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REVIEW

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Bioinspired Functional Surfaces for Medical Devices

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Abstract

Medical devices are a major component of precision medicine and play a key role in medical treatment, particularly with the rapid development of minimally invasive surgery and wearable devices. Their tissue contact properties strongly affect device performance and patient health (e.g., heat coagulation and slipperiness on surgical graspers). However, the design and optimization of these device surfaces are still indistinct and have no supporting principles. Under such conditions, natural surfaces with various unique functions can provide solutions. This review summarizes the current progress in natural functional surfaces for medical devices, including ultra-slipperiness and strong wet attachment. The underlying mechanisms of these surfaces are attributed to their coupling effects and featured micro-nano structures. Depending on various medical requirements, adaptable designs and fabrication methods have been developed. Additionally, various medical device surfaces have been validated to achieve enhanced contact properties. Based on these studies, a more promising future for medical devices can be achieved for enhanced precision medicine and human health.

Keywords: Bioinspired functional surfaces, Medical devices, Wet attachment, Interfacial liquid, Micro-nano structures, Wearable devices

1 Introduction

Precision medicine has become a national development strategy and has attracted worldwide attention in recent years based on increasing concerns regarding the overall health of the population [1, 2]. As a main component of precision medicine, medical devices for implantation and minimally invasive surgery (MIS) have gradually become more dominant based on the advantages of reduced injury, low infection risk, rapid healing, and high personalization. During medical operations, contact with tissue or organ surfaces is necessary and can have severe consequences for patients, including the biocompatibility of implanted devices, high-temperature coagulation on electrosurgical scalpels [3], and device tissue slipping on surgical graspers [4–6]. With the rapid progress in wearable devices, soft and sweaty skin can significantly reduce device fixation and distort detected signals [7, 8]. To eliminate these disadvantages, the regulation of interfacial contact states has become critical, which is challenging based on its multidisciplinary characteristics involving the fields of material engineering, mechanical engineering, and bioscience.

After millions of years of evolution, nature has shaped creatures with various remarkable surface functions to adapt to complex environments, including hydrophobic self-cleaning on the lotus [9], ultra-slipping on the *Nepenthes alata* peristome, and strong dry/wet attachment on gecko and tree frog feet [10, 11]. The unique functions of such natural surfaces stem from the interfacial interactions of air, liquids, solids, and energy fields at the micro or even nanoscale, which have caused enormous difficulties in terms of characterization and hampered the understanding of their mechanisms. After decades of development of micro-nano characterization methods, these underlying mechanisms have been studied

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intensively. Generally, the key features of natural sample surfaces are material properties (mechanical properties, wettability, electromagnetic properties, thermal properties, chemical properties, etc.) and micro-nano structures (single-level/hierarchical, random/patterned, and static/dynamic). Coupling effects at the micro-nano scale can lead to the creation of macroscale surface functions. Based on revealed mechanisms, theoretical models of surface attachment functions can be established, which provide principles for the design of bioinspired medical device surfaces.

Compared to the living environment in natural life, the operating environments of medical devices are significantly different. For example, tissues are always covered with mucus, which is stickier and more slippery than water, tissues or organs are much softer and more vulnerable than natural substrates, and surface biocompatibility is a constant concern. To apply bioinspired mechanisms to medical devices, the design of bioinspired surfaces must be specifically adjusted and optimized based on target medical operating scenarios. The fabrication of bioinspired surfaces is also difficult and is a long-term research topic because functional surfaces are typically constructed from micro-nano hierarchical structures and the materials of such surfaces are carefully selected. Various methods have been developed to obtain bioinspired surfaces, from mature semiconductor manufacturing processes to newly developed micro-nano self-assembly methods with low cost and large area production advantages.

In this review, we summarize the discovery of natural functional surfaces with ultra-slippery and strong wet adhesive properties that satisfy the requirements of medical devices. The underlying mechanisms of the coupling effects of surface materials and featured structures are elucidated. The applications of these bioinspired surfaces in medical devices are presented. Finally, a beneficial perspective is provided for the future exploration of bioinspired medical surfaces (Figure 1) [1].

2 The Underlying Mechanisms of Natural Functional Surfaces for Medical Devices

2.1 Basic Principles for Interfacial Contacts

Various natural creatures have evolved fascinating surfaces to achieve all sorts of important contact functions, including the ultra-slippery surfaces of *Nepenthes alata's* peristome and pitcher plants, strong dry/wet attachment ability of gecko and tree frog toe pads, and insensible penetration of skin by the proboscis of a mosquito [10, 11]. To realize these unusual functions, these surfaces possess special material properties and unique micro-nano structures that integrate mutual effects from surface chemistry, liquid/fluid mechanics, and surface mechanical interactions. Exploring their underlying mechanisms can provide novel strategies for addressing urgent and critical demands in the medical device field.

Common interfacial contacts consist of interactions between solid surfaces, occasionally under the influence of liquids. Solid surfaces have intrinsic material properties such as elasticity and surface chemistry features, as well as morphologies in different types of structures at micro or nanoscales (e.g., pillars, bumps, grooves, or random roughness). During dry contact, material properties and morphologies can significantly affect attachment performance, including adhesion and friction. Specifically, surface chemistry affects contact interactions at

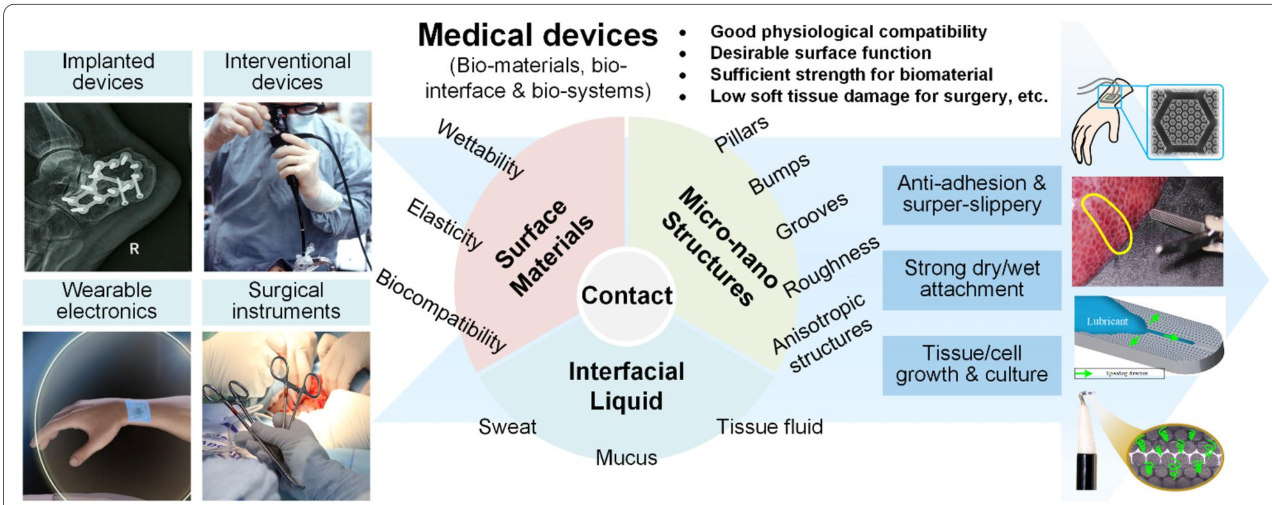

Figure 1 Nature offers novel strategies for functional surface design based on surface micro-nano structures, material properties, and their combination for creating interfacial liquid adjustment effects

the molecular scale based on strong covalent bonds generated by highly active chemical groups or weaker hydrogen bonds or van der Waals bonds created by electrostatic forces (Figure 2(a)). Surface morphologies modifying material elasticity can alter attachment by creating or removing mechanical interlocks at interfaces (Figure 2(b)). In wet contact, the liquid in an interface is another important factor determining contact properties based on the characteristics of the liquid, including strong capillarity action at the micro-nano scale, phase transition with increasing temperature, and significant hydrodynamics during shearing or pressure application (Figure 2(c), (d)). These features can regulate liquid movement or generate forces between contact interfaces, which promotes solid contact interactions to create unique functions to adjust attachment performance. By revealing such interfacial contact mechanisms, profound design strategies for medical device surfaces can be established for improved medical applications.

2.2 Natural Surfaces for Anti-adhesion and Ultra-slipperiness

Typical natural surfaces that reduce attachment forces to achieve anti-adhesion or slippery properties have been discovered in dry contact on maize leaves and the *Nepenthes alata's* inner pitcher wall, and in wet contact on the *Nepenthes alata's* peristome and earthworm skin. On maize leaves, surfaces covered with transverse and longitudinal ridges can help trap air between interfaces and reduce the effective contact area, thereby decreasing attachment forces. When the temperature increases and interfacial water vaporizes, these closed meshed ridges can also generate a vapor cushion to separate the contact further and form anti-adhesion, even at high temperatures (Figure 3(a)) [12, 13]. As a carnivorous plant, *Nepenthes alata* uses its slippery pitcher inner wall to restrain insects that fall into it by creating a low-adhesion surface. This surface has been characterized to be waxed and arrayed with crescent-shaped bulges. Under the coupling effects of low-surface-energy surface materials and micro-nano hierarchical structures, the surface exhibits superhydrophobicity with ultra-slippery properties (Figure 3(b)) [14]. Such featured surface structures and materials are critical for creating anti-adhesive surfaces for dry contact. However, based on the solid-solid mechanical interlocks in these contacts, attachment force cannot be reduced further.

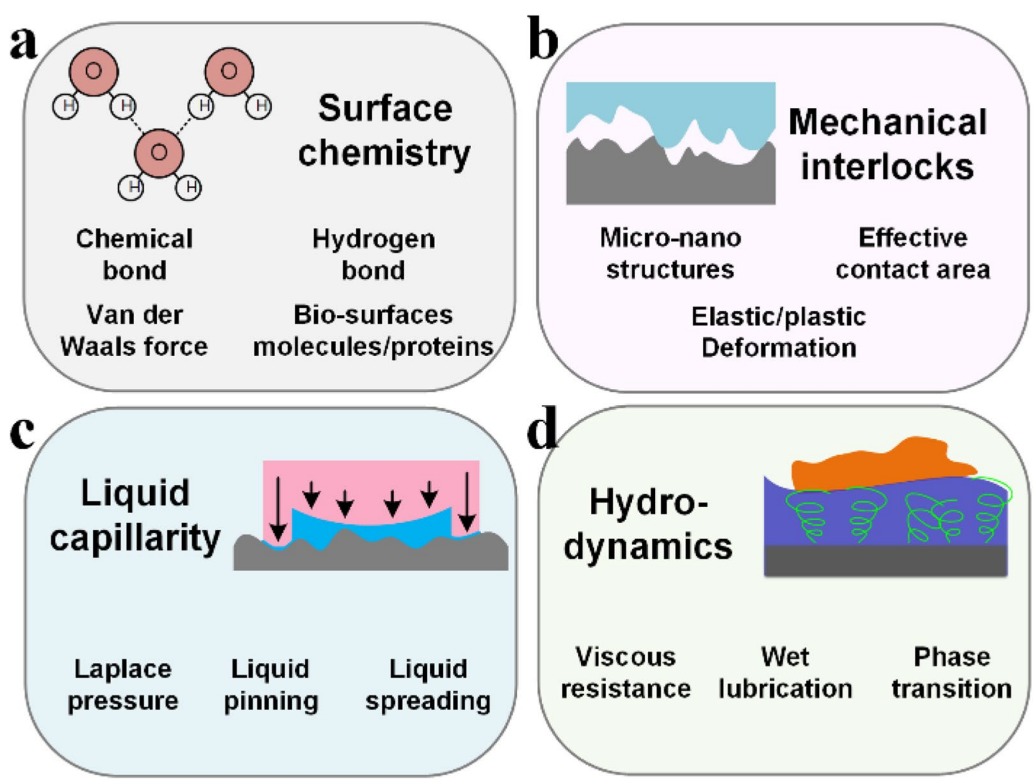

Figure 2 Featured influence factors that affect interfacial contact mechanisms: (**a**) surface chemistry, (**b**) mechanical interlocks, (**c**) liquid capillarity, and (**d**) hydrodynamics

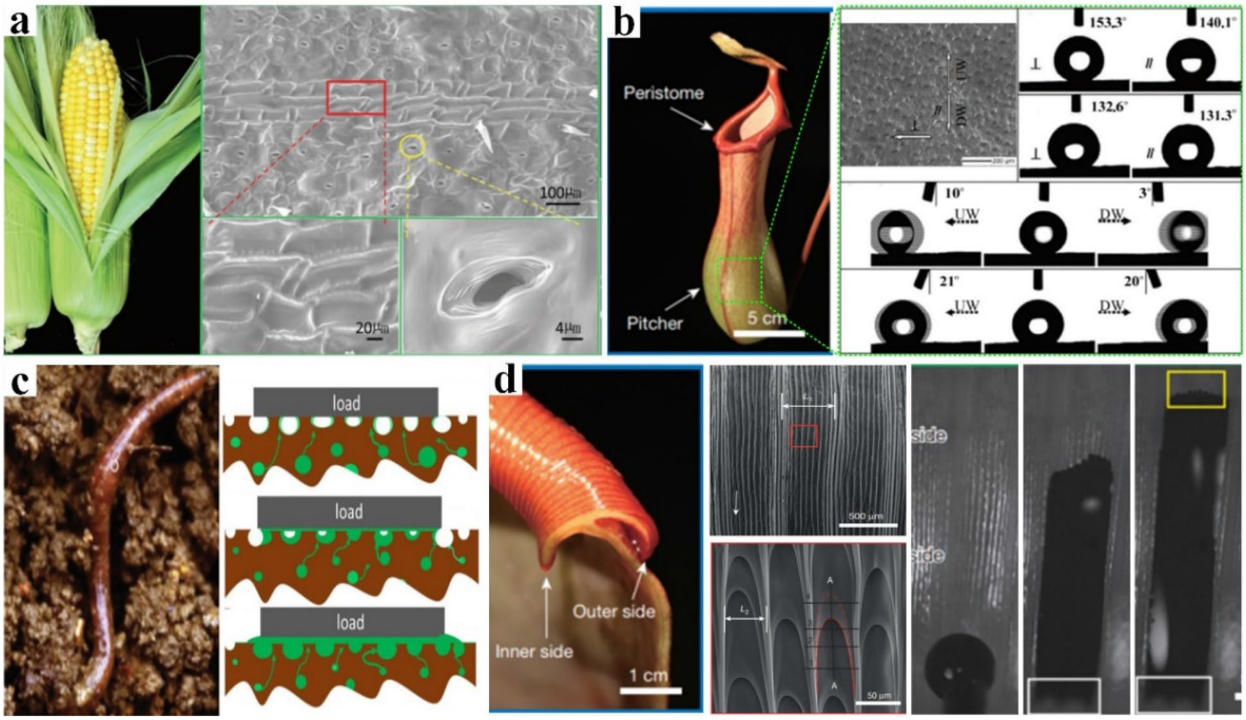

Figure 3 Anti-adhesion and slipping discovered on natural surfaces: (**a**) maize leaf with a grid-like structure, (**b**) superhydrophobic surface of *Nepenthes alata*, (**c**) earthworm-inspired self-replenishing lubrication surfaces, (**d**) unidirectional liquid spreading on the peristome of *Nepenthes alata*

A liquid with hydrodynamic attributes can act as a lubricant to reduce attachment strength significantly by altering solid-solid mechanical interlocks to achieve laminar flow liquid slip. Under this mechanism, earthworm skin evolves a layer of moist and sticky secretions for easier drilling into the soil and protection from solid scratches (Figure 3(c)) [15]. In particular, because it is arrayed with pit microstructures, this skin can prevent the secretion from scratching away during worm climbing to achieve long-term lubrication. In addition to lubricant preservation, the continuous transport of lubricants to the contact area is another strategy for long-term lubrication. The peristome surface of *Nepenthes alata* has developed a function that can rapidly and directionally transport nectar from the pitcher inner wall to the outer wall to attract and trap insects in the pitcher with its ultra-slippery properties (Figure 3(d)) [10]. Characterizations have revealed that this surface is superhydrophobic and consists of two-level microgrooves with duckbill-shaped arches aligned at the bottom of each second-level microgroove. These material properties and unique microstructures can enhance liquid spreading in one direction with a strong wedged capillarity effect while preventing liquid from flowing in the opposite direction with a sharp edge pinning effect, eventually forming a fast-directional liquid transport. With this unique functionality, the interfacial liquid film can be continuously spread over the peristome surface to keep it in an ultra-slippery state. By revealing such interfacial contact mechanisms, profound design strategies for medical device surfaces can be established for improved medical applications.

2.3 Natural Surfaces for Strong Attachment

In natural environments with various types of anti-adhesive or slippery surfaces, a strong attachment ability to resist such slipping is necessary for many creatures. The most common solution for creating strong attachment is to form mechanical interlocks between interfaces. Many insects have sharp, rigid, and hook-shaped claws or spines for climbing by either locking into rough bumps on a substrate or piercing through the substrate. The mosquito has evolved a complex proboscis to pierce the skin with extremely low force (Figure 4(a)) [16, 17]. The mantis can alter the tilt angle of its spines following substrate penetration to enhance attachment strength further (Figure 4(b)) [18]. However, this mechanical interlock approach cannot attach to smooth substrates with no bumps for engaging interlocks or stiff substrates that

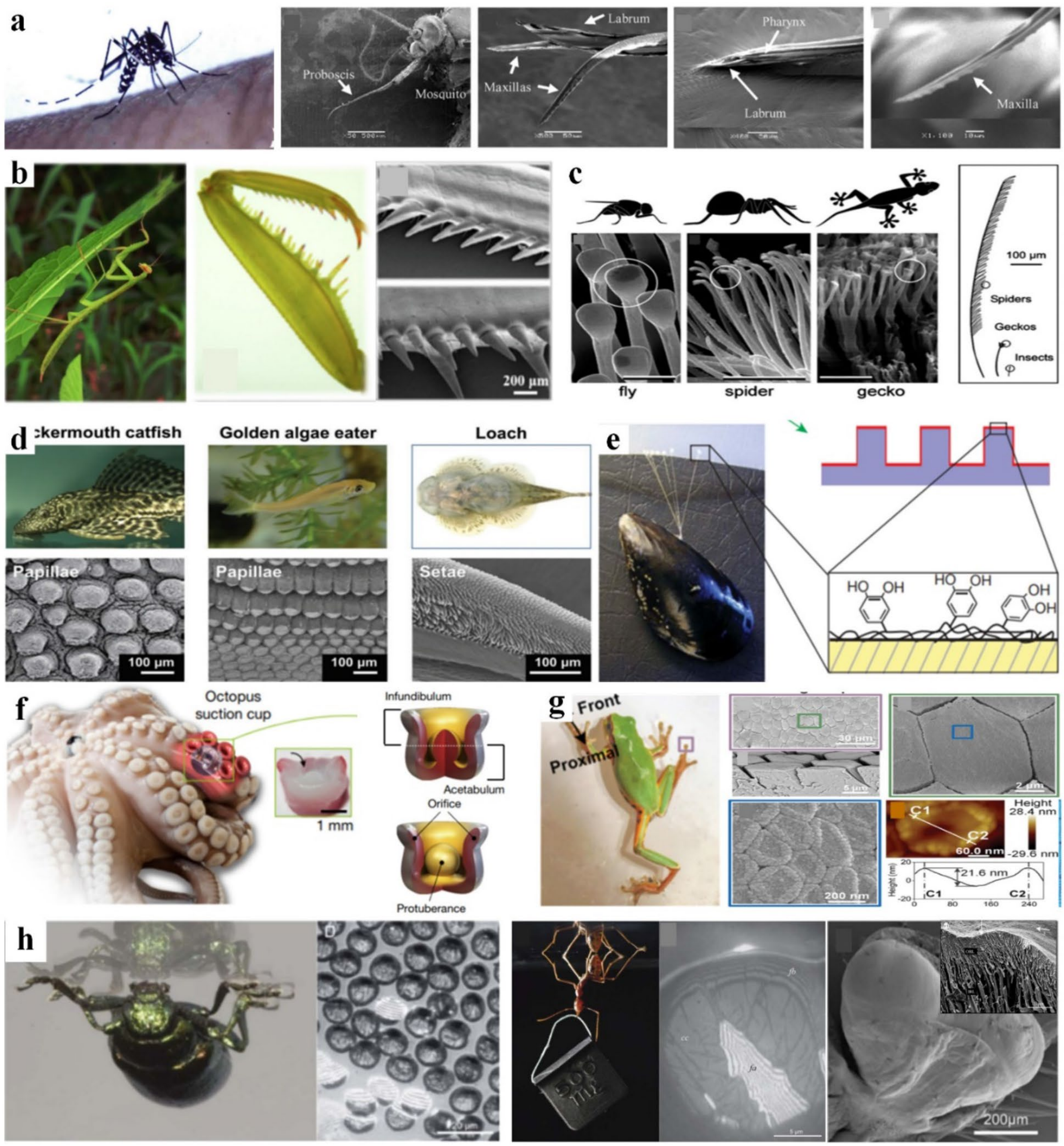

Figure 4 Strong attachment discovered on natural surfaces: (**a**) mosquito and its proboscis, (**b**) mantis and spines, (**c**) arrayed setae on insects, (**d**) strong attachments of creatures in wet environments, (**e**) mussel with its special adhesive proteins, (**f**) octopus vacuum suction, (**g**) hierarchical pillar array on the toe pad of a tree frog, and (**h**) insect adhesion with liquid capillarity

cannot be penetrated. Additionally, preload pressure is always necessary for mechanical interlocks, making it difficult for an insect to climb an overhanging surface. Van der Waals forces such as molecular interactions at the nanoscale can hardly be observed at the macroscale because the roughness of most natural surfaces prevents large-area contact in the acting range of such forces. Many creatures such as beetles, flies, spiders, and geckos have evolved arrayed setae hundreds of micrometers in height and tens of nanometers in diameter (Figure 4(c)) [19]. Each seta can form a much closer contact on a rough substrate to generate strong van der Waals forces, thereby creating strong attachment for their climbing. This strategy requires no external or preloaded forces, which helps these creatures be more adaptable to complex environments.

When a contact is in a wet condition, the van der Waals force is largely reduced by the interfacial liquid film. Therefore, other strategies such as wet adhesive materials, vacuum suction, and liquid capillary adhesion have been developed to help creatures form strong attachments in wet environments (Figure 4(d)) [20]. The mussel, with its special secreted adhesive proteins, can strongly cling to surfaces underwater. It has been revealed that the critical composite of this adhesive is catechuic amino acid 3,4-dihydroxy-L-phenylalanine, which can form strong molecular bonds on surfaces such as glass, Teflon, metal, and plastic (Figure 4(e)) [21, 22]. The mucus of a slug also demonstrates strong adhesion as a result of its interpenetrating positively charged proteins [23]. Based on these inspirations [24], various types of bioadhesives have been used for wound recovery and surgical suturing. On suckermouth fish or octopuses, vacuum suction can be generated by cup-shaped footpads after a preload is applied to expunge the interfacial air or liquid (Figure 4(f)) [25]. Their soft materials allow vacuum suction to form more easily on rough substrates [26]. Unlike one-time adhesive materials, such vacuum suction generates strong adhesion that can be generated repeatedly because no consumed ingredients are required. The toe pad of the tree frog is covered by a micro-nano hierarchical pillar array with a cavity on each nanopillar (Figure 4(g)) [11]. When an external force is applied, the connected channels between the pillars can squeeze out the interfacial liquid to form closer contact with the substrate and generate stronger wet friction. Additionally, with unique interfacial liquid adjusting effects (liquid self-splitting and self-sucking) from the hierarchical pillars, a nanoscale liquid film can form between the pillars and substrate to generate a Laplace capillary pressure several times the atmospheric pressure. Such strong capillarity firmly presses the interfaces and creates strong wet friction, even without the application of any external normal force [11]. A similar wet attachment strategy has also been discovered in wet climbing creatures such as stick insects (Figure 4(h)) [24]. This capillarity action promotes wet friction without the need for an external preload, which may be suitable for tissue fixation and manipulation based on the fragility of tissues or organs.

The coupling effect of material properties and featured micro-nano structures is the fundamental theory for creating a functional surface. These advantages offer various strategies for solving functional defects in medical devices. To realize these bioinspired medical surfaces, additional adaptive work on design and fabrication must be performed.

3 Application of Bioinspired Functional Surfaces in Medical Devices

3.1 Bioinspired Anti-adhesive or Ultra-slippery Surfaces for Medical Devices

Electrosurgical scalpels are commonly used as surgical instruments in MIS for tissue cutting and blood coagulation via electrical heating. In this process, cautery is the application of energy as heat to the target tissues. This can easily generate tissue conglutination or adhesion on the scalpel surface, which may lead to surgical failure and potential danger to patients. Inspired by special anti-adhesive and slippery surfaces in nature, researchers have attempted to mimic these functions on medical instruments.

3.1.1 Bioinspired Anti-adhesive Coating

Inspired by the gird-like topographic microstructure of maize leaves, Han et al. developed electrosurgical scalpels with ripple-like microgrids and microgrooves combined with TiO_2 coatings, as shown in Figure 5(a). Laser-engraving and 3D printing methods were integrated to fabricate these surfaces. The results indicate that this coupled bionic electrode exhibits an effective anti-adhesive property that can reduce the adhesion mass by approximately 71.43% [12, 27]. Femtosecond laser pulse (FLP)-induced modification is also an easy-to-implement method for developing anti-adhesion surfaces [28–30]. For example, Lin et al. tested an FLP-modified micro/nanostructured surface, as shown in Figure 5(b), which provides enhanced anti-adhesion properties that reduce the adhesion mass by approximately 75.14% with an injury area reduction of approximately 36%. Furthermore, the introduction of other coating materials has been explored to achieve anti-adhesion to soft tissues. Biocompatible films of diamond-like carbon (DLC) are considered to be valuable for their smoothness, low friction, and anti-corrosion properties. Cheng et al. created a Cu-incorporated DLC (DLC-Cu) film to form an antibacterial and anti-adhesion surface on medical devices and achieved excellent anti-adhesion characteristics for an adhesion mass reduction of approximately 76.6%, as shown in Figure 5(c), with an approximately 31.2% reduction in thermal injury area [31–33]. They further explored a CrN-coated surface to reduce the thermal injury during surgery and an approximately 45.4% reduction in the thermal injury area indicated that the plating of electrodes with a CrN film is a beneficial method for wound remodeling (Figure 5(d)) [34]. However, a 66.7% decrease in the adhesion mass of the CrN-coated surface

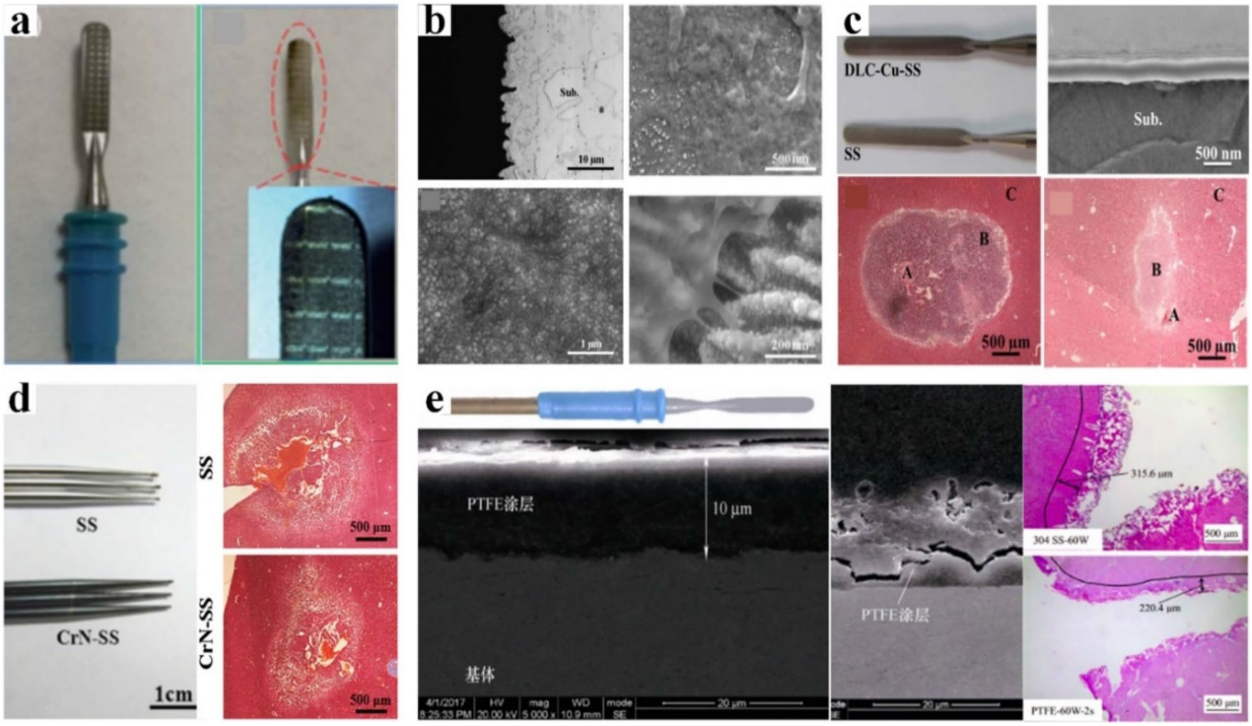

Figure 5 Dry anti-adhesion strategies for surgical scalpels: (**a**) maize-leaf-inspired grid-like hydrophobicity surface, (**b**) femtosecond laser pulse modification micro-nanostructured surface, (**c**) DLC-Cu coated anti-adhesion surface, (**d**) CrN coated anti-adhesion surface, and (**e**) PTFE-coated anti-adhesion surface

suggested that this is not an ideal approach for the anti-adhesion of electrodes using only microstructures or coatings. Additionally, based on their low surface energy, PTFE-coated electrodes have also been used for anti-adhesion to soft tissue. Although they initially exhibit high incision efficiency, they also exhibit inferior anti-adhesion durability, as shown in Figure 5(e) [35]. Therefore, developing medical devices using surfaces with excellent anti-adhesion capabilities remains a challenge.

3.1.2 Bioinspired Liquid-Infused Ultra-slippery Surfaces

Inspired by *Nepenthes alata*, liquid-infused slippery surfaces have been investigated as another form of anti-adhesion strategy in medical surfaces for the anti-adhesion of soft tissue. By using a direct chemical etching method and silicon oil infusion, Zhang et al. fabricated a liquid-infused slippery surface on stainless steel that can sustain high temperatures and exhibits stable anti-adhesion properties, as shown in Figure 6(a) [36]. To achieve a controllable microstructure for holding adequate lubricants, photolithography-assisted chemical etching was used to fabricate textured surfaces on stainless steel. The adhesion force and adhesion mass decreased by approximately 80% and 89%, respectively, exhibiting excellent stability (Figure 6(b)) [37]. The thermal effects of the injury were also analyzed, as shown in Figure 6(c), where the liquid-infused slippery surface exhibited the minimum thermal injury area with a reduction of approximately 72% [38]. Additionally, self-lubricated liquid-infused slippery surfaces have been investigated to improve the durability of anti-adhesion properties by introducing a gradient microstructure on the surface of scalpels. Cycle test results indicated that the stability of the scalpel was greatly improved as the adhesion force decreased by approximately 90% and the adhesion mass was reduced by approximately 75.6% (Figure 6(d)) [39]. Because medical devices are diverse in shape, Liu et al. attempted to create liquid-infused surfaces on curved device surfaces such as those used in electrocautery (Figure 6(e)) [40]. By using a rotary transform of the photoresist and chemical etching process, microstructures were successfully fabricated on the curved surfaces of electrocautery instruments, demonstrating the feasibility of this method for application to complex surfaces. Other methods for strengthening slippery surfaces to maintain anti-adhesion capabilities have been developed by Aizenberg et al., as shown in Figure 6(f), who developed stable, self-healing slippery liquid-infused surface that exhibits excellent stability for anti-adhesion [41]. Inspired by animal corneas, Tian et al. fabricated

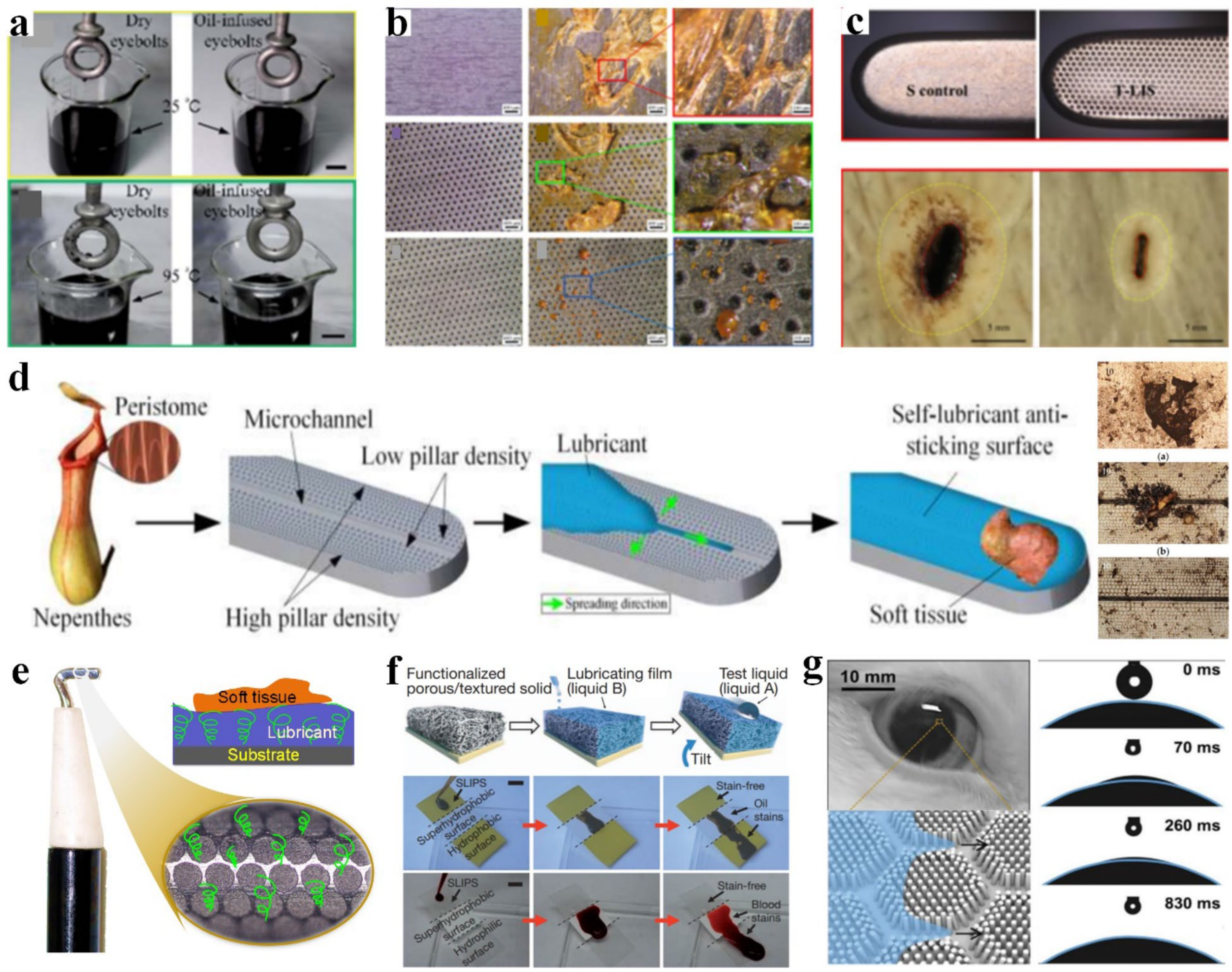

Figure 6 Liquid-infused slippery strategies for anti-adhesion on surgical scalpels: (**a**) stable liquid-infused slippery surface, (**b**) liquid-infused textured surfaces on stainless steel, (**c**) liquid-infused textured surfaces for low damage effects, (**d**) self-lubricating slippery anti-adhesion surface, (**e**) slippery surface on electrocautery instrument for the anti-adhesion of soft tissue, (**f**) stable and self-lubricating slippery liquid-infused porous surface, and (**g**) enhanced rapid super-spreading surface

an enhanced rapid super-spreading surface, as shown in Figure 6(g), where a microchannel and nanofiber array are involved [42]. This surface facilitates spreading more than 26 times faster than conventional superamphiphilic surfaces, indicating tremendous potential for application to slippery anti-adhesion surfaces. In summary, liquid-infused slippery surfaces have excellent potential for application to medical devices for the anti-adhesion of soft tissue. Postsurgical tissue adhesion is another significant clinical challenge that must be addressed. Various types of materials and functional surfaces have been investigated to prevent postsurgical tissue adhesion. Wang et al. developed a membrane that was synthesized through the reaction of polygalacturonic acid (PGA) with 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC), which exhibited promising anti-adhesion potential (Figure 7(a)) [43]. Additionally, Lee et al. explored the effects of poly(l-lactic acid)-polyethylene glycol (PEG) diblock copolymers for the prevention of tissue adhesion and indicated that this membrane is effective at preventing cell or tissue adhesion on film surfaces [44]. Another membrane of polylactide-polyethylene glycol tri-block copolymer (PELA) was proposed by Yang et al. to prevent cell or tissue adhesion and has achieved effective results based on the hydrophilic properties of polyethylene glycol (Figure 7(b)) [45]. In addition to these membranes, hydrogels have attracted significant attention as a barrier for the prevention of postoperative adhesion. Ding et al. synthesized a biodegradable and thermo-reversible PCLA-PEG-PCLA hydrogel as a convenient and highly

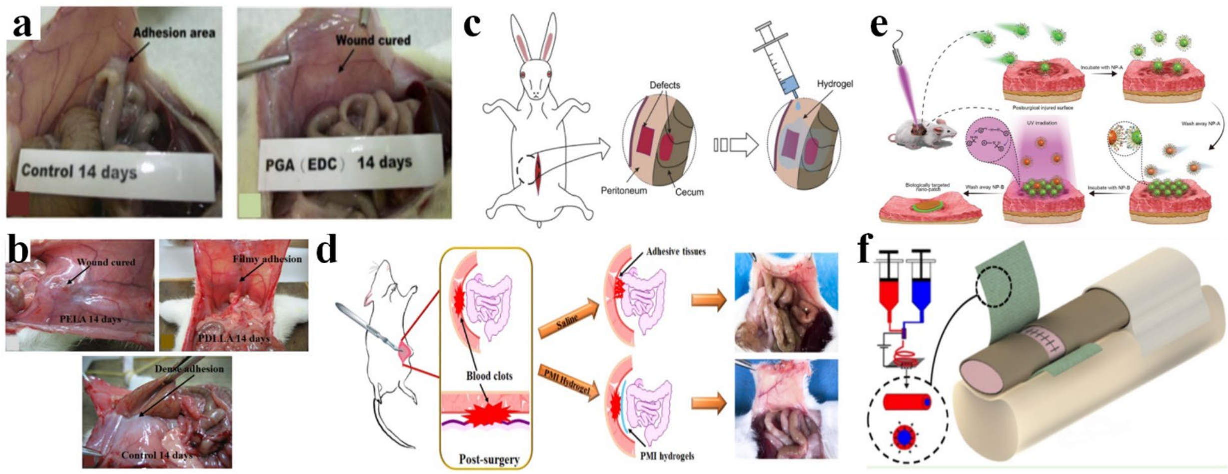

Figure 7 Surfaces to prevent postsurgical tissue adhesion: (**a**) PGA-EDC, (**b**) PELA, (**c**) PCLA-PEG-PCLA, (**d**) H-bonding supramolecular hydrogels, (**e**) pCNP, and (**f**) electrospun nanofibrous membranes

effective method to reduce the formation of intraperitoneal postoperative intestinal adhesion (Figure 7(c)) [46]. Cheng et al. proposed H-bonding supramolecular hydrogels of imidazolidinyl urea (hydrogen bonding reinforced factor) with biodegradable and high-toughness materials, as shown in Figure 7(d) [47]. However, the simplest and most direct method may be a biodegradable barrier such as a N, O-carboxymethyl chitosan/oxidized regenerated cellulose (N, O-CS/ORC) composite gauze [48], sandwiched electrospun scaffold loaded with ibuprofen [49], biologically targeted photo-crosslinked nanopatch (pCNP) (Figure 7(e)) [50], or nanofibrous membrane, which can act as a physical barrier to prevent or minimize the adhesion of a repaired tendon to its surrounding sheath (Figure 7(f)) [51]. All of these techniques are convenient and highly effective as barriers to prevent the postsurgical adhesion of the soft tissue.

3.2 Bioinspired Strong Attachment Surfaces for Medical Devices

With the rapid progress in wearable electronics and precision medicine, device-tissue contact has gradually become an important topic. Based on the vulnerability and slipperiness of soft tissues, such contact surfaces should possess the properties of strong wet attachment, similar to surgical graspers or wearable devices. By applying bioinspired strong attachment strategies to medical instruments, the deformation of tissue can be significantly reduced and wet attachment can be enhanced to achieve secure contact with tissues or skin.

3.2.1 Bioinspired Chemical Adhesives

Strong adhesives in a wet environment are necessary for medical procedures such as heart repair [52], wound seaming [53], blood vessel hemostasis [54], and skin adhering [55]. Common adhesives cannot be used in medical processes as a result of the slippery nature of mucus/sweat and requirements for biocompatibility. Inspired by natural strong wet adhesive components, various types of adhesives with robust adhesion to biological surfaces and good biocompatibility have been developed [56]. Mooney et al. developed a tough adhesive inspired by slugs with a positively charged layer and energy-dissipating matrix layer [57]. This adhesive can form a covalent bond with a bio-surface in several minutes, even under the impact of a bio-fluid, where the adhesion strength is approximately eight times greater than that of typical adhesives (Figure 8(a)). Another type of strong attachment strategy uses a typical adhesive polymer that works as a glue to bond a patch and substrate. The polymer, which is inspired by mussel protein, contains a catechol-modified polymer solution (e.g., dopamine) that can adhere to hydrogel patches on many types of materials, including glass, mica, PDMS, or even bio-surfaces such as liver tissue and skin (Figure 8(b)) [58]. Similarly, Zhao et al. developed a double-sided tape consisting of biopolymer composites and crosslinked poly (acrylic acid) with N-hydrosuccinimide ester (Figure 8(c)) [59]. This tape can form fast temporary bonds with bio-surfaces by absorbing interfacial bio-fluids, which is accompanied by amine group crosslinking to enhance the attachment strength further and achieve sturdy fixation within five seconds. By replacing traditional materials with

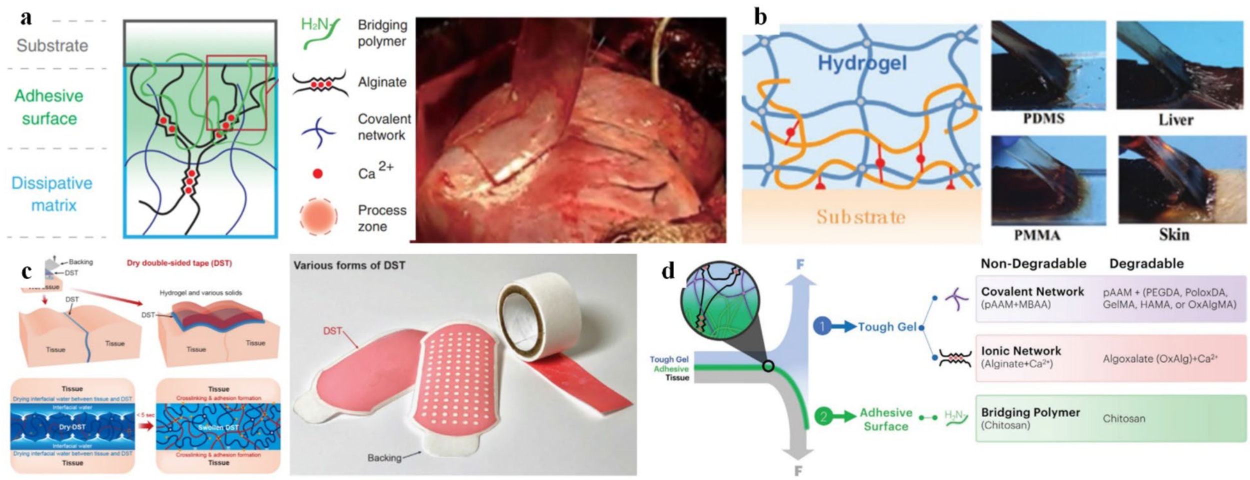

Figure 8 Bioinspired adhesives for medical devices: (**a**) tough adhesive for wet surfaces, (**b**) tough adhesive for wet and soft materials, (**c**) dry tape for wet tissues and devices, and (**d**) tough adhesive hydrogels

acrylate-functionalized crosslinks and oxidized alginate (algoxalate) polymers, a degradable adhesive can be completely degraded in two weeks with no appearance of toxicity, which further enhances its clinical practicality (Figure 8(d)) [60].

3.2.2 Bioinspired Microneedles

An easy way to introduce drugs or extract blood from the human body is through the skin using sharp and long metal needles [61]. With the rapid development of medical technology, drug delivery using slow- or long-term release features has attracted significant attention for the administration of oligonucleotides, vaccines, peptides, hormones, and cancer-targeted drugs. Park et al. fabricated arrayed microneedles using semiconductor-assisted methods, which can enhance permit entry and lateral diffusion by one to two orders of magnitude (Figure 9(a)) [62]. Cheng et al. introduced a microneedle patch integrated with cardiac stromal cells, which facilitated closer communication for heart cell regeneration (Figure 9(b)) [52]. Inspired by the clutching spines on the legs of the mantises, a microneedle patch with magnetized materials can deform needles under a certain magnetic field to lock them to a substrate with a much stronger attachment force (Figure 9(c)) [18]. Inspired by endoparasitic worms, Karp et al. developed a microneedle patch in which the needle swells after contact with water to form stronger mechanical interlocks (Figure 9(d)) [63]. Blood extraction with less invasive and low-pain characteristics is another application of microneedles (e.g., daily blood glucose monitoring or blood tests) [64]. Inspired by the imperceptible skin-piercing ability of a mosquito's proboscis, microneedles have been fabricated through laser cutting or chemical etching processes (Figure 9(e)) [16]. Their piercing force has been measured to be extremely small at approximately 18 μN and the sharpening angle of the needles has been optimized. By applying PZT actuators to a jagged microneedle, piercing motion was realized for practical medical applications (Figure 9(f)) [17]. Additionally a hydrophilic capillary microtube on a microneedle allows blood plasma to be extracted effectively (Figure 9(g)) [65].

3.2.3 Bioinspired Repeatable Wet Adhesion

Compared to single-time and permanent strong biosurface attachments from adhesives or microneedles, adhesion that can be generated easily and repeatedly for easy detachment is more important for instruments such as surgical graspers or wearable devices. To meet such requirements, the vacuum sucking approach of octopuses or suckermouth catfish is suitable and various surfaces with arrayed suckers on millimeter and micrometer scales have been developed with the assistance of the bubble capillary effect (Figure 10(a)) [25, 66, 67]. Such a vacuum-sucking surface can generate an adhesion force of approximately 25 kPa, which is one-quarter of atmospheric pressure and approximately three times greater than that of an unpatterned surface. Such a surface can work repeatedly under both dry and wet conditions, and using non-adhesive materials reduces the potential for contamination. In contrast to this vacuum sucking strategy, which requires a high external preloaded pressure to extrude the interfacial air/liquid, the strong wet attachment of the toe pad of a tree frog utilizes liquid strong capillarity action at the nanoscale to generate strong wet friction without external normal force, which makes it

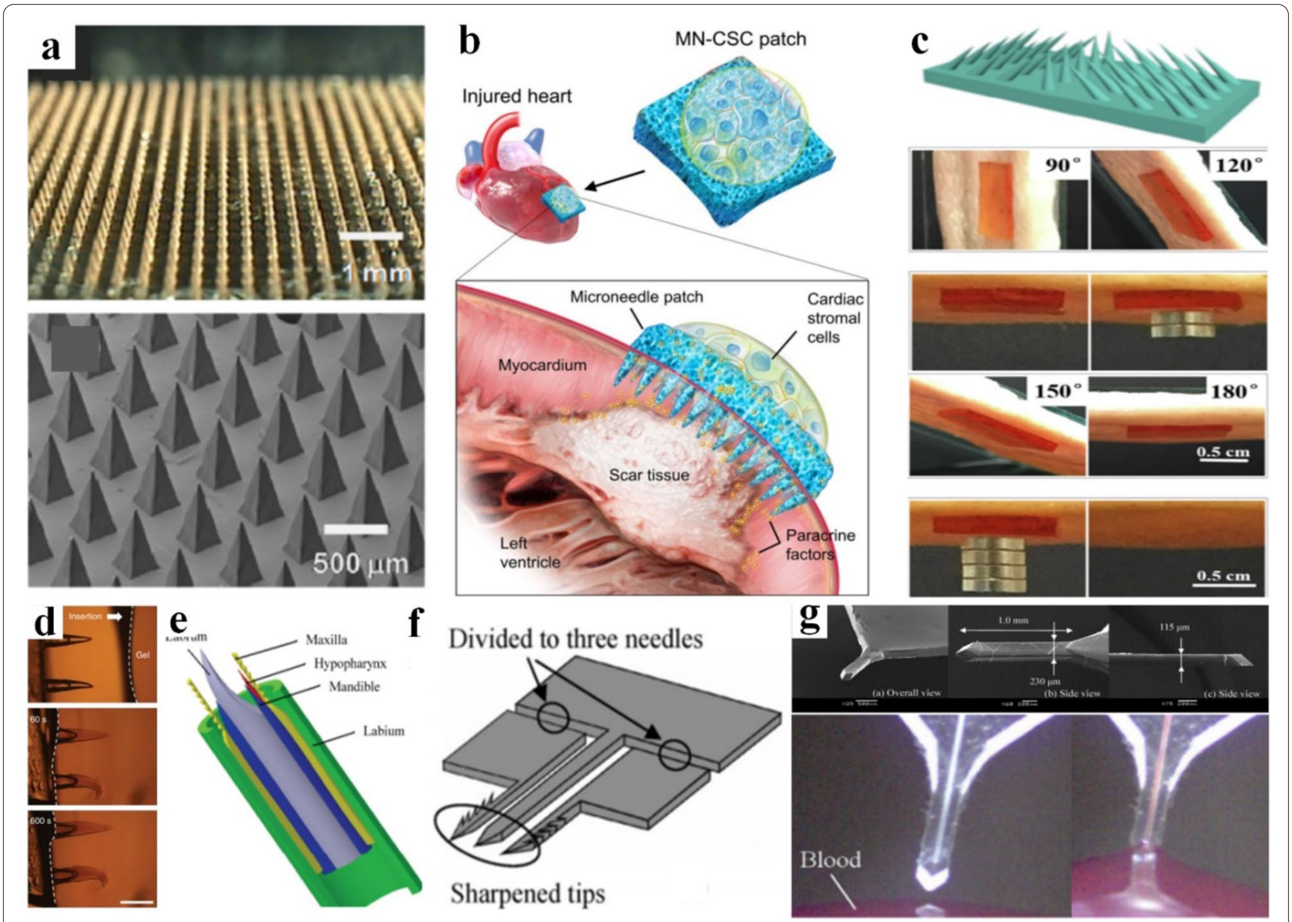

Figure 9 Microneedles for drug injection: (**a**) microneedle array for drug delivery, (**b**) cardiac cell-integrated microneedle patch, (**c**) bioinspired clamping microneedle array, (**d**) bioinspired swellable microneedle for tissue interlocking, (**e**) mosquito-proboscis-inspired needle, (**f**) mosquito-proboscis-inspired needle, and (**g**) microneedle for blood extraction

suitable for medical attachment considering the vulnerability of tissues and organs (Figure 10(b)). A tree-frog-inspired metal surgical grasper surface was fabricated using chemical spray etching methods to produce a sharp micropillar array. When testing the surface's attachment to a pig liver, the friction was found to be approximately five times the normal force and approximately times greater than that of traditional sharp-tooth surgical graspers. Because the associated structures are on the microscale, the tissue deformation induced by bioinspired surgical graspers is only approximately 90% of that of traditional graspers (Figure 10(c)).

Additionally, by applying this bioinspired surface to wearable devices, strong attachment can significantly enhance detected signal strength [11, 68].

4 Conclusions and Perspectives

In summary, significant progress has been made in the application of bioinspired surfaces to medical devices. With the discovery of all types of creatures with peculiar functional surfaces, the underlying mechanisms between contact interfaces have been revealed through micro/nano-scale interactions with an intervening liquid, including anti-adhesion/slippery functionality and strong attachment properties. The natural anti-adhesion function on maize leaves or *Nepenthes alata* pitcher walls has been attributed to their unique micro-nano bumps and low surface energy materials, which reduce the effective contact area and contact energy. The slippery functionality of earthworms and the *Nepenthes alata* peristome surface has been attributed to lubricative fluid and continuous liquid transportion capabilities. Additionally, natural strong attachment can be generated by mechanical interlocks at micro-nanoscales (i.e., mosquito proboscis or insect claw) or

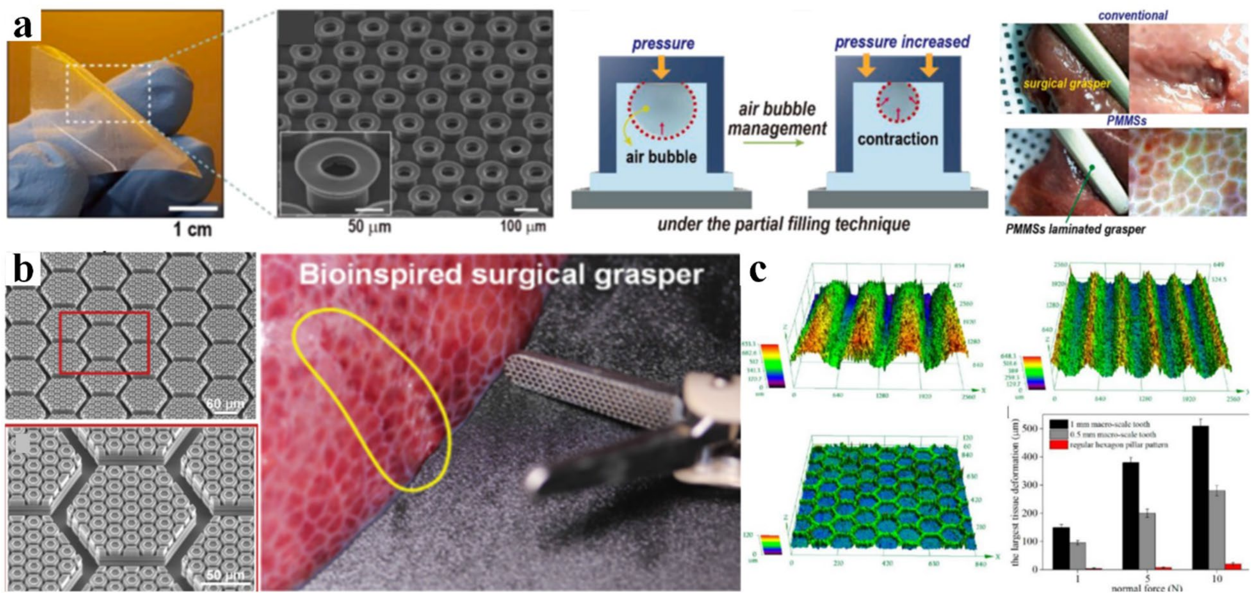

Figure 10 Bioinspired strong wet attachment based on liquid capillarity action: (**a**) moisture-tolerant adhesive patch inspired by the cups of an octopus, (**b**) tree-frog-toe-pad-inspired strong wet friction surface, and (**c**) tissue deformation of bioinspired surgical graspers

formed by van der Waals forces at the macroscale by the nano-setae arrays on insect and gecko footpads. Under wet conditions, vacuum sucking and nano-liquid capillarity strategies were identified on the sucking cups of the octopus and toe pads of the tree frog. These unique natural attachment mechanisms have been established based on the coupling effects of surface materials and micro-nano structures.

By revealing the underlying mechanisms of natural surfaces, bioinspired functional surfaces have been fabricated and tested to overcome potential dangers in the operation of medical devices, including blood coagulation on surgical electric scalpels and wet slipping on surgical graspers or wearable devices. Bioinspired dry and wet anti-adhesive surfaces have been applied to surgical scalpels, where the wet anti-adhesive strategy exhibits better cutting performance with its continuous liquid slipping effect. For strong attachment, bioinspired adhesive patches from mussels have been synthesized and have exhibited strong biocompatible adhesion to tissue and organ surfaces, even under the action of bio-fluids. Repeatable wet attachment surfaces have been designed and fabricated based on inspiration from the octopus and tree frog. Such surfaces exhibit strong attachment and less tissue injury for surgical graspers and wearable devices. Through applications in medical devices, bioinspired approaches have offered promising strategies for solving the inadequate functions of surfaces in the medical field in innovative ways.

Despite these significant achievements, more efforts still need to be devoted to the study of bioinspired surfaces for medical devices. Currently, most natural surface functions are discovered and studied at macro or micro scales, whereas functions at the nanoscale are still intangible based on the difficulty of observation and characterization, particularly for in situ interfacial liquid movement characterization. Novel techniques must be applied to these studies to expand the understanding of functions at a smaller scale further. The manufacturing of bioinspired medical devices is another important research area, including the selection and synthesis of new materials, and design and fabrication of more complex hierarchical micro-nano structures. Furthermore, the biocompatibility of bioinspired surfaces is fundamental for applications in medical devices and must be carefully addressed. With the continuous development of bioinspired interfacial contact mechanisms and fabrication techniques, a promising future for medical devices can be realized for enhanced precision medicine and human health.

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Author Contributions
LZ and GL contributed equally to this work. HC, DZ and LZ conceived the idea of this study; LZ and GL wrote the manuscript; HC and LZ optimized the presenting structure; and LZ, GL, YG, and YW provided the data. All the authors have read and approved the final manuscript.

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Competing Interests
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