Prediction of Chromatographic Selectivity, Retention Times, and Peak Widths for New Capillary Stationary Phases and Columns

Frank L. Dorman, Paul D. Schettler, and Chris English

How is GC Learned/Used?

- GC thought of, and often taught as “Separation by boiling point”
- Where mobile and stationary phases “do chemistry” in HPLC, in GC column dimensions and temperature program are typically adjusted
- GC applications are not usually optimized, and separations are compromised to fit existing columns and stationary phases
- Most phases not designed with any application in mind, and common phases are similar in selectivity (-1s & -5s)

Needs for Difficult GC Separations:

- Stationary phase selectivity should be optimized for particular separation, to maximize resolution and minimize run time
- Column dimensions should be matched to analytical requirements (flow, capacity, etc.)
- Current offerings of stationary phases and functionalities are limited
- Selection of phase and column, and optimization of separations needs to be easy for end user

General Equation for Resolution:

$$R = 1/4 \sqrt{L / h} \times (k / k+1) \times (\alpha-1 / \alpha)$$

Selectivity Factor (α) – addressed by stationary phase modeling

not commonly done by end user

Capacity Factor (k), and Column Factor – addressed by physical modeling

can be simultaneous with, or independent of stationary phase modeling

Stationary Phase Optimization Techniques

- Empirical Modeling:
  - Window diagramming approach
  - Computer simulation of phase selectivity, independent of column dimensions (ezGC™)
  - Computer prediction of optimized stationary phase composition and column dimensions, with specific resolution factors (times and peak widths)
- Molecular Modeling:
  - Computer prediction of solute/stationary phase interactions for <u>new polymer designs</u>

Stationary Phase Optimization

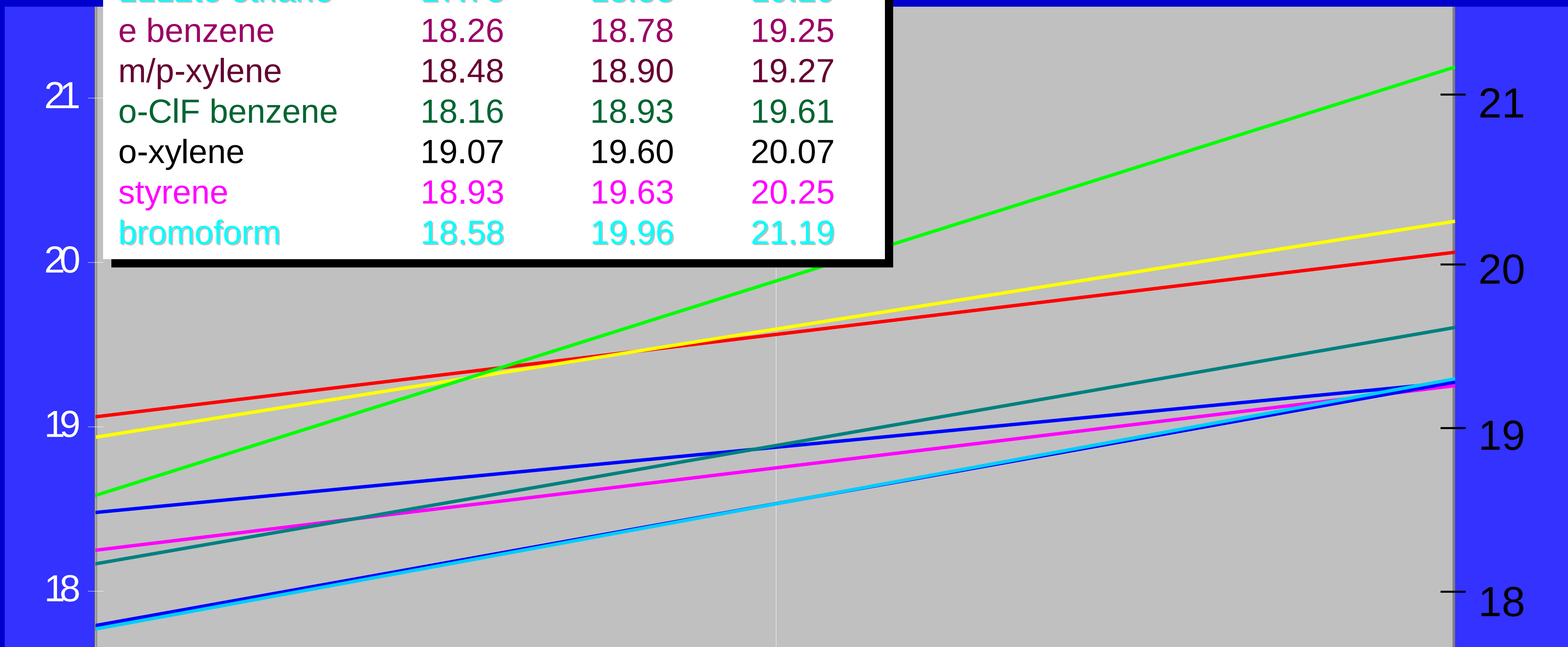
- Window diagramming (Rtx-502.2)
- Computer simulation of selectivity, independent of column dimensions (ezGC™)
  - Rtx®-CLPesticides, Rtx-CLPesticides2
- Computer prediction of optimized stationary phase composition and column dimensions
  - Rtx-TNT, Rtx-TNT2, Rtx-VMS, Rtx-VGC, Rtx-5SilMS, Rtx-VRX
- Computer prediction of solute/stationary phase interactions for new polymer designs

Window Diagrams

- Maier and Karpathy ('60s):
  - Demonstrated that mixing phases together could yield unique selectivity for packed column applications
- Laub and Purnell ('70s)
  - Mixed phase packed column applications
- Jennings et al ('80s)
  - Packed column applications, and capillary work based on lengths of dissimilar columns
  - DB™-1301 developed using DB™-1 and DB™-1701

Window Diagramming

	Rtx®-1	Rtx®-502	Rtx®-35
chlorobenzene	17.79	18.57	19.27
1112te ethane	17.78	18.58	19.29
e benzene	18.26	18.78	19.25
m/p-xylene	18.48	18.90	19.27
o-ClF benzene	18.16	18.93	19.61
o-xylene	19.07	19.60	20.07
styrene	18.93	19.63	20.25
bromoform	18.58	19.96	21.19



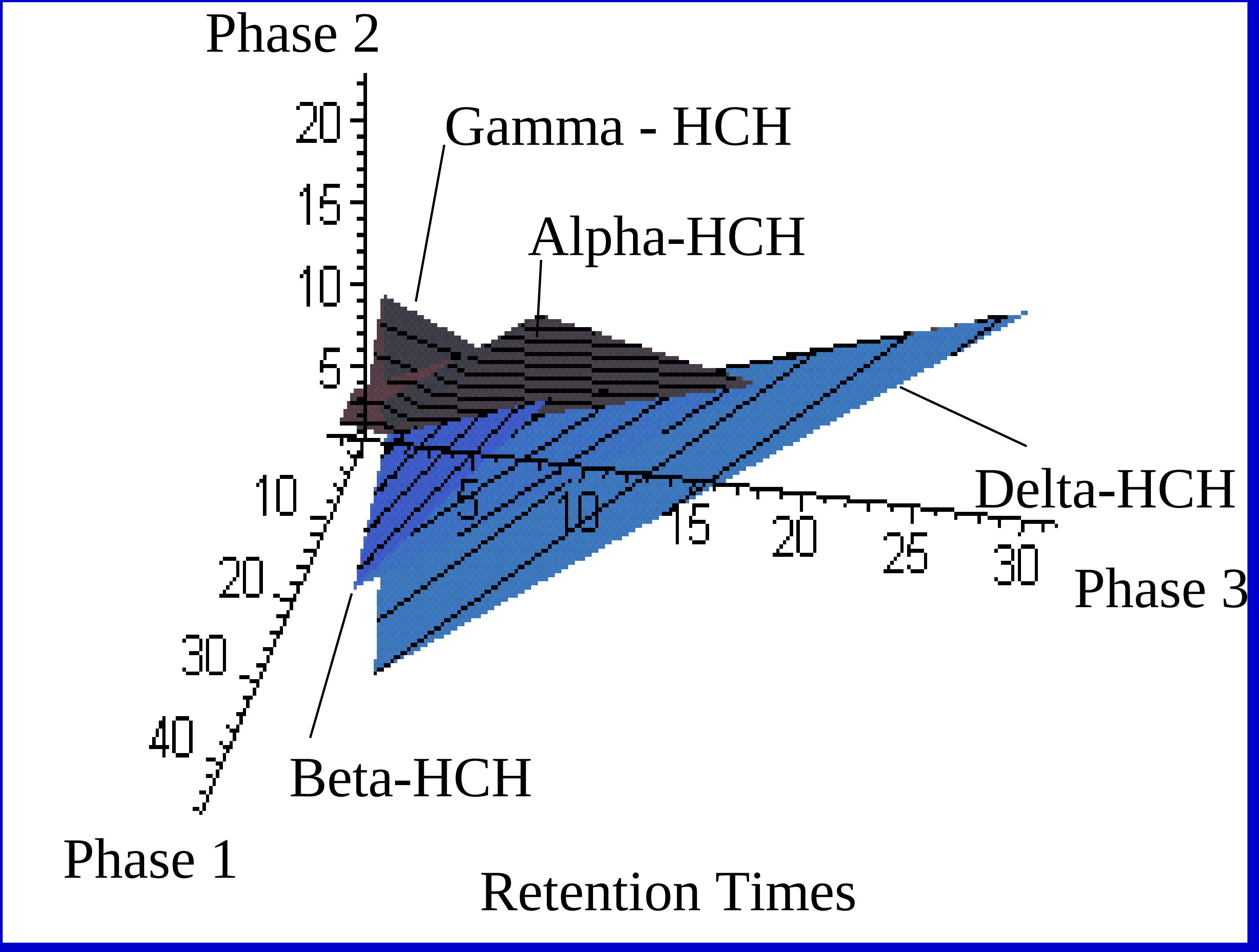
Stationary Phase Optimization

- Window diagramming
- Computer simulation of phase selectivity, independent of column dimensions (ezGC™)
  - Rtx®-CLPesticides, Rtx-CLPesticides2
- Computer prediction of optimized stationary phase composition and column dimensions
  - Rtx®-CLPesticides, Rtx-CLPesticides2, Rtx-TNT Rtx-TNT2, Rtx-VMS, Rtx-VGC, Rtx-5SilMS, Rtx-VRX
- Computer prediction of solute/stationary phase interactions for new polymer designs

Computer simulation of phase selectivity, independent of column dimensions (ezGC™)

- “Fix” Run Conditions
- Input data is normalized for column and program parameters
- Search for optimum solution by varying the stationary phase composition
- Program tracks up to 8 dimensions of phase functionalities
- No solution requires separate re-optimization of input data

3-Space Selectivity Surface for 4 Pesticide Compounds



Rtx®-CLPesticides Column Benefits

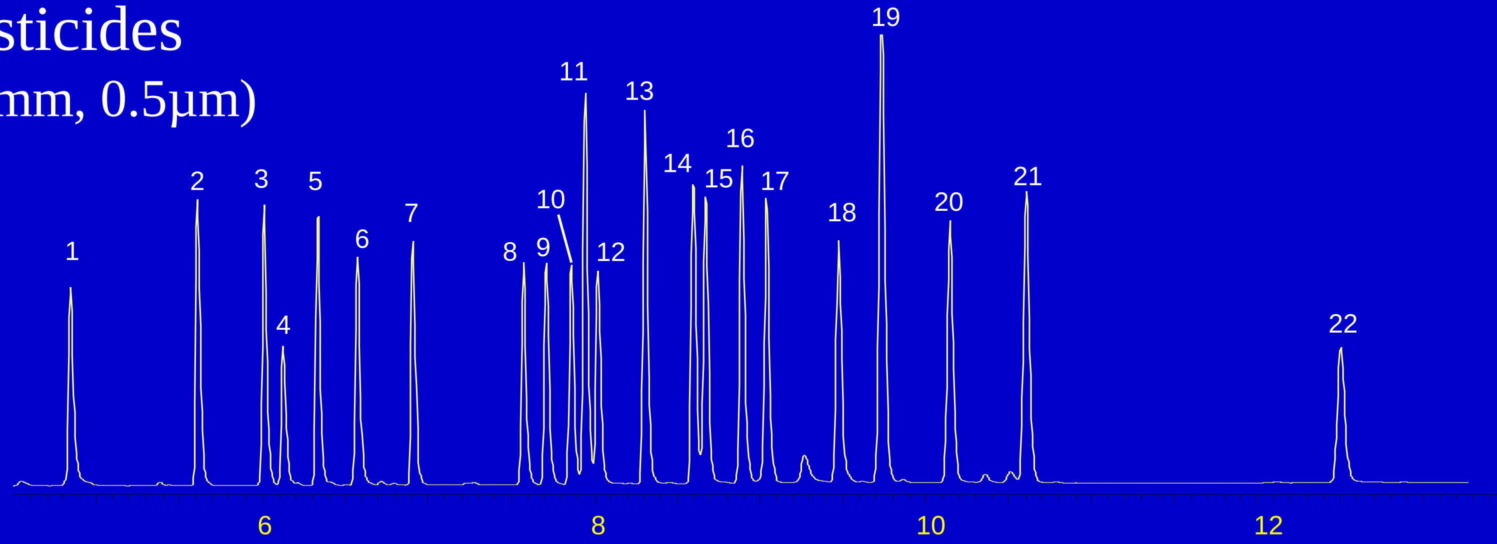
- Baseline resolution of all 22 compounds
- < 25 minute analysis time
- Available in all common dimensions
  - 0.18, 0.25, 0.32 and 0.53mm ODs
- Very low electron capture detector (ECD) bleed levels
- High thermal stability
  - 330°C maximum temperature

Confirmation Column?

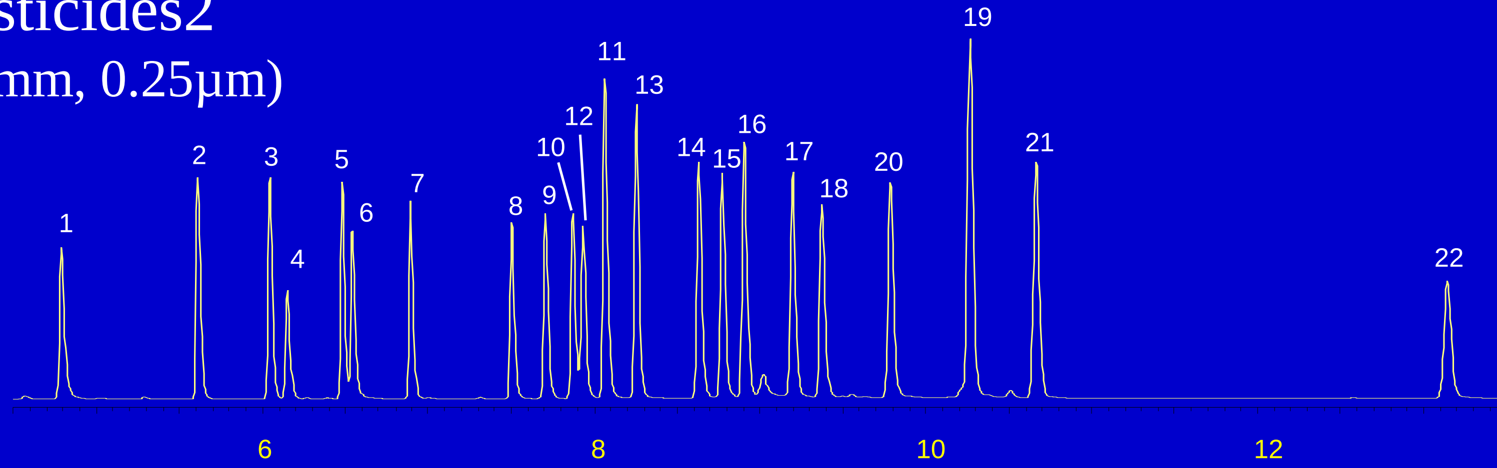
- Requirements
  - Same analysis conditions as primary column
  - Different elution order
  - Baseline resolution desirable
  - High thermal stability and inertness
  - Similar analysis times
- Rtx®-CLPesticides2 column meets requirements

Chlorinated Pesticides
Fast Runs

Rtx-CLPesticides
(30m x 0.32mm, 0.5µm)



Rtx-CLPesticides2
(30m x 0.32mm, 0.25µm)



Chlorinated Pesticides

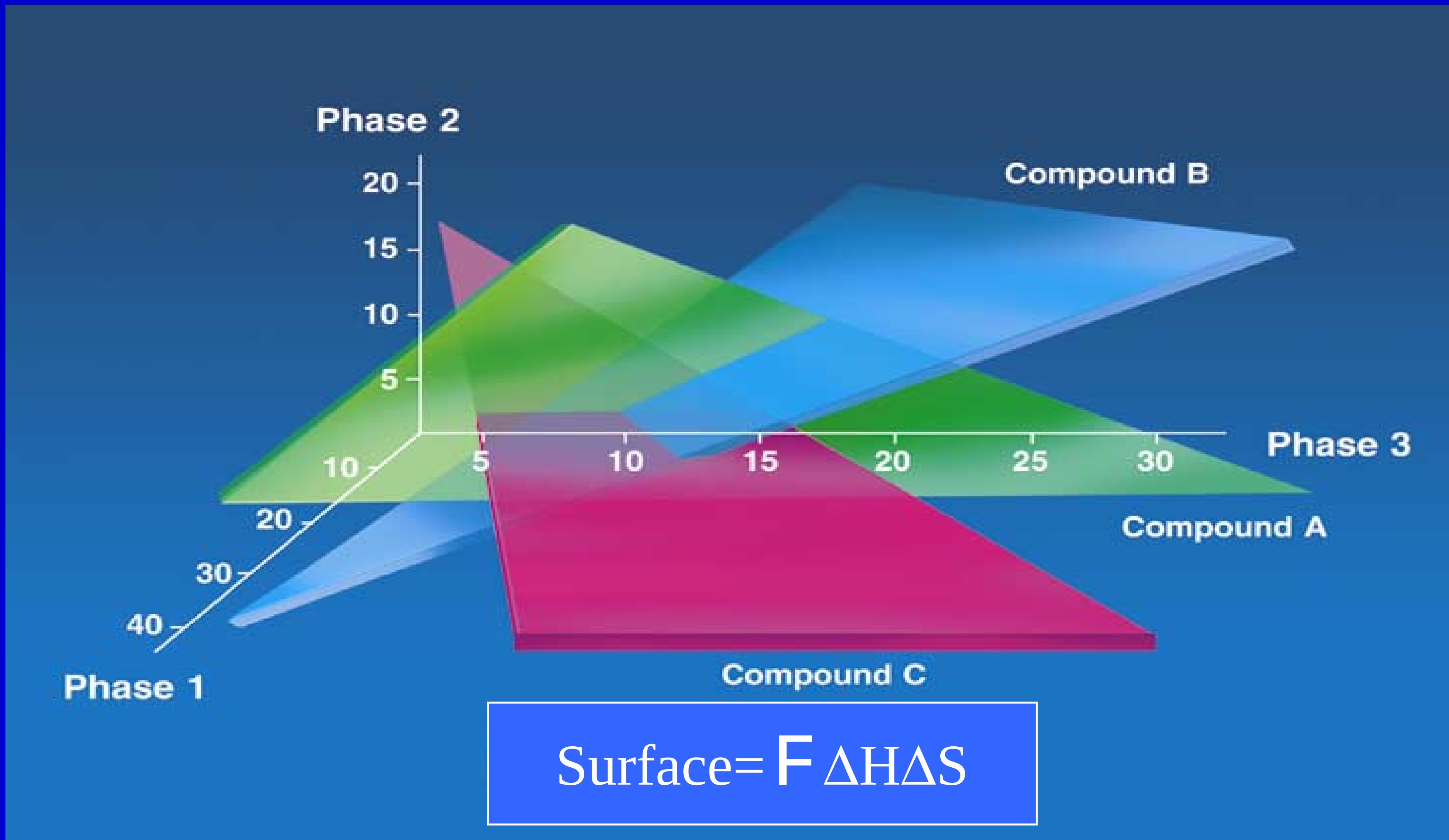
1 2,4,5,6-tetrachloro-m-xylene
2 alpha BHC
3 gamma BHC
4 beta BHC
5 delta BHC
6 heptachlor
7 aldrin
8 heptachlor epoxide
9 gamma chlordane
10 alpha chlordane
11 4,4'-DDE

12 endosulfan I
13 dieldrin
14 endrin
15 4,4'-DDD
16 endosulfan II
17 4,4'-DDT
18 endrin aldehyde
19 methoxychlor
20 endosulfan sulfate
21 endrin ketone
22 decachlorobiphenyl

Stationary Phase Optimization

- Window diagramming
- Computer simulation of phase selectivity, independent of column dimensions (ezGC™)
- Rtx®-CLPesticides, Rtx-CLPesticides2
- Computer prediction of optimized stationary phase composition **AND** column dimensions
  - Rtx-TNT Rtx-TNT2, Rtx-VMS, Rtx-VGC, Rtx-5SilMS, Rtx-VRX, Rtx-OPPesticides2, Customer-specific columns
- Computer prediction of solute/stationary phase interactions for new polymer designs

3-Space Selectivity Model for 3 Compounds



Surface= $F\,\Delta H \Delta S$

Explosives Analysis by HRGC

- HRGC more common than HPLC
- Selective detection using ECD
- Direct flash injection of ACN extract
- Simultaneous dual column analysis

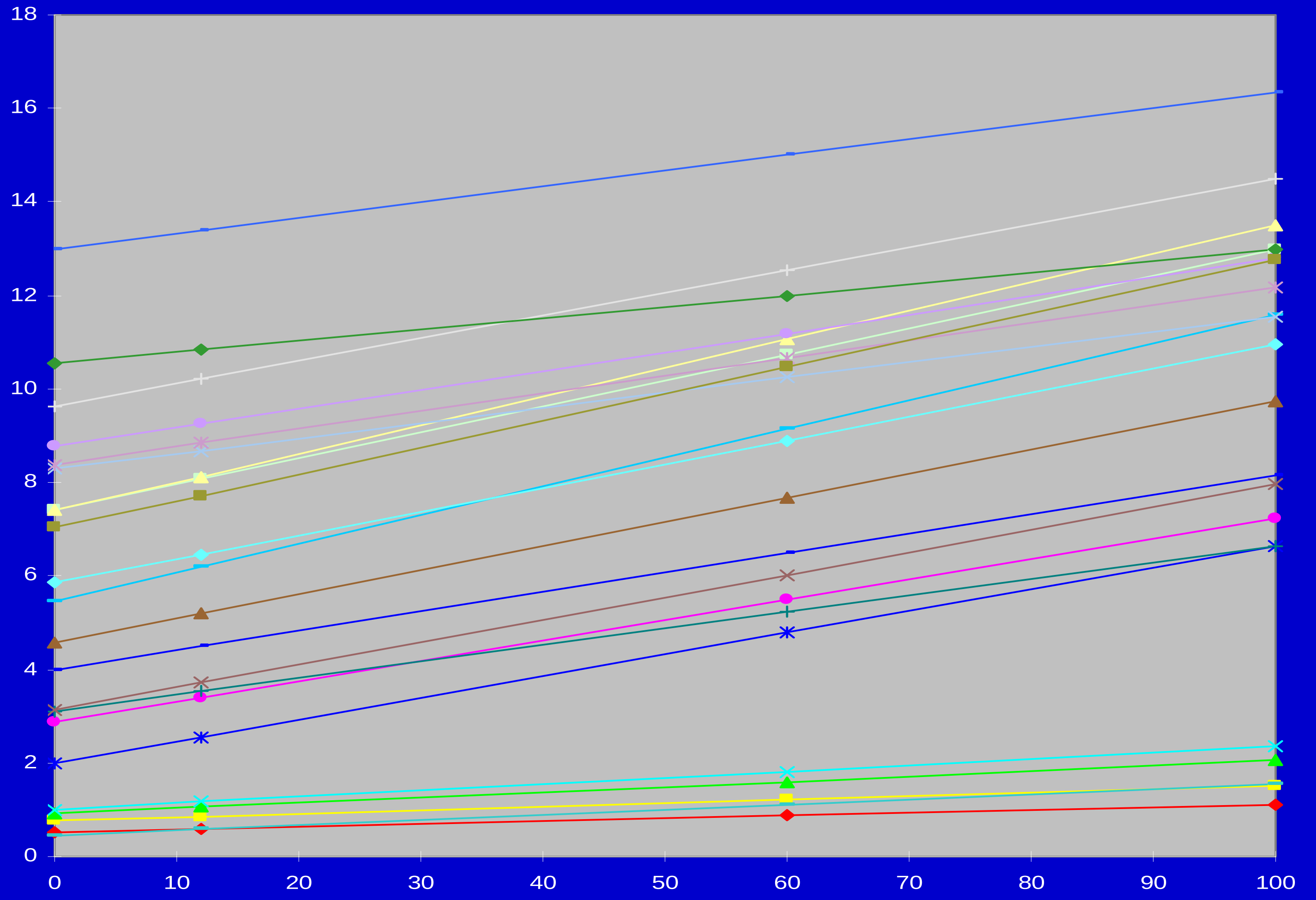
Explosives Target List EPA 8095

1 EGDN
2 nitrobenzene
3 2-nitrotoluene
4 3-nitrotoluene
5 4-nitrotoluene
6 nitroglycerine coelutes with 2,6-dinitrotoluene on Rtx-200
7 1,3-dinitrobenzene
8 2,6-dintrotoluene co-elutes with nitroglycerine on Rtx-200
9 1,2-dinitrobenzene (surrogate)
10 2,4-dinitrotoluene
11 3,4-dinitrotoluene (internal standard)
12 1,3,5-trinitrobenzene
13 trinitrotoluene
14 picric acid
15 PETN co-elutes with RDX on Rtx-1, co-elutes with 2-amino-4,6-dinitrotoluene on Rtx-200
16 RDX co-elutes with PETN on Rtx-1
17 4-amino-2,6-dinitrotoluene co-elutes with 3,5-dinitroaniline on Rtx-5
18 3,5-dinitroaniline co-elutes with 4-amino-2,6-dintrotoluene on Rtx-5
19 2-amino-4,6-dinitrotoluene co-elutes with PETN on Rtx-200
20 tetryl
21 nitroguanidine
22 HMX does not elute as a peak when the run time is longer than 20 minutes

Design Criteria

- Short Column, Wide-bore, Standard d_f , High μ
- Analysis Time < 20 min.
- Low Bleed with ECD
- Baseline Resolution
- Column Inertness

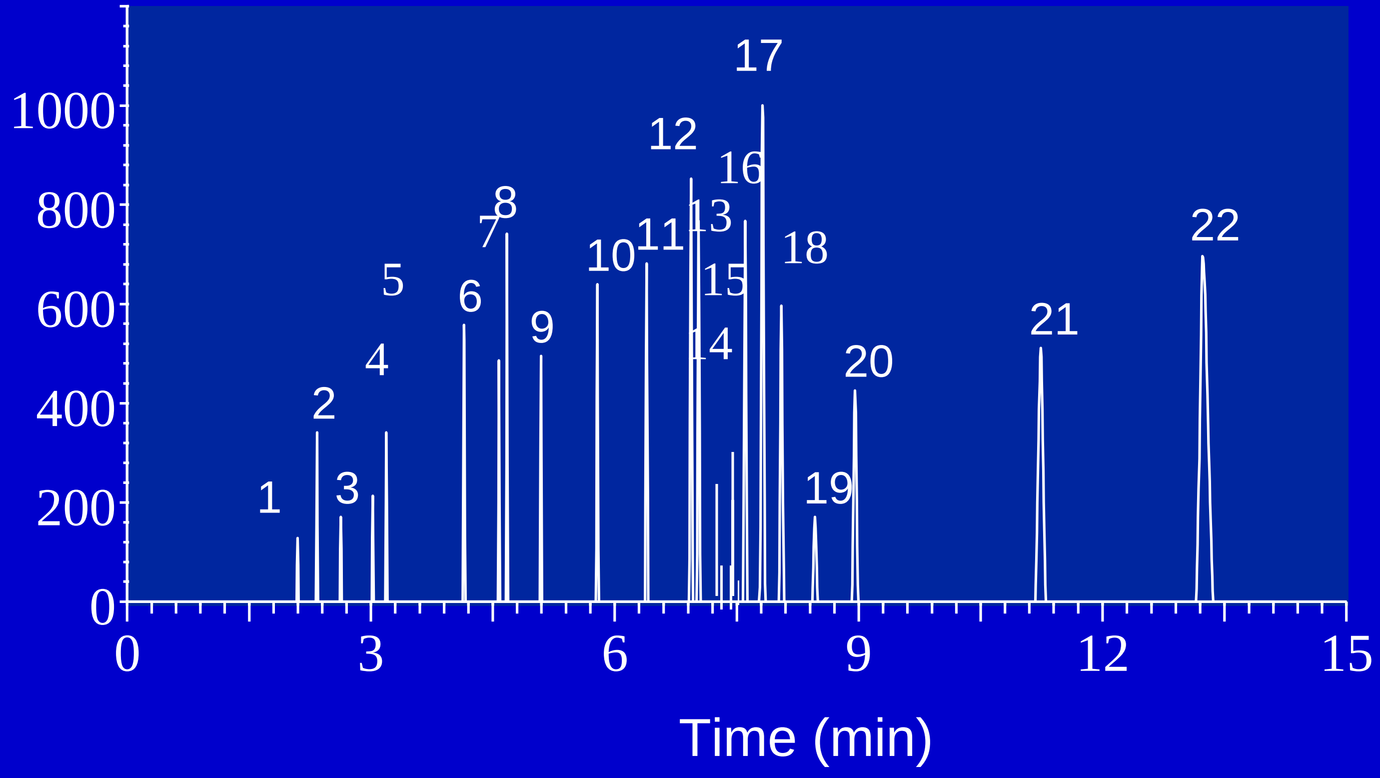
Modeling for Explosives



First Optimization Rtx-TNT

Rtx-TNT1 6 m x 0.53 mm x 1.5 µm Direct Inj 250C ECD 300C He@10mls/min.

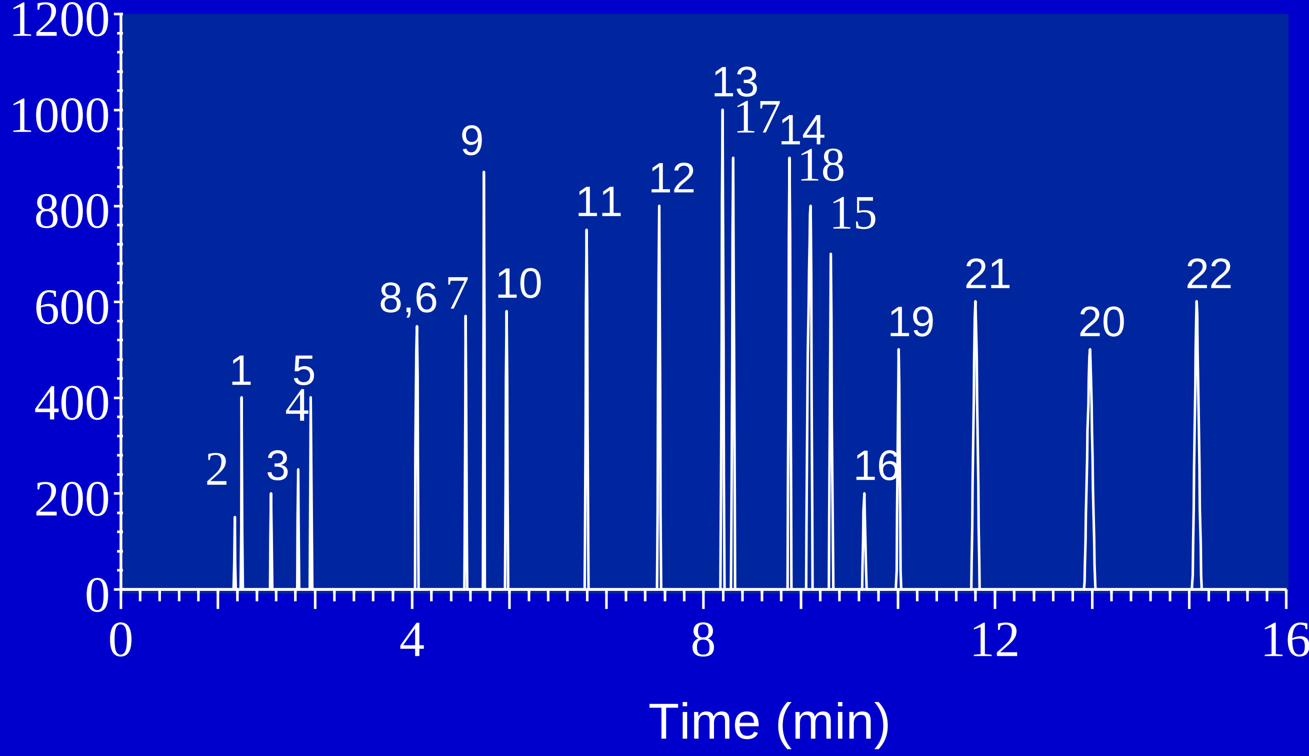
100°C 2min.to 200°C @ 10°C/min to 250°C @ 20°C/min.(10)



Second Optimization Rtx-TNT2

Rtx-TNT2 6 m x 0.53 mm x 1.5 µm Direct Inj 250C ECD 300C He@10mls/min.

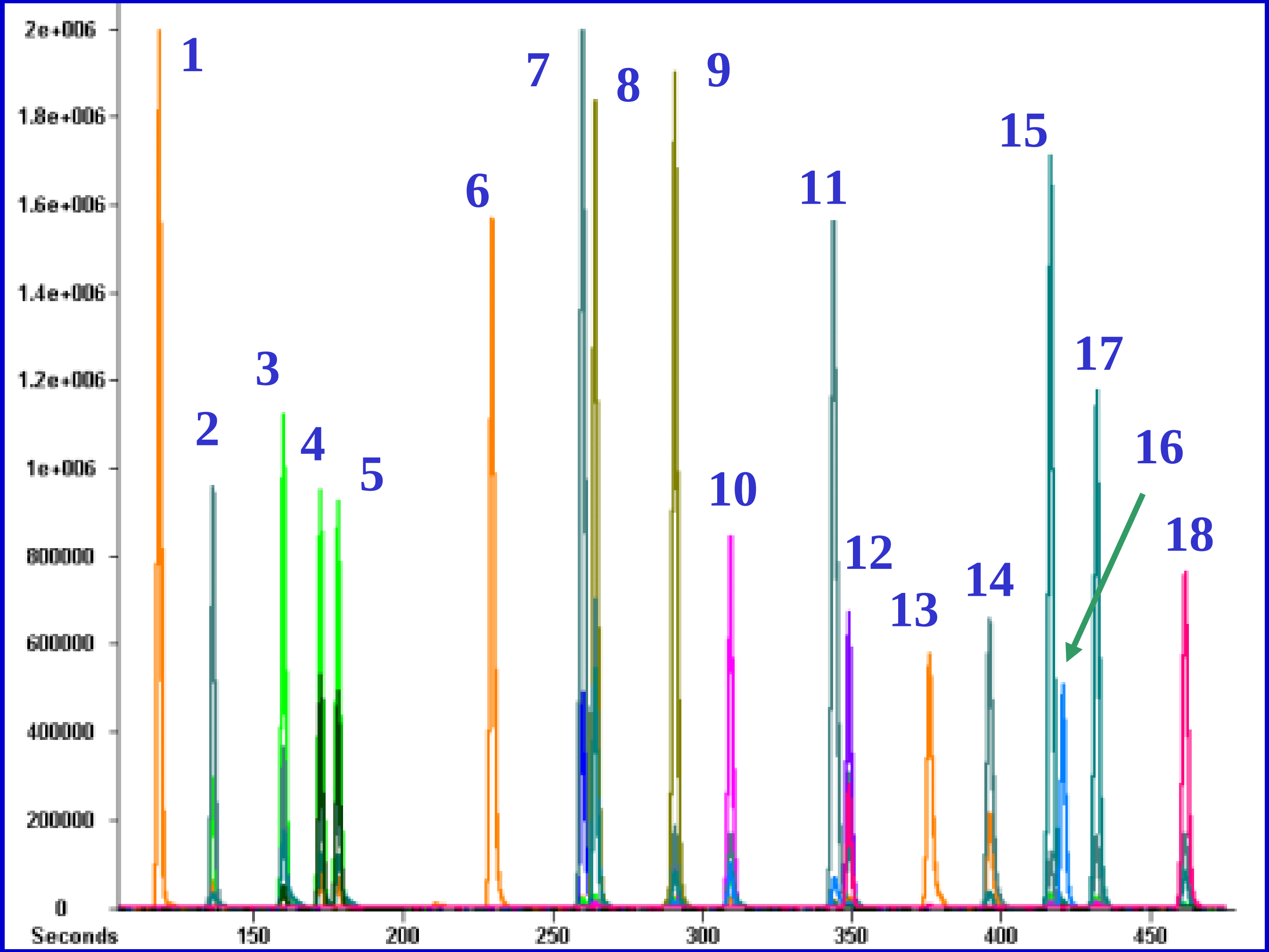
100°C 2 min. to 200° C @ 10°C/min to 250°C @200°C/min. (10)



On-Column Injection Rtx-TNT

1. Ethylene glycol dinitrate
2. Nitrobenzene
3. 2-Nitrotoluene
4. 3-Nitrotoluene
5. 4-Nitrotoluene
6. Nitroglycerin
7. 1,3-Dinitrobenzene
8. 2,6-Dinitrotoluene
9. 2,4-Dinitrotoluene
10. 3,4-Dinitrotoluene
11. 1,3,5-Trinitrobenzene
12. TNT
13. PETN
14. RDX
15. 4-Amino-2,6-dinitrotoluene
16. 3,5-Dinitroaniline
17. 2-Amino-4,6-dinitrotoluene
18. Tetryl

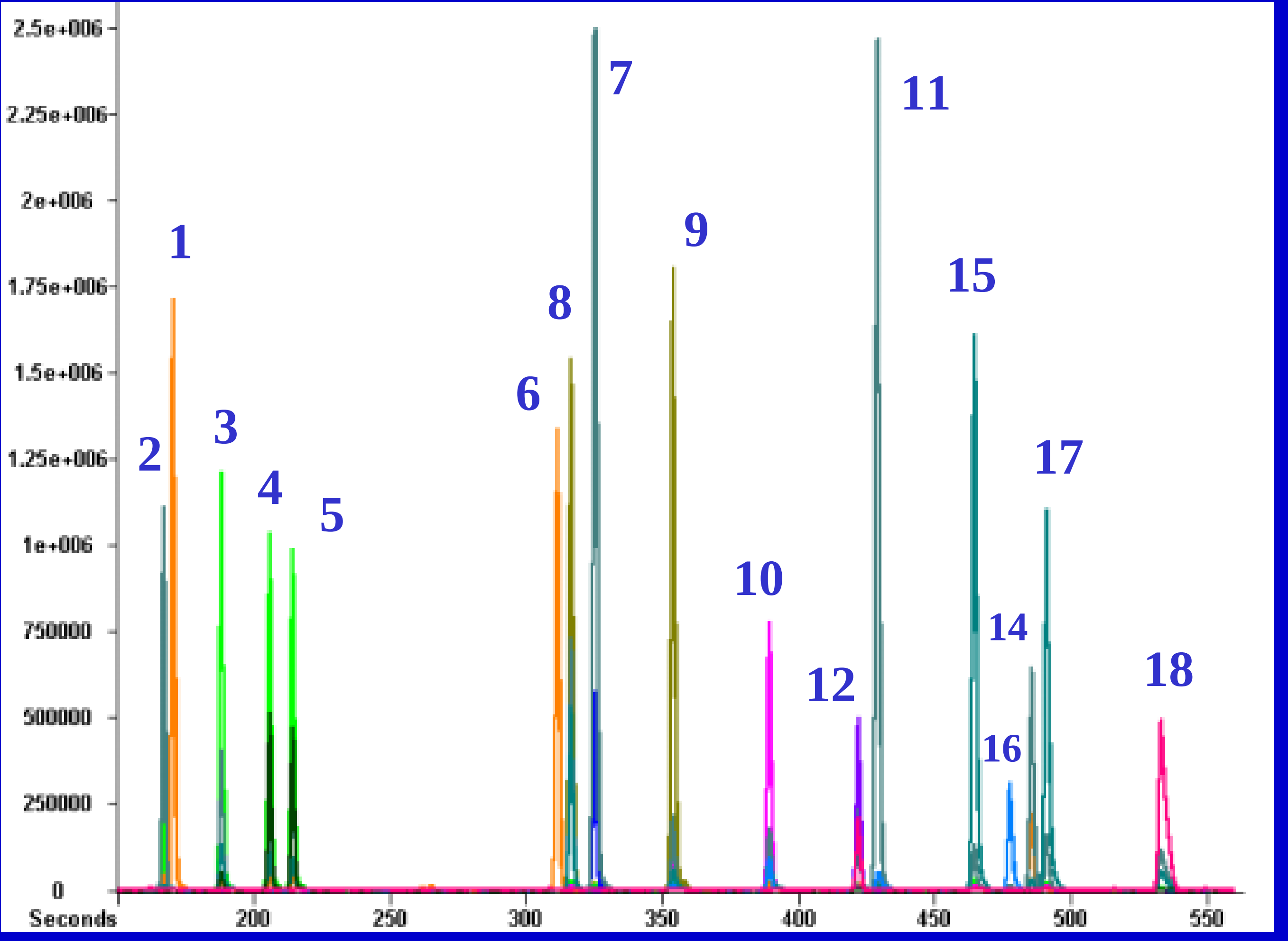
Less than 8 minutes!



On-Column Injection Rtx-TNT2

1. Ethylene glycol dinitrate
2. Nitrobenzene
3. 2-Nitrotoluene
4. 3-Nitrotoluene
5. 4-Nitrotoluene
6. Nitroglycerin
7. 1,3-Dinitrobenzene
8. 2,6-Dinitrotoluene
9. 2,4-Dinitrotoluene
10. 3,4-Dinitrotoluene
11. 1,3,5-Trinitrobenzene
12. TNT
13. PETN
14. RDX
15. 4-Amino-2,6-dinitrotoluene
16. 3,5-Dinitroaniline
17. 2-Amino-4,6-dinitrotoluene
18. Tetryl

9 minutes.



PETN is thermally degraded.

What If No Selective Functionality Can be Found?

- Accept less than ideal separation
  - Effect on quantitation and/or run time
- Use “old method” of trial and error
  - Slow, and inefficient
  - No guarantee that solution will be found
- Test functionalities electronically
  - Unproven technique for GC applicaiton
  - CPU intensive
  - Faster than trial and error

Stationary Phase Optimization

- Window diagramming
- Computer simulation of phase selectivity, independent of column dimensions (ezGC™)
- Computer prediction of optimized stationary phase composition and column dimensions
  - Rtx®-CLPesticides Rtx-CLPesticides2, Rtx-TNT Rtx-TNT2, Rtx-VMS, Rtx-VGC, Rtx-5SilMS, Rtx-VRX
- Computer prediction of solute/stationary phase interactions for new polymer designs

Computer Modeling: 2 Approaches

- Molecular Dynamics Approach:
  - Molecules are treated as harmonic oscillators, and forces of interaction are minimized to determine orientation.
- Quantum Mechanical Approach:
  - Wave functions are calculated, and molecular orbital structure is determined.

- Two techniques are complementary

Achieving Analyte Separation

Resolution

$$R = 1/4 \sqrt{L / h} \times (k / k+1) \times (\alpha\text{-}1 / \alpha)$$

Capacity Factor

$$k = (t_R - t_0) / t_0$$

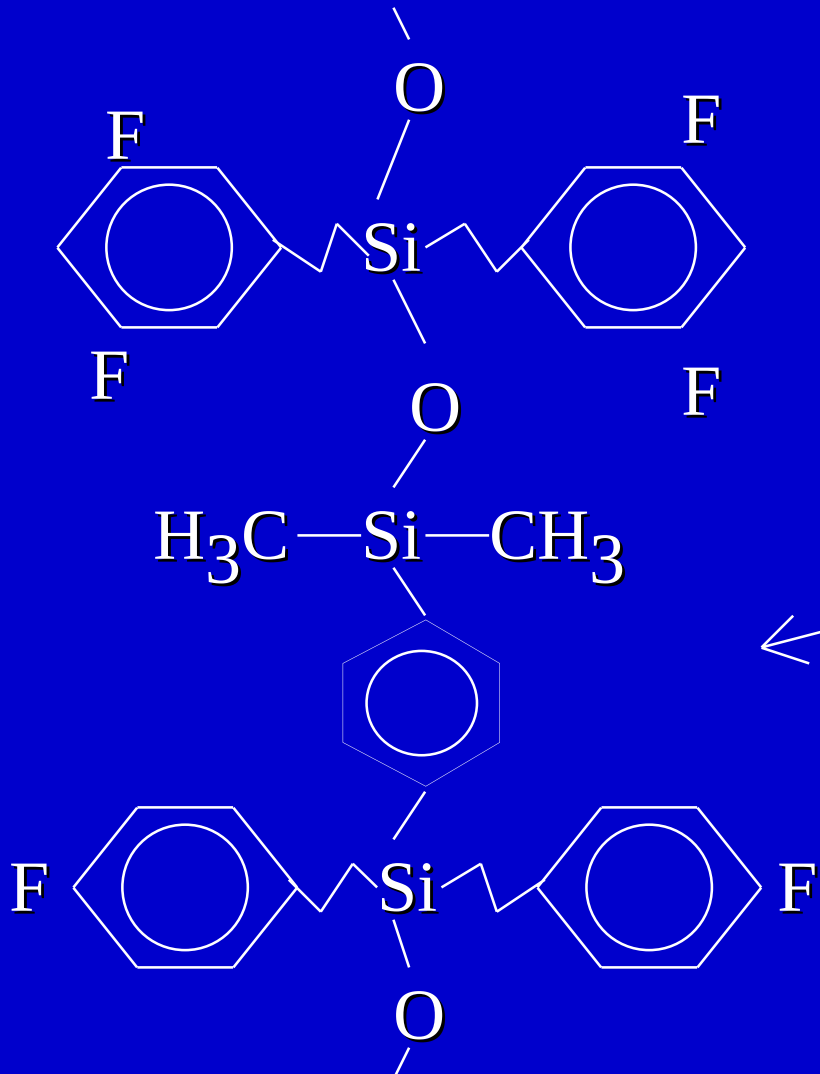
Selectivity

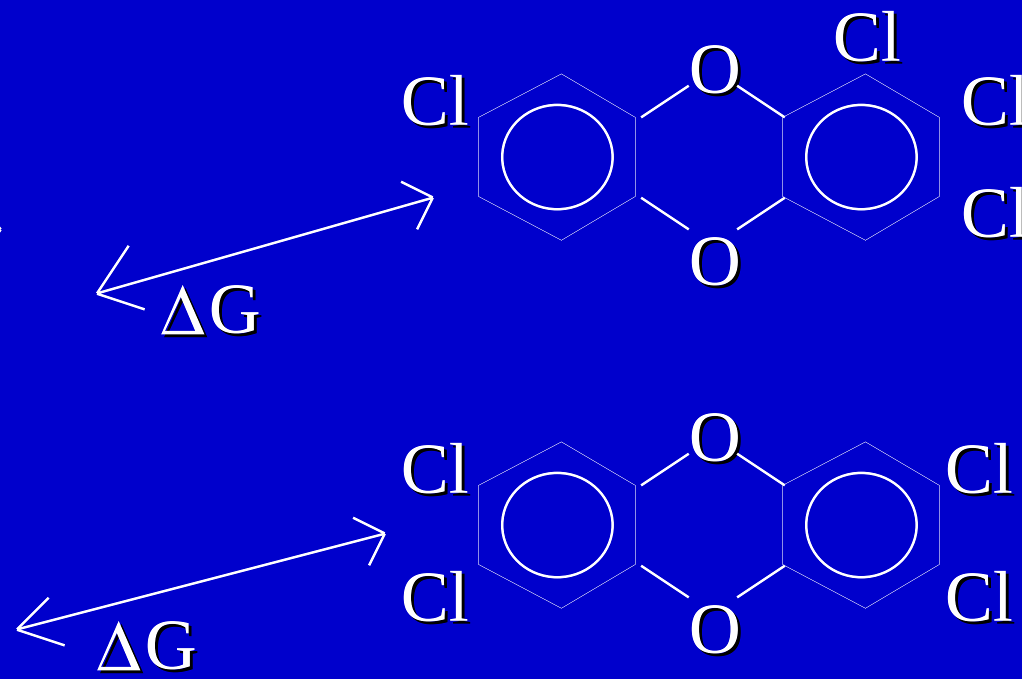
$$\alpha = k_2 / k_1$$

Thermodynamics:

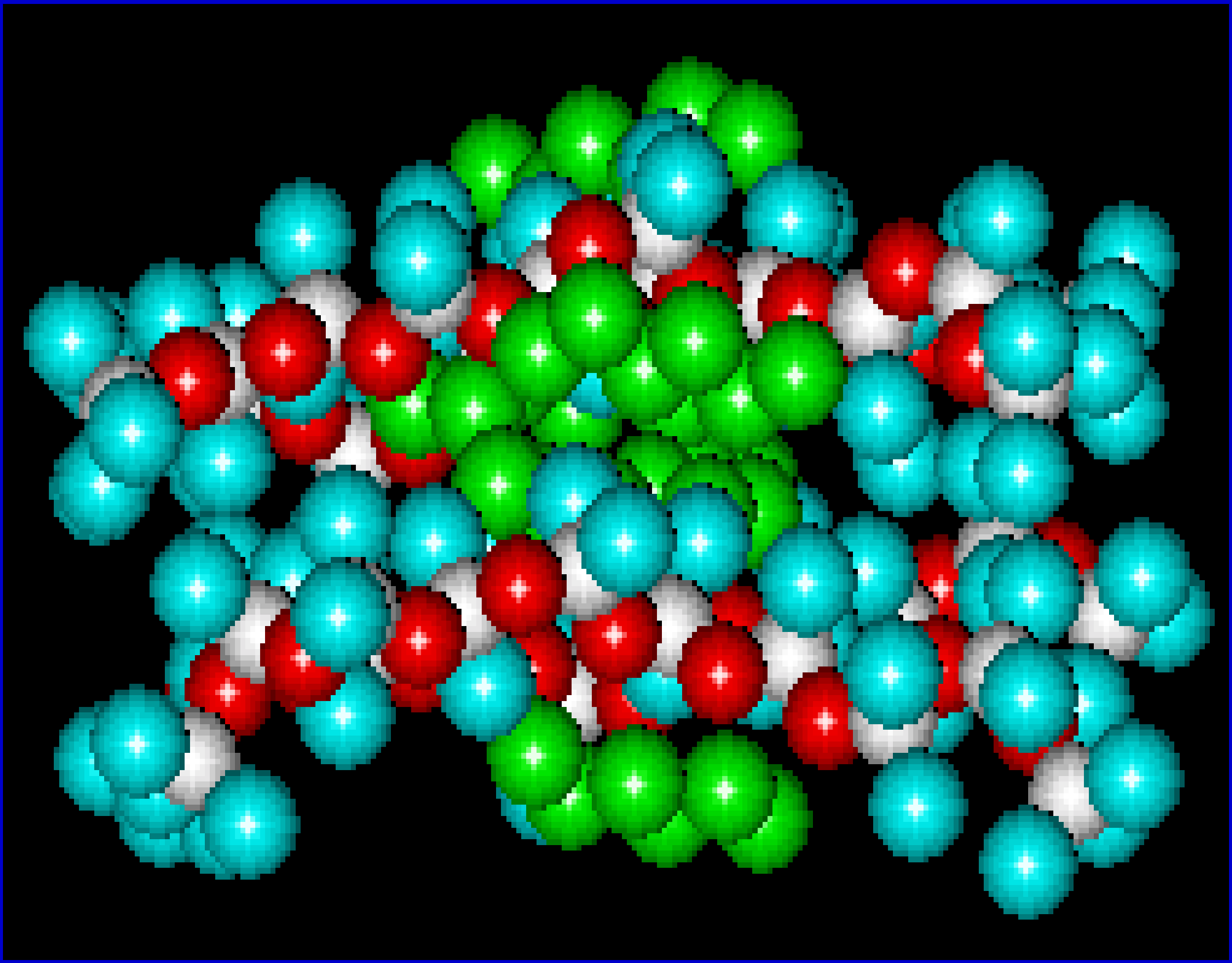
$$\Delta G = \Delta H - T\Delta S \qquad \Delta G = -RT \ln K_D$$

Modeling - Energies of Interaction





Separation $(\Delta\alpha) = \Delta\,\Delta G$



Molecular Modeling Results:

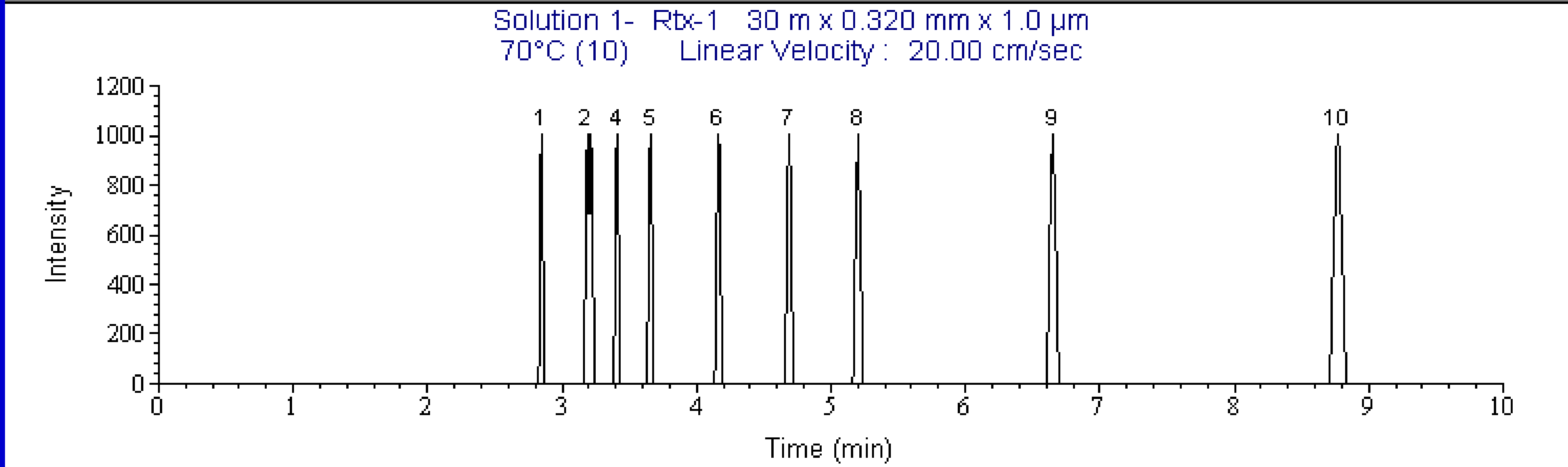
- Initial attempts were not successful
- Evaluated different force fields – AMBER
- Modified calculations based on work of A.Z. Panagiotopoulos

- Demeton-O on PDMS phase:
  - Observed ΔG = -1.14E4 J/mol
  - Calculated ΔG = -1.13E4 J/mol

Physical Parameter Optimization

- Chromatographers need ability to optimize separations to make most efficient possible use of time
  - Aids column choice
  - Excellent teaching tool
  - Allows for run-time and separation optimization for common compounds, or specific user compounds

Solution 1 - 8 out of 10 components resolved >= 4.06



Solution 1 - Tabular

#	Component Name	tR (min)	Width (min)	Rs
1.	acetone	2.843	0.0417	8.10
2.	1-propanol	3.183	0.0466	0.65*
3.	pentane	3.214	0.0471	0.65*
4.	methylethylketone (MEK)	3.407	0.0499	4.06
5.	hexane	3.654	0.0535	4.93
6.	1-butanol	4.162	0.0610	8.57
7.	3-pentanone	4.688	0.0687	7.36
8.	heptane	5.197	0.0761	7.36
9.	1-pentanol	6.650	0.0974	18.94
10.	octane	8.770	0.128	21.60

* < Minimum Resolution

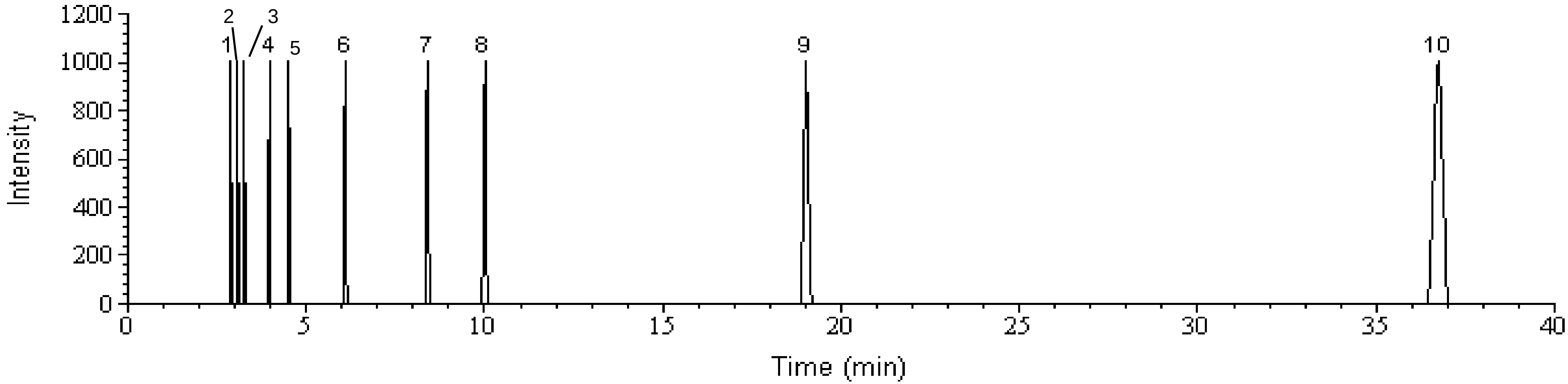
Pro ezGC for Windows

File Solutions Experimental Indices Calculator View Window Help

Solution 1 - 10 out of 10 components resolved >= 4.00

Solution 1- StabilWax 30 m x 0.320 mm x 1.0 µm

70°C (41) Linear Velocity : 20.00 cm/sec



Solution 1 - Tabular

#	Component Name	tR (min)	Width (min)	Rs
l.	hexane	2.882	0.0422	4.48
2.	pentane	3.072	0.0450	4.00
3.	heptane	3.254	0.0477	4.00
4.	octane	3.960	0.0580	9.10
5.	acetone	4.492	0.0658	9.10
6.	methylethylketone	6.079	0.0890	23.94
7.	3-pentanone	8.386	0.123	12.95
8.	1-propanol	9.988	0.146	12.95
9.	1-butanol	19.011	0.278	61.23
0.	1-pentanol	36.737	0.538	63.20

Start Inbox - Microsoft Outlook Pro ezGC for Windows 9:26 AM

What about my compounds?

- User libraries are easy to create
  - Compounds analyzed using two different temperature programs
  - Must measure dead times for column
  - Input directly or via spreadsheet
- Two runs necessary to determine optimum set of physical parameters for compound list

For the Routine User:

- Pro EZ-GC is relatively simple to operate
- Allows rapid selection of optimal program
  - Flow rates, carrier types and temperatures
- Transportable from PC to PC
- Low cost
- Can aid in column choice for common analyses
- Excellent teaching tool

Summary

- Stationary Phase Modeling:
  - Allowed for 10 new commercially-available phases over last three years
  - Individual customer columns can be cost effective
  - Most important factor for resolution is choosing a highly selective stationary phase
- Physical Modeling:
  - Pro ezGC reintroduced for operation under current operating systems. Low cost, and allows for physical optimization.