Integrally formed asymmetric hydrogel for biomaterials and bioelectronic interfaces

Haowen Lin,[1] Shuhuai Pang,[1] Jiahao Wu,[1] Chunbao Li,[2,3,*] and Fengyu Li[1,*]

[1]College of Chemistry and Materials Science, Su Bingtian Center for Speed Research and Training, Jinan University, Guangzhou 510075, China

[2]Department of Orthopedics, the Fourth medical center, Chinese PLA General Hospital, Beijing 100853, China

[3]Department of Cardiovascular Surgery, Chinese PLA General Hospital, Beijing 100853, China

*Correspondence: lifengyu@jnu.edu.cn (F.L.); cli301@foxmail.com (C.L.)

Received: August 12, 2025; Accepted: March 12, 2026; Published Online: March 13, 2026; https://doi.org/10.59717/j.xinn-mater.2026.100222

Citation: Lin H., Pang S., Wu J., et al. (2026). Integrally formed asymmetric hydrogel for biomaterials and bioelectronic interfaces. *The Innovation Materials* **4**:100222.

Hydrogels are widely used in biomedicine due to their excellent flexibility, adhesion, and biocompatibility. However, there are some bottlenecks in their structural design and functional application. The Janus structure, inspired by the ancient Roman double-sided protector, provides a different idea for material design in complex biomedical scenarios due to its unique "asymmetric" characteristics, which has been widely used in the field of biomaterials. The asymmetric Janus hydrogel breaks the limitation of the traditional hydrogel "isotropic". The two sides of asymmetric hydrogels have different physical, chemical, or biological properties, showing the characteristics of asymmetric properties. Among them, the two asymmetric properties represented by "adhesion-antiadhesion" and "hydrophobicity/hydrophilicity" have been widely studied. In this paper, the structural characteristics and preparation techniques of different types of asymmetric hydrogels are discussed, and the possible future development of Janus hydrogels is also proposed.

INTRODUCTION

As a kind of three-dimensional network soft material formed by physical or chemical cross-linking of hydrophilic polymer chains, hydrogels have shown irreplaceable application value in biomedical fields due to their unique high-water content, excellent biocompatibility, good flexibility, and interfacial adhesion, such as wound dressings, drug carriers, tissue engineering scaffolds, and biosensors.[1] However, the single structure and performance of traditional homogeneous or isotropic hydrogels face many limitations in the practical application of complex in vivo environments, and it is difficult to meet the multi-functional requirements in multiple scenarios. In the scenario of tissue wound repair after clinical surgery, the ideal hydrogel dressing should achieve the dual functions of "precise adhesion" and "selective anti-adhesion" at the same time. On the one hand, it should adhere closely to the surface of the damaged tissue to provide a stable microenvironment for cell proliferation and tissue regeneration, and prevent repair failure caused by dressing migration. On the other hand, excessive adhesion with surrounding healthy tissues should be avoided to reduce secondary damage to new tissues during dressing change and reduce the risk of inflammatory response. However, traditional homogeneous hydrogels either have poor fixation effect due to insufficient adhesion, or adhesion of surrounding tissues due to high adhesion, which cannot balance this core contradiction. In addition, in the application of electrophysiological signal monitoring in wet environment in vivo, as an interface material between electrodes and tissues, hydrogels need to form close contact with the wet tissue surface through hydrophilic water to ensure efficient transmission of electrical signals. In addition, it is necessary to block the excessive penetration of body fluids by hydrophobic surface to avoid structural damage of the gel network due to water absorption and swelling, thereby affecting the stability and accuracy of signal monitoring. These complex requirements highlight the performance limitations of traditional homogeneous hydrogels and promote the development of asymmetric hydrogels. The structural strategy of Janus provides a rich solution for expanding the application scenarios of hydrogels. The term "Janus" is derived from the two-sided god of Roman mythology.[2] In the field of materials, it refers specifically to materials with "bilateral heterogeneity" two surfaces or regions of which have significant differences in chemical composition, microstructure, physicochemical properties (such as hydrophilicity, hydrophobicity, adhesion, electrical conductivity, mechanical properties, etc.), or even completely opposite properties. Examples include one side being hydrophilic and one side being hydrophobic, or one side being highly adherent and one side being antiadhesion. This asymmetric structure enables the material to integrate multiple opposing functions in the same system, thus adapting to the multifunctional requirements in complex environments. Janus hydrogels have the advantages of asymmetric structure and biocompatibility and hydrophilicity of hydrogels, which are more suitable for wet environment application scenarios in the biomedical field (such as in vivo wound repair and in vivo sensing). Therefore, Janus hydrogels have become the focus of current research. The preparation methods of Janus hydrogels mainly include "one-pot" synthesis, unilateral modification, and assembly of two different types of hydrogels. "One-pot" is the most common preparation method of Janus hydrogels, and its principle is mainly under the induction of external forces or external stimuli (such as stirring, centrifugation, gravity, or mold induction). Janus hydrogels were prepared by polymerization and cross-linking of the hydrogel precursors with asymmetric distribution of functional groups or particles. In this review, we summarize two kinds of Janus hydrogels with adhesion-anti-adhesion and hydrophilic/hydrophobic properties by "one-pot" method, as well as their preparation techniques and structural characteristics, and look forward to the potential applications of Janus hydrogels in the future.

STRATEGIES FOR THE PREPARATION OF JANUS HYDROGELS

Adhesive/anti-adhesive hydrogel is a kind of hydrogel with spatially asymmetric interface structure. One side of the hydrogel can form stable adhesion to target substrates (such as skin, tissue, metal, etc.), and the other side shows low adhesion to avoid excessive adhesion to non-target surfaces. The principle of hydrogel preparation is to modulate the chemical composition, microstructure, or surface energy of the two sides of the hydrogel by region-selective regulation. At present, the common preparation methods include unilateral surface chemical modification,[3] layered assembly,[4] and temperature response.[5] Liu et al. proposed a new preparation method of adhesive/anti-adhesive hydrogel.[6] The interface distribution of free -COOH on both sides of the hydrogel was controlled by the strategy of centrifugation and agitation (as shown in Figure 1A), and adhesive/anti-adhesive hydrogel with adhesion difference up to 20 times was synthesized. They used acrylic acid (AA), dodecyl methacrylate (LMA), cetyltrimethylammonium bromide (CTAB), and [2- (methacryloxy) ethyl] dimethyl - (3-sulfopropyl) ammonium hydroxide (DMAPS) as precursors of hydrogels, which were prepared at a relatively low stirring speed of 600 RPM. Produce emulsion droplets composed of hydrophobic monomers (LMA) and surfactants (CTAB) and tend to occupy the top surface of the hydrogel, which effectively blocks the exposure of -COOH on the top surface, the lower distribution of emulsion droplets inside the hydrogel and on the bottom surface induces the exposure of abundant -COOH groups on the bottom surface, Free -COOH exposed to the bottom surface of hydrogels has been shown to strongly bind to tissues through amide reactions or electrostatic interactions, showing firm adhesion to tissues, and differences in distribution of -COOH lead to differences in adhesion to tissues as well. The study highlights that stirring speed plays a key role in determining the size of these emulsion droplets, with slower stirring speeds leading to larger droplets, thus amplifying the structural and functional differences between the top and bottom layers of the hydrogel.

Hydrophobic/hydrophilic hydrogels are a class of smart soft materials that introduce hydrophobic groups and hydrophilic groups/domains in the same

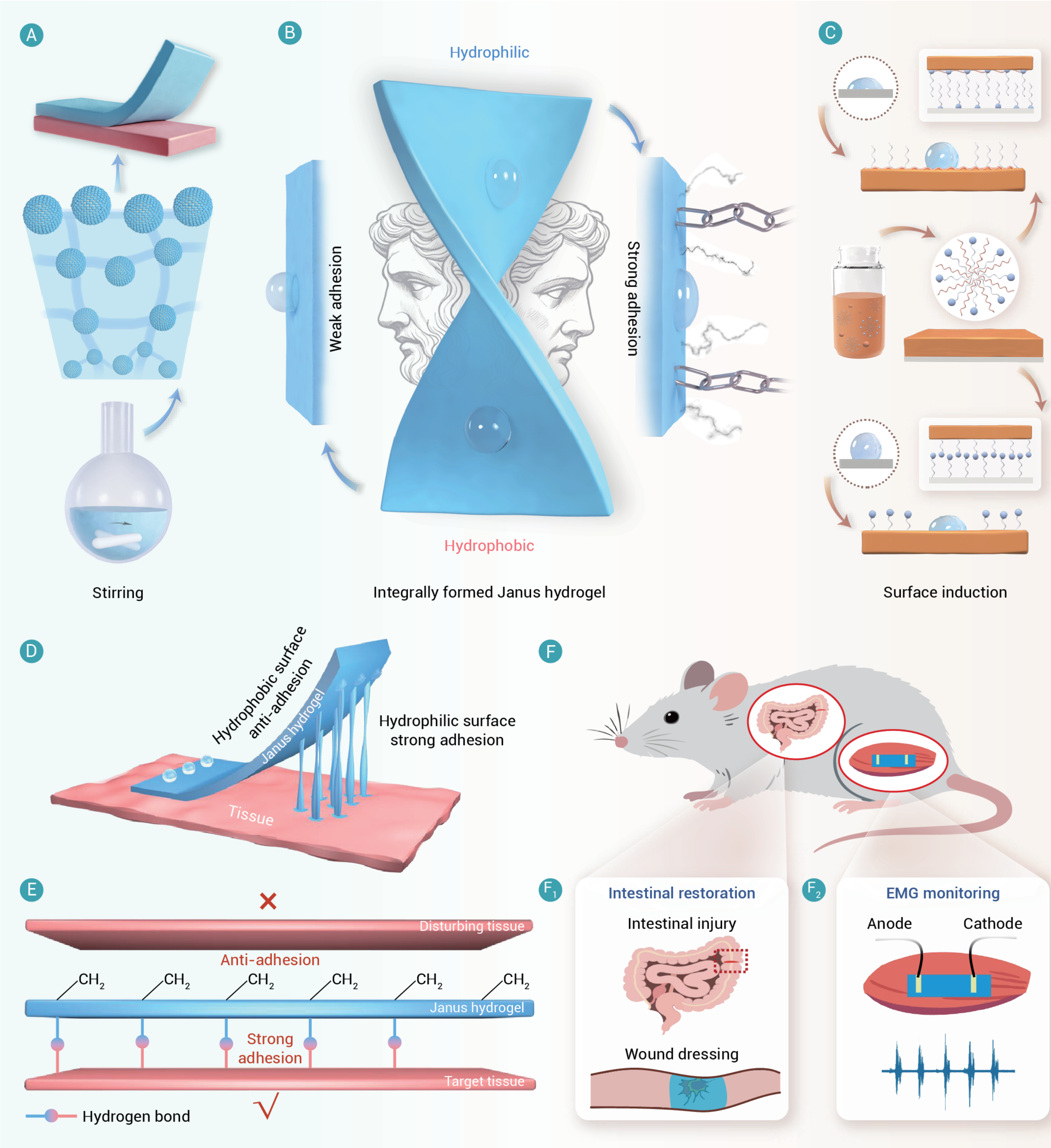

Figure 1. The schematic illustration of heterogeneous properties of the Janus hydrogel and application of Janus hydrogel (A) The aggregation of emulsion droplets is controlled by stirring. (B) The integrally formed Janus hydrogel with asymmetric adhesion and wettability. (C) The surface induction for the optional hydrogel surface.[10] Copyright 2024, Wiley. (D) The schematic illustration for Janus hydrogel bioadhesive. (E) Schematic diagram of selective adhesion of Janus hydrogel. (F) Janus hydrogel as a wound dressing F_1) and J Janus hydrogels were used as bioelectronic interfaces for Electromyography (EMG) monitoring F_2).

gel network by special design. It not only retains the core characteristics of traditional hydrogels "high water content, biocompatibility, and three-dimensional cross-linking network", but also obtains unique properties that traditional hydrogels do not have through the coordination and regulation of Hydrophobic/hydrophilic interactions. The nature of Hydrophobic/hydrophilic hydrogels is a "heterogeneous but stable" cross-linking network, which combines hydrophobic chain segments (or groups) and hydrophilic chain segments (or groups) in the same gel skeleton by chemical or physical means (as shown in Figure 1B). Current common preparation strategies include unilateral silanization,[7] multilayer assembly,[8] and electrical modulation.[9] Li et al. proposed a surface induction strategy to synthesize monolithic hydrophilic and hydrophobic hydrogels in one step based on the mechanism of hydrophobic surface induction in aqueous environment.[10] A novel mechanism for invasive inversion regulation is proposed by regulating the hydrophobic surface on the hydrophilic mold and the hydrophilic surface on the hydrophobic mold (Figure 1C). The asymmetric gel was easily obtained in a glass mold, and the difference in adhesive properties between the top and bottom surfaces of the gel was 2 times. In this micelle copolymerization system, iron ions with high ionic strength can promote the surfactant-hydrophobic micelle reorganization. During rapid gelation, the hydrophobic interaction between surfactants and different infiltration patterns leads to the differential distribution of hydrophilic and hydrophobic monomers on the surface. Flexible hydrophilic and hydrophobic mouldings can be used to modulate the top surfaces of the gels simultaneously, enabling selective design and patterning of the gels. Interestingly, benefiting from the reversible wetability induction of the surface, this Hydrophobic/hydrophilic hydrogel exhibits asymmetric adhesion, hydrophobic surfaces exhibit a relatively sparse distribution of hydrophilic functional groups. In contrast, hydrophilic surfaces are densely populated with hydrophilic groups such as hydroxyl groups, carboxyl groups, and quaternary ammonium cations. These hydrophilic groups can establish various intermolecular interactions with the functional groups on the surface of biological tissues. The disparity in the distribution of hydrophilic groups results in a two-fold difference in adhesion between the two sides of the Hydrophobic/hydrophilic hydrogel.

SUMMARY AND PROSPECT

In general, Liu et al. prepared adhesive/anti-adhesive hydrogel by controlling the distribution of the free-COOH interface on both sides of the hydrogel by stirring and centrifugation strategy. Li et al. used the surface-induced strategy to adjust the distribution of hydrophilic and hydrophobic monomers on the surface of the hydrogel by using the hydrophobic interaction between the hydrogel and different models, thus preparing the Hydrophobic/hydrophilic hydrogel. At the same time, thanks to the difference in the distribution of surface functional groups, they also exhibit adhesion-anti-adhesion properties. These two preparation methods provide new ideas for the preparation of Janus hydrogels by regulating the chemical composition distribution inside the hydrogel through different strategies.

Adhesion-anti-adhesion hydrogels and Hydrophobic/hydrophilic hydrogels have a wide range of applications in the field of biomedical materials. For example, in the in vivo wound dressing scenario, the adhesive surface of the adhesion/anti-adhesive hydrogel can adhere firmly to the gastric wound, thereby eliminating the need for tedious suture steps, while the antiadhesive surface can minimize damage to normal tissues and avoid excessive adhesion (Figures 1D-E & F_1). This novel strategy has shown great potential in the application of internal injury repair. In vivo monitoring of bioelectrophysiological signals (such as muscle electrophysiological signals), Janus hydrogel can be used as a coupling interface for acquisition. In addition to providing asymmetric adhesion properties, the hydrophobic surface can also prevent excessive tissue fluid from entering the hydrogel and avoid excessive swelling of the hydrogel. It ensures the fidelity of the collected electrophysiological signals and shows great potential in electrophysiological signal monitoring in vivo. (Figure 1F_2).

REFERENCES

1. Hou L., Liu X., Ge X., et al. (2023). Designing of anisotropic gradient surfaces for directional liquid transport: Fundamentals, construction, and applications. *The Innovation* 4:100508. DOI:10.1016/j.xinn.2023.100508
2. Zhuo S., Deng Z., Wu Z., et al. (2024). Janus gels for biomedical applications: Progress and future prospective. *Progr. Polym. Sci.* 155:101856. DOI:10.1016/j.progpolymsci.2024.101856
3. Chen S., Zheng Y., Fang Y., et al. (2024). Unilateral antibacterial Janus hydrogel hemostatic dressing prepared by the dragging effect of a brush. *Colloid. Surface. B* 247:114453. DOI:10.1016/j.colsurfb.2024.114453
4. Zhang X., Chen G., Wang Y., et al. (2024). Spatial tumor biopsy with fluorescence PCR microneedle array. *The Innovation* 5:100538. DOI:10.1016/j.xinn.2023.100538
5. Tristan Hessberger, Lukas B. Braun, Rudolf Zentel, et al. (2018). Interfacial self-assembly of amphiphilic dual temperature responsive actuating Janus particles *Adv. Funct. Mater.* 28:201800629. DOI: 10.1002/adfm.201800629
6. Wang H., Yi X., Liu T., et al. (2023). An integrally formed Janus hydrogel for robust wet - tissue adhesive and anti - postoperative adhesion. *Adv. Mater.*35:202300394. DOI:10.1002/adma.202300394
7. Yi B. Yang B., et al. (2024). Surface hydrophobization of hydrogels via interface dynamics-induced network reconfiguration. *Nat. Commun.* 15:023–44646-5. DOI:10.1038/s41467-023-44646-5
8. Li S., Liu L., Qiao F., et al. (2024). Bioinspired asymmetric - adhesion Janus hydrogel patch regulating by zwitterionic polymers for wet tissues adhesion and postoperative adhesion prevention. *Adv. Healthc. Mater.* 13:202402268. DOI:10.1002/adhm.202402268
9. Shao H., Wei K., Gong T., et al. (2024). Elastic Janus microarray film strain sensors with heterogeneous modulus and conductivity for healthcare and braille identification. *Adv. Funct. Mater.* 52:123–138. DOI:10.1016/j.bioactmat.2025.06.006
10. Wu J., Xian J., He C., et al. (2024). Asymmetric wettability hydrogel surfaces for enduring electromyographic monitoring. *Adv. Mater.* 36:202405372. DOI:10.1002/adma.202405372

FUNDING AND ACKNOWLEDGMENTS

This work was financially supported by the National Natural Science Foundation of China (grant nos. 21874056 and 52003103). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.