

Review Article

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Advances of soft robotics for gastrointestinal tract applications

Min Du¹, Zhennian Xie², Xuelin Wang¹

¹Key Laboratory for Biomechanics and Mechanobiology of Ministry of Education, Beijing Advanced Innovation Center for Biomedical Engineering, School of Engineering Medicine, Beihang University, Beijing 100191, China.

²Department of Anorectal Surgery, Xiyuan Hospital of China Academy of Chinese Medical Sciences, Beijing 100091, China.

Correspondence to: Prof. Zhennian Xie, Department of Anorectal Surgery, Xiyuan Hospital of China Academy of Chinese Medical Sciences, Beijing 100091, China. E-mail: xiezhennian@163.com; Dr. Xuelin Wang, Key Laboratory for Biomechanics and Mechanobiology of Ministry of Education, Beijing Advanced Innovation Center for Biomedical Engineering, School of Engineering Medicine, Beihang University, Beijing 100191, China. E-mail: wangxuelin@buaa.edu.cn

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Abstract

Gastrointestinal (GI) robots overcome the limitations of conventional endoscopy, offering a noninvasive and precise approach for diagnosing and treating major GI diseases including colorectal cancer, gastric cancer, inflammatory bowel disease, and peptic ulcers. However, due to the dynamic, tortuous, mucus-rich, and pH-variable environment of GI tract, GI robots face serious challenges in achieving precise localization, stable operation, and reliable sensing. Leveraging the properties of tissue-matched modulus, adaptive deformation, and bioinspired design, soft robots can conform to the intestinal wall, minimizing mechanical damage and thereby offering new strategies for efficient sensing and treatment of GI diseases. Hereinto, this review presents a comprehensive GI soft robot system by integrating materials, structural designs, actuation modes, and physiological adaptability to achieve multifunctional performance and clinical reliability. Specifically, materials are classified into biocompatible elastomers, smart responsive polymers, and functionalized conductive materials to guide material selection and structural optimization. Subsequently, structural engineering methods including continuous encapsulation designs, modular-reconfigurable architectures, and biomimetic frameworks are introduced, alongside diverse actuation strategies of field-driven, fluid-driven, and chemically driven autonomous mechanisms. Following that, preclinical applications are highlighted as navigation and localization, drug delivery and controlled release, *in vivo* sensing, as well as minimally invasive manipulation and therapy. In the future, this integrated GI soft robotics technology will fundamentally reshape precision medicine, enabling a more intelligent and personalized therapeutic platform, and driving the evaluation of next-generation GI soft robotics.

Keywords: Soft robot, gastrointestinal, minimally invasive, diagnosis and treatment, soft actuators



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INTRODUCTION

Soft robots, with their high degrees of freedom, large deformability, flexibility, and strong environmental adaptability, have become a research focus in robotics^[1,2]. Their advantages in flexible deformation, actuation, and gripping offer great potential for applications in deep-sea exploration, medical rehabilitation, and pipeline inspection^[2,3]. For instance, Li *et al.* developed a deep-sea soft robot based on dielectric elastomers capable of operating at a depth of 10,900 m^[4]; Xie *et al.* designed a bioinspired octopus arm integrated with flexible electronics for sensing, locomotion, and interaction in complex environments^[5]. Hu *et al.* created a magnetic-elastic millimeter-scale robot that performs jumping, rolling, climbing, and landing in the stomach for targeted drug delivery and minimally invasive surgery^[6]. Actually, traditional robots generally employ rigid materials and feature stiff structures and joints, relying on high-precision control systems to perform tasks. However, such rigid designs pose significant safety risks in the biomedical domain, as interactions with patients may cause tissue damage and discomfort. Alternatively, soft robotics has demonstrated considerable potential in biomedical applications, where compliant materials can minimize tissue injury and enhance user comfort during interactions with biological tissues or organs^[7,8]. Recent advances in smart materials, micro/nanofabrication, and biomedical engineering have driven soft robotics from proof-of-concept to practical clinics. These technologies now find wide-ranging bio-applications in minimally invasive therapies^[6,9–11], rehabilitation and assistive devices^[12–14], drug delivery systems^[15,16], and medical monitoring^[17,18], diagnostic^[19], and therapeutic procedures^[20]. Collectively, soft robots composed of functional materials, remotely actuated by electrical, magnetic, optical, chemical, or mechanical stimuli to perform complex tasks, offer significant advantages for biomedical applications.

The human digestive tract transports nutrients and expels waste, and its dysfunction directly affects health. Soft robots designed for the gastrointestinal (GI) tract operate within its constrained environment by integrating sensing, actuation, power supply, and communication systems, progressively enabling precise diagnosis and treatment of GI diseases. In specific clinical scenarios, GI soft robots are capable of performing GI tract biopsies and sampling intestinal microbiota for early screening and detection of colorectal cancer^[21–23]. Furthermore, Mimee *et al.* integrated a probiotic sensor into the robot to enable effective detection of GI bleeding^[24]. Additionally, capsule endoscopy enables direct visualization of the GI mucosal surface and, when integrated with deep learning, facilitates the detection of pathological changes such as bleeding, ulcers, polyps, and inflammation^[25,26]. Besides, soft robots integrated into endoscopes assist in esophageal and colonic stricture dilation and stent placement^[27,28], thereby improving surgical precision and safety. A system designed by Del Bono *et al.* can autonomously inflate and expand colonic tissue^[29], reducing potential tissue damage while maintaining the colonic lumen patency. Meanwhile, site-specific drug delivery represents another critical application area^[30]. For example, Zhao *et al.* reported a protein-based soft robot capable of navigating closed spaces within the GI tract and releasing drugs on demand for precise therapy^[31]. For gastric ulcer treatment, Zhou *et al.* developed an acid-triggered charge-switching antibacterial hydrogel soft robot that effectively accelerates gastric mucosal wound healing^[32]. In parallel, for chronic GI disorders, Abramson *et al.* designed an orally ingestible soft robot that adheres to the GI wall and achieves precise control of gastric motility disorders through electrical stimulation^[33]. Overall, these representative preclinical devices demonstrate the feasibility of integrating multifunctional soft robots into the complex GI environment and lay a solid foundation for intelligent, multimodal diagnostics and therapeutics for GI diseases in the future.

However, as one of the most complex organ systems, the GI tract poses a highly challenging physiological environment for soft robot design and application. Firstly, the GI tract exhibits multiscale, multilayered structural features and dynamic behaviors. Its folded surface, viscous mucus layer, and distinctive peristaltic

motility hinder the precise localization and stable retention of soft robots^[34,35], while GI peristalsis, luminal folding, and the viscous mucosal layer further impede mechanical propulsion. These challenges necessitate soft robots with a high degree of freedom, compact and reconfigurable structures, and reliable responses to external field-driven or autonomous actuation. Moreover, the GI tract exhibits pronounced pH gradients^[36], with a strongly acidic stomach environment (pH 1-4), near-neutral pH in the small intestine (pH 6.5-7), and mildly alkaline conditions in the colon (pH 7-8). These pH variations impose specific requirements on the selection of materials for soft robotic systems. Variations in pH necessitate that materials for soft robotics either possess robust chemical stability and corrosion resistance, or are pH-sensitive to enable an intelligent response to pH gradients^[37,38]. In addition, digestive enzymes and diverse microbiota communities further affect the stability and functionality of soft robots^[39,40]. Natural polymers (such as gelatin, collagen, and cellulose) and certain synthetic polyesters, including polylactic acid (PLA) and polycaprolactone (PCL), are susceptible to enzymatic degradation by digestive enzymes^[41,42]. Their rapid decomposition and dissolution can lead to structural failure of soft robots. Furthermore, metallic functional components (including actuators, sensors, and embedded circuits) are vulnerable to corrosion by bodily fluids, which may impair the core operational capabilities of the robot and result in complete functional failure^[43,44]. Therefore, soft robots must be either encapsulated or designed to strategically exploit GI physiological features for targeted activation. The complex physiological environment of the GI tract necessitates systematic innovations in material selection, structural design, actuation control, and functional implementation to enable safe and effective *in vivo* diagnostics and therapeutics.

This review aims to systematically delineate the latest advances in GI soft robotics field by integrating insights across four key dimensions: materials science, structural engineering, actuation strategies, and functional implementations [Figure 1]. A function-oriented material classification system is proposed, encompassing three major categories: biocompatible soft elastomers, smart responsive materials, and functionalized conductive and magnetic materials. Subsequently, three structural design strategies (namely continuous-encapsulated, modular-reconfigurable, and biomimetic morphologies) are summarized. Furthermore, the diverse actuation mechanisms, including field-driven, fluid-driven, and chemical reaction-driven methods, are systematically analyzed with respect to their applicability and technical characteristics. Finally, the multifunctional applications are thoroughly elaborated, ranging from fundamental drug delivery to complex integrated diagnosis and therapy. Through this review, we aspire to guide theoretical and technological advances in soft robotics, and aim to accelerate the clinical translation of GI soft robotic technologies from laboratory to clinics.

MATERIALS

Considering the complex physiological characteristics of GI tract, materials should possess mechanical properties matched to biological tissues to minimize tissue damage. Meanwhile, to ensure safe operation *in vivo*, both the materials and their degradation products are required to have benign biocompatibility^[43]. Currently, elastomers^[45], hydrogels^[46], shape memory polymers (SMPs)^[47], and liquid metals (LMs)^[48] are widely employed for fabricating soft structures due to their desirable compliance and potential for functional integration^[49]. This section reviews material selection strategies and recent advances in GI soft robotics across three key areas: biocompatible soft elastomers, smart responsive materials, and functionalized conductive and magnetic materials.

Biocompatible soft elastomeric materials

Biocompatible elastomeric materials, including elastomers and hydrogels, constitute the fundamental material platform for GI soft robotics, with their selection directly influencing the safety and functionality of the robots. Elastomers (such as silicone rubber and polyurethane) primarily serve as the main structural

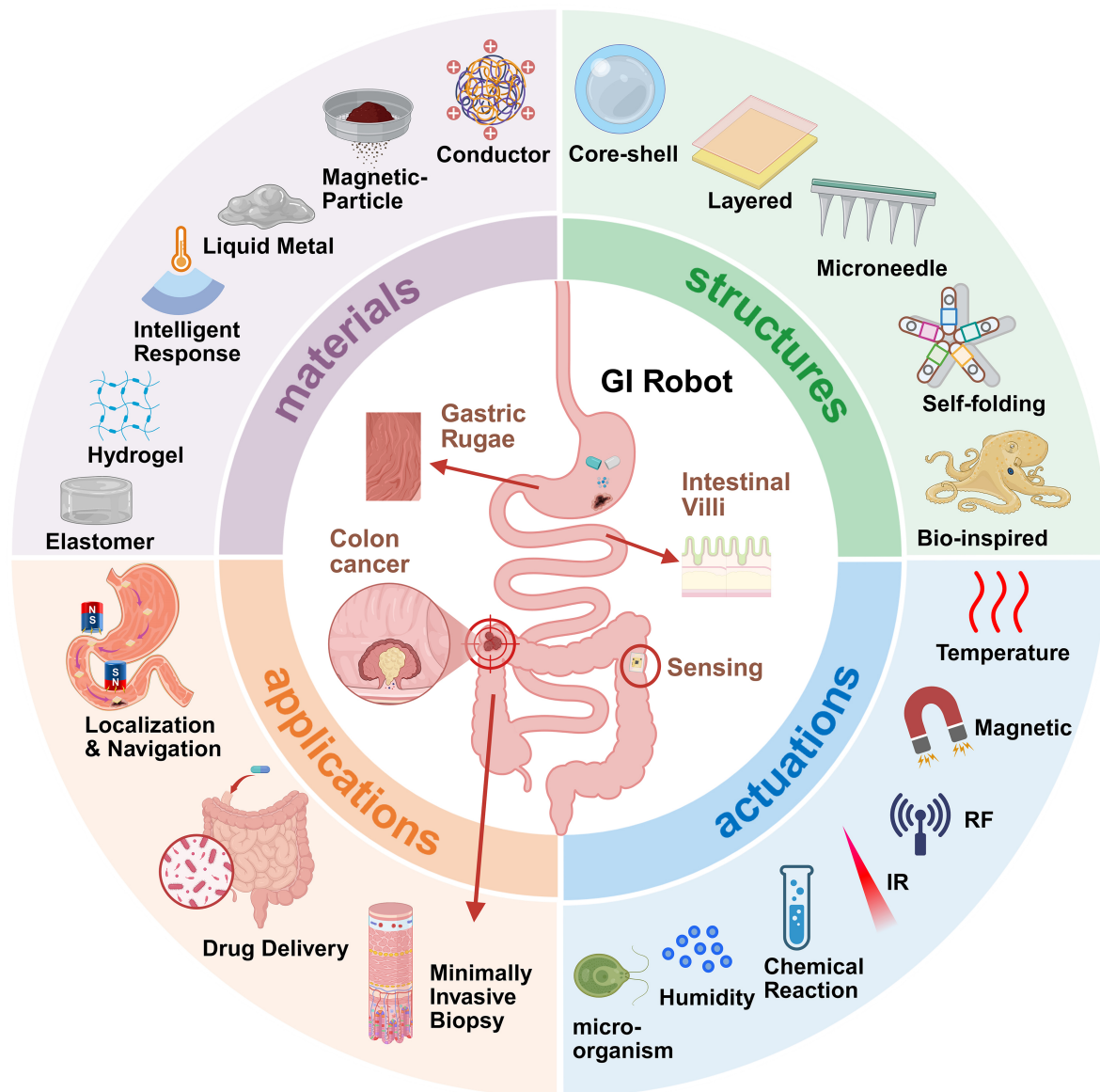


Figure 1. Overview of GI soft robots. The inner circle illustrates the gastric rugae and intestinal villi structure of the GI tract, as well as the functions of the GI robot for drug release and colon cancer sampling. The outer circle presents the aspects of GI soft robot, including materials, structure, actuation, and applications. Created with BioRender.com. GI: Gastrointestinal.

materials of the robot. Their core function is mechanical matching, requiring elastic modulus (typically ranging from tens of kPa to tens of MPa^[50]) aligned with GI soft tissues (~10 kPa) to minimize tissue damage and accommodate the deformation of the luminal environment. Additionally, their high fracture strain and superior fatigue resistance enable them to withstand cyclic strains, facilitating repetitive motions such as peristalsis and grasping. Silicone-based materials, as the most widely applied matrix materials [such as polysiloxanes, particularly polydimethylsiloxane (PDMS), and Ecoflex], exhibit low modulus, high strain capacity, and low hysteresis^[51]; PDMS-based soft robots have been extensively utilized as carriers and compliant actuators within simulated gastric and intestinal fluids. When combined with bioadhesive agents^[52], the robot demonstrated reliable operation exceeding 25 h under cyclic mechanical loading, effectively mimicking peristaltic environments. Similarly, the soft robot fabricated from Ecoflex exhibited

remarkable structural stability after prolonged immersion in acidic solutions ($\text{pH} = 1$)^[53], maintaining motion performance with negligible change in velocity ($0.21 \text{ cm}\cdot\text{s}^{-1}$ pre-immersion vs. $0.20 \text{ cm}\cdot\text{s}^{-1}$ post-immersion), indicative of superior corrosion resistance. Further validation in ex vivo porcine stomach models confirmed the structural integrity and operational feasibility of the robot, underscoring its potential for applications such as targeted bacterial infection therapy within the GI tract. Hydrogels, as three-dimensional (3D) polymer networks with high water content^[54], have attracted considerable attention for their unique hydrophilicity and bioactivity, serving key roles in cargo loading, controlled release, and mucoadhesion. Natural polymer hydrogels, including alginate, gelatin, and chitosan, both possess excellent biocompatibility and tunable mechanical properties via crosslinked networks^[55,56]. Moreover, hydrogels exhibit drug-loading capabilities. As illustrated in Figure 2A, sequential ingestion of a crosslinker solution containing calcium and dithiol crosslinkers, followed by a drug-loaded polymer solution of alginate and four-arm poly(ethylene glycol)-maleimide, forms a tough hydrogel in the stomach capable of withstanding pressures $\geq 13 \text{ kPa}$ ^[57], making it an ideal material for GI soft-robotic drug delivery. Hydrogels can also enhance adhesion performance; for instance, Figure 2B depicts robust hydrogel adhesives designed for gastric perforation repair that are acid-resistant^[58]. Thermoplastic elastomers, such as polyurethanes^[59], demonstrate distinct advantages in applications requiring frequent deformation due to their excellent elastic recoverability and ease of processing.

Smart responsive materials

Smart responsive materials endow GI soft robots with the capability to perceive environmental changes and autonomously react, representing a critical technological foundation for precision medicine. pH-sensitive materials exploit the pronounced pH gradient along the GI tract to achieve site-specific actuation^[60]. Polymers such as poly(acrylic acid) (PAA) and carboxymethyl chitosan (CMCS) exhibit significant swelling behavior changes in response to varying pH levels, making them ideal platforms for stomach-protective and intestine-targeted release systems^[61,62]. For example, Wen *et al.* developed Ca-alginate-based Janus capsules wherein hydroxypropyl methylcellulose phthalate (HPMCP) enteric microspheres dissolve under intestinal pH conditions to form microchannels^[63], enabling PAA to swell under alkaline environments and generate propulsion forces for targeted release in the intestine [Figure 2C]. Thermoresponsive polymers, such as poly(N-isopropylacrylamide) (PNIPAM)^[64], possess a lower critical solution temperature (LCST) near body temperature, facilitating phase transitions triggered by physiological heat or external stimuli. Ma *et al.* engineered a nanocellulose-mediated PNIPAM layer exhibiting hydrophobic contraction starting at $34.8 \text{ }^{\circ}\text{C}$ ^[65], enabling rapid bending actuation within typical gastric temperature ranges, thus providing swift and stable driving force for soft robots navigating confined and curved GI spaces. SMPs and liquid crystal elastomers (LCEs) endow the robot with programmable morphology and stimulus-responsive capabilities. SMPs actuate via entropy-driven phase transitions^[66], for instance, DiaPLEX MP3510^[67], with a transition temperature around $35 \text{ }^{\circ}\text{C}$, can be activated by body heat alone, mitigating safety concerns associated with external heating. As shown in Figure 2D, Peng *et al.* combined a temperature-responsive polyurethane SMP layer with a pH-sensitive PAA hydrogel layer to realize actuators that synergistically respond to dual stimuli^[68]. In addition, enzyme-responsive materials^[69], triggered by GI tract-specific enzymes, offer a novel approach for achieving spatiotemporally precise actuation. Besides, LCEs, combining the mechanical robustness of crosslinked polymers with the anisotropic ordering of liquid crystals^[70], also demonstrate dynamic responsiveness to stimuli such as temperature and light, further expanding the functional versatility of GI soft robotics^[71,72].

Functionalized conductive and magnetic materials

Functionalized conductive and magnetic materials constitute a vital material foundation for enabling remote actuation and multifunctional integration in GI soft robotics. Magnetic fillers are essential for wireless control with remote actuation forces. Specifically, hard magnetic materials, such as neodymium-

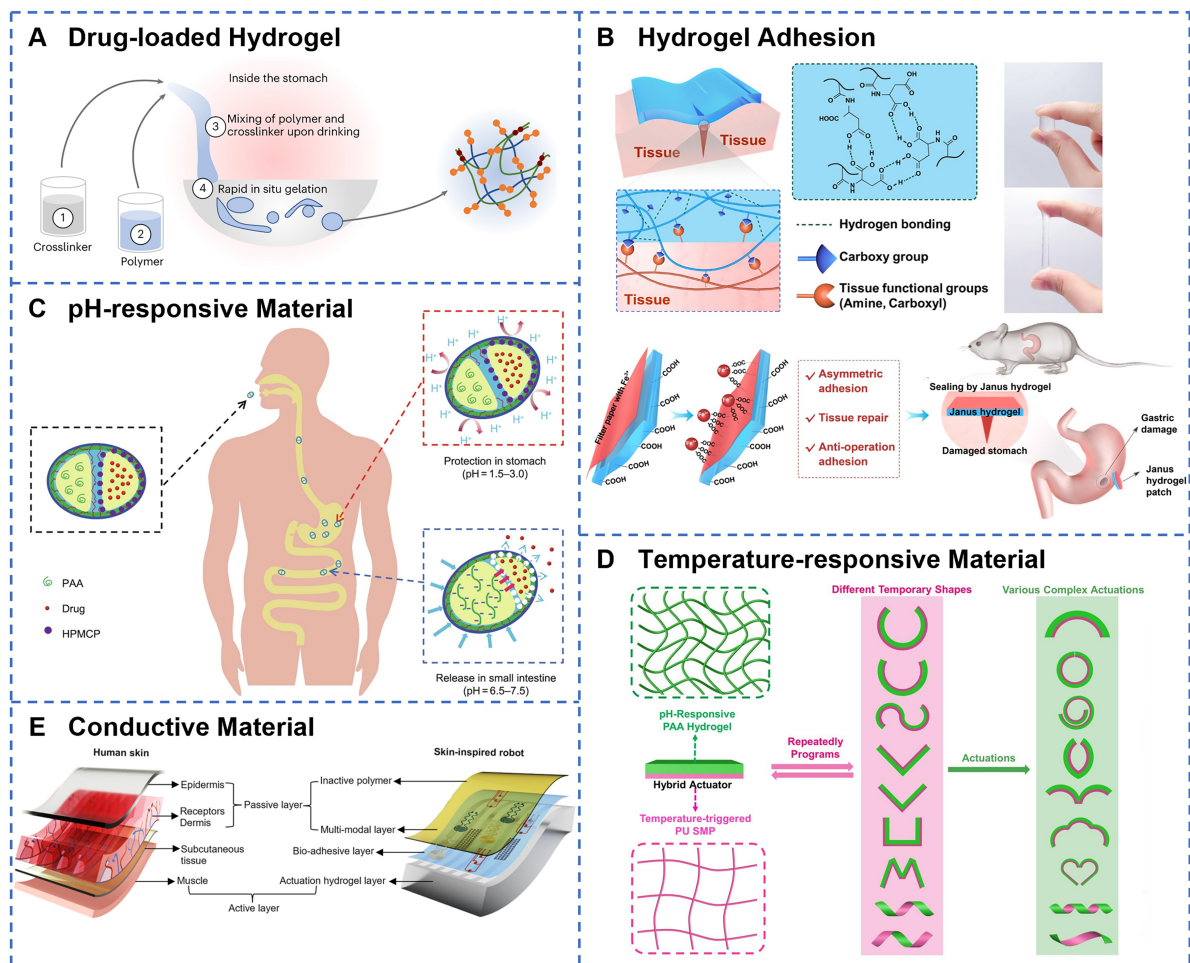


Figure 2. Material selection strategies for GI soft robots. (A) Liquid *in situ*-forming tough hydrogels form *in vivo* through sequential oral administration of crosslinker and polymer solutions, utilizing alginate and four-arm PEG-maleimide networks to create tough double-network systems capable of controlled drug release. Reprinted with permission from [57]. Copyright 2024, Springer Nature; (B) Poly(*N*-acryloyl aspartic acid) hydrogels demonstrate strong tissue adhesion through hydrogen bond crosslinked networks with Janus patch design, enabling gastric perforation repair while preventing. Reprinted with permission from [58]. Copyright 2022, Elsevier Ltd; (C) Cal-ginate-chitosan/protamine/silica capsules provide gastric protection for encapsulated indomethacin via acid-resistant composite shells, then enable rapid and controlled drug release in small intestine through pH-triggered opening of microchannels. Reprinted with permission from [63]. Copyright 2023, Elsevier Ltd; (D) Different response shapes of a novel SMP/hydrogel hybrid actuator. Reprinted with permission from [68]. Copyright 2023, MDPI; (E) Soft robot design mimics natural skin's hierarchical structure, integrating electronic sensing layers with artificial muscle components for adaptive robotic functionality. Reprinted with permission from [80]. Copyright 2024, Springer Nature. GI: Gastrointestinal; SMP: shape memory polymer.

iron-boron (NdFeB), possess high remanence and coercivity^[73], making them ideal candidates for magnetic actuation in GI soft robots. The application of an external alternating magnetic field (AMF) enables precise navigation, localization, and actuation of these robots. In contrast, ferromagnetic or soft magnetic materials (such as iron and iron oxides) exhibit magnetostrictive behavior^[74], undergoing deformation when subjected to external magnetic fields. Iron oxides, when used at appropriate dosages, demonstrate biocompatibility and can generate Joule heating under alternating high-frequency magnetic fields, making them suitable for magnetothermal therapy^[75,76]. In addition, they can serve as triggers for thermo-responsive material deformation and controlled drug release. Conductive elastomers incorporate conductive fillers to endow electrical functionalities. Typical conductive inclusions include poly(3,4-ethylenedioxythiophene):poly(styrene sulfonate) (PEDOT:PSS), silver nanowires (AgNWs), carbon nanotubes (CNTs), graphene,

and MXene, which collectively contribute to sensing capability^[77], adhesion property^[78], and multi-stimuli responsiveness^[79]. For instance, Zhang *et al.* integrated AgNWs, reduced graphene oxide (RGO), and PEDOT:PSS into a polymeric matrix to fabricate sensors with high spatiotemporal resolution [Figure 2E]^[80]. Besides, LMs such as gallium-indium alloys provide an ideal material for reversible deformation and flexible circuitry owing to their fluidity at room temperature and excellent conductivity^[81,82]. Their intrinsic radiopacity enables clear visualization under medical imaging modalities [e.g., X-ray, computed tomography (CT)], thereby facilitating precise tracking of soft robot motion. Photothermal materials (including CNTs and gold nanoparticles) can efficiently convert near-infrared light into thermal energy, underpinning light-driven actuation strategies^[83]. The integration of these functional materials transforms soft robots from mere mechanical devices into intelligent medical platforms endowed with sensing, decision-making, and actuation capabilities.

Material constraints and imaging considerations

In summary, biocompatible soft elastomers, stimuli-responsive materials, and functionalized conductive/magnetic materials all present distinct advantages in GI soft robots. However, to ensure reliable operation in the complex GI environment, these materials must satisfy a series of quantitative physiological and engineering constraints. Table 1 summarizes the critical material-related requirements for GI soft robotic systems with quantitative indicators, including elastic modulus ranges relevant to mucosal compliance, adhesion strength, pH/temperature responsiveness, allowable temperature during actuation, imaging compatibility, and *in vivo* residence/biodegradation timelines. By mapping specific material classes (elastomers, hydrogels, SMPs/LCEs, conductive/magnetic fillers, *etc.*) to these metrics, Table 1 provides a concise reference for evaluating suitability and guiding material selection in the GI environment.

In clinical imaging applications, it is essential to fully consider their compatibility to avoid imaging artifacts, localized overheating, and potential biosafety risks. Magnetic resonance imaging (MRI), a core modality for abdominal clinical imaging^[84], can be significantly affected by NdFeB permanent magnets, which cause significant magnetic field distortions in MRI, resulting in severe geometric distortion artifacts. In contrast, Fe₃O₄ superparamagnetic nanoparticles primarily affect signal intensity by altering local magnetic susceptibility, producing contrast enhancement or signal artifacts^[106]. Highly conductive gallium-based LMs may induce eddy currents under alternating radiofrequency fields^[107], leading to localized heating and risk of tissue burns^[108]. Mitigation strategies include the use of superparamagnetic fillers, reduction of filler concentration, polymer encapsulation layers, and optimization of MRI sequences [e.g., short echo time (TE) and spin-echo sequences]^[109,110].

In CT, high atomic number metals such as LMs absorb substantial X-rays, producing starburst-like beam hardening artifacts that can be alleviated by dilution or substitution with low-concentration contrast agents such as bismuth salts^[111,112]. Conventional X-ray radiography also relies on high contrast between metal and tissue. However, large metal components cause shadow artifacts, necessitating improved encapsulation designs or artifact suppression algorithms^[113].

By contrast, ultrasound imaging is highly compatible with most soft materials, such as hydrogels and elastomers, due to matched acoustic impedance with soft tissue, and active contrast can be achieved through microbubbles or using echogenic contrast agents^[114]. Among common conductive polymers and nanomaterials, PEDOT:PSS and CNTs are nearly “invisible” in MRI/CT with weak ultrasound echoes, making them suitable for stealth tracking. AgNWs and MXene, owing to higher atomic numbers or conductive paramagnetic properties, provide contrast in CT, X-ray, and MRI but may generate speckle artifacts in ultrasound^[115]. Graphene requires loading with high-Z metals or microbubble contrast agents to

Table 1. Key material classes for GI soft robotics and their performance parameters compared with GI tract

Category	Primary function	Elastic modulus (for mucosal compliance)	Mucoathesive strength	pH/Temperature transition point	Allowable temperature	Imaging compatibility	<i>In vivo</i> residence time/biodegradation period	References
GI tract	N/A	1-10 kPa Intestine: 20-40 kPa	N/A	Esophagus pH: 5-7 Stomach pH: 1-4 Intestine pH: 6.5-7	< 60 °C (At 60 °C protein coagulates)	MRI (assessment of inflammation and tissue characteristics) X-ray/CT Ultrasound imaging	Gastric emptying (2-5 h), small bowel transit (2-6 h), colonic transit (10-59 h) and whole gut transit (10-73 h)	[84-88]
Elastomer	Structural framework, mechanical matching, cyclic strain	10 kPa-20 Mpa	Matrix-dependent (typically requires modification)	N/A	> 60 °C (excellent thermal stability)	Generally compatible (ultrasound: excellent; CT/MRI: filler-dependent)	Mostly non-degradable; some degradable elastomers available	[89-92]
Hydrogels	Mucoathesion, drug loading	1-100 kPa PAA hydrogel: 6.7-9.3 kPa Ca-alginate hydrogels: 10-100 kPa	4.31-170 kPa	pH-responsive swelling/degradation (e.g., chitosan at pH < 6.5; PAA at pH 6-8)	< 60 °C (prone to dehydration)	Pure hydrogels show poor imaging contrast; compatibility improves when combined with various contrast agents	Hours to days (biodegradable)	[54,92-97]
SMP/LCE	Shape fixation; stimuli-responsive	MPa (rubbery state) → GPa (glassy state)	Tunable	T _g /T _n : -35-60 °C (actuation trigger)	N/A (intrinsically thermally actuated)	Generally compatible (US: excellent; CT/MRI: filler-dependent)	Tunable from days to biostable (dependent on chemical structure)	[98-101]
Liquid metal/Conductive composite	Circuits and sensing	Matrix-dependent (typically kPa to MPa)	Matrix-dependent	N/A	> 60 °C (excellent thermal conductivity)	CT-incompatible (high density); MRI/US (compatibility tunable). Radiogallium compounds as tumor imaging agents	Permanent (non-biodegradable)	[77,79,102-104]
Magnetic filler	Remote actuation and heating	Matrix-dependent	Matrix-dependent	N/A	N/A (serves as the heat source)	MRI: incompatible (artifact), CT/US: excellent	Permanent (non-biodegradable)	[74,76,104, 105]

Representative material classes (elastomers, hydrogels, SMPs/LCEs, conductive/magnetic fillers) and their quantitative performance indicators, including elastic modulus, adhesion strength, pH/temperature responsiveness, allowable temperature during actuation, imaging compatibility, and *in vivo* residence/biodegradation timelines. GI: Gastrointestinal; MRI: magnetic resonance imaging; CT: computed tomography; US: ultrasound; PAA: polyacrylic acid; SMP: shape memory polymer; LCE: liquid crystal elastomer.

enhance imaging visibility^[116]. Overall, material selection should balance functional performance and imaging requirements depending on application scenarios, with ultrasound or low-dose CT preferred for real-time tracking and safety assessment [Table 2].

Table 2. Imaging compatibility of materials in GI soft robotics

Imaging modality	Physical principle	Compatible material examples	Incompatible/risky material examples	Major effects and risks	Mitigation strategies	References
MRI	Magnetic field and RF pulses	Pure hydrogels, most elastomers, low-concentration Fe_3O_4	NdFeB magnets, high-concentration magnetic fillers, LMs	Severe artifacts or complete imaging failure, local heating risk, displacement forces due to magnetic gradients	Use superparamagnetic particles, dilute fillers, polymer encapsulation	[106,108,109,117,118,]
CT/ X-ray	X-ray attenuation	Low-atomic-number (Z) materials (polymers, hydrogels, soft tissues, iodine/barium/bismuth-based contrast agents in clinical doses)	High-Z materials (NdFeB magnets, LMs, high-concentration Bismuth/Barium)	Star-shaped beam-hardening artifacts, surrounding structure distortion	Dilution of high-Z components, optimized encapsulation, artifact-reduction algorithms	[111,112,119]
Ultrasound	Acoustic wave reflection	Hydrogels, elastomers, microbubbles	Large dense metal structures (e.g., NdFeB, LMs)	lower spatial resolutions, speckle artifacts	Add microbubbles, use of echogenic contrast agents	[114,120-122]

Comparison of representative materials under MRI, CT, X-ray, and ultrasound, highlighting compatible and risky categories, major artifacts or risks, and potential mitigation strategies. GI: Gastrointestinal; MRI: magnetic resonance imaging; RF: radio frequency; CT: computed tomography; X-ray: X-ray; Z: atomic number; LMs: liquid metals.

STRUCTURAL DESIGN

Structural design constitutes a critical aspect for realizing the intended functions of GI soft robots, necessitating the optimization of their locomotion performance, environmental adaptability, and operational capabilities while ensuring compliance with biocompatibility and safety requirements.

Continuous and encapsulated structure

Continuous and encapsulated structure represents a pivotal technological strategy for achieving both drug protection and site-specific release in GI soft robotics. Capsule-shaped architectures, a classical encapsulation design, fully protect internal functional components with continuous outer shells. As illustrated in [Figure 3A](#), a core-shell configuration comprising a hydrogel-encapsulated magnetic LM exhibits remarkable mechanical resilience^[123], enduring compressive strains up to 85% and impact forces equivalent to free falls from heights exceeding 14 meters, while demonstrating passive deformability, active rolling, and toughness. The RoboCap system employs grooved and protruding spiral surface designs to enable simultaneous mucus clearance and drug dispersion^[124], resulting in a 20- to 40-fold enhancement in bioavailability compared to conventional oral administration. Meanwhile, tubular structures capitalize on the inherent luminal geometry of the GI tract^[125], achieving propulsion via coordinated peristaltic and expansion motions. For instance, an untethered soft robot integrates capsule and tubular components^[126], with the tube facilitating propulsion through peristalsis and expansion [[Figure 3B](#)]. Nan *et al.* developed layered soft actuators by naturally depositing chitosan and magnetic nanoparticles into ordered stacks^[127], which actuate based on differential mechanical properties. A bilayer polysaccharide hydrogel system combines a supramolecular carboxymethyl cellulose (CMCL) inner network with a dialdehyde alginate (DAA)-crosslinked CMCS outer network to precisely modulate pH gradient responsiveness and controlled drug release^[128]. Besides, microneedle structures mark a significant evolution of encapsulation design towards active tissue penetration and drug delivery via sharp needle tips^[129,130]. As depicted in [Figure 3C](#), Chen *et al.* developed a dynamically omnidirectional adhesive microneedle platform^[131], opening new avenues for the oral delivery of macromolecular therapeutics.

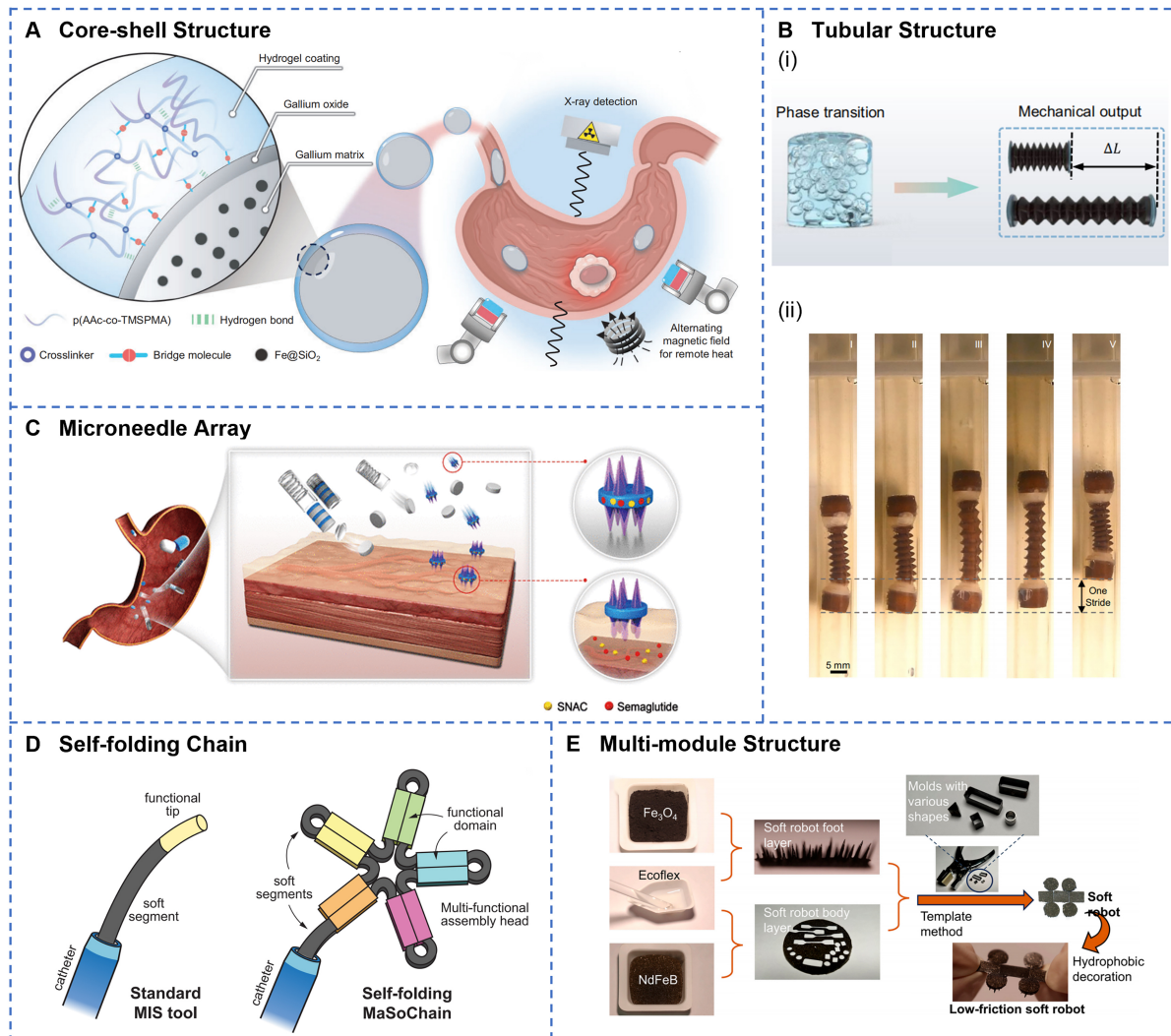


Figure 3. Design strategies of continuous and encapsulated structures, as well as modular and reconfigurable structures. (A) The hydrogel-coated containment capsule features a hierarchical core-shell architecture with remotely controlled thermal ablation capabilities via magnetic robotic arm manipulation under X-ray imaging guidance. Reprinted with permission from [123]. Copyright 2025, Oxford University Press; (B) Schematic illustration (i) and images (ii) of tubular robot expansion and peristaltic motion enabled by liquid-gas phase transition. Reprinted with permission from [126]. Copyright 2024, Springer Nature; (C) pH-responsive jack-in-the-box device deploys self-extending microneedle arrays to penetrate mucus and sustain localized drug release. Reprinted with permission from [131]. Copyright 2022, American Association for the Advancement of Science; (D) Self-folding chain exhibits modular self-folding architecture that transforms from linear configuration into large functional assemblies with multiple domains at the catheter tip. Reprinted with permission from [133]. Copyright 2023, Springer Nature; (E) The low-friction soft robot incorporates densely arranged cone structures with hydrophobic surface decoration to achieve ultra-low friction locomotion in viscous GI environments. Reprinted with permission from [53]. Copyright 2024, Beijing Institute of Technology Press. GI: Gastrointestinal.

Modular and reconfigurable structure

Modular and reconfigurable structure enables the execution of complex functions through the assembly and rearrangement of discrete functional units, representing a significant development direction in soft robotic architecture. A magnetically actuated origami millirobot [132], based on the Kresling pattern, dynamically interacts with its environment to perform rolling, flipping, and swimming motions, thus enabling amphibious locomotion. As illustrated in Figure 3D, a self-folding soft robot chain combines elastic energy

storage with magnetic assembly to autonomously transform from a slender^[133], catheter-constrained configuration into a larger functional structure. The multi-module MagCaps integrates two soft valve components containing different concentrations of NdFeB particles in parallel^[134], thereby achieving sequential or simultaneous release of distinct drugs by modulating only the amplitude of a single external magnetic field. A magnetic multilayer soft robot employs serially connected modules to provide a multi-degree-of-freedom motion and enable on-demand separation and reconfiguration for targeted adhesion^[52]. Moreover, a low-friction soft robot partitions its body and foot into modular functional zones [Figure 3E]^[53]. The foot incorporates a multi-cone structure and hydrophobic surface treatment, substantially reducing drag and enhancing locomotion speed within the mucus-rich GI environment. Additionally, a barbell-shaped soft microrobot utilizes asymmetric mass distribution and oppositely oriented axial magnetization in its head and tail to generate C-shaped bending deformation when exposed to a uniform magnetic field^[135], enabling fish-like swimming propulsion. Overall, these modular design strategies not only increase the functional density of soft robotic systems but also provide essential technological foundations for adapting to the complex and dynamic GI environment and diverse medical requirements.

Biomimetic structure

Biomimetic structure design, inspired by the locomotion mechanisms and morphological features of natural organisms, offers soft robots efficient movement strategies and enhanced environmental adaptability. The specific mechanisms involved encompass six aspects: geometric structure design, morphological features, material functional integration, mechanical responsiveness, tunable stiffness, and multimodal locomotion. To demonstrate this concept, researchers have developed various prototypes inspired by nature. The self-orienting millimeter-scale applicator adopts a mono-monostatic body design modeled after the leopard tortoise shell^[136], characterized by a shifted center of mass and a high-curvature upper shell. This bioinspired configuration enables rapid self-orientation within the gastric environment and imparts robustness against perturbations from peristaltic motion and fluid turbulence, thereby ensuring adaptability across fluids of varying viscosity and enabling precise and targeted drug delivery. As shown in Figure 4A, the starfish-inspired structure utilizes the contraction and expansion of star-shaped arms to achieve temperature-controlled drug release^[67]. Meanwhile, an octopus-inspired soft robot mimics suction cups through a constricted orifice, disk-like infundibulum, and dome-shaped acetabulum [Figure 4B]^[137]. By manipulating magnetic gradient fields, it generates dynamically controllable adhesion and detachment within the GI tract. Furthermore, Figure 4C illustrates an untethered magnetic robot modeled after the overlapping scales of a pangolin. This robot combines a flexible polymer matrix with metallic scales^[138]. Under radiofrequency fields, it attains localized heating above 70 °C, demonstrating potential for noninvasive hyperthermia within the GI tract. A microneedle robot inspired by the pufferfish's spiny organs expands to a diameter of 14 millimeters by absorbing intestinal fluids, forming a spiked vesicle^[139]. This soft robot structure can withstand and harness radial peristaltic pressure to penetrate the mucosal tissue with barbed drug-loaded microneedles. A stiffness-tunable velvet worm-inspired soft robot employs magnetorheological materials to replicate the worm's gland-based self-thickening secretion^[140], achieving controllable adhesion. Finally, a climbing plant-inspired actuator leverages the coiling and twisting mechanisms of plant tendrils to realize multimodal deformation^[141]. This actuator has been employed to fabricate a biomimetic quadruped robot capable of executing inchworm-like crawling locomotion [Figure 4D]. To sum up, bionic structural design significantly improves the locomotion efficiency and adhesion capability of GI soft robots while providing versatile strategies for actuation control and physiological task execution within the complex GI environment.

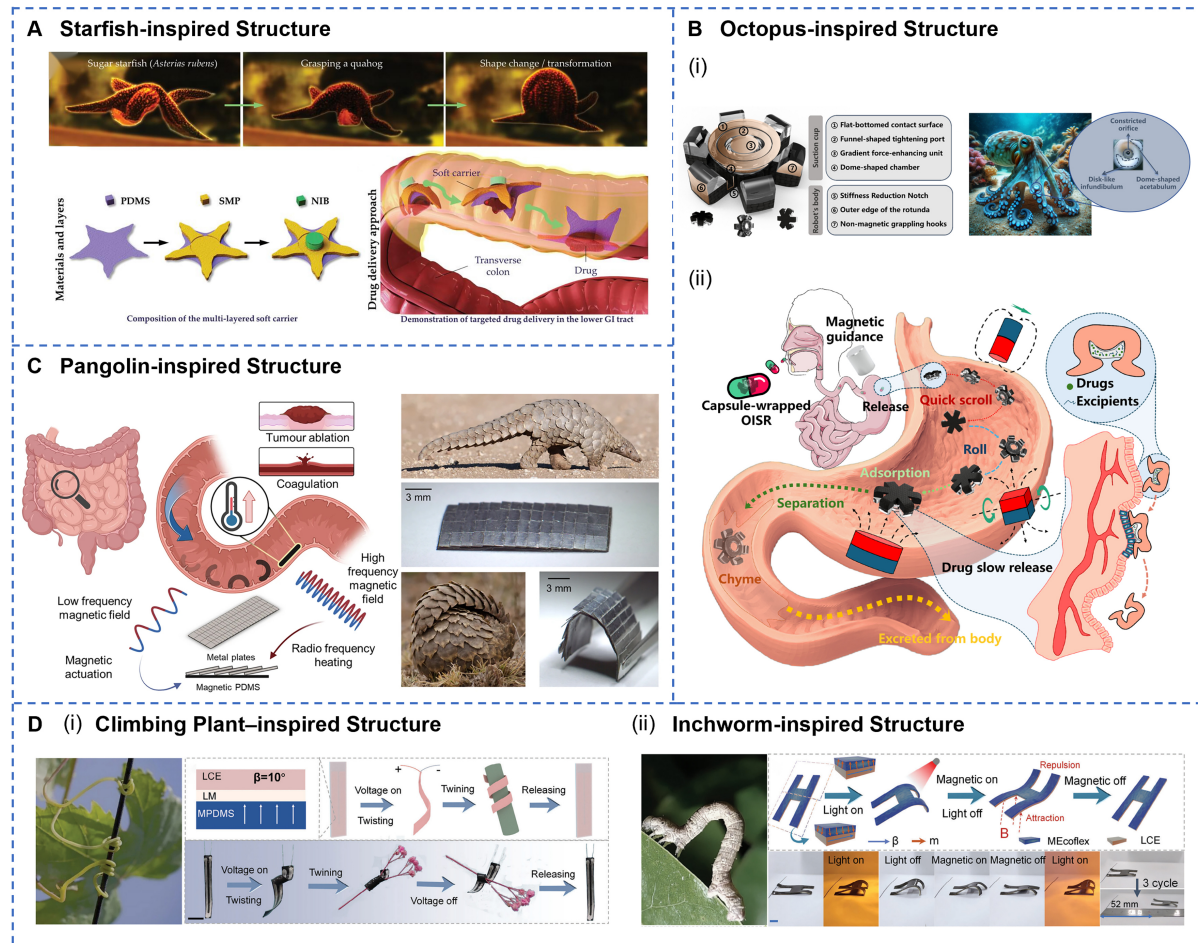


Figure 4. Structural designs to optimize the locomotion, environmental adaptability, and operational capabilities of GI soft robots. (A) Bio-inspired soft carrier with a starfish-mimetic structure, featuring a central disc and radiating arms. Reprinted with permission from^[67]. Copyright 2023, Wiley VCH; (B) OISR's biomimetic suction-cup architecture stores drug payloads and employs magnetic-gradient adhesion (i) and multimodal rolling motions for controlled gastric release (ii). Reprinted with permission from^[137]. Copyright 2024, MDPI; (C) Pangolin-inspired robot features overlapping metallic scale architecture that enables magnetic field-controlled locomotion while providing Joule heating capabilities exceeding 70 °C for therapeutic applications. Reprinted with permission from^[138]. Copyright 2023, Springer Nature; (D) Climbing plant-inspired smart tendrils demonstrating flower wrapping (i), alongside a schematic of an inchworm-inspired robot designed for locomotion on flat surfaces (ii). Reprinted with permission from^[141]. Copyright 2024, Wiley VCH. GI: Gastrointestinal.

ACTUATION METHODS

Actuation methods are the core technology to GI soft robots, governing locomotion performance and directly affecting control precision, response speed, energy efficiency, and operational safety. The unique GI environment precludes direct use of conventional motor-driven approaches, necessitating the development of innovative actuation technologies tailored to these biological conditions.

Field-driven actuation

Field-driven actuation enables wireless control of soft robots via external physical fields, and is considered as the most promising actuation approach for GI applications. Remote magnetic actuation offers strong tissue penetration and precise control capabilities. For example, a tri-reconfigurable magnetic robot achieves accurate navigation under a 7.42 mT magnetic field by embedding Fe_3O_4 magnetic nanoparticles^[142]. It reaches a maximum rolling speed of $7.23 \text{ mm}\cdot\text{s}^{-1}$ with a positioning error as low as

263 μm . The advantage of magnetic actuation lies in its ability to enable six degrees of freedom in motion control. By adjusting the strength, direction, and frequency of the magnetic field, translation, rotation, and deformation of the robot can be regulated^[143,144]. A magnetorheological elastomer exhibits tunable stiffness ranging from 0.477 to 2.03 MPa when subjected to an external magnetic field^[140], providing new opportunities for adaptive control of soft robots. Near-infrared light actuation utilizes the photothermal effect to achieve programmable deformation and phase-transition-driven motion^[83,145]. As shown in [Figure 5A](#), a magnetic patch robot employs a dual-shape-memory polymer system composed of poly (D-lactide) and poly(D,L-lactic acid-co-trimethylene carbonate)^[146]. Due to the differing glass transition temperatures of the two polymers, the robot exhibits multistage shape transformations. Combined with near-infrared heating, it can switch among helical, flat patch, and intermediate states, offering an innovative solution for the prevention of undesired postoperative adhesions. Light-driven actuation offers high energy density and rapid response but is limited by light penetration depth, making it primarily suitable for applications on superficial tissues. Ultrasound-triggered drug delivery systems achieve controlled release via acoustic mechanical and sonothermal effects^[126]. For instance, the barbell-shaped robot utilizes ultrasonic-triggered bubble oscillation technology for remote-controlled drug release [[Figure 5B](#)]^[135]. Meanwhile, electric field actuation enables precise deformation control through the response of electroactive materials. An electro-adhesive hydrogel interface achieves an adhesion strength of 16–17 kPa by inducing electrophoretic migration of cationic polymers under an applied direct current electric field^[147]. This system can maintain adhesion on pig gastric mucosa for up to 30 d. Electric actuation offers high response accuracy and low energy consumption; however, the biocompatibility of electrodes and effects of electrolysis products require careful consideration. Furthermore, a multi-motion robot employs electric heating for *in situ* magnetization reprogramming and couples with an external magnetic field to realize multimodal locomotion [[Figure 5C](#)]^[148]. Magnetothermal actuation combines magnetic control and thermal responsiveness. Magneto-thermal hydrogel swarms generate localized temperature increases when Fe_3O_4 particles are excited under high-frequency AMF^[149], triggering gel-sol phase transitions for shape morphing and drug release. Similarly, a magnetic LM capsule rapidly heats via magnetic hysteresis losses and eddy current effects under AMF^[123], reaching temperatures of 90 °C within 10 s. This enables precise energy delivery for localized thermal ablation therapy. Li *et al.* developed a triple-responsive actuator that bends under electrothermal or near-infrared heating^[150], undergoes plastic deformation to fix its shape, and recovers under a magnetic field in a thermal environment, enabling programmable shape memory and remote-controlled actuation. Field-driven actuation enables precise remote control with rapid response times^[151,152], facilitating flexible navigation and accurate positioning in the complex GI tract, making it suitable for controlled-path GI diagnosis and treatment. Its advantages include fast responsiveness, precise motion control, and the capability for non-contact wireless operation^[151,153]. However, it typically requires external device support, and the driving force presents limited penetration through human tissue^[154]. In summary, the development trend of multimodal field-driven actuation lies in integrating diverse field actuation techniques to achieve complementary functionalities and optimized performance.

Fluid-driven actuation

Fluid-driven actuation generates driving force for soft robots by compressing fluids, offering high actuation power and smooth response characteristics. Pneumatic actuation is the most classical form of fluid driving and achieves deformation of soft structures through controlled air inflation and deflation. For instance, a flexible over-the-tube device incorporates three pneumatically driven actuators [[Figure 5D](#)]^[155]. By precisely regulating air pressure, it enables gripping, advancing, and anchoring of the soft tether within a colonoscope. Melancon *et al.* integrated bistable origami modules into pneumatic actuators to develop modular origami structures with varying stability^[156], capable of locomotion through multimodal deformation. Hydraulic actuation leverages the incompressibility of liquids to transmit pressure and achieve precise control. Zhu *et al.* developed a hydraulically driven, motorless soft robot with a three-degree-of-

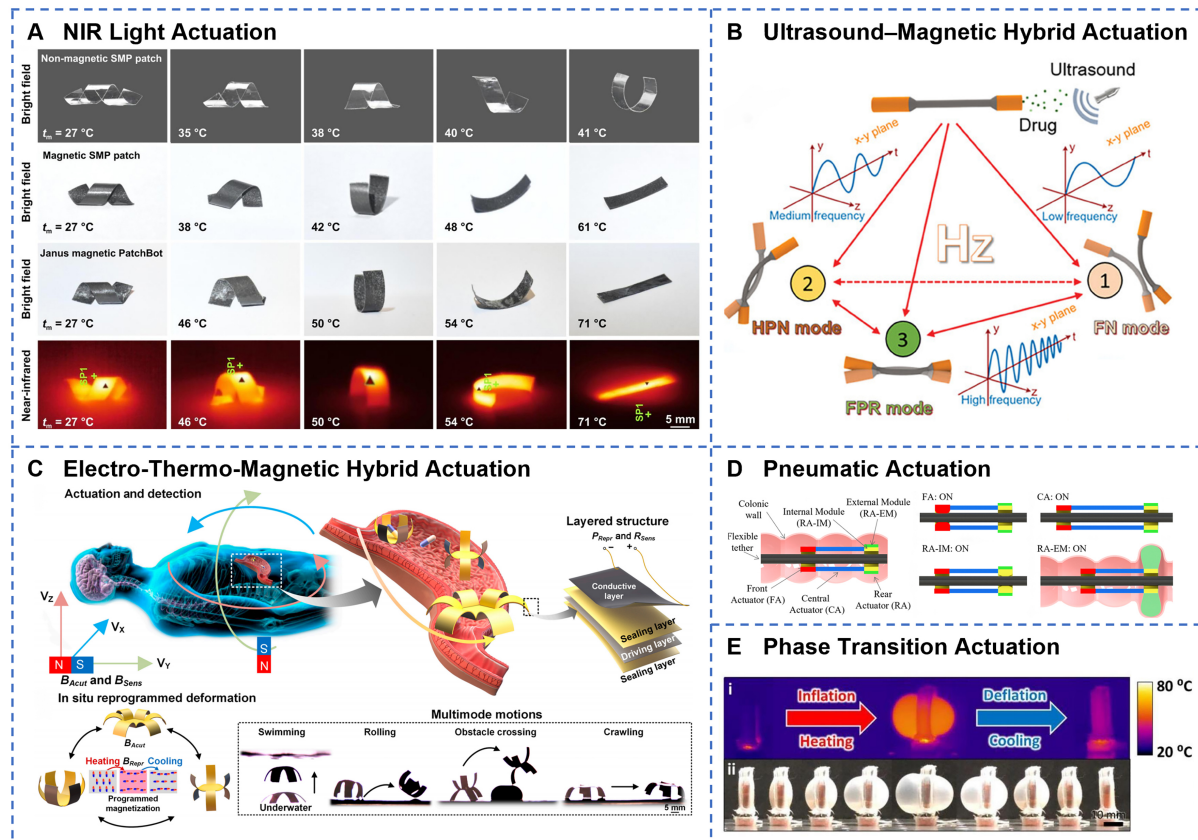


Figure 5. Field-driven and fluid-driven technologies for GI soft robots. (A) Near-infrared laser irradiation induces photothermal transformation of SMP PatchBots, with peak surface temperatures captured by NIR imaging. Reprinted with permission from^[146]. Copyright 2025, IOP Publishing Ltd; (B) Multimode control via ultrasound and external magnetic fields enables on-demand switching between distinct locomotion behaviors. Reprinted with permission from^[135]. Copyright 2024, Wiley VCH; (C) Hybrid electrothermal-magnetic actuation with *in situ* reprogrammable magnetic driving layer and conductive heating achieves versatile gastroscopic robot motions and pose sensing. Reprinted with permission from^[148]. Copyright 2023, Science and Technology Review Publishing House; (D) Pneumatic FOD design integrates FA, CA, and rigid actuator modules (RA-IM, RA-EM) for complex bending and extension. Reprinted with permission from^[155]. Copyright 2023, IEEE; (E) Liquid-gas phase-change STAM exhibits reversible inflation and deflation under thermal cycling, as shown in thermal and optical images. Reprinted with permission from^[161]. Copyright 2022, Elsevier B.V. GI: Gastrointestinal; FA: fluidic actuator; CA: compliant actuator.

freedom omnidirectional manipulator that supports lesion lifting, precise cutting, and en bloc foreign body removal^[157]. A handheld hydraulic soft robot uses a closed hydraulic system combined with an inner hydraulic filament artificial muscle to achieve bidirectional bending angles up to 180°^[158], with an average response time of approximately 0.0482 s. Fluidic actuation achieves robust and flexible motion by regulating internal fluid pressure to mimic biological peristalsis or bending movements^[159]. It is well-suited for applications requiring high environmental adaptability, excellent flexibility, and safe contact with the GI wall. Its advantages include a strong driving force, simple structure, and high compatibility with soft tissues. However, it often relies on external air or fluid supplies, which limits the miniaturization of the robot and its ability to operate untethered^[160]. To address the bulkiness of traditional pneumatic systems, researchers have developed a pumpless actuation technology based on liquid-gas phase change [Figure 5E]^[161]. A bidirectional thermoelectric-driven system controls heating and cooling of phase-change materials to inflate and deflate pneumatic chambers. Moreover, Beatty *et al.* introduced the FibroSensing Dynamic Soft Reservoir (FSDSR)^[162], where pressure applied to an external reservoir compresses an inner therapeutic reservoir, enabling active drug release and delivery. Therefore, pumpless fluid-driven soft robots offer a

novel actuation paradigm for GI soft robotics, combining rapid response and precise control. This integration provides robust power support for complex medical interventions. In conclusion, the development trend of fluid-driven systems lies in overcoming dependence on external supplies and advancing toward miniaturization and wireless operation, thereby enabling greater portability and autonomy.

Chemical autonomous actuation

Chemical autonomous actuation converts chemical energy directly into self-propulsion, eliminating the need for external power sources, and making it particularly ideal for *in vivo* applications. Bubble propulsion, driven by gases from chemical reactions, is a common strategy. For example, a rocket-inspired effervescent micromotor rapidly produces CO₂ bubbles through the acid-base neutralization reaction between sodium bicarbonate and citric acid [Figure 6A]^[163]. The resultant thrust propels the micromotor at an average speed reaching 750 $\mu\text{m}\cdot\text{s}^{-1}$, offering a novel strategy for oral delivery of macromolecular drugs such as insulin. Micromotors designed for GI drug delivery typically feature a core-shell architecture consisting of a reactive metallic core and an inert shell^[164]. In the dual-responsive micromotor pill^[165], magnesium particles react with intestinal fluid to generate hydrogen bubbles, achieving a chemical propulsion speed of 41.6 $\mu\text{m}\cdot\text{s}^{-1}$. Magnesium-based propulsion provides sufficient thrust while producing biocompatible reaction byproducts. Self-diffusiophoretic propulsion harnesses concentration and electrochemical gradients to achieve directed migration of molecules or ions. A dual-pH-responsive hydrogel actuator utilizes differential swelling of polyacrylamide (PAAm) and PAA to produce bidirectional bending with response times between 5 and 20 min^[166], offering an effective trigger mechanism for lipophilic drug delivery in GI pH environments. A Janus double-chamber capsule generates internal pressure through pH-responsive swelling of PAA polymers, enabling reactive pumping-controlled release via microchannels^[63]. Catalytic reaction-based actuation employs enzyme catalysis to convert biochemical energy. For instance, NO delivery microcapsules leverage reactive oxygen species (ROS) and inducible nitric oxide synthase (iNOS) at inflammatory sites to catalyze L-arginine into NO^[167], achieving combined antibacterial and anti-inflammatory effects [Figure 6B]. The selectivity of catalytic reactions enables activation of the robot in specific physiological or pathological environments, improving therapeutic precision. Chemical autonomous actuation relies on chemical reactants stored within soft robots to generate propulsion through chemical reactions, enabling self-powered motion^[168]. This actuation method is well-suited for fully autonomous microrobots that operate without external fields or equipment, with applications including localized *in vivo* cruising and positioning. Its advantages include high autonomy and miniaturization, although it is limited by low thrust and challenges in controlling the direction and speed of movement^[169]. Future advancements in chemical actuation aim to enhance reaction efficiency, regulate reaction kinetics, and optimize biocompatibility, thereby providing a technological foundation for fully autonomous biomedical robots.

Other actuation methods

Beyond the primary actuation techniques, the field of GI soft robotics also explores moisture-triggered and emerging biohybrid drive systems. Moisture-responsive soft robots absorb fluids within the GI tract and exhibit significant physical property changes. As illustrated in Figure 6C, a superabsorbent hydrogel-based robot swells to a diameter of 14 mm upon exposure to intestinal fluid^[139]. This expansion, combined with intestinal peristaltic pressure, enables barbed microneedles to penetrate the mucosa, facilitating painless oral delivery of insulin. Wei *et al.* designed a composite film actuator^[170]. The strong humidity sensitivity of cellulose nanofibers (CNF) and graphene oxide (GO), coupled with the rapid desorption properties of hydrophobic CNTs and the porous 3D nanochannels, results in fast and reliable moisture responsiveness. Under a relative humidity of 91%, another composite actuator produces bending angles up to 190 degrees^[171]. Relying solely on moisture-driven actuation within the GI tract is limited by insufficient driving

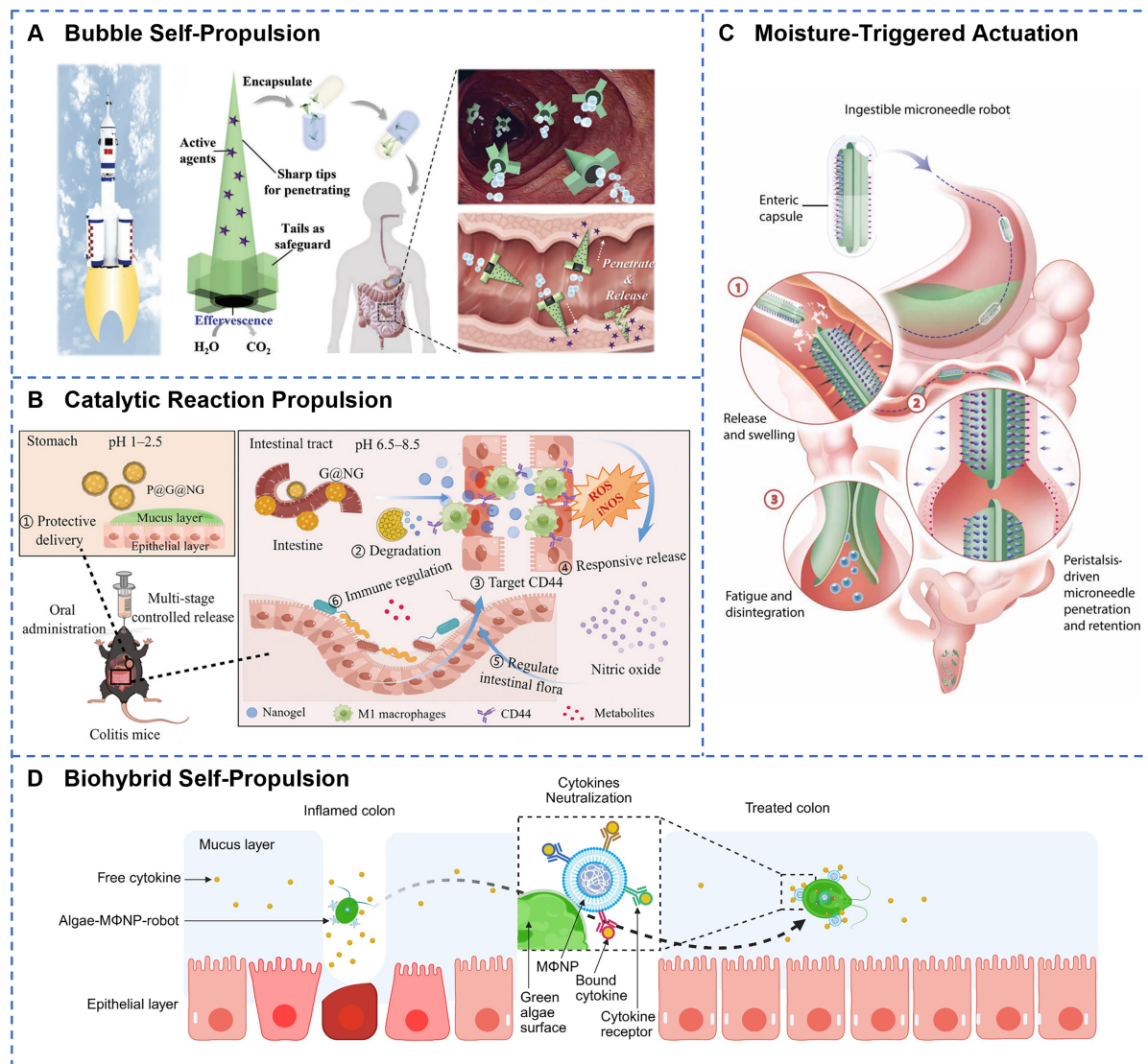


Figure 6. Chemical propulsion and other actuation technologies for GI soft robots. (A) Effervescent chemical reaction in rocket-like micromotors generates gas bubbles for self-propelled oral drug delivery *in vivo*. Reprinted with permission from [163]. Copyright 2023, Wiley VCH; (B) Catalytic degradation of P@G@NG releases NO in a multistage sequence along the GI tract to target colitis and modulate intestinal microbiota. Reprinted with permission from [167]. Copyright 2024, Wiley VCH; (C) Water-absorption-driven barbed microneedles swell and retain in tissue under peristaltic forces, with layered barb geometry optimizing retention strength. Reprinted with permission from [139]. Copyright 2024, American Association for the Advancement of Science; (D) Biohybrid algae-macrophage nanoparticle robots combine self-propulsion and immune cell targeting to treat inflammatory colitis, modified from [174]. Created with BioRender.com. GI: Gastrointestinal.

force and poor environmental adaptability. Therefore, integration with other responsive mechanisms, such as magnetic and chemical stimuli, is necessary to enhance locomotion performance. Biohybrid actuation combines the autonomous motility of living cells with the controllability of artificial materials [172], improving biocompatibility and biodegradability of soft medical robots. Magnetic particle-immobilized soft microrobots (MSCSMs) exemplify such biohybrid systems [173]. Mesenchymal stem cells provide exceptional tissue-like softness and biocompatibility, enabling adaptive *in vivo* morphology changes through reconfigurable transformations. By integrating the robust motility of green algae with the binding affinity of macrophage membrane-coated nanoparticles, Li *et al.* developed a biohybrid microrobot capable of

capturing and removing multiple proinflammatory cytokines *in vitro* [Figure 6D]^[174]. Although these novel actuation technologies remain in exploratory stages, they open new avenues for diversifying the capabilities of soft robotic systems.

FUNCTIONS AND APPLICATIONS

The functionalities and applications of GI soft robots represent the ultimate manifestation of their technological value, encompassing multiple levels ranging from fundamental navigation and localization to complex minimally invasive procedures. Based on clinical requirements and technological implementations, their primary functions can be categorized into four major areas: navigation and localization, drug delivery and controlled release, *in vivo* information acquisition, and minimally invasive manipulation and therapy. These functional modules can operate independently or synergistically through system integration, thereby providing comprehensive technical support for the diagnosis, treatment, and monitoring of GI diseases.

Navigation and localization

Significant advancements have been made in the precise intraluminal locomotion and stable positioning of GI soft robots. Magnetic actuation navigation systems enable free movement within 3D space through precise control of external magnetic fields. As shown in Figure 7A, a magnetic multilayer soft robot employs interlayer magnetic interactions to achieve on-demand detachment and simultaneous multi-target therapy^[52]. When the external magnetic field strength exceeds 15 mT, precise motion control is possible, allowing flexible navigation on the gastric tissue surface alongside prolonged adhesion. The shape-morphing magnetic patch robot (PatchBot) achieves complex morphological transformations via multilayer architecture and near-infrared laser actuation^[146], exhibiting high maneuverability and selective adhesion capabilities. Adaptation to the mucus-covered environment remains a critical challenge for GI navigation. A low-friction soft robot driven by AMF demonstrates efficient crawling on mucus-coated soft tissue surfaces^[53]. Its hydrophobic coating increases the surface contact angle beyond 120°, effectively minimizing mucus adhesion resistance. The development of real-time localization technologies provides robust support for precise navigation. Figure 7B illustrates a radio frequency identification (RFID)-based positioning system that utilizes received signal strength indication (RSSI) to achieve centimeter-level spatial resolution with a maximum detection depth of 15 cm^[82]. This system offers effective control of robots in visually occluded environments. A magnetically-actuated ultrasound capsule integrates magnetic actuation with ultrasound imaging^[175], allowing real-time *in vivo* tracking and delivering visual feedback for complex navigation tasks. A hydrogel-coated containment capsule of magnetic LM not only enables remote wireless magnetic hyperthermia therapy but also exhibits excellent radiopacity under X-ray imaging due to the high density of LM^[123], facilitating accurate *in vivo* localization and tracking. Localization techniques frequently combine medical imaging modalities, such as ultrasound and X-ray, with visual feedback to enhance navigation accuracy and safety^[176]. GI soft robots predominantly rely on external magnetic fields as wireless actuation sources. Combined with multimodal locomotion strategies, this approach effectively overcomes challenges imposed by GI tract peristalsis, mucus layers, and complex anatomical geometries^[177-179]. Nevertheless, the effective range of magnetic actuation remains limited, and reliance on large magnetic field generation equipment is significant. Further efforts are required to improve system portability and clinical applicability.

Drug delivery and controlled release

Drug delivery and therapeutic functions represent some of the most clinically valuable applications of GI soft robots. These systems significantly enhance the precision and efficacy of pharmacological treatments through targeted delivery, controlled release technologies, and protection of macromolecular drugs. The pH gradient within the GI environment provides a natural trigger mechanism for intelligent drug delivery systems. For instance, a double-layered polysaccharide hydrogel (DPH) leverages pH differences to achieve

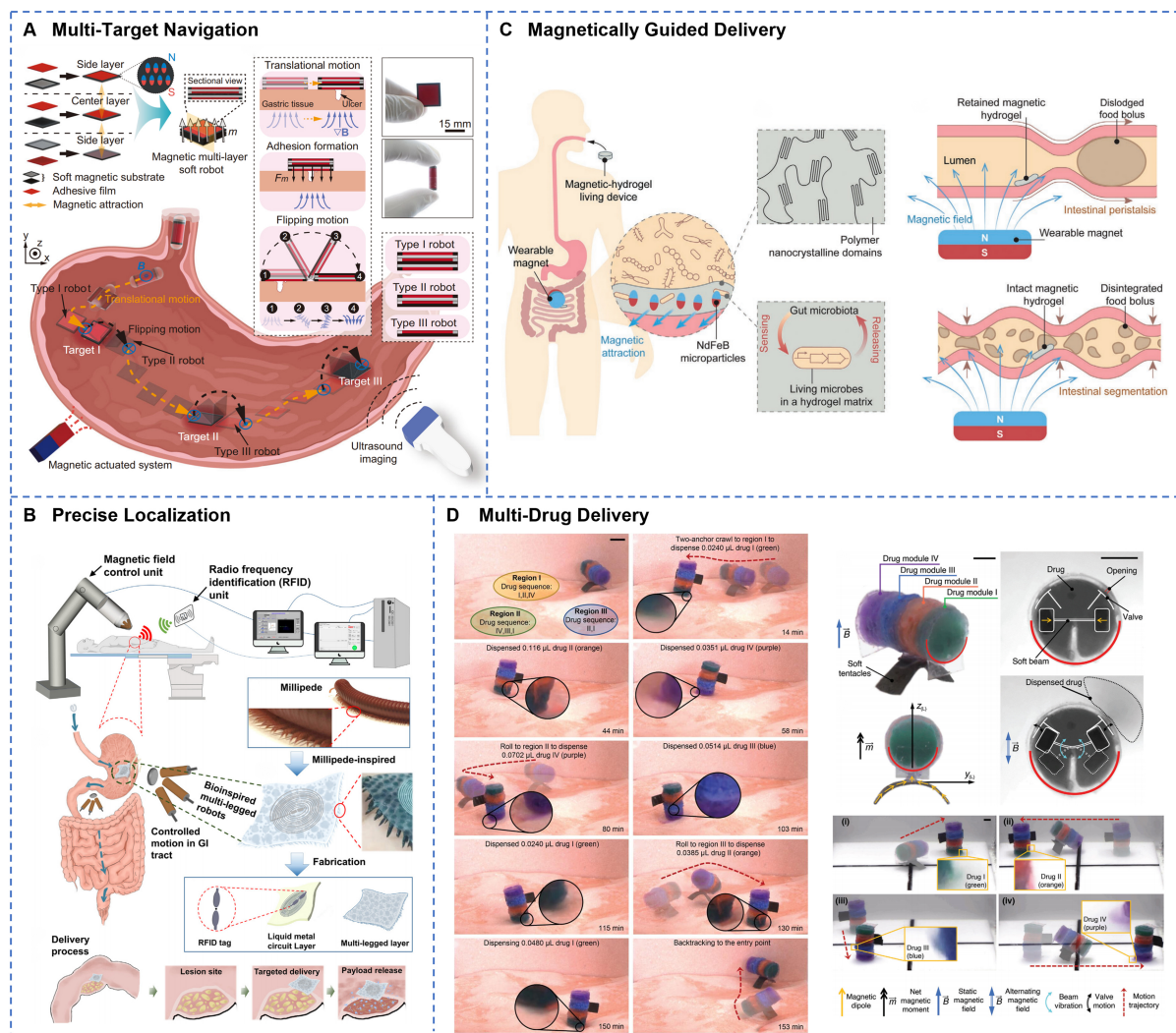


Figure 7. GI soft robots for precise navigation, localization, and targeted drug delivery within the digestive tract. (A) Magnetic multilayer soft robot achieves on-demand targeted drug delivery and adhesion to gastric ulcers through programmable flipping and translational motions under ultrasound guidance. Reprinted with permission from [52]. Copyright 2024, Springer Nature; (B) RFID-equipped millipede-inspired soft robot enables precise magnetic localization and controlled intragastric navigation for site-specific drug delivery throughout the digestive tract. Reprinted with permission from [82]. Copyright 2023, Elsevier Inc.; (C) A magnetic living hydrogel designed for targeted GI localization and retention via magnetic navigation. Reprinted with permission from [181]. Copyright 2021, Wiley VCH; (D) Programmable soft robot dispenses four distinct drugs with reprogrammable sequences and dosages at multiple targeted regions using magnetic two-anchor crawling locomotion. Reprinted with permission from [182]. Copyright 2024, Wiley VCH. GI: Gastrointestinal; RFID: radio frequency identification.

gut-specific release of probiotics [128]. The probiotics are protected by the closed cage structure of the DPH in the acidic gastric environment and are subsequently released at a rate of 90% within 6 h upon exposure to intestinal fluids. The probiotic count is increased by 239.5-fold compared to controls. A rocket-inspired effervescent micromotor uses chemically generated bubbles to propel and efficiently deliver macromolecular drugs such as insulin to the intestine [163]. Localized treatment is enabled by precise robot positioning and prolonged retention, facilitating high-concentration targeted drug administration. Nevertheless, the GI mucus layer and epithelial barrier impose limitations on drug penetration depth, local bioavailability, and retention time at target sites, thereby reducing therapeutic efficacy. To overcome these obstacles, several strategies have been proposed, including permeation enhancers to improve mucosal

penetration, microneedles or mechanical anchors to enhance local retention, magnetic targeting for prolonged localized release, and modulation of release kinetics to align with the *in vivo* residence time of the robotic device, thereby optimizing therapeutic outcomes. Wu *et al.* developed insulin-loaded, milk-derived exosomes (EXO@INS), enriched with negatively charged phospholipids and hydrophilic proteins^[180]. Their exosomal membranes serve as natural permeation enhancers, markedly improving traversal of the mucus barrier and demonstrating substantial potential for insulin delivery. A swellable microneedle robot enhances mucosal adhesion through peristaltic relaxation and barbed^[139], hook-like features, thereby overcoming gastric acid and enzymatic barriers to facilitate trans-mucosal penetration and sustained drug release within the intestine. As shown in Figure 7C, magnetically responsive hydrogels demonstrate site-specific retention in the murine intestine for up to seven days through attraction by external magnets^[181]. The integrated genetically engineered bacteria can detect biomarkers such as heme, thus enabling combined diagnostic and therapeutic functions. Tough *in situ*-forming gastric double-network hydrogels finely modulate the release rate by adjusting parameters such as network density and geometric dimensions^[57]. Using this hydrogel as a carrier, lumefantrine exhibits an area under the curve (AUC) comparable to the free drug, delivering equivalent total drug dosage at lower plasma concentrations and potentially mitigating drug toxicity. As depicted in Figure 7D, a multimodal reconfigurable capsule robot utilizes modular design to fulfill multi-site drug delivery requirements^[182], providing selective release of multiple therapeutics and sustained treatment effects. To conclude, soft robotic drug delivery systems have shown promising therapeutic potential in clinical models, including diabetes^[124], inflammatory bowel disease, intestinal microbiota modulation^[167], and colorectal cancer^[183]. However, systematic optimization is still required to address limitations related to drug-loading capacity, controlled dosage release, and long-term stability.

***In vivo* information acquisition**

GI soft robots integrate diverse *in vivo* information collection capabilities, including sample acquisition, biochemical sensing, and physiological monitoring. For example, Sun *et al.* developed a multimodal responsive magnetically actuated capsule featuring a unique dual-layer magnetic soft valve structure [Figure 8A]^[134]. This design enables efficient localized valve opening for drug release and sampling. The capsule's innovative helical shell facilitates active removal of the mucus layer on the intestinal wall during rotation, providing robust technical support for targeted sampling and delivery. Wireless millimeter-scale soft robots can navigate *in vivo* and deploy a microscale viscosity sensor to monitor intestinal mucus viscosity in real time^[184]. This capability enables *in situ* rheological sensing of deep tissue environments, applicable to disease monitoring in conditions such as cystic fibrosis. An ingestible device incorporating a sensing electrode ribbon expands upon this by unfolding within the stomach to contact the mucosa^[185]. It records high-quality bioelectrical signals from the gastric environment, including mucosal gastric slow waves, respiratory rate, and heart rate. Wang *et al.* demonstrated a method using soft robots to sense physiological tissue properties *in situ*^[186]. They utilized X-ray or ultrasound imaging *ex vivo* to measure adhesion, pH, and viscoelasticity of pig and mouse GI tissues, suggesting potential applications for sensing peptic ulcers *in vivo*. A miniaturized capsule combining genetically engineered probiotic biosensors with a custom photodetector chip enables real-time detection of labile inflammatory biomarkers within the GI tract and supporting wireless data transmission^[187]. In Figure 8B, a soft robot equipped with electronic armor achieves multiplexed simultaneous tactile and strain sensing via bioinspired artificial synapse mechanisms^[188]. This technology shows great promise in intelligent colonoscopy. Imaging and detection technologies further extend the capacity of soft robots for *in vivo* information acquisition. Artificial intelligence-driven wireless video capsule endoscopy performs real-time image processing that enhances visualization of the mucous layer^[189]. Through the integration of sensors and smart materials, these systems provide multidimensional sensing of complex physiological environments, supplying precise *in vivo* data to support disease diagnosis and therapy^[190-193]. Current challenges include ensuring the long-term stability of sensors, improving data transmission efficiency, and integrating imaging-based navigation within living systems.

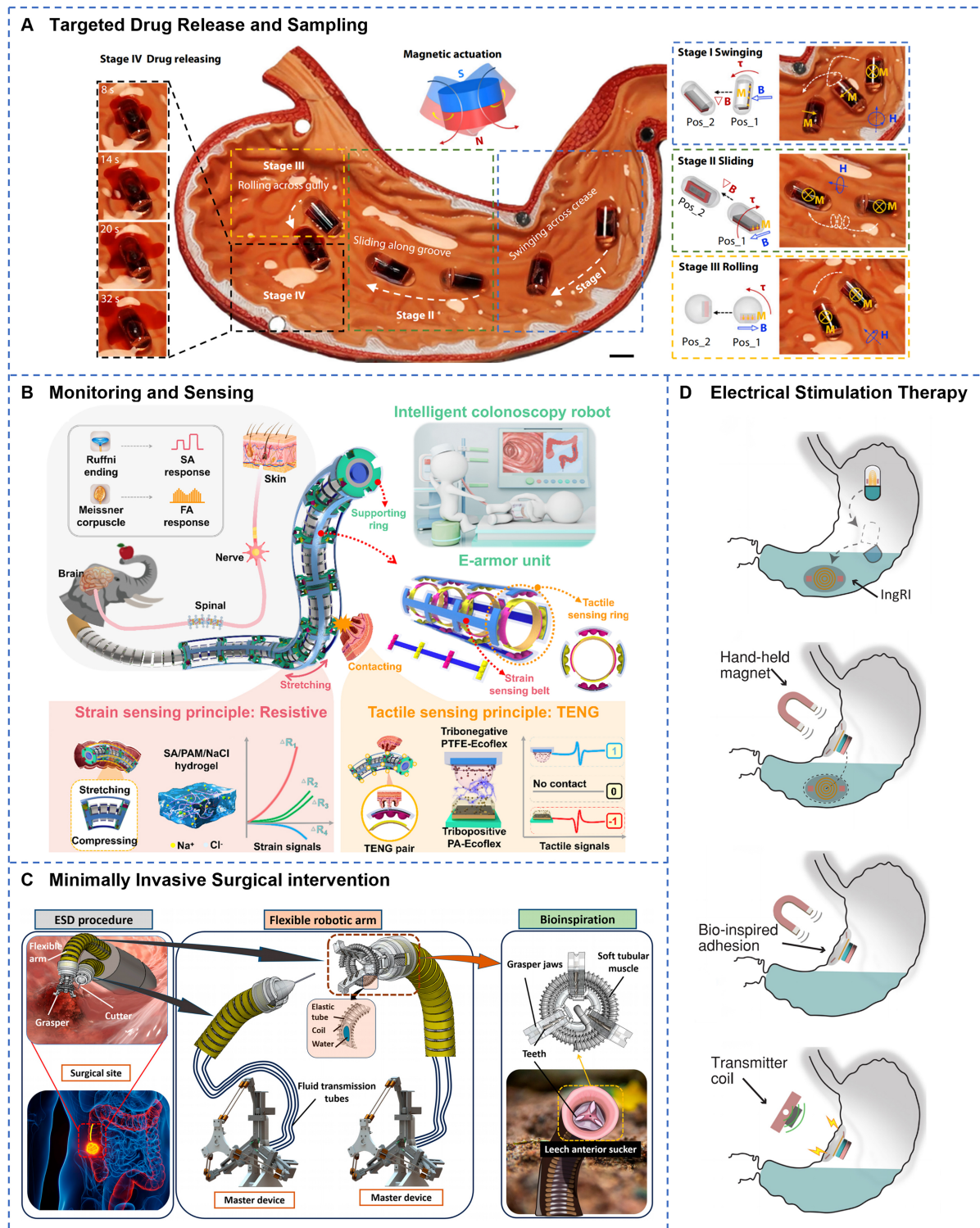


Figure 8. GI soft robots for *in vivo* information acquisition and minimally invasive therapies. (A) Magnetically actuated capsule robot performs targeted tissue sampling through four-stage operation: swinging, sliding, rolling, and high-frequency magnetic field-triggered drug release. Reprinted with permission from ^[134]. Copyright 2024, Springer Nature; (B) Triboelectric E-armor system integrates multimodal tactile sensing for real-time detection and acquisition of colonoscopic examination data. Reprinted with permission from ^[188]. Copyright 2025, Wiley VCH; (C) Hydraulic-driven soft endoscopic system features 3-DOF cutting arm and teleoperated grasper for minimally invasive colon lesion manipulation and surgical intervention. Reprinted with permission from ^[157]. Copyright 2025, Beijing

Institute of Technology Press; (D) Ingestible robotic interface delivers programmable electrical stimulation via near-field inductive coupling, adhering to gastric mucosa for chronic neuromodulation therapy. Reprinted with permission from^[196]. Copyright 2024, Springer Nature. GI: Gastrointestinal.

Minimally invasive manipulation and therapy

Minimally invasive procedures represent a crucial direction in the development of GI soft robot technology. These encompass biopsy, suturing, cutting, mucosal repair, foreign body removal, and functional actuation. A soft inflatable cable-driven parallel robot provides five degrees of freedom in spatial motion and variable stiffness control through pneumatic inflation and cable actuation^[194]. This system enables suturing tasks during GI endoscopic surgery. As shown in Figure 8C, Zhu *et al.* developed a biomimetic grasper-electrocautery hybrid system actuated by magnetic and hydraulic dual soft drives^[157]. Remote operation is achieved by pressure transmission, allowing submillimeter precision grasping and cauterizing within the colon. Nguyen *et al.* designed a motor-free soft robot that achieves positional errors below 300 μm ^[195]. By combining hydraulic actuation with microelectrodes and optical fibers, the robot can perform electrical impedance-based cancer lesion detection and radio-frequency ablation. It also supports *in situ* 3D printing for internal wound healing. These systems emphasize compliance and precise control in both structural design and actuation methods, significantly reducing the risk of tissue damage while improving surgical safety and accuracy. Beyond assisting surgical maneuvers, soft robots are also applied in the treatment of GI disorders. Nan *et al.* developed an ingestible, battery-free robotic interface driven by near-field inductive coupling technology [Figure 8D]^[196]. This device delivers noninvasive GI electrical stimulation, effectively increasing ghrelin levels. Wu *et al.* reported a biodegradable, self-powered electronic bandage fabricated from soft materials that accelerates intestinal wound healing^[197]. Addressing postoperative ileus, Srinivasan *et al.* designed an ingestible self-propelling device for intestinal reanimation^[198]. This system restores peristalsis through luminal electrical stimulation and demonstrated a 44% improvement in intestinal contraction in anesthetized animals. Integration of multifunctional capabilities is a key trend in minimally invasive intervention. Combining diagnostics, therapy, and monitoring on a single platform facilitates one-stop medical services^[199,200]. Future developments should focus on improving force feedback, real-time imaging, and automation control technologies to achieve higher levels of minimally invasive treatment.

CONCLUSION AND OUTLOOK

This review primarily elucidates the current technical characteristics and application scenarios of GI soft robots from materials, structures, actuations, and functional applications. Firstly, we summarize materials applied in GI soft robots, where biocompatible soft elastomers serve as the foundation, functional materials impart intelligent responsiveness, and the combination of various materials is increasingly adopted. Secondly, we focus on structural engineering, outlining design strategies from continuous encapsulation to modular-reconfigurable structures, and exploring the integration of existing robotic functional units with biomimetic structures. Furthermore, we systematically categorize major actuation manners of field-driven, fluid-driven, and self-driven chemical reactions, highlighting the diverse evolution of actuation mechanisms for the complex GI environment. Finally, we extensively explore the applications of GI soft robots across multiple levels, spanning navigation, localization, and minimally invasive interventions.

However, GI soft robots still face a range of challenges. Firstly, precise navigation and targeting remain limitations due to the complex intestinal environment, where robots struggle to reach specific sites and oral delivery faces premature degradation in gastric acid and poor targeting in the intestine. Meanwhile, limited

battery life remains a major challenge for GI soft robots, as current devices typically have low-capacity power sources that restrict operating time and overall performance. Moreover, environmental adaptability is also critical, as GI soft robots must navigate the uneven GI surface. Current technologies, however, lack precise positional control, fail to conform to lesion sites, and leave certain regions inaccessible, creating diagnostic and therapeutic blind spots. Besides, current soft robots face issues in precision, flexibility, and accessibility within confined GI spaces, while these robots must operate safely *in vivo* and be excreted or degraded, imposing strict demands on material selection and design.

GI soft robotics technology is entering a new era characterized by noninvasiveness, targeted functionality, and intelligent capabilities. In response to the associated challenges, feasible solutions and a clear development roadmap are proposed. In the short term, over the next 12 to 18 months, four major technological breakthroughs can address key current bottlenecks. Firstly, in navigation, localization, and drug delivery, integrated magnetic-RFID-ultrasound tracking technologies can achieve sub-centimeter spatial accuracy, while enteric coatings or pH-responsive polymer encapsulation can overcome premature degradation in the gastric environment and improve intestinal targeting in oral delivery. Secondly, regarding power and endurance, incorporating wireless power transfer and energy harvesting modules or employing battery-free triggering mechanisms can significantly extend operational time and enhance overall performance. Thirdly, to improve environmental adaptability, low-friction coatings, variable-stiffness materials, and shape-memory structures can be applied to robot surfaces to achieve effective attachment and detachment control on the uneven GI mucosa. Lastly, for operational safety, controllable biodegradable or excretable materials should be selected, guided by comprehensive toxicological evaluation systems to minimize *in vivo* residual risks.

In the long term, GI soft robots must meet critical requirements for clinical translation. First, they must demonstrate *in vivo* biocompatibility and safety by utilizing biocompatible materials to prevent toxic reactions and immune rejection, while ensuring safety for long-term implantation or *in vivo* operation. Second, comprehensive large animal safety and efficacy evaluations conforming to Good Laboratory Practice (GLP) standards are required to reliably validate performance and comply with regulatory requirements. Third, the robots must ensure compatibility with clinical imaging modalities such as X-ray, CT, and MRI to avoid significant interference and imaging artifacts. Furthermore, safety thresholds for localized tissue heating and electromagnetic stimulation should be established to protect surrounding tissues from damage.

By fulfilling these preclinical prerequisites, GI soft robots are expected to evolve from simple drug carriers into highly integrated diagnostic and therapeutic platforms, driving precision medicine toward minimally invasive, intelligent, and personalized approaches. Ultimately, they will become a new generation of noninvasive, targeted, and smart systems for the diagnosis and treatment of GI diseases. In terms of diagnosis, they are suitable for home-based assessment of acute symptoms, integrating big data and hospital networks to enable coordinated management. For therapy, these robots can achieve precise drug release and long-term sustained delivery, significantly enhancing drug utilization and enabling home treatment of chronic diseases. In summary, GI soft robots are reshaping digestive healthcare by surpassing the spatial and functional limits of conventional medical tools. Their development paves the way for next-generation systems towards minimally invasive, site-specific, and intelligent diagnosis and therapy of GI diseases.

DECLARATIONS

Authors' contributions

Designed and organized the project: Du, M.; Xie, Z.; Wang, X.

Manuscript writing: Du, M.

Manuscript supervision: Xie, Z.; Wang, X.

All authors have given approval to the final version of the manuscript.

Availability of data and materials

Not applicable.

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Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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