Combi 2001

Keynote Address:

Economic Impact of Combinatorial Chemistry on Industry and Society

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http://www.atp.nist.gov/www/ccmr/ccmr_off.htm

Agenda

- NIST's Mission and role in HTE methods
- The Advanced Technology Program
- ATP funding in HTE/combinatorial methods
- Increased productivity and profitability
- Vision 2020 Road Map of Research Needs
- Conclusion

NIST Assets Include:

Advanced Technology Program

Partnership with private industry to accelerate the development of high-risk, enabling technologies with broad benefits for the entire economy and for society.

Measurements and Standards Laboratories

Nation's ultimate reference point for measurements, standards, and technology research to support industry, science, health, safety, and the environment.

Manufacturing Extension Partnership

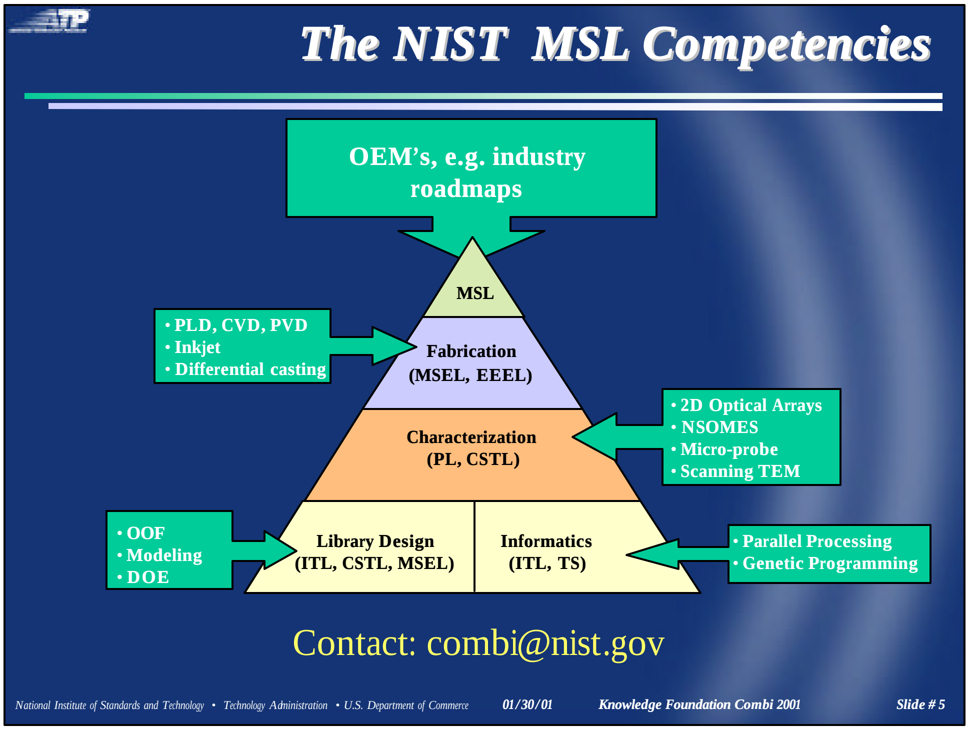
Network of centers offering technical assistance and best business practices to the 385,000 smaller manufacturers in all 50 states and Puerto Rico.

Baldrige National Quality Program

Promotes business performance excellence and quality achievement by U.S. companies.

HTE at NIST

- Support new parallel methodologies and measurement tools tailored to specific industrial applications and properties;
- Validate new and existing measurement methods and models for small sample sizes analyzed using parallel or high throughput approaches;
- Supply comprehensive standard reference materials libraries and data (faster and/or better);
- Demonstrate application of HTE/combinatorial methods to new materials and R&D problems.


The NIST MSL Competencies
OEM's, e.g. industry roadmaps
MSL
• PLD, CVD, PVD
• Inkjet
• Differential casting
Fabrication (MSEL, EEEL)
Characterization (PL, CSTL)
• 2D Optical Arrays
• NSOMES
• Micro-probe
• Scanning TEM
• OOF
• Modeling
• DOE
Library Design (ITL, CSTL, MSEL)
Informatics (ITL, TS)
• Parallel Processing
• Genetic Programming
Contact: combi@nist.gov
National Institute of Standards and Technology • Technology Administration • U.S. Department of Commerce
01/30/01
Knowledge Foundation Combi 2001
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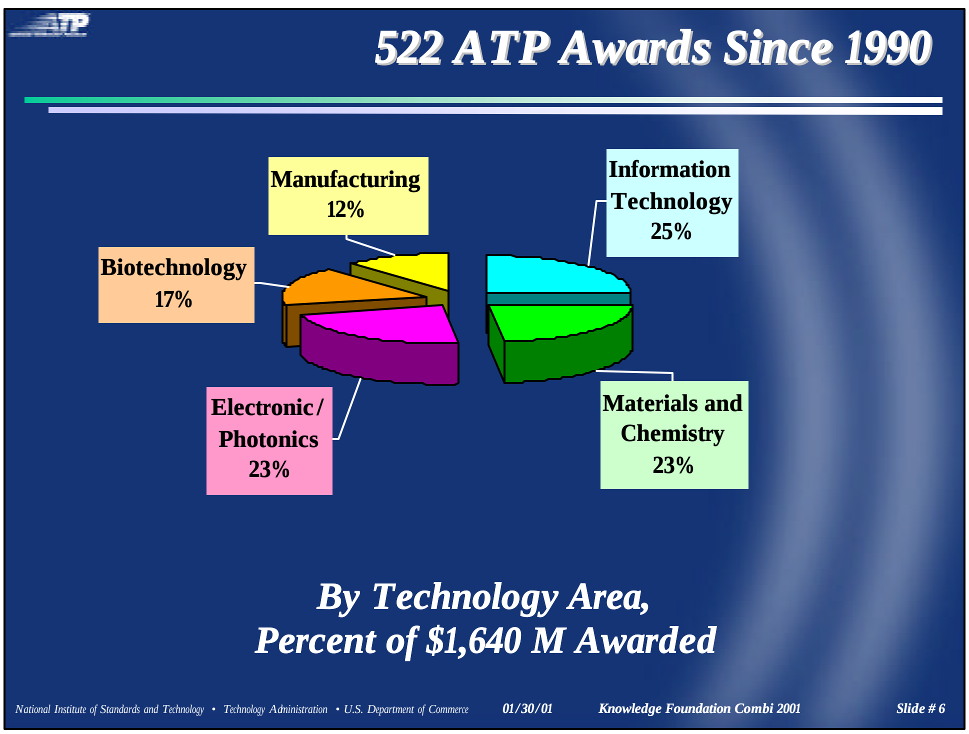
522 ATP Awards Since 1990
Manufacturing 12%
Information Technology 25%
Biotechnology 17%
Electronic/ Photonics 23%
Materials and Chemistry 23%
By Technology Area,
Percent of $1,640 M Awarded
National Institute of Standards and Technology • Technology Administration • U.S. Department of Commerce
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ATP Technology Cluster

Nonlinear Dynamics/UOP LLP $14,715K (ATP) + $15,186 (5 yrs.)
"Combinatorial Tools and Advanced Data Analysis Methods for Heterogeneous Catalysts"
Develop novel combinatorial methods for the discovery of new, more effective heterogeneous catalysts used by the chemical industry, thereby increasing the efficiency of catalyst research and development.

GE/Avery-Dennison $3,127K (ATP) + $3,200K (3 yrs.)
"Combinatorial Methodology for Coatings Development"
Develop combinatorial methods to achieve several orders of magnitude increase in the rate of screening of new coatings for the automotive and information display industries, accelerating the introduction of new products while also improving their quality.

ChemCodes, Inc. $2,000K (ATP) + $2,603K (2 yrs.)
"Experimental Generation of the First Complete Chemical Reaction Database"
Use high-throughput reaction screening coupled with quantitative mass spectrometry to create the first comprehensive, experimentally derived chemical reactivity database for organic molecules, leading to novel and efficient pathways for synthesizing new compounds.

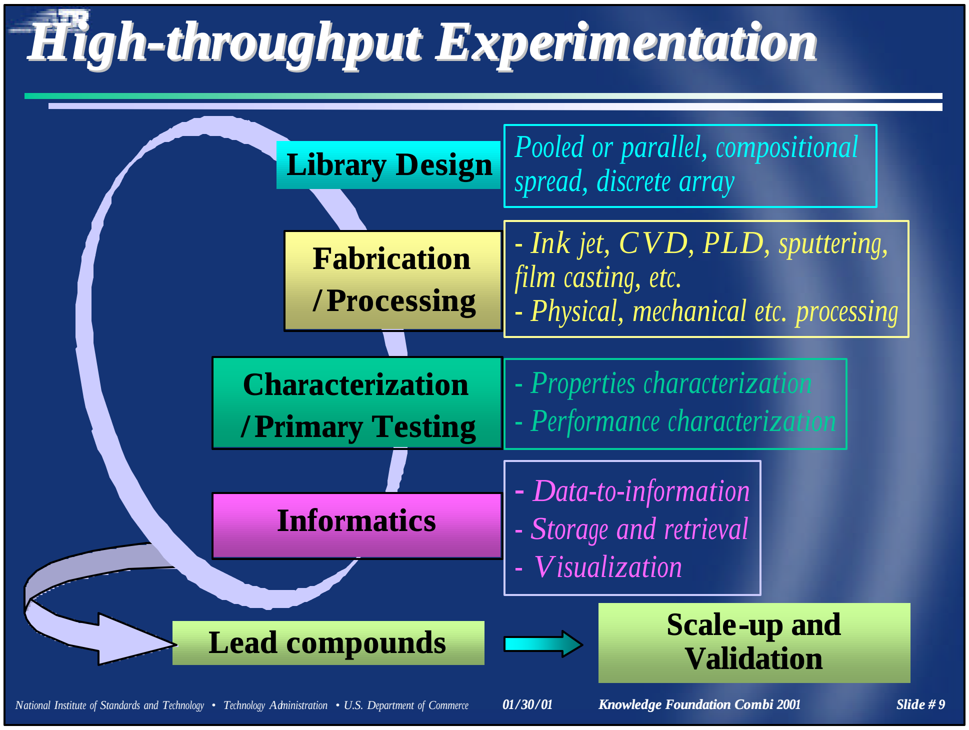
Albemarle Corporation $1,989K (ATP) + $2,143K (3 yrs.)
"Single-Site Catalysis: The Next Frontier"
Develop new families of well-characterized, highly efficient catalytic activators for use with metallocenes and other single-site catalysts to reduce costs and enable better product control in the production of polyolefin plastics.

ATP Intramural Support at NIST

Lab	ATP Intramural Funding: Technical Area
MSEL-Ceramics	NEXAFS: Scanning X-Ray Studies of Supported Catalysts
CSTL	Micro-hotplates and micro-sensors
MSEL-Polymers	Polymer Scaffolds for Engineered Tissue
ITL	Genetic programming for Data Visualization and Mining
CSTL/MSEL/ITL	Microwave microscopy of BST Thin Layer Dielectrics
Physics Lab	2-D FTIR. imaging

CSTL - Chemical Sciences and Technology Lab
MSEL - Materials Science and Technology Lab
ITL- Information Technologies Lab

Continuing FY2001 Ended FY2000



HTE improves innovation processes

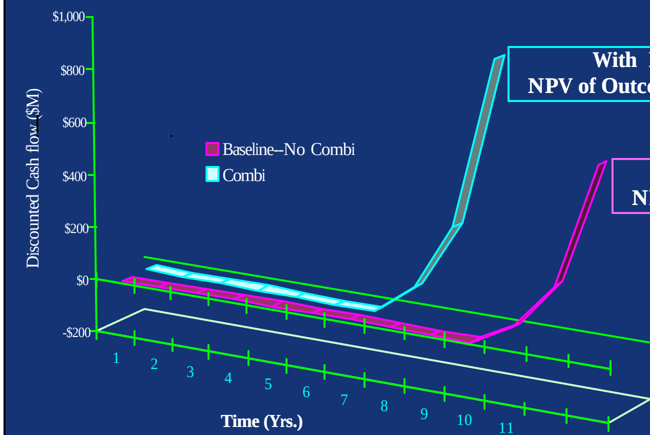
- **Reduced innovation cycle times across organization**
  - *Implementation in discovery phase can save two years off of usual 10-year commercialization cycle in chemical industry*
  - *Implementation in process and product development (emerging)*
  - *Implementation in customer service and (flexible) manufacturing (vision)*
- **More efficient use of R&D and manufacturing**
  - *ROI of R&D $'s*
  - *Decreased labor cost per experiment using using automation (>100-fold)*
- **Enables discovery in huge experimental spaces**
  - *Probability of success in discovery phase increases from 20-30% to >50%*
  - *Broadens spectrum of materials in development*

The Value of HTE in Discovery

Pro Forma example

Basis: Pharmaceutical / Chemical Company

ASSUMPTIONS: Company Implements Combi discovery	
Total BR time	0.3
No. chemists needed	4
No. compds Tested	~9,000
No. of Serial rounds	1
No. compds/Round	~9,000
Cost of screen/round	$10,000
Total costs-chemists	$167,000
Cost/Comp'd	$19



With HTE
NPV of Outcome: $286 M

Without HTE
NPV of Outcome: $203 M

ASSUMPTIONS: Pharmaceutical Industry w/out Combi Discovery	
Total BR time	5 years
No. chemists needed	15
No. comp'ds Tested	3,750
No. of Serial rounds	250
No. comp'ds/Round	38
Cost of screen/round	$10,000
Total costs-chemists	$18.75M
Total cost/Comp'd	$5,000

Economic Benefits

Broad-based economic benefits are expected from materials and process discovery using HTE methods:

- **Downstream impacts of new materials**
- **Diffusion to other industries**
- **Diffusion to other processes**

SYSTEMS & COMPONENTS $ 4 T

U.S. Sales* ($M)	
BASIC CHEMICALS	**$115,576**
SPECIALTY POLYMERS	**$ 29,415**
OPTOELECTRONICS	**$ 14,000**
SPECIALTY CHEMICALS	**$ 50,124**

CATALYST R&D $3,585M

A Developing Service Industry

Parent	Daughter	J/V Partners, Clients
(A. Zafaroni)	Symyx Technologies	Hoechst AG, Celanese AG, Bayer AG, BASF, Unilever, etc. IPO-11/19/99
ArQule Inc.	Alveus Technologies	N/A
MPI-Kohlenforschung BASF (silent partner)	hte GmbH hte North America	MPI-Kohlenforschung BASF (client) Molecular Simulations Inc.
Charybdis	Scylla	(single clients)
SRI International	SRI International	(single clients)
Catalytica Advanced Tech.	Catalytica NovoTec	
Shell International Chemicals (NL)	Avantium Technologies NV Avantium Technologies Inc.	Universities of Delft, Twente, Eindhoven; The Netherlands; GSE Technologies, Inc.; SmithKline Beecham/S.R. One; Alpinvest; The Generics Group, W.R. Grace, etc.

Market opportunity in catalysts is $ 300-500M

RD&E Early Adopters

Chemical Companies Utilizing HTE Methods

- Air Liquide
- Air Products
- Akzo Nobel
- Albemarle
- Alcoa
- Arch Chemicals
- Avery Dennison
- BASF
- BP
- Cabot
- Celanese
- Ciba Specialty Chemicals
- Clariant
- Cytec Industries
- DSM
- Dow Chemical
- DuPont
- Eastman Chemical
- ElfAtoFina
- Engelhard
- Geon
- General Electric
- Lucent Technologies
- Rohm and Haas
- Shell Oil
- UOP
- W.R. Grace

Vision 2020 Road Map

- *Technology Vision 2020* is a call to action, a strategic plan, for the U.S. chemical industry
  - CCR, ACS, AIChE, SOCMA, ACC
  - New Chemical Science and Engineering Technology (CCR)
- June 2, 2000 at NIST re: combi methods for materials
  - Approx. 40 participants from industry, government, academia
  - Vision and research needs out to the year 2020
  - Final report due March, 2001

Key Research Needs Identified

Challenges for High Throughput RD&E

Computational

- **Library Design**
  - *Computational/Modeling: QSPR*
  - *Statistics and control of error*
  - *Design of Experiments*
- **Informatics**
  - *Increasing Information/Bandwidth*
  - *Experimental complexity*
  - *Data integration/analysis*
  - *Hardware control / interfacing*
  - *Expert systems for data analysis*

Micro-Reactor Technologies

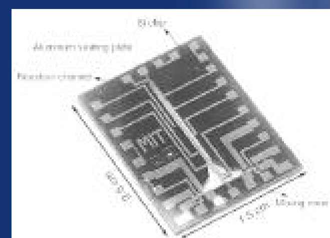
- **MEMS**
  - *Lab-on-chip*
  - *Embedded sensors*
  - *Mechanical sensors*
- **Automation**
  - *10^2 -10^3 throughput increase*
  - *Reproducibility*
- **Economies of scale**

Key Issues—Fabrication and Characterization

Micro-Reactor Technology

Integration of reactors, sensors, controllers on-chip

- Understanding and exploiting surface effects (CFD/modeling)
- Chip substrates: reactivity, thermal properties, machining
- Fluidic and electronic interconnects
- Mixing, separations, heat transfer
- Sample deposition
- Scalability Predictions
  - *Interfacial properties*
- Process control
  - *Temperature/pressure at much higher throughput*



Ref. Gleason et al., http://web.mit.edu/cheme/www/People/Faculty.

Key Issues--Informatics

Advanced Data Handling

- High-performance data mining tools to extend utility of a database management system;
- Atomic level chemistry to engineering design by developing relationships:
  - Properties = f (chemistry, processing, microstructure…)
- Integration of diverse databases to functionally specific data bases;
- Quantitative Structure Property Relationships (QSPR);
- Development of a query language that links different methods for querying the data.

Conclusions

Step-change processes are noted by industry as necessary in the following:

- Information technologies
  - *Chem- and Bio-informatics leverage the convergence of inexpensive computational engines and distributed data warehouses*
- Micro-reactor technologies
  - *MEMS-based reactors for both distributed manufacturing systems and in R&D settings provide higher densities and mass production drive economies of scale for high throughput screening*

ATP National Meeting

Funding Opportunities for High-Risk Research

June 4-6, 2001

Wyndham Baltimore Inner Harbor Hotel
101 West Fayette Street
Baltimore, Maryland

Check for Regional Meetings
www.atp.nist.gov
1-800-ATP-FUND

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http://www.atp.nist.gov/www/ccmr/ccmr_off.htm

Vision 2020

BACK-UP SLIDES

Vision 2020: Preliminary Conclusions

Library Design

Vision

- Close integration between experimentation and modeling
- Economic and business models will be used for decision making
- Most experiments done "virtually"
- Ability to solve a chemical field

Research Needs

- Integration of equipment and theory
- Models that span multiple scales: interface between micro-meso-macro scales
- Paradigm shift in experiment design
  - *Ability to process multiple experiments and results*
  - *Make the first experiment right (but integrate results from failures)*
  - *Pharmacology example*

Vision 2020: Preliminary Conclusions

Library Fabrication

Vision

- Libraries are achievable-a standard footprint is available
- Informatics/design/production are linked and web-accessible
- Virtual libraries have the ability to accurately predict
- Libraries that explore both compositional and process variables
- Vendors supply standardized equipment, universal standards for processing and calibration

Research Needs

- Sample Handling
  - *Technology for precise handling and mixing of powders and viscous liquids over high temperature, pH, pressure ranges*
- Scalability
  - *Lab scale to pilot scale predictability*
  - *Between thin films and bulk properties*

Vision 2020: Preliminary Conclusions

Library Characterization

Vision

- Correlation of performance and properties
- Scalability: micro measurements to performance levels

Research Needs

- Size/Scale Issues
  - *Small samples don't necessarily tell you how the whole will perform*
- Integration from sample to end-use
  - *Integrate analytical equipment with reactors*
  - *Microfluidic reactors coupled to detectors*
- Mechanical Properties
  - *Develop tool to measure stress-strain curves, tensile testing for 100 micro-samples*
- Structure
  - *Structural characterization—robust, sensitive, accurate, fast (x-ray system)*
- Tools (general)
  - *Catalyst performance measurements*
  - *Low cost tools to measure gloss, hardness, etc.*

Vision 2020: Preliminary Conclusions

Informatics

Vision

- Open collaboration through standard data structures
- Platform independence, central data storage
- Decision-making and knowledge infrastructure for R&D
- Researchers will move to probability-based approaches

Research needs

- Develop expanded data visualization tools
- Modular tool kit—infrastructure for many different applications
  - *Develop standard interface for instrumentation in general*
- Robustness and quality (six sigma)
- Develop alternative to current relational database technology
  - *Reducing work in database design, implementation, modifications*
  - *Dynamically updateable architectures*
- Tools to integrate and analyze structured and unstructured data

Project Selection Criteria

- **Scientific and Technological Merit *(50%)***
  - *Innovation in technology*
  - *High technical risk and feasibility*
  - *Quality of R&D plan*
- **Potential for Broad-Based Economic Benefits (*50%*)**
  - *Economic benefits*
  - *Need for ATP funding*
  - *Pathway to Economic Benefit*

Changes to the Proposal Submission Process

- **Streamlined proposal process (STAGE-GATE)**
- **Continual acceptance of proposals (Jan. 10th start date)**
- **Project selection criteria and review remain the same**
- **Electronic submissions of proposals (2002?)**
- **Regional workshops will include how to apply and opportunity to meet ATP staff for 1:1 discussions**
  - *Las Vegas-Alexis Park: February 1, 2001*
  - *NIST-Gaithersburg: February 6, 2001*

check our website (*www.atp.nist.gov/regionalmeeting*)

Common Proposal Weaknesses: Technical

- **Lack of sufficient detail**
  - *How you will reach technical objectives*
  - *What's innovative ("What is the technological nugget?")*
  - *Why a risky technical approach is needed*
- **Unsupported assertions**
- **Outside ATP mission**
  - *Low risk - product development*
  - *Lacks demonstrated feasibility - basic research*
  - *Scale-up or demo to only prove economics*
- **Lacks connection between technical goals & business opportunity**

Common Proposal Weaknesses: Business

- **Lacks connection between technical goals and business opportunity**
  - *Competitive analysis is lacking*
- **Poorly developed (or no) commercialization plan that does not incorporate business partners, distribution channels, business development/marketing/sales personnel, manufacturing, OR CUSTOMERS (!)**
  - *Include MOU's/LOA's/etc. only if favorable to proposal*
- **Business plan too innovative !**
- **Insufficient evidence of economic benefits**
  - *How will technology benefit company and also benefit U.S. economy*
  - *BE AS QUANTITATIVE AS POSSIBLE!*

Common Proposal Weaknesses: Combi

- **Outside ATP mission**
  - *"Low risk - product development"*
  - *"Lacks demonstrated feasibility - basic research"*
  - *"Edisonian--we don't fund boundary-less projects"*
  - *"What's so innovative about systems integration?"*
  - *"Why is this risky?…it's just software and hardware engineering best practices"*
  - *Insufficient evidence of broad economic benefits*
- **Doesn't paint the big picture early on**
  - *You need to communicate a multi-disciplinary project to specialists*

HAVE AN INDEPENDENT PARTY READ PROPOSAL!