Organic Polymer Chemistry in the Context of Novel Processes

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ABSTRACT: This article was written to shed light on a series of what some have stated are not so obvious connections that link polymer synthesis in supercritical CO_2 to cancer treatment and vaccines, nonflammable polymer electrolytes for lithium ion batteries, and 3D printing. In telling this story, we also attempt to show the value of versatility in applying one's primary area of expertise to address pertinent questions in science and in society. In this Outlook, we attempted to identify key factors to enable a versatile and nimble research effort to take shape in an effort to influence diverse fields and have a tangible impact in the private sector through the translation of discoveries into the marketplace.

INTRODUCTION

To have a rapid, significant, and measurable societal impact through research, we have chosen to pursue the convergence of diverse fields and ideas, as well as the translation of that research into commercial processes and devices. Seeing connections among different disciplines, designing studies (and entire research programs) around globally relevant questions, conducting the right experiments, and capturing and reporting the key data have been critical aspects of our research program. Convergence—a problem-solving approach in research that emphasizes the integration of knowledge, people, and ways of thinking from fields including the life, physical, engineering, social, and behavioral sciences—can thrive through the development and utilization of a collaborative team of scientists and engineers with diverse backgrounds and experience.[1] Having gained traction in recent years in science policy, this paradigm provides an exceptional opportunity for accelerating scientific discovery in the context of identifying and addressing the most pressing questions in modern society, including those related to the environment, human health, and energy storage. Convergence fosters real interactions and dialogue that bring about learning, understanding, problem solving, and discoveries that would not be possible within a single field of knowledge. Beyond discovery itself, a vision for the realization of impactful discoveries must be developed and communicated effectively to promote actions leading to commercialization. This vision is key to our translation of scientific discoveries into real-world solutions to address issues of the human condition. We believe that relating our story will illuminate important lessons about conducting convergent research in academia and having the ability to successfully translate that research to industry.

Where To Play and How To Win. Research is defined by the Merriam-Webster dictionary as, "investigation or exper-imentation aimed at the discovery and interpretation of facts, revision of accepted theories or laws in the light of new facts, or practical application of such new or revised theories or laws". More poetically, Henry Rosovsky, former Dean of the Faculty of Arts and Sciences at Harvard, is quoted as saying, "Research is an expression of faith in the possibility of progress. The drive that leads scholars to study a topic has to include the belief that new things can be discovered, that newer can be better, and that greater depth of understanding is achievable. Research, especially academic research, is a form of optimism about the human condition."[2] Scientists embody that optimism when they apply their expertise to explore their specialized fields more deeply or use new techniques to investigate old ideas or unexplained phenomena in a given discipline. Equally important is the exciting, innovative research that takes place in the space between disciplines, where different fields converge to address questions that demand the application of expertise from more than one discipline. These fertile areas provide some of the greatest opportunities for real-world application and impact. Using our case as an example, material science can be applied to develop or, in the context of novel processes, to solve problems in medicine, environmental science, energy, or mechanical engineering, providing some of the greatest opportunities for real-world application and impact.

The reality is that research requires funding, which typically requires more than optimism to obtain and maintain. Traditional government funding, in particular, is awarded based on a peer review process, meaning that the proposed research is expected to be based on established knowledge and beliefs. This approach is most likely to result in incremental changes to a research topic or small expansions of the

knowledge base. The awarded funds are restricted to the proposed research and allocated for specific purposes. In Peter Thiel's recent book, *Zero to one: Notes on Startups, or How to Build the Future*, he frames breakthrough ideas as zero-to-one ideas and incremental ideas as one-to-*n* ideas.[3] His thesis in the book is that a truly innovative, zero-to-one idea is often associated with a core belief that an inventor has that no one else has. This is exciting and alarming at the same time, especially for academic researchers, since the primary mechanism for funding research is the peer review system which requires one's peers to agree with you in order to get funding. Given this reality, researchers pursuing such zero-to-one ideas will need financial support that is not of the standard peer review type. Such alternative funding could include endowed professorships, certain unrestricted federal funds like the NIH Director's Pioneer Award, and the ability to work with the venture capital community doing translational research or academic entrepreneurship.

Pursuing translational research is the most direct way for academic researchers to improve the health, well-being, and economic vitality of a society. For an academic scientist, entrepreneurship provides a compass that helps to navigate where important problems are. It also enables a scientist to benefit from peer review on steroids! Certainly, peer review associated with publishing a paper makes papers stronger. In analogy, it is our experience that the peer review associated with financing one's startup is likewise helpful in identifying the key milestones and uncertainties of one's research ideas, thereby making the science better. In addition, this experience leads to improved grantsmanship, as it forces one to articulate the differences and benefits of one's own science: the value proposition. Further, the resources associated with company formation can provide an opportunity for scale-up of critical technologies to allow the expansion of one's ideas in ways not possible otherwise. And finally, a key benefit of academic entrepreneurship is that it intrinsically requires one's science to be valid: if it is not, mistakes will be identified quickly.

Convergence and Flexibility as a Mantra. It is ironic that one of the few places where entropy is not at play is at universities! Indeed, most academic institutions have entrenched divisions that group like researchers together and isolate them from other types of researchers. Nonetheless, communicating and collaborating with researchers in fields other than one's own can give rise to new insights and perspectives that amplify the ability to join knowledge from diverse fields to both identify and address important, societally relevant research questions. Large multidisciplinary research centers, such as government-funded science and technology centers, provide excellent platforms for convergent research to lead to new discoveries, and indeed, there has been significant momentum in recent years to find ways to better support convergent research. Most recently, for example, the National Science Foundation revealed an agenda, in the form of nine "big ideas", aimed at guiding the agency's approach to addressing urgent societal challenges in the coming decades; "Growing Convergent Research at NSF" is among these major priorities.[4] Turning to management, having a team that can work together effectively within a large research center requires excellent leadership and commitment for success. Providing leadership that fosters relationships and interactions is a necessary skill for a successful research director, especially in a convergence framework. One advantage of large funded research centers is that they can provide greater opportunity to

leverage innovations within the center and pivot from the original focus to a new focus within a larger context area of research. The longer-term nature of centers also allows for the development of continuity within a collaborative group, where group members work together long enough and deeply enough to learn extensively from one another, gain new expertise, and become multilingual with respect to research topics. More informal opportunities for collaboration can be found through participation in scientific societies, government panels, and workshops. The best collaborations are enabled through intentional actions that stretch one's comfort zone, where you adopt a vulnerable trust[5] and are clear about what you do not know, while learning and communicating with others about what you do know.

Successful academic groups focused on translational research apply the findings of fundamental science to the development of useful outcomes in society and may include students and professionals in chemistry, engineering, biology, physics, pharmacy, immunology, and others. A diverse group of people working and sharing their research with one another enables new understandings and problem-solving approaches. Fostering respect and inclusion of diversity of all types, not only in experience and educational background but also in identity— including race, religion, gender, culture, nationality, sexual orientation, personality, and socioeconomic background— encourages new ideas and approaches that can blossom into unexpected and innovative discoveries.[6]

The Importance of a Supportive University Home for Faculty. The University of North Carolina at Chapel Hill and North Carolina State University have formed an extremely supportive environment for me and my research group over the past 25 years. We have had access to an enabling infrastructure, leadership, and programs that have helped us to become extremely proficient at translating research to the private sector. This has included opportunities to partner with multiple corporations over the years, something that required extra administrative oversight by the university, which was not always easy nor was it inexpensive. The university also enabled my students and me to start several new companies based on our research. This helped our research to reach a scale to truly impact society, but, even more importantly, the close ties between these startup companies and my academic lab allowed us to further our research in ways that would not have been possible otherwise. One key example of this involved Liquidia Technologies. Liquidia was formed based on a nano- and micromolding technology developed at UNC-CH and NC State that we referred to as PRINT (*vide infra*). As part of their corporate development plans, Liquidia's investors poured millions of dollars into this technology to develop a process to make molds to form nano- and microparticles. These molds were provided to my academic laboratory in a form that could be run on a laboratory-scale roll-to-roll machine at the university. This allowed us to make large quantities of particles that we could not make otherwise. Such a capability enabled us to ask new questions about the fate of particles in *in vivo* experiments, which triggered many preclinical animal studies that would not have been possible otherwise.

A key part of this translational research environment was the ability of our university to file patent applications. For academic research to lead to products, commercial interests must get involved to provide the funds for scale-up and market development. This translation of research requires a significant investment, often in the range of hundreds of millions of
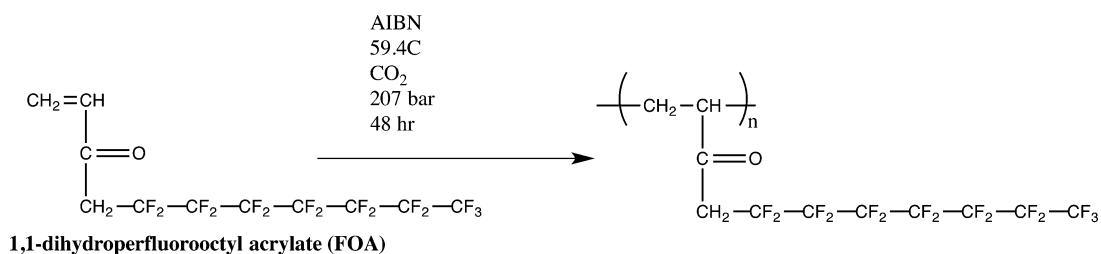
Figure 1. Homopolymerization of fluorinated octyl acrylate in CO_2.

dollars. The return on this investment must have a high potential, and as such, the filing of patent applications is often a necessary prerequisite. Without it, commercial interests will never get involved. Continuing this line of thinking, imagine a scenario where a faculty colleague and her research group come up with a key breakthrough that could lead to the cure of a dreaded disease like AIDS or a particular form of cancer. If her university does not have the resources to file for a patent application prior to her publication, then for all practical purposes that publication will negate the attainment of a strong patent. Without the potential for a strong patent to emerge, the ability to garner the hundreds of millions of dollars necessary to convert that breakthrough into a viable therapy is low. While a moral obligation to publish and share seminal and/or key research results is often argued, the commercial reality begs the question: does a university have the moral obligation to have the resources necessary to file a patent application too? Key patents, whether supported through the university or developed outside of the university setting, must be in place. Otherwise, groundbreaking research may never make it outside the laboratory to become game-changing, widely available technology.

RESULTS AND DISCUSSION

Our group has focused on synthetic organic polymer chemistry integrated with novel processes. We have built and maintained a group that is multidisciplinary and diverse to encourage innovation in and among convergent disciplines and that has respect for individuals in an environment where people can collaborate, impart unique expertise, and challenge one another to look at problems from different perspectives. Having the courage to learn new things and perform research in new areas to us has been most effective through collaborations.

One Thing Led to Another, Which Led to Another... We began our research in 1990 with the focus of performing free radical polymerizations in supercritical carbon dioxide (scCO$_2$). We discovered unexpected solubility and controlled reactivity of fluoropolymers in this medium that we exploited to develop an environmentally friendly synthetic option for manufacturing industrially important fluoropolymers with the potential to change the industry. Further research into the development of surfactants for CO_2 was largely supported through the National Science Foundation Science and Technology Center (NSF STC) for Environmentally Responsible Solvents and Processes (CERSP), which involved participants from the University of North Carolina at Chapel Hill (UNC), North Carolina State University (NCSU), North Carolina A&T University (NCAT), University of Texas at Austin (UT), and the Georgia Institute of Technology (GIT). At our home institutions, UNC and NCSU, our research led us to develop the use of CO_2 as an environmentally friendly dry cleaning process for fabrics and semiconductor processes. As a result of the long-range structure within the NSF STC, we had the advantage of being able to pivot into new opportune areas of research over the course of the center lifetime (1999−2009). Our synthetic processes were used to produce new fluoropolymers with new properties that we adapted to the fields of microfluidics and photolithography, leading us to develop a brand new industrial process for producing medically relevant nanoparticles with controlled shape and size called particle replication in nonwetting templates (PRINT). As a result of the pivot of our research focus to nanoparticle production and the use of nanoparticles to pursue novel approaches to vaccine design and cancer treatment, we have been fortunate to help launch and then be able to work within the Carolina Center for Cancer Nanotechnology Excellence (CCNE) funded by the National Cancer Institute (NCI), currently one of only six CCNEs in the country. Concurrently, we maintained research interests outside of the opportunities offered by PRINT. While investigating the development of nonfouling marine coatings based on our fluoropolymers, we discovered the ability to solubilize lithium salts and applied efforts to investigating perfluoropolyethers as nonflammable electrolytes in lithium ion batteries. The unique properties of these perfluorinated polymer electrolytes are still being explored and may yet provide an opportunity for innovative leaps in lithium battery technology. Additionally, our early fluoropolymer technology development has helped to propel an innovative leap in additive manufacturing. Harnessing the competing chemical reactions of free radical polymerization and oxygen inhibition, we developed continuous liquid interface production (CLIP). This unique 3D printing technology that is changing the potential of manufacturing in America is possible through the innovative use of a highly oxygen permeable transparent window made from some of our early fluoropolymer materials. In summary, we developed a process to create new materials. Those new materials led to the development of additional new processes that translated to the development of new products that are affecting society.

Polymerizations in Carbon Dioxide and Related Surfactants. While conducting graduate research with Jim McGrath at Virginia Tech, one of the authors (J.M.D.) was exposed to supercritical fluid extraction processes[7,8] that were used to fractionate copolymers to determine their chemical composition distribution.[9] The supercritical fluid extraction process was a powerful tool due to the fine control of solvating power as a function of temperature and especially pressure. Our research program at UNC was based on this early exposure to the power and potential of supercritical fluids (SCFs). Our UNC group performed research in the 1990s and 2000s synthesizing and characterizing fluoropolymers and fluorinated copolymers in scCO$_2$, with new compositions and architectures being developed to explore new properties and applications for this class of materials. Fluoropolymer synthesis in scCO$_2$ has

been reviewed that includes our numerous contributions to the field.[10] After filing our patent applications through the support of the chemistry department at UNC, we first reported our new synthetic technique for fluoropolymers in a 1992 *Science* paper.[11] Our UNC research began with the idea that free radical polymerizations in SCFs could be very interesting due to the unique properties of SCFs. We proposed that while $scCO_2$ has the density of a liquid, it has the viscosity of a gas[12] and, since free radical polymerizations are diffusion controlled, the diffusivities would be much higher in CO_2 radical reactions, which could have positive effects on the kinetics and molecular weight. Other advantages were that there can be no chain transfer to solvent. Prevailing theory at the time was that radical reactions would be quenched in CO_2. We found that fluoropolymers in particular had extremely high solubility in $scCO_2$, and we demonstrated the synthesis of high molecular weight perfluorinated octyl acrylate (FOA) homopolymer (Figure 1) and statistical copolymers of FOA with traditional hydrocarbons such as styrene, methyl methacrylate, butyl acrylate, and ethylene. This discovery became very important because at the time there was in impending ban on the use of chlorofluorocarbon (CFC) solvents that were used for the industrial synthesis of many fluoropolymers. Typical hydrocarbon solvents are incompatible with the synthesis of high molecular weight fluorocarbons via free radical chain polymerization due to the highly reactive nature of electrophilic radicals associated with fluorocarbons, which leads to high degrees of chain transfer with hydrogen containing solvents. Homogeneous polymerizations in CFC solvents were the option of choice for the manufacture of nonaqueous grades of important fluoropolymers, such as electronics grades of polytetrafluoroethylene and its derivatives, commonly known as Teflon, which are used in many important industries (e.g., wire coatings for high speed communications, high temperature lubricants, nonstick coatings, and corrosive chemical linings and coatings). An important alternative method of polymerization, still utilized today, was emulsion polymerization of tetrafluoroethylene (TFE) using perfluorinated surfactants, such as perfluorooctanesulfonate (PFOS), which have been shown, along with the acid form, perfluorooctanoic acid (PFOA), to have a wide and persistent presence in water, soil, and biological systems after many years of use in industrial processes and products.[13] In 1995 we reported the successful synthesis of tetrafluoroethylene-based fluoropolymers in $scCO_2$.[14] In 1996−1998 three U.S. patents were issued to the University of North Carolina for the $scCO_2$ synthesis of fluoropolymers.[15−17] In April of 1999 it was announced that DuPont Co., having exclusively licensed the technology from UNC, had begun construction on a $40 million, 2.5 million lb/year development and manufacturing facility to make melt-processable fluoropolymers using a process based on $scCO_2$.[18] The $scCO_2$ based licensed technology was not pursued to a significant extent by DuPont after internal corporate decisions to proceed with production using only the emulsion process based on PFOS. This result was a disappointing one for us, and for society, because of the environmental implications of continuing the use of the PFOS surfactant based technology. The demonstrably safer licensed technology using $scCO_2$ was not scaled up and utilized beyond the initial investment due to political and economic based decisions within DuPont. This is an important example of how even the best technology can succumb to the pressures of "business" in the hands of entrenched corporate interests. In many ways this negative experience with DuPont drove our

entrepreneurial interests and diminished our interests in partnering exclusively with existing companies that could, for whatever reason, not drive technology forward in a manner in which we would have, had we controlled our own destiny.

The success of using $scCO_2$ for fluoropolymer synthesis triggered our proposal for and award of one of five NSF Science and Technology Centers in 1999. Our initial developments were solution polymerizations in $scCO_2$. We were also interested in conducting heterogeneous polymerizations in $scCO_2$ such as commercially relevant emulsion polymerizations. Traditional emulsion polymerizations utilize surfactants to disperse organic reactants, and the resultant colloidal reaction products, in water. For our purposes we needed to develop surfactants that would disperse organic reactants in $scCO_2$.

We developed fluoropolymer-based surfactants specifically for CO_2 that benefited many industrial solvent intensive processes by reducing the use of organic and halogenated solvents. We designed the CO_2 surfactants to include a "CO_2-philic" portion and a "CO_2-phobic" portion (Figure 2) and
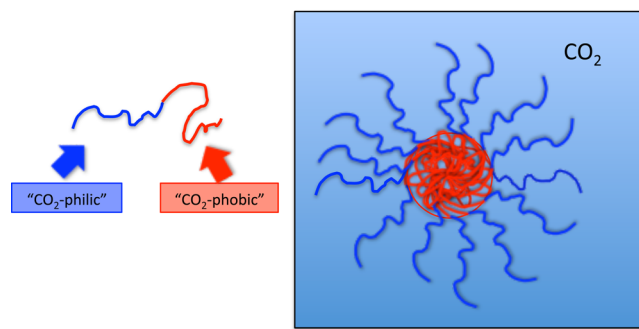

Figure 2. Block copolymer surfactant design for CO_2.

developed a variety of compositions and architectures.[19−22] Typical surfactants for water-based emulsions combine a hydrophilic portion and a lipophilic (or hydrophobic) portion. In an early example we synthesized a series of block copolymers incorporating a polystyrene block (CO_2-phobic) and a poly(1,1-dihydroperfluorooctyl acrylate) (PFOA) block (CO_2-philic).[23] Through a very successful collaboration with George Wignall at Oak Ridge National Laboratories, small angle neutron scattering (SANS) was used to characterize micelles formed by these block copolymer surfactants in $scCO_2$ and demonstrate the emulsification of a hydrocarbon oligomer at up to 20 wt %.[19] In 1997 we further demonstrated the use of dendritic CO_2 surfactants, where a perfluoroether acid fluoride was used to functionalize an amine terminated fourth generation hydrophilic dendrimer, creating a hydrophilic/CO_2-phobic core with a CO_2-philic shell. The resulting surfactant was insoluble in water but soluble in CO_2 at a variety of temperatures, including room temperature, at pressures >76 atm. This dendritic surfactant was used to extract water-soluble/CO_2 insoluble organic dyes, including methyl orange, from water into a CO_2 phase without agitation, at room temperature. This functionality had significant potential impact in environmental remediation of contaminated water, the extraction of pharmaceutical products, the encapsulation of drugs for targeted delivery, and the transport of reagents for chemical reactions (such as polymerizations) in liquid and supercritical CO_2 solvents, thereby avoiding unwanted organic and hydrocarbon solvents.[21] With our patented technology we started a company to replace toxic

we demonstrated the utility of PFPE as a highly effective material for imprint lithography of organic materials on the nanoscale.[32] Using a patterned silicon wafer master with square channel features of 2 μm in width and spacings that were 5 μm deep, we prepared PFPE molds by coating the master with the PFPE liquid resin and photocuring for 1 min. The cured PFPE elastomer was easily peeled from the master. The performance of the PFPE mold was compared to a PDMS mold prepared using the same master. The PDMS required that a fluorinated pretreatment be applied to the master to allow good release of the mold after the 15 h 80 °C cure. Photocured acrylate based replicates prepared using the PFPE mold were of significantly higher quality than acrylate replicates prepared using the PDMS mold. The PDMS mold swelled in the presence of the uncured acrylate, and had some adhesion to the cured acrylate that distorted the shapes of the replicate and endowed it with small pieces of torn PDMS mold that could be seen at high magnification (see Figure 5G). As a true test of nanoscale
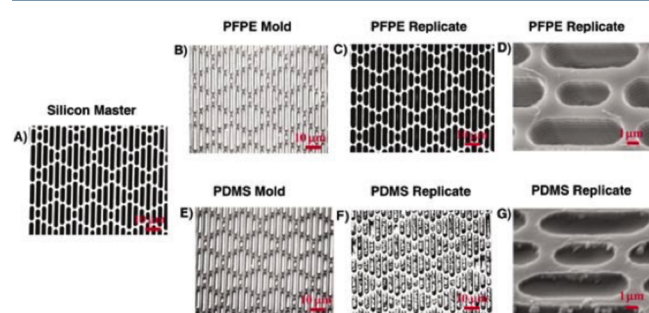

Figure 5. Images of a silicon master with 2 mm features (A), PFPE and PDMS molds made from this master (B, E), and replicate molds of TMPTA using the corresponding stamps (C, D, F, G). While both elastomers produced molds of high quality, the TMPTA replicate made with the PDMS mold contains residual PDMS that was ripped from the mold presumably because of adhesion (F, G). In contrast, the low surface energy PFPE mold was easily released from the TMPTA replicate (D). The submicron striated features on the replicate in panel D are present on the silicon master and are a result of multiple etching steps used during its fabrication.[32]

fabrication, we applied the PFPE to a silicon wafer master with much smaller features, having a width of 140 nm, spacing of 70 nm, and a depth of approximately 50 nm, and created a PFPE nanomold. The nanomold was used to produce photocured acrylate based replicates that looked identical to the master. The PFPE nanomold was easily removed from the cured acrylate replicate due to its low surface energy and flexibility. Useful PDMS molds of the nanoscale master could not be produced. The finding of the effectiveness of the PFPE elastomers as nanomolding materials was a huge development, as it enabled a much easier method for fabrication of nanoscale devices that could have applications in important and growing technology areas such as medicine, electronics, and sensors.

The potential to mold organic materials into nanoscale structures was evident using the PFPE mold materials. Concurrent to this work, local collaborations with the Department of Pharmacology, the School of Pharmacy, and the Gene Therapy Center at UNC, as well as the Department of Engineering at NCSU, were focused on a different process, inverse microemulsion polymerization, to produce nanoparticles for the purpose of cellular gene and antisense delivery.[33] It occurred to us that the nanofabrication micromolding process could open up opportunities in the area of

nanoscale organic particles for gene therapy as well as drug delivery. We realized that imprint lithography using PDMS, silicon, glass, or quartz molds was ineffective because the organic liquids to be molded showed significant interfacial interaction with the surfaces of molds and left a very thin layer of material between the mold surfaces upon filling and closing. This very thin layer, known as a "scum", served to hold the nanoparticles together. The advantage of using a PFPE nanomold and cover sheet was that the very low surface energy of the PFPE caused it to be only partially wetting to most organic liquids, and therefore the PFPE surfaces could come together cleanly and isolate the molding material into the mold cavities under small pressure. We coined this nanomolding technique as "PRINT", which stands for particle replication in nonwetting templates (Figure 6). The intentional
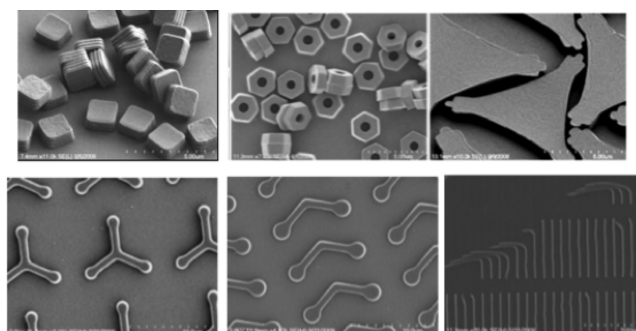

Figure 6. Examples of PRINT fabricated particles with a range of shapes, sizes, and physical and chemical properties.

creation of this recognizable acronym to describe our process was a driver for differentiation of our work from the alternative processes. It allowed us to take ownership of the process and materials, which helped to illustrate the uniqueness of the products produced using it and the opportunities for wide application of the process.

In 2005 we demonstrated the broad potential for PRINT, showing the production of isolated nanoparticles of commercially relevant materials including poly(ethylene glycol) (PEG), poly(D-lactic acid) (PLA), and poly(pyrrole) (PPy).[34] We produced nanoparticles using different synthetic routes with PRINT, including free radical polymerization, metal-catalyzed high temperature polymerization, and oxidative coupling using a strong acid, demonstrating flexibility and range in the process. The ability to choose the chemistry of the particle opens up the options for drugs and other agents to be successfully encapsulated in the particles for later application in areas such as oncology and vaccine design. The ability to change the shape enables control of interaction, delivery, transport, and packing in colloidal particles. We showed that a range of relevant sizes (<100 nm) and shapes of nanoparticles could be produced with PRINT for applications including drug delivery and sensing. We also used PRINT to load relevant cargoes into nanoparticles such as an oligonucleotide, avidin (a biologically active protein), and doxorubicin (an important chemotherapy agent). We showed that the agents were dispersed, available, and active from PRINT nanoparticles. The introduction of PRINT laid the foundation for a broad set of research activities that proceeded over the next decade in our UNC-CH and NC State laboratories, leading to a significant growth in the life sciences component of the research group and significant

collaborations with medical and pharmaceutical research-ers.[35−40]

With PRINT's broad potential to lead to commercial products, we also secured key patents leading to the launch of a startup company, based on PRINT, Liquidia Technologies. Through careful implementation of a thorough conflict of interest management plan by UNC-CH, our academic laboratory and the company were able to forge an amazing partnership that drove the technology in new directions and into the clinic. Liquidia was successful at winning venture capital funding to scale up the PRINT process, which further enabled research in new areas applicable to PRINT to continue at UNC. Molds manufactured at Liquidia were shared with the UNC lab as part of a research agreement between Liquidia and the DeSimone group at UNC, and UNC groups collaborated closely with Liquidia, preparing and testing PRINT nano-particles with different properties for a wide variety of applications. This relationship was highly beneficial to the growing company and to the university. As the company has grown and changed, focusing on economic drivers required in commercial industries, the range of the Liquidia/UNC collaboration has been narrowed as a result of greater separation in immediate and long-term goals.

In the mid to late 2000s fluorinated polymers, in conjunction with highly hydrophilic polymers, were being investigated as environmentally friendly amphiphilic anti-biofouling coatings for application in marine environments. Christopher Ober's group was designing grafted block copolymers of aliphatic fluorocarbons and poly(ethylene glycol) (PEG).[41,42] Karen Wooley's group was using hyperbranched highly fluorinated poly(styrene)s and poly(arylene ether)s cross-linked with PEG to create amphiphilic cross-linked networks.[43,44] All of these approaches were remarkably successful at reducing biofouling of both hydrophobic based and hydrophilic based marine organisms, which led us to consider the use of perfluoroethers for this application. Through funding from the Office of Naval Research (ONR), we began to focus on the development of nonfouling marine coatings based on amphiphilic hybrid materials using PFPEs and hydrophilic poly(ethylene glycol) (PEG).[45] Surprisingly, we found that low molecular weight (1000 g/mol) PFPE could be blended with low molecular weight PEG (<1000 g/mol) to provide optically transparent blends. We found this to be true for both the diol and dimethacrylate end-capped oligomer forms. We functionalized the oligomers with dimethacrylate end groups and photocured films of the PFPE/PEG blends to create a range of film compositions that showed a range of morphologies indicating nanophase separation shown by atomic force microscopy (AFM) and dynamical mechanical thermal analysis (DMTA). The films showed the potential to reduce fouling even with low levels of PEG, but the highly interesting finding from this research was the unexpected miscibility of the PFPE/PEG blends.

We began to explore other applications, focusing in areas where PEG had utility but faced drawbacks that the inclusion of PFPE might address. PEG and PFPE are both aliphatic polyethers with a subambient T_g, although the T_g of PFPE is substantially lower and PFPE does not crystallize. Being a fluorocarbon, PFPE also offers the potential for improved thermo-oxidative stability. Once armed with the surprising discovery that PFPE and PEG were miscible, we began to explore the phase equilibria of a ternary system of PFPE, PEG, and lithium salts, because it was well-known that PEG would

dissolve lithium salts, and perhaps, we hypothesized, given the thermo-oxidative stability of PFPEs, such a ternary system would be nonflammable. Perhaps not unexpectedly, we found that a 50:50 blend of PFPE and PEG could dissolve lithium salts. But very surprisingly, when we started to vary the stoichiometry of the ternary system, we discovered that pure PFPE, without PEG, could dissolve lithium salts! Given the hydrophobic nature and the electron deficient ether bonds of the PFPE, this was a real shocker to us.

In collaboration with Nitash Balsara's group at the University of California, Berkeley (UCB), we explored the electrochemical properties of PFPE blends with the well-known bis-(trifluoromethane)-sulfonimide lithium salt (LiTFSI).[46] The solubility of LiTFSI in the PFPE oligomers decreased inversely with molecular weight and increased with a synthetic modification of the hydroxyl end groups to methyl carbonate end groups. Electrochemical measurements showed that the conductivity of the PFPE/LiTFSI polymer electrolytes was significantly lower than that of analogous PEG/LiTFSI polymer electrolytes. However, the transference number, which is a value related to battery performance, was measured to be very near unity, an unprecedented high value relative to all other electrolytes for lithium ion batteries. Understanding the fundamental chemistry in the PFPE system leading to this high transference number and utilizing that information could lead to important breakthroughs in the field of lithium ion batteries leading to high performance, long lasting, nonflam-mable batteries for critical, portable applications including transportation. This opportunity for liquid PFPEs is being collaboratively explored between the DeSimone and Balsara groups through funding from the Department of Energy (DOE) through a large, multi-institution collaborative Energy Frontier Research Center (EFRC), the Center for Mesoscale Transport Properties (m2M). Alternative solid state perfluori-nated polymers are being explored as battery electrolytes through a National Science Foundation (NSF) grant held jointly by UNC and UCB. Recently published work has shown the utility of PFPE in a hybrid single ion conducting solid state electrolyte for lithium ion batteries.[47] These preliminary hybrid materials exhibit very high conductivities on the order of 10^{-4} S/cm, a cation transference number of close to unity, excellent stability, and low dissolution of lithium polysulfides, making them potentially ideal candidates for Li−S cells. The develop-ment of the materials, test cells, and electrochemical character-ization to attain such rapid progress in the battery field was made feasible through the strong collaborations with the Balsara group. This collaboration has also spawned a startup company, Blue Current, which is now pursuing the develop-ment of high performance lithium ion batteries.

Rapid and Continuous 3D Printing? Photopolymeriza-tion is an important industrial process for applications including coatings, adhesives, inks, microelectronics, dental fillings, and 3D printing, to name a few. The majority of these applications utilize free radical chain polymerizations of solvent free resins incorporating acrylated and/or methacrylated oligomer and monomer formulations.[48] The advantages of utilizing a photopolymerization process include significant positive environmental impacts such as reduction or elimination of the use of organic solvents and low temperatures that use less energy and cooling water. One of the major issues with free radical photopolymerization, though, is its high sensitivity to oxygen, which inhibits the reaction and can lead to low, surface specific conversion. There are a number of physical and

chemical strategies that have been utilized to reduce oxygen inhibition for industrial processes.[49]

Stereolithography is a 3D printing technique that utilizes photopolymerization to fabricate 3D structures in a layer by layer process, which, stated in another way, is a 2D process repeated over and over. In the example of a bottom up stereolithography apparatus (SLA), each individual photopolymer layer is formed in a closed environment between a build plate and a transparent window. The layer then has to be individually removed from the window, additional photopolymer resin has to be applied to the forming space, and then the layer is precisely lowered back down to create the forming zone again.[50] We conjectured that we could turn the "disadvantage" of oxygen inhibition into an advantage that enabled continuous 3D printing. The key to enabling this was the need for a window material that would be simultaneously transparent to UV light, highly permeable to oxygen, and impervious to swelling by organic liquid resins. An ideal candidate material is Teflon AF.

Understanding the potential of convergent research, by bringing together scientists with backgrounds in a range of areas in chemistry, physics, and engineering, a novel 3D printing process was developed resulting in the launch of a new company called Carbon. Our idea was to develop a technique that allowed us to continuously grow a solid part out of a liquid resin similar to the T-1000 Terminator that grows from a vat of liquid metal in the movie *Terminator 2*. A Teflon AF membrane, with its high oxygen permeability, low surface energy, and excellent chemical stability, was identified as the key enabler in the technique now known as continuous liquid interface production (CLIP). CLIP is a breakthrough process for additive manufacturing that has also led to the development of many new classes of photocurable 3D printing materials, ranging from elastomers to high performance, highly thermally stable materials. CLIP allowed for a fundamental change in 3D printing; we have shifted the field from its focus on simple prototyping, to what we refer to as functional prototyping that yields real parts and speeds that are 25−100 times faster.[51] We believe that the manufacture of real parts at game-changing speeds will usher in a new industrial category we refer to as 3D manufacturing. The rapid development of the software and hardware for the production machinery, along with new directly suited materials with unprecedented mechanical properties, has been made possible through the resources available from the venture capital community and strategic partnerships (approximately $200 million) to Carbon. What we do at Carbon is exploit the benefits derived from the intentional emphasis on diversity, convergence, and collaboration, especially at the intersection of hardware, software, and molecular science. CLIP today is the essence of software controlled chemical reactions to create final parts for designers, engineers, and manufacturers. Critical factors that can be varied to affect the form and function of the product being fabricated include the resin reactivity, light absorption, viscosity, and green strength. Other factors include the flux of oxygen, the flux of light, and the geometry and design of the part being fabricated. The optimization and growth of this model is enabling this future at Carbon. The fields of application include automotive, aerospace, consumer electronics, industrial, athletic footwear, and medical applications, to name a few. Moreover, a research agreement between Carbon and UNC supports long-term research in applications related to drug delivery, medical devices, and the production of microscale features.[52]

■ CONCLUSION

New Processes Can Change the Game. Commercial processes widely used to produce industrial and consumer products have a significant impact on the environment, the economy, and the products available to consumers. Novel processes developed on a small scale may provide opportunities for significant economic savings through reduced environmental impacts or improved products, but entrenched processes are often perpetuated due to the perceived imbalance of the cost of infrastructure investment into new processes. Successfully bringing a novel process to market is a tricky proposition that must be carefully addressed by a team, including a range of scientists, engineers, and business professionals, through an intentionally orchestrated sequence of events and technical developments.

It is exciting to consider the creation of a future fabricated with light. We like to consider light as our chisel for fabricating things. The metaphor of light as a chisel is a powerful one, and it helps to illustrate to our partners, customers, and investors what such a new future could mean. Currently polymers are made by a polymer supplier and provided to product manufacturers who process that polymer further to produce a polymer part. The polymer making up that part is always impacted by factors such as aging, contamination, and thermal-oxidative degradation to some extent, and therefore the polymer in the product does not have the same properties as the polymer that was originally made by the polymer manufacturer. Fabrication with light skips a step in this traditional manufacturing model. The polymer is produced simultaneously with the part, and therefore their properties are the same. The product properties are what become important, and those are a function of the starting materials, the process, and the design, which all come together in a single fabrication step. This could truly change the market as polymer producers change their strategies to produce better resins which are processed, packaged, shipped, and stored differently than current thermoplastic resins typically utilized to mold plastic parts. This is not to say that all thermoplastic molding will be replaced through fabrication with light. The greatest value in the fabrication with light is the potential to make parts that cannot be molded or mass customized, or bespoke parts like materials for applications in dentistry, hearing aids, and even footwear.

The job of a research-active professor is a many faceted one. Contributing to department organization and structure; teaching and grading college and graduate students in their fields of study; writing grant proposals and reports; purchasing, maintaining, and organizing laboratories and equipment; directing graduate and collaborative research; and authoring and editing publications of research all require a driven and persevering personality along with good interpersonal and organizational skills. To be successful in all of these areas requires the development of a team that is effective. Running a good research group with an emphasis on translating discoveries into real-world applications has many similarities to running a small company organizationally, although the financial structure, intentionally high personnel turnover rate, goals, and outputs differ significantly.

While it is not the typical outcome, the optimism with which a scientist approaches research through the translation of fundamental scientific discoveries into practical solutions for society can be highly motivating and rewarding. Being awarded

a proposal for scientific research funding can enable the exciting transition from ideas to discovery, then from discovery to practical application. Identifying the key discoveries, and translating those into solutions, is most effectively accomplished through convergent, collaborative research involving multiple disciplines and groups of people with diverse backgrounds and expertise. The successful development and commercialization of products relies on the unique capacities found in private industry, which provides a very different environment compared to an academic research group or center. Becoming familiar with the economies of starting materials and scale-up factors coupled with legal and regulatory requirements, packaging, marketing, and distribution can be overwhelming to an uninitiated scientist, and therefore a fruitful translation of academic research to the marketplace typically depends on outreach to, and collaboration with, experts in the area of business. Many universities are now emphasizing technology transfer offices, campus incubator spaces, and other campus-based resources designed to help lower the barriers associated with an endeavor to commercialize innovations spawned from academic research.

Finally, in business and in research alike, we have found that perhaps the biggest factor for success is understanding the convergence paradigm and operating in it by bringing together a diverse group of people; facilitating open and respectful communication of ideas, knowledge, and perspectives; and working collaboratively toward shared goals. This enables maximum leveraging of knowledge with respect to identifying and addressing the key questions that bear relevance to societal needs and challenges, leading to successful translation of science to real world solutions.

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Notes
The authors declare the following competing financial interest(s): Professor DeSimone is a stakeholder in Liquidia Technologies, Blue Current, and Carbon.

■ REFERENCES

(1) National Research Council. *Convergence: Facilitating Transdisciplinary Integration of Life Sciences, Physical Sciences, Engineering, and Beyond*; National Academies Press: Washington, DC, 2014.
(2) Rosovsky, H. *The University*; W. W. Norton & Company: New York, 1991.
(3) Thiel, P.; Masters, B. *Zero to One*; Crown Publishing: New York, 2014.
(4) Mervis, J. NSF Director Unveils Big Ideas. *Science* **2016**, *352* (6287), 755−756.
(5) Lencioni, P. M. *The Advantage*; Jossey-Bass: San Francisco, CA, 2012.
(6) DeSimone, J. M.; Farrell, C. L. Driving Convergence with Human Diversity. *Sci. Transl. Med.* **2014**, *6*, 238.
(7) Yilgor, I.; McGrath, J. E. Novel Supercritical Fluid Techniques for Polymer Fractionation and Purification, 1. Background. *Polym. Bull.* **1984**, *12*, 491−497.
(8) Yilgor, I.; McGrath, J. E. Novel Supercritical Fluid Techniques for Polymer Fractionation and Purification, 2. Fractionation and Characterization of Functional Siloxane Oligomers. *Polym. Bull.* **1984**, *12*, 499−506.
(9) DeSimone, J. M.; Hellstern, A. M.; Siochi, E. J.; Smith, S. D.; Ward, T. C.; Gallagher, P. M.; Krukonis, V. J.; McGrath, J. E. Homogeneous and Multiphase Poly(methyl methacrylate) Graft Polymers via the Macromonomer Method. *Makromol. Chem., Macromol. Symp.* **1990**, *32*, 21−45.
(10) Du, L.; Kelly, J. Y.; Roberts, G. W.; DeSimone, J. M. Fluoropolymer Synthesis in Supercritical Carbon Dioxide. *J. Supercrit. Fluids* **2009**, *47*, 447−457.
(11) DeSimone, J. M.; Guan, Z.; Elsbernd, C. S. Synthesis of Fluoropolymers in Supercritical Carbon Dioxide. *Science* **1992**, *257*, 945−947.
(12) Debenedetti, P. G.; Reid, R. C. Diffusion and Mass Transfer in Supercritical Fluids. *AIChE J.* **1986**, *32*, 2034−2046.
(13) Weber, R.; Watson, A.; Forter, M.; Oliaei, F. Review Article: Persistent Organic Pollutants and Landfills - a Review of Past Experiences and Future Challenges. *Waste Manage. Res.* **2011**, *29*, 107−121.
(14) Romack, T. J.; DeSimone, J. M.; Treat, T. A. Synthesis of Tetrafluoroethylene-Based, Nonaqueous Fluoropolymers in Supercritical Carbon Dioxide. *Macromolecules* **1995**, *28*, 8429−8431.
(15) US5496901, Method of Making Fluoropolymers, March 5, 1996.
(16) US5688879, Method of Making Fluoropolymers, November 18, 1997.
(17) US5739223, Method of Making Fluoropolymers, April 14, 1998.
(18) Basta, N. New DuPont Fluoropolymer Plant Will Use Supercritical Carbon Dioxide Process. Chemical Online. April 22, 1999. http://www.chemicalonline.com/doc/new-dupont-fluoropolymer-plant-will-use-super-0001.
(19) McClain, J. B.; Betts, D. E.; Canelas, D. A.; Samulski, E. T.; DeSimone, J. M.; Londono, J. D.; Cochran, H. D.; Wignall, G. D.; Chillura-Martino, D.; Triolo, R. Design of Nonionic Surfactants for Supercritical Carbon Dioxide. *Science* **1996**, *274*, 2049−2052.
(20) Fulton, J. L.; Pfund, D. M.; McClain, J. B.; Romack, T. J.; Maury, E. E.; Combes, J. R.; Samulski, E. T.; DeSimone, J. M.; Capel, M. Aggregation of Amphiphilic Molecules in Supercritical Carbon Dioxide: A Small Angle X-ray Scattering Study. *Langmuir* **1995**, *11*, 4241−4249.
(21) Cooper, A. I.; Londono, J. D.; Wignall, G.; McClain, J. B.; Samulski, E. T.; Lin, J. S.; Dobrynin, A.; Rubinstein, M.; Burke, A. L. C.; Frechet, J. M. J.; DeSimone, J. M. Extraction of a Hydrophilic Compound From Water Into Liquid CO_2 Using Dendritic Surfactants. *Nature* **1997**, *389*, 368−371.
(22) Keiper, J. S.; Behles, J. A.; Bucholz, T. L.; Simhan, R.; DeSimone, J. M.; Lynn, G. W.; Wignall, G. D.; Melnichenko, Y. B.; Frielinghaus, H. Self-Assembly of Phosphate Fluorosurfactants in Carbon Dioxide. *Langmuir* **2004**, *20*, 1065−1072.
(23) Guan, Z.; DeSimone, J. M. Fluorocarbon-Based Heterophase Polymeric Materials. 1. Block Copolymer Surfactants for Carbon Dioxide Applications. *Macromolecules* **1994**, *27*, 5527−5532.
(24) Bunyard, W. C.; Romack, T. J.; DeSimone, J. M. Perfluoropolyether Synthesis in Liquid Carbon Dioxide by Hexafluoropropylene Photooxidation. *Macromolecules* **1999**, *32*, 8224−8226.
(25) Hong, J. W.; Quake, S. R. Integrated Nanoliter Systems. *Nat. Biotechnol.* **2003**, *21*, 1179−1183.
(26) Hansen, C. L.; Sommer, M. O. A.; Quake, S. R. Systematic Investigation of Protein Phase Behavior with a Microfluidic Formulator. *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 14431−14436.

(27) Hansen, C. L.; Skordalakes, E.; Berger, J. M.; Quake, S. R. A Robust and Scalable Microfluidic Metering Method that Allows Protein Crystal Growth by Free interface Diffusion. *Proc. Natl. Acad. Sci. U. S. A.* **2002**, *99*, 16531−16536.

(28) Fu, A. Y.; Spence, C.; Scherer, A.; Arnold, F. H.; Quake, S. R. A Microfabricated Fluorescence-Activated Cell Sorter. *Nat. Biotechnol.* **1999**, *17*, 1109−1111.

(29) Liu, J.; Hansen, C.; Quake, S. R. Solving the "World-to-Chip" Interface Problem with a Microfluidic Matrix. *Anal. Chem.* **2003**, *75*, 4718−4723.

(30) Rolland, J. P.; Van Dam, R. M.; Schorzman, D. A.; Quake, S. R.; DeSimone, J. M. Solvent-Resistant Photocurable "Liquid Teflon" for Microfluidic Device Fabrication. *J. Am. Chem. Soc.* **2004**, *126*, 2322−2323.

(31) Whitesides, G. The 'Right' Size in Nanobiotechnology. *Nat. Biotechnol.* **2003**, *21*, 1161−1165.

(32) Rolland, J. P.; Hagberg, E. C.; Denison, G. M.; Carter, K. R.; De Simone, J. M. High-Resolution Soft Lithography: Enabling Materials for Nanotechnologies. *Angew. Chem., Int. Ed.* **2004**, *43*, 5796−5799.

(33) McAllister, K.; Sazani, P.; Adam, M.; Cho, M. J.; Rubinstein, M.; Samulski, R. J.; DeSimone, J. M. Polymeric Nanogels Produced via Inverse Microemulsion Polymerization as Potential Gene and Antisense Delivery Agents. *J. Am. Chem. Soc.* **2002**, *124*, 15198−15207.

(34) Rolland, J. P.; Maynor, B. W.; Euliss, L. E.; Exner, A. E.; Denison, G. M.; DeSimone, J. M. Direct Fabrication and Harvesting of Monodisperse, Shape-Specific Nanobiomaterials. *J. Am. Chem. Soc.* **2005**, *127*, 10096−10100.

(35) Merkel, T. J.; Herlihy, K. P.; Nunes, J.; Orgel, R. M.; Rolland, J. P.; DeSimone, J. M. Scalable, Shape-Specific, Top-Down Fabrication Methods for the Synthesis of Engineered Colloidal Particles. *Langmuir* **2010**, *26*, 13086−13096.

(36) Gratton, S. E. A.; Ropp, P. A.; Pohlhaus, P. D.; Luft, J. C.; Madden, V. J.; Napier, M. E.; DeSimone, J. M. The Effect of Particle Design on Cellular Internalization Pathways. *Proc. Natl. Acad. Sci. U. S. A.* **2008**, *105*, 11613−11618.

(37) Herlihy, K. P.; Nunes, J.; DeSimone, J. M. Electrically Driven Alignment and Crystallization of Unique Anisotropic Polymer Particles. *Langmuir* **2008**, *24*, 8421−8426.

(38) Gratton, S. E. A.; Williams, S. S.; Napier, M. E.; Pohlhaus, P. D.; Zhou, Z.; Wiles, K. B.; Maynor, B. W.; Shen, C.; Olafsen, T.; Samulski, E. T.; DeSimone, J. M. The Pursuit of a Scalable Nanofabrication Platform for Use in Material and Life Science Applications. *Acc. Chem. Res.* **2008**, *41*, 1685−1695.

(39) Xu, J.; Wong, D. H. C.; Byrne, J. D.; Chen, K.; Bowerman, C.; DeSimone, J. M. Future of the Particle Replication in Nonwetting Templates (PRINT) Technology. *Angew. Chem., Int. Ed.* **2013**, *52*, 6580−6589.

(40) Xu, J.; Wang, J.; Luft, J. C.; Tian, S.; Owens, G., Jr.; Pandya, A. A.; Berglund, P.; Pohlhaus, P.; Maynor, B. W.; Smith, J.; Hubby, B.; Napier, M. E.; DeSimone, J. M. Rendering Protein-Based Particles Transiently Insoluble for Therapeutic Applications. *J. Am. Chem. Soc.* **2012**, *134*, 8774−8777.

(41) Krishnan, S.; Ayothi, R.; Hexemer, A.; Finlay, J. A.; Sohn, K. E.; Perry, R.; Ober, C. K.; Kramer, E. J.; Callow, M. E.; Callow, J. A.; Fischer, D. A. Anti-Biofouling Properties of Comblike Block Copolymers with Amphiphilic Side Chains. *Langmuir* **2006**, *22*, 5075−5086.

(42) Martinelli, E.; Menghetti, S.; Galli, G.; Glisenti, A.; Krishnan, S.; Paik, M. Y.; Ober, C. K.; Smilgies, D.-M.; Fischer, D. A. Surface Engineering of Styrene/PEGylated-Fluoroalkyl Styrene Block Copolymer Thin Films. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 267−284.

(43) Bartels, J. W.; Cheng, C.; Powell, K. T.; Xu, J.; Wooley, K. L. Hyperbranched Fluoropolymers and Their Hybridization Into Complex Amphiphilic Crosslinked Copolymer Networks. *Macromol. Chem. Phys.* **2007**, *208*, 1676−1687.

(44) Xu, J.; Bartels, J. W.; Bohnsack, D. A.; Tseng, T.-C.; Mackay, M. E.; Wooley, K. L. Hierarchical Inorganic-Organic Nanocomposites Possessing Amphiphilic and Morphological Complexities: Influence of Nanofiller Dispersion on Mechanical Performance. *Adv. Funct. Mater.* **2008**, *18*, 2733−2744.

(45) Hu, Z.; Chen, L.; Betts, D. E.; Pandya, A.; Hillmyer, M. A.; DeSimone, J. M. Optically Transparent, Amphiphilic Networks Based on Blends of Perfluoropolyethers and Poly(Ethylene Glycol). *J. Am. Chem. Soc.* **2008**, *130*, 14244−14252.

(46) Wong, D. H. C.; Thelen, J. L.; Fu, Y.; Devaux, D.; Pandya, A. A.; Battaglia, V. S.; Balsara, N. P.; DeSimone, J. M. Nonflammable Perfluoropolyether-Based Electrolytes for Lithium Batteries. *Proc. Natl. Acad. Sci. U. S. A.* **2014**, *111*, 3327−3331.

(47) Villaluenga, I.; Wujcik, K. H.; Tong, W.; Devaux, D.; Wong, D. H. C.; DeSimone, J. M.; Balsara, N. P. Compliant Glass−Polymer Hybrid Single Ion-Conducting Electrolytes for Lithium Batteries. *Proc. Natl. Acad. Sci. U. S. A.* **2016**, *113*, 52−57.

(48) Yagci, Y.; Jockusch, S.; Turro, N. J. Photoinitiated Polymerization: Advances, Challenges, and Opportunities. *Macromolecules* **2010**, *43*, 6245−6260.

(49) Ligon, S. C.; Husár, B.; Wutzel, H.; Holman, R.; Liska, R. Strategies to Reduce Oxygen Inhibition in Photoinduced Polymerization. *Chem. Rev.* **2014**, *114*, 557−589.

(50) Melchels, F. P. W.; Feijen, J.; Grijpma, D. W. A Review on Stereolithography and Its Applications in Biomedical Engineering. *Biomaterials* **2010**, *31*, 6121−6130.

(51) Tumbleston, J. R.; Shirvanyants, D.; Ermoshkin, N.; Januszewicz, R.; Johnson, A. R.; Kelly, D.; Chen, K.; Pinschmidt, R.; Rolland, J. P.; Ermoshkin, A.; Samulski, E. T.; DeSimone, J. M. Continuous Liquid Interface Production of 3D Objects. *Science* **2015**, *347*, 1349−1352.

(52) Johnson, A. R.; Caudill, C. L.; Tumbleston, J. R.; Bloomquist, C. J.; Moga, K. A.; Ermoshkin, A.; Shirvanyants, D.; Mecham, S. J.; Luft, J. C.; DeSimone, J. M. Single-Step Fabrication of Comuputationally Designed Microneedles by Continuous Liquid Interface Production. *PLoS One* **2016**, in press.