

*Comparison of the Retention and Efficiency of Polybutadiene Coated Zirconia (PBD-ZrO<sub>2</sub>) and Various Octadecyl Bonded Silica Based Columns (ODS) Using Cationic Drugs*

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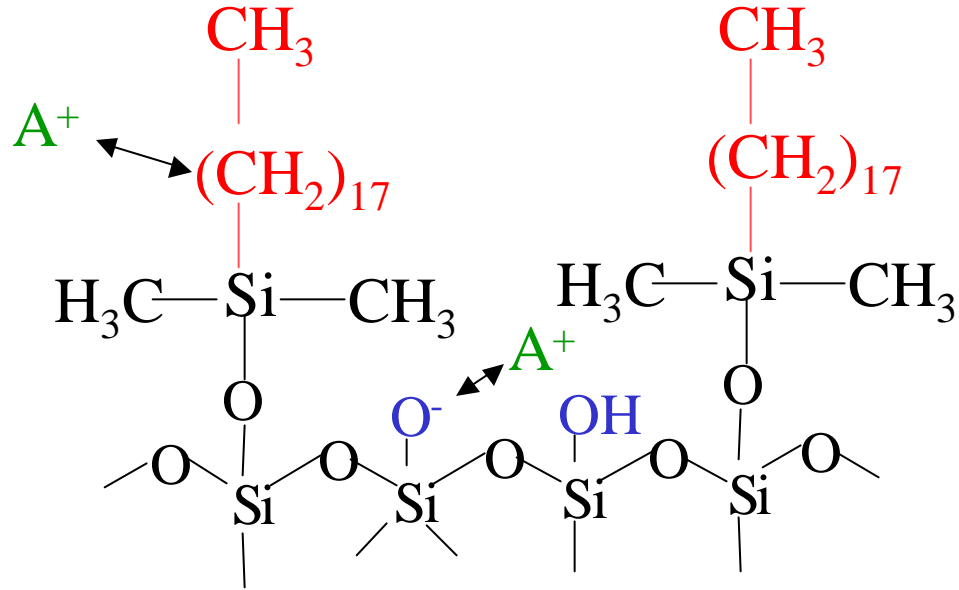
# Outline

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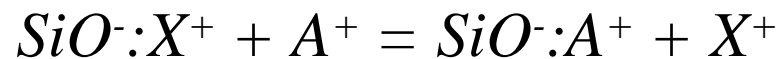
- Comparison of Silica and Zirconia Stationary Phases.
- Chromatography of Basic Analytes on ODS and PBD-ZrO<sub>2</sub>:
  - Comparison based on amitriptyline and acenaphthene.
  - Comparison based on 17 basic drugs.
- Conclusions:
  - Use of a small number of probes is not reliable for column ranking.
  - ODS and PBD-ZrO<sub>2</sub> have very different selectivity for basic drugs.

# Mixed-Mode Separation on ODS

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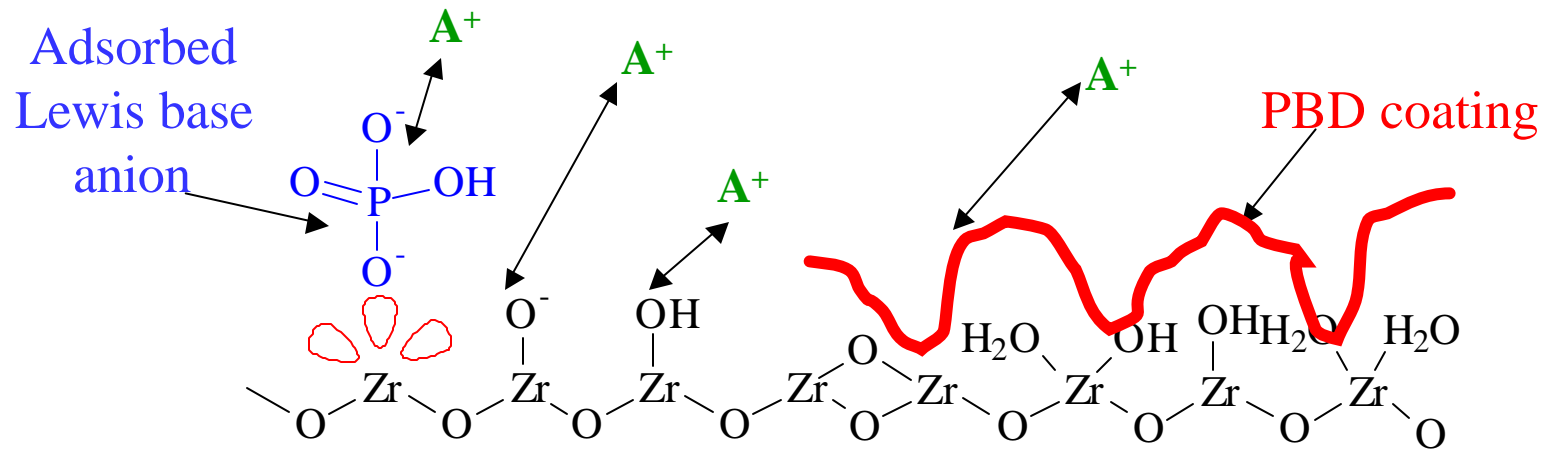


- Bonded C<sub>18</sub> Chains—**Reversed-Phase (RP)** Moieties
- Ionized Silanol Groups — **Ion-Exchange (IEX)** Sites

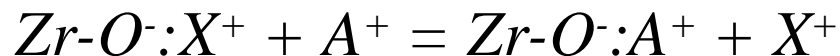
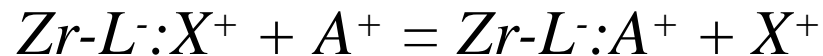


A<sup>+</sup>: analyte cation, X<sup>+</sup>: counterion

# Mixed-Mode Separation on PBD-ZrO<sub>2</sub>



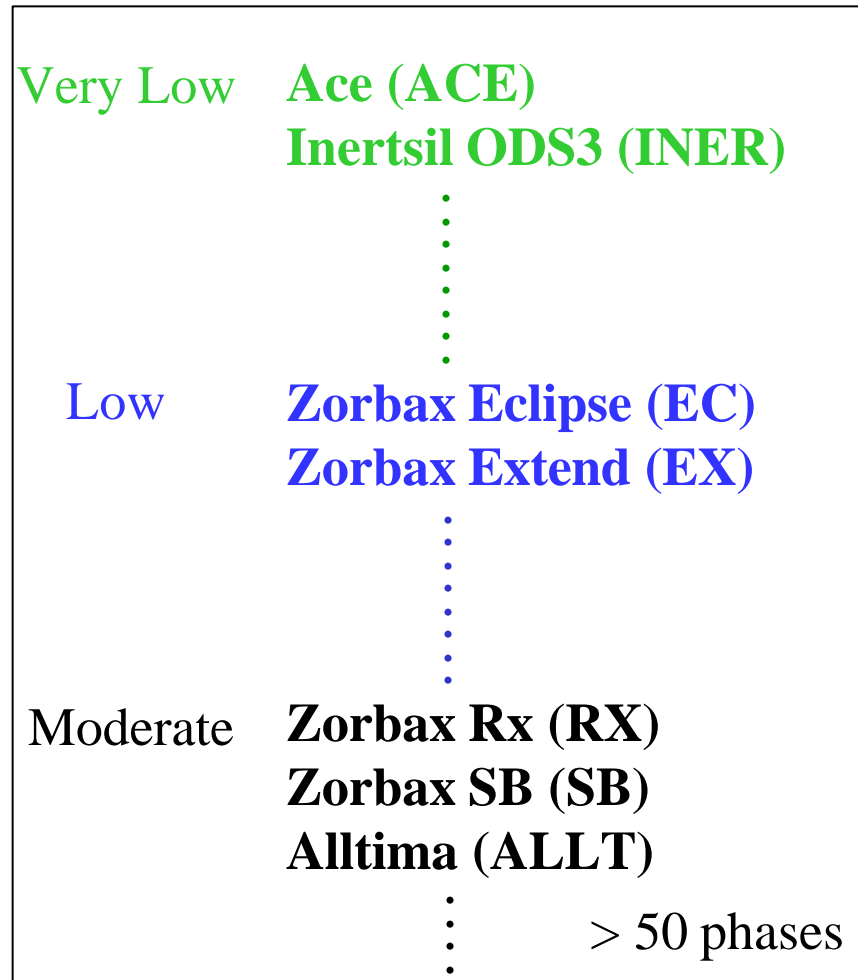
- PBD Coating — **Reversed-Phase (RP)** Moieties
- Lewis Base Anions — **Ion-Exchange (IEX)** Sites



A<sup>+</sup>: analyte cation, X<sup>+</sup>: counterion, L<sup>-</sup>: adsorbed Lewis base anion.

# Silanol Activity Ranking of Stationary Phases

## Silanol Activity of Different ODS Columns \*



\* Adapted from Mac-Mod Analytical, Inc. “*Column Comparison Guide*”, based on plate count of amitriptyline

# Characteristics of ODS and PBD-ZrO<sub>2</sub> Columns

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Column	Designation	Surface Area (m <sup>2</sup> /g)	Pore Size (Å)	Carbon Content (% w/w)
ACE	<b>ACE</b>	300	100	15.5
Zorbax Eclipse	<b>EC</b>	186	80	10
Inertsil ODS-3	<b>INER</b>	436	95	14.7
Zorbax Extend	<b>EX</b>	179	80	10
Alltima	<b>ALLT</b>	350	100	16
Zorbax SB	<b>SB</b>	180	80	10
Zorbax RX	<b>RX</b>	172	80	10
PBD-ZrO <sub>2</sub>	<b>PBD</b>	11.2	500	2.5

✓ PBD-ZrO<sub>2</sub> phase has **much less surface area** and **lower carbon content**

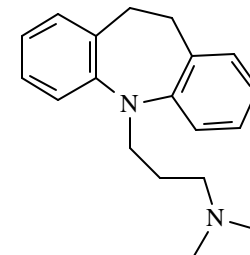
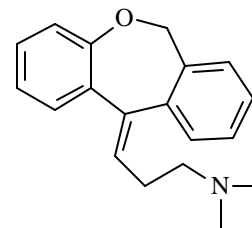
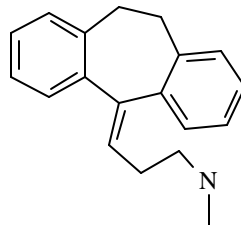
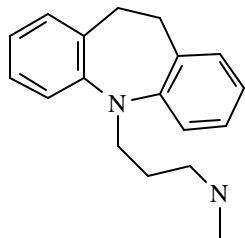
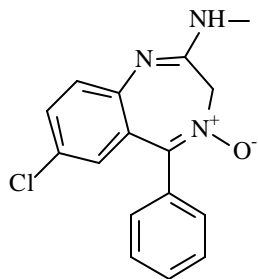
# Comparison of Different Phases Based on Ion-Exchange and Hydrophobic Interactions

Column	$k'_{am}$ *	$k'_{ac}$ *	$N_{am}$	Rank 1	$As_{am}$	Rank 2	$k'_{am}/k'_{ac}$	Rank 3
PBD	5.16	0.88	52,600	1	0.90	3	5.89	8
ACE	1.90	3.76	50,700	2	0.99	1	0.51	2
EC	2.32	4.21	49,600	3	0.81	5	0.55	3
INER	3.02	5.46	37,500	4	0.95	2	0.55	4
EX	2.07	4.38	35,600	5	0.67	6	0.47	1
ALLT	4.51	5.26	33,700	6	0.25	8	0.86	6
SB	3.2	3.25	28,300	7	1.13	4	0.99	7
RX	2.97	4.09	11,000	8	0.31	7	0.73	5

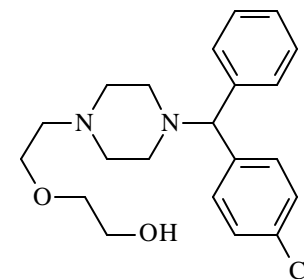
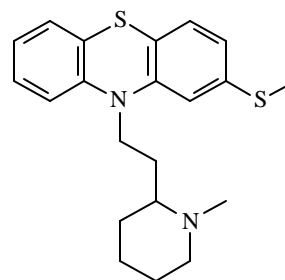
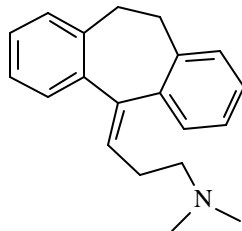
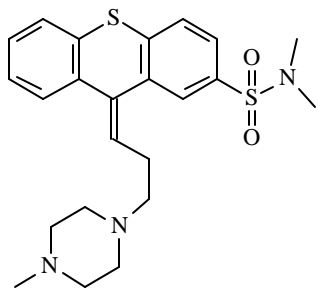
\* am: amitriptyline; ac: acenaphthene; N: plate count; As: asymmetry factor  
80/20 MeOH/25mM ammonium phosphate buffer, pH 6, temperature ambient (about 28 °C), 1.0 ml/min

✓ Ranking orders are **different** using **different methods**

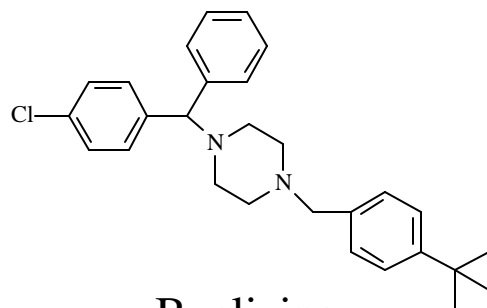
# Solutes--Antidepressants



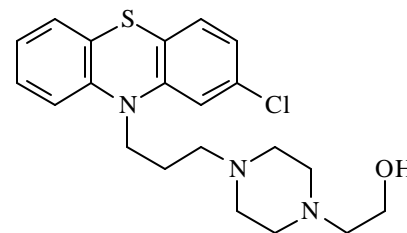
Clordiazepoxide (4.8) Desipramine (10.4) Nortriptyline (9.7) Doxepin (8.9) Imipramine (9.5)



Thiothixene (7.7, 7.9) Amitriptyline (9.4) Thioridazine (9.5) Hydroxyzine (2.0, 7.1)



Buclizine

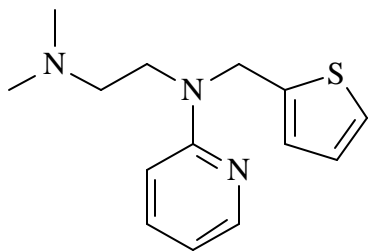


Perphenazine (3.7, 7.8)

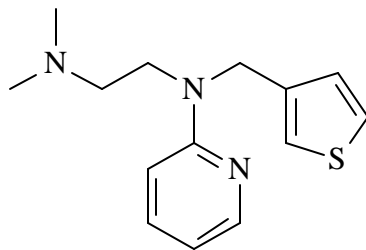


# Solutes--Antihistamines

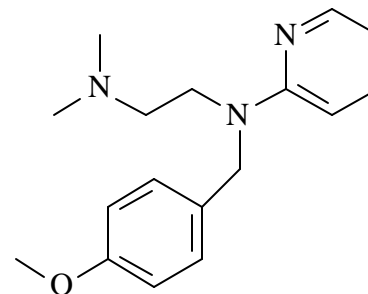
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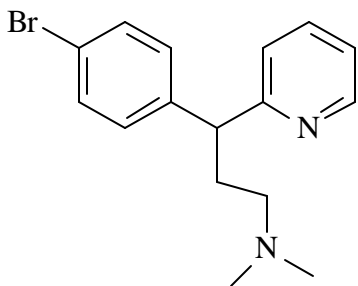
Methapyrilene  
(3.7, 8.9)



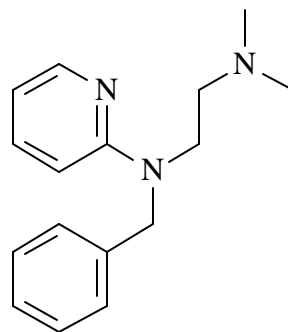
Thenyldiamine  
(8.9, 3.9)



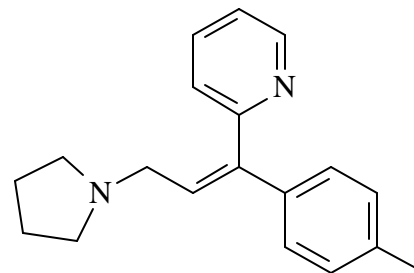
Ppyrilamine  
(4.0, 8.9)



Brompheniramine  
(9.8, 3.6)

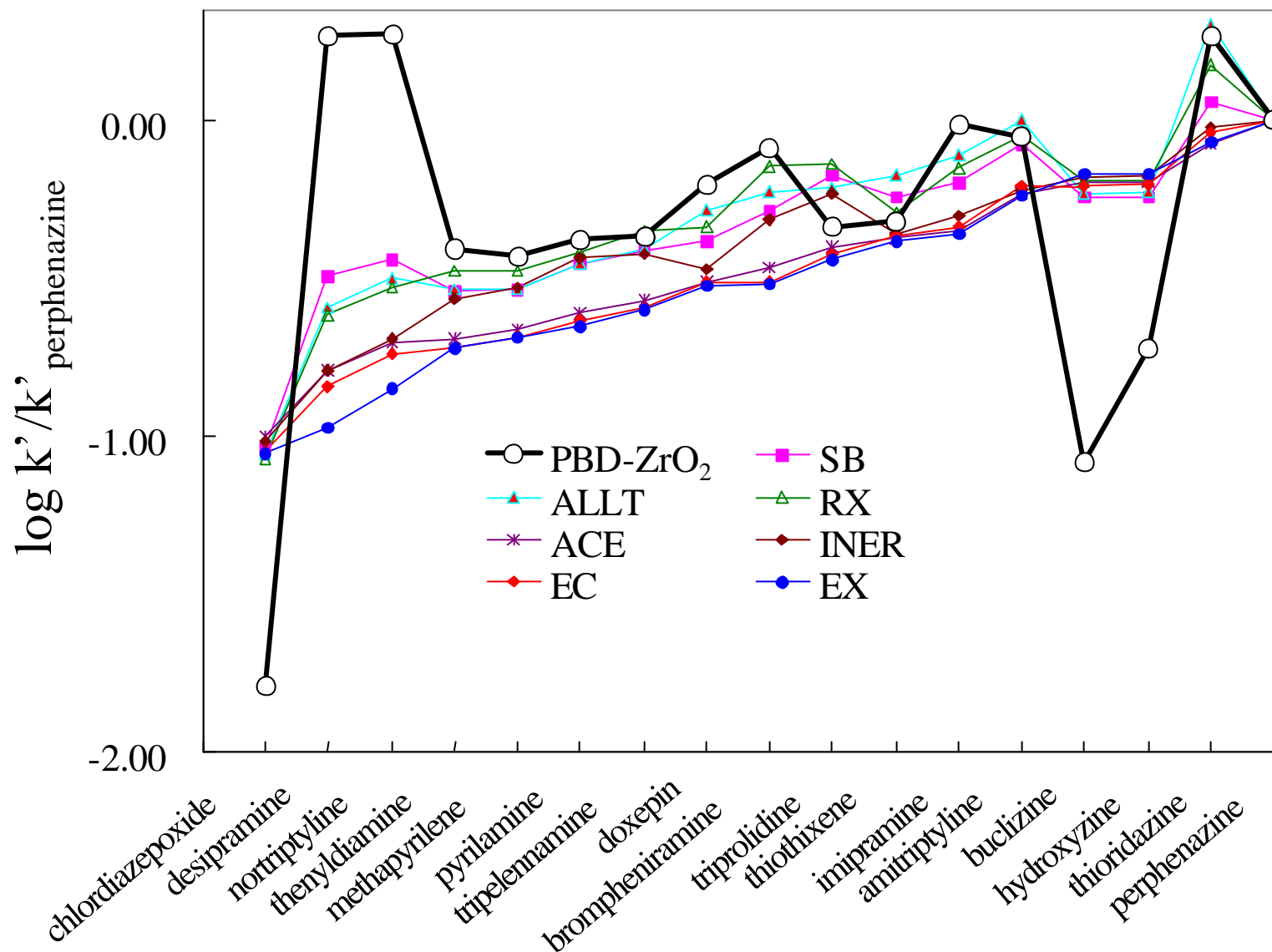


Tripeleennamine  
(4.2, 8.7)



Triprolidine  
(6.6)

# Comparison of Selectivity via Relative Retention



Condition: 72 % MeOH for antidepressants, 60% MeOH for antihistamine, 25 mM phosphate, pH=6.0, 35 °C, 1 mL/min.

✓ PBD-ZrO<sub>2</sub> is very different.

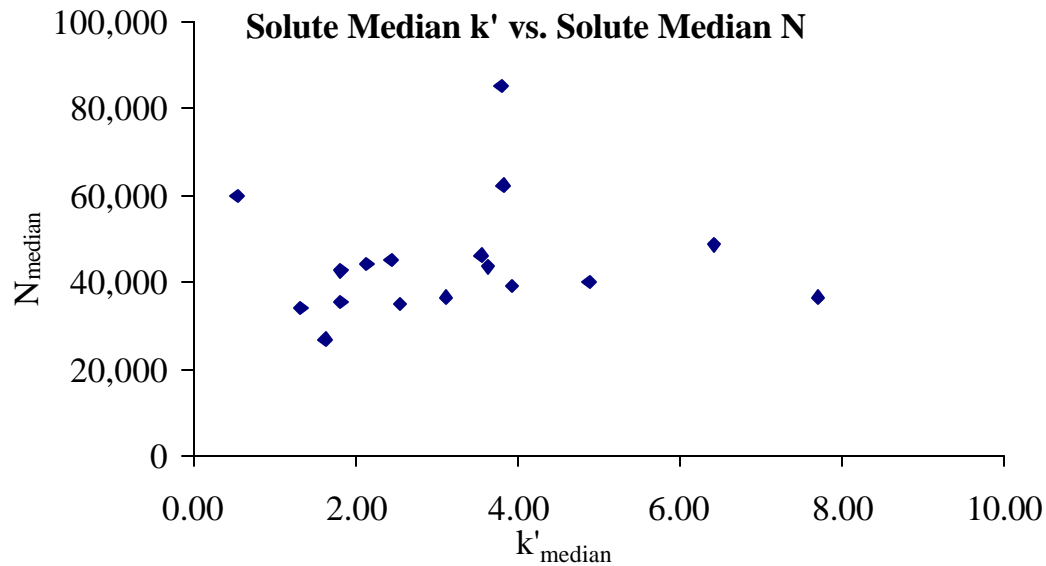
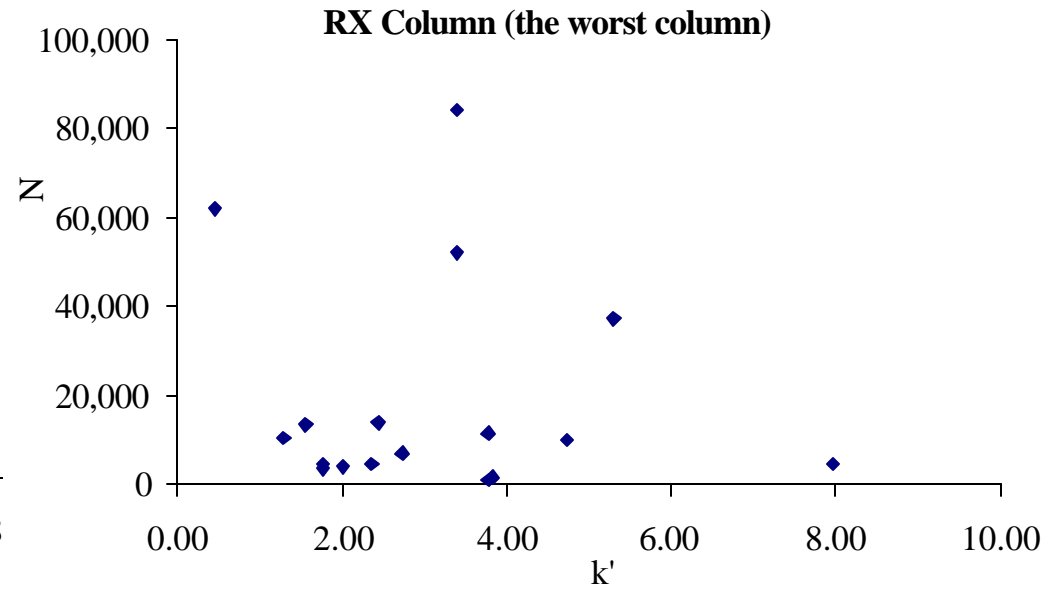
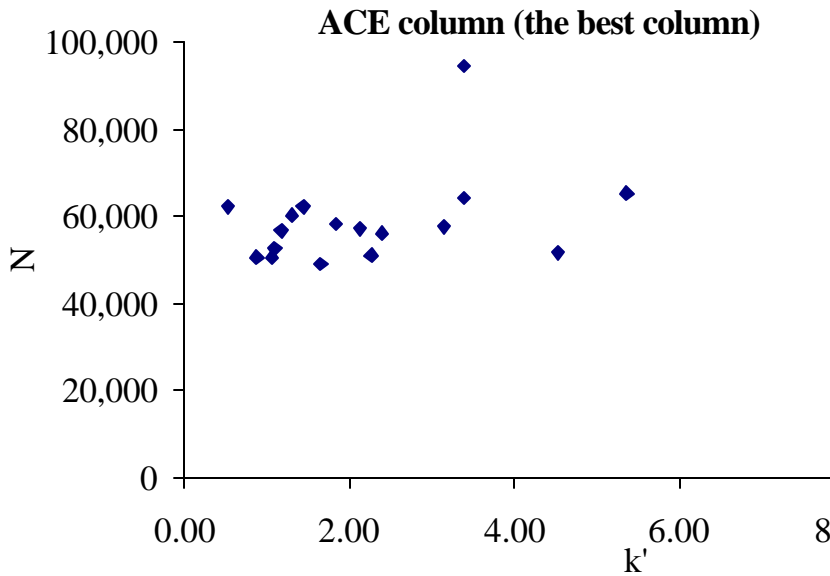
# Comparison of Normalized Plate Count

	Median	Normalized Plate Count, $N/N_{\text{solute median}}$							
Solute	per meter	ACE	EC	INER	EX	SB	ALLT	RX	PBD
	solute median	57,300	56,000	42,400	40,550	33,300	18,900	9,900	51,300
nortriptyline	26,700	1.90	1.67	0.88	0.99	1.01	0.39	0.50	2.12
desipramine	34,050	1.49	1.34	0.72	0.86	1.14	0.38	0.30	1.60
doxepin	34,800	1.41	1.40	1.05	0.95	0.96	0.56	0.40	1.04
thenyldiamine	35,650	1.48	1.45	1.25	0.75	0.59	0.53	0.13	1.58
thiothixene	36,400	1.40	1.40	0.98	1.11	0.93	0.65	0.19	1.02
thioridazine	36,600	1.41	1.49	1.05	0.93	0.95	0.19	0.13	1.29
imipramine	39,000	1.44	1.42	1.01	0.92	0.99	0.46	0.30	1.32
amitriptyline	39,900	1.44	1.39	1.04	0.96	0.70	0.33	0.25	1.29
methapyrilene	42,450	1.33	1.33	1.04	0.77	0.68	0.96	0.08	1.35
triprolidine	43,500	1.32	1.33	0.97	1.03	0.19	0.25	0.03	1.13
pyrilamine	44,350	1.35	1.34	0.97	1.03	0.48	0.40	0.09	1.18
tripelennamine	45,400	1.37	1.35	1.01	0.99	0.43	0.34	0.10	1.24
brompheniramine	46,100	1.26	1.21	0.89	0.94	0.13	1.15	0.02	1.06
perphenazine	48,750	1.33	1.29	0.95	1.05	1.07	0.81	0.77	0.31
chlordiazepoxide	59,750	1.04	1.14	0.81	0.95	1.07	0.96	1.04	0.66
hydroxyzine	62,450	1.03	0.97	1.12	0.82	1.38	1.36	0.84	0.70
buclizine	85,400	1.11	1.10	0.85	1.01	1.04	0.93	0.99	0.67

**N** below  $N_{\text{solute median}}$  (median for that solute on 8 columns); **best N** for that solute.

✓ No **universal** trend in plate count among the columns involved in the present study is observed. Column performance is very **solute dependent**.

# Retention Factor vs. Plate Count



✓ **Very little** relationship between  $k'$  and  $N$

# Conclusions

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- ✓ Basic analytes generally undergo **RP/IEX mixed-mode retention mechanism** on PBD-ZrO<sub>2</sub> and ODS phases
- ✓ Basic solute separations are both **condition** and **solute** dependent. **Column ranking** based on one or two probes is not reliable.
- ✓ **Dramatically different selectivity** on PBD-ZrO<sub>2</sub> and ODS phases
- ✓ No **universal** trend in plate count among the studied columns is observed. Column performance is very **solute dependent**

# Acknowledgments

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National Institutes of Health  
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