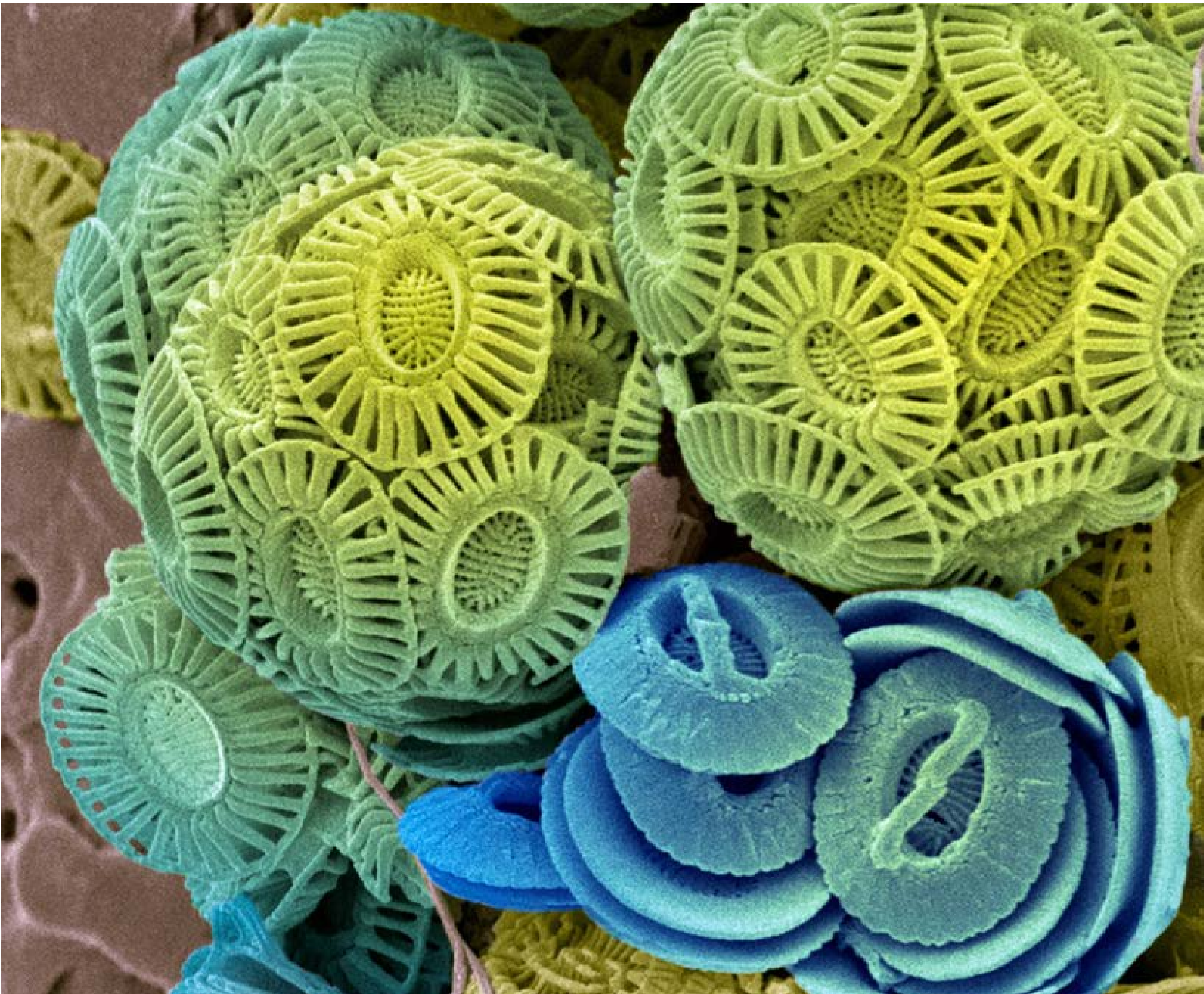
BIOMATERIALS WORKSHOP REPORT

Lawrence Berkeley National Laboratory

July 16-17, 2018

Organizers:
Caroline Ajo-Franklin, Peter Fischer, and Jay Keasling



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BERKELEY LAB

BioSciences

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EXECUTIVE SUMMARY

Biomaterials, materials made within biological systems through either natural or unnatural processes, provide a significant opportunity for applications for energy production, storage, and conservation, biomanufacturing, and environmental cleanup. However, much of the work done to date on biomaterials has focused on using biological systems to replicate conventional materials derived from petroleum feedstocks. While the natural world can be mined for a diversity of biomaterials that serve functions from encoding information (DNA) to structural support (bones), very little is known about the genes that encode many of these materials, how these materials are organized into hierarchical structures, and how that knowledge can be applied for creation of 'unnatural' biomaterials using synthetic biology. In this report, 'natural' biomaterials are those that are made by organisms through natural processes encoded by their genomes; 'unnatural' biomaterials are those that are purposefully designed to be produced by organisms or other processes (e.g. cell-free systems) for specific materials properties and applications. For biomaterials to be useful, a host of new computational, characterization, and synthesis methods are necessary. These tools would leverage existing capabilities in DNA sequencing and functional genomics, materials characterization methods including imaging, and computational and statistical methods to analyze data and to design new, unnatural biomaterials. Beyond existing capabilities, a robust effort to understand biomaterials will need to include efforts to discover and catalog unique biomaterials and the organisms that make them, new methods to characterize materials, and novel methods to biosynthesize sufficient quantities of biomaterials. A multidisciplinary approach that combines biology, chemistry, materials science, computing, and engineering is needed to discover and understand natural biomaterials, apply that knowledge to engineer organisms that can make unnatural biomaterials, and to develop biomaterials that can address a range of potential applications.

On July 16-17, 2018, Lawrence Berkeley National Laboratory hosted a one-and-a-half day workshop to bring together local biologists, chemists, materials scientists and others to define a Berkeley Lab view of biomaterials, identify grand challenges and applications for biomaterials development, and to network to increase communication across broad scientific disciplines. During this workshop, attendees also heard presentations from four speakers involved in biomaterials research that served as inspiration for discussions in breakout groups. During the workshop, participants identified challenges for biomaterials development that included lack of knowledge of mechanisms of natural biomaterials synthesis, a need to better correlate genes with functions in those mechanisms, adapting characterization methods from existing inorganic materials synthesis to biomaterials synthesis by organisms, and a need to develop computational and statistical methods for design of biomaterials based on desired properties and production systems. In addition, participants discussed a variety of applications for novel biomaterials, including energy generation and storage and environmental remediation. The types of biomaterials that could be used to address a wide range of applications included biomaterials that have self-healing properties, ones that can be made into hierarchical structures using biological systems, and those that can be deployed and constructed in resource-poor environments by tailored organisms.

ABOUT THE WORKSHOP

On July 16-17, 2018, Lawrence Berkeley National Laboratory (Berkeley Lab) hosted a one-and-a-half-day workshop to discuss and identify paths forward for biomaterials research at Berkeley Lab, across the national laboratory complex, at universities, and in the private sector that would enable the creation of new materials with performance-advantaged properties. This workshop continues the program development efforts established through the recent Advanced Biogenic Chemicals and Materials Laboratory-Directed Research and Development initiative established at Berkeley Lab in 2017. It also served as the first time Berkeley Lab had convened a workshop to bring together researchers representing the breadth of multidisciplinary research needed for a large-scale biomaterials effort. Through this convening, participants developed a shared definition of biomaterials and identified possible research collaborations, a key step in expanding Berkeley Lab's efforts beyond internally funded research. Because this was a preliminary and limited workshop, we look forward to extensive community engagement for refinement and expansion of the concepts outlined in this report.

The Biomaterials Workshop focused on three themes: grand challenges for the development of biomaterials, research programs that could address those challenges, and capabilities that could be leveraged (or would need to be built) to create those research programs. Workshop participants discussed the workshop themes in three sets of breakout groups, each structured to ensure diverse scientific perspectives. At the end of each breakout session, the whole group assembled and listened to report-outs from each breakout group.

46 attendees participated in the workshop, 38 of which represented four of Berkeley Lab's six Areas and the Laboratory Directorate. Researchers from University of California, Berkeley were in attendance, reflecting the strong integration of research between the two institutions. In addition, four speakers were invited to provide inspirational presentations on their biomaterials products or research. These speakers were David Breslauer from Bolt Threads, Arash Komeili from UC Berkeley, Eli Groban from Autodesk, and Maneesh Gupta from the Air Force Research Laboratory.

The desired outputs for this workshop were 1) a workshop report summarizing participants' discussions, 2) a shared understanding of biomaterials research opportunities for Berkeley Lab and UC Berkeley researchers, and 3) concepts for new research programs catalyzed by the Advanced Biogenic Chemicals and Materials initiative.

This workshop was funded with Berkeley Lab Strategic Planning Support Activity funds.

INTRODUCTION

The traditional definition of biomaterials is materials found inside living systems or made by living systems. Examples of these materials are protein, silk, DNA, cellulose, lignin, and silica shells, to name a few. A more expansive view of biomaterials would also include unnatural materials made by an engineered living system, made from monomers made by an engineered living system, made using biological components, or that mimic biomaterials. Examples of the latter include bionylon, polylactic acid, and DNA nanomaterials.

Natural biomaterials are unique in many ways. They tend to be much more complex, and therefore have greater functionality, than their synthetic counterparts. They are often hierarchical and have structures on multiple length scales. Some natural biomaterials are dynamic and adaptable to changes in environmental conditions, and some biomaterials will even self heal. Many natural biomaterials, particularly soft-hard composites, have unusual combinations of functionality, e.g. high strength and high toughness, that are not found in synthetic materials. Finally, many natural biomaterials are synthesized under ambient conditions and able to undergo morphogenesis, with the information for their development encoded in genetic information, such that they do not need to be molded.

Biomaterials can provide significant benefits in a range of applications that utilize the United States' abundant biomass resources, sense and remove contaminants or threats from the environment, contribute to energy conversion and storage, and improve human health. Biomaterials, across applications, hold the promise to have novel functions inaccessible with traditional synthesis methods, improved or new properties for a wide range of parameters, and reduce the energy intensity of materials production.

Biomaterials, at least those made by biology, have been useful products for centuries. Wood is used for building materials and energy production. Natural rubber is another biomaterial, a polymer made from isoprene and other compounds produced in plants. Even the silica shells of diatoms have been used in water filtration. More recently, biomaterials have been developed to displace petroleum-derived materials. Polylactic acid produced through fermentation and made into polymers has become a ubiquitous material for drinking cups and disposable utensils. Many of these materials, like the PLA-based plastic, offer certain performance advantages like improved biodegradability over their petroleum counterparts. Other biomaterials take greater inspiration from nature than petrochemistry, including the production of synthetic spider silk using microbes for use in textile production. Many more companies and researchers are looking towards biology and renewable plant feedstocks to create monomers (adipic acid, 1,3-butanediol) for polymers that can be used in production of polymers that might otherwise be made from petroleum. Lastly, biomaterials that incorporate living cells have been used to make environmentally-responsive and self-healing materials. For example, bacterial spores have been incorporated into cement, so that when cracks form, the spores trigger production of calcium carbonate to self-repair the cement.

Biomaterials are becoming a popular focus for companies. While biomaterials companies have traditionally focused on drug delivery and other health-related applications, recently started companies are focusing on other aspects of biomaterials for clothing (e.g., Bolt Threads is developing spider silk and leather substitutes), structural materials (e.g. Ecovative, MycoWorks, and Biomason), non-allergenic components in foods (Perfect Day) and other products.

While there have been many advances in biomaterials research and development in recent years, there are still many science and technology gaps for the development of biomaterials. One example is the engineering of yeast to produce spider silk. While we can produce the exact polypeptide sequence of spider silk, we still do not fully understand how the spider spins the protein into silk. Similarly, while we know the compositions of silica shells around diatoms and the calcite shells around coccolithophores, we don't fully understand how they are made into their distinct shapes. Understanding the materials and methods of synthesis will allow us to produce materials of defined shapes for a range of applications. New biomaterials, especially those with novel functions or properties, will require a multidisciplinary research programs that bring together biologists, chemists, materials scientists, and computer scientists. To succeed, these programs will need to probe biological function for fundamental understanding of biological materials synthesis; develop the tools and techniques to manipulate, engineer, and exploit those functions; develop chemical and materials synthesis approaches to create and characterize new materials; and develop computational tools for retrosynthesis, to correlated materials structure to desired materials properties, and to predict performance.

To develop biomaterials, integrated research programs across disciplines--including biology, chemistry, materials science, and computing--are needed. For example,the development of new biodegradable polymers for a variety of disposable consumer goods requires computational design tools to relate macroscopic polymer properties and physical-chemical relationships to chemical structure of the monomer, enzyme and microbial host design to synthesize polymer monomers, and scale-up methods to synthesize large quantities of the polymer. Another example is the development of hard materials with defined pore sizes for filtration/separation: it will be necessary to integrate structural biology with chemistry and physics to understand silica deposition and synthetic biology with structure and in vitro biology to reproduce silica deposition in vitro or in vivo in a heterologous host. Berkeley Lab is home to leading programs in basic and use-inspired research in these fields. In fiscal year 2018, Berkeley Lab invested LDRD funding in the Advanced Biogenic Chemicals and Materials program to bring together multidisciplinary teams to create new chemicals and materials and new routes to produce existing and new materials.
As a next step, Berkeley Lab staff held a workshop on July 16-17, 2018 to build a larger vision for biomaterials research.

For the purposes of this report, 'natural' biomaterials are those that are made by organisms through natural processes encoded by their genomes; 'unnatural' biomaterials are those that are purposefully designed to be produced by organisms or other processes (e.g. cell-free systems) for specific materials properties and applications.

WORKSHOP FINDINGS

Science Drivers

At the Biomaterials workshop, participants were asked to identify grand challenges for biomaterials development. Many of these grand challenges identified some key science drivers for biomaterials research that crossed boundaries of applications and types of biomaterials.

Discovery and characterization of natural biomaterials: While there are many known biomaterials, there are many more with interesting and potentially useful properties that have yet to be characterized and understood. Efforts to identify a greater breadth of biomaterials, especially biomineralized materials, are needed, as well as efforts to apply materials sciences characterization methods to those materials. By applying characterization methods to these biomaterials, researchers would be able to develop design principles for biomaterials that could be used in the development of computational and statistical methods to design new, unnatural (e.g. engineered using synthetic biology) biomaterials and to predict their properties and performance for specific applications.

Genotype to function for biomaterials: Related to discovery and fundamental understanding of natural biomaterials, one critical science driver necessary for development of novel biomaterials is understanding how natural biomaterials are encoded in an organism's genome. By applying functional genomics and other techniques, researchers could develop a fundamental understanding of how biomaterials are synthesized, a key challenge identified by the workshop participants. For some biomaterials production, the proteins involved in synthesis have been annotated to have very different functions. Another important element to this science driver is expanding the range of organisms surveyed for materials; coccolithophores, magnetotactic bacteria, sandworms, and spiders were identified as inspiration for developing a "zoo" of organisms that produce biomaterials useful for a range of applications.

Genetically-encoded biomaterials: Many of the applications and broad categories of biomaterials identified at the workshop will require the ability to engineer organisms to produce unnatural biomaterials. Organisms will need to be the factory, assembly plant, and processing facility for biomaterials. To do that, the design principles for biomaterials assembly must be understood, as well as the genes needed to develop new biosynthetic pathways and accessory pathways for biomaterials development. Many organisms that naturally produce biomaterials are genetically intractable and unculturable. New techniques for modifying these organisms will be necessary. In addition, scaling these organisms to relevant production levels will need to be considered as part of biomaterials development.

Retrosynthesis (reverse engineering) of biomaterials from desired properties and performance: Advances in computer-assisted design for biological systems and the Materials Genome Initiative, as well as efforts to develop a "(bio)materials genome" can be leveraged, along with the three above science drivers, to design computational tools (for example, those that incorporate partial differential equations, statistics, machine learning) that will allow researchers and engineers to design organisms that produce novel unnatural biomaterials with properties needed for the desired application. The development and validation of a retrosynthesis tool would allow for researchers to create biomaterials with performance improvements and unique applications.

Opportunities for Biomaterials Research

Discussions at the Berkeley Lab internal Biomaterials workshop centered on biomaterials with performance-advantaged characteristics that exploit the natural diversity of chemistry present in nature. Among the guiding principles for the scientific discovery and the deployment of novel biomaterials towards applications will be hierarchy, sustainability, adaptability, functionality, and topology of the desired materials. A wide variety of materials made possible through this diversity were identified, many of which can be classed into the following broad categories.

Determining the biological pathways to enable 3D-bioprinting: Workshop participants were inspired by naturally-occurring hierarchical materials created by organisms, many of which contain unique features and multi-scale structures not currently obtainable through traditional materials synthesis. These hierarchical materials are created by special structures present in organisms, such as the glands of spiders used for making silk and the organelles that print the calcite plates of coccolithophores, or are unique structures themselves, like the mineralized mandibles of sandworms. Hierarchical materials made by biology hold promise for new applications, including textiles and structural materials. Workshop participants discussed methods for identifying these hierarchical materials, the organisms that synthesize them, and structures that make these kinds of materials so that the organisms and biological methods could be engineered or reconstructed in other ways to produce novel materials similar to additive manufacturing or 3D printing. Synergistic research activities, particularly with materials science, that explore new avenues for additive manufacturing for structural materials can be anticipated.

Developing new platform technologies to produce regenerative or self-healing biomaterials: Participants discussed unique opportunities for materials that could regenerate or self-heal in response to damage. A material originally made through biology (or other methods) could be impregnated or coated with an organism that can repair damage to that material or remake the material while in place (e.g., like repairing a plane's skin while the plane is in flight). These materials could also belong to the category of additive biomaterials.

Developing platform hosts for deployable biomaterials: Unlike plastics or other human-made materials, biomaterials are unique in that molds are generally not needed to produce the final structure; the structure information is carried in the DNA sequence of the producing organism. Imagine if we could encode all the needed information for making any given biomaterial (natural or unnatural) in an easily transportable and deployable manner. Workshop participants discussed how--through use of microbes, fungi or even plants--all the needed information for making a biomaterial can be contained and then introduced into the right conditions for materials synthesis in the appropriate place. Organisms engineered to produce deployable biomaterials could be valuable in areas where resources are constrained or are not abundant.

Developing synthesis technologies for no-waste or green biomaterials: Many biomaterials currently in development or commercial use are polymers that can replace incumbent (e.g., petroleum-derived) materials with similar or slightly better performance. Because biology can be used to specifically produce single molecules of interest, monomers and co-monomers can be developed with engineered organisms. The monomers could then be polymerized in vivo or in vitro using enzymes or non-biological reactions. These single molecules can offer functional groups that cannot be derived through available synthesis methods and could result in performance improvements over existing materials. It is also possible to use biology to produce new polymers that are more easily recycled and have a high bio-content. Additionally, biology can be used to make proteins for polymers, a current area of interest for companies interested in producing new fibers for textiles.

Understanding and exploiting chirality and topology in biomaterials: Topology is a powerful concept in materials sciences that has led to the recent discovery of novel materials, e.g., topological insulators that could revolutionize information technologies. Likewise the concept of chirality (handedness) is driving new developments in spin-based electronics. As chirality is one of basic properties of most biological materials, one could envision new chiral biomaterials that leverage theoretical and computational materials science approaches. Computational materials sciences could predict the properties of unnatural biomaterials in which (non-biological) metals are substituted into naturally formed biominerals, e.g. introduction of dopants into magnetite biominerals. Lastly, rules-of-design for mechanical properties from materials science could be used to inspire designer materials, especially composite materials.

Applications for Novel Biomaterials

At Berkeley Lab's biomaterials workshop, participants were asked to think about the applications for novel biomaterials. The participants considered unique uses for biomaterials that could be pursued with the categories of biomaterials listed in the previous section.

Mobilizing lignocellulosic biomass: Use of the United States' abundant biomass resources enables sustainability targets while offering feedstocks that contain carbon, oxygen, and hydrogen in the form of lignocellulose that can be made into novel biomaterials. Leveraging biology, chemistry, and materials science, biomaterials could be developed that efficiently use the chemical building blocks of lignocellulose while providing unique performance benefits and added value for those crops. Current efforts in biomaterials have focused on plant plastics that can replace plastics made from fossil feedstocks. These plastics are often more biodegradable or compostable than traditional plastics, yet often perform poorly for the desired function (e.g., containing hot liquids). There is opportunity to use lignocellulosic feedstocks for new biomaterials that take advantage of the feedstocks' chemical composition for improved performance, reduced energy intensity of production, and increased value of products derived from those feedstocks. Waste streams comprised of lignocellulosic biomass provide yet another opportunity to match biomaterials properties and performance to specific feedstock characteristics. Native plant polymers (cellulose, hemicellulose, lignin, and suberin) could also be targets for engineering; by altering the properties of these materials, plants could be factories that produce new materials of interest or be engineered to have additional functionalities within the plant itself.

Biomaterials from CO_2: Biomaterials produced from CO_2 as a feedstock are attractive because they provide an alternative to materials produced from sugars, eliminating the requirement for obtaining feedstocks from lignocellulose, and they provide a means for some materials (e.g. building materials) to both valorize and sequester CO_2. Biomaterials can be produced from CO_2 using plants, algae, cyanobacteria and chemoautorophs, all of which can be engineered to convert CO_2 using heterologous pathways. CO_2 can also be used as to chemically transform intermediates produced from sugars to upgrade precursors for polymers.

Environmental remediation and water purification: Biomaterials, particularly those that can be deployed in resource-poor environments, could be used for environmental remediation tasks. A biomaterial with the appropriate properties could detect, bind, and sequester a desired contaminant. This same concept could be applied to recycling of useful elements or molecules; for example, rare earth metals could be collected using deployable biomaterials and recycled for future use in other products. Additionally, biomaterials made in the same manner as the silica shells made by diatoms or the calcite plates of coccolithophores could be used as highly robust filtration media with very consistent pore sizes. Embedding catalysts in these silica or calcite membranes would enable catalysis and simultaneous separation.

Energy harvesting and conversion: Similar to the way that leaves of plants collect the energy of sunlight, biomaterials could be engineered to collect sunlight and fix carbon dioxide.

Complex 3-D structures for catalysis and energy storage: As mentioned above, biomaterials have unique three dimensional structures, and unlike conventional materials, biomaterials do not need to be molded to attain the 3-D structure. These 3-D structures could be used for embedding various catalysts, specifically enzymes, in an architecture that would enable multi-step synthetic pathways. The 3-D structures might also be functionalized with various metals and used as energy capture and/or storage devices.

Lightweight, strong biomaterials: Many biomaterials are exceedingly strong for their weight. These biomaterials (or derivatives or mimics of them) could be used to reduce the weight of automobiles and airplanes, which in turn would save energy. If these lightweight, strong biomaterials can be synthesized using renewable carbon, they might also be produced using less energy than traditional materials and without the need for critical metals.

Biomaterials electronics: Many biomaterials are extremely effective at transporting electrons. These biomaterials or mimics of them could be used to create conducting biopolymers for electronics.

Biomanufacturing: The methods biology uses to manufacture materials could serve as next generation additive manufacturing. For example, diatoms are able to lay down/extrude silica shells in intricate 3-D patterns under ambient temperatures and pressures. Similarly, coccolithophores are able to extrude calcite plates, also with intricate patterns, at ambient temperatures/pressures. Mastering these biomanufacturing methods could lead to low-energy, low-cost ways to produce a variety of materials for all of the applications listed above.

Tissue and organ replacement: Biomaterials can serve as the substrate for the development of tissues and organs to replace diseased tissues and organs. The biomaterials will need to adopt specific 3-D structures to reconstruct the organ. New biomaterials are needed for replacement joints bones that will more closely mimic their natural counterparts.

Drug delivery: Biomaterials have been traditionally used for delivering therapies to the human body, since the biomaterials can be designed to degrade, dissolve or subsumed in the body. New biomaterials are always needed for new classes of drugs and therapies.

Research Capabilities

During the biomaterials workshop, participants were asked to identify existing and leverageable capabilities for biomaterials research, as well as identify gaps and new capabilities that would be needed. The participants also discussed which capabilities are appropriate for biomaterials development at national laboratories as fits their multidisciplinary, team science mission.

Leverageable (i.e. existing) Capabilities

Biology

- Biological engineering
- ‘Omics (genomics, transcriptomics, proteomics, metabolomics)
- Biomanufacturing platforms
- Metabolic modeling
- Structural characterization (crystallography, cryo-electron microscopy, electron microscopy, light microscopy, fluorescence microscopy)

Chemistry

- Synthesis and characterization of polymeric materials, including peptoids and protein-based polymers
- Hybrid chemical/biochemical routes for monomer production
- Compositional characterization

Materials Science

- Materials design for soft-hard composites
- Materials synthesis
    - Organic/inorganic hybrid materials
- Materials processing
- Structural characterization of hard and composite materials
- Functional characterization: mechanical, optical, chemical

Computing

- Materials prediction for inorganic materials
- Materials modeling

Existing User Facilities, large research programs, and collaboration/development units

- Advanced Leadership Computing Facilities and National Energy Research Scientific Computing Center: predicting biomaterials structures; calculating retrobiosynthesis routes for new materials
- Applied Energy Programs development units: engineering biomaterials organisms, engineering into industrial microbes and plants the ability to make biomaterials, production and purification of small amounts of natural or unnatural biomaterials for testing, scale-up of materials processes.

- Bioenergy Research Centers: engineering plants and microbes for natural and unnatural biomaterials synthesis
- DOE Systems Biology Knowledgebase: biomaterials data analysis
- Environmental Molecular Sciences Laboratory and Joint Genome Institute: genomics, mass spectrometry, microscopy, and spectroscopy for understanding natural and unnatural biomaterials synthesis
- Materials Genome Initiative (Materials Project): prediction of soft and hard biomaterials characteristics and synthesis routes
- Nanoscience Research Centers: characterization of natural biomaterials and their biosynthesis pathways; synthesis of unnatural biomaterials
- X-Ray Light Sources (Advanced Light Source and ALS-U) and Neutron Scattering Facilities: characterization of natural biomaterials and their biosynthesis pathways

Needed Capabilities

- ***Understanding and cataloguing of natural biomaterials:*** A wealth of biomaterial exist in nature. It is critical that we identify and characterize the organisms that synthesize these biomaterials and that we catalogue the structures and synthesis methods of these biomaterials. The genomes of the organisms that produce these interesting biomaterials should be sequenced, and the relationship between the genome sequence and the structures of the biomaterials should be elucidated.
    - Fundamental understanding of natural biological materials and the organisms that create those materials
    - Database of molecular and structural characteristics of natural biological materials
- ***Intentional alignment of existing characterization tools:*** Biomaterials, especially hierarchically-ordered biomaterials, require structural characterization that spans the nanometer to millimeter length scales. While many of the imaging and spectroscopic characterization tools exist, it can be a labyrinthine process to combine and align these tools into a coherent scientific program. Moreover, there are no facile ways to measure the same region of a biomaterial sample using different tools. Creating of streamlined access to these instruments and strategies to identify the same region are needed.
- ***Biomaterials characterization tools:*** Biomaterials are significantly different from chemically-synthesized materials. Many of the tools used to characterize synthetic materials are insufficient for characterizing biomaterials (e.g., will cause damage to the biomaterial). New characterization tools are needed, particularly ones that work in aqueous, in-situ and in-operando environments to tailor, design, and understand functionality, or that can be used to probe structure in a non-destructive manner.
    - New characterization methods for biomaterials dynamics (including self-healing), hierarchical structure, and protein assembly
    - Performance assays and requirements
- ***Computational biomaterials tools:*** In order to synthesize biomaterials for a variety of applications, we will need predictive computational design tools that correlate structure and function. These models must be multiscale as biomaterials generally occupy many length scales. In addition, we need retrobiosynthesis models that can predict the chemical structure of a given monomer or material that will achieve a desired materials property.

  - Biomaterials properties predictions and retrosynthetic tools
  - Multiscale modeling techniques for structure and function
  - Semi-automated data analysis that supports higher throughput rates as assays become smaller, cheaper, and faster
  - Design rules for biomaterials
  - Unsupervised learning for novelty detection and computational steering of catalogue development
- ***Biomaterials synthesis:*** Traditional methods for synthesizing materials are insufficient for production of biomaterials. We need to be able to scale biological methods for synthesizing biomaterials so that the resulting biomaterials can be produced in sufficient quantity for testing. In some cases, this will involve growing the biomaterials producer in large scale bioreactors. In other cases, this will involve recapitulating the biosynthesis method ex vivo (e.g., recapitulating and scaling silica and calcite biodeposition without cells). In addition, we need to perform technoeconomic and life-cycle assessments of these synthesis routes.
  - Recyclability assessments for biomaterials
  - Predictive scale-up and scale-down
  - Techno-economic and life cycle assessments for new biomaterials

Existing Funding Landscape for Biomaterials

Given the many types and applications for biomaterials, there are a variety of existing and potential sponsors of this research. To generalize, the National Institutes of Health (NIH) is a significant sponsor of biomaterials research directed towards improving human health, including supporting large, >$10M/yr multidisciplinary centers focused on drug delivery and tissue engineering. Research efforts directed toward creating biomaterials for energy, environment, and defense are sponsored by the Departments of Energy and Defense. However, these research programs are relatively small in number, are supported at modest levels, (e.g. 2-3 Principal Investigators and <$300k/yr), and most critically, do not link computational design, synthesis, and multi-scale characterization in a highly-interconnected and multidisciplinary way envisioned in this workshop.

Within the Department of Energy (DOE), the Office of Basic Energy Sciences (BES) has several biomaterials related programs. The Materials Science and Engineering (MSE) Division at BES has a Biomolecular Materials program, which supports small teams of investigators to discover, design and synthesize biomimetic and bioinspired functional materials and complex structures, and materials aspects of energy conversion processes based on principles and concepts of biology. The Chemical Sciences, Geosciences, and Biosciences (CSGB) Division at BES has a Physical Biosciences program, that combines experimental and computational tools, biochemistry, and molecular biology to gain a fundamental understanding energy conversion and storage energy in living systems. Thus this BES program informs how living cells could potentially used as biomaterials, but does not support manipulation of these cells and their application as biomaterials. Additionally, there is a current Funding Opportunity Announcement from the Office of Energy Efficiency and Renewable Energy (EERE) focused on utilization of biomass for bioproducts production. Characterization capabilities at BES User Facilities, including the Nanoscience Research Centers (NSRC), the X-ray Light Sources, and the neutron sources, are actively leveraged for understanding of natural biomaterials. Currently, neither the Office of

Biological and Environmental Research (BER) or Advanced Scientific Computing Research (ASCR) have dedicated programs in biomaterials, although the capabilities and user facilities of both offices could contribute significantly in this domain.

The Department of Defense has a handful of small extramural biomaterials programs within the individual Service research offices. For example, the Air Force Office of Scientific Research and Office of Naval Research have biomaterials programs that support teams of 1-2 principal investigators. DARPA's Biotechnology Office recently launched the Engineered Living Materials program, which seeks to revolutionize military logistics and construction by developing living biomaterials that combine the structural properties of building materials with the attributes of living systems. While this program provides more robust support than other efforts within DoD, e.g. 4-7 principal investigators at ~$1-4M/yr, it is tightly focused on synthetic biology approaches to structural biomaterials and does not intentionally link to computational biomaterials design or multi-scale characterization capabilities.

While there are numerous companies that are engaged in the production of biomaterials for biomedical applications, an emerging biomaterials production sector is creating unnatural biomaterials for a range of consumer focused applications. Bolt Threads has developed a spider silk thread that uses proteins found in spiders in yeast; textiles made from this process are being used for apparel and other applications. Other companies have focused on using starch, sugar, and lignocellulose as starting materials for sustainable plastic production. Companies in the biomaterials space often face long development times and challenges competing with existing products, leading to high costs of product development. Some companies in this space fund one-off projects with universities and national laboratories for access to expertise and equipment that cannot be justified as in-house capabilities. These projects are often used to solve a particular scientific question that is impeding progress or to perform specific, one-time assays. While opportunities to work with companies are frequent, the scope of work can be unpredictable, unconnected to a fundamental scientific question, and limited in its application to other applications. Additionally, intellectual property considerations prevent full and open transfer of knowledge to the wider scientific community.

CONCLUSION

The LBNL Biomaterials Workshop was a success in terms of the interest it generated at Berkeley Lab, the connections we made to researchers outside Berkeley Lab, and the ideas for future research generated. Biomaterials research is a significant opportunity for both basic sciences and commercial developments. The development of tools to study biomaterials and the organisms that make them will lead to new synthetic methods for biomaterials and unnatural materials. These tools include DNA sequencing, functional analysis, and cataloguing organisms that produce interesting biomaterials; characterization methods for natural and unnatural biomaterials; computational tools to analyze data generated by the analytical and imaging methods as well as to design novel biomaterials; and new methods to biosynthesize sufficient quantities of biomaterials to allow their characterization.

APPENDIX 1: WORKSHOP AGENDA

Day 1

9:00 — 9:30	Welcome and Introduction – **Jay Keasling** and **Peter Fischer**	Gray Auditorium
9:30 — 10:15	TALK: Better Materials for Better World: Silk without Spiders and Leather without Cows (30 minutes talk, 15 minutes discussion) – **David Breslauer**, Chief Scientific Officer and Co-founder, Bolt Threads	Gray Auditorium
10:15 — 10:45	**Break** (Regroup in breakout rooms)	
10:45 — 12:00	Breakout Session 1: Big Ideas and Grand Challenges for Novel Biomaterials – Breakout Leaders: **Blake Simmons, Tom Russell, Corie Ralston**	Gray Auditorium Room# 181A Room# 248
12:00 — 12:30	Regroup and Report-out: (Breakout Leaders)	Gray Auditorium
12:30 — 13:30	Networking	Atrium
13:30 — 14:15	TALK: Lipid-based Bacterial Organelles: An Unexplored Vehicle for Synthetic Biology Applications (30 minutes talk, 15 minutes discussion) – **Arash Komeili**, Associate Professor, Plant and Microbial Biology, UCB	Gray Auditorium
14:15 — 14:45	**Break** (regroup in breakout rooms)	
14:45 — 16:00	Breakout Session 2: Research Opportunities for LBNL with Novel Biomaterials – Breakout Leaders: **Jay Keasling, Brett Helms, Ting Xu**	Gray Auditorium Room# 181A Room# 248
16:00 — 17:00	**Regroup and Report-out** (Breakout Leaders)	Gray Auditorium
17:00 — 18:30	Networking Reception	Atrium

Day 2

8:50 — 9:00	Intro to Day 2 and Recap of Day 1 – **Jay Keasling** and **Peter Fischer**	Gray Auditorium
9:00 — 9:45	TALK: Ramblings on Economics and Software in the Emerging Bioeconomy (30 minutes talk, 15 minutes discussion) – **Eli Groban**, Head of Science, Autodesk Life Sciences	Gray Auditorium
9:45 — 10:30	TALK: Synthetic Biology for Materials and Manufacturing (30 minutes talk, 15 minutes discussion) – **Maneesh Gupta**, Research Materials Engineer, Air Force Research Lab	Gray Auditorium
10:30 — 11:00	**Break** (Regroup in breakout rooms)	
11:00 — 12:15	Breakout Session 3: Building Biomaterials Capabilities at a Local and National Scale – LBNL and Beyond – Breakout Leaders: **Peter Fischer, Caroline Ajo-Franklin, Aindrila Mukhopadhyay**	Gray Auditorium Room# 181A Room# 248
12;15 — 12:45	**Regroup and Report-out** (Breakout Leaders)	Gray Auditorium
12:45 — 13:00	Wrap Up, Next Steps – **Jay Keasling** and **Peter Fischer**	Gray Auditorium

APPENDIX 2: PARTICIPANTS

Name	**Affiliation**
Paul Adams	LBNL, Molecular Biophysics and Integrated Bioimaging
Caroline Ajo-Franklin	LBNL, Molecular Foundry
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