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1-1 What are Biomedical Sensors?

Biomedical sensors are **devices** that can **detect** and **measure** various **biological** and **physiological information**, **converting** biological or chemical signals into electrical or other forms of signals that <u>can be processed and analyzed</u>. They play a crucial role in medical diagnosis, monitoring of physiological conditions, and biomedical research. For example, in a blood glucose meter, the sensor detects the concentration of glucose in the blood and converts it into an electrical signal that can be displayed as a numerical value for the user to read.

1-2 To take examples to explain the classification of biomedical sensors.

(1) Physical Sensors

Physical sensors are those constructed **based on physical properties and effects.** A large number of such sensors are exemplified by metal resistance strain sensors, semiconductor piezoresistive sensors, piezoelectric sensors, and photoelectric sensors. Metal resistance strain sensors work on the principle that when a metal is subjected to strain, its resistance changes proportionally. This property allows them to measure mechanical forces accurately. Semiconductor piezoresistive sensors, on the other hand, utilize the piezoresistive effect in semiconductors, which is highly sensitive to pressure changes. Piezoelectric sensors generate an electric charge when mechanical stress is applied, making them useful for detecting vibrations and pressure variations. Photoelectric sensors, as the name implies, operate based on the interaction between light and electricity, such as converting light intensity into an electrical signal.

These physical sensors find extensive applications in various medical devices. Sphygmomanometers, which are used to measure blood pressure, often incorporate pressure-sensitive physical sensors. Thermometers rely on sensors that can detect temperature-induced changes in physical properties, such as the expansion of a liquid in a traditional mercury thermometer or the change in electrical resistance in an electronic thermometer. Electrocardiographs use sensors to detect the weak

electrical signals generated by the heart during its normal functioning. Stethoscopes, although not strictly electronic sensors in the traditional sense, are designed to amplify the physical sounds of the heart, lungs, and other internal organs, which can be considered as a form of physical signal detection. These sensors are crucial for detecting and monitoring a wide range of physiological parameters including blood pressure, breath, body temperature, heart sounds, heart electrical signals, blood viscosity, flow velocity, and flux.

(2) Chemical Sensors

Chemical sensors are designed **in accordance with chemical properties and effects.** They typically employ ion-selective sensitive films to convert non-electrical quantities like chemical components, content, and density into relevant electrical quantities. Examples of chemical sensors include various ion-sensitive electrodes, ion-sensitive tubes, and humidity sensors. Ion-sensitive electrodes are highly selective for specific ions in a solution. For instance, a pH-sensitive electrode is designed to measure the hydrogen ion concentration in a solution, which is expressed as the pH value. It works based on the principle of a chemical reaction that generates an electrical potential difference across the electrode membrane, proportional to the concentration of the target ion. Ion-sensitive tubes operate in a similar manner but may have different structural designs for specific applications. Humidity sensors detect the moisture content in the air or in a sample by measuring the change in a chemical property, such as the electrical conductivity of a hygroscopic material when it absorbs or releases water vapor.

These chemical sensors are used in devices like pH meters, which are essential for measuring the acidity or alkalinity of substances. Ion sensors are crucial for detecting and monitoring various ions in biological fluids. In the human body, the pH values of body liquids such as blood, sweat, and urine are important indicators of health. Chemical sensors can also detect and monitor substances like oxygen and carbon dioxide, which are involved in respiration processes, as well as important ions

in the body such as Na+, K+, Ca+, Cl -, and heavy metal ions. Abnormal levels of these ions can indicate various health issues, so accurate detection by chemical sensors is vital.

(3) Biological Sensors

Biological sensors are characterized by **using biological active materials as a molecule-recognition system**. They often utilize enzymes to catalyze specific biochemical reactions or detect the types and contents of large organic molecules through specific binding mechanisms. Enzymes are highly specific proteins that can accelerate biochemical reactions. For example, an enzyme sensor may use an enzyme to react with a target substrate in a sample. The reaction produces a detectable change, such as the generation of a product that can be measured electrochemically or optically. Microorganism sensors use whole microorganisms to detect specific substances. These microorganisms have specific metabolic pathways that can be affected by the presence of certain molecules in the sample, and this change can be detected as a signal. Immunity sensors are based on the immune response of the body. They use antibodies or antigens to specifically bind to target molecules, and the binding event can be detected through various techniques, such as fluorescence or electrochemical methods. Tissue sensors utilize living tissue or tissue-like materials to detect specific analytes. DNA sensors are designed to detect specific DNA sequences. They can be used to identify genetic markers related to diseases or to study gene expression.

Biological sensors are a relatively new development, emerging mainly in the second half of the century. They are used for **detecting and monitoring a wide range of biological entities** including tissues, cells, enzymes, antigens, antibodies, hormones, gallbladder substances, acetylcholine, 5-HT (serotonin), and DNA, RNA. These sensors play a crucial role in medical diagnosis, environmental monitoring, and food safety assessment, as they can provide highly specific and sensitive detection of biological substances.

1-3 To take examples to list the specific requirements of biomedical sensors.

High Sensitivity: Biomedical sensors need to be able to detect very small changes in the measured quantity. For example, in detecting trace amounts of biomarkers in the blood for early cancer diagnosis, the sensor should be sensitive enough to detect biomarkers present in extremely low concentrations, such as detecting specific proteins or nucleic acids that may indicate the presence of cancer cells at an early stage.

High Selectivity: They should be able to distinguish the target substance or signal from other interfering substances or signals. For instance, a glucose sensor in the body should only respond to glucose and not be affected by other sugars or substances in the blood.

Good Biocompatibility: The sensor should not cause any harmful effects or immune responses when in contact with the biological environment. For example, implantable sensors, such as pacemaker leads, must be made of biocompatible materials like titanium or certain polymers to avoid tissue rejection and ensure long-term functionality.

Stability: The sensor should maintain its performance over time. In continuous blood glucose monitoring systems, the sensor needs to provide accurate readings for an extended period, usually several days or weeks, without significant drift or degradation in performance.

Fast Response Time: The sensor should be able to quickly detect and respond to changes in the measured quantity. In monitoring heart rate, the sensor should be able to update the readings in real-time, accurately reflecting the changes in the heart's rhythm within a short period, typically within a few seconds.

1-4 What are Biomimetic Sensors?

Biomimetic sensors are sensors that **mimic the sensing mechanisms or**

structures of biological systems. They draw inspiration from nature to achieve highly efficient and specific sensing functions.

For example, some biomimetic sensors are designed to mimic the olfactory receptors in the human nose. These sensors can detect and identify specific odors in a similar way to how the human olfactory system works. They use artificial receptor materials that can bind to specific odor molecules and generate electrical or other signals, enabling the detection and discrimination of different odors.

Another example is the biomimetic vision sensors that imitate the structure and function of the human eye or the visual systems of other organisms. These sensors can capture and process visual information more efficiently and adaptively than traditional optical sensors, which have applications in fields such as robotics and computer vision.

1-5 To take examples to describe the trends of modern biomedical sensors and measurement.

(1) Miniaturization and Integration: Wearable devices like smartwatches with built-in heart rate and blood oxygen sensors integrate multiple sensing functions into a small, portable form, enabling daily physiological parameter monitoring.

(2) Multiplexing and Multi-modal Sensing: Some medical imaging systems combine X-ray, CT, and MRI, and biosensors are being developed to detect multiple biomarkers in a single sample, such as glucose, lactate, and ketone bodies in body fluids.

(3) Wireless and Remote Monitoring: Implantable wireless sensors can transmit internal body data like pressure and temperature to external receivers, facilitating remote patient health monitoring for timely medical intervention.

(4) Intelligence and Self-Calibration: Glucose sensors can self-calibrate based on reference values and environmental factors, and intelligent sensors can analyze data in real-time, providing early warning and diagnosis, like predicting hypoglycemia or hyperglycemia from glucose trends.

(5) Invasive and Non-Invasive Detection: There is a shift towards non-invasive or minimally invasive detection methods as they are more acceptable to patients, reliable, easy to operate, and sterilize, with examples like non-invasive blood glucose meters and percutaneous blood gas sensors.

(6) Multi-Parameter Detection: These sensors are small-sized, multi-functional systems that can measure multiple parameters simultaneously. For example, an integrated blood electrolyte sensor can monitor 5 parameters, offering higher accuracy, stability, and cost-effectiveness compared to using multiple sensors.

(7) In vitro and in vivo Detection: In vitro detection is important for clinical laboratory tests, becoming more multi-functional, continuous, and automatic, such as in vitro allergen detection. In vivo detection, like with brain-computer interfaces, allows real-time observation of physiological and pathological processes.

(8) Intelligent Artificial Viscera: These are designed to have all normal organ functions, and equipping anti-rejection molecular systems on transplanted organs can address the rejection problem in xenotransplantation.

(9) Bedside Monitoring and Wearable Devices: Bedside monitoring sensors are simple, durable, lightweight, and can operate continuously or semi-continuously. Wearable devices, especially smart textiles with fabric-based physical sensors, are used for bio-monitoring, rehabilitation, and telemedicine.

(9) Micro-Nano System: The integration of CPU and miniature sensors on the same silicon chip promotes intelligent microsensor technology, as seen in intellectual pills for in-vivo on-line detection.

(10) Biomimetic Sensors: These new-principle sensors, like receptor sensors, nerve cell sensors, and biomimetic nerve cell sensors, as well as electronic nose and tongue, are an important development direction in biomedical sensor technology, with potential applications in biomedicine, food, and environmental protection.

1-1 什么是生物医学传感器？

生物医学传感器是能够检测和测量各种生物与生理信息的装置，它将生物或化学信号转换为可处理和分析的电信号或其他形式的信号。这类传感器在医学诊断、生理状态监测和生物医学研究中起着关键作用。例如，在血糖仪中，传感器检测血液中的葡萄糖浓度，并将其转换为电信号，以数值形式显示供用户读取。

1-2 举例说明生物医学传感器的分类

（1）物理传感器

物理传感器基于物理性质和效应构建，典型代表包括金属电阻应变传感器、半导体压阻传感器、压电传感器和光电传感器。

金属电阻应变传感器：原理是金属受应变时电阻成比例变化，可精确测量机械力。

半导体压阻传感器：利用半导体的压阻效应，对压力变化高度敏感。

压电传感器：受机械应力时产生电荷，适用于检测振动和压力变化。

光电传感器：基于光与电的相互作用，如将光强度转换为电信号。

应用场景：

- 血压计采用压敏物理传感器测量血压；
- 温度计通过检测温度引起的物理性质变化(如传统水银温度计的液体膨胀或电子温度计的电阻变化）工作；
- 心电图仪利用传感器检测心脏正常工作时产生的微弱电信号；
- 听诊器虽非严格意义上的电子传感器，但通过放大心脏、肺部等内脏的物理声音，可视为一种物理信号检测形式。
  这些传感器用于检测和监测血压、呼吸、体温、心音、心电信号、血液黏度、流速和流量等广泛的生理参数。

（2）化学传感器

化学传感器依据化学性质和效应设计，通常使用离子选择性敏感膜将化学成分、含量和浓度等非电量转换为相关电量。典型例子包括各种离子敏感电极、离子敏感管和湿度传感器。

- **离子敏感电极**：对溶液中的特定离子具有高选择性。例如，pH 敏感电极通过化学反应产生与氢离子浓度（pH 值）成比例的电势差，用于测量溶液的酸碱度。

- **离子敏感管**：工作原理类似，但结构设计可能针对特定应用优化。
- **湿度传感器**：通过测量吸湿材料吸收或释放水蒸气时的化学性质变化（如电导率），检测空气或样品中的水分含量。

应用场景：

- pH 计依赖化学传感器测量物质的酸碱度；
- 离子传感器用于检测和监测生物体液中的各种离子（如血液、汗液、尿液的 pH 值是健康的重要指标）；
- 化学传感器还可检测呼吸过程中的氧气和二氧化碳，以及体内重要离子（如 Na^+、K^+、Ca^{2+}、Cl^- 和重金属离子），这些离子的异常水平可提示多种健康问题。

（3）生物传感器

生物传感器的核心是使用生物活性材料作为分子识别系统，常利用酶催化特定生化反应，或通过特异性结合机制检测大型有机分子的类型和含量。

- **酶传感器**：利用酶与样品中的目标底物反应，通过检测反应产物（如电化学或光学信号变化）实现测量。
- **微生物传感器**：利用完整微生物的特定代谢途径，通过检测微生物对样品中特定分子的响应信号实现分析。
- **免疫传感器**：基于人体免疫反应，利用抗体或抗原与目标分子特异性结合，通过荧光或电化学等技术检测结合事件。
- **组织传感器与 DNA 传感器**：分别利用活组织或类似材料、特定 DNA 序列检测目标分析物，可用于疾病相关遗传标记的鉴定或基因表达研究。

应用场景：
生物传感器是 20 世纪下半叶新兴的技术，用于检测和监测组织、细胞、酶、抗原、抗体、激素、胆酸、乙酰胆碱、5－羟色胺（血清素）及 DNA/RNA 等生物实体，在医学诊断、环境监测和食品安全评估中实现高特异性和高灵敏度的生物物质检测。

1-3 举例说明生物医学传感器的具体要求

（1）高灵敏度

传感器需能检测被测量的微小变化。例如，在早期癌症诊断中检测血液中的痕量生物标志物时，传感器需足够灵敏以识别极低浓度的特定蛋白质或核酸（这些物质可能提示早期癌细胞的存在）。

（2）高选择性

传感器应能从其他干扰物质或信号中区分目标物质或信号。例如，体内的葡萄糖传感器应仅对葡萄糖响应，不受血液中其他糖类或物质的影响。

（3）良好的生物相容性

传感器与生物环境接触时不应引起有害效应或免疫反应。例如，植入式传感器（如心脏起搏器导线）必须由钛或特定聚合物等生物相容性材料制成，以避免组织排斥并确保长期功能。

（4）稳定性

传感器需长期保持性能。在连续血糖监测系统中，传感器需在数天或数周内提供准确读数，无显著漂移或性能退化。

（5）快速响应时间

传感器需快速检测并响应被测量的变化。在心率监测中，传感器需实时更新读数，数秒内准确反映心律变化。

1-4 什么是仿生传感器？

仿生传感器是模仿生物系统的感知机制或结构的传感器，其设计灵感源于自然界，以实现高效、特异性的传感功能。

- **仿嗅觉传感器**：模仿人类鼻腔的嗅觉受体，通过人工受体材料结合特定气味分子并产生电信号，实现气味的检测与识别，类似人类嗅觉系统的工作方式。
- **仿视觉传感器**：模仿人眼或其他生物视觉系统的结构与功能，比传统光学传感器更高效、自适应地捕获和处理视觉信息，应用于机器人和计算机视觉等领域。

1-5 举例说明现代生物医学传感器与测量技术的发展趋势

（1）小型化与集成化

智能手表等可穿戴设备内置心率和血氧传感器，将多种传感功能集成于小巧便携的形态中，实现日常生理参数监测。

（2）多 iplexing 与多模态传感

部分医学成像系统融合 X 射线、CT 和 MRI，生物传感器则向单样本多生物标志物检测发展（如同时检测体液中的葡萄糖、乳酸和酮体）。

（3）无线与远程监测

植入式无线传感器可将体内压力、温度等数据传输至外部接收器，支持远程患者健康监测，便于及时医疗干预。

（4）智能化与自校准

葡萄糖传感器可根据参考值和环境因素自校准，智能传感器能实时分析数据并提供预警（如根据血糖趋势预测低血糖或高血糖）。

（5）有创与无创检测

趋势向无创或微创检测发展（如无创血糖仪、经皮血气传感器），因其更易被患者接受，且操作、灭菌更便捷可靠。

（6）多参数检测

小型化多功能系统可同时测量多个参数（如集成式血液电解质传感器监测 5 项指标），较单一传感器更精准、稳定且成本效益高。

（7）体外与体内检测

- **体外检测**：临床检验向多功能、连续化、自动化发展（如体外过敏原检测）；
- **体内检测**：脑机接口等技术实现生理病理过程的实时观测。

（8）智能人工脏器

设计具备正常器官功能的人工脏器，在移植器官上配备抗排斥分子系统，解决异种移植中的排斥问题。

（9）床旁监测与可穿戴设备

床旁监测传感器简洁耐用、轻便，支持连续或半连续工作；可穿戴设备（尤其是基于织物物理传感器的智能纺织品）用于生物监测、康复和远程医疗。

（10）微纳系统

CPU 与微型传感器在同一硅芯片上的集成推动智能微传感器技术发展，如用于体内在线检测的智能药丸。

（11）仿生传感器

受体传感器、神经细胞传感器、仿生神经细胞传感器及电子鼻 / 舌等新原理传感器，是生物医学传感器技术的重要发展方向，在生物医学、食品和环境保护领域具有潜力。