DROP-ON-DEMAND INKJET BIOPRINTING: A PRIMER*

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Engineering complex biological structures for regenerative medicine, in vitro tissue analysis, and pharmaceutical testing require new fabrication techniques that can place specific cells in specific target locations. Conventional cell seeding methods cannot achieve this level of spatial resolution. Biofabrication is a rapidly advancing field that uses a variety of delivery mechanisms to achieve the spatial resolution necessary to place cells, biomaterials, and bioactive macromolecules in specific target locations. One new technique within this field is bioprinting, which uses drop-on-demand delivery mechanisms to fabricate biological structures. This review focuses on drop-on-demand inkjet bioprinting and provides a primer for researchers seeking to enter the field.

Keywords: Tissue engineering; regenerative medicine; biofabrication; bioprinting; methods; gene transfection.

Introduction

The fields of tissue engineering and regenerative medicine seek to construct biological substitutes to restore and maintain normal function in diseased and injured tissues (Atala, 2004 and 2009). Biological structures are highly organized and heterogeneous, as they are composed of multiple different cell types and extracellular matrix (ECM) components that exist in precise locations. Even “simple” structures that are composed of only one cell type, such as articular cartilage, contain highly organized ECM arranged in ways that facilitate the biological functions of that structure. Therefore, biological substitutes must mimic the normal structure as much as possible to provide the same functionality as the native tissue. Engineering these complex tissue components requires new methods of combining cells, growth

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factors, and biomaterials in ways that facilitate tissue and organ morphogenesis (Bramfeldt et al., 2010; Mikos et al., 2006; Yeatts and Fisher, 2010). In addition, tissue engineering can be used to create in vitro test systems to evaluate pathologies for various conditions and develop novel pharmaceuticals (Adissu et al., 2007; Dash et al., 2009; Desai et al., 2010; Khetani and Bhatia, 2006; Yamada and Cukierman, 2007).

The limitations of conventional tissue engineering have become apparent as our understanding of biological systems has grown. Most notably, the discovery of the complex spatial interplay among multiple different cell types and ECM has highlighted the importance of placing specific biological components in specific locations. Traditional tissue engineering techniques such as manual cell seeding or cell spraying are incapable of achieving the proper level of spatial resolution to place specific cells in specific locations. Furthermore, placement of extracellular components, including growth factors and biomaterials, is of equal importance. As a result, new fabrication methods with high spatial resolution are now being developed for production of biological structures.

Biofabrication is a burgeoning field that seeks to combine living and non-living components of biological structures in a controlled manner. The challenge of biofabrication is to spatially arrange both the living and non-living components of biological structures to achieve functionality specific to the target application. Techniques for controlled micro-deposition of materials have been available for decades. The first dot-matrix printers were released for commercial use in the 1970s with the advent of the LA30 (Digital Equipment Corporation, Maynard, MA). The concept of placing small dots of material in specific locations is the underpinning of modern inkjet and laser printing technology, although the size of the dots has been significantly reduced as technology has improved.

Robotic spotting systems were developed in the 1980s for precise micro-scale deposition of biological substrates for medical diagnostics (MicroFab Technologies Inc., Plano, TX). The cost and complexity of these robotic spotting systems prevented them from gaining widespread acceptance in research, although such systems are still present in many commercial applications for micro-scale deposition. At the same time, the work of Klebe et al. in the area of cytoscribing laid the groundwork for precise controlled deposition of proteins and cells (Klebe et al. 1988 and 1994). In the late 1990s, desktop inkjet printers attained orifice diameters of 50 µm and drop resolutions of 80 µm. With this technological advent, researchers earnestly began to examine the use of inkjet printing as a low-cost alternative to robotic spotting systems for controlled delivery of both living and non-living components of biological structures. This gave rise to the field of bioprinting, which seeks to leverage drop-on-demand delivery systems to create biological structures.

Drop-on-demand bioprinting systems have been used in many different applications; however, there are significant issues that must be overcome before this type of bioprinting is a truly viable biofabrication technique (Burg et al., 2010; Wilson and Boland, 2003). There are a variety of delivery methods including laser-assisted
bioprinting that have various advantages and disadvantages in comparison to drop-on-demand inkjet bioprinting (Barron et al., 2004 and 2005; Guillemot et al., 2010b and 2010a). This report will focus on drop-on-demand inkjet bioprinting.

Drop-on-Demand Biofabrication

Types of drop-on-demand bioprinting

There are three major types of drop-on-demand bioprinters: thermal, piezoelectric, and mechanical (Fig. 1). All types have the same basic structure. A cartridge is filled with the material to be printed (“bio-ink”), which is then forced through a microfluidic chamber to an output orifice. The properties of the ink drop are dependent on the mechanism used to force the ink through the orifice and the properties of the output orifice itself. Thermal inkjets use a heating element that creates a bubble in the ink, forcing the ink through the orifice. Piezoelectric inkjets use a material that changes shape with voltage to force the ink out. There is a wide

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**Fig. 1. Schematic representation of three different inkjet printing methods.**

(a) A thermal inkjet printhead uses a heating element adjacent to the ink reservoir to rapidly raise the temperature in the reservoir. This creates a bubble in the reservoir that forces a small amount of ink through the output orifice. (b) A piezoelectric printhead uses a material that changes shape with voltage to push the ink through the output orifice. (c) A pressure-drive printhead uses a pressure source behind the reservoir to produce a force on the reservoir. A gate opens to allow ink to flow through the output orifice.
variety of mechanical bioprinting systems, with the two most common printing methods being air pressure and pump-based systems (Smith et al., 2004).

**Parameters for bioprinting**

The ultimate resolution of the bioprinting system is dependent on the type of printhead used for the application. Specifically, the minimum droplet size is dependent on the type of printhead. This resolution is separate from the final resolution of the bioprinted construct as the droplet will spread on the surface. For example, our pressure-drive microvalves deliver approximately 500 cells per droplet but these droplets spread over 1 mm of the bioprinting surface. Pressure-driven microvalves are the easiest type of printhead to incorporate into a custom device. This type of valve-driven bioprinting system typically has lower spatial resolution but higher throughput than thermal or piezoelectric printheads. Thermal and piezoelectric printheads are ubiquitous in desktop inkjet printers and some stand-alone printing systems. Newer inkjet printers are not suited for cell bioprinting because the orifice size on the new printheads is significantly less than the size of a cell. Older printheads released in the late 1990s are theoretically capable of single cell precision depending on the size of the output orifice. Single cell precision is dependent on the specific model of inkjet cartridge as a function of the average drop volume of the cartridge. For a HP26 cartridge, a concentration of $7.7 \times 10^6$ cells/mL corresponds on average to one cell per droplet (Parzel et al., 2009). Although these cartridges should be able to reliably print single cells, in practice there are sources of resolution error that researchers must take into account when performing a bioprinting experiment.

Imperceptible sources of resolution error can significantly affect the practical spatial resolution of a bioprinting system. When creating biological structures with micro-scale fabrication techniques, the slightest movement (only a few micrometers) changes the final outcome. The main sources of resolution error are the printhead itself, the distance from the printhead to the substrate where the drop will be placed (drop distance), and mechanical vibrations. Inkjet printheads are designed to place drops of material in a specific area such that multiple drops create an intended spatial distribution. Such printheads are not designed to repeatedly deliver material to an exact point. This error is dependent on the type of printhead used and cannot be changed — it must be included in the design of the biological structure. The error associated with drop distance is similar to the printhead error. Printheads are typically held several millimeters above their intended target and any errors in the direction of the ink drop will be magnified as the distance from the printhead to the target increases. Finally, when creating structures on a micrometer scale, tiny vibrations originating from movement of the system or even the air conditioning in the room can significantly affect the final resolution of the printing system. These sources of error can be somewhat overcome by holding the printhead on a stationary
platform and using a moveable stage beneath the printhead to create the biological structure.

In creating a biological structure, drop-on-demand bioprinting replaces the ink in the printhead with either living or non-living biological components in a bio-ink delivery matrix, typically a hydrogel (Fedorovich et al., 2007). Biological structures are created using layer-by-layer fabrication, where each pass of the printhead successively generates another layer of the printed construct. The choice of biomaterial for the delivery matrix plays a major role in determining the final properties of the bioprinted biological structure (Burg et al., 2010; Calvert, 2007; Fedorovich et al., 2007 and 2008). Typically the delivery matrix is a material that is liquid in the printhead but is cross-linked by a reaction with another agent to become semi-solid. A wide variety of hydrogels has this property and has been used for bioprinting. Two of the most common matrices are type I collagen and alginate, although new matrices are continually evaluated. The matrix provides structural stability for each layer so that a full construct can be built without collapsing. In addition, the biological properties of the matrix can affect the proliferation of bioprinted cells. As a result, the type of matrix chosen for bioprinting a structure must be specific to that particular application. The interactions between the living and non-living components of the biological structure guide the final characteristics of the structure (Jakab et al., 2004a and 2004b), to the point where self-assembly of structures may be a more viable approach to bioprinting than placing every cell in its specific niche. Bioprinting small pieces of tissue designed to undergo fusion into a full biological structure is an approach that can leverage developmental biology into organ printing (Mironov et al., 2003 and 2009; Norotte et al., 2009).

Each application of bioprinting requires a separate set of cell types and matrices. Studies of cell viability in thermal inkjet printheads have shown cell survival to be 70–90%, although some groups have determined that cells require a recovery period after bioprinting to restore membrane integrity (Chang et al., 2008; Cui et al., 2010; Nair et al., 2009; Xu et al., 2006). Typically, bioprinting researchers examine cell viability and proliferation using a variety of proprietary bioprinting mechanisms with specific cell types and a limited number of delivery matrices. However, the bioprinting of complex constructs will require multiple cell types and matrices. A comprehensive analysis of cell viability and proliferation using many different cell types, matrices, and bioprinting mechanisms is necessary before the goal of building complex constructs can be a reality.

Creating a bioprinting system: modifying desktop inkjet printers

Drop-on-demand bioprinting is commonly used with modified desktop inkjet printers. Modification of desktop printers is both an advantage and disadvantage of this technique. The hardware interfacing with the printhead already exists and has been quality tested by the manufacturer. However, this hardware is designed to print on
paper and contains numerous checks to prevent the printer from performing outside its normal specifications. Depending on the bioprinting application, the printer hardware must either be reverse-engineered or modified to bioprint. A printer can be modified to bioprint by using a bioprinting stage on one side of the printer and feeding paper through the other side to bypass the paper checks. Reverse engineering provides control of individual inkjet channels which is extremely beneficial for studying the fundamentals of inkjet bioprinting, especially with regard to channel throughput and clogging. However, reverse engineering a desktop printer may be beyond the capabilities of research groups that do not focus on engineering. Therefore, several groups have used the existing printer hardware with modifications to facilitate bioprinting.

One of the major modifications made to desktop inkjet printers is the addition of a Z axis in the paper tray (Boland et al., 2006; Nakamura et al., 2005; Roth et al., 2004; Xu et al., 2004 and 2005). Since a desktop printer only prints two-dimensional sheets of paper, stacking multiple layers at once requires an additional mechanism to lower the printing area with each successive layer. This is typically performed by adding an electronic elevator to the paper tray that lowers upon receiving a signal from the operator to print another layer. In this way, additional layers can be stacked upon each other to create a three-dimensional construct from two-dimensional layers.

Our group has chosen not to reverse engineer the hardware of desktop printers due to the numerous throughput issues that inkjet bioprinting faces. However, we have developed an inexpensive method of modifying Hewlett-Packard Deskjet 640 printers for bioprinting purposes. We combine the software power of the Printer objects built into the Microsoft .NET Framework (Microsoft Corp., Redmond, WA) with simple hardware modifications to the printer. The Printer objects in .NET provide built-in support for interfacing with desktop printers and provide a Graphics object that can be sent to the printer. The Graphics object allows the user to control the color of every pixel that will be printed, enabling both the black cartridge and the color cartridge to be used to print up to four different cell types or biomaterials. Combining the Graphics object with the Printer object provides the ability to bioprint an arbitrary number of structural layers in the form of additional “pages”.

From a hardware perspective, the HP 640 series of printers is simple to modify. Adding a trigger switch and solenoid allows us to override the normal operation of the printer, forcing the printer to print without any paper loaded in the machine. The printer requires a signal that indicates that paper is loaded in the paper roller before it will begin printing. The paper signal is provided by a photosensor on the back of the printer. This sensor is triggered only when the printhead reaches the end of the print bar. Thus, we place a trigger switch at the end of the print bar that changes the input of the photosensor only when the printhead is in the proper position. If the timing of these events is not correct, the printer will sense a paper jam and stop printing. When the printhead reaches the end of the print bar a second time, the trigger switch releases the photosensor so the printer will move to
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Fig. 2. HP Deskjet 640c series inkjet printer modified to print without paper. (Top) Three modifications are necessary to override the paper mechanisms. A control board is added to the back of the printer to manage the trigger and solenoid. The trigger switch is placed in the left dock position for the printhead. The solenoid is placed next to the photosensor and moves the sensor bar up and down. (Bottom) Schematic representation of the trigger and solenoid during the printing process with the print area displayed in green. When the printhead docks on the left side of the print bar it hits the trigger which drives the solenoid to block the photosensor. The printer will print without any paper loaded. When the printhead docks on the left side of the print bar for the second time the trigger causes the solenoid to release the photosensor.

This approach to modifying inkjet printers has advantages and disadvantages. First, the entire modification can be completed for less than $200. Approximately half of that expense is for an interface board to properly control the timing between the next “page” (Fig. 2). These modifications preclude any need to reverse engineer the printer hardware. In addition, we can leverage some of the protective measures included in the printer hardware to prevent clogging, including the docking function for the printhead that uses a sponge to wipe excess fluid from the printhead.
the trigger switch and solenoid. The .NET Framework and Visual Studio Express Editions can be downloaded free from Microsoft, eliminating the expense of licensing development software. Second, we can use the protections built into the printer hardware to prevent the printer from operating outside of its specifications. Third, the Graphics and Printer objects allow biological structures to be created programmatically using computer-assisted models, algorithms, or artificial intelligence (Fig. 3). Finally, the software can be built using a range of programming languages from Basic to C++, enabling researchers to tailor their bioprinting systems to their

```csharp
void Printer::PrintVasculature(System::Object ^sender,
   System::Drawing::Printing::PrintPageEventArgs ^e)
{
   // The first FOR loop defines the X coordinate for each blood vessel
   for (int x = 0; x < vasculature_size; x += vessel_spacing)
   {
      // The second FOR loop defines the number of cells to print
      // in the Y direction for each blood vessel
      for (int drop = 0; drop < vessel_length; drop += 1)
      {
         e->Graphics->FillRectangle(cell_type, x, drop, 1, 1);
      }
   }
   // Add more layers in the Z direction if necessary
   if (additional_layers = true)
   {
      e->HasMorePages = true;
   }
   else
   {
      e->HasMorePages = false;
   }
}
```

Fig. 3. Visual C++ code for programmatically creating a series of lines for vasculature bioprinting. The Printer object contained in the Microsoft .NET Framework provides functions for interacting with inkjet printers. This object provides a PrintPage that in turn provides a Graphics object for creating the picture to be printed. In this case the user has provided the total size of the vasculature (vasculature_size), the space between each blood vessel (vessel_spacing), the length of each blood vessel (vessel_length), the cell type, and the number of layers to be bioprinted. The FillRectangle() function from the Graphics object requires four arguments: color, X coordinate, Y coordinate, number of pixels in the X direction, and number of pixels in the Y direction. Here we use a nested FOR loop to create a line using one pixel at a time in the Y direction. The COLOR argument for the FillRectangle() function corresponds to the cell type — for example, cells bioprinted from the red portion of the color cartridge would be represented by the red (255, 0, 0) color programmatically. More layers can be added by setting the HasMorePages property to TRUE. This type of programmatic bioprinting can be used to rapidly create constructs with complex arrangements in each layer.
level of engineering expertise. Even with these capabilities, this system suffers from the issues related to inkjet bioprinting and does not provide control over individual channels in the printhead.

**Issues with inkjet bioprinting**

Despite the numerous applications of inkjet bioprinting that have been described in the literature, and the burgeoning field surrounding the technology, there are two major issues that prevent single-cell inkjet bioprinting from reaching its full potential. The first issue is the limited mobility of the printhead if no reverse engineering is performed. In the normal configuration the printhead is limited to 8.5 inches on the X axis and the length of the printhead on the Y axis. Thus, only biological structures of limited size can be created with this type of bioprinting system. Second, as noted above, inkjet cartridges suffer from low throughput. This is mainly due to deposition of salts in the microfluidic channels during the printing process. This often occurs when evaporation of water from the bio-ink drop leaves behind solid salts that block the channel orifice. Once the channel is clogged, it is virtually impossible to restore full functionality to that channel. Furthermore, cellular debris and other contaminants can clog the microfluidic chambers as well. As a result, inkjet cartridges typically can only print 400,000 cells per cartridge before failure (Parzel et al., 2009). This throughput is too low to produce large tissue constructs. Recently, Parzel et al. experimented with adding a chelating agent (EDTA) to the bio-ink as an anti-aggregant and they were able to significantly increase the longevity of inkjet cartridges (Parzel et al., 2009).

**Creating a custom bioprinting system**

One of the best ways to overcome the limitations of desktop inkjet printers is to develop a specialized bioprinting system. For example, Lee et al. designed a system for bioprinting fibroblasts and keratinocytes using microvalves instead of inkjet printheads (Lee et al., 2010) and leveraged this design to bioprint neural structures (Lee et al., 2009). Another type of system leverages extrusion printing to bioprint cells embedded in hydrogels. These hydrogels form fused droplets to form biological structures (Moon et al., 2010). Depending on the type of delivery system these custom designs can have significantly different throughput and precision than desktop printers.

One of our areas of focus is the bioprinting of skin constructs in situ and high throughput takes precedence over precise delivery for those applications. Our inkjet valves sacrifice precision for throughput by delivering approximately 500 cells per drop. In the context of bioprinting fibroblasts and keratinocytes, this design avoids the pitfalls associated with single-cell inkjet bioprinting. This system is cartridge-based and allows any cell type or biomaterial that can be packaged into a cartridge to be bioprinted in a specific location in a wound (Fig. 4).
Fig. 4. Schematic diagram of in situ skin bioprinter. (a) The printhead mounts on XYZ moveable axes that are mounted to a portable frame. This portable system mounts over the patient bed or operating table to bioprint skin cells directly in a wound. (b) Magnified view of the scanning system and printhead. The scanning system scans a wound and creates a map of the wound for the printer to follow. This printhead is cartridge-based so any material that can be packaged into a cartridge can be bioprinted in specific locations directly in a wound. The printhead uses inkjet microvalves instead of thermal or piezoelectric orifices to avoid problems with clogging. In this way the in situ skin bioprinter can bioprint an exact copy of the skin that the patient is missing.

Applications of bioprinting

One of the main advantages of the cartridge-based delivery system is the ability to bioprint many different substances by plugging in a new cartridge (Ilkhanizadeh et al., 2007; Pont-Lezica, 2009). Examples of this ability include repairing calvarial defects using bone morphogenic protein-2 patterned in three dimensions (Cooper et al., 2010) or directing the fate of stem cells by creating specialized microenvironments with growth factors (Phillippi et al., 2008). The ability of bioprinting to create spatial patterns was shown in the development of capillary networks generated from endothelial cells (Cui and Boland, 2009) as well as the generation of bone constructs from bone marrow stromal cells (Fedorovich et al., 2008). Drop-on-demand bioprinting allows the creation of test structures for mechanistic and pharmaceutical testing. For example, a microprinting system was used to develop liver tissue for metabolism studies (Chang et al., 2011). We demonstrated that the inkjet printing system can be used for high-throughput production of single-cell microparticles for high-throughput drug screening or examining stem cell differentiation (Xu et al., 2008). In this case, the choice of hydrogel was able to influence the formation of encapsulated cell droplets, resulting in an inexpensive high-throughput method of producing single cell microparticles.
We have also shown that the properties of the thermal inkjet printhead allow the bioprinter to act as a high-throughput transfection mechanism for transient transgene expression (24–48 hours post-transfection; Xu et al., 2009). The inkjet process induces transient membrane pores that close over the course of several hours (Cui et al., 2010; Xu et al., 2009). We hypothesized that these pores are introduced through a combination of the heat flux through the cell and the shear stress induced by pushing a cell through the output orifice (Fig. 5). The transient damage to the cell can be leveraged by combining cells and a plasmid vector in the printhead such that the two components are bioprinted together. During the bioprinting process, the transient cell damage causes the plasmid to insert in the cell. Whether inkjet-mediated transfection leads to direct transfer of DNA into the nucleus (e.g. nucleofection or lentiviral vector transduction: Trompeter et al., 2003; Naldini et al., 1996) or relies on cell division for transgene nuclear transfer (e.g. basic retroviral vector transduction or cationic liposome delivery: Miller et al., 1990; Tseng et al., 1999) remains to be determined. In any cases, we have shown that inkjet transfection is dependent on the size of the plasmid, the concentration of plasmid, and the type of printhead used (Fig. 6). The size of the plasmid must be compatible with the size of the transient pores created in the cell membrane and with an efficient transfer into the nucleus in order to lead to transgene expression. The transfection efficiency initially increases with increasing levels of plasmid but further increases in concentration do not increase the efficiency. Different inkjet printheads also have different transfection efficiencies due to differences in the

Fig. 5. Schematic drawing of the postulated mechanism for inkjet-induced gene transfection. When cells and gene plasmid pass through the ink channels of the printhead during the printing process, high shear stress and heat generated upon nozzle firing may cause temporary micro disruption of the cell membrane. Plasmids can then be transferred into the cells. Ejected droplets containing the transfected cells are subsequently sprayed at specific locations on a substrate following a predesigned program. Reproduced from Xu et al., Tissue Eng Part A, 15: 95–101 (2009) with permission from Mary Ann Liebert, Inc.
Fig. 6. Effects of the printing parameters and conditions on gene transfection. The higher plasmid concentrations exhibited higher transfection efficiency (a). The use of the HP 29 ink cartridge caused higher gene expression than the use of the HP 26 ink cartridge which has a larger nozzle size (b). Compared with the larger plasmid, pIRES-VEGF-GFP, the smaller pmaxGFP plasmid exhibited higher transfection efficiency of the porcine aortic endothelial (PAE) cells (c). Of note, transgene expression is measured 24–48 hours post-transfection (transient expression condition). Reproduced from Xu et al., Tissue Eng Part A, 15: 95–101 (2009) with permission from Mary Ann Liebert, Inc.

output orifices. While the transfection efficiency was significantly lower than that of electroporation, the cell viability was significantly higher than electroporation (Fig. 7). More research is necessary to improve inkjet bioprinting as a transfection method; however, the power of combining high-throughput gene manipulation with targeted delivery cannot be understated. Although bioactive factors can be precisely bioprinted in a construct, these factors will not be continually produced by the biological construct and will eventually degrade. In contrast, stable transfected cells are able to continually express bioactive factors to improve construct development and tissue regeneration. Whether inkjet transfection leads to significant
Fig. 7. **In vitro gene printing.** (a) Electrophoresis analysis of printed plasmid DNAs. 1: Size marker; 2: printed pmaxGFP; 3: nonprinted pmaxGFP; 4: printed pRES-VEGF-GFP; 5: nonprinted pRES-VEGF-GFP. The lower plasmid band is the supercoiled form and the upper is the nicked (single-stranded break) form. (b–e) Morphologies of printed and nonprinted cells. The printed PAE cells exhibited normal morphology on the collagen gels 2 days after printing (size bar = 5 µm) (b). A number of cells in the printed samples exhibited strong cytoplasmic green fluorescence (c). The nonprinted cells (controls) also showed normal morphology (size bar = 5 µm) (d), but were not detectably transfected with the GFP plasmid (e). (f, g) Viability and transfection efficiency comparison of the inkjet transfection method with other common gene transfection methods. Compared with the common chemical (Lipofectamine)-or electroporation (Nucleofection)-associated method, the inkjet transfection method had higher cell viability after transfection (f). The total transfection efficiency (combined with viability) of the inkjet method is lower than that of the Nucleofection method but higher than the Lipofectamine method (g). Of note, transgene expression is measured 24–48 hours post-transfection (transient expression condition). Reproduced from Xu et al., *Tissue Eng Part A*, 15: 95–101 (2009) with permission from Mary Ann Liebert, Inc.
levels of stable transfectants is not yet known. However, the fact that it provides for efficient transient transgene expression suggests that, combined with the use of designed site-specific endonucleases, it could be instrumental in the development of high-throughput hazard-free protocols for efficient targeted transgene integration (Moehle et al., 2008) or endogenous gene repair (Urnov et al., 2005), thereby leading to breakthrough applications both for regenerative medicine (stable expression of integrated transgenes) and basic gene therapy for inherited diseases (transgene correction or gene repair/inactivation).

Conclusions

Although great strides have been made in the field of drop-on-demand biofabrication, much more work is necessary before the major obstacles are overcome. Most notably, the field is still young and the comprehensive analyses of cell viability and proliferation in various delivery matrices using different delivery methods have yet to be performed. In the near future we expect to see biological structures engineered using a variety of delivery methods tailored to one specific task. We have provided a primer for researchers seeking to modify desktop inkjet printers for bioprinting purposes. However, most researchers and commercial enterprises seeking to enter this field would do well to choose a specific type of biological structure to engineer and customize a bioprinting machine to those specifications. This field has significant potential and rapid progress in engineering complex tissues is expected in the next few years.

References


