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Fabricating biomedical origami: a state-of-the-art review

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Abstract

Purpose—Origami-based biomedical device design is an emerging technology due to its ability to be deployed from a minimal foldable pattern to a larger volume. This paper aims to review state-of-the-art origami structures applied in the medical device field.

Methods—Publications and reports of origami structure related to medical device design from the past 10 years are reviewed and categorized according to engineering specifications, including the application field, fabrication material, size/volume, deployment method, manufacturability, and advantages.

Results—This paper presents an overview of the biomedical applications of devices based on origami structures, including disposable sterilization covers, cardiac catheterization, stent grafts, encapsulation and microsurgery, gastrointestinal microsurgery, laparoscopic surgical grippers, micrograppers, microfluidic devices, and drug delivery. Challenges in terms of materials and fabrication, assembly, modeling and computation design, and clinical adoptability are discussed at the end of this paper to provide guidance for future origami-based design in the medical device field.

Conclusion—Concepts from origami can be used to design and develop novel medical devices. Origami-based medical device design is currently progressing, with researchers improving design methods, materials, fabrication techniques, and folding efficiency.

Keywords

Origami; Surgical; Biomedical; Paper folding; Biomaterials

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Meredith Johnson and Yue Chen are co-first authors.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Human and animals rights This article does not contain any studies with human participants or animals performed by any of the authors.

Introduction

In recent decades, the ancient art of paper folding known as origami [1] has been studied on a mathematical level. Origami mathematics, also called Origamics [2–5], covers the basic principles of origami design, kinematics, and structural properties [2–6]. All forms of origami can be achieved using folding methods defined by six Huzita Axioms (HAs) and one Hatori Axiom [7–11]. Each axiom defines a folding method by combining preexisting points and lines together. With advanced computational simulation technology, the process of testing an origami design is accelerated and the development cost is reduced. Combining modern 2D and 3D rapid prototyping techniques with parametric graphical software for origami design—such as TreeMaker [12], Origamizer [13], Rigid Origami Simulator [14], and E-origami system [15]—origami designers can transform an idea into reality within hours.

Origami has a flat form and a deployed form; transformation between these two forms is made possible with folds in the paper. Folds can be used in a similar way in other items, allowing transformation from a functional form to a compact form for shipping or storage. This concept has already been successfully used to create multipurpose, space abiding packages and furniture [16–19]. In addition, foldable products can be designed to reduce manufacturing costs by requiring fewer materials and simplifying construction. Design concepts from origami could be used to improve medical devices. For example, disposable medical devices need to be as inexpensive as possible, so origami-inspired designs could be aimed at reducing manufacturing costs. For minimally invasive surgical procedures, an origami-based medical device could be inserted into the body through a small incision in its compact form, travel through the body to previously inaccessible areas, and then deploy into its functional form at its destination. Small robots and MEMS (microelectromechanical systems) with medical applications could also benefit from origami-based design [20].

In this paper, we review the current status of origami's influence in biomedical and clinical applications. A biomedical device design—based on origami fabrication methods—consists of a variety of folds, cuts, and creases on a single sheet of material. The key features of these devices include a simple fabrication process, cost-effective and disposable design (which is ideal for clinical applications that require high standards of sterilization), low cost, and highly adaptable designs for medical applications. Depending on the application, designs range from the nano- to milli-scale. The current challenges and the future directions of each concept in the field are examined.

Biomedical applications

By applying concepts from origami, medical devices can be fabricated in a simple and precise manner using modern rapid prototyping techniques. Origami designs can start in a compact form and then deploy into a functional form, thus enabling a novel and less invasive method of treatment delivery in which medical devices travel through the body to previously unreachable areas. Origami's influence can be seen in a wide range of medical devices, from an X-ray shroud to tetherless microgrippers [21]. The majority of medical origami devices focus on traveling to previously inaccessible sites in vivo to perform a procedure such as catheterization or biopsy [22–24]. This section reviews biomedical origami designs, highlighting applications in cardiac catheterization, drug delivery, encapsulation, gastrointestinal microsurgery, laparoscopic surgical gripper, microfluidic devices, microgrippers, sterilization, and stent grafts (Table 1).

Cardiac catheterization

Schmidt et al. [22] of Harvard Medical School presented the first intracardiac magnetic resonance imaging (ICMRI) catheter design (Fig.1). The ICMRI catheter consists of deployable intracardiac imaging coils located at the end of an electrophysiology abolition catheter. Chen et al. of the University of Georgia further improved the ICMRI catheter's mechanical design by increasing the diameter of the deployed mechanism [25] (Fig. 2). This design provided control during MRI-guided radiofrequency ablation (RFA) procedures. Taylor et al. changed the structure of the deployment mechanism to an origami design [26] (Fig. 3), allowing an increased amount of electronics to be mounted in the catheter and subsequently deployed into the targeted area in the heart. The ICMRI catheter consists of an origami MR imaging coil, and tracking microcoils, at the catheter's tip. The origami structure is modified from the Palmer-Shafer origami flasher. Imaging coils are attached to the microcoaxial cables located near the end of the catheter. The ICMRI catheter enters the femoral artery and is then maneuvered to the source of arrhythmia to perform RFA. The deployable MR imaging coil allows visualization of the procedure. MR images obtained by ICMRI, versus Invivo array coils, have 2–4 times the signal-to-noise ratio (SNR) increment. The ICMRI catheter also allows for 4–16 times faster imaging during MR-guided RFA. Overall, the ICMRI catheter has the potential to improve the accuracy and reliability of MRI-guided RFA delivery.

Drug delivery

Zhu et al. [27] of the University of Maryland have demonstrated how hydrogenation-assisted graphene origami (HAGO) can achieve molecular mass uptake, storage, and release (Fig. 4). By applying an external electric field to HAGO nanostructures, the geometry of the origami becomes mechanically "programmable." The nanoscale origami is formed with graphene, cut atomically thin. The chemical properties of graphene allow the structure of the origami to be manipulated mechanically with controllable external electric fields. The graphene starts out in the shape of a building block and can be configured into various origami structures. These folded graphene nanostructures could potentially serve as nano-containers for drug delivery in molecular vessels. Imperfect formation of the nanostructure during hydrogenation is a concern, as it could lead to inaccurate formation of HAGO. Also, the deployment mechanism becomes less effective as the size of HAGO increases. Nonetheless, nanofabricated origami has the potential to improve drug delivery.

Encapsulation microsurgery

Miyashita et al. [24] of the Massachusetts Institute of Technology (MIT) created a self-folding origami robot that can accomplish tasks and then disintegrate into the given environment (Fig. 5). Three layers along with four square electromagnetic coils comprise the planar sheet. A heat-sensitive contraction film (polyvinyl chloride) is sandwiched by two rigid structural layers of liquid-soluble material. Gaps are left on the front and back face of the structural layer to create the self-folding crease pattern. The robot's transformation from a planar to 3D structure is catalyzed by global heating. The folds begin at ~ 65 °C and complete in ~1 min. By controlling the electromagnetic coils with a joystick, the robot can be made to walk, swim, carry, and dig. Incomplete removal of the robot from the body after use and unexpected flipping are still concerns.

Gastrointestinal microsurgery

Shuhei et al. [28] of MIT developed an ingestible, controllable, and degradable origami robot (Fig. 6). Once the origami robot reaches the stomach after being swallowed, it is directed to the desired location by an external magnetic field to patch a wound, remove a foreign body, or deliver drugs. Although the design is significantly different, the robot is an extension of previous work on a self-folding origami robot (Fig. 7) [29]. The robot was tested on dried pig intestine with a central magnet (15 × 30 × 5 mm, length × width × height). For easy ingestion, the origami robot is engulfed in an ice capsule, which melts once in the stomach. Miniature origami robots can perform various minimally invasive gastrointestinal procedures, especially when used in conjunction with imaging technologies, as they can move with a high degree of control.

Imaging tools

Brigham Young University (BYU) and GE Healthcare designed a cover for the extendable arm of a medical X-ray machine [21] (Fig. 8). The cover expands and contracts using origami-inspired engineering. By incorporating the Miura-ori folding pattern, the cover is able to move and adjust to the extendable X-ray arm's geometry. Miura-ori folding allows for the continuous folding and unfolding motion of rigid bodies, in any direction. The cover is made of Tyvek, a synthetic paper product produced by DuPont. The cover keeps the extendable arm sterile during its movement. In comparison with plastic drapes previously used to shroud movable X-ray arms, this design is more cost-effective and time-efficient since the plastic drapes need manual replacement with every rotation in and out of the sterile field. This design utilizes foldable origami to decrease surgical costs.

Laparoscopic surgical gripper

Researchers of BYU are integrating origami techniques to create smaller grippers (3 mm in diameter) for Intuitive Surgical's Da Vinci Surgical System [30,31] (Fig. 9). The Da Vinci Surgical System performs surgeries robotically with the use of grippers. The grippers can hold a needle, suture, grasp objects, etc. BYU's new design was inspired by the origami pattern known as "Choppers." The simple origami design allows one-third of the number of parts as the original. Also due to the design, the parts are less complex, giving the gripper the ability to be scaled down further. The gripper is inserted into a tiny incision and then deployed inside the body to carry out a specific surgery. These origami-inspired designs may enable less invasive robotic surgery due to the small scale.

Microfluidic devices

Liu et al. of the University of Texas at Austin incorporated the principles of origami to develop a simple method for fabricating three-dimensional paper microfluidic devices (oPAD, Fig.10) [32]. The microfluidic device is folded from one piece of paper in a photolithographic step, regardless of the number of layers, whereas previously, sequential layer-by-layer fabrication was the only approach. This reduces cost and fabrication time. Simple folding can be completed in less than 1min without the use of tools. The device can then be unfolded, thus allowing for parallel analysis. Detection points can be placed on any layer of the oPAD, due to the easily unfolded design. The 3D microfluidic devices are formed by photolithographically patterned channels and detection reservoirs on chromatography paper (100 μm thick). This origami-based method for 3D paper microfluidic devices can lower costs and simplify fabrication.

Microgrippers

Leong et al. of Johns Hopkins University developed a tetherless microgripper that can be activated by temperature or chemical actuation, under biologically relevant conditions [33] (Fig. 11). The microgripper's function is the capture and retrieval of objects and biopsies. The grippers are remotely guided in vivo to desired cells. Once there, the gripper is actuated by exposure to heat (40–60°C) or by a variety of chemicals, including organic solvents and caustics. The gripper is 190 μm when closed, and 700 μm when open. Grippers with six rotationally symmetric digits, each digit consisting of three polymer joints, resulted in the most successful design. The overall design is modeled after biological appendages, including a hand. For in vivo guidance to prevent premature lodging, the grippers will need the incorporation of MRI or computed tomography (CT). The tetherless microgripper represents the development of biocompatible, minimally invasive, autonomous microtools.

Bassik et al. [34] of John Hopkins University expanded on this concept by focusing on specific enzyme-substrate biomolecular interactions to trigger the microgrippers. By choosing a biopolymer (to be placed in the joints of the gripper) which pairs with predetermined proteolytic enzymes that are naturally secreted from cancer cells, the microgripper is only triggered in cancerous environments. This microgripper is a representative example of the development of materials and devices with the ability to reconfigure autonomously in response to specific biological environments.

Stent grafts

Kuribayashi et al. [35] of the University of Oxford engineered a self-deployable origami stent graft (Fig. 12). The origami stent graft is comprised of a single, Ni-rich titanium/nickel (TiNi) shape memory alloy (SMA) foil with hill and valley folds. Once the foil is connected adhesively, it creates a cylinder with a diameter of 25.4 mm and length of 44 mm. The folds for the origami stent are etched using a negative photochemical etching process. Current stents are formed of wire mesh, which can lead to restenosis, wire mesh fractures, and graft ruptures. The new SMA stent graft is first packed into a sheath and then maneuvered to the designated site where the sheath is removed and the stent is delivered thermally (body temperature) or mechanically. The Ni-rich TiNi SMA stent graft would allow for minimally invasive surgery, such as those requiring esophageal and aorta stent grafts.

Challenges

Any device designed for use in a clinical environment needs to meet specific requirements addressing issues such as sterilization, biocompatibility, and safety. Although many origami-based medical devices have been tested experimentally and have been shown to possess advantages compared to conventional devices, a significant amount of work is needed for any individual device to reach clinical readiness. In this section, we present four technical challenges of origami-based medical device design based on the feedback of our clinical collaborators, namely material and fabrication, assembly issue, modeling and computation design, and clinical adoptability.

Materials and fabrication

The creases of an origami design store strain energy elastically. Different amounts of strain energy in the creases are required for different designs. A crease can be described with a hinge index. To raise the hinge index, heavy perforation and deep scoring can be used. These techniques will change the cross-sectional area of the crease, thereby changing the hinge index. The properties and dimensions of materials used in the design affect the amount of strain energy that can be stored in the creases and therefore affect the hinge index. Materials with a low hinge index, such as polymers and metals, can be used to store more strain energy in the creases. Different materials also have different effects on the rigidity of the panels and the amount of deflection experienced at the creases. The thickness of the materials must also be taken into consideration in order to achieve the desired level of stiffness or compliance. Monolithic and composite materials, as well as sandwiched membranes, have been used for origami designs [36]. There are many challenges to the manufacturing process of origami designs. Computer numeric controlled (CNC) manufacturing methods are the most feasible for creating creases in the material prior to folding. Plasma cutting, abrasive water jet cutting, laser cutting, incremental sheet forming, and nibbling are among the proposed CNC methods for origami design fabrication [37].

Assembly issue

Many assembly methods are possible for origami-based designs, but the two methods at the forefront are (a) using automated robots or intelligent machines to fold the material into the final product [38–40], and (b) creating self-folding designs. Origami engineers have suggested that self-folding designs could be achieved with the use of an intelligent material capable of spontaneously folding from a sheet into the final product. However, current self-folding technology requires subsystems in addition to the main material—typically joints and/or creases, folding actuators, a motion controller, and a power supply.

Designs for self-folding origami share certain characteristics with deployable solar panels, antenna deflectors [41,42], and programmable matter self-folding sheets [43]. One shared feature is a surface composed of polygons joined by crease joints. Large-scale origami is similar to the solar panels and antenna deflectors in that the actuators used for moving the joints must generate a relatively large amount of power, so the actuators are generally motors or springs. Small-scale origami is more similar to the programmable matter self-folding sheet in that the shape memory alloy (SMA) crease joints are also the actuators. Actuation in these joints is controlled by manipulating the temperature of the material, which causes the material to transition between a martensite and austenite phase. For both types of actuation, an external device is normally required to help control folding motions.

Modeling and computation design

Software can be used to facilitate the modeling and designing of a crease pattern for an origami structure. TreeMaker, frequently used for this purpose, requires the designer to input a tree graph which approximates the desired shape [44,45]. The software uses the desired shape to design a uniaxial base; this process is equivalent to a disk packing problem [46] and is carried out with a disk packing algorithm. A crease pattern is then generated, if possible. If the first pattern generated is undesirable, the designer can use Treemaker’s interface to request other variations, which are created with alternate disk packing problems. The designer then prints out the crease pattern and attempts to fold it first into a base with uniaxial flaps and then into the final shape. The patterns are often too difficult or even impossible to fold by hand, so the designer must make modifications in TreeMaker. Although it is an excellent tool for creating a preliminary prototype of a design, the user must be experienced in manual origami design.

Demaine et al. created an origami designing software called Origamizer, which divides a model’s surface mesh into flat triangular sections [47], and arranges the sections into a planar sheet. The sections are connected by jointed tucking molecules. Origamizer therefore creates the surface of the desired shape out of a sheet [47] which is organized as a triangular mesh. Creating a triangular mesh is equivalent to rearranging triangular facets in a plane without overlapping, plus inserting jointed tucking molecules. Origamizer has good efficiency, generally achieving a successful mesh design after several iterations.

The computational complexity of the two aforementioned origami design methods is determined by the problem solved by the software. TreeMaker’s complexity for any given design is equal to the complexity of the disk packing problem used to generate the uniaxial base. Origamizer’s complexity for any given design is equal to the complexity of facet arrangement and tuck molecule assignment used to generate the triangular mesh.

Demaine et al. created another method of origami design, in which orthogonal structures can be created from a set of existing hinge patterns [48,49]. The flat sheet is first divided into a grid of squares, and then each square block in the grid is assigned one molecule from a set of crease pattern molecules until a crease pattern for folding the desired orthogonal structure is achieved. The crease pattern design method has been demonstrated to be very efficient.

All three of the discussed methods are only suitable for desired final shapes which have specific geometric characteristics: TreeMaker can only realize shapes based on a uniaxial base, Origamizer can only realize meshed surfaces, and the orthogonal method can only realize shapes comprised of orthogonal surfaces. Also, each of the methods requires the desired shape of the final structure to be explicitly defined. Additionally, all of the methods are deductive, resulting in high accuracy and efficiency in achieving desired results.

Clinical adoptability

Origami-based medical devices have the potential to be more flexible, dexterous, safe, and accurate than existing devices and therefore can contribute to the implementation of minimally invasive procedures [50,51]. In order for origami-based designs to be approved for clinical use, they must be robust, easy, and reliable to use, and have consistent performance for high repeatability of procedures. Ease of use is important because clinicians will be able to learn to operate the device more quickly, reducing the cost of implementation. Clinicians should be consulted during the design process and asked to give input on the functions the device should perform and how the device should be operated. Input from clinicians should be used to ensure that the device improves upon existing technology and is likely to be approved for use in clinical applications.

Conclusion

The concepts used in the ancient art of paper folding can be used to create innovative medical devices. Researchers have explored the possibility of using origami designs to improve disposable sterilization covers, cardiac catheterization, stent grafts, encapsulation and microsurgery, gastrointestinal microsurgery, laparoscopic surgical grippers, microgrippers, microfluidic devices, and drug delivery. Origami engineering is currently progressing, with researchers improving designs and design methods, materials, fabrication techniques, and folding efficiency. Although the use of origami mathematics in biomedical engineering is rare at the present, progress in developing algorithms based on the fundamental concepts of origami (e.g., defining the limits of folding and unfolding) is paving the way for future clinical applications.

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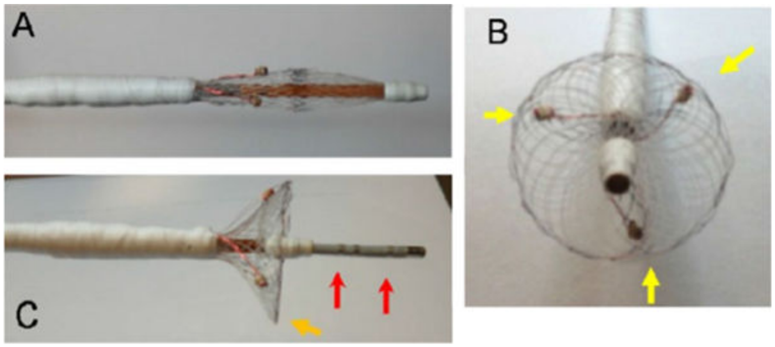

Fig. 1.

Origami structure deployed at: **a** 0%, **b** 30%, **c** 70%, and **d** 100% [26]

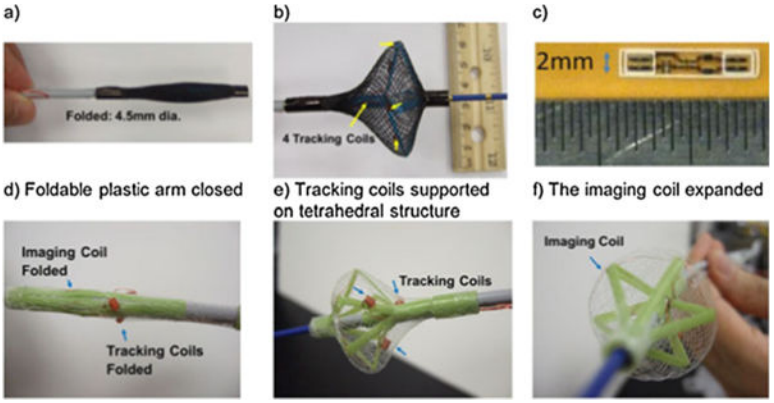

Fig. 2.

ICMRI origami catheter with imaging coil **a**–**b** collapsed and expanded; **c** tuning/matching microelectronics. ICMRI without nylon mesh, during closing (**d**) and opening (**e**–**f**) [25]

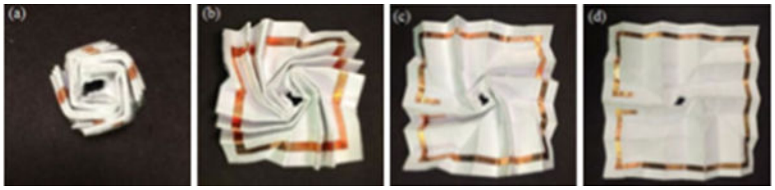

Fig. 3.

a Side view of the distal end in the fold configuration; **b** front view of the expanded catheter; **c** side view of the expanded catheter [22]

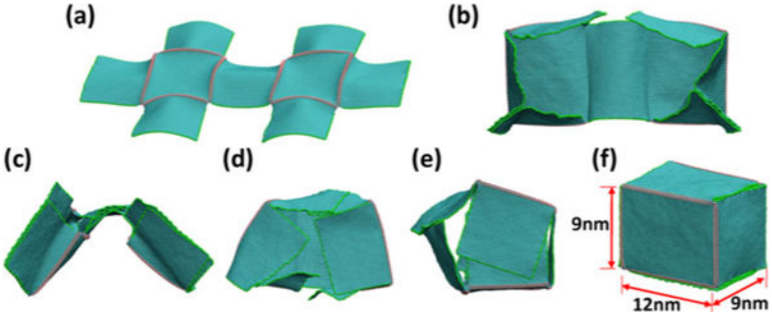

Fig. 4.

Nanoscale origami structure for drug delivery [27]

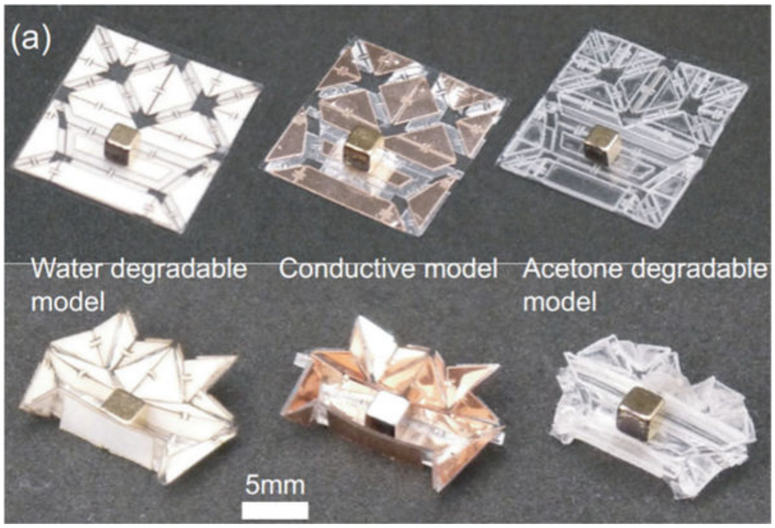

Fig. 5.

Different models of encapsulation origami robot [24]

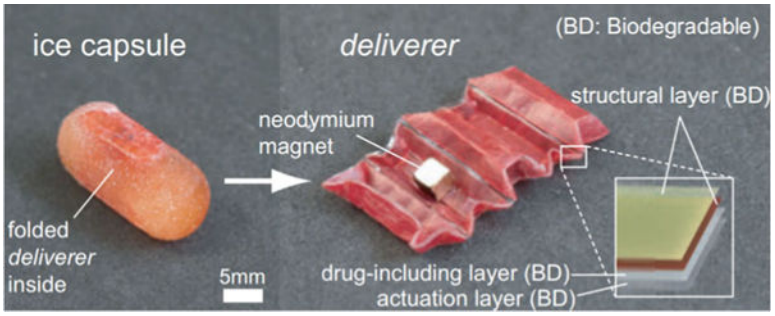

Fig. 6.

Ice capsuled gastrointestinal microsurgery origami robot [28]

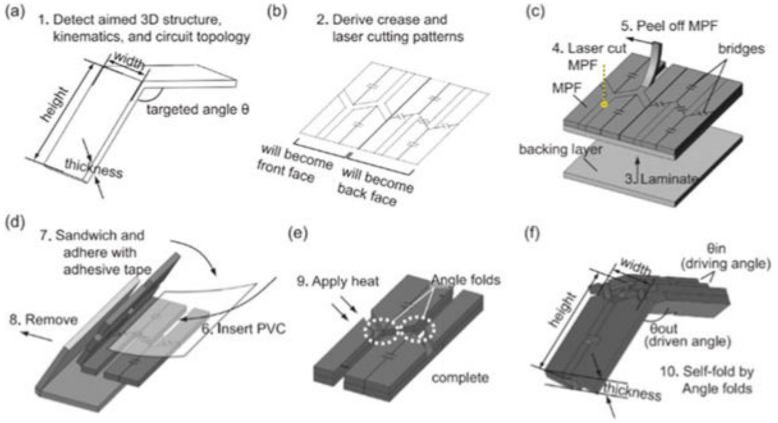

Fig. 7.

Fabrication process of the self-folding elastic electric origami devices [29]

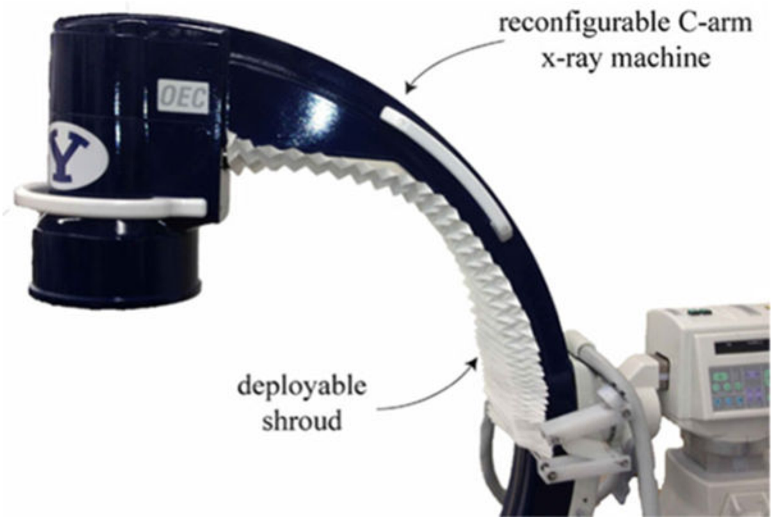

Fig. 8.

Origami cover of the X-ray shroud arm [21]

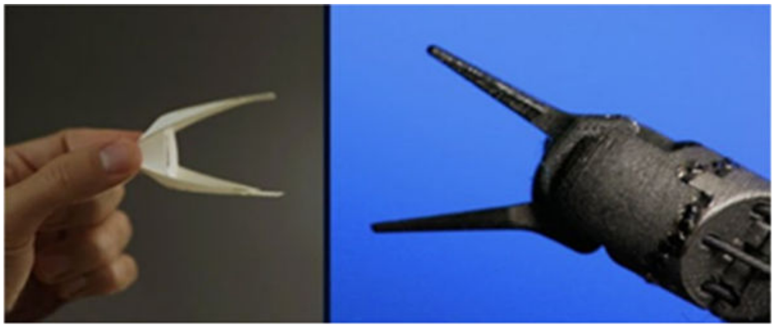

Fig. 9.

Origami gripper [30]

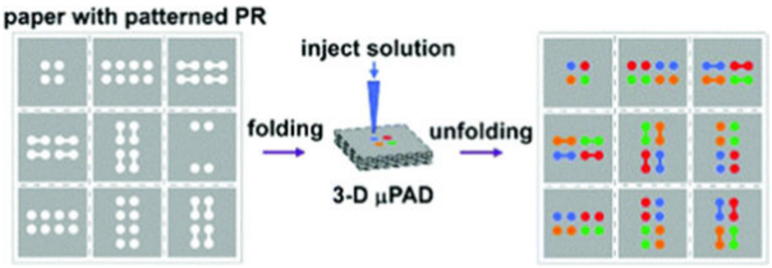

Fig. 10.

Origami-based design of the 3D paper microfluidic device [32]

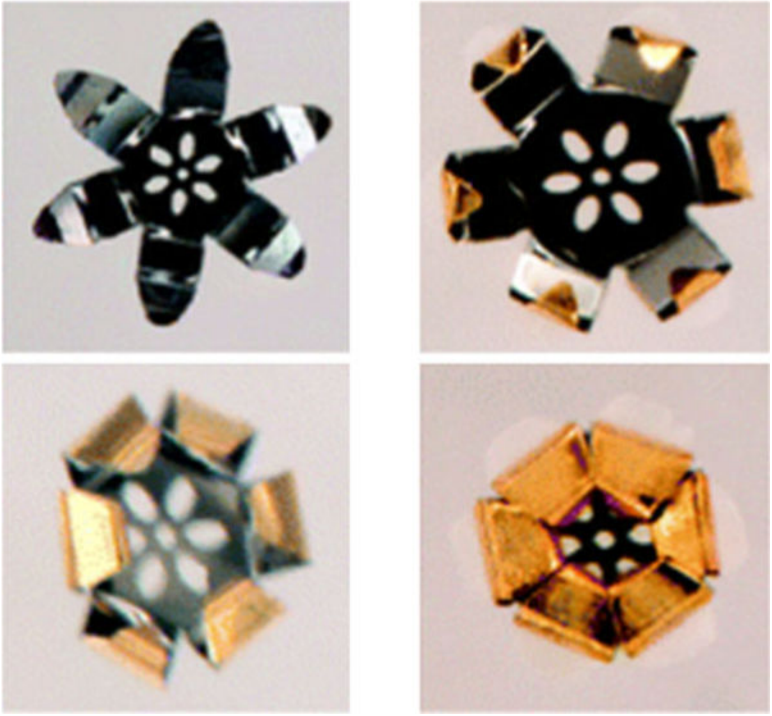

Fig. 11.

Kinetics of enzymatic triggering of the origami tool [34]

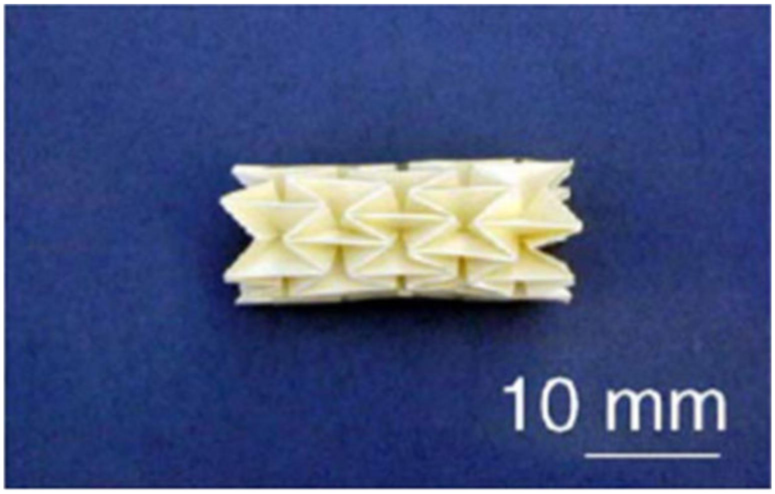

Fig. 12.
Self-deployed origami stent graft [35]

Table 1

Origami Designs with Medical Applications

Application	Material	Size/volume	Deployment/mechanism/control	Advantages	Figures	References
Heart catheterization	Biocompatible polycaprolactone	60 mm × 60 mm	A deployable origami MR imaging coil and tracking microcoils at the end of a catheter	The catheter design including the deployment mechanism and the MRI tuning and match electronics can be fabricated through a flexible printed circuit board	See Fig. 1	[26]
Heart catheterization	Biocompatible plastic	∅4.5 mm closed and ∅40 mm expanded	Tracking coils supported on a tetrahedral structure	The ICMRI catheter allows for 4–16 times faster imaging during MR-guided RFA. Can also improve accuracy and reliability in MRI-guided RFA operations	See Fig. 2	[25]
Heart catheterization	Biocompatible plastic	∅22 mm when expanded	Imaging coils in a tetrahedron MR-Tracking array on the end of a catheter	~Ten times the SNR over ~2.5 × 2.5 × 1.5 cm^3 FOV	See Fig. 3	[22]
Drug delivery through programmable molecular mass storage	Graphene	Tens of nm	Hydrogenation folds the graphene and external electric fields open and closes the graphene structure. The deployment mechanism is less effective as the size increases	Hydrogenation-assisted graphene origami can achieve molecular mass uptake, storage, and release	See Fig. 4	[27]
Encapsulation microsurgery robot	Water-degradable material, aluminum coated polyester and acetone-degradable material	1.7 cm	The robot can be remotely controlled by an external magnetic field.	Capable of performing different tasks, including swimming, delivering/carrying blocks, climbing and digging. All components except the built-in magnet can be degraded by water	See Fig. 5	[24]
Gastrointestinal microsurgery robot	Pig intestine and an iron magnet	15 × 30 × 5 mm	The origami robot is encapsulated in ice to be ingested. Once in the stomach the ice melts away. The robot can then move with the use of an external electric field	Less invasive and easy to produce, less cost	See Fig. 6	[28]
Gastrointestinal microsurgery self-folding robot	polyvinyl chloride, liquid-soluble paper	10 mm	A heat-sensitive contraction film (polyvinyl chloride; PC) is sandwiched by two rigid structural layers of liquid-soluble material. Electromagnetic coils control movements	This concept presents the capability a robot to operate various applications in previously unreachable sites encountered in both in vivo and bionic biological treatment	See Fig. 7	[29]
X-ray imaging machine shroud	Tyvek	~1 meter	The cover expands and contracts using the Miura-ori folding pattern	This design is a solution to lower cost and shorten duration of surgeries	See Fig. 8	[21]
Laparoscopic surgical gripper	Stainless steel	3 mm in diameter	The grippers can hold a needle, suture, grasp objects etc. Inserted into a tiny	Less invasive surgeries	See Fig. 9	[30]

Application	Material	Size/volume	Deployment/mechanism/control	Advantages	Figures	References
			incision and then deployed inside the body to carry out a specific surgery			
Microfluidic device	Chromatography paper	100 μ m thick paper	oPADS can be folded in one step, no tools required	Lower cost and manufacturing time, simple design, no tools	See Fig. 10	[32]
Microgrippers	Multilayer photolithography on water soluble sacrificial polyvinyl alcohol layer, trilayer joints composed of a polymer	600 μ m closed and 1.1 mm open	The gripper is activated with the contact of the specific biomolecular interaction which matches the enzyme	Less invasive, autonomous microtools, biocompatible, mass-producible	See Fig. 11	[34]
Stent grafts	Ni-rich titanium/nickel (TiNi) shape memory alloy (SMA)	∅25.4 mm× 44 mm	First packed into a sheath and then maneuvered to the designated site where the sheath is removed and the stent is deployed thermally (body temperature) or mechanically	Less invasive and easy to produce	See Fig. 12	[35]