that this is the source of bone electricity. However, it was discovered that new bone-forming cells or osteoblasts accumulate on the surface of pure hydroxyapatite, which has neither collagen nor streaming ions. The researchers wondered what was attracting these osteoblasts to a pure mineral.

As reported in a recent issue of *Advanced Materials* (doi:10.1002/adma.201705316), G. Catalan of the Barcelona Institute of Science and Technology and colleagues first looked at whether hydroxyapatite itself was piezoelectric. This is still a contentious issue; piezoelectricity originates from a fundamental asymmetry in the distribution of charges in a mineral, and structural studies disagree about whether the symmetry of hydroxyapatite is consistent with piezoelectricity. Laboratory measurements of the piezoelectric properties of hydroxyapatite by the team, however, revealed that the mineral is not piezoelectric.

However, even if a material is microscopically symmetric, a differential strain acting on the body can cause an asymmetry. This is called flexoelectricity, which is a coupling between a strain gradient in a body (flexure) and the amount of charge generated on the surface. As the name suggests, “flexure” leads to electricity. Tiny hairs in the inner ear, for example, have evolved to use this phenomenon for converting air waves to neural signals, thereby making flexoelectricity fundamentally important in auditory functioning. The researchers then set out to carefully flex natural bone and synthetic hydroxyapatite in the laboratory, measuring the bending-induced current using a lock-in amplifier. The flexure-induced current in synthetic hydroxyapatite and natural bone were remarkably similar, suggesting that flexoelectricity does indeed play a major role in generating electricity in bones. Moreover, because synthetic hydroxyapatite has no collagen, the quantitative similarity between the results rules out collagen piezoelectricity as a relevant contributor to the flexoelectricity of bone.

To fully understand the extent that flexoelectricity plays in bone regeneration, the researchers calculated the flexoelectric potential at a micro-crack in a bone. They found that even a small stress can be magnified at the apex of a crack tip, generating very high flexoelectric potentials. These flexoelectric potentials were compared with the electric fields that biologists had previously established to be sufficient to “electrostimulate” the beginning of the process of healing. As the crack starts healing, the apex shifts thereby serving as a beacon in directing the flow of healing cells. Thus flexoelectricity allows a micro-crack to call for help without the need for collagen piezoelectricity or streaming ions.

Brian Rodriguez at the University College Dublin, who is not connected to this research, says, “This work underscores the significance and ubiquity of flexoelectricity and clarifies several nagging and, until now, unresolved issues related to our understanding of bone remodeling.”

Vineet Venugopal
The researchers attributed this discrepancy to the existence of grain boundaries. They first constructed four typical grain boundaries observed in Li,OCl and evaluated their corresponding energy. The results suggested that the formation of grain boundaries was more favorable in Li,OCl than in perovskite oxides such as SrTiO3. At normal battery operating temperatures (~0–150°C), all of these grain boundaries exhibited 0.05–0.30 eV higher Li-ion migration energy barriers than the grain-boundary-free bulk counterpart, which suggested that the grain boundaries impeded Li-ion migration. Because previous simulations do not take the grain boundaries into consideration, the simulations overestimate the true Li-ion conductivity in real Li,OCl samples.

The researchers further developed a polycrystalline model and elucidated the relationship between Li-ion conductivity and the grain size of Li,OCl. This relationship can guide future experimental studies by choosing the optimal conditions for the synthesis of solid electrolytes, as the grain size is closely related to the preparation methods.

Feng Lin of Virginia Polytechnic Institute, who was not involved in the study, says, “For practical polycrystalline solid electrolytes, grain boundaries are complicated due to dynamic evolution of local crystal orientation, defects, and secondary phase impurities. This study provides a nice nucleation point for future elaborate studies considering these practical factors, and will lead to better design of solid-state Li-ion batteries to eliminate the challenges related to ionic conductivity, area specific resistance, lithium dendritic growth, etc.”

“Our approach provides valuable fundamental insights into the role of grain boundaries, which we are extending to other high-performance materials including LISICON and garnet-type solid electrolytes,” Islam says.

Tianyu Liu

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**Bio Focus**

**Health monitoring reaches new heights with human trials of ingestible sensor**

A sci-fi concept of an ingestible capsule to monitor human health is becoming a reality with the first human pilot trials, as reported in a recent issue of *Nature Electronics* (doi:10.1038/s41928-017-0004-x). This milestone is a joint effort between teams of Australian researchers at RMIT University, Monash University, and CSIRO.

This research presents a turning point in the history of direct human health monitoring. The designed and tested ingestible capsule monitors oxygen (O2), hydrogen (H2), and carbon dioxide (CO2) gases in the gut. The inside of the capsule consists of thermal conducting and semiconducting sensors that detect these gases.

Kourosh Kalantar-Zadeh, distinguished professor at RMIT University and director of the Centre for Advanced Electronics and Sensors, who is a lead researcher in this study, says, “H2 appears in the pathway of most of the microbiome species of the gut.” The microbiome (around 1.5 kg) and the human body are in a symbiotic relationship. The health of a human gut heavily relies on the correct performance of the microbiome. Kalantar-Zadeh says, “Correct function means a healthy H2 profile.” The H2 profile changes in the range of detectability when the ecosystem of the microbiome changes, which makes it important to measure and monitor its profile in the gut. The O2 levels vary in each organ, so its measurement provides information about the location of the capsule in the body. Oxygen gas content variation and its relation to the presence in an organ was confirmed through an ultrasound imaging technique.

In order to create benchmark profiles, the fiber content in the diet was varied in the trials to identify the effects of different fiber diets on the gas profiles. With the intake of a high fiber diet, the capsule resided in the stomach, small intestine, and large bowels for 12, 7, and 4 hours, respectively. A low fiber diet could retain the capsule for a longer period and the capsule remained in the stomach, small intestinal transit, and large intestine for 13, 5.5, and 54 hours, respectively. On the fourth day of the trial, dietary fiber was introduced to help release the capsule. The researchers conducted these tests on four healthy volunteers. The gas profiles were successfully monitored while modulating gut microbial fermentative activities with different fiber content in their diets. Experiments were successful in evaluating the small and large intestinal transit times.

Christopher J. Bettinger of Carnegie Mellon University praises this study. “Real-time monitoring of biomarkers in the GI tract is an exciting prospect. In this work, the authors create an ingestible microelectronic sensor that can monitor dissolved gases in the GI tract. The authors use chemical signatures to understand the composition of the microbiome. This device could be useful in many applications related to metabolic health,” Bettinger says.

Rahim Munir