# Inverse design in search of materials with target functionalities

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Abstract | Solid-state chemists have been consistently successful in envisioning and making new compounds, often enlisting the tools of theoretical solid-state physics to explain some of the observed properties of the new materials. Here, a new style of collaboration between theory and experiment is discussed, whereby the desired functionality of the new material is declared first and theoretical calculations are then used to predict which stable and synthesizable compounds exhibit the required functionality. Subsequent iterative feedback cycles of prediction–synthesis–characterization result in improved predictions and promise not only to accelerate the discovery of new materials but also to enable the targeted design of materials with desired functionalities via such inverse design.

Technologies are becoming increasingly reliant on the highly specialized properties of unique materials. Think about photocatalysts for reactions such as water-splitting that produce inexpensive and renewable solar fuels, or transparent conductors that make up the 'see-through' electrical contacts in efficient solar cells, touch-screen devices and flat panel displays, or topological insulators (bulk insulators whose surface is a conductor) that may see use in quantum computers. The discovery and/or synthesis of a material that is 50% more efficient than standard cells at converting sunlight into electricity, or batteries with tenfold higher energy density or light-metal alloys that can sustain high aerospace temperatures are some of society's grand challenges that rely on our ability to identify, out of an astronomically large space of possible materials, the few that carry such target, highly specific functionalities.

Materials can be defined by their constituent atoms (as encoded by atomic numbers), composition (stoichiometric or non-stoichiometric ratio of elements) and structure (crystallographic, nanostructure, microstructure or alloy short-range order), that is, ACS. Different materials (including those obtained by different processing conditions, temperatures and pressures) generally have different ACS and thus different electronic, magnetic, mechanical or optical properties. For example, allotropes (compounds with the same atomic identities and compositions but different structures) can have an entirely different colour, conductivity or hardness, as perhaps best illustrated by the allotropes of carbon: diamond, graphite and C<sub>60</sub>. Even the tiniest changes in composition or configuration could alter a superconductor into a magnet, transform a direct-bandgap (that is, light absorbing) semiconductor to an indirect-bandgap material, or convert a topological insulator into an ordinary insulator or a transparent conductor into an opaque insulator. Small changes in composition or configurations could also entirely suppress the enzymatic activity of an active site.

The duality between materials (encoded by their ACS) and the properties of materials (for example, superconductivity, magnetism, optical response, magneto-resistivity, topological insulation and thermoelectricity) is the modern incarnation in natural sciences of the classic body and soul duality in philosophy<sup>1</sup>, which has sprung periodically in and out of philosophical fashion for hundreds of years. As envisioned by Descartes, the body has a position in space, volume, structure and mass, as well as physically measurable properties that are inextricably yet inexplicably connected with the body. Because properties live in certain ACSs and not in others, the fundamental question in solid-state chemistry, condensedmatter physics, metallurgy and organic matter is: can we uncover the 'genetic code' of structure-property (or body-soul) relations?

The properties required to realize a particular device are often known, but the specific materials that harbour such properties are generally unknown and are difficult to identify. The conditions needed for water splitting, the defining qualities of coexisting transparency and conductivity in transparent conductors, and the reason for the coexistence of electrical conductivity and thermal insulation in thermoelectrics are understood in theory, but materials with these ideal properties remain generally unknown. Not surprisingly, materials with functionalities of relevance to technology were often discovered by a combination of intuition-driven trial and error and lucky accidents. Examples include the historic cases of light bulb filament material, penicillin or Teflon, as well as the more recent discoveries of C<sub>60</sub>, oxide superconductors and transparent conductors. However, accidental discovery can have crucial limitations, as target functionalities are difficult to find by accident. The easy-to-find materials were found decades ago, and today, we have to dig far deeper into the space of possible materials to find the specific solids that have the properties we really want. Furthermore, the current culture of such intuition-driven experimental explorations generally involves searching for the right properties in the chemical neighbourhood of known classes of materials, a process unlikely to result in outstanding or unexpected discoveries.

This Perspective reflects the opinions distilled from the author's experience in material design from the first inverse design idea<sup>2</sup> to his founding of the Energy Frontier Research Center (EFRC) (through the US Department of Energy (DOE)), the NSF center on 'Designing materials to revolutionize and engineer our future', and his ongoing work with the Materials Genome Initiative. These research groups all involve theorists and experimentalists working in concert. This article is not intended as a review but as a perspective. The reader interested in

specific chronological referenced details is directed to more specialized articles cited throughout this article.

#### Obstacles to deliberate discovery

One might wonder why the deliberate discovery of materials with specific properties has been so slow to come and difficult to accomplish. Identifying the obstacles that have contributed to the slow discovery of materials with target functionalities would clarify the rationale behind the types of strategies later adopted to overcome them. This analysis has led to the identification of seven major obstacles, described in the seven sections below.

Incremental improvements. The traditional use of functional materials has often focused on incremental improvements of the first discovered material, rather than on the search of more appropriate materials. This common approach for researching new compounds with specific functionalities might sometimes keep us away from the right material. An example is given by recent developments in materials for photovoltaic solar cells. Thin-film solar cell absorbers, such as CuInSe<sub>2</sub>, have now reached ~20% efficiency, with slow incremental increases on the order of 0.1–1% per year in each of the  $\sim$ 35 years of government investment<sup>3</sup>. However, a long-ago synthesized but unappreciated class of hybrid organic-inorganic halide perovskites  $AM^{IV}X^{VII}_{3}$  (where A is a small organic molecule, M<sup>IV</sup> is a group-IV metalloid and X<sup>vII</sup> is a halogen) was reconsidered recently by the photovoltaics community, enabling rapid progress from an initial 4% efficiency in 2009 to 22% only 7 years later<sup>4</sup>. It is possible that the initial slow progress in this field was partially due to the early decision to work with a given compound (such as CuInSe<sub>2</sub>) and incrementally improve its performance through a slow learning curve, rather than scan a broad range of compounds, searching for those that satisfy at least the minimum required properties. One might wonder how many other photovoltaic materials we have not found yet and, in general, how we can improve our traditional approaches to the selection and identification of materials with desired target properties.

*Missing data*. A number of physical properties of most synthesized materials are still unknown, a situation that limits our ability to select the right materials for a given function. MgB<sub>2</sub>, for example, has

long been known, but its superconductivity has only recently been recognized<sup>5</sup>; CuAlO<sub>2</sub> (delafossite) is a known mineral, but its transparent conductivity was discovered only a few years ago<sup>6</sup>. Not knowing the basic properties (optical, magnetic and/or mechanical) of the vast majority of already synthesized materials poses a serious obstacle to their use in groundbreaking technologies.

Quantum mechanical calculations are now helping us unravel previously unreported properties of synthesized materials. Many properties of known materials are now reported in material databases7and experimental compilations<sup>10,11</sup>, which are then used to sift through the data and discover previously unknown and interesting properties in known materials. Computational approaches have helped, for example, in the prediction of promising photovoltaic functionalities in previously known halide perovskite, with unappreciated physical properties12, and CuBX absorbers (in which B and X are group-V and group-VI elements, respectively<sup>13</sup>). Density functional theory (DFT) calculations by Cedar and co-workers screened thousands of cathode materials and identified and experimentally verified several of them, including a monoclinic form of LiMnBO<sub>3</sub> (REF. 14), layered  $\text{Li}_9\text{V}_3(\text{P}_2\text{O}_7)_3(\text{PO}_4)_2$  (REF. 15) and Cr-doped LiVO, (REF. 16). DFT calculations have been useful for the identification of thermoelectric materials17 and Mn<sub>2</sub>V<sub>2</sub>O<sub>7</sub> as a photocatalytic material for water splitting<sup>18</sup>. Experimental characterization within the same study confirmed a stable photocurrent at high pH but also revealed that a co-catalyst is needed for efficient oxygen evolution. Jain et al. provided a comprehensive table of DFT predictions of energy-related materials that have been confirmed by experiments18.

*Unknown compounds.* There are many compounds that have never been synthesized before but that appear to be chemically plausible. These unreported compounds may exhibit properties useful to technological developments. Studies of fundamental physicochemical properties, such as electronegativity or phase-transition behaviour, have generally focused on known compounds<sup>10,11</sup> and exclude numerous unreported but chemically plausible compounds. For example, some of the compounds belonging to the 1:1:1 class (including the half-Heusler subgroup, such as LiZnP) exhibit novel properties, such as thermoelectricity and piezoelectricity, and some of them can be used as transparent conductors or topological insulators. However, only 83 out of 483 possible compounds have been reported so far, and several  $8e^-$  and  $18e^-$  filled ABX tetrahedral structures have still not been synthesized<sup>19–21</sup>. A similar outcome of unidentified materials might also be expected in other leading groups of electronic and energy materials, such as  $ABX_2$ ,  $A_2BX_4$ ,  $ABX_3$ and  $A_3BX_4$ .

Finding 'missing compounds' could be important for a couple of reasons. First, our current formulation of physicochemical rules and trends reflects deductive reasoning, naturally based on the behaviour of known compounds. Discovering the structures and properties of currently unreported compounds (should they exist) could improve or even alter our understanding of the nature of physicochemical rules and trends. Second, the search for unreported materials can lead us to additional surprising discoveries. Indeed, the history of solid-state chemistry and materials science suggests that new compounds that have eluded synthesis for a long time either represent materials on the verge of some interesting metastability or require a non-intuitive set of growth conditions. Such complex and difficult to make materials often end up driving new science. For example, a recent study<sup>21</sup> predicted that compounds composed exclusively of heavy elements, such as TaIrGe, that had never been made before can have large bandgaps (TaIrGe is, in fact, transparent and conductive) in defiance of the standard expectation that heavy element compounds have small bandgaps (and are optically opaque). Finding new compounds, however, may not be easy. An unreported ACS can, in principle, appear in any of a large number of crystal structures, as illustrated in FIG. 1. Finding which of these structures is stable (red frame in FIG. 1) or exhibits an interesting, non-trivial property is challenging.

Material design based on quantum mechanics techniques is now making a difference in predicting unknown compounds that are stable and have interesting properties. Many compounds that have never been synthesized before have recently been predicted to be stable and synthesizable<sup>12-22</sup>, dozens of which have actually been made and tested, including new 18e<sup>-</sup> ABX compounds<sup>19</sup>, energy-related semiconductors<sup>18</sup> and semiconductors with indirect bandgaps (such as some ternary metal pnictides), which are promising in

Figure 1 | Theoretical prediction, experimental synthesis and characterization of previously unreported compounds belonging to the 18e-**ABX group. a** | Theoretical predictions have been used to scrutinize the chemical space of 18e<sup>-</sup> ABX compounds and select potentially stable space groups and structures that need to be examined. For the previously unreported compound TalrGe, the AgMgAs-type structure (F-43m space group, highlighted by the red frame) was found to be the most stable among other ABX structures as well as with respect to its possible decomposition products. A further theoretical model of optical transparency and creation of free carriers was then used to filter the stable compounds that are likely to also be transparent conductors. Transparency is expected for compounds with band structures featuring large interband transition energy gaps, whereas the propensity for the creation of free charge carriers is based on the existence of defects that induce the low-energy formation of charge carriers, such as Ge-on-Ta anti-site defects<sup>19</sup>. **b** | X-ray (left) and transmission electron microscopy (right) confirmations of the experimental isolation of the TalrGe structure following theoretical prediction. c | Measured transmission spectra (left) and images of the quartz substrate and TalrGe film illustrating its transparency (right)<sup>21</sup>. Hole conductivity was found with a remarkable mobility of 2,750 cm<sup>2</sup> sec<sup>-1</sup>. Parts **b** and **c** are adapted from REF. 21, Macmillan Publishers Limited.

photovoltaic devices<sup>22</sup>. It is particularly interesting that all such unexpected discoveries of relevant functionalities arise from the domain of previously unknown compounds that are now predicted to be stable, highlighting the need for theoretical searching tools. However, we have barely scratched the surface here, as only a small percentage of the missing compounds has been found.

Artificial nanostructures. Low-dimensional materials offer, in principle, an astronomically large space of potentially useful new compounds, but only a tiny fraction can be practically made.  $\mathcal{O}(10^5)$ inorganic compounds, known to be thermodynamically stable or weakly metastable in bulk<sup>10,11</sup>, can be combined to generate a vast number of artificial configurations. Furthermore, 0D, 1D or 2D building blocks<sup>23-25</sup> can be stacked by means of molecular beam epitaxy (MBE)<sup>25</sup>, focused ion beam or nanolithography, or by positioning individual atoms on a substrate by a scanning tunnelling microscope (STM) tip<sup>23,24</sup>, leading to new structures. Examples are the magnetoelectric multiferroic (LuFeO<sub>3</sub>)/(LuFe<sub>2</sub>O<sub>4</sub>) 2D superlattice<sup>26</sup>, zinc-blende (ZB)/wurtzite (WZ) superlattice





Theoretically stable











Figure 2 | **Examples of artificial structures that can be grown. A** | Layer-by-layer stacks of two (or more) 2D building blocks (here, LuFeO<sub>3</sub> and LuFe<sub>2</sub>O<sub>4</sub>) creating an almost arbitrarily selected 'genomic sequence'. The electron microscopy image of LuFeO<sub>3</sub>/LuFe<sub>2</sub>O<sub>4</sub> superlattice has been recorded along the [100] direction of LuFeO<sub>3</sub> (REF. 26). **B** | A 1D heterostructure made of different types of zinc-blende (ZB) and wurtzite (WZ) (REFS 27.28). **C** | Cross-sectional STM image of quasi-0D self-assembled lnAs quantum dot grown on 311B lnGaAs (part **Ca**) and capped by GaAsSb (part **Cb**) (REF. 29). Each configurational modification of such 2D, 1D or 0D structures could have different properties (such as optical absorption). Part **A** is adapted from REF. 26, Macmillan Publishers Limited. Part **C** is adapted from Ulloa, J. M. et al. Effect of a lattice-matched GaAsSb capping layer on the structural properties of lnAs/lnGaAs/lnP quantum dots. *J. Appl. Phys.* **107**, 074309 (2010), with the permission of AIP Publishing (REF. 29).

nanowire27,28 and InGaAs-capped and GaAsSb-capped InAs QDs29 as depicted in FIG. 2. Other examples include Si-Ge superlattices, which are produced by the layer-by-layer MBE growth of target sequences of Si and Ge layers. After the concerted opening and closing of the shutters of the Si and Ge growth chambers, the temperature is lowered so that atomic diffusion is kinetically forbidden<sup>25</sup>. These types of artificially grown structures are often globally thermodynamically metastable, because a specific layer sequence is forced during high-temperature growth by opening and closing shutters that release certain atomic species and then quenched to low temperatures at which atomic diffusion is rather slow<sup>25</sup>. However, such superstructures can be long-lived because once cooled to low temperatures, there are considerable kinetic barriers for atoms to diffuse and arrange into more stable structures<sup>25</sup>. Some of these artificial metastable structures have been found to exhibit exciting new physics quantum Hall effect<sup>30</sup> or Coulomb and spin blockade<sup>31</sup> — that could be used in technologies such as transistors and lasers. What makes such superstructures interesting is that often their intrinsic interfaces manifest properties that are absent in their constituent building block compounds. For example, even though bulk LaAlO<sub>3</sub> and SrTiO<sub>3</sub> are insulators, the LaAlO<sub>2</sub>/SrTiO<sub>2</sub> interface is conducting<sup>32</sup>. Therefore, one wonders whether genomic design (for example, the selection of sequence-controlled superlattice configurations) can lead to smart materials that Mother Nature did not make. The problem is that even restricting ourselves to two building blocks

(such as Si and Ge) and to the simplest structures — 2D superlattices — there are  $\mathcal{O}(2^N)$  stacking variants, with the number of layers *N* varying from 100 to 100,000. The astronomically high number of possible configurations makes it practically impossible to find, in an exhaustive manner, the right sequence of components by treating one case at a time. Indeed, even high-throughput computational or combinatorial growth techniques could not establish exhaustive databases of so many variants. So how are we going to find this needle in the combinatorial haystack?

Material design is making a difference in designing layer sequences in superstructures with target properties. The combination of quantum mechanics with evolutionary algorithms, discussed below, is now identifying such artificial superstructuresthat feature different properties from their individual building blocks. Remarkably, this can be done by calculating only a tiny fraction of all possibilities. Liu et al.33 have shown that the CdTe/InAs interface is a topological insulator despite its components being non-topological semiconductors. In addition, 2D superlattices<sup>34</sup> or 1D coremultishell quantum wires<sup>35</sup> characterized by a desired direct gap (that is, strongly absorbing) can be made by combining indirect-gap semiconductors (that is, weakly absorbing) such as Si and Ge. Other unsuspected direct-gap Si structures were designed in REFS 36–38, and a guaternary InAs/GaSb ordered alloy exhibiting absorption in the mid-infrared spectral region (~300 meV) needed for imaging has also been proposed<sup>39</sup>. Theoretical predictions have identified a complex Si-based superstructure that maximizes the conduction band valley splitting, useful

for quantum computer applications<sup>40</sup>, and the layer sequence of PbTiO<sub>3</sub> and SrTiO<sub>3</sub> that produces a superstructure with an electrical polarization far higher than that of its constituents<sup>41</sup>. It is unlikely that we could discover any of these unsuspected and non-intuitive configurations by treating one case at the time or using conventional pencil and paper physics. Indeed, the use of search and optimization methods has proved necessary.

#### Counterintuitive combinations of

properties. Technological applications often demand compounds with what would appear to be a counterintuitive combination of two or more properties. Such compounds harbouring what appears as contradicting attributes are rather difficult to identify and discover. For example, compounds that can photocatalyse water splitting into O<sub>2</sub> and H, for the production of renewable fuels need to satisfy a set of complex conditions regarding the location of their valence and conduction band edges with respect to a fixed set of redox potentials42. However, such conditions invariably lead to materials with a valence band edge that is high in energy, rendering the compound prone to photocorrosion<sup>42</sup>. Another example is provided by the transparent conductors<sup>43</sup> used in see-through metallic contacts for flat panel displays, as these conductors need to be optically transparent (that is, have a large energy bandgap) but also electrically conductive (that is, have high carrier concentration, which generally requires low bandgaps). Furthermore, normally transparent materials, such as transparent glasses, tend to be insulators, whereas metallic conductors, such as

copper, tend to be opaque. Extraordinary and rare exceptions of transparent conductive substances, such as In<sub>2</sub>O<sub>2</sub> (bixbyite) doped with Sn (REF. 44) and CuAlO<sub>2</sub> (delafossite)<sup>6</sup>, were discovered accidentally and are non-optimal in terms of performance parameters. Another example of contraindicated yet useful properties is illustrated by photovoltaic absorbers: optimal photovoltaic materials require the coexistence of strong optical absorption (associated with parallel energy bands in wavevector space or, better, flat energy bands that have a high joint density of states) and high carrier mobility (requiring dispersed energy bands that have, instead, light effective masses)13. These conditions are basically contradictory. Yet another illustration is that thermoelectric materials require the coexistence of high electrical conductivity (normally associated with structurally perfect metallic compounds) and large thermal insulation (normally created by structural imperfections that block phonon transport); again, these properties are generally contradictory in crystalline matter and exist, to some extent, in nanostructured narrow-gap semimetals, such as PbS-SrS-CaS (REF. 45). One might be tempted to conjecture that materials that have internally contradictory properties would be prime candidates for interesting technological applications that depend on unusual functionalities. Finding materials that harbour such rare combinations of essentially contradictory properties represents a difficult problem that cannot be solved by the traditional trial and error search of compounds, as it instead requires deliberate design.

Material design can play an important role in identifying rare compounds that harbour nearly contradictory traits. By combining quantum mechanics with a hierarchical set of functionality filters applied to large ensembles of a candidate material, a small number of unique bulk compounds manifesting almost contradictory but technology-crucial properties were predicted. These include thermochemical water splitting compounds46; high-performance thermoelectric compound SnSe (REF. 47); new classes of transparent hole conductors<sup>21,48–51</sup>, such as the unusual  $d^5$ system Li-doped Cr<sub>2</sub>MnO<sub>4</sub> (REF. 48) or the metallic ceramic Ba<sub>3</sub>Nb<sub>5</sub>O<sub>15</sub> that is transparent<sup>51</sup>; and a new class of Cu-B-X bulk photovoltaic absorbers13,22. Many of these predictions await experimental testing. However, the strategy of using theory to

reduce an enormous space of possibilities to just a few best-in-class candidates promises to considerably accelerate the traditional experimental process of discovery.

Defect induced functionalities. Materials in which extraordinary properties are defect induced are particularly difficult to define and design. Semiconductor technology has taught us that the presence of an extremely small number of lattice defects or the addition of a tiny amount of dopant can drastically change the material properties, instilling conductivity in insulators or recombination centres in crystals with perfect carrier transport<sup>52</sup>. This explains why costly chemical purification techniques (attempting the removal of unwanted impurities) and deliberate doping techniques (attempting the introduction of desired impurities) are such a central part of semiconductor technology. Would it be possible to design not only perfect crystals with target properties but also defects and dopants that deliver target functionality?

Material design is also starting to provide important contributions to the area of impurities by design. Recent theoretical approaches treat impurities and dopants not just as perturbations to the theory of perfect crystals but as new compounds in their own right, thereby allowing design. The recognition of particular clusters of N cluster impurities in light-emitting GaP that would deliver target energy and target strain for the ensuing bandgap levels53 is one such example that was distilled theoretically via generic algorithms from millions of candidate configurations. Another example is the identification of the configuration that Mn impurities should take in GaAs host crystal to create the highest predicted ferromagnetic Curie temperature, to the benefit of spintronic technologies<sup>54</sup>. Indeed, we have barely scratched the surface of the emerging field of impurities by design.

*Methodological obstacle.* Theoretical approaches that are independent of materials make it difficult to look for target materials. Model Hamiltonian approaches in condensed-matter physics<sup>55</sup> generally do not provide information on the identity of a system (its ACS) in which a given predicted effect will 'live', posing a methodological obstacle to the design of materials that exhibit said effects. In the model Hamiltonian approach, one specifies as input a set of preselected effective interactions (such as nearest-neighbour hopping integral, interelectronic Coulomb repulsion, strength

of spin-orbit coupling or nearest-neighbour atom-atom potentials) and produce as output the physical effect or property P set-up by such selected Hamiltonians. Model Hamiltonian approaches include Ising<sup>56</sup>, Hubbard57, Heisenberg58 and wavevectormomentum expansion<sup>59</sup>, to name a few. This generally results in a 'property diagram', mapping P in the space of the assumed interaction type, such as Coulomb repulsion or strength of spin-orbit coupling<sup>60</sup>. This approach provides deep conceptual understanding of new physical effects as a result of a postulated set of assumed effective interactions. It tells us which output properties are, in principle, possible for a given scenario of input effective interactions but does not guide the search of elements or compilation of compounds that exhibit such effects. Because the effective interactions used as input are generally not expressible (or mappable) in terms of the periodic table, there is generally no recognizable rational path between model Hamiltonian predictions and the realization of actual materials. In other words, the theory is not invertible. In addition, because the total electron and ion energy of the system is generally not computed or optimized with respect to the structural degrees of freedom, it is difficult to assess whether the predicted properties (such as exotic superconductivity and quantum spin liquids) will be found in stable (or nearly stable) recognizable compounds. Successful exceptions are few and include the model Hamiltonian realization that the previously known band-inverted HgTe quantum well in the CdTe barrier is in fact a topological insulator with new implications on the nature of its edge states61.

The way that contemporary material design science is addressing the seven obstacles and difficulties described in the seven sections above is discussed below.

#### Direct versus inverse design

The conventional approach to the discovery of materials with target properties generally involves studying experimentally and explaining theoretically the properties of a given material. Using this so-called direct approach involves the use of the three descriptors of a material (atomic identities, composition and structure, or ACS) as input to derive the ensuing material properties P(ACS) (symbolically (ACS) $\rightarrow$ P(ACS)) (see FIG. 3). Generally, in this 'function follows form' approach, there is no deliberate attempt to obtain a desired target functionality P(ACS) outcome. The

direct approach can be performed in a high-throughput mode or one compound at a time. The graph in the bottom part of FIG. 3 illustrates existing compounds (blue squares) with atomic numbers  $Z_{A}$  and  $Z_{B}$ , known composition and structure, and chemically plausible but so far unreported compounds (question mark area). The contour plot in the upper part of FIG. 3 schematically represents the variation of a certain physical property as a function of the material atomic identities, composition and structure in the bottom part. In the direct approach, the material search moves from the bottom graph to the upper graph, building a database of materials7-11. This computational analogue of combinatorial chemistry enables the identification of previously known materials with hitherto unrecognized (or not measured) properties from a database of known compounds.

What we often really would like to have is an inverse approach to material deign (hence, inverse design), in which the desired target properties are used as input to predict the ACS that exhibits them (symbolically  $P(ACS) \rightarrow (ACS)$ ). In this 'form follows function' inverse design philosophy, one guides research in a deliberate effort to identify a wanted target functionality ('functionality-first', a term coined by Walter Kohn in one of our many conversations) and necessarily works with ensembles (ACS) of possible materials. The focus is hence on search and optimization strategies, rather than on the creation of databases of general materials and general properties per se.

An illustration of the direct and inverse approaches is provided by the structure versus spectra problem in quantum dots. 0D epitaxialy grown nanostructures are generally made of a core quantum dot of a given shape, composition and size embedded in a matrix material of given composition. FIGURE 2c illustrates a cross-sectional STM image of an InAs QD capped by GaAsSb matrix<sup>29</sup>. Unlike the case of discrete molecules, these nanostructures can be made in a huge range of quasicontinuous shapes and sizes, with different types of matrix materials. Furthermore, each of these nanostructures would have its own characteristic spectroscopic fingerprints, such as a discrete series of ultrasharp excitonic emission lines consisting of single excitons and bi-excitons, as well as charged multi-excitons<sup>62</sup>. Given a particular sequence of sharp excitonic emission lines (referred to as a spectroscopic bar code<sup>63,64</sup> for an optical encryption or single photon application<sup>65</sup>), it would be useful to know

what shapes and sizes of quantum dots and matrix materials would give rise to this spectroscopic barcode. The direct approach may not be practical because it involves the synthesis and spectroscopic characterization of many nanostructures. Potentially more useful is the inverse approach, whereby one calculates the spectroscopic barcodes of a few nanostructures and uses this information to design one with a target barcode. The latter approach was demonstrated by Mlinar et al.63,64 using an atomistic, many-body theory of spectra, which, when combined with a Bayesian data reduction algorithm, enabled learning of the structure-property landscape and prediction of target nanostructures. Interestingly, computing just ~10-15 excitonic barcode lines of ~200 different nanostructures sufficed to identify - out of a far larger potential set of thousands of nanostructures — the nanostructure sizes. shapes and compositions most likely to produce a given target barcode64. This result provides an optimistic outlook on our growing capability to invert a spectroscopic signature of a rather complex, correlated many-body problem of multi-excitons in nanostructures to the benefit of directing the synthesis of nanostructures with given spectroscopic signature.

#### Approaches for direct design

Theoretical material-dependent approaches can be classified on the basis of three ways in which they complement experimental observations.

- Descriptive approaches. Most common joint theory-experiment publications pertain to cases where theory and models are used to interpret existing observations. Theoretical approaches here are largely 'postictive' not predictive.
- Predictive approaches. This approach predicts previously unreported behaviours of a material. Most often, this focuses on a given system or a narrowly defined group of systems.
- Predictive approaches for the discovery and design (D&D) of materials via consideration of ensemble of systems. Here, predictions involve navigation through non-trivial ensembles and, generally, a non-intuitive space of possibilities in search of the ACS with the target functionality. One explores both existing and missing materials, those with known or unappreciated properties, artificially grown (locally stable but globally metastable) or thermodynamically grown bulk materials while looking

for ACSs that have a target functionality (even contraindicated). This D&D approach represents the main focus of this Perspective and, along with material-dependent predictive approaches, is the essential factor enabling transformative changes in the science of new functional materials.

#### Material-dependent quantum approaches. Unlike model Hamiltonian theories in which the chemical identity of atoms in solids is relinquished in favour of describing interactions between electrons, spins and so forth, explicitly material-dependent approaches in condensed-matter physics represent a return to atomism. They specify as input the ACS descriptors with full atomistic resolution and consider only Hamiltonians that are capable of explicitly recognizing the 'chemical personality' of the system. By this, we mean that the Hamiltonian specifies the electron-ion potential, $V_{\text{ext}} = -\Sigma Z_{\alpha}/(r-R_{\alpha})$ , defined by all atoms of type $\alpha$ of atomic number *Z* located at lattice sites (*r*-*R*), thus explicitly accounting for ACS. Such approaches give access to the properties that emerge from a given ACS and the total (ion and electron) energy $E_{tot}(ACS)$ , enabling assessment of the thermodynamic stability of the assumed ACS (hence, possible refinement of the results by seeking the properties of more stable structures). Examples of this class of material-dependent theories with atomic resolution include DFT, as well as higher-level theories that include, to various degrees, dynamic correlation effects, such as DFT-DMFT (dynamic mean field theory)66 and DFT-QMC (quantum Monte Carlo)<sup>67</sup>. Although the insistence on a realistic description of the material via its actual ACS may create apparent complexity, understanding the underlying physics can be achieved by mapping the numerical results of the ACS-based calculation on simpler models, without scarifying realism. Examples include mapping the DFT total energy calculations of many crystal structures and compositions on a generalized cluster expansion68, in which the interatomic interactions are not assumed but rather derived from the mathematical mapping process of the ab initio total energies itself. Another example is the mapping of dynamic displacement models onto model Hamiltonians that can be conveniently used for understanding ferroelectricity<sup>69</sup>. Such approaches to the direct problem benefit from both chemical realism and the ability to explain the final result in reasonably simple, pedagogical terms. As usual, any such

theoretical approach can be limited by the underlying accuracy of the description of interelectronic interactions, such as accuracy of currently known exchange and correlation energy functionals in DFT.

#### Direct evaluation of properties via fast

but approximate learning from prior data. Evaluating the P(ACS)s for each material can be computationally expensive either because the property is a complex quantity (that is, superconductive critical temperature, defect-related energy and photovoltaic efficiency) or because numerous material configurations need to be considered. As the size of the available data sets (calculated or measured) of compounds and their corresponding properties is constantly increasing, one wonders if it is possible to use previous calculations to approximate the value of a property of a new material without directly measuring or calculating it. This can be done by machine learning<sup>70-73</sup> or by cluster expansion<sup>74–75</sup>. These approaches are useful in both direct and indirect approaches, when access to a large number of cases is needed.

Machine learning provides a set of strategies based on distilling approximate property evaluations from prior (experimental or calculated) data. In this case, the prediction of target properties, without calculating all of them, requires constructing data sets of materials and their calculated and/or measured properties and identifying factors (often called features, fingerprints or descriptors) that are proved or hypothesized to have a causal correlation with the target property. Such factors can assume the form of understanding-based physical models (or even a derived formula) showing how a given property depends on a particular descriptor (also called design metrics). Alternatively, the factors can be heuristic features for which causal relationship to the property currently does not exist (features). Examples of the first class of design metrics are quantitative models for photovoltaic efficiency based on optical properties (spectroscopic limited maximal efficiency<sup>22</sup>) and the ratio of average power factor to grain size for nanothermoelectrics76. Examples of the second kind represent a continuum of intuitive chemical properties derived from heuristic constructs<sup>71–73</sup>, such as various scales of electronegativity and atomic sizes. Finally, the properties are mapped to features of known materials by means of machine-learning algorithms (that is, classification of current knowledge). Once this classification step is complete, this method is applied to materials outside the data set, thus providing many more property values P(ACS) than originally available.

Early examples of the use of machine learning for the search of materials with target properties include the diagrammatic classification and prediction of different crystal structures of octet and non-octet



Figure 3 Direct and inverse approaches for the design of materials. The bottom graph shows the possible compounds that can be formed from components with atomic numbers  $Z_A$  and  $Z_B$ . The blue squares represent existing compounds of known composition and structure, whereas the question mark area represents chemically plausible but so far unreported compounds. The contour plot in the upper graph schematically represents the variation of a certain physical property as a function of the atomic identity, composition and structure of the material, given in the bottom part. In the direct approach to material design, all compounds depicted in the bottom graph are investigated, and for each, the presence and extent of a certain property and/or functionality are calculated. In functionality-directed material discovery or inverse design, only those compounds with the target (or maximal) functionality are investigated. R. Henning is acknowledged for assistance with this figure.

### PERSPECTIVES

compounds via chemical properties, such as electronegativity and size (Mooser and Pearson<sup>77</sup>), pseudopotential orbital radii<sup>78</sup> or Pettifor numbers<sup>79</sup>. Modern applications to multivariable diagrammatic classification can be found in REFS 70–73 and provide predictions of values for cases not included in the training data set.

Another useful approach is offered by cluster expansions of P(ACS). When the calculation of the physical property arising from a particular structure becomes computationally expensive, such as in the case of ferromagnetic, superconducting or ferroelectric transition temperatures of multicomponent systems, a broad configurational search of millions of candidates is not practical. Indeed, even binary A–B systems with N atomic sites per cell can result in  $M = 2^N$ configurations. This problem can be addressed by parameterizing the directly calculated properties of a set of *n* << *M* input configurations ( $S_i$ , with i = 1, ..., n) in terms of configuration variables (cluster expansion<sup>74–75</sup>) representing the contribution of various multisite interactions (for example, pairs, three-body and four-body) to the property. The expansion is mathematically exact74 if all *M* coefficients are retained. In practice, convergence with respect to the number of terms included is examined and crossvalidated, and in many cases, about 50-100 coefficients suffice. Once established and cross-validated, this expansion allows one to search almost effortlessly the properties of a few million arbitrary configurations. This approach can also be applied to search for the configuration of dopants in solids, not just for ideal pristine bulk solids. An example is the arrangement of Mn impurities in a GaAs host crystal that results in the highest ferromagnetic Curie temperature obtained by cluster-expanding the Curie temperatures of a set of ~50 accurately calculated configurations and applying the expansion to millions of other configurations<sup>54</sup>. Cluster expansions have been used to identify a special sequence in a ferroelectric PbTiO<sub>3</sub>/SrTiO<sub>3</sub> superlattice that has a considerably larger polarization than what would be expected from interpolating the polarization of the constituents<sup>41</sup>. Cluster expansion predictions are naturally compared with direct DFT calculations as part of the method, so accuracy is demonstrated, thus assuring us that the predictions can be used to replace direct calculations. Such comparison between predictions

#### a Modality 1: cubic Si in SiGe Atomic configuration 9,000 3,000 4,000 5,000 0 1.000 2.000 6.000 7.000 8.000 Barrier z [001] 8 6 VS (meV) Si well 4 Barrier 2 Substrate 100 200 300 400 GA generation **b** Modality 2: halide perovskites [M]<sup>+</sup> = Ammonium [DEA]MX [DA]MX<sub>3</sub> [GA]MX [MA]MX [Cs]<sup>+</sup> = Caesium [Cs]MX [HA]MX **FMIMX** [FA]MX [EA]MX [M]MX [HA]<sup>+</sup> = Hydroxylamine Materials [DA]<sup>+</sup> = Diamine [MA]<sup>+</sup> = Methylammonium [FM]<sup>+</sup> = Formamidium Stability ΠH [FA]<sup>+</sup> = Formamidinium [EA]<sup>+</sup> = Ethylamine Bandgap [GA]<sup>+</sup> = Guanidine amine [DEA]<sup>+</sup> = Dimethylamine m\_\*, m\_\* Pb Br Cl M Exciton Selected Abandoned bindina Sn Defect Ge tolerant Lead free c Modality 3: 18e<sup>-</sup> ABX A B X II- X -VI I- X VII III- X -V IV- X -IV Hq S HgTe In Bi O La Bi Hf Pb + Rb Cl 0 \_ 1 1 Cd S Cd Te Ga Bi 0 Y Bi 🗸 1 1 Zr Pb + + K Cl Zn Te Zn S Al Bi Sc Bi ✓ 1 Ti Pb + Na Cl Ba S Ba Te La Sb 🗸 1 In Sb + + 1 Hf Sn ✓ ✓ Li Cl Sr S Sr Te Y Sb 🗸 1 Ga Sb + 1 Zr Sn 🗸 Au Cl Ca S Ca Te Sc Sb ✓ 1 Ti Sn ✓ + Al Sb + 1 Ag Cl Mg S Mg Te + La As 1 Hf Ge ✓ ✓ In As + + Cu Cl Be O Be Te Ga As Y As + + 1 Zr Ge 🗸 🗸 Hg O Rb F Hg Se Al As Sc As + Ti Ge ✓ ✓ + Cd O Cd Se K F La Р 1 In P 1 1 Hf Si √ ✓ Zn O Zn Se Na F Y Р Zr Si 🗸 🗸 🗸 Ga P 1 + 1 Ba O Ba Se Li F Sc Ρ Ti Si 🗸 🗸 Sr O AL P + 1 + 1 Sr Se Au F La N Hf C Ca O In N + Ca Se Ga N

Previously unknown Previously unknown Previously known and predicted unstable and predicted stable

Mg Se

Be Se

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Ni Pd Pt

Al N

Ni Pd Pt

and high-level direct calculations is not always available in machine learning, but is desirable.

Mg O

Be O

Ni Pd Pt

Ag F

Cu F

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Ni Pd Pt

We next discuss how direct, materialdependent theoretical techniques can be used in the inverse design approach to affect the deliberate discovery and design of functional materials.

#### Inverse design and its modalities

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Sc N

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Ni Pd Pt

There are different approaches to finding compounds with desired target properties. The most fundamental approach involves mathematical inversion of the Schrödinger equation, as discussed extensively in the early mathematical literature<sup>80</sup>. In this case, one attempts to explicitly mathematically

Figure 4 | The three modalities of inverse design of materials. a | The evolution of valley splitting (VS) in the normally degenerate conduction band of silicon as a function of the genetic algorithm (GA) generation. The insert on the right shows a nanostructure composed of a Si slab (light blue) of initially unknown thickness d embedded within a Si-Ge well (green and yellow stripes) with initially unknown composition and periodicity, grown on a substrate with initially unknown composition and lattice constant. Modality 1 of inverse design was used to define the precise composition and structure of this nanostructure. In this case, Schrödinger equations have been solved to find materials exhibiting a VS of at least 1 meV, which is the minimum value needed for a material to be used in a Si-based qubit for quantum computing. However, this study disclosed that certain structures exhibit an even higher VS of 8 meV. Interestingly, the motif of four monolayers of Ge embedded in Si was detected to be the perfect structure to achieve a large VS<sup>40</sup>. **b** | The schematics of modality 2 used to explore chemical space for the discovery of promising AMX<sub>3</sub> perovskites. Ten cations were chosen for the A site, three group-IVA metalloids were chosen for the M site and three halogen anions were chosen for the X site. In this case, a hierarchical screening process was applied, in which successive sets of design metrics (different rows) were applied, including stability with respect to decomposition, appropriate solar bandgap, light hole and electron effective masses ( $m_e^*$  and  $m_b^*$ , respectively), low exciton binding energy, ability to tolerate defects (that is, non-deep centres) and compound toxicity (lead-free compounds). Each column corresponds to blocks of nine chemical compositions with fixed A and varying M and X. Within each block of nine possibilities, the red squares refer to materials that passed the screening (selected) and the grey ones refer to those that failed the screening (abandoned)<sup>12</sup>. c | A schematic overview of the modality 3 of material design, by which previously unreported compounds belonging to the family of 18e<sup>-</sup> ABX compounds were predicted. In this case, the B atom (blue) was chosen to have ten valence electrons, while A and X (in green and red, respectively) were changed to fulfil the 18-electron rule. Some of these compounds were already known, some were predicted to be unstable and some previously unreported compounds were predicted to be stable<sup>19</sup>. Part a is adapted from REF. 40, CC-BY-3.0 http://creativecommons.org/licenses/by/3.0/ Part **b** is adapted with permission from REF. 12, American Chemical Society. Part c is adapted from REF. 19, Macmillan Publishers Limited.

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Ni Pd Pt

Zr C

Ti C

+ +

1 1

> invert the Schrödinger equation, finding the potential that yields the wanted eigenvalue or using as the input the given phase shifts to construct the scattering potential that would produce such properties. However, the mathematical restrictions on the model are often so severe that it is not practical to find a unique and realizable physical

system that corresponds to the inverted conditions. I believe, however, that more effective mathematical approaches still remain to be discovered or implemented for direct inversion of the general Schrödinger equation such that the realistic atomic compositions and structures corresponding to desired target properties can be identified.

Contemporary approaches to inverse design do not attempt mathematical inversion of the relevant integro-differential equations of the electronic structure but instead manipulate a large set of direct approach calculations (ACS) $\rightarrow$ P(ACS) to effectively search for the right material (denoted (ACS)\*) harbouring the target property (P(ACS)\*). Note that it is incorrect to assume that methods that use the direct calculation of P(ACS) cannot be considered in approaches for the inverse design of materials. Indeed, we often use a few, reliable directly calculated P(ACS) values to anchor a general inverse design search that includes P(ACS) values often outside the original, directly calculated set.

Different classes of design problems may require different approaches. For example, searching for which configurations of a fixed chemical composition (such as in a locally stable superlattice) exhibit a target property does not require finding globally thermodynamically stable ground states. However, in searching for different chemical substitutions of bulk compounds, co-evaluation of the target property and thermodynamic stability may be required.

Modern strategies to search for ACSs corresponding to a target functionality can be grouped into three modalities (FIG. 4). The first modality of the inverse design of a material is mainly directed by the configurational search of materials and involves searching the target (ACS)\* on the fly by combining the direct computations of P(ACS) with evolutionary (Darwinian or Lamarckian) search algorithms. This modality does not require exhaustively computing all configurations or searching for a global thermodynamic minimum. The second modality involves the search of compounds by scrutinizing databases of computed or measured P(ACS) for known (ACS)\* and imposing a hierarchical set of property filters. In this case, we search for different chemical identities (A) that have target properties. The properties P(ACS) are either calculated directly or are approximated by auxillary methods that use a few directly obtained P(ACS) to approximate additional P(ACS) (cluster expansion or machine learning). The third

modality is analogous to the second, with the goal to find missing compounds.

Modality 1: searching artificial superstructures with target functionality. Consider an artificial superlattice whose specific superstructure patterns (A), /(B), //  $(A)_n/(B)_n/\dots$  (in which  $n, m, p, n'\dots$ are periodic repetitions of the building block compounds A and B) need to be found. The specific search is devoted to finding the sequences and orientations of A and B (or C, and so on) layers (n, m, p, n'...) (FIG. 2) that give the optical, magnetic or mechanical property of interest. This approach, known as the genomic approach<sup>2</sup>, uses genetic algorithms (BOX 1) or other optimization methods (BOX 2) to guide on-the-fly quantum mechanical calculations to find the answer<sup>2,34,35,39,40,53</sup>. Although the formation of simple random allovs of constituents A and B often leads to properties P(x) that are the average of the concentration (*x*)-weighted properties of the constituents,  $\langle P(x) \rangle = x P_A + (1 - x) P_B$ (Vegard's law-like behaviour), the allure of superstructuring A and B building blocks is that it can lead to functionalities that are qualitatively absent from the constituent compound (emergent properties and/or functionalities). What makes this problem difficult is that the sheer number of genomic-like layer sequences is astronomic and cannot be studied exhaustively. This calls for effective search methods that do not require exploring all points in the configuration space.

The resulting multi-layered configuration illustrated in FIG. 2 (for example, superlattices, quantum wells, core-shell nanostructures and structures created by positioning atoms via STM tips) is either stabilized by coherent epitaxial and interfacial effects<sup>81,82</sup> or is kinetically stabilized by insurmountable energy barriers. Thus, in modality 1 of inverse design, one looks for the layer sequence delivering the target functionality by performing a configurational search for fixed chemical identities of the basic species while performing only local energy optimization. This means that coherently strained epitaxial configurations are found by optimizing the local displacements of atoms without allowing possible atom swaps that would alter the configuration itself. This is different from modalities 2 or 3, which pertain to stable or near-stable bulk compounds, for which a global stability search is required.

Modality 1 of inverse design uses

optimization and search methods (such as evolutionary algorithms) to directly follow the functionality surface, thus directly identifying the structures and configurations whose functionality comes close to the desired target needed for a particular application. Evolutionary methods learn the structure-property landscape, eventually leading to a more effective search of the target configuration (for more details, see REFS 83–84 and BOX 1), as only a small fraction of the total number of configurations generally needs to be explored, typically a couple of thousand in a size space of 10<sup>14</sup>–10<sup>20</sup>. A good optimization and/or search algorithm explores only a tiny fraction of all possible compounds. This approach is guided by design principles, that is, a physical model (not a heuristic numerical descriptor) that relates atomic identities, composition and structure to the property being sought. Generally, a hierarchical set of design principles is used, in which compounds that fulfil early design principles pass on and are tested for fulfilment of the next design principles.

Examples of materials found via modality 1 of inverse design include a direct-gap semiconductor composed of a specific sequence of indirect-gap Si and Ge building blocks<sup>34</sup>, a 1D core-multishell wire with direct and optically strong absorption<sup>35</sup> and quaternary alloys of InAs/GaSb designed to exhibit bandgaps that result in the much wanted mid-infrared range (~300 meV)<sup>39</sup>. Modality 1 of inverse design has also been used to identify the configuration (composition and strain of various layers) of a Si-Ge quantum well that maximizes the conduction band valley splitting, which is useful for quantum computer applications<sup>40</sup>. We have shown that the CdTe/InSb interface behaves as a topological insulator despite its components being non-topological semiconductors<sup>33</sup>. A ferroelectric superlattice composed of PbTiO<sub>3</sub> and SrTiO<sub>3</sub> building blocks has a considerably larger polarization than that expected from interpolating the polarization of its constituents<sup>41</sup>. The arrangement of Mn atoms in a GaAs host crystal resulting in the highest ferromagnetic Curie temperature has also been disclosed<sup>54</sup>. Recent theoretical advances treat impurities and dopants as compounds in their own right and not as simple perturbations to the ideal crystal structure. Modality 1 of inverse design assisted by genetic algorithms has been used to identify the arrangement of the lowest level of nitrogen impurities in GaP that leads to the lowest strain value<sup>53</sup>. BOX 2 and REFS 85–88 discuss the exciting

#### Box 1 | Darwinian evolution in inverse design

In a typical genetic algorithm approach, one designates a superlattice configuration as a bit string of (0;1) denoting the occupations of lattice sites, for example, by Si or Ge. Each 'gene' corresponds to a single configuration, such as (0,1,1,00,11,...). Quantum mechanics calculations are performed for each configuration in order to optimize the structure and find the desired target properties. The fitness of the individual configuration or gene is represented by the difference between the value of the calculated property (for example, oscillator strength or bandgap) and the value of the target property. The selected configurations are mutations allowed to evolve by creating and mating them with different configurations . Important deviations from such Darwinian evolution by using Lamarckian approaches<sup>83</sup> are very promising. Metaheuristic algorithms that evolve a population of solutions by combining subsets of its members to produce new members enable rapid definition of the relevant part of phase space, avoiding evaluation of the total number of structures in that space. Prominent instances of evolutionary search include genetic algorithms, scatter search and path relinking, as well as hybrids joining these methods with Tabu search algorithms<sup>84</sup>.

The Darwinian theory of evolution implies that the genetic makeup inherited at birth is the one passed on during mating to new offspring, in which case, evolution is a product of environmental pressure and chance. In addition to this mechanism, Lamarck surmised that individuals could also pass on traits acquired during their lifetime. We found<sup>83</sup> that the configuration with the target property can be found much faster if the conventional Darwinian genetic progression — mating configurations and letting the lowest-energy fittest offspring survive — is allowed to experience Lamarckian-style fitness improvements during its lifetime, consisting of  $A \rightarrow B$  transmutations of some atomic sites (not just atomic relaxations). The remarkable statistical rate of success of these search strategies and their practical applicability were documented for finding the configuration of a binary alloy with target energy<sup>83</sup>.

yet unfulfilled promise of extending the search of configurations for a fixed composition into a search of configuration and composition. This might be done by converting the discrete variables (a site can be occupied by either atom A or atom B) into a continuous variable (a site is occupied by a potential that represents a fraction x of atom A and a fraction 1-xof atom B) so that it is possible to use continuous optimization and follow the gradient towards a composition that gives the target properties.

## Modality 2: searching the space of chemical compound for target functionality.

Modality 2 of inverse deign explores bulk materials for which the structure is often known but the related properties are unknown. The idea here is to search the chemical space (defined by the atomic identities and their stoichiometry) to design a material with the set attributes that results in the optimal value of the target functionality. In modality 2, there is no need to compute many properties of a broad range of compounds, albeit that information could be useful for data-driven discovery approaches. Modality 2 is based on a hierarchical approach by using certain design principles as a set of filters. These filters correspond to physical models designed to capture the property of interest (that is, strength of absorption or topological response). Finding the right

physical models that reflect the functionality needed in terms of ACS is the key step.

An example that illustrates the central importance of formulating design principles that guide the search is the case of finding the new Dirac fermion. These are particles that are defined, for example, by certain features of the electronic band structure, such as fourfold band degeneracy and cubic dispersion of the energy bands (the so-called cubically dispersed Dirac semimetal (CDSM)89, considered a new state of matter). Understanding of the theoretical nature of this fermion is needed to define the requirements (design principles) for searching the first material realization of this new particle. For example, to establish in-plane cubic dispersion at the band crossing, one needs at least three symmetry filters: inversion, C<sub>6</sub> rotation and the presence of non-symmorphic operations, such as screw axis or glide reflection. These requirements already exclude most of the space groups and leave only four possibilities (Nos 176, 192, 193 and 194). However, space groups 193 and 194 have three mirror planes parallel to the  $C_6$ axis. Therefore, only compounds belonging to space groups 172 and 192 can host cubic Dirac fermions in terms of crystal symmetry. This process of developing an understanding of the CDSM established the following design principles: inversion, C<sub>6</sub> rotation, non-symmorphic symmetry, projected angular momentum  $l_z = 1$  or -1 states<sup>89</sup> and an odd number of electrons per formula

unit. On the basis of these design principles, one can perform a material database search guided by such filters and find that a group of  $A(MoX)_3$  monochalcogenide compounds (where A is a monovalent cation and X is a chalcogen atom) with space group *P*63/*m* are ideal candidates for CDSM. Subsequent DFT calculations of the stability and band structure verified this prediction.

Modality 2 (FIGS 4,5) has been used, for example, to investigate the properties of a family of AMX<sub>3</sub> halide perovskites useful for photovoltaic applications by using a successive set of filters based on the evaluation of thermodynamic stability, solar bandgap, light effective mass and presence of non-toxic elements12. Other examples of the hierarchical identification of compounds with target properties include the theoretically proposed and experimentally realized class of Cu-Sb-S solar absorbers<sup>13,22</sup>, new compounds for thermochemical water splitting<sup>46</sup>, high-performance thermoelectric compounds47 and a new class of transparent hole conductors<sup>48-51</sup>. Other interesting examples of materials with target functionalities discovered by means of the modality 2 approach include a material for a Li battery cathode in which non-transition metals, such as Al, are partially substituted with transition metals, such as Co (REF. 14). This material was identified by Ceder et al.14 by means of DFT calculations of intercalation potentials and was also experimentally verified. Sokolov et al.90 identified various substitutions of a specific parent molecular skeleton to obtain good hole mobility. The novel derivative compounds were then found experimentally, exhibiting a greater than twofold improvement in mobility with respect to the parent molecule. Layered materials that have low exfoliation energies and thus can be easily used to create monolayers are also the focus of recent material searches. Ashton et al.91, for example, screened the crystal structures listed in the materials project crystal structure database8 for materials possessing layered motifs in their crystal structures and identified 826 stable layered materials. DFT calculations predicted 612 materials with exfoliation energies below 100 meV atom<sup>-1</sup>. Cheon et al.<sup>92</sup> applied a different data-mining algorithm to the crystal structures listed in the material-project databases to determine the dimensionality of weakly bonded motifs within bulk materials and identified 1,173 layered materials92. A review by Curtarolo et al.93 describes the techniques that can be used to screen a material database by applying a hierarchy of descriptors (that is,

computing the relevant design principle that reflects the target macroscopic property) to identify new stable compounds with the target property.

*Modality 3: exploring missing compounds for target functionality.* Modality 3 is analogous to modality 2 in that the goal is to discover unknown compounds. Therefore, it requires theoretical tools that can predict structures and their thermodynamic stability so that it is possible to establish which of the previously unreported compounds are inherently unstable (thus, understandably missing) and which are predicted to be stable (thus, just overlooked). One of the outcomes of modality 3 is the accelerated experimental isolation of new compounds and materials.

The general approach used in high-throughput DFT calculations of compounds<sup>7-9</sup> is to consider the convex hull, which identifies the structures and compositions that are stable with respect to competing phases. Such calculations are often performed assuming a temperature of 0 K. To date, this stability metric, which identifies structures lying on the convex hull (see REF. 75), is arguably the most successful predictor of the ability to experimentally isolate a compound in its ground state structure7-11. However, some structures can be explicitly stabilized only at higher temperatures, for example, by entropy. Finite temperature corrections (that is, inclusion of the entropy term -TS) can be done routinely by including the phonon and configurational entropy94-97. For instance, phonon calculations of target compounds, along with their competing phases, are used to calculate vibrational free energies and help identify the range of temperatures over which certain phases are stable. In this way, compounds that are stabilized at high temperature will be identified, regardless of whether these phases correspond to ground states. In addition, cluster expansion techniques are used to determine configurational entropies, off-stoichiometry compounds and their temperature dependences94-97. Note that predicting via DFT a particular stable structure at T = 0, P = 0 and the subsequent observation of another structural form at high temperature T (or pressure P) is not

#### Box 2 | Extending evolutionary searches from discrete to continuous variables

Generally, optimization methods are separated into local search methods (such as the conjugate gradient approach) and global search methods (such as evolutionary algorithms). The challenge for searching compounds with different atom types for a target property is to transform the discrete problem of decorating lattice sites with either A-type or B-type atoms into a continuous problem in which discrete atoms are replaced by virtual atoms that change continuously from pure A to pure B. This type of approach first surfaced in structural design engineering as early as 1988 (REF. 85) but has been used only recently for material design by Wang et al.<sup>66,87</sup>. The virtual-atom approach is an alternative local search approach for obtaining the global optimum that uses information contained within the gradient of the function  $\delta O(\sigma)$ . The virtual-atom approach replaces the discrete spins with continuous spins, which represent mixtures of a fraction  $x_i$  of A-type atoms with  $(1-x_i)$  of B-type atoms with spin  $S_i$  at each site *i*. The derivative  $\delta O(\sigma)/\delta S_i$  represents how desirable it is for site *i* to be occupied by one type of atom rather than the other. With this derivative in hand, gradient-driven local search methods can be used to optimize discrete configuration problems.

There are two problems with the application of gradient-driven local search methods to the virtual-atom problem. First, the virtual configuration  $\sigma_0$  obtained from a gradient-driven method is not necessarily a physically realizable configuration (in which each site is occupied by either an A-type or B-type atom). Second, the physical minimum-energy configuration is not necessarily the configuration closest to the continuous minimum-energy configuration nor indeed does it have to be in its neighbourhood. For these reasons, we introduce a local search method that uses only physical atoms yet still makes use of the virtual-atom gradient to jump discontinuously from one physical realization to the next<sup>83</sup>. Starting from a physical configuration  $\sigma_0$ , a spin direction  $S_i$  is picked and its gradient  $\delta O(\sigma_0)/\delta S_i$  is computed. If the gradient is positive, we proceed to another spin direction. Otherwise, the prediction offered by the gradient is checked by evaluating the physical prospect  $O(\sigma_1)$  of the neighbouring physical structure  $\sigma_1$  in direction  $S_1$ . We then iterate from the better structure  $\sigma_0$  or  $\sigma_1$ . Convergence is deemed achieved when all spin directions have been explored without finding a better physical structure. In this way, the algorithm hops from one physically realizable structure to the next, avoiding the pitfalls associated with unphysical structures. A similar algorithm has been proposed recently<sup>87</sup> with the difference that all gradient directions are evaluated at each step and that the algorithm moves in the direction indicated by the lowest gradient. 'Computation alchemy' (REF. 88) constitutes the implementation of such fictitious gradients ab initio; this, to the best of our knowledge, has never been used for material design and represents an exciting opportunity to be combined with continuous variable optimization and the aforementioned jump method.

necessarily a manifestation of a metastable phase, but often a statement that there are different thermodynamically stable phases at different temperatures and pressures.

Examples of materials discovered through modality 3 include laboratory isolations of ~20 compounds predicted to be stable and never found before<sup>19,21</sup> (FIG. 1). A recent example of a functionality search includes the discovery of a previously missing half-Heusler compound TaIrGe that was predicted to be stable and exhibited a wide bandgap (despite the strongly held intuition that high-Z compounds are generally narrow-gap materials or metals) but also conductive behaviour<sup>21</sup>. This new type of transparent conductor was recently isolated and confirmed experimentally to exhibit high hole mobility<sup>21</sup>. Dyer et al.<sup>98</sup> showed how a combination of layers in extended module materials assembly can propose new materials, such as by the stacking of AO rock-salt and BO<sub>2</sub> square layers to form ABO<sub>3</sub> perovskite structures. In the latter case, new phases in the Y-Ba-Ca-Fe-O system were identified. Emery et al.<sup>46</sup> calculated the stability of ABO3 perovskites from a set of candidate structure types and found that out of the 383 compounds predicted to be stable, 213 were not reported in the literature and thus represented new compounds.

#### Experiment and theory dialogue

The approach of functionality-directed materials discovery shows a number of potential advantages over more conventional empirical material selection processes, especially in its relation to experimental searches. First, it is possible to choose the type of functionality filters to be applied before starting the selection process; therefore, many potential candidates can be quickly eliminated without being examined (for example, using toxicity or the cost of rare elements as filters). Detailed examination of the remaining functionalities is then postponed to the stage at which the initial chemical space (hundreds to millions of candidates) is reduced to a handful of best candidates. A reasonable strategy is to divide all needed functionalities into groups and apply the most crucial filters first. In the case of photovoltaic absorbers, one might use as primary filters those that select stable, low-cost and non-toxic compounds with suitable bandgap energies and strong absorption. The filters omitted in the first stage are postponed to the final stage, which includes only the few best-in-class compounds that survived the hierarchical selection process. For photovoltaic purposes,



Figure 5 | **New material stability tests. a** | The most stable crystal structure of an ABX compound (dark red bar) obtained either from a fixed list of candidate structure types through high-throughput calculations<sup>19,20</sup> or from generic-algorithm global space group minimization<sup>106</sup> was compared with the corresponding lowest-energy decomposition products to give the heat of formation  $\Delta H_{\rm P}$  ldeally, the latter are higher in energy than the ABX compound. In practice, a range of metastability of about 100 meV is contemplated, in which ABX could be kinetically protected against decomposition by some energy barriers. **b** | The second stability test can be explained by looking at the 'chemical potential stability triangles' of possible compounds including Ta, Ir and Ge. The x and y axes of each triangle correspond to the Ta and Ir chemical potentials ( $\Delta \mu_{Ta}$  and  $\Delta \mu_{\rm Ir}$ ), respectively, whereas the Ge chemical potential is given by the condition that the sum of the chemical

potentials of the three elements is the calculated compound formation energy. The green areas in each triangle correspond to the stable domains with respect to a set of possible competing phases. When the competing phases are the elements Ta, Ir and Ge, the triangle is fully green, indicating full stability over that chemical potential domain. As additional competing phases are progressively considered, more of the green area is cut away, indicating the reduced stability domain. The final surviving green domain (bottom right) is the thermodynamically allowed region for the compound containing Ta, Ir and Ge. Such diagrams identify the competing phases that are closest in energy to the final allowed domain; selective metastability could then be explored by kinetically stabilizing the target compound specifically with respect to the competing phase that is closest in energy<sup>109</sup>. Part **b** is adapted from REF. 21, Macmillan Publishers Limited.

the final best materials can be filtered for low recombination loss, long minoritycarrier lifetime, appropriate defect-tolerant structure and good metal contact, among other factors. At this point, one might revert to conventional detailed experimental research, in which everything is checked, as well as more accurate calculations (that is, using high-precision methods). Note that the last step needs to be done only for a handful of final compounds, not for all or most candidates, as this is an extremely slow process that could take many years if applied to the unfiltered chemical space.

Functionality filters are best constructed from understanding-based physical models (design principle) rather than ad hoc heuristic models. For example, in focusing on the functionality of photovoltaic absorbers, one of the heuristic models that has been broadly used is based on the search of direct-gap semiconductors. However, a model based on first-principles calculations indicated that some indirect-gap materials (with suitable positioning of the various transitions) are better than direct-gap solids<sup>10</sup>. Using understanding-based filters (constructed on first-principles calculations or well-reasoned principles of solid-state chemistry) opens the way for the discovery of pertinent principles and not just materials.

What has been learned with great clarity over the past two decades of practice with material-dependent theories is the importance of a continued dialogue between theory, synthesis and characterization. Using quantum data to develop a Rosetta Stone for designing new materials is extraordinarily ambitious. The need for both an interactive and iterative approach to the predictionsynthesis-characterization loop stems both from the need to establish a common language among the different disciplines and because experiment often informs theory of initially naive assumptions, which are then rectified in the next set of this ping-pong game.

Examples of this iterative experiment– theory ping-pong include the theoretical identification that one out of the  $O(10^{40})$ possible configurations of the Si–Ge superstructure has a direct bandgap (as opposed to the constituents Si and Ge)<sup>34</sup>, which met with the experimental difficulty of realizing atomically sharp interfaces. Theoretical prediction then had to start from a new genetic algorithm, looking for superstructures with the target property while allowing the interfaces to be locally intermixed to a given degree<sup>34</sup>. This resulted in another, perhaps more realistic prediction. Another example is the case in which the inverse design of ordered  $Ga_{x}In_{1-x}P$  alloys with the maximal possible bandgap for a given alloy composition x (REF. 2) resulted in an answer that was initially not experimentally friendly — the layer orientation (201) is not a standard growth orientation<sup>25</sup>. Theoretical searches of bandgaps in a constrained space of layer orientations provided the target maximal bandgap for experimentally friendly growth directions (001) and (111). Yet another example involves the search of the space of A<sub>2</sub>BO<sub>4</sub>-type spinels for transparent hole conductors, which resulted in the identification of Co<sub>2</sub>ZnO<sub>4</sub> (REF. 99). This compound is predicted to generate Zn-on-Co anti-site defects that induce the formation of acceptor centres (producing holes), whereas the opposite, nominal hole-quencher defect Co-on-Zn anti-site was predicted to be electrically inactive and cannot affect the formation of the holes even if the defect

exists in large quantities. The experimental need to achieve a much larger concentration of free holes than initially predicted from the equilibrium concentration of Zn-on-Co anti-sites was addressed in the subsequent experiment–theory iteration by designing off-equilibrium growth conditions that maximized the Zn-on-Co acceptor without precipitation of Zn-rich competing phases<sup>99</sup>. The lessons distilled from the theory– experiment dialogue are often implementable as additional search constraints in the next iteration of theory, as illustrated above, representing a learning experience that does not exist in theory-only enterprises.

#### **Challenges in design and discovery** *Predicting exciting properties of*

impossible compounds. The widespread accessibility of first-principles electronic structure codes and fast multiprocessor computational platforms have quickly increased the prediction of new materials. A possible unfortunate outcome might be the theoretical prediction of exciting new physical properties or even new physics in structures and compounds very unlikely to ever exist because they violate basic principles of bonding. Examples of proposed structures with spectacular properties that do not have the additional virtue of being stable, or weakly metastable, include BiO<sub>2</sub>, in the assumed SiO<sub>2</sub><sup>-</sup> structure predicted to be a 3D Dirac semimetal<sup>100</sup> or the predicted new topological insulators in the assumed half-Heusler cubic structure<sup>101</sup>. Sometimes there is a desire to illustrate exotic properties that are possible in principle, despite issues with thermodynamic stability. However, if a compound has interesting exotic properties in a somewhat bizarre set of bonding circumstances leading to high energy, this could perhaps tell us that the exciting theoretically assumed property might itself be creating thermodynamic instability. Indeed, some physical properties may be contraindicated in principle owing to their thermodynamic stability (see, for example, the conjecture that the emptying of bonding levels and occupation of antibonding levels needed for topological insulation may conflict with the thermodynamic stability of the compound if the inversion occurs in a large volume of the Brillouin zone<sup>102</sup>). BaBiO<sub>3</sub> could be a great topological insulator in the assumed cubic phase if its Fermi energy could be shifted upwards (via doping) by ~1-2 eV. Unfortunately, such a shift in the Fermi energy is predicted to destabilize the

cubic structure, instead stabilizing another structure that is not topological, as shown in REF. 102. In addition, one understands that a high-throughput materials search will have little value if it predicts materials that cannot be made. I am concerned that such frequent occurrences in the published literature and in many computational databases will reflect negatively on the brand of predictive theories. While metastable materials can sometimes be made, we need to be reasonable and use the tools of total energy calculations (introduced in momentum space DFT calculations of periodic solids nearly 40 years ago<sup>103</sup>) to identify the degree of instability of the compounds we propose as having new and exciting properties.

It is understood, however, that metastable structures that are energetically somewhat above the ground state (<100 meV atom<sup>-1</sup>) can sometimes still be made<sup>104</sup>. Indeed, modalities 2 and 3 of the inverse design of materials have sometimes resulted in metastable materials<sup>20,105</sup>, to the benefit of future experimental attempts to grow them by off-equilibrium methods. At the same time, we generally strive to identify stable inorganic bulk structures that could withstand the perturbations normally applied under device conditions. For example, InBiO<sub>3</sub> in the assumed cubic perovskite Pm-3m crystal structure is predicted by band theory to be a band-inverted topological insulator material; however, once the octahedral units in this structure are allowed to tilt, the stability is greatly improved, the energy bands rearrange and there is no longer band inversion or topological behaviour9. Hence, there is a need to co-evaluate the property of interest and the thermodynamic stability of the particular structural form that hosts the target electronic property. By evaluating both functionality and stability, we aim to find exciting properties that have the additional virtue of potentially being found in realizable structures. Let us not put in jeopardy our reputation as theorists with our experimental colleagues by sending them on a wild goose chase.

#### **Rounding up the usual suspects.** A noteworthy concern about the theoretical discovery of stable compounds via high-throughput calculations or modality 3 functionality-driven design is the possible occurrence of a false-positive prediction of new compounds and false-negative disqualification of previously made compounds as being unstable. In these high-throughput approaches (REFS 7–9), one calculates the

total energy of the target compound and compares the result with the total energies of a preselected list of competing phases (FIG. 5a). The preselected competing phases include alternative crystal structures of the target compound ABC itself and decomposition products of the target compound (such as A + B + C or  $AC + BC_2$ ). A target compound with lower energy than that of the competing phases is declared a stable ground state structure. FIGURE 5b illustrates this idea for previously unmade TaIrGe (REF. 21). We show the allowed chemical potential domains of the elements Ta and Ir. If the only competing phases are the elemental phases Ta, Ir and Ge, then the whole triangle is stable and coloured green. As additional competing phases are considered and their energy computed, FIG. 5b shows that more slices are cut out of the green domains. In the case of TaIrGe, there is a surviving green area, indicating the stability domain. For many of the compounds we tried in the past, we did not find any remaining stability area, suggesting unstable prediction. Co-evaluation of the thermodynamic stability along with the propensity to have large bandgaps and defect structures that produce free holes led to the identification of TaIrGe as a stable transparent conductor<sup>21</sup>.

The reliability of the high-throughput approach depends on the size and type of the pool of competing candidate structures. Thus, a prediction of an unstable compound might be a false negative because more stable structures of the target compound were missed from the preselected competing group. Similarly, a prediction of a stable new compound may be a false positive if the preselected list of candidate decomposition products is not sufficiently complete. In both cases, the potential flaw comes from the use of a fixed list of known structure types. The solution known to date is reliable but costly, namely, using a global minimization method. Instead of confining the minimization space to the neighbourhood of the initial guessed structure type, one can use methods that are not symmetry restricted and do not restrict the computational cell to a fixed number of atoms. An example is genetic-algorithm-based global space group optimization<sup>106-108</sup>, which visits many disconnected local minima and can thus avoid the limitations of high-throughput methods. Hence, there is a need to find effective methods to extend the selection of stable crystal structures so as to avoid false-positive predictions and false-negative rejections.

Close and iterative interaction between

theorists and experimentalists. As much as the techniques for predictive material-dependent calculations based on first-principles theory have advanced over the past couple of decades, the design and discovery of new and promising functional materials depend on close and iterative collaboration between theory and experiment. For example, experiment needs to inform theory on the degree to which the initial assumptions (such as the degree of perfectness of an interface or the type of possible defects) have been fulfilled under experimental conditions. Theory can inform experiment on previously unsuspected structures and compositions with promising functionalities. The process leading to the successful discovery and design of materials is iterative in nature. In this respect, it is a regrettable state of affairs that most government funding practices are still directed towards single individual disciplines (such as theory alone or engineering alone) or small groups of 2-3 researchers in a couple of disciplines (notable examples that permit groups of experimentalists and theorists to be co-funded, such as the US DOE EFRC, are unfortunately rather rare). It should be recognized that the current maturity of material-dependent approaches based on first-principles theory could benefit society much more if broad interdisciplinary groups comprising theory, synthesis, characterization and device engineering are promoted.

#### The future

*Current approaches to the laboratory synthesis of new materials for technological applications are in need of considerable acceleration.* The crucial unresolved bottleneck is the synthesis and physical realization of hundreds and, in the near future, thousands of newly predicted materials.

The conventional synthetic approach for the production of new materials typically comprises sequential individual reactions under a specific set of conditions (combined with experience and intuition), the resulting products of which are recovered and analysed. This conventional approach may require many months or longer to define the optimal reaction conditions (for example, time, temperature profile, starting materials and composition) that yield the new desired material. This is extremely inefficient and labour intensive and covers a small section of potential phase space. During a typical graduate student tenure, one material per 6–12 months can be expected. This trial-and-error approach for materials synthesis and discovery has continued largely unchanged for decades. Thus, a major challenge is how to accelerate the experimental synthesis of predicted compounds in a theory-guided and automatic fashion.

The laboratory discovery of new functional materials without prior information to narrow the likely compositions and structures can be challenging. In addition to the large number of possible combinations of elements, unknown crystal structures can complicate the process of identification and structure determination, as one cannot a priori classify and identify a set of non-indexed diffraction peaks as belonging to a specific new phase. As a consequence, many unreported synthetic attempts, so-called dark reactions, are carried out to identify a new phase among known and unknown phases and to isolate it for further structural characterization.

In the future, it would be ideal if one was able to develop guidelines for synthetic conditions from first-principles theory along with a fully automated experimental feedback loop including process variation and artificial intelligence-based structure identification. A potential automated workflow would include structural determination measurements of materials obtained from external theoretical prediction and synthesis to provide feedback and guidance for a new cycle of theoretical calculations and syntheses. This automated workflow could radically transform the way we learn to identify and synthesize new materials using new strategies or theory-assisted automated discovery. The main ingredients of the present proposal include developing guidelines for synthetic conditions from first-principles theory along with a fully automated experimental feedback loop including process variation and artificial intelligence-based structure identification. This work will fully implement the original vision of the Materials Genome Initiative by enabling autonomous materials development from theory to synthesis of phase-pure samples.

#### **Concluding thoughts**

A new style of research that applies quantum theory to examine ensembles of materials, rather than one compound at a time, using inverse design and high-throughput discovery holds the potential to revolutionize the way materials for crucial technological applications are discovered. We have barely scratched the surface. One could imagine searching for unexplored functionalities such as superconductivity, new forms of magnetism, spin liquids or dopability of quantum materials, to name a few. One could leverage quantum mechanics domain ideas from optimization theory and artificial intelligence previously used for business applications and language learning, thus accelerating the quantum ensemble search problem beyond imagination.

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## PERSPECTIVES

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#### **Competing interests**

The author declares no competing interest.

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