Academic vs industry perspectives in 3D bioprinting

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INTRODUCTION

Reviews of the scientific literature afford the opportunity to summarize critical concepts in a field; these publications can be extremely helpful for novice readers and can help rapidly build an understanding of the state of the art. While almost all reviews summarize their topic, few offer a critical opinion of their field. Even fewer provide a perspective on the future direction of the field, i.e., what important questions remain unanswered, which questions are the most crucial to answer immediately, etc. *APL Bioengineering* recently introduced the "Perspective" manuscript format where we seek the opinion of thought leaders in their fields as to their answers for these critical questions.

While Perspectives on a subject can be helpful, they offer only one opinion. Yet in the course of academic discussions, viewpoints from multiple sides can get muddled or lost, especially if they originate in different fields or via non-academic partners including biotechnology and other industries. In that sense, single Perspective pieces may not present the full range of opinions. In an effort to bridge this divide in topic areas for *APL Bioengineering*, we are launching a periodic "Viewpoints" series, where we present a point vs counterpoint discussion on a rapidly developing area in bioengineering, aiming to specifically highlight and provide a forum where both positions can be succinctly summarized and argued. While we intend for this debate to be robust with the manuscripts published in our Viewpoints series by *APL Bioengineering*, they are not meant to be finite; we anticipate that this point vs counterpoint series will serve as a "launching pad" for each topic area covered.

POINT/COUNTERPOINT: 3D BIOPRINTING

To that end, our inaugural Viewpoints topic is 3D Bioprinting, a field which was originally termed "Additive Manufacturing" and which has seen tremendous hype in the popular press. Conventional 3D printing has seen robust translation for surgical planning, medical devices, and instrumentation, and so many have tried to show that novel bioprinting technologies are ready for patient use.[1,2] Whether it is the announcement of new bioinks[3] or printing of functional organ subunits,[4] such as ventricles[5] or vascularized tissue,[6,7] significant investments and promise have dominated news in the field. However, these discoveries may have set high market expectations.[8,9] Others have pointed to the need for additional development and characterization of these bioprinted products,[10] hence the need for a point-counterpoint perspective series on 3D Bioprinting.

Our first Perspective provides an academic viewpoint from Placone *et al.*[11] Their Perspective on 3D Bioprinting is that the printing materials used remain highly variable, e.g., bioinks composed of decellularized extracellular matrix (ECM), and validation of their material properties is often undefined or not attempted. This creates problems for reproducibility and for eventual industry regulation. Their solution to such concerns lies in additional training and rigor in the field such that additive manufacturing becomes standardized. Given the growth in non-biological printing applications and the training and regulation in those sectors, the authors end by expressing that standardization can help expand biological applications to academic, clinical, and commercial settings. This call for additional standardization is one that has been echoed more recently in academic analyses of their field,[12] which provides credence to the idea that the field has focused on diverse applications rather than standard processes required for commercial applications.

Our other Perspective comes from an industry viewpoint, provided by Birla and Williams.[13] They provide their viewpoint from BIOLIFE4D, a company involved in translating bioprinting to cardiac

applications. Unlike Placone *et al.*, who express concerns over printing materials, Birla and Williams posit that current bioinks, along with computer assisted design, have enabled industry partners to create tissues already and that these tissues often resemble microphysiological systems. They further argue that additive manufacturing will enable the community to examine the function of specific parts of tissues in ways not possible to existing methods; the assembly of those parts, e.g., valves, papillary muscles, vessels, cardiac muscle, etc., will soon enable us to create whole organs. Moreover, imaging methods could permit customization of the heart to fit an individual patient. Their concern for the field, however, lies not in the materials but rather in the cells used within bioinks, e.g., induced pluripotent stem cells (iPSCs) and their maturity or lack thereof. This is a common concern among stem cell biologists using iPSCs for cardiovascular applications,[14,15] despite the recent success of electromechanical stimulation.[16]

Where both Perspectives agree is in the need for additional technical training of staff and in funding for further development of these technologies. For conventional 3D printing, there are no fewer than 12 courses ranging in duration, including those online, e.g., Coursera and Skillshare, and in-person, e.g., MIT. However, for biological printing applications with bioinks, no such training exists. Our authors further agree that applications for these technologies will require further assessment, although they point to different concerns for future: bioinks vs cells. With recent setbacks at some key players in the industry,[17] further characterization would certainly appear to be needed to translate research[4–7] into industry successes.

These two Perspectives are the first of many of our *Viewpoints* series. We see that providing a forum for robust, evidence-based point vs counterpoint discussions on key developments in bioengineering represents an important and needed contribution to the field. These types of discussions will not only help the field define the future state of research and the challenging problems to be addressed, they will spur additional discussion and reflection, and ultimately stimulate new research and discovery. We hope you enjoy them.

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