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Supplementary Material

Method Optimisation in Hydrophilic Interaction Liquid Chromatography by Design of Experiments Combined with Quantitative Structure-Retention Relationships*

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Table S1. Plan of experiments defined by two-level full factorial design.

nr.	Acentonitrile cont	pH	Salt concentration
1	70	3	10
2	90	3	10
3	70	7	10
4	90	7	10
5	70	3	20
6	90	3	20
7	70	7	20
8	90	7	20
9	80	5	15
10	80	5	15
11	80	5	15

Table S2. Coefficients of the obtained DoE models for 16 nucleosides and their statistical evaluation on zwitterionic column.

Name of compounds	β_0 (p)	β_1 (p)	β_2 (p)	β_3 (p)	β_4 (p)	Q^2	R^2	R^2 adj.
2'-Deoxyadenosine	3.23 (0.00)	1.32 (0.00)	0.08 (0.00)	0.64 (0.00)	0.07 (0.00)	1.00	1.00	1.00
2'-Deoxycytidine	4.44 (0.00)	4.38 (0.00)	0.70 (0.00)	3.06 (0.00)	0.68 (0.00)	0.99	1.00	1.00
2',3'-Dideoxyadenosine	2.86 (0.00)	0.73 (0.00)	0.00	0.28 (0.00)	0.00	0.95	0.99	0.98
2'-Deoxyguanosine	4.38 (0.00)	4.88 (0.00)	0.67 (0.01)	3.47 (0.00)	0.66 (0.01)	0.98	0.99	0.99
3'-Deoxyguanosine	4.15 (0.00)	4.39 (0.00)	0.59 (0.01)	3.12 (0.00)	0.59 (0.01)	0.98	0.99	0.99
5'-Methyluridine	2.98 (0.00)	1.36 (0.00)	0.25 (0.00)	0.80 (0.00)	0.25 (0.00)	0.98	0.99	0.99
Adenosine	3.50 (0.00)	1.94 (0.00)	0.23 (0.00)	1.11 (0.00)	0.23 (0.00)	1.00	1.00	1.00
Cytidine	5.01 (0.00)	6.84 (0.00)	1.62 (0.00)	5.15 (0.00)	1.60 (0.00)	0.99	1.00	1.00
Guanosine	4.95 (0.00)	7.45 (0.00)	1.43 (0.01)	5.66 (0.00)	1.43 (0.01)	0.96	0.99	0.98
Inosine	4.23 (0.00)	4.35 (0.00)	0.97 (0.00)	3.03 (0.00)	0.96 (0.00)	0.97	0.99	0.99
Thymidine	2.66 (0.00)	0.75 (0.00)	0.08 (0.00)	0.37 (0.00)	0.09 (0.00)	0.99	1.00	0.99
Uridine	3.28 (0.00)	1.85 (0.00)	0.41 (0.00)	1.14 (0.00)	0.40 (0.00)	0.97	0.99	0.99
Acyclovir	4.21 (0.00)	4.03 (0.00)	0.60 (0.00)	2.79 (0.00)	0.63 (0.00)	0.98	1.00	0.99
2'-Deoxyuridine	2.89 (0.00)	1.03 (0.00)	0.16 (0.01)	0.56 (0.00)	0.19 (0.00)	0.97	0.99	0.99
3'-Deoxythymidine	2.27 (0.00)	0.31 (0.00)	0.00	0.13 (0.00)	0.00	0.98	0.99	0.99
2'-Deoxyinosine	3.79 (0.00)	2.91 (0.00)	0.52 (0.00)	1.89 (0.00)	0.54 (0.00)	0.97	0.99	0.99

DoE model is $t_R = \beta_0 + \beta_1 \times$ acetonitrile content $+ \beta_2 \times$ salt concentration $+ \beta_3 \times$ (acetonitrile content)^2 + $\beta_4 \times$ (acetonitrile content $\times$ salt concentration). p is the significance of the variables in the model.

Table S3. Coefficients of the obtained DoE models for 16 nucleosides and their statistical evaluation on amide column.

Name of compounds	β_0 (p)	β_1 (p)	β_2 (p)	β_3 (p)	β_4 (p)	Q^2	R^2	R^2 adj.
2'-Deoxyadenosine	3.15 (0.00)	1.11 (0.00)	0.06 (0.00)	0.57 (0.00)	0.06 (0.00)	1.00	1.00	1.00
2'-Deoxycytidine	4.32 (0.00)	3.87 (0.00)	0.00	2.56 (0.00)	0.00	0.99	0.99	0.99
2',3'-Dideoxyadenosine	2.95 (0.00)	0.72 (0.00)	0.02 (0.02)	0.33 (0.00)	0.00	1.00	1.00	1.00
2'-Deoxyguanosine	3.94 (0.00)	3.23 (0.00)	0.24 (0.00)	2.18 (0.00)	0.28 (0.00)	1.00	1.00	1.00
3'-Deoxyguanosine	3.86 (0.00)	3.12 (0.00)	0.24 (0.00)	2.13 (0.00)	0.29 (0.00)	1.00	1.00	1.00
5'-Methyluridine	2.89 (0.00)	0.93 (0.00)	0.09 (0.00)	0.51 (0.00)	0.10 (0.00)	1.00	1.00	1.00
Adenosine	3.34 (0.00)	1.49 (0.00)	0.12 (0.00)	0.84 (0.00)	0.13 (0.00)	1.00	1.00	1.00
Cytidine	4.55 (0.00)	4.78 (0.00)	0.34 (0.00)	3.31 (0.00)	0.40 (0.00)	1.00	1.00	1.00
Guanosine	4.26 (0.00)	4.33 (0.00)	0.40 (0.00)	3.08 (0.00)	0.48 (0.00)	1.00	1.00	1.00
Inosine	3.58 (0.00)	2.37 (0.00)	0.25 (0.00)	1.52 (0.00)	0.29 (0.00)	1.00	1.00	1.00
Thymidine	2.70 (0.00)	0.62 (0.00)	0.05 (0.00)	0.30 (0.00)	0.05 (0.00)	1.00	1.00	1.00
Uridine	2.95 (0.00)	1.02 (0.00)	0.11 (0.00)	0.56 (0.00)	0.13 (0.00)	1.00	1.00	1.00
Acyclovir	3.68 (0.00)	2.53 (0.00)	0.23 (0.00)	1.65 (0.00)	0.27 (0.00)	0.99	0.99	0.99
2'-Deoxyuridine	2.77 (0.00)	0.71 (0.00)	0.07 (0.00)	0.34 (0.00)	0.07 (0.00)	0.99	1.00	0.99
3'-Deoxythymidine	2.48 (0.00)	0.33 (0.00)	0.02 (0.01)	0.14 (0.00)	0.01 (0.03)	0.99	1.00	1.00
2'-Deoxyinosine	3.37 (0.00)	1.79 (0.00)	0.18 (0.00)	1.08 (0.00)	0.21 (0.00)	0.98	0.99	0.99

DoE model is $t_R = \beta_0 + \beta_1 \times$ acetonitrile content $+ \beta_2 \times$ salt concentration $+ \beta_3 \times$ (acetonitrile content)^2 $+ \beta_4 \times$ (acetonitrile content $\times$ salt concentration). p is the significance of the variables in the model.

Table S4. Coefficients of the obtained DoE models for 16 nucleosides and their statistical evaluation on amine column.

Name of compounds	β_0 (p)	β_1 (p)	β_2 (p)	β_3 (p)	β_4 (p)	Q^2	R^2	R^2 adj.
2'-Deoxyadenosine	3.34 (0.00)	1.43 (0.00)	0.23 (0.00)	0.74 (0.00)	0.18 (0.00)	0.99	1.00	0.99
2'-Deoxycytidine	4.96 (0.00)	5.30 (0.00)	1.35 (0.00)	3.64 (0.00)	1.29 (0.00)	1.00	1.00	1.00
2',3'-Dideoxyadenosine	2.91 (0.00)	0.81 (0.00)	0.09 (0.02)	0.36 (0.00)	0.00	0.98	0.99	0.99
2'-Deoxyguanosine	4.87 (0.00)	5.82 (0.00)	1.49 (0.00)	4.27 (0.00)	1.45 (0.00)	0.99	1.00	1.00
3'-Deoxyguanosine	4.62 (0.00)	5.33 (0.00)	1.36 (0.00)	3.94 (0.00)	1.31 (0.00)	0.98	1.00	0.99
5'-Methyluridine	3.29 (0.00)	1.80 (0.00)	0.56 (0.00)	1.19 (0.00)	0.53 (0.00)	0.98	0.99	0.99
Adenosine	3.71 (0.00)	2.25 (0.00)	0.59 (0.00)	1.40 (0.00)	0.54 (0.00)	0.99	1.00	0.99
Cytidine	5.89 (0.00)	9.30 (0.00)	3.57 (0.00)	7.16 (0.00)	3.48 (0.00)	0.90	0.98	0.96
Guanosine	5.69 (0.00)	9.53 (0.00)	3.48 (0.00)	7.64 (0.00)	3.31 (0.00)	0.92	0.98	0.97
Inosine	4.98 (0.00)	5.94 (0.00)	2.18 (0.00)	4.40 (0.00)	2.14 (0.00)	0.95	0.99	0.98
Thymidine	2.85 (0.00)	0.95 (0.00)	0.28 (0.00)	0.56 (0.00)	0.22 (0.00)	0.97	0.99	0.99
Uridine	3.64 (0.00)	2.44 (0.00)	0.99 (0.00)	1.72 (0.00)	0.91 (0.00)	0.93	0.98	0.97
Acyclovir	4.67 (0.00)	3.95 (0.00)	0.00	2.61 (0.00)	0.00	0.90	0.95	0.93
2'-Deoxyuridine	3.12 (0.00)	1.00 (0.00)	0.00	0.56 (0.02)	0.00	0.86	0.95	0.92
3'-Deoxythymidine	2.55 (0.00)	0.30 (0.00)	0.00	0.00	0.00	0.51	0.68	0.65
2'-Deoxyinosine	4.33 (0.00)	2.87 (0.00)	0.00	1.93 (0.00)	0.00	0.89	0.96	0.94

DoE model is $t_R = \beta_0 + \beta_1 \times$ acetonitrile content $+ \beta_2 \times$ salt concentration $+ \beta_3 \times$ (acetonitrile content)^2 + $\beta_4 \times$ (acetonitrile content $\times$ salt concentration). p is the significance of the variables in the model.

Table S5. Coefficients of the obtained DoE models for 16 nucleosides and their statistical evaluation on bare silica column.

Name of compounds	β_0 (p)	β_1 (p)	β_2 (p)	β_3 (p)	β_4 (p)	Q^2	R^2	R^2 adj.
2'-Deoxyadenosine	1.74 (0.00)	0.61 (0.00)	0.04 (0.02)	0.30 (0.00)	0.00	0.99	1.00	1.00
2'-Deoxycytidine	2.05 (0.00)	1.93 (0.00)	0.50 (0.00)	1.41 (0.00)	0.49 (0.00)	0.94	0.99	0.98
2',3'-Dideoxyadenosine	1.72 (0.00)	0.39 (0.00)	0.00	0.14 (0.01)	0.00	0.95	0.97	0.96
2'-Deoxyguanosine	1.89 (0.00)	1.77 (0.00)	0.52 (0.00)	1.30 (0.00)	0.50 (0.00)	0.93	0.98	0.97
3'-Deoxyguanosine	1.82 (0.00)	1.58 (0.00)	0.47 (0.00)	1.17 (0.00)	0.46 (0.00)	0.93	0.98	0.97
5'-Methyluridine	1.44 (0.00)	0.51 (0.00)	0.19 (0.00)	0.32 (0.01)	0.17 (0.00)	0.90	0.98	0.96
Adenosine	1.76 (0.00)	0.81 (0.00)	0.17 (0.01)	0.47 (0.00)	0.15 (0.01)	0.96	0.99	0.98
Cytidine	2.14 (0.00)	2.83 (0.00)	1.11 (0.01)	2.24 (0.01)	1.09 (0.01)	0.83	0.96	0.93
Guanosine	1.96 (0.00)	2.50 (0.00)	1.02 (0.01)	1.98 (0.01)	1.00 (0.01)	0.85	0.96	0.94
Inosine	1.85 (0.00)	1.71 (0.00)	0.69 (0.01)	1.27 (0.02)	0.67 (0.02)	0.79	0.95	0.91
Thymidine	1.40 (0.00)	0.30 (0.00)	0.08 (0.02)	0.13 (0.03)	0.06 (0.04)	0.90	0.97	0.95
Uridine	1.53 (0.00)	0.69 (0.00)	0.30 (0.01)	0.44 (0.02)	0.28 (0.01)	0.81	0.95	0.92
Acyclovir	2.03 (0.00)	1.63 (0.00)	0.43 (0.00)	1.11 (0.00)	0.40 (0.00)	0.95	0.99	0.98
2'-Deoxyuridine	1.49 (0.00)	0.39 (0.00)	0.13 (0.01)	0.00	0.10 (0.03)	0.87	0.96	0.93
3'-Deoxythymidine	1.35 (0.00)	0.13 (0.00)	0.00	0.00	0.00	0.74	0.79	0.77
2'-Deoxyinosine	1.86 (0.00)	1.19 (0.00)	0.34 (0.01)	0.75 (0.00)	0.31 (0.01)	0.91	0.98	0.96

DoE model is $t_R = \beta_0 + \beta_1 \times$ acetonitrile content $+ \beta_2 \times$ salt concentration $+ \beta_3 \times$ (acetonitrile content)$^2 + \beta_4 \times$ (acetonitrile content $\times$ salt concentration). p is the significance of the variables in the model.

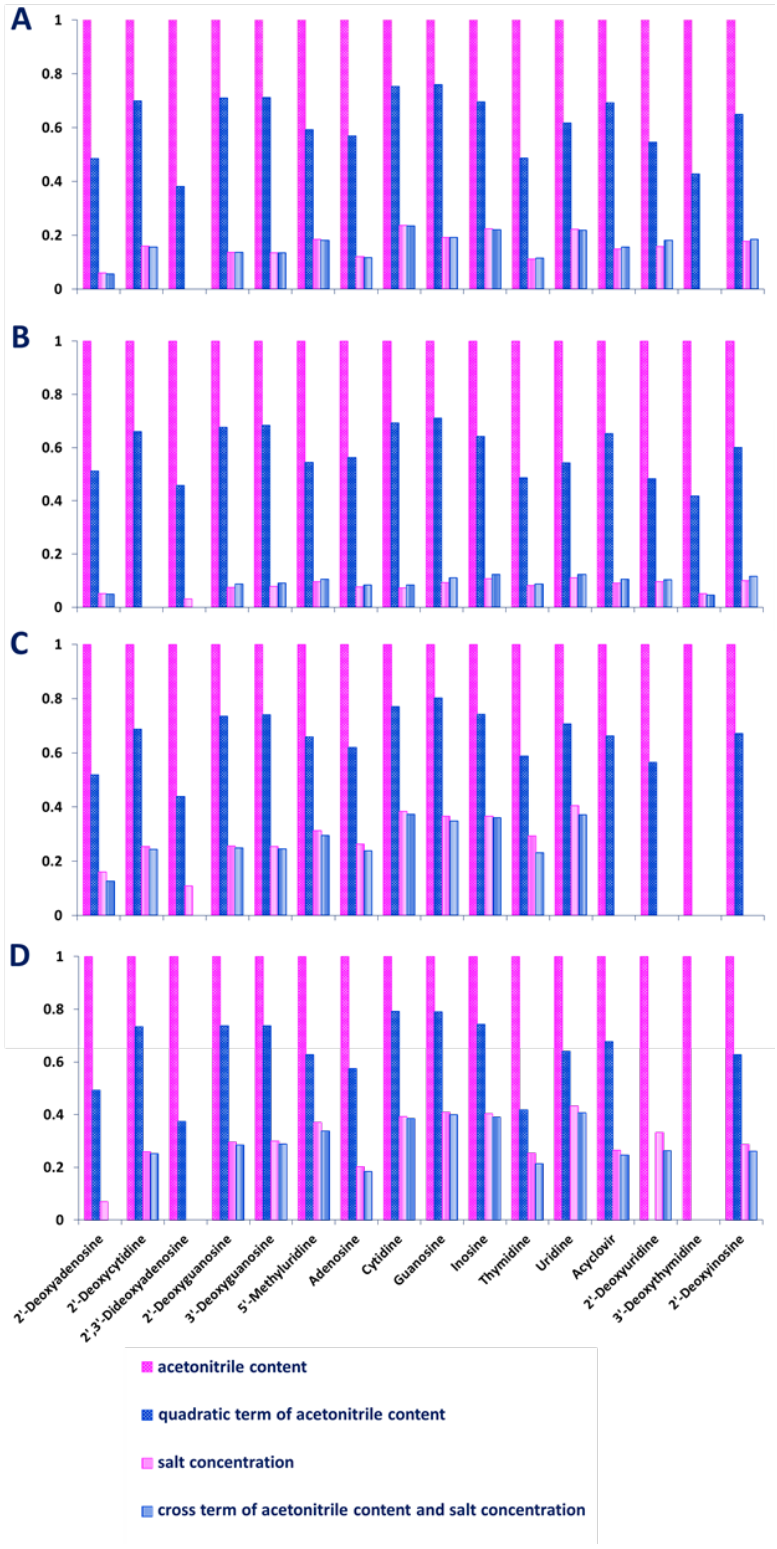

Figure S1. DoE model term ranking chart for 16 nucleosides over (A) zwitterionic, (B) amide, (C) amine, and (D) bare silica systems.

Table S6. Predictive performance of local GA-PLS models on internal validation under all 11 mobile phase compositions corresponding to the used DOE and over zwitterionic, amide, amine, and bare silica HILIC stationary phases.

	Zwitterionic		amide		amine		baresilica	
	RMSECV	Q^2_{cv}	RMSECV	Q^2_{cv}	RMSECV	Q^2_{cv}	RMSECV	Q^2_{cv}
1	0.01	0.99	0.00	0.99	0.01	0.99	0.01	0.99
2	0.09	0.98	0.09	0.98	0.12	0.98	0.04	0.99
3	0.01	0.99	0.01	0.99	0.01	0.99	0.00	0.99
4	0.16	0.97	0.06	0.99	0.10	0.98	0.03	0.99
5	0.01	0.99	0.01	0.98	0.03	0.97	0.01	0.99
6	0.17	0.98	0.09	0.98	0.31	0.98	0.09	0.98
7	0.01	0.98	0.01	0.99	0.01	0.99	0.01	0.99
8	0.18	0.98	0.07	0.99	0.21	0.99	0.12	0.99
9	0.02	0.98	0.02	0.99	0.03	0.98	0.01	0.99
10	0.02	0.99	0.02	0.98	0.02	0.98	0.01	0.99
11	0.02	0.99	0.02	0.98	0.02	0.99	0.01	0.99
Average	0.06	0.98	0.03	0.98	0.08	0.98	0.03	0.99

Numbers in row are operating conditions of the full factorial design (Table S1).

Table S7. The predicted retention times of test compounds on the chromatographic conditions corresponding to the used DoE matrix over zwitterionic HILIC column by using QSRR-DOE models.

	Predicted Retention Factors										
	K 1	*K* 2	*K* 3	*K* 4	*K* 5	*K* 6	*K* 7	*K* 8	*K* 9	*K* 10	*K* 11
2'-Deoxyadenosine	0.58	1.74	0.63	2.01	0.60	2.13	0.64	2.34	0.94	0.93	0.94
2'-Deoxycytidine	0.97	4.97	0.92	5.49	1.01	7.19	0.96	7.05	1.74	1.81	1.79
2',3'-Dideoxyadenosine	0.57	1.53	0.53	1.37	0.57	1.71	0.57	1.45	0.94	0.87	0.90
2'-Deoxyguanosine	0.87	5.30	0.93	5.90	0.93	8.23	0.96	8.75	1.77	1.86	1.82
3'-Deoxyguanosine	0.83	5.09	0.95	6.46	0.89	7.40	0.96	7.10	1.73	1.84	1.78
5'-Methyluridine	0.54	1.74	0.55	2.07	0.56	2.76	0.60	2.70	0.91	0.97	0.95
Adenosine	0.65	2.50	0.67	2.52	0.69	3.02	0.72	3.04	1.20	1.21	1.21
Cytidine	1.09	6.45	0.98	7.56	1.08	11.68	1.09	11.67	1.90	2.01	2.01
Guanosine	0.84	5.98	0.98	8.92	0.98	10.81	0.93	10.84	1.86	2.00	1.83
Inosine	0.89	5.72	0.92	6.08	0.86	7.80	1.01	7.22	1.66	1.80	1.92
Thymidine	0.43	1.12	0.51	1.25	0.46	1.45	0.49	1.43	0.66	0.67	0.68
Uridine	0.55	1.92	0.66	2.21	0.59	3.74	0.63	2.92	0.95	1.02	0.97
Acyclovir	0.82	4.14	0.93	5.22	0.86	6.34	0.91	6.06	1.47	1.54	1.57
2'-Deoxyuridine	0.51	1.35	0.56	1.65	0.53	2.20	0.58	2.08	0.82	0.84	0.85
3'-Deoxythymidine	0.39	0.57	0.40	0.75	0.41	0.90	0.44	0.90	0.57	0.57	0.52
2'-Deoxyinosine	0.71	3.07	0.80	3.45	0.77	4.69	0.81	5.01	1.35	1.41	1.39

Numbers in row are operating conditions of the full factorial design (Table S1).

Table S8. The predicted retention times of test compounds on the chromatographic conditions corresponding to the used DoE matrix over amide HILIC column by using QSRR-DOE models.

	Predicted Retention Factors										
	K 1	*K* 2	*K* 3	*K* 4	*K* 5	*K* 6	*K* 7	*K* 8	*K* 9	*K* 10	*K* 11
2'-Deoxyadenosine	0.41	1.42	0.41	1.54	0.40	1.59	0.44	1.74	0.72	0.68	0.66
2'-Deoxycytidine	0.57	4.02	0.59	3.82	0.56	4.65	0.63	4.48	1.23	1.18	1.14
2',3'-Dideoxyadenosine	0.39	0.98	0.37	1.24	0.39	1.33	0.40	1.26	0.68	0.65	0.61
2'-Deoxyguanosine	0.58	4.07	0.59	4.01	0.58	4.27	0.62	4.32	1.25	1.20	1.15
3'-Deoxyguanosine	0.56	3.61	0.55	3.43	0.55	4.27	0.58	4.25	1.11	1.10	1.05
5'-Methyluridine	0.35	1.21	0.33	1.19	0.34	1.53	0.35	1.40	0.59	0.58	0.56
Adenosine	0.44	1.71	0.43	1.73	0.43	1.98	0.46	1.98	0.83	0.80	0.77
Cytidine	0.63	5.34	0.67	5.18	0.63	5.93	0.74	6.02	1.51	1.46	1.39
Guanosine	0.61	4.47	0.61	4.50	0.60	5.70	0.65	5.42	1.11	1.07	1.03
Inosine	0.55	3.19	0.52	3.19	0.51	3.81	0.53	3.77	1.24	1.21	1.18
Thymidine	0.32	0.89	0.28	0.96	0.31	1.09	0.33	1.04	0.48	0.48	0.46
Uridine	0.35	1.28	0.34	1.29	0.34	1.51	0.36	1.55	0.61	0.60	0.58
Acyclovir	0.55	3.29	0.60	3.23	0.55	3.56	0.60	4.01	1.12	1.11	1.02
2'-Deoxyuridine	0.31	0.97	0.30	0.95	0.31	1.10	0.32	1.14	0.52	0.51	0.49
3'-Deoxythymidine	0.27	0.56	0.27	0.60	0.26	0.63	0.28	0.70	0.40	0.40	0.40
2'-Deoxyinosine	0.45	2.14	0.44	2.09	0.44	2.46	0.47	2.72	0.86	0.85	0.81

Numbers in row are operating conditions of the full factorial design (Table S1).

Table S9. The predicted retention times of test compounds on the chromatographic conditions corresponding to the used DoE matrix over amine HILIC column by using QSRR-DOE models.

	Predicted Retention Factors										
	K 1	*K* 2	*K* 3	*K* 4	*K* 5	*K* 6	*K* 7	*K* 8	*K* 9	*K* 10	*K* 11
2'-Deoxyadenosine	0.66	1.73	0.72	1.91	0.70	2.34	0.71	2.33	0.98	0.96	0.98
2'-Deoxycytidine	1.11	5.54	1.23	5.28	1.01	9.05	1.20	8.34	2.12	2.05	2.04
2',3'-Dideoxyadenosine	0.62	1.58	0.61	1.36	0.65	1.41	0.61	1.58	0.91	0.93	0.91
2'-Deoxyguanosine	1.15	6.16	1.24	6.05	1.15	10.97	1.20	9.45	2.20	2.07	2.08
3'-Deoxyguanosine	1.20	6.03	1.23	5.86	1.32	10.18	1.17	8.45	2.21	2.05	2.05
5'-Methyluridine	0.75	2.10	0.76	1.88	0.72	3.39	0.78	3.37	1.15	1.10	1.09
Adenosine	0.82	2.47	0.84	2.48	0.76	4.06	0.84	3.54	1.30	1.30	1.27
Cytidine	1.25	8.11	1.35	7.52	1.19	16.35	1.37	13.13	2.45	2.51	2.27
Guanosine	1.23	7.21	1.29	7.00	1.29	16.61	1.26	12.82	2.42	2.24	2.10
Inosine	1.23	5.21	1.33	5.72	1.26	12.23	1.28	10.11	2.22	2.08	2.22
Thymidine	0.60	1.27	0.60	1.29	0.68	1.70	0.57	1.67	0.76	0.77	0.75
Uridine	0.80	2.20	0.82	2.06	0.92	3.90	0.79	3.70	1.22	1.17	1.09
Acyclovir	0.98	4.62	1.12	4.65	0.99	6.24	1.08	6.01	1.77	1.74	1.84
2'-Deoxyuridine	0.70	1.65	0.69	1.56	0.82	2.40	0.70	2.09	0.97	0.95	0.96
3'-Deoxythymidine	0.51	0.91	0.53	0.74	0.62	0.97	0.50	0.90	0.67	0.57	0.54
2'-Deoxyinosine	0.99	3.77	1.12	3.88	1.86	5.20	1.07	4.54	1.79	1.67	1.64

Numbers in row are operating conditions of the full factorial design (Table S1).

Table S10. The predicted retention times of test compounds on the chromatographic conditions corresponding to the used DoE matrix over bare silica HILIC column by using QSRR-DOE models.

	Predicted Retention Factors										
	K 1	*K* 2	*K* 3	*K* 4	*K* 5	*K* 6	*K* 7	*K* 8	*K* 9	*K* 10	*K* 11
2'-Deoxyadenosine	0.44	1.41	0.46	1.50	0.47	1.56	0.47	1.79	0.71	0.67	0.70
2'-Deoxycytidine	0.54	3.23	0.54	3.37	0.57	5.13	0.56	6.20	1.04	1.00	1.04
2',3'-Dideoxyadenosine	0.44	1.43	0.48	1.29	0.48	1.40	0.44	1.12	0.74	0.69	0.73
2'-Deoxyguanosine	0.43	2.88	0.48	3.10	0.47	4.86	0.51	6.16	0.92	0.87	0.92
3'-Deoxyguanosine	0.40	2.69	0.44	3.00	0.46	4.70	0.49	5.62	0.90	0.88	0.91
5'-Methyluridine	0.24	0.89	0.28	0.94	0.24	1.55	0.30	2.03	0.47	0.40	0.46
Adenosine	0.40	1.58	0.44	1.68	0.42	2.06	0.46	2.39	0.76	0.68	0.74
Cytidine	0.54	3.60	0.55	3.71	0.57	6.33	0.57	7.96	1.08	0.97	1.12
Guanosine	0.38	2.97	0.48	3.40	0.44	6.20	0.51	7.61	0.93	0.90	0.96
Inosine	0.38	2.56	0.46	2.79	0.43	4.40	0.49	6.27	0.85	0.82	0.88
Thymidine	0.27	0.77	0.30	0.76	0.29	0.94	0.31	1.03	0.38	0.41	0.40
Uridine	0.24	0.94	0.29	1.03	0.29	1.67	0.32	2.15	0.49	0.51	0.49
Acyclovir	0.47	2.67	0.50	3.05	0.50	3.61	0.51	4.99	0.89	0.82	0.90
2'-Deoxyuridine	0.26	0.84	0.30	0.89	0.33	1.30	0.32	1.66	0.45	0.52	0.47
3'-Deoxythymidine	0.26	0.53	0.27	0.50	0.28	0.66	0.30	0.62	0.32	0.40	0.39
2'-Deoxyinosine	0.39	2.05	0.45	2.23	0.45	3.06	0.47	3.81	0.82	0.81	0.82

Numbers in row are operating conditions of the full factorial design (Table S1).

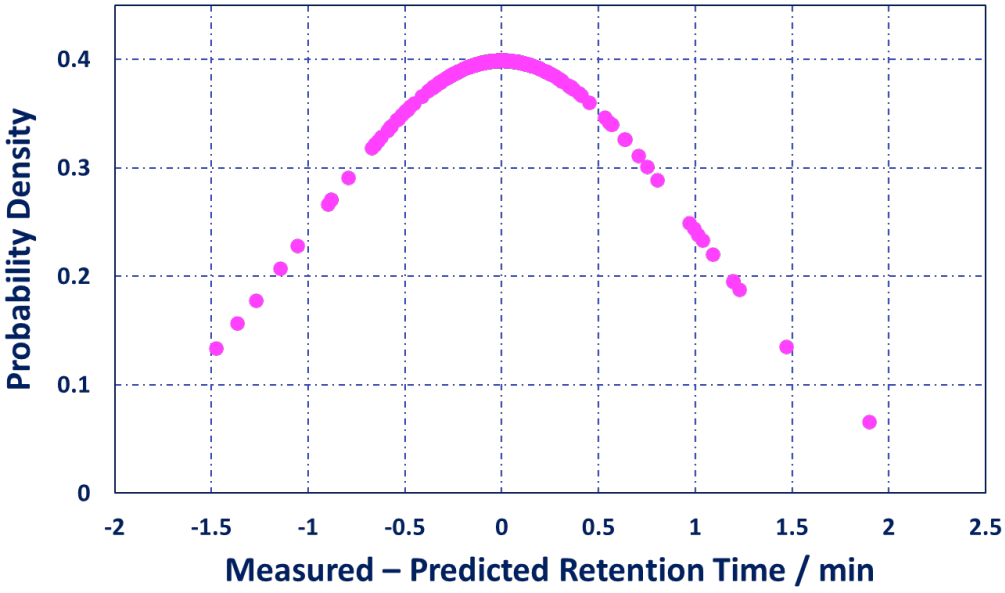

Figure S2. The residual plots of prediction errors using dual-filtering-based GA-PLS models for test set of 16 nucleosides over all experimental conditions corresponding to the used DOE matrix for zwitterionic, amide, amine, and bare silica systems.

Table S11. The experimental retention data and predicted retention times of test compounds on the selected working conditions over zwitterionic, amide, amine, and bare silica HILIC columns by using QSRR-DOE models.

	Zwitterionic		Amide		Amine		Bare Silica	
	Observed t_R	Predicted t_R	Observed t_R	Predicted t_R	Observed t_R	Predicted t_R	Observed t_R	Predicted t_R
2'-Deoxyadenosine	4.91	5.08	4.46	4.74	4.94	5.06	2.24	2.12
2'-Deoxycytidine	10.79	12.21	9.10	8.89	12.61	12.97	3.46	3.64
2',3'-Dideoxyadenosi	3.62	4.19	3.83	3.96	3.47	4.15	2.07	2.03
2'-Deoxyguanosine	11.60	13.89	7.77	7.65	13.97	14.63	3.09	3.51
3'-Deoxyguanosine	10.70	13.15	7.57	8.49	12.96	14.67	2.90	3.47
5'-Methyluridine	4.91	5.62	3.92	4.37	6.12	6.54	1.81	2.01
Adenosine	6.17	6.10	5.06	5.15	6.68	6.55	2.37	2.32
Cytidine	15.00	16.07	10.31	11.07	19.50	18.04	3.96	4.07
Guanosine	16.29	17.79	9.24	10.09	21.48	19.67	3.45	3.89
Inosine	10.66	12.55	6.17	8.04	14.38	15.19	2.90	3.40
Thymidine	3.65	3.95	3.43	3.84	4.16	4.23	1.61	1.75
Uridine	5.94	5.68	4.06	4.46	7.57	6.15	1.97	2.05
Acyclovir	9.89	10.42	6.54	8.47	11.32	10.52	3.14	3.12
2'-Deoxyuridine	4.26	4.78	3.53	3.91	4.89	5.58	1.74	1.94
3'-Deoxythymidine	2.61	3.08	2.90	3.26	2.77	3.57	1.40	1.61
2'-Deoxyinosine	7.80	8.31	5.32	5.99	9.51	8.99	2.70	2.79