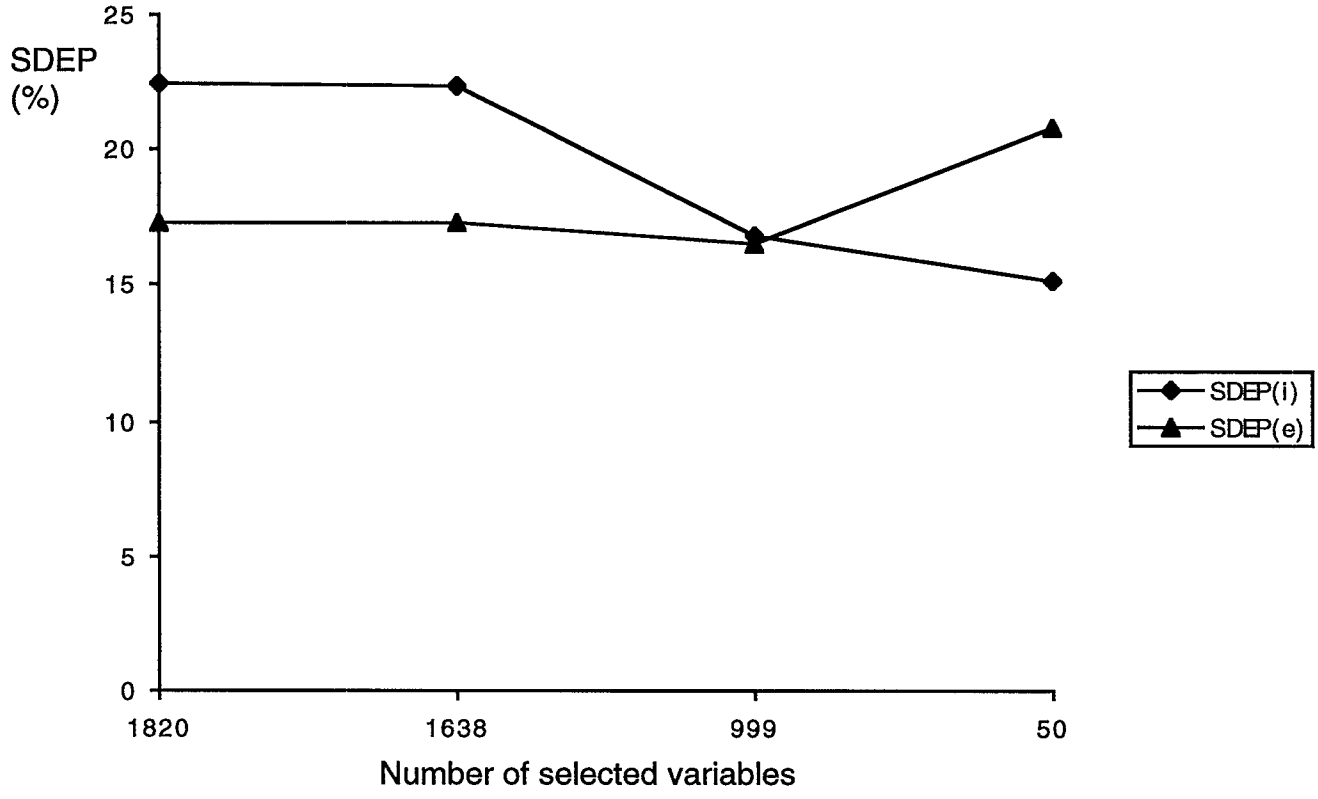

Figure 4. Comparison of internal ($SDEP_{(i)}$) and external ($SDEP_{(e)}$) standard deviations of errors in prediction as a function of the number of selected variables in the model. Results for three steps in variable selection are shown: 1) D-optimal selection (1820 -> 1638); 2) FFD selection without elimination of uncertain variables (1638 -> 999); 3) FFD selection with elimination of uncertain variables (999 -> 50). The B-G-C matrix and test set 1 (6 compounds) were used.

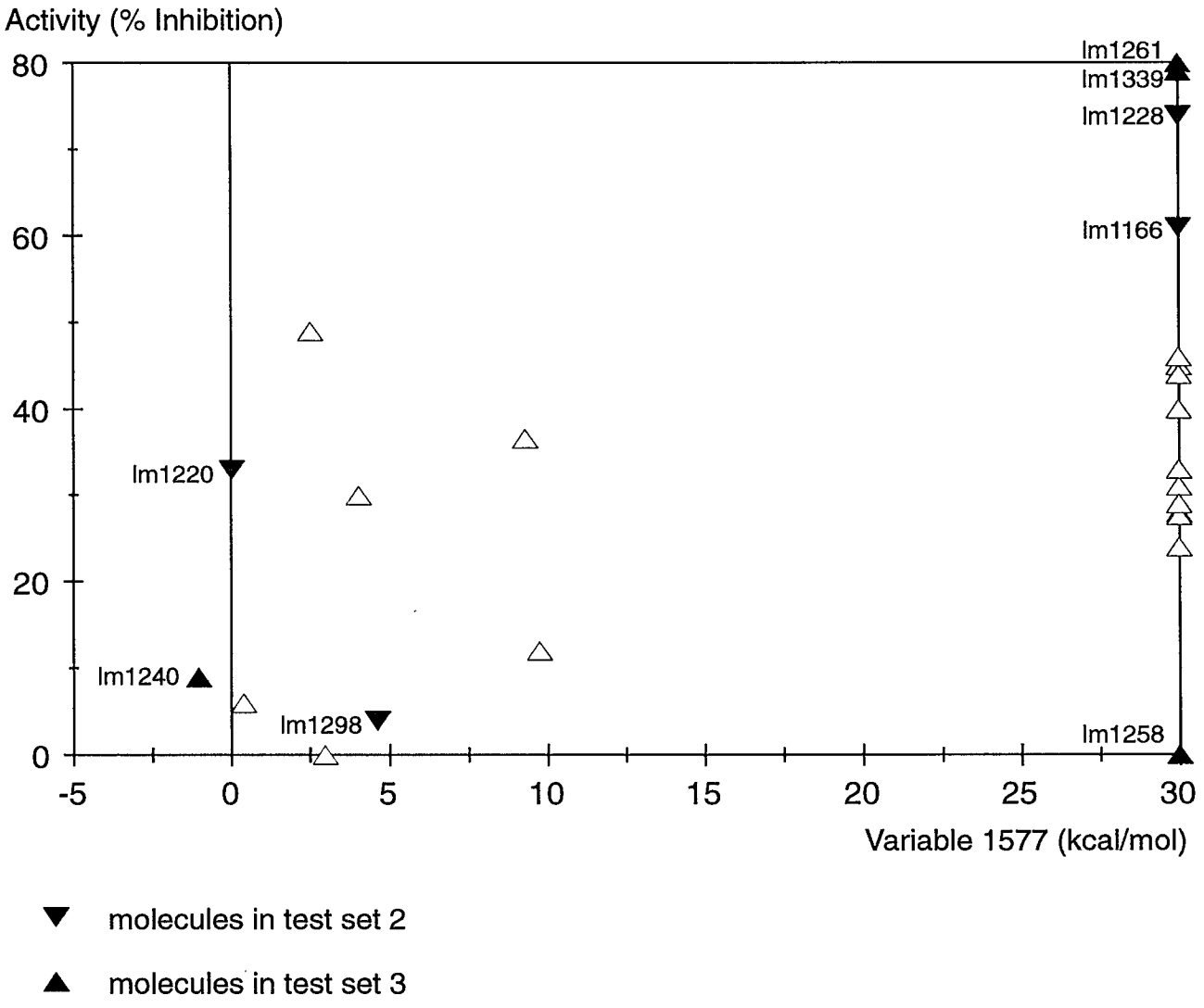

Figure 5. Scatter plot of X-variable 1577 against activity for the 26 inhibitors