Received: 18 April 2024 | Accepted: 28 April 2024

DOI: 10.1002/bmm2.12087

PERSPECTIVE

BMEMat WILEY

Breaking piezoelectric limits of molecules for biodegradable implants

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Funding information
Taishan Scholars Program of Shandong Province, Grant/Award Number: tsqn201909180

Abstract

In the quest for optimizing biodegradable implants, the exploration of piezoelectric materials stands at the forefront of biomedical engineering research. Traditional piezoelectric materials often suffer from limitations in biocompatibility and biodegradability, significantly impeding their in vivo study and further biomedical application. By leveraging molecular engineering and structural design, a recent innovative approach transcends the conventional piezoelectric limits of the molecules designed for biodegradable implants. The biodegradable molecular piezoelectric implants may open new avenues for their applications in bioenergy harvesting/sensing, implanted electronics, transient medical devices and tissue regeneration.

KEYWORDS

biodegradable implants, molecular ferroelectric, piezoelectric biosensors, self-powered electronics, transient bioelectronics

The piezoelectric effect entails the generation of electric charge which accumulates in certain materials under mechanical stimuli. This phenomenon has been widely employed in actuators, sensors, transducers, ultrasound scanners for medical imaging, and more recently, in the frontiers of biomedicine. Conventional piezoelectric materials, such as inorganic ceramic oxides like barium titanate (BTO), lead zirconate titanate (PZT), lead magnesium niobate-lead titanate (PMN-PT) and ferroelectric polymers like polyvinylidene fluoride (PVDF), have been prevalent choices. However, these materials face challenges related to flexibility, biocompatibility, and especially, biodegradability when utilized in implantable bio-devices and various biomedical applications. Although current biodegradable polymers like poly-L-lactic acid (PLLA), glycine, collagen, and others have been investigated, these natural or synthetic biodegradable piezoelectric polymers encounter limitations due to their low piezoelectric coefficient. The demand for biodegradable piezoelectric materials exhibiting high piezoelectric performances is pressing. In the recent Research Article published in *Science*,[1] Ren-Gen Xiong and co-workers have discovered a new molecular crystal, $HOCH_2(CF_2)_3CH_2OH$ [2,2,3,3,4,4-hexafluoropentane-1,5-diol] (HFPD), that exhibits remarkable piezoelectric properties (Figure 1a). Briefly, Han-Yue Zhang et al.[1] recrystallized transparent single crystals of HFPD using a solvent diffusion method and experimentally discovered that HFPD exhibited exceptional piezoelectric response with a large piezoelectric coefficient (d_{33}) of approximately 138 pC/N and a high piezoelectric voltage constant (g_{33}) of around 2450×10^{-3} Vm/N under no poling conditions. These values are significantly larger than those observed in other organic molecular crystals or ferroelectric polymer of PVDF (Figure 1b). Encouragingly, such a HFPD showed ferroelectricity with switchable spontaneous polarization. Additionally, HFPD demonstrated good biosafety and desirable biodegradation characteristics.

In order to overcome rigid and brittle weaknesses of crystal, the research team made flexible piezoelectric composite films by combining HFPD with polyvinyl alcohol and therefore explore its potential applications in flexible devices compatible with the human body. The resulting films exhibited excellent flexibility along with good biocompatibility and no apparent toxicity to biological cells. They also demonstrated significant piezoresponse with a d_{33} value of 34.3 pC/N. The finding of this study presents an important step forward in the development of molecular piezoelectric materials and opens up new possibilities for transient implantable electromechanical devices.[2] Particularly, it is inspiring that the acoustic impedance for HFPD matches that of the body reasonably well, which should be helpful for implantable ultrasound applications.

Looking ahead, one potential application for molecular piezoelectric biomaterials is in biosensing or healthcare monitoring[3] (Figure 1c). These flexible and biodegradable piezoelectric materials can be integrated into wearable or transient devices to monitor vital signs, detect biomarkers, and provide real-time feedback on an individual's health status. This has significant implications for personalized healthcare, allowing for early detection and intervention in various diseases. Additionally, biodegradable molecular piezoelectric materials may contribute to tissue regeneration efforts (Figure 1c). By incorporating the piezoelectric molecules into scaffolds or implants, it will be possible to generate electric signals under exogenous or enogenous mechanical stimuli, that facilitate the cellular growth and tissue regeneration. This could revolutionize regenerative medicine by enhancing the body's natural healing processes through bioactive implants or self-powered electric stimulation scaffolds.[4–6] Certainly, optimizing some factors including mechanical strength, tailored service longevity as well as the balance

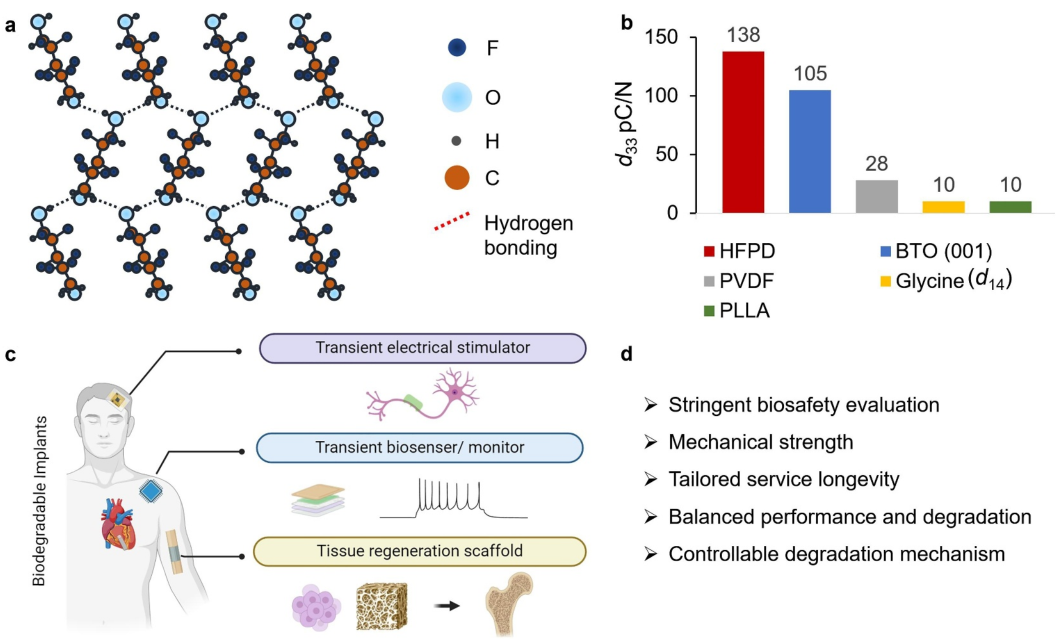

FIGURE 1 (a) HFPD molecules connected with the adjacent molecules to form a two-dimensional (2D) hydrogen bond network through O–H···O interactions of terminal hydroxyls in molecules, resulting in the biodegradability of the HFPD crystal. (b) Excellent piezoelectric properties (d_{33} of ~138 pC/N) of HFPD comparable to inorganic BTO. (c) Potential applications of biodegradable molecular piezoelectric implants. (d) Future investigation directions of biodegradable molecular piezoelectric biomaterials.

between performance and degradation is a critical challenge for degradable implantable biomaterials (Figure 1d). Furthermore, a stringent biosafety evaluation is imperative, including assessing degradation product metabolism, dose-dependent reproductive toxicity, genetic toxicity and carcinogenicity. Moreover, more investigations into the development of new strategies for biodegradation mechanisms are primarily designable. Regarding the research result published in *Science*,[1] the degradation of the HFPD molecular crystal is attributed to its water-solubility, involving the disruption of hydrogen bonding between molecules. Numerous studies have highlighted the molecular bond-breaking mechanisms that respond to various physiological signals (such as enzymes, pH, etc.) in the body's environment and external physical stimuli. Thus, when designing molecular piezoelectric materials, it is essential to take into account these mechanisms to achieve responsive and controllable degradation in biological settings.[7]

ACKNOWLEDGMENTS

We appreciate the Research Fund for the Taishan Scholars Program of Shandong Province (tsqn201909180).

CONFLICT OF INTEREST STATEMENT

All authors declare no financial/commercial conflicts.

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How to cite this article: J. Hao, N. A. N. N. Malek, W. H. A. Kamaruddin, J. Li, *BMEMat* **2024**, *2*(2), e12087. https://doi.org/10.1002/bmm2.12087