Perspective

# Combinatorial Materials Science: Paradigm Shift in Materials Discovery and Optimization

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In many respects materials science and related fields are driven by the discovery process. The discovery of materials exhibiting significantly enhanced performance or offering truly unique capabilities often leads to a virtual stampede of scientific and technological activity focusing on developing an understanding of these materials. Special sessions on this topic appear at conferences and symposia. Sections of or entire journals are devoted to a single material or class of materials. Startup companies seek to capitalize on these new capabilities. Recent examples include high-temperature (cuprate) superconductors and rare earth permanent magnets (e.g., $Nd_2Fe_{14}B$). In too many cases, however, the promise provided by the initial discovery falls somewhat short of expectations due to the inability to make additional improvements in performance, failure to solve integration issues, and processing difficulties.

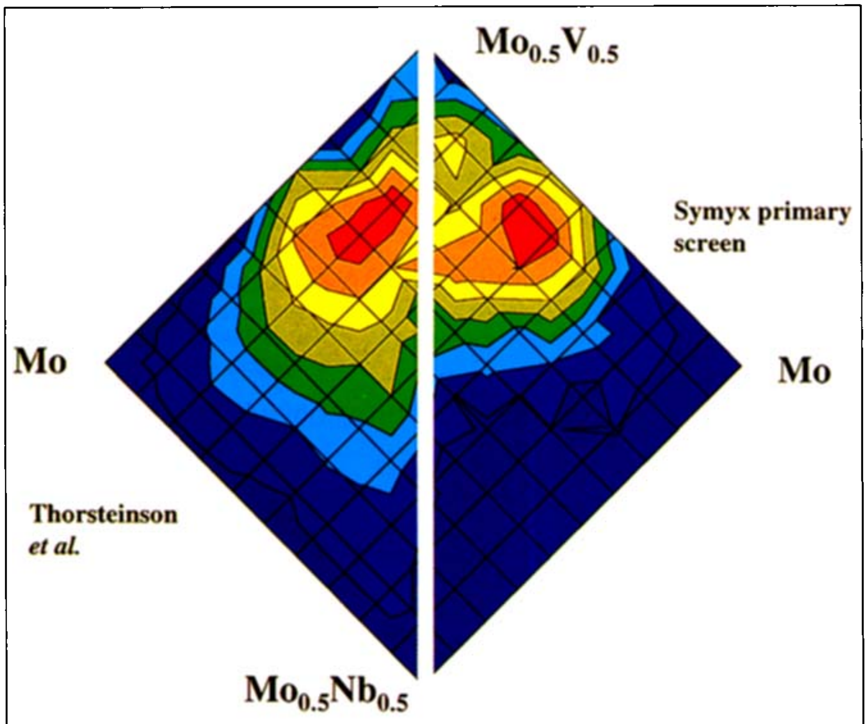

**Figure 1. Conversion of ethane to ethylene over Mo-V-Nb mixed metal oxide catalysts (arbitrary units).**

Mirror images of the Mo rich "quadrant" of the Mo-V-Nb ternary phase space: the left side is work conducted at Union Carbide (Thorsteinson et al., 1978); the right side is from work at Symyx Technologies (Cong et al., 1999).

One can reasonably question whether too much time and effort are being placed on optimization and implementation of known materials, recently discovered or not, as opposed to engaging in activities directed at the *bona fide* discovery of new materials. For example, the ability to generate not just a single material with improved properties, but multiple materials (of different structure and/or composition) with these properties would, no doubt, increase the probability that at least one of these candidates could be integrated successfully into a commercial technology.

Combinatorial chemistry—the technique of creating vast numbers of compounds by reacting a set of components in all possible combinations at once—has been adopted nearly universally by the pharmaceutical industry in their search for new drugs. Over the last decade-and-a-half, this field has matured rapidly and has become rather standardized concerning synthesis (e.g., solution-based routes in 96 and 384-well plates) and screening strategies (e.g., detection of receptor binding by fluorescence). *Combinatorial materials science* seeks to borrow from these *philosophies* developed in the pharmaceutical industry (Gordon et al., 1996), while extending them, and inventing entirely new strategies for the discovery of a myriad of new materials with applications in the chemical and electronics industries.

Synthetic strategies in these industries, unlike pharmaceuticals, vary from thin film methods such as physical and chemical vapor deposition to more traditional bulk techniques and the use of electrochemical methods. Screening strategies can also vary widely, depending on the targeted application of the material. Catalysts are judged by their ability to rapidly convert reactants to products (activity), particularly the formation of the desired product (selectivity). Luminescent materials are judged by their ability to produce a particular spectral output given a specific kind of stimulus—from photons, electrons, or some other source of excitation. A chemical formulation could be judged by its ability to produce a polymer that possesses a specific set of mechanical properties. Thus, a major challenge in combinatorial materials science is the development of not only a diverse set of synthetic strategies, but also screening strategies that can *quickly* assess the chemical, optical, mechanical and electronic properties of large arrays of materials. Clearly, it is far from a simple matter to overlay the techniques and strategies developed for pharmaceutical research and drug discovery to those appropriate for catalysts, polymers, and electronic materials. Indeed, it is impossible. Rather, one must start afresh in developing entirely new technologies.

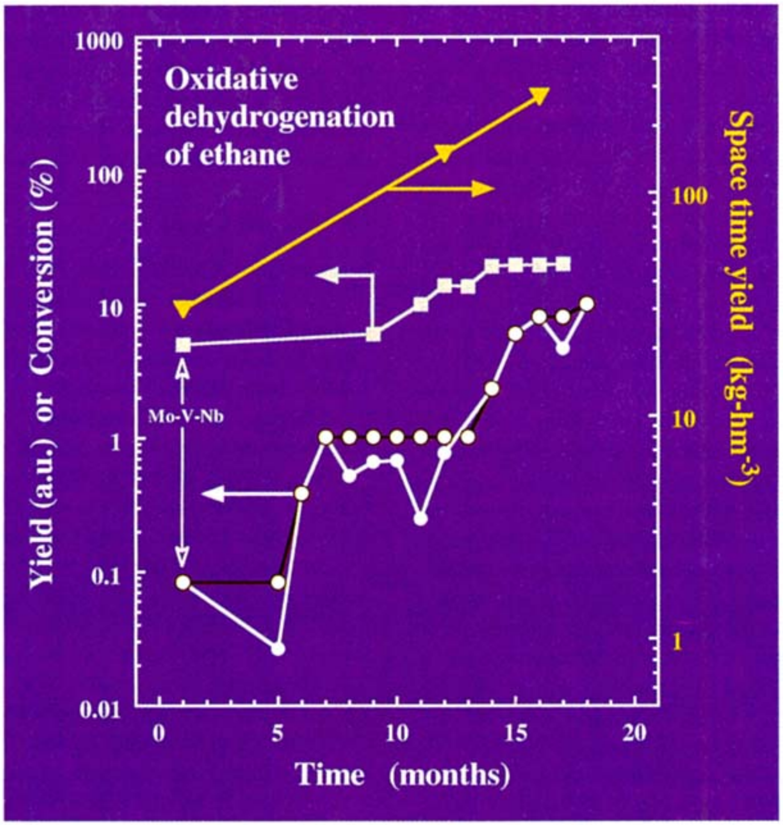

**Figure 2. Progress in catalyst development at Symyx Technologies for the oxidative dehydrogenation of ethane to ethylene using the Mo-V-Nb system as the benchmark.**

Data points in white circles are from the primary screen (conversion in arbitrary units, cumulative best given by black line). Data points in grey squares are from the secondary screen (conversion in %), whereas those in gold triangles represent results (space time yields) produced using bench-scale laboratory reactors.

Work over the past several years strongly suggests that combinatorial approaches to materials discovery will ultimately be successful, leading to significant technological breakthroughs impacting a variety of industries. Peter G. Schultz and colleagues at Lawrence Berkeley Laboratory were the first in 1995 to fully exploit the power of combinatorial materials science, examining high $T_c$ superconductors (Xiang et al., 1995) and giant magnetoresistive materials (Briceno et al., 1995). Their work has spawned a number of other studies, all supporting the great promise of the approach. For example, shortly after this pioneering work, Earl Danielson, Martin D. Devenney, and colleagues at Symyx Technologies began applying the combinatorial approach to investigate luminescent materials from both optimization (Danielson et al., 1997) and discovery (Danielson et al., 1998) points of view. This work (Danielson et al., 1998) led to a *bono fide* discovery, namely an unusual luminescent inorganic oxide, $Sr_2CeO_4$. In the course of work on this and other phosphor materials, these studies led to the demonstration of an important feature of their approach that the photophysical properties of thin film materials (about 1 μm thick and 1 $mm^2$ in area) were equivalent to those obtained from bulk samples synthesized by more traditional means. Recently, complex multicomponent oxides have been investigated by Bruce van Dover and colleagues (1998) at Lucent Technologies using a scheme possessing conceptual similarities to the combinatorial approach and drawing heavily from work conducted by Joseph J. Hanak (1970). In this case, part of a ternary phase diagram was investigated to optimize both the (high) dielectric coefficient and the (high) breakdown field.

In the area of heterogeneous catalysis, infrared thermography has been employed as a gauge of catalytic activity by a number of groups. In a proof of concept study, Richard C. Willson and coworkers at the University of Houston examined a small array (16 elements) of supported single-component catalysts for their activity concerning the oxidation of hydrogen (Moates et al., 1996). This approach (IR thermography) has also borne fruit in the case of homogeneous catalysis, where Steven Taylor and James Morken (1998) from the University of North Carolina at Chapel Hill examined nucleophilic acylation catalysts on encoded polymer beads. From a collection of approximately 7,000 beads, the "hottest" 23 were identified and subsequently decoded, revealing the structure of the most active catalysts. IR thermography has also been employed by the groups of Wilheim F. Maier (Holzwarth et al., 1998) and Manfred T. Reetz (1998), both at the Max-Planck Institut für Kohlenforschung in Mulheim an der Ruhr.

In another proof of concept study, Selim Senkan of the University of California at Los Angeles has employed resonant enhanced multiphoton ionization to examine the catalytic dehydrogenation of cyclohexane to benzene (Senkan, 1998; Senkan and Ozturk, 1999). Finally, Peijun Cong, Shenheng Guan, and colleagues at Symyx Technologies have developed and employed a rapid serial screening technology based on mass spectrometry to examine the oxidation of carbon monoxide by both $O_2$ and NO (Cong et al., 1999a). In the latter case, the use of a discriminating detection scheme (unlike IR thermography), a quadrupole mass spectrometer, permitted an examination of both catalytic selectivity and activity. This is of considerable importance, since, from a commercial point of view, selectivity is often of more importance than absolute activity.

As a final example illustrating the power of the combinatorial approach, we consider heterogeneous catalysts for the oxidative dehydrogenation of ethane to ethylene. Partial oxidation of alkanes represents an important class of reactions in industrial catalysis. The reaction $C_2H_6+{}^1/_2O_2\rightarrow C_2H_4+H_2O$ is favored thermodynamically ($\Delta G^\circ_{rxn}=-30.5$ kcal·mol$^{-1}$), although complete combustion ($C_2H_6+{}^7/_2O_2\rightarrow 2CO_2+3H_2O$), of course, is even more favorable ($\Delta G^\circ_{rxn}=-344.6$ kcal·mol$^{-1}$). Thus, this reaction provides an important test case for the combinatorial approach on both scientific and technological grounds, since an undesirable consecutive reaction must be avoided (unlike the oxidation of $H_2$ or CO by $O_2$).

On the order of 20 years ago, Young and coworkers at Union Carbide (Thorsteinson et al., 1978) investigated this reaction over mixed metal oxides and found that those composed of Mo, V and Nb provided superior performance, particularly at low temperatures (about 200°C), with the composition $Mo_{0.61}V_{0.31}Nb_{0.08}$ being optimum. Supported (on α-alumina) and unsupported catalysts showed similar results. Can a primary screen identify such a "hot" spot in the Mo-V-Nb oxide ternary phase diagram? The answer is a definitive yes! Figure 1 shows the results obtained both by the Union Carbide group and Cong et al. (1999b) using a variant of Symyx's rapid serial primary screen. Due to interfering (electron impact) mass spectrometric fragmentation patterns, an alternative approach was developed for the detection of $C_2H_4$ in the presence of a large background of $C_2H_6$ that is based on the principle of photothermal deflection (PTD) (Cong et al., 1996b). Even though the primary screen represents conversions of less than 0.01%, we see that the two data sets exhibit excellent agreement.

To improve on the Mo-V-Nb system, one should seek to introduce both *complexity* and *diversity*. Along these lines, in any discovery program, combinatorial or otherwise, considerable thought must be placed on *design of the library*—the array or set of materials to be investigated. A simple analysis will bear out the fact that a complete search of phase space (the periodic table) is not practical even using combinatorial approaches. If we designate the factor $P=1/\Delta x$, where $\Delta x$ is the precision in mol fraction and the factor $g$ represents the compound complexity ($g$=2 for a binary, 3 for ternary, etc.), then the number of distinct compositions ($G$) in a library is given by $(P+g-1)!/P!(g-1)!$. Thus, for a ternary with 5% precision, $G=22!/(20!2!)=231$, whereas for a quaternary with 10% precision $G=13!/10!3!=286$. Of course, a discovery program will seek to investigate many possible compounds. Given $n$ elements, there are $N=n!/(n-g)!g!$ possible combinations. Thus, if we restrict ourselves to 25 elements, we need to synthesize and screen $N=25!22!3!=2{,}300$ ternaries. If we form these at 5% precision, the total number of compositions is approximately equal to $N\times G=2{,}300\times 231=531{,}300$ (the exact number is 399,025). One sees that even for modest precision ($\Delta x=0.05$), complexity ($g=3$), and diversity ($n=25$), the numbers get very large and the experimental "boost factor" provided by high throughput combinatorial approaches is required.

In light of these facts, Yumin Liu, Daniel Giaquinta, Robert Doolen, and others at Symyx Technologies have embarked on a discovery program to improve the Mo-V-Nb system for the oxidative dehydrogenation of ethane. Their progress to date is illustrated by the data in Figure 2 obtained from Symyx's primary screen (PTD), secondary screen (packed-bed microreactors), and tertiary screen (bench-scale laboratory reactors). The former are related directly to conversion, whereas the latter are given in terms of space time yields (STY). At the primary screen level, catalyst performance has been increased by a factor of more than 100 in the space of 15 months by virtue of discovery and optimization of entirely new families of catalysts for this chemical transformation. In the larger-scale tests, the STY has been increased by nearly an order of magnitude over the prior state of the art. These results clearly demonstrate the promise of combinatorial approaches to speed the discovery process in a very challenging application.

Although we have focused the discussion on compositional phase space, one can also expect that the processing phase space will also become a target of high throughput experimentation. Successful strategies will involve not only thoughtful synthesis of inorganic and organic compounds, but equally fast screening of their properties using in many cases custom-designed, automated hardware, and evaluation and interpretation of vast data sets by sophisticated software tools. We are still in the early stages of the development of a new approach to materials discovery and optimization based on combinatorial strategies. Although the approach is arguably less than five years old, considerable progress has already been made and clearly one can expect significant discoveries to be made with these methodologies in the areas of heterogeneous and homogeneous catalysts, and polymeric and electronic materials in the very near future.

## Literature Cited

Briceno, G., H. Chang, X. Sun, P. G. Schultz, and X. D. Xiang, "A Class of Cobalt Oxide Magnetoresistance Materials Discovered with Combinatorial Synthesis," *Science*, **270**, 273 (1995).

Cong, P., R. D. Doolen, Q. Fan, D. M. Giaquinta, S. Guan, E. W. McFarland, D. M. Poojary, K. Self, H. W. Turner, and W. H. Weinberg, "High-Throughput Synthesis and Screening of Combinatorial Heterogeneous Catalyst Libraries," *Angew. Chem. Int. Ed.*, **38**, 484 (1999a).

Cong, P., A. Dehestani, R. Doolen, D. M. Giaquinta, S. Guan, V. Markov, D. Poojary, K. Self, H. Turner, and W. H. Weinberg," "Combinatorial Discovery of Oxidative Dehydrogenation Catalysts within the Mo-V-Nb-O System," *Proc. Natl. Acad. Sci. USA*, **96**(20), 11077 (1999b).

Danielson, E., J. H. Golden, E. W. McFarland, C. M. Reaves, W. H. Weinberg, and X. D. Wu, "A Rare-Earth Phosphor Containing One-Dimensional Chains Identified Through Combinatorial Methods," *Nature*, **389**, 944 (1997).

Danielson, E., M. Devenney, D. M. Giaquinta, J. H. Golden, R. C. Haushalter, E. W. McFarland, D. M. Poojary, C. M. Reaves, W. H. Weinberg, and X. D. Wu, "X-Ray Powder Structure of $Sr_2CeO_4$: A New Luminescent Material Discovered by Combinatorial Chemistry," *Science*, **279**, 837 (1998).

Gordon, E. M., M. A. Gallop, and D. V. Patel, "Strategy and Tactics in Combinatorial Organic Synthesis. Applications to Drug Discovery," *Acc. Chem. Res.*, **29**, 144 (1996).

Hanak, J. J., " 'Multiple-Sample Concept' in Materials Research: Synthesis, Compositional Analysis, and Testing of Entire Multicomponent Systems," *J. Mater. Sci.*, **5**, 964 (1970).

Holzwarth, A., H.-W. Schmidt, and W. F. Meier, "Detection of Catalytic Activity in Combinatorial Libraries of Heterogeneous Catalysts by IR Thermography," *Angew. Chem. Int. Ed.*, **37**, 2644 (1998).

Moates, F. C., M. Somani, J. Annamalai, J. T. Richardson, D. Luss, and R. C. Willson, "Infrared Thermographic Screening of Combinatorial Libraries of Heterogeneous Catalysts," *Ind. Eng. Chem. Res.*, **35**, 4801 (1996).

Reetz, M. T., M. H. Becker, K. M. Kuhling, and A. Holzwarth, "Time-Resolved IR-Thermographic Detection and Screening of Enantioselectivity in Catalytic Reactions," *Angew. Chem. Int. Ed.*, **37**, 2647 (1998).

Senkan, S. M., "High-Throughput Screening of Solid-State Catalyst Libraries," *Nature*, **394**, 350 (1998).

Senkan, S. M., and S. Ozturk, "Discovery and Optimization of Heterogeneous Catalysts by Using Combinatorial Chemistry," *Angew. Chem. Int. Ed.*, **38**, 791 (1999).

Taylor, S. J., and J. P. Morken, "Thermographic Selection of Effective Catalysts from an Encoded Polymer-Bound Library," *Science*, **280**, 267 (1998).

Thorsteinson, E. M., T. P. Wilson, F. G. Young, and P. H. Kasai, "The Oxidative Dehydrogenation of Ethane Over Catalysts Containing Mixed Oxides of Molybdenum and Vanadium," *J. Catal.*, **52**, 116 (1978).

van Dover, R. B., L. F. Schneemeyer, and R. M. Fleming, "Discovery of a Useful Thin-Film Dielectric Using a Composition-Spread Approach," *Nature*, **392**, 162 (1998).

Xiang, X.-D., X. Sun, G. Briceno, Y. Lou, K.-A. Wang, H. Chang, W. G. Wallace-Freedman, S.-W. Chen, and P. G. Schultz, "A Combinatorial Approach to Materials Discovery," *Science*, **268**, 1738 (1995).