

Chromatography Past, Present and Future

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Chemical and Pharmaceutical
Solutions

Overview

- Past
- Present
- Future

Past

History of Chromatography



History of Chromatography

- 1903: Russian Botanist Mikhail Tswett coins the term “Chromatography”-Color Writing
- Column Adsorption Chromatography
 - Separation of pigments by different adsorption

History of Chromatography

- Tswett's methods were not readily accepted and one of his greatest opponents was Dr. Willstatter (1915 Nobel Prize winner for analyzing Chlorophyll and other plant pigments)
- Methods different but the results were the same.

History of Chromatography

- 1922: L.S. Palmer used Tswett's techniques on various natural products
- 1931: Richard Kuhn (student of Dr. Willstatter) used this method to separate isomers of polyene pigments

History of Chromatography

- Dr. Heinrich Wieland (Nobel Laureate)
 - “Up to now, we have learned with much effort to distill, crystallize, and recrystallize, and now they come along and just pour the stuff through a little tube.”

History of Chromatography

- Liquid-Liquid Partition Chromatography
 - Archer John Porter and Richard Laurence Millington Synge-1941 create Liquid-Liquid Partition Chromatography one of the most significant tools linking analytical chemistry to life sciences
 - Separate various amino acids

History of Chromatography

- Paper Chromatography
 - Archer Porter Martin (1952 Nobel Prize) created Paper Chromatography in 1944
- Gas Chromatography
 - Fritz Cremer separated Oxygen and Carbon Dioxide in 1947
- Gas-Liquid Partition chromatography
 - Martin and colleagues develop Gas-Liquid to separate natural products

History of Chromatography

- Thin Layer Chromatography
 - 1938-N.A. Izmailov and M.S. Shraiber developed drop chromatography on horizontal plates
 - 1945-Meinhard and N.F. Hall separate terpenes
 - 1950-Justus Kirchner perfected the method using silicic acid with starch binder was applied to glass plates

History of Chromatography

- High Pressure Chromatography
 - 1966-Dr Horvath (Yale) coined the name
 - 1970-popularity grows with the development of silanized silica packing material which allowed for smaller volumes and longer columns

History of Chromatography

- Ion Exchange Chromatography
 - 1850-Thompson and Way treated various clays with ammonium sulfate or carbonate to generate ammonia and release calcium
 - 1927-first zeolite mineral column was used to remove interfering calcium and magnesium ions from a solution used to measure sulfate concentration in water
 - 1970-H. Small and co-workers at Dow used to determine low concentrations of ions (used for environmental and water quality studies)

History of Chromatography

- Affinity Chromatography
 - 1930-used to study enzymes and other proteins
 - 1948 Arne Wilhelm Tiselius Nobel Prize develop many gel types for specific biochemical adsorption

History of Chromatography

- Simulated Moving Bed
- Super Critical Fluid Chromatography

Present

Current Situation



History of Chromatography

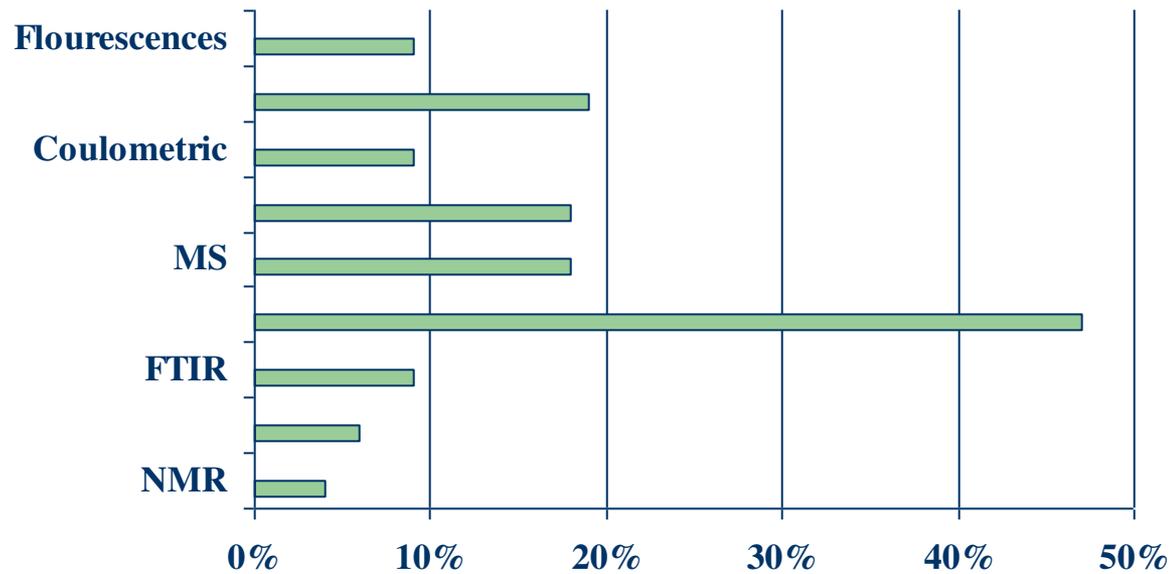
- Market Size
 - LC-\$3billion
 - GC-700million
 - 45% for Chemical/Petrochemical
 - 25% Environmental
 - 15% Food and Beverage

Market Size

- 2003-Market for material characterization instruments was placed at \$21.8billion
 - 59% for instruments
 - Chromatography was the fast growing segment
 - Estimate growth per year is placed at 12.9%

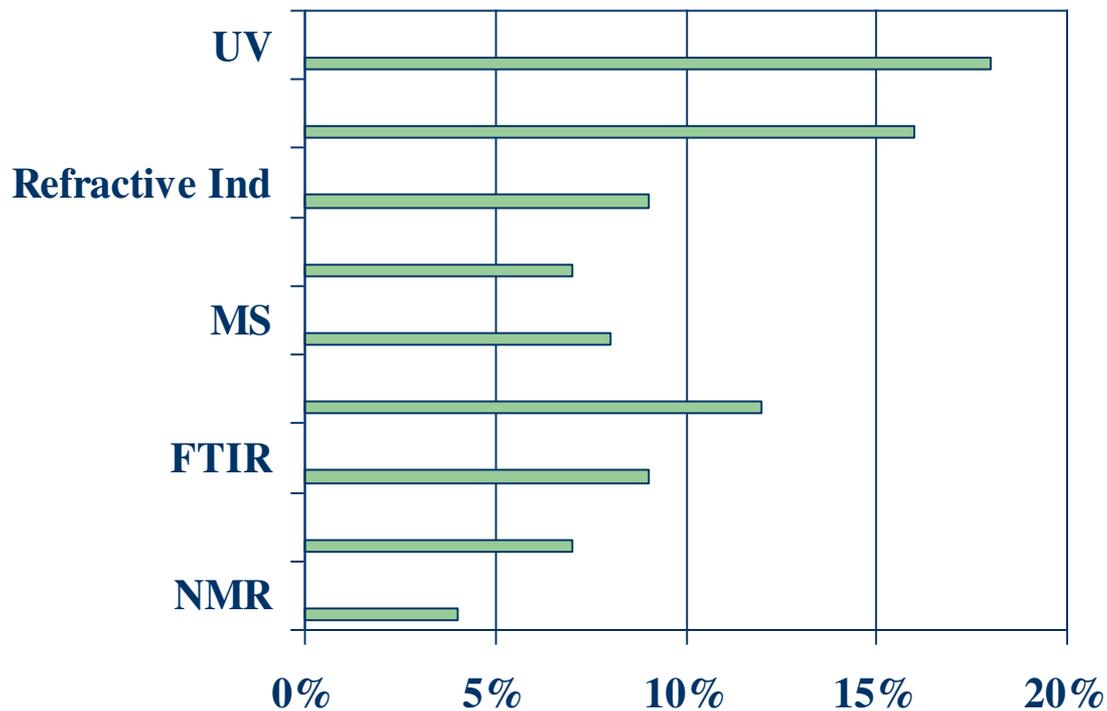
Future

Detectors/Separator Today



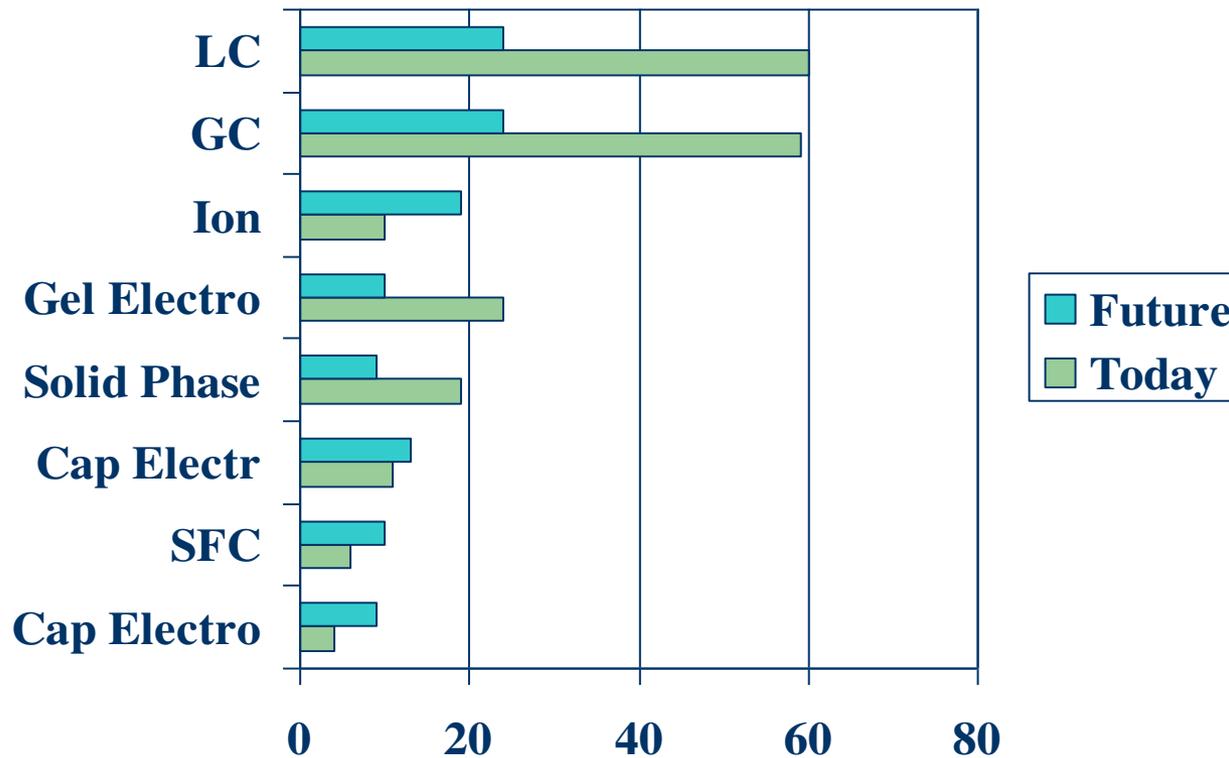
Future

Detector/Separator

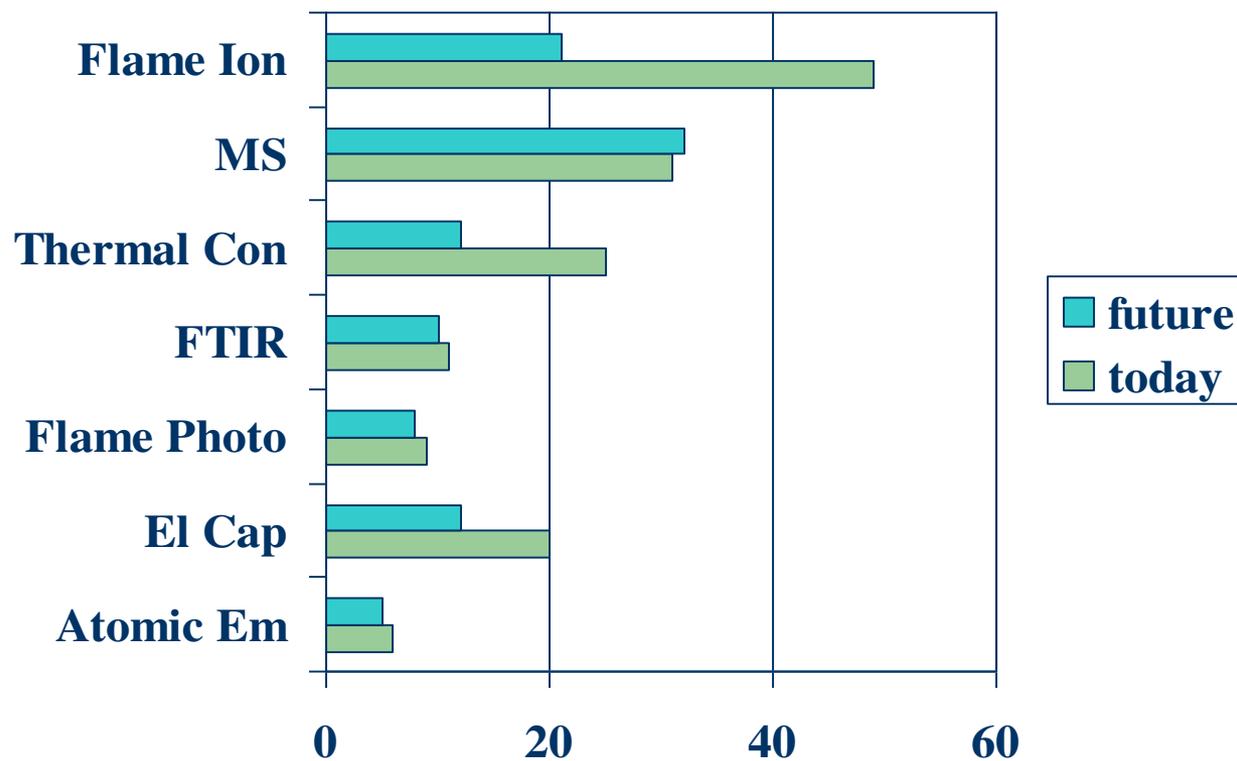


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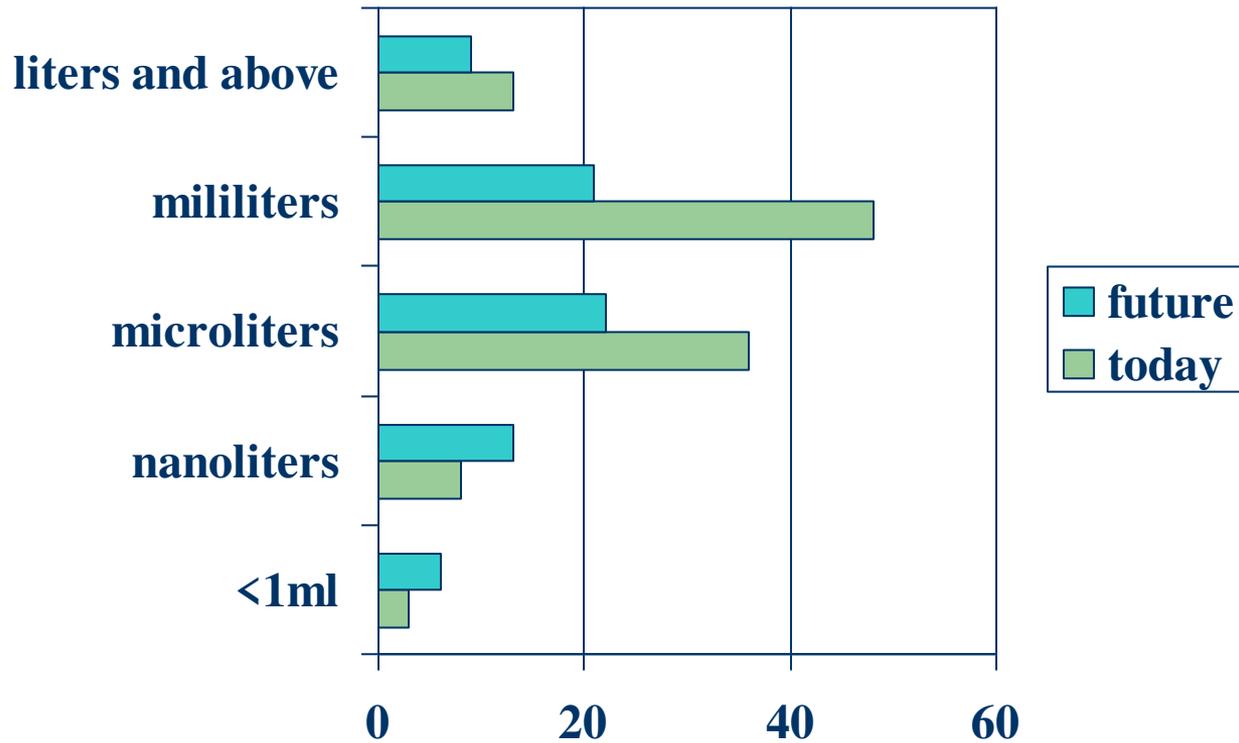
Technologies



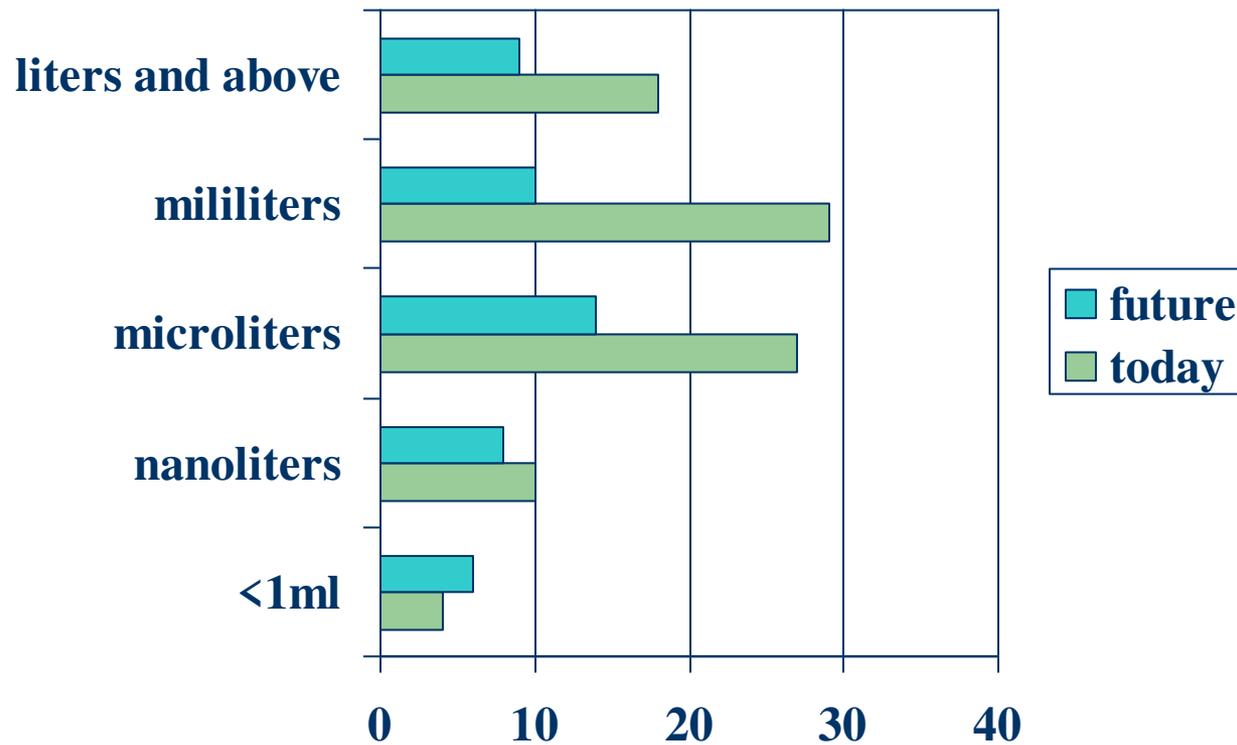
Detectors



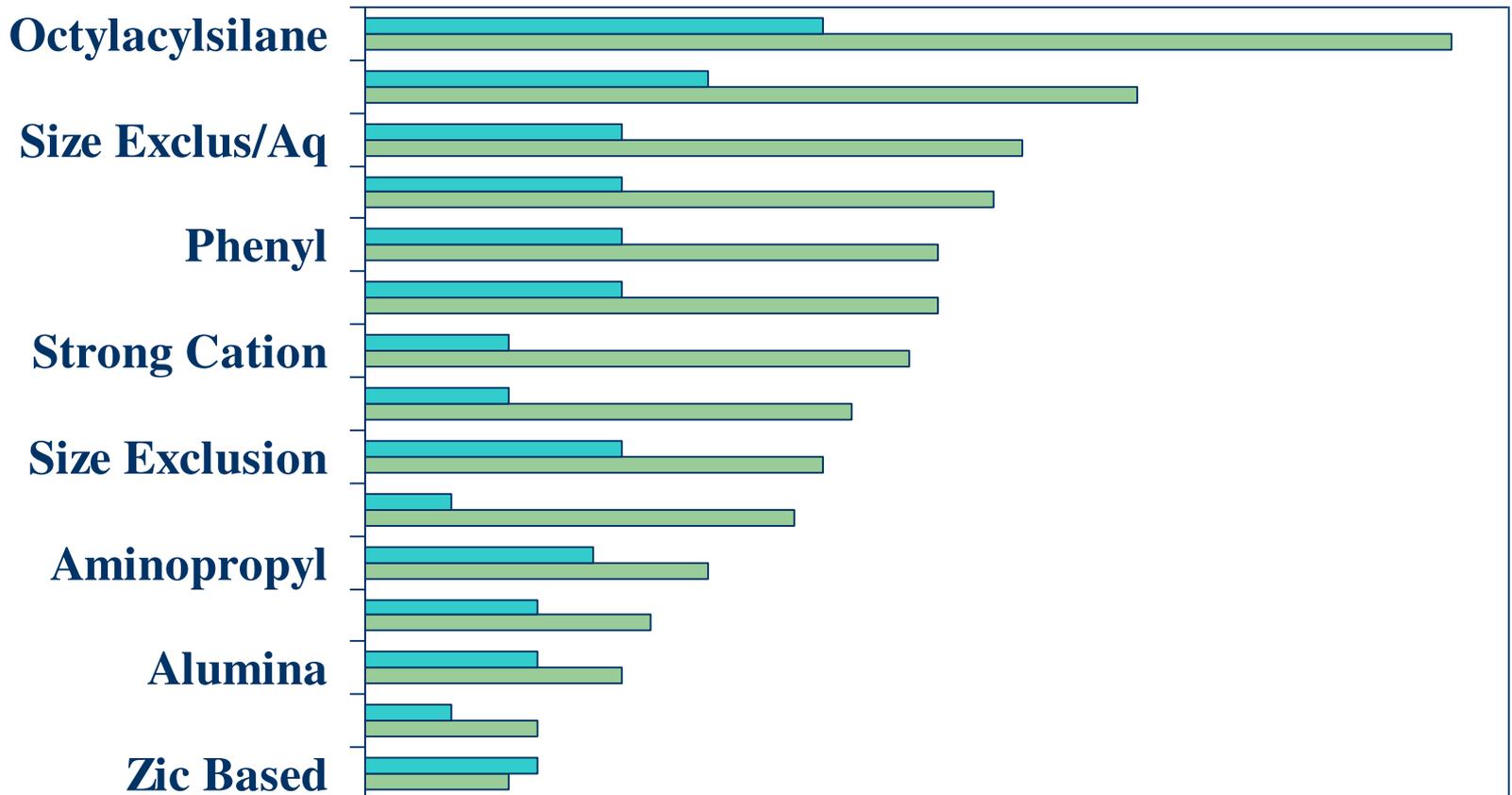
Sample Size/LC



Sample Size/GC

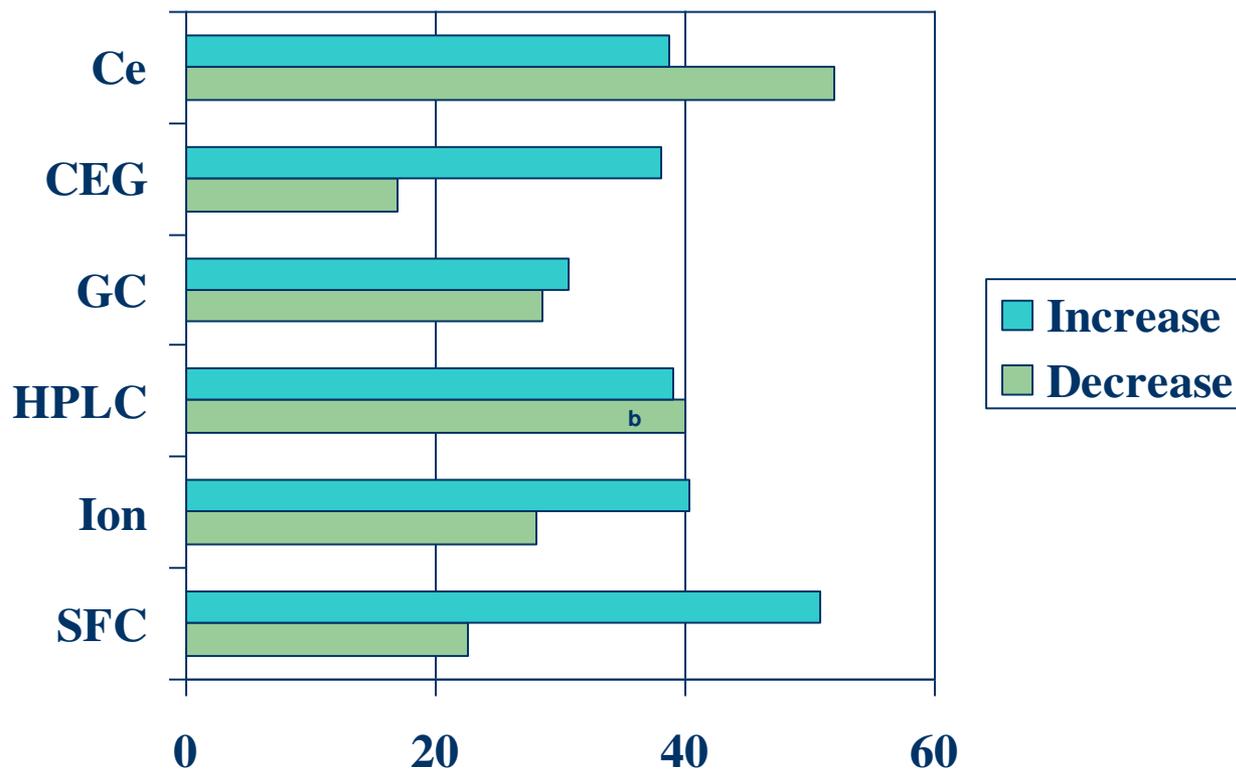


LC Stationary Phase



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Changes in chromatography used over the next 10 years



FUTURE

Next Generation



Future

- Equipment
- In the Unit
- Around the Unit

Future

- Equipment
 - Expect limited improvements
 - No major advances in technology

Future

- Drivers
 - Nanoflow Injection Schemes and improved hyphenated detection techniques
 - NMR/MS/NMR
 - Detectors

Future

- HPLC
 - Syringe Pumps
 - Fast-fill pumps
 - Teflon seal using motor driven cams
 - Diaphragm pumps using a movable membrane

Future

- GC
 - Column Improvements
 - Temperature control
 - Better Injection and Computational analysis techniques
 - Multidimensional hyphenated and tandem techniques
 - IR and NMR

Future

- GC cont.,
 - Improvements in Heating GC columns are improving analysis time (minutes to seconds)

Future

- TLC
 - Recent work in the area of separating enantiomers through the use of specialized cyclodextrin coatings

SMB

- 1950's: SMB begins with UOP
- 1997: First Chiral application run at UCB on a production scale
- 2001: the first FDA inspection of an SMB unit for an API

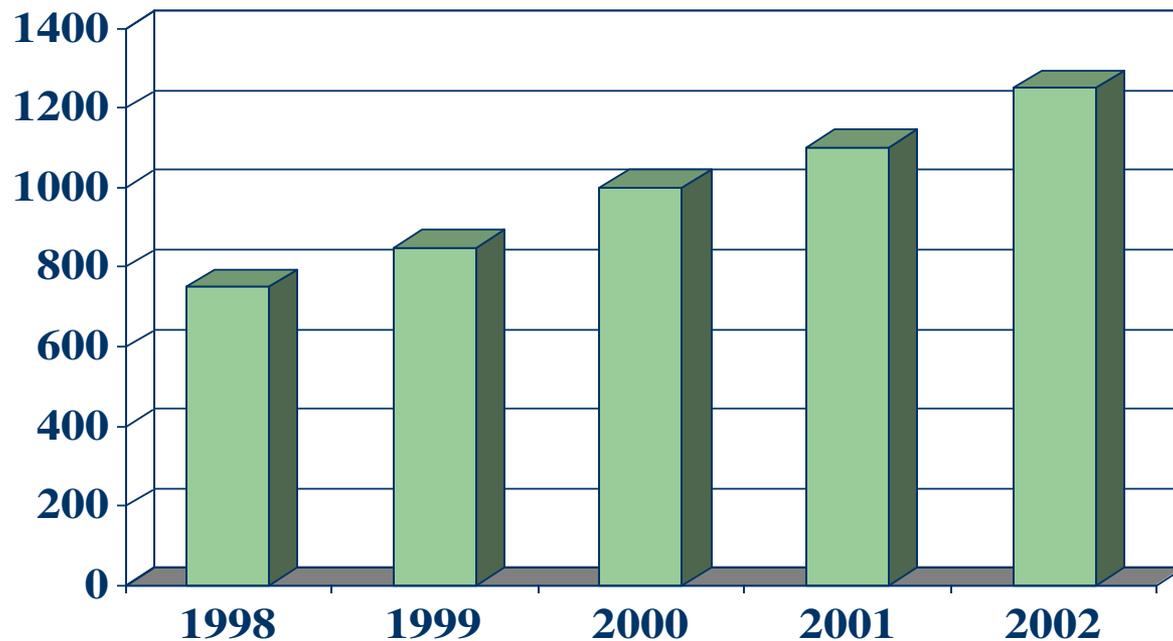
SMB

- 1990's other invest including Aerojet, Lundbeck, Carbogen and Bayer
- 2003: Aldrich invests in plant in Buchs
- 2006: Aerojet expects to commission their 100 cm unit.

HPLC

- 2001: Roche takes delivery of 80 cm column in Boulder, CO
- 2002: Novasep build the largest unit
- 2002: Novasep installs the first commercial unit in India

Prep and Process Scale Chromatography Demand (\$US Millions)



Market Growth

- 2003-approaching \$1.4 billion
- Double Digit growth

In the Equipment

CPS

Feedstock



Chiral Stationary Phases

- Silica Based
 - Polysaccharide Derived CSP
 - Amylose-helix
 - Cellulose-linear
- Resins
- New Products in the future

Packing Material

- High loadability
- Mechanical strength
- Chemical Stability
- Spherical Particles with narrow particle size ranges.

Packing Material

- Fullerenes
- Modified Silica
- Modified Organics
- More Specific and Higher performance

Packing Material

- Chiral Technologies
- PhosphonicS
- Nano-C
- Engelhard

Packing Material Chiral Technologies

CHIRALPAK® IB is the second in a new series of columns that has been prepared using a novel immobilization technology that results in a completely solvent-stable chiral stationary phase (CSP). These columns retain the high selectivity and versatility of the existing range of Daicel columns. Rapid chiral separations with longer column lifetime and excellent selectivity are now possible with this immobilized polysaccharide column.

- Standard Packing Material
- Improved Materials

Packing Material

Nano-C

- Nano-C manufactures commercial grades of fullerenes with a wide range of purities and compositions that can be tailored to customer applications
 - Modify the fullerenes cage
 - Functionalize the structures

Packing Material PhosphonS

PhosphonicS materials embody phosphonate groups covalently attached to a silica-type framework and a full range of phosphonate derivatives is available

- Thermal Stability
- High Loading
- No Swelling

Packing Material Engelhard

- Material Surface Scientists
 - Scavenging agents
 - Modified Silica and other supports
 - Separation and purification platforms

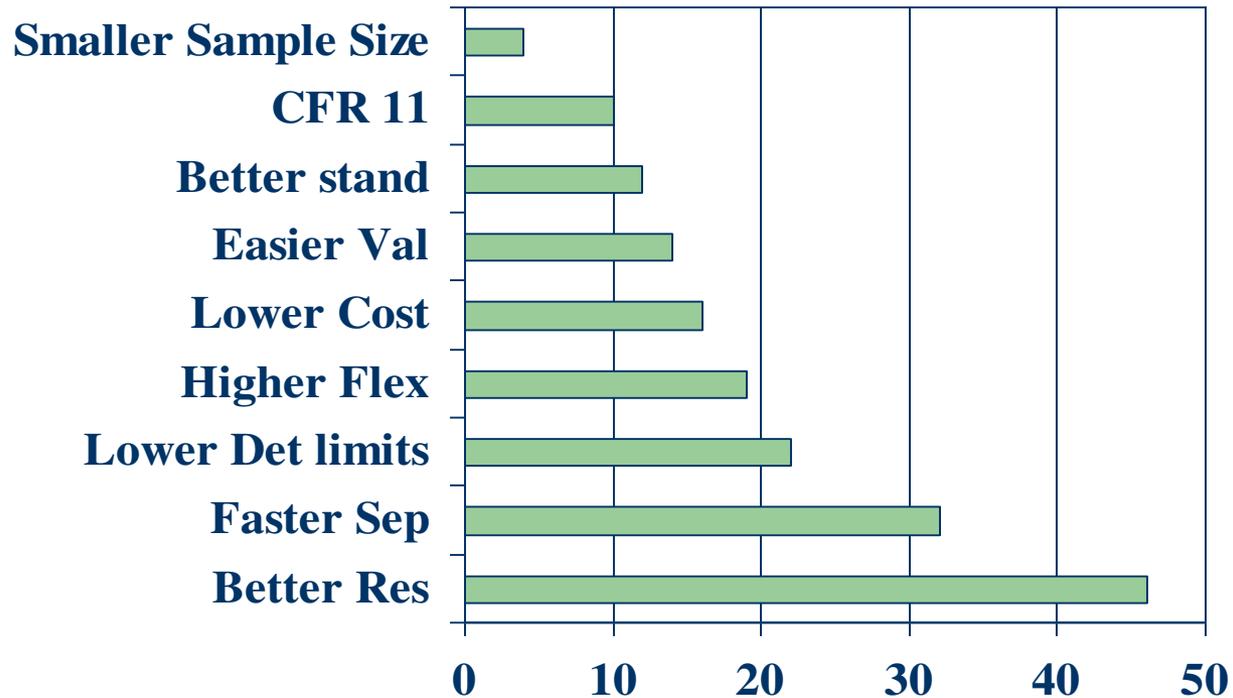
Feedstock

- Quality
 - Impurities
 - Solvents
 - Unwanted Isomers
- Reproducibility
 - Development Samples Approximates Production Material

Around the Equipment

- Guard Bed Technologies
- Distillation and Purification methods
- Pre-Treatment
- Micro-Reactors
- Down-Stream Chemistry

Current Challenges



Technology Trends

- Use of low skilled operators
- Addition of Sophisticated detectors
- Micro and Nano-Flow rates
- Standards and Support for Software and Hardware are likely to increase support
- Better ways to collect store and analyze data
- Software tools and methods to make regulatory compliance easier

Technology Trends

- Increase use of Sophisticated automation
- Improve Productivity
- Simplify data collection
- Improve quality and reliability

Technology Recommendations

- Standardized software and hardware interfaces
- Web-based client server technologies
- Nano-technologies can be used to provide low-cost chromatography's based sensors
- Multi-enhancements detection methods
- Develop faster, wider, deeper performance

Technology Recommendations

- Reduce the System's impact on corporate resources
 - Shrinking the physical footprint
 - Reducing the cost per analysis
 - Reduce volume of material consumed as analyte, eluent or carrier gas
 - Simplifying the operation to reduce training and personnel cost
 - Improve System Maintainability

Support

- Chiral Technologies
- Engelhard
- Lanxess
- Nano-C
- Novasep

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Thank You

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