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Materials-by-Design: Computation, Synthesis, and Characterization from Atoms to Structures

Jingjie Yeo^{1,2}, Gang Seob Jung¹, Francisco J. Martín-Martínez¹, Shengjie Ling^{1,3}, Grace X. Gu¹, Zhao Qin¹, Markus J. Buehler^{1,*}

¹Laboratory for Atomistic and Molecular Mechanics, Massachusetts Institute of Technology, Cambridge, MA 02139, USA

²Institute of High Performance Computing, Agency for Science, Technology and Research (A*STAR), Singapore 138632

³School of Physical Science and Technology, ShanghaiTech University, Shanghai, 201210, China

Abstract

In the 50 years that succeeded Richard Feynman's exposition of the idea that there is "*plenty of room at the bottom*" for manipulating individual atoms for the synthesis and manufacturing processing of materials, the materials-by-design paradigm is being developed gradually through synergistic integration of experimental material synthesis and characterization with predictive computational modeling and optimization. This paper reviews how this paradigm creates the possibility to develop materials according to specific, rational designs from the molecular to the macroscopic scale. We discuss promising techniques in experimental small-scale material synthesis and large-scale fabrication methods to manipulate atomistic or macroscale structures, which can be designed by computational modeling. These include recombinant protein technology to produce peptides and proteins with tailored sequences encoded by recombinant DNA, self-assembly processes induced by conformational transition of proteins, additive manufacturing for designing complex structures, and qualitative and quantitative characterization of materials at different length scales. We describe important material characterization techniques using numerous methods of spectroscopy and microscopy. We detail numerous multi-scale computational modeling techniques that complements these experimental techniques: DFT at the atomistic scale; fully atomistic and coarse-grain molecular dynamics at the molecular to mesoscale; continuum modeling at the macroscale. Additionally, we present case studies that utilize experimental and computational approaches in an integrated manner to broaden our understanding of the properties of two-dimensional materials and materials based on silk and silk-elastin-like proteins.

Keywords

Materials physics; design; resilience; multiscale; modeling; materiomics

*Corresponding author, mbuehler@MIT.EDU.

1. Introduction

In 1959, Richard Feynman expressed his vision around the concept that there exists “*plenty of room at the bottom*” for manipulating individual atoms for the synthesis and manufacturing processing of materials¹. More than 50 years after this visionary idea, recent advances in nanotechnology, materials characterization, additive manufacturing, synthetic procedures, and supercomputing have made it possible to develop innovative materials with sophisticated structures and multiple material functions, in accordance with specific rational designs, from the molecular to the macroscopic scale. This new materials-by-design paradigm, deeply rooted in Feynman’s belief, resulted in a paradigm shift towards a powerful integrated approach that connects theoretical design at the atomic level, modeling of materials at the nano-meso-micro-scale, and additive manufacturing, synthetic chemistry, and process engineering at the macroscale (Figure 1). Achieving such a precise level of control over materials manufacturing strongly impacts our society as it contributes to unprecedented advances in the development of more sustainable technologies, energy sources, miniaturization, and countless fields of science and engineering. The potential of this paradigm arises due to the convergence of several important factors: new manufacturing technologies; more developed material characterization techniques; new modeling methods; increased computational power; new optimization algorithms; and artificial intelligence.

The resulting material-by-design paradigm is highly influential in current developments of biomaterials, proteins, polymers and nanomaterials. Accordingly, in this article we provide an overview of different techniques of experimental synthesis, characterization, and computational modeling that combine to give rise to such a paradigm shift of manipulating materials on the atomic scale, together with some examples of biological, biomimetic, or nature-inspired materials where that interdisciplinary approach is already being proven successful by incorporating designs from atoms to structures. These studies will show that the “*room at the bottom*” dreamed by Feynman is already being filled up.

2. Materials-by-Design: Synthesis & Characterization (Experimentation)

Materials synthesis and their corresponding characterization must be tightly coupled and developed simultaneously to push the boundaries of bottom-up materials-by-design. Clearly, a great multitude of organic and inorganic material synthesis, fabrication, and characterization technologies are in existence, such as gas condensation and sol-gel techniques. However, not all such methods can synergize well with computational design. Therefore, in this section, we will examine several pertinent and promising methods of synthesizing or fabricating biological, biomimetic, or nature-inspired materials from atoms to structures: recombinant DNA technology, protein self-assembly, and additive manufacturing. Correspondingly, we will also discuss the techniques for characterizing these materials through spectroscopy and microscopy.

2.1. Material Synthesis and Fabrication Techniques

Recombinant DNA Technology—Recombinant protein technology is a biosynthesis method that produces peptides and proteins with tailored sequences encoded by recombinant DNA^{2,3}. The core methodology of such recombinant protein methods is the recombinant

DNA technology, which constructs defined DNA molecules using genetic recombination methods (such molecular cloning) that integrate multiple genetic materials into one sequence, leading to the expression of any mutant protein⁴. This biosynthesis technique is a *de novo* design strategy to produce peptides and proteins with tailored sequences, molecular weight, conformation, and even complex tertiary structures⁵. Figure 2a summarizes the four critical steps to obtain reconstructed protein via recombinant DNA technology.

The first step is the design and assembly of the protein or peptide genes into genetic “cassettes”. The sequences used for building recombinant DNA molecules can originate from any species or sources, and can even be computationally designed. Smaller monomeric gene sequences can be synthesized to be as short as single-stranded oligonucleotides (up to 100 base pairs) by commercial oligonucleotide synthesis, while large oligomeric sequences are usually constructed by using concatemerization, step-by-step directional approach, and recursive ligation⁶.

In the second step, the designed DNA segments are inserted into a DNA vector, which can be derived from plasmids or viruses. This is usually a small DNA molecule with all necessary genetic signals for replication in the living cell. A series of methods, such as the Gibson assembly method that joins DNA fragments in a single, isothermal reaction, and restriction enzyme/ligase cloning, can be applied to connect DNA segments with vectors. The resultant recombinant DNA vectors are transferred into the host organism for further expression. A series of heterologous host systems have been explored to express the recombinant proteins, such as bacteria, yeast, insects, plants, and even mammalian cell lines and transgenic animals⁶. Among these host systems, the bacteria, *Escherichia coli*, is the most well-established biosynthesis system due to its low cost, short generation time, and easier manipulation and scalability⁷. Not all of the expressed organisms will contain the reconstructed DNA vectors; these organisms must be selected and purified to isolate those that definitely contain the desired DNA inserts.

The final step is protein purification to isolate the designed proteins. Protein purification typically consists of a series of steps to isolate the desired proteins from the complex mixtures derived from the cells or organisms. These separation processes are usually distinct depending on the proteins being isolated, since they are directly related to the protein size, biological activity, binding affinity, and physicochemical properties.

Protein Self-assembly—Compared to other synthetic polymers, a unique feature of proteins is their inherent tendency to assemble into sophisticated hierarchical structures^{10,11}. The self-assembly processes can be initiated or triggered by an external stimuli, i.e., pH, ions, heat, chemical species, or any other environmental factors able to induce a conformational transition of the protein¹¹. Protein self-assembly has become a fundamental strategy to construct advanced functional protein materials. In particular, its ability to position molecules or nano-scale entities with nanometric spatial resolution poses unprecedented opportunities for the *de novo* synthesis of one- to three-dimensional nano-architectures with exceptional structure and functions tailored for applications in biomedicine and nanotechnology¹².

Although there is a vast array of different proteins and self-assembling mechanisms, this review focuses on two self-assembly regulation routes of silk fibroin^{8,12,13}, which is an abundant protein in nature and has a wide range of applications in biomedicine, water treatment, and optical and electronic devices^{9,14–18}. The two main methods, ethanol-induced self-assembly and heat-induced self-assembly, induce the silk fibroin to self-assemble into silk nanofibrils in a simple and environmentally harmless procedure (Figure 2b). Although these methods are discussed in the context of silk fibroin assembly, they are suitable for other protein systems as well, such as amyloid fibrils¹⁹ and soy proteins²⁰. The ethanol-induced self-assembly method uses silk fibroin aqueous solution as starting material (seed) with ethanol solution being added. The heat-induced self-assembly method uses the same starting materials without any ethanol while being incubated at a mild temperature (60–80 °C for example). Furthermore, the self-assembly process can be tuned by regulating the processing conditions. The silk nanofibrils obtained from these two self-assembly methods are necklace-like topological structures connected by homogeneous nanoglobules. Compared to other silk fibroin-based materials, these silk nanofibrils typically have higher β -sheet content (~50%), and their moduli are comparable with amyloid and collagen fibrils. The diameters of single nanofibrils are around of 3–5 nm, while their lengths can reach up to tens of micrometers⁸. Similar to other protein-based nanomaterials such as amyloid fibrils and collagen fibrils, silk nanofibrils have several unique advantages for biomedical and nanotechnology applications. For example, silk nanofibril is an all-protein nanomaterial that have similar structural and mechanical properties as collagen fibrils, thus they can serve as *in-vitro* extracellular matrix materials⁹. Furthermore, silk nanofibrils can be directly used for making porous nanomaterials, due to their fine dimensions and high specific surface area. Our previous works have indicated that the pore size of silk nanofibril material are tunable in the range of several to hundreds of nanometers¹⁷, which is a pore size range that other silk-based materials cannot attain. Thus, silk nanofibrils are good candidates for nano/ultra-filtration or other cutting-edge technologies, such as batteries, biosensors, or optical devices.

Additive Manufacturing—Additive manufacturing has revolutionized component and system-level materials fabrication by enabling the design of complex structures that consist of a miscellany of internal voids, multiple materials, and irregular shapes²¹. Using different manufacturing methods, traditional engineering materials such as polymers, metals (e.g. aluminum, titanium), and ceramics can be formed into arbitrary or carefully-designed shapes that were infeasible with conventional synthesis tools and traditional manufacturing techniques such as mills, lathes, and molds^{21–23}. Among all different techniques and emerging technologies within the field of additive manufacturing, there are seven different types of additive processes that we can emphasize as being mostly used nowadays: Vat polymerization, material jetting, binder jetting, material extrusion, powder bed fusion, sheet lamination, and direct energy deposition (DED)²⁴. A brief overview of these additive manufacturing technologies are presented below; a more detailed description is given by Gibson *et al.*^{24,25}.

Vat polymerization processes involve using a moving laser beam to build models layer-by-layer by tracing the shape of the printed object with mostly photopolymer resins, which cure or harden upon contact with UV light. This method provides the best surface finish, part

accuracy, and feature resolution compared to other additive manufacturing processes. *Material jetting*, in some cases known as PolyJet™ technology, uses a printing head to jet liquid photopolymers from a nozzle onto a build platform, where they are then cured with UV light *in situ*. This method offers high resolution printing and can produce materials that consist of multiple colors and properties by jetting out multiple materials simultaneously, providing near perfect adhesion. Additionally, this process allows different materials to be mixed to create other materials with intermediate mechanical properties. A disadvantage for this method is the limited number of materials available to use for the drop deposition process. The *binder jetting* process involves a powder based material and a binder, where the binder acts as an adhesive between powder layers. The print head deposits alternating layers of the build material and binding material. *Fused deposition modeling* (FDM) is a technique that consists of depositing semi-molten thermoplastics in ultra-fine beads along the extrusion path as indicated by the computer model. Compared to other 3Dprinting processes, FDM differs in the addition of the material, which is added through a nozzle under constant pressure and in a continuous stream. The *powder bed fusion* process includes the following common printing techniques: Electron beam melting (EBM), selective laser melting (SLM), and selective laser sintering (SLS). This method either uses a laser or electron beam to melt and fuse material powder together. SLS synthesizes structures using an expensive, high power laser to selectively sinter polymer powders, making it a very costly procedure. SLS has limitations when it comes to surface finish and feature resolution but can process a wide array of materials such as nylon, glass, ceramics, and metals. SLM uses a high-power laser beam to fully melt metallic powders such as aluminum and titanium into 3D objects. EBM uses a computer controlled electron beam under high vacuum to melt metallic powder at high temperatures. *Sheet lamination* processes include laminated objective manufacturing (LOM), which fuses adhesive-coated layers of paper, plastic, or metal laminates under high heat and pressure. Afterwards, the object is shaped by using a laser cutter or knife. A DED machine consists of a nozzle that deposits melted material onto a surface where it solidifies thereafter. The process can be used with polymers, ceramics, and metals. Overall, the selection of the additive method depends on the applications and user needs, which implies choosing the most suitable and cost-effective for the design at hand.

Limitations in Additive Manufacturing—Additive manufacturing has demonstrated its utility and effectiveness across many fields with applications in medicine, aerospace, and automotive industries, to name a few, yet certain limitations exist. These limitations pose substantial hurdles in establishing additive manufacturing as a primary, large-scale, industrial, processing method^{21–23}. While a complete review on the state-of-the-art and future prospective of additive manufacturing is beyond the scope of this work, a few key hindrances are outlined in this section. An immediate practical limitation is the cleaning process of the support material, which is especially difficult and sometimes infeasible when dealing with complicated structures with voids. Additionally, additive manufacturing also suffers from the limited range of materials that can be printed, which precludes the design space of optimized structures. When multiple materials are printed, however, interfaces are created and printing across material boundaries is very limited, constraining the design of heterogeneous objects. Of course, time and space also constrain additive manufacturing, although these are controlled by the type of process and the build tray size. Finally, there is

tradeoff in printing resolution. Otherwise stated, printers that print at the nanoscale need a significantly long time printing at the macroscale. Commercial 3D printers still have these limitations and much research is underway to improve additive manufacturing.

Applications in Material Design—Many engineering materials possess inherently conflicting mechanical properties, such as toughness and strength²⁶. For instance, metals are very tough but not very stiff, whereas, ceramics are very stiff but not very tough. Natural materials often circumvent these intrinsic tradeoffs through their intricate, hierarchical structures. As a result, many research groups strive to mimic nature's complex micro- and nano-architectures to improve the mechanical properties in engineering materials^{27–29}. Due to the complexity of hierarchical and heterogeneous geometries, additive manufacturing is an excellent method to fabricate these bio-inspired designs³⁰.

Additive manufacturing provides a tool for understanding how the nature-designed architectures overcome the tradeoffs for better mechanical properties. Buehler *et al.* have investigated various aspects of bio-inspired design by using a multimaterial printer called Connex 3. This printer uses polyjet technology that can print up to three materials simultaneously, allowing contrasting materials to be mixed to create materials with intermediate mechanical properties. Dimas *et al.* designed composites inspired by bone and nacre, 3D-printed them, and tested them to compare with simulations (Figure 3a)³¹. The generated composites have a soft matrix phase with stiff reinforcements and they discovered that these nature-inspired designs can deflect cracks better than their homogeneous counterparts, and as a result, have higher toughness. Mirzaeifar *et al.* expanded on the work and studied the effect of adding hierarchy to similar geometries (Figure 3b)³². Through the use of simulation and experiments with 3D-printed samples, they showed that increasing the level of hierarchy improved the defect tolerance of the composites. These two studies are largely concerned with nacre-like designs and the brick-and-mortar scheme. However, current literature shows that structural features such as mineral bridges also contribute to its high toughness and strength. Due to manufacturing difficulties, work on the effects of mineral bridges is limited to a small range of volume fractions and number of mineral bridges. Gu *et al.* systematically evaluated the effects of structural parameters, such as volume fraction of mineral phase and material hierarchy, on the mechanical response of nacre-inspired additive manufactured composites (Figure 3c)³³. Their results demonstrate that it is possible to tune composite properties by controlling the size and content of structural features in a heterogeneous material.

Not constraining the discussion of natural materials to nacre, Libonati *et al.* designed bone-like additive manufactured composites by mimicking the fundamental microstructural features of cortical bone such as osteons and showed that the toughening mechanisms demonstrated in their synthetic composites are very similar to those seen in real cortical bone (Figure 3e)³⁴. These toughening mechanisms include crack deflection and branching, micro-cracking, and fibril bridging. Expanding on similar work, Gu *et al.* combined finite element simulations and drop-tower experiments to show how nacre-like synthetic materials are superior to their constituent materials in impact resistance (Figure 3d)³⁵. They showed that the nacre-like 3D-printed designs were able to bring the energy of the impact down to a zero-impact velocity, while the stiff homogeneous material was only able to reduce the

energy of the impact by half. The authors further studied the conch shell, which is reported to have ten times higher toughness than nacre.

Most biomimetic literature focused on nacre and bone because the three-tiered microstructure in conch shells proved to be a significant modeling challenge to study and emulate. With the use of additive manufacturing, the authors created the first 3D prototype and finite element model of conch shells (Figure 3f). They studied the effects of added levels of hierarchy on impact properties and discovered that geometries demonstrating second level hierarchy absorbed 70% more energy than geometries with first level hierarchy and 85% more than the monolithic (no hierarchy) constituent material³⁶. Future work in this field will be to optimize these structural features for increased impact resistance. The advent of additive manufacturing offers the opportunity to do so by offering freedom in geometrical design.

2.2. Characterization

Qualitative and quantitative characterization of materials at different length scales is critical for understanding the relation between material composition, structure, property, and function. Since this characterization is based on the physical and chemical interaction between the samples and the characterization tool, characterization also provides opportunities for improvement and control over the synthesized samples. The most demanding feature of characterization is to provide accuracy to improve our understanding, synthesis, and production of materials. Currently, a plethora of experimental techniques are available not only to characterize but also to simultaneously interact *in situ* with the structure of the materials. This level of characterization has enabled the existence of nanoscience and nanotechnology as we understand them today, as well as the development of the “materials-by-design” paradigm that is expounded in this review. Describing in detail all the techniques available will require an entire monographic work, and such an endeavor goes beyond the purpose of the present review. However, we will briefly describe some techniques that have major roles in nano- and biomaterials science.

X-ray spectroscopy is a family of different spectroscopy techniques for investigating the local atomic structure of materials using X-ray radiation (Figure 4b). It is mostly based on X-ray emission, although X-ray absorption spectroscopy (XAS) is also applicable in materials characterization. X-ray radiation spectra are analyzed by different techniques, mainly energy-dispersive X-ray spectroscopy (EDS) for elemental analysis and wavelength dispersive X-ray spectroscopy (WDS), which provides diffraction patterns for a single wavelength. From an historical perspective, Wilhelm Conrad Rontgen received the first Nobel Prize in Physics in 1901 for discovering the X-ray, an electromagnetic radiation having a wavelength ranging from 0.01 to 10 nanometers. Subsequently, Max von Laue, William Henry Bragg, and William Lawrence Bragg were awarded Nobel Prizes in Physics in 1914 and 1915 for their contribution to X-ray spectroscopy, where diffraction patterns are generated from injection of X-ray to lattices of atoms in crystalline formations. It is also common knowledge that the helical structure of deoxyribonucleic acid (DNA)³⁷, was first reported in 1953 with X-ray spectroscopy performed by Watson and Crick for which they were awarded the Nobel Prize in Physiology or Medicine in 1962. Since then, technologies

based on X-rays have contributed to numerous fields of science and were crucial in the award of more than 20 Nobel Prizes in Medicine and Chemistry. In our daily life, X-ray radiation is most commonly known for its application in the medical field, in which radiography is a common technology that provides images of the insides of the human body.

As a spectroscopic technique, *Raman spectroscopy* is based on the interaction between matter and electromagnetic radiation (Figure 4a). While X-ray spectroscopy mainly utilizes elastic scattering, also known as Rayleigh scattering, where the high-energy electromagnetic radiation is scattered without changing in energy, Raman spectroscopy makes use of inelastic scattering where the low frequency of the emitted light changes due to the interaction between photons and molecules. The incident photon changes the vibrational, rotational, and any other low-frequency modes of the molecular system, thus generating excited states. The energy difference between the two states of molecules results in shifts in the frequency. When the light loses its energy to the vibration of molecules, it is called Stokes scattering and it is responsible for the more common spectra, while anti-Stokes scattering refers to the light gaining extra energy from molecules. This technique can provide information on chemical compounds that are present in the system based on their vibration because each bond type has a corresponding specific Raman shift, which cannot be easily characterized in other spectroscopy technology.

Transmission electron microscopy (TEM), a technique where electron beams are transmitted into the samples to visualize their images, was developed in early 1930s. TEM utilizes the short wavelength of electrons rather than light or UV, which allows much higher resolutions than optical microscopy because the wavelength of electrons is much shorter than visible light or UV. The electron beam can generate diffraction patterns from crystals (selected area diffraction patterns), which is a useful tool for studying the crystallinity of materials⁴³. Various versions of TEM have been developed for higher resolutions and better image quality, such as scanning TEM, cryo-TEM, and aberration corrected (AC)-TEM. Currently, sub-Angstrom resolutions are achievable, thus playing a critical role in studying atomic structures and charge redistribution of chemical bonds.

Unlike previously described microscopy techniques, *atomic force microscopy* (AFM)⁴⁴ actually touches the surface of materials by utilizing a cantilever beam and a probe tip (Figure 4d). AFM can provide three-dimensional surface profiles in contrast to the two-dimensional profiles from other microscopy techniques. Although the scanning speed is limited, AFM can perform well in ambient conditions and near-physiological conditions⁴⁵ in contrast to TEM, and this allows the probing of biological materials in ambient conditions such as hydrated environments. Furthermore, Steven Chu developed the technique of optically trapping of particles in water⁴⁶. Called *optical tweezers* (Figure 4c), a focused laser can trap nano- to micro-scale dielectric particles for studying the behaviors and forces associated with biological molecules^{47,48}. The pulling force can be much smaller than AFM, from 0.1 to 100 pN. The mechanical properties of biomolecules can also be directly compared with MD simulations⁴⁹. These two techniques significantly expanded the capabilities beyond merely visualizing atomic structures as the mechanical properties can be accurately determined in a variety of environments.

3. Materials-by-Design: Modeling & Optimization (Computation)

A critical driver of rapid advances in the materials-by-design paradigm in biological, biomimetic, or nature-inspired materials is the combination of multiscale computational models and the extensive utilization high-performance supercomputing with different techniques of experimental synthesis and characterization. This partnership between theory, computational simulations, and experiments is the key catalyst that enables the high-throughput design and detailed manipulation of materials from atoms to structures. In this section, multiscale computational techniques will be reviewed: density functional theory; molecular dynamics modeling such as atomistic and coarsegrained simulations and how these can be validated with experimental techniques of WAXS, SAXS, Raman, and infrared spectroscopy; continuum modeling; and numerical optimization.

3.1. Density Functional Theory

Density functional theory (DFT) is probably one of the most successful approaches to compute the electronic structure of matter. In its original formulation, it provides the ground-state energy and the electron density of atoms and molecules. In quantum mechanics, the wave function that arises from solving the Schrodinger equation contains all the information available about a given molecular system, and its square provides the electron density. Since it is impossible to solve the Schrodinger equation analytically for a system of more than two interacting particles, successive approximations have been implemented in computational chemistry to provide useful solutions. The first and most basic of these approximations is the Bom-Oppenheimer approximation, which assumes that the motion of the nuclei is much slower than that of the electrons since the nuclei are significantly more massive in comparison to the electrons. Thus, the electrons are assumed to respond instantaneously to the motion of the nuclei and the nuclei are fixed to solve the movement of the electrons. Within this approximation, DFT states that the energy of electrons is a functional, i.e. a function of a function, of the electron density in the homogenized electron gas, which allows us to approximate the problem of N - N interacting electrons (for a system consisting of N electrons) as a simpler system of one electron interacting with a homogenous external and effective potential. Therefore, the ground state properties of a A -electron system with $3N$ spatial coordinates are uniquely determined by an electron density that depends only on 3 spatial coordinates with the effective electron potential. In short, the functional constitutes the total energy that is determined from the electron density, which accounts for electron exchange effects coming from Pauli's exclusion principle and electron correlation effects coming from homogenization. However, the exact form of the exchange-correlation function has not been identified. Hence, the implementation of exchange-correlation functionals in DFT generates a plethora of different functional flavors that correspond to different approaches and subsequent approximations to describe the behavior of the electrons. Some examples are the local density approximation (LDA), generalized gradient approximation (GGA), meta-GGA, hybrid functionals. In LDA, the functional depends only on the (local) density at a given point, an example of which is the SVWN functional, while the functional in GGA depends on the local density and its gradient, such as the PW91 and LYP and the B88 exchange functional. In meta-GGA, the functional depends on the local density, its gradient, and its second derivative, for instance in the M06-L functional. Finally, in hybrid

functionals, a mix of Hartree-Fock exchange with either LDA, GGA, or meta-GGA, depending on the class, is implemented. Among the last family, B3LYP, which is a hybrid GGA, and M05-2X and M06-2X, which are hybrid meta-GGAs, are the most extensively employed.

Despite the challenges associated to its implementation, DFT provides a sound basis for developing several computational strategies for obtaining information about the energetics, structure, and properties of molecular systems at much lower costs than traditional *ab initio* wave function techniques. Nowadays, the original formulation has been generalized to deal with many different situations: spin polarized systems, time-dependent phenomena, reactivity descriptors and excited states, just to mention a few.

Within DFT, *conceptual DFT* is a branch of DFT that quantitatively define chemical concepts like chemical potential, electronegativity, or chemical hardness, within the formal formulation of DFT. Conceptual DFT provides a family of reactivity descriptors that have been proven useful in the design of new materials from the molecular scale. However, one of the greatest challenges in this context is to implement the conceptual DFT descriptor for usage in periodic systems and bulk materials.

3.2. Molecular Dynamics Modeling

Atomistic Molecular Dynamics Modeling—While extremely detailed characteristics of atoms can be determined through *ab initio* quantum chemical simulations or DFT calculations, this level of detail comes at a significant computational cost that will be insurmountable for systems that extends beyond hundreds of atoms. Molecular dynamics simulations simplified the interactions between atoms to be simple functions and the point masses are moving according to classical Newtonian equations of motions^{50,51}. While the greatly-reduced computational cost allows systems with millions of atoms to be simulated, a major downside is the loss of chemical or electronic details such that the accurate determination of chemical reactions or charge transport is not possible. However, MD simulations are useful for solving classical many-body problems which generally lack analytical solutions. Although MD is underpinned theoretically by Newton's laws of motions in its simplest form involving punctual particles, increasing complexity of problems mandates the incorporation of Euler equations, Hamilton's quaternions, and Lagrange's method of geometric constraints to formulate the equations of motion in a manner that enable greater ease of obtaining numerical solutions⁵².

By averaging out the motion of the electrons, the Hamiltonian of a system of atoms can be expressed as a function of their nuclear variables through the Born-Oppenheimer approximation. Assuming a classical description of a system is adequate, the Hamiltonian, H , of a system of N number of particles can be expressed as a sum of its potential, U , and kinetic, K energy functions. K and U in turn are functions of the set of coordinates $\mathbf{q}_i$ and momenta $\mathbf{p}_i$ of each atom i , where the variables in bold refer to vectors. From the Hamiltonian, equations for position and momentum can be derived, and trajectories are calculated by numerically integrating equations⁵³.

A wide variety of MD potentials have been parameterized to describe a great multitude of interatomic interactions and to produce numerous material properties. One of the most fundamental of these potentials is the Lennard-Jones (LJ) potential, which typically takes the form

$$U(r_{ij}) = 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] \quad (\text{Equation 1})$$

where ϵ is the potential depth, σ is the distance where the potential value is zero, and r_{ij} is the distance between two particles. Although its mathematical formulation is comparatively simple, it can accurately model the properties of several low-density gases, such as argon^{53,54}. More significantly, the LJ potential can be coupled to other interatomic potentials, providing dispersive interactions to model a much broader range of materials^{55–58}. To approximate interactions between chemically dissimilar atoms, the Lorentz-Berthelot mixing rules⁵⁰ can be applied.

However, greater complexity is demanded when modeling chemical species that have complex bonding structures, such as those in carbon and silicon compounds. For instance, in the case studies presented in the subsequent sections, highly detailed mathematical formulations have been derived, optimized, and validated against DFT and experimental results. These include many body potentials, e.g., Adaptive Intermolecular Reactive Empirical Bond Order (AIREBO) potential⁵⁵, the Tersoff potential⁵⁹, and classical potentials like those belonging to the large family of the Chemistry at HARvard Macromolecular Mechanics (CHARMM) potentials with harmonic forces⁶⁰, just to name a few. These advanced potentials can account for accurate interatomic bond, angle, and dihedrals, bond breaking and formation, and Coulombic interactions. An example of such an advanced mathematical form exemplifying the above can be given by

$$U(\mathbf{r}_1, \dots, \mathbf{r}_N) = \sum_{bonds} \frac{k_i}{2} (l_i - l_{i0})^2 + \sum_{angles} \frac{k_i}{2} (\theta_i - \theta_{i0})^2 + \sum_{torsions} \frac{V_n}{2} (1 - \cos(n\omega - \gamma)) + \sum_{i=1}^N \sum_{j=i+1}^N \left(4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] + \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}} \right) \quad (\text{Equation 2})$$

where l is the bond length; θ the bond angle; ω the dihedral angle; and q the atomic charge, which accounts for the Coulombic interactions. The subscript 0 denotes the reference or equilibrium values. Furthermore, these potentials can be parameterized from, or validated against, structural data obtained from WAXS/SAXS or Raman and IR spectroscopy.

WAXS and SAXS—The diffraction patterns from X-ray or electrons include information of the materials' structures. Conventional MD simulations utilize a vast number of atoms in the system, which complicate the analysis of structures and the validation of the models. The powdered samples' diffraction can be obtained based on Debye's equation⁶¹:

$$I(Q) = \sum_i \sum_j f_i f_j \frac{\sin(Qr_{ij})}{Qr_{ij}} \quad (\text{Equation 3})$$

where Q , r_{ij} and f are the scattering vector, distance between two atoms i and j , and atomic scattering factor, respectively. The empirically obtained scattering factors depend on the atom type and scattering vector Q . The scattering intensity of graphene, graphene oxide, and graphite as a function of scattering angle are shown in Figure 4b. This virtual diffraction calculation is critical for validating the structural evolution of materials obtained from MD simulations, such as self-assembly and crystal growth⁶². The angle dependence is included in the equation of the scattering vector, $Q = 4\pi \sin\theta/\lambda$, where θ is a half-angle of the diffraction and λ is the wavelength of the X-ray. Typically, if Bragg's peaks of crystal structures appear in the range of wide angles, the X-ray diffraction pattern is usually termed as wide-angle X-ray scattering (WAXS). In contrast, small angle X-ray scattering (SAXS) typically looks at the angles between 0.1 to 10 degrees, which can be applicable to non-crystallized systems such as macromolecules. The scattering information basically provides the size distributions of the constituent particles or molecules. Also, it can provide the overall shapes of unknown structures without crystallization. As an example, a SAXS-derived structure of tropoelastin is shown in Figure 4b. More comparisons between calculations and structures are found in the work by Hura *et al*⁶³.

Raman and Infrared spectroscopy—Raman and IR spectra depend on the vibrational mode of atoms in the systems. IR spectroscopy observes the absorption of light due to molecular vibration while Raman spectroscopy observes the scattered light due to the vibration of molecules. There is a rule of mutual exclusions for a molecule with a center of symmetry: the normal mode has either Raman or IR active but not both. In general, for more complex molecules, a strong IR intensity of a molecule corresponds to weak Raman intensity. As described previously, the parameters for MD potentials are fitted to their ground states using simple analytical functions such as harmonic potentials. The frequency of the normal mode is sensitive to the interatomic potential shape, which limits the ability of classical MD to obtain correct normal modes, and thus most calculations for obtaining the Raman and IR spectra rely on *ab-initio* or first principles calculations. Due to limitations in computational costs, only small molecules or unit cell systems can be applied to compare the spectra to experiments but theory could provide valuable tools to characterize the states of the systems, which conventional electron micro spectroscopy is hardly able to provide. For example, strain-induced Raman shifts of monolayer MoS₂ can be characterized by calculating the changes in the frequency of normal modes with the strains⁶⁴, and also with different stacks of MoS₂ and WSe₂⁶⁵ as shown in Figure 4a.

Coarse-grained Molecular Dynamics Modeling—Coarse-grain (CG) models are efficient methods for simulating and investigating systems in which the response, property, and/or behavior of interest is intrinsically at a spatiotemporal scale that are inaccessible to numerical methods that capture phenomena on a much smaller scale. Furthermore, through hierarchical “handshaking” between the various scales, progressive multiscale transitions from atomic to mesoscale to macroscale structure-property-function relationships can be

determined synergistically. This “finer-trains-coarser” approach immensely fortify the ability to design materials from the bottom-up by incorporating a comprehensive theoretical foundation for the prediction, characterization, and optimization of multiple properties in these novel materials.

Methods of coarse-graining in mesoscale numerical simulations of biological and polymeric materials can be broadly classified in three distinct categories: physics-based, knowledge-based, or structure-based approaches⁶⁶. Physics-based approaches are the most widely used, where forcefields are constructed based on experimental data or quantum-mechanical calculations, in a similar manner as fully atomistic MD simulations. As a result of this close resemblance to MD, physics-based forcefields can be conveniently incorporated into existing MD software, which provide greater portability and broader usage. One of the most widely used CG forcefield for biological materials is the MARTINI forcefield^{67,68}. Initially, it is parameterized to model lipids only⁶⁹. Subsequent developments standardized the methodology to systematically reproduce the free energies of hydration, vaporization, and partitioning of polar and apolar phases of numerous chemical compounds including hexadecane, chloroform, ether, and octanol⁶⁷. Atoms are clustered into four main types of polar (P), nonpolar (N), apolar (C), and charged (Q) CG beads and four heavy atoms with their corresponding hydrogen atoms are mapped into a single bead. Remarkably, this relatively simple representation of molecules has been parameterized for a whole host of materials, including proteins^{70,71}, DNA⁷², numerous polymers and block co-polymers such as PEG (polyethylene glycol) and PEO (polyethylene oxide)⁷³, and polysaccharides⁷⁴ (Figure 5a). The only major downside is the inability to capture conformational changes in proteins, as the secondary structures have to be constrained via an elastic network. Therefore, only tertiary structures can be determined from this MARTINI CG method.

Another physics-based method of coarse-graining is dissipative particle dynamics (DPD)^{78,79} where the CG beads are typically bonded with soft Hookean springs or the finitely extensible nonlinear elastic (FENE) model⁸⁰. In DPD simulations, the total force exerted on the CG beads consists of three components: a dissipative force, a random force, and a conservative linear repulsive force. The dissipative and random forces serve as a thermostat for maintaining the system’s temperature while the conservative force mimics excluded-volume interactions to confer each CG bead with a corresponding chemical identity. Similar to the MARTINI forcefield, DPD simulations have been widely applied to polymers^{76,81}, proteins^{27,82,83}, biomembranes⁸⁴, and complex fluids⁸⁵. For instance, critical parameters for the processing of bio-inspired silk fibres have been examined with DPD in order to predictively design hierarchical materials²⁷. Optimal ratios of the hydrophobic and hydrophilic domains in the copolymer and their ideal lengths are determined, which led to the formation of fibres with excellent mechanical properties, and these are verified experimentally. This work is extended further to examine how terminal modification of the peptides affects fibrillation⁸³. It is found that increasing the molecular weight at the terminals while decreasing the hydrophobicity will enhance the alignment of the peptide chains under shear. The mechanical strength and elasticity will also be improved at the cost of diminished extensibility and toughness. The properties of ultraviolet inks for 3D inkjet printing in nanoscale additive manufacturing have also been modelled with DPD⁷⁶ and it is shown that sodium dodecyl sulphate is an effective surfactant that can decrease the average

size and enhance the uniformity of agglomerates of polyethylene glycol and polystyrene (Figure 5b).

Many other methods are also gaining prominence, particularly those which are integrated into the Versatile Object-oriented Toolkit for Coarse-graining Applications (VOTCA)^{77,86,87} (Figure 5c). These are a family of structure-based CG methods. One such method is the iterative Boltzmann inversion (IBI) approach⁸⁸ which aims to reproduce experimentally or numerically determined radial distribution functions (RDFs) by iteratively improving a coarse-grained pair potential that has the mathematical form

$$U_{i+1}^{CG}(r_{ij}) \cong U_i^{CG}(r_{ij}) - k_b T \ln \left(\frac{\rho_i^{CG}(r_{ij})}{\rho_{target}(r_{ij})} \right) \quad (\text{Equation 4})$$

Successful convergence for a given RDF, $\rho_{target}(r_{ij})$, ensures a unique CG pair potential. The inverse Monte Carlo (IMC) method⁸⁹ is also implemented in VOTCA which, in a similar manner as IBI methods, aims to reproduce a coarse-grained Hamiltonian through iterative convergence of a linear combination of forcefield terms to a target RDF. A third method of relative entropy minimization⁹⁰ is that a CG ensemble can mimic a target fully atomistic simulation by optimizing the CG potential parameters such that the relative entropy between the CG and atomistic systems is minimized. This is possible because the overlap between the configurational phase-space of two molecular ensembles can be characterized by their relative entropy. A final notable method of coarse-graining is through force-matching where CG pairwise forces are derived from atomistic forces calculated from several reference sites⁹¹.

3.3. Continuum Modeling

Continuum modeling and simulations can be harnessed to probe material phenomena that are beyond the mesoscale, due to limitations in computational resources that are capable of determining the interactions between atoms or CG beads that number more than several orders of magnitude larger than those discussed in previous sections. This problem is circumvented by modeling the systems of interest as continuous media, in contrast to the discrete particles modeled in DFT, MD, or CGMD, and it is assumed that the infinitesimal subdivision of the material still retains the same material properties as those of the bulk. In a typical macroscopic continuum model, a set of coupled partial differential equations (PDEs) are constructed from fundamental physical laws, including conservation of mass, momentum, and energy, together with information regarding the materials' properties, known as constitutive relations. These equations can then be solved with specific boundary conditions. However, a purely analytical solution to this set of equations can usually only be found for relatively simple systems. Therefore, numerical methods that approximate the solutions to these equations are needed.

One such numerical method is the finite element method (FEM). FEM has been widely used to solve a large number of engineering problems in structural optimization, solid mechanics, heat transfer, and fluid flow, just to name a few. True to its name, FEM entails the division of the system of interest into simpler domains (finite elements) that are connected through

nodes. This representation of finite elements and nodes is also known as the *mesh* and it enables the continuum analysis of systems with complex geometries. In conventional FE analyses of the mechanics in linear systems, a system of linear equations is constructed based on the distribution of nodes and the nodal forces, displacement, and stiffnesses. This system of equations can then be solved using quite a number of different methods such as Gauss elimination, LU decomposition, or advanced multigrid method. As FEM is an extremely popular computational method that has been covered in a large number of publications, including undergraduate and graduate level textbooks^{92–96}, a detailed exposition of FEM is beyond the scope of this review. As the FEM analysis of macroscopic material properties is extremely flexible and rapid, it can be combined very effectively with additive manufacturing to design and create novel bio-inspired materials. This is discussed extensively in Section 1 and 3.4 of this review.

However, FEM has its drawbacks, particularly due to the need for a properly predefined mesh to connect the nodes⁹⁷. The meshing process consumes significant amounts of resources and time as an analyst needs to customize the mesh to suit the problem, especially when there are complex three-dimensional geometries. Conventional FEM formulations also assume that the displacement field is piecewise continuous, resulting in discontinuous stresses at the interfaces of the elements. This leads to inaccurate prediction of stresses, requiring special techniques to circumvent this issue. FEM also encounters significant difficulties in modeling systems undergoing large deformations or experiencing fracture⁹⁸. These problems arise from the fundamental need for a mesh of the system, therefore a broad class of modeling techniques, known as meshfree methods, seeks to remove this need for a user-predefined mesh to discretize the computational models⁹⁹. This is achieved by dispersing nodes both within and on the boundary of the domain of interest, thereby representing, in contrast to discretizing, the problem domain without forming a mesh. This means that the relationship between the nodes need not be known *a priori*. The main downside of meshfree methods is that they are relatively new in comparison to FEM and many categories of meshfree methods are under active development to solve broader classes of problems. There is also a lack of broadly distributed software that enables the rapid application of meshfree methods to generalized problems¹⁰⁰. Despite these limitations, meshfree methods have been applied to numerous specific problems in structural and fracture mechanics¹⁰¹.

While numerous computational methods can be applied at different discretized spatiotemporal scales, the hierarchical variations in material properties across these scales may not be as obvious. A simple illustration of this is the fact that a smaller object has a larger ratio of surface area to volume compared to another object that has the same geometry and material but with greater dimensions. For instance, the surface area of a sphere scales according to the square of its radius but the volume scales with the cube of the radius. However, similar scaling in material properties become much more difficult to derive analytically for objects that have complex geometries and non-uniform material distribution. Therefore, computational modeling can aid in the understanding of how these material properties vary according to size by approximating the underlying scaling laws, thereby aiding the design of the same material at different length scales.

For example, scaling laws related to density have been derived for the mechanical and thermal properties of three-dimensional (3D) porous graphene that has gyroidal geometry^{102,103}. On the one hand, it was demonstrated that higher densities led to better mechanical properties and this was verified experimentally through mechanical tests of 3D-printed polymeric gyroid structures¹⁰². On the other hand, gyroid graphene's thermal conductivity did not show significant variation with density, in contrast to typical porous materials such as silica aerogels^{104–106}. These studies provide critical insights into design rules for light, stiff, and thermally insulating 3D porous graphene structures at different length scales with varying hierarchical features.

3.4. Optimization

The designs of natural materials follow a form-function relation in which structure dictates properties. At the same time, requisite properties defined by the environment and needs for survival carve out efficient material structures through natural selection. Many of nature's materials are optimized for their own survival needs; these needs may include self-cleaning and hunting, for example^{107,108}. Engineering materials, on the other hand, need to meet certain requirements for their applications, which may include stiffness, strength, toughness, and low weight. Work on optimization of various materials for high performing mechanical properties is prevalent in literature. Many works are related to optimization of composite laminate designs using genetic algorithms, which are based on evolutionary algorithms and concepts^{109,110}. Topology optimization groups strive to optimize properties such as structural compliance based on known loads and boundary conditions, showing how an initial starting geometry slowly forms an optimized truss-like structure^{111–115}. Researchers have also studied how to optimize composite topologies with three materials for thermal conductivity properties¹¹⁶. All of these works lead to an emerging trend of materials-by-design in which properties of materials can be tuned to meet desired functions and applications.

The structural complexity of optimized solutions has often served as a barrier to manufacturing. As a result, most of the optimization work, a lot of which are topology, in the past has been limited to theoretical work^{117,118}. Recent advances in additive manufacturing have enabled researchers to physically create specimens with designs obtained from optimization algorithms^{119–127}. Gaynor *et al.* used topology optimization to optimize multiple materials for compliance and used additive manufacturing to fabricate the designs and experiments to gauge their performance¹¹⁹. Recently, the authors developed an optimization algorithm to tune the distribution of stiff and soft phases, optimized for toughness, in a composite material with a given crack¹²⁸. Applications for this work include designing materials to alleviate high stress concentrations at crack tips and preventing a pre-existing crack from propagating. A representative design obtained from the optimization algorithm with 12.5% volume fraction of soft material is shown in Figure 6b, where the grey zones represent a relatively stiff material compared to the black zones, which represent the softer material. It can be seen that the soft material surrounds the crack tip area to protect it and forms a wing-like shape around the crack tip. The strain field is shown in Figure 6b and it can be seen that the strain is no longer localized at the crack tip, but rather more distributed where the highest strained areas incorporate soft material that can handle more

strain. Details of the simulation and parameters used can be found in the publication by Gu *et al.*¹²⁸. What is more astonishing is that the design, obtained purely from mathematics and modeling, looks very similar to the design of dragonfly wings near the nodus point where cracks are most likely to initiate. Figure 6a shows a model representation of scanning electron microscope images of the dorsal and ventral structures near the nodus point¹²⁹. It can be seen that at the nodus point in the ventral side there is a wing-like shape of soft material, similar to the shape obtained from optimization. This suggests that natural materials, exemplifying the same mathematical conclusion, have crack deflecting mechanisms that minimize damage. With multi-material 3D-printing, researchers can now study algorithmically optimized designs and develop future engineering materials with crack-deflecting mechanisms that perform as well as dragonfly wings, for example. In this work, optimization was carried out using an algorithm that constantly searches for better designs through iteration.

Another approach to design new composites is using machine learning. Machine learning is a branch of artificial intelligence that uses a variety of techniques that allows computers to learn from past experience to detect patterns that hard to discern in large complex data sets. Machine learning is useful for problems that have a pattern associated with it, have lots of data, and are difficult to solve mathematically. Recently, Gu *et al.* applied machine learning to explore new geometric patterns with stiff and soft distributions of materials¹³⁰. The study showed that machine learning was able to accurately predict composite material properties, such as fracture and strength, and learn the patterns for geometries that performed the best. Additionally, machine learning was able to accelerate the exploration processes compared to finite element methods and other traditional evaluation models. In fact, the study showed that machine learning was orders of magnitudes faster than a finite element approach when it comes to predicting material properties. Therefore, machine learning can be an instrumental tool for designing new materials for future engineering applications.

4. Materials-by-Design: Case Studies and Impacts

The materials-by-design paradigm is strongly driven by the powerful integrated connection between experimental techniques in synthetic chemistry, additive manufacturing, and process engineering at the macroscale, as discussed in Section 2, with theoretical design at the atomic level and modeling of materials at the nano-meso-micro-scale, as detailed in Section 3. To provide concrete examples of this integration, three case studies are presented here. Firstly, for the design of 2D materials, we discuss how their electronic band structures can be analyzed and tailored through DFT calculations for advanced implementations in electronic devices. The mechanical properties of 3D structures derived from these 2D materials can also be determined with MD simulations to inform experimental synthesis and characterization. Secondly, we examine the interplay between *in silico* prediction and the *de novo* design of a versatile ultrafiltration membrane derived from silk proteins. Thirdly, we detail the integration of recombinant protein technology with MD simulations for the production of novel stimuli-responsive hydrogels based on silk-elastin-like proteins.

4.1. Two-dimensional Materials Design

Graphene and Other Two-dimensional Materials—Atomically thin two-dimensional materials and their unique mechanical, electrical and optical properties make them ideal for functional bio-mimicry designs such as in material toughening, electrical and optical sensing, and smart active designs. After the initial development of transistors in 1948 at the Bell Laboratory¹³¹, electronic devices have changed our life very significantly. At the fundamental level, most electronic devices are designed to control system or process information by controlling electrical currents through the applied external voltage to open a current channel in semiconducting materials. Therefore, the electronic properties of materials, such as the band structures, density of states, electron transport, resistance, and conductivity, are key factors that have to be considered in the manufacture and implementation of electronic devices. The applied voltage experiences a process of screening that is inherent to the bulk structure of the constituent material. This screening is diminished if the thickness is reduced and the electrons are confined in at least one of the spatial directions. Accordingly, thin structured materials are ideal for the development of electronic devices. This effect is maximized in atomically thin two-dimensional (2D) materials. The confinement helps to reduce the screening of the applied voltage. Among the 2D materials, graphene is specially known for its extremely intriguing properties, such as high mobility of electrons, which were predicted theoretically^{132,133}. Informed by previous theoretical research, graphene was isolated and characterized for the first time in 2004¹³⁴ by Andre Geim and Konstantin Novoselov who were awarded the Nobel Prize in Physics in 2010 for their innovative way of obtaining graphene samples from graphite¹³⁵. Since graphite is an allotrope of carbon that consists of stacked graphene layers by π - π interactions, Geim and Novoselov were able to exfoliate single-layered graphene from graphite by using Scotch tape. This simple but innovative technique can produce high quality micron-sized samples while also being equally applicable to other 2D materials that are multilayered bulk systems. In the case of graphene, its mechanical, electrical, and thermal properties are found to be exceptional: the thermal conductivity is estimated to be 5,000 W/mK¹³⁶; the electron mobility is approximately 15,000 cm²/V·s at room temperature¹³⁴; the high elastic modulus is around 1 TPa and its high intrinsic strength is around 130 GPa¹³⁷. These properties have placed graphene as one of the leading materials for innovation in the field of condensed matter physics and materials science.

High-quality, single-crystalline graphene can be obtained from physical exfoliation. However, it has limited ability to produce large-area graphene in sufficient quantities for practical applications. Chemical vapor deposition (CVD) is one of the most successful way for large scale production¹⁴¹. The nucleation of carbon atoms on a metallic substrate (Ni or Cu) initiates the growth of graphene flake into large domains. Due to the grain boundaries of the metal substrates, the graphene produced by CVD also has grain boundaries where the boundaries are well-stitched with pentagon and heptagon defects^{142,143}. The grain boundary affects the various properties of graphene based on their atomistic arrangements. However, the grain size obtained from CVD has improved significantly to produce inch-sized single-crystalline graphene¹⁴⁴.

Although graphene is well known for its ballistic transport and high electron mobility, it has no band gap. Possessing a band gap is vital for various electronic applications, such as transistors¹⁴⁵. It is possible to open the band gap of graphene by processing them in the form of nano-ribbons¹⁴⁶ or applying uniaxial mechanical strain¹⁴⁷. However, the mobility drops significantly to around $100 \sim 200 \text{ cm}^2/\text{V}\cdot\text{s}$ for a 150 meV bandgap because the high mobility of electrons in graphene is a direct consequence of not having a band gap. Thus, researchers have expanded their attention to other two-dimensional materials, such as molybdenum disulfide (MoS_2) and their transition metal dichalcogenide (TMD) family, hexagonal boron nitride (h-BN), black phosphorous, and many other 2D materials. In particular, monolayer MoS_2 has attracted significant attention due to its excellent electron transport with intrinsic direct bandgap (1.8 eV)¹⁴⁸. Figure 7a shows some representative two-dimensional materials of graphene, MoS_2 , h-BN, and their band structures.

The properties of graphene devices are strongly affected by their substrates as they are atomically thin, which limits their integration with conventional silicon-based devices. Utilizing h-BN as a substrate for graphene devices improved the mobility by approximately an order of magnitude as compared to devices with SiO_2 substrates¹⁴⁹. This research inspired other studies of new material systems with van der Waals heterostructures, including graphene, h-BN, MoS_2 , and WSe_2 ^{150,151} as shown in Figure 7b¹⁵², which are emerging candidates for the next generation of electronic devices. Moreover, wafer-scale heterostructures of WS_2 , MoS_2 , and MoS_2 were reported¹⁵³. Alternatively, instead of weak binding by stacking vertically, laterally bonded structures between h-BN and graphene show great promise for atomically thin circuits¹⁵⁴. Subsequently, in combination with the TMD family, various lateral heterostructures were proposed^{155–157}. Through epitaxial growth, atomically sharp interfaces between MoS_2 - WSe_2 lateral junction was also reported and this is illustrated in Figure 7c¹⁵⁸. Through permutations of these atomically thin graphene and other two-dimensional materials with lateral and vertical heterostructures, highly efficient and flexible devices can be realized.

We briefly introduced that graphene and two-dimensional materials have shown great promise as materials for electronic devices with their astonishingly excellent properties. Another exceptional property of graphene is its mechanical strength that is known to be 200 times stronger than steel. However, it is simply not possible to utilize graphene's mechanical advantages for large-scale construction materials due to its atomistic thickness. Thus, researchers have tried to transfer the properties of 2D graphene to 3D bulk materials. There are well-known examples of different dimensionalities from 2D graphene building blocks. The main feature of graphene as a carbon allotrope is its chemical bonding type: the sp^2 bond. Wrapping graphene into 0D or rolling into 1D structures result in fullerenes or carbon nanotubes respectively, which preserves the sp^2 bonds. Stacking graphene into 3D structures is graphitic in nature. The van der Waals interactions required for stacking graphene is extremely weak, and this limits graphene's application in 3D bulk systems. To overcome this problem, triply periodic minimal surfaces can be utilized for 3D graphene assembly, where the gyroid shape is proposed to be a good candidate for light and strong graphene materials¹⁰².

Recently, by building 3D structures inspired by origami and kirigami, the traditional Asian arts of paper folding and cutting, stretchable transistors can be constructed¹⁵⁹ (Figure 8a). It might be counterintuitive to fold graphene into 3D origami structures because the 3D structures are not stable with low bending stiffness. However, it was revealed that the static ripples in the graphene membrane increased graphene's effective thickness and thus served to stiffen the membrane. Moreover, controlling the crumpling and unfolding of large-area graphene on a polymer substrate, which are reversible due to its flexibility and robustness, was reported and tunable properties such as wettability and transmittance were demonstrated¹⁶¹. Self-assembling graphene ribbons from self-tearing and peeling from the substrate was observed at micrometer scale, which were activated by thermal fluctuation and may lead to self-assembled patterning in the future¹⁶⁰ (Figure 8b). The large area re-foldable crumpling of graphene generated by relaxation on pre-stretched polymers showed multiple functionality, such as tunable hydrophobicity, transparency, and resistance (Figure 8c).

All these observed behaviors indicate that there are many possible ways to build 3D structures from graphene, and it is crucial to understand the role of the atomic thickness in modulating the properties of the generated structures.

Computational Modeling and Design—In this section, we provide more specific details on how computational modeling can assist in understanding and tailoring the properties of 2D materials. In the case of graphene-like nanomaterials, theoretical band structures of graphite with zero band gap were reported seventy years ago¹⁶². Other theoretical modeling and simulations of graphene studied the Dirac fermion, spin-orbit coupling, and quantum hall effects¹⁶³. Currently, large-area graphene can be produced albeit with polycrystalline features. The grain boundaries include topological defects, i.e., pentagon and heptagon features, which are known to degrade the electrical, thermal, and mechanical properties drastically. These pentagon and heptagon rings are mostly located at the boundaries based on the relative rotational angles between grains. Modeling, such as with tight-binding (TB) methods or DFT calculations, allows us to study the differences in electronic properties due to specific atomic arrangements. For example, DFT calculations show how the band gap can be controlled by tailored periodic grain boundaries¹⁶⁴, which opens the gap to ~ 1 eV. Due to relatively long-range strain field from these defects, DFT cannot handle the system sizes in many cases to determine mechanical and thermal properties. As discussed in Section 3.2, reactive forcefields with MD simulations can model bond breaking and formation in larger system sizes compared to those achievable by DFT or TB methods.

From the experimental point of view, AFM nano-indentation of suspended CVD graphene showed that their mechanical strength did not degrade as much as the electronic and thermal properties with increasing numbers of grain boundaries in comparison with single crystalline graphene. It was also demonstrated that crack propagates into the grains¹⁶⁵. Their statistical results showed that smaller grain sizes had lower strength but broader distributions¹⁶⁶, which implied that the strength of polycrystalline graphene depends on randomized defect distribution. MD simulations with realistic randomly oriented grains also reported different trends with the grain sizes¹⁶⁷. The trend that the Young's modulus increases as the grain size increases is consistent. However, the trend for the strength of polycrystalline graphene varied

significantly. Kotaki and Yang reported size-independent strength^{168,169} while Sha and Chen reported increasing strength as the grain size increased. Both models were built in a similar way, however models that showed size-independent strengths had small voids at the boundaries. The regions that had voids can be considered as having an initial crack, and the pertinent property that must be considered in the presence of a crack is the fracture toughness. Based on the Griffith criteria²², the fracture toughness of CVD graphene was measured to be $4.0 \pm 0.6 \text{ MPa/m}^{1/2}$. The MD study revealed that there was enhancement of fracture toughness in polycrystalline graphene as the stress-concentration was delocalized (Figure 9a). The study showed that the mechanism was activated with the out-of-plane deformation¹⁷⁰. Pentagon-heptagon defects causes out-of-plane deformation, where the elastic modulus is lower and becomes more stretchable locally in comparison with the regions of pristine, hexagonal lattices. Thus, it can be considered to be a composite of soft and stiff materials with enhanced fracture toughness as discussed with 3D printed polymer composites, implying that complexities in the mechanical behaviors of polycrystalline graphene can arise not only from the defects themselves but also from their out-of-plane deformation.

Furthermore, graphene aerogels are 3D porous materials that utilize graphene's excellent mechanical strength, high electrical conductivity, and low thermal resistance¹⁷¹. Recently, newly developed methods to produce these aerogels by 3D printing were also proposed^{172,173}. Although these 3D structures possessed light weight and good mechanical stability overall, the reported quality and properties had a wide range of variations. It is intriguing to determine the limit of the properties of 3D graphene assemblies. The gyroid shape was utilized to idealize the 3D graphene structure in MD simulations with all bonds being sp^2 hybridized and having minimal surfaces^{102,103}. The results showed that the mechanical strength could be greater than 10 times that of mild steel at a mere 4.6% of the density of mild steel¹⁰², and the thermal properties is low and density-insensitive¹⁰³. These studies demonstrate that computational modeling can help to predict superior structures for designing 3D graphene materials (Figure 9b and c).

Due to its atomic thickness and high crystallinity, 2D materials are flexible and easily deformable by mechanical loading. Theoretically, strain engineering is expected to enable control over the electronic properties of TMD materials through mechanical strains^{174,175}. It was confirmed experimentally that strain induced tunable band gaps in WSe_2 and MoS_2 ^{176,177}, indicating that strain engineering is an effective method for tuning the optical and electronic properties of TMD materials. Polycrystalline MoS_2 was synthesized with CVD where triangular grains was grown with MoO_3 and S precursors¹⁷⁸. Unlike graphene, many types of defect structures at the grain boundaries of polycrystalline MoS_2 were reported^{179,180}, and these can be studied systematically with modeling in the future.

Characterization (in-situ, and quantitative comparison to modeling)—In the previous sections, we briefly explored the history and modeling of graphene and other 2D materials. Here, we explain different ways of integrating experimental characterization and computational modeling. Transmission electron microscopy (TEM) is one of the most fundamental methods of imaging an atomic structure. The hexagonal atomic structure of the suspended monolayer graphene was observed with TEM in a previous study¹⁸¹. Also, the

electron diffraction patterns in this study revealed the natural corrugation of graphene without substrates. Furthermore, high-resolution transmission electron microscopy (HRTEM) allowed the analysis of not only the atomic structures but also the charge redistribution due to chemical bonds such as nitrogen-doped point defects in graphene, which could be directly compared with the results of DFT¹⁸². Interestingly, the electron beam utilized in aberration-corrected transmission electron microscopy (AC-TEM) enabled the *in situ* manipulation and monitoring of atomic configurations, such as well-designed defects¹⁸³ and monitoring behaviors of dislocation pairs in graphene¹⁸⁴. Recently, the dynamics of the propagation of an atomically sharp crack tip was tracked *in situ* at the atomic level for two-dimensional materials (MoS₂) with the AC-TEM technique (Figure 10a). The interaction between the crack tip and defects in the system were observed directly and compared with MD modeling, thus paving the way towards understanding the fundamental behaviors of materials fracture and enabling the bottom-up design of materials with enhanced fracture toughness¹⁸⁵.

Likewise, scanning transmission electron microscopy (STEM) with annular dark field (ADF) imaging can distinguish atoms in MoS₂-WSe₂ lateral junctions based on the fact that the ADF signal is proportional to the atomic number ($\sim Z^{1.7}$). This property enabled the qualities of the sharp interface junctions to be characterized and mapped directly to the atomic structures¹⁵⁸. Recently, a MoS₂ channel that had a width of a few nanometers was embedded in WSe₂ by utilizing the 5/7 dislocation catalyst at the junction, and the difference between MoS₂ and WSe₂ was also clearly observed with ADF-TEM¹⁸⁶ (Figure 10b). For measuring strains in graphene or other 2D materials, Raman spectroscopy is a sensitive and convenient technique that can also be compared with DFT calculations¹⁸⁷. Moreover, multiple layers of graphene or MoS₂ also produce uniquely identifiable Raman spectra^{38,188}. Thus, precise characterization of the number of layers in 2D materials is possible with this technique. Furthermore, the quality of 3D printed graphene aerogel was quantified by looking at the 2D and G band from Raman spectroscopy¹⁷², where the G and 2D bands are the main spectra of graphene and they vary sensitively according to the number of layers. More distinct bands indicated the high quality of graphene without functional groups such as oxides.

4.2. Silk Ultrafiltration Membrane Design

Water purification membranes received significant attention in recent years with the aim of addressing global challenges in water pollution and the scarcity of potable water. Compared to other water-purification techniques, such as coagulation, flocculation, and sedimentation, membrane-based methods are more energy- and cost-efficient for removing molecular-level contaminants. However, it remains a significant challenge to fabricate low-cost water purification membranes while retaining excellent mechanical strength and high purification performance. A series of studies demonstrated that nanomaterial-based multilayer filtration membranes, such as graphene, graphene oxide, CNTs, tungsten disulfide, and molybdenum disulfide, can solve this problem^{189,190}, due to their unique advantages of having a low-pressure drop, high molecular loading capacity, enhanced throughput, and high filtration efficiency. However, there is still a large room for improvement in the filtration-efficiency of these membranes since nano-porous structures can only be developed through complex

processing and water can only permeate between gaps and interlayer spaces between the nanosheets during filtration.

Ling *et al.* produced *de novo* designs of a versatile ultrafiltration membrane by integrating computational modeling and experimental fabrication⁸. The first step for such a *de novo* design was to use computational modeling to predict the conditions under which systems that contain protein nanofibrils and nano-sized flakes of minerals can be assembled into multilayer structures. The authors established coarse-grained models of protein nanofibrils and mineral plates and simulated their self-assembly behaviors during vacuum filtration. The simulation results revealed that the multilayer structure of these two components could only form with weak interactions between nanofibrils and mineral plates. From this *in silico* prediction, a series of protein/mineral systems were scanned and finally a system that contained silk nanofibrils and hydroxyapatite were selected for experimental fabrication. In good agreement with the *in silico* prediction, the silk nanofibril/hydroxyapatite membranes formed highly ordered nano-sized multilayer structures. Remarkably, the resultant membranes not only showed ultrafast water penetration that was over five times greater than other reported ultrathin membranes with similar thickness, but it also exhibited universal and high efficiency in removing and even reusing (in some cases) heavy metal ions, dyes, proteins, and nanoparticles. More importantly, this synergistic integration of computational modeling and experimental fabrication is not only suitable for this specific case of silk nanofibril and hydroxyapatite systems. It is also useful for constructing multilayer nanoporous structures from different natural protein-based engineered peptides (e.g., amyloid, collagen fibril, etc.), protein-based fibrils (e.g., silk-, silk-elastin-, silaffin-, apatite-binding-peptide-based peptides and proteins) and their corresponding biomineral systems (e.g., calcification, silicification, etc.). Therefore, this design and fabrication strategy for membrane synthesis can lead to the production of functional materials for water purification and other practical applications.

4.3. Designing Silk-Elastin-Like Proteins: Going Beyond Nature

The field of biochemistry underwent a dramatic revolution as the technology to synthesize recombinant proteins matured over the past few decades. This technology led to the ability to rapidly express and purify large volumes of proteins with customized sequences for a wide variety of uses in scientific research, industrial processing, and development of commercial products. In particular, the production of biomaterials based on proteins, DNA, and cells was a major beneficiary¹⁹¹. The various mechanisms of producing recombinant proteins were covered extensively in numerous textbooks¹⁹² and reviews³, so they will not be described extensively here. Instead, the design, production, and characterization of recombinantly synthesized silk-elastin-like proteins (SELPs) will be the focus in this case study. SELPs are block co-polymers of tandemly repeating units of elastin-like and silk-like protein sequences. The elastin-like portion is derived from the hydrophobic domain of tropoelastin and has the protein sequence GXGVP, where varying the residues in the X position determines the particular stimuli-response the SELP can undergo, such as structural transitions with changes in temperature, pH, or light. The silk-like portion has the protein sequence of GAGAGS and it is derived from the β -sheet forming heavy chain domain of the

Bombyx Mori silkworm silk. It can serve as tunable crosslinks through β -sheet formation, thereby tuning the mechanical properties of the resulting biomaterials.

The precise protein sequence of SELPs can be customized through the construction of different expression vectors and standard protocols in molecular biology¹⁹⁷, including the use of pET expression vectors with the T7 promoter¹⁹⁵. The nomenclature of the synthesized SELPs depend on the ratio between the silk- and elastin-like blocks, as well as the residues in the X position, such that different SELP constructs are labeled as S_mE_nX . For instance, if a SELP construct has a silk-to-elastin ratio of 1:8 and a tyrosine at the X position, it will be labeled as SE₈Y. As a result of this diversity and ease of tailoring SELPs on a molecular level, numerous engineering applications were proposed to take advantage of the stimuli-responsive nature of SELPs. For instance, SELPs were spun into fibers through various methods, such as wet-spinning¹⁹⁴ (Figure 11b) and electro-spinning¹⁹⁸. SELPs were also found to be capable of self-assembly (Figure 11c), such as the formation of nanofibers on mica surfaces¹⁹⁹ or thermally triggered formation of micellar-like nanoparticles while interacting with hydrophobic drugs like doxorubicin¹⁹⁶. Plasmonic nanodevices were developed and they responded to thermal stimuli¹⁹³. These were made from functionalized gold nanoparticles and thermoresponsive SELPs (Figure 11a). Self-assembly was demonstrated through thermally reversible conformational switching in the elastin-like block while silk-like blocks stabilized the transition by forming β -sheets. Thermal cycling of these aggregates changed the UV-vis extinction spectra reversibly, showing their versatility for applications in plasmonic nanodevices. SELPs are also highly suitable for drug delivery vehicles and tissue engineering²⁰⁰, particularly when they are crosslinked to form hydrogels through horseradish peroxidase-catalyzed tyrosine crosslinking²⁰¹.

SELPs can now be characterized with molecular precision through the incorporation of computational molecular modelling^{201–203}, especially with fully atomistic and coarse-grained molecular dynamics. For example, through replica exchange molecular dynamics (REMD) simulations of SELP peptides, a transition temperature between 300K and 320K was determined for SELPs with valine as the X-residue, whereas this temperature transition was suppressed for a lysine residue, which corroborated experimental findings²⁰¹. Further REMD studies were performed on SELPs with tyrosine at the X position to probe the underlying molecular mechanisms responsible for the structural transitions²⁰³. The incorporation of tyrosine residues conferred thermos-responsiveness to the resulting SELP hydrogel and SE_gY constructs were experimentally determined to have transition temperatures around 21°C²⁰¹. Above this temperature, the hydrogel shrank to less than 10% of its original volume. This was attributable to a decrease in the end-to-end lengths of each SELP molecule as well as diminishing radius of gyration, accompanied by increasing amounts of hydrogen bonds. Tensile tests were also performed through steered MD where unfolding mechanisms were found to be highly dependent on temperature and the free energy barrier is significantly lower at colder temperatures. It is anticipated that this synergistic interplay between computational simulations and experiments will eventually realize the prospect of high throughput molecular design of SELP constructs by accurately predicting the structural and mechanical properties computationally before experimental synthesis.

5. Conclusions

In this review, we detailed the development of the materials-by-design paradigm through synergistic integration of experimental material synthesis and characterization with computational modeling and optimization. This paradigm creates the possibility to develop materials according to specific, rational designs from the molecular to the macroscopic scale and we present case studies that utilize this paradigm for materials development. In experimental material synthesis and characterization, we discussed extremely promising techniques that span recombinant protein technology that produces peptides and proteins with tailored sequences encoded by recombinant DNA, self-assembly processes induced by conformational transition of proteins, additive manufacturing for designing complex structures, and qualitative and quantitative characterization of materials at different length scales. We also detailed numerous multi-scale computational modeling techniques that fully complements these experiments: Density Functional Theory at the atomistic scale; fully atomistic and coarse-grain molecular dynamics at the molecular to mesoscale; continuum modeling at the macroscale. These experimental and computational approaches are utilized in an integrated manner to broaden our understanding of the properties of two-dimensional materials and materials based on silk and silk-elastin-like proteins. As the materials-by-design paradigm starts to become a reality, many limitations will impede its progress. Therefore, the next generation of computational techniques capable of simulating larger and more realistic predictive models must be developed to access the mesoscale gap in multi-scale modeling of materials, a gap that lies between atomistic and continuum models that must be filled in the future by the development of faster computers and novel methods.

Looking forward, machine learning is expected to provide a new revolution in computer science which, together with quantum computing, can boost the theoretical framework in which materials are currently designed and simulated. The development of these new computing avenues will impact many different aspects of our society beyond materials, including opportunities in the Internet of things (IoT), cyber-infrastructure, and robotics. All these will have to be coupled with further improvements in characterization techniques, as well as synthetic procedures that are more scalable. In the case of additive manufacturing, substantial hurdles in establishing additive manufacturing as a primary, large-scale, industrial, and processing method need to be addressed. Better cleaning processes of support materials, larger numbers of materials to print, better control over interfaces and material boundaries are some of the challenges that are hindering the growth of additive manufacturing into an established manufacturing technique. Overall, the achievement of these new, revolutionary advances in materials synthesis will help to tackle many of the grand challenges defined by the National Academy of Engineering (NAE). These include making solar energy far more economical, restore and improve urban infrastructure, provide access to clean water, or develop carbon sequestration methods. More importantly, achieving success in many of these NAE challenges will contribute significantly to the greater goals for sustainable development globally, defined by UN to include clean water and desalination, affordable and clean energy, sustainable cities and communities, and climate action.

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Figure 1.

The 'materials-by-design' paradigm that integrates numerous aspects of computation, synthesis, and characterization. List of acronyms: CVD – Chemical Vapor Deposition; DNA – Deoxyribonucleic Acid; FEM – Finite Element Method; CG – Coarse-grained; MD – Molecular Dynamics; DFT – Density Functional Theory; XRD – X-ray Diffraction; AFM – Atomic Force Microscopy; TEM – Transmission Electron Microscopy; IR – Infra-Red.

Figure 2.

The typical routes of protein recombination and silk fibroin self-assembly. a) Schematic of the processing steps of recombinant protein technology⁵. Adapted with permission from Ref [5]. Copyright (2017) American Chemical Society. b) Pathways of silk fibroin self-assembly^{8,9}. Adapted from Ref [6] licensed under CC BY-NC 4.0 from AAAS, and also adapted from Ref [7] with permission of The Royal Society of Chemistry.

Figure 3.

Biomimicry leads to materials with exceptional mechanical properties. a) Simulation, additive manufacturing, and mechanical testing form the framework used to characterize complex natural material microstructures such as those seen in nacre and bone³¹. Adapted from Ref [28] with permission from John Wiley and Sons. b) Using the same framework, the effects of structural hierarchy levels (1H, 2H, 3H) on defect tolerance of nacre and bone-like materials are examined³². Adapted with permission from Ref [29]. Copyright (2015) American Chemical Society. c) Systematic exploration of small structural features of nacre,

such as mineral bridges (left), is possible using additive manufacturing. Simulation of nacre-like composites with mineral bridges (right)³³. Adapted from Ref [30], Copyright (2017), with permission from Elsevier. d) Impact testing of nacre-like composites in simulation are compared to experiments on additive manufactured samples³⁵. e) Testing and fabrication of bone-inspired composites using additive manufacturing show toughening mechanisms in real bone can be recovered in synthetic bone-like materials³⁴. Adapted from Ref [32] with permission from John Wiley and Sons. f) Designs inspired by conch shells (left) show superior impact resistant properties (middle) with crack arresting mechanisms gained from their complex architectures (right)³⁶. Adapted from Ref [33] with permission from John Wiley and Sons.

Figure 4.

a) Schematic of Raman spectroscopy and measured Raman shift for different layers of MoS_2 from 488 nm laser line, showing two distinct shifts: $E'_{2g} \sim 383 \text{ cm}^{-1}$ and $A_{1g} \sim 408 \text{ cm}^{-1}$ shifts according to the number of layers³⁸. Adapted from Ref [34] with permission from John Wiley and Sons. b) Schematic of X-ray diffraction and a sample of small-angle X-ray diffraction (SAXD) pattern for elastin molecule. Powered wide-angle X-ray diffraction (WAXD) pattern for graphene, graphene oxide (GO), and reduced graphene oxide (rGO)³⁹, adapted from Ref [35] with permission of The Royal Society of Chemistry, and nanostructure of tropoelastin⁴⁰ obtained from SAXD, adapted from Ref [36] licensed under CC BY-NC 4.0 from AAAS. c) Schematic of an optical tweezer and a sample from collagen and the force-extension curve for a single type II collagen molecule⁴¹. Adapted from [37], Copyright (2004), with permission from Elsevier. d) Schematic of atomic force microscopy (AFM) and the force-extension behavior obtained from silk. The force-extension curve for the unfolding of pS(4+1) silk protein shows several rupture peak forces which are fitted with worm-like-chain (WLC) polymer model curves⁴². Adapted from [38] with permission from the National Academy of Science, USA.

Figure 5.

Coarse-grained MD simulations can be performed on a wide variety of material and biological systems, such as a) lipid membranes and transmembrane proteins with the MARTINI forcefield⁷⁵, adapted from Ref [63] licensed under CC BY from Nature Publishing Group. b) DPD simulations of polymer aggregation in inks for 3D printing⁷⁶, adapted from Ref [64] with permission from John Wiley and Sons, and c) hydrocarbons with the VOTCA methodologies⁷⁷. Adapted with permission from Ref [65]. Copyright (2009) American Chemical Society.

Figure 6.

Design by optimization. a) A model representation of scanning electron microscope (SEM) images of the dorsal and ventral structures of dragonfly wings near the nodus point, where cracks are most likely to initiate¹²⁹. Adapted from Ref [115], Copyright (2014), with permission from Elsevier. b) A representative design obtained from the optimization algorithm with 12.5% volume fraction of soft material, where the grey zones represent the stiffer material, and the black zones represent the softer material. It can be seen that the soft material surrounds the crack tip area to protect it and forms a wing-like shape around the crack tip. The strain field shows that strain is no longer localized at the crack tip, but rather

more distributed where the highest strained areas coincide with the soft material enabling it to handle more strain¹²⁸. Designs obtained purely from mathematics and from modeling look similar to the wing-like shape of soft material near the nodus point of the dragonfly wing, highlighted in the blue dotted areas.

Figure 7.

a) The atomic structures of 2D materials, including graphene, MoS₂, and h-BN, and their band structures. Band structures are obtained with DFT calculations in the Quantum-Espresso package¹³⁸ using the Perdew-Burke-Ernzerhof (PBE) functional¹³⁹ and norm-conserving type pseudopotential¹⁴⁰. b) Heterostructures with van der Waals interaction: hBN-Graphene-MoS₂-Graphene-hBN. c) Lateral heterostructure of MoS₂-WSe₂.

Figure 8.

a) Stretchable graphene electrode. Kirigami in-plane spring with (i) paper and (ii) graphene, and (iii) the graphene kirigami spring¹⁵⁹ being stretched by 70%. Adapted by permission from Nature Publishing Group: Nature, Ref [157], copyright (2015). b) A series of snapshots of graphene ribbon self-assembly with self-tearing by van der Waals interaction and thermal energy¹⁶⁰. Adapted by permission from Nature Publishing Group: Nature, Ref [158], copyright (2016). c) Multifunctional re-stretchable crumpled graphene on polymer¹⁶¹. (i) Schematic of the deformation of graphene on the pre-stretched biaxial polydimethylsiloxane (PDMS). (ii) Delamination and buckled geometry of graphene after uniaxial relaxation of the substrate. (iii) Crumples after the biaxial relaxation of the substrate. Adapted by permission from Nature Publishing Group: Nature Materials, Ref [159], copyright (2013).

Figure 9.

Molecular dynamics (MD) simulations with a reactive interatomic forcefield: constructing the models, deformation under mechanical loads, and stress-strain behaviors. a) Polycrystalline graphene¹⁷⁰. Adapted from Ref [169], Copyright (2015), with permission from Elsevier, (i) The 5-7 ring defects at the grain boundary caused intrinsic out-of-plane deformations. (ii) The spatial stress distribution of polycrystalline graphene at the failure points in panel a-(iii). (iii) The stress-strain curves of the polycrystalline and pristine graphene. b) 3D graphene assembly¹⁰². (i) $11 \times 11 \times 11$ nm 3D graphene assembly fused via randomly distributed graphene flakes with spherical inclusions. The structures under tension and compression with $\epsilon_x = -0.5, 0.0$, and 0.6 for (ii) to (iv) respectively. (v) Stress-strain curve of the assembly under compression and tension. c) Gyroid porous graphene¹⁰². (i) Representative geometry of 3D gyroid graphene. The deformation and fracture under compression with $\epsilon_x = 0.0, 0.1$, and 0.15 for (ii) to (iv) respectively. (v) Stress-strain curves of 3D gyroid graphene with different porosity sizes from 3 nm to 20 nm¹⁰². (b-d) are adapted from Ref [100] licensed under CC BY-NC 4.0 from AAAS.

Figure 10.

in-situ characterization with AC-TEM. a) A crack propagating through monolayer MoS₂. (i) *in-situ* AC-TEM images. (ii) Geometries obtained from MD simulation¹⁸⁵. Adapted with permission from Ref [184]. Copyright(2016) American Chemical Society. b) SEM images of (i) 1D MoS₂ channel embedded in WSe₂ from (ii) an atomically sharp MoS₂-WSe₂ hetero junction. (iii) MD simulations of the channel growth. The 5-7 ring play a catalytic role in promoting 1D MoS₂ channel growth¹⁸⁶. Adapted by permission from Nature Publishing Group: Nature Materials, Ref [185], copyright (2017).

Figure 11.

Applications of SELPs in a) plasmonic nanodevices¹⁹³, adapted with permission from Ref [192]. Copyright (2014) American Chemical Society, b) wet-spun fibers¹⁹⁴, adapted with permission from Ref [193]. Copyright (2009) American Chemical Society, and c) self-assembled nanoparticles^{195,196}, adapted with permission from Ref [194], Copyright (2011) American Chemical Society, and also adapted from Ref [195], Copyright (2014) American Chemical Society.