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# The applications of flexible electronics in dental, oral, and craniofacial medicine

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Dental, oral, and craniofacial diseases jeopardize health and reduce the quality of life. Accessing disease-related signals in advance is beneficial to prevent the occurrence or progression of those diseases. However, the inconvenience of periodical in-hospital examinations and the difficulty of sustaining daily health monitoring challenge personal compliance and possibly lead to limited prevention or treatment. Medical flexible electronics are electric devices fabricated on soft and extensible substrates to fit the human skin and enable non-invasive continuous monitoring of biophysical/biochemical signals. They provide the possibility of long-term, continuous, comfortable, and wireless healthcare monitoring and are expected to alleviate time and economic consumption by avoiding in-hospital examinations and treatment. Therefore, flexible electronics have emerged for early diagnosis and disease monitoring in stomatology. It is noteworthy that special biophysical/ biochemical characteristics and the environment of dental, oral, and craniofacial areas bring distinct challenges that flexible electronics need to address ingeniously to ensure their stability, selectivity, and sensitivity. This review summaries flexible electronics and their specificity when used in dental, oral, and craniofacial applications, including monitoring saliva or cavity-gas related biosignals, sensing the mechanical fluctuation from facial muscle/respiratory activities or orthodontic forces, and executing special functions in the prevention or postoperative recovery of relevant diseases. Furthermore, after analyzing current challenges and proposing potential solutions, the "51" principles of imperceptibility, intelligence, individualization, integration, and inexpensiveness are presented to help guide the future development of flexible electronics and promote their commercialization for dental, oral, and craniofacial medicine.

Dental, oral, and craniofacial health is closely related to the quality of both physical and social life. Commonly, dental, oral, and craniofacial diseases include caries, periodontal disease, oral mucosal disease, malocclusion, and benign/malignant tumors in the oral/craniofacial region. Treatment of these diseases is not only time-consuming and causes inconvenience and embarrassment in daily life but also induces a great financial burden<sup>1</sup>. Given that the progression of most oral and craniofacial diseases is slow, implementing diagnosis and treatment at early pathological stages can effectively prevent exacerbation, significantly improve the prognosis and the quality of life, and also avoid potential time/economy consumption relating to

treatment. However, existing diagnostic methods in stomatology mainly rely on artificial examination and imaging technologies and thus have limitations in real-time health monitoring and disease diagnosis regardless of time and place<sup>2</sup>. After sufficient treatment, monitoring therapeutic effects and recovery also challenges patient compliance due to the inconvenience and excessive costs of re-examination in the hospital. The lack of point-ofcare diagnosis hinders the implementation of primary prevention to sustain dental, oral, and craniofacial health.

Medical flexible electronics are electric devices fabricated on soft and extensible substrates that fit the human skin to enable non-invasive

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continuous monitoring of health and even participate in disease treatment/ recovery<sup>3</sup>. These miniaturized devices have the advantages of portability and wearability to realize continuous and prolonged monitoring of biophysical or biochemical signals without limitations in time and places. These benefits help to avoid interference with daily life, alleviate the economic burden, and thus endow the devices with great potential for application in point-of-care diagnosis. Currently, flexible electronics have been widely used in everyday life as well as medical practises<sup>4</sup>. In the field of stomatology, flexible electronics have also been gradually utilized for preventing the progression of dental, oral, and craniofacial diseases and judging the corresponding prognosis. After adjusting the design, construction, and material constituents according to the special biophysical/biochemical properties and environment in dental, oral, and craniofacial areas, flexible electronics can detect the levels of various factors relating to oral hygiene, orthodontic forces, and even cancer biomarkers, and thus help to make predictions of oral health status in time.

In this review, we summarize the mechanisms and applications of flexible electronics applied in teeth, oral cavity, and craniofacial regions, and analyze challenges in the current medical practices of these promising devices. Finally, we discuss the potential strategies to improve the device performance and prospect the future trend of flexible electronics in stomatology.

# A brief introduction to flexible electronics and their specificity when applied in stomatology

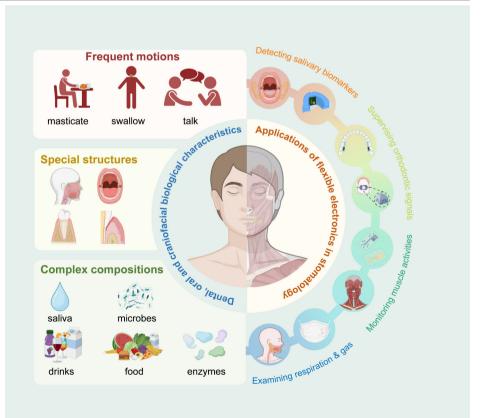
Generally, flexible electronics are designed as wearable sensors<sup>5</sup>. In daily life, they often present in the form of wireless electronic devices coupled to wristwatches to monitor basic physiological characteristics such as heart rate and skin temperature<sup>6</sup>. With the development of micromachining, electronics, and sensors, the types of flexible electronics expand greatly. These devices can be mainly categorized into two groups according to their functions of monitoring biophysical or biochemical signals: the former examines electrophysiology, motions (e.g., feedback from prosthetics),

temperature changes, intrinsic thermal, electrical, or mechanical properties of the skin, and vascular dynamics, while the latter detects metabolites and electrolytes in body fluids such as saliva, sweat, tears, and interstitial fluid<sup>7</sup>. Flexible electronics usually consist of a substrate, stretchable interconnects, and sensing elements. The substrate is required to be both flexible and elastically stretchable to ensure that it fits the human skin perfectly. The materials used for substrate fabrication also need to be durable to maintain their sufficient lifespan. Besides adopting intrinsically-specific or chemically-modified materials for fabricating the substrate and interconnection, deterministic geometries, such as serpentine, rotating square tessellations, nanocurve circuits, and wavy structures, are also utilized to enhance the device flexibility and scalability<sup>3,8,9</sup>. Conductive interconnects are fabricated on the substrate to enable electronic functions such as information transmission or electrochemical detection, mainly using micro/ nano-fabrication methods to deposit or print either metals or non-metallic but conductive materials (carbon nanotubes (CNTs), graphene, conductive hydrogels, etc.). Sensors used for flexible electronics are either biosensors or electronic sensors<sup>10</sup>. Biosensors access biological activities by targeting biomolecules based on immobilized bioactive molecules onto the constructed electrodes. Electronic sensors usually adopt materials with specific electric properties to enable the detection or measurement of the targets. For example, some devices utilize piezo-elastomeric substrates to capture mechanical signals of human tissues, and some other devices use optoelectronic nanohybrids that allow photon absorption, exciton dissociation, and charge-carrier transfer and transport to achieve optical signal acquisition<sup>11,12</sup>.

Compared to devices applied to other parts of the body, flexible electronics used in dental, oral, and craniofacial areas have to address some special situations (Fig. 1):

(1) Due to the frequent motions of both craniofacial muscles and the tongue during speaking, chewing, and swallowing, flexible electronics for dental, oral, and craniofacial applications are subjected to much more times of deformation and friction (e.g., against teeth and tongue) compared to

Fig. 1 | Flexible electronics applied in stomatology. Dental, oral, and craniofacial regions have specific features such as frequent motions, special structures, and complex compositions, which bring special challenges for flexible electronics applied here. Currently, applications of flexible electronics in stomatology focus on salivary biomarkers detection, orthodontic signals supervision, facial activities monitoring, and cavity-gas/respiration detection.



other kinds of wearable devices. Therefore, they require great extensibility and durability, meanwhile, they should keep good adhesion to the craniofacial skin or the moist surface of teeth, tongue, or oral cavity. It is noteworthy that flexible electronics applied inside the oral cavity should avoid the possibility of accidental detachment, which may lead to respiratory tract block. Moreover, comfort should be considered as well, given the long-time wear and frequent facial motions in daily life.

(2) Materials for fabricating flexible electronics in dental, oral, and craniofacial applications should ensure sufficient biocompatibility. Since these devices adhere to the surface of human tissues for a long time, the substrates, as well as adhesives, need to be chemically friendly to the skin or mucosa and would not cause irritation nor immune response<sup>13,14</sup>. Especially since that oral cavity directly connects the digestive tract and flexible electronics applied here in long-term contact with various acidic/alkaline substances (from food/drink or microbial metabolism) and enzymes in saliva, materials used for device fabrication should have excellent chemical inertness or been well-encapsulated by other inert and biocompatible materials, or they should be non-toxic and edible (both the materials themselves and their degradation/abrasion products) when intaken into digestive tract<sup>15</sup>.

(3) The functions of flexible electronics should be stable enough to endure the complex environment with various pH conditions in the moist oral cavity that contains enzyme-rich saliva, food/drink residue, and abundant bacteria. The abundant bioactive molecules and bacteria in the oral cavity greatly challenge the selectivity and sensitivity for target detection and analysis.

According to these peculiarities, various strategies have been developed to ensure the performance of dental, oral, and craniofacial flexible electronics and also the health of the users, mainly through adopting specific materials for device fabrication. Hydrogels that can be attached to skin and have great self-healing ability and load-bearing performance have been excellent choices for fabricating flexible substrates in stomatology scenarios. For instance, organic resin materials such as polyethylene terephthalate (PET), polyimide (PI), and polydimethylsiloxane (PDMS) are widely used due to their excellent durability and flexibility properties. To adapt to the frequent deformation during speaking, chewing, and swallowing, some additives are mixed into the aforementioned hydrogels to increase their stretchability. Some researchers added gallium (Ga) into hydrogel fabricated from sodium alginate (SA) and polyacrylamide (PAm) and obtained good performance when executing repeated mechanical movements since that the dynamic cross-linking between hydrogel ingredients and Ga ions strengthened mechanical properties<sup>16,17</sup>. MXene is another additive that can improve the hydrogel with satisfactory structural stability and excellent deformability<sup>18-20</sup>. Otherwise, chitosan-rich hydrogel, CNTs, and graphene oxide (GO) nanosheets can also endow flexible electronics with great mechanical properties<sup>17,21-23</sup>. For fabricating electrodes, adopting Cu/PI organic-inorganic composite can help improve deformability when maintaining essential conductivity<sup>24,25</sup>. It is also necessary to design specific structures (e.g., serpentine) of the electrodes to enable the tensile strength<sup>26</sup>. In order to enhance the adhesion of flexible electronics to facial skin, silk, poly(N-isopropylacrylamide) (PNIPAM), and other materials can be used to modify hydrogels to increase the covalent and non-covalent interactions<sup>21</sup>, while some other flexible electronics used to detect physical and biological signals in the oral cavity are mainly attached to mouth guards by using medical-grade epoxy or pastes<sup>27-29</sup>. In addition, for moist surfaces, it has been reported that flexible devices using water-soluble tape or silk can closely attach to the tooth surface after being dissolved by saliva<sup>24,30</sup>.

For flexible electronics in dental, oral, and craniofacial applications, especially those used inside the oral cavity, the biocompatibility of materials used should be good enough when experiencing various enzymes and pH conditions of saliva. Many natural hydrogels that are edible, such as chitosan and cellulose, are adopted for device fabrication<sup>17,19</sup>. Another strategy is employing chemically inertial materials (e.g., PDMS, silk film (SF), parylene, and silicone) to embed electric materials<sup>19,31–34</sup>. When constructing the electrodes of flexible electronics, metals like Ag, Pt, and Au, and conductive nano-materials such as CNTs and MXene, which have been proven to show

little toxicity under limited dosage, are employed to ensure ample biological safety<sup>19,21,22,31,35</sup>. For sensors that are commonly attached to mouthguards, aligners, or pacifiers, it is crucial to disinfect these items beforehand to ensure their sterility and biosafety<sup>29</sup>, and their constituents also mainly adopt biocompatible materials such as Prussian-blue (PB) transducer and fluorescent zinc oxide quantum dots (ZnO QDs)<sup>27,28,34,35</sup>.

In order to ensure the good working performance of dental, oral, and craniofacial flexible electronics, it is important to encapsulate their electrodes and sensors<sup>31,35,36</sup> to resist the humid and complex environment in the oral cavity or breathing gas. For example, carbon nanofibers mats are added beneath the surface of mask-like sensors to resist humidity<sup>36</sup>. In other flexible electronics, inert or hydrophobic PDMS, poly(MPC-co-EHMA-co-MBP) (PMEHB), polyvinyl butyral (PVB), polyethylene naphthalate film, and acrylic pressure sensitive adhesive have been used for package. For instance, to minimize biofouling and interference effects from saliva constituents, poly-orthophenylenediamine (PPD) is utilized for packaging an entire oral sensor<sup>27,28</sup>, while PMEHB, silicone, Nafion solution, and PVB mainly help to minimize the interference on electrodes<sup>31,35,37,38</sup>. Additionally, cellulose acetate (CA) membrane can be specifically employed to combat various bacteria present in the mouth<sup>35</sup>.

Furthermore, it is necessary to enhance the selectivity of flexible electronics applied in complex oral environments. PPD could be embedded in those devices to enhance the performance of enzymatic, ionophore-based, or electrochemical determination of biochemical signals in saliva and oral gases<sup>28</sup>. For electrochemical analysis, the utilization of multiple capacitive channels can assist in mitigating interference among diverse analytes, thereby improving the accuracy and reliability of the measurements<sup>27</sup>. Other highly sensitive materials (e.g., MXene, PNIPAM)<sup>19,32</sup> can be used as well. For example, the modified polyaniline (PANI) and PVB with increased porous structures coated on electrodes can enhance their ability to enrich ions, thereby boosting the sensitivity of the sensing process<sup>31</sup>. In addition, improving the electrode patterns or array shapes can also improve the sensitivity<sup>21,26</sup>.

# Flexible electronics applied in oral, dental, and craniofacial scenarios

Flexible electronics have the advantages of good sensitivity, short response time, and non-invasiveness<sup>39</sup>, therefore they can be applied in the dental, oral, and craniofacial areas to realize the real-time monitoring of health state and play an important role in the prevention of disease occurrence/progression, timely feedback of therapeutic effects and finally benefit long-term oral health maintenance.

#### **Detecting biochemical signals**

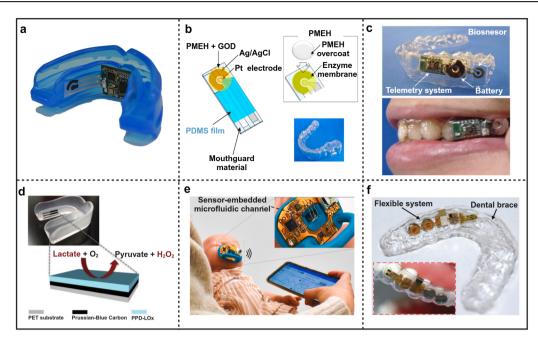
Biochemical signals in the oral cavity coming from saliva or cavity gas can be used as indicators for oral health status (Table 1). Common saliva-based biomarkers include uric acid (UA), glucose, lactic acid (LA), and various electrolytes, while oral cavity gas-based biomarkers are mainly ammonia (NH<sub>3</sub>), volatile sulfide compounds (VSCs), and so on.

#### Saliva-based biomarkers

Metabolites, biomolecules, and a variety of ionic compounds in saliva can reflect the health status of human body<sup>40,41</sup>. Measuring levels and changes of various substances in saliva by flexible electronics can guide disease diagnosis and treatment, and is a good alternative to invasive tests such as blood tests.

Uric acid is a biomarker for a variety of diseases such as gout and hyperuricemia. Kim et al. fabricated a mouthguard biosensor to monitor UA in saliva using a well-established method by screen-printing the sensor on a flexible polyethylene terephthalate substrate (Fig. 2a)<sup>27</sup>. A working electrode, PB transducer, was made by crosslinking the uricase enzyme and electropolymerizing o-phenylenediamine. A Bluetooth low energy chipset was integrated to achieve wireless connectivity with smartwatches, cell phones, or computers. The device employed the uricase to implement high selectivity, sensitivity, and stability to measure salivary UA and avoid

Applications	Device characteristics	(6			Targets	Real-world trials	l trials				Reference
	Substrate	Sensor	Structure	Size		Device Lifespan	Conducting real-world trials	Participant number	Participant situation	Trial duration	
Detecting saliva- based biomarkers	Flexible PET substrate	PB transducer	*	$1.8 \times 1.9 \text{ cm}^2$	SUA levels	Five days	Yes	Two	Healthy or with hyperuricemia	Four days (three times a day)	27
	PETG	Platinum and silver/sil- ver chloride electrodes, GOD immobilized in PMEH	Cavity structure	$2.5 \times 0.5 \mathrm{cm^2}$	Saliva glucose	*	°N	*	*	*	38
	PETG	Platinum and silver/sil- ver chloride electrodes, GOD with CA coating	Cavity structure	$2.5 \times 0.5 \text{ cm}^2$	Saliva glucose	*	Yes	*	*	*	35
	Flexible PET substrate	Printable PB transducer and a PPD/LOx reagent layer	*	*	Saliva lactate	*	Yes	*	*	Two hours	28
	Film ISE	lon sensors	Microfluidic channel	0.05 cm long	Saliva sodium and potassium levels	Several hours	Yes	*	Infants	*	29
	Water-soluble silk fibroin films and large- area graphene monolayers	Bifunctional graphene- AMP biorecognition sensor	Coil structure	*	Bacteria on tooth enamel	*	N	*	×	*	30
	Polyimide substrate	Electrochemical sen- sors for Ca <sup>2+</sup> and pH sensing	*	31.5 × 8.5 × 1.35 mm <sup>3</sup>	Salivary Ca <sup>2+</sup> con- centration and pH values	Twenty hours	Yes	Ten	Caries-free or suf- fering from dental caries	Several minutes	31
	PDMS	PANI	Serpentine tracks	$10 \times 8 \times 1.5 \text{ mm}^3$	Salivary pH values	*	Yes	Two	*	During day time	50
	PET with Ag/AgCl reference electrode	Ca <sup>2+</sup> , pH and PO4 <sup>3–</sup> sensors	*	*	Ca <sup>2+</sup> , pH and PO4 <sup>3+</sup> in oral environment	One month	Yes	Two	*	Ten days	37
Detecting cavity gas-based biomarkers	Au/PET substrate	Bacterial cellulose/ Ti <sub>3</sub> C <sub>2</sub> T <sub>x</sub> MXene bioaerogel	3D porous structure	*	NH <sub>3</sub>	*	Yes	*	*	*	19
	ZnO-PDMS nano- composite material	Fluorescent ZnO QDs	Nanoporous structure	*	VSC gases	*	Yes	Eight	Healthy or with dental lesions.	Seven hours	34



**Fig. 2** | **Flexible electronics applied for detecting saliva-based biomarkers. a** A mouthguard biosensor monitoring salivary uric acid<sup>27</sup>. **b** A cavity sensor measuring salivary glucose<sup>38</sup>. **c** A cavity sensor for glucose detection with a cellulose acetate coating<sup>35</sup>. **d** A lactate detection mouthguard sensor based on the LOx products-

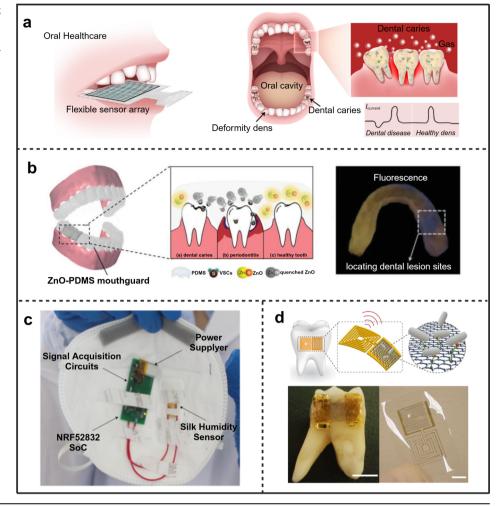
selective ability of Prussian blue<sup>28</sup>. **e** A smart pacifier continuously monitoring salivary electrolytes<sup>29</sup>. **f** A sensor monitoring the distribution of Ca<sup>2+</sup> and pH values on the tooth surface<sup>31</sup>. Panels **a**–**e** reproduced with permission. Panel **f** reproduced under Creative Commons (CC BY) license.

interference from ascorbic acid. It could respond stably to 300 µM UA, showing sufficient sensitivity when the abnormal UA value usually exceeded greater than 400 µM. Diabetes is a common cardiovascular disease whose diagnosis mostly depends on blood sugar detection (with fasting blood sugar (FBS) higher than 7 mmol  $L^{-1}$ <sup>42</sup>. Researches reveal that salivary glucose levels of healthy people (ranging from 0.5 to 4.8 mg  $dL^{-1}$ ) are statistically lower than diabetic patients (ranging from 1.26 to  $11 \text{ mg dL}^{-1}$ <sup>43,44</sup>, and the correlation of saliva glucose and blood glucose in individuals can be quantitatively determined as previously reported:  $FBS = 76.548 + (0.423 \times saliva glucose)$  for healthy people,  $FBS = 106.35 + (0.116 \times saliva glucose)$  for pre-diabetic patients, and  $FBS = 51.064 + (2.964 \times saliva glucose)$  for diabetic patients<sup>45</sup>. Accordingly, Arakawa et al. invented a cavity sensor to measure glucose in saliva, thus avoiding conventional invasive blood glucose testing and facilitating continuous dynamic monitoring of diabetes (Fig. 2b)<sup>38</sup>. The measurement of salivary glucose was mainly implemented by detecting the concentration of hydrogen peroxide produced by the enzymatic reaction of glucose oxidase (GOD). GOD was embedded within poly(2-methacryloyloxyethyl phosphorylcholine-co-2-ethylhexyl methacrylate) (poly(MPC-co-EHMA) or PMEH) and fixed on a customized monolithic mouthguard bracket with a wireless transmitter. This device ensured the specific monitoring of salivary glucose concentrations ranging from 1 to 1000  $\mu$ mol L<sup>-1</sup>, covering the concentration variation of 20–200  $\mu$ mol L<sup>-1</sup> required for medical monitoring. Afterward, they attached a CA coating to this sensor to prevent contamination from saliva (Fig. 2c)<sup>35</sup>. Kim et al. developed a mouthguard sensor based on a printable PB transducer and a PPD/lactate oxidase (LOx) reagent layer (Fig. 2d)<sup>28</sup>. This miniaturized and integrated device could be worn without professional guidance, enabling continuous noninvasive monitoring of lactate levels in a point-of-care manner for widespread scenarios. PB is highly selective for the products of LOx to detect lactate with a sensitivity of 0.1–1.0 mM. Newborns usually have difficulty in cooperating with invasive blood tests, and routine blood tests may lead to infections and even pediatric blood clots, sepsis, etc.<sup>46</sup>. Lim et al. developed a smart pacifier that continuously monitors salivary electrolytes in real-time. Several miniature ionic sensors made of fine metal wires were mounted in a microfluidic channel and inserted into a commercial pacifier. The microfluidic device was able to continuously draw saliva from the baby's mouth to monitor sodium (5.7–9.1 mM) and potassium (4.2–5.2 mM) levels in newborns (Fig. 2e)<sup>29</sup>. This device avoided the pain and risks associated with skin pricking during traditional blood tests, enabled continuous monitoring of the salivary electrolyte status of infants, and increased the cooperation of newborns with essential diagnosis.

Biomacromolecules in saliva can indicate the physiological/pathological status of the oral cavity as well. Mannoor et al. designed graphene nanosensors coupled with silk membranes and self-assembled antimicrobial peptides onto graphene monolayers to achieve biorecognition<sup>30</sup>. This device could monitor Helicobacter pylori in the oral cavity and thus prevent gastric ulcers. Li et al. designed a flexible conducting polymer electrode that could monitor salivary steroid hormones with low concentrations to reflect the female menstrual cycle<sup>47</sup>. The sensitivity of this device could reach  $11 \pm 4$  fM and eliminate a series of interferences in saliva such as urea, LA, glucose, and ascorbic acid.

Besides, salivary Ca<sup>2+</sup> concentration and pH values, as a reflection of the degree of enamel demineralization, can also indicate the situation and risk of individual caries<sup>48,49</sup>. Ling et al. designed a Ca<sup>2+</sup> and pH sensor electrode fabricated using Ca2+ ionophore II (ETH 129) and polyaniline, supplemented with a temperature sensor to reflect the effect of temperature fluctuation on electrochemistry (Fig. 2f)<sup>31</sup>. This sensor enabled the monitoring of the distribution of Ca<sup>2+</sup> and pH values on the tooth surface. The Ca<sup>2+</sup> sensor exhibited a linear response from 0.25 to 4 mM with a sensitivity of 30.3 mV decade<sup>-1</sup>, and the pH sensor exhibited a linear response to pH values from 4 to 8 with a sensitivity of 60.6 mV decade<sup>-1</sup> based on electrochemical measurement. The device contained PVB to enhance stability and electrodeposited gold nanoparticles (AuNPs) on the electrodes to improve the sensing performance, whose lifetime could last more than 20 days. In addition, the monitoring of pH variation in the oral microenvironment using a dental patch was realized<sup>50</sup>. Some flexible electronics could detect ion variation caused by dental caries during orthodontic treatment<sup>51,52</sup>. Liu et al. designed an integrated multiplex sensing clear aligner system that could attach to transparent aligners<sup>37</sup>. The device could reflect the varied  $Ca^{2+}$ , pH, and  $PO_4^{3-}$  in the oral environment in a real-time

**Fig. 3** | **Flexible electronics applied for detecting respiration or intraoral gas. a** A multifunctional flexible sensing platform detecting the localized release of NH<sub>3</sub><sup>19</sup>. **b** A wearable fluorescent mouthguard detecting the local release of volatile sulfur compounds<sup>34</sup>. **c** A CNT/SF hybrid materials combined into a facial mask to monitor respiration<sup>22</sup>. **d** Flexible electronics attached to teeth to achieve biorecognition<sup>30</sup>. Panels **a**–**d** reproduced with permission.



manner with electrochemical sensitivity of  $29.52 \text{ mV} \text{ decade}^{-1}$  of concentration for the Ca<sup>2+</sup> sensor,  $-10.52 \text{ nA} \text{ mM}^{-1}$  for the PO<sub>4</sub><sup>3-</sup> sensor, and 54.38 mV pH<sup>-1</sup> for the pH sensor, so as to prompt tooth demineralization.

In order to detect more than a single metabolite, Liu et al. proposed a dual-channel electrochemical biosensor for the simultaneous detection of lactose (with a sensitivity of 21.8  $\mu A$  mM $^{-1}$  cm $^{-2}$ ) and glucose (with a sensitivity of 18.7  $\mu A$  mM $^{-1}$  cm $^{-2}$ ) in saliva $^{53}$ . Since lactate is an intermediate product of glucose metabolism, simultaneous detection of dynamic trends of both lactate and glucose levels is important for preventing diabetic complications. This dual-channel biosensor was based on a flexible screen-printed PET-based electrode with two working electrodes so that the sensitivity and linear range of the two substances could be distinguished, thus avoiding interference between the two channels.

#### Cavity gas-based biomarkers

Detection of gases from the oral cavity, when dental caries or periodontitis occurs, is helpful for early diagnosis of these diseases. Pathogenic anaerobes potentially inducing periodontal disease and dental caries produce NH<sub>3</sub> and VSCs when consuming food residues<sup>54,55</sup>. Jin et al. utilized a degradable bacterial cellulose/Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub> MXene (BC/MXene) bioaerogel sandwiched between the patterned Au/PET substrates to design a multifunctional flexible sensing platform, which could detect the localized release of NH<sub>3</sub> (Fig. 3a)<sup>19</sup>. The 3D porous structure of BC/MXene bioaerogels ensured good gas sensitivity, and this material was easy to degrade to achieve environmental protection. Experiments proved that the device could use gas signals to reveal imperceptible dental lesions. Li et al. designed a transparent, wearable fluorescent mouthguard consisting of the zinc oxide–poly(dimethylsiloxane) (ZnO-PDMS) nanocomposite

to detect the local release of VSCs (Fig. 3b)<sup>34</sup>. Through observing fluorescence brightness variation, the device not only located VSCs to screen hidden dental lesion sites but also reflected the degree of the lesion. Although this research ruled out the influence of VSCs in gas and liquid states, factors such as different food residues would impact the results and the detection accuracy still needed to be improved for oral flexible electronics.

#### **Detecting biophysical signals**

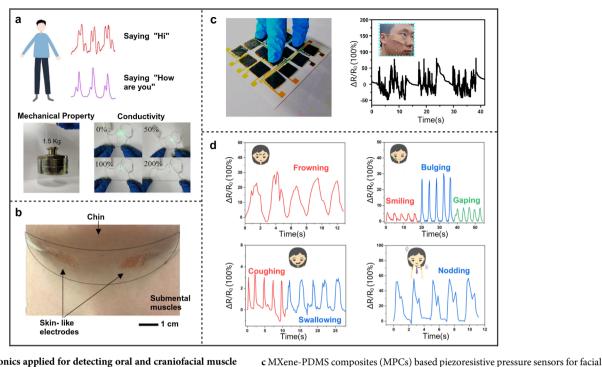
Dental, oral, and craniofacial biophysical signals mainly cover mechanics, temperature, humidity, and fluid dynamics (Table 2). Appropriate stress on oral tissues is vital to maintain the health of teeth and periodontal tissues, and the mechanical movements of craniofacial muscles are related to functions such as pronunciation, facial expression, and swallowing. In addition, the dynamic temperature, humidity, and gas flow can reflect the state of breathing as well.

#### **Muscle activities**

Beyond applications for detecting the above biochemical signals, flexible electronics also have a wide range of applications for monitoring physical signals from dental, oral, and craniofacial muscle functions<sup>56</sup>. Cao et al. prepared a composite hydrogel with covalently crosslinked polyacrylamide as flexible "elastin", Ca<sup>2+</sup> crosslinked SA as rigid "collagen" and Ga as active conductive soft "filler", whose properties were very similar to the human skin (Fig. 4a)<sup>16</sup>. The SA/PAm/Ga hydrogel strain sensors made from this material could monitor the subtle changes in facial muscles and generate and transmit signals through the resistance variety corresponding to different pronunciations. This device could help people with speech disorders

Applications	Device characteristics	Targets				Real-world trials	ld trials				Reference
	Substrate	Sensor	Structure	Size		Device lifespan	Conducting real-world trials	Participant number	Participant situation	Trial duration	
Muscle activities	SA/PAm/Ga hydrogel	×	Synergistic net- work structure	$60 \times 10 \times 3 \text{ mm}^3$	Speech function	*	Yes	*	*	*	16
	Elastomeric and poly- vinylalcohol film	Au-electrode	Fractal curves structure	*	Swallowing exercise	*	Yes	Four	Healthy	*	24
	Hollow-structured MPCs	Piezoresistive pres- sure sensors with compressible 3D gra- phene networks	3D	15 × 10 × 1.5 mm³	Stereo sound and ultrasonic vibration, swallowing, facial muscle movement, and various intense motion	*	Yes	*	*	*	18
	Chi-g-PANI copolymers	Strain sensor	*	*	Facial muscle movement	*	Yes	*	*	*	17
Orthodontic forces	Island-bridged poly- propylene piezoelectret film; PDMS arrays	PEFG	The island bridge and ser- pentine electro- des stucture	$60 \times 45 \times 12 \text{ mm}^3$	OTM	*	No (animal trial)	*	Young and aged rat	Eighteen days	26
	Acrylic	Six-dimensional force sensor	Enon-and- mortise structure	$7 \times 7 \times 7 \text{ mm}^3$	Orthodontic force in orthodontic treatment	*	°N N	*	*	*	58
	PDMS or dimethicone	Force sensor	Single semi- sphere structure	radius = 1.5 mm	Directional ortho- dontic force	*	No	*	*	*	33
	Flexible substrate compris- ing a 50-µm-thick PI layer and a 50-µm-thick copper layer (THKS100520)	MLCCs sensor	*	2 × 1.25 × 1.25 mm <sup>3</sup>	Force distribution on an occlusal surface	*	No	*	*	*	59
Respiratory dynamics	Flexible carbon nanofibers mats infiltrated with PDMS	Flexible pressure sensor and tempera- ture sensor	×	*	Respiration pattern	*	Yes	*	*	*	36
	MWCNT/PDMS composite	Humidity sensor	IDE pattern	$15 \times 10 \text{ mm}^2$	Respiration pattern	*	Yes	One	Healthy	Several min- utes (five times)	21
	CNT/SF hybrid con- ductive fibers	Humidity sensor	Nanofibrils network	$50 \times 25 \times 2.5 \text{ mm}^3$	Respiration pattern	*	Yes	*	*	457 seconds	22
	Water-soluble silk fibroin films and large-area gra- phene monolayers	Bifunctional graphene-AMP bior- ecognition sensor	Coil structure	*	Respiration	*	N	*	*	*	30
	ZnS:Cu phosphors and liquid polydimethylsiloxane	AgNWS/GO FTCE	Nanofibrils network	$1.5 \times 1.5  \text{cm}^2$	Bacteria	*	No	*	*	*	23

# **Review article**



**Fig. 4** | **Flexible electronics applied for detecting oral and craniofacial muscle activities. a** Hydrogel that could be applied for the function recovery of oral and craniofacial muscles<sup>16</sup>. **b** A skin-like electrode assisting swallowing training<sup>24</sup>.

to recover their speech function. Lee et al. designed a skin-like electrode that could reduce motion artifacts compared to rigid electrodes and assist patients suffering from dysphagia in swallowing training (Fig. 4b)<sup>24</sup>. This electrode had a significantly lower false-positive detection rate for sub-chin muscle monitoring than rigid electrodes and could distinguish swallowing from other movements. Song et al. fabricated a structurally stable and highly sensitive hollow structure of MXene-polydimethylsiloxane composites (MPCs) (Fig. 4c)<sup>18</sup>. MPCs were piezoresistive pressure sensors allowing fine measurement of the vibration of facial muscles by detecting the resistance change of compressive strain, which might help facial paralysis patients to practice more effectively in their rehabilitation exercises. Du et al. utilized functionalized adenine molecules and chitosan-grafted polyaniline copolymer (chi-g-PANI) to form conductive hydrogels to sensitively measure the activity of facial muscles for a long period. Polyaniline endowed the material with electrical conductivity, and chitosan compensated for the brittleness of PANI (Fig. 4d)<sup>17</sup>. The quaternate adenine here not only acted as an adhesive modulator by breaking the hydrogen bond between PANI and chitosan but also promoted the dispersion of the rigid polymer network to avoid the deterioration of mechanical and electrochemical properties.

#### Orthodontic forces

Traditional orthodontic treatment requires patients to make regular followup visits and adjust their orthodontic plan several times, which is likely to cause a decrease in patient compliance, leading to poor treatment results or even failure<sup>57</sup>. Wang et al. integrated a piezoelectric electret field generator into a personalized mechanical orthodontic aligner, which could stimulate the proliferation and differentiation of osteoclasts and osteoblasts through electrostimulation (Fig. 5a)<sup>26</sup>. This device could promote orthodontic tooth movement through a piezoelectric-excited alternating electric field for bone remodeling. Furthermore, the six-dimensional force sensors could help orthodontists refine their protocols, given that the device could keep directional tracking and precise monitoring while applying complex multiaxial stimuli. Hu et al. mimicked mortise and tenon structures to fabricate flexible sensors that could be interlocked between the upper and lower structures by concave and convex interlocking and integrated them with an orthodontic aligner (Fig. 5b)<sup>58</sup>. This device could effectively detect the magnitude and direction of orthodontic forces on the teeth to minimize potential side effects and treatment periods. Lee et al. developed a flexible hemispherical sensor that could be affixed between the tooth surface and a clear aligner (Fig. 5c)<sup>33</sup>. The thermoplastic hemispherical sensor fixed its semicircular bottom on the tooth surface, and its top side touched the clear aligner. When the aligner was stressed, the contact area between the top of the hemispherical sensor and the aligner surface changed, which could be measured by a portable microscope to quantify orthodontic forces. In order to measure the large loads of biting force and ensure the sensitivity, Lin et al. utilized a combination of multilayer ceramic capacitors (MLCCs) that had good piezoelectric properties and flexible small force sensors made of polyimide to form an MLCC force sensor (Fig. 5d)<sup>59</sup>. This device could be tightly attached to the teeth and was able to measure the force distribution on the occlusion surface or the force response during actual food chewing, which would be beneficial in aiding dental treatment.

expression rehabilitation<sup>18</sup>. **d** Conductive hydrogel that could be applied as flexible

electronics for measuring facial muscles<sup>17</sup>. Panels **a-d** reproduced with permission.

#### **Respiratory dynamics**

Flexible electronics are also able to measure the flow rate of gas, which endows them with the ability to determine the respiratory status and prevent the adverse effects of mouth breathing on intraoral dentition and craniofacial development. In order to prevent mouth breathing from adversely affecting mandibular development, cranial shape, or dental occlusion<sup>60</sup>, Pang et al. designed a flexible pressure and temperature dual-mode smart mouthpiece that could continuously monitor and recognize eight different respiratory conditions, including coughing, breath-holding, mouth-normal breathing, and slow breathing, to prevent the occurrence and progression of mouth-breathing syndrome<sup>36</sup>. Using a humidity sensor to replace the monitor of airflow rate, the inaccuracy detection of respiration caused by the displacement of flexible electronics could be avoided<sup>61</sup>. Thiyagarajan et al. used multi-walled carbon nanotubes (MWCNT)/PDMS composite materials on a cellulose paper surface to detect respiration<sup>21</sup>. Porous cellulose paper was very sensitive to the moisture of the environment and changed the ionic conductivity according to the change of relative humidity during breathing. Flexible nanowires applied in masks could also realize high antibacterium for medical treatment. Ma et al. reconstructed the mesoscopic structures of the bombyx mori SF materials with carbon nanotubes to give

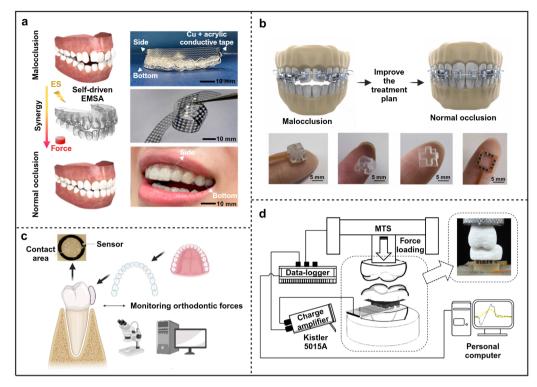


Fig. 5 | Flexible electronics applied for detecting the mechanical signals from orthodontic forces. a Piezoelectric electret field generator (PEFG) promoting orthodontic tooth movement<sup>26</sup>. b Flexible sensors for orthodontic forces detection<sup>58</sup>. c A hemispherical sensor for orthodontic forces detection<sup>33</sup>. d A multilayer ceramic

capacitor (MLCC) force sensor for detecting force distribution on the occlusal surface<sup>59</sup>. Panels **a**, **b**, **d** reproduced with permission. Panel **c** reproduced under Creative Commons (CC BY) license.

them stable mesoscopic structures (Fig. 3c)<sup>22</sup>. The CNT/SF hybrid materials showed great superiorities in biocompatibility, electrical conductivity, pressure sensitivity, and humidity sensitivity, which were then combined into facial masks to monitor respiration. This device could quickly respond to the change of humidity and had long-term stability in a humid environment, laying a foundation for oral and craniofacial telemedicine. Mannoor et al. printed the resonant coil onto water-soluble silk film substrates to fabricate graphene nanosensors (Fig. 3d)<sup>30</sup>. The silk membrane dissolved rapidly when contacting with water to ensure strong binding of the graphene-Au electrode structure onto oral tissues. The sensor could monitor respiration through signal changes as well because the conductivity of graphene could change in real-time with breathing. Sim et al. investigated an Ag nanowires and GO nanosheet mixture to make a flexible and transparent conductive electrode and used this electrode to make a facial mask layer as a self-heating and antibacterial coating<sup>23</sup>. The special mask could fight against Staphylococcus aureus and Klebsiella pneumonia, with a high bacteriostatic rate of up to 99.7%.

#### Other applications

Besides the above applications, flexible electronics also apply to beauty, diet, and other aspects (Table 3). Li et al. designed a hyaluronic acid-deliverable stretchable electronic facial mask that could increase skin moisture content by 20% with the help of sonophoresis<sup>25</sup>. The single-side soft pressing technique made the bending curvature of the mask reach 0.04 mm<sup>-1</sup>, corresponding to a radius of 2.5 cm, so it could perfectly fit human skin with the same bending curvature. In addition, experiments showed that the maximum temperature of the device could be maintained at 42 °C, making individuals feel comfortable. In the diet aspect, flexible electronics are helpful in evaluating the relationship between dietary intake and nutrition with low burden and, therefore, are helpful for monitoring the nutritional recovery of patients after surgery. Tseng et al. designed radiofrequency-trilayer sensors to monitor oral food consumption, and the sensitivity (in vitro) could reach around 0.6 MHz in 1 g L<sup>-1</sup> of glucose<sup>32</sup>.

They used broadside-coupled, split ring resonators to sandwich sensing interlayer and encapsulated this device with hygroscopic silk film. The sandwich structure provided a short-term reservoir to average the concentration of solution over time so as to cope with the transient nature of the solution in the mouth. Zhao et al. reported a self-powered wearable taste bud-mimicking e-skin based on enzyme-modified ZnO nanowire arrays on a patterned flexible substrate<sup>62</sup>. The e-skin modified with ascorbic acid oxidase and alcohol oxidase could reflect the ascorbic acid or alcohol content in food through the piezoelectric-enzyme reaction coupling process. The e-skin was able to taste beverages or fruits, for instance, to distinguish fruits such as cherries and oranges. This device showed potential applications in treating taste-related diseases. In addition, there is research on the application of flexible temperature sensors in the postoperative monitoring of dental implants so as to respond to the subtle changes of temperature rise caused by inflammation<sup>63,64</sup>. Kim et al. designed an implantable microtemperature sensor attached to the abutment wing of the dental implant<sup>65</sup>. The temperature measurement range could reach 20-100 °C, and it had high functional stability and biocompatibility. Although the physical stability was affected by the processing conditions, the device could still adapt to the moist conditions in the oral cavity.

#### **Challenges and prospects**

Flexible electronics need to fulfill three principles (3 S): stability, selectivity, and sensitivity<sup>66</sup>, which, however, encounter various challenges when applied in the field of stomatology. Temperature and stress are two major factors influencing the stability of flexible sensors. Complex environments or changes in external physical conditions, such as the oral cavity, which often undergo drastic temperature changes during various functional activities, can exacerbate the instability of the device material. In the continuously moist or fluidic environment of the oral cavity, biological receptors, such as enzymes in the sensors, are prone to lose their biometric functions<sup>67</sup>. Additionally, accumulated biological contaminants can also challenge the stability of sensors, leading to issues like incomplete

Applications	Device characteristics				Targets	Real-world trials	trials				Reference
	Substrate	Sensor	Structure	Size		Device lifespan	Conducting real- Participant world trials number	Participant number	Participant situation	Trial duration	
Other applications	Silicone layers	Cu/PI/Cu stretchable island-bridge mesh circuit	Serpentine	*	Transdermal admin- istration of HA	*	Yes	Five	*	Ten days	25
	Hygroscopic silk film or hydrogel-based interlayers	Hygroscopic silk film or Radiofrequency-trilayer hydrogel-based sensors interlayers	BC-SRR geometry	$2 \times 2 \text{ mm}^2$	Oral cavity and food consumption	*	Yes	*	*	One week	32
	Flexible Kapton substrate	Sensor-based on piezoelectric-enzymatic reaction	*	$0.5 \times 0.5 \mathrm{cm}^2$	$0.5 \times 0.5 \text{ cm}^2$ Taste bud functions Two to three day	Two to three days	Yes	*	*	*	62
	Polyimides	Implantable temperature sensor	Long serpentine	*	Micro-temperature of Two dental implant mont	Two months	No	*	×	*	65

attachment and artifacts between sensors and the target surface. Selectivity refers to the ability of a sensor to distinguish the analyte of interest from possible interferences<sup>68</sup>. Due to the complexity of the oral and craniofacial biological environment and frequent movement/deformation of the oral cavity, flexible electronics often work under conditions with a variety of chemical compounds (chemical/biological signals) or under persistent mechanical stresses (physical signals), making it difficult to realize monitoring of a specific target signal. High sensitivity is crucial for accurate monitoring of oral and craniofacial status, especially considering that the concentration of many biological indicators in oral biofluid is much lower than in blood<sup>69</sup>. Moreover, transmitting wireless signals from within the mouth across the cheeks to the exterior is highly challenging<sup>70</sup>. All these above challenges can reduce the sensitivity of flexible electronics. Flexible electronic devices also suffer from single function and delayed response time, and functional integration of the devices may be a potential solution<sup>53</sup>. Furthermore, the promotion of advanced technologies requires that flexible electronics are practical, and their future applications should cover the prevention, treatment, and monitoring of treatment effects and prognosis of oral and craniofacial diseases.

At present, in order to meet the 3 S challenges of flexible electronics for dental, oral, and craniofacial medicine, the experience of flexible electronics applied in other fields can be utilized. To overcome the challenges of stability, introducing compensating elements such as temperature sensors or using temperature-insensitive materials can be considered to avoid the effect of temperature. And the challenge of biofouling can be solved by using a protective film to prevent biological contamination. Also, encapsulating the key components, such as enzymes, into the electrodes using 3D printing helps to improve the device package and to prevent unwanted detaching<sup>70</sup>. Artificial receptors that collect target signals can be employed to improve stability as well. Compared to natural receptors like enzymes, artificial receptors are also simpler to process and thus can reduce costs<sup>71</sup>. The protective film or encapsulation can also help flexible electronics used in dental, oral, and craniofacial environments to resist moisture and corrosion. Besides, the challenges of selectivity can be solved by the efforts that have been made by several researchers: (1) For measuring chemical/biological signals, highly selective enzyme-based methods or techniques using artificial receptors are developed<sup>71,72</sup>. Moreover, it is possible to use selective sensor arrays to identify different analytes and achieve accurate analysis of the target<sup>70</sup>. (2) For measuring physical signals, designing sensor geometry to stretch in a specific direction when subjected to a force helps to achieve response and analysis of the mechanics of a single direction<sup>73</sup>, thus realizing the measurement of physical signals with a certain orientation. One possible solution to improve sensitivity is to find other highly-concentrated biomarkers that correlate with corresponding diseases<sup>5</sup>, meanwhile, improving the sensitivity of the sensor itself is also a critical issue. Using signal amplifier transistors to improve signal transduction or labeling with fluorescent proteins are reliable ways to improve sensitivity. For example, based on chemical stripping lithography, field effect transistors (FETs) with nanoscale strips could be produced, and they showed greater sensitivities than conventional methods due to the fact that these FETs had a high specific surface area to access many more targets<sup>74</sup>. To resolve signal transmission obstacles caused by cheeks, the intensity of the emitted signal or the sensitivity of the receiver for detecting radio signals can be enhanced. The improvement of the power supply capacity and antenna design, as well as the use of high-frequency signals, are also expected to benefit the signalreceiving performance75,76

However, beyond the 3 S principles, flexible electronics have yet to be improved in terms of biosafety, price, comfort, intelligence, and so on. In our opinion, the prospect of the applications of flexible electronics in oral and craniofacial clinical practises should follow the 5I principles: imperceptibility, intelligence, individualization, integration, and inexpensiveness (Fig. 6). (1) Imperceptibility can promote the acceptance of flexible electronics in stomatology by providing high comfort and esthetics to device wearers while minimizing interference with their daily lives. To achieve comfort, imperceptibility requires flexible electronics to be soft and small

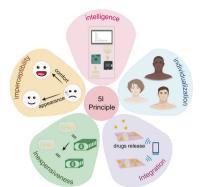


Fig. 6 | The 5I principles indicate improving the performance of flexible electronics in imperceptibility, intelligence, individualization, integration, and inexpensiveness.

enough to fit the complex biological structure and sensitive organs in oral, dental, and craniofacial regions. Otherwise, the device may irritate the oral mucosa and increase saliva secretion, potentially leading to flexible electronics shedding. For esthetics, they prefer to be invisible or disguised by applying transparent substrates and electrodes (such as metals, metal oxides, and metal carbides). (2) Intelligent, flexible electronics possess the capability to not only transmit data to associated electronic devices but also process the data, diagnose and analyze diseases in a real-time manner, and provide suggestions and emergency measures without assistance from doctors. The real-time data analysis and decision-making support not only conserves medical resources but also contributes significantly to enhancing the accuracy of diagnosis. Besides, this intelligent device should be able to detect various biomarkers concurrently or simultaneously monitor physical signals, chemical signals, and biological signals to realize multi-functional integration and even achieve comprehensive dynamic simulation and modeling of the oral cavity and craniofacial region. (3) Flexible electronics are expected to be more individualized. Given the significant variations in oral health status and dental morphology among individuals arising from genetic and habitual differences, it is crucial to design individualized flexible electronics that cater to the specific needs of each individual, encompassing esthetics, size, and comfort, among other factors. (4) Realize the integration of advanced techniques of diagnosis and treatment into flexible electronics. For instance, flexible electronics could combine drug delivery systems such as microneedle patches to automatically trigger drug release when monitoring pathological situations. (5) Additionally, identifying low-cost and high-performance materials is paramount for promoting the widespread applications of flexible electronics in dental clinics. Inexpensive, flexible electronics can alleviate the financial burden on patients, preventing them from incurring high inspection costs in hospitals.

The development of flexible electronics also needs a combination of multidiscipline technologies. For example, the lack of long-term energy supply in flexible electronics is an important reason for the lack of durability. Research has demonstrated that flexible electronics can collect the energy generated during the specific movement of the attachment site, thus providing continuous energy for wearable devices77. In addition to maintaining the self-power supply of the device, it is also possible to code the program to detect at intervals and then remain in "sleep mode" at other times, thus improving endurance. Currently, the diverse bacterial population in the oral cavity makes it possible to quickly form an acquired film that absorbs a large number of bacteria after cleaning teeth, posing a threat to oral hygiene, especially for flexible electronics attached to this area. To address this issue, it is crucial to reduce bacterial adhesion on flexible electronics or apply an antibacterial coating to the surface of device78-80. In addition, incorporating a self-heating electrode into the flexible electronic mask can eliminate bacteria through heating<sup>23</sup>. Moreover, according to market research, mechanical mismatches in Young's moduli between the human body and flexible electronics can lead to poor sensing accuracy<sup>81</sup>. If flexible electronics dislocate from soft body surfaces during eating or swallowing, the artifact arises and results in inaccurate data records. Consequently, the use of conductive hydrogel with excellent adhesion as a substrate has gradually become prevalent<sup>82-84</sup>. Furthermore, the employment of ionic additives that enhance stretchability and electrical conductivity can lower the materials Young's modulus<sup>85</sup>. Oral flexible electronics require attachment to mouthguards or orthodontic accessories, thereby necessitating a higher degree of miniaturization. Employing semi-solid/solid electrolytes under the technique of 3D printing and thin-film sputtering makes possibilities to construct microscale flexible electronics<sup>86</sup>. It could also develop smaller and ultrathin sensors based on flexible semiconducting materials (e.g., crystalline silicon carbide nanomembranes)<sup>87</sup>. Researchers have designed microneedle sensors for sample extraction, where the embedded electrodes or responsive materials at the microneedle tips can detect biomarkers. Integrating these microneedle sensors into a flexible patch is expected to further reduce the device size<sup>50</sup>. The size of the wireless system can be diminished by shifting from near-field or radio frequency identification-like approaches, which necessitate bulky proximal reader devices, to far-field radios capable of communicating with compact receivers that can potentially be situated at considerable distances<sup>27</sup>. When implanting flexible electronics in a moist oral environment, it can realize precise surface fit with the help of water-responsive super contractile polymer (WRAP) films<sup>88</sup>. When relative humidity exceeds 80%, WRAP films can contract instantly, achieving Young's modulus of less than 100 kPa after contraction. Hydrogels can also be integrated with moisturedriven energy generators to provide a long-term energy supply for flexible electronics in humid environments<sup>89,90</sup>. The substrate for dental, oral, and craniofacial flexible electronics must possess sufficient flexibility and stretchability to withstand and recognize complex muscle movements. It is also a strategy to apply self-healing materials in flexible electronics for both electronic devices and substrates<sup>91,92</sup>. For example, adding materials such as SF and tannic acid to the hydrogel to enhance the chemical force, such as hydrogen bonds inside the hydrogel<sup>93</sup>, or using hydrogel that can heal itself under the stimulation of water<sup>94</sup>, can be used to improve the self-healing ability of flexible electronics.

Moreover, it is noteworthy that most of the medical flexible electronics in stomatology are currently still in the proof-of-concept stage, therefore extensive clinical studies should be conducted to advance the applications of flexible electronic devices in preclinical and clinical situations<sup>29</sup>. It is insufficient that most of the clinical trials of flexible electronics in oral and craniofacial contain no more than ten participants. At present, the results of these clinical experiments show that the measurement of flexible electronics is reliable, including the monitoring of various components and pH of saliva or oral cavity gases, which can meet the requirements of clinical pathological detection and accurately judging facial expressions or muscle movements according to the frequency of different electrical signals. However, the results of a small number of clinical investigations are inaccurate and non-universal, so it is necessary to carry out large-scale clinical experiments to verify the practicability and accuracy of flexible electronics.

#### Conclusion

Flexible electronics have been emerging in the clinical practices of stomatology, which greatly aids in preventing the development of dental, oral, and craniofacial diseases and in assessing disease prognosis. With their assistance, it is anticipated that individuals will be able to reformulate the management of their oral healthcare status and reduce the time/economic costs associated with treating oral diseases. Currently, flexible electronics can detect the level of a variety of substances in saliva and cavity gas and determine the status of systemic diseases as well as monitor oral bacterial conditions and pH changes to prevent caries and safeguard periodontal health. By measuring mechanical signals, flexible electronics can also be utilized to assist in the development and adjustment of orthodontic strategies, the reconstruction of taste and smell sensations, and the analysis of respiratory dynamics. Moreover, flexible electronics contribute to the monitoring of postoperative recovery levels, facilitating training in swallowing and occlusal functions. As a result of the achievements in various technologies, flexible electronics combine multiple disciplines, such as materials science, physics, algorithm and software development, and clinical medicine, to facilitate innovative and patient-centered diagnostic, monitoring, and therapeutic approaches. They can achieve non-invasive and portable testing around the clock without interfering the life quality. These advantages assist oral patients as well as stomatologists in establishing regimes pertaining to primary prevention and treatment, assistance in rehabilitation, and improvement of prognostic tracking.

The application potentiality of flexible electronics in dental, oral, and craniofacial is magnificent. 5I principles are expected to steer the field development and facilitate the realization of this ambitious plan. In the future, flexible electronics should have the ability to adapt to the intricate environment in dental, oral, and craniofacial regions, such as dynamic temperature and pressure, humid environments, and the interference of various food residues. We believe that by fostering the utilization of flexible electronics, the prevention of oral diseases can be significantly advanced, leading to a more equitable distribution of medical resources.

#### Data availability

The graphical data and other findings in this paper are available from the corresponding author upon reasonable request.

#### Code availability

All custom codes regarded as central to the conclusions are available from the corresponding authors upon reasonable request.

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## **Competing interests**

The authors declare no competing interests.

# **Additional information**

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