**REVIEW**

# Bioinspired superwetting surfaces for biosensing

### Abstract

Inspired by nature, scientists and researchers have studied the wetting behaviors on various creatures and mimicked their structures to fabricate diverse functional superwetting materials. As one kind of emerging application, the bioinspired superwettable surfaces used for biosensing have been aroused wide interests. In this review, we summarized the recent developments of bioinspired superwettable surfaces in the field of biosensing. In the first part, superwettable creatures in nature, namely, superhydrophobic self-cleaning lotus leaf, high-adhesion superhydrophobic rose petal, amphiphobic springtail, patterned wetting desert beetles, slippery pitcher plant, were introduced. In sequence, we successively described the special wetting models of superhydrophobicity, superamphiphobicity, responsive wettability, patterned wettability, and slipperiness. Then, biosensing applications based on the respective patterned wettable, superhydrophobic, responsive wettable, and slippery substrates that were combined with the common detection approaches (colorimetry, fluorescence, surface-enhanced Raman scattering (SERS), electrochemistry) were shown in detailed. At last, an insight of remaining challenges and future development for bioinspired superwetting materials applied in biosensing was provided.

### Keywords

biosensing, detecting technologies, nature, superwettable

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1. **INTRODUCTION**

Nature, the most distinguished, inspires the development and progress of mankind. From the past to the present, learning from nature is a timeless topic. As a common phenomenon, special wetting behaviors have attracted plenty of attentions. From a work by Barthlott and co-workers, the lotus leaves can always keep themselves clean in dirty conditions, arising from superhydrophobicity and self-cleaning property induced by the microstructures and low surface energy substance of wax. 

In followed, Jiang's group observed much smaller structures, convexities in nanoscale, on the micropapillaes. So, the micro/nano hierarchical structures and waxy layer are proved to contribute to superhydrophobicity on lotus leaf, where water drops roll freely randomly on such surface to clear contaminations. Since then, a great deal of fantastic superwettable animals and plants have been studied. The romantic rose petals also show super water-repellency. But, in contrast with lotus leaf, water drops can be hung on even upside down due to high-adhesion forces generated on rose petal surfaces. Besides
bioinspired superhydrophobicity, (super)amphiphobicity inspired by bacterial (*Bacillus subtilis*) biofilm colonies, springtails, leafhoppers, and pellicles,15-20 patterned wettablity inspired by Namib Desert beetles (*Stenocara* sp.),21 slippery inspired by *Nepenthes* pitcher plant22 have been widely researched as well nowadays. Inspired by these natural creatures, biomimetic superwettable materials have been numerous developed via texture constructions and chemical modifications.23-26 Meanwhile, the corresponding applications based on these bioinspired wettabilities emerge in last several decades, such as self-cleaning,27,28 liquids separation,29,30 anticing,31,32 antifouling,33,34 antifogging,35,36 fog harvesting,37,38 and so on.

In the field of analytical chemistry, biosensing application is an important tool to detect biological and chemical molecules (ie, metal ions, H2O2, DNA, miRNA, proteins, glucose, etc).39-41 In recent years, the integrations between bioinspired superwettable surfaces and detecting techniques that include the common technologies of colorimetry, fluorescence, surface-enhanced Raman scattering (SERS), and electrochemistry on the same platforms have been put forward by scientists and researchers in quest of biosensing.42-43 For example, the beetle-inspired patterned wetting samples often possess (super)hydrophilic dots on the (super)hydrophobic substrates, whereby the (super)hydrophilic domains containing sensing entities to generate according signal output to realize the final application of biosensing.44-46 What is more, the surfaces with superhydrophobicity, superamphiphobicity, responsive wettability, and slipperiness have been also utilized for efficient biosensing in present.

In this review, we showed the progress of biosensing applications based on bioinspired superwetting materials in recent years. At first, the wetting characterizations of lotus leaf, rose petal, springtail, Namib Desert beetle, and *Nepenthes* pitcher plant are presented. Then, the wetting models of superhydrophobicity, (super)amphiphobicity, responsive wettability, patterned wettability, and slipperiness were respectively discussed. In followed, with the aid of frequently used detecting technologies (colorimetry, fluorescence, SERS, and electrochemistry), the aforementioned bioinspired superwettable surfaces as useful platforms in the field of biosensing were introduced. Finally, the highlights and challenges of bioinspired superwettable surfaces for biosensing were detailed.

2 | WETTAE NATURAL CREATURES

The special wetting behaviors play important roles on the survivals of plenty of plants and animals in nature. Here, we described the wettabilities on lotus leaf, rose petal, springtail, Namib Desert beetle, and *Nepenthes* pitcher plant, respectively.

### 2.1 | Superhydrophobicity inspired by lotus leaf

Lotus has been a symbol of purity and nobility in ancient Asian culture due to its self-cleaning property in dirty environment.47-49 Taken advantage of the technology of scanning electron microscope (SEM), nano-branches on the micropapillaes were found on lotus leaf by Jiang and coworkers (Figure 1A).10 Also, the low surface free energy of wax layer was also found on the surface. The micro- and nano-structures and wax layer are considered to be important for the self-cleaning superhydrophobic interface. Water drop on the lotus surface shows a water contact angle (WCA) larger than 160° and easily rolls away in any directions. Thus, the rolling drops can bring the dusts or dirties away from the surface, keeping a cleaning lotus leaf all the time.

### 2.2 | Superhydrophobicity inspired by rose petal

Different from the strong water-repellent lotus leaf, rose petals show high adhesion for water drops but still keep in superhydrophobic states.14 The red rose petals exhibit an array of micropapillae within nanoscale creases (Figure 1B). When water droplets are set on rose petal surface, the spherical shapes for water drops are observed, at the same time, water drops are found to be stucked on these surfaces even upside down.

### 2.3 | Omniphobicity inspired by springtails

Different from the creatures with superhydrophobicity, superhydrophobicity underwater superoleophobicity, it is once considered that no superoleophobic creature exists in nature. Artificial oleophobic or superoleophobic surfaces are predesigned through more complex structures and much lower surface energy. As an omniphobic insect, the springtail (*Orthonychiurus stachianus*) is featured with a comb-like structure with hexagonally arranged cavities (Figure 1C),10 whereby a regularly arranged but complex-shaped surface structures were constructed. The overhanging structures, such as mushroom and serif T structures, play important roles in omniphobicity on springtail, resulting in the non-wetting to low surface tension liquids.
Patterned wettablilty inspired by beetles

In dry and hot Namib Desert, there are several beetles showing superior water collections to feed themselves. In 2001, A. R. Parker et al. found the hydrophilic smooth “bumps” were distributed on superhydrophobic wax-covered valleys (Figure 1D). The “bumps” (0.5 mm in diameter) are randomly distributed in an array with 0.5-1.5 mm apart, and the wax layer constructs the hydrophobic valley. Therefore, the integration of alternated hydrophilicity and hydrophobicity are endowed the beetles with efficient fog-harvesting abilities. During the nighttime, the wind contained dense drops blow from nearby ocean brings amounts of water to the creatures in Namib Desert. Water in foggy atmosphere is captured by the hydrophilic regions and then coalesces into a bigger one, and finally transported to the hydrophobic area till to the maximal drop weight. It can be understood that water is captured on hydrophilic areas and transported by hydrophobic regions on the dorsal back of Namib Desert beetle to achieve fog harvesting.

Slippery inspired by pitcher

The peristome surface existed in *Nepenthes* pitcher plant is featured with relative regular microstructure, where straight rows of epidermal cells constructed first- and second-order radial ridges (Figure 1E). When rain water wetted peristome in a slippery state, a glossy surface is obtained without any individual droplets. The intermediary liquid is locked-in micro-textures on pitcher, forming a repellent layer. And, surface energies between liquid and solid are well matched, which is cooperated with micro-textural roughness to create a highly stable state and a continuous overlying film is obtained. So, amounts of ants are quickly captured and moved down to digestive fluid.

WETTING MODELS

Definition of wetting behaviors

Wetting behavior of a surface is defined by WCA. Previously, the value of 90° is considered as the boundary of hydrophobicity and hydrophilicity based on Young’s equation, shown as below:

$$\cos \theta = \frac{\gamma_{\text{SA}} - \gamma_{\text{WS}}}{\gamma_{\text{WA}}}$$

$\theta$ is the water contact angle (WCA) on the surface. $\gamma_{\text{WA}}$ means the interfacial tension between water and solid. $\gamma_{\text{WS}}$ and $\gamma_{\text{SA}}$ show the respective interfacial tensions of solid against air and water against air, which are usually called surface tensions. It is concluded when $\theta$ (WCA) is larger
than 90°, the value of \( \cos \theta \), also \( (\gamma_{SA} - \gamma_{WS})/\gamma_{WA} \), is less than 0, so a hydrophilic surface is determined. In contrast, hydrophobicity is defined with \( \theta > 90° \) and \( \cos \theta < 0 \). However, Young's equation is restricted to an absolutely smooth surface. In reality, WCA is strongly affected by micro- or nanoscale structures and chemical compositions on such surface. In followed, Jiang's group proposed that WCA of 65° was a limit to confirm hydrophobicity and hydrophilicity (Figure 2A).54-56 Superhydrophobicity (WCA > 150°) can be obtained via much rougher structures when surface WCA is larger than 65°. In the meantime, increased roughness can make a surface (WCA < 65°) more wettable and becomes superhydrophilic with a WCA < 10°.

### 3.2 Superhydrophobic wetting models

Through constructing special geometric structures and chemical composition treatments, superhydrophobic materials have attracted abroad interests. Among them, five typical models of superhydrophobicity, namely Wenzel state, Cassie state, Wenzel-Cassie transition state, “lotus” state and “gecko” state were demonstrated to study wetting characterizations. Meanwhile, surface free energy (SFEs) of the operated samples was discussed with wetting behaviors.

### 3.2.1 Wenzel state

Learning from rose petal, water drops are pinned with an adhesion force induced by the special wetting behavior, called Wenzel state.57 On the surface, water is occupied on rough structures (Figure 2B).

\[
\cos \theta_{O} = r \cos \theta_{I}
\]

\( \theta_{O} \) and \( \theta_{I} \) represent the WCA in respective apparent and original states. \( r \) means the roughness factor, determined by the ratio between the actual area of the rough surface and the projected surface area. It found that the values of \( \cos \theta_{O} \) and \( r \cos \theta_{I} \) are less than 1, further showing that \( r \) in Wenzel state should be controlled below than 1. However, the roughness factor \( r \) may be larger than 1 on a highly rough or porous substrate, where Wenzel model is not suitable for deep study.

### 3.2.2 Cassie state

Different from Wenzel state, water drops can easily roll on the Cassie stare surface,58 arising from air layer that fully filling the textured structures. This kind of superhydrophobicity (Figure 2C) is known as:
\[ \cos \theta_C = f_{SL} (r_f \cos \theta_I + 1) - 1 \] 

\( f_{SL} \) shows the fraction between the solid and liquid interface at the contacted area. \( r_f \) is the roughness ratio of the wet part to the solid surface when liquid contact rough surface. Herein, \( r_f \) is much lower than \( r \) in Wenzel state. So, wetting behaviors were influenced by both \( f_{SL} \) and \( r_f \).

### 3.2.3 Wenzel-Cassie state

There exists a transition state between Wenzel and Cassie models (Figure 2D),\(^{59}\) where water would not fully occupy the voids and air do not fully fill up the surface structures. Through the process of droplet press, impact, or vibration, Cassie to the Wenzel state will be varied in reality.

### 3.2.4 “Lotus” state

As a special model of Cassie state wetting, “lotus” state wetting inspired by lotus leaf is usually featured with much more complex structures (Figure 2E),\(^{60}\) namely micro- and nanoscale hierarchical structures, which still provides superhydrophobicity. So, in dirty ponds, contaminations on lotus surface can be removed by rolling-off water drops contributing to the strong water-repellency and self-cleaning.

### 3.2.5 “Gecko” state

Similar with water drop pinning on Wenzel-state superhydrophobic surface, “gecko” state superhydrophobic sample also show high adhesion for water drops (Figure 2F).\(^{61}\) In “gecko” state,\(^{106}\) there are two kinds of trapped air, one is the sealed air pockets trapped in the nanotubes, the other one is that air pockets are opened and linked to outside atmosphere. It is proved that the trapped air contributes to superhydrophobicity with a high CA and the negative pressure, produced by sealed air in the nanotubes, which generated the adhesive force for water. Therefore, the “gecko” state surface is featured with superhydrophobicity and high adhesion for water.

Besides the roughness, surface free energy (SFE) on a surface has an important effect on wetting behavior (Figure 2g).\(^{52-65}\) Setting the liquids with a range of surface tensions (STs) on certain samples in varied SFEs shows different wetting behaviors. It is known that STs and SFEs differ in physical quantities while they possess same values and dimensions. Water shows the ST with a value of about 72 mN/m, and here we determine the STs of a series of organic solvents with an average value of 28 mN/m.

According to ST and SFE analysis, the (super)hydrophobic as well as (super)oleophobic surfaces should be controlled at the relative low SFEs < 28 J/m\(^2\). The surface shows the (super)hydrophobicity and (super)oleophilicity when 28 J/m\(^2\) < SFE < 72 J/m\(^2\). As for (super)hydrophilicity, the substrate often manifests (super)oleophilicity in air since a largest SFEs > 72 J/m\(^2\) is achieved. Therefore, thorough regulating SFEs on the selected surface, the desirable wettabilities can be developed as well.

### 3.3 Special wetting models

#### 3.3.1 Superamphiphobicity

Through the studies of oil-repelled creatures from nature (ie, bacterial (Bacillus subtilis) biofilm colonies, pelli- cles, leafhoppers, springtails), superamphiphobic materials have been widely reported in recent years. Both nano- and microstructures are found on lotus-inspired and springtail-inspired surfaces with strong liquid repellency. But much lower surface free energy and more complex structures are required to achieve superamphiphobicity. During the preparation, multiscale structures,\(^{66-67}\) such as, overhangs, T-like structures (Figure 3A), mushroom-like structures, fibrous structures, and matchstick-like structures are of an essence. Meanwhile, the low surface chemicals should be chosen based on the substances containing fluorides with much low SFE.\(^{68-70}\) On this superamphiphobic surface, not only water drop but organic oils can be repelled as spherical shapes.

#### 3.3.2 Responsive wettability

Generally, a surface is sensitives to outer stimulus and responses with wetting changes,\(^{71-73}\) we often call this surface as smart responsive wettable material. Due to their significance in fundamental research and industrial practice, the wetting responsive surfaces has highly arisen increasing interest. To date, reversible wetting transitions between superhydrophilicity and superhydrophobicity on the functional surfaces have been widely reported (Figure 3B). And the external stimuli now can be concluded as pH, light irradiation, ion, temperature, electrical filed, solvent treatment, gas, and so on.\(^{74-76}\)

#### 3.3.3 Patterned wettability

Taken advantage of hydrophobicity-hydrophilicity patterned dorsal back, beetles living in Namib desert are able to harvest water from air. Thereby, water is captured on
FIGURE 3 Special wetting of superamphiphobicity, responsive wettability, patterned wettability, slippery. (A) On the T-like structural surface, both water and oil drops are repelled due to superamphiphobicity. (B) Superhydrophobicity and superhydrophilicity are switched upon the stimulus (pH, light, ion, etc.). (C) Water is captured on hydrophilic area and transported by hydrophobic area on patterned wettable beetle-inspired surface. (D) On slippery liquid-infused porous surfaces, water drop can easily slide away from the surface. Reprinted with permission.44 Copyright 2019, Elsevier

hydrophilic area and transported by hydrophobic regions due to the water-repellency.77-79 Often, it can be seen that water drops are also condensed on hydrophobic area (Drops 2-4). Then, thanks to the contrast wetting behaviors, water drops are transported to the hydrophilic domain by an imbalance force. At last, Drops 2-4 coalesce with Drop 1 previously adhered on hydrophilic area to become a larger drop, namely Drop 1+2+3+4. So, the “condensation,” “coalescence,” and “transportation” of water are conducted on beetles as well as their bioinspired surfaces (Figure 3C), which are followed by the “absorption” or “collection” process.

3.3.4 Slippery

The space among the microstructures was filled by rainwater on the slippery Nepenthes pitcher, then insects slide across peristome surface and then fell down to the interior of this plant. The slippery liquid-infused porous surfaces (SLIPS) are now prepared through the approach to lock lubricating liquid onto a micro/nanoporous substrate (Figure 3D). Three principles have been put forward to designing SLIPS.80-81 The first one is that the selected lubricating liquid must wick into, wet, and stably adhere to the substrate. In regard to the second one, the lubricating liquid should wet the solid surface to form a stable liquid layer. As for the third one, the lubricating liquid and tested solution should not be mixed and produce an immiscible state. The slippery surface shows superior repellency for water, organic solvents that are immiscible with lubricating liquid, paraffin, insects, polymers, and so on, also possessing the antifouling for easily-sliding behaviors.

4 BIOINSPIRED SUPERWETTING SURFACES FOR BIOSENSING

In recent years, detecting techniques, such as colorimetry, fluorescence, SERS, electrochemical, and visual assays (varied wetting states) are used in analytical chemistry.82-87 Herein, patterned wettable surfaces, superhydrophobic surfaces, responsive wettable surfaces, and slippery surfaces are combined respectively with various detecting techniques applied in the field of biosensing and are detailed below.

4.1 Patterned wettable surfaces for biosensing

Except for the well-known fog harvesting, the beetle-inspired patterned wettable surfaces have been also used for biosensing.88-91 The microdroplets can be well anchored on (super)hydrophilic points in small regions. At the same time, the concentration of the target solution was enriched, which is anticipated for high-throughput detection. Currently, (super)hydrophilic-(super)hydrophobic patterned materials have been the most popular candidates to cooperate with colorimetry, fluorescence, SERS, and electrochemistry for biosensing, which are detailed below.
4.1.1 | Colorimetric detection

As a facile, rapid and low-cost instrument, the concentrations of targeted colored analyte produce different color depth, which can be determined by colorimetry. Through the hydrophilic-hydrophobic pattern, the enhanced effect was integrated with molecularly imprinted polymer-photonic crystals (MIP-PC) colorimetric sensor by Hou et al to improve the sensitivity of detecting tetracycline. Just by the naked eye, colorimetric transition, larger than 200 nm, from cyan to red could be clearly observed depending on MIP-PC colorimetric sensor. Fukada et al developed the hydrophilic-superhydrophobic fabrics to detect caffeine. Based on dual extreme wetting substrate, that is, superhydrophilic-superhydrophobic microchips (Figure 4A), Wang and his team reported a biosensing platform to enable the detection of routine physiological markers toward microgravity applications. The superhydrophobic and superhydrophilic area showed the respective WCA of about 157.6° and 0° (Figure 4B,D), where water microdrops were repelled and adhered on (Figure 4C).
Through strong capillary force on superhydrophilic regions with regulated diameters, microdrops in changed volumes were hung on against gravity (Figure 4E,F). Moreover, this biosensing technology could detect calcium (Figure 4G), protein (Figure 4H), and glucose (Figure 4I).

4.1.2 Fluorescence

During a light absorption, initial electronic in a molecule is excited to induce an emission phenomenon, which is called fluorescence. When the excitation and emission are controlled in given wavelengths, biosensing detections can be achieved via the measurement of fluorescence intensity. In general, the fluorophore concentration that is in certain value would show a significant influence on fluorescence intensity with a proportional parameter. Huang et al prepared a multi-stopband photonic crystals (PC) microchip on a substrate with patterned hydrophilicity-hydrophobicity (Figure 5A-D), realizing a universal and high-performance multi-analyte discriminant testing method. The selective enhancement of fluorescence sensing in varied channels was operated on our microchip (Figure 5E,F). Remarkably, 12 of different metal ions (namely, Al$^{3+}$, Ca$^{2+}$, Cd$^{2+}$, Co$^{2+}$, Cr$^{3+}$, Cu$^{2+}$, Fe$^{2+}$, Hg$^{2+}$, Li$^+$, Mg$^{2+}$, Ni$^{2+}$, and Zn$^{2+}$) could be clearly recognized and analyzed just by our simple sensor (Figure 5G,H). The improvement of efficiency evaluation of discriminant analysis on the efficiency of PC microchip could be adjusted from five to only two PCs. Attributing to facile preparation and efficient sensing evaluation, the reported surface indicated huge significance to develop advanced discriminant analysis of complicated analytes in recent fluorescent sensing systems and assays. Advantaged by a novel aggregation-induced emission (AIE), another functional beetle-inspired microchip was introduced by our group, where the WCA of about 157.5° was on the superhydrophobic area and the WCA of nearly 0° was on the superhydrophilic site. The fluorescence of AIEgens was enhanced due to the combined effects of evaporation-induced enrichment on superhydrophilic microwells and aggregation-induced emission of AIEgens. Based on this functional surface, the detection of microRNA-141 could be achieved at an extreme low limit of 1 pM, which was also successful even in real samples. Wang’s group fabricated a series of superwettable microchips, possessing the abilities of detecting the biomolecules miRNA-141.
DNA, free prostate-specific antigen with respective detection limit of 88 pM, 2.3 × 10^{-16} M, 10 fg/mL.

4.1.3 Surface-enhanced Raman scattering

SERS is one of the most important techniques in studying the nano-structure surface of metals as it has high sensitivity and can obtain high-quality Raman signals. SERS is able to increase detecting rates via the enhanced Raman signal, even for detected substances in low concentrations. In recent years, SERS has been widely utilized in a variety of fields, including biomolecule imaging, molecule detection as well as environmental monitoring. Li and co-workers used the electrochemical deposition (Figure 6A) to synthesize SERS-active nanostructured Au microisland arrays (Figure 6B), which were deposited on previously prepared substrate with patterned superhydrophilicity-superhydrophobicity. Highly spiky and sharp edges and tips that resemble the areole structure were found on nanostructured Au microislands (Figure 6C), denoted as Au-areoles arrays, which contained plenty of active hot spots to produce strong electromagnetic field and further to ensure great Raman amplification. The superhydrophobic substrate shows strong water repellency and superhydrophilic areas exhibit favorable adhesion for liquid solution (Figure 6D), then the concentrations of target molecules were enhanced on the superhydrophilic Au-areoles pattern. With the
bioinspired surface, detections of adenine, dopamine (DA), glucose, and DA and methyl blue (MB) with high sensitivity and mutually independent multi-sample were realized even without interference (Figure 6E,F). By self-assembly and photocatalytic lithography,111 Lai et al fabricated superhydrophilic/superhydrophobic patterns with erasable and rewritable properties on a TiO2 nanotube array (TNA) sample, whereby the site-selective cell immobilization and reversible protein absorption were conducted on 2D scaffold TNA surface. Meanwhile, 3D functional patterns (calcium phosphate, silver nanoparticles, drugs, and biomolecules) with highly sensitive manners were obtained based on such wettable template, demonstrating SERS as well as antibacterial performance. What is more, miRNA-14112 and H2O2113 were detected by these patterned wetting surfaces through SERS.

4.1.4 | Electrochemical sensing

Through qualitatively and quantitatively measuring the current and/or potential originated from an electrochemical cell within the analytes, electrochemical analysis is a typical technique in biosensing because of the diverse advantages of high sensitivity, easy fabrication, low cost, and quick response.114-116 An electrochemical droplet microarray (Figure 7A,B) with high-density individually addressable feature was developed by Zhangetal,117 which was occupied by a layer of permeable porous hydrophobic-hydrophilic patterned polymethacrylate (Figure 7C,D). Here, redox-active molecules were on hydrophilic pattern and neighboring cells were spatially and effectively separated by water-repelled area, demonstrating electrochemical sensing of 1,4-benzoquinone (Figure 7E,F) and H2O2 (Figure 7G,H) within single droplets. In order to enhance the sensitivity and detection limit in an electrical label-free detection, Kim et al reported a biosensor with controlled wettable behaviors.118 A passivation layer, containing CYTOPTM, served as hydrophobic outer surface, and the inner ones were sensing regions with hydrophilicities. It found that the interactions of biomolecules between analytes and receptors were enhanced on the hydrophilic area, which were suppressed by outer non-wetting one. When the concentration of analyte was increased, the improvements both for sensitivity and limit of detection were obtained. In the meantime, the effect of detection
of cardiac troponin I was investigated upon different proportions between hydrophobicity and hydrophilicity. Patterened superhydrophobicity-superhydrophilicity integrated with a nanodendritic electrochemical biosensor was prepared by Xu et al., which could sensitively and selectively detect the prostate cancer biomarkers, such as miRNA-375, miRNA-141, and prostate-specific antigen.

4.2 | (Super)hydrophobic surfaces for biosensing

Superhydrophobic interfaces have been applied in multiple fields. What is more, these non-wetting materials can be also utilized in biosensing. Similar with beetle-inspired materials applied in biosensing, spherical shapes, and small contact lines of target solution are also observed on the superhydrophobic surface. However, the contact lines from the above two surfaces differ in wettabilities. The former is generated by the (super)hydrophilic domains, where the lengths of contact lines are firmly determined by the diameters of (super)hydrophilic domains. The latter is induced by the air-liquid-solid three-phase contact line due to super water-repellency. A spherical shape is observed when the aqueous solution drop containing analyte is set on superhydrophobic surface. Meanwhile, the relative small contact line between the drop and solid contributes to a highly concentrated domain and enhanced concentration after solvent evaporation. Therefore, detecting analytes even in trace amounts can be realized by this hydrophobic concentrating effect.

Compared with the passivation layer with hydrophilicity, the hydrophobic one shows an extreme enhancement for sensitivity of the biosensor. Choi’s group prepared an electrical biosensor with hydrophobic passivation by the revamped metal oxide semiconductor field-effect transistor that included a designed underlap area between drain and gate. This biosensor manifested the detection limit of up to 100-fold than that from hydrophilic passivation one. It is known that the natural rose petals show the advantageous features of the eco-friendly, low cost, and highly hydrophobic. Chen and co-workers use these rose petals to detail an interesting platform for ultrasensitive SERS, where the lower epidermis served as a bio-template. To address the shortcomings of highly diluted, small volume samples in detection test, Ling’s group constructed strong surface plasmon and chemical functionalization to obtain a superhydrophobic SERS platform, which could be applied in the trace detection just with 1 μL of sample volume. In 2011, Fabrizio’s group conducted a breakthrough work, they reported superhydrophobic delivery of molecules to plasmonic nanofocusing SERS structures. Once the sensor was in a nanoscale length (Figure 8A,B), the limit dictated by diffusion could be overcome (Figure 8C), arising from the combining effects of superhydrophobic samples and nanoplasmonics. It was seen that the drop containing extremely diluted solution on such non-wetting surface, keeping its quasi-spherical shape with the extending evaporation (Figure 8D,E). Taken advantage of this, operations of detecting few molecules were still achieved in highly diluted and a few nanoliters and microliters of initial targeted solution (Figure 8F,G).

A surface is superhydrophobic in air, also possessing the superareophilic property, so aqueous drops are repelled as spherical shapes on the sample due to the sufficient and constant air cushion occupied on the textured structures. The above works reported superhydrophobic sensor by virtue of the small contact line because of the feature of strong water-repellency. Different from these, Feng’s group synthesized a series of sensing devices based on the solid/liquid/air triphase interfaces although superhydrophobicity was still used. In one of their works, they prepared a perfect electrode system that contained superhydrophobicity-mediated air-liquid-solid joint interfaces (Figure 9A-C). Air was trapped in rough structures, then O2 could be transported from the outside environment at a rapid and continuous rate, ensuring a stable concentration of interfacial oxygen. The enzymatic product H2O2 was tested by cathodic measurement on the reported sensing assay (Figure 9D-F), also, a model analyte of glucose was detected with surprisingly high selectivity (≈2% signal modulation attributing to common biologic interferents), sensitivity (18.56 μA cm−2 mM−1), and a dynamic linear range up to 80 × 10−3 M. At the triphase interface, H2O2 reduction reaction was conducted on reliable sensing platform to highly detect glucose (Figure 9G), indicating wide interest in the fields of clinical diagnosis, medical research, environmental analysis, and so on.

4.3 | Responsive wettable surfaces for biosensing

Different from the traditional detecting techniques, as mentioned above, that is, colorimetry, fluorescence, SERS, electrochemistry, a new kind of approach called visual assay has been also developed in biosensing. The visual assay is mainly based on the variations of wetting behaviors on the selected superwettable substrates. Upon the
outer stimulus, a responsive surface with varied wetting can be accomplished. The changes of wetting behaviors, such as WCAs, rolling-off angles, before and after stimulus response can be easily served as detecting signal.\textsuperscript{134-135}

In 2016, an electrochemical chiral sensing route was established by Shi's group with the aid of screen-printed carbon electrodes, which depended on the stimuli-responsive copolymer/graphene hybrid.\textsuperscript{136} They showed high sensitivity and selectivity for monosaccharides. Subsequently, in 2017, their group reported another electrochemical biosensor based on a novel stimuli-responsive copolymer,\textsuperscript{137} which was applied for selectively and sensitively detecting sialic acid (SA) in mouse brain. Our group reported an effective point-of-care testing (POCT) device based on pH-responsive superwettable surfaces (Figure 10A),\textsuperscript{138} which were prepared by modifying silica nanoparticles with the organosilanes (3-[2-(2-amino ethylamino) ethylamino] propyl trimethoxy silane (AEPTMS) and octyl trimethoxy silane (OTMS)). Because of the switch between superhydrophobicity and superhydrophilicity, pH, urea, and glucose were specifically detected just by naked-eye. From the glucose oxidase-catalyzed reaction, pH of such solution was decreased by the produced gluconic acid. So, upon the growing concentration of glucose, the value of water CA was decreased (Figure 10B). What is more, we realized the non-invasive diagnoses of diabetes in urine and saliva on such surfaces simply by visible water CA variations (Figure 10C).

As light-responsive materials, TiO\textsubscript{2} nanoparticles (NPs) have been widely reported with reversible switching wetting behaviors.\textsuperscript{139-141} Our group prepared a superamphiphobic surface by the coating (Figure 11A) of dual-sized...
FIGURE 9 (A) Model of triphase enzyme electrode in an analyte solution was showed, whereby the reaction of glucose and H₂O₂ are exhibited. (B) SEM image to the carbon fiber electrode and the insert is the WCA of 153±2° on such surface. (C) After sequential immobilization of H₂O₂ electrocatalyst platinum and glucose oxidase, environmental SEM image of the electrode is shown. (D) For triphase electrode and normal electrode both at -0.1 V, the glucose concentration against background-subtracted current derived from the cyclic voltammograms (CVs) is shown. The inset is the enlarged view when the concentration is 0. (E) At 5 s, relation between glucose concentration and the background-subtracted current is shown with a linear detection upper limit of about 60 × 10⁻³ M. (F) In undiluted bovine serum (−0.1 V potential), the concentration of glucose was increased to 84.6 × 10⁻³ M when responded to triphase electrode chronoamperometric. (G) Interference effect for the detection of analytes on electrode response, whereby glucose was highly detected. Reprinted with permission. Copyright 2017, Wiley-VCH

TiO₂ NPs (21 nm, 60 ~ 200 nm) and perfluoroocetyltriethoxysilane (PFOTS), showing strong repellency for water, glycerol, olive oil, hexadecane with all of contact angles larger than 150° (Figure 11B). Under UV illumination (λ = 365 nm), a mask was used to remove away from such surface, thus leading to a gradient surface energy due to the PFOTS decomposed by TiO₂ NPs. When ethanol droplets with varied concentrations rolled away from our surface energy gradient surface, they showed different droplet-sorting performances for the movement distances in an incline angle. Thereby, attributing to the ATP-dependent rolling-circle amplification (RCA) and droplet-sorting property (Figure 11C), biosensing for ATP detection was also observed on our surface (Figure 11D).

4.4 Silppery surfaces for biosensing

Pitcher-inspired surfaces are famous for their anti-fouling and slippery. When applied in biosensing, the sliding behavior can be treated as an output signal to detect biomolecules. Our group fabricated an oil-swollen organogel material, possessing controllable sliding speed and critical sliding angle (CSA) of a droplet that contained varied DNA chain length. As for short-stranded DNA (ss DNA), it could be treated as a hydro trope to interact with selected organic solvent molecules, meanwhile, thickness and adhesion force of such interface were increased and then a droplet within ss DNA was firmly adhered on the reported surface (Figure 12A). In contrast, the drop containing long ssDNA that generated by ATP in an RCA reaction could easily slide away (Figure 12A), resulting from the nucleobase exposure decrease and low interfacial adhesion. micro RNA-21 (miR-21), as a primer probe, was also able to initiate RCA reaction. In absence of miR-21, no long ssDNA was produced in RCA drop, where drop was adhered (Figure 12B). But, the generated long ssDNA in RCA drop with miR-21 lead to an easily-sliding behavior (Figure 12C). What is more, the detection for protein (thrombin) was established on our surface thanks to a DNA-catalyzed strand displacement reaction combined with an RCA reaction.
FIGURE 10  (A) Working principle of the switching of the pH-responsive superwetting surface properties is shown, where a CA of water droplet decreased to $\sim 0^\circ$ at pH 1 and increased to $161.4^\circ \pm 6.2^\circ$ at pH 13. (B) Wetting states of droplets with different concentrations of glucose within the linear range. (C) Corresponding to hydrophobicity, and those from patients with diabetes decreased to nearly $50^\circ$, indicating the hydrophilicity of the surface. (D) Non-invasive detection of saliva and urine obtained from nine patients with diabetes and six normal people illustrating that the CA can be employed to distinguish between samples of people with diabetes and normal people. Reproduced with permission.138 Copyright 2018, Nature Publishing Group

FIGURE 11  (A) SEM image of TiO2 NPs. (B) Water, glycerol, olive oil, hexadecane drops were on the superamphiphobic surface with contact angles larger than $150^\circ$. (C) Mechanism of RCA. (D) In varied concentrations of ATP, the drops adhered on different positions along the surface energy gradient surface. (E) After RCA, liquid droplets that contain $250 \mu$M of AMP, GTP, UTP, CTP, and ATP were stuck on different positions on such surface, and specific ATP detection was achieved since ATP drop was hanging at the highest point. Reprinted with permission.142 Copyright 2018, Springer
The traditional biosensing usually required large volume of analyte, moreover, the analyte is extremely expensive or difficult to be obtained in some cases. Once for the ultralow concentrations of targeted substances, the detections become a challenge task. In the field of biosensing, the bioinspired superwetting materials are applied with several advantages (Table 1). On patterned wetting and superhydrophobic surfaces, the small contact lines between analytes and surfaces contribute to enhanced concentrations, sometimes as well as signal output amplification. At the same time, these surfaces often achieve anchoring ability for extremely low usages of analyte solutions with high sensitivities. Visual assays based on responsive wetting and slippery materials show the direct and rapid detections just by naked eyes, indicating convenient and simple platforms for biosensing.

5 | CONCLUSION

In summary, from the inspirations of natural creatures, the recent progresses of biomimetic superwettable materials applied in biosensing applications were presented. We described the special wettings of the lotus leaf, rose petal, springtail, desert beetles and pitcher plant, then showed the wetting models of superhydrophobicity, superamphiphobicity, responsive wetting, patterned wetting, slippery. Based on the detecting technologies (ie, colorimetry, fluorescence, SERS, electrochemical), bioinspired superwetting surfaces utilized in the application of biosensing were highlighted.

As a new type of application, superwetting materials for biosensing have emerged in large numbers. Although so, there are still some sever problems to be solved in regard to this application. Surface textured structures and chemical compositions are decisive for wetting properties. However, surface structures are easy to be destroyed and compositions are sensitively changed, leading to mechanical weakness and chemical corrosion. So, the unstable wettable surfaces cannot be well performed for a long time, let alone for continuous and effective sensing. At the same time, the preparation of these bioinspired superwettable materials usually required complex fabrications and high cost. For example, beetle-inspired surfaces should be constructed within both (super)hydrophobic and (super)hydrophilic patterns, extremely expensive fluorides with low surface energies are often used for superamphiphobicity, pitcher-inspired surfaces need roughness construction and unstable lubricate oils. Selectivity and sensitivity are highly demanded in analytical chemistry. But, as for biosensing with bioinspired superwettable surfaces, high sensitivity is often emphasized on, completely neglecting the selectivity.
**TABLE 1**  Fabrications, wettings, detecting techniques and analytes related to biosensing reported in this review were showed as below

| Material                          | Fabrication                           | Wetting                        | Detecting technique | Analyte                           | Reference |
|----------------------------------|---------------------------------------|--------------------------------|---------------------|-----------------------------------|-----------|
| Glass/PDMS/photonic-crystal      | Inkjet printing                       | Hydrophilic-hydrophobic       | Colorimetric        | TC                                | 95        |
| PET film                         | Dip coating                           | Hydrophilic-superhydrophobic  | Colorimetric        | Anhydrous caffeine                | 96        |
| Glass/nano silica                | CVD/ UV etching                       | Superhydrophilic-superhydrophobic | Colorimetric        | Glucose, calcium, protein         | 97        |
| Glass/PDMS/photonic-crystal      | Solvent evaporation                   | Hydrophilic-hydrophobic       | Fluorescence        | mRNA                              | 98        |
| ITO/photonic-crystal             | UV etching                            | Hydrophilic-hydrophobic       | Fluorescence        | Al$^{3+}$, Ca$^{2+}$, Cd$^{2+}$, Co$^{2+}$, Cr$^{3+}$, Cu$^{2+}$, Fe$^{2+}$, Hg$^{2+}$, Li$^+$, Mg$^{2+}$, Ni$^{2+}$, Zn$^{2+}$ | 101       |
| Glass slide/candle soot/nano silica | CVD/ UV etching                       | Superhydrophilic-superhydrophobic | Fluorescence        | miRNA-141                        | 102       |
| FTO/TiO$_2$ nanowires            | Hydrothermal/ UV etching              | Superhydrophilic-superhydrophobic | Fluorescence        | miRNA-141                        | 103       |
| Glass slide/nano silica          | CVD/ UV etching                       | Superhydrophilic-superhydrophobic | Fluorescence        | mRNA                              | 104       |
| Glass slide/candle soot/nano silica | CVD/ UV etching                       | Superhydrophilic-superhydrophobic | Fluorescence        | DNA                               | 105       |
| Silicon plate/AgNO$_3$/nano-Au   | CVD/ UV etching/Electrochemical deposition | Superhydrophilic-superhydrophobic | SERS                | Adenine, DA, glucose              | 106       |
| TNA                              | Electrochemically anodization         | Superhydrophilic-superhydrophobic | SERS                | Cell, protein                     | 107       |
| ITO/Ti/Au/ nano-Au               | CVD/Electrochemical deposition        | Superhydrophilic-superhydrophobic | SERS                | miRNA                             | 108       |
| Cu sheet/ nano-Au                | Chemical etching                      | Hydrophilic-superhydrophobic  | SERS                | H$_2$O$_2$                        | 109       |
| Silicon substrate/Au/SU-8 photoresist/HEMA-EDMA | UV Photolithography/ PVD | Hydrophilic-hydrophobic     | Electrochemical     | H$_2$O$_2$, 1,4-benzoquinone,     | 110       |
| FET /CYTOPTM                     | Photolithography / etching            | Hydrophilic-hydrophobic       | Electrochemical     | Cardiac troponin I                | 111       |
| ITO/Ti/Au/ nano-Au               | CVD/Electrochemical deposition        | Superhydrophilic-superhydrophobic | Electrochemical     | miRNA-141, miRNA-375              | 112       |
| Underlap FET/photoresist/SiO$_2$/Si$_x$N$_y$/CYTOPTM | LPCVD /HF etching                | Hydrophilic-hydrophobic     | Electrochemical     | anti-AI                           | 113       |
| Silicon wafers/Si1813/nano-Ag    | HF etching/ electroless deposition    | Superhydrophobic              | SERS                | Rhodamine, lambda DNA, lysozyme   | 114       |
| Rose petals/nano-Ag              | Physical deposition                   | Hydrophobic                   | SERS                | Rhodamine 6G                      | 115       |
| Silicon plate/Ag nanocubes       | thermal evaporator deposition         | Superhydrophobic              | SERS                | Rhodamine 6G                      | 116       |
| Microporous carbon fiber mesh/Pt | PTFE-treated                          | Superhydrophobic              | Electrochemical     | Glucose                           | 117       |
| SPCE/G-copolymer                 | Physical deposition                   | Hydrophilic to hydrophobic    | Electrochemical     | D-glucose, L-glucose              | 118       |

(Continues)
**TABLE 1** (Continued)

| Material                  | Fabrication                  | Wetting                     | Detecting technique | Analyte      | Reference |
|---------------------------|------------------------------|-----------------------------|---------------------|--------------|-----------|
| SPCE/nano-Au/ PNI-PBA-TP  | Electrochemically deposited/dip coating | Hydrophilic to hydrophobic | Electrochemical     | Sialic acid | 137       |
| Glass/pH-SiNPs            | Self-assembly process        | Superhydrophilic to superhydrophobic | Visual             | Urea, glucose | 138       |
| Glass/PTES/titanium (IV)/P25 | Spray-coating             | Superhydrophilic to superhydrophobic | Visual             | ATP, DNA    | 142       |
| Glass/PDMS/organic solvents | Spin-coating/immersed in organic alkane | Slippery                    | Visual             | ATP, miRNA, thrombin | 144       |

Abbreviations: PDMS, polydimethylsiloxane; CVD, Chemical vapor deposition; TC, tetracycline; PET, polyethylene terephthalate; MIP, molecularly imprinted polymer; PC, photonic crystals; OTS, octadecyltrichlorosilane; UV, ultraviolet; ITO, indium tin oxide; fPSA, free prostate specific antigen; FTO, fluorine-doped tin oxide; TNA, TiO2 nanotube array; PTES, 1H, 1H, 2H, 2H-perfluoroctyltriethoxysilane; DA, dopamine; FET, field-effect transistor; HEMA-EDMA, porous poly(2-hydroxyethyl methacrylate)-co-(ethylene dimethacrylate)polymeric film; PVD, physical vapor deposition; LPCVD, Low pressure chemical vapor deposition; Anti-AI, specific antibody; PTFE, polytetrafluoroethylene; SPCE, screen-printed carbon electrodes; pH-SiNPs, pH-responsive silica nanoparticles.

**SCHEME 1** Bioinspired superwetting materials for biosensing. Through surface roughness and chemical constructions, a number of superwetting surfaces (superhydrophobicity, patterned wettability, responsive wettability, slipperiness) are fabricated and applied in the emerging applications of biosensing. Reproduced with permission.125 Copyright 2011, Nature Publishing Group. Reprinted with permission.105 Copyright 2015, Wiley-VCH. Reproduced with permission.138 Copyright 2018, Nature Publishing Group. Reprinted with permission.144 Copyright 2018, Elsevier

during the application. Therefore, the specific recognition should be paid more attention on in future researches. Because of the lack of high-throughput and multifunctional abilities, the superwetting surface is limited to one target detection in biosensing now. And, just one signal output cannot prove the detection correction. So, in order to accomplish various recognitions of targeted analytes and diversified signal readouts, multimode and multifunctional sensing applications are advocated. Although there are still many difficulties to be solved for the bioinspired superwetting surfaces in the field of biosensing, we believe that their commercial productions will eventually be realized by the persistent attention and efforts of scientists.

**CONFLICT OF INTEREST**

The authors declare no conflict of interest.

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