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Is the Future of NMR on the Benchtop?

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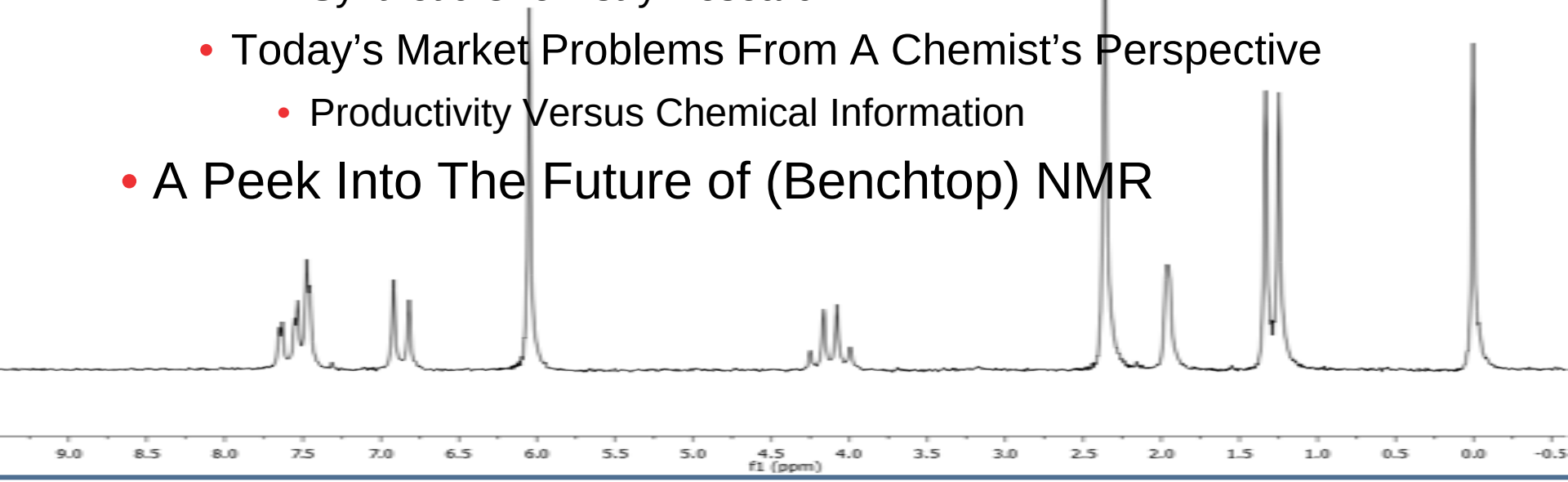
Welcome. Here's What We Have For You Today

- A Quick Look Into The Past : MS; HPLC; NMR
- A Longer Look At The Present
  - High-Field NMR From A Buyer's/Business Perspective
  - Today's Market Problems Where High-Field NMR "Disappoints"
    - Chemical Education
    - Process Research/Engineering
    - Synthetic Chemistry Research
  - Today's Market Problems From A Chemist's Perspective
    - Productivity Versus Chemical Information
- A Peek Into The Future of (Benchtop) NMR



The Classic ‘Onion Skin’ Approach to Technology

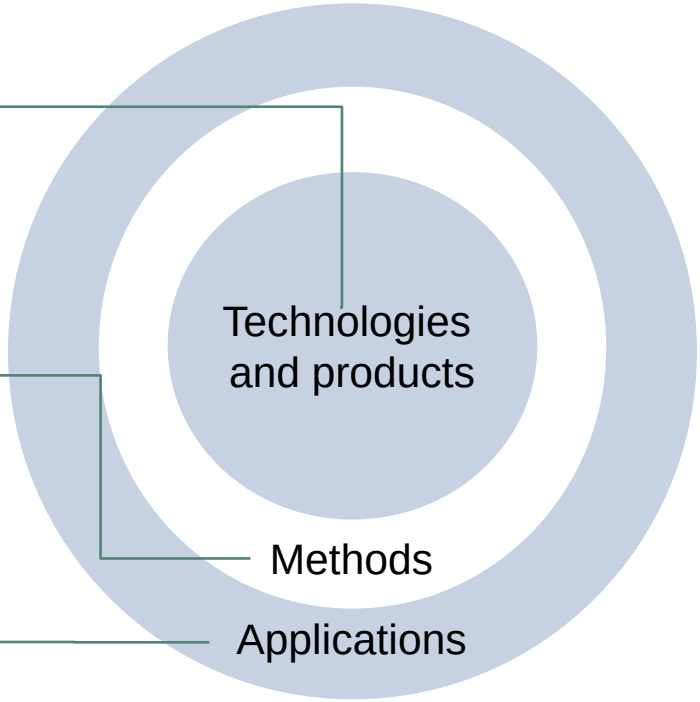
Successful companies need to focus on customer needs by:

- Understanding and embracing market problems
- Providing more integrated product offerings for less experienced customers, those interested in dedicated applications, or those conducting more routine analysis
- Remaining on the cutting edge of technology - change is constant

Enhancements to improve raw performance (e.g., sensitivity) and reduce cost/maintenance

New methods to aid in the analysis of complex samples, increase speed and enrich the information that can be gathered from an experiment

Fully developed experimental workflows from ‘sample to answer’ that enable new users to get quickly up to speed

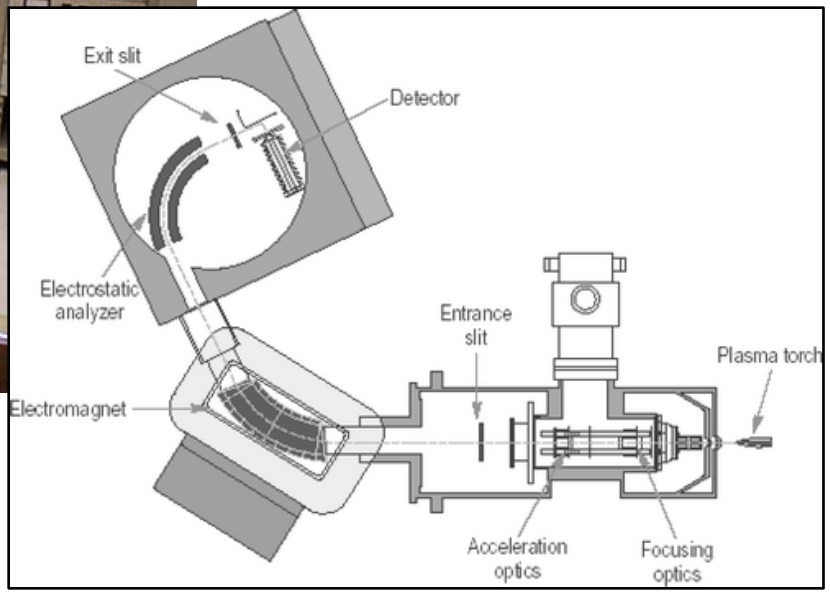


A parallel investment in systems integration, training tools, and service/support to ensure that when a customer buys a system from Thermo :

- It works the first time, every time
- Consistently generates quality data
- And if they have a problem, they get timely assistance at a fair price

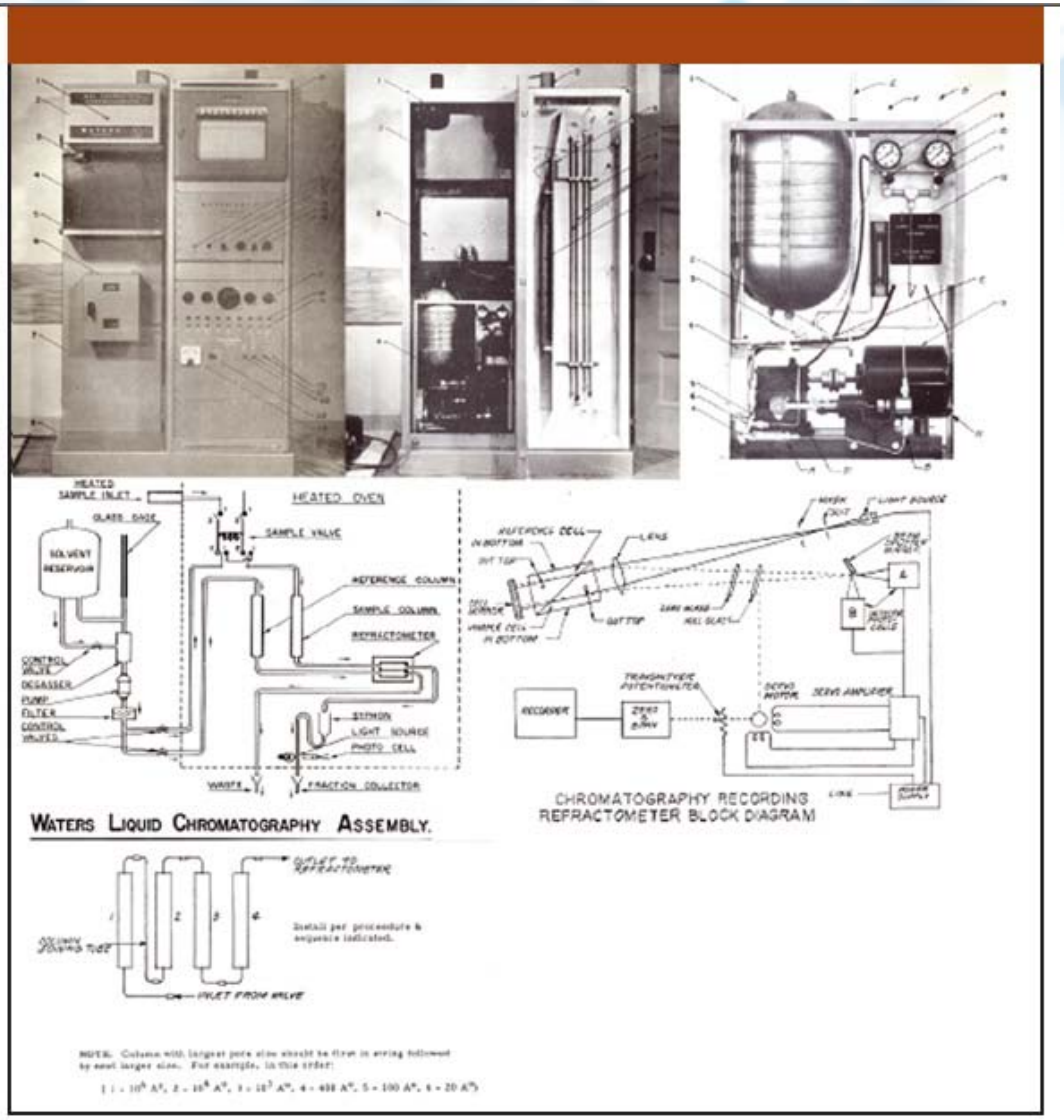
The Past : Mass Spectrometry

Magnetic Sector
Mass Spectrometer



1960's – 1990's

The Past : High Pressure Liquid Chromatography



First Waters
HPLC System
Circa1963

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The Present : LC-MS On The Bench

Thermo Scientific™
Dionex™ UltiMate™
3000 HPLC system

Thermo Scientific™
MSQ Plus
Mass Detector

LC-MS Single
Quadrupole
Benchtop
Spectrometer

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The Past : Nuclear Magnetic Spectroscopy

Varian DP-60
1962

The Present : High-Field Nuclear Magnetic Spectroscopy

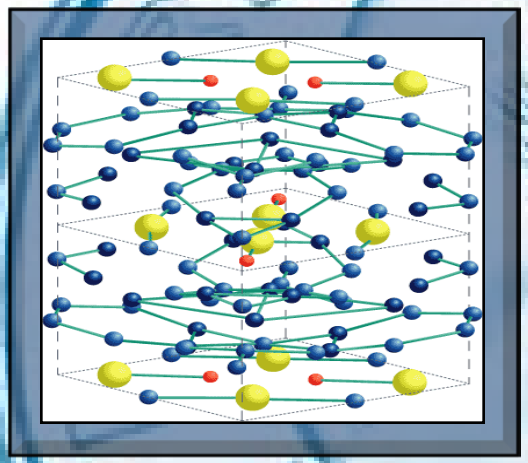
Bruker FT-300
Entry-level
Launched 2010

The Present : Bench-top Nuclear Magnetic Spectroscopy

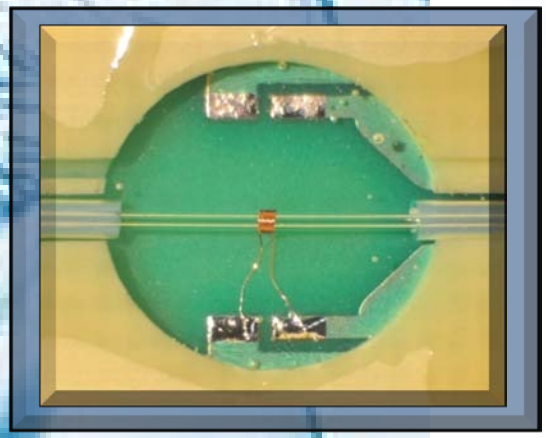
Thermo Scientific™ picoSpin™ 80 Launched 2013

How On Earth Do They Do That?

Magnetic Materials



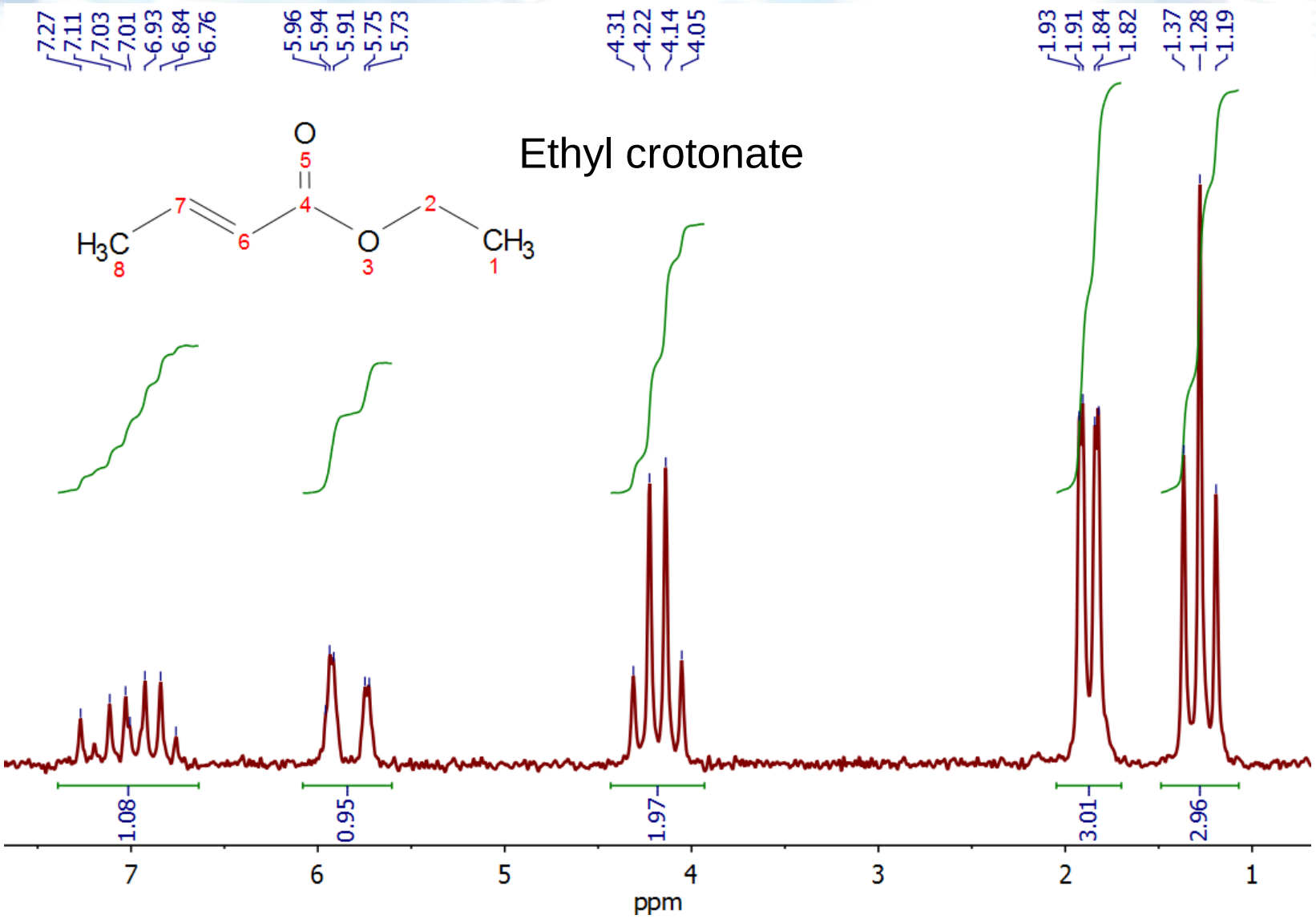
Micro Coil Technology



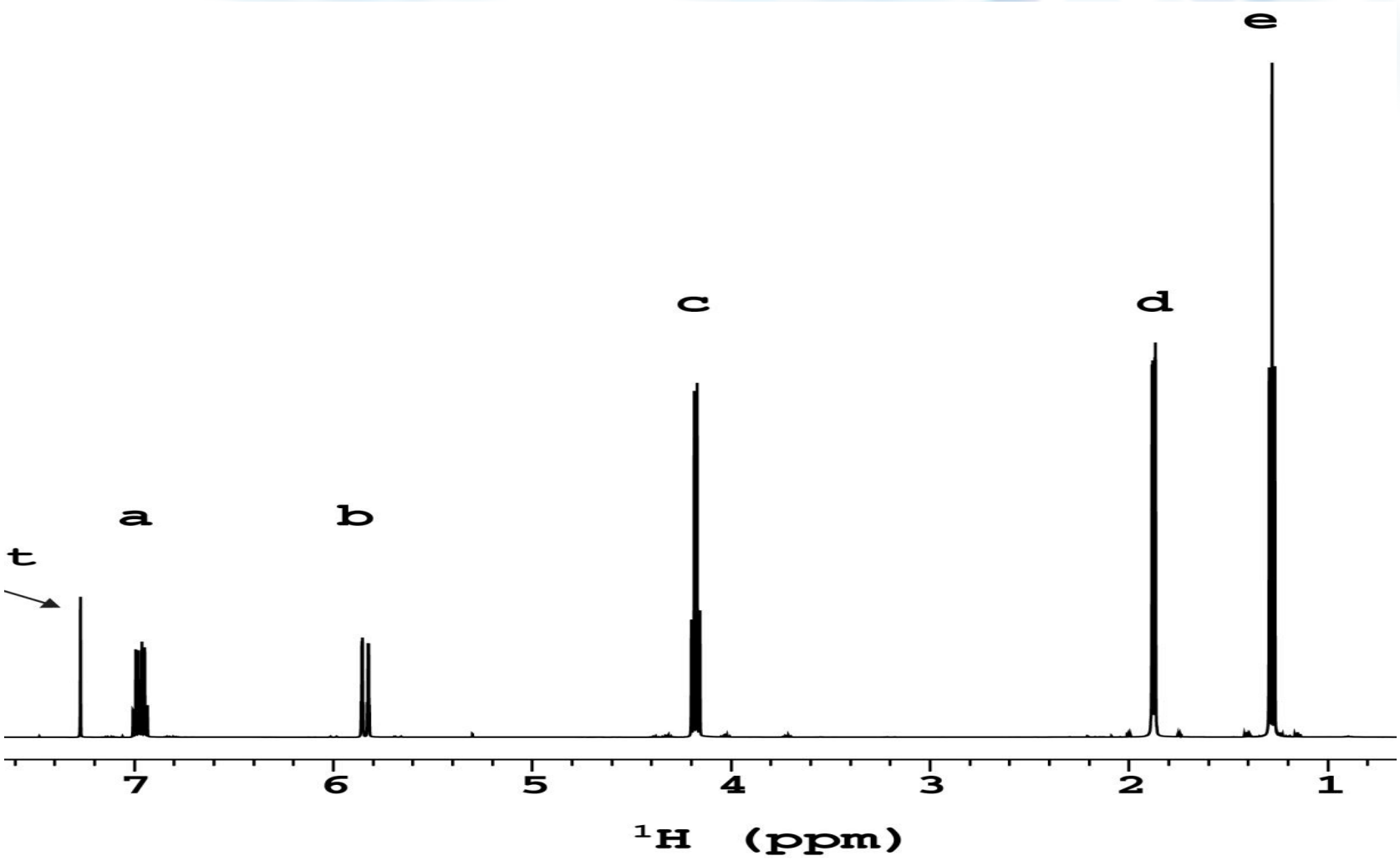
Radiofrequency Electronics

- **$Nd_2Fe_{14}B$ magnets**
- **Microcoil NMR experiments by A.G. Webb *et al*., U. of Ill.**
- **Advances in Rf (Tx and Rx) Electronics… (Mobile Phones)**

Typical ^{1}H Spectrum @ 82MHz : 15mins, 0.2M



Ethyl Crotonate @ 400MHz : Compare & Contrast



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^{1}H NMR Applications In An Organic Chemistry Lab

- Go-to technique for structure confirmation/verification
  - Often used daily for rapid decision making
    - “Did I Make What I Think I Made?”
- Used extensively for structure elucidation
  - Powerful tool when used in tandem with other techniques, e.g. LC/MS
    - “What Have I Got?”
- Ideal method to study mixtures & kinetics of reactions
  - Easily measure relative or absolute quantification
    - “How Much Do I Have?”
  - Reaction monitoring in real time can unveil mechanistic behavior
    - “How Did I Make What I Made?”
- Excels in determination of stereo- & regio-chemistry
  - Look “inside” the molecule at topological information
  - Structural fragments connect like jigsaw pieces

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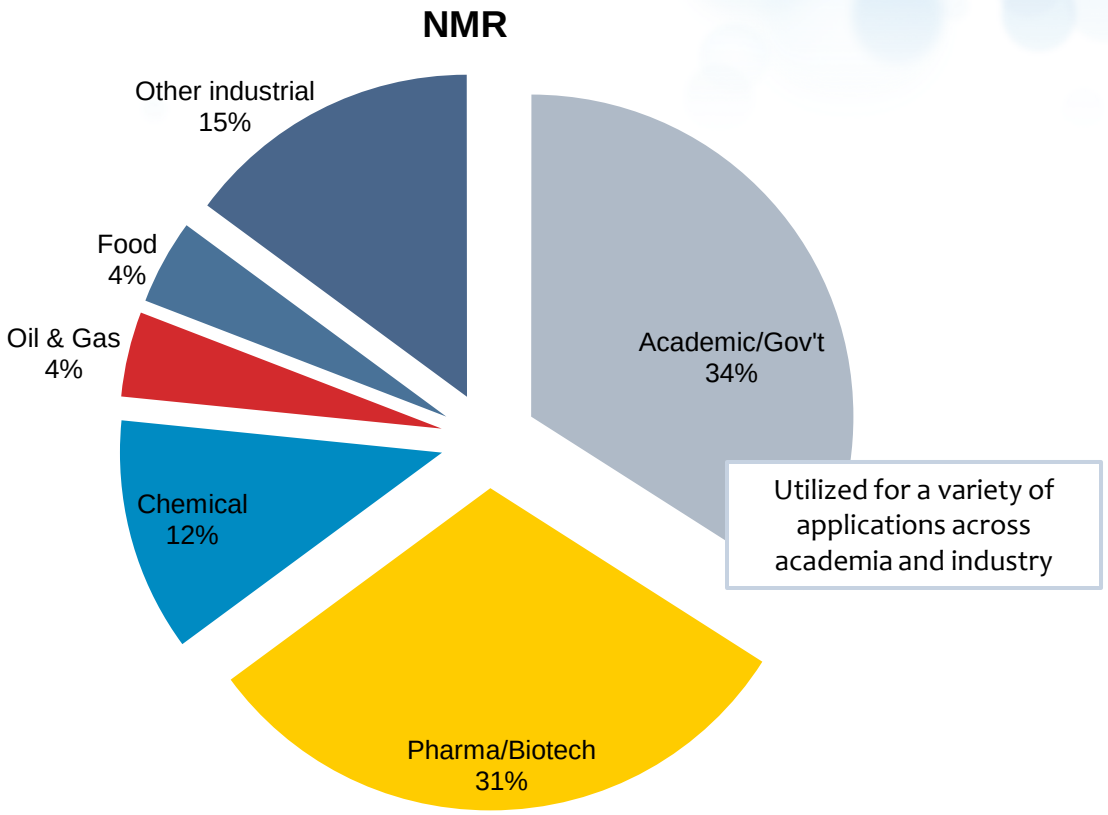
Facts And Myths

- 95+% of all NMR spectra measured are ^{1}H
- Remainder are other nuclei and other advanced techniques
  - ^{13}C, ^{31}P, ^{19}F, COSY, HSQC, HMBC, etc.
- Vast majority of all ^{1}H spectra are simple verification studies
  - ‘Did I Make What I Think I Made?’
- It’s a myth that you need 300+MHz to extract useful chemical information for verification studies
  - Previous generation low-field NMR had poor sensitivity and resolution
- Facilities buy high-field instruments to cover all requirements
  - Buying decision based on the need for the 5% of non-^{1}H measurements

High-Field NMR Market Distribution by Customer Type



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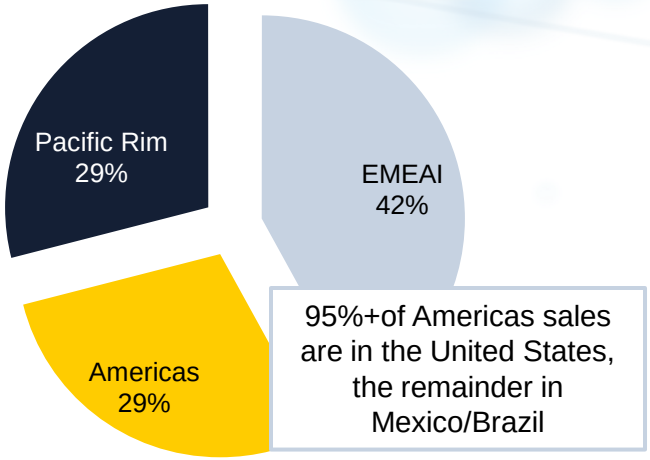
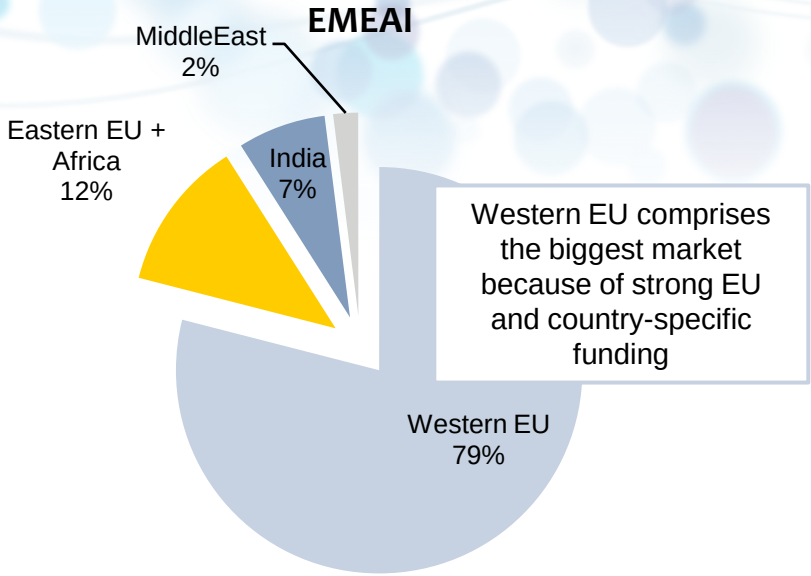
High-Field NMR Market Distribution by Geography

Worldwide



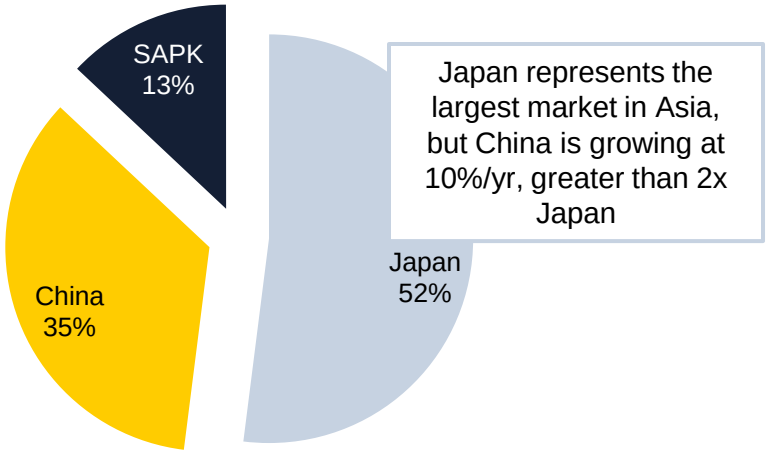
95%+of Americas sales are in the United States, the remainder in Mexico/Brazil

EMEAI



Western EU comprises the biggest market because of strong EU and country-specific funding

Asia Pacific



Japan represents the largest market in Asia, but China is growing at 10%/yr, greater than 2x Japan

EU agencies have proactively funded NMR technology development and invested in the build-out of academic core research facilities. Bruker has strongly benefited from these investments.

High-Field NMR Portfolio Markets

Market	TAM	Percent Served	SAM
Nuclear magnetic resonance	$475M	95%	$450M
Magnetic Resonance Imaging	$76M	72%	$55M
X-ray diffraction	$500M	18%	$89M
Total	$1051M	57%	$594M

Source: SDI market reports and competitive analysis

The three principal segments (NMR, MRI and X-ray) represent sizeable markets with annual growth rates ranging from 5-10% depending on product type and geography. There is considerable opportunity for growth through portfolio expansion & broader market coverage

High-Field NMR Market Segments

Segment	Segment Size	Sample type	Description
BioNMR	~ $85M	Large bio-molecules	Protein and/or DNA/RNA research focusing on answering structure/function correlations, binding studies and dynamics studies.
BioSolids	~ $37M	Large bio-molecules	Protein structure determination and binding site characterization for insoluble samples (e.g., drug targets like membrane proteins)
Chemists & Students	~ $55M	Small molecules	Small molecule structure verification for a host of applications including medicinal chemistry, process research & Mfg QA/QC. Teaching Universities w/ NMR classes.
Advanced Research	~ $49M	Mainly small molecules	Mixed applications - everything from structure verification to full structure determination to mixture analysis to studying some inorganic compounds. Often multi-user systems shared between groups within a chemistry department.
Sensitivity Challenged Research	~ $33M	Small molecules	Sample limited applications where mass sensitivity is important. Examples include natural products and metabolite analysis.
Materials Science - liquids	~ $17M	Small & large molecules	Samples include polymers , inorganic compounds and petroleum industry samples requiring observation of unusual nuclei and extended T range.
Materials Science - solids	~ $27M	Large & small molecules	The study of inorganic samples or nano materials utilizing solid-state NMR.
Metabolomics & Ligand Binding	~ $7M	Small molecules	High throughput, sensitivity limited studies focused on target-ligand binding and/or metabolite screening for biomarkers.
Food & Beverage	~ $4M	Small molecules & mixtures	Analysis of proteins, carbohydrates, fats or additives in consumable products during R&D, process development or Mfg QA/QC

High-Field NMR Market Segments: Benchtop Opportunities

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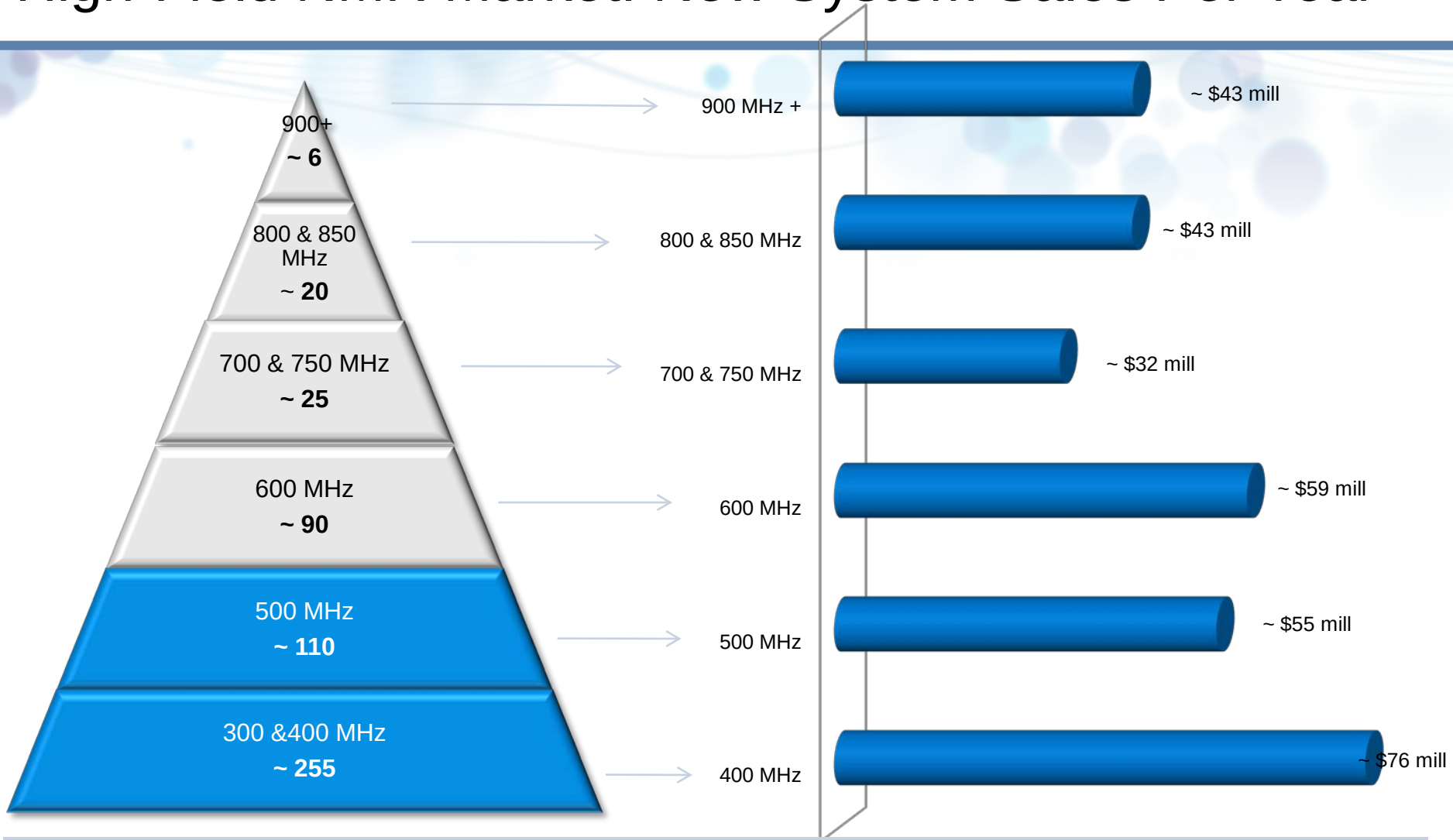
High-Field NMR Market: New System Sales Per Year



Although on a unit basis, the majority of volume resides in lower frequency systems, the extremely high cost of high-end systems (up to $15M/system),results in market revenues distributed along the continuum.

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Summary of Recent Market trends

Pharmaceutical and Industrial	Academic and Government
• Mergers are resulting in the consolidation of facilities and personnel • Although companies have older infrastructure, there are limited capital budgets for new equipment • Most are seeking increased productivity with existing systems (i.e., automation)	• Grant funding is tougher to get, especially for high-end instrumentation • New equipment orders often result from pooling of departmental funds • Government stimulus programs will result in stochastic purchases, though grants will be fairly concentrated

Due to the significant capital investment required to purchase new systems, many customers are focused on enhancing and/or upgrading the performance of their existing equipment. The performance and productivity bar is being set very high for the purchase of new equipment

Financial Aspects of Owning An NMR Spectrometer

- Cost of entry
  - Bruker FT-300 ~ $150k + installation
  - Agilent MR400 ~ $220k + installation

- Cost of Ownership / per Year
  - Cryogens
    - Liq. He ~ $4000 + delivery
    - http://www.rsc.org/chemistryworld/2013/05/helium-reserve-supply-shortage-price-rise
    - Liq. N_2 ~ $500 + delivery
  - Solvents & Tubes
    - Chloroform-d(+TMS) + 10x$3 tubes for 100 chemists ~ $25,000
  - Personnel
    - One Full-time Headcount with Bachelor's degree ~ $70,000
  - Service
    - Full service contract ~ $15,000, Partial ~$5,000

Understand and Embrace NMR Market Problems

Three Examples Today :

1. Chemical Education
   - E.g. Two-year college, 100 students, budget-limited
2. Process Research/Engineering
   - E.g. Chemical Development Group in Pharma
3. Synthetic Chemistry Research Laboratory
   - E.g. Postgraduate Research Lab

Challenges and Opportunities in Chemical Education

Example One : Two-Year College with 100 Students

- Can only dream of owning high-field NMR capability
  - Overkill for teaching basics of spectroscopy & simple ^{1}H spectra
  - Use simulated NMR problems for teaching – poor substitute
- Likely to give their students hands-on experience with:
  - FT-IR, e.g., iS5
  - UV/Vis, e.g., Spectronic 200
- Addition of NMR completes the portfolio of training
  - Gives students a head-start in later chemistry-related careers

First-time NMR Purchase: Cost Implications

Nothing

Purchase : $200k
Personnel : $70k/yr
Consum's : $30k/yr

Or

Nothing

Purchase : $60k
Personnel : $0/yr
Consum's : $5k/yr

Challenges and Opportunities in Process Research/Eng.

Example Two : Chemical Development Group in Pharma

- Reactors are large and placed remotely from NMR labs
  - Interested in reaction monitoring as much as structure confirmation
  - Need exclusive access to NMR spectrometer when needed
  - Often use R&D facilities, equivalent to buying time on the instrument
- Problematic solution is to set up small-scale reaction in NMR lab
  - Experience shows that experiment conditions cannot be mimicked
  - Compromises and assumptions cloud results
- Need proximal NMR solution with little sample preparation
  - Operators are possibly engineers, not chemists

Replace Existing NMR Services: Cost Implications

Send Samples Off-Site For NMR Analysis $10k-$50k / yr

Purchase : $200k
Personnel : $70k/yr
Consum's : $30k/yr

Or

Send Samples Off-Site For NMR Analysis $10k-$50k / yr

Purchase : $60k
Personnel : $0/yr
Consum's : $5k/yr

Challenges and Opportunities in Synthetic Chemistry Lab

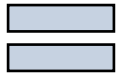
Example Three : Postgraduate Organic Chemistry Lab

- All share an open-access NMR instrument
  - High-field instrument - good ; Remote location - bad
  - Centralized facilities are expensive, and popular
    - That combination usually leads to an over-subscribed service
- Long wait times impact productivity
  - Robotic systems help but queues grow quickly at peak times
  - Even one hour can mean a half-day lost due to lab safety restrictions
- Proximity of instrument = precious time re-gained
  - Shorter wait times, even when longer acquisition time taken into account
  - Lightweight : can be hand-carried around the lab or between labs

Expand Current High-Field Facilities: Cost Implications

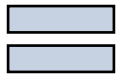
Purchase : $200k
Cost / yr : $100k

Or



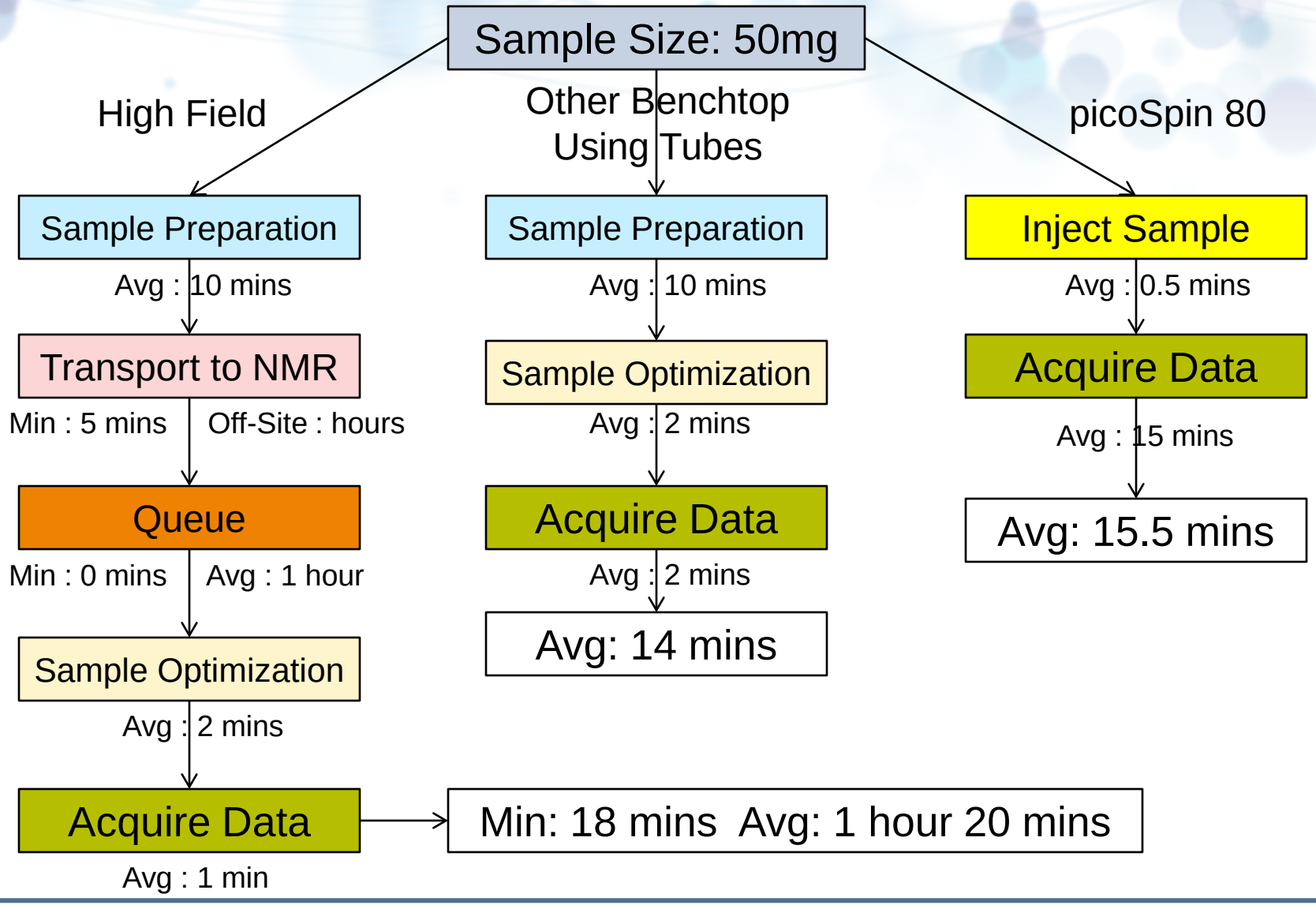
Purchase : $400k
Personnel : $70k/yr
Consum's : $60k/yr

Purchase : $200k
Cost / yr : $100k

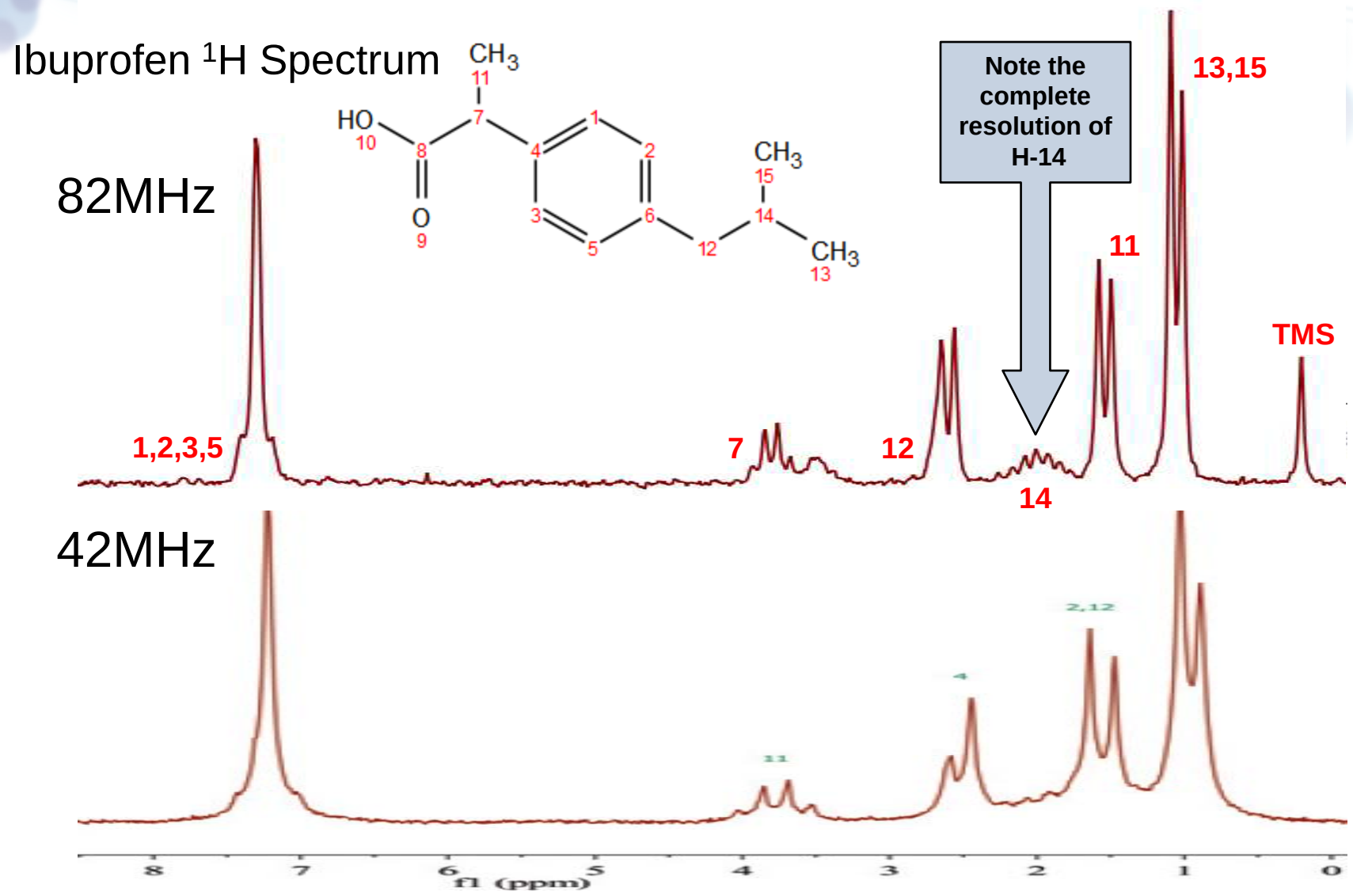


Purchase : $260k
Personnel : $70k/yr
Consum's : $35k/yr

Productivity Comparisons



What's More Important: Speed or Chemical Information?



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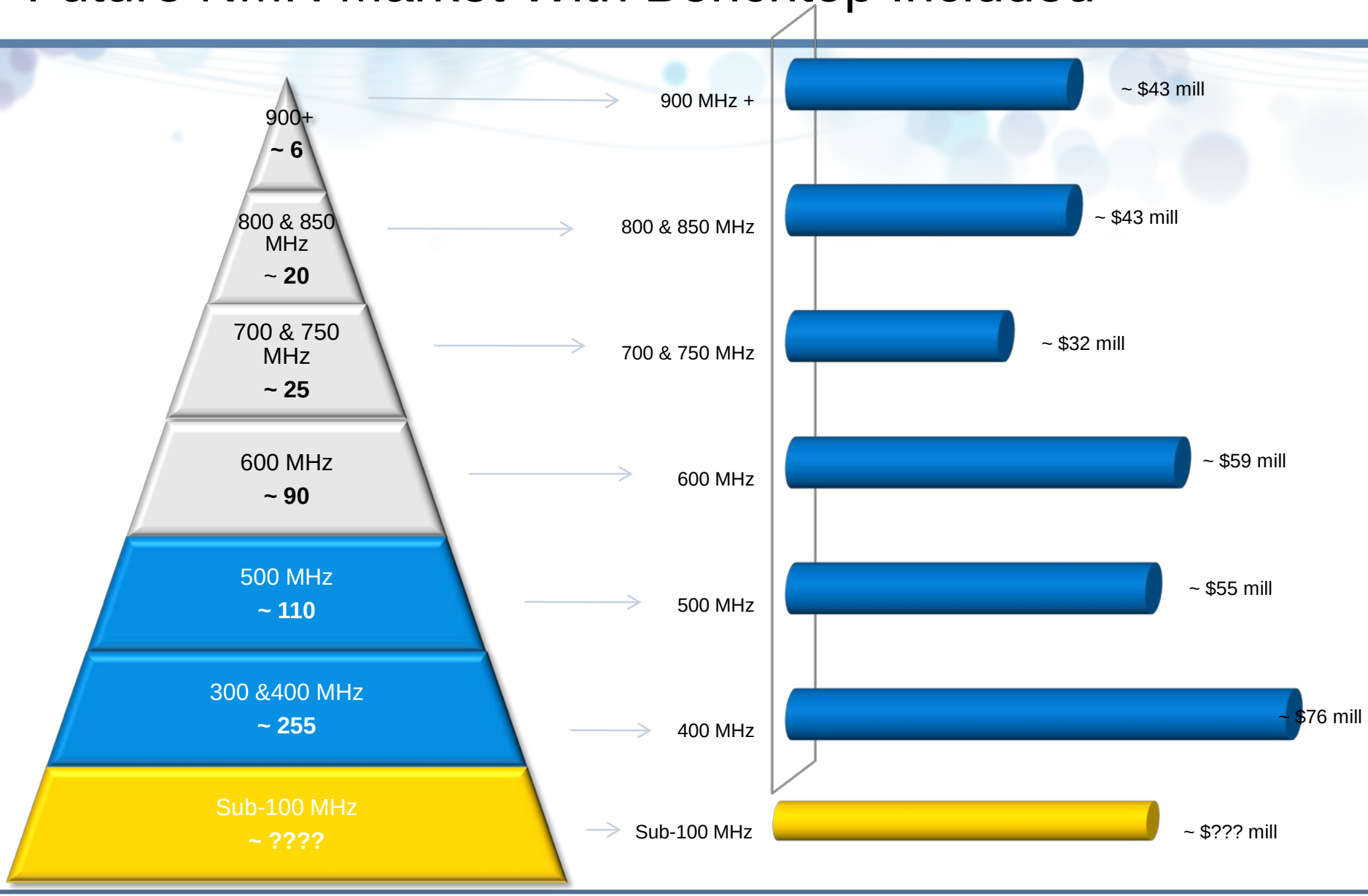
Future Outlook

- Immediate
  - Awakening
  - Enabling
  - Funding
- Medium term
  - Standard in education
  - Financial cost-benefit universally accepted
- Long term
  - Mature
  - Technology Advances
  - Complementary to high-field

Future NMR Market With Benchtop Included



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Thank You For Your Attention!

Questions?