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VIEWPOINT

The Importance of Phase Equilibria and Diffusion in High-Throughput and Autonomous Materials Discovery

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Abstract Machine learning has accelerated the prediction and screening of crystal structures, while automation has increased the number of compositions and processing conditions that can be explored experimentally. However, identifying a structure near the zero-temperature convex hull or detecting its signature in a synthesis product does not, by itself, establish materials discovery. In this perspective, we argue that finite-temperature phase equilibria and transformation kinetics should guide these eff orts from the outset. CALPHAD, combined with diff usion data, provides a framework for selecting compositions and processing conditions capable of producing the required phase constitution, including metastable states whose formation and persistence depend on the processing path. Rigorous characterization is then needed to establish what was produced and whether its properties and stability meet the intended requirements. Progress should be measured by reproducible processing windows that yield the required phase constitution, microstructure, and properties under manufacturing and service conditions.

Keywords materials discovery · CALPHAD · autonomous synthesis · Phase stability · finite temperature thermodynamics

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More recently, advances in machine learning and automation have extended this paradigm from high-throughput calculation and screening toward increasingly autonomous discovery. Machine-learning-guided crystal-structure searches, such as GNoME, can propose and screen vast numbers of plausible structures and estimate their energetic stability.[[1]] At the same time, autonomous synthesis laboratories, such as A-Lab, integrate artificial intelligence, robotics, and automated synthesis and characterization to produce and test proposed compounds.[[2]] These developments have substantially increased the rate at which hypothetical compounds can be proposed and evaluated. However, these computational approaches commonly assess stability using predicted zero-temperature energies relative to an approximate convex hull. Identifying a hypothetical compound on, or arbitrarily close to, the 0 K ground-state convex hull does not, by itself, constitute materials discovery. Similarly, compounds produced in autonomous laboratories require rigorous structural, compositional, and functional verification before a discovery claim can be made. Virtually generating a potentially stable crystal structure, or synthesizing a compound whose novelty and phase constitution have not been properly established, is not equivalent to discovering a material under finite-temperature processing and operating conditions.

This distinction is important because a crystal structure is not the same thing as a material. High-throughput calculations at the crystal structure level typically represent idealized, periodic, and often fully ordered phases with fixed compositions and few or no defects. Engineering materials, by contrast, exist at finite temperature and pressure, may be compositionally disordered or multiphase, and contain defects, interfaces, residual stresses, and microstructures inherited from arbitrarily-defined processing protocols. Their stability is governed by the Gibbs

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energy (or other relevant potentials, depending on the thermodynamic boundary conditions), including configurational, vibrational, magnetic, and electronic thermally excitable degrees of freedom, and by competition with every relevant phase in the system. A structure on the 0 K convex hull may not remain stable under synthesis or operating conditions, whereas a structure above the 0 K hull may become stable at finite temperature or may be accessible as a metastable state through kinetic stabilization. Zero-temperature screening is therefore useful, but it is not a substitute for knowledge of finite-temperature phase equilibria of a given materials system. CALPHAD (calculation of phase diagrams) provides the practical framework for connecting these predictions to finite-temperature phase stability, processing, and phase constitution.

Autonomous synthesis does not eliminate these considerations. The detection of diffraction peaks (or any other structural signature) consistent with a target structure is only an initial indication of synthesis. A convincing claim of materials discovery should establish composition, phase purity or phase fractions, structural disorder, reproducibility, processing history, and properties relevant to the intended application. It should also determine whether the resulting phase is stable, metastable, or transient under the conditions of synthesis and use. These requirements become especially important when automated platforms employ processing routes that differ substantially from those used in commercial manufacturing.

High-throughput experimentation itself is not new. Combinatorial thin-film libraries, diffusion couples, and diffusion multiples have long been used to explore composition and processing spaces efficiently.[[3,4]] Robotic materials discovery also preceded A-Lab. In 2020, Cooper and coworkers demonstrated a mobile robotic chemist that autonomously performed and evaluated 688 wet-chemistry experiments in search of improved photocatalyst formulations.[[5]] More recent powder-synthesis platforms extend this approach to the synthesis of predicted inorganic compounds. They increase the number of compositions and processing conditions that can be examined, but throughput and automation alone do not make the resulting materials feasible. Open-loop synthesis campaigns conducted without knowledge of the relevant phase equilibria are unlikely to yield materials with the desired phase constitution. They may instead produce phase mixtures, metastable states, or transient products specific to the synthesis route. Phase diagrams and diffusion data are therefore needed to select compositions and processing conditions, design appropriate heat treatments, and determine whether the desired phase constitution can be produced reproducibly.

The treatment of chemical disorder illustrates this problem. Most high-throughput density functional theory (DFT) workflows evaluate stoichiometric, fully ordered structures that can be represented using small periodic cells. Experimental phase diagrams, however, also contain nonstoichiometric phases and solid solutions with finite composition ranges and partial site occupancies. A chemically random solid solution cannot be represented by a single small periodic cell and, in the 0 K limit, will generally order or decompose into lower-energy states. Describing its stability at finite temperature requires a statistical treatment of configurational entropy using approaches such as special quasirandom structures, the coherent potential approximation, or cluster expansions.[[6–8]] Because these treatments are not routinely included in high-throughput screening, a substantial portion of experimentally relevant phase space is either simplified or omitted.

This limitation also affects how predictions are compared with experiments performed at elevated temperature. An ordered structure predicted at 0 K may disorder during synthesis, producing a solid solution with the same parent lattice but a different thermodynamic state.[[9]] Observation of that solid solution does not confirm the stability of the predicted ordered compound. Conversely, a calculation may identify a distinct ordered compound at a composition that lies within a broad solid-solution phase field at the temperature of interest. This distinction is particularly important in high-entropy and compositionally complex alloys, where predictions based on a small number of ordered configurations may not represent the equilibrium phase constitution.[[10,11]] Establishing the relationship between the predicted and observed states requires finite-temperature free energies and an explicit description of the corresponding order-disorder equilibria.

Lab-scale and combinatorial synthesis routes frequently produce metastable or compositionally inhomogeneous products. Thin-film deposition can retain amorphous phases or structures stabilized by substrate strain. Arc melting can leave segregation or incomplete homogenization, and additive manufacturing can preserve phases generated during rapid solidification. The formation of a phase by one of these methods establishes that it is accessible along that processing path. It does not establish equilibrium stability. Its formation, or non-formation, must be interpreted using the equilibrium phase relations, transformation kinetics, and thermal history of the experiment. Post-synthesis heat treatment may be required before the observed phase constitution can be compared with equilibrium predictions.

Phase diagrams should guide the design of high-throughput experiments rather than serve only as retrospective tools for interpreting synthesis products. They identify the relevant phase fields, competing phases, solubility ranges, invariant reactions, and transformation temperatures. Diffusion data provide the time and length scales needed to choose annealing schedules and assess whether local or bulk equilibrium is plausible. This information determines which compositions, precursors, temperatures,

and post-processing treatments should be explored. It also provides a basis for distinguishing a failed synthesis from a kinetically inaccessible target or an incorrect stability prediction. CALPHAD therefore remains an essential element of materials discovery. It identifies the composition-temperature-processing regions capable of producing the required phase constitution and provides the thermodynamic framework needed to direct synthesis, heat treatment, and manufacturing.

In alloy design, CALPHAD calculations can define the feasible region before property optimization begins. A composition that does not provide the required phase constitution, transformation temperatures, solidification range, or heat-treatment window should be excluded even if a property model predicts attractive performance. Earlier studies formulated this inverse phase-stability problem as the identification of composition-temperature regions that satisfy prescribed phase-constitution constraints.[[12,13]] Subsequent work applied constraints on FCC stability and solidification range, together with limits on density and thermal conductivity, to restrict the feasible alloy-design space before optimizing mechanical response. Five design-make-test-learn cycles identified a three-objective Pareto set after sampling only 0.15% of the feasible space.[[14]] Senkov et al. similarly used calculated phases and transformation temperatures to screen more than 130,000 multicomponent systems and select candidates for structural-alloy development.[[15]] In this issue, Endsley et al. applied phase-stability and aluminum-activity constraints to tens of thousands of Nb-Mo-Ti-Al-Hf compositions before synthesis, ultimately identifying alloys that formed continuous, adherent alumina scales at 1400 °C.[[16]] These studies show that phase-equilibrium calculations do not merely explain what was synthesized. Rather, they define the part of composition-processing space in which optimization is physically meaningful.

Even after a feasible phase field has been identified, a predicted crystal structure is not yet an engineering material. High-throughput DFT generally evaluates the zero-temperature energetic stability of a specified periodic crystal structure.[[17,18]] An alloy used in service may instead contain solid solutions, ordered and disordered domains, secondary phases, defects, interfaces, and a processing-dependent microstructure.[[19]] These features often control performance but are absent from the calculation that motivated synthesis. A low formation energy or small distance from the convex hull therefore does not establish that a useful material can be produced.[[20]] The relevant question is whether a practical processing route can generate and retain the required phase constitution and microstructure under manufacturing and service conditions.

Manufacturability imposes another set of thermodynamic and kinetic constraints. An alloy selected for phase stability and properties at its intended service temperature may still have a wide freezing range, form low-melting phases during solidification, segregate strongly, crack during casting or additive manufacturing, or require impractical homogenization treatments.[[21,22]] These are not secondary questions to be addressed after discovery. They determine whether a nominal composition can be converted into a reproducible bulk material. CALPHAD solidification calculations and diffusion simulations can be used to assess solidification paths, cracking susceptibility, and homogenization times.[[21,22]] Process models can then identify operating conditions that avoid keyholing, balling, and lack of fusion during additive manufacturing.[[23]] A phase that can only be obtained as a thin film, quenched droplet, or milligram-scale powder under narrowly controlled laboratory conditions has not yet been shown to be manufacturable.

None of this excludes metastable materials from consideration. Many engineering materials depend on metastable phases or microstructures retained by quenching, deformation, deposition, or other controlled processing.[[24,25]] Their use is possible because the transformation path, kinetic persistence, and limits of the metastable state are understood well enough to define a reproducible processing window.[[24–26]] The same standard should apply to high-throughput discovery. Producing a phase once is not sufficient. The process must reliably generate the required phase constitution at a relevant scale, and the material must retain it during subsequent processing and service.

Throughput alone does not solve the materials-discovery problem. A robotic platform can make more samples per day, but an open-loop search that ignores phase equilibria, diffusion, and manufacturing constraints will efficiently explore compositions that cannot produce the required phase constitution. Automation does not diminish the role of CALPHAD. It makes thermodynamic and kinetic models more valuable by directing experiments toward composition-processing regions in which the desired phase constitution can actually be produced and retained. Automated experiments should then test and refine those regions using characterization sufficient to establish composition, phases, microstructure, and properties. Success should not be measured by the number of structures predicted or samples synthesized. It should be measured by the identification of reproducible processing windows that yield the required phase constitution, microstructure, properties, and stability at a manufacturable scale.

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References

1. A. Merchant, S. Batzner, S.S. Schoenholz, M. Aykol, G. Cheon, and E.D. Cubuk, Scaling Deep Learning for Materials Discovery, *Nature*, 2023, **624**(7990), p 80–85. https://doi.org/10.1038/s41586-023-06735-9
2. N.J. Szymanski, B. Rendy, Y. Fei, R.E. Kumar, T. He, D. Milsted, M.J. McDermott, M. Gallant, E.D. Cubuk, A. Merchant, H. Kim, A. Jain, C.J. Bartel, K. Persson, Y. Zeng, and G. Ceder, An Autonomous Laboratory for the Accelerated Synthesis of Inorganic Materials, *Nature*, 2023, **624**(7990), p 86–91. https://doi.org/10.1038/s41586-023-06734-w
3. X.-D. Xiang, X. Sun, G. Briceño, 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*, 1995, **268**(5218), p 1738–1740. https://doi.org/10.1126/science.268.5218.1738
4. J.-C. Zhao, A Combinatorial Approach for Efficient Mapping of Phase Diagrams and Properties, *J. Mater. Res.*, 2001, **16**(6), p 1565–1578. https://doi.org/10.1557/JMR.2001.0218
5. B. Burger, P.M. Maffettone, V.V. Gusev, C.M. Aitchison, Y. Bai, X. Wang, X. Li, B.M. Alston, B. Li, R. Clowes, N. Rankin, B. Harris, R.S. Sprick, and A.I. Cooper, A Mobile Robotic Chemist, *Nature*, 2020, **583**(7815), p 237–241. https://doi.org/10.1038/s41586-020-2442-2
6. A. Zunger, S.-H. Wei, L.G. Ferreira, and J.E. Bernard, Special Quasirandom Structures, *Phys. Rev. Lett.*, 1990, **65**(3), p 353–356. https://doi.org/10.1103/PhysRevLett.65.353
7. P. Soven, Coherent-Potential Model of Substitutional Disordered Alloys, *Phys. Rev.*, 1967, **156**(3), p 809–813. https://doi.org/10.1103/PhysRev.156.809
8. J.M. Sanchez, F. Ducastelle, and D. Gratias, Generalized Cluster Description of Multicomponent Systems, *Physica A*, 1984, **128**(1–2), p 334–350. https://doi.org/10.1016/0378-4371(84)90096-7
9. A. van de Walle and G. Ceder, Automating First-Principles Phase Diagram Calculations, *J. Phase Equilib.*, 2002, **23**(4), p 348–359. https://doi.org/10.1361/105497102770331596
10. Y. Lederer, C. Toher, K.S. Vecchio, and S. Curtarolo, The Search for High Entropy Alloys: A High-Throughput ab-Initio Approach, *Acta Mater.*, 2018, **159**, p 364–383. https://doi.org/10.1016/j.actamat.2018.07.042
11. R. Feng, P.K. Liaw, M.C. Gao, and M. Widom, First-Principles Prediction of High-Entropy-Alloy Stability, *npj Comput. Mater.*, 2017, **3**(1), p 50. https://doi.org/10.1038/s41524-017-0049-4
12. R. Arróyave, S.L. Gibbons, E. Galvan, and R.J. Malak, The Inverse Phase Stability Problem as a Constraint Satisfaction Problem: Application to Materials Design, *JOM*, 2016, **68**(5), p 1385–1395. https://doi.org/10.1007/s11837-016-1858-5
13. A. Abu-Odeh, E. Galvan, T. Kirk, H. Mao, Q. Chen, P. Mason, R. Malak, and R. Arróyave, Efficient Exploration of the High Entropy Alloy Composition-Phase Space, *Acta Mater.*, 2018, **152**, p 41–57. https://doi.org/10.1016/j.actamat.2018.04.012
14. T. Hastings, M. Mulukutla, D. Khatamsaz, D. Salas, W. Xu, D. Lewis, N. Person, M. Skokan, B. Miller, J. Paramore, B. Butler, D. Allaire, V. Attari, I. Karaman, G.M. Pharr, A. Srivastava, and R. Arróyave, Accelerated Multi-Objective Alloy Discovery Through Efficient Bayesian Methods: Application to the FCC High Entropy Alloy Space, *Acta Mater.*, 2025, **297**, 121173. https://doi.org/10.1016/j.actamat.2025.121173
15. O.N. Senkov, J.D. Miller, D.B. Miracle, and C. Woodward, Accelerated Exploration of Multi-Principal Element Alloys with Solid Solution Phases, *Nat. Commun.*, 2015, **6**(1), 6529. https://doi.org/10.1038/ncomms7529
16. M.A. Endsley, C. McMullin, C.S. Holgate, G.G.E. Seward, A. Suzuki, M. Worku, N.R. Philips, C.G. Levi, and T.M. Pollock, Efficient Design of Quinary Alumina-Forming Refractory Multi-Principal Element Alloys, *J. Phase Equilib. Diffus.*, 2026. https://doi.org/10.1007/s11669-026-01261-3
17. A. Jain, S.P. Ong, G. Hautier, W. Chen, W.D. Richards, S. Dacek, S. Cholia, D. Gunter, D. Skinner, G. Ceder, and K.A. Persson, Commentary: The Materials Project: A Materials Genome Approach to Accelerating Materials Innovation, *APL Mater.*, 2013, **1**(1), 011002. https://doi.org/10.1063/1.4812323
18. C.J. Bartel, S.L. Millican, A.M. Deml, J.R. Rumptz, W. Tumas, A.W. Weimer, S. Lany, V. Stevanović, C.B. Musgrave, and A.M. Holder, Physical Descriptor for the Gibbs Energy of Inorganic Crystalline Solids and Temperature-Dependent Materials Chemistry, *Nat. Commun.*, 2018, **9**(1), 4168. https://doi.org/10.1038/s41467-018-06682-4
19. G.B. Olson, Computational Design of Hierarchically Structured Materials, *Science*, 1997, **277**(5330), p 1237–1242. https://doi.org/10.1126/science.277.5330.1237
20. A. Lee, S. Sarker, J.E. Saal, L. Ward, C. Borg, A. Mehta, and C. Wolverton, Machine Learned Synthesizability Predictions Aided by Density Functional Theory, *Commun. Mater.*, 2022, **3**(1), 73. https://doi.org/10.1038/s43246-022-00295-7
21. S. Kou, A Criterion for Cracking During Solidification, *Acta Mater.*, 2015, **88**, p 366–374. https://doi.org/10.1016/j.actamat.2015.01.034
22. A. Borgenstam, A. Engström, L. Höglund, and J. Ågren, DICTRA, a Tool for Simulation of Diffusional Transformations in Alloys, *J. Phase Equilib.*, 2000, **21**(3), p 269–280. https://doi.org/10.1361/105497100770340057
23. L. Johnson, M. Mahmoudi, B. Zhang, R. Seede, X. Huang, J.T. Maier, H.J. Maier, I. Karaman, A. Elwany, and R. Arróyave, Assessing Printability Maps in Additive Manufacturing of Metal Alloys, *Acta Mater.*, 2019, **176**, p 199–210. https://doi.org/10.1016/j.actamat.2019.07.005
24. Z. Li, K.G. Pradeep, Y. Deng, D. Raabe, and C.C. Tasan, Metastable High-Entropy Dual-Phase Alloys Overcome the Strength-Ductility Trade-Off, *Nature*, 2016, **534**(7606), p 227–230. https://doi.org/10.1038/nature17981
25. A. Inoue, Stabilization of Metallic Supercooled Liquid and Bulk Amorphous Alloys, *Acta Mater.*, 2000, **48**(1), p 279–306. https://doi.org/10.1016/S1359-6454(99)00300-6
26. M. Aykol, S.S. Dwaraknath, W. Sun, and K.A. Persson, Thermodynamic Limit for Synthesis of Metastable Inorganic Materials, *Sci. Adv.*, 2018, **4**(4), p eaaq0148. https://doi.org/10.1126/sciadv.aaq0148

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