Self-powered cardiovascular electronic devices and systems

Qiang Zheng[1,2], Qizhu Tang[3], Zhong Lin Wang[1,4]✉ and Zhou Li[1,2]✉

Abstract | Cardiovascular electronic devices have enormous benefits for health and quality of life but the long-term operation of these implantable and wearable devices remains a huge challenge owing to the limited life of batteries, which increases the risk of device failure and causes uncertainty among patients. A possible approach to overcoming the challenge of limited battery life is to harvest energy from the body and its ambient environment, including biomechanical, solar, thermal and biochemical energy, so that the devices can be self-powered. This strategy could allow the development of advanced features for cardiovascular electronic devices, such as extended life, miniaturization to improve comfort and conformability, and functions that integrate with real-time data transmission, mobile data processing and smart power utilization. In this Review, we present an update on self-powered cardiovascular implantable electronic devices and wearable active sensors. We summarize the existing self-powered technologies and their fundamental features. We then review the current applications of self-powered electronic devices in the cardiovascular field, which have two main goals. The first is to harvest energy from the body as a sustainable power source for cardiovascular electronic devices, such as cardiac pacemakers. The second is to use self-powered devices with low power consumption and high performance as active sensors to monitor physiological signals (for example, for active endocardial monitoring). Finally, we present the current challenges and future perspectives for the field.

[1]*CAS Center for Excellence in Nanoscience, Beijing Key Laboratory of Micro-Nano Energy and Sensor, Beijing Institute of Nanoenergy and Nanosystems, Chinese Academy of Sciences, Beijing, China.*

[2]*School of Nanoscience and Technology, University of Chinese Academy of Sciences, Beijing, China.*

[3]*Department of Cardiology, Renmin Hospital of Wuhan University, Wuhan, China.*

[4]*School of Materials Science and Engineering, Georgia Institute of Technology, Atlanta, GA, USA.*

✉*e-mail: zlwang@gatech.edu; zli@binn.cas.cn*

https://doi.org/10.1038/s41569-020-0426-4

Cardiovascular diseases are the primary cause of death globally[1]. The WHO estimated that 17.9 million people died from cardiovascular diseases in 2016 and that this number will increase to 23.6 million by 2030 (REF.[2]). Of these deaths, 85% are caused by myocardial infarction or stroke[2]. In these patients, early diagnosis and timely intervention are of great importance for survival. In the past 50 years, the emergence of cardiovascular electronic devices (CEDs), such as implantable pacemakers, implantable cardioverter–defibrillators (ICDs), cardiac resynchronization therapy devices and various implantable or wearable monitoring devices, has been hugely beneficial to cardiovascular health and has reduced morbidity and mortality associated with cardiovascular disease[3]. CEDs have evolved and are now smaller, with a longer battery life and improved functionality compared with previous devices. However, some limitations curtail the greater uptake and widespread application of this technology, mostly associated with finite battery life, miniaturization, sensing capacities, lead malfunction and device-related infections. In this Review, we discuss the next generation of CEDs, which involve self-powered technology[4] and which are designed to address some of the main limitations in the field. We also summarize the prospects in the near future for implantable and wearable 'intelligent' CEDs.

Current technologies for CEDs

Implantable CEDs

In 1958, the first implantable pacemaker was developed[5] and, since then, tremendous improvements in cardiovascular implantable electronic devices (CIEDs) have been made. Modern CIEDs, including implantable pacemakers, ICDs, cardiac resynchronization therapy devices, implantable loop recorders and implantable haemodynamic monitoring devices, have already saved millions of lives by providing more accurate and continuous diagnostic and therapeutic capability (FIG. 1). The growth, general ageing and increasing life expectancy of the worldwide population have resulted in increased prevalence of chronic diseases, such as heart failure and atrial fibrillation, meaning that CIEDs have an increasingly important role in modern health-care systems.

Cardiac pacemakers. Cardiac pacemakers are the best known and most widely used CIEDs and were initially used to correct electrical conduction disorders, such as bradycardia and syncope[6]. Each year, millions of patients undergo permanent implantation of a pacemaker to

Key points

- The introduction of implantable or wearable electronic devices has revolutionized diagnosis and therapy in cardiovascular medicine, reducing morbidity and mortality of millions for patients with cardiovascular disease.
- Current battery-powered cardiovascular electronic devices have a limited life and do not allow long-term, uninterrupted monitoring or treatment of cardiovascular disease, which is crucial for preventing death and/or improving quality of life.
- Abundant sources of energy exist in the human body and the surrounding environment, such as biomechanical, solar, thermal and biochemical energy.
- Self-powered technology, which converts energy from the human body or surrounding environment into electricity, can provide a sustainable source of power to replace or supplement battery technology.

prevent or treat life-threatening cardiac conditions. The design of pacemakers has continually evolved, reflecting both technological progress and increasing understanding of cardiac function. Today, pacemakers have the typical single-chamber and dual-chamber modes, as well as more advanced pacing methods, such as biventricular pacing (also known as cardiac resynchronization therapy[7–10]) and His-bundle pacing[11,12]. These new pacing modes require complex sensing capacities, alternative functions and improvements in system optimization, such as battery longevity, miniaturization, leadless design and software upgrades. For example, optimized software algorithms can iteratively test the pacing threshold and automatically adjust the output power, thereby prolonging the life of the pacemaker to a total of 10 years[13,14]. Other algorithms can be used to monitor atrioventricular nodal conduction and optimize pacing in patients with intermittent atrioventricular node block[15,16].

Implantable cardioverter–defibrillators. ICDs are another class of battery-powered CIED, commonly used for preventing sudden cardiac death in patients with known, sustained ventricular tachycardia or fibrillation. Studies have shown that ICDs can have a role in preventing cardiac arrest in individuals who have not had, but are at high risk of developing, life-threatening ventricular arrhythmias[17,18]. ICDs can also have the features of a pacemaker. New devices provide additional 'overdrive' pacing to electrically convert a sustained ventricular tachycardia or 'back-up' pacing if bradycardia occurs. ICDs also offer a host of other sophisticated functions, such as the abilities to record detected arrhythmic events and to perform electrophysiological testing[19]. Modern ICDs have a volume of <40 cm^3, similar to that of older-generation pacemakers. However, the life of ICDs (approximately 5 years) is shorter than that of pacemakers (approximately 12.5 years) because their continuous working mode requires greater power consumption. Therefore, extending the battery life of ICDs is a priority.

Implantable loop recorders. Implantable loop recorders are a type of CIED used for heart monitoring. Implantable loop recorders can record an individual's heart rhythm continuously for >3 years, providing a range of important information that cannot be obtained by other methods, which can assist with making a definite diagnosis and instituting effective treatment. For example, implantable loop recorders can capture infrequently occurring abnormal heart rhythms that are missed by standard electrocardiography or dynamic electrocardiography from a Holter monitor[20]. Implantable loop recorders are often used to diagnose arrhythmia-based syncope, which is difficult by other approaches[21]. Implantable loop recorders are also used to detect recurrences of atrial fibrillation or tachycardia after ablation procedures[22,23]. Battery life is also a major concern with this type of device.

Wearable or portable CEDs

Wearable electronic devices have revolutionized digital and mobile health monitoring by enabling health monitoring to be continuous and longitudinal, both within and outside the clinical setting[24]. In cardiovascular medicine, wearable electronic devices have an extremely broad range of potential applications in enabling the monitoring of vital signals to help to diagnose both acute and chronic forms of cardiovascular disease. Cardiovascular wearable electronic devices can be divided into four main categories on the basis of their function: electrocardiography and heart rhythm monitors, heart rate monitors, haemodynamic monitors[25] and daily activity monitors. Cardiovascular wearable electronic devices come in various designs, including wrist bands (cuffs)[26,27], smart watches[28–31], rings[32], vests[33], chest patches[34–36] and T-shirts[37] (FIG. 1).

Wearable electrocardiography and heart rhythm monitors. As early as the 1960s, "evanescent cardiac abnormalities and phantom arrhythmias" were being detected with the use of ambulatory electrocardiography to explain clinical syndromes[38]. With the development of cost-effective mobile communication technology, ambulatory electrocardiography signals could be recorded and data uploaded remotely via the mobile cardiac outpatient telemetry system developed in 2002 (REF. 25). Currently, smaller and more convenient wearable devices for recording electrocardiographic data have been approved for use, including the KardiaBand (AliveCor), Apple Watch (Apple) and ScanWatch (Withings). These devices can detect atrial fibrillation and classify heart rhythm as being normal or out-of-range in just a few seconds, providing clinicians with valuable diagnostic data.

Wearable heart rate monitors. Various wearable electronic devices for continuous, real-time heart rate monitoring have been developed. These wearable devices have evolved from chest-strap monitors to wristband monitors. The measurement of heart rate has advanced from the traditional, simple recordings taken by physicians to the continuous, daily monitoring taken by individuals wearing these devices. The most commonly used technology in wearable devices for the detection of heart rate is photoplethysmography, which measures changes in light absorbance through the skin[39,40] and has an error of <10%[41,42]. However, these measurements might be less accurate during exercise or in individuals with dark skin pigmentation, tattoos or high levels of body fat.

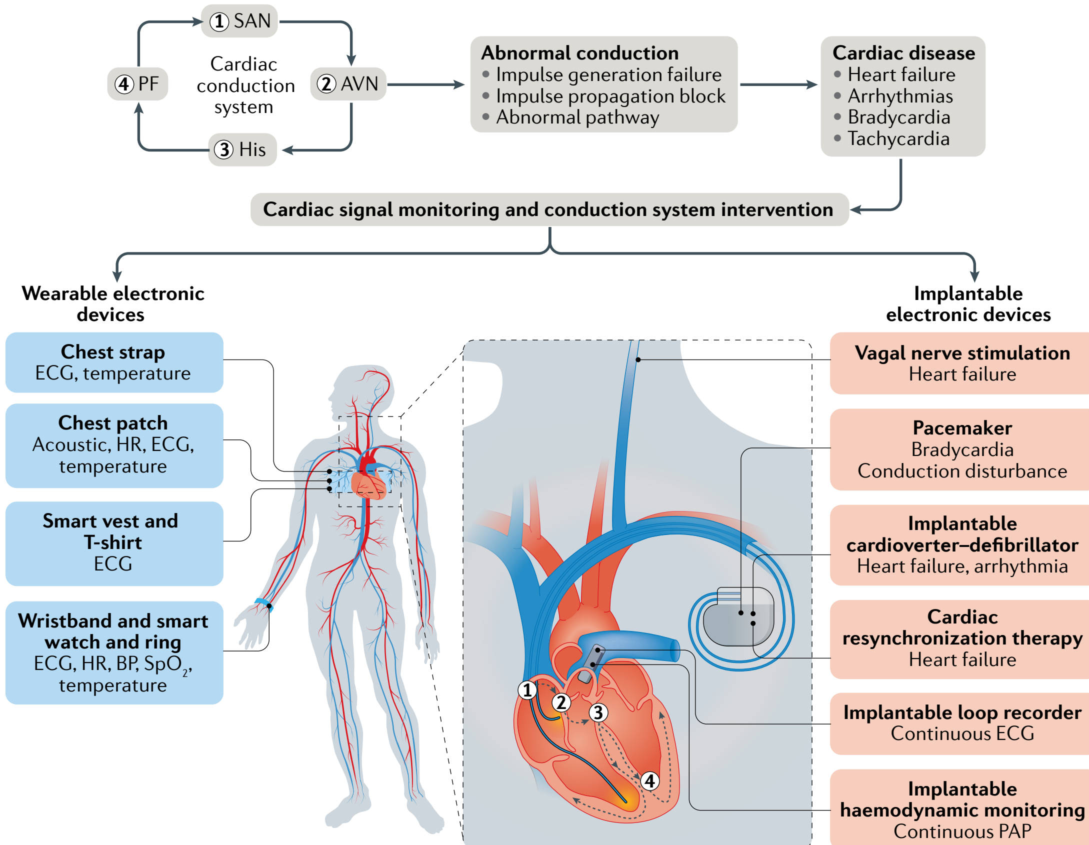

Fig. 1 | **Existing electronic devices for cardiac conduction disease.** The cardiac impulse originates in the sinoatrial node (SAN) and moves through the atrioventricular node (AVN), the His bundle (His), and the left and right bundle branches, and stimulates their terminal Purkinje fibres (PF). These structures (1–4) are identified in the image of the heart. Abnormal conduction of electrical signals in this pathway can cause a variety of cardiovascular diseases. Therefore, monitoring of cardiac signals and timely interventions targeting the conduction system are crucial. Cardiovascular electronic devices have been developed for the diagnosis and treatment of cardiac conduction disease. Existing devices can be divided into two classes: wearable electronic devices, mainly for monitoring cardiac-related signals, including chest straps and patches, smart vests and T-shirts, wristbands, and smart watches and rings; and implantable electronic devices, including vagal nerve stimulation devices, pacemakers, implantable cardioverter–defibrillators, cardiac resynchronization therapy devices, implantable loop recorders and implantable haemodynamic monitoring devices. BP, blood pressure; ECG, electrocardiogram; HR, heart rate; PAP, positive airway pressure; SpO_2, blood oxygen saturation.

Wearable haemodynamic monitors. Given the increasing prevalence of heart failure, tools that can detect early signs of decompensation are greatly needed[43,44]. Wearable devices for remote dielectric sensing and bioimpedance monitoring were developed for this purpose and can identify differences in the dielectric properties of different tissues to provide a quantitative analysis of the degree of pulmonary congestion and the levels of intrathoracic fluid[45]. The use of wearable bioimpedance monitors to detect transthoracic impedance is more convenient and sensitive than current clinical methods for predicting heart failure such as gain in body mass, which can also reflect the intrathoracic impedance and intrathoracic fluid level[46].

Wearable daily activity monitors. Daily activity data can be used to support cardiovascular clinical decision-making. These data can be used to predict the risk of cardiovascular disease and to help patients with chronic cardiovascular disease to make timely alterations to their therapeutic regimen. Activity monitors are usually mechanical motion sensors that rely on accelerometers to measure movement. The accelerometer can be integrated with other wearable equipment to record estimates of applied forces, body motions and the surrounding environment. However, several problems still constrain the widespread use of wearable daily activity monitors in clinical practice[47], and further validation is needed. For example, accelerometers are not suitable for assessing non-ambulatory activities, and the limited life of batteries makes the continuous use of wearable monitors a challenge[48].

Considerations for next-generation CEDs

The fundamental motivation for the invention of implantable and wearable CEDs was to free patients from the time and space constraints of repeated measurements in a health-care setting and to provide long-term, uninterrupted monitoring and treatment. To achieve these aims, a CED must have a sustainable energy supply and integrated functionality.

With current battery technologies, CEDs need to be replaced or recharged periodically, depending

Piezoelectric effect
The capacity of certain materials to generate an electrical charge in response to applied mechanical force.

Crystal
A solid material whose constituents (such as atoms, molecules and ions) are arranged in a highly ordered microscopic structure to form a crystal lattice that extends in all directions.

Electric dipole moment
The separation of a positive charge and a negative charge by a distance; a measure of the polarity of a system.

Wurtzite structure
A hexagonal crystal structure that occurs in various binary compounds; named after the mineral wurtzite.

C-axis
In crystal drawings, by convention, the c-axis is usually oriented vertically in the plane of the paper; all crystals except those with a cubic (or isometric) crystal structure have a c-axis.

Charge centre
The position in a charge distribution with non-zero total charge where the electric dipole moment vanishes.

Superposition
Superposition is the capacity of a quantum system to be in multiple states at the same time until it is measured.

Triboelectrification
A type of contact electrification whereby certain materials become electrically charged after they are separated from a different material with which they were in contact.

Electrostatic induction
A method to create or generate static electricity in a material by bringing an electrically charged object near to it, which causes the electrical charges to be redistributed in the material, resulting in one side having an excess of either positive or negative charges.

on utilization and battery volume. Developments in implantable devices over the past two decades have led to a reduction in the volume of ICDs from 70 cm^3 to 30 cm^3 and an extension in their life from 5 years to 10 years[49]. However, many patients still require replacement of their CED because of limited battery capacity as well as issues related to chemistry and physical structure (size and mass). Furthermore, physicians need to balance the life expectancy of the patient and the life of the CED because a mismatch can increase the likelihood of needing to change the CED, which is associated with a fourfold increased risk of infection and up to a fivefold increased risk of lead complications[50,51]. For rechargeable wearable devices, limited battery capacity greatly constrains patient freedom when using the device and reduces compliance.

Conversely, to meet the extensive requirements for clinical approval, future CEDs will require more functions, more powerful computing and remote communication capabilities, which will further increase the power consumption of the device. For example, the mean maximum predicted life of existing single-chamber and dual-chamber pacemakers is 12.0 ± 2.1 years and 9.8 ± 1.9 years, respectively (calculated using data on the six latest mainstream models of pacemaker) (TABLE 1). If more advanced features were incorporated, such as remote monitoring, pre-arrhythmia electrocardiogram storage and rate response, the life of devices would be reduced by approximately 0.5–3.6 years[51]. On the basis of these considerations, alternative energy sources, such as triboelectric nanogenerators (TENGs) and piezoelectric nanogenerators (PENGs), solar energy harvesters, thermal energy harvesters and biofuel cells, are currently being assessed in preclinical studies (FIG. 2a). These strategies, which convert energy from the human body or its surrounding environment into electricity to provide a sustainable power source, can be defined as self-powered technologies. These technologies can potentially be used to design the next generation of CEDs.

Existing self-powered technologies

Technologies to harvest energy to power CEDs sustainably are urgently needed. However, the energy sources available in biological systems are mainly the slow stretching of muscle, the slow flow of biofluids and blood, and possibly infrared light and sonic waves that can penetrate deep tissues. Biomechanical action is one of the major sources of power and has attracted a lot of attention. The following technologies have been developed to capture these energy sources (TABLE 2).

Piezoelectric nanogenerators

The piezoelectric effect is a way of generating an internal electric potential by applying a mechanical force[52,53]. Typically, when an external force is applied to a piezoelectric material, mutual displacement of anions and cations occurs in the crystal and produces an electric dipole moment. Cumulatively, this process generates a difference in the potential distribution throughout the material in the direction of the tension. PENGs, or piezoelectric generators when referring to non-nanomaterial systems, were invented using nanomaterials or bulk materials with a piezoelectric effect, including some inorganic materials, such as zinc oxide (ZnO), lead zirconate titanate (PZT), barium titanate, modified PZT, lead metaniobate, lead barium niobate and modified lead titanate, and some organic materials, such as polyvinyl chloride and polyvinylidene fluoride and its derivatives[54].

The currently available PENGs are mostly composed of external loads, piezoelectric components and flexible substrates. ZnO nanowire is a classic material for building a PENG[55,56], and ZnO is used here as an example to describe the functional mechanism of PENGs. ZnO has a wurtzite structure with asymmetric structures along and perpendicular to the c-axis, in which Zn^{2+} and O^{2-} are related in a tetrahedral configuration (FIG. 2b). In its original state, the charge centre of the cations and the charge centre of the anions overlap. When an external force is applied along the c-axis, the charge centres are displaced and a dipole moment is formed. A potential, called the piezoelectric potential, is macroscopically generated as a result of the superposition of the dipole moments from each of the crystal cells. Driven by this piezoelectric potential, electrons will flow in an external circuit and can power electronic devices. With repeated application and withdrawal of external forces, the PENG will produce a continuous alternating current to the connected external circuit. Various materials can be selected or synthesized for use in PENGs to make different types of device for use in particular scenarios.

Triboelectric nanogenerators

TENGs are another type of mechanical–electrical energy conversion device that function by combining triboelectrification and electrostatic induction[57]. The basic principle of this type of nanogenerator is that two materials with different electron-capture properties can carry different charges after contact and separation, thereby inducing an electric potential between the surfaces. Each material has an electrode attached to its back surface. The opposite charges on each material can generate electrostatic induction, which drives electrons in the metal electrode on the back of the friction material to flow in order to balance the difference in electric potential that has been created. When these two back electrodes are connected by an external circuit, the existing electric potential, called the triboelectric potential, can drive free electrons through the circuit, and an electric current is generated. TENGs can be classified into four different working modes[58] (FIG. 2c).

Vertical contact–separation mode. A traditional TENG operating on the basis of a vertical contact–separation mode usually consists of five parts: two different friction layers, two electrode layers and an external circuit. The two friction layers are moved vertically into contact and then separated during working cycles[59]. As this contact–separation process is repeated under a mechanical load, continuous alternating current output is generated by the TENG[60].

Lateral sliding mode. A lateral sliding mode TENG is composed of two layers aligned in parallel, with electrodes on the top and bottom of each layer. One layer slides in parallel to the other so that the two ends no

Table 1 | **Features and durability of cardiac implantable electronic devices**

Device model (manufacturer)	Mode	Volume (cm^3)	Usable battery capacity (A•h)	Battery chemistry	Features	Predicted life[a] (years)	Time from ERI to EOS (months)
Cardiac pacemakers							
Evia (Biotronik)	DR	12.0	1.2	Li–MnO_2	RF, HM, CLS, accelerometer	9.0–11.5	6
	SR	11.0	1.5			12.9–14.5	
Accolade EL (Boston Scientific)	DR	15.8	1.6	Li–CF_X	RF, HM, MV, accelerometer	10.9–12.4	3
Accolade (Boston Scientific)	DR	13.7	1.0	Li–CF_X	RF, HM, MV, accelerometer	7.2–8.3	3
	SR	13.2	1.0			8.7–9.4	
Kora 100 (LivaNova)	DR	8.0	0.8	Li–iodine	HM, MV, accelerometer	8.0–9.9	3
	SR	7.5	0.8			10.1–11.4	
Advisa and Ensura (Medtronic)	DR	12.7	1.1	Li–CF_X and SVO	HM, accelerometer	6.3–7.2	3
	SR	11.9	1.1			8.4–9.1	
Assurity (St. Jude Medical)	DR	10.4	0.91	QMR cell	RF, HM, accelerometer	9.1–10.9	6.5
	SR	10.4				13.5–15.3	9.4
ICD and CRT-D							
Iperia (Biotronik)	ICD (DR)	31	1.39	Li-CF_X or Li-SVO	RF, HM	9.4	3
	ICD (SR)	31	1.39			10.4	
	CRT-D	36	1.52			7.5	
Autogen EL and Autogen X4 (Boston Scientific)	ICD (DR)	29.5	1.78	Li-MnO_2	RF, HM	12.4	3
	ICD (SR)	29.5	1.78			13.0	
	CRT-D	29.5	1.75			10.4	
Platinium (LivaNova)	ICD (DR)	31.2	1.53	Li-CF_X or Li-SVO	RF, HM	17.5	11
	ICD (SR)	31.2	1.53			18.1	
	CRT-D	31.2	1.53			12.1	
Evera and Viva (Medtronic)	ICD (DR)	33	1.0	Li-CF_X or Li-SVO	RF, HM	9.7	3
	ICD (SR)	33	1.0			11.0	
	CRT-D	33	1.0			6.8	
Fortify and Quadra Assura (St. Jude Medical)	ICD (DR)	35	1.377	Li-CF_X or Li-SVO	RF, HM, accelerometer	11.1	4.9–5.4
	ICD (SR)	35	1.377			11.7	
	CRT	38	1.377			8.4	

All the estimates included in the table are under conditions of 2.5 V, 0.40 ms, 60 bpm and with a 500 Ω lead[51]. CF_X, carbon monofluoride; CLS, closed-loop stimulation; CRT-D, cardiac resynchronization therapy–defibrillator; DR, dual chamber; EOS, end of service; ERI, elective replacement indicator; HM, home monitoring; ICD, implantable cardioverter–defibrillator; MnO_2, manganese dioxide; MV, minute ventilation; QMR, quasar medium rate (combining the advantages of SVO and CF_X chemistry); RF, radiofrequency communication; SR, single chamber; SVO, silver vanadium oxide. [a]The data range given for cardiac pacemakers is for 100% to 50% pacing. The data given for ICD devices is for 0% pacing and assumes zero clinical shocks. The data given for CRT-D devices is for 15% atrial pacing, 100% biventricular pacing and zero clinical shocks. Each additional clinical shock reduces the life of the device by 16–47 days, which means that the actual service life of these devices is less than the manufacturer's predicted value (often by 4–6 years).

longer overlap. An electric field is generated owing to the spatial distribution of the surface triboelectrification charges. A current is generated if the two electrodes are connected by an external circuit[61].

Single-electrode mode. A single-electrode mode TENG consists of two dielectric layers but with only one layer being connected to an electrode, which is grounded. When the other layer is moved and the distance between the two layers varies, an electrostatic potential is created owing to the surface triboelectric charges. A current is then generated between the electrode and the ground[62].

Freestanding mode. A freestanding mode TENG is an optimized version of the single-electrode TENG[63]. To utilize all the induced potential from the two electrodes in the single-electrode TENG, two electrode plates are positioned alongside each other, below the dielectric layer. The mechanism of electricity generation is similar to that in the lateral sliding mode[64].

Pyroelectric nanogenerators

Pyroelectric nanogenerators (PyENGs) are energy collection devices that can convert thermal energy into electrical energy by using nanomaterials with pyroelectric effects[65,66]. The pyroelectric effect refers to changes

Electron-capture properties
During electron capture, an electron in the inner shell of an atom is drawn into the nucleus where it combines with a proton, forming a neutron and a neutrino; the neutrino is ejected from the atom's nucleus, and the overall effect is for an unstable atom to become more stable.

in the spontaneous polarization of some crystals when they are heated to different temperatures. When the temperature is constant, the spontaneous polarization intensity of the crystal remains unchanged, and no pyroelectric current is generated. However, when the temperature increases or decreases over time, the intensity of the spontaneous polarization will decrease or increase, respectively. If the crystal is connected to an external circuit, pyroelectric current is generated in the circuit. A continuous cycle of heating and cooling produces a constant electric current[67] (FIG. 2d).

Biofuel cells

Biofuel cells are an important approach to harvesting biochemical energy from the biofluid environment of living organisms to produce electricity. Biofuel cells generate power by a mechanism involving reduction–oxidation reactions, similar to that of commercial fuel

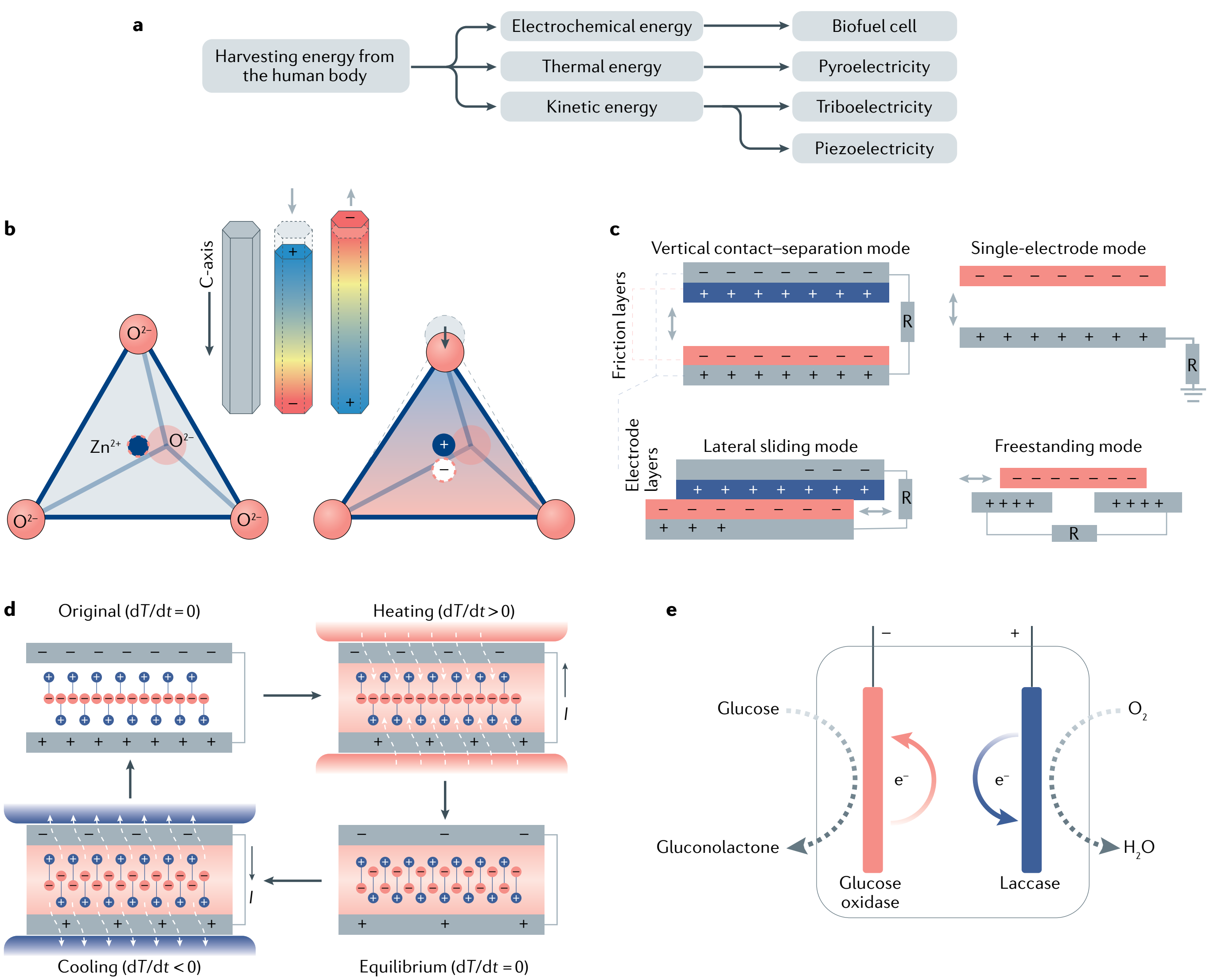

Fig. 2 | **Existing self-powered technologies and their fundamental features. a** | Types of energy present in the human body and different methods of harvesting these kinds of energy. **b** | The principle underlying a zinc oxide-based piezoelectric nanogenerator with a wurtzite crystal structure. The Zn^{2+} and O^{2-} ions are related in a tetrahedral configuration, and the charge centres of these cations and anions overlap (left). When an external force is applied along the c-axis (centre), the charge centres are displaced (right) and a dipole moment is formed. Superposition of the dipole moments generates a piezoelectric potential. **c** | The four fundamental working modes of triboelectric nanogenerators (TENGs). The triboelectric effect occurs at the interface between two different dielectric materials that are in contact. TENGs rely on the coupling of triboelectrification and electrostatic induction. When the two friction layers are brought into contact, triboelectric charges are transferred to the two surfaces. When the two friction layers are separated, an electrostatic field is created by the triboelectric charges, which can drive electrons to flow through an external circuit that has a resistance (R). The four different categories of TENG design are vertical contact–separation mode, single-electrode mode, lateral sliding mode and freestanding triboelectric layer mode. **d** | The principle underlying a pyroelectric nanogenerator based on the spin Seebeck effect. The pyroelectric effect refers to a phenomenon in which the polarization of some crystals spontaneously changes in response to a variation in temperature. As the temperature goes up and down over time (dT/dt), the intensity of the spontaneous polarization will decrease or increase, and pyroelectric current (I) will be generated in the circuit. **e** | The principle underlying biofuel cell based on a glucose redox reaction. A typical biofuel cell uses enzymes as catalysts for glucose oxidation at the anode and oxygen reduction at the cathode to generate electric power.

Table 2 | **Characteristics of implanted energy harvesters**

Energy harvester	Materials	Structures	Output in vivo (V)	Size	Implantation sites	Biocompatibility[a]	Implantation duration (animal)[b]	Cost	Refs
PENG	ZnO	Single nanowire	0.001–0.003	100–800 nm diameter	Heart, diaphragm	Good	NA (rat)	High	77
	PZT	Flexible multilayers	0.3–17.8	1.5–6.0 cm^2	Heart, lungs	Risk of lead poisoning	48 h (pig)	High	82–84,107,108
	PVDF	Thin film or nanofibres	0.014–4.8	0.25–6.50 cm^2	Heart, lungs, arteries	Good	5 days (rat)	High	106
TENG	Polymer or metal	Double contacting layers	3.7–65.2	1.5–23.8 cm^2	Heart, diaphragm, under chest skin	Good	72 h (pig)	Low	90–92,109,112,114,134
Oscillation generator	Metal	Bulk	0.6–0.9	~4 cm diameter	Heart	Fair	1 h (sheep)	Low	75,93,94
Biofuel cell	Enzyme and metal electrode	Thin film	0.2–0.6	0.25–0.75 cm^2	Jugular vein, retroperitoneal space, blood vessel in ear	Good	167 days (rat)	Low	70,132,133,136
Solar cell	Semiconductors	Bulk or thin film	3.00–5.67	0.14–4.60 cm^2	Under the skin	Good	7 months (rabbit)	High	98–100

Only devices that have been implanted in living animals are listed in the table, and all data were tested in vivo. NA, not available; PENG, piezoelectric nanogenerator; PVDF, polyvinylidene fluoride; PZT, lead zirconate titanate; TENG, triboelectric nanogenerator; ZnO, zinc oxide. [a]Based on the description in the referenced papers or the chemical properties of the material itself. [b]The longest implantation time reported to date is given.

cells (FIG. 2e). A typical biofuel cell uses enzymes as catalysts for glucose oxidation at the anode and oxygen reduction at the cathode to generate electric power[68–70]. These electrochemical reactions can be described as follows[71]:

$$\text{Anode: } C_6H_{12}O_6 + 2OH^- \rightarrow C_6H_{12}O_7 + H_2O + 2e^-$$

$$\text{Cathode: } \frac{1}{2}O_2 + H_2O + 2e^- \rightarrow 2OH^-$$

$$\text{Overall: } C_6H_{12}O_6 + \frac{1}{2}O_2 \rightarrow C_6H_{12}O_7.$$

The two electrodes (the anode and the cathode) are usually separated into two compartments and are connected to an external electrical circuit.

In addition to the generator systems mentioned above, other methods of generating electricity have been reported, such as solar cells that harness solar energy on the basis of the photovoltaic effect[72–74], oscillation generators that harness mechanical energy from the human body on the basis of the electromagnetic effect[75] and endocochlear potential cells that harness the potential difference between the perilymph (the extracellular fluid located within the inner ear) and the endolymph (the fluid contained in the membranous labyrinth of the inner ear) owing to K^+ transfer[76]. Each of these methods has its own characteristics, advantages and limitations when applied to biological self-powered systems. Some of the most promising progress is described below.

Photovoltaic effect
A process in which two dissimilar materials in close contact produce an electrical voltage when struck by light or other form of radiant energy.

Electromagnetic effect
A process in which either a stationary conductor is put in a moving magnetic field or a moving conductor is put in a stationary magnetic field, producing a voltage or electromotive force across the electrical conductor.

Applications of self-powered CEDs

Existing battery technology constrains many aspects of current CEDs, including service life, miniaturization, flexibility and biosecurity[49]. Therefore, replacing or supplementing batteries with a sustainable power source has the potential to revolutionize the field of CEDs, which is also the motivation behind the development of self-powered cardiovascular devices. The harvesting of kinetic energy from the heart by a PENG was first demonstrated in 2010 (REF.[77]) and, since then, various novel energy-harvesting devices have been built, initiating a wave of self-powered devices in the cardiovascular field designed using nanogenerator technology. Research into self-powered CEDs can be broadly divided into two categories: the use of nanogenerators to harvest energy from the human body or ambient environment as a sustainable power source for CIEDs, and the use of nanogenerators as active sensors for monitoring physiological signals (FIG. 3).

Sustainable power source for CIEDs

CIEDs need to function for as long as possible in the human body, preferably for the lifetime of the patient[49,78–80]. Multiple replacements of devices and the associated surgery bring huge health risks to patients as well as economic burdens to health-care systems. In addition, to ensure a minimum life of a battery, reducing the volume and mass of a CIED is difficult, which imposes limitations on optimizing the overall design of the device. The use of self-powered technology would be an ideal solution to address these limitations by ensuring a continuous energy supply and allowing new device designs and reductions in size.

Piezoelectric self-powered devices. The rhythmic contraction and relaxation of the heart to pump blood around the circulatory system provides an inexhaustible source of power for energy-harvesting devices[81] and generates sufficient kinetic energy to power a CIED. When implanted in the human body, a PENG can convert biomechanical energy into electricity (FIG. 4).

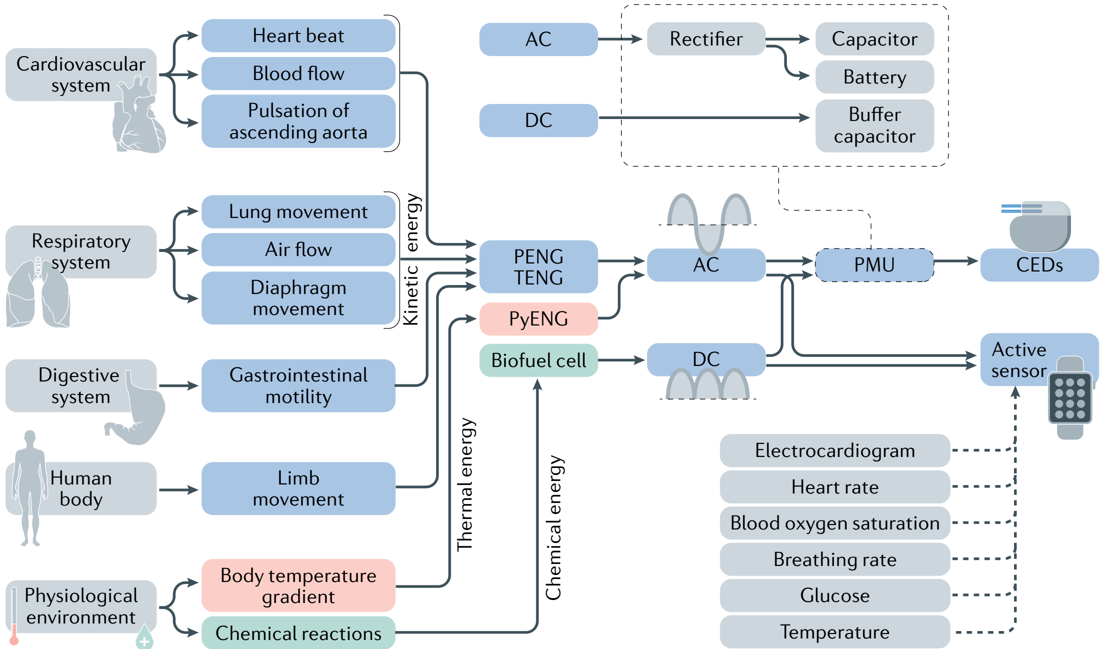

Fig. 3 | **Implementation path for building a self-powered cardiovascular electronic system.** Energy can be harvested from the motions of various organs and tissues as well as from temperature gradients in the body and the flow of bodily fluids. Various energy-harvesting strategies can be applied, including piezoelectric nanogenerators (PENGs), triboelectric nanogenerators (TENGs), pyroelectric nanogenerators (PyENGs) and biofuel cells. The energy is then stored in a power management unit (PMU) or used directly for downstream applications — for example, to power cardiovascular electronic devices (CEDs) and for active sensing of heart-related signals.

Open-circuit voltage
(V_{oc}). The difference in electric potential between two terminals of a device when disconnected from any circuit (no external load is connected and no external electric current is flowing between the terminals).

Short-circuit current
The excess current flowing through an electrical circuit as a result of an unintended path in the circuit with no or very low electrical impedance.

Rectifier
An electrical device that converts alternating current, which periodically reverses direction, into direct current, which flows in only one direction.

The first in vivo demonstration of the conversion of biomechanical energy from the beating heart into electrical energy by a PENG was reported in 2010 (REF.[77]). Various ZnO nanowire devices were implanted into a living rat. An AC output synchronized with the heart beat was obtained, with an open-circuit voltage (V_{oc}) of 3 mV and a short-circuit current (I_{sc}) of 30 pA.

In 2014, a flexible device consisting of PZT ribbons was reported[82]. This PZT-based device was integrated with a rectifier and a rechargeable microbattery and was encapsulated in polyimide. The device was implanted into several animal models and was able to harvest and store energy from the heart. The long-term stability of this PENG was tested under mechanical loading conditions for >20 million cycles in a moist environment[82]. Another group also reported a PZT-based piezoelectric device for harvesting energy from the heartbeat in vivo[83]. The output voltage reached 3 V, which roughly matches the operating voltage of some CIEDs, such as commercial cardiac pacemakers[83].

To improve the efficiency of energy harvesting to meet the energy consumption of CIEDs, more advanced piezoelectric materials have been proposed. In 2017, a piezoelectric energy harvester containing single-crystalline $(1-x)Pb(Mg_{1/3}Nb_{2/3})O_3-xPb(Zr,Ti)O_3$ (PMN–PZT) was reported, with a V_{oc} of 17.8 V and an I_{sc} of 1.74 μA at its highest output from pig heart beats[84]. The researchers also built a successful self-powered, wireless communication system.

Kinetic energy can also be harvested from the motion of organs and tissues other than the heart, including from the dilatation of arteries[85], movements associated with breathing[77,82,86] and peristalsis of the stomach[87]. This research provides many more options for building self-powered CIEDs.

Triboelectric self-powered devices. The first successful TENG was reported in 2012 (REF.[57]). Since then, this booming technology has benefited various fields, especially biomedicine[88,89]. The first use of an implantable TENG in cardiovascular medicine was reported in 2014 (REF.[90]) (FIG. 4). This TENG harvested the energy from periodic breathing to generate an AC output of 3.73 V at 0.14 μA (FIG. 5a). The converted electricity could be stored and used to power a prototype pacemaker, demonstrating for the first time the feasibility of building pacemakers that are self-powered by a TENG.

In 2016, the same group proposed improvements to the TENG and implanted the device into large animals for the first time. Driven by the heart beat of adult pigs, the TENG generated an output of 14 V at 5 μA, which was the highest achieved at that time. In addition, the device worked constantly for >72 h in an active animal, which was a substantial achievement[91].

Current efforts are mainly focused on optimizing the efficiency of energy harvesting and storage in order to achieve a truly self-powered implantable device. In 2019, the 'symbiotic pacemaker', a fully self-powered, implantable stimulator that uses TENG technology, was described[92]. The symbiotic pacemaker successfully corrected sinus arrhythmia in adult pigs (FIG. 5b–d). This remarkable device used the energy harvested in vivo from a large animal to achieve

Quartz clock
Inside a quartz clock or watch, the battery sends electricity to the quartz crystal through an electronic circuit; the quartz crystal oscillates (vibrates back and forth) at the precise frequency of 32,768 times per second.

complete pacing functions for the first time, an important breakthrough in the development of self-powered CIEDs.

Other strategies for powering CIEDs. Many strategies other than TENG and PENG have been reported that allow the extraction of energy from the human body or the ambient environment, such as PyENGs, biofuel cells, solar cells and oscillation generators. However, not all of these approaches have been used as implantable power sources for cardiovascular devices because of limitations associated with their operating mechanism, materials or output efficiency.

Before the use of PENGs and TENGs, oscillation generators were widely considered for harvesting biomechanical energy. In 1999, a device based on a quartz clock was implanted on the right ventricular wall of a dog to harvest the kinetic energy of the heart[75]. In 2013, a new type of oscillation generator was designed with imbalanced mass[93]. Biomechanical energy from the heart of a sheep was successfully harvested (11 μJ per heart beat), which could be stored and used by a cardiac pacemaker[93]. However, the device was fairly heavy (16.7 g), which might impose a burden on the heart. Therefore, optimization was focused on how to reduce the mass and size of the device. In 2017, a new oscillation generator with a radius of 3.8 mm and a mass of 7.7 g was designed. When implanted at an epicardial site, this new device could generate sufficient power to drive a prototype pacemaker[94].

Solar energy is one of the cleanest and most abundant sources of energy in the ambient environment. The equipment for utilizing solar energy to generate electricity has been commercialized for >50 years[95–97]. Accordingly, researchers have attempted to adapt solar cells to power CIEDs. In 2014, a device containing three small commercial solar cells was placed subdermally in a pig and used to power a pacemaker[98]. At an implantation depth of 3 mm, the device yielded >3,500 μW/cm^2 of power density. In the following year, the researchers used advanced monocrystalline solar cells with a power density of 1,963 μW/cm^2, further developed a low-light photovoltaic module and implanted the device in vivo to power a fully functional, battery-free, single-chamber pacemaker[99]. Another group reported an integrated, self-powered system consisting of ultrathin photovoltaic cells, a rechargeable battery and a pacemaker[100]. This system was implanted subdermally in mice to harvest solar energy, and electricity directly generated or stored by the device was used to operate a custom-made pacemaker. In the context of implantable power sources, the efficiency of energy conversion of a photovoltaic device is inversely related to the depth of implantation. Flexibility, miniaturization, comfort and safety while maintaining efficiency are still challenges for the implantation of existing photoelectric conversion devices.

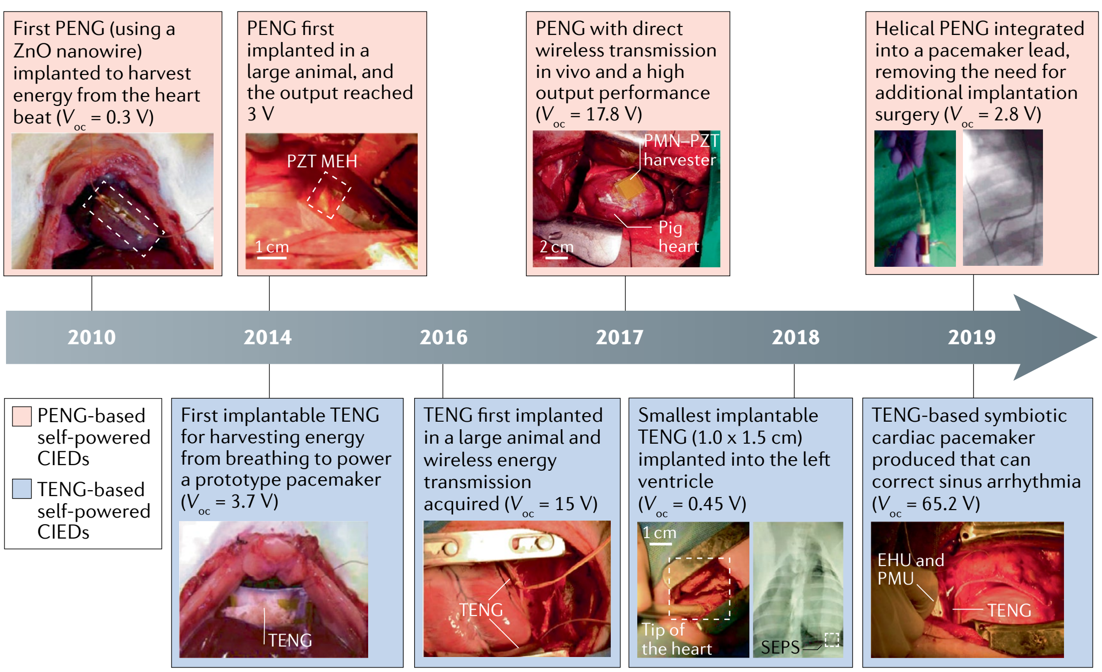

Fig. 4 | **Evolution of implantable PENGs and TENGs to build self-powered CIEDs.** Milestones in the development of implantable piezoelectric nanogenerators (PENGs) and triboelectric nanogenerators (TENGs) to produce self-powered cardiovascular implantable electronic devices (CIEDs). EHU, energy harvest unit; MEH, mechanoelectric harvester; PMN, (1–x)Pb(Mg$_{1/3}$Nb$_{2/3}$)O$_3$; PMU, power management unit; PZT, lead zirconate titanate; SEPS, self-powered endocardial pressure sensor; V_{oc}, open-circuit voltage; ZnO, zinc oxide. Top left image adapted with permission from REF.[77], Wiley. Top middle left image adapted with permission from REF.[82], PNAS. Top middle right image adapted with permission from REF.[84], Wiley. Top right image adapted with permission from REF.[137], Elsevier. Bottom left image adapted with permission from REF.[90], Wiley. Bottom middle left image adapted with permission from REF.[91], ACS. Bottom middle right image adapted from REF.[114], Wiley. Bottom right image adapted from REF.[92], CC BY 4.0 (https://creativecommons.org/licenses/by/4.0).

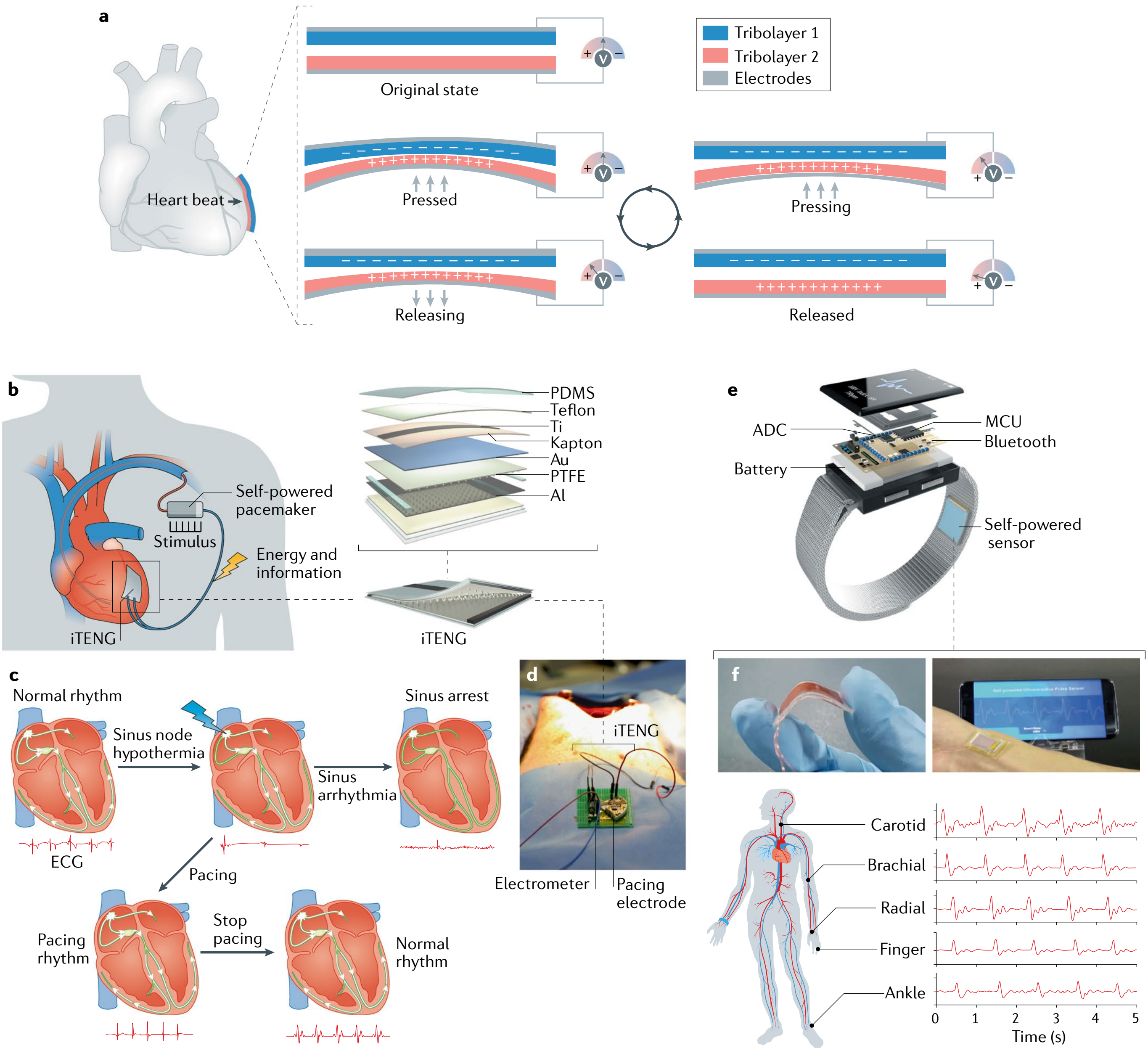

Fig. 5 | **Current self-powered cardiovascular electronic devices. a** | The principle of harvesting energy from the heart beat and the process of heart signal monitoring using a triboelectric nanogenerator (TENG). The motion of the heart beat brings the two friction layers of the TENG into and out of contact, generating triboelectric charges. The electrostatic field produced by these triboelectric charges can drive the flow of electrons in an external circuit. **b** | Illustration of the symbiotic cardiac pacemaker system (a self-powered pacemaker) and the structure of its implantable TENG (iTENG), containing layers of polydimethylsiloxane (PDMS), Teflon, titanium (Ti), Kapton, gold (Au), polytetrafluoroethylene (PTFE) and aluminium (Al). **c** | When hypothermia is applied to the sinus node, the heart enters sinus arrhythmia, which can lead to sinus arrest, as seen on the electrocardiogram (ECG). The arrhythmia is detected by the symbiotic cardiac pacemaker system and a pacing rhythm is applied for a short period that returns the heart to normal sinus rhythm. **d** | Photograph of the symbiotic cardiac pacemaker system being implanted in a large animal. **e** | A smart bracelet with a TENG-based active pulse sensor, containing an analogue-to-digital converter (ADC) and a microcontroller unit (MCU). **f** | Photograph of a flexible active pulse sensor and its real-time signal outputs when placed over the radial artery. The signal output of a pulse sensor when applied at various arterial positions is shown. Panels **b**–**d** adapted from REF.[92], CC BY 4.0 (https://creativecommons.org/licenses/by/4.0). Panels **e** and **f** adapted with permission from REF.[109], Wiley.

Active sensors of cardiovascular signals

Some physiological signals, such as heart rate and rhythm, radial artery pulse and blood pressure, glycaemic index, breathing wave, body temperature and daily movement, can provide information on cardiovascular health for the prevention of diseases through early diagnosis and intervention[101]. The development of wearable and implantable sensing devices allows real-time monitoring of these physiological signals. Currently, most wearable devices are designed to meet the needs of daily life. Their quality requirements, including battery life, data accuracy, equipment reliability and consistency of testing standards, are not strictly regulated and, therefore, these devices are generally unsuitable for medical applications. In medical practice, clinically approved devices need more complex functions, more stable and accurate data acquisition, more reliable and durable equipment, greater convenience for patients, better compliance to avoid missing any sudden changes in physiological signals in patients at high risk of a cardiac event, and continuous real-time monitoring of these signals at all times and in all places. These criteria represent the challenges associated with lifestyle wearable devices. For medical applications, wearable or implantable self-powered cardiovascular sensors with low power consumption, long life, high sensitivity and long-term stability are necessary. Two main strategies exist: active sensors, which can directly read, analyse and convert kinetic, chemical and/or thermal signals into electricity and monitor the status of the human body[102] (FIG. 5e), and devices that use nanogenerators to harvest energy to power medical sensors[103–105], which are similar in concept to the self-powered CIEDs. Therefore, the following discussion focuses mainly on the first strategy. With the active sensors described below, self-powered data acquisition, transmission and display can be simultaneously achieved in a system without a battery. However, if the device has integrated functions such as signal processing and wireless communication to form a fully self-powered system, the two strategies need to be combined[106].

Spin Seebeck effect
The generation of spin 'voltage' as a result of a temperature gradient; when a metallic magnet is subjected to a temperature gradient, it generates different driving powers of electrons in different spin channels along the temperature gradient.

n-Type organic semiconductor
Organic materials that are generally electrical insulators but which become semiconducting when charges are injected from appropriate electrodes; n-type organic semiconductors are electron acceptors with a low-lying lowest unoccupied molecular orbital.

Organic electrochemical transistor
A transistor in which the drain current is controlled by the injection of ions from an electrolyte into a semiconductor channel; the injection of ions in the channel is controlled through the application of a voltage to the gate electrode.

Wearable self-powered pulse sensors. Pulse sensing is an effective way to obtain data on cardiovascular parameters, such as radial artery pulse pressure and heart rate. The pulse can easily be detected on particular parts of the body surface with the use of a wearable device, which can provide important diagnostic parameters, such as amplitude, frequency and waveform. A PENG-based wearable self-powered pulse sensor, mounted on the skin, successfully measured subtle changes in radial artery augmentation index and pulse pressure velocity, with high sensitivity (~0.005 Pa) and fast response times (~0.1 ms)[107]. A piezoelectric device incorporating a Pb–PZT film was designed to detect dynamic radial or carotid artery pulsation and respiratory motion when attached to the wrist or neck[108]. Tiny pulse changes arising on the surface of the epidermis were detected, with good sensitivity (approximately 0.018 kPa^{-1}), a fast response time (approximately 60 ms) and good mechanical stability. A TENG-based, self-powered pulse sensor, which consisted of flexible thin films of polydimethylsiloxane and Kapton, showed excellent sensing capacity when applied as a patch on different parts of the human body[109] (FIG. 5f–h). Some cardiovascular diseases such as cardiac arrhythmia, atrial septal defect and coronary heart disease were diagnosed using this device. Another TENG-based pulse sensor was designed for non-invasive blood pressure measurement and had a high sensitivity of 45.7 mV/Pa, an ultrafast response time of <5 ms and no performance degradation after up to 40,000 motion cycles[110]. These self-powered devices are useful for the continuous assessment of an individual's health status and have the potential for detecting the early onset of cardiovascular disease.

Implantable active pulse sensors. Implantable sensors were invented to eliminate the interference of wearable devices with human activities and to meet the demand for higher fidelity and accuracy of acquired signals[102,104,111]. However, implantable sensors have inherent challenges, such as battery capacity, effective signal transduction and infections. Combining self-powered technology with implantable active sensors is a promising approach to reducing energy consumption and extending battery life to achieve long-term monitoring of cardiovascular signals in vivo. An implantable triboelectric active sensor (iTEAS) was designed using TENG-based self-powered technology for real-time monitoring of cardiovascular signals[112]. The iTEAS responded to heart contraction and relaxation, with a heart rate detection accuracy of 99% and some capacity to detect cardiac rhythm disturbances, such as atrial fibrillation and premature ventricular contraction. A piezoelectric thin-film-based implantable active sensor was designed to be wrapped around the aorta for blood pressure monitoring and had excellent linearity and accuracy ($R^2 = 0.99$)[113]. In 2019, a TENG-based, miniaturized (1.5 × 1.0 cm) active sensor was integrated with a surgical catheter for real-time endocardial pressure monitoring[114]. This device was implanted into the left ventricle or left atrium and achieved ultrasensitive, real-time monitoring in vivo. This device could detect arrhythmias such as premature ventricular contraction and ventricular fibrillation.

Active respiratory sensors. In 2018, a novel TENG-based active respiratory sensor was designed that could monitor respiratory rhythm[115], in which voltage peaks changed in accordance with breathing patterns. A PENG-based active respiratory sensor has also been developed. This flexible pressure sensor, made from a composite film of polyvinylidene fluoride–trifluoroethylene and multiwall carbon nanotubes, was positioned under the nose, and the respiratory airflow was harnessed to generate electrical signals[116]. A PyENG-based approach was used to produce an active breath sensor that could monitor temperature fluctuations during a breath, on the basis of the spin Seebeck effect[117,118]. The output of the PyENG was closely related to the temperature variation between exhaled gas and the ambient air[119]. The device could directly detect the respiratory rate and differentiate between three different patterns of breathing (normal, deep and rapid)[119].

Active blood sugar sensors. An active blood sugar sensor has been designed using an n-type organic semiconductor integrated with a biofuel cell[120]. The sensor consists of a polymer-based, flexible biofuel cell as the power generator and a small organic electrochemical transistor as the detector of glucose in bodily fluids. The sensor can detect a wide dynamic range of glucose levels (10 nmol/l to 20 mmol/l), with a sensitivity that can be adjusted by varying the conditions, and is a cost-effective, efficient and portable solution for blood sugar sensing.

Active body temperature sensors. Investigators have discussed the possibility of TENG-based or PENG-based active body temperature sensors using temperature-sensitive polyvinylidene fluoride film[121,122], which will help to evaluate physiological status and possibly to diagnose disease. A highly sensitive temperature–pressure dual-mode sensor was produced by combining PENG and PyENG technologies[123]. The flexible, self-powered sensor has a temperature resolution of <0.1 K and a pressure-sensing sensitivity of >20 kPa^{-1}.

Challenges and future perspectives

Interfacing with the human body

The functioning of a self-powered CED depends on the conversion of human-derived energy into electricity. No matter what kind of energy conversion method is used, the device must be in contact with the human body in a stable and close manner. Given the soft and curvilinear features of human tissues and organs (including the heart, diaphragm, lungs, stomach, muscles and skin) that the device will be implanted into or fixed on, the inability of rigid wearable and implantable systems to form a close interface remains a constraint. Reducing mechanical mismatch in the interface between the electronic device and the organism can effectively circumvent adverse immune responses during chronic implantation and thereby improve biosafety[124]. Indeed, soft and compliant integration of electronic devices with the human body is also necessary to improve the efficiency of energy conversion and sensing functions. Several approaches can be considered to achieve self-powered devices that conform to biological surfaces. First, further optimization of the structural design of electronic devices should be pursued, which might include the incorporation of ultrathin, porous, woven and/or other engineered materials[125,126] to introduce both flexible and stretchable properties to the entire device. Second, the development of intrinsically flexible and stretchable materials with low Young's modulus can provide tissue-level soft mechanical properties that eliminate the barrier at the interface between the electronics and the organism[127].

Miniaturization

With advanced microfabrication and nanofabrication techniques, CEDs can be made increasingly compact and integrated. A bulky battery or other form of traditional power source is one of the main obstacles to the miniaturization of CEDs. Therefore, finding solutions to reduce the mass and size of the power source, without compromising the energy supply, is of great importance. Self-powered technologies that harvest energy from human activities and/or the surrounding environment might mean that CEDs no longer need to be powered by a bulky battery. Reducing the mass and volume of these energy harvesters is central to achieving the aim of miniaturizing the overall device. For example, for devices designed to be placed in the pericardial space, a flat geometry is preferable. The thickness should ideally be <3 mm, but the area can be relatively larger. In addition, the mass of the device should typically be <1–2% of the mass of the heart (that is, <3–6 g), so as not to disturb cardiac contraction[128]. The mass of the smallest leadless pacemaker is currently approximately 2 g (REF.[129]).

As shown in TABLE 2, implantable PENGs and TENGs have been constructed using single-layered or double-layered thin flexible films, and their reported maximal thickness and mass are 0.9 mm and 1.9 g, respectively[92]. Therefore, these devices can easily be implanted into the narrow pericardial space or fixed (bio-bonded or stitched) onto the outside of the heart and will not disturb cardiac contraction. However, oscillation generators are a similar size to wristwatches, and their mass is often >10 g, exceeding the loading limit of the heart. The size and mass of electromagnet-based generators (EMGs) are also the main factors that hinder their clinical application in implantable or wearable cardiovascular devices. In a study evaluating the output voltages of different types of energy-harvesting device in relation to their mass, the values in PENGs, TENGs and EMGs were 28.0 V/g, 93.3 V/g and 0.3 V/g, respectively, indicating that increasing the output capacity of PENGs and TENGs will not substantially increase the mass of the device, and these devices have more potential for further miniaturization[130].

To maintain the output power while also miniaturizing self-powered CEDs, some possible directions should be considered, such as designing novel structures for higher outputs, the use of ultrathin encapsulation materials and methods, and the application of flexible integrated electronic circuits. Advances in materials science, electronic technology, and microprocessing and nanoprocessing technologies provide a great opportunity to develop smaller, more durable and more functional self-powered CEDs.

Power management

Appropriate power management can increase the efficiency of energy harvesting and energy use in self-powered devices. Efficient power management can be achieved by two main strategies. The first approach involves the conversion of unstable and pulsatile energy and storage of this energy via carefully designed electrical circuits. For example, PENGs and TENGs can be driven by periodic motions of the beating heart or breathing to generate a pulsatile output that cannot be used to power CEDs directly. The energy should be stored in batteries or capacitors for later use. In addition, the impedance mismatch between energy harvesters and common energy storage devices or CEDs can induce substantial energy loss or electrical failure, and is also a focus for future research.

For the second approach, some energy harvesters with a fairly stable, continuous and low-current output, such as biofuel cells, can be used to power CEDs directly. Here, the main strategy is to increase the output voltage. DC-to-DC converters and charge pumps can be used to increase the output voltage to meet the required operating voltage (2–3 V) of most CEDs. Other power management methods, such as buffer capacitors[98] and

Young's modulus
A measure of the capacity of a material to withstand changes in length when under lengthwise tension or compression.

Impedance mismatch
In electrical engineering, an impedance mismatch occurs when the input impedance of an electrical load does not match the output impedance of the signal source, resulting in signal reflection or an inefficient power transfer (depending on the type of matching required).

DC-to-DC converters
Electronic circuits or electromechanical devices that convert a source of direct current (DC) from one voltage level to another.

Charge pumps
DC-to-DC converters that use capacitors for electrical charge storage to raise or lower the voltage.

Buffer capacitors
A capacitor designed to suppress voltage surges that might otherwise damage other components in an electrical circuit.

Sputtered metals
A process by which metals form a thin layer of conducting material on a surface as a result of sputtering, a method of physical vapour deposition.

small rechargeable batteries[100], have been used during temporary energy shortages, for example, to power a solar-cell-based pacemaker at night.

Wireless technology

The existing mechanisms of wireless communication involve substantial power consumption, which limits the miniaturization of CEDs. However, incorporating wireless technology into CEDs gives physicians access to real-time data and the ability to make adjustments to treatment regimens without the need for patients to attend a hospital or clinic.

In the future, multiple medical devices located at different locations in the body (including, for example, leadless pacemakers positioned deep within the heart) might need to communicate with each other and work together[129]. The distance, depth and frequency of wireless transmission will be greatly increased, which will require more powerful communication capabilities. The optimization of wireless technology, including internal circuits, antennas and transmitters and a communication network within the body, together with the development of a self-powered energy supply and power management systems, will produce the next generation of self-powered CIEDs, with opportunities for miniaturization, complexity, robustness and increased functionality.

Standardization

Before their widespread use, standardized evaluation of self-powered CEDs must be conducted. These evaluations will also help to refine device design. The evaluation criteria should include the following aspects.

Output properties. To assess their suitability as sustainable power sources, the output performance of the various self-powered technologies should be standardized in order to facilitate the design and manufacture of medical electronic devices. These criteria include V_{oc}, I_{sc}, current density, internal resistance, maximum output and the efficiency of energy conversion. The specification of these values will help to establish widely accepted standards for practical applications of self-powered CEDs.

Connections. Connections are important for self-powered devices. Different components are most commonly connected using electrical wires. These wires are often made of gold[131], copper[132,133], polytetrafluoroethylene[87], carbon paste[70] or sputtered metals[83,107]. Furthermore, energy-conversion devices will be widely applied in future electrical devices, just as standard batteries are commonly used at present. Therefore, the connection between the energy harvester and the electronics needs to be standardized[134] to allow the assembly of a self-powered implantable electrical system. In addition to size specifications, the connector should have steady power transmission and long-term mechanical stability. Moreover, given that some implantable energy harvesters need to be located in soft and cramped positions inside the body, the connectors must be manufactured using conducting polymers to allow maximum flexibility.

Implantation-related evaluation. Providing sustainable energy to build implantable medical devices that can be used for a lifetime is one of the main motivations for the development of self-powered CEDs. Given that the device will stay inside the body for years or even decades and will be in contact with surrounding organs and tissues, strict in vivo evaluation criteria for biocompatibility, implantation method and site, and long-term durability must be applied[135]. Currently, these evaluations are neither systematic nor complete, and no unified evaluation standards or evaluation system have been established. Appropriate standardization of the surgical process is also essential. Considering the various possible implantation sites, such as the heart, lungs, diaphragm or aorta, the best implantation site and fixation strategy should be carefully studied and determined to guide future use.

Data handling. With either implantable or wearable CEDs, a large amount of data is continuously generated. Data collection, storage, transmission and analysis are performed using different platforms, algorithms and standards, and are difficult to translate to clinical practice. Therefore, one of the major challenges for the widespread adoption of self-powered CEDs into health-care systems is the identification and extraction of useful and actionable health-related information from the huge volume of data. With the increasing uptake of self-initiated physiological signal monitoring by individuals, applying big data analytical methodologies and machine learning to these datasets is a potential and inevitable solution. The increased computing power and ever-growing application of artificial intelligence will be used for the prediction of cardiovascular disease before the development of symptoms and to inform clinical decision-making.

Conclusions

Self-powered technology fits perfectly with the mobility, miniaturization and distribution of wearable and implantable CEDs. However, these devices are undergoing continuous evolution, with the latest generation of self-powered CEDs being smaller, softer, safer, more durable and more functionally complex than previous devices. With the integration of these advanced properties, self-powered CEDs will continue to improve, so that extremely long service lifetime, progressive miniaturization, better human conformability, improved sensing capacity, integrated functions with real-time data transmission, mobile data processing, and smart power utilization to adjust dynamically to power consumption and physiological needs will be achieved. Various self-powered CEDs are potentially available to meet the requirements of specific applications, such as in vivo diagnosis and treatment, real-time monitoring after surgery, and chronic disease monitoring and feedback. Meanwhile, device design and data processing technologies will be further tailored to specialized needs. In the future, self-powered implantable or wearable medical sensors and electronic devices are likely to be adopted as mainstream solutions in the field of cardiovascular diagnosis and treatment.

Published online: 07 September 2020

1. Beaglehole, R., Saracci, R. & Panico, S. Cardiovascular diseases: causes, surveillance and prevention. *Int. J. Epidemiol.* **30**, S1–S4 (2001).
2. World Health Organization. Cardiovascular diseases (CVDs) https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) (WHO, 2017).
3. Auricchio, A. & Moccetti, T. Electronic cardiac medicine: present and future opportunities. *Swiss Med. Wkly* **140**, w13052 (2010).
4. Wang, Z. L. Self-powered nanotech. *Sci. Am.* **298**, 82–87 (2008).
5. Larsson, B., Elmqvist, H., Ryden, L. & Schuller, H. Lessons from the first patient with an implanted pacemaker: 1958-2001. *Pacing Clin. Electrophysiol.* **26**, 114–124 (2003).
6. European Society of Cardiology. et al. 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy: the task force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). *Europace* **15**, 1070–1118 (2013).
7. Madhavan, M., Mulpuru, S. K., McLeod, C. J., Cha, Y. M. & Friedman, P. A. Advances and future directions in cardiac pacemakers: part 2 of a 2-part series. *J. Am. Coll. Cardiol.* **69**, 211–235 (2017).
8. Dotsenko, O., Barsheshet, A. & Huang, D. T. Cardiac resynchronization therapy for prevention of heart failure events in elderly patients with left ventricular dysfunction. *Expert Rev. Cardiovasc. Ther.* **10**, 1319–1327 (2012).
9. Moss, A. J. et al. Cardiac-resynchronization therapy for the prevention of heart-failure events. *N. Engl. J. Med.* **361**, 1329–1338 (2009).
10. Leclercq, C. et al. A randomized comparison of triple-site versus dual-site ventricular stimulation in patients with congestive heart failure. *J. Am. Coll. Cardiol.* **51**, 1455–1462 (2008).
11. Ellenbogen, K. A. & Vijayaraman, P. His bundle pacing: a new promise in heart failure therapy? *JACC Clin. Electrophysiol.* **1**, 592–595 (2015).
12. Keene, D. et al. His bundle pacing, learning curve, procedure characteristics, safety, and feasibility: insights from a large international observational study. *J. Cardiovasc. Electrophysiol.* **30**, 1984–1993 (2019).
13. Boriani, G. et al. Role of ventricular Autocapture function in increasing longevity of DDDR pacemakers: a prospective study. *Europace* **8**, 216–220 (2006).
14. Biffi, M. et al. Actual pacemaker longevity: the benefit of stimulation by automatic capture verification. *Pacing Clin. Electrophysiol.* **33**, 873–881 (2010).
15. Milasinovic, G. et al. Percent ventricular pacing with managed ventricular pacing mode in standard pacemaker population. *Europace* **10**, 151–155 (2008).
16. Gillis, A. M. et al. Reducing unnecessary right ventricular pacing with the managed ventricular pacing mode in patients with sinus node disease and AV block. *Pacing Clin. Electrophysiol.* **29**, 697–705 (2006).
17. Moss, A. J. et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N. Engl. J. Med.* **346**, 877–883 (2002).
18. Bardy, G. H. et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N. Engl. J. Med.* **352**, 225–237 (2005).
19. Glatter, K. A., Young, J. N. & McElvany, M. D. Implantable cardioverter-defibrillators: a new preventive medical option. *Prev. Cardiol.* **9**, 49–53 (2006).
20. Brignole, M. et al. Indications for the use of diagnostic implantable and external ECG loop recorders. *Europace* **11**, 671–687 (2009).
21. Farwell, D. J. & Sulke, A. N. Does the use of a syncope diagnostic protocol improve the investigation and management of syncope? *Heart* **90**, 52–58 (2004).
22. Roy, D. et al. Amiodarone to prevent recurrence of atrial fibrillation. Canadian trial of atrial fibrillation investigators. *N. Engl. J. Med.* **342**, 913–920 (2000).
23. Wyse, D. G. et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N. Engl. J. Med.* **347**, 1825–1833 (2002).
24. Dunn, J., Runge, R. & Snyder, M. Wearables and the medical revolution. *Per. Med.* **15**, 429–448 (2018).
25. Pevnick, J. M., Birkeland, K., Zimmer, R., Elad, Y. & Kedan, I. Wearable technology for cardiology: an update and framework for the future. *Trends Cardiovasc. Med.* **28**, 144–150 (2018).
26. National Heart Foundation and High Blood Pressure Research Council or Australia Ambulatory Blood Pressure Monitoring Consensus Committee. Ambulatory blood pressure monitoring. *Aust. Fam. Phys.* **40**, 877–880 (2011).
27. Mukkamala, R. et al. Toward ubiquitous blood pressure monitoring via pulse transit time: theory and practice. *IEEE Trans. Biomed. Eng.* **62**, 1879–1901 (2015).
28. Teplitzky, B. A. & McRoberts, M. in *2018 IEEE 15th International Conference on Wearable and Implantable Body Sensor Networks (BSN)* 58–61 (IEEE, 2018).
29. Vandenberk, T. et al. Clinical validation of heart rate apps: mixed-methods evaluation study. *JMIR Mhealth Uhealth* **5**, e129 (2017).
30. Orchard, J. et al. Screening for atrial fibrillation during influenza vaccinations by primary care nurses using a smartphone electrocardiograph (iECG): a feasibility study. *Eur. J. Prev. Cardiol.* **23**, 13–20 (2016).
31. Lau, J. K. et al. iPhone ECG application for community screening to detect silent atrial fibrillation: a novel technology to prevent stroke. *Int. J. Cardiol.* **165**, 193–194 (2013).
32. de Zambotti, M., Rosas, L., Colrain, I. M. & Baker, F. C. The sleep of the ring: comparison of the OURA sleep tracker against polysomnography. *Behav. Sleep Med.* **17**, 124–136 (2019).
33. Chung, M. K. et al. Aggregate national experience with the wearable cardioverter-defibrillator: event rates, compliance, and survival. *J. Am. Coll. Cardiol.* **56**, 194–203 (2010).
34. Selvaraj, N. in *2014 IEEE Healthcare Innovations Conference (HIC)* 83–86 (IEEE, 2014).
35. Turakhia, M. P. et al. Diagnostic utility of a novel leadless arrhythmia monitoring device. *Am. J. Cardiol.* **112**, 520–524 (2013).
36. Solomon, M. D. et al. Incidence and timing of potentially high-risk arrhythmias detected through long term continuous ambulatory electrocardiographic monitoring. *BMC Cardiovasc. Disord.* **16**, 35 (2016).
37. Glassninja. HeartIn ECG-monitoring T-shirt. *Cool Wearable* https://www.coolwearable.com/heartin-ecg-monitoring-t-shirt/ (2020).
38. Corday, E. et al. Detection of phantom arrhythmias and evanescent electrocardiographic abnormalities: use of prolonged direct electrocardiocording. *JAMA* **193**, 417–421 (1965).
39. Kamal, A. A., Harness, J. B., Irving, G. & Mearns, A. J. Skin photoplethysmography — a review. *Comput. Methods Prog. Biomed.* **28**, 257–269 (1989).
40. Allen, J. Photoplethysmography and its application in clinical physiological measurement. *Physiol. Meas.* **28**, R1–R39 (2007).
41. Cadmus-Bertram, L., Gangnon, R., Wirkus, E. J., Thraen-Borowski, K. M. & Gorzelitz-Liebhauser, J. The accuracy of heart rate monitoring by some wrist-worn activity trackers. *Ann. Intern. Med.* **166**, 610–612 (2017).
42. Wang, R. et al. Accuracy of wrist-worn heart rate monitors. *JAMA Cardiol.* **2**, 104–106 (2017).
43. Krumholz, H. M. et al. Patterns of hospital performance in acute myocardial infarction and heart failure 30-day mortality and readmission. *Circ. Cardiovasc. Qual. Outcomes* **2**, 407–413 (2009).
44. Adamson, P. B. Pathophysiology of the transition from chronic compensated and acute decompensated heart failure: new insights from continuous monitoring devices. *Curr. Heart Fail. Rep.* **6**, 287–292 (2009).
45. Amir, O., Rappaport, D., Zafrir, B. & Abraham, W. T. A novel approach to monitoring pulmonary congestion in heart failure: initial animal and clinical experiences using remote dielectric sensing technology. *Congest. Heart Fail.* **19**, 149–155 (2013).
46. Malfatto, G. et al. Correlation between trans and intra-thoracic impedance and conductance in patients with chronic heart failure. *J. Cardiovasc. Med.* **17**, 276–282 (2016).
47. Evenson, K. R., Goto, M. M. & Furberg, R. D. Systematic review of the validity and reliability of consumer-wearable activity trackers. *Int. J. Behav. Nutr. Phys. Act.* **12**, 159 (2015).
48. Chiauzzi, E., Rodarte, C. & DasMahapatra, P. Patient-centered activity monitoring in the self-management of chronic health conditions. *BMC Med.* **13**, 77 (2015).
49. Lau, E. W. Technologies for prolonging cardiac implantable electronic device longevity. *Pacing Clin. Electrophysiol.* **40**, 75–96 (2017).
50. Lekkerkerker, J. C. et al. Risk factors and time delay associated with cardiac device infections: Leiden device registry. *Heart* **95**, 715–720 (2009).
51. Munawar, D. A. et al. Predicted longevity of contemporary cardiac implantable electronic devices: a call for industry-wide "standardized" reporting. *Heart Rhythm* **15**, 1756–1763 (2018).
52. Wang, Z. L. & Song, J. H. Piezoelectric nanogenerators based on zinc oxide nanowire arrays. *Science* **312**, 242–246 (2006).
53. Wang, X., Song, J., Liu, J. & Wang, Z. L. Direct-current nanogenerator driven by ultrasonic waves. *Science* **316**, 102–105 (2007).
54. Xu, S. et al. Self-powered nanowire devices. *Nat. Nanotechnol.* **5**, 366–373 (2010).
55. Hu, Y., Zhang, Y., Xu, C., Zhu, G. & Wang, Z. L. High-output nanogenerator by rational unipolar assembly of conical nanowires and its application for driving a small liquid crystal display. *Nano Lett.* **10**, 5025–5031 (2010).
56. Wang, Z. L. From nanogenerators to piezotronics: a decade-long study of ZnO nanostructures. *MRS Bull.* **37**, 814–827 (2012).
57. Fan, F.-R., Tian, Z.-Q. & Lin Wang, Z. Flexible triboelectric generator. *Nano Energy* **1**, 328–334 (2012).
58. Wang, Z. L. Triboelectric nanogenerators as new energy technology and self-powered sensors – principles, problems and perspectives. *Faraday Discuss.* **176**, 447–458 (2014).
59. Zhu, G. et al. Triboelectric-generator-driven pulse electrodeposition for micropatterning. *Nano Lett.* **12**, 4960–4965 (2012).
60. Niu, S. et al. Theoretical study of contact-mode triboelectric nanogenerators as an effective power source. *Energy Environ. Sci.* **6**, 3576–3583 (2013).
61. Wang, S. et al. Sliding-triboelectric nanogenerators based on in-plane charge-separation mechanism. *Nano Lett.* **13**, 2226–2233 (2013).
62. Niu, S. et al. Theoretical investigation and structural optimization of single-electrode triboelectric nanogenerators. *Adv. Funct. Mater.* **24**, 3332–3340 (2014).
63. Wang, S., Xie, Y., Niu, S., Lin, L. & Wang, Z. L. Freestanding triboelectric-layer-based nanogenerators for harvesting energy from a moving object or human motion in contact and non-contact modes. *Adv. Mater.* **26**, 2818–2824 (2014).
64. Niu, S. et al. Theory of freestanding triboelectric-layer-based nanogenerators. *Nano Energy* **12**, 760–774 (2015).
65. Bowen, C. R. et al. Pyroelectric materials and devices for energy harvesting applications. *Energy Environ. Sci.* **7**, 3836–3856 (2014).
66. Cuadras, A., Gasulla, M. & Ferrari, V. Thermal energy harvesting through pyroelectricity. *Sens. Actuators A Phys.* **158**, 132–139 (2010).
67. Uchida, K. et al. Observation of the spin Seebeck effect. *Nature* **455**, 778–781 (2008).
68. Mano, N., Mao, F. & Heller, A. Characteristics of a miniature compartment-less glucose-O2 biofuel cell and its operation in a living plant. *J. Am. Chem. Soc.* **125**, 6588–6594 (2003).
69. Rapoport, B. I., Kedzierski, J. T. & Sarpeshkar, R. A glucose fuel cell for implantable brain–machine interfaces. *PLoS ONE* **7**, e38436 (2012).
70. Zebda, A. et al. Single glucose biofuel cells implanted in rats power electronic devices. *Sci. Rep.* **3**, 1516 (2013).
71. Dagdeviren, C., Li, Z. & Wang, Z. L. Energy harvesting from the animal/human body for self-powered electronics. *Annu. Rev. Biomed. Eng.* **19**, 85–108 (2017).
72. Tian, B. et al. Coaxial silicon nanowires as solar cells and nanoelectronic power sources. *Nature* **449**, 885–889 (2007).
73. Vazquez-Mena, O. et al. Performance enhancement of a graphene-zinc phosphide solar cell using the electric field-effect. *Nano Lett.* **14**, 4280–4285 (2014).
74. Chang, T. H. et al. Planar heterojunction perovskite solar cells incorporating metal-organic framework nanocrystals. *Adv. Mater.* **27**, 7229–7235 (2015).
75. Goto, H., Sugiura, T., Harada, Y. & Kazui, T. Feasibility of using the automatic generating system for quartz watches as a leadless pacemaker power source. *Med. Biol. Eng. Comput.* **37**, 377–380 (1999).
76. Mercier, P. P., Lysaght, A. C., Bandyopadhyay, S., Chandrakasan, A. P. & Stankovic, K. M. Energy extraction from the biologic battery in the inner ear. *Nat. Biotechnol.* **30**, 1240–1243 (2012).
77. Li, Z., Zhu, G., Yang, R., Wang, A. C. & Wang, Z. L. Muscle-driven in vivo nanogenerator. *Adv. Mater.* **22**, 2534–2537 (2010).

78. Ben Amar, A., Kouki, A. B. & Cao, H. Power approaches for implantable medical devices. *Sensors* **15**, 28889–28914 (2015).
79. Burleson, W., Clark, S. S., Ransford, B. & Fu, K. in *DAC Design Automation Conference 2012* 12–17 (IEEE, 2012).
80. Joung, Y. H. Development of implantable medical devices: from an engineering perspective. *Int. Neurourol. J.* **17**, 98–106 (2013).
81. Shi, B., Li, Z. & Fan, Y. Implantable energy-harvesting devices. *Adv. Mater.* **30**, e1801511 (2018).
82. Dagdeviren, C. et al. Conformal piezoelectric energy harvesting and storage from motions of the heart, lung, and diaphragm. *Proc. Natl Acad. Sci. USA* **111**, 1927–1932 (2014).
83. Lu, B. et al. Ultra-flexible piezoelectric devices integrated with heart to harvest the biomechanical energy. *Sci. Rep.* **5**, 16065 (2015).
84. Kim, D. H. et al. In vivo self-powered wireless transmission using biocompatible flexible energy harvesters. *Adv. Funct. Mater.* **27**, 1700341 (2017).
85. Zhang, H. et al. A flexible and implantable piezoelectric generator harvesting energy from the pulsation of ascending aorta: in vitro and in vivo studies. *Nano Energy* **12**, 296–304 (2015).
86. Lin, H.-I., Wuu, D.-S., Shen, K.-C. & Horng, R.-H. Fabrication of an ultra-flexible ZnO nanogenerator for harvesting energy from respiration. *ECS J. Solid State Sci. Technol.* **2**, P400–P404 (2013).
87. Dagdeviren, C. et al. Flexible piezoelectric devices for gastrointestinal motility sensing. *Nat. Biomed. Eng.* **1**, 807–817 (2017).
88. Zheng, Q. et al. Biodegradable triboelectric nanogenerator as a life-time designed implantable power source. *Sci. Adv.* **2**, e1501478 (2016).
89. Song, P. et al. A self-powered implantable drug-delivery system using biokinetic energy. *Adv. Mater.* **29**, 1605668 (2017).
90. Zheng, Q. et al. In vivo powering of pacemaker by breathing-driven implanted triboelectric nanogenerator. *Adv. Mater.* **26**, 5851–5856 (2014).
91. Zheng, Q. et al. In vivo self-powered wireless cardiac monitoring via implantable triboelectric nanogenerator. *ACS Nano* **10**, 6510–6518 (2016).
92. Ouyang, H. et al. Symbiotic cardiac pacemaker. *Nat. Commun.* **10**, 1821 (2019).
93. Zurbuchen, A. et al. Energy harvesting from the beating heart by a mass imbalance oscillation generator. *Ann. Biomed. Eng.* **41**, 131–141 (2013).
94. Zurbuchen, A. et al. Towards batteryless cardiac implantable electronic devices—the Swiss way. *IEEE Trans. Biomed. Circuits Syst.* **11**, 78–86 (2017).
95. Bereuter, L. et al. Energy harvesting by subcutaneous solar cells: a long-term study on achievable energy output. *Ann. Biomed. Eng.* **45**, 1172–1180 (2017).
96. Chaar, L. E., lamont, L. A. & Zein, N. E. Review of photovoltaic technologies. *Renew. Sust. Energ. Rev.* **15**, 2165–2175 (2011).
97. Hovel, H. J. in *Semiconductors and Semimetals* Vol. 11 (eds Willardson, R. K. & Beer, A. C.) 181–207 (Academic Press, 1975).
98. Haeberlin, A. et al. Successful pacing using a batteryless sunlight-powered pacemaker. *Europace* **16**, 1534–1539 (2014).
99. Haeberlin, A. et al. The first batteryless, solar-powered cardiac pacemaker. *Heart Rhythm* **12**, 1317–1323 (2015).
100. Song, K. et al. Subdermal flexible solar cell arrays for powering medical electronic implants. *Adv. Healthc. Mater.* **5**, 1572–1580 (2016).
101. Zhao, L. M., Li, H., Meng, J. P. & Li, Z. The recent advances in self-powered medical information sensors. *InfoMat* **2**, 212–234 (2020).
102. Sun, J. Y., Yang, A. P., Zhao, C., Liu, F. & Li, Z. Recent progress of nanogenerators acting as biomedical sensors in vivo. *Sci. Bull.* **64**, 1336–1347 (2019).
103. Liu, Z. et al. Wearable and implantable triboelectric nanogenerators. *Adv. Funct. Mater.* **29**, 1808820 (2019).
104. Feng, H. et al. Nanogenerator for biomedical applications. *Adv. Healthc. Mater.* **7**, e1701298 (2018).
105. Lin, Z. et al. Triboelectric nanogenerator enabled body sensor network for self-powered human heart-rate monitoring. *ACS Nano* **11**, 8830–8837 (2017).
106. Li, Z., Zheng, Q., Wang, Z. L. & Li, Z. Nanogenerator-based self-powered sensors for wearable and implantable electronics. *Research* **2020**, 8710686 (2020).
107. Dagdeviren, C. et al. Conformable amplified lead zirconate titanate sensors with enhanced piezoelectric response for cutaneous pressure monitoring. *Nat. Commun.* **5**, 4496 (2014).
108. Park, D. Y. et al. Self-powered real-time arterial pulse monitoring using ultrathin epidermal piezoelectric sensors. *Adv. Mater.* **29**, 1702308 (2017).
109. Ouyang, H. et al. Self-powered pulse sensor for antidiastole of cardiovascular disease. *Adv. Mater.* **29**, 1703456 (2017).
110. Meng, K. et al. Flexible weaving constructed self-powered pressure sensor enabling continuous diagnosis of cardiovascular disease and measurement of cuffless blood pressure. *Adv. Funct. Mater.* **29**, 1806388 (2019).
111. Mahmud, M. A. P., Huda, N., Farjana, S. H., Asadnia, M. & Lang, C. Recent advances in nanogenerator-driven self-powered implantable biomedical devices. *Adv. Energy Mater.* **8**, 1701210 (2018).
112. Ma, Y. et al. Self-powered, one-stop, and multifunctional implantable triboelectric active sensor for real-time biomedical monitoring. *Nano Lett.* **16**, 6042–6051 (2016).
113. Cheng, X. L. et al. Implantable and self-powered blood pressure monitoring based on a piezoelectric thinfilm: simulated, in vitro and in vivo studies. *Nano Energy* **22**, 453–460 (2016).
114. Liu, Z. et al. Transcatheter self-powered ultrasensitive endocardial pressure sensor. *Adv. Funct. Mater.* **29**, 1807560 (2019).
115. Wang, M. et al. Air-flow-driven triboelectric nanogenerators for self-powered real-time respiratory monitoring. *ACS Nano* **12**, 6156–6162 (2018).
116. Wang, A., Hu, M., Zhou, L. & Qiang, X. Self-powered wearable pressure sensors with enhanced piezoelectric properties of aligned P(VDF-TrFE)/MWCNT composites for monitoring human physiological and muscle motion signs. *Nanomaterials* **8**, 1021 (2018).
117. Wang, S., Wang, Z. L. & Yang, Y. A one-structure-based hybridized nanogenerator for scavenging mechanical and thermal energies by triboelectric-piezoelectric-pyroelectric effects. *Adv. Mater.* **28**, 2881–2887 (2016).
118. Wang, X. et al. Light-triggered pyroelectric nanogenerator based on a pn-junction for self-powered near-infrared photosensing. *ACS Nano* **11**, 8339–8345 (2017).
119. Xue, H. et al. A wearable pyroelectric nanogenerator and self-powered breathing sensor. *Nano Energy* **38**, 147–154 (2017).
120. Ohayon, D. et al. Biofuel powered glucose detection in bodily fluids with an n-type conjugated polymer. *Nat. Mater.* **19**, 456–463 (2020).
121. Wang, X. et al. Bionic single-electrode electronic skin unit based on piezoelectric nanogenerator. *ACS Nano* **12**, 8588–8596 (2018).
122. Xia, K., Zhu, Z., Zhang, H. & Xu, Z. W. A triboelectric nanogenerator as self-powered temperature sensor based on PVDF and PTFE. *Appl. Phys. A* **124**, 520 (2018).
123. Zhang, F., Zang, Y., Huang, D., Di, C. A. & Zhu, D. Flexible and self-powered temperature-pressure dual-parameter sensors using microstructure-frame-supported organic thermoelectric materials. *Nat. Commun.* **6**, 8356 (2015).
124. Feiner, R. & Dvir, T. Tissue–electronics interfaces: from implantable devices to engineered tissues. *Nat. Rev. Mater.* **3**, 17076 (2017).
125. Liu, J. et al. Syringe-injectable electronics. *Nat. Nanotechnol.* **10**, 629–636 (2015).
126. Hong, G., Yang, X., Zhou, T. & Lieber, C. M. Mesh electronics: a new paradigm for tissue-like brain probes. *Curr. Opin. Neurobiol.* **50**, 33–41 (2018).
127. Obidin, N., Tasnim, F. & Dagdeviren, C. The future of neuroimplantable devices: a materials science and regulatory perspective. *Adv. Mater.* **32**, e1901482 (2020).
128. Pfenniger, A., Jonsson, M., Zurbuchen, A., Koch, V. M. & Vogel, R. Energy harvesting from the cardiovascular system, or how to get a little help from yourself. *Ann. Biomed. Eng.* **41**, 2248–2263 (2013).
129. Tjong, F. V. & Reddy, V. Y. Permanent leadless cardiac pacemaker therapy: a comprehensive review. *Circulation* **135**, 1458–1470 (2017).
130. Tan, P. et al. A battery-like self-charge universal module for motional energy harvest. *Adv. Energy Mater.* **9**, 1901857 (2019).
131. Schwefel, J. et al. Wireless communication by an autonomous self-powered cyborg insect. *J. Electrochem. Soc.* **161**, H3113–H3116 (2014).
132. Cinquin, P. et al. A glucose biofuel cell implanted in rats. *PLoS ONE* **5**, e10476 (2010).
133. El Ichi, S. et al. Bioelectrodes modified with chitosan for long-term energy supply from the body. *Energy Environ. Sci.* **8**, 1017–1026 (2015).
134. Shi, B. et al. A packaged self-powered system with universal connectors based on hybridized nanogenerators. *Adv. Mater.* **28**, 846–852 (2016).
135. Yu, J. R. et al. Current and future perspectives on skin tissue engineering: key features of biomedical research, translational assessment, and clinical application. *Adv. Healthc. Mater.* **8**, e1801471 (2019).
136. Castorena-Gonzalez, J. A. et al. Biofuel cell operating in vivo in rat. *Electroanalysis* **25**, 1579–1584 (2013).
137. Dong, L. et al. In vivo cardiac power generation enabled by an integrated helical piezoelectric pacemaker lead. *Nano Energy* **66**, 104085 (2019).

Acknowledgements
The authors' work on self-powered medical devices is funded by the National Natural Science Foundation of China (no. 61875015 and 81971770), the Key Project of the National Natural Science Foundation (no. 81530012), the National Key R&D Project from the Ministry of Science and Technology, China (2016YFA0202703), the Beijing Natural Science Foundation (7204333), the University of Chinese Academy of Sciences and the National Youth Talent Support Program.

Author contributions
Q.Z. and Z.L. researched the data for the article and wrote the manuscript. All the authors discussed the content of the article and reviewed and/or edited it before submission.

Competing interests
The authors declare no competing interests.

Peer review information
Nature Reviews Cardiology thanks S.-G. Kim and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.

Publisher's note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.