pathogens induce pathologies (inflammation, diarrhea, and vomiting). In the case of norovirus, only a few virus particles are sufficient to quickly induce severe diarrhea and vomiting. With the idea that severe pathology can develop in a bystander cell–dependent manner, despite only a few infected cells, perhaps research should also focus on bystander cells in the case of norovirus infection. Similarly, between 10 and 30% of coronavirus disease 2019 (COVID-19) patients have gastrointestinal symptoms (*12*), and there is evidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) replication in the human intestinal epithelium (*13*, *14*). Although few infected cells have been detected in patient biopsies, bystander cells might be responsible for the gastrointestinal symptoms observed in COVID-19 patients.

Historically, infectious disease research has focused on the infected cell population because most analyses of host-pathogen interactions have been performed on bulk populations by using conditions in which most of the cells are infected by the pathogen of interest. With the development of single-cell methodologies, it is now possible to disentangle the participation of both the infected and noninfected bystander cells for the virus life cycle and induced pathologies. This will provide a better understanding of pathogenic mechanisms but also could provide new therapeutic targets to control the disease. This is exemplified by the study of Chang-Graham *et al.*, which showed that blocking the formation of ICWs in bystander cells, through the inhibition of P2Y purinoceptor 1 (P2Y1), resulted in a decrease of rotavirus-induced diarrhea severity in mice. As such, targeting the pathogen or the infected cells might not be the sole option to control infectious diseases and their induced pathologies. ■

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FLEXIBLE SENSORS

The more and less of electronic-skin sensors

Sensors can measure both strain and temperature or measure force without affecting touch

By **Xinyu Liu**[1,2]

Electronic skins (e-skins) are flexible electronic devices that emulate properties of human skin, such as high stretchability and toughness, perception of stimuli, and self-healing. These devices can serve as an alternative to natural human skin or as a human-machine interface (*1*–*3*). For on-skin applications, an e-skin should be multimodal (sense more than one external stimulus), have a high density of sensors, and have low interference with natural skin sensation. On pages 961 and 966 of this issue, You *et al.* (*4*) and Lee *et al.* (*5*), respectively, report advances of skin-like electronic devices. You *et al.* present a stretchable multimodal ionic-electronic (IE) conductor–based "IE^M-skin" that can measure both strain and temperature inputs without signal interference. Lee *et al.* describe an ultrathin capacitive pressure sensor based on conductive and dielectric nanomesh structures that can be attached to a human fingertip for grip pressure and force measurement without affecting natural skin sensation.

The human skin contains a large number of mechanoreceptors and thermoreceptors (nerve endings that sense deformation and temperature, respectively) that provide distinct perception of the spatial distributions of strain and temperature on our skin induced by touch stimulations (*6*). To replicate these sensory functions of the natural skin, different types of sensors that act as artificial receptors are integrated onto an e-skin for multimodal sensation (*7*). However, an e-skin containing a high-density array of sensory "pixels" of different types for sensing different physical quantities tends to have a complex structure and is challenging to manufacture.

A preferred strategy for realizing multimodal sensation on an e-skin is to use the same sensory unit for detecting different physical quantities without signal interference, an approach called decoupled multimodal sensing. Traditional stretchable sensors are sensitive to both strain and temperature and cannot be used as artificial multimodal receptors without signal interference. Targeting interference-free strain and temperature sensing by a single sensory unit, You *et al.* creatively used the ion relaxation dynamics of an ion conductor (an elastomer mixed with an ionic liquid) to decouple the strain and temperature measurement and developed the IE^M-skin composed of an array of artificial multimodal ionic receptors. They fabricated the IE^M-skin by sandwiching a thin layer of ion conductor with two layers of orthogonally patterned stretchable electrode strips (see the figure, top). A pixelated matrix of millimeter-sized artificial receptors formed between the top and bottom electrodes.

The electrical properties of each receptor are affected by the externally applied strain and temperature stimuli and can be measured through impedance measurement. You *et al.* used a strain-independent intrinsic electrical parameter of the ion conductor, the charge relaxation time, which reflects the ionic charge dynamics of the ion conductor and is equal to the ratio of material's dielectric constant and ion conductivity (*8*, *9*). The charge relaxation time is the signal readout for temperature and is not affected by the deformation of the IE^M-skin. For strain measurement, the bulk capacitance of the ion conductor is measured. The effect of temperature on the capacitance is eliminated through normalization against a reference capacitance at the temperature measured by the receptor. Thus, an external strain input only changes geometric parameters of the ion conductor, whereas a temperature input primarily modulates the intrinsic electrical properties (dielectric constant and ion conductivity) of the ion conductor.

Another enabling factor of the IE^M-skin design is its emulation of the epidermis and dermis bilayer of the human skin by suspending the receptor matrix layer over a low-friction interface layer filled with talcum powder. This design allows three-dimensional wrinkle-like deformations of the IE^M-skin under different contact modes (such as shear, pinch, tweak, and torsion) and permits the IE^M-skin to distinguish these contact modes through

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the measured temperature and strain profiles. Data confirm that the IE^M-skin can perform decoupled, real-time measurement of strain and temperature with high accuracy.

The IE^M-skin can serve as a human-machine interface that accepts tactile inputs of different contact modes and can be integrated into prosthetic and robotic devices to provide tactile and thermal feedback with high spatial resolution. The concept of using intrinsic electrical parameters, such as conductivity and dielectric constant of sensing materials, for strain-independent temperature sensing can be generalized to developing other types of stretchable multimodal sensors for humidity, chemicals, and biomolecules. One limitation is that the method for recognizing different tactile input modes through the measured temperature and strain profiles only works for interactions with hot or cold objects at temperatures different from that of the IE^M-skin. Alternative solutions may include the use of learning-based recognition models purely based on strain-distribution data or modulation of the temperature of the IE^M-skin (by adding a heating layer) based on the environment.

Skin-like electronic sensors also hold great potential for construction of hand-wearing devices such as instrumented gloves for quantifying tactile signals like force and pressure during finger or in-hand manipulation (*10*). Such data could facilitate the decoding of human hand sensation and its roles in object manipulation and enable better designs of robotic and prosthetic hands with biomimetic sensory feedback (*11*). Targeting imperceptible wearing and tactile sensing on fingertips, Lee *et al.* developed an ultrathin capacitive pressure sensor consisting of multilayers of conductive and dielectric nanomesh structures. This sensor design is derived from the design of conductive nanomesh electrodes proposed by Miyamoto *et al.* (*12*), which can be directly laminated on human skin during fabrication.

The electrode is fabricated by first electrospinning a water-soluble polymer, polyvinyl alcohol (PVA) into a multilayered mesh-like network of 300- to 500-nm-wide nanofibers. A 100-nm-thick gold layer is then deposited onto the PVA nanomesh sheet, and the gold-coated nanomesh sheet is transferred onto the skin surface. The sacrificial PVA nanofibers are washed off by water, but a residual layer of the dissolved PVA greatly facilitates the attachment of the resultant gold nanomesh layer onto the textured skin surface with excellent adhesion and conformal contact. The skin-integrated nanomesh electrode is stretchable and highly breathable and has exceptionally low bending stiffness, and so it creates no mechanical constraint or dermatological irritation to the skin.

To fabricate a nanomesh pressure sensor (see the figure, bottom), Lee *et al.* first laminated a nanomesh electrode on the skin surface and then sequentially attached a dielectric nanomesh layer made of electrospun polyurethane and parylene nanofibers and another nanomesh electrode layer to form a parallel-plate capacitor structure. Then, a nanomesh passivation layer of polyurethane nanofibers was attached to the top electrode layer with dissolved PVA nanofibers as the filler and adhesive. The total thickness of the nanomesh pressure sensor is ~13 μm. When fingers wearing such a pressure sensor grip an object, the grip force applied to the pressure sensor deforms the middle dielectric nanomesh layer and leads to a change in the capacitance measured between the top and bottom electrodes as the sensor readout.

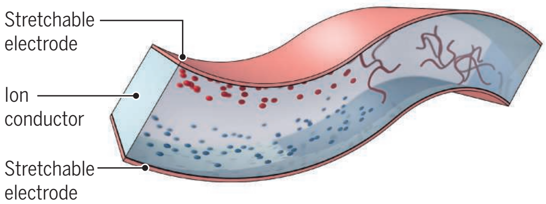
Through object-gripping experiments performed by human participants, Lee *et al.* investigated the effect of the finger-integrated pressure sensor on the natural fingertip sensation and found no decrease of the sensory feedback caused by the attachment of the pressure sensor. They hypothesized that the ultrathin and compliant structure of the nanomesh pressure sensor renders the device imperceptible on the fingertip. In addition, the intimate and conformal adhesion of the sensor's bottom nanomesh electrode layer to the skin surface may also contribute to the negligible interference of the finger skin sensation by the sensor attachment. This sensor also shows excellent mechanical durability under cyclic compression, shearing, and surface friction, which is attributed to the high mechanical robustness of the multilayered nanomesh structure of the pressure sensor.

This work highlights another new application of the previously reported skin-integrated nanomesh electronics (*12*) to wearable physical sensing with unprecedented performance. Future work may involve the further examination of fundamental mechanisms for the on-skin imperceptibility of the nanomesh pressure sensor, the systematic study of the skin-integrated pressure sensor performance for grasping objects of different materials and properties (such as insulating versus conductive, hard versus soft, and smooth versus textured), and the scalable fabrication of pixelated nanomesh pressure sensors in a large area with high density. The nanomesh pressure sensor could record tactile signals of human-hand manipulation that could provide superior sensing performance and zero data artifacts over existing instrumented gloves and e-skins.

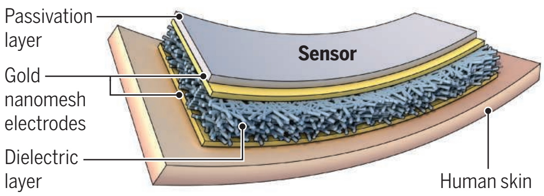
Multimodal sensation and nonobstructive skin integration are two important features that are desirable in e-skin designs. The studies reported by You *et al.* and Lee *et al.*, respectively, provide new solutions to better realize these attractive features with simplified device structures and enhanced sensing performance without impeding natural sensation. These results will inspire new sensor designs and lead to applications of e-skins as wearable health care monitoring, sensory prosthetic and robotic devices, and high-performance human-machine interfaces. ■

Improved electronic skins

Two goals in artificial touch sensors are to sense more than one stimulus with one receptor and to create wearable sensors that maintain natural skin sensation.



Receptor for decoupled sensing
For multimodal sensation, You *et al.* developed a stretchable ionic-electronic conductor receptor that detects both strain and temperature inputs without the signals interfering with each other.



Nanomesh-based pressure sensor
For on-skin sensing, Lee *et al.* attached an ultrathin capacitive pressure sensor based on conductive and dielectric nanomesh structures to a human, which did not affect natural skin sensation.

GRAPHIC: C. BICKEL/*SCIENCE*

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