Tools and techniques for electrical characterization of biosensors

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The growing field of bioelectronics has the potential to revolutionize personal healthcare, strengthen security systems, and help safeguard the environment, as well as protect food and water supplies. Emerging nanoscale technologies are making advances in noninvasive physical biosensors, lab-on-a-chip tools, prosthetics/implants, and medical telematics systems possible.

At their simplest, biosensors are devices used to detect an analyte, i.e., a substance or chemical constituent of interest. Essentially, they can allow for understanding bio-composition, structure, and function by converting a biological response into an electrical signal. Proper testing of the electrical portions of these sensors is essential to support their development.

Biosensors are devices that do one or more of the following:

1. Detect, record, convert, process, and transmit information regarding a physiological change or process.
2. Use biological materials to monitor the presence of various chemicals in a substance (analyte).
3. Combine an electrical interface (transducer) with the biologically sensitive and selective element.

More specifically, a biosensor contains a bioreceptora biomolecule that recognizes the target analyte. The transducer portion of the biosensor converts the recognition event into a measurable signal that correlates with the quantity or presence of the chemical or biological target of interest. Figure 1 illustrates a generalized biosensor model.
Performance criteria for a biosensor system include:

1. Speed and ease of use by non-technical personnel.
2. Selectivity to target analyte.
4. Linearity.
5. Accuracy/repeatability.
6. Dynamic range. High analyte concentrations will not degrade sensor usability.
7. Robustness (relatively insensitive to temperature, electrical noise, physical shock, vibration, etc.)
8. Usable lifetime/adaptability.
9. Safety/integrity (for personnel, equipment, and analytes.)

**Sensor Designs**

Various biosensor design approaches have been used over the years, including an oligonucleotide sensor and nucleic acid reaction to indicate the presence of a pathogen. Another design employs surface plasmon resonance (SPR) to detect biological molecules such as protein and DNA. An SPR-based sensor can provide label-free studies of molecular interactions in real time using a sensor chip interface that facilitates attachment of specific ligands to the transducer surface and provides a sensitive measurement of surface concentrations.

Tissue-based sensors are also being developed that use living cells on chips that can react functionally to the presence of both biological and chemical threat agents. Because they are designed to mimic the function of multi-cellular human tissue, these sensors should respond to both known and previously uncharacterized agents. The transducer senses small changes in electrical charges on the surface of the living cells.

Electrochemical biosensors are normally based on enzymatic catalysis of a reaction that produces or consumes electrons. The sensor substrate may contain three electrodes: a reference electrode, a
working electrode, and a counter electrode. The target analyte is involved in the reaction that takes place on the active electrode surface, and the reaction may cause either electron transfer across the double layer (producing a current) or can contribute to the double layer potential (producing a voltage). One can either measure the current (rate of flow of electrons is now proportional to the analyte concentration) at a fixed potential or the potential can be measured at zero current (which gives a logarithmic response)[1].

An electrochemical potentiometric biosensor (in which potential is produced at zero current) gives a logarithmic response with a high dynamic range. Such biosensors are often made by screen printing the electrode patterns on a plastic substrate that is coated with a conducting polymer, and then some protein (enzyme or antibody) is attached. They have only two electrodes and are extremely sensitive and robust.

All biosensors usually involve minimal sample preparation as the biological sensing component is highly selective for the analyte concerned. The signal is produced by electrochemical and physical changes in the conducting polymer layer due to changes occurring at the surface of the sensor. Field effect transistors (FETs), in which the gate region has been modified with an enzyme or antibody, can also detect very low concentrations of various analytes as the binding of the analyte to the gate region of the FET causes a change in the drain-source current.

Many recent advances in biosensors have come through the use of graphene, which offers unique physiochemical properties, and superior mechanical, thermal, and electrical properties. Graphene-based biosensors offer the potential for high sensitivity because graphene is a two-dimensional single atomic layer of graphite that can maximize the interaction between the surface dopants and adsorbates. Graphene has much lower Johnson noise (the noise in a resistive material caused by thermal motion of charge carriers) than carbon nanotubes that are functionalized for bio-detection applications. Therefore, a very small variation in the carrier concentration in a graphene biosensor can cause a notable variation in electrical conductivity that can be measured.

Depending on the analyte and bioreceptor, the transducer portion of a biosensor could employ any of these mechanisms:

- **Amperometric**: Amperometric devices detect changes in current. They measure currents generated when electrons are exchanged between a biological system and an electrode.
- **Potentiometric**: Some reactions cause a change in voltage (potential at constant current) between electrodes that can be detected or measure.
- **Conductive**: Conductimetric devices detect changes in conductivity between two electrodes.
- **Resistive**: Resistivity is the inverse of conductivity, and can be measured with similar method.
- **Capacitive**: When the biorecognition reaction causes a change in the dielectric constant of the medium near the bioreceptor, capacitance measurement method can be used as a transducer.
- **Piezoelectric**: In a piezoelectric material, there is a coupling between its mechanical and electrical properties. It can be used to create an electrical oscillator whose frequency can be varied and measured by varying a mass applied to its surface. In the case of a biosensor, that mass can change due to the reaction taking place on the surface.
- **Thermal**: These devices measure changes in temperature.
- **Optical**: Optical biosensors correlate changes in concentration, mass, or number of molecules to direct changes in the characteristics of light. For this method to work, one of the reactants or products of the biorecognition reaction has to be linked to colorimetric, fluorescent or luminescent indicators. An optical fiber is sometimes used for guiding light signals from the source to the detector.
Achieving a stable, reproducible interface between the biological affinity elements and an inorganic transducer element is a major challenge in biosensor design. Fast, accurate electrical characterization is essential for qualifying the sensor/transducer interface, as well as the ultimate operation of a biodetection system.

Developing or verifying performance metrics for the biosensor is an important part of biosensor development. Because of the complexity of extracting cell and tissue signatures of agent activity and response, it is often desirable to conduct direct current-voltage (I-V) characterization on key components of the biosensor. Although I-V characterization requires only a small fraction of the time needed for most types of functional testing, it is a powerful predictor of the device's actual performance in operation. For example, I-V data can be used to study anomalies, locate maximum or minimum curve slopes, and perform reliability analyses, often on sensors based on amperometric, potentiometric, conductive, resistive, and thermal principles.

I-V testing typically involves applying a voltage or current to the device under test (DUT) and measuring its response to that stimulus. Temperature measurements may also be taken. The test procedures may involve probing integrated circuits to apply the stimulus to certain connection pads and measure the DUT response on others. The signal levels involved are often extremely low, which demands the use of sensitive instrumentation and techniques that minimize external sources of error.

Biosensors are often designed for use in portable, battery-powered equipment, which can restrict their operational power requirements and may dictate the level of voltage or current output that can be provided to the measurement circuitry. In battery-operated systems, sensor output current can range from nanoamps to milliamps and voltage from nanovolts to volts. Different measurement techniques and tools are required for characterizing signals over these wide ranges.

Source measure unit (SMU) instruments can simplify the time-sensitive triggering involved in the I-V characterization process by handling. Essentially, SMU instruments integrate the capabilities of a precision power supply (PPS) with those of a high-performance digital multimeter (DMM) in a single instrument. They can simultaneously source or sink voltage while measuring current, and source or sink current while measuring voltage. Figure 2 illustrates an SMU instrument configured as a constant current source and voltmeter to measure the response from a DUT. SMU instruments allow storing many different test sequences in onboard program memory, which can then be executed with a simple trigger signal. Test data can be stored in a buffer memory until an I-V sweep is completed and then downloaded to a PC for processing and analysis.
Testing BioFET Sensors

As mentioned previously, a FET can be fabricated to work with bio-materials to become a biosensor. The FET is a transistor that uses an electric field to control the shape and, therefore, the conductivity of a channel of one type of charge carrier in a semiconductor material.

Figure 3 is a highly simplified illustration of what's involved in fabricating a bioFET semiconductor transducer. The dielectric layer, an oxide such as silicon dioxide, has two functions: to isolate the channel of the FET from the liquid and to couple the surface layer charge electrostatically into the channel. A biofunctionalized layer that exhibits immobilized biomolecule receptors capable of binding the desired molecule lies on top of the dielectric. The analyte is a solution that contains the dissolved sample molecules. The reference electrode allows adjusting the device in order to maximize its sensitivity. If the target molecules bind to the receptors, a change in the surface charge density occurs. This change alters the potential in the semiconductor and thus the conductivity in
Determining the I-V parameters of a bioFET helps ensure that it functions properly in its intended applications and that it meets specifications. **Figure 4** illustrates how to set up an I-V characterization system for a three-terminal bioFET using two Keithley Model 2450 SourceMeter SMU Instruments. The number of instruments required for testing depends on the number of FET terminals that must be biased and measured. The Model 2450 (Figure 5) is suitable for a wide range of I-V tests, including gate leakage, breakdown voltage, threshold voltage, transfer characteristics, and drain current. Just as important, its touchscreen-based graphical user interface make instrument navigation an intuitive experience by representing many functions and parameters graphically, which helps substantially reduce the learning curve associated with using a new instrument.

Although **Figure 6** illustrates the results of generating a drain family of curves (VDS-ID) on a three-terminal FET, the same techniques are applicable to bioFET devices.

**Figure 4.** Two Model 2450 SMU instruments configured to test a three-terminal bioFET.
**Figure 5.** The Model 2450s touchscreen GUI and context-sensitive help function allows even novice SMU instrument users to acquire the data they need quickly and with confidence.

**Figure 6.** Typical FET drain family of curves generated with two Model 2450 SMU instruments.

**Conclusion**

The right I-V instrumentation and characterization techniques can greatly simplify qualifying sensors for bio detection systems and analytical instruments. For more details on this process, download a free copy of Keithley Instruments application brief, [Biosensor/Transducer Qualification Using the Model 2450 Interactive SourceMeter SMU Instrument](http://www.keithley.com/aapp/2450.pdf).

**References**


Also see:

- Printable conductive gel promises low-cost biosensors, energy storage
- Ultra-sensitive biosensor for medical diagnostics

Sources for Further Reading


About the author

Jonathan Tucker is Senior Marketing and Product Manager for Keithley Instruments, which is part of the Tektronix test and measurement portfolio. He joined Keithley in 1987. During his tenure, he has served in a variety of positions, including manufacturing test engineer, applications engineer, applications manager, product manager, and business development manager.